

# Annals of the Rheumatic Diseases

The EULAR Journal



Annual European Congress of  
**RHEUMATOLOGY**

**EULAR 2018**

Amsterdam, 13-16 June 2018

Abstracts





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The EULAR Journal

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# Welcome Address

Dear Colleagues,

I wish you a warm welcome to the 19th EULAR Annual European Congress of Rheumatology in Amsterdam. Our annual EULAR Congress has become a major event in the calendar of world rheumatology, and Amsterdam 2018 will again provide a unique event for the exchange of scientific and clinical information. It offers a platform to facilitate interactions between medical doctors, scientists, health professionals, patients and professionals representing the pharmaceutical industry, from across Europe and around the world.

This will be a particularly exciting congress - we will launch the EULAR Strategy 2018-2023 and highlight remarkable progress in several recent initiatives, including the EULAR School of Rheumatology and our ground breaking "Don't Delay, Connect Today" campaign.

EULAR is built on three fundamental pillars, integrating patient (PARE), health professional and rheumatology national associations. This partnership underpinning the work of EULAR is a unique stimulus to prosper advances in our field, for example via treatment recommendations, political advocacy, and research leadership. Accordingly, our congress is of the highest quality delivering a rich resource of contemporary, yet accessible information, serving a vital role in our unstinting efforts to reduce the impact, burden and cost of rheumatic and musculoskeletal diseases for individuals and society.

EULAR 2018 will address a wide range of topics including innovation in population, health service, clinical, translational and basic science. The WIN/HOT track for the busy clinician requiring an update on What is New and How to Treat the major rheumatic diseases has become an admired and 'must see' highlight of the EULAR Congress. Sessions dedicated to People with Arthritis and Rheumatism in Europe (PARE), Health Professionals in Rheumatology (HPR) are further jewels in our programme. High quality health care industry sessions provide in depth and focussed insights. Our poster presentations and poster tours provide a highly interactive exchange of knowledge and solutions amongst participants. We will be discussing the best of the more than 5000 submitted abstracts, testament to the rich vein of creativity and energy currently evident in our discipline. In Amsterdam, together we will further promote the reputation of the EULAR Congress as the most innovative and informative venue for clinical research for the practising physician. Finally, it is a particular pleasure to celebrate the participation of the EULAR EMEUNET organisation of young rheumatologists that continues to attract young colleagues to the meeting. Together we must disseminate the message that rheumatology is one of the most attractive and successful disciplines in global medicine.

We are very happy to revisit the City of Amsterdam. In 2006, we relished the magnificent ambiance of canals and canalside houses, galleries, astonishing museums (think Rembrandt, Vermeer, Rubens, Steen and Van Gogh), the Anne Frank House, theatres, music and culinary pleasures. The city has flourished since, offering an ever more diverse and enriching experience, hopefully bathed in early summer sunshine! Whereas balmy warmth may be uncertain, there is no doubt that Amsterdam will provide an excellent background for scientific and clinical exchanges, international collaborations and renewal of friendships. We take great pleasure in welcoming you all to EULAR 2018, and hope that your stay in Amsterdam will be informative, educational and, last but not least, enjoyable.

Johannes W. J. Bijlsma  
EULAR President

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## **Speakers Abstracts**

# Speaker Abstracts

WEDNESDAY, 13 JUNE 2018

## WIN and HOT session

### SP0001 SYSTEMIC LUPUS: ISSUES ABOUT PREGNANCY

A. Tincani. *Rheumatology and Clinical Immunology Unit, University of Brescia, Brescia, Italy*

Angela Tincani and Francesca Crisafulli

The outcome of Systemic Lupus Erythematosus (SLE) pregnancies has dramatically improved over years thanks to pregnancy planning, multidisciplinary management and close monitoring. According to EULAR recommendations,<sup>1</sup> pre-pregnancy counselling with the identification (and management) of possible disease related risk factors (such as active or past lupus nephritis and presence of antiphospholipid antibodies or antiphospholipid syndrome, APS), assessment of disease activity during pregnancy (including renal function parameters, anti-dsDNA and serum C3/C4) together with obstetrical monitoring are necessary to achieve a good pregnancy outcome. A recent evaluation of our SLE pregnancy cohort recruited from 1987 to 2017 showed a number of losses not significantly different to that observed in the general obstetric population; it is of interest that all the patients enrolled received pre-pregnancy counselling and were prospectively followed during gestation by a multidisciplinary team. According to this finding, a recent paper with data derived from Norwegian Registries<sup>2</sup> underlines that adverse pregnancy outcomes (APO) occur more frequently in SLE patients only in the presence of active disease.

However, the data are not univocal. A recent meta-analysis<sup>3</sup> still underlines the higher frequency of APO such as preeclampsia (PE), spontaneous abortion, pre-term birth and small for gestational age (SGA) newborns in SLE patients. So much effort is still devoted to identify new predictors of APO and possible protective strategies.

The uterine artery Doppler applied to SLE pregnancies shows an increased mean pulsatility index while the same patients display a higher ratio of two angiogenic biomarkers (sFlit-1/PIGF) related to placental dysfunction.<sup>4</sup>

Furthermore, an increase of Bb and sC5b-9 levels during early phases of pregnancy was observed in SLE patients who later developed APO.<sup>5</sup> A more recent work shows higher levels of Pentraxin3 (PTX3) in the general obstetric population with early-onset PE.<sup>6</sup> Studying placental histology, a higher number of neutrophils and neutrophilic extracellular traps (NETs) were detected in both SLE and non-SLE pregnancies with PE as compared with controls.<sup>7</sup> Taken together these observations suggest that also innate immunity could play a role in the occurrence of APO observed in this condition.

Many studies have assessed the beneficial role of hydroxychloroquine (HCQ) in SLE pregnancies. The use of HCQ is associated with a lower frequency of preterm birth and intrauterine growth restriction, less disease flares and reduction of the risk of fetal loss and SGA in patients with lupus nephritis. On the other hand, the use of prednisolone was associated with lower birth weight and higher rate of preterm birth.<sup>2</sup> In our cohort, the exposure to corticosteroids in doses greater than 35 mg/week in the 1st trimester was associated with preterm birth (<37 th weeks), while in the 3rd trimester with severe preterm birth (<34 th weeks). A recent study had assessed the improvement of pregnancy outcome in women with refractory obstetric APS treated with pravastatin<sup>8</sup>; given the strong association between SLE and APS, this could be an interesting topic to develop in the future.

The interest in long-term outcome of children born to mother with SLE raises from few observational studies suggesting an increased risk of neurodevelopmental disorders, congenital heart defects and autoimmune diseases. However, the risk of these adverse outcomes is small, and the large majority of children are in good health. Recently, the neurodevelopmental status of 40 children (median age 7.4 years) born to women carrying antiphospholipid antibodies (with or without SLE) was investigated by child neurologists and psychiatrists. All the children resulted normally intelligent but a slight increase in the frequency of epilepsy, sleep disorders and learning disability was observed.<sup>9</sup> In this respect, a recent study performed in animals pointed out the role of HCQ as protector of fetal brain development, offering a possible future preventive strategy.<sup>10</sup>

In conclusion, most of the young women affected by SLE can now carry out one or more pregnancies thanks to the improvement in prevention, early recognition and treatment of pregnancies complications. Nevertheless, further studies are necessary to reduce the risk of pregnancy morbidity still reported in some patients.

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WEDNESDAY, 13 JUNE 2018

## Little arthritis in PsA and axSpA with newly onset arthritis – does it matter?

### SP0002 PSA BEYOND THE TYPICAL POLY-ARTICULAR PHENOTYPE: HOW TO DEAL WITH THIS IN CLINICAL PRACTICE?

E. Nikiphorou. *Academic Rheumatology, Kings College London, London, UK*

This lecture will focus on the case of a psoriatic arthritis (PsA) patient presenting primarily with entheselial disease rather than the usual poly-articular phenotype. The case discusses issues around misinterpretation of signs and symptoms leading to inappropriate diagnoses and failure to early disease recognition and therefore treatment. Consequences of delayed treatment and less typical presentations of PsA will be discussed in greater detail during the session, highlighting important diagnostic and management aspects of disease, relevant to routine clinical practice.

**Disclosure of Interest:** None declared

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### SP0003 AXSPA PATIENT WITH PERIPHERAL MANIFESTATIONS

A. Sepriano. *Rheumatology, Leiden University Medical Centre, Leiden, Netherlands*

A case of a 32 year old Caucasian, female patient referred to an outpatient rheumatology clinic with a 3 month history of low back pain and a 2 week duration severe left heel pain is presented. Disease presentation, including findings on physical examination, laboratory tests and imaging are discussed, as well as their potential impact on treatment decisions.

**Disclosure of Interest:** None declared

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### SP0004 EXTRA SPINAL MANIFESTATIONS IN AXIAL SPONDYLOARTHRITIS

M. Dougados. *Hopital Cochin, Paris, France*

The extra-spinal manifestations in axial spondyloarthritis can be categorised in 2 main sub-groups: the extra-spinal rheumatological manifestations on one hand and the extra rheumatological manifestations in the other hand.

The extra spinal manifestations comprise synovitis, dactylitis and enthesitis and extra rheumatological manifestations comprise mainly skin psoriasis, uveitis and inflammatory bowel disease.

In terms of diagnostic approach in case of a patient presenting with axial symptoms, the probability to detect any extra-spinal manifestations in the past-history of the patients and/or concomitantly to the axial symptoms is very high (>75% at the baseline visit of the DESIR cohort including patients with recent onset axial symptoms suggestive of spondyloarthritis). These manifestations (based on data from different databases: for example the DESIR cohort and the ASAS-COMO-SPA cross-sectional study) will be described

The long term follow-up of patients presenting with axial spondyloarthritis emphasises the possibility to observe these extra-spinal manifestations overtime (incident cases).

These data are strong arguments to

1. Justify the inclusion of these extra-spinal manifestations in the set of classification criteria of axial spondyloarthritis
2. Justify specific investigations (mainly interview and physical exam ) of the patients at the time of the diagnosis
3. Justify a systematic monitoring of these different extra-spinal manifestations during the entire course of the disease

**Disclosure of Interest:** None declared

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**WEDNESDAY, 13 JUNE 2018**

## Cancer and inflammation

**SP0005** **INFLAMMATION AND CANCER: FRIEND OR FOE**

*C.S. Roxburgh. Academic Unit of Surgery, University of Glasgow, Glasgow, UK*

Cancer associated inflammation and the host immune response are key determinants of progression and outcome in solid malignancies. There is now persuasive evidence that inflammation is key to tumourigenesis via dna damage, stimulation of angiogenesis and proliferation, and inhibition of apoptosis. there have long been suspicions that dysregulated immune and inflammatory responses promote the progression and dissemination of established cancers and there is a heightened risk of cancer development in individuals with chronic inflammatory diseases. the tumour microenvironment is now viewed as a battleground for pro-tumour and anti-tumour responses. We now see an increase array of novel therapeutic targets targeting innate and adaptive components of the immune response to cancer. ONCO-Immunology with immunotherapy are an established part of clinical practice differing from conventional anti-cancer treatments in that the strategies do not principally target cancer cells. This talk will focus on the evidence that inflammation influences malignant progression in gi malignancy discussing novel therapeutic strategies.

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**WEDNESDAY, 13 JUNE 2018**

## Psychological distress and pain; not all in the mind.

**SP0006** **DISTRESS AND PAIN: INTEGRATED BRAIN PATHWAYS**

*B. Sundermann. Institute of Clinical Radiology, University Hospital Muenster, Muenster, Germany*

The focus of functional and multimodal neuroimaging studies has been switching from individual brain areas to larger interacting networks in the human brain. Regions within a network as well as different networks interact with each other and are usually involved in multiple brain functions such as perception, attention or cognitive control. In this presentation we will review the current knowledge on brain networks which are involved in the processing of painful stimuli or altered in patients suffering from chronic pain and how these share network correlates implicated in distress.

**Disclosure of Interest:** None declared

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**SP0007** **DEALING WITH PSYCHOLOGICAL DISTRESS TO OPTIMISE OUTCOMES FOR ARTHRITIS PAIN**

*R.J. Smeets. Rehabilitation Medicine, Maastricht University, Maastricht, Netherlands*

As clinicians we are often confronted with patients who suffer from arthritis pain. As most of us working in the field of arthritis, we are specifically trained to assess and treat medical causes in order to relieve pain. However, in daily practice we experience that many patients will develop chronic pain with huge problems in staying active and experiencing moderate to high levels of disability and lower level of quality of life.

In my opinion all clinicians should be able to identify psychosocial factors that contribute to the persistence of arthritis pain associated disability and loss of quality of

life. Besides these patient relevant psychosocial factors, I will specifically focus on the important role clinician's beliefs/attitudes regarding pain in better treating and coaching patients with chronic arthritis pain.

Participants will learn how to look for these potentially contributing factors, how to diagnose the level of functioning of these patients and how to inform patients about their pain and role of important contributing psychosocial factors. I will discuss the way how you might better prescribe pain medication and other pain relieving treatments and finally how you can help them to stay active despite being in pain, reduce the risk of iatrogenic damage, and what type of treatments exist to address contributing psychosocial factors.

Finally, I will specifically elaborate on the Fear Avoidance Model as one of the currently most often used theoretical models to assess patients and on which basis a very successful treatment called graded exposure *in vivo* has been developed.

**Disclosure of Interest:** None declared

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**WEDNESDAY, 13 JUNE 2018**

## Inflammation in the shadow of fibromyalgia

**SP0008** **A RA WITH PERSISTANT HIGH DISEASE ACTIVITY UNDER BIOLOGICAL TREATMENT: HOW DOES CHANGING DIAGNOSIS CHANGE MANAGEMENT AND OUTCOME?**

*A.P. Trouvin. Pain Evaluation and Treatment Department, Hopital Cochin, Paris, France*

We shall discuss the clinical case of a 45 years old woman. She has been diagnosed with rheumatoid arthritis, rheumatoid factor and ACPA are positive, acute phase reactants were elevated and no erosion was detected on the initial X-Rays. After a first line treatment with a conventional DMARD during 18 months, she experienced new flares with multiple synovitis and with elevated acute phase reactants. A TNF-inhibitor treatment was initiated. After 3 months, low disease activity was not reached hence biologic treatment was switched to abatacept. After 3 months, the patient still complained of pain in her hands and feet but acute phase reactants normalised, DAS-28 score is 5,20 (TJC: 18 , SJC: 0, ESR 14 mm/h, VAS general health patient: 70/100). Question rose to change biological therapy once again. The case presentation will discuss how a possible fibromyalgia can, in this case, be confounding in the patient's clinical evaluation and therefore change the management of the patient.

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**Disclosure of Interest:** None declared

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**SP0009** **FIBROMYALGIA ONSET OF SYSTEMIC LUPUS ERYTHEMATOSUS?**

*N. Hassan. Rheumatology, University Hospital of Wales, Cardiff, UK*

Systemic lupus erythematosus (SLE) and fibromyalgia often pose a diagnostic challenge to clinicians. The two conditions can coexist and the presence of one can complicate the diagnosis and management of the other. There is an increased prevalence of fibromyalgia amongst SLE patients compared to the general population but the exact nature of this association is not yet fully understood. We describe a patient diagnosed with fibromyalgia who later went on to develop SLE.

**Disclosure of Interest:** None declared

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WEDNESDAY, 13 JUNE 2018

**Shaping the future in systemic sclerosis**

SP0010 FIBROBLAST-MATRIX-VESSEL: THE UNHAPPY TRIAD

C.P. Denton. Centre for Rheumatology, Royal Free Hospital and UCL Medical School, London, UK

Systemic sclerosis (SSc) is a complex multisystem disease that links autoimmunity, inflammation, vascular damage to development of fibrosis or scarring in target organs. The pathogenesis of the disease involves reciprocal interaction between the immunological, vascular and mesenchymal compartments and involves processes that are central to connective tissue growth and repair. However in the context of SSc this process is dysfunctional in that the amount of tissue damage is excessive or the repair process is dysregulated. Thus it seems likely that perturbation of the cross talk between cells and pathways that regulate the cell types involved are important in pathogenesis and represent appropriate targets for therapeutic intervention. It is likely that some emerging therapies can attenuate the pathogenesis of SSc by acting on multiple cell type and this is perhaps especially relevant to an approach such as autologous haematopoietic stem cell transplant. However it is likely that individual pathways or mediators can be modified in a less extreme manner and have benefit as potential disease modifying therapy. A number of key mediators and pathways are emerging including IL6, TGFbeta and intracellular pathways linked to nuclear hormone receptors. These are being targeted experimentally. Another strategy for treatment would be targeting the initiating cells such as monocytes, especially those with a profibrotic phenotype, or the effector cells in fibrosis such as myofibroblasts. Evidence supporting these strategies is emerging and it is likely that restoration of a more balanced interaction between vessels, extracellular matrix and fibroblasts would underpin effective therapies for the fibrotic and vascular components of SSc.

**Disclosure of Interest:** C. Denton Grant/research support from: Inventiva, CSL Behring, GSK, Bayer, Consultant for: GSK, Actelion, Inventiva, Roche, Bayer, Boehringer Ingelheim, EMD Serono, Sanofi Aventis  
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SP0011 IS THERE AN UNIVERSAL TRANSLATOR? WHICH (ANIMAL) MODELS TELL US MOST?

J. Distler. Department of Internal Medicine 3, University of Erlangen, Erlangen, Germany

We will review the key features of currently available preclinical models of SSc, highlight their strengths and limitations and analyse, which subsets of SSc patients individual models mimic. We will also discuss how to employ models to evaluate drug candidates with different modes of actions and how to combine different models for an optimal preclinical portfolio.

**Disclosure of Interest:** J. Distler Shareholder of: 4D Science, Grant/research support from: Anamar, Active Biotech, Array Biopharma, aTyr, BMS, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, GSK, Inventiva, Novartis, Sanofi-Aventis, RedX, UCB, Consultant for: Actelion, Active Biotech, Anamar, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, GSK, Inventiva, JB Therapeutics, Medac, Pfizer, RuiYi and UCB  
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SP0012 NOVEL THERAPIES THAT MAY MAKE IT INTO THE CLINIC IN SYSTEMIC SCLEROSIS

1,2,3D. Furst. <sup>1</sup>University of California Los Angeles, Los Angeles; <sup>2</sup>University of Washington, Seattle, USA; <sup>3</sup>University of Florence, Florence, Italy

**Introduction:** Many therapies have been tested in systemic sclerosis (SSc), often failing but new approaches to measuring effect may improve the probability of success. The Combined Response Index for Systemic Sclerosis (CRI SS) combines measurement of the skin, lungs, activities of daily living and global assessments of disease activity into a single number. Like the DAS 28, this measure may be more powerful than any single outcome measure such as modified Rodnan skin score (mRSS) or forced vital capacity (FVC).

Novel approaches:

Multiple therapies are being tested which modify the immune system and the vascular pathogenetic node underlying the pathogenesis of SSc. Among these are tocilizumab (an IL-6 inhibitor), abatacept (affecting CD8 receptors) and rituximab (a CD20 inhibitor), all of whom are being tested in late phase studies and for whom results can be expected soon.

A more novel approach involves inhibition of tyrosine kinases which, in turn, affect TGF-beta, PDGF, FGF beta and VEGF. Among these are nintedanib and a

nanoparticle preparation delivering imatinib selectively. Encouraging animal studies and early human studies are resulting in larger studies in SSC patients.

Other drugs affecting fibrosis and inflammation are also being tested, including a cannabinoid which has shown encouraging early results.

While hematopoietic stem cell therapy will soon become a standard of care, other cellular therapies such as adipose derived mesenchymal cells and mesenchymal products such as exosomes and microparticles are being tested in systemic sclerosis.

There may or may not be enough time to discuss even more novel approaches to treating systemic sclerosis, with good rationale and some early results, which may reach the clinic.

Overall, this is an encouraging time for novel therapies to treat systemic sclerosis.

**Disclosure of Interest:** None declared

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WEDNESDAY, 13 JUNE 2018

**Basic mechanisms of inflammation**

SP0013 S100-ALARMIN: POTENTIAL THERAPEUTIC TARGETS FOR ARTHRITIS

J. Roth. Inst. of Immunology, University of Münster, Münster, Germany

Innate immunity is a pivotal factor in the pathogenesis of rheumatic diseases. During the last years there is growing evidence that pro-inflammatory alarmins of the family of calcium-binding S100-proteins promote inflammation in rheumatic, auto-inflammatory and auto-immune diseases. Serum concentrations of S100A8/S100A9 correlate with disease activity in several rheumatic diseases and are useful surrogate markers for monitoring disease activity predicting response to treatment, systemic organ involvement, or relapses in several autoimmune diseases. We have now identified a novel mechanism of auto-inhibition in mice and man restricting S100-alarmin activity to local sites of inflammation. We identified specific peptide sequences within the second calcium-binding EF-hands of S100A8 and S100A9 binding to TLR4/MD2 and triggering inflammation. However, biological activity of S100A8/S100A9 is locally restricted by calcium-induced (S100A8/S100A9)<sub>2</sub>-tetramer formation hiding the TLR4/MD2-binding site within the tetramer interphase. This auto-inhibitory mechanism is essential to prevent fatal inflammation in mice *in vivo*. Since S100A8/S100A9 complexes are the most abundant alarmins in arthritis, blocking of active S100A8/S100A9-dimers may represent an innovative approach for local inhibition of inflammatory processes in rheumatic diseases.

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WEDNESDAY, 13 JUNE 2018

**Health professionals welcome session**

SP0014 HEALTH PROFESSIONALS IN RHEUMATOLOGY WELCOME

R.H. Moe<sup>1,2</sup>. <sup>1</sup>Rheumatology, NKRR, Diakonhjemmet Hospital, Oslo, Norway; <sup>2</sup>Rheumatology, NBRR, Diakonhjemmet Hospital, Oslo, Norway, Oslo, Norway

An increasing amount of people are diagnosed with Rheumatic and Musculoskeletal Diseases (RMDs). EULAR Health Professionals in Rheumatology (HPR) can through substantial knowledge and clinical expertise contribute significantly to better lives with RMDs. Examples of important HPR core competencies are education, evidence-based treatment, prevention, team-based rehabilitation, and the support of individuals to participate in work, or education. The presentation will address some of the important multidisciplinary contributions to reduce the individual and societal burden of RMDs in the future.

**Disclosure of Interest:** None declared

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SP0015 WHAT'S NEW? PRESENTATION OF THE HPR NEWSLETTER

K. Betteridge. N/A, London, UK

The presentation will aim to showcase HPR News – the newsletter for EULAR's Health Professionals in Rheumatology. HPR News is available twice a year and is published to support EULAR's commitment to enable networking and learning



amongst HPRs across Europe. It also shares information about the work of the HPR Standing Committee, Study Groups as well as showcasing projects being carried out by HPR country member associations. The new design for the newsletter will be highlighted, alongside the content structure and HPRs will be encouraged to contribute to ensure the newsletter stays relevant to its audience.

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WEDNESDAY, 13 JUNE 2018

## Statistics made simple: a practical approach to complex concepts

SP0016 **STEPWISE OR NOT TO STEPWISE? THE DO'S AND DONT'S OF MULTIVARIABLE MODELLING**

S. Lydersen, Norwegian University of Science and Technology, Trondheim, Norway

**Introduction:** Different types of regression analyses, including linear, logistic, and Cox regression, are commonly used methods in medical research. Usually, these analyses include more than one covariate as independent variables. This is particularly the case in observational studies: When investigating the possible association between an exposure and an outcome, there can be a large number of potential confounders. Examples are age, sex, body mass index, and lifestyle factors. How should we choose which variables to include in the model? Here I shall focus on two issues:

- Attempting to include too many covariates in the analyses
- Use of stepwise selection of covariates

These are among the most frequently encountered issues in statistical review of manuscripts submitted for the Annals of the Rheumatic Diseases Lydersen 2015 Limit the number of covariates

With a limited number of observations, how many covariates can you include? Traditional rules of thumb state that the ratio of observations per variable ought to be in the size of order 10. Some authors recommend 15, some 20, others state that 5 is sufficient. See Lydersen, 2015 and references therein.

Do not use stepwise selection

Stepwise selection of covariates basically means that only covariates that are statistically significant, typically with a p-value less than 0.05 or 0.10, are included in the model. A fundamental problem is the following: As always is the case in estimation, regression coefficients are estimated with some uncertainty. Hence, some are underestimated, and some are overestimated, that is, too far away from the null hypothesis. Including only covariates with small p-values causes overestimated coefficients to be more likely to be selected. This introduces bias away from the null hypothesis. Stepwise procedures used to be very popular, but today an increasing number of analyst criticise such methods. For example, Rothman et al. 2008 page 419 state: "There are several systematic, mechanical, and traditional algorithms for finding models (such as stepwise and best-subset regression) that lack logical and statistical justification and that perform poorly in theory, simulations and case studies ... One serious problem is that the P-values and standard errors ... will be downwardly biased, usually to a large degree".

**Recommendation:** Selection of covariates should be based on the research question at hand and on substantial knowledge such as what is biologically plausible. Chapter 10 'Predictor selection' in the book Vittinghoff et al. 2012 gives good guidance. Check that the number of covariates is small enough compared to the number of observations. Do not use stepwise selection.

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**Disclosure of Interest:** None declared

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WEDNESDAY, 13 JUNE 2018

## E-health for better care

SP0017 **BITS AND BYTES: FITTING MEDICAL INFORMATION – PICASO THE PLATFORM FOR IMPROVED PERSONAL, COORDINATED CARE**

J. Richter, on behalf of PICASO Consortium. *Polidinic and Hiller Research Unit for Rheumatology, Heinrich-Heine-University Duesseldorf, Duesseldorf, Germany*

Coordination of care plans between healthcare sectors and efficient management of patients with co-morbidities is of large demand. Rheumatoid arthritis (RA) patients are at increased risk of cardiovascular diseases. Different stakeholders are potentially involved in the EULAR recommended management processes. Optimised orchestration of accumulated information is of major importance to ensure data quality, meaningful management processes and cost effectiveness. A newly developed information and communications technology platform within the Horizon2020-funded PICASO-project ([www.picaso-project.eu](http://www.picaso-project.eu)) will support a continuum of care from hospitals and outpatient clinics to the home. The PICASO platform will be developed and trialled with patients and clinicians. First experiences will be reported. The platform will become available for RA-patients in routine care but also for wider applicability in Rheumatology and other chronic diseases.

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**Disclosure of Interest:** None declared

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SP0018 **SMART WEARABLES AND HEALTH APPS – THE RIGHT TOOL FOR HEALTH MONITORING AND IMPROVING QUALITY OF HEALTH?**

M. Silva, on behalf of E-health for better care. *ReumNet, Brussels, Belgium*

What role can technology play in enabling a shift from a traditional paternalistic model of care to a model based on empowered patient sharing ownership? In the traditional model, patients are fully reliant on the healthcare professional for information, diagnosis and treatment, with complexity to navigate through the ecosystem and where physicians are empowered rather than patients. Patient empowerment is enhanced thanks to technology enabled care, in which patients have access to their medical files, can use tools that allow them to be proactive and focus on prevention and where self-management is supported across the treatment pathway. Smart wearables and health apps are becoming more widespread and a commodity, while more and more research is being performed on the effectiveness of such devices on the quality of life of patients. The design of wearables and health apps itself can be approached in a patient-centric way, to maximise the benefits for patients and the uptake by patients. This presentation will discuss some evidences of the impact of technology on improvement of quality of life and how patients should be included in the design process.

**Disclosure of Interest:** M. Silva Shareholder of: Esperity SPRL, Simperium BVBA, Grant/research support from: EUPATI Belgium VZW, Consultant for: Janssen Pharmaceuticals, Novartis, Sanofi, Pfizer, ReumaNet

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WEDNESDAY, 13 JUNE 2018

## EULAR projects in paediatric rheumatology and UCAN

SP0019 **UCAN AND PRINTO ALIGNED TO LINK BED AND BEDSIDE: PERSPECTIVE FROM THE BENCHSIDE**

S.J. Vastert, *Pediatric Rheumatology and Laboratory for Translational Immunology, University Medical Center Utrecht, Utrecht, Netherlands*

In the past 2 decades we have gained important insights on the mechanisms of disease and therapy in children with Juvenile Idiopathic Arthritis (JIA). These insights have resulted in several game-changing therapeutic modalities in several

subtypes of JIA. In for example systemic JIA, we have learned that the systemic inflammatory mechanisms at onset of this disease, are primarily driven by innate immune cells and their inflammatory cascades. Both IL-1 and IL-6 blockade in sJIA have resulted in high response rates of sJIA patients.

Additional progress still has to be made in efficacy, cost reduction, minimization of side effects and taper and stop strategies of maintenance drugs. To ensure that the right goals are set, patients (and/or their parents in paediatric disease) should be involved in important research questions and goals. In addition, if we really aim to take the next step in improving the outcome and life of our patients, clinical innovations need to go hand in hand with basic discoveries to really affect care for patients.

Current clinical trials rely on the recognition of clinical phenotypes and have strict inclusion criteria. In these trials with more or less homogenous patient cohorts, response rates to a specific treatment are evaluated and compared to placebo or current standard therapeutics. This has resulted in the registration of multiple biologic therapies for various JIA subtypes and to significantly improved response rates and disease outcomes for most JIA patients. However, still a major question in clinical practice remains: which biological to start in which patient and when.

Agreement on several consensus treatment plans in clinical practice for different subtypes of JIA, will help in comparing responses to registered therapeutics. However, to book further progress in the care for JIA patients, what we really need is a more molecular based set of classification criteria, or disease taxonomy, of JIA subtypes and (sets of) biomarkers for disease course/therapy response and biomarkers to assess subclinical disease activity. These criteria and biomarkers will enable informed decisions on the start as well as tapering/stop of maintenance therapy. Such a classification, as well as the discovery and validation of novel/promising biomarkers are likely to be developed in collaborative cohort studies with new onset JIA patients that are prospectively followed and sampled over time.

Facilitating the translation from bench to bedside is crucial for addressing the major current challenges in JIA management. When successful, it will set new standards for safe, targeted and personalised medicine in JIA.

**Disclosure of Interest:** S. Vastert Grant/research support from: from SOBI in collaboration with ZonMW, rational pharmacotherapy program

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#### SP0020 HOW DIGITAL TOOLS CAN HELP TO CROSS BORDERS IN INTERNATIONAL COLLABORATIONS

*V. Seyfert-Margolis. My Own Med, Inc, Chevy Chase, USA*

When people think of digital health, they generally think of health and wellness mobile apps, or wearable sensor devices like Fit Bit or the Apple Watch. But digital technologies are much more than that. Today's advanced digital health has evolved into software platforms that can connect and support patients, their families and connect them to their health systems, enabling outcomes research and management with direct input from networks of patients that can connect across geographical divides. And these systems enable communication between medical systems, enabling hubs and spokes of networked researchers and their patients that promote data capture, information sharing and enhanced communications to patients- by meeting them where they are. These new models are driving the ability to study interventions in real world contexts including patients' between visit activities and their engagement with multiple layers of the healthcare teams thereby promoting integrated research and care. With all of these capabilities, the question remains, "will the medical research community be ready to embrace it?"

**Disclosure of Interest:** None declared

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WEDNESDAY, 13 JUNE 2018

### Ultrasound basic I

#### SP0021 HOW TO ASSESS DACTYLITIS+DEMO

*E. Naredo. Rheumatology and Joint and Bone Research Unit, Hospital Universitario Fundacion Jimenez Diaz, Madrid, Spain*

Dactylitis is a hallmark feature of psoriatic arthritis (PsA) and other spondyloarthritides, although it can also be present in other conditions such as sarcoidosis, gout or infections. Regarding PsA, dactylitis, which occurs in 30% to 50% of patients, is a highly discriminative feature for PsA diagnosis in early disease as well as a predictor factor for structural damage development. On ultrasound, dactylitis is a complex and heterogeneous "imaging syndrome" that includes a variety of elementary lesions, i.e. enthesitis (finger extensor tendon, collateral ligaments, flexor fibrous

sheaths, flexor pulleys, functional entheses), tenosynovitis, paratenonitis, synovitis, subcutaneous/peritendon tissue inflammation, and proliferative and erosive bone changes. High resolution B-mode ultrasound offers a detailed anatomical imaging of the different lesions present in dactylitis as well as Doppler ultrasound provides information on the inflammatory activity of the involved structures and tissues.

**Disclosure of Interest:** None declared

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#### SP0022 HOW TO ASSESS BONE EROSIONS – INDICATIONS, PITFALLS AND NEW TECHNIQUES + DEMO

*M. Szkudlarek. Dept. of Rheumatology, Koege Sygehus, Koege, Denmark*

Detection of bone erosions is essential for the early diagnosis, the prediction of future bone damage, and the monitoring of therapeutic outcomes in patients with rheumatoid arthritis (RA).

Yet, bone erosions are not pathognomonic for RA. They occur in many other disease entities. Presence of bone erosions is characteristic for mixed connective tissue disease, juvenile idiopathic arthritis, gout, hemochromatosis, pigmented villonodular synovitis, among others. It is not uncommon in osteoarthritis. Bone erosions can be detected at entheses in spondyloarthropathy and in the joints of patients with psoriatic arthritis. Erosive changes can also be seen in bone neoplastic disease.

Conventional radiography is still considered the basic imaging method of detection of bone erosions, as well as a monitoring tool. However, more modern imaging techniques are becoming more widely used. They include ultrasonography, magnetic resonance imaging and computed tomography. Apart from higher sensitivity for detection of bone erosions, the new techniques offer simultaneous visualisation of soft tissues. Their role in follow-up of patients with erosive disease as well as erosive progression is still a subject of research.

In the short time allowed, the presentation will also address localization, pitfalls and characteristic appearance of bone erosions in main rheumatological diseases.

**Disclosure of Interest:** None declared

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#### SP0023 HOW TO ASSESS MECHANICAL AND INFLAMMATORY TENDINITIS + DEMO

*U. Fredberg. Diagnostic Centre, Universitu Research Clinic of Innovative Patients Pathways, Silkeborg Regional Hospital, Silkeborg, Denmark*

Tendinopathy is a frequent disorder that may last for several years and impair the quality of life of athletes, non-athletes and patients with inflammatory joint diseases where tendinopathy is a frequent complication.

The diagnosis can often be made alone by clinical examination, but in the selected cases, imaging can be determined for the correct diagnosis and treatment.

US has several significant advantages over MRI. The greatest strength of the US is that it is interactive and the examiner is in contact with the patient, and any site of reported pain or tenderness can be directly correlated with its real-time scan appearance on the screen. The ultrasonographer can make use of the dynamic real-time character of US, so that tendons can be studied throughout their range of motion and side-to-side comparison is always available during the US examination. This unique advantage over other cross-sectional imaging modalities like MRI is of course especially applicable in the evaluation of mobile structures such as tendons. Tissue with few mobile protons emits little or no signal and, therefore, the internal architecture of the tendon is not well demonstrated in MRI. In contrast, US shows the fine internal structure of tendons, and US therefore pictures the anatomic border of the tendon more precisely than MRI, and in agreement with this the "standard deviation" (SD) and "range of the mean difference" from repeated measurement are less in US than in MRI. It is easy to change to a higher-frequency US transducer to obtain greater spatial resolution. The spatial resolution of US is much better than that of MRI if both examinations are performed with the most modern equipment. Furthermore, US can demonstrate the neovascularisation (Doppler) and the stiffness of the tissue (elastography) in tendinopathy.

In the lecture, the ultrasound typical findings of different mechanical and inflammatory tendinopathies are reviewed and completed with a live demonstration of ultrasound scan of a tendon.

**Disclosure of Interest:** None declared

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WEDNESDAY, 13 JUNE 2018

**New drugs – new perspectives: clinical and regulatory issues concerning biosimilars**

SP0024

**AN UP-DATE ON BIOSIMILARS***T.K. Kvien. Department of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway*

Biosimilars represent a new opportunity for lowering the cost of treatment with biological disease-modifying antirheumatic drugs (bDMARDs). Studies have demonstrated large inequities in the access to bDMARDs across countries and this inequity is related to economic parameters such as gross domestic product. Thus, reduced costs of bDMARDs should potentially lead to better treatment for more patients, especially in countries with low economy.

The regulatory agencies in Europe and in US have set up strict guidelines for approval of biosimilars which include extensive pre-clinical examinations (structure and functional characteristics) but less clinical data than for an originator product. The clinical part of this comparability exercise focuses on efficacy, safety, pharmacokinetics as well as immunogenicity.

Three biosimilars to adalimumab have also been approved but the patent of the reference product has not yet expired (expected to occur October 2018). (expected to occur October 2018). It is a growing acceptance about the use of these biosimilars, also in extrapolated indications when treatment are started or changed for medical reasons. Most rheumatologists will consider the biosimilars on the same level as originator products in these situations.

However, replacing an originator product by a biosimilar is more controversial, but is important because of the large cost-savings. Switching evidence is available from four different types of studies which will be discussed:

- Extension of phase 3 RCTs
- Switching within RCTs
- Real life data (eg from DANBIO)
- Randomising patients on stable long-term treatment

In the NOR-SWITCH trial – totally funded by the Norwegian government – 482 patients on stable treatment with the reference product infliximab across 6 indications (RA, SpA, PsA, UC, CD, PsO) were randomised to continued treatment with the reference product or switch to the biosimilar CT-P13; Jørgensen KK et al. *Lancet* 2017;389:2304–2316). The primary endpoint was occurrence of disease worsening, defined by the disease-specific composite measures or clinically significant worsening leading to a major change in treatment. Overall, disease worsening occurred in 26.2% of patients who continued treatment with the originator infliximab and in 29.6% of patients who switched to CT-13. The adjusted treatment difference (95% CI) was  $-4.4\%$  ( $-12.7$ – $-3.9$ ) which was within the prespecified non-inferiority margin of  $-15\%$ . The occurrence of adverse events, including infusion reactions, was similar across both groups. There were no differences between the two groups in secondary endpoints, including time to study drug discontinuation, remission rates, CRP levels, anti-drug antibody formation and drug trough levels. The extension study (not yet published) showed that switching from originator to biosimilar was not inferior to continued treatment with the biosimilar.

In conclusion, the NOR-SWITCH study demonstrated that switching to CT-P13 was not inferior to continued treatment with originator infliximab, adding to the increasing real-world evidence that switching from originator to biosimilar bDMARD is safe and efficacious.

**Disclosure of Interest:** T. Kvien Consultant for: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celgene, Celltrion, Eli Lilly, Epirus, Hospira, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, San-do and UCB

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SP0025

**SHARED DECISION MAKING IN SWITCHING TO BIOSIMILARS***T. French. Rheumatology, University Hospitals Bristol NHS Foundation Trust, Bristol, UK*

This presentation will focus on the speaker's experience of switching patients who are on an originator biologic therapy to a biosimilar, using a shared decision making approach. It will initially explore what constitutes shared decision making, why it is important when switching to biosimilars and the benefits of this approach.

The speaker will discuss how this change in therapy was achieved in practice when switching patients to both intravenous and subcutaneous biosimilars. There

will be a focus on the patient consultation itself, recognising patient anxiety and an exploration of why some patients declined to switch.

The speaker will share how loss of efficacy to the biosimilar was managed, and how this influenced the shared decision making approach.

Clinician's concerns will also be considered, specifically the inability to maintain pharmacovigilance (in not having sufficient nursing resources to add patients who had switched to a biosimilar to a national register). This is relevant to shared decision making as providing evidence and reassurance to patients regarding safety of biosimilars relies on this data collection.

The guidance referred to in this presentation is from NHS England, National Institute for Health and Care Excellence and the British Society for Rheumatology, so it has a UK focus. However, the main themes of the talk should be relevant to all audience members as it considers the opposing pressures on Rheumatology nurses to be change agents and make cost savings in implementing this switch to biosimilars. Whilst nurses also need to act as the patient advocate in ensuring shared decision making is a reality: that a face-to-face consultation takes place and that the patient can decline to switch and not feel penalised. The speaker will reflect on how the trust in her relationship with her patients was tested by this experience.

The main recommendation from this presentation is that rheumatology teams need to be proactive in managing this change and securing extra funding for nursing or pharmacy support. This 'invest to save' approach will enable appropriate consultation with patients to allow them to give informed consent to switch their therapy and feel supported whilst this switch takes place. It also enables maximum cost savings by ensuring the switch occurs quickly.

**Disclosure of Interest:** None declared

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SP0026

**BIOSIMILARS – THE CHANGING VIEWS OF PARE'S MEMBER ORGANISATIONS***D. Wiek. EULAR PARE, Huenxe, Germany*

After EULAR PARE's position paper "Biosimilars – what do patients need to consider" published in November 2015 more biosimilars for rheumatic diseases have been approved by EMA (European Medicine Agency), have entered the market in different European countries and more biosimilars will be marketed. New studies and data informing about the use of biosimilars, as well as feedback received from patient organisations and in particular from PARE organisations, have made it necessary to update PARE's 2015 position.

Biological therapies are enormous cost factors for the healthcare system and biological therapies have to be affordable, what is seen as difficult in various countries. But an optimal quality healthcare is enormously important for the individual patient (e.g. fewer sick days, less hospitalisation, less disabilities), prevents early retirement and thus saves costs and contributes to a country's economic and social system.

If so-called naïve patients should take a biologic, the less expensive biosimilar can be used, as long as there are no contraindications, the patient has been informed and the decision is based on a shared decision between rheumatologist and patient.

But transitioning users from an originator to a biosimilar is very controversial and seen critically by PARE's patient organisations. The talk will cover the changing views concerning extrapolation, one-time switch, multiple therapy switches, registries and the relevance of the application form for patients.

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WEDNESDAY, 13 JUNE 2018

**Don't delay, connect today!**

SP0027

**DON'T DELAY, CONNECT TODAY – IMPLEMENTATION OF THE EULAR CAMPAIGN IN ROMANIA***R. Ionescu. Department of Internal Medicine and Rheumatology, University of Medicine and Pharmacy "Carol Davila", Sf. Maria Hospital, Bucharest, Romania*

**Background** 22% of the population in Europe currently has, or had experienced "long-term muscle, bone and joint problems".<sup>1</sup> Early referral to a rheumatologist for appropriate diagnosis and treatment prevent structural damage, disability and decrease mortality.<sup>2</sup>

**Objectives:** To launch a patient oriented campaign in Romania in order to increase awareness of rheumatic musculoskeletal diseases (RMDs) – early



recognition of symptoms, ways of breaking down the barriers that delay early diagnosis. Also to educate the general public that rheumatic diseases may occur at any age and severe affect both children and young people.

The long term goal of the campaign is to decrease the number of people with disabilities, work loss or early retirement as well as the health care costs.

**Methods:** The launch event of the campaign will be attended by patients, rheumatologists, GPs, HPs, media and also national and local authorities.

A coordinated media plan will consist of pre-launch teasers, appropriate broad-casting of the event and post-event reminders as well as educational flyers/materials with the slogan "Don't delay, Connect today", handed out in shopping centres and other crowded areas.

Online posts on the [www.rheumatism.ro](http://www.rheumatism.ro) website and the dedicated FB page will stimulate communication and mutual support among patients as well as spread information on RMDs to the general public.

**Results:** Up to 100 participants are expected to attend the launching event and get direct/live benefit from the information on early diagnosis and early treatment.

Over 50% of the Romanian population will audience the campaign messages covered by 50 media articles (in Romanian) and over 10 000 people will receive e-messages (online and Facebook impressions/engagement). This coordinated media plan will stimulate communication and mutual support among people with RMDs.

**Conclusions:** The implementation of the EULAR campaign in Romania "Don't delay, Connect today" aims an early referral to the rheumatologist for diagnosis and treatment and for a normal quality of life of patients with inflammatory rheumatic diseases. The campaign will have a communication peak around the launching event. Until the end of the year an on-going media and online communication strategy will be implemented.

#### REFERENCES:

- [1] Health in the European Union Eurobarometer Special Report 272, September 2007.
- [2] Emery P, Breedveld FC, Dougados M, et al, Early referral recommendation for newly diagnosed rheumatoid arthritis: evidence based development of a clinical guide, *ARD* 2002.

**Disclosure of Interest:** None declared

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WEDNESDAY, 13 JUNE 2018

## Burning bones

### SP0028 EFFECTS OF INFLAMMATION ON BONE IN INFLAMMATORY ARTHRITIS

*E.M. Gravallesse. Medicine/Rheumatology, University of Massachusetts Medical School, Worcester, MA 01605, USA*

Research in my laboratory is devoted to the study of the pathogenesis of rheumatoid arthritis (RA), with a particular interest in the fundamental mechanisms of bone and cartilage destruction. Key research findings include the identification of osteoclasts as the cell type responsible for bone destruction in RA, and receptor activator of NF- $\kappa$ B ligand (RANKL) as the critical cytokine produced by cells within RA synovial tissues that promotes osteoclastogenesis. More recently, we have identified the inhibitory effects of synovial inflammation on bone formation in RA, and focused on the effects of inflammation in inhibiting the Wnt signalling pathway, resulting in the impairment of osteoblast function. We have also studied the mechanisms that prevent healing of bone erosions in RA, and will discuss a completed clinical trial that addresses the question of erosion healing. Mechanisms of bone loss in RA will be contrasted to mechanisms of bone formation in spondyloarthritis. Finally, we have identified specific pathways in the innate immune system that regulate bone remodelling in the setting of inflammation, and these appear to be directly relevant to inflammatory arthritis. This lecture will thus cover what we have learned about basic mechanisms, and will discuss the clinical implications of this work for the practicing physician.

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### SP0029 FINE STRUCTURE ANALYSIS TO DETECT BONE PORES

*M. Gunzer, on behalf of Basic and Translational Science Session. Institute for Experimental Immunology and Imaging, University of Duisburg-Essen, University Hospital, Essen, Germany*

The blood supply is essential for the many functions of bones. The bone marrow as well as blood cells generated within are particularly dependent on a functional circulation. Despite this fact there is a remarkable logical gap in our understanding of a closed circulatory loop in long bones. We have discovered a previously unknown type of blood vessels in long bones of mice that forms an intense connexion of bone marrow with the external circulation outside of the bone. These blood vessels transport the majority of blood into and out of bones and hence constitute an essential structural component of bone physiology. I will present a detailed characterisation of these vessels and also show evidence for similar structures in man.

**Disclosure of Interest:** None declared

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WEDNESDAY, 13 JUNE 2018

## Delay in treatment and the role of health professionals

### SP0030 REASONS FOR DELAY IN HELP SEEKING AT THE ONSET OF SYMPTOMS

*R.J. Stack. Psychology, Nottingham Trent University, Nottingham, UK*

Early intervention following the onset of chronic illnesses such as rheumatoid arthritis, lupus and Sjogren's syndrome can improve disease prognosis, reduce illness related disability and improve patient quality of life. Therefore, it is vital that the time between symptom onset and treatment is short, however, many patients experience long delays. The period of time between an individual's first detection of a bodily change and the first consultation with a healthcare professional is known as patient delay, while the time between first consultation and been referred to a rheumatologist for treatment is known as healthcare professional delay.

Patient delay can be attributed to a range of barrier to consultation, these include contextual barriers (e.g. geographical location, financial barriers and availability of health services), individual barriers (e.g. demographic characteristics and health literacy) the nature of symptom onset (e.g. intermittent symptoms or the experience of a symptoms commonly associated with many conditions such as fatigue) and psychological barriers (e.g. perceptions of illness, the normalising symptoms interpretation of symptoms and fear and worries about wasting the doctor's time).

Many interventions to reduce patient delay focus on educating the public about the typical symptoms associated with a specific illnesses in the hope that greater awareness will lead to better recognition of early symptoms. These interventions are based on the premise that the general public may hold misrepresentative stereotypes of what it is like to experience an illness or may even have no stereotypical belief (also known as a prototypical belief) to compare their current symptoms to. There is very little evidence about the evolution of early symptoms over time and how patients appraise these early symptoms and then decide to seek help. Furthermore, the non-specific nature of early symptoms for many rheumatological conditions can also be a significant barrier to patients recognising that symptoms are indicative of a chronic illness. For example, patients may attribute symptoms to stress, ageing or a temporary condition and actively choose not to seek help. Therefore, we must explore patients beliefs about symptom experience and not just focus on their beliefs about specific illnesses. Understanding early symptom presentation and the way that early symptoms are interpreted by patient is important for the development of robust help seeking interventions. However, interventions to promote prompt help-seeking based on symptom presentation must also take in to account for contextual, individual and psychological barriers which may interact with individual perceptions of early symptoms.

Understanding the factors which lead to patient delays and healthcare professional delays across rheumatological conditions can ensure that interventions to reduce delay are developed using a robust evidence base. Evidence based interventions such be multifaceted and may include the development of public health information (e.g posters, tv campaigns etc), the development of robust online information and challenging mis-information online, addressing health inequalities which may lead to delay (e.g. increasing the accessibility of health services and promoting health literacy in hard-to-reach communities) and developing educational information for healthcare professionals.

**Disclosure of Interest:** None declared

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**SP0031 ARE ILLNESS PERCEPTION AND COPING STYLE ASSOCIATED WITH PATIENT DELAY?**

*K. Van der Elst*<sup>1,2</sup>. <sup>1</sup>Rheumatology, University Hospitals Leuven; <sup>2</sup>Skeletal Biology and Engineering Research Centre, KU Leuven Department of Development and Regeneration, Leuven, Belgium

EULAR recommendations for rheumatoid arthritis (RA) management advocate early intensive treatment to target. Timely diagnosis and treatment initiation in RA depends on a multitude of factors, such as healthcare organisation and referral pathways. Nevertheless, individuals seem to have a large contribution themselves by delaying their first contact with a health professional after symptom onset. This pre-diagnosis period can be described as a daunting period for persons who are later diagnosed with RA, because of experiencing symptoms they do not fully understand yet. It has been shown that when confronted with particular new symptoms, persons develop or adjust certain beliefs and attitudes that determine their understanding of, and their way of dealing with these unknown symptoms. Consequently, how persons interpret (perception) and manage (coping) their initial RA-related symptoms could influence their help-seeking behaviour. The results presented in this lecture will introduce the role of illness perception and coping in the patient delay in recently diagnosed patients with early RA. The audience will learn about the role of psychosocial aspects in patients' help-seeking behaviour, and why such aspects are worthwhile to consider when aiming for a reduction in early RA treatment delay.

**REFERENCE:**

- [1] Van der Elst K, et al. Are illness perception and coping style associated with the delay between symptom onset and the first general practitioner consultation in early rheumatoid arthritis management? An exploratory study within the CareRA trial. *Scand J Rheumatol* 2016;45(3):171–8.

**Disclosure of Interest:** None declared

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**SP0032 THE PATIENTS' PERSPECTIVE ON DELAY IN TREATMENT**

*S. Makri*. CYPLAR, Limassol, Cyprus

**Background:** Delay in early start of treatment could cause serious problems for the patient with an RMD such as unnecessary pain suffering, deformations, depression and even disability. Often patients visit Orthopaedic doctors mainly out of ignorance. Often GPs delay for various reasons, referral to the specialist

**Objectives:** In order to achieve the goal of good quality of life, both and patient and the GP should be informed and educated so as to recognise early symptoms and seek immediate medical advice and treatment.

**Methods:** The use of Campaigns in the context of "Don't delay connect today" Slogan. Media appearances, with the aim of raising awareness amongst the public and patients are very useful. The use of mobile Clinique staffed by Health professionals, advising on how to recognise early symptoms, use of printed material to stress the importance of early diagnosis. Training of GPs and orthopaedics. Use of examples

**Results:** The patient, through education, realises the importance of early referral to a Rheumatologist for receiving personalised and effective treatment.

**Conclusions:** Early diagnosis and timely treatment allow the patient with RMDs to live a good quality life. Campaigning in this direction, through information and raising awareness, can empower the patient to seek help at the early stages of the disease.

**Disclosure of Interest:** None declared

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**SP0033 DELAY IN TREATMENT FROM THE GP PERSPECTIVE**

*B. Fautrel*. Rheumatology, Sorbonne Université – Paris 6/Assistance publique – Hôpitaux de Paris, Paris, France

Inflammatory joint disease (IJD), i.e., rheumatoid arthritis, psoriatic arthritis or spondyloarthritis, require rapid referral to rheumatologists to get optimal specialised care, since early diagnosis and early treatment are 2 key prognosis factors. To achieve this objective, education of general practitioners (GP) is of dramatic importance, since they have to detect early IJD symptoms which are sometimes partial and non specific.

The lecture will identify the key elements that have to be communicated to GPs to improve their skills in detecting IJD at very steps, as well as the most important elements to make rheumatologist appointment available to them.

**Disclosure of Interest:** None declared

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THURSDAY, 14 JUNE 2018

**Fat and fatty acids: targets for therapy?**

**SP0034 ADIPOSE TISSUE INFLAMMATION: ONCE FAT WAS FAT AND THAT WAS THAT**

*H. Schipper*<sup>1,2</sup>. <sup>1</sup>Pediatric Cardiology; <sup>2</sup>Laboratory of Translational Immunology, Wilhelmina Children's Hospital/University Medical Center, Utrecht, Netherlands

Until only 100.000 years ago, humans hunted smaller creatures and gathered what they could, meanwhile being hunted by larger predators. *Homo sapiens* showed a spectacular leap to the top of the food chain ever since. While mankind however advanced from a cavemen diet to fast food, our adipose tissue did not adapt so quickly. Here, the evolutionary origins of adipose tissue and its implications for systemic inflammatory conditions will be discussed.

A few decades ago, adipose tissue was considered a lipid sink, evolved to store energy in times of nutritional excess and release energy in times of shortage. Indeed, multicellular organisms depend on their ability to store energy to prevent starvation. Equally important though, they rely on their ability to fight infections. Several lines of evidence illustrate that adipose tissue in fact embodies the amalgamation of highly conserved metabolic and immune pathways. Whereas the fat body in *Drosophila melanogaster* comprises adipose tissue, liver and immunological moieties in one functional unit, adipocytes in humans and other higher organisms are reminiscent of their evolutionary origins by toll-like receptor expression, cytokine production and antigen-presenting capacities. From an evolutionary perspective, adipose tissue is fully equipped to respond to inflammatory stimuli, in order to fulfil the high energy demands of an acute immune response. In modern times however, the immunological capacities of adipose tissue are more of a burden. Both in nutritional overload and systemic inflammatory conditions, the inflammatory impetus of adipose tissue can have devastating consequences.

**Disclosure of Interest:** None declared

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**SP0035 INFLAMMATION-INDUCED FORMATION OF FAT ASSOCIATED LYMPHOID CLUSTERS**

*J. Caamano*, on behalf of Stroma-Immune Cell Interaction Group. Institute of Immunology and Immunotherapy, College of Medical and Dental Sciences – University of Birmingham, Birmingham, UK

Fat-associated lymphoid clusters (FALCs) are atypical lymphoid tissues located on adipose tissues in mucosal surfaces such as the mesenteries, omentum, mediastinum, pericardium, and gonadal fat in humans and mice. FALCs were originally identified in mouse and human mesenteries due to that they contain a high number of type 2 innate lymphoid cells (ILC). Our work has shown that FALCs contain B1, B2 and T lymphocytes as well as myeloid and other innate immune cell populations.<sup>1,2</sup> Inflammation induces the rapid formation of FALCs and significant changes in cellular composition. Immunizations have shown the development of adaptive immune responses including B cells undergoing a germinal centre reaction in mesenteric FALCs emphasising their function on local immunity.

Our recent results show that helminth or bacterial infections induce a significant increase in proliferation of ILC in FALCs and a massive expansion in the number of clusters at early time points. A recent report has demonstrated that mesenteric FALCs act as a reservoir of CD8 +T resident memory cells (Trm) that have been generated following infections with bacteria or parasites.<sup>3</sup>

Our current working model is that FALCs have a dual role during immune responses. At the initial stages of infection or inflammation FALCs support the activation and proliferation of innate lymphoid cells. At later stages FALCs act as reservoirs of tissue resident memory T cells through their stromal cell expression of survival factors and their association with adipocytes to support Trm metabolism and survival. Understanding what signals and cells are essential to FALC formation in homeostasis and following inflammation or infection will allow the development of therapies to reduce or prevent FALC formation during chronic inflammation and autoimmune diseases.

**REFERENCE:**

- [1] Benezech C, et al. *Nat Immunol* 2015;16:819.3.  
 [2] Cruz-Migoni et al. *Front. Immunol* 2016. <https://www.frontiersin.org/articles/10.3389/fimmu.2016.00612/full#B27>  
 [3] Han et al. *Immunity* 2017;47:1154.

**Disclosure of Interest:** None declared

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**SP0036 FREE FATTY ACIDS: GOOD OR BAD IN RHEUMATOLOGY?**

L.A. Joosten<sup>1</sup>, Leo AB Joosten<sup>2,3</sup>. <sup>1</sup>Internal Medicine, Radboud University Medical Center, Nijmegen, Netherlands; <sup>2</sup>Department of Internal Medicine, Radboud University Medical Center, Nijmegen, The Netherlands; <sup>3</sup>Department of Medical Genetics, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania

Free fatty acids (FFA's) are grouped based on the length of their carbon chains into short chain fatty acids (SCFAs), medium chain fatty acids (MCFAs) and long chain fatty acids (LCFAs). The most FFAs are released after breakdown of triglycerides in adipose tissue and the liver. However, SCFAs including acetate, propionate and butyrate are derived from the fermentation of fibres in the gut. In this presentation, the good or the bad properties of FFA's to control or aggravate inflammation in general will be discussed. With special focus on rheumatic disorders, such as rheumatoid arthritis and gout. In addition, the synergy of LCFAs with damage associated molecular patterns (DAMPs) will be addressed. Finally, the therapeutic value of SCFAs will be discussed in rheumatic disorders.

**Disclosure of Interest:** None declared

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THURSDAY, 14 JUNE 2018

**Inclusive school environment for young people with RMDs****SP0037 INCLUSION OF ILL CHILDREN INTO THEIR HOME SCHOOL BY REAL TIME EDUCATION**

E. Janssens. *Bednet vzw, Bednet, Leuven, Belgium*

The right to education, even when ill

It seems self-evident. Even when you are ill for a long time, you preserve the right to learn and keep your place in the social environment of your class group.

For 25 years now the right to education has been established as a right of every child, as formulated in the Convention on the Rights of the Child. Since 2006 Bednet makes sure that this fundamental right is fulfilled. Bednet takes care that children and youngsters who are absent for a shorter or longer period because of physical or mental illness, surgery or pregnancy, can continue attending the lessons – from their home and with their own class group. In the educational law it is called: synchronous internet education (SIE).

But it is only since 1 September 2015 that synchronous internet education (SIE) is structurally embedded in the educational system of the Flemish Community. This results in the right to SIE for every child with a chronic or long term illness.

Along with lessons, and all the rest

Bednet takes care that children and youngsters who are absent for a shorter or longer period because of physical or mental illness, surgery or pregnancy, can continue attending the lessons – from their home and with their own class group.

It is available for pre-school children from the age of 5, pupils of primary and secondary schools. The equipment and the counselling is free for schools and families, and this throughout the period in which the child needs it.

Bednet aims at limiting arrears in learning by providing a set of tailor-made lessons. This way 9 children out of 10 succeed in passing on to the next class despite their absence from school. Moreover Bednet makes an opening in the isolation of the child by enabling regular contacts with peers. The illness recedes to the background and the child is temporarily back with friends 'in his or her class group'. The non-profit organisation always collaborates with the parents, the school and other partners, such as the hospital schools and volunteers.

**Bednet in practice:** Bednet creates a live connexion between the pupil with an illness and his or her class group. The pupils and the teacher see the youngster on the flat screen at the back of the classroom. The child at home can direct a camera, enabling him or her to attend the lesson and/or talk to peers. Bednet uses a system that is easy to use. The pupil participates actively in the lesson, answers questions, can send and receive documents and take part in group work. Just as if the pupil were really sitting in the classroom.

Bednet operates with regional consultants in the different provinces. They do the follow-up of the children and confer with parents, hospital and school. They plan everything and take care of the concrete organisation. A technical helpdesk supports children and school throughout the project.

**Bednet in numbers:**

- In the first full school year during which Bednet was active (2007–2008), 37 children were supported.
- Since the start more than 1,900 children with a long time or chronic illness have used Bednet in 1,250 Flemish schools with synchronous internet education.

- The children and youngsters live in all parts of Flanders and Brussels. Two out of three Bednet users attend secondary school.
- Cancer remains the most common pathology with 21% of all users. Also patients with rheumatology belong to the target group of Bednet.

**The future:** Under the authority of the Flemish Government Bednet faces the big challenge of guaranteeing the right to SIE for each and every child with a long term illness. It is gradually being extended to cover all children with a long-term absence from school in the whole of Flanders. It is estimated that numbers could grow to 1.000 children in 2018.

**Disclosure of Interest:** None declared

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**SP0038 RAISING AWARENESS OF INVISIBLE ILLNESSES IN SCHOOLS AND EDUCATION**

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Introduction

RAiSE is a user-led research project inspired by the negative experiences that young people face while studying and living with an invisible illness. Many young people who live with chronic illnesses look no different to their healthy peers. The invisible nature of some illnesses can often lead to an invisible struggle, leading to misunderstandings, particularly in the case of young people. It can be a huge burden on the chronically ill to make the invisible, visible to others.

**Objective:** The main objective of RAiSE is to improve the standard of care given to young people with invisible illnesses in school and college and to create a resource to teach education professionals a series of strategies and techniques to support their students. RAiSE will also offer support to young people with invisible illnesses and aim to empower them to take control of their own health.

**Methods:** A young patient of Alder Hey NHS Children's Foundation Trust decided to raise awareness of living with an invisible illness. A network of young people, parents, education and health professionals was created and a series of workshop and focus groups allowed each stakeholder to share their experiences and expertise as they inspired and advised the production of the RAiSE information pack. It is important that young people are able to shape research based on their lived experiences. Several international charities and organisations have offered support and knowledge in advising the process.

**Results:** At early workshop meetings, young people with invisible illnesses and their parents were able to offer personal accounts and experiences which highlighted that the most common themes were problems with communication and trust, as well as difficulty in understanding the erratic nature of many chronic illnesses. From this research, a draft information pack was written by the RAiSE committee, which was later presented to young people, parents, health and education professionals and charity representatives. All stakeholders were able to offer their expertise from their respective fields. Feedback was overwhelmingly positive and any adjustments are to be made in the coming weeks. The final pack will be completed and ready for distribution by the end of summer 2018.

**Conclusion:** The project has been a successful example of young patient led research and highlights the importance of self-management in young people living with invisible chronic illnesses. The collaboration between young people, parents, and education and health professionals has highlighted the necessity for cooperation between all stakeholders for the benefit of the young person.

**Disclosure of Interest:** None declared

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**SP0039 I GRADUATED! EDUCATION FOR CHILDREN AND ADOLESCENTS WITH RMDs**

T.C. Wilhelmer. *Youth Ambassador, Austrian Rheumaliga, Lauterach, Austria*

Communication is the key to success in practically every situation. Without communicating to your counterpart, how should they understand your own situation?

When it comes to studying with a chronic illness we need to know how the illness affects our ability. We need to communicate what we are able to do and where we need support. When I started my Master Degree I have been honest from the very beginning. I never kept my rheumatic disease and the disability that comes with it a secret. Being open from the very beginning gives yourself and your university, school or even workspace the opportunity to adapt to your abilities. Hiding your disability will make it hard for yourself to keep up with your class. Your fellow students and teachers not knowing what your limitations are will most certainly lead to misunderstandings.

Many pupils and students do not know that there are laws and regulations that could help them to get through school easier. For example you are allowed to have longer writing times in exams, or use your computer for typing texts instead of having to write by hand. This helps to prevent pain in your joints. There are



even more ways in which your university or school can help you to get through your day than you would think of in the first place. Without asking for help, you will never find out what is actually possible. Through communicating with a disability-spokesperson you will most likely get even greater support.

In my lecture I will talk about my own story and how I managed to finish my Bachelor Degree whilst falling chronically ill with Adult Onset Still's Disease. I will give examples on how to handle a life with chronic illness. There will be some tips on what to do when your counterpart is not as understanding as he or she should be. I will explain what I do to get me through lectures and exams.

**Disclosure of Interest:** None declared

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#### SP0040 PARENTS SUPPORT FOR CHILDREN WITH RMDS IN EDUCATION

*M. Kopic. Society for Children with Immune Disease, Komenda, Slovenia*

My presentation will contain situation in schools all across the Europe (at least 13 countries/results from a survey and info which I get from our Associations, members of ENCA).

It is serious situation. First I will present the problems, we, parents, are struggling with every day. I will also prepare and present possible solutions. One country is extra good in solutions and they really take good care for children with autoimmune conditions and we can learn from them. I will also present a concrete good solution.

Solutions should be used as a prepared document for all the countries. That is a goal of ENCA.

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THURSDAY, 14 JUNE 2018

### WIN and HOT session

#### SP0041 WIN SESSION: WHAT IS NEW IN THE TREATMENT OF MYOSITIS?

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Much progress has been made over the last decade in the understanding of the inflammatory myopathies. It is heartening to see some of these developments now in clinical practice which is hopefully increasing the quality of care for myositis patients. This talk will summary the new upcoming treatments in myositis. However, treatment of a rare disease not only involves administering pharmacotherapeutic agents, but recognising when to treat and which poor prognostic groups required intensification. Antibody testing of the spectrum of newly identified myositis serology now allows for better stratification of patients and assists the physician with treatment, monitoring and prognosis. New EULAR/ACR criteria are available for classification to assist inclusion into clinical trials, as well as agreed definitions for minimal, moderate and major response. A better understanding of the pathogenesis has now led to randomised controlled trials now being conducted in the inflammatory myopathies, including targeting the innate immune pathway that will hopefully lead to a licensed treatment for this difficult orphan disease.

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#### SP0042 RECENT ADVANCES IN THE TREATMENT OF SYSTEMIC SCLEROSIS

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Few rheumatological diseases have seen as many false dawns as systemic sclerosis (SSc) and many drugs once hailed as promising have fallen by the wayside. Clinical trials have been plagued by poor accrual, difficulties with definitions of endpoints, clinical heterogeneity of disease manifestations and variability of disease course, resulting in inconclusive or negative trial results. Clinicians standing in the shadows of no man's land could be forgiven for not seeing the sparks of light around them. Yet our grasp of the pathological pathways operative in SSc,

consensus on endpoints and international collaboration have paved the way for clinical trials with novel antibiotic and immunomodulatory drugs (e.g. rociguat, JAK-STATi) that could change the way we treat SSc. For now we will have to stick to old friends such as methotrexate, MMF and cyclophosphamide in early diffuse cutaneous SSc, even though their clinical benefit is modest at best as shown in the ESOS study and expressed in recent guidelines.<sup>1-3</sup> Rituximab is increasingly being used based on observational studies in SSc and its proven potency in rheumatoid arthritis, but requires more robust data. Tocilizumab has shown unexpected benefit on lung function in a phase 2 trial,<sup>4</sup> which if confirmed with phase 3 trial could transform the way we manage SSc-ILD. As of yet, the only proven disease modifying therapy in early progressive SSc is autologous hematopoietic stem cell transplantation, shown to be effective in two prospective, controlled randomised clinical trials (ASTIS and SCOT, conducted in Europe and North America respectively).<sup>5,6</sup> Only a small group of patients qualify for this however and even fewer have access to centres with the necessary expertise. SSc continues to constitute an area of unmet need, yet progress is being made, albeit slow.

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### Can we halt progression of structural damage in axial SpA?

#### SP0043 HOW TO CAPTURE CLINICALLY RELEVANT STRUCTURAL PROGRESSION IN AXIAL SPA

*D. Van Der Heijde. Leiden University Medical Center, Leiden, Netherlands*

Structural damage in axial SpA usually refers to the sacro-iliac (SI) joints or the spine. The classic order of the progress of structural damage is in the SI joints, followed by the spine. Consequently, in early disease assessment of structural damage should be focused on the SI joints and in established disease (i.e. in patients with radiographic sacroillitis) evaluation of the spine becomes more useful.

The most striking abnormality representing structural damage in axial SpA is bone formation, although in early phases bone destruction can also be seen. Typically, structural damage is assessed on radiographs.

For radiographs there are two frequently used scoring methods: grading of the SI joints according to the modified New York (mNY) criteria and assessment of the spine by the modified Stoke Ankylosing Spondylitis Score (mSASSS). The mNY grades range from 0–4 per SI joint, 0–8 in total. Although it is well known that reliability of mNY grading is poor, this continuous grading has recently been successfully used as an outcome measure. The mSASSS is mainly based on bone formation in the anterior vertebral corners in the cervical and lumbar spine (range 0–72). It is a reliable measure but the progression observed by mSASSS is rather modest, resulting in a minimum follow-up of two years.

Imaging of structural damage by MRI is another option. Due to the imaging of the whole spine and the three-dimensional technique this seems an attractive alternative. However, especially bone formation is very hard to assess. Fatty deposition is a typical MRI abnormality, which can be seen as an intermediate step between inflammation visible on MRI and bone formation on radiographs. However, this finding is insufficiently validated to be able to consider it as a true surrogate for structural damage.

Finally, a CT scan is a method having the advantages of MRI (whole spine, tomographic technique) but also the best capabilities of bone imaging. The big disadvantage of CT scan is the radiation dose. Recently, it became possible to make images with good image quality but acceptable radiation, the so-called low-dose CT. A validated scoring system for CT exists: the CT scoring system (CTSS). Only bone proliferation is assessed in this method. In a direct comparison with mSASSS more progression was observed over a 2 year period. This was mainly due to the progression observed in the thoracic spine.

Only structural damage assessed by the mSASSS has shown a clear relationship with outcomes that are important for patients such as function and quality of life. No data on MRI or CTSS exist. However, it is hard to describe what defines a clinically relevant progression. The interval to assess progression to assess a

treatment effect is typically 2 years. Only small changes can be assessed over this period, normally about 1–2 mSASSS units. It is hard to define that this is clinically relevant. The most important for treatment is to show that there is inhibition of structural progression in comparison to untreated patients, especially as axial SpA is a lifelong disease and 1 unit over 30 years still leads to severe ankylosis of the spine.

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SP0044

#### WHAT DO WE LEARN FROM RCTS ON THE TREATMENT EFFECT ON STRUCTURAL PROGRESSION IN AXSPA?

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The introduction of tumour necrosis factor inhibitors (TNFi) about 20 years ago has led to the hope of disease modification of ankylosing spondylitis, since biologics showed for the first time a decrease of inflammatory activity on MRI, with the latter being theoretically also directly linked to new bone formation. However, the first open-label extensions of randomized-controlled trials with a treatment duration of 2 years failed to show any positive effect on the radiographic progression in AS patients when compared to historical cohorts that had not been exposed to biologics. Nevertheless, later data indicated that this lack of influence on radiographic progression might have been due to many different reasons that were not taken into account in these first analyses, such as the radiographic status of patients at baseline, CRP levels or insufficient duration of follow-up. Furthermore, most recent data from MRI studies also indicated that the most important link to influence radiographic progression with biologics might not be the suppression of inflammation but the protection of bone to show tissue metaplasia to post-inflammatory findings, while early suppression of inflammation might be the key to even completely inhibit radiographic progression in AS patients.

Indeed, most recent cohort data have been able to demonstrate an association between TNF-blocker treatment and reduced risk of spinal structural progression (e.g. formation of syndesmophytes). Furthermore, early escalation of treatment from NSAIDs to biologics and long-term treatment with biologics have also independently been able to show positive effects on radiographic progression in patients with AS. Finally, also newer biologics such as IL-17A inhibitors have also provided promising results in terms of overall low radiographic progression rates as measured by validated scoring systems.

Currently, first head-to-head trials of different biologics are underway to examine any possible differences between the available compounds with a primary outcome of their effect on spinal radiographic progression.

It remains to be shown whether and how these results will also become clinically relevant in terms of decrease or even inhibition of spinal mobility restrictions, in order to be able to postulate a 'real' disease modifying effect of biologic treatment in axial spondyloarthritis.

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THURSDAY, 14 JUNE 2018

### Reproductive issues in rheumatology

SP0045

#### OESTROGENS, IMMUNE RESPONSE AND AUTOIMMUNE DISEASES

*M. Cutolo, on behalf of Eular Study Group on Neuroendocrinology of the Rheumatic Diseases. Research Lab. Division Rheumatology. Dept Internal Medicine University of Genova Italy, genova, Italy*

Sex hormones are implicated in the immune response, with estrogens as enhancers at least of the humoral immunity and androgens and progesterone (and glucocorticoids) as natural immune-suppressors. Several physiological, pathological and therapeutic conditions may change the serum oestrogen milieu including the menstrual cycle, pregnancy, postpartum period, menopause, elderly, chronic stress, altered circadian rhythms, inflammatory cytokines, use of glucocorticoids, oral contraceptives, and steroid hormonal replacements. Cortisol and melatonin circadian rhythms are altered, at least in rheumatoid arthritis (RA), and partially involve also sex hormone circadian synthesis and levels. Abnormal regulation of aromatase activity (i.e. increased activity) by inflammatory cytokines production (i.e. TNF-alpha, IL-1, IL-6) may partially explain the abnormalities of peripheral oestrogen synthesis in RA (i.e. increased availability of 17-beta estradiol and possible metabolites in synovial fluids) and in systemic lupus erythematosus (SLE). In the synovial fluids of RA patients the increased oestrogen concentration are observed in both sexes and are more specifically characterised

by the hydroxylated forms, in particular 16alpha-hydroxyestrone, that is a mitogenic and cell proliferative endogenous hormone. Local effects of sex hormones in autoimmune rheumatic diseases seems to consist mainly in modulation of cell proliferation.

Epidemiological evidence indicates that during the fertile age women are more often affected by rheumatic diseases than men, particularly autoimmune diseases. As a matter of fact, rheumatic disorders with autoimmune involvement such as RA or SLE, result from the combination of several predisposing factors, that include the relationships between epitopes of the trigger agent (i.e. virus), the status of the stress response system including the hypothalamic-pituitary-adrenocortical axis (HPA) and mainly the effects of the gonadal hormones (hypothalamic-pituitary-gonadal axis – HPG).

The pre- or post-menopausal serum sex hormonal status is a further factor influencing the rate of rheumatic diseases. It is therefore important, whenever possible, to evaluate epidemiologic data broken down into age (for example 10 year age band) and sex-specific group before making inferences. Obviously, sex hormones seem to play an important role as modulators of both disease onset and perpetuation and show circadian rhythms together with cortisol.

Sex hormones are implicated in the immune response, with estrogens as enhancers at least of the humoral immunity and androgens and progesterone (and glucocorticoids) as natural immune-suppressors. Low concentrations of gonadal and adrenal androgens [testosterone (T)/dihydrotestosterone (DHT), dehydroepiandrosterone (DHEA) and its sulphate (DHEAS), respectively] levels, as well as reduced androgens/estrogens ratio, have been detected in serum and body fluids (i.e. blood, synovial fluid (SF), smears, salivary) of male and female RA patients, as well as in SLE, supporting the possible pathogenic role for the decreased levels of the immune-suppressive androgens. However, respect to serum levels of estrogens, interestingly they are not significantly changed which is in strict contrast to androgen levels in RA patients (reduced).

As a matter of fact, sex hormones can exert also local actions (paracrine) in the tissues in which they are formed or enter the circulation and both T and 17-beta estradiol seem to exert dose and time-dependent effects on cell growth and apoptosis. These effects, as well as important influences on gene promoter of Th1/Th2 cytokines and the recently discovered increased SF oestrogen concentrations, might suggest new interesting roles for estrogens at least in RA. Finally estrogens exert important epigenetic actions on cell proliferation. Estrogens act as key factors in cellular proliferation and differentiation as well as cancer development and progression (prostate). The expression of oestrogen receptor (ER)-β appears to be lost during prostate cancer progression through hypermethylation mechanism. Epigenetic drugs such as 5-aza-2'-deoxycytidine (5-AZAC) and Trichostatin A (TSA) showed efficacy in restoring ERβ expression in prostate cancer cells. These observations highlights that the strategy of merging epigenetic and hormonal therapies might be beneficial also in inflammatory/autoimmune diseases (synovial tissue)

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SP0046

#### WHAT WE NEED TO CONSIDER IN PHYSICIAN-PATIENT COMMUNICATION ON SEXUAL PROBLEMS IN DIFFERENT RHEUMATIC CONDITIONS

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Quality of life (QOL) is often reduced in patients with chronic diseases. Sexual activity and enjoyment constitute an important aspect of QOL. Sexuality is a neglected area of QOL in patients with rheumatic disease.

Sexual problems among patients are common and often increase with disease duration. Both disease related factors and the psychological response to chronic disease can impair sexual functioning. General disease symptoms like pain, fatigue, disease activity, and impaired physical function contribute to reduced sexual activity in both genders. However, psychological factors like depression, anxiety, negative body image and low self-esteem play an important role. Sexual dysfunction can create frustration and distress, and if chronic increase anxiety and depression, and damage interpersonal relationships.

Sexual health is rarely addressed by health professionals (HP), and it is as a rule not spontaneously reported by patients. HPs may feel awkward to intrude into the intimate sphere of a patient, and patients may feel ashamed of revealing their sexual dysfunction.

A first step to improve the physician-patient communication in this area is to include sexuality in the curriculum of health professionals teaching how to address and evaluate sexual function. Assessment of sexual function by validated instruments includes both frequency of intercourse as well as sexual desire, arousal, orgasm, and sexual satisfaction. In women vaginal lubrication and in men erectile function and ejaculation are part of the evaluation. Assessment of disease activity and comorbidities helps to detect physical components of sexual dysfunction. Barriers regarding communication on sexual activity should be identified and overcome. Assessment of sexual function may be assigned to a specially trained nurse, an occupational therapist or a psychologist of the interdisciplinary team. Referral to specialists in urology, gynaecology or sexual medicine may also help patients to get a better sex life. A major point for restoring sexual and reproductive health in patients of both genders is to achieve optimal disease control.

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#### SP0047 CHALLENGES IN THE MANAGEMENT OF DIFFERENT RHEUMATOLOGIC DISORDERS DURING PREGNANCY: LESSONS FROM THE REGISTRIES

*R. Fischer-Betz. Rheumatology, Heinrich-Heine-University, Duesseldorf, Germany*

Registers have considerably expanded our knowledge in many fields of rheumatology. In particular, the Biologics Registers contribute to an enormous increase in knowledge on the "real world" safety of the rapidly growing treatment options. Family planning in the case of RD is a particular challenge in the physician-patient relationship and requires an optimal strategy. The impact of pregnancy on the underlying disease or the impact of maternal disease on the outcome of pregnancy is not yet fully understood. In addition there is still a high unmet need of data on drug safety as women with wish to have children or pregnant women are excluded from registration studies for ethical reasons. Therefore, systematic and prospective observation in daily care is the best possibility to collect data on this subject. Data options range from clinical-based cohort studies (e.g. the PROMISSE study), prospective pregnancy exposure studies (e.g. the MotherToBaby studies) to national birth registries. Recently, pregnancy registers in women with RD have been established in several European countries. Together with other studies, these registers will hopefully add to improved expertise in the future

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THURSDAY, 14 JUNE 2018

#### Clinical challenges in giant cell arteritis in 2018\_\_\_\_\_

#### SP0048 A CASE OF PULSELESS STROKE

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Giant cell arteritis (GCA) is the most common form of vasculitis in individuals aged 50 years and over. GCA typically affects large and medium-sized arteries, with a predilection for the extracranial branches of the carotid artery. Patients with GCA usually present with symptoms and signs that are directly related to the artery that is affected, with or without constitutional manifestations. The most dreaded complication of GCA is visual loss, which affects about one in six patients and is typically caused by arteritis of the ophthalmic branches of the internal carotid artery. Before the advent of glucocorticoid treatment, the prevalence of visual complications was high. Increasing awareness by physicians of the symptoms of GCA and advances in diagnostic techniques over the past twenty years have also contributed to a substantial decline in the frequency of permanent visual loss. Ischaemic brain lesions are less common than visual lesions, and mostly result from vasculitis of the extracranial vertebral or carotid arteries. In the case of both the eye and the brain, ischaemic damage is thought to result from arterial stenosis or occlusion that occurs secondary to the inflammatory process.

A patients with giant cell arteritis with extensive extra and intracranial large vessel involvement effectively treated with cyclophosphamide followed by mycophenolate mofetil will be presented. Diagnosis and management of ischaemic complications in giant cell arteritis will be discussed.

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#### SP0049 HEAD GAMES WITH GCA AND GCS

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Case 1: This is a 65 y/o woman with osteoporosis, depression and recently diagnosed polymyalgia rheumatica characterised by shoulder and hip girdle pain and stiffness with elevated inflammatory markers. She developed recurrent symptoms and new-onset jaw and tongue claudication in the setting of a prednisone taper. She was found to have a bulging right temporal artery and biopsy confirmed giant cell arteritis. She was placed on prednisone 60 mg daily with resolution of her symptoms, but developed worsening symptoms of depression and anxiety with insomnia on high dose prednisone. She subsequently attempted suicide by intentional medication overdose and carbon monoxide poisoning. She was admitted to the psychiatry ward and additionally found to have a varicella zoster skin rash. Upon resolution of the zoster infection she was started on tocilizumab by subcutaneous injection weekly and prednisone was successfully tapered over 4.5 months without recurrence of symptoms.

Case 2: This is a 63 y/o man with ITP on monthly rituximab and chronic prednisone 10 mg daily, hypertension, hyperlipidemia and osteoarthritis who developed worsening shoulder and neck pain for two months with more recent onset of scalp tenderness and left-sided vision changes for two weeks. He was found to have left optic neuropathy, elevated inflammatory markers, and an MRI demonstrating enhancement of the left temporal artery. Left temporal artery biopsy was normal. He was given pulse dose intravenous methylprednisolone for suspected giant cell arteritis and transitioned to high dose oral prednisone with improvement in musculoskeletal symptoms, inflammatory markers and stabilisation of his vision. He subsequently developed insomnia, hyperactivity and talkativeness and was diagnosed with steroid-induced mania, which improved with antipsychotics and benzodiazepines as per the psychiatry service. He was discharged home and after three days developed new vision loss of the right eye on prednisone 60 mg daily. On exam, he was found to have progressive visual field loss of the left eye and new inferior visual field loss of the right eye with disc oedema of the right optic nerve. Right temporal artery biopsy was negative. He was again given pulse dose intravenous methylprednisolone followed by oral methylprednisolone and ultimately received tocilizumab intravenously prior to discharge.

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THURSDAY, 14 JUNE 2018

#### Do we still need biopsies to diagnose Sjögren's and autoimmune myositis?\_\_\_\_\_

#### SP0050 OPPORTUNITIES AND CHALLENGES OF IMAGING IN PRIMARY SJÖGREN'S

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Sjogren's syndrome (SS) is a chronic autoimmune inflammatory disorder of exocrine glands. Its diagnosis relies solely on a combination of clinical and laboratory findings. However, recent developments have shown that imaging techniques may have additional value in detecting salivary glands abnormalities in pSS. In general, sialography is considered to be the most reliable of the imaging methods. Salivary gland scintigraphy is very sensitive and especially useful in early stages of the disease. Nevertheless, both imaging techniques are used by only minority of rheumatologists for diagnosis of pSS because of the invasive character of sialography and the low specificity of scintigraphy. MRI has shown a good sensitivity and specificity to detect structural abnormalities in pSS but few centres have access to the specific know-how. A recent development is the increased interest in ultrasonography (US) as a tool to assess major salivary glands. Ultrasonography of the salivary glands (SGUS) appears to be an inexpensive commonly available noninvasive technique that does not cause complications and inconvenience to the patient, although the data are somewhat conflicting. Although, the recent but preliminary American classification criteria for Sjögren syndrome do not include salivary gland such imaging technique<sup>1</sup> this procedure has clearly demonstrated high impact on classification of Sjögren patients<sup>2-5</sup> and demonstrated good diagnostic properties.<sup>5</sup> A systematic literature review<sup>6</sup> has shown a paucity of data regarding the metric properties of ultrasound, making interpretation and



comparison of studies difficult. In particular, there are limited data describing a standardised scanning method and standardised definitions of US gland pathologies. Even if we obtained truth validity, discrimination validity (reliability) is not yet validated. Therefore, although SG-US is an upcoming modality in rheumatology, it is not yet ready to make diagnostic or therapeutic decisions regarding salivary glands in daily routine practice. It should still be considered to be a research tool, until we are able to demonstrate acceptable intra- and interobserver reliabilities. Preliminary work addressing these issues has been done so far by the USpSS study group consisting of both clinicians and ultrasonographers.<sup>6,7</sup>

More recently, a SG-US OMERACT task force group composed of international clinicians and ultrasonographers was created with the aim of developing a standardised scanning method using standardised definitions of gland pathology. A consensual Delphi process about definitions and scoring using B mode modality of SG-US was used and the intra and inter reliabilities between 18 sonographers showed good to excellent reliabilities (Light's kappa=0.81, Light's kappa=0.71 respectively) (article in preparation). Currently, there is an unmet need concerning the use of SGUS in the monitoring of patients. Even if it seems that structural damage are stable over time.<sup>8</sup> Another possible way to study SG in the disease course is to use Doppler. Doppler waveform analysis was found useful for detecting blood flow abnormalities in SG of patients with pSS compared to controls.<sup>9</sup> Given the importance of parotid and submandibular glands involvement in pSS, we believe that the vascularisation and B mode sonography should be evaluated routinely. A new US technique measuring the elasticity of SG parenchyma using elastography has recently emerged and could be implemented in the evaluation of SGUS pSS patients.<sup>10-12</sup> Some authors showed that stiffness of SG parenchyma was increased compared to healthy controls and suggested to adjunct this procedure to gray-scale ultrasonography for the clinical diagnosis of pSS. The last important challenge is to know if imaging techniques are capable to replace minor salivary glands biopsy. A recent study<sup>13</sup> has shown good agreement between SGUS and parotid gland and moderate with labial glands.

In conclusion, US has nearly completed the 3 pillars of the OMERACT process (truth validity, discrimination validity and feasibility). The use of different imaging technique and particularly ultrasonography should be educated and it is now of importance to train the rheumatologists to this technique as proposed by The US EULAR courses.

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THURSDAY, 14 JUNE 2018

## How monogenetic autoinflammatory diseases help to understand and treat rheumatic diseases

SP0051 **CLINICAL PRESENTATION OF AUTOINFLAMMATORY DISEASES IN CHILDREN AND ADULTS: HOW NOT TO MISS THESE PATIENTS**

*S. Ozen. Pediatric Rheumatology, Hacettepe University, Ankara, Ankara, Turkey*

Autoinflammatory diseases are diseases of the innate immune system, characterised by attacks of inflammation. The inflammatory attacks can manifest in a variety of forms; fever, is frequent, the skin and musculoskeletal system is often affected. Acute phase reactants are increased in almost all of the patients. The autoinflammatory diseases can be classified according to their leading manifestations such as: those with periodic fevers (and other various features), those with pyogenic

features, those with psoriasis, those with features of interferopathies and those with vasculopathy. With this large range of features these diseases are in the differential of many common diseases. Genetic testing is confirmatory but may not be widely available.

The differentiating features of especially the common autoinflammatory diseases will be reviewed.

**Disclosure of Interest:** S. Ozen Consultant for: Novartis, Speakers bureau: SOBI

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THURSDAY, 14 JUNE 2018

## Joint EULAR – EFIS session: I've got a B in my bonnet

SP0052 **POSTTRANSLATIONAL MODIFICATION OF AUTOANTIBODIES IN RA**

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Rheumatoid Arthritis (RA) is a common autoimmune disease in which autoantibodies serve as interesting biomarkers. In a large proportion of the patients several types of autoantibodies are present that target post-translationally modified proteins. Next to antibody responses against citrullinated proteins (ACPA) we now also describe antibody responses against carbamylated proteins (anti-CarP) in RA. The use of these autoantibodies in the prediction, diagnosis and prognosis will be discussed, as well as the clues, obtained in animal models, as to how such an antibody response may be initiated.

In addition the findings that antibodies themselves are also post-translationally modified and the functional consequences of such modifications will be highlighted both regarding carbamylation of IgG and modifications of ACPA IgG.

**Disclosure of Interest:** None declared

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SP0053 **MEMORY PLASMA CELLS IN CHRONIC INFLAMMATORY DISEASES – A ROADBLOCK TO TOLERANCE INDUCTION**

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Regeneration of tolerance is the Holy Grail of treating inflammatory rheumatic diseases. Obviously neither physiological nor therapeutic immunosuppression does achieve this for most patients. What are the roadblocks for therapies inducing therapy-free remission? We have identified memory plasma cells secreting pathogenic (auto)antibodies as one such roadblock. Such cells are often generated already before disease becomes clinically apparent. They persist over time in inflamed tissues and in the bone marrow, in niches which protect them from environmental stress, including conventional therapies. By constitutive secretion of pathogenic antibodies they fuel relapse and refractoriness. Any therapy aiming at induction of therapy-free remission will have to remove this roadblock. Recently we and others have developed therapeutic concepts to ablate memory plasma cells, based on a molecular understanding of their lifestyle. Such therapies, however, have two major inherent problems: they also ablate protective humoral immunity, increasing risk of infection, and the pathogenic memory plasma cells can be regenerated, if tolerance is not regenerated. To address the latter point, ablation of plasma cells has to be combined with tolerance-inducing therapeutic options, and until then, patients have to be protected passively by IV-Ig. For selective targeting of pathogenic memory plasma cells, differences in the lifestyle between protective and pathogenic plasma cells could be exploited, but few have been identified so far. We have now developed a novel technology to target plasma cells according to the specificity of the antibodies they secrete. Plasma cells are labelled *in vivo* with a given antigen, and those plasma cells secreting specific antibodies are selectively killed by their own antibodies. We have now demonstrated feasibility and efficacy of this therapeutic approach in a preclinical model. Apart from the therapeutic perspective, this technology also offers a unique option to identify pathogenic plasma cell specificities in experimental and clinical rheumatology.

**Disclosure of Interest:** None declared

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**SP0054 THE CONTRIBUTION OF REGULATORY B CELLS IN PROTECTING RHEUMATIC DISEASES**

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B cells are considered central to the pathogenesis of patients with rheumatic diseases (RD) including Systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA). In addition to producing autoantibodies, B cells suppressing inflammatory responses, known as regulatory B cells (Bregs) are numerically and functionally defective in rheumatic diseases. The production of interleukin 10 (IL-10) classically defines a Breg, however the stability and/or plasticity of this population is not well understood. In addition to producing autoantibodies, B cells suppressing inflammatory responses, known as regulatory B cells (Bregs) are numerically and functionally defective in RD patients. The production of interleukin 10 (IL-10) classically defines a Breg, however the stability and/or plasticity of this population is not well understood. Additionally, IL-10 +B cells have been shown to co-express pro-inflammatory cytokines such as TNF $\alpha$  and IL-6, further complicating Breg classification. Characterising the signals inducing Breg differentiation and the subsequent stability and/or plasticity of this population may aid in understanding the factors contributing to Breg dysfunction in RD patients. Novel findings unravelling the signals required and the stability of B regs versus B effector cells in RDs will be discussed.

**Disclosure of Interest:** None declared

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THURSDAY, 14 JUNE 2018

**Sustainable healthcare in rheumatology and the role of health professionals**

**SP0055 HOW CAN INTEGRATED HEALTHCARE CONTRIBUTE TO SUSTAINABLE HEALTHCARE IN RHEUMATOLOGY?**

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**Introduction:** According to the World Health Organisation (WHO) "an integrated, people-centred approach is crucial to the development of health systems that can respond to emerging and varied health challenges, including urbanisation, the global tendency towards unhealthy lifestyles, ageing populations, the dual disease burden of communicable and non-communicable diseases, multi-morbidities, rising health care costs, disease outbreaks and other health-care crises". In supporting health services to become more integrated and people-centred a Framework was developed that proposes five interdependent strategies: 1. Empowering and engaging people and communities; 2. Strengthening governance and accountability; 3. Reorienting the model of care; 4. Coordinating services within and across sectors; 5. Creating an enabling environment. Given that health systems are highly context-specific, the Framework does not propose a single model but interdependent (sub) strategies, policy options, and interventions that need to be adopted.<sup>1</sup> What is known about the adoption of these strategies for people with rheumatic and musculoskeletal diseases?

**Methods:** A convenience sample of recently published reports about redesigning health care for people with rheumatic and musculoskeletal diseases is assessed against the WHO Framework on integrated-people centred health services. The five interdependent strategies, including the policy options and interventions as defined under the Framework, are assessed for presence, implementation fidelity and outcomes. Implementation fidelity refers to the degree to which an intervention is delivered as intended (i.e. in line with the Framework). Outcomes of people-centred care include: equity in access, quality, responsiveness and participation, efficiency, and resilience.

**Results:** To be presented at the conference.

**Discussion:** It is anticipated to find a plethora of examples of mainly single policy options and interventions, but hardly any examples of combinations of strategies. This would indicate a need for a systems approach in achieving sustainable healthcare in rheumatology.

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**SP0056 SUSTAINABLE HEALTHCARE – IT TAKES A VILLAGE**

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Healthcare delivery is at a crossroads for potential paradigm change due to budget constraints, complexity of care, increasing performance measures and implementation of electronic health records. Additionally, recent reports of high levels of stress and burnout amongst healthcare providers has been linked to decreased patient safety and medical errors. Complicating matters for rheumatology, is shrinking of the available workforce. The model of interprofessional healthcare delivery holds promise as a means to improve both patient outcomes and provider wellbeing. This presentation addresses implementation of interprofessional teams in rheumatology and provides a review of successful models and guidelines for implementation.

**Disclosure of Interest:** None declared

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THURSDAY, 14 JUNE 2018

**SSc: From registries to trials – do we have sufficient data and the appropriate design?**

**SP0057 THE COURSE OF SYSTEMIC SCLEROSIS (SSC): WHAT CAN WE LEARN FROM REGISTRIES?**

*M. Matucci Cerinic. Professor of Rheumatology, Director Division of Rheumatology AOUC, University of Florence, Italy, Florence, Italy*

SSc is a heterogeneous connective tissue disease with an unpredictable course and a high mortality and morbidity. Although the identification of patients in early stages of disease is increasingly achievable thanks to the introduction of the new ACR/<sup>EULAR 2013</sup> classification criteria, the stratification of patients according to the risk of disease progression or of severity of disease is still an unmet need. Several potential predictive factors of disease evolution have been proposed over the years: SSc specific autoantibodies related to disease complications, serum biomarkers of internal organ involvement, age at diagnosis, sex, disease subset seem to have a prognostic value but unfortunately all these may be present in different combinations making it difficult to identify how the disease will evolve. Data from registries of different countries confirm that the clinical presentation depends on several factors. Data from EUSTAR group data base indicate that a late age at onset (>75 years) of SSc is associated with more aggressive disease as well as the male gender, that has a more severe phenotype and a worst prognosis than female, with an increased risk of occurrence of cardiovascular involvement. The analysis of geographic variations among different SSc presentations may suggest that eastern centres care for more severe SSc manifestations in Europe. Data from EUSTAR group reported also that the main causes of deaths in SSc are due to pulmonary fibrosis, pulmonary arterial hypertension (PAH) and heart involvement (mainly heart failure and arrhythmias). Independent risk factors for mortality and their seem to be proteinuria, the presence of PAH based on echocardiography, pulmonary, forced vital capacity below 80% of normal, dyspnoea above NYHA class II, reduction of dlco, patient age at onset of Raynaud's phenomenon and the modified Rodnan skin score. Interestingly, SSc patients show an increase risk of lung cancer (especially non small cell lung carcinoma) in association with interstitial lung disease and of esophageal or cardiac adenocarcinoma. Data from the database of the German Network for Systemic Scleroderma support the concept that SSc-overlap syndromes should be regarded as a separate SSc subset, distinct from lcSSc and dcSSc, due to a different progression of the disease, that had an intermediate rate of disease progression in between lcSSc and dcSSc, different proportional distribution of specific autoantibodies, and of different organ involvement. Therefore, the use of registries is today of paramount importance to obtain significant data about several unmet needs in SSc.

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THURSDAY, 14 JUNE 2018

## Patient involvement in research: The future of collaborative research. Lessons from the field of rheumatology and beyond

SP0058 PATIENT INVOLVEMENT IN RESPIRATORY RESEARCH

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The European Lung Foundation (ELF) mission is to bring together the public and patients with respiratory professionals to improve lung health. ELF was founded by and works in a unique partnership with the European Respiratory Society (ERS), a membership society for respiratory professionals. A core part of ELF's activities is to ensure that the perspectives of people living with a lung condition help to inform research, treatment and policy activities at a European level. ELF has extensive experience of facilitating patient engagement in research and clinical projects, including in EU-funded consortia, and has published extensively on the topic.

During this session, ELF will share its experience of involving patients in respiratory research collaborations. Focusing on three projects as exemplars of different stages of the research process, ELF will share some of the lessons, challenges, and key benefits of involving patients in research and will highlight how these can be transferred to projects beyond the respiratory field.

Research priority setting: the European Asthma Research and Innovation Partnership (EARIP) set out to develop a coordinated and integrated approach to the future of asthma research and development by creating a roadmap of the components needed to reduce the burden of asthma, in terms of the impact on individuals and on healthcare systems across Europe. ELF led a research priority setting process in which patient perspectives played a central role. The resulting research priorities have been taken forward by research funders and consortia, helping to ensure that the future research agenda is patient-centred.

Key lessons:

- how to involve patients in research priority setting
- how to build consensus between patient, clinical, research and industry stakeholders

### Clinical trials:

the ground-breaking U-BIOPRED (Unbiased Biomarkers for the Prediction of Respiratory Disease Outcomes) project involved patients with severe asthma as equal partners. Up until this point, many projects funded by the EU Innovative Medicines Initiative (IMI) had limited or no involvement of patients. As a result of the successful partnership between patients and professionals, IMI asked the project to develop a guide to patient involvement in EU-funded research so that the experience could be transferred to other disease areas. U-BIOPRED is still considered a pioneering project in terms of its level of patient involvement and many new studies use the approach as the exemplar for how to engage patients as partners.

Key lessons:

- how to involve patients as equal partners in clinical research
- how to maximise the opportunities for patient input
- where patients can add value to clinical projects

### Disease registries:

the European Multicentre Bronchiectasis Audit and Research Collaboration (EMBARC) is an ERS Clinical Research Collaboration dedicated to improving research and clinical care for people with bronchiectasis. EMBARC has created a European Bronchiectasis Registry, funded by the ERS and by the EU IMI Programme. Patients have played a central role in defining the scope, ethics, governance and data protection processes for the registry and the next phase of the project will include a patient-powered registry in order to capture patient-important outcomes directly from people affected by bronchiectasis.

Key lessons:

- patients' and clinicians' recommendations for involvement in research – dos and don'ts
- how to involve patients from rare disease communities in research

**Conclusion:** Patient involvement in respiratory research has grown significantly over the last decade. Patient perspectives are increasingly considered to be a core component of every research project and the wider respiratory community values the important role patients now play. ELF has facilitated the involvement of people with lung conditions in a wide range of research projects and the lessons learned are highly transferable to other disease areas and settings.

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SP0059 EULAR'S PATIENT RESEARCH PARTNER NETWORK – PATIENTS' FUTURE INVOLVEMENT IN RESEARCH

C. Zabalán. Romanian League Against Rheumatism, Bucharest, Romania

Research in the field of RMDs, particularly in Europe, has advanced significantly the last years. In particular, **the interest in developing Patient Reported Outcomes (PROs) and forms of participatory research has grown**. In the field of rheumatology there have been undertaken many initiatives to explore and implement participatory research.

Substantial unmet needs in the area of research, highlighted in the **RheumaMap** (developed by EULAR), will however require an altogether **higher level of commitment and innovation**. Implementation of the distinct elements contained in RheumaMap will rely on scientists, patients and health professionals.

In this regard EULAR PARE has developed **recommendations for patient-researcher collaboration** and also established a network of **40 trained patient research partners** of whom 6 have also graduated for the EUPATI training course.

Last year it was created a **platform** (under the name of **Study Group for Participatory Research**) for knowledge exchange regarding patient participation in rheumatology care and research with the aim of establishing a group of researchers and patient research partners with an interest in developing innovative methods to elicit the voice of patients in rheumatology research, to stimulate the dialogue about the rationale, principles and conditions for patient involvement in research and to discuss and develop the nomenclature and methodology of evaluating the process, results and impact of patient participation in research and health care innovation.

**The Learning Objectives** of the session are as follows:

- To learn from best practices of patient engagement in different disease areas
- To explore patient involvement in guideline development and health care innovations
- To explore how to evaluate patient involvement
- To explore how to cease the moment, how to have fun in the process

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THURSDAY, 14 JUNE 2018

**EULAR Projects in musculoskeletal imaging**

SP0060

**EULAR RECOMMENDATIONS FOR THE USE OF IMAGING IN MECHANICAL LOW BACK PAIN**

Bjarke B Hansen<sup>1</sup>, Lene Terslev<sup>1</sup>, Francis Berenbaum<sup>2</sup>, Ingrid Möller<sup>3</sup>, Mikael Boesen<sup>1</sup>, Jean Denis Laredo<sup>2</sup>, Francois Rannou<sup>2</sup>, Stefan Lohmander<sup>4</sup>, Martin Englund<sup>4</sup>, Xenofon Baraliakos<sup>5</sup>, Philip Conaghan<sup>6</sup>, Stéphane Genevay<sup>7</sup>, Clémence Palazzo<sup>2</sup>, David John Wilson<sup>8</sup>, Ross Wilkie<sup>9</sup>, Daniel Prieto-Alhambra<sup>8</sup>, Alison Kent<sup>8</sup>, Souzi Makri<sup>10</sup>, Victoria Navarro Compán<sup>11</sup>, Christelle Nguyen<sup>2</sup>, Maria Else Marie Bartels<sup>1</sup>, Cecilie Nordberg<sup>1</sup>, Antonietta D'Agostino<sup>2</sup>, Gilles Fournier<sup>1</sup>, G. L. Fournier<sup>12</sup>, on behalf of EULAR Task Force. <sup>1</sup>Copenhagen, Denmark; <sup>2</sup>Paris, France; <sup>3</sup>Barcelona Spain; <sup>4</sup>Lund, Sweden; <sup>5</sup>Ruhr, Germany; <sup>6</sup>Leeds, UK; <sup>7</sup>Genève Switzerland; <sup>8</sup>Oxford, UK; <sup>9</sup>Keele, UK; <sup>10</sup>Cyprus; <sup>11</sup>Madrid, Spain; <sup>12</sup>Rheumatology, Center for Rheumatology and Spine Diseases, Copenhagen (Frederiksberg), Denmark

**Background:** Low back pain is common and relates to a variety of overlapping pathologies. Imaging of the spine has a high priority in the assessment of patients with low back pain. However, studies have shown that clinicians vary widely in how frequently they obtain imaging tests for assessment of low back pain. Technical advances in the field of lumbar spine imaging are made at an increasingly high rate, and it seems likely that improved imaging procedures can indeed increase the understanding of low back pain and aid the diagnostic precision to the diagnostics of mechanical low back pain. The EULAR Task Force consists of radiologists, orthopaedic surgeons, rheumatologists, doctors in physical medicine and general medicine, physiotherapist and patients and the aim of the group was to develop evidence-based recommendations for the use of imaging modalities in low back pain with or without radiculopathy

Based on PICO established at the first meeting and using European League Against Rheumatism (EULAR) standardised operating procedures a systematic literature review was conducted to retrieve data on the role of imaging modalities including both conventional, contrast enhanced and dynamic approaches in radiography, ultrasound, MRI and CT. The recommendations will be based on the results of the systematic literature review and expert opinion and will be relevant for to all health care professionals who treat mechanical low back patients due to its multifactorial nature.

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THURSDAY, 14 JUNE 2018

**MRI**

SP0061

**HOW TO USE MRI IN THE DIAGNOSIS AND MANAGEMENT OF PSORIATIC ARTHRITIS + CLINICAL CASES**

M. Østergaard. Copenhagen Center for Arthritis Research, Copenhagen University Hospital Rigshospitalet, Glostrup, Denmark

Psoriatic arthritis (PsA) is an inflammatory joint disease characterised by presence of arthritis, enthesitis and/or spondylitis in patients with psoriasis. PsA presents a wide range of disease manifestations in various patterns. Imaging is an important part of management of PsA and is used for multiple reasons including establishing/confirming a diagnosis of inflammatory joint disease, determining the extent of disease, monitoring activity and damage, assessing therapeutic

efficacy, and identifying complications of disease or treatment, in the setting of clinical practice or clinical studies.

Magnetic resonance imaging (MRI) allows detailed assessment of all peripheral and axial joints and entheses involved in PsA and can visualise both inflammation and structural changes. This talk will provide an overview of the status and perspectives of MRI in diagnosis and management peripheral and axial PsA.

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SP0062

**HOW TO USE MRI IN THE DIAGNOSIS AND MANAGEMENT OF OSTEOARTHRITIS**

P.G. Conaghan. University of Leeds, Leeds, UK

The recent EULAR recommendations for the use of imaging in the clinical management of peripheral joint osteoarthritis (OA) provide an excellent, evidence-based, multi-disciplinary way background to this topic.

For diagnosis, the importance of a detailed history and thorough examination can never be underrated. Imaging should be used as only part of the diagnostic criteria for any rheumatic disease. One of the key EULAR recommendations is that imaging is often not required to make the diagnosis when patients present with a typical presentation of OA, with short-duration morning stiffness and increasing pain with prolonged weight bearing. The major benefit for imaging is in helping differential diagnosis in atypical presentations, and generally radiographs (weight-bearing for the knee) would be used first.

MRI brings its unique 3D strengths to diagnosis. MRI may play a role in the diagnosis of a meniscal tear, but this should only be considered where there is a clear history of locking or blocking to joint extension, rather than gelling (after prolonged immobility) or 'giving way', the latter being usually a sign of muscle weakness. When using MRI it is useful to remember that some degree of synovitis is common in osteoarthritis, and the presence of effusion or synovial hypertrophy does not automatically mean a primary inflammatory arthritis. Another common imaging feature is the bone marrow lesion (BML). This has similar juxta articular location in OA and rheumatoid arthritis, though the pathology is markedly different: BMLs represent osteitis in rheumatoid arthritis but areas of micro-fracture, necrosis and fibrosis in osteoarthritis. So clinical context is critical.

Routine imaging for OA follow up is usually not required unless there is an unexpected rapid progression of symptoms in which case a number of diagnoses should be considered. BMLs show areas of osteonecrosis, so a biopsy report suggesting this is should not be confused with avascular necrosis (AVN). AVN is a condition resulting from the disruption from the vascular supply to a particular bone, often the femoral head, leading to resorption of subchondral trabeculae and clinically related to prolonged corticoid use, alcohol excess or previous surgery. It's also been seen in connective tissue diseases. Patients may be under the age of 50, unlike the average age of rapidly progressive osteoarthritis (RPOA). RPOA is relatively uncommon and figures on its incidence vary widely. It is most commonly described again in the hip joint, and it may be the result of secondary osteonecrosis after subchondral fracture. This lesion is of importance because increased frequency of RPOA has been seen in trials of the anti-nerve growth factor monoclonal antibodies in the last decade, where there may be a link to concomitant NSAID use. Subchondral insufficiency fractures (SIF) are another cause of sudden onset pain, usually in the medial side of the knee and not associated with a previous history of trauma. There is a high prevalence of related meniscal tears. This tends to be seen in older females and is associated with the subchondral crescent sign indicating a fracture.

In terms of guiding treatment, at present we do not have evidence that the presence of particular pathologies such as BMLs or synovitis should indicate targeted therapies for those pathologies, though (appropriately) a lot of research is currently underway to see if these do represent legitimate targets for existing and novel therapies.

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THURSDAY, 14 JUNE 2018

**WIN and HOT session**

SP0063

**WIN SESSION: ABOUT DIAGNOSIS AND CLASSIFICATION OF SPONDYLOARTHRITIS**

*V. Navarro Compán. Rheumatology, University Hospital La Paz, IdPaz, Madrid, Spain, Madrid, Spain*

In patients with axial spondyloarthritis (axSpA) an early diagnosis is becoming progressively more relevant. Nowadays, several therapies have shown to be efficacious to control disease symptoms and signs and they are even more useful if administered in early stages of the disease. However, the aim of an early diagnosis is not easy to achieve. Similar to the majority of rheumatic diseases, axSpA is heterogeneous in its presentation, course, and outcome, and does not have a single clinical, laboratory, pathological, or radiological feature to serve as a gold standard in support of diagnosis. With the new therapies available, many research studies are focusing on how to make an early diagnosis of axSpA.

Additionally, some confusion remains about differences between classification and diagnosis of axSpA. In clinical practice, in the absence of diagnostic criteria, the classification criteria are often used to assist in the diagnostic process of a disease. Based on this, there is an ongoing debate about whether or not the current classification criteria should be revised. During this session, the new insights on diagnosis and classification in axSpA will be highlighted.

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SP0064

**HOT SESSION: RECENT ADVANCES IN THE MANAGEMENT OF SPONDYLOARTHRITIS**

*S. Ramiro<sup>1,2</sup>. <sup>1</sup>Rheumatology, Zuyderland Medical Center, Heerlen; <sup>2</sup>Rheumatology, Leiden University Medical Center, Leiden, Netherlands*

In the last years the treatment armamentarium for spondyloarthritis (SpA) has been expanded. In addition to non-steroidal anti-inflammatory drugs (NSAIDs) and tumour necrosis factor (TNF)-inhibitors, we nowadays count in daily clinical practice with IL-17-blockers for the treatment of patients with axial SpA. This increase in treatment options has led to an update of the ASAS-EULAR management recommendations, which will be discussed in this lecture, together with the evidence supporting them.

Currently, several studies on tapering to stop biologics in patients with axial SpA with inactive disease are being conducted and the first results available will be discussed. The path is being paved for a treat-to-target approach that is gaining shape in SpA. More evidence towards such an approach has been gathered throughout the last years and strategy trials are now ongoing.

Inhibition of structural progression remains a hot topic in SpA. Whether or not the current interventions we have can achieve such an outcome is not yet fully clear, and the challenges related to this will be discussed in this lecture. More data has come out to help us gain more insight into this complex relationship between disease activity and structural damage and the effect of therapy on it.

**Disclosure of Interest:** S. Ramiro Grant/research support from: MSD, Consultant for: Lilly, Novartis, AbbVie

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THURSDAY, 14 JUNE 2018

**To taper or not to taper in RA**

SP0065

**TO TAPER OR NOT TO TAPER NON BIOLOGICAL DMARDS IN RA REMISSION?**

*K.F. Baker, J.D. Isaacs. Musculoskeletal Research Group, Newcastle NIHR Biomedical Research Centre, Newcastle University and Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK*

Remission is now a realistic goal in rheumatoid arthritis (RA), with a third of patients achieving sustained remission through the use of conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) in modern treat-to-target strategies. Nevertheless, csDMARDs pose a risk of severe side-effects and require regular blood safety monitoring, which is both intrusive for patients and expensive for healthcare systems. This poses a therapeutic challenge – when is it appropriate to withdraw csDMARDs from patients with RA in sustained disease remission?

In the first part of this presentation we will use case histories to contrast the possible outcomes following withdrawal of csDMARDs from patients in sustained remission, highlighting the uncertainty facing patients and their clinicians in this scenario (presented by Dr Kenneth Baker). In the second section of this lecture (presented by Prof John Isaacs) we will discuss the criteria to consider when stopping csDMARDs, any potential risks to the strategy, and the potential to identify informative biomarkers to help guide management of the patient in remission.

**Disclosure of Interest:** None declared

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SP0066

**BIOLOGICAL DMARD CASE PRESENTATION**

*J. Kedra. Rheumatologie, Hôpital Pitié-Salpêtrière, Paris, France*

We present the case of a male patient, who developed in 2002 (at the age of 37) rheumatoid arthritis, at that time positive for RF and ACPA without erosions on X-rays. He was first treated with salazopyrine, stopped in 2003 because of residual disease activity and structural damage progression on X-rays (MTP 5 erosion, JSN on both carpal joints), then methotrexate, which was efficient but was finally stopped in 2004 for suspicion of MTX pulmonary toxicity (cough, short breath, with CT-scan abnormality). Leflunomide 20 mg/day was started with adequate response up to 2009, when loss of efficacy was recorded. Addition of adalimumab 40 mg every other week was decided, leading to sustained remission.

In 2011, he was on remission with this combination of treatments, and he stopped adalimumab abruptly on his own, resulting in a flare after 4 months (7 tender joints and 5 swollen joints). Adalimumab every other week was restarted, and remission was obtained a few weeks later.

In 2013, he remained on sustained remission, which led to his inclusion in a trial testing the progressive spacing of adalimumab. Every 6 months, the disease activity was assessed in consultation, and hands and feet X-rays were repeated every year: the patient remained on sustained remission according to DAS28, and there was no additional structural damage. Finally, in May 2017, DAS28 was at 1.71 with leflunomide 20 mg/day and adalimumab 40 mg every 2 months, so we were proposed to stop adalimumab.

When last seen, in November 2017, the patient was still on remission with leflunomide monotherapy.

**Disclosure of Interest:** None declared

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SP0067

**TO TAPER OR NOT TO TAPER BIOLOGICAL DMARD**

*B. Fautrel. Rheumatology, Sorbonne Université – Paris 6/Assistance publique – Hôpitaux de Paris, Paris, France*

Remission is more and more achievable in the course of rheumatoid arthritis (RA) or spondyloarthritis (SpA). Tapering strategies have been proposed to reduce the risk of overtreatment of patients with inactive disease. They have been tested in several observational or randomised controlled trials. On this basis, EULAR guidelines recommend to consider careful DMARD tapering in people with sustained remission.

The lecture will develop the potential benefits and risks of a tapering strategy for people affected by RA or SpA, in remission thanks to biologic agents. It will also highlight the residual unmet needs for the care of RA or SpA patients in remission.

**Disclosure of Interest:** None declared

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THURSDAY, 14 JUNE 2018

**Can we improve the care of gout?**

SP0068

**DECT IMAGING IN GOUT – READY FOR PRIME TIME?**

*N. Dalbeth. University of Auckland, Auckland, New Zealand*

Dual energy computed tomography (DECT) allows visualisation of urate crystal deposition in people with hyperuricaemia and gout. This technology is increasingly used in clinical practice for gout diagnosis, and can also guide treatment decisions in gout. The diagnostic properties of DECT will be described and compared with other advanced imaging methods such as ultrasonography. The potential for false positive results due to artefact, and false negative results in the case of small urate crystal deposits will be demonstrated. The role of DECT in



monitoring of treatment response, understanding mechanisms of disease, and facilitating patient understanding of the condition will be explored.

**Disclosure of Interest:** N. Dabeth Consultant for: Kowa, Horizon

**DOI:** 10.1136/annrheumdis-2018-eular.7767

#### SP0069 IMPROVING ADHERENCE IN GOUT THERAPY

**A. Abhishek.** *Academic Rheumatology, The University of Nottingham, Nottingham, UK*

Gout is the commonest inflammatory arthritis and affects between 2.5% and 3.9% of the adult population in the western world, with even higher prevalence estimates reported elsewhere. It is the only form of arthritis that can be "cured" with simple, inexpensive pharmacologic urate lowering treatment. Such medicines offer the potential for "cure" to most people with gout. However, despite this, gout patients have the lowest adherence to long-term pharmacologic treatment among people with different rheumatic diseases. The reasons for this are multifactorial but include misconceptions about the disease and its treatment among patients, physicians and the wider community.

The long-term management of gout is overseen by primary care physicians in most countries. Recent studies have explored alternate models of gout management and care, such as by community pharmacists and nurses. Such interventions have associated with a high uptake of urate lowering treatment and excellent persistence with treatment for upto five years.

This lecture will summarise the key barriers to the uptake of and adherence with urate lowering treatment. Recent randomised controlled trials and pilot studies examining the role of nurses and pharmacists in the management of gout using a treat-to-target approach will be discussed. New data about the mechanism by which such interventions may promote adherence with urate lowering treatment will be presented.

**Disclosure of Interest:** A. Abhishek Grant/research support from: AstraZeneca, Ironwood, OxfordImmuntech, Speakers bureau: Menarini

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#### SP0070 WHAT ARE GOUT GUIDELINES GOOD FOR ?

**T. Bardin.** *Rheumatology, hôpital Lariboisière, Paris, France*

Guidelines aim to help physicians to make decisions in daily practice for an individual patient with a given condition. Guidelines should therefore be clear, easily readable and understandable by all physicians involved in disease care. They should also be as simple and brief as possible to be easily memorised by physicians, and this is a real challenge when guidelines aim at a full coverage of gout management. Most importantly, they cannot be taken as strict rules with legal implications. The final decisions concerning an individual patient remain in the hands of the responsible physician.

Guideline methodology has improved over years but still varies across recently published works. Ad hoc committees regularly involve all specialities involved in the disease care, and in the case of gout, general practitioners, who take care of most gout patients are now included but their number vary. Patients are not always included, despite being the final target of guidelines. Conflicts of interest of participating physicians are taken into account to a varying extent. The guideline development process involves an evaluation of all evidence available at the time of writing. Treatment impact on outcome, and assessment of drug benefit ratios are unanimously considered as important in the elaboration of guidelines. Factors such as drug pricing, availability and local regulatory agency recommendations, for instance about reimbursement, also matter, as guidelines should be practical in order to help physicians, but are rarely taken into account in guidelines.

There are several levels of evidence and the best ones, such as randomised placebo-controlled trials (RCT) or RCT meta-analyses are not available in all aspects of gout management. A large part of the published guidelines on the management of gout therefore relies on expert opinion, which remains fragile and may vary from one group to the other.

The numerous guidelines presently available for gout management exhibit more or less striking differences, and this diversity does not help guidelines to reach their goal. In this regard, the major differences observed between the simple and short guidelines issued by the American College of Physicians and the usually more complicated recommendations from the Rheumatology societies are the most detrimental. Pursuing therapeutic research on gout management and improving guideline methodology appear as sine qua non conditions to reach consensus and improve gout management.

**Disclosure of Interest:** T. Bardin Consultant for: astraZeneca, ipsen menarini, novartis

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THURSDAY, 14 JUNE 2018

#### "Why does BMI matter?"

#### SP0071 IS OBESITY A RISK FOR RA?

**T. Uhlig.** *Rheumatology, Diakonhjemmet Hospital, Oslo, Norway*

According to the World Health Organisation (WHO) guidelines, individuals with a BMI of >30 kg/m<sup>2</sup> are classified as obese. Obesity is on a global scale rising in prevalence and is a recognised as a cause of chronic disability. As it threatens public health, obesity has attracted significant attention in the general population, especially due to its association with significant metabolic and cardiovascular complications.

In research on rheumatoid arthritis (RA) BMI is frequently reported as a demographic variable, but obesity has not been thoroughly studied. A link between obesity and RA is plausible, as in adipose tissue biologic mechanisms of inflammation exist and may be linked to chronic systemic inflammation.

Obesity has in performed studies been considered a controversial risk factor for RA. While several studies have examined the potential influence of obesity on the development of RA, the results have been inconsistent.

While a few studies from the United States have found no or only modest association between obesity and the risk of RA, some European studies found significant risks for an association between RA and obesity. The prevalence of obesity has risen sharply in recent years which may increase our ability to better study possible associations between obesity and RA in the future. Existing evidence may thus point toward a slightly increased of obesity for the risk of RA.

**Disclosure of Interest:** None declared

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#### SP0072 DOES OBESITY INFLUENCE RA OUTCOMES ?

**P.D. Kiely.** *Rheumatology, St Georges University Hospitals NHS Foundation Trust, London, UK*

The prevalence of obesity at diagnosis of rheumatoid arthritis (RA) has doubled in N. European and N. American populations from ~14% ten years ago to ~30% now. Several prospective studies of patients with early RA, treated with csDMARD regimens, have found an association of baseline obesity with worse short and long term outcomes including DAS28 remission, low DAS, HAQ, pain assessed by VAS and SF36 physical and mental components. The most recently published cohorts report O.R. of obese RA patients at baseline achieving DAS28 remission of 0.71 (0.55–0.93) at 2 years (versus non obese) and 0.53 (0.39–0.71) at 3 years (versus normal BMI). A variety of composite responses (DAS28, CDAI, SDAI, EULAR) to TNF inhibitors, whether given in fixed dose s.c. or weight dosed i.v. formulations are significantly worse in obese RA patients from trial and registry data. In contrast the DAS28 response to Rituximab in RA patients is not affected by BMI, and ACR responses in Abatacept and Tocilizumab treated RA patients, whilst numerically less good in obese patients, are not disadvantaged by fixed s.c. dosing in comparison to i.v. dosing adjusted by weight.

Obesity is an increasingly prevalent co-morbidity and is associated with worse outcomes, including DAS28 remission, HAQ and pain scores.

**Disclosure of Interest:** P. Kiely Speakers bureau: BMS, Pfizer, Roche

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THURSDAY, 14 JUNE 2018

#### Musculoskeletal pain; feeding the opioid epidemic

#### SP0073 OPIOID PRESCRIBING: WHAT'S THE PROBLEM?

**B.H. Smith<sup>1,2</sup>**, on behalf of Scottish Pain Research Community (SPaRC). <sup>1</sup>Pain Service, NHS Tayside; <sup>2</sup>Division of Population Health Sciences, University of Dundee, Dundee, UK

Opioids have been used for at least 7,000 years in the treatment of acute pain, to aid sleep and to promote euphoria. Their short-term benefits are well-recognised, but longer-term benefits are less well understood and associated harms well-known. For pain lasting beyond the acute period, the prescribed use of strong opioids was, until recently, mainly restricted to cancer and palliative care, when life expectancy is limited. More recently, however, we have seen rapidly increasing use of both strong and weak opioids for chronic non-malignant pain. This has particularly been in North America where an "opioid epidemic" is apparent, but similar patterns are emerging across the world, including Europe.

The commonest problems with long-term use of opioids include constipation, nausea and sedation. Other, perhaps more serious problems include hyperalgesia,

endocrine and immune dysfunction, mood disorders, tolerance, addiction and death. Our systematic review estimated an incidence of iatrogenic misuse or addiction of ~4% among all people prescribed an opioid. The other problem is with the lack of high quality evidence to support their effectiveness in the long-term relief of pain, as we will hear later. These concerns have prompted the International Association for the Study of Pain to issue a recent carefully-worded statement on the use of opioids in chronic pain, advising caution and close monitoring. This presentation will summarise these issues, and present evidence of the increasing use of opioids in recent years, focusing on Europe and particularly Scotland, where prescribing rates rose 65% in a 10 year period. I will present evidence of both good and potentially harmful prescribing, evidence that most prescribing is "appropriate" in that it is associated with severe chronic pain, and, despite this, that a very large proportion of people with chronic pain are not prescribed any opioid. Opioids may still have a role in chronic non-malignant pain, but the goals of their use need to be increased function and improved quality of life, and we need careful selection of patients and evaluation of outcomes.

**Disclosure of Interest:** B. Smith Grant/research support from: Scottish Government, Chief Scientist Office

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### SP0074 ARE ALL OPIOIDS THE SAME?

C. Stein. *Anesthesiology and Intensive Care Medicine, Charité – Freie Universität Berlin, Berlin, Germany*

Indiscriminate activation of opioid receptors provides pain relief but also severe central and intestinal side effects such as respiratory depression, sedation, addiction, nausea and constipation. Novel strategies to avoid adverse effects include the design of "biased agonists" and of environment-sensitive ligands. Exploiting pathological (rather than physiological) conformation dynamics of opioid receptor-ligand interactions might yield ligands without adverse actions. By computer simulations at low pH, a hallmark of injured tissue, we designed an agonist that, due to its low pKa, selectively activates peripheral mu-opioid receptors in injured/infamed tissue, i.e. at the source of pain generation. Unlike conventional opioids, this agonist showed pH-sensitive binding, G-protein subunit dissociation, and cAMP inhibition *in vitro*. It produced injury-restricted analgesia in rats with different types of inflammatory pain without exhibiting respiratory depression, sedation, constipation or addiction potential.

**Disclosure of Interest:** None declared

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### THURSDAY, 14 JUNE 2018

## What is lupus – syndrome or different entities?\_\_\_\_\_

### SP0075 AUTOANTIBODIES – NOT ALWAYS WHAT THEY SEEM

P.L. Meroni. *Immunorheumatology Research Laboratory, IRCCS Istituto Auxologico Italiano, 20095 Cusano Milanino, Milan, Italy*

Autoantibodies (autoAbs) are the most popular and used biomarkers for systemic rheumatic diseases (SRD). AutoAbs are becoming more and more important for: i) classification (including identification of disease subtypes), ii) diagnosis, iii) prognosis, iv) monitoring activity/organ-tissue damages as well as v) response to therapy. Moreover, autoAbs have been recently used as inclusion criteria in clinical trials and their presence is a formal requisite for prescribing some new drugs. The advent of new techniques, as well as the increasing number of autoimmune diagnostic laboratories, raise the issues of assay variability and reproducibility. In addition, the new techniques need to be validated versus the standard ones in order to determine and possibly improve the correct interpretation of their results. Harmonisation of the assays for autoAbs is becoming increasingly urgent and the availability of suitable reference material for calibration and quality control is emerging as a valuable tool for increasing assay reliability. Several international committees are joining their efforts in order to improve harmonisation and at the same time to avoid misdiagnosis, unnecessary repetition of tests and ultimately to optimise patient care and costs. On the other hand, the correct interpretation of the results depends on the technique used for detecting a given autoantibody and on its own characteristics (Meroni et al. *Nat Rev Rheumatol*. 10:35–43; 2014). The best example is the screening tests for antinuclear antibodies (ANA). Indirect immunofluorescence (IF) ANA testing has been suggested to be the golden

standard technique for ANA screening by the American College Rheumatology task force in 2010 (Meroni and Schur *Ann Rheum Dis*. 69:1420–2; 2010). While the sensitivity of IF ANA is high, its specificity is low as well as its post-test probability. So, the strength of a positive ANA should be evaluated in the clinical context to avoid mistakes (Mahler et al *J Immunol Res*. 2014:315179 2014). In addition, the isolated ANA positivity with specific staining pattern (i.e. dense fine speckled 79 – DFS70) does not support the diagnosis of a SARD and should not be taken into consideration for both classification and inclusion criteria (Mahler et al. *Autoimmun Rev*. 15:198–01; 2016). IF offered advantages in comparison with the screening solid phase assays (SPA) available at the moment of the ACR position paper; however the improvement of the solid phase assays in the last years changed the situation in a substantial way. Advantages and disadvantages of the two techniques have been reviewed and discussed by several groups and none of the two tests appears to satisfy completely our needs. However, the combination of IF and SPA that include the main nuclear (cytoplasmic) antigens diagnostic for SARD, has been reported to display higher specificity and post-test probability than the use of the single tests (Bossuyt et al *Ann Rheum Dis*. 73:e10; 2014). New tests that employ a panel of autoantigens specific for a given subset of SARD (e.g. lupus-like, scleroderma, myositis, anti-phospholipid syndrome) are now available or are going to be launched soon increasing their specificity/post-test probability in a significant manner. For example, the combination of IF and SPA for ANA screening could decrease the risk of "false positive or negative" results, while the use of one screening assay and the new ANA profiles in the context of a specific clinical setting might increase the diagnostic power. In conclusion, our strategy to autoAb testing is changing and we should take advantage of the combination of the new serological tools for better understanding the meaning of a given positive result. The combination of the new tests will be pivotal for addressing the need for a *Personalised Medicine* in rheumatology.

**Disclosure of Interest:** P. L. Meroni Speakers bureau: Pfizer, Abbvie, INOVA Diagnostics

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### THURSDAY, 14 JUNE 2018

## Genetics, epigenetics and disease: is it all in the genes?\_\_\_\_\_

### SP0076 GENOMIC DISSECTION OF IMMUNE-MEDIATED DISEASE: PROGNOSIS, VASCULITIS AND EOSINOPHILS

K.G. Smith. *Department of Medicine, University of Cambridge, Cambridge, UK*

Modern medicine has developed by classifying disease into defined diagnostic categories on clinical grounds. Even within a specific clinical diagnostic category, however, the features of a disease and the clinical course it takes can vary greatly between individuals. I will examine two examples of how application of genomic technologies to patient cohorts has provided insight into disease behaviour.

1. A distinct biology underlying immune-mediated disease prognosis?

This presentation will explore transcriptome data that defines a clinically useful prognostic biomarker in IBD, but also addresses the specific immunological mechanisms driving long-term outcome many immune-mediated diseases (including SLE and ANCA-associated vasculitis (AAV)), and the genetics that underpins this. Evidence will be presented suggesting that the biology underlying long-term disease outcome, or prognosis, is distinct from that driving specific diagnosis, and represent an under-investigated but clinically relevant aspect of disease pathogenesis.

2. Patient stratification in ANCA-associated vasculitis: GWAS highlights new disease entities.

AAV has been defined using pathological criteria into granulomatosis with polyangiitis (GPA, formerly Wegener's), microscopic polyangiitis (MPA) and eosinophilic granulomatosis with polyangiitis (EGPA, or Churg-Strauss syndrome). GWAS studies performed by the European Vasculitis Genetics Consortium have revealed 4 genetically distinct syndromes within AAV – which are aligned with autoantibody specificity, and better align with clinical phenotype, patient outcome and treatment response than the traditional clinically-defined syndromes. GWAS can therefore be a tool for enhancing patient stratification, and revealing new insights into disease susceptibility and perhaps therapy.

**Disclosure of Interest:** None declared

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THURSDAY, 14 JUNE 2018

## It's your move: promoting physical activity in people with RMD's

SP0077 NEW INSIGHTS INTO STRATEGIES TO EFFECTIVELY PROMOTE PHYSICAL ACTIVITY

K. Knittle. University of Helsinki, Helsinki, Finland

Physical activity is generally safe and beneficial for people with rheumatic diseases. Despite this, people with rheumatic diseases commonly engage in physical activity at levels which fall below common recommendations. Recent advances in behavioural science and health psychology offer healthcare professionals new tools and methods for promoting physical activity among people with rheumatic conditions. This lecture will present the most recent evidence on the interventions and behaviour change techniques that are most likely to increase motivation for physical activity, help individuals translate their motivation into action, and promote long-term maintenance of physical activity.

**Disclosure of Interest:** None declared

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SP0078 THE PATIENTS PERSPECTIVE ON PHYSICAL ACTIVITY AND WORK PARTICIPATION IN RMDs

K. Hamblly. School of Sport and Exercise Sciences, University of Kent, Medway, UK

Fatigue and musculoskeletal symptoms are shared features of many rheumatic and musculoskeletal diseases (RMDs) that often impact on physical activity and work participation. Physical activity is particularly important in the management and quality of life of people with RMDs. Participation in regular exercise can facilitate positive adaptations<sup>1</sup>, but people with RMDs tend to be less physically active than the general population.<sup>2,3</sup>

Two hundred and sixty-eight individuals with antiphospholipid syndrome (APS) participated in a cross-sectional online survey (85% female, mean age 47±11 years, 59% primary APS) on physical activity and exercise. It was found that 82% of participants wanted to increase the amount of physical activity and exercise that they do and 71% of participants were either motivated or very motivated to participate in physical activity and exercise. However, a range of barriers to increasing levels of physical activity and exercise were expressed as summarised in table 1.

**Abstract SP0078 – Table 1.** What is preventing you from increasing the amount of physical activity and exercise that you do?

<b>Energy Levels</b>	Exhaustion, tiredness, no energy after work, ADLs draining, 'payback', fatigue, mentally and physically exhausted, stressful job
<b>Symptoms</b>	Pain, aching, flare, muscle spasms, headaches, migraines, stiffness
<b>Strength, balance and mobility</b>	Bad falls, jelly legs, legs dead weight, balance, dizziness, giddiness, loss of control, mobility, light headed, lack of strength
<b>Fitness</b>	Level of fitness poor, lack of stamina/endurance, overweight, deconditioned
<b>Psychological</b>	Anxiety, depression, worry about side effects, stressful, scary, uncertain what can do, not sure if safe, no willpower, no motivation, no confidence, laziness, worry about negative effect on work
<b>Environment</b>	Resources, membership cost, travel costs
<b>Time</b>	Lack of time, work, carer, dependents, family demands, life too hectic, busy life, have to balance activities, do enough already

From a patient perspective, managing home and work priorities to get things done without compromising health is a tricky task! Self-management is an important skill for anyone with an RMD, but it is a challenging skill to learn as RMDs are often unpredictable and the art of listening to your body takes time and experience. Having the flexibility to adjust the cumulative load and stressors placed on your body and mind in response to your current health status is crucial. Exercise interventions need to be personalised and, importantly, be flexible so that they can be easily adjusted to reflect the health uncertainties and disruptions associated with many RMDs. These adjustments can be made to a variety of parameters including scheduling, type of exercise, volume, frequency, intensity or duration all of which need guidance for the patient. Flexibility can also be incorporated into work participation through changes to work tasks, location, start/finish times, breaks and working from home. In many countries, it is now a legal right to request flexible working and employers have legal obligations to provide reasonable adjustments for individuals with health conditions such as RMDs.

In our APS study, two-thirds of people said that they had not been given any advice regarding participation in physical activity and exercise and of those who

had received advice only 30% thought they had received adequate advice. The latest BMJ Best Practice for APS recommends in patient instructions "exercise regularly".<sup>(4)</sup> However, evidence from our study suggests that people are uncertain as what physical activity they can or should do and the specifics of exercise in terms of type, frequency, duration or intensity. People wanting to exercise looked for guidance from health care professionals as well as online, but found a lack of information regarding the types of exercise they should be doing and how to determine if they were doing too much or too strenuous exercise.

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**Disclosure of Interest:** None declared

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SP0079 MAJOR ACHIEVEMENTS AND FUTURE CHALLENGES IN PHYSICAL ACTIVITY

M.D. Iversen, on behalf of Physical activity working group. Department of Physical Therapy, Movement and Rehabilitation Sciences, Northeastern University, Bouve College of Health Sciences, Boston, USA

Research demonstrates that physical activity and exercise yield numerous health benefits for individuals with arthritis without adversely impacting joint health. Despite these data, individuals with arthritis remain less physically active than their healthy counterparts. Over the past decade, professional organisations and researchers have synthesised these data and incorporated information on the role of physical activity in management guidelines for clinicians and patients, and developed public health campaigns to motivate individuals to become more physically active. Corporations and researchers have also created and launched new software applications to measure, monitor, and promote physical activity for persons with arthritis that are easy to use and readily accessible. This presentation will highlight the major accomplishments related to the measurement of physical activity, promotion of knowledge and self-management skills to promote physical activity at the individual and population level and discuss future challenges regarding the development of effective population-based and individualised interventions to improve physical activity engagement among individuals with arthritis.

**Disclosure of Interest:** None declared

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THURSDAY, 14 JUNE 2018

## Data visualisation: tables and graphs for publication and presentation I

SP0080 DATA VISUALISATION: TABLES AND GRAPHS FOR PUBLICATION AND PRESENTATION

M. Boers. Epidemiology and Biostatistics; Amsterdam Rheumatology and immunology Center, VU University Medical Center, Amsterdam, Netherlands

This workshop (held both on Thursday and on Friday) is an introduction to the principles of good graph and table design as pioneered by Cleveland<sup>1</sup> and Tufte<sup>2</sup> and updated by Few<sup>3</sup> so that the participant can better answer the following questions: Which of the messages in my research results requires a graph or table?

Recognising how graphs improve on simple statistics and convey much more information. Knowing when a table is better, or when to keep the data in the body text.

How can I best convey the message?

Striving for clear vision by choice of graph, scaling, discrimination of data series, minimising non-data ink, avoiding chart junk. Striving for clear understanding through a balance between data and explanation. Using order, subheadings, formatting and rules to guide your reader through your table data.

Is my graph/table truthful?

Creating a direct proportion between graph and data quantities, avoiding forms prone to misinterpretation, labels to prevent ambiguity; keeping data in context,



avoiding more dimensions in the graph than in the data. Visualisation in Tables is further discussed in my recent article that is freely downloadable.<sup>4</sup>

This year's course will extend introductory material available via YouTube clips on the ARD website (ard.com)! Direct link: [https://www.youtube.com/playlist?list=PLXU14EQbU\\_V9JpmoAKsaCC0VjZbxzAN](https://www.youtube.com/playlist?list=PLXU14EQbU_V9JpmoAKsaCC0VjZbxzAN)

Note that you can also sign up for a **special lecture**,

"Theory of poster design and presentation" followed by a **poster tour** after the session, devoted to poster design!

Session Title: EULAR Projects – Challenging Projects in Education and Training

Date/Time: Saturday 16.06.2018 08:30–10:00

Room: Room: E106/E107

Followed by Poster Tour, sign up required!

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**Disclosure of Interest:** None declared

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THURSDAY, 14 JUNE 2018

## Challenges of patient organisations' in the 21 st century

### SP0081 PATIENT ORGANISATIONS' CHALLENGES IN A WORLD THAT IS GETTING OLDER – LESS – MORE COLOURFUL

*W. Koesters. Independent, Bergheim, Germany*

We have to see the demographic facts. The most important fact continues to be the birth rate, that is, how many children are born in a country. Because only when children are born, they can start their vocational training or go to college 16 to 18 years later and will be available as qualified workers a few years later. Only those people can in turn have children and bring them up in a way that is sustainable. Only those can become a member of a patient organisation, can be engaged voluntarily.

When you look at the 28 countries in the EU, you will notice that on the one hand the average birth rate is 1.55 (2013) while on the other hand there are still significant differences even within Europe. To keep a population stable, we need 2.08 children per woman aged 15 to 49 years.

The consequences are evident: in almost all European countries the population will shrink without further immigration from abroad or no longer grow on its own. In almost all countries more people will die than be born. This will also have repercussions on the ageing of society and naturally on the demand for products and services too, but also on the potential labour force. This will have consequences for patient organisations too.

At the same time the needs will change because in all countries people continue to get older and live longer. In their old age they will therefore require services for a longer period of time than previous generations: health, nursing care, culture, leisure, housing, support and assistance, travel.

The economy, all companies and professions, the public health, the organisation of daily life will have to face profound changes with long-term effects as well as the associated challenges.

This also against the background of medical doctors becoming older and scarcer as well.

**Disclosure of Interest:** None declared

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### SP0082 HOW A USER-LED ORGANISATION FOR RMDs ENABLES CITIZEN PARTICIPATION IN PORTUGAL

*E.F. Mateus. Liga Portuguesa Contra As Doenças Reumáticas, Lisbon, Portugal*

One of the first challenges faced by patients' organisations may be to become a user-led organisation. In Portugal, for instance, there is still a strong culture of paternalistic relationship between doctors and patients, which can be a barrier when it comes to recognising leadership skills in a patient. This means that

achieving a user-led model within the organisation depends on a) at least one person (patient or carer) feeling able to come forward and assume the leadership, b) this person's ability to gather more peers for the governing bodies, and c) that this team is accepted by the members of the organisation who are used to the paternalistic model. The important role of PARE and EULAR in providing tools and opportunities for developing skills for the empowerment of patients in advocacy, lobbying and as research partners, will be addressed in this lecture, since it can contribute to overcome some of the identified barriers.

Another challenge may be that the desirable concept of patients' organisations as user-led organisations should be duly recognised, for their acknowledgement as stakeholders in the decision-making processes, representing the people affected by those processes. In Portugal, although the National Health Plan for 2012–2016 and its extension to 2020 considers citizenship-based strategies, the predicted involvement of patients/citizens and their representatives, as a key strategic axis to maximise health gains, had been limited to a couple initiatives without significant patient or public. Several patient and citizen organisations have been advocating for increased and meaningful involvement in health decision-making. In 2015, a working group was established with representatives from 13 patient organisations (including the Portuguese League Against Rheumatic Diseases – LPCDR), one consumer organisation and a research centre. The main objective was to develop a Charter for Public Involvement in Health that could be widely accepted and recognised by health stakeholders. However, the group also felt the need to define a consensus on Eligibility Criteria for the Representation of People with or without Disease in Health Decision-Making in Portugal. The final version of the Charter was discussed with political and health stakeholders in a Forum held at the Portuguese parliament that count about 150 participants. The document will now be presented for a legislative procedure in Portugal and it has been accepted in the public consultation on information to be considered during the preparation of the draft guidelines on the effective implementation of the right to participate in public affairs by the Office of the United Nations High Commissioner for Human Rights (OHCHR). This lecture will also focus on lobbying with several tools, from EULAR EU Affairs, Stene competition, PARE conferences and engagement programme, to patients' organisations networks, as a process for a user-led organisation to be acknowledged as such.

The final challenge to be addressed will be the need to empower the citizens' involvement, through education, training and networking for patient advocacy, patients' involvement on health policy decision-making processes and on research. Several empowerment tools to help applying the «users'» arguments and getting involved in multiple areas, to improve access to care, social protection, sustainability, citizens' rights and patients' quality of life will be presented.

This lecture aims to address some strategies, sharing the Portuguese League Against Rheumatic Diseases (LPCDR) experience on engaging the «users», changing mindsets and tackling the citizen participation of people with Rheumatic and Musculoskeletal Diseases (RMDs) in Portugal.

**Disclosure of Interest:** None declared

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### SP0083 GAPS IN PATIENT TREATMENT – WHAT PATIENT ORGANISATIONS CAN DO?

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**Background:** Access to healthcare is a basic human right and one of the fundamental principles of European health systems, together with safety, quality, and equity. Unfortunately due to economic crisis and the cuts in healthcare budgets in many countries, inequalities in healthcare have been made worse. Furthermore the healthcare systems are facing increasing demands due to demographic change and the fact that the number of patients with chronic diseases is growing.

**Objectives:** To identify the inequalities in healthcare system and the degree to which the standards of care are affected.

To outline patients organisations challenges in such a demanding environment and their efforts to overcome the gaps in patients' healthcare.

**Methods:** Describe the gaps in patients' access to health care and the degree of their satisfaction from the offered health care services as reflected by the relative EPF survey conducted in 2016 among patients in European countries.

In these challenging conditions, patient organisations should help to fill the gaps and suggest specific solutions by raising awareness about the problems of the patients and the consequences of inadequate healthcare. At the same time they should develop collaborations with the scientific and academic community as well as with other patients' organisations.

**Conclusion:** Patients with chronic and long term conditions have valuable experience as a result of their interaction with the healthcare system and can identify important gaps and propose solutions in order to improve access to healthcare.

**Disclosure of Interest:** None declared

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THURSDAY, 14 JUNE 2018

## The EULAR Exercise recommendations for physical activity in people with inflammatory arthritis and osteoarthritis

SP0084 WHY PHYSICAL ACTIVITY EXERCISE WORKS

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Pain, inflammation, and decreased physical function are consequences of musculoskeletal disorders (MSDs), limiting patients' daily activities and restricting their participation in society. Physical activity and exercise have positive health effects for the circulatory, digestive, endocrine, excretory, immune, integumentary, muscular, nervous, respiratory and skeletal systems. Given the benefits of physical activity and exercise, physical activity is a primary component of symptom management for individuals with musculoskeletal disorders. This presentation will review the short- and long-term effects of physical activity and exercise in general and specifically, for individuals with musculoskeletal disorders, with a focus on the cardiovascular, immune and musculoskeletal systems.

**Disclosure of Interest:** None declared

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SP0085 THE EVIDENCE FOR PHYSICAL ACTIVITY IN INFLAMMATORY ARTHRITIS AND OSTEOARTHRITIS

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**Objective:** To evaluate the effectiveness of physical activity in people with rheumatoid arthritis, spondyloarthritis and osteoarthritis.

**Methods:** A Systematic review and meta-analysis were performed searching the databases Pubmed/Medline, CENTRAL, Embase, Web of Science, Emtree, PsycInfo up to April 2017. We included randomised controlled trials (RCTs) in adults ( $\geq 18$  years) with rheumatoid arthritis (RA), spondyloarthritis (SpA) and osteoarthritis (OA) investigating the effect of exercise or physical activity (PA) promotion on cardiovascular fitness, muscle strength, flexibility, neuromotor performance, and daily PA. Additionally we applied public health recommendations for PA based on the American College of Sports Medicine (ACSM) principles for effective interventions. Outcomes included assessments done directly after the intervention; If suitable, pooled in a meta-analysis using a random-effect model presented as standardised mean difference (SMD). Study registration in PROSPERO (CRD42017082131).

**Results:** The systematic review included 63 RCTs, of which 44 (3469 people with RA, SpA, OA) were included in the meta-analysis. Moderate effects were found of aerobic exercises and resistance training on cardiovascular fitness (SMD 0.6 (95% CI 0.38 to 0.81)) and muscle strength (SMD 0.54 (95% CI 0.35 to 0.72)) respectively, but no effect of combined exercises on flexibility (SMD 0.12 (95% CI -0.16 to 0.41)). PA promotion interventions produced a small increase in PA behaviour (SMD 0.21 (95% CI 0.03 to 0.38)).

**Conclusion:** Exercising and PA promotion according to public recommendations for PA were effective on cardiovascular fitness and muscle strength, with moderate, and thus clinically relevant effect sizes in people with SpA, RA and OA.

**Disclosure of Interest:** None declared

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SP0086 THE DEVELOPMENT AND PURPOSE OF THE EULAR RECOMMENDATIONS FOR PHYSICAL ACTIVITY IN PEOPLE WITH INFLAMMATORY ARTHRITIS AND OSTEOARTHRITIS

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**Objective:** Regular physical activity (PA) is increasingly promoted for people with rheumatic and musculoskeletal diseases as well as the general population. We evaluated if the public health recommendations for PA are applicable for people

with inflammatory arthritis (iA; Rheumatoid Arthritis and Spondyloarthritis) and osteoarthritis (OA) in order to develop evidence-based recommendations for advice and guidance on PA in clinical practice.

**Methods:** The EULAR standardised operating procedures for the development of recommendations were followed. A task force (including rheumatologists, other medical specialists and physicians, health professionals, patients and methodologists) from 16 countries met twice. In the first task force meeting, 13 research questions to support a systematic literature review (SLR) were identified and defined. In the second meeting, the SLR evidence was presented and discussed before the recommendations, research agenda and education agenda were formulated.

**Results:** The task force developed and agreed on four overarching principles and ten recommendations for PA in people with iA and OA. The mean level of agreement between the task force members ranged between 9.8 to 8.8. Given the evidence for its effectiveness, feasibility and safety, PA is advocated as an integral part of standard care throughout the course of these diseases. Finally, the task force agreed on a related research and education agenda.

**Conclusion:** Evidence and expert opinion inform these recommendations to provide guidance in the development, conduct and evaluation of PA interventions and promotion in patients with iA and OA. It is advised that these recommendations should be implemented considering individual needs and national health systems.

**Disclosure of Interest:** None declared

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SP0087 HOW TO DEAL WITH CARDIOVASCULAR RISK FACTORS FOR PHYSICAL ACTIVITY AND IMPLEMENT THE PA RECOMMENDATIONS IN THE RHEUMATOLOGIC PRACTICE?

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How to deal with cardiovascular risk factors for physical activity and implement the PA recommendations in the rheumatologic practice?

Nowadays, physical activity is increasingly advocated not only for the general population but also for patients with inflammatory arthritis as well as osteoarthritis. Generally, physical activity has favourable effects on cardiovascular risk factors. A recent systematic review revealed moderate, statistically significant improvements in blood pressure, LDL-cholesterol, and total cholesterol levels after about one year (additional) physical activity. Also the BMI improved and the effects appear to be a dose-related but not with all cardiovascular risk factors. Nevertheless, these favourable modest effects on cardiovascular risk factors could result in a clinically relevant reduction of cardiovascular events, provided that the physical activity remains enhanced albeit that thus far the evidence towards a reduction of cardiovascular events is not unequivocal.

It is important to realise that this review generally comprised persons without cardiovascular disease or risk factors for cardiovascular disease. It's well known that (very) high intensity exercise results in a small absolute increase of myocardial infarction in comparison to those who have less strenuous physical exertion. The risk is the highest in those who exercised less than one time per week.

Therefore, the American College of Sports Medicine (ACSM) developed an exercise preparticipation health screening process to mitigate these risks. Recommendations were developed for those 1) who should receive medical permission before starting a physical exercise program 2) with clinically significant disease(s) who may benefit from physical activity under medical supervision and 3) with medical conditions that excludes them from participation in physical activity programs. The health screening advices of the ASCM are based on an health screening logic model for aerobic exercise participation that takes the current level of physical activity, 2) presence of signs or symptoms and/or known cardiovascular disease/risk factors and 3) desired physical activity into account.

However, the ASCM guidelines do not apply for patients with inflammatory joint disorders such as rheumatoid arthritis (RA). RA is associated with increased overall mortality compared to the general population, with cardiovascular diseases as one of the main causes.

The optimisation of management of cardiovascular risk in RA patients is an important aim in the treatment. Active counselling is indispensable, including also attention to exercise, particularly in RA patients with a high CV risk, defined as a 10 year CV risk of 20% or higher. Physical exercise for these patients is necessary and challenging since professionals should take multiple factors into account, such as comorbid conditions related to CV risk (e.g. hypertension, diabetes mellitus and obesity). However, the effects of exercise therapy on CV risk in RA patients are unknown and the required intensity is also unknown.

Therefore, we are currently developing a tailor-made exercise therapy program for these complex patients that will evaluate the effects of exercise therapy on cardiorespiratory fitness and several secondary outcomes.

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**Disclosure of Interest:** None declared

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THURSDAY, 14 JUNE 2018

## Capillaroscopy I

### SP0088 THE IMPORTANCE TO DIFFERENTIATE NORMAL FROM ABNORMAL CAPILLAROSCOPIC IMAGES FOR AN EARLY DIAGNOSIS OF DISEASE

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Medical doctors frequently get patients with Raynaud's phenomenon (RP), a frequent symptom in the general population, referred. The importance of distinguishing normal capillaroscopic findings from (pathognomonic) abnormal (pathological) findings, lies in the fact that this distinction allows the differentiation between a primary RP (not connected to any connective tissue disease [CTD]) from a secondary RP due to systemic sclerosis (SSc) and diseases of the scleroderma spectrum.

What is normal in primary RP?

A normal capillaroscopic pattern, by qualitative assessment, is characterised by a homogeneous distribution of hairpin shaped capillaries as a "comb-like structure", with a density of between 9–14 capillaries per mm. Yet, there exists a wide intra- and inter-individual variety in a normal population which will be discussed in this session.

What is pathognomonic abnormal in patients with RP due to SSc?

Patients with the RP who have an underlying clinically recognisable (=with skin involvement) SSc show a very characteristic combination of capillary abnormalities in the nailfold, which can easily be assessed through qualitative assessment (=pattern recognition). Maricq et al. described last century, with the widefield technique (magnification X12–14) the scleroderma pattern. This pathognomonic combination contains the following: a striking widening of all three segments of the capillary loop (arterial, venous and intermediate), loss of capillaries and disorganisation of the nailfold capillary bed. Many branched "bushy" capillaries may also be observed.

In 2000, Cutolo et al. qualitatively assessed the nailfolds of an SSc cohort with patients fulfilling the American College of Rheumatology (ACR) criteria for SSc with the nailfold videocapillaroscopic (NVC) technique (magnification X200). According to the different proportions of the hallmark parameters of the scleroderma pattern (giants, capillary loss, haemorrhages and (neo) angiogenesis Cutolo et al. defined three patterns "early", "active" and "late".

The central role of capillaroscopy in distinction between a primary and secondary RP due to SSc is reflected by the fact that capillaroscopy is one of the new ACR/EULAR criteria for classifying a patient as having SSc.

Besides playing a paramount role in distinguishing a primary from secondary RP, capillaroscopy has an additional role. It can inform the rheumatologist dealing with a patient population with merely the RP and no other signs of a CTD, who will futurely develop SSc. This role is reflected by capillaroscopy playing a central role in the LeRoy and VEDOSS criteria for (very) early diagnosis of SSc.

What about capillaroscopic morphology in connective tissue diseases other than SSc?

No large scale prospective cohorts exist describing capillaroscopic morphology in connective tissue diseases other than SSc. Moreover, several morphologic

definitions exist across literature of different schools. The EULAR Study Group on microcirculation in Rheumatic diseases was set up in 2014 to tackle, in between others these working points.

#### SUGGESTED FURTHER READING:

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**Disclosure of Interest:** None declared

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### SP0089 HOW TO DISTINGUISH THE MAJOR CAPILLAROSCOPIC PATTERNS

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The most well-known pattern of capillaroscopic abnormality is the 'systemic sclerosis-pattern', characterised by dilated capillary loops, areas of avascularity, haemorrhages and distortion of the normal nailfold architecture. Cutolo and colleagues have described three patterns within this spectrum: 'early', 'active' and 'late', on the basis of numbers of giant capillaries and of microhaemorrhages, the extent of capillary loss and of disorganisation of the capillary architecture, and the presence of angiogenesis.<sup>1</sup> Systemic sclerosis-pattern abnormalities are also seen in patients with inflammatory muscle disease, especially in those with dermatomyositis, when areas of angiogenesis ('bushy' or 'ramified' capillaries), are very commonly seen.

Abnormalities have also been described in other diseases, but these are less specific. This lecture will illustrate the different patterns of abnormality with a focus on systemic sclerosis and inflammatory muscle disease. Capillaroscopic patterns which have been reported in systemic lupus erythematosus, antiphospholipid syndrome, and childhood connective tissue diseases will also be described.

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**Disclosure of Interest:** None declared

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THURSDAY, 14 JUNE 2018

## Ultrasound advanced I

### SP0090 US FOR PULLEY LESIONS – CLINICAL RELEVANCE

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In the human body the pulleys are represented as structures that change the path of a tendon as they pass over them. The pulleys are composed of fibrocartilage (finger pulleys), cartilage (trochlea of the eye), ligament (extensor retinaculum) or bone (lateral malleolus). The clinical relevance of the pulleys of the flexor digitorum tendons (FDT) of the hand is indisputable in that it affects the flexion and excursion efficiency of the FDT and can generate pain. This system is composed of the transverse carpal ligament, the palmar aponeurosis pulley, and the digital flexor pulley system. There is some controversy about the functional relevance of the injury of the different FDT pulleys including the palmar aponeurotic pulley.

Pulleys can be affected by different conditions including chondroid metaplasia, tenosynovial ganglions, traumatic or inflammatory lesions of the FDT sheet, sport practice or work activities. Changes in thickness have recently been identified in flexor pulleys in patients with psoriasis arthropathy with a history of dactylitis and have been related to the so-called Koebner response.

Musculoskeletal ultrasound allows the visualisation of these structures statically and dynamically while at the same time it is an instrument to increase the precision in steroid injection of the trigger finger when is needed

**Disclosure of Interest:** None declared

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**SP0091 US FOR PERIPHERAL NERVE ENTRAPMENTS + DEMO**

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Symptoms related to entrapment of the peripheral nerves of the upper and lower extremity are common in rheumatologic practice and are often misinterpreted as articular or non neurologic periarticular pathology. Owing to the variable trajectory and mobility of the peripheral nerves, high resolution musculoskeletal ultrasound (US) has many advantages over other imaging modalities including superior resolution, ability to perform a dynamic real-time examination, precise sonopalpation and comparison with the contralateral structures. Its availability, relative ease of application in experienced hands and tolerance argue for its use as the initial "intervention" when compared to electrophysiologic testing. Large, medium and many smaller nerves can be imaged directly (along with the musculoskeletal terrain through which they pass ) depending on the quality of the instrumentation, skill and anatomic knowledge of the sonographer. Even pathologic involvement of smallest "nonvisualized" small nerves may be deduced by secondary changes of the innervated musculature, the so-called "echo-myogram". Obviously a thorough knowledge of the peripheral neuroanatomy and musculoskeletal relationships along the nerve trajectory is the key to an enhanced and reliable evaluation. This presentation will focus on the principles of neuro-sonoanatomy of the major peripheral nerve of the extremities and the fundamentals of the peripheral nerve US examination will be demonstrated.

**Disclosure of Interest:** None declared

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**SP0092 US FOR SCORING SJÖGREN DISEASE**

S. Jousse-Joulin, on behalf of omeract task force. *rheumatology, cavale blanche hospital, brest, France*

Sjogren's syndrome (SS) is a chronic autoimmune inflammatory disorder of exocrine glands. Its diagnosis relies on solely a combination of clinical and laboratory findings. Recently, new imaging techniques as MRI or ultrasound, known to be less invasive than sialography have shown a good sensitivity and specificity to detect structural abnormalities in pSS. Ultrasonography of the salivary glands (SGUS) appears to be the most attractive imaging approach: it is an inexpensive commonly available noninvasive technique that does not cause complications and inconvenience to the patient, although the data are somewhat conflicting. A systematic literature review has highlighted the main keypoints to validate salivary glands ultrasonography has an outcome measure in particular, there are limited data describing a standardised scanning method and standardised definitions of US gland pathologies.<sup>1</sup> Until now, both parotid glands and submandibular glands were assessed using a scoring system first developed by de Vita et al.<sup>2</sup> later modified by other investigators. Five scoring systems are now published which are frequently modified by different operators<sup>3-6</sup> but their reliability were not always evaluated. In order to use SGUS in clinical routine, we need to have standardisation of the US procedure to assess SG and to be capable to have a simple and reliable score to rate structural damage of each. A SGUS OMERACT task force was created in 2016 and produce consensual US definitions of the 6 major salivary glands and a semi quantitative scoring. The intra and inter reliability of this scoring between international experts showed good inter reliability and excellent intra reliability. We will present to you the definitions and the new semi quantitative scoring with a live demo.

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**Disclosure of Interest:** None declared

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**THURSDAY, 14 JUNE 2018****Immune senescence and ageing****SP0093 RESETTING THE IMMUNE SYSTEM IN AUTOIMMUNITY**

E. Van Wijk. *Laboratory of Translational Immunology, University Medical Centre Utrecht, Utrecht, Netherlands*

Autologous hematopoietic stem cell transplantation (HSCT) is a last resort treatment for refractory autoimmune patients and the only therapy so far that can induce long-term drug-free remission in these patients. Understanding the mechanisms responsible for this regained immune tolerance may help to develop other, less aggressive immune-mediated interventions with a similar outcome. Although the underlying mechanisms are incompletely understood, extensive immune ablation followed by autologous stem cell infusion seems to be able to rewire a faulty immune system. It is so far unknown which cells need to be removed prior to autologous transplantation and which cells are important in controlling disease after transplantation. We have previously shown that transplantation restores immune tolerance by renewal and modulation of both the CD4 effector T cell (Teff) and FOXP3 Treg compartment in a proteoglycan induced arthritis (PGIA) mouse model. In the human setting we further looked into T cell renewal by TCR CDR3 b chain repertoire sequencing prior to and post HSCT of juvenile idiopathic arthritis and dermatomyositis patients. We found that TCR beta chain diversity of Treg was highly restricted prior to transplantation and that the TCR b chain diversity of Treg increased post-transplantation. The TCR beta chain diversity of the CD4 non-Treg compartment also expanded after aSCT, although not as strikingly as the Treg compartment, indicating that the Treg compartment is more affected. Interestingly, in patients these highly dominant T(reg) cell clones persist over time and (locally) expand with every relapse of disease. The question is now how HSCT or related therapies can efficiently target and stimulate T cell renewal in chronic autoimmune inflammation, with limited toxicity.

**Disclosure of Interest:** None declared

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**FRIDAY, 15 JUNE 2018****Special delivery: Intercellular communication****SP0094 NEW INSIGHTS INTO ANTIBODY-BASED THERAPIES AND DISEASE SUSCEPTIBILITIES REVEALED BY MICROSCOPY OF HUMAN NK CELLS**

D.M. Davis. *Manchester Collaborative Centre for Inflammation Research, University of Manchester, Manchester, UK*

**Background:** Natural Killer (NK) cells express the Fc receptor CD16 (FcγRIIIa), which can trigger antibody-dependant cellular cytotoxicity (ADCC) against opsonized cells. ADCC is clinically important as one of the mechanisms by which therapeutic antibodies work. The anti-CD20 mAb rituximab is, for example, widely used for targeting B cells in treatments of autoimmune disease and non-Hodgkin's lymphoma. Here, we set out to study individual NK cell-target cell interactions by microscopy to determine what happens as NK cells meet different target cells sequentially, some opsonised and some not.

In addition, genetic diversity in human NK cell receptors has been linked with resistance and susceptibility to many diseases, but underlying mechanisms remain unclear. The effect of this genetic diversity on the cell surface organisation and signalling of receptors is a major unknown. Thus, we set out to study the organisation and signalling of inhibitory Killer Ig-like receptors (KIR) encoded by different genes and alleles using super-resolution microscopy.

**Results:** We found that repeated activation via CD16 decreased the amount of perforin secreted. However, perforin secretion was restored upon subsequent activation via a different NK cell activating receptor, NKG2D. Repeated stimulation via NKG2D also decreased perforin secretion but this was not rescued by stimulation via CD16. These different outcomes of sequential stimulation could be accounted for by shedding of CD16 being triggered by cellular activation. Shedding of CD16 also increased NK cell motility and allowed for detachment of NK cells from target cells. In turn, this aided NK cell survival and boosted serial engagement of target cells.

In addition, we report that inhibitory NK cell receptors encoded by different genes and alleles organise differently at the surface of primary human NK cells. In particular, expression level has major effects on receptor organisation. KIR that are expressed at a low level assemble in smaller clusters than KIR that are highly expressed. Unexpectedly, upon receptor triggering, low-expressed receptors in smaller clusters generate more phosphorylated Crk than highly expressed receptors.



**Conclusions:** <sup>(1)</sup> Shedding of the Fc receptor CD16 has an unexpectedly complex impact on NK cell responses. Shedding this receptor renders NK cells less potent at CD16-mediated activation, as expected, but promotes the detachment from opsonized targets to aid sequential target cell surveillance. Thus, counter-intuitively, shedding of Fc receptor CD16 can positively impact immune responses.

<sup>(2)</sup> Genetic variation modulates the nanoscale organisation of inhibitory NK cell receptors, which in turn impacts receptor signalling. This may be important in how genetic variation impacts immune responses and disease susceptibilities.

**Disclosure of Interest:** None declared

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#### SP0095 INFLAMMATORY CYTOKINES AS KEY MESSENGERS OF THE IMMUNE SYSTEM

M.I. Koenders, *Experimental Rheumatology, Radboud university medical center, Nijmegen, Netherlands*

Intercellular communication is mediated by direct cell contact as well as via soluble factors like cytokines. Cytokines are signalling proteins that bind to a receptor on a recipient cell, thereby activating an intracellular signalling pathway. This in turn may affect various biological functions like activation, differentiation or proliferation of the cell.

In this lecture, the role of inflammatory cytokines as key messengers of the immune system will be discussed. Targeting of hallmark cytokines in rheumatic diseases, like TNF, IL-6, GM-CSF, and IL-17, has changed the therapeutic landscape, and novel pro-inflammatory cytokines are currently under investigation as therapeutic targets. Furthermore, anti-inflammatory cytokines may be applied as therapeutic agents.

Cytokines act on the innate and adaptive immune system, as well as on non-immune cells. How exactly do these key messengers control our immune system in health and disease?

To unravel the cytokine network that drives the dysregulated immune system in rheumatic diseases, findings from *in vitro* studies, animal experiments and clinical trials will be combined.

**Disclosure of Interest:** None declared

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FRIDAY, 15 JUNE 2018

### WIN and HOT session

#### SP0096 ADVANCES IN THE MANAGEMENT OF OSTEOPOROSIS

C. Roux, *Rhumatologie, Hôpital Cochin, Paris, France*

The number of fractures related to osteoporosis is expected to increase in the next few decades, because of the increasing number of frail elderly patients at high risk of falls and fractures. Guidelines are available worldwide for the screening of patients at high risk of fracture, and for appropriate treatment including non pharmacological treatments for falls prevention: A number of questions will be discussed during the session. Why should we treat? Because the burden of osteoporosis is related to fractures, and their consequences on morbidity, and even on mortality for the more severe ones. When should we treat? There is an immediate increase of sustaining a new fracture in the 2–3 years following a first one; this represents a unique window of opportunity for treatment. How should we treat? Treatments are effective in prevention of fracture, and re fracture, providing that we use the more effective treatment, with the appropriate sequences. How long should we treat? The treat to target strategy must be used in patients having a low bone mineral density, and obtaining a T score above –2 is a reachable target. A current challenge is the patients' view on side effects of the treatments; although they are very rare, their perception is very high. A number of qualitative studies sought to assess patients' fears and beliefs and provide wordings to clarify the fracture risk concept. The prevention of fragility fractures is now within our reach.

**Disclosure of Interest:** None declared

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#### SP0097 CHECK-POINT INHIBITORS: WHAT ARE THEY USED FOR, ABOUT SIDE-EFFECTS AND PREDICTION OF EFFICACY

E. Kapiteijn, *Medical Oncology, LUMC, Leiden, Netherlands*

The development of immune checkpoint inhibitors targeting cytotoxic T-lymphocyte antigen 4 (CTLA-4), programmed cell death-1 (PD-1) and programmed

death-ligand 1 (PD-L1) have significantly improved the treatment of a variety of metastasized cancers, such as melanoma, lung cancer, renal and bladder cancer. Immune checkpoint inhibitors enhance antitumor immunity by blocking negative regulators of T-cell function that exist both on immune cells and on tumour cells. Although these agents can lead to remarkable responses, their use can also be associated with unique immune-related adverse effects (irAEs).

Consensus guidelines regarding the treatment of the most common irAEs including rash, colitis, hepatitis, endocrinopathies, and pneumonitis have been established. The mainstay of irAE treatment consists of immunosuppression with corticosteroids or other immunosuppressant agents such as infliximab; most irAEs will resolve with appropriate management.

Nevertheless, a substantial proportion of patients treated with checkpoint inhibitors do not respond. Several markers have shown promising predictive value, including baseline and post-treatment changes in leucocyte counts, lactate dehydrogenase and C-reactive protein. To date, research on routinely available blood, biopsies and clinical markers has focused primarily on checkpoint inhibitors use in melanoma and lung cancer, but preliminary evidence is emerging for other cancer types.

**Disclosure of Interest:** None declared

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#### SP0098 HOT SESSION: IMMUNE RELATED ADVERSE EVENTS FROM CHECKPOINT INHIBITOR THERAPY

L. Calabrese, on behalf of IRaeS eular. *Rheumatology, Cleveland Clinic, - Cleveland, USA*

Advances in cancer immunotherapy have made it now one of the cornerstones of care for patients with malignancies. Much of these advances have come through the development of checkpoint inhibitors which target negative regulatory signals in the adaptive immune response leading to re-invigoration of cell mediated immunity which had become suppressed or exhausted within the tumoral environment. With such reinvigorated immune response a collateral effect has been the development of autoimmune and or autoinflammatory complications (known as immune related adverse events or irAEs) seen in virtually every organ system. Among these are rheumatic complications estimated to observe in 4%–7% of the exposed population and often requiring acute and chronic immunosuppression to adequately manage. Numerous rheumatic irAEs have been reported the most common of which is inflammatory arthritis as well as myositis, PMR, vasculitis and sicca and others. Rheumatologists are now increasingly seeing such patients as the proliferation of checkpoint therapy increases (three are estimated to be several hundred thousand patients on such therapy in the US with another 1 00 000 patients in varying clinical trial of cancer immunotherapeutics). irAEs in general have been posited to be the potential Achilles heel of cancer immunotherapy. Rheumatologist will be increasingly called upon to take key roles in the management of irAEs with a broad spectrum of immunosuppressive and targeted therapies.

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FRIDAY, 15 JUNE 2018

### Challenges in systemic lupus diagnosis

#### SP0099 A CASE OF PAINFUL DYSPNEA

M. Gatto, *Unit of Rheumatology, University of Padova, Padova, Italy*

A 20-year-old female patient was admitted to ER due to dyspnea and stinging chest and interscapular pain, associated with neck pain worsened by physical exercise.

She reported worsening of respiratory symptoms in the past ten days and concomitant onset of acrocyanosis. At physical examination she displayed tachycardia and tachypnea, no abnormalities at lung auscultation, with oxygen saturation 94% at pulse oxymeter. Arterial blood gas tests showed a decreased pO<sub>2</sub> and pCO<sub>2</sub>. Urgent blood examination showed low leucocyte count 2900/mm<sup>3</sup> and mild normocytic anaemia Hb 10.8 g/dl. Due to chest pain, dyspnea and concomitant gas findings, a CT scan was prompted in the suspicion of pulmonary embolism, yet no vascular abnormalities were shown, but a small rim of pleural fluid at the right base.

The patient was admitted to Internal medicine department where she underwent pulmonary function tests showing a restrictive respiratory pattern with decreased TLCO and but normal KCO. HRCT was performed ruling out interstitial lung disease. Elevation of right emidiaphragm was shown at AP imaging.



Upcoming blood and urine analysis showed increased serum creatinine with proteinuria 1 g/day and hematuria. Following interdisciplinary consultation immunologic investigations were performed showing elevated titres of ANA, anti-dsDNA and decreased complement levels.

The patient was diagnosed with SLE with shrinking lung and active renal involvement and was referred to Rheumatology Unit where treatment was initiated with prednisone 0.5 mg/kg/day and mycophenolate mofetil 2 g/day. Respiratory symptoms as well as pulmonary function tests improved within some days after initiation of steroid treatment.

After 12 months the patient displayed still abnormally restrictive respiratory pattern at pulmonary function tests, despite clinical improvement. She was also displaying proteinuria 0.8 g/day with active urinary sediment and rising anti-dsDNA antibodies. Thus, she underwent Rituximab 1 g 2 weeks apart with subsequent improvement of both renal and respiratory signs and symptoms. Improvement remained stable at 2 years.

**Disclosure of Interest:** None declared

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#### SP0100 NEUROPSYCHIATRIC LUPUS OR NOT?

A. Fanouriakis. *Rheumatology and Clinical Immunology, 4th Department of Internal Medicine, "Attikon" University Hospital, Athens, Greece*

A 30 year old woman with a 10 year history of SLE was admitted in the Emergency Department with severe headache, drowsiness and vertigo. Brain magnetic resonance imaging revealed an extensive ischaemic stroke in the cerebellum. During the month prior to the episode, the patient had not been feeling well, complaining for arthralgias, fatigue, hair-loss, low grade-fever and the progressively deteriorating headache.

Should this patient's ischaemic stroke be attributed to lupus? Moreover, if yes, does it represent a thrombotic or an inflammatory process?

The second patient, a 38 year old woman of Asian descent, was referred to our Unit due to refractory seizures and status epilepticus for the past two years. On initial presentation, she had fever, mild leukopenia, low C3 and C4 levels and positive ANA (titer 1:320). She had been previously treated by different neurologists, with a combination of antiepileptic drugs, with no success. Brain magnetic resonance imaging was repeatedly unremarkable and electroencephalogram revealed mild epileptiform changes.

Does this patient represent a case of *bona fide* neuropsychiatric lupus?

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FRIDAY, 15 JUNE 2018

### Understanding the language of basic research, epidemiology and health services articles

#### SP0101 UNDERSTANDING THE LANGUAGE OF EPIDEMIOLOGY ARTICLES

W.G. Dixon. *The University of Manchester, Manchester, UK*

'Clinical and Epidemiological Research' is one of two headings for original articles in the Annals of Rheumatic Disease. But what *is* epidemiological research? What do all those different types of bias mean? And what do all of those bizarre statistical terms mean? How can I make sense of the research, and how is it relevant to my practice? Answer: Attend the lecture and find out.

**Disclosure of Interest:** W. Dixon Consultant for: Google, Bayer

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#### SP0102 UNDERSTANDING THE LANGUAGE OF HEALTH SERVICES ARTICLES

L. Carmona. *IMusc, Madrid, Spain*

The only difference of Health services Research with other types of research is the study unit observed. This goes beyond individuals and it may likely refer to doctors, their clinics, or even countries. We still need to work on hypotheses, although some exploratory research can be done; and we always need to start with a research question. If you are unable to find a research question in an original article, remember: stop reading. We will review some of the top questions answered by health services research, such as performance of doctors and services, efficacy of complex interventions, and inequalities. In addition, we will review basic concepts, such as what is an indicator, very frequently used as outcome

measures, or what makes a best practice, as well as some special difficulties, such as multilevel (AKA hierarchical) models or instrumental variables. To end, we will review basic concepts in qualitative research, needed to understand the papers dealing with health services research.

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FRIDAY, 15 JUNE 2018

### Joint EULAR – ESSR session on: The role of MR imaging in rheumatic diseases and its clinical implications

#### SP0103 INDICATIONS AND CLINICAL IMPLICATIONS OF MR IMAGING IN RA

B. Ostendorf. *Rheumatology, Dept. of Rheumatology and Hiller-Institute for Experimental Rheumatology, Düsseldorf, Germany*

In clinical practice, rheumatologists most frequently use imaging techniques to explore bone and soft-tissue involvement in RA. MRI is the best noninvasive, observer-independent imaging modality technique that has advantages over clinical examination and conventional radiographs for assessing joint damage and soft tissue inflammation, which are common features even in the earliest stages of RA. MRI provides multiplanar images with a high degree of resolution without ionising radiation. Based on these characteristics, MRI identifies early signs of arthritis where other imaging modalities failed. Main indications for MRI in RA consequently are to determine joint involvement, differential diagnosis and early diagnosis of inflammation, such as synovial changes, changes in tendon sheaths and bursae, as well as bone marrow oedema (BME), not detected by clinical examination, BME even also not by ultrasound. The presence of BME has added benefits to modern diagnostic criteria, and anti-citrullinated peptide antibody positive patients have demonstrated higher osteitis scores. Additionally, MRI helps to assess and define prognosis and outcome, because synovitis and BME are risk factors for the progression of structural changes. Growing data on the validity of MRI in predicting and assessment of treatment response are available as well. Recent evidence has demonstrated that MRI inflammatory parameters are frequent findings in RA with clinical remission and low disease activity states, which has impact on treatment changes. MRI helps to identify at-risk individuals with arthralgia without clinical arthritis, furthermore these patients with defined RA and high risk for disease progression leading to therapy escalation and also may limit unnecessary treatment with potentially expensive biologic drugs. Studies that directly assess how MRI use in clinical care might even influence decision making, quality of care and cost effective delivery of that care. Clinical studies answering these questions of regular use of MRI are warranted.

**Disclosure of Interest:** None declared

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#### SP0104 INDICATIONS AND CLINICAL IMPLICATIONS OF MAGNETIC RESONANCE IMAGING IN SPONDYLOARTHRITIS

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Axial spondyloarthritis (axSpA) is a chronic inflammatory disease that affects the sacroiliac joints and the spine. Whereas early disease is characterised by inflammation, severe structural damage may occur later in the disease course.

Magnetic resonance imaging (MRI) can detect inflammatory lesions (bone marrow oedema (BME)/osteitis), and structural lesions (erosions, bone spurs, ankylosis and fat metaplasia).

In patients suspected for axial spondyloarthritis (axSpA) in clinical practice, MRI has a key role for early diagnosis of axial SpA, since MRI is by far the best available method for early detection of inflammation in the spine and sacroiliac joints. MRI is also more sensitive and accurate for assessment of structural sacroiliac changes than conventional radiography. Differential diagnoses, including anatomical variations, degenerative disease, osteitis condensans ilii, infections and others, should of course always be considered.

In patients with diagnosed axial SpA, MRI is the method of choice for sensitive objective monitoring of axial inflammation, and also peripheral inflammation and damage can be assessed. Whole-body MRI is a promising method, which may become important for simultaneous assessment of axial and peripheral disease manifestations in one examination. Furthermore, MRI can provide information which may help predict the response to therapy and the risk of subsequent progression of structural damage.

The present talk will describe the indications and implications of using MRI in spondyloarthritis in the diagnosis and management of SpA, taking a starting point in the "EULAR recommendations for the use of imaging in the diagnosis and management of spondyloarthritis in clinical practice"; Mandl et al, *Ann Rheum Dis* 2015 74:1327–1339), the "Recommendations of the ESSR Arthritis Subcommittee for the Use of Magnetic Resonance Imaging in Musculoskeletal Rheumatic Diseases"; Sudot-Szopińska et al, *Semin Musculoskelet Radiol* 2015 19:396–411) and the recent update from The Assessment in SpondyloArthritis International Society (ASAS) MRI working group; Lambert et al. *Ann Rheum Dis* 2016 75:1958–1963). However, selected data from important clinical studies will also be described.

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#### SP0105 MRI IN EARLY AND ESTABLISHED SPA: WHAT IS THE ADDED VALUE?

*I. Eshed. Diagnostic Imaging, Sheba Medical Center, Ramat Gan, Israel*

MRI of the sacroiliac joints (SIJ) and of the spine has revolutionised diagnosis of early spondyloarthritis (SpA).

With its high contrast resolution, it is able to detect inflammation of the SIJ in its early stage before structural damage occurs. The introduction of biological drugs from the has further emphasised the need for early diagnosis of sacroiliitis. Since the treatment is to be used in a narrow window of opportunity to reach disease control, MRI was rapidly embraced as a dominant diagnostic tool and at the same time included into the classification criteria for axSpA becoming the cornerstone of SpA diagnosis. In this presentation, the early and more established imaging characteristics of sacroiliitis will be discussed in context of other imaging modalities and potential differential diagnoses.

**Disclosure of Interest:** None declared

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FRIDAY, 15 JUNE 2018

### The stromal link to inflammation

#### SP0106 FIBROBLASTS: THEIR ROLES IN MATRIX AND VESSELS

*J. Distler. Department of Internal Medicine 3, University of Erlangen, Erlangen, Germany*

Persistent activation of fibroblasts is a common denominator of fibrotic diseases but mechanistically incompletely defined. In contrast to physiologic tissue repair responses, fibroblasts remain persistently active in fibrotic diseases and continue to release excessive amounts of extracellular matrix. We will discuss novel insights into the molecular mechanisms underlying the uncontrolled activation of fibroblasts in fibrotic diseases and potential implications of those findings for targeted antifibrotic therapies.

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FRIDAY, 15 JUNE 2018

### New approaches in measuring what matters to patients

#### SP0107 WHAT CAN BAYESIAN STATISTICS CONTRIBUTE TO MEASURING PATIENT PERSPECTIVES?

*V. Ritschl. Section for Outcomes Research, CMSIIS – Center for Medical Statistics, Informatics, and Intelligent Systems, Medical University of Vienna, Vienna, Austria*

Thomas Bayes (1701–1761) founded the Bayesian approach, published as "Essay Towards Solving a Problem in the Doctrine of Chances" in 1763 as a new philosophy in inferential statistics opposed to the classical, frequentist approach. Frequentists test whether a hypothesis is true or false with a certain probability. The Bayesian approach depends on conditional probability which takes prior

knowledge (a prior distribution of probabilities) into account. An example for the use of the Bayesian approach is a self-reported instrument that assesses function in rheumatic and musculoskeletal diseases. This instrument produces worse scores with higher age due to the increasing incidence of physical disability. The prior knowledge (higher age leading to a worse function score) should be taken into account when the scores of the instruments are interpreted.

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#### SP0108 NEW APPROACHES IN MEASURING WHAT MATTERS TO PATIENTS – DECISION AID TOOLS

*H. Bekker. Chair in Medical Decision Making, School of Medicine – University of Leeds, Leeds, UK*

**Purpose:** To explain what patient decision aids are, why they help patients engage more effectively with healthcare, and how their use enables health professionals to meet clinical guidance on delivering shared decision making about treatment choices.

People's healthcare decisions are emotionally and cognitively demanding, involving trade-offs between treatment options with negative consequences for themselves and their families. Health professionals are delivering increasingly complex care; patients live longer with co-morbidities and increased frailty, and new technologies lead to more treatments being offered. Decision science provides insight into how people make these decisions, and what can influence people's thinking encouraging them to make more or less reasoned choices.

Patient decision aids are resources developed with reference to decision science evidence on how to structure the health problem, present information about risks, benefits and consequences of options, elicit patient values and guide people to reach treatment choices that fit best in their lives (<http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD001431.pub5/full>). This talk provides an overview of the components within patient decision aids (<http://ipdas.ohri.ca/who.html>) known to support people make more reasoned decisions about their healthcare, using examples taken from patient decision aids developed and evaluated within the UK.

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FRIDAY, 15 JUNE 2018

### Innovative treatments for a better quality of life

#### SP0109 INVOLVEMENT OF A PATIENT ORGANISATION IN HEALTH TECHNOLOGY ASSESSMENT

*J. Clausen. Scientific Adviser, Deutsche Rheuma-Liga Bundesverband e.V., Bonn, Germany*

The term "Health Technology Assessment" (HTA) designates the systematic evaluation of therapies (drugs and non-drug interventions) and technologies for cost effectiveness, clinical effectiveness and safety to form the basis for evidence-based priority setting and policy decisions (reimbursement and coverage decisions). Usually, therapeutic or diagnostic interventions are subject to the assessment, but also complex programs (e.g. prophylactic screening programs) may be investigated. The involvement of patient organisations in Health Technology Assessments improves outcomes and offers additional insights. It guarantees that the perspective of the most important group – the patients as consumers – is adequately addressed.

A patient organisation may be involved in various ways in Health Technology Assessments: Patient organisations can identify gaps in healthcare coverage and initiate the generation of a respective Health Technology Assessment; they can provide additional registry data, complementing study data from randomised controlled trials for the Health Technology Assessment. The provision of information on patient-relevant outcomes and other patient-relevant aspects (e.g. mode of administration) is crucial to assess the benefit for patients of the therapy (or technology/program) under evaluation. Moreover, patient organisations may also be involved in the evaluation of the assessment report and in the execution of the results.

Generation of an HTA can be a time-consuming process and a very demanding one for patient organisations and the involved volunteers. Staff members of the patient organisation can be involved directly in the various tasks, or indirectly, supporting voluntary patients. If voluntary patients attend panel groups, most of them will need intensive support by their respective patient organisation depending on the complexity of the respective topic. Finding qualified volunteers, willing to

spend a substantial amount of their time and able to travel frequently, is another obstacle to overcome.

This presentation provides some examples of the involvement in Health Technology Assessments of the German Rheumatism League, Germany's largest patient organisation with about 3 00 000 members, and the essential prerequisites for the participation of patient organisations in that process.

**Disclosure of Interest:** None declared

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FRIDAY, 15 JUNE 2018

## EULAR Projects in investigative rheumatology

### SP0110 AUTOANTIBODY STANDARDISATION IN RHEUMATIC DISEASES. THE ROLE OF THE EUROPEAN CONSENSUS FINDING STUDY GROUP ON AUTOANTIBODIES IN RHEUMATIC DISEASES (ECFSG)

J. Rönneklid, on behalf of The European Consensus Finding Study Group on autoantibodies in rheumatic diseases (ECFSG). *Department of immunology, genetics and pathology, Uppsala University, Uppsala, Sweden*

The aim of the European Consensus Finding Study Group on autoantibodies in rheumatic diseases (ECFSG), a.k.a the EULAR autoantibody study group, is to achieve a common consensus in autoantibody diagnostics: a laboratory result should be the same, independent of the country or laboratory where the result is obtained. Since 1988, the ECFSG has yearly distributed unknown sera to European laboratories (presently 43) for evaluation in a clinical context. These sera are chosen to reveal differences between different laboratories. The results are discussed in conjunction to the European Workshop for Rheumatology Research (EWRR) every year. Use of reference materials helps to align test results by adopting internationally used measurement units, but reference materials are missing for many autoantibody specificities. Since 2014 an ECFSG focus has been on evaluating samples that might constitute new reference materials for companies producing autoantibody measurement assays, as well as for clinical laboratories. Hitherto investigated autoantibody specificities are provided in the table 1. In my talk I will present the work of ECFSG, including the characterisation of the samples that have constituted raw material for currently available reference materials. I will also tell about our first characterisation of a tentative new reagent sample, that thereafter was produced as reference material by the National Institute of Biological Standards and Control (NIBCS) in the UK. In November 2017 that reagent was endorsed by the World Health Organisation (WHO) to become the new international reference reagent for anti-double stranded DNA (anti-dsDNA) antibodies.

**Abstract SP0110 – Table 1.** Hitherto tested tentative or now existing reference reagents

2014	anti-dsDNA (now publicly available WHO standard, NIBSC 15/174)
2015	ACPA
2016	anti-PR3 (standard available from the EU Science Hub, ERM-DA483/IFCC)
2016	anti-MPO (standard available from the EU Science Hub, ERM-DA476/IFCC)
2016	IgG anti-b2GP1
2017	anti-GBM
2018	anti-DFS70

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### SP0111 HOW NEURO ENDOCRINE IMMUNOLOGY IMPACT RHEUMATIC DISEASES?

M. Cutolo, on behalf of EULAR Study Group on Neuroendocrine Immunology of Rheumatic Diseases (NEIRD). *Research Laboratory Division Rheumatology Dept Internal Medicine University of Genova Italy, Unicersity of Genova Italy, Genova, Italy*

The Neuro Endocrine Immune Network (NEI) is the most important communication-system in human body to maintain the health status. NEIRD evaluate the relationships between NEI and Rheumatic and Musculoskeletal Diseases (RMDs). The altered interaction between the nervous system, the immune/inflammatory cells and the endocrine system plays an important role in the pathophysiology of autoimmunity and chronic inflammation. The involvement of the adrenal steroid

hormones in the immune response is fundamental and follow a circadian rhythm (circadian rhythm studies obtained the Nobel Prize for Medicine in 2017). As Matter of fact, the nocturnal ability of the NEI system to mount an efficient immune and inflammatory response, with related clinical consequences, is matter of important chronotherapeutical approaches with exogenous steroids, in particular with glucocorticoids (GCs) (their discovery obtained the Nobel Prize in 1950 and still a pillar in the treatment of RMDs and not only). Other important steroid hormones involved in the NEI are the sex hormones (estrogens. E2 OH-metabolites are potent enhancers of cell proliferation) and the d-hormone (steroidal hormone structure of the final metabolite of Vitamin D). Clinical observations indicate a strong influence of the neuroendocrine system on immune function and *vice versa* in chronic inflammatory rheumatic diseases. The influence of hormones and neuronal pathways happens before and after the outbreak of the disease. Very recent data demonstrate the modulatory role of estrogens on epigenetic mechanisms (ie DNA methylation and gene upregulation). For example differentially expressed miRNA pathways linked to E2 in human endothelial cells through ER have been shown, and provide new insights by which oestrogen can modulate endothelial function. This point might be crucial in autoimmune diseases like systemic sclerosis (SSc) a disease prevalent in females and that start from damaged endothelium. We have started a large study on epigenetic and pregnancy on patients with RMDs such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). On the other hand, the disease process with an activated immune system influences several hormonal and neuronal pathways. In addition, the energy bottleneck leads to important disease sequelae such as sickness behaviour/fatigue/depressive symptoms, sleep disturbances, anorexia and malnutrition, bone loss, muscle wasting and cachectic obesity, insulin resistance with hyperinsulinemia (insulin-like growth factor-1 resistance), dyslipidemia, alterations of steroid hormone axes, disturbances of the hypothalamic-pituitary-gonadal (HPG) axis, elevated sympathetic tone, hypertension and volume overload, decreased parasympathetic tone, inflammation-related anaemia, and finally circadian (circannual) rhythms of symptoms. New therapeutic strategies should respect these findings because rheumatic patients die earlier due to the mentioned disease sequelae. It is suggested that disease sequelae must be treated more consequentially because they are inherent to chronic inflammatory systemic diseases (possible evolution for some of them in cancer). Therapeutic strategies in this field of NEIRD are slowly developing. Low-dose glucocorticoid therapy as supplementation of the "small adrenal engine", chronotherapy with glucocorticoids (night release) and vitamin D supplementation are the best examples of the successful utilisation of demonstrated concepts.

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### SP0112 MICROCIRCULATION IN RHEUMATIC DISEASES

V. Smith<sup>1,2</sup>, on behalf of the EULAR Study Group on Microcirculation in Rheumatic Diseases. <sup>1</sup>*Department of Internal Medicine, Ghent University;* <sup>2</sup>*Department of Rheumatology, Ghent University Hospital, Ghent, Belgium*

**Background:** The EULAR Study Group on Microcirculation in Rheumatic Diseases (SG MC/RD) aims to build an international network of expert centres to facilitate and exchange knowledge. It is a non-profit group and has no financial support. Both altered microvascular morphology and peripheral flow are the main focus of research.

**Objectives:** 1) To integrate different expertises to study the pathophysiology of disease processes. 2) To exchange knowledge and to facilitate standardisation concerning different techniques to assess the (micro)circulation such as nailfold capillaroscopy, laser doppler and laser speckle contrast analysis (LASCA). 3) To elaborate predictive indexes for disease progression and follow-up based on the integration of different tools and biomarkers. 4) To develop intervention protocols based upon an understanding of and targeting disease mechanisms (i.e. microvascular damage progression to fibrosis).

**Methods:** The EULAR SG MC/RD was accepted by the EULAR Executive committee in March 2014 and is being supervised by the EULAR Committee on Investigative Rheumatology, currently chaired by Prof. X. Mariette. Anno 2018 the number of members has risen to 79 (out of which 26 from 14 non-European countries). The EULAR study group meets half yearly (every EULAR/ACR) and



organises training courses every two years at Genova and supplies continuous training through the EULAR imaging library.

**Results:** The following projects resulted in publications: As standardisation of techniques to evaluate the microcirculation is one of the aims of the study group, a first activity was a multi-centre study to assess the reliability of simple capillaroscopic definitions to evaluate morphologies of single capillaries.<sup>1</sup> Optimisation of reliability of initial definitions has been obtained at the 7th EULAR course on capillaroscopy.<sup>2</sup> Secondly, the evaluation of interrater reliability of microcirculatory flow evaluation by LASCA was piloted by 2 of the founding members and has been published.<sup>3</sup> Thirdly, a cross-sectional, international SURvey on non-iNvaSive techniques to assess which tools are being used to evaluate the microcirculation in patients with Raynaud's phenomenon has been performed in between 471 eligible physicians.<sup>4</sup> A 4th publication resulted from a systematic review, analysing the role of capillaroscopy in systemic lupus erythematosus, based on standard interpretation of capillaroscopy according to the EULAR SG MC/RD.<sup>5</sup>

**Conclusions:** The relatively young EULAR SG MC/RD is thriving well, based on multi-centre joint forces to achieve standardisation of microcirculatory evaluation of rheumatic diseases as well as in achieving clinical as well as basic science research.<sup>6</sup>

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#### FRIDAY, 15 JUNE 2018

### Laboratory course – from the clinic to the lab and back

#### SP0113 NEW TRENDS IN BIOMARKERS IN INFLAMMATORY JOINT DISEASE

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This lecture provides an overview on new developments in biomarker research and standardisation in inflammatory joint diseases. The presentation includes an introduction of established and new biomarkers in serum and synovial fluid as well as methods for their detection. Furthermore, an overview on different modifications of auto-antigens (including citrullinated and carbamylated isoforms) and their role in immune response and pathogenesis of disease will be given. The diagnostic performance of new and established biomarkers will be discussed including antibodies against modified antigens also illustrated by difficult to diagnose cases. In this context, special attention will be attributed to the predictive value of biomarkers for diagnosis of disease and treatment response.

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#### FRIDAY, 15 JUNE 2018

### New assessments in clinical practice

#### SP0114 HOW TO PERFORM A QUICK AND RELIABLE PHYSICAL EXAMINATION IN RHEUMATOLOGY

M. Doherty. *Academic Rheumatology, University of Nottingham, Nottingham, UK*

The GALS (Gait, Arms, Legs, Spine) screen is a quick, reasonably sensitive way to detect common musculoskeletal (MSK) abnormalities as part of a wider medical assessment.<sup>1</sup> However, for someone with MSK complaints a detailed assessment is required to determine the diagnosis and impact of the condition on that person. The history is the key starting point. This needs to be holistic and individualised as the enquiry proceeds, since the impact of any condition is person-specific and influenced by many factors (e.g. psychosocial, illness perceptions, sleep, comorbidity etc.). A thorough history usually suggests the single most likely cause for the patient's problem(s) and should then guide the examination – an efficient

targeted “rapier” approach where the practitioner selects appropriate skills from a range of competencies according to specific history elements. This contrasts with a longer hypothesis-free “screen” where an identical set of procedures is undertaken in each patient.

This presentation covers key principles and considerations of assessment and illustrates how the history guides the subsequent “rapier” examination.<sup>2</sup> Examples include:

(1) in the *history*: determination of pain localisation and features associated with radiated pain; pain and stiffness characteristics that differentiate mechanical usage-related pain, inflammatory pain, acute crystal synovitis, destructive bone pain and neurogenic pain; non-specific symptoms of inflammation.

(2) in the *examination*: usual order of inspection at rest, inspection during movement, then palpation at rest and during movement of symptomatic regions; contrasting clinical findings that quickly differentiate joint and peri-articular problems; initial selection of the movement(s) that is affected first and most severely by arthritis – the tight pack position(s); detection of “stress pain” (pain worse in tight-pack but reduced/absent in loose-pack positions – the most sensitive sign of inflammation); examination for effusion, soft-tissue and firm swelling; use of resisted active movements and stress tests for peri-articular lesions; a targeted screen for asymptomatic disease prompted by the main diagnosis.

EULAR learning resources available at [http://www.eular.org/edu\\_training\\_dvd.cfm](http://www.eular.org/edu_training_dvd.cfm) include:<sup>1</sup> The “GALS” screen and<sup>2</sup> Principles of the musculoskeletal history and examination.

**Disclosure of Interest:** None declared

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#### SP0115 VALUE OF INFLAMMATORY BIOMARKERS IN CLINICAL DECISION MAKING

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Inflammation is known to play a major role in rheumatologic disorders. Inflammatory biomarkers can help clinicians diagnose rheumatic diseases and assess disease activity more accurately. These markers have been incorporated into classification criteria of several diseases to enable early diagnosis and timely initiation of treatment. Quantification of inflammation has become essential to tailor the treatment strategy, especially in patients with rheumatoid arthritis, polymyalgia rheumatica and vasculitides. Inflammation can be measured from different perspectives – the measures that quantify biomarkers participating in inflammation, surrogate markers of inflammation, and the by-products of the inflammation process.

Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels are among the most commonly used acute phase reactants in the detection and follow-up of rheumatologic disorders. These markers are not specific to trigger factors of inflammation, limiting their capacity to discriminate the cause for stimuli as well as the organs involved.

In the current presentation the advantages and limitations of new and established inflammatory biomarkers in clinical decision making will be discussed illustrated by case reports.

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#### SP0116 VALUE OF ULTRASOUND IN CLINICAL DECISION MAKING

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The use of ultrasound (US) has increased over the past 20 years for clinical decision making and for optimised patient care. The utility of US for correctly diagnosing the cause of musculoskeletal symptoms is known by many clinicians but little published data exist in this area. However, the value of US for diagnosing and handling treatment decisions especially in patients with rheumatoid arthritis (RA) has been well documented. US has been proven to be more sensitive than clinical joint evaluation.<sup>1,2</sup> This has resulted in the acknowledgement of US as an addition to the clinical joint evaluation in suspected RA patients for assessing a more elaborate joint involvement helping the clinician to correctly classify the patients according to the new RA classification criteria.<sup>3</sup> Likewise, in early undifferentiated inflammatory arthritis the use of US may assist in pinpointing those patients who will develop persistent inflammatory arthritis over time.<sup>4</sup> US may also impact diagnosis and treatment decisions. This has been shown both in situations with regional pain such as the painful foot in chronic inflammatory diseases and the possible need for corticosteroid injections but also in global disease activity assessment in RA patients where US provides additional disease activity information leading to altered treatment decisions as compared to regularly DAS28 assessment.<sup>5,6</sup> Also, in remission US may – by assessing subclinical inflammation



– detect those patients with the highest risk of flare.<sup>7</sup> US is a valuable part of future decision making in rheumatology.

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#### SP0117 ULTRASOUND SCANNING OF RA PATIENTS IN REMISSION

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The optimisation of the current therapeutic strategies for RA, with the establishment of early intensive treatment and with the availability of new drugs, has led to a dramatic change in the management of RA, and remission is the target of modern treatment in patients with RA.<sup>1,2</sup>

Remission is ideally characterised by the absence of clinically detectable disease activity, the absence of radiographic progression and the improvement of physical function.<sup>3</sup> However, in clinical practice it is frequently difficult to use a comprehensive definition of this condition and apply objective systems for assessing it. Then, subclinical disease activity may be present, even in patients who are in clinical remission, leading to joint damage progression<sup>4</sup> and disease flare.<sup>5</sup>

EULAR recommendations for the use of imaging in RA patients include ultrasound (US) as an assessment tool for inflammatory activity and remission, as it is able to detect joint inflammation and predict subsequent joint damage.<sup>6</sup> Recent studies have shown that US provides diagnostic and prognostic data in terms of risk of flare, disability and damage progression in RA.<sup>8</sup> Furthermore, in addition to joints, US allows the assessment also of periarticular structures, such as tendons, that have been demonstrated to be the site of inflammatory changes also in patients in clinical remission.<sup>7</sup>

Recently, 427 RA patients in clinical remission have been evaluated in a multicentre study which included the US assessment of wrist and hand tenosynovitis and synovitis by grey scale (GS) and power Doppler (PD).<sup>2</sup> Results of this study showed a high prevalence of tenosynovitis (52.5%–95% CI 0.48, 0.57 for GS and 22.7%–95% CI 0.19, 0.27 for PD) and synovitis (71.6%–95% CI 0.67, 0.76 for GS and 42%–95% CI 0.37, 0.47 for PD). Among clinical correlates, PD tenosynovitis associated with lower remission duration and morning stiffness while PD synovitis did not. Only PD tenosynovitis showed a significant association with the flare

questionnaire [OR 1.95 (95% CI 1.17, 3.26)]. No cross-sectional associations were found with the HAQ. The presence of radiographic erosions associated with GS and PD synovitis but not with tenosynovitis. This study demonstrated that US-detected tenosynovitis is a frequent finding in RA in clinical remission. Compared with intra-articular synovitis, active tenosynovitis was more associated with RA patients reporting unstable remission. Based on those results, US demonstrated to be a useful imaging modality for assessing tenosynovitis which may help in sub-setting RA patients in clinical remission.<sup>2</sup>

More recently, a multicentre longitudinal study in 361 consecutive patients with RA in clinical remission demonstrated that the conjunct presence of PD positive tenosynovitis and synovitis predicts flare in patients with RA in clinical remission.<sup>7</sup> US scanning of RA patients in remission has a crucial role in order to demonstrate active joint and tendon inflammation that are able to predict flare.

During this practical skills session at EULAR Congress 2018 the role of US in detecting subclinical inflammation at joint and tendon level will be discussed and practical demonstration on how to scan patients in remission will be performed.

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FRIDAY, 15 JUNE 2018

#### WIN and HOT session

#### SP0118 RECENT ADVANCES IN THE TREATMENT OF RHEUMATOID ARTHRITIS

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Modern management of rheumatoid arthritis (RA) is underpinned by the principle of establishing a clear treatment goal through the efficient strategic use of DMARDs in order to minimise adverse outcomes. With evolving ambitions and new targeted therapies, ongoing advances in the management of RA continue to be made: this HOT session will summarise our progress in the understanding and management across the RA disease continuum; including the state of at risk of RA status to early and later RA disease. In particular, the session will focus on studies that inform on (i) the ability to potentially abrogate progression from autoimmunity to development of RA disease (ii) currently identified strategies that offer the optimal opportunity for remission induction in ERA (iii) ability to drug taper and (iv) use of recently introduced synthetic and biologic targeted therapies. Finally, with co-morbidity outcomes including cardiovascular disease, another key focus in the contemporary management of RA, developments in improving this area of health concern will also be presented.

**Disclosure of Interest:** None declared

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FRIDAY, 15 JUNE 2018

## Advances in biologic therapy of small vessel vasculitis

### SP0119 THE EVOLVING ROLE OF MEPOLIZUMAB IN EGPA

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There is overwhelming evidence that eosinophiles play a key role in the pathogenesis of EGPA. IL-5 is the central cytokine for eosinophil maturation, eosinophil release from the bone marrow and eosinophil survival. Mepolizumab is an antibody neutralising IL-5, which proved efficient in the hyper-eosinophilic syndrome and eosinophilic asthma, amongst other conditions. Targeting this cytokine in EGPA therefore seemed plausible. Two small uncontrolled trials demonstrated the safety of mepolizumab in EGPA and indicated the potential for induction of remission, maintenance and steroid sparing. A randomised controlled trial (MIRRA) confirmed those findings and showed higher rates of accrued remission for mepolizumab when given as ad-on medication to conventional immunosuppressants and/or glucocorticoids. Steroid sparing properties were also confirmed. MIRRA and previous trials in different indications issued no major safety concerns. Based on this trial drug approval for EGPA might be feasible.

To date the major problems in the treatment of EGPA are 1) refractory disease 2) a high frequency of relapses and 3) the need for high glucocorticoid doses in many patients.

Mepolizumab could be used for induction of remission in addition to glucocorticoids. However, its not yet clear, which subgroup of patients might profit most. Especially patients with severe disease have not been investigated. For patients with refractors non-severe disease mepolizumab is a potential option. Mepolizumab also was efficient in preventing relapses and therefore may also be used for maintenance of remission, especially in patients suffering from prevalent relapses. Finally, patients with high need for glucocorticoids could profit from mepolizumab, particularly in case of steroid-sensitive comorbidities or steroid-induced complications.

**Disclosure of Interest:** F. Moosig Consultant for: Chugai, GSK  
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### SP0120 CURRENT CONTROVERSIES IN THE USE OF RITUXIMAB FOR INDUCTION AND MAINTENANCE OF AAV DISEASE

B. Terrier, on behalf of French Vasculitis Study Group. *Internal Medicine, Cochin Hospital, Paris, France*

Rituximab has now taken one of the first places in induction remission treatment of ANCA-associated vasculitides (AAVs) and is challenging cyclophosphamide. Rituximab is an anti-CD20 IgG1 mouse-human chimeric antibody that selectively depletes mature and memory B-cells.

Use of rituximab for induction

In AAVs, rituximab non-inferiority to cyclophosphamide as induction agent was clearly established. In the RAVE trial, which compared oral cyclophosphamide to rituximab as induction regimen, the remission rate at 6 months was 64% in the rituximab group and 53% in the cyclophosphamide group. Consequently, rituximab has revolutionised AAVs' standard-of-care and is now recommended as first-line therapy for many patients with granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA).

The RAVE trial prospectively compared two arms: induction with glucocorticoids combined with oral cyclophosphamide for 3–6 months followed by 12–15 months of azathioprine versus glucocorticoids and rituximab (375 mg/m<sup>2</sup>/week for 4 consecutive weeks) followed by placebo. At 12 and 18 months respectively, 48% and 39% of the rituximab–placebo recipients had sustained complete remission vs. 39% and 33% of the cyclophosphamide–azathioprine group. Those outcomes demonstrated that, after rituximab induction, azathioprine maintenance therapy is not useful. Nonetheless, both groups still had very high relapse rates, meaning that an effective maintenance regimen had not yet been found.

In contrast, these findings in induction phase could not be applied to AAVs forms excluded from the RAVE study, i.e. EGPA, vasculitis associated with anti-glomerular basement membrane antibodies (Goodpasture's syndrome), patients with alveolar haemorrhage requiring mechanical ventilation or those with rapidly progressive renal failure with creatinine exceeding 350 micromol/L. Also, studies are lacking to demonstrate that rituximab should be recommended as first-line therapy for patients who do not require cyclophosphamide for remission induction or patients with predominant granulomatous manifestations (granulomatous ear, nose and throat (ENT) lesion(s), isolated tracheal or bronchial stenosis, orbital tumour or pachymeningitis) that are life-and/or function-threatening.

Use of rituximab for maintenance

The idea to maintain remission with low-dose rituximab every 6 months for 18 months seemed reasonable than no intervention, as shown by MAINRITSAN trial results. In that prospective RCT, rituximab maintenance consisted of semestrial 500 mg infusions for 18 months. The first rituximab infusion was given 3–4 weeks after the end of cyclophosphamide induction therapy, followed by the second 2 weeks later and semestrial infusions thereafter. At the end of follow-up, 28 months post-randomization and 10 months after the last rituximab infusion, 5% of rituximab recipients vs. 28% of azathioprine-treated patients had relapsed. Prolonged follow-up of those patients showed that, at 60 months, although relapses had occurred in both groups, rituximab remained superior to azathioprine for sustaining remission. Although the results highlighted rituximab superiority in maintaining remission, it also became clear that relapses still occurred, frequently 18 to 24 months after the last rituximab infusion.

An answer to the optimal rituximab duration will be partially obtained with the MAINRITSAN 3 trial (ongoing), which is comparing, after randomization, four additional semestrial rituximab infusions (500 mg) to placebo, after patients had previously received rituximab during 18 months. It seems reasonable that, in the future, treatment duration will be adapted to prognostic factors and predictors of relapses.

Also, the impact of using higher dose of rituximab during maintenance will be addressed by the RITAZAREM trial (ongoing). This protocol evaluates rituximab infusions of 1 gram every 4 months for 20 months compared to oral azathioprine. Use of rituximab for EGPA

Data on rituximab's clinical benefits for eosinophilic granulomatosis with polyangiitis (EGPA) patients is currently restricted to low-evidence-based open-label studies and case reports. The main findings of these studies indicate a potential benefit in severe refractory/relapsing EGPA, especially in patients with positive ANCA. Two ongoing prospective studies in France are comparing rituximab to conventional immunosuppressants as induction (REOVAS trial) and maintenance phase (MAINRITSEG trial). It will help to define more precisely the indication of rituximab in EGPA patients and eventually highlight which patients would benefit from the drugs.

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FRIDAY, 15 JUNE 2018

## Tapering and flaring in PsA and SpA

### SP0121 TAPERING IN PSA – TO DO OR NOT TO DO?

L. Coates. *Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, UK*

This talk will discuss the current evidence regarding tapering or drug withdrawal in patients with psoriatic arthritis. With increasing numbers of patients achieving good outcomes such as remission, the issue of how long to continue treatment for has been raised. Given the cost of some of the newer therapies, this question also has significant cost effectiveness implications.

There is a limited amount of evidence but data from randomised and observational studies will be discussed as well as key research questions that remain outstanding.

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### SP0122 TAPERING IN AXIAL SPONDYLOARTHRITIS – TO DO OR NOT TO DO?

D. Poddubnyy. *Charité Universitätsmedizin Berlin, Berlin, Germany*

According to the current version of the ASAS-EULAR management recommendations for axial spondyloarthritis, tapering of a biological disease modifying anti-rheumatic drug (bDMARD) can be considered once a remission is achieved. Tapering is opposed to a complete discontinuation that is associated with a very high disease flare risk (70%–100%) in axial spondyloarthritis. The question of tapering in axial spondyloarthritis has been addressed in a number of small clinical trials: in the majority of the them, tapering (either dose reduction or increase of the injection/infusion interval) could be done without a disease flare. It is, however, not clear, whether the tapering has any beneficial effect for a patient (i.e., in terms of safety) in addition to a cost-saving effect. Further, a number of questions related to tapering still requires an evidence-based answer: a) what is the optimal time-point of the initiation of tapering (e.g., 3, 6 or 12 months after remission achievement)? b) what is the optimal tapering regimen? c) are there reliable predictors of sustained remission/disease flare during tapering? The question of a bDMARD tapering after remission achievement will be at least partially answered in ongoing

phase 4 trials with TNF blockers in non-radiographic axial spondyloarthritis. An appropriately designed and powered long-term trial is needed to investigate possible long-term benefits and risks of treatment tapering in axial spondyloarthritis.

**Disclosure of Interest:** None declared

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FRIDAY, 15 JUNE 2018

## Prevention of OA: yes we can!

SP0123

### WHY IS THE PREVALENCE OF KNEE OSTEOARTHRITIS INCREASING?

*D. Felson. Clinical Epidemiology Unit, Boston University School of Medicine, Boston, USA*

Invited speaker abstract submission

EULAR18-7734

WHY IS THE PREVALENCE OF KNEE OSTEOARTHRITIS INCREASING?

D. Felson

**I will give my lecture on:** Friday, 15 June 2018

**Disclosure of Interest:** None declared

Populations throughout the world are ageing and with ageing comes an increase in knee osteoarthritis. The prevalence of obesity is also rising and this further contributes to an increased risk of disease. Not surprisingly, the demand for knee replacements is rising quickly and is projected to increase further.

While the increase in osteoarthritis may be due in part to ageing and obesity of the population, there may be other causes. In a recent study, cadavers whose age and weight at the time of death were known were examined for evidence of knee osteoarthritis. It was found that, after adjustment for age and weight, knee osteoarthritis in our current postindustrial era was twice as common as knee osteoarthritis in the early industrial era. Reasons for this increase include changes in diet or in physical activity. They might also include changes in effects or severity of obesity. Understanding the increase in prevalence might provide new clues to osteoarthritis prevention.

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SP0124

### PHYSICAL ACTIVITY AND EXERCISE: OPPORTUNITIES AND CHALLENGES

*M. Englund. Clinical Epidemiology Unit, Orthopedics, Department of Clinical Sciences Lund, Lund University, Lund, Sweden*

Osteoarthritis (OA) is a steadily growing public health concern in particular as there is still a lack of curative therapeutic options in a biological sense. Thus, prevention of OA becomes an increasingly important topic.

Physical activity, and exercise are among the key modifiable risk factors associated with OA. Joints are built to be used, but overuse and joint injuries are also linked with incident OA. This presentation will provide some key opportunities with exercise to maintain joint health, but also the challenges when the window of opportunity is exceeded.

**Disclosure of Interest:** None declared

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FRIDAY, 15 JUNE 2018

## Big data for musculoskeletal research

SP0125

### HOW BIG DATA AND MACHINE LEARNING COULD CHANGE THE GAME

*S. Khalid. Nuffield Dept of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, UK*

With recent advances in the acquisition and digitisation of medical data, the use of routinely collected health data for research is on the rise. Routinely collected data comes with the promise of the 3 V's of "big data": volume, velocity, and variety. Recent recommendations by the UK National Institute for Health and Care Excellence and the Academy of Medical Sciences have therefore acknowledged the potential for data science methods to play an increasingly important role in health-care research.

Against this backdrop of growing data and increasing computational resources, the use of data science methods including machine learning is becoming popular for analysing large-scale medical datasets.

This talk provides a brief overview of machine learning methods for healthcare applications including an introduction to supervised and unsupervised learning, followed by real-world examples of data analysis using machine learning, such as (a) the development of prognostic models for clinical risk assessment, and (b) mining of electronic health records for detecting patterns and phenotypes within a population.

**Disclosure of Interest:** None declared

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SP0126

### BIG DATA FOR TREATMENT EFFECTIVENESS AND SAFETY

*L. Tomlinson. Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, London, UK*

While randomised clinical trials remain the gold-standard for examining drug-effects, there are limitations to the evidence they provide. For example, studies are usually too small or too short to detect rare and long-term adverse effects. This is particularly true for kidney-related outcomes where many trials were under-powered to detect outcomes of interest such as end-stage renal disease, too historic to collect data on newly-defined entities such as acute kidney injury or simply excluded patients with chronic kidney disease. In addition, disproportionate recruitment of Caucasian men in mid- to older-life limits the evidence base for understanding risk of adverse-effects in other population groups such as women, the elderly and people of non-Caucasian ethnicity. Determining these outcomes requires long-term surveillance of population databases, usually anonymised health care records, once a drug is in routine use.

In this talk I will discuss recent work from our group where we have used routinely collected renal function measurements from primary care to precisely examine kidney-related and other adverse effects. I will discuss some of the difficulties of this approach as well as the potential it offers to understand better the balance between risks and benefits of many drugs in common use.

**Disclosure of Interest:** None declared

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FRIDAY, 15 JUNE 2018

## From big data to personalised medicine in paediatric rheumatic diseases

SP0127

### FROM MENDELIOME TO PERSONALISED MEDICINE IN CHILDHOOD SLE

*A. Belot<sup>1,2</sup>, on behalf of Genial/Lumigene working group. <sup>1</sup>Pediatric Rheumatology Unit – National Reference Centre for Rheumatism and Autoimmune diseases – Raise, Chu Lyon; <sup>2</sup>U1111, INSERM, Lyon, France*

Pediatric-onset SLE is a rare condition where genetics traits are believed to play an important causal role. A few monogenic causes of SLE have been described mostly in familial forms, including complement deficiencies, so-called type I interferonopathies, and B cell-related defects. Genetic studies in mouse models and genome-wide associations studies in patients have also pointed to other genes potentially involved in juvenile SLE. However, large-scale sequencing analyses of paediatric SLE are lacking, and the overall contribution of genetic factors in disease onset is therefore unknown. Personalised medicine relies on the understanding of underlying mechanisms. Genetic discovery and functional characterization of the variants prefigure the precision medicine in complex diseases such as SLE.

We have designed a NGS panel comprising genes for which mutations are known lupus causing (KLC) (also reported as the Mendeliome) as well as prospective candidate genes, potentially lupus causing (PLC), and analysed 117 children who fulfilled ACR criteria for SLE from two large cohorts of pediatric-onset SLE in the UK and France. Genetic variants were identified and filtered to select rare (ExAC database frequency of <1% for homozygous variants and <0.01% for heterozygous variants) and predicted *in silico* as damaging by different algorithms.

We identified mutations in KLC genes for 8 patients. Variant segregation within families and functional analyses supported the causal role of these mutations. Other patients had monoallelic variants in recessive KLC genes, which may have contributed to disease onset and other patients displayed rare and pathogenic variants in PLC genes. This enrichment was specific to the lupus cohort compared to a control cohort of healthy patients.



This large-scale analysis led to the identification of monogenic causes of lupus in about 7% of analysed patients in an unselected paediatric population of *sLE*. 7/8 causes are related to an innate immune disorder with efferocytosis deficiency, emphasising the importance of apoptotic body clearance in the pathogenesis of lupus. Other variants in *KLC* or *PLC* genes may represent novel monogenic causes of lupus or could influence disease-onset by increasing the penetrance of more severe mutations. The treatment is still poorly adapted to the underlying mechanisms but progress in immunomonitoring together with the revolution in the field of genetics prompt clinician to set up targeted therapies considering genetic background and biomarkers.

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#### SP0128 FINDING THE NEEDLE IN THE HAYSTACK AND USING IT: GALECTIN-9 AS A BIOMARKER IN JUVENILE DERMATOMYOSITIS

*A. Van Royen-Kerkhof. Pediatric Immunology and Rheumatology, Wilhelmina children's Hospital of the University Medical Center Utrecht, Utrecht, Netherlands*

**Background:** Juvenile dermatomyositis (JDM) is a rare systemic immune-mediated disease involving skin and muscle. A high disease burden exists with risk of both under- and overtreatment due to the lack of reliable biomarkers.

**Methods:** A multiplex immunoassay was performed in a discovery cohort for plasma levels of 45 proteins related to inflammation in 25 well-defined JDM patients, determined by clinical activity and treatment.

Results were validated in two independent international external and internal validation cohorts (n=125).

In a longitudinal cohort (n=30), the performance of this biomarker over time was assessed with a median 2.8 years follow-up.

**Results:** In the discovery cohort we found a clustering of 10 mediators of which Galectin-9 and CXCL10 distinguished best between active disease and remission. Both biomarkers had a strong correlation with clinical parameters (Spearman *r* with Physician's global assessment (PGA)=0.75 for both). This was confirmed in the validation cohorts (Spearman *r*=0.7 with PGA, for both). In the longitudinal cohort galectin-9 and CXCL10 correlated with disease activity over time, and elevated levels could predict flares several months before clinical symptoms. Both cross-sectionally and longitudinally, galectin-9 and CXCL10 outperformed creatine kinase activity.

**Conclusion:** Galectin-9 and CXCL10 are robust biomarkers for disease activity in JDM. A short-term implementation into clinical practice is feasible and can facilitate individualised treatment.

**Disclosure of Interest:** None declared

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FRIDAY, 15 JUNE 2018

### Triple T: T cells, technologies and therapies

#### SP0129 STUDYING T CELL FUNCTION IN RA AND PSA

*L. Taams. Inflammation Biology, King's College London, London, UK*

Rheumatoid arthritis (RA) and spondyloarthritis (SpA) describe a group of inflammatory joint diseases affecting ~2% of the population. RA has strong genetic associations with *HLA-DR*, indicating a role for CD4 +T cells. CD4 +T cells are prominently present in the RA joint, where they can contribute to the inflammatory milieu. I will present recent data from our lab regarding the presence, regulation and function of different CD4 +T cell subsets that are present in the RA joint.

In contrast, SpA has strong genetic associations with *HLA-B/RUNX3* which imply a role for CD8 +T cells. Furthermore, genetic associations with *IL23R/TRAFF3IP2* and the clinical efficacy of IL-17 blockade in SpA, indicate a role for IL-17 in SpA. This provides a strong rationale to investigate the presence, phenotype and functional capacity of IL-17 +CD8+T cells in the joints of patients with SpA. I will present novel data regarding the presence, phenotype and potential function of IL-17 +CD8+T cells in the joints of patients with SpA. Collectively, our data indicate that IL-17 +CD8+T cells may be important contributors to the pathogenesis of SpA.

**Disclosure of Interest:** L. Taams Grant/research support from: GSK, UCB, Novo Nordisk A/S, Novartis

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#### SP0130 TOWARDS T CELL TOLERANCE IN RHEUMATOID ARTHRITIS

*R. Thomas. Diamantina Institute, University of Queensland, Brisbane, Australia*

Disease modifying strategies are available for treatment of rheumatoid arthritis (RA), and good response rates are achieved. However, limitations include toxicity, a response rate ceiling, cost and rationing of biologic therapies, inability to cure or permanently reverse RA pathology, and inability to prevent disease. Immunotherapies targeting checkpoint molecules are markedly changing the landscape of clinical oncology. In autoimmune diseases such as RA, dendritic cells represent an important target for antigen-specific immunotherapy for T cell tolerance. Antigen-specific strategies promise greater specificity and safety, without general immune suppression, and thus the potential for intervention in at-risk subjects before disease onset. In a proof-of-concept trial, delivery of autoantigenic peptides and autologous tolerogenic dendritic cells was safe and had immunomodulatory effects on T cells including reduction of effector T cells and a relative increase in regulatory T cells. We have developed and are trialling in RA patients, antigen-specific immunotherapy targeting dendritic cells *in situ* with liposomes encapsulating autoantigenic peptide and calcitriol with the aim of antigen-specific T cell tolerance. I will discuss the development of antigen-specific tolerance strategies and the parallel development of immune monitoring assays to determine T cell outcomes in clinical trials in RA.

**Disclosure of Interest:** R. Thomas Grant/research support from: Janssen Biotech Inc, Consultant for: Janssen Biotech Inc

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FRIDAY, 15 JUNE 2018

### Navigating the world of digital health

#### SP0131 ONLINE SOCIAL MEDIA PLATFORMS AND PUBLIC HEALTH INFORMATION: AN EXPLORATION INTO ARTHRITIS RELATED VIDEOS ON YOUTUBE IN 2017

*E. Heron. The University of Southampton, Southampton, UK*

**Background:** YouTube is one of the most used social media platforms from a desktop computer. YouTube provides a virtual platform that allows users to upload and view video content. Due to this functionality, YouTube is a valuable method for sharing and disseminating health information.

Patients with chronic conditions (including arthritis) are increasingly relying on online health information to help manage their symptoms, with 75% of patients living with chronic conditions reporting their healthcare decisions are influenced by information found online.

To date there have been no studies that have explored the information available for people searching for advice and support about arthritis on YouTube.

**Methods:** Patient and public involvement (PPI) representatives contributed to defining terms likely to be used by members of the public with arthritis searching for self-management strategies on YouTube. These included "joint pain", "knee pain", "hip pain", "hand pain" AND "helping" or "improving". From each of these search terms the top 10 videos sorted by view counts were chosen. Videos were included if the content was related to arthritis, in English and published in 2017. Videos were excluded if they were inappropriate or offensive, not related to humans or duplicates. The top 50 videos sorted by view count were included for analysis. This data set was systematically coded by the team lead (EH) and cross-checked by an additional team member (AC). Coded data were analysed using SPSS.

**Results:** Eighty videos were retrieved, 7 videos were irrelevant, 9 were duplicates and 11 were non-English language videos. Sixty-three videos were included for analysis. From the top fifty videos (sorted by view count), "Herbal Medicine" (n=14; 28%) was the most common category, followed by "Exercise and Stretching" (n=12; 24%). The most watched video relating to the self-management of arthritis was related to "Herbal Medicine" with a view count close to two million (n=1,930,905) within the four months since it had been posted online. Twenty five (69%) of the arthritis management related videos originated from the USA, with the UK producing only one video. Fifteen (30%) of the videos had been posted by self-reported health professionals. Nineteen (38%) of the videos were commercial. None of the videos produced links to research to back up their claims.

**Conclusion:** Sharing of health information on YouTube is unregulated. The most accessed videos include alternative approaches to self-management and are not posted by registered health care professionals (HCPs). Whilst a wide range of arthritis-related videos were retrieved, few were created by HCPs or reputable health care organisations. YouTube is a powerful tool for people with arthritis to



access and use health information. Current findings demonstrate scope for HCPs and established healthcare organisations to further utilise YouTube for the dissemination of quality-controlled, evidence-based information.

**Disclosure of Interest:** None declared

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#### SP0132 MEASURING DIGITAL HEALTH LITERACY, WHY AND HOW?

C. Drossaert. *Psychology Health and Technology, University of Twente, Enschede, Netherlands*

Digital health literacy or eHealth Literacy refers to a person's ability to search, select, appraise and apply online health information or appropriately use digital health applications. In this presentation I will address the issue of measurement of these skills. First, we will explore why it is important to measure digital health literacy and discuss the different aims of measuring. Second, we will address some of the currently available instruments, including the oldest and most used instrument, the eHealth Literacy Scale or EHEALS Norman & Skinner, 2006 and some more recent instruments, including the eHealth Literacy Questionnaire, eHLQ Kayser et al. 2018 and the Digital Health Literacy Instrument, DHLI. Van der Vaart & Drossaert, 2017. Of each instrument, I will briefly discuss its underlying theory, some empirical findings, and its strengths and weaknesses. I will conclude with discussing some general challenges in measuring digital health literacy and directions for future research.

**Disclosure of Interest:** None declared

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#### SP0133 PATIENT EXPERIENCES FROM A TELE-HEALTH INTERVENTION ON DISEASE ACTIVITY IN RA: THE KEEN AND THE RELUCTANT PATIENT

L.R. Knudsen. *Department of Rheumatology, Aarhus University Hospital, Aarhus, Denmark*

**Background:** Recently, the effectiveness of monitoring disease activity in rheumatoid arthritis (RA) through a patient-reported outcome (PRO)-based tele-health follow-up strategy was compared to usual outpatient follow-up in the TeRA trial.<sup>1</sup> Telemedicine interventions require patients taking an active role in the disease course and treatment, and assuming more responsibility for monitoring and identifying signs and symptoms of disease activity.<sup>2-3</sup> The TeRA study examines the effectiveness of tele-health follow-up, but provides no insight into how patients experience this new approach to disease control.

**Objectives:** To explore the experiences of a PRO-based tele-health follow-up from the perspective of patients with RA and their experiences of increasing their active role and responsibility for disease control in particular.

**Methods:** Adopting a strategy of *interpretive description*,<sup>4</sup> we conducted individual, semi-structured interviews with 15 RA patients participating in the tele-health follow-up. Participants were selected purposively and consecutive from both genders and with various ages, disease durations and disease severity. The analysis was inductive with a constant comparative approach. First, we identified the main themes conveying the participants' experiences. Then, we constructed patient typologies to explain different perspectives on the tele-health follow-up.

**Results:** Five themes covered the participants' experiences: 'A flexible solution', 'Responsibility', 'Knowledge of RA', 'Communication and involvement' and 'Continuity'. Two typologies: 'the keen patient' and 'the reluctant patient' represented opposite perspectives and preferences regarding the core value of and approach to the tele-health follow-up.

**Conclusions:** The participants had positive perceptions of the PRO-based tele-health follow-up and saw it as a flexible and resource-saving solution that can reduce the burden of unnecessary interruptions in everyday life. They reported disadvantages related to missing face-to-face contact with health professionals.

The two typologies, 'the keen' and 'the reluctant' patient, help us understand the patients' different needs, wishes and abilities to take part in tele-health follow-up. Our findings reveal a need for more insight into how tele-health follow-up could be integrated in routine clinical practice, paying special attention to how reluctant patients may be supported.

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**Disclosure of Interest:** None declared

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FRIDAY, 15 JUNE 2018

## The rheumatologist-orthopaedic surgeon connexion in secondary fracture prevention

#### SP0134 THE CONNEXION BETWEEN FRACTURE CARE AND SECONDARY FRACTURE PREVENTION

K. Åkesson. *Dept Clinical Sciences Malmö, Lund University, Malmö, Sweden*

That fracture begets fracture, is today an acknowledged reality. Nevertheless, there are still gaps in fracture care and many are far from reaching the optimal treatment pathway. Ultimately, each fracture should be appropriately managed from the moment of the fracture, through the acute management of the patient and the fracture, through to rehabilitation and secondary prevention. Optimisation of every step leads to better post-fracture functioning and quality of life, in addition to a reduced risk of new fracture events where the next fracture often is more severe than the previous.

Fracture treatment has improved with newer implants (plates, screws, nails, joint replacements etc) being developed specifically for fragile bone. Standardising procedures and checklists have made a difference in reducing complications. In the field of anaesthesia advances allows for surgery in the increasingly frail older person with acceptable perioperative risks and outcome. Similarly, tailored medical management is essential also to improve rapid post-operative recovery. The team approach to prompt regaining of function and rehabilitation allows for faster return to the home.

However, it has been more difficult to systematically improve the final step – prevention to avoid recurrence. It is a fact that patients at the highest risk of fracture, those who have already sustained a fracture, have overwhelmingly remain unidentified for osteoporosis treatment and falls prevention. Exceptions exist and they have become examples of best practice; whereby integrated, systematic identification, investigation and intervention were key components for secondary prevention of fractures. The cornerstone in such programs is the fracture coordinator; hence, they are commonly referred to as a fracture liaison service (FLS). They are the link between the orthopaedics and the osteoporosis clinic. Through the development of a best practice framework, the key components for developing secondary fracture prevention programs are outlined and tool kits on how to get started are available. The fundamental component is however, acceptance by the system in order to incorporate prevention as a required part of fracture management.

The presentation will provide an overview of main advances as well as tips on how to move forward.

**Disclosure of Interest:** K. Åkesson Speakers bureau: Invited lectures for Amgen, Lilly, Radius, UCB

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#### SP0135 THE EULAR/EFORT RECOMMENDATIONS FOR PATIENTS WITH RECENT FRACTURE

W.F. Lems, on behalf of Working Group in EULAR EFORT recommendations in patients 50 years and over with a fracture. *Rheumatology, location VUmc, Amsterdam Rheumatology and immunology Center, Amsterdam, Netherlands*

The European League Against Rheumatism (EULAR) and the European Federation of National Associations of Orthopaedics and Traumatology (EFORT) have recognised the importance of optimal acute care for the patient 50 years and over with a recent fragility fracture and the prevention of subsequent fractures in high risk patients, which can be facilitated by close collaboration between orthopaedic surgeons and rheumatologists or other metabolic bone experts. Therefore, the aim was to establish for the first time collaborative recommendations for these patients.

According to the EULAR standard operating procedures for the elaboration and implementation of evidence-based recommendations, 8 rheumatologists from 8

countries and 10 orthopaedic surgeons from 10 countries met twice under the leadership of 2 conveners, a senior advisor, a clinical epidemiologist and 3 research fellows. After defining the content and procedures of the task force, 10 research questions were formulated, a comprehensive and systematic literature search was performed, and the results were presented to the entire committee. Subsequently, 10 recommendations were formulated based on evidence from the literature and after discussion and consensus building in the group.

The 10 recommendations will be discussed at the meeting; they included appropriate medical and surgical peri-operative care which requires, especially in the elderly, a multidisciplinary approach including orthogeriatric care. A coordinator should build up an organisation with systematic investigations for future fracture risk in all elderly patients with a recent fracture. High-risk patients should have appropriate non-pharmacological and pharmacological treatment to decrease the risk of subsequent fracture.

#### REFERENCE:

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**Disclosure of Interest:** W. F. Lems Consultant for: Amgen, Eli Lilly, Merck, Speakers bureau: Amgen, Eli Lilly, Merck

**DOI:** 10.1136/annrheumdis-2018-eular.7721

FRIDAY, 15 JUNE 2018

## What's new: Latest advances in treatment in JIA and osteoarthritis

### SP0136 LAST ADVANCES IN TREATMENT AND MANAGEMENT OF OSTEOARTHRITIS

*M. Kloppenburg. Rheumatology, Leiden University Medical Center, Leiden, Netherlands*

Osteoarthritis is a highly prevalent disease that results in a considerable disease burden for patients that suffer from this disease. Osteoarthritis can affect any joint, but is especially prevalent in the knee, hips and hands. The management for osteoarthritis includes non-pharmacological, pharmacological and surgical options. But options depend on the location of osteoarthritis, since not all treatment options are equally effective for patients with different osteoarthritis phenotypes. Fortunately, the number of high-quality clinical trials has increased in the last years and have increased our insight in potential effective treatments for osteoarthritis. Non-pharmacological options include information and education, exercise possibly in combination with weight reduction in overweight patients with knee osteoarthritis or assistive technology in patients with hand osteoarthritis. Regarding effective pain alleviating medication research, including systematic reviews, network analyses and randomised clinical trials, has increased our insight in the clinical efficacy of different medications. This has led to the discussion about the role of acetaminophen in osteoarthritis. New pain alleviating medication has been developed and is currently investigated. Furthermore, currently used medication is investigated for alternative ways of application. The ultimate requirement to have a disease modifying drug available is not yet met, but studies have been undertaken and are ongoing to investigate disease modifying potential.

**Disclosure of Interest:** None declared

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FRIDAY, 15 JUNE 2018

## Assessment and prevention of RMDs, what have we learned?

### SP0137 PREVENTION OF RMDs – WHAT HAVE WE LEARNED?

*S.M. Verstappen<sup>1,2</sup>. <sup>1</sup>NIHR Manchester Biomedical Research Centre, Central Manchester University Hospitals NHS Foundation Trust, Manchester Academic Health Science Centre; <sup>2</sup>Arthritis Research UK Centre for Epidemiology, Centre for Musculoskeletal Research, Division of Musculoskeletal and Dermatological Sciences, The University of Manchester, Manchester, UK*

Rheumatic and Musculoskeletal Diseases (RMDs) cause the greatest burden of disability in Europe and is increasing. The WHO Europe Action Plan for the Prevention and Control of Non-communicable Diseases recently recognised this burden and recommends action to promote prevention and improve health in the

general population and those with musculoskeletal health. Targeted screening and prevention in individuals at high-risk of developing RMDs will only be successful if there is a good understanding of the underlying mechanisms of the disease and of possible genetic and environmental risk factors associated with the risk of developing RMDs. The main focus of this presentation is on the evidence of the association between modifiable lifestyle factors and the risk of developing RMDs and the effectiveness of drugs administered during the preclinical phase of RMDs.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.7783

### SP0138 WHY NOT ALL EFFECTIVE INTERVENTIONS ARE WORTHWHILE

*F. Guillemin. Université de Lorraine, APEMAC, Nancy, France*

Economic decisions in the health sector should be made to reach both efficiency and improvement of health in the most equitable way in the population. Comparative assessment of innovation with usual or current standard practice allows measuring the incremental benefit per individual. The comparison should bear both on effectiveness, ie health effect, and on costs of alternatives, considering appropriate stakeholders and payers. Moreover, according to diseases and treatment target, the time horizon should be relevant to its expected effect, from a few weeks for painkillers to a lifetime for disease modifying drugs in inflammatory arthritis, joint prosthesis in osteoarthritis, or prevention of osteoporosis.

Various scenarios can result from an economic analysis, with four possibilities for a new treatment or health care technology: more efficient at lower cost (optimal), less efficient at higher cost (worse issue), less efficient at lower cost (needing a decision to lose some effectiveness), or more efficient at higher cost – ie cost-effective – (needing to identify what the society is ready to pay off). This is done by calculating an incremental cost-effectiveness ratio, illustrating a marginal benefit per individual, at best using data from clinical trials. Therefore, not all effective interventions can be candidate for diffusion.

Because there is a need to make decisions before larger diffusion of the innovation, a set of methods are also available to anticipate its potential benefit, using a modelling approach. Sensitivity analyses are also conducted in varying conditions of application in reasonable range, using deterministic and stochastic methods. More recently, another perspective has been developed, ie the calculation of the net budgetary impact. This approach allows an extension of the costs to the targeted people in the whole population at a country level. It should take all indirect costs into account. Using these approaches, it is possible to observe that sometimes promising health technology sometimes need to be abandoned, given the too high cost to society for low additional benefit to individuals.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.7788

FRIDAY, 15 JUNE 2018

## High-end imaging: looking for the invisible

### SP0139 THE ROLE OF PHAGOCYTES AT THE INFLAMMATORY SITE

*S. Uderhardt, on behalf of Ronald N Germain. Laboratory of Systems Biology, National Institute of Allergy and Infectious Diseases, Bethesda, USA*

Inflammation is a highly conserved, multicellular response to infection or injury ensuring host defense and tissue integrity. Immune cell activation, however, can cause substantial collateral damage, often further amplifying the inflammatory response and significantly contributing to disease pathology (e.g. influenza, myocardial infarction). Hence, mechanisms are required not only to promote and resolve inflammation, but also to regulate the primary events that initiate this process in order to avoid unwanted and potentially harmful immune responses.

Using state-of-the-art intravital and static multi-parameter imaging techniques in mice, our lab seeks to understand the complex interactions and functions of different immune cells types in the execution and regulation of the inflammatory responses to sterile damages in peripheral tissues. With primary focus on the innate immune system, we're particularly interested in the dynamic interplay of embryonically-derived tissue macrophages and recruited neutrophils, which can prevent unwanted immune cell activation and thereby fine-tune the threshold for the onset of damaging inflammation.

This presentation will provide novel insights into the multi-layered regulation of the very initial steps in an inflammatory response to tissue damage, and will further discuss the differential roles of different populations of phagocytes at sites of inflammation.

This research was supported by the Intramural Research Program of the NIAID.

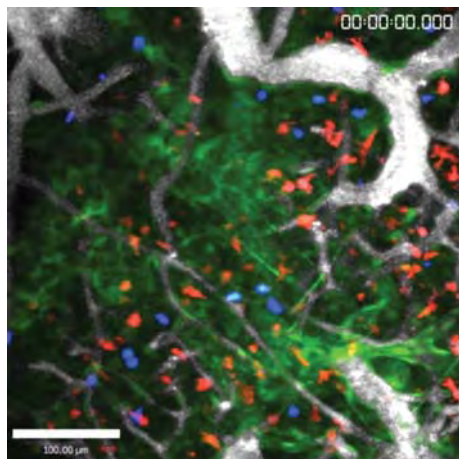
**Disclosure of Interest:** None declared

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#### SP0140 IMAGING THE ARTHRITIC JOINT

**J. Brewer.** *Institute of Infection, Immunity and Inflammation, University of Glasgow, Glasgow, UK*

Advanced imaging approaches such as multiphoton laser scanning microscopy (MPLSM) enable the real-time visualisation of cellular behaviour throughout the development of immune responses *in vivo*. These techniques have brought new insights into the spatial and temporal organisation of the immune system, for example the T cell/Dendritic cell interactions in the lymph node during the decision to induce immunological priming versus immunological tolerance. We believe that understanding cellular interactions in the joint will similarly transform our understanding of the importance of time and tissue specific regulation of the immune system in homeostasis and in diseases such as Rheumatoid Arthritis. Furthermore, using cell fate mapping, we have integrated imaging data in different cellular locations with transcriptional analysis to reveal the underlying molecular basis of these interactions. We propose that the key T cell/DC interactions controlling the development of immune responses and their molecular basis are influenced by the distinct anatomical and temporal context in which they take place, providing targets for therapeutic intervention as well as indicating biomarkers to report immune function.



Abstract SP0140 – Figure 1

**Disclosure of Interest:** None declared

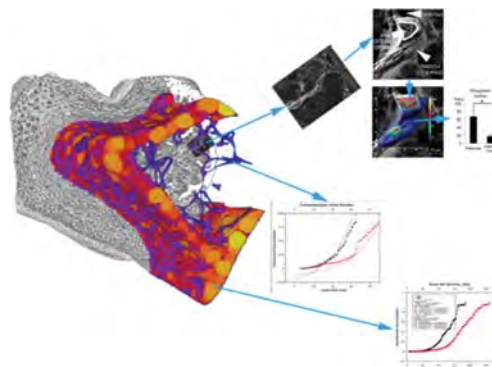
**DOI:** 10.1136/annrheumdis-2018-eular.7787

#### SP0141 IMPROVING THE STUDY OF BONE DISEASES BY CORRELATIVE ELECTRON-, ION- AND X-RAY MICROSCOPY INCLUDING THEIR ANALYTICAL TECHNIQUES

**S.H. Christiansen,** on behalf of S.H. Christiansen, L. Kling, G. Sarau, R. Keding, L. Pillatsch, J. Michler, P. Milovanovic, B. Busse, M. Herrmann, G. Schett. *Helmholtz Zentrum Berlin für Materialien und Energie, 14109 Berlin, Germany*

In the last decades a lot of knowledge was gathered on the structure and composition of bone. Cutting-edge correlative high-resolution microscopy and spectroscopy permits reaching the next level of understanding: Correlative workflows starting from X-ray microscopy volume analysis with voxel sizes of <1 μm, over large scale scanning electron data acquisition, to dual beam microscope analysis (focused electron- and ion beam) permit the scale bridging investigation of bone architectures and thus merging the “big picture” and the underlying ultrastructure with statistical significance. In combination with additional analytical add-ons, physical properties such as optical, mechanical, compositional, structural etc. deliver a highly detailed correlative dataset of bone.

The present paper utilises the comprehensive data acquisition to study bone degradation as it occurs in diseases such as osteoporosis and inflammatory osteoarthritis in mouse models.



Abstract SP0141 – Figure 1

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.7872

SATURDAY, 16 JUNE 2018

### WIN and HOT Lancet session

#### SP0142 WHAT CAN NEW INSIGHTS IN THE PATHOGENESIS OF PSORIATIC ARTHRITIS TELL US?

**D. Veale**<sup>1,2</sup>. <sup>1</sup>University College Dublin; <sup>2</sup>St. Vincent's Hospital, Dublin, Ireland

Psoriatic arthritis is a chronic immune-mediated inflammatory arthropathy, of unknown cause that presents with low grade inflammation of the skin, joints and/or entheses including the axial skeleton. Psoriatic arthritis is associated with increased mortality from cardiovascular disease. Diagnosis is primarily according to clinical phenotype due to the diverse clinical features. Increased understanding of the pathogenesis has led to specific new therapeutic agents and treatment strategies that prevent disease progression and improve quality of life, however 40% or more subjects show partial response or fail to respond. Despite this several unmet needs remain. There are no validated biomarkers for diagnosis, prediction of therapeutic response or remission, therefore it remains difficult to accurately assess disease activity, predict which subjects will respond to a specific therapy, and identify those in remission. This review will address specific recent advances in translational research that inform the pathogenesis of psoriatic arthritis.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.7769

SATURDAY, 16 JUNE 2018

### The GI tract in systemic sclerosis – is there light at both ends?

#### SP0143 ARMFUL HIDDEN TELANGIECTASIA

**C. Frantz.** *Rheumatology A, Cochin Hospital, Paris Descartes University, Paris, France*

Patients with systemic sclerosis (SSc) develop a broad spectrum of vascular manifestations including the almost universal Raynaud's phenomenon, commonly digital ulceration and more rarely critical digital ischaemia. In parallel, within this very heterogeneous disease, some patients will develop vascular related organ damages leading to heart or kidney failure. In addition, SSc patients commonly exhibit telangiectasia that are visible macular, dilated superficial blood vessels. They can develop near the surface of the skin or the mucous membranes. Cutaneous telangiectasia are now included in the classification criteria and may be a marker of more aggressive vascular phenotype. Furthermore, telangiectasia can occur in the gut and promote the development of more structured damages like vascular ectasias and sometimes the very specific gastric antral vascular ectasia. All these vascular lesions induce severe and recurrent chronic iron-deficiency anaemia that can require specific local treatments to stop the bleeding. They also occur in subsets of SSc patients at risk of other SSc complications that will be highlighted in the clinical cases to be presented.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.7662



**SP0144 THE IMPORTANCE OF MAINTAINING CONTROL**K.E.N. Clark. *University College London, London, UK*

The clinical impact of lower gastrointestinal tract involvement in systemic sclerosis will be illustrated by case presentations. This will describe problems including pseudo-obstruction, severe malnutrition, and electrolyte imbalance and anorectal disease. The interplay with comorbidities such as cardiac scleroderma will also be described. Potential therapeutic strategies for these different complications will be introduced through these cases.

**Disclosure of Interest:** None declared**DOI:** 10.1136/annrheumdis-2018-eular.7672**SP0145 LIGHT AT THE LOWER GASTROINTESTINAL TRACT IN SYSTEMIC SCLEROSIS**C.P. Denton. *Centre for Rheumatology, Royal Free Hospital and UCL Medical School, London, UK*

Gastrointestinal tract manifestations of systemic sclerosis are common and represent a high burden of the disease. Whilst some aspects can be treated the lower bowel involvement is especially challenging. The midgut is affected with dysmotility and functional impairment including the consequences of impaired absorption and exocrine pancreatic insufficiency. Midgut hypomotility can lead to stagnation of bowel contents and small intestinal bacterial overgrowth that contributes to bloating, diarrhoea and malnutrition. Colonic involvement contributes to chronic constipation and anorectal disease is a major non-lethal burden leading to incontinence. This has enormous impact on quality of life. The end result is a constellation of symptoms and clinical problems that require integrated management to ensure appropriate investigation and treatment. Strategies that can be helpful include broad spectrum antibiotics to address small intestinal bacterial overgrowth and prokinetics to address issues of pseudo-obstruction. The latter is best managed conservatively. Occasionally patients develop nutritional failure that requires parental nutrition. This can be successfully delivered as part of a home care programme and is generally parenteral supplementation, for example with overnight feeds, rather than total parenteral nutrition. Constipation and diarrhoea require opposite strategies for treatment and often a high degree of patient self-management. Recent trials of techniques to improve anorectal incontinence have been promising for strategies such as posterior tibial nerve stimulations and this may represent useful option in some cases.

**Disclosure of Interest:** C. Denton Grant/research support from: Inventiva, CSL Behring, GSK, Bayer, Consultant for: GSK, Actelion, Inventiva, Roche, Bayer, Boehringer Ingelheim, EMD Serono, Sanofi Aventis

**DOI:** 10.1136/annrheumdis-2018-eular.7621**SATURDAY, 16 JUNE 2018****RA: is it all in your head?****SP0146 THE LINK BETWEEN INFLAMMATION AND DEPRESSION**N. Harrison. *Neuroscience, Brighton and Sussex Medical School, Brighton, UK*

Inflammation is increasingly implicated in the etiology of depression. Patients with idiopathic depression have been shown to express increased circulating pro-inflammatory cytokines and 30% of patients receiving chronic Interferon-alpha for the treatment of Hepatitis-C develop major depression. Recently, anti-inflammatory agents, including 'biologics' developed for rheumatoid arthritis, have shown potential efficacy for the treatment of idiopathic depression. However, the utility of these medications is highly variable emphasising the importance of identifying biomarkers that may predict treatment response. Interestingly, neuroimaging studies have recently demonstrated that increases in inflammation can rapidly alter brain function and microstructural integrity. Further, these acute changes in brain structure/function can additionally predict the later development of depressive response during sustained inflammatory challenge. For example, in patients with Hepatitis-C given Interferon-alpha over a prolonged period, acute changes in ventral striatal microstructure (observed within 4 hours of the first injection of Interferon) predict the magnitude of fatigue/motivational impairment experienced 4 weeks later while acute changes in amygdala processing of emotionally valenced stimuli predicts the magnitude of depressive symptoms. Conversely, inhibitors of Tumour Necrosis Factor (TNF) reduce amygdala reactivity to emotional stimuli, which correlate with improvement in mood. Together, these studies

highlight the importance of inflammatory processes in depression and support ongoing trials of anti-inflammatory agents in this common and functionally impairing disorder.

**Disclosure of Interest:** N. Harrison Grant/research support from: Janssen, Consultant for: GSK

**DOI:** 10.1136/annrheumdis-2018-eular.7813**SATURDAY, 16 JUNE 2018****Gut bacteria: the boss of the immune system****SP0147 HOW THE GUT MICROBIOTA AND ITS METABOLITES IMPACT ON BONE HOMEOSTASIS**M.M. Zaiss. *Department of Internal Medicine 3 – Rheumatology and Immunology, Friedrich-Alexander-University Erlangen-Nürnberg (FAU), Erlangen, Germany*

Microbial metabolites are known to modulate immune responses of the host. The main metabolites derived from microbial fermentation of dietary fibres in the intestine, short-chain fatty acids (SCFA), affect local and systemic immune functions. Here we show that SCFA are regulators of osteoclast metabolism and bone mass *in vivo*. Treatment of mice with SCFA as well as feeding with a high-fibre diet significantly increases bone mass and prevents postmenopausal and inflammation-induced bone loss. The protective effects of SCFA on bone mass are associated with inhibition of osteoclast differentiation and bone resorption *in vitro* and *in vivo*, while bone formation is not affected. Mechanistically, propionate (C3) and butyrate (C4) induce metabolic reprogramming of osteoclasts resulting in enhanced glycolysis at the expense of oxidative phosphorylation, thereby downregulating essential osteoclast genes such as TRAF6 and NFATc1. In summary, these data identify SCFA as potent regulators of osteoclast metabolism and bone homeostasis.

**Disclosure of Interest:** None declared**DOI:** 10.1136/annrheumdis-2018-eular.7900**SATURDAY, 16 JUNE 2018****Multi-disciplinary management of complex persistent pain****SP0148 PAIN: THE ROLE OF PSYCHOLOGY**L. Knudsen. *Spinal Cord Injury Centre of Western Denmark, Viborg, Denmark*

Pain is a multidimensional experience, and chronic ongoing pain may have wide-ranging social and psychological implications. A biopsychosocial model of understanding is generally considered to be the best pain model, and it is well-established that interdisciplinary pain management is the most effective treatment approach. Psychological management plays an important role in such treatment. This lecture will cover the link between psychological factors and pain as well as psychological pain management.

**Disclosure of Interest:** None declared**DOI:** 10.1136/annrheumdis-2018-eular.7799**SP0149 THE PATIENT'S PERSPECTIVE OF LIVING WITH COMPLEX REGIONAL PAIN SYNDROME**R. Connert. *Select, Royal Devon and Exeter Hospital, Exeter, Devon, UK, Exeter, UK*

There is wide acknowledgement in medical literature that CRPS is a very painful condition that can be severely debilitating and adversely affect quality of life. In an attempt to assist the many highly caring, gifted and dedicated clinicians who want to understand what this actually means from the perspective of those who live with the condition relentlessly day by day, I shall attempt to bring such a statement to life. I shall speak mainly from my own journey of learning to live with CRPS since 2001, but shall also draw on the experiences fellow sufferers have shared with me, and humbly contribute some key messages for the clinicians who come into contact with patients pre or post diagnosis.

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**SP0150 FUNCTIONAL REHABILITATION FOR THE RELIEF OF COMPLEX PERSISTENT PAIN**

*C. McCabe. Royal National Hospital for Rheumatic Diseases, Royal United Hospitals Nhs Foundation Trust, Bath, UK*

Persistent pain, by definition, is a long-term condition that cannot be resolved by available medical or other treatments. Historically, the focus for pain and rehabilitation specialities has been on management, to improve quality of life and function in the presence of pain. However, most patients seek pain relief.

Research by the Bath Pain group, and other published literature indicates that people make hypotheses about bodily feelings based on prior performance and the current environment. This is an active process. Pain related adaptations to the sensory and motor systems ensure we act to minimise potential threats. These adaptations impact on bodily feelings and modify autonomic and limbic systems. The degree of adaptation can be minor and brief, or significant and persistent. Where adaptive mechanisms continue to engage beyond what is deemed as useful, this can be considered hyper-adaptive.

I will present clinical evidence of pain related hyper-adaptations that people with persistent pain describe in clinic. For example, perceived changes in the painful limb, ownership, temperature, and size, as well as feelings of peculiarity, discomfort, pain, and altered movement trajectory when motor output does not match expected sensory feedback. People with Rheumatoid Arthritis, Fibromyalgia, Complex Regional Pain Syndrome, or after limb fracture all describe altered body perceptions. Individuals may, for example, perceive a painful hand (and an object held within it), as excessively heavy and enlarged (when in reality it is not), report clumsiness, and difficulty moving the hand due to a perceived inability to 'engage' with it. We have described visual neglect and emotional changes about the painful limb, and consequent impacts on motor and autonomic function.

The sensory system encodes the characteristics and location of stimuli and determines if these are harmful or innocuous. This process is impaired in a painful body part. The ability to determine the texture or temperature of materials applied to the painful skin is commonly lost; or non-painful stimuli, such as light touch, are perceived as painful (allodynia).

This session will describe work that has focused on aiming to increase our understanding of the pain-related adaptations in sensorimotor processing and associated behaviours, in order to design interventions that help to redefine this hyper-adaptive response, essentially broadening sensorimotor function, and relieving persistent pain.

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**SATURDAY, 16 JUNE 2018**

**Osteoarthritis: a vascular disease**

**SP0151 DOES IMAGING SUPPORT THE VASCULAR NATURE OF OSTEOARTHRITIS?**

*P.G. Conaghan. Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, UK*

There are a number of ways in which vascular disease may contribute to either the initiation or structural progression of osteoarthritis (OA). We should keep in mind that atherosclerotic vascular disease, like OA, occurs with increasing frequency as people age and consequently understanding their inter-relationship and any potential causal relationship is difficult. Of interest is the suggested epidemiological links between cardiovascular mortality and OA, though again this is difficult to discern the casual part of the relationship. Links between vascular disease and osteoarthritis may of course be mediated through a common disease association, obesity. One hypothesis is that osteoarthritis is a differentiation disorder involving altered lipid metabolism.

It should also be remembered that articular cartilage is avascular, and it receives much of its nutrition from the subchondral bone or synovial fluid. Vascular disease in the subchondral bone may accelerate structural progression through alterations in cartilage nutrition or through direct ischaemic effects on bone. Imaging plays a key role in hypotheses about vascular involvement in OA, since it is commonly used for diagnosis and assessing progression. It has been suggested that the MRI subchondral bone changes typical of OA (termed bone marrow lesions) are similar to those seen in avascular necrosis, especially in the hip.

How might vascular changes effect OA? Certainly OA structural changes have been proposed because of secondary vascular changes in the high-pressure subchondral bone environment. These have been described in terms such as 'venous outflow obstruction' and also 'localised hypercoagulabilities', and have been described in animal and human studies. Venous outlet syndrome in the subchondral region can result in ischaemia of bone and the adjacent cartilage. Dynamic contrast enhanced (DCE-)MRI and positron emission tomography (PET) have

demonstrated that venous outflow obstruction results in decreased perfusion and that venous stasis is associated with trabecular remodelling, in animal OA models. Another potential role for vascular perturbation is in the synovitis commonly seen in OA. Given the frequency of synovitis in (especially knee) OA, it is possible that a patchy distribution of reduced blood flow (local ischaemia) happens in areas of greater inflammation. Greater levels of synovial inflammation have been associated with OA progression.

Another hypothesis is that atheromatous disease might directly effect OA pathology progression. Computed tomography (CT) has been used in the spine to demonstrate an association between arterial calcification and the degree of disc degeneration, and there has also been shown to be a relationship between disc degeneration and adjacent bony end plate damage. These spinal changes are similar to OA joint pathologies. Another study demonstrated an association between hand osteoarthritis imaging findings and aortic calcification.

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**SP0152 HYPERTENSION, BONE MARROW LESIONS AND OSTEOARTHRITIS (OA)**

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Elements of the metabolic syndrome except for hypertension such as dyslipidemia and central adiposity are not consistently associated with knee osteoarthritis once obesity is adjusted for. However, after adjustment for obesity, hypertension is modestly associated with an increased risk of knee and even, in some studies, hand OA. A recent meta-analysis reported consistency across large cohort and case control studies; those with hypertension had a 1.49 fold increased odds of OA ( $p < 0.001$ ).

There are several possible explanations for this association especially if hypertension compromises the supply of nutrients to the joint. First, as OA develops, subchondral bone remodelling is accompanied by angiogenesis which could be inhibited by vascular insufficiency. In findings that are probably related, bone marrow lesions seen on MRI in OA represent lesions of bone trauma and, in these lesions, the number of vessels increases and the vessels have especially thick walls for their size. Bone marrow lesions have been linked to intraosseous hypertension that is probably not a consequence of arterial but rather of venous hypertension within bone. Further, NSAID use in persons with OA could raise blood pressure and create a spurious association of OA with hypertension. Given this range of potential explanations and the potential for identification of causal factors that may offer clues to OA treatment, further exploration of the biology of this relationship is needed.

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**SATURDAY, 16 JUNE 2018**

**Workshop: Is there a diet for people with RMDs?**

**SP0153 WHAT EVIDENCE IS THERE THAT DIETS HELP PEOPLE WITH RMDs?**

*<sup>1,2</sup>A. Linauskas. <sup>1</sup>Department of Rheumatology, Aarhus University Hospital, Aarhus; <sup>2</sup>Department of Rheumatology, North Denmark Regional Hospital, Hjoerring, Denmark*

Throughout history patients with Rheumatic diseases (RMD) have used different diets trying to improve the symptoms and dietary manipulation is still widely used today. There are several potential mechanisms by which diet may be related to pathways involved in inflammation, such as decreasing the inflammatory process, increasing antioxidant levels, changing the lipid profile, influencing composition of the intestinal bacterial flora.

The common dietary programs used by people with RMD include vegetarian or vegan, Mediterranean, elimination diets or fasting periods. Moreover, many

dietary supplements are available both as combination formulas and as single-ingredient supplements.

The most studies, investigating diet influence on RMD symptoms in human, were conducted among Rheumatoid Arthritis (RA) patients as an adjunctive therapy. Further, there is a wide variation in evidence robustness probably due to the complexity of studying the relationship between diet and disease activity.

**Diets:** Several controlled studies among RA patients have been performed.

Mediterranean diet intervention studies have shown tendency to pain reduction and improvement of physical function after 3–6 months.

An intervention study, comparing 7–10 days fasting followed by 13 months vegetarian diet and the ordinary diet, showed significant pain reduction in the intervention group. Though, there was no significant difference in physical function or morning stiffness compared to RA patients adhered to an ordinary diet.

Vegan diet intervention studies did not report statistical significant difference in pain, physical activity or morning stiffness compared to an ordinary diet.

One study compared 6 weeks of elimination diet to an ordinary diet. Due to inadequate data reporting, no between-group analyses were possible, the authors of the study concluded: "When the dietary and placebo groups were compared the dietary group did better for all 13 variables for which differences between them were significant".

Cholesterol lowering diet study among 17 Systemic Lupus Erythematosus (SLE) patients showed increased quality of life (measured by questionnaire) after 12 weeks study period compared to the control group.

Ramadan fasting study among 40 SLE patients did not reveal any influence of fasting on disease activity or patients' quality of life during the fasting period or 3 months after fasting compared to non-fasting SLE patients.

Non-randomised controlled low-salt, uncooked vegan diet study among 53 fibromyalgia patients revealed improvements in pain, joint stiffness, quality of sleep, quality of life and general health after 3 months of study period.

**Dietary supplements:** Several studies of fish oil supplementation have been performed among RA patients and have generally shown positive results on pain reduction, morning stiffness, and improvement in physical activity and decreased use of pain relief medications. The potential benefit of eating whole foods with high omega-3 content has not been evaluated.

Studies, investigating Vitamin D supplementation in RA patients did not find any disease modifying effect.

Interventional studies of antioxidant supplementation in patients with RMD have been inconclusive.

Current data regarding potential therapeutic effects of probiotics suggest plausible benefits, though evidence grade is still low.

There is some evidence that herbal therapy containing Gama Linolenic Acid oils (evening primrose, borage, or blackcurrant seed oil) reduce some RA symptoms.

**Alcohol:** Studying effects of alcohol on RMD activity is complicated not least in relation to the treatment. Two observational studies among RA patients, showed tendency towards an inverse association between alcohol use and disease severity.

**Conclusion:** The effects of dietary manipulation in RMD patients are still uncertain due to small study samples and potential risk of bias. Higher drop-out rates and weight loss in the groups with manipulated diets indicate that potential adverse events should not be ignored.

However, there is some evidence that fasting followed by a vegetarian diet and Mediterranean diet improve pain, but not stiffness and physical function among RA patients, when compared to an ordinary diet.

Several controlled studies showed that dietary supplements of moderate-to-high doses of omega-3 fatty acids have a beneficial effect on several parameters of RA activity.

Evidence regarding diet influence on RMD's other than RA is very weak.

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## SP0154 HOW TO OFFER SEMINARS ON NUTRITION

C. Elling-Audersch, *Deutsche Rheuma-Liga (German Rheumatism League), Berlin, Germany*

Deutsche Rheuma-Liga (German Rheumatism League)

Deutsche Rheuma-Liga (DRL) is a patient organisation that offers support to people with all rheumatic and musculoskeletal diseases (RMDs). We offer to our members information, various seminars, exercise classes and advice services. The main goal is to improve a patient's self-management.

Most patients have questions concerning medication, but would like to know as well what other measures can be taken to improve their health. Nutrition and the question of a rheumatism diet is one of the great patients' demands.

Based on a survey of our organisation (DRL) patients' information priorities are obvious and have led to offerings for patients.

Our seminars for patients about nutrition are based on our nutrition booklet, on evidence-based information and on avoiding an esoteric content.

All seminars deal with three key elements of self-management: nutrition, exercise and ergonomic kitchen aids.

Based on the key messages of nutrition, the important aspects are not only to educate, but also to exercise, to communicate, to exchange experiences, to cook, to taste, to smell and to enjoy. We show ergonomic kitchen aids and explain their daily usefulness.

My talk will consider organisational aspects as well, if an organisation wants to offer such seminars.

In our experience combining nutrition, exercise and ergonomic aids are essential aspects of a healthy life and contribute to a person's rheumatic and/or musculoskeletal treatment successfully.

**Disclosure of Interest:** None declared

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## SP0155 NUTRITION – HOW TO TALK ABOUT IT

V. Krafft, *Rheumaliga Schweiz, Zurich, Switzerland*

When it comes to the subject of nutrition and rheumatism, particularly in relation to inflammatory rheumatism, opinions are sharply divided. Holistically oriented physicians and therapists believe that a change in diet can replace medication in the treatment of chronic inflammation and they thus pursue the goal of reducing the need for medication through an anti-inflammatory diet. Rheumatologists by contrast staunchly defend drug therapy and still approach the subject of nutrition with great reserve, disinterest, or even reject its effects out of hand. Some warn that patients who stray from a balanced diet with a mix of foods may risk nutritional deficiencies.

These opposing views leave many of those affected by rheumatism unsure of how to approach nutrition. Can a change in diet really help alleviate the symptoms of inflammatory rheumatism? Which diet rules can I trust? And what's more: How do I speak about it with my rheumatologist? Will he advocate a change in diet and view it as part of my arthritis therapy – or see it merely as a supporting measure, quite a nice idea but without any therapeutic value?

Anyone wanting to provide rheumatism patients with some guidance in this regard must ward against possible bias. The Swiss League against Rheumatism makes sure its communications on this controversial issue take into account the whole spectrum of existing medical pluralism. On the question of nutritional benefits, it thus provides information from the point of view of conventional medicine as well as that of complementary medicine and all the shades in between.

Objectives of the Swiss League against Rheumatism

The Swiss League against Rheumatism endeavours on the one hand to ensure that its communication about nutrition is not one-sided but rather presents the different viewpoints. On the other hand, those affected should be given access to knowledge that can help them to form their own opinion.

To achieve these goals, the Swiss League against Rheumatism continually invests human and financial resources into research on this topic, interviews and exchanges with experts, as well as ongoing updates of their contributions.

**Communication channels:** The Swiss League against Rheumatism informs people about the topic of nutrition through the following communication channels:

- Website
- Facebook
- Brochures
- Lectures

The main focus is on articles on the website.

Standpoint of the Swiss League against Rheumatism

The Swiss League against Rheumatism includes the subject of nutrition in its communications because there is a great need for information among those affected.

The Swiss League against Rheumatism itself takes no position for or against a described measure but rather only makes recommendations based on scientific criteria. On the basis of these scientific criteria, it can be assumed that nutrition, in particular a Mediterranean diet, can have a "positive influence" on various rheumatic diseases.

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SATURDAY, 16 JUNE 2018

**Challenging projects in education and training****SP0156 THEORY OF POSTER DESIGN AND PRESENTATION**

*M. Boers, Epidemiology and Biostatistics; Amsterdam Rheumatology and Immunology Center, VU University Medical Center, Amsterdam, Netherlands*

This lecture introduces basic elements of poster design, and is followed after the session by a special poster tour devoted to design. It strongly links to the concepts discussed in my workshop on data visualisation.

To design an effective poster, its message and the intended audience must be clear. Effective posters stand out because they convey their main message almost instantly, and then seduce participants to stay longer and learn more. Much more than oral presentations, posters are about selling your work in competition with all those other people presenting in your session.

In a good poster, all elements work together like a symphony orchestra:

Title, headings, text, tables, graphs, format, colours, layout, handouts, gimmicks, and ... you!

For the design process, you need a good plan (including timelines!), good tools (templates, software!) and a ruthless editor. Editing is about throwing out more and more stuff, until finally you reach the point where throwing out more destroys understanding. So the 'orchestra' has single instrumentation, and is wonderfully transparent.

Posters are not 'comprehensive'! All the details you love can go into a specially designed handout (NOT an exact replica of your poster).

Your role as presenter is special: you must be visible but unobtrusive, and flexible to accommodate different viewer styles, and have different modes of presentation (eg. walkthrough, answer questions, respond to critique). Also make sure your contact details are visible and correct (if no handout, be sure to have business cards). If you are playful you can use gimmicks to increase your visibility: match your clothes to your colour scheme, make something in real 3D on your poster, use sound, etc. But don't overdo it: this is just the icing on the cake: this is a science, not a commercial exhibit.

When we go to assess posters in the upcoming poster tour, we will be looking for the following elements:

1. Overall message clear?
2. Text quality: brevity, clarity
3. Table quality: clear vision, clear understanding
4. Graph quality: clear vision, clear understanding
5. Design elements: layout, choice of font, color
6. Handout: not a replica, elements 1–5 repeated
7. Presenter: style, contact details

**Disclosure of Interest:** None declared

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**SP0157 THE EULAR SCHOOL OF RHEUMATOLOGY. A CHALLENGING EDUCATIONAL EULAR PROJECT. WHERE ARE WE NOW?**

*A. Iagnocco, Scienze Cliniche e Biologiche, Università degli Studi di Torino, Turin, Italy*

EULAR has traditionally been a strong advocate of training and education in rheumatology, which has made EULAR the pre-eminent provider and facilitator of high-quality educational offerings for physicians, health professionals in rheumatology, and people with rheumatic and musculoskeletal diseases. Indeed, the international rheumatology community is set to benefit from high levels of education in rheumatology, with the aim of delivering significant relief to the lives of people with musculoskeletal and rheumatic diseases worldwide.

In June 2017, the EULAR School of Rheumatology was launched at the Annual EULAR Congress. This is as a fully integrated operational entity contained within EULAR which combines all educational offers, whether they are live courses, online courses, books, webinars or any other material, under one roof. This new system has the aim of greatly facilitating access to all products, giving personalised overviews and allowing, for those who sign up for a membership, to use the various incentives and special offers. The School will also provide the members a secure means of storing their gained certifications and other personal information. In addition, members of the EULAR School of Rheumatology will be able to benefit from a new accumulative credit point system, which adds points according to educational hours spent in EULAR courses, either live or on-line. Members will also

be regularly informed regarding the developments of the School and new educational and training materials.

With the purpose of optimising and improving the already very solid educational offerings of EULAR, during the last two years, seven groups of eminent experts in education actively worked to develop new products to be added to the existing educational material of EULAR. Many different projects are currently being developed by these "classrooms" and are addressed to the whole rheumatology community (i.e. rheumatologists, undergraduates, trainees, teachers, researchers, health professionals, and people with rheumatic and musculoskeletal diseases). Indeed, in today's digital era, education and training possibilities are undergoing constant changes with new approaches, products and technologies coming up. Thus, the EULAR School of Rheumatology represents a model of future learning, reflecting the changing needs of the rheumatology community through offering new educational materials across this medical discipline and the greatest levels of access to the highest quality of education in the field.

With the modern developments of the rheumatology discipline, EULAR School of Rheumatology is today taking its educational offerings, services and products to a global audience worldwide.

For information about ongoing and new initiatives of the EULAR School of Rheumatology, please go to [www.eular.org/school\\_of\\_rheumatology.cfm](http://www.eular.org/school_of_rheumatology.cfm).

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SATURDAY, 16 JUNE 2018

**Recommendation session ESSCA****SP0158 UPDATE OF EULAR RECOMMENDATIONS FOR VACCINATION OF PATIENTS WITH AUTOIMMUNE INFLAMMATORY RHEUMATIC DISEASES**

*O. Elkayam, on behalf of Eular task force. Rheumatology, Tel Aviv Medical Center, Tel Aviv, Israel*

**Objectives:** A European League Against Rheumatism (EULAR) Task Force was established to update the recommendations for vaccination of patients with autoimmune inflammatory rheumatic diseases (AIIRD) published in 2011.

**Methods:** Following the latest version of the EULAR Standardised Operating Procedures (SOP), three systematic literature reviews were conducted to present the new evidence published between 2009–2017 regarding the prevalence of vaccine preventable diseases among patients with AIIRD, the efficacy and safety of vaccines recommended for adults, and the effect of disease modifying drugs on the response to vaccines. After the presentation of the new evidence to the Task Force, overarching principles and recommendations were formulated. Evidence was graded in categories I–IV, the strength of recommendations was graded in categories A–D, and Delphi voting was applied to determine the level of agreement between the experts of the Task Force.

**Results:** A total of 6 overarching principles and 9 recommendations were formulated. The first two overarching principles focus on the responsibility of the treating physician for a yearly assessment of the vaccination status of AIIRD patients. An individualised vaccination program should be suggested and explicitly discussed with all patients. The next overarching principles address the timing of vaccination. Preferably patients are vaccinated during stable disease and prior to planned immunosuppression, in particular prior to B-cell depleting treatment. Non-live vaccines can be safely provided to AIIRD patients under immunomodulating treatments, whereas the administration of live attenuated vaccines should be avoided under immunomodulating treatment, with the possible exceptions of herpes zoster and MMR. Recommendations 1 to 7 refer to the administration of specific vaccines. Influenza and pneumococcal (a combination of PCV 13 and PPSV23) vaccines should be strongly considered for all patients with AIIRD. Herpes zoster, human papilloma virus, hepatitis A and B, yellow fever, and tick-borne encephalitis vaccines should be considered in AIIRD patients at risk. Newly formulated recommendations 8 and 9 address the vaccination approach to household members and newborns of patients with AIIRDs. Immunocompetent household members of patients with AIIRD should be encouraged to receive vaccines according to national guidelines with the exception of oral poliomyelitis vaccine. Live attenuated vaccines should be avoided during the first 6 months of life in newborns of mothers treated with biologics during the second half of pregnancy

**Conclusions:** The 2017 EULAR recommendations provide an up-to-date guidance on the management of vaccinations in patients with AIIRDs. The dissemination of the data to health professionals and patients and implementation of the recommendations will help to prevent vaccine preventable diseases in the AIIRD population.

**Disclosure of Interest:** None declared

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**SP0159 EULAR RECOMMENDATIONS FOR THE MANAGEMENT OF SJÖGREN'S SYNDROME**

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Sjögren's syndrome (SjS) is a systemic autoimmune disease that affects 0.1% of the European population and that presents with a wide spectrum of clinical manifestations. Primary SjS has no cure, and their therapeutic management has not changed significantly over the past decades. The current approach is still based upon symptomatic treatment of sicca symptomatology and broad-spectrum immunosuppression directed against systemic disease. In spite of the several therapeutic options available, there is insufficient information on their differential efficacy and safety, making that treatment decisions remain challenging in clinical practice. Over the last decade, research has centred on investigating more effective SS-targeted therapies, with the development of various randomised controlled trials (RCT) unfortunately with the absence of game-changing results. With these discouraging results, national effort promoted by some scientific societies have led to the development of several sets of recommendations.

The European League Against Rheumatism (EULAR) promoted and supported in 2010 an international collaborative study (EULAR SS Task Force) aimed at developing consensual disease activity indexes in SS. This work was very successful with the development of the first international specific scores for SjS (ESSPRI and ESSDAI), now widely used both in clinical and research settings. The wide consensus obtained on the development of the ESSDAI/ESSPRI scores provided an excellent opportunity to advance in the development of international recommendations for the therapeutic management of SS. Therefore, we continued the work of the Task Force with the development of evidence-, consensus-based official EULAR recommendations following the Delphi methodology, with the aim to provide physicians and patients with a rational therapeutic approach to SjS patients.

**Disclosure of Interest:** None declared

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**SP0160 2018 EULAR RECOMMENDATIONS FOR THE USE OF GLUCOCORTICOID THERAPY**

F. Buttgerit. Department of Rheumatology and Clinical Immunology, Charité University Medicine Berlin, 10117 Berlin, Germany

Glucocorticoids (GC) are potent anti-inflammatory and immunosuppressive drugs which are used successfully to treat many disorders, including rheumatoid arthritis, polymyalgia rheumatica, giant cell arteritis, myositis, systemic lupus erythematoses and other rheumatic diseases. However, these drugs also have the potential to cause severe adverse effects, particularly if high doses are used for prolonged periods. Therefore, the benefits of GC therapy must be balanced against the potential risks. Key strategies to achieve this goal include (i) following guideline recommendations regarding GC therapy dosing, monitoring for potential adverse events, and adverse event prevention and management, (ii) using or developing new therapeutic advances to improve the therapeutic balance.

The EULAR Glucocorticoid Task Force has already published several recommendations over the last years such as those on the standardised nomenclature for GC dosages and treatment regimens, on the management of systemic GC therapy in rheumatic diseases, and on monitoring adverse events of low-dose GC therapy. Recent work of this group dealt with the question under which conditions long-term treatment with GC has an acceptably low level of harm. As a result, the task force members agreed that the risk of harm is low for the majority of patients at long-term dosages of  $\leq 5$  mg prednisone equivalent per day, whereas at dosages of  $>10$  mg/day the risk of harm is elevated. At dosages between  $>5$  and  $\leq 10$  mg/day, patient-specific characteristics determine the risk of harm. This means general and glucocorticoid-associated risk factors and protective factors such as a healthy lifestyle should be taken into account when evaluating the actual and future risk.

Another new information on the use of GCs has been recently provided by EULAR 2016 update of RA recommendations: "Short-term GCs should be considered when initiating or changing csDMARDs, in different dose regimens and routes of administration, but should be tapered as rapidly as clinically feasible." This wording does acknowledge that there are several different regimens for oral use, intramuscular injection, and intravenous pulse therapy. It is now also being stated more clearly that GCs should be given as bridging therapy together with csDMARDs, either as part of the initial strategy or subsequently if this has failed.

In contrast, GCs are usually not needed as a bridging therapy when bDMARDs or tsDMARDs are used. This recommendations reconfirms that GCs should be gradually reduced and ultimately stopped, ideally within 3 to 6 months.

Finally, the role of GCs in the management of polymyalgia rheumatica as has been described and discussed by the recent EULAR/ACR recommendations will be briefly discussed.

**Disclosure of Interest:** F. Buttgerit Grant/research support from: Mundipharma, Horizon, Pfizer, Consultant for: Horizon, Pfizer, Speakers bureau: Horizon, Pfizer,

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**SP0161 2018 EULAR RECOMMENDATIONS FOR THE MANAGEMENT OF HAND OSTEOARTHRITIS**

M. Kloppenburg, on behalf of Task force for the update of EULAR recommendations for the management of hand osteoarthritis. *Rheumatology, Leiden University Medical Center, Leiden, Netherlands*

Hand osteoarthritis is a prevalent osteoarthritis phenotype, with high disease burden. With regard to the management of patients with hand osteoarthritis European League Against Rheumatism (EULAR) recommendations have been formulated in 2007. However, new evidence has emerged and therefore the recommendations have been updated by an international task force of experts, including rheumatologists, health professionals, plastic surgeon and patient representatives.

First, a systematic literature review was performed, collecting evidence regarding non-pharmacological, pharmacological and surgical treatment options. Second, based on the evidence and expert opinion, five overarching principles were formulated, referring to treatment goal, information provision, individualised treatment, shared-decision making and need to consider multidisciplinary and multimodal treatment approaches. In addition ten recommendations were formulated, describing non-pharmacological, pharmacological and surgical options, and considerations about follow-up. Finally, a level of evidence, grade of recommendation and level of agreement were allocated by all experts to each statement.

With the updated EULAR recommendations evidence-based up-to-date guidance can be provided on the management of hand OA.

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**SATURDAY, 16 JUNE 2018**

**Fractures: more than bone alone**

**SP0162 LOOK AT THE CASCADE : CLINICAL OBSERVATIONS**

K. Briot. *Rheumatology, Cochin Hospital, Paris, France*

Vertebral fracture (VF) is the most common osteoporotic fracture, and a strong risk factor of subsequent vertebral fracture. Prospective studies have shown that a recent VF increases an imminent risk of a subsequent one, and attention has been paid recently to a possible cascade phenomenon i.e. the occurrence of multiples VFs in less than one year after discontinuation of denosumab (rebound vertebral fractures) in postmenopausal osteoporosis and in patients receiving aromatase inhibitors. Vertebral fracture cascade has been reported in secondary causes of osteoporosis (after the initiation of systemic glucocorticoids, in endocrine disease, benign hemopathies as mastocytosis and in pregnancy-and lactation-associated osteoporosis). We reported the clinical observations of patients with multiples vertebral fractures occurring over one year and we discussed the causes, the potential risk factors and the appropriate management.

**Disclosure of Interest:** None declared

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**SP0163 A CASE OF SEVERE OSTEOPOROSIS AND ISCHAEMIC HEART DISEASE; WHAT WILL BE THE FUTURE CARDIOVASCULAR RISK?"**

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**Case description:** A 63-year-old female recently presented to metabolic bone clinic with vertebral fractures at L4 and L5. DEXA scan showed osteoporosis with T-scores at the spine  $-4.0$  and left hip  $-3.8$ . Patient was commenced on weekly



Alendronic acid 70 mg, calcium and vitamin D supplements. Patient had severe vitamin D deficiency and was commenced on treatment at primary care. She is on analgesics and physiotherapy for back pain, which was of moderate severity. She was on oral prednisolone for 5 years for polymyalgia rheumatica in the past and weaned off year ago. Other past medical history includes coronary artery disease; a myocardial infarction requiring coronary artery bypass graft 3 years back. She does not have diabetes or hypertension. She has hypercholesterolaemia; probably polygenic in origin and is on lipid lowering medications since the age of 50 years.

Her alcohol intake is minimal, and is a non-smoker. There is no family history of osteoporosis or cardiovascular disease. Her milk consumption accounted for 300 mg of calcium per day. She has reached menopause at 43 years of age and has not been on hormonal replacement therapy. Her current medications are Aspirin, Atorvastatin, Bisoprolol and Omeprazole. There is no history of indigestion or dental concerns.

Except mild local tenderness at L4–5 region, rest of the clinical examination is unremarkable.

Recent blood investigations showed normal calcium, inorganic phosphate, PTH and vitamin D. Alkaline phosphatase (195 IU/L) and P1NP (55 ug/L) were raised. Renal functions showed normal creatinine with eGFR of 62 mL/min. Full blood count is unremarkable. Serum and urine electrophoresis excluded multiple myeloma.

**Summary:** This is a case of severe osteoporosis involving vertebral fractures requiring osteoporosis treatment. Possible causes for osteoporosis would be previous use of oral steroids for long time and severe undiagnosed vitamin D deficiency. Hypercholesterolaemia and significant history of ischaemic heart disease are other concomitant diagnoses.

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## Emerging topics in the management of the antiphospholipid syndrome

### SP0164 HOW TO MANAGE ASYMPTOMATIC CARRIERS OF ANTIPHOSPHOLIPID ANTIBODIES

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Individuals who do not display the classical features of the Antiphospholipid Syndrome (APS) (vascular and obstetric disease)<sup>1</sup> are referred to as “aPL carriers”. They can be patients affected by systemic autoimmune diseases who are screened for antiphospholipid antibodies (aPL). aPL may be found in patients with “non-criteria” manifestations or in women undergoing investigations for infertility. The presence of aPL can be serendipitously discovered before a surgical procedure because of a prolonged thromboplastin time. Are these subjects at increased risk for thrombosis and adverse pregnancy outcomes (APO)? Since aPL are pathogenic autoantibodies, the answer should be “yes”. However, the magnitude of the risk can be variable from patient to patient, accordingly to the multifactorial origin of aPL-related vascular and obstetric manifestations.

According to international consensus,<sup>2</sup> the thrombosis risk stratification should consider: 1) the aPL profile (type, titer, persistence), 2) the coexistence of other thrombotic risk factors, and 3) the presence of an underlying autoimmune disease, mainly systemic lupus erythematosus (SLE). The definition of “high-risk” aPL profile comprises positivity for Lupus Anticoagulant (LA), or ‘triple positivity’, i. e. LA+anti cardiolipin antibodies (aCL) +anti-beta2glycoprotein I antibodies (anti-B2GPI) or medium-high titers of IgG aCL or IgG anti-B2GPI. Conversely, patients with isolated, intermittently positive aCL or anti-B2GPI at low-medium titers could be considered at low risk for thrombosis.

According to the literature, aPL carriers seem to have a low annual incidence of acute thrombosis, ranging from 0% to 3.8%.<sup>3</sup> These figures are not much different from the estimated incidence of thrombosis in unselected cases (about 1% patient-years), which is also equivalent to that of major bleeding associated with the use of low dose aspirin (LDA), the most frequently used drug for primary prophylaxis.<sup>4</sup> Therefore, the dilemma in clinical practice is to correctly select those aPL carriers for whom the expected benefit of therapy outweigh the risk.

Over years, the management of aPL carriers have been investigated in several studies enrolling different patients groups (SLE, pure obstetric APS, asymptomatic aPL carriers) and evaluating the efficacy of various interventions: LDA,<sup>5</sup> low intensity warfarin,<sup>7</sup> low molecular weight heparin (LMWH) in high risk situations such as surgery, prolonged immobilisation, and puerperium.<sup>8,9</sup>

Aside from drugs acting on platelets and on the coagulation system, there is evidence that immunomodulatory agents may be beneficial in primary prophylaxis of aPL carriers. Hydroxychloroquine (HCQ) is a well-recognised key-drug in the management of SLE patients and has an anti-thrombotic effect.<sup>10</sup> The use of HCQ as primary prophylaxis has been proposed also for non-SLE patients.<sup>11</sup> Statins may be useful in aPL carriers not only for the correction of a proatherogenic lipid profile, but also for reducing proinflammatory and prothrombotic biomarkers.<sup>12,13</sup>

Turning to the obstetric field, the detection of aPL antibodies has been increasingly performed in asymptomatic women, mainly for obstetrical reasons (e.g. before assisted reproductive techniques, after APO that are not included in APS classification criteria). Therefore, it is not infrequent to take the responsibility to recommend or not a treatment in “healthy” pregnant women carrying aPL. General obstetric risk should be assessed (age, hypertension, obesity, etc.). It is currently under discussion whether different aPL profiles confer the same degree of obstetric risk.<sup>14</sup> LA<sup>15</sup> and triple aPL positivity<sup>16</sup> seem to be the major predictors of APO, although APO have been described also in patients with a “low-risk” aPL profile (e.g., IgM isotype or medium to low aPL titers).<sup>17,18</sup> A key drug for primary obstetric prophylaxis is LDA and many physicians prescribe it to pregnant aPL carriers.<sup>20</sup> The immunomodulatory properties of HCQ have been advocated to be beneficial in pregnant patients with aPL<sup>21</sup> and clinical retrospective studies supported its effectiveness in refractory obstetric APS.<sup>22,23</sup> Puerperium is considered a high-risk period for thrombosis for all women. Women who carry aPL should be considered for LMWH for 4–6 weeks after delivery.<sup>19</sup>

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### SP0165 THE COMPLEX INTERPLAY BETWEEN SYSTEMIC LUPUS ERYTHEMATOSUS AND ANTIPHOSPHOLIPID SYNDROME

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The antiphospholipid syndrome (APS) was first described in the 1980's. It is diagnosed when antiphospholipid antibodies (aPL) i.e. anti-cardiolipin (aCL), anti-β<sub>2</sub>Glycoprotein-I (aβ<sub>2</sub>GPI) or positivity in the functional lupus anticoagulant test (LA) occur together with any type of thrombosis (e.g. myocardial infarction(MI), stroke, venous or microvascular thromboses) or obstetric complications.<sup>5</sup> aPL recognise protein co-factors, most importantly the scavenger protein β<sub>2</sub>GlycoproteinI (β<sub>2</sub>GPI), that bind to membrane phospholipids. It is not fully understood how complexes of β<sub>2</sub>GPI and anti-β<sub>2</sub>GPI antibodies initiate a pro-thrombotic state, but activation of platelets, endothelial cells and the complement cascade are associated features.

Approximately 80% of APS patients are women, many are young and severely ill. There is a considerable overlap between APS and SLE. Approximately 30%–40% of SLE patients are aPL positive but only about half of them develop clinical symptoms fulfilling the APS classification criteria.

Several prospective studies have demonstrated that aPL are predictive of vascular events in patients with SLE. Though conflicting results exist, we have not noted positive associations between aPL and accelerated atherosclerosis in SLE, rather we believe that it is the pro-thrombotic state, which is the major cause of vascular events in the aPL positive SLE subgroup. Microvascular disease is an often unrecognised and difficult to diagnose feature in the aPL positive SLE subgroup. We have noted that up to 15% of patients diagnosed with nephritis have microvascular pathology in accordance with APS nephropathy in renal biopsies.

The aPL positive SLE subgroup has also been demonstrated to have a more rapid accrual of damage, where in addition to vascular damage neuropsychiatric damage makes a notable contribution.

When investigating primary APS patients, we and others have noted traits that are normally seen and attributed to SLE, such as low platelets, complement consumption, a low grade of systemic inflammation and even low titers of anti-DNA antibodies. Thus, the distinction between these two groups, APS secondary to SLE and primary APS, is not always clear.

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### SP0166 ALL YOU NEED TO KNOW ABOUT KIDNEY DISEASE IN ANTIPHOSPHOLIPID SYNDROME

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Antiphospholipid syndrome (APS) can affect any vascular bed and is characterised by a plethora of clinical manifestations related with different organ systems involvement. Accordingly, APS can affect any part of kidney vasculature and parenchyma such as renal arteries and veins, intra-renal arteries and arterioles, and glomerular capillaries. APS-associated nephropathy was first described in patients with primary APS, characterised by acute thrombotic lesions in glomeruli and/or arterioles (thrombotic microangiopathy) and chronic vascular lesions such as fibrous intimal hyperplasia of arterioles and interlobular arteries, organised thrombi with or without recanalisation, and fibrous arterial and arteriolar occlusions or focal cortical atrophy.<sup>1</sup> APS nephropathy lesions have also been later described in patients with SLE-associated APS and SLE patients with positive antiphospholipid antibodies but without APS, independently of lupus nephritis.<sup>2, 3</sup> The most common clinical manifestations of APS nephropathy include hypertension, microscopic hematuria, proteinuria (from mild to nephrotic range), and a usually mild renal insufficiency. Arterial thromboses (especially stroke), pulmonary embolism, livedo reticularis, anticardiolipin antibodies, and lupus anticoagulant were strongly associated with histologic lesions of APS nephropathy. During the follow-up period, manifestations of APS (especially arterial thromboses) developed more frequently in SLE/non-APS patients with APS nephropathy than in those without APS nephropathy lesions. In the Sydney classification criteria for APS, APS nephropathy has been included in non-criteria APS manifestations.<sup>4</sup> The significant association between the presence of APS nephropathy and antiphospholipid antibodies suggests a pathogenetic role of antiphospholipid antibodies in the development of this nephropathy. Data from experimental and clinical studies support also a potential role of complement cascade activation, tissue factor activation, and activation of mTORC in APS nephropathy pathogenesis. Currently, there is no consensus on the treatment of APS nephropathy. Updated evidence about the role of anticoagulation, hydroxychloroquine, statins, and targeted therapies such as B-cell directed therapies, complement inhibition, tissue factor inhibition, and mTOR pathway inhibition will be discussed.

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## The links between gout and kidney function

### SP0167 RENAL URATE TRANSPORTERS (SUMMARY FOR CLINICIANS)

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Gout was, and still is in some academic environments, a “metabolic” disease. The advent of allopurinol in the mid of the XXth century, the first xanthine-oxidase inhibitor, precluded that most subjects with “primary gout” were to suffer from overproduction of uric acid. No actual overproduction was neatly demonstrated and some empiric observations showed that “renal underexcretion” was working in most patients with gout.

In 2002, Enomoto and coworkers characterised the first renal urate transporter, URAT1, encoded by SL22A12, showing that the human knockout for URAT1 was associated with familial hypouricemia. A bunch of uric acid transporters have been characterised since then, polymorphisms of some of them being associated with variability in renal handling of urate. The function of transporters is complex: PDZK1 (also known as NHERF3) is a scaffolding protein that binds to several urate transporters such as URAT1, OAT4, and NPT1. Therefore, PDZK1 plays a pivotal role in forming a urate-transporting multimolecular complex (also named “urate transportome”) in humans. Hyperuricemia is no more a metabolic disease: it is a “transportopathy”. In addition, linkage of urate transporters to Na, P, and sugars may help understanding some comorbid conditions associated to hyperuricemia and gout, such as diabetes and hypertension.

In addition to the previously referred, ABCG2 is a cassette binding protein expressed in the kidney and more importantly in the intestine, where is involved with active excretion. The discovery of ABCG2 helped to explain that apparent overproduction in some patients is a “renal overload” due to impaired intestinal excretion.

A summarised knowledge on the urate transporters may be useful for clinicians implicated in the management of gout, as it may explain why XOIs efficacy does differ in patients with apparent overproduction, why allopurinol response may be blunted in some patients, how targeting transporters may be helpful for the development of new urate-lowering molecules, and how to explain efficacy and safety models for uricosurics and combination therapies.

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### SP0168 THE USE OF XO INHIBITORS IN CKD – PROS AND CONS

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The association of chronic kidney disease (CKD) and hyperuricaemia is well established, and many observational studies have reported that hyperuricaemia is associated with development and progression of CKD. Potential mechanisms of this observation will be discussed, including the potential for urate as an ‘innocent bystander’ or as a causal mediator contributing directly to kidney injury. Xanthine oxidase inhibitors (XOIs) are the most widely used urate-lowering drugs. Current evidence for efficacy and safety of XOIs for preventing or delaying progression of chronic kidney disease will be presented, both in the general population and in people with gout. The challenges of XOI use in people with CKD will also be discussed, with specific reference to allopurinol dosing in CKD, and cardiovascular safety of febuxostat.

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## Big data in pre-clinical research

### SP0169 INTEGRATION OF OMICS DATA FOR PREDICTING RESPONSE TO ANTI TNF TREATMENT

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Successful development of biologics for targeting specific molecules, like TNF, was a hallmark of new era in therapy of inflammatory and rheumatic diseases.

However, the approach based on interfering with TNF exceeds simple neutralisation of inflammatory cytokine and, possibly, this is why the prediction of response remains elusive. High costs of the treatment and irreversible tissue damage in non-responders have forced multiple attempts to predict response to anti TNF treatment using clinical, laboratory and molecular markers. There are several issues related to this type of studies that may include genetically heterogeneous groups of patients, different types of anti-TNF treatment, multiple types of response measures and are typically underpowered. Nowadays, an enormous amount of genetic, epigenetic and genomic data revived new expectations and stimulates producing of models for prediction of anti TNF response. We performed several studies based on different omics data in genetically homogeneous Swedish population that raises importance of disease subgrouping and interference of environmental factors on prediction values.

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## How do you sleep?

### SP0170 RE-EVALUATE LIFE WHEN BROKEN SLEEP HAS A NEGATIVE EFFECT ON INFLAMMATORY ARTHRITIS

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Despite improved possibilities for early diagnosis and medical treatment rheumatoid arthritis (RA) still causes stiffness and swelling in the joints. Poor sleep, chronic pain, fatigue, reduced physical function, depression and reduced quality of life are consequences of these symptoms and the inflammation is.<sup>1-3</sup> About 60%–80% of patients with RA report poor sleep compared to 10%–30% in the background population.<sup>4-6</sup> Patients with RA indicate sleep as one of the most important parameters evaluating their medical treatment with anti-rheumatics, which indicate the impact sleep can have on physical and mental well-being.<sup>7</sup> Common meanings of good and bad sleep in a healthy population is characterised by subjective satisfaction, appropriate timing, adequate duration, high efficiency, and sustained alertness during waking hours.<sup>8</sup> Thereby, sleep health is seen as a multidimensional pattern of sleep-wake-fulness, adapted to individual, social, and environmental demands, that promotes physical and mental well-being.

Initially, this lecture will focus on “state of the art” regarding sleep and inflammatory joint diseases. Also different suggestions of non-pharmacological treatments targeting improved sleep quality will be presented.

Subsequently, experiences from a nurse-led sleep outpatient clinic which was established in 2016 in the Department of Rheumatology and Spine diseases, Rigshospitalet – Glostrup, will be presented focusing on how the clinic is organised and how specialised nurses are meeting patients with poor sleep with non-pharmacological interventions. We have systematically collected data about the patients sleep when included in the clinic for treatment and when discharged from the clinic. We will present results from these patients.

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### SP0171 SLEEP DISTURBANCES IN PRIMARY SJÖGREN’S SYNDROME: EVIDENCE FROM THE LITERATURE, PATIENT SLEEP DIARIES AND A QUALITATIVE FOCUS GROUP STUDY

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Primary Sjögren’s syndrome is a systemic autoimmune disease which targets secretory glands resulting in dryness. Extra-glandular features include fatigue, pain and sleep disturbances. There are few studies exploring the specific sleep disturbances experienced by PSS patients; the impact of these disturbances and the potential acceptability of interventions to address some of these problems. In this talk, I will present work which begins to map the landscape of sleep disturbances in PSS:

Firstly, a systematic review of the literature explores sleep disturbances in PSS patients and identifies particular sleep symptoms which are problematic in these patients.<sup>1</sup>

Secondly, I will explore the relationship between daytime sleepiness (hyper-somnolence) and other clinical parameters in patients recruited to the UK Primary Sjögren’s Syndrome Registry.

Thirdly, I will report on sleep diary data from 30 patients attending a multidisciplinary fatigue clinic in the North East of England.

Finally, I will present findings from focus groups conducted with PSS patients and their partners. In this qualitative study, we explored the impact of sleep disturbances on patients and their families and potential acceptability of a non-pharmacological intervention (cognitive behavioural therapy for insomnia) to address specific sleep disturbances.<sup>2</sup>

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### SP0172 WHAT EFFECT DOES EXERCISE HAVE ON SLEEP IN RMD?

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Circadian rhythms are physical, mental and behavioural changes that follow a daily cycle. Sleep is an essential aspect in maintaining the body’s circadian rhythm and maintain health-related quality of life (HQoL) therefore, sleep disturbances can have a detrimental impact on same. The Outcome Measures in Rheumatology (OMERACT) has identified sleep as one of the key outcomes important to RMD patients.<sup>1</sup> Patients with various immune-mediated inflammatory diseases, including rheumatoid arthritis, have reported disturbed sleep and reduced sleep duration, further adding to their disease burden.<sup>2, 3</sup> It has been well established that being physically active and taking regular exercise are important for those who have been diagnosed with RMD’s.<sup>4</sup> Exercise has been identified as an important part of the nonpharmacological management of poor sleep duration and in improving sleep quality however, in a 2013 Cochrane review that examined exercise and fatigue in RA, it was noted by the authors that sleep quality was yet to be examined in this population.<sup>5</sup> Moreover, it is known that in general exercise improves mood state, which can also be an additional factor in improving sleep duration and sleep quality.<sup>5</sup>

Exercise offers a potentially attractive alternative or adjuvant treatment for those people with RMD who have sleep issues. The position stand from the American College of Sports Medicine (ACSM) regarding exercise for those with chronic conditions is categorised by cardio-respiratory exercise, resistance exercise, flexibility exercise and neuro-motor exercise. This presentation will consider the evidence regarding the effect exercise has on sleep in general and how the examination of a participants exercise habits prior to any study might be important, as it may have an impact on its effectiveness. A key message from the talk will be the presentation of evidence of exercise programmes in people with RMD, according to the Frequency, Intensity, Time and Type (FITT) principle will be presented.<sup>8</sup>



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## Stratifying connective tissue diseases

### SP0173 STRATIFYING PRIMARY SJÖGREN'S SYNDROME PATIENTS

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The clinical manifestations of primary Sjögren's syndrome (PSS) vary considerably between individual patients. The pathogenesis of PSS is not fully understood and although many aberrant biological pathways have been identified, the relationships between these pathways and clinical manifestations remain unclear. Furthermore, there is substantial heterogeneity in long-term outcomes and in health economic cost among patients with PSS. Stratification of PSS into more homogeneous subsets will facilitate better understanding of the pathogenesis of the disease, development of more cost-effective management strategies and accelerate therapeutic development programmes of targeted therapies in PSS. The establishment of several large cohorts of clinically well characterised PSS cohorts with associated biobanked materials has provided a rich resource for stratified medicine research in PSS. The growing number of datasets from clinical trials in PSS provide an excellent opportunity to evaluate the potential impact of stratified approach to therapy development in PSS.

In this presentation, different approaches to identify clinically and biologically meaningful PSS subsets will be considered. In addition, the key challenges and potential future directions in Stratified Medicine in PSS will be discussed.

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### SP0174 THE VALUE OF TYPE I INTERFERON SIGNATURE TO STRATIFY PATIENTS

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Since the first reports 2003 of an increased expression of type I interferon (IFN) regulated genes in cells from patients with SLE, a number of studies have demonstrated that many systemic inflammatory autoimmune diseases display this over-expression of type I IFN regulated genes, now known as an IFN signature. This is

true for a majority of patients with SLE, but also large proportion of patients with primary Sjögren's syndrome, myositis, systemic sclerosis and rheumatoid arthritis (RA). The so called type I interferonopathies is a group of rare Mendelian diseases with a very strong IFN signature. Other autoimmune diseases, such as type I diabetes, also display an IFN signature. Type I IFN seems to be most important for inducing the IFN signature, but it's clear that type II and type III IFNs can contribute to the IFN signature. Besides the expression of type I IFN regulated genes, recent studies have shown that patients with SLE and other autoimmune disease, have epigenetic changes in IFN regulated gene, which are hypomethylated. Thus, there are strong evidences that type I IFN system activation is a key event in many autoimmune diseases. Can the IFN signature help us to stratify patients in order to predict risk for major organ manifestations, disease outcome or response to treatment? Early studies showed that patients with active disease and more severe disease manifestations usually have a more prominent IFN signature, which still is true. However, recent studies have revealed that the IFN signature needs to be combined with a broader analysis of expressed genes. For instance, a plasmablast signature seems to correlate best with SLE disease activity and a neutrophil signature associates with lupus nephritis. For treatment stratification, it's perhaps not surprising that SLE patients with a high IFN signature have a better treatment response to type I IFN inhibition, compared to IFN low patients. At least when type I IFN receptor inhibition has been used to downregulated the type I IFN response. In RA, the IFN signature at baseline predict a poor response to TNF-alpha treatment as well as nonresponse to B-cell depleting therapy. In conclusion, there are several indications that the type I IFN signature is a valuable biomarker for patient stratification. However, we are just at the brink of the understanding how to apply this signature in clinical practice.

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### SP0175 HETEROGENEITY OF MYOSITIS AND THERAPEUTIC CONSEQUENCES

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Idiopathic inflammatory myopathies, or myositis, are a heterogeneous group of chronic inflammatory disorders affecting striated muscle leading to muscle weakness and impaired function. In addition, other organs are variably involved including the skin, lungs, heart, joints, and the gastrointestinal tract contributing to morbidity and mortality and to low health-related quality of life. Treatment decisions are often guided by the most prominently affected organ. The best recognised disease subsets are polymyositis (PM), dermatomyositis (DM), juvenile PM and DM, sporadic inclusion body myositis (sIBM), and immune-mediated necrotizing myopathy (IMNM). Muscle specific autoantibodies and muscle associated autoantibodies are frequently found in different forms of myositis and collectively they can be detected in approximately 80% adults and 60% children with myositis. They can identify homogeneous subsets, and have both diagnostic and prognostic value. The worst functional outcomes in terms of muscle involvement are often seen in patients with sIBM and with anti-SRP antibodies. sIBM patients are notoriously non-responsive to any treatment. Patients with anti-SRP display necrotizing myopathy in the muscle biopsy and treatment effect is usually low. In some patients an improvement or at least stabilisation can be achieved with the use of rituximab. The other patients with IMNM are those with anti-HMGCR antibodies and with statin medication history. Here the response to glucocorticoids (GC) and immunosuppressives (IS) is mostly good, although some patients require treatment with intravenous immunoglobulins (IVIg) to which they respond very well even without concomitant GC. Patients with antisynthetase syndrome are characterised by the presence of interstitial lung disease, which may be in some cases the prevailing manifestation of the disease with only mild or none muscle weakness. Treatment is often successful with calcineurin inhibitors, mycophenolate mofetil (MMF), cyclophosphamide, or rituximab in these patients. Subgroup of patients with anti-NXP2 antibodies is characterised with strong association with calcinosis, both in children and adults, and the treatment represents a difficult problem. The effect was reported with the use of calcium channel blockers, warfarin, bisphosphonates, sodium thiosulfate, aluminium hydroxide, probenecid, colchicine as well as IVIGs, rituximab, abatacept, infliximab, and thalidomide. In any case, patients need to be treated aggressively if calcinosis progresses. Muscle disease in dermatomyositis is often responsive but the treatment of cutaneous manifestations may occasionally prove difficult. Antimalarials are usually prescribed first, sometimes in combination with systemic treatment using IVIGs, tacrolimus, MMF, or other IS. Patients with anti-MDA5 antibodies often develop clinically amyopathic or hypomyopathic DM, but at the same time their ILD can be rapidly progressive. Aggressive treatment with high dose GC and IS needs to be started early to increase the chance for survival. A proportion of patients with myositis manifests high type I interferon signature and the clinical trial suggests that these are the patients who benefit most from the treatment with interferon type I inhibition. In the future careful considerations based on the disease subsets,



presence of autoantibodies, transcriptome and proteomic analysis will facilitate stratification into defined disease subtypes and help to guide targeted therapies in idiopathic inflammatory myopathies.

**Disclosure of Interest:** None declared

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**SATURDAY, 16 JUNE 2018**

## Work and rehabilitation – key priorities for people with RMDs

**SP0176** **IT WORKS?! EMPLOYMENT SUPPORT FOR PEOPLE WITH RMDs**

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**Background:** In Germany, approximately 17 million people are suffering from RMDs (Rheumatic and Musculoskeletal Diseases). Due to the ageing society, increasing numbers are to be expected. As all people with disabilities and chronic diseases, patients suffering from RMDs have a significantly higher risk of unemployment or invalidity pension and they take slower profit of economic recovery in the job market.

**Objectives:** Give an overview on German efforts to get patients with RMDs back into work again or to sustain their ability to work

**Methods:** Main results of recent surveys will be presented. In the light of these data, current changes of the German social and health legislation will be discussed, as well as connected pilot projects.

**Results:** The online survey "Rheuma eine Stimme geben" of Deutsche Rheuma-Liga was conducted between March and May 2017 including 930 participants. Work is identified as an important issue and identified as target for highly needed improvements. After medical care and pensions, work is considered the most important topic. Well known problems are reflected: during a rheumatoid flare, still more than 50 percent of patients are waiting more than seven days for an appointment with a rheumatologist. Two of three patients have had problems with the approval of medical rehabilitation. More than 80 percent would appreciate to be entitled to work from home. As benefits, participants name the prolongation of their working life, more flexibility of working hours in accordance with their illness as well as being better able to combine work and necessary therapies. With regard to negative consequences, three out of five patients fear that they (would have to) work also in case of illness. Another problem is stigmatisation: still, one out of five patients does not inform their colleagues and the management. Most important reasons are fears of job loss and fear of troubles in the job.

Following the new ...Bundesteilhabegesetz" (from 01/2018), several measures were introduced to improve access and participation of people with disabilities to work. One of these, the "Budget for work", will improve possibilities for people with disabilities working in sheltered workshops to access the job market. In the spirit of CRPD Article 27, this instrument should be accessible to all people with disabilities, who are capable to work at least some hours a day under normal work conditions. Furthermore, it will be outlined, how the new programme rehapro intends to evaluate new models, methods and measures to prevent an (impending) disability or reduction in earning capacity as early as possible.

**Conclusions:** Action Plan for People with Rheumatic Diseases (2017)

In order to overcome these problems, the Deutsche Rheuma-Liga, representing 300.000 individual members and 11.000 volunteers, has issued an action plan. Key Claims connected to improvement of work conditions for people with RMDs are ...

- Ensure good and early treatment and improved medical care for people with RMDs in order to maintain their ability to work.
- Promote better collaboration between health care providers and health services (e.g. introduction of DMPs)
- Implement more consequently the principle "rehabilitation instead of invalidity pension" as well as a patient-centred rehabilitation
- Promote knowledge on grants e.g. for work place adjustments or trainee programs
- Optimize job trainings with regard to the real needs of people with RMDs
- Enhance the use of the instrument "Betriebliches Eingliederungsmanagement", especially for small and medium enterprises
- Promote the use of flexible working time models or support workers
- Evaluate and implement new forms of working models for people with chronic diseases
- Create incentives for jobs, that may be combined with partial instead of full invalidity pension

**Disclosure of Interest:** None declared

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**SP0177** **QUALITY OF LIFE AT THE WORKPLACE – HOW EARLY INTERVENTIONS OF HEALTH PROFESSIONALS CAN SUPPORT PEOPLE WITH RMDs**

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It is widely acknowledged that work has huge impact on health and well-being. As people affected by rheumatic and musculoskeletal diseases (RMDs) often have problems in participating in work, they should be supported by the multidisciplinary health care team. Health professionals in rheumatology play an important role in early interventions to support people with RMDs at their work places. This presentation will set out to explore important issues which need to be addressed when enabling people with RMDs to stay employed or return to work from the perspective of health professionals in rheumatology. The presentation will focus on paid work, but also include unpaid work.

With reference to ongoing clinical and research work in this field, the author will discuss possibilities and challenges in identifying work related problems, setting goals in a collaborative way, as well as providing different secondary and tertiary preventive strategies, interventions and workplace adaptations. By using a participatory multi-methods approach, facilitating self-management, evaluating and adapting work tasks and the environment, and providing ergonomic devices, people with RMDs can be supported.

And as the right time point for doing something for health and more quality of life at the work place is now, some innovative, easy-to-transfer ideas for patients, health professionals and rheumatologists will also be presented.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.7825



# **Scientific Abstracts**

## Oral Presentations

WEDNESDAY, 13 JUNE 2018

### Cancer and inflammation

OP0001

#### RISK OF MALIGNANCY IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS: A REGISTER-BASED COHORT STUDY

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**Background:** The risk of malignancies, in particular malignant lymphomas, in Juvenile Idiopathic Arthritis (JIA) patients is low but has been reported to be elevated compared to the general population.

**Objectives:** To assess the risk of cancer in patients with JIA in comparison to non-JIA individuals.

**Methods:** Register-based cohort study of patients with a first JIA diagnosis recorded from 1987 to 2015, based on data retrieved from the Swedish Patient Register (with information on hospitalizations (1987 and onwards) and outpatients visits (2001 and onwards)), and the Swedish Cancer Register (compiling data on all invasive cancers in Sweden (since 1958)). JIA patients were matched (on sex and age) to five non-JIA individuals sampled from the Swedish child population. All participants were followed up from six months after date of 2nd visit with a JIA diagnosis (for JIA patients) or the corresponding date (for non-JIA individuals) until the first date of the following events: cancer diagnosis, migration, death, 18 years of age, or 31 December 2015. The occurrence of malignancies was compared through standardised incidence rates (SIR). The same analysis was rerun allowing participants to be followed up through adult ages (age at 31 December 2015).

**Results:** 7461 JIA patients and 36 747 non-JIA individuals were identified and followed up, with a median follow up time of 4.7 years. Twelve malignancies (among which 6 lymphomas) were recorded among the JIA patients and 40 (7 lymphomas) among the non-JIA individuals, giving a rate for all cancers of 30/100000 person-years and 20/100000 person-years respectively, and a rate ratio of 1.48 (95% Confidence Interval (CI): 0.78 to 2.82). When defining the outcome as a malignant lymphoma, the rates for JIA and non-JIA were 15 and 3.5/100000 person-years, respectively, and the rate ratio was 4.2 (95% CI: 1.4 to 12.5).

Allowing the follow-up to cover ages above 18 did not substantially alter these two rate ratios.

When restricting the study period to new-onset JIA diagnosed from July 2005 to December 2015, the rate for all cancers were 19.8/100000 person-years (JIA) and 21.1/100000 person-years (non-JIA), providing a rate ratio of 0.94 (95% CI: 0.27 to 3.22) when the age at the end of follow-up was 18 years. The rate ratio was 1.60 (95% CI: 0.68 to 3.74) when the follow-up covered all ages until end of 2015 (maximum 29 years of age). There were too few outcome cases to further restrict to malignant lymphomas.

**Conclusions:** JIA patients are at increased risk to develop malignant lymphoma. The low numbers of cancer cases in JIA patients underscores that the absolute risk is low, but hampered modelling inferences on the association between cancer and DMARDs in this cohort of JIA patients followed from disease onset.

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OP0002

#### NO DIFFERENCE IN THE RISK OF MALIGNANCY IN TOCILIZUMAB VERSUS TNF INHIBITOR INITIATORS IN PATIENTS WITH RHEUMATOID ARTHRITIS: A MULTI-DATABASE COHORT STUDY

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**Background:** Few studies have conducted head-to-head comparisons of malignancy risk between different types of biologics in rheumatoid arthritis (RA).

**Objectives:** To examine the rate of incident malignancy excluding non-melanoma skin cancer (NMSC) in RA patients newly treated with tocilizumab (TCZ) versus TNF inhibitors (TNFi).

**Methods:** We conducted a cohort study using data from 3 U.S. healthcare claims databases (2010–2015) – Medicare, IMS PharMetrics Plus or Truven MarketScan. Adults aged  $\geq 18$  years with RA who newly started TCZ or a TNFi after

failing a different TNFi, abatacept or tofacitinib were included. The primary outcome was incident malignancy excluding NMSC based on 2 diagnosis codes within 2 months (specificity >98%). The 10 most frequently occurring cancers, leukaemia and human papilloma virus-related cancer and all-cause mortality were analysed as individual secondary endpoints. (table 1). For the primary as-treated analysis, follow-up time started the day after cohort entry and ended on treatment discontinuation, outcome occurrence, disenrollment, death, or the end of study period. To control for >60 potential confounders, TCZ starters were propensity score (PS)-matched to TNFi starters with a variable ratio of 1:3 within each database. Hazard ratios (HR) from the 3 PS-matched cohorts were combined by a fixed-effects model.

**Results:** We included a total of 10,393 TCZ initiators PS-matched to 26,357 TNFi initiators. A total of 118 malignancies occurred in TCZ starters and 322 in TNFi starters across the three databases. The IR of malignancy per 100 person-years ranged from 0.81 (IMS) to 2.18 (Medicare) in TCZ and from 0.98 (MarketScan) to 2.16 (Medicare) in TNFi. The risk of incident malignancy was similar between the two groups across all three databases (table 1), with a combined HR of 0.92 (95% CI: 0.74 to 1.14) in TCZ versus TNFi. Secondary analyses by cancer subtype and all-cause mortality showed similar results.

**Abstract OP0002 – Table 1.** Combined HR (95% confidence interval) of incident malignancy: a 1:3 variable ratio PS matched analysis comparing TCZ to TNFi.

Outcome	TCZ (n=10,993)		TNF inhibitors (n=26,357)
	As Treated	ITT-365d	
<i>Primary</i>			
<b>Malignancy excluding NMSC</b>	0.92 (0.74–1.14)	0.96 (0.78–1.18)	REFERENCE
<i>Secondary</i>			
<b>Non-Hodgkin's lymphoma</b>	1.56 (0.69–3.49)	1.21 (0.52–2.78)	REFERENCE
<b>Bladder cancer</b>	1.61 (0.49–5.28)	0.96 (0.26–3.62)	REFERENCE
<b>Breast cancer</b>	1.27 (0.80–1.99)	1.25 (0.81–1.91)	REFERENCE
<b>Colorectal cancer</b>	0.73 (0.22–2.43)	0.95 (0.41–2.23)	REFERENCE
<b>HPV-related cancer</b>	1.34 (0.47–3.82)	1.01 (0.31–3.24)	REFERENCE
<b>Kidney cancer</b>	0.77 (0.15–3.95)	1.39 (0.38–5.07)	REFERENCE
<b>Lung cancer</b>	0.97 (0.56–1.69)	1.06 (0.66–1.71)	REFERENCE
<b>Melanoma</b>	0.87 (0.43–1.75)	0.65 (0.29–1.45)	REFERENCE
<b>Prostate cancer</b>	1.15 (0.46–2.87)	0.81 (0.30–2.13)	REFERENCE
<b>Thyroid cancer</b>	0.72 (0.08–6.45)	0.51 (0.11–2.30)	REFERENCE
<b>Leukaemia</b>	0.79 (0.24–2.55)	0.61 (0.12–3.03)	REFERENCE
<b>Uterine cancer</b>	3.16 (0.79, 12.7)	3.21 (0.85, 12.19)	REFERENCE
<b>All-cause mortality</b>	0.66 (0.49–0.89)	0.96 (0.76–1.22)	REFERENCE

ITT-365d: intent-to-treat analysis up to 365 days of followup.

**Conclusions:** This large multi-database cohort study found no difference in the risk of malignancy excluding NMSC in patients with RA who newly start TCZ versus TNFi.

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WEDNESDAY, 13 JUNE 2018

### Psychological distress and pain; not all in the mind.

OP0003

#### ASSOCIATION BETWEEN DISEASE SEVERITY AND ONSET OF DEPRESSION IN KNEE OSTEOARTHRITIS

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**Background:** Osteoarthritis (OA) is a heterogenous condition characterised by structural pathology of the joint and pain and disability that represent patients' experience of the illness. Disease progression may lead to deteriorating

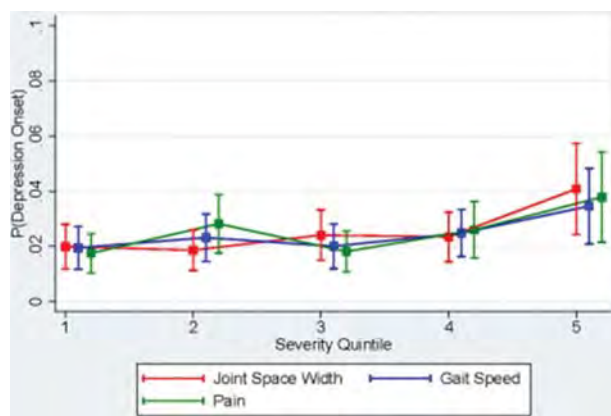


psychosocial health, but it is not clear what components of OA disease severity are related to depression onset in these patients.

**Objectives:** The aim was to determine the components of OA disease severity that contribute to depression onset among individuals with radiographic knee OA.

**Methods:** Eligible participants (n=1,652) were from the Osteoarthritis Initiative with radiographic disease (Kellgren-Lawrence [K-L] grade 2, 3, or 4), complete baseline covariate data, and were below the screening threshold for probable depression (Centre for Epidemiological Studies Depression [CES-D] Scale≤16). OA disease severity was assessed at baseline and three annual follow-up visits using minimum joint space width (millimetres), 20-metre gait speed (metres per second), and pain subscale of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). OA disease severity predictors were evaluated as a moving average at each time point then categorised in quintiles. Joint space width and gait speed categories were inverted so that increasing quintile corresponded to greater disease severity. Depression onset was assessed at four annual follow-up visits using the CES-D. Potential confounders included time-invariant and time-varying measures: demographics, lifestyle factors, socioeconomic status, Charlson comorbidity index, K-L grade, and WOMAC functional disability and joint stiffness; and CES-D score, body mass index, analgesic use, and knee injuries, respectively. Marginal structural models that account for time-dependent confounding and selective attrition modelled the association between each time-varying disease severity predictor and depression onset.

**Results:** There was a non-linear probability (figure 1) for onset of depression by disease severity quintiles for the three predictors. Moreover, the risk of depression was greatest in the highest severity quintiles and reached statistical significance for all three predictors. Odd ratios comparing highest to lowest severity quintiles in order of increasing magnitude were 1.80 (95% confidence interval [CI]: 1.00, 3.24) for gait speed, 2.10 (95% CI: 1.17, 3.75) for joint space width, and 2.21 (95% CI: 1.14, 4.30) for pain.



**Conclusions:** Findings demonstrate that the presence of greater structural disease severity and pain and decreased physical performance increases the risk of depression onset among individuals with radiographic knee OA. Thus, it is necessary to also intervene on OA disease severity when treating depression to effectively manage these patients. A combined treatment strategy consisting of two interventions delivered in parallel to simultaneously treat each condition may be the most effective form of medical care for OA patients who have comorbid depression.

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#### OP0004 COGNITIVE IMPAIRMENT IN RHEUMATOID ARTHRITIS PATIENTS: A CASE-CONTROL STUDY

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**Background:** Rheumatoid arthritis (RA) is the most common autoimmune inflammatory arthritis in adults.<sup>1</sup> Extra-articular manifestations of RA can occur in about 40% of patients, either in the beginning or during the course of their disease.<sup>2</sup> Recent studies have suggested that RA may have an important relation in the

development of cognitive and neurological dysfunction.<sup>3</sup> However, the bond between RA and the brain is still uncertain.

**Objectives:** The purpose of this study was to assess the frequency and the clinical predictors of cognitive impairment in rheumatoid arthritis (RA) patients.

**Methods:** A cross-sectional and case-control study was performed including consecutive RA patients seen in a rheumatology outpatient clinic of referral tertiary hospital. The control group included 100 healthy subjects. We registered clinical and demographic data including age, sex, level of education, time of disease, time of diagnosis, drugs in use, cardiovascular risk factors and other comorbidities. Functional capacity was assessed using the Health Assessment Questionnaire (HAQ). Neurological appraisal was made with standardised questionnaires: Mini-Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA) and the Hospital Anxiety and Depression (HAD). Analysis of the data was performed using chi-square and t-tests and a multivariate analysis (SPSS 22.0). Significance level was set as <0.05.

**Results:** We included 102 patients (88 were female) with a mean age of 57.4 (±10.7) years; among these patients, 92 (90.2%) used corticosteroids, 66 (64.7%) methotrexate, 5 (4.9%) sulfasalazine, 43 (42.1%) leflunomide, 18 (17.6%) chloroquine and 25 (24.5%) biologic therapy. The mean age of RA diagnosis was 42.9 (±12.7) years. In both univariate and multivariate analysis, compared to the control group, patients with RA presented significant lower MMSE (22.5±4.0) and MoCA (17.1±4.5) scores (p<0.05). Adjusting for level of education, just 31 and 25 patients presented normal MMSE and MoCA scores (p<0.01), respectively. Cognitive decline was associated with higher HAQ scores (functional outcome due to RA) and prolonged time of disease (p<0.05). No correlation was found between sex, disease-modifying antirheumatic drugs, rheumatoid factor, C-reactive protein levels and the neurological impairment. The mean HAD score was 17.2 (±8.2) and anxiety and depression were more prevalent in RA patients than in control group (p<0.01).

**Conclusions:** Patients with rheumatoid arthritis may present with cognitive decline and dementia as extra-articular manifestations of the disease. Neurological impairment is usually disregarded and might be under-diagnosed in RA patients. Future studies are necessary in order to better understand the relationship between RA and the Brain.

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**Disclosure of Interest:** None declared

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WEDNESDAY, 13 JUNE 2018

#### Shaping the future in systemic sclerosis

#### OP0005 PATTERNS OF 31 NEW AUTOANTIBODIES AGAINST G PROTEIN-COUPLED RECEPTORS AND GROWTH FACTORS IN SYSTEMIC SCLEROSIS CAN BE DESCRIBED BY LATENT FACTORS

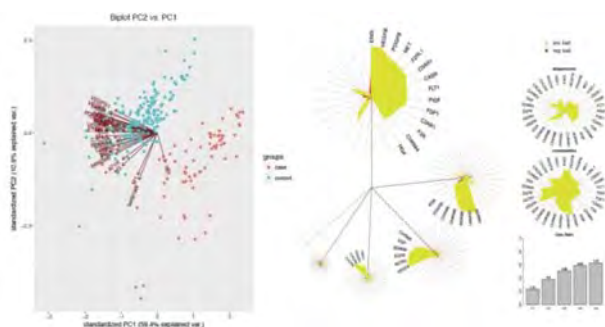
H. Bittern<sup>1</sup>, A. Carvalho-Marques<sup>1</sup>, O. Cabral-Marques<sup>1</sup>, C. Fouodo<sup>2</sup>, I. König<sup>2</sup>, H. Heidecke<sup>3</sup>, G. Riemekasten<sup>1</sup>, S. Schinke<sup>1</sup>. <sup>1</sup>Rheumatology and Clinical Immunology UKSH Lübeck; <sup>2</sup>Institute of Medical Biometry and Statistics, -, Lübeck; <sup>3</sup>CellTrend GmbH, Biotechnology, Luckenwalde, Germany

**Background:** Systemic sclerosis (SSc) is a rare autoimmune multisystemic disease with a significant disease burden and impact on life quality and survival. Disease specific, diagnostic and prognostic antibodies (ab) are known such as Scl70 and centromere (ACA) ab<sup>1</sup> or recently endothelin or angiotensin receptors.<sup>2</sup> Functional ab can bind G protein-coupled receptors (GPCR) regulating immune function and were reported in the pathogenesis of various inflammatory and non-inflammatory diseases.<sup>3</sup>

**Objectives:** We analysed 31 ab against GPCRs and growth factors in a retrospective cohort of 71 SSc patients compared to 196 sera from healthy controls (HC). Ab levels were related to disease manifestations such as sex, age, SSc phenotype in order to hypothesise functional ab and new pathogenic targets in SSc.

**Methods:** The retrospective clinical characterisation of 14 male and 57 female SSc patients (26–82 years) included mRSS, organ involvement assessed by laboratory tests, spirometry and imaging such as CT-scan or echocardiography. 30/71 had active disease (EUSTAR activity score). Ab were measured by ELISA and normalised to a standard serum. Median ab levels from SSc were compared to HC (Mann Whitney Test). Ab patterns were analysed using different statistical approaches (factor analysis, principal component analysis (PCA), linear discriminant analysis (LDA), cluster analysis and biserial correlation).

**Results:** Clinical SSc subgroups (diffuse/limited cutaneous, male/female) differ in ab levels and form separate clusters (LDA method). Moreover, 5 resp. 7 latent factors group ab and clinical disease manifestations. Factor analysis reveals VEGFR2 and YBX1 ab to be more unique with the lowest communalities. The biserial correlation shows moderate associations between ab patterns and SSc specific symptoms such as Raynaud's, calcinosis or akroosteolysis but also unspecific symptoms such as polyneuropathy. Compared to association of ETAR ab with Raynaud's and skin sclerosis HGFR ab are inversely correlated. In HC most ab levels against GPCR and growth factors are higher than in SSc except for YBX1 which has the highest ab levels in SSc patients. In HC ab levels against YBX1 ab are associated with male sex and family history of rheumatic diseases. Yet, ADRB2 ab are linked to the absence of GI symptoms or depression and ab against ENG, ETAR, PAR2, PAR1 with normal troponine levels (absence of heart involvement).



**Abstract OP0005 – Figure 1.** (a) Projection of individuals (points) and variables (arrows), representing the measured proteins, in the space of the two principle components. The almost perfect separation between controls (cyan) and cases (orange) is explained by higher protein levels for almost all proteins in the HD groups against lower values in the SSc group. By contrast, only the YBI\_P18 protein presents a tendency to be higher in the SSc group and lower in the other group. *M1* and *betaladr* proteins have lowest contributions for separating HG from SSc participants. (b) Dandelion plot displays 5 latent factors the cluster antibodies against GPCR and growth factors in SSc

**Conclusions:** We describe 31 new ab against GPCR and growth factors in SSc. Ab as well as SSc disease manifestations could be clustered by latent factors. Most ab titers in SSc were lower than in HC. Some ab were linked to the absence of SSc manifestations. Thus, we postulate that a dysbalance of functionally protective autoantibodies, that can be found in healthy individuals, and the appearance of SSc specific ab such as Scl70 contribute to its pathogenesis. Considering the preliminary character of our data, the functional impact of ab against GPCR and growth factors has to be validated *in vitro* and statistical correlations to be confirmed in a prospective independent patient cohort.

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**Disclosure of Interest:** None declared

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OP0006

#### SAFETY AND EFFICACY OF LENABASUM (JBT-101) IN DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS SUBJECTS TREATED FOR ONE YEAR IN AN OPEN-LABEL EXTENSION OF TRIAL JBT101-SSC-001

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**Background:** Lenabasum (JBT-101) is a selective cannabinoid receptor type 2 agonist that activates resolution of innate immune responses in humans and reduces inflammation and fibrosis in animal models of SSc. It is a synthetic, oral, non-immunosuppressive small molecule. Lenabasum had acceptable safety and tolerability and showed evidence of clinical benefit in diffuse cutaneous SSc (dcSSc) in Phase 2 trial JBT101-SSC-001 (NCT02465437).

**Objectives:** The objective of this study was to provide long-term open-label safety and efficacy data in dcSSc subjects who received lenabasum in that trial.

**Methods:** Subjects who completed the double-blind placebo-controlled (DBPC) part of JBT101-SSC-001 were eligible to receive lenabasum 20 mg BID in an open-label extension (OLE).

**Results:** 36/38 (95%) eligible subjects enrolled in the OLE and 34/36 (94%) were on baseline immunosuppressive drugs. The mean interval off study drug from the end of DBPC dosing to the start of OLE dosing of 9.5 weeks (range 4.7 to 56 weeks). At the time of data cut-off, the duration of OLE dosing was median 51.4 weeks, mean 45 weeks (range 26, 418 weeks), and 19 subjects had completed Week 60. Three subjects discontinued, 2 for AEs and 1 for withdrawal of consent. Adverse events (AEs, n=171) occurred in 33/36 (92%) subjects in the OLE. By maximum severity, 1 (3%) subject had life threatening AE, 3 (8%) subjects had severe AEs, 21 (58%) subjects had moderate AEs and 8 (22%) had mild AEs. Seven (19%) subjects had AEs considered related to lenabasum. The AEs that occurred in ≥10% of subjects (n,% of subjects) were upper respiratory tract infection (8, 22%), urinary tract infection (5, 14%), diarrhoea (4, 11%) and skin ulcers (4, 11%). Mild intermittent dizziness occurred in 3 (8%) subjects. One subject developed renal crisis 7 days after starting 60 mg/day prednisone prescribed by a non-study physician and had 2 severe and 1 life-threatening/serious AEs related to the renal crisis and deemed unrelated to lenabasum. During the OLE, there was improvement in multiple efficacy outcomes from both the study start and the OLE start. For example, in the 25 subjects who had completed OLE Week 52 at the time of data cut-off, the mean (SE) improvements from study start were: ACR CRISS score=56% (9%); modified Rodnan Skin Score=-8.6 (1.5); HAQ-DI=-0.14 (0.11), Physician Global Assessment=-0.9 (0.5), and 5-D Itch Questionnaire=-2.3 (0.8). Forced vital capacity% predicted was stable from study start with mean (SE) change=0.4% (0.7%).

**Conclusions:** In OLE of Phase 2 trial JBT101-SSC-001, lenabasum continues to have acceptable safety and tolerability in dcSSc with no severe or serious AEs. Multiple efficacy outcomes improved, although open-label nature of dosing with lenabasum is acknowledged. These data support Phase 3 testing of lenabasum for treatment of dcSSc.

**Disclosure of Interest:** R. Spiera: None declared, L. Hummers: None declared, L. Chung: None declared, T. Frech: None declared, R. Domsic: None declared, V. Hsu: None declared, D. Furst: None declared, J. Gordon: None declared, M. Mayes Consultant for: Boehringer-Ingelheim, Mitsubishi-Tanabe, Astellas, Roche-Genentech, R. Simms: None declared, E. Lee Employee of: Corbus Pharmaceuticals, Inc., N. Dgetluck Employee of: Corbus Pharmaceuticals, Inc., S. Constantine Employee of: Corbus Pharmaceuticals, Inc., B. White Employee of: Corbus Pharmaceuticals, Inc.

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WEDNESDAY, 13 JUNE 2018

#### Basic mechanisms of inflammation

OP0007

#### GROWTH DIFFERENTIATION FACTOR 11 ATTENUATES INFLAMMATORY ARTHRITIS THROUGH ANTAGONISING NF-KB SIGNALLING PATHWAY

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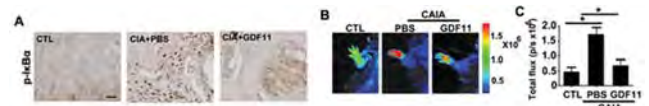
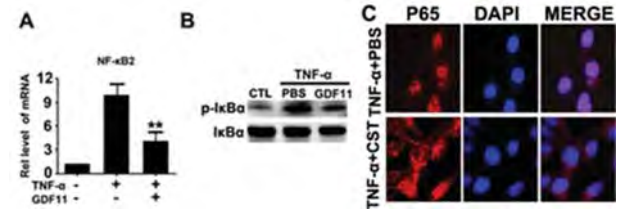
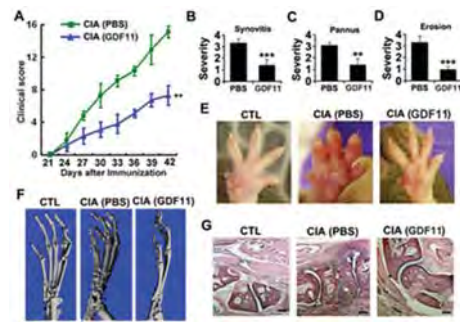
**Background:** It is well established that the tumour necrosis factor- $\alpha$  (TNF- $\alpha$ ) plays a dominant role in rheumatoid arthritis (RA)<sup>1</sup> and other arthritis models.<sup>2,3</sup> Growth Differentiation Factor 11 (GDF11) is recently reported to be closely

associated with various inflammatory diseases. However, whether GDF11 interacts with TNF- $\alpha$  and plays a role in RA still remains unknown.

**Objectives:** To investigate the potential role of GDF11 in development of RA, and to testify the underlying mechanisms involved.

**Methods:** NF- $\kappa$ B-luciferase transgenic mice (Balb/c strain), DBA-1 mice, micro-CT, *in vivo* imaging system (IVIS), mice bone marrow-derived macrophages (BMDM), cell immunostaining, collagen induced arthritis model (CIA), collagen antibody induced arthritis model (CAIA), GDF11 recombinant protein, co-immunoprecipitation Co-IP, Western blot, real time PCR, Histology, immunohistochemistry, unpaired t-tests (Mann-Whitney), paired t-tests, and ANOVA.

**Results:** The interaction between GDF11 and TNFR1/TNFR2 in BMDM was implied by co-immunoprecipitation (Co-IP) (figure 1A-B). BMDM cells were cultured with stimulation of 10 ng/ml TNF- $\alpha$ , in the presence or absence of 10  $\mu$ g/ml GDF11. Inflammation-associated cytokines, including IL-1 $\beta$ , IL-6 and inducible nitric oxide synthase (iNOS) were assessed at 12 hour time point through real time PCR (figure 1C-1E), and expression level of IL-1 $\beta$  was assayed through ELISA at 72 hour time point (figure 1F). As a result, GDF11 suppressed TNF- $\alpha$ -induced expression of inflammatory cytokines. Every experiment was repeated for three times. Collagen-induced arthritis (CIA) mice model was established in DBA-1 mice, and intraperitoneal injection of GDF11 attenuated clinical score (figure 2A), synovitis, pannus and bone erosion (figure 2B-2D) compared with PBS control group (n=7 for each group). Representative pictures of the paw (figure 2E), micro-CT (figure 2F) as well as HE staining (figure 2G) revealed that GDF11 greatly suppressed joint destruction in CIA model. In addition, GDF11 inhibited TNF- $\alpha$ -induced expression of biomarkers for activation of NF- $\kappa$ B signalling pathway, including NF- $\kappa$ B2 (figure 3A), phosphorylation of I $\kappa$ B $\alpha$  (figure 3B) and nuclear translocation of p65 (figure 3C) in BMDM, which were tested through real time PCR, Western blot and cell immunostaining, respectively. To testify the function of GDF11 in activation of NF- $\kappa$ B signalling pathway *in vivo*, p-I $\kappa$ B $\alpha$  expression was detected through immunohistochemistry in CIA model, and GDF11 diminished phosphorylation of I $\kappa$ B $\alpha$  (figure 4A) compared with PBS group (n=5). Moreover, CAIA arthritis model was established in BALB/C strain-based NF- $\kappa$ B luciferase mice, and GDF11 markedly repressed intensity of bioluminescence signal in the paws of CAIA model (figure 4B-4C). The values are the mean  $\pm$ SD. \*p<0.05, \*\*p<0.01 and \*\*\*p<0.005 vs control group.



**Conclusions:** These results reveal GDF11 as potential antagonist for inflammatory function of TNF- $\alpha$ . Besides, GDF11 displays promising protective function in inflammatory arthritis mice models. In conclusion, GDF11 may shed light on treatment of inflammatory arthritis and provide a potential therapeutic instrument for RA in the future.

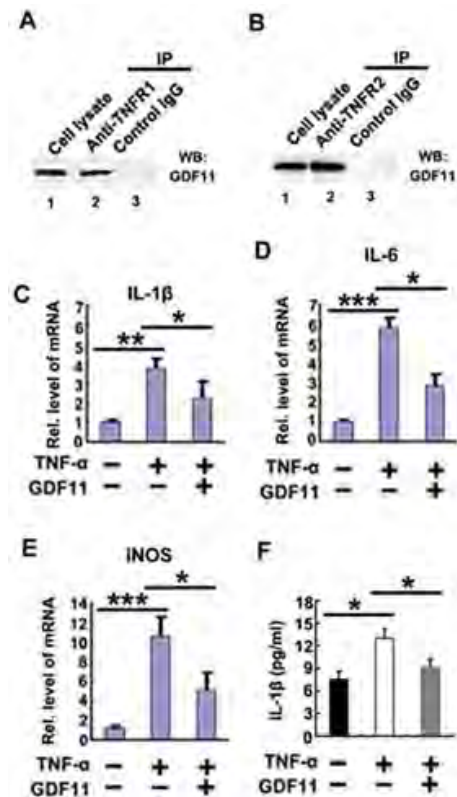
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**Disclosure of Interest:** None declared

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**OP0008 MODELLING AN AUTOINFLAMMATORY IMMUNOPROTEASOME DISEASE NAKAJO-NISHIMURA SYNDROME WITH HUMAN PLURIPOTENT STEM CELL-DERIVED MYELOID CELL LINES**

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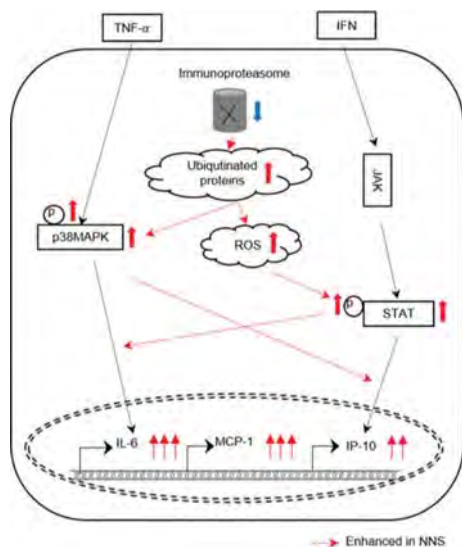
**Background:** Nakajo-Nishimura syndrome (NNS) is an immunoproteasome-associated autoinflammatory disorder caused by a mutation of PSMB8 gene.<sup>1</sup> Although dysfunction of immunoproteasome causes various cellular stresses attributed to the overproduction of inflammatory cytokines and chemokine in NNS, precise underlying mechanisms of autoinflammation are still largely unknown.

**Objectives:** We aim to investigate and understand the detailed mechanisms and signal pathways in NNS and to seek potential therapeutic candidates.

**Methods:** We established a panel of isogenic pluripotent stem cell (PSC) lines with the homozygous G201V mutation in PSMB8 gene using CRISPR/Cas9-mediated genome editing system. Myeloid cell lines (MLs) were established from each clone and used for functional analysis.<sup>2,3</sup>

**Results:** Immunoproteasome activity of PSMB8-mutant PSC-derived MLs (MTMLs) reduced even without stimulation, compared to that of the isogenic wild-type counterparts. When stimulated, MT-MLs showed overproduction of inflammatory cytokines and chemokines, with elevated reactive oxygen species (ROS). The levels of phosphorylated p38 MAPK and STAT1 also increased. Treatment with a p38 MAPK inhibitor, a JAK inhibitor and anti-oxidants dose-dependently decreased the abnormal production of cytokines and chemokines in MT-MLs. Both unstimulated and stimulated MT-MLs showed distinct transcriptional profiles, indicating the ML-MLs were already in a 'primed' state before stimulation.





**Conclusions:** The current PSC models revealed a specific ROS-mediated inflammatory pathway and provide a platform for studying the pathophysiology of NNS and searching for the alternative therapeutic options for NNS and related immunoproteasome disorders.

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WEDNESDAY, 13 JUNE 2018

## Statistics made simple: a practical approach to complex concepts

OP0009

### RISING PREVALENCE OF FUNCTIONAL DISABILITY IN PATIENTS WITH RHEUMATOID ARTHRITIS OVER 20 YEARS

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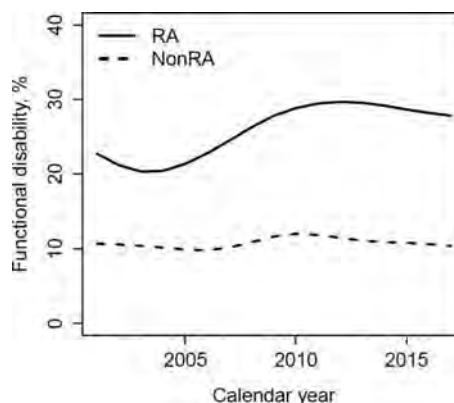
**Background:** Despite the advances in treatment of rheumatoid arthritis (RA) over the recent decades many patients with RA do not achieve remission or full physical functioning. The trends in prevalence of functional disability (FD) in patients with RA are not fully understood.

**Objectives:** To assess the prevalence of patient-reported FD in patients with RA compared to subjects without RA over the past two decades of calendar time, across different age categories and over the duration of RA disease.

**Methods:** This retrospective population-based cohort study included Olmsted County, MN residents who met 1987 ACR criteria for RA from 1/5/1999 to 12/31/2013 and a cohort of subjects without RA matched by age and sex from the same underlying population. Each non-RA subject was assigned an index date matching RA incidence date of a corresponding RA patient. Activities of Daily Living (ADL) were recorded annually over the past 20 years at patients' routine medical care visits based on patient provided information about performing six ADL without assistance including feeding oneself, dressing, using the toilet, bathing, walking, housekeeping. FD was defined as having difficulty with  $\geq 1$  of the six ADLs. Analyses were performed using age- and sex-adjusted logistic regression models with random subject effects to account for multiple measures per patient.

**Results:** Five hundred eighty-six patients with RA (mean age 55, 70% females) and 531 non-RA subjects (mean age 56, 70% females) have completed 7446 questionnaires (4,301 RA and 3145 non-RA) from 1/5/1999 to 1/5/2018 on or

following their RA incidence/index date. There has been a significant increase in the prevalence of FD among patients with RA compared to the non-RA cohort over the past two decades ( $p=0.003$ , figure 1). When analysing by age group, patients with RA compared to the non-RA subjects had at least a 15% excess in the proportion of FD at any given age up to the 8–9th decade of life while the proportions were similar in both cohorts. When analysing FD over the duration of RA disease, its prevalence was significantly higher in the RA compared to non-RA subjects, starting at RA incidence/index date (26% in RA vs 11% in non-RA subjects,  $p<0.001$ ), with persistent excess in prevalence over the entire follow-up time. When FD was defined as having difficulty with  $\geq 2$  of the six ADLs the trends were similar for calendar year, age categories and RA disease duration, although the proportion of patients affected with functional disability was smaller.



**Conclusions:** Patients with RA have significantly higher prevalence of FD compared to their non-RA counterparts. The prevalence of FD in RA has increased in the recent decades with a persistent excess in the proportion of affected patients in the RA compared to the non-RA cohort across the age-range and over RA disease duration. This substantial and growing FD burden is despite the recent advances in controlling RA disease activity with modern antirheumatic therapies. More studies are needed to understand the underlying causes for these trends in FD and to improve outcomes in patients with RA.

**Disclosure of Interest:** None declared

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OP0010

### USE OF CLAIMS AND ELECTRONIC MEDICAL RECORD DATA TO PREDICT RA DISEASE ACTIVITY

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**Background:** Prior studies have demonstrated challenges in developing and validating claims-based algorithms that accurately predict RA disease activity.<sup>1,2</sup> The ability to adjust for and predict RA disease activity would be a powerful epidemiological tool for studies that lack direct disease activity measures such as the DAS28.

**Objectives:** We used machine-learning methods to incorporate claims and electronic medical record (EMR) data to develop models to predict DAS28 (CRP) as a continuous measure, and to distinguish moderate-to-high disease activity from low activity/remission.

**Methods:** We identified 300 adults ( $\geq 18$  years of age) with RA enrolled in a single academic centre cohort with  $\geq 1$  year of linked Medicare insurance claims preceding a DAS28 (CRP) measurement between 2006 and 2010. Of these, 95 had Medicare Part D pharmacy data. From claims we included demographics, co-morbidities, joint replacement surgery, physical therapy visits, numbers of RA-related codes, laboratory values and imaging studies, and healthcare utilisation. For those with Part D pharmacy data we included medications (steroids, analgesics, DMARDs) and switches between drugs. From the EMRs we obtained smoking status, BMI, blood pressure, medication use, laboratory values for seropositivity (RF or anti-cyclic citrullinated peptide antibodies), haematocrit, ESR and CRP. We constructed models with claims only, claims with medications and claims with EMR data. We examined these models with DAS28 (CRP) as a continuous measure and as a binary outcome (moderate/high activity vs low activity/remission). We used adaptive least absolute shrinkage and selection operator (LASSO), which avoids model overfitting by penalising large coefficients and selects a subset of variables by shrinking some coefficients to zero. We used adjusted  $R^2$  to compare continuous model fit and C-statistics to compare binary models.



**Results:** In models that included DAS28 as a continuous measure, using claims alone explained 11% of the DAS28 variability. Adding medications and EMR data to claims improved the adjusted  $R^2$  by 6% (table 1). In models that included DAS28 as a binary outcome (moderate/high activity vs low activity/remission), our claims-only model yielded a C-statistic of 0.68, which increased to 0.79 after inclusion of medications and EMR data.

**Abstract OP0010 – Table 1.** Model Fit Statistics for Continuous DAS28 (CRP) (Adjusted  $R^2$ ) and Binary Categories (Moderate/High vs Low/Remission; C-Statistic)\*

	Model 1: claims only	Model 2: claims +Medicare medications	Model 3: claims +Medicare and EMR medications	Model 4: EMR data**	Model 5: claims +Medicare medications +EMR data**
<b>Adjusted <math>R^2</math></b>	0.11	0.12	0.14	0.16	0.17
<b>C-statistic</b>	0.68	0.74	0.77	0.76	0.79

\*n=300 except for Model 2 (n=95)

\*\*EMR data includes medications, laboratory tests, BMI, blood pressure and smoking status

**Conclusions:** Incorporating medications, EMR data and laboratory values into a claims-based index did not significantly improve the ability to predict DAS28 scores as a continuous measure. However, models that include claims, medications and EMR data may be used to reasonably distinguish moderate-to-high disease activity from low disease activity/remission.

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WEDNESDAY, 13 JUNE 2018

## E-health for better care

### OP0011-PARE A WEEK TO TWEET: FINDINGS FROM YOUNG PARE'S ONLINE COURSE FOR TWITTER NOVICES

S.R. Stones<sup>1,2,3</sup>, on behalf of Young PARE Working Group. <sup>1</sup>*Fibromyalgia Action UK, Paisley, UK*; <sup>2</sup>*Young PARE, Zürich, Switzerland*; <sup>3</sup>*School of Healthcare, University of Leeds, Leeds, UK*

**Background:** Twitter is a social networking platform that enables individuals to publish short posts called tweets. Twitter enables individuals to reach over 270 million active users on the platform each month.<sup>1</sup> A useful way to develop individuals' confidence on Twitter can be through participating in tweet chats and by conversing at conferences through the use of a preselected hashtag.<sup>2</sup> Young PARE identified a need among the patient community to provide some training for individuals to get started on Twitter. This mirrored the ongoing work provided by EMEUNET for rheumatology professionals.

**Objectives:** The aim of the course was to deliver a structured online Twitter learning experience, and to evaluate participants' use and perceptions of the course.

**Methods:** The course was hosted on Mailchimp over a period of seven days, from Thursday 16 until Wednesday 22 February 2017. Participants wishing to take part signed up to the course via a form advertised by email and online. Participants received an email with a task to complete at 09:00 each day. Despite the daily prompt, the course was self-paced, enabling participants to participate at their own convenience. An anonymous evaluation survey, hosted by bos, was distributed to participants immediately after the course. A combination of 5-point Likert scales, multiple allowable answers and open-ended comments were employed.

**Results:** A total of 95 individuals subscribed to the course, with 11% responding to the survey (n=11). Of the respondents, 63.7% were aged 35 years or older. The course was rated as either good (63.6%) or excellent (36.4%), with 63.6% stating that the course met their expectations. The most favoured topics rated as strongly liked or liked by 90.9% of respondents were: (i) Using twitter at conferences; (ii) Public and protected tweets; (iii) Embedding Twitter feeds; (iv) Hashtags; and (v) Sending tweets. However, some participants felt that Twitter was not applicable to their country. Participants also provided constructive feedback for future courses; including more screenshots to guide textual prompts, and the option to house the course in a single, online location that can be accessible at any time.

**Conclusions:** 'A week to tweet' challenged the misconception that social media is just for young people under 35. The course provided a simplified account of Twitter, from the basics of getting started, through to more complex functions. It appeared to be a welcomed resource for twitter novices, though the instructional content could be simplified, particularly for participants whose first language is not English. Cultural issues were also raised, with some participants feeling that Twitter wasn't relevant in their country. This highlights the need for better awareness of the global functionality of Twitter, and the capabilities of this social networking platform. For future instances, course content should be accessible from an online repository, so that participants can access the course at their own pace. There may be scope for the course to be hosted under the EULAR School of Rheumatology in the future.

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**Disclosure of Interest:** None declared

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### OP0012-HPR CREATION OF THE FIRST DIGITAL TRAINING DESIGNED FOR PATIENTS WITH RHEUMATOID ARTHRITIS BY PATIENT ORGANISATION IN RHEUMATOLOGY

S. Trope<sup>1</sup>, J.-D. Cohen<sup>2</sup>, C. Beauvais<sup>3</sup>, G. Dugoua Jacques<sup>1</sup>, D. Poivre<sup>4</sup>, A. Sarau<sup>5</sup>, D. Vacher<sup>1</sup>, H. Barkatz<sup>6</sup>, P. Lacoste<sup>6</sup>, V. Weill<sup>6</sup>, G. Thibaud<sup>1</sup>, on behalf of ANDAR patient organisation. <sup>1</sup>*ANDAR, Paris*; <sup>2</sup>*Hospital, Montpellier*; <sup>3</sup>*St Antoine Hospital, Paris*; <sup>4</sup>*Hospital, Metz*; <sup>5</sup>*hospital, Brest*; <sup>6</sup>*Dr SPOC, Paris, France*

**Background:** People with chronic conditions face the disease more effectively when they develop psychosocial skills and self-care. Health authorities thus recommend the organisation of therapeutic patient education (TPE)... suffering from different limitations.

**Objectives:** A patient organisation had the idea to develop a digital training solution, accessible everywhere, complementary to TPE, for patients with rheumatoid arthritis.

**Methods:** The choice was made for an online training program such as Massive Open Online Courses (MOOC).

A preliminary survey was carried out among the patients via an electronic questionnaire via social networks and an emailing to the organisation members.

A steering committee (COPIL) made up of representatives of the patients' association, expert patients and rheumatologists with the support of a specialised agency, determined the timetable, the educational objectives, the contents, the speakers and the evaluations.

**Results:** The initial investigation was stopped at 100 responses, obtained in 3 days. 85.9% planned to follow the MOOC on their computer, but to meet the needs of all, the device is responsive. 61% had never participated in a TPE program and 94% were interested in joining MOOC to learn new information about the disease (78.8%), treatments (71.7%), have expert views (67.7%), share experience with other patients (56.6%), and better live with the disease (50.5%).

The MOOC: Using the Learning Management System platform drspoc.com, Intervention of the experts via videos and live courses, evaluation of the achievements and, during two annual sessions, tutoring by patients trained specifically. At the beginning and end of the session, learners are invited to answer different questionnaires (knowledge, skills, satisfaction).

COPIL identified 15 experts (patient-experts, rheumatologists, occupational therapist, physiotherapist, nutritionist, social worker, psychologist, sexologist, nurse) who wrote the content of their speech. All texts have been validated by a pedagogical engineer and the director of the association.

215 people pre-registered during the month preceding the launch, 154 persons active and 446 posts shared during the first session. 217 pre-registered, 238

actives, 1 257 posts during the second sessions, tutored by peer patients with a dedicated training.

Some participants were health care professionals and their extremely positive feedbacks prove the value in offering MOOC access to every people interested in. **Conclusions:** This is the first digital training strategy for people with rheumatoid arthritis. It proved to be useful to patients, offering an alternative or complement to TPE.

It will be necessary to evaluate the impact of this MOOC on the quality of life of the patients and their perception on its usefulness after several sessions. We decided to propose an e-learning version without peer patient intervention and accessible at any time in addition to the MOOC version with a specific educational path.

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WEDNESDAY, 13 JUNE 2018

## EULAR projects in paediatric rheumatology and UCAN

OP0013

### PREGNANCY OUTCOMES IN DMARD EXPOSED PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS – RESULTS OF THE BIOLOGIC REGISTER JUMBO

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**Background:** Juvenile idiopathic arthritis (JIA) often persists into adult life. Young women and men with JIA are often still exposed to disease modifying anti-rheumatic drugs (DMARDs). Little is known about the impact of DMARDs on pregnancy and its outcome, and there has been no approved DMARD for pregnant or lactating women so far.

**Objectives:** To investigate the course and outcome of pregnancies in female JIA patients and male JIA patients with pregnant partners who were exposed to DMARDs.

**Methods:** In the JIA biologic registry JuMBO (Juvenile arthritis MTX/Biologics long-term Observation), patients (or partners of patients) with pregnancies were identified. Standardised patient interviews were conducted and the course and outcome of pregnancy inquired. In addition, prospectively collected physician-reported data were considered in the analysis.

**Results:** Out of the 1300 patients enrolled in JuMBO, a total of 222 pregnancies in 116 women and in 25 partners of men with JIA were reported. Until January 2018, information was available for 149 pregnancies of 96 women with JIA and for 34 pregnancies of 20 male patients with pregnant partners.

The majority of the 96 women had polyarticular JIA (75%). The median age at first conception was 24 years (ys, IQR 20–27) and the median disease duration was 14 ys (IQR 9–18). All women were ever exposed to DMARDs, 84% to a biological (b) DMARD. Among the 149 pregnancies, 64 occurred upon DMARD exposure (29 bDMARDs, 23 bDMARDs plus synthetic (s)DMARDs, 12 sDMARDs). DMARDs were discontinued in most exposed patients 6 weeks (median, IQR 4–9) after conception. In the groups of pregnancy exposed (n=64) and unexposed (n=85) to a DMARD at conception were the outcomes as follows: 36 and 64 live births, 16 and 6 elective pregnancy terminations, 8 and 12 spontaneous abortions, 2 and 0 extra-uterine gravidity, and 0 and 1 stillbirth, respectively. Among the 100 pregnancies with live births, most frequent complications were gestational diabetes in 9 cases and bleeding in 7 cases. Three women suffered from preeclampsia. Twelve children were born before the 37th week of gestation (5 (13.9%) of exposed and 7 (10.9%) of unexposed mothers) and 38 were born by Caesarean section. Six children were born with malformations, of which four are to be considered as major anomalies according to the EUROCAT classification<sup>1</sup> (2 (5.5%) in exposed patients and 2 (3.1%) in unexposed patients).

Of the 34 pregnancies in partners of male patients, in 26 cases the expectant fathers had been exposed to DMARDs at conception. Most pregnancies (29/34, 85.2%) resulted in a live birth, 3 (8.8%) ended in a spontaneous abortion and 1 (2.9%) pregnancy was terminated. Two (6.9%) children were born with congenital malformation

**Conclusions:** Women and men with JIA who are still undergoing treatment in young adulthood often become pregnant or procreate children under medication, why more information on drug safety in pregnancy is needed. For this, more patient data must be evaluated in connexion with therapy, disease activity and the JIA category.

## REFERENCE:

- [1] European Surveillance of Congenital Anomalies, EUROCAT Guide 1.3, chapter 3.3: Coding of EUROCAT subgroups of congenital anomalies. Available from [www.eurocat-network.eu](http://www.eurocat-network.eu) (Accessed 30 January 2018).

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WEDNESDAY, 13 JUNE 2018

## Opening plenary abstract session

OP0014

### SERUM URATE, GOUT, AND CARDIOVASCULAR DISEASE IN A RANDOMISED CONTROLLED TRIAL OF CANAKINUMAB: A CANTOS SECONDARY ANALYSIS

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**Background:** Serum urate is a risk marker for both gout and cardiovascular disease, but trial data demonstrating that drugs which reduce gout also reduce cardiovascular event rates is scarce. It is also uncertain if any such effects are mediated through urate levels.

**Objectives:** We examined the relationships between serum urate (SUA), canakinumab, and incidence rates for gout and cardiovascular events in the Canakinumab Anti-inflammatory Thrombosis Outcomes Study (CANTOS), a randomised double-blind placebo controlled trial of IL-1 $\beta$  inhibition.

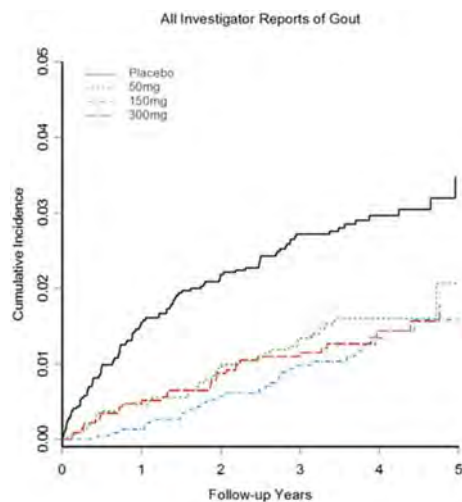
**Methods:** 10 061 patients with stable atherosclerosis (prior myocardial infarction) and hsCRP  $\geq 2$  mg/L were randomly allocated to placebo or to one of three doses of canakinumab (50 mg, 150 mg, or 300 mg), administered subcutaneously once every three months. Serum urate and hsCRP were tested at baseline and every 3 months for the first year and then annually. A physician diagnosed history of gout was ascertained at baseline and subsequent attacks were assessed during follow-up as part of the systematic adverse event reporting. The rates of gout and major adverse cardiovascular events (myocardial infarction, stroke, re-vascularisation, and cardiovascular death) were compared across different baseline SUA levels and by randomised treatment assignment.

**Results:** The groups were well balanced with respect to baseline characteristics with a median follow-up of 3.7 years. Median age was 61 years, 74% were male, median BMI was 29.8kg/m<sup>2</sup>, and median SUA at baseline was 6.1 mg/dl (IQR: 5.2, 7.2). In the placebo group, rates for both gout and major adverse cardiovascular events increased across baseline SUA strata. Rates were 0.28, 1.36, and 5.94 per 100 person years for gout and 4.1, 5.3, and 5.6 for major adverse cardiovascular events per 100 person years for SUA levels of <6.9, 6.9–8.9, and  $\geq 9.0$  mg/dL, respectively. Random allocation to all dosages of canakinumab reduced rates of incident gout (see figure 1). This reduction in gout by canakinumab was observed at all baseline SUA levels (see table 1), and canakinumab had no effect on SUA levels over time but did reduce hsCRP.

**Abstract OP0014 – Table 1.** Gout risk by treatment assignment, stratified by baseline serum urate

		Placebo		Canakinumab (all dosages)			
		N	Events	N	Events	Rate (95% CI)	HR (95% CI)
<b>Gout events</b>							
SUA	<6.9 mg/dl	2326	24	4614	19	0.28 (0.18–0.41)	0.40 (0.07–0.73)
	6.9–8.9 mg/dl	831	41	1684	41	1.36 (1.00–1.85)	0.65 (0.48–0.74)
	$\geq 9.0$ mg/dl	186	34	418	36	5.94 (4.25–8.32)	2.55 (1.84–3.54)

SUA, serum urate; Rate per 100 person-years; HR, hazard ratio; CI, confidence interval. Hazard ratios calculated using placebo as reference.



**Conclusions:** The CANTOS trial confirms that serum urate is a risk marker for both gout and cardiovascular events and demonstrates that IL-1 $\beta$  inhibition is effective in preventing both of these inter-related conditions. However, canakinumab had no effects on serum urate itself.

#### REFERENCE:

- [1] Ridker PM, Everett BM, Thuren T, et al. Antiinflammatory therapy with canakinumab for atherosclerotic disease. *N Engl J Med* 2017;377:1119.

**Disclosure of Interest:** D. Solomon Grant/research support from: Astra Zeneca, R. Glynn: None declared, J. MacFadyen: None declared, P. Libby: None declared, T. Thuren Employee of: Novartis, B. Everett: None declared, P. Ridker: None declared

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#### OP0015 MORTALITY OF THE COBRA EARLY RHEUMATOID ARTHRITIS TRIAL COHORT AFTER 23 YEARS FOLLOW UP

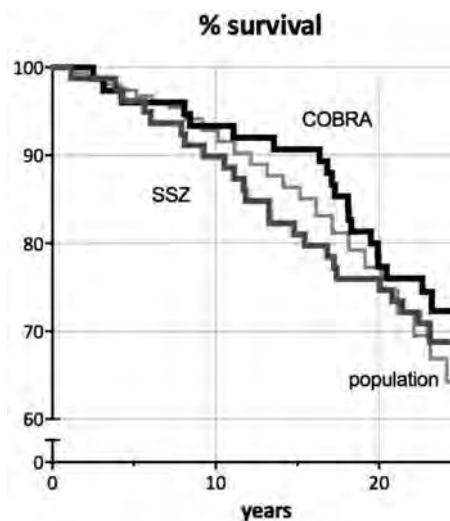
P.B.M. Poppelaars<sup>1</sup>, L.H.D. van Tuyl<sup>1</sup>, M. Boers<sup>1,2</sup>. <sup>1</sup>Amsterdam Rheumatology and Immunology Center | VU University Medical Center; <sup>2</sup>Epidemiology and Biostatistics, VU University Medical Center, Amsterdam, Netherlands

**Background:** Mortality in patients with rheumatoid arthritis (RA) is higher than the general population. Most cohorts show that the adverse effect of RA becomes apparent only after more than a decade of follow up. Whether early, intensive treatment can improve this is still unknown. COBRA combination therapy (COmbinatietherapie Bij Rheumatoïde Artritis) showed long-term effectiveness for treatment of early RA without undue harm.<sup>1</sup> In 2010, after 11 years of follow up, the COBRA follow up study showed lower mortality in patients with COBRA treatment compared to patients with sulphasalazine monotherapy.<sup>2</sup>

**Objectives:** Our aim was to investigate mortality in the COBRA-trial cohort after 23 years and compare this mortality to a reference sample of the general population in the Netherlands.

**Methods:** In the COBRA trial, patients with early RA (median disease duration, 4 months) were treated with sulphasalazine monotherapy (SSZ, n=79) or a combination of SSZ, low-dose methotrexate and initially high, step-down prednisolone (COBRA, n=76). In the current study, we investigated mortality in the COBRA trial with the help of the Dutch state registry for mortality (Centrum van familiegeschiedenis, CBG). We compared the mortality in this cohort to a reference sample of the general population in the Netherlands matched for age and gender (data from Statistics Netherlands). The Standardised Mortality Ratio (SMR) compared the trial groups and the general population.

**Results:** With data of 154 out of the 155 patients, follow up was nearly complete. Duration of follow up was mean 23 (in patients alive, range 22–24) years. In total 44 patients died (28%, SMR=0.80 [95% CI: 0.59 to 1.06]); 20 of 75 COBRA patients (27%, SMR 0.75; [0.47–1.14]) and 24 of 79 SSZ patients (30%, SMR 0.85 [0.56–1.25]); the difference in mortality was not significant (p=0.61). In the reference sample of the general population (n=154) 55 people (36%) died. The positive trend for COBRA over SSZ decreased over time (figure 1).



**Conclusions:** This prospective cohort study of early RA is one of the first to show a normalisation of RA mortality compared to the general population after 23 years of follow up. In fact, this trial population had a numerically lower mortality than expected. This confirms that early, intensive treatment of RA (that can include glucocorticoids) has long-term benefits, and strongly suggests these benefits include normalisation of mortality.

#### REFERENCES:

- [1] Boers M, et al. *Lancet* 1997;350:309–18.  
[2] van Tuyl LH, et al. *Ann Rheum Dis* 2010;69:807–12.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.3675

#### OP0016 A MULTICENTRE RANDOMISED CONTROLLED TRIAL OF ZOLEDRONIC ACID FOR OSTEOARTHRITIS OF THE KNEE WITH BONE MARROW LESIONS

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**Background:** No disease-modifying drugs are currently available for the treatment of osteoarthritis (OA). Bone marrow lesions (BMLs) visualised on magnetic resonance imaging (MRI) have been identified as a promising therapeutic target. Our pilot study showed that a single infusion of zoledronic acid (ZA) reduced knee pain and BML size in knee OA patients over 6 months.<sup>1</sup> A longer, larger study was required to assess whether these improvements can be reproduced in a larger multicentre design.

**Objectives:** To compare the effect of once-yearly intravenous infusion of ZA to placebo on knee pain and BML size over 24 months in knee OA patients with significant knee pain and BMLs.

**Methods:** The Zoledronic Acid for Osteoarthritis Knee Pain (ZAP2) study is a multicentre, randomised, double-blinded, placebo-controlled trial over 24 months. Patients  $\geq 50$  years who had significant knee pain (defined as a visual analogue scale (VAS)  $\geq 40$  mm) and MRI-detected knee BML were randomised to receive either ZA (5 mg in 100 ml saline) or placebo (100 ml saline) once-yearly. Those with severe knee OA (joint space narrowing (JSN) on X-ray of Grade 3 using the Osteoarthritis Research Society International (OARSI) atlas) were excluded. Outcomes included knee pain and function by the Western Ontario and McMasters Universities Osteoarthritis Index (WOMAC), knee pain by VAS and change in knee total BML size (sum of medial femoral, lateral femoral, medial tibial, lateral tibial and patellar sites) by proton density weighted MRI from baseline to 24 months. Effect modification of the absence or presence of radiographic OA (JSN grade 0 or grade 1–2) was pre-specified. Mixed effect modelling using an intent-to-treat design was performed for data analyses. Adjustment for baseline values were performed for knee pain and function outcomes due to baseline imbalances.

**Results:** 223 patients (mean  $\pm$ SD age 62.0 $\pm$ 8.0 years, 117 females) were enrolled. At baseline, mean  $\pm$ SD knee WOMAC pain (0–500), WOMAC function (0–1700) and VAS pain scores (0–100) were 200.0 $\pm$ 105.0, 656.9 $\pm$ 352.9 and 51.0



$\pm 20.5$ , and median BML size was 489.6 mm<sup>2</sup>. After 24 months, there was no significant difference in changes in knee pain (WOMAC pain: -37.5 vs -58.0,  $p=0.205$ ; VAS pain: -11.5 vs -16.8,  $p=0.17$ ) or function scores (-134.9 vs -159.2,  $p=0.65$ ), or knee BML size (-33.5 mm<sup>2</sup> vs -11.7 mm<sup>2</sup>,  $p=0.68$ ) between the ZA group and the placebo group. Pre-specified analyses consistently showed that ZA was more effective than placebo in patients without radiographic OA (JSN Grade 0) on changes in WOMAC pain (-88.3 vs -42.6,  $p=0.21$ ), VAS pain (-21.8 to -8.3,  $p=0.11$ ), WOMAC function (-296.9 vs -78.5,  $p=0.06$ ) and BML size (-67.4 vs 98.2,  $p=0.14$ ). Adverse events were more frequent in the ZA group, primarily flu-like symptoms and musculoskeletal pain and stiffness.

**Conclusions:** Once-yearly infusion of ZA did not significantly reduce knee pain or BML size overall in knee OA patients over 24 months but may have symptomatic benefit in milder disease.

#### REFERENCE:

[1] Laslett LL, et al. *Ann Rheum Dis* 2012;71:1322-8.

**Disclosure of Interest:** None declared

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### OP0017 THE IMPACT OF THE DURATION OF BISPHOSPHONATE DRUG HOLIDAYS ON HIP FRACTURE RATES

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**Background:** Given FDA warnings, drug holidays (temporary or permanent discontinuation) of bisphosphonates (BPs) after long-term (3-5 years) continuous therapy is becoming increasingly common in the United States (US). However, the benefits and risks of stopping BPs, and the optimal timing to restart, remain unclear.

**Objectives:** We conducted a population-based cohort study of women on long term BP therapy to evaluate the rate of hip fracture following a drug holiday.

**Methods:** We used Medicare data (2006-2014) to identify all women with medical and pharmacy coverage who initiated a BP and were at least 80% adherent for  $\geq 3$  years ('baseline'), at which follow-up time began. Patients using other bone therapies (e.g. denosumab, oestrogen, teriparatide, calcitonin) were excluded or censored if they started after follow-up began. We calculated crude rates of hip fracture for continuing BP therapy and among those who discontinued, for categories of time since discontinuing (i.e., length of drug holiday), extending up to 3 years. We used Cox proportional hazards models to evaluate the risk of discontinuing per the length of the drug holiday, using age as the time axis and controlling for potentially confounding factors, with and without adjusting for death as a competing risk.

**Results:** We identified 1 56 236 women who were highly adherent, long-term BP users. The mean (SD) age was 78.5 (7.5) years. The most commonly used BPs were alendronate (71.7% ever use, 52% exclusive use) and zoledronic acid (16.2% ever use, 8.9% exclusive use). During a median (IQR) followup of 2.1 (1.0, 3.3) years, 62 676 (40.1%) of women stopped BP therapy for at least 6 months or more. Among these women, 7947 (12.7%) subsequently restarted any BP. Overall, 16 904 (10.8%) died.

A total of 3745 hip fractures occurred during follow-up. Hip fracture rates were lowest among women who were current users, and gradually increased as the length of the drug holiday increased, achieving their maximum with a drug holiday >2 years (table 1).

**Abstract OP0017 - Table 1.** Hip fracture rate by duration of BP drug holiday, adjusting for competing risk of death

Time since Bisphosphonate Discontinuation (yrs)	Number of hip fractures, n	Crude Incidence Rate per 1000 person-years	Adjusted* Hazard Ratio (95% CI)
0 (i.e. current use)	1958	9.6 (9.2-10.1)	1.0 (reference)
>0 to $\leq 3$ months	530	13.1 (12.0-14.3)	1.29 (1.17-1.42)
>3 months $\leq 1$ year	539	12.0 (11.0-13.1)	1.12 (1.02-1.24)
>1 to $\leq 2$ years	422	13.3 (12.0-14.6)	1.21 (1.09-1.35)
>2 to $\leq 3$ years	235	15.7 (13.7-17.8)	1.39 (1.21-1.59)

\*adjusted for age, region, race, rural or urban, median income, calendar year, comorbidity (fragility fracture, charlson comorbidity index score), DXA, number of physician visits, care by a rheumatologist or endocrinologist, long term care residence, vitamin D deficiency, glucocorticoids, and proton pump inhibitors

**Conclusions:** In a large cohort of U.S. women, a BP drug holiday greater than 2 years was associated with a significantly increased risk for hip fracture of up to 39% compared to continued BP use.

**Disclosure of Interest:** J. Curtis Grant/research support from: AbbVie, Amgen, BMS, Corrona, Janssen, Lilly, Myriad, Pfizer, Roche/Genentech, UCB, Consultant for: AbbVie, Amgen, BMS, Corrona, Janssen, Lilly, Myriad, Pfizer, Roche/Genentech, UCB, R. Chen Grant/research support from: Amgen, Z. Li Grant/research support from: Amgen, T. Arora Grant/research support from: Amgen, K. Saag Grant/research support from: Amgen, Merck, Consultant for: Amgen, Merck, Radius, N. Wright: None declared, S. Daigle: None declared, M. Kilgore Grant/research support from: Amgen, E. Delzell: None declared

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### OP0018 THE VALUE OF ADDING MRI TO A CLINICAL TREAT-TO-TARGET STRATEGY IN RHEUMATOID ARTHRITIS PATIENTS IN CLINICAL REMISSION: CLINICAL AND RADIOGRAPHIC OUTCOMES FROM THE IMAGINE-RA RANDOMISED CONTROLLED TRIAL

S. Møller-Bisgaard, K. Hørslev-Pedersen, B. Ejbjerg, M. Hetland, L. Ørnbjerg, D. Glinatsi, J. Møller, M. Boesen, R. Christensen, K. Stengaard-Pedersen, O. R. Madsen, B. Jensen, J. Villadsen, E.-M. Hauge, P. Bennett, O. Hendricks, K. Asmussen, M. Kowalski, H. Lindegaard, S.M. Nielsen, H. Bliddal, N. Krogh, T. Ellingsen, A.H. Nielsen, L. Balding, A.G. Jurik, H. Thomsen, M. Østergaard. *Depts of Rheumatology and Radiology, Musculoskeletal Statistics Unit, Hospitals at Slagelse, Graasten, Gentofte, Aarhus, Frederiksberg, Silkeborg, Hjørring, Odense, Herlev, the Parker Institute and Rigshospitalet, Zealand, Funen and Jutland, Denmark*

**Background:** Targeting MRI remission in rheumatoid arthritis (RA) patients in clinical remission may improve clinical outcome and halt joint damage progression.

**Objectives:** To determine whether a treat-to-target (T2T) strategy based on structured MRI assessments targeting absence of osteitis/bone marrow oedema (BME) would lead to improved clinical and radiographic outcomes, compared with a conventional T2T strategy in RA patients in clinical remission.

**Methods:** The IMAGINE-RA study was a 2 year investigator-initiated, randomised, open-label multicentre study. Two hundred RA patients in clinical remission (defined as: DAS28-CRP < 3.2 and no swollen joints) receiving conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) were randomly assigned 1:1 to a conventional DAS28-CRP guided T2T strategy, targeting

**Abstract OP0018 - Table 1.** Primary and secondary outcomes at 24 months

	MRI T2T	Conventional T2T	Difference between groups	P value*
<b>Primary endpoints</b>				
<b>Radiographic:</b>				
No radiographic progression, n (%)	49 (66.2%)	58 (62.4%)	OR, 1.19 (0.04 to 39.47)	0.922
<b>Clinical:</b>				
DAS28-CRP remission (DAS28-CRP < 2.6), n (%)	64 (85.3%)	63 (88.2%)	OR, 1.03 (0.31 to 3.43)	0.958
<b>Secondary endpoints</b>				
<b>Clinical</b>				
ACR-EULAR Boolean remission, n (%)	37 (49.3%)	30 (31.9%)	OR, 4.19 (1.30 to 13.57)	0.017
SDAI remission (SDAI < 3.3), n (%)	48 (64.0%)	56 (62.2%)	OR, 1.67 (0.59 to 4.71)	0.336
CDAI remission (COAH < 2.8), n (%)	53 (69.7%)	59 (64.8%)	OR, 2.75 (0.90 to 8.36)	0.075
DAS28-CRP	1.9 (0.1)	2.1 (0.1)	-0.2 (-0.3 to 0.0)	0.093
Morning stiffness, min	18.1 (3.2)	10.1 (2.9)	3.0 (-5.4 to 11.4)	0.486
Tender joint count (0-28)	0.2 (0.1)	0.5 (0.1)	-0.2 (-0.6 to 0.1)	0.173
Swollen joint count (0-28)	0.0 (0.1)	0.3 (0.1)	-0.3 (-0.5 to -0.0)	0.038
Patient VAS global (0-100)	15.5 (1.8)	21.2 (1.6)	-5.7 (-10.4 to -0.9)	0.019
Patient VAS pain (0-100)	14.2 (1.7)	18.7 (1.6)	-4.5 (-9.0 to 0.0)	0.052
Patient VAS fatigue (0-100)	21.8 (1.9)	24.4 (1.7)	-2.6 (-7.7 to 2.4)	0.311
Physician VAS global (0-100)	4.7 (0.8)	6.9 (0.8)	-2.3 (-4.4 to -0.1)	0.041
<b>Radiographic</b>				
Change in TSS	1.0 (0.3)	1.3 (0.3)	-0.3 (-1.1 to 0.6)	0.558
<b>Function and quality of life</b>				
Change in HAQ	-0.052 (0.024)	0.091 (0.028)	-0.148 (-0.209 to -0.078)	<0.001
Patient with normal function (HAQ $\leq 0.5$ ), n (%)	61 (80.3%)	75 (79.3%)	OR, 0.73 (0.08 to 7.14)	0.790
Change in SF-36 PCS	1.1 (1.0)	-0.2 (0.9)	1.3 (-1.3 to 4.0)	0.330
Change in SF-36 MCS	-0.5 (1.0)	-0.9 (0.9)	0.5 (-2.1 to 3.0)	0.727
Change in EQ-5D	0.040 (0.015)	0.019 (0.013)	0.021 (-0.017 to 0.060)	0.279

95% CI, 95% confidence interval; ACR=American College of Rheumatology; CDAI=Clinical Disease Activity Index; CRP=C-reactive protein; DAS28-CRP=Disease activity score in 28 joints based on four variables, including CRP; EQ-5D=EuroQol-5 dimensions; EULAR=EULAR Boolean remission; HAQ=Health Assessment Questionnaire; MCS=Mental Component Summary score; MRI=Magnetic Resonance Imaging; PCS=Physical Component Summary score; RA=RA; RAI=RAI remission; SDAI=Simplified Disease Activity Index; SF-36=Short Form 36 item questionnaire; T2T=treat-to-target; TSS=Total Sharp/van der Heijde score; VAS=Visual Analogue Scale. Data are presented as least square means (SE) unless otherwise stated. Analyses are based on full analysis set (patients having a baseline visit and at least one follow-up visit) with no data imputation to replace missing data. \*P values are based on repeated-measures logistic regression models. For some of the variables, fewer patients were included in the analyses due to missing data, with the minimum being 86 patients in the MRI T2T arm (range 86-98) and 91 (range 91-99) in the conventional T2T arm.



DAS28-CRP<3.2 and no swollen joints or an MRI guided T2T strategy based on the same clinical T2T strategy and MRI targeting absence of BME. Patients were followed every 4 months over a 2 year follow-up period. In the MRI T2T arm contrast-enhanced MRI of the dominant hand 2nd-5th metacarpophalangeal joints and wrist was performed ahead of the clinical visit and evaluated for presence/absence of BME. Treatment was escalated according to a predefined treatment algorithm if target was not reached, starting with increments in csDMARD mono/combination therapy and then adding biologic DMARDs. The co-primary endpoints were 1) proportion of patients achieving DAS28-CRP remission (DAS28-CRP<2.6) and 2) proportion of patients with no radiographic progression (change in total Sharp/vdHeijde score  $\leq 0$ ) 24 months from baseline. Secondary outcomes included various clinical, functional, radiographic and MRI variables. Pearson's chi-square statistics and repeated-measures logistic regression models were used to assess primary and secondary outcomes.

**Results:** Primary and secondary clinical and radiographic outcomes at 24 months are presented in the table 1. 76 patients in the MRI T2T arm and 95 patients in conventional T2T arm completed the study. Of them 64 patients (85%) in the MRI T2T arm and 83 patients (88%) in the conventional T2T arm reached the primary clinical endpoint (chi-square=0.324,  $p=0.569$ ) and 49 patients (66%) in the MRI T2T arm and 58 (62%) in the conventional T2T arm reached the primary radiographic endpoint (chi-square=0.265,  $p=0.606$ ). ACR/EULAR remission rates, swollen joint count, patient VAS global and HAQ favoured the MRI T2T arm ( $p<0.038$ ).

**Conclusions:** Targeting absence of MRI BME in addition to a conventional T2T strategy in RA patients in clinical remission had no effect on the probability of achieving DAS28-CRP remission or halt radiographic progression. However, more patients achieved ACR/EULAR remission and improvements in physical function when MRI was used for treatment guidance.

Clinicaltrials.gov Identifier: NCT01656278

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Abstract OP0019 – Table 1

	PBO (n=105)	Bari 2 mg (n=105)	Bari 4 mg (n=104)
<b>Efficacy measure</b>		<b>Week 24</b>	
Resolution of arthritis or rash (SLEDAI-2K)	56 (53.3)	61 (58.1)	70 (67.3)*
SRI-4	50 (47.6)	54 (51.4)	67 (64.4)*
Flare (SFI, any severity)	54 (51.4)	45 (42.9)	34 (32.7)*
Flare (SFI, severe)	12 (11.4)	10 (9.5)	6 (5.8)
LLDAS	27 (25.7)	35 (33.3)	40 (38.5)*
DTJC	-5.59	-6.50	-6.86*
DSJC	-4.60	-4.12	-4.76
DCLASI activity score	-2.80	-1.66	-2.27
DWorst pain	-0.56	-1.17	-1.31*
DWorst fatigue	-1.18	-1.13	-1.52
<b>Safety measure</b>		<b>Weeks 0–24<sup>‡</sup></b>	
TEAEs	68 (64.8)	75 (71.4)	76 (73.1)
SAEs	5 (4.8)	11 (10.5)	10 (9.6)
Serious infections	1 (1.0)	2 (1.9)	6 (5.8)
Deep vein thrombosis	0	0	1 (1.0)

Disease Activity State (LLDAS), and tender joint count (TJC) change from baseline were also significantly improved for Bari 4 mg compared to PBO (table 1). No statistically significant differences were observed between Bari 2 mg and PBO in any of the above endpoints. Rates of AEs leading to treatment discontinuation and SAEs were higher for both Bari dose groups compared to PBO. There were no deaths, malignancies, major adverse cardiovascular events, tuberculosis, or serious herpes zoster infections; one SAE of deep vein thrombosis was reported in a patient with risk factors (Bari 4 mg group).

Data are n (%) patients, unless otherwise indicated. D=least squares mean change from baseline. <sup>‡</sup>Includes up to 30 days post treatment. CLASI=Cutaneous Lupus Erythematosus Disease Area and Severity Index; n=number of patients in the analysis population; n=number of patients in the specified category; TEAE=treatment emergent adverse event. \* $p\leq 0.05$ .

**Conclusions:** In patients with SLE receiving standard background therapy, once-daily oral Bari 4 mg was associated with significant clinical improvements compared to PBO and an acceptable benefit/risk profile. These findings support further study of Bari 4 mg as a potential therapy for patients with SLE.

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OP0019

**BARICITINIB IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE): RESULTS FROM A PHASE 2, RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY**

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**Background:** Baricitinib (Bari), an oral selective inhibitor of Janus kinase (JAK)1 and JAK2, has been approved for the treatment of RA in the EU and Japan.

**Objectives:** To report results from a 24 week (wk) global, Phase 2, double-blind, placebo (PBO)-controlled study of Bari in patients with SLE receiving standard therapy.

**Methods:** Patients with SLE (positive ANA or anti-dsDNA, clinical SLEDAI-2K $\geq 4$ , arthritis or rash required) receiving stable background SLE therapy were randomised 1:1:1 to PBO, or Bari (2- or 4 mg) once daily. The primary endpoint was resolution of SLEDAI-2K arthritis or rash at wk 24.

**Results:** Of 314 patients randomised, 79%, 82%, and 83% completed 24 wks of treatment in PBO, Bari 2 mg, and Bari 4 mg groups, respectively. At wk 24, a significantly greater proportion of patients in Bari 4 mg group compared to PBO achieved resolution of SLEDAI-2K arthritis or rash (67% vs 53%,  $p<0.05$ ); and SRI-4 response (64% vs 48%,  $p<0.05$ ). At Wk24, the proportion of patients achieving flare reduction (SELENA-SLEDAI Flare Index [SFI]), Lupus Low

OP0020

### VALIDATION OF NEW SYSTEMIC LUPUS ERYTHEMATOSUS CLASSIFICATION CRITERIA

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**Background:** This 4 phase project<sup>1</sup> jointly supported by EULAR and ACR has led to draft criteria.<sup>2</sup>

**Objectives:** To simplify and validate the new criteria in a large international cohort.

**Methods:** 23 expert centres each contributed up to 100 patients with SLE and with non-SLE diagnoses. Diagnoses were verified by 3 independent reviewers for 1,193 SLE and 1059 non-SLE patients. 500 randomly selected SLE and non-SLE patients formed the derivation cohort and the remainder the validation cohort.

**Results:** The criteria were fine-tuned and simplified, using ANA of  $\geq 1:80$  as entry criterion and a classification threshold of 10.

Renal	Class III/IV nephritis	10	Class II/V nephritis	8	Proteinuria $\geq 0.5$ g/day	4
Specific antibodies	Anti-Sm or Anti-dsDNA	6				
Mucocutaneous	ACLE	6	SCLE or DLE	4	Alopecia or oral ulcers	2
Serosa	Acute pericarditis	6	Effusion	5		
Musculoskeletal	Arthritis	6				
CNS	Seizures	5	Psychosis	3	Delirium	2
Blood	Autoimmune hemolysis or thrombocytopenia	4	Leukopenia	3		
Complement	Low C3 and C4	4	Low C3 or C4	3		
Anti-phospholipid	Anti-Cardiolipin or anti- $\beta$ 2-GPI or lupus anticoagulant	2				
Constitutional	Fever	2				

Sensitivity was close to the SLICC 2012 criteria, specificity maintained at the level of the ACR 1997 criteria. This performance was independently confirmed in the validation cohort.

	ACR 1997 criteria	SLICC criteria	New criteria
<b>Derivation</b>			
Sensitivity	84.63	96.81	98.00
Specificity	95.20	90.00	96.40
<b>Validation</b>			
Sensitivity	82.76	96.70	96.12
Specificity	93.38	83.62	93.38

**Conclusions:** The new criteria developed with EULAR/ACR support achieved sensitivity close to the SLICC criteria, while maintaining the specificity of the ACR criteria.

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OP0021

### DRAFT CLASSIFICATION CRITERIA FOR THE ANCA ASSOCIATED VASCULITIDES

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**Background:** Classification criteria for the ANCA-associated vasculitides (AAVs) were developed in the 1980s prior to the use of ANCA testing and newer imaging techniques. The Diagnostic and Classification of the Systemic Vasculitides (DCVAS) study is an international project to update classification criteria for the systemic vasculitides.

**Objectives:** Development of draft classification criteria for Granulomatosis with Polyangiitis (GPA), Microscopic Polyangiitis (MPA) and Eosinophilic Granulomatosis with Polyangiitis (EGPA).

**Methods:** Three phases: 1) Expert panel review of cases to identify gold standard set of new cases of small vessel vasculitis; 2) Item reduction of >8000 individual DCVAS items using data-driven and consensus methodology; 3) Lasso logistic regression models within each development set comparing each of the AAV types to other small and medium vessel vasculitides. Final criteria derived through clinical consensus, tested in validation set. The classification project has received financial support from the ACR and EULAR.

**Results:** The expert review process approved 2072/2871 (72%) of physician diagnosed DCVAS cases, including [724 GPA, 291 MPA, 226 EGPA, 51 polyarteritis nodosa (PAN), 220 other small vessel disease (SVV)]. Data driven and expert consensus resulted in 91 items retained. Draft criteria, and sensitivity and specificity in table 1.

**Abstract OP0021 – Table 1.** Draft classification criteria for the ANCA-associated vasculitides. \*Cartilagenous involvement: Inflamed ear or nose cartilage or hoarse voice/stridor, endobronchial involvement or saddle nose deformity

Granulomatosis with polyangiitis (GPA)	Microscopic polyangiitis (MPA)	Eosinophilic granulomatosis with polyangiitis (EGPA)
Blood nasal discharge, ulcers, crusting, congestion or blockage, or septal defect/perforation+3	Pauci-immune glomerulonephritis+3	Obstructive airways diseases+3
Cartilagenous involvement*+2	Bloody nasal discharge, ulcers, crusting, congestion or blockage, septal defect/perforation –3	Nasal polyps+3
Conductive or sensorineural hearing loss+1	pANCA or MPO-antibody positive+6	Mononeuritis multiplex or motor neuropathy+1
Pauci-immune glomerulonephritis+1	Fibrosis or ILD on chest imaging+3	Eosinophil count $\geq 1 \times 10^9/L$ +5
cANCA or PR3-antibody+5	cANCA or PR3-antibody –1	Extravascular eosinophilic predominant inflammation/eosinophils in bone marrow +2
pANCA or MPO-antibody –1	Eosinophil count $\geq 1 \times 10^9/L$ –4	cANCA or PR3-antibody –3
Eosinophil count $\geq 1 \times 10^9/L$ –4		Microscopic haematuria –1
Granuloma, extravascular granulomatous inflammation, or giant cells on biopsy+2		
Nodules, mass, cavitation on chest imaging+2		
Inflammation, consolidation, or effusion of the nasal/paranasal sinuses on imaging +1		
<b>Total score of <math>\geq 5</math> is needed for classification Sensitivity 93%, Specificity 94%</b>	<b>Total score of <math>\geq 6</math> is needed for classification Sensitivity 87%, Specificity 96%</b>	<b>Total score of <math>\geq 5</math> is needed for classification Sensitivity 88%, Specificity 98%</b>

**Conclusions:** Draft classification criteria for GPA, MPA and EGPA have been created which reflect current practice and have good sensitivity and specificity.

**Acknowledgements:** DCVAS sites and expert panel members

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WEDNESDAY, 13 JUNE 2018

## From NSAIDs to bDMARDs in SpA: what is new?\_\_\_

### OP0022 IS A PRIMARY GOOD RESPONSE TO NSAIDS PREDICTIVE OF THE SUBSEQUENT RESPONSE TO THE FIRST TNF INHIBITOR IN PATIENTS WITH RECENT AXIAL SPONDYLOARTHRITIS?

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**Background:** Good response to NSAIDs is a SpA feature included in classification criteria for axial spondyloarthritis (axSpA). Among patients eligible for a TNF inhibitor (TNFi), some patients may have never responded to NSAIDs (non-responders to NSAIDs) while others initially responded (responders to NSAIDs) but have secondarily escaped and need to be treated with biologics.

**Objectives:** Our aim was to determine if the initial response to NSAIDs is an independent predictive factor of a subsequent good response to the first TNFi in axSpA.

**Methods: Patients:** Patients from the prospective observational DESIR cohort of early axSpA cohort who started a TNFi over the 5 years of follow-up.

NSAIDs response and TNFi response definitions

NSAIDs response was defined by the item 'good response to NSAIDs according to Amor's criteria' at the inclusion visit. TNFi response was defined by the BASDAI50 response between the 'baseline' visit (last cohort visit before TNFi initiation) and the 'follow-up' visit (visit taking place after at least 8 weeks of TNFi treatment).

**Analysis:** We compared the characteristics of the NSAIDs responder to the non-responders and their response to the first TNFi.

We performed a multivariate logistic regression modelling the impact of an NSAID response to the TNFi response. We included known predictive factors of TNFi response in this model (age, gender, HLAB-B27, activity of the disease [ASDAS-CRP], CRP, X-ray and MRI sacroiliitis). To account for selection bias and for confirmation purpose, we applied a propensity score with Inverse Probability Weighting (IPW) method to predict TNFi response (SAS, version 9.2).

**Results:** Among the 708 patients of the cohort, 236 were included in the analysis. At the inclusion, the main characteristics were the following: 106 (44.7%) males, mean age 33.8±3.9 years, mean BASDAI 54.5±17.3 and 202 (85.6%) were NSAIDs responders.

The NSAIDs responder and non-responder groups were comparable at M0 except for HLA-B27 positive status: 59.9% vs 40.1%, p=0.041, CRP level: 13.4±20.3 mg/L vs 6.3±6.6 mg/L, p=0.027, history of psoriasis: 17.8% vs 35.3%, p=0.001 and BASDAI: 53.0±18.1 vs 61.8±13.2, p=0.001, in responder and non-responder patients, respectively.

The percentage of TNFi responders was 32.2% (65/202) and 23.5% (8/34) in the NSAIDs responder and non-responder groups, respectively (univariate analysis [OR 1.54 [95% CI: 0.7 to 3.6], p=0.313).

The multivariate logistic regression found the following independent factors of the TNFi response: gender [adjusted OR (aOR)=2.9 [CI95%: 1.4–6.0], p=0.004], age [aOR=0.9 [95% CI: 0.91 to 0.99], p=0.026], HLA-B27 status [aOR=2.5 [CI95%: 1.2–5.3], p=0.02], ASDAS-CRP score [aOR=1.6 [95% CI: 1.1 to 2.4], p=0.016], and MRI sacroiliitis [aOR=2.0 [CI95%: 1.0–4.2], p=0.054]. Response to NSAIDs was not significantly associated to the response to the TNFi [aOR=1.93 [95% CI: 0.6 to 6.3], p=0.275]. The IPW aOR confirmed the non-association between NSAIDs good response and TNFi good response: 1.60 [CI95%: 0.7–3.3], p=0.20.

**Conclusions:** The good response to NSAIDs according to the Amor's criteria does not seem to be an independent predictive factor of a good response to the first TNFi in early axSpA patients.

**Disclosure of Interest:** None declared

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### OP0023 EFFECT OF ANTERIOR UVEITIS, PSORIASIS AND INFLAMMATORY BOWEL DISEASE ON DRUG-SURVIVAL FOR TNF-INHIBITORS IN ANKYLOSING SPONDYLITIS

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**Background:** Tumour necrosis factor inhibition (TNFi) is the mainstay treatment for ankylosing spondylitis (AS) with a high disease activity. Whereas disease activity and sex have been shown to affect drug-survival for TNFi in AS, the impact of typical AS-comorbidities, such as anterior uveitis, psoriasis and inflammatory bowel disease (IBD), on the drug-survival of TNFi in AS is less well understood.

**Objectives:** To determine the impact of comorbidity with anterior uveitis, psoriasis and IBD on drug-survival in patients with AS starting treatment with a first TNFi.

**Methods:** Swedish biologics-naïve patients with AS starting a 1st TNFi July 1 2006 – December 31 2015, were identified in the Rheumatology Quality Register, and followed from treatment start until treatment discontinuation. Censoring occurred at the first of: December 31 2015, death, emigration, or loss of follow-up. Comorbidities, and potential confounders, were identified through linkage to six other national registers.

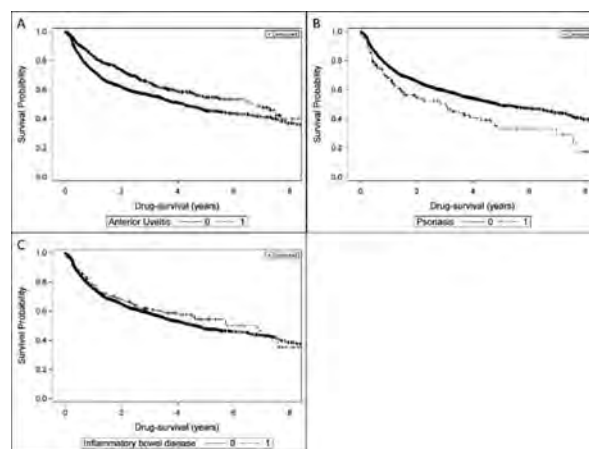
We calculated survival curves and hazard ratios (HRs) for each comorbidity and the risk of TNFi discontinuation. HRs were adjusted for sex, age, CRP, peripheral arthritis, type of TNFi and BASDAI at baseline. Additional models were also adjusted for other chronic morbidities (cardiovascular disease, affective disease, diabetes, malignancies, chronic lung disease and chronic kidney failure), and for socioeconomic status (length of education, household income, sick-leave, country of birth and civil status), respectively.

**Results:** 2577 patients (71% men) were identified, 27% had a previous history of anterior uveitis, 7% IBD and 6% psoriasis. A history of anterior uveitis was associated with a lower risk of TNFi discontinuation (HR 0.72; 0.62–0.83), whereas presence of psoriasis was associated with an increased risk (HR 1.48; 1.18–1.86). No association was found between presence of IBD and risk of TNFi discontinuation. Models adjusting for disease activity, morbidities, and socioeconomic status resulted in an attenuated association for psoriasis (table 1). The impact of each comorbidity on drug-survival is visualised in figure 1.

**Abstract OP0023 – Table 1.** HR for association between inflammatory comorbidities and risk of discontinuation of TNFi treatment in AS

Comorbidity	A	B	C	D
Anterior uveitis	0.72 (0.62–0.83)	0.71 (0.60–0.84)	0.72 (0.61–0.85)	0.75 (0.62–0.90)
Psoriasis	1.48 (1.18–1.86)	1.35 (1.04–1.76)	1.28 (0.98–1.67)	1.33 (0.99–1.78)
IBD	0.91 (0.71–1.16)	0.84 (0.65–1.09)	0.82 (0.63–1.07)	0.83 (0.62–1.10)

A)univariable; B-D) adjusted for baseline measures; C) also adjusted for other morbidity and D) also adjusted for socioeconomic status.



**Abstract OP0023 – Figure 1** Survival probability (Kaplan-Meier plots) for persisting on a first-line TNFi, for patients with ankylosing spondylitis, dependant on having a history of (A) anterior uveitis, (B) psoriasis or (C) inflammatory bowel disease.



**Conclusions:** Comorbidities typically associated with AS affect TNFi drug survival, but in different directions. Possible explanations include a differential effect of TNFi on these morbidities themselves, or other inherent differences in the AS inflammatory phenotype. The association with psoriasis decreased after adjustment, suggesting the influence of other factors. The role of inflammatory comorbidities in determining response and persistence of TNFi should be further examined.

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OP0024

#### WHAT HAPPENS TO PATIENTS WITH ANKYLOSING SPONDYLITIS WHO START A FIRST BIOLOGIC? A SWEDISH STUDY OF TREATMENT TRAJECTORIES IN CLINICAL PRACTICE

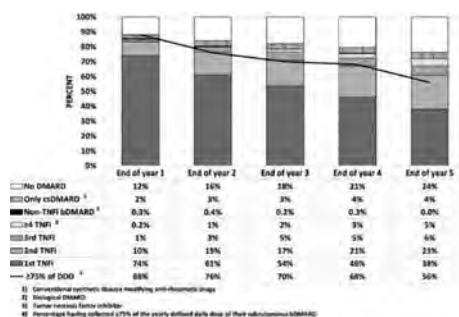
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**Background:** Clinical trials have shown that 40%–50% of patients with ankylosing spondylitis (AS) achieve a good response ( $\geq 40\%$  improvement) to treatment with tumour necrosis factor inhibitors (TNFi). By contrast, observational studies indicate that less than two out of three patients continue their first biological disease modifying anti-rheumatic drug (bDMARD) up to two years. During the past six years, five TNFi and one IL-17-inhibitor have been marketed for AS in Sweden. Yet, an assessment of long-term treatment trajectories in AS is lacking. In particular, there is a need for a better understanding of the proportion of patients who fail their first bDMARD, when this happens, and which drugs become their ensuing treatments.

**Objectives:** To describe contemporary five-year treatment trajectories for patients initiating a first ever bDMARD in AS, and to explore whether the dose of bDMARD is gradually tapered in those patients who remain stable on their bDMARD treatment.

**Methods:** Swedish patients with AS starting a first ever bDMARD in 2010–2015 were identified in the Swedish Rheumatology Quality Register (SRQ). At the end of each full year (1–5 years) after treatment start, the treatment status of each patient was determined. Censoring occurred at the first of: death, emigration, 31 December 2015 or loss to follow-up. In addition, data on collected prescriptions for the subcutaneous bDMARDs were retrieved from the National Prescribed Drug Register. For patients remaining on their first subcutaneous bDMARD, according to SRQ, the proportion of patients collecting  $\geq 75\%$  of the yearly 'defined daily doses' (DDD) at a pharmacy during each full year was determined.

**Results:** 1698 patients with AS starting a first bDMARD in the study-period were identified, all of which were TNFi. After the end of the first year, 74% remained on their first bDMARD and after five years 38% (figure 1). Of the 72% of patients who remained on any bDMARD after five years, 85% were on their first or second bDMARD. After five years 24% were not on any DMARD and around five percent of the patients discontinuing bDMARD treatment did so due to low disease activity or remission. Among those remaining on their first subcutaneous bDMARD the proportion collecting  $\geq 75\%$  of the yearly DDD gradually decreased from 88% to 56% over the 5 years of follow-up (black line in figure 1).



**Abstract OP0024** – Figure 1 Proportion of patients with ankylosing spondylitis on each treatment after 1–5 years of follow-up from initiating their first bDMARD

**Conclusions:** While a minority of patients with AS remain on their first-line bDMARD after 5 years of treatment, most are still on any bDMARD. Further, despite a low rate of discontinuation due to remission, one fourth of patients no longer use any bDMARDs treatment after 5 years. Patients remaining stable on treatment gradually but substantially decrease their use over time.

**Disclosure of Interest:** U. Lindström: None declared, T. Olofsson: None declared, S. Wedrén: None declared, I. Qirjazo: None declared, J. Askling Grant/ research support from: JA has received grants from Abbvie, BMS, Merck, Pfizer, Roche, Samsung, UCB, mainly for safety monitoring via the Swedish ARTIS system

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OP0025

#### IDENTIFICATION OF PREDICTORS OF STRUCTURAL DAMAGE PROGRESSION IN THE SACROILIAC JOINTS IN PATIENTS WITH EARLY AXIAL SPONDYLOARTHRITIS ON A LONG-TERM ANTI-TNF TREATMENT

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**Background:** Several observational studies showed a low, but still detectable progression of structural damage in the sacroiliac joints (SIJ) in patients with axial spondyloarthritis (axSpA) over 2 to 5 years. Few predictors of progressions, such as elevated C-reactive protein (CRP) and active inflammation on magnetic resonance imaging (MRI), have been identified, mostly in patients not treated with TNF inhibitors. To date, it is not clear whether these predictors also work in patients treated with anti-TNF agents and whether anti-TNF therapy is able to retard such a progression.

**Objectives:** To evaluate the radiographic progression in the sacroiliac joints (SIJ) and to identify predictors of such a progression during long-term (up to six years) treatment with tumour necrosis factor (TNF) blocker etanercept in patients with early axSpA.

**Methods:** In the ESTHER trial<sup>1</sup> a total of 76 patients with early (up to 5 years symptom duration) and active axSpA were randomised to be treated with either etanercept or sulfasalazine for one year. Between year 1 and year 6, all patients who continued in the study were treated with etanercept. X-rays of SIJ were collected at baseline and every 2 years thereafter. Two trained readers, who were blinded for all clinical data, scored independently the SIJ x-rays in a concealed and randomly selected order, according to the grading system of the modified New York (mNY) criteria (grade 0 to 4). Patients with bilateral sacroiliitis of grade  $\geq 2$  or unilateral of grade  $\geq 3$  were classified as radiographic axSpA (r-axSpA), and as non-radiographic axSpA (nr-axSpA) otherwise. The sacroiliitis sum score (0–8) was calculated as a sum of means of both readers for the left and right SIJ. Active and chronic inflammatory changes on MRI of SIJ were assessed at baseline, year 2 and year 4 according to the Berlin MRI scoring system. A longitudinal mixed model analysis was performed to identify predictors of the radiographic sacroiliitis progression.

**Abstract OP0025 – Table 1.** Longitudinal mixed model analysis of the association between structural damage in the sacroiliac joints (sacroiliitis sum score) and disease-related parameters in patients with early axSpA treated with etanercept for up to 6 years.

Disease-related parameters	Univariable analysis $\beta$ (95% CI)	Model 1 $\beta$ (95% CI)	Model 2 $\beta$ (95% CI)
Elevated CRP ( $>5\text{mg/l}$ )	0.44 (0.13 – 0.75)	-	0.45 (0.11 – 0.78)
SIJ osteitis score on MRI (0-24)	0.05 (0.01 – 0.09)	0.04 (0.01 – 0.08)	-
Age, years	0.00 (-0.02 – 0.01)	-0.00 (-0.02 – 0.01)	-0.00 (-0.02 – 0.01)
Male sex	-0.03 (-0.35 – 0.27)	-0.18 (-0.53 – 0.16)	0.00 (-0.33 – 0.33)
HLA-B27 positivity	-0.07 (-0.47 – 0.32)	-0.08 (-0.55 – 0.38)	-0.08 (-0.54 – 0.36)
Treatment duration with ETN, years	-0.04 (-0.13 – 0.03)	-0.03 (-0.15 – 0.09)	-0.01 (-0.12 – 0.09)
Symptoms duration, years	-0.01 (-0.07 – 0.05)	0.01 (-0.07 – 0.11)	0.01 (-0.07 – 0.10)

axSpA, axial spondyloarthritis; CRP, C-reactive protein; CI, confidence interval; ETN, etanercept; MRI, magnetic resonance imaging; SIJ, sacroiliac joints.

**Results:** Totally, 55 patients with axSpA contributing with 159 SIJ radiographs were included in the analysis. At baseline, 19 patients were classified as r-axSpA and 36 as nr-axSpA based on the independent SIJ reading. Radiographic progression from nr- to r-axSpA was observed in 5 (18%) patients between baseline and year 2. Progression decelerated to 4.1% between year 2 and 4, and no further progression was observed up to year 6. The mean  $\pm$ SD change of sacroiliitis sum score was  $0.13 \pm 0.73$ ,  $-0.26 \pm 0.76$  and  $-0.09 \pm 0.67$ , in the time intervals baseline-year 2, year 2 year 4, and year 4 year 6, respectively. In the longitudinal mixed model analysis, elevated CRP (model 2) and osteitis on MRI (model 1) were independently and significantly associated with a higher sacroiliitis sum score (table 1).



**Conclusions:** Long-term therapy with a TNF blocker seems to decelerate progression of structural damage in the SIJ. Elevated CRP and presence of osteitis in MRI were independently associated with SIJ radiographic progression.

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**Disclosure of Interest:** V. Rios Rodriguez Consultant for: Abbvie, Novartis, K.-G. Hermann Speakers bureau: Abbvie, MSD, Pfizer, UCB, H. Haibel: None declared, C. Althoff: None declared, O. Behmer Employee of: Pfizer, J. Sieper Grant/research support from: Abbvie, MSD, Pfizer, Consultant for: Abbvie, MSD, Pfizer, UCB, D. Poddubnyy Grant/research support from: Abbvie, MSD, Novartis, Consultant for: Abbvie, BMS, MSD, Novartis, Pfizer, UCB, Speakers bureau: Abbvie, BMS, Janssen, MSD, Novartis, Pfizer, Roche, UCB

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#### OP0026 ADALIMUMAB SERUM CONCENTRATION FAILS TO PREDICT ACHIEVEMENT OF SUSTAINED REMISSION OR ABSENCE OF FLARE FOR PATIENTS WITH NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS IN THE ABILITY-3 STUDY

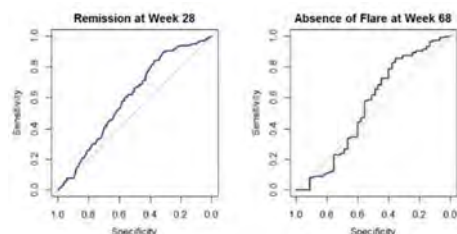
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**Background:** In patients (pts) with active non-radiographic axial spondyloarthritis (nr-axSpA) in the ABILITY-3 study who achieved sustained remission with adalimumab (ADA), continued ADA therapy was associated with significantly fewer pts flaring than treatment withdrawal. Sustained remission is an important treatment goal in pts with nr-axSpA, but factors predicting sustained remission and absence of flare are unknown.

**Objectives:** To determine whether an ADA concentration threshold is predictive of achievement of sustained remission and absence of flare in pts with nr-axSpA.

**Methods:** ABILITY-3 included a 28-wk open-label (OL) ADA (40 mg every other wk) lead-in in which pts who achieved sustained remission (ASDAS <1.3 at wks 16, 20, 24, and 28) were randomised to double-blind (DB) placebo (PBO) or continued ADA for 40 wks (68 wks total). Pts not achieving remission were discontinued at wks 20, 24, or 28. The primary efficacy variable was the proportion of pts who did not experience a flare (ASDAS  $\geq 2.1$  at 2 consecutive visits) by wk 68. Pts who flared received OL ADA rescue. ADA trough concentrations at wks 12 or 28 were used to predict achieving sustained remission by wk 28 (all OL patients, n=673) and absence of flare at wk 68 (patients randomised to DB ADA, n=152). Threshold analysis was conducted by constructing receiver operating characteristic (ROC) curves (R Ver 3.3.3) to assess predictive ADA trough concentration thresholds based on specificity and sensitivity values.

**Results:** Of 673 pts enrolled in the OL phase, 305 met criteria for remission at wk 28 and were randomised to DB treatment. Mean  $\pm$ SD ADA trough concentrations were  $6.68 \pm 5.23$   $\mu$ g/mL at wk 12 and  $8.36 \pm 5.27$   $\mu$ g/mL at wk 28. During the DB phase, 81 and 45 pts flared and 68 and 36 pts received  $\geq 12$  wks of OL ADA rescue in PBO (n=153) and ADA (n=152) arms, respectively. ADA mean  $\pm$ SD trough concentration at wk 68 for pts randomised to DB ADA with flare ( $7.64 \pm 5.22$   $\mu$ g/mL) was slightly lower than for DB ADA pts without flare ( $8.12 \pm 4.35$   $\mu$ g/mL). ROC curves showed AUC values  $\leq 0.6$  for achieving sustained remission by wk 28 and absence of flare at wk 68, with no concentration threshold meeting sensitivity and specificity criteria for reliable prediction of such endpoints (figure 1).



Abstract OP0026 – Figure 1 Receiver operating characteristic curves to predict sustained remission by week 28 and absence of flare at week 68 by adalimumab serum concentration

**Conclusions:** ROC analyses did not identify an ADA trough concentration threshold that reliably predicted whether a pt with nr-axSpA would achieve sustained remission (by wk 28) or absence of flare (at wk 68).

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**Disclosure of Interest:** N. Kwatra Employee of: AbbVie, M. Magrey Grant/research support from: Amgen, AbbVie, and UCB Pharma, Consultant for: UCB and Janssen, P. Mease Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Lilly, Novartis, Pfizer, Sun Pharma, and UCB, Consultant for: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Lilly, Novartis, Pfizer, Sun Pharma, and UCB, Speakers bureau: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Genentech, Janssen, Novartis, Pfizer, and UCB, J. Sieper Consultant for: AbbVie, Janssen, Lilly, Merck, Novartis, Pfizer, Sun Pharma, and UCB, Speakers bureau: AbbVie, Janssen, Lilly, Merck, Novartis, Pfizer, and UCB, R. Landewe Grant/research support from: Abbott, Amgen, Centocor, Novartis, Pfizer, Roche, Schering-Plough, UCB, and Wyeth, Consultant for: Abbott/Abbvie, Ablynx, Amgen, Astra-Zeneca, Bristol Myers Squibb, Celgene, Janssen (formerly Centocor), Galapagos, GlaxoSmithKline, Novartis, Novo-Nordisk, Merck, Pfizer, Roche, Schering-Plough, TiGenix, UCB, and Wyeth, Speakers bureau: Abbott/Abbvie, Amgen, Bristol Myers Squibb, Janssen (formerly Centocor), Merck, Pfizer, Roche, Schering-Plough, UCB, and Wyeth, X. Wang Employee of: AbbVie, A. Lertratanakul Employee of: AbbVie, J. Anderson Employee of: AbbVie, N. Mostafa Employee of: AbbVie

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#### OP0027 CHARACTERISTICS OF CYTOKINES AND CHANGES IN INTERLEUKIN-17 LEVELS IN THE SYNOVIAL FLUID OF PATIENTS WITH ANKYLOSING SPONDYLITIS ON TREATMENT WITH BIOLOGICS

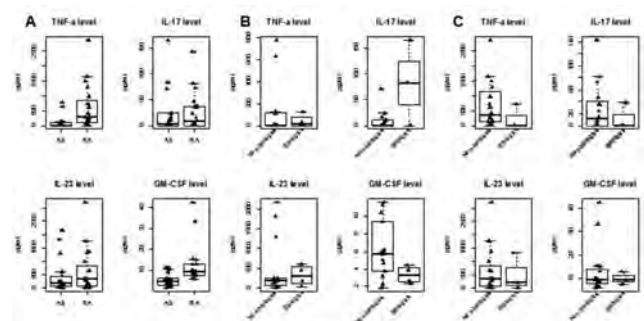
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**Background:** Biologic drugs targeting the inflammatory cytokines have been recommended in rheumatoid arthritis (RA) and ankylosing spondylitis (AS). Yet, some patients require a change in treatment because an adequate response is not achieved.

**Objectives:** The current study aimed to evaluate the levels of tumour necrosis factor alpha (TNF- $\alpha$ ), interleukin (IL)-17, IL-23, and granulocyte-macrophage colony-stimulating factor (GM-CSF) in the joint fluid in patients with AS and RA and identify the important cytokines related with treatment-response.

**Methods:** Synovial fluid was obtained from 18 patients with AS and 19 with RA who suffered from arthritis of the knee; and the levels of the cytokines were measured. The differences in their levels between patients with AS and RA, and between patients treated with and without biologics (biologics group and non-biologics group) were analysed.

**Results:** TNF- $\alpha$  and GM-CSF levels in patients with AS were significantly lower than those in patients with RA (figure 1A, both  $p < 0.01$ ); however, IL-17 and IL-23 levels were not significantly different between the two groups. Furthermore, levels of IL-17 were markedly elevated in the biologics group compared with the non-biologics group in AS (figure 1B,  $p = 0.04$ ). However, in RA, there were no significant differences between the non-biologics and biologics group (figure 1C).



**Conclusions:** In AS, IL-17 in synovial fluid is a good marker of non-response to biologics and may be a good target for non-responders to TNF inhibitor.

**Disclosure of Interest:** None declared

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OP0028

### EFFICACY AND SAFETY OF BCD-085, A NOVEL IL-17 INHIBITOR, IN ANKYLOSING SPONDYLITIS. RESULTS OF PHASE 2 CLINICAL STUDY

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**Background:** BCD-085 is an innovative humanised monoclonal antibody against interleukin-17 with genetically modified Fc- and CDR-regions, aimed to improve treatment outcomes in patients with several autoimmune disorders.

**Objectives:** This abstract presents the results of double-blind placebo controlled dose-finding phase II clinical study of efficacy and safety of subcutaneous BCD-085 in patients with ankylosing spondylitis.

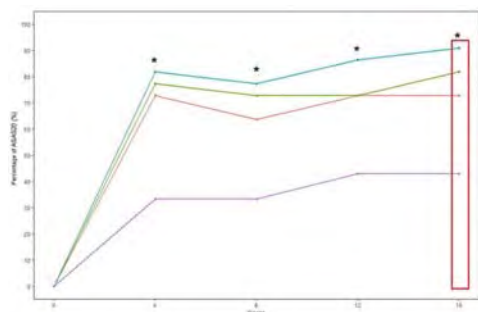
**Methods:** The study was conducted as international multicenter randomised double-blind placebo controlled study. The study enrolled 88 adults with active AS. Patients were randomised in 4 study arms in 1:1:1:1 ratio to receive 40, 80 or 120 mg of BCD-085 or placebo. In the active period of the study, patients received the test drug/placebo SC injections once weekly for the first three weeks of treatment and then every other week till Wk 12. After Wk 12 all patients underwent follow-up for 4 weeks.

**Results:** Efficacy: BCD-085 is superior to placebo in doses 80 and 120 mg. ASAS20 at wk 16 was reached by 81.82%, 90.91% and 42.86% of patients in BCD-085 80 mg, 120 mg and placebo arm respectively ( $p=0.008$ , 95% CI for difference in proportion [12.36%; 65.56%];  $p=0.001$ , 95% CI: 23.71% to 72.39%), superiority margin 10%). Significant reduction of AS activity was revealed for all BCD-085 arms: by Wk 4 BASDAI and ASDAS-CRP scores decreased and maintained achieved levels till the end of the study. Other secondary endpoints (ASAS40, ASAS5/6, BASMI, BASFI, BASDAI, MASES, chest expansion, QoL, spinal pain) had the corresponding dynamics: by the time of second evaluation (Wk 1 for spinal pain, Wk 4 for other endpoints) significant improvement with no further negative changes was revealed. For all evaluated endpoints the most pronounced response was established for BCD-085 120 mg arm. In placebo arm no significant dynamics was shown.

**Safety:** All arms had highly similar safety profiles. Most of AEs were presented as mild or moderate laboratory abnormalities (ANC decreased, WBC increased) and moderate arterial hypertension. The rates of AEs were equivalent for all BCD-085 doses and placebo. There were no cases of SAEs, treatment discontinuation due to safety reasons or local reactions. Immunogenicity assessment did not detect formation of binding antibodies.

Abstract OP0028 – Table 1. Summarised safety data

Parameter	Arm				P-value
	BCD-085 40 mg (n=22)	BCD-085 80 mg (n=22)	BCD-085 120 mg (n=22)	Placebo (n=22)	
Any AE	11 (50.00%)	6 (27.27%)	4 (18.18%)	7 (31.82%)	0.183
Therapy-related AEs	5 (22.73%)	4 (18.18%)	1 (4.55%)	5 (22.73%)	0.354
Grade 3-4 AEs	1 (4.55%)	2 (9.09%)	0	1 (4.55%)	0.900



Abstract OP0028 – Figure 1. ASAS20 response throughout the study (\* – statistically significant difference between BCD-085 and placebo arms).

**Conclusions:** Treatment with BCD-085 leads to significant improvement in all AS symptoms in comparison with placebo. The dose of 120 mg of BCD-085 had

the most pronounced effect. The drug was well tolerated in all doses with no differences with placebo in safety profiles.

**Disclosure of Interest:** V. Mazurov: None declared, S. Erdes: None declared, E. Kunder: None declared, N. Soroka: None declared, P. Shesternya: None declared, S. Smakotina: None declared, T. Raskina: None declared, D. Krechikova: None declared, T. Dubinina: None declared, A. Ereemeeva Employee of: JCS BIOCAD, E. Dokukina Employee of: JCS BIOCAD, E. Chernyaeva Employee of: JCS BIOCAD, R. Ivanov Employee of: JCS BIOCAD

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OP0029

### CLINICAL EFFECT OF VEDOLIZUMAB ON ARTICULAR MANIFESTATIONS IN PATIENTS WITH SPONDYLOARTHRITIS ASSOCIATED WITH INFLAMMATORY BOWEL DISEASE

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**Background:** Data on the effects of vedolizumab on joint manifestations remain controversial.<sup>1,2</sup>

**Objectives:** The purpose of this study was to evaluate baseline characteristics of crohn's disease (CD) and ulcerative colitis (UC) patients treated with vedolizumab, assess the effect of vedolizumab on joint manifestations in patients with inflammatory bowel disease (IBD)-associated Spondyloarthritis (SpA), and evaluate new onset of SpA under VDZ.

**Methods:** This single-centre, retrospective and observational study was conducted from July 2014 to July 2017. The charts of all patients with IBD who had undergone treatment with vedolizumab for more than 3 months were reviewed. The patients' demographic and clinical characteristics were collected. Data on IBD-associated SpA were collected as well as new onset of SpA under VDZ. The ASAS criteria were used to establish the diagnosis of SpA.

**Results:** Patient characteristics and main results are shown in table 1. A total of 171 patients diagnosed with IBD were treated with vedolizumab from July 2014 to July 2017. Notably, 97.1% of patients had been previously treated with at least one TNF- $\alpha$  inhibitor. All patients included in this study completed the induction phase at last observation, and the mean follow-up of the entire cohort was 14.3  $\pm$  12.0 months. Ten (5.8%) patients had a history of IBD-associated SpA but were in clinical remission at the time of initiation of VDZ, whereas 4 (2.4%) had active SpA when VDZ was started. First, no clinical benefit on SpA following initiation of VDZ was found in those 4 patients with active SpA. Second, exacerbation of SpA in patients with clinical remission at initiation of VDZ was found in 6/10 patients whereas no effect was reported in the remaining 4/10 patients. All those 14 patients with IBD-associated SpA were under TNF inhibitors just before starting VDZ. Finally, new onset of SpA induced by VDZ was reported in 1 patient.

Abstract OP0029 – Table 1. Characteristics of patients and main results

Variable	n=171
Age (years), mean $\pm$ SD	37.8 $\pm$ 12.9
Female gender, n (%)	110 (64.3)
Body mass index (kg/m <sup>2</sup> ), mean $\pm$ SD	23.7 (4.8)
Type of disease, n (%)	104 (60.8)
- Crohn's disease	67 (39.2)
- Ulcerative colitis	
Duration of disease (years), mean $\pm$ SD	10.5 (7.6)
Duration of follow-up under vedolizumab (months), mean $\pm$ SD	14.3 (12.0)
IBD-associated SpA, n (%)	157 (91.8)
- No history	10 (5.8)
- History (inactive at initiation of VDZ)	4 (2.4)
- Active at initiation of VDZ	
Clinical benefit on SpA following initiation of VDZ (n=4)	4/4 (100)
- No clinical benefit	0/4 (0)
- Improvement	
Exacerbation of SpA in patients with clinical remission at initiation of VDZ (n=10)	6 (60)
- Yes	4 (40)
- No	
New onset of SpA induced by VDZ	1 (<1)

**Conclusions:** Vedolizumab does not seem to show any efficacy in IBD-associated SpA and might even induce exacerbation or new onset of SpA. Inception cohort studies are needed to better evaluate the effect of vedolizumab on joint manifestations.

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**Disclosure of Interest:** None declared

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**WEDNESDAY, 13 JUNE 2018:** RA therapy – new molecules and new strategies

OP0030

**CORTICOSTEROID BRIDGING STRATEGIES WITH METHOTREXATE MONOTHERAPY IN EARLY RHEUMATOID AND UNDIFFERENTIATED ARTHRITIS; A COMPARISON OF EFFICACY AND TOXICITY IN THE TREACH AND IMPROVED STUDIES**

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**Background:** What is the optimal glucocorticoid (GC) bridging therapy with MTX monotherapy in early arthritis?

**Objectives:** To compare short term clinical efficacy of high and low dose GC tapering schedules with MTX monotherapy in 2 clinical trials in early rheumatoid arthritis (RA) and undifferentiated arthritis (UA) patients.

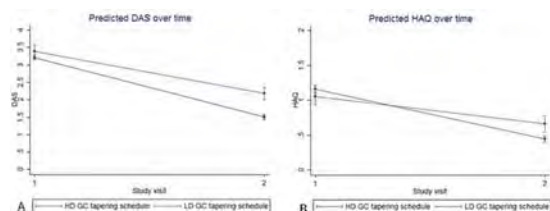
**Methods:** In tREACH, early RA and UA (arthritis in  $\geq 1$  joint(s), <1 year symptoms) patients were randomised to 3 different treatment arms. For this analysis we only use the data of arm C: oral GCs (prednisone) (15 mg/day, tapered to 0 in 10 weeks) with MTX monotherapy (25 mg/week); low dose GC tapering schedule (LDGC).

In IMPROVED RA and UA (arthritis in  $\geq 1$  joint and  $\geq 1$  other painful joint, <2 years symptoms) patients were treated with prednisone (60 mg/day, tapered in 7 weeks to 7.5 mg/day, continued to 4 months)+MTX monotherapy (25 mg/week); high dose GC tapering schedule (HDGC). We compared %DAS-remission (<1.6) and low disease activity ( $\leq 2.4$ ) at first evaluation (3 months tREACH, 4 months IMPROVED) and DAS and HAQ over time. After multivariate normal imputation we applied generalised estimating equations (GEE) for linear outcomes and logistic regression models for binary outcomes, adjusted for potential baseline confounders (figure 1). Adverse events were compared between treatment arms using  $\chi^2$ -square tests.

**Results:** Patients with a HDGC (n=610) had shorter symptom duration and higher HAQ, were less often seropositive (ACPA positive 56.0% vs 77.3%, RF positive 58.1% vs 65%) and more often had UA (20.3% vs 2.1%) than patients with a LDGC (n=97). Baseline DAS was comparable.

At the first evaluation time point (median 3.06 (IQR 2.99–3.22) months in LDGC, 4.01. (3.8–4.17) in HDGC) DAS and HAQ had decreased significantly less after 3 months LDGC: DAS  $\beta$  (95% CI) 0.500 (0.276; 0.725), and HAQ 0.330 (0.189; 0.470) than after 4 months HDGC (figure 1).

Compared to the HDGC patients, patients with the LDGC had a significantly lower chance of achieving DAS-remission 63.4% vs 28.9% (OR (95% CI) 0.215 (0.124; 0.373) and low disease activity 80.6% vs 55.7% ((OR (95% CI) 0.249 (0.143; 0.435)). Presence of ACPA was positively associated with achieving DAS-remission in the HDGC group, but not in the LDGC group. Per 100 patient years, 7.98 serious adverse events were reported in the HDGC and 23.4 in the LDGC (p=0.004). Hypertension, hyperglycemia (>7.8 mmol/L), gastrointestinal complaints and liverenzymes above normal were reported in similar frequencies across all groups. In patients with a LDGC more headaches, skin rashes, creatinine above normal range and any decrease in haematology blood counts were reported (data not shown).



**Abstract OP0030** – Figure 1 A: Predicted DAS over time, B: Predicted HAQ over time. All predictions are from multiple imputed models, adjusted for age, gender body mass index, presence of ACPA, presence of rheumatoid factor, symptom duration, effect over time (in GEE) and baseline DAS (for binary out-comes). DAS, Disease Activity Score; HAQ Health Assessment Questionnaire; HD GC, high dose glucocorticoids, LD GC, low dose glucocorticoids

**Conclusions:** In early arthritis patients, GC bridging therapy with prednisone 60 mg daily tapered in 7 weeks to and continued at 7.5 mg daily in combination with MTX monotherapy was associated with better clinical outcomes and without additional effects than prednisone 15 mg daily tapered to nil in 10 weeks in combination with MTX monotherapy, after correction for baseline age, gender, DAS, body mass index, presence of ACPA, presence of rheumatoid factor, symptom duration, and (in GEE) time from baseline.

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OP0031

**THE IMPORTANCE OF ASSESSING MULTIPLICATIVE AND ADDITIVE INTERACTION: EXAMINING THE EFFECT OF GLUCOCORTICOID THERAPY ON MORTALITY IN PATIENTS WITH RHEUMATOID ARTHRITIS AND CONCOMITANT TYPE II DIABETES**

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**Background:** Glucocorticoids (GC) are widely used to treat rheumatoid arthritis (RA), however they are known to have risks associated with them. It has been shown that GCs increase the risk of diabetes mellitus (DM). A few studies have investigated the long-term effects of GC use on outcomes in DM, but not in RA specifically. As people with RA already have increased risk of cardiovascular (CV) disease, the additional burden of DM and GCs may be important. If the effect of GCs was dependent on DM we would say there is effect modification and this can be on the additive scale, corresponding to variation in the absolute treatment effect, e.g. the risk difference (RD), across DM status, or the multiplicative scale, corresponding to variation in the relative treatment effect e.g. the rate ratio (RR).<sup>1</sup>

**Objectives:** To examine in patients with RA 1) whether all-cause and CV mortality rates differ by GC and DM status, and 2) whether DM modifies the relationship between GC and all-cause and CV mortality on multiplicative and additive scales.

**Methods:** Patients with RA and linkage to mortality data were identified from the Clinical Practice Research Datalink (n=9085), a database of primary care electronic medical records in the UK. RR and RD for ever GC use were calculated by DM status. Cox proportional hazards (PH) regression models were fitted with an interaction term for DM and use of GC to assess multiplicative interaction. Additive interaction was measured with the Relative Excess Risk due to Interaction (RERI)<sup>2</sup> where a value different from zero indicates a difference in the absolute effect of treatment.

**Results:** Those with DM and ever treated with GCs had a 3-fold increased all-cause mortality RR (95% CI: 2.27, 4.09) whilst those without DM had a slightly higher RR (3.46 (95% CI: 2.95, 4.07)). However those with DM had a higher RD: 36.46 deaths per 1000 patient years (pyrs) (95% CI: 27.5, 45.41) compared to those without DM: RD 22.83 deaths per 1000 pyrs (95% CI: 19.83, 25.82) because of higher baseline mortality rates. A similar pattern was seen for CV mortality. The adjusted Cox PH model for all-cause mortality showed no evidence of multiplicative interaction, but there was significant additive interaction (RERI 0.86 (95% CI: 0.18, 1.54)). For CV mortality there was no interaction on either scale.

**Conclusions:** Methodologically, this study showed assessing interaction on the additive and multiplicative scales can lead to different conclusions and should be considered carefully. In this study significant interaction was seen on additive scale but not on the multiplicative scale due to higher baseline rates in patients with DM. Clinically, this study provides some evidence that long-term GC therapy may be particularly harmful in patients with RA and DM.

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OP0032

### MALIGNANCIES AND SERIOUS INFECTIONS IN RANDOMISED CONTROLLED TRIALS OF JANUS KINASE INHIBITORS IN PATIENTS WITH RHEUMATOID ARTHRITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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**Background:** Two JAK inhibitors are currently approved by different agencies worldwide for their use in patients with rheumatoid arthritis. The safety profile of these agents has been of interest since the approval of the first JAK inhibitor, particularly the risk of developing malignancies or serious infections.

**Objectives:** We conducted a systematic review and meta-analysis of phase 2 and phase 3 trials to evaluate these two outcomes in patients receiving JAK inhibitors for rheumatoid arthritis.

**Methods:** We performed a search in 5 electronic databases and also searched clinicaltrials.gov, Food and Drug Administration, and European Medicines Agency. In addition, the bibliography list of included studies was also screened to search for further citations not retrieved from other sources. We included controlled trials evaluating the efficacy of a JAK inhibitor (i.e., tofacitinib baricitinib, filgotinib, peficitinib, ABT-494, or decenotinib). Two reviewers independently screened studies, evaluated their risk of bias, and extracted data. Primary outcome data included number and type of malignancies and infections and time point of occurrence when available. The reported publications was considered the primary source of data for all trials. Serious infections were defined as those meeting the criteria for a serious adverse events such as a fatal, life threatening, or leading to hospitalisation.

**Results:** Thirty-one trials were analysed, reporting data on 13 945 patients. Follow-up of the included trials ranged between 4 and 52 weeks with a median of 24 weeks. The risk of attrition bias was judged low for most studies. The reported rates of malignancies and serious infections across studies ranged from 0% and 0.7% to 2.0%, and 5.4%, respectively. Most commonly reported malignancies were lung cancer, melanoma, nonmelanoma skin cancer, basal cell and squamous cell carcinoma. Patients receiving the combination of JAK inhibitor plus methotrexate or JAK inhibitor monotherapy had higher rates of malignancies, compared with methotrexate between 12 and 24 weeks before the rescue treatment was implemented, but the difference did not reach statistical significance (odds ratio (OR) 2.48, 95% confidence interval (CI) 0.76 to 8.11 and 1.39, 95% CI: 0.21 to 9.11, respectively). Regarding serious infections, the JAK inhibitor groups had similar rates to those observed in the control groups (OR 0.90, 95% CI: 0.38 to 0.92, 95% CI: 0.35 to 2.43, respectively). However, there was a dose-response effect with higher rates of serious infections observed in those patients receiving higher doses of JAK inhibitors.

**Conclusions:** Although not reaching statistical significance, in the currently available RCTs, the rates of malignancy were higher in the JAK inhibitors groups compared to their controls. The rates of serious infections were similar between JAK inhibitor groups and their controls, but were dose-dependent. Future studies should aim to indirectly compare each JAK inhibitor to evaluate if these safety signals are also drug dependent and to assess risk per type of malignancy or infection.

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OP0033

### EFFECT OF A STEP-UP OR STEP-DOWN IN TOFACITINIB DOSE ON EFFICACY AND SAFETY IN PATIENTS WITH RHEUMATOID ARTHRITIS IN LONG-TERM EXTENSION STUDIES

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**Background:** Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA). Efficacy and safety of tofacitinib 5 and 10 mg BID have been shown in long-term extension (LTE) studies up to 114 months.<sup>1</sup>

**Objectives:** To assess the impact of tofacitinib dose changes on efficacy and safety in patients (pts) who increased (step-up) or who decreased (step-down) dose, vs pts who remained on the same dose when entering LTE studies.

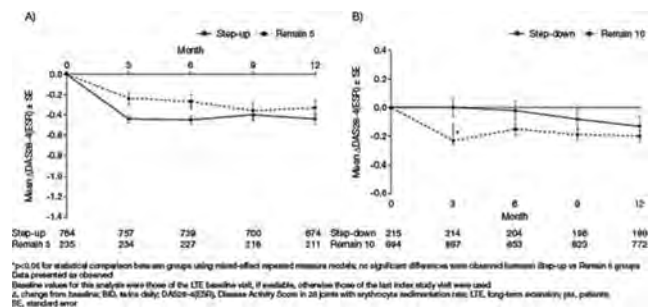
**Methods:** In this exploratory, post hoc analysis, data were pooled from 2 open-label LTE studies (NCT00413699 [ongoing; database not locked at Jan 2016 data-cut]; NCT00661661) of pts with RA who had participated in Phase (P) 1/2/3 tofacitinib index studies and had  $\geq 81$  days of tofacitinib exposure (to allow  $\geq 2$  assessments) in each period (P1/2/3 index and LTE). Dose changes from index study dose were mandated by protocol (at LTE entry) or at the investigator's discretion (during LTE). This analysis only included pts who remained on their initial/changed dose in the LTE. Pts were analysed in 4 groups: 5 mg BID [index]  $\rightarrow$  10 mg BID [LTE] (Step-up; n=833); 5 mg BID [index]  $\rightarrow$  5 mg BID [LTE] (Remain 5; n=248); 10 mg BID [index]  $\rightarrow$  10 mg BID [LTE] (Remain 10; n=951); 10 mg BID [index]  $\rightarrow$  5 mg BID [LTE] (Step-down; n=234). To determine if initial efficacy (last index study assessment) affects response following dose change on LTE entry, sub-groups for the Step-up and Remain 5 groups were defined based on initial ACR20 response, and sub-groups for the Step-down and Remain 10 groups were defined based on initial ACR50 response. Efficacy was assessed up to Month 12 in the LTE based on  $\Delta$ DAS28-4(ESR). Exposure-adjusted event rates (pts with events/100 pt-yrs) are presented for the most common adverse events (AEs) for the entire LTE study exposure.

**Results:** No statistically significant differences in  $\Delta$ DAS28-4(ESR) were observed between the Step-up and Remain 5 groups (figure 1A), whether or not they had an initial ACR20 response (data not shown). In general, no significant differences in  $\Delta$ DAS28-4(ESR) were observed between the Step-down and Remain 10 groups (figure 1B), whether or not they had an initial ACR50 response (data not shown). The rates and types of AEs were similar across all groups (table 1).

Abstract OP0033 – Table 1. Summary of AEs in the LTE study

	Step-up: 5 to 10 mg BID N=833	Remain on 5 mg BID N=248	Step-down: 10 to 5 mg BID N=234	Remain on 10 mg BID N=951
Total years of exposure	2729	807	822	3030
Discontinued due to AEs, n	207	53	46	221
Most common AE system organ classes, n (EASR) EASR >10.00 in any group				
Infections and infestations	578 (21.18)	171 (18.88)	141 (17.16)	563 (21.88)
Gastrointestinal disorders	257 (8.41)	92 (10.25)	93 (10.10)	295 (8.77)
Musculoskeletal and connective tissue disorders	223 (11.83)	78 (8.59)	58 (6.81)	286 (12.58)
Most common AE preferred terms, n (EASR) EASR >3.00 in any group				
Nasopharyngitis	101 (3.70)	70 (7.71)	83 (7.68)	148 (4.81)
Upper respiratory tract infection	139 (5.09)	37 (4.07)	33 (4.01)	179 (5.90)
Bronchitis	90 (3.82)	41 (4.81)	20 (2.43)	137 (6.52)
Urinary tract infection	121 (4.43)	12 (1.32)	18 (2.19)	115 (3.79)
Herpes zoster	94 (3.44)	34 (3.74)	18 (2.19)	95 (3.13)

EASR, events per 100 pt-yrs; AE, adverse event; EASR, exposure-adjusted event rate; LTE, long-term extension; pt, patient



Abstract OP0033 – Figure 1. Mean  $\Delta$ DAS28-4(ESR) over time for A) Step-up pts and those who remained on tofacitinib 5 mg BID and B) Step-down pts and those who remained on tofacitinib 10 mg BID

**Conclusions:** In pts with RA, the safety profile was similar regardless of dose change. Step-up from tofacitinib 5 to 10 mg BID, or step-down from 10 to 5 mg BID, did not affect efficacy over 12 months vs remaining on the same dose, and was not influenced by initial response. Conclusions were limited by small pt numbers in some groups, the open-label design and inclusion of pts in the LTE who showed tolerability for tofacitinib and drug retention.

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OP0034

**LONG-TERM EFFECTIVENESS OF THE COBRA SLIM REMISSION INDUCTION AND TREAT TO TARGET STRATEGY IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS LACKING CLASSICAL MARKERS OF POOR PROGNOSIS: 2 YEAR RESULTS OF THE CARERA TRIAL**

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**Background:** EULAR guidelines recommend to treat all patients with early Rheumatoid Arthritis (eRA) with a combination of methotrexate (MTX) and a short-term course of Glucocorticoids (GC). The COBRA Slim strategy with MTX and a moderately dosed tapering down scheme of GC was effective, also in patients without classical markers of poor prognosis during the first year.

**Objectives:** To compare the outcomes of MTX with or without initial step-down GC in Low-Risk patients during the second year of the CareRA trial, in terms of disease control, safety and DMARD use.

**Methods:** CareRA is a two-year prospective investigator-initiated pragmatic multicentre RCT. DMARD naïve eRA patients were stratified into a High- or Low-Risk group based on classical prognostic markers (presence of erosions, RF, anti-CCP and DAS28-CRP). Low-Risk patients (n=90) were randomised to either Tight-Step Up (TSU) with MTX 15 mg weekly without GC or to COBRA Slim, a combination of MTX 15 mg weekly and prednisone tapering down scheme starting at 30 mg, tapered to 5 mg daily from w6 and stopped at w34. A treat-to-target approach was applied until year 1 and afterwards treatment was at the discretion of the rheumatologist. Proportions of DAS28-CRP remission at year 2 was a co-primary CareRA endpoint. Secondary outcomes were efficacy according to other remission criteria, EULAR/ACR response rates and functionality measured by HAQ (ITT analysis, last observation carried forward). Adverse events (AEs) and concomitant medication were registered.

**Results:** At year 2, 67.4% of Slim and 70.2% of TSU patients were in remission according to DAS28CRP (p=0.777). Out of patients in DAS28CRP remission at year 1, 80.0% (24/30) in the Slim group, versus 69.0% (20/29) in the TSU group remained in remission at every three-monthly evaluation until year 2. Remission rates defined by Boolean criteria were higher in patients of the Slim (39.5% versus TSU group (19.1%) (p=0.033). Functionality measured by mean area under the HAQ curve over 2 years was better in Slim patients (38.3±47.2) than in TSU patients (56.4±48.7) (p=0.025). Other secondary efficacy outcomes did not differ

Abstract OP0034 – Table 1 Clinical outcomes during the second year per treatment arm

	COBRA slim (n=43)	TSU (n=47)	p-value
Remission DAS28-CRP year 2	29 (67.4%)	33 (70.2%)	0.777
DAS28-CRP change BL-year 2	2.2±1.8	2.2±2.0	0.929
DAS28-CRP change year 1-year 2	0.1±0.8	0.0±0.9	0.486
Mean AUC of DAS28CRP	248.9±110.8	266.1±82.3	0.119
Good EULAR response at year 2	55.8%	61.7%	0.571
ACR50 improvement at year 2	25 (58.1%)	23 (48.9%)	0.382
ACR70 improvement at year 2	19 (44.2%)	15 (31.9%)	0.230
Remission CDAI year 2	20 (46.5%)	15 (31.9%)	0.156
Remission SDAI year 2	20 (46.5%)	15 (31.9%)	0.156
Remission Boolean year 2	17 (39.5%)	9 (19.1%)	0.033
Mean AUC of HAQ	38.3±47.2	56.4±48.7	0.025
Clinically meaningful HAQ change at year 2	53.5%	59.6%	0.561
HAQ = 0 at year 2	48.8%	36.2%	0.224

DAS28-CRP= 28 Joint disease activity score calculated with C-reactive protein; good EULAR response = low disease activity with a DAS28-CRP change (BL-year 2) >1.2; AUC = Area Under the Curve (BL-year 2); HAQ= health assessment questionnaire; clinically meaningful HAQ change (BL-year 2) = HAQ change >0.22.

between the treatment arms. The total numbers of AEs reported as related to study therapy, were 69 in 34 TSU patients and 63 in 28 Slim patients. Biologicals were started in 14 Low-Risk patients (15.6%), more specifically in 8 Slim and 6 TSU patients during the CareRA trial. At the year 2 visit 62.5% of Slim patients were on MTX monotherapy and 12.5% on a combination of csDMARDs. In the TSU group 58.5% was taking MTX as only DMARD, and 19.5% took a combination of csDMARDs. Out of all Low-Risk patients 11.0% (8/73) was taking oral GC at the year 2 visit, 5 patients in the TSU group and 3 patients in Slim group, all at a low dosages.

**Conclusions:** In eRA patients lacking classical markers of poor prognosis COBRA Slim showed persistently high remission rates and good disease control 2 years after initiating therapy in a treat to target setting. COBRA slim seems to be slightly more effective than TSU according to the year 2 Boolean remission criteria and the 2 year functionality AUC but the CareRA study was not powered for this analysis.

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OP0035

**UPADACITINIB AS MONOTHERAPY: A PHASE 3 RANDOMISED CONTROLLED DOUBLE-BLIND STUDY IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS AND INADEQUATE RESPONSE TO METHOTREXATE**

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**Background:** Upadacitinib (UPA), an oral JAK inhibitor, showed efficacy in rheumatoid arthritis (RA) patients (pts) with an inadequate response to csDMARDs or bDMARDs on continuing stable csDMARD(s).<sup>1,2</sup>

**Objectives:** Safety and efficacy of switching to UPA 15 mg or 30 mg monotherapy vs continuing methotrexate (MTX) as a blinded study drug was evaluated in pts with inadequate response to MTX (MTX-IR).

**Methods:** Pts with active RA (TJC ≥6, SJC ≥6, hsCRP ≥3 mg/L) on stable MTX were enrolled and randomised 1:1:1 in a double-blind manner to once-daily (QD) UPA 15 mg or 30 mg monotherapy or to continue MTX (cMTX) at their prior stable dose. At BL, all pts discontinued prior MTX without washout and received PBO (for pts on UPA) or MTX at prior dose (cMTX) as blinded study drug. The primary endpoints at Week (Wk) 14 were the proportion of pts achieving ACR20, and the proportion achieving DAS28-CRP ≤3.2 (NRI).

**Results:** 648 pts were randomised, all received study drug; 598 (92.3%) completed 14 wks. BL demographics and disease characteristics were generally similar across arms. Both primary endpoints were met (p<0.001); at Wk 14, a significantly greater proportion of pts receiving UPA monotherapy (15 mg and 30 mg) vs cMTX achieved ACR20 (67.7% and 71.2% vs 41.2%), and DAS28-CRP ≤3.2 (44.7% and 53.0% vs 19.4%) (table 1). All key secondary endpoints also showed UPA 15 and UPA 30 monotherapy to be superior to cMTX, including ACR50 (41.9% and 52.1% vs 15.3%), ACR70 (22.6% and 33.0% vs 2.8%), DAS28-CRP <2.6 (28.1% and 40.5% vs 8.3%), ΔHAQ-DI (-0.65 and -0.73 vs -0.32). ΔSF-36 PCS and ΔMorning Stiffness data are also shown (table 1). The proportion of pts achieving CDAI ≤10 was significantly greater with UPA 15 and 30 vs cMTX (34.6% and 46.5% vs 24.5%).

Adverse events (AEs) were reported at similar frequencies across arms; serious AEs were numerically higher in UPA 15 but similar between cMTX and UPA 30 (table 1). Numerically more infections were reported in cMTX and UPA 30 vs UPA 15. One serious infection each was reported in UPA 15 and cMTX, and none in UPA 30. Herpes zoster was more frequent in UPA 30 vs UPA 15 or cMTX. 3 malignancies (1 in cMTX and 2 in UPA 15) and 3 adjudicated MACE (1 in UPA 15 and 2 in UPA 30) were reported. One adjudicated pulmonary embolism was reported (UPA 15) in a pt with known risk factors (BMI 36; on oestrogen therapy). One death (haemorrhagic stroke due to ruptured aneurysm) was reported in UPA 15. No TB, renal dysfunction or GI perforation was reported. Rates and types of laboratory abnormalities were consistent with prior UPA RA studies to date.

Abstract OP0035 – Table 1

EFFICACY ENDPOINTS AT WEEK 14 <sup>a</sup>			
	cMTX, N=216	UPA 15, N=217	UPA 30, N=215
ACR20 (%)	41.2%	67.7% <sup>***</sup>	71.2% <sup>***</sup>
DAS28-CRP≤3.2 (%)	19.4%	44.7% <sup>***</sup>	53.0% <sup>***</sup>
ACR50 (%)	15.3%	41.9% <sup>***</sup>	52.1% <sup>***</sup>
ACR70 (%)	2.8%	22.6% <sup>***</sup>	33.0% <sup>***</sup>
DAS28-CRP<2.6 (%)	8.3%	28.1% <sup>***</sup>	40.5% <sup>***</sup>
CDAI-1 (D)	24.5%	34.6% <sup>*</sup>	46.5% <sup>***</sup>
ΔDAS28-CRP (LSM)	-1.20	-2.29 <sup>***</sup>	-2.61 <sup>***</sup>
ΔHAQ-DI (LSM)	-0.32	-0.65 <sup>***</sup>	-0.73 <sup>***</sup>
ΔSF-36 PCS (LSM)	4.32	8.28 <sup>***</sup>	10.19 <sup>***</sup>
ΔMorning Stiffness Duration (min.) (LSM)	-53.0	-94.6 <sup>**</sup>	-102.3 <sup>***</sup>
ADVERSE EVENT SUMMARY, n (%)			
	cMTX, N=216	UPA 15, N=217	UPA 30, N=215
Any Adverse Event (AE)	102 (47.2)	103 (47.5)	105 (48.8)
Serious AE	6 (2.8)	11 (5.1)	6 (2.8)
AE Leading To Study Drug D/C	6 (2.8)	8 (3.7)	6 (2.8)
Infection	57 (26.4)	42 (19.4)	54 (25.1)
-Serious Infection <sup>†</sup>	1 (0.5)	1 (0.5)	0
-Opportunistic Infection <sup>‡</sup>	1 (0.5)	0	3 (1.4)
-Herpes Zoster	1 (0.5)	3 (1.4)	6 (2.8)
Hepatic disorder <sup>§</sup>	4 (1.9)	4 (1.8)	5 (2.3)
Any Malignancy (including NMSC) <sup>¶</sup>	1 (0.5)	2 (0.9)	0
-NMSC	1 (0.5)	0	0
MACE (adjudicated) <sup>  </sup>	0	1 (0.5)	2 (0.9)
Venous Thromboembolism (adjudicated)	0	1 (0.5) <sup>  </sup>	0
Death	0	1 (0.5)	0

cMTX, Continuing MTX as a blinded study drug; LSM, least square means; Δ, Change from baseline; CPK, creatine phosphokinase; NMSC, non-melanoma skin cancer; MACE, major adverse cardiovascular event (cardiovascular death, non-fatal MI, non-fatal stroke)

<sup>a</sup>Results for binary endpoints are based on NRI. Results for DAS28-CRP and HAQ-DI are based on Multiple Imputation. Results for other endpoints are based on Mixed Effect Model Repeat Measurement. \*, \*\*, \*\*\* p < 0.05, < 0.01 and 0.001 respectively

<sup>†</sup>Serious infection events: cMTX: uricospirit; UPA 15: abscess limb

<sup>‡</sup>Opportunistic infection events: cMTX: fungal oesophagitis; UPA 30: 2 oral candidiasis, 1 oropharyngeal candidiasis

<sup>§</sup>Hepatic disorders: Except for 1 case of mild hepatic cyst, all due to liver enzyme elevation

<sup>¶</sup>Malignancies: cMTX: basal cell carcinoma; UPA 15: 1 non-Hodgkin's lymphoma, 1 breast cancer

<sup>||</sup>MACE (adjudicated): UPA 15: 1 hemorrhagic stroke due to ruptured aneurysm (fatal), investigator deemed as unrelated to study drug; UPA 30: 1 myocardial infarction, 1 stroke; investigators reported both events as unrelated to study drug

<sup>||</sup>VTE: Pulmonary embolism (BMI 35, estrogen hormone therapy); investigator deemed as unrelated to study drug

**Conclusions:** In this MTX-IR study population, switching to UPA as monotherapy at 15 mg and 30 mg QD showed significant improvements in RA signs and symptoms vs continuing MTX. Numerically higher responses were observed for UPA 30 mg vs 15 mg, particularly for more stringent efficacy criteria. Safety observations were similar to those in prior UPA studies.

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OP0036

## A PHASE 3 RANDOMISED, PLACEBO-CONTROLLED, DOUBLE-BLIND STUDY OF UPADACITINIB (ABT-494), A SELECTIVE JAK-1 INHIBITOR, IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS WITH INADEQUATE RESPONSE TO CONVENTIONAL SYNTHETIC DMARDS

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**Background:** Upadacitinib (UPA) is an oral, selective JAK-1 inhibitor in development for the treatment of patients (pts) with moderate to severe rheumatoid arthritis (RA) and other immune-mediated diseases.

**Methods:** This Phase 3 study in pts with inadequate response (IR) to csDMARDs included a double-blind placebo (PBO)-controlled period (Period 1, reported here), during which pts were randomised 1:1:1 to receive once-daily (QD) extended-release formulation of UPA at 15 mg or 30 mg, or PBO for 12 weeks (wks). The primary efficacy endpoints were the proportion of pts who achieved an ACR20 response and the proportion who achieved DAS28-CRP low disease activity (LDA, ≤3.2) at Wk 12, using non-responder imputation (NRI).

**Results:** Of 661 pts who were randomised, all received study drug, and 618 (93.5%) completed Period 1. At baseline, demographics and disease characteristics were similar across arms. The study met all primary and key secondary endpoints with p values < 0.001 for both doses. At Wk 12, significantly more pts receiving UPA 15 mg and 30 mg QD vs PBO achieved an ACR20 response (63.8% and 66.2% vs 35.7%, p < 0.001), and DAS28-CRP LDA (48.4% and 47.9% vs 17.2%, p < 0.001) (table 1). Onset of action was rapid with significantly more pts in both UPA arms achieving ACR20 at Wk 1 vs PBO. At Wk 12, significantly more pts met ACR50 and ACR70 in the UPA 15 mg (38% and 20.8%) and 30 mg QD arms (43.4% and 26.5%) vs PBO (14.9% and 5.9%). Significantly more patients receiving UPA 15 mg and 30 mg QD vs PBO achieved DAS28-CRP < 2.6 (30.8% and 28.3% vs 10%, p < 0.001) and CDAI-LDA (40.3% and 42% vs 19%, p < 0.001), and pts receiving UPA at both doses experienced significantly greater improvements in DAS28-CRP, HAQ-DI, morning stiffness and FACIT-F vs PBO (p < 0.001).

Adverse events (AEs) and serious AEs were numerically higher with UPA than PBO (table 1). The overall incidence of infection was higher for UPA 15 mg and 30 mg QD vs PBO, but few were serious infections. There were 4 cases of herpes zoster/Varicella Zoster Virus infection (1 on PBO). Asymptomatic CPK elevations were only reported for patients on UPA. Two malignancies and 3 adjudicated cardiovascular events were reported. No PE/DVT were reported. There were no deaths, cases of TB or GI perforations. Types and frequency of laboratory abnormalities were similar to findings in Phase 2 studies with UPA.

Abstract OP0036 – Table 1

Efficacy Endpoints <sup>a</sup>			
	PLACEBO N=221	UPADACITINIB 15 MG QD N=221	UPADACITINIB 30 MG QD N=219
Primary Endpoints			
ACR20 (%)	35.7	63.8 <sup>***</sup>	66.2 <sup>***</sup>
DAS28-CRP LDA (%)	17.2	48.4 <sup>***</sup>	47.9 <sup>***</sup>
Key Secondary Endpoints			
ACR20 at Week 1 (%)	6.6	22.2 <sup>***</sup>	28.3 <sup>***</sup>
ACR50 (%)	14.9	38.3 <sup>***</sup>	43.4 <sup>***</sup>
ACR70 (%)	5.9	20.8 <sup>***</sup>	26.5 <sup>***</sup>
DAS28-CRP < 2.6 (%)	10.0	30.8 <sup>***</sup>	28.3 <sup>***</sup>
CDAI LDA (%)	19.0	40.3 <sup>***</sup>	42.0 <sup>***</sup>
Δ DAS28-CRP	-1.02	-2.29 <sup>***</sup>	-2.34 <sup>***</sup>
Δ HAQ-DI	-0.25	-0.59 <sup>***</sup>	-0.54 <sup>***</sup>
Δ SF-36 PCS	3.03	7.56 <sup>***</sup>	8.01 <sup>***</sup>
Δ Morning Stiffness Duration (min.)	-31.2 <sup>†</sup>	-82.36 <sup>***</sup>	-85.13 <sup>***</sup>
Δ FACIT-F	3.96	7.81 <sup>***</sup>	7.74 <sup>***</sup>
Summary of Adverse Events, n (%)			
Any Adverse Event (AE)	100 (45.3)	125 (56.6)	118 (53.9)
Serious AE	5 (2.3)	8 (4.1)	6 (2.7)
AE Leading To Discontinuation Of Study Drug	7 (3.2)	7 (3.2)	13 (5.9)
Severe AE	5 (2.3)	8 (3.6)	7 (3.2)
AE of Special Interest			
Infection	47 (21.3)	64 (29.0)	69 (31.5)
Serious Infection <sup>†</sup>	1 (0.5)	1 (0.5)	3 (1.4)
Opportunistic Infection <sup>‡</sup>	1 (0.5)	0	3 (1.4)
Anemia	3 (1.4)	0	3 (1.4)
Neutropenia	1 (0.5)	4 (1.8)	0 (0.0)
Herpes Zoster	1 (0.5)	1 (0.5)	2 (0.9) <sup>§</sup>
Hepatic disorder	5 (2.3)	4 (1.8)	6 (2.7)
CPK elevation <sup>¶</sup>	0	5 (2.3)	6 (2.7)
Malignancy (including NMSC) <sup>  </sup>	0	0	2 (0.9)
Cardiovascular event (adjudicated) <sup>  </sup>	0	2 (0.9)	1 (0.5)
MACE	0	0	1 (0.5)
Other adjudicated CEs	0	2 (0.9)	0

Δ, Change from baseline; \*\*\*p < 0.001

<sup>a</sup>Results for binary endpoints are based on NRI analysis. Results for continuous endpoints based on Multiple Imputation or Mixed Effect Model Repeat Measurement analysis

<sup>†</sup>Serious infection events: PBO: pneumonia; UPA 15 mg: enterococcal infection; UPA 30 mg: 1 bacterial zoster; 1 viral upper respiratory tract infection; 1 Mycoplasma pneumoniae infection

<sup>‡</sup>Opportunistic infection events: PBO: oral candidiasis; UPA 30 mg: 2 oral candidiasis; 1 varicella zoster pneumonia

<sup>§</sup>1 patient on UPA 30 mg was exposed to chicken pox and had primary varicella infection

<sup>¶</sup>All asymptomatic

<sup>||</sup>Malignancies: UPA 30 mg: 1 case of basal cell carcinoma in patient with history of skin cancer; 1 case of chronic lymphocytic leukemia/lymphoma. Both were deemed unrelated to study drug by the investigator

<sup>||</sup>Cardiovascular events (adjudicated): MACE: ischemic stroke in patient with history of hypertension (upadacitinib 30 mg); Other adjudicated CEs: 1 congestive cardiac failure (upadacitinib 15 mg); 1 stroke (placebo in patient with prior history of angina, coronary artery disease and transient ischemic attack (upadacitinib 15 mg))

Abbreviations: CPK, creatine phosphokinase; NMSC, non-melanoma skin cancer

**Conclusions:** The efficacy of UPA at 15 mg and 30 mg QD vs PBO was demonstrated in this csDMARD-IR study population. The most notable responses were observed in the more stringent endpoints of LDA (by either DAS28-CRP or CDAI)



and ACR70. The safety and tolerability profile was consistent with observations in the Phase 2 studies with UPA.

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OP0037

#### EFFICACY OF TOFACITINIB AFTER TEMPORARY DISCONTINUATION IN PATIENTS WITH RHEUMATOID ARTHRITIS: ANALYSIS OF DATA FROM OPEN-LABEL LONG-TERM EXTENSION STUDIES

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**Background:** Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA). Given the chronic nature of RA, there may be situations when therapy is temporarily discontinued. It is important to understand loss of response during temporary discontinuation and the ability to regain disease control following treatment reinitiation. Re-establishment of tofacitinib efficacy following temporary discontinuation/reinitiation has been previously demonstrated in patients (pts) with RA participating in the vaccine sub-study of the long-term extension (LTE) study ORAL Sequel.<sup>1</sup>

**Objectives:** To further assess tofacitinib efficacy and safety after temporary discontinuation and reinitiation in pts with RA in LTE studies.

**Methods:** Data were pooled from two open-label LTE studies (NCT00413699 [database lock: March 2017] and NCT00661661) of pts with RA who had completed qualifying Phase 1/2/3 index studies. Pts received tofacitinib 5 or 10 mg twice daily as monotherapy or with conventional synthetic disease-modifying antirheumatic drugs. Pts who received continuous tofacitinib for  $\geq 4$  months, temporarily discontinued tofacitinib for 14–30 days and then resumed treatment were included in the analysis. Efficacy outcomes were analysed at the pre-interruption visit ( $\leq 90$  days before discontinuation) and at the post-interruption visit (within 14–42 days of resuming treatment); data from the interruption period were not analysed. Efficacy outcomes included: ACR20/50/70 response rates, mean tender and swollen joint counts, mean C-reactive protein levels and mean DAS28–4 (ESR), CDAI, HAQ-DI, Patient Global Assessment of arthritis, Pain and Physician Global Assessment of arthritis scores. Safety was analysed from Day 1 of temporary discontinuation to the post-interruption visit and included adverse events (AEs), serious AEs (SAEs) and discontinuations due to AEs that occurred within the time range.

**Results:** 261 pts met the criteria for temporary discontinuation. Median (range) duration of temporary discontinuation was 19<sup>14–30</sup> days. Pt demographics are shown in table 1. Efficacy outcomes were generally similar at pre- and post-interruption visits (table 2). From Day 1 of discontinuation to the post-interruption visit, AEs, SAEs and discontinuations due to AEs occurred in 142 (54.4%), 29 (11.1%) and 4 (1.5%) pts, respectively.

Abstract OP0037 – Table 1 Patients demographics and baseline disease characteristics<sup>1</sup>

	All tofacitinib (N=261)
Age (years), mean (SD)	53.7 (11.3)
Sex, n (%)	
Female	224 (85.8)
Race, n (%)	
White	173 (66.3)
Black	7 (2.7)
Asian	63 (24.1)
Other	18 (6.9)
BMI (kg/m <sup>2</sup> ), mean (SD)	26.8 (6.4)
Duration of disease (years), mean (SD)	9.4 (8.2)
TJC, mean (SD)	25.1 (15.2)
SJC, mean (SD)	15.4 (8.6)
CRP (mg/L), mean (SD)	20.6 (23.9)
DAS28-4(ESR), mean (SD)	6.4 (1.0)
CDAI, mean (SD)	36.6 (12.1)
HAQ-DI, mean (SD)	1.5 (0.7)
PtGA, mean (SD)	60.4 (22.1)
Pain-VAS, mean (SD)	58.8 (23.3)
PGA, mean (SD)	61.1 (16.9)
Background csDMARD use, n (%) <sup>b</sup>	181 (69.3)

<sup>a</sup>Baseline values were those of the index study if patients began LTE study treatment  $\leq 14$  days from the last tofacitinib dose in the index study. Otherwise, LTE baseline values were used; <sup>b</sup>At LTE baseline

BMI, body mass index; CDAI, Clinical Disease Activity Index; CRP, C-reactive protein; csDMARD, conventional synthetic disease-modifying antirheumatic drug; DAS28-4(ESR), Disease Activity Score in 28 joints, erythrocyte sedimentation rate; HAQ-DI, Health Assessment Questionnaire-Disability Index; LTE, long-term extension; PGA, Physician Global Assessment of arthritis; PtGA, Patient Global Assessment of arthritis; SD, standard deviation; SJC, swollen joint count; TJC, tender joint count; VAS, visual analogue scale

Abstract OP0037 – Table 2 Efficacy endpoints at the pre-interruption visit ( $\leq 90$  days before temporary discontinuation) and post-interruption visit (within 14–42 days of resuming treatment)

	All tofacitinib (N=261)	
	Pre-interruption visit	Post-interruption visit
ACR20, % (95% CI)	75.5 (69.8, 80.6)	74.3 (68.6, 79.5)
ACR50, % (95% CI)	54.4 (48.2, 60.6)	51.0 (44.7, 57.2)
ACR70, % (95% CI)	31.8 (26.2, 37.8)	31.4 (25.8, 37.4)
TJC, mean (95% CI)	6.1 (4.9, 7.2)	8.0 (6.4, 9.6)
SJC, mean (95% CI)	3.4 (2.8, 4.1)	5.0 (3.9, 6.2)
CRP (mg/L), mean (95% CI)	0.48 (0.38, 0.58)	0.46 (0.37, 0.56)
DAS28-4(ESR), mean (95% CI)	3.6 (3.4, 3.7)	3.9 (3.7, 4.0)
CDAI, mean (95% CI)	10.0 (8.9, 11.1)	11.8 (10.3, 13.2)
HAQ-DI, mean (95% CI)	0.94 (0.85, 1.03)	0.98 (0.88, 1.07)
PtGA, mean (95% CI)	28.4 (25.8, 31.0)	29.3 (26.6, 32.1)
Pain (VAS), mean (95% CI)	28.1 (25.4, 30.8)	28.8 (26.0, 31.7)
PGA, mean (95% CI)	17.1 (15.3, 18.9)	18.0 (16.0, 19.9)

Median (range) time from the pre-interruption visit to Day 1 of temporary discontinuation was 43 (0–90) days and the median (range) time from resuming treatment to the post-interruption visit was 28 (14–42) days

N is the total number of patients in the analysis; the number of patients evaluable for each endpoint may be fewer than N

ACR, American College of Rheumatology; CDAI, Clinical Disease Activity Index; CI, confidence interval; CRP, C-reactive protein; DAS28-4(ESR), Disease Activity Score in 28 joints, erythrocyte sedimentation rate; HAQ-DI, Health Assessment Questionnaire-Disability Index; PGA, Physician Global Assessment of arthritis; PtGA, Patient Global Assessment of arthritis; SJC, swollen joint count; TJC, tender joint count; VAS, visual analogue scale

**Conclusions:** In pts with RA who temporarily discontinued tofacitinib, similar efficacy responses were observed at pre- and post-interruption visits, suggesting that there is no loss of efficacy after temporary withdrawal and reinitiation of tofacitinib. The safety profile was consistent with previous tofacitinib reports in LTE studies over 9 years.<sup>2</sup>

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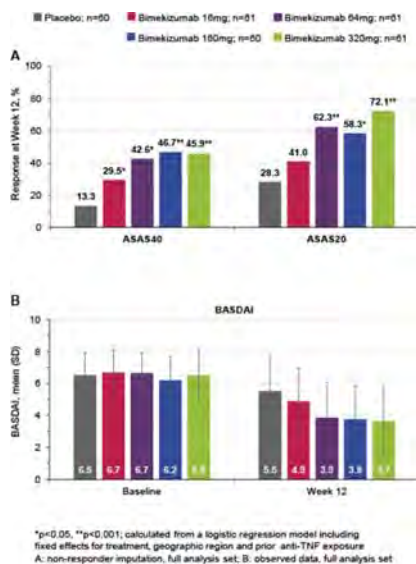
LB0001

### DUAL NEUTRALISATION OF IL-17A AND IL-17F WITH BIMEKIZUMAB IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS (AS): 12-WEEK RESULTS FROM A PHASE 2B, RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED, DOSE-RANGING STUDY

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**Background:** Dual neutralisation of IL-17F, in addition to IL-17A, reduces inflammation<sup>1</sup> to a greater extent than inhibition of IL-17A alone in disease-relevant cell models. Bimekizumab, a monoclonal antibody that potently and selectively neutralises both IL-17A and IL-17F, provided rapid and substantial clinical improvements in studies evaluating patients with psoriasis<sup>2</sup> and psoriatic arthritis.<sup>1</sup>

**Objectives:** Assess 12 week efficacy and safety of bimekizumab in patients with active AS; the primary objective was to assess the ASAS40 dose-response relationship at Week 12.



**Abstract LB0001** – Figure 1 A) non-responder imputation, full analysis set; B) observed data, full analysis set

**Methods:** In this ongoing 48 week study (NCT02963506: double blind to Week 12 then dose blind to Week 48), 303 patients with active (BASDAI  $\geq 4$ ; spinal pain  $\geq 4$  [0–10 numerical rating scale]) AS, fulfilling the modified New York criteria, were randomised 1:1:1:1:1 to receive subcutaneous bimekizumab 16 mg, 64 mg, 160 mg, 320 mg or placebo Q4W, for 12 weeks. Prior exposure to 1 anti-TNF therapy was permitted. The primary endpoint was ASAS40 response rate at Week 12. Secondary endpoints (ASAS20 and ASAS5/6 response rate and change from baseline in BASDAI and ASDAS-CRP at Week 12) and safety were also assessed.

**Results:** Overall, 297 (98.0%) patients completed the 12 week double-blind period. The majority of patients were male (84.5%) with a mean (SD) age of 42.2 (11.8) and median (min, max) symptom duration of 13.3 (0.3, 48.2) years; baseline characteristics were similar among treatment groups (median [min, max] hs-CRP: 12.1 [0.3, 130.6] mg/L; mean [SD] BASDAI: 6.5 [1.4]; ASDAS-CRP: 3.9 [0.8]; prior anti-TNF exposure: 11.2%). At Week 12, there was a significant ( $p < 0.001$ ) dose-response for ASAS40. A greater percentage of bimekizumab-treated patients achieved ASAS40 (primary endpoint) than placebo (Figure:  $p < 0.05$ , all doses). More patients receiving bimekizumab than placebo also achieved ASAS20 (figure 1;  $p < 0.05$ , 64 mg–320 mg doses) and ASAS5/6 (16mg: 29.5%; 64 mg: 39.3%; 160 mg: 50.0%; 320 mg: 52.5%; placebo: 5.0%;  $p < 0.05$ , all comparisons). Compared with placebo, greater reductions from baseline were achieved with bimekizumab for both BASDAI (figure 1) and ASDAS-CRP (LS mean [SE] change from baseline: 16 mg:  $-1.0$  [0.15]; 64 mg:  $-1.6$  [0.15]; 160 mg:  $-1.4$  [0.16]; 320 mg:  $-1.5$  [0.16]; placebo:  $-0.4$  [0.16];  $p < 0.001$ , all doses). The overall incidence of TEAEs was 86/243 (35.4%) for bimekizumab-treated patients versus 22/60 (36.7%) for placebo. No unexpected safety risks were observed; the most frequently reported events were nasopharyngitis and headache.

**Conclusions:** The primary and key secondary objectives were achieved; dual neutralisation of IL-17A and IL-17F with bimekizumab provided clinically meaningful improvements in disease outcome measures. No new safety signals were observed versus previous studies.<sup>1,2</sup>

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**Disclosure of Interest:** D. van der Heijde Consultant for: AbbVie; Amgen, Astellas, AstraZeneca, BMS, Boehringer Ingelheim, Celgene, Daiichi, Eli-Lilly, Galapagos, Gilead, Glaxo-Smith-Kline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, UCB, Employee of: Director of Imaging Rheumatology BV, L. S. Gensler Grant/research support from: AbbVie, Amgen, UCB, Consultant for: Novartis, Lilly, Janssen, A. Deodhar Grant/research support from: AbbVie, Eli Lilly, Janssen, Novartis, Pfizer, UCB, Consultant for: AbbVie, Eli Lilly, Janssen, Novartis, Pfizer, UCB, X. Baraliakos Grant/research support from: Abbvie, Pfizer, MSD, UCB, Novartis, Consultant for: AbbVie, BMS, Boehringer Ingelheim, Celgene, Chugai, Janssen Biologics, Novartis, Pfizer, UCB, Galapagos, Speakers bureau: AbbVie, Chugai, Janssen, Novartis, Pfizer, UCB, D. Poddubnyy Grant/research support from: Abbvie, MSD, Novartis, Consultant for: Abbvie, BMS, Janssen, MSD, Novartis, Pfizer, UCB, M. K. Farmer Employee of: UCB Pharma, D. Baeten Employee of: UCB Pharma, T. Kumke Employee of: UCB Pharma, M. Oortgiesen Shareholder of: UCB Pharma, Employee of: UCB Pharma, M. Dougados Grant/research support from: UCB, Lilly, Pfizer, AbbVie, Merck, Consultant for: UCB, Lilly, Pfizer, AbbVie, Merck

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WEDNESDAY, 13 JUNE 2018

### Doctor, how bad will my rheumatoid become? RA – prognosis, predictors and outcomes

OP0038

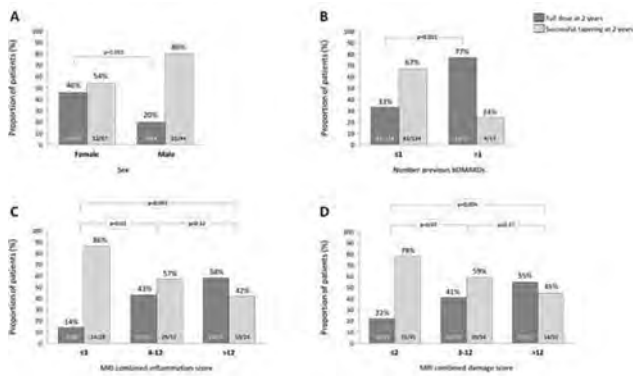
#### DOSE TAPERING AND DISCONTINUATION OF BIOLOGICAL THERAPY IN RHEUMATOID ARTHRITIS PATIENTS IN REMISSION IN ROUTINE CARE – 2-YEAR OUTCOMES AND IDENTIFICATION OF PREDICTORS

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**Background:** A cohort of routine care rheumatoid arthritis (RA) patients in sustained remission had biological disease-modifying anti-rheumatic drugs (bDMARDs) tapered according to a treatment guideline. Little is known about predictors of successful tapering and discontinuation of bDMARDs.

**Objectives:** We studied: 1) the proportion of patients whose bDMARD could be successfully tapered or discontinued; 2) unwanted consequences of tapering/discontinuation; 3) potential baseline predictors of successful tapering and discontinuation.





**Abstract OP0038** – Figure 1 Observed association between potential predictors and the proportion patients with successful tapering (i.e. less than full dose) versus full dose at year 2

**Methods:** One-hundred-and-forty-three patients with sustained disease activity score (DAS28-CRP) ≤ 2.6 and no radiographic progression the previous year were included. bDMARD was reduced to 2/3 of standard dose at baseline, 1/2 after 16 weeks, and discontinued after 32 weeks. Patients who flared (defined as either DAS28-CRP > 2.6 and DAS28-CRP ≥ 1.2 from baseline, or erosive progression on X-ray and/or MRI) stopped tapering and were escalated to the previous dose level.

**Results:** One-hundred-and-forty-one patients completed 2 year follow-up. At 2 years, 87 patients (62%) had successfully tapered bDMARDs, with 26 (18%) receiving 2/3 of standard dose, 39 (28%) 1/2 dose and 22 (16%) having discontinued; 54 patients (38%) were receiving full dose. DAS28-CRP<sub>0-2yrs</sub> was 0.1 ((-0.2)–0.4) (median(interquartile range)) and mean Total-Sharp-Score<sub>0-2yrs</sub> was 0.01 (1.15) (mean(SD)). Radiographic progression was observed in 9 patients (7%). Successful tapering was independently predicted by: ≤ 1 previous bDMARD, male gender, low baseline MRI combined inflammation score and low MRI combined damage score. Negative IgM-rheumatoid factor predicted successful discontinuation. The association between potential predictors and the proportion of patients with successful tapering of bDMARDs is shown in figure 1.

**Conclusions:** By implementing a clinical guideline, 62% of RA patients in sustained remission in routine care were successfully tapered, including 16% successfully discontinued at 2 years. Radiographic progression was rare. IgM-RF was an independent predictor for successful discontinuation of bDMARDs. Maximum one bDMARDs, male gender, and low baseline MRI combined inflammation and MRI combined damage scores were independent predictors for successful tapering.

**Disclosure of Interest:** None declared

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**OP0039 HIGH DISEASE ACTIVITY AND DISABILITY AT ONE YEAR IN TWO CLUSTERS OF PATIENTS WITH RHEUMATOID ARTHRITIS DEFINING THEMSELVES AS IN AN ACCEPTABLE STATE AT TREATMENT INITIATION**

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**Background:** A significant proportion of patients with rheumatoid arthritis (RA) define themselves as in a ‘patient acceptable symptom state’ (PASS) at methotrexate (MTX) initiation. Within this heterogeneous group, there are likely to be clinical phenotypes associated with poor outcome.

**Objectives:** To identify distinct phenotypes of symptoms within patients in PASS at baseline and to compare disability and disease activity scores of these patients over one year.

**Methods:** The Rheumatoid Arthritis Medication Study (RAMS) is a one year prospective cohort of patients with RA starting MTX. At baseline, patients reported demographics, completed the Health Assessment Questionnaire (HAQ), pain/fatigue visual analogue scales (VAS) and the Hospital Anxiety and Depression Scale (HADS). A research nurse conducted a 28 swollen and tender joint count and the Disease Activity Score (DAS28) was calculated. DAS28 and HAQ were assessed again at 12 months. Patients also answered the dichotomous question ‘Is your current condition satisfactory, when you take your general functioning and your current pain into consideration?’ Only those answering yes at baseline were

included in the analysis. Phenotypes were identified using K-medians cluster analysis based on baseline swollen/tender joint count, HAQ, VAS-pain, VAS-fatigue and HADS-depression. The ‘elbow method’ was used to select the number of clusters. Quantile regression was used to compare the 12 month HAQ and DAS28 scores between clusters, controlling for age and gender.

**Results:** Five clusters were identified within the 300 patients in PASS at baseline (mean (sd) age=61.4 (12.1) years, 186 (62%) women) (table 1). Compared to Cluster 1, patients in higher clusters had worse HAQ (median difference (95% CI) vs Cluster 1: Cluster 2=0.36 (0.11, 0.61); Cluster 3=0.19 (-0.11, 0.49); Cluster 4=0.74 (0.47, 1.00); Cluster 5=0.89 (0.54, 1.24)) and worse DAS28 at 12 months (median difference (95% CI) vs Cluster 1: Cluster 2=0.43 (-0.06, 0.91); Cluster 3=0.40 (-0.19, 0.99); Cluster 4=0.89 (0.36, 1.41); Cluster 5=1.28 (0.59, 1.96).

**Abstract OP0039** – Table 1 Baseline characteristics of the five clusters

Cluster	N	Baseline scores, Medians						Clinical characteristics matrix §					
		SJC28	TJC28	HAQ	Pain	Fatigue	Dep	SJC28	TJC28	HAQ	Pain	Fatigue	Dep
1	50	2	1	0	8	8	0	M	L	L	L	L	L
2	109	2	3	0.5	25	25	4	M	M	M	M	M	M
3	44	13.5	10.5	0.5	20	12.5	2	H	H	M	M	M	M
4	71	4	5	1.13	50	64	7	M	M	H	H	M	H
5	26	12	23	1.25	56.5	66	5	H	H	H	H	H	M

§ Dep = depression, measured using the Hospital Anxiety and Depression Scale; HAQ = Health Assessment Questionnaire; N = number; SJC28 = swollen joint count (28); TJC28 = tender joint count (28); L = Low (L), Medium (M) and High (H) defined based on median and interquartile of each characteristic in the total cohort of patients in a PASS; SJC28: L=0-1, M=2-3, H=4-10; TJC28: L=0-1, M=2-7, H=8-26; HAQ: L=0.00-0.19, M=0.20-1.12, H=1.13-3.00; pain: L=0-14, M=15-46, H=47-100; Fatigue: L=0-10, M=11-55, H=56-100; depression: L=0-1, M=2-6, H=7-24

**Conclusions:** Despite all patients reporting they were satisfied with their condition at baseline, five distinct clinical phenotypes were identified. These clusters can identify ‘reticent’ patients who are likely to have poor outcomes in the future.

**Disclosure of Interest:** None declared

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**OP0040 SYNOVIAL CELL INFILTRATION IN ACPA-VE PATIENTS DISPLAYS SIMILAR SIGNATURES TO OTHER SERONEGATIVE INFLAMMATORY ARTHRITIS. RESULTS FROM THE PATHOBIOLOGY OF EARLY ARTHRITIS COHORT (PEAC)**

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**Background:** There is increasing evidence to suggest that ACPA +ve and ACPA-ve RA are distinct diseases. Current data demonstrates overlap in classification criteria between ACPA-ve RA and other sero negative inflammatory arthritides such as PsA. Associated with this is a variable prognosis and response to treatment for patients with ACPA-ve RA. Biomarkers capable of refining diagnosis and improving on current classification criteria early in the disease course for patients with ACPA-ve RA are thus urgently needed. Data examining the synovial pathophysiological relationship between PsA and ACPA ±RA is currently limited although has the potential to identify disease specific synovial cellular and molecular signatures.

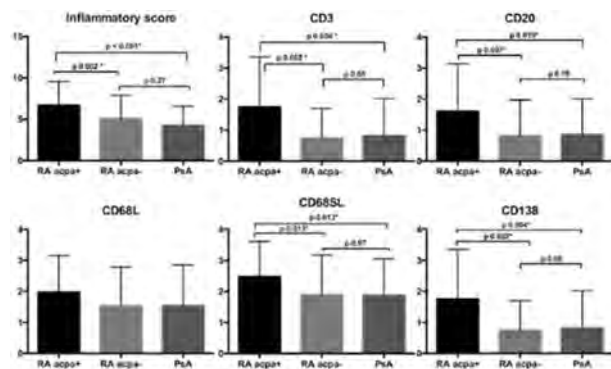
**Objectives:** Therefore, the aim of this study is to examine in a cohort of therapy naïve, early inflammatory arthritis patients, whether ACPA-ve RA can be defined at disease initiation according to synovial pathobiological signatures.

**Methods:** A total of 186 consecutive DMARD naïve inflammatory arthritis patients (disease duration <1 year) recruited as part of the multicentre PEAC study at Barts Health NHS Trust were evaluated. All patients underwent a baseline synovial biopsy of a clinically active joint along with collection of inflammatory markers (CRP). Following H and E staining, sections underwent immunohistochemical staining and semi-quantitative scoring (0–4) to determine the degree of CD20 +Bcells, CD3 +T cells, CD68 +lining (l) and sublining (sl) macrophage and CD138 +plasma cell infiltration. Sections were categorised into three phenotypes: (i) Fibroid(F):(CD68 SL <2 and or CD3, CD20, CD138 <1), (ii) Myeloid(M):(CD68SL >2, CD20 <1 and or CD3 >1) and (iii) Lymphoid(L):(grade 2–3 CD20 +aggregates, CD20 >2).

**Results:** 90/186 patients were classified as ACPA+ve RA, 55/186 as ACPA-ve RA and 41/186 as PsA. 80% of synovial samples were collected from small joints (wrist, MCP, PIP). All 186 samples were suitable for analysis. Results confirmed that C-reactive protein (CRP) as inflammatory marker does not differentiate between subgroups (p 0.41). Significantly higher degree of immune cell infiltration was seen between ACPA+ve vs ACPA-ve and ACPA+ve vs PsA but not between ACPA-ve and PsA (figure 1). When grouping patient between clinical subgroups

(ACPA+ve vs ACPA-ve vs PsA) and pathotypes (fibroid, myeloid and lymphoid) (table1) we demonstrated a significantly higher prevalence of a lymphoid pathotype in ACPA+ve RA vs ACPA-ve or PsA.

	RA acpa + N90 9ungraded	RA acpa- N55 12ungraded	PsA N41 0ungraded	P value fisher test	P value acpa+vs acpa-	P value acpa+vs PsA	P value acpa- vs PsA
F	15 (16%)	17 (31%)	15 (36%)	0.01*	0.03*	0.005*	0.41
M	25 (28%)	14 (25%)	11 (27%)				
L	41 (45%)	12 (22%)	10 (24%)				



**Conclusions:** Our results suggest that the synovial cell infiltrate (B cells, T cells, macrophages and plasma cells) in ACPA-ve RA is significantly different from ACPA +ve patients. They also suggest shared pathophysiological mechanisms between PsA and ACPA-ve RA and support a role for future refinement of diagnosis of ACPA-ve RA according to synovial pathobiology.

**Disclosure of Interest:** None declared

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OP0041

#### DOES TREATMENT STRATEGY INFLUENCE THE ABILITY TO ACHIEVE AND SUSTAIN DMARD-FREE REMISSION IN RA?; RESULTS OF A LONGITUDINAL STUDY COMPARING AN INTENSIVE DAS-STEERED TREATMENT STRATEGY WITH TREAT-TO-TARGET IN ROUTINE CARE

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**Background:** Disease-modifying anti-rheumatic drug (DMARD)-free remission is an achievable outcome in rheumatoid arthritis (RA). The influence of treatment strategy on the ability to achieve and sustain this outcome is unclear. Therefore, we compared the prevalence and sustenance of DMARD-free remission in RA-patients treated in a trial with intensive DAS-steered care aimed at DMARD-free remission versus RA-patients treated to target in routine care.

**Methods:** 279 consecutive RA-patients (2010-criteria), diagnosed in the Leiden University Medical Centre between March 2007-September 2010, were studied. Of these, 155 participated in a DAS <1.6 steered trial aimed at DMARD-free remission (IMPROVED-study). These patients were initially treated with high-dose prednisone (60 mg/day) and methotrexate. Medication was intensified in case of a DAS ≥1.6 and tapered in case of a DAS <1.6. The other 124 RA-patients were treated according to routine care, consisting of initial methotrexate and subsequent DAS <2.4 steered treatment. The median follow-up was 7.8 years. Medical records were studied on achieving DMARD-free remission, defined as the absence of synovitis for ≥1 year after DMARD-cessation, and 'late flares', defined as recurrence of clinical synovitis ≥1 year after DMARD-cessation. Sustained DMARD-free remission was defined as the sustained absence of clinical synovitis after DMARD-cessation for ≥1 year and the total follow-up duration; i.e. patients with a late flare were not in this group. Percentages of remission and late flares were compared between the two treatment strategies, in all patients and after stratification by ACPA.

**Results:** Patients receiving intensive treatment were more often ACPA-positive (59% vs 40%). DMARD-free remission was achieved by 35% of patients receiving intensive treatment and by 29% of patients receiving routine care (HR 1.2, 95% CI: 0.8 to 1.8). Within the ACPA-positive and ACPA-negative strata patient characteristics were similar, except for a younger age in patients receiving intensive treatment. Within ACPA-positive patients, DMARD-free remission was achieved more often in the intensive treatment group than in the routine care group (25% vs 6%, HR 4.9, 95% CI: 1.4 to 17, corrected for age). In ACPA-negative patients no differences were observed (49% vs 44%, HR 1.1, 95% CI: 0.6 to

1.8, corrected for age). A late flare occurred in 20% of patients receiving intensive treatment and in 8% of patients receiving routine care (HR 2.3, 95% CI: 0.6 to 8.3). After excluding late flares from the remission group, the prevalence of DMARD-free sustained remission was not different for both treatment strategies in the total group (28% vs 27%, HR 1.0, 95% CI: 0.6 to 1.5). Also in the ACPA-positive group no significant effect remained (17% vs 6%, HR 3.1, 95% CI: 0.9 to 11, corrected for age).

**Conclusions:** An intensive treatment strategy was not associated with a higher prevalence of DMARD-free sustained remission compared to up-to-date routine treatment. Within ACPA-positive RA, intensive treatment resulted in more remission but also in more late flares. Together these data do not provide evidence to prioritise the studied intensive treatment strategy above current routine care.

**Disclosure of Interest:** None declared

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OP0042

#### IN ACPA POSITIVE AT-RISK INDIVIDUALS, WHICH MRI AND US FINDINGS BEST PREDICT DEVELOPMENT OF CLINICAL SYNOVITIS?

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**Background:** ACPA +individuals with non-specific MSK symptoms are at risk of inflammatory arthritis (IA) and may benefit from early intervention. Clinical, serological and US markers have previously been assessed to determine risk of progression.<sup>1</sup>

**Objectives:** Evaluate the value of MR and US imaging in characterising and quantifying risk in a large ACPA +cohort.

**Methods:** Eligible ACPA +individuals without clinical synovitis had gadolinium enhanced 3.0 T MRI of the dominant hand and wrist. Images were scored by 2 radiologists for synovitis, bone marrow oedema (BME), erosions and tenosynovitis (TSV) according to OMERACT RAMRIS. Joint counts for each abnormality at each joint were corrected for age using a healthy controls reference range.<sup>2</sup> US of the same regions were scored using OMERACT definitions. Maximum MRI and US abnormality scores observed per patient across all joints scored were dichotomised <2, ≥2. Potential associations between baseline US (greyscale (GS) and powerDoppler (PD)) and MRI findings and i) progression to IA and ii) development of clinical synovitis within a joint were identified using Cox and penalised regression.

**Results:** Imaging of 98 individuals (mean age 47, 69% female) was available. 30% (29/98) progressed to IA. Median time to progression was 31 weeks (IQR 24, 67). BME and erosions scores ≥2 were reported in 10%, preferential location to the carpal bones/wrist joints. Synovitis score ≥2 was present in 9%, preferential location at MCP5 and radial carpal/intercarpal joints. TSV was the most frequent reported abnormality with 22% scoring ≥2, 40% scoring 1. US GS and PD scores ≥2 were reported in 23% and 9% respectively. The unadjusted analysis HRs for all imaging abnormalities were high, indicating potential association with risk of progression. Controlling for variables, MRI TSV was associated with time to IA with an increased HR. US GS and PD were also independently associated with time to progression and confirmed on penalised regression, table 1. At the joint level MRI TSV, BME and US GS were associated with the risk of progression to clinical synovitis, HR=7.03 p<0.001, HR 4.22 p=0.076 and HR 8.04 p<0.001 respectively.

**Abstract OP0042 – Table 1.** Patient-level Cox regression proportional hazard modelling of associations between maximum observed score per patient for baseline MRI abnormalities and time to IA (n=95)

Abnormality	No IA% (n=66)	IA% (n=29)	Unadjusted HR (90% CI), P value	Adjusted HR (90% CI), P value	Penalised HR
Small joint tenderness	44(29)	55(16)	1.60 (0.87,2.97), p=0.207	1.20 (0.58,2.46), p=0.679	1
RF and/or ACPA>3ULN	83(55)	93(27)	2.14 (0.64,7.16), p=0.301	1.02 (0.27,3.80), p=0.981	1
EMS≥30 min	27(18)	45(13)	2.00 (1.08,3.71), p=0.064	1.52 (0.69,3.37), p=0.384	1
US PD≥2	2 (1)	28(8)	7.21 (3.62,14.36), p<0.001	5.09 (1.93,13.44), p=0.006	4.37
US GS≥2	11(7)	52(15)	4.97 (2.69,9.19), p<0.001	2.69 (1.14,6.34), p=0.059	2.17
MRI erosion≥2	6 (4)	17(5)	2.15 (0.96,4.82), p=0.120	0.59 (0.20,1.76), p=0.431	1
MRI BME≥2	8 (5)	17(5)	2.30 (1.01,5.23), p=0.097	1.55 (0.56,4.27), p=0.482	1
MRI synovitis≥2	3 (2)	24(7)	4.22 (2.03,8.75), p=0.001	1.08 (0.46,2.54), p=0.881	1
MRI TSV≥2	14(9)	41(12)	3.51 (1.89,6.55), p=0.001	4.02 (1.91,8.44), p=0.002	3.16

**Conclusions:** ACPA +at risk individuals have features on imaging which assists prediction of development to IA. MRI TSV provides additional predictive ability over and above the clinical and US variables.

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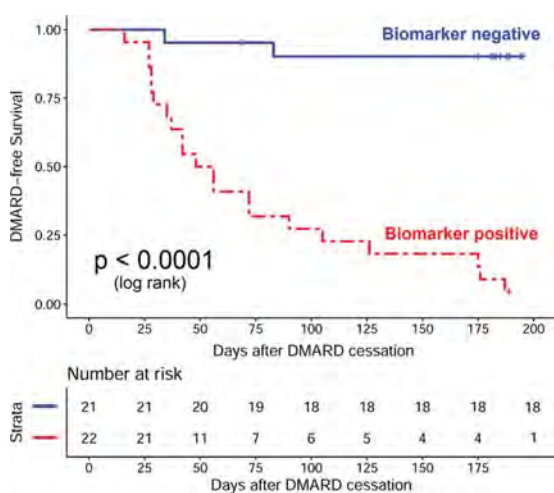
#### OP0043 PREDICTORS OF DRUG-FREE REMISSION IN RHEUMATOID ARTHRITIS: RESULTS FROM THE PROSPECTIVE BIOMARKERS OF REMISSION IN RHEUMATOID ARTHRITIS(BIORRA) STUDY

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**Background:** Remission is now a realistic and achievable target for many patients with rheumatoid arthritis (RA) using disease-modifying anti-rheumatic drugs (DMARDs) prescribed in modern treat-to-target regimens. However, DMARDs carry risks of potentially serious adverse effects, and require regular and expensive blood monitoring. Recent studies suggest that half of patients with RA in remission can discontinue DMARDs without a flare of arthritis activity, though this cannot currently be reliably predicted.

#### Abstract OP0043 – Table 1

Demographic	Value
Satisfied 2010 ACR/EULAR classification criteria: n (%)	44 (100%)
Age: median (IQR) [range]	66.5 (54.5–71.3) [35 – 82]
Female: n (%)	23 (52%)
Years since RA diagnosis: median (IQR) [range]	5.5 (3–11) [1–40]
Seropositive (rheumatoid factor and/or anti-citrullinated peptide antibody): n (%)	32 (73%)
Current methotrexate use: n (%)	38 (86%)
Baseline DAS28-CRP: median (IQR) [range]	1.07 (0.99–1.63) [0.96–2.34]
ACR/EULAR Boolean remission: n (%)	29 (66%)
Presence of joint erosion on baseline 7-joint ultrasound scan: n (%)	29 (70%)



**Objectives:** To identify baseline biomarkers that can predict sustained drug-free remission (DFR) versus arthritis flare following DMARD cessation.

**Methods:** Patients with established RA satisfying clinical (disease activity in 28 joints with CRP [DAS28-CRP]<2.4) and ultrasound (absence of power Doppler synovitis on a blinded 7-joint scan) remission criteria discontinued conventional synthetic DMARDs (methotrexate, sulfasalazine, and/or hydroxychloroquine) and

were monitored for 6 months. The primary outcome was time-to-flare, defined as DAS28-CRP $\geq$ 2.4. Baseline clinical and ultrasound parameters (synovial/tenosynovial greyscale and joint erosions), circulating levels of 26 cytokines/chemokines, and gene expression by peripheral CD4 +T cells (RNA sequencing) were assessed for their ability to predict time-to-flare and flare/DFR status by multivariate Cox regression and receiver-operating characteristic (ROC) analysis.

**Results:** 44 patients were eligible for DMARD cessation (table 1); 23 (52%) experienced an arthritis flare at a median (IQR) of 48 (31.5–86.5) days. A composite score incorporating five variables (three genes [currently subject to patent application], one cytokine [IL-27], and one clinical [ACR/EULAR Boolean remission]) differentiated future flare and DFR with an area under the ROC curve of 0.96 (95% CI: 0.92 to 1.00), sensitivity 0.91 (0.78–1.00) and specificity 0.95 (0.84–1.00) (figure 1).

**Conclusions:** Our study provides proof-of-concept evidence for the existence of biomarkers of DFR in RA. If validated in an external cohort, these biomarkers may hold promise in guiding DMARD withdrawal, with consequent minimisation of medication adverse events and healthcare costs.

**Acknowledgements:** KB was supported by the Wellcome Trust [102595/Z/13/A] and the NIHR Newcastle Biomedical Research Centre [BH136167/PD0045]. A patent application is currently in process regarding the gene expression biomarkers, the identify of which will subsequently be disclosed.

**Disclosure of Interest:** None declared

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#### OP0044 AFTER HOW LONG OF DISEASE DURATION DOES THE INCREASED MORTALITY RISK APPEAR IN RECENT ONSET RHEUMATOID ARTHRITIS?

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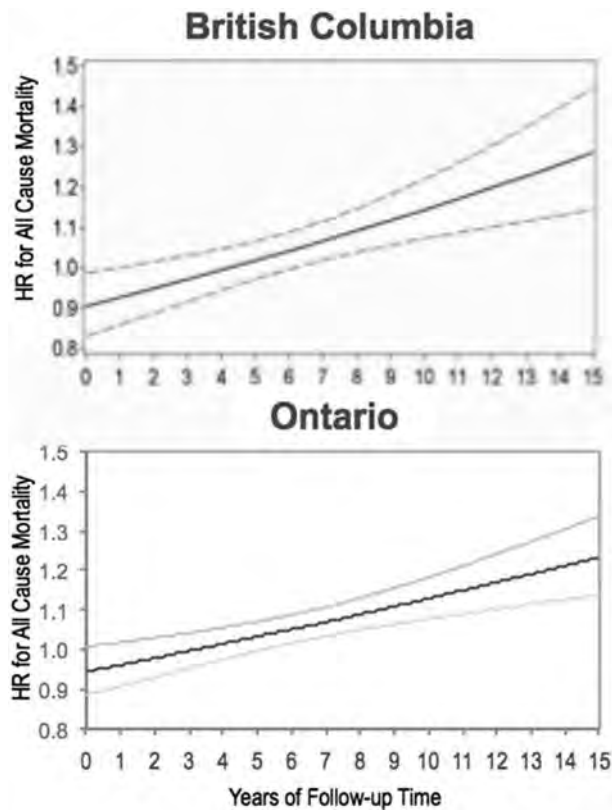
**Background:** For decades studies showed that rheumatoid arthritis (RA) patients died earlier than their general population counterparts. Some inception cohorts have failed to detect an increased mortality risk, possibly due to limited followup or to improvement in mortality risk in cohorts of more recent onset.

**Objectives:** To evaluate the risk of all-cause mortality in incident RA patients and to estimate when the increased risk appears amongst two Canadian inception cohorts with RA onset after 2000

**Methods:** Using a common protocol, we conducted 2 independent population-based cohort studies, using administrative health data, of incident RA patients in British Columbia (BC) and Ontario (ON), Canada over 2000 to 2015. In each province, we identified all RA patients (using validated criteria) diagnosed between 2000 and 2005 (to allow a minimum of 10 years of follow-up), and identified non-RA general population comparators for each RA patient, matched 1:2 on age, sex and index years. All patients were followed from index date until death (ascertained from vital statistics), out-migration, or end of study period (2015). Adjusted hazard ratios (HRs) and 95% CIs were estimated using multivariable Cox regression, controlling for baseline comorbidities, healthcare use, and socio-demographic factors. To estimate when the increased mortality risk appeared in incident RA patients, and to assess the proportional hazards assumption, we included an interaction between RA diagnosis and follow-up time in the multivariable model, to detect if and how the HR varied according to RA duration. Quadratic and logyear interactions were tested in the multivariable Cox models to assess linearity of the interaction.

**Results:** Among 13 834 incident RA patients in BC (27 668 matched comparators), 66% were female with a mean (SD) age of 58<sup>16</sup> years at cohort entry. Among 27 405 incident RA patients in ON (54 810 matched comparators), 70% were female with a mean (SD) age of 56<sup>16</sup> years. The prevalence of individual comorbidities at baseline was comparable across RA cohorts. During follow-up, 3139 (23%) of BC RA patients and 6270 (23%) ON RA patients died, with corresponding crude mortality rates of 2.3 deaths per 100 person-years in both provinces. Crude mortality rate ratios for BC and ON were 1.11 (95% CI: 1.07 to 1.16) and 1.27 (95% CI: 1.23 to 1.31), respectively. Multivariable analyses detected an increased risk of all-cause mortality in incident RA (relative to non-RA) patients by 6 years of follow-up, with a linear relationship suggesting further increase over time (figure 1). By 10 years of followup, the adjusted HR for RA was 1.14 (95% CI: 1.07 to 1.22) in BC and 1.13 (95% CI: 1.08 to 1.18) in ON.





**Abstract OP0044** – Figure 1 Adjusted HR (solid black line) and 95% CIs (grey line) for all-cause mortality, over time since cohort entry

**Conclusions:** In 2 large Canadian RA population-based inception cohorts, a small increased mortality risk appeared after 6 years of RA duration and increased to a 14% (in BC) and 13% (in ON) increased risk after 10 years. While these findings represent an improvement in the mortality risk associated with RA compared to previous reports in older historical cohorts, the increasing mortality risk associated throughout the disease course suggests increased efforts to prevent disease progression and optimise comorbidity management are needed.

**Disclosure of Interest:** None declared

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#### OP0045 ADVERSE EVENT REPORTING RATES AND PLACEBO/STANDARD-OF-CARE-ARM ACR RESPONSES VARY BY REGION IN RHEUMATOID ARTHRITIS TRIALS

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**Background:** Clinical trials are increasingly globalised, with more trials conducted in Asia, Latin America, and the Russian Federation and Eastern Europe (RFEE).<sup>1</sup> Adverse event (AE) reporting rates and placebo (or standard-of-care-arm) response may differ by geographic region and level of economic development<sup>2-4</sup>; efficacy and safety may not be generalizable across regions. This potential heterogeneity and its implications for rheumatoid arthritis (RA) trials have not been studied in detail.

**Objectives:** To assess potential regional differences in rates of ACR responses and AE reporting using patient-level data (PLD) from RA trials in the TransCelerate initiative.<sup>5</sup>

**Methods:** We obtained PLD for all 17 RA trials available through TransCelerate as of August 2017 and analysed data from 7 trials with geographic information available (NCT01198002, NCT01202760, NCT01202773, NCT01404585, NCT00605735, NCT00048581, NCT00647270). We grouped patients by region and evaluated differences in demographics, AE reporting rates, and ACR response. Pairwise comparisons were made between regions using Fisher's exact test, with false discovery rate (FDR) correction for multiple comparisons. All patients were included in analyses of AE reporting. Only patients with data sufficient to calculate ACR scores were included in analyses of ACR response. Demographics for patients in each region are shown in table 1.

**Results:** The lowest rates of AE reporting and ACR50 response were seen in RFEE. The highest rate of ACR20 response was seen in Asia. After FDR

correction, significantly lower 12 week and 52 week AE reporting rates were seen in RFEE than in Asia, Latin America, or the United States. Only the ACR50 response difference between RFEE and Latin America survived FDR correction; however, ACR20 rates in Asia remained significantly higher than in RFEE and the United States (table 2).

**Abstract OP0045** – Table 1 Patient demographics by region

Region	AE Analysis, n	ACR Response Analysis, n	Female, %	Median Age, y (SD; range)
US	369	268	81	55 (11; 21-78)
RFEE	213	160	81	51 (12; 25-79)
Latin America	167	132	89	51 (12; 22-76)
Asia	164	107	88	52 (12; 18-83)

**Abstract OP0045** – Table 2 Proportions of patients attaining ACR50/20 response at 12 week and/or reporting  $\geq 1$  AE at 12 and 52 weeks across regions

Attaining ACR50	6	9*	7	1
Attaining ACR20	17	24	29**	15
With AE at 12 weeks	53*	49*	51*	22
With AE at 52 weeks	68*	58**	65*	39

\*p < 0.05 vs RFEE. \*\*p < 0.05 vs US. All p values corrected for multiple comparisons.

**Conclusions:** Patient-level data from placebo arms in the TransCelerate initiative revealed significant regional differences in AE reporting rates and ACR50/ACR20 response rates. Differences in Latin America, RFEE, and Asia were especially notable; future patient populations from these regions may show distinct efficacy/safety profiles regardless of treatment. Given ongoing globalisation of clinical trials, country- and region-specific treatment patterns, patient populations, and safety issues should be explored to avoid misguided inferences across regions. Capping recruitment by region to balance these factors may be warranted.

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**Disclosure of Interest:** D. Keebler Shareholder of: Roche, Employee of: Genentech, E. Teng Employee of: Genentech, J. Chia Employee of: Genentech, D. Lee Employee of: Genentech, J. Galanter Employee of: Genentech, J. Peake Employee of: Genentech, K. Tuckwell Shareholder of: Roche, Employee of: Genentech

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**WEDNESDAY, 13 JUNE 2018:** Immunobiology of vasculitis

#### OP0046 EFFECT OF A SELECTIVE C5aR ANTAGONIST, AVACOPAN (CCX168), ON PLASMA COMPLEMENT LEVELS IN ANCA ASSOCIATED VASCULITIS (AAV)

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**Background:** The interaction between primed neutrophils and anti-neutrophil cytoplasmic autoantibodies (ANCA) releases factors that activate the alternative complement pathway, initiating an amplification loop that is thought to sustain necrotizing inflammation during flares of AAV.<sup>1</sup> Avacopan (CCX168), a selective, orally available, small molecule C5aR1 antagonist, was associated with rapid clinical benefit in the Phase 2 CLEAR trial in patients with AAV,<sup>2</sup> indicating that therapeutic intervention in this pathogenic process can be accomplished by inhibiting the C5aR1-dependent cellular response to C5a, without broad inhibition of upstream complement functions important to host defense.

**Objectives:** The present study was designed to confirm the reported elevated levels of complement activation products in AAV,<sup>2</sup> demonstrate that inhibiting cellular (e.g. neutrophil) activation by C5a with avacopan is effective in AAV while preserving upstream functions of complement, and compare effects of avacopan to those of high dose prednisone.

**Methods:** The CLEAR trial compared 3 regimens in 67 patients with AAV:<sup>1</sup> full dose prednisone (60 mg daily, tapered);<sup>2</sup> avacopan 30 mg twice daily plus low dose prednisone (20 mg, tapered);<sup>3</sup> avacopan 30 mg twice daily plus no



prednisone. All also received either cyclophosphamide or rituximab. Bb, C3a, C5a, sC5b-9 and properdin were analysed by ELISA in plasma collected at baseline and at intervals in AAV patients, and in 20 healthy controls matched for age, gender and ethnic background. Paired t-test was used for within group comparison and unpaired t-test was used for between group comparisons using log transformed data. P-values were corrected for multiple comparisons.

**Results:** Before treatment, levels of C3a, C5a, sC5b-9 and properdin were significantly elevated in AAV patients compared to matched healthy controls (geomean [95%], C3a, 67.2 [57.5–78.7] vs 23.2 [16.9–31.9] ng/mL,  $p < 0.001$ ; C5a, 7.55 [6.50–8.78] vs 5.19 [3.87–6.95] ng/mL,  $p < 0.05$ ; sC5b-9, 241(222–262) vs 155 (136–178) ng/mL,  $p < 0.001$ ; Properdin, 18.4 [16.9–20.0] vs 13.1 [11.4–15.6]  $\mu\text{g/mL}$ ,  $p < 0.001$ ). In subjects treated with full dose prednisone, levels of Bb, C3a, and C5a decreased significantly on Day 8 and 29 rising again at day 85, coincident with tapering. Consistent with its mode of action (inhibition of C5aR1, the receptor at the terminus of the complement cascade), avacopan did not impact circulating complement levels. There were no changes from baseline in mean plasma sC5b-9 or properdin levels in any treatment group.

**Conclusions:** Avacopan was associated with rapid improvement in AAV disease activity without apparent impact on assembly of C5b-9 (the membrane attack complex) or upstream activities of the complement system important for host defense (e.g. bacterial infections) and tissue repair. In contrast, glucocorticoids were associated with dose-dependent reduction of circulating levels of upstream complement activation products.

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#### OP0047 CIRCULATING CD24<sup>hi</sup>CD38<sup>hi</sup> REGULATORY B CELLS INFLUENCE TH17 CELL RESPONSES IN PATIENTS WITH ANCA-ASSOCIATED VASCULITIDES

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**Background:** CD24<sup>hi</sup>CD38<sup>hi</sup> regulatory B cells (Bregs) exhibit suppressive function and modulate pathogenic T cell responses. Persistent expansion of pathogenic IL-17-producing T cells (Th17) has been demonstrated in patients with anti-neutrophil cytoplasmic autoantibody (ANCA)-associated vasculitides (AAV). In addition, a reduction in numbers of CD24<sup>hi</sup>CD38<sup>hi</sup> Bregs was described in active AAV patients whereas no difference was found in patients in remission compared to healthy controls (HCs).

**Objectives:** To investigate whether there is a direct relation between increased proportions of Th17 cells and diminished proportions Bregs in AAV patients.

**Methods:** Frequencies of both Bregs and Th17 cells were determined by FACS in blood samples from 44 AAV patients in remission. None of the AAV patients received immunosuppressive treatment. Bregs were defined within the CD19<sup>+</sup> population as CD24<sup>hi</sup>CD38<sup>hi</sup> cells, and Th17 cells were defined within the CD3<sup>+</sup>CD4<sup>+</sup>CD45RO<sup>+</sup> population by their specific chemokine receptor expression as CXCR3<sup>+</sup>CCR4<sup>+</sup>CCR6<sup>+</sup> cells. In addition, CD3<sup>+</sup>CD4<sup>+</sup> Th cells were sorted from 4 AAV patients and 3 HCs and co-cultured with either Breg-depleted B cells or total B cells. Cultured cells were stimulated with SEB and CpG-ODN and frequencies of both IL-17<sup>+</sup> (Th17) and IFN $\gamma$ <sup>+</sup> (Th1) T cells were determined at baseline and day 5 upon restimulation with PMA and Ca<sup>2+</sup> ionophore.

**Results:** The frequency of circulating Bregs in AAV-patients correlated negatively with circulating Th17 cells ( $r = -0.390$ ;  $p = 0.009$ ), whereas no such correlation was observed with other B cell subtypes. The co-culture experiments revealed that the frequency of IFN $\gamma$ <sup>+</sup> T cells was unaffected when Bregs were depleted in both HCs and AAV patients (undepleted samples median: 10.6%; range: 5.5%–19.7% vs Breg-depleted samples median: 11%; range: 4.9%–19.2%). Remarkably, a significant increase in the frequency of IL-17<sup>+</sup> Th cells was detected in Breg-depleted samples (median: 1.6%; range: 1%–3.8%) compared to undepleted samples in both HCs and patients ( $p = 0.03$ ; undepleted samples median: 1.2%; range: 0.9%–2.9%). Moreover, the IFN $\gamma$ <sup>+</sup>:IL-17<sup>+</sup> T cell ratio was not different between

undepleted (median: 13.8, range: 5.1–39.3) and Breg-depleted samples at baseline (median: 11, range: 7.3–30), whereas a significant decrease was found in the Breg-depleted samples (median: 5.6; range: 3.3–9.1) after 5 days of culture ( $p = 0.016$ ; undepleted median: 6.3; range: 4.2–10.6) indicating a change in the Th1:Th17 ratio.

**Conclusions:** CD24<sup>hi</sup>CD38<sup>hi</sup> Bregs modulate Th17 responses in AAV patients. Future treatment of AAV could aim at expanding CD24<sup>hi</sup>CD38<sup>hi</sup> Bregs to suppress pathogenic Th17 cells.

**Disclosure of Interest:** None declared

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#### OP0048 THE UTILITY OF SERUM ANGIOPOIETIN-1 AND ANGIOPOIETIN-2 IN PATIENTS WITH ANTI-NEUTROPHIL CYTOPLASMIC AUTOANTIBODY-ASSOCIATED VASCULITIS

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**Background:** Angiotensin-1 (Ang-1) and Angiotensin-2 (Ang-2) are antagonistic ligands which bind with similar affinity to the extracellular domain of the tyrosine kinase with Ig-like and epidermal growth factor-like domains 2 (Tie-2) receptor, which is almost exclusively expressed by endothelial cells. Ang-1/Tie-2 signalling maintains vessel integrity, inhibits vascular leakage, suppresses inflammatory gene expression and prevents recruitment and transmigration of leukocytes. In contrast, binding of Ang-2 disrupts protective Ang-1/Tie-2 signalling and facilitates endothelial inflammation. Recently, serum Ang-2 levels have been reported to be elevated in autoimmune disorders such as rheumatoid arthritis, systemic lupus erythematosus, and anti-neutrophil cytoplasmic autoantibody-associated vasculitis (AAV).

**Objectives:** To examine the serum Ang-1 and Ang-2 levels in patients with AAV, and investigate the utility as biomarkers.

**Methods:** Seventy-one patients who had been diagnosed as AAV and referred to Niigata University Medical and Dental Hospital between 2009 and 2017, were participated in this study. Serum Ang-1 and Ang-2 levels were measured by enzyme-linked immunosorbent assay, before the initiation of remission-induction therapy. Laboratory findings, disease activity using Birmingham vasculitis activity score (BVAS) at the time of diagnosis, and patients' kidney and overall prognosis at August 2017, were corrected from patients' clinical records. The correlations between these findings and serum Ang-1, Ang-2 levels, and Ang-1/Ang-2 ratio were analysed by Pearson correlation coefficient and stepwise multiple regression analysis. A value of  $p < 0.05$  was taken to indicate statistical significance.

**Results:** In Pearson correlation coefficient analysis, serum Ang-1 was negatively correlated with serum creatinine (Cr) ( $r = -0.3490$ ,  $p = 0.0151$ ), urinary protein/Creatinine ratio (UP/Cr) ( $r = -0.3147$ ,  $p = 0.0312$ ), and positively correlated with estimated glomerular filtration ratio (eGFR) ( $r = 0.4091$ ,  $p = 0.0039$ ). Serum Ang-2 was positively correlated with BVAS ( $r = 0.3024$ ,  $p = 0.003$ ), serum Cr ( $r = 0.3778$ ,  $p = 0.0081$ ), and the initiation of hemodialysis therapy ( $r = 0.4196$ ,  $p = 0.0151$ ), and negatively correlated with eGFR ( $r = -0.2999$ ,  $p = 0.0383$ ). The Ang-1/Ang-2 ratio was positively correlated with BVAS ( $r = 0.3527$ ,  $p = 0.0139$ ), serum Cr ( $r = 0.7419$ ,  $p < 0.0001$ ), UP/Cr ( $r = 0.4799$ ,  $p = 0.0006$ ), and the initiation of hemodialysis therapy ( $r = 0.6151$ ,  $p < 0.0001$ ), and negatively correlated with eGFR ( $r = -0.4758$ ,  $p = 0.0006$ ). In stepwise multiple regression analysis, eGFR was selected as a positive independent variable for serum Ang-1 levels ( $\beta = 0.3769$ ,  $p = 0.0014$ ) and Ang-1/Ang-2 ratio ( $\beta = 0.4060$ ,  $p = 0.0005$ ), whereas the initiation of hemodialysis therapy was selected as a positive independent variable ( $\beta = 0.5850$ ,  $p < 0.0001$ ), and UP/Cr ( $\beta = -0.5780$ ,  $p < 0.0001$ ) and eGFR ( $\beta = -0.4311$ ,  $p = 0.0003$ ) were selected as negative independent variables for serum Ang-2 levels.

**Conclusions:** These findings showed the protective effect of kidney functions for Ang-1 and the utility of Ang-2 as a predictive factor for kidney prognosis.

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**Disclosure of Interest:** None declared

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**OP0049** **ABERRANT VISTA EXPRESSION ON CD45RA+CD25DIM TH-CELLS IN GIANT CELL ARTERITIS**

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**Background:** A broad naïve Th-cell repertoire is needed to face novel antigenic challenges and mounting an optimal immune response.<sup>1,2</sup> The replenishment of naïve T-cells is severely restricted by thymic involution with ageing.<sup>3</sup> In the past, our group provided new insight into the homeostasis of human Th-cells, identifying CD45RA<sup>+</sup>CD25<sup>dim</sup>Th-cells as a subset of post-thymically expanded naïve Th-cells in healthy aged individuals.<sup>4</sup> Immune homeostasis of naïve Th-cells is especially important to understand defective immune responses in age-related immune disorders such as Giant Cell Arteritis (GCA). Recently, a loss of immunoinhibitory checkpoints has been implicated in GCA.<sup>5,6</sup> The possible contribution of immune checkpoint pathways to the dysregulation of Th-cells, especially in CD45RA<sup>+</sup>CD25<sup>dim</sup>Th-cells in GCA has not yet been studied.

**Objectives:** In this study, we aimed to investigate the expression of different immune checkpoint molecules on circulating CD45RA<sup>+</sup>CD25<sup>dim</sup>Th-cells of GCA-patients and compare it with matched healthy controls (HCs).

**Methods:** In a cross-sectional study, fresh blood samples were obtained from 33 GCA-patients with/without immunosuppressive treatment (glucocorticoids) and 12 sex/age-matched HCs. The frequency of the expression of different immune checkpoints including CD28, Cytotoxic T-Lymphocyte-associated antigen-4 (CTLA-4), Programmed death-1 (PD-1), and V-domain Ig suppressor of T cell activation (VISTA) were determined on CD45RA<sup>+</sup>CD25<sup>dim</sup>Th-cells of GCA-patients and HCs by flow cytometry.

**Results:** Proportion of circulating CD45RA<sup>+</sup>CD25<sup>dim</sup>Th-cells in GCA-patients was not different when compared to HCs, whereas significant increase in these cells was observed only in treated GCA-patients when compared to HCs. The proportion of CD28, CTLA-4 and PD-1 expression on CD45RA<sup>+</sup>CD25<sup>dim</sup>Th-cells did not differ between GCA-patients and HCs. Interestingly, proportion of VISTA expression on these cells was significantly decreased in GCA-patients. Furthermore, decreased frequency of VISTA expression was seen in both untreated and treated patients.

**Conclusions:** In GCA-patients (untreated and treated), lower frequencies of VISTA<sup>+</sup>CD45RA<sup>+</sup>CD25<sup>dim</sup>Th-cells were noted. Decreased VISTA expression in GCA-patients could play a role in the regulation of Th-cell activation/inhibition. The functional consequences of immune checkpoint modulation within particular subsets requires further investigation.

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**Disclosure of Interest:** None declared

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**OP0050** **GENE POLYMORPHISMS OF THE GLUCOCORTICOID RECEPTOR AND 11B-HYDROXYSTEROID DEHYDROGENASE TYPE 1 AFFECT RELEVANT CLINICAL OUTCOMES IN ANCA ASSOCIATED VASCULITIS**

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**Background:** High doses of exogenous glucocorticoids (e.g., prednisolone) are a standard part of treatment for ANCA-associated vasculitis.<sup>1</sup> Efficacy and toxicity of glucocorticoid treatment differ widely between individuals.<sup>2</sup> We hypothesised

that this can be partly explained by genetic polymorphisms of the glucocorticoid receptor (GR) and 11 $\beta$ -hydroxysteroid dehydrogenase type 1 (HSD11B1) that influence glucocorticoid sensitivity.

**Objectives:** To investigate whether five haplotypes of the Glucocorticoid Receptor gene (NR3C1) and a single nucleotide polymorphism of 11 $\beta$ -hydroxysteroid dehydrogenase type 1 (HSD11B1) are associated with treatment efficacy and toxicity in ANCA associated vasculitis.

**Methods:** A total of 241 ANCA associated vasculitis patients were genotyped for five polymorphisms of the glucocorticoid receptor gene and one polymorphism of the HSD11B1 gene. Glucocorticoid receptor gene haplotypes were predicted based on genotyping results. Relapse free survival, mortality, renal survival, metabolic adverse events and infections were compared between carriers and non-carriers of glucocorticoid receptor haplotypes and the HSD11B1 genotype.

**Results:** Carriers of the ER22/23EK haplotype of the glucocorticoid receptor had a significantly higher risk of 10 year mortality (Hazard Ratio (HR) 3.0, 95% confidence interval, CI: 1.2 to 7.3), more frequently required plasmapheresis treatment (p=0.04) and had a higher risk of developing end-stage renal disease (HR 7.4, 95% CI: 1.9 to 28.7). Carriers of a minor variant of HSD11B1 more frequently experienced relapse (HR 2.5, 95% CI: 1.5 to 4.1), except if they also carried the BcI haplotype of the glucocorticoid receptor. Homozygous carriers of the BcI haplotype had a higher risk of developing hypertension (HR 2.7, 95% CI: 1.2 to 5.7) and dyslipidemia (HR 4.1, 95% CI: 1.8 to 9.6). Occurrence of infections neither differed between GR haplotypes, nor between HSD11B1 genotypes.

**Conclusions:** The ER22/23EK and BcI haplotype of the glucocorticoid receptor and a polymorphism of the gene for HSD11B1 are associated with clinically relevant inflammatory and metabolic outcomes in ANCA associated vasculitis.

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**OP0051** **EVOLUTION OF THE VASCULAR INVOLVEMENT OBJECTIFIED BY PET/TAC IN PATIENTS WITH GIANT CELL ARTERITIS TREATED WITH TOCILIZUMAB**

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**Background:** Giant cell arteritis (GCA) is a large-vessel vasculitis which can involve the aorta and/or its major branches. Tocilizumab (TCZ) seems to be effective in giant cell arteritis (GCA).<sup>1–4</sup>

**Objectives:** Our aim was to assess if the clinical and analytical improvement yielded in patients with GCA treated with TCZ is accompanied by a reduction of the vascular inflammation evaluated by PET/CT.

**Methods:** Study of 36 patients who had a baseline and follow-up PET/CT from a multicenter series of 134 patients with GCA in treatment with TCZ. The evolution of the vascular involvement objectified by PET/CT was assessed. In addition clinical efficacy, analytical improvement (acute phase reactants) and the reduction of corticosteroid dose was studied.

**Results:** The 36 patients (28 women and 8 men) had an mean age of 69.83±8.66 years. After TCZ onset, a rapid and maintained clinical improvement was observed (table 1). In addition, during the first twenty-four months of follow-up, C-reactive protein decreased from 2.4 [0.9–6.8] to 0.1 [0.0–0.5] mg/dL and the erythrocyte sedimentation rate from 41.5 [16.7–58.5] to 4 [2–12.5] mm/1 st hour. On the other hand, the levels of haemoglobin experienced an increase from 12.3 [11.3–13.0] to 13.3 [13.0–13.9] g/dL. The median dose of prednisone decreased from 12.5 [9.4–26.2] to 0.0 [0.0–0.0] mg/day. However, the decrease in F18-fluorodeoxyglucose uptake in the PET/CT study was not as evident.

## Abstract OP0051 – Table 1

	Baseline	Month 6	Month 12	Month 18	Month 24
<b>Clinical improvement n, (%)</b>					
Complete		26/26 (80)	24/27 (88.9)	21/23 (95.4)	17/18 (94.4)
Partial		5/35 (14.3)	3/27 (11.1)	1/22 (4.5)	1/18 (5.5)
No improvement		2/35 (5.7)	0 (0)	0 (0)	0 (0)
<b>Laboratory markers, median [IQR] #</b>					
ESR	41.5 [16.7-58.5] (36)	4 [2-8] (36)*	4.5 [2-12] (28)*	5 [2.5-11] (23)*	4 [2-12.5] (19)*
CRP	2.4 [0.9-6.6] (36)	0.1 [0.0-0.7] (33)*	0.3 [0.1-0.6] (27)*	0.1 [0.1-0.5] (23)*	0.1 [0.0-0.5] (18)*
Dose of corticosteroids (mg/day), median [IQR] #	12.5 [8.4-28.2] (36)	5.0 [1.2-6.0] (33)*	0.0 [0.0-4.2] (28)*	0.0 [0.0-2.5] (21)*	0.0 [0.0-0.6] (19)*
<b>Improvement in PET/CT</b>					
Complete		0/8 (0)	3/13 (23)	3/11 (27.3)	1/4 (25)
Partial		6/8 (75)	6/13 (46.1)	7/11 (63.6)	2/4 (50)
No improvement		2/8 (25)	4/13 (30.8)	1/11 (9.1)	1/4 (25)

\*p&lt; 0.0001 (Wilcoxon test)

**Conclusions:** Although TCZ seems to be an important therapeutic agent in the treatment of GCA, achieving a rapid and sustained clinical and analytical improvement, the decrease in vessel inflammation assessed by F18-fluorodeoxyglucose uptake seems to take a slower course.

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OP0052

### MICROPARTICLES AS POTENTIAL BIOMARKERS OF DISEASE ACTIVITY IN ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODY – ASSOCIATED VASCULITIS

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**Background:** Microparticles (MPs) are submicron particles, which are released from plasma membrane upon cell activation and during the early phase of apoptosis. Increased levels of circulating MPs, mainly of endothelial cell origin, but also platelet derived, have been shown to correlate with autoinflammatory disease activity, such as anti-neutrophil cytoplasm antibody (ANCA) – associated vasculitis (AAV).

**Objectives:** The aim was to evaluate levels of activity markers expressed on MPs from patients with AAV, during active disease and remission, compared to healthy control subjects.

**Methods:** Our study included 46 AAV patients and 23 healthy age and gender matched control subjects. We analysed the concentration of MPs in plasma by flow cytometry. MPs were phenotyped by expression: CD142 (tissue factor-TF), anti-H3cit (citruinated Histone 3 directed against neutrophil extracellular traps – NETs), anti-pentraxin3 (pentraxin3), HMGB1 (high mobility group box 1 protein-HMGB1), anti-TWEAK (tumour necrosis factor-like weak inducer of apoptosis-TWEAK), anti-plasminogen (plasminogen), anti-C3a (C3a) and anti-C5a (C5a). The assessment of vasculitis disease activity was performed using the Birmingham Vasculitis Activity Score (BVAS), where active disease was defined as BVAS ≥ 1 and inactive (remission) as BVAS=0.

**Results:** Half of the patients group<sup>23</sup> had active vasculitis (13 male/10 female, mean age 61±14 years) and 23 had inactive disease (12 male/11 female, mean age 64±13 years). Concentration of MPs expressing TF, H3cit, pentraxin-3 and HMGB1 in active patients were significantly higher than in those in remission and healthy controls (p<0.01, p<0.0001, respectively). MPs expressing C5a and C3a were significantly higher in both active and inactive patients compared to controls (p<0.001). Additionally, levels of MPs expressing C5a and C3a strongly correlated with BVAS in patients with active disease (r=0.78, p<0.0001; r=0.5, p<0.01, respectively), while there was no significant correlation between other explored markers and BVAS.

**Conclusions:** Our results support recently postulated role of the complement system in AAV pathogenesis and disease activity. Evaluated proteins expressed

on MPs, especially C5a and C3a, could be used as potential biomarkers which might reflect inflammation and disease activity in AAV patients. Further investigations are necessary to confirm our preliminary results and to validate the most promising biomarker in AAV.

**Disclosure of Interest:** None declared

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OP0053

### INFLAMMATORY DISORDERS ASSOCIATED WITH TRISOMY 8 MYELODYSPLASTIC SYNDROMES : FRENCH RETROSPECTIVE CASE CONTROL STUDY

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**Objectives:** We report myelodysplastic syndrome (MDS)-associated systemic inflammatory and autoimmune diseases (IADs) with cytogenetic trisomy 8, and describe their outcome, treatments efficacy and impact on MDS survival in a French multicenter retrospective study.

**Methods:** In this study, 21 patients with trisomy 8-MDS and IADs were analysed and compared to 103 MDS patients with trisomy 8 without IADs.

**Results:** The median age was 67 [59 – 80] years and the male/female ratio 0.9. The IADs were Behçet's or Behçet's-like disease in 11 (52%) cases, inflammatory arthritis in 4 (19%) cases, Sjögren's syndrome, autoimmune hemolytic anaemia, aseptic abscesses, polyarteritis nodosa, Sweet's syndrome and unclassified vasculitis in one case each. Trisomy 8 karyotype was isolated in 8 cases (38%) and associated with other abnormalities in remaining cases. Seventeen (81%) IADs patients were treated (88% with steroids) with complete and partial response in 35% and 47%, respectively. A second-line therapy was required for steroid dependence or relapse in 38% of cases. The effect of MDS treatment on IADs could be assessed in 7 patients treated with Azacitidine : 5/13 (38%) achieved remission and 2/13 (15%) partial response of IADs. Compared with 103 trisomy 8-MDS/CMML patients without IADs, IADs patients were more often non-Caucasian (p=0.004), MDS subtype tended to be more frequently CRDM (p=0.09) and had more often a poor karyotype (p<0.001). No survival difference was seen between patients with trisomy 8-MDS-associated IADs and without IADs.

**Conclusions:** The spectrum of IADs associated to trisomy 8-MDS is dominated by Behçet's disease, but may also be other various immune disorders. Steroid therapy is often effective, but sparing therapies are mostly necessary.

**Disclosure of Interest:** None declared

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WEDNESDAY, 13 JUNE 2018

### Envisioning new horizons for people with osteoarthritis

OP0054

### PAIN IN HAND OSTEOARTHRITIS AND THE ASSOCIATIONS WITH RADIOGRAPHIC OSTEOARTHRITIS SEVERITY AND PSYCHOLOGICAL FACTORS

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**Background:** Pain is the most preferred area of improvement for patients with hand osteoarthritis (OA). Whereas only weak associations have been found between radiographic OA severity and pain, few studies have explored whether psychological factors are associated with pain.

**Objectives:** To examine whether radiographic severity, depression, anxiety and pain catastrophizing are associated with self-reported pain in patients with hand OA, and to explore possible interactions between psychological factors and radiographic severity.

**Methods:** The Nor-Hand study is an observational cohort study of 300 (89% women) hand OA patients with median (IQR) age of 61 [57–66] years. Participants completed questionnaires, including Numeric Rating Scale (NRS, 0–10 scale) about hand pain, Australian/Canadian (AUSCAN) hand pain subscale (0–20 scale), Hospital Depression and Anxiety Scale (HADS, 0–42 scale) and Pain



Catastrophizing Scale (PCS, 0–52 scale) at the baseline examination in 2016–2017. Bilateral interphalangeal, metacarpophalangeal, first carpometacarpal and the scaphotrapezotrapezoidal joint were scored for radiographic OA according to the Kellgren-Lawrence (KL) index (sum score: 0–132 scale). Using linear regression analyses, we analysed whether KL sum score, HADS sum score and PCS sum score (independent variables) were associated with AUSCAN pain (dependent variable). Separate models were applied for each independent variable with adjustment for age, sex and body mass index (BMI). Thereafter, all independent variables were included in the same model. Analyses were repeated using NRS hand pain as the dependent variable. Interactions between KL sum score and HADS/PCS were explored.

**Results:** Patients reported wide range of pain severity with mean (SD) AUSCAN pain of 8.2 (4.0) and mean (SD) NRS hand pain of 3.8 (2.3). Their radiographic severity ranged from minimal to severe with a median (IQR) KL sum score of 28 (15–44). Most patients reported low levels of anxiety, depression and pain catastrophizing with median (IQR) HADS sum score of 6 (3–10) and PCS sum score of 9 (5–15).

The HADS and PCS sum scores were associated with hand pain, both when analysed separately and in the same model together with KL sum score (table 1). Increasing radiographic severity was not associated with hand pain in the age, sex and BMI-adjusted models. When including HADS and PCS in the models, the associations between radiographic severity and pain became stronger for both pain outcomes and statistically significant for AUSCAN pain (table 1).

We found interactions between KL sum score and HADS. In the 61 persons with HADS depression and anxiety subscale scores below 8, the KL sum score was significantly associated with AUSCAN pain ( $B=0.03$ , 95% CI: 0.003 to 0.06,  $p=0.03$ ) and NRS pain ( $B=0.02$ , 95% CI: 0.002 to 0.03,  $p=0.03$ ) (adjusted for age, sex, BMI and PCS), whereas no associations between radiographic severity and pain was found in persons with HAD depression and/or anxiety subscale scores of 8 or more.

Abstract OP0054 – Table 1

	AUSCAN pain (B, 95% CI)		NRS hand pain (B, 95% CI)	
	Model 1*	Model 2**	Model 1*	Model 2**
KL sum score	0.01 (-0.01, 0.04); $p=0.35$	0.03 (0.001, 0.05); $p=0.04$	0.005 (-0.01, 0.02); $p=0.52$	0.01 (-0.002, 0.03); $p=0.09$
HADS sum score	0.19 (0.11, 0.26); $p<0.001$	0.12 (0.04, 0.20); $p=0.01$	0.11 (0.07, 0.15); $p<0.001$	0.08 (0.03, 0.12); $p=0.001$
PCS sum score	0.17 (0.12, 0.23); $p<0.001$	0.14 (0.08, 0.20); $p<0.001$	0.10 (0.07, 0.13); $p<0.001$	0.07 (0.04, 0.11); $p<0.001$

\* separate models for KL, HADS and PCS, respectively, with adj. for age, sex and BMI \*\* KL, HADS and PCS included in the same model with adj. for age, sex and BMI.

**Conclusions:** Depression, anxiety and pain catastrophizing were associated with pain in hand OA, emphasising that pain in hand OA should be treated in a biopsychosocial framework. Importantly, radiographic severity was associated with pain only in persons with no or low levels of depression and anxiety.

**Disclosure of Interest:** None declared

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### OP0055 A NOVEL METHOD FOR ASSESSING PROXIMAL TIBIOFIBULAR JOINT ON MR IMAGES IN PATIENTS WITH KNEE OSTEOARTHRITIS

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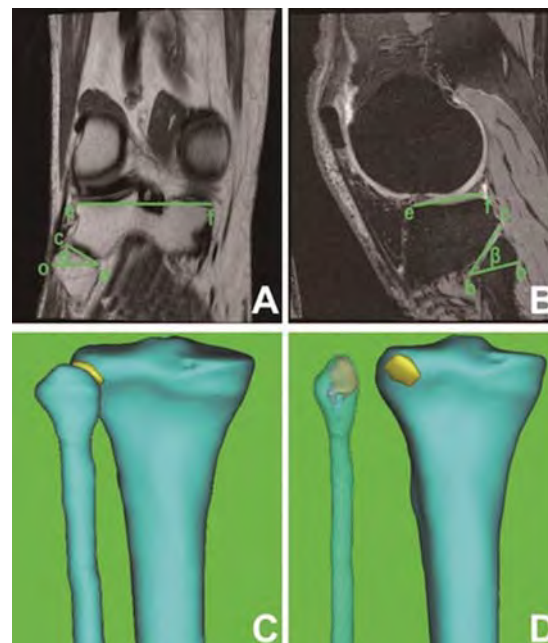
**Background:** Proximal tibiofibular joint (ProxTibFibJ) is a synovial sliding joint that has been estimated to transmit one-sixth of the leg's static load. One study has reported that proximal fibular osteotomy could significantly improve the clinical outcomes in patients with medial compartment OA. However, no study has delineated the measurement of ProxTibFibJ morphological parameters (ProxTibFibJ contacting area, load-bearing area, lateral stress-bolstering area and posterior stress-bolstering area) on magnetic resonance imaging (MRI) and investigated their correlations with knee OA structural abnormalities.

**Objectives:** To validate a pragmatic method to measure the morphological parameters of the ProxTibFibJ and to describe their associations with knee structural abnormalities in patients with knee osteoarthritis (OA).

**Methods:** A total of 408 participants with knee OA were selected. The morphological status of ProxTibFibJ were measured on coronal and sagittal magnetic resonance images (MRI). We calculated the contacting area of ProxTibFibJ (S), and its projection areas onto the horizontal (load-bearing area, St), sagittal (lateral stress-bolstering area, S $\varphi$ ) and coronal plane (posterior stress-bolstering area, S $\nu$ ), respectively. Knee structural abnormalities including cartilage defects, bone

marrow lesions (BMLs) and cartilage volume were evaluated. Clinical construct validity was examined through describing the associations between the morphological parameters of ProxTibFibJ and knee structural abnormalities. The reliabilities were examined by calculating the intra- and inter-observer correlation coefficients.

**Results:** The average ProxTibFibJ fibular contacting area was  $2.4\pm 0.7$  cm<sup>2</sup>. The intra- and inter-observer correlation coefficients for all measures were excellent (all  $\geq 0.90$ ). In cross-sectional analyses, the ProxTibFibJ morphological parameters (S, St, S $\nu$  and S $\varphi$ ) were significantly associated with radiographic medial JSN (OR 1.72 for S; 2.20 for St; 1.65 for S $\nu$ ), radiographic medial osteophyte (OR 0.51 for S $\varphi$ ) and MRI-assessed knee joint structural abnormalities including cartilage volume ( $\beta -0.07$  for S;  $-0.09$  for St), cartilage defects (OR 1.63 for S; 1.95 for St) and BMLs (OR 1.54 for S; 1.74 for St) at medial tibiofemoral compartment. In longitudinal analyses, S (RR, 1.45) and St (RR, 1.55) of ProxTibFibJ were significantly and positively associated with an increase in medial tibial cartilage defects over 2 years, after adjustment for age, gender, height, weight, ROA, tibial plateau bone area and intervention. St ( $\beta, -0.07$ ), S $\nu$  ( $\beta, -0.07$ ) and S ( $\beta, -0.06$ ) of ProxTibFibJ were significantly and negatively associated with change in medial tibial cartilage volume, after adjusted for above covariates. St (RR, 1.55) of ProxTibFibJ was positively associated with an increase in medial tibial BML, and S $\varphi$  (RR, 0.35) was negatively associated with an increase in medial femoral BMLs.



**Conclusions:** This novel method to assess the morphological parameters of ProxTibFibJ using MRI is reproducible, and has clinical construct validity. The longitudinal associations with osteoarthritic changes suggest that higher load-bearing area of ProxTibFibJ is a potential risk factor for medial compartment OA.

**Disclosure of Interest:** None declared

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### OP0056 MOLECULAR AND STRUCTURAL BIOMARKERS OF INFLAMMATION AT 2 YEARS AFTER ACUTE ACL INJURY DO NOT PREDICT STRUCTURAL KNEE OSTEOARTHRITIS AT 5 YEARS

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**Background:** Trauma-induced cytokine response and local inflammation after knee injury may be important in the development of posttraumatic osteoarthritis (OA). It has been reported that synovial fluid levels of inflammatory markers remain increased up to 5 years after anterior cruciate ligament (ACL) injury, indicative of extended local inflammation in the injured joint.<sup>1</sup> Inflammation potentially represents a valid target for treatment in the early and subacute phase after joint trauma in order to prevent or delay onset of post-traumatic knee OA.

**Objectives:** To determine the role of inflammatory biomarkers at 2 years after anterior cruciate ligament (ACL) injury for predicting radiographic and magnetic resonance imaging (MRI)-defined knee OA 5 years post injury. Secondary aim was to estimate the concordance of inflammatory biomarkers assessed by MRI and in synovial fluid.

**Methods:** We studied 113 patients with acute ACL injury. 1.5 Tesla knee MRIs were read for Hoffa- and effusion-synovitis. Biomarkers of inflammation included IL-6, IL-8, IL-10, TNF- $\alpha$  and IFN- $\gamma$  in serum and synovial fluid, and IL-12p70 in serum. The outcome was radiographic knee OA (ROA) or MRI-defined OA (MROA) at 5 years. Area under receiver operating characteristic curve (AUC), sensitivity and specificity were evaluated in models including MRI features only (M1), inflammation biomarkers only (serum [M2a] – synovial [M2b]) or both MRI and serum [M3a] or synovial [M3b] markers. Linear regression was used for evaluating association between MRI and synovial biomarkers.

**Results:** At 5 years, ROA was present in 26% and MROA was present in 32% of patients' injured knee. The AUCs (95% CI) for ROA were 0.44 (0.42–0.47;M1), 0.62 (0.59–0.65;M2a), 0.58 (0.55–0.61;M2b), 0.53 (0.50–0.56;M3a) and 0.50 (0.46–0.53;M3b) for each model. The corresponding AUCs for MROA were 0.67 (0.64–0.70), 0.49 (0.47–0.52), 0.65 (0.61–0.68), 0.56 (0.52–0.59) and 0.69 (0.66–0.72) (table 1). The associations between MRI and synovial biomarkers were weak and not statistically significant, apart from effusion-synovitis and IL-8 (log 10 IL8 levels were 0.23 and 0.43 higher in persons with grade 1 or 2/3, respectively).

**Abstract OP0056** – Table 1 Discriminatory accuracy of imaging and serum/synovial fluid biomarkers at 2 years with respect to knee osteoarthritis (OA) development at 5 year according to 4 definitions using logistic regression model maximising area under receiver operating characteristic curve (AUC)

Outcome @ 5 years	MRI features only (Model 1)		Serum biomarkers only (Model 2a)		MRI and serum biomarkers (Model 3a)		Synovial biomarkers only (Model 2b)		MRI and synovial biomarkers (Model 3b)	
	AUC	95% CI	AUC	95% CI	AUC	95% CI	AUC	95% CI	AUC	95% CI
MRI OA	0.67 (0.64-0.70)	0.62 (0.59-0.65)	0.44 (0.42-0.47)	0.58 (0.55-0.61)	0.53 (0.50-0.56)	0.67 (0.64-0.70)	0.49 (0.47-0.52)	0.65 (0.61-0.68)	0.56 (0.52-0.59)	0.69 (0.66-0.72)
Sens	0.69 (0.61-0.78)	0.65 (0.57-0.73)	0.44 (0.42-0.47)	0.58 (0.55-0.61)	0.53 (0.50-0.56)	0.67 (0.64-0.70)	0.49 (0.47-0.52)	0.65 (0.61-0.68)	0.56 (0.52-0.59)	0.69 (0.66-0.72)
Spec	0.68 (0.57-0.79)	0.64 (0.53-0.75)	0.44 (0.42-0.47)	0.58 (0.55-0.61)	0.53 (0.50-0.56)	0.67 (0.64-0.70)	0.49 (0.47-0.52)	0.65 (0.61-0.68)	0.56 (0.52-0.59)	0.69 (0.66-0.72)
ROA	0.44 (0.42-0.47)	0.62 (0.59-0.65)	0.44 (0.42-0.47)	0.62 (0.59-0.65)	0.53 (0.50-0.56)	0.67 (0.64-0.70)	0.49 (0.47-0.52)	0.65 (0.61-0.68)	0.56 (0.52-0.59)	0.69 (0.66-0.72)
Sens	0.44 (0.42-0.47)	0.62 (0.59-0.65)	0.44 (0.42-0.47)	0.62 (0.59-0.65)	0.53 (0.50-0.56)	0.67 (0.64-0.70)	0.49 (0.47-0.52)	0.65 (0.61-0.68)	0.56 (0.52-0.59)	0.69 (0.66-0.72)
Spec	0.44 (0.42-0.47)	0.62 (0.59-0.65)	0.44 (0.42-0.47)	0.62 (0.59-0.65)	0.53 (0.50-0.56)	0.67 (0.64-0.70)	0.49 (0.47-0.52)	0.65 (0.61-0.68)	0.56 (0.52-0.59)	0.69 (0.66-0.72)
TF OA	0.68 (0.65-0.71)	0.62 (0.59-0.65)	0.44 (0.42-0.47)	0.62 (0.59-0.65)	0.53 (0.50-0.56)	0.67 (0.64-0.70)	0.49 (0.47-0.52)	0.65 (0.61-0.68)	0.56 (0.52-0.59)	0.69 (0.66-0.72)
Sens	0.68 (0.65-0.71)	0.62 (0.59-0.65)	0.44 (0.42-0.47)	0.62 (0.59-0.65)	0.53 (0.50-0.56)	0.67 (0.64-0.70)	0.49 (0.47-0.52)	0.65 (0.61-0.68)	0.56 (0.52-0.59)	0.69 (0.66-0.72)
Spec	0.68 (0.65-0.71)	0.62 (0.59-0.65)	0.44 (0.42-0.47)	0.62 (0.59-0.65)	0.53 (0.50-0.56)	0.67 (0.64-0.70)	0.49 (0.47-0.52)	0.65 (0.61-0.68)	0.56 (0.52-0.59)	0.69 (0.66-0.72)
PF OA	0.62 (0.58-0.66)	0.64 (0.61-0.67)	0.44 (0.42-0.47)	0.62 (0.59-0.65)	0.53 (0.50-0.56)	0.67 (0.64-0.70)	0.49 (0.47-0.52)	0.65 (0.61-0.68)	0.56 (0.52-0.59)	0.69 (0.66-0.72)
Sens	0.62 (0.58-0.66)	0.64 (0.61-0.67)	0.44 (0.42-0.47)	0.62 (0.59-0.65)	0.53 (0.50-0.56)	0.67 (0.64-0.70)	0.49 (0.47-0.52)	0.65 (0.61-0.68)	0.56 (0.52-0.59)	0.69 (0.66-0.72)
Spec	0.62 (0.58-0.66)	0.64 (0.61-0.67)	0.44 (0.42-0.47)	0.62 (0.59-0.65)	0.53 (0.50-0.56)	0.67 (0.64-0.70)	0.49 (0.47-0.52)	0.65 (0.61-0.68)	0.56 (0.52-0.59)	0.69 (0.66-0.72)

ROA= radiographic OA, TF=tibiofemoral, PF=patellofemoral, AUC= area under the receiver operating characteristic curve

**Conclusions:** Neither MRI-defined inflammation, nor synovial/serum inflammation biomarkers at 2 years as analysed here predicted ROA or MROA at 5 years. The concordance between MRI and synovial inflammatory biomarkers was weak. Additional studies with longer follow-up will be needed to confirm or refute our findings and to more firmly define the role of inflammation for OA development following acute ACL injury.

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OP0057

#### EFFICACY AND SAFETY OF A DISTRACTION-ROTATION KNEE BRACE (ODRA) IN MEDIAL KNEE OSTEOARTHRITIS – A PHASE III RANDOMISED CONTROLLED TRIAL (ERGONOMIE STUDY)

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**Background:** According to EULAR and OARS1 guidelines, evidence is inconclusive for the symptomatic benefits of an unloader knee brace in medial knee osteoarthritis (OA).

**Objectives:** The objective of this multicenter randomised controlled trial (RCT) (*ClinicalTrials Id. NCT02765685*) was to compare the efficacy and safety of the ODRA brace, a distraction-rotation custom-made knee brace versus usual care over one year in medial knee OA.

**Methods:** Patients with symptomatic medial knee OA (VAS pain scores at rest >40/100 for the medial compartment) and Kellgren-Lawrence (KL) grade II-IV were randomised in two groups: brace group (ODRA +usual care) vs usual care alone (UCA). Patients were followed up every two months for one year. Usual care consisted of all the pharmacological and non-pharmacological treatments used for the management of knee OA. The primary end-point was the difference of VAS-pain between M0 and M12. Secondary end-points included patient global assessment of disease severity (PGA) on VAS,% of patients reaching the PASS (VAS-pain <30/100) and MCII (delta VAS-pain >20/100) thresholds at M12, KOOS scores, OA-specific quality of life questionnaire (OAKHQOL), as well as drug intake. Safety and compliance were evaluated by recording side effects and average knee brace duration of wear, respectively.

**Results:** Overall 120 patients (57% women) from 7 centres were included. Their characteristics were the following: mean age 63.6±11.4 years; BMI 29.6±5.5 kg/m<sup>2</sup>; OA duration 5.8±6 years; 52% KL III; 21% KL IV. The VAS pain decrease was statistically higher in the ODRA group (from 61.9±17.4 (M0) to 38.8±25.3 (M12) than in the UCA group (54.9±18.2 to 45.5±23.8) in the intent to treat bivariate and multivariate analyses (delta VAS-pain: 13.1±4.9, p<0.01). At M12, ODRA patients experienced a significant higher improvement than the UCA patients for PGA, all KOOS domains and for 3 of 5 domains of OAKHQOL (Pain, Physical activities, Mental health). Patients reaching PASS threshold at M12 were 42% in ODRA group vs 27% in UCA group (OR=3.04; 95% CI: 1.11 to 8.30; p<0.05) and were 46% vs 28% for MCII respectively (OR=2.65, 95% CI: 1.01 to 6.96; p<0.05). The overall analgesic use decreased more frequently in the ODRA group at M12 than in the UCA group (32.7% vs 15.4%, p<0.05) except for NSAIDs, HA or steroid injections. The compliance was good: the brace was worn for a median [IQR] duration of 5.7 [4.0–7.0] hours a day between M0 and M6 and 5.3 [3.7–6.3] hours a day between M6 and M12. Non-serious side effects were more common in the ODRA group (p<0.05) which justified the definitive withdrawal of the brace in 8 ODRA patients (13%), mainly for cutaneous side effects.

**Conclusions:** In this RCT, the use of the ODRA brace in addition to usual care was shown to be superior to usual care alone in reducing symptoms and improving quality of life of patients suffering from medial knee OA, with good compliance.

**Disclosure of Interest:** None declared

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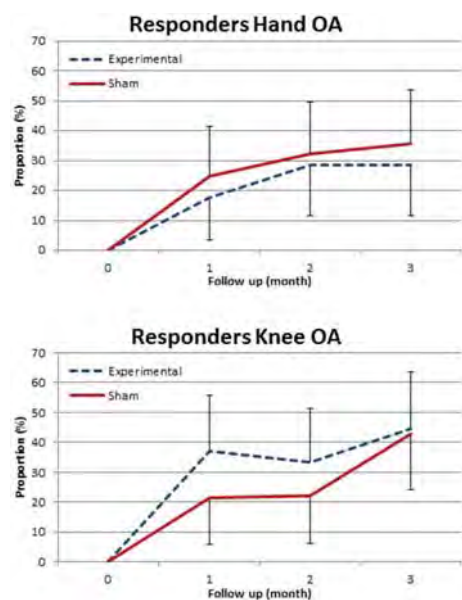
OP0058

#### LOW-DOSE RADIATION THERAPY AS TREATMENT FOR HAND AND KNEE OSTEOARTHRITIS: TWO DOUBLE-BLIND RCT'S

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**Background:** Synovial inflammation plays an important role in osteoarthritis (OA) pathophysiology. In some countries, low-dose radiation therapy (LD-RT) is widely used as treatment for OA, while relatively unknown in others. Studies *in vitro* and in OA animal models have shown anti-inflammatory effects of LD-RT. However, systematic literature review has shown that high-level evidence for beneficial effects in clinical practice is lacking.

**Objectives:** To assess the effect of LD-RT on clinical outcomes and inflammation in patients with hand or knee OA, using two parallel prospective RCTs.



Abstract OP0058 – Responders over time with 95%CI

Abstract OP0058 – Table 1

	Hand OA		Knee OA	
	LD-RT (n=28)	Sham (n=28)	LD-RT (n=27)	Sham (n=28)
Male/Female, n	4/24	8/20	12/15	15/13
Age (years)	67 (1)	62 (12)	62 (9)	68 (9)
BMI (kg/m <sup>2</sup> )	26 <sup>24-27</sup>	29 <sup>26-31</sup>	29 <sup>25-30</sup>	26 <sup>24-31</sup>
Pain (0–100) #	54 (19)	56 (15)	41 (14)	39 (17)
Functioning (0–100) #	55 (25)	59 (16)	40 (17)	38 (19)
Effusion*	6 <sup>5-8</sup>	5 <sup>5-8</sup>	6 <sup>4-8</sup>	5 <sup>4-7</sup>
Synovial thickening*	3 <sup>1-4</sup>	1 <sup>1-3</sup>	2 <sup>1-3</sup>	2 <sup>1-3</sup>
Power Doppler*	1 [0–2.5]	1 [0–3]	NA	NA
MRI effusion/synovitis (0–12)	NA	NA	5 <sup>5-8</sup>	4 <sup>2-7</sup>

Mean (sd) or median [25%–75%]; lower scores indicate better health status  
#: AUSCAN or WOMAC, respectively; \* Hand: joint count (0–18), Knee: thickness (mm); NA: not assessed

**Methods:** Patients with hand OA (n=56) or knee OA (n=55) according to ACR-criteria, with a pain score  $\geq 5/10$ , not responding to analgesics and exercise therapy were included. They were randomly allocated 1:1 to the LD-RT (6 × 1 Gy LD-RT in two weeks) or sham (6 × 0 Gy in two weeks) intervention, stratified for pain score (<8 vs  $\geq 8$ ). The primary outcome was the number responders according to the OMERACT-OARSI responder criteria, 3 months post-intervention. Secondary outcomes were inflammatory aspects assessed by ultrasound (US; both knee and hand) and MRI (knee only). In hand OA, joints were scored semi-quantitatively (0–3) for US effusion, synovial thickening and power Doppler signal. In knee OA, we assessed the mean US effusion and synovial thickness (mm) at three locations, and the summed MRI effusion/synovitis (semi-quantitatively; 0–3) from four locations. Logistic and linear regression analyses were used to assess differences in dichotomous and continuous outcomes, respectively. Analyses were adjusted for pain stratum.

**Results:** Baseline characteristics are shown in table 1. The proportion of responders over time is shown in figure 1. After 3 months, in hand OA, there were 8 (29%) responders in the LD-RT group and 10 (36%) in the sham group (OR 0.69; 95% CI: 0.22 to 2.17). In knee OA, there were 12 (44%) responders in the LD-RT

group and 12 (43%) in the sham group (OR 1.09; 95% CI: 0.37 to 3.19). In both hand and knee OA, no significant changes in clinical outcomes and inflammatory aspects were observed in both groups.

**Conclusions:** We were unable to demonstrate a beneficial effect of LD-RT on pain and functioning, nor on inflammatory processes, in patients with hand or knee OA. In light of absence of other high-level evidence, we advise against the use LD-RT as treatment for hand and knee OA.

Dutch Trial Register: NTR4574

**Disclosure of Interest:** None declared

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#### OP0059 EFFICACY AND SAFETY OF INTRA-ARTICULAR SPRIFERMIN IN SYMPTOMATIC RADIOGRAPHIC KNEE OSTEOARTHRITIS: PRE-SPECIFIED ANALYSIS OF 3-YEAR DATA FROM A 5-YEAR RANDOMISED, PLACEBO-CONTROLLED, PHASE II STUDY

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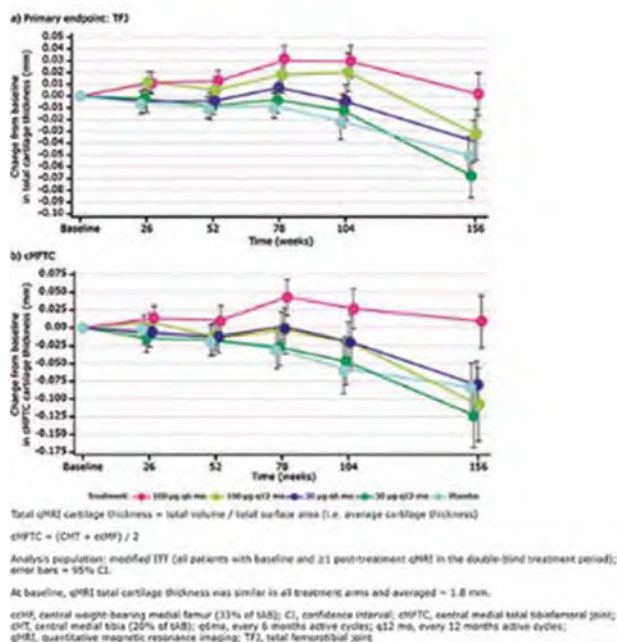
**Background:** Sprifermin, a novel recombinant human fibroblast growth factor 18, is currently being investigated as a potential disease-modifying osteoarthritis (OA) drug. Two-year results of the 5 year phase II FORWARD study showed a statistically significant dose-dependent cartilage thickness increase in the total femorotibial joint (TFJ), and in the medial, lateral and central medial sub-region TFJ compartments by quantitative magnetic resonance imaging (qMRI).

**Objectives:** Here we report the pre-specified 3 year results.

**Methods:** Patients (pts) aged 40–85 years with symptomatic radiographic knee OA, Kellgren-Lawrence grade (KLG) 2 or 3, and medial mJSW  $\geq 2.5$  mm in the target knee were randomised (1:1:1:1) to receive 3 weekly i.a. injections with double-blinded placebo (PBO) or sprifermin, administered q6mo (0, 6, 12, and 18 months) or q12mo (0 and 12 months). The primary endpoint was the change in TFJ cartilage thickness from baseline (BL) to Year 2 with pre-specified analyses at Year 3. The intent-to-treat (ITT) population (all randomised pts) was used for non-qMRI endpoints; and the modified ITT population (all ITT pts with BL and  $\geq 1$  post-treatment MRI up to Year 2) for qMRI endpoints.

**Results:** 549 pts were randomised (median age 65 years, 69% women, 80% white, 69% KLG2, and ~70% predominantly medial disease); of which 18.4% (sprifermin) and 24.1% (PBO) discontinued the study within 3 years. TFJ cartilage thickness decreased from Year 2 to 3 in all treatment groups; however, the 0.05 mm difference between sprifermin 100  $\mu$ g q6mo and PBO was maintained (0.00 vs –0.05 mm; p<0.001; figure 1a). Additionally, significant differences in mean cartilage thickness change from BL to Year 2 were maintained up to Year 3 with sprifermin 100  $\mu$ g vs PBO in both the medial (100  $\mu$ g q6mo –0.01 vs –0.06 mm; p=0.025) and lateral TFJ compartments (100  $\mu$ g q6mo and q12mo: +0.01 and 0.00 vs –0.04 mm; p<0.001 and p=0.003, respectively), and central medial (100  $\mu$ g q6mo: +0.009 vs –0.084 mm; p=0.008; figure 1b) and central lateral (100  $\mu$ g q6 and q12mo: +0.038 and +0.017 vs –0.053 mm; p<0.001 and p=0.003, respectively) TFJ sub-regions. The significant mean change from BL to Year 2 in lateral (but not medial) mJSW by X-ray was maintained up to Year 3 with both sprifermin 100  $\mu$ g groups vs PBO (100  $\mu$ g q6 and q12mo: +0.13 and +0.10 vs –0.11 mm; p=0.014 and p=0.040, respectively). By Year 2 total WOMAC scores were improved by ~50% in all treatment groups including PBO, and maintained up to Year 3 (18 months after last injection) without a significant difference between treatment groups. AEs and serious AEs remained balanced between groups at Years 2 and 3.





**Abstract OP0059** – Figure 1 Mean change from baseline in cartilage thickness (by qMRI) over 3 years in: a) and b)

**Conclusions:** The 3 year results of the FORWARD study are consistent with the 2 year results: although cartilage thickness declined in all treatment groups between Year 2 and 3, the difference at Year 2 with sprifermin 100 µg vs PBO was maintained up to Year 3. Based on qMRI sprifermin is effective at increasing cartilage thickness in a dose-dependent manner in knee OA patients, and has an acceptable safety profile.

**Disclosure of Interest:** M. Hochberg Consultant for: Bioiberica SA, Bristol Myers Squibb, EMD Serono, Inc., Galapagos, IBSA Biotechniq SA, Novartis Pharma AG, Pfizer Inc., Plexxikon, Samumed LLC, Theralogix LLC and TissueGene Inc, A. Guermazi Consultant for: OrthoTrophix, GE Healthcare, Merck Serono, AstraZeneca, Sanofi, TissueGene and Pfizer, Employee of: Boston Imaging Core Lab, LLC, H. Guehring Employee of: Merck KGaA, A. Aydemir Employee of: EMD Serono, Inc., S. Wax Employee of: EMD Serono, Inc., P. Fleuranceau-Morel Employee of: EMD Serono, Inc., A. Reinstrup Bihlet Shareholder of: Nordic Bioscience, Employee of: Nordic Bioscience, I. Byrjalsen Employee of: Nordic Bioscience, J. Ragnar Andersen Shareholder of: Nordic Bioscience, Employee of: Nordic Bioscience, F. Eckstein Shareholder of: Chondrometrics GmbH, Consultant for: Merck KGaA, Samumed LLC, Abbvie, Bioclinica, TissueGene, Servier and Roche, Employee of: Chondrometrics GmbH  
DOI: 10.1136/annrheumdis-2018-eular.2181

## OP0060 KNEE JOINT DISTRACTION COMPARED WITH HIGH TIBIAL OSTEOTOMY AND TOTAL KNEE ARTHROPLASTY: TWO-YEAR CLINICAL, STRUCTURAL, AND BIOMARKER OUTCOMES

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**Background:** Knee joint distraction (KJD) is a new joint-preserving surgery technique that, like high tibial osteotomy (HTO), aims to delay total knee arthroplasty (TKA) especially in younger patients with knee osteoarthritis (OA). One year after treatment, KJD demonstrated similar beneficial outcomes compared to HTO and compared to TKA.<sup>1,2</sup>

**Objectives:** To compare radiographic joint space width and clinical outcome over two-years for KJD vs TKA and for KJD vs HTO and to additionally study KJD cartilage repair by evaluation of systemic collagen type II markers.

**Methods:** End-stage knee OA patients considered for TKA were randomised to KJD (n=20; KJD<sub>TKA</sub>) or TKA (n=40). Medial compartmental knee OA patients with a varus deviation of <10° considered for opening wedge HTO were randomised to KJD (n=23; KJD<sub>HTO</sub>) or HTO (n=46). Distraction surgery was performed by use of

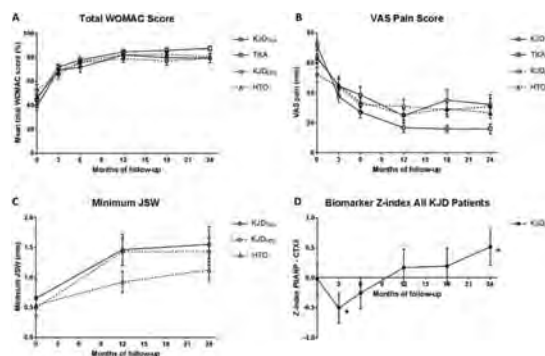
two external fixators with built in springs, placed lateral and medial of the knee joint. The knee was distracted 5 mm for 6 weeks and weight-bearing was encouraged.

WOMAC questionnaires (100 best) and VAS pain scores (0 best) were assessed at baseline (0), 3, 6, 12, 18 and 24 months. In the KJD groups, serum PIIANP and urine CTXII levels, as markers for collagen type II synthesis and breakdown, were determined over time. Normalised Z-indexes were calculated ( $Z_{index} = Z_{PIIANP} - Z_{CTXII}$ ) to express net collagen type II synthesis. The minimum and mean joint space width (JSW) of the most affected compartment (MAC) were measured with KIDA software on standardised radiographs taken at 0, 12 and 24 months.

**Results:** Of the 129 included patients, 1, 6, 3, and 5 patients were lost in the KJD<sub>TKA</sub>, TKA, KJD<sub>HTO</sub>, and HTO group respectively, for various reasons. One-year structural and clinical outcomes were statistically significantly improved as reported before, and these beneficial effects sustained for at least two years after treatment when compared to baseline (figure 1A-C).

At 24 months, there were no significant differences between the KJD<sub>HTO</sub> and HTO groups (all p>0.25) and between the KJD<sub>TKA</sub> and TKA group, except for VAS pain score in favour of TKA at 24 months (p=0.037; figure 1B).

Compared to baseline, the ratio of synthesis over breakdown of collagen type II biomarkers (figure 1D) was significantly decreased at 3 months (-0.45±0.20; p=0.032) after which this reversed towards an increase over time (at 24 months +0.59±0.19; p=0.004).



**Abstract OP0060** – Figure 1 Change in A) total WOMAC score and B) VAS pain score after treatment with knee joint distraction (KJD), total knee arthroplasty (TKA) and high tibial osteotomy (HTO). KJD patients are divided in KJD<sub>TKA</sub> (from the trial including patients for KJD and TKA) and KJD<sub>HTO</sub> (from the trial including patients for HTO and TKA). C) change in minimum joint space width (JSW) measured on radiographs after KJD and HTO. D) biomarker Z-index changes for all KJD patients (KJD<sub>TKA</sub> and KJD<sub>HTO</sub> combined) after treatment.  $Z_{index} = Z_{PIIANP} - Z_{CTXII}$ , where the Z-values for both biomarkers are relative to baseline and (\*) indicates statistically significant changes compared to baseline. In all graphs, the mean values ±SEM are given.

**Conclusions:** Sustained improvement of clinical benefit and increase in JSW after KJD is demonstrated for over 2 years of follow-up in case of treatment of patients with medial compartmental knee OA indicated for HTO or patients with end-stage knee OA indicated for TKA. The structural cartilage repair observed on radiographs is supported by a beneficial change in systemic biomarkers for collagen type II. For the HTO-indicated population, results of KJD patients were similar to those of HTO. For the TKA-indicated patients, TKA appeared to result in a slightly better clinical outcome, however at the expense of the native knee joint.

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**Disclosure of Interest:** None declared

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## OP0061 TREATMENT OF KNEE OSTEOARTHRITIS WITH SM04690 IMPROVED WOMAC A1 'PAIN ON WALKING' – RESULTS FROM A 52 WEEK, RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PHASE 2 STUDY OF A NOVEL, INTRA-ARTICULAR, WNT PATHWAY INHIBITOR

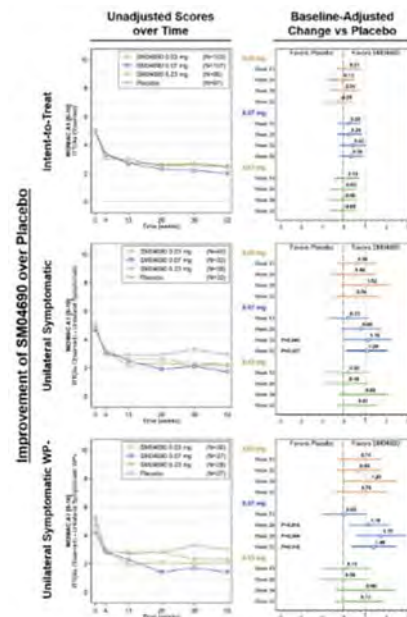
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**Background:** Knee osteoarthritis (OA) is characterised by pain, disability and joint deformity due to articular cartilage degradation and bone remodelling. Wnt

signalling is involved in these cellular processes. SM04690, a small molecule, intra-articular (IA), Wnt pathway inhibitor, is in development for treatment of knee OA as a potential disease modifying drug.

**Objectives:** A phase 2, multicenter, 52 week, randomised, double-blind, placebo-controlled (PBO) trial of SM04690 was conducted. Safety and efficacy outcomes including the Western Ontario and McMaster Universities Arthritis Index (WOMAC) question A1 were evaluated.

**Methods:** Subjects with ACR-defined knee OA, Kellgren-Lawrence (KL) grades 2–3, received a single 2 mL IA injection of SM04690 (0.03, 0.07 or 0.23 mg) or PBO in the target (most painful) knee. WOMAC was assessed at baseline and 4, 13, 26, 39 and 52 weeks post-injection. WOMAC question A1, ('how much pain have you had when walking on a flat surface?'), was analysed as an exploratory outcome. Analysis of covariance adjusted for WOMAC A1 baseline in the intent-to-treat (ITT) population was conducted. Two subgroups identified in the primary analysis<sup>1</sup> were also explored: 1) subjects with unilateral symptomatic knee OA (pre-specified) and 2) subjects with unilateral symptomatic knee OA without widespread pain or comorbid symptoms (Widespread Pain Index $\leq$ 4 and Symptom Severity $\leq$ 2 [WP-], post-hoc).



**Abstract OP0061 – Figure 1.** Change and ladder plots depicting average WOMAC A1 improvement in SM04690 over placebo adjusted for baseline WOMAC A1. \*Minimal clinically improvement difference (MCID) defined as 10% of WOMAC A1.

**Results:** 455 subjects, mean age 60.3 [ $\pm$ 8.7] years, BMI 29.9 [ $\pm$ 4.6] kg/m<sup>2</sup>, female 58.9%, KL 3 [64.1%], with unilateral symptomatic OA [36.0%] were enrolled (n=402 [88.4%] completers). No safety signals were observed.

For WOMAC A1, in the ITT population, no statistically significant differences between treatment groups and PBO were seen, although the 0.07 mg dose demonstrated improvements compared to PBO at all timepoints (figure 1). In unilateral symptomatic subjects, 0.07 mg showed statistically significant improvements in WOMAC A1 compared to PBO at Weeks 39 (-1.2, 95% CI: [-2.3 to -0.0], p=0.043) and 52 (-1.1, 95% CI: -2.0 to -0.1, p=0.027).

In unilateral symptomatic WP- subjects, the 0.07 mg dose showed statistically significant improvements in WOMAC A1 compared to PBO at Week 26 (-1.2, 95% CI: -2.1 to -0.2, p=0.015), through Weeks 39 (-1.8, 95% CI: -3.0 to -0.6, p=0.004) and 52 (-1.4, 95% CI: -2.5 to -0.4, p=0.010).

**Conclusions:** In this phase 2 study, improvements compared to PBO in WOMAC A1 were seen in clinically relevant unilateral symptomatic and unilateral symptomatic WP- subgroups. The improvements seen in this combined, multi-dimensional outcome of pain and function suggested SM04690 has a potential role in the treatment of signs and symptoms of knee OA.

#### REFERENCE:

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**Disclosure of Interest:** S. Kennedy Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, H. Ghandehari Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, C. Swearingen Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, J. Tambiah Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, M. Hochberg Consultant for: Bioberica, EMD Serono, Novartis

Pharma AG, Plexixikon, Pfizer, Proximagen, Regeneron, Samumed, LLC, Theralogix LLC

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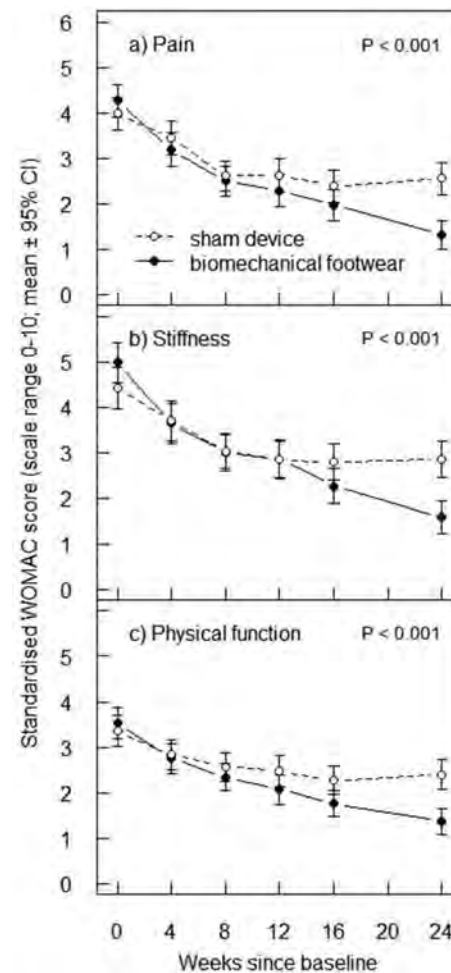
#### LB0002 BIOMECHANICAL THERAPY FOR OSTEOARTHRITIS OF THE KNEE: A RANDOMISED CONTROLLED TRIAL (BIOTOK)

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**Background:** Biomechanics plays an important role in knee osteoarthritis (OA). A new biomechanical footwear system aims at altering knee loading patterns and retraining neuromuscular control of the lower extremities. It consists of shoes with two adjustable convex pods at the soles, which are adjusted based on gait analysis, with the hypothesis that adjustments of the location of the pods will alter limb biomechanics so as to unload diseased compartments of the knee and that walking on the convex pods will facilitate muscular retraining.

**Objectives:** The aim of this trial was to compare the efficacy and safety of the new biomechanical footwear with an identical appearing shoe with flat pods (the sham device) in relieving pain and improving physical function in patients with knee OA.

**Methods:** In this randomised sham-controlled trial, patients with radiological knee OA (Kellgren-Lawrence grade  $\geq$ 2), knee pain lasting for  $\geq$ 6 months, and moderate pain on the WOMAC pain subscale ( $\geq$ 3 on a standardised scale from 0 to 10) were randomly assigned 1:1 to the biomechanical footwear or the sham device. The same shoe or device was provided for bilateral use. Patients in both groups were instructed to use the footwear for 30 minutes/day during the first week, and to increase use by 10 minutes/day each week to a maximum of 5 hours/day at 24 weeks. After 4, 8, 12, and 16 weeks, each patient's footwear



**Abstract LB0002 – Figure 1**

was re-calibrated by technicians. Because the sham device had no adjustable pods on the soles, technicians pretended to make appropriate changes.

The primary endpoint was knee pain at the end of treatment in the knee with more pain at screening, assessed with the WOMAC pain subscale. Secondary outcomes were WOMAC physical function and stiffness subscales. All subscales were standardised to range from 0 to 10. These outcomes were analysed using linear models adjusted for baseline values and the two stratification factors uni- vs. bilateral, and medial vs. lateral osteoarthritis at randomization, using multiple imputation.

**Results:** Of 697 patients assessed for eligibility, 220 were randomised: 111 to the experimental footwear and 109 to the sham device. The mean age was 65.2 years (SD 9.2) and the mean body mass index was 28.0 (SD 4.6). Overall, 47.3% were women and 88.2% had medial knee OA in the index knee. The mean WOMAC pain score at baseline was 4.1 (SD 1.9). Seven patients in the experimental group and 13 in the sham group dropped out. At the end of the trial, the adjusted mean difference for WOMAC pain was 1.34 (95% CI: 0.92 to 1.77) in favour of the experimental footwear. The adjusted mean difference was 1.42 (0.93 to 1.91) for WOMAC stiffness and 1.12 (0.73 to 1.50) for WOMAC physical function (figure 1). Three serious adverse events occurred in the experimental group, compared with 9 in the sham group; none were treatment-related. Thirty adverse events occurred in the experimental group, compared with 36 in the sham group; 18 and 17 of these, respectively, were possibly treatment-related.

**Conclusions:** This trial suggests that the new biomechanical footwear system is both efficacious and safe in relieving knee pain in patients with knee OA.

**Disclosure of Interest:** S. Reichenbach Grant/research support from: Mäxi Foundation, S. Heldner: None declared, A. Lenz: None declared, D. Felson: None declared, P. Jüni: None declared

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WEDNESDAY, 13 JUNE 2018

## Fracture risk and consequences

### OP0062 OSTEOPOROTIC HIP FRACTURES IN MEN: A RISING CONCERN

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**Background:** Osteoporosis screening and treatment is often exclusively targeted at post-menopausal women. The US Preventive Task Force guidelines recommend bone density screening in women starting at age 65, but do not make any similar recommendation for men, even though men have higher mortality than women after a hip fracture.<sup>1</sup> Recent improvements in health care has led to increasing lifespan of men in US. As more men enter the seventh and eighth decades of their life, they are at more risk for developing osteoporosis and osteoporotic hip fractures.

**Objectives:** To study the number and prevalence of hospitalizations for osteoporotic hip fractures in the men and women aged 50 years and up in the US over 23 years (1993–2015).

**Methods:** The National Inpatient Sample (NIS) is a stratified random sample of all US community hospitals and is the only US national hospital database with information on all patients, regardless of payer, including persons covered by Medicare, Medicaid, private insurance, and the uninsured. We examined all inpatient hospitalizations in NIS from 1993 to 2015 with a primary diagnosis of non-traumatic (osteoporotic) hip fractures in individuals 50 years and older. Patients were excluded if there was any evidence of major trauma, open fractures, or primary or secondary femoral tumours. US population estimates and projections for the resident US population were obtained from the US Census Bureau. All prevalence rates were expressed per 1 00 000 of the US population.

**Results:** From 1993 to 2015, we studied 6.3 million osteoporotic hip fracture hospitalizations in 1.99 billion person-years of observation in individuals who were 50 years or older. Of these, 74% occurred in women. Hip fracture hospitalizations in women decreased from 2 09 052 in 1993 (prevalence 562 per 1 00 000 person-years) to 2 01 435 in 2015 (340 per 1 00 000 person-years), even as the population of 50 years and older women increased from 37 million in 1993 to 59 million in 2015 (59% increase in population), perhaps reflecting increasing awareness, screening and treatment for osteoporosis in elderly women. However, in men aged 50 years and older, osteoporotic hip fracture hospitalizations increased from 64 339 in 1993 to 83 885 in 2015, even as the prevalence decreased from 218 per 1 00 000 person-years in 1993 to 162 per 1 00 000 person-years in 2015. The 30% increase in the absolute number of hip fracture hospitalizations, despite decreasing prevalence, is coincident with the 75% rise in the number of the 50 years and older men population, from 29.6 million in 1993 to 51.7 million in 2015.



Abstract OP0062 – Figure 1. Hip fracture hospitalisation in the US

**Conclusions:** Despite an overall decrease in prevalence, the absolute number of osteoporotic hip fracture hospitalizations increased in 50 years and older men. More attention needs to be paid to prevention of osteoporotic hip fractures in this cohort.

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- [1] Hawkes WG, et al. Gender differences in functioning after hip fracture. *J Gerontol A Biol Sci Med Sci* 2006;61(5):495–9.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.2291

### OP0063 PERIPHERAL ARTERIAL DISEASE AND RISK OF OSTEOPOROTIC HIP FRACTURE: A SYSTEMATIC REVIEW AND META-ANALYSIS OF COHORT STUDIES

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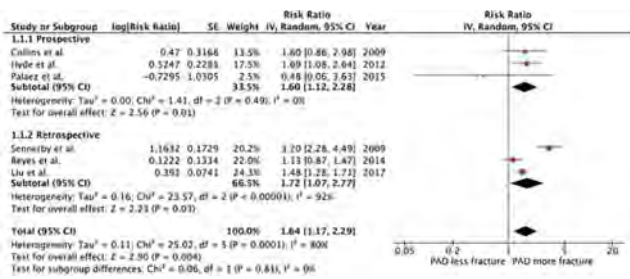
**Background:** Previous studies have demonstrated that patients with peripheral arterial disease (PAD) had lower bone mineral density, particularly in the femur, compared with general population. Therefore, it is possible that patients with PAD may have a higher risk of osteoporotic hip fracture.

**Objectives:** To compare the risk of developing hip fracture between patients with PAD and individuals without PAD.

**Methods:** A systematic literature search was conducted using EMBASE and MEDLINE database from inception to November 2017 to identify all cohort studies that investigated the risk of incident hip fracture among patients with PAD compared with individuals without PAD. The systematic literature review was independently conducted by the first two investigators using the search strategy that included the terms for 'peripheral arterial disease' and 'hip fracture'. Eligible studies must be cohort studies (either prospective or retrospective) that reported the risk of incident hip fracture among patients with PAD. Comparators must be individuals without PAD. Eligible studies must provide the effect estimates (relative risks (RR) or hazard ratios (HR)) with 95% confidence intervals (CI) for the calculation of pooled effect estimates. Adjusted point estimates from each study were combined together using the random-effect, generic inverse variance method as described by DerSimonian and Laird.

**Results:** Of 8464 retrieved articles, 6 cohort studies (3 prospective cohort studies and 3 retrospective cohort studies) involving 15 895 patients with PAD and 2 33 835 comparators without PAD met the eligibility criteria and were included in the meta-analysis. We found a significantly increased risk of incident hip fracture among patients with PAD compared with individuals without PAD with the pooled RR of 1.64 (95% CI: 1.17 to 2.29). The statistical heterogeneity was high with an  $I^2$  of 80%. Subgroup analysis by study design showed a significantly increased risk of incident hip fracture among patients with PAD for both prospective studies (pooled RR 1.60; 95% CI: 1.12 to 2.28;  $I^2$ 0%) and retrospective studies (pooled RR 1.72; 95% CI: 1.07 to 2.77;  $I^2$ 92%) as shown in figure 1.





**Conclusions:** In summary, this study demonstrated a significantly increased risk of incident hip fracture among patients with PAD compared with individuals without PAD.

**Disclosure of Interest:** None declared

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### OP0064 GENERAL BONE LOSS IN PATIENTS WITH EROSIVE AND NON-EROSIVE HAND OSTEOARTHRITIS DURING THREE YEARS

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**Background:** Hand osteoarthritis (OA) and its more severe subset erosive hand OA are common causes of pain and morbidity. Some metabolic factors were suggested to be implicated in erosive disease. Few studies investigated differences in systemic bone loss between erosive and non-erosive hand OA.

**Objectives:** To compare the change of bone mineral density (BMD) between patients with erosive and non-erosive hand OA in a longitudinal study after three years.

**Methods:** American College of Rheumatology (ACR) criteria were used to assess hand OA. Erosive hand OA was defined by at least one erosive interphalangeal joint. All patients underwent clinical assessments of joint swelling and radiographs of both hands. DEXA examination of lumbar spine, total femur and femur neck was performed at baseline and after three years. Metabolic risk factors (body mass index, hypertension, diabetes, dyslipidaemia) were collected.

**Results:** Altogether, 144 patients (15 male) with symptomatic nodal HOA were included in this study and followed between April 2012 and January 2018. Out of these patients, 82 had erosive disease after three years. The disease duration (p<0.01) was significantly higher in patients with erosive compared with non-erosive disease.

Most patients took symptomatic slow acting drugs (SYSADOA) twice a year, non-steroidal anti-inflammatory drugs (NSAIDs) and analgesics on demand.

Baseline population characteristics did not differ between both groups. Osteoporosis (T-score <-2.5 SD) was diagnosed in 12.5% (9/72) of patients with erosive hand OA and in 8.06% (5/57) of patients with non-erosive hand OA. Although BMD did not significantly differ between the groups (BMD of lumbar spine 1,05 g/cm<sup>2</sup> vs 1,13 g/cm<sup>2</sup>, p<0.05, total femur 0,90 g/cm<sup>2</sup> vs 0,97 g/cm<sup>2</sup>, p<0.01 and femur neck 0,86 g/cm<sup>2</sup> vs 0,91, p<0.05), T-scores of lumbar spine (-0.96 vs -0,41 SD, p<0.05), total femur (-0.69 vs

-0,33SD, p<0.05) and femur neck (-1,14 vs -0,88 SD, p<0.05) were significantly lower in patients with erosive compared with non-erosive disease.

After three years, the decrease in T- score of lumbar spine was significantly higher in erosive hand OA compare to non-erosive disease (-3,66% vs 15,52%, p<0.01), also the decrease of T-score in total femur was significantly higher in erosive hand OA compare to non-erosive disease (-4,29% vs 7,68%, p<0.05).

The decrease of bone mineral density was also significantly higher in patients with erosive hand OA after three years. The decrease of BMD of lumbar spine was significantly higher in erosive hand OA after three years compare to non-erosive disease (-3,30% vs 1,06%, p<0,05), the decrease of BMD in femur neck was significantly higher in erosive hand OA after three years compare to non-erosive disease (-3,2% vs 0,02%, p<0,05), the decrease of BMD total femur neck was significantly higher in erosive hand OA after three years compare to non-erosive disease (-1,58% vs 0,82%, p<0,05).

**Conclusions:** These results suggest that patients with erosive hand OA are at higher risk for development of deep general bone loss.

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**Disclosure of Interest:** None declared

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### OP0065 OSTEOPOROSIS AND VERTEBRAL FRACTURES ARE ASSOCIATED WITH DISEASE ACTIVITY AND RADIOGRAPHIC DAMAGE IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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**Background:** Osteoporosis (OP) and vertebral fractures (VF) are common comorbidities of axial Spondyloarthritis (axSpA) with deleterious effects for the physical function of the patients.

**Objectives:** To evaluate the relationship between disease activity and radiographic damage and bone mineral density (BMD), 25 (OH) vitamin D levels and VF in patients with axSpA (ASAS Criteria).

**Methods:** Cross-sectional study. Activity variables: Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Ankylosing Spondylitis Disease Activity Score (ASDAS); ESR and CRP. Vitamin D insufficiency if <30 ng/mL. Lumbar Spine (LS) and femoral neck (FN) Dual X-ray absorptiometry (DXA) performed. Evaluation of VF with semiquantitative method (Genant) in thoracolumbar X-rays. Bivariate analysis to evaluate the associations with the presence of OP and/or VF, then binary and multiple logistic regression models, by using SPSS (v23); p values<0.05 considered significant.

**Results:** We studied 206 patients (62 women/144 men); 86% AS/14% nr-axSpA and associated peripheral involvement in 42%. Mean ±standard deviation (SD) values: age 52±14; activity (BASDAI 3.6±2.2, ASDAS-CRP 2.2±0.95, ASDAS-ESR 2.5±0.99, CRP 4.97±8.97 mg/L, ESR 18.2±14, 8 mm); physical function (BASFI 3.3±2.7); radiographic damage: mSASSS total 20.46±19.14, lumbar 10.41±9.89 and cervical 10.05±10.78; 25 (OH)vitD 19.83±9.25 ng/mL, 85.7% of the patients had insufficiency. Low LS BMD in 25.7% (z-score) and 28.9% (t-score) and low FN BMD in 45.2% (z) and 28.9% (t) of the patients. OP prevalence in LS 3.2%(z)/6.9%(t) and in FN 9.1% (z)/13.4% (t). Morphometric VF were identified in 34% of the patients.

Bivariate analysis: ESR, ASDAS-ESR, age, male sex, low 25 (OH) vitD levels and the mSASSS were associated with low FN BMD. Multivariate models confirmed the association between disease activity (ASDAS-ESR [OR 3.32 (95% CI: 2.35 to 4.55); p=0.016], 25(OH)D [OR 0.95 (95% CI: 0.86 to 0.98); p=0.029] and low FN BMD (z score).

An association was confirmed between CRP [OR 2.34 (95% CI: 1.10 to 4.98); p=0.027], radiographic damage [lumbar mSASSS OR 1.06 (95% CI: 1.03 to 1.10) p=0.001], high LS BMD [OR 296 (95% CI: 5.07 to 12258); p=0.006] and low FN BMD [OR 0.11 (95% CI: 0.03 to 0.12); p=0.000] and the presence of VF.

**Abstract OP0065 – Table 1.** Differences between patients without or with VF

	Without VF	With VF	p value
CRP (mg/L)	5.10±1.6	9.51±2.1	p=0.003
ESR (mm/h)	15.87±4.8	23.12±6.2	p=0.002
25OHvitD (ng/mL)	20.80±4.6	18.04±3.7	p=0.049
cervical mSASSS	8.02±2.5	13.11±4.8	p=0.002
lumbar mSASSS	8.93±3.7	12.36±6.5	p=0.000
total mSASSS	17.66±7.3	27.13	p=0.000
		±10.7	
LS BMD	1.090	1.191	p=0.002
	±0.09	±0.13	
FN BMD	0.912	0.773	p=0.000
	±0.11	±0.18	

**Conclusions:** In patients with axSpA, low FN BMD is associated with disease activity and vitamin D insufficiency and VF are associated with CRP and low hip bone mass. Furthermore, the presence of radiographic damage, even when 'falsely' increases LS BMD, is associated with the presence of fractures.

#### REFERENCE:

[1] Van der Heide, et al. 2016 update of the ASAS-EULAR management recommendations of axial SpA. *Ann Rheum Dis* 2017 Jun;76(6):978–991.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.2491

OP0066

### RISK OF FRACTURE AND LOW MINERAL DENSITY IN ADULTS WITH INFLAMMATORY BOWEL DISEASES. A SYSTEMATIC LITERATURE REVIEW WITH META-ANALYSIS

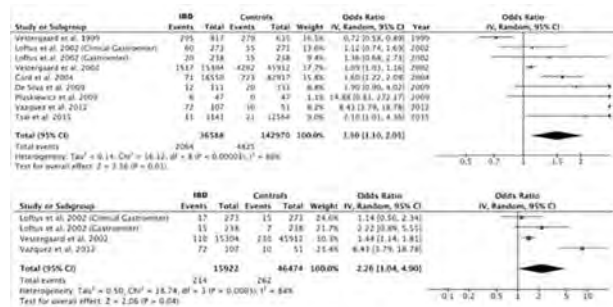
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**Background:** Inflammatory bowel disease (IBD) such as Crohn's disease (CD) and ulcerative colitis (UC) is associated with decreased mineral density caused by chronic inflammation and corticosteroid use. However, the increase of fracture risk is unknown and differs according to studies.

**Objectives:** The aim of our study is to assess the risk of fracture and low bone mineral density (BMD) in patients with IBD compared to the general population.

**Methods:** A systematic search of literature up to 1 st February 2017 was conducted using databases including: MEDLINE (via PUBMED), EMBASE, the Cochrane library and abstracts from the ACR, ASBMR and EULAR congresses from 2014 to 2016. Prospective and retrospective cohort studies were included if they reported the incidence of fractures and/or the measure of BMD by dual energy X-ray absorptiometry (DEXA) (expressed in g/cm<sup>2</sup>) in IBD patients in comparison with healthy controls. Meta-analysis was performed to assess odds-ratios (OR) for each studied group using the inverse variance approach to estimate pooled OR with their 95% confidence interval. Heterogeneity was assessed according to Cochran's Q-test and I<sup>2</sup> values. Calculations were made with the Cochrane RevMan 5.3 software. P-values less than 0.05 were considered as significant. Data was extracted by two independent investigators.

**Results:** The literature search identified 1165 articles and no congress abstracts; a manual search did not retrieve any articles. Finally, 25 studies met the inclusion criteria. 9 of them reported 2065 fracture events among 42,615 IBD patients and 4825 fracture events among 2 03 240 healthy controls. Global risk of fracture was increased in IBD patients compared with controls with pooled OR at 1.50 (95% CI: 1.10 to 2.05; p=0.01). The pooled OR of vertebral fracture was 2.26 (95% CI: 1.04 to 4.90; p<0.001). Fracture risk was not significantly increased for any other site (arm, hip, wrist). The analysis of 17 studies concerning BMD showed the significant decrease of BMD and Z-score at three sites. At femoral neck, mean difference (MD) of BMD was -0.05 (95% CI: -0.08 to -0.02; p=0.001) and MD of Z-score -0.48 (95% CI: -0.64 to -0.33 P<0.00001). At total femur, this values was respectively -0.08 (95% CI: -0.11 to -0.05, p<0.00001) and -1.01 (95% CI: -1.52 to -0.50 ; p=0.07), and at lumbar spine -0.06 (95% CI: -0.10 to -0.03, p=0.0003) and -0.51 (95% CI: -0.68 to -0.34 ; p<0.0001).



**Conclusions:** IBD patients have an increased risk of fractures, especially vertebral ones, suggesting the need for regular follow-up and preventing measures.

**Acknowledgements:** This work was initiated during sessions on performing meta-analyses organised by AbbVie. AbbVie had no role in the study design or in the collection, analysis, or interpretation of the data, the writing of the manuscript, or the decision to submit the manuscript for publication. Publication of this article was not contingent upon approval by AbbVie. This study was not financially supported by AbbVie.

**Disclosure of Interest:** None declared

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OP0067

### DICKKOPF-1 (DKK1) SERUM LEVELS AND BONE QUALITY (TBS EVALUATION) IN PATIENTS WITH SYSTEMIC SCLEROSIS AND RHEUMATOID ARTHRITIS

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**Background:** Systemic sclerosis (SSc) as well as rheumatoid arthritis (RA) patients present an increased risk of osteoporosis (OP) as a result of the chronic inflammatory state, low vitamin D, immobilisation and other causes. The Wnt/ $\beta$ -catenin pathway is signalling identified like a key promoters of the osteoblastogenesis hence of the new bone formation in inflammatory conditions. Dickkopf-1 (DKK1) is a natural inhibitor of Wnt signalling pathway that could be involved in promoting osteoclastogenesis through suppression of osteoprotegerin.<sup>1</sup> Trabecular Bone Score (TBS) is an index of bone quality extracted from dual-energy X-ray absorptiometry (DXA) analysis.<sup>2</sup>

**Objectives:** In this study, bone mineral density (BMD) and Dkk-1 levels were evaluated in SSc patients, in order to investigate possible associations between systemic OP and/or osteopenia and Dkk-1 concentrations, according to their different nailfold videocapillaroscopic (NVC) patterns of microangiopathy (NVC patterns 'Early', 'Active', and 'Late')<sup>3</sup> in SSc patients and to compare the results regarding bone quality with RA patients and healthy subjects (CNT).

**Methods:** Eighty-four SSc patients, 98 rheumatoid arthritis (RA) and 60 CNT were studied. Dkk-1 serum levels were measured by ELISA methods (Quantikine Human DKK-1 Immunoassay R and D System, Minneapolis, USA). Bone Mineral Density (BMD, g/cm<sup>2</sup>) of the lumbar spine (L1-L4) was analysed by dual-energy X-ray absorptiometry (DXA) scan. Lumbar spine bone quality was derived from each spine DXA examination using the TBS analysis. Nailfold videocapillaroscopic (NVC) patterns were analysed as previous reported.<sup>3</sup> 25 hydroxyvitamin D (25(OH)D ng/ml) serum concentration was evaluated in all subjects.

**Results:** Serum DKK-1 levels were significantly higher in patients with SSc than in CNT (2892±1121 pg/ml vs 2044±692 pg/ml, p<0.007). Dkk-1 levels were statistically significantly higher in patients with 'Late' SSc pattern than in those both 'Active' and 'Early' pattern (3467±954.1 pg/ml, 2290±487.8 pg/ml, 1827±888.3 pg/ml respectively, p<0.0001). A negative correlation between Raynaud's phenomenon duration (years expressed) (p<0.01) and Dkk-1 levels (p<0.001) was also observed. TBS values were found statistically higher in SSc with a 'Early' NVC pattern, compared to the 'Active' or 'Late' pattern. (p<0.001). Only in the 'Late' NVC pattern group a significant negative correlation was observed between TBS and Dkk-1 values (p<0.001). No statistical significant difference was observed in the three groups about DXA values (p=0.13, for all areas). Serum levels of 25 (OH) D were statistically significantly higher in patients with 'Early' SSc pattern than in those both 'Active' and 'Late' NVC pattern (19.1±7.5, 15.1±5.3, 12.1±7.1 respectively, p=0.002).

**Conclusions:** The data obtained showed a significantly increased of Dkk-1 serum concentrations together and a decreased bone mass (lower TBS and BMD) in SSc patients compared to CNT. The bone quality seems lower in SSc patients with more altered microvasculature ('Late' NVC pattern).

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OP0068

### SHORT TERM EFFECTS OF AMBIENT AIR POLLUTION ON OSTEOPOROTIC HIP FRACTURE. AN ECOLOGICAL STUDY IN A PERIOD OF 16 YEARS

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**Objectives:** To examine the short-term effects of outdoor air pollution on the incidence of osteoporotic HFx in a southern European region.

**Methods:** This is a retrospective cohort study based on data from three databases. Daily HFx incidence was calculated using discharge data from the hospital of Alcorcón for the period 2000–2015. Daily weather conditions were compiled from records of the national meteorological station (AEMET). Daily air pollutant levels (mcg/m<sup>3</sup>) were calculated from data from the Ministry of Environment for the Madrid Community: sulfur dioxide (SO<sub>2</sub>), nitrogen monoxide (NO), nitrogen dioxide (NO<sub>2</sub>), ozone (O<sub>3</sub>) and particulate matter in suspension <2.5 µm (PM<sub>2.5</sub>) and <10 µm (PM<sub>10</sub>), for the same period. Pollutant concentrations were categorised into quartiles (Q1 to Q4, lowest to highest). Associations between HFx incidence and air pollutant levels were examined through Generalized Additive Models (GAM) at a daily level with Poisson link function. Models were adjusted for a penalised spline function of time.

**Main outcome measures:** Daily hospital admissions for hip fracture.

**Results:** HFx incidence showed a direct association with NO, NO<sub>2</sub>, PM<sub>2.5</sub> and PM<sub>10</sub> and inverse association with O<sub>3</sub> levels. Incidence rate ratios for Q1vsQ2, Q1vsQ3 and Q1vsQ4 respectively were: 1.171 (1.103–1.244), 1.245 (1.173–1.322) and 1.331 (1.253–1.414) for NO; 1.057 (0.996–1.122), 1.185 (1.116–1.259) and 1.276 (1.199–1.357) for NO<sub>2</sub>; 1.028 (0.943–1.12), 1.092 (1.006–1.185) and 1.146 (1.049–1.253) for PM<sub>2.5</sub>; 1.083 (1.016–1.155), 1.099 (1.034–1.168) and 1.213 (1.136–1.294) for PM<sub>10</sub>; and 0.975 (0.914–1.04), 0.868 (0.815–0.924) and 0.814 (0.765–0.867) for O<sub>3</sub>. These associations persisted when the models were corrected for season, day of the week and weather conditions. When participants were stratified by age and sex, associations persisted only in women older than 75 years.

**Conclusions:** A short-term effect was observed of several indicators of air pollution on hip fracture incidence. This is the first study that finds this association.

**Disclosure of Interest:** None declared

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OP0069

#### THE RELATIONSHIP BETWEEN ESTIMATED BONE STRENGTH BY FINITE ELEMENT ANALYSIS AT THE PERIPHERAL SKELETON TO AREAL BMD AND TBS AT LUMBAR SPINE IN ADULTS

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**Background:** Bone strength, estimated by finite element (FE) analysis based on high resolution peripheral quantitative computed tomography (HR-pQCT) images is an important contributor to understanding risk of fracture. However, it is a peripheral device and cannot be evaluated *in vivo* at lumbar spine L1-L4.

**Objectives:** The aim of this study was to investigate if the axial bone quality can be predicted by strength measurements of peripheral bone.

**Methods:** Peripheral bone microarchitecture, areal bone mineral density (aBMD) and trabecular bone score (TBS) were measured in adults individuals (n=262, 60 years and older; 63% women). Stiffness and failure load were estimated by FE analysis at HR-pQCT images at radius and tibia. Areal BMD and TBS were measured by dual energy X-ray absorptiometry (DXA) at L1-L4. Correlations between peripheral and axial data were estimated for each gender adjusted by age, weight, and height.

**Results:** Areal BMD L1-L4 resulted in weak to moderate significant correlations with stiffness and failure load at radius (women: R<sup>2</sup>=0.178, p<0.05 and R<sup>2</sup>=0.187, p<0.001, respectively; men: R<sup>2</sup>=0.454 and R<sup>2</sup>=0.451, p<0.001, respectively) and at tibia (women: R<sup>2</sup>=0.211 and R<sup>2</sup>=0.216, p<0.001, respectively; men: R<sup>2</sup>=0.488 and R<sup>2</sup>=0.502, p<0.001, respectively). TBS showed a very weak or no correlation with stiffness and failure load at radius (women: R<sup>2</sup>=0.148 and R<sup>2</sup>=0.150, p<0.05, respectively; men: R<sup>2</sup>=0.108 and R<sup>2</sup>=0.106, p<0.05, respectively) and at tibia (women: R<sup>2</sup>=0.146 and R<sup>2</sup>=0.150, p<0.05, respectively; men: R<sup>2</sup>=0.072 and R<sup>2</sup>=0.078, respectively).

**Conclusions:** These data suggest that aBMD L1-L4 was better explained by peripheral bone strength characteristics than the TBS, mainly in men and tibia is generally the site with a better relationship.

**Disclosure of Interest:** None declared

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WEDNESDAY, 13 JUNE 2018

## New drugs – new perspectives: clinical and regulatory issues concerning biosimilars

### OP0070-HPR IS PATIENTS' SATISFACTION WITH BEING SWITCHED TO A BIOSIMILAR MEDICATION ASSOCIATED WITH THEIR LEVEL OF HEALTH LITERACY? RESULTS FROM A NORWEGIAN USER SURVEY

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**Background:** Economically motivated switching to biosimilar medication has been practiced in Norway since March 2016. There are several studies comparing the efficacy, safety and immunogenicity of biosimilars, however no studies have yet described patients' experiences and attitudes towards economically motivated switching.

**Objectives:** The aim of this study was to describe patients' experiences regarding being switched to an alternative medication (the switch) and further to investigate possible associations between such switching and health literacy.

**Methods:** Potential users of Etanercept or Infliximab were asked to participate using three patients' interest associations. Data from this convenience sample was collected using a web-survey in January 2017. Attitudes and experiences with a possible switch to an alternative medications were assessed using several questionnaires. In addition, data on gender, age and marital status were collected. Patients' experiences, attitudes and satisfaction were assessed using a self-developed questionnaire. In addition, health related literacy was measured using The Health Literacy Questionnaire<sup>1</sup> a multi-dimensional validated questionnaire. We used three domains covering patients' ability to actively engage with health care providers (Scale 6), ability find good health information (Scale 8) and understanding health information well enough to know what to do (Scale 9). Data were analysed using multiple logistic regression and the results expressed as odds for being satisfied with the switch.

**Results:** Of all included responders (n=290), 155 reported being switched to a biosimilar medication in 2016. Median age was 51 years, range 20–74. The majority of responders were females, 61% (n=176) and more than half (51%) completed higher education. Over 80% of those who were switched (economically motivated switch to a biosimilar drug) were neutral or satisfied with their new medication. Patients who were dissatisfied with being switched had lower levels of health related literacy compared to patients who were satisfied. Further, older patients reported more often being satisfied compared to younger patients. Only 14% reported that they were involved when a decision to being switched was made, male patients significantly more often compared to female patients (p=0.02). Self-assessed good health was strongly associated with higher probability of being satisfied with the switch, only 9/74 patients who reported bad health also reported being satisfied. When adjusted for age and self-assessment of one's own health, scales 6 and 8 but not scale 9, were significantly associated with higher odds for being satisfied with being switched (OR=2.5, 95% CI: [1.2 to 5.2] and OR=2.7, 95% CI: [1.2 to 5.9], for scale 6 and 8, respectively).

**Conclusions:** A great majority of patients reported being satisfied with being switched to a cheaper biosimilar medication, however, almost one in five (19%) reported being dissatisfied. Our findings suggest that patients' attitudes and level of satisfaction are associated with being given sufficient and necessary information concerning their health.

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WEDNESDAY, 13 JUNE 2018

## Movement in musculoskeletal pain; from risk to management

OP0071

### THE PREVALENCE OF PAIN FLARES: IMPACT OF DEFINITION

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**Background:** Rapid acute pain exacerbations, colloquially called *pain flares*, affect quality of life and are a key driver for patients to seek healthcare. There is no standardised definition of pain flare.<sup>1</sup> Daily collection of patient-reported symptoms with mobile technology enables monitoring pain flares in real-time. The



choice of definition may identify different people and patterns of pain severity. If remote monitoring of flares is to inform clinical practice and research, it is important to understand the implications of these choices.

**Objectives:** Investigate the frequency of pain flares from daily pain symptoms under various definitions in a population with chronic pain.

**Methods:** Participants with chronic ( $\geq 3$  months) musculoskeletal pain in the smartphone study Cloudy with a Chance of Pain<sup>2</sup> reported daily pain severity and impact of pain on a 5-point scale. Pain flares were defined in five ways:

1. *Worse than average:* pain severity higher than personal median
  2. *Above threshold:* pain value 4 or 5
  3. *Move to above threshold:* pain value 1 or 2 or 3 yesterday to 4 or 5 today
  4. *Absolute change:* 2-point increase in pain since yesterday
  5. *Composite:* 2-point increase in pain severity since yesterday and impact 4 or 5
- Daily pain-flare rate was calculated by dividing the number of pain flares by the number of days a pain flare would have been possible, hereafter called *at-risk days* (def. 1+2: total days of symptom entry; def 3 to 5: days of data entry for which participant also entered data on preceding day). Monthly pain-flare rates per person were calculated by multiplying the rate by 30.

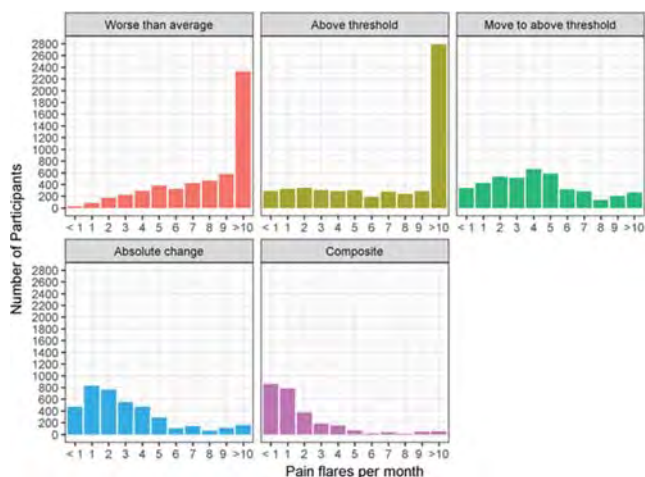
**Results:** The study smartphone app was downloaded by 13 256 people. After excluding people that never reported pain severity ( $n=2020$ ), did not complete the baseline questionnaire ( $n=947$ ), stayed in the study for less than 7 days ( $n=3418$ ), and reported non-musculoskeletal chronic pain ( $n=728$ ), 6143 were eligible for analysis.

**Abstract OP0071 – Table 1.** Participants with pain flares and monthly pain flare rates under 5 definitions

	Participants with $\geq 1$ flare (%)	Flares	Monthly pain flare rate
<b>Worse than average</b>	5304 (86.3)	1 09 616	8.0
<b>Above threshold</b>	5627 (91.6)	1 18 596	8.7
<b>Move to above threshold</b>	4246 (69.1)	33 661	3.2
<b>Absolute change</b>	3940 (64.1)	22 173	2.1
<b>Composite</b>	2577 (42.0)	9531	0.9

Table 1 shows that the portion of eligible people with at least one pain flare varies by definition, with 42% reporting at least one pain flare according to the most restrictive classification criterion. Depending on the criterion used, the monthly pain-flare rate per ranges from 0.9 to 8.7.

Under the 'worse than average' and 'above threshold' definition, most participants have more than 10 pain flares per month (figure 1). Under the two most stringent definitions, most participants have between 0 and 3 pain flares per month.



**Conclusions:** The five plausible definitions for a pain flare are demonstrated to generate quite different flare rates through time. Pain flares in people with chronic musculoskeletal pain, however, remain common even as classification criteria become increasingly strict. As daily data collection of patient-generated data becomes possible, careful thought must be given to flares should best be defined for clinical practice and research.

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#### OP0072 SLEEP PROBLEMS AND FATIGUE AS A PREDICTOR FOR THE ONSET OF CHRONIC WIDESPREAD PAIN OVER A 5- AND 18-YEAR PERSPECTIVE. A 20-YEAR PROSPECTIVE STUDY

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**Background:** If localised pain represent one end of a pain spectra, with overall better general health, chronic widespread pain (CWP) and fibromyalgia represent the other end of the spectra with worse general health and more comorbidities with other somatic diseases and mental illness. Sleep problems and fatigue are common among individuals reporting CWP and previous research indicate that sleep problems may be an important predictor for pain prognosis.

**Objectives:** The aim of this population-based study was to investigate if sleep problems and fatigue predict the onset of CWP 5 and 18 years later.

**Methods:** In order to get more stable baseline classifications of CWP, a wash-out period was used, including only individuals who had not reported CWP (according to <sup>ACR 1990</sup> criteria for fibromyalgia) at baseline (-98) and three years prior baseline (-95). In all, data from 1249 individuals entered the analyses for the 5 year follow-up (-03) and 791 entered for the 18 year follow-up (-16). Four parameters related to sleep (difficulties initiating sleep, maintaining sleep, early morning awakening and non-restorative sleep), and one parameter related to fatigue (SF-36 vitality scale) were investigated as predictors for CWP. Binary logistic regression analysis were used for analyses.

**Results:** All investigated parameters predicted the onset of CWP five years later (problems with initiating sleep (OR 1.91; 1.16–3.14), maintaining sleep (OR 1.85; 1.14–3.01), early awakening (OR 2.0; 1.37–3.75), non-restorative sleep (OR 2.27; 1.37–3.75) and fatigue (OR 3.70; 1.76–7.84)) in a model adjusted for age, gender, socio-economy and mental health. All parameters except problems with early awakening predicted the onset of CWP also 18 years later. In all, 785 individuals did not report any of the sleeping problems at baseline (fatigue not included), 268 reported one of the problems, 167 two, 128 three and 117 subjects reported to have all four sleep problems. Reporting all four sleep problems was significantly associated with CWP at follow-up at both time points when adjusting for age, gender, socio economy and mental health (OR 4.00; 2.03–7.91 and OR 3.95; 1.90–8.20); adjusting for age, gender, socio economy and number of pain regions (OR 2.94; 1.48–5.82 and OR 2.65; 1.24–5.64) and in a model adjusting for age, gender, socio economy and pain severity (OR 2.97; 1.53–5.76; and OR 3.02; 1.47–6.21) for the 5 year and 18 year follow-up respectively, compared to not reporting any of the sleep problems at baseline.

**Conclusions:** Both sleeping problems and fatigue predicts the onset of CWP 5- and 18 years later. The results highlight the importance of the assessment of sleep quality in the clinic.

**Disclosure of Interest:** None declared  
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#### OP0073 CENTRAL SENSITISATION PREDICTS FATIGUE INDEPENDENTLY OF MUSCULOSKELETAL PAIN

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**Background:** Fatigue is a common musculoskeletal (MSK) pain comorbidity that is associated with increased healthcare use and poor quality of life. Central sensitisation (CS), the amplification of sensory input across multiple systems, has been associated with MSK pain. It has been hypothesised that similar mechanisms may explain the co-occurrence of fatigue, but data are conflicting.

**Objectives:** To test the hypothesis that CS was associated with the presence of fatigue, and to establish whether the relationship was independent of the relationship between MSK pain and fatigue.

**Methods:** 2455 participants in a prospective cohort study completed a baseline questionnaire collecting data on fatigue (Chalder Fatigue Scale, score 0–33 (CFQ); pain (body map, score range 0–44); demographics (date of birth, sex); Rapid Assessment of Physical Activity (RAPA); analgesic use; and mental health (Hospital Anxiety and Depression (HAD) scale). During a clinic visit a random sample of participants ( $n=290$ , 11.8%) had a wind-up ratio test (the perceived intensity of a single 256mN pinprick/intensity of a series of 10 pinpricks) at the thenar eminence of the right hand (WUR-H) and dorsum of the left foot (WUR-F) to assess CS, and bioelectric impedance (Tanita BC-418 Segmental Body

Composition Analyzer) to determine proportion body fat. All participants were followed up 12 months later, at which time they completed the CFQ. Linear regression, with inverse probability sampling weights, tested the relationship between WUR at baseline and CFQ at 12 months, adjusted for baseline CFQ, demographics, lifestyle factors, HAD and in a final model baseline MSK pain. Results are expressed as beta coefficients with p values.

**Results:** The median (IQR) WUR-H and WUR-F were similar (2.4 (1.5, 3.8) and 2.5 (1.6, 4.0) respectively), did not differ by sex but were significantly lower in older people. After adjusting for age and sex, WUR-H ( $\beta=0.17$ ,  $p=0.00$ ) and WUR-F (0.18, 0.00) predicted CFQ at follow-up. In a fully adjusted model, WUR-H (Model 1: 0.13, 0.00) and WUR-F (Model 2: 0.13, 0.00) predicted CFQ at follow-up, independently of baseline MSK pain. Independent predictors of CFQ were age, MSK pain, depression, anxiety, physical activity and body fat (table 1).

#### Abstract OP0073 – Table 1

Baseline predictors of fatigue at 12 months		
	Model 1 – Hand ( $\beta$ , p-value)	Model 2 – Foot ( $\beta$ , p-value)
Wind-up ratio	0.13–0.00	0.13–0.00
Age	0.03–0.00	0.04–0.00
Gender	–0.41, 0.05	–0.46, 0.05
HAD Depression	0.18–0.00	0.18–0.00
HAD Anxiety	0.30–0.00	0.30–0.00
RAPA	–0.25, 0.00	–0.19, 0.00
% body fat	0.03–0.004	0.04–0.002
Analgesic use	0.03–0.34	0.05–0.12
MSK pain	0.11–0.00	0.10–0.00

**Conclusions:** Fatigue is predicted by CS, independently of the presence of MSK pain. For those seeking to treat fatigue, the potential benefit of interventions which reduce sensitisation should be investigated.

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**Disclosure of Interest:** None declared

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#### OP0074 ASSOCIATION BETWEEN BRAIN-DERIVED NEUROTROPHIC FACTOR GENE POLYMORPHISMS AND FIBROMYALGIA IN A KOREAN POPULATION: A MULTI-CENTRE STUDY

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**Objectives:** Several lines of evidence suggest that brain-derived neurotrophic factor (BDNF) is involved in the pathophysiology of fibromyalgia (FM) and studies have found that FM patients have altered serum and plasma BDNF levels. However, it is not known whether polymorphisms of the *BDNF* gene are associated with FM. In this study, we explored the association between polymorphisms of the *BDNF* gene with FM susceptibility and the severity of symptoms.

**Methods:** The study enrolled 409 patients with FM and 423 controls from 10 medical centres that participated in the Korean nationwide FM survey study. Alleles at 10 positions in the *BDNF* gene were genotyped: rs2883187 (C>T), rs7103873 (G>C), rs7103411(C>T), rs10835210 (C>A), rs11030104 (A>G), rs12273539 (C>T), rs11030102(C>G), rs11030101 (A>T), rs6265 (G>A), and rs7124442 (C>T).

**Results:** The allele and genotype frequencies of *BDNF* rs11030104 differed significantly between the FM patients and controls ( $p=0.031$ ). The GG genotype of rs11030104 had a protective role against FM ( $p=0.016$ ) and the G allele of rs11030104 was negatively associated with the presence of FM compared with the A allele ( $p=0.013$ ). In comparison, although the allele and genotype frequencies of *BDNF* rs12273539 did not differ between the FM patients and controls, the TT genotype of *BDNF* rs12273539 was associated with susceptibility to FM ( $p=0.038$ ). Haplotype analyses suggested that some *BDNF* haplotypes have a protective role against FM. Finally, we found that that some genotypes and haplotypes of the *BDNF* gene contribute to the specific symptoms of FM.

**Conclusions:** This study is the first to evaluate the associations of *BDNF* gene polymorphisms with FM. Our results suggest that some *BDNF* single-nucleotide polymorphisms and haplotypes are associated with susceptibility to, and contribute to the symptoms of, FM.

**Disclosure of Interest:** None declared

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#### OP0075 ULTRASOUND-DETECTED SHOULDER PATHOLOGIES CLUSTER INTO GROUPS WITH DIFFERENT CLINICAL ASSOCIATIONS: DATA FROM A PROSPECTIVE STUDY OF 500 COMMUNITY REFERRALS FOR SHOULDER PAIN

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**Background:** Shoulder pain is common and its management remains challenging, often resulting in poor outcomes: 50% of people continue to have shoulder pain at 18 months. This may be in part due to inaccurate clinical diagnosis. Ultrasound offers accurate detection of pathology and its use is increasing. However, the relationship between ultrasound findings and clinical phenotype is unclear.

**Objectives:** A prospective study was undertaken to explore latent class groupings and explore the association between patient reported outcome measures and the different groups.

**Methods:** 500 primary care patients attending for shoulder ultrasound were prospectively recruited. Radiologists and sonographers underwent training to ensure standardised reporting. Baseline data was collected via self-reported questionnaires. Outcome measures collected included pain, function, quality of life, treatments received, activity, self-efficacy and levels of acceptable symptom states. These measures underwent Rasch analysis. Latent class analysis was undertaken to identify groups.

**Results:** Mean age was 53.6% and 52% were female. Latent class analysis confirmed the existence of 4 groups: limited bursitis; extensive inflammation; RC tears; limited pathology. The oldest age group were those with RC tears, and the youngest was those with limited bursitis. The rotator cuff tear group had the highest levels of pain and disability, and the lowest levels of acceptable symptom states. Those with limited pathology had the highest levels of acceptable symptom states. The extensive inflammation group had the lowest activity scores.

Summary statistics for classes obtained prior to covariate adjustment (complete data only)

	Bursitis (limited inflammation)	Bursitis (extensive inflammation)	RC tear	Limited pathology
% of sample	49	18	15	18
Age, years: mean (95% CI)	47.4 (45.3–49.6)	64.4 (61.1–67.7)	66.1 (63.4–68.9)	49.1 (46.3–51.9)
Female:%	53	58	41	52
Duration of symptoms, months: median (IQR)	6 (3–14)	7 (4–23)	5 (3–12)	6 (4–15)
RC tear (y/n):%	4	44	>99	2
Full thickness RC tear:%	<1	20	92	<1
Bursitis:%	>99	88	34	6
Impingement:%	70	58	94	2
Calcific tendinitis:%	10	6	2	12
ACJ degeneration:%	34	83	63	33
Glenohumeral OA:%	1	2	15	2
Adhesive capsulitis:%	3	5	6	25
Biceps tenosynovitis:%	<1	17	10	<1
Rotator cuff tendinopathy:%	22	81	12	14
EQ5D-5L VAS: median (IQR)	75 (61–85)	66 (49–80)	80 (70–90)	75 (60–85)
Brophy activity score: mean (95% CI)	7.2 (6.9–7.5)	5.5 (4.9–6.0)	7.1 (6.6–7.7)	6.7 (6.2–7.2)
Total SPADI: mean (95% CI)	49.9 (48.6–51.1)	51.8 (48.6–55.1)	56.2 (54.0–58.4)	50.2 (47.7–52.6)
P-SEQ: mean (95% CI)	34.7 (33.3–36.1)	32.2 (29.3–35.1)	33.2 (30.6–35.7)	34.3 (31.8–36.8)
PASS:%	17	30	11	34

VAS=visual analogue scale; SPADI=shoulder pain and disability index; P-SEQ=patient self-efficacy questionnaire; HADS=hospital and depression scale; PASS=patient acceptable symptom state

**Conclusions:** This study confirms that ultrasound pathologies cluster into groups. These groups appear to differ in symptom associations at baseline; expanding the LCA to include covariates will allow us to formally explore these associations. A longitudinal study will provide understanding of the relevance of these groups to long-term patient outcomes.

**Disclosure of Interest:** None declared

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OP0076

### ISOTEMPORAL SUBSTITUTION OF SEDENTARY TIME WITH PHYSICAL ACTIVITY IN FIBROMYALGIA: ASSOCIATION WITH QUALITY OF LIFE AND DISEASE IMPACT. THE AL-ANDALUS PROJECT

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**Background:** There is an awareness of detrimental health effects of sedentary time (ST) in fibromyalgia.<sup>1</sup> However, data are limited on how replacing ST with physical activities of different intensities may be related to the typically reduced quality of life of these patients. Increasing time in one behaviour requires decreasing time in another but classic regression models are not able to directly target these substitutions. Hence, the isomodal substitution paradigm (a novel model to study the estimated effects of one activity for another<sup>3</sup>), might allow us to better understand the relationship between ST, physical activity and perceived health status in fibromyalgia.

**Objectives:** To investigate the association of replacing ST with light physical activity (LPA) or moderate-to-vigorous physical activity (MVPA) with quality of life and disease impact in women with fibromyalgia.

**Methods:** In total, 407 women with fibromyalgia (51.4±7.6 years old) were included in this cross-sectional study. The time spent in ST and PA intensity levels was objectively measured with triaxial accelerometry. Quality of life and disease impact were assessed using the 36-item Short-Form Health Survey (SF-36) and the Revised Fibromyalgia Impact Questionnaire (FIQR), respectively. An isomodal substitution approach was used to estimate the associations between the substitution of 30 min of ST with an equivalent time of LPA or MVPA and the outcomes. Analyses were controlled for age, current occupational status, fat percentage, and antidepressant consumption.

**Results:** Substituting 30 min of ST with LPA in the isomodal model was associated with better bodily pain ( $B=0.55$ ), vitality ( $B=0.74$ ) and social functioning ( $B=1.45$ ) of SF-36 and better scores at all of the domains of FIQR (function, overall impact, symptoms severity, and total impact) ( $B$  ranging from  $-0.95$  to  $-0.27$ ), all  $p<0.05$ . When 30 min of ST were replaced with MVPA, significantly better physical role ( $B=2.30$ ) and social functioning ( $B=4.11$ ) of the SF-36 and function of FIQR ( $B=-0.73$ ) were observed (all  $p<0.05$ ).

**Conclusions:** Allocating time of sedentary behaviour to either LPA or MVPA was generally associated with better quality of life and lower disease impact in women with fibromyalgia. The isomodal models suggest that LPA may be beneficial for a larger number of domains, while MVPA may establish greater changes in the outcomes. These results reinforce the importance of moving towards less sedentary lifestyle in fibromyalgia, although these findings should be investigated in longitudinal, experimental research.

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**Disclosure of Interest:** None declared

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OP0077

### EFFECTIVENESS OF 8-WEEKS SUPERVISED AND NON-SUPERVISED AEROBIC EXERCISE PROGRAMSON CLINIC FINDINGS,FUNCTIONAL STATUS AND QUALITY OF LIFE IN THE PATIENTS WITH FIBROMYALGIA SYNDROME

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**Background:** Fibromyalgia syndrome, aerobic exercise.

**Objectives:** This study was planned to evaluate the effectiveness of 8 weeks supervised and non-supervised aerobic exercise programs on clinic findings, functional status and quality of life in the patients with fibromyalgia syndrome.

**Methods:** A total of 120 patients who received the diagnosis of fibromyalgia syndrome according to <sup>ACR 2010</sup> Fibromyalgia classification criteria were enrolled into the study. Patients were randomised into three groups ;Supervised aerobic exercise group (Group 1, 40 subjects), non-supervised aerobic exercise group (Group 2, 40 subjects), and control group (Group 3, 40 subjects). Fatigue, depression,

functional status, physical function, and quality of life of patients were evaluated before and after the treatment. Visual Analogue Scale (VAS) was used to assess the fatigue level. The level of depression was evaluated by Zung Depression Scale (ZDS). The evaluation of functional status was performed using Fibromyalgia Impact Questionnaire (FIQ). The quality of life of patients was investigated by Nottingham Health Profile (NHP). 6-metre walking distance test was used for the assessment of the physical function.

**Results:** After the exercise program, it was observed that there was a statistically significant improvement in both exercise groups for all evaluated parameters (fatigue, depression,functional status, physical function and quality of life), compared to the baseline ( $p<0.05$ ).When compared with control group, it was found that the improvement in both groups was statistically significant better than control group ( $p<0.05$ ).The improvement in fatigue,depression, functional status, physical function, and the Physical mobility subgroup of the quality of life was found to be better in supervised exercise group compared to the non-supervised home-based exercise group ( $p<0.05$ ). As for the patients in the control group, it was observed that there was no improvement in any of the evaluated parameters.

**Conclusions:** In this study it was demonstrated that both supervised and non-supervised aerobic exercisepograms have positive effects on clinic findings, functional status and quality of life ofpatients with fibromyalgia. However, further-studies with a larger sample size and with a longer follow-up period are needed to support the findings of our study about the positive effects of supervised and non-supervisedaerobic exercises.

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OP0078

### IS THE EFFICACY OF PHYSICAL THERAPY RELATED TO THE PAIN IN THE PATIENT'S MIND?

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**Background:** The degree of improvement in functionality and pain after physical therapy in the patients with knee osteoarthritis (OA) may be due to various peripheral factors and used modalities. Additionally, in some patients, modifiable psychological factors such as pain catastrophizing and depression may influence the therapy outcome.<sup>1</sup>

**Objectives:** The aim of this study was to investigate the impact of pain catastrophizing and depression on pain and functionality in the patients with knee OA who were treated with physical therapy.

**Methods:** The prospective cohort study participants were 89 patients with knee OA who underwent 10 sessions of physical therapy consist of hot-pack, transcutaneous electrical nerve stimulation (TENS), and ultrasound (US). Socio-demographic and clinical data were initially recorded. At baseline, pain catastrophizing and depression were measured with the standardised questionnaires including Pain Catastrophizing Scale (PCS) and Beck Depression Inventory-II (BDI-II).The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and the visual analogue scale (VAS) were performed at baseline, at the end of therapy and at first month after therapy.

**Results:** The patients' mean age was 60.38 (0.97), 82% were women, and 58.4% were not working. At baseline, the mean VAS and WOMAC scores were 7.39 (1.07) and 43.03 (19.47), respectively. 47.20% of the patients had clinically proper catastrophizing. The baseline demographic and clinical characteristics, except BDI-II score, VAS, and WOMAC were not different among the low catastrophizing and high catastrophizing groups (table 1). The patients who had high



scores on pain catastrophizing had a lower improvement in VAS and WOMAC scores at the end of therapy and at first month after therapy (figure 1).

**Abstract OP0078 – Table 1.** Demographic data of all patients

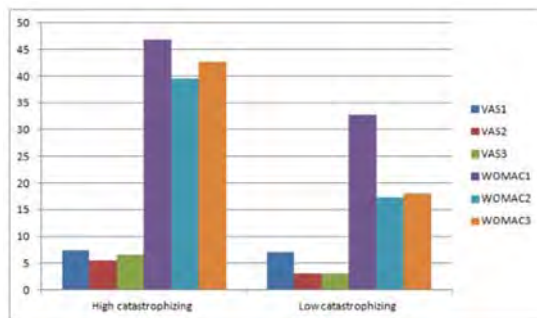
	Low catastrophizing (n:47)	High catastrophizing (n:42)	Total (n:89)	p
Age, mean±SD (years)	58.93±9.68	62.00±8.54	60.38 ±0.97	0.11
Gender n (%)	37 (78.7)	36 (85.7)	73 (82)	0.39
Female	10 (21.3)	6 (14.3)	16 (18)	
Male				
BMI, mean±SD	29.18±3.62	29.51±3.72	29.34 ±0.38	0.52
BDI-II, mean±SD	9.19±5.69	16.30±8.41	12.55 ±7.91	<0.001*
Employment Status n (%)	21 (44.7)	31 (73.8)	52 (58.4)	0.096
Not working	3 (6.4)	1 (2.4)	4 (4.5)	
Labourers	6 (12.8)	3 (7.1)	9 (10.1)	
Retail trading	13 (27.7)	5 (11.9)	18 (20.2)	
Retired	4 (8.5)	2 (4.8)	6 (6.7)	
Government employee				
Initial VAS, mean ±SD	6.97 (1.01)	7.85 (0.95)	7.39 (1.07)	<0.001*
Initial WOMAC, mean±SD	31.63 (15.03)	55.78 (15.65)	43.03 (19.47)	<0.001*

PCS: Pain Catastrophizing Scale, VAS: Visual Analogue Scale, WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index

High catastrophizing was described as total PCS score  $\geq 30$ .

Low catastrophizing was described as total PCS score  $< 30$ .

\* Statistically significant value ( $p < 0.05$ )



**Abstract OP0078 – Figure 1** The comparing of differences of VAS and WOMAC scores among low catastrophizing and high catastrophizing groups.

**Conclusions:** We suggest that high levels of initial PCS score may cause lower improvement on pain and functional levels in the patients who underwent physical therapy. Screening for pain catastrophizing and depression in the patients who receive physical therapy and taking necessary precautions may improve outcomes.

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**Disclosure of Interest:** None declared

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**WEDNESDAY, 13 JUNE 2018:** Don't delay, connect today!

#### OP0079-PARE 'AWARENESS WEEK FOR RHEUMATIC DISEASES- 8–14 MAY 2017'

B. Boteva, H.L. Bankova. Sofia, Bulgaria

**Background:** Among the main priorities that Bulgarian Organisation for people with rheumatic diseases follow is the dissemination of knowledge and information about RMD's.

An important initiative is the annual awareness week about RMD's which is organised since 2015. The awareness week is organised in May and the idea occurred after EULAR's Knowledge transfer program in which BOPRD took part in 2013.

**Objectives:** In 2017 the focus was on two of the rheumatic diseases – SLE and fibromyalgia. SLE and fibromyalgia are not well known in our country that is why we decided to spread awareness among general public and policymakers.

The main goal of the 2017 awareness week for RMD's was to:

- inform the society and policymakers about the social significance of SLE and fibromyalgia
- Spread awareness about the most common symptoms of SLE and fibromyalgia
- Inform people with SLE, fibromyalgia and other RMDs how they can manage symptoms as anxiety, depression, and tension.

**Methods:** The 2017 awareness week about RMDs was organised in the period 8–14 May 2017.

One of the most important accents was a seminar, organised on 8 of May. We have invited as lecturer Gergana Radovich who is one of the international T-Tapp trainers. She holds a Master degree in Cognitive science, as well as certificates for Psych-K Facilitator and EFT Practitioner.

T-Tapp is a series of movements designed to put the body in proper functional alignment, restore metabolic function and stands on its own as a complete workout. Such a seminar for people with RMDs was not organised before. The participants had the chance to learn more about EFT and T-Tapp and how these techniques can benefit their condition and help them fight fear, tension, and anxiety.

At 10-th of May – World lupus day a discussion about the problems that people with SLE face was organised.

In the evening the National Palace of Culture (a famous building in the capital of Bulgaria) was lit in purple light to support people with SLE.

**Results:** The 2017 awareness week for RMDs was very successful.

All publications and media interviews that were published at the organisation's website and in other websites reached more than 4000 people in total.

88 people liked the organisation's Facebook page in the period 8–14 May 2017.

We have managed to continue to offer online EFT and T-Tapp lessons to the members of the organisation

**Acknowledgements:** Miglena Ivanova; Snezhana Bozhinova; Janeta Cherpokova; PRCare;Bozhidar Ivkov;Hristina Bankova

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.7407

#### OP0080-PARE PHOTO ALBUM OF PEOPLE WITH RHEUMATIC DISEASES UNDER THE TITLE: 'THERE ARE SOME PEOPLE... OUR PEOPLE!!!'

K. Koutsogianni, E. Tsourlidaki, J. Papadakis, R. Stara, L. Papadaki, on behalf of The Arthritis Foundation of Crete. *The Arthritis Foundation of Crete, Heraklion, Crete, Greece*

**Background:** The impact of rheumatic diseases in the daily life of people is sometimes quite dramatic, causing abundance of everyday pleasures and activities even one's hobbies. The burden of RMDs is not adequately communicated to the public or to the state, so that this important aspect is not generally met with relevant seriousness.

**Objectives:** The goal of our campaign was: a. to give a clear picture of the difficulties that people with rheumatic diseases face in their everyday life and b. to prove that some people manage to overcome their serious movement problems, their pain and dysfunction and show, with dignity and strength, that the artistic part inside them is vividly alive. The message we would like to communicate here is: THE POWER OF MIND IS STRONGER THAN BODY WEARENESS AND CHRONIC PAIN.

**Methods:** Firstly we got in touch with members of our Association that their skills could be presented in the album and discussed our idea, which was gladly accepted by them.

10 members of the association are included in the album, all of which are people with severe inflammatory rheumatic diseases. Ignoring their obvious moving problems and putting aside their other engagements, these wonderful people follow their talents and become sculptors, icon painters, pastry chefs etc. After the nomination of the sponsor for the project, a professional photographer was selected to capture the talents, the dedication to their art and the inner feelings of those people, in a way that can only be detected through the photographer's eye.

The shooting started in March 2017 and was finished in September 2017. Each of the artists had the chance to spend time with the photographer, express their feelings and show their way of life to him. This face to face contact enabled George (the photographer) to depict on his photos the real personality of these special people.

After the shooting, a website was created where the pictures were uploaded with underlined personal remarks of both the artists and the professional photographer. Information about the inflammatory rheumatic diseases and the importance of early diagnosis was added to the album. Additionally, during October 2017, a 45 s video was promoted through TV, targeting the serious problems that people with RMDs are facing in their everyday life but also revealing the strength and courage of this great artists' team. A press conference was as well organised to support the visit of the particular website.

**Results:** Results: 173.000 people have visited the website from October to January, with another 16.800 visits through YouTube.



**Conclusions:** Through an artistic approach a patient organisation can trigger the awareness of the public, communicate the important message of the seriousness of RMDs and also underline the endless dedication and the seek for dreams to come true, even if one has to live along with a rheumatic disease all your life.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.2907

WEDNESDAY, 13 JUNE 2018:

## Let's improve diagnosis and treatment of orphan diseases

### OP0081 PHENOTYPIC SUBGROUPS IN IGG4-RELATED DISEASE – A CLUSTER ANALYSIS

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**Background:** IgG4-related disease (IgG4-RD) is a multi-organ immune-mediated condition of uncertain etiology characterised by substantial organ-specific morbidity if not diagnosed and treated promptly. Identifying IgG4-RD subgroups based on the distribution of organ involvement may influence the understanding of pathogenesis and guide clinical management.

**Objectives:** To identify phenotypic clusters of IgG4-RD that may differentiate clinically meaningful subgroups using an unbiased method.

**Methods:** The study cohort consisted of 493 IgG4-RD subjects diagnosed by 76 IgG4-RD specialists from North America, South America, Europe, and Asia. For each case, investigators included details regarding age at disease onset and diagnosis, race/ethnicity, organ involvement, biopsy findings, and lab results. We performed latent class analysis (LCA) using SAS procedure PROC LCA to identify subgroups representing distinct patterns of organ involvement by IgG4-RD (figure 1). We fitted LCA models with 2–5 subgroups and chose the best model based on Akaike information criteria and adjusted Bayesian information criterion. The posterior probability of subgroup (cluster) membership for all cases was determined and cases were assigned to the cluster in which they had the highest probability of membership. We compared the distribution of organ involvement and other baseline features between clusters using Chi square tests and analysis of variance, where appropriate.

**Results:** Of the 493 IgG4-RD subjects, 65% were male, 40% were Caucasian, 45% were Asian, and 12% were Hispanic. The mean age at diagnosis was 59.5 (±14.0) years. Using LCA, we identified four clusters of IgG4-RD (table 1), each of which accounted for between 19% and 32% of the cohort. Cluster 1

('Hepatobiliary') included 158 (32%) patients characterised by hepatobiliary involvement. Cluster 2 ('Orbital') included 88 (19%) patients characterised by orbital and/or sinus disease. Cluster 3 ('Mikulicz') included 109 (22%) patients who had features of classic Mikulicz (dacryoadenitis plus major salivary gland involvement), often accompanied by renal and lung disease. Cluster 4 ('Retroperitoneal Fibrosis (RPF)') included 138 (28%) patients with RPF and/or aortic involvement. The clusters differed significantly with regard to age at symptom onset ( $p<0.001$ ), gender and race distribution ( $p<0.001$ ), serum IgG4 concentration ( $p=0.02$ ), and presence of hypocomplementemia ( $p<0.001$ ). In contrast to the other clusters, cluster 2 ('Orbital') included a majority of female patients who tended to be younger. Cluster 3 ('Mikulicz') was characterised by the highest serum IgG4 concentrations and cluster 4 ('RPF') by the lowest. Hypocomplementemia, which occurred in only a minority of patients overall (9%), tended to segregate in cluster 3 ('Mikulicz'), a group in which renal disease was common.

Abstract OP0081 – Table 1

Variable (mean ±SD or median [IQR])	Cluster 1	Cluster 2	Cluster 3	Cluster 4	P-Value
Sample Size	158 (32%)	88 (19%)	109 (22%)	138 (28%)	
Organ Involvement	Hepatobiliary	Orbital - Sinusitis	Mikulicz - Renal - Lung	RPF - Aorta	
Male	79%	35%	52%	72%	<0.0001
Age at Diagnosis	62 (12.8)	56 (14.1)	60.1 (12.9)	58.3 (14.5)	0.008
Age at Symptom Onset	61.2 (13.0)	53.3 (14.5)	57.7 (13.9)	56.5 (15.7)	0.0004
Diagnostic Delay	0.87 (1.7)	2.7 (3.7)	2.5 (3.8)	1.9 (3.9)	<0.001
Race/Ethnicity					
White	46%	35%	19%	53%	<0.0001
Asian	39%	52%	51%	31%	
Hispanic	10%	9%	20%	9%	
Number of Organs	2.2 (1.0)	2.3 (1.3)	5.0 (1.9)	2.3 (1.3)	<0.0001
IgG4 (mg/dL) Concentration	325 (160, 667)	334.5 (169.8, 943)	809 (300, 1365)	216 (85, 640)	0.02
Hypocomplementemia	5%	5%	20%	6%	<0.0001

**Conclusions:** Using an unbiased method, we identified four phenotypic clusters of IgG4-RD patients. In addition to the differences in organ involvement, clusters were distinguished by age at diagnosis as well as race/ethnicity and gender distribution, serum IgG4 concentrations, and frequency of hypocomplementemia. These clusters may identify patients with IgG4-RD resulting from different risk factors or exposures and those likely to respond differently to treatment.

**Disclosure of Interest:** None declared

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### OP0082 APREMILAST FOR BEHÇET'S SYNDROME: A PHASE III RANDOMISED, PLACEBO-CONTROLLED, DOUBLE-BLIND STUDY (RELIEF)

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**Background:** Oral ulcers (OU) are the most common sign of Behçet's syndrome (BS) and are observed in nearly every patient. Due to their severity and frequency of recurrence, OU can be disabling and have a substantial effect on quality of life. There is an unmet need for effective treatment for OU in BS. Apremilast (APR), an oral phosphodiesterase 4 inhibitor that modulates inflammatory pathways, demonstrated efficacy in the treatment of oral and genital ulcers of BS in a phase II study.

**Objectives:** Phase III study to further evaluate the efficacy and safety of APR for OU in BS pts with active OU previously treated with  $\geq 1$  medication.

**Methods:** In this phase III, multicenter, randomised, placebo (PBO)-controlled study, 207 eligible pts were randomised (1:1) to APR 30 mg BID (n=104) or PBO (n=103) for 12 weeks, followed by a 52 week active-treatment extension. Pts had active BS, with  $\geq 3$  OU at randomization or  $\geq 2$  OU at screening +randomization, without active major organ involvement. Primary endpoint was area under the curve (AUC) for total number of OU over 12 weeks. AUC reflects the change in the number of OU over time, accounting for the clinical characteristic that OU repeatedly remit and recur. Secondary endpoints assessed other measures of OU, including pain, OU resolution (OU-free), maintenance of OU resolution, and time to resolution. Effects on genital ulcers were also assessed. A prespecified hierarchical testing procedure was used for multiplicity adjustment.

**Results:** AUC for total number of OU over 12 weeks was statistically significantly lower in the APR group compared with the PBO group (table 1). This treatment effect is supported by statistically significant benefits in the APR group compared with PBO for secondary endpoints assessing OU, including pain, OU resolution, maintenance of OU resolution, and time to resolution. A numerically greater proportion of pts achieved resolution of genital ulcers at Week 12 in the APR group compared with PBO.



The incidence of treatment-emergent adverse events (AEs) was comparable between APR and PBO during the PBO-controlled period (78.8% vs 71.8%, respectively). Serious AEs were observed in 3 APR pts (migraine, oral ulcer flare, genital ulcer, arthralgia, soft tissue injury) and 4 PBO pts (diarrhoea, genital and fungal infections, oral ulcer flare, acne, acute febrile neutrophilic dermatosis, erythema multiforme).

Endpoints	P Value	Adjusted Treatment Difference (or HR)	APR vs. PBO (LS Mean, Median Time or %)
AUC for the number of OU from baseline through Week 12	<0.0001	-92.6	129.5 vs 222.1
Change from baseline in the pain of OU as measured by VAS at Week 12	<0.0001	-24.8	-40.7 vs -15.9
Proportion of subjects achieving OU resolution by Week 6 who remain OU free for ≥6 additional weeks (maintenance of OU resolution)	<0.0001	25.1%	29.8% vs 4.9%
Time to OU resolution, during the PBO-Controlled Treatment Phase	<0.0001	HR = 2.400	Median time in weeks: 2.1 vs 8.1
Proportion of subjects achieving resolution of OU at Week 12	<0.0001	30.6%	52.9% vs 22.3%
Proportion of subjects achieving resolution of genital ulcers at Week 12 for subjects who had genital ulcers at baseline	0.1100	28.4%	70.6% vs 41.2%

**Conclusions:** APR effectively reduced the number and pain of OU, improved time to oral ulcer resolution, and maintained the resolution of OU, the most common manifestation of BS. Favourable treatment effects were also observed for genital ulcer resolution. The safety profile was consistent with the known safety profile of APR.

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### OP0083 TEMPORAL TRENDS AND MORTALITY OF HOSPITALISED PATIENTS WITH ADULT ONSET STILL'S DISEASE: A NATIONWIDE ESTIMATE

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**Background:** There is a dearth of epidemiological studies on Adult Onset Still's Disease (AOSD). Majority of studies are from single centres or are regional. The largest AOSD epidemiological study till date describes 512 patients.<sup>1</sup>

**Objectives:** To describe the demographics, complications, mortality and trends of hospitalised patients with AOSD in United States. Also, to understand the factors associated with mortality in these patients.

**Methods:** All adult (>18 years) hospitalised patients between 2009 and 2013 from a nationwide inpatient sample (NIS) database were captured. AOSD patients were identified using the ICD-9 code 714.2. Patients also coded for Rheumatoid Arthritis, Lupus, Myositis, Polymyalgia Rheumatica, Ankylosing Spondylosis and Psoriatic Arthritis were excluded. This was done in order to capture patients with strictly AOSD. NIS is the largest all-payer inpatient care database in the United States with approximately 8 million hospitalizations each year. Discharge weights were used to enable nationwide estimates. Descriptive statistics were represented as means/medians for continuous and as frequencies and percentages for categorical variables. A survey weighted logistic regression model was used to describe the associations with in-hospital death.

**Results:** Between 2009 and 2013, 5,820 AOSD patients were hospitalised (table 1). AOSD patients had a mean age of 53.6 (SE - 0.61) years, 3817 (65.6%) were females. The racial/ethnic distribution showed that 56% white, 15% African American, 11.7% Hispanic and 3% Asian patients were affected. Over the years, the number of white patients that are hospitalised seems to have increased. 37.6% were hospitalised in urban teaching hospitals. 100 (1.7%) of patients developed Macrophage Activating Syndrome (MAS). 66 (1.1%) patients had disseminated intravascular coagulation (DIC) and 25 (0.4%) had thrombotic thrombocytopenic purpura (TTP). Mean length of stay was 6.9 days. There were 154 inpatient deaths in 5 years (mortality 2.6%). The patients who died in the hospital had a higher mean age of 62.4 (SE- 3.1) years, had a higher proportion of Asians

(13.9%) and had increased number of comorbid conditions. Asians had 6.4 times the risk of in-hospital death compared to Whites. The risk for in-hospital death is 30 times higher if a AOSD patient had concurrent DIC.

**Abstract OP0083 – Table 1 AOSD characteristics**

Variables, n (%) / Mean (SD) when specified	2009 n = 846	2010 n = 995	2011 n = 1434	2012 n = 1380	2013 n = 1265	Total N = 5820
Age in Years, Mean (SE)	53.6 (1.3)	52.3 (1.6)	54.9 (1.2)	52.8 (1.2)	53.9 (1.1)	53.6 (0.6)
Female	320 (38.1%)	645 (64.9%)	952 (66.2%)	870 (63.1%)	990 (78.4%)	3817 (65.6%)
Race						
White	437 (51.4%)	555 (55.8%)	819 (57.1%)	750 (53.4%)	730 (57.7%)	3291 (56.4%)
Black	117 (13.9%)	168 (16.9%)	243 (16.9%)	230 (16.3%)	163 (12.9%)	874 (15.0%)
Hispanic	96 (11.3%)	110 (11.0%)	141 (9.9%)	120 (8.7%)	205 (16.2%)	673 (11.5%)
Asian	25 (3.0%)	47 (4.7%)	29 (2.0%)	25 (1.8%)	50 (3.9%)	176 (3.0%)
Native American + Others	21 (2.5%)	20 (2.0%)	79 (5.5%)	80 (5.8%)	38 (3.0%)	238 (4.1%)
Missing values	150 (17.7%)	125 (12.6%)	122 (8.5%)	115 (8.3%)	80 (6.3%)	591 (10.2%)
Insurance						
Medicare	311 (36.7%)	318 (31.9%)	539 (37.6%)	525 (37.9%)	570 (44.9%)	2333 (40.2%)
Medicaid	104 (12.3%)	157 (15.7%)	170 (11.9%)	145 (10.5%)	160 (12.6%)	736 (12.6%)
Private including HMO	311 (36.7%)	371 (37.1%)	474 (33.3%)	475 (34.4%)	375 (29.6%)	2040 (35.2%)
Self-pay	60 (7.1%)	79 (7.9%)	95 (6.6%)	85 (6.1%)	80 (6.3%)	399 (6.8%)
No charge/other	20 (2.4%)	49 (4.9%)	96 (6.7%)	50 (3.6%)	75 (5.9%)	292 (5.0%)
Length of stay (days), Mean (SE)	6.1 (0.5)	6.7 (1.1)	7.0 (1.1)	6.6 (0.4)	6.3 (0.4)	6.9 (0.3)
Total Charges in USD, Mean (SE)	533,152 (2404)	525,501 (3024)	529,833 (2450)	532,080 (2590)	512,347 (2137)	510,887 (858)
Median household income						
\$1-\$1099	305 (34.2%)	274 (27.7%)	234 (16.3%)	340 (24.6%)	315 (24.9%)	1469 (24.4%)
\$1900-\$4299	217 (25.7%)	221 (22.3%)	213 (14.9%)	235 (16.9%)	318 (24.9%)	1262 (21.7%)
\$48000-\$62999	166 (19.6%)	275 (27.7%)	370 (26.1%)	326 (23.6%)	305 (24.1%)	1443 (24.8%)
\$63000+	236 (27.9%)	188 (18.9%)	498 (34.7%)	335 (24.2%)	315 (24.9%)	1972 (33.9%)
Setting of the hospital						
Small	51 (6.0%)	70 (7.0%)	123 (8.5%)	175 (12.7%)	140 (11.1%)	565 (9.7%)
Medium	169 (20.0%)	150 (15.0%)	270 (19.0%)	305 (22.1%)	270 (21.3%)	1333 (22.9%)
Large	341 (40.3%)	384 (38.5%)	462 (32.6%)	640 (46.4%)	610 (48.2%)	2438 (41.9%)
Missing values	285 (33.7%)	375 (37.7%)	620 (43.2%)	160 (11.5%)	345 (27.3%)	1685 (29.0%)
Location/teaching status of hospital						
Rural	60 (7.1%)	83 (8.3%)	88 (6.2%)	65 (4.7%)	100 (7.9%)	496 (8.5%)
Urban non-teaching	233 (27.8%)	240 (24.2%)	379 (26.4%)	345 (24.9%)	340 (26.9%)	1537 (26.4%)
Urban teaching	247 (29.1%)	284 (28.5%)	347 (24.2%)	720 (51.8%)	580 (45.8%)	2278 (39.3%)
Missing values	235 (27.9%)	375 (37.7%)	620 (43.2%)	160 (11.5%)	345 (27.3%)	1685 (29.0%)
Table 2: Factors associated with In-Hospital Death						
Variable	Odds ratio (95% CI)				p-value	
Age	1.03 (0.99-1.06)				0.154	
Female	1.32 (0.5-2.49)				0.619	
Race						
White	Reference					
Asian	6.39 (1.77-23.1)				0.005	
Black, Hispanic and Others	0.84 (0.26-2.75)				0.772	
Number of Chronic conditions	1.20 (1.05-1.37)				0.006	
Median Household income						
\$1-\$1099	Reference					
\$1900-\$4299	1.36 (0.41-4.29)				0.596	
\$48000-\$62999	0.95 (0.36-2.57)				0.858	
\$63000+	2.57 (0.57-11.62)				0.222	
Disseminated Intra-vascular Coagulation	29.69 (5.5-160.4)				<0.001	

**Conclusions:** In hospitalised American AOSD patients, the average age was higher than previously described in cross sectional studies. This may indicate an ageing population with a higher number of comorbidities that justify hospitalisation. More patients were in large or urban teaching hospitals compared to small or rural hospitals. In-hospital death was associated with increased comorbid conditions and was significantly higher among Asians and patients with DIC. To our knowledge, this is the largest epidemiological study of AOSD.

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### OP0084 SERUM FIBROBLAST GROWTH FACTOR 2 IS A USEFUL BIOMARKER TO DISTINGUISH ADULT ONSET STILL DISEASE FROM SEPSIS

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**Background:** The precise cytokine networks in the serum of individuals with adult onset still disease (AOSD) that are associated with its pathogenesis have been unknown. Serum levels of interleukin (IL)-1β, IL-6 and IL-18 have been reported as useful serum biomarkers for diagnosis and disease evaluation among AOSD patients,<sup>1,2</sup> but these cytokines are also elevated in other inflammatory diseases including severe infection.



**Objectives:** We attempted to identify specific biomarkers to distinguish AOSD from sepsis.

**Methods:** We measured serum levels of 45 cytokines in 66 AOSD patients, 17 sepsis patients and 133 age-matched controls by multi-suspension cytokine array. Japan College of Rheumatology-certified rheumatologists diagnosed with AOSD based on the Yamaguchi criteria. Cytokines were ranked by their importance by a multivariate classification algorithm. We performed a logistic regression analysis to determine specific biomarkers for discriminating AOSD from sepsis patients. To identify specific molecular networks, we performed a cluster analysis of each cytokine.

**Results:** Serum fibroblast growth factor 2 (FGF-2), vascular endothelial growth factor (VEGF), granulocyte-colony stimulating factor (G-CSF), and IL-18 levels were significantly elevated in the AOSD group versus the sepsis group. Multivariate classification algorithms followed by a logistic regression analysis revealed that the measurement FGF-2 distinguished AOSD patients from sepsis patients with the highest accuracy (cut-off value=28.5 pg/mL, sensitivity 100%, specificity 88.2%, accuracy 96.7%).

Abstract OP0084 – Table 1

variables (AOSD vs sepsis)	sensitivity	specificity	accuracy	AUC	AIC
FGF-2	1.000	0.882	0.967	0.972	24.50
IL-18	0.930	0.824	0.900	0.895	50.90
G-CSF	0.837	0.706	0.800	0.721	75.30
FGF-2 + IL-18	0.977	0.941	0.967	0.986	21.70

**Conclusions:** We have demonstrated that FGF-2 can be the best biomarker for differential diagnosis between AOSD and sepsis based on the measurement of multiple cytokines. Although the differential diagnosis between rheumatic diseases and infectious conditions is a great challenge in clinical practice, these findings help to improve the diagnostic performance of AOSD in daily practice.

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OP0085

#### SAFETY OF LONG-TERM (UP TO 6 YEARS) CANAKINUMAB THERAPY (<2, 2–<4 AND 4–<8MG/KG) IN PATIENTS AGED <4 TO 65 YEARS FROM BETA-CONFIDENT REGISTRY

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**Background:** The  $\beta$ -confident registry (NCT01213641), a multicenter, long-term (6 years; yrs), prospective, observational study has demonstrated the safety and effectiveness of canakinumab (CAN) in real life CAPS patients (pts) according to their phenotypes.<sup>1</sup> Here we report long-term safety of CAN in pts with CAPS and other autoinflammatory syndromes, enrolled in the  $\beta$ -confident registry, according to their age and dose administered.

**Objectives:** To monitor the long-term safety of different CAN doses (<2, 2–<4 and 4–<8 mg/kg) across different age groups (<4 to 65 years) in pts with CAPS and other autoinflammatory syndromes.

**Methods:** Cumulative safety data were reported as exposure adjusted incidence rate per 100 pt-years (IR/pyr) from the enrollment of the first pt (November 2009) until end of study (December 2015). Pts were followed up for at least 1 year. The protocol did not mandate any visits or procedures. All observed and reported AEs and SAEs were recorded for the following age groups:<4-, 4–<12-, 12–<18-, 18–<65 and  $\geq$ 65 years.

**Results:** Of the 285 pts enrolled, 21% (n=60) discontinued the study mainly due to loss of follow-up (35%, n=21) followed by AEs (10%, n=6), poor efficacy (8%, n=5) and pt preference (3%, n=2). In total, 1114 AEs and 155 SAEs were reported in 223 pts (110.7 IR/100 pyr) and 83 pts (15.4 IR/100 pyr), respectively. Exposure adjusted incidence rate of AEs (IR/100 pyr) among pts in the <4 and 4–<12 year age group, were lowest in the pts who received <2 mg/kg dose (130.3 and 59.7, respectively) compared to pts who received 2–<4 mg/kg (450.8 and 169.6, respectively) and 4–<8 mg/kg (121.5 and 90.0, respectively) CAN dose. In pts

aged 12–<18 years, IR/100 pyr were lowest in pts who received 2–<4 mg/kg dose (118.2) compared to pts who received <2 mg/kg (169.6) and 4–<8 mg/kg (139.4) CAN dose. Similarly, in the 18–<65 year age group, IR/100 pyr were lowest in pts who received <2 mg/kg dose (93.1) compared to pts who received 2–<4 mg/kg (100.7) and 4–<8 mg/kg (154.4) CAN dose. In the  $\geq$ 65 year age group, IR/100 pyr decreased with increase in dose (<2 mg/kg: 26, 2–<4 mg/kg: 17). Overall, 5, 13, 19, 84 and 7 SAEs were reported in <4-, 4–<12-, 12–<8-, 18–<65 and  $\geq$ 65 year age groups, respectively. One death (metastatic rectal adenocarcinoma in a 76-yr-old MWS patient) was reported.

**Conclusions:** The  $\beta$ -confident registry is the largest CAPS cohort documented in a registry. In general, incidence of adverse events in each dose group increased with age (<4–<65 years). However, no meaningful pattern of AEs was observed with increased dose for each age group. Long-term treatment with canakinumab demonstrated favourable safety profile which was similar to that reported earlier<sup>2</sup> and is well tolerated in CAPS patients aged <4 to 65 years.

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OP0086

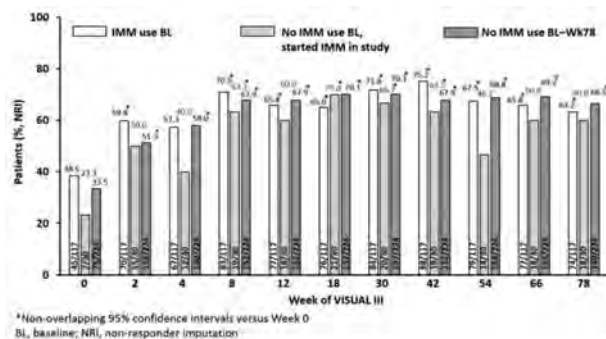
#### LONG-TERM EFFICACY AND SAFETY OF ADALIMUMAB BY IMMUNOSUPPRESSANT USE IN PATIENTS WITH NON-INFECTIOUS UVEITIS IN THE VISUAL III TRIAL

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**Objectives:** To evaluate the long-term safety and efficacy of adalimumab in patients with non-infectious intermediate, posterior, or panuveitis, by immunosuppressant (IMM) use.

**Methods:** Adult patients who completed or had a treatment failure in the VISUAL III trials were eligible to enter the Phase III open-label extension study, VISUAL III. Patients received adalimumab 40 mg every other week in VISUAL III, and interim follow-up data were collected through Weeks 0 to 78. Efficacy measures assessed included proportion of patients with: no active inflammatory lesions in both eyes; anterior chamber (AC) cell grade  $\leq$ 0.5 + in both eyes; vitreous haze (VH) grade  $\leq$ 0.5 + in both eyes; quiescence (defined as no active inflammatory lesions AND AC cell grade  $\leq$ 0.5 + AND VH grade  $\leq$ 0.5+); and steroid-free quiescence. Mean steroid dose and mean best corrected visual acuity (BCVA) were also assessed. Missing data were imputed using non-responder imputation for categorical endpoints, last observation carried forward for continuous variables, and as-observed for steroid dose. Efficacy was analysed by IMM (methotrexate, cyclosporine, mycophenolate mofetil, or azathioprine) use. Adverse events (AEs) were reported from first adalimumab dose in VISUAL III through interim cut-off date of Oct 31, 2016, with analysis by IMM use.

**Results:** Of 371 patients included in the intent-to-treat analysis, 117 (31.5%) were using IMM at VISUAL III baseline (BL) and 30 (8.1%) started IMM during VISUAL III. The proportion of patients with quiescence improved over time irrespective of IMM use; compared with Week 0, 95% confidence intervals were non-overlapping at most time points (figure 1). Numeric improvements were achieved in steroid-free quiescence, steroid dose reduction, and BCVA, with no difference by IMM use. No new safety signals were detected through 130 weeks of treatment and AE rates were generally consistent with previous VISUAL trials; some AEs, notably serious infections and malignancies, were slightly higher with concomitant IMM use.



**Abstract OP0086 – Figure 1.** proportion of patients in quiescence by IMM use in VISUAL III

**Conclusions:** Exploratory analyses from the VISUAL III trial demonstrated that efficacy in adalimumab-treated patients was sustained or improved through 78 weeks of treatment, irrespective of IMM use. AE rates were consistent with previous VISUAL trials, although numerically higher rates for a subset of AEs were observed in patients taking IMM.

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OP0087

### INCREASED RISK OF ISCHAEMIC HEART DISEASE AND MORTALITY AMONG FMF PATIENTS – PERSPECTIVE FROM A BIG DATABASE

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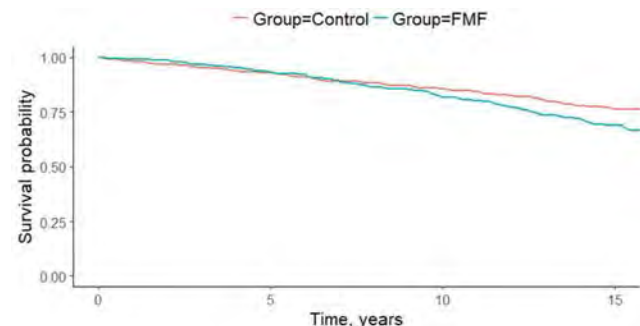
**Background:** Familial Mediterranean fever (FMF) is a systemic autoinflammatory monogenic disease. It has been previously reported that FMF patients are prone to develop ischaemic heart disease (IHD),<sup>1,2</sup> mostly due to increased inflammatory activity and endothelial dysfunction.<sup>3,4</sup> However, large-scale information regarding the extent and prognosis of IHD among FMF patients is lacking.

**Objectives:** To check whether an association exists between FMF and IHD, and to assess the long-term prognostic significance of IHD among FMF patients using a big data registry with a 15 year follow-up period.

**Methods:** Utilising the medical records of Clalit Health Services, the largest HMO in Israel, we extracted a cohort of FMF patients along with their age-and-sex matched controls. Dates of registration in the medical records of FMF, IHD and death, as well as anthropometric information and medical comorbidities were extracted from the database. To compare the distribution of variables across the cohort strata, univariate analysis was performed using Chi-square and student t-test. Multivariate analysis using a logistic regression model was used to find variables associated with IHD. Survival analysis using Cox proportional hazards method and a log-rank test was performed to find variables associated with increased risk of all-cause mortality.

**Results:** The cohort included 7,670 FMF patients and 7670 age-and-sex matched controls. The mean age of both groups was 39.1, and both consisted 50.1% females. IHD was observed among 491 FMF patients (6.4%) vs 375 controls (4.89%),  $p < 0.001$ . In multivariate logistic regression, FMF was found to be

independently associated with a diagnosis of IHD (OR 1.44, 95% CI: 1.21 to 1.72). After over 15 years of follow-up, 345 (4.5%) of FMF patients had died, compared to 271 (3.53%) of the controls ( $p < 0.001$ ). In multivariate survival analysis, both FMF and IHD were found to be significantly associated with increased risk to all-cause mortality (HR 1.29, 95% CI: 1.10 to 1.53 and HR 1.57, 95% CI: 1.29 to 1.9, respectively).



**Conclusions:** IHD is associated with worse prognosis among FMF patients compared to controls. Proper screening methods are recommended to assess whether early identification and treatment may improve life expectancy.

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OP0088

### IMMUNE-RELATED ADVERSE EVENTS OF CANCER IMMUNOTHERAPY – WHEN INFLAMMATORY SIDE EFFECTS ARE ASSOCIATED WITH SURVIVAL: A SINGLE-CENTRE PROSPECTIVE COHORT STUDY

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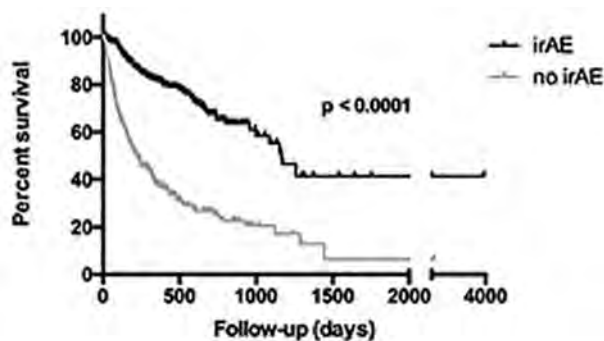
**Background:** Immune checkpoint inhibitors (ICI) represent a new standard of care for the treatment of selected advanced cancers and are still being investigated in many other tumour types. By enhancing the T-cell activation, a unique spectrum of inflammatory side effects has emerged, also known as immune-related adverse events (irAEs), including various well-described rheumatic manifestations. Data regarding the association between irAEs and patient outcomes are conflicting.

**Objectives:** To evaluate the incidence and characteristics of irAEs in patients receiving ICI, as well as the correlation with tumour response and patient survival.

**Methods:** This was a single-centre prospective observational study including all cancer patients receiving ICIs. The occurrence of irAEs, tumour response and patient outcomes were assessed on a regular basis. Overall survival has been considered from the start of ICI.

**Results:** From May 2015 to September 2017, 636 patients (70% male, mean age 64 years) have been included in this cohort while receiving anti PD-1 (n=435), anti PD-L1 (n=66) or anti CTLA-4 (n=3) as single agent or as sequential (n=100) or combined (n=32) therapies. Cancer types were mainly melanoma (n=293), non-small cell lung cancer (n=150) and renal carcinoma (n=83). Overall, 274/633 patients (43%) experienced irAEs, either 1 irAE (n=162), 2 irAEs (n=78) or  $\geq 3$  irAEs (n=34), with a median exposure time of 52 days<sup>30-31</sup> for the first irAE. Dermatological irAEs were by far the most frequent (n=160), followed by digestive

(n=80), endocrine irAEs (n=67), rheumatic (n=49) and pulmonary irAEs (n=17). So far, evaluation of tumour response was available for 551 patients, including 190 responders (complete response n=36 and partial response n=154), 192 patients with stable disease and 169 with progressive disease. 122/189 responders (65%) and 107/192 with stable disease (56%) experienced at least one irAE while reported only in 40/169 non responders (24%). Patients experiencing at least one irAE had an increased overall survival (median of 1169 days versus 224 days,  $p < 0.0001$ , figure 1), without statistical difference according to organ system. Of note, there was also no statistical difference regarding tumour response or irAEs occurrence among the 9.4% of patients with preexisting inflammatory or autoimmune disease (60/636).



Abstract OP0088 – Figure 1. Overall survival according to irAE occurrence

**Conclusions:** Although irAE occurrence is not required for treatment benefit, it strongly associates with overall survival. Optimal multidisciplinary management of irAEs, including rheumatologists when needed, is worthwhile to maintain beneficial responses.

**Disclosure of Interest:** None declared

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WEDNESDAY, 13 JUNE 2018:

## New driving molecules in systemic sclerosis

### OP0089 ABATACEPT IS EFFECTIVE IN EXPERIMENTAL DIGESTIVE AND LUNG TISSUE FIBROSIS

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**Background:** Cytotoxic T-lymphocyte associated molecule-4 (CTLA-4) is an immunoregulatory membrane receptor resulting in the down-regulation of T-cell responses. A previous report showed that abatacept (CTLA4-Ig) prevented and induced regression of inflammation-driven dermal fibrosis in two different mouse models of systemic sclerosis (SSc).<sup>1</sup>

**Objectives:** We aimed to assess the effects of abatacept in two complementary mouse models reflecting digestive involvement, lung fibrosis and pulmonary hypertension (PH), mimicking severe SSc organ damage.

**Methods:** Abatacept was given in the chronic graft-versus-host disease (cGvHD) mouse model, characterised by digestive involvement, and in the Fra-2 mouse model which is characterised by non-specific interstitial pneumonia and pulmonary vascular remodelling leading to PH. Mice were treated by intraperitoneal injections of abatacept (1 mg/mL in the cGvHD model for 6 weeks; 1 mg/mL or 10 mg/mL in the Fra-2 mouse model for 4 weeks) or human IgG1 (100 mg) used as a negative control.

**Results:** In the cGvHD model, treatment of allogeneically mice with abatacept led to a significant reduction of alanine aminotransferase (24%,  $p=0.014$ ) and aspartate aminotransferase levels (61%,  $p<0.001$ ). Pathological analysis of colon revealed decreased inflammatory infiltrates and destruction of crypts in allogeneically mice receiving abatacept.

When assessed by chest micro-CT imaging, Fra-2 mice treated with abatacept displayed a 12% decrease in lung density (10 mg/ml,  $p=0.037$ ) as well as an increase in functional residual capacity as compared to IgG1-treated mice (16% for 1 mg/ml,  $p=0.001$  and 14% for 10 mg/ml,  $p=0.005$ ).

Consistent with these results, abatacept 10 mg/L decreased histological fibrosis score (Ashcroft score) as well as hydroxyproline content by 79% ( $p=0.009$ ) and 31% ( $p=0.044$ ) respectively, as compared to IgG1-treated mice.

Treatment with abatacept 10 mg/mL markedly reduced protein levels in the lesional lungs of Fra-2 mice of the fibrogenic markers MCP1 by 79% ( $p=0.043$ ) and osteopontin by 87% ( $p=0.039$ ). Levels of TGF- $\beta$  were also reduced with abatacept (61% for 1 mg/mL,  $p=0.037$  and 69% for 10 mg/mL,  $p=0.013$ ). Further, abatacept decreased M1 and M2 macrophages infiltration as well as T-cell proliferation in the lesional lungs of Fra-2 mice.

Upon treatment with abatacept a reduction of right ventricular systolic pressure ( $28.1 \pm 1.5$  mmHg vs  $36.0 \pm 5.1$  mmHg,  $p=0.037$  for 10 mg/mL) and right ventricular hypertrophy ( $0.29 \pm 0.01$  vs  $0.33 \pm 0.010$ ,  $p=0.037$  and  $29 \pm 0.01$  vs  $0.33 \pm 0.01$  for 10 mg/mL,  $p=0.037$ ) was observed compared to IgG1-treated mice. Consistent with these findings, abatacept 10 mg/mL was associated with significant decrease in percent medial wall thickness and numbers of muscularized distal pulmonary arteries.

**Conclusions:** We demonstrate that treatment with abatacept improves digestive involvement, prevents lung fibrosis and attenuates PH in SSc pre-clinical mice models. These findings suggest that abatacept might be an appealing therapeutic approach for severe internal organ involvement in SSc beyond its already demonstrated effects on skin fibrosis.

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**Disclosure of Interest:** None declared

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### OP0090 MITOCHONDRIAL DNA MUTATIONS AND RESPIRATORY CHAIN DYSFUNCTION IN LUNG FIBROSIS OF SYSTEMIC SCLEROSIS

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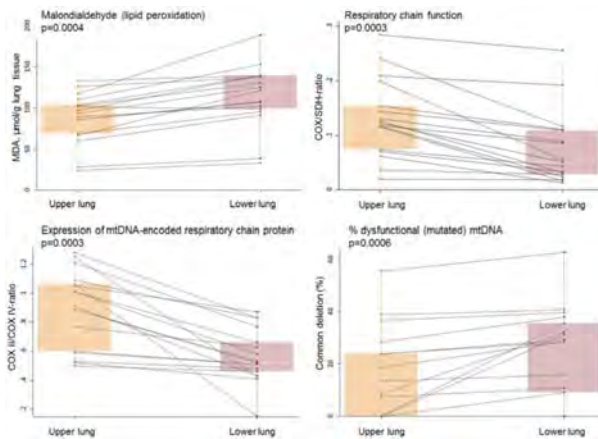
**Background:** Recent data have implemented reactive oxygen species (ROS) in the etiology of interstitial lung disease (ILD) in systemic sclerosis.

**Objectives:** To investigate a role of large-scale somatically acquired mutations in mitochondrial DNA (mtDNA) and consecutive respiratory chain dysfunction as a trigger of ROS formation and lung fibrosis.

**Methods:** Lung biopsies from patients with idiopathic interstitial pneumonitis and systemic sclerosis (n=31) were analysed for mitochondrial functions and compared with biopsies from 13 healthy controls (HC). From 17 patients we had simultaneous biopsies from the upper and lower lung.

**Results:** Malondialdehyde as a marker of ROS formation was increased in ILD ( $p=0.007$ ). The median proportion of mtDNA containing the pathogenic common deletion was 22.5% in ILD patients, compared to 0% in HC. This translated into a 3.8-fold diminishment of mtDNA-encoded cytochrome c-oxidase (COX2), but not nucleus-encoded (COX4) respiratory chain subunits in ILD compared to controls ( $p<0.0001$ ) and a 33% diminishment of mtDNA-encoded cytochrome c-oxidase activity ( $p=0.001$  vs controls). In all patients, the more fibrotic lower lungs had significantly more malondialdehyde ( $p=0.0004$ ), mtDNA deletions ( $p=0.0006$ ), and cytochrome c-oxidase dysfunction ( $p=0.0003$ ) than the less-fibrotic upper lung counterparts. Conversely, lower lungs had significantly less ( $p=0.0003$ ) mtDNA-encoded COX2 subunits in comparison to non-mtDNA-encoded COX4 subunits (figure 1). There was no association of any mitochondrial parameter with smoking status or age, and no difference between biopsies from patients with systemic sclerosis and non-specific interstitial pneumonitis.





**Abstract OP0090 – Figure 1.** Mitochondrial parameters in lung biopsies simultaneously obtained in both, upper and lower lungs, of patients with fibrotic lungs. Lines connect values of the same patients.

**Conclusions:** Our data support a role of mtDNA-mutations and consecutive respiratory chain dysfunction as a trigger and perpetuator of ROS formation in both, idiopathic interstitial pneumonitis and ILD of patients with systemic sclerosis.

**Disclosure of Interest:** None declared

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#### OP0091 CXCL10/CXCL11 SERUM MEASUREMENT AS POTENTIAL PREDICTOR OF SYSTEMIC SCLEROSIS

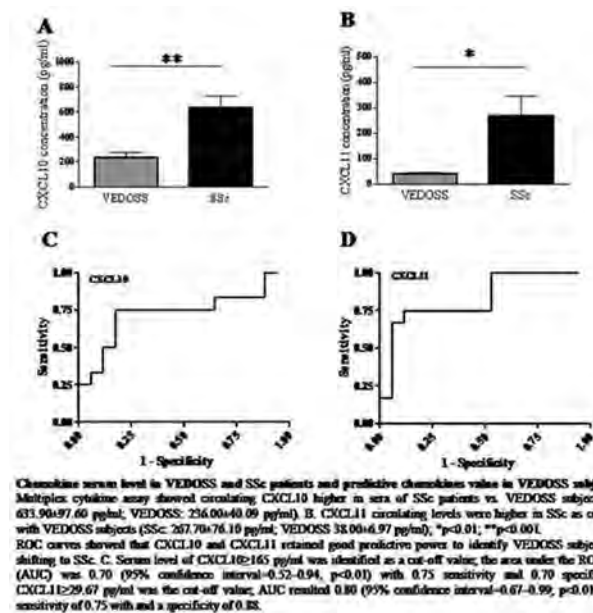
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**Background:** Systemic sclerosis (SSc), amongst autoimmune rheumatic disorders, shows a heterogeneous and unpredictable course from stable/mild involvement to progressive/late stage, when irreversible multiorgan fibrosis occurs.<sup>1</sup> Early SSc diagnosis remains a clinical challenge; a delay in diagnosis leads, in turn, to therapy delay and more severe patient disability.<sup>2-3</sup> Earliest vascular immune-mediated alterations are critical in SSc, which, indeed, has been referred to as a 'vascular' disease.<sup>4</sup> Recognition of biomarker(s) involved in earliest vascular derangements might represent a clinical tool potentially useful for therapeutic approach. Blood level of chemokines IFN $\gamma$ -inducible protein 10 (IP-10/CXCL10) and IFN-inducible T cell alpha chemoattractant (I-TAC/CXCL11), both involved in endothelial dysfunction, has been shown to associate with worse SSc prognosis.<sup>5,6</sup>

**Objectives:** To investigate possible modifications of circulating CXCL10/CXCL11 in the shift from very early diagnosis of SSc (VEDOSS), when vasculopathy and fibrosis are still at very low degree, to definite SSc. Associations between chemokines and capillaroscopic pattern, autoantibody positivity were evaluated.

**Methods:** Multiplexed luminex technology was used to analyse CXCL10/CXCL11 in total 62 sera, 34 from VEDOSS and 28 from SSc patients, fulfilling the new ACR/EULAR 2013 classification criteria; none of the subjects were treated for SSc. Within VEDOSS group, we selected 29 sera of subjects with follow up (40.67 $\pm$ 5.46 months) and, for each patient of this subcohort, chemokine levels were assessed at follow up (T1) and compared with basal level (T0). Appropriate tests were used for sample distribution and statistical analysis.

**Results:** Serum CXCL10/CXCL11 were significantly lower in all VEDOSS (CXCL10: 236.00 $\pm$ 40.09 pg/ml; CXCL11: 38.00 $\pm$ 6.97 pg/ml) vs all SSc sera (CXCL10: 633.90 $\pm$ 97.60 pg/ml; CXCL11: 267.70 $\pm$ 76.10 pg/ml; p<0.001 and p<0.01, respectively). Moreover, in VEDOSS subcohort, basal chemokine values (T0) were significantly higher (p<0.001) in sera of subjects who subsequently shifted to SSc (CXCL10: 237.34 $\pm$ 27.34 pg/ml; CXCL11: 45.12 $\pm$ 7.18 pg/ml) vs subjects not developing SSc (CXCL10: 140.06 $\pm$ 16.17 pg/ml; CXCL11: 20.17 $\pm$ 4.06 pg/ml). Sera analysed at follow up (T1) showed a significant increase of both chemokines vs T0 values only in patients who developed SSc (CXCL10: 536.18 $\pm$ 54.98 pg/ml; CXCL11: 250.21 $\pm$ 86.53 pg/ml; p<0.001). CXCL10/CXCL11 retained significant predictive values for SSc development with 165 pg/ml and 29.67 pg/ml cut-off values, respectively, as shown by receiver operating characteristic (ROC) analysis. Significant correlation of CXCL10/CXCL11 with nailfold capillaroscopic pattern was observed.



Correlations	Rho ( $\rho$ )	P
CXCL10/CXCL11	0.6 (Pearson)	<0.0001
CXCL10/NVC	0.6 (Spearman)	<0.0001
CXCL11/NVC	0.5 (Spearman)	<0.001

Serum CXCL10 and CXCL11 concentrations also significantly correlated (Pearson's Rho  $\rho$  0.6; <0.0001) and correlated with capillaroscopic pattern (Spearman's  $\rho$  0.6 and 0.5, respectively; p<0.001 and p<0.0001). NVC=nailfold videocapillaroscopy

**Conclusions:** CXCL10/CXCL11 blood level measurement in VEDOSS patients potentially represents a noninvasive biomarker associated with vascular modifications – as shown by capillaroscopic pattern – predictive of SSc.

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**Disclosure of Interest:** None declared

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#### OP0092 DECREASED DICKKOPF-1 EXPRESSION IN CLINICALLY UNINVOLVED SKIN FROM PATIENTS WITH SYSTEMIC SCLEROSIS

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**Background:** Evidence suggests that the Wnt pathway is a critical mediator of the fibrotic process. The activity of the pathway is tightly regulated by several soluble inhibitors such as Dickkopf-1 (Dkk-1). We, among others, have previously shown that Dkk-1 is absent from scleroderma skin in sharp contrast to skin from healthy subjects where it is clearly expressed.<sup>1,2</sup>

**Objectives:** Up until now, Dkk-1 skin expression has only been assessed in established fibrosis, in biopsies obtained from clinically involved areas. We aimed to assess whether the striking lack of Dkk-1 skin expression is also evident in a)

clinically uninvolved skin from patients with SSc and b) very early disease at the puffy/edematous phase, prior to skin thickening.

**Methods:** Skin biopsies were obtained from a) 12 patients with SSc from lesional skin of the forearm, b) 5 patients with SSc from the upper back which was not affected clinically, c) 2 patients with systemic sclerosis (SSc) with very early disease (<12 months). These patients had puffy hands but no skin thickening; the biopsy was obtained from the distal part of the forearm, in close proximity to the edematous area d) 5 healthy subjects. Dkk-1 expression was immunohistochemically assessed using a mouse anti-human monoclonal antibody (R and D Systems) by a semi-quantitative method (high/moderate/weak/no expression).

**Results:** Healthy skin displayed a high Dkk-1 immunoreactivity in basal cells of the epidermis as well as in the fibroblasts of the dermis in sharp contrast to clinically involved scleroderma skin that displayed no Dkk-1 immunoreactivity. Clinically uninvolved skin was obtained from 5 patients with SSc (4 diffuse-1 limited) with a median age of 50<sup>46-72</sup> and disease duration of 6<sup>2-13</sup> years. In all 5 biopsies Dkk-1 was only moderately expressed in basal cells of the epidermis and dermal fibroblasts. Clinically uninvolved scleroderma skin could be differentiated by immunohistochemical means from both skin from healthy subjects (high Dkk-1 expression) and clinically involved scleroderma skin (no Dkk-1 expression). Skin from very early disease at the edematous phase, prior to skin thickening, displayed only a weak Dkk-1 immunoreactivity in basal cells of the epidermis as well as in the fibroblasts of the dermis.

**Conclusions:** The decrease in Dkk-1 expression in clinically uninvolved scleroderma skin substantiates previous evidence that the skin in SSc is universally affected underlying the systemic nature of the disease. The downregulation of Dkk-1 at the edematous phase of the disease indicates that the Wnt pathway is involved early in the disease process, prior to establishment of fibrosis a finding with potential pathogenetic implications

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**Disclosure of Interest:** None declared

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#### OP0093 LOW RUNX3 EXPRESSION ALTERS DENDRITIC CELL FUNCTION IN PATIENTS WITH SYSTEMIC SCLEROSIS AND CONTRIBUTES TO ENHANCED FIBROSIS

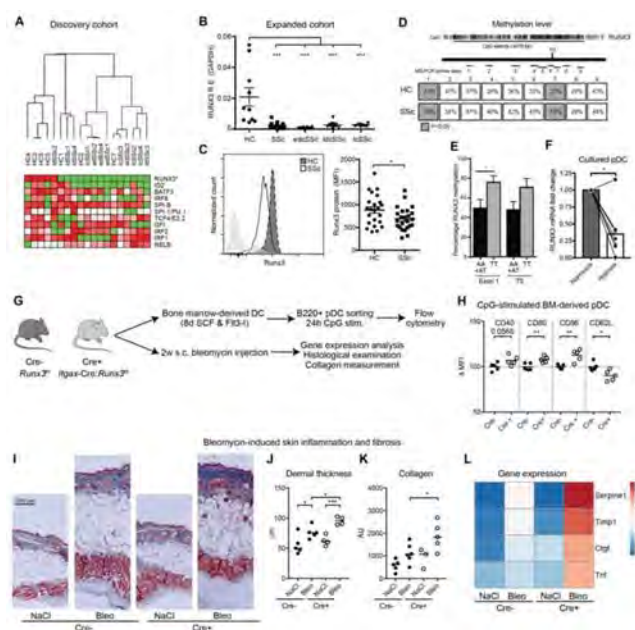
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**Background:** Systemic sclerosis (SSc) is an autoimmune disease with unknown pathogenesis manifested by inflammation, vasculopathy, and fibrosis in skin and internal organs. The type I IFN signature found in SSc propelled us to study plasmacytoid dendritic cells (pDCs) in this disease.

**Objectives:** To identify candidate pathways underlying pDC aberrancies in SSc and to validate its function on pDC biology.

**Methods:** PCR-based transcription factor profiling and methylation status analyses, SNP genotyping by sequencing, and flow cytometry analysis were performed in pDCs from healthy controls or SSc patients. pDCs were also cultured under hypoxia and RUNX3 levels were determined. To study Runx3 function in DCs, *Ilgax-Cre:Runx3<sup>fl/fl</sup>* mice were used in an *in vitro* functional assays and bleomycin-induced SSc skin inflammation and fibrosis model.

**Results:** Transcription factor RUNX3 was significantly downregulated in SSc pDCs on RNA and protein levels. A higher methylation status of the *RUNX3* gene correlated with RUNX3 gene expression level and disease susceptibility. After sequencing of the *RUNX3* promoter region, we identified a non-synonymous SNP rs6672420 associated with SSc and hypermethylation of *RUNX3*. Additionally, pDCs cultured in hypoxic conditions showed a significantly lower RUNX3 expression. Furthermore, mouse pDCs deficient of *Runx3* showed enhanced expression of co-stimulatory molecules upon CpG stimulation. Finally, in SSc bleomycin model, mice with DC-specific deletion of *Runx3* showed increased skin inflammation and fibrosis.



**Conclusions:** We found low RUNX3 expression in pDCs of SSc patients. The presence of a SNP and higher methylation status of RUNX3, and downregulation in hypoxic condition, suggest at least three pathways underlying the low RUNX3 expression observed in SSc pDCs. We demonstrate a detrimental role of RUNX3-obliterated DCs in a mouse SSc model further underscoring the role of pDCs in this disease. Further research is warranted to explore the potential therapeutic effect of RUNX3 targeting in fibrotic disease.

**Disclosure of Interest:** None declared

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#### OP0094 SLIT2/ROBO4 AXIS MAY CONTRIBUTE TO ANGIOGENESIS DISTURBANCE IN SYSTEMIC SCLEROSIS (SSc)

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**Background:** In SSc, vascular involvement is a primary event characterised by vascular tone dysfunction and microcirculatory abnormalities. Many classes of guidance molecules, such as members of the secreted glycoproteins Slits and their Roundabout (Robo) receptors, play critical roles in angiogenesis. Among these, Robo1 and Robo4 are expressed in endothelial cells. In particular, it has been demonstrated that the interaction of Slit2 with Robo1 promotes angiogenesis, while the Slit2/Robo4 axis inhibits VEGF-mediated endothelial cell migration and tube formation *in vitro* and neovascularization *in vivo*.

**Objectives:** To evaluate the possible involvement of the Slit/Robo axis in SSc defective angiogenesis.

**Methods:** Serum Slit2 levels were measured by ELISA in 78 SSc patients, 64 patients with a very early diagnosis of SSc (VEDOSS) and 74 age- and sex-matched healthy controls. Slit2, Robo1 and Robo4 protein expression was evaluated by immunofluorescence in skin biopsies from 15 SSc patients and 10 controls. Slit2 and Robo4 expression in dermal microvascular endothelial cells isolated from 5 SSc patients (SSc-MVECs) and 5 healthy controls (H-MVECs) was analysed by quantitative real-time PCR, Western blot and immunocytochemistry. Proliferation, wound healing and capillary-like tube formation were assessed in H-MVECs challenged with recombinant human (rh) Slit2 or SSc sera (n=6) in the presence/absence of an anti-Slit2 blocking antibody, as well as in SSc-MVECs treated with anti-Slit2 antibody or Robo4 siRNA.

**Results:** Circulating Slit2 levels were significantly increased in either SSc (median 11.12 ng/ml, IQR 8.02–16.25 ng/ml) or VEDOSS (median 11.27 ng/ml, IQR 8.46–18.60 ng/ml) compared with healthy controls (median 8.79 ng/ml, IQR

6.68–12.13 ng/ml) ( $p=0.002$  and  $p=0.001$ , respectively). Serum Slit2 was elevated in SSc patients irrespective of the nailfold videocapillaroscopy (NVC) pattern or the presence/absence of digital ulcers. Interestingly, differences in serum Slit2 levels were found between VEDOSS patients with early/active NVC pattern and controls ( $p<0.0005$ ), while Slit2 concentrations were similar in VEDOSS with normal NVC and controls. In SSc, Slit2 and Robo4 expression was higher in clinically affected skin and cultured MVECs in respect to controls. No difference was found in Robo1 expression. Cell viability, wound healing capacity and capillary-like tube formation in H-MVECs were all significantly reduced after challenge with rh Slit2 or SSc sera. These inhibitory effects were significantly attenuated when SSc sera were preincubated with anti-Slit2 blocking antibody. Cell viability, wound healing capacity and *in vitro* angiogenesis were severely compromised in SSc-MVECs and could be significantly ameliorated by Slit2 neutralisation or Robo4 gene silencing.

**Conclusions:** In SSc, increased circulating levels of Slit2 and activation of the Slit2/Robo4 antiangiogenic axis may contribute to peripheral microangiopathy since the very early phase of the disease.

**Disclosure of Interest:** None declared

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#### OP0095 SOLUBLE CD163 AS A POTENTIAL BIOMARKER IN SYSTEMIC SCLEROSIS

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**Background:** Recent accumulating evidences indicate a crucial role of macrophage lineage in the pathogenesis of fibrotic diseases including systemic sclerosis (SSc). CD163 is a surface marker expressed by M2 macrophages that accumulate during the healing phase of acute inflammation. It is actively released from the plasma membrane in response to certain inflammatory stimuli and enters the circulation in its soluble form (sCD163).

**Objectives:** In this study, we aimed to evaluate the performance of serum and urinary sCD163 concentrations as possible biomarker in SSc.

**Methods:** Urine and serum samples were obtained from SSc patients, fulfilling the 2013 ACR/EULAR classification criteria for SSc, and age- and sex-matched controls. Serum and urinary sCD163 concentrations were measured by commercially available ELISA kit (R and D systems) and evaluated for their significance as potential biomarkers. Statistical analysis was carried out using Mann-Whitney U test and the relationship between parameters was statistically examined by Spearman's rank test.

**Results:** Two hundred and three SSc patients were included, 163 (80%) were female, with a mean  $\pm$ standard deviation (SD) age of  $59\pm 13$  years and a mean  $\pm$ SD disease duration of  $12\pm 9$  years. Eighty-one (41%) patients had diffuse cutaneous SSc and mean  $\pm$ SD mRSS was  $6.6\pm 7.7$ . Lung fibrosis on imaging was observed in 33% of the patients, 7% had pulmonary arterial hypertension, 44% had history of digital ulcers and 41% were taking immunosuppressive therapy. Control group consisted of 47 age- and sex-matched patients with non-inflammatory diseases, being osteoporosis for the very large majority.

Serum sCD163 levels were significantly higher in SSc patients compared with controls (mean  $\pm$ SD:  $529\pm 251$  vs  $385.1\pm 153$  ng/ml;  $p<0.001$ ). Urinary sCD163 concentrations in SSc patients were also higher than those in controls, but this did not reach significance ( $236.9\pm 498$  vs  $176.2\pm 173$  ng/mg uCr;  $p=0.580$ ). When looking at the subsets according to skin disease or disease duration, no difference could be identified. Furthermore, when the organ involvements were investigated, no subpopulation could be identified as having higher concentrations.

**Conclusions:** To our knowledge this is the first evaluation of both serum and urinary sCD163 levels in SSc. Our results show a significant difference for sera values that should be prioritised for further studies as compared to urinary concentrations conversely to what has been described in lupus. Our results further support that the M2 macrophages/CD163 signalling system may play a role in the pathogenesis of SSc. However, further studies are required to address the exact role of CD163 in the pathogenesis of SSc and to determine whether it could help in the risk-stratification of the patients in this heterogeneous disease.

**Disclosure of Interest:** None declared

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WEDNESDAY, 13 JUNE 2018

## A rollercoaster from bench to bedside and back again: paediatric rheumatology in the 21st century...

#### OP0096 ADENO-ASSOCIATED VIRUS VECTOR-MEDIATED INTERLEUKIN-10 INDUCTION PREVENTS VASCULAR INFLAMMATION IN A MURINE MODEL OF KAWASAKI DISEASE

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**Background:** Kawasaki disease (KD), which is a common paediatric heart disease, is characterised by coronary vasculitis and subsequently aneurysm formation. Although the administration of intravenous immunoglobulin (IVIG) is effective for reducing aneurysm formation, approximately 10%–20% of patients are resistant to this therapy. Therefore, additional therapeutic approaches for treating the IVIG-resistant patients need to be developed.

*Candida albicans* water-soluble fraction (CAWS)-induced vasculitis on coronary arteries and root of aorta is a frequently used murine model of KD. It has been considered that C-type lectin receptor Dectin-2 recognises CAWS. Recent studies showed CAWS-resistant strains of mice have higher serum IL-10 levels, which suggested that IL-10 might negatively regulate the development of CAWS-induced vasculitis.

**Objectives:** The aim of the study is to investigate the therapeutic effect of IL-10 in CAWS-induced vasculitis and elucidate the underlying pathogenesis of KD.

**Methods:** To induce the expression of IL-10 *in vivo*, Adeno-associated virus (AAV) vectors encoding IL-10 were injected into DBA/2 mice. After the induction of IL-10, the mice were treated intraperitoneally with CAWS to induce vasculitis. Cardiac functions by echocardiography, inflammation and fibrosis by histological analyses, gene expression of inflammatory cytokines and fibrosis-related factors in the heart, and infiltrating cells by flow cytometry were assessed to evaluate the effects of IL-10.

For *in vitro* study, bone marrow-derived macrophages (BMDM) were stimulated with CAWS in presence or absence of IL-10. TNF- $\alpha$  and IL-6 produced by the BMDM and Dectin-2 expressions on the BMDM were assessed.

**Results:** AAV-mediated induction of IL-10 significantly attenuated CAWS-induced cardiac functions (%FS and LVEDD). Histological analyses revealed that IL-10 markedly attenuated the vascular inflammation and fibrosis in the aortic root and coronary artery. Accordingly, increased gene expressions of inflammatory cytokines or fibrosis-related factors in the heart of CAWS-treated mice were significantly reduced by IL-10. The predominant infiltrating inflammatory cells in vascular walls were Dectin-2<sup>+</sup>CD11b<sup>+</sup> macrophages, and they were also decreased by IL-10.

Furthermore, we showed GM-CSF induced Dectin-2 expression on BMDM, and the GM-CSF-treated BMDM produced TNF- $\alpha$  and IL-6 upon CAWS-stimulation. IL-10 had no effect on the Dectin-2 expression but significantly inhibited the production of the cytokines. Finally, the AAV-mediated induction of IL-10 prevented the expression of TNF- $\alpha$  and IL-6 in the heart of the mice treated with CAWS for 24 hours (at the early phase), but not GM-CSF and Dectin-2. These results suggest that GM-CSF mediates CAWS-induced vasculitis via Dectin-2 upregulation and IL-10 inhibits the downstream of GM-CSF and Dectin-2 signalling.

**Conclusions:** Our study has shown that IL-10 may have therapeutic application in the prevention of coronary vasculitis and aneurysm formation, and provided new insights into the mechanism underlying the pathogenesis of KD.

**Disclosure of Interest:** None declared

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#### OP0097 STIMULATED MONOCYTE-DERIVED MACROPHAGES FROM PATIENTS WITH ENTHESITIS RELATED ARTHRITIS SECRETE HIGHER LEVELS OF IL23 AND LOWER LEVELS OF INTERFERON GAMMA COMPARED TO HEALTHY CONTROLS

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**Background:** Enthesitis related arthritis (ERA) is the subtype of juvenile idiopathic arthritis most closely related to adult spondyloarthritis (SpA).



Macrophages, the IL23/IL17 pathway and dysregulation of IFN $\gamma$  are strongly implicated in the pathogenesis of adult SpA but remain relatively unexplored in ERA.

**Objectives:** To compare levels of IL23 and IFN $\gamma$  produced by monocyte-derived macrophages (MDMs) in the presence of lipopolysaccharide (LPS) from patients with ERA compared to healthy controls. The effect of clinical features such as enthesitis, peripheral and axial arthritis on IL23 and IFN $\gamma$  expression was also studied.

**Methods:** Peripheral blood monocytes from 39 patients (68% HLA B27 positive, 84% male, median age 16 years 4 months, median disease duration 3 years 10 months) and 21 age and gender-matched healthy controls were differentiated *in vitro* with macrophage-colony stimulating factor in to macrophages. Differentiated cells were treated with IFN $\gamma$  for 24 hours to upregulate HLA B after which the cells were washed and stimulated with LPS (50 ng/mL). IL23 and IFN $\gamma$  expression from the cell culture supernatants were measured by ELISA and luminex assay respectively.

**Results:** IL23 expression was significantly higher in patients with ERA [median 53580 pg/mL (IQR 35735–83945 pg/mL) vs 32110 pg/mL (IQR 13745–48235 pg/mL),  $p=0.01$ ], particularly in patients who were HLA B27 positive [median 64650 pg/mL (IQR 36400–99650 pg/mL),  $p=0.0067$ ]. IL23 was not significantly different between patients with and without peripheral arthritis or axial arthritis. However, patients who had active enthesitis (assessed clinically or on scan within 6 months of the sample) had significantly higher IL23 expression compared to patients without enthesitis [median 75905 pg/mL (IQR 36728–99425 pg/mL) vs 38485 pg/mL (IQR 29923–63725 pg/mL),  $p=0.014$ ] and healthy controls [ $p=0.0017$ ]. Interestingly, patients who had both HLA B27 and active enthesitis had even higher levels of IL23 [median 79380 pg/mL (IQR 36540–103200 pg/mL),  $p=0.0018$ ]. Conversely, levels of IFN $\gamma$  were found to be lower from MDMs of patients with ERA compared to healthy controls, at baseline [median 3985 pg/mL (IQR 2820–6849 pg/mL) vs 6305 pg/mL (IQR 3938–8744 pg/mL),  $p=0.0054$ ] and after LPS stimulation [median 9146 pg/mL (IQR 7438–11255 pg/mL) vs 11693 pg/mL (IQR 9481–13435 pg/mL),  $p=0.013$ ]. No difference was found between patients who were HLA B27 positive and negative, although there was a trend towards lower levels of IFN $\gamma$  in patients with enthesitis, this was not statistically significant.

**Conclusions:** IL23 expression is significantly higher from stimulated MDMs of patients with ERA compared to healthy controls, especially in HLA B27 positive patients with active enthesitis. This suggests a role for IL23 in the pathogenesis of ERA and supports the hypothesis that this sub-population of patients might benefit from IL23 blockade. Interestingly, IFN $\gamma$  expression is lower in patients with ERA. Dysregulation of IFN $\gamma$  has been shown to cause upregulation of the IL23/17 pathway in animal models<sup>1</sup> and thus may also contribute to the pathogenesis of ERA.

#### REFERENCE:

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#### OP0098 CLINICAL PICTURE AND SPECTRUM OF CONDITIONS ASSOCIATED WITH NLRP12 GENE MUTATIONS

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**Background:** NLRP12-related autoinflammatory disease (NLRP12-AID) is an exceptionally rare autosomal-dominant disorder caused by germ-line mutations in NLRP12 gene. Very few patients with NLRP12-AD have been identified worldwide, therefore there is a scarcity of data on phenotypic presentation of this syndrome.

**Objectives:** Here we provide evidence that NLRP12-AID may have clinical manifestations characteristic for primary immune deficiencies (PID).

**Methods:** 246 children with periodic fever (PF) of unknown origin were subjects to the next generation sequencing (NGS) analysis; 213 of these patients had signs of primary immunodeficiency (PID) manifested by recurrent infections, while 33 kids had isolated PF. The NGS panel was composed of 302 genes implicated in PID and/or AID.

**Results:** NLRP12 variants were detected in 20 cases (see the table 1). Median age of first AID-related fever episode was 12 months, ranging from 2 months to 13 years. Increased association with immune-mediated diseases ( $n=15$ , 75%) was observed. Nine patients demonstrated increased susceptibility to infection and two children suffered from Crohn's disease. Administration of short courses of

NSAID or corticosteroids resulted in resolution of the disease flare. In one severe case canakinumab (anti-interleukine-1 $\beta$  antibody) was successfully used.

**Abstract OP0098 – Table 1**

NLRP12 mutation	ID, sex	NLRP12 related symptoms	Comorbid disease
p.H304Y	PK, f	PF, 1d/week	CVID, AIHA, pancytopenia, S, ILD Severe CD, food and drug allergy
	RI, m	Cyclic vomiting with hCRP since newborn	
	AA, f	Permanent aphthous stomatitis, PFAPA, AP	
Asn715>Ser	ZV, m	PF (infections?) PF 5–7d/month	Congenital red-cell aplasia, AIHA, S, LA
	KA, m	with LA, redness, eye pain	
	VM, m		
p.F402L	GA, f	PF	Chronic posterior scleritis
	GE, m	PF	
Thr861Ser	CA, m	PF (infections)	Episodes of severe respiratory infection Severe CD, S
	KS, m	Episodic AP, diarrhoea	
Gln417Leu	AR, m	1d PF	Meningitis, septic shock, otitis,
	SK, m	Persistent fever	
Arg352Cys	DE, f	PF, S, A, AP, urticaria, growth delay,	Severe recurrent MAS, ILD
p.Ala57Ser	AK, m	Respiratory and intestinal infections with PF	Bacterial meningitis
p.Ala5Glu	HT, m	PFAPA-like syndrome headaches +eye pain	
p.Arg723Gln	BA, f	PF, A	
p.Val936Leu	GA, f	PF (infections?)	Recurrent purulent sinusitis w/o fever
p.Tyr246Cys	ES, f	FCAS, relapsed aseptic peritonitis	
p.Gly52Ser	KV, f	PF (infections?)	
p.R738fs	SD, m	1–4d of PF, cold-induced, 3–4/ year,	pneumonia, febrile seizures, brain oedema

Abbreviations: A-arthritis, ABA-abatacept, AIHA-autoimmune hemolytic anaemia, AP-abdominal pain, CD-Crohn's disease, CKB-canakinumab, CVID-common variable immunodeficiency, d-day, ILD-interstitial lung disease, LA-lymphadenopathy, PF-periodic fever, S-splenomegaly

**Conclusions:** Significant number of patients with genetically assigned diagnosis of NLRP12-AID have clinical features which close resemble PID. This phenotypic overlap may result in underdiagnosis of NLRP12-AID among patients with PID.

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**Disclosure of Interest:** None declared

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#### OP0099 REMISSION IN JIA CAN BE PREDICTED FROM ONE YEAR FOLLOWING DIAGNOSIS IN A UK MULTICENTRE INCEPTION COHORT

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**Background:** One of the primary aims for children and young people with JIA is remission. Early improvement in disease likely predicts greater chance of remission in the longer-term.

**Objectives:** To assess the association between change in disease activity over the first year of disease and later occurrence of remission.

**Methods:** Children and young people with oligoarticular, RF-negative or RF-positive polyarticular JIA recruited to the Childhood Arthritis Prospective Study prior to January 2014 were selected for analysis.

Two definitions of remission based on clinically inactive disease at two consecutive study follow-ups were explored: 1) Wallace's preliminary criteria and 2) the clinical Juvenile Arthritis Disease Activity Score in 10 joints (cJADAS10). Association between changes in JIA core outcome variables and pain over the first year of disease and later occurrence of remission were analysed using logistic regression models, adjusting additionally for age, gender, symptom duration and predictor value at presentation. Oligoarticular and polyarticular JIA were modelled separately. Multiple imputation accounted for missing data.

**Results:** A total of 1045 children were included. Of these, 70% were female and the majority had oligoarticular JIA (67%). The median age at presentation was 7 years (IQR 3, 11). Within three years, 25% achieved remission according to Wallace's criteria and 39% according to cJADAS10. More children with oligoarticular JIA achieved remission than those with polyarticular JIA (table 1).

Remission using Wallace's criteria was predicted in oligo and polyarthritis respectively by improvements in physician's global (OR: 3.1, 95% CI: 1.9 to 5.3; OR: 4.8, 95% CI: 1.4 to 16.7) and parental global (OR: 1.5, 95% CI: 1.2 to 1.8; OR: 1.4, 95% CI: 1.5 to 2.0). For oligoarthritis, additional predictors included improvement in active joint count (OR: 1.7, 95% CI: 1.0 to 2.3) and ESR (OR: 1.1, 95% CI: 1.0 to 1.2). Improvement in limited joint count also predicted remission in polyarticular JIA (OR: 1.2, 95% CI: 1.0 to 1.4) (table 1).

Remission using cJADAS10 was predicted in oligo and polyarthritis respectively by improvements in physician's global (OR: 2.1, 95% CI: 1.6 to 2.8; OR: 2.3, 95% CI: 1.5 to 3.6), parental global (OR: 1.9, 95% CI: 1.4 to 2.6; OR: 2.0, 95% CI: 1.3 to 3.0), active joint count (OR: 1.6, 95% CI: 1.1 to 2.2; OR: 1.3, 95% CI: 1.1 to 1.7), limited joint count (OR: 1.4, 95% CI: 1.1 to 1.9; OR: 1.1, 95% CI: 1.3 to 2.3), CHAQ (OR: 2.2, 95% CI: 1.4 to 3.3; OR: 2.7, 95% CI: 1.5 to 5.0) and pain (OR: 1.2, 95% CI: 1.1 to 1.4; OR: 1.3, 95% CI: 1.1 to 1.5) (table 1).

**Abstract OP0099** – Table 1 Achievement and predictors for remission according to wallace's preliminary criteria and the cJADAS10

	Oligoarthritis (n=704)		Polyarthritis (n=341)	
	Wallace's preliminary criteria	cJADAS10	Wallace's preliminary criteria	cJADAS10
Follow-up	Percent remission			
2 years	19	35	15	21
3 years	19	35	15	22
Ever	27	45	20	28
Improvement over the first year in one unit of:	Odds ratios for ever remission (95% CI)			
Active joint count	1.7 (1.0, 2.3)	1.6 (1.1, 2.2)	1.4 (0.9, 2.0)	1.3 (1.1, 1.7)
Limited joint count	1.3 (0.58, 1.7)	1.4 (1.1, 1.9)	1.2 (1.0, 1.4)	1.1 (1.3, 2.3)
Physician global assessment (cm)	3.1 (1.9, 5.3)	2.1 (1.6, 2.8)	4.8 (1.4, 16.7)	2.3 (1.5, 3.6)
Parent global assessment (cm)	1.5 (1.2, 1.8)	1.9 (1.4, 2.6)	1.4 (1.5, 2.0)	2.0 (1.3, 3.0)
CHAQ	1.3 (0.8, 2.0)	2.2 (1.4, 3.3)	1.6 (0.9, 2.9)	2.7 (1.5, 5.0)
ESR (mm/hr)	1.1 (1.0, 1.2)	1.0 (1.0, 1.1)	1.1 (1.0, 1.2)	1.0 (1.0, 1.1)
Pain (cm)	1.1 (1.0, 1.1)	1.2 (1.1, 1.4)	1.1 (1.0, 1.3)	1.3 (1.1, 1.5)

cJADAS10: Clinical Juvenile Arthritis Disease Activity Score in 10 joints; CI: Confidence Interval; CHAQ: Childhood Health Assessment Questionnaire; ESR: Erythrocyte Sedimentation Rate

**Conclusions:** Both improvements in the physician's and parental global assessments over the first year of disease predict remission in JIA. However, improvements in function and pain predict higher odds of remission on the cJADAS10 but not Wallace's preliminary criteria. These factors may be helpful in predicting well-being but not a lack of inflammation.

**Disclosure of Interest:** None declared

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OP0100

### INCREASE IN DIRECT HEALTHCARE COSTS IN JUVENILE IDIOPATHIC ARTHRITIS OVER THE PAST 10 YEARS – RESULTS OF A HEALTH INSURANCE CLAIMS DATA ANALYSIS

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**Background:** Biological disease-modifying anti-rheumatic drugs (bDMARDs) are effective but expensive treatment options in juvenile idiopathic arthritis (JIA). The extent to which the healthcare costs of JIA have changed as a result of their increasing use has hardly been investigated.

**Objectives:** The aim of this study was to analyse resource utilisation and direct healthcare costs in patients with JIA since the introduction of treatment with biologic agents.

**Methods:** Using health insurance claims data in Germany, resource utilisation and direct healthcare costs of children and adolescents with a diagnosis of JIA (International Classification of Diseases, Tenth Revision, [ICD-10] code M08, M09.0, L40.5) between January 1, 2007 and December 31, 2016 were assessed. Direct healthcare costs comprised costs for outpatient care (i.e., visits to physicians, laboratory tests, emergency department visits, and outpatient hospital services), costs for inpatient care (i.e., hospital admissions), costs for pharmacotherapy and other treatment costs (i.e., non-physician visits [e.g., visits to physical therapists] and aids/adaptations).

**Results:** Data from 12 652 children and adolescents with a diagnosis of JIA were included in the analyses. Mean direct healthcare costs per patient increased by 33% from € 4577 in 2007 to € 6109 in 2016. Pharmacological treatment was the cost domain with the highest increase (table 1). This increase was almost entirely caused by an increasing prescription of bDMARDs (from 8.6% to 15.7%). Costs for inpatient care also increased, whereas other treatment costs slightly decreased.

Total costs per patient were calculated as the sum of the domains outpatient care, hospital admissions, pharmacotherapy and other treatment costs. bDMARDs, biological Disease-Modifying Anti-Rheumatic Drugs; csDMARDs, conventional synthetic Disease-Modifying Anti-Rheumatic Drugs.

\* excluding costs for pharmacotherapy.

**Conclusions:** Direct healthcare costs in JIA considerably increased over the past 10 years, mainly caused by an expanding use of biologic agents. The results also showed that the rise in costs for treatment with biologic agents has been at a plateau since 2014. The healthcare costs incurred must, of course, always be placed in the context of indirect and intangible costs and the long-term prognosis of patients.

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**Abstract OP0100** – Table 1. Mean direct healthcare costs (in euros) per patient per year.

	2007 n=1067	2008 n=1057	2009 n=1125	2010 n=1160	2011 n=1219	2012 n=1302	2013 n=1344	2014 n=1414	2015 n=1448	2016 n=1516
Outpatient care*	834	877	691	731	687	707	775	826	810	812
Hospital admissions*	1549	1602	1532	1559	1843	1878	2097	2028	1924	1749
Pharmacotherapy	1701	1791	2021	2021	2219	2346	2924	3264	3396	3131
csDMARDs	159	151	147	137	165	158	189	201	187	153
bDMARDs	964	1153	1424	1446	1653	1831	2250	2599	2557	2494
Glucocorticoids	9	8	8	7	7	7	8	13	9	6
Other treatment costs	492	469	412	438	434	437	424	449	417	417
Non-physician visits	353	340	307	332	314	317	312	323	312	279
Aids and adaptations	139	129	105	106	120	120	112	126	105	138
Total direct costs	4577	4739	4655	4749	5182	5367	6220	6566	6547	6109

OP0101

### EXPLORING PAIN AND THE IMPACT OF JIA ON ADOLESCENTS AND YOUNG ADULTS: A MIXED-METHODS STUDY

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**Background:** Young people with Juvenile Idiopathic Arthritis (JIA) have emphasised concerns about the extent to which factors beyond inflammation affect their daily lives, particularly with persistent pain, despite effective clinical management into adulthood. Pain experience and impact on daily life remains relatively unexplored in the adolescent and young adults (AYAs).

**Objectives:** This study aimed to: a) establish prevalence of current pain in AYAs with JIA, b) determine associations with pain intensity, and c) qualitatively explore perceived impact of JIA on daily life.

**Methods:** This cross-sectional mixed methods study recruited 85 JIA patients attending AYA Rheumatology clinics in London. It assessed pain intensity (APPT) as the primary outcome, with the following predictor variables: mood (HADS), illness perceptions (B-IPQ), fatigue (FACIT-F), functioning (WSAS), quality of life (MSK-HQ), demographics and disease activity. Analysis was conducted using Spearman's correlations and hierarchical multiple linear regression. Semi-structured interviews about the impact of JIA with a subset of 15 participants were conducted and analysed via inductive thematic analysis. Ethical/R and D approvals and informed consent were obtained.

**Results:** Participants completing the survey were predominantly female (68.2%), White British (65.9%), aged 16–25 (mean=19.63, SD=2.23), with Polyarticular (40%) the most common subtype, and 10.43 years mean disease duration (SD=5.16). Prevalence of current pain was 91.8%, with 37% reporting medium-to-severe pain. In interviews (66% female, 33% white British, mean age 19.92, mean disease duration 12 years), despite high prevalence, pain was only ranked fourth (6/15) as most impacting on daily life by those interviewed. The other top areas chosen were: fatigue (9/15), mood (8/15), social aspects (8/15), and impairments in functioning (5/15). Pain was reported in terms of impact on personal relationships (e.g. changes to mood linked to pain) and other restrictions preventing life as a 'normal' young person. In the survey, pain intensity was moderately associated with biological variables, e.g. active joints ( $r_s=0.27$ ), and strongly associated with psychological variables, e.g. depression and illness related distress ( $r_s=0.53$  and  $r_s=0.50$ ). Demographic and clinical variables (Step 1) explained 13.4% of variance in pain intensity. Adding distress, fatigue and functioning (Step 2) explained an additional 24.8%, and illness perceptions (Step 3) explained a further 30.4%. Identity and Consequences illness perceptions accounted for 70.5% of the association between active joints and pain.

**Conclusions:** Findings support an approach of the biopsychosocial model of pain in clinical practice. The impact of JIA occurs during active disease but also persist during remission, going beyond pain and inflammation. These impacts need to be monitored by healthcare

**Disclosure of Interest:** None declared

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OP0102

### PROLONGED IMAGE ACQUISITION TIME AFTER CONTRAST AGENT ADMINISTRATION RESULTS IN INCREASED SYNOVIAL THICKNESS ON POST-CONTRAST MRI OF JIA PATIENTS: STANDARDISATION IS KEY

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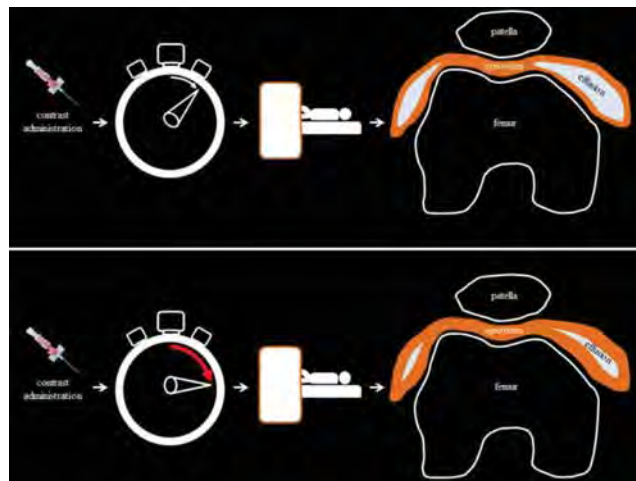
**Background:** Timing of acquisition of post-contrast MR images for the assessment of the synovial membrane is important: delayed acquisition can result in

contrast washout into synovial fluid.<sup>1</sup> Several authors demonstrated the importance of this timing using qualitative data (membrane appearance on MRI).<sup>1–4</sup> Nonetheless, there is no international consensus on timing of post-contrast images in arthritis, leading to acquisitions at 1 to 10 min after contrast injection.<sup>1–5</sup> This could result in incorrect measurement of synovial thickness and thus imprecise assessment of disease activity and over or under treatment of patients.

**Objectives:** To quantitatively measure and compare thickness of the synovial membrane on early and late post-contrast knee MRI in patients with juvenile idiopathic arthritis (JIA).

**Methods:** Prospectively collected dynamic contrast-enhanced T1 MRIs of children with JIA were used to measure synovial thickness at time point 1 (TP1), 1 min and TP2, 5 min after contrast administration. Written and verbal informed consent for participation in our IRB-approved study was obtained. Two experienced readers, who were blinded for the time point, independently measured synovial thickness on a predefined, marked location in the patellofemoral compartment on randomised images. The Wilcoxon test was used to compare the mean synovial thickness measurements from TP1 and TP2. Moreover, we studied the number of patients judged to have active synovial inflammation (synovium >2 mm) on both time points.

**Results:** Measured synovial thickness in 53 patients with JIA (median age 13.5 years, 58.6% female) increased with prolonged time-after-contrast (TP1 1.4 mm and TP2 1.5 mm,  $p<0.001$ ). Moreover, we found a 25% relative increase of patients with active synovial inflammation (synovial membrane >2 mm) when comparing the measurements at TP2 versus TP1.



**Conclusions:** Our study is the first to add quantitative data to the literature showing that synovial thickness as measured on post-contrast MRI increases with a prolonged interval between contrast administration and acquisition of the post-contrast images. Our data, together with previous studies<sup>1–4</sup> indicate that it is questionable whether one can reliably measure synovial thickness without standardisation of the interval between contrast administration and acquisition of post-contrast sequences. This could not only influence clinical interpretation and quantitative scoring in JIA, but possibly also impacts other rheumatologic diseases in which synovial thickness is quantified in scoring systems, such as rheumatoid arthritis and osteoarthritis.<sup>6,7</sup>

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**Disclosure of Interest:** None declared

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OP0103

### IDENTIFICATION OF OPTIMAL SUBCUTANEOUS DOSES OF TOCILIZUMAB IN CHILDREN WITH SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS

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**Background:** Efficacy and safety of intravenous (IV) tocilizumab (TCZ) were demonstrated in patients (pts) with systemic juvenile idiopathic arthritis (sJIA) in the phase 3 TENDER study<sup>1</sup> (WA18221). Study WA28118 (ClinicalTrials.gov, NCT01904292) investigated dosing regimens of subcutaneous (SC) TCZ in pts with sJIA by bridging to IV TCZ data to identify the optimal SC regimen.

**Objectives:** To characterise the pharmacokinetics (PK), pharmacodynamics (PD), and safety of TCZ SC in pts with sJIA; efficacy was an exploratory objective.

**Methods:** This phase 1b multicenter, open-label study evaluated PK, PD, and safety of TCZ SC in pts aged 1–17 years with sJIA and inadequate response to glucocorticoids and nonsteroidal anti-inflammatory drugs. Interim analysis (IA) was conducted after 24 pts had received TCZ SC for 14 weeks. Pts could be either TCZ-naive or switch from TCZ IV to SC at baseline. TCZ SC was administered for 52 weeks according to body weight: <30 kg, either 162 mg every 10 days (before IA) or 162 mg every 2 weeks (Q2W, after IA); ≥30 kg, 162 mg every week (QW).

**Results:** Among enrolled pts (n=51), 25 weighed <30 kg (8 before and 17 after IA) and 26 weighed ≥30 kg. Twenty-six pts (51%) were TCZ naive and 25 (49%) switched from TCZ IV. Median steady state C<sub>min</sub> was similar for pts <30 kg receiving TCZ 162 mg Q2W and those ≥30 kg receiving TCZ 162 mg QW, and the range largely overlapped (table 1). More than 95% (49/51) of pts treated with TCZ SC had model-computed steady state C<sub>min</sub> higher than the 5th percentile achieved with TCZ IV. Median and range of AUC<sub>2weeks</sub> were similar for both weight groups (table 1). Changes in interleukin-6, C-reactive protein, and erythrocyte sedimentation rate were similar for both weight groups. Most pts had ≥1 adverse event (AE; n=50; 98%). Injection site reactions (ISRs) occurred in 21 pts (41%); most were mild and none led to treatment interruption/withdrawal. AE rate was 1200.3/100 patient-years (PY) (909.3/100 PY excluding ISRs). The most common AEs were viral upper respiratory tract infection (13; 25.5%), neutropenia (13; 25.5%), and cough (12; 23.5%). Nine serious AEs occurred in 7 pts (13.7%; 19.3/100 PY); 5 were infections, all in the <30 kg group. Two deaths occurred, both in the <30 kg group. Median Juvenile Arthritis Disease Activity Score-71 improved (decreased) from baseline to week 52 for TCZ-naive pts (<30 kg, -13.9; ≥30 kg, -12.4) and was maintained or improved further for pts who switched from TCZ IV (<30 kg, -0.7; ≥30 kg -0.2).

Abstract OP0103 – Table 1

	TCZ SC (WA28118)		TCZ IV (WA18221)	
	<30 kg TCZ 162 mg Q2W n=25	≥30 kg TCZ 162 mg QW n=26	<30 kg TCZ 12 mg/kg Q2W n=46	≥30 kg TCZ 8 mg/kg Q2W n=43
Model-computed steady state PK parameters, median (range)				
C <sub>min</sub> µg/mL	64.2 (16.6-135.9)	72.4 (19.5-157.8)	65.9 (19.0-135.5)	70.7 (5.3-126.6)
C <sub>max</sub> µg/mL	126.6 (51.7-265.8)	89.8 (26.4-190.2)	274.4 (148.8-444.0)	253.0 (119.6-404.3)
AUC <sub>2weeks</sub> µg/mL·day	1298 (539-2792)	1154 (334-2370)	1734 (840-2712)	1631 (526-2779)

**Conclusions:** A PK-based strategy successfully bridged TCZ SC to TCZ IV in pts with sJIA. Dosing regimens of 162 mg Q2W in pts <30 kg and 162 mg QW in pts ≥30 kg provided adequate exposure to support efficacy comparable to that of TCZ IV. Except for ISRs, safety was consistent with the known safety profile of TCZ IV in sJIA.

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**Disclosure of Interest:** H. Brunner: None declared, N. Ruperto Consultant for: AbbVie, Amgen, Biogenidec, Alter, AstraZeneca, Baxalta Biosimilars, Biogenidec, Boehringer, BMS, Celgene, CrescendoBio, EMD, Speakers bureau: AbbVie, Amgen, Biogenidec, Alter, AstraZeneca, Baxalta Biosimilars, Biogenidec, Boehringer, BMS, Celgene, CrescendoBio, EMD, D. Lovell Grant/research support from: National Institutes of Health, NIAMS, Consultant for: Astra-Zeneca, Bristol Meyers Squibb, AbbVie, Pfizer, Roche, Novartis, UBC, Forest Research Institute, Horizon, Johnson and Johnson, Biogen, Takeda, Genentech, GlaxoSmithKline,

Boehringer Ingelheim, Celgene, Janssen, Speakers bureau: Genentech, I. Calvo-Penedes: None declared, G. Horneff: None declared, M. L. Gamir Gamir: None declared, M. Hufnagel: None declared, J. Hsu Employee of: Roche, M. Bao Employee of: Roche, W. Douglass Employee of: Roche, N. L. Mallalieu Employee of: Roche, C. Wells Shareholder of: Roche, Employee of: Roche, C. M. Mela Employee of: Roche, F. De Benedetti Grant/research support from: Novartis, Roche, Pfizer, SOBI, AbbVie, Novimmune, BMS, Sanofi

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WEDNESDAY, 13 JUNE 2018: Burning bones

OP0104

### ANTIBODIES AGAINST CARBAMYLATED PROTEINS ARE INVOLVED IN OSTEOCLASTOGENESIS BY INDUCING RANKL EXPRESSION IN OSTEOBLASTS IN VITRO

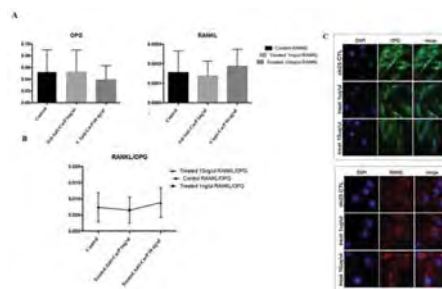
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**Background:** Citrullinated peptide are one of the main target of immune response in Rheumatoid Arthritis (RA) and antibodies to citrullinated peptides (ACPA) are involved in bone resorption. One of the target antigens – citrullinated vimentin – is expressed on the surface of osteoclast precursors where it can bind the antibodies starting the differentiation in mature osteoclast. Moreover, recent data demonstrated that serum levels of receptor activator of nuclear factor-κB ligand (RANKL) are higher in ACPA-positive RA patients. RANKL is the main osteoblast-derived cytokine inducing osteoclastogenesis. Antibodies directed against carbamylated proteins (Anti-CarP) have been recently described in RA patients with Rheumatoid Arthritis. The effect of anti-CarP on bone resorption has not been yet addressed.

**Objectives:** The aim of the study was to investigate *in vitro* the effect of anti-CarP on Osteoprotegerin (OPG) and RANK ligand (RANKL) production in osteoblast cultures.

**Methods:** Anti-CarP were investigated by ELISA in the sera of 88 RA patients using carbamylated fetal calf serum (CarFCS) and non-modified FCS as antigens. Anti-CarFCS were purified from the sera of 3 RA patients who tested highly positive for anti-CarP. Osteoblasts were isolated from the femoral head of 3 patients undergoing total hip arthroplasty and cultured in three different conditions – 1 ng/ml of anti-CarFCS, 10 ng/ml of anti-CarFCS or control medium for 4–6 days, until confluence. RNA was extracted from cell lysates and OPG and RANKL mRNA expression was analysed by Real-time PCR. Moreover, OPG and RANKL expression was investigated by immunofluorescence on treated and non-treated cells. Differences were determined either with two-way repeated measures analysis of variance (ANOVA) with Bonferroni's multiple comparison test, using Prism 5.0 software. A p value < 0.05 was considered significant.

**Results:** In osteoblast cultures, anti-CarFCS decreased the expression of OPG and increased the expression of RANKL in a dose-dependent manner, leading to an increase in RANKL/OPG ratio (figure 1A and 1B). The result was confirmed by the immunofluorescence analysis demonstrating the subcellular co-location of OPG and RANKL in osteoblast cultures (figure 1C).



Abstract OP0104 – Figure 1. Expression of mRNA for RANKL and OPG (A) and RANKL/OPG ratio (B) in osteoblast cultures treated with anti-CarFCS; sub-cellular location of RANKL and osteoprotegerin in osteoblasts' cultures (C).

**Conclusions:** The results of the study confirm that anti-CarFCS can be detected in nearly 40% of RA patients. The increase of RANKL/OPG ratio in the osteoblast cultures treated with anti-CarFCS suggests an effect of such autoantibodies on osteoclastogenesis and osteoclasts activity, supporting their possible involvement in the development of bone erosions.

**Disclosure of Interest:** None declared

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OP0105

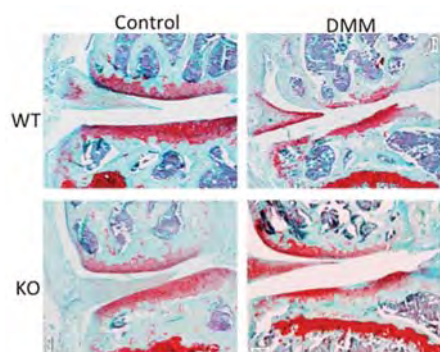
**ZCCHC6 DELETION DOWNREGULATES IL-6 AND REDUCES THE SEVERITY OF EXPERIMENTAL OSTEOARTHRITIS IN MICE**M.Y. Ansari, M.N. Khan, I. Ahmad, T.M. Haqqi. *Anatomy and Neurobiology, Northeast Ohio Medical University, Rootstown, USA*

**Background:** Osteoarthritis (OA) is the most common joint disease in elderly and is a major cause of disability. Currently no disease modifying agents exist to treat OA. ZCCHC6 (zinc-finger CCHC-domain containing protein 6) is a member of family of terminal uridylyltransferases (TUTs) and is known to carry out template independent addition of Uridine at the 3' ends of miRNAs. ZCCHC6 has been implicated in miRNA-mediated regulation of cytokine gene expression; however, the role of ZCCHC6 in the pathogenesis of OA is unknown.

**Objectives:** The aim of this study was to investigate the effect of ZCCHC6 deletion on proinflammatory cytokine, IL-6, expression in human and mouse chondrocytes and to study the role of ZCCHC6 in OA pathogenesis *in vivo* using Zcchc6<sup>-/-</sup> mice.

**Methods:** Human or mouse chondrocytes were prepared by sequential enzymatic digestion and treated with recombinant human or mouse IL-1 $\beta$  to mimic OA pathogenic conditions. Cytokine profiling was done using qPCR array and multiplex assay. IL-6 expression in chondrocytes was analysed by qPCR and immunoblotting/ELISA. IL-6 mRNA stability was determined by Actinomycin-D chase experiments. The 3'-uridylation of miRNAs was analysed by deep sequencing of small RNAs using Illumina MiSeq. ZCCHC6 and IL-6 expression in OA cartilage was analysed by immunohistochemistry. For *in vivo* studies, OA was induced by surgical destabilisation of medial meniscus (DMM) in the knee joints of mice. The severity of OA was assessed by safranin O/fast green staining followed by OARSI scoring.

**Results:** ZCCHC6 expression was upregulated in OA cartilage. Cytokine expression profiling in ZCCHC6 depleted human and Zcchc6<sup>-/-</sup> mouse chondrocytes revealed IL-6 as a major target of ZCCHC6. Depletion of ZCCHC6 expression in human chondrocytes resulted in decreased expression of IL-6 at mRNA and protein levels. ZCCHC6 depletion suppressed IL-1 $\beta$  induced expression of IL-6. Overexpression of ZCCHC6 in human chondrocytes resulted in increased expression of IL-6 in the presence or absence of IL-1 $\beta$ . Chondrocytes from Zcchc6<sup>-/-</sup> mice also showed decreased levels of IL-6 expression compared to Zcchc6<sup>+/+</sup>. Furthermore, overexpression of mouse Zcchc6 in Zcchc6<sup>-/-</sup> chondrocytes rescued IL-6 expression. IL-6 mRNA half-life was significantly reduced in Zcchc6<sup>-/-</sup> mouse chondrocytes and ZCCHC6 depleted human chondrocytes. Deep sequencing of small RNAs in ZCCHC6 depleted human chondrocytes showed reduced 3'-uridylation of IL-6 targeting miRNAs miR-26a/26b. Human chondrocytes transfected with miR-26a/26b mimic suppressed IL-6 expression, however, miR-26b mimic with additional 'UU' failed to suppress IL-6 expression. Zcchc6<sup>-/-</sup> mice expressed low levels of MMP13 and showed lesser matrix degradation in the joints with DMM surgery. Zcchc6<sup>-/-</sup> mice developed less severe OA as determined by safranin O/fast green staining followed by OARSI scoring. Synovitis was also decreased in the Zcchc6<sup>-/-</sup> mice DMM joints in comparison to Zcchc6<sup>+/+</sup> +DMM joints.



**Conclusions:** Our data demonstrate that ZCCHC6 is upregulated in OA cartilage and regulates IL-6 expression via miR-26b 3'-uridylation. These data identify a previously unknown function of ZCCHC6 in OA pathogenesis and identifies a potential therapeutic target for the management of OA.

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**Disclosure of Interest:** None declared

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WEDNESDAY, 13 JUNE 2018

**Delay in treatment and the role of health professionals**

OP0106

**WHO IS NOT REACHING REMISSION IN EARLY RA AND WHY? PREDICTORS FOR PERSISTENT DISEASE ACTIVITY IN THE FIRST YEAR DIFFER IN MEN AND WOMEN AND ARE RELATED TO LIFESTYLE AND TREATMENT**

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**Background:** Although early identification and aggressive treatment of RA improves outcomes, we have shown that 45% of early RA participants receiving guideline-based care do not achieve remission in the first year. Moreover, fewer women reached remission than men.

**Objectives:** To compare predictors of persistent disease activity (LDA/MDA/HAD) in the 1st year of RA treatment in men and women.

**Methods:** Sample included adults in CATCH (Canadian Early Arthritis Cohort) from 2007–2016 with active disease at baseline and  $\geq 12$  m F/U. Standardised visits included clinical assessments, questionnaires, and lab tests. Logistic regression with backward selection was used to identify predictors of failing to achieve remission (DAS28 <2.6) by 12 months among baseline sociodemographic and RA characteristics and patient reported outcomes.

**Results:** The sample included 1628 adults with classifiable RA, who were mostly female (72%) with a mean (SD) age of 55, (15) with 2 (2) comorbidities, and symptom duration of 6 (3) months. At enrollment, 95% had active disease (DAS28 MDA (42%); HDA (53%)), most were initially treated with csDMARDS (any 92%; MTX 75%). 46% of women and 38% of men did not reach remission by 12 months. Among women, multivariable results showed obesity more than doubled the likelihood of not achieving remission; other key predictors were minority status, lower education, and higher TJC and fatigue scores at baseline (table 1). In men, current smoking was associated with a 3.5 greater odds of not achieving remission in the first year; other predictors included older age, and higher pain. Not using MTX increased the likelihood of not achieving remission in women by 28% and men by 45%. Longer symptom duration and higher ESR were associated with not achieving remission in all. Factors not related to persistent disease activity included family history of RA, RF/ACPA status, erosions, SJC, HAQ and depressive symptoms at baseline.

Abstract OP0106 – Table 1

	Women	Men
N	1179	449
<b>Sociodemographics</b>		
Age (each 10 years)	1.04 (0.95, 1.14)	1.48 (1.22, 1.79)
Minority race	1.46 (1.07, 2.00)	Not selected
Education = high school	1.41 (1.09, 1.82)	Not selected
Comorbidities	1.12 (1.05, 1.21)	Not selected
Obese (BMI $\geq 30$ kg/m <sup>2</sup> )	2.06 (1.49, 2.83)	1.65 (0.95, 2.85)
Current smoking	Not selected	3.45 (2.06, 5.77)
<b>RA Characteristics</b>		
Symptom duration (month)	1.10 (1.05, 1.14)	1.15 (1.07, 1.24)
Family history of RA	Not selected	1.62 (0.95, 2.77)
RF+ or ACPA+	1.23 (0.87, 1.75)	Not selected
Erosions	Not selected	Not selected
MTX Use	0.72 (0.54, 0.95)	0.55 (0.33, 0.90)
Oral Steroids (Y vs N)	0.80 (0.60, 1.07)	1.45 (0.92, 2.27)
Parenteral Steroids (Y vs N)	Not selected	Not selected
ESR (mm/h)	1.01 (1.01, 1.02)	1.02 (1.01, 1.03)
Swollen Joint Count (28)	Not selected	Not selected
Tender Joint Count (28)	1.03 (1.01, 1.06)	Not selected
<b>Patient Reported Outcomes</b>		
High depressive symptoms	Not selected	Not selected
Pain (0-10)	Not selected	1.11 (1.03, 1.20)
HAQ-DI (0-3)	Not selected	Not selected
Fatigue (0-10)	1.05 (1.00, 1.09)	Not selected
<b>Fit Statistics</b>		
AIC	1519	535
BIC	1801	581
Area under the curve	0.69	0.74

**Conclusions:** In this large pan-Canadian cohort of early RA patients receiving guideline-based arthritis care, obesity in women and current smoking in men were the strongest predictors of not achieving remission in the first 12 months followed by non-use of MTX, higher baseline inflammation and longer symptom duration. Additional poor prognostic indicators in women included minority status, lower



education, and higher fatigue, whereas older age and greater pain were associated with persistent disease activity in men. Smoking cessation in men and weight reduction in women, and optimising MTX use may facilitate rapid reduction of inflammation, an essential goal of treatment in early RA.

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**Disclosure of Interest:** None declared

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THURSDAY, 14 JUNE 2018

## Fat and fatty acids: targets for therapy?\_\_\_\_\_

### OP0107 ADIPOCYTOKINES IMBALANCE IS ASSOCIATED WITH VASCULAR DAMAGE IN SYSTEMIC SCLEROSIS

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**Background:** Adipocytokines are implicated in the development of fibrosis, vasculopathy and immune abnormalities through a variety of biological effects, but their role in systemic sclerosis (SSc) is not fully investigated. Chemerin is implicated in chemotaxis of immune cells, in promoting angiogenesis and it is involved in inflammation. Adiponectin (APN) has metabolic actions and anti-inflammatory properties, while Leptin (LEP) mediates actions in endothelial cells, such as angiogenesis, vasodilation, NO production and upregulates various mediators of vascular inflammation.

**Objectives:** In this study we investigated Chemerin, LEP and APN levels in SSc patients according to disease subtypes and clinical characteristics.

**Methods:** Chemerin, LEP and APN levels were evaluated in 100 SSc patients and in sex, age and BMI matched healthy controls. Clinical and demographical characteristics were available for all patients.

**Results:** Chemerin, APN and LEP levels were lower in SSc patients compared to healthy controls (Chemerin: 58.7±27.6 ng/ml vs 74.0±29.0 ng/ml, p=0.004; LEP: 19.6±18.3 ng/ml vs 28.5±23.8 ng/ml, p=0.03, APN: 6.5±3.9 µg/ml vs 12.8±6.0 µg/ml, p<0.001)

Chemerin levels were lower in patients with anti-topoisomerase antibodies (50.2±22.7 ng/ml) respect to patients with other autoantibodies (64.6±29.7 ng/ml), p=0.018.

Regarding capillaroscopic damage, Chemerin levels were lower in patients with late pattern (44.8±18.9 ng/ml) compared to patients with early (64.3±28.5 ng/ml) and active pattern (71.7±29.9 ng/ml), p<0.001. APN levels inversely correlate with IL-6 levels (R=-0.4, p<0.001), while directly correlate with capillary density (R=0.3, p=0.03). Patients with avascular areas presented lower levels of APN (5.3±3.9 µg/ml) compared to patients without avascular areas (7.3±3.4 µg/ml), p=0.005. LEP levels directly correlate with vascular density on nailfold capillaroscopy (R=0.3, p=0.02), confirming the role of LEP in endothelial homeostasis. Furthermore, patients with avascular areas presented lower LEP levels (15.5±13.0 ng/ml) compared to patients without avascular areas (31.1±28.4 ng/ml), p=0.003. LEP levels were lower in patients with active digital ulcers (9.3±6.6 ng/ml), compared to patients without ulcers (9.3±6.6 ng/ml), p=0.01. The anti-inflammatory and endothelium protective role of APN emerged also when we considered the lung involvement: in fact patients with DLCO >50% presented higher levels of APN (7.0±3.9 µg/ml) compared to patients with DLCO <50% (5.8±3.8 µg/ml), p=0.05.

Considering the cardiopulmonary involvement, LEP levels inversely correlate with PAPs on echocardiography (R=-0.24, p=0.02). Finally LEP levels inversely correlate with skin score (R=-0.3, p=0.009) and patients with early disease presented lower LEP levels (15.1±13.2 ng/ml) compared to patients with long lasting disease (29.9±28.7 ng/ml), p=0.006.

**Conclusions:** Our data suggest an imbalance of the levels of adipocytokines in SSc, their down-regulation in patients with a more aggressive pattern on nailfold videocapillaroscopy and organ damage, suggesting a possible role of Chemerin, LEP and APN in the impaired angiogenesis and in the development of vasculopathy of SSc patients.

**Disclosure of Interest:** None declared

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### OP0108 DIET INDUCED METABOLIC CHANGES IN AN OSTEOARTHRITIS MOUSE MODEL

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**Background:** Adipose tissue is not only an energy depot, but also secretes bioactive factors such as adipokines. Several of these factors are known to regulate immune responses. Osteoarthritis (OA) is one of the most common joint diseases with obesity being a well known risk factor. Therefore, an obesity model (High-fat diet, HFD) was combined with an established model for OA (DMM, destabilisation of the medial meniscus) to evaluate the role of adipokines in this setting.

**Objectives:** This work evaluates the influence of different adipokines on OA progression and obesity comparing systemic vs local effects at different time points.

**Methods:** The study was performed in C57Bl/6 mice fed with HFD or ND (normal diet) prior to OA induction. Mice were sacrificed and analysed 4, 6 and 8 weeks after surgery. For systemic analysis, sera were evaluated for adipokines such as adiponectin, leptin and visfatin and inflammatory markers. Diet induced systemic changes were also analysed using a fatty liver score and evaluation of crown-like structures (CLS) in adipose tissue. OA progression was scored and quantified based on histological stainings of the joints (H/E, safranin O). Immunohistochemical stainings of the joints were performed to evaluate local distribution of adipokine positive cells and the respective cell types. Metabolic parameters were correlated to the local progression of OA.

**Results:** The numbers of CLS were significantly lower comparing HFD (0.2±0.1553, n=7) with ND (5.219±0.9831, n=8) in mice. Fatty-liver score was significantly higher in HFD compared to ND. OA induction was significant at every time-point vs healthy control and higher in HFD (e.g.: OA score at 6 weeks HFD 3.7 vs ND 1.4). In the OA groups, there was a positive correlation between bodyweight and OA score (r<sup>2</sup>=0.33). Correlation level of OA score with liver score or serum leptin level was low, even though leptin was significantly induced by HFD. However, DMM decreased leptin levels at all time points, independent from diet (e.g. 4 weeks: HFD healthy 18.4 ng/ml vs HFD DMM 3.7 ng/ml). The different parameters for metabolic changes (fatty liver score and bodyweight) were positively correlated with serum leptin level. HFD, DMM or the combination of both did not show significant effects on serum levels of adiponectin, visfatin or IL-6. Local adipokine secretion in the joints was independent from systemic metabolism parameters.

**Conclusions:** Our data show that similar to observations in humans, OA is deteriorated by HFD which correlates mainly with the bodyweight and to a lower extend with metabolic changes induced by obesity. Local adipokine expression was especially detectable in the damaged meniscus showing increased amounts of adiponectin and leptin producing cells. Interestingly, local adipokine expression was independent from systemic adipokine levels.

**Disclosure of Interest:** None declared

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## Biologics in RA. Improving and maintaining the response\_\_\_\_\_

### OP0109 IN RA PATIENTS WITH INITIAL RESPONSE TO RITUXIMAB, EARLY DEPTH OF B CELL DEPLETION IS ASSOCIATED WITH LONG TERM MAINTENANCE OF THERAPY

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**Background:** B-cell depletion is a fundamental effect of rituximab (RTX). The speed/depth of initial B-cell depletion is associated with clinical response, and non-responders largely having incomplete depletion.<sup>1, 2</sup> However, some patients with incomplete depletion still show clinical improvement (ID-R). Little is known about factors associated with complete depletion; the long-term outcome of the two responder groups according to their level of depletion has not been studied yet.

**Objectives:** To assess factors that are associated with complete depletion and clinical response (CD-R) and compare the 3 year RTX retention between the two RTX responder groups (CD-R vs ID-R), with a view to inform practice on the optimal use of RTX in RA.

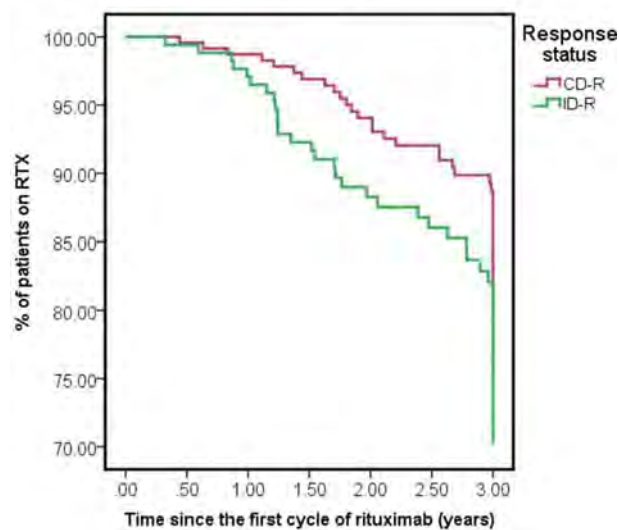
**Methods:** A prospective observational study was conducted in patients with RA who were treated with RTX in Leeds. Each initial cycle of RTX consisted of 2 × 1000 mg infusions, repeated either on clinical relapse or fixed 6 monthly



retreatment strategy. B-cells were measured at 0, 2 weeks and every 6 months using highly sensitive flow cytometry (as previously described). Complete depletion was defined as total B cell count  $<0.0001 \times 10^9/L$  at week 2. Patients were classified into 4 groups based on B-cell depletion (CD=complete,) and EULAR response (R=good/moderate, NR=no response). Multiple imputation was used for missing data. Factors for predicting CD-R in cycle 1 (C1) were tested using logistic regression analyses. In the survival analysis, an event was defined as RTX cessation either due to death, safety or switching to other biologics.

**Results:** A total of 693 patients were treated with RTX in Leeds. Of these, 624 had clinical data at 6 months and were included in the analysis. Total follow-up was 2826 patient-years. In cycle 1, 418/624 (67%) had EULAR response. Of these, 242/418 (58%) had CD-R. In univariable analysis, age, concomitant MTX/LEF, non-smoker, pre-RTX lower naïve, memory B-cell and plasmablasts were associated with CD-R in C1. However, in a multivariable analysis, only concomitant MTX/LEF (OR 2.1 95% CI: 1.3 to 3.5), non-smoker (1.6, 1–2.6) increased the odds while lower plasmablasts (0.89, 0.83–0.95) decreased the odds of CD-R. After adjusting for confounders including age, gender, concomitant MTX/LEF and previous exposure to TNF- $\alpha$ , there was a trend to longer maintenance on RTX (surrogate for response) in the CD-R vs ID-R groups; HR 0.70 (95% CI: 0.46 to 1.05);  $p=0.058$  (figure 1).

**Rituximab retention 3 years after the administration of the first cycle**



**Abstract OP0109** – Figure 1 Rituximab retention 3 years after the administration of the first cycle

**Conclusions:** Among patients with good initial clinical response to RTX, we observed differences in immunological response. This had important long term consequences: in patients with early complete B-cell depletion accompanied by good clinical response, RTX treatment was sustained over 3 years numerically, while responses of ID were less durable. Therefore, treatment with anti-CD20 mAb should aim to achieve CD for sustained maintenance on rituximab. CD-R can be predicted by concomitant use of MTX/LEF, non-smokers and those with low baseline plasmablasts.

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OP0110

#### SERUM TOCILIZUMAB TROUGH CONCENTRATIONS ARE ASSOCIATED WITH CLINICAL DISEASE ACTIVITY INDEX SCORES IN ADULT RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Serum trough levels of TNF $\alpha$  inhibitor biologics have been found to be associated with clinical responses in rheumatoid arthritis (RA) patients. It is unknown whether serum trough levels of tocilizumab (TCZ) administered as a fixed dose subcutaneous injection, also associate with clinical disease activity responses.

**Objectives:** To ascertain whether serum TCZ trough levels at weeks 12 and 24 after beginning treatment with a 162 mg once weekly regimen of SC tocilizumab, were associated with clinical disease activity outcomes in RA patients.

**Methods:** We analysed data sets from the Israeli branch (TASC, NCT01988012) of the Roche multinational umbrella study TOZURA, which evaluated a SC TCZ treatment regimen of 162 mg once weekly as monotherapy or in combination with methotrexate or other csDMARDs in a real-life clinical setting. The study comprised of 100 patients. A paired-samples T test was used to compare mean serum TCZ levels at week 12 relative to week 24. Clinical disease activity index (CDAI) scores were natural log-transformed in order to achieve normal distribution. Generalised estimating equations were used to evaluate associations between the predictors (TCZ levels, soluble IL-6 receptor (sIL6R) levels) and the study outcomes (CDAI scores, HAQ scores, CDAI remission/low disease activity status, HAQ DI remission). Generalised estimating equations were also used to evaluate associations between age, sex, weight, BMI, baseline CRP levels, serum TCZ and sIL6R serum levels. P values below 0.05 were considered significant.

**Results:** Serum trough levels of TCZ at week 24 (mean 41.1, SD 23.2) were higher than at week 12 (mean 36.3, SD 18.1).

In a univariate analysis, for every increase of 1 microgram/ml in the serum concentration of TCZ there was a corresponding decrease of 1.3% (95% CI: 0.4% to 2.3%) in the CDAI score and for every increase of 100 ng/ml in the serum concentration of sIL6R there was a corresponding decrease of 12.6% (95% CI: 2% to 22%) in the CDAI score.

In a multivariate model which included age, sex, visit date and both sIL6R and TCZ levels, only the associated between TCZ levels and CDAI scores remained significant. Similarly, every increase of 10 microgram/ml in the serum concentration of TCZ was associated with an odds ratio of 1.35 (95% CI: 1.07 to 1.72) of being in a state of CDAI remission or low disease activity versus moderate/high disease activity state. TCZ and sIL6R serum levels were not associated with HAQ DI scores.

Female sex was associated with an increase of 12.9 microgram/ml in the serum TCZ concentrations (95% CI: 5.9 to 20.0). Also, every increase of 1 BMI unit was associated with a decrease of 1.5 microgram/ml in the serum TCZ concentrations (95% CI: 0.8 to 2.2) and every increase of 1 kg in weight was associated with a decrease of 0.6 microgram/ml in the serum TCZ concentrations (95% CI: 0.3 to 0.9).

**Conclusions:** In the first year of TCZ treatment with a fixed dose regimen of 162 mg SC injection once a week, serum trough concentrations of TCZ are associated with CDAI scores and a state of CDAI remission/low disease activity. Body weight and BMI are inversely associated with serum TCZ concentrations. These results suggest that personalising the dose of SC TCZ to body weight may improve clinical outcomes of RA disease activity.

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**Disclosure of Interest:** None declared

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OP0111

#### TOCILIZUMAB DISCONTINUATION AFTER ATTAINING REMISSION IN PATIENTS WITH RHEUMATOID ARTHRITIS WHO WERE TREATED WITH TOCILIZUMAB ALONE OR IN COMBINATION WITH METHOTREXATE: RESULTS FROM A PROSPECTIVE, RANDOMISED, CONTROLLED STUDY (THE SECOND YEAR OF THE SURPRISE STUDY)

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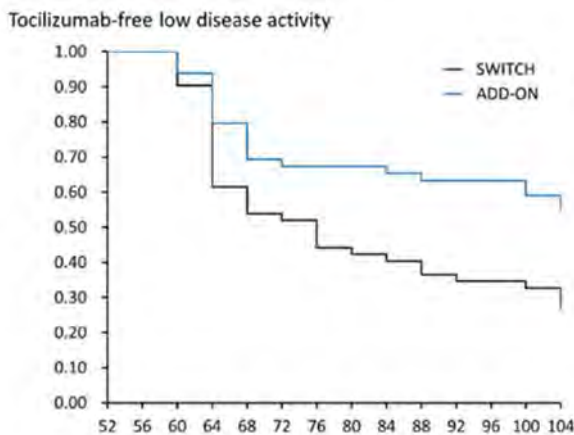
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**Background:** Feasibility of discontinuation of biologic agents in patients with rheumatoid arthritis (RA) who have reached stable remission has been investigated. Although evidence has been accumulating regarding tumour necrosis factor inhibitors, the possibility of tocilizumab-free strategy is still unclear.

**Objectives:** To evaluate the sustained remission and low disease activity after discontinuation of tocilizumab in patients with RA who were treated with tocilizumab alone or in combination with methotrexate.

**Methods:** The SURPRISE study was a 2 year randomised, controlled study. Patients with active RA despite methotrexate were randomised to tocilizumab added to methotrexate (ADD-ON) or switch to tocilizumab alone (SWITCH). At week 52, tocilizumab was discontinued in patients who achieved remission based on disease activity score for 28 joints (DAS28-ESR<2.6). The endpoints of the second year included tocilizumab-free sustained remission rates at week 104, sustained low disease activity rates, radiological outcomes assessed with the modified total Sharp score (mTSS), and safety. The efficacy of re-instituted tocilizumab/methotrexate was also assessed.

**Results:** 105 patients who achieved remission at 52 week discontinued tocilizumab; 51 in the ADD-ON continued methotrexate and 54 in the SWITCH were observed without medication. Whereas sustained DAS28 remission rates at week 104 were 24% for the ADD-ON and 14% for the SWITCH (p=0.29), sustained low disease activity rate was significantly higher in the ADD-ON than in the SWITCH (55% vs 27%, p=0.005, figure 1). Radiographical progression was comparable in the 2 groups (mTSS; 0.37 vs 0.64, p=0.36). Re-start of tocilizumab induced remission in all patients except two irrespective of concurrent methotrexate after 36 weeks while re-start of methotrexate was effective only in a half of patients.



Abstract OP0111 – Figure 1 Tocilizumab-free low disease activity

**Conclusions:** Sustained low disease activity after tocilizumab discontinuation could be maintained with continued methotrexate in more than half of patients. Re-treatment with tocilizumab led remission in more than 90% patients.

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#### OP0112 THERAPEUTIC DRUG MONITORING TO OPTIMISE SWITCHING BETWEEN BIOLOGIC AGENTS IN RHEUMATOID ARTHRITIS

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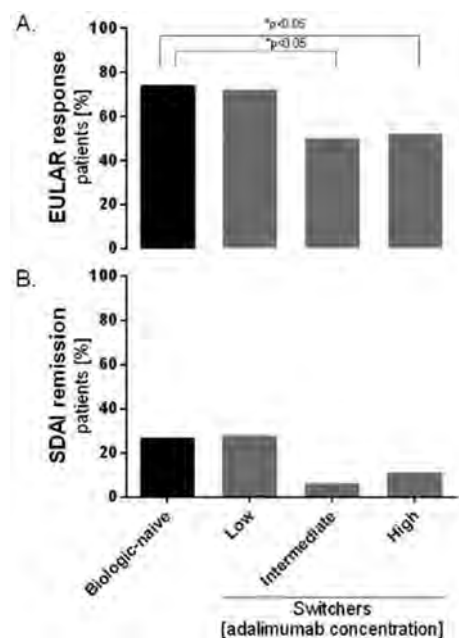
**Background:** Many patients with rheumatoid arthritis (RA) are treated with tumour necrosis factor inhibitors (TNFi). It is, however, unclear whether to switch to a second TNFi or to another mode of action drug in case of non-response. The detection of anti-drug antibodies (ADAs) have shown to be related to the response rate of a second TNFi.<sup>1</sup> The detection of ADAs is, however, to a large extent dependent of the type of assay used and, moreover, the efficacy of the drug is determined by the pharmacokinetics. Therefore, it more logical to use drug levels in daily clinical practice.

**Objectives:** To investigate whether serum drug concentration of patient's first TNFi, adalimumab, was related to the effectiveness of a second TNFi, etanercept.

**Methods:** Consecutive patients with RA treated with etanercept were followed in the Reade Rheumatology Registry, an observational cohort (NTR no.6868). Patients who were treated with adalimumab 40 mg every other week previously (switchers; n=69) were compared to patients starting etanercept without prior biologic agents (biologic-naïve; n=380). Patients received etanercept 50 mg weekly or 25 mg twice a week. Switchers were divided into three groups; respectively low- (<0.5 µg/mL), intermediate- (0.5 and 5.0 µg/mL) and high- (>5.0 µg/mL) adalimumab concentration. The last available serum sample before adalimumab discontinuation was assessed for adalimumab concentrations by enzyme linked immunosorbent assay (ELISA). ADAs were measured using the antigen binding test (ABT). Clinical endpoints were percentage of patients achieving European League Against Rheumatism (EULAR) good or moderate response and the Simplified Disease Activity Index remission criteria (SDAI <3.3) after 52 weeks.

**Results:** Median (IQR) adalimumab concentration of the switcher-groups with low (n=18), intermediate (n=18) and high concentrations (n=27) were, respectively 0.0 µg/mL (0.0–0.05), 2.5 µg/mL (1.5–4.3) and 7.4 µg/mL (6.0–11.8). ADAs were detected in, respectively 16 patients (89%), 6 patients (33%) and 3 patients (11%). Response rate of switchers with low adalimumab concentrations was

comparable to biological-naïve patients, whereas switchers with intermediate and high concentrations responded worse regarding EULAR response criteria (respectively 74%, 72%, 50% and 52%; figure 1A) and SDAI remission (respectively 27%, 27%, 6%, 11%; figure 1B).



**Conclusions:** For the first time, we showed that the response rate of switchers with low adalimumab concentrations was comparable to biological-naïve patients, whereas switchers with intermediate and high concentrations responded worse. Therefore, drug concentration assessment may optimise switching, as it helps to identify those patients that may benefit from a second TNFi.

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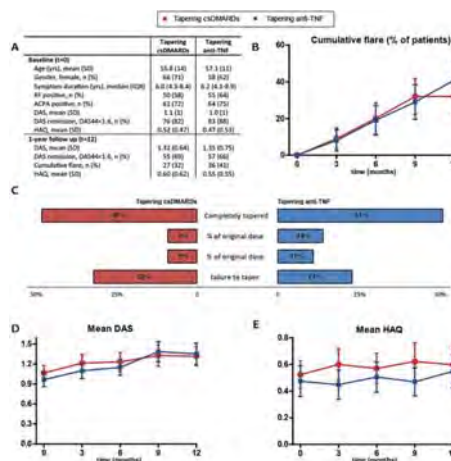
OP0113

#### GRADUAL TAPERING TNF BLOCKERS VERSUS CONVENTIONAL SYNTHETIC DMARDS IN PATIENTS WITH RHEUMATOID ARTHRITIS IN SUSTAINED REMISSION: FIRST YEAR RESULTS OF THE RANDOMISED CONTROLLED TARA-STUDY

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**Background:** Clinical and radiographic outcomes in rheumatoid arthritis (RA) have improved enormously in the last two decades, due to early detection of the disease, early initiation of 'intensive' therapy and a treat-to-target approach. As a result, 50%–60% of early RA patients will achieve sustained remission during the first year of follow-up. In aforementioned cases current guidelines recommend to consider tapering treatment, but an optimal approach to gradually de-escalate conventional synthetic or biologic DMARDs (respectively csDMARDs and bDMARDs) is currently lacking.

**Objectives:** The aim of this study is to evaluate the effectiveness of two tapering strategies, namely gradual tapering of csDMARDs and anti-TNF therapy during one year of follow-up.



**Abstract OP0113** – Figure 1 (A) Baseline characteristics and results after 12 months of follow-up of both tapering groups. (B) Cumulative flare over time, error bars indicate 95% confidence intervals. (C) Treatment at 12 months. Columns indicate the percentage of patients that tapered medication until the indicated amount of the original dose. (D) Mean DAS over time, error bars indicate 95% confidence intervals. (E) Mean HAQ over time, error bars indicate 95% confidence intervals. Abbreviations: ACPA; anti-citrullinated protein antibody, csDMARDs; conventional synthetic DMARDs, DAS; disease activity score, HAQ; health assessment questionnaire, RF; rheumatoid factor.

**Methods:** In this multicenter single-blinded randomised controlled trial RA patients in sustained remission for at least 3 consecutive months, defined as a DAS<sub>44</sub>≤2.4 and a swollen joint count (SJC)≤1, which was achieved with csDMARDs and a TNF blocker were included. Eligible patients were randomised into gradual tapering csDMARDs followed by the TNF blocker or vice versa. Medication was tapered in three steps over the course of 6 months. Gradual tapering was done by cutting the dosage into half, a quarter and thereafter it was stopped. The primary outcome for the clinical effectiveness was disease flare defined as DAS44 >2.4 and/or SJC >1. Secondary outcomes were quality of life and functional ability.

**Results:** A total of 187 patients were randomly assigned to tapering csDMARDs (n=93) or tapering anti-TNF (n=94). Patients had an average symptom duration of 6.7 years and were predominantly female (66%) with an average age of 56.4 years (figure 1A). The cumulative flare ratio in the csDMARD and anti-TNF tapering group was respectively 32% and 41% (figure 1B), which corresponds with a hazard ratio of 0.91 (95% CI: 0.68 to 1.22, p=0.55). In the last 3 months the increase in cumulative flare ratio differs the most between the two groups. On the other hand, in 48% and 51% of patients respectively tapering csDMARDs or anti-TNF the medication could be completely withdrawn (figure 1C). Percentages of patients which are not completely tapered are higher than the flare ratios, due to loss of remission without a disease flare. Furthermore, mean DAS and mean HAQ over time, and after 1 year, did not differ between both tapering groups (figure 1D and E).

**Conclusions:** There were no significant differences in flare ratios, disease activity and functional ability between both tapering strategies during the first year of follow-up. Therefore, in RA patients who are in sustained remission we advise to taper anti TNF first, but before tapering therapy rheumatologists should take the risk of a disease flare and patient's wishes into account.

**Disclosure of Interest:** None declared

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OP0114

#### ANA DEVELOPMENT IS ASSOCIATED WITH POOR RESPONSE TO BIOLOGICAL DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** It has been well known that anti-TNF- $\alpha$  treatment for patients with rheumatoid arthritis (RA) is associated with anti-nuclear antibody (ANA)



development. Using data of 110 RA patients treated with infliximab (IFX), we previously reported that ANA development along with ANA levels at base line were associated with poor outcomes of IFX.<sup>1</sup> However, no replication studies have been reported. In addition, whether the findings are true to general biological disease-modifying anti-rheumatic drugs (bDMARDs) is uncertain.

**Objectives:** To replicate an association between poor response and development of ANA during IFX treatment in patients with RA. To analyse whether the association is found in other bDMARDs.

**Methods:** We analysed a data of Japanese RA patients treated with (n=721) or without (bDMARDs-naïve; n=1050) bDMARDs (IFX, etanercept ETN, adalimumab ADA, golimumab GLM, certolizumab pegol CZP, tocilizumab TCZ, abatacept ABT) as a first line bDMARD from a single comprehensive RA cohort. All of the participants were not included in our previous study. We conducted multiple logistic linear regression analysis to assess effects of ANA development on treatment outcomes. We further analysed correlates of ANA development. ANAs were determined by indirect immunofluorescence with HEp-2 cells, and ANA development was defined as more than two times increase from baseline values.

**Results:** We found that ANA development at 3 months after starting bDMARDs was significantly associated with cessation of bDMARDs due to insufficient response within a year (OR 3.70, p=0.037). We further found that RA patients who did not develop ANA at 3 months but developed ANA within a year showed a significant association with treatment failure between 12 and 24 months (OR 7.11, p=0.044). ANA levels at baseline showed significant association with or tendency of insufficient response in both situations (OR 1.21 and 1.69, respectively), independently on ANA development. We still found associations of ANA development after conditioning on IFX usage, indicating that the associations are not limited to IFX. Female was associated with ANA development (OR 1.85) and high levels of ANA at baseline (OR 2.41, p=0.006), which is consistent with previous data in healthy population.<sup>2</sup> bDMARDs use (OR 2.09, p=0.056) was also a risk for ANA development. Among bDMARDs, anti-TNF agents, especially IFX, were risk factors of ANA development (OR 6.34, p<0.0001).

**Conclusions:** ANA development during treatment is associated with poor response to bDMARDs, which is not limited to IFX. Female and IFX usage are risk factors for ANA development.

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#### OP0115 IMPROVED RESPONSE TO ETANERCEPT IS ASSOCIATED WITH SERUM VITAMIN D LEVELS IN RHEUMATOID ARTHRITIS

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**Background:** Although treatment of rheumatoid arthritis (RA) has significantly improved during the past decades, many patients do not adequately respond or become resistant to current treatments. It is currently unknown why some patients respond well and others do not, and how the response rate could be improved.

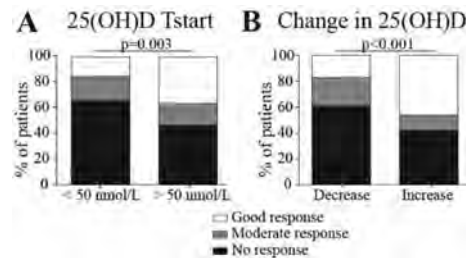
Vitamin D has strong immunomodulatory properties and it has been shown RA patients have a lower serum 25(OH)D level than healthy individuals. Moreover, vitamin D levels are correlated with disease severity.<sup>1,2</sup> Interestingly, *in vitro* studies have shown that vitamin D augments the suppressive effects of etanercept in a simplified model for synovial inflammation.<sup>3</sup> This suggests that vitamin D could improve the therapeutic response to etanercept in RA patients.

**Objectives:** To investigate if etanercept response is related to serum vitamin D (25(OH)D) levels in RA patients.

**Methods:** For this study, data were used from the tREACH trial, a multicenter stratified single blinded randomised clinical trial. RA patients, according to the 2010 classification criteria, who started with etanercept within the first 12 months of the study were included in the analysis. Serum vitamin D (25(OH)D) levels were

determined at the start of treatment (Tstart) and 3 months later using the LIAISON 25 OH Vitamin D TOTAL assay. Correlation coefficients between vitamin D levels and the disease activity score (DAS) were calculated. Treatment response was determined with the EULAR response criteria, and difference in response rates was assessed using Chi-Square tests.

**Results:** 91 patients started etanercept in the first 12 months of the study, of which 24 did not have serum for 25(OH)D measurements at both start of treatment and three months later. Therefore, a total of 67 patients was included in this study, of which 82% was female. At baseline, 45 (67%) and 48 (73%) were positive for rheumatoid factor and anti-citrullinated protein antibodies, respectively. DAS after etanercept treatment was weakly inversely correlated with serum 25(OH)D after treatment (r=-0.29, p=0.02) and the change in 25(OH)D during treatment (r=-0.25, p=0.04). After correcting for DAS and serum 25(OH)D at the start of treatment the aforementioned correlations were still found. Importantly, EULAR response rate was significantly lower in patients who were vitamin d-deficient at the start of treatment (34.6% vs 59.4%) and in patients with decreasing 25(OH)D levels during treatment (39.2% vs 57.7%) (figure 1).



**Conclusions:** RA patients with a serum 25(OH)D level below 50 nmol/L at the start of etanercept treatment or a decreasing level during treatment have a lower EULAR response rate. Therefore, increasing serum 25(OH)D level in vitamin D deficient patients may be important to achieve optimal effects of TNF $\alpha$  blocking therapy.

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#### OP0116 IMPACT OF TNF INHIBITORS ON NEED FOR JOINT REPLACEMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS: A MATCHED COHORT ANALYSIS OF UK BIOLOGICS REGISTRY DATA

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**Background:** Previous ecological data from the UK and Denmark suggest a decline in the incidence of joint replacements for RA patients following the introduction of tumour necrosis factor inhibitors (TNFi). However, patient-level data on the comparative effectiveness of TNFi compared to conventional synthetic DMARD (csDMARD) use on the need for total hip (THR) or knee (TKR) replacement are lacking.

**Objectives:** To estimate the impact of TNFi use on subsequent need for THR or TKR (primary outcomes) or other joint replacement (OJR) (secondary outcome) in RA.

**Methods:** A propensity score (PS) matched cohort was analysed using the British Society for Rheumatology Biologics Registry (2001 – 2016) for Rheumatoid Arthritis (BSRBR/RA) data. Exclusion criteria were: previous THR or TKR (all analyses) or OJR (secondary analysis), less than 6 months follow-up, prevalent biological DMARD use, or first biological DMARD use that was not a TNFi. Patients were followed from date of registration up to the earliest of date of outcome, death, loss-to-follow-up or change of TNFi exposure status (stopping, switching or starting).

Multiple imputation was used to deal with missing data. The PS (i.e. the probability of receiving TNFi conditional on observed characteristics) was estimated using logistic regression. This included age, gender, ethnicity, index of multiple deprivation, BMI, smoking, year of registration, duration of RA, DAS-28, HAQ, SF36, ACR criteria, comorbidities, and comedications. A PS calliper of 0.2 was used to match all TNFi users to csDMARD users (with replacement) using a 1:1 ratio. Weighted Cox regression was used to estimate the impact of TNFi use on study outcomes, adjusted for any confounders that remained unbalanced.

**Results:** Our 1:1 matched cohort contained a total of 19 116 patient records. THR rate was 6.30/1,000 PYs [95% CI: 4.24 to 9.76] and 5.22/1,000 PYs [CI: 4.66 to 5.88] in the csDMARD and TNFi cohorts, respectively. TKR rate was 8.09/1,000 PYs [CI: 5.32 to 12.89] and 8.89/1,000 PYs [CI: 8.13 to 9.72], respectively. There was no significant association between TNFi use and THR or TKR (HRs=0.86 [CI: 0.60 to 1.22] and 1.11 [CI: 0.84 to 1.47], respectively), although when analyses were restricted to patients with DAS >5.1 (as per NICE guidance) these HRs were 0.74 [CI: 0.51–1.05] and 0.95 [CI: 0.71 to 1.26], respectively. Among those over 60 years old, TNFi was associated with a significant reduction in THR (HR=0.60 [CI: 0.41–0.87]) but not TKR (HR=1.31 [CI: 0.87–1.99]). THR but not TKR rates were also reduced among those with an above average HAQ score. Overall, no significant associations were found for OJR.

**Conclusions:** Our findings suggest TNFi use may reduce the need for THR in older and more severe RA patients, although no evidence was found for a reduction in younger or less severe patients or in rates of TKR or OJR. Further work is needed to confirm these results.

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THURSDAY, 14 JUNE 2018

## SLE, Sjögren's and APS- new criteria, novel diagnostic tools and co-morbidities

OP0117

### SAFETY AND IMMUNE RESPONSE OF A LIVE ATTENUATED HERPES ZOSTER VACCINE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A RANDOMISED PLACEBO-CONTROLLED TRIAL

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**Objectives:** To evaluate the safety and immune response of a live attenuated herpes zoster (HZ) vaccine in patients with systemic lupus erythematosus (SLE) in a randomised placebo-controlled trial.

**Methods:** Adult patients who fulfilled  $\geq 4$  ACR criteria for SLE and had a SLEDAI score  $< 6$  with stable immunosuppressive treatment for 6 m were recruited. Exclusion criteria were: active infection; lymphocyte  $< 500/\text{mm}^3$ ; reduced serum IgG/A/M level; serum creatinine  $> 200 \mu\text{mol/L}$ ; a history of cancer; and high-dose immunosuppressive treatment (prednisone  $> 15 \text{ mg/day}$ , azathioprine  $> 100 \text{ mg/day}$ , MMF  $> 500 \text{ mg/day}$ , cyclosporin  $> 100 \text{ mg/day}$ , tacrolimus  $> 3 \text{ mg/day}$ , CYC and biologics). Participants were randomly assigned to receive HZ vaccine (Zostavax) or placebo (same volume of normal saline) given subcutaneously. Anti-VZV IgG reactivity (baseline and 6 weeks post-vaccination) was measured by an ELISA coated with inactivated varicella-zoster viral antigen (Vidas VZV IgG, bioMerieux, Marcy l'Etoile, France). Cell-mediated response to HZ was assessed by a specific VZV-stimulated IFN $\gamma$  enzyme linked immunospot (ELISPOT) assay. Disease activity of SLE was assessed by the SLEDAI and PGA. Adverse events (AEs) and immune responses to HZ of the two groups were compared.

**Results:** 90 SLE patients were recruited (age  $45.6 \pm 14.1$  years; 93% women): 45 assigned to HZ vaccine and 45 to placebo. All participants had a history of HZ/

chickenpox infection. The baseline clinical profile of the two groups of patients was similar. Only 3 patients in the vaccine and 1 patient in the placebo group had mild SLE activity (all mild thrombocytopenia). Baseline SLEDAI and PGA scores of the two groups were not significantly different ( $1.58 \pm 1.8$  vs  $1.64 \pm 1.7$ ;  $p=0.86$  and  $0.21 \pm 0.18$  vs  $0.27 \pm 0.25$ ;  $p=0.18$ , respectively). The proportion of patients receiving various immunosuppressive agents, lymphocyte count, serum creatinine, IgG/A/M levels were also similar in the two groups. The mean baseline VZV IgG index value was  $3.28 \pm 1.19$  and  $3.45 \pm 1.07$  in the vaccine and control group of patients, respectively ( $p=0.48$ ). The paired VZV IgG titer at week 6 was significantly higher in the vaccine than control group, even after adjustment for baseline value ( $4.16 \pm 1.26$  vs  $3.32 \pm 1.01$ ;  $p<0.001$ ), lymphocyte count, Ig levels, SLEDAI, and other clinical variables. The% increase in VZV IgG antibody was significantly higher in the vaccinated than control patients ( $+59.8\%$  vs  $-2.1\%$ ;  $p=0.01$ ), indicating an effect of vaccine. 21 and 6 AEs were reported in the vaccinated and control patients, respectively, but none were serious. Significantly more vaccinated patients reported pain and erythema at the injection site than controls (31% vs 7%;  $p<0.01$ ) (mild in all and subsided in a few days). Other AEs more commonly reported with vaccination included dizziness (2%), arthralgia (2%) and subjective fever (4%). Two vaccinated patients (4.4%) had mild flare of skin/joint disease, and one control patients (2.2%) had mild increase in proteinuria between week 0 and 6. None of the patients had clinical HZ infection post-vaccination.

**Conclusions:** In patients with stable SLE who were not receiving intensive immunosuppression, the live attenuated HZ vaccine was well tolerated and provoked an expected antibody response. Study of the cell-mediated response to HZ post-vaccination is in progress.

**Disclosure of Interest:** None declared

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OP0118

### DEVELOPMENT OF METABOLIC SYNDROME IN PATIENTS WITH SLE: RESULTS FROM AN INCEPTION COHORT

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**Background:** Individuals with systemic lupus erythematosus (SLE) are at increased risk of cardiovascular disease, which is possibly related to metabolic syndrome (MetS). Previous studies suggest that inflammation may be an important underlying mechanism in MetS development, but include patients with prevalent MetS only. In order to assess whether the development of incident MetS could be predicted, we examined the association between the onset of MetS and disease activity, therapeutic exposure, and biomarkers of inflammation overtime in patients with SLE.

**Objectives:** 1) To identify the clinical characteristics of patients with recently diagnosed SLE who develop incident MetS during first two years of follow-up; 2) To determine whether metabolic and inflammatory biomarkers improve the ability to predict incident MetS during follow-up.

**Methods:** We studied 1687 recently diagnosed SLE patients ( $< 15$  months) enrolled into the SLICC Inception Cohort from 11 countries. Clinical, therapeutic and laboratory data were recorded at baseline and annually at follow-up visits. Serum concentrations of adiponectin, B-lymphocyte stimulator, high sensitivity C-reactive protein, interleukin (IL)-6, IL-18, IL-18 binding protein, insulin, leptin and tumour necrosis factor alpha were measured, if samples were available. A complete-case analysis was performed. Only patients with both MetS status available at baseline, year 1 and year 2 visits were analysed. Logistic regression was performed to analyse which factors were predictive of the development of incident MetS in the first 2 years of follow-up. Patients who developed incident MetS were compared with those who were free of MetS throughout follow-up.

**Results:** Overall, 436 (26%) patients were included in this complete-case analysis. Of these, 243 (56%) were free of MetS throughout the follow-up period, 87 (20%) had persistent MetS at each visit, and 106 (24%) developed incident MetS during follow-up. In a multivariable logistic regression model that excluded biomarkers, clinical factors associated with future onset of MetS included increased age, Hispanic ethnicity, active renal disease, higher disease activity and current corticosteroid use. This model performed 'fairly' when identifying patients likely to develop incident MetS (Area Under Receiver Operator Characteristics Curve (AUC ROC)=0.77). In a multivariable model that included the inflammatory and

metabolic biomarkers, increasing age, Korean ethnicity, higher disease activity and increased serum leptin performed similarly (AUC ROC=0.75).

**Conclusions:** SLE patients who develop incident MetS exhibit a more inflammatory disease phenotype, with higher corticosteroid exposure in the preceding visit. Increased serum leptin concentration is independently associated with future onset of MetS. These factors can help predict those at increased risk of developing future MetS and may help target patients for more focused cardiovascular disease prevention.

**Disclosure of Interest:** None declared

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OP0119

#### PROGRESSION OF SUBCLINICAL ATHEROSCLEROSIS IN SYSTEMIC LUPUS ERYTHEMATOSUS OF LOW DISEASE ACTIVITY: THREE-YEAR FOLLOW-UP AND COMPARISON TO RHEUMATOID ARTHRITIS

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**Background:** Both systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) are characterised by accelerated atherosclerosis compared to the general population. Prospective studies have shown that atherosclerosis progression is halted in patients with RA of low disease activity, but it is unclear if maintaining lupus low disease activity state mitigates accelerated atherosclerosis due to SLE.

**Objectives:** To prospectively assess the risk and determinants of atherosclerosis progression in SLE versus RA patients of low disease activity.

**Methods:** We performed carotid and femoral artery ultrasound to detect atherosclerotic plaques at baseline on 345 participants with SLE, RA, and healthy controls, individually matched for age and gender, after excluding patients with atherosclerotic cardiovascular disease, malignancy and diabetes. After 3 years of follow-up, patients with SLE (n=89) and RA (n=64) maintaining low disease activity<sup>1</sup> for >75% of the follow-up time, and their matched controls (n=72) underwent repeat ultrasound to identify those with atherosclerosis progression, as defined by the development of new plaques compared to baseline. We applied multiple logistic regression models to assess the odds of atherosclerosis progression between SLE, RA, and control participants, and used the stepwise backward elimination algorithm (p<0.1) to examine potential associations with SLE damage index, anti-phospholipid antibodies, corticosteroids, hydroxychloroquine, immunosuppressives, and disease duration in patients with SLE, adjusting for use of antiplatelet agents, statins, and traditional cardiovascular risk factors with the European Society of Cardiology's SCORE risk estimation of 10 year fatal cardiovascular disease.

**Results:** Atherosclerotic plaque progression was detected in 21% of SLE patients, 17% of RA patients, and 8% of controls (p=0.078). After controlling for SCORE, antiplatelet agent use and statins, the rate of atherosclerosis progression compared to healthy controls was significantly higher in SLE (OR=3.05, 95% Confidence Interval (CI) 1.06–8.79, p=0.039), but not in RA (OR=2.11, 95% CI: 0.72 to 6.23, p=0.176). In patients with SLE, longer disease duration at baseline (OR=1.11, 95% CI: 1.02 to 1.21, p=0.015), antiphospholipid antibody positivity (OR=7.04, 95% CI: 1.57 to 31.58, p=0.011 cumulative corticosteroid dose during follow-up (OR=1.16, 95% CI: 0.99 to 1.35, p=0.069), treatment with antiplatelet agents (OR=0.21, 95% CI: 0.05 to 0.99, p=0.049), and the SCORE prediction (OR=1.67, 95% CI: 0.91 to 3.08, p=0.099) were included in the multivariable model as determinants of atherosclerosis progression. No disease-related determinants were significantly associated with atherosclerosis progression in patients with RA.

**Conclusions:** Unlike RA, atherosclerosis progression is accelerated in SLE even in the setting of low disease activity. In addition to SCORE, longer disease duration at baseline, antiphospholipid antibody positivity, and higher cumulative corticosteroid dose during follow-up increase the odds of atherosclerosis progression in patients with SLE of low disease activity.

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OP0120

#### INFLUENCE OF EPIDEMIOLOGY AND ETHNICITY ON SYSTEMIC EXPRESSION OF PRIMARY SJÖGREN SYNDROME IN 9974 PATIENTS

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**Objectives:** To analyse the influence of epidemiology and ethnicity on the clinical systemic presentation at diagnosis of primary Sjögren syndrome (SjS).

**Methods:** The Big Data Sjögren Database included 10 475 worldwide patients from 22 countries fulfilling the 2002 criteria. Age at diagnosis, gender and ethnicity (77% White, 14% Asian, 6% Hispanic, 1% Black/African American, 2% others) were correlated with systemic involvement at diagnosis (retrospectively scored in 9974 patients using ESSDAI/clinESSDAI)

**Results:** Men had higher mean ESSDAI (8.0 vs 5.9, p<0.001) and clinESSDAI (8.4 vs 6.1, p<0.001) in comparison with women; the domains more active in men included lymphadenopathy (p<0.001), glandular (p<0.001), pulmonary (p=0.001), PNS (p<0.001) and CNS (p<0.001). Highest scores were also reported in patients with young-onset disease (<35 years) with respect to older onset (>65 years) for ESSDAI (6.5 vs 5.6, p=0.002) and clinESSDAI (6.4 vs 5.8, p=0.034). Highest ESSDAI scores were reported in Black/African American, followed by White, Asian and Hispanic patients (6.7 vs 6.3 vs 5.4 vs 4.9, respectively, p<0.001). BAA patients showed the highest frequency of activity in lymphadenopathy, articular, PNS, CNS and biological domains, Whites in glandular, cutaneous and muscular, Asians in pulmonary, renal and haematological and Hispanics in the constitutional domain.

**Conclusions:** This study provides the first evidence for a strong influence of epidemiology and ethnicity on the systemic phenotype at diagnosis of primary SjS

**Disclosure of Interest:** None declared

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OP0121

#### LUPUS ANTICOAGULANT IS ASSOCIATED WITH THROMBOTIC EVENTS IN HEALTHY CARRIERS: RESULTS FROM A PROSPECTIVE LONGITUDINAL STUDY

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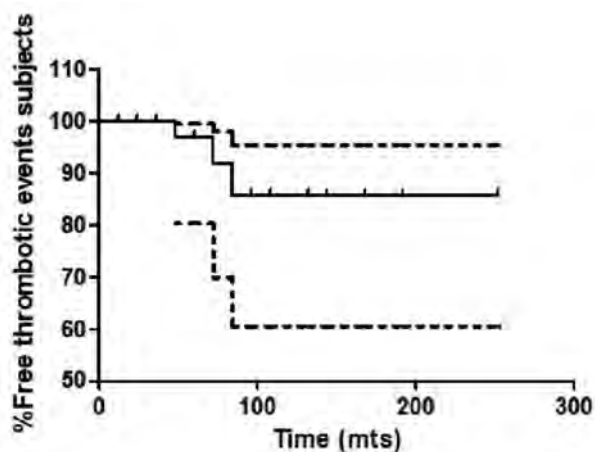
**Background:** Antiphospholipid syndrome (APS) is an autoimmune disease characterised by thrombotic events and/or pregnancy morbidity in combination with persistent positivity for antiphospholipid antibodies (aPL) [lupus anticoagulant (LA), anticardiolipin (aCL), anti b2 glycoprotein I (anti-β2GPI) in medium/high titers]. These antibodies could be identified not only in other pathological



conditions (i.e. autoimmune diseases), but also in healthy subjects (aPL carriers). In this subset, the risk of developing thrombotic events or pregnancy morbidity ranges from 0% to 3.8%, and it is higher in subjects with LA positivity, triple positivity (LA+aCL+anti-β2GPI) and aCL positivity at high/medium titer. Nonetheless, 70% of aPL carriers described so far showed a concomitant autoimmune disease, being itself a risk factor for thrombotic events.

**Objectives:** We longitudinally followed up a cohort of healthy subjects persistently positive for aPL to evaluate the risk of developing thrombotic events.

**Methods:** Healthy subjects positive for aPL in at least 2 consecutive determinations (aPL carriers) were enrolled. Medical history was recorded and the following parameters were registered: presence of traditional risk factors (smoking, diabetes mellitus, hypertension, dyslipidemia, hormone therapy); obstetric history (infertility, miscarriages); family history of autoimmune and cardiovascular diseases with an early onset; recent infectious episodes. Laboratory evaluation was performed, including aCL IgG/IgM, anti-β2GPI IgG/IgM, LA, antinuclear antibody, C3/C4 serum levels, thrombophilia screening. All subjects were evaluated every 6 months.



Abstract OP0121 – Figure 1. Reports the Kaplan-Meier curve of aPL carriers free from thrombotic events.

**Results:** We enrolled 47 aPL carriers (M/F 9/38, median age at first visit 45.5 years, IQR 17). Thirty-six subjects (76.6%) were aCL+ (30.5% at medium/high titer), 30 (63.8%) anti-β2GPI+ (36.7% at medium/high titer), 24 (51.1%) LA+. Thirty-one subjects (65.9%) were positive for more than one aPL and 12 (25.5%) showed a triple positivity. The aPL carriers were longitudinally followed up for a median of 60 months (IQR 48). Twenty-four subjects were treated with low dose aspirin (LDA) and 3 with hydroxychloroquine. During this observational period, 5 subjects were lost to follow-up and 5 became persistently negative for aPL after a median of 54 months (IQR 39). Considering the remaining 37 aPL carriers, 3 (1F, 2M) experienced a thrombotic event (2 arterial and 1 venous). This patients were treated with LDA at the time of the event and were all LA+. In one case, the episode was preceded by a flu-like event. Interestingly, the LA prevalence resulted significantly higher in the subjects experiencing thrombotic events in comparison with those who did not (p=0.0001). We observed an absolute risk of thrombotic events of 0.08 (CI: 0.02 to 0.2) and an incidence rate of 1.1 (CI: 0.3 to 2.9).

**Conclusions:** In this prospective study, specifically designed to evaluate the incidence of APS related clinical manifestations in aPL positive healthy subjects, LA positivity resulted the most important risk factor of thrombotic events.

**Disclosure of Interest:** None declared

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**OP0122 VALIDATION OF REMISSION AND LUPUS LOW DISEASE ACTIVITY STATE AS PREDICTORS OF ORGAN DAMAGE IN SLE**

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**Background:** Outcome measures that combine control of SLE activity and prednisone reduction are clinically relevant. A clinical goal in SLE is to reduce risk of long-term organ damage.

Abstract OP0122 – Table 1. Rates of new damage, in subgroups defined by past levels of disease activity

Percentage of Prior Months in:	Number of person-months observed	Number of months with an increase in SLICC/ACR Damage Index	Rate of damage per 100 person months	Rate Ratios	P-values
Clinical Remission	-	-	-	-	-
None	35 772	406	1.13	1.0 (Ref)	-
Not none, but<25%	14 358	102	0.71	0.60	<0.0001
25% to 50%	6573	50	0.76	(0.48,0.75)	0.023
50% to 75%	3845	27	0.70	0.66	0.035
75%+	1641	10	0.61	(0.46,0.94)	0.12
				0.63	
				(0.42,0.97)	
				0.58	
				(0.30,1.15)	
Clinical Remission on Treatment	-	-	-	-	-
None	16 491	250	1.52	1.0 (Ref)	-
Not none, but<25%	20 169	170	0.84	0.54	<0.0001
25% to 50%	14 344	103	0.72	(0.44,0.67)	<0.0001
50% to 75%	8396	54	0.64	0.46	<0.0001
75%+	2789	18	0.65	(0.36,0.60)	0.0019
				0.43	
				(0.30,0.60)	
				0.45	
				(0.27,0.75)	
LLDAS	-	-	-	-	-
None	30 366	343	1.13	1.0 (Ref)	-
Not none, but<25%	10 880	106	0.97	0.86	0.18
25% to 50%	5012	40	0.80	(0.69,1.07)	0.037
50% to 75%	8494	60	0.71	0.70	0.0010
75%+	7527	46	0.61	(0.51,0.98)	<0.0001
				0.63	
				(0.48,0.83)	
				0.54	
				(0.40,0.73)	
LLDAS on Treatment	-	-	-	-	-
None	7656	117	1.53	1.0 (Ref)	-
Not none, but<25%	10 555	134	1.27	0.83	0.14
25% to 50%	12 686	129	1.02	(0.65,1.06)	0.0013
50% to 75%	18 151	133	0.73	0.66	0.0010
75%+	13 141	82	0.62	(0.51,0.85)	<0.0001
				0.48	
				(0.37,0.61)	
				0.40	
				(0.30,0.54)	

**Objectives:** We assessed whether two recently proposed disease activity outcomes were predictive of future damage.

**Methods:** For each month of follow-up in a large SLE cohort, we determined whether the patient was in Clinical Remission (as defined by the DORIS working group) or lupus low disease activity state (LLDAS) (as defined by Franklyn et al). Clinical Remission was defined as a PGA<0.5, clinical SLEDAI=0 and no prednisone or immunosuppressants. Clinical Remission on Treatment allowed for prednisone ≤5 mg/day and immunosuppressant use. LLDAS was defined as a SLEDAI ≤4, PGA≤1.0, no major organ activity, and no new activity. LLDAS on treatment allowed for prednisone use ≤7.5 mg/d and immunosuppressants. Damage was defined using the SLICC/ACR Damage index.

**Results:** There were 81 118 person-months observed among 2026 patients (92% female, 53% Caucasian, 39% African-American). table 1 shows the rates of damage, per person month, in subgroups defined by Remission or LLDAS. Damage rates were relatively low when LLDAS was achieved at least 50% of the time. These rates were similar to those experienced by patients who met a more stringent treatment restriction with Remission on Treatment at least 50% of the time.

**Conclusions:** Percent time in LLDAS had a clear dose response for rate ratios of organ damage. The equivalence of LLDAS and DORIS remission on treatment is welcome news, as LLDAS on treatment >50% of the time is an easier goal to achieve (3 times more person-months observed in our cohort) and more realistic as a clinical trial outcome.

**Disclosure of Interest:** None declared

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OP0123

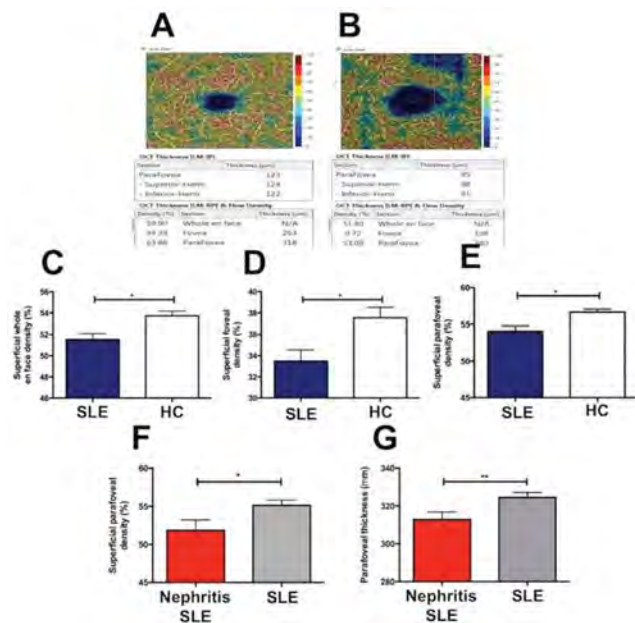
### EVALUATION OF RETINAL MICROVASCULATURE BY OPTICAL COHERENCE TOMOGRAPHIC ANGIOGRAPHY IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS MIRRORS SYSTEMIC INVOLVEMENT

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**Background:** Optical coherence tomographic angiography (OCTA) is a novel imaging modality that visualises retinal microvasculature in a noninvasive manner. It may have value in managing retinopathy, correlate with visual outcome and mirror systemic involvement in autoimmune diseases.

**Objectives:** Aim of this study was to evaluate retinal microvasculature in systemic lupus erythematosus (SLE) patients and correlate abnormal vascular maps with disease activity, damage accrual, treatment and visual outcome.

**Methods:** In a prospective cross-sectional study, OCTA was used to examine density maps, by means of a 6 mm scan, based on superficial retinal layer and deeper retinal layer images in patients and healthy controls (HC) (figure 1A-B) from November 2015 to December 2017. Vessel density, based on a map with vessels of 1-pixel width was measured.



**Results:** 52 eyes from 26 SLE patients and 40 healthy eyes from 20 HC were imaged (table 1). The eyes from SLE patients had a lower superficial whole en face density, superficial fovea density and superficial parafoveal density ( $p=0.02$  for all comparisons) compared with healthy eyes (figure 1C-E). A negative correlation was demonstrated in SLE patients between age and superficial whole en face density ( $p=0.0005$ ,  $r=-0.5$ ), superficial foveal density ( $p=0.006$ ,  $r=-0.4$ ), superficial parafoveal density ( $p=0.004$ ,  $r=-0.4$ ), deep whole en face density ( $p=0.003$ ,  $r=-0.4$ ) and deep parafoveal density ( $p=0.001$ ,  $r=-0.4$ ). SLEDAI correlated inversely with superficial en face density ( $p=0.002$ ,  $r=-0.4$ ), superficial parafoveal density ( $p=0.0003$ ,  $r=-0.5$  and  $p=0.002$ ,  $r=-0.5$ ), deep whole en face density ( $p=0.01$ ,  $r=-0.4$ ) and deep parafoveal density ( $p=0.002$ ,  $r=-0.4$ ). A negative correlation was found between SLICC and superficial whole en face density ( $p=0.0001$ ,  $r=-0.5$ ), superficial parafoveal density ( $p<0.0001$ ,  $r=-0.6$ ), deep whole en face density ( $p<0.0001$ ,  $r=-0.6$ ) and deep parafoveal density ( $p<0.0001$ ,  $r=-0.7$ ). Patients with nephritis displayed reduced parafoveal vessel density and parafoveal thickness compared to those of patients without nephritis ( $p=0.02$  and  $p=0.008$ , figure 1F-G). A positive correlation was found between hydroxychloroquine (HCQ) cumulative dose and both superficial and deep parafoveal density ( $p=0.009$ ,  $r=0.4$  and  $p=0.04$ ,  $r=0.3$ ). Best-corrected visual acuity in SLE positively correlated with superficial whole en face density, superficial parafoveal density, deep whole en

face density, and deep parafoveal density ( $p<0.0001$ ,  $r=0.7$  for all correlations). A negative correlation was found with fovea thickness ( $p=0.01$ ,  $r=-0.5$ ).

Abstract OP0123 – Table 1

	HC (n=20)	SLE (n=26)
Age (years)	46±8.9	49.6±13.6
Female n (%)	16 (80)	23 (88.5)
Disease duration (months)	-	181.5±93
SLEDAI	-	4.3±4.2
SLICC	-	1.9±1.5
HCQ cumulative dose (g)	-	738.8±486.8
Kidney involvement (n/%)	-	10/40
NPSLE (n/%)	-	8/32
aPL positive (n/%)	-	10/40

**Conclusions:** SLE patients, in particular those with kidney involvement, displayed a reduced retinal microvascular density compared with normal subjects. Vessel density provides a quantitative metric of capillary network that correlated with age, best-corrected visual acuity and clinical features as SLE disease activity and damage accrual. Hydroxychloroquine might have a protective role preserving the microvascular structures.

**Disclosure of Interest:** None declared

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OP0124

### IN SLE PATIENTS IN SUSTAINED LOW DISEASE ACTIVITY, NOVEL INTERFERON ASSAYS PREDICT FLARES AND GLUCOCORTICOID REQUIREMENTS

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**Background:** Objectives of therapy in SLE are to maintain low disease activity and minimise glucocorticoid exposure. Disease activity is unpredictable with periods of low disease activity followed by flares. Once disease is controlled, there is an unmet need for predictors of sustained remission or flares to decide when glucocorticoids can be safely tapered. Type 1 interferon (IFN-I) activity is associated with disease activity in SLE. We recently validated two novel assays for IFN-I. First, a 2-score gene expression system that is continuous and accounts for molecularly of the IFN transcriptome. Second, the flow cytometric biomarker tetherin that allows measurement of IFN status in individual cell subsets, with memory B cell tetherin (tetherin) correlating best with disease activity.

**Objectives:** To determine whether IFN assays can predict flare and glucocorticoid requirements in patients with lupus

**Methods:** Retrospective notes review was done in 165 consecutive patients with SLE who submitted IFN biomarker samples between 2011–2015. The reviewer was blinded to biomarker status.

For the interferon scores, RNA was extracted from PBMCs and a custom Taqman array was used to measure expression of 30 interferon stimulated genes normalised to *PP1A* and then calculate IFN Score A (12 genes predominantly responsive to IFN-alpha) and IFN Score B (14 genes also responsive to other IFN subtypes and inflammatory mediators). For tetherin, PBMCs were analysed fresh with conventional surface staining. MFI of CD317 (tetherin) was measured on CD19+CD27+CD38 lymphocytes.

We performed two analyses:<sup>1</sup> In patients in sustained low disease activity (defined as no BILAG A or B in the six months prior to IFN biomarker sampling), prediction of new disease activity in the following six months (defined as new BILAG A or B).<sup>2</sup> The association between IFN biomarkers and change in mean monthly glucocorticoid dose following biomarker sampling (defined as same or increased vs decreased or no glucocorticoid prescription). Since tetherin is measured on B-cells we excluded patients who were B cell depleted after rituximab. IFN biomarkers were compared between groups using Mann-Whitney U Tests.

**Results:** Of 165 patients, 92 were in sustained low disease activity prior to biomarker sampling. Of these, new BILAG A/B activity occurred within 6 months of sampling in 16 (17%). New BILAG A/B activity was associated with higher levels of IFN Score A ( $p=0.027$ ,  $n=83$ ), IFN Score B ( $p=0.097$ ,  $n=83$ ) and tetherin ( $p=0.026$ ,  $n=92$ ).

Of 143 patients with complete data, glucocorticoid doses were increased or maintained after sampling in 45 and decreased or not prescribed in 98. Increased/maintained glucocorticoids were associated with higher IFN Score A ( $p=0.003$ ,  $n=113$ ), IFN Score B ( $p=0.013$ ,  $n=113$ ) and tetherin ( $p=0.043$ ,  $n=84$ ).

After adjustment for age, gender, pre and post-sampling glucocorticoid dose, substantive associations with flare remained for IFN Score A (OR=1.44/unit, 95% CI: 0.998 to 2.082,  $p=0.051$ ) and tetherin (OR=3.135/1000 units, 95% CI: 1.179 to 8.335,  $p=0.022$ ).

**Conclusions:** SLE patients in low disease activity with high IFN Score A, Score B and tetherin levels have an increased risk of disease activity and/or glucocorticoid exposure in the months that follow biomarker testing. There is a potential role for use of these IFN assays as predictive biomarkers in SLE in the future.

**Disclosure of Interest:** None declared

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THURSDAY, 14 JUNE 2018

### The 'A-B-C' of PsA (Assessment, Biologicals, Co-morbidities)

#### OP0125 DAPSA AND ULTRASOUND SHOW DIFFERENT PERSPECTIVES OF PSORIATIC ARTHRITIS ACTIVITY: RESULTS FROM A LONGITUDINAL OBSERVATIONAL STUDY OF PATIENTS STARTING TREATMENT WITH BIOLOGIC DMARDS

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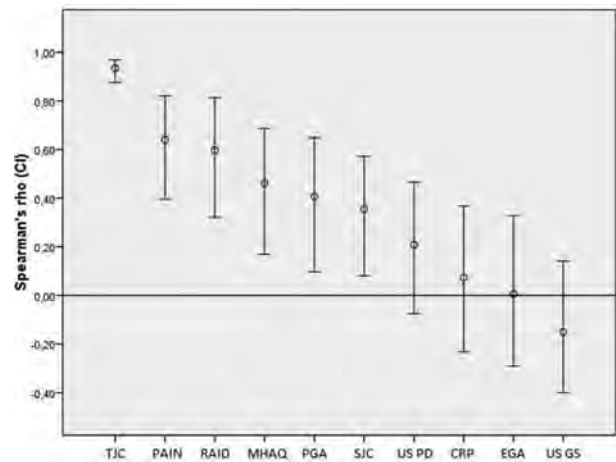
**Background:** Clinical disease activity in patients with psoriatic arthritis (PsA) may be assessed by DAPSA- a sum score of tender (of 68) and swollen (of 66) joints, CRP (mg/dl), patient's global assessment of disease activity (PGA) and patient's pain (0–10 VAS for both). Ultrasound (US) with grey scale (GS) and power Doppler (PD) is used to detect inflammation in joints as well as extra-articular structures. Discrepancies have previously been described between DAPSA and US.<sup>1</sup>

**Objectives:** To explore the associations between DAPSA and US assessments of disease activity during follow-up of patients with PsA starting bDMARD treatment.

**Methods:** Patients with PsA were included when initiating bDMARDs, and examined at 0, 3, 6, 9 and 12 months including 66 swollen/68 tender joint counts (SJC/TJC), examiner's global assessment VAS (EGA), patient reported outcome measures (PROMs; PGA, patient's pain, RAID, MHAQ), laboratory measures (CRP, ESR, calprotectin) and US (46 joints, 8 flexor tendons, 14 entheses and 4 bursae with calculated GS and PD sum scores). DAPSA was calculated. PD sum score zero was defined as US remission. Generalised Estimating Equations (GEE) was used for longitudinal analysis.

**Abstract OP0125 – Table 1** Median (IQR) of clinical, laboratory and US assessments during bDMARD treatment

	Baseline (n=47)	3 months (n=42)	6 months (n=36)	9 months (n=33)	12 months (n=31)
DAPSA	19.8 (13.9–30.9)	13.1 (4.9–20.9)	10.5 (2.6–18.7)	10.2 (3.5–20.5)	9.0 (2.4–20.6)
TJC (of 68)	7 (2–15)	2 (0–11)	1 (0–9)	2 (0–9)	2 (0–11)
SJC (of 66)	1 (0–3)	0 (0–1)	0 (0–1)	0 (0–0)	0 (0–0)
PGA (VAS 0–10)	5.2 (3.3–6.9)	2.8 (1.0–5.1)	2.0 (0.9–4.3)	3.3 (0.5–5.4)	2.7 (0.5–4.9)
PAIN (VAS 0–10)	5.4 (3.0–6.8)	3.1 (1.0–4.1)	2.8 (0.9–5.8)	2.6 (1.1–5.4)	2.2 (0.7–5.4)
MHAQ	0.50 (0.25–0.88)	0.25 (0.00–0.50)	0.13 (0.00–0.44)	0.25 (0.00–0.44)	0.13 (0.00–0.50)
RAID (0–10)	5.1 (4.0–6.0)	2.9 (0.9–5.1)	2.3 (1.3–4.7)	3.0 (0.9–5.2)	2.6 (1.1–4.9)
CRP mg/L	3 (1–7)	1 (1–3)	2 (1–4)	2 (1–3)	2 (1–3)
ESR mm/h	11 (6–17)	6 (3–12)	7 (3–11)	9 (3–13)	7 (4–14)
Calprotectin µg/L	826 (487–1202)	511 (307–741)	431 (305–669)	459 (267–1005)	432 (294–768)
EGA (VAS 0–10)	2.4 (2.0–2.8)	1.5 (1.0–2.2)	1.2 (0.8–1.6)	1.2 (0.8–1.6)	1.0 (0.5–1.2)
Sum score	4 (2–9)	2 (0–5)	2 (0–3)	3 (0–6)	4 (1–8)
GS					
Sum score	1 (0–4)	0 (0–2)	0 (0–2)	0 (0–2)	0 (0–2)
PD					



**Abstract OP0125 – Figure 1.** Baseline correlations with DAPSA

**Results:** 47 patients (mean (SD) age 48.4 (12.8) years, disease duration 12.7 (10.9) years, 60% women) were included (68% biologic-naïve). The figure depicts high correlation between DAPSA and subjective assessments at baseline, while PD sum score was more strongly associated with SJC ( $r=0.49$ ,  $p<0.001$ ), EGA ( $r=0.29$ ,  $p=0.05$ ) and DAS28 ( $r=0.35$ ,  $p=0.015$ ), but not with DAPSA ( $r=0.21$ ,  $p=0.16$ ) or PROMs. There was significant improvement at 3 months in all variables ( $p=0.046$ – $<0.001$ ) (table 1). Longitudinally, TJC and patient's pain had strongest association with DAPSA (standardised  $\beta$  0.86 vs 0.52, both  $p<0.001$ ). DAPSA remission was obtained in 27%–33% of the patients and PD remission in 60%–70%, but their association was weak and not statistically significant (OR 1.4, 95% CI: 0.69 to 2.95,  $p=0.33$ ).

**Conclusions:** In our observational PsA cohort DAPSA was mostly influenced by TJC and patient's pain and had no significant association with a comprehensive US examination. This finding indicates possible limitations of using DAPSA in T2T strategy in PsA.

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**Disclosure of Interest:** None declared

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#### OP0126 EVALUATING LOW DISEASE ACTIVITY DEFINITIONS IN PSORIATIC ARTHRITIS USING ULTRASOUND

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**Background:** Cut offs for low disease activity (LDA) using psoriatic arthritis (PsA) specific composite scores have recently been proposed.<sup>1–3</sup> Whether these definitions adequately reflect the absence of inflammation is unknown.

**Objectives:** To evaluate these definitions against a low level of activity according to ultrasound examination.

**Methods:** We performed a prospective study on 83 PsA patients undergoing clinical and ultrasound examinations at two study visits scheduled 6 months apart. LDA was assessed using the Disease Activity index for Psoriatic Arthritis (DAPSA $\leq 14$ ), the Psoriatic Arthritis Disease Activity Score (PASDAS  $\leq 3.2$ ), the Composite Psoriatic Disease Activity Index (CPDAI $\leq 4$ ), the Disease Activity Score 28 CRP (DAS28-CRP $\leq 2.8$ ) and the Minimal Disease Activity criteria (MDA).

Ultrasound (US) evaluation was performed at 68 joints (evaluating synovia, peritendinous tissue, tendons and bony changes) and 14 entheses.

Minimal ultrasound disease activity (MUDA) was defined as a Power Doppler (PD) score  $\leq 1$ , respectively at joints, peritendinous tissue, tendons and entheses.

**Results:** LDA was present in 33.7%–65.0% of patients at baseline and in 44.3%–80.6% at follow-up examination, depending on the criteria used. MUDA was observed in 16.9% at baseline and in 30% at follow-up.

At baseline only the DAPSA-LDA definition was useful to identify MUDA patients (78.6% of patients identified correctly), whereas at follow up >80% of MUDA



patients were correctly classified as LDA according to DAPSA, PASDAS, CPDAI and DAS28-CRP.

Only DAPSA (Sensitivity (S)=88.2%, Specificity (Sp)=40.5,  $p=0.033$ ), PASDAS (S=88.2%, Sp=55.0%,  $p=0.002$ ) and the MDA criteria (S=71.4%, Sp=67.3%,  $p=0.003$ ) were able to discriminate patients with and without MUDA at follow-up. A global ultrasound inflammation subscore for joints and entheses (GUIS-j/e), containing the above mentioned US variables, was significantly higher in patients with active disease versus patients in LDA according to DAPSA ( $p=0.002$ ) and PASDAS ( $p=0.013$ ) at baseline and DAPSA ( $p=0.007$ ), PASDAS ( $p=0.001$ ), CPDAI ( $p=0.021$ ) and the MDA criteria ( $p<0.001$ ) at follow up.

**Conclusions:** Of all tested LDA definitions, DAPSA was overall the most efficacious in differentiating between high and low ultrasound scores and better identified patients with MUDA as compared to the other tested scores.

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OP0127

#### CAN ACHIEVING MINIMAL DISEASE ACTIVITY (MDA) PREVENT PROGRESSION OF SUBCLINICAL ATHEROSCLEROSIS AND ARTERIAL STIFFNESS? A TWO-YEAR PROSPECTIVE COHORT STUDY IN PSORIATIC ARTHRITIS

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**Background:** PsA patients have higher CVD risk due to underlying inflammation. While achieving MDA was associated with articular benefits, its effect on CVD risk remained uncertain

**Objectives:** To investigate effect of achieving MDA on subclinical atherosclerosis and arterial stiffness

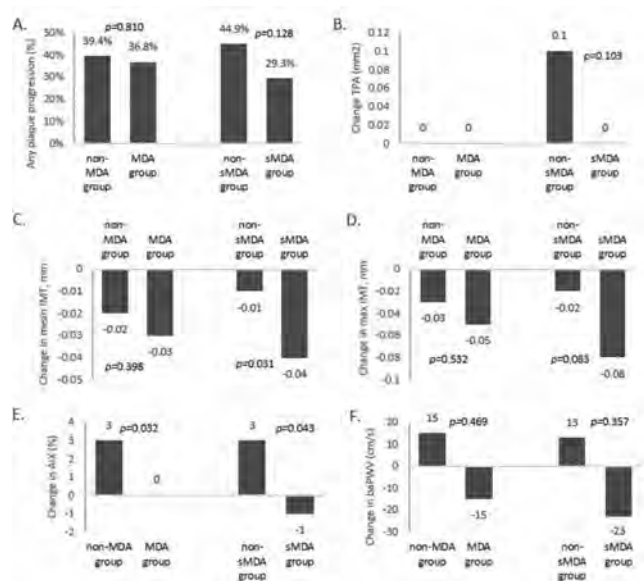
**Methods:** Subjects without CVD were recruited and received protocolised treatment aiming at MDA for 2 years. High-resolution ultrasound (for subclinical atherosclerosis) and arterial stiffness were assessed yearly. The primary objective was to investigate the effect of achieving MDA (MDA group) at 12 months on the progression of subclinical atherosclerosis (carotid intima-media thickness [IMT] and plaque) over 2 years. Secondary objectives were to compare 1) changes in arterial stiffness (branchial-ankle pulse wave velocity [PWV]) and augmentation index [AIX] over 2 years between MDA and non-MDA group; 2) changes in vascular outcomes in patients who could or could not achieve sustained MDA (sMDA, defined as achieving MDA from month 12 to 24). Carotid plaque progression was defined as an increase in number/region harbouring plaque compared with baseline

**Results:** 90 patients [male: 52 (58%); age: 50±11] were included. At 24 months, 62 (69%) were on csDMARDs, 20 (22%) were on anti-TNF- $\alpha$  and 8 (9%) were on Secukinumab. Proportion of patient achieved MDA increased significantly (baseline: 17%; 12 months: 64%; 24 months: 69%) after intensive treatment. Vascular outcomes were similar between MDA and non-MDA group (figure 1). 41 (46%) patients achieved sMDA. At baseline, a higher prevalence of subjects in the non-sMDA group were smokers, treated with NSAIDs and csDMARDs; fewer subjects were on bDMARDs, and they had higher disease activity compared with the sMDA group. 34 (38%) of them had plaque progression and prevalence was numerically higher in the non-sMDA group [22 (45%) vs 12 (29%),  $p=0.13$ ]. Using multivariate analysis, achieving sMDA had protective effect on plaque progression [OR=0.27, 95% CI: 0.09 to 0.84,  $p=0.03$ ] after adjustment of baseline difference (table 1). Achieving sMDA was also related to less progression of total plaque area (TPA), mean and maxIMT, PWV and AIX (table 1)

**Conclusions:** Effective suppression of inflammation by achieving sustained MDA may prevent subclinical atherosclerosis and arterial stiffness progression in PsA patients

**Abstract OP0127 – Table 1.** Multivariate analysis on vascular outcomes

Outcome	Baseline covariates	OR/ $\beta$	95% CI	p
<b>Plaque progression</b>	Age	1.07	1.01–1.13	0.02
	VAS Physician Global	0.96	0.93–0.99	0.02
	LDL-C	2.63	1.31–5.49	0.01
	bDMARDs use	0.11	0.01–0.65	0.02
<b>TPA change</b>	sMDA	0.27	0.09–0.85	0.02
	BMI	-0.43	-0.76, -0.10	0.01
	LDL-C	2.83	0.72–4.93	0.01
<b>meanIMT change</b>	sMDA	-3.92	-7.18, -0.66	0.02
	bDMARDs use	-0.03	-0.07, -0.00	0.03
	sMDA	-0.04	-0.07, -0.01	0.01
<b>maxIMT change</b>	Any plaque progression	-0.07	-0.13, -0.01	0.02
	sMDA	-0.07	-0.13, -0.01	0.03
<b>PWV change</b>	Age	4.95	0.92–8.99	0.02
	PWV	-0.48	-0.68, -0.29	<0.001
	sMDA	-71.4	-143.2, 0.23	0.05
	sMDA	-71.4	-143.2, 0.23	0.05
<b>AIX change</b>	Sex	3.32	0.11–6.56	0.04
	sMDA	-3.06	-6.07, -0.05	0.05



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**Disclosure of Interest:** None declared

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OP0128

#### THE PHENOTYPE OF AXIAL PSORIATIC ARTHRITIS: IS IT DEPENDENT ON HLA-B27 STATUS?

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**Background:** Up to 50% of patients with psoriatic arthritis (PsA) have associated spinal involvement similar to ankylosing spondylitis (AS). HLA-B27 positivity is lower in PsA compared to other SpA which may affect the disease phenotype.

**Objectives:** Our aim was to compare axial phenotype in PsA patients with and without HLA-B27 with AS patients.

**Methods:** A large international collaboration collected BASDAI, CRP, HLA-B27 status and sacroiliac joints (SIJ) and spine radiographs. These were read centrally by two blinded readers using consensus on the modified New York criteria, mSASSS and PASRI. AP spine radiographs were examined for symmetry (score difference  $\geq 2$  between sides) and morphology of syndesmophytes (typical marginal vs atypical chunky/non-marginal) were compared.

**Results:** Eight sites contributed 244 (25% HLA-B27+) PsA patients and 198 (75% HLA-B27+) AS patients. Mean BASDAI, mSASSS and PASRI were higher in AS. When categorised by diagnosis and HLA-B27 there were significant differences for age, sex, disease duration, mSASSS, PASRI and syndesmophyte symmetry. Regression analysis, with mSASSS and PASRI as dependent variables revealed significant associations with age, sex, duration of disease, and group (HLA-B27 and diagnosis).

Binary multivariate logistic regression was used to investigate associations of age, sex, HLA-B27 status, diagnosis (PsA v AS) and concomitant diabetes with radiographic features. Sacroiliac symmetry showed no significant associations, whilst syndesmophyte symmetry was associated with increasing age and HLA-B27 positivity. Typical marginal syndesmophytes were associated with age, HLA-B27 status and disease duration: in the cervical spine significant associations with age, sex and HLA-B27 status; in the lumbar spine with age, HLA-B27 and diagnosis. Atypical chunky syndesmophytes were associated only with increasing age and male sex.

Abstract OP0128 – Table 1

	Psoriatic arthritis		Ankylosing spondylitis		Statistic	p (2 way)
	B27- (n=184)	B27+ (n=60)	B27- (n=50)	B27+ (n=148)		
Age, y mean (sd)	55.3 (13.4)	50.5 (13.7)	48.5 (14.1)	48.5 (14.3)	7.7*	0.0001
Males n (%)	106 (58)	38 (63)	32 (64)	114 (77)	13.9+	0.003
Duration of disease, y mean (sd)	11.8 (10.3)	14.2 (11.0)	8.4 (9.5)	13.3 (12.3)	3.3*	0.02
Symmetry at SIJ n (%)	165 (90)	54 (90)	43 (86)	132 (89)	7.1+	Ns
Symmetry in spine n/N (%)	36/62 (58)	21/29 (72)	14/24 (58)	67/84 (80)	9.5+	0.02
Marginal syndesmophytes, n (%)	94 (51)	39 (65)	25 (50)	89 (60)	5.5+	Ns
Atypical syndesmophytes, n (%)	41 (22)	17 (28)	12 (24)	29 (20)	1.9+	Ns

\* F statistic from one way analysis of variance. +chi squared statistic

**Conclusions:** This analysis suggests less difference in radiographic phenotype between AS and axial PsA than previously thought. HLA-B27 negative PsA patients have less severe disease as measured by mSASSS and PASRI with less typical marginal syndesmophytes and symmetry, whilst HLA-B27 positive PsA appears similar to AS.

**Disclosure of Interest:** None declared

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#### OP0129 DRUG SURVIVAL ON ANTI-TNF-ALPHA IN PSORIATIC ARTHRITIS PATIENTS WITH AXIAL INVOLVEMENT AND ANALYSIS OF PREDICTORS

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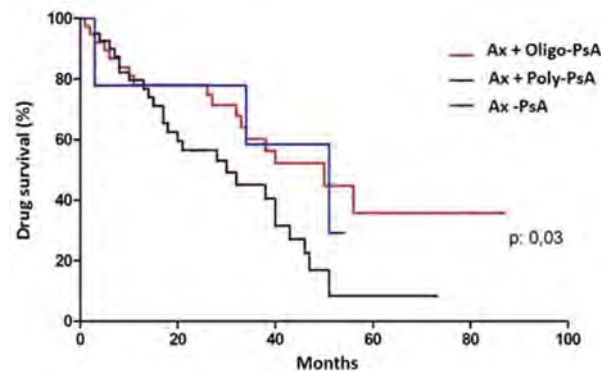
**Background:** A few studies have focused on the clinical outcomes in predominant axial Psoriatic Arthritis (PsA) patients treated with anti-TNF- $\alpha$  agents<sup>1-3</sup> in real-life settings.

**Objectives:** Primary endpoint: to evaluate drug survival on anti-TNF- $\alpha$  agents in PsA patients with axial involvement or axial and either polyarticular or oligoarticular peripheral arthritis. Secondary endpoints: to evaluate the presence of any predictor of discontinuation of anti-TNF in PsA patients with axial involvement and to investigate whether peripheral arthritis may impact the discontinuation for ineffectiveness in patients with axial disease.

**Methods:** 415 biologic therapy-naive PsA patients (CASPAR criteria) starting a first TNF-inhibitor from January 2010 to December 2016 were screened. Among these, 87 had axial involvement (ASAS criteria) with imaging arm (X-ray or MRI) and were enrolled: 40 with axial and polyarticular peripheral PsA (Axe +Poly PsA), 38 with axial and oligoarticular peripheral PsA (Axe +Oligo PsA) and 9 with only axial disease (Ax-PsA). At baseline and at last available visit or drug discontinuation, we collected age, gender, disease duration, BMI, HLA-B27, nail psoriasis and/or dactylitis, TJC, SJC, ESR, CRP, enthesitis, LEI, DAPSA, BASDAI, ASDAS-CRP, PASI, HAQ, intake of glucocorticoids and DMARDs, anti-TNF therapy discontinuation and reasons of discontinuation. Drug

survival was evaluated by Kaplan-Meier life table method, comparison of survival curves with Log-rank test and baseline predictors of drug discontinuation with Cox regression analysis.

**Results:** At baseline, Axe +Poly PsA patients had significantly higher peripheral (DAPSA) and axial disease activity (BASDAI, ASDAS-CRP). Stratifying patients by subset of disease, the median of treatment was 51 months (95% IQR 24.87–77.13) for Ax-PsA group, 50 months (95% IQR 28.39–71.61) for Axe +Oligo PsA group, 30 months (95% IQR 11.84–48.15) for Axe +Poly PsA group (figure 1). Axe +Oligo PsA patients had significantly higher persistence on TNFi rather than Axe +Poly PsA patients (log rank test, p=0.03). Axe +Poly PsA patients had higher risk of stopping TNFi (Cox regression, HR 3.75) and significantly higher percentage of discontinuation for ineffectiveness rather than for an adverse event ( $\chi^2$  test, p=0.0009). At last observation, Axe +Poly PsA patients had higher DAPSA but no difference in axial disease activity (t-STUDENT test, Mann-Whitney test).



Abstract OP0129 – Figure 1. Drug survival on TNF-inhibitor in Ax-PsA, Axe+Oligo-PsA and Axe+Poly-PsA patients (Kaplan-Meier life table method, log rank test)

**Conclusions:** PsA subsets seems to have different features, behaviour, clinical response and drug survival on TNF-inhibitors. Axe +Poly PsA subset seems to be more aggressive and difficult to treat. Anti-TNF- $\alpha$  blockers may perform differently in PsA: a more accurate analysis of the clinical disease subsets may improve our knowledge and better management of PsA in daily practice.

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**Disclosure of Interest:** None declared

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#### OP0130 RISK OF CANCER IN PATIENTS WITH PSORIASIS/ PSORIATIC ARTHRITIS: A POPULATION-BASED STUDY IN THE PROVINCE OF BRITISH COLUMBIA

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**Background:** Psoriasis (PsO) is a relapsing chronic autoimmune disease of the skin. Up to one-third of patients (pts) also develop inflammatory arthritis, known as psoriatic arthritis (PsA). PsO/PsA, like other forms of chronic inflammatory arthritis, are often associated with complications such as cardiovascular disease and infections. However, data on the risk of cancer in pts with PsO/PsA at population level are limited.

**Objectives:** To assess the risk of cancer in pts with newly diagnosed PsO/PsA at the population level.

**Methods:** We created a population-based matched retrospective cohort of PsO/PsA pts diagnosed between 1 January 1997 and 31 December 2012 using administrative health data from British Columbia, Canada. We identified all incident cases of PsO/PsA and an equal number of controls matched on sex, age and calendar year. PsO/PsA cases met  $\geq 1$  of the following: 1 diagnostic code for PsO/PsA by a rheumatologist/dermatologist;  $\geq 2$  diagnostic codes for PsO/PsA,  $\geq 2$  months apart in a 2 year period by a non-rheumatologist/dermatologist; or  $\geq 1$  hospitalisation with diagnostic code for PsO/PsA. We evaluated incident cancers during follow-up from the Cancer Registry in both cohorts. Adjusted risk of cancers

was estimated using a generalised estimating equation extension of multivariate Poisson regression models.

**Results:** We identified 81 568 incident cases of PsO/PsA (mean age 48.5 years [SD 17.8], 51.5% female). Individuals with PsO/PsA were at significantly higher risk of being diagnosed with 8/41 types of cancer examined, including eye and orbit (4 fold), female genital (3 fold), non-melanoma skin (2 fold), prostate (males; 1.1 fold) (table 1). Incidence of rectal and colon cancer was lower among PsO/PsA pts relative to the non-PsO/PsA cohort (table 1).

**Abstract OP0130 – Table 1.** Incidence Rate (IR) and Incidence Rate Ratio (IRR) of Cancer Among PsO/PsA Pts Compared With the General Population

Outcome	PsO/ PsA events	Non- PsO/ PsA events	PsO/PsA follow-up (PY)	Non-PsO/ PsA follow-up (PY)	PsO/ PsA IR (per 100,000 PY)	Non- PsO/ PsA IR (per 100,000 PY)	IRR (95% CI)
Eye and orbit	13	<5	623,843.5	<5	2.08	-	4.25 (1.21–14.91)
Female genital other than cervix uteri, corpus uteri and ovary	55	21	623,625.8	611,542.1	8.81	3.43	2.57 (1.55–4.25)
Other urinary	31	16	623,818.6	611,585.4	4.97	2.62	1.90 (1.04–3.47)
Non-melanoma skin	401	217	621,233.8	610,223.9	64.54	35.56	1.82 (1.54–2.14)
Lung	705	589	622,877.2	610,834.8	113.18	96.42	1.17 (1.05–1.31)
Prostate	760	664	620,065.8	608,124.9	122.57	109.19	1.12 (1.01–1.25)
Melanoma	218	200	6 22 791	610,672.1	35.00	32.75	1.07 (0.88–1.29)
Colon	286	332	622,845.1	610,410.5	45.91	54.39	0.84 (0.72–0.99)
Rectum	157	194	623,196.9	610,811.7	25.19	31.76	0.79 (0.64–0.98)

PY=patient years

**Conclusions:** This general population-based study demonstrates that pts with PsO/PsA have an increased risk of several types of cancer, and a decreased risk of rectal and colon cancer. This association highlights the need to further explore potential risk factors and pathways that contribute to these complications.

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#### OP0131 INNATE LYMPHOID CELLS CORRELATE WITH DISEASE ACTIVITY AND BONE REMODELLING IN PSORIATIC ARTHRITIS

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**Background:** Evaluation of actual immunopathology in psoriatic arthritis (PsA) is challenging. Current composite measures approved for PsA are very useful tools to assess disease activity in clinical routine. Nonetheless, because of subjective patients' estimations that widely affect the scoring, in particular the distinction between remission and low disease activity is a common question of debate.

Innate lymphoid cells (ILC) subsets may couple different aspects of PsA disease activity.

**Objectives:** To address whether PsA is associated with an altered composition of innate lymphoid cells and whether such changes are associated with disease activity and structural damage in PsA.

**Methods:** 124 patients satisfying the Classification Criteria for Psoriatic Arthritis (CASPAR) and 26 healthy volunteers were enrolled in the study. Information regarding clinical features, laboratory parameters were collected and disease activity score 28 (DAS28), disease activity in psoriatic arthritis (DAPSA), minimal disease activity score (MDA) were calculated. MRI and high-resolution peripheral CT were taken and PsA MRI score (PsAMRIS) was assessed. Flow cytometric analysis was performed and IFNg-producing ILC1s, IL-4/IL-5-producing ILC2s and IL-17/IL-22-producing ILC3s were identified among ILCs. Multivariate linear regression and Receiver-Operating Characteristic (ROC) Curve analysis was performed using the IBM SPSS Statistics software.

**Results:** Total number of circulating ILCs were increased in PsA patients compared to healthy controls (p<0,001). Linear regression analyses of the relationship between disease activity and circulating ILC counts showed that ILC2 negatively and ILC1 and ILC3 positively correlated with DAPSA score. The strongest correlation was observed when the ratio of ILC2 to ILC3 was analysed (R=-0.5709; p<0.0001). ILC2/3 ratio was also reduced in patients with active psoriatic skin disease, presence of enthesitis or a history of concomitant uveitis. Extend of synovitis or tenosynovitis or presence of bone erosions or osteophytes on MRI was inversely correlated with the ILC2/3 ratio (R=-0.6753; p<0.0001, R=-0.5828; p=0.0011 and p<0.001 respectively). Consistently, presence of erosions and/or osteoproliferation assessed by HR-pQCT was correlated with a significant lower ILC2/3 ratio. Furthermore, ROC Curve was used to test the performance of the ILC2/3 ratio as marker in differentiating between remission and disease activity of PsA. Indeed, a cut-off 0.57 exhibited highest sensitivity (92.9%) and a 84.7% specificity in identifying remission.

**Conclusions:** The ILC2/3 ratio correlates with various facets of PsA manifestations and might be a useful tool to evaluate disease activity in PsA patients.

**Disclosure of Interest:** None declared

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#### OP0132

#### STRUCTURAL AND MICROSTRUCTURAL INTRA-ARTICULAR BONE CHANGES AT THE METACARPAL HEADS IN PATIENTS WITH PSORIATIC ARTHRITIS COMPARED TO CONTROLS: A HR-PQCT STUDY

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**Background:** Located inside the joint capsule,<sup>1</sup> the entire metacarpal head (MCH) is directly exposed to intra-articular inflammatory milieu in patients with psoriatic arthritis (PsA). We hypothesise that bone loss and new bone formation in the MCH will be more prominent in PsA compared to healthy controls.

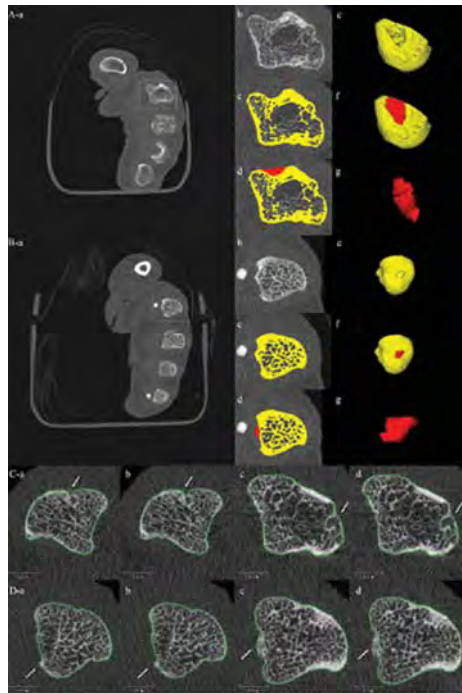
**Objectives:** To investigate structural (bone erosion and enthesiophyte) and microstructural intra-articular bone changes in patients with PsA at the second and third MCH (MCH 2 and 3) compared with controls.

**Methods:** 139 subjects (77PsA, 62 control) underwent HR CT scanning at the MCH 2 and 3 and distal radius. 15 patients with joint destruction<sup>2</sup> were excluded from further analysis. An integrative CART-EBEE approach was developed to investigate the structural and microstructural bone changes. CART method (AB) was used to calculate volume of bone erosion and enthesiophyte [Crop of metacarpal bone(a,b); Automated segmentation of periosteal surface (c,e);Restoration of the missing cortical boundary based on anatomic curve(d,f);Three-dimensional calculation of volume(g)]; EBEE method was used to calculate volumetric bone mineral density (vBMD) and microstructure before and after exclusion of Bone Erosion (C) and Enthesiophyte (D).

**Results:** 62 patients with PsA and controls were comparable in age, gender and body mass index. PsA patients had a significantly increased number (mean  $\pm$ SD/patient 2.4 $\pm$ 1.4 vs 1.3 $\pm$ 1.1, p<0.001) and total volume of enthesiophytes (8.75  $\pm$ 6.92 vs 4.36 $\pm$ 4.90 mm<sup>3</sup>, p<0.001); but a similar number of bone erosion (mean  $\pm$ SD/patient 2.9 $\pm$ 1.2 vs 2.7 $\pm$ 1.4, p=0.408) and a trend suggestive of an increase in total volume of bone erosion (11.88 $\pm$ 7.82 vs 9.64 $\pm$ 5.96 mm<sup>3</sup>, p=0.076) per person compared with control. Depth of each individual bone erosion was greater in PsA than control; while no differences in the maximal height of each individual enthesiophyte was found between PsA and control. With regards to the microstructure, PsA showed a significantly decreased total vBMD, cortical vBMD (Ct.vBMD) and Ct. thickness at the distal radius; while a preferential bone loss at the trabecular (Tb.) compartment [Tb. vBMD; trabecular bone volume



fraction [BV/TV] and Tb. thickness] was observed at the MCH compared to control. After excluding of enthesiophyte, a further deterioration in the Ct. compartment (vBMD, perimeter, thickness) in PsA patients was observed. Regression model in PsA and controls indicated that PsA was independently associated with an increased total volume of enthesiophytes per person. Regression model in PsA showed that CRP, older age and higher BMI were independently associated with an increase in the total volume of bone erosion. On the other hand, older age was independently associated with an increase in total volume of enthesiophyte per person.



**Conclusions:** Intra-articular trabecular bone loss and enthesal new bone formation was more prevalent in the MCH of patients with PsA.

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**Disclosure of Interest:** None declared

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THURSDAY, 14 JUNE 2018

## RA: such a pain, and beyond

OP0133

### UNACCEPTABLE, REFRACTORY PAIN DESPITE INFLAMMATION CONTROL IN EARLY RHEUMATOID ARTHRITIS AND ITS RELATION TO TREATMENT STRATEGY: RESULTS FROM THE RANDOMISED CONTROLLED SWEFOT TRIAL

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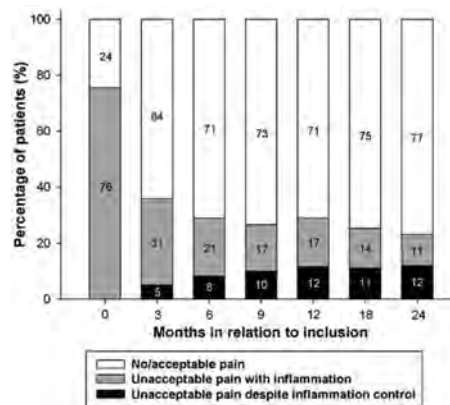
**Background:** Pain is a major concern of RA patients and earlier work has defined the level considered not acceptable by patients (unacceptable pain according to the patient acceptable symptom state (PASS)<sup>1</sup>). While a lot of focus has been put on the occurrence and management of inflammatory pain, less is reported on refractory pain despite inflammation control, and its pattern in early RA.

**Objectives:** The aim of this study was to investigate the prevalence of unacceptable pain despite inflammation control during the first 2 years after treatment start in new-onset RA patient and to compare the impact of biological vs conventional combination therapy on the occurrence of this pain status.

**Methods:** The SWEFOT (SWedish FarmacoTherapy) trial was designed as a randomised, active-controlled, open-label study, enrolling early (<1 year) RA patients Oct 2002 to Dec 2005 After a 3 month run-in period on methotrexate (MTX), patients reaching DAS28  $\leq 3.2$  continued monotherapy (n=147), while the others were randomised to addition of infliximab (IFX; n=128) or sulfasalazine +hydroxychloroquine (SSZ+HCQ; n=130). Results for disease activity and radiographic data were published earlier. Here, we used a measure of unacceptable pain despite inflammation control as outcome (combining VAS pain  $>40$  mm<sup>100</sup> with CRP  $<10$  mg/L<sup>2</sup> and  $\leq 1$  swollen joint (of 28)). When comparing the randomised arms, last observation carried forward in case of protocol breach was used, while for analyses of the whole material we used all data irrespective of protocol breach. Differences in prevalence were analysed by Mc Nemar's test, while differences between patients randomised to IFX vs SSZ+HCQ as well as between EULAR response groups were estimated by logistic regression, adjusting for age, sex and VAS pain at baseline.

**Results:** In the whole material (including all 3 groups, n=405), the frequency of unacceptable pain despite inflammation control increased gradually from inclusion, reached 12% at 1 year (difference from inclusion;  $p<0.001$ ), and then remained stable until the 2 year follow-up; at that point accounting for more than half of all unacceptable pain (figure 1). The frequency was unrelated to EULAR response from inclusion to the 2 year follow-up (11.4% of good responders vs 10.4% of non-responders,  $p=0.95$ ). Furthermore, no difference in unacceptable pain despite inflammation control at 2 years was found between patients randomised to IFX vs SSZ+HCQ, (adjusted odds ratio 1.1 [95% CI: 0.5 to 2.4];  $p=0.75$ ).

**Conclusions:** After 2 years of early active treatment in new-onset RA patient, a substantial portion had unacceptable pain despite inflammation control. This pain status was as common in EULAR good responders as in non-responders and no difference was found between patients randomised to IFX compared to SSZ+HCQ. These data are in line with insufficient effects of current treatment strategies to prevent development of inflammation-independent pain in a subgroup of patients, strongly warranting alternative treatment strategies in these patients.



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- [2] Lourduoss, et al. *Arthritis Care Res*. doi:10.1002/acr.23245

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OP0134

### MULTIFACTORIAL EXPLANATORY MODEL OF FATIGUE IN PATIENTS WITH RHEUMATOID ARTHRITIS: A PATH ANALYSIS

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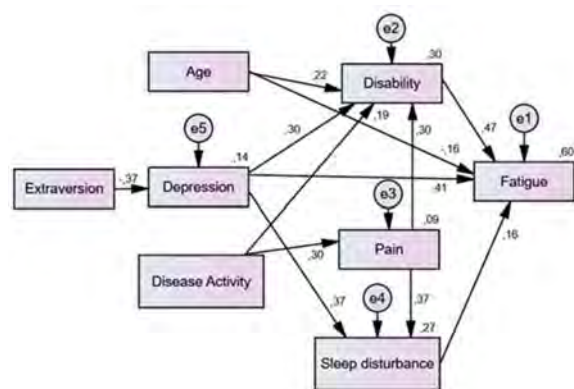
**Background:** Fatigue is one of the most prevalent and disabling symptoms among patients with Rheumatoid Arthritis (RA). However, it is also one of the most

neglected by health professionals. Much of this problem is due to health professionals' poor understanding of the etiology of fatigue and, also, the absence of effective strategies to prevent or treat it.

**Objectives:** This study aimed at developing a multidimensional explanatory model of fatigue in patients with RA as means to foster better understanding and care of this symptom.

**Methods:** This was an ancillary analysis of an observational, cross-sectional, single centre study. Patients completed a questionnaire that included demographic data and measures of sleep (0–10 Numeric Rating Scale (NRS)), pain (0–10 NRS), disability (HAQ), anxiety and depression (HADS), and personality (TIPI). Fatigue was assessed by the Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F). Disease activity (DAS28-CRP3v) and haemoglobin levels were also assessed. Path analysis was performed to test and improve a hypothesised model for fatigue.

**Results:** In total, this analysis included 142 patients (83.1% females, mean (SD) age of 61.1 (11.7) years). The final path analysis model (figure 1) presented acceptable fit (Goodness of Fit Index, GFI=0.92; Comparative Fit Index, CFI=0.89; Root Mean Square Error of Approximation, RMSEA=0.10), and explained 60.0% of the variance of fatigue. Depression and disability had the greater direct influences upon fatigue ( $\beta=0.412$ ;  $p<0.001$  and  $\beta=0.465$ ;  $p<0.001$ , respectively). Sleep disturbance also influenced directly fatigue but at a lower intensity ( $\beta=0.157$ ;  $p=0.007$ ). Disease activity and pain had only an indirect influence on fatigue through disability and sleep disturbance ( $\beta=0.149$ ,  $p=0.005$ , and  $\beta=0.199$ ,  $p=0.005$ , respectively). Age was negatively associated with fatigue ( $\beta=-0.162$ ,  $p=0.003$ ). Extroverted patients presented less depressive symptoms and, consecutively, less fatigue ( $\beta=-0.224$ ,  $p=0.002$ ).



Abstract OP0134 – Figure 1 Final path analysis model with standardised direct coefficients.

Goodness of fit index=0.92; Comparative fit index=0.89; Root mean square error of approximation=0.10.

All coefficients in the model presented  $p<0.05$ .

**Conclusions:** Depression, disability and sleep disturbance appear to be the main factors explaining fatigue in patients with RA. Disease activity and pain seem to play only a secondary role. These findings foster a shift in the paradigm of patient care towards a more holistic management of fatigue, integrating adjunctive therapies in association with measures driven solely towards abrogation of the inflammatory process.

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**OP0135 FOETAL-NEONATAL AND MATERNAL OUTCOMES IN WOMEN WITH RHEUMATOID ARTHRITIS**

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**Background:** Pregnancy involves adaptation to the immune system to prevent rejection of the foetus and this might have consequences on the activity of the rheumatoid arthritis (RA). Equally the aberrant immunity and disease activity of the RA might influence the pregnancy and foetal-neonatal outcomes.

**Objectives:** This study was designed to estimate the risk of adverse foetal-neonatal and maternal outcomes in pregnancies in women with RA.

**Methods:** We identified 2,350,339 singleton pregnancies using the Taiwan National Health Insurance database and birth registry between 2001 and 2012. Maternal history of RA, SLE, Sjögren's syndrome, systemic sclerosis, vasculitis and poly/dermatomyositis were ascertained; among them, 845 individuals had RA. Odds ratios (ORs) and 95% confidence intervals (CIs) for pregnancy outcomes were estimated using an adjusted generalised estimating equation model.

**Results:** Pregnancies in women with RA were associated with an OR (95% CI) of 1.65 (1.37–1.98) for low birthweight (<2500 g) (n=114), 1.41 (1.128–1.68) for prematurity (<37 week) (n=124), and 1.62 (1.36–1.92) for small for gestational age (n=132). Maternal outcomes in pregnancies of women with RA were just associated with an OR (95% CI) of 1.34 (1.06–1.68) for preterm labour (n=74). Women with RA did not have an increased risk of post-partum death, cardiovascular complications, surgical complications, and the other systemic organ dysfunction.

Abstract OP0135 – Table 1

Foetal-neonatal outcomes in pregnancies of women with RA, SLE, Sjögren's syndrome, systemic sclerosis, vasculitis and poly/dermatomyositis (different AIRDs).

	RA	SLE	Sjögren's syndrome	Systemic sclerosis	Vasculitis	Poly/dermatomyositis
Stillbirth	1.91 (0.99-2.98)	3.43 (2.71-4.33)*	1.29 (0.56-3.11)	1.58 (0.22-11.1)	N/A	1.21 (0.17-8.57)
exposed stillbirth	1.06 (0.15-7.58)	0.48 (0.07-3.48)	N/A	N/A	N/A	N/A
unexposed stillbirth	1.69 (0.95-2.71)	3.75 (2.97-4.75)*	1.44 (0.60-3.46)	1.73 (0.24-12.3)	N/A	1.34 (0.19-9.49)
Low birth weight (<2500 g)	1.63 (1.37-1.98)*	2.36 (2.07-2.56)*	2.06 (1.34-3.16)*	2.46 (1.40-4.32)*	0.71 (0.18-2.86)	2.22 (1.34-3.69)*
Pretermity (<37 week)	1.41 (1.18-1.68)*	2.34 (2.14-2.56)*	1.36 (0.95-1.75)	2.34 (1.39-3.95)*	1.14 (0.45-3.05)	1.71 (1.02-2.90)*
Small for gestational age	1.62 (1.36-1.92)*	2.43 (2.21-2.66)*	1.93 (1.58-2.48)*	2.11 (1.22-3.63)*	0.53 (0.14-2.10)	1.51 (0.88-2.60)
Large for gestational age	0.31 (0.39-0.87)	0.34 (0.27-0.42)	0.59 (0.33-0.77)	0.13 (0.02-1.03)	0.64 (0.21-1.99)	0.76 (0.36-1.60)
Apgar score 1 min (<7)	0.94 (0.65-1.40)	3.02 (2.58-3.59)*	2.45 (1.41-4.22)*	1.93 (0.63-5.97)	1.1 (0.16-7.91)	1.82 (1.02-3.26)*
Apgar score 5 min (<7)	0.17 (0.02-1.21)	2.97 (1.83-5.01)*	0.97 (0.24-3.89)	2.48 (1.45-4.22)*	N/A	1.83 (0.26-13.6)
Fetal distress	1.21 (0.93-1.57)	1.33 (1.13-1.56)*	1.81 (1.28-2.55)*	2.59 (1.24-4.95)*	N/A	1.95 (1.02-3.75)*
Fetal abnormalities, any	1.15 (0.89-1.50)	1.25 (1.06-1.48)*	1.29 (0.88-1.87)	1.45 (0.60-3.48)	0.80 (0.26-2.31)	1.24 (0.56-2.77)
Central nervous system malformations	1.71 (0.85-3.03)	1.39 (0.84-2.33)	2.14 (0.80-5.71)	N/A	N/A	N/A
Chromosomal abnormalities	1.34 (0.64-2.81)	0.63 (0.38-1.03)	N/A	N/A	N/A	N/A
Decreased fetal movements	0.59 (0.31-1.14)	0.46 (0.29-1.24)	0.41 (0.13-1.27)	0.92 (0.13-6.21)	0.98 (0.14-6.83)	0.59 (0.08-4.18)
Obstetrical abnormalities	1.51 (1.06-2.17)*	1.34 (1.06-1.70)*	2.41 (1.72-3.36)*	1.42 (0.35-5.87)	N/A	2.64 (1.19-6.33)*

\*Adjusted for age, sex, Charlson comorbidity index, urbanization, income, occupation, birth year, maternal nationality.  
 Abbreviation: AIRDs, autoimmune rheumatic diseases; RA, rheumatoid arthritis; N/A, not applicable; SLE, systemic lupus erythematosus.  
 \*p<0.05

**Conclusions:** Pregnancies in women with RA were at a higher risk for multiple adverse foetal-neonatal outcomes, especially low birthweight (<2500 g), prematurity (<37 week), and small for gestational age. Maternal outcomes showed that just preterm labour was more common in women with RA. Women with RA should not be discouraged to seek pregnancy based on the disease alone.

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OP0136

### SIBLINGS OF PATIENTS WITH RHEUMATOID ARTHRITIS ARE AT INCREASED RISK OF ACUTE CORONARY SYNDROME

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**Background:** Patients with rheumatoid arthritis (RA) are at increased risk of cardiovascular disease such as acute coronary syndromes (ACS), which cannot entirely be explained by traditional cardiovascular risk factors. Studies have shown an association between RA disease severity and risk of ACS, speaking for a contribution of the RA disease *per se* to the excess ACS risk. In a recent report, however, we demonstrated that despite more efficient control of inflammation in RA during the recent years, the excess risk for ACS among patients with RA compared to the general population remains<sup>1</sup>. This finding suggests that besides effects related to the RA disease *per se*, there may be a shared susceptibility. If the excess risk of ACS in patients with RA were increased due to this, an increased risk of ACS would be observed also in individuals with a similar genetic set-up and background as the patients with RA, such as their siblings.

**Objectives:** To investigate any potential shared susceptibility between RA and ACS by estimating the risk of ACS in full siblings of patients with (vs. without) RA.

**Methods:** We used the Swedish Rheumatology Quality register (SRQ) to identify an early RA cohort diagnosed between 1996–2015, which was linked to the Swedish Multigeneration Register, Patient Register, the Cause of Death register, and the Total Population Register. Through this, we sampled five general population comparator subjects to each patient with RA, matched by birth year and sex, and identified all full siblings to patients with RA and for their comparator subjects born within five years of their index case. The comparators, and all siblings, were required to be alive and living in Sweden at the time of the index patient's RA diagnosis (=start of follow-up). All unique individuals were then followed for ACS (defined as first ever hospitalisation for ACS (ICD10: I21 or I20.0) or MI listed as the cause of death), and censored at death, migration, RA diagnosis (for non-RA subjects) or the end of the study (Dec 31 st 2015). We calculated hazard ratios (HR) using a Cox proportional hazards model, adjusting for age, sex and calendar period of diagnosis. Confidence intervals (CI) were estimated using a robust sandwich estimator.

**Results:** We identified 7492 patients with RA who had 10 671 full siblings, and 35 120 population comparator subjects with 47 137 full siblings. The HR for ACS was 1.44 (95% CI: 1.25 to 1.66) and 1.23 (95% CI: 1.09 to 1.40) for patients with RA and their siblings, respectively, compared to the comparator subjects. A direct comparison between the RA patients and their RA-free siblings confirmed the familial association between RA and ACS, HR 1.19 (95% CI: 1.02 to 1.38).

**Conclusions:** The increased risk of ACS in siblings of patients with RA a) provide evidence of shared susceptibility between RA and ACS, the nature of which needs to be further investigated, and b) suggests that to bring down the CV risk in RA to that in the general population, cardiopreventive measures must go beyond optimised RA disease control.

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**Disclosure of Interest:** H. Westerlind: None declared, M. Holmqvist: None declared, L. Ljung: None declared, T. Frisell: None declared, J. Askling Grant/research support from: Johan Askling has or has had research agreements with Abbvie, BMS, MSD, Pfizer, Roche, Astra-Zeneca, Eli Lilly, Samsung Bioepis, and UCB, mainly in the context of safety monitoring of biologics via ARTIS. Karolinska Institutet has received remuneration for JA participating in advisory boards arranged by Pfizer and Eli Lilly.

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OP0137

### ASSESSING THE RISK OF RA PATIENTS FOR COMORBID CONDITIONS THROUGH A STRUCTURED NURSE-LED INTERVIEW – THE ERIKO STUDY

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**Background:** Assessment of comorbidities in rheumatoid arthritis (RA) has proven to be difficult for the rheumatologist due to lack of time leading to considerable deficits. Nurse-led programs on RA comorbidity management might solve this problem and have been reported to be beneficial.<sup>1</sup>

**Methods:** The cluster randomised multicentre study ERIKO longitudinally assessed the general health status of patients with RA in Germany applying a

nurse-led scoring algorithm for individual risk profiles (ERIKO-Score). The ERIKO-Score is a composite score evaluating the following risk factors: cardiovascular (CV) risk (ESC-guideline), infection risk (RABBIT risk calculator), vaccination status (guideline), fracture risk (FRAX), tooth status (PSI), depression (PHQ-9) and health-related quality of life (hrQoL, RAID). The outcome was translated into a three-level ordinal score defined by the categories low, intermediate or high risk with 0, 1 and 2 points, respectively. Afterwards the treating rheumatologist discussed the outcomes with the patient. The primary endpoint, the change in ERIKO-Score between baseline and after one year of follow-up as a consequence of the structured assessment (active arm) was assessed using a mixed model in order to account for a random centre effect. Furthermore, comorbidity management in the active arm versus expert guided assessment following standard of care (SOC, control arm) was evaluated using Fisher's exact test and the Cochran-Armitage trend test.

**Results:** The analysis included 341 patients from 42 rheumatology centres with 210 patients in the active arm (mean disease duration 12.0 years (sd 8.8), mean DAS28 2.6 (sd 1.1)) and 131 patients in the control arm (mean disease duration 9.7 years (sd 7.4), mean DAS28 2.6 (sd 1.2)). After one year of follow-up the structured assessment led to a significant mean decrease in total ERIKO-Score by -0.45 (95% CI ranging from -0.67 to -0.23, p<0.001). This decrease was driven by an improvement in vaccination status, tooth status and depression risk. No difference in comorbidity management was detected between the structured assessment and SOC. At the end of follow-up, the mean ERIKO-Scores for both arms were 4.85 with 95% CIs ranging from 4.59 to 5.11 and 4.47 to 5.24 for the active arm and the control arm, respectively. A significant improvement in risk categorisation after one year of follow-up was observed for vaccination status and depression risk with better outcomes in the active arm as compared to the control arm.

**Conclusions:** A nurse-led comorbidity risk assessment in rheumatology practices resulted in a significant improvement after one year of follow-up. However, improvement was small and there was no benefit compared to expert-opinion based SOC. In clinical routine, applying the ERIKO-Score based on validated tools seems to be feasible. Nurse-led comorbidity assessment seems to be able to reduce existing deficits.

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OP0138

### INVESTIGATION OF BIOPSYCHOSOCIAL ASSESSMENTS IN PATIENTS WITH RHEUMATIC DISEASE

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**Background:** The daily living activities, functions, depression and anxiety of patients with rheumatic diseases can be affected at various levels.<sup>1</sup> This condition explains the biopsychosocial dimension of chronic pain, it also requires the multi-dimensional assessment of the disease.<sup>2</sup>

**Objectives:** The aim of this study was to investigate biopsychosocial assessments of patients with rheumatic diseases.

**Methods:** Patients with rheumatic diseases were included in this prospective study. Demographic informations of patients were recorded. Health Assessment Questionnaire (HAQ) was used to assess daily living activities, the Hospital Anxiety and Depression Scale (HADS) was used to assess the anxiety and depression levels and Cognitive Exercise Therapy Approach Scale (the authors request that the abbreviation stay as 'BETY' as the original in Turkish) was used to assess biopsychosocial status of the patients.<sup>3</sup> Data obtained from 352 patients were analysed by correlation analysis.

**Results:** 352 patients (82.4% women, 17.6% men, mean age: 46.01±11.6 years) were included in this study. Descriptives of the assessment results were given in table 1. There was a statistically significant correlation between the BETY and the



anxiety and depression subscales of HADS, respectively, strong and moderately strong, in the positive direction ( $r=0.618$   $p<0.001$  and  $r=0.572$   $p<0.001$ ). A statistically significant, strong correlation was found between the BETY and HAQ scores in the positive direction ( $r=0.650$   $p<0.001$ ) (table 2). It was observed that patients showed depression characteristics according to HADS cut-off values ( $>7$ ).

Abstract OP0138 – Table 1 Characteristics of patients

n=352	Min-Max	X±SD
Age (year)	19–75	46,01±11,6
Height (cm)	130–190	162,54±8,42
Weight (kg)	40–125	73,19±14,9
BMI (kg/m <sup>2</sup> )	15,21–52,76	27,8±5,8
HADS-A	0–21	8,71±5,1
HADS-D	0–21	7,49±4,6
HADS-T	0–42	16,20±8,9
HAQ	0–53	12,21±10,4
BETY	2–120	62,65±26,3

X: Mean, SD: Standard Deviation BMI: Body Mass Index

Abstract OP0138 – Table 2 Correlations

n=352		HADS-anx	HADS-dep	HAQ
BETY	r	,618*	,572*	,650**
	p	,000	,000	,000

\*: Pearson Correlation Test \*\*: Spearman Correlation Test  $p<0,05$

**Conclusions:** It was concluded that the cognitive functions of patients with rheumatic diseases were affected by anxiety-depression levels and daily living activities. Therefore, when the patient changes his/her cognition about his/her illness, it is thought that anxiety and depression levels may change positively. It was decided that the cognitive functions of the patients should be emphasised in the assessment of rheumatic patients.

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## OP0139 CHARACTERISTICS OF DIFFICULT-TO-TREAT RHEUMATOID ARTHRITIS: RESULTS OF AN INTERNATIONAL SURVEY

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**Background:** The EULAR and ACR recommendations regarding rheumatoid arthritis (RA) mainly focus on early phases of the disease and on pharmacological management. Nevertheless, some patients remain symptomatic despite treatment according to the current recommendations, which makes them difficult-to-treat.<sup>1</sup> The estimated prevalence of difficult-to-treat RA is around 5%–20%. A difficult-to-treat RA classification needs to be defined to enable creation of recommendations on its comprehensive management.

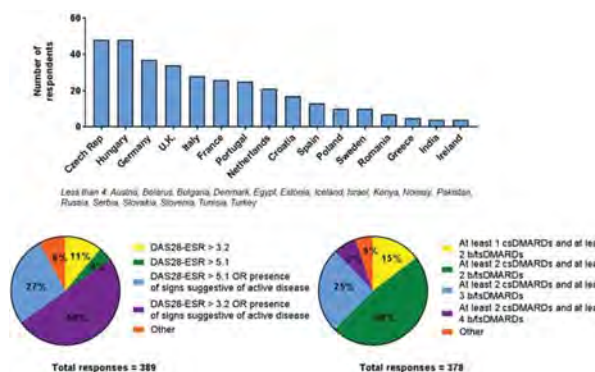
**Objectives:** To compose a definition of difficult-to-treat RA and to explore items on its comprehensive management not covered by the current EULAR RA management recommendations.

**Methods:** An online survey was distributed among rheumatologists (in training). It consisted of 9 questions regarding the background of the respondents, aspects to be included in the definition of difficult-to-treat RA and missing items on its comprehensive management in the current EULAR management recommendations. Multiple-choice questions were used to assess the necessity of incorporating the following items into the definition: the disease activity level, e.g. the disease activity score assessing 28 joints (DAS28-ESR), presence of fatigue, number of disease-modifying anti-rheumatic drugs (DMARDs) that failed and the inability to reduce oral glucocorticoid (GC) treatment. Optional open questions were used to identify additional features for the definition of difficult-to-treat RA and to collect items on its comprehensive management not covered by the current EULAR recommendations.

**Results:** 390 rheumatologists (a few of them in training) from 31 countries completed the survey between July and December 2017 (figure 1a). 50% of the respondents would include signs suggestive of active disease or a DAS28-ESR score  $>3.2$  in the definition (figure 1b) and 41% fatigue. The most selected option for the number and category of DMARDs that had to have been used to be included in the definition was 1) Failure to  $\geq 2$  conventional synthetic DMARDs and (Boolean) 2)  $\geq 2$  biological or targeted synthetic DMARDs with different mechanisms of action (figure 1c). 89% suggested including inability to taper oral GCs below 5 or 10 mg. Over 400 responses to open questions were submitted, of which a selection is listed in table 1.

Abstract OP0139 – Table 1 Most frequent answers to the open questions

Please define any additional features and suggested criteria for difficult-to-treat RA	Please mention any clinically relevant situations which are not covered by the current EULAR RA recommendations
Time span with active disease despite treatment	Treatment adherence
Rapidly progressive erosions despite treatment	Persistent chronic pain without objective inflammatory signs
Adverse events to multiple agents	Coping problems
Comorbidities, e.g. fibromyalgia	Extra-articular manifestations



**Abstract OP0139 – Figure 1 a)** origin and number of respondents, b) what should be the definition for not well-controlled disease in the definition of difficult-to-treat RA? c) which and how many anti-rheumatic drugs should at least be tried with insufficient effect (failed) for the definition of difficult-to-treat RA?

**Conclusions:** This survey shows that difficult-to-treat RA is seen as a heterogeneous condition; next to signs of active disease, failure to DMARDs and inability to taper GCs may be included in the definition. The large number of respondents and of responses with regard to items not covered by the current EULAR RA management recommendations underscore the need for recommendations on comprehensive management of difficult-to-treat RA.

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OP0140

### PATTERN AND INFLUENTIAL FACTORS IN PROMOTING TREAT-TO-TARGET (T2T) FOR FOLLOW-UP RA PATIENTS WITH A RHEUMATOLOGIST-PATIENT INTERACTIVE SMART SYSTEM OF DISEASE MANAGEMENT (SSDM): A COHORT STUDY FROM CHINA

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**Background:** Treat-to-Target (T2T), achieving a DAS28 score lower than 2.6 (remission, Rem) or below 3.2 (low disease activity, LDA), is the main management strategy recommended by ACR and EULAR. The Smart System of Disease Management (SSDM) is an interactive mobile disease management tool, including the doctors' and patients' application system. The patients can perform self-evaluation, including DAS28, morning stiffness duration (MSD) and HAQ, and enter medical records (including medication and laboratory test results) through the mobile application. The data synchronises to the mobiles of authorised rheumatologists through cloud data base and advices could be delivered.

**Objectives:** The objective of this study is to evaluate the patterns of T2T and related influential factors among RA patients after applying SSDM in real world.

**Methods:** Patients were registered through downloading the SSDM application, then were trained to master SSDM by health professionals in clinics. The first assessment for DAS28 were performed as baseline. The patients were required to perform repeated assessments once a month after leaving clinics.

**Abstract OP0140** – Table 1 Results at baseline and in the final follow up from 2,264 patients with RA

	Baseline Total (2,264)	Achiever of T2T (908, 40%)		Failure of T2T (1,356, 60%)	
		Maintainer of T2T 643 (71%)	Relapser 265 (29%)	Maintaining failure of T2T 835 (62%)	Achiever of T2T 521 (38%)
Age (years): mean ± SD		49.21 ± 13.38	48.82 ± 13.70	50.99 ± 14.02	48.45 ± 13.82
Disease duration (months): mean ± SD		61.35 ± 86.11	63.98 ± 84.11	61.96 ± 72.49	65.67 ± 85.42
Times of patient self-evaluation and data entry: mean ± SD		5.29 ± 1.39	2.81 ± 1.20*	2.95 ± 1.44	5.38 ± 1.45*
DAS28: mean ± SD	Baseline	2.28 ± 0.61	2.48 ± 0.58	4.87 ± 1.16	4.33 ± 0.94
	Final follow up	2.15 ± 0.63	4.14 ± 0.84	4.51 ± 0.96	2.34 ± 0.60
MST median (IQR), mean ± SD	Baseline	0(0-0)	0(0-10)	29.16 ± 34.26	15.26 ± 20.25**
	Final follow up	0(0-2)	18.15 ± 22.14	13.93 ± 22.10***	0(0-5)
HAQ: median (IQR), mean ± SD	Baseline	0(0-0)	0(0-1)	4.68 ± 3.52	1.98 ± 2.15**
	Final follow up	0(0-0)	3.26 ± 2.47	2.18 ± 2.25***	0(0-0)

DAS28: disease activity score in 28 joints; HAQ: health assessment questionnaire; MST: morning stiffness duration.

\*: P<0.01; \*\*: P<0.001; One-way analysis of variance was used for comparisons in different groups.

†††: P<0.001; One-way analysis of variance was used for comparisons in the same group between baseline and final follow up.

**Results:** From Jun 2014 to Jan 2018 2,264 RA patients from 154 hospitals across China were followed up for more than 6 months through SSDM, and the results at baseline and in final follow up were shown in table 1. The rate of T2T achievers were 40% (908/2,264) at baseline, and improved significantly to 51% (1,164/2,264) after 6 month follow up, p<0.05. Among T2T achievers at baseline, 71% (643/908) maintained T2T, 29% (265/908) relapsed. Compared with relapsers, T2T maintainers performed more self-evaluation and data entry (5.29 vs 2.81, p<0.01). Among patients failed to achieve T2T at baseline, 38% (521/1,356) achieved T2T after 6 months. Comparing with 6 month failure (835/1,356), new T2T achievers got shorter MSD (15.26±20.25 vs 29.16±34.26 min, p<0.001), lower HAQ score (1.98±2.15 vs 4.68±3.52, p<0.001) at baseline, performed more times of self-evaluation and data entry (5.38 vs 2.95, p<0.01). However, even in

patients of 6 month failure, the MSD and HAQ score were improved significantly in final follow up comparing with those at baseline (13.93±22.16 vs 29.16±34.26, p<0.001; 2.18±2.25 vs 4.68±3.52, p<0.001, respectively).

**Conclusions:** After proactive disease management via SSDM for more than 6 months, the rate of T2T in RA patients increased significantly. The patients who perform more self-evaluations through SSDM had lower probability of relapse and higher T2T maintaining and achievement. SSDM is a valuable tool for long term RA follow-up through empowering patients. Future RCT of improving T2T outcome through intervention of above influential factors with SSDM is warranted.

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THURSDAY, 14 JUNE 2018

### Quickly emerging: science in SSc, myositis and related syndromes

OP0141

### ULTRASOUND DIAGNOSTIC AND PREDICTIVE VALUE OF INTERSTITIAL LUNG DISEASE IN SYSTEMIC SCLEROSIS. DIAGNOSTIC AND PREDICTIVE VALUE OF ULTRASOUND IN THE ASSESSMENT OF INTERSTITIAL LUNG DISEASE

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**Background:** Interstitial lung disease (ILD) is a common complication of Systemic Sclerosis (SSc) and frequently may be cause of death of patients. High resolution computed tomography (HRCT) is the reference imaging tool for the assessment of ILD; however, its use may be limited for both ionising radiation and costs. In this way, pulmonary ultrasound (US) is revealing interesting potential in the assessment of ILD.

**Objectives:** To determine the validity of pulmonary US in detecting subclinical ILD in SSc and to determine its predictive value for detecting disease progression.

**Methods:** We included 133 SSc patients ≥ 18 years-old without respiratory symptoms. Individuals with previous diagnosis of ILD or other pulmonary diseases were excluded. A rheumatologist performed the Borg scale dyspnea index, Rodnan skin score (RSS) and lung auscultation to confirm the subclinical respiratory status. Chest X-ray and respiratory function tests (RFT) were performed the same day in all patients. US was performed by a rheumatologist expert who was blinded to clinical assessment. To determine the concurrent validity HRCT was performed. Finally, serologic tests (anti-centromere, anti-Scl70) were obtained. HRCT findings were scored according to Warrick score, whereas US findings were classified according the previously proposed semiquantitative scale (0=normal, ≤5 B-lines; 1=slight, ≥6 and ≤15 B-lines; 2=moderate, ≤16 and ≥30 B-lines; 3=severe, ≥30 B-lines). In order to evaluate the inter-observer reliability, 50% of patients were assessed by 2 rheumatologists with different experience in US; both blinded to clinical data. A healthy control group matched for age and gender was included.

A follow-up including US, RFT and Borg scale was done every 3 months until 12 months.

**Results:** A total of 54 of 133 patients (40.6%) showed US signs of ILD in contrast to healthy controls (4.8%) (p=0.0001). The clinical and laboratory variables associated with ILD were: anti-centromere antibodies (p=0.005), Borg scale (p=0.004) and RSS (p=0.004). A positive correlation was demonstrated between the US and HRCT findings (p=0.001), confirmed also with the Chi square test (p=0.006). No association was shown with gender, age, disease duration, chest X-ray or RFT. Sensitivity and specificity of US in detecting ILD was 91.2% and 88.6% respectively. A Moderate inter-observer reliability of US findings was observed (kappa 0.50).

In follow-up, a total of 30 patients (22.6%) that demonstrated ILD during first evaluation, showed US worsening in their ILD status. Interestingly, 9 of those 30 patients (30%) became symptomatic by the Borg scale. The elapsed time in which progression of ILD or clinical conditions was documented was between 6 and 9 months of follow-up.

**Conclusions:** US showed a high prevalence of subclinical ILD in SSc patients. It demonstrated to be a valid, reliable and feasible tool to detect ILD in SSc and to follow-up its evolution. On the basis of our results we believe that US can be implemented as a screening tool for diagnosis of subclinical ILD in SSc.

**Disclosure of Interest:** None declared

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**OP0142 RITUXIMAB IN SYSTEMIC SCLEROSIS : SAFETY AND EFFICACY DATA FROM THE EUSTAR NETWORK**

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**Background:** Few small-sized observational studies have suggested that rituximab might be a promising treatment in systemic sclerosis (SSc)

**Objectives:** To evaluate the outcomes of SSc-patients receiving in routine care Rituximab

**Methods:** Retrospective longitudinal multicenter observational study which included SSc-patients treated with rituximab upon the decision of their physician within the framework of EUSTAR. We interrogated the participating centres and EUSTAR database to determine epidemiological and clinical characteristics, the indication for initiating the treatment, and the following parameters at baseline and at the last visit under treatment: modified Rodnan Skin Score (mRSS), joint, lung and gastrointestinal involvements, treatment, laboratory tests and safety events.

**Results:** 248 patients were included: 70 (28%) men, mean age: 51±13 years, mean disease duration: 7±7 years; 150 (65%) had diffuse cutaneous-SSc, 54% were positive for anti-topoisomerase and 71% had lung fibrosis. Overlap disease was noticed in 62 patients (26%) including 23 with rheumatoid arthritis. The indication for the treatment was lung involvement (56%) followed by articular (42%) and skin involvements (30%). At baseline, 175 patients were treated with steroids and 132 with DMARDs. Mean follow-up was 2.4 (±1.9) years.

In the whole sample, mRSS decreased from 15±11 to 10±8 (p<0.01).

For SSc-patients treated for lung with baseline FVC <70%, FVC improved from 56 ±9% to 59±12%; p=0.02. In patients with articular involvement (n=83), tender joint and swollen joint counts decreased from 9±7 to 4±6 and from 3±5 to 1±3, respectively (p<0.01).

In the whole population, 45 patients could stop steroids and mean dose decreased from 10 mg to 7 mg in the other.

During the follow-up, 78 (31%) patients had side effects including 35 (14%) with severe side effects leading to discontinuation of the treatment in 10%. Six deaths were recorded (1 heart failure, 1 sepsis, 2 respiratory insufficiencies, 2 sudden deaths). 76 patients had infection, requiring hospitalisation in 20 patients.

**Conclusions:** In this study, skin, lung and joint involvement appeared to improve under rituximab. Infections and other severe adverse events were frequently

reported. A comparative study including control patients from EUSTAR centres is ongoing.

**Disclosure of Interest:** M. Elhai: None declared, O. Distler Grant/research support from: Actelion, Bayer, Boehringer Ingelheim, ChemomAb, espeRare foundation, Genentech/Roche, GSK, Inventiva, Lilly, medac, Medimmune, Mitsubishi Tanabe Pharma, Novartis, Pfizer, Sanofi, Sinoxa and UCB in the area of potential treatments of scleroderma and its complications, V. Smith : None declared, M. Matucci-Cerinic: None declared, J. J. Alegre-Sancho : None declared, M.-E. Truchetet: None declared, Y. Braun-Moscovici: None declared, F. Iannone: None declared, F. Chotchaeva: None declared, A. Lescoat : None declared, E. Siegert : None declared, I. Castellvi: None declared, P. Airo : None declared, S. Vettori: None declared, E. Hachulla: None declared, A. Erler : None declared, L. Ananieva : None declared, M. Krusche: None declared, F. López-Longo : None declared, J. Distler : None declared, N. Hunzelmann : None declared, A.-M. Hoffmann-Vold : None declared, V. Ricciari: None declared, V. Hsu: None declared, M. Pozzi: None declared, C. Ancuta : None declared, E. Rosato : None declared, C. Mihai: None declared, M. Kuwana: None declared, Y. Allanore Grant/research support from: Actelion, Bayer, Boehringer Ingelheim, ChemomAb, Genentech/Roche, Inventiva, Pfizer, Sanofi, Servier, in the area of potential treatments of scleroderma and its complications.

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**OP0143 REGIONAL GRAFTING OF AUTOLOGOUS ADIPOSE TISSUE IS EFFECTIVE IN INDUCING PROMPT HEALING OF INDOLENT DIGITAL ULCERS IN PATIENTS WITH SYSTEMIC SCLEROSIS: RESULTS OF A MONOCENTRIC RANDOMISED CONTROLLED STUDY**

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**Background:** Adipose-derived stromal/stem cells (ADSCs) are believed to be pluripotent cells with characteristics similar to BMSCs. Preliminary attempts of cell therapy with ADSCs have been carried out with the purpose of inducing ulcer healing in peripheral vascular impairment that can be observed in animal models and human conditions. In a recent pilot open study from our group it has been demonstrated that lipofilling with autologous adipose tissue-derived cell fractions, which are known to contain both ADSCs and a stromal/vascular cell component, was effective in inducing a prompt healing of long lasting digital ulcers (DU) localised in the fingertips of a small number of patients with Systemic Sclerosis (SSc). The DU healing was accompanied by the rapid disappearance of local ischaemic pain and evidence of a partial restoration of capillary bed in the involved digits when assessed by nailfold videocapillaroscopy (NVC).

**Objectives:** A randomised controlled trial (RCT) was performed to confirm preliminary uncontrolled data indicating that regional adipose tissue (AT) grafting (G) is effective in inducing DU healing in patients with SSc.

**Methods:** Patients with SSc, fulfilling the 2013 ACR/EULAR classification criteria and suffering from a DUs lasting for at least 6 weeks prior to enrolment time and showing no tendency to heal, were randomised to be blindly treated with AT-G or a sham procedure (SP). AT-G consisted of injection at the base of the finger with DU of 0.5–1 ml of AT after centrifugation of fat aspirate from abdominal adipose tissue. SP consisted of a false liposuction followed by the injection of 0.5–1 ml of 0.9% saline solution at the base of the affected finger. Weekly iloprost infusion (0.5–2 ng/Kg/min), and calcium-channel blockers (oral nifedipine 20 mg daily) were administered during the entire observation time to all of the patients enrolled in both arms of the study.

The primary end-point was to compare the cumulative prevalence of healed DUs in the two groups within the following 8 weeks. Secondary end points to be assessed were: (i) pain intensity modification (measured by VAS), and (ii) variation of the number of capillaries in the affected digits (recorded by nailfold videocapillaroscopy) in patients receiving AT-G compared to those who underwent SP.

**Results:** AT-G and SP were performed in 25 and 13 patients, respectively. The two groups were comparable for age, gender, disease duration and SSc subtypes.

DU healing was observed in 23/25 and 1/13 patients treated with AT-G and SP, respectively (p<0.0001). The 12 patients who received the unsuccessful SP underwent a rescue AT-G. Also in all of them DU healing was observed after 8 weeks of observation. It was noticeable that only in the patients treated with AT-G either a significant reduction of pain intensity or an increase of capillary numbers in the affected finger were recorded after both 4 and 8 weeks (p<0.0001 in all the comparisons).

**Conclusions:** This RCT strongly confirm previous preliminary and uncontrolled data indicating that AT-G may be a successful option for inducing improvement and healing in ischaemic SS-related fingertip DUs that are resistant to more traditional therapeutic approaches.

**Disclosure of Interest:** None declared

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OP0144

### INTRAVENOUS VERSUS ORAL CYCLOPHOSPHAMIDE (CYC) FOR THE TREATMENT OF INTERSTITIAL LUNG INVOLVEMENT (ILD) AND SKIN INVOLVEMENT IN SYSTEMIC SCLEROSIS (SSC): SAFETY AND EFFICACY EVALUATION IN A LARGE MULTI-CENTRE SCLERODERMA COHORT

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**Background:** In the last decade, oral CYC has shown modest but significant effect on SSc-ILD and skin thickness in two large randomised controlled trials, with superiority to placebo and similar efficacy to mycophenolate. However, many centres give priority to monthly IV CYC for expected milder toxicity.

**Objectives:** To compare efficacy and safety of oral versus iv CYC for treating ILD and/or skin involvement in SSc.

**Methods:** SSc patients treated with oral or iv CYC for at least 6 months were followed for 1 year from the last administration. Data were obtained from the EUSTAR database and the Scleroderma Lung Studies I and II regarding safety [both serious (SAEs) and non-serious adverse events (AEs)] and efficacy (%FVC, %DLCO, mRSS) at end of treatment and after one-year follow-up were analysed [mean ±SD or median(IQR) as appropriate].

**Results:** 322 patients were eligible: 149 patients received oral CYC with median daily dose 106(93–134) mg, treatment duration 365(364–366) days, while 153 patients received IV CYC median monthly dose 1000(700–1200) mg, treatment duration 335(291–374) days. Ethnicity, previous DMARD exposure, previous and concomitant steroid exposure and dosage, current/previous smoking exposure, prevalence of digital ulcers and arterial hypertension were different between the two groups (see table 1 for further details).

For efficacy: despite different baseline%FVC and%DLCO, adjusted changes in pulmonary measures from end of treatment (EOT) vs baseline and follow-up visit (FU) vs EOT were, respectively: %FVC [0(–5–5) vs 0(–7–7) and 1(–6–4) vs –2(–7–4), p=NS], %DLCO [–4(–9–3) vs –3(–9–6), 1(–6–5) vs –1(–9–6), p=NS] and mRSS [–3(–5–0) vs –1(–5–0), –1(–4–1) vs 0(–3–1), p=NS]. In a multivariate analysis, no independent variable significantly influenced%FVC change at any visit.%DLCO change was influenced by baseline%DLCO and history of SSc-related cardiomyopathy at EOT assessment and by history of SSc-muscle involvement at FU visit. Baseline mRSS was the only variable having a significant impact on mRSS change.

For safety: in the oral group, there were more leukopenia (WBC <2500 ×10<sup>9</sup>/mm<sup>3</sup> at least once – 21.6% vs 1.2%, p<0.001), haemorrhagic cystitis [5.5% (8 instances) vs 0%, p=0.011] at EOT visit. In contrast, there were more SAEs (9% vs 19%, p=0.025), need for oxygen supplementation (5% vs 14%, p=0.016) and SSc-related cardiomyopathy onset (2% vs 9%, p=0.024) during follow-up in the IV group.

**Abstract OP0144 – Table 1** Baseline significant differences between study population groups.

	Oral CYC (149 pts)	Intravenous CYC (153 pts)	P
Caucasian race, n(%)	104 (69.8)	146 (95.4)	<0.001
Afro-american race, n(%)	23 (15.4)	0 (0)	<0.001
Previous steroid exposure, n(%)	42 (28.4)	70 (46.7)	0.001
Previous DMARD exposure, n(%)	35 (23.5)	62 (41.3)	0.001
Steroid treatment at baseline, n(%)	51 (34.6)	111 (72.5)	<0.001
CYC treatment duration (days), mean	365 (365-366)	343 (194-514)	0.035
CYC daily dose (mg), mean (IQR)	106.6 (93.1-132.3)	33.3 (23.3-40)	0.001
Smoking history, n(%)	21 (14.6)	10 (6.6)	0.035
%FVC at baseline, mean (IQR)	69 (60-75)	83 (68-96)	<0.001
%DLco at baseline, mean (IQR)	51 (40-63)	56 (42-71)	0.022
History/presence of digital ulcers, n(%)	40 (26.8)	64 (42.1)	0.008
History/presence of arterial	40 (26.8)	25 (16.3)	0.035

CYC=cyclophosphamide, DMARD=disease modifying ant rheumatic drug, FVC=forced vital capacity, DLco=lung diffusion of carbon oxide.

**Conclusions:** In this hypothesis generating study, similar efficacy of one year of oral and iv CYC were seen. In contrast, a different safety profile for AE time courses and types of AEs were seen in the two groups. Although significantly higher dosage of steroids at all visits and prevalence of DMARDs use were

present in the IV CYC group (as a post-treatment maintenance), these did not have an impact on either safety or efficacy. Case-control or randomised studies are warranted to extend and confirm our data.

**Disclosure of Interest:** None declared

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OP0145

### SCLERODERMA RELATED INTERSTITIAL LUNG DISEASE AND MYCOPHENOLATE : LONG TERM OUTCOMES

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**Background:** Interstitial lung disease [ILD] is a leading cause of mortality in scleroderma. <sup>1</sup> Scleroderma lung study-II clearly illustrates the equivalent efficacy and a better side-effect profile of mycophenolate mofetil [MMF] as compared to cyclophosphamide.

**Objectives:** To study the long term outcomes of mycophenolate mofetil in scleroderma related interstitial lung disease (SSc-ILD) in terms of change in forced vital capacity (FVC)

To determine the effect of MMF on longitudinal high resolution computed tomography (HRCT) scores.

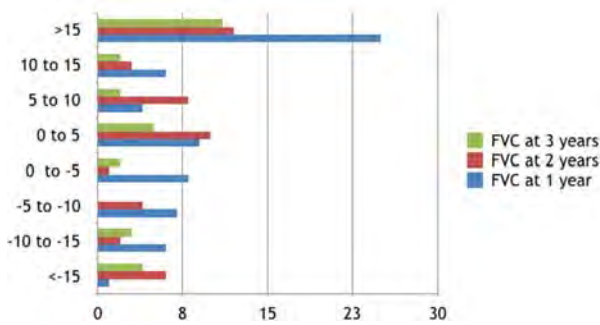
**Methods:** All patients of SSc-ILD from 2013 till date who had a baseline FVC and follow up FVC were taken for analysis. All patient received an average dose of 2 g/day of MMF for a median duration of 2 years and were tapered as per the standard protocol. FVC was measured using standard protocols. The FVC change was computed as percentage relative change from baseline FVC value. According to American Thoracic society recommendations, improvement is defined as an increase in FVC ≥10%, stabilisation by change in FVC <10% and worsening by a reduction in FVC ≥10%.

**Results:** We had 88 patients with a baseline and followup FVC data. Of these 66 patients had a 1 year follow up; 46 patients had a 2 year followup and 29 patients had a 3 year followup data. The absolute median (IQR) increase in the FVC value at the end of 1 year, 2 years, 3 years were 4.15 (-2.3 to 10.5), 2.85 (-3.4 to 7.2) and 3.8 (-0.6 to 10.4) respectively. At the end of 1 year, 2 years and 3 years 89.4%; 82.6% and 75.9% respectively had a stable or improved relative FVC change from baseline.

Of the 52 individuals who had a baseline as well as repeat HRCT, stable/improved scores in ground glass opacity, fibrosis and honey combing was seen in 80.8%, 86.5% and 86.5% respectively. There was no difference in the extent of FVC change between those with limited vs extensive disease.

**Abstract OP0145 – Table 1**

Baseline Characteristics	Value
Age, yr. mean(SD)	33.8 (±11.3)
Female sex, n (%)	75 (85.2%)
Type of SSc	5
Limited	71
Diffuse	6
Sine scleroderma	
Disease duration, months, mean (SD)	46.6 (±42.1)
Antibodies	70
Scl-70	1
Anti centromere	
MRSS, mean (SD) n=52	20.4(±13.2)
FVC% predicted, mean (SD)	61.2 (±17.9)
HRCT pattern [n=85]	68
NSIP (cellular)	11
NSIP (fibrotic)	6
UIP	
HRCT determined disease extent [median(IQR)] ; n=52	0.33 (0–1.3)
Maximum fibrosis score (0–4)	1 (0–1.5)
Maximum ground glass opacity (0–4)	0 (0.08)
Maximum honeycombing (0–4)	
Maximum fibrosis score n=52	29 (55.8%)
1%–25%	23 (44.2%)
26%–100%	
<b>HRCT change over 2 years</b>	<b>Frequency (Percentage)</b>
Ground Glass opacity	42 (80.8%)
Stable/Improved	10 (19.2%)
Worsened	
Fibrosis	45 (86.5%)
Stable/Improved	7 (13.5%)
Worsened	
Honey combing	45 (86.5%)
Stable/Improved	7 (13.5%)
Worsened	



Abstract OP0145 – Figure 1 Relative change in FVC from base line at different time points

**Conclusions:** A vast majority of individuals of scleroderma ILD patients on MMF in our cohort had a stable disease or improvement over short and long term follow up both in terms of FVC change from baseline as well as HRCT scoring.

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**Disclosure of Interest:** None declared

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#### OP0146 IDIOPATHIC INFLAMMATORY MYOPATHIES & INTERSTITIAL LUNG DISEASE

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**Background:** Idiopathic inflammatory myopathies (IIM) is associated with interstitial lung disease (ILD). IIM associated ILD ranges from subclinical disease, to rapidly progressive ILD (RPILD). Early recognition of these patients is essential for determining treatment.

**Objectives:** A retrospective case-control study in a tertiary referral centre to identify: a) Clinical features associated with ILD in IIM.

b) Whether antibodies e.g. anti-ENA and myositis specific antibodies (MSA), may aid recognition of ILD or RPILD.

c) Whether intensive immunosuppressants have implication on prognosis of ILD.

**Methods:** The clinical records of IIM patients who were followed up in rheumatology clinic or admitted into our hospital from Jan 2013 to Dec 2016 were reviewed. We analyse the clinical characteristics (*rash, arthritis, myositis, Raynaud's phenomenon, mechanic hands, and cutaneous ulcers with blood tests*), antibody profile (*anti ENA: anti-Jo1, Ro, La, Sm, RNP, Scl 70 and MSA: anti Oj, E, PL7, PL12, SRP, PM-Sci75, PM-Sci100, Ku, SAE1, NXP2, TIF1γ, MDA5, Mi2*), treatment and survival. We compare these parameters in IIM-ILD patients against those without ILD. Chi-squared and Mann-Whitney U tests were used to analyse categorical and continuous variables. Log rank test was used to compare survivals.

**Results:** Among the 101 IIM patients, the mean age was 62 years old with 71% female. 74 patients (73%) had dermatomyositis, 17 (17%) had polymyositis and 10 (10%) clinical amyopathic dermatomyositis. 53 patients (52%) had ILD; 48 (48%) had no ILD. In ILD group, 11/53 patients (21%) were RPILD.

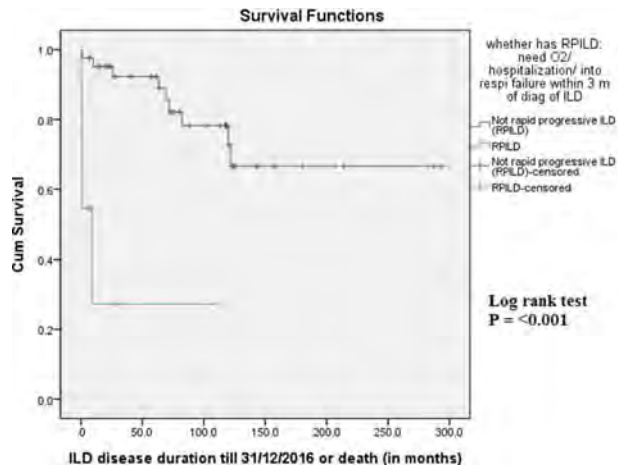
All patients had anti-ENA checked. 59/101 patients (58%) had MSA profile.

Significantly more ILD patients had arthritis, mechanic hands, anti Jo1, anti Ro and anti MDA5 than those without ILD. 21/101 patients had cancers associated with IIM, but cancers were less common in ILD group. Subgroup analyses revealed arthritis, mechanic hands and anti MDA5 were again significantly more common in RPILD compared to other ILD patients (table 1). Anti MDA5 were more commonly found in deceased versus alive patients (40% vs 8.2%,  $p=0.02$ ; OR=7.5). Deceased patients also had significantly higher median peak ferritin (2475 vs 553 pmol/L,  $p=0.008$ ), so did the ILD group (2332 vs 484 pmol/L,  $p=0.02$ ).

ILD patients received more intensive immunosuppressants (high dose steroid, cyclophosphamide, MMF, tacrolimus, IVIg or even rituximab) than non ILD group. The survival was not significantly different between ILD and non ILD groups. However despite intensive immunosuppressants, RPILD patients' survival was still much worse than the other ILD patients (figure 1).

Abstract OP0146 – Table 1 Features with  $P<0.05$  and the odds ratios (OR)/relative risks (RR)

	ILD (%)	Non ILD (%)	P value	OR/ RR	RPILD (%)	Other ILD (%)	P value	OR/ RR
Arthritis	53	21	0.001	4.3	73	33	0.02	5.3
Mechanic hands	17	0	0.003	2.1	36	6	0.008	9.7
Carcinoma	8	35	0.001	0.2				
Anti Jo1	20	5	0.03	5				
Anti MDA5	24	0	0.02	2	50	8	0.008	11.8
Anti Ro	40	17	0.01	3.3				



Abstract OP0146 – Figure 1 Kaplan Meier curves of RPILD & ILD groups

**Conclusions:** Certain clinical features and MSA aid recognition of IIM-ILD. Anti MDA5 is related to ILD, RPILD and mortality. Ferritin may be a disease activity and prognostic marker for IIM-ILD. With immunosuppressants, survival of IIM patients with or without ILD is similar. For RPILD patients, the survival is significantly worse despite active treatment.

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**Disclosure of Interest:** None declared

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#### OP0147 ABERRANT ACTIVATION OF TYPE I INTERFERON SYSTEM IN ANTI-MDA5 DERMATOMYOSITIS PATIENTS

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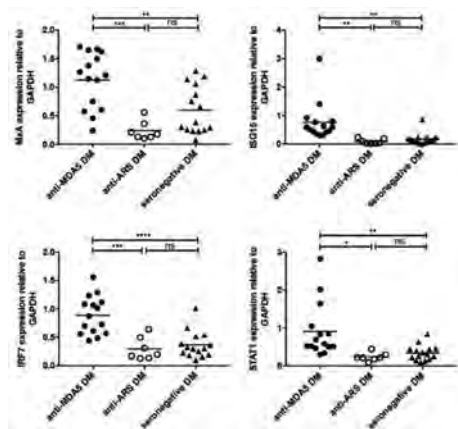
**Background:** Anti-melanoma differentiation-associated gene 5 (MDA5) DM patients have an increased risk of interstitial lung disease (ILD), with a potentially fatal course.<sup>1</sup> Viral infection has been speculated to be the putative trigger for anti-MDA5 DM.<sup>2,3</sup> The molecular pathogenesis remains largely unknown.

**Objectives:** In this study, we aimed to explore the role of type I interferon (IFN) system in the pathogenesis of anti-MDA5 DM.

**Methods:** We studied 20 anti-MDA5 DM patients and compared them with anti-aminoacyl-tRNA synthetase (ARS) DM patients (n=10) and seronegative DM patients (n=30). The levels of IL-1b, IL-4, IL-6, IL-8, IL-10, IL-12, IL-18, TNF-a, IFN-a, IFN-b, IFN-g, B cell activating factor (BAFF), Krebs von den Lungen-6 (KL-6) in blood were tested by enzyme-linked immunosorbent assay and multiplex assay. Expressions of mRNA for sensor molecules (TLR3, TLR4, TLR7, TLR9, MDA5, RIG-1) and type I IFN inducible genes (IRF7, STAT1, MxA, ISG15) in peripheral blood mononuclear cell (PBMC) were detected by real-time polymerase chain reaction analysis. Expressions of STAT1, MxA, ISG15 proteins in skin lesions from anti-MDA5 DM were analysed by immunohistochemistry technique.

**Results:** Anti-MDA5 DM patients had higher levels of plasma type I IFN (IFN-a, IFN-b), IL-6, IL-10 and TNF-a than seronegative-DM patients. In comparison to anti-ARS DM patients, IFN-a alone displayed heightened level in anti-MDA5 DM patients. Among these 3 subsets of patients, PBMC from anti-MDA5 DM patients

have the significant upregulation of TLR3, TLR7, MDA5, RIG-1 sensors as well as IRF7, STAT1, MxA, ISG15 genes. And skin biopsies from anti-MDA5 DM patients were characterised by strong expression of STAT1, MxA, ISG15 proteins. Furthermore, overexpression of plasma BAFF was observed in anti-MDA5 DM patients. BAFF level was showed to be positively correlated with IFN- $\alpha$  level. Additionally, BAFF level, synergizing with IFN- $\alpha$ , was of great relevance to KL-6 in anti-MDA5 DM patients with higher plasma IFN $\alpha$  concentration.



**Conclusions:** Our data suggest that aberrant activation of the type I IFN system associated with BAFF may be implicated in the pathogenesis of ILD in anti-MDA5 DM. The discovery may drive the development of new therapeutic strategies for the type of DM patients.

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OP0148

#### A VALIDATION OF THE 2017 EULAR/ACR IDIOPATHIC INFLAMMATORY MYOPATHIES CLASSIFICATION CRITERIA IN AN EXPERT-DEFINED SINGLE-CENTRE TEN YEAR INCIDENT COHORT

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**Background:** The recently published 2017 European League Against Rheumatism (EULAR) and American College of Rheumatology (ACR) classification criteria for adult and juvenile idiopathic inflammatory myopathies (IIM) and their major subgroups reflect a long-appreciated need for more accurate case definition in

ongoing research in these complex and heterogenous diseases.<sup>1</sup> However a number of issues remain unresolved. There was a high frequency of missing data in both the derivation and validation samples, only one of the now numerous myositis specific autoantibodies is included, and certain well recognised IIM subtypes are not specifically classified despite their well phenotyped and differing natural histories, clinical features and treatment modalities.<sup>2,3</sup>

**Objectives:** To perform an external validation of the EULAR/ACR classification criteria in an incident IIM cohort and examine how classification criteria-assigned IIM subtype correlates with expert opinion.

**Methods:** Adults with newly diagnosed IIM attending Salford Royal NHS Foundation Trust Neuromuscular services were identified. A retrospective review of all putative cases was performed, and cases fulfilling a consensus expert-opinion diagnosis of definite IIM included. A broad range of clinical, serological and histological data were collected and each case assigned a single IIM subtype by expert opinion. The EULAR/ACR classification criteria were applied and sensitivity, specificity, positive and negative predictive value calculated, presented with 95% confidence intervals (CI).

**Results:** A total of 922 cases were screened with 255 expert opinion definite IIM identified. The sensitivity to diagnose an IIM was 99.6% (97.2–100) and 80.9% (76.0–85.8) for the classification criteria cut-points of 'probable' and 'definite' respectively. The sensitivity for 'definite' IIM improved to 90.2% (86.5–93.8) when biopsy data for 24/34 initially missed cases were excluded. In 94/255 cases the IIM subtype differed between expert opinion and classification criteria, most strikingly in the group subtitled 'polymyositis' using the EULAR/ACR criteria, where there was discrepancy in the majority (87/161).

**Abstract OP0148 – Table 1.** PM, polymyositis; DM, dermatomyositis; IBM, inclusion body myositis; ADM, amyopathic dermatomyositis; IMNM, immune-mediated necrotizing myopathy; ASS, anti-synthetase syndrome; OM, overlap myositis.

Classification Tree-assigned IIM Subtype

	PM	DM	IBM	ADM	Totals
PM	37	0	0	0	37
DM	3	54	0	0	57
IBM	0	0	56	0	56
Expert-assigned IIM Subtype					
ADM	0	0	0	14	14
ASS	29	5	0	0	34
IMNM	25	0	0	0	25
OM	30	2	0	0	32
Total	124	61	56	14	255

**Conclusions:** The criteria performed with high sensitivity in identifying IIM in an external cohort of IIM patients. However, substantial disagreement exists in subtype assignment, especially resulting in a larger proportion of cases of 'polymyositis' with heterogeneous features, important to consider in the application of these criteria to subsequent research.

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**Disclosure of Interest:** None declared

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## Can imaging improve diagnosis and outcome in rheumatic diseases

OP0149

### AN MRI GUIDED TREAT-TO-TARGET STRATEGY IN RHEUMATOID ARTHRITIS PATIENTS IN CLINICAL REMISSION IMPROVED MRI INFLAMMATION BUT NOT DAMAGE PROGRESSION – RESULTS FROM THE IMAGINE-RA RANDOMISED CONTROLLED TRIAL

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**Background:** Magnetic Resonance Imaging (MRI) bone marrow oedema (BME)/osteitis and MRI synovitis have been identified as predictors of structural damage progression in rheumatoid arthritis RA.<sup>1,2</sup> Targeting MRI remission may reduce inflammation and halt damage progression.

**Objectives:** To investigate whether a 2 year treat-to-target (T2T) strategy targeting MRI remission (defined as absence of BME) suppresses MRI-determined measures of disease activity and structural joint damage in RA patients in clinical remission.

**Methods:** In the two year investigator initiated, randomised, open label multi-centre IMAGINE-RA study, 200 RA patients in clinical remission (defined as DAS28-CRP <3.2 and no swollen joints) receiving conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) were randomised 1:1 to a conventional DAS28-CRP guided T2T treatment strategy targeting DAS28 <3.2 and no swollen joints or an MRI guided T2T treatment strategy applying the same clinical T2T strategy and in addition targeting absence of MRI BME. Patients were followed every 4 months over a 2 year follow-up period. In all patients contrast-enhanced MRIs of the 2nd–5th metacarpophalangeal (MCP) joints and wrist of the dominant hand were performed at baseline, 12 and 24 months. In the MRI T2T arm MRI was performed every 4 months ahead of the clinical visit and assessed for presence/absence of BME by one blinded evaluator so the result was available for the investigator at the visit. In the conventional T2T arm MRI findings were blinded to the investigator. If treatment target was not met treatment was escalated according to a predefined treatment algorithm starting with increment in csDMARD and then adding biologic DMARDs. MRIs (0, 12 and 24 months) were evaluated according to the RAMRIS scoring system, with known chronology by one blinded experienced reader. Pearson's chi-square statistics and repeated-measures logistic regression models were used to assess outcomes.

**Results:** MRI outcomes of inflammation and damage at 24 months are presented in the table 1. The MRI T2T arm showed statistically significant reductions at 24 months in all inflammatory endpoints (osteitis, tenosynovitis and total inflammation score,  $p < 0.018$ ), except synovitis, ( $p = 0.074$ ), compared to the conventional T2T arm. No differences between treatment strategies were seen in damage progression.

Abstract OP0149 – Table 1 MRI outcomes at 24 months

MRI outcomes at 24 months				
	MRI T2T	Conventional T2T	Difference between groups (95% CI)	P value*
<b>MRI</b>				
<b>Inflammation</b>				
Change in osteitis (RAMRIS) score	-1.8 (0.6)	-0.1 (0.5)	-1.8 (-3.2 to -0.3)	0.018
Change in synovitis (RAMRIS) score	-0.5(0.3)	0.3 (0.3)	-0.8 (-1.8 to 0.1)	0.074
Change in tenosynovitis (RAMRIS) score	-0.9 (0.3)	0.3 (0.3)	-1.2 (-2.1 to -0.3)	0.007
Change in total inflammation (RAMRIS) score	-2.9 (1.0)	0.7 (1.0)	-3.6 (-6.4 to -0.8)	0.013
<b>Damage</b>				
Change in erosion (RAMRIS) score	0.5 (0.2)	0.6 (0.2)	-0.1 (-0.6 to 0.4)	0.663
Change in JSN (RAMRIS) score	0.1 (0.2)	0.4 (0.1)	-0.3 (-0.7 to 0.2)	0.235
Change in total damage (RAMRIS) score	0.6 (0.3)	1.0 (0.3)	-0.3 (-1.2 to 0.5)	0.395
No progression in erosion (RAMRIS), n (%)	59 (79.7%)	70 (75.3%)	OR, 1.06 (0.02 to 66.59)	0.976

95% CI, 95% confidence interval; JSN=joint space narrowing; MRI=Magnetic Resonance Imaging; RAMRIS=RA magnetic resonance imaging scoring system; T2T=treat-to-target; total damage score=sum score of MRI erosion and JSN; total inflammation score=sum score of MRI synovitis, osteitis and tenosynovitis. Data are presented as least square means (SE) unless otherwise stated. Analyses are based on full analysis set (patients having a baseline visit and at least one follow-up visit) with no data imputation to replace missing data. \*P values are based on repeated-measures logistic regression models. For some of the variables, fewer patients were included in the analyses due to missing data, with the minimum being 85 (range 85-89) in the MRI T2T arm and 90 (range 90-95) in the conventional T2T arm.

**Conclusions:** An MRI T2T strategy, aiming to eliminate MRI BME, was more effective than a conventional T2T strategy in reducing MRI inflammation but not MRI damage progression. The reduced inflammatory load caused by the MRI T2T strategy may reduce long-term structural joint damage and improve patient-

reported outcomes, but more than two years follow-up data are needed to clarify this.

Clinicaltrials.gov Identifier: NCT01656278

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OP0150

### ULTRASOUND POWER DOPPLER ACTIVITY PREDICTS CLINICAL JOINT SWELLING IN EARLY RHEUMATOID ARTHRITIS PATIENTS: SECONDARY ANALYSES FROM THE ARCTIC TRIAL

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**Background:** Ultrasound is increasingly applied in the management of rheumatoid arthritis (RA). It is important to detect synovitis early to prevent future joint damage and disability. It is not known whether subclinical ultrasound inflammation in a joint precedes clinical joint swelling.

**Objectives:** We aimed to investigate whether ultrasound power Doppler (PD) activity in a joint is associated with subsequent clinical joint swelling in early RA patients.

**Methods:** In the treat-to-target ARCTIC trial, DMARD naïve early RA patients were randomised to follow-up with or without ultrasound, with the same treatment algorithm applied in both arms. Patients were assessed by 44 swollen joint count at all visits (13 visits over two years). Ultrasound examinations were performed using a validated 0–3 semi-quantitative scoring system.<sup>1</sup> with assessments at all visits in the ultrasound arm and at baseline, 12 and 24 months in the conventional arm. We calculated the risk of next-visit clinical joint swelling according to ultrasound inflammation status in clinically non-swollen joints at the preceding visit. We estimated the odds ratio of a joint being swollen at next visit in joints with different PD activity (PD score: 1, 2 or 3), compared to non-swollen joints with no PD activity (PD score=0). These calculations were performed in a logistic mixed-effects model with random intercepts for patient and joint in order to account for within-patient and -joint dependencies, and were adjusted for age, gender, ACPA status, DMARD treatment and strategy arm. Joints injected with corticosteroids were excluded. Data from the two strategy arms were pooled and analysed together, as clinical and radiographic outcomes were similar in the two arms after two years.<sup>2</sup>

**Results:** 230 patients were included (118 in the ultrasound strategy arm, 112 in the conventional strategy arm). Mean (SD) age was 51.4 (13.7) years, 61% were female and mean baseline DAS was 3.46 (1.17). The risk of clinical joint swelling at the next visit increased with grade of PD activity (table 1).

Abstract OP0150 – Table 1. Risk of swollen joint at the next visit in joints with subclinical synovitis

Ultrasound assessment	Joint swelling at the next visit n (%)	OR	p-value
PD 0	706/42819 (1.7%)	Reference:	
PD 1	37/469 (7.9%)	3.6 [2.3–5.5]	<0.001
PD 2	33/189 (17.5%)	11.8 [6.9–20.1]	<0.001
PD 3	7/45 (15.6%)	12.1 [4.1–35.7]	<0.001

PD=Power Doppler. Odds ratios are adjusted for within-patient and within-joint dependencies, gender, age, DMARD treatment, ACPA status and strategy arm.

**Conclusions:** We found PD activity in non-swollen joints to be strongly associated with development of clinical joint swelling at the next visit, and the risk increased with higher power Doppler activity. This study supports the use of ultrasound as a tool to detect joints at risk for developing clinical synovitis.

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OP0151

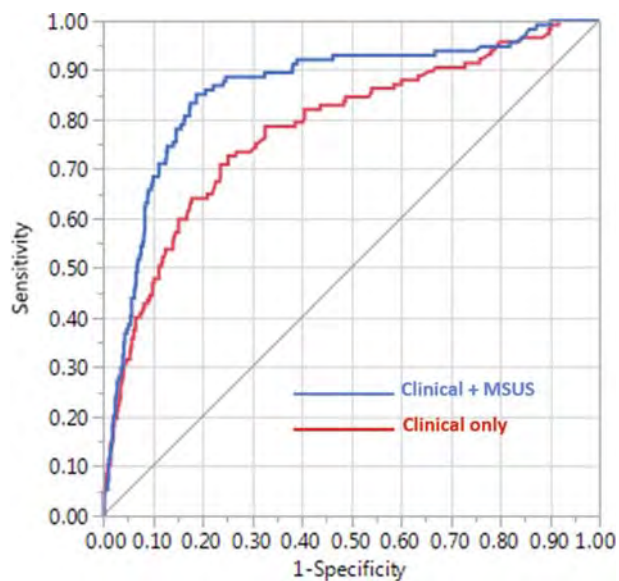
### ROUTINELY RECORDED MUSCULOSKELETAL ULTRASOUND FINDINGS IMPACT CLINICIANS' DIAGNOSTIC BEHAVIOUR MAXIMALLY IN AUTOANTIBODY-SERONEGATIVE PATIENTS ATTENDING AN EARLY ARTHRITIS CLINIC

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**Background:** Musculoskeletal ultrasound (MSUS) is a popular assessment tool, but its contribution to diagnostic practice over and above standard clinical and laboratory parameters has proved difficult to quantify.

**Objectives:** A published 7-joint ultrasound algorithm<sup>1</sup> has been adapted for pragmatic application during 15 min screening appointments forming part of initial patient assessments in the Newcastle Early Arthritis Clinic (NEAC). Its additive contribution to diagnostic classification in this routine setting was appraised.

**Methods:** Detailed baseline clinical and laboratory parameters were recorded. Semi-quantitative MSUS scoring (0–3, grey scale and power Doppler) of the most symptomatic wrist (midline and ulnar dorsal longitudinal views), 2nd/3rd MCPs and PIPs and 2nd/5th MTPs (all longitudinal views) was recorded by sonographers, along with the 'sonographer's scan impression' ('definitely inflammatory,' 'possibly inflammatory' or 'non-inflammatory'). All MSUS findings were available to rheumatologist diagnosticians during subsequent consultations, and persistent inflammatory arthritis (PIA) was classified only where patients were started on  $\geq 1$  disease modifying anti-rheumatic drug (DMARD). Stepwise multiple logistic regression was employed to identify clinical variables that independently predicted IA diagnosis; the additive contribution of MSUS parameters to resultant models was assessed by comparing areas under receiver operator characteristic curves (AU ROCs).



**Abstract OP0151** – Figure 1 ROC curves depicting additive discriminatory utility of MSUS 'scan impression' with clinical parameters alone (red), with respect to PIA diagnosis amongst seronegative early arthritis patients.  $\Delta$  AU AOC=0.08;  $p < 0.001$

**Results:** 847 patients were enrolled (17% seropositive for anti-citrullinated peptide autoantibody, ACPA); final outcomes of PIA were recorded in 29% and 18% of the overall and ACPA-seronegative cohorts, respectively. SJC, CRP, age and ACPA status were non-redundant clinical/laboratory predictors of a PIA diagnosis by consulting rheumatologists in the overall cohort (AU ROC 0.85; 95% CI: 0.81 to 0.88), their discriminatory utility being diminished in the seronegative sub-cohort (AU ROC 0.78; 95% CI: 0.72 to 0.82). Although the additive contribution of

summed parameters from the 7-joint MSUS algorithm to the model was statistically significant ( $p < 0.001$ ) it was numerically small ( $\Delta$  AU ROC 0.03 and 0.05 in the overall and seronegative cohorts, respectively). The 'sonographer's scan impression' was a potentially more useful diagnostic tool, its additive contribution to diagnostic outcome over clinical parameters alone being most evident in ACPA-negative patients where it increased the AU ROC by 10% ( $\Delta$  AU ROC 0.08;  $p < 0.001$ ; figure 1).

**Conclusions:** In this large, un-blinded observational study, the clinical utility of a 15 min MSUS screen for diagnosing PIA requiring DMARDs was particularly evident amongst ACPA negative patients attending an EA clinic.

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OP0152

### IS SONOGRAPHIC PHENOTYPE OF LATE-ONSET RHEUMATOID ARTHRITIS DIFFERENT FROM YOUNG-ONSET RHEUMATOID ARTHRITIS? RESULTS FROM THE BIRMINGHAM EARLY ARTHRITIS COHORT

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**Background:** The incidence of rheumatoid arthritis (RA) is generally seen as a bimodal age distribution, which consists of young-onset RA (YORA) and late-onset RA (LORA). Although a retrospective study has reported some differences in sonographic changes between LORA and YORA, little is known whether there are any differences in the clinical and sonographic phenotypes between these two groups during the early disease phases.

**Objectives:** To compare the clinical and sonographic characteristics between YORA and LORA during the early phases of disease.

**Methods:** DMARD-naïve patients with clinically apparent synovitis of at least one joint and symptom duration of three months or less were included in the analysis. Patients underwent clinical, ultrasonography and radiological assessments at baseline and final outcomes were determined at 18 months; patients were classified as having RA (according to either the 1987 ACR and/or 2010 ACR/EULAR criteria), a non-RA persistent arthritis or a resolving arthritis. Sonographic assessment included MCP, PIP, wrist, MTP, knee, ankle, elbow joints and wrist, hand flexor, bicep tendon, anteromedial-lateral tendon compartments. The presence and absence of joint synovitis and tenosynovitis were recorded according to the EULAR/OMERACT consensus definition.

	Young-onset RA (n=37)	Late-onset RA (n=36)	Non-RA persistent arthritis (n=27)	Resolving arthritis (n=50)	P (YORA vs LORA)
Age (years)	50 (45–56)	67 (63–73)	39 (31–60)	46 (35–59)	<0.001
EMS (mins)	75 (30–120)	120 (60–240)	60 (10–180)	30 (0–68)	0.808
DAS-28 CRP	5.02 (3.60–5.73)	5.11 (4.49–6.10)	3.77 (3.02–4.95)	3.35 (2.98–4.43)	1.00
RF%					
High Positive	15 (40.5)	10 (27.8)	1 (3.7)	2 (4)	0.568
Low Positive	5 (13.5)	7 (19.4)	4 (14.8)	1 (2)	
Negative	17 (45.9)	19 (52.8)	22 (81.5)	47 (94)	
ACPA %					
High positive	17 (45.9)	14 (38.9)	2 (7.4)	2 (4)	0.722
Low positive	1 (2.7)	2 (5.6)	0 (0.0)	0 (0.0)	
Negative	19 (51.4)	20 (55.6)	25 (92.6)	48 (96.0)	
Symptom duration (weeks)	8 (4–10)	8 (6–10)	6 (4–8)	5 (4–8)	1.00
Bilateral MTP squeeze, n (%)	22 (59.5)	10 (27.8)	4 (14.8)	10 (20.0)	0.09

**Results:** 150 patients were included in the analysis. At 18 months, 37 patients developed YORA, 36 developed LORA, 27 developed non-RA inflammatory arthritis and 50 patients had resolving arthritis. The clinical characteristics

between YORA and LORA were not significantly different at initial presentation (table 1). The ultrasound characteristics differed between these two groups. LORA patients were more likely to have shoulder biceps tendon tenosynovitis (GS;  $p=0.026$ , PD; 0.037), elbow joint synovitis (GS;  $p=0.010$ , PD;  $p=0.037$ ), MCP1 (PD;  $p=0.032$ ) and MCP5 (GS;  $p=0.035$ ) synovitis, compared to YORA patient. YORA patients were more likely to have MTP synovitis (GS;  $p=0.013$ ) compared to LORA patients.

**Conclusions:** This is the first study to describe the difference of both clinical and sonographic inflammation of YORA and LORA in recent-onset DMARD-naïve RA patients in a longitudinal study. There are differences in US-detected joint and tendon inflammation despite similarities in clinical characteristics. The prognostic value of the differences in US pathology between these two groups should be further explored.

**Disclosure of Interest:** None declared

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**OP0153 RESOLUTION OF SYMPTOMS OF PATIENTS WITH CLINICALLY SUSPECT ARTHRALGIA IS PARALLELED BY DISAPPEARANCE OF MRI-DETECTED SUBCLINICAL INFLAMMATION; A LONGITUDINAL STUDY**

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**Background:** It is known that MRI-detected subclinical inflammation in patients with Clinically Suspect Arthralgia (CSA) precedes the development of clinically evident Inflammatory Arthritis (IA). However, there are no longitudinal studies in CSA patients that did not progress to IA. The course of joint symptoms in these patients is unknown. Furthermore, it is unknown if subclinical inflammation resolves spontaneously in parallel with disappearance of joint symptoms.

**Objectives:** To determine the course of joint symptoms and of MRI-detected subclinical joint inflammation, and mutual time relationships, in patients that presented with CSA but did not progress to IA during 2 year follow-up.

**Methods:** Between April 2012-April 2014, 149 patients were included in the CSA cohort. These patients had no clinically evident arthritis but recent-onset (<1 year) arthralgia of small joints that was clinically considered at risk for IA by the rheumatologist. None of the patients were treated with DMARDs. Patients underwent MRI at baseline and when arthritis developed or after 2 years (when follow-up ended). The patients that did not progress to IA within 2 years and had serial MRIs, as well as longitudinal clinical data and questionnaires (e.g. the HAQ), were studied ( $n=60$ ). 1.5T MRIs of wrist, MCP2-5, and MTP1-5 joints were scored for synovitis, tenosynovitis and bone marrow oedema (BME) (summed in the total MRI inflammation score) according to RAMRIS, blinded for order in time and clinical information. Paired t-tests were used.

**Results:** After 2 year follow-up, 20 patients (33%) had complete resolution of symptoms whereas 40 patients (66%) did not. The remaining symptoms in the latter group were diagnosed as: persistent inflammatory arthralgia ( $n=26$ ), osteoarthritis ( $n=6$ ) and tendinomyalgia ( $n=8$ ). In the total group, the mean total MRI-inflammation score decreased from 3.2 at baseline to 2.5 at 2 years ( $p=0.046$ ). When the patients with persistent symptoms were studied, there were no significant changes in MRI-inflammation scores. Analysing the patients with resolution of symptoms separately, the total MRI-inflammation score decreased significantly ( $3.3$  to  $2.3$ ;  $p=0.019$ ). Also the total synovitis and tenosynovitis scores decreased significantly ( $1.3$  to  $0.82$  and  $0.83$  to  $0.30$ , respectively;  $p=0.043$  and  $p=0.029$ ), whereas BME scores remained unchanged ( $1.2$  and  $1.2$ ;  $p=0.87$ ). After 2 year follow-up the absolute MR-scores of these patients were compared to data from age-matched symptom-free controls; no differences were found for synovitis, suggesting normalisation. Physical functioning, measured with HAQ, remained similar in patients with persistent symptoms ( $0.56$  to  $0.51$ ;  $p=0.61$ ), whereas HAQ normalised in patients with resolution of symptoms (mean score of  $0.15$  at 2 years,  $p=0.053$  compared to baseline).

**Conclusions:** Approximately one-third of the patients that presented with CSA and that did not convert to IA had resolution of symptoms, this was paralleled by normalisation of MRI-detected inflammation as well as physical functioning. This is the first study showing that subclinical inflammation in individuals at risk for developing RA can resolve spontaneously. The data suggest that subclinical inflammation was causally related to joint pain.

**Disclosure of Interest:** None declared

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**OP0154 PROSPECTIVE OBSERVATIONAL STUDY TO EVALUATE THE USE OF MUSCULOSKELETAL ULTRASONOGRAPHY TO IMPROVE RHEUMATOID ARTHRITIS MANAGEMENT: INTERIM ANALYSIS OF THE ECHO STUDY**

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**Background:** Musculoskeletal Ultrasound (MSUS) has been shown to be superior to clinical examination in the detection of synovitis in patients with Rheumatoid Arthritis (RA), and can be used to improve diagnostic accuracy and potentially monitor disease changes in order to make treatment decisions aimed at optimising patient care. Since the creation of the Canadian Rheumatology Ultrasonography Society (CRUS) in 2010, an increasing number of rheumatologists has been trained in the use of MSUS.

**Objectives:** The overall study objective is to compare the effectiveness of MSUS to Routine Care (RC) as a disease management tool in patients with moderate-to-severe RA for whom a change in treatment is indicated. In addition, the predictive power of MSUS assessments has been assessed here.

**Methods:** 'Echo' is a prospective two-cohort, quasi-experimental study of patients diagnosed with active moderate-to-severe RA managed either with MSUS (within CRUS) or as per RC. To be eligible for the study patients must require a change in treatment as per the judgment of the treating physician. Patients are followed for 1 year with assessments at baseline, 3, 6, 9, and 12 months. Key outcome measures of interest include CDAI LDA/Remission, DAS-28 LDA/Remission, patient satisfaction (TSQM) and patient perception of participation in disease management (PAM-13).

**Results:** A total of 383 patients (71.5% female) with a mean (SD) age of 58.7 (11.7) years and disease duration of 7.0 (10.0) years were enrolled, without any significant differences between treatment groups.

At baseline, a greater proportion of patients in the MSUS group were treated with a biologic DMARD (bDMARD; 50.3% vs 35.8%,  $p=0.004$ ); patients in the RC group were more likely to be treated with a non-biologic DMARD (nbDMARD; 84.2% vs 91.5%,  $p=0.027$ ). Over time, a comparable proportion of patients in the two groups started/switched a bDMARD (21.6% vs 15.6%,  $p=0.126$ ) or added/switched a nbDMARD (18.7% vs 23.6%,  $p=0.248$ ). The overall number of treatment modifications was also similar between groups (3.0 vs 2.7,  $p=0.236$ ).

Upon adjusting for age, gender, previous bDMARD treatment, and baseline parameter level, no differences between the two treatment groups with respect to CDAI LDA/Remission, DAS-28 LDA/Remission, and TSQM score were observed during follow-up. However, the PAM-13 score was significantly higher in the MSUS group (69.6 vs 64.2,  $p=0.02$ ).

In the MSUS group, higher total US erosion score at baseline was associated with a lower rate of CDAI LDA at 12 months (OR=0.86;  $p=0.047$ ); higher total PD synovitis score at baseline was associated with a lower rate of CDAI LDA at 6 months (OR=0.90;  $p=0.010$ ), and; higher total synovitis GREY scale at baseline was associated with lower rates of DAS28 LDA (OR=0.93;  $p=0.026$ ) and DAS28 remission (OR=0.94;  $p=0.061$ ) at 6 months.

**Conclusions:** MSUS assessments can be useful predictors of future disease remission in patients with RA. MSUS may be associated with increased patient perception of participation in disease management and patient activation.

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**OP0155 ULTRASOUND AS AN OUTCOME MEASUREMENT TOOL FOR OPTIMISED MONITORING OF GOUT. VALIDATION OF THE OMERACT ULTRASONIC DEFINITIONS OF GOUT ELEMENTARY LESIONS**

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**Objectives:** To evaluate ultrasound (US) as an outcome measurement instrument for monitoring gout patients during urate lowering therapy using the OMERACT US Working Group's 2015 definitions of US elementary lesions in gout.

**Methods:** US examination (28 joints, 26 tendons) were performed in patients with microscopically verified gout who either initiated or increased urate lowering therapy. Joints and tendons were evaluated for the four OMERACT elementary lesions of gout (Double contour, Tophus, Aggregates and Erosions). Furthermore, subcutaneous (SC) oedema was registered and synovitis was graded by grey scale (GS) and colour Doppler (CD) (both graded 0-3). A sum score was



calculated for each component for each patient (table 1). Patient Reported Outcomes (PROs) regarding pain (visual analogue scale), numbers of attacks within the last 3 months and physical function (Health Assessment Questionnaire) were obtained, as were C-reactive protein (CRP), p-urate and clinical joint examination. All examinations were repeated after 3 (n=29) and 6 months (n=15, follow-up still ongoing) and changes in scores were evaluated using Wilcoxon-Pratt signed-rank test.

**Results:** 29 patients (28 males, 1 female), mean age of 68 (39 – 89) years were included. US showed a numerical, but statistically non-significant (p=0.13), decline in DC count from baseline to 3 months' follow up, while at 6 months a statistically significant decline was observed (p=0.033). The tophus count decreased non-significantly at both 3 and 6 months' follow up, whereas the aggregate and erosion counts by large were unchanged. GS synovitis showed a statistically non-significant decrease at follow ups, whereas CD synovitis and SC oedema counts declined significantly at 3 months' follow up (p=0.033 and 0.044, respectively). P-urate levels decreased statistically significant from baseline to both 3 and 6 months' follow-up (both p-values<0.001), as did clinical markers such as CRP, joint evaluation, pain and attack frequency.

**Abstract OP0155** – Table 1 Course of US, biochemical and clinical variables during urate lowering therapy

Variable (possible range)	Baseline (n=29)		3 months' follow up (n=29)		p-value*
	Mean	Median (range)	Mean	Median (range)	
<b>Ultrasound scores**</b>					
Double contour (0-28)	3.8	4 (0-10)	2.3	2 (0-9)	0.13
Tophi (0-54)	2.8	2 (0-8)	2.4	2 (0-8)	0.42
Aggregates (0-54)	5.6	4 (2-14)	5.2	5 (2-13)	0.85
Erosions (0-28)	2.3	2 (0-5)	2.4	2 (0-5)	0.88
Grey Scale synovitis (0-132)	8.5	8 (1-19)	6.9	6 (1-19)	0.22
Color Doppler synovitis (0-132)	3.4	3 (0-10)	2.0	2 (0-6)	0.033
Subcutaneous oedema (0-28)	2.8	0 (0-12)	1.2	0 (0-12)	0.044
<b>Biochemical and clinical variables</b>					
P-urate (mmol/L)	0.48	0.47 (0.32-0.60)	0.35	0.35 (0.24-0.51)	<0.001
Serum C-reactive protein	15.9	11.0 (0.30-120)	4.0	1.8 (0.30-20.0)	0.009
Synovial joints (0-40)***	2.3	2 (0-14)	1.3	0 (0-14)	0.011
Tender joints (0-40)***	3.0	2 (0-18)	1.3	0 (0-7)	0.008
Patient VAS (0-100)	40.6	40 (0-95)	17.5	10 (0-75)	0.009
Numbers of attacks within last 12 weeks	2.1	2 (0-4)	0.4	0 (0-3)	<0.001
HAQ (0-3)	0.185	0 (0-1.125)	0.129	0 (0-1.125)	0.52
<b>SUBPOPULATION</b>					
Variable	Baseline (n=15)		6 months' follow up (n=15)		p-value*
	Mean	Median (range)	Mean	Median (range)	
<b>Ultrasound scores**</b>					
Double contour (0-28)	4.1	4 (0-9)	1.8	2 (0-7)	0.038
Tophi (0-54)	3.4	2 (0-8)	2.3	2 (0-8)	0.28
Aggregates (0-54)	5.6	4 (2-14)	5.1	3 (2-10)	0.97
Erosions (0-28)	2.7	2 (0-5)	2.7	2 (0-4)	1.00
Grey Scale synovitis (0-132)	8.8	10 (1-19)	7.5	8 (2-17)	0.58
Color Doppler synovitis (0-132)	3.7	4 (0-9)	3.1	3 (0-7)	0.60
Subcutaneous oedema (0-28)	3.5	5 (0-12)	0	0 (0-0)	0.004
<b>Biochemical and clinical variables</b>					
P-urate (mmol/L)	0.48	0.47 (0.32-0.60)	0.33	0.30 (0.23-0.51)	<0.001
Serum C-reactive protein	22.2	14.0 (0.3-120)	8.7	2.3 (0.30-14.0)	0.018
Synovial joints (0-40)***	3.1	2 (0-14)	1	0 (0-4)	0.030
Tender joints (0-40)***	4.1	3 (0-18)	0.7	0 (0-5)	0.005
Patient VAS (0-100)	39	40 (0-85)	11	5 (0-60)	0.017
Numbers of attacks within last 12 weeks	2.4	2 (0-4)	0.5	0 (0-3)	<0.001
HAQ (0-3)	0.150	0 (0-1.125)	0.150	0 (0-1.125)	0.70

\*p-values are calculated using Wilcoxon-Pratt signed rank test, two-sided p-values. Values in bold indicate p<0.05.  
 \*\* joints evaluated by US: Metatarsophalangeal, wrist, elbow, metatarsophalangeal, distal and proximal joints. Tendon compartment evaluated by US: Extensor tendons of the wrist (divided in compartments 1-6), biceps brachii and brachii radialis and ulnaris tendons were evaluated for tenosynovitis (TS) and CD; aggregates and tophi. Triceps, Achilles, quadriceps and patella tendons were only evaluated for aggregates and tophi.  
 \*\*\* Tender and swollen joint counts include proximal and distal interphalangeal joints of the hands and feet, metacarpal and metatarsophalangeal joints, wrist, elbow, knee/leg, ankle and knee.

**Conclusions:** Of the four OMERACT US elementary gout lesions only DC count showed a statistically significant decrease as a response to 6 months of urate lowering therapy. The number of tophi had decreased at both 3 and 6 months' follow up, but not statistically significant. Aggregates and erosions count did not markedly respond to the 6 month treatment.

The study indicates that US assessing the OMERACT elementary lesions, particularly DC, is a feasible tool for monitoring gout lesions. However, a follow-up of at least 6 months may be needed to detect change of crystal deposits, as reflected by DC, and presumably an even longer follow-up period is needed to evaluate more massive deposits as tophi.

**Disclosure of Interest:** None declared

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**OP0156 SIMPLE ASSESSMENT OF CONVENTIONAL 18F-FDG PET/CT ACCURATELY DIAGNOSES CRANIAL ARTERITIS IN GLUCOCORTICOID-NAÏVE GCA PATIENTS: A CASE-CONTROL STUDY**

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**Background:** Although older studies argue that fluorine-18-fluorodeoxyglucose (FDG) positron emissions tomography (PET)/CT cannot demonstrate inflammation in cranial arteries the spatial resolution of modern PET systems have greatly

improved allowing for more precise diagnostics of small structures. FDG PET/CT is widely used to diagnose large-vessel (LV) giant cell arteritis (GCA). Recognising FDG uptake in cranial arteries potentially adds to FDG PET/CTs diagnostic accuracy for GCA.

**Objectives:** To evaluate the diagnostic accuracy of conventional FDG PET/CT of the cranial arteries in GCA.

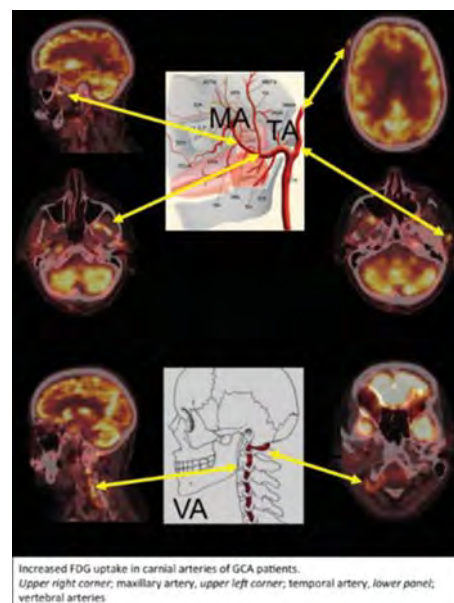
**Methods:** In a cohort of consecutively included glucocorticoid-naïve patients suspected of new-onset GCA, patients full-filling 1990 ACR criteria for GCA were identified. Conventional FDG PET/CT and clinical assessment was performed before treatment. Controls were age- and sex-matched patients with malignant melanoma (MM) who had a metastatic-disease-free follow-up FDG PET/CT<sub>≥</sub>6 months after MM resection.

All PET images were evenly cropped to include only head and neck. Images were randomly assessed by 2 nuclear medicine physicians (10 years experience) blinded to clinical symptoms and findings. Training included review of 5 GCA-PET examinations (not part of cohort). Temporal (TA), maxillary (MA) and vertebral (VA) arteries were visually scored bilaterally. Arterial FDG uptake above surrounding tissue was considered indicative of inflammation and graded low or high. If disagreement between readers occurred, final score was settled by an expert nuclear medicine physician.

Student t test was used for quantitative data. Inter-reader agreement was evaluated by Cohens weighted kappa (disagreement on diagnosis weighted 0, disagreement on FDG uptake intensity weighted 0.2).

**Results:** A total of 44 patients and 44 controls were identified. In both case and control group, the mean age was 69 years (p=0.45) and 25/44 were women. Large-vessel involvement was seen in 39/42 patients, and 35/42 were temporal artery biopsy positive. GCA patients' median global assessment of disease activity was 8 (IQR: 5–10) and median CRP was 70 (95% CI: 58; 85) mg/L.

Considering only FDG uptake in TA and/or MA, diagnostic sensitivity and specificity was 66% (95% CI: 50%–80%) and 100% (95% CI: 92%–100%). Including VA, sensitivity increased to 86% (95% CI: 73%–95%) and specificity remained high, 98% (95% CI: 88% to 100%). Cohens weighted kappa was 0.82 (agreement 93%, p=0.000) in a per segment analysis and kappa was 0.84 (agreement 92%, p=0.000) in diagnosis.



**Abstract OP0156** – Figure 1 FDG PET/CT of cranial arteries in patients with giant cell arteritis

**Conclusions:** Inter-reader agreement on FDG uptake in cranial arteries is almost perfect, and cranial arteritis in glucocorticoid-naïve GCA patients can be readily and accurately diagnosed by conventional FDG PET/CT. The high diagnostic specificity suggests that TAB can be avoided in patients with FDG uptake in cranial arteries. Moreover, FDG PET/CT performed in patients with suspected vasculitis should always include head and neck.

**Disclosure of Interest:** None declared

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THURSDAY, 14 JUNE 2018

**HPR Singing power to the people****OP0157-HPR AGREEMENT BETWEEN JIA PATIENTS AND PARENTS ON DISEASE PERCEPTION ANALYSED BY THE NORWEGIAN VERSION OF THE JAMAR QUESTIONNAIRE**

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**Background:** Juvenile Idiopathic Arthritis (JIA) has a broad impact on the child and family life. There is an increasing interest in the importance and recognition of the value of parent/patient reported outcome (PRO). Juvenile Arthritis Multidimensional Assessment Report (JAMAR) assesses essential aspects of the child's disease perception and Health Related Quality of Life (HRQoL). The intention is to enhance adequate medical decisions and to improve patient care in routine clinical setting.

**Objectives:** To determine the level of agreement between patients with JIA and their parents on the quantitative items of the Norwegian version of JAMAR, the direction of potential differences and if sex, age, disease activity and duration influence the level of agreement.

**Methods:** 129 patient/parent dyads participated in the study. The patients, aged 12 to 18 years, were included consecutively at Oslo University Hospital, St. Olavs Hospital in Trondheim, and the University Hospital of Northern Norway in Tromsø during 2012–2013. Both patients and parents completed the JAMAR questionnaire. Demographic and disease specific data were recorded. The study examined the level of agreement for the seven quantitative items in JAMAR. Pain, disease activity (DA) and wellbeing (WB) were measured by a 21-numbered circle VAS, physical function with Juvenile Arthritis Functional Score (JAFS) and HRQoL with Paediatric Rheumatology Quality of Life Scale (JQL) total score including the sub- dimensions Physical Health (JQLPH) and Psychosocial Health (JQLPsH). Both the direction of the differences in scores and whether sex, age, disease activity (MDGlobal), and duration influenced the degree of agreement were investigated. Intraclass correlation coefficient ICC was used for analysis together with paired and independent t-test.

**Results:** Median age for patients were 15 years, 66% were girls, 37% had oligoarticular JIA, 25% had polyarticular RF negative JIA, 4% had systemic JIA, 34% belonged to other categories, and median MDGlobal was 1 (range 0–7). As a group, patients and parents median scores were similar, except for JQLPH, where patients scored better than parents (p=0.002). Correlations between answers from patients and parents were significant for all items (p<0.001), strength varying from ICC 0.70 for JQLPsH to strongest correlation for pain with ICC 0.93. Individual dyads agreement was low showing discordance ( $\geq 1$ ) in at least one item in up to 70% of the pairs.<sup>2</sup> Male patients scored better and female patients scored worse for WB than their parents (p=0.03). Patients with MDGlobal  $\leq 1$  scored less pain and patients with MDGlobal  $>1$  scored more pain than their parents (p=0.01).

**Conclusions:** The Norwegian version of JAMAR is a PRO- and HRQoL-tool suitable for standard clinical care. The study shows high level of agreement between patients and parents as groups, but the strength of the agreement varies between the items. Comparing dyads showed substantial differences on all items. Thus it is important that both adolescent patients and parents complete the questionnaire, and that both reports are used to support adequate clinical assessment and care.

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**Disclosure of Interest:** None declared

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**OP0158-HPR EFFECTIVENESS OF AN E-HEALTH TAILORED SELF-MANAGEMENT PROGRAM FOR PATIENTS WITH RHEUMATOID ARTHRITIS: AN EXPLORATIVE RCT**

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**Background:** E-health programs have potential to support RA patients in self-management. However, many of these programs are developed without involving patients. As a consequence, patient preferences for program use are not well

known and these programs may not well suit patient's needs for self-management support. We developed a tailored e-health self-management program for patients with RA with the help of a patient panel. While self-management interventions are complex interventions, it is informative to perform an explorative RCT before embarking on a larger trial.

**Objectives:** 1) Evaluate the potential effectiveness in patients with RA of a 12 month tailored e-health self-management program, versus 'usual care', on self-management behaviour, self-efficacy, general health status, focus on fatigue and the level of pain and fatigue; 2) exploration of floor and ceiling effects of the potential outcome measures at baseline and effect sizes at 6 and 12 months after baseline were used to identify outcome measures most likely to capture potential benefits

**Methods:** The RCT was performed in out-patients from two hospitals in the Netherlands. Inclusion criteria were RA patients 18 years or older, being able to speak and read Dutch and having access to internet. Patients were randomised to 'e-health' in addition to 'usual care' or to 'usual care' alone. The 'e-health' group received 12 months access to the online self-management program. Assessment of outcomes occurred at baseline, 6 and 12 months. Outcome measures included self-management behaviour (PAM-13, SMAS-S), self-efficacy (RASE, PEPPI-5), general health status (RAND-36), focus on fatigue (MPCI-F), pain and fatigue (NRS scales). A linear mixed model for repeated measures, using the intention to treat principle was used to study differences between intervention and control groups. A sensitivity analysis was performed to study the influence of high and low compliance in the intervention group

**Results:** In total 157 patients (n=78 intervention group versus n=79 control group) were included in the study. A statistically significant (p<0.05) between-group difference was only shown for the RAND-36 vitality after 12 months, in favour of the 'e-health' group. Effect sizes were low. Compared with the patients with non or low compliance, patients with a high compliance to the intervention scored statistically significant better on RAND-36 perception after 12 months. Here also, effect sizes were low. Floor and ceiling effects were not apparent in the outcomes used.

**Conclusions:** Based on these results it is not possible to conclude on possible positive effects of the intervention: for all outcomes the effect sizes were low. Consequently, it is not possible to select outcome measures to be regarded as primary/main secondary outcomes for a larger trial. A process evaluation should be performed to give an explanation for the findings of this study.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.6542

**OP0159-HPR REUMANET BERNHOVEN: INTRODUCTION AND EVALUATION OF AN ONLINE SELF-MANAGEMENT TOOL AND PERSONAL HEALTH ENVIRONMENT FOR PATIENTS WITH RHEUMATOID ARTHRITIS(RA)**

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**Background:** Over the past 15 years, there has been a huge shift in the management of RA: the armamentarium has increased but also the way antirheumatic drug are being used has changed, e.g.treat to target. This has implications for how the communication between professional and patient needs to occur: hence shared decision making part of most guidelines. Therefore, healthcare must be organised in a different way: patients should be more involved in their treatment and patient's self-management should play a very important role. The use of a personal health environment can be an effective tool to involve patients in their disease management and helps to optimise the communication between the patient and health professionals.

**Objectives:** The aim of this project was to create an online personal health environment with self-management tools for patients with rheumatoid arthritis (RA) and determine the factors limiting patients to use this environment.

**Methods:** Since April 2017 a new online personal health environment was developed in the Netherlands especially for patients with RA, called Reumanet Bernhoven. It includes: 1. an overview of the medication and comorbidities, 2. a graphic of disease-related values (e.g.DAS28, anti-ccp, SR, BMI, 36-Item Short Form Health Survey (SF-36), Health Assessment Questionnaire (HAQ) and RA Impact of Disease (RAID)), 3. a diary, 4. questionnaires such as the different VAS scales (pain, fatigue, general health), Health Assessment Questionnaire HAQ, SF-36 and RAID questionnaire to prepare the outpatient visit. 5. an application to send messages to the health professional. 6. a library with useful disease-specific information. 7. a graphic overview of the DAS28 in combination with the RAID questionnaire to self monitor disease activity. After six months those patients who did not use Reumanet yet were contacted to reveal the cause.

**Results:** By November 2017, 997 RA-patients were included in Reumanet Bernhoven. 56% (n=557) used it at least once in this 6 month period. 13% (n=70) of them used the self monitoring tool. The remaining patients, 44% (n=440) were questioned for not using Reumanet at home. 55% (n=242) of these patients responded and 14% (n=62) do want to participate yet, 26% (n=114) did not have a computer or email address, 16% (n=71) did not want to using a digital environment at home.

**Conclusions:** Half of the RA-patients used Reumanet at home of which 13% performed self-monitoring of their disease activity in this online personal health environment. Reumanet will be seen as a promising tool to involve patients in their disease management and can be helpful for shared decision making between patient and health professional. In future, more research is needed to optimise patient self-management in a digital health environment in order to increase its usage.

**Disclosure of Interest:** None declared

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#### OP0160-HPR DETERMINANTS OF HAPPINESS AND QUALITY OF LIFE IN PATIENTS WITH RHEUMATOID ARTHRITIS: A STRUCTURAL EQUATION MODELLING APPROACH

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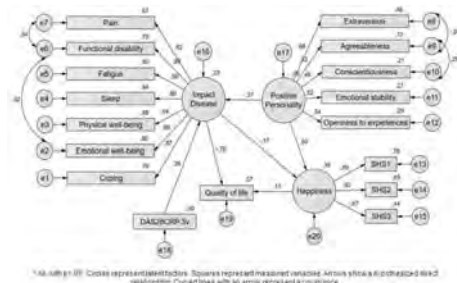
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**Background:** Remission is the core target of disease management in rheumatoid arthritis (RA), but the ultimate goal of medical care is to improve patients' enjoyment of life, a concept akin to happiness. What is the contribution of disease control towards happiness and what other means may the health professional consider towards that goal?

**Objectives:** To examine the determinants of happiness and quality of life (QoL) in patients with rheumatoid arthritis (RA), with emphasis on disease activity, disease impact and personality traits.

**Methods:** This is an ancillary analysis of an observational, cross-sectional study. Consecutive patients were assessed on disease activity, disease impact, personality, QoL and happiness. Structural equation modelling estimation was used to assess the associations between these dimensions, pursuing three hypotheses: H<sub>1</sub> – Disease activity and perceived impact of disease are negatively associated to overall QoL and happiness in patients with RA; H<sub>2</sub> – 'Positive' personality traits are related to happiness both directly and indirectly through perceived disease impact; H<sub>3</sub> – Happiness has a mediating effect in the relation between impact of disease and QoL.

**Results:** Data from 213 patients was analysed. Results obtained in the structural equation measurement model indicated a good fit [ $\chi^2/df=1.38$ ; CFI=0.98; GFI=0.92; TLI=0.97; RMSEA=0.04] and supported all three driving hypotheses (figure 1). Happiness was positively related to 'positive' personality (total effect of 0.56, with a direct effect of  $\beta=0.50$ ,  $p<0.001$  and an indirect effect of  $\beta=0.06$ ,  $p=0.03$ ) and, to a lesser extent, negatively related with perceived impact of disease ( $\beta=-0.17$ ;  $p=0.02$ ). This impact, in turn, was positively related to disease activity ( $\beta=0.36$ ;  $p<0.001$ ) and mitigated by 'positive' personality traits ( $\beta=-0.37$ ;  $p<0.001$ ). Impact of disease had a much stronger relation with QoL than with happiness (total effect of 0.72, of which  $\beta=-0.02$ ,  $p=0.04$  was an indirect effect vs  $\beta=0.17$ ;  $p=0.02$ , respectively). Happiness mitigated the negative effect of disease impact upon QoL ( $\beta=0.13$ ;  $p=0.01$ ). Moreover, disease activity had a negative indirect effect of  $-0.26$  ( $p=0.003$ ) on QoL and also a negative indirect effect of  $\beta=-0.06$  ( $p=0.04$ ) on happiness.



**Abstract OP0160-HPR – Figure 1.** Estimated standardised direct effect for the proposed model.

**Conclusions:** Optimisation of QoL and happiness of people with RA requires not only effective control of the disease process but also improvement of the disease impact domains. Personality, and its effects upon the patient's perception and experience of life, seems to play a pivotal mediating role in these relations and should deserve paramount attention if happiness and enjoyment of life is taken as the ultimate goal of health care.

**Disclosure of Interest:** None declared

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#### OP0161-HPR THE DEVELOPMENT OF SELF-MANAGEMENT TRAINING FOR INNOVATIVE DEPARTMENTS (STRIDE): A SKILLS-TRAINING PROGRAMME FOR RHEUMATOLOGY TEAMS TO ENHANCE SUPPORT FOR SELF-MANAGEMENT

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**Background:** Integrating self-management support into clinical practice is a key NHS, UK, EU and USA policy.<sup>1-3</sup> A survey with >1000 UK patients with inflammatory arthritis showed that many would like support to manage the impact of symptoms (82%), emotions (57%), and depression (34%).<sup>4</sup> However, rheumatology teams rated the support they offer as inadequate, and one of the main reasons is the lack of appropriate skills-training for healthcare professionals.<sup>5</sup> Evidence suggests that self-management support provision works best when it is condition-specific and has team and organisational support.<sup>6,7</sup>

**Objectives:** To develop a skills-training programme for rheumatology teams to enhance support for self-management provision through enhancing current skills and facilitating self-management strategy development.

**Methods:** The steering team comprised clinicians, academics with expertise in self-management and HP education, and two patient partners. To inform the practicalities and structure of the programme and optimise feasibility and acceptability, qualitative telephone interviews were performed with 11 rheumatology healthcare professionals, focusing on barriers and enablers of providing self-management support, and how to optimise buy-in.

**Results:** Interviews identified key considerations and practical recommendations for programme development including: the challenge vs value of involving the whole team; providing opportunities to practice skills; focusing on how to implement skills in clinical practice; and using peer support and prompts to develop and maintain skills. The Self-Management Training for Innovative Departments (STRIDE) programme was therefore formulated to comprise two 3 hour training sessions to whole teams at local departments, approximately 4-6 weeks apart (6 CPD hours). It contains modules on self-management, motivational interviewing, collaborative care and agenda setting, communication and acceptance, and signposting (eg for psychological or peer support) and the opportunity for teams to review their own practice and patient pathways. Delivery involves presentation of the evidence base, group discussion, 4 patient videos, skills demonstrations, and practice and feedback opportunities, facilitated by two expert trainers. Teams are provided with a localised support package after each session, which includes individual behavioural/attitudinal issues and team care provision points discussed during training and raised as potential areas to take forward.

**Conclusions:** Interviews highlighted the challenges in developing team training, and enabled the development of a practical, brief training programme. The STRIDE programme is currently being piloted and evaluated with five rheumatology teams across England. Evaluation involves assessment of healthcare professional skills, knowledge and confidence (pre and post training questionnaires); healthcare professional experiences of training (qualitative interviews); and a patient-based evaluation (pre and post training questionnaires).

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**Disclosure of Interest:** None declared

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**OP0162-HPR ESTIMATING HEALTH-RELATED QUALITY OF LIFE FOR GOUT PATIENTS: A POST-HOC ANALYSIS OF UTILITIES FROM THE CLEAR TRIALS**

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**Background:** Prior studies of health-related quality of life (HRQoL) in gout patients have shown significant disutilities associated with flares and tophi or serum uric acid (sUA).<sup>1,2</sup> However, no prior study has explored the simultaneous impact of all three aspects of gout severity.

**Objectives:** Estimate the impact of gout flares, tophi, and sUA levels on HRQoL through post-hoc analysis of SF-36 data collected in two randomised, double-blind, placebo-controlled Phase 3 studies of urate lowering therapies in gout patients (CLEAR 1 and CLEAR 2).<sup>3,4</sup>

**Methods:** Linear regression analysis was used to estimate the effects of patient and disease characteristics on SF-6D scores at month 6 and month 12. Multiple regression methods and out-of-sample testing were used to select the final model from covariates representing tophus burden, the number of flares during each six-month period, serum urate levels, baseline characteristics, and comorbidities. Predicted mean utility scores were calculated by evaluating the model at the mean values of the covariates (excluding location-specific covariates) in the pooled CLEAR 1 and CLEAR 2 intent-to-treat population.<sup>3,4</sup>

**Results:** The final regression model (table 1) includes significant disutilities associated with the presence of tophi at screening (0.0418; SE: 0.0073; p<0.001), the number of gout flares (0.0036 per flare; SE: 0.0005; p<0.001), and median sUA on-treatment (0.0083 per mg/dL in excess of 6 mg/dL; SE: 0.0031; p=0.007). The predicted mean utility scores for patients with zero flares and no tophi are 0.7718 for sUA <6 mg/dL; 0.7552 for sUA 6 to <8 mg/dL; 0.7386 for sUA 8 to <10 mg/dL; and 0.7220 for sUA ≥10 mg/dL.

**Abstract OP0162HPR – Table 1.** Regression model of SF-6D utilities

Coefficient	Mean	SE	p value
Intercept	0.9182	0.0235	<0.001
Region Europe	–	0.0092	<0.001
Country New Zealand	0.0641	–	–
Age <sup>†</sup>	0.0523	0.0200	0.009
Female	–	0.0003	0.003
Black race	0.0009	–	–
Body mass index <sup>‡</sup>	–	0.0140	0.084
Diabetes mellitus <sup>‡</sup>	0.0242	–	–
Hypertension <sup>‡</sup>	–	0.0098	0.002
Unemployed <sup>‡</sup>	0.0307	0.0005	<0.001
Disabled or retired due to illness <sup>‡</sup>	0.0020	–	–
Number of gout flares	–	0.0080	0.007
Tophi present at screening	0.0215	0.0067	0.010
sUA <sup>‡</sup> per mg/dL in excess of 6 mg/dL	0.0172	0.0103	<0.001
	0.0596	–	–
	–	0.0121	<0.001
	0.1125	–	–
	–	0.0005	<0.001
	0.0036	0.0073	<0.001
	0.0418	–	–
	–	0.0031	0.007
	0.0083	–	–

R<sup>2</sup>: 0.1788; Adjusted R<sup>2</sup>: 0.1730; Residual standard error: 0.1217 on 1857 degrees of freedom. <sup>†</sup>Baseline characteristics. <sup>‡</sup>Median sUA on-treatment. Abbreviations: SE, standard error; SF-6D, Short form 6D questionnaire; sUA, serum uric acid.

**Conclusions:** The present analysis is unique in that it explored the simultaneous effects of flares, tophi, and sUA on HRQoL. The results indicate that high sUA levels are associated with significant disutility when controlling for the effects of flares, tophi, and other patient covariates. The clinical rationale is that uncontrolled sUA creates a state of chronic inflammation, contributing to underlying ill health in addition to its effects on flares, tophi, and comorbidities.

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**OP0163-HPR DEVELOPMENT OF AN ONLINE SELF-MANAGEMENT PLATFORM FOR PEOPLE WITH RHEUMATIC AND MUSCULOSKELETAL CONDITIONS (MSKHUB.COM)**

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**Background:** Patient information and education have been shown to improve pain and self-efficacy and increase overall quality of life in people with chronic musculoskeletal conditions (MSCs). Informed patients are better able to distinguish and manage symptoms, use treatments effectively, access services needed, manage work and cope better with the psychological impact of their conditions. However, there is a need to improve the access to high quality specialist health information for people with rheumatic and MSCs.

**Objectives:** This study aimed to test the usability and acceptability of an online self-management platform developed for people with rheumatic and MSCs to facilitate access to (i) valid and reliable health information (ii) evidence-based Patient Reported Outcome Measures (PROMs) (iii) advice on self-help, assistive technologies and rehabilitation (iv) and peer support via an online community.

**Methods:** Phase 1 involved the MSKHUB community development through service-user and health professionals group formation. People with Rheumatic and MSCs (n=15) and their family/carers (n=5) were purposively identified via social media networks and brought in as collaborators to form the MSKHUB Patient and Public Research Advisory Group (PRAG). A multi-disciplinary group of health professionals (n=7) were also identified through the academic and clinical networks to form the MSKHUB Health Professionals Reference Group (HPRG). A digital-lead specialising in health technologies and social media networks also supported the development of the online content and social networks. The digital lead, PRAG and HPRG had face-to-face and online meetings throughout the Phase 1 to inform the development of the MSKHUB through an iterative process. Following the Phase 1, 25 participants with rheumatic and MSCs used the website on their own devices at home and provided feedback by completing a user-experience survey assessing ease of use, helpfulness, and satisfaction with the MSKHUB.

**Results:** Participants completed the registration process and all PROMs on the MSKHUB site in an average of 1.5 hours (SD 30 min); some PROMs required more to complete due to their size and complexity but all PROMs were deemed as relevant and important to include. Participants' comments were addressed to improve the user-friendliness and ease of use. Participants reported high levels of usefulness and satisfaction in the user-experience survey (80% rated the usefulness as 9/10% and 92% rated satisfaction as 7/10 [1=not useful/not satisfied at all to 10=extremely useful/satisfied]). All participants indicated they would continue using the MSKHUB and recommend it to their families and/or friends with rheumatic and MSCs.

**Conclusions:** MSKHUB Development (Phase 1) involved the creation and testing the usability and acceptability of an online self-management platform for people with rheumatic and MSCs, which is an important step in developing appropriate and user-friendly online health education platforms. Our study suggested that community dwelling people with rheumatic and MSCs demonstrated a high degree of acceptance of the MSKHUB and could use it easily. The Phase 2 will involve a wider testing of the MSKHUB for general site activity, use and evaluation through a variety of embedded appraisal methods within the site is currently underway.

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**Disclosure of Interest:** None declared

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**OP0164-HPR** **IMPACT OF A NURSE-LED PROGRAM OF PATIENT SELF-ASSESSMENT AND SELF-MANAGEMENT AXIAL SPONDYLOARTHRITIS: RESULTS OF A PROSPECTIVE, MULTICENTRE, RANDOMISED, CONTROLLED TRIAL (COMEDSPA)**

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**Background:** Nurses should promote self-assessment and self-management skills in order that patients might achieve a greater self efficacy and improvement in patients with axSpA.

**Objectives:** To evaluate the impact of a nurse-led program of self-management/assessment for disease activity program in axSpA.

**Methods:** Prospective, randomised, controlled, open, 12 month trial (NCT02374749). **Participants** 1/Patients: consecutive Axial SpA patients (according to rheumatologist) attending a clinic of the participating centres were invited 0.2/Nurses :all participated at a 1 day meeting prior the start of the study.

**Study treatment:** a program including: 1) Self-management=a) a video explaining the disease, the interest of smoking cessation in axial SpA, the role of NSAIDs as cornerstone treatment in axSpA in the absence of contra-indications, the interest of physical activity and exercise, followed by a discussion with the nurse; b) physical examination by the nurse to check for the presence of spinal deformities and depending on the absence/presence of such deformities projection of a specific video of home-based exercises. 2) Self-assessment: Video presentation of the rationale of the use of a composite index (ASDAS/BASDAI), followed by discussion with the nurse. Explanation by the nurse of the collection, calculation of BASDAI and ASDAS **Treatment allocation:** after written informed consent, the treatment was allocated randomly via an electronic system. **Outcome variables:** Primary: The level of coping (0–10, where 0=very well) after 12 months. Other variables: Successful smoking cessation, NSAID intake, Number of home-based or supervised exercise, international physical activity questionnaire (IPAQ).

**Results:** Baseline characteristics of the 502 recruited patients (250 and 252 in the active and control groups, respectively): Age: 46.7±12.2 years, male gender: 62.7%, disease duration: 13.7±11.0 y, Xray sacroiliitis 62.8%, MRI sacroiliitis 65.7%, current biologic treatment: 78.3%, ASDAS-CRP: 1.9±0.8, BASFI: 25.6±22.3. After 1 year, coping levels were lower in the active group, but not significant (2.8±2.0 vs 3.0±2.1, p=0.3). However, there was a significant decrease in the BASDAI in the active group (-1.2±15.8 vs +1.4±15.7, p=0.03), a significant increase in the number (6.1±28.8 vs -0.4±26.9, p=0.03) and duration (4.3±20.1 vs -1.7±20.7, p<0.01) of the home-exercises in the active group, and a greater IPAQ score in the active group at the end of follow-up (138.4±227 vs 95.6±173, p=0.02).

**Conclusions:** This study highly suggests a short-term benefit of a nurse led program on the self-management and self-assessment for disease activity in a young axSpA population in particular with regard to the frequency and the duration of home exercises.

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THURSDAY, 14 JUNE 2018

**Fires and firefighters: switching the immune system on and off**

**OP0165** **JOINT-SPECIFIC DIFFERENCES IN THE ACTIVATION OF THE JAK-STAT PATHWAY IN RHEUMATOID ARTHRITIS**

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**Background:** Synovial fibroblasts (SF) promote chronic joint inflammation and joint destruction in rheumatoid arthritis (RA). We have shown recently that SF

from different joints exhibit profound differences in their transcriptomes, epigenomes and functions, which creates a unique microenvironment in each joint. This might influence the susceptibility of distinct joints to develop RA or lead to joint-specific differences in the disease severity or therapeutic response.

**Objectives:** To analyse differences in the JAK-STAT pathway in SF from different joints.

**Methods:** SF were isolated from knee, shoulder and hand joints of RA and osteoarthritis patients undergoing joint replacement surgery and from knee synovial biopsies of non-arthritic subjects with arthralgia. Transcriptomes and epigenomes of SF were determined by RNA-seq, Illumina HiSeq 2000 (n=21), ChIP-seq (Illumina HiSeq 2500, n=7) and Infinium HumanMethylation450 BeadChip (n=12). We used MetaCore (Thomson Reuters) for the pathway enrichment analysis of RNA-seq data. SF were stimulated with IL-6/soluble IL-6 receptor (IL-6/sIL-6R, 50 ng/ml each). The amount of STATs and phospho-STAT3 (p-STAT3) was measured by Western blot with normalisation to  $\alpha$ -tubulin.

**Results:** The JAK-STAT pathway was enriched in knee SF versus hand and shoulder SF (FDR<0.05). JAK1 (normalised reads – mean  $\pm$ SD: 10673 $\pm$ 2084) and STAT1 (15520 $\pm$ 2678) were the top expressed Janus kinase and STAT mRNAs in SF, respectively, whereas the expression of JAK3 (40 $\pm$ 26) and STAT4 (164 $\pm$ 91) mRNAs was low. Looking into joint-specific differences, STAT1 mRNA was higher in knee SF and shoulder SF compared with hand SF (p<0.05, FDR<0.15). Accordingly, STAT1 protein was increased in knee SF (STAT1/ $\alpha$ -tubulin ratio: 0.83 $\pm$ 0.02, p=0.02, n=4) and shoulder SF (1.02 $\pm$ 0.02, p=0.001, n=5) versus hand SF (0.57 $\pm$ 0.02, n=3). JAK1, STAT2 and STAT5B mRNAs were higher in knee compared with hand SF (p<0.05, FDR<0.05) and STAT2 and STAT6 mRNAs were higher in knee versus shoulder SF (p<0.05, FDR<0.05). TYK2 mRNA was high in hand SF compared with shoulder and knee SF (p<0.05, FDR<0.05). SF from different joints exhibited comparable DNA methylation at the promoters of these genes. Activating histone marks H3K4me3 and/or H3K27ac were enriched at the promoters of JAK1, STAT1, STAT2 and STAT5B in knee versus hand SF. This indicated that the abundance of activating histone marks at gene promoters might shape joint-specific expression of a subset of Janus kinase and STAT genes. Stimulation of SF with IL-6/sIL-6R increased the phosphorylation of STAT3 in knee (p-STAT3/ $\alpha$ -tubulin ratio 1.8 $\pm$ 1.0, p=0.03, n=5) and shoulder SF (1.8 $\pm$ 0.7, p=0.03, n=6) compared with hand SF (0.9 $\pm$ 0.5, n=6). The basal amount of STAT3 protein and the ratio pSTAT3/STAT3 was higher in knee SF (STAT3/ $\alpha$ -tubulin ratio: 0.8 $\pm$ 0.1; p-STAT3/STAT3: 2.2 $\pm$ 0.8, n=3) and shoulder SF (0.6 $\pm$ 0.4; 2.1 $\pm$ 1, n=4) versus hand SF (0.3 $\pm$ 0.02; 1.0 $\pm$ 0.4, n=2).

**Conclusions:** Here we show substantial quantitative and qualitative differences in the JAK-STAT signalling pathway in SF from different joints. Knee SF, in particular, exhibit increased expression of Janus kinase and STAT genes and enhanced JAK-STAT signalling upon stimulation with IL-6/sIL-6R. This suggests that RA in different joints might not be equally sensitive to Janus kinase inhibitors or blockade of IL-6. This has important implications in clinical practice and drug discovery in RA.

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**OP0166** **COMPARATIVE EVALUATION OF CELLULAR AND MOLECULAR CHANGES ASSOCIATED WITH RESPONSE TO SELECTIVE IL-23 BLOCKADE VS DUAL IL-12/23 BLOCKADE IN PSORIASIS SKIN**

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**Background:** Emerging clinical data indicate that selective blockade of interleukin 23 (IL-23) can achieve greater efficacy compared to dual blockade of IL-12/23 in patients with moderate-to-severe psoriasis (PsO).<sup>1</sup> Ustekinumab (UST) targets the p40 subunit common to IL-12 and IL-23, whereas guselkumab (GUS) specifically targets the IL-23-specific p19 subunit. While differences in antibody potency may explain therapeutic differences between UST and GUS, we explored cellular and molecular changes in the skin of PsO patients treated with UST or GUS to understand the mechanism underlying selective IL-23p19 inhibition.

**Methods:** UST data were derived from the ACCEPT study (NCT00454584, n=85), in which PsO patients received either 45 mg or 90 mg of UST at weeks (wks) 0 and 4, and GUS data were from the first-in-human study (NCT00925574, n=24) that tested single subcutaneous doses of GUS. Skin biopsies were collected at baseline (BL), and wks 1 and 12 post-treatment from each study to evaluate 1) histologic improvement via epithelial thickness, T cells (CD3), and myeloid DCs (CD11c) counts and 2) molecular response to drug via microarray. Biopsies from healthy subjects served as controls. GUS 100 mg and 300 mg groups were combined to increase analytic power. The IC<sub>50</sub> of each drug was evaluated by cell-based bioassays.

**Results:** The two cohorts are comparable in BL demographics, disease characteristics, skin histopathology, PsO lesional molecular expression profiles, and significantly enriched canonical pathways. Blockade of IL-23 with GUS resulted in a significantly greater reduction in CD3 and CD11c counts in the skin at wk12 relative to BL when compared to UST blockade (>90% vs ~70%). In pts who achieved >50% improvement in PASI score, GUS (n=9) showed a larger impact on the PsO transcriptomic profile than UST 90 mg (n=12) by wk1 and greater enhancement was achieved by wk12. GUS neutralised 74% of the PsO disease profile by >80%, while UST resolved only 21% at wk12. Expression of PsO disease markers such as defensin Beta 4A and lipocalin 2 were fully resolved by GUS beyond the level observed in non-lesional skin of PsO pts, while UST only resolved these markers by 32% and 63%, respectively. *In vitro*, GUS showed higher potency (2–14 fold) than UST in inhibiting IL-23 activity, which may contribute to stronger neutralisation of PsO disease markers by GUS.

**Conclusions:** In conclusion, this comparative study demonstrates that GUS inhibits psoriasis-associated pathology and resolves the skin transcriptomic PsO disease profile more strongly than UST.

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OP0167

#### A LOW MOLECULAR WEIGHT BAFF SIGNALLING INHIBITOR, BIK-13, AMELIORATES B CELL ACTIVATION *IN VITRO* AND *IN VIVO* AUTOIMMUNE MODELS AND CONSEQUENTLY SUPPRESSES PRODUCTION OF IGG AND CYTOKINES

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**Background:** We reported that BAFF robustly increases IL-6 production by peripheral monocytes of patients with primary Sjögren's syndrome (pSS) and that the BAFF-induced IL-6 production and serum IgG levels of the patients were positively correlated with the expression level of a BAFF receptor (BR3) in pSS monocytes. Moreover, we found that IgG production by pSS B cells *in vitro* was significantly enhanced by BAFF-stimulated monocytes. These results collectively suggest that BAFF signalling via BR3 is involved in IgG overproduction and that is a possible therapeutic target to treat autoimmune diseases, such as pSS. We successfully discovered a pyrrolopyrimidine derivative, BIK-13, which inhibits BAFF binding to BR3 by our original high throughput screening.

**Objectives:** To explore the possibility of BIK-13 as a drug to treat autoimmune diseases.

**Methods:** Human PBMC were stimulated *in vitro* with a mixture of soluble BAFF (sBAFF), recombinant human IL-21, and anti-IgM and anti-CD40 antibodies ('multiple stimulation') to differentiate B cells into plasma blasts and/or plasma cells. BIK-13 was added to the culture and the differentiation of B cells was monitored by the expression levels of CD19/CD38/IgD and Activation-induced cytidine deaminase (AID) analysed by FACS and quantitative RT-PCR, respectively. The amounts of IL-6, IL-10 and IgG in the culture supernatants were measured by ELISA. BIK-13 was administered intraperitoneally to MRL/lpr mice and serum levels of an anti-dsDNA antibody, IL-6 and IL-10 were measured by ELISA. The proportion of B cells among splenic lymphocytes of the mice was analysed by FACS. Production of cytokines *in vitro* by stimulated splenic lymphocytes was measured

by ELISA. Infiltration of lymphocytes into organs was analysed by immunohistochemistry.

**Results:** FACS analysis of multiple-stimulated human PBMC indicated that differentiation of B cells into plasma blasts and/or plasma cells was inhibited by BIK-13 in a dose dependent manner. Interestingly, increased IgG, IL-6 and IL-10 production by the stimulated PBMC were concomitantly and significantly suppressed by BIK-13. In addition, the expression level of AID in the cells was also suppressed by BIK-13, suggesting that an IgG class switching was impaired. Administration of BIK-13 to MRL/lpr mice for 16 weeks decreased the serum levels of an anti-dsDNA antibody, IL-6 and IL-10 as compared to the control. Notably, immunohistochemical analysis revealed that infiltration of B cells into salivary and lacrimal glands was remarkably suppressed in BIK-13-treated mice. Moreover, the proportion of B cells among splenic lymphocytes was also decreased in BIK-13-treated mice as compared to the control. In addition, production of IL-6 and IL-10 by activated splenic lymphocytes of the BIK-13-treated mice was also remarkably suppressed as compared to control mice.

**Conclusions:** Our data collectively suggest that BIK-13, a low molecular weight BAFF-signalling inhibitor, suppresses B cell activation/differentiation *in vitro* and consequently inhibits production of IgG and cytokines, such as IL-6 and IL-10, by the cells. The compound inhibited infiltration of B cells into organs of model mice of autoimmune diseases. These data suggest that the compound is a promising drug candidate to treat autoimmune diseases, such as pSS.

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OP0168

#### NIK-IKK COMPLEX INTERACTION CONTROLS NF-KB DEPENDENT INFLAMMATORY ACTIVATION OF THE ENDOTHELIUM IN RESPONSE TO LTBR LIGATION

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**Background:** Sites of chronic inflammation, such as rheumatoid arthritis (RA) synovial tissue, are characterised by neovascularization and often contain tertiary lymphoid structures with characteristic features of lymphoid organs such as high endothelial venules (HEV), and sometimes even true germinal centres. Ligation of the lymphotoxin (LT)- $\beta$  receptor (LT $\beta$ R) results in activation of both canonical and NF- $\kappa$ B-Inducing Kinase (NIK)-dependent noncanonical NF- $\kappa$ B signalling in endothelial cells (EC) and plays a crucial role in lymphoid neogenesis. Noncanonical NF- $\kappa$ B signalling in EC promotes inflammation-induced angiogenesis and triggers the development of the cuboidal HEV appearance. However, the relative contribution of the individual pathways to the acquisition of leukocyte traffic-regulating properties by EC is less well understood.

**Objectives:** To identify the molecular pathways by which LT $\beta$ R drives inflammatory activation of EC to promote interactions with leukocytes.

**Methods:** Primary human EC were treated with LT $\beta$  or LIGHT to activate LT $\beta$ R, followed by analysis of downstream NF- $\kappa$ B signalling pathways and expression of inflammatory cytokines and adhesion molecules. To repress canonical NF- $\kappa$ B signalling pathway, a small molecule inhibitor of IKK $\beta$  was used, and noncanonical NF- $\kappa$ B signalling was repressed with siRNA targeting NF $\kappa$ B2. The role of NIK in LT $\beta$ R signalling was investigated using small molecule inhibitors and siRNA targeting NIK, as well as adenoviral overexpression of NIK. The role of NF- $\kappa$ B signalling in RA was measured by stimulating EC with RA synovial fluid (RASf) followed by analysis of inflammatory mediators.

**Results:** LT $\beta$ R triggering in EC resulted in activation of both canonical and non-canonical NF- $\kappa$ B signalling pathways and induced inflammatory cytokine expression and immune cell adhesion. IKK $\beta$  inhibition completely repressed LT $\beta$ R-induced inflammatory activation of EC, indicating that this process was mediated through canonical NF- $\kappa$ B signalling. Interestingly, inactivation of NIK with small molecule inhibitors and siRNAs significantly decreased LT $\beta$ R-induced expression of inflammatory cytokines and adhesion of immune cells to endothelium, whereas silencing of NF $\kappa$ B2 had no effect. This suggests that the noncanonical pathway is dispensable for NIK-dependent activation of EC through the canonical NF- $\kappa$ B pathway. Further analyses, including silencing of NIK and NIK overexpression, demonstrated a role for NIK in activation of the canonical NF- $\kappa$ B pathway by amplifying IKK complex activity. RASf stimulation of EC resulted in activation of canonical and noncanonical NF- $\kappa$ B signalling, and increased the expression of inflammatory cytokines and adhesion molecules, which could be blocked by targeting NIK.

**Conclusions:** These findings suggest that in addition to regulating noncanonical signalling, NIK can serve as an amplifier of canonical NF- $\kappa$ B signalling and associated inflammatory responses in EC, which may play a role in development and



maintenance of chronic inflammation. Consequently, NIK may be an attractive therapeutic target.

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**OP0169 A COMBINATION OF PROTEINS AS MEASURED WITHIN THE MULTI-BIOMARKER DISEASE ACTIVITY SCORE AT PRESENTATION OF RA IDENTIFIES A GROUP OF ACPA-NEGATIVE RA PATIENTS WITH HIGH LIKELIHOOD OF DEVELOPING DMARD-FREE SUSTAINED REMISSION**

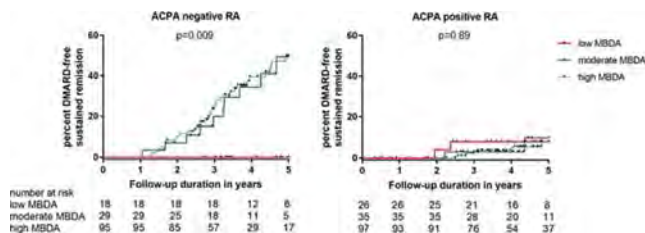
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**Background:** Rheumatoid arthritis (RA) typically requires lifelong treatment. However, some RA patients achieve sustained disease-modifying antirheumatic drug (DMARD)-free remission, which is a proxy for cure of RA that has become increasingly achievable, as reported previously. DMARD-free sustained remission has been reported mostly in autoantibody-negative RA, yet the underlying mechanism is unknown. The multi-biomarker disease activity (MBDA) score combines 12 serum biomarkers and is developed to measure RA disease activity. We hypothesise that the subgroup of RA patients that is most likely to achieve DMARD-free sustained remission is identifiable at disease presentation by cytokines such as those combined in the MBDA score.

**Objectives:** To evaluate whether the MBDA score or its component cytokines at the presentation of RA are associated with ability to later achieve DMARD-free sustained remission.

**Methods:** 300 patients with RA (by the 1987 and/or 2010 criteria) who had been consecutively enrolled in the Leiden Early Arthritis Clinic between 2010 and 2015 were studied. At time of diagnosis, before DMARD treatment was started, the MBDA score, with a scale of 1–100, was determined from the serum concentrations of 12 biomarkers (VCAM-1, EGF, VEGF-A, IL-6, TNF-RI, MMP-1, MMP-3, YKL-40, Leptin, Resistin, CRP, SAA) with a pre-specified, validated algorithm. Patients were categorised as having a low (<30), moderate<sup>30–44</sup> or high (>44) MBDA score. DMARD-free sustained remission was defined as the absence of synovitis (by physical examination) that sustained after discontinuation of all DMARD therapy (including biologics and systemic and intra-articular corticosteroids) for the entire follow-up period, but had to extend to at least one year after DMARD withdrawal. Analyses were stratified for ACPA and restricted to 5 years follow-up as thereafter the number of patients became small. The median follow-up duration of all patients was 4.3 years.

**Results:** A total of 54 RA patients (18%) had achieved DMARD-free sustained remission. For the total group of RA patients, baseline MBDA category ( $p=0.03$ ) and ACPA-negativity ( $p<0.001$ ) were associated with achieving DMARD-free sustained remission. For ACPA-positive RA patients, the MBDA category at baseline was not associated with achieving DMARD-free sustained remission ( $p=0.89$ , figure 1). By contrast, among ACPA-negative RA patients, none of those with low MBDA score achieved DMARD-free sustained remission during 5 years follow-up, whereas the estimated rate of remission was 50% for those with moderate or high MBDA scores ( $p=0.009$ , figure 1). Of the 12 biomarkers in the MBDA test, only SAA showed a significant difference between ACPA-negative patients with and without DMARD-free sustained remission ( $p=0.01$ ).



**Conclusions:** ACPA-negative RA patients who achieved DMARD-free sustained remission were characterised by moderate to high MBDA scores at disease presentation. This is the first evidence that a cytokine profile at disease onset can identify a subgroup of ACPA-negative RA patients with a high likelihood of maintaining clinical remission after treatment withdrawal.

**Disclosure of Interest:** None declared

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**OP0170 HUMAN IL-38 REDUCES JOINT INFLAMMATION IN A MOUSE MODEL OF GOUTY ARTHRITIS**

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**Background:** Interleukin-38 (IL-38) is the last member of the IL-1 family of cytokines to be fully investigated for its functions. IL-38 is proposed as an anti-inflammatory cytokine in various auto-inflammatory diseases, such as psoriasis and rheumatoid arthritis. For example, IL-38 knockout mice have exacerbated autoantibody-induced arthritis. Current understanding of the capacity of IL-38 in gout, a prototype IL-1 $\beta$  driven auto-inflammatory disease, is unknown.

**Objectives:** We hypothesised that *in vivo* treatment with human recombinant IL-38 results in a reduction in joint inflammation in a mouse model of gouty arthritis.

**Methods:** We treated C57/Bl6 mice with 1  $\mu$ g recombinant IL-38 (3–152 AA) intraperitoneally at 24, 12 and 2 hours before induction of gouty arthritis with intra-articular injection of albumin-opsonized monosodium urate crystals (300  $\mu$ g) and palmitic acid (200  $\mu$ M) in 10  $\mu$ L PBS. Joint inflammation was scored after 4 hours. The synovial lining was cultured in RPMI for 2 hours to allow cytokines to be secreted, and cytokines in the synovium were extracted with Triton-X 100 to obtain total cytokines (membrane and intracellular). In the synovial culture fluid and extract, IL-1 $\beta$ , IL-6 and KC were measured by ELISA. Data

**Results:** Mice treated with recombinant IL-38 exhibited significantly reduced joint swelling and redness on a three-point macroscopic inflammation scale: Vehicle-treated 1.5 $\pm$ 0.25 vs IL-38 Treated 0.75 $\pm$ 0.25 (n=10,  $p<0.0001$ , Mann Whitney-U test). The 2 hour synovial membrane culture fluid contained significantly lower levels of IL-1 $\beta$  (1207 $\pm$ 480 vs 379 $\pm$ 184 pg/mL,  $p<0.05$ ), IL-6 (10783 $\pm$ 2490 vs 5321 $\pm$ 2935 pg/mL,  $p<0.05$ ) and KC (4390 $\pm$ 931 vs 1081 $\pm$ 750 pg/mL,  $p<0.05$ ). In extract of the synovial membrane, there is a reduction in IL-1 $\beta$  (1505 $\pm$ 397 vs 624 $\pm$ 509 pg/mL,  $p<0.05$ ), IL-6 (11059 $\pm$ 2299 vs 3597 $\pm$ 2509 pg/mL,  $p<0.01$ ) and KC (1505 $\pm$ 397 vs 624 $\pm$ 509 pg/mL,  $p<0.05$ ).

**Conclusions:** Human recombinant IL-38 reduces swelling and redness of the joint, and pro-inflammatory cytokines secreted by and contained in the synovial membrane in a mouse model of gouty arthritis. These data reveal that recombinant IL-38 has therapeutic benefit in an IL-1 $\beta$  mediated model of inflammation.

**Disclosure of Interest:** None declared

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**OP0171 LEPTIN LEVELS, OVERWEIGHT AND P GINGIVALIS PRESENCE CONTRIBUTE TO THE MECHANISM OF SYSTEMIC INFLAMMATION IN FIRST-DEGREE RELATIVES OF RHEUMATOID ARTHRITIS INDIVIDUALS**

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**Background:** Association studies in rheumatoid arthritis (RA) have been focused in the pre-clinical phases of the disease in first-degree relatives (FDR). Data has shown that obesity, ACPA and the periodontal condition may modulate the severity and the clinical presentation of RA

**Objectives:** To investigate the levels of adipokines in FDR and establish their association with the state of rheumatic and periodontal condition

**Methods:** 124 FDR individuals and 124 healthy controls matched by age and gender were included. Rheumatologic (clinical and serological markers) and periodontal assessment was performed. It was quantified the adiponectin, leptin, IL6 levels. HLA-DRB1 was determined. Serum markers of RA (rheumatoid factor, erythrocyte sedimentation rate, C reactive protein (CRP), and ACPA. *P gingivalis* and IgG1/IgG2 *P gingivalis* were measured. Radiographs of hands and feet were evaluated the Sharp-van der Heijde score. An association analysis was made to evaluate the relationship between adipokines and periodontal, rheumatologic conditions using X2 test, and logistic regression model was performed to confirm this associations

**Results:** In FDR group, 71.77% were women with a mean age of 39.24 $\pm$ 12.22 years. 37.09% had overweight and 4.83% had obesity. Among the controls, 70.97% were women, with an average age of 39.31 $\pm$ 12.30 years. 27.41% had overweight and 4.83% had obesity. Leptin levels were found in 37.66% vs 18.42% in controls ( $p=0.002$ ). In FDR, 60.48% had periodontal disease of which 62.66% moderate, *P gingivalis* in 62.10%. In controls, 55.64% had periodontal disease, of which 63.76% moderate with 42.74% *P gingivalis* positive ( $p=0.002$ ). In the FDR, radiography of hands and feet showed in 25.28% of them had some alteration, 68.18% had  $\geq 1$  erosion, 45.45% had  $\geq 1$  joint space narrowing and in 6.89% juxta-articular osteopenia. An association of leptin levels with the low economic level was found  $p=0.006$  and high levels of leptin in individuals with BMI  $\geq 30$   $p=0.031$ .

IL6 was found to be associated with severity of periodontal disease, with higher levels being found frequently in mild periodontal disease  $p=0.039$ . The condition of FDR was significantly associated with high leptin levels adjusted for presence of swollen joints, presence of *P. gingivalis* and low levels of IL6 OR=2.57, 95% CI: 1.14 to 5.95. In this group, the individual with leptin at moderate levels adjusted with BMI >25, has a lower probability of presenting CRP >3 mg/L OR=0.43 95% CI: 0.20 to 0.90.

**Conclusions:** High levels of leptin, the presence of *P. gingivalis* and swollen joints may be relevant conditions associated with the development of RA in FDR. Leptin levels and overweight can modulate the production of acute phase proteins in this group of individuals contributing to the mechanism of systemic inflammation. The clinical implications of our findings propose regulated exercise programs, oral hygiene, and weight control in FDR

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**Disclosure of Interest:** None declared

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#### OP0172 LPS-INDUCED PERIODONTITIS PROMOTES ARTHRITIS DEVELOPMENT IN MICE

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**Background:** Although *in vivo* studies have demonstrated that periodontitis aggravates experimental arthritis, there are no animal models that mimic the co-occurrence of these diseases.

**Objectives:** To investigate the arthritogenic effect of lipopolysaccharide (LPS) in a mouse model of periodontal disease.

**Methods:** Periodontitis was induced in CD1 mice by injection of 0.01 or 0.05 µg of LPS in 5 µl of PBS every 48 hour into the vestibular gingiva of the second molar on the left maxilla. Untreated mice or injected with LPS at the tail were used as controls. Mice (n=10 per condition) were monitored daily and arthritis was estimated by conventional visual scoring method (scale 0–5) and recording the paw swelling with a calliper. 2 weeks after the 9th injection mice were sacrificed to collect blood, maxilla and paw samples. The left maxilla was analysed by microCT and the alveolar bone loss was assessed measuring the distance between the cementum-enamel junction (CEJ) and the alveolar bone crest (ABC) of each molar. Ultrasound (US) was performed to measure the ankle joint space. Periodontal and paw tissues were processed for histological analysis. Inflammation, vascular proliferation and bone resorption were scored (0–3) in maxilla. Inflammation, pannus formation, cartilage and bone destruction were scored (0–5) in ankle joints. CXCL1, IL-1β, IL-6 and TNF serum levels were determined by ELISA.

**Results:** Ankle swelling and inflammation were noted after the 5th periodontal injection of 0.05 µg of LPS, picked at day 18 and continued for the next 15 days with paw swelling and score higher than those of untreated mice (at the sacrifice  $p<0.001$ ). 0.01 µg of LPS did not induce paw changes. Therefore, the subsequent assessments were conducted only in mice injected with 0.05 µg of LPS. The CEJ-ABC distance was greater in the inoculated (0.29±0.08 mm) than in the control (0.17±0.05 mm) mice ( $p<0.001$ ). Histological analysis showed that LPS induced a mild vascular proliferation (score 0.8±0.42) in periodontal tissue and a substantial alveolar bone resorption (score 1.8±0.42), but not inflammation. US revealed the presence of effusion and a 1.5-fold higher joint space in the ankle of mice with periodontitis than in controls ( $p<0.05$ ). Leukocyte infiltration (score 2.36±1.56) and synovial proliferation (score 2.09±1.54) were observed after histology in ankle joints of mice injected orally. The same sections had slight cartilage (score 1.32±1.21) and bone destruction (score 0.68±0.72). Animals that received LPS tail injection did not show any clinical and histological signs of arthritis. CXCL1 and TNF were higher in arthritic mice (CXCL1:2226.87±264.38 pg/ml; TNF:24.55±7.0 pg/ml), than in controls (CXCL1:445.97±92.09 pg/ml; TNF:3.22±1.04 pg/ml). Although there was no statistical difference, IL-1β and IL-6 were highest in LPS-mice (IL-1β:79.49±11.99 pg/ml; IL-6:196.02±40.62 pg/ml).

**Conclusions:** This study shows that experimental arthritis and periodontal disease can co-occur after LPS oral injection in mice. Our model may be useful to improve the understanding of the mechanisms underlying the link between periodontitis and arthritis.

**Disclosure of Interest:** None declared

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THURSDAY, 14 JUNE 2018

#### Inclusive school environment for young people with RMDs

#### OP0173-PARE YOUTH-R-COACH, A PROGRAM FOR YOUTH WITH A CHRONIC DISEASE

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**Background:** Youth-R-Coach is a project for youth (aged 15–25) with a chronic illness. It is a project set up by the Centre for Chronically Ill and Work (CCZW) in cooperation with Youth-R-Well.com, the Dutch organisation for youth with RMDs. Youth-R-Coach is based on CCZW's program for the certification of 'experience expertise'.

**Objectives:** Youth-R-Coach focusses on the development of experts-by-experience, and making those experiences available for others to learn from. A distinctive element is the creative aspect: the development of writing talent.

**Methods:** The participants reflect individually on personal experiences with their disease, as well as their personal competencies. This process is supported by a portfolio of assignments and a mentor who also has an RMD. The participants also incorporate their personal experience with the disease in a self-written book with support of a writing coach. Even though the process is an individual one, the program starts with a group of participants. There is a kick-off meeting, a weekend training and a final group meeting. In this way, the participants get to know each other and learn from each other's personal experiences with the disease. They stay in contact during the program and help each other with the portfolio and writing of their book. During the meetings, workshops are provided to teach them new skills, such as 'online coaching' and 'presenting'.

**Results:** Youth-R-Coach worked with a group of 7 participants who followed the program in 2016, and a group of 7 participants who started in 2017. Both groups are currently busy finalising their portfolios and books, which will be ready in May 2018.

The books are intended to make personal experiences in dealing with an RMD available for peers, for whom the books can be a source of support in dealing with the disease. The books are also interesting for a wider audience, because they provide insights into living with a chronic illness as a young person. The books are all very different. Some wrote short columns, while others wrote an entire novel. What all the books have in common is that they are all based on personal experiences of living with a chronic illness.

Developing expertise-by-experience and writing about their experiences has helped the participants to better cope with their disease, and has made them ambassadors. Some of them have been, or are still, involved in activities for patient organisations since the start of the program. For example, some have volunteered as a mentor for an RMD youth holiday camp, or given presentations based on personal experience with an RMD. Some participants will continue coaching their peers after finishing the program, and some continue writing about their personal experiences in a blog. How participants will continue to use their new-found skills is down to personal interests and competencies, but whatever they do, the program has given them useful tools for coping with and teaching others about the disease.

**Conclusions:** Fourteen participants (aged 18–27) developed their expertise-by-experience in dealing with an RMD and are now able to act as a coach for their peers. Their experiences in dealing with the disease will be published in self-written books and made available to a wide audience. All of the current participants had an RMD, but the project would also be useful for youths who have other chronic illnesses.

**Acknowledgements:** Youth-R-Coach was made possible with the financial support of the FNO Foundation.

**Disclosure of Interest:** None declared

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THURSDAY, 14 JUNE 2018

#### The building blocks of systemic inflammation

#### OP0174 ALTERATION OF MEDIATORS OF VASCULAR INFLAMMATION BY ANIFROLUMAB IN THE PHASE IIB MOUSE STUDY IN SLE

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**Background:** Cardiovascular disease remains one of the leading causes of death for patients with systemic lupus erythematosus (SLE), and the disease is

widely known to feature premature atherosclerosis promoted by immune dysregulation. Neutrophil extracellular traps (NETs) can induce endothelial dysfunction and promote inflammatory events. Furthermore, sources of reactive oxygen species released during NET formation promote oxidised HDL, leading to deficient cholesterol efflux capacity (CEC). Type I interferons (IFNs) stimulate NET formation and inhibit vascular repair. Anifrolumab is a fully human, IgG1  $\kappa$  monoclonal antibody that binds to IFNAR1 and blocks signalling of all type I IFNs. Thus, anifrolumab may decrease mechanisms of vascular damage in SLE.

**Objectives:** We evaluated the ability of anifrolumab to reduce *in-vivo* NET formation and improve CEC relative to standard of care (SOC) in the MUSE study.<sup>1</sup>

**Methods:** Baseline IFN gene signature (IFNGS) test status (high or low) of MUSE patients was determined as described.<sup>1</sup> Plasma samples from fasting patients (n=190) were obtained at days 1 and 365 of the MUSE study. Plasma MPO-, HNE- and CitH3-DNA NET complexes were quantified by ELISAs in the MUSE and healthy donor (HD) samples (n=20) as described.<sup>2</sup> Wilcoxon rank-sum test was used to assess differences between groups. Post-treatment samples from the placebo (n=52) and 300 mg anifrolumab (n=73) groups were compared with baseline samples. Significance of change from baseline was determined using Wilcoxon signed-rank test. CEC was tested as described.<sup>3</sup> Reproducibility of the CEC assay was assessed using percent coefficient of variation (CV) from the analysis of variance (ANOVA). SLE patients with defective baseline CEC were identified as those with CEC <2 standard deviations from the HD mean value in the same testing run.

**Results:** All three neutrophil NET complexes (NNCs) were elevated in SLE patients (p<0.01) and were significantly enriched in IFN test-high patients (p<0.05). Anifrolumab significantly decreased all three NNCs at Day 365 vs Day 1 (p<0.05), whereas in the placebo group, complexes did not change or increased. The CEC assay was reproducible (16.4% CV) across 2 days of testing for a subset of 26 baseline samples, and longitudinal changes in steroid dosage for the placebo group did not affect CEC. Greater baseline NET complex levels significantly correlated with poor baseline CEC (p<0.05). Anifrolumab significantly increased CEC in IFNGS test-high patients with defective CEC at baseline (p<0.001), whereas no significant changes occurred in the placebo group.

**Conclusions:** Circulating NNCs were significantly elevated in patients with moderate to severe SLE as compared with HDs. Anifrolumab decreased circulating NNCs. Although changes in steroid dosages during MUSE did not affect CEC, anifrolumab significantly improved CEC over SOC. This work supports continued assessment of anifrolumab effects on vascular inflammation and endothelial damage in SLE.

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**Disclosure of Interest:** W. White Shareholder of: AstraZeneca, Employee of: MedImmune, N. Seto: None declared, M. Playford: None declared, K. Casey Shareholder of: AstraZeneca, Employee of: MedImmune, M. Smith Shareholder of: AstraZeneca, Employee of: MedImmune, P. Carlucci: None declared, B. Yu Shareholder of: AstraZeneca, Employee of: MedImmune, L. Wang Shareholder of: AstraZeneca, Employee of: MedImmune, G. Illei Shareholder of: AstraZeneca, Consultant for: MedImmune, N. Mehta Grant/research support from: Abbvie, Novartis, Janssen, Celgene, Employee of: NHLBI, M. Kaplan Grant/research support from: MedImmune

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OP0175

#### INTERFERON SIGNATURE MIGHT SERVE AS EARLY BIOMARKER FOR DEVELOPMENT OF LUPUS AND CORRELATES STRONGLY WITH MYXOVIRUS-RESISTANCE PROTEIN A

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**Background:** Incomplete systemic lupus erythematosus (iSLE) marks a group of patients with typical features of SLE, who do not meet classification criteria. Up to 55% progress to SLE, but there are no predictive markers available. Interferon (IFN) type-I is an important early mediator in SLE. The majority of SLE patients show upregulation of interferon-inducible genes. Levels of IFN-related soluble markers, which are more easily applicable, are also increased in SLE.

**Objectives:** To measure IFN signature and IFN-related soluble markers in iSLE patients to determine if these can serve as predictors of SLE.

**Methods:** Thirty iSLE patients (ANA titer  $\geq 1:80$ , disease duration <5 years,  $\geq 1$  ACR clinical feature), 39 SLE patients with quiescent disease (fulfilling ACR or SLICC criteria, SLEDAI  $\leq 4$ ) and 11 healthy controls (HC) were included. Clinical and serological data were retrieved from medical charts.

RNA was isolated from whole blood using PAXgene tubes, reversely transcribed to cDNA and quantitatively analysed by Real time PCR. IFN score was calculated based on cumulative expression of 12 IFN-related transcripts (IP-10, IFI44L, IFIT3, LY6E, MX1, SERPING1, IFITM1, IRF7, STAT1, C1QA, IFI16 and IRF9). A positive IFN-score was defined as >2 SD of the mean of the control group. Levels of IFN-related mediators, including IFN- $\gamma$  induced protein 10 (IP-10) and Myxovirus-resistance protein A (MxA) were measured using ELISA.

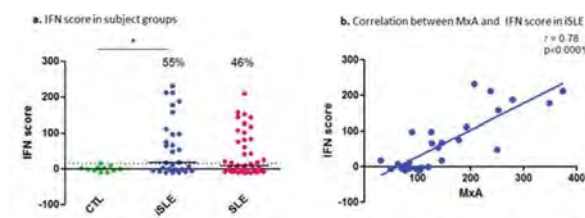
Statistical significance between groups was tested with Mann-Whitney U tests. Correlations of continuous data were calculated using Spearman's r test.

**Results:** Baseline characteristics are shown in table 1. An increased IFN score was present in 55% of iSLE patients (p=0.05) and 46% of SLE patients (p=0.07) (figure 1a). In iSLE, IFN score correlated positively with ESR (r=0.52, p=0.004), SSA titer (r=0.64, p=0.02) and cumulative number of ENA (r=0.57, p=0.001), and negatively with leukocyte count (r=-0.38, p=0.04), Hb (r=-0.39, p=0.04), and C4 (r=-0.47, p=0.01). SLEDAI, clinical symptoms, nor use of hydroxychloroquine were correlated with IFN score.

Abstract OP0175 – Table 1

	CTL (n=11)	iSLE (n=30)	SLE (n=39)
Female gender, n(%)	10 (91)	25 (79)	32 (82)
Age (median, range)	28 (25–65)	45 (20–83)	41 (19–76)
Disease duration, years median (range)		1.4 (0.1–4.6)	2.7 (0.5–6.8)
ACR criteria, median (range)		3 (1–3)	5 (2–9)
SLICC criteria, median (range)		3 (2–4)	5 (4–9)
SLEDAI median range)		0 (0–6)	2 (0–4)
Hydroxychloroquine use, n (%)		10 (33)	33 (85)
Immunologic features, n (%)			
ANA or SSA-pattern		30 (100)	39 (100)
Anti-dsDNA		9 (30)	33 (85)
Anti -SSA		14 (47)	12 (31)
Anti-Sm		3 (10)	6 (15)
Decreased complement		4 (13)	26 (67)

Levels of MxA correlated strongly with IFN score in both iSLE (r=0.78, p<0.0001) (figure 1b) and SLE (r=0.6, p<0.0001). IP-10 levels correlated with IFN score in iSLE (r=0.45, p=0.02), but not in SLE.



Abstract OP0175 – Figure 1 a) IFNscore in subject group, b) correlation between MxA and IFN score in iSLE

**Conclusions:** IFN-signature is present in 55% of patients with iSLE and correlates with ESR, autoantibody number, leukopenia, anaemia and hypocomplementemia. Interestingly, MxA levels correlated strongly with IFN-gene upregulation and thus might be a suitable and easily applicable surrogate marker for IFN type-I activity. iSLE patients with IFN upregulation might be those at most risk for disease progression; longitudinal data however should be awaited.

**Disclosure of Interest:** None declared

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OP0176

### RNA SEQUENCING DETECTION OF GENE DYSREGULATION IN B CELLS SORTED FROM SALIVARY GLAND TISSUE AND PERIPHERAL BLOOD REVEALS NEW PATHWAYS INVOLVED IN SJÖGREN'S SYNDROME PATHOPHYSIOLOGY

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**Background:** Primary Sjögren's syndrome (pSS) is a chronic auto-immune disorder characterised by lymphocytic infiltrates and destruction of the salivary glands (SG). Chronic B cell activation, the secretion of autoantibodies and the critical role of BAFF have been demonstrated. However, mechanisms leading to B cells dysregulation remain partially understood.

**Objectives:** To establish transcriptomic maps of the B cells sorted from the SG and from blood using RNASeq analysis.

**Methods:** Patients had pSS according to 2016 EULAR/ACR criteria and controls had sicca symptoms without any antibodies and with normal SG biopsy. B cells were sorted from SG biopsies and from blood using a FACS ARIA. Total RNASeq profiling was performed using MiSeq (Illumina). Statistical analysis (DESeq2) identified differentially expressed genes between pSS and controls in B cells sorted from SG (9 pSS and 4 controls), from blood (16 pSS and 7 controls); and between B cells sorted from SG and blood in the same patients (4 pSS). Functional enrichment analysis was performed using Ingenuity Pathway Analysis.

**Results:** The pSS vs controls comparison in B cells sorted from SG identified up-regulated genes involved in activation of B cells including CD48, CD22 and CD40. TLR10, which is involved in innate immunity was also up-regulated in pSS. The analysis of the non-coding expressed RNAs showed an up-regulation of Mir155 which is essential for B cell differentiation and antibody production (table 1A).

In B cells sorted from blood, TLR7 and the downstream signalling molecule IRF7 were up-regulated in pSS. Additionally, IL-6 which is involved in B cells growth was up-regulated (table 1B). Enrichment analysis highlighted EIF2 signalling pathway, interferon (IFN) signalling pathway and role of JAK in IFN signalling.

The paired comparison between B cells from SG and from blood identified up-regulated genes including CD138, a plasma cell marker, IL-6, TLR5 and IFN induced genes (table 1C). Mir155HG was also up-regulated.

These results need to be confirmed by RT-qPCR and additional analysis of the non-coding expressed RNA is ongoing.

Table 1 Selection of genes differentially expressed between pSS and controls in B cells sorted from biopsy (1A), blood (1B) and between SG and blood B cells from the same pSS patients (1C)

	Gene Symbol	log2 fold-change	p-value
1A	<b>Salivary B cells (pSS vs controls)</b>		
	CD48	2.59	0.009
	CD22	2.29	0.048
	CD40	2.64	0.017
	TLR10	5.67	0.002
	Mir155HG	4.94	0.002
1B	<b>Blood B cells (pSS vs controls)</b>		
	TLR7	1.40	0.008
	IRF7	0.76	0.041
	IL-6	1.54	0.006
1C	<b>Salivary vs blood B cells in pSS</b>		
	CD138	6.92	9.63e-05
	IL-6	3.05	0.004
	TLR5	8.86	8.26e-06
	Mir155	3.10	0.011

**Conclusions:** This study allowed exploring the mechanisms that support B cell activation in pSS focusing on tissue resident and circulating cells. Our data confirmed the B cell activation and differentiation through several markers including CD40, CD22, CD48, CD138 and highlighted the role of innate immunity with the TLRs and key pathways including IFN and JAK signalling. Lastly, the role of an epigenetic regulation of Ig secretion is suggested in tissue infiltrating B cells through mir155 expression. Precise understanding of these dysregulation should offer development of new targeted therapeutic perspectives for patients.

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**Disclosure of Interest:** None declared

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OP0177

### BCL6 IDENTIFIES ECTOPIC GERMINAL CENTRES IN SALIVARY GLAND BIOPSIES IN PRIMARY SJÖGREN'S SYNDROME PATIENTS

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**Background:** Primary Sjögren's syndrome (pSS) patients who exhibit germinal centres (GCs) within salivary gland parenchyma have higher focus scores and present with more disease activity than GC negative pSS patients. Moreover, presence of GCs might be of clinical importance for stratification of treatment. However, there is considerable heterogeneity in reported findings concerning the presence of GCs. This can partially be explained by the difficulty in identifying GCs in diagnostic H and E sections and the lack of uniform histopathological criteria.

**Objectives:** The aim of this study was to assess the most appropriate way to identify unequivocally GCs in parotid and labial gland biopsies of pSS patients.

**Methods:** As part of routine diagnostic work-up for pSS, both parotid and labial salivary gland biopsies were taken from 100 consecutive patients suspected for pSS. Forty-two patients were classified as having pSS according to the ACR-EULAR criteria, the remaining 58 patients were classified as non-pSS sicca patients. Diagnostic salivary gland biopsies were formalin fixed, paraffin embedded and serially sectioned at 3–4 µm thickness. Sections were stained with H and E as well as immunohistochemically for CD3, CD20, CD21, CD45, Ki67 and Bcl6. Presence of GCs, the number of GCs/mm<sup>2</sup> salivary gland parenchyma and level of lymphoid organisation were determined in all sections.

**Results:** According to diagnostic H and E staining, in 15% and 2% of pSS patients GCs were present in parotid and labial salivary glands, respectively. Staining for the proliferation marker Ki67 and the GC-B cell associated transcription factor Bcl6, showed higher percentages: 23% and 25%. Much higher percentages of follicular dendritic cell (FDCs) networks were revealed by CD21L (45% and 55%, for parotid and labial glands, respectively) compared to the number of GCs seen in tissue sections stained for Bcl6. Similarly, the median number of CD21+ FDC networks/mm<sup>2</sup> was significantly higher than the number of GCs/mm<sup>2</sup> as revealed by H and E, Ki67 and Bcl6. Careful evaluation of the consecutive sections stained for CD21L and Bcl6, showed that only roughly half of the FDC networks, also harbour GCs. Finally, not all sections that showed clearly defined GCs by Bcl6 staining, also revealed GCs by Ki67 or H and E staining.

**Conclusions:** Due to the difficulty in GC recognition, use of diagnostic H and E leads to an underestimation and incorrect identification of GCs, while using anti-CD21L overestimates GC counts. This suggests that, although CD21+ FDC networks play an essential role in GC development and T/B cell compartmentalization, positivity for CD21+ FDC networks does not always imply presence of ectopic GCs. Furthermore, since Ki67 is an excellent marker for solely the dark zone of GCs, small GCs can be overlooked while other proliferative areas might be mistakenly identified as GCs. This study shows that staining for Bcl6 allows easy and unequivocal identification of GCs and should therefore be implemented in the histopathological evaluation of salivary gland biopsies of pSS patients.

**Disclosure of Interest:** None declared

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OP0178

### ANALYSIS OF B-CELLS SUBSETS IN FIRST DEGREE RELATIVES OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Systemic lupus erythematosus (SLE) is an autoimmune, multi-organ disease characterised by periods of activity and remission. In lupus, one of the fields that has most helped his knowledge is the study of lymphocyte subpopulations through flow cytometry. Specifically, in the SLE some alterations have been detected at the level of B lymphocytes as the increase of B-cells subsets such as plasmablasts, plasma cells, transitional cells. There are no studies to date that have analysed the behaviour of B cells subsets in first -degree relatives of patients affected by lupus

**Objectives:** To analyse if there quantitative difference in the B-cells subsets of the first-degree relatives of SLE with respect to the control population (healthy) and the lupus population

**Methods:** Transversal descriptive study. We included 13 patients diagnosed with SLE according to the criteria of the American College of Rheumatology (ACR) with positivity for antinuclear antibodies (ANA) and anti-DNA, 34 first-degree relatives and 50 healthy controls between the months of May 2016 and March 2017. None of the subjects evaluated received treatment with rituximab or belimumab. We analysed B-cells subsets (negative double, naïve B-cells, unswitched memory B-cells, switched memory B-cells) in all the subjects included in our study. The 95% confidence intervals were obtained for both the means and the percentage difference. The level of statistical significance was established at  $p < 0.05$ . The data was analysed with IBM SPSS software Statistics 19 and EPIDAT 4.1.

**Results:** 47 subjects were analysed between relatives and patients, of which 33 (70.20%) were women. 13 subjects (27.70%) were diagnosed with lupus. 100% of those diagnosed with lupus were women. The mean (X) and confidence intervals (95% CI) for the different subgroups (healthy subjects, subjects diagnosed with SLE, relatives of the first degree) is shown in table 1. In none of the subpopulations analysed in patients diagnosed with SLE in front of relatives of 1 st grade it has reached statistical significance. When analysing B cells subsets of the three groups of subjects, we did find statistically significant differences between unswitched memory B cells of healthy subjects and 1 st degree relatives (being lower in the group of healthy subjects) This finding has not been described in any previous study, although it should be noted that the sample before us is small.

Abstract OP0178 – Table 1

B-CELLS SUBSETS		HEALTHY	SLE	RELATIVES
Naïve (%)	Mean	70,4 (95% CI:	69,3 (95% CI:	65,8 (95% CI:
	(CI95%)	68,2 to 72,7)	62,2 to 76,3)	60,4 to 71,2)
Doubles Negative (DN) (%)	Mean	4,1 (95% CI: 3,5	6,2 (95% CI: 4,8	2,9 (95% CI: 1,9
	(CI95%)	to 4,6)	to 7,6)	to 4,0)
Unswitched (%)	Mean	9,6 (95% CI: 8,2	13,0 (95% CI: 7,4	17,2 (95% CI:
	(CI95%)	to 11,1)	to 18,7)	13,4 to 21,1)
Switched (%)	Mean	11,4 (CI95%	11,5 (95% CI: 6,3	14,0 (95% CI:
	(CI95%)	=10,1–12,7)	to 16,7)	11,2 to 16,8)

**Conclusions:** There are quantitative differences between unswitched memory B-cells of healthy subjects and relatives of 1 st grade of SLE. More studies with a larger sample size are necessary to see the behaviour of the rest of B-type lymphocyte subpopulations

**Disclosure of Interest:** None declared

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OP0179

#### MOLECULAR DOCUMENTATION OF THE CLONAL EVOLUTION OF A DIFFUSE LARGE B-CELL LYMPHOMA OUT OF CLONALLY EXPANDED RHEUMATOID FACTOR-EXPRESSING B CELLS IN A SJÖGREN'S SYNDROME PATIENT

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**Background:** Sjögren's syndrome (SS) is the autoimmune disease with the highest risk of lymphoma development. SS patients develop most frequently MALT lymphoma and to a lesser extent diffuse large B-cell lymphoma (DLBCL). Previously, we have shown that at least 40% of salivary gland MALT lymphomas express groups of near identical (also called stereotypic) B-cell receptors, which display *in vitro* mono-specific rheumatoid factor (RF) reactivity<sup>1</sup>. Recently, we have analysed the B-cell immunoglobulin heavy variable (IGHV) repertoire in 4 SS labial salivary glands. In 2 out of 4 salivary glands only one minor stereotypic RF B-cell clone was detected. Interestingly, in one salivary gland of patient SG22 a highly expanded stereotypic RF-expressing B-cell clone was present, which was also detected in peripheral blood. Twenty six months later, a clonally-related DLBCL was diagnosed<sup>2</sup>.

**Objectives:** To study the molecular alterations present in the RF-expressing B cell clones of salivary gland, peripheral blood and in the DLBCL of SS patient SG22.

**Methods:** From peripheral blood 4 RF-expressing immortalised B-cell clones with identical IGHV rearrangements were isolated. These 4 RF-clones were analysed by whole exome sequencing and the identified non-synonymous exome mutations were traced in the salivary gland and in the DLBCL, using targeted next generation sequencing.

**Results:** In total we identified 56 exome mutations in the 4 RF B-cell clones. Twelve non-synonymous mutations were shared between all 4 RF-clones, of which one was a missense mutation in *CARD11*, a well-known oncogenic mutation of DLBCL. In the salivary gland all shared 12 non-synonymous mutations were detected, whereas in the DLBCL only 4 of these mutations were detected.

Remarkably, the *CARD11* mutation was not detected in the DLBCL. The exome mutations were analysed for typical characteristics of induction by the B-cell specific mutator AID. This revealed that the large majority of mutations (80%) were (i) not located within 1,5 kB of the transcription initiation site of the genes, (ii) did not concern C/G nucleotides in AID hotspots (WRC/GYW) and (iii) were not in genes expressed by B cells. This lack of evidence for AID involvement, suggests that the exome mutations of the RF-clones were due to replication errors, obtained during their clonal expansion. Interestingly, as compared to the RF-clones of peripheral blood, the DLBCL accumulated 44 extra somatic mutations together in IGHV and IGKV. As expected, these new IGHV/IGKV mutations showed the characteristics of AID involvement, indicating that in an ancestor RF-clone, AID activity was induced.

**Conclusions:** We have documented the clonal outgrowth and diversification of a RF-specific B-cell clone in a SS patient and the evolution of this clone into a DLBCL. Our analysis are indicative for AID activity in the lymphoma cells, represented by accumulation of IGHV/IGKV mutations. However, we have no evidence that AID is instrumental in the accumulation of the non-IG mutations in the RF-clones from peripheral blood.

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**Disclosure of Interest:** None declared

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OP0180

#### TYPE I INTERFERON IS PRODUCED BY NON-HAEMATOPOIETIC TISSUE RESIDENT CELLS BUT NOT PDCs IN PRE-CLINICAL AUTOIMMUNITY AND SLE

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**Background:** Systemic Lupus Erythematosus (SLE) is characterised by persistently high type I interferon (IFN) activity. Plasmacytoid dendritic cells (pDCs) produce large amounts of IFNs in viral infection, although these immunogenic properties are usually strictly regulated. *In vitro*, pDCs are responsive to nucleic acids and they have therefore been postulated to be the main source of type I IFNs in SLE. However, their function is not fully established in human SLE.

**Objectives:** To investigate the dysregulated IFN axis in patients with pre-clinical autoimmunity and SLE.

**Methods:** Patients with SLE who met 2012 ACR/SLICC criteria were recruited. We also recruited healthy controls (HC) and therapy-naïve individuals presenting with ANA and 1–2 clinical symptoms, but not meeting ACR/SLICC criteria, of whom 17% progressed to SLE (At-Risk). IFN activity was evaluated by measuring a score of IFN-responsive genes in the PBMCs using TaqMan. pDCs were immunophenotyped as well as studied *in vitro* for production of proinflammatory cytokines and induction of T cell responses using flow cytometry. pDCs were sorted and sequenced using high-sensitive RNA sequencing. IFN expression was visualised in skin biopsies using *in situ* hybridisation. Keratinocytes were isolated from fresh skin biopsies and cultured *in vitro*; IFN production was measured by qPCR and ELISA.

**Results:** Most of the SLE and At-Risk patients had increased IFN activity, which correlated with disease activity and clinical features. In contrast, circulating pDCs were decreased in both SLE and At-Risk patients and their numbers did not correlate with any clinical features or IFN status. *In vitro* stimulation revealed that pDCs from SLE and At-Risk patients could not produce IFN- $\alpha$  and TNF- $\alpha$  upon stimulation with TLR9 or TLR7 agonists. In addition, they induced significantly less T cell activation and proliferation compared to HC pDCs. RNA-seq data analysis showed an upregulation of IFN-responsive genes in most of the SLE and At-Risk pDCs but not transcripts of any IFN subtypes. Other upregulated pathways were related to immune regulation and senescence. Phenotypically, SLE pDCs were characterised by upregulation of regulatory receptors and increased telomeric erosion. *In situ* hybridization revealed high IFN expression in the epidermis but not in lymphocyte-infiltrating areas of lesional biopsies from SLE patients. High expression of IFN was also observed in epidermis of At-Risk individuals without any signs of cutaneous inflammation. *In vitro* stimulation of freshly isolated keratinocytes also showed a notable increase in IFN production.

**Conclusions:** In SLE, non-haematopoietic tissue resident cells are a dominant source of IFN and this is present prior to clinically overt disease. Meanwhile, the professional IFN-producing pDCs have lost their immunogenic properties. These findings suggest an important role for tissue resident cells in autoimmunity and may facilitate novel therapeutic interventions.

**Disclosure of Interest:** None declared

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**OP0181** **PATIENT PERSPECTIVES OF PEOPLE WITH PRIMARY SJÖGREN'S SYNDROME: A MULTICENTRE QUALITATIVE EUROPEAN STUDY**

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**Background:** Primary Sjögren's syndrome (pSS) is one of the most common systemic autoimmune disorders and leads to an impaired health related quality of life. However, treatment mainly focuses on the management of physical manifestations. Little is known about the lived experiences of people with pSS, including the impact on people's life, functioning and their social relationships.

**Objectives:** To explore the perspectives of people with pSS from different European countries with various cultural backgrounds in order to achieve a broad understanding of concepts that are important and meaningful to people with pSS. This study is a part of a project which aims to evaluate the coverage of the patient perspectives by patient reported outcome measures in pSS, which is funded by the Austrian Association of Rheumatology.

**Methods:** A multicentre focus group study was performed in five European countries, namely Austria, Germany, Italy, Romania and Sweden. Patients were recruited from the outpatient clinics of the local centres. Focus groups were chaired by a trained moderator and followed an interview guide which included questions about impairments and limitations in body structures, body functions, activities and participation as well as contextual factors and resources, such as coping strategies. Focus groups were audiotaped and transcribed. We conducted a content-analysis of each focus group and subsequently combined the extracted concepts from each country, using the International Classification of Functioning, Disability and Health as a frame of reference.

**Results:** A total of 12 focus groups was conducted in seven participating centres in five countries. Fifty people (48 women; 96%) with pSS participated in the focus groups (ranging from two to four groups per country). All focus groups had a total duration of 1030 min and resulted in 252 pages of transcript. From qualitative analysis we derived concepts meaningful to people with pSS from all countries, especially those concepts that were linked to a physical dimension. However, we identified differences in the description of these experiences in daily life, for example for pain-concerning sensations or for the impact on social relationships. Furthermore, the attitudes towards the treatment and towards the disease differed between the participants. People with pSS had various coping strategies, such as gaining more knowledge about the disease or utilising non-pharmacological treatment.

**Conclusions:** This is the first multicentre qualitative European study which investigated the patient perspectives in pSS with a cross-cultural understanding. Clinicians, health professionals and researchers need to know about the perspectives, experiences and needs of people with pSS in order to ensure a comprehensive treatment.

**Disclosure of Interest:** None declared

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THURSDAY, 14 JUNE 2018

**The crystal maze – etiology and management**

**OP0182** **GOUT AND DEMENTIA IN THE ELDERLY: A MEDICARE CLAIMS STUDY**

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**Background:** The pursuit of a link between gout/hyperuricemia and dementia has led to contradictory results. Most observational studies, including population-based studies, showed that hyperuricemia was associated with a higher risk of dementia and less cognitive dysfunction, while a few studies found hyperuricemia to be associated with a lower risk of dementia. Recently, a large French population-based study in the elderly (65 years or older) showed that hyperuricemia was associated with a higher risk of dementia and with MRI changes of ageing in the brain.

**Objectives:** To assess whether gout in the elderly is associated with a risk of incident dementia.

**Methods:** We used the 5% Medicare claims data for this observational cohort study. We used multivariable-adjusted Cox proportional hazard models to assess the association of gout with incident dementia, adjusting for potential confounders/covariates including demographics (age, race, gender), comorbidities (Charlson-Romano comorbidity index), and medications commonly used for cardiac diseases (statins, beta-blockers, diuretics, and angiotensin converting enzyme (ACE)-inhibitors) and gout (allopurinol and febuxostat).

**Results:** In our cohort of 1.23 million Medicare beneficiaries, 65 324 had incident dementia. The crude incidence rates in people without and with gout were 7.36 and 13.58 per 1000 person-years, respectively. In multivariable-adjusted analyses, gout was independently associated with a significantly higher hazard ratio of incident dementia, with a hazard ratio [HR] of 1.17 (95% CI, 1.13, 1.21); sensitivity analyses confirmed the main findings. Compared to age 65 to <75 years, older age groups were associated with 3.3 and 6.3-fold higher hazards of dementia; hazards were also higher for females, Black race or people with higher medical comorbidity.

Subgroup analyses indicated that gout was significantly associated with dementia in patients without key comorbidities (CAD, hyperlipidemia, CVD, diabetes, hypertension) with HR ranging 1.20–1.57, but not in patients with each of these comorbidities, except CAD, with HR 0.97–1.07 (table 1).

**Abstract OP0182 – Table 1.** Association of gout with incident dementia, in pre-defined subgroups of presence/absence of CAD, hyperlipidemia, CVD, diabetes or hypertension

	Multivariable-adjusted (Model 1)		Multivariable-adjusted (Model 1)	
	HR (95% CI)	P-value	HR (95% CI)	P-value
	<b>No CAD</b>		<b>CAD</b>	
Gout	1.20 (1.15–1.25)	<0.0001	1.07 (1.01–1.14)	0.032
	<b>No Hyperlipidemia</b>		<b>Hyperlipidemia</b>	
Gout	1.33 (1.27–1.40)	<0.0001	1.02 (0.97, 1.07)	0.56
	<b>No CVD</b>		<b>CVD</b>	
Gout	1.23 (1.18–1.28)	<0.0001	0.97 (0.90–1.05)	0.46
	<b>No Diabetes</b>		<b>Diabetes</b>	
Gout	1.24 (1.19–1.29)	<0.0001	1.04 (0.98–1.10)	0.23
	<b>No Hypertension</b>		<b>Hypertension</b>	
Gout	1.57 (1.46–1.68)	<0.0001	1.01 (0.97–1.05)	0.76

Gout\*CAD p-value<0.0001; Gout\*hyperlipidemia p-value<0.0001; Gout\*CVD p-value<0.0001;

Gout\*diabetes p-value<0.0001; Gout\*hypertension p-value<0.0001;

**Conclusions:** Gout was independently associated with 17%–20% higher risk of incident dementia in the elderly. Future studies need to understand the pathogenic pathways involved in this increased risk.

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**Disclosure of Interest:** J. Singh Grant/research support from: Takeda, Savient, Consultant for: Savient, Takeda, Regeneron, Merz, Iroko, Bioiberica, Crealta/Horizon and Allergan pharmaceuticals, WebMD, UBM LLC and the American College of Rheumatology, J. Cleveland: None declared

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**OP0183** **ASSOCIATION BETWEEN HFE GENOTYPES AND CLINICAL SEVERITY CHARACTERISTICS OF CALCIUM PYROPHOSPHATE CRYSTAL ARTHRITIS**

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**Background:** Several metabolic disturbances that reduce the activity of pyrophosphatases have been associated with development of calcium pyrophosphate crystal arthritis (CPPCA), but there is scarce data on their influence on clinical manifestations, as such disease-specific variables are not recorded in most available databases.

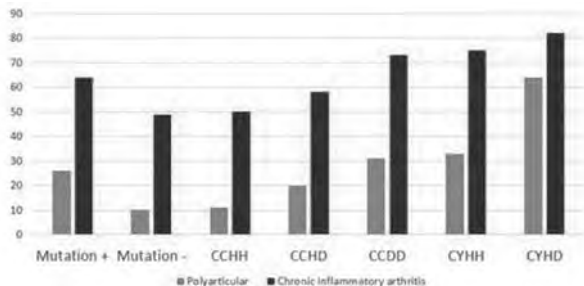
**Objectives:** To evaluate factors associated to severity of clinical joint involvement in patients with definite CPPCA.

**Methods:** Transversal study with prospective recruitment of cases (patients with CPPCA diagnosis confirmed by microscopy showing CPP crystals within



leucocytes in synovial fluid plus presence of X-ray chondrocalcinosis in at least one joint) and controls (patients with synovial effusion shown to have no CPP crystals and no chondrocalcinosis in hands and knee X-rays), paired by age and gender. Patients with hemochromatosis or primary hyperparathyroidism were not included. General variables were included along with plausible metabolic variables (Ca, P, Mg, iPTH, iron saturation [satFe%], ferritin, diuretics and type of diuretic, and HFE genotype), and distribution of joint involvement (mono-oligo-polyarticular) and clinical manifestations (acute [A-CPPCA] and chronic inflammatory [CI-CPPCA]), as in EULAR recommendations.

**Results:** 340 patients and 316 controls were recruited, 53% were men, age at inclusion was 67±10 year (IC range 62–75), time from onset of symptoms 5.2 ±5.3 year (IC range 1–8). Regarding cases, A-CPPCA was present in 147 (43.2%), CI-CPPCA in 193 (56.8%), with monoarticular involvement in 102 (30.0%), oligoarticular in 176 (51.8%), and polyarticular in 62 (18.2%). Patients showed higher serum ferritin levels and lower Mg levels than controls (253 and 2.00 vs 204 and 2.08, respectively), along with higher rate of HFE gene mutations (Odds ratio 2.30, 95% CI: 1.66 to 3.20). Genotypes including homozygous mutations of H63D allele, heterozygous mutations for C282Y allele, and double heterozygous mutations for C282Y and H63D were statistically associated with higher frequency of polyarticular involvement and with CI-PPA (figure 1). Clinical variables were also associated with higher SatFe% levels, but not Mg or ferritin levels. S65C gene mutations were not increased in patients compared to controls and did not show any association with clinical phenotype.



**Abstract OP0183** – Table 1 Rate (%) of polyarticular and chronic inflammatory clinical pattern impact of presence of any mutation and genotypes of FHE genes

**Conclusions:** Patients with definite CPPCA show differences in serum Mg and Ferritin levels compared to that of controls, and may contribute, along with other factors, to development of CPPCA. Nevertheless, only presence of some HFE genotypes involving C282Y and H63D genes were associated with more severe phenotype of clinical involvement.

**Disclosure of Interest:** None declared

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#### OP0184 THE FREQUENCY OF FLARES IN SUBJECTS WITH CHRONIC REFRACTORY GOUT TREATED WITH PEGLOTICASE IS RELATED TO VARIATION IN THE LEVEL OF PLASMA URATE

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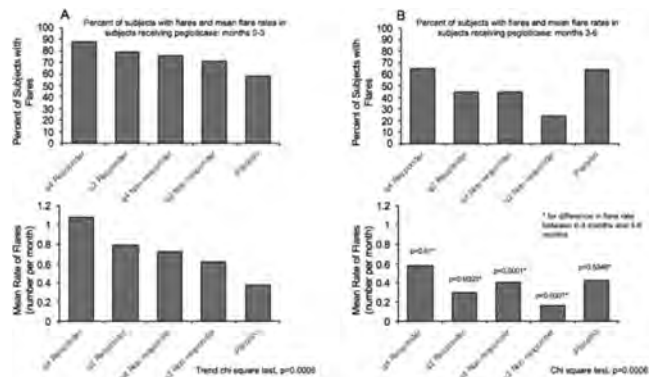
**Background:** Lowering plasma urate in subjects with gout is associated with an increase in flares because of an altered equilibrium between soluble urate and uric acid crystals.<sup>1</sup> Details of the relationship between plasma urate lowering and gout flares have not been fully delineated. Pegloticase is a mammalian recombinant uricase conjugated to polyethylene glycol approved for the treatment of chronic gout refractory to conventional oral urate lowering therapy.<sup>2–4</sup> Results from the two 6 month randomised clinical trials (RCTs) of pegloticase showed that during months 1–3, there was an increase in pegloticase-treated subjects experiencing gout flares vs those receiving placebo. However, the reported analysis did not separate results for subjects who did and did not respond to pegloticase with a sustained reduction in plasma urate levels or relate flares to plasma urate levels.

**Objectives:** To determine factors associated with the occurrence of flares in subjects who did and did not respond to pegloticase in the two RCTs for this therapy.

**Methods:** This analysis used results from 2 pivotal RCTs<sup>2</sup> of pegloticase (8 mg every 2 weeks [q2] or every 4 weeks [q4]) vs placebo in subjects with chronic refractory gout. A responder was defined as a subject with plasma urate <6.0 mg/dL ≥80% of the time from the week-9 infusion to just prior to the week-13 infusion and from the week-21 infusion to the week-25 final study visit. Gout flares were defined as acute joint pain and swelling requiring treatment. Gout flare prophylaxis

(colchicine, 0.6 mg once or twice daily, or a NSAID) was initiated 1 week before the first infusion and continued throughout the study.

**Results:** There were increases in the frequency of subjects experiencing flares and the mean flare frequency in the pegloticase group vs placebo during the first 3 months of the trial (figure 1A). In contrast, there were marked reductions in both outcomes during months 3–6 (figure 1B). The increase in flares in the first 3 months was most evident (p=0.0006) and the decrease during the second 3 months was least marked (p=0.0006) in subjects receiving q4 pegloticase. Previous analysis indicated that q2 pegloticase caused persistently lowered plasma urate in responders, whereas q4 administration resulted in a more saw tooth pattern.<sup>5</sup> Multivariate linear regression analysis indicated that the only variable associated with flares in the treated subjects was the absolute change in plasma urate prior to these events. Assessment of plasma urate at both 2 weeks and immediately before flares indicated that larger differences between these two values were associated with increased flare occurrence (p=0.002).



**Conclusions:** Flares associated with pegloticase treatment in subjects with chronic refractory gout were increased most markedly in responders to monthly administration and were significantly associated with fluctuations in plasma urate levels. Such fluctuations are much more common with monthly administration of pegloticase vs the recommended biweekly treatment regimen.

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**Disclosure of Interest:** L. Calabrese: None declared, T. Fields Consultant for: Horizon Pharma, Takeda, Ironwood, Speakers bureau: Horizon Pharma, Takeda, Ironwood, A. Yeo Consultant for: Horizon Pharma, P. Lipsky Consultant for: Horizon Pharma

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#### OP0185 EMERGENCY DEPARTMENT VISITS FOR GOUT: A DRAMATIC INCREASE IN THE PAST DECADE

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**Background:** Several studies have suggested that the prevalence of gout has been increasing worldwide, perhaps related to lifestyle factors.<sup>1–3</sup> In the US, the NHANES study found a significantly higher age-adjusted prevalence (3.9%) in 2007–2008 than the estimate in 1988–1994 (2.9%). This trend paralleled an observed increase in hyperuricemia.<sup>1</sup>

**Objectives:** To study emergency department visits due to gout in the US over 9 years (2006 to 2014).

**Methods:** The Nationwide Emergency Department Sample (NEDS) is the largest all-payer emergency department (ED) database in the United States, yielding national estimates of hospital-based ED visits. It contains information from 31 million ED visits at 945 hospitals in 34 states that approximate a 20-percent stratified sample of U.S. hospital-owned EDs. Weighted, it estimates roughly 143 million ED visits. We studied all ED with primary diagnosis of Gout (ICD9 code 274.xx) from 2006–2014 and calculated prevalence in different age groups. Population data was obtained from US census bureau.

**Results:** Over last 9 years, 1.7 million people visited EDs with a primary diagnosis of acute gout. The total number of ED visits per year increased from 1 68 580 in 2006 to 2 13 780 in 2014, an increase of 26.8%. The prevalence of emergency room visits with primary diagnosis of gout increased from 56.5/100,000 population

in 2006 to 67/100,000 in 2014 ( $p < 0.001$ ). The largest increase in ED visits was a 28% increase in prevalence among the 45–64 years age group from 91/100,000 to 116/100,000 (27%,  $p < 0.001$ ). Men were responsible for 78% of the ED visits in both 2006 and 2014.

Age in years	Total number of ED visits in 2006	Prevalence of ED visits/100,000 population in 2006	Total number of ED visits in 2014	Prevalence of ED visits/100,000 population in 2014
18–44	49 265	44	55 216	48
45–64	68 544	91	97 081	116
65–84	44 358	137	53 206	133
85+	6242	128	8126	132
All ages	2 05 905	56.5	2 13 780	67

**Conclusions:** Emergency Department visits have increased dramatically in the US over the last 9 years, and this increase is mostly in the 45–64 years age group perhaps reflecting the undermanaged burden of uncontrolled gout. Education, improved recognition and long-term management as well as increased use of preventive strategies is needed.

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OP0186

#### NEPHROLITHIASIS AS A COMPLICATION OF GOUT: A CROSS-SECTIONAL STUDY WITH HELICAL COMPUTED TOMOGRAPHY

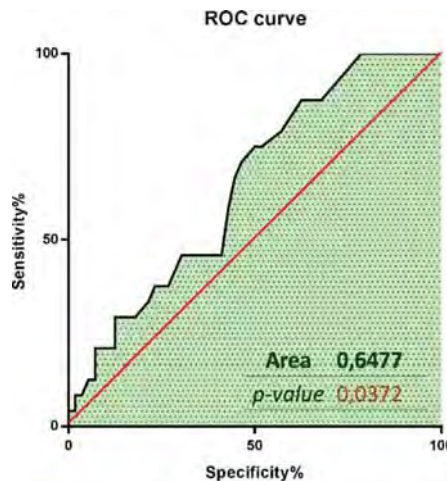
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**Background:** Gout is the most prevalent inflammatory arthritis, secondary to persistent hyperuricemia. It has been associated with development and progression of cardiometabolic diseases and chronic kidney disease. Several studies have shown a relationship between hyperuricemia and history of nephrolithiasis, although cut-off levels for uric acid and other related risk factors are still not well established.

**Objectives:** To determine the frequency of nephrolithiasis (NL) detected by helical computed tomography (h-CT) and its associated risk factors in patients with gout in a tertiary hospital of São Paulo, Brazil.

**Methods:** This cross-sectional study, conducted from 2016 to 2017, included 80 patients with a diagnosis of gout, according to the criteria of the ACR/EULAR-2015. They were questioned about the previous history of NL and submitted to h-CT for NL. Two groups were established: with and without NL; and later, unilateral and bilateral lithiasis. Anthropometric data, disease duration, serum uric acid (UA), creatinine, urinary pH (pH) and urinary UA of groups were compared. Statistical analysis included: mean, standard deviation, relative percentages, t-student test, chi-square test and ROC curve. Comparison of time to event-rate was performed by Kaplan-Meier method with log rank test.  $p < 0.05$  was considered statistically significant.

**Results:** NL was confirmed by h-CT in 30% of patients. However, only 16% reported previous history of NL. Groups with NL and without NL were similar in mean age ( $65,96 \pm 5,54$  and  $68,89 \pm 9,58$  years,  $p = 0.147$ ), disease duration ( $16,63 \pm 11,49$  and  $11,77 \pm 9,74$  years,  $p = 0.056$ ) and BMI ( $29,72 \pm 5,09$  and  $28,82 \pm 5,08$ ,  $p = 0.470$ ). The NL group had higher pre-treatment UA compared with patients without NL ( $9,36 \pm 1,09$  and  $8,80 \pm 1,08$  mg/dL,  $p < 0.05$ ) and the most acidic pH ( $5,26 \pm 0,42$  and  $5,74 \pm 0,62$ ,  $p < 0.05$ ). In addition, patients with bilateral NL presented higher BMI than unilateral patients ( $p = 0.036$ ). According to ROC curve analysis, the best cutoff value for pre-treatment UA was 8.5 mg/dL, yielding sensitivity and specificity of 75% and 50%, respectively, for predicting NL events in this study. Kaplan-Meier analysis showed that after 20 years of disease, 55% of patients with pre-treatment AU  $\geq 8.5$  mg/dL had NL, while only 18% of patients with pre-treatment AU  $< 8.5$  mg/dL.



AU $\geq 8,5$ mg/dL		
Sensitivity	75%	95% IC: 53% - 90%
Specificity	50%	95% IC: 36% - 64%
		Without NL
AU $< 8,5$ mg/dL	27	6 (18%)
AU $\geq 8,5$ mg/dL	29	18 (38%)

**Conclusions:** Since prevalence of NL in gout patients cannot be determined reliably from the clinical history, an active screening test for NL should be performed in these patients. Our study suggests that urine acidification and UA  $\geq 8.5$  mg/dL are associated with an increased risk of NL during follow-up of gout patients and should be corrected in their treatment.

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**Disclosure of Interest:** None declared

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OP0187

#### FRUCTOSE-CONTAINING BEVERAGES IS AN INDEPENDENT RISK FACTOR FOR GOUT EARLY-ONSET IN SOUTH CHINA

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**Background:** A trend of earlier onset of gout has been reported even though its incidence increases in a linear fashion with age until 70 years. Dietary factors have been supposed to be contributed to the early onset of gout.

**Objectives:** To investigate diet characteristics of gout and their impact on the early onset of gout.

**Methods:** Consecutive gout patients who fulfilled the 2016 ACR/EULAR classification criteria were recruited between Dec 2016 and Dec 2017. A cross-section survey on dietary factors before gout onset was conducted with semi-quantitative diet questionnaire. The questionnaire included alcohol, fructose-containing beverages, soup, animal organs, sea-foods, hotpot, tea and coffee, which impact on

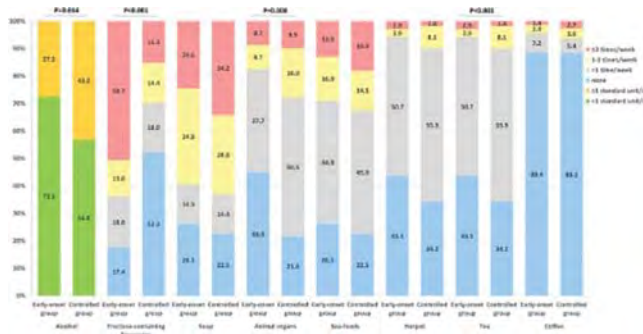
serum uric acid (sUA) and aren't major macronutrient provider in Chinese dietary patterns. The patients with gout onset before age 30 years were defined as early-onset group while the others were defined as control group.

**Results:** Among 180 gout patients recruited, there were 69 (38.3%) patients in early-onset group and 111 (61.7%) in control group. Compared with control group, gout patients in early-onset group presented significantly higher level of sUA, estimated glomerular filtration rate and proportion of obesity, but lower fraction excretion of uric acid and prevalence of hypertension (table 1, p<0.05). The results of diet questionnaire showed that more patients in early-onset group consumed fructose-containing beverages ≥3 times/week, but less alcohol, animal organs and tea (all p<0.05, figure 1). There were no significantly difference in the consumption of soup, seafood, hotpot and coffee. Consuming fructose-containing beverages ≥3 times/week [OR 8.3 (2.5, 27.1), p<0.001], alcohol ≥1 standard unit/d [OR 0.27 (0.10, 0.80), p=0.017] and tea ≥3 times/week [OR 0.33 (0.12, 0.92), p=0.033] were associated with early-onset gout after adjusted by variables which were significantly different between early-onset group and control group (table 1).

**Abstract OP0187 – Table 1.** Comparison of clinical characteristics between the early-onset group and control group

Characteristics	all patients (n=180)	early-onset group (n=69)	control group (n=111)	P
Male, n(%)	168 (93.3)	68 (98.6)	100 (90.1)	0.027
Age, years	42.5±15.5	28.3±7.2	51.4±12.4	<0.001
Age of onset, years	37.8±15.1	23.5±5.1	46.7±12.1	<0.001
Duration of gout, years	3.0 (1.0,8.0)	3.0 (2.0,5.0)	3.0 (1.0,7.0)	0.782
Family history, n (%)	63 (35.0)	29 (42.0)	34 (30.6)	0.148
Tophi, n (%)	31 (17.2)	10 (14.5)	21 (18.9)	0.544
sUA, mg/dl	9.0±2.4	9.9±2.1	8.7±2.1	<0.001
FEUA,%	3.9 (2.8,5.2)	3.2 (2.3,4.7)	4.2 (3.0,5.7)	0.002
eGFR, ml/min <sup>1</sup> /1.73m <sup>2</sup>	83.2±19.7	91.3±17.3	78.3±19.5	<0.001
Hypertension, n (%)	58 (32.2)	11 (15.9)	47 (42.3)	<0.001
Diabetes mellitus, n (%)	26 (14.4)	7 (10.1)	19 (17.1)	0.276
Dyslipidemia, n (%)	117 (65.0)	44 (63.8)	73 (65.8)	0.873
Body mass index kg/m <sup>2</sup>	25.4±3.5	25.7±4.1	25.2±3.0	0.352
Obesity, n (%)	46 (25.6)	24 (34.8)	22 (19.8)	0.034

sUA: serum uric acid; FEUA: fraction excretion of uric acid; eGFR: estimated glomerular filtration rate.



**Conclusions:** Fructose-containing beverages may be an independent risk factor for gout early-onset in south China. Patient education should emphasise diet management.

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**Disclosure of Interest:** None declared

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**OP0188 EFFECTS OF ALLOPURINOL VERSUS FEBUXOSTAT ON CARDIOVASCULAR RISK IN KOREAN PATIENTS WITH GOUT: A NATION-WIDE COHORT STUDY**

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**Background:** Gout is associated with an increased risk of cardiovascular (CV) disease.

**Objectives:** We aimed to investigate comparative CV risk among gout patients who initiated allopurinol versus febuxostat.

**Methods:** Using the 2002–2015 Korean National Health Insurance Service (KNHIS) data for the whole Korean population, we conducted a cohort study on patients aged ≥40 years who had ICD-10 diagnosis code for gout and initiated allopurinol or febuxostat without prior history of urate lowering therapy, excluding those with chronic kidney disease, cancer, or dialysis treatment. The primary outcome was a composite CV endpoint of hospitalisation for myocardial infarction, stroke/transient ischaemic attack, or coronary revascularisation. Secondary outcomes were individual components of the primary outcome, and hospitalisation for heart failure (HF). Follow-up time started from the day after the first date the study drug was initiated and continued through to the earliest date among the following censoring events: discontinuation of the study drugs, outcome occurrence, disenrollment, end of study dataset, or death. After propensity score (PS)-matching with a 4:1 ratio for allopurinol and febuxostat initiators to adjust for baseline confounding, we estimated hazard ratio (HR) and 95% confidence interval (CI) of CV risks in allopurinol initiators versus febuxostat.

**Results:** We included 39 636 allopurinol initiators PS-matched on 9909 febuxostat initiators with a mean age of 59 years and 78% male. Before PS matching, baseline CV risk factors including hypertension, dyslipidemia, diabetes, and previous ischaemic heart disease were more prevalent in febuxostat initiators. The incidence rate per 100 person-years for primary composite endpoint was 2.33 in allopurinol and 2.12 in febuxostat initiators in the primary as-treated analysis. The HR (95% CI) for the primary outcome associated with allopurinol was 1.18 (0.98–1.42) versus febuxostat. Secondary outcome analyses showed similar results (table 1).

**Abstract OP0188 – Table 1.** Risk of cardiovascular events in allopurinol versus febuxostat initiators

	Allopurinol (n=39,636)		Incidence rate per 100 person-year	Febuxostat (n=9,909)		Incidence rate per 100 person-year	HR (95% CI)
	Events (n)	person-years		Events (n)	person-years		
<b>AS-TREATED ANALYSIS</b>							
<b>Primary outcome</b>							
Composite CV end point	735	31 605	2.33	133	6272	2.12	1.18 (0.98–1.42)
<b>Secondary outcomes</b>							
MI	105	31 528	0.33	20	6269	0.32	1.03 (0.64–1.68)
Coronary revascularisation	215	31 546	0.68	31	6269	0.49	1.42 (0.97–2.08)
Stroke/TIA	498	31 572	1.58	94	6271	1.50	1.14 (0.91–1.43)
Heart failure	956	30 611	3.12	206	6108	3.37	1.15 (0.99–1.34)

Propensity-score matching was used to adjust more than 50 covariates including demographic characteristics, medical comorbidities such as CV risk factors, use of gout specific and non-specific medications, and health care utilisation pattern. CI=confidence interval; CV=cardiovascular; HR=hazard ratio; MI=myocardial infarction; TIA=transient ischaemic attack

**Conclusions:** In this large Korean population-based cohort study, CV risks appear to be numerically, but not statistically significantly, elevated among allopurinol initiators compared to febuxostat initiators.

**Disclosure of Interest:** None declared

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**OP0189 IDENTIFICATION OF NEW AND RARE VARIANTS IN ABCG2, SLC22A1 AND ALDH16A1 GENES IN CRYSTAL-PROVEN EARLY-ONSET GOUT**

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**Background:** Early-onset or juvenile gout (EOG) without hypoxanthine-guanine phosphoribosyltransferase enzyme deficiency (*HPRT*, OMIM 300323) and not related to familial juvenile hyperuricemic nephropathy (*UMOD*, OMIM 300323) is a rare gout phenotype characterised by a first flare in adolescence or in young adulthood. While numerous genome wide association studies (GWAS) have been done in classical and late-onset gout, very few studies have been performed in EOG patients. Moreover, until now most genetic studies only assess association between pre-defined single nucleotide polymorphisms (SNP) and gout.

**Objectives:** Our aim was to identify the genetic variants of clinically confirmed EOG by screening all exons of gout-associated genes with targeted Next-Generation Sequencing (NGS) approach.

**Methods:** Twenty-six urate crystal-proven gout patients with first flare occurring before the age of 30 years were included. Gout history, comorbidities and patient characteristics were recorded. All participants provided written informed consent to genetic analysis. After DNA extraction from total blood samples, the NGS libraries were prepared with surselect QXT (Agilent) and sequencing was performed with miseq (Illumina).

The multigene panel included 80 genes described in GWAS and genes involved in rare diseases such as *HPRT* and *UMOD*.

**Results:** Twenty-six patients (24 men, 20 Caucasians, 5 Asians and 1 African) with crystal-proven gout had experienced their first flare at a mean age of 22.8 years [14–29]. Gout duration was 11.5 years [1–46] and clinical tophi observed in 9 patients. Mean age was 37.5 [24–69] years and mean body mass index 27.6 kg/m<sup>2</sup> [20.1–40.7]. Ten patients were overweight, 5 had obesity, 1 hypertension, 0 diabetes mellitus, 7 dyslipidemia and 10 chronic kidney disease stages 2–4. Mean serum urate level was 527 µmol/L [270–803]. Amongst 26 affected patients, 7 had a molecular anomaly (26.9%). Six patients harboured one rare or novel variant in *ABCG2* (three Caucasian patients), *ALDH16A1* (two Caucasian patients) and *SLC22A11* (one African patient). Two other patients (one Caucasian and one Asian) carried an association of variants in both *ABCG2* and *ALDH16A1*. All variants had a Minor Allele Frequency (MAF) below 0.3% or were never described in public databases. All variant were considered as probably pathogenic according to *in silico* predictive algorithms. Interestingly, the well-known p.Gln141Lys SNP of *ABCG2* was identified in 3 Asian patients (11.5%) at homozygous level.

**Conclusions:** Our finding of very rare and novel pathogenic variants in *ABCG2*, *ALDH16A1* and *SLC22A11* genes provides better insights of the molecular pathogenesis in early-onset juvenile gout. However, our results also highlight the involvement of yet undetermined genes in this population.

**Disclosure of Interest:** None declared

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THURSDAY, 14 JUNE 2018

**Treatments: friend or foe?**

**OP0190 THE ROLE OF NSAIDS IN THE ASSOCIATION BETWEEN OSTEOARTHRITIS AND CARDIOVASCULAR DISEASES: A POPULATION-BASED COHORT STUDY**

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**Background:** Worldwide, osteoarthritis (OA) is a major musculoskeletal disorder. Recent research suggests that OA is an independent risk factor for cardiovascular disease (CVD).<sup>1</sup> The relationship is complicated because non-steroidal anti-inflammatory drugs (NSAIDs), a proven risk factor for CVD, are frequently used for the treatment of OA.<sup>2</sup> Researchers have hypothesised that NSAID use in the causal pathway between OA and CVD is what may ultimately impact these patients to develop CVD, this pathway has yet to be studied.<sup>3,4</sup>

**Objectives:** The objective of this study was to disentangle the role of NSAID in the increased risk of CVD among OA patients.

**Methods:** This longitudinal study was based on linked health administrative data from British Columbia, Canada. From a population-based cohort of 720,055 British Columbians, we matched on age and sex to assemble 7,743 OA patients and 23 229 non-OA controls (1:3 ratio). We used multivariable Cox proportional hazards models to estimate the risk of developing incident CVD (primary outcome) as well as ischaemic heart disease (IHD), congestive heart failure (CHF) and stroke

(secondary outcomes). To estimate the mediating effect of NSAIDs, defined as current use of NSAID using linked prescription dispensing records, in the OA-CVD relationship, we implemented a marginal structural model.

**Results:** People with OA had 23% higher risk of developing CVD compared to people without OA after adjusting for SES, BMI, hypertension, diabetes, hyperlipidemia, COPD, and Romano comorbidity score, adjusted HR (95% CI) was 1.23 (1.17, 1.29). Adjusted HR (95% CI) was 1.42 (1.33, 1.52), 1.17 (1.10, 1.27), 1.14 (1.08, 1.24) for CHF, IHD and stroke, respectively. Approximately 67.51% of the total effect of OA on the increased risk of CVD was mediated through current NSAID use. Among the secondary outcomes, approximately 44.77% of increased CHF risk was mediated through current NSAID use. More than 90% of the total effects on IHD and stroke was mediated through the current NSAID use.

**Conclusions:** Our study is the first to evaluate the mediating role of NSAID use in the OA-CVD relationship based on population-based health administrative data. The results of this study also indicate that OA is an independent risk factor for CVD. Our findings suggest that the mediating role of NSAID use substantially contributes to the OA-CVD association.

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**Disclosure of Interest:** None declared

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**OP0191 ALL-CAUSE MORTALITY AND CARDIOVASCULAR DEATH IN HYDROXYCHLOROQUINE USERS IN RHEUMATOID ARTHRITIS PATIENTS – A POPULATION BASED DANISH COHORT STUDY**

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**Background:** Rheumatoid arthritis (RA) is associated with a marked increase in cardiovascular comorbidity and mortality.<sup>1</sup> The increased risk is present from the earliest stages of the disease and evidence suggests an overlap in the pathogenic features leading to RA and atherosclerosis.

Hydroxychloroquine (HCQ) is used to treat RA in combination with methotrexate and has been associated with decreased risk of type II diabetes and dyslipidaemia among RA patients. Also HCQ has improved survival rates when used to treat other inflammatory diseases, e.g. systemic lupus erythematosus.<sup>1</sup> The evidence regarding RA patients is scarce.

**Objectives:** We wish to examine whether HCQ would affect the incidence rates of cardiovascular diseases, type II diabetes, cardiac – and all-cause mortality among Danish RA patients in an observational cohort study.

**Methods:** We identified all incident RA patients during the period of 2004 through 2014 in Denmark. HCQ initiators were compared with non-users of HCQ, stratified on rheumatoid factor positivity. Each HCQ initiator was matched to a non-HCQ initiator by their propensity score (PS). In the PS all relevant available cardiovascular drugs and comorbidities were included. All together we had 3,742 RA patients in each group.

**Results:** We found a significant reduction in all-cause mortality and cardiovascular related death among HCQ initiators, with a hazard ratio of 0.83 (95% confidence interval [CI] 0.71–0.97) and 0.78 (95% CI: 0.61 to 0.99), respectively. We did not find any association between HCQ use and development of type II diabetes or specific ischaemic events (myocardial infarctions and ischaemic strokes).



**Conclusions:** The beneficial properties on survival seen with HCQ use in other inflammatory diseases seem also applicable to RA patients. These results need confirmation in a randomised setting but justifies the use of HCQ in combination with other conventional synthetic disease-modifying antirheumatic drugs even though the effect of HCQ, *per se*, on RA disease activity is limited.

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**Disclosure of Interest:** None declared

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#### OP0192 METHOTREXATE USE AND THE RISK FOR CARDIOVASCULAR DISEASE AMONG RHEUMATOID PATIENTS INITIATING BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS

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**Background:** Methotrexate (MTX) has been associated with reduced risk for CVD in several studies conducted among rheumatoid arthritis (RA) patients never exposed to biologic disease-modifying antirheumatic drugs (bDMARDs). Effect of concomitant MTX use on CVD risk among RA patients initiating bDMARDs remains unknown.

**Objectives:** The objective of this study was to assess the CVD risk associated with MTX use among RA patients initiate bDMARDs, overall, and by each bDMARDs initiated.

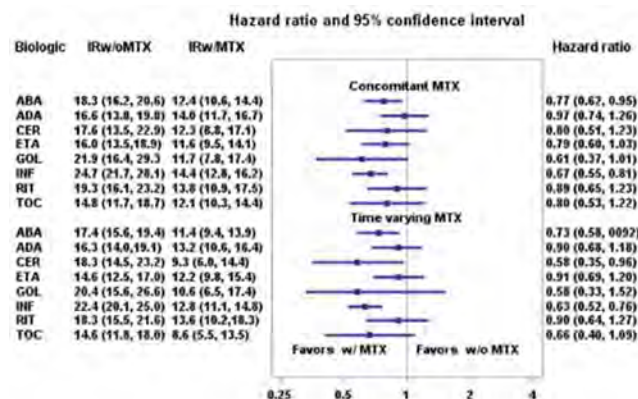
**Methods:** A retrospective cohort study was conducted using 2006–2015 Medicare claims data for RA patients. Follow up started at initiation (index date) and ended at earliest of 1) end of exposure of the specific bDMARDs agent (days of supply plus 90 days extension), 2) switched to other bDMARDs or tofacitinib, 3) CVD event, 4) death date, 5) loss of Medicare coverage, 6) end of study (September 30, 2015). MTX use was defined as 1) concomitant MTX use, with prescription for MTX within 120 days after index date and 2) time varying MTX, defined as prescription date to prescription date plus days of supply without extension. For sensitivity analysis, a 90 day extension was added to days of supply. The primary outcome was composite of incident MI, incident stroke and fatal CVD. Fatal CVD were identified by a claims based algorithm with PPV  $\geq 80\%$ .

Incidence rates (IR) and 95% confidence intervals (CI) were calculated using Poisson regression. Overall association between MTX use (versus no MTX) and risk of CVD were assessed using Cox regression. Given that the interactions between MTX and background bDMARDs was significant, we performed contrast (MTX Yes vs No) to examine the association between MTX and risk for CVD for each underlying bDMARDs in one model. A subgroup analysis limited the cohort to RA patients with previous exposure to MTX was conducted to ensure consistency of findings.

**Results:** A total of 88,255 DMARDs initiations (64 218 patients) were included in this study. The average age at initiation was 64.6 (12.3) years, 84.0% were female, 68.2% were non-Hispanic white. The crude IRs for CVD were 13.1 (95% CI: 12.2 to 14.0) and 18.7 (95% CI: 17.6 to 19.9) events per 1000 person years for RA patients with and without concomitant MTX respectively. The crude IRs for CVD were 12.1 (95% CI: 11.1 to 13.2) and 17.9 (95% CI: 16.9 to 18.8) events per 1000 person years for RA patients with and without time varying MTX respectively. IRs for individual bDMARDs are shown in figure. P-value for interaction

between concomitant MTX and background bDMARDs was 0.0189 and p-value for interaction between time varying MTX and background bDMARDs was 0.0030. The contrast HRs for concomitant MTX ranged from 0.61 (0.37, 1.01) for golimumab initiators to 0.97 (0.74, 1.26) for adalimumab initiators (figure 1). The contrast HRs for time varying MTX ranged from 0.58 (0.35, 0.96) for certolizumab initiators to 0.90 (0.68, 1.18) for adalimumab initiators.

Results were robust in sensitivity and subgroup analyses.



**Conclusions:** Our observational study suggests an overall 23% reduction of CVD risk associated with concomitant MTX use. The effect sizes vary among background bDMARDs.

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#### OP0193 TOCILIZUMAB AND THE RISK FOR CARDIOVASCULAR DISEASE EVENTS AMONG RHEUMATOID ARTHRITIS PATIENTS: A DIRECT COMPARISON IN REAL WORLD SETTING

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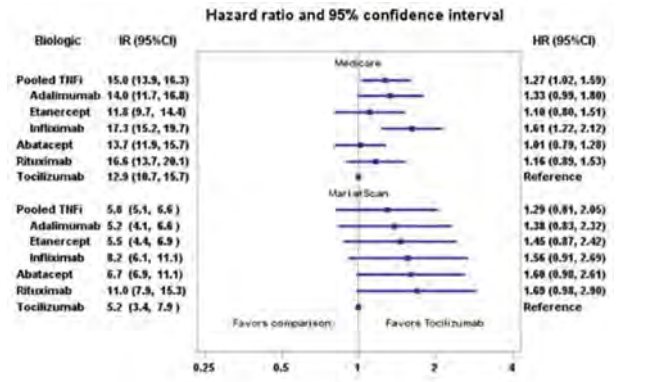
**Background:** Multiple studies have observed unfavourable changes in lipid profile associated with tocilizumab (TCZ, anti-IL6 receptor antagonists) and some other rheumatoid arthritis (RA) therapies. The real-world cardiovascular disease (CVD) risk associated with the first anti-IL-6R medication for RA, TCZ, remains uncertain.

**Objectives:** The objective of this study was to assess the CVD risk associated with TCZ compared to individual tumour necrosis inhibitor (TNFi) therapies, as well as to other biologics used for RA (e.g. rituximab, abatacept).

**Methods:** Using 2006–2015 Medicare and MarketScan claims data, we conducted a retrospective cohort study among RA patients who initiated biologic disease-modifying antirheumatic drugs (bDMARDs) after January 1, 2010 and had at least 365 days medical and pharmacy coverage before initiation. The primary outcome was a composite of myocardial infarction (MI), stroke, and fatal CVD assessed using a validated method. Subgroups analyses were done for RA patients experienced to other bDMARDs before initiation and by stratifying patients with respect to key CVD risk factors to identify both higher and lower CVD risk patients. We provided descriptive statistical for each exposure group. Incidence rates and 95% confidence intervals were calculated using Poisson regression. COX regression was used to generate unadjusted and adjusted hazard ratio.

**Results:** We identified 3 54 486 (Medicare 206,275+MarketScan 148,211) RA patients and 4 63 446 (Medicare 271,832+MarketScan 191,614) initiations of bDMARDs. After applying inclusion and exclusion criteria, the final cohort contained 88 463 (Medicare 46,648+MarketScan 41,815) RA patients and 1 17 493 (Medicare 61,715+MarketScan 55,778) episodes. The mean (SD) age was 64.7 (12.1) in Medicare and 52.2 (12.3) in MarketScan. The majority of patients were female (83.9% in Medicare and 80.5% in MarketScan), and 68.6% were non-Hispanic White in Medicare. TCZ users were similar to abatacept and rituximab users except that TCZ users were less likely to be naïve to bDMARDs. Compared to TNFi users, TCZ users were more likely to be white, with history of CVD (other than MI or stroke), heart failure, atrial fibrillation, hospitalisation and had more

physician visits in baseline. TCZ users were less likely to be diabetic, use methotrexate in the baseline, and to be naïve to bDMARDs. The crude incidence rate (IR) per 1000 patient-years for composite CVD among Medicare patients ranged from 13.3 (95% CI: 11.1 to 16.0) for etanercept to 19.4 (95% CI: 16.3 to 20.9) for rituximab users. The crude incidence rate for pooled TNFi users was 16.4 (15.2–17.7). Compared to TCZ, the adjusted hazard ratios were 1.03 (0.82–1.29) for abatacept, 1.25 (0.96–1.61) for rituximab, 1.13 (0.84–1.52) for etanercept, 1.33 (0.99–1.80) for adalimumab, and 1.57 (1.21–2.05) for infliximab (figure 1). There were no significant differences in CVD risk between tocilizumab and any other biologic using MarketScan data. Results were robust in numerous subgroup analyses.



Abstract OP0193 – Figure 1. Incidence rates and adjusted hazard ratios of CVD events in RA patients

**Conclusions:** Consistent with findings of a recently completed safety trial in RA, tocilizumab was associated with a comparable CVD risk compared to etanercept, as well as a number of other RA biologics, in two large data sources.

**Disclosure of Interest:** F. Xie: None declared, H. Yun Grant/research support from: BMS, E. Levitan Grant/research support from: Amgen, Consultant for: Amgen, Novartis, P. Muntner: None declared, J. Curtis Grant/research support from: AbbVie, Amgen, BMS, Corrona, Janssen, Lilly, Myriad, Pfizer, Roche/Genentech, UCB, Consultant for: AbbVie, Amgen, BMS, Corrona, Janssen, Lilly, Myriad, Pfizer, Roche/Genentech, UCB  
**DOI:** 10.1136/annrheumdis-2018-eular.5807

**OP0194 THE ASSOCIATION BETWEEN SERUM URIC ACID AND ARTERIAL STIFFNESS IN A LOW-RISK, LARGE POPULATION OF MIDDLE-AGED KOREAN**

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**Background:** Arterial stiffness occurs because of biologic ageing and arteriosclerosis, and is most commonly measured by pulse-wave velocity. Several studies have reported that high serum uric acid may contribute to the development of a number of metabolic and haemodynamic abnormalities, and multivariate analyses in epidemiologic studies have suggested that hyperuricemia is an independent risk factor for arterial stiffness in those with comorbidities such as diabetes, hypertension, and chronic kidney disease. However, there are few reports about the association between SUA and arterial stiffness in apparently healthy populations. **Objectives:** We aimed to investigate the association between serum uric acid (SUA) and arterial stiffness as evaluated by brachial ankle pulse wave velocity (baPWV) in a low-risk, large, middle-aged Korean population.

**Methods:** We conducted a cross-sectional study of 66,917 Koreans (38 170 men, 28 747 women) who received yearly screening with available PWV and SUA results. None of the participants had coronary heart disease, diabetes, or hypertension. SUA was divided into quintiles for assessment of its association with baPWV by multiple linear regression analysis.

**Results:** The average SUA level was 5.23±1.4 mg/dl, and SUA values were higher in men than in women (6.1±1.2 mg/dl vs 4.1±0.8 mg/dl). In multiple regression analysis, PWV was significantly higher in SUA quintiles 2–5 compared to the lowest group (reference) (coefficient=11.52, 18.19, 24.73, and 31.02 cm/s, respectively). In female subjects, the average difference (cm/s) of PWV between quintiles 2–5 and quintile 1 of SUA was 13.1, 22.9, 34.6, and 32.1, respectively.

Fully adjusted linear coefficient  $\beta$  (S.E.) was 6.62 (0.70) and 12.43 (1.33) in all participants and female subjects, respectively ( $p<0.001$ ). In contrast, there was a J-shaped association between PWV and SUA quintile among males. When modelled continuously, each 1 mg/dl higher SUA level was associated with 0.27 higher baPWV ( $p<0.001$ ) in the adjusted analysis.

**Conclusions:** These findings indicate that higher SUA levels could have an unfavourable impact on arterial stiffness as measured by baPWV in a low-risk, large, middle-aged Korean population.

**Disclosure of Interest:** None declared  
**DOI:** 10.1136/annrheumdis-2018-eular.1848

**OP0195 ROLE OF SEROPOSITIVITY ON MORTALITY IN RA AND THE IMPACT OF TREATMENT WITH DMARDS**

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**Background:** Previous studies showed that RF positivity (+) in RA was associated with increased overall mortality, and that cause-specific mortality rates differed by autoantibodies. Anti-citrullinated protein antibodies (ACPAs) have been associated with cardiovascular death, and RF with death due to neoplasm and respiratory disease.<sup>1</sup>

**Objectives:** To evaluate the association of serostatus (in particular, antibody [Ab] titres) with mortality and its modification by DMARDS.

**Methods:** Administrative claims data from Optum Clinformatics Data Mart and Humana databases (2006–2016) were used. Inclusion criteria: 2 diagnosis codes for RA plus 1 DMARD prescription; age  $\geq 18$  years (y);  $\geq 6$  months (M) baseline (BL); +/-3 M from index date. Index date was the first test date for ACPA or RF (main analysis) or the DMARD prescription date (DMARD effect on mortality analysis). Patients (pts) with ankylosing spondylitis, Crohn's disease, lupus, psoriatic arthritis or ulcerative colitis at/before index date were excluded. Based on BL Ab test, pts were categorised into Ab status of ACPA+/-, RF +/- and double +/-.

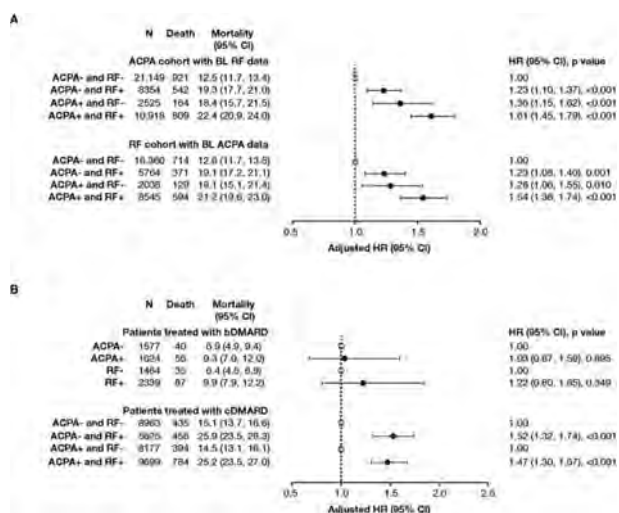
Ab +pts were then categorised into 2 groups based on Ab titres. DMARD-exposed pts were categorised into biologic (b)DMARD (use of any bDMARD) and conventional (c)DMARD (use of a cDMARD but never a bDMARD) cohorts. Crude mortality rates per 1000 pt-y, as well as adjusted analysis using traditional multivariate regression and disease risk score methods, were used. Covariates were age, sex, region, physician office visits in past 3 M, indicator variable for RA diagnosis before ACPA/RF testing, past hospitalisation, medication use (steroids, NSAIDs, salicylates), DMARD use and co-morbidities. **Results:** A total of 53 849 and 79 926 pts with RA had evaluable ACPA and RF status, respectively. The average (SD) age was 61.4 (15.2) and 61.8 (15.6) y in the ACPA and RF cohorts, respectively. For both ACPA and RF, mortality rates were significantly higher in Ab +vs Ab- pts, and were highest in pts with the highest Ab titres (table 1). The hazard ratios (HRs) for mortality were highest in pts with double positivity (figure 1A). HRs were higher in Ab +vs Ab- pts exposed to cDMARDs. There was no difference in mortality between Ab +vs Ab- pts in the bDMARD-exposed group (figure 1B).

Abstract OP0195 – Table 1 Crude mortality rates and HRs in patients categorised by serostatus

	Patients, n	Deaths, n	Pt-y	Crude mortality, incidence rate/1000 pt-y (95% CI)	Adjusted HR (95% CI)	P value
ACPA-	36 667	1798	1 26 451	14.2 (13.6–14.9)	1.00	
ACPA+	17 182	1276	57 719	22.1 (20.9–23.4)	1.48 (1.37–1.60)	<0.001
ACPA +Group	8321	606	29 518	20.5 (18.9–22.2)	1.38 (1.25–1.52)	<0.001
ACPA +Group 1*	8861	670	28 201	23.8 (22.0–25.6)	1.60 (1.45–1.76)	<0.001
RF-	46 376	2522	1 79 247	14.1 (13.5–14.6)	1.00	
RF+	33 550	2688	1 18 583	22.7 (21.8–23.5)	1.44 (1.36–1.53)	<0.001
RF +Group	16 758	1098	60 393	18.2 (17.1–19.3)	1.18 (1.09–1.27)	<0.001
RF +Group 1*	16 792	1590	58 190	27.3 (26.0–28.7)	1.79 (1.51–2.11)	<0.001

\*Based on antibody titre: Group 1=lower titre; Group 2=higher titre





**Abstract OP0195** – Figure 1 Mortality rates and HRs in patients categorised by (A) double ACPA and RF serostatus; (B) serostatus and DMARD exposure

**Conclusions:** Elevated ACPA and RF titres were independently associated with increased mortality among pts with RA. The associations between ACPA/RF and mortality persisted in those treated with cDMARDs but not with bDMARDs. Further studies are warranted to evaluate the effect of bDMARDs on mortality in seropositive pts.

#### REFERENCE:

[1] Ajejanova S, et al. *Ann Rheum Dis* 2016;75:1924–32.

**Disclosure of Interest:** E. Alemao Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Z. Guo Employee of: Bristol-Myers Squibb, M. Weinblatt Grant/research support from: Amgen, Bristol-Myers Squibb, Crescendo Bioscience, Sanofi, Consultant for: Amgen, Bristol-Myers Squibb, Crescendo Bioscience, AbbVie, Lilly, Pfizer, Roche, Merck, Samsung Novartis, N. Shadick Grant/research support from: BRASS registry, Amgen, Bristol-Myers Squibb, and Mallinckrodt, Consultant for: Bristol-Myers Squibb  
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OP0196

#### SAFETY AND EFFICACY OF IMMUNE CHECKPOINT INHIBITORS IN PATIENTS WITH CANCER AND PREEXISTING AUTOIMMUNE DISEASES: A NATIONWIDE MULTICENTER RETROSPECTIVE STUDY

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**Background:** Immune Checkpoint Inhibitors (ICI) have revolutionised the management of several cancers, enhancing the anti-tumoral immune response. However they are responsible for many Immune Related Adverse Effects (IRAE), and therefore most patients with Preexisting Autoimmune Diseases (PAD) have been excluded from clinical trials.

**Objectives:** The aim of this study was to evaluate the safety and efficacy of ICI in patients with PAD.

**Methods:** Three national expert networks, focusing respectively on skin cancers, thoracic cancers and inflammatory diseases participated in this study. All patients who received an ICI despite a PAD in clinical practice were included in this nationwide retrospective study.

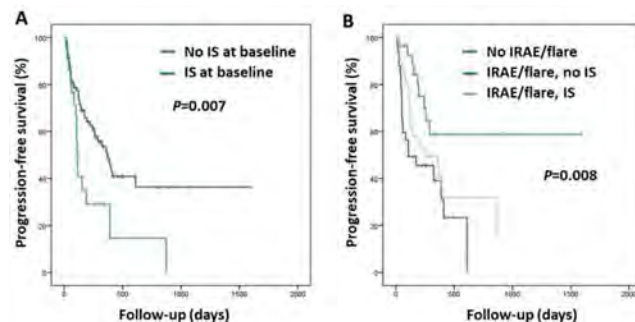
**Results:** 112 patients were included: 64 men (57.1%), median age 66.5. Most patients received an anti-PD1 or anti-PD-L1 drug (84.8%). Main cancer types were melanoma (n=66, 58.9%) and Non-Small Cell Lung Carcinoma (NSCLC) (n=40; 35.7%). Median follow-up was 8 months [0–52].

Most frequent PAD were psoriasis and psoriatic arthritis (27.6%), rheumatoid arthritis (17.8%), inflammatory bowel disease (12.5%), spondyloarthritis (4.5%), lupus (6.3%), polymyalgia rheumatica and/or giant-cell arteritis (6.3%). 24 patients (21.6%) were receiving an immunosuppressive therapy (IS) at ICI initiation

(including steroids in 15, sDMARD in 10 and rituximab in 1). 37 patients (33%) had an active disease.

PAD flares were frequent (n=47; 42%) and 30.4% of them were severe (grade CTCAE 3–4). 26 patients (56.5%) received an IS treatment for a flare (22 received steroids and 7 a DMARD). Other IRAEs not related to the PAD occurred in 43 patients (38.4%), 41.5% were severe. 23 patients (56.1%) required an IS (including a DMARD in 4). 36 patients (32.1%) discontinued ICI temporarily or definitively because of a flare or an IRAE. One patient died due to an IRAE.

Concerning the anti-tumoral response, the Overall Response Rate (ORR) was 48.3% for melanoma and 53.8% for NSCLC. The median Progression Free Survival (PFS) was 12.4 months for melanoma and 9.7 for NSCLC. Median overall survival (OS) was not reached in any group. PFS and OS were shorter in patients receiving an IS treatment at ICI initiation (p=0.007, figure 1A, and p=0.003, respectively). PFS and OS were longer in patients who experienced a PAD flare or other IRAE, but this gain was lost when an IS was used to treat the flare/IRAE (p=0.008, figure 1B, and p=0.01, respectively). Conversely, this gain was not impacted with ICI discontinuation.



**Conclusions:** PAD flares and other IRAEs are frequent during ICI therapy and may be severe. The OS, ORR and PFS seem high in patients with PAD. The occurrence of a flare/IRAE is associated to a better outcome, gain lost when IS are used, while ICI discontinuation has no impact on PFS. Further prospective studies are needed to confirm our findings.

**Disclosure of Interest:** None declared

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OP0197

#### RHEUMATIC AND MUSCULOSKELETAL ADVERSE EVENTS ASSOCIATED WITH IMMUNE CHECKPOINT INHIBITORS: DATA MINING OF THE US FOOD AND DRUG ADMINISTRATION ADVERSE EVENT REPORTING SYSTEM

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**Background:** Immune-modulating monoclonal antibodies directed against immune checkpoints (cytotoxic T lymphocyte-associated antigen 4 (CTLA-4), programmed cell death-1 receptor (PD-1) and its ligand PD-L1), have demonstrated tremendous promise in the treatment of diverse solid tumour types, including melanoma, non-small cell lung cancer, among others and have improved survival rates of these cancer patients. However, these advances have created a new set of challenges in identifying and managing toxicities.

**Objectives:** To identify emerging trends of rheumatic and musculoskeletal adverse events by immune checkpoint inhibitor (ICI) treatment in the US Food and Drug Administration (FDA) Adverse Events Reporting System (FAERS).

**Methods:** We used AERSMine, an open-access web based application to mine the FAERS database from the first quarter (Q1) of 2011 to the third quarter (Q3) of 2017, approximately 7.1 million patients. Measures of disproportionality were calculated using well-established pharmacovigilance metrics, Relative Risks (RR) and safety signals (information component, (IC)), in a subset of patients with a cancer diagnosis. Terminology used for categorization of adverse events was as included in the FAERS. Fisher's exact test was used to determine significant adverse event differences by ICI treatment and age.

**Results:** We identified 30 939 unique patients with cancer and reports of immune checkpoint inhibitor associated toxicities. More than half of these reports were in relation with anti PD-1 inhibitors. Statistically significant adverse events associated with ICI therapy identified as toxicity signals with different agents included: NIVOLUMAB: myositis (n=102; RR, 1.35; p<0.01; IC, 0.43), rheumatoid arthritis (n=67; RR, 1.52; IC, 0.61), psoriatic arthropathy (n=20; RR, 1.93, IC, 0.95),

musculoskeletal pain (n=76; RR, 1.37; IC, 0.45) and myasthenia gravis (n=66; RR, 1.42; IC, 0.50);<sup>2</sup> PEMBROLIZUMAB: arthralgia (n=151; RR, 1.43; IC, 0.52) and pain in an extremity (n=58; RR, 1.35; IC, 0.43);<sup>3</sup> DURVALUMAB: polymyositis (n=2; RR, 4.41; IC, 2.15), rhabdomyolysis (n=4; RR, 2.68; IC, 1.42), and autoimmune arthritis (n=2; RR, 8.83; IC, 3.14);<sup>4</sup> IPILIMUMAB: muscular weakness (n=157; RR, 1.70; IC, 0.76) and back pain (n=105; RR, 1.27; IC, 0.34). In general, rates of rheumatic and musculoskeletal adverse events were higher in men and in the elderly population (>65 years).

**Conclusions:** A wide spectrum of rheumatic and musculoskeletal toxicity signals were detected with ICI's. Clinicians need to be vigilant about these rare but debilitating complications. Future studies to explore mechanisms and optimal management strategies of these toxicities are warranted.

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[1] Sarangdhar M, Tabar S, Schmidt C, et al. Data mining differential clinical outcomes associated with drug regimens using adverse event reporting data. *Nat Biotechnol* 2016;34:697–700.

**Disclosure of Interest:** None declared

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THURSDAY, 14 JUNE 2018

## Can we halt progression of structural damage in axial SpA?

### OP0198 COMBINED EFFECTS OF TUMOUR NECROSIS FACTOR INHIBITORS AND NSAIDS ON RADIOGRAPHIC PROGRESSION IN ANKYLOSING SPONDYLITIS

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**Background:** The potential of TNFi or NSAIDs to reduce radiographic progression in AS is uncertain and causal effects of both exposures on radiographic progression have not been convincingly demonstrated. In addition, no study has evaluated whether effects are comparable among different NSAIDs in this setting.

**Objectives:** The objective of this study was to explore causal effects of NSAIDs and TNFi on radiographic progression in Ankylosing Spondylitis (AS) and to compare effects of celecoxib to other NSAIDs.

**Methods:** We included all patients meeting the modified New York criteria in a prospective cohort with at least 4 years of clinical and radiographic follow up. Clinical and medication data were collected every 6 months and radiographs were performed at baseline and every 2 years. We used longitudinal targeted maximum likelihood estimation to estimate the causal effect of TNFi and NSAIDs (using the NSAID index) on radiographic progression as measured by the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) at 2 and 4 years, accounting for time-varying covariates. We controlled for sex, race/ethnicity, education, symptom duration, enrollment year, number of years on TNFi, symptom duration at time of TNFi start, baseline mSASSS, ASDAS-CRP, current smoking, and missed visit status.

Abstract OP0198 – Table 1

	TNF use	No TNF use	Mean Difference	P-value
Comparing TNF use vs no TNF use, given no NSAID (=0) at time t:				
mSASSS @ 2 years	13.94	14.92	-0.98 (-2.77, 0.81)	0.28
mSASSS @ 4 years	16.12	15.62	0.50 (-0.63, 1.64)	0.38
Comparing TNF use vs no TNF use, given low NSAID (>0 and <50) at time t:				
mSASSS @ 2 years	15.43	15.49	-0.06 (-1.63, 1.51)	0.94
mSASSS @ 4 years	15.52	16.76	-1.24 (-1.80, -0.68)	<0.001
Comparing TNF use vs no TNF use, given high NSAID (>=50) at time t:				
mSASSS @ 2 years	14.79	15.13	-0.34 (-1.46, 0.78)	0.56
mSASSS @ 4 years	14.17	17.47	-3.31 (-4.02, -2.59)	<0.001
Comparing TNF use vs no TNF use, NSAID=celecoxib at time t:				
mSASSS @ 2 years	11.63	15.62	-3.98 (-4.51, -3.45)	<0.001
mSASSS @ 4 years	14.37	19.06	-4.69 (-5.08, -4.30)	<0.001

**Results:** Of the 519 patients, 75% were male with a baseline mean (SD) age and symptom duration of 41.4 (13.2) and 16.8 (12.5) years respectively. The baseline mean (SD) mSASSS was 14.2 (19.6). At baseline, NSAIDs were used in 66% of

patients, of which ½ used an index <50 and ½ an index ≥50). TNFi were used in 46% of patients at baseline. In the setting of TNFi use, the addition of NSAID therapy was associated with less radiographic progression in a dose-related manner at 4 years. When NSAID specific effects were examined, celecoxib in combination with TNFi use was associated with the greatest reduction in radiographic progression and this was significant at both 2 and 4 years (table 1).

**Conclusions:** Dose related use of NSAIDs together with TNFi in AS patients has a synergistic effect in slowing radiographic progression with the greatest effect in those using both high-dose NSAIDs and TNFi. Celecoxib appears to confer the greatest benefit in decreasing progression with effect at both 2 and 4 years.

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### OP0199 SUSTAINED REMISSION OF INFLAMMATION IS ASSOCIATED WITH REDUCED STRUCTURAL DAMAGE ON SACROILIAC JOINT MAGNETIC RESONANCE IMAGING IN PATIENTS WITH EARLY AXIAL SPONDYLOARTHRITIS: EVIDENCE TO SUPPORT THE CONCEPT OF TREAT-TO-TARGET

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**Background:** Treat-to-target is acceptable in RA; however, it is unknown whether it will reduce/prevent disability, impairment of mobility, and structural damage in early axial spondyloarthritis (axSpA) without radiographic sacroiliitis.

**Objectives:** To evaluate the impact of sustained clinical remission on MRI structural parameters. We hypothesised that patients with sustained inactive disease according to the ankylosing spondylitis disease activity score (ASDAS <1.3) are more likely to achieve reduction in erosion (structural damage) and increase in backfill (a reparative process) on MRI of the SI joints (SIJ).

**Methods:** EMBARK (NCT01258738) and DESIR (NCT01648907) enrolled patients with early axSpA. EMBARK included 12 weeks of double-blind placebo-control, then open-label etanercept for 92 weeks. Patients in the DESIR observational cohort had no history of biologics and received no biologics for 2 years. T1 weighted MRI images of SIJ at baseline and 104 weeks were combined and anonymized; readers were unaware of film chronology and original patient cohort. Three experienced readers evaluated MRI images using the SpondyloArthritis Research Consortium of Canada SIJ Structural Score. Lesion change was considered present if ≥2 of 3 readers measured change in same direction. ASDAS endpoints were assessed sequentially: sustained (≥2 visits 6 months apart) inactive disease (ASDAS <1.3) or moderate disease activity (≥1.3 to <2.1); or no sustained response (≥2.1). Net proportions of patients with decrease in erosion and increase in backfill were determined, unadjusted and adjusted for covariates that may affect development of lesions on MRI.

**Results:** From EMBARK and DESIR, 161 and 76 patients, respectively, were included. For patients in EMBARK with sustained ASDAS <1.3, a greater percentage had decrease in erosion (34/104, 32.7%) than increase (5/104, 4.8%); p<0.0001; without sustained response, 5/24 (20.8%) had decrease in erosion and 1/24 (4.2%) had increase. This trend was also present in DESIR. Patients with sustained ASDAS <1.3 in EMBARK: 22.1% had increase in backfill, 0% had decrease; p<0.0001; in DESIR, 21.7% had increase, 0% had decrease; p<0.05. For those without sustained response, difference between increase and decrease was smaller. Net percent of patients (adjusted) with sustained ASDAS <1.3 and erosion decrease: 22.6% and 9.3% for EMBARK and DESIR, respectively; without sustained response: 13.3% and -10.1%. Net percent of patients with sustained ASDAS <1.3 and backfill increase: 19.6% and 25.7% for EMBARK and DESIR, respectively; without sustained response: 8.7% and 6.0%.

**Conclusions:** These data demonstrate a link between sustained ASDAS inactive disease and MRI structural endpoints. Clinical relevance of change in MRI SIJ erosion and backfill and their relationship to ankylosis development requires study.

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Pfizer, Roche, UCB, Lilly, M. de Hooge Employee of: Selfemployed without other personnel (registered company under the Belgium law) MdH Research. Additional Affiliation: Ghent University, Ghent, Belgium., R. Lambert Consultant for: AbbVie, Bioclinica, Janssen, Parexel, UCB, R. Landewé Grant/research support from: Abbott, Amgen, Centocor, Novartis, Pfizer, Roche, Schering-Plough, UCB, Consultant for: AbbVie, Ablynx, Amgen, Astra-Zeneca, Bristol Myers Squibb, Celgene, Janssen, Galapagos, GlaxoSmithKline, Novartis, Novo-Nordisk, Merck, Pfizer, Roche, Schering-Plough, TiGenix, UCB, Employee of: Director of Rheumatology Consultancy BV, which is a registered company under Dutch law, Speakers bureau: Abbott/AbbVie, Amgen, Bristol Myers Squibb, Janssen, Merck, Pfizer, Roche, Schering-Plough, UCB, A. Molto Grant/research support from: Pfizer, Consultant for: Merck,UCB, D. van der Heijde Consultant for: AbbVie, Amgen, Astellas, AstraZeneca, BMS, Boehringer Ingelheim, Celgene, Daiichi, Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, UCB, Employee of: Director of Imaging Rheumatology bv., J. Bukowski Shareholder of: Pfizer, Employee of: Pfizer, H. Jones Shareholder of: Pfizer, Employee of: Pfizer, I. Logeart Shareholder of: Pfizer, Employee of: Pfizer, L. Marshall Shareholder of: Pfizer, Employee of: Pfizer, R. Pedersen Shareholder of: Pfizer, Employee of: Pfizer, A. Szumski Employee of: InVentiv Health, B. Vlahos Shareholder of: Pfizer, Employee of: Pfizer, M. Dougados Grant/research support from: Pfizer, AbbVie, UCB, Merck, Lilly, Consultant for: Pfizer, AbbVie, UCB, Merck, Lilly  
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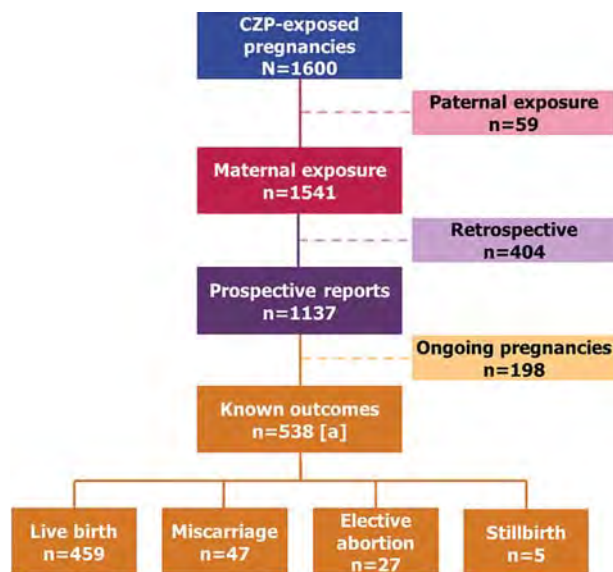
## Reproductive issues in rheumatology

OP0200

### CHARACTERISTICS AND OUTCOMES OF PROSPECTIVELY REPORTED PREGNANCIES EXPOSED TO CERTOLIZUMAB PEGOL FROM A SAFETY DATABASE

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**Background:** Anti-tumour necrosis factor medications (anti-TNFs) are effective in controlling chronic inflammatory diseases, but information about their use and safety in pregnancy is limited. Consequently, anti-TNFs are often discontinued early in gestation. Certolizumab pegol (CZP), an Fc-free, PEGylated anti-TNF approved for treatment of rheumatic diseases and/or Crohn's disease, has no active placental transfer.



Abstract OP0200 – Figure 1 Overview of pregnancy reports

**Objectives:** This project provides information on pregnancy outcomes in women receiving CZP, especially those with early pregnancy exposure.

**Methods:** Prospective and retrospective data on maternal CZP exposure, including timing and duration, outcomes, comorbidities, and major malformations were extracted from the UCB Pharma safety database through 6 March 2017. This analysis was limited to prospective reports to avoid bias associated with retrospective submissions. Numbers of live births, miscarriages, elective abortions, stillbirths, and major congenital malformations were ascertained.

**Results:** From a total of 1541 maternal CZP-exposed pregnancies, 1137 were reported prospectively, of which 528 pregnancies (including 10 twin pregnancies) had 538 known outcomes: 459 live births (85%), 47 miscarriages (9%), 27 elective abortions (5%), and 5 stillbirths (1%) (figure 1). Of the 459 live births, 8 (2%) cases of major congenital malformations were reported (vesicoureteral reflux, club foot, congenital heart disease, cerebral ventricle dilatation, polydactyly, anal fistula, accessory auricle, and hydronephrosis). Of the 528 prospective pregnancies with known outcomes, 436 (83%) were exposed during the 1st trimester, when most organogenesis occurs; 201 pregnancies were exposed during the entire pregnancy.

**Conclusions:** This analysis represents the largest published cohort of pregnant women exposed to an anti-TNF for management of chronic inflammatory diseases. Analysis of pregnancy outcomes does not indicate a malformative effect of CZP compared to the EU general population (2%–3%), nor an increased risk of foetal death. These data are reassuring for women of childbearing age considering treatment with CZP; however, the ongoing collection of post-marketing surveillance data, including the ongoing MotherToBaby study from the Organisation of Teratology Information Specialists, will provide further important information.

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## Do we still need biopsies to diagnose Sjögren's and autoimmune myositis?

OP0201

### CLINICAL OUTCOMES AND RESPONSE TO ANTI-THROMBOTIC TREATMENT AMONG PATIENTS WITH CONCOMITANT LUPUS NEPHRITIS AND THROMBOTIC MICROANGIOPATHY: A MULTICENTER COHORT STUDY

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**Background:** In addition to glomerular lesions, renal vascular involvement is an important prognostic marker of lupus nephritis (LN). Among patients with various vascular changes, individuals with thrombotic microangiopathy (TMA) present with severe clinical manifestations and have a high mortality.

**Objectives:** We sought to assess renal outcomes and response to anti-thrombotic treatments in addition to conventional immunosuppression in patients with biopsy proven LN and TMA.

**Methods:** Clinical and renal histopathological data for 97 patients with biopsy-proven LN and TMA were retrospectively analysed. Antibody profiles, induction and maintenance therapies for LN, and anti-thrombotic treatments were collected. TMA lesions were classified into acute and chronic (table 1). A complete renal response (CR) was defined as proteinuria <0.5 g/24 hour and normal or near-



normal (within 10% of normal GFR if previously abnormal) GFR. Partial Response (PR) was defined as a  $\geq 50\%$  reduction in proteinuria to subnephrotic levels and normal or near-normal GFR. Renal outcomes were assessed at one year post biopsy. **Results:** The mean age of the patients was  $38.9 \pm 15.2$  years (range, 13–69 years). The study included 85 females (87.6%) and 12 males (12.4%). The clinical presentations were nephrotic syndrome, nephritic syndrome, and asymptomatic urinary abnormalities in 38 (39.2%), 20 (20.6%), 39 (40.2%) patients, respectively. Nine patients were classified Class III (9.3%, including 2 as Class III +V), 82 as Class IV (84.5%, 10 as Class IV-segmental (IV-S) (10.3%) and 72 as Class IV-global (IV-G) (74.2%), including 4 as Class IV-G+V and 6 as Class V (6.2%). Forty-two (43%) patients presented with acute and 55 (57%) with features of chronic TMA. All patients had received treatment with standard immunosuppressants (55% mycophenolate, 39% cyclophosphamide, 6% other regimen) and steroids.

Abstract OP0201 – Table 1

Acute TMA features	Chronic TMA features
• Endothelial swelling with partial or complete occlusion of lumina;	• Capillary wall thickening with double contours;
• Microthrombi, focal or global;	• Organizing capillary thrombi;
fragmented RBC on glomerular subendothelial space and/or mesangial areas;	• Glomerular ischemic collapse with afferent arteriolar occlusion;
• Mesangiolysis, focal, segmental/global;	• Segmental/global glomerulosclerosis
• Glomerular congestion with efferent arteriolar occlusion	

At 12 months, CR was observed in 37 patients (38.1%), PR in 22 (22.6%) and no response in 38 (39.1%). Sixty-one patients (62.9%) were antiphospholipid positive (aPL) and 37 (38.1%) received anticoagulation with vitamin-K antagonist (VKA) and/or heparins. Presence of aPLs (OR, 2.4; 95% confidence interval-CI, 1.2–7.3;  $p=0.03$ ), anti-DNA positivity (OR, 12.8; 95% CI: 3.0 to 71.3;  $p=0.002$ ), and chronic features of TMA (OR, 3.0; 95% CI: 1.2 to 17.5;  $p=0.04$ ) were all found to be associated with no response. When limiting the analysis to aPL positive patients, after adjusting for type of immunosuppressant therapy and LN class on biopsy, variables that were significantly associated with CR +PR were features of acute TMA rather than chronic (OR, 8.62; 95% CI: 1.4 to 97.1;  $p=0.03$ ) and the use of VKA/heparins (OR, 2.1; 95% CI, 1.02–16.2;  $p=0.046$ )

**Conclusions:** In patients with concomitant LN and TMA, the presence of aPL and chronic features of TMA were associated with poorer renal outcomes. In patients with aPL, the use of anticoagulation appeared protective and warrants further investigation as a therapeutic tool, especially in the setting of acute TMA.

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#### OP0202 GENE EXPRESSION PROFILES IN PRIMARY SJÖGREN'S SYNDROME WITH AND WITHOUT SYSTEMIC MANIFESTATIONS

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**Background:** Different phenotypes characterise the clinical spectrum of primary Sjögren's syndrome (SjS). Patients with a clinical expression limited to glandular features (GFs) are classically distinguished from patients with extra-glandular manifestations (EGMs). The former patients often complain higher level of fatigue and widespread pain (WP). (Segal et al. 2013) This suggests that gene expression pattern may be different in the two subgroups.

**Objectives:** To investigate the differences of gene expression in SjS patients with GFs and in those with EGMs.

**Methods:** Nineteen patients with SjS were selected for the study. Gene expression in peripheral blood mononuclear cells (PBMCs) was analysed in 4 patients with EGMs and 4 patients with GFs alone using Clariom D human Affymetrix gene chip (Affymetrix, Santa Clara, CA, USA), and compared to that found in healthy controls. Differences in gene expression were evaluated by analysis of variance (ANOVA) and Step-Up FDR-controlling procedure, being FDR corrected  $p$  value  $\leq 0.01$  and fold change  $> 2$  considered as statistically significant.

Validation of the gene overexpression was performed by quantitative Real Time (qRT)-PCR in PBMCs from all the selected SjS patients, using the  $\Delta\Delta Ct$  method for comparing relative fold expression differences.

**Results:** All the enrolled SjS patients (18 females and 1 male) had a positive lip biopsy, while anti-SSA/Ro antibodies were detected in 10/11 and 6/8 of the patients with EGMs and with GFs alone, respectively. ESSDAI value ranged from 7 to 55 in patients with EGMs (median 17), and from 0 to 2 in patients with GFs alone (median 1).

In both types of patients, the functional analysis of the two transcriptomes showed a large number ( $> 1000$ ) of modulated genes that are involved in the well-known pathological processes of SjS, i.e., apoptosis, inflammatory response, immune response, type I and type II interferons, and Toll-like receptors signalling.

Genes modulated only in patient with EGMs showed a significant enrichment of the biological processes associated with immune response (79% of all enriched processes) and, namely, of the molecular pathways related to B cell activation. The analysis of the transcripts expressed only in patients with GFs alone showed instead a preponderant enrichment in different metabolic processes (43%) and in processes associated with the central perception of the stimuli. Indeed, genes involved in sensory perception and in nociceptive signals (i.e., ANPEP, TNFRF1, P2RY1, IFNG) were modulated exclusively in patients with GFs alone. The significant differential expression of selected genes in the two SjS subgroups was confirmed by the qRT-PCR analysis.

**Conclusions:** These data indicate that in SjS patients with GFs alone a dysregulation of pain pathways (namely beta-adrenergic receptor and Notch signalling) may play a role in the development of WP that is common in this subset of patients. The biological mechanisms triggering the activation of these genes remain to be completely clarified.

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## How monogenetic autoinflammatory diseases help to understand and treat rheumatic diseases

OP0203

### SAFETY AND EFFICACY OF INTRAVENOUS ADMINISTRATION OF BONE-MARROW DERIVED MESENCHYMAL STROMAL CELLS IN THERAPY REFRACTORY JUVENILE IDIOPATHIC ARTHRITIS PATIENTS, A PHASE IB/IIA PILOT-STUDY

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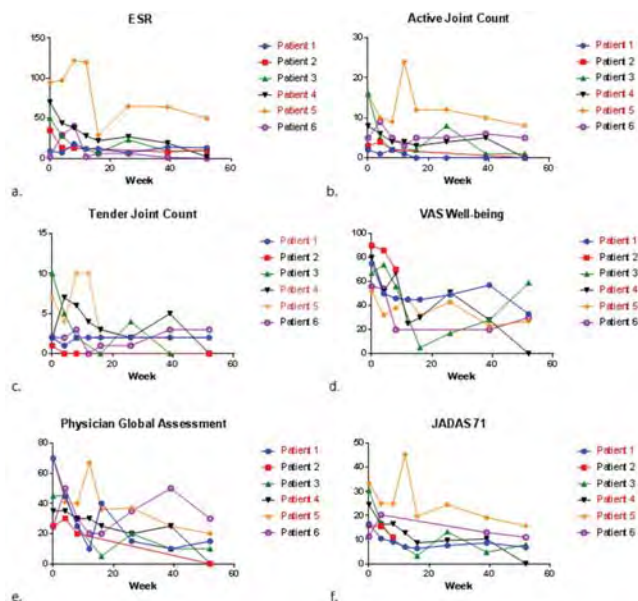
**Objectives:** To compare the total number of adverse events (AE's) before and after mesenchymal stromal cell (MSC) infusion in refractory JIA and to evaluate its effectiveness.

**Methods:** Single-centre Phase Ib/IIa, open label intervention study in JIA patients previously failing all biologicals registered for their diagnosis. Six patients will receive 2 million/kg intravenous infusions of allogeneic bone-marrow derived MSC. In case of ACR-Ped30-response but subsequent loss of response one and maximal two repeated infusions are allowed.

**Results:** Six JIA patients with 9.2 years median disease duration, still active arthritis and damage were included. All had failed methotrexate, corticosteroids and median 5 different biologicals. MSC were administered twice in 3 patients. No acute infusion reactions were observed and a lower post-treatment incidence in AE's was found. The one sJIA patient had again an evolving macrophage activation syndrome, 9 weeks after tocilizumab discontinuation and 7 weeks post- MSC infusion.

Eight weeks after one MSC infusion, 4 patients showed less active joints, 5 patients improved in many clinical parameters and inflammatory parameters decreased in 3/4. After 1 year, we found significantly lower active joint counts,

improved well-being scores, normalised median ESR- and CRP-levels. Inactive disease was reached by 3 patients at 1 year.



**Conclusions:** MSC infusions in refractory JIA patients are safe, although in sJIA stopping the 'failing' biologic treatment carries a risk of a MAS flare since the drug might still suppress the systemic features. Furthermore, intravenous administration of MSC might be efficacious even in multiple biological-failing JIA patients with damage.

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## Joint EULAR – EFIS session: I've got a B in my bonnet

OP0204

### DOMINANT B CELL RECEPTOR CLONES IN PERIPHERAL BLOOD PREDICT ONSET OF ARTHRITIS IN INDIVIDUALS AT RISK FOR RHEUMATOID ARTHRITIS – A VALIDATION COHORT

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**Background:** A phase characterised by the presence of specific autoantibodies and arthralgia's in the absence of clinically evident synovial inflammation often precedes the onset of rheumatoid arthritis (RA). However, only a subset of these *RA-risk* individuals will develop active disease in the short term<sup>1</sup>. Recent findings show that dominant B-cell receptor (BCR) clones in peripheral blood can accurately predict imminent onset of arthritis in these *RA-risk* individuals.<sup>2</sup>

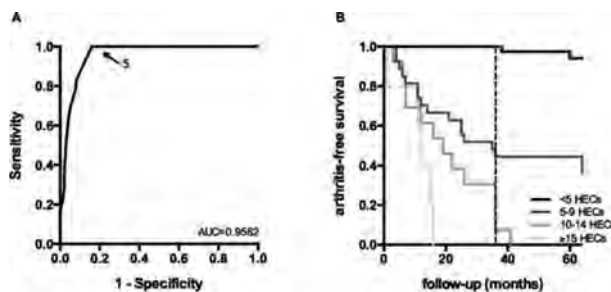
**Objectives:** To validate the predictive role of BCR clones in peripheral blood in *RA-risk* individuals in a larger cohort.

**Methods:** The BCR repertoire in peripheral blood was analysed using next-generation BCR sequencing in a prospective cohort study of 129 *RA-risk* individuals from Reade. Like earlier, BCR clones expanded beyond 0.5% of the total repertoire were labelled highly expanded clones (HECs), shortly referred to as dominant BCR clones, and individuals were labelled BCR-positive if peripheral blood at study baseline showed  $\geq 5$  dominant BCR clones.

**Results:** We observed that the number of dominant BCR clones was increased in *RA-risk* individuals who developed arthritis within 3 years, compared to *RA-risk* individuals who did not  $10.6 \pm 5.3$  vs  $2.2 \pm 2.8$  (mean  $\pm$ SD;  $p < 0.0001$ ). When creating a ROC curve we could replicate that the most optimal cut-off for this test is at  $\geq 5$  dominant BCR clones in the peripheral blood (figure 1A), dividing the cohort

in 45 BCR-positive individuals and 84 BCR-negative individuals. None of the BCR-clone negative individuals developed arthritis within 36 months. Within the total follow-up of 104 months only 8% of the BCR-clone negative individuals developed arthritis compared to 76% of the BCR-clone positive individuals, resulting in a relative risk of 9.1 (95% CI: 4.4 to 18.8,  $p < 0.0001$ ).

To test whether a higher number of dominant BCR clones correlates with higher risk of arthritis BCR-clone positive individuals were subdivided into three groups: 5–9 HECs ( $n=27$ ), 10–14 HECs ( $n=13$ ) and  $\geq 15$  HECs ( $n=5$ ). The Kaplan-Meier curve for all groups is shown in figure 1B (logrank test between BCR-clone negative group and positive subgroups:  $p < 0.0001$ ). Having 10 or more HECs corresponded with a positive predictive value of 83% and a negative predictive value of 87% within 3 years. The BCR clonality test clearly added to existing indices of RA risk in *RA-risk* individuals (data not shown).



**Abstract OP0204** – Figure 1 Predictive value of dominant BCR clones (A) receiver operating characteristic (ROC) curves for the number of dominant clones, in at-risk individuals (dotted line at 36 months)

**Conclusions:** In this external validation cohort we could replicate the fact that dominant BCR clones in peripheral blood predict imminent onset of clinical symptoms of RA in seropositive arthralgia patients with high accuracy. Furthermore, a highly significant association correlating a higher number of dominant BCR clones with higher risk was shown. We hope these results will support evaluation of early interventions that prevent onset of arthritis.

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**Acknowledgements:** Intellectual property PCT/EP2017/067047. N. de Vries, PP Tak, ME Doorenspleet, PL Klarenbeek. 'METHOD FOR DETERMINING THE RISK OF DEVELOPING ARTHRITIS'.

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OP0205

### APRIL INDUCES A NOVEL SUBSET OF IGA-REGULATORY B CELLS THAT SUPPRESS INFLAMMATION THROUGH THE EXPRESSION OF IL-10 AND PD-L1

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**Background:** Regulatory B cells (Bregs) are immunosuppressive cells that modulate immune responses through multiple mechanisms, such as the production of IL-10 and the skewing of T cell differentiation in favour of a regulatory phenotype. However, the signals required for the differentiation and activation of these cells remain still poorly understood. We have already shown that overexpression of the TNF family member A Proliferation-Inducing Ligand (APRIL) reduces the incidence and severity of collagen-induced arthritis (CIA) in mice.

**Objectives:** As we have also found that APRIL promoted IL-10 production and regulatory functions in human B cells, we hypothesised that APRIL, but not BAFF, may be involved in the induction and/or activation of IL-10 producing Bregs that suppress inflammatory responses *in vitro* and *in vivo*.

**Methods:** Peripheral blood-derived naïve B cells were cultured in the presence of IL-21 +TGF- $\beta$ , IL-21 +APRIL or IL-21 +BAFF to induce class switch recombination to IgA. Regulatory B cell functions and phenotypes were assessed on the class switched IgA B cells.

**Results:** We describe that APRIL promotes the differentiation of naïve human B cells to IL-10-producing IgA<sup>+</sup> B cells. These APRIL-induced IgA<sup>+</sup> B cells display a regulatory B cell phenotype and inhibit T cell and macrophage responses *in vitro* through expression of IL-10 and PD-L1. Moreover, APRIL-induced IL-10 producing regulatory B cells suppress inflammation *in vivo* in experimental autoimmune encephalitis (EAE) and contact hypersensitivity (CHS) models. Finally, we showed a strong correlation between APRIL and IL-10 in the inflamed synovial tissue of inflammatory arthritis patients.

**Conclusions:** We identified a novel subset of regulatory B cells within the IgA switched B cell population that suppresses inflammation *in vitro* and *in vivo*, which indicate the potential relevance of this subset of B cells for immune homeostasis and immunopathology.

**Disclosure of Interest:** C. Fehres: None declared, N. van Uden: None declared, N. Yeremenko: None declared, L. Fernandez: None declared, G. Franco Salinas: None declared, L. van Duivenvoorde: None declared, B. Huard: None declared, J. Morel: None declared, H. Spits Shareholder of: AIMM Therapeutics., M. Hahne: None declared, D. Baeten: None declared

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THURSDAY, 14 JUNE 2018

## Sustainable healthcare in rheumatology and the role of health professionals

### OP0206-HPR OUTPATIENT FOLLOW UP ON DEMAND FOR PATIENTS WITH RHEUMATOID ARTHRITIS – A TWO-YEAR RANDOMISED CONTROLLED TRIAL

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**Background:** Medical treatment and care are often life-long in patients with rheumatoid arthritis (RA). During periods of stable illness, patients typically attend routine visits every 3–8 months at the rheumatology outpatient clinic. The arthritis may flare up between scheduled medical visits, but it may be difficult to get acute appointments with the rheumatologist. Scheduled routine visits may be in a stable and 'good' period without any symptoms and with no need for control and adjustment of treatment and care. Consequently, there is a demand for developing outpatient control procedures that cater to the needs of the individual patient and which support the patient's experience of active participation in the control and treatment of their own disease.

**Objectives:** To compare a new outpatient system based on patient self-controlled outpatient follow up (Open Outpatient Clinic System (OOCs)) with traditional scheduled routine visits at a rheumatology outpatient clinic.

**Methods:** A two-year RCT with RA patients aged 18 to 80 years with a disease duration of at least one year. Patients were recruited consecutively from the rheumatology outpatient clinic of a major university hospital in the Copenhagen area of (Denmark from Feb 2015 to Jan 2017) Patients were randomised electronically and stratified regarding bio-medicine. Joints were examined by a blinded rheumatologist. Patients in the intervention group received information about the disease, symptoms, treatment and use of the OOCs. Appointments for the control group were scheduled according to routine procedures. Outcome measures were collected at baseline, year 1 and year 2. Clinical parameters: Disease Activity Score 28 (DAS28), CRP, Visual Analogue Scale (VAS) pain and fatigue, number of tender and swollen joints (28 joints), X-ray of hands and feet. Psychological parameters: VAS patient satisfaction, VAS patient trust, VAS patient involvement and quality of life (EQ-5D).

**Results:** 289 patients were included, 253 completed the 1 st year, 158 the 2nd year. The OOCs at year one and two was comparable to traditional scheduled routine procedures regarding clinical and psychological outcome measures. No radiological progression was detected. Patients in the intervention group made more phone calls to the clinic (244 versus 55) and had fewer visits compared to the control group (424 versus 513). Main results are shown in the table 1.

Abstract OP0206HPR – Table 1. Preliminary results Jan 2018

RA patients Diagnosis codes:M059, M060, M069	Baseline OOCs	Baseline ctrl	1 year OOCs	1 year ctrl	2 years OOCs	2 years ctrl
Number of patients	144	145	125	128	75	83
Age (median)	62	64	-	-	-	-
Female, percent of patients	77	75	-	-	-	-
Male, percent of patients	23	25	-	-	-	-
Total number of visits, telephone visits excluded	-	-	424	513	211	354
Total visits per patient, telephone visits excluded (median)	-	-	3	4	2	4
Total number of telephone visits	-	-	244	55	72	13
Telephone visits per patient (median)	-	-	1	0	0	0
DAS28crp (median)	2.7	2.8	2.3	2.4	2.2	2.1
VAS patient satisfaction, 0 worst, 100 best (median)	96	95	94	93	93	93
VAS patient trust, 0 worst, 100 best (median)	97	96	94	95	94	97
VAS pt involvement, 0 worst, 100 best (median)	96	94	93	93	93	95

**Conclusions:** The OOCs met RA patient preferences for RA appointments and was comparable with traditional scheduled routine procedures regarding clinical and psychological outcomes after one year. Thus, the OOCs could provide a basis for a future organisation of outpatient care for patients with RA.

**Disclosure of Interest:** None declared

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THURSDAY, 14 JUNE 2018

## SSc: From registries to trials – do we have sufficient data and the appropriate design?

### OP0207 THE OUTCOMES OF LIMITED CUTANEOUS SYSTEMIC SCLEROSIS PATIENTS: A EUSTAR DATABASE STUDY

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**Background:** Several studies have consistently showed that the extent of skin involvement has a major impact on disease prognosis in the diffuse cutaneous subtype of systemic sclerosis. The large majority of the ongoing clinical trials aim at identifying efficient drug in this subset. By contrast, little is known about the limited cutaneous subset (LcSSc) and the translation of the data coming from DcSSc to LcSSc is uncertain.

**Objectives:** Therefore, our aim was to investigate skin and lung involvement trajectories of LcSSc patients using the large EUSTAR registry.

**Methods:** We analysed the longitudinal data extracted from the EUSTAR cohort collected before February 2017. Worsening of skin fibrosis was defined by an increase in modified Rodnan skin score (mRSS) >3.5 points from baseline to 2nd visit. Interstitial lung disease (ILD) was defined by any fibrosis on imaging (X-ray/computed tomography). Worsening of ILD was defined by a decrease of



FVC >10% from baseline to 2nd visit. For predicting models, predictors with  $p < 0.02$  in the univariate analysis were included in the logistic regression analysis.

**Results:** 8013 LcSSc were included with a mean follow-up of about  $3.3 \pm 3.7$  years. At baseline, mean  $\pm$ SD mRSS was  $6 \pm 5$  and ILD was present in 28.4% of all patients.

Worsening of skin fibrosis was observed in 6.4% (19/298), 7.8% (97/1248) and 9.8% (289/2957) of LcSSc patients at 6, 12 and 24 months follow-up respectively. In multivariate analysis, variables predicting skin fibrosis progression were elevated European Scleroderma Study Group activity index (ESeSG-AI) (OR [95 IC]: 1.22 [1.05–1.4],  $p = 0.007$ ) for 12 months progression and ESeSG-AI (1.24 [1.13–1.38],  $p < 0.001$ ) and mRSS (0.95 [0.93–0.98],  $p = 0.001$ ) for 24 months progression.

Worsening of ILD was observed in 11.7% (23/196) and 19.9% (65/326) of LcSSc patients with ILD at baseline, at 12 and 24 months follow-up respectively. In multivariate analysis, variables predicting ILD progression at 24 months were ESeSG-AI >3 (OR [95 IC]: 3.8 [1.51–9.56],  $p = 0.005$ ), FVC (1.03 [1.01–1.04],  $p < 0.001$ ) and LVEF (0.91 [0.85–0.97],  $p = 0.005$ ).

**Conclusions:** It appears that only few LcSSc patients progress for skin fibrosis; this limits the use of mRSS in this subset and the potential of anti-fibrotic drugs of skin disease. However, a substantial rate of ILD progression was identified as well as relevant predictors. These results support the inclusion of LcSSc patients in SSc-ILD trials evaluating anti-fibrotic drugs. Our predictive models will be helpful to define enriched population in future clinical trials.

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OP0208

#### A PROOF-OF-CONCEPT DOUBLE-BLIND RANDOMISED PLACEBO-CONTROLLED TRIAL OF PROBIOTICS IN SYSTEMIC SCLEROSIS ASSOCIATED GASTROINTESTINAL DISEASE

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**Background:** Hypothesis: Gastrointestinal (GI) microbiota is a co-founding factor contributing to systemic sclerosis (SSc) and GI manifestations. Probiotics reduced GI symptoms by modulating microbiome composition in an open-label study.<sup>1</sup>

**Objectives:** To determine whether probiotics result in reduction of GI symptoms in SSc patients, assessed using the UCLA Gastrointestinal Tract questionnaire (GIT 2.0).

**Methods:** In this double-blind placebo-controlled trial, 40 subjects with SSc (total GIT0.1) were randomised to receive 60 days of probiotics (900 billion units/day, composite of lactobacilli, bifidobacteria and streptococcus) or placebo, followed by 60 days of probiotics in both groups. Subjects on probiotics or antibiotics 30 days prior were excluded. Enrolled subjects were required to have stable doses of prednisolone, immunosuppression and GI medications 30 days prior and during the trial. Between group differences in total GIT change was assessed after 60 days (primary endpoint) and 120 days (secondary endpoint). Stool microbiome composition was analysed using 16S next generation sequencing. We performed principle coordinate analysis, alpha diversity and taxonomic level analyses. Two-sample t-tests were used to evaluate between-group differences, reported as mean  $\pm$ SD. An intention-to-treat and last observer carried forward analysis was done.  $P$ -value < 0.05 was considered statistically significant.

**Results:** 40 subjects were randomised to placebo ( $n = 21$ ) or probiotics ( $n = 19$ ). Baseline characteristics are summarised in table 1. At the primary endpoint, change in total GIT was not statistically significant between placebo ( $-0.14 \pm 0.27$ ) and probiotic groups ( $-0.13 \pm 0.31$ ;  $p = 0.85$ ). At the secondary endpoint, there was greater reduction in total GIT in the probiotic ( $n = 13$ ;  $-0.18 \pm 0.26$ ) than the initial placebo group ( $n = 15$ ;  $-0.05 \pm 0.22$ ), though not reaching statistical significance ( $p = 0.14$ ). There was a statistically significant reduction in GIT-reflux subdomain in the probiotic group ( $-0.22 \pm 0.16$  vs initial placebo group  $0.05 \pm 0.27$ ;  $p = 0.0037$ ). Subjects on probiotics had greater abundance of lactobacillus, bifidobacterium and streptococcus, and exhibited high alpha diversity, whereas those on placebo had a decreasing trend of alpha diversity. Majority of adverse events were grades I and II.

**Abstract OP0208** – Table 1 Baseline characteristics of subjects

	Probiotic (n=19)	Placebo (n=21)
Fulfill EULAR/ACR 2013 criteria, n (%)	19 (100)	21 (100)
Mean $\pm$ SD Age, years	51.4 (13.7)	50.7 (7.9)
Females, n (%)	19 (100)	16 (76.2)
Disease duration from non-Raynaud's onset, years	44.5 (14.2)	41.3 (9.7)
Diffuse subtype, n (%)	3 (15.8)	6 (28.6)
Anti-Centromere positive, n (%)	7 (36.8)	2 (9.5)
Anti-Topo-I positive, n (%)	2 (10.5)	10 (47.6)
Mean $\pm$ SD total GIT	0.42 (0.29)	0.41 (0.27)
Mean $\pm$ SD GIT Reflux	0.45 (0.44)	0.39 (0.39)
Mean $\pm$ SD GIT Distension	1.13 (0.70)	0.93 (0.74)
Mean $\pm$ SD GIT Diarrhoea	0.26 (0.44)	0.36 (0.60)
Mean $\pm$ SD GIT Fecal soilage	0.26 (0.71)	0 (0)
Mean $\pm$ SD Body Mass Index	23.6 (2.8)	22.9 (3.0)
Hydrogen breath test positive, n (%)	2 (10.5)	3 (14.3)
Prednisolone, n (%)	6 (31.6)	8 (38.1)
GI medications	13 (68.4)	18 (85.7)
GI: Proton-pump inhibitor	11 (57.9)	17 (81.0)
GI: Pro-motility agent	7 (36.8)	7 (33.3)
Immunosuppressive medications	10 (52.6)	13 (61.9)

**Conclusions:** This trial demonstrated safety of probiotics in SSc. The primary outcome at 60 days was not achieved. A prolonged course of probiotics (120 days) resulted in greater improvement of GI reflux. There was a possible positive association between reduced GI stress (evidenced by greater alpha diversity of the GI microbiota) and lower GIT scores in the probiotic group. This study provides justification for a larger definitive trial of probiotics in SSc.

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**Disclosure of Interest:** None declared

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THURSDAY, 14 JUNE 2018

#### Patient involvement in research: The future of collaborative research. Lessons from the field of rheumatology and beyond

OP0209-PAR

#### THE PATIENT VOICE IN ARTHRITIS RESEARCH: A COLLABORATIVE APPROACH TO EMBEDDING PPI INTO RESEARCH STRATEGY

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**Background:** Public and Patient Involvement (PPI) encompasses a variety of ways researchers engage with people for whom their research holds relevance. Active and formal PPI can result in increased patient support for research and improved likelihood of patient involvement in the case of clinical research, including improved relevance to patient quality of life. As a research centre, we decided to develop our own PPI initiative. In order to develop a meaningful and productive partnership, we have developed this initiative from conception with our patient insight partners.

**Objectives:** The overall objective is to improve our research quality, relevance and outcomes. We aim to ensure that the real-life experiences of people living with arthritis are considered in the decision making processes around arthritis research.

**Methods:** A community approach to recruitment of patient insight partners was used. Social media, advocacy charities, and local community events were the predominant source of recruitment. Three initiatives were proposed: steering committee, patient insight panels, and a patient educator programme. A discussion forum between patients and researchers was used to determine the feasibility, interest and accessibility of proposed initiatives. An independent facilitator was commissioned to prepare an unbiased report of the discussion forum, upon which the PPI strategy was developed.

**Results:** Patient support for the PPI initiative was overwhelmingly positive. A number of potential barriers to participation were identified.

1) Steering committee:

Risk of tokenism and the potential intimidation of a structure that was too formal. Mechanisms to overcome included multiple patient representatives, detailed terms of reference and a supportive environment with a rotating chair. Our patient insight partners proposed a three-tier structure: a patient focus group that

nominates the steering committee members and a plenary meeting to be kept informed about research they are involved in.

#### 2) Insight Panels:

Access to technology was viewed as the major barrier to remote involvement. Mechanisms to overcome included multiple modes of communication: online, telephone, postal communication. Providing the opportunity for face-to-face or speaking directly with a researcher in an informal setting was seen as crucial in building interpersonal relationships and sustaining involvement.

#### 3) Patient Educator:

Extremely well received. Barriers to participation revolved largely around travel and physical accessibility. This can be overcome with in-house resources.

Our research strategy is being revised with the PPI strategy as a central tenet. We are adopting the new steering committee under the three-tier format and yearly research meeting with plenary session. We have a PPI newsletter, the editorial board for which is made up of researchers and patient insight partners. A patient educator module is under review for incorporation into a new PhD programme. We have expanded our research into multidisciplinary areas, with new sociology researchers and psychology collaborators.

**Conclusions:** The development of a true patient partnership in our group has fundamentally changed the scope and remit of our research, allowing us to expand our biomedical and clinical research into a more holistic model.

**Disclosure of Interest:** None declared

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### OP0210-PARE DUTCH JUVENILE IDIOPATHIC ARTHRITIS PATIENTS, CARERS AND CLINICIANS CREATING A RESEARCH AGENDA TOGETHER FOLLOWING THE JAMES LIND ALLIANCE METHOD

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**Background:** Biomedical research should support patients, carers and clinicians to take important decisions in the consulting room and eventually to improve the lives of patients.<sup>1</sup> Thus far the end-users of Juvenile Idiopathic Arthritis (JIA) research have not been involved in the prioritisation of future research. The JIA research community clearly sees the unmet need and has repeatedly expressed the wish to do something about this. As Parsons et al. have put it: 'Understanding young people's research priorities is important to develop research that is in tune with their needs.'<sup>2</sup> Putting this into practice starts with a search for relevant issues, working together with the end users of scientific knowledge on JIA – patients, carers and clinicians – and to prioritise research questions that can really make a difference.<sup>3</sup>

**Objectives:** In 2018 Dutch organisations of patients, carers and clinicians will collaboratively develop a research agenda for JIA, following the James Lind Alliance methodology.<sup>3,4</sup> An established research agenda, created by patients, carers and clinicians, will inform researchers and research funders about what the most important, relevant research questions for JIA are.

**Methods:** The James Lind Alliance (JLA) methodology enables us to do a systematic search for unanswered questions that are relevant to patients, carers and clinicians.<sup>4</sup> In a 'Priority Setting Partnership' (PSP), we will gradually establish a top 10 list of the most important unanswered research questions for JIA. In this process the input from patients and their carers will be given the same weight as that from clinicians.

The Dutch JIA PSP will be led by a steering group. This steering group coordinates the PSP and organises the activities. It will include representatives of patients (for JIA: young and adult JIA-patients), carers (for JIA: parents and spouses) and clinicians (for JIA: paediatric rheumatologists, physiotherapists, nurses, psychologists, social workers, ophthalmologist, etc.).

**Results:** The Dutch JIA organisations support the agenda; also financially. Following the JLA method it will take approximately twelve to eighteen months to formulate a research agenda, so the research agenda for JIA will be published in 2019.

**Conclusions:** A research agenda that will be jointly inspired by patients, carers and clinicians can really make a difference for decision-making in the consulting room and for the lives of JIA-patients.

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**Disclosure of Interest:** None declared

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THURSDAY, 14 JUNE 2018

### Can we improve the care of gout?\_\_\_\_\_

#### OP0211 ULTRASOUND SHOWS RAPID REDUCTION OF URIC ACID LOAD DURING A TREAT-TO-TARGET APPROACH IN GOUT PATIENTS: RESULTS FROM A LONGITUDINAL STUDY (NOR-GOUT)

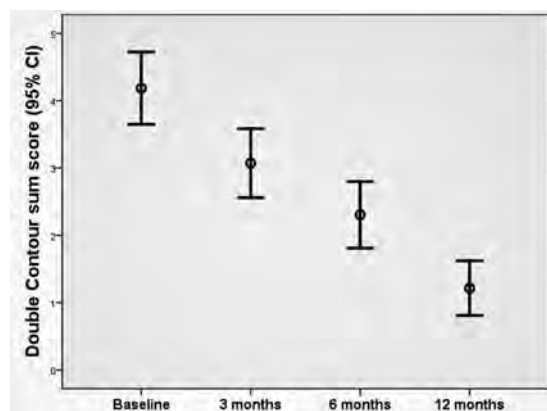
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**Background:** Ultrasound (US) has received an increasing attention in detecting uric monosodium urate (MSU) deposits, and is included as a domain in the ACR/EULAR classification criteria for gout. The OMERACT US group has developed definitions for US elementary lesions in gout including the double contour sign (DC) (deposits of crystals on the surface of cartilage), tophus (larger hypo-echoic aggregation of crystals, usually well delineated), aggregates (small hyper-echoic deposits) and erosions. MSU deposits may be found in many different regions with some predilection sites, but only a few small studies have explored the decrease of deposits during treatment.

**Objectives:** To explore by US the longitudinal resolution of MSU deposits during a treat-to-target approach with urate lowering therapy (ULT) in patients with gout.

**Methods:** In a prospective observational study, patients with crystal-proven gout were included if they presented after a recent gout flare and had increased serum urate levels (>360 µmol/L/>6 mg/dl). In a treat-to-target approach using ULT and increasing drug doses with monthly follow-up until treatment target was met (<360 µmol/L, or <300 µmol/L if clinical tophi). An extensive US assessment was performed (GE E9 machine, grey scale 15MHz) at baseline and after 3, 6 and 12 months to detect MSU deposits, using the OMERACT definitions for DC, tophi and aggregates with bilateral assessment of radiocarpal joints, MCP 2, insertion of triceps and quadriceps, proximal and distal patellar tendon, the Achilles tendon and cartilage of distal femur (maximal flexed knee) and the talar cartilage of tibio-talar joint and MTP 1 joint. The degree of elementary lesions was semi-quantitatively scored 0–3 (0=none, 1=possible, 2=certain, 3=major deposits). Sum scores of DC, tophi and aggregates, as well as total sum score of all lesions, were calculated for each visit. Changes from baseline were explored by paired samples T-test and response by Standardised Response Mean (SRM).

**Results:** 161 patients were included at baseline (93.3% men, mean (SD) age 57.0 (14.1) years, disease duration 8.0 (7.7) years). The mean (SD) serum urate level decreased from 487 (82) µmol/L at baseline to 312 (52) µmol/L at 12 months, with 72% reaching the target at 3 months, and 84% at 12 months. Sum scores of deposits decreased over 12 months (table 1, with \*p<0.05, \*\*p<0.001), and the numeric decrease was largest for DC (figure 1). SRM from baseline to 3, 6 and 12 months was 0.73, 1.02 and 1.26 for DC, 0.06, 0.57 and 0.91 for tophi and 0.20, 0.51 and 0.66 for aggregates.



Abstract OP0211 – Table 1

	Baseline (n=161)	3 months (n=124)	6 months (n=115)	12 months (n=88)
Double Contour score	4.2 (3.4)	3.1 (2.8)**	2.3 (2.7)**	1.2 (1.9)**
Tophi score	6.5 (6.6)	6.3 (5.7)	5.4 (6.1)**	4.2 (5.3)**
Aggregates score	9.1 (5.3)	8.8 (4.9)*	7.9 (5.2)**	6.7 (4.9)**
Double Contour, tophi and aggregates sum score	19.8 (13.6)	18.1 (12.0)**	15.6 (12.8)**	12.1 (10.9)**

**Conclusions:** During a treat-to-target approach with ULT all deposits decreased, and most extensively for DC. This study shows that reduction of the uric acid load in gout during treat-to-target ULT can be visualised by US, and that DC may be the most sensitive to change.

**Disclosure of Interest:** None declared

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#### OP0212 MOBILE PHONE TEXT MESSAGES FOR IMPROVING ALLOPURINOL ADHERENCE: A RANDOMISED CONTROLLED TRIAL OF TEXT MESSAGE REMINDERS

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**Background:** Medication adherence is important to treatment success, particularly in gout where the target level achievement is critical. However, there is no evidence that mobile phone text message reminder is effective in improving treatment adherence and clinical outcomes for gout.

**Objectives:** To evaluate the effect of mobile phone text messaging on the adherence to allopurinol treatment and serum uric acid (SUA) level of patient with gout in a randomized-controlled trial.

**Methods:** Adult patients who were diagnosed of gout by 1977 ARA classification criteria for gout, receiving at least 1 month of allopurinol, and had estimated glomerular filtration rate greater than 30 mL/min/1.73 m<sup>2</sup> were enrolled and randomly assigned to 2 groups by block randomization. Patients in the intervention group received a daily short message reminder to take allopurinol for 90 days. Patients in the control group received a weekly short message information about non-pharmacologic treatment for gout in plain language. The primary outcomes were allopurinol adherence, defined as the Medication Taking Behaviour for Thai patient (MTB-Thai) score >21, and SUA level at 12 weeks. The primary analysis was by intention-to-treat. This trial is registered with Thai Clinical Trials Registry, TCTR20171229004.

**Results:** Eighty-two patients were randomised, with 42 in the intervention group and 40 in the control group. No significant different of baseline characteristic, SUA (7.66±1.24 vs 7.78±1.17 mg/dL) and MTB-Thai score (18.38±0.73 vs 18.37±0.95) between two groups. At week 12, 37 patients (88.1%) in the intervention group achieved adherence compared with none of patient in the control group (RR for adherence 71.5, 95% CI: 4.54 to 1126.80; p=0.002). SUA level was decreased significantly from baseline in both study groups, however, the reduction in the intervention group was significantly greater than in the control group (-1.47±0.86 vs -0.28±0.39 mg/dL, p<0.001). Serum creatinine was significantly decreased in the intervention group (-0.03±0.09 mg/dL, p<0.031), while serum creatinine was unchanged in the control group (0.01±0.08 mg/dL, p=0.84).

**Conclusions:** Patients who received daily short message reminder had significantly improved adherence and reduction in SUA compared with the control

individuals. Mobile phones text reminders may be an important tool to enhance allopurinol adherence and help in controlling SUA level in gout patients.

**Disclosure of Interest:** None declared

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THURSDAY, 14 JUNE 2018

#### 'Why does BMI matter?'

#### OP0213 WHAT IS THE IMPACT OF POOR PROGNOSTIC FACTORS ON THE ACHIEVEMENT OF LOW DISEASE ACTIVITY OR REMISSION IN PATIENTS WITH RHEUMATOID ARTHRITIS?

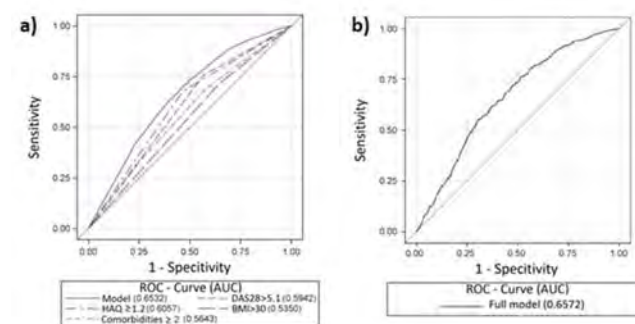
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**Background:** Poor prognostic factors were initially developed using radiologic progression as outcome. In the 2016 update of the EULAR recommendations it is proposed to use these factors for decision whether or not a biologic should be started. However, the treatment target is not radiologic progression but low disease activity (LDA) or remission.

**Objectives:** To investigate the impact of indicators of unfavourable prognosis on the achievement of LDA and remission in patients with RA.

**Methods:** Patients from the German biologics register RABBIT switching from 1 st to 2nd csDMARD were studied. High disease activity (DAS28 >5.1), autoantibodies (RF/ACPA positive), prevalent erosions, functional limitation (HAQ ≥1.2), comorbidities (≥2), obesity (BMI >30kg/m<sup>2</sup>), and smoking were evaluated as prognostic factors. Generalised regression analyses were applied to investigate the role of prognostic factors regarding the achievement of LDA (DAS28 <3.2) or remission (DAS28 <2.6). Receiver operating characteristic (ROC) curves were calculated to compare the ability of the prognostic factors (baseline values) to discriminate patients achieving LDA from those maintaining moderate or high disease activity within six months. The prognostic value of all factors was determined by the area under the ROC curve (AUC).

**Results:** A total of 1613 patients were studied (mean age 58.9 years, mean disease duration 4.8 years). 35% had DAS28 >5.1, 60% were RF/ACPA positive, 27% had erosions, 44% functional limitation, 37% ≥2 comorbidities, 32% were obese, and 26% current smokers. LDA was achieved by 33% of patients with DAS28 >5.1, by 30% if also autoantibodies and erosions were present, and by 20% if DAS28 >5.1, HAQ ≥1.2, ≥2 comorbidities and obesity were present. DAS28 >5.1 (OR 0.41 [95% CI: 0.32 to 0.52]), HAQ ≥1.2 (0.58 [0.46;0.74]), ≥2 comorbidities (0.66 [0.47 to 0.90]) and obesity (0.72 [0.57;0.91]) independently decreased the probability of LDA within six months. Current smoking (0.67 [0.48;0.93]) was negatively associated with remission. RF/ACPA and erosions were not associated. The ROC curves for achieving LDA for the significant factors (DAS28 >5.1, HAQ ≥1.2, ≥2 comorbidities and obesity) and a model containing only these four factors are shown in figure 1(a). The AUC of the model is higher than the one of the single curves. The AUC for the full model (figure 1(b)) which was additionally adjusted for age, sex, autoantibodies, erosions, current smoking, therapy and time is similar to the one of the reduced model.



**Conclusions:** High disease activity, functional limitation, comorbidities and obesity had significant negative impact on LDA and remission. They should be considered as poor prognostic factors in csDMARD-treated patients. It appears that a combination of the factors is better than using single ones.



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OP0214 **BASELINE COMORBIDITIES AND OVERWEIGHT PREDICT FUNCTIONAL STATUS AND HEALTH-RELATED QUALITY OF LIFE 9 YEARS LATER – A LONGITUDINAL COHORT STUDY OF 428 PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING STANDARD CARE**

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**Background:** Health-related quality of life (HRQOL) and functional status are markedly reduced in patients with rheumatoid arthritis (RA) leading to a significant societal and individual burden. Comorbidities and sociodemographic factors are associated with reduced HRQOL and functional status in cross-sectional studies of RA,<sup>1</sup> but their predictive value is largely unknown as longitudinal studies are lacking.

**Objectives:** To investigate whether comorbidities and sociodemographic factors predict HRQOL and functional status 9 years later in real-world patients with RA.

**Methods:** Consecutive patients with RA were recruited from a university hospital outpatient clinic between July 2006 and July 2007. Data regarding sex, age, disease duration, disease activity score of 28 joints and CRP (DAS28), number of comorbid conditions, marital status (married/cohabiting vs living alone), smoking (ever, previously or currently), exercise ( $\geq$ once a week vs not regularly), body mass index (BMI), educational level (elementary, training or higher), functional status (the health assessment questionnaire (HAQ)) and HRQOL (Euroqol 5 dimensions (EQ-5D)) were registered in the clinical database DANBIO; patients then continued routine care.

EQ-5D includes 5 dimensions of health (mobility, self-care, usual activities, pain/discomfort, anxiety/depression), each divided into three levels of severity, yielding 243 possible health states. A validated algorithm converts each health state into an index score between 0 (death) and 1 (perfect health).<sup>2</sup>

HAQ and EQ-5D scores at the most recent follow-up visit were retrieved from DANBIO on Sept 30th 2017. Two linear regression models were built with scores for HAQ and EQ-5D at follow-up as outcomes, respectively, all baseline variables were entered as possible explanatory variables and stepwise backward selection was employed. Sex, age, disease duration and baseline HAQ/EQ-5D were forced into the models.

**Results:** 564 patients with RA were recruited (81% women, median (IQR) age: 60<sup>49–68</sup> years, disease duration: 7 (3–16) years, DAS28: 2.9 (2.1–3.7), HAQ: 0.63 (0.25–1.25), EQ-5D: 0.74 (0.66–0.82) and followed in routine care for a median of 9<sup>5–10</sup> years. 428 and 256 patients had complete HAQ and EQ-5D scores, respectively at follow-up (HAQ: 0.75 (0.25–1.4), EQ-5D: 0.78 (0.69–0.86)). Patients without complete HAQ and EQ-5D scores at follow-up were older at baseline (10 and 6 years, respectively,  $p < 0.0001$ ), while sex, disease duration, DAS28, HAQ and EQ-5D scores were similar.

High HAQ, BMI 26–30 kg/m<sup>2</sup>, and 3 or more comorbid conditions at inclusion were all independently associated with poorer functional status and low EQ-5D 9 years later (table 1). The models with HAQ or EQ-5D as outcome explained 51% and 31% of the variation (Adj R<sup>2</sup>), respectively.

**Abstract OP0214** – Table 1 Multivariable linear regression model with HAQ and EQ-5D at follow-up as outcomes.

Explanatory variables	HAQ at follow up			EQ-5D at follow up		
	Coefficient	95% CI		Coefficient	95% CI	
Women	0.19	0.06	0.33	-0.03	-0.08	0.02
Age (50–75 yrs)	0.06	-0.05	0.18	0.03	-0.01	0.07
Age (>75 yrs)	0.03	-0.22	0.28	0.01	-0.10	0.11
Disease duration (3–10 yrs)	0.10	-0.03	0.23	-0.01	-0.06	0.04
Disease duration (>10 yrs)	0.12	-0.02	0.25	-0.02	-0.07	0.03
Baseline HAQ (per unit increase)	0.72	0.63	0.81	-0.10	-0.14	-0.05
Baseline EQ-5D (per unit increase)	NS	-	-	0.13	-0.05	0.30
BMI (<18.5 kg/m <sup>2</sup> )	0.27	-0.08	0.62	-0.09	-0.23	0.04
BMI (26–30 kg/m <sup>2</sup> )	0.22	0.10	0.33	-0.09	-0.13	-0.04
BMI (>30 kg/m <sup>2</sup> )	0.16	0.01	0.32	-0.03	-0.08	0.03
One comorbid condition	0.13	0.01	0.26	-0.02	-0.07	0.02
Two comorbid conditions	-0.03	-0.18	0.12	0.03	-0.03	0.08
$\geq 3$ comorbid conditions	0.30	0.14	0.47	-0.14	-0.20	-0.08
Constant	0.39	0.07	0.72	0.79	0.64	0.94

Adjusted R<sup>2</sup>: HAQ: 0.51, EQ-5D: 0.31.

Reference groups: male, age: < 50 years, disease duration: 0–2 years, BMI: 18.5–25 kg/m<sup>2</sup>, comorbid conditions: none.

**Conclusions:** Potentially modifiable factors (overweight and comorbidities) were independently and consistently associated with worse functional status and HRQOL at follow-up 9 years later in patients with RA receiving standard care. The findings suggest that focus on lifestyle and comorbidities in patients with RA may improve important long-term outcomes.

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**Disclosure of interest:** None declared

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THURSDAY, 14 JUNE 2018

**Musculoskeletal pain; feeding the opioid epidemic**

OP0215 **TIME-RELATED TRENDS IN OPIOID PURCHASES AMONG PATIENTS WITH EARLY INFLAMMATORY ARTHRITIDES**

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**Background:** Treatment outcomes in inflammatory arthritis (IA) have improved during the past decades; however, pain management remains a great challenge. There has been a concern of overprescription of opioids during recent years.

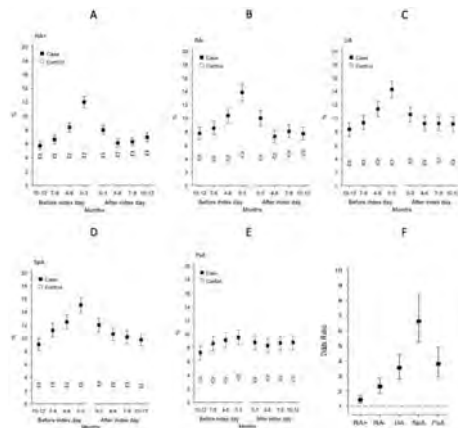
**Objectives:** The aim of this study was to explore the frequency of opioid users in patients with newly-onset IA in comparison with the general Finnish population and discover the proportion of long-term opioid users.

**Methods:** From the nationwide register maintained by the Social Insurance Institution of Finland we collected all incident adult patients with the five most common IAs between 2010–14. For each case, three eligible controls were randomly selected and individually matched according to age, sex, and place of residence. Opioid purchases between 2009–2015 were obtained from the drug prescription register and evaluated one year before and after the index date (decision of special reimbursement for antirheumatic drugs), further dividing the observation time into 3 month periods. Long-term use was defined as opioid purchases at least in three of these periods per year. All opioids from mild to strong were included.

**Results:** Data on different diagnosis groups are presented in table 1. The proportion of opioid purchasers among IA patients and their controls are shown in figure 1A-E. Also, odds ratio for long-term opioid use after the index date is shown in figure 1F.

**Abstract OP0215 – Table 1.** Number (N), proportion of females (%), and mean ages at baseline of incident patients with inflammatory arthritides between 2010 and 2014 in Finland.

	RA+ n=6186	RA- n=2970	UA n=2959	SpA n=3577	PsA n=2670
Age, mean (SD)	58 (15)	57 (17)	49 (17)	38 (12)	49 (13)
Proportion of females (%)	66.4	67.2	67.4	52.3	48.8



**Abstract OP0215 – Figure 1.** Proportion of opioid purchasers among patients with incident A) seropositive rheumatoid arthritis (RA+), B) seronegative rheumatoid arthritis (RA-), C) unspecified arthritis (UA), D) spondyloarthritis [(SpA), including ankylosing spondylitis and non-radiographic axial spondyloarthritis], and E) psoriatic arthritis (PsA) and their controls one year before and after the index date. F) Odds ratio for long-term opioid use among incident RA+, RA-, UA, SpA, and PsA patients versus controls after the index date.

**Conclusions:** IA patients are more likely to buy opioids one year before and one year after the diagnosis and prescription of antirheumatic medication than controls from the general population. The opioid purchases peak just before the index date in most IA patients. Long-term opioid use is also more common among patients with newly-onset IA, especially among those with SpA.

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#### OP0216 EXAMINING MODIFIABLE PSYCHOLOGICAL & SOCIAL HEALTH FACTORS ASSOCIATED WITH USE OF OSTEOARTHRITIS ORAL ANALGESIC TREATMENT

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**Background:** EULAR recommends the use of non-opioid oral medicines (acetaminophen, NSAIDs, or COX-2 inhibitors) for the management of knee osteoarthritis (OA). Opioids are also recommended when these other therapies fail. There are known demographic and clinical differences in OA treatment use. Patients' social and psychological health may also influence use of medications, yet their association with the utilisation of opioid or non-opioid oral OA treatments is unknown.

**Objectives:** Determine which modifiable social and psychological health factors are associated with use of oral opioid and non-opioid medications for OA.

**Methods:** Baseline data from a randomised controlled trial that examined the effects of a positive psychological intervention on pain in veterans with knee OA were used. For our study, patients were categorised based on self-reported use of the following oral medications for OA at baseline: opioids (with/without other oral analgesic treatments), non-opioid analgesics, and no oral analgesic treatment.

We used  $\chi^2$  or analysis of variance to compare sociodemographic, clinical, social, and psychological health variables by baseline OA treatment use. We used multinomial logistic regression models to estimate adjusted relative risk ratios (RRRs) of using an opioid or a non-opioid analgesic (vs. no oral analgesic treatment),

comparing patients by levels of social support (Medical Outcomes Study), health literacy ('How confident are you filling out medical forms by yourself'), and depressive symptoms (Patient Health Questionnaire-8). All models were adjusted for age, sex, race, income, OA symptom severity (WOMAC), self-reported Charlson comorbidity index, and body mass index.

**Results:** In this sample, 30.6% (n=110) reported taking opioid analgesics for OA, 54.2% (n=195) reported non-opioid use, and 15.3% (n=55) reported no oral analgesic use. Compared to the other groups, those taking opioids were younger (mean age 62.5 vs 64.3 vs 67.1, respectively, p=0.002) and had higher mean WOMAC scores (54.5 vs 45.7 vs 42.7, p<0.001). Opioid users also had lower mean social support scores (10.0 vs 10.5 vs 11.9, p=0.007) and were more likely to have moderate-severe depression (42.7% vs 24.1% vs 14.5%, p<0.001). Having adequate health literacy did not differ by treatment group type.

**Abstract OP0216 – Table 1** Social and psychological variables associated with oral analgesic treatment use\*

	Adjusted relative risk ratio	95%CI	p-value
<b>Non-Opioid Oral Analgesic Use †</b>			
Social support	0.94	(0.86,1.03)	0.188
Adequate health literacy	0.52	(0.21,1.30)	0.160
Depression, moderate to severe	1.93	(0.72,5.12)	0.189
<b>Opioid Use †</b>			
Social support	0.92	(0.83,1.02)	0.120
Adequate health literacy	0.53	(0.20,1.42)	0.207
Depression, moderate to severe	2.96	(1.08,8.07)	0.035
<b>Opioid Use ‡</b>			
Social support	0.98	(0.92,1.05)	0.601
Adequate health literacy	1.02	(0.55,1.89)	0.954
Depression, moderate to severe	1.53	(0.87,2.71)	0.140

\*Multinomial model adjusted for age, sex, race, income, WOMAC, comorbidity, BMI

†Reference: No oral medication use for OA

‡Reference: Non-opioid oral analgesic use

The table 1 shows the associations between the social and psychological health measures with oral analgesic use, adjusted for sociodemographic and clinical factors. Having moderate-severe depression was associated with higher risk of opioid analgesic use compared to no oral analgesic use (RRR 2.96, 95% CI: 1.08 to 8.07) when adjusted for sociodemographic and clinical factors. Depression level was not significantly associated with non-opioid oral medication use, compared to no oral analgesic medication use, in a similarly adjusted model. Neither social support nor health literacy was associated with opioid or non-opioid oral analgesic use in fully adjusted models.

**Conclusions:** Knee OA patients with more severe depression symptoms, compared to those without, were more likely to report using opioid (vs. non-opioid) analgesics for OA. Social support and health literacy were not significantly associated with oral analgesic use for OA when sociodemographic and clinical factors were accounted for.

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THURSDAY, 14 JUNE 2018

#### What is lupus – syndrome or different entities?\_\_\_\_\_

#### OP0217 A PERMEABLE BLOOD-BRAIN BARRIER IS NOT REQUIRED FOR NEUROPSYCHIATRIC MANIFESTATIONS IN SLE AND PSS

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**Background:** A prevailing hypothesis for neuropsychiatric (NP) manifestations in systemic lupus erythematosus (SLE) and primary Sjögren's syndrome (pSS) is that brain reactive autoantibodies can enter the brain through an impaired blood-brain barrier (BBB) during inflammatory conditions. Based on murine models the cytokine TWEAK could contribute to NP phenomena by binding Fn14 on brain endothelial cells. This will open the BBB and allow brain-reactive autoantibodies produced in the periphery to reach their targets in the brain.

**Objectives:** The aim of this study was to investigate the role of the BBB's permeability for NP manifestations in human SLE and pSS. Also, we wished to investigate whether increased TWEAK concentrations could be attributed to brain

involvement as previously documented in the animal models of SLE. We compared TWEAK with markers of BBB permeability and astrocyte activation. Also, we estimated intrathecal B-cell activation, anti-NR2 abs, and explored whether these variables were associated with NP manifestations.

**Methods:** In a population-based cohort of 50 SLE (all fulfilling the ACR criteria) and 52 pSS patients (all fulfilling the AECG criteria) NP manifestations were classified according to the ACR recommendations for NP-SLE. TWEAK, anti-NR2 antibodies (abs) were measured in serum and cerebrospinal fluid (CSF), S100b in CSF, and IgG index and Q-albumin were calculated.

**Results:** TWEAK concentrations in serum/CSF, as well as S100B and anti-NR2 abs in CSF, Q-albumin and IgG indices are shown in table 1. Associations between intrathecal TWEAK and S100B, Q-albumin and IgG index are given in table 2. No associations were found between TWEAK in serum/CSF and NP manifestations in the SLE, nor in the pSS group. Further, no associations were revealed between NP manifestations and S100B, Q-albumin or IgG index. Anti-NR2 abs in CSF were associated with increased OR for dysfunction in the cognitive domains visuospatial processing (OR 4.9,  $p=0.03$ ) and motor functioning (OR 6.0,  $p=0.006$ ) when corrected for age, gender, disease duration and education.

**Abstract OP0217** – Table 1 Demographic and other selected data in 50 SLE- and 52 pSS patients

	SLE	pSS	<i>p</i> -value
Age, years, mean (SD)	43 (12)	57 (12)	<0.001
Females (%)	43 (86)	44 (85)	0.84
Disease duration, years, mean (SD)	12 (9)	7 (5)	<0.001
No with NP manifestations (%)	46 (92)	48 (92)	0.95
TWEAK, serum, pg/ml	655 (200-4644)	925 (451-1508)	<0.001
TWEAK, CSF, pg/ml	887 (369-2351)	1351 (481-5184)	<0.001
S100B in CSF, pg/ml	221 (110-420)	264 (138-544)	0.005
Q-albumin, ratio	4.71 (1.98-12.2)	4.24 (1.69-10.8)	0.99
IgG index, ratio	0.17 (0.10-0.39)	0.18 (0.09-1.12)	0.19
Anti-NR2 in CSF, ratio	0.37 (0.14-2.2)	0.41 (0.15-3.0)	0.20

Abbreviations: Abs, antibodies

Anti-NR2 ab values given as a ratio against an internal calibrator with defined signal intensity.

Laboratory data are presented as median and ranges.

**Abstract OP0217** – Table 2 Associations\* between TWEAK in CSF and selected laboratory variables in 50 SLE- and 52 pSS patients

Dependent variables	SLE			pSS		
	$\beta$	R <sup>2</sup>	<i>p</i> -value	$\beta$	R <sup>2</sup>	<i>p</i> -value
Q-albumin	0.11	0.01	0.45	0.11	0.01	0.44
S100B, pg/ml	0.50	0.25	<0.001	0.45	0.20	0.001
IgG index	-0.14	0.02	0.32	0.37	0.12	0.007

\* Univariable regression analyses

**Conclusions:** Although several studies show that TWEAK seems necessary for CNS involvement in murine SLE, no clinical NP manifestations could be attributed to TWEAK concentrations in CSF/serum in the SLE- or pSS patients. Further, no associations were found between NP manifestations and the integrity of the BBB (Q-albumin), nor astrocyte activation.

The TWEAK concentration was higher in CSF than blood in both the SLE- and pSS patients, indicating an intrathecal production.

TWEAK in CSF covaried with S100B in CSF possibly reflecting a common ongoing intracerebral process.

We hypothesise that TWEAK is neuroprotective in human SLE and pSS. Brain residing immune cells produce brain reactive abs, for example anti-NR2 abs. These abs bind to neurons, and the cellular stress induced in the neurons leads to production of TWEAK. Concurrently, the activated B cells secrete proinflammatory cytokines that among other actions activate astrocytes that in turn produce S100B, also a neuroprotective protein.

**Disclosure of Interest:** None declared

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THURSDAY, 14 JUNE 2018

## Genetics, epigenetics and disease: is it all in the genes?

OP0218

### INVESTIGATING THE REGULATORY SNPs AT THE RUNX3 LOCUS ASSOCIATED WITH ANKYLOSING SPONDYLITIS

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**Background:** Among the 100 genes associated with ankylosing spondylitis (AS), *RUNX3* a transcription factor (TF) involved in diverse immunological processes has a very robust ( $10^{-15}$ ) association.<sup>1</sup> The biggest challenge following association studies remain to understand the mechanism behind this association and get insights of the disease. We have recently demonstrated that the association between AS and the single nucleotide polymorphism (SNP) *rs4648889* located in a 2 kb regulatory locus upstream the promoter of *RUNX3* can be explained by allele-specific effects on TF recruitment that alter gene expression, specifically in CD8 +T cells.<sup>2</sup> In addition, another closely adjacent SNP, *rs4265380* shows functional effects (i.e. TF recruitment, histone marks enrichment and cell count) on CD14 +monocytes.<sup>3</sup>

**Objectives:** The main objectives of this work are: 1) to dissect the functional effects of the different SNPs at the *RUNX3* locus, acting in different cell types (especially CD8 +T cells and monocytes); 2) to identify the different interacting partners (i.e. TFs) binding at the *RUNX3* locus in the presence of the AS-associated alleles.

**Methods:** We used publicly available dataset to define the epigenetic landscape of the *RUNX3* locus. *In vitro* functional studies were performed to characterise the effects of these specific genetic variants, providing critical functional evidence for their role in AS.

**Results:** (1) Roadmap data revealed a robust peak for open chromatin and specific histone modifications associated with regulatory elements. Hi-C data showed the interaction of *RUNX3* with different genomic loci within chromosome 1, in GM12878 lymphoblastoid cell line, CD8 +T cells and monocytes; (2) ChIP-qPCR experiments on monocytes and CD8 +T cells from AS patients revealed the enrichment for several histone modifications (i.e. H3K79Me2 and H3K4Me1) at the *RUNX3* locus overlapping the SNPs of interest; (3) preliminary DNA pull-down experiments, followed by Mass Spectrometry, started to identify the whole range of proteins and TFs (DNA/protein 'interactome') that bind at the *RUNX3* locus in the presence of the AS-associated alleles, evaluated in both CD8 +T cells and monocytes; (4) initial pathway enrichment analysis highlighted the distinct contribution of proteins involved in the transcriptional machinery (AS-risk VS protective alleles).

**Conclusions:** We provide first evidence that the 2 kb region upstream the *RUNX3* gene has a plausible functional role in AS. These new observations are critically important not only in identifying specific cell types that play a pathogenic role in AS, but also in defining dysregulated pathways and potential therapeutic drug targets.

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**Disclosure of Interest:** None declared

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THURSDAY, 14 JUNE 2018

## It's your move: promoting physical activity in people with RMD's

### OP0219-HPR THE EFFICACY OF MOTIVATIONAL COUNSELLING AND SMS-REMINDERS ON DAILY SITTING TIME IN PATIENTS WITH RHEUMATOID ARTHRITIS: 22 MONTHS FOLLOW-UP OF A RANDOMISED, PARALLEL-GROUP TRIAL

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**Background:** Patients with rheumatoid arthritis (RA) have high amounts of daily sitting time and do not meet recommendations for moderate to vigorous physical activity (PA). Previously, we reported results from a randomised controlled trial (RCT) investigating the efficacy of a four-month individually tailored behavioural intervention, targeting reduction of sedentary behaviour (SB) in patients with RA.<sup>1</sup> The four-month post intervention results showed that patients in the intervention group reduced their daily sitting time; moreover patient-reported outcomes (PROs) and total cholesterol levels improved compared to the usual lifestyle control group.

**Objectives:** To investigate 18 month post-intervention efficacy of the four-month individually tailored, behavioural intervention on daily sitting time in patients with RA.

**Methods:** In the observer-blinded RCT, we included 150 RA patients from a rheumatology outpatient clinic. The intervention group (n=75) received three motivational counselling sessions and tailored text messages aimed at increasing light intensity PA through reduction of SB. The control group (n=75) maintained usual lifestyle. Primary outcome was change from baseline in objectively measured daily sitting time. Secondary outcomes included PROs and cardio-metabolic biomarkers (blood pressure, lipids and HbA1c). All outcome measures were analysed with a mixed effects repeated measures ANCOVA model on the intention-to-treat population.

**Results:** At 22 months follow-up from baseline, 12 participants were lost to follow-up (three and nine, respectively). Compared to baseline, daily sitting time in the intervention group decreased 1.10 h/day, and in the control group it increased 1.32 h/day; between-group difference of -2.43 h/day (95% CI: -2.99 to -1.86; p<0.0001) in favour of the intervention group. Likewise, for most secondary outcomes between-group results favoured intervention: VAS-pain: -15.51 mm (-23.42 to -7.60), VAS-fatigue: -12.30 mm (-20.71 to -3.88), physical function: -0.39 HAQ-units (-0.53 to -0.26), total cholesterol: -0.86 (-1.03 to -0.68), triglyceride: -0.26 (-0.43 to -0.09) and HbA1c: -1.15 (-1.39 to -0.91) mmol/l.

**Conclusions:** Even 18 months after completed intervention results showed an effect on daily sitting time and improvements in PROs, lipids and HbA1c in favour of the intervention group. Findings suggest that an individually tailored, behavioural approach may be beneficial in promoting health in addition to current clinical practise for patients with RA.

#### REFERENCE:

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**Disclosure of Interest:** None declared

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THURSDAY, 14 JUNE 2018

## Challenges of patient organisations' in the 21st century

### OP0220-PARE DEVELOPMENT OF THE SWISS NATIONAL STRATEGY 'MUSCULOSKELETAL DISEASES' 2017-2022 BY THE SWISS LEAGUE AGAINST RHEUMATISM

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**Background:** To support countries in their national efforts, the WHO developed a Global Action Plan for the Prevention and Control of Noncommunicable Diseases

2013-2020, which included cardiovascular diseases, cancers, chronic respiratory diseases and diabetes.<sup>1</sup> Although rheumatic or musculoskeletal diseases were not considered by the WHO, the Federal Office of Public Health (FOPH) of Switzerland included them within the National Strategy for the Prevention of Noncommunicable Diseases (NCD strategy).<sup>2</sup> This valuable national strategy and the corresponding action plan focus mainly on primary and secondary prevention with the aim to prevent diseases before their occurrence and to decrease associated risk factors. As a consequence, numerous organisations started to prepare disease-specific national strategies with focus on tertiary prevention and the main intention of supporting people with chronic illness.

**Objectives:** The objective of this project of the Swiss League against Rheumatism was to develop the Swiss National Strategy 'Musculoskeletal Diseases' 2017-2022. The strategy focused on patients affected by a rheumatic disease in order to complete the objectives that had already been undertaken by the Swiss government.

**Methods:** The structure of the Swiss League against Rheumatism (non-profit organisation) required a streamlined process. The theoretical framework, as part one in a two-part strategy, was developed from scientific literature. For the second part of the strategy, the identification of different measures in various fields of action, an expert group with advisory role was built in September 2015. This expert group was composed of different organisations: the Federal Office of Public Health, the Swiss Conference of the Regional Directors of Health Care, the Swiss Society of Rheumatologists, the Swiss Society of Orthopaedics and Traumatology, the Swiss Association of Physiotherapy, the Swiss Association of Occupational Therapy and the Swiss League against Rheumatism. Several interviews were conducted with experts from those and other organisations to determine the need for action in the field of musculoskeletal diseases for the upcoming six years. In summer 2016 the various recommendations of possible measures were prioritised.

**Results:** In summer 2017 as a result of this process, the Swiss League against Rheumatism was able to present the National Strategy 'Musculoskeletal Diseases' 2017-2022 with various measures grouped in the categories of 'prevention and early detection', 'care' and 'research and education'.<sup>3</sup>

**Conclusions:** Using this approach, a national strategy was developed with a reasonable amount of personal and financial resources. The current challenge of the implementation process is to motivate the involved organisations to realise specific measures on their own or in collaboration. These measures enable a better support of persons with musculoskeletal conditions during the full course of their disease.

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**Disclosure of Interest:** None declared

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### OP0221-PARE KNOW THEIR NUMBERS: WHAT DO RA PATIENTS KNOW ABOUT THEIR OWN BIOMEDICAL DATA?

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**Background:** Evidence shows that patients with a higher knowledge regarding their health, experience better health and have better outcomes, this leads to lower costs for the National Health Service. The Blood Pressure Association UK encourages the public to know their biomedical data. Similarly, there is a desire for patients with chronic diseases such as rheumatoid arthritis (RA) to know their biomedical data (blood pressure, lipid profile, DAS 28 score, BMI, blood sugar etc). It is well documented that patients with RA are at a high risk of developing cardiovascular disease.

**Objectives:** The aims of this study were to ascertain the existing knowledge that patients have on their biomedical data, understand the barriers of knowing these health indicators and enquire how their knowledge can be improved.

**Methods:** 50 consecutive patients with RA seen in a nurse-led clinic were asked to complete an anonymised questionnaire. The questionnaire consisted of 10 questions which assessed demographics, the patients' knowledge of their current biomedical data and the importance of knowing this information. It also enquired if patients knew what the term 'know your numbers' meant, reasons for not knowing and what could be done to increase their knowledge in knowing their numbers.

**Results:** 80% (n=40) questionnaires were returned. The estimated mean age (mean ±SD, years) was 58.1±13.4. A majority of the respondents were female

(87.5%). The highest category of disease duration for the cohort was between 2–5 years with 40% (n=16) patients. 30% (n=12) of the respondents were aware of the 'know your numbers' concept. 27.5% (n=11) knew their cholesterol while 80% did not know their last blood sugar. The majority 90% (n=36) did not know their BMI. Only 25% of the respondents knew their DAS score. 50% knew the significance of the numbers. 40% (n=16) reported that no one had informed them about the numbers. 95% (n=38) of the participants showed interest in knowing their numbers and 27.5% (n=11) suggested that a written record explained and regularly updated would be appropriate whilst 35% (n=14) proposed that a multidisciplinary input would be useful in regularly informing them of the numbers.

**Conclusions:** Although cardiovascular disease risk assessment and the management has improved in RA. There still remains a gap in patient engagement and activation in taking responsibility in knowing the risks and what they mean. It is well documented that patients with increased level of activation are more likely to engage in positive health behaviours resulting better outcomes. Our study has shown that although patients do not know much about their biomedical data they are interested in knowing about them. Knowing their biomedical may encourage them to take more ownership of their health even leading to more self-managing their RA.

**Disclosure of Interest:** None declared

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THURSDAY, 14 JUNE 2018

## The EULAR exercise recommendations for physical activity in people with inflammatory arthritis and osteoarthritis

### OP0222-HPR PHYSICAL CAPACITY CONTRIBUTES marginally IN EXPLAINING VARIATIONS OF FATIGUE IN PERSONS MODERATELY AFFECTED BY RHEUMATOID ARTHRITIS

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**Background:** Fatigue is a prominent problem for persons with rheumatoid arthritis (RA). Physical activity, including planned and structured exercise, is an important non-pharmacological intervention that positively affects fatigue. Physical capacity including variables as aerobic capacity, muscle strength and lower limb capacity, are modifiable and their relative contributions to fatigue are thus of interest to better understand and address this detrimental consequence of RA.

**Objectives:** To explore the contributions of physical capacity in explaining variations in fatigue among people with rheumatoid arthritis (RA).

**Methods:** This cross-sectional study included 269 participants (82% women, mean age 60 years, mean DAS28 2.8, mean HAQ-DI 0.5) recruited for a physical activity intervention. Data were collected from the Swedish Rheumatology Quality Registers, from questionnaires on fatigue, activity limitation, perceived health, pain and anxiety/depression and from physical capacity tests (lower limb function, grip strength, aerobic capacity). We used logistic regression to estimate the association between severe fatigue ( $\geq 50$ , VAS 0–100) and A) independent variables related to disease and disease impact and B) model A plus physical capacity tests. Pooled odds ratio tests compared model fit.

**Results:** Severe fatigue was reported by 95 participants (35%). The three variables which were statistically significantly associated with severe fatigue ( $p < 0.05$ ) in both models were perceived health, pain and anxiety/depression. Anxiety/depression demonstrated the largest effect size with odds ratios of 2.43 (95% CI: 1.20 to 4.94) in model A and 2.58 (95% CI: 1.25 to 5.32) in model B. The likelihood ratio test indicated that model B was a better fit to the data than model A with  $\chi^2$  (df 3)=2.65,  $p=0.048$ .

**Conclusions:** We found that disease impact variables rather than physical capacity variables are predictors of severe fatigue in people with RA. Further studies are needed to assess correlations between physical capacity and fatigue using multidimensional assessments of fatigue to enable separate analyses of physical and mental fatigue respectively.

**Disclosure of Interest:** None declared

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THURSDAY, 14 JUNE 2018

## Immune senescence and ageing

### OP0223 TARGETING CHONDROCYTE PLASTICITY VIA CONNEXIN43 MODULATION ATTENUATES CELLULAR SENESCENCE IN OSTEOARTHRITIS

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**Background:** Chondrocytes in articular cartilage undergo phenotypic changes and senescence, restricting cartilage regeneration and favouring the osteoarthritis (OA) progression, a chronic disease characterised by degeneration of articular cartilage leading to physical disability and pain. Like other wound healing disorders, chondrocytes from OA patients show a chronic increase in the transmembrane channel protein connexin43 (Cx43), which through the exchange of factors or recruitment/release of signalling factors to the membrane regulates signal transduction. Immature or stem-like cells are found in cartilage isolated from OA patients, yet their origin and role in disease progression are unknown.

**Objectives:** Our objective was to investigate the role of Cx43 in chondrocyte plasticity during osteoarthritis.

**Methods:** Human mesenchymal stem cells and chondrocytes from osteoarthritic donors were used in this study. Protein levels were evaluated by western blot, immunofluorescence and flow cytometry. RNA expression was evaluated by RT-qPCR. Cell communication was studied by scrape loading assay and flow cytometry.

**Results:** Here we show that Cx43 acts as a positive regulator of the reversion of human chondrocytes to a less differentiated state. Overactivity of Cx43 in the membrane largely maintain this stem-like phenotype by increasing the basic helix-loop-helix transcription factor TWIST-1 and tissue remodelling and proinflammatory factors such as MMPs and IL-6, which in turn lead to cellular senescence by upregulation of p53 and p16INK4a, contributing to the senescence-associated secretory phenotype (SASP). Downregulation of Cx43 leads to redifferentiation of osteoarthritic chondrocytes (OAc) into more differentiated state decreasing MMPs, proinflammatory cytokines production and cellular senescence. Collectively, these results identify a causal Cx43-sensitive circuit in chondrocytes that regulates dedifferentiation and redifferentiation events involved in wound healing and tissue repair. In addition we show that chronic dedifferentiation drives catabolic processes and cellular senescence.

**Conclusions:** Targeting Cx43 allows dedifferentiated chondrocytes to revert to a chondrocyte-specific phenotype and its subsequent recovery in a predictable manner. These findings support the use of Cx43 as an appropriate therapeutic target to halt OA progression and to promote cartilage regeneration

**Disclosure of Interest:** None declared

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FRIDAY, 15 JUNE 2018

## Special delivery: intercellular communication

### OP0224 ADAMTS-12 PROTECTS AGAINST INFLAMMATORY ARTHRITIS THROUGH INTERACTING WITH PROINFLAMMATORY CTGF

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**Background:** It has been reported that a disintegrin and metalloproteinase with thrombospondin motifs-12 (ADAMTS-12) is a susceptibility gene for rheumatoid arthritis (RA) development, and its level was significantly increased in RA patients. In addition, ADAMTS-12 was also reported to be required for normal inflammation.

**Objectives:** This study aims to determine the role of ADAMTS-12 and the underlying mechanisms in the pathogenesis of inflammatory arthritis.

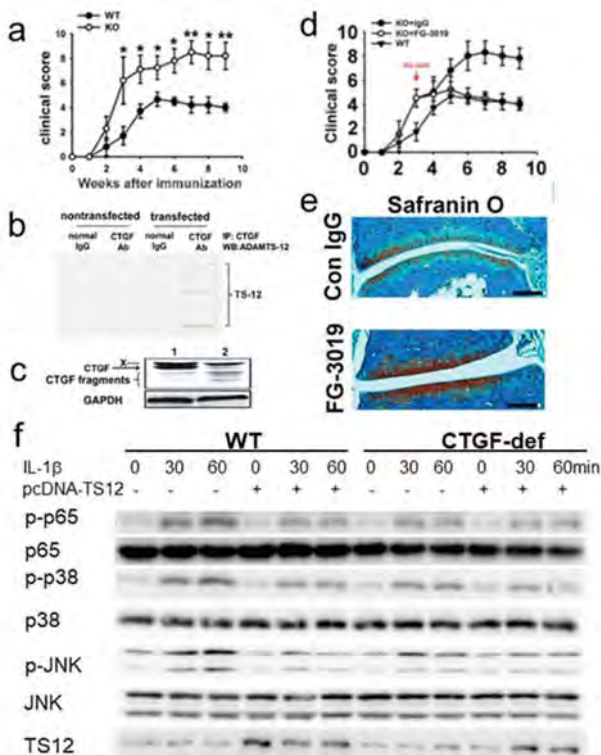
**Methods:** Collagen-induced arthritis (CIA) was established in ADAMTS-12<sup>-/-</sup> mice and their control littermates to determine the role of ADAMTS-12 *in vivo*. Connective tissue growth factor (CTGF) deficient Raw264.7 were used to

determine their functional interplays. Protein-protein interaction assays were performed to detect the interactions of ADAMTS-12 with CTGF

**Results: ADAMTS-12<sup>-/-</sup> mice are more susceptible to collagen-induced arthritis.** Accelerated disease onset, significant increase in the arthritis score and arthritis incidence, were observed in ADAMTS-12<sup>-/-</sup> mice (figure 1a). Histological analysis of whole ankle joints demonstrated a significant increase in synovitis, destruction of bone and cartilage loss in ADAMTS-12<sup>-/-</sup> mice. ELISA results indicated that ADAMTS-12<sup>-/-</sup> CIA mice exhibited enhanced release of pro-inflammatory and reduced secretion of anti-inflammatory cytokine. Collectively, these data demonstrate that ADAMTS-12<sup>-/-</sup> renders mice highly susceptible to CIA.

**ADAMTS-12 interacts with and cleaves CTGF, and ADAMTS-12-mediated signalling depends on CTGF during inflammation.** It is known that CTGF plays a pro-inflammatory role in the pathogenesis of inflammatory arthritis. We co-transfected CTGF and ADAMTS-12 into 293 T cells and found ADAMTS-12 bound to (figure 1b) and digested CTGF (figure 1c). *In vivo* studies also demonstrated that CTGF was accumulated in the synovium of ADAMTS-12<sup>-/-</sup> CIA mice. To further determine whether CTGF is a critical regulator of ADAMTS-12 mediated signalling, we generated CTGF deficient Raw264.7. Overexpression of ADAMTS-12 and CTGF deficiency could decrease the activation of inflammatory signalling markers such as NFκB, p38 and JNK in response to IL-1β at a comparable level. More importantly, overexpression of ADAMTS-12 in CTGF deficient Raw264.7 failed to further inhibit the activation of these signal molecules as compared to CTGF deficient Raw264.7 (figure 1f). Taken together, these results suggest that CTGF is a critical regulator of ADAMTS-12 mediated signalling during inflammation.

**Blocking CTGF attenuates inflammatory arthritis in ADAMTS12-deficient CIA mice model.** To determine whether the accelerated inflammation in ADAMTS-12<sup>-/-</sup> mice resulted from the accumulated CTGF, we administered CTGF antibody to ADAMTS-12<sup>-/-</sup> CIA model after disease onset. The arthritis score in ADAMTS-12 deficient mice was significantly reduced in presence of CTGF antibody (figure 1d). Moreover, histological analysis indicated CTGF abrogated further tissue destruction and inflammation (figure 1e).



**Abstract OP0224** – Figure 1 ADAMTS-12 protects against inflammatory arthritis through interacting with CTGF. (a) Clinical arthritis scores in WT and KO CIA mice. (b) Co-IP assays detect the associations of ADAMTS-12 with CTGF. (c) Western blotting of CTGF cleavage by ADAMTS-12. (d) Clinical arthritis scores in WT, control IgG-treated KO and CTGF antibody-treated KO mice with CIA. (e) Safranin O staining. (f) WT or CTGF-deficient (CTGF-def) Raw264.7 were transfected with pcDNA-ADAMTS 12 for 48hrs, then cells were treated with or without IL-1β for indicated time. Cell lysate were separated in SDS-page and probed with indicated antibodies.

**Conclusions:** ADAMTS-12-mediated regulation of inflammatory arthritis is probably through, at least in part, its interplay with CTGF and blockage of CTGF has been shown to be effective in treating inflammatory arthritis.

**Disclosure of Interest:** None declared

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#### OP0225 S100A9 MEDIATES ACUTE NOCICEPTIVE PAIN IN EXPERIMENTAL SYNOVITIS

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**Background:** Synovitis-associated pain is an important aspect of arthritis pathology. Several inflammatory mediators released by the synovium have been implicated in the regulation of pain, including S100A8 and S100A9. These mediators may regulate pain either via direct stimulation of TLR4 on the nerve endings in the synovium or via stimulation at the site of the dorsal root ganglia (DRG), thereby enabling an increased phagocyte infiltration that may cause sensitisation.

**Objectives:** To elucidate the role of S100A9 in the pain response after induction of an acute synovitis using streptococcal cell walls (SCW) as a trigger, by comparing S100a9<sup>-/-</sup> mice and their wild type controls.

**Methods:** Acute synovitis was induced by a single intraarticular injection of SCW in the knee joint of C57Bl/6 (WT) mice and S100a9<sup>-/-</sup> mice (also functional knock-outs for S100A8). Control mice received a saline injection. Serum S100A8/A9 levels were investigated by ELISA. Joint swelling and cell influx was assessed by <sup>99m</sup>Tc accumulation and histology. Pain response were investigated using an Incapacitance Tester (weight bearing), Catwalk (gait analysis) and von Frey's filaments (mechanical allodynia). Gene expression of inflammatory mediators and neuron activation markers in DRG were determined by q-PCR. Monocyte influx and protein expression was monitored by immunohistochemistry (IHC).

**Results:** A single intraarticular injection of SCW resulted in acute synovitis, accompanied by a strongly increased synovial expression of S100A8 and S100A9 and increased serum S100A8/A9 levels at day 1, which returned to basal levels at day 7. However, joint swelling and cell influx were similar in WT and S100a9<sup>-/-</sup> mice at day 1, excluding a role for S100A8/9 on pain perception via increased synovitis. WT mice showed a marked and significant decrease in the percentage of weight bearing on the SCW injected hind paw (28%) compared to saline injection (47%, p<0.001) at day 1, whereas S100a9<sup>-/-</sup> mice did not. In addition, the stand-phase of the unaffected paws was significantly increased in WT mice 1 day after injection, while in S100a9<sup>-/-</sup> mice these parameters were not altered. Both mouse strains showed a similar reduction of paw withdrawal threshold, excluding a role for S100A8/9 in allodynia. Analysis of DRG showed no increased phagocyte infiltration after SCW injection and no change in gene expression of the chemokines MCP-1 and KC (for monocytes and neutrophils respectively), and pro-inflammatory cytokines IL-1β and TNF was measured. In addition, F4/80 staining was comparable between WT and S100a9<sup>-/-</sup> mice. However, expression of the neuron activation markers NAV1.7, ATF3 and GAP43 was significantly increased at 1 day after SCW injection in WT mice as compared to saline injected mice (p=0.022, 0.004 and 0.030 respectively) while no regulation of these factors was found in S100a9<sup>-/-</sup> mice, which is in line with the reduced pain response observed earlier in S100a9<sup>-/-</sup> mice. The difference in NAV1.7 expression in the DRG was further confirmed at protein level with IHC.

**Conclusions:** These findings show that S100A9 is an important mediator of inflammatory nociceptive pain response in the knee, rather than being involved in peripheral sensitisation. During the acute phase of inflammation S100A8/A9 is likely regulated via direct activation of TLR4 on nerve endings in the synovium and not via monocyte infiltration in the DRG.

**Disclosure of Interest:** None declared

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FRIDAY, 15 JUNE 2018

#### Biologics in RA. More, more and more about safety.

#### OP0226 RISK OF HOSPITALISED INFECTION AND INITIATION OF ABATACEPT VERSUS TNF INHIBITORS AMONG PATIENTS WITH RHEUMATOID ARTHRITIS: A PROPENSITY SCORE-MATCHED COHORT STUDY

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**Background:** Rheumatoid arthritis (RA) patients receiving biologic therapy are at an increased risk of infection. TNF inhibitors (TNFi) and abatacept are used similarly in RA as the first line biologic. Few studies conducted a head-to-head



**Abstract OP0226 – Table 1.** Risk of hospitalised infection in Abatacept versus TNFi initiators: PS-matched analysis

	Event	Abatacept (n=11,248)			TNF inhibitors (n=11,248)		
		Person-years	IR	HR (95% CI)	Person-years	IR	HR (95% CI)
Primary outcome	Hospitalised infection	1024	40.01	0.97 (0.89–1.06)	1031	41.21	1.0
Secondary outcomes	Bacterial infection	635	23.99	1.04 (0.93–1.16)	598	23.10	1.0
	Herpes zoster	402	15.06	1.01 (0.88–1.16)	391	14.94	1.0
	Bone/joint infection	53	1.93	1.33 (0.88–2.01)	39	1.45	1.0
	Cardiac infection	0	0	-	3	0.11	1.0
	Gastrointestinal infection	158	5.81	1.21 (0.96–1.52)	128	4.79	1.0
	Genitourinary infection	130	4.77	1.20 (0.93–1.55)	106	3.97	1.0
	Respiratory infection	351	13.11	0.91 (0.79–1.05)	378	14.45	1.0
	Skin/soft tissue infection	178	6.55	0.92 (0.75–1.13)	189	7.12	1.0
	Neurologic infection	2	0.07	0.20 (0.04–0.90)	10	0.37	1.0

comparison of infection risk specific to different types of biologics used in a real-world setting.

**Objectives:** To evaluate the risk of hospitalised infection among RA patients who initiate abatacept versus TNFi.

**Methods:** We identified RA patients aged  $\geq 18$  years with  $\geq 2$  RA diagnoses separated by 7–365 days using insurance claims data from Truven MarketScan database (2005–2015). New users of abatacept or TNFi (adalimumab, etanercept, certolizumab, golimumab, and infliximab) were included. To balance RA duration or severity between the groups, we excluded patients who previously used rituximab, tocilizumab or tofacitinib. We also excluded patients with malignancy, dialysis, HIV/AIDS, or organ transplantation. The primary outcome was a composite endpoint of hospitalised infection including bacterial, viral or opportunistic infection. Secondary outcomes were bacterial infection, herpes zoster, and infections affecting different organ systems. To control for over 50 baseline confounders, we performed 1:1 propensity score (PS) matching. We estimated incidence rate (IR) and hazard ratio (HR) with 95% confidence interval (CI) of risk of hospitalised infection.

**Results:** We included 11,248 PS-matched pairs of abatacept and TNFi initiators with median age of 56 years. 83% were female. In the 1 year baseline period, 68% had any use of oral steroids and 55% used methotrexate. 18% had diabetes and 3% had hospitalised infection. Over the mean 2.3 year of followup, 1024 abatacept and 1,031 TNFi initiators were hospitalised for infection (table 1). The risk of any hospitalised infection was similar (HR 0.97, 95% CI: 0.89 to 1.06) between the two groups with the IR per 1000 person-years of 40.01 in abatacept and 41.21 in TNFi initiators. We found consistent results in the analyses of secondary outcomes. IR=events per 1000 person-years

**Conclusions:** In this large cohort of RA patients who used abatacept or TNFi as a first or second-line biologic agent, we found no difference in the risk of hospitalised infection between the two groups.

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#### OP0227 TIMING OF ABATACEPT BEFORE ELECTIVE ARTHROPLASTY AND POST-OPERATIVE OUTCOMES

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**Background:** Guidelines recommend holding biologic DMARDs before major surgery, but few studies have examined perioperative timing of individual biologic therapies.<sup>1</sup>

**Objectives:** We aimed to determine whether holding abatacept infusions before elective hip or knee arthroplasty is associated with lower risk of adverse post-operative outcomes.

**Methods:** This retrospective cohort study using U.S. Medicare claims data from 2006-September 2015 evaluated adults with  $\geq 2$  ICD9 codes for RA who received abatacept by infusion within 6 months of inpatient primary or revision total hip or knee arthroplasty. Infusions were selected as these procedures can be precisely dated in claims data. Patients with hip fracture, malignancy, pre-existing infection, non-elective procedures, or surgery after hospital day 3 were excluded. Logistic and Cox regression were used to assess associations between abatacept stop timing (time between most recent infusion and surgery in 4 week intervals based on dosing interval) and adverse outcomes: 1) hospitalised infection within 30 days (from discharge diagnoses, PPV >80%), 2) rate of prosthetic joint infection (PJI, ICD9 996.66) within 1 year, and 3) 30 day readmission (among patients with discharge to home, rehabilitation facility, or skilled nursing facility). Propensity scores based on the probability of being in each abatacept stop timing group were used to balance confounders across exposure groups using inverse probability weighting. Risk of hospitalised infection associated with methotrexate or with average glucocorticoid dose in the 3 months prior to surgery was assessed in abatacept treated patients using a reduced multivariable logistic regression model.

**Results:** Among 1537 surgeries in 1410 patients, there were 158 (10.3%) hospitalised infections within 30 days (most commonly urinary, skin/soft tissue, and pneumonia), 34 (2.6/100 person-years) PJI within 1 year, and 108/1448 (7.5%) 30 day readmissions. There were no significant differences in the rates of hospitalised infection, prosthetic joint infection, or 30 day readmission in patients who received abatacept within 4 weeks of surgery vs patients with longer stop timing (table 1). Among abatacept treated patients, glucocorticoid use (vs. none) was associated with a dose-dependent increase in the risk of hospitalised infection:  $\leq 5$  mg [aOR 1.32 (0.88–1.98)], 5–10 mg [aOR 2.40 (1.54–3.73)], >10 mg [aOR 1.73 (0.74–4.06)]. Concomitant use of methotrexate was not associated with hospitalised infection risk [aOR 0.97 (0.68–1.38)] (table 2).

**Abstract OP0227 – Table 1** Association between abatacept stop timing and post-operative outcomes, from logistic and Cox regression with inverse probability weighting

Abatacept Stop Timing	30-day hospitalized infection		Prosthetic joint infection within 1 year		30-day readmission*	
	N (%)	aOR (95% CI)	N (inc/100py)	aHR (95% CI)	N (%)	aOR (95% CI)
< 4 weeks (n = 394)	61 (10.3)	Reference	11 (2.4)	Reference	44/572 (7.7)	Reference
4-8 weeks (n = 670)	80 (9.0)	0.98 (0.66-1.45)	15 (3.1)	1.22 (0.55-2.73)	45/627 (7.2)	0.97 (0.62-1.53)
≥ 8 weeks (n = 273)	37 (13.6)	1.11 (0.69-1.79)	6 (3.0)	0.71 (0.25-2.08)	19/249 (7.6)	0.94 (0.51-1.73)

\*Readmissions assessed among patients with discharge to home, rehabilitation facility, or skilled nursing facility. Adjusted odds ratios (aOR) and hazard ratios (aHR) from logistic and Cox regression with inverse probability treatment weights. inc/100py = incidence per 100 person years.

**Abstract OP0227** – Table 2 Association between glucocorticoids and methotrexate with post-operative hospitalised infection among abatacept treated patients, logistic regression model

Average glucocorticoid dose	Adjusted OR (95% CI)	p-value
None (n = 764)	Reference	–
≤5mg (n = 454)	1.32 (0.88-1.98)	0.18
5-10mg (n = 252)	2.40 (1.54-3.73)	<0.001
>10mg (n = 67)	1.73 (0.74-4.06)	0.21
Methotrexate use (n = 573)	0.97 (0.68-1.38)	0.86

Included in the reduced multivariable model but not shown: abatacept stop timing, age, disability, sex, race, median household income, surgery type, chronic kidney disease, surgeon volume. Tested but excluded (p > 0.2): osteonecrosis, diabetes, congestive heart failure, asthma/COPD, obesity, Charlson score, previous biologic, hospitalizations, hospitalized infections, number outpatient visits, hospital volume, skilled nursing facility residence, extra-articular RA, region, urban, antibiotics/NSAIDs/opioids past 90 days, year.

**Conclusions:** Holding intravenous abatacept for ≥4 weeks (one dosing interval) was not associated with a lower risk of hospitalised infection, prosthetic joint infection, or 30 day readmission. Glucocorticoid use even at 5–10 mg per day was associated with significantly greater risk of post-operative infection.

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**OP0228** **COMPARATIVE RISK OF BIOLOGIC THERAPIES AND RISK OF GLUCOCORTICOIDS IN PATIENTS WITH RHEUMATOID ARTHRITIS UNDERGOING ELECTIVE ARTHROPLASTY**

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**Background:** Patients with RA undergoing major surgery are at high risk for infection. Different biologic DMARDs may be associated with different infection risks.<sup>1</sup>

**Objectives:** Goals were 1) to compare post-operative infection risk after arthroplasty in patients with RA exposed to different biologics, and 2) examine associations between glucocorticoid use and post-operative infection.

**Methods:** A retrospective cohort study using U.S. Medicare data from 2006-September 2015 evaluated adults with ≥2 ICD9 codes for RA undergoing elective inpatient primary or revision total knee or hip arthroplasty. Eligible patients received an infusion or prescription for abatacept, adalimumab, etanercept, infliximab, or tocilizumab within 8 weeks or a rituximab infusion within 16 weeks of surgery. Patients with hip fracture, malignancy, pre-existing infection, or non-elective surgery were excluded. Average glucocorticoid dose in the 3 months before surgery was calculated from oral prescriptions. Logistic or Cox regression evaluated associations between biologic exposure and post-operative outcomes: 1) hospitalised infection within 30 days (from discharge diagnoses, PPV >80%), 2) rate of prosthetic joint infection (PJI, ICD9 996.66) within 1 year, and 3) 30 day readmission among patients with discharge to home, skilled nursing facility, or inpatient rehab. Propensity scores based on the probability of receiving a specific biologic treatment were used to balance confounders across treatment groups using inverse probability weighting. Similar analyses were used to evaluate associations between glucocorticoid dose and outcomes in the same cohort, using inverse probability weighted analyses based on the probability of being in each glucocorticoid treatment category.

**Results:** Among 7929 surgeries in 7138 patients, there were 717 (9.0%) hospitalised infections within 30 days of surgery (most commonly urinary, skin/soft tissue, and pneumonia), 192 (2.8/100 person-years) PJI within 1 year, and 465/7554 (6.2%) 30 day readmissions. There was no significant difference in the risk of

hospitalised infection, PJI, or 30 day readmission across biologic treatment groups (table 1). Glucocorticoid dose >10 mg/day (mean 13.5±3.5 mg/day) was associated with a significantly greater risk of hospitalised infection [aOR 2.37 (1.63–3.44)] and prosthetic joint infection [aHR 2.04 (1.09–3.84)] compared to no glucocorticoid use (table 1). Patients with glucocorticoid dose >10 mg also had a numerically greater risk of 30 day readmission that did not reach statistical significance [aOR 1.61 (0.99–2.61)] (table 1).

**Abstract OP0228** – Table 1 Associations between preoperative biologic exposure or glucocorticoid dose and post-operative outcomes

	30-day hospitalized infection		1-year prosthetic joint infection		30-day readmission***	
	N (%)	aOR (95% CI)	N (inc/100py)	aHR (95% CI)	N (%)	aOR (95% CI)
<b>Associations with biologic exposure before surgery</b>						
Abatacept (n = 1369)	126 (9.2)	Reference	27 (2.3)	Reference	92/1296 (7.1)	Reference
Adalimumab (n = 1284)	108 (8.4)	0.86 (0.63-1.18)	50 (3.5)	0.83 (0.47-1.46)	78/1225 (6.4)	0.89 (0.62-1.28)
Etanercept (n = 1896)	173 (9.4)	1.03 (0.79-1.35)	27 (2.7)	1.00 (0.62-1.61)	112/1767 (6.3)	1.03 (0.74-1.43)
Infliximab (n = 2798)	249 (8.9)	0.86 (0.75-1.24)	58 (2.6)	1.08 (0.68-1.73)	143/2673 (5.4)	0.85 (0.62-1.16)
Rituximab (n = 337)	33 (9.8)	1.10 (0.69-1.75)	3 (1.2)	N/A**	21/314 (6.7)	1.03 (0.58-1.83)
Tocilizumab* (n = 305)	28 (9.2)	1.01 (0.62-1.63)	9 (5.1)	N/A**	19/279 (6.8)	0.85 (0.49-1.49)
<b>Associations with average glucocorticoid dose before surgery</b>						
None (n = 3966)	342 (7.8)	Reference	93 (2.5)	Reference	107/2045 (5.2)	Reference
≤5mg (n = 1915)	205 (9.6)	1.18 (0.98-1.42)	54 (3.0)	1.13 (0.80-1.59)	90/1026 (8.8)	1.31 (1.04-1.63)
5-10mg (n = 1093)	121 (11.0)	1.28 (1.01-1.62)	31 (3.4)	1.16 (0.75-1.79)	51/530 (9.6)	1.29 (0.98-1.71)
>10mg (n = 181)	49 (16.1)	2.37 (1.63-3.44)	14 (5.0)	2.04 (1.09-3.84)	13/152 (8.3)	1.61 (0.99-2.61)

Adjusted odds ratios (aOR) and hazard ratios (aHR) from logistic and Cox regression with inverse probability weights, with separate analyses for biologics and glucocorticoids. \*Tocilizumab (n = 305) compared to abatacept (n = 841) year 2011-2015 only. \*\*Excluded from adjusted analyses because of inadequate outcomes. \*\*\*Readmissions assessed among those with discharge to home, rehabilitation facility, or skilled nursing facility. Inc/100py = incidence per 100 person years. Bolded values are statistically significant with p < 0.05.

**Conclusions:** Risk of hospitalised infection, prosthetic joint infection, and readmission after arthroplasty was similar in patients with RA treated with different biologics. In contrast, glucocorticoid use, especially >10 mg/day, was associated with greater risk of hospitalised infection and PJI.

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**OP0229** **THE ASSOCIATION OF BIOLOGIC DRUG-LEVELS WITH INFECTION RISK: RESULTS FROM THE BRITISH SOCIETY FOR RHEUMATOLOGY BIOLOGICS REGISTER FOR RHEUMATOID ARTHRITIS**

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**Background:** High dose tumour necrosis factor inhibitor (TNFi) drugs are associated with an increased serious infection (SI) risk. It is feasible that high biologic levels predict dose-dependent adverse events such as SI. No registries have systematically evaluated the effect of drug levels on infection risk.

**Objectives:** To assess the effect of biologic drug levels in rheumatoid arthritis (RA) patients on (i) all infections (AI) (ii) SI (infections requiring hospitalisation, IV antibiotics or lead to death)

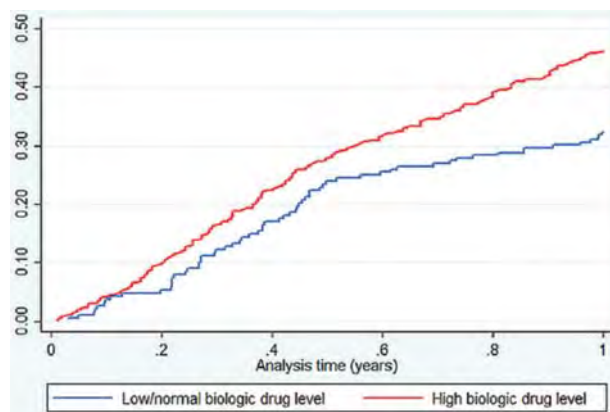
**Methods:** Patients recruited to both the British Society for Rheumatology Biologics Register-RA (safety data) and the Biologics in RA Genetics and Genomics Syndicate (serological samples) were included. Both are large national prospective RA cohorts. Biologic drug levels were measured at 3/6/12 months after biologic initiation and stratified as low/normal or high drug levels (HL) as per thresholds defined using concentration-effect curves for each drug. The risk of first and total infections within the first year was analysed. Events occurring on drug or within 90 days of last dose were included. The risk of an event was compared between low/normal vs HL groups using Cox proportional-hazard models. Factors affecting both drug levels and infection risk were adjusted for in the models.

**Results:** 703 patients (286 etanercept, 179 adalimumab, 120 certolizumab, 104 tocilizumab and 14 infliximab) had clinical data and serological samples. 74% were women, mean (SD) age 58<sup>12</sup> years, on a first biologic (89%). The crude rate/1000 pyrs was 314 and 464 for AI; 54 and 76 for SI in the low/normal and HL groups respectively. The adjusted hazard ratio for AI within the first year differed significantly between the two groups with the HL group having 50 percent higher risk of AI (HR: 1.51; 95% CI: 1.14, 2.01) (table 1). The most common types of AI in the HL group were lower (34%) and upper (16%) respiratory tract infections, urinary tract infections (15%), skin infections including shingles (8%).

Abstract OP0229 – Table 1

	Low/normal drug level (n=241)	High drug levels (n=462)
<b>All events with follow up censored at 1 year (95% CI)</b>		
<b>All infections (n)</b>	63	232
Crude rate (/1000 pyrs)	314 (245–401)	464 (408, 528)
Unadjusted HR	Ref	1.44 (1.09, 1.91)*
Adjusted HR †	Ref	1.51 (1.14, 2.01)*
<b>Serious infections (n)</b>	11	38
Crude rate (/1000 pyrs)	54 (30–98)	76 (55–104)
Unadjusted HR	Ref	1.36 (0.70–2.67)
Adjusted HR†	Ref	1.17 (0.58–2.30)
<b>First event within 1 st year (95% CI)</b>		
<b>All infections (n)</b>	46	150
Crude rate (1000 pyrs)	229 (172–256)	300 (256–352)
Unadjusted HR	Ref	1.24 (0.89–1.73)
Adjusted HR †	Ref	1.26 (0.91–1.78)
<b>Serious infections (n)</b>	6	22
Crude rate (/1000 pyrs)	29 (13–67)	44 (28–67)
Unadjusted HR	Ref	1.39 (0.56–3.44)
Adjusted HR†	Ref	1.26 (0.50–3.16)

\*p<0.05 † Adjusted for age, gender, DAS score, methotrexate use



Abstract OP0229 – Figure 1 All infection Nelson-Aalen cumulative hazard estimates

**Conclusions:** RA patients with high biologic drug levels have a higher risk of infection. Monitoring drug levels may be helpful in prediction of infection. In disease remission patients with HL, biologic dose tapering may lower infection risk.

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OP0230

#### PREDICTORS OF HYPOGAMMAGLOBULINEMIA DURING RITUXIMAB MAINTENANCE THERAPY IN RHEUMATOID ARTHRITIS: A 12-YEAR LONGITUDINAL MULTI-CENTRE STUDY

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**Background:** Rituximab (RTX) is an anti-CD20 monoclonal antibody that selectively depletes B-cell population. One of the drawbacks of a prolonged peripheral B-cell depletion is the suppression of protective antibodies and an increased risk for infectious events. However, few long-term data are available on predictors for the development of low levels of serum immunoglobulins in patients receiving repeated courses of RTX.

**Objectives:** We aimed at the identification of predictors for hypogammaglobulinemia occurrence in RA patients long-term treated with RTX in a 'real-life' setting.

**Methods:** Multicenter longitudinal observational usual care study including RA patients according to ACR<sup>1987</sup> and/or ACR/EULAR<sup>2010</sup> classification criteria followed and treated with RTX. A previous study assessing the safety profile of RTX in patients with RA reported a median follow-up of 30 months.<sup>1</sup> Therefore, we decided to include RA patients on RTX maintenance therapy, after a minimal exposition of 30 months. Serum protein electrophoresis was performed before each RTX infusion. Hypogammaglobulinemia and severe hypogammaglobulinemia were defined as total gammaglobulin <6 g/L and <4 g/L, respectively. Safety monitoring included the collection of all adverse events (AE) in particular severe infections.

**Results:** 134 patients met inclusion criteria: 113 female subjects (84.3%); mean age 52.1±11.4 years. Mean follow-up was 79.5±24.6 months and analysis was based on 854.9 patient-years (pt-yrs). Mean RTX cumulative dose was 12.0±4.9 g. Hypogammaglobulinemia (<6 g/L) occurred during the follow-up period in 23 patients (2.7 events per 100 pt-yrs), leading to an incidence of 17.1%. The mean time to development of hypogammaglobulinemia was 64±23 months. A total of 9.7% of patients had severe infections (1.5 events per 100 pt-yrs). Patients who developed hypogammaglobulinemia were more likely to experience severe infections (26.1% vs 6.3%, p=0.033). Univariate Cox analysis identified age over 65 years (HR 4.28 [95% CI: 0.92 to 19.97], p<0.001), low gammaglobulin levels prior the first RTX infusion (<8 g/L) (HR 7.35 [95% CI: 1.82 to 29.68], p<0.001) as predictors of protective factor (HR 0.26 [95% CI: 0.08 to 0.87], p=0.03).

**Conclusions:** Our results show that gammaglobulin levels of less than 8 g/L at baseline is a strong independent risk factor for developing subsequent hypogammaglobulinemia, whereas concomitant MTX therapy seems to be a protective factor in RA patients treated long-term with RTX. Identifying such predictors will raise clinicians' awareness and allow more tailored monitoring of RA patients long-term treated with RTX.

#### REFERENCE:

[1] Isvy, et al. *Joint Bone Spine* 2012.

**Disclosure of Interest:** None declared

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OP0231

#### GASTRO-INTESTINAL PERFORATIONS AMONG RHEUMATOID ARTHRITIS PATIENTS TREATED WITH BIOLOGIC DMARDS: A NATIONWIDE SWEDISH COHORT STUDY

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**Background:** Use of glucocorticosteroids and NSAIDs for the treatment of RA has been associated with an increased risk of gastrointestinal (GI) perforations. The introduction of disease modifying agents, such as methotrexate or tumour necrosis factor inhibitors (TNFi) provided a seemingly safer treatment option, but the safety of other types of biologics relative to TNFi remains unclear.

**Objectives:** To estimate the incidence of gastro-intestinal perforations among Swedish RA patients treated with TNFi and non-TNFi biologics, and compare it with the incidence among bionative patients with RA and a matched general population comparator group.

**Methods:** We performed a register-based cohort study, including all Swedish RA patients, with follow-up between 2010 and 2015. For these, all treatment initiations with biologic disease modifying anti-rheumatic drugs were identified through the Swedish Rheumatology register (SRQ), and grouped by class into TNFi and non-TNFi drugs (10 857 and 5823 treatment starts). Biologics naïve patients with RA were identified by recorded diagnosis in the Swedish National Patient Register (NPR), since 2001 (n=54,732). Five general population controls were matched to



each biologic-treated patient with RA (n=53,214) by sex, age, and geographical region. A patient could participate to several of these exposure cohorts. For each patient, follow-up under a cohort ended either with an outcome event (GI perforation identified in the NPR as an ICD10 code from a predefined list) or with the first of any of the following censoring events: emigration from Sweden, death, transition to another cohort, discontinuation of treatment (+90/+180 days lag time) or end of study period. Crude incidence rates were tabulated for each cohort and adjusted hazard ratios (HR) and 95% confidence intervals were estimated in multivariable Cox regressions, controlling for baseline differences. The final adjusted model included the following covariates: sex, age, line of biologic treatment, disease characteristics, co-medication at treatment start, co-morbidities and a history of GI perforation.

**Results:** We found 31 GI perforations among 18 604 person-years (pyr) exposed to TNFi, and 31 GI perforations among 10 947 pyr exposed to non-TNFi, corresponding to crude incidence rates of 1.67 and 2.83 per 1000 pyr, respectively. The crude incidence rate among the biologics-naïve was 2.54 while among the general population comparators it was 0.94. The rate of GI perforations remained higher in patients with RA compared to the general population after adjustment for patient characteristics, HR of 1.78 (95% CI: 1.44 to 2.17), whereas the seemingly increased rate among bionative and non-TNFi users vs TNFi was largely explained by differences in age and disease history at start of follow-up, with adjusted HRs of 1.10 (0.68–1.78) for TNFi vs bionative and 1.10 (0.63–1.91) for TNFi vs non-TNFi, respectively.

**Conclusions:** Although patients with RA had a higher rate of GI perforations than matched general population comparators, no significant differences in risk remained between bionative, TNFi or non-TNFi treated RA patients after adjusting for baseline patient characteristics.

**Disclosure of Interest:** None declared

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OP0232

#### FEMALE GENDER AND POSITIVE RHEUMATOID FACTOR PREDICT LOW SERUM INFlixIMAB LEVELS AND POSITIVE ANTI-DRUG ANTIBODIES, WHICH ASSOCIATE WITH TREATMENT FAILURE ON INFlixIMAB IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS. REPORT FROM THE SWEFOT TRIAL POPULATION

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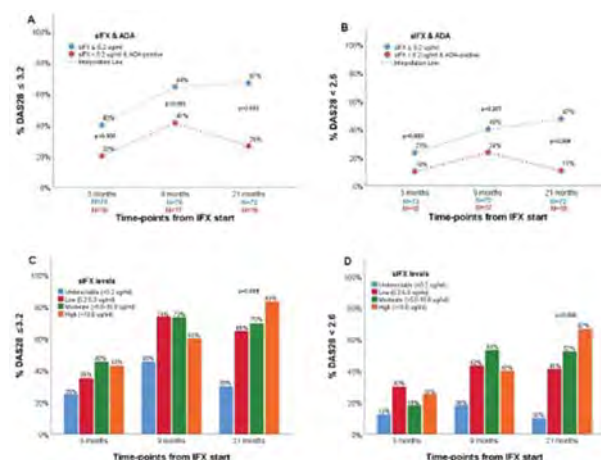
**Background:** Tumour necrosis factor (TNF) inhibitors, with infliximab (IFX) first on the market, have revolutionised treatment of patients with rheumatoid arthritis (RA). However, in a substantial proportion of patients, they lose efficiency, and up to 44% of patients have been found to develop anti-drug antibodies (ADA), leading to low serum IFX (sIFX) levels. Despite this, sIFX measurement is still rarely used for clinical decision making, and standardised clinical threshold titre levels have not been clearly defined.

**Objectives:** In an early RA trial adding IFX to methotrexate (MTX) in patients not achieving low disease activity (LDA=DAS28≤3.2) after 3 months monotherapy, we studied whether sIFX or ADA were associated with treatment outcome, and whether easily available baseline parameters predicted ADA development.

**Methods:** Of IFX-treated SWEFOT patients (n=128), 101 had available serum samples at follow-up, which were analysed for sIFX levels at 3, 9 and 21 months (routine ELISA). Samples with undetectable sIFX (<0.2 µg/ml) were analysed further for ADA using direct ELISA with plate-bound TNF. Primary and secondary outcome measures were LDA and remission (DAS28 <2.6) at 21 months. Clinical and demographic characteristics of patients at start of IFX therapy (baseline) were tested as potential predictors of ADA development, using uni- and multivariate logistic regression.

**Results:** At 3, 9 and 21 months from IFX add-on to MTX, 15%, 23% and 28% of patients, respectively, had undetectable sIFX, and 34% were ever ADA-positive. Significantly higher proportion of patients achieved LDA among those with detectable sIFX, versus undetectable sIFX and positive ADA (67% vs 26%, p=0.002, figure 1A), with similar difference for remission (47% vs 11%, p=0.004, figure 1B). When sIFX levels were further stratified into <0.2, 0.2–5.0, 5.0–10.0 and >10 µg/ml, there was a significant trend across the groups in achievement of LDA (30%, 65%, 70% and 83% respectively, p=0.008, figure 1C) or remission (10%; 41%, 52% and 67%, respectively, p=0.004, figure 1D). Women had undetectable sIFX at 21 months more often than men (35% vs 7%, p=0.006). In multivariate logistic regression analysis, the following baseline characteristics were significant

predictors of ever ADA-positivity: female gender, RF-positivity, higher tender joint count, erythrocyte sedimentation rate and lower health assessment questionnaire score (data not shown).



**Abstract OP0232** – Figure 1 Clinical outcome of patients at 3, 9 and 21 months stratified for sIFX and ADA status at the same time points. Proportion of patients in LDA (A) and remission (B) among patient with detectable sIFX level (blue dots) and ADA positive patients with undetectable sIFX levels (red dots). Proportion of patients in LDA (C) and remission (D) among four strata of patients according to sIFX levels undetectable (<0.2 µg/ml) – blue bars, low (0.2–5.0 µg/ml) – red bars, moderate (>5.0–10.0 µg/ml) – green bars, and high (>10.0 µg/ml) – orange bars.

**Conclusions:** In early RA patients receiving add-on IFX therapy, ADA-positivity or lower serum IFX levels were associated with a higher risk of not reaching treatment targets, that is LDA or remission. RF positivity and female gender, factors known to be associated with worse clinical outcomes, predicted development of ADA.

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OP0233

#### LONG-TERM SAFETY OF ADALIMUMAB IN ADULT PATIENTS FROM GLOBAL CLINICAL TRIALS ACROSS MULTIPLE INDICATIONS: AN UPDATED ANALYSIS IN 29,987 PATIENTS REPRESENTING 56,951 PATIENT-YEARS

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**Background:** Adalimumab is an anti-tumour necrosis factor- $\alpha$  (TNF- $\alpha$ ) agent indicated for the treatment of immune-mediated diseases. The long-term safety of adalimumab was previously reported in 23 458 patients representing up to 12 years of clinical trial exposure in rheumatoid arthritis (RA), juvenile idiopathic arthritis, ankylosing spondylitis (AS), psoriatic arthritis (PsA), plaque psoriasis (Ps), and Crohn's disease (CD).

**Objectives:** Here we report an updated analysis examining the long-term safety of adalimumab in adult patients with RA, AS, non-radiographic axial spondyloarthritis (nr-axSpA), peripheral SpA (pSpA), PsA, Ps, hidradenitis suppurativa (HS), CD, ulcerative colitis (UC), and non-infectious uveitis (UV).

**Methods:** Here we report an updated analysis examining the long-term safety of adalimumab in adult patients with RA, AS, non-radiographic axial spondyloarthritis (nr-axSpA), peripheral SpA (pSpA), PsA, Ps, hidradenitis suppurativa (HS), CD, ulcerative colitis (UC), and non-infectious uveitis (UV).

**Results:** This analysis included 29 987 patients, representing 56 951 patient-years of exposure (table 2). The majority of adalimumab exposure was in RA studies. The most frequently reported SAE of interest was infection (highest incidences in CD, RA, UV, and UC). Overall and for most of the adalimumab populations (AS, PsA, Ps, UC, CD, and RA), the observed number of deaths was below what would be expected in an age- and sex-adjusted population (table 1). For HS, nr-axSpA, pSpA, and UV studies, the small size of these trials precluded accurate assessment of the standardised mortality ratio, and the 95% CIs all included 1.0.

**Abstract OP0233** – Table 1 Standardised mortality ratios across indications

Indication	SMR	95% CI
RA (n=15,511)	0.74	0.63–0.87
AS (n=2026)	0.14	0.00–0.77
nr-axSpA (n=863)	1.22	0.14–4.40
pSpA (n=165)	1.84	0.21–6.65
PsA (n=837)	0.34	0.04–1.24
Ps (n=3732)	0.34	0.15–0.64
HS (n=733)	1.50	0.40–3.84
CD (n=3896)	0.44	0.14–1.02
UC (n=1739)	0.37	0.12–0.87
UV (n=464)	1.23	0.45–2.68
Total (n=29,986)	0.65	0.57–0.74

AS, ankylosing spondylitis; CD, Crohn's disease; HS, hidradenitis suppurativa; nr-axSpA, non-radiographic axial SpA; Ps, plaque psoriasis; PsA, psoriatic arthritis; pSpA, peripheral SpA; RA, rheumatoid arthritis; SMR, standardised mortality ratio; SpA, spondyloarthritis; UC, ulcerative colitis; UV, uveitis.

**Abstract OP0233** – Table 2 Incidence rates of serious adverse events of interest\*

Characteristic	RA	AS	nr-axSpA	pSpA	PsA	Ps	HS	CD	UC	UV	Total
n	15,511	2026	863	165	837	3732	733	3896	1739	464	29,987
Exposure, PYs	24,922	2120	709	101	993	5479	1198	4359	2407	1151	56,951
Serious infection	4.6	1.8	2.5	1.0	2.8	1.8	2.8	6.9	3.5	4.1	3.7
Tuberculosis	0.3	0.1	0.1	0.3	0.2	0.2	0	0.2	0.1	0.4	0.2
Active	0.5	0.1	0.1	0	0.2	0.2	0	0.1	0.1	0.2	0.2
Latent	<0.1	0	0	0.3	0	0	0	<0.1	0	0.3	<0.1
Opportunistic infection <sup>†</sup>	<0.1	0	0.1	0	0	0	0	<0.1	<0.1	0.4	<0.1
Demyelinating disorder	<0.1	<0.1	0	0	0	0	0	0.1	<0.1	0.3	<0.1
Lupus-like syndrome	<0.1	<0.1	0.1	0	0	0	0	<0.1	<0.1	<0.1	<0.1
CHF	0.2	<0.1	0	0	0	0.1	0.2	0	<0.1	<0.1	0.2
Fe new onset/ worsening	<0.1	<0.1	0	0	0.1	<0.1	<0.1	<0.1	<0.1	0	<0.1
Malignancy <sup>‡</sup>	0.7	0.2	0.1	0.3	0.2	0.3	0.3	0.4	0.6	0.7	0.6
Lymphoma	0.1	<0.1	0	0	0.2	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1
NMSC	0.2	0.2	0	0	0.1	0.1	<0.1	<0.1	<0.1	0.2	0.1
Melanoma	<0.1	<0.1	0	0	0	0.2	0	0	<0.1	0	<0.1
Sarcoidosis	<0.1	<0.1	0	0	0	0	0	0	0	<0.1	<0.1
Any AE leading to death	0.7	<0.1	0.3	1.0	0.3	0.2	0.5	1.1	0.1	0.6	0.5

AE, adverse event; AS, ankylosing spondylitis; CD, Crohn's disease; CHF, congestive heart failure; HS, hidradenitis suppurativa; NMSC, non-melanoma skin cancer; nr-axSpA, non-radiographic axial SpA; Ps, plaque psoriasis; PsA, psoriatic arthritis; pSpA, peripheral SpA; PY, patient-year; RA, rheumatoid arthritis; SpA, spondyloarthritis; UC, ulcerative colitis; UV, uveitis.  
\*Rates in events/100 PYs.  
†Total includes the 10 populations shown plus 20 patients with Behçet's disease (35.5 PY).  
‡Excludes oral candidiasis and tuberculosis.  
§Excludes lymphoma, hepatosplenic T-cell lymphoma, leukemia, NMSC, and melanoma.

**Conclusions:** This analysis of data from clinical trials of adalimumab demonstrated an overall safety profile consistent with previous findings and with the TNF inhibitor class. No new safety signals or tolerability issues with adalimumab treatment were identified and, for most indications, the mortality rate was below what would be expected in an age- and sex-adjusted population. Efficacy and safety data continue to support the well-established benefits of adalimumab for the approved indications.

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FRIDAY, 15 JUNE 2018

**Clinical and therapeutic aspects of vasculitis**

**OP0234 INFLIXIMAB THERAPY IN PATIENTS WITH TAKAYASU ARTERITIS**

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**Background:** Takayasu arteritis (TAK) is a chronic inflammatory disease that predominantly affects the aorta and its main branches. Glucocorticoids (GCs) are the cornerstones of the initial treatment of TAK. However, most patients relapse with steroid withdrawal.

**Objectives:** To evaluate the efficacy and safety of infliximab (IFX) in Korean patients with active TAK.

**Methods:** Patients with active TAK were enrolled in a single-centre prospective open label trial. Active disease was defined according to the National Institutes of Health (NIH) criteria. Concomitant GCs were tapered to prednisone ≤10 mg/day or equivalent at 2 weeks prior to the initiation of IFX. Patients received intravenous infusions of IFX, at a starting dose of 5 mg/kg at weeks 0, 2, 6, and then every 8 weeks, up to week 46, and were followed up to week 54. At week 30, patients with partial remission received increased dose of IFX by 1.5 mg/kg, and patients who failed with IFX terminated the study. At week 38 and 46, patients with symptom of active disease or high serum level of erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP), were instructed to increase the IFX dose by 1.5 mg/kg, up to 9.5 mg/kg, at each point. All the patients underwent Positron Emission Tomography-Computed Tomography (PET-CT) at baseline and week 30. The primary efficacy end point was the achievement of partial or complete remission at week 30.

**Results:** Twelve patients with TAK were enrolled and treated with IFX; 1 patient with study violation was excluded from analysis. At week 30, 3 patients (27.3%) achieved complete remission and 6 patients (54.5%) achieved partial remission. Statistically significant improvements were seen at week 30 for all of major secondary measures, including change from baseline in Indian Takayasu Clinical Activity Score 2010 ITAS 2010 (median 11.0, interquartile range [IQR] 10.0–11.8; 6.0, IQR 5.0–9.0, p=0.004), ITAS.A (14.0, IQR 12.0–14.0; 7.0, IQR 6.0–10.5, p=0.003) and serum levels of ESR (56.0, IQR 44.0–82.5; 26.0, IQR 20.0–56.5, p=0.031) and CRP (1.3, IQR 0.7–2.6; 0.2, IQR 0.1–2.1, p=0.019). PET parameters were significantly reduced, including maximum standardised uptake value (3.50, IQR 3.10–3.84; 3.10, IQR 2.49–3.27, p=0.023), target-to-vein ratio (1.34, IQR 1.13–1.95; 1.31, IQR 1.05–1.45, p=0.032), and target-to-liver ratio (2.38, IQR 1.47–3.05; 1.92, IQR 1.51–2.18, p=0.014) from baseline to week 30. Serum levels of pentraxin-3, soluble human leukocyte antigen-E (sHLA-E), interleukin-6 tended to decrease, while tumour necrosis factor-α level increased after IFX therapy. There were no serious adverse events (SAEs) or AEs necessitating discontinuation of IFX.

**Conclusions:** Treatment with IFX may lead to remission or improvement with lower glucocorticoid requirement in TAK (clinicaltrials.gov NCT02457585).

**Disclosure of Interest:** None declared

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OP0235

### INTERFERON-FREE ANTIVIRALS FOR HEPATITIS C VIRUS-ASSOCIATED CRYOGLOBULINEMIA VASCULITIS: A LONG-TERM FOLLOW-UP STUDY

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**Background:** In small-size and short term studies of hepatitis C virus (HCV)-cryoglobulinemia vasculitis (CryoVas), direct antiviral agents (DAAs) showed a better response rate and tolerance than interferon containing regimens.

**Objectives:** To evaluate the effectiveness and tolerance of all oral interferon-free DAA in a large CryoVas cohort with long-term follow-up.

**Methods:** This prospective international multicenter cohort study included 148 symptomatic HCV-CryoVas patients (53.7% with cirrhosis and 49.3% antiviral-naïve). They all received DAA, i.e. sofosbuvir (SOF) plus daclatasvir (n=53), SOF plus ribavirin (n=51), SOF plus ledipasvir (n=23), or SOF plus simeprevir (n=18), for 12 or 24 weeks. The primary endpoint was the clinical response of CryoVas symptoms at week 12 after stopping DAAs.

**Results:** 106 (72.6%) patients showed a complete response, 33 (22.6%) a partial response and 7 (4.8%) no response of CryoVas symptoms. Cryoglobulinemia was no longer found in 53.1%. A sustained virological response was obtained in 97.2%. Premature DAA withdrawal was noted in 4.1%. Two factors were associated with a poor response: a severe form of CryoVas [OR 0.33, 95% CI: 0.12 to 0.91; p=0.03] and peripheral neuropathy [OR 0.31, 95% CI: 0.11 to 0.84; p=0.02]. After a median follow-up of 15.3 months, 4 (2.8%) patients died. The final clearance rates of CryoVas manifestations were as follows: purpura (97.2%), renal involvement (91.5%), arthralgia (85.7%), neuropathy (77.1%) and cryoglobulinemia (53.8%). Only SOF plus ledipasvir regimen showed significant superiority [OR 4.09, 95% CI: 1.19 to 19.00; p=0.04].

**Conclusions:** The different DAA combinations showed high response rates of HCV-CryoVas symptoms. The tolerance was good, and the mortality rate was very low. We identified prognosis factors of response to DAA.

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OP0236

### RISK OF CARDIOVASCULAR DISEASE AND VENOUS THROMBOEMBOLISM AMONG PATIENTS WITH INCIDENT ANCA-ASSOCIATED VASCULITIS: A 20 YEAR POPULATION-BASED COHORT STUDY

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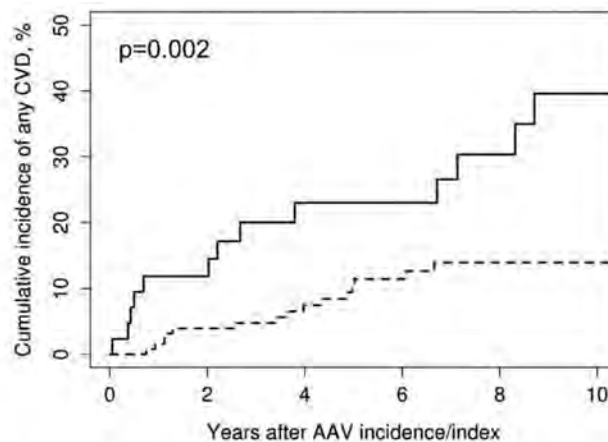
**Background:** Although modern treatments have greatly improved survival in ANCA-associated vasculitis (AAV), many patients suffer cardiovascular and thrombotic complications during long-term follow up.

**Objectives:** We aimed to assess the cardiovascular disease (CVD) and venous thromboembolism (VTE) risks among patients with newly diagnosed AAV.

**Methods:** A population-based incident AAV cohort of 58 patients diagnosed between 1996 and 2015 in Olmsted County (Minnesota, USA) was identified by medical record review. For each patient, 3 age- and sex-matched non-AAV comparators were randomly selected from the same population and assigned an index date corresponding to the AAV incidence date. Medical records of cases and comparators were reviewed for CVD events, which included cardiac events (coronary artery disease, heart failure and atrial fibrillation), cerebrovascular accidents (CVA), peripheral vascular disease (PVD) and VTE, which included deep vein thrombosis (DVT) and pulmonary embolism (PE).

**Results:** Baseline total cholesterol, high-density lipoprotein and current smoking rate were lower in AAV than comparators (p=0.03, p=0.01 and p=0.04, respectively), while other CVD risk factors and Framingham risk score were not significantly different between the 2 groups. CVD events developed in 13 patients and

17 comparators, corresponding to a >3 fold increased risk (hazard ratio [HR] 3.15; 95% confidence interval [CI]: 1.51–6.57) (figure 1). By subtypes, risks were increased for cardiac events (HR 2.96, 95% CI: 1.42 to 6.15) and CVA (HR 8.16, 95% CI: 2.45 to 27.15), but not for PVD. The HR for VTE was 3.26 (95% CI: 0.84 to 12.60), significantly increased for DVT (HR 6.25, 95% CI: 1.16 to 33.60), but not for PE (HR 1.33, 95% CI: 0.23 to 7.54).



**Conclusions:** Despite a similar prevalence of CVD risk factors at baseline, the risk of CVD is >3 fold higher and for CVA 8-fold higher in patients with incident AAV than matched comparator subjects.

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- [2] Morgan MD, et al. Increased incidence of cardiovascular events in patients with antineutrophil cytoplasmic antibody-associated vasculitides: A matched-pair cohort study. *Arthritis Rheum* 2009;60(11):3493–500.

**Disclosure of Interest:** None declared

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OP0237

### A COMPARISON OF PK AND PD OUTCOMES OF TOCILIZUMAB IN GIANT CELL ARTERITIS AFTER SC AND IV DOSING

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**Background:** Tocilizumab (TCZ), a humanised anti-interleukin-6 (IL-6) receptor monoclonal antibody, was recently approved for the treatment of patients with giant cell arteritis (GCA). Evidence was based on results of a double-blind randomised controlled trial (RCT) in GCA patients given 162 mg TCZ either weekly (QW) or every other week (Q2W) via subcutaneous (SC) route (GiACTA trial<sup>1</sup>). A second RCT conducted using 8 mg/kg TCZ given intravenously (IV) every 4 weeks (Q4W) also showed positive outcomes in GCA patients.<sup>2</sup> The double-blind dosing portion of each study lasted approximately 1 year. All three regimens (SC 162 mg QW, SC 162 mg Q2W, IV 8 mg/kg Q4W) resulted in positive outcomes for sustained remission of GCA. However, a higher benefit was noted in some key secondary efficacy outcomes with the QW vs the Q2W SC regimen.<sup>1</sup>

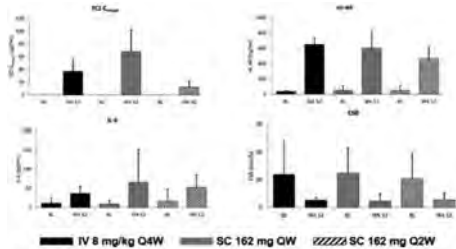
**Objectives:** To characterise the pharmacokinetics (PK) of TCZ in the GCA population and to assess the impact of the exposure differential from the three regimens on pharmacodynamic (PD) markers.

**Methods:** TCZ levels and PD biomarkers (soluble IL-6 receptor [sIL-6R], IL-6, erythrocyte sedimentation rate [ESR], and C-reactive protein [CRP]) were measured using validated assays at regular intervals throughout the dosing period from all patients in each trial. A comparison of PK and PD outcomes was conducted to understand the dose exposure–response relationships.

**Results:** At week 52, mean trough steady state exposure (C<sub>trough</sub>), a primary PK driver of TCZ efficacy, was highest from SC 162 mg QW, followed by IV 8 mg/kg Q4W, and finally SC Q2W (figure 1). Of the PD end points, at week 52, sIL-6R levels were similar for the SC QW and IV regimens but lower for the SC Q2W regimen



(figure 1), possibly demonstrating a higher level of target engagement from the SC QW and IV regimens compared with the Q2W regimen. IL-6 levels increased vs baseline after TCZ administration for all three regimens, reflecting displacement of bound, endogenous IL-6 from its receptor, consistent with the mechanism of action of TCZ. ESR levels decreased to a similar extent in response to TCZ administration with all three regimens. Change from baseline in CRP was comparable between the two SC regimens (~79%–93% reduction from baseline from the QW and Q2W regimens, respectively). Quantitative changes in CRP values are not available for the IV study.



**Abstract OP0237** – Figure 1 Mean (SD) baseline and week 52 PK/PD markers after chronic dosing with TCZ after IV and SC regimens in GCA patients.

**Conclusions:** Comparison of  $C_{trough}$  after 52 weeks of dosing with TCZ from the 8 mg/kg IV regimen with that obtained from two SC regimens showed that exposures from the IV regimen were within the range of exposures of the QW and Q2W regimens. Comparison of PD outcomes showed that all three regimens had comparable results, with the possible exception of lower levels of sIL-6R (a mechanistic marker reflecting serum concentration and target engagement) from the SC Q2W regimen. Comparability of PD results is consistent with the similar efficacy outcomes seen in the SC and IV trials.

#### REFERENCES:

- [1] Stone JH, et al. *N Engl J Med* 2017;377:317–328.
- [2] Villiger PM, et al. *Lancet* 2016;387:1921–1927.

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**Disclosure of Interest:** N. L. Mallalieu Shareholder of: Roche, Employee of: Roche, J. H. Stone Grant/research support from: Roche, Genentech, Xencor, Consultant for: Roche, Genentech, Xencor, P. Villiger: None declared, M. Klearman Employee of: Genentech, L. Brockwell Employee of: Roche, S. Dimonaco Employee of: Roche, J. E. Charon Employee of: Roche  
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#### OP0238

### ASSOCIATION BETWEEN AGE AT DIAGNOSIS AND CLINICAL PRESENTATION AND OUTCOMES OF ANCA-ASSOCIATED VASCULITIS. ANALYSIS FROM THE DCVAS STUDY

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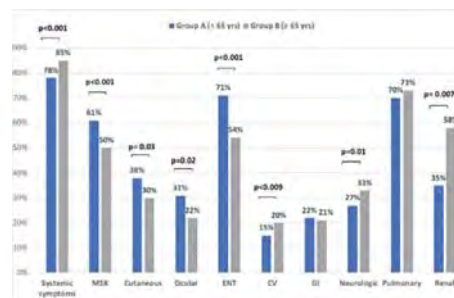
**Background:** ANCA-associated vasculitis (AAV) can affect all age groups. Nevertheless, the differences in disease presentation and outcome between younger and elderly-onset patients are still incompletely understood.<sup>2</sup>

**Objectives:** To identify distinguishing characteristics of clinical presentations, short-term outcomes and accumulated damage for AAV, based on age of disease onset.

**Methods:** We included patients with a final diagnosis of AAV: granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), eosinophilic granulomatosis with polyangiitis (EGPA) enrolled in The Diagnostic and Classification Criteria for Primary Systemic Vasculitis (DCVAS) study through May 2017. We divided the population according to age at diagnosis: <65 years old (group A) or ≥65 (group B).

**Results:** We included 1338 patients. 66% had a disease onset <65 years of age (male:50%; mean age 48.4±12.6 years); 34% had an elderly-onset (male: 46%; mean age 73.6±6). The diagnoses of GPA and EGPA were more frequent in group A (73% and 74% of patients, respectively) compared to MPA (56%),  $p<0.001$  for comparisons within each diagnostic group. P-ANCA/anti-MPO positivity was more frequent in group B (48% vs 27%,  $p=0.001$ ); c-ANCA/PR3

predominated in group A (48% vs 35%;  $p<0.001$ ). The clinical presentation at onset significantly differed between the two groups. Patients from group A had higher rates of ocular, cutaneous, and musculoskeletal involvement compared to patients in group B who experienced more systemic, renal, cardiovascular, and neurological manifestations (figure 1). Pulmonary and gastrointestinal manifestations were equally distributed between the two age groups. Vasculitis Damage Index (VDI) was significantly higher in patients from group B, with 12% of patients with a 6 months VDI score ≥5, compared to 7% in group A;  $p=0.01$ . There were 13 (1.5%) deaths amongst patients belonging to group A compared to 22 (4.8%) in group B, HR 3.44 (1.65–7.18);  $p=0.001$ .



**Abstract OP0238** – Table 1. Clinical characteristics and outcome according to age groups

	Group A (<65 years) n=878	Group B (≥65 years) n=460	p
Mean Age	48.4±12.6	73.6±6	<0.001
Diagnostic delay	14.6±34.4	11.8±32.2	0.036
Symptoms duration	19.9±35.1	18.1±33.1	0.145
<b>Type of AAV:</b>			
GPA	536 (61%)	199 (43%)	<0.001
EGPA	148 (17%)	186 (40%)	<0.001
MPA	189 (22%)	66 (14%)	0.004
p-ANCA/anti-MPO	240 (27%)	222 (48%)	0.001
c-ANCA/anti-PR3	421 (48%)	161 (35%)	<0.001
<b>VDI at 6 months follow-up</b>			
=0	236 (28%)	90 (22%)	base
=1/2	378 (44%)	184 (41%)	0.186
=3/4	187 (22%)	116 (26%)	0.010
≥5	57 (7%)	55 (12%)	0.001

**Conclusions:** Patients with AAV with elderly-onset disease display a different pattern of organ-involvement and an increased risk of significant damage and mortality compared to younger patients. A better understanding of the influence of age of onset on the clinical course of AAV could improve diagnostic and classification criteria and has implications on their pattern of presentation and subsequent clinical course.

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- [1] Watts RA, et al. *Epidemiology of systemic vasculitis. Arthritis Rheum* 2000;43:414–19.
- [2] Chen M, et al. *Antineutrophil cytoplasmic autoantibody-associated vasculitis in older patients. Medicine* 2008;87:203–9.

**Disclosure of Interest:** None declared

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#### OP0239

### PREGNANCY OUTCOMES IN PATIENTS WITH IGA VASCULITIS

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**Background:** IgA vasculitis (IgAV) is usually a self-limiting condition, but women with a history of IgAV are reported to have an increased risk of complications during pregnancy. There is however little international data regarding obstetric outcomes and risk factors for IgAV patients<sup>1</sup>.

**Objectives:** To compare pregnancy outcomes between matched controls and patients hospitalised for IgA vasculitis in Western Australia (WA), where birth centres attached to public hospitals are the principal source for delivery of free midwifery-led care.

**Methods:** Cohort study of IgAV patients (ICD-9-CM 287.0/ICD-10-AM D69.0) using non-exposed age-matched controls (1:3), where pregnancy-related events and outcomes (see table 1 for ICD codes) were extracted from state-wide hospital morbidity data for period 1980 to 2015. Results are presented as odds ratios (95% CI) versus controls.

**Results:** Pregnancy-related contacts (n=1,440) occurred in 49.5% of all female IgAV patients (n=347) and in 37% of all female controls (n=914). IgAV patients were younger at first pregnancy (23.7 vs 26.4 years, p<0.01) and had a higher overall mean number of hospital pregnancy contacts than controls (5.4 vs 3.1, p<0.001). IgAV patients experienced 168 uncomplicated live births, 93 complicated (including preterm) deliveries and 32 abortive pregnancies. The risk for abortion (OR 1.3, CI: 0.7 to 2.3), complicated delivery (OR 0.9, CI: 0.7 to 1.3) or classification as high-risk pregnancy (OR 0.94, CI: 0.74 to 1.24) was similar for IgAV patients compared to controls, despite a higher risk of hypertensive disorders (OR 4.4 CI:1–9.1).

**Abstract OP0239 – Table 1.** Diagnostic codes used for data extraction from health registries

Definition	ICD9 codes	ICD10 codes
Any pregnancy event	630–80, V22–V24, V27, V30–V40	O00–O85, Z33–Z35, Z37–Z39
Normal delivery healthy child	650.1–9	O80.1–9
Complicated delivery	652–670	O81–O85
Abortive outcome	630–640, 656.4	O00–O08.9, Z33.2
High risk pregnancy	V23–V24	O09–O09.9
Hypertension in pregnancy	642–643	O10–O15.9

**Conclusions:** In this large population-based longitudinal study, the risk for abortion or complicated pregnancies/deliveries was not increased for IgAV patients. The more frequent hospital contacts and increased risk of hypertension during pregnancy in IgAV patients had little impact on pregnancy outcome.

#### REFERENCE:

- [1] Tayabali S, Andersen K, Yoong W. Diagnosis and management of Henoch-Schonlein purpura in pregnancy: A review of the literature. *Arch Gynecol Obstet* 2012;286:825–29.

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#### OP0240 FAVOURABLE LONGTERM OUTCOME IN PATIENTS WITH GIANT CELL ARTERITIS TREATED WITH TOCILIZUMAB. REAL LIFE DATA FROM A SWISS CENTRE

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**Background:** Tocilizumab (TCZ) has been shown to be effective for achieving sustained glucocorticoid (GC)-free remission in patients with giant cell arteritis (GCA) <sup>1,2</sup>. However, data on real life patients and longterm follow up is still limited.

**Methods:** We included all patients with GCA or polymyalgia treated with TCZ iv (8 mg/kg/month) in our division from 1/2013 to 1/2018. Safety and efficacy were analysed retrospectively.

**Results:** 42 patients were analysed (69% female). Patients with involvement of cranial vessels (n=20) were older than patients without cranial involvement (n=16) (72.8±6.4 vs 63.2±10.3 years, p=0.05). Initially, 9 patients had AION, vascular stenosis was detected in 10 and aneurysms in 9 patients.

Initial vascular imaging included MR/CT angiography in 36 and 14 patients, ultrasound in 23 patients and PET CT in 8 patients.

Mean duration of TCZ therapy was 18.2±9.6 months with treatment ongoing in 33 patients. Since 2013, the time between diagnosis and initiation of TCZ as well as the number of immunosuppressants before TCZ decreased. All patients initially received iv methylprednisolone followed by standard oral tapering of prednisone starting with 1 mg/kg/d. PMR patients were started on oral GC. Low dose ASS or oral anticoagulants were used in 83% and statins in 55% of GCA patients.

Before the first RCT of TCZ in GCA was reported<sup>3</sup>, TCZ was initiated in 25 patients after failure of conventional immunosuppressives after a mean disease duration of 12.7±11.2 months. TCZ was started after failure of one immunosuppressant in 19/25 patients, 6/25 patients failed to at least 2 immunosuppressants. Since 12/2015, 17 patients were started on TCZ with a significantly shorter disease duration

(mean 4.1±5.4 months) (p=0.0047). 14/17 patients received TCZ after GC alone, in only 3 patients MTX was used before TCZ.

GC free remission was achieved in 24/33 patients (73%) with ongoing TCZ treatment. GC free and TCZ free remission was achieved in 6 patients only (4/6 PMR, 2/36 patients with GCA). Therefore, a favourable outcome was noted in 30/42 patients (76.2%). In 12 patients, TCZ was stopped in patients with GC free remission. 3/11 patients relapsed after 11, 11 and 3 months and responded to reinitiation of TCZ and GC, all achieving GC free remission again. 3 GCA patients stopped TCZ in GC free remission, but died of vascular complications during follow-up.

Infections during TCZ treatment included 2 patients who developed herpes zoster, one patient with RSV pneumonia and one patient with bronchitis, all occurring within the first 6 months of TCZ treatment and during concomitant GC therapy (9.5%). TCZ was reinitiated in all of these patients without subsequent complications. 3 patients developed ischaemic vascular complications (7.1%) during treatment with TCZ: 1 patient with cerebral infarction and 2 patients developed progressive vascular stenosis.

**Conclusions:** TCZ resulted in GC free remission in 76% of patients. Unfavourable events were limited to infections and vascular complications. However, sustained remission without TCZ was observed infrequently and was mainly limited to patients with PMR. Our data suggest that patients with GCA benefit from continuous treatment with TCZ.

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- [1] Stone JH, et al. *NEJM* 2017;377:317.  
 [2] Villiger PM, et al. *Lancet* 2016;387:1921.  
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**Disclosure of Interest:** None declared

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#### OP0241 EFFICACY OF TOCILIZUMAB IN TAKAYASU ARTERITIS: MULTICENTER FRENCH RETROSPECTIVE STUDY OF 46 PATIENTS

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#### Background:

**Objectives:** We report the long term outcome of 46 TA patients treated with tocilizumab, describe the factors of response and compare the vascular event free survival to DMARDS.

**Methods:** retrospective nationwide french study

**Results:** We observed a decrease in the NIH scale; in C-reactive protein levels and in daily prednisone dose at 3 and 6 months, respectively; p<0.0001) under tocilizumab. The overall tocilizumab failure free survival was 81% [95% CI: 0.7 to 0.95], 72% [95% CI: 0.55 to 0.95] and 48% [95% CI: 0.2 to 0.1] at 12, 24 and at 48 months, respectively. The presence of constitutional symptoms at the time of tocilizumab initiation (hazard ratio 5.6 [95% CI: 1.08 to 29], p=0.041), C-reactive protein level (hazard ratio 1.16 [95% CI: 1.01 to 1.31] for every 10 mg/L, p=0.003) were significantly associated with tocilizumab-failure-free survival. The incidence of vascular complications of TA decreased significantly under tocilizumab compared to DMARDS therapy.

**Conclusions:** This nationwide study shows that tocilizumab may reduce the incidence of vascular complications in TA.

**Disclosure of Interest:** None declared

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FRIDAY, 15 JUNE 2018

## Axial spondyloarthritis: on the interface between healthy and diseased

OP0242 **FATTY LESIONS DETECTED ON MRI SCANS IN PATIENTS WITH ANKYLOSING SPONDYLITIS ARE BASED ON THE DEPOSITION OF FAT IN THE VERTEBRAL BONE MARROW**

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**Background:** Fatty lesions (FL), similar to bone marrow oedema (BME) and sclerosis (SCL), are characteristic findings in MRI examinations of patients with ankylosing spondylitis (AS) and degenerative disc disease (DDD). It has recently been shown that FL are associated with syndesmophyte formation in AS. The anatomic correlate of FL has not been studied to date. Current assumptions are solely based on non-invasive data.

**Objectives:** To examine the cellular composition of FL in the edges of vertebral bodies of patients with AS or DDD by histology.

**Methods:** Patients with AS or DDD undergoing planned kyphosis correction surgery by spinal osteotomy (in AS) or surgery to correct spinal stenosis (in DDD) were included into this biopsy study. The spinal surgeon (HB) took all biopsies mainly in the area close to the vertebral edge in many of which FL had been seen by MRI (figure 1a for AS and 1b for DDD). Biopsies were decalcified, embedded in paraffin, cut and stained by hematoxylin and eosin. The marrow composition was analysed and the cellularity graded (% surface area) by two different investigators blinded to patients' diagnosis. Four different marrow compositions could be differentiated: (i) fat, (ii) fibrosis, (iii) inflammation and (iv) hematopoiesis (normal).

**Results:** A total of 60 biopsies mostly obtained from the lower thoracic spine and the lumbar spine of 21 AS patients (mean age 51.7 years, mean disease duration 24.6 years) and of the lumbar spine in 18 DDD patients (mean age 60.1 years) were available. On the patient level, the histological appearance of MRI-FL was different between the groups: fat marrow was present in biopsies of 19 AS (90%) but in only 5 DDD (28%) patients. Inflammatory marrow changes, resembling mononuclear infiltrates, were found in 8 AS (38.1%) and 14 DDD (77.8%) patients at areas with concomitant FL and BME on MRI, while marrow fibrosis was seen in 6 AS (28.6%) and 4 DDD (22.2%) patients at areas with concomitant FL and SCL on MRI. In the semiquantitative histopathological analysis, the mean distribution ( $\pm$ standard deviation) of the various bone marrow tissue types in the biopsies differed between the AS vs DD in a similar way, with 43% ( $\pm$ 26.3%) vs 16% ( $\pm$ 30.3%) for fatty marrow, 11% ( $\pm$ 15.5%) vs 55% ( $\pm$ 42%) for inflammatory marrow and 9% ( $\pm$ 16.1%) vs 13% ( $\pm$ 27.8%) for fibrotic marrow, respectively.

**Conclusions:** The presence of FL on MRI corresponds to fat deposition in the bone marrow of patients with advanced AS. These data show that the MRI change termed 'fatty lesion' is indeed based on the deposition of fat in the vertebral bone marrow in AS. Since vertebral bone marrow is physiologically harbouring hematopoiesis, AS seems to lead to a change in the bone marrow microenvironment with local disruption of hematopoiesis and replacement by fat. The link between fat and new bone formation should be studied in earlier disease stages.



**Disclosure of Interest:** None declared

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OP0243 **PREVALENCE OF INFLAMMATORY AND CHRONIC CHANGES SUGGESTIVE OF AXIAL SPONDYLOARTHRITIS IN MAGNETIC RESONANCE IMAGES OF THE AXIAL SKELETON IN INDIVIDUALS <45 YEARS IN THE GENERAL POPULATION AS PART OF A LARGE COMMUNITY STUDY (SHIP)**

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**Background:** Magnetic resonance imaging (MRI) is crucial for classification and diagnosis of axial spondyloarthritis (axSpA). Characteristic MRI lesions of axSpA are bone marrow oedema (BME) or structural fatty lesions (FL) of the sacroiliac joints (SIJ) and spine. However, the specificity of these lesions has been questioned, since patients with chronic back pain but no axSpA may also have a positive MRI, as shown in recent cohort studies.

**Objectives:** To investigate the prevalence of BME and FL on MRI of the spine and the SIJ in the general population.

**Methods:** Volunteers <45 years of the population based Study of Health in Pomerania (SHIP)<sup>1,2</sup> underwent MRI examinations of the spine (sagittal orientation, T1 and T2 MRI sequences) and the SIJ (coronal orientation, STIR sequences), independently of clinical symptoms. Two trained readers blinded for age and gender of the examined persons evaluated the prevalence of BME (SIJ and spine) and FL (spine) suggestive of axSpA using the ASAS definitions: a lesion in the SIJ was considered positive if located periarticularly and in the middle part of the joint and a lesion in the spine was considered positive if detected at the edge of the vertebral body). Clearly degenerative lesions involving the vertebral endplate or being accompanied by abnormalities of the intervertebral disc (protrusion or prolapse) were not counted.

**Results:** A total of 802 complete MRI sets (spine and SIJ) of 394 male (49.1%) and 408 female volunteers (50.9%) was evaluated. The mean age of all patients was 37.5 $\pm$ 6.2 years. BME in the SIJ suggestive of axSpA were found in 144 individuals (18%), with an equal distribution between males (n=74, 18.8%) and females (n=70, 17.2%). A similar pattern of BME was found in the spine, again with no differences between males and females. However, the location of the lesions was different: 9.5% had  $\geq$ 1 lesion in the cervical, 18.6% in the thoracic and 7.4% in the lumbar spine. Overall, 88.6% male and 84.6% female volunteers were found to have  $\geq$ 1% and 54.6% male and 46.1% female volunteers were found to have at  $\geq$ 3 positive spinal lesions in any spinal region. In comparison, the prevalence of FL was higher (36.7% volunteers in the cervical, 72.4% in the thoracic and 52.7% in the lumbar spine). Overall, 86.5% volunteers were found to have  $\geq$ 1% and 50.2% volunteers were found to have  $\geq$ 3 positive spinal lesions in any spinal segment.

Logistic regression analysis showed that age was the only demographic characteristic that independently contributed to the occurrence of both BME (RR=1.22, 95% CI: 1.03 to 1.46, p<0.025) or FL (RR=1.12, 95% CI: 1.07 to 1.19, p<0.001).

**Conclusions:** In this large population-based study with healthy volunteers a relatively high prevalence of inflammatory and structural MRI lesions was found. Whether these lesions are to be explained by mechanical stress needs to be further studied. The high prevalence of BME and FL in the axial skeleton in the general population indicates a limited diagnostic value of these MRI findings. Thus, those should be interpreted with caution in relation to diagnosis, classification and assessment of disease activity.

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**Disclosure of Interest:** None declared

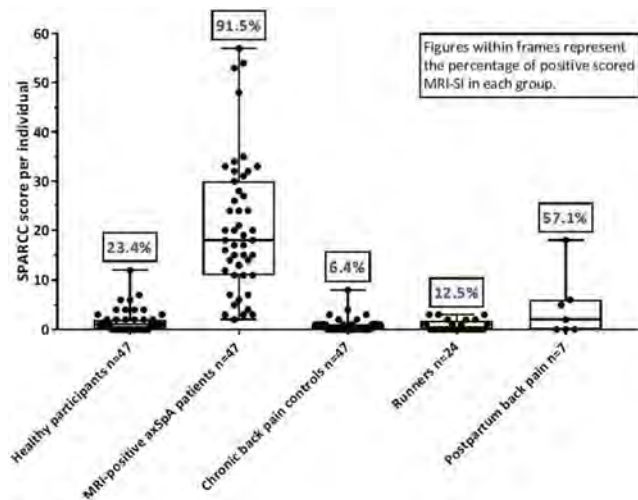
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**OP0244 AN ASAS-POSITIVE MRI OF THE SACROILIAC JOINTS CAN ALSO OCCUR IN HEALTHY INDIVIDUALS, RUNNERS AND WOMEN WITH POSTPARTUM BACK PAIN**

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**Background:** Inflammation shown on MRI of the sacroiliac joint (MRI-SI) is prevalent in axSpA (±30%) but the specificity is not well known.  
**Objectives:** To compare MRI of the sacroiliac joints (MRI-SI) of healthy, symptomless individuals and those with known mechanical strain acting upon SI joints to axial spondyloarthritis (axSpA) and chronic back pain (CBP) patients.  
**Methods:** Three trained, calibrated and blinded readers randomly scored MRI-SI of 172 subjects: 47 healthy individuals without current/past back pain; 47 axSpA patients from the SPondyloArthritis Caught Early (SPACE) cohort (with a previously confirmed positive MRI-SI); 47 CBP controls (irrespective of MRI-SI results) from the SPACE cohort; 7 women with postpartum back pain; and 24 frequent runners. Readers scored according to the ASAS definition and SPARCC score.  
**Results:** Of the 47 healthy volunteers, 11 (23.4%) had a positive MRI-SI, compared to 43 of 47 (91.5%) positive axSpA patients and 3 of 47 (6.4%) CBP patients. Of the runners, 3 of 24 (12.5%) and of the women with postpartum back pain 4 of 7 (57.1%) had a positive MRI-SI. Using a SPARCC cut-off of ≥2 for positivity, 12/47 and healthy volunteers (25.5%), 46/47 positive axSpA patients (97.9%), 5/47 CBP controls (10.6%), 4/24 runners (16.7%) and 4/7 women with postpartum back pain (57.1%) were positive. 'Deep' BME-lesions were not found in healthy volunteers, CBP patients and runners, but in 38 of 47 positive axSpA patients (80.9%) and in 1 of 7 women with postpartum back pain (14.3%).



**Conclusions:** A substantial proportion of healthy individuals without current/past back pain has a positive MRI-SI according to the ASAS definition. Deep (extensive) BME lesions are exclusively found in axSpA patients.

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**Disclosure of Interest:** None declared

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**OP0245 ABILITY OF MRI OF THE SACROILIAC JOINTS TO DIFFERENTIATE PATIENTS WITH AXIAL SPONDYLOARTHRITIS FROM WOMEN, WHO HAVE GIVEN BIRTH, PATIENTS WITH DISC HERNIATION, PERSONS WITH HARD PHYSICAL WORK, LONG-DISTANCE RUNNERS AND HEALTHY MALES**

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**Background:** Sacroiliitis detected by MRI plays a central role in the ASAS (Assessment of Spondyloarthritis International Society) classification criteria for axial spondyloarthritis (axSpA)<sup>1</sup>. However, both false positives and false negatives have been reported. We have little knowledge of the best MRI approach to separate AxSpA from other conditions that may appear like sacroiliitis.

**Objectives:** To assess the value of different types of MRI SIJ lesions to differentiate axSpA from other conditions.

**Methods:** In this prospective cross-sectional study, the MASH study, 204 participants, age ≤45 years were enrolled. All participants with pain should have VAS pain >2 (on a scale 0–10) for ≥2 months. Women with and without pain after pregnancy, patients with disc herniation and all participants without pain were not allowed to have any clinical SpA features or rheumatologic conditions. Information on HLA-B27 and CRP were not available until after the study. The study included 41 patients with axSpA, 46 women with and 14 without pain respectively related to pregnancy/labour; 12 months, 25 patients with lumbar disc herniation, 26 persons with hard physical jobs (cleaning assistants), 23 long-distance runners (≥30 km/week) and 29 healthy men. All participants underwent clinical, laboratory and MRI examination including STIR and T1-weighted sequences of the SIJs. MRIs were evaluated in random order according to the Spondyloarthritis Research Consortium of Canada SIJ MRI scores for inflammation<sup>2</sup> and structural lesions<sup>3</sup> by two experienced readers blinded to all clinical data.

**Results:** The 204 participants comprised 41.2% males, had a mean (min-max) age of 33.2 (19; 45) years, and 22% were HLA-B27 positive. The table 1 below shows the clinical characteristics within each participant group, and the preliminary MRI results based on one reader. MRI bone marrow oedema, fat metaplasia and erosions were frequently present in patients with axSpA, but were also seen in the other groups of study participants with and without pain, particularly in women with postpartum pain. MRI backfill and ankylosis were only seen in patients with axSpA.

**Abstract OP0245 – Table 1.** Clinical characteristics, SPARCC scores and distribution of SPARCC scores

Clinical characteristics, SPARCC scores and distribution of SPARCC scores							
	AxSpA (N=41)	Post-partum w/pain (N=46)	Post-partum w/o Pain (N=14)	Disc herniation (N=25)	Cleaning staff (N=26)	Long distance Runners (N=23)	Healthy men (N=29)
Age	30.9 30.0 (19; 44)	32.6 32.5 (26; 41)	33.1 32.5 (27; 41)	35.2 37.0 (21; 43)	39.1 39.0 (28; 45)	32.7 32.0 (22; 43)	30.9 30.0 (20; 43)
Male sex	26 (63.4)	0 (0)	0 (0)	11 (44.0)	0 (0)	18 (78.3)	29 (100.0)
HLA-B27	33 (80.5)	5 (10.9)	1 (7.1)	0 (0)	0 (0)	1 (4.3)	4 (13.8)
CRP (mg/L)	11.4 4.0 (0.3; 38)	1.6 0.0 (0.3; 7.1)	2.4 0.7 (0.3; 13)	2.2 0.9 (0.3; 14)	2.6 1.0 (0.3; 20)	1.4 0.4 (0.3; 7.4)	0.9 0.3 (0.3; 4.9)
Child births	1.7 2.0 (0; 7)	1.5 1.0 (1; 4)	1.9 2.0 (1; 3)	1.6 2.0 (0; 3)	2.5 2.5 (0; 5)	0.5 0 (0; 2)	NA
SPARCC Inflammation*	11.4 10.0 (0; 43)	4.2 1.0 (0; 23)	1.5 0 (0; 8)	0.3 0 (0; 5)	0.7 0 (0; 5)	0.3 0 (0; 4)	0.2 0 (0; 2)
SPARCC Fat	11.6 0 (0; 40)	0.6 0 (0; 14)	0.6 0 (0; 7)	0.4 0 (0; 4)	0.2 0 (0; 2)	0.4 0 (0; 5)	0.7 0 (0; 13)
SPARCC Erosion	4.6 1 (0; 15)	0.6 0 (0; 17)	0 0 (0; 0)	0 0 (0; 1)	0.1 0 (0; 2)	0.1 0 (0; 2)	0.1 0 (0; 3)
SPARCC Backfill	5.9 3.0 (0; 20)	0 0 (0; 0)	0 0 (0; 0)	0 0 (0; 0)	0 0 (0; 0)	0 0 (0; 0)	0 0 (0; 0)
SPARCC Ankylosis	4.0 0 (0; 20)	0 0 (0; 0)	0 0 (0; 0)	0 0 (0; 0)	0 0 (0; 0)	0 0 (0; 0)	0 0 (0; 0)
SPARCC Inflammation*	score ≥1	28 (68)	24 (52)	5 (36)	3 (12)	5 (19)	4 (14)
	≥5	26 (63)	21 (46)	4 (29)	1 (4)	3 (12)	1 (4)
	≥8	25 (61)	13 (28)	1 (7)	1 (4)	1 (4)	0 (0)
	≥10	21 (51)	8 (17)	0 (0)	0 (0)	0 (0)	0 (0)
SPARCC Fat	≥1	33 (81)	5 (11)	2 (14)	3 (12)	2 (8)	3 (10)
	≥5	29 (71)	3 (7)	1 (7)	2 (8)	0 (0)	2 (7)
	≥8	27 (66)	2 (4)	1 (7)	0 (0)	0 (0)	1 (4)
	≥10	20 (49)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)
SPARCC Erosion	≥1	27 (66)	4 (9)	0 (0)	1 (4)	1 (4)	2 (7)
	≥5	18 (44)	2 (4)	0 (0)	0 (0)	0 (0)	1 (3)
	≥8	16 (39)	2 (4)	0 (0)	0 (0)	0 (0)	0 (0)
	≥10	10 (24)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)
SPARCC Backfill	≥1	23 (56)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
SPARCC Ankylosis	≥1	17 (42)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

In cells with 1 row, values are N (%). In cells with 2 rows, values are mean (upper row) and median (lower row).  
 \*MRI SIJ scores were for SPARCC. Spondyloarthritis Research Consortium of Canada SIJ MRI scores for inflammation and structural lesions.  
 †Without scores for depth and ankylosis.  
 ‡CRP: C-Reactive Protein, HLA-B27: Human Leucocyte Antigen B27

**Conclusions:** Inflammatory lesions, fat metaplasia and erosions were most frequently occurring in patients with axSpA, but also in women with postpartum pain. The SPARCC-scores cannot separate the different groups entirely. Further detailed analysis of lesions may help differentiate axSpA from other conditions.

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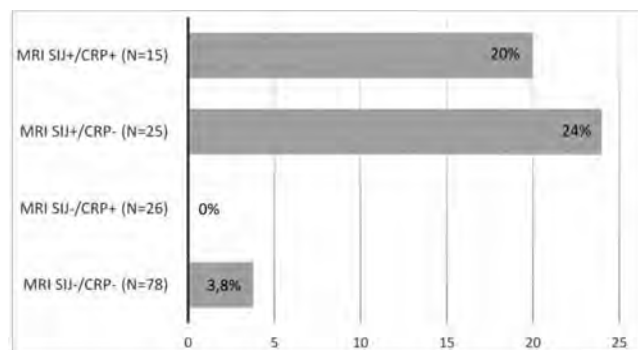
#### OP0246 INFLAMMATION ON MRI OF SPINE AND SACROILIAC JOINTS IS HIGHLY PREDICTIVE OF STRUCTURAL DAMAGE IN AXIAL SPONDYLOARTHRITIS: THE 5 YEARS DATA OF THE DESIR COHORT

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**Background:** The effect of local inflammation on structural damage in patients (pts) with axial spondyloarthritis is not well known.

**Objectives:** We aimed to test the possible effect of inflammation on structural damage both assessed by MRI and at the level of the spine and the SIJ.

**Methods:** Pts with recent onset ( $\leq 3$  years) axSpA (according to the treating rheumatologist) from the DESIR cohort were included. MRI of the SIJ (MRI-SIJ) and spine (MRI-spine) were obtained at baseline (BL), 2 and 5 years and scored by 3 trained central readers unaware of the chronology. Bone Marrow Oedema (BME) at MRI-SIJ was assessed according to ASAS definition and at the MRI-spine by the presence of  $\geq 3$  lesions. Structural damage in the SIJ (MRI-SIJ-STR) and in the spine (MRI-spine-STR) was defined by  $\geq 3$  fatty lesions. The% of structural net progression (number of 'progressors' minus the number of 'regressors' divided by the total number of pts) was assessed in subgroups according to CRP and BME status at BL. The effect of BME on MRI-SIJ on MRI-SIJ-STR and of BME on MRI-spine on MRI-spine-STR was evaluated using two types of binomial generalised estimating equations (GEE) models: i. effect at BL on 5 years incorporating measurements from all readers (GEE adjusted for reader); ii. effect of BME over 5 years (longitudinal time-lagged models with auto-regression). The final models were adjusted for variables proved to confound the association of interest (variables tested: age, gender, HLA-B27, smoking status, CRP, BASDAI, ASDAS, treatment with NSAIDs and TNFi).



**Abstract OP0246** – Figure 1 Net progression from MRI-SIJ-STR negative to MRI-SIJ-STR positive ( $\geq 3$  fatty lesions) according to baseline objective inflammatory markers:

**Results:** In total, 151 and 145 pts had complete 5 year MRI-SIJ and MRI-spine data available from 3 readers, respectively. Of the 151 pts with complete MRI-SIJ data, the net% pts who switched from MRI-SIJ-STR negative to positive ranged from 3.8% to 24% according to the presence of objective signs of inflammation at BL (figure 1). Low number of pts did not allow for similar analysis in the spine. In the multivariable analysis, both the presence of BME at MRI-SIJ (OR=4.2 [95% CI: 2.4 to 7.3]), and BME at MRI-spine (OR=8.9 [95% CI: 2.1–38.7]) at baseline were highly predictive of MRI-SIJ and MRI-spine structural progression respectively 5 years later, adjusting for CRP (only factor found to confound the association of interest). Similar positive associations were found in the longitudinal models testing the effect of BME on MRI-SIJ-STR and MRI-spine-STR over 5 years (table 1).

**Abstract OP0246** – Table 1 Effect of inflammation on MRI (ASAS definition of sacroiliitis and BME in the spine) on binary MRI structural outcomes

	$\geq 3$ fatty lesions on MRI-SIJ	$\geq 3$ fatty lesions on MRI-Spine
<b>Effect of BMI on:</b>	OR (95% CI) (n=144–197)	OR (95% CI) (n=145–197)
By GEE adjusted for reader	<b>4.2 (2.4; 7.3)*</b>	<b>8.9 (2.1; 38.7)*</b>
By longitudinal GEE adjusted for reader and repeated measurements	<b>5.1 (2.7; 9.6)£</b>	<b>15.6 (4.8; 50.3)£</b>

\* Adjusted for CRP at baseline; £ adjusted for time-varying lagged ASDAS-CRP.

**Conclusions:** Our results show that local inflammation is strongly associated with the development of structural damage over 5 years both in the SIJ and spine in early axSpA and that this effect is independent of systemic inflammation.

**Disclosure of Interest:** None declared

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#### OP0247 PERFORMANCE OF REFERRAL STRATEGIES FOR SPONDYLOARTHRITIS: A POPULATION-BASED NATIONWIDE STUDY

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**Background:** Several strategies have been proposed to promote early referral of patients with axial spondyloarthritis (axSpA), but consensus on the 'best' strategy is yet to be achieved. Moreover, few studies compared referral strategies (RS) head-to-head and, up to now, none has neither evaluated these in a 'nationwide' setting (external validity) nor assessed the entire spectrum of SpA (i.e. axSpA and peripheral SpA).

**Objectives:** To evaluate the performance of the screening strategy for SpA of a nationwide epidemiological study (EpiReumaPt), as compared to previously proposed RS.

**Methods:** EpiReumaPt was a three-stage national health survey (2011–2013) where, in the first phase, 10 661 adult participants were randomly selected and interviewed using a structured face-to-face questionnaire that included screening for rheumatic diseases (RD), such as SpA. In the second phase, positive screenings for  $\geq 1$  rheumatic complaint plus 20% negative screenings were invited for an assessment by the rheumatologist. Finally, 3 rheumatologists revised all the information and defined the final diagnosis by consensus. All participants of the second phase were included (n=3,877). Each RS (table 1) was tested against the SpA revised diagnosis using the following metrics: sensitivity, specificity, positive predictive value (PPV), and post-test probability of disease given a negative test (1-negative predictive value). RS with an imaging (e.g. MRI) or laboratory component (e.g. CRP, HLA-B27) were modified (by excluding these components) given limited data obtained in the survey (table 1). A weighting factor was used to take the survey design into account.

**Results:** From the total 3877 participants, 92 received a SpA diagnosis [weighted prevalence: 1.6% (95% CI: 1.2 to 2.1)], 3107 other RD diagnosis [e.g. knee osteoarthritis (31%)] and 678 no RD diagnosis. The ASAS RS was the most sensitive (85%) followed by the EpiReumaPt strategy (72%) (table 1). The ASAS and EpiReumaPt RS had the lowest post-test probabilities of SpA in the presence of negative screening (0.6% and 0.7% respectively), thus, yielding a marked decrease in the probability of disease if negative [(1.6–0.6)/1.6\*100=63%; (1.6–0.7)/1.6\*100=56% respectively]. On the other hand, the likelihood of SpA increased by 38% (2.2–1.6)/1.6\*100 and 119% (3.5–1.6)/1.6\*100 in case of a positive ASAS and EpiReumaPt RS, respectively. Brandt III was the least sensitive strategy in this study and not contributive to excluding SpA (1-NPV: 1.5%; pre-test probability: 1.6%), but expectedly increased the likelihood of SpA by 3.8 times if positive. The performance of the remaining RS is described in the table 1.



**Abstract OP0247** – Table 1 Performance of the referral strategies against the rheumatologist clinical diagnosis (N=3,877; pre-test probability: 1.6% – weighted national SpA prevalence)

	Sensitivity (%)	Specificity (%)	PPV (%)	1-NPV (%)
ASAS	85.4	38.8	2.2	0.6
EpiReumaPt	72.1	67.6	3.5	0.7
CafaSpA one	56.3	69.7	2.9	1.0
Brandt I	49.2	79.3	3.7	1.0
Braun IBP	47.5	78.7	3.5	1.1
MASTER	36.7	87.7	4.6	1.2
Brandt II	27.7	92.4	5.6	1.3
Hermann	22.4	93.2	5.1	1.3
CafaSpA two	15.2	95.2	4.9	1.4
Braun 2 step	15.1	95.7	5.3	1.4
Brandt III	7.9	98.4	7.6	1.5

ASAS (≥1/5+): IBP (ASAS definition), good response to NSAIDs, family history of SpA, peripheral manifestations (arthritis, enthesitis and/or dactylitis), extra-articular manifestations (uveitis, psoriasis and/or IBD); EpiReumaPt (≥1/5+): previous SpA/PsA diagnosis, IBP (≥ 3/8 features), CBP (≥ 3 months) starting <45 years and ≥ 1/6 SpA features, dactylitis, enthesitis; CafaSpA one (≥1/3+): IBP (ASAS definition), good response to NSAIDs, family history of SpA; CafaSpA two (≥2/3+): see CafaSpA one; Brandt I (≥ 1/1+): IBP (morning stiffness>30 min, pain at night/early morning, improvement by exercise; ≥1/3); Brandt II (≥ 1/1+): ≥2/3 IBP features (see Brandt I); Brandt III (≥ 1/1+): ≥3/3 IBP features (see Brandt I); Braun IBP (≥ 2/5+): start BP≤35 years, waking second half of the night, alternating buttock pain, improvement by movement, not rest; MASTER (≥ 2/3+): IBP (morning stiffness>30 min, improvement exercise, not rest, awakening in the night because of BP), good response to NSAIDs, family history of AS; Hermann (≥1/1): IBP (Callin's criteria); Braun 2 step (≥ 2/3): psoriasis, alternating buttock pain, improvement BP by exercise. HLA-B27 excluded from ASAS, Brandt I-III and Braun 2 step; elevated CRP/ESR excluded from ASAS.

**Conclusions:** For the first time, a wide range of SpA RS were tested head-to-head in a population-based setting where the ASAS and EpiReumaPt RS were shown to be the most sensitive. Our data suggest that these strategies can be effectively used as screening tools for SpA especially when laboratory and imaging data are not available.

**Disclosure of Interest:** None declared

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OP0248

#### POTENTIAL DIFFERENCES IN AXIAL SPONDYLOARTHRITIS DISEASE ACTIVITY CATEGORIZATION USING DIFFERENT MINIMUM VALUES FOR HIGH-SENSITIVITY CRP IN ANKYLOSING SPONDYLITIS DISEASE ACTIVITY SCORE CALCULATION AND DIFFERENT DEFINITIONS OF DISEASE FLARE

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**Background:** It has been recommended that the lower limit of high-sensitivity CRP (hsCRP) be restricted to 2 in the Ankylosing Spondylitis Disease Activity Score (ASDAS) calculation. Also, a definition of flare of ASDAS increase ≥0.9 was recently proposed.

**Objectives:** Using non-radiographic axial SpA (nr-axSpA) trial data, this analysis evaluated potential differences in patient (pt) categorization using different minimum values for hsCRP in the ASDAS calculation and different definitions of disease flare.

**Methods:** ABILITY-3 (NCT01808118) assessed the impact of continuation versus withdrawal of adalimumab (ADA) in nr-axSpA pts who achieved sustained remission with open-label ADA. All pts received open-label ADA 40 mg every other wk during a 28-wk lead-in period. Pts who achieved remission, defined as ASDAS inactive disease (ID, ASDAS <1.3) at wks 16, 20, 24, and 28 were randomised to 40-wk, double-blind ADA (continuation) or PBO (withdrawal). ASDAS was calculated with the full range of hsCRP (protocol-defined) and limiting hsCRP to the lowest possible value of 2 mg/L (rederived). Flare was calculated as 2 consecutive study visits with ASDAS >2.1 (protocol definition) or with ASDAS increase ≥0.9 (modified definition). Data are reported as observed (open label) and by nonresponder imputation (double blind).

**Results:** 673 pts were enrolled. At open-label baseline, mean ASDAS using the protocol-defined ASDAS calculation was 3.6 vs 3.7 when rederived. At wk 28, 295 (43.8%) pts achieved protocol-defined ASDAS ID vs 272 (40.4%) pts using the rederived ASDAS; mean ASDAS at double-blind baseline was 0.7 vs 0.9, respectively. At wk 68, significantly more pts treated with ADA vs PBO had no flare per protocol definition (69.7% vs 47.1%; p<0.001; table 1). Similar results were observed with modified definitions (table 1). At wk 68, significantly greater proportions of ADA vs PBO pts achieved ASDAS endpoints (all p<0.001), with similar results for protocol-defined and rederived ASDAS calculations, respectively: ID (57.2% vs 33.3% and 52.0% vs 29.4%), major improvement (58.6% vs 32.0% and 50.0% vs 30.7%), and clinically important improvement (67.1% vs 45.1% and 67.1% vs 44.4%).

**Abstract OP0248** – Table 1 Percentage of patients not experiencing disease flare at week 68 using protocol-defined or rederived ASDAS and/or modified flare definitions

Variable, n (%)	Adalimumab (40 mg EO/W) n=152*	Placebo n=153*	Difference, %	P value
Protocol-defined ASDAS and flare	106 (69.7)	72 (47.1)	22.7	<0.001
Rederived ASDAS, protocol-defined flare	100 (65.8)	69 (45.1)	20.7	<0.001
Protocol-defined ASDAS, modified flare definition	97 (63.8)	56 (36.8)	27.2	<0.001
Rederived ASDAS and modified flare definition	99 (65.1)	65 (42.5)	22.6	<0.001

ASDAS, Ankylosing Spondylitis Disease Activity Score; EO/W, every other week; ID, Nonresponder imputation; P value using 2-sided Pearson chi-square test. \*Efficacy outcomes were calculated based on the number of patients randomized, rather than those who would have qualified for randomization based on rederived ASDAS calculations.

**Conclusions:** At both open-label and double-blind baseline, mean ASDAS was similar, regardless of the hsCRP value cut-off used. Fewer pts in both treatment groups were categorised as not experiencing a flare when limiting the lowest possible hsCRP value to 2 mg/L in the ASDAS calculation and/or using a modified flare definition. However, treatment differences remained similar compared with the protocol-defined methodology. Results suggest infrequent clinically relevant differences in ASDAS values with use of either definition for minimum hsCRP and that the use of ASDAS >2.1 or ASDAS increase ≥0.9 as the definition of flare is reasonable.

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OP0249

#### THE CONTRIBUTION OF STRUCTURAL MRI LESIONS TO DETECTION OF SACROILIITIS IN PATIENTS IN THE ASSESSMENTS IN SPONDYLOARTHRITIS INTERNATIONAL SOCIETY (ASAS) CLASSIFICATION COHORT

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**Background:** Active lesions typical of axial spondyloarthritis (axSpA) in the sacroiliac joint (SIJ) were reported by local site readers in about 40% of patients in the ASAS classification cohort (ASAS-CC) when this study was conducted over 10 years ago<sup>1</sup>. There has been no data reported on the occurrence of structural lesions in this cohort. Since this study was conducted, there has been considerable progress in our understanding of SIJ lesions observed on MRI, which raises the possibility that MRI scans of patients in the ASAS-CC could now be interpreted substantially differently.

**Objectives:** To determine the added contribution of structural lesions in the SIJ to the evaluation of sacroiliitis in an inception cohort of patients with axSpA.

**Methods:** Recently updated MRI lesion definitions for axSpA (ASAS\_MRI\_def<sup>m</sup>) were recorded in an eCRF that comprises global assessment (lesion present/absent) and detailed scoring (SPARCC SIJ inflammation, SPARCC SIJ structural). MRI scans were available in a variety of formats (DICOM (n=175), JPEG (n=71), DICOM film(n=32)) and sequences, axial and semicoronal orientations, from 278 of the 495 cases who had MRI performed in the ASAS-CC. Image quality



was considered sufficient to record global data by 6 central readers in all cases. An additional reader assessed only images in DICOM format (n=175). Comparison of active and structural lesion frequencies typical of axSpA was assessed descriptively according to individual and majority of central readers data.

**Results:** Active lesions typical of axSpA were recorded in about 30% of cases in the cohort. Active or structural lesions typical of axSpA were recorded in about 40% of patients (table 1). Similar data was observed when active sacroiliitis was defined using the ASAS definition of a positive MRI. Structural lesions alone, without any active lesions typical of axSpA, were recorded in 6.6% of cases. Active lesions alone, without any structural lesions typical of axSpA, were recorded in 7.8% of cases. Both active and structural lesions typical of axSpA were recorded in 23.1% of cases. The frequencies of these categories were only slightly lower when majority reader data was analysed.

**Abstract OP0249** – Table 1 Contribution of structural MRI lesions to detection of sacroiliitis in the ASAS-CC. (\*Individual data from Reader; \*majority reader ( $\geq 4$ ) data)

Variable	Mean% (Range)*	Number (% of Cases)*
Active lesions typical of axSpA	31.5 (24.5-38.5)	79 (28.4%)
Active lesions typical of axSpA but not structural lesions typical of axSpA	7.8 (4.6-11.8)	7 (2.9%)
Structural lesions typical of axSpA	31.4 (23.5-39.9)	68 (28.6%)
Structural lesions typical of axSpA but not active lesions typical of axSpA	6.6 (4.2-12.7)	7 (2.9%)
Active and structural lesions typical of axSpA	23.1 (16.0-29.0)	51 (21.4%)
Active or structural lesions typical of axSpA	39.2 (28.2-48.7)	99 (41.6%)
Active lesions typical of axSpA and meets ASAS definition for positive MRI	30.0 (22.6-37.4)	79 (28.4%)
ASAS positive MRI but not structural lesions typical of axSpA	7.2 (3.4-11.3)	7 (2.9%)
Structural lesions typical of axSpA but not ASAS positive MRI	8.8 (5.0-13.0)	7 (2.9%)
ASAS positive MRI and structural lesions typical of axSpA	22.6 (15.6-28.6)	51 (21.4%)
ASAS positive MRI or structural lesions typical of axSpA	38.4 (27.7-47.9)	99 (41.6%)

**Conclusions:** Structural lesions typical of axSpA may be observed without any active lesions typical of axSpA in 5%–10% of cases presenting with undiagnosed back pain in the ASAS-CC. This is the same proportion of the cohort for which active lesions typical of axSpA are seen without any structural lesions typical of axSpA. In view of the concomitant presence of both lesions, contextual interpretation seems optimal.

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**Disclosure of Interest:** None declared

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FRIDAY, 15 JUNE 2018

## Present and future treatments for SLE, Sjögren's and APS

OP0250

### A RANDOMISED, DOUBLE-BLIND STUDY TO ASSESS THE SAFETY, TOLERABILITY AND PRELIMINARY EFFICACY OF LENIOLISIB (CDZ173) IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME

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**Background:** Primary Sjögren's syndrome (pSS) is a systemic and progressive autoimmune disease characterised by lymphoid infiltration and progressive alteration of exocrine glands secretory function. Ectopic germinal center-like structures harbour plasma cells that generate autoantibodies leading to immune complex formation. Leniolisib (CDZ173) is an oral low molecular weight compound that selectively inhibits the lipid kinase PI3K $\delta$ . In animals, leniolisib blocks PI3K $\delta$ -dependent B cell functions, disrupts germinal centre formation and immune cell trafficking, supporting the rationale for a PI3K $\delta$ -targeted therapy in pSS

**Objectives:** To evaluate the safety, tolerability, pharmacokinetics (PK) and preliminary clinical efficacy of multiple oral doses of leniolisib, after 12 weeks of treatment, in pSS patients

**Methods:** Double-blind, randomised, placebo-controlled, parallel-design study recruited 30 seropositive pSS patients with moderate to severe disease activity as determined by EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) $\geq 6$ , EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI) $\geq 5$  and stimulated

whole salivary flow rate  $>0$  mL/min. Patients were randomised in a 2:1 ratio to receive leniolisib (70 mg b.i.d) or placebo. The primary outcome was change in ESSPRI at week 12. Secondary outcomes included PK, changes in ESSDAI, the Short Form-36 (SF-36), Multidimensional Fatigue Inventory (MFI) and global Visual Analogue Scales (VAS) completed by patients and physicians. Additional assessments included lacrimal gland function and biomarkers relevant to pathway and disease

**Results:** Overall safety and tolerability profile of leniolisib was acceptable, but appeared less favourable than placebo. In particular, rash occurred more frequently in the leniolisib group (11/20 patients) compared to placebo (1/10 patients). There was a slight improvement (not statistically significant) in ESSPRI scores (dryness, pain and fatigue) favouring leniolisib. Similar trends were observed in secondary endpoints (SF-36/mental and physical, MFI, VAS completed by patients and physicians). After 12 weeks of treatment, there was a slight improvement (not statistically significant) in the lacrimal gland function in the leniolisib group compared to placebo. The observed PK profile was as expected based on healthy volunteer data. Biomarker results suggest a strong and sustained target and pathway engagement, as evidenced by inhibition of phosphorylated Akt in *ex-vivo* stimulated B cells, significant decrease in serum CXCL13 and reduced frequency of circulating Follicular T helper-like cells. There was a trend of decreasing autoantibody levels in leniolisib-treated patients

**Conclusions:** Leniolisib had an acceptable safety and tolerability profile, but caused rashes a known class effect of PI3K inhibitors. Target and pathway engagement were confirmed, however no clear efficacy signal for leniolisib was seen based on ESSPRI and ESSDAI in this Proof-of-Concept study at the studied dose.

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OP0251

### ATTAINMENT OF LOW DISEASE ACTIVITY AND REMISSION IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS WITH HIGH DISEASE ACTIVITY IN THE ATACEPT PHASE IIB ADDRESS II STUDY AND ITS LONG-TERM EXTENSION

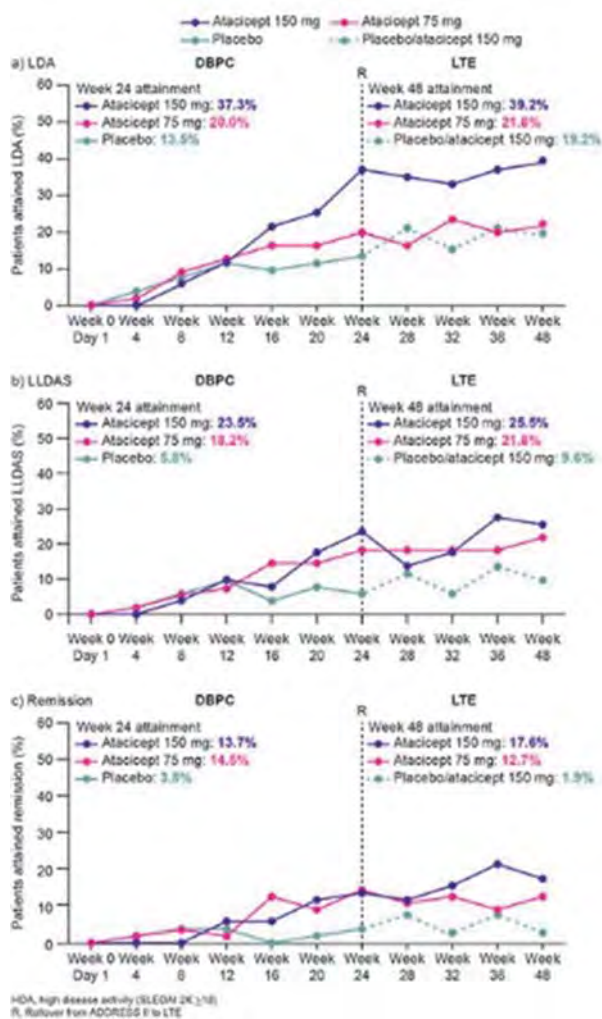
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**Background:** Low disease activity (LDA) and remission are consummate goals of SLE treatment.<sup>1</sup> Lupus Low Disease Activity State (LLDAS) is associated with reduced damage accrual,<sup>2</sup> and has been shown to be a feasible clinical trial endpoint.<sup>3</sup> In the Phase IIb ADDRESS II study,<sup>4</sup> atacept improved SRI-6 response rates and flare prevention at Week (Wk) 24 vs placebo (PBO), in patients with High Disease Activity (HDA; SLEDAI-2K $\geq 10$ ) at Screening, with an acceptable safety profile.

**Objectives:** Post-hoc analysis of ADDRESS II and its long-term extension to describe 48-wk rates of LDA and remission in patients with HDA at Screening.

**Methods:** Pts were randomised 1:1:1 to weekly subcutaneous PBO or atacept 75 or 150 mg for 24 wks in ADDRESS II. Completers entered the extension study at the same dose, except PBO patients who switched to atacept 150 mg (PBO/atacept 150 mg). This analysis includes: LDA (SLEDAI-2K $\leq 2$ ); LLDAS (SLEDAI-2K $\leq 4$  without major organ activity, no new disease activity vs previous visit, Physician's Global Assessment [PGA] $\leq 1$ , prednisone-equivalent  $\leq 7.5$  mg/day, and stable immunosuppressants); and remission (clinical SLEDAI-2K=0, PGA  $< 0.5$ , prednisone  $\leq 5$  mg/day) per definitions proposed by DORIS.<sup>1</sup>

**Results:** Of 306 ADDRESS II pts, 158 (52%) had HDA at entry; 42.4% achieved SRI-6, 23.4% LDA, 15.8% LLDAS and 10.8% remission at Wk 24. At Wk 48, 52.5% achieved SRI-6, 26.6% LDA, 19.0% LLDAS and 10.8% remission. Among the 83 HDA patients with an SRI-6 response at Wk 48, LDA, LLDAS, and remission represented increasingly stringent subsets (49.4% [n=41] attaining LDA, 34.9% [n=29] LLDAS, and 20.5% [n=17] remission). LDA, LLDAS and remission rates were higher in patients treated with atacept 150 mg vs 75 mg and PBO/atacept 150 mg (table 1; figure 1).



Abstract OP0251 – Figure 1. LDA, LLDAS and remission in patients with HDA at screening (a. LDA; b. LLDAS; c. remission)

Abstract OP0251 – Table 1 LDA, LLDAS and remission at Wk 48 of patients with HDA at screening

Endpoint	Statistics	PBO/Atacicept 150 mg* (n=52)	Atacicept 75 mg (n=55)	Atacicept 150 mg (n=51)
LDA	Attainment, n (%)	10 (19.2)	12 (21.8)	20 (39.2)
	OR [95% CI]		1.17 [0.46–3.00]	2.71 [1.11, 6.60]**
LLDAS	Attainment, n (%)	5 (9.6)	12 (21.8)	13 (25.5)
	OR [95% CI]		2.62 [0.85–8.06]	3.22 [1.05, 9.82]**
Remission	Attainment, n (%)	1 (1.9)	7 (12.7)	9 (17.6)
	OR [95% CI]		7.44 [0.88–62.71]	10.93 [1.33, 89.78]**

\*PBO pts who switched to atacicept 150 mg after Week 24; \*\*p<0.05; CI, confidence interval; OR, odds ratio

**Conclusions:** At 48 wks, patients entering the ADDRESS II study with HDA who received atacicept 150 mg were more likely to attain LDA, LLDAS and remission than those treated with 75 mg or PBO/atacicept 150 mg. These endpoints were more stringent and discriminatory than SRI-6, confirming LLDAS, LDA, and remission to be robust and meaningful endpoints for SLE trials, and adding further support for future studies of atacicept in SLE.

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**OP0252 ORGAN DAMAGE PROGRESSION AND LONG-TERM SAFETY OF BELIMUMAB (BEL) IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE): AN EXTENSION OF PIVOTAL PHASE 3 BLISS STUDIES**

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**Background:** Non-United States completers of the Phase 3 BLISS-52 (BEL110752) and BLISS-76 (BEL110751) studies could continue treatment with BEL.

**Objectives:** To evaluate long-term safety, tolerability and organ damage progression in patients with SLE treated with BEL.

**Methods:** In this multicentre, open-label long-term study (BEL112234/NCT00712933), patients received intravenous BEL every 4 weeks, plus standard SLE therapy. Safety was assessed at each visit. Organ damage (Systemic Lupus International Collaborative Clinics/American College of Rheumatology Damage Index [SDI]) was assessed as a safety endpoint every 48 weeks. The study continued until BEL was commercially available in each patient's country and included an 8 week follow-up period.

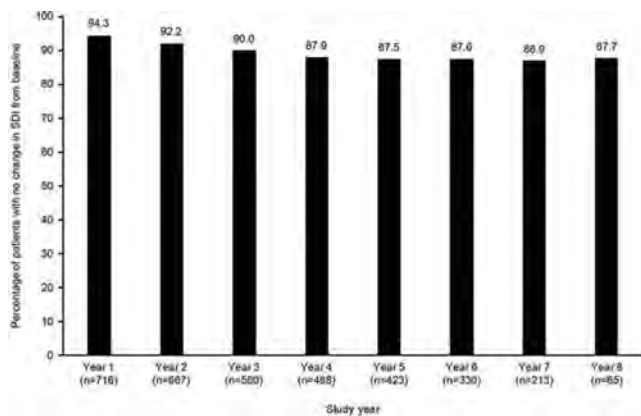
**Results:** In total, 738 patients entered the long-term study and were treated for up to 9 years (3352 patient-years). Of these, 735 (99.6%) received ≥1 dose of BEL; the mean (SD) number of infusions was 56.4 (27.02). The incidence of adverse events (AEs) remained stable or declined over time (table 1). The most common AEs were headache (n=205, 27.9%), nasopharyngitis (n=155, 21.1%), diarrhoea (n=143, 19.5%), arthralgia (n=136, 18.5%) and influenza (n=134, 18.2%). Sixty-nine patients (9.4%) experienced an AE resulting in discontinuation of BEL or study withdrawal. Eleven deaths occurred, one of which (cardiogenic shock) was possibly related to BEL. Three serious AEs of suicide attempt/ideation (0.4%) occurred. The mean (SD) SDI score was 0.6 (1.02) at baseline (prior to the first dose of BEL). At Year 8 87.7% of patients had no change in SDI score from baseline, indicating low organ damage accrual (figure 1).

<sup>a</sup>Number of patients; <sup>b</sup>included opportunistic infections, tuberculosis, herpes zoster (recurrent and disseminated) and sepsis; <sup>c</sup>two deaths during post-treatment follow-up.

**Conclusions:** BEL displayed a stable safety profile with no new safety signals. There was minimal organ damage progression.

## Abstract OP0252 – Table 1

Safety results, n <sup>a</sup> (%)	Any time post baseline n=735	Year 0–1 n=735	Year 1–2 n=701	Year 2–3 n=620	Year 3–4 n=514	Year 4–5 n=442	Year 5–6 n=345	Year 6–7 n=219	Year 7–8 n=65	Year 8 + n=6
≥1 AE	706 (96.1)	617 (83.9)	502 (71.6)	441 (71.1)	344 (66.9)	261 (59.0)	181 (52.5)	92 (42.0)	26 (40.0)	3 (50.0)
≥1 AE resulting in treatment discontinuation	69 (9.4)	13 (1.8)	13 (1.9)	20 (3.2)	10 (1.9)	7 (1.6)	5 (1.4)	0	0	0
≥1 serious AE	231 (31.4)	78 (10.6)	58 (8.3)	66 (10.6)	44 (8.6)	27 (6.1)	16 (4.6)	11 (5.0)	1 (1.5)	0
Serious infections/infestations	107 (14.6)	36 (4.9)	24 (3.4)	26 (4.2)	17 (3.3)	14 (3.2)	6 (1.7)	5 (2.3)	1 (1.5)	0
Infections of special interest <sup>b</sup>	95 (12.9)	32 (4.4)	16 (2.3)	20 (3.2)	21 (4.1)	10 (2.3)	11 (3.2)	2 (0.9)	0	0
All malignant neoplasms (except non-melanoma skin cancer)	6 (0.8)	1 (0.1)	1 (0.1)	1 (0.2)	2 (0.4)	1 (0.2)	0	0	0	0
Depression/suicide/self-injury	86 (11.7)	40 (5.4)	24 (3.4)	14 (2.3)	14 (2.7)	4 (0.9)	4 (1.2)	4 (1.8)	0	0
Death	11 (1.5) <sup>c</sup>	2 (0.3)	1 (0.1)	2 (0.3)	2 (0.4)	2 (0.5)	0	0	0	0



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OP0253

**A PHASE III RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY TO EVALUATE THE EFFICACY AND SAFETY OF ABATACEPT OR PLACEBO ON STANDARD OF CARE IN PATIENTS WITH ACTIVE CLASS III OR IV LUPUS NEPHRITIS**

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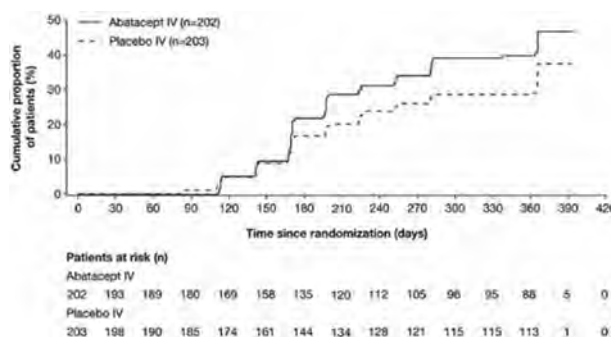
**Background:** The tenets of novel treatment strategies for active class III or IV lupus nephritis (LN) aim to improve renal response rates as well as the speed, robustness and durability of responses; decrease extra-renal SLE disease activity; reduce glucocorticoid exposure; ensure tolerability and provide acceptable treatment-related safety profile.

**Objectives:** Compare efficacy and safety of IV abatacept (ABA), a selective T cell co-stimulation modulator, vs placebo (pbo), on background therapy for active proliferative LN.

**Methods:** This was a 24-mth, randomised, Phase III, multicentre, double-blind study with an open-ended, blinded long-term extension. Patients (pts) were randomised to pbo or ABA IV 30 mg/kg for 3 mths, followed by ABA~10 mg/kg every 4 wks on a background of mycophenolate and glucocorticoids. The primary endpoint, complete response (CR) at 1 year, was a composite measure that required maintenance of glomerular filtration rate, urine protein-to-creatinine ratio

(UPCR) ≤0.5, absence of urinary cellular casts and prednisone ≤10 mg/day. We report Yr 1 data and available post-Yr 1 data for all pts, all double-blind.

**Results:** 405 pts were randomised (ABA n=202; pbo n=203). At baseline, mean age was 33 years, mean UPCR=3.78, mean serum creatinine=0.93 mg/dL and mean GFR=95 mL/min. Yr 1 study completion rates were ABA 77%, pbo 79%; fewer ABA pts discontinued during Yr 2 (ABA 14%, pbo 22%) and beyond. There were no significant differences between treatment arms in the proportion of pts with CR after 52 wks of treatment (ABA 35.1%, pbo 33.5%, p=0.73; primary endpoint). Achievement of sustained CR (2 successive visits) occurred earlier and more frequently in ABA-treated pts (figure 1). These benefits were driven by improvement in proteinuria which was seen as early as Day 85 (adjusted mean change in UPCR ABA -2.50, pbo -2.00; adjusted difference from pbo [95% CI] -0.50 [-0.84,-0.16]) and was sustained beyond Yr 2 (Yr 2: ABA -3.13, pbo -2.72; adjusted difference from pbo [95% CI] -0.41 [-0.79,-0.03]). There was no negative impact of ABA on renal function (eGFR). Few non-renal adjudicated BILAG A or B events occurred in Yr 1 (ABA=13 [BILAG A=0], pbo=12 [BILAG A=2]). Safety in Yr 1 was consistent with the known profile of ABA (serious adverse event [SAE] rate ABA 24%, pbo 19%). SAE rates after Yr 1 improved (ABA 6%, pbo 13%). The death rate was similar at Yr 2 (ABA 7, pbo 6). Improvements in SLE-related pharmacodynamic markers (C3, C4 and anti-dsDNA autoAb) were more sustained in ABA-treated pts.



**Abstract OP0253** – Figure 1 Kaplan-meier plot of time to first sustained complete renal response during year 1 of double-blind period: all randomised and treated patients

**Conclusions:** The study failed to meet its primary endpoint of higher CR rate in pts with active class III or IV LN after 1 year of abatacept treatment. Abatacept-treated pts had more rapid improvement in proteinuria, which led to earlier, sustained CR. There was a favourable safety profile extending beyond 2 years of treatment.

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OP0254

#### A PROPENSITY SCORE-MATCHED (PSM) ANALYSIS OF ORGAN DAMAGE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) FROM THE POOLED BLISS LONG-TERM EXTENSION (LTE) TRIALS VERSUS THE TORONTO LUPUS COHORT (TLC)

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**Background:** A pooled analysis of the open-label BLISS LTE studies (BEL112233/BEL112234) reported low levels of organ damage accrual (measured by Systemic Lupus International Collaborating Clinics [SLICC]/American College of Rheumatology Damage Index [SDI]) in patients who received belimumab (BEL) plus standard therapy (SoC) over a 5 year period. However, the LTE studies had no SoC arm. This post-hoc study (206347) used PSM to match BLISS LTE patients to TLC patients to define a SoC treatment comparison cohort.

**Objectives:** To assess damage accrual in patients with SLE treated with BEL plus SoC compared with PSM patients from the TLC treated with SoC alone.

**Methods:** This analysis compared the mean SDI change from baseline (over 5 years), time to SDI event (on all patients with  $\geq 1$  year follow-up), and magnitude of year-to-year SDI change (over 5 years), from baseline to Year 5 in patients treated with BEL plus SoC (pooled United States [US] and non-US data from the BLISS LTE studies), and SoC alone. Patients in the LTE and TLC were 1:1 PSM based on 16 clinical variables with a propensity score calliper  $\pm 20\%$ . Regression augmented inverse propensity score weighting (IPSW) tested the robustness of the PSM results.

**Results:** For the 5 year analysis, 181 LTE patients were matched to 181 TLC patients (mean bias 3.8%) from a larger pool of 973 patients (BLISS LTE n=592; TLC n=381). Time-to-event PSM resulted in 323 LTE and 323 TLC patients (mean bias 3.7%) from a larger pool of 1541 patients (BLISS LTE n=949; TLC n=592). The mean SDI score change from baseline in the BEL group was 0.265 (95% confidence interval [CI]: 0.180, 0.350) compared with 0.718 (95% CI: 0.547, 0.889) in the SoC group, resulting in a BEL treatment effect of  $-0.453$  fewer SDI units (95% CI:  $-0.646, -0.260$ ;  $p < 0.001$ ) over 5 years compared with SoC alone. The IPSW model produced similar results ( $-0.374$ , 95% CI:  $-0.512, -0.236$ ;  $p < 0.001$ ). Patients treated with BEL were 60% less likely to progress to a higher SDI score over any given year of follow-up compared with SoC patients (hazard ratio 0.397, 95% CI: 0.275, 0.572;  $p < 0.001$ ). A patient receiving BEL has a 3.1% annual probability of organ damage progression compared with a 7.5% annual probability with SoC. Among the 646 time-to-event matched patients, there were 49 increases in SDI over the first 5 years in the BEL group and 102 in the SoC group. Of these, 4.1% (n=2/49) of the BEL group had an SDI increase  $\geq 2$  compared with 25.5% (n=26/102) of the SoC group. Therefore, for patients who experienced any increase, the likelihood of experiencing a  $\geq 2$  point SDI increase was 6-times greater in the SoC group (25.5/4.1=6.22;  $p=0.002$ ).

**Conclusions:** This PSM analysis demonstrates that BEL plus SoC reduces, and slows the rate of organ damage progression and reduces the magnitude of progression compared with SoC alone.

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OP0255

#### IDENTIFICATION OF CLINICAL AND SEROLOGICAL PREDICTIVE FACTORS OF RESPONSE TO RITUXIMAB TREATMENT IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) PATIENTS

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**Background:** Response to Rituximab (RTX) varies significantly between SLE patients. Ethnicity may play a role in these differences, and a possible relationship has been suggested between the clinical response to RTX and the presence of certain auto-antibodies (ab) (anti-ENA and anti-dsDNA ab) and C3 levels at baseline.

**Objectives:** The aim of this study was to identify biomarkers that could predict the response to RTX treatment in SLE patients.

**Methods:** This was a cross-sectional study of 121 SLE patients treated with RTX in UCLH between 2000 and 2016. Demographic, clinical and serological data were analysed. Disease activity was evaluated using the BILAG index. Patients were categorised as 'Responders' if all or some of the As and Bs from the BILAG score at the time the RTX was given were lost at 6 and at 12 months, and as 'Non-Responders' if none of the As and Bs were lost. Relapse after RTX treatment was defined as development of a new BILAG Grade A or B in any system. A uni and multivariate regression analysis were performed to identify predictive factors of response to RTX utilising a combination of clinical and biological markers.

**Results:** At 6 and at 12 months, 85% and 70% respectively of our patients had responded clinically to the RTX treatment. 24% of patients relapsed during the year after RTX. In the univariate analysis, constitutional symptoms at diagnosis (crude OR (95% CI): 5.66 (1.53–20.88),  $p=0.009$ ) and the absence of musculoskeletal disease at the time of RTX (0.27, (0.09–0.81),  $p=0.019$ ) were related to response at 6 months. In the multivariate analysis, both remained significant, (adjusted OR (95% CI)): 5.33 (1.39–20.41),  $p=0.014$  and 0.26 (0.08–0.81),  $p=0.021$  respectively. With respect to the response at 12 months, in the univariate analysis the presence of arthritis as the main indication for RTX (3.16 (1.31–7.58),  $p=0.010$ ), the absence of renal disease at diagnosis (0.36 (0.15–0.86),  $p=0.022$ ) and of cardiorespiratory disease at the time of RTX (0.29 (0.09–0.89),  $p=0.031$ ), less than one anti-ENA ab (0.28 (0.12–0.66),  $p=0.003$ ), low levels of C3 at diagnosis (0.29 (0.09–0.89),  $p=0.031$ ), increased anti-dsDNA ab levels (0.38 (0.17–0.89),  $p=0.025$ ) and decreased C3 levels (0.27 (0.11–0.63),  $p=0.002$ ) before RTX were related to the response. In the multivariate analysis, only the absence of more than one anti-ENA showed significance (0.30 (0.11–0.82),  $p=0.020$ ). Having more than one anti-ENA was related to relapse (3.30 (1.36–8.05),  $p=0.009$ ), while having arthritis as the main indication for RTX therapy was associated with a lower risk of flare (0.26 (0.10–0.64),  $p=0.004$ ). On the multivariate analysis, having arthritis remained significant (0.29 (0.11–0.75),  $p=0.010$ ).

**Conclusions:** There is a relation between the presence of more than one anti-ENA ab and a worse response to treatment at 12 months and a higher risk of flaring. Having arthritis at the time of RTX leads to a negative response at 6 months but a lower risk of flare before 1 year.

**Disclosure of Interest:** None declared

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OP0256

#### HYDROXYCHLOROQUINE REDUCES RISK OF INCIDENT DIABETES MELLITUS IN PRIMARY SJÖGREN SYNDROME PATIENTS: A PROPENSITY SCORE MATCHED POPULATION-BASED COHORT STUDY

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**Background:** HCQ is an antimalarial drug that is widely prescribed for the treatment of Sjögren syndrome. Glucocorticoids may alter glucose metabolism and contribute to diabetes mellitus. Treatment for primary Sjögren syndrome (SS) sometimes requires glucocorticoids that may worsen glucose homeostasis. HCQ can reduce diabetes risk in SLE and RA.

**Objectives:** This study aimed to investigate the association of HCQ use and diabetes mellitus risk in primary SS patients.

**Methods:** This nationwide, population-based cohort study was conducted using the Taiwan National Health Insurance Research Database. In the period 2002–13, 7311 newly diagnosed primary SS patients were identified after excluding those with a previous diagnosis of RA, SLE or diabetes mellitus. The propensity score matched 4874 patients with at least 6 month hydroxychloroquine exposure after diagnosis and 2437 patients without. Incidence of diabetes mellitus was identified as a new diagnostic code using a diabetes mellitus-specific medication.

**Results:** Four hundred and ninety-seven newly diagnosed diabetes mellitus patients were identified among primary SS patients (4874 had taken HCQ and 2437 had never taken HCQ), with an average follow-up period of 4.9 years. Compared with patients without HCQ treatment, the hazard ratio (HR) of diabetes

mellitus in patients taking HCQ at a cumulative dose  $\geq 175$  g was reduced [HR 0.60 (95% CI: 0.45 to 0.80),  $p < 0.001$ ]. Higher prednisolone-equivalent dose ( $\geq 88$  defined daily dose) was associated with increased risk of developing diabetes mellitus [HR 1.50 (95% CI: 1.11 to 2.03),  $p = 0.001$ ], which was reduced by concomitant HCQ use at a cumulative dose  $\geq 374$  g [HR 0.34 (95% CI: 0.22 to 0.56),  $p = 0.001$ ].

**Conclusions:** This propensity score matched analysis of Taiwanese patients with primary SS found that use of HCQ is associated with reduced risk of incident diabetes mellitus in a dose-dependent manner. High-dose glucocorticoids increase the risk of diabetes, which can be decreased by concomitant HCQ use.

**Disclosure of Interest:** None declared

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**OP0257 DECREASE OF AUTOPHAGY IN PERIPHERAL BLOOD MONONUCLEAR CELLS FROM SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS TREATED WITH BELIMUMAB**

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**Background:** Autophagy is a conserved catabolic process that degrades cytoplasmic constituents and organelles in the lysosome, promoting the recycling of cellular nutrients, and is also a key mechanism for protein homeostasis and quality control<sup>1</sup>.

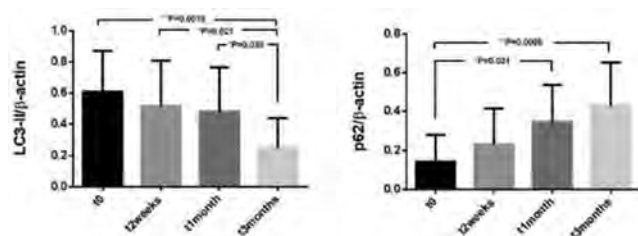
T lymphocytes from patients with systemic lupus erythematosus (SLE) are resistant to induction of autophagy<sup>2</sup>.

Belimumab (BLM), a human monoclonal antibody that inhibits B lymphocyte stimulator (BLYS), is the first biological drug to be approved for the treatment of SLE. BLM seems to play a role in modulating the signalling cascade involved in the regulation of autophagy, blocking the binding of soluble BLYS to its receptors (B cell activating factor receptor, BAFF-R; B cell maturation antigen, BCMA; transmembrane activator and calcium modulator and cytoplasmic ligand interactor, TACI), mainly expressed on B cells and plasmacells<sup>3</sup>.

**Objectives:** The aim of this study was to evaluate the autophagy process by means the expression of LC3-II and p62 markers in lysates of peripheral blood mononuclear cells (PBMCs) from SLE patients at baseline (t0) and after 2 weeks (t2weeks), 1 month (t1month), and 3 months (t3months) of treatment with BLM. We also investigated the presence of BLYS receptors on T cell subsets.

**Methods:** We enrolled 15 consecutive patients who started treatment with BLM (M/F, 0/15; mean age, 44.3 years, range 30–54 years; mean disease duration, 242.6 months, range 48–432 months). All patients fulfilled the American College of Rheumatology revised classification criteria<sup>4</sup>. PBMCs from SLE patients were lysed in lysis buffer and analysed to evaluate autophagy, monitoring LC3-II and p62 levels by Western blot. Flow cytometry was performed for surface phenotyping of freshly isolated PBMCs, using conjugated monoclonal antibodies against human CD4 and CD8; anti-human BAFF-R, BCMA, and TACI polyclonal antibodies were used to detect BLYS receptors on T cells subsets.

**Results:** LC3-II expression levels in PBMCs from SLE patients decreased after 3 months of BLM therapy and, in the same lapse, p62 levels increased (figure 1;  $p < 0.05$  for all the experimental conditions). BAFF-R and BCMA were expressed on CD4<sup>+</sup> (Mean Fluorescence Intensity -fold increase-, MFI=1.6 and 1.2, respectively;  $p < 0.05$ ) and CD8<sup>+</sup> (MFI=1.6 and 2.5;  $p < 0.05$ ) T cells, while TACI was expressed only on CD8<sup>+</sup> T cells (MFI=1.2;  $p < 0.05$ ).



**Conclusions:** In the present study we demonstrated, for the first time, the expression of BAFF-R, TACI and BCMA in CD4<sup>+</sup> and CD8<sup>+</sup> T cells from SLE patients, and that BLM treatment was able to decrease the levels of autophagy in PBMCs. We can speculate that BLM could mediate this effect by blocking the binding of BLYS with its receptors.

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FRIDAY, 15 JUNE 2018

**From cartilage to bone**

**OP0258 EFFICACY OF THE HIGHLY SELECTIVE ADAMTS-5 INHIBITOR GLPG1972 IN THE RAT MENISCECTOMY MODEL**

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**Background:** Aggrecan cleavage is an early process in cartilage degradation observed in OA. As a result, aggrecanase inhibition is an attractive therapeutic strategy for the treatment of OA.<sup>1,2</sup> A disintegrin and metalloproteinase with thrombospondin motifs-5 (ADAMTS-5) is an aggrecanase playing a key role in the catabolic events leading to OA.<sup>3</sup> We previously described the pharmacological characterisation of GLPG1972, a potent, selective and orally bioavailable ADAMTS-5 inhibitor showing anti-catabolic activity in cartilage explants and displaying disease-modifying OA drug (DMOAD) potential in the destabilisation of the medial meniscus (DMM) model in mice.<sup>4,5</sup>

**Objectives:** In this communication we report the activity of GLPG1972 in a second model of surgery-induced OA, the rat meniscectomy (MNX) model.<sup>6</sup>

**Methods:** OA pathology was induced by meniscectomy in the right hind leg of each rat. On day 1 post surgery, rats were randomly assigned to a treatment group (n=20 per group) according to their body weight. GLPG1972 was administered orally over 3 weeks at dose levels of 10, 25 and 50 mg/kg b.i.d. At sacrifice, the right tibias were collected and processed for histological analysis. OA development in the tibial plateau was evaluated using the OARSI score. The following structural parameters were measured by imaging histomorphometry analysis: subchondral bone plate thickness, proteoglycan content and fibrillation index. Blood samples were collected at steady state at predose, 1, 3 and 6 hour post-dose for the determination of GLPG1972 plasma concentrations.

**Results:** Three weeks post-surgery, a significant reduction in OARSI score compared to vehicle-treated rats was observed with GLPG1972 at 25 and 50 mg/kg b.i.d. (–24% and –23%, respectively). Treatment with GLPG1972 also resulted in a significant reduction in cartilage fibrillation as of 25 mg/kg b.i.d. and prevented proteoglycan loss and subchondral bone plate thickening at all doses. At 25 mg/kg b.i.d. GLPG1972 average plasma concentration over 24 hour was found to be in line with the value observed in other rat MNX experiments (385 ng/mL). GLPG1972 bio-distribution in the target tissue was also determined: the average condyle to plasma ratio was found to be 0.14.

**Conclusions:** Oral dosing with GLPG1972 in rat MNX model resulted in significant chondroprotection confirming the DMOAD potential of GLPG1972. A Phase 1 first-in-human study was successfully completed with GLPG1972 (NCT02612246), and a dose-escalation Phase 1b study in OA patients is ongoing (NCT03311009). GLPG1972 is a promising OA drug candidate and a Phase 2 program is currently under preparation.

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OP0259

### ZCCHC5, A LTR RETROTRANSPONON-DERIVED NEOFUNCTIONALIZED GENE, IS ESSENTIAL FOR THE TRANSCRIPTIONAL ACTIVITY OF SOX9 AND THE EXPRESSION OF COL2A1 IN CHONDROCYTES AND IS DOWNREGULATED IN OA CARTILAGE

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**Background:** Retrotransposon-derived DNA sequences occupy approximately 40% of the mammalian genome, compared with only 1.5% of protein coding genes, and are a source of variation in the genome. LTR-derived gene *ZCCHC5* (*Mart3*) is a member of *gag*-related retrotransposon family that has lost the ability to retrotranspose. *ZCCHC5* gene encode a protein of approximately 53 Kd and contains a nucleic acid binding domain (CX<sub>2</sub>CX<sub>4</sub>HX<sub>4</sub>C), a *gag*-like region within the intact ORF and a homeobox associated leucine zipper motif indicating that this gene may have acquired new function(s) in the cell. Expression and function of *ZCCHC5* in degenerative joint diseases such as OA or other diseases has not been explored.

**Objectives:** The aim of this study was to investigate whether *ZCCHC5* is expressed in OA cartilage and chondrocytes and whether it is involved in the regulation of catabolic and/or anabolic factors in chondrocytes and its modulation under pathological conditions.

**Methods:** Chondrocytes were derived by the enzymatic digestion of human OA and normal C57BL6 mouse cartilage. Total RNA was prepared using Trizol and was made DNA-free using on-column digestion. mRNA expression was quantified using TaqMan assays. Protein expression was determined by immunohistochemistry (IHC) and Western blotting (WB) with validated antibodies. siRNA mediated depletion or plasmid mediated overexpression of *ZCCHC5* gene was used to study its role in chondrocyte function under pathological conditions. Luciferase reporter vectors were used to study promoter activity in human chondrocytes.

**Results:** TaqMan, WB and IHC analyses revealed that the expression of *ZCCHC5* was very low in the damaged OA cartilage compared to the levels detected in normal cartilage and the unaffected cartilage of the same patient. Stimulation of human and mouse chondrocytes with IL-1 $\beta$  significantly decreased the expression of *ZCCHC5* ( $p < 0.05$ ) which correlated with the inhibition of COL2A1 expression and upregulation of MMP-13. Overexpression of *ZCCHC5* upregulated the COL2A1 mRNA and protein levels which were not suppressed by stimulation with IL-1 $\beta$ . Importantly, in these cells expression of MMP-13 was low and remained suppressed under pathological conditions. In contrast siRNA mediated depletion of *ZCCHC5* expression in chondrocytes abrogated the protective effect on COL2A1 expression and increased the level of MMP-13 mRNA and protein upon treatment with IL-1 $\beta$ . Additionally, depletion of *ZCCHC5* eliminated the SOX9 activity and COL2A1 promoter activation in human chondrocytes but this was reversed by reintroduction of *ZCCHC5* expression indicating that *ZCCHC5* plays an important role in SOX9 activity and COL2A1 transcription.

**Conclusions:** Our data for the first time demonstrate that a LTR retrotransposon-derived neogene *ZCCHC5* plays a key role in maintaining the differentiated functions of adult articular chondrocytes. Its repression in OA may contribute to cartilage deterioration by blocking chondrocyte anabolic functions and by enhancing expression of catabolic factors. Taken together, our data revealed a previously unidentified role of *ZCCHC5* in a disease pathogenesis and uncovered a potential therapeutic approach to limit/reverse cartilage damage in OA.

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**Disclosure of Interest:** None declared

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OP0260

### TARGETING NEUTROPHIL MICROVESICLES TO DAMAGED CARTILAGE USING ANTIBODIES TO POST-TRANSLATIONALLY MODIFIED COLLAGEN II

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**Background:** Microvesicles (MV) are extracellular vesicles released from the plasma membrane of cells. MV derived from neutrophils (PMN) have been shown to penetrate cartilage and exert chondro-protective effects in inflammatory arthritis 1-2.

Collagen type II (CII) is the most abundant protein found in cartilage. Inflammation in the joint results in post-translational modification of collagen II (CII) by reactive oxygen species (ROS). We have produced a single chain variable fragment (scFv) antibody specific to CII modified by ROS, namely anti-ROS-CII<sup>3</sup>. We hypothesise that loading anti-ROS-CII upon MV will localise them to the arthritic cartilage.

**Objectives:** The main objectives of this study were: i) Load anti-ROS-CII upon MV using aqueous energy dissemination; ii) Assess incorporation of anti-ROS-CII upon MV *in vitro* and iii) Validate the localisation and therapeutic potential of the enriched microvesicles in an *in vivo* model of arthritis.

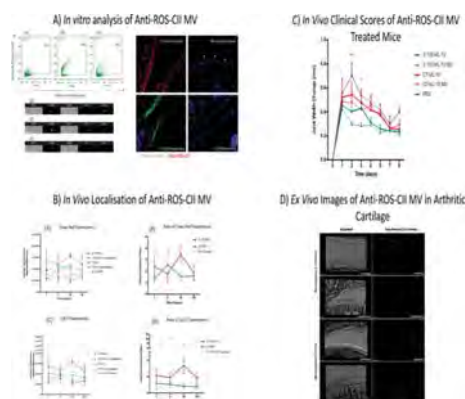
**Methods:** Anti-ROS-CII were produced in house. Human PMN MV from healthy donors were isolated as previously described<sup>4</sup>. Anti-ROS-CII were intercalated upon MV using 100 ug 1,2-dioleoyl-*sn*-glycero-3-phospho-L-serine by aqueous energy dissemination, as previously described<sup>4-5</sup>. Incorporation was assessed by ImageStream<sup>X</sup> (IS<sup>X</sup>), ELISA, NanoSight and immunofluorescence.

*In vivo* experiments were performed in an Antigen Induced Arthritis (AIA) mouse model. Localisation was assessed by IVIS Imaging following intravenous treatment of enriched MV. *Ex vivo* IVIS imaging was performed to confirm *in vivo* data. *In vivo* experiments were also conducted using MV enriched with anti-ROS-CII fused to vIL-10 and anti-mTNF therapies. Clinical scores were assessed throughout. Knee joints were harvested and snap frozen to detect the presence of enriched MV in the arthritic cartilage by confocal microscopy, and for qPCR analysis.

**Results:** Incorporation of anti-ROS-CII upon MV was observed by ImageStream. Antibodies present on the MV retained their binding capabilities, as shown by ELISA. Strong microvesicle fluorescence was detected in the arthritic cartilage of mouse tissue sections when using anti-ROS-CII enriched MV as a primary incubation.

*In vivo* studies exhibited the ability of the enriched MV to localise specifically in the arthritic joint. *Ex vivo* IVIS knee imaging confirmed *in vivo* results. *Ex vivo* knee cryosections showed the presence of enriched MV specifically within the arthritic cartilage.

*In vivo* treatment studies using anti-ROS-CII fused to anti-inflammatory therapeutics led to a significant reduction in knee swelling.



**Conclusions:** In this study we have demonstrated the ability to use aqueous energy dissemination to successfully enrich MV with antibodies. These enriched MV are able to localise in the arthritic joint and deliver anti-inflammatory therapeutics.

Overall, this study demonstrates the attainability of targeting a biological scaffold to the arthritic joint. The potential of co-delivering MV alongside anti-inflammatory therapeutics is paramount to simultaneously protect cartilage and reduce inflammation.

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**Disclosure of Interest:** None declared

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OP0261

### RETINOIC ACID IS REGULATED BY CARTILAGE INJURY AND IS ANTI-INFLAMMATORY IN HAND OSTEOARTHRITIS

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**Background:** A Genome-Wide Association Study (GWAS) in hand OA has identified the association of hypomorphic variants within *ALDH1A2* and severe hand OA (Styrkarsdottir U, et al. 2014). This gene encodes the enzyme catalysing the production of all-trans retinoic acid (atRA). atRA has an essential role in embryonic limb development, but its role in adult cartilage and in OA remains unclear. Previous work from our lab has shown that cartilage injury activates inflammatory signalling and regulates the expression of inflammatory genes.



Trapeziectomy is a surgical treatment for patients with intractable base of thumb OA and is a good source of hand OA cartilage.

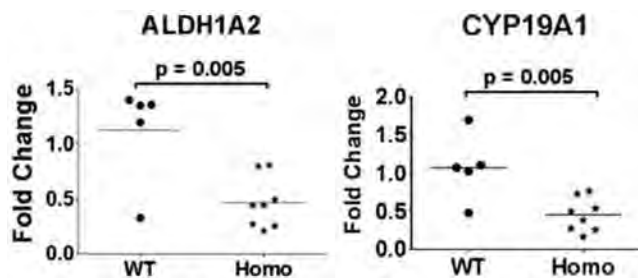
**Objectives:** The aim of this study was to investigate the expression of atRA-dependent and inflammatory genes in the cartilage of patients and to examine these with respect to the presence/absence of polymorphic ALDH1A2 variants. We also investigate the regulation of atRA upon cartilage injury and its effect on injury-induced inflammatory gene regulation.

**Methods:** We collected 26 trapeziectomy samples, and dissected the cartilage within one hour of collection. Genomic DNA was extracted for the identification of the two common variants (SNP rs4238326 and SNP rs3204689). Expression levels of atRA-dependent and inflammatory genes were tested by RT-PCR.

Healthy cartilage was obtained from femoral heads of 5-week-old mice and porcine metacarpophalangeal joints of 3–6 months old pigs. Gene regulation upon cartilage injury was tested. To examine the role of specific injury-induced pathways, porcine joints were pre-injected with selective inhibitors to: TGF $\beta$ R, FGF2R, TAK1 and CYP26, 1 hour prior to injury.

**Results:** Polymorphic variants in ALDH1A2 were common in this patient population and we identified 8 patients homozygous for both variants, and 5 patients who were wild type for both variants. mRNA levels of ALDH1A2 and atRA-dependent gene CYP19A were significantly lower in the homozygous group compared to wild type (figure 1). There were also trends in the regulation of several other atRA-dependent genes. Conversely, inflammatory genes such as HAS1, TSG6 and ADAMTS5 showed a general increase in homozygous patients.

Cartilage injury in both porcine and murine tissue led to a rapid down-regulation of atRA-dependent genes (CYP26s and RARs). Injecting joints with a potent TAK1 inhibitor prevented the drop of atRA-dependent genes. Prior injection of the joint with a CYP26 (enzymes that normally break down atRA) inhibitor, restored levels of atRA-dependent genes after injury and suppressed injury-induced inflammation genes.



**Conclusions:** Polymorphic variants in ALDH1A2 are associated with significantly lower levels of ALDH1A2 and CYP19A1 mRNA in hand OA cartilage. Adult articular cartilage constitutively produces atRA, and this is strongly suppressed by mechanical injury through TAK1 activation. Preventing the drop in cellular atRA upon injury, by pre-incubating the joint with a CYP26 inhibitor, restores atRA levels and leads to a reduction in inflammatory gene regulation. These results indicate that atRA plays an important anti-inflammatory role in cartilage and provides a potential novel therapeutic strategy to treat hand OA.

**Disclosure of Interest:** None declared

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#### OP0262 DISEASE MODIFYING EFFECTS OF THE CANINE IL4-10 FUSION PROTEIN IN THE CANINE GROOVE MODEL OF OSTEOARTHRITIS

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**Background:** An ideal disease modifying osteoarthritis (OA) drug should have analgesic, chondroprotective and anti-inflammatory effects. A fusion protein of Interleukin 4 and 10 (IL4-10FP) might have these effects.

**Objectives:** This study evaluates the effects of canine IL4-10FP (cIL4-10FP) in the canine Groove model of OA.

**Methods:** In 8 skeletally mature dogs, knee OA in the right leg was induced according to the Groove model. After 6 weeks of OA development, intra-articular injections in the affected knee with either PBS (500  $\mu$ l; n=4) or cIL4-10FP (10  $\mu$ g/500  $\mu$ l; n=4) were given weekly for 10 weeks. The contra-lateral joints served as a healthy control.

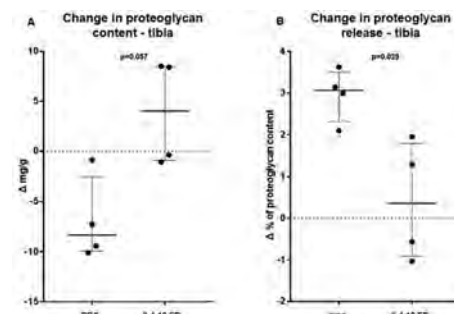
Force plate analysis (FPA) was used to determine joint loading as a surrogate marker of pain. The ratio of the affected over the contra-lateral control joint was calculated for each dog for each time point. FPA was performed before OA

induction to determine baseline values, and before and 24 hours after the 1<sup>st</sup>, 6<sup>th</sup> and 9<sup>th</sup> intra-articular injection. A linear mixed model was used to evaluate effects of injections. After 10 weeks of treatment dogs were euthanized and tissue samples were harvested. Serum Immunoglobulin G (IgG) titers against cIL4-10FP were evaluated to check for potential antibody formation.

Cartilage proteoglycan content and release of proteoglycans were determined *ex vivo* by Alcian Blue assay. Synovial inflammation was evaluated by HE-staining using OARSI grading. Changes in outcomes in the affected/treated joints compared to contra-lateral control joints were calculated.

**Results:** After OA induction a clear reduction in joint loading (increase in pain) was found (standing force and braking force). After cIL4-10FP injections these forces increased toward normalisation (cIL4-10FP vs PBS group, p=0.002 and p=0.01, respectively). No IgG elevation was detected after 10 injections. Compared to contra-lateral controls, proteoglycan content of OA PBS injected knees suggested tissue degeneration (27 vs 34 mg/g). In the cIL4-10FP treated group proteoglycan content in right knees was not different from the contralateral controls (33 vs 31 mg/g). The mean change in proteoglycan content compared to contra-lateral controls was different with a p value of 0.057 (figure 1). A similar pattern was found for the change in release of proteoglycans from the cartilage, which was less increased in the cIL4-10FP group compared to the PBS group (0.4% vs 3.0%; p=0.029, figure 1).

Synovial inflammation was mild (characteristic of this model) and did not change after intra-articular injections (0.4 and -1.3 points out of 18 for cIL4-10FP and PBS respectively).



**Abstract OP0262** – Figure 1 Chondroprotective effects of cIL4-10 fusion protein. (A) change in proteoglycan content between left (control) and right (injected) knees. Values are expressed per animal, representing a mean of 8 samples, and as median  $\pm$  IQR. (B) change in release of proteoglycans between left (control) and right (injected) knees. Values are expressed per animal, representing a mean of 8 samples, and as median  $\pm$  IQR.

**Conclusions:** Repetitive intra-articular injection with canine IL4-10FP in dogs did not lead to antibody formation. Dogs treated with cIL4-10FP showed improved joint loading compared to PBS treated dogs, reflecting an analgesic effect. Recovery of proteoglycan content and normalisation of release in cIL4-10FP treated dogs indicate a chondroprotective effect. Synovial inflammation in the Groove model was too mild to be changed significantly. These results clearly warrant further research to develop IL4-10FP as a DMOAD.

**Acknowledgements:** This work is supported by the Dutch Arthritis Foundation project NR12-2-202

**Disclosure of Interest:** None declared

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#### OP0263 CLAUDIN-11 REGULATES BONE HOMEOSTASIS VIA BIDIRECTIONAL EPHB4-EPHRIN2 SIGNALING

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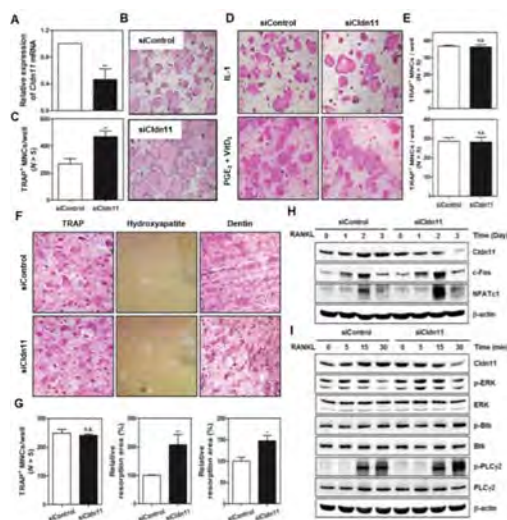
**Background:** Claudins (Cldns) are well-established components of tight junctions (TJs) that play a pivotal role in the modulation of paracellular permeability. Several studies have explored the physiologic aspects of Cldn family members in bone metabolism. However, the effect of Cldn11, a major component of central nervous system myelin, on bone homeostasis has not been reported.

**Objectives:** This study was performed to identify the effects of Cldn on bone metabolism via regulation of osteoclast and osteoblast differentiation and their function

**Methods:** We performed various *in vitro* and *in vivo* studies using gain- and loss-of function of Cldn11 that is belong to the Cldn group. Osteoclast formation from bone marrow cells (BMC) and Osteoblast formation was evaluated in specific condition with over-expression or down-regulation of Cldn11. The expression of osteoclast associated gene and osteoblast related gene mRNA were assessed

by RT-PCR. The levels of c-fos and NFATc1 protein were assessed by western blot. Also the mitogen-activated protein (MAPK)s and important signal pathways were measured using Western blot analysis. Osteoclast function was evaluated with resorption pit assay and osteoblastic effects of Cldn11 was evaluated with new bone formation of mouse calvaria. With LPS and co-treated Recombinant protein of Cldn11 on mouse calvaria, we evaluated the effects of Cldn11 on LPS induced bone loss by using histologic analysis.

**Results:** We found that Cldn11 played a negative role in receptor activator of nuclear factor kappa B ligand dependent osteoclast (OC) differentiation by down-regulating the phosphorylated form of extracellular signal-regulated kinase (ERK), Bruton's tyrosine kinase, and phospholipase C gamma 2, in turn impeding c-Fos and nuclear factor of activated T cells c1 expression. Osteoblast (OB) differentiation by positive feedback of Cldn11 was achieved through the phosphorylation of Smad1/5/8, ERK, and c-Jun amino-terminal kinase. Importantly, this Cldn11-dependent dual event arose from targeting EphrinB2 ligand reverse signalling into OC and EphB4 receptor forward signalling into OB. In agreement with these *in vitro* effects, subcutaneous injection of Cldn11 recombinant protein exerted similar effects on local calvarial regions in mice.



**Conclusions:** These findings suggest that Cldn11 is a novel regulator in bone homeostasis.

**Disclosure of Interest:** None declared

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## OP0264 GLUCOSEPANE : A NEW BIOMARKER OF THE SEVERITY OF OSTEOARTHRITIS

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**Background:** Glycation, oxidation and nitration of proteins are reactions involved in accelerated ageing of tissues. The products of these reactions are used as biomarkers of chronic pathologies such as diabetes or chronic inflammatory states.

**Objectives:** In this work, we studied by mass spectrometry the levels of amino acids and glycated, oxidised or nitrated proteins in culture media of chondrocytes cultivated in multi-layers and in the blood of guinea pigs or osteoarthritis patients.

**Methods:** Sixty male, 3-week-old Dunkin-Hartley guinea pigs were used in this work. At 4-weeks-old and 8 week intervals until week 36, twelve animals were sacrificed and histological severity of knee osteoarthritis evaluated and cartilage rheological properties. Human patients with early and advanced osteoarthritis and healthy subjects were recruited. Human chondrocytes cultured in multilayers were treated for 10 days with interleukin (IL) -1 $\beta$ . Amino acids and glycated, oxidised and nitrated proteins were analysed in the serum of guinea pigs, osteoarthritis patients and in the culture medium conditioned by chondrocytes by stable isotopic dilution analysis liquid chromatography-tandem mass spectrometry using the Acquity UPLC system.

**Results:** Severity of osteoarthritis increased progressively in guinea pigs with age. Glycated, oxidised and nitrated amino acids were increased markedly at week 36. Glucosepane and dityrosine increased progressively from weeks 20

and 28, respectively. Glucosepane was positively correlated with the OA histological severity ( $r=0.58$ ,  $p<0.0001$ ) and the Young's modulus ( $r=0.52-0.56$ ,  $p<0.0001$ ). Oxidation free adducts were positively correlated with OA severity ( $p<0.0009-0.0029$ ) and hydroxyproline with cartilage thickness ( $p<0.0003-0.003$ ). In the clinical study, plasma glucosepane was increased 38% in patients with early osteoarthritis ( $p<0.05$ ) and 6-fold in patients with advanced osteoarthritis ( $p<0.001$ ) compared to healthy subjects. IL-1 $\beta$  increased the release of glycated, oxidised and nitrated products from chondrocytes *in vitro*.

**Conclusions:** The glycation, oxidation and nitration of proteins are reactions related to the severity of osteoarthritis. The products of these reactions are measurable in blood by mass spectrometry and could be biomarkers of osteoarthritis. More specifically, glucosepane is an advanced glycation product very strongly increased in the severe form of the disease. In conclusion, serum glucosepane is a potential biomarker for diagnosis and progression of osteoarthritis.

**Disclosure of Interest:** None declared

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## OP0265 LOCAL REACTIVATION OF GLUCOCORTICOIDS BY 11 $\beta$ -HYDROXYSTEROID DEHYDROGENASE TYPE 1 MEDIATES THE DEVELOPMENT OF GLUCOCORTICOID-INDUCED BONE LOSS

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**Background:** Due to the potent immunomodulatory and anti-inflammatory nature of glucocorticoids (GCs) they are routinely used in the treatment of inflammatory diseases such as rheumatoid arthritis. However their therapeutic potential is limited due to the prevalence of adverse side effects associated with long term GC exposure such as osteoporosis, insulin resistance and obesity. 11 $\beta$ -hydroxysteroid dehydrogenase type 1 (11 $\beta$ -HSD1) is a bi-directional enzyme that primarily converts inactive GCs to their active counterparts. Previously, local reactivation of GCs by 11 $\beta$ -HSD1 has been shown to play a major role in the metabolic side effects associated with GC excess.

**Objectives:** We aim to assess whether local reactivation of GCs by 11 $\beta$ -HSD1 mediates the adverse effects of therapeutic GCs on bone.

**Methods:** Wild-type (WT) mice and transgenic mice with a global 11 $\beta$ -HSD1 knockout (11 $\beta$ KO) were treated with the active murine GC corticosterone (CORT) (100 mg/ml) for 4 weeks. Tibia and humerus bones were excised post-mortem for micro-CT analysis, gene expression analysis and three point flexure strength (TFS) tests. Serum was collected from mice for ELISA analysis of TRAcP-5b and P1NP.

**Results:** Micro-CT analysis of bone volume to tissue volume (BV/TV), trabecular thickness (TT) and trabecular number (TN) found no significant differences between untreated WT and 11 $\beta$ KO mice (BV/TV: WT 8.5% $\pm$ 0.66 vs 11 $\beta$ KO 7.5% $\pm$ 0.76, NS; TT: WT 96.5  $\mu$ m $\pm$ 3.8 vs 11 $\beta$ KO 95.8  $\mu$ m $\pm$ 6.4, NS; TN: WT 0.0009 1/ $\mu$ m $\pm$ 0.00004 vs 11 $\beta$ KO 0.0008 1/ $\mu$ m $\pm$ 0.00004, NS). Humerus TFS tests of WT and 11 $\beta$ KO animals also showed no significant differences (WT 51.2 MPa $\pm$ 15.1 vs 11 $\beta$ KO 49.2 MPa $\pm$ 4.9, NS). All bone parameters were decreased in CORT fed WT mice indicating the development of osteoporosis, whilst 11 $\beta$ KO mice were protected against many of the detrimental effects of CORT (BV/TV: WT 4.2% $\pm$ 0.38 vs 11 $\beta$ KO 7.2% $\pm$ 0.71,  $p\leq 0.05$ ; TN: WT 0.0006 1/ $\mu$ m $\pm$ 0.00004 vs 11 $\beta$ KO 0.0009 1/ $\mu$ m $\pm$ 0.00008,  $p\leq 0.001$ ; HBS: WT 27.1 MPa $\pm$ 5.6 vs 11 $\beta$ KO $\pm$ 5.0 MPa $\pm$ 5.1,  $p\leq 0.05$ ). ELISA analysis of mouse serum showed no significant differences in the bone resorbing osteoclast marker TRAcP-5b amongst the groups, whereas analysis of the bone forming osteoblast marker P1NP revealed a significant increase in CORT fed 11 $\beta$ KO mice compared with CORT fed WT mice (11 $\beta$ KO 158.6 ng/ml $\pm$ 53.1 vs WT 31.4 ng/ml $\pm$ 7.4,  $p\leq 0.05$ ). Gene expression of the mature osteoblast markers ALP (alkaline phosphatase) and BGLAP (osteocalcin) showed significant increases in CORT fed 11 $\beta$ KO animals compared to CORT fed WT animals (ALP: 11 $\beta$ KO 0.0074 AU  $\pm$ 0.0012 vs WT 0.0022 AU  $\pm$ 0.0007,  $p\leq 0.01$ ; BGLAP: 11 $\beta$ KO 0.27 AU  $\pm$ 0.04 vs WT 0.02 AU  $\pm$ 0.01,  $p\leq 0.001$ ). No significant differences were observed between untreated WT and 11 $\beta$ KO animals.

**Conclusions:** These data suggest that local reactivation of GCs by 11 $\beta$ -HSD1 mediates the development of glucocorticoid-induced osteoporosis by inhibiting osteoblastic bone formation.

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**Disclosure of Interest:** None declared  
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FRIDAY, 15 JUNE 2018:

## Seeking the pathophysiology of rheumatoid arthritis and spondylarthritis

### OP0266 SYNOVIAL TISSUE PROFILING IN AUTOANTIBODY POSITIVE AT RISK INDIVIDUALS REVEALS GENE SIGNATURES ASSOCIATED WITH LATER DEVELOPMENT OF RHEUMATOID ARTHRITIS

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**Background:** Previous work has suggested subtle infiltration of synovial T cells<sup>1</sup> in the absence of overt synovial inflammation<sup>2</sup> in individuals at risk of developing rheumatoid arthritis (RA).

**Objectives:** To study the molecular changes in synovium preceding arthritis development in preclinical RA.

**Methods:** We included sixty-seven individuals who were IgM rheumatoid factor (RF) and/or anti-citrullinated protein antibody (ACPA) positive and without any evidence of arthritis. All individuals underwent mini-arthroscopic synovial biopsy sampling of a knee joint at inclusion and were prospectively followed. First, an explorative genome-wide transcriptional profiling study was performed on synovial biopsies obtained from 13 individuals using Agilent arrays (test cohort). Survival analysis was used to identify transcripts with a significant association with arthritis development. The expression level of differentially expressed genes was validated using quantitative real-time PCR in the total cohort. Immunohistochemistry was used to study gene candidates at protein level *in situ*.

**Results:** Six of the 13 individuals in the explorative study developed RA after a median follow up time of 20 months (IQR 2–44). The 7 individuals who did not develop RA had a median follow up time of 85 months (IQR 69–86). Using a False Discovery Rate of <5% we found that increased expression of 3151 transcripts correlated with a higher risk of arthritis development, and increased expression of 2437 transcripts correlated with a lower risk. Gene Set Enrichment Analysis revealed that synovial biopsies of individuals who developed RA after follow up display higher expression of genes involved in several immune response-related pathways (e.g. T cell and B cell receptor pathways, cytokine and chemokine signalling and antigen processing and presentation) compared with biopsies of individuals who did not develop RA. In contrast, lower expression was observed for genes involved in e.g. extracellular matrix receptor interaction, Wnt-mediated signal transduction and lipid metabolism. Subsequently, the expression level of a selection of 27 differentially expressed genes was validated by quantitative real-time PCR in 61 RA-risk individuals. Two-way hierarchical cluster analysis classified the individuals into two groups, where those individuals who developed RA (n=16) showed a preference to cluster together in the left arm of the dendrogram (Chi2 p=0.03).

Immunohistochemistry analyses (n=54) showed an abundant expression of CXCL12 and CXCR4 already in most RA-risk individuals. Synovial biopsies from RA-risk individuals who developed arthritis were more likely to show a positive gp38 staining and lower lipid staining.

**Conclusions:** This study clearly shows molecular changes appearing in synovial tissue before onset of arthritis in the absence of overt synovitis. Preclinical synovial alterations in immune response genes and lipid metabolism were associated with development of arthritis.

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**Disclosure of Interest:** L. Van Baarsen: None declared, M. de Hair: None declared, J. Semmelink: None declared, I. Choi: None declared, D. Gerlag Employee of: GlaxoSmithKline, UK. GlaxoSmithKline was not involved in this study., P. Tak Employee of: GlaxoSmithKline, UK. GlaxoSmithKline was not involved in this study.

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OP0267

### THE PADI4 GENE PROMOTER METHYLATION LEVEL IS ASSOCIATED WITH ANTI-PADI4 ANTIBODIES LEVEL AND RA ACTIVITY

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**Background:** Rheumatoid arthritis (RA) is a chronic, autoimmune, inflammatory disease that predominantly affects the synovial membrane leading to joint destruction. Anti-citrullinated protein antibodies (ACPA) are important markers of RA. They recognise post-translationally modified auto-antigens generated by enzymes peptidylarginine deiminases (PADIs) mostly type 4 (PADI4), which transform arginine to new amino acid citrulline in various proteins. There were also identified anti-PADI4 antibodies (anti-PADI4) which are a specific marker of RA. DNA methylation plays a key role in the control of gene expression. The process concerns CpG islands in promoter regions of about 75% of genes and leads to gene silencing when over-expressed. It is possible that PADI4 production is also regulated via methylation.

**Objectives:** We aimed to identify if there is an association between PADI4 gene promoter methylation degree, anti-PADI4 antibodies level and RA activity.

**Methods:** A total of 155 unrelated patients, 125 with RA, 83.2% female, aged 52.2±12.3 years (mean ±SD) and 30 healthy controls (HC), 76.7% female, aged 53.2±8.1 years, were enrolled. RA patients were divided according DAS28 score into 4 groups as shown in table 1. Whole blood and serum samples were collected and stored at -80°C until analysis. DNA was extracted from whole blood and stored at -80°C until analysis. Two single-nucleotide polymorphisms (SNPs) of the PADI4 gene (PADI-94, rs2240340 and PADI-104, rs1748033) were determined by TaqMan genotyping. Quantitative real-time methylation-specific PCR (qMSP) was used to analyse the methylation status of promoter region in PADI4 gene. Anti-PADI4 antibodies were evaluated in serum by ELISA.

**Results:** We found the differences in anti-PADI4 level between RA severe and HC group (p<10<sup>-5</sup>), RA moderate and HC (p<10<sup>-5</sup>), RA low activity and HC (p<0.05) and in PADI4 methylation group between RA severe and RA remission (p<0.05), RA moderate and RA remission (p<10<sup>-3</sup>) and RA moderate and HC (p<10<sup>-2</sup>). What is interesting is that methylation level in the RA remission group is higher than in the HC. The intensity of PADI4 methylation correlates with anti-PADI4 antibodies level and DAS28 score with r<sub>s</sub>=-0.2 and -0.36 respectively (both p-values<0,05) and anti-PADI4 level is associated with DAS28 score (r<sub>s</sub>=0.38).

Abstract OP0267 – Table 1

	RA Severe DAS28>5.1; 27.2%	RA Moderate DAS28>3.2– 5.1; 36.8%	RA Low (DAS28>2.6– 3.2; 15.2%)	RA Remission (DAS28≤2.6; 20.8%).	Healthy Control (HC)
PADI4	1.32	1.14	1.98	2.12	1.86
Metylation	[0.79–2.27]	[0.69–1.82]	[1.37–2.48]	[1.73–2.94]	[1.62–3.49]
Anti-PADI4	731.03	716.11	589.57	455.54	293.25
[U/ml]	[477.98– 1288.1]	[400.85– 1250.8]	[306.08– 2380.2]	[271.26– 1104.9]	[234.39– 389.12]

Data are given by median [interquartile range]

**Conclusions:** We demonstrate the novel finding that elevated methylation of PADI4 gene promoter is associated with lower RA activity and lower level of anti-PADI4 antibodies and might play a role in pathophysiology of RA or be used as future therapeutic target. The data suggest that PADI4 enzyme synthesis is epigenetically regulated by its gene promoter methylation.

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OP0268

### APOPTOSIS OF SYNOVIAL FIBROBLASTS INDUCED BY P53-DERIVED HYBRID PEPTIDES THROUGH DISSOCIATING THE BINDING OF P73 WITH IASPP TO INCREASE PUMA AND BAX EXPRESSION

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**Background:** In rheumatoid arthritis (RA) synovial fibroblasts (SFs), mutant p53 can lead to transformation-like features resistant to the apoptosis induction.<sup>1</sup> Deficiency in p53-mediated suppression by its dominant-negative counterpart is observed in human cancers with activating p73 as a therapeutic strategy in such patients.<sup>2</sup> A p53-derived hybrid peptide 37 amino acid (37AA) can inhibit the p73 binding with inhibitory apoptosis stimulating protein of p53 (IASPP), thus activating the downstream apoptosis signalling pathway in tumour cells.<sup>3</sup>

**Objectives:** We hypothesised that p73 is involved in the RA pathogenesis, and examined whether p53-derived hybrid peptides can activate p73 to induce apoptosis of SFs by using adenoviral vectors encoding 37AA (Ad37AA) to transduce SFs *in vitro* and inject collagen-induced arthritis (CIA) joints *in vivo*.

**Methods:** Mononuclear cells (MNCs) from RA patients before and after receiving the adalimumab therapy were examined for iASPP expression by real-time RT-PCR. Synovial tissues and SFs from RA patients and CIA rats were subjected to immunohistochemical and immunofluorescent staining and real-time RT-PCR for the p73 and iASPP expression. SFs transduced with Ad37AA, were subjected to TUNEL assay for apoptotic status and real-time RT-PCR for the expression of downstream apoptosis signalling molecule PUMA and Bax. SFs were transduced with lentiviral vectors-encoding short hairpin p73 RNA to produce p73-silenced SF transfectants. Therapeutic effects of Ad37AA injection were evaluated on CIA joints. Immunohistochemical staining and TUNEL assay were used to analyse synovial cadherin-11/PUMA/IL-6 expression and apoptotic cells, respectively.

**Results:** There were reduced iASPP levels by targeting TNF in RA MNCs, and increased p73 with co-localised iASPP expression in synovial lining layers and SFs from RA patients and CIA rats. Enhanced cell apoptosis, increased PUMA and Bax expression and lower iASPP-associated p73 levels were identified in Ad37AA-transduced SFs, and silencing p73 abrogated the increased PUMA and Bax expression. Articular indexes and histologic scores were reduced in Ad37AA-injected joints with decreased SF densities, increased apoptotic cells, higher PUMA expression and lower IL-6 levels.

**Conclusions:** These results demonstrate that injecting p53-derived hybrid peptides can induce apoptosis of SFs through the activation of p73 in the rheumatoid joint, suggesting that strengthening the p73-dependent apoptotic mechanism is a potential therapeutic strategy in RA patients.

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OP0269

### ACTIVATION OF MERTK+CD206+ SUBPOPULATION OF HUMAN SYNOVIAL TISSUE-RESIDENT MACROPHAGES LIMITS INFLAMMATORY RESPONSE

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**Background:** Current therapies have transformed the management of rheumatoid arthritis. However, there are still a substantial proportion of patients who do not respond to treatments, and among those who respond, only small proportion achieve disease remission. We showed previously that human synovial tissue macrophages (STMs) are a heterogeneous population; and a sub-population of CD206<sup>+</sup>MertK<sup>+</sup> positive STMs predominates in RA patients in sustained remission, in contrast to patients with active RA. Their surface receptors, e.g. MerTK, and distinct transcriptomes suggest that they may play a pivotal role in re-enforcing joint homeostasis during remission.<sup>1</sup> Thus, we hypothesise that activation of

CD206<sup>+</sup>MerTK<sup>+</sup> human synovial tissue macrophages contribute to the resolution of inflammation.

**Objectives:** We aimed to investigate whether activation of MerTK in STM sub-population promotes an anti-inflammatory environment in the synovium.

**Methods:** Using flow cytometric techniques and with a specific antibody panel design,<sup>1</sup> STMs from digested RA synovial biopsies (n=36) were phenotyped and/or harvested. Patients' group included 28 patients with active disease and 8 patients in remission (DAS28 ESR <2.6 and power doppler negative). After excluding all other cell types, macrophages were gated based on the expression of CD64 and CD11b (CD45<sup>pos</sup>CD64<sup>pos</sup>CD11b<sup>pos</sup>HLA-DR<sup>pos</sup>).<sup>1</sup> Two distinct sub-populations: CD206<sup>+</sup>MerTK<sup>+</sup> and CD206<sup>-</sup>MerTK<sup>-</sup> were sorted and cultured on a collagen coated 96-well plate at 1000 cells per well in the presence of with LPS (10 ng/ml)±Gas6, a MerTK ligand (200 ng/ml), for 24 hour. TNF production was measured with a high sensitivity ELISA.

**Results:** As previously shown,<sup>1</sup> RA patients in sustained remission have a majority of CD206<sup>+</sup>MerTK<sup>+</sup> STMs whilst patients with active RA show an increased number of CD206<sup>-</sup>MerTK<sup>-</sup> macrophages. The percentage of CD206<sup>+</sup>MerTK<sup>+</sup> macrophages negatively correlated with the disease activity score. Stimulation of FACS-Aria sorted CD206<sup>+</sup>MerTK<sup>+</sup> and CD206<sup>-</sup>MerTK<sup>-</sup> macrophages with TLR4 ligand induced TNF production. However, activation of MerTK pathway by Gas6 inhibited LPS-induced TNF production by CD206<sup>+</sup>MerTK<sup>+</sup> subpopulation.

**Conclusions:** CD206<sup>+</sup>MERTK<sup>+</sup> macrophages, which predominate in RA patients in remission, have Gas6-mediated negative feedback mechanism limiting TNF production. Thus, Gas6/MerTK pathway in synovial tissue macrophages could drive the resolution of inflammation and synovial tissue homeostasis. Further functional and transcriptomics studies will reveal the therapeutic potential of CD206<sup>+</sup>MERTK<sup>+</sup> macrophages.

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OP0270

### IGA ANTI-CCP ANTIBODIES ARE DETECTABLE IN THE SALIVA BUT NOT SPUTUM OF INDIVIDUALS AT-RISK OF DEVELOPING RHEUMATOID ARTHRITIS

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**Background:** Recent evidence suggests the initiation of rheumatoid arthritis (RA) – related autoimmunity may occur by local citrullination at the oral mucosa and lungs. IgA antibodies are the hallmark of mucosal immunity; the majority of saliva IgA antibodies are locally produced whereas IgG antibodies are largely serum derived.<sup>1</sup> Furthermore, IgA anti-CCP antibodies have recently been described in the sputum of at-risk individuals.<sup>2</sup> The relative importance of the oral and lung mucosa in disease initiation is, however, unclear and the prevalence of saliva and sputum anti-CCP antibodies in the same at-risk individuals has not been reported.

**Objectives:** To investigate the prevalence of IgA anti-CCP antibodies in the saliva and sputum of seropositive individuals at risk of developing RA.

**Methods:** Anti-CCP positive individuals with no evidence of clinical synovitis (CCP+), anti-CCP positive RA patients (RA) and healthy controls (HC) matched for age and smoking status were recruited. Unstimulated saliva and serum samples were collected. Induced sputum samples were obtained using 7% saline via ultrasonic nebuliser (UltraNeb 3000 DA, Devilbiss, Germany). Sputum was mixed with phosphate buffered saline, mechanically disrupted and centrifuged to obtain supernatant. IgA and IgG anti-CCP antibodies (anti-CCP2, immunocap assay, Phadia) were measured in all saliva, sputum and serum samples. IgA and saliva/sputum IgG anti-CCP titres exceeding the 95th centile in HC were considered positive.

**Results:** 55 CCP+, 40 RA and 32 HC were recruited and had saliva and serum collected. 24 CCP+, 14 RA and 22 HC had sputum and serum collected. Of these, 23 CCP +and 7 RA patients provided simultaneous saliva, sputum and serum samples. 8/55 (15%) CCP +and 10/40 (25%) RA patients had positive saliva IgA anti-CCP levels compared with 1/31 (3%) HC. 23/54 (43%) CCP +and 21/48 (44%) RA patients had positive serum IgA anti-CCP levels compared with 1/32 (3%) HC (table 1). Of note, 7/18 (39%) patients with a positive saliva IgA anti-CCP test had a negative serum IgA anti-CCP test, suggesting localised production and accumulation of IgA anti-CCP antibodies rather than transfer from the serum. Only 1/24 CCP+ (4%) and 1/14 (7%) RA patients had positive sputum IgA anti-

CCP levels. No patients had IgA anti-CCP detectable in both saliva and sputum samples.

#### Abstract OP0270 – Table 1

	Anti-CCP positive results (%)					
	Saliva IgA	Sputum IgA	Serum IgA	Saliva IgG	Sputum IgG	Serum IgG
HC	1/31 <sup>(1)</sup>	1/22 <sup>(1)</sup>	1/32 <sup>(1)</sup>	1/31 <sup>(1)</sup>	0/22 (0)	0/32 (0)
CCP+at-risk	8/55 <sup>(15)</sup>	1/24 <sup>(1)</sup>	23/54 <sup>(43)</sup>	23/54 <sup>(43)</sup>	10/24 <sup>(42)</sup>	50/54(93)
RA	10/40 <sup>(25)</sup>	1/14 <sup>(7)</sup>	21/48 <sup>(44)</sup>	23/42(55)	9/14(64)	47/48(98)

**Conclusions:** We found an increased prevalence of saliva but not sputum IgA anti-CCP antibodies in seropositive at-risk individuals. These findings support the concept that localised RA-related autoimmunity in at risk individuals can be site specific. IgA anti-CCP antibodies at the oral mucosa precede arthritis and may represent an important step in the initiation and propagation of disease.

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#### OP0271 GASTROINTESTINAL DAMAGE AND MICROBIAL TRANSLOCATION ARE INVOLVED IN THE DEVELOPMENT OF IMMUNE SYSTEM ACTIVATION IN INFLAMMATORY BOWEL DISEASE-ASSOCIATED SPONDYLOARTHRITIS

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**Background:** The altered composition of the gastrointestinal (GI) microbiota, known as dysbiosis, can induce and modulate the systemic inflammation, through microbial translocation and T-cell activation, in several immuno-mediated diseases, such as inflammatory bowel disease (IBD), HIV infection, and ankylosing spondylitis.

**Objectives:** In a cohort of 85 patients with inflammatory bowel disease-associated spondyloarthritis (SpA/IBD), we assessed gut bacterial infiltration and intestinal damage. In systemic circulation, GI epithelial damage, microbial translocation and immune system activation were assessed with intestinal-fatty acid binding protein (I-FABP), lipopolysaccharide (LPS), soluble CD14 (sCD14), respectively. Moreover, the *in vitro* activity of the latter two was evaluated on osteoblast cells.

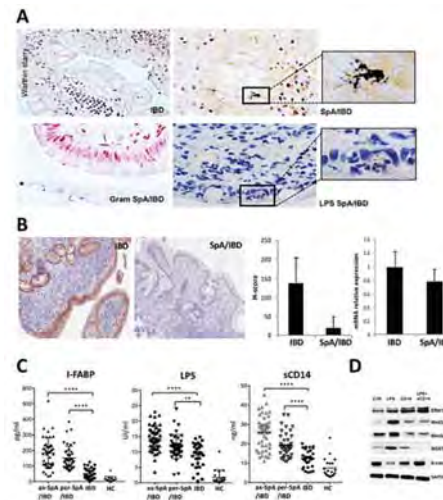
**Methods:** I-FABP, LPS, sCD14, sclerostin (SOST) and anti-SOST antibodies (anti-SOST-IgG) were assayed with ELISAs. LPS and sCD14 were used *in vitro* to stimulate the MG63 human osteoblast-like cell line. Occludin, claudin-1, claudin-4, and the presence of bacteria were assessed, respectively, by real-time-PCR analysis and immunohistochemical staining of the ileum.

**Results:** Bacteria were detectable in the ileal epithelium of IBD patients, but only in SpA/IBD they were associated with epithelial damage and downregulation of occludin, claudin-1 and claudin-4 (figure 1A-B).

The serum levels of I-FABP, LPS and sCD14 resulted significantly higher in axial (187.9, 14.03, and 26.97, respectively) and peripheral SpA/IBD (130.3, 11.55, and 18, respectively) than in IBD patients (IFABP 43.65,  $p < 0.0001$  for both patients' groups; LPS 9.625,  $p < 0.0001$  vs Ax-SpA/IBD and =0.007 vs Per-SpA/IBD; sCD14 12.34,  $p < 0.0001$  for both patients' groups) (figure 1C).

In the SpA/IBD cohort, SOST was weakly correlated with I-FABP ( $r = -0.2683$ ), LPS ( $r = -0.3063$ ) and sCD14 ( $r = -0.3075$ ), and anti-SOST-IgG with LPS ( $r = 0.3959$ ) and sCD14 ( $r = -0.3414$ ). Moreover, sCD14 showed significant correlation with I-FABP ( $r = 0.3316$ ) and LPS ( $r = 0.5649$ ).

*In vitro*, LPS, but not sCD14, significantly induced SOST expression through the upregulation of both Wnt3a and Wnt5a and the downregulation of the b-catenin proteins (figure 1D). On the opposite, the combination of LPS and sCD14 downregulated SOST expression through the upregulation of ERK1/2 and b-catenin protein (figure 1D).



**Abstract OP0271 – Figure 1** A. immunohistochemical staining of ileal bacteria. Ten ileal samples of patients affected by SpA/IBD or IBD were stained for bacteria infiltration (upper panel). Lower (from left to right): Gram and LPS staining of the same samples. B. Analysis of ileal tight-junctions proteins expression. From the left to the right: Ten ileal samples of patients affected by SpA/IBD or IBD were stained for occludin (and claudin-1 and -4, data not shown); count of occludin positive cells and quantitative real-time-PCR of occludin (and claudin-1 and -4, data not shown) expression in the same ileal samples. C. analysis of I-FABP, LPS and sCD14 serum levels in SpA/IBD and IBD patients. ELISAs assays were carried out in 45 patients with axial and 40 patients with peripheral SpA/IBD, and compared with IBD or HC. D. Western-blot analysis of MG-63 osteoblast-cells. The MG-63 osteoblast-like cell line was stimulated with LPS ± sCD14 *in vitro* and then cells were harvested for western blot analysis. Semi-quantitative densitometric analysis of the protein bands was carried out on the blot (data not shown). Statistical analysis: Kruskal-Wallis analysis. \*\* $p < 0.01$ ; \*\*\*\* $p < 0.0001$ ; if not reported:  $p$  non significant. Abbreviations. SpA/IBD: inflammatory bowel disease-associated spondyloarthritis; ax-SpA/IBD: axial SpA/IBD; peripheral SpA/IBD; IBD: Inflammatory bowel disease; HC: healthy controls; I-FABP: intestinal fatty acid binding protein; LPS: bacterial lipopolysaccharide; sCD14: soluble CD14; ERK 1/2: extracellular Signal-regulated Kinase-1/2. Wnt: wingless protein family; SOST: sclerostin.

**Conclusions:** The role of gut inflammation and microbial translocation in the onset of arthritis in IBD patients are still under investigation. We have demonstrated that in SpA/IBD there is a significant bacterial infiltration of the ileal tract, associated with the downregulation of tight-junctions' proteins (occludin, claudin-1 and claudin-4) and epithelial damage, that cause microbial translocation and higher plasma levels of I-FABP, LPS, and sCD14. LPS and sCD14, thus, could trigger a complex systemic inflammatory response acting on several biochemical pathways, linking the immune system (anti-SOST-IgG) and the bone (SOST).

**Disclosure of Interest:** None declared

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#### OP0272 INFLAMMATION AT BARRIER TISSUES SUCH AS SKIN AND GUT TRIGGERS MILD JOINT INFLAMMATION AND IS INFLUENCED BY BIOMECHANICAL STRESS INDUCED BY FORCED-RUNNING

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**Background:** The factors triggering the onset of psoriatic arthritis (PsA) and other forms of spondyloarthritis (SpA) are mostly unknown. These joint diseases are clinically associated with psoriasis (PsO) and inflammatory bowel disease (IBD). The three pathologies share the common leitmotiv of chronic inflammation and all of them have an at least partially shared genetic susceptibility. Enteses, the attachment sites of tendons and ligaments into the bones, are considered as a primary disease localization and a site of biomechanical stress. Increasing evidence supports the hypothesis that biomechanical stress, together with inflammatory triggers such as antigens and changes in the microbiome, can contribute to the onset of PsA and SpA by inducing local microdamage in the enteses.

**Objectives:** Here, we aim to understand early events leading to PsA and SpA by combining a protocol of forced exercise in mice with simultaneous locally-induced cutaneous or intestinal inflammation.

**Methods:** Forty 8 weeks old C57/Bl6 male mice were used to induce the PsO- or IBD-like disease, respectively by serial applications of imiquimod cream (IMQ) on a shaved area of the back skin, and administration to the intestine of dextran sodium sulphate (DSS) dissolved in drinking water. Forty control mice were left

untreated. After induction of inflammation, we applied a protocol of forced treadmill running to increase biomechanical stress in half of the mice. Control mice with or without IMQ or DSS treatment did not run. We evaluated skin and gut disease severity clinically and by histology, and performed microCT scans, histological and immunohistochemical analyses of the knees and the paws, to investigate eventual changes occurring in the joints.

**Results:** Clinical and histological assessment of the skin or gut confirmed successful induction of cutaneous and intestinal inflammation. The exercise protocol slightly affected the severity of the PsO- but not of the IBD-like disease in mice. In both models, disease was not confined to the target organs as systemic inflammation was demonstrated by trabecular bone loss, as indicated by microCT analyses, and by changes in spleen size. The exercise protocol did not appear to have an additional effect on these systemic disease manifestations, but it is associated with increased articular cartilage thickness and cellularity. Signs of mild joint inflammation were seen for both the IMQ and DSS models. Mild synovitis was triggered by skin and gut disease. At the entheseal level, immunohistochemical detection for CD45<sup>+</sup> cells showed that forced exercise boosts inflammation in the presence of inflammation triggered at a distant site.

**Conclusions:** Induction of PsO- or IBD-like inflammation by local treatments of immune-privileged barrier tissues, such as skin and gut, also triggers a systemic response with inflammation-associated bone loss and discrete signs of joint disease. Forced running exercise increased the degree of enthesitis in this setting, providing new support for the hypothesis that biomechanical stress contributes to disease manifestations in PsA and other forms of spondyloarthritis.

**Disclosure of Interest:** None declared

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#### OP0273 TRANSMEMBRANE TNF SIGNALLING THROUGH TNF-RI INDUCES SPA-LIKE INFLAMMATION, WHEREAS SIGNALLING THROUGH TNF-RII IS CRUCIAL FOR NEW BONE FORMATION

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**Background:** TNF can drive strictly distinct inflammatory pathologies depending on its expression form. Previously, we have shown that transmembrane (tm) TNF rather than soluble TNF contributes to key pathological features of spondyloarthritis (SpA), including new bone formation.<sup>1</sup>

**Objectives:** Delineate the cellular and molecular mechanisms by which selective tmTNF overexpression leads to SpA-like pathology.

**Methods:** tmTNF tg mice (TgA86)<sup>2</sup> were crossed with TNF-RI or TNF-RII knock out mice. Animals were followed for 100 days for clinical symptoms of arthritis and spondylitis development. Histology was performed at the end of the study on both peripheral and axial joints. Calvarial mouse fibroblasts were cultured in osteogenic conditions. Differentiation towards osteoblasts was analysed by alizarin red staining, alkaline phosphatase (ALP) staining as well as by qPCR for collagen type I, II, and X, ALP and RUNX2.

**Results:** Clinical arthritis, visualised by swelling and deformation of front- and hind paws, was observed in 100% of the tmTNF<sup>+/WT</sup> (>20) as well as in all tmTNF<sup>+/WT</sup>xTNF-RII<sup>-/-</sup> mice (7/7) but not in tmTNF<sup>+/WT</sup>xTNF-RI<sup>-/-</sup> mice (0/9). Histologically, peripheral synovitis, osteitis and enthesitis were observed in all tmTNF<sup>+/WT</sup> and tmTNF<sup>+/WT</sup>xTNF-RII<sup>-/-</sup> mice, confirming previous findings that tmTNF-mediated synovitis requires the presence of the TNF-RI receptor.<sup>2</sup> Similarly, hunch back formation and crinkled tails were observed in the tmTNF<sup>+/WT</sup> and the tmTNF<sup>+/WT</sup>xTNF-RII<sup>-/-</sup> mice but not in tmTNF<sup>+/WT</sup>xTNF-RI<sup>-/-</sup> mice. Histology confirmed the presence of inflammatory cellular infiltrates at the edge of the intervertebral units in all tmTNF<sup>+/WT</sup> tg mice and all tmTNF<sup>+/WT</sup>xTNF-RII<sup>-/-</sup> mice, but not in tmTNF<sup>+/WT</sup>xTNF-RI<sup>-/-</sup> mice. Whereas these data indicate that TNF-RI is required for tmTNF-induced inflammation, it was striking that 50% (10/20) of the tmTNF<sup>+/WT</sup> versus none (0/7) of the tmTNF<sup>+/WT</sup>xTNF-RII<sup>-/-</sup> mice depicted clear histological signs of endochondral new bone formation. To test whether TNF-RII is involved in pathological new bone formation in this model, calvarial fibroblasts skulls from tmTNF<sup>+/WT</sup>, tmTNF<sup>+/WT</sup>xTNF-RI<sup>-/-</sup>, tmTNF<sup>+/WT</sup>xTNF-RII<sup>-/-</sup> or WT were differentiated with osteogenic medium with or without IL-17A. tmTNF overexpressing fibroblasts enhanced the osteogenic differentiation as observed by ALP and alizarin red staining and increased mRNA levels of Collagen type I and ALP compared to WT. This enhancement in osteogenesis was maintained in tmTNF<sup>+/WT</sup>xTNF-RI<sup>-/-</sup>-derived fibroblasts but abolished in tmTNF<sup>+/WT</sup>xTNF-RII<sup>-/-</sup>-derived fibroblasts.

**Conclusions:** The SpA-like phenotype in tmTNF tg mice is crucially dependent on TNF-RI to drive peripheral and axial inflammation, but TNF-RII signalling is required to drive the pathological new bone formation under inflammatory conditions.

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FRIDAY, 15 JUNE 2018

#### HPR Supporting self-management

##### OP0274-HPR A FUNCTIONAL EXERCISE PROGRAM IMPROVES PAIN AND HEALTH RELATED QUALITY OF LIFE IN PATIENTS WITH FIBROMYALGIA: A RANDOMISED CONTROLLED TRIAL

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**Background:** Fibromyalgia (FM) is a syndrome characterised mainly by chronic generalised pain that affects the physical fitness and functional capacity of patients. There is increasing evidence of the benefits of physical exercise in improving FM symptoms, making these interventions part of therapeutic arsenal.

**Objectives:** To evaluate the effectiveness of a program of functional exercises in reducing pain, improving functional capacity, increasing muscle strength, improving flexibility, balance and quality of life of patients with FM.

**Methods:** It is a controlled and randomised study, with blind evaluator. A total of 82 female patients with FM were included, with age between 18 and 65 years, randomised into two groups, intervention and control. The intervention group (FEG) performed functional exercise training for 45 min twice a week for 14 weeks. The control group (SEG) performed stretching exercises with the same duration and frequency. Evaluation instruments were: VAS – Visual Analogue Scale for pain assessment; FIQ- Fibromyalgia Impact Questionnaire, for assessing health-related quality of life; Time-up and go test for functional performance evaluation; 1RM, for evaluation of muscle strength; Bank of Welss, for the assessment of flexibility; Berg Balance Scale, to evaluate balance; and SF-36 to evaluate general quality of life. Also, the amount of analgesics used during the intervention period was assessed.

**Results:** 41 patients were randomised to the FEG and 41 patients to the SEG. After intervention, the FEG presented a reduction in pain and an improvement in the quality of life related to the disease, which was statistically significant compared to SEG. Regarding general quality of life, functional capacity, muscle strength, flexibility and balance, there was no difference between the groups.

**Conclusions:** Functional exercise training proved to be effective in reducing pain and improving the health-related quality of life of patients with FM when compared to stretching exercises.

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**OP0275-HPR** THE EFFECTS OF EXERCISE ON DEPRESSIVE AND ANXIETY SYMPTOMS IN RHEUMATOID ARTHRITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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**Background:** Exercise reduces depressive and anxiety symptoms among the general population, and those with a chronic illness. Elevated depressive and anxiety symptoms are prevalent co-morbidities in Rheumatoid Arthritis (RA) therefore, addressing same through exercise may have an important impact on their health related quality of life (HQoL). Evidence does support the effect of exercise on these outcomes however, quantitative synthesis of evidence from randomised controlled trials (RCTs) of exercise effects, on these critically important symptoms in RA, has yet to be conducted.

**Objectives:** To quantify the overall population effect of exercise on depressive and anxiety symptoms, fatigue, and pain, derived from available RCTs, and to explore the extent to which participant and trial characteristics moderated the mean effect.

**Methods:** Articles published before September 2017 were located by two independent reviewers using Google Scholar, PsycINFO, PubMed, and Web of Science. Trials included both randomization to exercise and non-exercise control using validated measures of depression and anxiety, assessed at baseline and post-intervention. Hedges' *d* effect sizes (95% CI) were computed and random effects models were used for all analyses. Sources of bias were also assessed independently by two reviewers using the Cochrane bias assessment tool for RCTs and Newcastle–Ottawa Quality Assessment Scale for non-RCTs.

**Results:** Seventeen studies were included, with 1214 participants, of which 12 RCTs contributed to the meta-regression analysis. Participants were aged 49±9 years and 83%±14% female. Exercise training consisted on average of 3±1 weekly sessions, 60±17 min per session, and 11±5 weeks in duration. Interventions were diverse with a mix of aerobic and/or resistance training including, 4 different types of Yoga, 2 dance based and 1 Tai-chi. Mean reported adherence was 87%±11%. For depression, 18 of 20 effects (90%) were >0. The mean effect size  $\Delta$  was 0.20 (0.10–0.31;  $p<0.001$ ). For anxiety, seven of seven effects (100%) were >0. The mean effect size  $\Delta$  was 0.50 (0.27–0.74;  $p<0.001$ ). Seven of 16 effects reduced pain by a mean effect delta of 0.04 (95% CI: –0.14 to 0.21;  $z=0.41$ ;  $p>0.69$ ). Six of 11 effects (54.5%) did not reduce fatigue with the mean effect delta being –0.01 (95% CI: –0.20 to 0.19;  $z=-0.09$ ;  $p>0.93$ ). Depressive or anxiety symptoms were not the primary outcome in any of the included trials.

**Conclusions:** Pharmacologic interventions have improved the management of RA however, research indicates that exercise remains an important part of the overall treatment. This quantitative synthesis of evidence from RCTs of the effects of exercise shows significant small-to-moderate reductions in depressive and anxiety symptoms. It has been reported that the degree of depression and anxiety in people with RA is a preceding sign of physical disability that may appear later in life therefore, aiming to target both through exercise may help to improve HQoL. Future trials should focus on depression and/or anxiety as the primary outcome. Exercise prescription is a core skill for physiotherapists therefore, they should be confident in prescribing exercise to people with RA, who have depression and anxiety, as it significantly reduces their symptoms.

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**OP0276-HPR** OCCUPATIONAL BALANCE AND ITS RELATION TO PERFORMANCE OF VALUED LIFE ACTIVITIES IN PERSONS WITH RHEUMATOID ARTHRITIS IN WORKING AGE

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**Background:** Experience of balance in everyday activities where work is an essential part is important to health and well-being,<sup>1</sup> as has also been observed in previous studies in people with rheumatoid arthritis (RA).<sup>2</sup> The Valued life activity scale (VLA-swe) is a questionnaire in which patient's first report if the separate activities are valued or not to perform and secondly difficulties to perform these activities.<sup>3</sup> Occupational Balance Questionnaire (OBQ) focuses on satisfaction with the amount and variation of occupations.<sup>4</sup>

**Objectives:** The objectives were to 1) describe the relationship between performance of valued activities and experienced occupational balance, and to 2) identify aspects associated with low occupational balance in persons with RA.

**Methods:** 368 persons (age 18–65 years, 77% women) with RA responded to a questionnaire measuring occupational balance (OBQ)<sup>4</sup> and performance of

valued life activities (VLA-swe).<sup>3</sup> Other aspects of interest were activity limitations measured by Health Assessment Questionnaire (HAQ), pain (measured by VAS), continuous stress (stressed continuously for more than a month during the last 12 months), children at home, education, and living situation. The relation between OBQ and performance in VLA across genders and Workers/Non-workers were analysed using non-parametric correlation analyses. To identify the impact of different aspects on the likelihood that participants would report lower occupational balance, OBQ was analysed using workers/nonworkers, stress, gender, age, pain and difficulties performing valued activities as independent variables in logistic regressions models. The study was approved by the Regional Ethics Committee (Dnr2011/452–31).

**Results:** The OBQ was significantly related to difficulties to perform valued activities reported by VLA ( $r=-0.41$ ,  $p<0.001$ ). Having more difficulties performing valued activities was the strongest predictor of lower occupation balance and increased the risk of reporting lower occupation balance with nearly five times (OR=4.54,  $p<0.001$ ). Continuous stress increased the risk of having lower occupation balance more than three times (OR=3.27,  $p<0.0001$ ) than those who not reported being stressed. The other variables show no significant impact on the likelihood that the participants would report lower occupational balance.

**Conclusions:** The results showed support for the relationship between occupation balance and performance of valued life activities and highlights to identify what's important for the individual and to assume that in the rehabilitation. The results also show the importance of ability to manage stress, in order to enable for retaining ability to work and achieve high occupational balance.

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**OP0277-HPR** EVALUATION OF THE EFFECTIVENESS OF A PROGRESSIVE RESISTANCE TRAINING PROGRAM FOR PATIENTS WITH FIBROMYALGIA: A RANDOMISED CONTROLLED TRIAL

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**Background:** Fibromyalgia (FM) is a chronic pain syndrome, not inflammatory, characterised by the presence of diffuse pain and painful points. Commonly, it is linked to other symptoms such as fatigue, sleep disorders, morning stiffness; and psychological disorders such as anxiety and depression. The medical treatment of FM brings benefits in the short term. For long-term benefits it is usually associated with non-medicated treatment, such as patient education, physical conditioning, rehabilitation and psychological therapy. In this study, we used the progressive resistance training, which is muscle strengthening performed through the gradual increase of load during the training period.

**Objectives:** To evaluate the impact of a global progressive resistance training program on pain, quality of life, functional capacity and muscular strength in patients with fibromyalgia

**Methods:** Sixty patients were randomised into 2 groups: experimental group and control group. Patients in the experimental group underwent a progressive resistance training program, performed twice a week for 12 weeks. The charge intensity was progressively increased from 40% to 80% of 1RM. The following muscle groups were worked: trunk flexors and extensors, elbow flexors and extensors, knee flexors and extensors, hip abductors and adductors and shoulder abductors. In addition to strength training, the experimental group also received a structured education program in one hour class once a week for five weeks. Patients in the control group received the same education program.

**Results:** After the intervention, significant improvements were observed in the experimental group in comparison with control group over time for the following parameters: pain ( $p=0.004$ ), FIQ ( $p=0.021$ ), quality of life (with statistically significant improvement for all the SF-36 domains), functional capacity, assessed by the 6 min walk test ( $p=0.045$ ), and muscle strength (with statistically significant improvement for all muscle groups trained). The intergroup and intragroup comparisons were showed in table 1.

Abstract OP0277-HPR – Table 1 Intergroup and intragroup comparisons

	Experimental group				Control group				p-value*	Adjusted p-value*
	T0	T6	T12	Δ	T0	T6	T12	Δ		
Number of pain scales (n)	6.90 ± 1.50	5.00 ± 1.30	5.20 ± 2.50	<0.001	6.90 ± 1.40	7.50 ± 1.80	6.80 ± 2.00	0.50	0.002	0.002
F42 score	5.60 ± 1.20	5.30 ± 1.70	4.70 ± 1.80	<0.001	6.00 ± 1.20	6.90 ± 1.90	6.90 ± 1.30	0.70	0.001	0.001
VAS: Pain score	6.91 ± 2.07	5.41 ± 2.22	5.11 ± 2.53	<0.001	7.07 ± 1.74	7.51 ± 2.04	6.73 ± 2.18	0.67	<0.001	<0.001
Δ Pain score										
Physical functioning	48.39 ± 21.39	58.30 ± 18.70	61.30 ± 19.40	0.001	37.90 ± 22.80	38.00 ± 23.40	35.70 ± 23.00	0.70	0.004	0.002
Physical role functioning	16.04 ± 24.20	32.52 ± 26.10	38.20 ± 28.10	0.001	24.20 ± 26.80	18.00 ± 25.10	13.70 ± 26.10	0.60	<0.001	<0.001
Health status	37.43 ± 16.40	46.10 ± 14.50	46.80 ± 14.80	0.002	33.20 ± 17.10	37.70 ± 17.40	32.50 ± 16.30	0.80	0.002	0.002
General health perception	43.69 ± 22.70	45.80 ± 25.90	51.80 ± 25.50	0.044	38.70 ± 22.30	41.50 ± 24.30	37.80 ± 21.50	0.3	0.004	0.004
Δ Health status	48.80 ± 18.90	50.30 ± 24.00	52.20 ± 22.60	<0.001	37.60 ± 17.80	38.30 ± 18.70	34.50 ± 18.90	0.60	0.002	0.002
Visual Analogue Scale	60.82 ± 21.40	64.20 ± 24.80	62.80 ± 27.20	0.312	48.20 ± 22.80	48.40 ± 22.60	41.70 ± 24.20	0.302	0.013	0.013
Emotional role functioning	12.20 ± 25.00	41.03 ± 40.50	41.70 ± 42.80	<0.001	26.70 ± 45.00	26.30 ± 42.80	23.20 ± 41.20	0.745	0.001	0.001
Δ Visual Analogue Scale	49.50 ± 23.00	55.70 ± 24.80	52.00 ± 22.50	<0.001	45.50 ± 18.60	43.70 ± 17.80	43.50 ± 19.00	0.701	<0.001	<0.001
S: Statistic with trend (p-value)	447.70 ± 80.90	410.50 ± 83.30	483.50 ± 72.90	<0.001	420.60 ± 112.00	427.70 ± 103.40	428.40 ± 114.50	0.861	0.041	0.041

**Conclusions:** The progressive resistance training program was effective in improving pain, quality of life, functional capacity and muscular strength of patients with fibromyalgia.

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**OP0278-HPR PATIENT REPORTED OUTCOMES AND SAFETY IN PATIENTS UNDERGOING SYNOVIAL BIOPSY: COMPARISON OF ARTHROSCOPIC, ULTRASOUND-GUIDED PORTAL-FORCEPS AND ULTRASOUND-GUIDED NEEDLE BIOPSY TECHNIQUES, IN FIVE CENTRES ACROSS EUROPE**

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**Background:** Synovial tissue analysis could provide a step towards personalised medicine in daily clinical practice for patients with inflammatory arthritis. However systematic reports comparing the patient's perspective when undergoing synovial biopsy according to different synovial sampling techniques is currently missing from the literature. We here present a multicenter study across Europe, comparing patient reported outcomes (PRO) and safety data from patients undergoing synovial biopsy procedures using either ultrasound guided needle biopsy (US-NB), ultrasound guided portal and forceps (US-PF) or conventional arthroscopy.

**Objectives:** 1. Describe PRO data on joint indices of pain, stiffness and swelling, procedural discomfort and willingness to undergo a second biopsy for each biopsy technique. 2. Describe and compare safety data. 3. Evaluate the impact of intramuscular (IM) or intra-articular (IA) corticosteroid as part of the biopsy procedure, on PRO data and safety. 4. Evaluate how sequential biopsy procedures impacted on PRO and safety data.

**Methods:** Information on PROs, safety, diagnosis, disease activity and treatment were collected from five European biopsy centres. Joint pain, swelling and stiffness indices were recorded as 0–100 mm VAS; qualitative variables on balanced 5-point Likert scales. PRO data delta values between post and pre-values were calculated. Between group comparisons with unadjusted and adjusted robust linear regression, adjusting for disease activity, corticosteroid use during biopsy procedure and when relevant pre-biopsy value.

**Results:** 524 synovial biopsy procedures were included; 329 (78%) had Rheumatoid Arthritis and biopsies were primarily from wrist (n=296, 57%). PRO and safety data are presented in table 1. None of the biopsy techniques caused increase in pain, swelling or stiffness, and there were no differences in post biopsy and delta PROs between biopsy procedures. There was 9 adverse events (1.7%) with no difference between biopsy methods(p=0.85). 71.7% reported none or mild

discomfort during biopsy and 86.5% were positive or neutral to rebiopsy. Corticosteroid use, IM (n=62) or IA (n=38), did not result in more adverse events (p=0.81). However, it was associated with a reduction in post-swelling (p=0.005), but not pain or stiffness. Sequential biopsy procedures (n=103 patients), did not result in more adverse events (p=0.61) or worsening in PRO data between baseline and second biopsy procedure.

Abstract OP0278-HPR – Table 1 Patient reported outcomes and safety

	Needle	Portal & Forceps	Arthroscopic	Total	p-value	Adjusted p-value*
Biopsy procedures, n (%)	402 (76.7)	65 (12.4)	57 (10.9)	524 (100.0)		
<b>Pain, swelling and stiffness before and after biopsy</b>						
Pre pain, mean (SD)	52.21 (29.14)	45.60 (32.90)	62.44 (23.98)	52.51 (29.36)	<0.01	<0.01
Post pain, mean (SD)	39.47 (29.94)	32.46 (27.42)	43.16 (22.62)	38.91 (29.03)	0.06	0.19
Pre swelling, mean (SD)	50.28 (30.70)	41.02 (33.11)	53.09 (29.26)	49.40 (30.90)	0.07	<0.01
Post swelling, mean (SD)	35.95 (30.47)	31.18 (26.66)	36.46 (26.00)	35.45 (28.52)	0.22	0.17
Pre stiffness, mean (SD)	51.48 (30.33)	47.28 (31.89)	48.79 (30.13)	50.62 (30.77)	0.56	0.03
Post stiffness, mean (SD)	37.72 (30.45)	33.75 (28.01)	36.14 (24.91)	37.61 (29.57)	0.56	0.18
Delta pain, mean (SD)	-12.90 (27.74)	-13.14 (30.36)	-20.94 (28.91)	-13.76 (28.27)	0.17	0.19
Delta swelling, mean (SD)	-14.67 (29.57)	-8.83 (27.74)	-18.68 (35.03)	-14.43 (29.96)	0.28	0.17
Delta stiffness, mean (SD)	-13.70 (28.62)	-13.52 (32.25)	-14.18 (37.49)	-13.72 (30.32)	0.99	0.18
<b>Safety</b>						
Syncope or presyncope, n (%)	2 (0.8)	0 (0.0)	0 (0.0)	2 (0.4)		
Tamponovitis	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)		
Neurological affection, n (%)	4 (1.0)	1 (1.5)	0 (0.0)	5 (1.0)		
Tendon damage, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)		
Haemarthrosis, n (%)	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)		
Deep vein thrombosis	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)		
Joint infection	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.85*	

\* adjusted for biopsy method, disease activity, intra-articular or intramuscular corticosteroid injection during biopsy; used in Post and delta values also pre-values.

† Test for difference in total number of adverse events between groups, by Fisher's exact test.

**Conclusions:** Overall, our results do not suggest a significant difference in tolerability or safety between US-NB, US-PF or arthroscopic synovial sampling. Further, data suggests that use of IM or IA corticosteroid, as part of the biopsy procedure, is safe and improves tolerability. Finally, sequential synovial biopsies were well tolerated and safe when performed using all biopsy techniques.

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**OP0279-HPR A NATIONAL SURVEY OF THE UTILISATION AND EXPERIENCE OF HYDROTHERAPY IN THE MANAGEMENT OF AXIAL SPONDYLOARTHRITIS: THE PATIENTS' PERSPECTIVE**

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**Background:** Hydrotherapy is recommended in the United Kingdom (UK) by the National Institute for Health and Care Excellence (NICE) as an adjunctive therapy in the management of Axial Spondyloarthritis (AS). Despite these guidelines, NHS hospital hydrotherapy services are in decline. The impact on utilisation and patient experience are poorly understood.

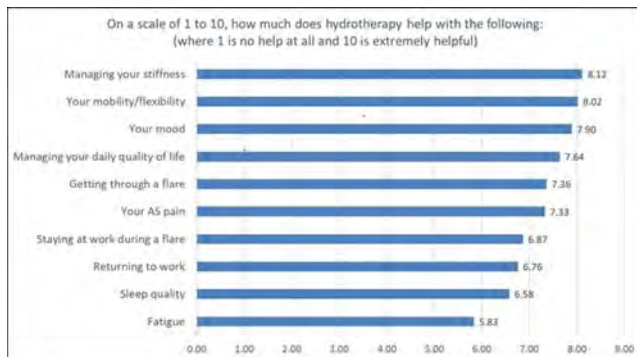
**Objectives:** To identify the utilisation of hospital hydrotherapy services for AS in the UK and capture the patients' experience to inform future services and research.

**Methods:** An online survey was distributed to the National Ankylosing Spondylitis Society (NASS) patient membership between September and November 2017, with social media updates. The survey design included open and closed questions. Thematic analysis of the qualitative responses was conducted.

**Results:** 250 members completed the survey (40.4% male; average age 50.4 years; average delay to diagnosis 11.4 years). **Utilisation:** 157 (65.7%) accessed a hospital hydrotherapy service. 102 (63.0%) were referred by rheumatology, 26 (16.0%) via a specialist AS Physiotherapist and 3 (1.9%) self-referring via a telephone helpline. The most frequent service offered was six weekly sessions. 85 (62.5%) reported no access to hospital hydrotherapy when in flare. Barriers to access in a flare included long waiting times, a limit on the sessions offered and pool closures. 'Pay as you Go' hospital hydrotherapy sessions were accessed by 35 (16.1%) with 119 (77.3%) interested in doing so. 59 (26.9%) received written hydrotherapy resources for continuation in a non-hospital pool following discharge. 77 (50.7%) were advised to continue with hydrotherapy for self-management. Barriers to utilising a non-hospital pool were high cost, lower pool temperature, pool crowding and a lack of knowledge of exercises. 28 (18.5%) reported a current threat of closure of their hospital hydrotherapy pool. **Experience:** Five themes emerged from the qualitative data. 1) *Emotional well-being:* Patients described greater control over their condition when exercising in water. 2) *Exercise Behaviour:* Patients performed a wider variety of exercise, often challenging themselves, and not attempted on land. 3) *Group Effect:* Patients described a sense of motivational support when exercising with others. 4) *Professional Support:* Patients cited the benefit of hydrotherapy sessions led by a physiotherapist who shared their expertise and discussed problems. 5) *Pool Environment:* Patients described gains from non-impact exercise and

weightlessness in the water. The warmer pool temperature was stated as a reason for the benefits obtained.

Reported benefits of hydrotherapy are illustrated in graph 1:



**Conclusions:** This survey suggests variability in utilisation of hospital hydrotherapy services by a national AS patient group in the UK, with barriers to access, lack of promotion and pool closures. Similar benefits of hydrotherapy to those stated in the NICE guidance were experienced.<sup>1</sup> Future service recommendations which focus on flexible access for flare management, 'Pay as you Go' schemes, group exercise and self-management may increase utilisation, optimise experience and reverse decline. Research to assess the benefits of these service recommendations in a clinical population is needed.

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[1] <http://www.nice.org.uk/guidance/ng65>

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#### OP0280-HPR PHYSICAL ACTIVITY IN ESTABLISHED RA AND VARIABLES ASSOCIATED WITH PHYSICAL ACTIVITY MAINTENANCE OVER A SEVEN YEAR PERIOD

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**Background:** Interventions to promote a healthy lifestyle also in patients with rheumatoid arthritis (RA) have been in focus over the last years. Physical activity (PA) defined as moderate-to-vigorous physical activity (MVPA) has the possibility to reduce disease burden in RA and may contribute to improved quality of life (QoL). It is well known that a large number of patients with RA have a sedentary life style and are less active than their healthy peers. However, less information is known about the long term change of MVPA and possible associated variables.

**Objectives:** To study self-reported change of MVPA over seven years in a well-defined RA cohort.

**Methods:** A lifestyle questionnaire was sent twice to patients in the BARFOT cohort, in 2010 (n 1525) and in 2017 (n 1046) with a response rate of 73% and 68% respectively and 950 patients responded to both questionnaires. All patients fulfilled the ACR criteria for classification of RA and had a disease duration at inclusion (1992 to 2006) of  $\leq 12$  months. Patients were dichotomized as being active on recommended levels of MVPA (MVPA<sub>rec</sub>; physically active on a moderate level  $\geq 150$  min/week (MPA) or on an intense level  $\geq 75$  min/week (VPA)) or not (sedentary). The patients reported body mass index, smoking habits, tender (TJC) and swollen joint count (SJC, 28-joints), patient global assessment (PatGA), pain intensity (NRS) and distribution (pain mannequin), fatigue (NRS), physical function (HAQ), health related QoL (EQ5D), comorbidities and medical treatment. Possible associated variables with meeting MVPA<sub>rec</sub> at both time points or not (dependent variable) was studied by using a logistic regression analysis. All variables were adjusted for age, gender and smoking habits.

**Results:** Forty-one percent (n 389) of the patients met MVPA<sub>rec</sub> at both occasions, and they reported better EQ5D scores compared with the sedentary group (mean 0.77 (SD 0.18) vs 0.68 (0.27)). The patients who met MVPA<sub>rec</sub> were younger, (mean age (SD) 59<sup>13</sup> years vs 62<sup>13</sup> years, p<0.001) and were to higher extent never smokers 46% vs 38%, p=0.021. There was a negative association

with meeting MVPA<sub>rec</sub> and being overweight (OR 0.58, 95% CI: 0.43 to 0.96) or obese (OR 0.38, 95% CI: 0.25 to 0.59), the presence of cardiovascular (OR 0.56, 95% CI: 0.41 to 0.75) and pulmonary diseases (OR 0.51, 95% CI: 0.31 to 0.85), TJC (OR 0.98, 95% CI: 0.95 to 0.995), high pain intensity (OR 0.99, 95% CI: 0.987 to 0.998), and pain distribution (OR 0.93, 95% CI: 0.90 to 0.96), worse fatigue (OR 0.99, 95% CI: 0.998 to 0.997) and a worse physical function (HAQ, OR 0.58, 95% CI: 0.45 to 0.76). Patients with higher values in QoL (EQ5D, OR 3.1, 95% CI: 1.52 to 6.2) were positively associated with meeting MVPA<sub>rec</sub>. In 2010 there were no differences in medical treatment between the groups, p=0.377. In 2017 the group meeting MVPA<sub>rec</sub> included a lower number of untreated patients compared to 2010 (25% vs 34%, p=0.017).

**Conclusions:** Only four out of ten patients with established RA reported to maintain recommended levels of PA over a seven year period. Experiencing high quality of life seems to be important for PA maintenance together with lower levels of pain, fatigue and better physical function. Health care professionals need to take the patient perspective into account and support maintenance of physical activities accordingly.

**Disclosure of Interest:** None declared

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#### OP0281-HPR PREFERENCES OF PATIENTS WITH RHEUMATOID ARTHRITIS REGARDING DISEASE MODIFYING ANTI-RHEUMATIC DRUGS: A DISCRETE CHOICE EXPERIMENT

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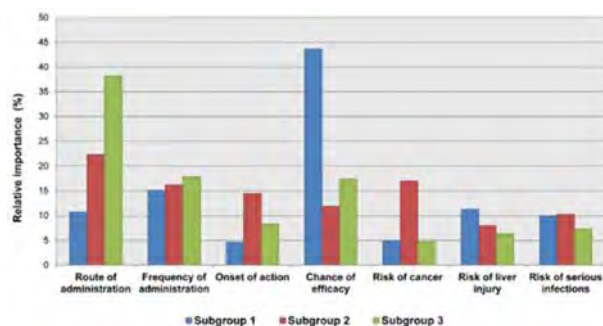
**Background:** Adherence to disease modifying anti-rheumatic drugs (DMARDs) is suboptimal in rheumatoid arthritis (RA) patients. Adherence rates vary from 30% to 90%, which may be partly due to patients' preferences regarding treatment benefits and drawbacks of DMARD therapy. Tailoring treatment options to these preferences might motivate patients to adhere to their drugs and eventually improve adherence.

**Objectives:** The primary objective is to identify subgroups in RA patients based on their preferences towards DMARD characteristics. The secondary objective is to identify characteristics associated with subgroup membership.

**Methods:** A discrete choice experiment (DCE) based on a literature review, expert recommendations and focus groups was used to elicit preferences in RA patients. Patients were asked to state their choice over two different hypothetical treatment options, which were described by seven DMARD characteristics and three levels within each characteristic (e.g. route of administration with the levels: oral, subcutaneous and intravenous). Patients were eligible to participate if they were diagnosed with RA according to the ACR/EULAR 2010 criteria, current user of at least one DMARD, and aged  $\geq 18$  years. Latent class analysis was used to identify subgroups based on stated preferences towards DMARD characteristics and multinomial logistic regression was used to identify characteristics (i.e. beliefs about medicines, patient- and disease-related variables) associated with subgroup membership.

**Results:** A total of 1317 RA patients were invited to participate in this study with an overall response rate of 24.8% (n=326). Three subgroups with segment sizes of 46.5% (SG1), 24.6% (SG2) and 28.9% (SG3) were found. SG1 was most strongly influenced by chance of efficacy, which contributed for 43.6% in their choice for a DMARD. In contrast with SG1, route of administration, risk of cancer and frequency of administration contributed most in SG2 (relative importance (RI) of 22.3%, 17.0% and 16.2% respectively). In SG3, route of administration (RI:38.2%) contributed most in their choice for a DMARD with a strong preference for tablets/capsules. Current and previous use of other cDMARDs (i.e. leflunomide, azathioprine, ciclosporin or gold therapy) and indifferent (low necessity, low concerns) beliefs were significantly associated with assignment to SG2 (Relative Risk Ratio (RRR) 6.03, p=0.0012, RRR=3.64, p=0.013 and RRR:14.91, p=0.003 respectively). Current and previous use of sulfasalazine, other cDMARDs, medium educational level and (early) retirement were significantly associated with assignment to SG3 (RRR:3.91, p=0.009; RRR:0.34, p=0.010, RRR:3.38, p=0.020, RRR:3.12, p=0.005 and RRR:0.358, p=0.034).





Abstract OP0281-HPR – Figure 1 Relative importance of attributes for each subgroup

**Conclusions:** DCE data revealed that RA patients had different preferences for DMARD characteristics, which resulted in the identification of three subgroups. Integrating preferences of these subgroups in patient-tailored treatment decisions and the effect on medication adherence should be part of future research.

#### REFERENCE:

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**Disclosure of Interest:** None declared

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FRIDAY, 15 JUNE 2018

## From gene to function

### OP0282 NEW SYSTEMIC SCLEROSIS RISK LOCI IDENTIFIED THROUGH A META-GWAS STRATEGY

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**Background:** In systemic sclerosis (SSc), previous GWASs have identified several loci associated with the disease, but their rate of discovery has been limited due to modest sample sizes. Extensive collaborative efforts have enabled us to gather the largest cohort of SSc patients. In the present study, we have performed a large meta-GWAS taking advantage of our well-powered cohort.

**Objectives:** To continue unravelling the complex genetic component of SSc.

**Methods:** The complete set of individuals enrolled for this study comprised a total of 26 679 genome-wide genotyped individuals of European ancestry. PLINK and EIGENSTRAT were used for quality control and population stratification adjustments. Genotype imputation was performed with IMPUTE2 and the 1000 Genome Project Phase 3 as reference panel.

**Results:** Twenty-three loci reached the genome-wide significance level ( $p$ -value  $< 5 \times 10^{-8}$ ) in our large-scale meta-analysis. Twelve out of the total significant signals represented new associations and involved novel pathways in the pathophysiology of the disease. Significant enrichment was observed for epigenetic marks of active promoters and active enhancers in critical cell types for the disease. In addition many of the interrogated variants correlated with eQTLs thus altering gene expression.

**Conclusions:** Using a large meta-GWAS, we have identified twelve novel associations for SSc susceptibility and confirmed several previously reported risk loci. These results considerably increase our understanding of the genetic basis of SSc and shed light on the pathogenesis of the disease providing important information to discover new therapeutic targets genetically validated.

**Disclosure of Interest:** None declared

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### OP0283 CROSS-DISEASE META-ANALYSIS IN FOUR SYSTEMIC AUTOIMMUNE DISEASES TO IDENTIFY SHARED GENETIC ETIOLOGIES

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**Background:** Cross-disease genome-wide association studies (GWAS) in autoimmune diseases (AIDs) has become a powerful tool to expose new genetic variants associated with disease susceptibility and to reveal shared biological mechanisms in the pathophysiology of these conditions.

**Objectives:** The goal of our study was to identify shared genetic etiologies by performing a large-scale meta-analysis of four systemic AIDs in individuals from European-descent populations, including rheumatoid arthritis [4595 cases and 3372 controls], systemic lupus erythematosus [3154 cases and 8775 controls], systemic sclerosis [2255 cases and 4407 controls] and myositis [1674 cases and 3150 controls]

**Methods:** PLINK and EIGENSTRAT were utilised for quality control and population stratification adjustments. Genotype imputation was performed using Minimac in the Michigan Imputation Server and the Haplotype Reference Consortium as reference panel.

**Results:** We meta-analysed ~6.5 million single nucleotide polymorphisms (SNPs) (MAF >1%, R<sub>sq</sub> >0.3) across the four diseases and were able to identify 27 genome-wide significant independent loci with at least two diseases leading the association. Our new findings include five unreported shared risk loci: *NAB1*, *KPNA4-ARL14*, *DGQK*, *LIMK1*, and *PRR12*. The results from the meta-analysis were functionally enriched in transcription factor binding sites, promoter and enhancer histone marks and DNase cleavage hotspots in immune cell lines, as well as in epithelial and epidermal cell lines. This is consistent with the clinical manifestations across diseases related to the immune system and the connective tissue. Interestingly, several associated variants were able to modify the expression of the nearest genes and constitute shared expression quantitative trait loci across diseases.

**Conclusions:** These studies offer the opportunity to uncover new biological pathways, address patient classification based on their molecular taxonomy and provide an opportunity for drug repositioning by targeting shared mechanisms across diseases.

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**Disclosure of Interest:** None declared

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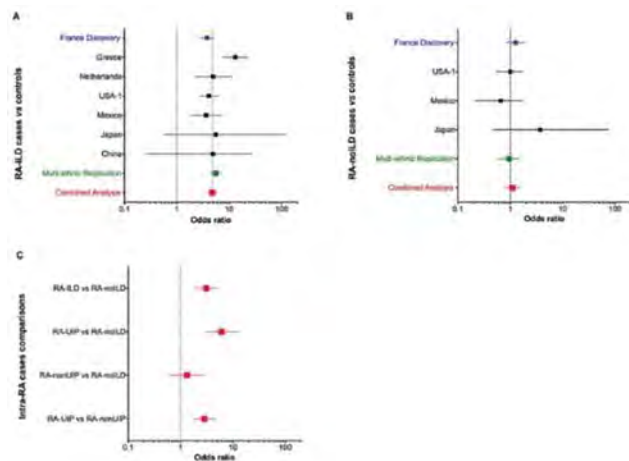
**OP0284 MUC5B PROMOTER VARIANT RS35705950 IS A RISK FACTOR FOR RHEUMATOID ARTHRITIS – INTERSTITIAL LUNG DISEASE**

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**Background:** Rheumatoid arthritis-associated interstitial lung disease (RA-ILD) and idiopathic pulmonary fibrosis (IPF) share phenotypic similarities. The gain-of-function *MUC5B* promoter variant rs35705950 is the strongest risk factor for development of IPF

**Objectives:** We hypothesised that rs35705950 would also contribute to the risk of ILD in RA patients.

**Methods:** Using a French discovery population and multi-ethnic validation populations from 6 different countries, we tested the association of the *MUC5B* promoter variant in RA-ILD (n=620), RA without ILD (n=614), and unaffected controls (n=5448).



**Results:** The discovery population revealed an association of the *MUC5B* promoter variant with RA-ILD when compared to unaffected controls ( $OR_{adj}=3.8$  95% CI: 2.8 to 5.2;  $p=9.7 \times 10^{-17}$ ) (figure 1A). Similar to the discovery cohort, the *MUC5B* promoter variant was significantly over-represented among the cases of RA-ILD in the multi-ethnic study cohorts when compared to unaffected controls ( $OR_{adj}=5.5$  95% CI: 4.2 to 7.2;  $p=4.7 \times 10^{-35}$ ) (figure 1A), and when the discovery population and the multi-ethnic cohorts were combined ( $OR_{combined}=4.7$  95% CI: 3.9 to 5.8;  $p=1.3 \times 10^{-49}$ ) (figure 1A). Additionally, the *MUC5B* promoter variant was found to increase the risk of ILD among patients with RA ( $OR_{combined}=3.1$  95% CI: 1.8 to 5.4;  $p=7.4 \times 10^{-5}$ ), however, no statistical association with the *MUC5B* promoter variant was observed for RA without ILD (figure 1B). The association of the *MUC5B* promoter variant with RA-ILD increased significantly when

restricted to the usual interstitial pneumonia (UIP) by high-resolution computed tomography ( $OR_{combined}=6.1$  95% CI: 2.9 to 13.1;  $p=2.5 \times 10^{-6}$ ) (figure 1C). Immunohistochemical and *in-situ* hybridization analysis of RA-ILD lung tissue demonstrated expression of *MUC5B* by type 2 alveolar epithelial cells undergoing endoplasmic reticulum stress.

**Conclusions:** Our findings demonstrate that *MUC5B* promoter variant rs35705950 is a risk factor for RA-ILD specifically associated with radiologic evidence of UIP.

**Disclosure of Interest:** None declared

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**OP0285 IDENTIFICATION OF RARE CODING VARIANTS IN IL-1-RELATED PATHWAYS IN PATIENTS WITH ADULT-ONSET STILL'S DISEASE**

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**Background:** Adult-onset Still's disease (AOSD) is a rare autoinflammatory disease characterised by fever, arthritis, and multi-organ involvement. Inflammation in AOSD is mediated by interleukin (IL)–1 $\beta$ , as confirmed by the dramatic clinical efficacy of selective blockers of this cytokine. The genetic predisposition to this rampant IL-1-driven inflammation remains nevertheless elusive. Previous studies failed to identify associations between polymorphisms in the genes encoding IL-1 and AOSD, thus pointing at more complex genetic mechanisms. This 'missing heritability' cannot be adequately investigated with traditional techniques for genetic partitioning, such as GWAS, which only assess common variants and polymorphisms. Studies focusing on highly penetrant rare variants or different types of mutations (i.e. small copy-number variations; insertions/deletions) are warranted.

**Objectives:** We hypothesised that genetically determined changes in IL-1-related pathways resulting in excessive IL-1 $\beta$  activity lead to the development of autoinflammation in AOSD. Scope of this study was to unravel the combined mutational variation of a network of IL-1-related receptors, pathways, counter-regulators, and cellular processes possibly involved in the pathogenesis of AOSD and IL-1-mediated inflammation in general.

**Methods:** We collected clinical, demographic, and genetic data from a large cohort of 76 AOSD patients and developed an innovative platform based on molecular inversion probes (MIP) technology for performing highly multiplexed targeted-resequencing. This allows efficient sequencing of the coding sequence of 48 genes related to the IL-1-pathway, and allows studying rare and common variants in one assay. We have also screened 500 healthy controls, and 1000s of samples with other disorders using the same assay.

**Results:** We identified rare and unique (i.e. private variants) in the IL1 pathway in several individuals with AOSD. Whether any these are involved in a strong predisposition to AOSD is currently followed-up. Rare genetic variants have been identified in six IL-1-pathway 'clusters':

1. Deregulated activation of the inflammasome and release of IL–1 $\beta$  and IL–18.
2. IL–1 family receptors and intracellular signalling mediators.
3. Other pro-inflammatory cytokines and receptors.
4. Regulatory molecules, including IL–1Ra or IL–37.
5. Cellular processes regulating production of IL–1 and IL–18 (i.e. autophagy).
6. Production of ROS, which function as markers of cellular damage and trigger inflammation.

**Conclusions:** Unravelling the genetic bases of inflammation in AOSD deepens our understanding of the human innate immunome. Of note, this study platform may serve for the genetic analysis of other IL-1-mediated conditions, including gout and other autoinflammatory diseases, whose genetic predisposition remains elusive. Equally important, the identification of pathways amenable to targeting with small molecules or biologics may translate into remarkable clinical implications.

**Disclosure of Interest:** None declared

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OP0286

### GENOTYPIC EFFECTS OF ANKYLOSING SPONDYLITIS ASSOCIATED IL7R POLYMORPHISMS ARE MEDIATED THROUGH MONOCYTES IN INFLAMMATION

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**Background:** Interleukin 7 (IL-7) plays a key role in T cell survival and proliferation. Both cell-surface expressed and soluble forms of the IL-7 receptor (sIL7R) are recognised. sIL7R has been shown to prolong IL-7 activity in inflammation.<sup>1</sup> IL7R polymorphisms are associated with multiple inflammatory diseases including ankylosing spondylitis (AS). Higher levels of circulating sIL7R are present in those carrying the risk variant but the cellular sources of soluble IL7R are unclear. Expression quantitative trait loci (eQTL) studies have shown genetically regulated IL7R gene upregulation in monocytes after innate immune stimuli.<sup>2</sup>

**Objectives:** This study aims to characterise the genotypic effects of IL7R polymorphism on monocyte protein surface expression and sIL7R release.

**Methods:** Monocyte cell surface IL7R expression was measured by flow cytometry in the presence or absence of LPS or TNF in a cohort of volunteers recruited from the Oxford biobank. Soluble IL7R was quantified by ELISA in purified monocyte cultures stimulated with LPS. RNA sequencing was performed for 8 paired samples of control and recombinant IL-7 exposed stimulated monocytes.

**Results:** Surface IL7R expression was induced after 24 hours of LPS stimulation both in isolated monocytes (n=84, p<8.9e-19) and CD14 +cells in whole PBMC cultures (n=103, p<3.9e-31). We find the key genotypic regulator of this response to be rs6897932, previously associated with AS predisposition, both in isolated monocytes (n=85, p=9e-7) and CD14 +cells in whole PBMC cultures (n=103, p=9.4e-5). There was no genotypic effect seen in unstimulated monocytes. Notably IL7R positivity of CD4+, CD8 +and CD56+cells measured within the PBMC culture both before or after LPS stimulation showed no association with rs6897932. The addition of anti-TNF (Infliximab) abrogated the genotypic effect. In a second independent cohort, genotype-specific surface IL7R induction was also observed after stimulation with recombinant human TNF (n=62, p=0.0007). In a third cohort, release of soluble IL7R was observed to be under genetic control after stimulation with LPS (n=99, p<3.1e-11). RNA sequencing of isolated monocytes stimulated with LPS and recombinant IL-7 showed differential expression of 3240 transcripts (FDR<0.05) compared with LPS alone (n=8). Direct *ex-vivo* staining of monocytes from inflamed synovial fluid of SpA showed significant upregulation of IL7R compared to paired PBMC monocytes (n=4, p<0.015).

**Conclusions:** Monocytes upregulate IL7R expression and soluble IL7R secretion after LPS treatment in a functional, genotype- and TNF $\alpha$ -dependent manner. SpA synovial monocytes express IL7R suggesting preactivation. These data draw attention to an unappreciated key myeloid role for AS risk variants at IL7R.

#### REFERENCES:

- [1] Lundström W, et al. *PNAS* 2013.
- [2] Fairfax BP, et al. *Science* 2014.

**Acknowledgements:** BPF and PB contributed equally to this work

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.3704

OP0287

### GENE ENHANCERS ASSOCIATED WITH AN INCREASED RISK OF DEVELOPING JIA FAIL TO DOWN REGULATE RUNX1 AFTER CELL STIMULATION

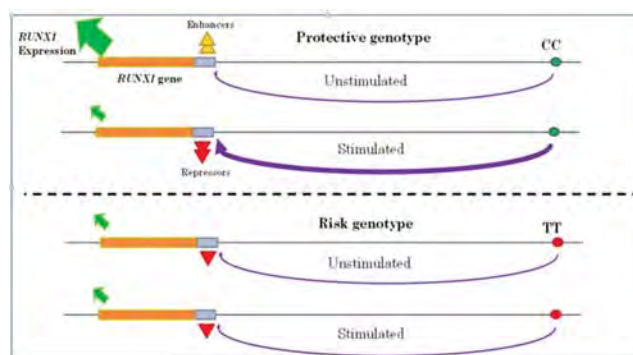
A. Yarwood, C. Taylor, A. Hinks, S. Smith, K. Duffus, A. McGovern, W. Thomson, S. Eyre. *Arthritis Research UK Centre for Genetics and Genomics, Centre for Musculoskeletal Research, Manchester Academic Health Science Centre, University of Manchester, Manchester, UK*

**Background:** In recent years there have been tremendous strides in determining the genetic component of complex diseases, not least in Juvenile Idiopathic Arthritis (JIA). We now have 17 genetic loci robustly associated with an increased risk of developing JIA.<sup>1</sup> In JIA, like all complex diseases, the regions of the genome harbouring genetic changes are found outside protein coding DNA, in regions of the genome shown to control gene expression, often sited some distance from the closest gene. One of these JIA associated regions, on chromosome 21q22, is labelled with the *RUNX1* gene, although the associated variants are situated over 450 kb from the gene. We have previously demonstrated, through Capture HiC analysis, that the genomic region containing the JIA associated variants makes a physical contact with the *RUNX1* promoter. The next challenge in this region, therefore, is to determine how a risk genetic background effects the expression of the gene, contributing to the susceptibility to JIA.

**Objectives:** Determine the function and mechanism of how the gene enhancer region, situated over 450 kb upstream of the *RUNX1* gene, works to increase the risk of developing JIA.

**Methods:** B-lymphocyte cell lines, containing either a risk or protective JIA genetic background at the 'RUNX1' loci were interrogated for potential causative functional mechanism. Allele specific interactions were investigated using chromosome conformation capture (3C), enhancer activity (H3K4me1) with chromatin immunoprecipitation (ChIP), and the resultant expression of the *RUNX1* gene analysed by qPCR in both stimulated (IL4/anti CD40) and unstimulated cell lines.

**Results:** The enhancer region associated with JIA interacts with the *RUNX1* promoter in B-cell lines. A stimulation specific effect is observed in B-cell lines harbouring the protective alleles. In this protective context, prior to stimulation *RUNX1* expression is higher than in the risk genotype with enhancer enrichment detected near the proximal promoter. After stimulation the interaction between the enhancer and *RUNX1* promoter is much stronger, and whilst no enhancer enrichment was detected, this increased interaction frequency after stimulation corresponds to a sharp downregulation of *RUNX1* expression. In contrast, the risk genotype showed no stimulation dependant change, maintaining both interaction and expression levels.



**Conclusions:** 3C and ChIP experiments were performed to investigate genotype and stimulation specific DNA-DNA and DNA-protein interactions and identify correlation with gene expression. These results suggest that the ability for B-cells to switch from relatively high expression of the *RUNX1* transcript to low expression upon stimulation is crucial to an appropriate immune response.

#### REFERENCE:

- [1] Hinks A, et al. Dense genotyping of immune-related disease regions identifies 14 new susceptibility loci for juvenile idiopathic arthritis. *Nat Genet* 2013 Jun;45(6):664–9.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.3883

OP0288

### TRANSCRIPTIONAL PERTURBATION OF RA-RISK ENHANCER BY CRISPR-DEADCA9 REGULATES LONG RANGE GENE TARGETS

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**Background:** Findings from genome wide association studies in complex diseases indicate over 90% of genetic variants associated with risk of developing disease are found outside protein coding regions, suggesting regulation of gene expression is key to disease susceptibility. For rheumatoid arthritis (RA) it has been demonstrated that risk variants are found in gene regulation regions, and are significantly enriched in T-cell specific enhancers. In addition, a significant proportion of associated variants lay some distance from the nearest gene and enhancers may not necessarily regulate the closest gene, effectively 'skipping' genes. Using chromatin conformation technology (HiC) we have demonstrated that an enhancer region intronic of the *COG6* gene, containing variants associated with RA, make robust physical contact with the promoter of *FOXO1*, almost 1 Mb away on the linear chromosome. *COG6* is not an obvious candidate risk gene for RA, whilst *FOXO1* is involved in T-cell development and shown to be over expressed in RA synovium. The challenge now is to provide empirical evidence that the enhancer found within *COG6* does regulate *FOXO1* expression, and how an RA risk genetic background affects this regulation.

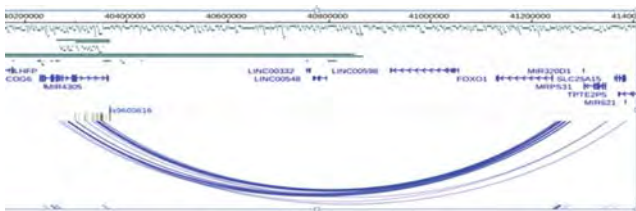


**Objectives:** Use CRISPR-Cas9, to perturb the COG6 intronic enhancer region and measure the downstream effect on the expression of FOXO1.

**Methods:** We utilised a modified form of the Cas9 enzyme, dead Cas9 (dCas9), that can precisely target DNA, but will not induce a cut. Using the dCas9 attached to either enhancers (p300) or repressors (KRAB) of expression we investigated how perturbation of the enhancer intronic of COG6 changed the expression of FOXO1.

We designed 3 guides across the COG6 enhancer, and transduced a cell line (HEK293) using a lentiviral dCas9 CRISPR system, with either dCas9-KRAB or dCas9-p300 and each of the three guides. We cultured the cells until 70%–80% confluent, GFP sorted the cells and then extracted RNA. A quantitative PCR was performed (QuantStudio) for both COG6 and FOXO1 gene transcript expression and normalised to housekeeping genes.

**Results:** Up to 90% of HEK cells were transduced with the dCas9 enzyme and guide, and these were sorted by FACS using GFP to sort the top 60%. The 3 guides gave consistently increased levels of FOXO1 expression with the dCas9-p300, compared to both control and dCas9-KRAB ( $p=0.02$ ). This was particular evident for guide 3, with a 40% increase (p300) and 10% decrease (KRAB) of FOXO1 expression observed. Expression of COG6 was also perturbed, but in a less consistent manner, with both increase and decrease expression for KRAB and p300.



**Conclusions:** Over 90% of HEK cells were transduced with the dCas9 enzyme and guide, and these were sorted by FACS using GFP to sort the top 60%. The 3 guides gave consistently increased levels of FOXO1 expression with the dCas9-p300, compared to both control and dCas9-KRAB ( $p=0.02$ ). This was particular evident for guide 3, with a 40% increase (p300) and 10% decrease (KRAB) of FOXO1 expression observed. Expression of COG6 was also perturbed, but in a less consistent manner, with both increase and decrease expression for KRAB and p300.

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[1] Martin P, et al. Capture Hi-C reveals novel candidate genes and complex long-range interactions with related autoimmune risk loci. *Nat Commun* 2015 Nov 30.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.3946

OP0289

#### INTEGRATION OF CHROMATIN CONFORMATION, TRANSCRIPTOME AND GENOME-WIDE LANDSCAPE OF BRD2 AND BRD4 BINDING MOTIFS IDENTIFIES MECHANISMS OF BET INHIBITOR ACTION IN RHEUMATOID ARTHRITIS SYNOVIAL FIBROBLASTS

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**Background:** Rheumatoid arthritis (RA) is a chronic autoimmune disease characterised by infiltration of immune cells into the synovium and hyperplasia of the synovial lining, resulting in the formation of pannus that degrades cartilage and bone. Fibroblast-like synoviocytes (FLS) are the main cell types of the rheumatoid synovium and possess phenotypic and molecular characteristics of transformed cells. JQ1, an inhibitor of the bromodomain and extra terminal domain (BET) family that includes BRD2, BRD3, BRD4 and BRDT has shown efficacy *in vitro* on RA-FLS proliferation and *in vivo* in a murine model of arthritis.

**Objectives:** We sought to elucidate the mechanism of action of BET proteins in FLS biology and determine the potential therapeutic utility of targeting BRD2/BRD4 for RA disease treatment and interception.

**Methods:** To understand the mechanism of JQ1 action, we subjected JQ1-treated RA-FLS to transcriptional profiling by RNA-Seq and determined BRD2 and BRD4 cistromes by identifying global BRD2/BRD4 chromatin binding sites by ChIP-Seq. In addition, Assay for Transposable Accessible Chromatin by high throughput Sequencing (ATAC-Seq) was employed to identify open and closed regions of chromatin in JQ1-treated RA-FLS.

**Results:** We demonstrate that the active isomer of JQ1 but not its inactive isomer inhibits IL-1b-induced RA-FLS activation and proliferation. Through an integrated analysis of RNA-Seq, ATAC-Seq to profile changes in chromatin accessibility and ChIP-Seq of BRD2/4 and Pol2 proteins, we found that JQ1 inhibited multiple key inflammatory pathways, and altered the genome wide occupancy of crucial transcription factors involved in inflammatory signalling. Specifically, JQ1 treatment resulted in reduced occupancy of both BRD2 and BRD4 in approximately 2000 regions genome-wide, and a loss of Pol2 occupancy in approximately 600 genomic regions. Collectively we found that 105 genes had altered occupancy in all three proteins (BRD2, BRD4 and Pol2) and were also differentially expressed. Most prominently, JQ1 resulted in down regulation of IL6, IL8, p38 MAP kinase and HMGB1/TLR4 signalling pathways. In addition, we have identified BRD2/BRD4 super-enhancer genes and demonstrate that JQ1 altered BRD2/BRD4 occupancy in the IL6 and IL8 super-enhancer regions, and significantly down-regulated IL6, IL8, TLR4 and IL1b expression.

**Conclusions:** Our results suggest pleiotropic effects of JQ1 on pathways that have been individually targeted and shown to be efficacious for the treatment of RA. These studies provide a strong rationale for targeting of BRD2/BRD4 in RA.

**Disclosure of Interest:** S. Nagpal Shareholder of: Johnson and Johnson, Grant/research support from: Johnson and Johnson, Employee of: Johnson and Johnson, V. Krishna Shareholder of: Johnson and Johnson, Grant/research support from: Johnson and Johnson, Employee of: Johnson and Johnson, X. Yin Shareholder of: Johnson and Johnson, Grant/research support from: Johnson and Johnson, Employee of: Johnson and Johnson, D. Pocalyko Shareholder of: Johnson and Johnson, Grant/research support from: Johnson and Johnson, Employee of: Johnson and Johnson, A. Walsh Shareholder of: Johnson and Johnson, Grant/research support from: Johnson and Johnson, Employee of: Johnson and Johnson, K. Bachman Shareholder of: Johnson and Johnson, Grant/research support from: Johnson and Johnson, Employee of: Johnson and Johnson, I. Anderson Shareholder of: Johnson and Johnson, Grant/research support from: Johnson and Johnson, Employee of: Johnson and Johnson, L. Madakamutil Shareholder of: Johnson and Johnson, Grant/research support from: Johnson and Johnson, Employee of: Johnson and Johnson

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FRIDAY, 15 JUNE 2018

#### PARE abstract session

#### OP0290-PARE KEEP AN EYE OUT FOR INVISIBLE PAINS – A DANISH CAMPAIGN

C.R. Ziegler. *Gigtforeningen, Gentofte, Denmark*

**Background:** How does it feel to live with a RMD and have chronic pain? How do you explain pain caused by RMD to your friends and family? How do you make others understand how pain affects your daily life? The communication department of the Danish Rheumatism Association needed to convey living with invisible pains, because it is of such importance to people with RMDs. Based on interviews with the users (people with RMDs) we found the best way of making others understand was to create a film, which illustrated living with invisible pain.

**Objectives:** We wanted to increase the general understanding of RMDs and living with invisible pain in society. The secondary objective was to brand awareness of the Danish Rheumatism Association and to generate leads for further processing, e.g. signing up for membership.

**Methods:** Based on a few interviews with users and several posts from Social Media we focused on making invisible pain visible. By choosing the media of a film we could show what the users found difficult putting into words. The film had to be short to make it possible to share, e.g. on Facebook, and by choosing a film without speak we avoided language barriers. Through adverts we retargeted visitors to our website and generated more members of the association.

**Results:** We launched the film on World Arthritis Day 2017 In 3½ weeks the film reached 1 million users and more than 1000 comments on Facebook, and the number of followers went up by 2000. The total impact of the film will be presented in June 2018.

**Conclusions:** In the presentation we will show how and why the campaign could be such a success. We will focus on how to follow-up the positive results of generating leads and making invisible pain visible.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.2902

**OP0291-PARE RUNNING WITH RHEUMATISM: A 7-WEEK TRAINING PROGRAMME FOR NOVICE RUNNERS WITH INFLAMMATORY RHEUMATIC DISEASE**

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**Background:** In the Netherlands, running is the second most practised sport. Running is also becoming increasingly popular among people with inflammatory rheumatic diseases, according to the growing number of running-related questions to the Dutch Arthritis Foundation and rheumatologists. Frequently asked questions are: 'Am I allowed to run?' and 'How can I start in a safe way?'.

**Objectives:** Given the increasing demand from the target group, and the potential positive health consequences of high-intensity exercise,<sup>1</sup> we developed a 7 week running programme for novice runners with inflammatory rheumatic disease, and explored its feasibility and safety.

**Methods:** First we performed a needs assessment among 228 participants with different inflammatory rheumatic diseases. In all, 200 (88%) participants were interested in practicing the sport of running. Then, a rheumatologist, specialised physical therapist, patient representatives and experienced running trainers developed the running programme, based on the proven effective 'Start to Run' programme of the Dutch Athletics Federation. The programme aims to prepare participants in 7 weeks for a 20 min run without breaks, and consists of one supervised group training session and one or two non-supervised training sessions per week. In addition to gradual progression of joint load (by starting with running on soft even surfaces) and running volume, special attention is paid to development of muscle strength and coordination, optimal movement pattern and running at an own comfortable pace. During the programme, the running trainer is in close contact with a rheumatologist and/or specialised physical therapist who can be consulted for advice.

**Results:** Of the first 24 participants of 'Running with Rheumatism', 12 participants completed the programme successfully, 4 participants developed a running related injury, 1 participant dropped out due to rheumatic symptoms, and 7 participants dropped out due to other reasons (e.g. surgery, infectious mononucleosis, burn-out). Participants indicated that they felt safe and comfortable during the group training sessions, and were surprised to be able to achieve so much progress in a short time period. They felt that they had become stronger and got to know their body and physical capabilities better.



**Conclusions:** The first running groups were successful. The incidence of running related injuries did not significantly differ from incidence rates reported from

comparable programmes for regular novice runners in the Netherlands. Therefore, we aim for nationwide implementation.

**REFERENCE:**

- [1] Jong ZD, Munneke M, Zwiderman AH, et al. Is a long-term high-intensity exercise program effective and safe in patients with rheumatoid arthritis? Results of a randomized controlled trial. *Arthritis & Rheumatism* 2003;48:2415–24.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.3782

**OP0292-PARE THE CREATION OF THE 'AQUA RE-ACTION'. A METHODOLOGICALLY BASED AQUATIC PHYSICAL INTERVENTION/REHABILITATION PROGRAM FOR PEOPLE WITH RMD'S**

A. Iacovou. Cyprus League Against Rheumatism, Limassol, Cyprus

**Background:** As an Aquatic Instructor and an OA patient myself, I faced with other RMD patients the demand for an aquatic physical conditioning program that can meet our needs. After contacting with Patient Leagues and Aquatic Fitness Training Organisations, I found out that there was no such a specific program and it was essential to create one.

**Objectives:** My first objective was to get trained and create an aquatic program that could improve the quality of life through improving the ROM, muscular strength, flexibility, balance and aerobic capacity. My next objective was to accommodate people with variables like having or not fear of water, with minimum or increased joint mobility, with different affected joints and connective tissues. Hence to that I had to approach and convince Rheumatologists, Orthopaedics, Physiotherapists and patients for the benefits of this specific Aquatic program and have it as an option to their rehabilitation. Moreover, I had to use water as my basic instrument and use it's principles (Laws of physics) to estimate the programs intensity. Finally I decided to offer that knowledge through an Instructor course.

**Methods:** In order to get trained, I followed specific training in Aquatic fitness and Rehabilitation by International Aquatic Organisations like the Aquatic Exercise Association, International Aquatic Therapy Faculty and BECO Academy and spending hours in the pool testing exercises and designing the program. Methodologically, I implemented the Principles of Aquatic Environment like buoyancy, hydrostatic pressure, inertia, and biomechanics like, hydrodynamics, movement speed, levers, to estimate the exercise in low to medium intensity and I emphasised on the the quality and the execution of the movement. The program was focused on no pain moves in the biggest possible ROM, using all joints and muscle groups, working on muscle flexibility strength and aerobic capacity. I created a shallow and a deep water program in order to classify participants based on certain criteria.

I contacted meetings with Physicians, and the Cyprus League Against Rheumatism. Published article about Aquatic workout benefits to RMD's at the Cyprus League Against Rheumatism (Cyplar) Journal, I gave lectures and special offer to Cyplar members.

The creation of the Instructors course, needed to start from registering a name, logo and manual. It was also essential to build a business structure to obtain financial and human resources.

**Results:** Based on the participants testimonies there was an improvement on quality of life, their joints range of motion, muscle strength, flexibility and aerobic capacity. Hence to that they mention less pain, move quality night sleep and generally better social life with out depression. All the above was mentioned also from their Physicians and therapists that lead to increasing their trust towards the program benefits. Hence to that our collaboration with CYPLAR continued by organising a joined annual Swimming charity event.

AQUA Re-Action is the registered name of the program, and Logo and Manual are in an ongoing process of final registrations.

**Conclusions:** Having an active lifestyle through an aquatic physical conditioning program, which is under the guidance of a specialised Aquatic Instructor, for at least 3 times per week, can lead to a significant improvement on patients Quality of life within few weeks.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.1674

**OP0293-PARE** **PROBLEMS, GOALS AND URGENT WISHES OF YOUNG AUSTRIANS DIAGNOSED WITH RHEUMATIC DISORDERS: A REPORT**

P. Wegscheider, G. Schaffer. *Austrian Rheumatism League, Maria Alm, Austria*

**Background:** The Austrian Rheumatism League provides information about rheumatic disorders in order to improve the quality of life. It helps to get in contact with professional health caregivers and supports the sharing of personal experience. Because we suspected that young patients often have very different problems, goals and urgent wishes than their older counterparts, we conducted a survey addressing these questions.

**Objectives:** We sent a questionnaire to young people between 15 and 35 years old diagnosed with 'rheumatism' and in order to get information about their diagnosis, their daily lives, their problems, goals and urgent wishes.

**Methods:** 52 persons between 15 and 35 years old and diagnosed with juvenile idiopathic arthritis, rheumatoid arthritis, psoriatic arthritis, Mb. Bechterew, systemic lupus erythematoses, Sjögren-Syndrome, Sharp-Syndrome or fibromyalgia filled out a questionnaire. The subjects were divided into two groups (15–25, 25–35 years). The questions covered gender, province of residence, education, job, retirement, pregnancies/family as well as the problems and goals of the subjects. We also asked where they obtain necessary information about their condition (doctor, web).

**Results:** 55% of the participants were 15–25 years old and 45% were between the age of 25–35 years. 72% were female. Of these, 15 live in the province of Salzburg, 15 in Upper Austria and 15 in Vorarlberg. There were 5 participants each from other provinces (Vienna, Lower Austria, Styria, Carinthia, Tyrol and Burgenland). Most young adults got their information from their doctors (50%) or from the internet (39%). 39% graduated with A-level, 27% graduated at university and 34% completed specialised job training. 78% of these young Austrians were able to earn their living; 22% were not able to work. 29% never got the chance to start working. 35% had enough support to get pregnant and to manage a family. There was a strong desire (81%) for a meeting (which was never held before in Austria). 50% expressed willingness to help us or to run their own group. The most urgent wish of young people diagnosed with a rheumatic disorder is to be healed or to receive the ideal therapy in order to go into remission. The participants felt that there is a lack of understanding and appreciation of young people with painful chronic diseases. Some participants would like to be treated by younger rheumatologists. They feel that this would facilitate 'eye level' consultations. There is also a lack of understanding and support in schools, in civil service settings and in government agencies. A big issue mentioned was inflexible thinking, especially in job settings. Applicants with rheumatic disorders must compete with healthy individuals for forty-hour jobs. For people with a rheumatic disorder a forty-hour job is often too much, but they can do good work in a job with shorter working hours. Young people feel it is necessary to force our society and our doctors to feel responsible for the concerns of young people with rheumatism.

**Conclusions:** Following the positive feedback the Austrian Rheumatism League organised a first meeting for those young people with rheumatism. A program of sports and relaxation in a beautiful natural setting was planned with the aim of enhancing positive, constructive thinking and well-being. We must encourage young people with rheumatic disorders to participate in the activities of the Austrian Rheumatism League, and encourage our society to give up black and white thinking. Everyone should be educated to accept and appreciate handicapped colleagues in their work setting, and to treat them as equals. Furthermore, our government should make it possible for persons with rheumatic disorders to stay at work and with their families even if they are not able to work forty hours a week. All doctors working with rheumatic patients should be familiar with their thoughts, beliefs, aims and problems in order to support them not only with drug prescriptions but also with understanding.

**Disclosure of Interest:** None declared

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**OP0294-PARE** **ADDRESSING KEY CHALLENGES OF LAY INVOLVEMENT IN MUSCULOSKELETAL RESEARCH: CO-APPLICANTS AND TRIAL STEERING COMMITTEES**

A. Higginbottom, S. Blackburn, R. Taylor, C. Rhodes, L. Campbell, K. Dziedzic. *Research Institute for Primary Care and Health Sciences, Keele University, Keele, UK*

**Background:** Patient and Public Involvement (PPI) in research is a requirement of funding in the UK. It has shown to improve the relevance and quality of research. For over 10 years, a Research User Group (RUG) of over 100 patients with musculoskeletal and other long term conditions who actively work with a Research Institute.<sup>1</sup> Researcher and anecdotal feedback from RUG members and researchers have highlighted two challenging PPI roles: lay co-applicants on research grants and lay membership of trial study steering committees (TSCs).

For some RUG members, this has resulted in a less positive experience and a disinterest in having these important roles in the future

**Objectives:** To address the challenges of involving RUG members as co-applicants and as members of TSCs, and to describe ways of supporting RUG members in these roles.

**Methods:** Information to improve understanding of the challenges of these roles were gathered during group meetings and informal conversations with 13 RUG members, and a workshop with 35 researchers. PPI and researcher perspectives were captured on flipcharts, notes and meeting minutes. This information shaped the development of resources and approaches to support RUG members as lay co-applicants and TSC members.

**Results:**

**Abstract OP0294PARE – Table 1.** Challenges and support of lay co-applicants and TSC lay members

	Challenges	Support provided
Lay co-applicant	Understanding the role and time commitment Managing expectations Difficulties with online grant submission process Research jargon	Guidance and advice provided for RUG members and research teams Early meetings encouraged between research teams and RUG members to discuss and agree roles Personal and technical support provided for lay members during the grant submission process Glossary
Lay members of TSCs	Understanding the role and process of TSCs Understanding study background, aim and design Sustaining interest during extended periods between meetings Uncertainty about what, how and when to contribute in meetings Awareness of role by other TSC members Lack of training Teleconference meetings Volume of emails and paperwork to review Research jargon	Training module for RUG members Guides for Chairs, RUG members and researchers Pre-meetings with Chair and post meeting support (debrief) Two RUG members to attend for mutual support PPI as a set agenda item and lay contribution encouraged throughout meetings PPI Support Worker attend meetings to support RUG member Hard copies of paperwork sent, sections relevant to lay input highlighted Glossary

**Conclusions:** Providing support to RUG members and researchers can sustain active and long-term lay involvement in these challenging yet important research roles.

**REFERENCE:**

[1] Jinks, et al. *Res Involv Engagem* 2016;2:1.

**Acknowledgements:** We thank all RUG members for their contribution to our research, and R Taylor, C Ingram, C Walker, S Dent, P Callaghan for their input to training and guidance. We thank the Primary Care Consortium and Arthritis Research UK for supporting the RUG. KD is part-funded by a NIHR Knowledge Mobilisation Research Fellowship (KMRF-2014–03–002).

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.6328

**OP0295-PARE** **'KWEK BEGRIP': THE LAUNCH OF OUR CREATIVE CAMPAIGN ACROSS THE NETHERLANDS ON WORLD ARTHRITIS DAY AIMS TO INCREASE AWARENESS ABOUT RMDs IN GENERAL AND PEOPLE LIVING WITH RMDs IN PARTICULAR**

S. De Jong. *Patient advocacy, Dutch Arthritis Foundation, Amsterdam, Netherlands*

**Background:** With two million patients, RMDs are one of the most common chronic diseases in the Netherlands. A 2016 Nivel survey showed that 50% of all RMD patients deal with people who know too little about RMDs in order to understand their situation. RMDs are not always visible, and symptoms may vary from day to day. This often leads to friends, colleagues, neighbours and even relatives showing incomprehension. For RMD patients this can lead to loneliness, insecurity and a sense of not being accepted. Understanding RMDs and being able to show compassion starts with knowing about RMDs.

**Objectives:** By launching a national creative campaign about incomprehension, the Dutch Arthritis Foundation aims to raise general awareness of RMDs to promote understanding of people with a RMD and to reduce their sense of loneliness.



**Methods:** The Dutch Arthritis Foundation started its campaign on World Arthritis Day: 'Grow awareness, plant a bulb!'. To 'grow understanding', we created two special tulip bulb fields, one online and one offline, for participants to plant the special 'Anita Witzier' tulip bulb. Anita Witzier is a well-known Dutch television host who suffers from rheumatoid arthritis. She has been ambassador for the Dutch Arthritis Foundation since 2001.

With the help from 70% of all local RMD patient organisations and a number of garden centres, we handed out a total of 15 000 bags of tulip bulbs across the Netherlands. The campaign kick-off was on World Arthritis Day. The event, held on a tulip breeder's field, hosted presentations about incomprehension, and served to share real-life stories.

We also developed a website where people could plant bulbs digitally. Every week, participants receive a video, cartoon, update or article with information about RMDs. The campaign will run until 21 May 2018 when the (real-life) tulips will bloom in our RMD field. All participants can then visit the field to pick a bunch of flowers.

**Results:** The campaign received a great deal of national media attention on WorldArthritisDay, and featured on television programmes, in newspapers and on online platforms. 8000 people have since signed up for the online tulip field, sharing the information with others in their network. The campaign site drew 68 000 visitors between 12 Oct and 31 Oct. The campaign also resonated with people on Facebook. In October, our campaign posts reached 1,869,000 visitors, with more than 65 000 interactions (respond, share, like, watch video, conversion to campaign site).

**Conclusions:** Raising awareness for incomprehension can be difficult. A creative approach can help to kickstart a public debate. Responses generally show that people with RMDs appreciate this complicated subject being put on the map.

**Disclosure of Interest:** None declared

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OP0296

#### THE RISK OF DELIBERATE SELF-HARM IN RHEUMATOID ARTHRITIS AND ANKYLOSING SPONDYLITIS: A POPULATION-BASED COHORT STUDY

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**Background:** Inflammatory arthritis is associated with the development of mental health disorders. However, there is limited data on the risk of serious mental health outcomes following a rheumatoid arthritis (RA) or ankylosing spondylitis (AS) diagnosis.

**Objectives:** To estimate the risk of deliberate self-harm in patients with ankylosing spondylitis or rheumatoid arthritis compared with the general population.

**Methods:** We evaluated population-based cohorts of RA (n=53,240) and AS (n=13,964), each matched 1:4 by age, sex, and calendar year (at diagnosis) with non-IA comparator cohorts in Ontario, Canada. Individuals with a history of mental illness or prior episode of deliberate self-harm were excluded. The outcome was a first emergency room presentation for deliberate self-harm, subsequent to RA or AS diagnosis, between April 1, 2002 and March 31, 2016. We estimated hazard ratios (HR) and 95% confidence intervals (95% CI) for RA and AS, separately, versus the comparator groups, adjusting for demographic, clinical and health service utilisation variables.

**Results:** Individuals with AS were more likely to deliberately self-harm (incidence rate [IR] of 6.79/10,000 person years [PY] compared to 3.19/10,000 PY in comparators, with an adjusted HR 1.82 (95% CI: 1.26 to 2.62). Deliberate self-harm was also increased for individuals with RA (IR 3.51/10,000 PY) compared to comparators (IR 2.45/10,000 PY) only before (HR 1.43, 95% CI: 1.16 to 1.75), but not after covariate adjustment (HR 1.09, 95% CI: 0.88 to 1.36). The most frequent method of self-harm was poisoning (64% of attempts in AS, 81% in RA) or self-mutilation (36% in AS, 18% in RA).

**Conclusions:** There is a significantly increased rate of self-harm attempt in inflammatory arthritis and the risk is particularly elevated following a diagnosis of AS. These findings highlight the need for routine evaluation of self-harm behaviour as part of the management of chronic inflammatory arthritis. Understanding the mechanisms contributing to deliberate self-harm attempts will help tailor preventive strategies to reduce morbidity associated with this serious mental health outcome.

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**Disclosure of Interest:** None declared

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FRIDAY, 15 JUNE 2018

#### More money or more education and collaboration?\_

OP0297

#### DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS PATIENTS IS INFLUENCED BY COUNTRIES' SOCIOECONOMICS: RESULTS FROM THE METEOR REGISTRY

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**Background:** The treatment and prognosis of rheumatoid arthritis (RA) patients have improved tremendously, but patients across the world may not benefit similarly. One of the potentially critical factors may be poorer access to expensive biological (b)DMARDs.

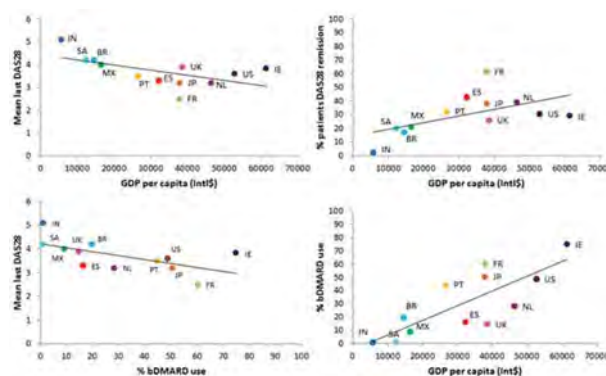
**Objectives:** To investigate daily practice data regarding bDMARD-use in different countries worldwide and assess if a lower country's socioeconomic status (SES) is associated with worse clinical outcomes and lower usage of bDMARDs.

**Methods:** Data on disease activity and drug use from countries that contributed  $\geq 100$  RA patients after 1–2000 were extracted from the daily practice, observational METEOR database. Missing data were imputed using multi-variate normal imputation (30 cycles). Gross domestic product (GDP) per capita in international dollar (Int\$) was used as indicator of SES. Per country average DAS28 and the proportion of patients in DAS28-remission (DAS28 <2.6) were calculated by taking the average of all patients at the last available visit. Univariable logistic regression analyses were performed to assess associations between GDP, bDMARD use and disease outcomes at a country level.

**Results:** In total, 20,379 patients were included from 12 countries: United States, Mexico, South-Africa, Japan, Brazil, United Kingdom, Spain, Ireland, Portugal, France, India and the Netherlands. The number of patients ever using a bDMARD varied between 0.9% (South-Africa) and 75% (Ireland). The proportion of patients in remission at the final visit varied between 2% (India) and 39% (Netherlands).

Patients in countries with a higher GDP per capita had a lower average DAS28 and consequently, a higher proportion of them were in DAS28-remission:  $\beta$  (95% CI)  $-0.32$  ( $-0.41$ ;  $-0.021$ ) lower DAS28 and an additional 4.2% (0.14; 8.26) of patients in DAS28-remission for every 10,000 Int\$ additional GDP.

To underscore the assumption that the association between SES and DAS28 is mediated by bDMARD use, we assessed whether SES was associated with bDMARD use per country. Indeed, a higher GDP per capita was associated with a higher proportion of patients using a bDMARD:  $\beta$  (95% CI) 11.2 (4.82; 17.5), indicating an additional 11% of patients using a bDMARD per 10,000 Int\$ increase in GDP per capita. Furthermore, DAS28 was  $\beta$  (95% CI)  $-0.14$  ( $-0.28$ ;  $-0.0054$ ) lower and 2.8% ( $-0.13$ ; 5.8) more patients achieved DAS28-remission per 10% increase in proportion of patients using a bDMARD, figure 1.



**Abstract OP0297** – Table 1 Associated between 'GDP per capita (Int\$)', '% bDMARD use' and 'disease activity'.

**Conclusions:** RA patients in countries with a lower SES had worse disease activity. Although patients in countries with a lower SES less often used bDMARDs, the effect of bDMARD use on disease activity was smaller than expected, indicating that other factors than access to bDMARDs may contribute to the effectiveness of RA treatment.

**Disclosure of Interest:** None declared

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OP0298

### THE COMPARATIVE EFFECTIVENESS OF CYCLING TUMOURNECROSIS FACTOR INHIBITOR (TNFI) VERSUS SWAPPING TO A NONTNFI ON PATIENT-REPORTED FUNCTIONAL ABILITY OF PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Data on patient-reported functional ability to evaluate the optimal strategy for patients who have failed to first TNFi is scarce. Patient-reported outcomes are a critical component of assessing whether clinicians are improving the wellbeing of patients.

**Objectives:** We conducted a systematic review and meta-analysis to evaluate the comparative effectiveness of two strategies, cycling versus swapping, on patient-reported functional ability and other patient-reported outcomes.

**Methods:** Four electronic databases were searched (MEDLINE, EMBASE, Cochrane Library, and Web of Sciences). Sources of grey literature (unpublished records) were searched through clinicaltrials.gov and other websites. The selection process, risk of bias assessment, and data extraction were performed by two independent reviewers. We included controlled trials evaluating patient-reported outcomes in patients either cycling to a second TNFi or swapping to a targeted drug with an alternative mechanism of action. Other outcomes reported included pain, patient global assessment, fatigue, and quality of life.

**Results:** We included 13 studies reporting data on 4394 patients. The reported cycling strategies were adalimumab, certolizumab, etanercept, golimumab, or infliximab; swapping strategies were abatacept, rituximab, tocilizumab, or tofacitinib. For the individual comparisons, TNFi versus disease modifying antirheumatic drug (DMARD), there was a statistically significant increase in functional ability from baseline to 14 weeks, favouring those patients receiving the cycling strategy (Mean Difference (MD) -0.20, 95% CI: -0.34 to -0.06; scores ranging from 0 to 3). Differences favouring cycling when compared to a DMARD were also observed for pain, fatigue, and patient global assessment. Similarly, when comparing nonTNFi versus DMARD, there was a statistically significant increase in functional ability from baseline to 24 weeks, favouring those patients receiving the swapping strategy (MD -0.31, 95% CI: -0.35 to -0.27; scores ranging from 0 to 3). Differences favouring cycling when compared to a DMARD were also observed for pain, sleep, fatigue, patient global, and quality of life (SF-36 physical and mental components). Three RCTs directly compared the two strategies. There was no statistically significant differences in the functional disability reported between those patients assigned to the cycling strategy compared with those assigned to the swapping strategy at 12, 24, 36 or 52 weeks (MD at 52 weeks -0.05, 95% CI: -0.18 to 0.09; score ranging from 0-3).

**Conclusions:** Although evidence from previous reports suggest that swapping may be more effective than cycling when evaluating some clinical outcomes our results suggest that with the current evidence both strategies are equally effective in improving functional disability and other patient-reported outcomes.

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OP0299

### COST-EFFECTIVENESS OF TAPERING TNF BLOCKERS VERSUS CONVENTIONAL SYNTHETIC DMARDS IN RHEUMATOID ARTHRITIS: FIRST YEAR RESULTS OF THE RANDOMISED CONTROLLED TARA-STUDY

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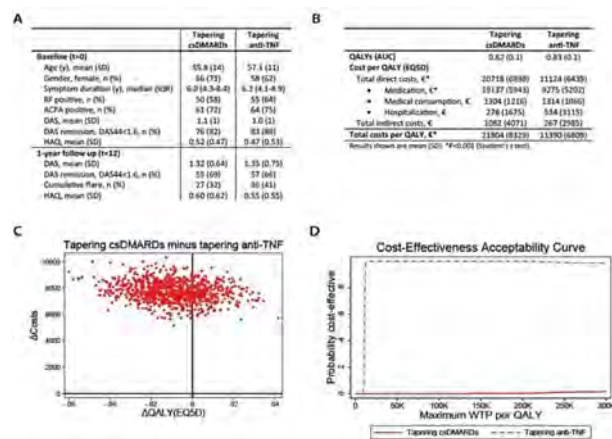
**Background:** Current guidelines recommend to consider tapering treatment in rheumatoid arthritis (RA) patients who are in sustained remission, but the optimal approach to de-escalate conventional synthetic and biological DMARDs (respectively csDMARDs and bDMARDs) remains unknown. The benefits of tapering are a decreased risk of long-term adverse events and a reduction of health care costs, especially when bDMARDs are tapered. However, tapering treatment may lead to more transient or persistent disease flares, which have a direct impact on patients' lives and societal costs.

**Objectives:** The aim of this study is to evaluate the difference in cost-effectiveness of tapering csDMARD or anti-TNF therapy during one year of follow-up.

**Methods:** The TARA trial is a multicenter single-blinded randomised controlled trial. Included were RA patients that used a combination of csDMARDs and anti-TNF and who were at least for 3 months in sustained remission, defined as a DAS<sub>2.4</sub> and a swollen joint count (SJC) ≤1. Patients were randomised into

gradual tapering csDMARDs followed by the TNF blocker or vice versa. Medication was tapered in three steps over the course of 6 months. Gradual tapering was done by cutting the dosage into half, a quarter and thereafter it was stopped. Data on QALYs (measured with the Dutch EuroQol [EQ5D]), direct, and indirect costs were used to calculate the Incremental Cost Effectiveness Ratio (ICER). Direct costs comprises costs for treatment and medical consumption, while indirect costs comprises costs due to loss of productivity (i.e. sick leave and unemployment).

**Results:** A total of 187 patients were randomly assigned to tapering csDMARDs (n=93) or tapering anti-TNF (n=94). Patients had an average symptom duration of 6.7 years and were predominantly female (66%) with an average age of 56.4 years (figure 1A). Average QALYs (SD), over 1 year, for tapering csDMARDs or anti-TNF were, respectively, 0.82 (0.1) and 0.83 (0.1) (figure 1B). One year after inclusion a none significant difference in cumulative flare ratio of 9% was observed (overall flare ratio 36%). Patients in the anti-TNF tapering group had lower costs per QALY (SD) (€11 390 (6809)) compared to patients in the csDMARD tapering group (€21 804 (8329)). The difference in costs per QALY were mainly determined by the medication costs (figure 1B). The Incremental Cost Effectiveness Ratio (ICER, 95% CI) between tapering csDMARDs and anti-TNF was €31 922 (-€920572, €984416) (figure 1C). Tapering anti-TNF was >95% cost-effective across all willingness-to-pay thresholds compared to tapering csDMARDs (figure 1D).



**Abstract OP0299** – Figure 1 Summary of economic evaluation. (A) baseline characteristics and results after 12 months of follow-up of both tapering groups. (B) total costs per QALY after 1 year of follow-up. (C) cost effectiveness and plane of costs of tapering csDMARDs minus costs for tapering anti-TNF. (D) acceptability curves for tapering csDMARDs and tapering anti-TNF. Abbreviations: AUC; area under the curve, csDMARDs; conventional synthetic DMARDs, EQ-5D; Dutch EuroQol, QALY; quality adjusted life year, WTP; willingness to pay.

**Conclusions:** Tapering anti-TNF is more cost-effective compared to tapering csDMARDs. Therefore, in RA patients who are in sustained remission we advise to taper anti-TNF first, but before tapering therapy rheumatologist should take the risk of a disease flare and patient's wishes into account.

**Disclosure of Interest:** None declared

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OP0300

### REDUCING AVOIDABLE BIOLOGIC DRUG WASTAGE THROUGH COLLABORATION BETWEEN PATIENTS AND CARE PROVIDERS: THE LEEDS SPONDYLOARTHRITIS SERVICE EXPERIENCE

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**Background:** The Leeds rheumatology department manages a cohort of approximately 4,000 patients with inflammatory arthritis receiving biologic therapies with an estimated annual cost of £15,000,000. Of these, approximately 1,000 have axial Spondyloarthritis or Psoriatic arthritis (SpA). Biologic drug wastage with self-injectable drugs can occur when patients have no further use for their existing stockpile of drug (typically occurring when receiving further stock around the time of stopping, pausing or switching drugs). Wastage is recorded by home-delivery companies on receiving returned 'unusable' stock. With intravenous drugs, wastage occurs when patients don't attend infusions. Reducing risk of self-injectable wastage has been achieved (1) but reducing self-injectable and intravenous biologic wastage has not.

**Objectives:** To establish whether a patient information letter could be used to reduce measured biologic drug wastage.

**Methods:** All SpA patients receiving biologic therapies (infusion or self-injectable) were identified by prescription records. Wastage (recorded by the infusions ward & home-delivery companies) was reviewed from January 2016 until May 2017. A patient information leaflet (PIL) was developed and sent simultaneously to all patients advising how to minimise wastage (ie: call the infusions ward or delivery companies early when unable to attend and pausing, stopping or switching biologics respectively). The same wastage was measured for 4 months afterwards.

**Results:**

Time.frame	16 .months Jan.2016 to.May.2017	4 .months May.to. Sep.2017	12 .month.projection
Biologic Drug wasted	Pre.intervention.wastage (negative.value)	Post. intervention. wastage	Projected.annual. savings.(positive.value)
Adalimumab	-£12,598.33	£0.00	+£9,448.75
Certolizumab	£0.00	£0.00	£0.00
Golimumab	£0.00	£0.00	£0.00
Tocilizumab	-£1,612.80	£0.00	+£1,209.60
Ustekinumab	-£2,147.00	£0.00	+£1,610.25
Secukinumab	£0.00	£0.00	£0.00
Infusions(infliximab and biosimilar)	-£64,680.00	£0.00	+£48,510.00
Total financial value	-£81,038.13	£0.00	+£60,778.60

In the 16 months prior to the PIL intervention an estimated £81,000 of wastage was measured. Of this, 80% was due to infusion ward wastage (n=45 infliximab infusions) and 20% was due to self-injectable biologics. Following the PIL intervention, no wastage was measured either on the infusion ward or for self-injectable biologics. This resulted in a projected annual saving of £61,000 (80% of which was related to avoidable infliximab wastage). During the observation period the total number of patients taking biologics did not change significantly. No adverse events have been associated with this PIL. Limitations include; a standardised infliximab dose banding was introduced during the final month which may have reduced wastage; Etanercept/etanercept biosimilar data are incomplete as the project is ongoing and are therefore excluded from the analysis.

**Conclusions:** This is the first intervention demonstrating a reduction in measured biologic drug wastage. It represents a simple, reproducible and sustainable intervention through a collaborative effort between patients and health care providers and offers potential significant savings in a time of austerity.

**REFERENCE:**

[1] Whiteman, et al. *Rheumatology* April 2016;55(suppl 1):i119.

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**Disclosure of Interest:** None declared

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**OP0301 TWO YEAR COST-EFFECTIVENESS ANALYSIS OF THE CARERA TRIAL IN EARLY RA: A PIGGY BACK STUDY**

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**Background:** Rheumatoid arthritis (RA) causes high individual, medical and societal costs. EULAR guidelines suggest treating early, intensively and to target using disease modifying anti-rheumatic drugs (DMARDs), preferably with initial glucocorticoid (GC) bridging. COBRA slim, a combination of methotrexate (MTX) with a moderate dose prednisone step down bridge scheme showed a positive efficacy/tolerability balance in the Care in early RA (CareRA) trial. COBRA Slim in comparison to DMARD combination therapy with GC bridging, has the necessary intensity to induce remission, but with a lower risk of severe discomfort or adverse events, decreasing the early need for biologic (b)DMARDs.

**Objectives:** Perform an economic evaluation on the 2 year pragmatic randomised CareRA trial.

**Methods:** Patients with early RA (≤1 year) naïve to DMARDs were randomised to monotherapy or synthetic (cs)DMARD combination with or without GC bridging, after risk stratification based on classical prognostic markers. Clinical and patient-reported data were collected at each visit (≥ 10 times in 2 years).

Direct costs of visits and RA medication (systemic GCs, cs and bDMARDs) over 2 years were calculated for each patient from each of the 5 treatment arms (table 1).

For cost-effectiveness analysis, benefits were expressed as the proportion of patients with DAS28CRP<2.6 at year 2. Missing data was imputed per item with expectation maximisation.

For cost-utility analysis, utilities were calculated using a validated mapping algorithm reconstructing EQ-5D scores based on age, sex, HAQ and pain scores at relevant study visits. Quality-adjusted life years (QALYs) encapsulating the impact of treatment on a patient's length of life and health-related quality of life, were calculated as the time-weighted average of all available EQ-5D scores (area under the curve).

Incremental cost-effectiveness ratios (ICERs) from each strategy were calculated. ICERs compare the additional costs a strategy imposes over another with the additional benefits it delivers. Means and medians based methods were calculated with confidence intervals via bootstrapping.

**Results:** From the initial CareRA cohort (n=379), cost/benefit data of 326 patients was used for a 2 year economic analysis. The mayor driver of direct costs was bDMARDs (57%>87% of total costs). Number of consultations were comparable (±11) across all treatment strategies.

The cost-effectiveness analysis in the high risk population showed a higher ICER for COBRA Avant Garde (mean € 198.65/1%, median € 78.41/1%) and a dominated ICER for COBRA Classic (mean € -181.40/1%, median € -35.01/1%) compared to the Slim. In the low risk arm, ICERs for COBRA Slim compared to Tight Step Up (TSU) were € 46.75/1% (mean) and € 43.64/1% (median).

Cost-utility analysis in the high risk arm showed an incremental cost of € 1 469.36 for an increased utility of 0.012555 QALYs for COBRA Classic compared to COBRA Slim, resulting in an ICER of € 117 033.85/QALY.

The ICER of COBRA Avant Garde vs COBRA Slim was € 69 329.19/QALY. In the low risk arm, the comparison of COBRA Slim to TSU yields an ICER of € 1 342.78 per QALY.

**Abstract OP0301 – Table 1**

Treatment strategy	Direct costs		Effectiveness		Utility			QALYs of 2 years	
	Mean (95% CI)	Median (IQR)	Mean ± SD	% <2.6 at Y2	Y1	Y2	Mean ± SD		
HIGH RISK	COBRA Slim n=67	€ 238.62 (€1 713.15, €2 896.13)	€ 1 145.37 (1034.96-1588.07) BS-CI €3 192.64, €1 267.93	2.20 ± 0.87	75.9 % BS-CI 67.8%, 83.9%	0.57	0.82	0.82	1.64 ± 0.31 BS-CI 1.57, 1.69
	COBRA Classic n=67	€ 707.98 (€2 942.15, €4 923.24)	€ 1 428.92 (1 342.46, 1 878.27) BS-CI €1 378.84, €1 481.98	2.30 ± 0.88	87.3 % BS-CI 58.6%, 75.9%	0.53	0.82	0.81	1.65 ± 0.32 BS-CI 1.58, 1.72
	COBRA Avant Garde n=77	€ 410.83 (€2 287.62, €5 933.28)	€ 1 608.01 (1305.72-1763.05) BS-CI €1 591.61, €1 929.40	2.03 ± 0.83	81.3 % BS-CI 74.6%, 93.6%	0.56	0.82	0.86	1.65 ± 0.34 BS-CI 1.58, 1.72
LOW RISK	COBRA Slim n=34	€ 3055.64 (€1 596.07, €5 383.40)	€ 1 124.04 (1029.76-1825.78) BS-CI €1 040.66, €1 286.20	1.95 ± 0.86	79.4 % BS-CI 67.6%, 88.2%	0.60	0.87	0.87	1.72 ± 0.31 BS-CI 1.67, 1.83
	Tight Step up n=41	€ 877.99 (€ 1 262.42, €4 740.37)	€ 968.19 (809.85-1555.25) BS-CI € 897.13, €1 186.03	2.23 ± 1.03	75.6 % BS-CI 63.4%, 85.4%	0.66	0.84	0.82	1.59 ± 0.35 BS-CI 1.49, 1.68

BS-CI: 95% confidence intervals resulting from 1000 bias-corrected and accelerated bootstrapped replications; QoL: quality of life; QALYs: quality-adjusted life years; SD: standard deviation; IQR: interquartile range; BS: baseline; Y1: year 1; Y2: year 2

**Conclusions:** COBRA Slim which consists of an initial combination of MTX and a moderate dosed GC remission induction scheme has a favourable cost-effective and cost-utility profile for patients with early RA independent of their prognostic factors.

**Disclosure of Interest:** S. Pazmino: None declared, R. Westhovens: None declared, J. Joly: None declared, V. Stouten: None declared, D. De Cock: None declared, K. Van der Elst: None declared, P. Verschueren Grant/research support from: Unrestricted Pfizer Chair in the management of early rheumatoid arthritis

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**OP0302 AN EVALUATION OF UTILISATION PATTERNS AND APPROPRIATENESS OF LABORATORY TESTS AMONG NEW REFERRALS TO RHEUMATOLOGISTS: CHOOSING UNWISELY!**

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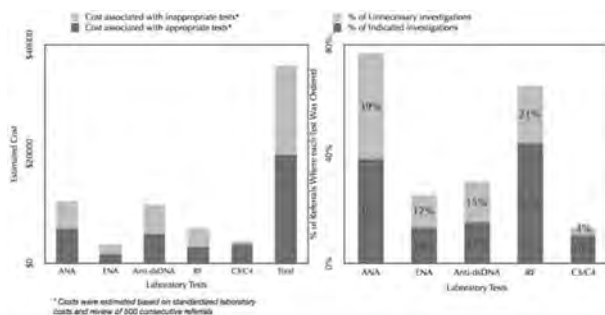
**Background:** Laboratory testing including autoantibodies are common investigations ordered by physicians in diagnosing rheumatic diseases. Tests such as rheumatoid factor (RF) and antinuclear antibody (ANA) have been shown to have low positive predictive value and questionable clinical utility in general practice. <sup>1-3</sup>Optimizing value in medical care is a worldwide concern. In addition, overuse of diagnostic tests can increase health resource use, lead to unnecessary referrals, and cause anxiety associated with positive results. To that end, the Canadian Rheumatology Association (CRA) joined the national Choosing Wisely Canada Campaign and developed a list of 5 tests with evidence indicating they may not be adding value and in fact be harmful. Among these, ANA testing was identified as one of the tests often inappropriately ordered. <sup>3</sup> When combined with extractable nuclear antibodies (ENA) and anti-dsDNA, these tests impose a significant cost.



**Objectives:** To evaluate the utilisation patterns, appropriateness, and associated cost of tests (ANA, ENA, anti-dsDNA, RF, and complement levels) in patients referred to rheumatologists 2 years after release of CRA choosing wisely guidelines.

**Methods:** A chart audit reviewing the records of all referred patients to five rheumatologists at an academic university out-patient rheumatology clinic over one year (including referrals that were rejected) was conducted. Specific tests requested prior to referral and their indication based on clinical presentation were extracted. Other data included reason for referral and the final diagnosis. The number of unnecessary laboratory tests and associated costs were calculated.

**Results:** Over 500 patients were reviewed. Most common referrals were for possible diagnosis of rheumatoid arthritis, lupus, and seronegative spondyloarthropathies. Prior to referral: 77% had undergone ANA testing at least once, in one-third of cases, ANA was repeated; 25% had ENA testing and 30% had anti-dsDNA. Among all ANA tests, 25% were requested when there was no clinical suspicion for connective tissue diseases based on American College of Rheumatology criteria. Half of ENA and anti-dsDNA testing was requested in the context of negative ANA. RF was requested in 65% of the referrals and in one third, there was no clinical suspicion of inflammatory arthritis.



**Abstract OP0302 – Figure 1.** Utilisation patterns and associated costs of laboratory investigations among referrals to rheumatologists

**Conclusions:** RF, ANA, ENA, and anti-dsDNA are among commonly ordered investigations prior to referral to rheumatology. Despite the recommendations by choosing wisely campaigns, up to 50% of investigations are inappropriately ordered. Based on our cost estimation, more selective ordering of the above tests, and minimising inappropriate investigations would lead to 45% cost reduction.

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#### OP0303

### SYSTEMATIC SCREENING OF COMORBIDITIES IMPROVES VACCINATION RATES, SKIN CANCER SCREENING AND VITAMIN D SUPPLEMENTATION IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: RESULTS OF THE COMEDSPA PROSPECTIVE, CONTROLLED, ONE YEAR RANDOMISED TRIAL

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**Background:** Specific recommendations for the detection/prevention of comorbidities have been proposed for patients with SpA. However, we know that often a gap exists between recommendation and their implementation in daily practice

**Objectives:** To evaluate the impact of a program of systematic screening of comorbidities and its management (detection/prevention).

**Methods:** Prospective, randomised controlled open, 12 month trial (NCT02374749). Patients: Axial SpA (according to rheumatologist). Study treatment: Collection of data by the nurse during a specific out-patient visit for the 5

studied SpA comorbidities (i.e. cardiovascular disease (CVD), osteoporosis, cancer, infection and peptic ulcer) according to the recommendations of the French Society of Rheumatology. In the event of non-agreement with the recommendation the patient was informed. A report summarising the results of this program prepared by the nurse was sent to the patient's attending physician and rheumatologist. Treatment allocation: After written informed consent, the study treatment was allocated randomly. Outcome variables: the main outcome was the change after one year of a comorbidity score. This weighted composite comorbidity score ranged from 0 to 100, where 0=optimal management of the 5 studied comorbidities and its weights were derived from the percentage of attributed mortality in SpA to each comorbidity in the literature, i.e. 40 points for CV disease, 20 points for cancer and infection, 10 points for osteoporosis and 10 points for peptic ulcer. The number of patients with actions undertaken against comorbidities according to the recommendations during the 12 months following this program were defined as secondary variables

**Results:** There were no differences in the baseline characteristics of the 502 recruited patients (252 and 250 in the active and control groups, respectively): Age: 46.7±12.2 years, male gender: 62.7%, disease duration: 13.7±11.0 y, Xray sacroiliitis 62.8%, MRI sacroiliitis 65.7%, current biologic treatment: 78.3%, ASDAS-CRP: 1.9±0.8, BASFI: 25.6±22.3. During the 1 year follow-up period, the comorbidity score decreased more in the active group, but this difference was not significant (−3.20 vs −1.85).

The number of actions per patient was statistically higher in the group comorbidities : 4.54±2.08 vs 2.65±1.57 (p<0.001); the number of patients with actions performed to be in agreement with recommendations during the 12 months follow-up was higher in the active group for infections (flu vaccination : 28.6% vs 9.9%, p<0.01; pneumococcal vaccination:40.0% vs 21.1%,p=0.04), skin cancer screening (36.3% vs 17.2%; p=0.04), and osteoporosis (BMD performed: 22.6% vs 8.7%, p<0.01; Vitamin D supplementation initiation: 51.9% vs 9.4%, p<0.01).

**Conclusions:** This study highly suggests the short-term benefit of program on the systematic screening of comorbidities for its management in agreement with recommendations, even if this young age population of axSpA patients.

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#### OP0304

### MULTIDISCIPLINARY COLLABORATION AMONG YOUNG SPECIALISTS: RESULTS OF AN ONGOING INTERNATIONAL SURVEY BY YOUNG ORGANISATIONS

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**Background:** Young clinicians and researchers frequently work alongside other medical specialists in order to share expertise, knowledge and skills. Multidisciplinary work is worthwhile but may be sometimes challenging.

**Objectives:** To describe current clinical and research collaboration among young specialists and to identify some perspectives to develop such collaborations.

**Methods:** An online survey was disseminated by email and social media (facebook and twitter) to members of the Emerging European League Against Rheumatism Network (EMEUNET), the Young Nephrologists' Platform (YNP), the Paediatric Rheumatology European Society Emerging Rheumatologists and Researchers (PReS EMERGE), and the European Academy of Allergy and Clinical Immunology Junior Members (EAACI JM).

**Results:** Of 354 respondents from 40 countries, 60% were female, 23% were aged below 30 years and 67% 31–40 years. Young rheumatologists were the most represented (36%), followed by young nephrologists (24%), young paediatricians (18%), young allergologists (11%) then young internists (3%) and several other specialties (as clinical immunology, dermatology, pulmonology, orthopaedics). 60% were certified specialists, 34% in training and 6% were researchers without clinical work. Overall, the top 3 specialties for clinical collaboration in daily practice were radiology, cardiology and dermatology. Collaborations were reported frequently by phone and email, also by various combined clinics while common local multidisciplinary meetings were uncommon. Of note, 71% of respondents found collaboration with young colleagues easier than with senior specialists. Research collaboration usually started by knowing other specialists (73%) and/or by attending common meetings (39%). 96% would like to develop

clinical research collaborations and 69% basic research collaborations. The majority of young specialists would be interested in online (84%) and/or 1–2 days (86%) common courses including cases discussion (80%) and training workshops (84%), as well as webinars recorded with several specialists on a specific disease (96%). Respondents were a bit less enthusiastic with developing collaboration through social media (facebook 61%, twitter 58%) but interested in common apps (71%).

**Conclusions:** This collaborative initiative highlighted wishes from young specialists for developing 1) regular local multidisciplinary meetings to discuss complex patients 2) clinical research collaboration with combined grants and 3) multidisciplinary online projects such as common courses, webinars and apps.

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## The changing therapeutic landscape of PsA

### OP0305 DISEASE INTERCEPTION IN PSORIASIS PATIENTS WITH SUBCLINICAL JOINT INFLAMMATION BY INTERLEUKIN 17 INHIBITION WITH SECUKINUMAB – DATA FROM A PROSPECTIVE OPEN LABEL STUDY

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**Background:** Musculoskeletal changes precede the onset of psoriatic arthritis (PsA). A subset of psoriasis patients is characterised by arthralgia as well as inflammatory changes in the joints visible by MRI assessment. These patients have a high risk to progress into PsA.

**Objectives:** To test the concept of a very early intervention in PsA we exposed psoriasis patients with subclinical joint inflammation to the anti-interleukin (IL)–17A antibody secukinumab. We hypothesised that IL-17A inhibition disrupted the early link between skin and joint disease in psoriasis.

**Methods:** Psoriasis (but not PsA) patients were included in the open prospective 24 weeks 'Interception in Very Early PsA' (IVEPSA) study. To fulfil the inclusion criteria patients had to have a PASI score greater than 6 or nail or scalp involvement as well as inflammatory or erosive changes in MRI or high-resolution peripheral quantitative computed tomography (HRpQCT) at baseline. Patients received treatment with secukinumab 300 mg sc. for 24 weeks. MRI scans and HRpQCT of the dominant hand were performed at baseline and at 24 weeks. MRI was scored according to PsAMRIS. HRpQCT evaluated for erosions and enthesiophytes.

**Results:** 20 patients (median age 49.5 years (IQR 42.8, 59), 70% males) with a median disease duration of 14 years (IQR 5, 20), were included into the study. At baseline, 85% reported arthralgia assessed by a Visual Analogue Scale (VAS) and 40% had tender joints on examination (TJC78). 83.3% had at least one inflammatory lesion in the MRI, 66.7% synovitis, 55.6% tendinitis/enthesitis, 27.8% osteitis and 16.7% periarticular inflammation. Erosions were present in 72.2% and 58.8% in the MRI and HRpQCT, respectively, while enthesiophytes were found in 33.3% and 41.2%. One patient was discontinued early due to lack of improvement (wk12) and one patient was unable to perform the follow-up MRI. Psoriatic skin disease (total PASI and BSA) significantly improved (both  $p < 0.05$ ) and also arthralgia (VAS pain, tender joint count) significantly declined after secukinumab treatment (both  $p < 0.05$ ). Total PsAMRIS score and synovitis subscore significantly improved at week 24 ( $p = 0.005$  and  $p = 0.008$ , respectively). Importantly, improvement in total PsAMRIS score significantly correlated with the improvement in arthralgia ( $p < 0.05$ ). Finally, neither erosions nor enthesiophytes in MRI and HRpQCT progressed during the 24 weeks of treatment. There was no new safety signal in the study.

**Conclusions:** IL-17 inhibition by secukinumab over 24 weeks led to resolution of inflammation and no progression of bone changes in the joints in psoriasis patients with subclinical peripheral joint involvement. These data suggest that very early disease interception in PsA is a feasible approach. IVEPSA also provides the guide for further very early interventions in PsA providing concepts for imaging-based identification and the sensitivity to change subclinical inflammation through biological disease modifying anti-rheumatic drug therapy.

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OP0306

### SUBCUTANEOUS SECUKINUMAB INHIBITS RADIOGRAPHIC PROGRESSION IN PSORIATIC ARTHRITIS: ANALYSIS BY PRIOR ANTI-TNF THERAPY AND CONCOMITANT METHOTREXATE USE

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**Background:** Psoriatic arthritis (PsA) is associated with joint inflammation, characterised by synovitis, presence of erosions, joint space narrowing (JSN) and new bone formation leading to structural damage, increased disability and reduced quality of life. Secukinumab (SEC) provided significant and rapid clinical efficacy, and inhibition of radiographic progression in PsA patients (pts) in the FUTURE 5 study.<sup>1</sup>

**Objectives:** To assess the effect of subcutaneous (sc) SEC on radiographic progression by prior anti-TNF therapy or concomitant methotrexate (MTX) use in the FUTURE 5 study.

**Methods:** Adults (n=996) with active PsA, stratified by prior anti-TNF therapy (naïve and inadequate response/intolerance [IR]), were randomised 2:2:2:3 to sc SEC 300 mg with loading dose (LD), 150 mg LD, 150 mg no LD, or placebo (PBO) at baseline (BL), Wks 1, 2, 3, 4, and every 4 wks thereafter. At Wk 16, PBO non-responders were switched to SEC 300 or 150 mg. Concomitant MTX ( $\leq 25$  mg/week) was allowed. Radiographic progression (mean change in van der Heijde-modified total Sharp score for PsA [vdH-mTSS] and its components: erosion and joint space narrowing [JSN] scores from BL to Wk 24) was based on hand/wrist/foot X-rays obtained at BL, Wks 16 (non-responders) assessed by two blinded readers (plus an adjudicator if required). Average scores were used. Statistical analyses used linear extrapolation at Wk 24 for all PBO non-responders and for all other pts with missing Wk 24 X-rays.

**Results:** At BL, 30% pts were anti-TNF-IR and 50% were on concomitant MTX. Radiographic progression was significantly inhibited at Wk 24 in the overall population with SEC vs PBO; mean change from BL in vdH-mTSS was 0.08 (300mg;  $p < 0.01$ ), 0.17 (150mg;  $p < 0.05$ ), -0.09 (150mg no LD;  $P < 0.01$ ) vs 0.50 (PBO). Lower radiographic progression (vdH-mTSS, erosion and JSN scores) was observed with SEC vs PBO regardless of prior anti-TNF therapy or concomitant MTX use (table 1).

**Abstract OP0306 – Table 1.** Radiographic findings (mean change in scores from BL to Wk 24)

Radiographic findings (mean change in scores from BL to Wk 24)	SEC 300mg		SEC 150mg		PBO
	LD	LD	No LD		
Anti-TNF-naïve	n=152	n=149	n=151	n=214	
vdH-mTSS	0.01 <sup>1</sup>	0.12 <sup>2</sup>	-0.25 <sup>2</sup>	0.48	
Erosion	0.03 <sup>1</sup>	0.09 <sup>2</sup>	0.01 <sup>2</sup>	0.36	
JSN	-0.02	0.03	-0.25 <sup>2</sup>	0.12	
Anti-TNF-IR	n=65	n=64	n=69	n=82	
vdH-mTSS	0.23	0.29	0.31	0.54	
Erosion	0.10	0.19	0.27	0.30	
JSN	0.13	0.10	0.04	0.24	
Without concomitant MTX	n=107	n=106	n=95	n=151	
vdH-mTSS	0.06 <sup>1</sup>	0.16	-0.17 <sup>2</sup>	0.46	
Erosion	0.07 <sup>2</sup>	0.13	-0.09 <sup>2</sup>	0.41	
JSN	-0.01	0.03	-0.07	0.05	
With concomitant MTX	n=110	n=107	n=115	n=145	
vdH-mTSS	0.10 <sup>1</sup>	0.18 <sup>1</sup>	-0.03	0.54	
Erosion	0.04 <sup>1</sup>	0.11	0.22	0.27	
JSN	0.06	0.07	-0.25 <sup>1</sup>	0.26	

<sup>1</sup> $P < 0.0001$ ; <sup>2</sup> $P < 0.001$ ; <sup>3</sup> $P < 0.01$ ; <sup>4</sup> $P < 0.05$  un-adjusted P-values vs. PBO

**Conclusions:** Subcutaneous secukinumab 300 mg with loading dose, and 150 mg with and without loading dose, inhibited radiographic progression in patients with active PsA. Low rates of radiographic progression were observed regardless of previous anti-TNF therapy or concomitant MTX use.

#### REFERENCE:

[1] ] Mease PJ, et al. *Arthritis Rheumatol* 2017;69(suppl 10).

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Abstract OP0307 – Table 1. Summary of efficacy results at week 24\*

Endpoints	Risankizumab (RZB)				Placebo
	Arm 1 N=42	Arm 2 N=42	Arm 3 N=39	Arm 4 N=20	Arms 1-4 N=143
ACR20 (%)	42.9	47.6	59.0**	40.0	48.3*
ACR50 (%)	19.0	16.7	33.3**	20.0	22.4**
ACR70 (%)	11.9	11.9	15.4*	15.0	13.3**
PASI 75 (%) <sup>†</sup>	68.8***	70.0***	69.6***	55.8*	67.6***
PASI 90 (%) <sup>†</sup>	60.0***	52.9**	47.6**	55.6**	53.2***
PASI 100 (%) <sup>†</sup>	46.7**	35.3**	28.6*	44.4*	37.1***
MDA (%)	19.0	28.6**	25.6*	30.0*	25.2**
DAS28(CRP) <sup>‡</sup>	-1.1	-1.4**	-1.6***	-1.7***	-1.4***
ΔDactylitis Count <sup>§</sup>	-1.3	-2.3	-3.6	-3.5	-2.5
ΔSPARCC Enthesitis Index <sup>¶</sup>	-1.3	-2.7*	-1.6	-3.4*	-2.0
ΔPain-VAS <sup>  </sup>	-6.9	-11.2	-19.1**	-6.4	-11.5*
HAQ-DI <sup>  </sup>	-0.19	-0.11	-0.21	-0.13	-0.16
ΔmTSS <sup>  </sup>	-0.3	0.2	-0.5*	-0.2	-0.2*

Arm 1: 150 mg RZB at weeks 0, 4, 8, 12, and 16; Arm 2: 150 RZB at weeks 0, 4, and 16 (PBO at weeks 8 and 12); Arm 3: 150 mg RZB at weeks 0 and 12 (PBO at weeks 4, 8, and 12); Arm 4: 75 mg RZB at week 0 (PBO at weeks 4, 8, 12, and 16); Arm 5: PBO at weeks 0, 4, 8, 12, and 16.

Ph-values for comparison versus placebo: \*\*\*, P<0.001; \*\*, P<0.01; \*, P<0.05.

\*Categorical endpoints are based on NRI analysis using Cochran-Mantel-Haenszel test; continuous variables are based on MMRM analysis and mTSS is based on ANCOVA. †PASI responses calculated only in patients with psoriasis affecting ≥3% BSA at baseline; Arm 1, N=18; Arm 2, N=20; Arm 3, N=23; Arm 4, N=9; Arm 5, N=21. ‡LS Mean for change from baseline are presented. §Dactylitis count and SPARCC enthesitis index assessed only in patients with active dactylitis (Arm 1, N=8; Arm 2, N=11; Arm 3, N=11; Arm 4, N=6; Arm 5, N=8) and enthesitis (Arm 1, N=28; Arm 2, N=34; Arm 3, N=26; Arm 4, N=11; Arm 5, N=26) at baseline, respectively. ACR20/50/70 = ≥20/50/70% improvement in American college of rheumatology score; ANCOVA = analysis of covariance; BSA = body surface area; DAS28(CRP) = 28-joint disease activity score based on C-reactive protein; Δ = change from baseline to week 24; HAQ-DI = health assessment questionnaire-disability index; MDA = minimal disease activity; MMRM = mixed effect model; repeat measurement; mTSS = modified total Sharp score; NRI = non-responder imputation; PASI75/90/100 = 75/90/100% improvement in psoriasis area and severity index; PBO = placebo; RZB = risankizumab; SPARCC = Spondyloarthritis Research Consortium of Canada; VAS=visual analog scale.

OP0307

### EFFICACY AND SAFETY OF RISANKIZUMAB, A SELECTIVE IL-23P19 INHIBITOR, IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS OVER 24 WEEKS: RESULTS FROM A PHASE 2 TRIAL

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**Background:** Interleukin-23 (IL-23), a key regulator of multiple effector cytokines, has been implicated in the pathogenesis of psoriatic arthritis, synovitis, enthesitis, and bone erosion. Risankizumab (RZB) is a humanised IgG1 monoclonal antibody that binds to p19 subunit of IL-23, selectively inhibiting this critical cytokine.

**Objectives:** To report the efficacy and safety of different doses of RZB in patients (pts) with active psoriatic arthritis (PsA) over 24 weeks.

**Methods:** In this double-blind, parallel-design, dose-ranging Phase 2 study, pts with active PsA (stratified by prior TNFi use and concurrent MTX use) were randomised in a 2:2:2:1:2 ratio to receive RZB (150 mg at weeks [Wks] 0, 4, 8, 12, and 16 [Arm 1], 150 mg at Wks 0, 4, and 16 [Arm 2], 150 mg at Wks 0 and 12 [Arm 3], 75 mg single dose at Wk 0 [Arm 4]) or matching placebo (PBO, Arm 5). Pts completing Wk 24 visit had an option to enter a separate open-label extension (OLE) study; pts not entering the OLE were followed until Wk 32. Efficacy assessments included ACR20/50/70, PASI, minimal disease activity (MDA), DAS28(CRP), dactylitis count, SPARCC enthesitis index, pain-VAS, HAQ-DI, and mTSS scores.

**Results:** Of the 185 pts who received the study drug, 173 (93.5%) completed 16 Wks of treatment and 145 (78.4%) entered OLE at Wk 24. The primary endpoint of ACR20 response at Wk 16 was achieved by pts in each of the RZB arms.<sup>†</sup> At Wk 24, ACR20/50/70 responses were significantly higher in pts receiving RZB (pooled across all RZB arms) compared with PBO (table 1). PASI75/90/100 responses at Wk 24 were significantly higher in RZB-treated pts compared with PBO. At Wk 24, RZB-treated pts achieved significantly higher MDA responses as well as greater improvements in DAS28(CRP) and Pain-VAS. Improvements in HAQ-DI and enthesitis from BL were numerically greater in RZB arms. At Wk 24, RZB-treated pts (pooled across all RZB arms) showed significant improvement from BL in mTSS compared with PBO. Treatment-emergent adverse events (TEAEs), collected up to Wk 32, were comparable across treatment arms (table 2); the most common TEAE was infection. There were no deaths or cases of tuberculosis in RZB-treated pts; 2 adjudicated major adverse cardiovascular events (TEAEs) were reported in RZB arms.

Abstract OP0307 – Table 2. Overview of treatment-emergent adverse events (TEAEs) over 32 weeks

TEAEs, n (%)	Risankizumab (RZB)				Placebo
	Arm 1 N=42	Arm 2 N=42	Arm 3 N=39	Arm 4 N=20	Arm 5 N=42
Any AE	27 (64.3)	22 (52.4)	27 (69.2)	13 (65.0)	31 (73.8)
Drug related AEs <sup>a</sup>	8 (19.0)	7 (16.7)	8 (20.5)	4 (20.0)	8 (19.0)
Serious AE <sup>b</sup>	3 (7.1)	0	2 (5.1)	3 (15.0)	2 (4.8)
Drug related serious AE <sup>b</sup>	1 (2.4)	0	2 (5.1)	1 (5.0)	0
Severe AE	3 (7.1)	0	2 (5.1)	1 (5.0)	4 (9.5)
AE leading to drug discontinuation	3 (7.1)	0	0	1 (5.0)	2 (4.8)
Infection <sup>c</sup>	16 (38.1)	13 (31.0)	16 (41.0)	6 (30.0)	12 (28.6)
Serious infection	0	0	0	2 (10.0) <sup>d</sup>	0
Serious hypersensitivity	1 (2.4) <sup>e</sup>	0	0	0	0
Adjudicated MACE	1 (2.4) <sup>f</sup>	0	0	1 (5.0) <sup>g</sup>	0
Malignancy	0	0	0	1 (5.0) <sup>h</sup>	0
Depression	0	0	2 (5.1)	0	0

Arm 1: 150 mg RZB at weeks 0, 4, 8, 12, and 16; Arm 2: 150 RZB at weeks 0, 4, and 16 (PBO at weeks 8 and 12); Arm 3: 150 mg RZB at weeks 0 and 12 (PBO at weeks 4, 8, and 12); Arm 4: 75 mg RZB at week 0 (PBO at weeks 4, 8, 12, and 16); Arm 5: PBO at weeks 0, 4, 8, 12, and 16.

<sup>a</sup>Investigator assessed AE as possibly related to study drug. <sup>b</sup>No serious adverse event type was reported in more than one patient. <sup>c</sup>The most frequently reported AE was upper respiratory tract infection. <sup>d</sup>1 patient with urinary tract infection, influenza, and sepsis. <sup>e</sup>1 patient with gastroenteritis and pyelonephritis. <sup>f</sup>An event of investigator reported anaphylactic reaction occurred after the 1<sup>st</sup> injection of risankizumab. The sponsor assessed the event details as not consistent with IgE-mediated anaphylaxis. <sup>g</sup>1 patient with ischemic stroke. <sup>h</sup>1 patient with type 1 myocardial infarction. <sup>i</sup>1 patient with ovarian cancer.

AE = adverse event; IgE = immunoglobulin E; MACE = major adverse cardiovascular event; PBO = placebo; RZB = risankizumab; TEAE = treatment-emergent adverse event.

**Conclusions:** Pts with active PsA treated with RZB maintained improvement in joint and skin symptoms through 24 wks. RZB-treated pts (pooled across all RZB arms) showed evidence for inhibition of radiographic progression. RZB was well-tolerated with no new or unexpected safety findings.

#### REFERENCE:

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**OP0308 EFFICACY AND SAFETY RESULTS OF GUSELKUMAB IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS OVER 56 WEEKS FROM A PHASE 2A, RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY**

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**Objectives:** Evaluate efficacy and safety of guselkumab (GUS) in patients (pts) with active psoriatic arthritis (PsA) over 56 weeks (wks).

**Methods:** Pts w/active PsA (defined as  $\geq 3$  tender and  $\geq 3$  swollen joints, C-reactive protein  $\geq 3$  mg/L) and  $\geq 3\%$  body surface area (BSA) of plaque psoriasis despite current or previous treatment w/standard-of-care therapies, including previous TNF inhibitor therapy, were eligible to participate and were randomised 2:1 to receive GUS 100 mg subcutaneously or placebo (PBO) at wk 0, 4, and every 8 wks thereafter through wk44. At wk16, pts from either group with  $<5\%$  improvement from baseline in both swollen and tender joint counts were eligible for early escape (EE) to open-label ustekinumab. All remaining PBO pts crossed-over to receive GUS 100 mg at wks24, 28, 36, and 44. At wk56, a post-treatment follow-up visit was conducted. Efficacy post wk24 through wk44 and wk56 was evaluated in pts who did not EE and continued treatment at wk24 (post wk24 efficacy analysis set) based on observed data. The wk24 data in this population were included as a reference.

**Results:** 149 pts were randomised to receive study agent (PBO: 49, GUS: 100). The study met its primary and all secondary endpoints through wk24. At wk24, 29 pts in the PBO group crossed over to receive GUS, of which 28 completed treatment through wk44. 86 pts in the GUS group continued treatment at wk24 and 84 pts completed treatment through wk44. Post wk24, ACR 20/50/70 and PASI 75/90/100 responses improved in PBO to GUS crossover pts and were well-maintained in GUS pts through wk44 (last efficacy assessments while on drug) and wk56 (final follow-up visit) (table 1). The efficacy results from wk24 through wk44 and wk56 are summarised in table 1.

Through wk56, 17.2% of PBO—GUS, 46.0% of GUS, and 39.5% of the combined GUS pts had  $\geq 1$  AEs, of which infections and infestations were the most commonly reported (3.4%, 27.0%, and 21.7%, respectively). Post wk24, there was no disproportional increase in overall AE frequency, or infections and infestations among GUS pts with longer exposure. Through wk56, among 129 pts who received GUS, there was 1 pt with malignancy (basal cell carcinoma), 1 pt with 2 serious infections (both pneumonia), 6 pts reported  $\geq 1$  SAEs (myocardial infarction, osteoarthritis, pupils unequal, radius fracture, pneumonia, ulcerative keratitis), 2 pts discontinued treatment due to AEs, 1 pt had neutropenia meeting NCI-

CTCAE toxicity grade 3, and 6 pts were positive for antibodies to GUS. No deaths occurred through wk56.

**Abstract OP0308** – Table 1 Efficacy results from Wk24 through Wk44 and Wk56 in post Wk24 efficacy analysis set based on the observed data

Efficacy Endpoints	PBO→GUS			GUS		
	Week 24*	Week 44	Week 56	Week 24	Week 44	Week 56
ACR 20	9/29 (31.0%)	21/28 (75.0%)	22/27 (81.5%)	57/86 (66.3%)	65/94 (69.1%)	61/83 (73.5%)
ACR 50	5/29 (17.2%)	13/28 (46.4%)	18/27 (66.7%)	34/86 (39.5%)	39/94 (41.5%)	44/83 (53.0%)
ACR 70	1/29 (3.4%)	7/28 (25.0%)	8/28 (28.6%)	14/86 (16.3%)	22/94 (23.4%)	27/83 (32.5%)
PASI 75	6/29 (20.7%)	23/28 (82.1%)	22/27 (81.5%)	71/86 (81.4%)	75/93 (80.6%)	70/82 (85.4%)
PASI 90	3/29 (10.3%)	21/28 (75.0%)	20/27 (74.1%)	61/86 (70.9%)	68/93 (73.1%)	64/82 (78.0%)
PASI 100	3/29 (10.3%)	15/28 (53.6%)	15/27 (55.6%)	38/86 (44.2%)	53/93 (57.0%)	47/82 (57.3%)
Mean (SD) change from baseline in HAQ-DI score	-0.19 (0.881)	-0.69 (0.612)	-0.67 (0.558)	-0.46 (0.583)	-0.54 (0.598)	-0.55 (0.621)
Median (IQR) percent change from baseline in Entesis Score	-30.0 (-100.0, 0.0)	-100.0 (-100.0, -66.0)	-100.0 (-100.0, -35.0)	-100.0 (-100.0, -60.0)	-100.0 (-100.0, -50.0)	-100.0 (-100.0, -50.0)
% of patients with unresolved arthritis	12/18 (66.7%)	8/17 (47.1%)	5/16 (31.3%)	26/57 (45.8%)	25/96 (26.0%)	19/65 (29.2%)
Median (IQR) percent change from baseline in dactylitis	-46.0 (-70.8, 0.0)	-100.0 (-100.0, -100.0)	-100.0 (-100.0, -80.0)	-100.0 (-100.0, -80.0)	-100.0 (-100.0, -100.0)	-100.0 (-100.0, -95.0)
% of patients with unresolved dactylitis	13/16 (81.3%)	2/16 (12.5%)	1/16 (6.3%)	30/50 (60.0%)	10/49 (20.4%)	12/48 (25.0%)
Mean (SD) change from baseline in SF-36 physical component summary (PCS) score	2.33 (7.365)	8.02 (8.647)	N/A	7.40 (7.448)	8.34 (8.783)	N/A
Mean (SD) change from baseline in SF-36 mental component summary (MCS) score	0.51 (6.770)	5.93 (9.033)	N/A	5.45 (9.081)	4.56 (9.548)	N/A
% of patients achieving Minimal Disease Activity (MDA)	1/29 (3.4%)	8/28 (28.6%)	N/A	23/86 (26.7%)	29/94 (30.9%)	N/A

\*Among the patients with arthritis at baseline

\*Among the patients with dactylitis at baseline

\*Measured prior to receiving guselkumab

**Conclusions:** In pts with active PsA and  $\geq 3\%$  BSA of psoriasis, GUS demonstrated substantial benefits on joint symptoms, physical function, psoriasis, enthesitis, dactylitis, and quality of life, and efficacy was well-maintained through wk56. GUS was well-tolerated with no unexpected safety findings in this population after ~1 year of exposure.

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**OP0309 CHARACTERISATION OF CLINICAL BENEFITS IN SUBJECTS CLASSIFIED AS ACR20 NON-RESPONDERS AT WEEK 104 OF APREMLAST TREATMENT: SUBANALYSIS OF 3 LONG-TERM, PHASE III TRIALS**

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**Background:** The PALACE 1, 2, and 3 trials evaluated the efficacy and safety of apremilast (APR) in subjects with active psoriatic arthritis (PsA) despite prior conventional disease-modifying anti-rheumatic drugs and/or biologics.

**Objectives:** The aim of this analysis is to further characterise the clinical benefits associated with long-term APR exposure in subjects who failed to achieve an ACR20 response at Week 104.

**Methods:** Subjects were randomised (1:1:1) to receive placebo (PBO), APR 30 mg BID (APR30), or APR 20 mg BID at baseline. Subjects who were randomised to APR30 at baseline and classified as ACR20 non-responders (ACR20NRs) at Week 104 were considered for this analysis. At Weeks 24, 52, and 104, ACR core components were examined as well as the proportions of

subjects achieving PASI-75/PASI-50 among those with psoriasis involvement  $\geq 3\%$  of the body surface area at baseline, and dactylitis count and MASES of 0 among those with dactylitis or enthesitis at baseline. Safety is described for the overall PALACE 1–3 population.

**Results:** A total of 109 subjects randomised to APR30 treatment at baseline were ACR20NRs at Week 104. Baseline ACR core components were similar for ACR20NRs and ACR20 responders at Week 104. Among these ACR20NRs, several core components of ACR response, including swollen/tender joint counts and Physician's Global Assessment of Disease Activity (visual analogue scale) scores, showed sustained improvements from baseline through Week 104 (table 1). Importantly, of the 109 ACR20NRs at Week 104, 50.0% achieved a PASI-50 response after continued treatment with APR30 through Week 104 (table 1). Among ACR20NRs with baseline dactylitis (n=44) or enthesitis (n=74), 68.2% achieved a dactylitis count of 0 and 33.8% achieved a MASES of 0 at Week 104. More limited improvements in Subject's Global Assessment of Disease Activity, Subject's Assessment of Pain, Health Assessment Questionnaire-Disability Index, and C-reactive protein outcomes most commonly had an impact on subjects' ability to achieve an ACR20 response. In the overall subject population, no new safety concerns were identified through 104 weeks.

Abstract OP0309 – Table 1

	ACR20NRs at Week 104 With APR30 From Baseline (n=109)		
	Week 24	Week 52	Week 104
Swollen joint count (0-76), mean and median % change	-52.2, -71.4	-62.8, -73.3	-58.0, -75.0
Tender joint count (0-78), mean and median % change	-32.5, -47.4	-45.8, -53.5	-41.7, -51.7
PhGA (VAS 0-100 mm), mean and median % change	-37.9, -43.6	-49.8, -54.2	-44.3, -48.7
Dactylitis=0, n/m (%) <sup>a</sup>	23/44 (52.3)	29/44 (65.9)	30/44 (68.2)
MASES=0, n/m (%) <sup>b</sup>	20/74 (27.0)	27/74 (36.5)	25/74 (33.8)
PASI-75, n/m (%) <sup>c</sup>	17/50 (34.0)	22/50 (44.0)	18/50 (36.0)
PASI-50, n/m (%) <sup>d</sup>	31/50 (62.0)	33/50 (66.0)	25/50 (50.0)

Data are as observed at Week 24, Week 52, and Week 104 for all subjects who were randomized to APR30 at baseline and were ACR20NRs at Week 104 and with a value at the time point indicated.  
<sup>a</sup>Examined among subjects with dactylitis at baseline. <sup>b</sup>Examined among subjects with enthesitis at baseline. <sup>c</sup>Examined among subjects with  $\geq 3\%$  psoriasis involvement of the body surface area at baseline. PhGA=Physician's Global Assessment of Disease Activity; VAS=visual analog scale; n/m=number of subjects achieving response/number of subjects with evaluable data at the time point; MASES=Maastricht Ankylosing Spondylitis Enthesitis Score; PASI-75/50= $\geq 75\%/\geq 50\%$  reduction from baseline Psoriasis Area and Severity Index score.

**Conclusions:** ACR20NRs receiving APR30 demonstrated significant improvements in core PsA domains. The data may explain why subjects who failed to achieve an ACR20 response remained on long-term APR treatment. These findings suggest that some subjects with PsA may experience meaningful clinical improvement that is not completely captured by the assessment of ACR20 response criteria. Outcome measures specifically designed for PsA subjects, may be more suitable to evaluate treatment response in PsA subjects.

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#### OP0310 PREVALENCE OF RISK FACTORS AND CARDIOVASCULAR EVENTS ACROSS PSORIATIC ARTHRITIS PATIENTS TREATED WITH BIOLOGICAL THERAPY

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**Background:** Psoriasis and psoriatic arthritis (PsA) are described as associated with more frequency of risk factors and cardiovascular events.

**Objectives:** To determine the prevalence of risk factors and cardiovascular events in a cohort of patients with PsA treated with biological therapy and its correlation with gender.

**Methods:** We included all PsA patients (met CASPAR criteria) following treatment with bDMARDs (reference population 2.055.000). We obtained data of high

blood pressure, hyperlipidemia, hyperuricemia, type 2 diabetes mellitus, obesity (BMI  $\geq 30$ ), non-infectious liver disease, ischaemic cardiopathy, myocardial infarction, ischaemic stroke or transient ischaemic attack. For this analysis included gender, age, disease duration, current bDMARDs with or without current co-medication with csDMARDs and HLA-B27 status. Continuous variables were reported as mean  $\pm$  standard deviation. Categorical variables were reported as percentages and frequencies. All analyses were performed using SPSS software. Differences were considered statistically significant if  $p < 0.05$  (two-tailed).

**Results:** Data were obtained from 598 PsA patients who have been treated with bDMARDs. Three-hundred and twenty-five (54.3%) patients were men, mean age was 53.3 $\pm$ 12.6 years (men 53.3 $\pm$ 12.9 and women 53.2 $\pm$ 12.3,  $p=0.943$ ) and disease duration of PsA was 12.4 $\pm$ 8.7 years. No differences were seen for disease duration of PsA, nail disease, dactylitis, uveitis or HLA-B27. The prevalence of high blood pressure, hyperlipidemia, hyperuricemia, type 2 diabetes mellitus, obesity, non-infectious liver disease, ischaemic cardiopathy, myocardial infarction (MI) and ischaemic stroke/transient ischaemic attack (IS) was 36.0%, 43.6%, 16.0%, 12.5%, 26.3%, 12.5%, 5.5%, 3.8% and 1.3%, respectively. Men had most prevalence of type 2 diabetes mellitus, hyperuricemia, non-infectious liver disease, ischaemic cardiopathy, myocardial infarction and brain stroke event (see table 1). Patients with MI or IS had more prevalence of CV risk factors.

Abstract OP0310 – Table 1

	Female (273)	Male (325)	P
High blood pressure, n(%)	98 (35.9)	117 (36.0)	0.979
Hyperlipidemia, n(%)	111 (40.7)	150 (46.2)	0.177
Hyperuricemia, n(%)	13 (4.8)	82 (25.3)	<0.001
Diabetes mellitus, n(%)	21 (7.7)	54 (16.6)	0.001
Liver disease, n(%)	19 (7.6)	49 (16.7)	0.002
Ischaemic cardiopathy, n (%)	8 (2.9)	25 (7.7)	0.011
Myocardial infarction, n (%)	5 (1.8)	18 (5.5)	0.019
Brain stroke event, n (%)	1 (0.2)	7 (2.2)	0.058

**Conclusions:** Type 2 diabetes mellitus, hyperuricemia, non-infectious liver disease, ischaemic cardiopathy, myocardial infarction and brain stroke event were more prevalent in men than in women with PsA. Male gender had correlation with the prevalence of cardiovascular events or their risk factors.

#### REFERENCE:

[1] Husted JA, et al. Cardiovascular and other comorbidities in patients with psoriatic arthritis: A comparison with patients with psoriasis. *Arthritis Care Res (Hoboken)* 2011 Dec;63(12):1729–35.

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**Disclosure of Interest:** None declared

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#### OP0311 NOTABLE EVOLUTIONS IN THE CHARACTERISTICS OF PSORIATIC ARTHRITIS CLINICAL TRIALS POPULATIONS IN THE ERA OF BIOLOGICAL TREATMENTS

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**Background:** Psoriatic arthritis is a chronic inflammatory disease that affects the musculoskeletal system. It can include arthritis, spondylitis, dactylitis and enthesitis, and is strongly associated with the presence of psoriasis. The introduction of biological therapies as a treatment option has brought a significant improvement in disease control for these patients.

**Objectives:** In this study, we wanted to detect emerging differences in demographic and clinical characteristics of the PsA-patient study population since the introduction of biologicals.

**Methods:** We selected 12 phase II- and phase III-trials and divided them into 3 treatment periods based on different time windows and working mechanisms of the particular biologicals or targeted DMARDs. Published tables with the baseline demographic and clinical characteristics of study population from the individual studies were used. For inclusion of a specific parameter, it had to be present in at least one study of each period. An exception to this rule was made for the 'number of patients with prior anti-TNF therapy', only present in studies from the second and third period. Parameters were defined in different categories: patient characteristics (gender, age, race, weight), disease characteristics (duration of PsA, presence of dactylitis, presence of enthesitis, psoriasis body surface area), disease activity parameters (swollen joint count, tender joint count, C-reactive protein



(CRP)-level, visual analogue scale of disease activity and pain, disease activity score, psoriasis area severity index (PASI)-score, disease effects (total Sharp score, health assessment questionnaire disability index (HAQ-DI)-score) and prior treatments. For the continuous data, we calculated a weighted mean and standard deviation (SD) per period. Data not available in the form of mean  $\pm$ SD in the original studies were therefore not included. For the discrete data, we summed up the patients meeting the criterion from all the studies in a given period and calculated a percentage. We used the RStudio software. For the normally divided data, we used ANOVA-test for a group analysis to find significant differences between the time periods. For the discrete data, we used Chi-square test.

**Results:** Detailed analysis of the baseline characteristics showed some remarkable differences between the three different treatment periods with most data indicating that these shifts have occurred between the first and the second period. In comparison to the initial trials with etanercept, infliximab and adalimumab, gender and race show more diversity, patients are older but have a shorter disease duration, show lower swollen and tender joint counts, but more enthesitis, and have lower CRP-levels. Although several of these parameters suggest an overall lower disease activity in the second and third period of trials, this is not reflected in the physician's and patient's perspective of disease activity and the HAQ-DI score.

**Conclusions:** Our analysis found significant differences in patient characteristics, disease characteristics, disease activity, disease effects and use of prior treatments between the 3 periods of treatment drugs since the introduction of biologicals. Patients appear to be considered earlier and with less severe disease albeit that the subjective evaluation of disease activity goes in the opposite direction.

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OP0312

#### INTERNATIONAL LEAGUE OF ASSOCIATIONS FOR RHEUMATOLOGY (ILAR) TREATMENT RECOMMENDATIONS FOR PSORIATIC ARTHRITIS IN RESOURCE-POOR COUNTRIES

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**Background:** The European League Against Rheumatism (EULAR) and the Group for Research and Assessment of Psoriasis and PsA (GRAPPA) updated their respective recommendations for the management of PsA in 2015. However, these guidelines are primarily based on studies conducted in resource replete countries; hence they may not be applicable to countries in Central and South America, and Africa. Therefore, new ILAR recommendations have been developed for these regions adapted from existing recommendations.

**Objectives:** To establish ILAR recommendations for the management of PsA in resource poor settings, particularly Central/South America and Africa, using an expert local panel, adaptation of existing EULAR and GRAPPA treatment recommendations and a new systematic literature review (SLR) for specific issues in resource-poor countries.

**Methods:** The ADAPTE Collaboration process<sup>1</sup> for guideline adaptation was followed to assess and adapt the EULAR and GRAPPA treatment recommendations for PsA covering the Americas and Africa. The process was conducted according to its three phases: set-up phase (identifying and seeing agreement from a panel of participants from the relevant countries), adaptation phase (defining health questions using the PIPOH tool, assessing the two source recommendations, conducting an SLR to answer health questions not addressed in the two source recommendations, assessing quality of source recommendations, assessing applicability of principles contained in the source recommendations, and drafting adapted recommendations), and finalisation phase (external review, aftercare planning and final production).

**Results:** Five principles for the management of PsA were developed addressing 1. Goals of therapy, 2. Assessment of domains, 3. Assessment of relevant comorbidities, 4. Safety of pharmacotherapy and shared decision making, and 5. Frequency of follow up. Six recommendations for the management of PsA were also developed addressing 1. Goals of therapy, 2. Screening and management of

tuberculosis, HIV, HBV, HCV, Chagas' disease, leishmaniasis, leprosy, and other concomitant comorbidities, 3. Frequency of monitoring in resource poor countries, 4. Safety and efficacy of pharmacotherapy in all domains, 5. Efficacy and safety of combination therapy, and 6. Safety and efficacy of biosimilars and intended copies.

**Conclusions:** ILAR recommendations for the management of PsA in resource-poor countries are now available, developed by adapting principally the GRAPPA recommendations, but also the EULAR recommendations, supplemented by expert opinion from these regions.

#### REFERENCE:

[1] The ADAPTE Collaboration. The ADAPTE Process: Resource Toolkit for Guideline Adaptation, Version 2.0 2009. [Available from] <http://wwwwg-i-n.net>

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FRIDAY, 15 JUNE 2018

#### T/B be or not T/B: adaptive or innate immunity – that is the question

OP0313

#### MOLECULAR ANALYSIS OF ANTI-CITRULLINATED PROTEIN ANTIBODY VARIABLE REGIONS INDICATES ABERRANT SELECTION PROCESSES DURING ACPA B-CELL DEVELOPMENT

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**Background:** Anti-citrullinated protein antibodies (ACPA) represent the most specific biomarker in Rheumatoid Arthritis (RA) and have been associated with RA pathogenesis. ACPA-IgG are heavily N-glycosylated in the variable domain. Recently, we showed that >80% of ACPA-IgG clones harbour N-glycosylation sites in their variable regions that result from somatic hypermutation (SHM). The reason for this remarkable phenomenon is incompletely understood. Elucidation of its molecular basis might provide insights into mechanisms by which ACPA-expressing B cells breach tolerance.

**Objectives:** To understand the molecular origin of ACPA variable domain N-glycosylation based on B-cell receptor (BCR) sequence analyses.

**Methods:** ACPA-expressing B cells were isolated from peripheral blood of 12 ACPA-positive RA patients using CCP2-streptavidin tetramers and fluorescence activated cell sorting. Full-length immunoglobulin (Ig) transcripts of heavy chains (HC) and light chains (LC) were obtained using anchoring reverse transcription of Ig sequences and amplification by nested PCR. Sequences were analysed for the degree of SHM and the presence of N-glycosylation sites (defined as sequences encoding N-X-S/T (X  $\neq$  Proline) in the protein backbone). Sites that required a single nucleotide mutation to be generated were defined as s-SHM sites, whereas sites requiring multiple mutations were defined as m-SHM sites. IgG sequences of 12 healthy donors were used as control.

**Results:** 67% of ACPA-Ig $\kappa$  LC and 47% of ACPA-Ig $\lambda$  LC contained  $\geq$ 1 n-glycosylation sites compared to 82% of ACPA-IgG HC. Nucleotide mutation rates were similar for ACPA-Ig $\kappa$  LC and ACPA-Ig $\lambda$  LC (88.2% $\pm$ 5.7% and 87.3% $\pm$ 5.3% similar to germline, respectively) and lower compared to the mutation rate of ACPA-IgG HC (82.4% $\pm$ 5.8% similar to germline). The distribution of sites in ACPA-Ig $\kappa$  LC and ACPA-IgG HC was similar, with most sites located in framework region (FR) 3 (42% and 49%, respectively). In contrast, 65% of all N-glycosylation sites in ACPA-Ig $\lambda$  LC clones were located in FR1 and only 7% were located in FR3. Furthermore, 26% of all N-glycosylation sites in ACPA-IgG HC were m-SHM sites compared to 15% in IGHV-matched IgG clones derived from healthy donors. 28% and 44% of all N-glycosylation sites were m-SHM sites in ACPA-Ig $\kappa$  LC and ACPA-Ig $\lambda$  LC, respectively. No correlation was observed between the number of nucleotide mutations and the number of total N-glycosylation or m-SHM sites in ACPA clones.

**Conclusions:** Our analyses revealed an abundance of N-glycosylation sites in ACPA-IgG HC, ACPA-Ig $\kappa$  LC and ACPA-Ig $\lambda$  LC. N-glycosylation sites in ACPA are frequently m-SHM sites. Intriguingly, the generation of such sites requires multiple somatic mutations suggesting that m-SHM sites in specific positions in ACPA variable regions could be advantageous for the survival of ACPA-expressing B cells. This indicates that the introduction of N-glycosylation sites might be a selective process that could allow these B cells to escape from putative tolerance checkpoints.

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OP0314

**B CELL PHENOTYPE AND FUNCTION IN THE SYNOVIUM OF ACPA+ AND ACPA- RHEUMATOID ARTHRITIS PATIENTS**

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**Background:** Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease of unknown and complex etiology with severe detrimental effects for the patient's quality of life. While rheumatoid factors (RF) and anti-citrullinated protein antibodies (ACPA) have been used extensively for the diagnosis of RA, no clear mechanism of action towards disease pathogenesis and progression has been identified. Importantly, both seropositive and seronegative RA patients experience significant improvement in disease severity following B cell depletion. Therefore, we hypothesised that B cells have a central role in ACPA<sup>+</sup> and ACPA<sup>-</sup> RA irrespective of their capacity to produce auto-antibodies.

**Objectives:** The characterisation of B and T cell populations in the peripheral blood and synovium of ACPA<sup>+</sup>, ACPA<sup>-</sup> and arthralgia patients.

The identification of non-antibody mediated B cell function under the hypoxic conditions of the inflamed joint.

**Methods:** Peripheral blood, synovial fluid and tissue was obtained from ACPA<sup>+</sup>, ACPA<sup>-</sup> and arthralgia patients. Following enzyme digestion of the tissue, several 15-colour panels were used for the flow cytometric analysis of T and B cell populations of ACPA<sup>+</sup>, ACPA<sup>-</sup> and arthralgia patients compared to healthy subjects. Activation and function of healthy, sorted B cells, cultured *in vitro* and stimulated by CD40 and BCR mediated signals under normoxic (21% O<sub>2</sub>) and hypoxic (1% O<sub>2</sub>) conditions was examined.

**Results:** Pro-inflammatory cytokine production by peripheral blood CD4<sup>+</sup> T cells is not significantly different between ACPA<sup>+</sup>, ACPA<sup>-</sup> and arthralgia patients when compared to healthy controls. However, a significant reduction in CD27<sup>+</sup> switched memory B cells was observed between healthy subjects and ACPA<sup>+</sup> RA patients. The aforementioned decrease in memory B cells is potentially a result of increased susceptibility to FAS induced apoptosis since healthy B cells cultured with RA patient plasma showed increased activation, CD80/CD86 and FAS expression.

In the synovial fluid and synovial tissue, CD4 T cell pro-inflammatory cytokine production was increased when compared to peripheral blood CD4 T cells. Interestingly, ACPA<sup>-</sup> RA patient CD4<sup>+</sup> T cells produced reduced amounts of pro-inflammatory cytokines when compared to ACPA<sup>+</sup> RA patient CD4<sup>+</sup> T cells. Despite accumulation of switched and double negative (DN) memory B cells in the synovial fluid and tissue, compared to peripheral blood, no differences in synovial B cell subpopulation composition between ACPA<sup>+</sup> and ACPA<sup>-</sup> RA patients was observed. Interestingly, sorted B cells from healthy subjects showed increased sensitivity to *in vitro* stimulation with increased expression of CD80 and CD86 when cultured under hypoxic conditions, while co-culture with RA patient synovial fibroblasts did not enhance this effect.

**Conclusions:** The increased capacity of ACPA<sup>+</sup> compared to ACPA<sup>-</sup> RA patient synovial CD4<sup>+</sup> T cells to produce pro-inflammatory cytokines, could be responsible for the more severe disease progression of ACPA<sup>+</sup> compared to ACPA<sup>-</sup> RA. The accumulation of memory B cells in both ACPA<sup>+</sup> and ACPA<sup>-</sup> RA, underlines a common, antibody independent, contribution of B cells in synovial inflammation. While B cell activation under hypoxic conditions and increased CD80/CD86 expression is potentially an important mediator for the emergence of auto-reactive T cells and disease progression in RA.

**Disclosure of Interest:** None declared

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OP0315

**JUVENILE IDIOPATHIC ARTHRITIS PATIENTS EXHIBIT PERSISTENCE IN CD4 MEMORY T CELLS AND DISTINCT TRANSCRIPTOMIC SIGNATURE DESPITE BIOLOGICS THERAPY**

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**Background:** JIA patients respond well to anti-TNFA biologics, with up to 80% of patients achieving clinical remission. In spite of this success, 50%–80% will relapse upon therapy withdrawal, indicating a large proportion of patients had yet to fully resolve their disease. Compounded by concerns with drug toxicities and financial burden, there is a genuine interest to find predictors for successful drug cessation and devise new avenues of therapy.

**Objectives:** To determine how subclinical persistence of disease occurs despite therapy, we compare JIA individuals destined to flare or remain inactive, prior to (To) and after therapy withdrawal (Tend). Previous publications have reveal that CD4 T cells play a vital role in disease pathogenesis in JIA patients. We aim to dissect the CD4 landscape (a) through CyToF, to decipher the CD4 subsets responsible for disease persistence, (b) to unravel the pathways involved through mRNA analysis with Nanostring.

**Methods:** Patients treated with anti-TNF-alpha biologics were recruited with clinically inactive disease on treatment and initiated with therapy discontinuation. The patients designated as flare (n=24) and inactive (n=24) based on 6 JIA core set parameters. Healthy paediatric controls (n=17) with no inflammatory disease were recruited pre-operatively during day surgeries. A separate study with active JIA patients recruited pre/post treatment (n=4 paired) with anti-TNFA biologics and achieving recent clinical remission.

**Results:** Interrogation of PBMCs with CyToF reveal the persistence of a subset of CD3 +CD4+inflammatory memory CD45RA- TNFA +PD1- CTLA4- T cells (p<0.05) in flare (To) versus inactive (To) individuals. Intriguingly an additional subclinical subset, TNFA +IL-6+, was detected (p<0.05) in flare (To) versus healthy individuals. Upon therapy withdrawal, this subclinical subset expands (p<0.05) in flare (Tend) individuals versus inactive (Tend). Notably we also observe a distinct early increase in CD3 +CD4+CD45 RA- CXCR5 +T cells in flare versus inactive (To) individuals which subsides after therapy withdrawal, indicating early T-B interaction. We noted strong but likely inadequate compensatory enrichment of CD45RA- subset of Tregs in flare versus inactive (To/Tend) individuals. To decipher the mechanism that leads to incomplete disease resolution, we sorted CD3 +CD4+CD45 RA- CD45RO+T cells from flare and inactive (To/Tend) patients, and observed striking dysregulation in several major pathways, (a) TCR activation, (b) TNFA signalling, (c) Apoptosis, (d) NF-kB signalling, (e) MAPK signalling. This dysregulation also extends to a separate cohort of active JIA patients naive to anti-TNFA biologics therapy and persisting till recent onset clinical remission.

**Conclusions:** These results highlight a strong immunological memory dysregulation in a subset of CD4 T cells in JIA patients that is predictive of clinical fate and providing new therapeutic insights.

**Disclosure of Interest:** None declared

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OP0316

**INCREASED EXPRESSION OF MICRORNA-142-3P IS ASSOCIATED WITH THE FUNCTIONAL DEFECT OF REGULATORY T CELLS IN ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODY ASSOCIATED VASCULITIS**

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**Background:** Circulating regulatory T cells (Tregs) in anti-neutrophil cytoplasmic antibody associated vasculitis (AAV) are frequently functionally deficient. The mechanism behind their impaired function is however unknown. Small non-coding microRNA (miR) are post-transcriptional regulators of protein synthesis and previous studies have shown that differently expressed miRs in T cells are associated with auto immunity.

**Objectives:** To investigate whether the dysfunctionality of Tregs in AAV is due to altered microRNA (miR) expression.

**Methods:** Tregs (CD4<sup>+</sup>CD45RO<sup>+</sup>CD25<sup>+</sup>CD127<sup>-</sup>) of healthy controls (HC) and AAV patients in remission without treatment (AAV-REM) were FACS-sorted, and total RNA was isolated. Samples from 8 HCs and 8 AAV-REMs were subjected to miRNA microarray analysis. Based on relative expression and fold change, 5 differentially expressed miRs were validated in an independent cohort using qRT-PCR and a database and literature search was performed to identify potential targets.

**Results:** Nineteen miRs differentially expressed were detected by microarray analysis, of which Let-7g, miR-20a-5p, miR-26a-5p, miR-142-3 p, miR-146a-5p were validated in an independent cohort. Of these, miR-142-3 p was confirmed to be significantly upregulated (2-fold, p=0.03) in Tregs from AAV-REM patients compared to HC Tregs (n=23, n=22). To study the functional impact of miR-142-3 p overexpression, HC Tregs were transfected using either a mimic-miR-142-3 p or a scrambled (SCR)-control. After transfection, live Tregs were co-cultured with T effectors (CD4<sup>+</sup>CD25<sup>+</sup>) in a suppression assay to test their suppressive capacity. Transfection with mimic-miR-142-3 p significantly increased the miR-142-3 p levels (2.4 fold, p=0.03) and reduced the suppressive capacity compared to SCR-transduced Tregs (1.9 fold reduction, p=0.02). Moreover, miR-142-3 p levels tended to correlate to the suppressive function of Tregs (p=0.06, rho=-0.591). A database and literature search identified adenyl cyclase 9 (AC9) as a promising target of miR-142-3 p. mRNA levels of AC9 tended to be lower in AAV-REM patients compared to HC (3.8 fold, p=0.07). In addition, cAMP

levels, which are partly produced by AC9, were significantly lower in Tregs from AAV-REM patients after 48 hour of stimulation with anti-CD3 and anti-CD28 (1.7 fold,  $p=0.003$ ).

**Conclusions:** Increased expression of miR-142-3p in Tregs of AAV-REM patients is associated with their functional impairment, potentially by targeting the AC9/cAMP mediated suppression.

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### OP0317 SCREENING OF AN AUTOANTIBODY SIGNATURE OF EARLY KNEE OSTEOARTHRITIS: DATA FROM THE OSTEOARTHRITIS INITIATIVE

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**Background:** The immune system can detect the changes involved in the osteoarthritic (OA) joint, triggering the production of immunoglobulins against self-proteins (Autoantibodies or AABs). As AABs might be generated in a stage prior to the disease, they can be potentially used to identify an increased risk for the disorder, allowing the diagnosis of asymptomatic OA.

**Objectives:** The discovery of an AAb signature useful for the early diagnosis of knee OA.

**Methods:** Nucleic Acid-Programmable Protein Arrays (NAPPA) were used to screen the presence of AABs against 2200 human proteins in sera belonging to two different subcohorts from the Osteoarthritis Initiative (OAI): Incidence and Non-exposed subcohorts. Participants in the incidence subcohort had not developed any symptomatic knee OA at baseline, but they did present an increased risk of developing the disease. Non-exposed subcohort incorporate participants which have no radiographic findings or symptoms of knee OA, nor any reported risk factors. A hundred sera from both subcohorts at baseline were used. In order to know if the profile of AABs was specific of asymptomatic OA, samples belonging to the same patients selected from the incidence subcohort were analysed after 72 months of follow up, when all of them have developed OA. Data were normalised following the Biodesign Institute criteria. A 1.1 cutoff was used to determine reactivity and all proteins over the cutoff were analysed by Wilcoxon test. The Partial Area Under the Curve (pAUC) at 95% specificity was analysed with a  $p$  value < 0.05.

**Results:** We detect AABs against six proteins showing different reactivity (see table 1) in a stage prior to the disease –samples from the incidence subcohort at baseline compared with the non-exposed subcohort–. These proteins were implicated in the cholesterol biosynthesis (Diphosphomevalonate decarboxylase, MVD), and the elimination of potentially toxic xenobiotic or endogenous compounds (ASB7 and UGT1A7, respectively). We also found a GTPase from the Rho family (RAC3), the Vacuolar protein sorting-associated protein 4B (VPS4B), which has been recently reported to facilitate chondrocyte apoptosis in a OA rat model, and Methionine adenosyltransferase 2 subunit beta (MAT2B). The latter is the regulatory subunit of the enzyme responsible of the catalysis of S-adenosylmethionine, a dietary supplement widely used in the management of OA symptoms. None of the six AABs were found after the disease has been established (samples from the incidence subcohort at 72 months).

Abstract OP0317 – Table 1

Acc number	Symbol	Wilcoxon test (pvalue)	Specificity at 95%	AUC	AUC (p value)
O75351	VPS4B	0.005	80.80%	0.855	0.4732
Q9NZL9	MAT2B	0.005	80.80%	0.86	0.0497
P53602	MVD	0.002	75.60%	0.9	0.0426
P60763	RAC3	0.003	76.30%	0.88	0.0496
Q9HAW7	UGT1A7	0.015	79.59%	0.82	0.0481
Q9H672	ASB7	0.002	76.90%	0.885	0.0499

**Conclusions:** This work is the first to screen a large number of human proteins for the discovery of OA-associated AABs. We define a panel of six AABs, which are increased prior to the development of symptomatic knee OA. These results suggest that a serum AABs signature can facilitate the discovery of early OA biomarkers useful for clinical diagnosis.

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**Disclosure of Interest:** None declared

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### OP0318 NETOSIS-INHIBITING T-ACPA THERAPY FOR USE IN DIFFERENT NET-DRIVEN HUMAN AUTOIMMUNE DISEASES

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**Background:** Aberrant Neutrophil Extracellular Trap (NET) formation contributes to the induction and propagation of inflammation and plays a key role in causing tissue damage in conditions like sepsis, SLE, RA and vasculitis. Citrullination of proteins is involved in the formation of NETs, autoimmunity, and the breaking of tolerance in NET-driven autoimmune diseases. In SLE and RA, neutrophils undergo enhanced NETosis, and NET components are observed in blood, inflamed tissues and joints.

**Objectives:** Our objective is to develop a novel first in class NET-inhibiting therapeutic anti-citrullinated protein antibody (tACPA) targeting citrullinated histones 2A and 4, for the treatment of human diseases in which aberrant NET formation add to the severity of the pathology with an initial focus on autoimmune diseases. Here, we demonstrate the utility of tACPA for different NET-based diseases beyond RA, including SLE, vasculitis, gout and idiopathic pulmonary fibrosis (IPF).

**Methods:** Previously, using two RA animal models, the therapeutic properties of tACPA have been demonstrated.<sup>Chirivi et al., 2013</sup> In the current studies, neutrophils from RA and SLE donors, as well as biological NET-inducing stimuli, such as RA synovial fluid (SF), gout SF and activated platelets, have been used to demonstrate the NETosis-inhibiting properties of tACPA in different human disease contexts. We have further expanded tACPA's therapeutic utility by testing it in a surrogate model for NET-mediated organ damage (sepsis) and IPF.

**Results:** NETosis in human RA and SLE neutrophils have been induced with a calcium ionophore and could be inhibited by tACPA treatment (40%–100% reduction). Similar results were obtained using RA and gout SF or activated platelets as NETosis inducers in combination with neutrophils from healthy donors. These observations have been confirmed with multiple NET readouts such as MPO activity, MPO/DNA ELISA, DNA quantification as well as imaging readouts. In addition, we demonstrated that in an LPS-induced sepsis model 30% of tACPA-treated mice survived (compared to 0% in placebo controls), showing protection against organ failure. In a bleomycin-induced IPF mouse model, tACPA protected mice from the development of lung fibrosis (compared to placebo controls). When determining neutrophil counts in bronchoalveolar lavage samples, we found that in tACPA-treated mice, neutrophil levels were normal, while levels in placebo-treated mice were elevated.

**Conclusions:** In a sepsis and IPF mouse model, tACPA prevented NET-mediated organ damage, providing evidence that tACPA could be a promising therapeutic strategy for diseases where NET-mediated endothelial toxicity causes organ damage like SLE, vasculitis and IPF. Central to our strategy for generating a preclinical data package supporting clinical testing, is to demonstrate that patient NETosis can be significantly inhibited *ex vivo*. We will present data that confirm that tACPA can block human SLE NETosis as well as human NETosis induced by activated platelets or gout SF.

**Disclosure of Interest:** R. Chirivi Shareholder of: Citryll BV, Employee of: ModiQuest BV, J. van Rosmalen Employee of: ModiQuest BV, K. Kambas: None declared, G. Schmets: None declared, H. Kalisvaart: None declared, G. Bogatkevich: None declared, T. Shaw: None declared, H. van Es Shareholder of: Citryll BV, J. Raats Shareholder of: Citryll BV

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OP0319

### LOW AND MODERATE PHYSICAL ACTIVITY REDUCES LOCALISED IL-1B IN AN ACUTE MOUSE MODEL OF GOUT BY DOWN-REGULATING TLR2 EXPRESSION ON CIRCULATING NEUTROPHILS

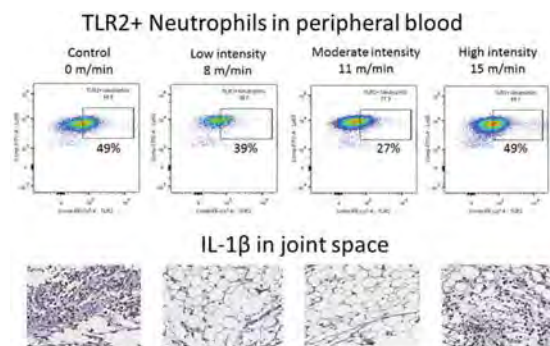
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**Background:** While physical activity was originally believed to exacerbate inflammation in rheumatic disease, recent studies have shown significant reductions in inflammation with regular exercise. It has been previously shown that down-regulation of toll-like receptor (TLR)2 and TLR4 expression correlates with increased physical activity in humans. Furthermore, both TLR2 and TLR4 knockout mice are resistant to monosodium urate (MSU) crystal-induced gout. Additionally, mesenchymal stem cells (MSCs) can be immunosuppressive by secreting IL-1 receptor antagonist (IL-1RA) and have also been shown to be up-regulated with exercise.

**Objectives:** The aim of this study was to investigate the mechanism by which exercise suppresses gouty inflammation and to define the potential roles of TLR2, TLR4, and MSCs in the process.

**Methods:** NFκB reporter mice [BALB/C-Tg(NFκB-RE-luc)-Xen] were exercised daily by treadmill walking (45 min/day for 2 weeks) at low intensity (35% VO<sub>2</sub>max; 8 m/min), moderate intensity (55% VO<sub>2</sub>max; 11 m/min), and high intensity (75% VO<sub>2</sub>max; 15 m/min). Mice were then injected with MSU crystals (0.5 mg) into the tibio-tarsal joint (ankle). Localised NFκB activity was measured 16 hours later in the injected ankle by bioluminescent imaging. Tissue was collected and processed for immunohistochemical (IHC) analysis and whole blood was collected for both flow cytometry and serum analysis.

**Results:** Mice in the low/moderate intensity exercise groups had decreased inflammation, F4/80<sup>+</sup> macrophages, and MPO<sup>+</sup> neutrophils at the site of MSU injection compared to high intensity and non-exercised controls. Similarly, bioluminescent imaging of NFκB activity was significantly reduced locally in both low/moderate intensity groups compared to high-intensity and non-exercised controls. Surface expression of TLR4 on peripheral monocytes or neutrophils showed little difference by flow cytometry, while TLR2 expression on peripheral neutrophils was significantly reduced. In concordance, localised IL-1β expression via IHC was reduced in low/moderate intensity exercise conditions. IL-1RA expression correlated with IL-1β induction locally by IHC and was elevated in serum. Also, bone marrow-derived MSCs were significantly reduced in low/moderate intensity exercise compared to high-intensity or non-exercised controls.



**Conclusions:** These data show that while low/moderate intensity exercise regimens can reduce the localised MSU crystal-induced inflammation, high intensity training negates this response. Moreover, the exercise-mediated suppression of NFκB activity and IL-1β expression locally can be partially explained by a reduction in peripheral neutrophil recruitment via downregulation of TLR2 expression in the peripheral blood. Although not clearly defined mechanistically in this study, our results also suggest that MSCs may contribute to this immunosuppressive response and are mobilised out of the bone marrow with low/moderate intensity exercise.

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OP0320

### S100A9 HAMPERS OSTEOCLAST DIFFERENTIATION FROM CIRCULATING PRECURSORS BY REDUCING THE EXPRESSION OF RANK

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**Background:** High levels of the damage-associated molecular patterns (DAMPs) S100A8 and S100A9 are produced in the synovium during both experimental and human rheumatoid arthritis (RA). These alarmins have been implicated in inflammation-induced bone resorption. We and others have previously shown that stimulation of mature osteoclasts with S100A8/A9 results in increased numbers and bone resorptive activity. In agreement, reduced bone destruction was observed after induction of experimental RA models in S100a9<sup>-/-</sup> mice. However, the effects of S100A8/A9 on monocyte-to-osteoclast differentiation remain elusive.

**Objectives:** Here, we investigated the effects of S100A9 on CD14<sup>+</sup> monocytes and their potential to differentiate into osteoclasts.

**Methods:** CD14<sup>+</sup> monocytes were isolated from buffy coats of healthy donors using density gradient centrifugation and magnetic cell sorting. Cells were differentiated into osteoclasts with macrophage colony-stimulating factor (M-CSF) and Receptor activator of nuclear factor kappa-B (RANK) ligand (RANKL) in the presence or absence of S100A9. mRNA expression was determined by RT-qPCR and protein expression was determined using Luminex analysis. Moreover, osteoclast differentiation was assessed using Tartrate-resistant acid phosphatase (TRAP) staining and the resorptive capacity was determined using mineral-coated plates. RANK protein expression was assessed using FACS.

**Results:** We observed that S100A9 stimulation of monocytes resulted in a strong induction of various pro-inflammatory factors, such as interleukin (IL)1β, IL6, IL8, and tumour necrosis factor (TNF)α after 24 hours, both on the mRNA and protein level. Interestingly, we observed a strong decrease in the number of multinucleated osteoclasts as determined by TRAP staining, at day 6 and 8 after start of the cultures. In agreement with this, the cells showed a strongly reduced resorptive capacity after 10 days of culture. We demonstrated that already a 24 hour stimulation with S100A9 strongly reduced the osteoclastogenic potential of the CD14<sup>+</sup> monocytes. Finally, to determine the mechanism of how this short S100A9 stimulation might reduce the osteoclast development, we determined the protein expression of the RANK receptor, which is crucial for osteoclast differentiation. We observed that S100A9 stimulation hampered the M-CSF-induced upregulation of RANK after 24 hours, suggesting that this underlies the hampered osteoclast differentiation. Interestingly, this S100A9-induced decreased RANK expression could be reversed by addition of the TNFα-inhibitor etanercept, but not by addition of IL1 receptor antagonist.

**Conclusions:** Whereas S100A8/A9 have been previously shown to stimulate the numbers and resorptive capacity of mature osteoclasts, we here show that stimulation of monocytes with S100A9 strongly inhibits their osteoclastogenic potential, possibly via TNFα-induced reduction of RANK expression. This suggests that S100A8/A9 does not solely stimulate osteoclast formation and function but rather that the timing of exposure to S100A8/A9 is an important determinant for monocyte-to-osteoclast differentiation.

**Disclosure of Interest:** None declared

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FRIDAY, 15 JUNE 2018

### Pathophysiology and biomarkers in PsA: what impact?

OP0321

### PRECISION MEDICINE USING DIFFERENT BIOLOGICAL DMARDS BASED ON CHARACTERISTIC PHENOTYPES OF PERIPHERAL T HELPER CELLS IN PSORIATIC ARTHRITIS

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**Background:** Biological DMARDs targeting TNF-α, IL-17, and IL-12/23 (p40) are available. The high efficacy of these drugs has been proven in numerous clinical trials. However, there are some cases in which a change from one bDMARDs to another one is necessary because of the refractory nature of the disease, and there is no established method to select the optimal bDMARDs according to the individual case, despite the fact that various drugs are available.

**Objectives:** We sought to investigate the selection of specific biological DMARDs based on characteristic lymphocyte phenotypes for treating PsA.

**Methods:** we performed this study to evaluate the efficacy of biologics therapy in 64 patients with PsA after 6 months of therapy, and to compare the results of



peripheral lymphocyte phenotyping using 8-colour flow cytometry, with specific focus on helper T cell subsets, between 26 patients with PsA and healthy donors. In addition, the therapeutic response of 26 patients in whom the optimal bDMARDs was strategically chosen based on the results of peripheral lymphocyte analysis was evaluated at 6 months of treatment intervention in comparison with 38 patients in whom the standard biological product was used based on the 2011 and 2015 EULAR recommendations. Thus, the possibility of the optimisation of drug selection for bDMARDs therapy based on peripheral blood lymphocyte phenotyping was investigated.

**Results:** The 26 patients with PsA in the strategic treatment group were classified into the following 4 types based on the peripheral blood analysis: a CXCR3<sup>+</sup>CCR6<sup>+</sup>CD38<sup>+</sup>HLA-DR<sup>+</sup> activated Th1 cell-predominant type, CXCR3<sup>+</sup>CCR6<sup>+</sup>CD38<sup>+</sup>HLA-DR<sup>+</sup> activated Th17 cell-predominant type, Th1/Th17-high type, and Th1/Th17-low type. Accordingly, ustekinumab was administered to the activated Th1 cell-predominant patients, secukinumab to the activated Th17 cell-predominant patients, secukinumab or TNF inhibitor to the Th1/Th17-high patients, and TNF inhibitor to the Th1/Th17-low patients. At 6 months of strategic treatment, there was a significant decrease in SDAI (from 16.2 to 3.52), DAS28 (ESR) (from 4.13 to 2.27), and PASI (from 8.36 to 2.40). There were no statistically significant differences in background factors at baseline between these 2 groups. Moreover, the proportion of patients with the combined use of MTX was significantly lower in the strategic bDMARDs treatment group. There were significant decreases in TJC, SJC, PGA, CRP, ESR, DAS28 (ESR), SDAI, and PASI in both groups at 6 months of therapy. There were no significant differences in the amounts of these decreases between the two groups. However, at 6 months of therapy, the rate of low disease activity achievement according to SDAI, DAS28 (ESR), and ACR20 response rate was significantly higher in the strategic bDMARDs treatment group.

**Conclusions:** Strategic treatment in which different bDMARDs were selected according to phenotypic differences in helper T cells showed significantly higher efficacy than standard bDMARD therapy. The results of this study provide an important guide to the implementation of more effective therapeutic intervention.

**Disclosure of Interest:** None declared

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FRIDAY, 15 JUNE 2018

## The art of diagnosis of axial SpA

OP0322

### ARE WE TREATING WITH BIOLOGICAL THERAPIES WOMEN PATIENTS WITH REAL NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS?

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**Background:** As a result of the development of the ASAS criteria for axial spondyloarthritis (axSpA), a new entity (non-radiographic axSpA –nr-axSpA) was created. In some countries major concerns have been raised with regard to this entity because this could imply administrating TNF inhibitors (TNFi) to non-SpA patients. Especially the possibility of treating women with fibromyalgia has been mentioned.

**Objectives:** To evaluate if the gender distribution and the pattern of patients have changed in clinical practice since TNFi were approved for nr-axSpA.

**Methods:** Dataset from a prospective cohort including all patients with axSpA treated with biological therapy (BT) since 2000 till August-2017 in a tertiary hospital was analysed. Patients' and disease' characteristics and disease activity parameters were collected at baseline. Based on the starting date for the first BT, patients were classified in two groups: i) before 2013 and ii) during or after 2013, since the nr-axSpA approval-date for TNFi in the country was July 2012. Gender distribution and other characteristics were compared between both groups using Chi-square and Student-t tests.

**Results:** In total, 385 axSpA patients initiated BT. Out of these, 266 initiated BT in period i) and 119 in period ii). The characteristics of patients in both groups are depicted in table 1. Importantly, no differences between period i) and ii) were observed regarding gender distribution (38% and 39% of women; p=0.8, respectively). Additionally, during period ii), the percentage of patients with nr-axSpA was similar for both genders and out of all patients with nr-axSpA, the majority (60%) were men. Overall, disease duration was shorter in period ii) for both genders. Women in period ii) had significantly higher ASDAS, BASMI and CRP than women in period i) and higher ASDAS, BASDAI and BASFI than men in period ii).

**Abstract OP0322** – Table 1 Patients characteristics stratified for starting first TNFi period and gender

	2000-2012			2013-2017		
	Total n=266	Males n=164	Females n=102	Total n=119	Males n=72	Females n=47
Age, yrs (mean [SD])	43.7 (11.9)	43.7 (11.4)	43.6 (12.8)	45.1 (14.1)	43.9 (13.8)	47.0 (14.5)
Smokers %	44	47	39	49	47	51
Disease duration, months (mean [SD])	61.0 (125.0)	63.5 (136.5)	55.5 (118.0)	51.0 (119.0)	62.5 (139.5)	49.0 (106.0)
HLA-B27 %	60	65	54	57	57	57
BASDAI (mean [SD])	6.0 (2.3)	5.7 (2.5)	6.9 (2.4)	6.0 (2.4)	5.8 (2.2)*	6.5 (2.6)*
ASDAS (mean [SD])	3.3 (0.9)	3.3 (1.0)	3.3 (0.9)	3.4 (1.0)	3.2 (1.0)*	3.6 (3.4)*
BASFI (mean [SD])	5.0 (3.8)	4.9 (3.7)	5.3 (3.0)	4.7 (3.8)	4.3 (4.1)*	5.7 (2.9)*
BASMI (mean [SD])	2.1 (2.2)	2.4 (2.4)	2.0 (1.4)*	2.4 (2.0)	2.2 (2.2)	2.7 (1.7)*
CRP (mean [SD])	4.1 (10.1)	4.3 (6.8)	3.2 (7.4)*	7.5 (16.7)	6.8 (17.0)	10.2 (21.9)*
PGA (mean [SD])	69 (30.0)	67 (30.0)	70 (30.0)	70 (30.0)	70 (30.0)	70 (30.0)
PGA (mean [SD])	45 (40.0)	40 (40.0)	50 (40.0)	45 (30.0)	40 (30.0)	45 (30.0)
Peripheral involvement, %	43	35	57	48	46	51
DMARDs, n	49	47	51	51	46	60
Nr-axSpA, %	-	-	-	51	50	53

\*p<0.05

**Conclusions:** In clinical practice, the frequency of women initiating BT have not increased since its approval for nr-axSpA. Additionally, women treated nowadays with BT have more objective parameters of disease activity than they used to do. This supports that when treating axSpA women (including nr-axSpA) with BT, we are currently treating axSpA -and not fibromyalgia- patients.

**Disclosure of Interest:** None declared

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OP0323

### ARE GENDER-SPECIFIC APPROACHES NEEDED IN DIAGNOSING EARLY AXIAL SPONDYLOARTHRITIS? DATA FROM THE SPONDYLOARTHRITIS CAUGHT EARLY COHORT

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**Background:** Although gender differences have been observed in the severity of axial spondyloarthritis (axSpA), gender differences in disease presentation of early axSpA have not been thoroughly investigated.

**Objectives:** Our aim was to assess if the disease presents differently in males and females, and to evaluate if this has an impact on the diagnostic process.

**Methods:** Baseline data from the SpondyloArthritis Caught Early cohort, which includes patients with chronic back pain (CBP; ≥3 months, ≤2 years, onset <45 years), were analysed. Patients underwent a full diagnostic workup, including MRI and radiograph of the sacroiliac joints (MRI-SIJ and X-SIJ), to establish a diagnosis of axSpA. Characteristics of male and female patients with a definite diagnosis of axSpA (based on a level of confidence about the diagnosis ≥7, as expressed by the physician on a 0–10 rating scale) were compared. Regression models were built for 1) the whole CBP cohort stratified by gender to study which SpA features were associated most with diagnosis in each gender, and 2) for axSpA patients to test if gender was associated with imaging positivity (MRI SIJ+and/or X-SIJ+).

**Results:** Of the 719 CBP patients, 275 were male. With 146/275 (53.1%) males and 155/444 (34.9%) females diagnosed as axSpA, males were more likely to be diagnosed with axSpA (OR 2.1, 95% CI: 1.5 to 2.9). Despite similar symptom duration, male axSpA patients were younger at diagnosis (27.4±7.5 vs 29.5±7.8 years; p=0.021). Presence of SpA features was similar in male and female axSpA patients (table 1) except for HLA-B27 and imaging positivity, which were more common in male axSpA patients (HLA-B27 +80% vs 60%; p<0.0001 and positive imaging 78% vs 64%; p=0.007). Nevertheless, both these SpA features were still more prevalent in female axSpA patients than in non-axSpA patients, either females (HLA-B27 +23% and imaging 7%) or males (HLA-B27 +34% and positive imaging 11%) (all p<0.001). Moreover, in multivariable models with diagnosis as

outcome, HLA-B27 and imaging positivity were associated with a diagnosis of axSpA in both sexes (male patients: HLA-B27+: OR 3.8, 95% CI: 1.7 to 8.8; MRI-SIJ+: OR 24.3, 95% CI: 9.7 to 60.6; X-SIJ+: OR 2.7, 95% CI: 0.7 to 9.4 and female patients: HLA-B27+: OR 6.7 95% CI: 3.2 to 14.0; MRI-SIJ+: OR 32.6 95% CI: 14.2 to 75.0; X-SIJ+: OR 6.9 95% CI: 1.4 to 32.7). In models with imaging positivity as the outcome, male gender and HLA-B27 positivity were both independently associated with MRI+and/or X-SI+ (OR 1.8, 95% CI: 1.0 to 3.1 and OR 1.8 (1.0–3.3).

**Abstract OP0323** – Table 1 Characteristics of patients with a definite diagnosis of axial spondyloarthritis (level of confidence  $\geq 7/10$ ), comparison between genders (n=301)

	Male N=146	Female N=155	p-value
<b>Age at CBP onset (years), mean (SD)</b>	<b>27.4 (7.5)</b>	<b>29.5 (7.8)</b>	<b>0.021</b>
<b>Duration BP (months), mean (SD)</b>	13.3 (7.1)	13.4 (7.0)	0.49
<b>Alternating buttock pain</b>	65 (60)	64 (51)	0.15
<b>IBP</b>	125 (84)	129 (84)	0.98
<b>Response to NSAIDs</b>	92 (64)	98 (66)	0.79
<b>Family history of SpA</b>	68 (47)	69 (45)	0.79
<b>Peripheral arthritis</b>	37 (25)	34 (22)	0.52
<b>Heel enthesitis</b>	46 (31)	51 (33)	0.73
<b>Dactylitis</b>	16 (11)	16 (10)	0.87
<b>Uveitis</b>	19 (13)	20 (13)	0.98
<b>Psoarthritis</b>	22 (15)	37 (24)	0.051
<b>IBD</b>	10 (7)	12 (8)	0.75
<b>HLA-B27 positive</b>	<b>114 (80)</b>	<b>92 (60)</b>	<b>&lt;0.001</b>
<b>Elevated CRP/ESR</b>	71 (49)	64 (42)	0.23
<b>SpA features without imaging or HLA-B27, mean (SD)</b>	3.5 (1.7)	3.5 (1.6)	0.99
<b>MRI-SIJ+/X-SIJ-</b>	65 (45)	68 (44)	0.91
<b>MRI-SIJ-/X-SIJ+</b>	5 (3)	5 (3)	0.92
<b>MRI-SIJ+/X-SIJ+</b>	<b>44 (30)</b>	<b>26 (17)</b>	<b>0.006</b>
<b>Any positive imaging</b>	<b>114 (78)</b>	<b>99 (64)</b>	<b>0.007</b>

Results are presented as n (%) unless otherwise indicated. AxSpA= axial spondyloarthritis; CBP=chronic back pain; HLA=human leukocyte antigen; IBP=inflammatory back pain; IBD=inflammatory bowel disease; NSAIDs=non-steroidal anti-inflammatory drugs; CRP= C reactive protein; ESR=erythrocyte sedimentation rate; MRI=magnetic resonance imaging; SIJ= sacroiliac joints; X=X rays; any positive imaging= MRI-SIJ+ and/or X-SIJ+. All features were complete in at least 95% of patients unless specified otherwise. Bold indicates significant results.

**Conclusions:** Although our data show clear gender differences in early axSpA, they highlight that in both genders HLA-B27 and imaging are key elements for a diagnosis of axSpA. Therefore, our study does not suggest that separate diagnostic strategies are required for men and women.

**Disclosure of Interest:** None declared

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FRIDAY, 15 JUNE 2018

## Understanding the language of basic research, epidemiology and health services articles

### OP0324 RISK OF SERIOUS INFECTIONS IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH ABATACEPT, RITUXIMAB AND TOCILIZUMAB IN DENMARK AND SWEDEN

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**Background:** Safety concerns have been raised regarding the risk of serious infections (SI) with the different available biologic disease-modifying anti-rheumatic drugs (bDMARDs). Little is known about the risk of SI in patients with rheumatoid arthritis (RA) treated with non-tumor-necrosis-factor-inhibitors (non-TNFi) bDMARDs.

**Objectives:** In RA patients treated in routine care with the three non-TNFi, abatacept, rituximab and tocilizumab 1) to compare crude as well as adjusted incidence

rates (IR) of SI after the first year of treatment, and 2) to estimate the relative risk (RR) of SI across these drugs after 1 year of treatment.

**Methods:** Collaborative observational cohort study conducted in Denmark (DK) and Sweden (SE) in parallel. RA patients in DANBIO (DK) and ARTIS/SRQ (SE) who started a non-TNFi treatment<sup>Jan 2010-Dec 2015</sup> were included and their clinical characteristics at baseline were identified. Baseline comorbidities, reimbursed antibiotic prescriptions and incident SI (hospitalisation listing infection as major cause of admission) were identified through linkage to National Patient Registries and Prescription Drug Registries. IR of SI per 100 patient years (adjusted for age and sex) and rate ratios (as estimates of RR, adjusted for additional covariates) during 1 year treatment were assessed via Poisson regression.

**Results:** 8987 treatment episodes were identified (abatacept 2,725/rituximab 3,363/tocilizumab 2,899). Differences in baseline characteristics between the three drugs were observed (table 1). During the first year of treatment, 456 SI were identified. Across all three non-TNFi there was a non-significant tendency towards higher IRs in DK than in SE. Age/sex-adjusted IRs for SI were similar across treatments in each country (abatacept/rituximab/tocilizumab for SE 6.0/6.4/4.7 and for DK 7.1/8.1/6.1, respectively). The 1 year adjusted between-drug comparisons (=RR) were formally non-significant (table 1).

**Abstract OP0324** – Table 1 Baseline characteristics, IR and RR of RA patients starting non-TNFi stratified by drug and country

Variable	ABA, N=2725		RTX, N=3363		TCZ, N=2899	
	DK	SE	DK	SE	DK	SE
Treatment episodes, n	830	1895	718	2645	1098	1801
Female gender, %	78	81	78	78	78	79
Age, years	59(50-67)	61(51-68)	61(52-69)	64(54-71)	59(50-67)	59(49-67)
Disease duration, yrs	7(3-16)	11(6-21)	11(6-19)	13(6-21)	8(3-16)	11(5-20)
DAS28	4.7(3.9-5.5)	4.9(4.1-5.7)	4.9(4.0-5.6)	5.0(4.1-5.8)	5.0(4.1-5.8)	5.1(4.2-6.0)
HAQ	1.4(0.8-1.9)	1.3(0.9-1.8)	1.5(1.1-2)	1.3(0.9-1.8)	1.4(1.1-2)	1.3(0.9-1.8)
CRP, mg/L	8(2-29)	8(4-21)	10(4-25)	10(4-25)	11(4-30)	11(4-30)
Previous cancer, %	1	4	2	11	1	4
<b>Incidence rates (IR) of serious infections, 0-12 months</b>						
Person years	568	1472	571	2189	906	1426
infections, n	40	80	50	158	55	85
IR (95%CI)*	7.1(5.1, 9.9)	6.0(4.8, 7.5)	8.3(5.9, 11.0)	6.4(5.3, 7.7)	6.1(4.6, 8.1)	4.7(3.7, 6.1)
<b>Risk Ratios (RR) for serious infections, 0-12 months**</b>						
	ABA vs TCZ (ref)		ABA vs RTX (ref)		TCZ vs RTX (ref)	
Adjusted RR (95%CI)	1.15 (0.69, 1.90)	1.13 (0.83, 1.54)	0.84 (0.55, 1.60)	0.86 (0.66, 1.13)	0.92 (0.50, 1.36)	0.77 (0.57, 1.03)

DK=Denmark, SE=Sweden

\*adjusted for age and gender. \*\* Adjusted for age, sex, DAS28, smoking, disease duration, HAQ, previous serious infection, previous cancer, previous chronic obstructive pulmonary disease and terility of antibiotic prescriptions. Numbers are medians (IQR) unless otherwise stated. End of follow-up was July 2015 in DK and December 2015 in SE

**Conclusions:** The risk of SI across treatment with non-TNFi ranged between 4.7 and 8.1/100 patient years after 1 year, but no significant differences were observed between specific drugs. The numerical between-drug differences may partly be explained by differences in baseline characteristics.

**Acknowledgements:** Partly funded by Foreum and Nordforsk. The Swedish part of the study forms part of the ARTIS safety monitoring programme. For this, ARTIS has or has had agreement with Abbvie, BMS, MSD, Pfizer, Roche, Astra-Zeneca, Eli Lilly, Samsung Bioepis, and UCB. The Danish part of the study forms part of a post-marketing safety surveillance agreement with BMS.

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### OP0325 EFFECT OF THREE HEALTH IT INTERVENTIONS ON RA DISEASE ACTIVITY SCORE DOCUMENTATION IN AN ACADEMIC RHEUMATOLOGY CLINIC

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**Background:** Routine assessments of disease activity are a key part of high quality rheumatoid arthritis (RA) care. Recommendations published in 2012 detailed the preferred disease activity measures, but little has been published about how to best implement these measures to guide routine clinical practice.

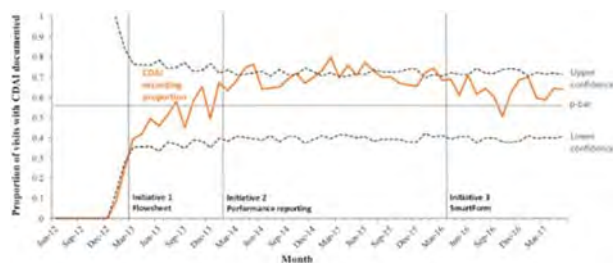
Customization of the electronic health record (EHRs) provides an opportunity to systematically collect disease activity scores in order to adequately implement treat-to-target approaches to RA treatment.

**Objectives:** To evaluate the overall impact of three health information technology (IT) initiatives at the point of care on the proportion of RA patient visits with disease activity scores recorded in an academic outpatient clinic.

**Methods:** We studied three initiatives designed to facilitate disease activity score documentation: 1. An EHR flowsheet, 2. Public reporting of physicians' performance, 3. An EHR SmartForm to facilitate the calculation and documentation of a validated RA measure, the Clinical disease activity index (CDAI). The initiatives were implemented at different time points over the study period. The study cohort included all adult RA patients with at least 2 face-to-face encounters in the outpatient rheumatology clinic at University of California, San Francisco between June 2012 – June 2017. Clinical data and covariates were retrieved from the EHR data warehouse.

To examine trends in CDAI documentation over time, we created a quality control chart (p-chart) (figure 1, where vertical lines indicate onset of each of the initiatives). For each initiative, we analysed our data using a two-pronged pre-post approach. First, we developed multiple logistic regression models in which the outcome was documentation of CDAI, controlling for patient age, sex, race/ethnicity, language and insurance category as well as physician sex and years in practice. Second, logistic mixed effect models were used to account for repeated visits by patients to the clinic and clustering by physicians.

**Results:** We included data from 7406 encounters from 978 unique patients. Mean (SD) age was 58.9 (16) years, 82% were female, 44% were racial/ethnic minorities, and 59% had public insurance. Over a 60 month period, overall documentation of CDAI scores per month in the clinic increased from 0% to 64% (figure 1). Results from mixed effect logistic modelling showed that Initiative 1 significantly increased CDAI recordings (OR=40.14 p<0.001); Initiative 2 further increased recordings (OR=2.86, p<0.001); Initiative 3 decreased the probability of CDAI being recorded (OR=0.61, p<0.001). No systematic differences were found across patient demographics or provider sex and years in practice.



**Abstract OP0325** – Figure 1 proportion of visits per month with CDAI documentation during implementation of quality improvement initiatives

**Conclusions:** Introduction of a flowsheet and public reporting of physician performance within the practice significantly improved performance, but institution of the SmartForm did not further improve on these gains. However, gains were maintained through the end of the five-year study period. Future work should focus on whether improved CDAI documentation is associated with improved patient outcomes, such as lower disease activity and improved physical function.

**Disclosure of Interest:** None declared

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FRIDAY, 15 JUNE 2018

## The stromal link to inflammation

OP0326

### MODELLING THE INTERACTION BETWEEN DISEASE MICROENVIRONMENT AND MESENCHYMAL STEM CELLS IN SCLERODERMA

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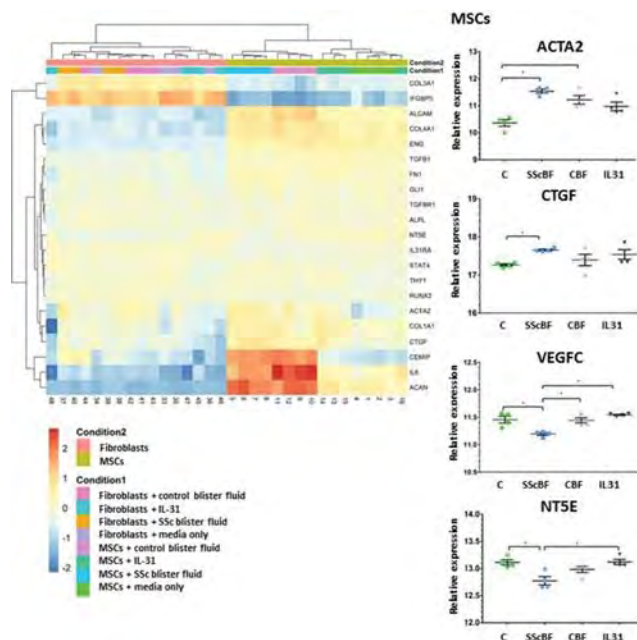
**Background:** Mesenchymal stem cells (MSCs) are pleuripotent bone marrow and tissue resident cells implicated in homeostasis and tissue repair. Systemic

sclerosis (scleroderma, SSc) is a severe connective tissue disease characterised by progressive fibrotic thickening of the dermis, accompanied by loss of subcutaneous fat and microvasculature. Aberrant activation of MSCs within the disease microenvironment may underly the persistent fibrotic repair process, or account for the failure of adipogenesis and dysregulated vascular repair.

**Objectives:** We sought to: 1) determine whether activated MSCs are present within the SSc involved skin lesions, 2) test whether SSc suction blister fluid (BF) derived from involved forearm skin can induce phenotype changes in MSCs, 3) fully profile the altered gene expression in MSCs exposed to SSc BF, 4) investigate the role of key factors present at increased level in SSc BF (IL-31, lactate).

**Methods:** Novel post-fixation collagenase tissue dissociation techniques applied to 1 mm tissue sections, combined with Feulgen staining of DNA, were used to identify MSCs undergoing metakaryotic division within the involved skin of SSc patients. Fat derived MSCs from healthy controls were treated in tissue culture with blister fluid derived from the fibrotic skin lesions or from matched sites in healthy individuals, or exposed to key constituent factors, including cytokines (IL-31, 50 ng/ml), metabolites (lactate, 25 mM), and enhanced stiffness matrix (50 kPa gels). The responses of MSCs were studied by analysis of next generation sequencing (NGS) and phenotype changes.

**Results:** MSCs undergoing metakaryotic division were identified in SSc skin biopsy material but not in healthy control (HC) tissue (SSc vs HC, superficial dermis 0 vs 0, mid dermis 1.1 vs 0 p<0.0001, deep dermis 1.4 vs 0 p<0.0001 metakaryotic cells per x20 field). SSc BF (diluted 1:125 in media) induced disease-relevant phenotype changes in MSCs, such as  $\alpha$ SMA expression (p<0.05), collagen gel contraction (p<0.002) and scratch wound repair (p<0.016), as well as loss of adipogenic potential, more than control BF or media alone, due in part to elevated IL-31 and lactate. NGS indicated that SSc blister fluid induced treatment-specific gene expression in MSCs (figure 1), more differentially than in normal dermal fibroblasts, consistent with activation of fibrosis, wound repair, migration, osteogenesis, connective tissue formation and loss of angiogenesis/vascular repair. Induction of  $\alpha$ SMA in MSCs was dependent on the matrix stiffness in medium.



**Conclusions:** Factors present at elevated levels in the disease microenvironment, including cytokines and metabolites, as well as the stiffened ECM, are capable of promoting the migration and differentiation of fat derived MSCs, towards tissue reparative cells implicated in the fibrotic process. Conversely, the adipogenic and vascular regenerative potential of these cells may be reduced by exposure to the SSc microenvironment.

**Disclosure of Interest:** None declared

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OP0327 **CXCL4 DRIVES FIBROSIS BY PROMOTING SEVERAL KEY CELLULAR AND MOLECULAR PROCESSES**

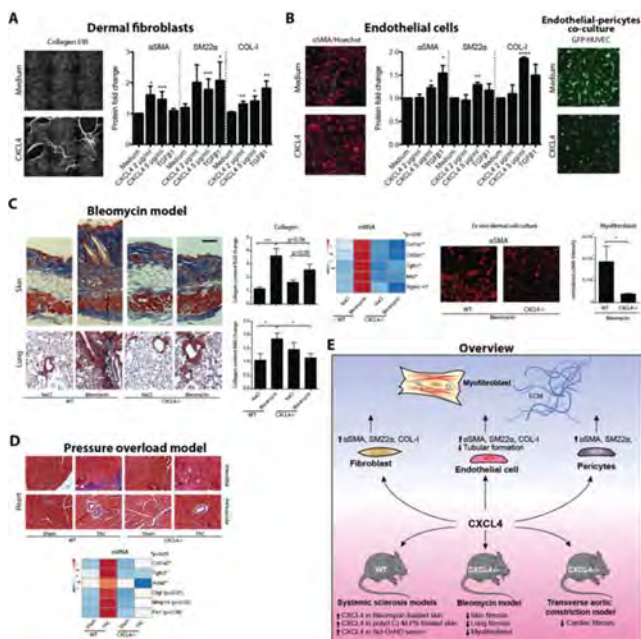
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**Background:** Fibrosis, characterised by excessive accumulation of extracellular matrix (ECM) through myofibroblasts, is a leading cause of mortality worldwide<sup>1,2</sup>. Understanding the pathways involved in myofibroblasts activation is crucial to develop novel treatment strategies. Systemic sclerosis (SSc) is a prototypic fibrotic disease in which we previously identified CXCL4 to be strongly correlated with skin and lung fibrosis<sup>3</sup>.

**Objectives:** We aimed to elucidate the role of CXCL4 in fibrosis development using *in vitro* and *in vivo* assays.

**Methods:** Human primary dermal fibroblasts, endothelial cells, and pericytes, were (co-) cultured in the presence or absence of recombinant human CXCL4. CXCL4<sup>-/-</sup> mice were used in bleomycin-induced skin and lung fibrosis model, and pressure-overload cardiac fibrosis model. Gene expression was assessed by qPCR, protein expression was determined by western blot or immunofluorescence, and collagen content was measured by trichrome staining or hydroxyproline assay.

**Results:** We found that CXCL4 induced the expression of myofibroblast markers  $\alpha$ SMA and SM22 $\alpha$ , and collagen synthesis in human dermal fibroblasts, endothelial cells, and pericytes. CXCL4 also suppressed endothelial cell tubular formation in a co-culture with pericytes. In mice, CXCL4 expression was increased in a variety of mouse inflammatory and fibrotic models. Using CXCL4<sup>-/-</sup> mice, we confirmed the essential role of CXCL4 in promoting fibrotic events in the skin, lung, and heart using two independent fibrosis models.



**Conclusions:** CXCL4 drives myofibroblast transformation from different precursors and it is required for fibrosis development across organs. Our findings implicate a pivotal role of CXCL4 in fibrosis further substantiating the potential role for neutralising CXCL4 as a novel therapeutic strategy.

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**Disclosure of Interest:** None declared

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FRIDAY, 15 JUNE 2018

**New approaches in measuring what matters to patients**

OP0328-HPR **PATIENTS' VIEWS ON ROUTINE COLLECTION OF PATIENT-REPORTED OUTCOMES IN RHEUMATOLOGY CARE – A DANBIO FOCUS GROUP STUDY**

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**Background:** Patient Reported Outcomes (PROs) are important for shared decision-making regarding treatment. The DANBIO registry, which has included >60 000 patients (>5 00 000 visits), routinely collects PROs (health assessment questionnaire (HAQ), visual analogue scales for pain, fatigue and global health, patient acceptable symptom state (PASS) and an anchor) on touch-screens in the waiting room, as part of rheumatology standard care.<sup>1</sup> The aims of DANBIO are to 1) monitor the disease in individual patients, 2) improve treatment quality, 3) conduct research. Patients' experience with the collection of PROs in DANBIO has not been explored.

**Objectives:** To explore patients' views on the collection of PROs in rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS)

**Methods:** We conducted a qualitative study based on one semi-structured focus group interview in each of the five geographical regions in Denmark. The analysis of the transcribed interviews was based on content analysis.<sup>2</sup> Four patient research partners were involved in all phases of the study

**Results:** In total, 32 adult patients with RA (n=21), PsA (n=6) or AS (n=5) participated. 21 (66%) were female, mean age 60 years (range 32–80).

The analysis identified an overarching theme **Potential for improvement of communication** referring to patients' perception that PROs have the potential to inspire both patients and clinicians to prepare for and improve dialogue in the consultation. In addition, four subthemes emerged.<sup>1</sup> **Lack of information about why the data is collected** referring to patients' uncertainty as to whether the PROs aimed primarily at monitoring their own disease, to save money or for research purposes. Questions regarding who gets access to data (in addition to the rheumatologist or nurse), and if data were sold to external parties, were also expressed.<sup>2</sup> **Validity of the data** referring to patients' concerns about how to reply 'correctly'. The fluctuations in disease activity and timing in relation to pharmacological treatment affected the patients' answers. They were uncertain whether answers should reflect their present state or an average of disease manifestations since their last visit. Patients were also uncertain regarding the reference; should they compare to healthy individuals or to when the arthritis is as good as it can be. Some chose to answer as if they were doing worse or better than they actually felt, in order to enter into dialogue with the clinician or because they were worried that medical treatment would be withdrawn.<sup>3</sup> **Inclusion of the PROs in the consultation** referring to patients' experiences varying from no use of the PROs at all to detailed review with the rheumatologist or nurse

**Conclusions:** Systematic information and continuous dialogue regarding the purpose of the collection of PROs, how to answer the PROs and active use of the answers in the consultations are important for patients with arthritis

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**Disclosure of Interest:** None declared

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**OP0329-HPR** **OUTCOMES THAT MATTER TO PEOPLE LIVING WITH INFLAMMATORY ARTHRITIS; A GLOBAL STANDARD SET, DEVELOPED BY THE INTERNATIONAL CONSORTIUM FOR HEALTH OUTCOME MEASUREMENT (ICHOM) WORKING GROUP FOR INFLAMMATORY ARTHRITIS**

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**Background:** Value-based health care (VBHC) is a framework for improving efficiency of healthcare in which competition on value for patients is the central concept. Public reporting of patient outcomes by healthcare providers is proposed as a mechanism that will accelerate identification and adoption of innovations that increase value, through shared learning and sparking competition on outcomes that matter to patients. A key barrier to the implementation of VBHC in inflammatory arthritis (IA) is the absence of a universally accepted set of patient outcomes and risk adjustment variables that are appropriate and feasible to implement in different healthcare systems worldwide.

**Methods:** The International Consortium for Health Outcomes Measurement (ICHOM) assembled a multidisciplinary international working group (WG), consisting of 24 experts, including six patient representatives, to develop a standard set of patient-centred outcomes for IA. The process followed a structured approach using a modified Delphi process to reach consensus on 1) medical conditions to be covered by the set, 2) outcome domains, 3) outcome measures, 4) case mix variables and – definitions. Each step was supported by systematic literature reviews and consultation of (external) experts on the topic under consideration.

**Results:** The WG decided to include rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis and juvenile idiopathic arthritis in the IA Standard Set. Twenty-four outcome domains were initially identified in the 130 randomised trial reports and 28 qualitative studies that were found in the systematic literature reviews. Ultimately, pain, fatigue, activity limitations, overall physical and mental wellbeing, work/school/housework ability and productivity, inflammatory disease activity including therapeutic response (i.e. has the patient achieved the treatment target?), and serious adverse events were included. The measurement properties of 21 patient-reported outcome measures were assessed for all of the included domains. 20 of these were linked to an item response theory-based common reporting metric. This allows users of the ICHOM IA set to choose their preferred instrument while allowing comparison of outcomes. A number of risk adjustment variables and time points for collection were recommended to allow global benchmarking.

**Conclusions:** We present the ICHOM standard set of outcomes for Inflammatory Arthritis, that we encourage providers of care to implement to facilitate global comparison of outcome data and stimulate shared learning.

**Disclosure of Interest:** None declared

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FRIDAY, 15 JUNE 2018

**Innovative treatments for a better quality of life**

**OP0330-PARE** **LOVE YOUR HEART, AN ONLINE, INTERACTIVE CARDIOVASCULAR RISK ASSESSMENT PROGRAMME FOR PEOPLE WITH RA/IA**

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**Background:** Having RA doubles the risk of most heart problems, including heart attack, stroke and atherosclerosis — the build-up of fat, cholesterol and cellular debris (plaque) on blood vessel walls. Studies show that approx. 50% of people with RA die prematurely due to cardiovascular disease (CVD) one of the most common co-morbid risks. Many patients and even health professionals are unaware of this leading potentially to poorer long-term outcomes. UK Rheumatologist, Dr. Holly John originally developed and piloted this programme in group face to face format in Dudley which achieved very good results, but the format limited the number of people who could access it and benefit from it. NRAS, with Dr. John's permission, wanted to make it as widely available as possible to all with RA. Being unaware of these risks means that people with RA can be less likely to address factors, firmly within their own control, such as smoking, exercise, weight and diet.

**Objectives:** In order to make this programme freely available to all, we had to convert a face to face paper-based programme into an on-line, interactive video which would not only educate but enable people to assess their own personal CVD risks and set goals to mitigate such risks. We have also included within the programme baseline and 6 month follow up assessments to measure intended and actual behaviour change. The overall purpose of the programme is to achieve a healthier heart lifestyle thereby reducing premature mortality due to CVD.

**Methods:** Using the paper participant manual created for the group programme and working closely with Dr. John and other health professional specialists (exercise, smoking cessation, nutrition) at Dudley as well as patients who had attended the programme, we reviewed with our creative film production team the best way to adapt this to create a really engaging, interactive on-line educational experience which would allow participants to undertake the programme over time whilst working through the goal-setting and evaluation process. 2 days of filming were done in Dudley and Maidenhead at the end of 2016 followed by 12 months' period of editing, review, some re-filming and software development. The programme piloted with 20 people with RA at the end of 2017 and their feedback has been incorporated. The programme launches in the UK on 14th February, St. Valentine's Day. Heart-shaped business cards and A4 posters describing the programme with links to register, will be sent to all rheumatology units across the UK in February/March encouraging HCPs to refer their patients to Love your Heart.

**Results:** Many people have registered interest in this programme and we anticipate a high take up immediately post launch. Numbers who have participated by early June, together with anonymised baseline assessment details including intention to change behaviour will be available by June/EULAR should we be successful in having this abstract accepted.

**Conclusions:** It is too early to make any conclusions but we hope that by <sup>EULAR 2019</sup> we will have some interesting conclusions to report on. We anticipate that this programme is more likely to encourage patients to make heart healthy lifestyle choices than being advised to 'exercise, eat healthily, lose weight, stop smoking' by health professionals during routine clinic appointments.

**Acknowledgements:** We would like to acknowledge the input and commitment of our technology partner Streaming Well Ltd.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.4635

**OP0331-PARE** **BEHAVIOUR CHANGE EXPERIENCES AND NEEDS OF PERSONS WITH RHEUMATIC DISEASE**

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**Background:** Persons with rheumatic diseases have a higher rate of surgery as well as a need of beneficial lifestyle behaviours, in order to control risk factors associated with surgery and disease co-morbidities.

**Objectives:** The objective was to explore behaviour change experiences and needs of individuals similar to patients undergoing knee and hip surgery.

**Methods:** A survey was designed with focus on current lifestyle behaviours; experience of behaviour changes; desire to change behaviours; and attitudes and willingness to adopt digital tools in the behaviour change process. The survey was distributed via a web system to 13864 Swedish Rheumatism Association (SRA) members with a rheumatic disease.

**Results:** 1660 consented to participate of whom a majority were women, 1/2 between 45 and 64 years of age and 1/3 older than 65, where 2/3 had experienced at least 1 surgery and 2/3 of these 2–3 surgeries, with 1/4 concerning knee or hip surgery. 20% had experienced complications. Almost all respondents had access to a smartphone, computer and the internet. The most problematic current behaviour was insufficient physical activity, with less than 1/5 engaging in recommended levels of physical activity/week. Less than 1/10 smoked and about 1/20 gave indications of risky alcohol consumption. Regarding healthy eating, a large majority ate breakfast daily, 3/4 ate fruits and vegetables daily, and slightly under 1/2 ate fish 2–3 times a week. However, about 2/3 consumed unhealthy foods several times/week, with 1/5 indicating consumption 1–2 times/day. Accordingly, 2/3 indicated they would like to increase physical activity level and over 1/2 wanted to improve eating habits. 20% wanted to change other behaviours such as weight loss, consumption of sugary foods, and stress management. Fewer than 10% wanted to change their smoking habits and less than 1/20 wanted to change their alcohol habits. A majority had attempted prior behaviour change, 3/4 focused on physical activity, 2/3 on healthy eating, 1/5 on smoking and 1/20 on alcohol. Regarding the duration of the change, it was permanent for 2/5. Among those who succeeded in maintaining the change during a shorter period, 44% succeeded for 3–6 months, 1/20 for 6–12 months and about 1/10 for periods of 1–2 years. Regarding types of support used for implementing behaviour change, 1/3 had no support but only 1/10 found this helpful. Almost half used self-help, 1/5 used social support, 1/6 used professional support, and 1/10 used digital support. Most helpful were self-help, followed by social, professional and digital support, respectively.

Respondents were asked about use of a digital tool to support lifestyle behaviour change. Over 3/4 were open to using digital tools. Regarding the respondents' preferences: the top three preferences were for reminders, contact with peers and information on the importance of changing the behaviour in question.

**Conclusions:** The survey suggests that SRA members have digital access despite 1/3 being older than 65. The focus for current and future behaviour change is physical activity and to a lesser extent, healthy eating. Smoking and risky alcohol use behaviours are low in this group. Willingness to engage in a digital tool is high, and preferences are clear, with interest in human contact with professionals and peers through the digital tool, as well as automated functions.

**Disclosure of Interest:** None declared

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FRIDAY, 15 JUNE 2018

## Advances in biologic therapy of small vessel vasculitis

### OP0332 PAEDIATRIC OPEN-LABEL CLINICAL STUDY OF RITUXIMAB FOR THE TREATMENT OF GRANULOMATOSIS WITH POLYANGIITIS (GPA) AND MICROSCOPIC POLYANGIITIS (MPA)

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**Background:** Rituximab in combination with glucocorticoids (GC) is approved to treat adult patients (pts) with GPA or MPA; however, limited data exist on the safety and efficacy of rituximab in paediatric pts with these potentially life- and organ-threatening diseases.

**Objectives:** To report the interim safety, pharmacokinetics (PK) and exploratory efficacy data from the 6 month remission induction phase of a Phase IIa international, open-label, 18 month clinical study of rituximab in paediatric pts with GPA or MPA.

**Methods:** Pts aged  $\geq 2$  to  $\leq 18$  years with newly diagnosed or relapsing GPA/MPA received 4 intravenous (IV) rituximab infusions of 375 mg/m<sup>2</sup> body surface area (BSA) on Days 1, 8, 15 and 22 with concomitant GC 1 mg/kg/day (max 60 mg/day) tapered to 0.2 mg/kg/day minimum (max 10 mg/day) by Month 6. All pts received 3 doses of pulse IV methylprednisolone (30 mg/kg/day, max 1 g/day) prior to first rituximab infusion and mandatory prophylaxis for *Pneumocystis jirovecii* infection. Pts were also pre-medicated with acetaminophen and an antihistamine, 1 hour before each rituximab infusion. Adverse events (AEs) and laboratory data were measured at each study visit (1, 2, 4 and 6 months). Plasma samples for PK analysis were collected throughout the study; clearance and area under the curve (AUC) were calculated using population PK modelling from the RAVE study of rituximab in adult pts with GPA/MPA.<sup>1</sup> For exploratory efficacy assessment, the Paediatric Vasculitis Activity Score (PVAS) was measured at each study visit.

**Results:** Of the 25 pts enrolled, 19 (76%) had GPA and 6 (25%) had MPA (median [range] age 14<sup>6-17</sup> years; 80% female). Median (range) disease duration was 0.5 (0.2-0.72) months; 2 pts had received prior cyclophosphamide therapy. All received 4/4 rituximab infusions and completed the 6 month induction phase. By Month 6, all pts had experienced  $\geq 1$  AE. The most common AEs by system organ class were infections and infestations in 16 pts (64%). AE terms reported in  $\geq 3$  pts are listed in the table 1. Eleven serious AEs occurred in 7 pts (28%), including 3 serious infections (viral gastroenteritis, one lower and one upper respiratory tract infection). 32% of pts had  $\geq 1$  infusion related reaction (IRR). No serious IRRs or deaths were reported. The relationship between AUC and BSA was flat and comparable to adult pts. A total of 13 pts (52%) achieved remission by 6 months, defined as PVAS of 0 and GC dose 0.2 mg/kg/day (max 10 mg/day) or PVAS of 0 on 2 consecutive readings  $\geq 4$  weeks apart irrespective of GC dose.

Abstract OP0332 – Table 1 Adverse events reported in  $\geq 3$  patients

Adverse event	Number of events (% of pts with $\geq 1$ AE)
Headache	6 (24%)
Upper respiratory tract infection	5 (20%)
Abdominal pain (upper)	3 (12%)
Back pain	3 (12%)
Blood IgG decreased	3 (12%)
Chest pain	3 (12%)
Cough	3 (12%)
Epistaxis	3 (12%)
Hypertension	3 (12%)
Nausea	3 (12%)
Pyrexia	3 (12%)
Vomiting	3 (12%)

AE, adverse event; IgG, immunoglobulin G.

**Conclusions:** In the initial 6 months of this first global clinical trial of rituximab in paediatric pts with GPA/MPA, rituximab was generally safe and well tolerated. The overall safety profile and PK parameters were comparable to adults with GPA/MPA. No new safety signals were observed. However, the study size and interim nature of the analysis limit firm conclusions. The clinical trial and additional efficacy, PK and safety analyses are ongoing.

#### REFERENCE:

[1] Stone, et al. *NEJM* 2010;363:221-32.

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**Disclosure of Interest:** P. Brogan Grant/research support from: Roche, SOBI, Novartis, Chemocentryx, Consultant for: Roche, SOBI, UCB, Speakers bureau: SOBI, Novartis, G. Cleary Speakers bureau: AbbVie, O. Kasapcopur: None declared, S. Rangaraj: None declared, R. Yeung Consultant for: Novartis, Eli Lilly, P. Brunetta Shareholder of: Roche, Employee of: Genentech, Inc., J. Cooper Employee of: Genentech, Inc., P. Pordeli Employee of: Roche, P. Lehane Employee of: Roche

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### OP0333 SURVIVAL IN ANCA ASSOCIATED VASCULITIDES: A RETROSPECTIVE MULTICENTRIC ANALYSIS IN NORTHERN ITALY

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**Background:** Patients affected by ANCA associated vasculitides (AAV) show lower survival than general population, even if the mortality decreased significantly in the last decade.

**Objectives:** Aim of our study is to analyse the early mortality (within 6 months) and the long-term survival in a multicentric Italian cohort of AAV patients.

**Methods:** we identified all patients affected by AAV, diagnosed from 1995 until 2017, followed routinely in four vasculitis referral centres in Northern Italy. We enrolled patients with diagnosis of granulomatosis with polyangiitis (GPA) and micro polyangiitis (MPA), fulfilling EMA algorithm or <sup>CHCC 2012</sup> definitions, with complete survival data at last follow up. The analysis focused on early mortality, long-term survival and their predictors.

**Results:** We enrolled 200 AAV patients (F/M 110/90, Caucasian 98%) with a median age at diagnosis of 54.6 $\pm$ 15.2 years. 157 (78.5%) were affected by GPA and 43 (21.5%) by MPA. Data about ANCA antibodies were available in 181 patients and 157 (87%) resulted ANCA positive: 100 c-ANCA/PR3, 56 p-ANCA/MPO and one with double specificity PR3-MPO-ANCA.

During the follow up period [53<sup>26-100</sup> months], we registered 21 (10.5%) deaths, 6 (28.5% of all mortality) within 6 months after diagnosis: 9 patients died due to infectious complications, 1 due to hepatic cancer, 1 due to end stage heart failure, 1 due to massive cholestasis and 9 due to unknown causes.

Early mortality was significantly associated with a higher frequency of alveolar haemorrhage (p=0.01; OR 11.1 IC95% 2.1-60.1) and respiratory failure (p<0.001, OR 28.3 95% CI: 4.7 to 170.6).

The long-term survival, analysed with Kaplan-Maier method, did not show significant differences between GPA and MPA patients, while a significant poorer



survival was observed in p-ANCA/MPO patients than c-ANCA-PR3 and ANCA negative patients (Log rank test: p=0.04).

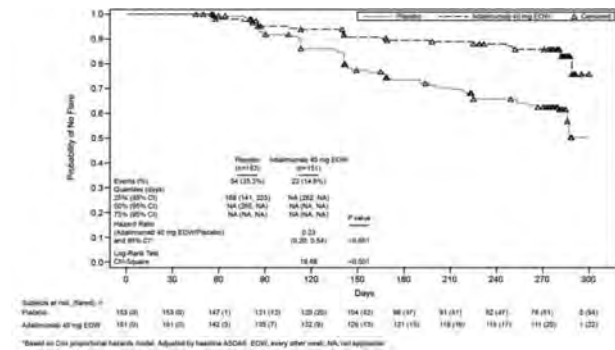
At univariate analysis of baseline data, deceased patients resulted older at disease onset (p=0.001) with more comorbidities (p<0.001) and presented at diagnosis a higher frequency of respiratory failure (p=0.002, OR 7.1 IC95% 2.2–22.2) and renal insufficiency (p=0.003, OR 4.7 95% CI: 1.6 to 13.7). No significant differences were noted in term of infections/year, relapses/year and cancer development.

**Conclusions:** In this large cohort of Italian patients we confirm a higher short and long-term survival in AAV patient than reported in literature. Nevertheless, up to one third of deaths occurred within 6 months after diagnosis and infection diseases resulted the most frequent cause of death. Moreover, our data confirm the prognostic importance of ANCA pattern and the poor outcome of patient with severe lung and renal involvement.

**Disclosure of Interest:** None declared

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**FRIDAY, 15 JUNE 2018:** Tapering and flaring in PsA and SpA



**Abstract OP0334 – Figure 1** Time to flare by week 68

**OP0334 EFFICACY AND SAFETY OF CONTINUING VERSUS WITHDRAWING ADALIMUMAB (ADA) IN MAINTAINING REMISSION IN PATIENTS WITH NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS (NR-AXSPA)**

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**Background:** It is not known whether TNF blockers can be stopped in nr-axSpA patients (pts) who are in remission.

**Objectives:** ABILITY-3, reported here, assessed if ADA can be discontinued or should be continued in nr-axSpA pts in sustained remission after a 28-wk open-label period.

**Methods:** ABILITY-3 enrolled adult pts diagnosed with nr-axSpA, fulfilling ASAS criteria but NOT modified New York criteria who had objective evidence of active MRI inflammation in the SI joints or spine or elevated high-sensitivity CRP at screening, active disease at baseline (ASDAS ≥2.1, BASDAI ≥4, total back pain ≥4), and inadequate response to ≥2 NSAIDs. Pts who achieved ASDAS inactive disease (ASDAS <1.3) with open-label ADA 40 mg every other wk at wk 16, 20, 24, and 28 were randomised to 40-wk, double-blind PBO (withdrawal) or ADA (continuation) in period 2. Primary efficacy endpoint was proportion of pts who did not experience a flare (ASDAS ≥2.1 at 2 consecutive study visits) during period 2. Secondary endpoints were also assessed up to wk 68 (nonresponder imputation).

**Results:** Of 673 enrolled pts, 305 (45%) were randomised to double-blind treatment. A significantly greater proportion of pts treated with ADA vs PBO had no flares (70% vs 47%; p<0.001) at wk 68; relative risk of flare with treatment withdrawal was 1.77. Time to flare analysis showed significantly lower risk of flare for ADA vs PBO (figure 1). At wk 68, significantly greater proportions of ADA vs PBO pts achieved secondary endpoints, except for HAQ-S (table 1). Among pts who received ADA at any time, 77% reported adverse events (AEs) and 4% reported a serious AE; nasopharyngitis (17%), upper respiratory tract infection (12%), worsening of axSpA (9%), headache (8%), and diarrhoea (6%) were the most common. During period 2, incidence of AEs was similar for ADA and PBO (65% vs 69%), incidence of serious AEs was higher for PBO vs ADA (7% vs 1%), and the most common AEs in both the ADA and PBO groups were nasopharyngitis (16% vs 13%), upper respiratory tract infection (13% vs 8%), and worsening of axSpA (6% vs 14%; none serious).

**Abstract OP0334 – Table 1** Efficacy outcomes at week 68

Wk 68, n (%)	ADA (40 mg EOW) n=152	PBO n=153	P Value
No flare	106 (70)	72 (47)	<0.001
ASDAS ID	87 (57)	51 (33)	<0.001
ASDAS MI	89 (59)	49 (32)	<0.001
ASDAS CII	102 (67)	69 (45)	<0.001
ASAS20	107 (70)	72 (47)	<0.001
ASAS40	100 (66)	70 (46)	<0.001
ASAS 5/6	87 (57)	49 (32)	<0.001
ASAS PR	64 (42)	41 (27)	0.005
BASDAI50	103 (68)	72 (47)	<0.001
Change from baseline in BASFI, LSmean±SE	-3.97±0.11 n=111	-3.51±0.13 n=77	0.007
Change from baseline in HAQ-S, LSmean ±SE	-0.68±0.04 n=112	-0.58±0.04 n=79	0.088

**Conclusions:** In pts with nr-axSpA who achieved sustained remission with ADA, continued therapy was associated with significantly more pts maintaining remission and lower disease activity than treatment withdrawal. These results support the continuation of ADA therapy after achievement of sustained remission. Safety findings were consistent with established safety profile of ADA.

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**OP0335 HIGH NEED FOR ANTI-TNF THERAPY AFTER WITHDRAWAL STRATEGY IN EARLY PERIPHERAL SPONDYLOARTHRITIS**

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**Background:** Treatment with TNFi in early stages of peripheral Spondyloarthritis (pSpA) results in higher rates of clinical remission, compared to treatment in more longstanding disease.<sup>1</sup> When remission is reached, the recently updated T2T-recommendations suggest tapering of treatment. In the CRESPA-trial pSpA patients were treated with golimumab monotherapy; we demonstrated that – after reaching sustained remission – discontinuation of golimumab led to biological-free remission in 53% of patients; conversely 47% experienced a disease flare. It is currently unknown if concomitant administration of DMARDs could lead to higher rates of biological-free remission.

**Objectives:** To explore – in pSpA patients in clinical remission – the possibility that co-medication with methotrexate would allow discontinuation of the TNFi.

**Methods:** The CRESPA-trial included patients with active pSpA and symptom duration <12 weeks; the primary study results have been reported previously (reference). In the CRESPA-Extension protocol, patients were included that either did not reach remission (but had substantial improvement with golimumab treatment), or that experienced recurrence of arthritis, enthesitis or dactylitis within 1 year after discontinuation of golimumab. These patients received additional open-label golimumab 50 mg SC every 4 weeks for 2 years. At week 104, patients were offered an additional 12 weeks of golimumab treatment, but now in combination with methotrexate 15 mg weekly. At week 116, patients in clinical remission continued methotrexate, but discontinued golimumab. Patients were prospectively followed to assess the rate of sustained biological-free clinical remission. In

case of relapse of arthritis, enthesitis or dactylitis under methotrexate monotherapy, golimumab was restarted.

**Results:** Currently, twenty three of the original 60 pSpA patients included in the CRESPA-trial, completed the 2 year CRESPA-Extension protocol; of these, 21 (91%) were in clinical remission at week 104 when methotrexate was added. The mean follow-up period after completion of the extension part, was 80±28 w. 5 patients (24%) are still in sustained remission (n=5) under methotrexate monotherapy whereas in 16 patients (76%), golimumab needed to be re-installed because of relapse of disease activity (n=14) or development of adverse events related to methotrexate (n=2). Recurrence of disease was characterised by development of arthritis in all patients with a median of 4 tender and 3 swollen joints. In 50% (n=7) of the cases, concomitant dactylitis was present. 64% (9/14) were having concomitant psoriasis which was mild since all had a BSA <5%. The mean time for recurrence was 28.6 weeks. Restarting golimumab treatment promptly restored clinical remission in all patients within 12 weeks.

**Conclusions:** In patients with pSpA in clinical remission after 2 years of golimumab monotherapy, concomitant administration of methotrexate before discontinuation of the TNFi, did not significantly raise the percentage of patients in biological-free remission. In 76% of patients, golimumab had to be restarted, underscoring the overall weak efficacy of methotrexate in pSpA.

#### REFERENCE:

- [1] Carron P, et al. Anti-TNF-induced remission in very early peripheral spondyloarthritis: The CRESPA study. *Ann Rheum Dis* 2017 Feb 17.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.4287

**FRIDAY, 15 JUNE 2018:** Prevention of OA: Yes we can!

#### OP0336 THE EFFECT OF TIMING AND DURATION OF STATIN EXPOSURE ON THE RISK OF REVISION FOLLOWING TOTAL HIP OR KNEE ARTHROPLASTY: A POPULATION-BASED COHORT STUDY

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**Background:** Total hip/knee replacement (THR/TKR) are safe and effective interventions for the treatment of osteoarthritis. However, around 2.5% of patients who undergo a THR/TKR in the UK require revision surgery within 5 years. Experimental studies have suggested that statins may have a beneficial effect on bone by promoting osteoblast formation and reducing osteoclastic bone resorption. Statins have been linked to improved strength of the bone-implant interface and may also attenuate the inflammatory response to particulate wear debris and subsequent periprosthetic osteolysis. Observational data suggest that postoperative exposure to statins may reduce the risk of revision arthroplasty. However, the influence of timing of statin exposure on revision risk has not previously been investigated. This may be significant since statins may affect biological processes occurring at different postoperative periods.

**Objectives:** To determine whether the timing of statin exposure relative to the primary arthroplasty influences the risk of revision arthroplasty. Also to determine whether the duration of exposure is associated with the risk of revision arthroplasty.

**Methods:** Subjects from the Clinical Practice Research Datalink, a population-based clinical database, who had THA/TKA from 1988–2016 were included. Cox regression models were used to determine the association between statin exposure and the risk of revision THA/TKA, i) at any time and ii) if first exposed 0–1, 1–5, or >5 years following THA/TKA. Cox regression was also used to determine the association between total duration of statin exposure (<1, 1–2, 2–3, 3–4, 4–5, >5 years) and revision risk. The Cox regression models were adjusted for the propensity score for statin exposure in each period, which was calculated using a logistic regression model including demographic factors, selected comorbidities and selected medication. Missing data for covariates were imputed using multiple imputation by chained equations with 10 iterations.

**Results:** 1 51 305 participants were included. 57 003 (37.7%) were exposed to statins during follow up and 3500 (2.3%) had revision arthroplasty. In a propensity score adjusted model, exposure to statins was associated with a reduced risk of revision arthroplasty (HR (95% CI) 0.82 (0.75, 0.90)). Participants first exposed within 1 year and between 1 and 5 years following THA/TKA (vs unexposed) had a reduced risk of revision arthroplasty (HR (95% CI) 0.82 (0.74, 0.91) and 0.76 (0.65, 0.90), respectively), while first exposure >5 years following THA/TKA was not associated with revision risk. In relation to duration of statin therapy, participants exposed for more than 5 years in total (vs <1 year) had a reduced risk of revision (HR (95% CI) 0.74 (0.62, 0.88)).

**Conclusions:** Statin therapy initiated up to 5 years following THA/TKA may reduce the risk of revision arthroplasty. The mechanisms by which statin therapy is linked with a reduced risk of revision surgery are not completely understood, though does not appear to be related solely to an effect on osseointegration of the primary prosthesis, which occurs primarily in the early (<1 year) postoperative period.

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**Disclosure of Interest:** None declared

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#### OP0337 ASSOCIATION BETWEEN METABOLIC SYNDROME AND TRAJECTORIES OF KNEE PAIN: A 10.7-YEAR FOLLOW-UP STUDY

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**Background:** Metabolic syndrome (MetS) has been suggested as having a role in the pathogenesis of osteoarthritis (OA). However, no study has assessed whether MetS and its components are associated with knee pain and its change over time.

**Objectives:** To identify distinct trajectories of MSP over 10.7 years in an older population, and to examine risk factors for identified trajectories.

**Methods:** 1099 participants (mean age 63 years) from the population-based Tasmanian Older Adult Cohort study were recruited at baseline. 875, 768 and 563 participants attended years 2.6, 5.1 and 10.7 follow-up, respectively. Demographic, psychological, lifestyle and comorbidities data were obtained at baseline. Knee radiographic OA was assessed by X-ray at baseline. Group-based trajectory modelling was applied to identify distinct trajectories of MSP. Multi-nominal logistic regression was used for the analyses with adjustment for potential confounders.

**Results:** 985 participants were included for the analyses, three pain trajectories were identified: 'Mild pain' (52%), 'Moderate pain' (33%) and 'Severe pain' (15%) with 32% of participants having Mets. MetS was significantly associated with increased risk of both 'Moderate pain' (relative risk [RR]: 1.47, 95% confidence interval [CI]: 1.10 to 1.96) and 'Severe pain' (2.22, 1.54 to 3.20) relative to 'Mild pain' in univariate analysis. After adjustment for age, sex, smoking, physical activity, emotional problems, comorbidities and radiographic OA, central obesity was associated with increased risk of both 'Moderate pain' (1.70, 1.17 to 2.49) and 'Severe pain' (3.28, 2.16 to 4.98), and MetS and its components (hypertriglyceridemia and low HDL) were only associated with increased risk of 'Severe pain' (p<0.05). However, these associations became weak and non-significant after further adjustment for body mass index (BMI), but hypertension became significantly protective with 'Moderate pain' (0.70, 0.50 to 0.99). Similar associations were found in those with knee OA (RR: 1.70 to 2.75, all p<0.05).

**Conclusions:** The Mets is predominantly associated with knee pain trajectories through central obesity, and hypertriglyceridemia and low HDL can predict 'Severe pain' trajectory in those with Mets. An unexpected inverse association between hypertension and moderate pain trajectory needs a further investigation, which may reflect an interaction between blood pressure and pain sensitivity in 'Moderate pain' trajectory.

**Disclosure of Interest:** None declared

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**FRIDAY, 15 JUNE 2018**

#### Big data for musculoskeletal research

#### OP0338 RELATIONSHIP OF PROVIDER DENSITY ON TOTAL JOINT REPLACEMENT OUTCOMES

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**Background:** The proportion of providers in a geographical location (provider density) has been associated with improved surgical outcomes in hand and wrist surgery, appendicitis and other high-volume procedures, demonstrating the importance of access to care.

**Objectives:** The purpose of this study is to assess the association of provider density with Total Knee Replacement (TKR) and Total Hip Replacement (THR) outcomes.



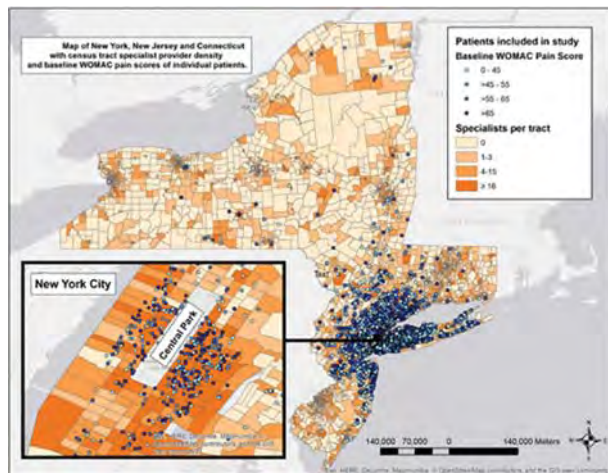
**Methods:** Individual patient-level variables were obtained from a single institution TKR and THR registry between 5/1/07 and 2/1/11. Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain and function scores at baseline and 2 years after elective TKR and THR were collected and retrospectively analysed. We included patients living in New York, Connecticut and New Jersey which is the catchment area for the hospital. Individuals' geocodable addresses were used to obtain the number of primary care physicians (PCPs) and specialists in each census tract using the ArcGIS software. Provider density was calculated and broken down into percentage quartiles. Comparisons were made using Kruskal-Wallis tests.

**Results:** A total of 3606 TKR, and 4295 THR patients were included. (figure 1) Mean number of PCPs was 5.4(SD 9.5) and specialists were 15.8(SD 41.1) per census tract. The median number of PCPs were 2 (IQR 1, 6) and specialists were 3 (IQR 1, 13). Neighbourhood poverty or education correlated poorly with the number of PCPs and specialists. Baseline WOMAC pain and function scores (table 1) are statistically significantly better in neighbourhoods with a higher proportion of specialists, but not PCPs. These differences were no longer present 2 years after surgery.

**Abstract OP0338** – Table 1 Association of specialist proportions in neighbourhoods with WOMAC\* scores

Proportion of Specialists per census tract	Baseline WOMAC* median (IQR)	p-value	2-year WOMAC* median (IQR)	p-value	Baseline WOMAC* median (IQR)	p-value	2-year WOMAC* median (IQR)	p-value
<b>Pain</b>								
Total Hip Replacement								
Quartile 1 (Lowest)	50 (40,65)	<0.001	100 (80,100)	0.59	50 (40,65)	<0.001	85 (80,100)	0.76
Quartile 2	50 (40,65)		100 (80,100)		55 (45,65)		85 (80,100)	
Quartile 3	55 (45,65)		100 (80,100)		55 (45,65)		85 (80,100)	
Quartile 4 (Highest)	55 (45,65)		100 (80,100)		58.3 (45.7-70)		85 (80,100)	
Total Knee Replacement								
Quartile 1 (Lowest)	46.9 (35.3-58.8)	<0.001	95.6 (86.8-100.0)	0.49	50.0 (39.7-61.8)	<0.001	81.2 (75.0-98.4)	0.37
Quartile 2	43.3 (38.8-61.8)		85.9 (88.8-100.0)		52.9 (42.7-66.2)		90.6 (79.5-97.1)	
Quartile 3	50.0 (39.7-64.7)		96.9 (88.2-100.0)		52.9 (42.7-66.2)		89.9 (77.9-97.1)	
Quartile 4 (Highest)	50.0 (39.4-63.3)		96.9 (88.2-100.0)		55.9 (44.1-69.1)		91.2 (78.3-98.5)	

\*WOMAC - Western Ontario and McMaster Universities Osteoarthritis Index



**Abstract OP0338** – Figure 1 Map of New York, New Jersey and Connecticut with census tract specialist provider density and baseline WOMAC pain scores of individual patients.

**Conclusions:** Patients from neighbourhoods with fewer specialists seek arthroplasty with worse baseline pain and function than those from neighbourhoods with more specialists. However, once these patients receive arthroplasty (i.e. specialty care), these differences resolve by 2 years. These data suggest that once a patient can access specialty care in the health care system, their outcomes improve despite worse baseline pain and function.

**Disclosure of Interest:** B. Mehta: None declared, J. Szymonifka: None declared, S. Dey: None declared, I. Navarro-Millan: None declared, L. Mandl Grant/research support from: Boehringer-Ingelheim, A. Bass Grant/research support from: Abbott, Pfizer, L. Russell: None declared, M. Parks Grant/research support from: Zimmer, Consultant for: Zimmer, M. Figgie Shareholder of: Mekanika, J. Nguyen: None declared, S. Goodman: None declared

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**OP0339 DEVELOPMENT OF A PREDICTIVE MODEL OF RADIOLOGICAL DAMAGE IN PATIENTS WITH RHEUMATOID ARTHRITIS BASED ON ARTIFICIAL INTELLIGENCE**

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**Background:** Rheumatoid arthritis (RA) is a chronic inflammatory disease associated with increased mortality and disability. Although different factors associated with prognosis have been identified, it is still difficult to predict the evolution of a specific patient.

**Objectives:** Our objective is to train and validate a predictive model of disease severity using radiological damage as a surrogate marker, based on Artificial Intelligence techniques, and using clinical and genetic data.

**Methods:** Four independent cohorts were included (892 patients with 1667 hand X-rays). Radiological damage was measured with the Sharp/van-der-Heijde score (SvdH). The variables to be predicted [total value of SvdH, erosion component (ES) and joint narrowing (NS)] were logarithmically transformed. As clinical predictors, age at onset of symptoms, sex, duration of the disease at the time of each radiograph, year of onset of symptoms and presence of rheumatoid factor were used. As genetic variables, the single nucleotide polymorphism data obtained from the Immunochip genotyping platform (Illumina) were used. In addition, an interaction between each polymorphism and the duration of the disease was introduced. Three cohorts were used for the selection of variables, generation of predictive models and internal validation. The fourth cohort was used to perform the external validation of the models. Regression trees with random effects were generated using the R package 'REEMtree'. The goodness of fit of the models was measured using the root mean squared error (RMSE) and the intraclass correlation coefficient (ICC).

**Results:** In the cohorts where the predictive models were developed, the RMSEs for total SvdH, ES and NS were 3.16, 1.02 and 2.29 units of the Sharp/van-der-Heijde score, respectively. The ICCs were 0.96, 0.87 and 0.95, respectively. In the external validation cohort, the RMSEs were 7.13, 3.53 and 4.81 units of the Sharp/van-der-Heijde score, respectively. The ICCs were 0.90, 0.78 and 0.88.

For the total SvdH, the best fit model contained the variables 'age of onset of the symptoms of RA' and the interaction between duration of the disease and 3 polymorphisms: rs10752907, rs4405161 and rs2501617. For the ES, it contained the variables 'age of onset of AR symptoms', the polymorphism rs7769752 and the interaction between disease duration and 6 polymorphisms: rs12410412, rs117029499, rs72925969, rs869186, rs11258464, rs4781952. For the NS, it contained the variables 'age of onset of AR symptoms', 'gender', and the interaction between disease duration and 9 polymorphisms: rs3814055, rs1020822, rs13157991, rs152294, rs2914190, rs10824537, rs2637229, rs114136906 and rs4958241.

**Conclusions:** It is possible to generate predictive models of radiological damage of great precision using Artificial Intelligence techniques. This could allow early stratification of patients according to prognosis.

It is necessary to validate these models in other populations.

**Disclosure of Interest:** None declared

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FRIDAY, 15 JUNE 2018

**From big data to personalised medicine in paediatric rheumatic diseases**

**OP0340 EVIDENCE BASED RECOMMENDATIONS FOR CORTICOSTEROID TAPERING/DISCONTINUATION IN NEW ONSET JUVENILE DERMATOMYOSITIS PATIENTS FROM THE PRINTO TRIAL**

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**Background:** At present no clear evidence based guidelines exist to standardise the tapering and discontinuation of corticosteroids (CS) in juvenile dermatomyositis (JDM).

**Objectives:** To provide evidence-based recommendations for CS tapering/discontinuation through the analysis of the patients in the PRINTO new onset JDM trial. Secondary objective of the study was to identify predictors of clinical remission and CS discontinuation.



**Methods:** New onset JDM children were randomised to receive either prednisone (PDN) alone or in combination with MTX or CSA. All children were given initially intravenous methylprednisolone, and then PDN starting with 2 mg/kg/day. Gradual tapering according to a specific protocol could lead to the safe dose of 0.2 mg/kg/day by month 6, then discontinued at month 24. Major therapeutic changes (MTC) were defined as the addition or major increase in the dose of MTX/CSA/ other drugs or any other reasons for which patients were dropped from the trial. Patients were divided according to clinical remission (CR) (CMAS=52 and MD global=0 for 6 continuous months) into two major groups. Group 1 included those on CR, who could discontinue PDN, with no MTC (reference group). Group 1 was compared with those who did not achieve CR, without or with MTC (group 2 and 3, respectively). JDM core set measures (CSM) were compared within the 3 groups. We also calculated the gold standard group 1 median change in the CSM in the first 6 and over 24 months and applied a logistic regression model to identify predictors of CR with PDN discontinuation.

**Results:** 139 children were enrolled in the trial: 47 on PDN, 46 on PDN +CSA and 46 on PDN +MTX. We identified 30 (21.6%) patients for group 1, 43 (30.9%) for group 2 and 66 (47.5%) for group 3. At baseline all 3 groups had no differences in the CSM. Already in the first 2 months a clear differential trend in disease activity measures, according to clinical remission status and PDN discontinuation, could be identified. From the observation of the median change in the CSM of group 1 in the first 6 months, the following recommendations could be extrapolated: decrease corticosteroids from 2 to 1 mg/kg/day in 2 months if the MD-global, parent-global, CHAQ, DAS, CMAS, MMT or Phs measures have changed of at least 50%; from 1 to 0.5 mg/kg/day in the following 2 months if the MD-global, CHAQ, DAS, CMAS show a change of at least 20%; in the following 2 months (month 4–6) corticosteroids can be tapered up to the safe dose of 0.2 mg/kg/day, if the disease activity measures remain at low/normal values. We finally ran a logistic regression model that showed that the achievement of PRINTO criteria 50–70–90 at 2 months from disease onset, an age at onset >9 years and the combination therapy PDN +MTX, increase the probability of clinical remission from 4 to 7 times (table 1).

**Abstract OP0340** – Table 1 Logistic regression model for the outcome: achievement of remission (n/tot: 28/130; 21.5%)

	OR (95% CI)	P <sup>a</sup>
<b>Responder at 2 months:</b>		0.0076
Printo-50 (vs. not responder/Printo-20)	5.41 (1.37 - 21.32)	
Printo-70 (vs. not responder/Printo-20)	6.90 (1.91 - 24.99)	
Printo-90 (vs. not responder/Printo-20)	4.46 (1.08 - 18.38)	
Age at onset > 8.53 years (≤ 8.53 years)	4.64 (1.69 - 12.71)	0.0017
Treatment group: PDN+MTX (vs. PDN / PDN+CSA)	3.63 (1.30 - 10.09)	0.0116
AUC of the model: 0.80		

OR: Odds Ratio; 95% CI: 95% Confidence Interval; P<sup>a</sup>: Likelihood Ratio test

**Conclusions:** We propose evidence based specific cut-offs for corticosteroid tapering/discontinuation based on the change in JDM CSM of disease activity, and to identify the best predictors for clinical remission and corticosteroid discontinuation.

**Disclosure of Interest:** None declared

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FRIDAY, 15 JUNE 2018

## Triple T: T cells, technologies and therapies

### OP0341 INCREASED FREQUENCY OF CIRCULATING CD4 +CXCR5-PD1HI PERIPHERAL HELPER T (CTPH) CELLS IN PATIENTS WITH SEROPOSITIVE EARLY RHEUMATOID ARTHRITIS (RA)

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**Background:** A novel population of CD4 +T cells with B cell helping capacity has been described in the synovial tissues and peripheral blood of seropositive RA

patients with an established disease, and termed 'peripheral helper' (Tph) cells. (Rao DA et al, Nature 2017) Tph cells are characterised by the lack of CXCR5 together with a bright expression of PD-1 (CD4 +CXCR5-PD-1<sup>hi</sup> T cells). As opposed to CD4 +CXCR5+PD-1<sup>hi</sup> follicular helper T cells (Tfh), Tph cells are not located in lymphoid organs but accumulate in inflamed tissues. Tph cell numbers have not been previously examined in early RA (eRA).

**Objectives:** To study the frequency of circulating CD3 +CD4+CXCR5-PD-1<sup>hi</sup> Tph cells (cTph), in patients with eRA.

**Methods:** Peripheral blood was drawn from DMARD-naïve early RA patients (eRA) (2010 ACR criteria) with a disease duration <24 weeks (n=42), and healthy controls (HC) matched for age and gender (n=42). For comparison, blood was also drawn from 66 patients with established RA (disease duration >2 years), 45 patients with Spondyloarthritis (SpA), and their age and gender-matched HC (one HC per patient). In addition, synovial fluid from 7 patients with established RA and 3 patients with SpA was examined. Established RA patients were receiving low-dose oral methotrexate and were naïve for biological agents. SpA patients were receiving NSAIDs, low-dose oral methotrexate and/or sulphasalazine and were naïve for biologicals. After isolation by Ficoll-Hypaque gradient, PBMCs were stained with antibodies to CD3, CD4, CXCR5, ICOS and PD-1, and examined by flow cytometry.

**Results:** The frequency of circulating CXCR5- cells gated for CD4 +T cells was not different among the studied groups. In contrast, eRA patients demonstrated an increased frequency of circulating CD4 +CXCR5-PD-1<sup>hi</sup> Tph and CD4 +CXCR5-PD-1<sup>hi</sup>ICOS+ T cells. When examining seropositive (RF and/or ACPA+, n=25) and seronegative eRA patients (RF- and ACPA-, n=17) separately, it was evident that the above described alterations were only apparent in seropositive eRA. Likewise, increased cTph numbers were observed in seropositive (n=47) but not seronegative (n=19) established RA, and not in SpA patients (n=45), which is consistent with data reported by Rao et al. Interestingly, this increased cTph cell frequency was observed only in seropositive RA patients with an active disease (DAS28 >2.6, n=24), whereas the numbers of cTph cells in established RA patients who had achieved remission (DAS28 <2.6, n=23) were not different from HC. Furthermore, Tph cells were present in the synovial fluid of seropositive RA (n=4) but not of seronegative RA (n=3) or SpA (n=3).

**Conclusions:** Tph cells may play an important role in the pathogenesis of seropositive but not seronegative RA. An increased cTph cell frequency is a marker of active, seropositive RA.

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[1] Rao DA, et al. Nature 2017;542(7639):110–114.

**Disclosure of Interest:** None declared

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### OP0342 ALTERED FREQUENCY AND FUNCTION OF MAIT CELLS IN SYSTEMIC SCLEROSIS REVEALED BY HIGH DIMENSIONAL MASS CYTOMETRY AND TRANSCRIPTOME ANALYSIS

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**Background:** Systemic sclerosis (SSc) is an autoimmune disease characterised by excessive fibrosis of skin and internal organs, and vascular dysfunction<sup>1</sup>. Association of T and B cell subsets have been reported in SSc, however there is lack of systematic studies of functional relations between immune cell subsets in this disease<sup>2,3,4</sup>. This lack of mechanistic knowledge hampers targeted intervention.

**Objectives:** In the current study we ought to determine differential immune cell composition and heterogeneity in peripheral blood of SSc patients and its impact on disease severity and progression.

**Methods:** Mononuclear cells from blood of SSc patients with interstitial lung disease (ILD, n=10) or No ILD (n=10) and healthy controls (n=10) were analysed by mass cytometry using a 36 marker (cell-surface and intracellular) panel to aid in identification of major PBMC lineages including T cells, B cells, monocytes and NK cells and their subsets. Transcriptome analysis (m-RNA sequencing) was performed on sorted T and B cell subsets. Unsupervised clustering of mass cytometry data was performed using in-house developed analysis software MARVIS. This software combines dimension reduction and clustering steps to identify all possible cellular subsets. Further, custom R scripts helped in identifying nodes that were differentially expressed between the study groups and also phenotype of these nodes.

**Results:** Unsupervised clustering performed revealed significant differences in the frequencies of T cell and B cell subsets. Most strikingly we identify a 3 fold decrease in frequencies of Va7.2+CD161+mucosal associated invariant T cells (MAIT) in SSc patients and 2 fold increase in total B cells, particularly

CD19 +CD27 naive cells. A subset of memory CD8 +T cell, expressing CXCR3 was found to be increased in SSc patients as compared to healthy controls. Transcriptome analysis of sorted B cell and T cell subsets showed decrease in genes related to survival and increased expression of apoptotic genes in CD4,CD8 T and MAIT cells from SSc patients. Genes related to exhaustion and leukocyte migration were highly expressed in T cells from patients.

**Conclusions:** This study provides an in depth analysis of systemic immune composition in SSc with the potential to delineate mechanisms of pathogenesis and identify diagnostic and/or therapeutic targets. This is the first demonstration of dysfunction of MAIT cells in SSc and further characterisation of their function in this context is required.

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## Navigating the world of digital health

### OP0343-HPR AN ECONOMIC EVALUATION OF A TAILORED GUIDED INTERNET-BASED COGNITIVE BEHAVIOURAL INTERVENTION FOR PATIENTS WITH RHEUMATOID ARTHRITIS AS AN ADDITION TO USUAL CARE

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**Background:** Within the field of rheumatoid arthritis (RA), patients report decreased health-related quality of life (HRQoL) as a result of living with physical factors such as pain and psychological factors such as negative mood. As these factors are associated with the disease trajectory, health care utilisation, and workplace disability of patients, these factors lead to significant societal health expenses. In a recent randomised controlled trial, improvements in especially psychological functioning (e.g., depressed mood) were found by offering tailored, therapist guided cognitive behavioural therapy online.<sup>1</sup> Although internet-based cognitive behavioural therapy holds promise for implementation and cost-reductions, scarce research is available on the cost-effectiveness of these treatments.

**Objectives:** A cost-effectiveness study from a societal perspective was conducted alongside a randomised controlled trial on a tailored and therapist-guided internet-based cognitive behavioural intervention (ICBT) for patients with elevated levels of distress, as an addition to usual care alone in order to inform stakeholders on implementation of this treatment.

**Methods:** Data were collected at baseline/pre-intervention, 6 months/post-intervention, and three-monthly thereafter during one year follow-up. Effects were measured in quality-adjusted life years (QALYs) and costs from a societal perspective including healthcare sector costs (including healthcare use, medication, and intervention costs), patient travel costs for healthcare use, and costs associated with loss of labour.

**Results:** The intervention improved quality of life compared to usual care alone ( $\Delta$  QALYs=0.059), but also led to higher costs ( $\Delta$ =€ 4.211,44), which reduced substantially when medication costs were left out of the equation ( $\Delta$ =€ 1.862,72). Most (93%) of the simulated ICERS were in the north-east quadrant, suggesting a high probability that the intervention is effective in improving HRQoL, but at a greater monetary cost for society compared to usual care alone.

**Conclusions:** A positive effect on quality-adjusted life years is seen in the intervention group compared to the control group. However, cost-ratios show that this comes at a greater cost to society. The substantial costs in this population are generated by medication costs, for which no group differences could be found. The cost-benefit ratio improves when the costs for medication are not taken into account.

Based on the effects for improvement of quality of life, implementation of the intervention is recommended, yet on the side of costs, further study is warranted.

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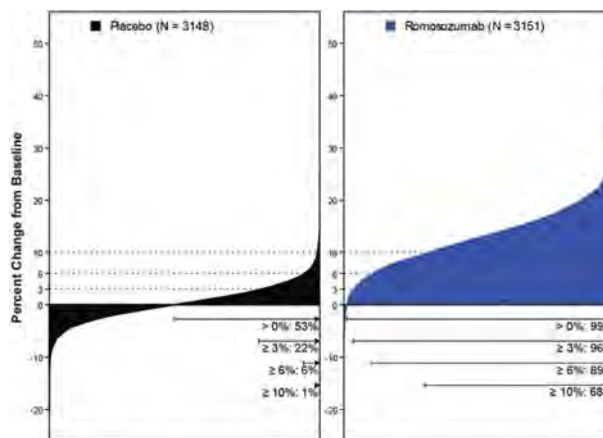
## The rheumatologist-orthopaedic surgeon connexion in secondary fracture prevention

### OP0344 FRAME STUDY: THE FOUNDATION EFFECT OF REBUILDING BONE WITH ONE YEAR OF ROMOSUZUMAB LEADS TO CONTINUED LOWER FRACTURE RISK AFTER TRANSITION TO DENOSUMAB

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**Objectives:** Romosozumab (Romo), a sclerostin antibody, has a dual effect of increasing bone formation and decreasing bone resorption. In the FRAME study (NCT01575834), one year of Romo treatment resulted in large bone mineral density (BMD) increases at the lumbar spine (LS) and total hip (TH) versus placebo (Pbo).<sup>1</sup> The differences between groups remained after all subjects transitioned to denosumab (DMAb) during the second year of study. Here, we further characterise the BMD gains seen during the FRAME study and examine the effect of building bone with Romo on fracture-risk reduction after transition to DMAb.

**Methods:** Subjects in FRAME were randomised to receive monthly Romo 210 mg or Pbo for 12 months, after which all subjects received 6-monthly DMAb 60 mg for an additional 12 months. Endpoints for the current analysis were mean change from baseline in BMD T-score, percentage of subjects with a BMD gain, and fracture incidence in the second year of the FRAME study, including new vertebral, clinical (nonvertebral and symptomatic vertebral), and other fracture categories.



N = Number of subjects with values at baseline and at least one post-baseline visit at or before month 12. Data are percent change in BMD from baseline to month 12 by individual subject at the lumbar spine. N = included subjects with baseline and  $\geq 1$  post-baseline measurement; missing data were imputed by last observation carried forward. X-axis represents each individual subject. Dotted horizontal lines reflect 3%, 5%, and 10% BMD gain from baseline to month 12. Lines with arrowheads below the X-axis represent the percent of subjects with the indicated BMD gains (> 0%,  $\geq$  3%,  $\geq$  5%, and  $\geq$  10%). BMD, bone mineral density.

**Abstract OP0344** – Figure 1 Percent change in lumbar spine BMD from baseline to month 12 by individual subject

**Results:** 7180 subjects were included in the study (Romo, n=3589; Pbo, n=3591). At month 12, the mean change from baseline in LS BMD T-score was 0.88 for Romo and 0.03 for Pbo. At month 24 (after both treatment groups received DMAb in the second year) mean increases in LS BMD T-score were 1.11 for Romo/DMAb and 0.38 for Pbo/DMAb. At month 12, the mean changes in TH BMD T-score were 0.32 for Romo and 0.01 for Pbo. At month 24, mean changes in TH BMD T-score were 0.45 for Romo/DMAb and 0.17 for Pbo/DMAb. In the Romo group, 99% of subjects showed an increase in LS BMD at month 12, with 89% achieving  $\geq 6\%$  gains (figure 1). Administration of Romo during the first year led to reductions versus Pbo in the relative risk of fractures during the second year, despite both groups receiving DMAb in the second year (reductions of 81% for vertebral fractures [ $p < 0.001$ ]; 32% for clinical fractures [ $p = 0.052$ ]; 39% for major osteoporotic fractures [ $p = 0.034$ ]).

**Conclusions:** Romo versus Pbo resulted in substantially higher BMD T-score increases after one year. After transition to DMAb, BMD gains in both treatment groups were similar in the second year. One year of Romo treatment, followed by transition to DMAb, resulted in unprecedented gains in BMD and substantially reduced fracture rates during the second year even though subjects in both groups received DMAb. These data support the clinical benefit of rebuilding the skeletal foundation with Romo treatment before transition to DMAb.

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[1] Cosman F, et al. *N Engl J Med* 2016;375:1532–43.

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OP0345

#### DENOSUMAB COMPARED WITH RISEDRONATE IN GLUCOCORTICOID-TREATED SUBJECTS: RESULTS FROM THE FINAL 24-MONTH ANALYSIS OF A RANDOMISED, DOUBLE-BLIND, DOUBLE-DUMMY STUDY

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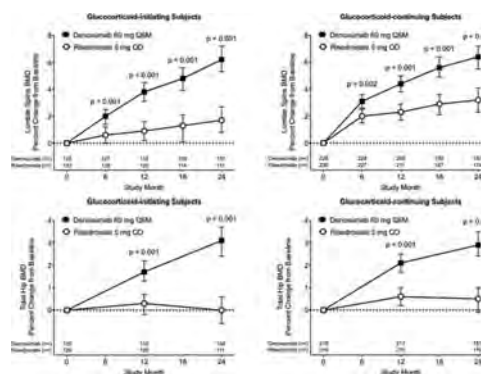
**Background:** Denosumab 60 mg subcutaneously Q6M increased spine and hip BMD significantly more than risedronate 5 mg orally QD at 12 months in glucocorticoid-treated subjects (as previously reported<sup>1</sup>).

**Objectives:** This analysis compared the BMD effects of denosumab vs risedronate and further characterised denosumab safety in this population at 24 months.

**Methods:** This phase 3, randomised, double-blind, double-dummy study enrolled adults  $\geq 18$  years receiving  $\geq 7.5$  mg daily prednisone (or equivalent) for  $< 3$  months (glucocorticoid-initiating subpopulation) or  $\geq 3$  months (glucocorticoid-continuing subpopulation). All subjects  $< 50$  years had history of osteoporotic fracture. Glucocorticoid-continuing subjects  $\geq 50$  years had lumbar spine (LS), total hip (TH), or femoral neck BMD T-scores  $\leq -2.0$ , or  $\leq -1.0$  and history of fracture. Subjects were randomised 1:1 to denosumab 60 mg subcutaneously Q6M or risedronate 5 mg orally QD for 24 months. This analysis assessed denosumab superiority over risedronate for percentage change from baseline in LS and TH BMD at 24 months.

**Results:** Of 795 randomised subjects, 590 (74.2%) completed the 24 month study (glucocorticoid-initiating: 109/145 denosumab, 117/145 risedronate; glucocorticoid-continuing: 186/253 denosumab, 178/252 risedronate). Denosumab

was superior to risedronate for increases from baseline in LS and TH BMD at all timepoints assessed through 24 months in each subpopulation (figure 1). Adverse events, serious adverse events (including infection), and fractures were similar between groups.



**Abstract OP0345** – Figure 1 Bone mineral density percentage change (95% CI) from baseline through month 24

**Conclusions:** In conclusion, denosumab was superior to risedronate for increases in spine and hip BMD through 24 months. The overall safety profile was similar between groups. Denosumab may offer a valuable osteoporosis treatment option for patients receiving glucocorticoids.

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FRIDAY, 15 JUNE 2018

#### What's new: latest advances in treatment in JIA and osteoarthritis

#### OP0346-PARE A PARTNERSHIP IN IMPLEMENTATION: ADAPTING AN OSTEOARTHRITIS GUIDEBOOK ACROSS EUROPEAN CULTURES – WITH PATIENTS, FOR PATIENTS

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**Background:** A guidebook for patients with osteoarthritis (OA) was co-developed with UK patients during an OA research study.<sup>1–3</sup> The JIGSAW-E project is now disseminating and implementing the OA management guidelines and Guidebook in clinical practice in UK, Netherlands, Norway, Denmark and Portugal.<sup>4</sup>



**Objectives:** To study the translation and cultural adaptations of the OA Guidebook appropriate for local context and use by patient champions and health professionals together.

**Methods:** A project launch meeting led to the creation of an international panel of Patient Champions and the adaptation of the OA Guidebook as a priority project. 15 Patient Champions with OA were collaborative partners of the project's local Communities of Practices (CoP) (UK:2, Norway:2, Netherlands:5, Denmark:5, Portugal:1) (figure 1). CoPs also engaged with OA patient organisations. Cultural adaptation of the OA Guidebook by CoPs: 1) review of UK OA Guidebook and existing written patient information; 2) translation; 3) cultural adaptation: review of content, images and layout; 4) consistency check with national guidelines; 5) production; 6) review and approval; 7) shared learning across countries via Skype. Each CoP adopted a process appropriate to their specific context

**Results:**

**Abstract OP0346-PARE** – Table 1 Development of culturally adapted versions of the OA Guidebook in each country.

Country	Developments to date
Netherlands	The Dutch team produced a full version of the OA Guidebook, revised the translated text and recommended new images to better reflect Dutch patients. Now available in hard copy and on a OA patient website: <a href="http://www.poly-artrose.nl/">www.poly-artrose.nl/</a>
Norway	The Norwegian CoP supplemented an existing OA handbook ('ActiveA') with a 'Feeling Positive' chapter from the UK version. The Patient Champions commented on the new chapter which will be made available on the JIGSAW-E website.
Denmark	The Danish team produced a concise version of the OA Guidebook, containing vital written information for patients at first consultation. The Patient Champion helped to adapt translations for the short version.
Portugal	The Portuguese team are working with the local health administration and patient organisations to culturally adapt a full Portuguese translation of OA Guidebook



**Abstract OP0346-PARE** – Figure 1 The JIGSAW-E international panel of patient champions

**Conclusions:** It is feasible and effective to involve patient champions in the cultural adaptation and dissemination of consistent and accurate patient information to support the implementation of OA guidelines in clinical practice.

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**Acknowledgements:** Thank you to all the Patient Champions for their contributions to JIGSAW-E. A. Rosager and L. Baumbach led the Danish adaptation. JIGSAW-E is funded by EIT Health. KD is part funded by a NIHR Knowledge Mobilisation Research Fellowship (KMRF201403002). The MOSAICS study was funded by NIHR Programme Grant (RP-PG-0407–10386).

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OP0347

#### SHARE DECISION MAKING AID FOR JUVENILE IDIOPATHIC ARTHRITIS: MOVING FROM INFORMATIVE PATIENT EDUCATION TO INTERACTIVE CRITICAL THINKING

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**Background:** Shared decision making (SDM) is an emerging trend in paediatrics. Currently available SDM interventions are mere information on the disease or medication and often fail to engage the children in the medical decision process. It has been suggested that future decision aids should consider developing separate more appropriate tools in order to better engage the children.

**Objectives:** To develop, and evaluate an illustrated and interactive evidence-based SDM aid for children living with inflammatory arthritis, able to inform them about the pros and cons of their disease as well as the available treatment options, and help them to make an informed shared decision.

**Methods:** A multidisciplinary team defined criteria for the SDM as to design, medical content and functionality, for children. Development was according to the international standard (IPDAS). Eight categories emerged as highly important for shared decision making: 1. What is arthritis? 2. Why do we treat arthritis? 3. What are my targets? 4. What are the available treatment options? 5. Progressometer/ my chances of improvement? 6. How soon will the medications kick in and how to take them? 7. Potential side effects? 8. For how long shall I take the medication. Each category is supported by simple illustrations showing the state of the joint in the different scenarios whether the child take treatment or not, whereas at the end of each category the child is asked to make a decision in view of the information given. 94 children with juvenile idiopathic arthritis, evaluated the tool, in a randomised controlled study, in comparison to control group composed of 95 patients treated according to standard protocols.

**Results:** The shared decision making aid was developed to offer information about the disease, the risks and benefits of treatment. 97.5% of the children included reported comprehensibility of >90/100. the progressometer helped the children identify the importance of taking treatment for their disease. The patients' adherence to anti-rheumatic therapy was significantly ( $p<0.01$ ) higher in the SDM group, whereas stopping DMARDs for intolerance was significantly ( $p<0.01$ ) higher in the control group at 12 months of treatment. There was significant improvement in the functional ability as well as quality of life measures in the SDM group ( $p<0.01$ ), whilst absence from school was significantly higher in the control group ( $p<0.01$ )

**Conclusions:** This Illustrated-interactive SDM aid for children living with idiopathic inflammatory arthritis was found to be a simple, user-friendly tool which can be implemented in standard clinical practice. The illustration and interactive style made it more attractive to the children. The developed SDM offered the children evidence-based information about the pros and cons of treatment options, improved their understanding of the disease, communication with their treating clinician as well as their ability to make an informed decision.

**Disclosure of Interest:** None declared

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FRIDAY, 15 JUNE 2018

#### High-end imaging: Looking for the invisible\_\_\_\_\_

OP0348

#### MASS SPECTROMETRY IMAGING ANALYSIS OF SYNOVIUM DIFFERENTIATE PATIENTS WITH PSORIATIC AND RHEUMATOID ARTHRITIS

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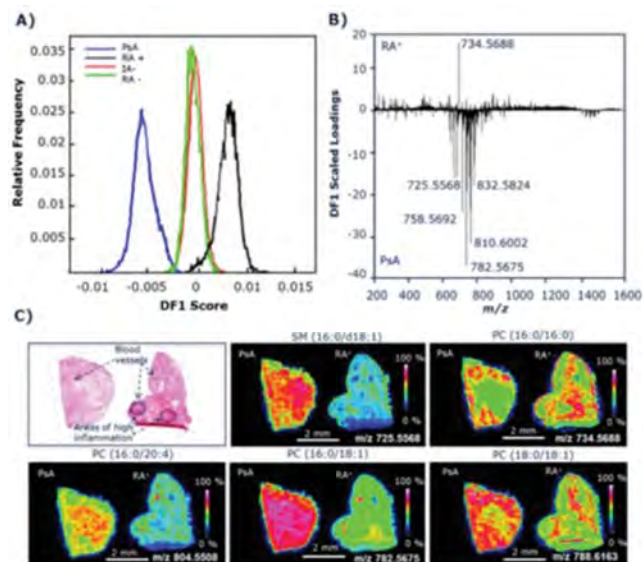
**Background:** Rheumatoid arthritis (RA) and Psoriatic arthritis (PsA) are systemic inflammatory diseases characterised by a chronic form of arthritis, often leading to

irreversible joint damage. Both are highly heterogeneous and complex disorders, presenting major challenges in diagnosis and treatment. The signs and symptoms of RA and PsA are similar especially at the earlier phases of the disease, so it can be difficult to distinguish them on clinical grounds. Lipids and metabolites have been associated with pathological events in both diseases as contributors of the inflammation process. Accordingly, the local lipidome and metabolome from the inflamed tissue may be more reliable in predicting the disease status than the current diagnostic methods, since the synovium is one of the main target tissues of both pathologies.

**Objectives:** To identify lipid and metabolic profiles in the synovium using Mass Spectrometry Imaging (MSI) that would have the potential to distinguish between patients with RA and PsA.

**Methods:** Synovium biopsies from 25 patients with PsA, 21 with RA (16 seropositive and 5 seronegative) and 10 with IA (Indeterminate arthritis) were included. Tissue sections were deposited on conductive slides and coated with different matrices for lipid and metabolite extraction. MALDI images were acquired on a rapifleX MALDI TissueTyper time-of-flight instrument. Multivariate data analysis was used to look for the lipids and metabolites with the highest differences among groups.

**Results:** MALDI-MSI revealed differential lipid and metabolic profiles among all compared groups. Discriminant analysis (DA) performed on lipid data acquired in positive ion mode displayed a good separation of patients with PsA and RA, especially seropositive RA (figure 1A). PsA showed higher lipid content, mainly phospholipids and sphingolipids, compared to seropositive RA (figure 1B and 1C). Some of them showed a specific localization within tissue. Experiments performed in negative ion mode showed that phosphatidylinositols and phosphatidic acids content varied among groups. Accordingly, DA allowed the separation of PsA from RA and IA patients, mainly from seronegative RA. PsA and RA groups were also distinguished based on synovium metabolic signatures. Sugars including *N*-acetylhexosamine 6-sulfate (*m/z* 282.0276), glucuronic acid 1-phosphate (*m/z* 273.0026) and *N*-acetylneuraminic acid (*m/z* 290.0876) displayed a stronger intensity in RA synovium when compared to PsA.



**Abstract OP0348 – Figure 1.** A) Histogram distribution and B) Discriminant function 1 (DF1) loading plot. DF1 negative scores are specific to PsA synovial tissue and positive scores to seropositive RA. C) Spatial mapping positive-lipid ions in synovium sections. Scale bar shows normalised intensities. **Conclusions:** For the first time, PsA and RA synovial membranes have been classified by MALDI-MSI. PsA synovium was characterised by a higher content of phospholipids compared to seronegative and seropositive RA. However, sugar metabolites displayed a stronger intensity in RA synovium when compared to PsA. Metabolic and lipid signatures here reported could support clinical decision-making in the diagnosis of RA and PsA.

**Disclosure of Interest:** None declared

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SATURDAY, 16 JUNE 2018

## RA: is it all in your head?

OP0349

### REMAINING PAIN AND WIDESPREAD PAIN DISTRIBUTION DURING THE FIRST 12 MONTHS AFTER RA DIAGNOSIS

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**Background:** The incidence of fibromyalgia (FM), a chronic widespread pain syndrome, is highest in the first year after RA diagnosis.<sup>1</sup> These 12 months may represent a critical window during which acute inflammatory pain transitions to chronic non-inflammatory pain. To prevent this transition, more data are needed about the course and predictors of pain during this time.

**Objectives:** 1) To describe the evolution of pain during the 12 months after RA diagnosis, and 2) to identify predictors of remaining pain and widespread pain (previously described as ‘fibromyalgic RA’)<sup>2</sup> at 12 months.

**Methods:** Data were obtained from early RA patients in the Canadian Early Arthritis Cohort (CATCH), a prospective inception cohort. Primary outcomes were: 1) remaining pain above the Patient Acceptable Symptom State (PASS), defined as 4/10 on a pain intensity numerical rating scale,<sup>3</sup> and 2) widespread pain, defined by tender joint count (TJC28) – swollen joint count (SJC28) ≥ 7.<sup>2</sup> Descriptive statistics were used to summarise the frequency of remaining pain and widespread pain over 12 months. Logistic regression models were used to identify predictors of remaining pain and widespread pain at 12 months. Variables forced into the multivariable models included age, sex, SJC28, ESR, depression, back pain, OA, sleep problems, HAQ-disability index (DI), MTX use, non-MTX conventional synthetic DMARD (csDMARD) use and NSAID use. Additional variables considered for inclusion via a backward selection process were race, education, income, FM, number of comorbidities and steroid use. Both models were adjusted for their respective baseline values.

**Results:** 1270 patients were included, with mean (SD) age of 53.9 (14.5) years, symptom duration of 5.8 (3.0) months and baseline DAS28 of 5.0 (1.4). The percentage of patients with remaining pain decreased from 64% at baseline to 24% at 12 months. The percentage of patients with widespread pain decreased from 9% to 5%. The strongest predictors of 12 month remaining pain were sleep problems (highest quartile OR 2.2, 95% CI: 1.2 to 3.9), pain intensity >4/10 (OR 2.1, 95% CI: 1.3 to 3.4) and higher HAQ-DI score (OR 1.5, 95% CI: 1.1 to 2.0). The strongest predictors of 12 month widespread pain were higher HAQ-DI score (OR 1.8, 95% CI: 1.1 to 3.1) and higher number of comorbidities (OR 1.2, 95% CI: 1.0 to 1.5). Baseline non-MTX csDMARD use was associated with lower likelihood of widespread pain (OR 0.5, 95% CI: 0.3 to 0.8).

**Abstract OP0349 – Table 1** Multivariable logistic regression models for the association between baseline characteristics and a) remaining pain (pain NRS>4), and b) widespread pain distribution (TJC28-SJC28≥7)

Baseline characteristics	Remaining Pain <sup>1</sup> OR (95% CI)	Widespread pain <sup>2</sup> OR (95% CI)
Age (for change of 10 yrs)	0.8 (0.7, 1.0)	0.7 (0.6, 0.9)
Baseline pain intensity > 4/10	2.1 (1.3, 3.4)	2.1 (0.8, 5.4)
Sleep problems, quartiles		
≥0 and <2	REF	REF
>2 and ≤5	1.8 (1.1, 3.1)	0.7 (0.3, 1.9)
>5 and ≤8	1.8 (1.1, 3.0)	0.9 (0.4, 2.2)
>8 and ≤10	2.2 (1.2, 3.9)	1.0 (0.3, 2.7)
Missing	0.6 (0.1, 5.6)	2.2 (0.2, 24.3)
HAQ-DI	1.5 (1.1, 2.0)	1.8 (1.1, 3.1)
Number of comorbidities	1.1 (1.0, 1.3)	1.2 (1.0, 1.5)
Non-MTX csDMARD use	0.8 (0.6, 1.1)	0.5 (0.3, 0.8)

<sup>1</sup>Adjusted for sex, education, income, SJC28, ESR, depression, back pain, osteoarthritis, MTX use, NSAID use  
<sup>2</sup>Adjusted for sex, SJC28, ESR, depression, back pain, osteoarthritis, MTX use, NSAID use, baseline pain distribution

**Conclusions:** Despite improvements in pain during the first year after RA diagnosis, 24% continued to report remaining pain above the PASS, and 5% reported widespread pain at 12 months. Patients at greatest risk for 12 month remaining pain were those with sleep problems, severe pain and disability at baseline. Patients at greatest risk for widespread pain were those with high baseline disability and many comorbidities. Baseline inflammation was not associated with 12 month pain outcomes.

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OP0350

**DEPRESSION AND ANXIETY IN AN EARLY RHEUMATOID ARTHRITIS INCEPTION COHORT. ASSOCIATIONS WITH EPIDEMIOLOGICAL, SOCIOECONOMIC AND DISEASE FEATURES**

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**Background:** Co-morbid depression and anxiety occur in the context of rheumatoid arthritis (RA). Their characteristics, including associations with RA features, have not been examined previously in an early RA inception cohort with longitudinal follow up data.

**Objectives:** To examine the frequency of anxiety and depression in patients with early RA, over time and to explore associations with epidemiological, socioeconomic and disease-related features.

**Methods:** The Scottish Early Rheumatoid Arthritis (SERA) inception cohort recruited newly diagnosed RA patients (fulfilling ACR-EULAR 2010 criteria) followed-up thereafter every 6 months. Pre-specified clinical, laboratory and psychosocial features, including anxiety and depression scores (measured by the hospital anxiety and depression scale; score range: 0–21 for each one), were recorded at baseline and at follow-up. Non-parametric tests and logistic regression models were used to examine the nature and magnitude of associations.

**Results:** Data from 848 RA patients were available. Frequency of anxiety and depression at baseline was 19.0% and 12.2% with a reduction at month 12% to 13.4% and 8.2% ( $p=0.004$  and  $p=0.01$ , respectively). Anxiety and depression scores were correlated with DAS28 at all time points, including baseline (all  $p<0.0001$ ). Change in DAS28 (final-baseline) was correlated with change in depression and anxiety scores at month 6 ( $p<0.0001$ ,  $r=0.265$  and  $p=0.001$ ,  $r=0.230$ ) and 12 ( $p<0.0001$ ,  $r=0.288$  and  $p<0.0001$ ,  $r=0.217$ ). In univariate analyses, anxiety and depression scores were associated with various features, at different time points (table 1). CRP was highly associated with depression but not anxiety scores at all time points, with change in CRP correlating with change in depression scores (month6;  $p<0.0001$ ,  $r=0.185$  and month12;  $p<0.0001$ ,  $r=0.302$ ). Multivariable analysis indicated that anxiety score at baseline was associated with female gender ( $p=0.01$ ,  $\text{Beta}=0.133$ ), younger age ( $p=0.007$ ,  $\text{Beta}=-0.181$ ) and patient global assessment score (PGA) ( $p<0.0001$ ,  $\text{Beta}=0.201$ ), and at month 6 and 12 with low BMI (month 6,  $p=0.024$ ,  $\text{Beta}=-0.091$ ; month 12,  $p=0.002$ ,  $\text{Beta}=-0.139$ ), PGA (month 6,  $p<0.0001$ ,  $\text{Beta}=0.222$ ; month 12,  $p<0.0001$ ,  $\text{Beta}=0.248$ ) and baseline anxiety scores (month 6,  $p<0.0001$ ,  $\text{Beta}=0.623$ ; month 12,  $p<0.0001$ ,  $\text{Beta}=0.586$ ). For depression scores, multivariable analysis indicated association at baseline with PGA ( $p<0.0001$ ,  $\text{Beta}=0.286$ ) and at month 6 and 12 with PGA (month 6,  $p<0.0001$ ,  $\text{Beta}=0.306$ ; month 12,  $p<0.0001$ ,  $\text{Beta}=0.320$ ), CRP levels (month 6,  $p=0.006$ ,  $\text{Beta}=0.150$ ; month 12,  $p=0.002$ ,  $\text{Beta}=0.171$ ) and baseline depression (month 6,  $p<0.0001$ ,  $\text{Beta}=0.422$ ; month 12,  $p<0.0001$ ,  $\text{Beta}=0.356$ ) and anxiety scores (month 6,  $p<0.0001$ ,  $\text{Beta}=0.189$ ; month 12,  $p=0.008$ ,  $\text{Beta}=0.170$ ).

**Abstract OP0350 – Table 1** Variables associating with high anxiety and/or depression score at baseline and at month 6 and 12. 1) ANOVA test, compared to employed and to retired individuals, 2) patient global VAS used for DAS28 calculation. 3) average alcohol units/week. NA: not applicable, BMI: body mass index, IM: intramuscular. \*by mouth, \*intramuscular

Anxiety score						
Factors/confounders	Baseline		6 months		12 months	
	p value	r	p value	r	P value	r
Age	<0.001	-0.187	<0.001	-0.158	0.001	-0.131
BMI					0.944	-0.084
Female gender	0.002	NA				
Smoking			0.008	NA	0.039	NA
Unemployment <sup>1</sup>	0.001	NA	<0.001	NA	<0.001	NA
Anxiety baseline			<0.001	0.691	<0.001	0.632
Depression baseline			<0.001	0.507	<0.001	0.443
DAS28 baseline			<0.001	0.175	0.020	0.114
Patient global VAS <sup>2</sup>	<0.001	0.210	<0.001	0.397	<0.001	0.387
Depression score						
Factors/confounders	Baseline		6 months		12 months	
	p value	r	p value	r	P value	r
Age	0.004	-0.101				
BMI	0.037	0.075				
Alcohol units <sup>3</sup>	0.002	-0.107				
Smoking			0.021	NA	0.002	NA
Unemployment	0.001	NA	<0.0001	NA	<0.0001	NA
Anti-CCP negative	0.013	NA				
Corticosteroids			0.017*	NA	0.005*	NA
Anxiety baseline			<0.001	0.488	<0.001	0.423
Depression baseline			<0.001	0.602	<0.001	0.519
DAS28 baseline			<0.001	0.223	<0.0001	0.172
Patient global VAS	<0.0001	0.328	<0.001	0.500	<0.001	0.522
ESR	0.016	0.116			0.029	0.130
CRP	<0.0001	0.163	<0.0001	0.152	0.004	0.112

**Conclusions:** Depression and anxiety are significant comorbidities at the time of RA diagnosis. While there are also associations with socioeconomic and other

variables, the close relationship between CRP and depression provides further support to the already compelling data linking inflammation and depression. Changes in the anxiety and depression scores, in tandem with disease activity over time, requires further investigation.

**Disclosure of Interest:** None declared

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SATURDAY, 16 JUNE 2018

**Battling hyperinflammation in paediatric rheumatic diseases**

OP0351

**FIRST DIAGNOSIS OF UVEITIS IS NOT HIGHER AMONG JUVENILE IDIOPATHIC ARTHRITIS (JIA) PATIENTS RECEIVING ETANERCEPT COMPARED TO METHOTREXATE**

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**Background:** Uveitis is a common comorbidity among patients with juvenile idiopathic arthritis (JIA), occurring in approximately 1 in 10 JIA patients. Among other risk factors such as early age at JIA onset, shorter disease duration and oligoarticular subtype, the use of etanercept (ETN) may also increase the risk of developing uveitis. However, previous studies have produced conflicting results, often limited by small sample sizes and limited follow-up time.

**Objectives:** To determine if patients receiving ETN have a higher risk of developing uveitis for the first time compared to patients receiving methotrexate (MTX).

**Methods:** The study population comprised JIA subjects recruited to the BSPAR ETN Cohort Study at point of starting ETN or MTX. Only patients with no prior history of uveitis were included. This was an on-drug analysis, whereby events were only included if the patient was on ETN or MTX at the time of uveitis onset. Follow-up began from date of first treatment to first uveitis diagnosis, discontinuation of ETN or MTX, most recent follow-up up to 30/11/16 or death, whichever came first. Crude incidence rates of uveitis per 100 person years (pyears) were calculated. Hazard ratios (HR) comparing risk of uveitis with ETN versus MTX were calculated using propensity adjusted Cox regression.

**Results:** Of 1517 patients, 1009 were registered to the ETN cohort (all receiving ETN) and 508 to the MTX cohort. ETN patients were older, with longer disease duration, and were less likely to have persistent oligoarthritis. The mean age at uveitis diagnosis was 8 years in the ETN cohort versus 5 years in the MTX cohort. The HR adjusted for age and gender, disease scores, disease duration, baseline steroid use, co-morbidity, ILAR subtype, and ethnicity found a lower risk of developing uveitis in patients receiving ETN compared to MTX (0.30, 95% CI (0.10–0.90)) (table 1).

**Abstract OP0351 – Table 1**

	Patients taking MTX	Patients taking EN
Subjects (n)	508	1009
Age, median (IQR)	9 (3–13)	11 (8–14)
Gender, % female	71	69
Disease duration (years), median (IQR)	1 (0–1)	3 (1–6)
CHAQ score, median (IQR)	0.9 (0.3–1.5)	1.0 (0.3–1.6)
ILAR subtype, n (%)		
Persistent oligoarthritis	84 (17)	53 (5)
Other non-systemic JIA	424 (83)	955 (95)
Person years exposure	908	2471
New diagnosis of uveitis	18	15
Crude incidence rates per 100 pyears	2.4 (1.4–3.9)	0.6 (0.3–1.0)
Unadjusted HR (95% CI)	ref	0.24 (0.11–0.52)*
Age & Gender adjusted HR (95% CI)	ref	0.41 (0.18–0.95)*
Fully adjusted HR (95% CI)	ref	0.30 (0.10–0.90)*

\* $p<0.05$

**Conclusions:** Within this cohort of UK children with JIA, a new diagnosis of uveitis is not more common among children receiving ETN compared to MTX, even after taking into account differences in age and disease duration between the cohorts. This is reassuring given there is a possible increased risk of uveitis among children with JIA receiving ETN. Age appears to be a major influencing factor as patients in the MTX cohort were younger thus at a higher risk of uveitis. For patients with a high uveitis risk other treatment options could have been



selected, leading to possible confounding by indication, which in turn makes ETN look protective. Researchers should take these selection biases into account when analysing their results.

**Disclosure of Interest:** None declared

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## Gut bacteria: the boss of the immune system

OP0352

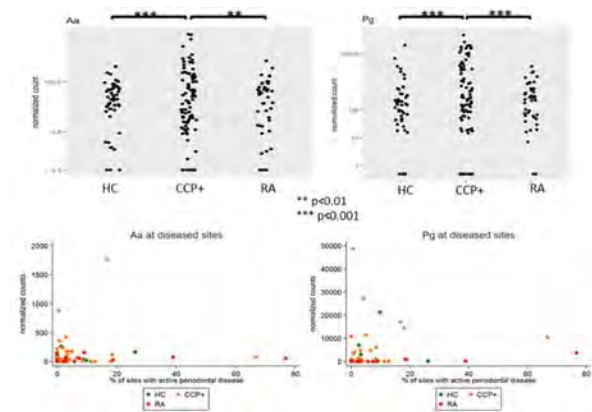
### AN INCREASED PREVALENCE OF PERIODONTAL DISEASE, PORPHYROMONAS GINGIVALIS AND AGGREGATIBACTER ACTINOMYCETEMCOMITANS IN ANTI-CCP POSITIVE INDIVIDUALS AT-RISK OF INFLAMMATORY ARTHRITIS

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**Background:** The prevalence of periodontal disease is increased in RA, and periodontitis is associated with the bacterium *Porphyromonas gingivalis* (Pg), which can citrullinate arginine residues.<sup>1</sup> These observations suggest periodontitis may be a key initiator of RA-related autoimmunity. Importantly, clinical periodontal disease, and the relative abundance of periodontal bacteria have not been described in seropositive individuals at risk of developing RA who do not have synovitis.

**Objectives:** To investigate the prevalence of periodontal disease and the relative abundance of key periodontal bacteria in anti-CCP positive at-risk individuals without synovitis.

**Methods:** Anti-CCP positive individuals with musculoskeletal symptoms but no clinical synovitis (CCP+), early RA (RA) patients and healthy controls (HC) were recruited. CCP +underwent a 38 joint ultrasound (US) assessment. Periodontal examination was performed by a dentist; six sites per tooth were assessed for clinical attachment level (CAL), pocket depth (PD) and bleeding on probing (BOP). Periodontal disease sites (PDD) were defined as CAL $\geq$ 2 mm and PD  $\geq$ 4 mm. A clinical consensus was agreed for each case by three dentists. DNA, isolated from subgingival plaque from diseased and healthy periodontal sites, was paired-end sequenced (Illumina HiSeq3000). Taxonomic and functional profiles were obtained from MG-Rast and differences between groups studied using DESeq2. Mann-Whitney U tests were used to compare groups and Spearman Rho used for correlations. For metagenomic data, Wald test was used to compare relative abundance.



**Abstract OP0352** – Figure 1 Relative abundance of *Aggregatibacter actinomycetemcomitans* (Aa) and *Porphyromonas gingivalis* (Pg) according to RA status and extent of periodontal disease

**Results:** 48 CCP+, 26 RA and 32 HC were recruited. Groups were balanced for age, sex and smoking. All but 2 (96%) CCP +had no US synovitis (greyscale  $\geq$ 1 and power Doppler $\geq$ 1). Dentists classified 73% CCP+, 38% HC (p=0.02) and 54% RA as having clinical periodontitis. The percentage of periodontal sites with CAL  $\geq$  2 mm, PD  $\geq$  4 mm, BOP, PDD and active PDD (PDD +BOP) were all greater in CCP +compared to HC (p<0.05) and similar to RA. In non-smokers, PDD and active PDD were more prevalent in CCP +compared to HC. Metagenomic data indicated CCP +had increased relative abundance of both Pg

and *Aggregatibacter actinomycetemcomitans* (Aa) compared to HC (p<0.001) and RA (p<0.01). However, clinical periodontitis was only associated with increased relative abundance of Pg (p<0.001) but not Aa. Furthermore, the relative abundance of Pg was associated with the percentage of sites with active PDD in CCP+ (p=0.05) and HC (p=0.04) but this was not seen for Aa (figure 1).

**Conclusions:** We report an increased prevalence of periodontal disease, Pg and Aa in anti-CCP positive at-risk individuals without synovitis. Interestingly, relative abundance of Pg, but not Aa, was associated with periodontitis, suggesting potential mechanistic differences that require further exploration. These data support the concept that periodontal inflammation and periodontopathic bacteria may both be important in the initiation of RA-related autoimmunity.

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## Multi-disciplinary management of complex persistent pain

OP0353-HPR

### THE EFFECTS OF ARTHRITIS GLOVES ON HAND PAIN IN PEOPLE WITH RHEUMATOID OR INFLAMMATORY ARTHRITIS: A RANDOMISED CONTROLLED TRIAL (A-GLOVES TRIAL)

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**Background:** Arthritis (compression) gloves are commonly provided to people with rheumatoid arthritis (RA) and undifferentiated inflammatory arthritis (IA) in the UK health service. These apply pressure and warmth to relieve hand pain, stiffness and improve hand function. A systematic review identified little evidence to support their use.<sup>1</sup>

**Objectives:** This randomised controlled trial tested effectiveness and cost-effectiveness of mid-finger length compression (intervention) gloves (20% Lycra: commonest glove model provided) with control gloves (i.e. oedema gloves: 11% Lycra: fitted at least one size too big) in people with RA and IA.

**Methods:** Both gloves, which had similar thermal qualities although the control gloves did not provide compression, were provided by rheumatology occupational therapists, following training.<sup>2</sup> Participants were also given brief advice on hand exercise and joint protection. Adults with RA/IA and persistent hand pain were randomised 1:1 to the two glove types, stratified by disease modifying anti-rheumatic drug (DMARD) change in previous 12 weeks. The primary outcome was dominant hand pain on activity Visual Analogue Scale (VAS:0–10); other outcomes included night hand pain, hand stiffness (both 0–10 VAS); Measure of Activity Performance Hand (MAP-HAND: 0–3). Multiple linear regression was undertaken to estimate the effect of group allocation on hand pain during activity, adjusting for the stratification variable and baseline values. Cost-effectiveness used individual patient level costs (intervention plus healthcare utilisation) and health benefit data (EQ-5D) to calculate costs and QALYs.

**Results:** 206 participants were randomised (103 to each glove type): median age 59 years [IQR 51,67]; women:166 (81%); mean disease duration: 8.2 (SD 9.5) years; employed:76 (37%); right hand dominant:185 (90%). Of these, 163 (79%) completed 12 week follow-up questionnaires. Both groups reported similar adherence to glove wear (mean 5.2 days/week). At 12 w, hand pain scores in both groups similarly improved: the between-groups mean difference of 0.1 was not statistically significant (95% CI: -0.47 to 0.67;p=0.72). There were no significant differences between groups on any measures, with both groups improving similarly between baseline and 12 w. 73% in both groups considered gloves beneficial. Intervention gloves had higher costs (£552 (SD £464); control £391 (SD £543) but comparable benefits to control gloves. Intervention gloves would cost £83 700 to gain one QALY and were not likely to be cost-effective.

**Conclusions:** Compression (intervention) and loose-fitting arthritis (control) gloves had similar effects on hand pain, stiffness and function. Therefore, compression is not the 'active ingredient' in arthritis gloves. Loose fitting gloves providing warmth were perceived as equally effective by participants. We do not know if the therapist effect is important or whether ordinary gloves providing warmth would provide similar results.

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[1] Hammond, et al. Clin Rehabil 2016 30:213–24.

[2] Prior, et al. Rheumatology 2017. www.abstractsonline.com/pp8/#!/4205

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**Osteoarthritis: a vascular disease**

**OP0354 RADIOGRAPHIC EROSIONS ARE ASSOCIATED WITH FLUORESCENCE OPTICAL IMAGING ENHANCEMENT IN HAND OSTEOARTHRITIS**

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**Background:** Erosive hand osteoarthritis (OA) is a phenotype characterised by more inflammation and erosions of the subchondral bone. Fluorescence optical imaging (FOI) is a novel imaging technique demonstrating altered microcirculation in wrist and finger joints as a sign of inflammation. No previous hand OA study has explored the validity of FOI against radiography.

**Objectives:** The aim of the current study was to explore the association between radiographic findings and FOI enhancement in the distal (DIP) and proximal interphalangeal (PIP) joints.

**Methods:** The NOR-HAND study is an observational hand OA study, in which 251 patients (88% female, median age 61 (interquartile range 56–66) years, 35% erosive hand OA) underwent FOI and x-rays of both hands. The FOI-scan was performed after the administration of an intravenous fluorescence dye (indocyanine green, ICG) and 360 images (1/second) were produced in 6 min. Based on the inflow and washing out of the dye the pictures were divided into 3 phases. Finally, the prima vista mode (PVM) represented a composite picture of the first 240 images of the examination. For each phase, fluorescence enhancement in the joints was graded from 0–3 based on signal intensity. Radiographic severity of the joints was evaluated with the Verbruggen Veys (VV) anatomical phase scoring system, which is based on the assumption that OA in finger joints will progress through different phases. To study whether more advanced radiographic phases were associated with FOI enhancement in the same joint, we applied logistic regression analyses with generalised estimating equations adjusting for age, sex, BMI and absence/presence of erosive hand OA, defined at patient level as having at least one DIP and PIP joint(s) in the erosive or remodelled phase.

**Results:** FOI demonstrated no and uncommon enhancement of the metacarpophalangeal and thumb base joints, respectively, thus we analysed DIP and PIP joints only. FOI enhancement was most commonly seen in phase 2 and PVM, also in the non-affected joints (table 1). The frequency of enhancement was lower for phase 3 and in particular for phase 1. Joints in the erosive phase had statistically significantly higher odds of FOI enhancement in phase 1, 2 and PVM as compared to the non-affected joints (table 1). Having erosive hand OA in other DIP and PIP joints was also associated with FOI enhancement (p<0.05 in all phases except in phase 1), and our stratified analyses confirmed that FOI enhancement in the non-erosive phases was more common in the erosive vs the non-erosive hand OA patients.

**Abstract OP0354 – Table 1 Odds of FOI enhancement in joints with increasing radiographic severity according to the verbruggen veys anatomical phase scoring system**

Odds of FOI Enhancement in Joints with Increasing Radiographic Severity According to the Verbruggen Vey's Anatomical Phase Scoring System.												
	FOI phase 1, Grade 1-3			FOI phase 2, Grade 1-3			FOI phase 3, Grade 1-3			FOI PVM, Grade 1-3		
	N (%)	OR	95% CI	N (%)	OR	95% CI	N (%)	OR	95% CI	N (%)	OR	95% CI
<b>All Hand OA Patients</b>												
N phase*	15/1618 (1)			1125/3582 (7)			333/1575 (2)			978/1632 (6)		
1 phase*	26/2269 (1)	1.36	0.58-3.33	1587/2212 (7)	0.80	0.64-1.00	334/2202 (2)	0.62	0.51-0.76	1111/2298 (5)	0.71	0.62-0.87
2 phase*	3/213 (1)	1.71	0.53-5.88	158/205 (7)	1.05	0.7-1.59	40/205 (2)	0.41	0.28-0.61	128/212 (6)	0.79	0.57-1.10
3 phase*				150/160 (9)	1.87	1.18-3.08	70/160 (4)	0.85	0.58-1.29	136/172 (8)	1.62	1.02-2.56
P phase*	12/294 (4)	4.52	1.52-10.65	96/116 (8)	1.93	0.65-5.72	85/116 (3)	0.50	0.33-0.76	74/124 (6)	0.66	0.42-1.05
<b>Erosive Hand OA</b>												
N phase*	2/191 (1)			154/198 (8)			20/188 (3)			184/196 (7)		
1 phase*	15/858 (2)	2.63	0.62-11.2	613/818 (7)	0.79	0.50-1.27	247/818 (3)	0.68	0.46-1.02	529/849 (6)	0.76	0.51-1.13
2 phase*	2/158 (1)	2.68	0.34-20.9	123/154 (8)	1.11	0.62-1.98	38/154 (2)	0.51	0.33-0.83	102/138 (6)	0.88	0.54-1.44
3 phase*				150/169 (9)	1.91	1.04-3.52	70/169 (4)	0.94	0.60-1.51	136/172 (8)	1.70	0.98-2.95
P phase*	12/294 (4)	7.91	1.37-47.4	96/116 (8)	1.93	0.62-5.94	85/116 (3)	0.57	0.36-0.90	74/124 (6)	0.70	0.40-1.20
<b>Non-erosive Hand OA</b>												
N phase*	13/1427 (1)			971/1384 (7)			263/1387 (3)			840/1436 (6)		
1 phase*	13/1431 (1)	0.85	0.36-2.01	969/1384 (7)	0.79	0.61-1.01	282/1384 (2)	0.60	0.47-0.76	782/1439 (5)	0.72	0.56-0.87
2 phase*	1/53 (2)	2.95	0.66-13.3	16/52 (6)	0.88	0.44-1.76	2/51 (4)	0.14	0.04-0.54	26/54 (8)	0.62	0.36-1.04

**Conclusions:** Joints in the erosive phase have more frequent FOI enhancement than non-affected joints. Furthermore, FOI enhancement in non-erosive phases is more common in patients with erosive vs non-erosive hand OA, suggesting that erosive hand OA is a more inflammatory phenotype. FOI enhancement in phase 2, 3 and PVM was common in joints without radiographic pathology, whereas enhancement in phase 1 was uncommon in joints with severe pathology. Thus,

there is a need to consider other FOI scoring methods for the assessment of FOI enhancement in hand OA.

**Disclosure of Interest:** None declared

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**Emerging topics in the management of the antiphospholipid syndrome**

**OP0355 PULMONARY THROMBOECTOMY IS A CURATIVE RESOLUTION FOR CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION ASSOCIATED WITH PRIMARY ANTIPHOSPHOLIPID SYNDROME: A RETROSPECTIVE COHORT STUDY**

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**Background:** Chronic thromboembolic pulmonary hypertension (CTEPH) is a rare and life-threatening condition with a poor prognosis in antiphospholipid syndrome (APS) patients. A specialised and multidisciplinary evaluation are needed for APS associated CTEPH. As a curative option for CTEPH, pulmonary thromboendarterectomy (PTE) requires careful risk and benefit assessment in APS patients.

**Objectives:** This retrospective cohort study aimed to investigate the clinical manifestations and prognosis of CTEPH in APS patients with or without PTE.

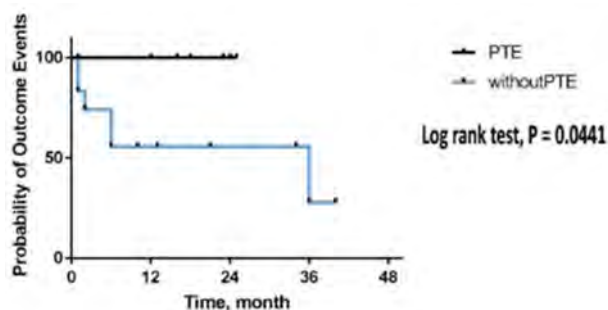
**Methods:** Consecutive patients with APS associated CTEPH diagnosed between January 2012 to September 2017 at Peking Union Medical College Hospital were retrospectively evaluated. Patients were divided into two groups by whether underwent PTE or not. Demographics, clinical manifestations, antiphospholipid antibodies profiles, target medications, treatment were collected as possible influencing factors. Chi-square test was used to analyse the short-term prognosis while Kaplan Meier curve and log rank test were used to analyse long-term prognosis (outcome events: deterioration of cardiac function or death).

**Abstract OP0355 – Table 1 Baseline demographic and clinical characteristics of 20 APS associated CTEPH patients**

Variables	Total (n=20)	With PTE (n=8)	Without PTE (n=12)	P-value
<b>Female, n(%)</b>	13 (65.0)	4 (50.0)	9 (75.0)	0.27
<b>Median age, yrs</b>	29 <sup>(19-51)</sup>	28 <sup>(22-32)</sup>	34 <sup>(19-51)</sup>	0.09
<b>APS median duration, months</b>	36 <sup>(1-252)</sup>	48 <sup>(1-76)</sup>	32 <sup>(1-152)</sup>	0.49
<b>APL profiles</b>	14 (70.0)	6 (75)	8 (66.7)	1.00
ACL, n(%)	17 (85.0)	7 (87.5)	10 (83.3)	1.00
Anti-β2GP1, n(%)	16 (80.0)	8 (100)	8 (66.7)	0.12
LA, n(%)				
<b>Diagnosis</b>	8 (40.0)	6 (75.0)	2 (16.7)	0.02
Primary APS, n(%)	12 (60.0)	2 (25.0)	10 (83.3)	
SLE-APS, n(%)				
<b>CTEPH Median duration, n(months)</b>	18 <sup>(1-144)</sup>	48 <sup>(1-76)</sup>	7 (1-144)	0.89
<b>Manifestations</b>	5 (25)	2 (25.0)	4 (33.3)	1.00
Chest pain, n(%)	20(100)	8 (100.0)	12(100)	-
DOE, n(%)	4 (20)	0	4 (33.3)	0.12
Cough, n(%)	7 (35)	2 (25.0)	5 (41.7)	0.64
Hemoptysis, n(%)				
<b>Other Thrombotic Events, n(%)</b>	17(85)	7 (87.5)	10 (83.3)	1.00
<b>Target therapies</b>	10 <sup>(50)</sup>	5 (62.5)	5 (41.7)	0.65
PDESi	4 (20)	2 (25.0)	2 (16.7)	1.00
Baselent				
<b>Baseline WHO FC</b>	7 (35.0)	3 (37.5)	4 (33.3)	0.33
II, n(%)	11 (55.0)	5 (62.5)	6 (50.0)	
III, n(%)	2 (10.0)	0	2 (16.7)	
IV, n(%)				
<b>Posttreatment WHO FC</b>	10 (50.0)	7 (87.5)	3 (25.0)	0.01
I, n(%)	7 (35.0)	1 (12.5)	6 (50.0)	
II, n(%)	3 (15.0)	0	3 (25.0)	
III, n(%)				

**Results:** A total of the 20 APS associated CTEPH patients were enrolled, 8 underwent PTE and 12 without PTE. Common CTEPH developed by these patients included chest pain, dyspnea on exertion, cough and hemoptysis. Chi-square test (p=0.01) and Kaplan Meier curves (Log rank test, p=0.04) showed that there was statistically significant difference in both short-term and long-term prognosis among patients with PTE and without PTE. On the other hand, Cox regression analysis showed diagnosis (PAPS or SLE-APS), aPL (antiphospholipid antibody) profiles, thrombocytopenia, other Thrombotic Events, target therapies,

baseline WHO FC have no effects on the prognosis of CTEPH in patients with APS.



**Abstract OP0355** – Figure 1 Kaplan-Meier survival curves of APS patients associated CTEPH after treatment (anticoagulation and/or PTE).

**Conclusions:** After a full specialised and multidisciplinary risk-benefit evaluation to limit the risk of thrombosis or bleeding and to manage possible thrombocytopenia, for those CTEPH developed in APS patients, PTE is a curative resolution.

**Disclosure of Interest:** None declared

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**OP0356** **PLASMA BLAST PROLIFERATION IS ASSOCIATED WITH TOLL LIKE RECEPTOR 7 POLYMORPHISMS AND UPREGULATION OF TYPE I INTERFERON, CONTRIBUTING TO THE ANTIBODY PRODUCTION IN ANTIPHOSPHOLIPID SYNDROME**

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**Background:** Antiphospholipid antibodies (aPL) as pathogenic autoantibodies in systemic lupus erythematosus (SLE) and antiphospholipid syndrome (APS) are supported by a number of clinical, *ex vivo* and animal studies. Nevertheless, aPL are not eliminated by corticosteroid administration or immunosuppression. Novel therapy targeting aPL production is currently unmet needs, in contrast, little is known on its pathological mechanism.

**Objectives:** This study aimed to clarify the mechanism of aPL production by lymphocyte subset analysis, genomic analysis and *ex vivo* experiments.

**Methods:** B cell and T cell subsets, a total of 21 subsets, were evaluated in peripheral blood mononuclear cells (PBMC) of 26 primary APS (PAPS), 18 SLE-associated APS (SLE/APS) patients and 10 healthy controls by flow cytometry. Twenty-one single nucleotide polymorphisms (SNP), which were shown to be associated with autoimmune or thrombotic diseases, were analysed in genomic DNA of those patients by TaqMan genotyping assay. Interferon (IFN) score was calculated based on the mRNA expression of Ly6e, Mx1, IFIT1 and IFIT3 in PBMC. To evaluate the aPL-producing capability of plasmablasts, PBMC obtained from APS patients were cultured following depletion of CD19 +CD20+ or CD19+CD20 cells and the culture supernatants were applied to aPL measurements by enzyme-linked immunosorbent assay and cell assay using  $\beta$ 2GPI/HLA-DR7 overexpressing HEK293T cells.<sup>1</sup>

**Results:** In PAPS and SLE/APS patients, plasmablasts, Th2 cells and Th17 cells were increased while pre- and post- switched memory B cells, regulatory B cells and regulatory T cells were decreased compared to healthy controls. Genomic analysis revealed that the increase of plasmablasts ( $p=0.032$ ) and the decrease of memory B cells ( $p=0.013$ ) were more pronounced in patients with a risk allele of SNP in toll like receptor 7 (TLR7) gene (rs3853839). IFN score was significantly higher in the TLR7 SNP risk allele carriers, confirming the downstream signalling of TLR7 ( $p=0.029$ ). *Ex vivo* experiments showed that aPL, including anti-cardiolipin/ $\beta$ 2-glycoprotein I-HLA class II complexes -IgG and -IgM, were present in the culture supernatant of CD19 +CD20+depleted PBMC from APS patients, but not in that of CD19 +CD20 depleted cells.

**Conclusions:** Our data indicate an important role of plasmablasts in the production of aPL. Furthermore, plasmablast proliferation was associated with TLR 7 and type I IFN, suggesting a common pathophysiology in SLE and APS. Targeting plasmablasts might be a novel, immunological therapeutic approach in the treatment of APS.

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**Disclosure of Interest:** None declared  
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SATURDAY, 16 JUNE 2018

**The links between gout and kidney function**

**OP0357** **HYPERECHOIC DEPOSITS IN THE RENAL MEDULLA ARE ASSOCIATED WITH SEVERE GOUT AND DECREASED EGFR: A TRANSVERSAL STUDY IN 503 VIETNAMESE PATIENTS**

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**Background:** Renal medulla crystal deposits have been demonstrated by pathology in severe gout but little studied by ultrasound (US) scan.

**Objectives:** To assess the frequency of hyperechoic renal medulla (HERM) in gouty patients and factors associated with their development.

**Methods:** Renal US scan using a Ecube 9 echograph (Alpinion S. Korea), was performed in gout patients (ACR/EULAR criteria) consecutively seen at the Vien Gut general clinic, Ho Chi Minh City, Vietnam, and receiving no ULT at presentation. Age and sex of patients, gout features, associated diseases, serum (S) uric acid (UA), eGFR (MDRD), urinary lab stick parameters, urine UA/creatinine ratio, and fractional clearance of urate (FCU) were recorded. Patients with HERM were counted and compared with those who had no medullary deposits by the Wilcoxon rank sum test for continuous variables and the Fischer exact test for categorical variables. Multivariable logistic model was used to assess relation between variables at inclusion in the study and presence of medulla deposits.

**Results:** 503 consecutive patients (500 males) were included. They had a median age of 46 years, median BMI of 25 kg/m<sup>2</sup>, median gout duration of 4 years. 280 (56%) had clinical tophi, 154 (31%) urate arthropathy, 28; 56% urolithiasis, 112 (22%) hypertension, 58 (11.5%) type 2 diabetes, 5 (1%) coronary heart disease. Their median eGFR was 78 ml/min, SUA 423 micromol/L, FCU 0.063, urine UA/creatinine ratio 0.253, urinary pH 6.

Diffuse and bilateral HERM on the B mode with frequent twinkling artefacts on the Doppler mode was identified in 181 (36%) of the 503 patients. Univariate analysis showed that HERM associated with higher age, longer duration of gout, clinical tophi, urate arthropathy ( $p<0.0001$  for each of the variables), higher uricemia ( $p=0.001$ ), hypertension ( $p=0.0008$ ), CHD ( $p=0.0006$ ), lower eGFR ( $p<0.0001$ ), leucocyturia ( $p=0.02$ ), proteinuria ( $p=0.02$ ). No association with US-diagnosed urolithiasis, hematuria, urine UA/creatinine ratio, FCU and urinary pH was found. In multivariate analysis, log of the duration of gout (OR: 2.22 (CI: 1.63–3.08),  $p<0.001$ ), clinical tophi (OR: 8.21 (4.23–16.91)  $p<0.001$ ), urate arthropathy (OR: 3.74 (2.18–6.52,  $p<0.001$ ), and lower eGFR (OR: 0.86 (0.75–0.99) for each 10 ml/min decrease,  $p=0.04$ ) were significantly associated with HERM.

**Conclusions:** In our gout population, HERM was observed in 36% of patients, correlated with decreased renal function, and clearly associated with severe gout, but not with features of uric acid lithiasis.

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**OP0358** **WHY DO NOT ALL CHRONIC KIDNEY DISEASE PATIENTS GET GOUT? IMPAIRED NEUTROPHIL CHEMOTAXIS IN HYPERURICEMIA-RELATED CKD**

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**Background:** One characteristic feature of acute gout is the infiltration of neutrophils into the inflamed joints, where they recognise monosodium urate (MSU) crystals leading to an acute inflammatory response. The development of chronic kidney disease (CKD) is associated with increased serum uric acid (UA) levels also known as hyperuricemia, a major risk factor for gout. Despite hyperuricemia, acute gout is less frequent in CKD patients. However, the effects of hyperuricemia on leukocyte chemotaxis in CKD are not fully understood.



**Objectives:** We hypothesised that hyperuricemia affects neutrophil chemotaxis in CKD patients. Furthermore, we made use of a novel mouse model of chronic uric acid nephropathy.

**Methods: Human study:** Serum was collected and neutrophils isolated from CKD patients or healthy subjects. Serum BUN (blood urea nitrogen), creatinine and uric acid levels were measured. Neutrophil transwell assays were carried out and the number of migrated neutrophils towards fMLP, human IL-8 determined by flow cytometry. **Animal study:** Six week old Alb-creERT2;Glut9<sup>lox/lox</sup> mice (ki/ki) and mice without active Cre (+/+) were injected with tamoxifen. The ki/ki mice received either a high fat diet with Inosine (HFD+Ino) to induce hyperuricemia-associated CKD or a chow diet with Inosine (Chow+Ino) to induce only hyperuricemia without CKD. Control +/-mice either received HFD+Ino or Chow+Ino diet. After two weeks, all groups were injected either with MSU crystals or vehicle into a preexisting air pouch, a mouse model for acute gouty arthritis. After 12 hours, neutrophil infiltration and the extent of inflammation were assessed via flow cytometry, ELISA, and colorimetric assays.

**Results: Human study:** Compared to healthy subjects, CKD stage 5 patients presented with significant higher levels of serum BUN (14.1 vs 52.1 mg/dl,  $p=0.001$ ), creatinine (1.5 vs 9.3 mg/dl,  $p=0.001$ ) and UA (2.3 vs 10.3 mg/dl,  $p=0.001$ ). Neutrophils from CKD patients showed an impaired migratory ability due to the down-regulation of the adhesion molecules P-Selectin and  $\alpha\beta$ Integrin.

**Animal study:** Two weeks post-HFD +Ino, ki/ki mice developed hyperuricemia-associated CKD (serum UA: 10–14 mg/dl; BUN: 80 mg/dl), whereas the ki/ki mice on Chow+Ino diet became hyperuricemic without CKD. Control +/-mice on both diets did neither develop hyperuricemia nor CKD. Interestingly, the number of infiltrating neutrophils into the air pouch was reduced in hyperuricemic ki/ki mice with CKD as well as in hyperuricemic ki/ki mice without CKD compared to +/-control mice. We observed less inflammation indicated by decreased IL-1 $\beta$ , TNF $\alpha$ , CXCL1 and myeloperoxidase levels, and a down-regulation of adhesion molecules on infiltrated neutrophils in hyperuricemic ki/ki mice with CKD compared to +/-control mice.

**Conclusions:** Our data show that neutrophils from CKD patients are less able to migrate, which was consistent with data from our novel mouse model demonstrating that hyperuricemia impairs neutrophil chemotaxis in MSU crystal-induced inflammation. This indicated that the mechanism for defective neutrophil migration might be responsible for the lower incidence of acute gouty arthritis in hyperuricemic CKD patients.

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## Big data in pre-clinical research

OP0359

### EXPLORATION OF T-CELL SIGNATURES FOLLOWING TCR STIMULATION USING SINGLE CELL RNA-SEQ TO INFORM TREATMENT RESPONSE STUDIES IN RHEUMATOID ARTHRITIS

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**Background:** For rheumatoid arthritis (RA), as with many other rheumatic diseases, the importance of determining which therapy will work best, early in disease, to prevent further progression, is an important area of research. Progress in treatment response has been limited, possibly due to the complex interplay between various cell types. As such, specific T-cell signatures, determined by single cell RNA-Seq (scRNA-Seq), could be predictive of future response to treatments such as anti-TNF biologic therapies.

**Objectives:** Our aim was therefore to determine the optimal study design and to assess the potential of scRNA-Seq to identify T-cell signatures under resting and stimulated conditions to inform future studies.

**Methods:** Primary CD4 +T cells were either stimulated using anti-CD3/CD28 beads or subjected to the same conditions without stimulation for 4 hours. Single cells were isolated using the 10X Genomics Chromium Controller with a target recovery of 6000 cells. Each scRNA-Seq library was sequenced on 4 Illumina HiSeq 4000 lanes (~200K reads/cell) and processed using the cellranger pipeline. Further quality control and cluster analysis was performed using Seurat.

**Results:** For the unstimulated sample 5,586 cells were recovered and after quality control and filtering, 5,387 cells remained. Similarly, for the stimulated sample, 4,621 cells were recovered and 4,473 remained. This resulted in an average of 1094 and 1456 genes per cell. Similar clusters were seen after downsampling the stimulated dataset to 1 lane (~379M reads, ~82K reads/cell), suggesting that

CD4 +T cells are defined by large gene expression changes rather than subtle variations, consistent with protein expression data. Cluster exploration allowed the identification of several typical CD4 +T cell populations, including naïve, helper and regulatory. Furthermore, alignment of the two conditions in Seurat, identified classical and non-classical markers of activation, such as CD69, CCR7, MYC and PIM3. Finally, the relative cluster location and the expression of indicative markers suggested evidence of a progression from a naïve cell state to an 'active' effector state.

**Conclusions:** This data has provided important insights into future study design and confirmed the potential of scRNA-Seq to identify T-cell signatures. Importantly, despite obvious expression changes, cluster identity was maintained between stimulatory conditions. This implies it is possible to directly compare scRNA-Seq expression profiles between patient samples showing different disease activity without confounding the conclusions and enable the use of scRNA-Seq to investigate its predictive potential in RA treatment response. We are therefore in the process of expanding this work to study patient samples and different cell types. For example we have already generated similar data for monocytes on 3 RA samples and 3 healthy samples.

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OP0360

### RNA-SEQUENCING OF 800 HUMAN BLOOD SAMPLES REVEALS SHARED AND UNIQUE EXPRESSION PROFILES ACROSS SEVEN SYSTEMIC AUTOIMMUNE DISEASES

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**Background:** Systemic autoimmune diseases (SADs) are chronic inflammatory conditions with limited treatment options. Although SADs encompass different clinical diagnoses, many of them share common pathophysiological mechanisms and have similar clinical manifestations. Therefore, defining a precise diagnosis and consequently an appropriate treatment is complex.

**Objectives:** We aimed to identify characteristic expression profiles for patients diagnosed with different SADs and find specific biomarkers for each disease based on whole blood RNA-seq data.

**Methods:** As part of the ongoing IMI PreciseSADS project we generated and analysed globin-depleted, polyA-selected RNA-seq data from an initial subset of 800 peripheral blood samples of healthy controls and patients with seven different SADs: systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), systemic sclerosis (SSc), Sjögren's syndrome (SSj), mixed connective tissue disease (MCTD), undifferentiated connective tissue disease (UCTD) and primary antiphospholipid syndrome (PAPS). Differential gene expression analysis was performed with DESeq2 and biomarker discovery was achieved using linear support vector classifier-based feature elimination and logistic regression-based estimator with cross-validation.

**Results:** We identified unique and common genes that were differentially expressed between controls and each of the seven SADs. The greatest extent of transcriptional dysregulation was found in SLE and MCTD patients, while UCTD, SSc and RA showed fewest differentially expressed genes. We found large and statistically significant overlaps between the lists of differentially expressed genes for each disease, with SLE, MCTD, Sjs and UCTD showing most pronounced similarity at the gene expression level. The overlapping genes were enriched in interferon signalling pathway and the classical complement pathway. Low overlap was found between Sjs and RA, and Sjs and SSc.

We also looked for unique gene expression patterns in each disease with the aim of identifying potential biomarkers. We were able to define gene signatures differentiating between SADs and controls and also between SAD pairs.

**Conclusions:** Even though we were able to identify a limited number of disease specific signature genes, there are extensive and statistically significant overlaps in gene expression profiles of the seven investigated SADs. Similar to the clinical manifestations, the data presented here suggest that also on the molecular level, these diseases share a large portion of their pathophysiology. Work is ongoing to expand the dataset for confirmation of these preliminary data.

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**How do you sleep?****OP0361-HPR SLEEPING PROBLEMS AND ANXIETY IS ASSOCIATED TO CHRONIC MULTISITE MUSCULOSKELETAL PAIN IN SWEDISH HIGH SCHOOL STUDENTS**

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**Background:** The relationship between chronic multisite musculoskeletal pain (CMP) and sleep is complex, where pain can lead to sleeping problems and lack of sleep can intensify the pain perception. Most previous studies relates to adults, but adolescents may also suffer from CMP, and there is a need for more knowledge regarding the relationships between CMP and sleeping problems, stress, anxiety, depression, and health status.

**Objectives:** To study background factors associated to CMP in first year Swedish high school students.

**Methods:** First year Swedish high school students (n=296) were invited to complete questionnaires on chronic pain (mannequin with 18 body regions), sleeping problems (Uppsala Sleep Inventory, four items scored from 1–5), stress (ELO questions, scored from 1–5), anxiety and depression (Hospital Anxiety and Depression Scale, scored from 0–21), health status (EQ-5D, scored from 0 to 1, worst to best) and physical activity (International Physical Activity Questionnaire, categorised into low, moderate and high levels). Stress and sleeping items were dichotomized into 1–3 points (best) vs 4–5 points (worst). Individuals scoring at least severe problems (4 points) at one or more sleeping items were classified as having severe sleeping problems. HADS were categorised as non-cases (0–7), possible<sup>7–10</sup> and probable cases (11–21 points). Students were grouped as having CMP (pain present in ≥3 regions) or not (no chronic pain or chronic pain in 1–2 regions). Multiple logistic regression analyses (adjusted for sex) with CMP as dependent variable were performed in SPSS, version 24.

**Results:** 254 students (86% of total sample, 87 boys and 167 girls) with a mean age of 16.1 (SD 0.6) years participated in the study. CMP was present in 25 (9.8%) students with no differences between boys and girls (8.0% vs 10.8%; p=0.488). Having CMP was associated with reporting severe sleeping problems (OR 2.49, 95% CI: 1.06 to 5.81, p=0.035) with initiating sleep, maintaining sleep, early morning awakenings and/or not feeling restored after sleep in comparison to the other students. Students with CMP were more likely to be categorised as probable cases for anxiety (OR 3.06, 95% CI: 1.09 to 8.61, p=0.034), but there were no associations for possible cases for anxiety (OR 1.15, 95% CI: 0.38 to 3.51, p=0.800), possible cases (OR 2.03, 95% CI: 0.63 to 6.54), or probable cases for depression (OR 3.35, 95% CI: 0.33 to 33.83). There was a nearly significant association between stress and belonging to the CMP group (OR 2.31, 95% CI: 0.97 to 5.53, p=0.059). A higher self-reported health status was associated to a lower likelihood for CMP (OR 0.04, 95% CI: 0.01 to 0.27, p=0.001). Distribution of physical activity levels of low, moderate and high was not significantly associated to having CMP in comparison with not having it.

**Conclusions:** One in ten high school students fulfilled criteria for having chronic multisite musculoskeletal pain. CMP was associated to sleeping problems, anxiety, and a worse health status. The results from this study may be used by school health-care professionals in their preventive work to promote student's health.

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**Stratifying connective tissue diseases****OP0362 NOVEL GENE VARIANTS ASSOCIATED WITH CARDIOVASCULAR DISEASE IN SYSTEMIC LUPUS ERYTHEMATOSUS AND RHEUMATOID ARTHRITIS**

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**Background:** Patients with Systemic Lupus Erythematosus (SLE) and Rheumatoid Arthritis (RA) have increased risk of cardiovascular disease (CVD).

**Objectives:** We investigated whether single nucleotide polymorphisms (SNPs) at autoimmunity risk loci were associated with CVD in SLE and RA.

**Methods:** SLE patients (n=1045) were genotyped using the 200K Immuchip SNP array (Illumina). The allele frequency was compared between patients with and without different manifestations of CVD. Results were replicated in a second SLE cohort (n=1043) and in an RA cohort (n=824). We analysed publicly available genetic data from the general population, performed electrophoretic mobility shift assays and measured cytokine levels and occurrence of anti-phospholipid antibodies (aPLs).

**Results:** We identified two new putative risk loci associated with increased risk for CVD in two SLE populations, which remained after adjustment for traditional CVD risk factors. An *IL19* risk allele was associated with stroke/myocardial infarction in SLE (OR 2.3 (1.5–3.4), p=8.5×10<sup>-5</sup>) and RA (OR 2.8 (1.4–5.6), p=3.8×10<sup>-3</sup>), meta-analysis (OR 2.5 (2.0–2.9), p=3.5×10<sup>-7</sup>), but not in population controls. The *IL19* risk allele affected protein binding and SLE patients with the risk allele had increased levels of plasma-IL10 (p=0.004) and aPL (p=0.01). An *SRP54-AS1* risk allele was associated with stroke/transient ischaemic attack in SLE (OR 1.7 (1.3–2.2), p=2.5×10<sup>-5</sup>) but not in RA. The *SRP54-AS1* risk allele is an expression quantitative trait locus for four genes.

**Conclusions:** The *IL19* risk allele was associated with stroke/myocardial infarction in SLE and RA, but not in the general population, indicating that shared immune pathways may be involved in the CVD pathogenesis in inflammatory rheumatic diseases.

**Disclosure of Interest:** None declared

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**OP0363 OPTIMISINGPRECISION MEDICINE BY USING GENETICS TO ASSIGN DIAGNOSTIC PRIOR PROBABILITIES TO PATIENTS WITH SYNOVITIS – PROOF OF PRINCIPLE**

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**Background:** In patients with synovitis, the question is 'Which disease does this patient have?' However, traditional tests often only inform us about disease presence yes/no and disease discriminating symptoms often take a while to arise. Time independent information, such as genetics, might accelerate the diagnostic process. As increasing number of patients have genotyping data available in medical records prior to their visit, the question emerges: can genetic data facilitate disease differentiation in early disease?

**Objectives:** Proof of principle study to test the differentiating ability of genetic profiles in patients with synovitis.

**Methods:** We studied the most common rheumatologic diseases: rheumatoid and psoriatic arthritis, SLE, spondyloarthritis and Gout. The population level

disease probability for each disease comprised a sex adjusted disease prevalence and a weighted genetic risk score comprised of risk SNPs' odds ratio from literature. Within case genetic probabilities (GProb) were obtained through normalisation of the population risk assuring a patient's total disease probability of 1. So, each patient got a probability for each disease. GProb was developed in a simulated dataset and tested in

- Validation dataset of 1,211 rheumatology cases identified with ICD codes from 62,512 patients
- Replication dataset of 248 rheumatology cases identified by chart-review from 15,047 patients
- Clinical setting of prospective selected patients that presented with synovitis at the rheumatology outpatient clinic (n=242). Here, GProb was calculated for the five diseases plus the category 'Other'.

Having multiple GProbs for each patient, we tested whether the GProbs referring to the patient's real disease were higher than those that referred to the other phenotypes.

We used multinomial logistic regression with the six diseases as the dependent variables to test the additive value of GProb on top of clinical information.

**Results:**

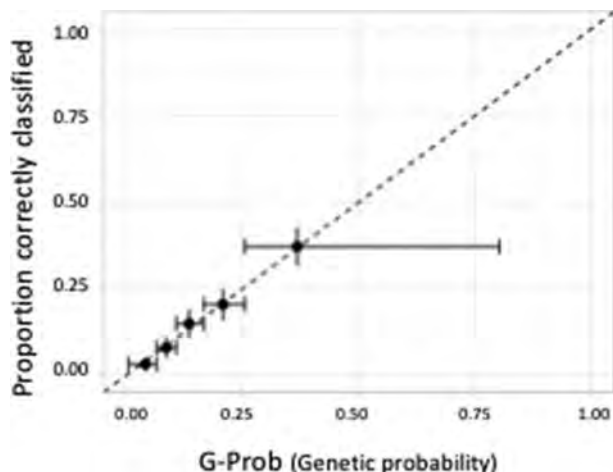
- There was a strong significant correlation between GProb and the disease status ( $r=0.27$   $P<0.0001$ ) with an AUC of 0.68.
- We observed a higher correlation with disease status in the more precisely identified cases ( $r=0.49$   $P<0.0001$ ) and a high AUC 0.82
- Also in a prospective setting, the GProb performed well ( $P<0.0001$  AUC 0.74 figure 1) especially in ruling out diseases (table 1).

The clinical information alone explained 41% of the variance in the final diagnosis. Adding GProb significantly improved the predictive value (expl. variance increased to 51%  $p=0.0008$ ).

Sensitivity analysis showed that the results were not driven by one disease.

**Abstract OP0363** – Table 1 Performance of G-Prob in ruling out diseases in the prospective dataset (n=242)

Selection	% of total G-Probs	% of G-Prob that correctly rejected disease
G-Prob < 0.05	14%	97%
G-Prob < 0.20	70%	89%



**Abstract OP0363** – Figure 1 Ability of GProb to differentiate six disease outcomes (RA, PsA, SLE, SpA, Gout, Other) in a prospective selection of patients with synovitis.

The graph depicts the mean GProb (with range) of each quintile of GProbs on the x-axis and the corresponding proportion of those GProbs that matched with the patient's real disease on the y-axis. The graph demonstrates that the genetic probability of the disease highly resembles the real disease risk. In case of a perfect test performance, the dots would lie exactly on the diagonal (dashed) line.

**Conclusions:** This study developed methodology for disease-discriminating tests.

In patients with synovitis, genetic data can facilitate decision making in early disease by ruling out and pointing towards the most likely phenotype. Seeing the increasing importance of an early diagnosis in patients with synovitis, genetics can be considered as part of a patient's medical history.

Additional prospective studies will further need to validate this proof of principle study.

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**Work and rehabilitation – key priorities for people with RMDs**

**OP0364-PARE WORK STATUS AND WORK BARRIERS IN PATIENTS RECEIVING bDMARDs AS INFUSIONS IN RHEUMATOLOGY HOSPITAL CLINICS IN NORWAY. A CROSS-SECTIONAL STUDY**

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**Background:** Preventing work disability is an important treatment goal for people with rheumatic diseases. New treatment modalities with introduction of bDMARDs have led to better control of disease activity, symptoms and improvement of functional capacity. Still, sick leave and forced retirement is common, and studies have shown that work status at start of therapy is a predictor of work ability later in the disease course.

**Objectives:** The objective of this study was to explore work status, concerns about future work capacity and work barriers in a group of patients receiving bDMARDs as infusions in rheumatology hospitals in Norway.

**Methods:** This is a cross-sectional study. In March and April 2017, patients at two rheumatology hospitals were invited to participate in a survey. Participation was voluntary with anonymous response. Information about background, disease, and start of bDMARD infusions was self-reported in a questionnaire. Further, respondents who were working or on sick leave (full- or part time), answered questions about work capacity and degree of concern about future work capacity on NRS-scales from 1–10 (10=best capacity and high degree of concern). They also scored their experienced barriers related to seven different topics selected from the Work Experience Survey-Rheumatic Conditions (WES-RC) on 5 point Likert scales (5=severe problems).

**Results:** Of 343 eligible patients, 317 responded (92%). Mean (SD) age were 52.3 (14.9) years, 81% were under 67 (age of retirement in Norway). The largest diagnostic groups were rheumatoid arthritis (47%) and spondylarthritis (26%). Mean (SD) disease duration was 13.8 (10.6) years. Half of the respondents aged <67 years reported reduced work ability, of these 27% were on sick leave and 23% were on disability pension. The proportion of patients on sick leave was highest among those who started with bDMARD infusions within the last 3 months (42.3%), and lowest in the group who had started 25 to 36 months earlier (21.4%). For disability pension the numbers were opposite, with the largest amount in the group that received treatment for more than 36 months (29.7%).

There were significant differences in ratings of work capacity and concerns about future work capacity among respondents working full time and those on sick-leave. Mean (SD) scores of work capacity were 8.0 (1.7) and 5.5 (3.0) ( $p<0.001$ ) in full time workers and participants on sick-leave, respectively. Corresponding scores for concerns about future work capacity were 5.2 (2.5) and 7.0 (2.7), ( $p<0.001$ ). Thirty percent of respondents in full-time work scored 7 or higher on degree of concern about future work capacity. Regardless of work status, 'physical work demands', 'mental work demands' and 'balance between work and private life' was rated as the most severe barriers for work ability.

**Conclusions:** This cross-sectional study shows that approximately half of the patients receiving bDMARD infusions at two hospitals in Norway report reduced work ability, and nearly one third was concerned about future work capacity. Early identification of patients who, despite optimal treatment, experience work barriers is important. Activity regulation, ergonomic advice and self-management strategies for managing work demands and imbalance between work and private life should be further tested.

**Disclosure of Interest:** None declared

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**OP0365-PARE** **WORK MATTERS: A UK WIDE SURVEY OF ADULTS WITH RHEUMATOID ARTHRITIS AND JUVENILE IDIOPATHIC ARTHRITIS ON THE IMPACT OF THEIR DISEASE ON WORK**

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**Background:** 10 years ago, NRAS ran a survey and found that people with RA are less likely to be in employment than the general population, and that there are significant barriers to work.

**Objectives:** To understand how the situation has changed over the last 10 years, NRAS surveyed over 1500 people with RA to understand their experiences.

**Methods:** NRAS worked with the University of Manchester (UoM) to develop open and closed questions to explore the current state of employment of people with RA, as well as barriers to remaining in and returning to employment. The survey was developed jointly with UoM and contained validated questionnaires on absenteeism and presenteeism. The survey was distributed by NRAS to its members through email and non-members through social media.

**Results:** 63.3% of people surveyed were in employment, an increase from 2007 when this figure was at 54.8%. However, a significant number of people were concerned about the possibility of remaining in the job if there were any changes to the nature of the work. Participants commented on the challenges and advantages of work, with the primary advantages being financial security, sense of purpose and enjoyment, and the employer/working environment. However, many of the barriers to work included the role being too demanding, RA symptoms, lack of reasonable adjustments, the commute, and the lack of an understanding employer/colleagues. Almost 40% of participants stated that their employers did not understand the disease and that help that was not available. Nearly half of all respondents had to use annual leave in order to deal with their RA; this being just one example of how employers had breached the Equality Act 2010. The survey found that low numbers of people claimed benefits with Disability Living Allowance and/or Personal Independence Payments and Blue Badge being the most commonly claimed. Many participants had co-morbidities, with high numbers of people reporting mental health issues.

**Conclusions:** Fewer people are losing their job or retiring early due to the disease which may be due to better and earlier treatment. However, the attitudes of employers and colleagues can have a great impact on the ability of someone with RA to remain in work. Progress must be made to raise awareness of employers' responsibilities in relation to employees with disabilities, but also to signpost employers to help that is readily available for them.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.1833

**SATURDAY, 16 JUNE 2018**

**The challenges of rheumatology trainees in the clinical learning environment**

**OP0366** **AMBULATORY RHEUMATOLOGY TEACHING DAY – A 360-DEGREE EVALUATION OF STAKEHOLDER EXPERIENCES**

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**Background:** The Dunedin School of Medicine, New Zealand, include an ambulatory teaching day for 5th year medical students within their rheumatology

curriculum. This day involves clinical lectures, examination skills, and clinical assessment of patient volunteers. This is often the students' first experience of conducting a rheumatology consultation.

**Objectives:** To evaluate the effectiveness of the Ambulatory Rheumatology Teaching Day from the perspective of all involved stakeholders, to inform ongoing development of this teaching programme.

**Methods:** Independent focus groups of patients (two groups, n=12), consultants/clinical lecturers (one group, n=4), and 5th year medical students (four groups, n=19) involved in ambulatory rheumatology teaching days were conducted. Transcripts were analysed using thematic analysis, and themes compared across the three stakeholder groups.

**Results:** All stakeholder groups found the ambulatory day well-structured, educational, and inclusive. Patient contact provided a bridging opportunity between theory and practice; students reported a broader perspective on the lived experience of rheumatic conditions, and improved clinical and examination skills. Consultants found the one-day format created scheduling issues with their clinical workload, and suggested two half-day sessions would enable all rheumatology consultants to input into at least one of the sessions. Students and patients supported this format; students further suggested radiology and laboratory diagnostic tutorials prior to the ambulatory day, to aid their clinical assessment experience. All stakeholders observed that student diagnosis was mainly dependent on pronounced clinical presentation. Students were competent in diagnosing rheumatoid arthritis and gout, but failed to diagnose ankylosing spondylitis and calcium pyrophosphate dihydrate crystal deposition (CPPD). Greatest knowledge gains were reported for the conditions of ankylosing spondylitis and psoriatic arthritis. While students reported no interaction issues with the patients, both consultants and patients observed that several students were hesitant to conduct the physical examination, appearing concerned they may cause pain to the patient. Accordingly, students expressed a preference for more clinical supervision during the patient examinations; whereas the consultants favoured the student being independent, developing their questioning skills to improve their examination technique. Patients supported this independent approach to teaching the clinical assessment, and suggested the use of prompt sheets to engage the students in questioning regarding clinical presentation, symptoms, and medications.

**Conclusions:** The ambulatory rheumatology teaching day provided a supportive and effective learning environment for introducing 5th year medical students to the patient consultation process. Students gained both clinical skills and a valuable understanding of the patient perspective of a variety of rheumatic conditions. Students would further benefit through prior tutorials on diagnostic skills, with a focus on interpretation of radiology and laboratory results. Additionally, enhancing the role of the patient as teacher will aid the examination process, and highlight the importance of both clinical and patient outcome priorities.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.4252

**OP0367** **USING YOUTUBE TO TEACH THE FUNDAMENTALS OF RHEUMATOLOGY: A TWO-YEAR RETROSPECTIVE ANALYSIS OF FOUR ONLINE LECTURES**

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**Background:** Duesseldorf has a dedicated rheumatology unit; therefore, education in rheumatology takes up an increased portion of the medical curriculum. Furthermore, most medical schools in Germany have very few or no lectures on topics in rheumatology. According to the German Society of Rheumatology, one reason for the lack of lectures is the absence of dedicated rheumatology teaching units. To improve education in rheumatology offered to medical students at these universities, we hypothesise the use of online platforms such as YouTube to be a potential in delivering content.

**Objectives:** Investigating the potential of YouTube to deliver online lectures in rheumatology.

**Methods:** Online lectures were created by a physician from the Department of Rheumatology at University in Duesseldorf and the e-Learning platform Amboss. Content was matched with the educational goals of the Department of Rheumatology from the 2016 curriculum and the educational goals for rheumatology from the IMPP ('Institut für medizinische und pharmazeutische Prüfungsfragen'), which is responsible for the medical state examination ('Staatsexamen') in Germany. Lectures were produced in German and the overall length of the content was 36 min and 27 s. The content was divided into four short lectures (range, between 6:49 min and 13:27 min) and made available to the public via the online streaming platform YouTube. Information on the age, sex, and location of viewers was collected and analysed. Lectures were analysed for the number of clicks, total watch time, average watch time, and the types of devices used to access content. Analysis was performed over a 20 month period (04/16–01/18). The integrated feature of the platform YouTube Analytics was used for analysis.

**Results:** Viewers from 108 different countries accessed the content, with 95.1% streaming from three countries with German as a native language (Germany,

Austria, Switzerland). Males comprised 55.6% of the viewers and females 44.4%. Twenty percent of viewers were aged between 18 and 24 years, 56% were between 24 and 34 years of age, 14% were aged between 35 and 44 years old, and the remaining 10% were over the age of 45 years.

All four videos were clicked 82 373 times (first video, 31,296; second, 18,674; third, 15,928; fourth, 16 475 times). Viewers spent an average of 4:37 min watching the videos. In total, 381,514 min of content was delivered. Approximately 58% of the content was accessed through mobile devices such as smartphones and tablets.

**Conclusions:** YouTube and YouTube Analytics were found to be exceptionally successful in delivering and analysing online lectures. Mobile phones were the

most commonly used device by viewers, demonstrating the growing importance of adapting content for these devices. A comparison of the delivered educational minutes with the traditional setting of delivering knowledge at a university in a 45 min lecture to an average audience of 100 individuals amounts to approximately 847 lessons. In conclusion, the use of online lectures to deliver medical content especially in universities where rheumatology is not represented by a dedicated faculty is highly recommended.

**Disclosure of Interest:** None declared

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## Poster Presentations

THURSDAY, 14 JUNE 2018

### Genomics, genetic basis of disease and antigen presentation

#### THU0001 DIFFERENTIAL METHYLATION AS A PREDICTOR OF METHOTREXATE RESPONSE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Methotrexate (MTX) is recommended as the first-line disease modifying anti-rheumatic drug (csDMARD) for the treatment of rheumatoid arthritis (RA), but up to 40% patients do not respond adequately, or experience adverse effects<sup>1</sup>; therefore, identifying blood-based biomarkers that predict treatment response is a research priority. DNA methylation is an epigenetic marker that modifies but does not alter DNA sequence; MTX may act, at least in part, by inhibiting intracellular methyl donor transfer leading to DNA hypomethylation<sup>2</sup> so DNA methylation may act as a biomarker of MTX response.

**Objectives:** To identify differential DNA methylation signatures in whole blood associated with response to MTX in patients with RA.

**Methods:** DNA methylation was measured using the HumanMethylation450 BeadChip in DNA samples from individuals recruited to the Rheumatoid Arthritis Medication Study (RAMS). Demographic and clinical data were collected prior to starting MTX (baseline) and at 6 months after commencing MTX. DNA was extracted from whole blood samples collected at baseline and at 4 weeks from patients who, at 6 months, had a EULAR good response (n=36) or EULAR poor response (n=36) to MTX. Differentially methylated positions (DMPs) between baseline and 4 weeks, and between good and poor response groups were identified using a linear model, adjusting for gender, age, cell composition, baseline disease activity score (DAS28), and smoking status. Additional analyses were performed to assess the association between methylation and change in DAS28 score and the individual DAS28 components over 6 months. DMPs with significant differences were selected for replication by pyrosequencing in an independent group of 100 patients with both baseline and 4 week samples available for testing. Using genome-wide genotype data for the same patients, replicated DMPs were investigated for methylation QTLs (meQTLs).

**Results:** The initial analysis identified differential methylation between good and poor responders at 2 CpG sites (DMPs) in samples taken at 4 weeks, with response status determined at 6 months (p-value<10<sup>-5</sup>). Three other DMPs were associated with change in tender joint count, another 3 DMPs with change in swollen joint count, and a further 4 DMPs were associated with change in C-reactive protein (CRP). Of the 12 DMPs, 4 showed replicated association with improvement of swollen joint count and lower CRP levels at 6 months in the pyrosequencing dataset (p-value<0.01). However, there were no meQTLs identified at these loci.

**Conclusions:** These results suggest DNA methylation may provide a biomarker of MTX response but requires replication in other larger data sets.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.4680

#### THU0002 NOVEL PATHOGENIC STOP CODON MUTATION IN THE NF-KB P65 SUBUNIT (RELA) ASSOCIATED WITH BOTH BEHÇET'S DISEASE LIKE SYNDROME AND NEUROMYELITIS OPTICA IN AN IRISH FAMILY

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**Background:** Behçet's disease (BD) has a complex multifactorial pathogenesis and presents with phenotypic heterogeneity predominantly mucocutaneous ulcerations, ocular lesions and skin manifestations. More recently, there have been reported cases of monogenic spectrum defects presented with BD-like similarities or phenotype.

**Objectives:** We investigated an Irish Caucasian family of eleven that included two half-sisters with early-onset BD, and another sister with neuromyelitis optica, all who were born to asymptomatic non-consanguineous parents. More recently, one of the sisters' daughter developed recurrent oral aphthosis at the age of 10 years old.

**Methods:** Peripheral blood mononuclear cells were extracted from patients and non-affected donor blood using standard fractionation methods. Following quality assessment and quantification whole exome sequencing was performed on all participants.

**Results:** Whole exome sequencing data identified segregation of a novel pathogenic stop codon mutation in the nuclear factor NF-κB p65 subunit (RelA) resulting in a non-functional protein. The mutation involves cytosine deletion and results in a His487ThrfsTer7 frameshift (His487ThrfsTer7) *RelA* resulting in loss of transcription activation-1 (TA1) and a portion of TA2 from RelA. The mutation was seen within the three generations, including the three half-sisters, their father as well as one of the proband's daughter, potentially describing a new syndrome.

**Conclusions:** Our study suggests that loss-of-function mutations in the NF-κB pathway, a pivotal mediator of inflammation and apoptosis, are linked with the development of familial early-onset BD-like syndromes. Better insights and further understanding of this "orphan" immunogenetic syndrome carries high clinical impact to assist early disease recognition and potential discoveries of novel targeted therapies.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.3889

#### THU0003 COMPREHENSIVE EVALUATION OF THE EFFECTS OF RARE AND COMMON EXONIC ABCG2 VARIANTS ON GOUT SUSCEPTIBILITY

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**Background:** Gout is the most common form of inflammatory arthritis and is caused by hyperuricemia. Many previous studies have indicated that common dysfunctional variants of the gene encoding ATP-binding cassette transporter subfamily G member 2/breast cancer resistance protein (ABCG2/BCRP) increase the risk of gout and hyperuricemia. In addition, we recently showed that rare non-synonymous variants are also risk factors for gout. However, we have not evaluated the effects of synonymous and splice-site variants of



*ABCG2*. Thus, to estimate the risk of genetic variants of *ABCG2* more comprehensively, we analysed the association between all exonic variants and gout susceptibility.

**Objectives:** The main purpose of this study was to perform comprehensive *in silico* evaluation of the effects of all types of rare and common exonic *ABCG2* variants on gout susceptibility in Japanese population.

**Methods:** We previously sequenced all the exons of *ABCG2* in 480 patients with gout and 480 healthy controls (Japanese males) and performed functional analyses of non-synonymous variants. In this present study, we analysed the correlation between urate transport function and scaled C-score of CADDv1.3 (CADD score) of non-synonymous variants. We additionally performed Receiver Operating Characteristic (ROC) curve analysis and selected variants with altered function of more than 50% compared to wild-type *ABCG2*. Stratified association analyses and multivariate logistic regression analysis were performed to evaluate the effects of selected rare and common *ABCG2* variants on gout susceptibility.

**Results:** We identified 4 common and 26 rare exonic or closely situated intronic variants of *ABCG2*. CADD scores showed significant correlation with the results of functional analyses on urate transport ( $p=0.014$ ,  $r=-0.539$ ). ROC curve analysis showed an area under the curve (AUC) of 0.775. The optimal cutoff value of CADD score was 15 for classifying variants with altered function of more than 50% compared to wild-type *ABCG2* (sensitivity=0.88, specificity=0.67). Therefore, we selected variants with a CADD score greater than 15 for downstream analyses. All intronic or synonymous variants had low CADD scores and thus were removed. Multivariate logistic regression analysis showed that the rare variants of *ABCG2* were associated with a significantly increased risk of gout and the size effect of these rare variants (odds ratio [OR]=2.7,  $p=0.012$ ) was similar to that of the common variants, Q126X (OR=3.3,  $p=4.8 \times 10^{-6}$ ) and Q141K (OR=2.3,  $p=8.6 \times 10^{-6}$ ).

**Conclusions:** This study confirmed that both common and rare variants in *ABCG2* increase gout susceptibility. Furthermore, our *in silico* analyses suggest that synonymous and splice-site variants of *ABCG2* may not play a key role in the pathogenesis of gout.

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**Disclosure of Interest:** None declared

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#### THU0004 A DE NOVO NON-SENSE ERAP1 POLYMORPHISM IN TWO HLA-B\*27-NEGATIVE TWINS WITH AXIAL SPONDYLOARTHRITIS

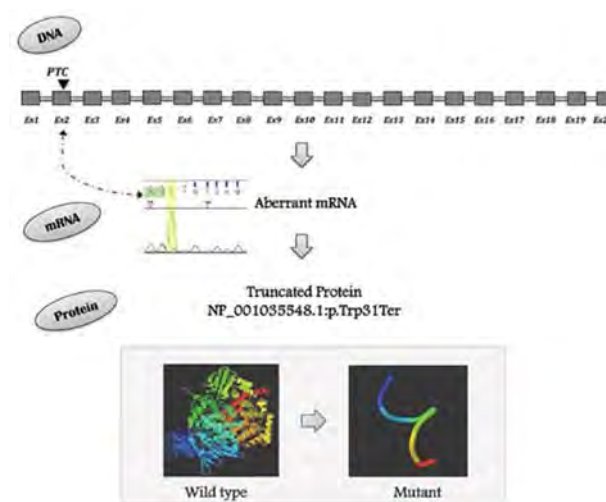
M.C. Padula<sup>1,2</sup>, G. Martelli<sup>2</sup>, R. Giuzio<sup>2</sup>, C. Amato<sup>2</sup>, T. Carbone<sup>1</sup>, M. Gilio<sup>1</sup>, P. Leccese<sup>1</sup>, G. Tramontano<sup>1</sup>, A.A. Padula<sup>1</sup>, S. D'Angelo<sup>1</sup>. <sup>1</sup>Department of Rheumatology, Rheumatology Institute of Lucania (IReL) and Rheumatology Department of Lucania, San Carlo Hospital of Potenza and Madonna delle Grazie Hospital of Matera, Italy; <sup>2</sup>Department of Science, University of Basilicata, Potenza, Italy

**Background:** Axial spondyloarthritis (axSpA) is a group of inflammatory disorders primarily affecting the spine that includes ankylosing spondylitis (AS) and non-radiographic axSpA. AS is strongly associated with HLA-B\*27. A small percentage of HLA-B\*27-positive subjects develop AS, suggesting the role of other genes in AS susceptibility.<sup>1,2</sup> Among these genes, *ERAP1* acts as "molecular ruler". It encodes the endoplasmic reticulum aminopeptidase 1 protein, responsible for the peptides trimming for the efficient binding to class I major histocompatibility complex (MHC). Several common gene SNPs (single nucleotide polymorphisms) were associated with the susceptibility to AS, but the presence of other *ERAP1* polymorphisms was supposed to explain the genotype-phenotype correlation.<sup>1,3,4</sup>

**Objectives:** The aim of this study is to genotype the *ERAP1* gene whole structure searching for common and additional polymorphisms in two HLA-B\*27-negative twins.

**Methods:** We integrated a bioinformatics and a second level molecular approach in order to characterise *ERAP1* gene. Specific primer pairs were designed for the coverage of all gene regions. Genomic DNA was isolated from the whole blood of two 36 years-old axSpA male twins. They are HLA-B\*27-negative (HLA-A\*02, HLA-A\*32; HLA-B\*07; HLA-CW\*07). The coexistence of Crohn's disease (CD) was documented in both patients after the initial diagnosis of axSpA. Primer-specific polymerase chain reaction (PCR) was carried out. PCR products were sequenced and bioinformatics tools (BlastN and Mutation Surveyor) were queried for the mutational analysis. Phyre2 on line software was used for predicting the protein tertiary structure.

**Results:** Molecular characterisation of *ERAP1* gene identified a *de novo* homozygous guanine to adenine substitution at 15 132 position of exon 2 nucleotide sequence (NG\_027839.1:g.15312G>A). This substitution is a stop-codon variation that directly generates an early premature termination codons (PTC). The 3D model of the protein showed a significant difference of the folding when wild-type and mutant protein were compared. The non-sense transcript could result in the production of a truncated protein, formed by 30 amino acids (NP\_001035548.1:p.Trp31Ter) (figure 1).



**Abstract THU0004 – Figure 1.** The effect of the novel stop-codon variant at DNA, RNA and protein level. The novel substitution generates a PTC in *ERAP1* exon 2, that could be responsible for the production of an aberrant mRNA and of the truncated protein. The protein tertiary structure prediction by Phyre2 software is shown.

**Conclusions:** A *de novo* stop-codon *ERAP1* variant was identified for the first time in axSpA. We suggest that the PTC-related *ERAP1* protein could contribute to AS risk by affecting the protein role.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.5405

#### THU0005 WHOLE GENOME LINKAGE AND EXOME SEQUENCING ANALYSES IN TAKAYASU ARTERITIS FAMILIES

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**Background:** Takayasu arteritis (TA) is an inflammatory large vessel vasculitis affecting mainly aorta and its branches. Inflammation in vessels causes thickening

of walls, fibrosis, dilatation and nonspecific symptoms such as fever, hypertension and arthralgia. It is a rare disorder with unknown etiology and the worldwide incidence is 0.4 to 2.6 per million.

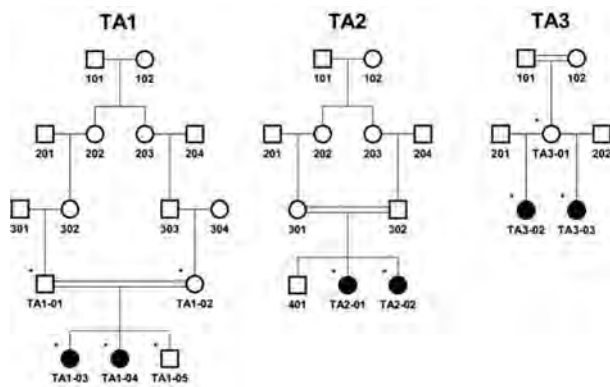
**Objectives:** We studied three consanguineous families with consisting of two affected daughters each and their healthy parents in order to identify the disease locus and the causative mutation

**Methods:** In two of the families, genome-wide single nucleotide polymorphism (SNP) genotyping was performed for available family members using Illumina OmniExpress-24 BeadChip targeting ~700,000 SNP markers. Using genotyping data, we performed multipoint parametric linkage analysis assuming recessive inheritance and complete penetrance. Also exome sequencing was performed for four of the patients to search for rare, homozygous deleterious variants. For TA1 and TA2 families whether the variants were located in a region IBD (identical by descent) in affected sisters or not was investigated.

**Results:** Whole genome linkage and exome analyses identified homozygous, rare (MAF <0.01) candidate variants shared by the affected sister pairs in the first two families. Candidate variants for the first family were in *ANXA8L1*, *EHBP1L1*, *TULP2*, *MYH14* and *SHANK1* and for the second family in *AP4B1*, *RIMBP3*, *VCX3B* and *NXF2*. In the third family, no candidate homozygous variant was common for the affected sibs, who had different fathers. *In silico* functional predictions of the candidate variants shared by each sister-pair were determined.

Abstract THU0005 – Table 1. *In silico* functional predictions of candidate variants

Family	Gene	Change	SIFT	PolyPhen2	MutationTaster
TA1	<i>ANXA8L1</i>	c.449C>T (p.T150M)	Deleterious	Probably damaging	Disease Causing
	<i>EHBP1L1</i>	c.3595C>T (p.R1199C)	Deleterious	Probably damaging	Polymorphism
	<i>TULP2</i>	c.1300T>C (p.Y434H)	Tolerated	Benign	Polymorphism
	<i>MYH14</i>	c.565C>T (p.R189C)	Deleterious	Probably damaging	Disease Causing
	<i>SHANK1</i>	c.3947G>A (p.G1316D)	Tolerated	Possibly damaging	Disease Causing
TA2	<i>AP4B1</i>	c.263C>T (p.T88I)	Tolerated	Benign	Disease Causing
	<i>RIMBP3</i>	c.3788A>C (p.E1263A)	Tolerated	Benign	Polymorphism
	<i>VCX3B</i>	c.44A>G (p.K15R)	Tolerated	Possibly damaging	Polymorphism
	<i>NXF2</i>	c.1301+1G>A	-	-	Disease Causing



**Conclusions:** This is the first whole genome linkage analysis and subsequent exome sequencing in TA patients with suggestive recessive inheritance. Possible candidate variants in two out of the three families were determined. However, we could not find any genetic change in terms of genetic mutations, exonic deletions or structural variations shared by these families. We had hoped that the study in these rare families with a pair of TA sibs would unravel a gene responsible for TA. We now question whether the inheritance is dominant with reduced penetrance which requires more familial cases to be studied.

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**Disclosure of Interest:** None declared

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THU0006

## APPLICATION OF MACHINE LEARNING METHODS FOR PREDICTION MODELLING OF PSORIATIC ARTHRITIS IN PATIENTS WITH PSORIASIS

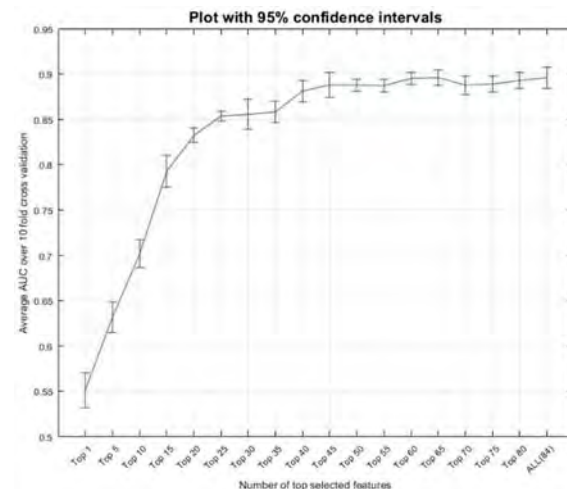
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**Background:** Approximately 30% of patients with psoriasis develop a chronic inflammatory arthritis referred to as psoriatic arthritis (PsA). The ability to accurately predict which psoriasis patients will develop PsA would enable early intervention and help prevent disability. Both psoriasis and PsA have a substantial genetic risk component, however the utility of using genetic risk factors for the prediction of PsA is currently unknown. Alleles of the human leukocyte antigen (HLA) genes represent the largest genetic effects observed for both psoriasis and PsA (HLA-C\*0602 and HLA-B\*27 respectively); these genes are highly polymorphic with extensive linkage disequilibrium (LD) which will make variable (feature) selection using statistical models very challenging. Machine learning methods, such as information theoretic criteria, are well suited to this challenge and will find a subset of the original variables that enable more accurate prediction.

**Objectives:** To apply machine learning methods for feature selection of HLA alleles and evaluate the accuracy of these feature for the prediction of PsA.

**Methods:** Feature selection was performed using information theoretic criteria methods which are classifier independent methods that provide a ranking of genetic features that differentiate PsA from cutaneous-only psoriasis. Multiple methods were tested; mutual information maximisation (MIM), joint mutual information (JMI), minimal-Redundancy-Maximal-Relevance (mRMR) and conditional mutual information maximisation (CMIM). Two principal components (population stratification) and age of psoriasis onset were included as potential confounders. The Bagged Trees method was used for classification and the performance of the predictive models were assessed using area under the receiver operating characteristic curve. These methods were applied to a dataset of 1462 PsA cases and 1132 cutaneous-only psoriasis cases using 2-digit and 4-digit classical HLA alleles imputed using the SNP2HLA algorithm.

**Results:** The single most important features based on rank were identified as HLA-B\*27 (2-digit) and HLA-B\*2705 (4-digit) by the four different feature selection techniques; this is consistent with previous analyses of this data using regression based methods. However, the predictive accuracy of these single features was found to be poor (AUC 0.55 HLA-B\*27). Sequentially adding additional HLA features based on rank substantially improved the performance of the classification model where 20 2-digit features selected by JMI demonstrated an average AUC of 0.84 based on 10 cross-fold validation (figure 1).



**Conclusions:** The results demonstrate that classification models constructed from multiple HLA alleles substantially outperform classification based solely on

the previously reported PsA risk allele (HLA-B\*27). Importantly, the study demonstrates that this additional information is efficiently captured using information theoretic criteria methods which capture correlations between markers.

**Disclosure of Interest:** None declared

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**THU0007 GENETIC VARIANTS IN SLE SUSCEPTIBILITY LOCI, XKR6 AND GLT1D1, ARE ASSOCIATED WITH CHILDHOOD-ONSET SLE IN A KOREAN COHORT**

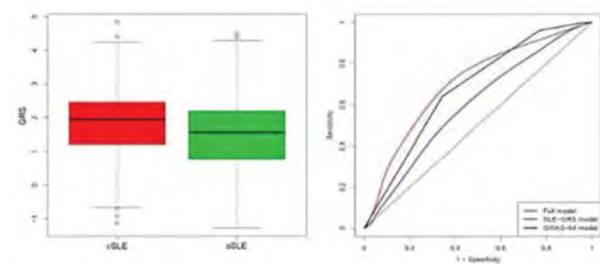
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**Background:** Systemic lupus erythematosus (SLE) is a polygenic autoimmune disease that occurs in all ages. It has been well documented that younger age of SLE onset is associated with more severe clinical manifestations and worse outcomes. However, impact of genetic variants on age of SLE onset was not fully understood.

**Objectives:** We investigated a cumulative effect of reported SLE-risk variants on childhood-onset SLE and searched for new risk loci of childhood-onset SLE using a genome-wide SNP analysis.

**Methods:** We analysed 96 Korean childhood-onset (<16 years old) and 685 adult-onset SLE (≥16 years old) who were previously genotyped by both Immuno-chip and genome-wide SNP arrays. Individual genetic risk scores (GRS) from well-validated SLE susceptibility loci (45 Asian confirmed non-HLA loci and an HLA-DRB1 amino acid haplotype model) were calculated and tested for their association with childhood-onset SLE. Association of each genetic variant with childhood-onset SLE was analysed using a multivariable logistic regression adjusting for population substructure.

**Results:** Mean age of SLE onset was 12.5±2.5 years in childhood-onset SLE and 29.0±9.4 in adult-onset SLE. GRS from SLE susceptibility loci was significantly higher in childhood-onset SLE than adult-onset SLE (p=0.001). Two SNPs, rs7460469 in *XKR6* and rs7300146 in *GLT1D1*, showed the most significant associations with childhood-onset SLE (p=1.26×10<sup>-8</sup>, OR=0.18, and p=1.49×10<sup>-8</sup>, OR=0.35, respectively). Especially, rs7300146 in *GLT1D1* was the cis expression quantitative trait locus (eQTL) for *SLC15A4*, which has been known an SLE susceptibility gene in a Chinese population. The model consisting of SLE GRS and the two newly identified loci to predict childhood-onset SLE attained an area under curve (AUC) of 0.71 in a receiver operating characteristics (ROC) curve.



**Abstract THU0007 – Figure 1.** A) association of genetic risk score else. cSLE; childhood-onset, aSLE; adult-onset SLE, GRS; genetic risk score and B) ROC curve for SLE-GRS, GWAS-hitand full model. ROC; receiver operating characteristics, SLE; Systemic lupus erythematosus, GWAS; genome-wide association study

**Conclusions:** Childhood-onset SLE is associated with a high cumulative SLE-risk effect and two novel SNPs rs7460469 and rs7300146, providing the first predictive model for childhood-onset SLE in Koreans.

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**Disclosure of Interest:** None declared

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**THU0008 LINKING GENETICS TO T-CELL PHENOTYPE IN JIA: RATIONAL FOR IL-2 THERAPY**

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**Background:** Several genetic regions associated with susceptibility to juvenile idiopathic arthritis (JIA), harbour genes involved in the interleukin-2 (IL-2) response which is pivotal in the function of regulatory T cells (T-regs) and their ability to suppress effector T cells. Genetically JIA is similar to type 1 diabetes (T1D) which also demonstrates an enrichment of genes related to IL-2 regulation and response. Early clinical trial data has indicated recombinant IL-2 to be successful in enhancing T-regs in T1D. I hypothesise that IL-2 regulation and response is critical to the development of JIA and therefore IL-2 therapy represents an exciting and viable therapeutic option for JIA.

**Objectives:** We aim to identify a subset of JIA patients who carry a high burden of genetic risk variants in genes related to IL-2 regulation and response, who could then be targeted for IL-2 therapy. Secondly we will link genetics to cellular phenotypes using CyTOF to identify a subset of cells that are most perturbed in JIA and determine the effects of IL-2 on these cellular subsets.

**Methods:** A weighted genetic risk score (wGRS) was generated using 9 JIA susceptibility SNPs considered to be within or near to genes involved in interleukin (IL-2) regulation and response.<sup>1</sup> The IL-2 wGRS was tested in an independent set of UK cases (1435) and controls (5181). The risk of developing JIA was assessed by subtype, using logistic regression. A CyTOF panel containing 33 antibodies targeting markers of T cells and T-regulatory cells was developed and tested in CD3 +T cells from two healthy individuals after 12 hour stimulation (anti CD3/CD28 beads plus recombinant IL-2). Cells were stained for all antibodies, iridium and cisplatin and analysed on the CyTOF Helios. Data will be analysed with traditional biaxial gating as well commercially available packages such as cytofit.

**Results:** The IL-2 wGRS demonstrated an increased percentage of individuals in the high risk group in the extended oligoarthritis, RF negative and RF positive polyarthritis subtypes suggesting a higher burden of IL-2 related loci. The odds of developing JIA for those in the highest risk group (quintile 5) compared to all others was increased in these subtypes (OR 2 95% CI 1.45–2.76, OR 2.39 95% CI 1.87–3.04, OR 2.14 95% CI 1.49–3.09, respectively). Comparing this to a wGRS generated from JIA susceptibility loci excluding IL-2 related genes shows that this enrichment is specific to the IL-2 wGRS. Biaxial gating of CyTOF data showed increases in activation markers after stimulation (CD25, CD69, CD38 and HLA-DR, decrease CCR7). We demonstrated that our panel can successfully identify traditional CD4 +T cell subsets showing differences between stimulated and unstimulated cells and between individuals.

**Conclusions:** Our analysis has shown that patients with oligoarthritis and polyarthritis have an increased burden of JIA susceptibility variants in genes related to IL-2 regulation and response suggesting these individuals may benefit from IL-2 therapy. Using the CyTOF panel we can now analyse individuals with high and low GRS allowing us to identify cellular subsets which may be altered by these genetic variants.

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**Disclosure of Interest:** None declared

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THU0009

### TOWARDS PRECISION MEDICINE IN CONNECTIVE TISSUE DISEASES: GENOMIC AND TRANSCRIPTOMIC STUDIES

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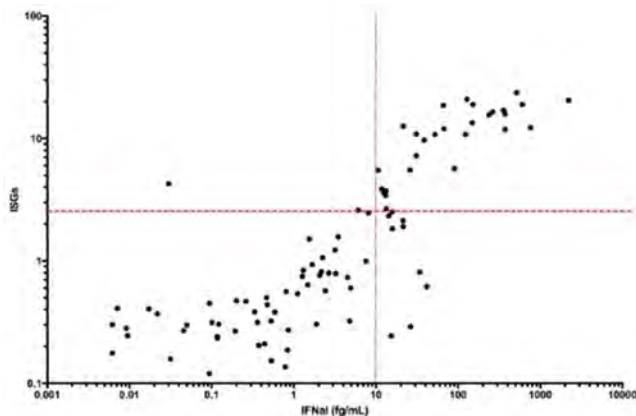
**Background:** To date, 18 genotypes linked with enhanced interferon signalling and severe inflammatory multi-system disease, have been identified. Functional studies in these disorders has led to significant advances in the understanding of type I interferon signalling. Understanding the role of these same genes in the pathogenesis of Connective Tissue Diseases (CTDs) may help guide precision medicine in this field.

**Objectives:** To study the relationship between phenotypic, serological, genomic and transcriptomic characteristics in adults with Connective Tissue Diseases (CTDs).

**Methods:** Following clinical and serological phenotyping, targeted exome sequencing was performed in 100 adults with CTDs. The CTDs include: systemic lupus erythematosus, Sjogren's syndrome, mixed and undifferentiated CTD, limited and diffuse cutaneous systemic sclerosis and dermatomyositis. The targeted 200-gene panel was designed based on data from human or animal studies associating gene function with autoimmune diseases, particularly lupus. Type I interferon stimulated gene (ISG) signature score was calculated from quantitative PCR assessment of six interferon stimulated genes<sup>1</sup> and interferon alpha was directly assayed by single-molecule array (Simoa) digital ELISA technology<sup>2</sup> in all cases.

**Results:** Targeted exome sequencing in adults with CTD identified potential monogenic causes in 5% of cases, with causative genes including known type I interferon-associated genes, such as TREX1, C1q and PEPD.

An ISG signature was present in 35% of the cohort and showed significant correlation with the Simoa interferon alpha assay ( $r=0.854$ ) (figure 1).



**Conclusions:** Drug development in CTDs is notoriously slow. However, recent drug developments in type I interferon modulation in terms of JAK-STAT inhibition and interferon receptor antibodies offer great promise for a subset of patients. Our work demonstrates that through deep phenotyping of patients with corollary 'omic studies, a CTD subset, that is not restricted to a single diagnostic grouping, can be identified in whom targeted anti-interferon therapy would likely be of great value.

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**Disclosure of Interest:** None declared

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THU0010

### POLYMORPHISMS IN PHASE I-METABOLISING ENZYME AND HORMONE RECEPTOR GENES INFLUENCE THE RESPONSE TO ANTI-TNF THERAPY

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**Background:** Although the etiology of rheumatoid arthritis (RA) remains unclear, there are evidences suggesting a role of sex steroid hormones in determining the onset and progression of the disease.

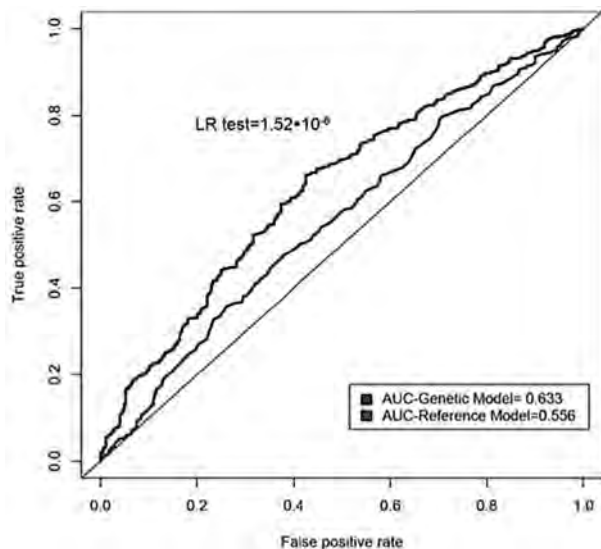
**Objectives:** The aim of this study was to evaluate whether 47 single nucleotide polymorphisms (SNPs) in steroid hormone-related genes are associated with the risk of RA and anti-TNF drug response.

**Methods:** We conducted a case-control study in 3 European populations including 2936 RA patients and 2197 healthy controls. Of those a total of 1985 RA patients were treated with anti-TNF blockers. The association of potentially interesting markers with RA risk or drug response in the discovery population was validated through meta-analysis with data from DREAM and DANBIO registries. Results were corrected for multiple testing (Meff method;  $p=0.0011$ ).

The value of steroid hormone-related variants for prediction of anti-TNF drug response was also assessed using stepwise logistic regression analyses. The area under the curve (AUC) of a receiver operating characteristic (ROC) curve analysis and a  $-2 \log$  likelihood ratio (LR) test were used to assess whether the genetic model fitted significantly better the data compared to the reference model. A randomization test (50.000 iterations) was run to confirm the consistency of the results.

**Results:** Although none of the selected variants played a relevant role in modulating RA risk, the meta-analysis of the linear regression data with those from the DREAM and DANBIO registries showed a significant correlation of the CYP3A4<sub>rs11773597</sub> and CYP2C9<sub>rs1799853</sub> variants with changes in DAS28 after the administration of anti-TNF drugs ( $p=0.00074$ , and  $p=0.006$ ). An overall haplotype

analysis also showed that the *ESR2*<sub>GGG</sub> haplotype significantly associated with a reduced chance of having poor response to anti-TNF drugs ( $p=0.0009$ ). Finally, a ROC curve analysis confirmed that a model built with 8 steroid hormone-related variants significantly improved the ability to predict drug response compared with the reference model including demographic and clinical variables (AUC=0.633 vs. 0.556;  $P_{LRtest}=1.52 \cdot 10^{-6}$ ).



**Conclusions:** These data suggest that steroid hormone-related genes play a role in determining the response to anti-TNF drugs.

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THU0011

#### LOCATION AND INTERACTION OF IGG HYPERVARIABLE REGIONS WITH PORPHYROMONAS GINGIVALIS PEPTIDYLARGININE DEIMINASE CITRULLINATED PEPTIDES, A HIGHLIGHT TO UNDERSTAND THE ASSOCIATION MODEL OF RHEUMATOID ARTHRITIS AND PERIODONTAL DISEASE: IN SILICO ANALYSIS

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**Background:** IgG antibodies against citrullinated peptides are one of the most specific biomarkers used in the classification of the disease. The relationship between RA and periodontal disease is based on the process of citrullination. The enzyme in the most important bacteria related with periodontitis (*Porphyromonas gingivalis*) the Peptidylarginine Deiminase (PPAD) modify arginine residues to citrulline

**Objectives:** To model *in silico* the binding of PPAD peptides with the hypervariable regions of IgG

**Methods:** One PPAD peptide with 15 residues was selected *in silico* by its recognition by B cells (Bcepred y ABCpred) and T lymphocytes (ProPred, MHCpred). The peptide arginines were changed *in silico* by citrulline (Cit) with the ACD/ChemSketch software, obtaining four different peptides, natural, Arg1 changed, Arg1-Arg8 changed and a random sequence. The 3D peptide modelling was obtained using PEP-FOLD Server and the 3D structure of variable domains of the heavy and light chain of IgG was obtained with the SwissModel. The amino acids of the hypervariable regions capable of interacting were defined using ConSurf Server. The peptides and variable domains were prepared using Openbabel. Docking models were performed by Patchdock and PyMOL tool was used to rendering the structural complexes obtained

**Results:** The 3D structure of IgG variable domains had a QMEN6 z-score <1. Modelling of the topological disposition of the amino acids was obtained and the interaction scores between the four peptides and light and heavy chain hypervariable regions were high, although the better score was in the natural peptide and light chain interaction. The heavy chain showed also a high score during the *in silico* interaction with the Cit1-Cit8 modified peptide. The approximate interface area of the receptor-ligand complex and the contact atomic energy (ACE) between the ligand and the receptor revealed the energy required for the interaction allowing its stability. The PPAD-IgG complexes showed the atomic contact maps in which the heavy chain hypervariable region contacted seven amino acids in all four peptides while only six contacts occurred between light chain and the peptides. The model showed the interactions between light chain and natural peptide (Arg1 with Gly100, Arg8 with Glu1) and for Cit1-Cit8 peptide, Cit8 interact with Thr10 (Cit1 has no contact). Regarding the heavy chain, Arg1 of natural peptide interacted with Trp47 while for Cit1-Cit8 peptide were Cit1 with Lys43 and Cit8 with Pro40

**Conclusions:** The *in silico* model shows bacterial PPAD peptides with and without citrullination interact with the hypervariable regions of human IgG. The citrulline residues modify the 3D structure influencing the contact area with the heavy and light chain variable regions. Peptide with modifications of two arginine residues by citrulline presented a high interaction score indicating that may have an effective recognition for IgG

**Disclosure of Interest:** None declared

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THU0012

#### TARGETED RE-SEQUENCING OF 128 RHEUMATOID ARTHRITIS SUSCEPTIBILITY GENES UNCOVERS NOVEL RISK LOCI IN THE SINGAPORE CHINESE POPULATION

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**Background:** Rheumatoid arthritis (RA) is a fairly common inflammatory autoimmune disease with a prevalence of 1% to 1.5%. Patients experience chronic joint pain, swelling and overtime irreversible joint damage. Genetic variants known to contribute to rheumatoid arthritis (RA) susceptibility have been reported in more than 120 genes, including the HLA, PTPN22, CTLA4, TNFAIP3, PADI4, FCRL3, CD4, CD244 and CD40. The genetic susceptibility to RA has not been studied in the Singapore population.

**Objectives:** To identify novel risk variants in candidate genes previously reported to be associated with rheumatoid arthritis (RA) in Singapore Chinese RA patients positive for anti-citrullinated peptide antibodies (ACPA).

**Methods:** All the 128 known candidate genes associated with RA identified through GWAS were sequenced in 48 RA patients and 45 controls. The resultant data was analysed for association using single variant association and pathway-based association enrichment tests. In addition, the genetic burden due to rare variants was assessed using the C-alpha test. The candidate variants that showed significant association were validated in a larger cohort of 500 RA cases and 500 controls using mass array and Taqman technologies.

**Results:** 39 variants in 18 genes were identified using single variant association analysis and C-alpha test. IL6ST, with stepwise filtering. Among these, the missense variant in IL6ST, 5:55260065 (p.Cys47Phe) was significantly associated with RA in the Singapore Chinese patients ( $p=0.0194$ ). The insignificant results of additional potential rare variants such as IL6ST, 5:55237103 and PXR rs199881366 is highly due to the limitations of our small sample size.

**Conclusions:** Our results suggest that IL6ST, 5:55260065, 5:55237103 and PXR rs199881366 confer risk of RA in ACPA-positive Chinese patients.

**Disclosure of Interest:** None declared

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**THU0013 DOWNREGULATION OF MICRORNA MAY CONTRIBUTE TO ACTIVATION OF THE INTERFERON SIGNALLING PATHWAY IN THE IDIOPATHIC INFLAMMATORY MYOPATHIES**

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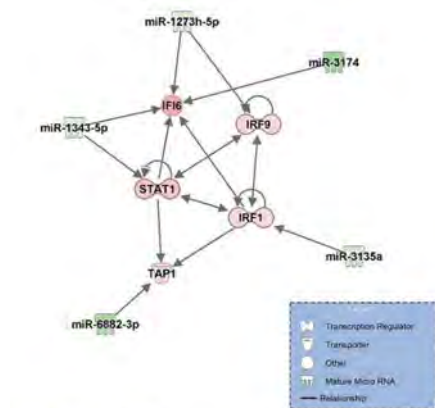
**Background:** The idiopathic inflammatory myopathies (IIM) are a group of rare autoimmune conditions characterised by weakness and inflammation of skeletal muscle. MicroRNA are short single stranded RNA which regulate gene expression by binding to particular target mRNA and suppressing translation or inducing degradation. MicroRNA are known to play a role in muscle homeostasis and immune regulation and therefore may be involved in IIM pathology.

**Objectives:** To profile both microRNA and mRNA in whole blood samples from polymyositis (PM), dermatomyositis (DM) and inclusion body myositis (IBM) patients compared to non-myositis controls using next generation RNA sequencing.

**Methods:** Whole blood samples in tempus tubes were collected as part of the myositis research tissue bank held at the University of Manchester. Total RNA was extracted from 7 PM, 7 DM, 5 IBM and 5 non-myositis control samples and both microRNA and mRNA profiles were determined by sequencing on the Illumina HiSeq 4000.

**Results:** Analysis of microRNA expression identified 19 microRNAs as significantly differentially expressed (DE) ( $p < 0.05$ ) for PM, 11 for DM and 27 for IBM, compared to controls. Analysis of myositis specific autoantibody anti-Jo1 positive cases (four PM and one DM) vs controls identified 18 DE microRNAs, 12 of which were not identified for any of the clinical subgroups.

Gene expression analysis identified 129 significantly DE genes for PM (false discovery rate  $< 0.05$ ), 53 for DM, 24 for IBM and 691 for anti-Jo1 compared to controls. Ingenuity pathway analysis (IPA) of RNAseq data identified the most significant canonical pathway as 'Interferon signalling' which was predicted to be upregulated in PM, DM and anti-Jo1 subgroups. The anti-Jo1 subgroup had a higher number of DE genes and a higher activation score in the interferon signalling pathway compared to PM or DM. The IPA tool microRNA target filter was used to match DE microRNA with corresponding DE mRNA predicted or previously observed to be targets. When mRNA targets were filtered for involvement in interferon signalling, two downregulated microRNA targeted two upregulated mRNA in PM and five downregulated microRNA targeted five upregulated mRNA in the anti-Jo1 group as shown in figure 1. No microRNAs targeting mRNA involved in the interferon signalling pathway were identified for DM or IBM.



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**Abstract THU0013 – Figure 1.** Relationship between differentially expressed microRNA in anti-Jo1 samples versus controls and mRNA targets involved in the interferon signalling pathway. Green colouring indicates downregulation; red colouring indicates upregulation and darker shades indicate greater fold change.

**Conclusions:** To our knowledge this is the first mRNA and microRNA profiling study in whole blood from myositis patients using RNA sequencing. Grouping by anti-Jo1 positivity identified different microRNA and increased predicted activation of interferon signalling compared to the clinical subgroups analysed. Our results suggest that increased activation of the interferon pathway in anti-Jo1 positive patients may be due to downregulation of microRNAs which target genes in this pathway.

**Disclosure of Interest:** None declared

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**THU0014 GENETIC SCREENING FOR IDENTIFYING HUMAN GENES REGULATING FIBROSIS IN SYSTEMIC SCLEROSIS**

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**Background:** Systemic sclerosis (SSc) is a prototypic multi-systemic fibrotic disease. Fibrosis involves exacerbated collagen production. A lack of effective therapies has partly been due to incomplete understanding of the mechanisms of fibrosis and inadequate subsetting of this heterogeneous disease to allow targeted treatment. Identification of a collagen-synthesis gene signature in SSc will enhance our ability to molecularly subset SSc patients. We reasoned that there exists several unidentified genes regulating collagen synthesis, whose dysregulation play key roles in fibrosis underlying SSc.

**Objectives:** To discover novel genes/pathways involved in elevated collagen synthesis

**Methods:** We conducted a pioneering forward-genetics approach using genome-wide ribonucleic acid interference (RNAi) –screening. We performed RNAi-screening in dermal fibroblasts from three patients with early diffuse cutaneous systemic sclerosis (onset from the first non-Raynaud's manifestation of less than 3 years). Dermal fibroblasts were immortalised using ectopic expression of human telomerase. The assay used a collagen promoter driver reporter system for identifying genes regulating collagen transcription.

**Results:** The genetic screen identified 187 genes whose silencing altered the activation of collagen promoter activity. This included 82% and 18% positive and negative regulators, respectively. A system-level view of genes and signalling pathways regulating collagen synthesis was generated using bioinformatics analysis.

**Conclusions:** We anticipate that this catalogue of collagen expression regulating genes will help to unravel the dysregulated genetic regulatory modules of fibrosis and may aid in the diagnostics of different clinical subsets of SSc.

**Disclosure of Interest:** None declared

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**THU0015 OESTROGEN DEPENDENT REGULATION OF MICRO-RNA IN RHEUMATOID ARTHRITIS**

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**Background:** Oestrogen has ameliorating effects on rheumatoid arthritis (RA). Oestrogen receptor (ER) signalling affects micro-RNA (miR) expression and processing in breast cancer, while its effect on miR profile in RA have never been studied.

**Objectives:** To study the effect of the oestrogen replacement therapy and oestrogen receptor signalling on the miR transcription and bioprocessing in RA patients.

**Methods:** The expression of the key miR processing enzymes Dicer, Drosha and DGCR8 was measured in the leukocytes of the peripheral blood of 145 female RA patients (age 53 years, disease duration 9.8 years) by RT-PCR and analysed with respect to the levels of ER $\alpha$ , used as surrogate marker of active ER $\alpha$  signalling. Total RNA was prepared from the serum samples of 46 postmenopausal female RA patients who received treatment with oestradiol (E2), noretisterone acetate, vitamin D<sub>3</sub> and calcium (n=22, mean E2 levels 229.4 $\pm$ 143.2 pg/ml) or vitamin D<sub>3</sub> and calcium supplementation only (n=24, mean E2 levels 30.8 $\pm$ 8.7 pg/ml). Serum was obtained after 12 and 24 months of treatment and was stored at  $-70^{\circ}\text{C}$  until the time of analysis. MicroRNA transcription was performed by 3D-Geno microarray measuring >2560 miRs (TATAA Biocenter, Gothenburg).

**Results:** A higher ER $\alpha$  expression in RA female patients was associated with increased transcription of the major miR processing proteins Dicer ( $p=0.0057$ ), Drosha ( $p=0.019$ ) and DGCR8 ( $p=0.0095$ ). This activated transcription of miR biomachinery could indicate a higher demand and a facilitated miR maturation. The E2-treatment significantly changed the profile, but not the levels, of miRs in serum, where only 50% of the miR transcripts were present both in E2-treated and control samples. Also the profile of miRs related to RA and of those regulating translation of ER $\alpha$  and Dicer, Drosha, and DGCR8 proteins was affected. Extensive bioinformatic analysis of the miR-targeting genes affected during E2-treatment, revealed a reduction of gene clusters aiding autoimmune pathology and the RA-associated molecular processes including DNA replication ( $p=2.6 \times 10^{-4}$ ), peptidyl-serine phosphorylation ( $p=2 \times 10^{-4}$ ), protein localization to nucleus and nuclear import ( $p=5 \times 10^{-4}$ ).



**Conclusions:** Activation of ER $\alpha$  significantly enhances the miR processing, and affects the profile of miR transcription in female RA patients. The change in miR profile during E2-treatment could contribute to a significantly change in the miR landscape and disposition of intracellular processes in RA.

**Disclosure of Interest:** None declared

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**THU0016 TRANSMITOCHONDRIAL CYBRIDS SHOW THAT OXPHOS VIA, BUT NO GLYCOLYSIS VIA, IS INVOLVED IN THE ATP REDUCTION OF OA HUMAN CHONDROCYTES**

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**Background:** Mitochondrial dysfunction is well documented in OA and has the capacity to alter chondrocyte function and viability, contributing to cartilage degeneration. It is important to evaluate the influence of mitochondria in the pathogenesis of OA using an *in vitro* model to explain the functional consequences of this association and help us to identify potential diagnostic biomarkers and/or therapeutic targets. Transmitochondrial cybrids are a useful cellular model to study the mitochondrial biology and function implications in the cellular behaviour, since they carry different mitochondrial variants with the same nuclear background, therefore, excluding the variations because of nuclear genome.

**Objectives:** The aim of this work is test mitochondrial activity in the OA chondrocytes using transmitochondrial cybrids with mtDNA from healthy donors (without OA) and from patients with OA.

**Methods:** Cybrids were developed using 143B.TK<sup>-</sup> Rho-0 cell line (nuclear donor) and platelets (mitochondrial donors) from healthy and OA donors. Human articular chondrocytes were obtained from patients with hip replacement. The mtDNA copy number was measured by real-time PCR method. The ROS production was evaluated using flow cytometry. The metabolic status was evaluated by glucose consumption and glucose oxidation. The glycolytic activity was measured after addition of glucose, oligomycin and 2-dioxylglucose using Seahorse XFp (ECAR). The OXPHOS function was evaluated by SeaHorse XFp (OCR) after addition of oligomycin, FCCP and Rotenone/Antimycin. Appropriate statistical analyses were performed with GraphPad Prism v6.

**Results:** The analysis of mtDNA copy number showed that the OA have higher levels than N in cybrids and human chondrocytes. The analysis of ROS production showed that OA had higher levels than N in both types of cells. The metabolic status analysing glucose consumption, glucose oxidation and total glucose cellular uptake reflected higher values in OA cybrids than N cybrids. But the analysis of glycolysis data showed lower values in OA than N cybrids. The analysis of ATP obtained through glycolysis did not show any difference between cybrids. The analysis of OXPHOS function showed that OA had lower basal respiration and maximal respiratory capacity than N in both types of cells. The ATP obtained via OXPHOS was lower in OA than in N.

**Conclusions:** The analysis of OXPHOS function supports the participation of mitochondria in cybrids and human chondrocytes metabolism. Both types of cells use the mitochondria to obtain ATP and OXPHOS via, but no glycolysis, is involved in the reduction of ATP synthesis by OA cells. All these data support that N cybrids and chondrocytes use mitochondria with more efficiency.

**Disclosure of Interest:** None declared

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**THU0017 DNA METHYLATION OF REGULATORY SITES OF HAND OSTEOARTHRITIS SUSCEPTIBILITY GENES IN FINNISH WOMEN**

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**Background:** Despite the hard effort in OA genetic studies only a small part of the estimated effect has been found so far and thus the focus has been changing from genetic to epigenetic studies. The most widely studied epigenetic control mechanism is DNA methylation. There are only few studies on hand OA concerning DNA methylation but their results are promising.

**Objectives:** Our aim was to study methylation of the regulatory sites of our previously found hand OA susceptibility genes and to replicate some previously reported methylation sites associated with hand OA, in our Finnish women hand OA material.

**Methods:** The study design was cross-sectional. Bilateral hand radiographs of 542 occupationally active Finnish female dentists and teachers aged 45 to 63 and

classified them according to the presence of OA by using reference images. Radiographic hand OA at least mild, in at least three joints (ROA2\_3), and radiographic findings summary score (OASUM) were used to define hand OA status. The methylation percentages were determined by bi-sulfite converted DNA pyrosequencing with commercial CpG Assays. Statistical analyses were performed using hierarchical multiple linear regression.

**Results:** Of the studied methylation sites the COL2A1\_1 methylation site was associated with ROA2\_3 (p=0.04). Also ALDH1A2\_01 methylation site was associated with OASUM (p=0.02). When the data was stratified by occupation the association was only significant, and stronger, in teachers but not in dentists (COL2A1\_1 p=0.02 vs. p=0.36 for ROA2\_3, and ALDH1A2\_1 p=0.01 vs. p=0.36 for OASUM, respectively). The studied methylation sites in TGFB1, RRP9 and TRAPP5 genes had methylation percentages under the detection limit and they were excluded from the analysis.

**Conclusions:** Our results lend further support to COL2A1 and ALDH1A2 being hand OA susceptibility genes at the epigenetic level.

**Acknowledgements:** The study was financially supported by a grant from the Finnish Work Environment Fund (113369).

**Disclosure of Interest:** None declared

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**THU0018 MIRNAS-146A AND -499 GENE EXPRESSION AND THEIR POLYMORPHISMS AS DIAGNOSTIC MARKERS FOR RHEUMATOID ARTHRITIS**

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**Objectives:** To investigate the expression of miRNAs-146a and -499 and their polymorphisms in Egyptian patients with RA and to evaluate their relationship to clinical manifestations and disease activity.

**Methods:** Fifty-two RA patients and 56 matched controls were studied. Disease activity score-28 was assessed. MicroRNAs expression and polymorphisms were assayed by polymerase chain reaction (PCR).

**Results:** Patients mean age was 39.5±10.8 years and the disease duration of 7±5.1 years. The DAS28 was 3.1±1.7; 23 were in remission, 5 had mild disease activity, 18 moderate and 6 severe. There was a 15.5±27.2 fold increase in miRNA-146a and 3.3±6.1 in miR-499. The fold change of miRNA-146a was significantly higher in those without joint deformities (n=18) (28.1±42.6) compared to those with (8.8±8.4; p=0.01). Both miRNA-146a and -499 fold change were significantly decreased in those with a positive ANA (n=7) (2.5±2.1 and 0.07±0.08) compared to those with a negative test (18.1±29.6 and 3.8±6.5; p=0.002 and p=0.001 respectively). The fold changes tended to be higher in those in remission compared to active patients. However, miRNA-499 in those with severe disease activity tended to be higher. There was no significant correlation of the fold change of the miRNAs with the clinical manifestations or medications received. Only ANA positivity significantly inversely correlated with the fold increase in miRNA-146a (r=-0.42, p=0.003). The fold change in miRNA-146a significantly correlated with miRNA-499 (r=0.56, p<0.0001).

**Conclusions:** Both miRNAs-146a and -499 are highly expressed in RA patients and can be considered as diagnostic markers. Increased expression of miRNA-146a expression is protective in those with negative ANA and both in those without joint deformities.

**Disclosure of Interest:** None declared

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**THU0019 ARE MICRORNAS A MOLECULAR CLOCK? THE NEWCASTLE THOUSAND FAMILIES COHORT STUDY**

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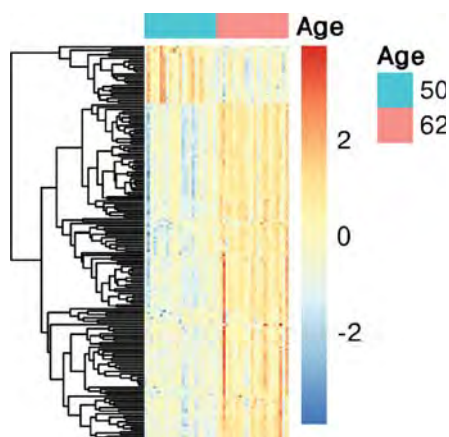
**Background:** No single biomarker has been identified for monitoring ageing trajectory. To date, biological clocks are based on DNA methylation, telomere length, p16<sup>ink4a</sup> expression and microsatellite mutations<sup>1</sup>. Body ageing is a complex phenomenon, including a progressive, pro-inflammatory state, termed 'inflammaging'. MicroRNAs have been linked with cellular senescence and inflammaging. MicroRNAs are short, non-coding sequences of RNA regulating post-transcriptional gene expression with impressive stability and ubiquitous presence, making them ideal candidate biomarkers. Previous studies of circulating microRNAs in ageing were small-scale<sup>2</sup> or compared individuals of different ages, which is methodologically less robust<sup>3</sup>. MicroRNA biomarkers can bring greater understanding to

ageing mechanisms, diagnosis/prognosis of age-related disease and even novel treatment targets.

**Objectives:** To quantify relationships between circulating microRNA expression and biological ageing and determine whether microRNAs may be a molecular clock.

**Methods:** This pilot work is a nested substudy within a prospective, longitudinal birth cohort from May/June 1947 (the Newcastle Thousand Families Study NTFs). Serum samples from 23 subjects taken at ages 50 and 62 years were extracted from the biobank. HTG EdgeSeq microRNA whole transcriptome assay was performed, measuring expression of 2083 human microRNA transcripts using an array followed by next generation sequencing. Global microRNA expression profiles were generated and analysed using this technology, profiling all known microRNAs from a small volume of serum (<15  $\mu$ L). NIHR funding has been secured for whole cohort analysis.

**Results:** Resulting data has shown very strong associations (up to  $p < 10^{-12}$ ) for biological ageing, with 84 microRNAs meeting  $p$ -values  $< 0.05$  (see heat map). Analysing the whole cohort will independently validate and extend the findings, in order to identify an ageing signature; the molecular clock.



**Conclusions:** This study suggests very strong changes in microRNAs in individuals between 50 and 62, suggesting microRNA signature is a molecular clock. These observations need to be confirmed and extended to validate serum microRNAs as biomarkers for ageing, for early detection of age-related disease and as tools to monitor ageing trajectory.

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#### THU0020 TOCILIZUMAB DECREASES THE PRO-INFLAMMATORY ROLE OF PLATELETS IN RHEUMATOID ARTHRITIS: IDENTIFICATION OF A NEW MECHANISM OF ACTION ASSOCIATED WITH POSITIVE RESPONSE?

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**Background:** Tocilizumab (TCZ), a humanised monoclonal antibody directed against IL-6 receptor, is an efficient treatment for rheumatoid arthritis (RA) but its mechanisms of action are not yet well understood.

**Objectives:** To identify new mechanisms of action of TCZ, by the study of gene expression fluctuations, between baseline (BL) and 3 months of treatment (T<sub>3m</sub>), in RA patients.

**Methods:** TOSCA study has been realised to evaluate efficiency and tolerance of TCZ administrated subcutaneously in active RA patients. Among the 125 patients of TOSCA study, 38 were ranked according to their treatment response after 3 months: 29 good responders (GR), 19 of which were also treated by methotrexate (MTX) and 10 non responders (NR), 7 of which were treated by MTX (GR: DAS 28-ESR<sub>3m</sub> <3,2 and Delta DAS28-ESR<sub>(BL-3m)</sub> ≥3; NR: DAS 28-ESR >3,2 and Delta DAS28-ESR<sub>(BL-3m)</sub> <3). A transcriptomic analysis was performed using a 44K whole human genomic DNA microarray (Agilent) on whole blood cells collected at BL and at T<sub>3m</sub>. We identified genes with statistically significant expression fluctuations between BL and T<sub>3m</sub> specifically in GR group (and not in NR group), treated by TCZ in monotherapy (excluding genes which fluctuated only with the association TCZ-MTX). Functional bio-informatics analysis was applied to this set of transcripts, by interrogation of Gene Ontology database, using Single Experiment Analysis tool and Natural Language Processing algorithms.

**Results:** Overall, 1089 transcripts significantly dysregulated were identified only in GR group at T<sub>3m</sub> (t test,  $p < 0.05$ ). This first set of transcripts was reduced to 783 by exclusion of transcripts that were fluctuated specifically when MTX was associated with TCZ in GR group. The functional analysis with these 783 genes dysregulated under TCZ in monotherapy enabled the identification of 8 transcripts (*CLU*, *F13A1*, *ITGA2B*, *ITGB3*, *SELP*, *SNCA*, *SPARC*, *TREML1*) whose relative abundances were significantly reduced at T<sub>3m</sub>. These genes were enriched in "platelet alpha granule" GO functional category. Proteins encode by these genes, either released in blood circulation or expressed at the cell membrane in case of platelet activation, have a pro-inflammatory activity through an interaction between platelets and immune cells.

**Conclusions:** This transcriptomic analysis suggests a new mechanism of action of TCZ in RA and the importance of platelets activation in RA pathophysiology. Indeed, genes linked with the pro-inflammatory role of platelets were down regulated. Further functional studies will be necessary to validate the direct effect of TCZ on platelets in RA.

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#### THU0021 DIFFERENTIAL EFFECTS OF TR14 VERSUS DICLOFENAC ON COX/LOX PATHWAYS REVEALED BY RNASEQ

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**Background:** Anti-inflammatory agents are used widely in treating numerous pain and inflammatory conditions. With a focus on the COX/LOX pathways in cutaneous wound repair in mice, the therapeutic activities of Tr14 (Traumeel), a multicomponent/multitarget natural product, and diclofenac (NSAID), a non-selective cyclooxygenase (COX) inhibitor were compared. The COX enzymes convert arachidonic acid into prostaglandins and thromboxanes, while the lipoxygenase (LOX) pathway generates more pro-inflammatory leukotrienes. Differential effects were identified via transcriptome analysis (RNAseq).

**Objectives:** To compare the transcriptomic changes after administration of Tr14 or diclofenac in a mouse cutaneous wound healing model, with particular emphasis on the COX/LOX pathway.

**Methods:** After abrasive wounding, the wounds were treated with topical Tr14 (34 mg/ml) in combination with subcutaneous Tr14 injections (9.5 mg/ml), or with subcutaneous Tr14 injections only, or topical diclofenac at clinically relevant doses (2 mg/ml). Skin samples were analysed for RNA transcript profiling by RNAseq at specific times (12 hour, 24 hour, 36 hour, 72 hour, 96 hour, 120 hour, 192 hour) after injury. Differentially expressed genes (DEGs) were computed at each time point between diclofenac vs control or Tr14 vs control, using EdgeR.

**Results:** At early time points (12–36 hour), both control and Tr14-treated wounds showed marked increase in the inducible COX2 enzyme mRNA, while diclofenac-treated wounds did not, likely due to blocking the PGE2 necessary for the feedback induction. Tr14, in contrast, had a striking inhibitory effect on mRNA levels

for leukotriene A4 hydrolase, which converts LTA4 to LTB4; microsomal glutathione S-transferase, which converts LTA4 to LTC4; and gamma-glutamyltransferase (LTC4 >LTD4). In contrast, Tr14, but not diclofenac strongly induced Nrf2 mRNA at 12–36 hours.

**Conclusions:** Tr14 and diclofenac had very different effects on the COX/LOX synthetic pathway after cutaneous wounding. Tr14 allowed normal autoinduction of COX2 mRNA by PGE2, but suppressed mRNA levels for the key enzymes in the leukotriene synthetic pathway. A likely explanation for these effects is that Tr14 strongly induced Nrf2 mRNA, which is known to co-repress the leukotriene enzymes via transcription factor Bach1.

**Disclosure of Interest:** None declared

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### THU0022 ANALYSIS OF 47 NON-MHC ANKYLOSING SPONDYLITIS SUSCEPTIBILITY LOCI REVEALS SHARED ASSOCIATED VARIANTS ACROSS CAUCASIANS AND CHINESE HAN

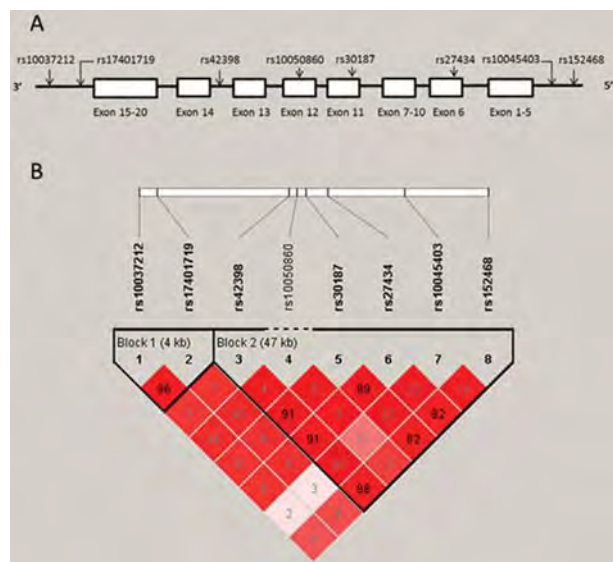
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**Background:** Genetic factors play a prominent role in AS pathogenesis. So far over 40 non-MHC Ankylosing Spondylitis(AS) susceptibility loci with genome-wide or suggestive significance have been initially reported in Caucasians, however, lack of association evidence of most loci was seen in Chinese Han and some results seemed controversial.

**Objectives:** Here, we present a systematic evaluation of 47 non-MHC AS susceptibility loci using GWAS datasets in Chinese Han.

**Methods:** Totally 1853 AS cases and 4048 newly matched controls in 4 cohorts were obtained, after imputation meta-analysis results of 93 589 variants within 47 reported loci were extracted. Best-guess genotype data were used for interaction analysis and weighted genetic risk score model construction which was then assessed by receiver operator characteristic analysis. Functional annotation was conducted using HaploReg, RegulomeDB and rVarBase Database.

**Results:** We revealed 14 AS-associated variants with nominal association in Chinese Han, including rs10865331(p=2.96E-9), rs10050860 (p=1.84E-4) and rs8070463(p=2.81E-4) and found potential associated variants within these loci. We then extracted variants in ERAP1 as well as HLA-B27 tag snp rs13202464 for HLA-B27-ERAP1 interaction analysis (figure 1). Epistatic association between ERAP1 (rs30187, rs10045403) and HLA-B27 (rs13202464) was confirmed. Among those 14 variants, rs30187 showed weaker risk effect in Chinese while rs10050860 and rs12504282 seemed to attribute more risk (Table 1). Genetic prediction model combining 14 variants in 11 loci with HLA-B27 achieved better discrimination ability(AUC=0.884, 95%CI=0.873~0.895) than HLA-B27 alone (p=2.17E-6). We also identified some likely functional variants at these loci.



Abstract THU0022 – Figure 1

**Abstract THU0022 – Table 1.** Comparison of 14 shared associated non-MHC SNPs across European and Chinese

Locus	SNP	Nearby Gene(s)	Risk allele	RAF% (CEU/CHN)	OR (CEU/CHN)	PARP% (CEU/CHN)
1 p36	rs6600247	RUNX3	C	0.50/0.69	1.16/1.15	7.41%/9.42%
2 p15	rs10865331	Intergenic	A	0.38/0.49	1.34/1.27	11.44%/11.60%
3 p24	rs10510607	CMC1	C	0.83/0.54	1.15/1.14	11.07%/7.03%
4q21	rs12504282	ANTXR2	T	0.54/0.91	1.14/1.20	7.03%/15.38%
5 p13	rs11742270	IL7R	G	0.73/0.84	1.11/1.14	7.43%/10.53%
5q15	rs30187	ERAP1	T	0.34/0.53	1.32/1.11	9.81%/5.47%
5q15	rs10045403	ERAP1	A	0.73/0.82	1.20/1.18	12.74%/12.92%
5q15	rs10050860	ERAP1	C	0.78/0.95	1.18/1.45	12.31%/30.01%
6q15	rs639575	BACH2	T	0.61/0.49	1.08/1.10	4.65%/4.69%
14q13	rs8006884	PPP2R3C	C	0.35/0.40	1.11/1.09	3.71%/3.44%
17q11	rs2297518	NOS2	A	0.19/0.16	1.13/1.11	2.41%/1.72%
17q21	rs9901869	NPEPPS	A	0.52/0.62	1.15/1.14	7.24%/7.95%
17q21	rs8070463	TBKBP1	C	0.51/0.44	1.14/1.16	6.66%/6.64%
21q22	rs2836883	Intergenic	G	0.74/0.83	1.19/1.16	12.33%/11.71%

**Conclusions:** Our results provided a detailed spectrum of non-MHC AS susceptibility loci in Chinese Han and highlighted 2 p15, ERAP1 and TBKBP1 may play a critical role in AS pathogenesis.

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**Disclosure of Interest:** None declared

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THURSDAY, 14 JUNE 2018:

### Adaptive immunity (T cells and B cells) in rheumatic diseases

#### THU0023 COMPLEX IMMUNOPHENOTYPING STRATIFIES PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME, SYSTEMIC LUPUS ERYTHEMATOSUS AND SECONDARY SJÖGREN'S SYNDROME ASSOCIATED WITH SYSTEMIC LUPUS ERYTHEMATOSUS INTO DISTINCT CLINICALLY RELEVANT GROUPS WITH POTENTIAL THERAPEUTIC IMPLICATIONS

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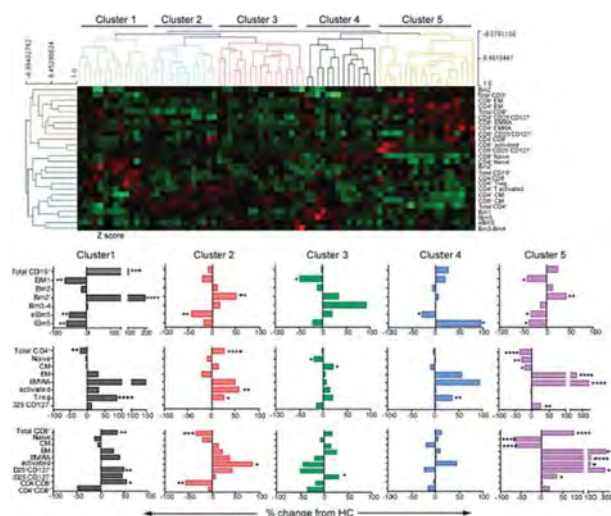
**Background:** Similarities in the clinical and laboratory features of patients with primary Sjögren's syndrome (pSS) and systemic lupus erythematosus (SLE) have led to attempts to treat pSS and SLE patients with similar biologic therapeutics. However, the results of many clinical trials are disappointing and no effective treatments are available for pSS and few for SLE patients with refractory disease.

**Objectives:** To identify novel patient endotypes using in depth immune phenotyping that facilitates the selection of biological therapies for patients regardless of diagnostic labels.

**Methods:** Peripheral blood was collected from patients with pSS (n=55), SLE (n=38), SS/SLE (n=15) and age/sex-matched healthy controls (HCs) (n=34). In-depth phenotyping of peripheral B and T-cell subsets by flow-cytometry, followed by unsupervised cluster analysis were performed. ROC analysis identified immune signatures characteristic for every cluster (endotype).

**Results:** Patients with pSS, SLE and SS/SLE had both unique and shared defects in immune cell phenotype. Hierarchical clustering of CD19<sup>+</sup> B-cells, CD4<sup>+</sup> and CD8<sup>+</sup> T-cells across the three disease groups identified five distinct endotypes spanning diagnostic boundaries. Three of the endotypes had distinct immune signatures, characterised by predominantly B-cell, T-cell memory or CD4<sup>+</sup>/CD8<sup>+</sup> T-cell subset fingerprints respectively, while two clusters had no distinct immune profiles. Notably, clinical and disease features were not significantly different between clusters.





**Conclusions:** The results demonstrated that immune cell biomarkers could be used to re-classify patients in a manner that reflects their underlying immunopathogenesis. Characterisation of a patient's endotype could lead to better stratification of patients for selection of therapeutic targets in clinical trials.

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#### THU0024 TREATMENT WITH IMMUNE CHECKPOINT INHIBITORS AND THE BREAK OF B-CELL TOLERANCE TO AUTOANTIGENS

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**Background:** The field of autoimmunity may benefit from the knowledge gained by studying immune checkpoint inhibitors. These agents, which have proven remarkably successful in treating various types of cancer, inhibit negative costimulatory signals to T-cells, thereby enhancing anti-tumour T-cell responses. This can come at the cost of severe immune-related adverse effects (irAEs) including arthritis, colitis, endocrine diseases, hepatitis, and various skin abnormalities. However, it is currently unknown to which extent or to which autoimmune disease-associated autoantigens autoantibodies are formed (as a reflection of breaking of tolerance to self-antigens) under checkpoint inhibitor therapy and whether this is associated with irAEs.

**Objectives:** To investigate whether patients treated with immune checkpoint inhibitors develop autoantibodies, and whether this trait is associated with irAEs.

**Methods:** In pre- and (12 weeks) post-treatment sera of 133 patients with Stage III or IV melanoma treated with ipilimumab (anti-CTLA-4), we determined antibodies associated with rheumatoid arthritis (RF IgM, anti-CCP2), autoimmune hepatitis (anti-smooth muscle, anti-mitochondria, anti-liver-kidney-microsome), thyroiditis (anti-thyroid peroxidase (TPO), anti-thyroglobulin (TG)), Coeliac's disease (anti-endomysium, anti-gliadin IgG), adrenal insufficiency (anti-adrenal cortex), and autoimmune connective tissue diseases (anti-nuclear antibodies, anti-dsDNA, anti-ENA, and specific ENA tests: anti-SSA, anti-SSB, anti-RNP70, anti-U1RNP, anti-Sm, anti-Jo1, anti-CENP, anti-PMSCL, anti-RNA polymerase 3, anti-Scl70). We used McNemar's exact test for paired data to test whether autoantibody positivity increased post-treatment, and investigated by Fisher's exact tests whether developing autoantibodies was associated with system-specific (Grade 3 or 4) irAEs.

**Results:** In total, post-treatment positivity for any autoantibody was seen in 19.2% (19/99) of patients that were fully autoantibody-negative pre-treatment ( $p < 0.0001$ ). A significant association was observed between development of any

autoantibodies and any irAEs: 14/19 (73.7%) patients that developed autoantibodies had irAEs, versus 37/80 (46.3%) patients that did not develop autoantibodies (OR: 3.3 [95% CI: 1.1 to 9.9]). Regarding specific autoantibodies, predominantly anti-TPO (4.8%, 6/125) and anti-TG antibodies (6.0%, 8/132) developed in patients negative for these autoantibodies at baseline ( $p=0.03$  and  $p=0.008$ , respectively). However, development of these antibodies was not associated with development of thyroid disease. For most other autoantibodies, including RA-associated antibodies, post-treatment positivity increased only marginally and was not associated with occurrence of irAEs in the organ system related to the specificity of the autoantibody.

**Conclusions:** Breaking of humoral tolerance as measured by development of autoantibodies is relatively common under treatment with ipilimumab and is associated with the development of irAEs. The nature of the autoantigens towards which tolerance is broken is not reflected in the phenotype of the irAEs.

**Disclosure of Interest:** None declared

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#### THU0025 FLORID SYNOVITIS AFTER PD1 ANTAGONIST THERAPY IS CHARACTERISED BY A MARKED ABSENCE OF PD1+ INFILTRATING T CELLS

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**Background:** Although immunological blockade of checkpoint inhibitors (CIs) for cancer therapy is known to be associated with exacerbated inflammation recapitulating many features of autoimmunity<sup>1</sup>, including synovitis resembling rheumatoid arthritis (RA)<sup>2</sup>, no reports have investigated cellular infiltrates in synovial tissue (ST) of these patients. Here we provide the first report on ST cell infiltration, in particular PD1 expressing T cells, after a PD1 inhibitor-induced (Nivolumab) immune related adverse event (irAE) and severe synovitis.

**Objectives:** To characterise ST cellular infiltration in PD1 inhibitor induced arthritis with particular reference to PD1 positive T cells and compare these changes with active early RA ST.

**Methods:** Arthroscopic ST biopsies, parallel synovial fluid (SF) and PBMCs were collected from a DMARD-naïve nivolumab-treated small cell lung cancer (SCLC) patient with severe peripheral inflammatory polyarthritis (negative RF and ACPA; no axial or extra-articular irAE); 3 DMARD-naïve patients with seropositive early RA (<12 months duration; fulfilling 2010 ACR/EULAR criteria) were used as comparators.

Serial sections from fresh-frozen ST blocks were stained with H and E, CD3, CD45RO, CD55 and CD68 and semi-quantitatively scored as described<sup>3</sup>. ST, SF and PBMC cell suspensions were stained with Zombie UV (BioLegend), CD45RO, PD1, CD3, ICOS, CD8, CD4, CD20 (all BD) prior to flow cytometry. Cells were gated on live, singlet, lymphocytes, CD3+ and CD4+ T cells, and CD20+ and CD8+ T cells were excluded from endpoint PD1+, ICOS+ and CD45RO+ analysis.

**Results:** CD68 +macrophage, CD20+ B cell and CD3+ T cell and CD45RO +memory T cell infiltration in IC-irAE was comparable to RA ST on semi-quantitative scoring, while TNF; staining was markedly elevated in CI-irAE compared to RA (CI-irAE-TNF; 4, RA-TNF; 2). Flow cytometry identified a striking absence of PD1+ ICOS+ CD4+T cells in IC-irAE SCLC in all compartments (CI-irAE: ST; 0.06, SF; 0.01, PBMCs; 0.00) compared to RA (RA: ST mean and SEM; 22.13 ±3.63; SF; 45.95±1.85; and to a lesser extent in PBMCs; 0.41±0.13; n=3 for each), despite comparable CD4 +T cell frequency in each compartment (frequency of CD3 +cells, CI-irAE: ST; 57.8, SF; 64.7, PBMCs; 38.2, RA: ST; 45.9 ±15.3, SF; 49.5±11.2, PBMCs; 62.2±13.8, figure 1).

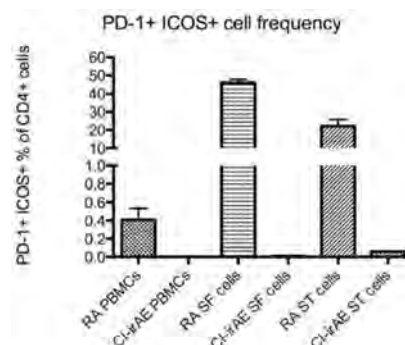


Figure 1 PD-1 +ICOS + T cells are absent in CI-irAE. Showing the PD-1 +ICOS + frequency of CD4 +T cells gated on live, singlet, lymphocytes, and

CD3+, CD20- and CD8-cells. (RA: ST mean and SEM; 22. 13±3.63: SF; 45.95 ±1.85 n=3 for each, CI-irAE: ST; 0.06, SF; 0.01, PBMCs; 0.00, n=1 for each).

**Conclusions:** While ST infiltration in CI-irAE SCLC recapitulates many features of RA histopathology, PD1 expression principally distinguishes RA from irAE ST T-cell infiltration. Despite abundant CD4 and CD45RO memory T cell infiltration in CI-irAE comparable with RA, we found a conspicuous absence of PD1 positive T-cells. Further research is needed to fully understand the nature of reduced PD1 expression in this setting and the source of elevated TNF, which could shed light on the pathogenesis of CI-irAE and guide CI-irAE management.

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**Disclosure of Interest:** None declared

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#### THU0026 ORGANISED B CELLS AND PLASMA CELLS IN THE AORTA OF GIANT CELL ARTERITIS PATIENTS

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**Background:** Giant cell arteritis (GCA) is the most common type of systemic vasculitis. Currently, two forms of GCA are described: a cranial(C)-GCA and a systemic, large-vessel (LV)-GCA. LV-GCA frequently occurs without specific symptoms and late complications are aortic aneurysms or aortic rupture. Based on the analysis of temporal artery biopsies (TAB), GCA is postulated to start at the adventitial site and to be T cell-mediated. In the temporal artery infiltrates, T cells clearly outnumber B cells. Interestingly, we recently documented decreased numbers of B cells and elevated BAFF levels in newly diagnosed GCA patients prompting further research into the pathogenic role of B cells in GCA. Recent work in TAB of C-GCA patients demonstrated the presence of B cells and their organisation into artery tertiary lymphoid organs (ATLOs).

**Objectives:** Our objective was to investigate the presence and organisation of B cells in the aorta of patients with

#### LV-GCA:

**Methods:** Aorta tissue samples of 9 histologically-proven LV-GCA patients who underwent surgery due to an aortic aneurysm were studied by immunohistochemistry. Staining was performed with antibodies detecting CD20 (B cells), CD3 (T cells), CD21 (follicular dendritic cells (FDC)), PNA<sup>ad</sup> (high endothelial venules (HEV)), bcl6 (germinal centre B cells), CD138 (plasma cells) and adipophilin (atherosclerotic plaque/macrophages). None of the patients received immunosuppressive treatment at the time of surgery. For comparison, 22 aorta samples from age- and sex-matched atherosclerosis patients with an aortic aneurysm were included.

**Results:** Aorta tissues of LV-GCA patients showed massive infiltration of B cells. The infiltrating B cells were mainly found in the adventitia and were frequently organised into high density B cell areas. In contrast to the temporal artery, B cells clearly outnumbered T cells in the aorta. ATLOs contained co-localised high density B cells and T cells, a FDC network, HEV and sometimes a germinal centre. ATLOs were observed in 77.8% of LV-GCA patients as opposed to only 36.4% of atherosclerosis patients. The number of ATLOs per patient was significantly higher in the LV-GCA group. Strikingly, ATLOs in aortas of LV-GCA patients contained more plasma cell niches and these niches also contained more plasma cells compared to aorta's of the atherosclerosis group. No association between the number of ATLOs and the number of atherosclerotic plaques was observed.

**Conclusions:** In conclusion, aorta tissues from patients with histologically-proven LV-GCA showed massive B cell infiltrates, predominantly located in the adventitia, that were organised into ATLOs. Moreover, these ATLOs frequently contained plasma cell survival niches. The predominance of organised B cells and plasma cells at the site of inflammation in LV-GCA suggests an involvement of B cell-mediated immune mechanisms in LV-GCA to be further explored.

**Disclosure of Interest:** None declared

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#### THU0027

#### NON-RESPONSE TO RITUXIMAB THERAPY IN RHEUMATOID ARTHRITIS ASSOCIATES WITH INCOMPLETE DISRUPTION OF THE B-CELL RECEPTOR REPERTOIRE IN THE PERIPHERAL BLOOD

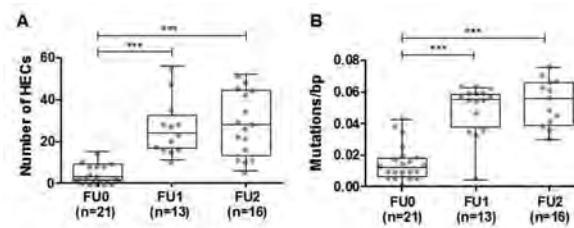
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**Background:** Rituximab (RTX) induces more than 98% depletion of the CD20 +B cells in blood after a single injection, yet 35% to 50% of RA treated patients show a poor response to the therapy<sup>1</sup>. Despite the identification of many different biomarkers, mostly in the B cell compartment<sup>2</sup>, adequate prediction of response to RTX treatment is still quite challenging.

**Objectives:** To test the hypothesis that non-response to rituximab can be predicted by analysing B-cell receptor (BCR) repertoire characteristics before and shortly after rituximab therapy.

**Methods:** Paired peripheral blood (PB) samples and synovial tissue (ST) samples were available from a total of 21 patients before therapy with RTX, and at 4 and 16/24 weeks after treatment. Next-generation sequencing was used to analyse the BCR repertoire, and assess the frequency of high expanded clones (HECs: >0.5% of the sequenced reads)<sup>3</sup> and load of somatic hypermutation (SHM). Clinical response was evaluated at 6 month following EULAR response criteria.

**Results:** In spite of the complete depletion of B cells (measured using CD19) with conventional flow cytometry, we detect a complete BCR repertoire at week 4 and 16/24 after RTX treatment. The post-treatment PB BCR repertoire is composed of fewer, but more expanded and more mutated clones compared to baseline (figure 1). Non-response associates with a higher number of HECs at week 4 (p<0.01) and with a higher overlap in the top-50 clones between the baseline and week 4 repertoire (p=0.03). In fact, in all non-responders some of the HECs detected at week 4 were already present at baseline. In these persisting clones the SHM load was higher than the median in the total repertoire. In the synovial tissue BCR repertoire the number of clones and HECs does not significantly change after RTX treatment. Like in PB, an increase in SHM load is observed after treatment but at the later time point (week 16). In ST the overlap within the top-50 clones with baseline is largely maintained at week 4, but then decreases at week 16. No baseline predictors of response to RTX treatment were identified.



**Abstract THU0027 – Figure 1.** HECs (A) and SHM load (B) in PB BCR repertoire before (FU0) and after (FU1 and FU2) treatment with RTX.

**Conclusions:** Incomplete depletion of the baseline BCR clonal repertoire in peripheral blood within the first month of treatment predicts poor clinical response at 6 months, revealing the persistence of “rituximab-resistant” BCR clonal signatures associated with treatment failure. In all patients the PB BCR repertoire at 4 weeks after rituximab is dominated by few but highly expanded and highly mutated BCR clones, most likely CD20-negative plasmablasts, while less pronounced and delayed effects are observed in the ST BCR repertoire.

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**Disclosure of Interest:** None declared

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**THU0028 INTERLEUKIN-6 RECEPTOR INHIBITION, AS FIRST-LINE B-DMARD, AFFECTS B CELL SUBPOPULATIONS DISTRIBUTION THROUGH EPIGENETIC MODIFICATIONS IN RHEUMATOID ARTHRITIS PATIENTS**

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**Background:** Despite IL-6R inhibition was found to influence B cell subpopulations distribution in Rheumatoid Arthritis (RA), no data are available on the effect on epigenetic signature of RA B cells by this treatment. It is well known that B cell maturation is under control of the microRNA-155 (miR-155)/PU.1 axis significantly influenced by IL-6 stimulation<sup>1</sup>.

**Objectives:** To investigate the effect of IL-6R inhibition on the epigenetic signature of B cells (miR-155/PU.1 axis) in RA patients.

**Methods:** Twenty-nine RA patients [18 (62.1%) female; 57.2±14.9 years old; disease duration 1.3±0.7 years] starting IL-6R inhibitor treatment as first b-DMARD, have been enrolled. At study entry and after 3–6–12–18 months follow-up, CD19<sup>+</sup> cells were isolated from peripheral blood (PB) by magnetic microbeads (Miltenyi) and B cells subpopulations were assessed through FACS according to the IgD/CD27 classification. MiR-155 and PU.1 endogenous expression was determined in PB-derived CD19<sup>+</sup> cells by RT-PCR at baseline and after 3–6–12–18 months follow-up. IL-6 plasma level was assessed by ELISA at study entry for each patient. ACR/EULAR criteria were used to assess the response rate to IL-6R inhibitor treatment for each RA patient. PB-derived CD19<sup>+</sup> cells of healthy individuals (HC) were used as comparison group.

**Results:** At study entry, RA patients showed higher percentage of IgD<sup>+</sup>/CD27<sup>+</sup> CD19<sup>+</sup> cells (p<0.05) and IgD<sup>+</sup>/CD27<sup>+</sup> CD19<sup>+</sup> cells (p<0.05) than HC. Moreover, IgD<sup>+</sup>/CD27<sup>+</sup> CD19<sup>+</sup> cells percentage directly correlated with Disease Activity Score (p=0.04) and IL-6 plasma levels (p=0.06) in RA patients. IL-6R inhibition lead to DAS and SDAI remission achievement in 73.9% and 52.2% of RA patients after 18 months follow-up, respectively, and significantly reduced IgD<sup>+</sup>/CD27<sup>+</sup> CD19<sup>+</sup> cells percentage after 18 months follow-up (p<0.02). Stratifying RA patients based on the remission achievement during the follow-up, RA patients who achieved DAS remission under IL-6R inhibition showed a significant decrease of IgD<sup>+</sup>/CD27<sup>+</sup> CD19<sup>+</sup> cells percentage compared to patients not achieving this outcome (p<0.05), reaching IgD<sup>+</sup>/CD27<sup>+</sup> CD19<sup>+</sup> cells percentage comparable to HC (p>0.05). Analysing the epigenetic profile in B cells of RA patients, at baseline, PB-derived CD19<sup>+</sup> cells of RA patients showed significantly higher endogenous expression of miR-155 (p=0.04) than HC. Moreover, RT-PCR showed that IL-6R inhibition significantly represses endogenous miR-155 expression in PB-derived RA B cells already after 3 months of treatment (p<0.05) and restores PU.1 expression in PB-derived B cells after 6 months (p<0.05) only in RA patients achieving disease remission.

**Conclusions:** IL-6R inhibitor, used as first b-DMARD treatment, acts restoring B cells homeostasis through epigenetic modulation in RA. In particular, IL-6R inhibition significantly represses endogenous expression of miR-155 in PB-derived CD19<sup>+</sup> cells conversely restoring PU.1 expression mirrored by the decrease of IgD<sup>+</sup>/CD27<sup>+</sup> B cell rate in RA patients achieving disease remission.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.4809

**THU0029 CTLA-4-IG TREATMENT INDUCES MODULATION OF B-CELL FUNCTION AND DIFFERENTIATION**

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**Background:** CTLA-4 modulates T-cell activation by inducing inhibitory signalling in T-cells. To date the direct effect of CTLA-4-Ig (abatacept) on B-cells has not been studied in detail. We hypothesise that CTLA-4 modulates B-cell function, B-cell homeostasis and B-cell receptor signalling in a T-cell-dependent and T-cell-independent manner.

**Objectives:** To assess the impact of abatacept on 1. B-cell activation and function *in vitro*; 2. B-cell signalling *in vitro*; 3 maintenance and specificity of memory B-cells specific for citrullinated protein antigens *in vivo*.

**Methods:** The time kinetic of CD80 and CD86 expression was measured by flow cytometry on isolated B-cells after stimulation via CD40, IL-21R, TLR9, and BCR in presence and absence of CTLA-4-Ig. Human B-cells lines (BJAB) deficient either for CD80 or CD86 were created using the CRISPR Cas9 technology and the effect of abatacept on CD80 respectively CD86 expression was assessed in

these K.O. cell lines. CD80 and CD86 internalisation upon abatacept binding was studied by fluorescence microscopy. The effect of abatacept on PI3K-, NF-κB, PLCγ-signalling and Ca-flux in B-cells was assessed. The effect of CTLA-4-Ig *in vivo* on the pool of memory cells specific for anti-citrullinated protein antigens was studied by limiting dilution assays performed before and during CTLA-4-Ig treatment.

**Results:** The expression of CD80 and CD86 on isolated human B-cells peaked at day 2–3 of culture after stimulation with CD40-L and IL-21. CTLA-4-Ig led to a decrease in CD80 and CD86 expression. These results were confirmed in human B-cell lines deficient either for CD80 or CD86. By fluorescence microscopy we were able to demonstrate, that abatacept treatment of cultured B-cells leads to a reduction in CD80 and CD86 expression mediated by a mechanism that involves internalisation of the receptors and bound CTLA-4-Ig. To test if CTLA-4-Ig binding activates signalling pathways, we stimulated B-cells with CTLA-4-Ig or via BCR or CD40. We detected phosphorylation of p65 indicating activation of the canonical NF-κB pathway. The effect of CTLA-4-Ig *in vivo* on the pool of memory cells specific for autoantigens (anti-citrullinated protein antigens) was studied by limiting dilution assays in patients with rheumatoid arthritis. This assay is based on polyclonal stimulation of memory B-cells that leads to blast formation and antibody secretion in the supernatant. We performed limiting dilution experiments before and after start of CTLA-4-Ig treatment and observed a significant reduction of the absolute frequency of citrullinated antigen specific memory B-cells in response to treatment.

**Conclusions:** CTLA-4-Ig-treatment leads to a decrease in B-cells' CD80 and CD86 expression, mediated by a mechanism that involves internalisation of the receptors and bound CTLA-4-Ig. CTLA-4-Ig activates the canonical NF-κB pathway in B-cells. *In vivo* CTLA-4-Ig treatment reduces the frequency of citrullinated antigen specific memory B-cells in patients with rheumatoid arthritis.

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**THU0030 MOLECULAR MECHANISMS OF AUTOPHAGIC MEMORY IN PATHOGENIC T CELLS IN HUMAN RHEUMATOID ARTHRITIS**

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**Background:** One of the key elements of immune pathogenesis of human autoimmune arthritis is the resilience of pathogenic T cells. We have previously described that CD4 +T cells in patients with arthritis have an increased level of autophagy than their healthy equivalents. Here, we sought to explore at epigenetic and transcriptional levels the concept of persisting increased autophagy as the consequence of "autophagic memory", as one of the mechanisms conferring resilience to pathogenic T cells, in particular to a subset of CD4 +T cells (CPL: Circulating Pathogenic-like Lymphocytes), which are significantly more represented in patients with active arthritis and resistant to therapy with biologics

**Objectives:** To understand molecular mechanism of resilience and persistence in pathogenic T cells in rheumatoid arthritis.

**Methods:** Autophagy in T cells were analysed using CytoID autophagy detection kit. Jurkat cells pre-starved and control were harvested at various time points, and RNA was extracted for RNA-sequencing and DNA methylation analysis. Illumina paired end sequencing was performed and data was analysed using open source tools in R statistical programming software. CD4 +memory and naive T cells were sorted using flow cytometer for qPCR analysis. The CD4 +memory and naive cells were sorted using Flow cytometer. RNA extracted and converted to cDNA for qPCR analysis of key genes

**Results:** First, we demonstrated elevated autophagic levels in CD4 +memory T cells when compared to naive CD4 +T cells. Second, we showed that autophagic levels are increased in naive and CD4 +T cells from RA patients compared to healthy controls. Using next generation RNA-sequencing, transcription factor gene regulatory network (TF-GRN) and methylation analyses, we identified MYC as key regulator of autophagic memory in a human T cell line. Transcriptome and network analysis of RNA-seq data from patients' CPLs confirmed MYC as key modulator of autophagy. Importantly, inhibitor of MYC increases autophagy



**Conclusions:** The present study suggests that autophagic memory is retained both at the transcriptional and epigenetic levels as an integral part of mechanisms of efficient activation and survival of memory T cells. This mechanism is particularly relevant for cells subsets, such as CPLs, which are relevant to the immunopathogenesis of autoimmune diseases, such as arthritis. These studies have a direct translational valency as they identify autophagy and its metabolic controllers as a novel therapeutic target.

**Disclosure of Interest:** None declared

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**THU0031 PHENOTYPE OF FOXP3+ REGULATORY T-CELLS EXPANDED BY THE IL-2 MUTEIN, AMG 592 IN HEALTHY SUBJECTS IN PHASE 1, FIRST-IN-HUMAN STUDY**

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**Background:** Low-dose interleukin-2 (IL-2) therapy expands regulatory T cells (Treg) and provides clinical benefit for inflammatory diseases. AMG 592 is an investigational IL-2 mutein designed to expand Treg more selectively than recombinant IL-2 (aldesleukin). In a phase 1, double-blind, placebo (PBO)-controlled first-in-human (FIH) study, we investigated the safety and tolerability of AMG 592 and pharmacodynamic (PD) effects on Treg.

**Objectives:** We recently presented FIH study results including summary of safety, PK and PD.<sup>1</sup> Here we extend those findings by exploring phenotypes of AMG 592 expanded Foxp3<sup>+</sup> Treg subsets using flow cytometry. We compared both analysis using predefined gates and unsupervised gating. Potential implications for dose selection and mechanism of action will be discussed.

**Methods:** In the FIH study, healthy subjects in multiple ascending dose cohorts received a single subcutaneous dose of AMG 592 (n=6 per cohort) or placebo (n=2 per cohort). Pharmacodynamic response was evaluated for 28 days after treatment. In addition to enumerating CD4<sup>+</sup> Foxp3<sup>+</sup> Treg we evaluated changes in Treg subsets after AMG 592 treatment. Changes from baseline were analysed with linear mixed effects models with visit, dose level, and baseline result as main effects. To identify cell subsets, independent of predefined gates the same data were also evaluated with unsupervised gating tools using raw data from days 1, 8, 15 and 22.

**Results:** We observed a robust, dose-dependent expansion of Tregs that peaked at day 8 (~4–5 fold increase) and remained elevated above baseline up to day 29 for the highest doses. Expanded Tregs had increased levels of CD25 and Foxp3, and were enriched for CD31<sup>+</sup> recent thymic emigrants (RTE). Both naïve and memory Treg increases peaked at day 8, however, naïve Treg including RTE persisted at elevated levels through day 29 while memory Treg returned to normal levels earlier. The majority of Treg expressed the transcription factor Helios. Furthermore, expanded Tregs expressed higher proportions of PD-1. Unsupervised gating analysis identified several primary clusters of expanded Treg, one including naïve and RTE Treg and another including memory Treg with elevated levels of HLA-DR expression. Evaluation of these clusters over time suggests that both increase initially at day 8 followed by preferential persistence of cells in the naïve over memory Treg cluster by day 22.

**Conclusions:** Foxp3<sup>+</sup> Treg were expanded in a dose dependent fashion in healthy subjects treated with AMG 592. The phenotype of expanded Treg included elevation of CD25 and Foxp3 as well as enrichment for PD-1 positive subsets. Taken together the increase in Treg with an RTE phenotype and persistence of naïve Treg suggests that AMG 592 may increase diversity of the Treg pool as a possible mechanism of action in addition to effects on memory Treg.

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**THU0032 CCR6+CD4+ T CELLS DRIVE ANTIGEN-INDUCED ARTHRITIS VIA THE IL-23R PATHWAY**

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**Background:** The IL-23/IL-17A immune pathway is important for the progression of T cell-mediated arthritis. However, it is not known where IL-23R<sup>+</sup> T cells locate during the different stages of arthritis and which IL-23R<sup>+</sup> T cells drive joint inflammation.

**Objectives:** We aimed to identify IL-23R<sup>+</sup> T cells in the secondary lymphoid organs and synovium during the development and progression of antigen-induced arthritis (AIA). Furthermore, we studied which IL-23R<sup>+</sup> T cells drive full-blown AIA.

**Methods:** To induce AIA, IL-23R<sup>+/+</sup> (WT), heterozygous IL-23R<sup>+GFP</sup> (IL-23R-GFP, KI reporter), and IL-23R<sup>GFP/GFP</sup> (IL-23RKO) mice were immunised with methylated bovine serum albumin (mBSA) in Complete Freund's Adjuvant. After 7 days mice were injected in the knee joints with mBSA. Mice were macroscopically scored at different time points and knees were used for histological analysis of inflammation and bone erosion. The spleen, inguinal and popliteal lymph nodes (LN), and the synovium were collected and analysed for the expression of GFP<sup>+</sup>/IL-23R<sup>+</sup> T cells.

To study which T cells drive AIA, CCR6<sup>+</sup> T helper (CD4<sup>+</sup>) cells and  $\gamma\delta$  T cells from CFA/mBSA immunised WT mice were adoptively transferred into IL-23RKO recipient mice prior to AIA induction and disease severity was assessed at the peak of AIA.

**Results:** AIA disease progression was mainly driven by the IL-23R pathway since IL-23RKO mice had significantly lower arthritis scores and less bone damage. During arthritis, total cell numbers of lymphoid tissues were lower in IL-23RKO mice, suggesting involvement of IL-23R pathway in cell proliferation. Heterozygous IL-23R reporter mice had similar disease scores to WT mice, indicating that half of the receptor expression is sufficient to drive disease. Flow cytometric analysis of GFP/IL-23R in T cells of naïve and arthritic IL-23R reporter mice revealed that a fraction of CCR6<sup>+</sup>CD4<sup>+</sup> T cells and  $\gamma\delta$  T cells, but not CD8<sup>+</sup> T cells, expressed IL-23R in the lymphoid tissues. Already one day after AIA induction, the fractions of both IL-23R<sup>+</sup> CCR6<sup>+</sup>CD4<sup>+</sup> T cells and  $\gamma\delta$  T cells were increased in the draining LNs from the joints. However, these IL-23R<sup>+</sup> T cells were decreased during the peak of disease, possibly due to their migration towards the synovium. Indeed, CD4<sup>+</sup> T cells and  $\gamma\delta$  T cells were abundantly present in the WT joints during the peak of disease, but decreased in IL-23RKO joints. Adoptively transferred CCR6<sup>+</sup>CD4<sup>+</sup> T cells, but not  $\gamma\delta$  T cells, were able to restore AIA in IL-23RKO mice, indicating that CCR6<sup>+</sup>CD4<sup>+</sup> T cells are the main drivers of AIA.

**Conclusions:** The IL-23R signalling pathway is essential for full-blown AIA. Both CCR6<sup>+</sup>CD4<sup>+</sup> T cells and  $\gamma\delta$  T cells, but not CD8<sup>+</sup> T cells, express IL-23R during naïve and inflammatory conditions. Total cell number in the lymphoid tissues of arthritic IL-23R deficient mice is lower. Interestingly, adoptive transfer of CCR6<sup>+</sup>CD4<sup>+</sup> T cells but not  $\gamma\delta$  T cells, can rescue arthritis in IL-23R deficient mice.

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**THU0033 AGE-ASSOCIATED B CELLS IN EARLY DRUG-NAÏVE RHEUMATOID ARTHRITIS PATIENTS**

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**Background:** Rheumatoid arthritis (RA) is a chronic autoimmune disorder characterised by joint inflammation and bone destruction. The presence of autoantibodies, years before the clinical onset of disease, and the efficacy of Rituximab, a B-cell depleting therapy, highlight a pathogenic role for B cells. Different groups have recently identified a novel subset of B cells named age-associated B cells (ABCs). Studies in mice autoimmune models and patients suffering from autoimmune diseases described these cells as CD19<sup>high</sup> CD21<sup>-</sup> CD11c<sup>+</sup>. Moreover, a subset of synovial fluid B cells with low levels of CD21, expresses FcRL4 and produces the cytokine RANKL, which stimulates the differentiation and activation of osteoclasts. The ABCs found in peripheral blood could therefore be the precursors of this FcRL4 positive subset found in synovia.

**Objectives:** We aimed to investigate the proportion and phenotype of peripheral blood ABCs in patients suffering from early drug naïve RA.

**Methods:** Newly presenting patients, naïve to immunomodulatory treatment, were recruited from the Newcastle Early Arthritis Clinic, and followed until diagnoses were confirmed. B-cell subsets in peripheral blood were detected and phenotyped using flow cytometry.

**Results:** Our work showed increased proportions of ABCs in seropositive RA compared to other inflammatory arthritis controls, highlighting a potential link between autoantibody production and ABCs. Moreover, patients with high disease activity had higher proportions of ABCs in peripheral blood. Interestingly, the FcRL4<sup>+</sup>, the proliferating Ki67<sup>+</sup> and the T-bet expressing B cells were enriched in the ABC population compared to the other B cell subsets. Furthermore, ABCs expressed high levels of MHC class II and co-stimulatory molecules, as well as the activation marker, CD69.

**Conclusions:** These data supports a possible pathogenic role of ABCs in RA, potentially via autoantibody and T cell stimulatory ability, but further characterisation of this subset and functional studies are needed.

**Disclosure of Interest:** None declared

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#### THU0034 SALMONELLA TYPHI VI IGG AS A MARKER OF IMMUNOSUPPRESSION IN RHEUMATIC DISEASE

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**Background:** Measurement of vaccine response may be used as a diagnostic tool to aid determination of antibody deficiency. The IgG response to pneumococcal polysaccharide vaccination (PPV) is currently used to assess T cell independent responses, however additional polysaccharide vaccines are under evaluation. In patients with rheumatic diseases (RD) treatment regimens can result in immunosuppression and subsequently secondary immune deficiency (SID).

**Objectives:** To measure the IgG response to Typhi Vi vaccination (TV) in RD patients presenting with antibody deficiency. To correlate immunosuppression with TV responses, as well as TV responses to clinical presentations, B cells and total IgG. Further, we interpret the responses in combination with the responses to PPV.

**Methods:** 35 RD patients were referred for immunological evaluation at Hospital Clínico San Carlos, Madrid, Spain. The responses to TV and PPV were measured using commercial human anti-*Salmonella* Typhi Vi IgG and pneumococcal capsular polysaccharide (PCP) IgG ELISAs kits. A TV responder was defined as achieving  $\geq 32$  IU/mL (lower limit of the normal range), a PCP IgG responder ( $>50$  mg/L), B cells were measured by flow cytometry (responder  $\geq 6.6\%$ ) and total IgG by nephelometric assay (responder  $\geq 600$  mg/dL). For all measurements (+) indicates a responder and (-) indicates a non-responder.

**Results:** A greater percentage of TV- patients previously received non-biological treatment (79% vs 43%), specifically steroid treatments (68% vs 28%) and biological treatments (particularly CD20 and TNF alpha targets; 46% vs 14%). At presentation, TV non-responsiveness was associated with a higher frequency of upper respiratory tract infections (75% vs 57%), serious bacterial infections (21% vs 14%) and required slightly higher antibiotic usage (93% vs 71%).

Stratification of the RD patients using the response to the TV and PPV identified four groups of activity: TV+/PCP+, TV-/PCP+, TV+/PCP- and TV-/PCP-. In the presence of a normal response to PPV, the failure to respond to TV (TV-/PCP+) correlated with a higher frequency of previous non-biological treatment (84% vs 43%), biological treatment (47% vs 14%), steroids treatment (68% vs 29%) and were currently undergoing treatment (84% vs 29%,  $p=0.01$ ) compared to those who responded to TV (TV+/PCP+). At presentation TV-/PCP+ patients had a greater incidence of upper respiratory tract infections (74% vs 57%), serious bacterial infections (16% vs 14%) and antibiotic usage (95% vs 71%). Non-responders to both vaccinations (TV-/PCP-) had a higher incidence of serious bacterial infections (25% vs 16%) and pneumonia (50% vs 32%) when compared to the TV+/PCP- group. When correlated with B cell number, 58% of B cells had a concentration of TV antibodies  $<32$  U/mL.

**Conclusions:** The response to TV correlated with underlying disease treatment and immunological presentation. Assessing the response to two polysaccharide vaccinations, TV and PPV, may provide a greater understanding of the T cell independent pathway and provide more clinical information for the clinician.

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#### THU0035 A CD8 ALPHA-NEGATIVE SUBSET OF CD4+SLAMF7+ CYTOTOXIC T CELLS IS EXPANDED IN PATIENTS WITH IGG4-RELATED DISEASE AND DECREASES FOLLOWING GLUCOCORTICOID TREATMENT

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**Background:** IgG4-Related Disease (IgG4-RD) is a fibro-inflammatory disorder characterised by tumefactive lesions, frequent elevation of serum IgG4 levels, and tissue fibrosis.<sup>1</sup> Glucocorticoids represent the treatment of choice to induce IgG4-RD remission but their effect on the cells orchestrating the disease remains unknown.<sup>1</sup> We recently described an unconventional population of clonally expanded CD4<sup>+</sup>SLAMF7<sup>+</sup> cytotoxic T effector memory (T<sub>EM</sub>) cells (CD4<sup>+</sup>CTLs) and causally linked it to IgG4-RD in view of their capacity to secrete pro-fibrotic molecules and to infiltrate affected organs.<sup>2-4</sup>

**Objectives:** In order to better clarify the mechanisms of action of glucocorticoids in IgG4-RD and the pathogenic relevance of CD4<sup>+</sup> CTLs, we herein aim to describe the effects of corticosteroid treatment on CD4<sup>+</sup> CTLs.

**Methods:** CD8 $\alpha$ , granzyme A, perforin, and SLAMF7 expression within the effector/memory compartment of CD45RO (T<sub>EM</sub>) and CD45RA (T<sub>EMRA</sub>) CD4<sup>+</sup> T cells was quantified by flow cytometry in 18 active IgG4-RD patients at baseline and after 6 months of glucocorticoid treatment. Eighteen healthy subjects were studied as controls. Next-generation sequencing of the T-cell receptor  $\alpha$  and  $\beta$  chain gene was performed on circulating CD4<sup>+</sup>CTLs in patients with IgG4-RD before and after treatment, and in affected tissues.

**Results:** Circulating CD4<sup>+</sup> T<sub>EM</sub> and T<sub>EMRA</sub> cells were not expanded in IgG4-RD patients compared to healthy controls. CD4<sup>+</sup>SLAMF7<sup>+</sup> T<sub>EM</sub> cells (but not T<sub>EMRA</sub> cells) were significantly increased among IgG4-RD patients. Within CD4<sup>+</sup>SLAMF7<sup>+</sup> T<sub>EM</sub> cells, CD8 $\alpha$ <sup>+</sup> but not CD8 $\alpha$ <sup>low</sup> cells were elevated in IgG4-RD patients. The same dominant clones of CD8 $\alpha$ <sup>+</sup>CD4<sup>+</sup>SLAMF7<sup>+</sup> T<sub>EM</sub> cells found in the peripheral blood were also identified in affected tissue. Both CD8 $\alpha$ <sup>+</sup> and CD8 $\alpha$ <sup>low</sup> CD4<sup>+</sup>SLAMF7<sup>+</sup> T<sub>EM</sub> cells expressed cytolytic molecules. Clonally expanded CD8 $\alpha$ <sup>+</sup> but not CD8 $\alpha$ <sup>low</sup> CD4<sup>+</sup>SLAMF7<sup>+</sup> T<sub>EM</sub> cells decreased following glucocorticoid-induced disease remission.

**Conclusions:** A subset of CD8 $\alpha$ <sup>+</sup>CD4<sup>+</sup>SLAMF7<sup>+</sup> cytotoxic T<sub>EM</sub> cells is oligoclonally expanded in patients with active IgG4-RD. This population contracts following glucocorticoid-induced remission. Further characterisation of this cell population may provide prognostic information and targets for therapeutic intervention.

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#### THU0036 ABATACEPT INCREASES REGULATORY B CELL EFFECT ON T CELL PROLIFERATION THROUGH THE PRODUCTION OF IL-10 AND TGF-BETA IN VITRO AND IN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Abatacept is a CD152 agonist known to inhibit T cell proliferation but recent data suggest that it could act directly on B cells.<sup>1-2</sup>

**Objectives:** To demonstrate the effect of Abatacept (versus IgG control) on regulatory functions of B cells on T cell proliferation in an established *in vitro* co-culture model. To evaluate its role, *in vivo*, by measuring the regulatory functions of B cells from rheumatoid arthritis patients before and after the Abatacept treatment.

**Methods:** Peripheral and tonsillar T cell and B cell from healthy controls were purified. The biotinylation of Abatacept was used to study its binding on T and B cells by flow cytometry and confocal microscopy. A well-established co-culture model between CpG-stimulated B cells and anti-CD3/anti-CD28 stimulated T cells was set up in which Abatacept or an IgG control was added to evaluate any change in B cell regulatory functions. Activation markers (e.g. CD25, CD69, CD40, CD152) and regulation markers (e.g. FoxP3, TGF- $\beta$ ) were assessed by flow cytometry. Similar analysis was also performed on rheumatoid arthritis patients before and three months after Abatacept therapy. All patients gave their informed consent.

**Results:** Abatacept increases the inhibition of T cell proliferation by B cells compared to IgG control in the co-culture model ( $p=0.03$ ). Interestingly, alone, Abatacept does not modify T cell proliferation. This can be explained by the increase in IL-10 and TGF- $\beta$  producing B cells and the CD152 expression. Abatacept is able to bind B cells at day 0 of co-culture and B and T cells at day 4.5 of co-culture. Abatacept has a direct effect on B cells by increasing the CD25 ( $p=0.03$ ) and CD152 expression ( $p=0.02$ ) reflecting a higher activation level. Nevertheless, Abatacept had no direct effect on B cell proliferation. In RA patients, the treatment with Abatacept resulted in an increased regulation of T cell proliferation and this effect is related to a higher percentage of IL-10 secreting B cells 3 months after the therapy ( $p=0.03$ ).

**Conclusions:** In our *in vitro* and *in vivo* models, Abatacept has a direct effect on B cells leading to an increase capability of regulation of T cell proliferation which directly linked to higher production of IL-10 and TGF $\beta$ .

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**Disclosure of Interest:** None declared

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#### THU0037 LEPTIN ENHANCED THE EXPRESSION OF AUTOANTIBODIES AND INFLAMMATORY CYTOKINES OF B CELLS VIA ACTIVATING ERK1/2 AND JAK/STAT3,5 PATHWAYS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** B lymphocytes derived from patients with systemic lupus erythematosus (SLE) displayed abnormal activation and overexpression of auto-antibodies. It was reported that leptin was elevated in the sera of SLE patients and lupus mice, and blockade of leptin also remarkably improved the disease activity and renal pathology of lupus mice. Therefore, our study is to explore whether leptin in SLE regulates the activation and function of B cells.

**Objectives:** Our study is to explore whether leptin in SLE regulates the activation and function of B cells.

**Methods:** The sera and peripheral blood monocyte cells (PBMC) were isolated from healthy controls and SLE patients with Ficoll, then B cells were acquired through magnetic activated cell sorting (MACS). The sera were incubated in 56° for 30 min (complement inactivation). B cells were cultured in normal or SLE serum, with or without recombinant leptin. Anti-leptin antibody or inhibitions of the signalling pathways were added in SLE sera in order to observe the effects of B cells induced by leptin. Cell proliferation was detected by flow cytometry and carboxyfluorescein diacetate succinimidyl ester (CFSE), and the levels of auto-antibodies and inflammatory cytokines were examined by ELISA. The total and phosphorylated protein was tested with Western Blot analysis.

**Results:** Leptin R on B cells showed increased levels in SLE patients [(3.33  $\pm$  1.28)% v.s. (2.76  $\pm$  1.06)%,  $p<0.01$ ]. Leptin could upregulate the activated markers (CD80, CD86), also increase the proliferation (CFSE) of B cells. Recombinant leptin promotes IgG/IgM production [ IgG: leptin 0 (45.50  $\pm$  3.87)ng/ml vs. leptin 100 (61.24  $\pm$  3.66)ng/ml,  $p<0.01$ ; IgM: leptin 0 (60.75  $\pm$  19.60)ng/ml vs. leptin 100 (118.90  $\pm$  26.16)ng/ml,  $p<0.01$ ], as well as inflammatory cytokines (IL-6, IL-10, TNF- $\alpha$ ) secreted by B cells derived from SLE patients. [IL-10: leptin 0 (20.45  $\pm$  5.17)pg/ml vs. leptin 100 (23.81  $\pm$  5.45)pg/ml,  $p<0.01$ ; IL-6: leptin 0 (156.10  $\pm$  32.64)pg/ml vs. leptin 100 (244.20  $\pm$  54.23)pg/ml,  $p<0.05$ ; TNF- $\alpha$ : leptin 0 (13.33  $\pm$  2.38)pg/ml vs. leptin 100 (18.85  $\pm$  2.69)pg/ml,  $p<0.001$ .] Compared with Nor serum, SLE serum enhanced the levels of IgG/IgM and inflammatory cytokines, such as IL-6, IL-10, TNF- $\alpha$ . Moreover, blockade of leptin could partially reverse these effects. SLE serum or recombinant leptin could activate p38 MAPK, ERK1/2, and Jak/stat3,5 pathways, but not PI3K/Akt or Jak/stat1 pathways. In addition, blocking ERK1/2 and Jak/stat3,5 pathways could partially reverse the effects of enhanced secretion of autoantibodies and inflammatory cytokines induced by recombinant leptin or SLE serum.

**Conclusions:** Leptin promote the activation and proliferation of B cells in SLE. Recombinant leptin or serum leptin from SLE patients both enhanced the

expression of autoantibodies and inflammatory cytokines (IL-6, IL-10, TNF- $\alpha$ ) of B lymphocytes. Additionally, ERK1/2, and Jak/stat3,5 signalling pathways might play a vital role in this process.

**Disclosure of Interest:** None declared

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#### THU0038 INCREASE OF CIRCULATING MEMORY B CELLS AFTER GLUCOCORTICOID-INDUCED REMISSION IDENTIFIES PATIENTS AT RISK OF IGG4-RELATED DISEASE RELAPSE

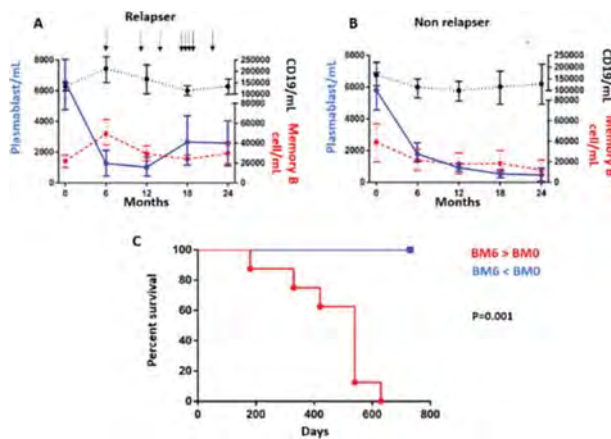
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**Background:** IgG4-related disease (IgG4-RD) is relapsing-remitting systemic fibro-inflammatory condition characterised by elevated serum IgG4 concentration and by tumor-like lesions<sup>1</sup>. Glucocorticoids represent the treatment of choice to induce IgG4-RD remission but relapses occur in almost 50% of patients at two years.<sup>2</sup> Several evidences suggest that B cells are central to the pathogenesis of IgG4-RD, the most significant being (i) the clinical improvement induced by B-cell depletion with rituximab, and (ii) the oligoclonal expansion of circulating plasmablasts in the vast majority of patients.<sup>3</sup>

**Objectives:** To describe alterations of B-lymphocyte subpopulations that might predict IgG4-RD relapse in patients treated with a first course of glucocorticoids according to international guidelines

**Methods:** Thirty patients with IgG4-RD were treated with glucocorticoids according to international consensus guidelines. Flow cytometry analysis of circulating CD19<sup>+</sup> and CD20<sup>+</sup> cells, naïve B cells, memory B cells, plasmablasts, and plasma cells was performed at baseline and every 6 months after the initiation of corticosteroid treatment.

**Results:** Patients with active untreated IgG4-RD showed reduced CD19<sup>+</sup> B cells, CD20<sup>+</sup> B cells, and naïve B cells compared to healthy controls ( $p<0.05$ ), but expanded plasmablasts and plasma cells ( $p<0.01$ ). Glucocorticoids treatment led to disease response in all patients. Clinical improvement was accompanied by a significant reduction of naïve B cells, circulating plasmablasts, and plasma cells, and by a significant increase of memory B cells compared to baseline ( $p<0.01$ ). Increase of circulating memory B cells was observed only in patients experiencing disease relapse and not in patients who maintained remission at two years of follow-up (HR:14.40, 95% CI 2.96–70.1,  $p<0.01$ , figure 1 A-B). Relapse rates at 12 and 24 months were 25% and 100% with memory B cell increase at 6 months (figure 1C), respectively. No B-cell subpopulations were found to predict IgG4-RD relapse at disease onset.



**Conclusions:** The efficacy of glucocorticoids in IgG4-RD is associated with selective effects on different B-cell subpopulations. IgG4-RD relapse may be predicted by the increase of memory B-cells after glucocorticoid-induced remission

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**Disclosure of Interest:** None declared

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**THU0039 INSULIN-LIKE GROWTH FACTOR 1 RECEPTOR REGULATES THE PHENOTYPE AND FUNCTION OF CD21+ B CELLS**

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**Background:** Ligand to the inducible T cell costimulator (ICOSL) on B cells is essential for the ICOS-dependent follicular recruitment of activated T cells. In patients with rheumatoid arthritis (RA) the IGF1-IGF1R axis is altered. Inhibition of IGF1R alleviated arthritis by reducing IL-6-dependent formation of Th17 cells.<sup>1</sup> Here we study the role of IGF1R on CD21+ cells in experimental arthritis.

**Methods:** Female Balb/c mice were immunised with methylated BSA or with CII. Consequences of the IGF-1R inhibition for arthritis were studied in mBSA and CII-immunised mice treated with NT157 compound promoting degradation of insulin receptor substrates or using shRNA producing construct (shIGF1R). At termination three sub-populations of CD21+ cells were analysed: follicular dendritic cells (FDc, CD21+CD19-CXCR5-); marginal zone B cells (MZBc, CD21+CD19+CXCR5-); follicular B cells (FBc, CD21+CD19+CXCR5+). Supernatants of LPS-stimulated splenocytes were analysed for production of cytokines, chemokines using Cytokine Array. Serum levels of antigen specific and autoantibodies were measured in an ELISA.

**Results:** In spleen of mBSA-immunised mice, ICOSL expression on CD21+ cells correlated to IGF1R ( $r=0.70$ ,  $p=0.007$ ). Inhibition of IGF1R induced a 20% reduction in ICOSL expression in all CD21+ subsets ( $p=0.007$ ) followed by an increase in the number of MZBc ( $p=0.003$ ), while FDc and FBc were unchanged. Inhibition of IGF1R had no effect on the expression of ICOSL on CD4 T cells or the subset of CXCR5+follicular T cells. Reduction of the ICOSL+CD21+B cells was associated with lower production of IL-13. Inhibition of IGF1R signalling by NT157 and by shRNA, reduced production of CXCL13 and CXCL12, the chemokines essential for B cell migration towards follicles. In contrast, the production of chemokines CCL5 and CXCL12 preventing intra-follicular migration was increased, which explains the increase of MZBc. Additionally, the insufficient ICOSL signalling significantly reduced the production of IL-7 and IL-4, regulating class switching of B cells in germinal centres and differentiation of B cells into plasma cells. The described disbalance in the cytokines aiding B cell development led to the reduced production anti-inflammatory IL-10 and of mBSA-specific IgM ( $p=0.005$ ) and increased production of autoreactive RF-IgM levels ( $p=0.001$ ).

**Conclusions:** The study shows that IGF1R controls B cell development through the expression of ICOSL on CD21+ cells. Insufficient ICOSL signalling disturbs a balance between antigen-specific response and autoantibody production in experimental arthritis.

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**Disclosure of Interest:** None declared

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**THU0040 ENHANCEMENT OF EARLY HUMAN B CELL DEVELOPMENT BY JAK INHIBITION**

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**Background:** Rheumatoid arthritis is an immune-mediated disease, in which immune cell activation leads to destructive inflammation of the joints. In this context the treatment with JAK inhibitor tofacitinib has been proven to be effective. In mice treatment with tofacitinib resulted in reduced specific antibody responses, failure to generate germinal centres, and partial block of B cell development in the bone marrow. Conversely *in vivo* treatment of psoriasis arthritis patients as well as of rheumatoid arthritis patients with tofacitinib results in an increase of relative

and absolute numbers of B cells in the first 4–8 weeks from beginning of treatment. It is known that mouse early B cell development is strongly dependent on IL-7 signalling, while this is not essential in humans. Nevertheless other cytokines are important in determining the fate and development of B lymphocytes. Hence, the outcome of JAK inhibition in early B cell development remains to be studied

**Objectives:** To assess the impact of JAK inhibition on early B cell development *in vitro*

**Methods:** We used a *in vitro* model in which CD34+ cells isolated from cord blood are cultivated subsequently in SCF, Flt3-L and IL-6, then SCF, Flt3-L and IL-7 and finally in cytokine-free medium.<sup>1</sup> The culture reproduces all stages of development from common lymphocytes progenitors to immature B cells.

**Results:** With the addition of tofacitinib to the *in vitro* culture we observed an increase in the absolute numbers of lymphoid precursors developing *in vitro* especially at week 5 and 6 of culture. Specifically, JAK inhibition led to an increase of pre-B and immature B cells by week 5 and 6. These data are in contrast with the early B cell development block observed in the tofacitinib treated mouse, but are in line with the rapid increase of B cells in peripheral blood after 4–8 weeks of tofacitinib treatment in patients. Analysis of induction of fate determining genes (EBF, E2A, PAX-5) showed an earlier and stronger induction of fate determining genes.

**Conclusions:** Our data indicate that JAK inhibition may promote early B cell development by enhancing the commitment of lymphoid precursors to the B cell compartment, contributing to a temporary increase in relative and absolute numbers of B cell in peripheral blood of treated patients. These data contribute to our understanding of human B cell development, prompt us to further analyse the quality of B cell output from the bone marrow in JAK inhibited patients, and may provide cues to understand the outcome of JAK inhibition treatment in rheumatic diseases.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.5190

**THU0041 THE EFFECTS OF ABATACEPT ON HUMAN B CELL ACTIVITIES**

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**Background:** Abatacept is a cytotoxic T lymphocyte antigen-4 (CTLA-4) fusion protein approved for rheumatoid arthritis (RA) treatment worldwide. Abatacept mimics the natural CTLA-4 and competes with CD28 for binding the CD80/CD86 on antigen presenting cells to prevent T cell activation. However, the impacts of CTLA-4-Ig through its interaction with CD80/CD86 on B cells are not fully understood.

**Objectives:** The aim of this study was to test whether CTLA-4 regulates human B cell functions

**Methods:** We assayed the effect of abatacept on human B cells in both *in vitro* and *in vivo* conditions. Blood was taken from 20 patients with RA before and after abatacept treatment and the expression of surface proteins on B cells was detected using immunofluorescent staining. Serum level of rheumatoid factor (RF) and anti-cyclic citrullinated protein antibody (ACPA) was measured by ELISA. Purified human B cells from healthy donors were stimulated in the presence of abatacept and cell proliferation, cytokine production, plasma cell differentiation, and antibody production were measured.

**Results:** In RA patients, abatacept treatment transiently reduced the level of CD80/CD86 on peripheral blood memory B cells and increased the naïve to memory B cell ratio. Also, abatacept reduced IgM-RF level in 10 out of 12 patients, which correlates with patients' disease activity, but it had no significant effects on serum levels of anti-citrullinated protein antibody or anti-tetanus toxoid antibodies during the 6 months of abatacept treatment. In the *in vitro* assays, we observed that the CD80 and CD86 induced by T-independent (TI) but not T-dependent (TD) stimulation was significantly downregulated by abatacept at both the mRNA level and protein level. Some TI-induced cytokine production by B cells from healthy donors was also reduced by abatacept. Neither TI nor TD-stimulated B cell proliferation was reduced by abatacept in <sup>3</sup>H-thymidine incorporation assay. Abatacept had no significant effect on CD38<sup>high</sup> CD27<sup>high</sup> plasma cell differentiation. Finally, abatacept inhibited Daudi-B cell induced allogeneic T cell proliferation, indicating a significant blockade of T-B interaction by abatacept.

**Conclusions:** In RA patients, abatacept may decrease RF level by interfering the interaction of CD28 with CD80/CD86, therefore preventing B cells from T cells'



**THU0044 IMPAIRED AUTOPHAGY INDUCES DEFECTIVE FUNCTION OF REGULATORY B CELLS IN ANKYLOSING SPONDYLITIS**

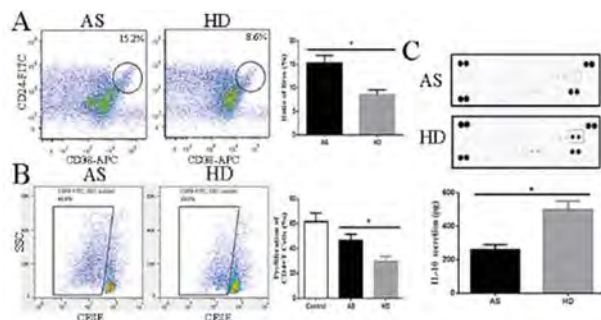
C. Shuizhong, X. zhongyu, Z. guan, S. huiyong, W. yanfeng. *Department of Orthopedics, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, China*

**Background:** Ankylosing spondylitis (AS) is an autoimmune disease characterised by pathological osteogenesis and chronic inflammation. Large number studies shown that Regulatory B cells (Bregs) has immunosuppressive function, which could be involved in many rheumatic disease, such as systemic lupus erythematosus (SLE), rheumatoid arthritis (RA). But the Bregs in AS are poorly understood.

**Objectives:** To investigate the ratio and function of Bregs in AS, and illuminate the under lying mechanism, which might help to further understand the pathology of AS.

**Methods:** (1) Peripheral blood mononuclear cells (PBMCs) were collected from 9 AS patients and 9 healthy controls, then the Bregs were detected by using flow cytometry with the following antibodies: CD19-PE, CD24-FITC and CD38-APC.<sup>2</sup> B cells were purified with a CD19 magnetic bead, the Bregs were sorted by using the flow cytometry. Bregs were added to the upper chamber with 1.5 ml medium, while CD4 +T cells were added to the lower chamber with 2.6 ml medium at a ratio of 1:1 Bregs(1 × 10<sup>6</sup> cells): CD4 +T cells(1 × 10<sup>6</sup> cells). CD4 +T cells were incubated with 5 μM CFDA-SE. The CD4 +T cell proliferation was analyse in the fifth day.<sup>3</sup>The cytokines of Bregs were detected with a proteome profiler kit, and confirmed by using Elias and Western Blot.<sup>4</sup> We detected the Bregs autophagy between AS and HD. And we regulate the autophagy with rapamycin and 3-methyladenine (3-MA), then detected the IL-10 secretion of Bregs and the CD4 +T cell proliferation among groups.

**Results:** (1) The ratio of Bregs in AS was higher that in healthy group.<sup>2</sup> Bregs from AS shown a impaired function in suppressed the CD4 +T cell proliferation compared with HD.<sup>3</sup> Bregs of AS expressed and secreted less IL-10 than healthy control, and might explain the impaired function of Bregs of AS.<sup>4</sup> Exogenous IL-10 recovered the immunosuppressive capacity of AS Bregs, whereas exogenous anti-IL-10 antibody reduced the immunosuppressive capacity of HD Bregs.<sup>5</sup> Autophagy impaired in AS Bregs compared with HD Bregs. Induce autophagy in AS Bregs could increase the IL-10 secretion and strengthened its immunosuppressive capacity, while 3-MA shown the opposite results.



**Conclusions:** Even increasing ratio of Bregs in AS, but they had a impaired function in suppressed CD4 +T cell proliferation compared with the HD. We further found that impaired autophagy could induces less IL-10 secretion, which further affected the immunosuppressive capacity of Bregs of AS.

**Acknowledgements:** This study was supported by the National Natural Science Foundation of China (81271951, 81401850), the Science and Technology Project of Guangdong Province (2015 B020228001) and by the Engineering Technology Research Centre for Comprehensive Diagnosis and Treatment of Ankylosing Spondylitis of Guangdong Higher Education Institutes (GCZX-A1301).

**Disclosure of Interest:** None declared

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**THU0045 EXPANSION OF ACTIVATED CXCR5+ICOS+ TFH CELLS AND PLASMA BLASTS INDUCED BY SEASONAL INFLUENZA VACCINE IS IMPAIRED IN ANTI-IL-6R TREATED RHEUMATOID ARTHRITIS PATIENTS**

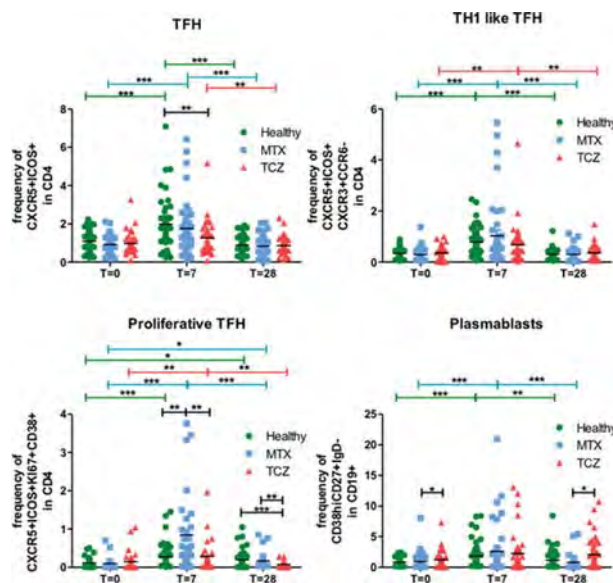
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**Background:** T follicular helper (Tfh) cells are essential for the generation of high affinity neutralising antibodies elicited following vaccination and are involved in the pathogenesis of rheumatoid arthritis (RA). Interleukin (IL)-6 has been shown to be critical for Tfh differentiation in mice, while its importance in humans has been less clear, given the lack of adequate *in vivo* assessment.

**Objectives:** To investigate the importance of IL-6 for the *in vivo* differentiation of human Tfh cells, taking advantage of influenza vaccination in patients under anti-IL-6R therapy.

**Methods:** Blood was collected before, 7 and 28 days after vaccination from established RA patients treated with tocilizumab (TCZ, IL-6R blocker), methotrexate (MTX) ± other DMARDs and age- and sex-matched healthy donors (HD). We analysed the frequency of Tfh (CD3<sup>+</sup>CD4<sup>+</sup>CD25<sup>+</sup>Foxp3<sup>-</sup>CXCR5<sup>+</sup>CD45RO<sup>+</sup>), T follicular regulatory (Tfr, CD3<sup>+</sup>CD4<sup>+</sup>CD25<sup>+</sup>Foxp3<sup>+</sup>CXCR5<sup>+</sup>) and B cell populations at each time point. We used non-parametric tests, deemed significant at p<0.05.

**Results:** We included 137 participants (42 TCZ, 42 MTX, 53 HD) with similar age and gender distribution. Patients from the TCZ group had more active and severe disease. At baseline, patients treated with TCZ had higher frequency of Tfh and Tfr-Th2-like cells (CXCR3<sup>+</sup>CCR6<sup>-</sup>) and lower frequency of Tfr-Th1-like (CXCR3<sup>+</sup>CCR6<sup>+</sup>) and B cells. Following influenza vaccination, the overall blood Tfh and Tfr populations remained unchanged in all groups. However, as previously reported, there were marked changes in specific subsets at day 7 of HD following vaccination. We found a marked expansion of activated CXCR5<sup>+</sup>ICOS<sup>+</sup> Tfh cells at day 7, in HD and MTX-treated patients, but this was impaired in the TCZ group (figure 1). The increase in activated CXCR5<sup>+</sup>ICOS<sup>+</sup> Tfh cells was mainly due to a Tfh-Th1-like subpopulation, greatly increased in HD and MTX-treated patients (figure 1). Of note, CXCR5<sup>+</sup>ICOS<sup>+</sup> Tfh-Th17-like cells also accumulated in HD but not in RA patients. The proliferative capacity of CXCR5<sup>+</sup>ICOS<sup>+</sup> Tfh cells seemed to be partially impaired in patients under IL-6R blockade, that displayed marked reduction of Ki67<sup>+</sup>CD38<sup>+</sup> proliferative cells within that compartment (figure 1). Anti-IL-6R treatment also impaired expansion of CD19<sup>+</sup>IgD<sup>-</sup>CD27<sup>+</sup>CD38<sup>hi</sup> plasmablasts following vaccination, when compared with both MTX and HD groups (figure 1). Changes in CXCR5<sup>+</sup>ICOS<sup>+</sup> Tfh and plasmablasts were significantly correlated in all groups.



Abstract THU0045 – Figure 1. Frequency of cell populations within the CD4+ in the blood. All tests are paired and non-parametric. Healthy N=53, MTX N=42, TCZ N=42.



**Conclusions:** Anti-IL-6R treatment limits proliferative ability of activated CXCR5<sup>+</sup>ICOS<sup>+</sup> Tfh cells, blocking their emergence as well as plasmablast accumulation following influenza vaccination. Our data suggest that IL-6 is crucial for optimal *in vivo* generation of activated Tfh cells in humans.

**Disclosure of Interest:** None declared

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**THU0046 SMALL MOLECULE INHIBITOR OF THE WNT PATHWAY (SM04755) AS A POTENTIAL TOPICAL TREATMENT FOR PSORIASIS**

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**Background:** Psoriasis (PSO) is an autoimmune disease, causing patches of thick, inflamed, scaly skin due to excessive proliferation of skin cells<sup>1</sup>. Wnt signaling plays an important role in PSO, regulating inflammation and keratinocyte proliferation. SM04755, a novel, topical small-molecule Wnt pathway inhibitor was previously shown to inhibit inflammation and keratinocyte proliferation *in vitro* and in an IMQ-induced mouse PSO model<sup>2</sup>.

**Objectives:** In this study, the effects of SM04755 on inflammation and skin health were evaluated in two models that closely resemble human PSO pathophysiology: reconstitution of ICR *scid* mice with minor histocompatibility mismatched naïve CD4<sup>+</sup> T lymphocytes<sup>3</sup> and an IL-23 intra-dermal injection model<sup>4</sup>.

**Methods:** For (A) immune reconstitution model, peripheral blood mononuclear cells were isolated from F<sub>2</sub> (BALB/c x 129/SvJ) mice and analysed by flow cytometry to identify H-2D<sup>d</sup> haplotype donor mice. CD4<sup>+</sup>/CD45RB<sup>Hi</sup> cells from donor mice spleens were purified and injected intravenously into CB17/ICR-Tac Prkdc/*scid* (ICR *scid*) mice (5 × 10<sup>5</sup> cells/mouse). Skin appearance and ear thickness were evaluated weekly. At the first visible PSO-like signs, mice were randomised and treated with SM04755 (400 µg/cm<sup>2</sup>) or vehicle. After 14 weeks, body and spleen weights were measured, and inflammation was evaluated by measuring cytokines (IL-1β, TNF-α, IL-6) in tissues from skin, ears, spleen and plasma using ELISA. Epidermal thickness and skin immune cell infiltration were histologically evaluated. For (B) the IL-23 model, rIL-23 was injected intra-dermally into mouse ears, every other day for 35 days. Mice were randomised on Day 16 and treated with SM04755 (400 µg/cm<sup>2</sup>) or vehicle or Clobetasol daily for 20 days. Ear thickness was measured every 3 days. Skin immune cell infiltration was histologically evaluated.

**Results:** (A) Immune reconstitution of ICR *scid* mice resulted in PSO-like signs, with skin lesions and increased thickness of the skin and ears. Treatment with topical SM04755 (400 µg/cm<sup>2</sup>) significantly (p<0.01) decreased skin and ear thicknesses and improved skin appearance compared to vehicle. Body weights were significantly (p<0.05) higher in treated compared to vehicle mice. SM04755 significantly reduced histologically measured epidermal thickness (p<0.05) and immune cell infiltration in the skin compared to vehicle. Further, inflammatory cytokine levels in the skin, ears, spleen and plasma and spleen weight were significantly (p<0.05) reduced in SM04755 treated animals compared with vehicle. (B) Intra-dermal IL-23 injection into mouse ears resulted in inflammation and ear thickening by day 16 compared to sham. Treatment with topical SM04755 (400 µg/cm<sup>2</sup>) significantly (p<0.05) decreased ear thickness, immune cell infiltration, and improved appearance compared to vehicle.

**Conclusions:** In two mouse models of (A) minor histocompatibility mismatched T lymphocyte reconstitution-induced PSO and (B) IL-23 injection-induced PSO, topically applied SM04755 inhibited key pathophysiological features of PSO at macro- and microscopic levels, compared to vehicle. SM04755 has potential as a topical therapy for PSO. Clinical trials are ongoing.

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**THU0047 1,25(OH)<sub>2</sub>D<sub>3</sub> AND DEXAMETHASONE ADDITIVELY SUPPRESS SYNOVIAL FIBROBLAST ACTIVATION BY CCR6+ TH MEMORY CELLS AND ENHANCE THE EFFECT OF TNF-ALPHA BLOCKADE**

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**Background:** Despite improvement in treatment of rheumatoid arthritis (RA) over the past decades, insufficient treatment response and treatment resistance in many patients demonstrate the need to develop new therapeutic strategies. Chronic synovial inflammation could be suppressed by targeting activation of RA synovial fibroblasts (RASf) by for example IL-17A-producing CCR6 +T helper memory (memTh) cells. Previously, we have shown that dexamethasone (DEX) combined with the active vitamin D metabolite 1,25(OH)<sub>2</sub>D<sub>3</sub> reduces pathogenicity of memTh cells.

**Objectives:** To study the additive effect of 1,25(OH)<sub>2</sub>D<sub>3</sub> and DEX on suppressing the pro-inflammatory loop between RASf and CCR6 +memTh cells and explore potential therapeutic applications.

**Methods:** CCR6 +memTh cells from PBMC of healthy donors or treatment-naïve early RA patients were cultured alone or with RASf from established RA patients for three days and treated with or without 1,25(OH)<sub>2</sub>D<sub>3</sub>, DEX or etanercept. Treatment effects were assessed using ELISA and flow cytometry.

**Results:** CCR6 +memTh produces less of the pro-inflammatory cytokines IL-17A, IL-22 and IFNγ upon exposure to 1,25(OH)<sub>2</sub>D<sub>3</sub>, and to a lesser extent by DEX. TNFα was only inhibited by the combination of 1,25(OH)<sub>2</sub>D<sub>3</sub> and DEX. In contrast, in RASf cultures DEX was the strongest inhibitor of IL-6, IL-8 and tissue-destructive enzymes. As a result, 1,25(OH)<sub>2</sub>D<sub>3</sub> and DEX additively inhibited inflammatory mediators in CCR6 +memTh RASf co-cultures. Interestingly, low doses of mainly DEX, but also 1,25(OH)<sub>2</sub>D<sub>3</sub>, combined with etanercept better suppressed synovial inflammation in this co-culture model compared to etanercept alone.

**Conclusions:** This study suggests that 1,25(OH)<sub>2</sub>D<sub>3</sub> and DEX additively inhibit synovial inflammation through targeting different pro-inflammatory mechanisms. Furthermore, low doses of DEX and 1,25(OH)<sub>2</sub>D<sub>3</sub> enhance the effect of TNFα blockade in inhibiting RASf activation, providing a basis to improve RA treatment.

**Disclosure of Interest:** None declared

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**THU0048 PRO-INFLAMMATORY IL-17A-PRODUCING CCR6+ T HELPER MEMORY CELLS CHANGE INTO ANTI-INFLAMMATORY CELLS WITH REGULATORY CAPACITY UPON EXPOSURE TO ACTIVE VITAMIN D**

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**Background:** In autoimmune diseases such as rheumatoid arthritis (RA), an important therapeutic goal is to normalise the imbalance between pro- and anti-inflammatory cells. In RA, especially pro-inflammatory CCR6 +T helper (Th) memory cells, characterised by IL-17A production and RORC expression, are elevated and more activated compared to healthy controls. Therefore, modulating these cells to become anti-inflammatory could contribute to restoring the immunological balance. Interestingly, the active vitamin D metabolite 1,25(OH)<sub>2</sub>D<sub>3</sub> inhibits pro-inflammatory cytokine production by CCR6 +Th memory cells.

**Objectives:** We investigated whether 1,25(OH)<sub>2</sub>D<sub>3</sub> can induce an anti-inflammatory phenotype in these memory CCR6 +Th cells.

**Methods:** CCR6 +Th memory cells, excluding Tregs, were sorted from treatment-naïve early RA patients or healthy controls and cultured with or without 1,25(OH)<sub>2</sub>D<sub>3</sub>. Effects were analysed using microarray, RT-PCR, ELISA or flow cytometry. Functional properties were assessed via suppression and chemotaxis assays.

**Results:** 1,25(OH)<sub>2</sub>D<sub>3</sub> inhibits pro-inflammatory cytokines such as IL-17A, IL-17F and IL-22 in CCR6 +Th memory cells from both healthy controls and RA patients. This is accompanied by induction of anti-inflammatory factors, including IL-10 and CTLA4. Interestingly, these formerly pathogenic cells suppress proliferation of autologous CD3 +T cells, similar to classical Tregs. Importantly, the modulated memory cells still migrate towards the site of inflammation, modelled by synovial fluid, and retain their suppressive capacity in this environment.

**Conclusions:** Committed pro-inflammatory IL-17A-producing CCR6<sup>+</sup>Th memory cells shift towards anti-inflammatory cells with functional regulatory capacities upon exposure to active vitamin D. This process can contribute to restoring the immunological balance and inhibiting synovial inflammation in RA.  
**Disclosure of Interest:** None declared  
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**THU0049 DEVELOPMENT OF TFH-TH1 LIKE CELLS THROUGH EPIGENETIC MODIFICATION BY STATS FAMILY FACTORS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS**

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**Background:** Systemic lupus erythematosus (SLE) is a prototype of autoimmune disease characterised by chronic immune activation and multiple immunologic phenotypes<sup>(1)</sup>. Among several types of immune cells, T follicular helper (Tfh) cells serve important roles in the development and progression of SLE<sup>(2)</sup>.

**Objectives:** To assess the characteristics and mechanisms of differentiation of Tfh cells, we probed the phenotype of T helper cells in patients with SLE and underlying epigenetic modifications by cytokine-induced signal transducer and activators of transcription (STAT) family factors.

**Methods:** Naive CD4<sup>+</sup> T cells and memory CD4<sup>+</sup> T cells were isolated and stimulated by various cytokines and T cell receptor (TCR) *in vitro*. Expression of characteristic markers of Tfh-Th1-cells and phosphorylation of STATs were analysed by flow cytometry and qPCR. Histone modifications were evaluated by chromatin immunoprecipitation. Peripheral blood mononuclear cells from SLE patients and healthy controls were analysed by flow cytometry and productions of cytokines in serum were tested by cytometric bead array.

**Results:** Differentiation of CXCR5<sup>+</sup>CXCR3<sup>+</sup>Bcl-6<sup>+</sup>T-bet<sup>+</sup>IL-21<sup>+</sup>IFN- $\gamma$ <sup>+</sup> Tfh-Th1-like cells was induced by IL-12. Among STAT family, STAT1 and STAT4 were phosphorylated simultaneously by IL-12 independent of IFN- $\gamma$  and directly bound on Bcl-6 and T-bet gene loci accompanied by suppression of trimethylated histone 3 lysine 27. Compared with healthy controls, responsiveness of activation of STAT1 and STAT4 by IL-12 and proportion of activated Tfh-Th1-like cells were increased in patients with SLE.

**Conclusions:** Our findings suggest that IL-12-mediated co-activation of STAT1 and STAT4 alter histone modification, resulting in development of Tfh-Th1-like cells that are characteristically expanded in patients with SLE. These findings could be one of underlying pathogenesis of SLE and potentially helpful towards development of cell-specific treatment.

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THURSDAY, 14 JUNE 2018

**Rheumatoid arthritis – etiology, pathogenesis and animal models**

**THU0050 HYPOXIA INDUCES PRODUCTION OF CITRULLINATED PROTEINS IN HUMAN FIBROBLAST-LIKE SYNOVIOCYTES THROUGH REGULATING HIF1A**

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**Background:** Hypoxia is a prominent microenvironment feature in a range of disorders including cancer, rheumatoid arthritis (RA), atherosclerosis, inflammatory bowel disease (IBD), infection and obesity. Hypoxia promotes biological functions of fibroblast-like synoviocytes via regulating hypoxia-inducible factor 1 $\alpha$  (HIF1 $\alpha$ ). Dysregulated protein citrullination in RA drives the production of antibodies to citrullinated proteins, a highly specific biomarker of RA. However, the mechanisms promoting citrullination in RA are not yet fully elucidated.

**Objectives:** In the present study, we investigated whether pathophysiological hypoxia as found in the rheumatoid synovium modulates the citrullination in human fibroblast-like synoviocytes (HFLS).

**Methods:** HFLS were incubated in a hypoxic chamber (5% CO<sub>2</sub> and 1% O<sub>2</sub>, balanced with N<sub>2</sub> as indicated) or in a normal incubator containing 5% CO<sub>2</sub> and approximately 20% O<sub>2</sub>. The realtime quantitative PCR and western blotting were used to detect the expression of peptidylarginine deiminase 2, peptidylarginine deiminase 4 and citrullinated proteins. HFLS were transfected with HIF1 $\alpha$  siRNA to block the HIF1 $\alpha$  pathway.

**Results:** In the present study, we found that peptidylarginine deiminase 2 (PAD2) and citrullinated proteins were increased in HFLS after exposed to hypoxia. Moreover, knocking down HIF1 $\alpha$  by hif1 $\alpha$  siRNA ameliorated the expression of PAD2 and citrullinated proteins.

**Conclusions:** Collectively, the present study provide a new mechanism involved in generating citrullinated proteins: hypoxia promote citrullination and PAD production in HFLS. Concurrently, we also proposed a novel hypoxia involved mechanism in RA pathogenesis. The present study deepens our understanding of the role of hypoxia in the pathogenesis of RA and provides potential therapeutic strategy for RA.

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**THU0051 TNF RECEPTOR 2 PLAYS AN IMMUNOREGULATORY AND ANTI-INFLAMMATORY ROLE IN ARTHRITIS**

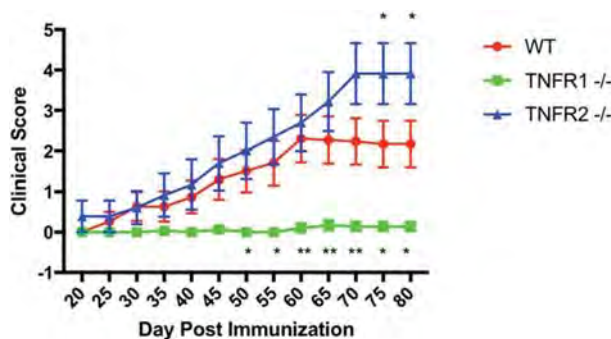
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**Background:** Despite the overall success of TNF $\alpha$  inhibitors in rheumatoid arthritis (RA), up to half of patients are classified as either primary or secondary non-responders<sup>1</sup>. One hypothesis put forward to explain resistance to anti-TNF $\alpha$  therapy is an ascendant effect of dysregulated regulatory T cells and increased Th17 responses following TNF $\alpha$  blockade. Previous studies have demonstrated that TNFR2 is critical for stabilisation and suppressive function of regulatory T cells<sup>2,3</sup>. However, TNFR2 also activates pro-inflammatory signalling cascades and, to date, the net effect of TNFR2 on the pathogenesis of RA remains unclear.

**Objectives:** In this study we address this question by assessing the progression of collagen-induced arthritis (CIA) in mice deficient for TNFR1 or TNFR2.

**Methods:** C57Bl/6N.Q (H-2<sup>q</sup>) mice were immunised with bovine type II collagen emulsified in complete Freund's adjuvant. The mice were monitored daily for arthritis and scored clinically from the day of onset of disease. Mice were culled on day 10 after arthritis onset and spleens, lymph nodes, serum and paws were collected for further analysis.

**Results:** As expected, TNFR1<sup>-/-</sup> mice were found to be largely resistant to arthritis both clinically and histologically (figure 1). In contrast, there was significantly enhanced disease activity at the clinical and histological levels in TNFR2<sup>-/-</sup> mice (figure 1) and this was accompanied by increased expression of the pro-inflammatory cytokines, TNF $\alpha$  and IL-6, reduced numbers of regulatory T cells, reduced FoxP3 expression and reduced expression of the immune inhibitory molecules, PD-1 and LAG3, in TNFR2<sup>-/-</sup> mice compared to WT mice.



Abstract THU0051 – Figure 1. Progression of CIA in mice deficient for TNFR1 or TNFR2

**Conclusions:** This study has shown that TNFR2 signalling plays immunoregulatory and anti-inflammatory roles in CIA. First, it contributes to promotion of regulatory T cell generation and FoxP3 expression, and second, it limits the expression of pro-inflammatory cytokines. TNFR2 also regulates the expression immune inhibitory

molecules during inflammation. The results support the rationale to for development of TNFR1 specific antagonists or TNFR2 agonists for the treatment of RA.

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### THU0052 A CIRCULATING PROTEIN SIGNATURE CORRELATES WITH SYNOVIAL PATHOTYPES IN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Rheumatoid arthritis (RA) is a disease characterised by high clinical variability and an underlying cellular and molecular heterogeneity. Efforts to find tools for the classification of the different disease phenotypes and patient stratification are essential to develop tailored therapies and improve its management. According to this, specific pathological phenotypes of synovial tissue (pathotypes) have emerged as associated with diverse clinical evolution and response to therapy.<sup>1</sup>

**Objectives:** To identify signatures of circulating proteins associated with specific synovial pathotypes in RA patients.

**Methods:** A proteomic analysis was carried out on samples from patients enrolled in the Pathobiology of Early Arthritis Cohort. Ultrasound-guided synovial biopsies from these patients allowed their classification into three groups: lymphoid (L), myeloid (M) or fibroid (F), according to the pathotype. The study was performed using 54 serum samples at baseline. Sera were analysed by nanoliquid chromatography coupled to mass spectrometry using a SWATH strategy on a triple TOF (Sciex). The proteomic data were processed using ProteinPilot and PeakView. A two-stage support vector machine (TSSVM) with RBF kernel and 10 cross-fold validation for each meta-model was applied using the Classyfire, e1071 and caret R packages.

**Results:** The proteomic analysis led to the identification and quantification of 229 proteins in all samples. A screening was performed on a group of 30 samples (Train set: 10 L, 10 M and 10 F). Data were pre-processed by PCA for dimension reduction. Then, application of machine learning tools led to the identification of a panel of 11 proteins whose different abundance is associated with a specific synovial phenotype (either L, M or F) in RA patients. As shown in the table 1, a very high accuracy and Kappa coefficient were achieved with this classification tool. The results were confirmed on an independent validation set of 24 samples (12 L, 8 M and 4 F) with also good performance. This protein signature allowed the correct classification of the samples into the three pathotypes with very high sensitivity and specificity (see table 1).

**Abstract THU0052 – Table 1.** Metrics of the classification performance of the 11-protein panel identified in this work as associated with the synovial pathotype of the patient. Cut-off for significance was p-value<0.05.

Train set	Classes in the train set						
				Fibroid	Lymphoid	Myeloid	
Accuracy	0.9667	95% CI	(0.8278–0.9992)	Sensitivity/	1.000/	1.000/	0.9091/
				Specificity	1.000	0.9524	1.000
Kappa	0.95	P-Value	4.48E-09	Pos/Neg	1.000/	0.9000/	1.000/
				Pred Value	1.000	1.000	0.9500
Validation set	Classes in the validation set						
				Fibroid	Lymphoid	Myeloid	
Accuracy	0.875	95% CI	(0.6764–0.9734)	Sensitivity/	1.000/	0.8462/	0.8750/
				Specificity	0.9524	0.9091	0.9375
Kappa	0.7907	P-Value	0.0005881	Pos/Neg	0.7500/	0.9167/	0.8750/
				Pred Value	1.000	0.8333	0.9375

**Conclusions:** A signature of 11 circulating proteins has been identified as associated with synovial pathotypes in RA patients. The putative correlation of this signature with the clinical evolution and/or response to therapy of the patients remains to be elucidated.

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**Disclosure of Interest:** None declared

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### THU0053 ANTI-FRACTALKINE MONOCLONAL ANTIBODY AMELIORATES JOINT DESTRUCTION IN COLLAGEN-INDUCED ARTHRITIS MODEL BY INHIBITION OF OSTEOCLAST PRECURSOR CELL SURVIVAL AND MIGRATION

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**Background:** In the Phase 1/2 clinical study, E6011, a novel humanised anti-fractalkine (FKN) mAb demonstrated a promising efficacy in active RA patients who were inadequately controlled by MTX and/or TNF- $\alpha$  inhibitors (NCT 02196558). FKN is expressed on endothelial cells and fibroblast-like synoviocytes in synovium and also expressed on osteoblasts. CX3CR1 is expressed on monocytes/macrophages and osteoclast precursor cells (OPCs). Therefore, FKN-CX3CR1 interaction could play pivotal roles in migration, differentiation and activation of those cells. However, the precise mechanism(s) of FKN-CX3CR1 axis in RA, especially on joint destruction remains to be elucidated.

**Objectives:** We examined the roles of FKN-CX3CR1 axis in joint destruction, particularly focused on osteoclast precursor cells in *in vitro* and *in vivo* by using anti-mouse FKN mAb (anti-mFKN mAb).

**Methods:** DBA/1J mice were immunised with intradermal injections of bovine type II collagen to induce arthritis (CIA). Anti-mFKN mAb or control IgG were intraperitoneally injected twice a week. The clinical arthritis score was monitored, and joint destruction was evaluated by soft X-ray and histopathology. Plasma levels of joint destruction markers were assessed by ELISA. FKN expression in joint tissues were assessed by immunohistochemistry. Cell survival of bone marrow-derived OPCs without or with immobilised FKN was also assessed by FACS. In *in vivo*, OPCs were labelled by fluorescein and transferred to CIA mice to evaluate migration of OPCs into inflamed synovium. Anti-mFKN mAb or control IgG were injected before the cell transfer. The number of fluorescein-labelled OPCs that migrated into the CIA joint tissue were analysed.

**Results:** In both prophylactic and therapeutic treatments, anti-mFKN mAb clearly reduced the clinical arthritis score, soft X-ray score. Plasma levels of cartilage oligomeric matrix protein (COMP) and matrix metalloproteinase-3 (MMP-3) were also decreased after treatment with anti-mFKN mAb. Histological analysis revealed that anti-mFKN mAb inhibited synovitis, pannus formation, cartilage destruction, and that it suppressed bone damage with marked reductions in the number of tartrate-resistant acid phosphatase (TRAP)-positive cells. In *in vitro*, RANKL-induced osteoclast differentiation was enhanced by immobilised FKN, and anti-mFKN mAb suppressed FKN-dependent enhancement of osteoclast formation. FKN also enhanced cell survival of OPCs and eventually increased the number of OPCs. In *in vivo*, increasing expression of FKN was detected on endothelium in synovial tissue of CIA mice, and fluorescein-labelled OPCs migrated into the affected synovium. Anti-mFKN mAb clearly abrogated their migration into synovium.

**Conclusions:** Anti-mFKN mAb remarkably ameliorated the joint destruction with the marked reduction of osteoclasts by the inhibition of both OPC survival and OPC migration in inflamed joint tissues. These results strongly indicate that inhibition of FKN-CX3CR1 axis by a humanised anti-FKN mAb, E6011, is an attractive and affected joints-selective therapeutic strategy for the treatment of both inflammatory synovitis and joint destruction in RA patients.

**Disclosure of Interest:** None declared

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### THU0054 LONG NON-CODING RNA GAPLINC PROMOTES PROLIFERATION AND INVASION OF FIBROBLAST-LIKE SYNOVIOCYTES AS MICRORNA SPONGING IN RA PATIENTS

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**Background:** Accumulating evidence suggested that long non-coding RNAs (lncRNAs) play diverse functional roles in many autoimmune diseases including



rheumatoid arthritis (RA). However, there is a dearth of knowledge in what role these transcripts play in fibroblast-like synoviocytes (FLSs) of RA patients. LncRNA GAPLINC, a novel long non-coding RNA, was first described in gastrointestinal cancer tissues and associated with bad behaviours of tumour cell as well as poor prognosis in patients.

**Objectives:** This study was undertaken to explore the expression and roles of LncRNA GAPLINC in RA-FLSs and investigate its possible mechanism.

**Methods:** RA-FLSs and trauma-FLSs were cultured from synovial specimens. The expression of RNA was detected by qRT-PCR. GAPLINC suppression was transfected by siRNA. Cell viability analysis was taken by CCK-8 assay and flow cytometry. Cell invasion was using transwell chamber methodology. The bioinformatics analysis was performed using miRanda, PITA, RNAhybrid algorithms, as well as KEGG and Gene Ontology(GO) analysis.

**Results:** The relative expression of LncRNA GAPLINC was significantly higher in RA-FLSs than trauma-FLSs ( $p < 0.05$ ). Transfection of GAPLINC-siRNA significantly decreased the expression of LncRNA GAPLINC in RA-FLSs. GAPLINC suppression in RA-FLSs revealed significant alterations in cell proliferation and invasion. In the GAPLINC-siRNA group, a inhibition rate in growth was first observed ( $15.29\% \pm 0.38\%$ ) at 24 hour after transfection, then a significant suppression was observed ( $28.75\% \pm 2.34\%$ ) at 48 hour, more apparent ( $36.63\% \pm 7.93\%$ ) at 72 hour and largely maintained ( $35.97\% \pm 3.67\%$ ) at 96 hour after siRNA treatment, compared to the negative control group (NC-siRNA). Moreover, flow cytometry assay showed GAPLINC-siRNA group had an accumulation of cells in the G0/G1 phase and the decreased number of RA-FLSs in the S and G2/M phase. In the invasive assay, the membrane-invading RA-FLSs numbers decreased significantly in the treatment group with GAPLINC knockdown ( $45.0 \pm 3.0$ ) compared to values observed in the NC-siRNA group ( $149.0 \pm 7.0$ ). Above comparisons were all statistically significant ( $p < 0.05$ ). The bioinformatics analysis predicted that some of microRNAs and mRNA may be the downstream molecules of LncRNA GAPLINC, we thus simulated a gene co-action network model based on the competitive endogenous RNA (ceRNA) hypothesis. Further verification of this model demonstrated that silencing of GAPLINC increased miR-382-5 p and miR-575 expression.

**Conclusions:** The results suggest that elevated LncRNA GAPLINC expression promote the proliferation and invasion of RA-FLSs and it may function as a novel microRNAs sponging agent. Additionally, LncRNA GAPLINC may regulate RA-FLS pathological behaviours in an miR-382-5 p-dependent and miR-575-dependent manner. Based upon these findings, LncRNA GAPLINC may provide a novel valuable therapeutic target for RA patients.

**Acknowledgements:** This work was supported by grants from Province Natural Science Fund of Guangdong, China<sup>No.2014A030313080</sup> and National Natural Science Foundation of China (No.81771750).

**Disclosure of Interest:** None declared  
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#### THU0055 AN ANATOMICALLY DISTINCT PATHOGENIC FIBROBLAST SUBSET DRIVES INFLAMMATION IN ARTHRITIS

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**Background:** Fibroblasts are key effector cells in the persistence of synovial inflammation and joint damage. It is not yet known whether specific subsets of synovial fibroblasts exist, and if so, if they are responsible for the distinct fibroblast mediated features observed in inflammatory arthritis, such as invasion of cartilage, bone damage, and persistence of inflammation.

**Objectives:** Here we identify and describe the biology of a functionally distinct pathogenic fibroblast cell type marked by the co-expression of Thy1.2 and Podoplanin (Pdpn), that is responsible for persistence of synovial inflammation.

**Methods:** We used the serum transfer arthritis (STA) model to induce joint inflammation. To identify putative subsets of fibroblasts we used flow cytometry using established markers of stromal cells, on enzymatically digested synovial tissue. These cells were localised in tissue sections using immunohistochemistry or immunofluorescence staining. Proliferation of subsets *in vivo* during the time course of STA was determined by BrdU incorporation studies. Transcriptomic analysis was performed using ultra-low input RNA sequencing on flow sorted populations of cells and single cell analysis performed on CD45 negative gated cells.

**Results:** Using FAP as a biomarker of activated synovial fibroblasts we have been able to identify and define distinct subsets of synovial fibroblasts based on their co-expression of Thy1.2 and Pdpn. These subsets reside in distinct compartments of the synovial microanatomy including the lining layer (LL), sub-lining layer (SL) and a subset of pericytes. We found that FAP +cells within the SL are highly proliferative and their expansion in cell number positively correlates with

inflammation. Global deletion of FAP +mesenchymal cells in the synovium using a FAP-DTR mouse attenuated synovial inflammation; protected against erosive bone damage and lead to reduced leucocyte accumulation as a result of reduced chemokine and cytokine production by synovial fibroblasts within the membrane. Collectively these data suggest a pathogenic pro-inflammatory role for these cells.

Transcriptomic analysis by both ultra-low input bulk RNA sequencing and single cell analysis revealed these subsets to be transcriptionally distinct with the greatest transcriptional differences observed between LL and SL cells, demonstrating a site specific transcriptional program for cells within these compartments. Gene signature analysis of SL FAP +cells was consistent with an immune effector cell phenotype, in contrast to lining layer cells that express genes associated with matrix remodelling. Finally, to test this hypothesis we injected FAP +LL cells and FAP +SL cells into inflamed ankle joints of mice. The injection of FAP +SL cells lead to more severe and prolonged joint inflammation, whereas injection of LL FAP +cells had no effect. Finally, we identified these cell subsets within human synovial tissue and have demonstrated the expansion of SL cells with inflammation.

**Conclusions:** Synovial inflammation is associated with the expansion, activation and differentiation of fibroblasts into distinct functional subsets of cells that regulate those specific aspects of inflammatory joint pathology. Direct targeting of specific pathogenic subsets of synovial fibroblasts may provide a novel, non-immunosuppressive approach to the treatment of inflammatory arthritis.

**Disclosure of Interest:** None declared  
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#### THU0056 14-3-3 IS A MOLECULAR SWITCH REGULATING MACROPHAGE POLARISATION IN INFLAMMATORY ARTHRITIS

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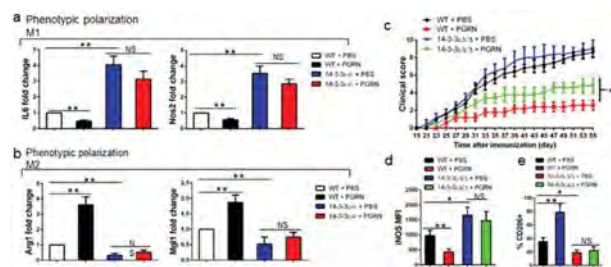
**Background:** Functional heterogeneity is a hallmark of macrophages, which can be classified into 2 major phenotypes with opposite role in inflammation termed M1 (inflammatory or classically activated) macrophages and M2 (alternatively activated) macrophages. In addition, M1-M2 polarisation of macrophages is a highly dynamic process and the phenotype of polarised macrophages can be switched under physiological and pathological conditions. Progranulin (PGRN), a multiple functional growth factor, binds to TNF receptor 2 (TNFR2) and activates the protective and anti-inflammatory pathway in inflammatory arthritis. In addition, 14-3-3e was identified as a component of PGRN/TNFR2 complexes in Raw264.7 macrophages.

**Objectives:** In this study, we examined whether 14-3-3e regulated macrophage polarisation and if so, whether this was important for PGRN's anti-inflammatory action in inflammatory arthritis.

**Methods:** LysMCre and 14-3-3e F/F mouse line was obtained from Jackson Laboratory.

**Results:** 14-3-3e regulates macrophage polarisation *in vitro*. We found that 14-3-3e deficiency enhanced M1 while inhibited M2 polarisation (figure 1a, b). Interestingly, PGRN showed reverse effects on macrophage polarisation. In addition, PGRN's effects were largely lost in 14-3-3e deficient BMDMs (figure 1a, b). Together, these data indicate that 14-3-3e is a critical downstream mediator of PGRN regulation of macrophage polarisation.

**Macrophage-specific 14-3-3e contributes to control of inflammatory arthritis and is critical for PGRN's anti-inflammatory action.** We then explored the role of macrophage-specific 14-3-3e in inflammatory arthritis and whether PGRN's anti-inflammatory activity depended on 14-3-3e *in vivo*. We established CIA in 14-3-3eF/F (serve as WT) and 14-3-3eΔ/Δ mice, followed by i.p. injection of recombinant PGRN. The clinical arthritis score demonstrated that 14-3-3eΔ/Δ mice displayed increased severity of CIA compared with WT CIA. In addition, PGRN's protective effects against inflammatory arthritis was compromised in 14-3-3eΔ/Δ mice (figure 1c), suggesting that 14-3-3e is critical downstream mediator of PGRN's anti-inflammatory effects. In addition, FACS analysis showed that total numbers of F4/80 cells were not different in all WT and knockout CIA mice. However, analysis of CD45 +CD11b+cell population in spleen demonstrated a significant increase in mean fluorescence intensity (MFI) of iNOS and a significant decrease of CD206 +cells in PBS treated 14-3-3eΔ/Δ CIA mice as compared with PBS treated WT CIA mice; moreover, there was a significant decrease of iNOS MFI while a dramatic increase of CD206 +cells in PGRN-treated WT mice compared to that in PBS-treated mice. Further PGRN-mediated effects on macrophage polarisation was lost in 14-3-3eΔ/Δ CIA mice (Fig 1d, e). Collectively, these results indicate that PGRN skews macrophage toward M2 polarisation to resolve inflammation and this effect depends on 14-3-3e.



**Abstract THU0056** – Figure 1. 14–3–3 $\epsilon$  is a critical mediator of PGRN<sup>1</sup> regulation of macrophage polarisation and contributes to PGRN's anti-inflammation action. (a, b) qPCR analysis of Il1b and Nos2 (a), or Arg1 and Mgl1 (b) mRNA expression in WT, or 14–3–3 $\epsilon$ -/- macrophages which are polarised to M1 (a) or M2 (b) in the absence or presence of PGRN (200ng/ml). (c) Clinical arthritis score of WT or 14–3–3 $\epsilon$  $\Delta\Delta$  CIA mice treated with or without PGRN. n=8 (d, e) CD45+CD11b+ cells were analysed for MFI of iNOS (d) and percentage of CD206+ cells (e). \* p<0.05, \*\* p<0.01, NS=no significance

**Conclusions:** Both *in vitro* and *in vivo* results indicate that 14–3–3 $\epsilon$  is a key molecule regulating macrophage polarisation which plays an important role in inflammatory arthritis, and it is an essential component for PGRN/TNFR2 mediated protective effect against inflammatory arthritis.

**Disclosure of Interest:** None declared

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### THU0057 MECHANICAL STRAIN DETERMINES THE SITE-SPECIFIC DIRECTION OF INFLAMMATION AND TISSUE DAMAGE IN ARTHRITIS

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**Background:** Many pro-inflammatory pathways leading to arthritis act systemically on the immune system rather than locally in the joint. However, the reason behind the regional and patchy distribution of arthritis represents a longstanding paradox.

**Objectives:** To explore the relation between mechanical strain and joint inflammation and to understand the underlying basis of joint pattern involvement in inflammatory rheumatic diseases.

**Methods:** Arthritis was induced by collagen-induced arthritis (CIA) and passive collagen antibody induced arthritis (CAIA) in respectively C57BL/6 and RAG2-/- (T- and B-cell deficient) mice. Animals were subjected to different regimens of mechanical strain. Increased strain occurred in voluntary running mice whereas tail suspension (unloading) abolished mechanical strain; both were compared to control housing conditions. The impact of different loading conditions was measured on clinical disease score, histology, micro-CT images and erosion quantification, gene induction in tendon and synovial tissue, immune cell recruitment *in situ*, development of anti-collagen antibodies and their pattern of sialylation and galactosylation.

**Results:** Voluntary running of CIA in C57BL/6 mice markedly induced an early onset and increased progression whereas no disease onset could be observed in the hind paws from animals in unloaded conditions. CAIA in running RAG2-/- mice also induced early arthritic symptoms and severe progression. Intriguingly, running conditions were sufficient to induce arthritis without the need of LPS as an inflammatory trigger. Mechanical strain did not alter however IgG autoantibody levels nor their levels of galactosylation and sialylation. Furthermore, we demonstrate that mechanical strain on stromal cells results in recruitment of classical monocytes into specialised mechano-sensitive regions characterised by a unique microanatomy. This promotes local inflammation and differentiation into local osteoclasts which induce regional erosions. A striking similarity was observed in the pattern of joint erosions in human patients with RA and SpA which were also confined to these mechanosensitive regions.

**Conclusions:** This study provides the first evidence that mechanical strain controls the transition from systemic autoimmunity into site-specific joint inflammation.

Homing of inflammation and development of erosions was confined to specific mechano-sensitive regions, characterised by a high number of attachment- and contact points for tendons. This represents a novel paradigm and explains why arthritis in mice and humans is characterised by a regional and patchy distribution. Curiously, this pathway does not rely on adaptive immunity but rather on stromal cells. Mechano-stimulation of mesenchymal cells induced CXCL1 and CCL2 permitting recruitment of classical monocytes which can differentiate into bone-resorbing osteoclasts. Thus, mechanical strain controls the site-specific direction of inflammation and tissue damage in arthritis.

**Acknowledgements:**

**Disclosure of Interest:** None declared

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### THU0058 TAS8274, A HIGHLY SELECTIVE JANUS KINASE 3 INHIBITOR, SHOWS POTENT EFFICACY, BUT DOES NOT AFFECT HOST DEFENSE, IN PRECLINICAL MOUSE MODELS

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**Background:** The family of Janus kinases (JAKs) plays important roles in signalling pathway mediated by various cytokine receptors. An aberrant activation of JAK-STAT signalling has been reported to be involved in the pathogenesis of autoimmune diseases<sup>1</sup>. Pan-JAK inhibitors have shown a good efficacy in patient with rheumatoid arthritis (RA)<sup>2</sup>. However, their use is limited due to safety concerns, including severe herpes zoster infection, by inhibiting JAK1-mediated interferon signaling<sup>3</sup>. Therefore, a selective JAK3 inhibitor would provide a better balance between efficacy and safety than pan-JAK inhibitors.

**Objectives:** We identified the characteristics of TAS8274, a novel highly selective inhibitor of JAK3, using *in vitro* assays, a mouse model of collagen-induced arthritis (CIA), and a mouse model of herpes simplex virus (HSV)-1 infection.

**Methods :** *In vitro* biochemical assay was performed using available kinase assay panels. The effects on anti-inflammatory responses were assessed by examining cytokine productions. IL-2, IL-3, and IFN- $\alpha$ -induced phosphorylation of STAT proteins in peripheral blood mononuclear cells (PBMCs) were analysed by a flow cytometry method. NK cell cytotoxicity in the presence of IFN- $\alpha$  was evaluated by Cr<sup>51</sup> release assay. In a mouse skin HSV-1 infection model, TAS8274 and tacrolimus were administered for 7 days before inoculation of the virus on the back skin, and then were administered for another ten consecutive days. At the end of this experiment, the number of papules on the back was counted. To evaluate the therapeutic efficacy using mouse CIA model, TAS8274 was orally administered to CIA mice after the disease onset. Disease severity was evaluated by clinical score of paw swelling, and the scores of inflammation, pannus, cartilage, and bone damage were performed using a modified Mankin score system.

**Results:** TAS8274 inhibited the enzymatic activity of JAK3 (IC<sub>50</sub>=0.16 nM), and showed more than 1000-fold selectivity against other JAK kinases. In the cell-based assays, TAS8274 strongly inhibited IL-17 production from differentiated Th17 cells. TAS8274 also suppressed the IL-2-induced STAT5 phosphorylation in PBMCs, but had much lower inhibitory effects on the IFN- $\alpha$ -induced STAT1 phosphorylation. In contrast, Tofacitinib and Baricitinib had robust inhibitory effects on the IFN- $\alpha$ -induced STAT1 phosphorylation. Furthermore, Tofacitinib and Baricitinib dose-dependently reduced the NK cell cytotoxicity, while TAS8274 had little effect on that. Tacrolimus-treated group significantly increased the number of papules compared with vehicle-treated group in a mouse HSV-1 infection model, but TAS8274-treated group did not increase the number of papules. In an established mouse CIA model, TAS8274 dose-dependently reduced the severity of arthritis and histopathological scores compared with vehicle-treated mice.

**Conclusions:** TAS8274 did not inhibit the JAK3-independent STAT signalling pathway *in vitro* and showed potent efficacy at dose range without exacerbation of the risk of HSV-1 infection. Our study demonstrates that TAS8274 would be an attractive therapeutic agent with excellent balance between efficacy and safety.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.1865

**THU0059 PLASMA EXOSOMAL MIR-92A ARE INVOLVED IN THE OCCURRENCE AND DEVELOPMENT OF BONE DESTRUCTION IN RA PATIENTS BY INHIBITING APOPTOSIS OF FIBROBLAST-LIKE SYNOVIOCYTES**

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**Background:** Rheumatoid arthritis (RA) is a chronic and progressive autoimmune disease that mainly affects joints. Bone erosion and bone destruction are the characteristic features of RA.<sup>1</sup> The mechanism of bone destruction is not fully understood at present. The decrease of apoptosis of human fibroblast-like synoviocytes (FLSs) originating from mesenchymal is involved in the occurrence and development of bone destruction in RA.<sup>2</sup> Exosomes are important mediators of biological information and play a part in the occurrence and development of various diseases including RA.<sup>3</sup>

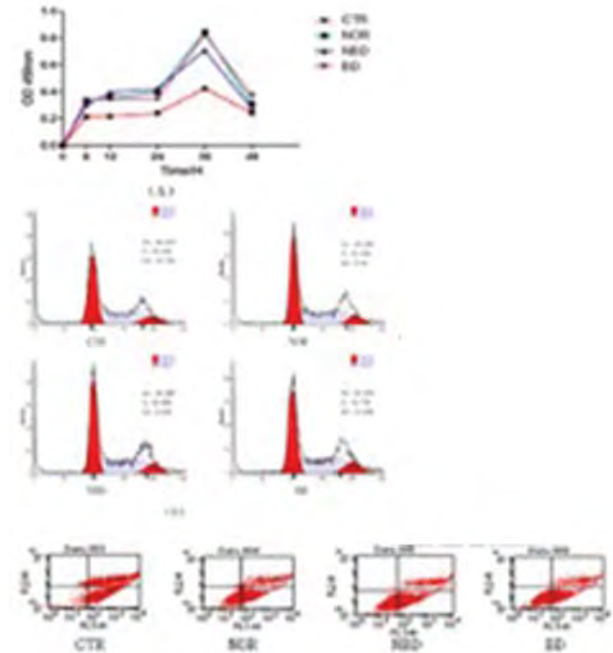
**Objectives:** The aim of study was to find whether exosomes participate in the pathogenesis of bone destruction in RA.

**Methods:** plasma was collected from 10 healthy people and 20 RA patients. According to Sharp-van der Heijde score (SHS), patients were divided into two groups named bone destruction group and non bone destruction group. Exosomes were extracted by Total Exosome Isolation reagent and confirmed by transmission electron microscope and western blot. The internalisation of exosomes was detected by immunofluorescence. Normal FLSs were stimulated with exosomes. Flow cytometry was utilised to detect the alteration of cell cycle and apoptosis rate. The cell proliferation was determined by CCK-8 assay. Apoptosis proteins (Bax, BCL-2 and caspase-3) were examined by western blot. The concentrations of TNF- $\alpha$  and IL-1 in the cell supernatants were measured by enzyme-linked immunosorbent assay (ELISA). High-throughput sequencing was used to detect the expression of miRNAs in exosomes.

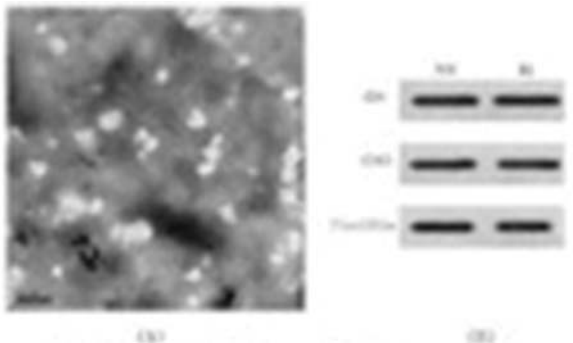
**Results:** There is no difference between exosomes of normal people and RA patients in promoting cell proliferation. However, the exosomes of RA patients can prohibit the cell apoptosis and promote the release of TNF- $\alpha$  and IL-1 from FLSs more effectively. Of these two RA groups, the abilities of bone destruction group exosomes are higher. The expressions of Bcl-2 and caspase-3 in bone destruction group are also significantly higher than that in the non bone destruction group and the normal group. Inversely the expression of Bax in bone destruction group is lower. Additionally, exosomal miR-92a are significantly over expressed in bone destruction group.

Table 1. The SHS and SHS/RF score of RA patients

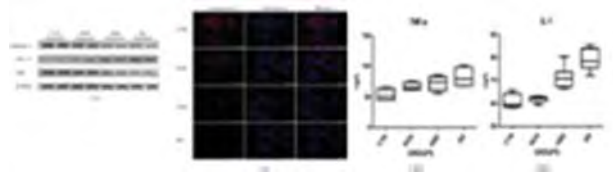
Number	SHS	RF	SHS/RF	SHS/RF
1	1	1	1	1.00
2	1	1	1	1.00
3	1	1	1	1.00
4	1	1	1	1.00
5	1	1	1	1.00
6	1	1	1	1.00
7	1	1	1	1.00
8	1	1	1	1.00
9	1	1	1	1.00
10	1	1	1	1.00
11	1	1	1	1.00
12	1	1	1	1.00
13	1	1	1	1.00
14	1	1	1	1.00
15	1	1	1	1.00
16	1	1	1	1.00
17	1	1	1	1.00
18	1	1	1	1.00
19	1	1	1	1.00
20	1	1	1	1.00



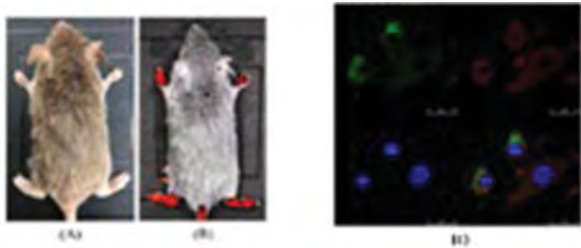
Abstract THU0059 – Figure 3



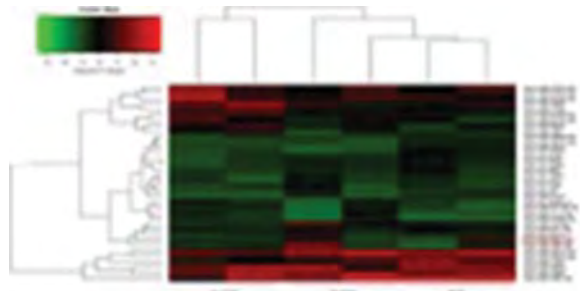
Abstract THU0059 – Figure 1



Abstract THU0059 – Figure 4



Abstract THU0059 – Figure 2



Abstract THU0059 – Figure 5



**Conclusions:** The study showed that exosomes in the serum of RA patients can prohibit the apoptosis of FLSs and enhance the secretion of inflammatory cytokines to promote bone destruction. Exosomes play an important role in the pathogenesis of RA. Exosomes can be used as a potential predictor for early bone destruction.

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**Disclosure of Interest:** None declared

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#### THU0060 ALTERATIONS OF SPLICING IN LEUKOCYTES FROM RHEUMATOID ARTHRITIS PATIENTS AND ITS INFLUENCE ON THE AUTOIMMUNE, INFLAMMATORY AND ATHEROTHROMBOTIC PROFILE OF THE DISEASE. POTENTIAL ROLE OF U4ATAC

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**Objectives:** The aim of this study was the identification, in leukocytes of Rheumatoid Arthritis (RA) patients, of the alterations present in the spliceosome and the machinery responsible for the splicing, as well as their influence on the activity of the disease and its atherothrombotic profile.

**Methods:** We evaluated, using a microfluidic qPCR array (Fluidigm), a set of 45 elements of the splicing machinery: the complete major and minor spliceosome components and a series of splicing factors with potential pathological role. Monocytes, neutrophils and lymphocytes of purified from 74 RA patients and 29 healthy donors (HD) were assessed. In parallel, extensive clinical/serological evaluation, and correlation and association analyses were carried out.

**Results:** A significant alteration in several components of the spliceosome was observed in all the three leukocyte subtypes from RA patients compared to HD. Various spliceosome components were specifically altered in different leukocyte subtypes; it should be noted that a general downregulation was observed. Likewise, it was striking that 7 elements, including two small nuclear RNA (snRNA) of the major spliceosome (U1 and U5), the snRNA of the minor spliceosome, U4atac, and the splicing factors RBM3, RBM17, SAM68 and SRSF10 showed the same alteration pattern: all significantly reduced in the 3 leukocyte subtypes of patients with RA, except for U4atac, which was consistently over expressed and virtually absent in HD leukocytes. Although this process needs further analysis, it is likely that the overexpression of U4atac could interfere in the normal functioning of the major spliceosome, by binding to U5, thus altering the splicing of most introns (>99%), favouring non-canonical splicing, and generating aberrant proteins involved in the development of this pathology. Correlation and association studies showed a significant association between the expression levels of the 7 splicing factors cited and several clinical/serological parameters, including the activity of the disease, the positivity for anti-CCP and RF antibodies, and the expression of different inflammatory mediators. Likewise, reduced values of other splicing factors, differentially deregulated in the three leukocyte subtypes, were associated with radiological involvement, as well as with the presence of atheroma plaques, hyperlipidemia and arterial hypertension.

**Conclusions:** We have identified specific alterations in the splicing machinery of leukocytes from RA patients, associated with the activity of the disease, as well as with its inflammatory and atherothrombotic profile. Altogether, the generalised reduction of multiple elements of the splicing machinery and the consistent elevation of U4atac will deem necessary to examine the possible role of this snRNA in the alteration of the spliceosome in the near future, as well as its specific implication in the regulation of the expression of key proteins in the pathology of RA.

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**Disclosure of Interest:** None declared

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#### THU0061 RESTRICTED AXL SYNOVIAL EXPRESSION AND INCREASED CLEAVAGE OF AXL ECTODOMAIN CORRELATE WITH HIGHLY INFLAMED SYNOVITIS AND MORE SEVERE RHEUMATOID ARTHRITIS

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**Background:** Tyrosine kinase Axl, member of the TAM family, is expressed by antigen presenting cells and behaves as a negative regulator of the inflammatory cascade. Inflammatory stimuli up-regulate Axl expression in bone-marrow-derived macrophages<sup>1</sup>. Soluble (s) Axl, generated by ADAM10, is a potent decoy for the TAM-ligand Gas6 and can impair TAM axis activation in lupus<sup>2</sup>. In rheumatoid arthritis (RA) dendritic cells, Axl is epigenetically down-regulated<sup>3</sup>. Emerging evidence has emphasised the significant role of Axl/sAxl in the pathogenesis and progression of autoimmune diseases, but little is known about TAM expression and regulation within the rheumatoid synovium.

**Objectives:** We aimed to quantify Axl/ADAM10 in synovial tissue (ST) and sAxl/Gas6 in synovial fluid (SF) and to correlate Axl/sAxl expression with synovial inflammation and disease severity in RA patients.

**Methods:** ST/SF were sampled from early treatment-naïve RA patients undergoing ultrasound (US)-guided synovial biopsy of the most inflamed accessible joint. RA was diagnosed according to ACR/EULAR2010 criteria. The Krenn's synovitis score of inflammation was determined by H and E. Immunohistochemistry (IHC) staining of CD3/CD20/CD138/CD68 allowed to define the synovial immune infiltrate. Axl/ADAM10/CD68 were assessed in ST by IHC/immunofluorescence (30 patients). sAxl/Gas6 were quantified in 17 SF by ELISA. Synovial gene expression data were obtained by next-generation sequencing (80 patients).

**Results:** Axl was predominantly expressed only by CD68-positive macrophages of the lining and co-localised with ADAM10. AXL synovial mRNA significantly negatively correlated with the Krenn's score and with the degree of infiltration by B/T lymphocytes, plasma cells, and sub-lining macrophages, but not lining macrophages. In SF, sAxl positively correlated with Gas6 and was significantly more abundant in patients with highly inflamed synovitis and more active disease. AXL synovial gene expression showed strong negative correlation with indexes of disease severity, including ESR, CRP, DAS28, and US synovial thickening/power-doppler, and with the mRNA of pro-inflammatory cytokines, e.g. TNF and IL6.

**Conclusions:** Our data demonstrate that, despite the highly-inflamed environment characterising RA synovia, Axl expression is restricted to the synovial lining, where it can be cleaved and released into the synovial fluid by ADAM10. There, sAxl can bind Gas6 with high affinity, preventing its interaction with transmembrane functional TAM receptors. Raised levels of sAxl and down-regulated AXL mRNA expression correlate with highly inflamed synovitis and more severe disease. Defects in the TAM system could provide an original mechanistic explanation of the persistent inflammation in the RA joints, representing a novel therapeutic target exploitable to regain tissue homeostasis.

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**Disclosure of Interest:** None declared

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#### THU0062 WNT5A INVOLVEMENT IN MIGRATION, INVASION AND THE PRO-INFLAMMATORY PHENOTYPE OF RHEUMATOID SYNOVIOCYTES

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**Background:** Fibroblast-like synoviocytes (FLS) are pivotal in the inflammation and joint damage of rheumatoid arthritis (RA). These cells acquire an aggressive phenotype; they migrate and invade articular structures perpetuating synovial inflammation. Also, they contribute to cartilage and bone damage by secretion of cytokines, metalloproteinases and cathepsins. The mechanisms modulating migration and invasion of FLS are not yet completely known. Recently, the role of the non-canonical pathway of Wnt5a has been highlighted in these processes, as well as, its contribution to osteoclastogenesis. Moreover, Wnt5a could be involved in other pathogenic aspects of RA, as suggested by its involvement in tissue

inflammation through regulation of cytokine, chemokine and metalloprotease expression. Thus, the study of the non-canonical pathway of Wnt5a in the aggressive phenotype of FLS and the inflammatory response may provide new therapeutic targets for the RA.

**Objectives:** To analyse the involvement of Wnt5a in the proliferation, migration, invasion and inflammatory responses of FLS from RA patients.

**Methods:** FLS were obtained from eight RA patients. Expression of Wnt5a was suppressed by siRNA transfection (Dharmacon). Cellular proliferation was determined using the CellTiter-Glo Luminescent Cell Viability Assay (Promega). Migration was analysed by the wound-healing assay using Ibidi inserts. The occupation area was determined by Image J. Invasion was tested by quantifying Giemsa stained cells on the bottom side of Matrigel coated trans-membrane (Millipore). The expression of inflammatory mediators and metalloproteases was analysed by real-time PCR after stimulation with recombinant Wnt5a protein (rWnt5a), TNF and combined treatment.

**Results:** We analysed the effect of the absence of Wnt5a and rWnt5a on the proliferation, migration and invasion of RA FLS. FLS lacking Wnt5a showed a significant migration decrease, 27.9% in basal condition and 16.9% after TNF stimulation, when compared with FLS transfected with siRNA control. Accordingly, migration of RA FLS treated with rWnt5a was increased by 48.5% when compared with cells treated with the vehicle. No change in migration was observed in TNF-stimulated FLS. Invasive capacity was reduced, reaching 71.4% of that observed in FLS transfected with siRNA control in basal conditions. In addition, invasion in FLS treated with rWnt5a was 35.7% higher than in controls. We also analysed the effect of rWnt5a on the inflammatory response of RA FLS. We found a significant increase of IL6, IL8, CCL2, CXCL5, MMP9 and MMP13 basal expression and the TNF-induced expression of IL6, IL8, CXCL5 and MMP3. Nevertheless, the lack of Wnt5a or the addition of rWnt5a did not modify the spontaneous or the TNF-induced proliferation.

**Conclusions:** These results indicate that Wnt5a contributes to the aggressive phenotype of FLS by potentiating their migration and invasion, and by stimulating the inflammatory response.

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**Disclosure of Interest:** None declared

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#### THU0063 CD11c+ DENDRITIC CELLS IN INFLAMMATORY ARTHRITIS

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**Background:** Dendritic cells (DCs) are important antigen presenting cells (APCs) and therefore they play an important role in bridging the innate and the adaptive immune response. DCs can be divided in different subsets with specific functions. As powerful APCs, DCs are thought to play an important role in the induction of autoimmune diseases such as rheumatoid arthritis. However, the active role of DCs in joint inflammation is not known yet.

**Objectives:** We analysed histological sections of K/BxN serum transfer arthritis as well as hTNFtg arthritis for the presence of CD11c+ cells by immunohistochemistry. We also performed synovial biopsies and analysed the cellular composition of the inflammatory infiltrate with respect to DCs. We used CD11c-diphtheria toxin receptor (DTR) transgenic mice, which express the human diphtheria toxin receptor under the CD11c promoter, allowing for specific depletion of CD11c+ cells by administration of diphtheria toxin (DT). K/BxN serum transfer arthritis was induced, and mice were given either DT or PBS or in wt and BARF3 deficient mice. In addition CD11c DTR mice were crossed into hTNFtg animals and also received either DT or PBS. The severity of arthritis was determined clinically and histologically.

**Methods:** We analysed histological sections of K/BxN serum transfer arthritis as well as hTNFtg arthritis for the presence of CD11c+ cells by immunohistochemistry. We also performed synovial biopsies and analysed the cellular composition of the inflammatory infiltrate with respect to DCs. We used CD11c-diphtheria toxin receptor (DTR) transgenic mice, which express the human diphtheria toxin receptor under the CD11c promoter, allowing for specific depletion of CD11c+ cells by administration of diphtheria toxin (DT). K/BxN serum transfer arthritis was induced, and mice were given either DT or PBS or in wt and BARF3 deficient mice. In addition CD11c DTR mice were crossed into hTNFtg animals and also received either DT or PBS. The severity of arthritis was determined clinically and histologically.

**Results:** We show that CD11c+ cells are present in significant numbers in the synovia of K/BxN and TNF driven arthritis. Both CD8+CD11c+ and CD11b+CD11c+, can be found in synovial tissue. Upon depletion of CD11c+ cells clinical signs of K/BxN serum transfer arthritis were significantly reduced. Histological analysis found reduced synovial inflammation after the depletion of CD11c+ cells in K/BxN arthritis. In addition, local bone destruction and the number of

osteoclasts was also significantly reduced. Analysis of K/BxN arthritis in wt mice and BATF3<sup>-/-</sup> mice, which lack a subset of DCs, namely CD8+CD11c+DCs, revealed no difference in arthritis severity between the two groups. In addition to K/BxN arthritis, we found that also in TNF-driven arthritis depletion of CD11c+ cells led to a striking reduction of synovial inflammation and a complete depletion of osteoclasts.

**Conclusions:** These data show that in addition to initiating an adaptive immune response, CD11c+ dendritic cells, are also involved in innate effector mechanisms of inflammatory arthritis. Especially CD11b+CD11c+ and monocyte derived inflammatory seem to play a role in inflammatory arthritis, suggesting that they could be an important therapeutic target for patients suffering from inflammatory arthritis.

**Disclosure of Interest:** None declared

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#### THU0064 ANTIBODIES AGAINST CARBAMYLATED PROTEINS FROM PATIENTS WITH RHEUMATOID ARTHRITIS ACTIVATE ENDOTHELIAL CELLS

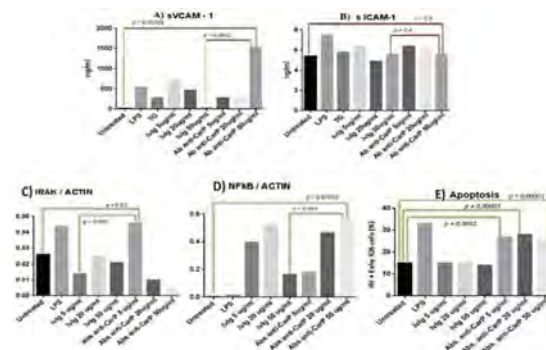
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**Background:** Inflammation contributes to the excess of cardiovascular morbidity in rheumatoid arthritis (RA), by promoting endothelial activation; this brings toward the production of adhesion molecules and the activation of signalling mediators. Antibodies against carbamylated proteins (anti-CarP) detected in RA patients correlate with subclinical atherosclerosis.

**Objectives:** Aims of the present study were: 1) to determine the effect of anti-CarP antibodies purified from the sera of RA patients, on the production of VCAM1 and ICAM1 as well as the activation of IRAK1 and NF- $\kappa$ B by human endothelial cell line EAhy926. 2) To evaluate endothelial cell apoptosis induced by anti-CarP.

**Methods:** An indirect ELISA was used to detect the presence of anti-CarP in the sera of RA patients. To purify anti-CarP, carbamylated-FCS used as an antigen was spotted onto a nitrocellulose filter and incubated with patient's sera that recorded the highest titer. Antibodies were eluted with glycine 100 mM, pH 2.5 and neutralised with Tris-HCl 1M, pH 8. Antibodies concentration was measured by using a colorimetric Bradford assay. The immortalised hybridoma cell line EAhy926 was cultured in Dulbecco's Modified Medium containing 10% fetal bovine serum, 1 mM l-glutamine, 100 U/ml penicillin and 10 ml HAT. After cell stimulation with purified anti-CarP at different time points (30 min-48 h) and different concentrations (5–20–50  $\mu$ g/ml), supernatants were gathered to investigate the production of VCAM-1, ICAM-1 using commercial ELISA kits while activation of IRAK1 and NF- $\kappa$ B was detected by Western Blot analysis using cell lysates. Apoptosis was measured using FITC-conjugated annexin V (AV) and a propidium iodide (PI) apoptosis detection kit at different times (30 min-48 h).

**Results:** After EAhy926 stimulation with anti-CarP we observed: 1) induction of VCAM-1 but not ICAM production in cell supernatants; 2) activation of IRAK1 and NF $\kappa$ B transcription factor in cell lysates and 3) induction of endothelial cell apoptosis.



**Abstract THU0064 – Figure 1.** Expression of adhesion molecules (A, B), activation of IRAK1 (C), NF $\kappa$ B (D) signalling and apoptosis (E) in EAhy 926.

**Conclusions:** These data suggest a potential involvement of anti-CarP antibodies in endothelial cell activation allowing to further speculate on its possible effect in excess cardiovascular risk in RA patients.

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**Disclosure of Interest:** None declared

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#### THU0065 RESULTS OF TREATMENT OF ARTHROSCOPIC AND TRADITIONAL SYNOVECTOMY OF THE KNEE JOINT IN RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis is a systemic inflammatory autoimmune disease of connective tissue with a predominant joint injury that occurs at any age, more often in women. It is characterised by a chronic course with periods of exacerbations and remissions

**Objectives:** To evaluate the results of arthroscopic and traditional synovectomy of the knee joint in patients with rheumatoid arthritis

**Methods:** The study involved 48 patients, 29 of them were women and 19 men, aged from 25 to 65 years old, who had a chronic synovitis of the knee joints. It was implemented at the department of traumatology, orthopaedics and GPH with neurosurgery of Tashkent Medical Academy and 1-Republic Clinical Hospital. In all patients, on the background of basic therapy and intraarticular injections of SCS, a persistent recurrent synovitis was formed within a few months. Sixteen patients underwent sinocapsulectomy (SCE) with the traditional method. 32 patients underwent arthroscopic synovectomy (ASE), for which the standard basic arthroscopic technique Dyonics (Smith and Nephew) was used. The functional condition of the knee joint before and after the operation was assessed using the KOOS scale (Knee and Osteoarthritis Outcome Score)

**Results:** The study showed that movements in the operated joint were allowed 3–5 hours after the operation, from the first day, isometric exercises were prescribed, active movements in the knee joint before the onset of pain. Results of treatment in terms of up to 3 months were tracked in all 48 patients. The degree of intraarticular changes determined by arthroscopy was evaluated according to the Outerbridge classification. In patients after SCE, pain in the joint, limiting the amplitude of motion, crunching during movement were noted. After ASE, there was a significant improvement in the function and condition of the knee joint: patients could walk for longer distances without additional support, did not experience discomfort while walking the stairs, complaints of pain, and no swelling. Repeated ASE with tunnelling was required in 2 patients with grade III chondromalacia

**Conclusions:** Thus, the SCE of the knee is indicated if the conservative treatment of recurrent synovitis in RA is unsuccessful for a long time. The ASE should be performed in the early stages of the RA, which drastically reduces the activity of the pathological process, makes it possible to maintain the functional capacity of the joint, and the timely adequate administration of the basic therapy allows the maximum achieved long-term functional result to be maintained for the longest time and reduces the risk of relapse and the need for repeated operations

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**Disclosure of Interest:** None declared

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#### THU0066 CIRCULATING MIRNAS AS POTENTIAL BIOMARKERS OF DISEASE AND CARDIOVASCULAR RISK IN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Circulating miRNAs have been proposed as attractive candidates as both diagnostic and prognostic biomarkers in various diseases, including a spectrum of autoimmune and cardiovascular conditions. Yet, the contribution of

circulating miRNAs to the cardiovascular pathogenesis of Rheumatoid Arthritis (RA) patients and their potential role as biomarkers are still unknown.

**Objectives:** To identify circulating miRNAs as potential biomarkers of disease features and cardiovascular (CV) risk in RA.

**Methods:** Plasma samples of 48 healthy donors (HDs) and 124 RA patients were collected. In the discovery phase, an array of 2083 human miRNAs was performed by using HTG EdgeSeq miRNA Whole Transcriptome Assay (Next generation sequencing) in 9 plasma samples (3 HDs, and 6 RA patients). Then, differentially expressed miRNAs, were selected and validated by RT-PCR in the whole cohort of patients and HDs. Potential targets of the validated miRNAs were identified by using Ingenuity Pathway Analysis (IPA) software and analysed at protein levels (Multiplex Assay). Correlation and association studies of altered miRNAs with analytical and clinical variables were also performed.

**Results:** The miRNA whole Transcriptome assay showed that 360 miRNAs were differentially expressed in RA patients in relation to HDs, including 261 upregulated and 97 downregulated. Functional classification (IPA) demonstrated that deregulated miRNAs were mainly involved in processes such as inflammatory response, connective tissue development and function, haematological disease, tissue development, and immunological disease. Nine microRNAs, selected among the most differentially expressed in the array, were selected for validation in all the subjects recruited (miR-299, miR-567, miR-4293, miR-135b, miR-6816, miR-346, miR-143, miR-199a, miR-106a, miR-148b). *In silico* analyses showed that these miRNAs had potential targets related to cytokine signalling, atherosclerosis pathway and intracellular signalling. The altered levels of selected miRNAs and its putative target proteins were validated in the whole cohort of patients.

A number of serum miRNAs in all the RA patients analysed were found inter-related and associated to autoimmunity (positivity for anti-CCPs and RF), bone erosion, inflammation (CRP, ESR, TNF $\alpha$ , IL6, IL8, IFN and IL-2), and evolution time. We could further identify a specific signature of four miRNAs (miR143, miR106, miR148b and miR567) that identified RA patients that had suffered previous CV events and specifically associated with the increase in the carotid intima-media thickness (CIMT) and with 'Framingham CV risk factors' such as diabetes, obesity or dyslipidemia.

**Conclusions:** We have branded novel and specific circulating miRNAs related to disease features and CV risk in RA patients, including, their autoimmune and inflammatory profile, the presence of Framingham risk factors and incipient atherosclerosis. These circulating miRNAs might be thus considered useful tools for the management of the disease in this autoimmune condition.

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**Disclosure of Interest:** None declared

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#### THU0067 ASSOCIATION OF HIGH TITERS OF ANTI-CARBAMYLATED PROTEINS ANTIBODIES WITH DECREASED BONE MINERAL DENSITY IN EARLY ARTHRITIS PATIENTS

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**Background:** Rheumatoid arthritis (RA) has a negative impact on bone homeostasis, in which multiple inflammatory mediators are involved together with the anti-citrullinated proteins antibodies (ACPA). These antibodies are able to promote osteoclastogenesis and bone loss even before the onset of synovitis. Accordingly, ACPA are associated with the three aspects of bone loss: joint bone erosion, juxta-articular bone loss and, as recently demonstrated<sup>1</sup>, decreased bone mineral density (BMD). Other RA specific autoantibodies, the anti-carbamylated protein antibodies (anti-CarPA), are associated with the presence, severity and progression of erosions with independence of ACPA. However, their implication in the other aspects of bone loss has not been studied.

**Objectives:** To evaluate the association of anti-CarPA with BMD in a cohort of early arthritis (EA) patients.

**Methods:** Clinical data and samples were obtained at the first visit of 548 patients from the Princesa Early Arthritis Register Longitudinal (PEARL) study, which recruits patients within one year from arthritis onset. BMD was assessed by dual-energy x-ray absorptiometry (Hologic QDR-4500, Elite, Mass, USA) at the lumbar spine (LS), total hip (TH) and metacarpophalangeal (MCP) joints. BMD was considered as Z-scores, except for MCP due to lack of reference data. Anti-CarPA were determined by ELISA using carbamylated fetal calf serum. The ELISA results were considered as negative, below the 98 percentile of healthy controls, low-positive, below the median of positive patients, and high-positive, otherwise. Data were analysed with linear regression including sex, age, BMI, and menopause as covariates.

**Results:** Anti-CarPA were positive in 25.9% of the EA patients. The positive patients did not show significant differences in BMD with the negative patients.



However, this lack of association was due to the similarity of negative and low-positive patients, because the high-positive patients showed significant decrease of BMD at LS ( $\beta = -0.39$ ,  $p = 0.01$ ) and TH ( $\beta = -0.30$ ,  $p = 0.02$ ). Nevertheless, we did not find significant association at the juxta-articular bone of the MCP joints. Given the overlap between anti-CarPA and ACPA, we included the two autoantibodies in multivariate analysis. The association with BMD was significant only in the ACPA positive/anti-CarPA high-positive subgroup at LS and TH ( $p = 0.007$  and  $0.005$ , respectively). In addition, the coefficients of regression were similar between the ACPA positive/anti-CarPA high-positive and the ACPA negative/anti-CarPA high-positive subgroups ( $\beta = -0.50$  vs.  $-0.52$  at LS, and  $\beta = -0.37$  vs.  $-0.30$  at TH).

**Conclusions:** We found significantly lower BMD at LS and TH in the patients with high anti-CarPA titers. These associations seem to be independent from the presence of ACPA, suggesting that anti-CarPA could contribute to systemic bone loss in EA patients.

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**Disclosure of Interest:** None declared

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#### THU0068 IDENTIFICATION AND VERIFICATION OF BIOMARKER CANDIDATES FOR MONITORING RHEUMATOID ARTHRITIS ACTIVITY BY MASS SPECTROMETRY

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**Background:** Rheumatoid arthritis (RA) is a long-lasting inflammatory autoimmune disorder that ultimately leads to the destruction of joint architecture. The activity of this disease is measured by the assessment of clinical symptoms.

**Objectives:** To apply a proteomic strategy to find serum biomarkers able to discriminate patients with different RA activities.

**Methods:** To facilitate the complex measurement of serum by proteomics, a simple, fast and reproducible albumin-specific depletion method using ethanol was optimised and applied to the samples employed in this study. 80 samples from the IMID consortium, classified according to the DAS28 score into low activity<sup>40</sup> and high activity<sup>40</sup> were analysed by mass spectrometry. Four independent pools of the high RA activity samples (10 samples per pool) and 4 pools of the low RA activity samples were firstly albumin-depleted, and then the remnant serum proteins were digested and differentially labelled with iTraQ 8-plex reagents. Subsequently, the 8 labelled pools were combined and cleaned using StageTips-C18. Finally, the pool mixture was fractionated by HPLC (Zorbax-C18) and the resulting fractions were analysed by nanoLC-MS/MS using MALDI-TOF/TOF, TripleTOF and LTQ-Orbitrap.

**Results:** The mass spectrometry analysis led to the identification of 186 proteins. In this screening step, the abundance of 9 proteins was found to be significantly different between patients with high (H) and low (L) RA activity. Orthogonal experiments, using Western Blot, protein bead arrays and Multiple Reaction Monitoring (MRM) with synthetic heavy-labelled peptides, were conducted in order to verify some of these biomarker candidates of RA activity. The results obtained from the verification phase, conducted by MRM on 50 samples from the same cohort, show a decrease of Apolipoprotein B (ratio H/L=0.84,  $p = 0.00$ ), Histidine Rich Glycoprotein (ratio H/L=0.86,  $p = 0.01$ ) and Plasma protease C1 inhibitor (ratio H/L=0.84,  $p = 0.02$ ). Furthermore, this verification phase shows also an increase of Haptoglobin (ratio H/L=1.34,  $p = 0.01$ ) and Serum Amyloid A1 (ratio H/L=1.64,  $p = 0.05$ ), in accordance with that observed in the screening. These proteins are related with the RA process and the effects caused by this type of disease (inflammation and immune disorder in joints).

**Conclusions:** In this proteomic study, 5 proteins were found to be quantitatively altered between patients with high and low RA activity using shotgun and targeted mass spectrometry.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.3517

#### THU0069 IN RA, BECOMING SERONEGATIVE OVER THE 1ST YEAR OF DMARD TREATMENT DOES NOT TRANSLATE TO BETTER CHANCES OF SUSTAINED DRUG-FREE REMISSION IN THE LONG-TERM

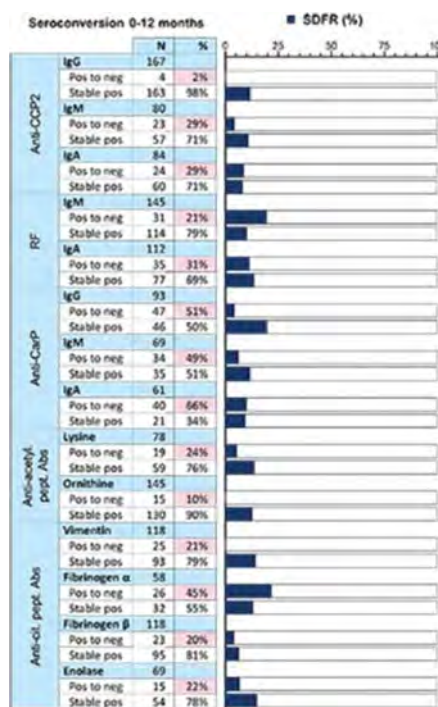
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**Background:** In rheumatoid arthritis (RA), autoantibodies are a reflection of the underlying B cell autoimmunity and an important predictor of long-term outcome. Baseline seropositivity is a poor prognostic factor for sustained drug-free remission (SDFR). However, autoantibody levels may change and patients may become seronegative under treatment. It is unknown how often this happens and whether some autoantibodies (depending on isotype use or antigen recognition) disappear more often than others. Furthermore, it is unclear whether becoming seronegative early in disease, indicating disappearance of serological autoimmunity, improves chances of SDFR.

**Objectives:** To longitudinally characterise the levels and presence of autoantibodies in RA patients and to investigate whether changes in these levels and/or presence associates with SDFR.

**Methods:** In sera of 399 seropositive RA patients in the IMPROVED study<sup>1</sup>, we measured, at 4-month-intervals over the first year of treatment: IgG, IgM, and IgA isotypes for anti-cyclic citrullinated peptide-2 (anti-CCP2) and anti-carbamylated protein antibodies (anti-CarP), IgM and IgA for rheumatoid factor (RF), and IgG autoantibodies against 4 citrullinated and 2 acetylated peptides. We investigated whether changes in antibody levels and seroconversion from positive to negative for each individual antibody was favourable for SDFR (drug-free DAS44 <1.6 lasting  $\geq 1$  year until last follow-up).

**Results:** For all 14 antibodies, median levels decreased significantly between baseline and 4 months and then stabilised. Most seroconversion to negative happened within the first 4 months of treatment (with prednisone and methotrexate), after which some patients converted back to seropositive. The prevalence of seroconversion varied substantially depending on the autoantibody. The percentage of patients who were seropositive at baseline and became seronegative by 12 months varied substantially depending on the autoantibody: 2% (anti-CCP2 IgG) to 66% (anti-CarP IgA) (see figure 1). We hypothesised that greater level decreases and seroconversion to negative might be favourable for the long-term outcome SDFR, but surprisingly, greater median decreases in levels were not associated with higher chance of SDFR for any antibody. Furthermore, using Chi-squared tests, we found no evidence that rates of SDFR were higher in patients who seroconverted to negative compared to those who stayed seropositive, for any of the 14 antibodies analysed (see figure 1).



Abstract THU0069 – Figure 1. Percentage of patients reaching SDFR (drug-free DAS44 <1.6 lasting  $\geq 1$  year until last follow-up), separated by whether patients

seroconverted from positive to negative ("Pos to neg") or remained positive ("Stable pos") or for the specified antibody, between 0–12 months.

anti-CCP2=Anti cyclic citrullinated peptide-2; RF=rheumatoid factor, anti-CarP=anti carbamylated protein antibodies; Anti-cit. pept. Abs=anti citrullinated peptide antibodies; Anti-acetyl. pept. Abs=anti acetylated peptide antibodies (IgG).

**Conclusions:** Autoantibody levels decrease and seroconversion from positive to negative occurs under treatment, but these changes do not translate to apparent clinical long-term benefits with regard to SDFR. This suggests that the disappearance of measurable serological autoimmunity does not lead to eradication of disease.

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[1] Heimans AR&T 2016;18:23.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.6356

#### THU0070 THE TRANSCRIPTION FACTORS IKAROS AND AIOLOS ARE EXPRESSED IN THE SYNOVIAL MEMBRANE OF EARLY RHEUMATOID ARTHRITIS PATIENTS IN ASSOCIATION WITH SYNOVIAL LYMPHOID AGGREGATES

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**Background:** IKZF1 (Ikaros) and IKZF3 (Aiolos) are transcription factors acting as regulators of the immune system development. Specifically, they are essential for the maturation, differentiation and survival of B cells. Polymorphisms of IKZF1 and 3 have been linked to systemic autoimmunity, and they are being explored as therapeutic targets in Systemic Lupus Erythematosus. However, their involvement in other autoimmune diseases is currently unknown.

**Objectives:** To evaluate the expression of IKZF1 and 3 in the synovia of patients with early Rheumatoid Arthritis (RA) naïve to treatment, in correlation with the clinical phenotype, including treatment response.

**Methods:** DMARD-naïve patients with early (<12 months) RA (n=41) fulfilling the 2010 ACR/EULAR criteria were recruited as part of the Pathobiology of Early Arthritis Cohort at Barts Health NHS Trust. Sections of paraffin embedded synovial tissue obtained by ultrasound-guided synovial biopsy were stained by immunohistochemistry (IHC) for IKZF1 and IKZF3, and a semi-quantitative score (0–3) was used to classify patients (IKZF1 +ve or IKZF3 +ve cells/visual field <5=0; 5–20=1; 20–50=2; >50=3). Sequential sections were stained by IHC for immune cells and patients were categorised into 3 synovial pathotypes according to the following criteria: i) Lymphoid (L) presence of grade 2–3 CD20+aggregates, (CD20 ≥2) and/or CD138 >2; ii) Myeloid (M) CD68SL ≥2, CD20 ≤1 and/or CD3 ≥1, CD138 ≤2 and iii) Fibroid (F) CD68SL <2 and CD3, CD20, CD138 <1.

**Results:** Ikaros and Aiolos were expressed in the synovia of 43.1% and 56.7% of early RA patients, respectively. IKZF1 +ve patients (defined as IKZF1 score ≥2) showed a higher prevalence of a lymphoid pathotype (9/9 in IKZF1 +ve vs 4/22 in IKZF1 -ve, p<0.001) and a higher prevalence of ACPA (9/9 vs 13/22, p=0.04) and RF (9/9 vs 12/22, p=0.02). IKZF3 +ve patients showed a similar association with local and systemic inflammation and autoantibody positivity. As shown in table 1, ikaros and aiolos synovial scores were significantly correlated with synovial cell infiltrate and systemic inflammation. Remarkably, ikaros showed a significant correlation with the baseline Sharp score. Accordingly, patients with high expression of Ikaros (sq score ≥2) had a significantly higher Sharp score (mean ±SD 4.75 ±3.3 vs 1.33±2.54, p=0.008).

**Conclusions:** Here, we show the expression of the transcription factors Ikaros and Aiolos in the synovia of early RA patients in correlation with lymphoid aggregates and systemic inflammation, and, for Ikaros, with baseline radiographic erosions. While additional analyses are needed in order to confirm the expression and function of ikaros and aiolos by synovial immune cells, our preliminary work suggest that they might be relevant in the pathogenesis of RA and therefore be considered as therapeutic targets in a subset of patients.

**Disclosure of Interest:** None declared

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**Abstract THU0070 – Table 1.** Spearman correlation coefficients

	Krenn	CD3	CD20	CD68L	CD68SL	CD138	ESR	CRP	DAS28	Sharp
IKZF1	0.659**	0.712**	0.816**	0.525**	0.432*	0.851**	0.553**	0.491**	0.333	0.410*
IKZF3	0.658**	0.652**	0.809**	0.581**	0.550**	0.812**	0.487*	0.474*	0.296	0.313

\*p<0.05; \*\*p<0.01

THU0071

#### MUSCLE LIPOTOXICITY ON SARCOPENIA DEVELOPMENT IN A MODEL OF COLLAGEN-INDUCED ARTHRITIS

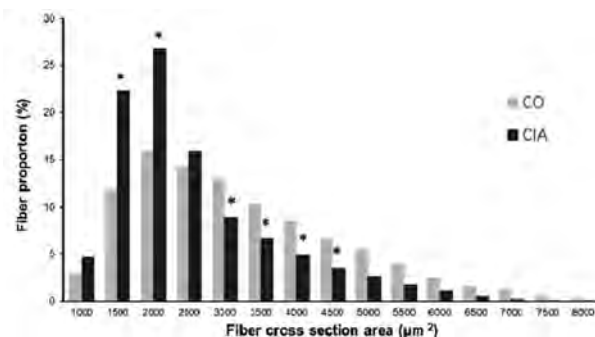
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**Background:** Alterations of body composition in Rheumatoid arthritis (RA) may contribute to the development of cardiometabolic disorders. RA patients have a decrease in muscle mass with a preserved or increased fat mass, notably accumulation of ectopic fat in the muscles, which define the sarcopenic obesity. The mechanisms leading to this sarcopenic obesity phenotype remain poorly understood. Accumulation of intramuscular lipids and the formation of lipotoxic compounds may affect intracellular signalling pathways and energy production, alter protein synthesis and thus promote sarcopenia.

**Objectives:** Our objective was to determine if muscular lipotoxicity promotes the development of sarcopenia in joint inflammatory condition, using rats with collagen-induced arthritis.

**Methods:** Male Sprague Dawley rats were divided into a control group (CO, n=12) and a collagen-induced arthritis group (CIA, n=11). After 5 weeks, hind leg muscles and epididymal adipose tissue were removed. Tissues were weighed at sacrifice and stored for histological analyses and evaluation of mitochondrial function, lipotoxicity, protein and gene expression levels. Statistical analyses were performed with t-test.

**Results:** Animals, adipose tissue and muscle weights tended to be lower in the CIA group. Only EDL muscle weight was significantly lower in the CIA group (p=0.05). Muscle histological analyses showed larger CSA (cross sectional area) in CO group. In the CIA group we observed a nonhomogeneous distribution of muscle fibre CSA with a predominance of small fibres (figure 1). Mean perimeter and mean diameter were also significantly decrease in CIA group but the shape of fibres remained similar between groups. Furthermore, there was an increased expression of MAFBx (a marker of catabolism) mRNA (40%, p=0.04) in the CIA group, while MyoD (a myogenesis marker) mRNA was decreased by 18% (p=0.01), indicating a catabolic state. Lipid content analysis showed an accumulation of intramuscular TAG (x 1.5, p=0.05), as well as an increased expression of cellular fatty acid transporter FATP1 (about 35%, p=0.01) and mitochondrial fatty acid transporter CPT1b (about 27%, p=0.02). Mitochondrial DNA copy number was decreased by 27% in CIA rats (p=0.01) and complex IV activity of mitochondrial respiratory chain also tended to be reduced in CIA group (-20%, p=0.18).



**Abstract THU0071 – Figure 1.** Fibre cross sectional area distribution

**Conclusions:** Collagen-induced arthritis induced fibres alterations in skeletal muscle. The association of increased muscle protein catabolism, mitochondrial dysfunction and fatty acid accumulation in skeletal muscle of animals with arthritis supports the hypothesis that lipotoxicity is involved in sarcopenia development during joint inflammation.

**Disclosure of Interest:** None declared

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THU0072

### GENE SIGNATURE OF PLASMACYTOID DENDRITIC CELLS REVEALS NOVEL PATHWAYS CONTRIBUTING TO TOLERANCE IN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Reestablishing immune tolerance and long term remission represent major therapeutic goals in rheumatoid arthritis (RA). Our laboratory previously demonstrated that plasmacytoid dendritic cells (pDCs) from RA patients in remission have the ability to induce IL-10 producing regulatory T cells (Tregs) *in vitro*.<sup>1</sup> However, the molecular pathway of RA pDC-mediated Treg induction remains elusive.

**Objectives:** Herein, we sought to identify the molecular mechanism through which pDCs contribute to restoration of tolerance in RA.

**Methods:** pDCs were isolated from peripheral blood of RA patients responding to anti-TNF therapy (remission based on disease activity score DAS28 <5.1) and healthy control subjects and DNA microarrays were performed. Flow cytometry and real time PCR were used to verify the expression of de-regulated genes in RA pDCs. Finally, *in vitro* cultures of pDCs activated with CpG A in the presence or absence of recombinant IL-6 (rIL-6) were performed to assess the functional importance of these gene signatures.

**Results:** pDCs from RA patients (n=5) exhibited a differential gene signature (6741 deregulated genes) compared to pDCs from healthy controls (n=5). Notably, IL-6 receptor (IL-6R) gene, exhibited increased expression levels in pDCs isolated from RA patients compared to healthy pDCs and the surface expression levels of IL-6 receptor were verified in a subsequent cohort of patients responding to therapy (n=9) versus active patients or healthy donors. Moreover, assessment of IL-6 signalling pathway in RA patients versus healthy donors revealed a significant increase of pSTAT1 expression levels in RA patients (n=9) compared with healthy donors (n=6) (mean fluorescence intensity  $\pm$ SEM, 7.98 $\pm$ 0.8 versus 12.65 $\pm$ 1.18, p value=0.0076). Importantly, IL-6-treated pDCs exhibited a vast decrease in TNF- $\alpha$  production (p value=0.0002) whereas no differences were found in the production of IFN- $\alpha$  and in their antigen presenting capacity between CpG-treated pDCs in the presence or absence of rIL-6. Moreover, confocal experiments in progress will assess the expression levels of TNF- $\alpha$  in pDCs isolated from RA patients in remission versus active or healthy donors. The functional importance of the previous findings will be addressed in coculture experiments of IL-6 stimulated pDCs with monocytes isolated from healthy donors and monitor their activation and maturation status.

**Conclusions:** We found that pDCs from RA patients in remission display increased IL-6R expression levels and an activated IL-6 signalling pathway. Activation of IL-6 signalling on pDCs *in vitro* significantly decreases the production of TNF- $\alpha$  whereas it does not alter IFN- $\alpha$  production and their antigen presenting capacity. This novel finding and the underlying mechanism that may drive pDCs towards a previously described tolerogenic phenotype, need to be further addressed.

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**Disclosure of Interest:** None declared

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THU0073

### A SUBSET OF NEUTROPHIL HIGHLY EXPRESSING CD49D AND VEGFR1 CAN ENHANCE PANNUS FORMATION VIA INCREASE FLS MIGRATION AND INVASION ABILITY BY UP-REGULATING MMP3 AND 13

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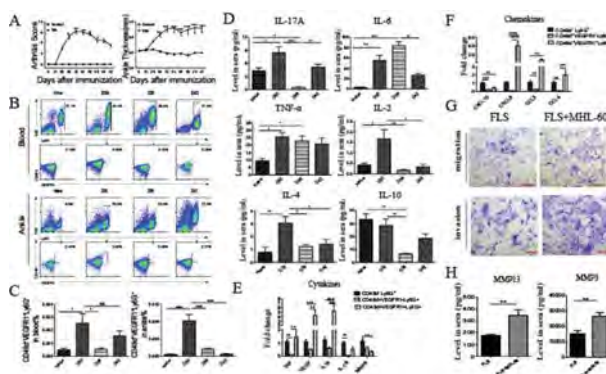
**Background:** Neutrophil is known to play an important role in the progression of rheumatoid arthritis (RA). Pannus formation requires hypoxia microenvironment

(<sup>1,2</sup>) and a small population of neutrophil highly expressing CD49d, VEGFR1 and CXCR4 is reported to induce angiogenesis at the sites of hypoxia(<sup>3</sup>).

**Objectives:** In the current study, we aim to identify this subset of neutrophil and investigate its function and role during the pannus formation.

**Methods:** Collagen-induced arthritis (CIA) model was applied in this study and CD49d<sup>+</sup>VEGFR1<sup>+</sup>Ly6G<sup>+</sup> neutrophil was monitored at the onset and remission of arthritis. The levels of IL-17, IL-4, IL-6, IL-10, TNF- $\alpha$  and IFN- $\gamma$  in CIA model sera were tested by ELISA at day 30, 36 and 42, respectively. mRNA expressions of cytokines including TNF- $\alpha$ , VEGF, IL18 and MMP9 were detected by RT-PCR. Meanwhile, chemokines genes of CXCL10, CXCL9, CLL3 and CLL4 expressed in CD49d<sup>+</sup>VEGFR1<sup>+</sup>neutrophil were also measured. *In vitro*, synovial fibroblast-like cells (FLS) was co-cultured with MHL60, expressing CD49d and VEGFR1, and the migration and erosion was measured.

**Results:** CD49d<sup>+</sup>VEGFR1<sup>+</sup> neutrophil was detected in the peripheral blood and ankle at various time points with the peak on day 30. The gene expression of TNF $\alpha$ , VEGF, IL-18 as well as CXCL10, CXCL9, CLL3 and CLL4 was significantly increased in CD49d<sup>+</sup>VEGFR1<sup>+</sup> neutrophil. Pre-coculture with MHL60 was able to increase FLS migration and erosion. Meanwhile, the expression of MMP13, MMP3 was robustly enhanced at the mRNA and protein level.



**Conclusions:** A subset of neutrophil highly expressing CD49d and VEGFR1 was detected for the first time in CIA mice. CD49d<sup>+</sup>VEGFR1<sup>+</sup> neutrophil is able to secrete various chemokine and cytokines. Meanwhile, it can enhance FLS migration and invasion ability via up-regulating MMP3 and 13.

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**Acknowledgements:** no

**Disclosure of Interest:** None declared

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THU0074

### EFFECTS OF RITUXIMAB ON THE INFLAMMATORY AND PRO-THROMBOTIC PROFILES OF NON-B CELLS OF THE IMMUNE AND VASCULAR SYSTEMS OF RHEUMATOID ARTHRITIS AND SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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**Background:** Treatment with B-cell depletion, including rituximab (RTX), has been proven successful in achieving remission from the active disease in Rheumatoid Arthritis (RA) and Systemic Lupus Erythematosus (SLE) patients. However, the effect of RTX on the Cardiovascular disease (CVD) associated to both autoimmune conditions has not been elucidated yet. The aim of this study was to investigate whether B-cell depletion therapy with RTX has an impact on activation of non-B cells of the immune and vascular systems in the context of CVD in RA and SLE patients



**Methods:** The analysis was carried out in plasma and purified leucocytes from 25 subjects, including 12 RA and 13 SLE patients. To evaluate the influence of B-cells depletion on the inflammatory profile of T-cells, purified lymphocytes from 6 RA and 7 SLE patients were treated with RTX (1 µg/ml) for 24 hours. B-cells depletion was assessed by flow cytometry and the changes occurred in the inflammatory profile of T cells were analysed by RT-PCR. The changes promoted in the activity of key intracellular regulators of pro-inflammatory cytokines were analysed by western blot in proteins purified from lymphocytes. In a second set of experiments, supernatants from cultured lymphocytes of 6 RA and 7 SLE patients was added—either, in the presence or in the absence of RTX—to cultured endothelial cells (HUVECs), monocytes, and neutrophils isolated from Healthy Donors (HDs) and incubated for 6 hour. The changes induced in the inflammatory/pro-thrombotic profile of these cells was analysed by RT-PCR. Finally, serum obtained from 6 RA and 6 SLE patients at baseline and after 3 months of therapy with RTX, was added to HUVECs, monocytes, and neutrophils isolated from HDs and the response was analysed by RT-PCR

**Results:** In parallel to the significant decline of B-cells, a downregulation of the pro-inflammatory profile of T-lymphocytes from RA and SLE patients was demonstrated, revealed by the significant drop of IL1, IL6, IL17, IFN $\gamma$ , and TNF $\alpha$  gene expression levels. A decrease in the phosphorylation status and protein expression levels of STAT-3 and p38 was also found in T-cells treated with RTX. HUVECs, monocytes, and neutrophils incubated with the supernatant of RTX-treated lymphocytes from RA and SLE patients showed a decrease in the expression levels of various pro-thrombotic factors (i.e. TF, IL8, and VEGF) and cell-adhesion molecules (i.e. V-CAM, I-CAM and e-Selectin). Likewise, HUVECs, monocytes, and neutrophils treated with serum of RA and SLE patients after 3 months of therapy with RTX, showed a reduced expression of genes related to their pro-thrombotic and pro-inflammatory profiles

**Conclusions:** Depletion of B-cells induced by RTX might promote a beneficial effect in the CV risk-profile of RA and SLE patients through the modulation of the inflammatory and pro-thrombotic shapes of leukocytes and vascular endothelial cells

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**Disclosure of Interest:** None declared

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**THU0075** **IMPACT OF OBESITY ON RHEUMATOID ARTHRITIS (RA) ONSET AND PROGRESSION. IN VIVO AND IN VITRO EFFECTS OF SYNTHETIC DMARDS ON THE RA-ASSOCIATED METABOLIC ALTERATIONS**

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**Objectives:** 1) To evaluate the impact of obesity in RA onset and progression, 2) To analyse the *in vivo* effects of synthetic disease-modifying antirheumatic drugs (sDMARDs) on the obesity and IR in an obese collagen-induced arthritis (CIA) mouse model. 3) To study the *in vitro* effects of sDMARDs on the lipid and glucose homeostasis in adipose tissue (AT).

**Methods:** CIA was developed in obese and lean mice. 55 C57Bl/6 mice (4–5 weeks) were used. Forty-one mice were fed with high fat diet (60%) until reaching 30 g (obese) (OB). OB-mice were treated with leflunomide (LFN)(10 mg/kg daily), methotrexate (MTX)(3 mg/kg three times/week) or hydroxychloroquine (HCQ) (60 mg/kg daily) for 15 days. After treatment, glucose tolerance test (GTT) was performed. Buffy coat, plasma and adipose tissue (AT) samples were collected. 3 T3-L1 adipocytes were treated with serum from RA patients (10%) alone or in combination with sDMARDs at day 9 of differentiation. Human subcutaneous AT samples were treated *ex vivo* with serum from RA patients (10%) alone or in combination with sDMARDs. Protein and gene expression of molecules involved in inflammation, insulin signalling and lipid accumulation was analysed through RT-PCR, western blot and ELISA in all the experiments.

**Results:** CIA-OB mice developed the arthritis earlier and more severe compared with CIA-lean mice. On the hand, arthritis increased the systemic levels of inflammation and HOMA-IR of OB-mice. The induction of arthritis in OB mice increased the inflammatory burden, accompanied by a reduction of genes involved in insulin signalling and lipid accumulation, inducing an aggravation of the insulin resistance (IR) state in AT.

The therapies more effective inhibiting the generation of inflamed digits were HCQ and MTX. HCQ significantly reduced the body weight, accompanying by a reduction in insulin and glucose plasma levels leading to a decrease of HOMA-IR values. AT of CIA-OB mice treated with MTX and HCQ had restored levels of genes involved in lipid accumulation, adipogenesis and insulin signalling.

Serum from RA patients elevated the levels of inflammatory markers, reduced the expression of genes related to lipid accumulation, adipogenesis and insulin signalling in 3 T3L1 adipocytes. Although LFN, MTX and HCQ *in vitro* treatment reduced inflammation, only MTX and HCQ regulated insulin sensitivity and lipid accumulation. These results were recapitulated in *ex vivo* treatments in human AT explants.

**Conclusions:** 1) Obesity accelerates the development and aggravates the outcome of the arthritis in mice. Arthritis exacerbates the inflammatory burden and the metabolic alterations in an obesity context. 2) *In vivo*, HCQ promotes a beneficial effect on the metabolism of CIA-OB mice, improving the insulin sensitivity at systemic and AT levels and reducing body weight. 3) *In vitro*, HCQ and MTX revert the metabolic alterations induced by RA serum in AT. Thus, HCQ and MTX might be considered as a valuable therapeutic strategy in RA patients to ameliorate the metabolic complications associated.

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**Disclosure of Interest:** None declared

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**THU0076** **ANTIBODIES TO CITRULLINATED PROTEIN ANTIGENS (ACPAS) INDUCE ADIPOSE TISSUE DYSFUNCTION IMPAIRING ADIPOCYTE DIFFERENTIATION, LIPID ACCUMULATION AND PROMOTING MACROPHAGE POLARISATION. IN VITRO EFFECT OF BIOLOGIC DMARDS**

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**Background:** Adipose tissue (AT) dysfunction is an important determinant of inflammation- or lipid-induced metabolic complications. Rheumatoid arthritis (RA) is closely associated with metabolic comorbidities such as obesity or insulin resistance (IR). ACPAs are involved in the development of cardiovascular disease associated to this disorder. However, the role of ACPAs on the adipose tissue (AT) function is unravelled.

**Objectives:** 1) To analyse the direct effects of ACPAs on the AT function: adipocyte differentiation, macrophage polarisation and lipid accumulation, and 2) To evaluate the effects tocilizumab (TCZ) or infliximab (IFX) on the metabolic alterations induced by ACPAs on AT.

**Methods:** IgGs-NHS (Normal Human Serum) and IgGs-ACPAs were isolated from serum of 20 controls and 20 RA patients. 3 T3-L1 fibroblast were treated with IgG-NHS or IgG-ACPAs alone or in combination with IFX or TCZ during several stages of the differentiation to adipocytes (day 0 and day 9). Lipid accumulation was analysed by oil red 0 (ORO) staining. M0 macrophages from THP-1 cells were treated with IgG-NHS or IgG-ACPAs alone for 12 hour or in combination with IFX and TCZ for another 12 hour. Macrophage polarisation was analysed by flow cytometry. Visceral and subcutaneous AT samples were obtained from 8 obese patients through bariatric surgery. AT samples were treated *ex vivo* with IgGs-NHS or IgG-ACPAs alone or in combination with biological DMARDs. Protein and gene expression of molecules involved in adipogenesis, inflammation, insulin signalling and lipid accumulation was analysed through RT-PCR, western blot and ELISA in all the experiments.

**Results:** *In vitro* treatment of M0 macrophages with IgG-ACPAs induced M1 polarisation state and impaired insulin signalling. 3 T3-L1 fibroblast treated with IgG-ACPAs at day 0 showed an impaired adipocyte differentiation shown by a reduction of genes involved in adipogenesis and lipid accumulation. Levels of accumulated lipids were also significantly reduced. Likewise, genes involved in insulin signalling were reduced. Treatment with IFX and TCZ after differentiation reverted the expression of these genes. At human adipose tissue level, the treatment with IgGs-ACPAs increased the levels of inflammatory markers, accompanied by a downregulation of genes involved in lipid accumulation, adipogenesis and insulin signalling. After treatment with biological DMARDs, inflammatory and metabolic alterations were reverted on human AT explants.

**Conclusions:** 1) ACPAs impairs AT function, acting in both, macrophages and adipocytes, inducing M1 macrophage polarisation and impairing adipogenesis and lipid accumulation in adipocytes, favouring an IR state. 2) TCZ and IFX might reverse the metabolic alterations induced in AT by ACPAs. 3) Targeting these autoantibodies would be an excellent therapeutic strategy to restore AT function and reduce the metabolic complications related to RA.

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**Disclosure of Interest:** None declared

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THU0077

### INCREASED FOLLICULAR HELPER T CELL REGULATES AUTOANTIBODY HYPOSIALYLATION IN GLUCOSE-6-PHOSPHATE ISOMERASE INDUCED ARTHRITIS

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**Background:** Circulating follicular helper T (Tfh) cells were reported to be increased and promote B cell activation and antibody production in rheumatoid arthritis. Recently, IL-23-Th17 cells axis and hyposialylation of antibodies were proved to be linked to the inflammation of experimental and rheumatoid arthritis. However it remains uncertain how Tfh, including IL-17 producing Tfh (Tfh17), is associated to arthritis and whether its function includes promotion of antibody hyposialylation.

**Objectives:** The aim of this study is to explore the relation between Tfh and auto-antibody hyposialylation in glucose-6-phosphate isomerase (GPI) induced arthritis (GIA), which mouse model was dependent on T cells, B cells and IL-17.

#### Methods:

1. Fluctuation of Tfh and its subsets in draining lymph nodes (dLNs) were analysed and expression of co-stimulatory molecules were assessed among these subsets. Their localization were examined by immunofluorescence (IF) staining. In order to explore the counterpart reaction, serial changes of plasmablast and plasma cell population in dLNs were also analysed.
2. To elucidate Tfh function in ex-vivo, naïve B cells were co-cultured with Tfh and the ratio of differentiated plasmablast was quantified. Anti-GPI antibody production from plasmablast was measured in the existence of Tfh.
3. The titers of anti-GPI antibodies in GIA sera were measured by ELISA.
4. DCs were stimulated with purified anti-GPI antibodies from day 7 (arthritis onset phase) and day 28 (resolving phase) GIA to examine the pathogenicity change of antibody. MRNA of ST6 beta-galactoside alpha-2,6-sialyltransferase 1 (st6gal1), the responsible protein for antibody sialylation, in plasmablast was quantified by PCR and detection of sialic acid in anti-GPI antibody was performed by lectin blotting.
5. Naïve B cells were co-cultured with Tfh and the st6gal1 expression in differentiated plasmablast was measured by flow cytometry.

#### Results:

1. Tfh cells were increased in GIA. It peaked at day 7, the onset of arthritis, and Tfh17 was specifically increased at the same time. Moreover, OX40 expression in Tfh17 was higher than other subsets. IF showed that Tfh and Tfh17 were accumulated in germinal centre of dLNs. As counterparts, plasmablasts and plasma cells were most increased at day 7 as well.
2. When co-cultured with Tfh, the frequency of differentiated plasmablast was much higher than other conditions, and anti-GPI antibody production was up-regulated in the existence of Tfh and GPI.
3. Conflicting with the results above, anti-GPI antibody titers in the sera were gradually elevated even after day 7 and this elevation continued while GIA peaked out.
4. DCs produced higher level of TNF-alpha when stimulated with the antibody from day 7 GIA than day 28. St6gal1 expression in plasmablast was significantly decreased at day 7 and recovered at day 28. In addition, the day 7 antibodies were tended to be contain less sialic acid.
5. Decreased expression of st6gal1 was observed in differentiated plasmablast co-cultured with Tfh.

**Conclusions:** Tfh, especially Tfh17 were increased in the induction phase of arthritis. Also, Tfh could have a crucial role in the development of arthritis via plasmablast activation and regulation of autoantibody hyposialylation in GIA.

**Disclosure of Interest:** None declared

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THU0078

### BERBERINE AMELIORATES BONE EROSIONS IN COLLAGEN-INDUCED ARTHRITIS RAT MODELS SUPPRESSING THE EXPRESSION OF IL-17A

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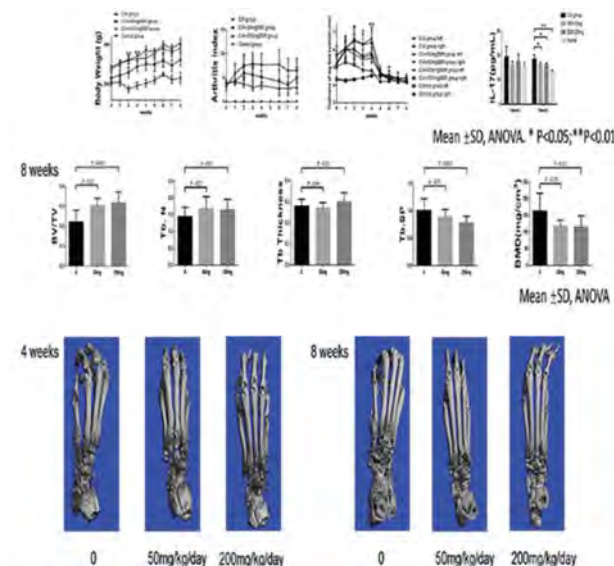
**Background:** Rheumatoid arthritis (RA) is a chronic progressive disease characterised by synovial inflammation, autoantibody production, cartilage and bone destruction. Bone erosions are a key feature of RA reflecting both disease severity and disease progression. An imbalance between Th17 and regulatory T cells (Treg cells) has been extensively recognised in both patients and model animals

of RA. Oral administration of berberine, an isoquinoline alkaloid, has been showed to ameliorate various symptoms of autoimmune diseases including RA.

**Objectives:** To verify whether berberine may prevent bone erosions during RA progression and to explore the potential mechanisms in Collagen-induced arthritis (CIA) rat model.

**Methods:** The severity of arthritis was expressed as mean arthritic index on a 0–4 scale according to the following criteria: 0=no oedema or swelling; 1=slight oedema and erythema limited to the foot and/or ankle; 2=slight oedema and erythema from the ankle to the tarsal bone; 3=moderate oedema and erythema from the ankle to the tarsal bone; and 4=severe oedema and erythema from the ankle to the entire leg. Each limb was graded, and thus the maximum possible score was 16 for each animal. The threshold score of rats with established CIA is 2. The CIA rats were divided into 3 groups: placebo group (n=4), low dose berberine group (50 mg/kg/day, n=4) and high dose berberine group (200 mg/kg/day, n=4). Placebo and berberine were intragastrically administered to all rats for 4 and 8 weeks after the CIA models were established. TNF- $\alpha$ , IL-1 $\beta$ , IL-6, IL-17A, and IgG in the serum were measured by ELISA kits (purchased from Abcam). The hind paws of rats were scanned by micro CT (Scanco, Switzerland).

**Results:** The thickness of the swollen hind paws was reduced in the high dose berberine group (200 mg/kg/day) compared with the placebo group (Fig A). No significant differences were observed in the levels of TNF- $\alpha$ , IL-1 $\beta$ , and IL-6 between the three groups. However, the levels of IL-17A and IgG were significantly decreased in the high dose berberine group when compared with the placebo group (Fig A). Micro CT data revealed that berberine could significantly improve the microstructure of CIA rats including the bone volume ratio (BV/TV), areal bone mineral density (aBMD) and trabecular separation (Tb Sp) (Fig B and C). Development of bone erosion had also been partially prevented.



**Figure 1** A; B microstructure; C 3D reconstruction

**Conclusions:** Berberine attenuated the symptoms of CIA rats and may prevent bone erosion progression by suppressing IL-17A in CIA. Human studies are required to confirm whether it may serve as a potential treatment for RA in the future.

**Disclosure of Interest:** None declared

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THU0079

### ADIPONECTIN AGGRAVATES BONE EROSION BY PROMOTING OSTEOPONTIN PRODUCTION IN SYNOVIAL TISSUE OF RHEUMATOID ARTHRITIS

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**Background:** We have previously reported that adiponectin (AD), an adipokine that is secreted by adipocytes, correlates closely with progressive bone erosion in rheumatoid arthritis (RA). The exact mechanism of AD towards promoting joint destruction remain unclear.

**Objectives:** Osteopontin (OPN) is required for osteoclast recruitment. We hypothesised that AD exacerbates bone erosion by inducing OPN expression in synovial tissue. This study aimed to evaluate a novel role for AD in RA.

**Methods:** The serum levels of AD and OPN were determined in 38 RA, 40 osteoarthritis (OA) patients, and 20 healthy controls using enzyme-linked immunosorbent assay (ELISA). AD and OPN production were measured by double immunofluorescence of RA and OA synovial tissue. Quantitative real-time PCR and immunofluorescence were used to evaluate the mRNA and protein expression levels of OPN in RA synovial fibroblasts (RASFs) and OA synovial fibroblasts after preincubation with AD, respectively. Migration of the RAW264.7 osteoclast precursors cell line was assessed using the Transwell migration assay and co-culture system. Bone destruction and osteoclastogenesis were assessed by immunohistochemistry, microcomputed tomography, and tartrate-resistant acid phosphatase (TRAP) staining in AD-treated collagen-induced arthritis (CIA) mice with or without OPN silencing. The expression levels of OPN and integrin  $\alpha_v\beta_3$  in the ankle joint tissues of the mice were examined by double immunofluorescence.

**Results:** Our results indicated that the AD and OPN expression levels increased noticeably and were associated with each other in the RA serum. The AD distribution was coincident with that of OPN in the RA synovial tissue. AD stimulation of RASFs increased OPN production in a dose-dependent manner. AD-treated RASFs promoted RAW264.7 cell migration, and the effect was blocked with a specific antibody against OPN. Silencing of OPN using lentiviral-OPN short hairpin RNA reduced the number of TRAP-positive osteoclasts and the extent of bone erosion in the AD-treated CIA mice. When bound to integrin  $\alpha_v\beta_3$ , OPN functions as a mediator of AD and osteoclasts.

**Conclusions:** Our study provides new evidence of AD involvement in bone erosion. AD induces the expression of OPN, which recruits osteoclasts and initiates bone erosion. These data highlight AD as a novel target for RA treatment.

**Disclosure of Interest:** None declared

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#### THU0080 SERUM IRISIN AND MYOSTATIN LEVELS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) patients have loss of muscle mass. The balance between muscle protein synthesis and degradation is regulated by cytokines and growth factors, named myokines, such as irisin and myostatin. Myokines are mainly expressed by skeletal muscle and exert systemic effects promoting crosstalk among different tissues. Irisin increases cortical bone mass and its low levels are related to muscle atrophy and obesity<sup>1, 2</sup> while myostatin is a negative regulator of muscle growth and regeneration and has a direct role in osteoclastogenesis of inflammatory bone destruction<sup>3, 4</sup>.

**Objectives:** To evaluate serum levels of irisin and myostatin and body composition of RA patients and controls.

**Methods:** 122 female patients with RA, mean age 53 years, mean disease activity score (DAS28) 4.09, mean disease duration 11.2 years and mean body mass index 27.33 kg/m<sup>2</sup> were included. 69 age and sex-matched healthy subjects were enrolled as control group. Irisin (Phoenix Pharmaceuticals) and myostatin (R and D Systems) serum levels were evaluated by ELISA. Fat mass index (FMI;Kg/m<sup>2</sup>) and appendicular lean mass index (ALMI;Kg/m<sup>2</sup>) were assessed by total body dual-energy x-ray absorptiometry. Student's t test and Spearman correlation were performed. Significance was set at p<0.05.

**Table 1.** Irisin and myostatin serum levels of RA patients and controls

	n	Irisin (mean ±SD)	Myostatin (mean ±SD)
RA patients treated with biologics	13	31,71±7,69 <sup>#</sup>	2448,64±1114,90 <sup>#</sup>
RA patients non-treated with biologics	27	25,93±6,89	3261,66±1156,28 <sup>*</sup>
Controls	30	30,36±10,95	4049,08±1610,01

\*p<0,05 RA patients treated with biologics vs controls; <sup>#</sup>p<0,05 RA patients treated with biologics vs RA patients non-treated with biologics; <sup>p</sup>>0,05 RA patients non-treated with biologics vs controls.

**Results:** RA patients had decreased serum levels of irisin (25,61±8,25 vs 30,36 ±10,95 ng/ml; p<0.05) and myostatin (3011,28±1271,11 vs 4049,08±1610,01 pg/

ml; p<0.05), decreased ALMI (6,09±0,88 vs 6,50±1,10; p<0.05) and increased FMI (11,26±3,30 vs 9,44±2,65; p<0.05), compared to controls. No correlations were observed among irisin and myostatin levels and ALMI and FMI. Of the 122 RA patients, 40 were analysed for the use of biologic medication. Serum levels of irisin and myostatin were different between RA patients treated and non-treated with biologics (table 1).

**Conclusions:** RA patients presented loss of lean mass and gain of fat mass, as well as lower irisin and myostatin serum levels, in comparison with controls. Additionally, the use of biologic medication by patients impacted on myokines serum levels. Further analyses are needed for a better comprehension of irisin and myostatin roles in RA, and to verify their correlation to other RA features.

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#### THU0081 IDENTIFICATION OF NOVEL AUTOANTIBODIES IN THE SYNOVIAL FLUID FROM PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is a chronic, autoimmune and inflammatory joint disease with a poorly understood etiology. Despite widespread diagnostic use of anti-citrullinated protein antibodies and rheumatoid factor, there is strong demand for novel biomarkers to improve the diagnosis of this disease.

**Objectives:** The purpose of present study is to investigate novel autoantibodies in the synovial fluid of RA patients.

**Methods:** 1) By using SEREX (Serological identification of antigens by recombinant cDNA expression cloning), we identified ten and several antigens from sera of RA patients. 2) Three epitope sites in the candidate antigens proteins were predicted and 18 mer peptides were synthesised. 3) Synovial fluid of the knees was obtained from 48 RA and 48 osteoarthritis (OA) patients. 4) Furthermore, Alpha-LISA was used to analyse the antibody levels in synovial fluid using synthetic polypeptide as antigens.

**Results:** Significantly higher proportion of antibodies against lamin A (LMNA, RA 19871+13924 VS OA 6726+3975, p<0.000001) and cell growth-regulating nucleolar protein (CGRN, RA 19673+13314 VS OA 10614+6391, p<0.00007) were found in synovial fluid of RA as compared with OA.

**Conclusions:** We identified two novel autoantibodies in the knee synovial fluid of RA patients. These antibodies would have the potential to become diagnostic biomarkers of RA.

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#### THU0082 IMPAIRED LEFT VENTRICULAR RELAXATION AND ITS ASSOCIATION WITH INFLAMMATORY MARKERS IN COLLAGEN-INDUCED ARTHRITIS

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**Background:** Patients with rheumatoid arthritis (RA) experience an increased risk of developing heart failure with a preserved ejection fraction. Although there is some evidence to support a role of chronic inflammation in the pathogenesis of impaired left ventricular (LV) function in RA,<sup>1</sup> the direct effects of inflammatory cytokines on the LV function in collagen-induced arthritis (CIA) (an experimental model most similar to RA) require further elucidation.



**Objectives:** The aim of this study was to determine LV systolic and diastolic function and their association with circulating inflammatory markers in CIA.

**Methods:** Male Sprague Dawley rats were randomly divided into two groups: a control group (n=12) and a collagen-induced arthritis group (CIA, n=21). Rats in the CIA group were immunised with 0.2 ml type-II bovine collagen emulsified in incomplete Freund's adjuvant at the base of the tail followed by a 0.1 ml booster injection 7 days later. Eight weeks post-immunisation, markers of LV systolic function and geometry including ejection fraction (EF), fractional shortening (FS), stroke volume (SV) and LV end systolic diameter (ESD) were assessed echocardiographically using two-dimensional directed M-mode imaging. Markers of LV diastolic function including the early-to-late diastolic filling velocity ratio (E/A), the lateral (Lat e') and septal (Sep e') wall myocardial tissue lengthening at the mitral annulus and the ratio between early mitral inflow velocity and mitral annular early diastolic velocity (E/e') were assessed using pulsed Doppler and tissue Doppler echocardiography. Serum concentrations of interleukin 6 (IL-6), interleukin 1 $\beta$  (IL-1 $\beta$ ), tumour necrosis factor alpha (TNF- $\alpha$ ) and C-reactive protein (CRP) were determined by an enzyme-linked immunosorbent assay.

**Results:** No significant differences in markers of systolic function or geometry (EF, FS, SV and ESD) were observed between the groups (p>0.05). Compared to the control group, E/A (control=2.17 $\pm$ 0.39; CIA=1.46 $\pm$ 0.46; p=0.0001) and Sep e' (control=3.75 $\pm$ 0.69; CIA=3.23 $\pm$ 0.47; p=0.04) were lower in the CIA group. By contrast, E/e' (control=29.94 $\pm$ 6.99; CIA=24.17 $\pm$ 8.49; p=0.13) and Lat e' (control=3.99 $\pm$ 0.43; CIA=3.79 $\pm$ 0.78; p=0.31) did not differ amongst the two groups. IL-6 (115 $\pm$ 70.09 versus 365.3 $\pm$ 88.96 pg/mL; p<0.0001), IL-1 $\beta$  (14.1 $\pm$ 55.7 versus 238.6 $\pm$ 49.01 pg/mL; p<0.0001), TNF- $\alpha$  (293.5 $\pm$ 87.16 versus 626.0 $\pm$ 119.7 pg/mL; p<0.0001) and CRP concentrations (0.23 $\pm$ 0.34 versus 0.97 $\pm$ 0.35 ng/mL; p<0.0001) were higher in the CIA compared to control group. A lower E/A was associated with TNF- $\alpha$  (r=-0.63; p=0.0003), IL-6 (r=-0.56; p=0.0001), IL-1 $\beta$  (r=-0.48; p=0.001) and CRP concentrations (r=-0.60; p=0.001) in the total sample. Lower TNF- $\alpha$  (r=-0.39 p=0.04) and IL-1 $\beta$  (r=-0.47, p=0.01) levels were associated with E/e' in the total sample.

**Conclusions:** Diastolic function is impaired in male Sprague Dawley rats with CIA. Our results indicate that exposure to high grade inflammation can reduce LV relaxation without impairing systolic function in CIA. Markers of inflammation were also associated with increased filling pressures in this animal model. Systemic inflammation may directly impact myocardial diastolic function in CIA.

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THU0083

#### CD30 APTAMER-SLAT-SHRNA CHIMAERAS INHIBIT TH17 DIFFERENTIATION BY ROR $\gamma$ T IN RHEUMATOID ARTHRITIS

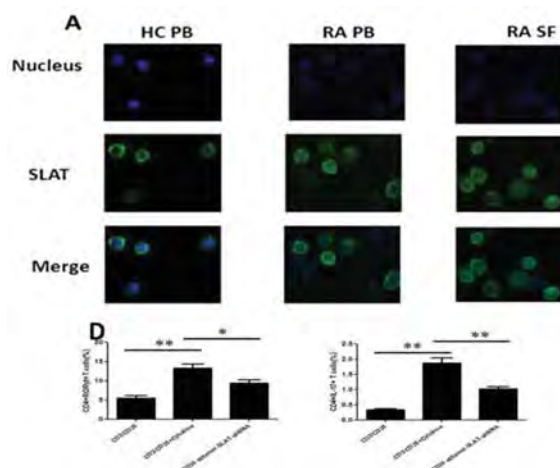
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**Background:** T helper 17 (Th17) cells play a central role in rheumatoid arthritis (RA) via the production of pro-inflammatory cytokines interleukin (IL)-17. SWAP-70-like adapter of T cells (SLAT) has recently emerged as an important regulator of Th17 differentiation. Aptamer-facilitated cell specific delivery of shRNA represents an attractive novel approach for efficient RNAi delivery. However, the role of CD30 aptamer-SLAT-shRNA chimaeras in regulating Th17 differentiation in patients with RA is unclear.

**Objectives:** SLAT play a crucial role in regulating Th17 cell differentiation and function. This study was undertaken to investigate the role and mechanism of SLAT in Th17 cells differentiation in patients with RA.

**Methods:** Peripheral blood CD4<sup>+</sup> T cells and synovial fluid CD4<sup>+</sup> T cells derived from RA patients and healthy controls were used to test the effect of SLAT *in vitro*. CD30 aptamer-SLAT-shRNA chimaeras were generated *in vitro* and transfected into CD4<sup>+</sup> T cells. The effect of CD30 aptamer-SLAT-shRNA chimaeras on Th17 production and differentiation was detected.

**Results:** SLAT was expressed mostly in cytoplasm and cell membrane of CD4<sup>+</sup> T cells. The protein levels of SLAT in peripheral blood and synovial fluid CD4<sup>+</sup> T cells of RA patients were higher than that of healthy controls. The effect of CD30 aptamer-SLAT-shRNA chimaeras on Th17 differentiation was due to its ability to sequester SLAT and prevent it from targeting the transcription factor ROR $\gamma$ T.



**Abstract THU0083 – Figure 1.** A. SLAT was expressed mostly in cytoplasm and cell membrane of CD4<sup>+</sup> T cells. D. CD30 aptamer-SLAT-shRNA chimaeras reduced the percentage of CD4<sup>+</sup>ROR $\gamma$ T<sup>+</sup> T cells and CD4<sup>+</sup>IL-17<sup>+</sup> T cells.

**Conclusions:** This study reveals new evidence of the role of SLAT in Th17 differentiation in CD4<sup>+</sup> T cells of RA patients.

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THU0084

#### HISTONE DEACETYLASE 1 (HDAC1): A NOVEL THERAPEUTIC TARGET IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Despite enormous efforts to develop new therapeutic strategies for treatment of rheumatoid arthritis (RA), the large number of non responding

patients to currently available drugs underlies the unmet need to identify new therapeutic targets.

**Objectives:** Certain CD4<sup>+</sup>T cell subsets, especially Th17 cells, have been shown to be major drivers of inflammation in patients with RA. The expression of their key transcription factors is controlled by histone modifications which includes acetylation of *lysine residues* mediated by histone deacetylases (HDAC). Indeed, pan HDAC inhibitors have been shown to be a potential therapeutic strategy. However, major side effects limited the clinical use and underline the need of more specific HDAC inhibitors. We therefore addressed the individual role of HDAC1 on the development of collagen-induced arthritis model (CIA).

**Methods:** Mice with a T cell specific deletion of HDAC1 (HDAC1 cKO) were generated by using the CD4Cre/LoxP system. Collagen induced arthritis (CIA) was induced at week 8. Animals were scored for paw swelling and grip strength. After 10 weeks, mice were sacrificed and paraffin sections of the affected joints were analysed for histomorphological signs of inflammation, cartilage and bone destruction. Anti-CII antibody levels were determined by ELISA. Serum samples were analysed for various cytokines by multiplex assays. CCR6 expression in CD4 T cells was analysed by flow cytometry.

**Results:** To address potential effects of HDAC1 in the pathogenesis of RA, CIA was induced in *HDAC1cKO* mice and *WT* mice. Surprisingly *HDAC1cKO* mice were completely protected from the development of arthritis. In line with the clinical data, histological analysis revealed no signs of inflammation, no bone erosion and no osteoclasts in the joints of *HDAC1cKO* mice. Anti-CII antibodies, including total IgG and IgG2c were detected in *HDAC1cKO* and *WT* mice. Surprisingly, IL-17 was significantly decreased in the serum of *HDAC1cKO* mice as compared to *WT* mice, suggesting a role of HDAC1 in the development of Th17 cells. To see whether HDAC1 is involved in the regulation of the chemokine receptor 6 (CCR6), the main marker of Th17 cells, we compared the upregulation of CCR6 in CD4<sup>+</sup> T cells from *WT* and *HDAC1cKO* mice. Indeed, CCR6 could not be upregulated in CD4<sup>+</sup> T cells from *HDAC1cKO* mice upon IL-6 *in vitro*. These data support the role of HDAC1 in the regulation of CCR6, an important chemokine receptor, which is necessary for the migration of pathogenic Th17 cells and therefore for the development of arthritis.

**Conclusions:** Our data show the importance of HDAC1 as a key immune regulator in the pathogenesis of T cell driven collagen induced arthritis. Therefore, it might be considered as an interesting novel therapeutic target in RA.

**Disclosure of Interest:** None declared

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**THU0085** CR6086, A NOVEL EP4 ANTAGONIST WITH IMMUNOMODULATORY PROPERTIES, DECREASES BONE LOSS IN THE RAT COLLAGEN-INDUCED ARTHRITIS (CIA) MODEL: A MICROTOMOGRAPHY (MICROCT) STUDY

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**Background:** CR6086 is a novel PGE2 EP4 receptor antagonist showing favourable immunomodulatory properties, striking DMARD effects in rodents, and an anti-inflammatory activity targeted to immune-mediated diseases and distinct from that of NSAIDs. Besides its role in controlling T cells, PGE2 is implicated in the aggressive bone erosion of rheumatoid arthritis (RA).

**Objectives:** To characterise CR6086 activity on the bone compartment mostly affected by erosion in the CIA model in rats.

**Methods:** 15 male Lewis rats were immunised by intradermal injection with collagen II in CFA. 5 naïve animals were the sham group. 3 days after boost, oedema was assessed and rats assigned to treatment with vehicle or CR6086 (3 or 10 mg/kg qd). Oedema was measured again on days 7 and 14, and hindlimb joints were blindly scored for clinical signs of arthritis (scale 0–4; from normal=0 to maximally inflamed limb with involvement of multiple joints=4). At sacrifice, hindlimb calcaneus underwent high-resolution X-ray microCT (total and cancellous bone), a sensitive method that allows the reduction of experimental animals in compliance with the 3R rule. Parameters were expressed as the mean of left and right paw. Joints were then scored for histological features. Statistics were performed by ANOVA, correlations by Spearman analysis.

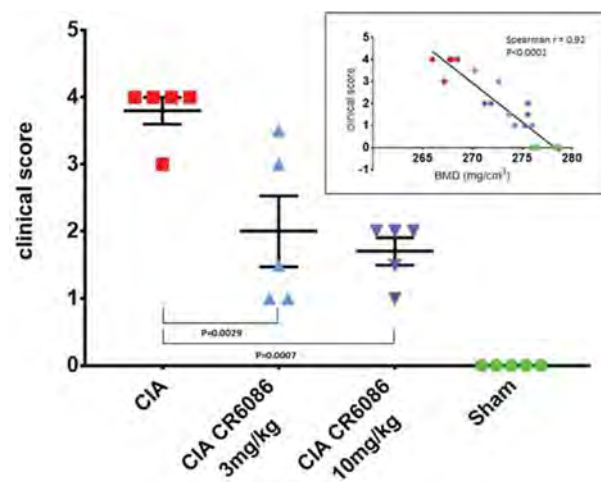
**Results:** CR6086 significantly reduced bone loss in CIA rats (table 1), even at the low dose of 3 mg/kg. The effect on cancellous bone plateaued already at 3 mg/

kg, confirming the sensitivity of the metabolically more active districts of bone to the action of EP4 antagonists.

	Sham-vehicle	CIA-vehicle	CIA-CR6086 3mpk	CIA-CR6086 10mpk
<b>Total bone, mean (SD)</b>				
<b>BMD (mg/cm<sup>3</sup>)</b>	277.20 (1.25)	267.40 (0.95)	273.50 (2.09) p 0.0004#, 0.0167\$	273.90 (2.17) p 0.0002#, 0.0322\$
<b>BV/TV (%)</b>	82.53 (10.11)	60.64 (2.68)	76.02 (5.57) p 0.0005#, n.s.\$ p 0.0004\$	76.77 (5.30) p 0.0003#, n.s.\$
<b>BS/BV (mm<sup>-1</sup>)</b>	6.10 (0.78)	13.64 (0.83)	9.00 (1.48) p 0.0001#, 0.0044\$	8.61 (1.25) p 0.0001#, 0.0134\$
<b>Cancellous bone, mean (SD)</b>				
<b>BMD (mg/cm<sup>3</sup>)</b>	270.44 (2.17)	261.20 (1.20)	267.31 (1.87) p 0.0007#, n.s.\$	266.24 (2.61) p 0.0032#, 0.0225\$
<b>BV/TV (%)</b>	71.09 (4.99)	42.76 (3.74)	61.66 (6.81) p 0.0009#, n.s.\$	58.17 (7.57) p 0.0040#, 0.0165\$
<b>BS/BV (mm<sup>-1</sup>)</b>	14.51 (2.67)	30.31 (1.84)	20.83 (3.30) p 0.0008#, 0.0196\$	21.84 (3.81) p 0.0019#, 0.0067\$
<b>Trabecular thickness (µm)*</b>	143.02 (31.94)	66.94 (4.39)	98.49 (14.38) p 0.0041#, 0.0111\$	94.25 (16.38) p 0.0105#, 0.0055\$
<b>Trabecular separation (µm)**</b>	56.46 (3.51)	90.85 (9.00)	60.51 (8.85) p 0.0004#, n.s.\$	66.85 (9.28) p 0.0023#, n.s.\$
<b>Trabecular number (mm<sup>-1</sup>)</b>	3.64 (0.39)	3.31 (0.10)	4.01 (0.26) p 0.0001#, n.s.\$	3.93 (0.13) p 0.0003#, n.s.\$

\* 2x(BV/BS); \*\* 2x(TV-BV)/BS; \$ vs. sham; # vs. CIA; BMD, Bone Mineral Density; TV, Total Volume; BV, Bone Volume; BS, Bone Surface; mpk, mg/kg

There was a strict correlation between clinical score and bone parameters (BMD; figure 1 inset), confirming that bone erosion in CIA is closely associated with arthritis severity.



**Conclusions:** CR6086 is an EP4 antagonist in clinical development for RA (NCT03163966). Besides its immunomodulatory activity, CR6086 effectively decreases the aggressive bone erosion that characterises both the CIA model and the early phases of human RA.

**Disclosure of Interest:** M. Lanza Employee of: Rottapharm Biotech, G. Caselli Employee of: Rottapharm Biotech, F. Ferrari Employee of: Rottapharm Biotech, A. Grotti Employee of: Rottapharm Biotech, R. Cavagnoli Employee of: Rottapharm Biotech, M. Perrella: None declared, F. Daubine Employee of: Atlantic Bone Screen, V. Ayer Employee of: Rottapharm Biotech, L. Rovati Employee of: Rottapharm Biotech

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**THU0086 INTERLEUKIN 17 RECEPTOR D (IL-17RD) REDUCES INCIDENCE OF COLLAGEN INDUCED ARTHRITIS**

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**Background:** IL-17RD is a member of the IL-17 receptor family. In contrast to the other IL-17 receptors, IL-17RA, -RB, -RC and -RE, little is known about the ligand and function of IL-17RD. Recently, IL-17RD has been described to negatively regulate a selection of IL-17A responsive genes. IL-17RD is therefore proposed to limit IL-17A signalling.

**Objectives:** In this study we examined IL-17RD expression in multiple cells types and its role in the development of collagen induced arthritis.

**Methods:** Human synovial fibroblasts from Rheumatoid Arthritis (RA) patients were stimulated with tumour necrosis factor  $\alpha$  (TNF $\alpha$ ), interleukin 1  $\beta$  (IL-1 $\beta$ ) or IL-17A for multiple time points. IL-17RD expression levels were measured via qPCR. Collagen induced arthritis (CIA) was induced in IL-17RD knockout mice and wildtype littermates. At days 1 and 21, mice were immunised intradermally with chicken collagen type II in complete Freund's adjuvant (CFA). Mice were scored 3 times a week for clinical disease defined as swollen joints with a maximum score of 8. Due to ethical reasons, mice were removed from the experiments when they reached a score of 6. CD4<sup>+</sup> memory T cells, CD8<sup>+</sup> memory T cells, CD19<sup>+</sup> B cells and monocytes were isolated from WT spleens and analysed for IL-17RD expression. Blood neutrophil migration assays were performed *in vitro* using WT and IL-17RD deficient (IL-17RD KO) mouse synovial fibroblasts.

**Results:** Human synovial fibroblasts from RA patients have baseline expression of IL-17RD. Upon stimulation with TNF $\alpha$  a significant downregulation of IL-17RD expression was measured from 24 hours onwards. IL1 $\beta$  stimulation had a similar effect as TNF $\alpha$  on IL-17RD expression. Lack of IL-17RD did not result in differences in CIA severity, but the incidence of CIA was reduced. IL-17RD is mainly expressed in synovial fibroblasts. IL-17RD KO synovial fibroblasts attract less neutrophils likely by lower production of neutrophil attractants.

**Conclusions:** An inflammatory environment causes synovial fibroblasts to downregulate IL-17RD expression. Lack of IL-17RD reduces the incidence CIA, which is an IL-17-driven model. The decrease in CIA incidence is likely explained via the reduced attraction of neutrophils to the site of inflammation.

**Disclosure of Interest:** None declared

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**THU0087 MICRORNA-1915-3P IN SERUM EXOSOME IS ASSOCIATED WITH DISEASE ACTIVITY OF RHEUMATOID ARTHRITIS IN KOREA**

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**Background:** Rheumatoid arthritis (RA) is a chronic inflammatory disease that is characterised by severe tissue damage and chronic synovial inflammation.<sup>1</sup> Using analysis of gene polymorphism, biochemical assays, and proteomics approaches, several promising biomarkers for treatment response have been proposed, including red blood cell (RBC) MTX polyglutamate levels, as well as serum levels of proteins such as cytokines, growth factors, and autoantibodies.<sup>2</sup> However, these markers need further development and refinement to attain sufficient sensitivity and specificity.

**Objectives:** In this study, we used a miRNAarray approach to identify new miRNA in exosome that are related to disease activity in patients with RA who showed inadequate response to treatment. We also examined the relationship between the levels of expression of the RNAs and various serologic parameters of the patients.

**Methods:** Forty-two RA patients were included in the study. Disease activity was measured using the 28-joint disease activity score with ESR (DAS28-ESR). Patients with RA were stratified according to the following criteria: the clinical remission (CR) group (n=22), DAS28-ESR $\leq$ 2.6; and the non-CR group (n=20), DAS28-ESR $>$ 2.6. By exosome preparation, miRNA array, and Reverse Transcription-qPCR reactions, several miRNAs were as potent markers for disease activity.

**Results:** After data processing for relative quantification of miRNA in exosome between the CR and non-CR groups, we identified 47 miRNAs with a relative fold change (non-CR/CR) $>$ 2. The expression levels of 37 miRNAs were found decreased in non-CR group, while 10 miRNAs increased in non-CR group. To validate these results, five miRNAs were selected (hsa-miR-1915-3 p, hsa-miR-4516, hsa-miR-6511b-5p, hsa-miR-3665, hsa-miR-3613) showing at least 2-fold change between the CR and non-CR groups. Both levels of hsa-miR-1915-3 p and hsa-miR-6511b-5p were significantly increased in CR group; hsa-miR-1915-3 p was 43.75 in the CR group and 24.68 in the non-CR group (p=0.004), and

hsa-miR-6511b-5p was 3.02 in the CR group and 2.45 in the non-CR group (p=0.03).

**Conclusions:** hsa-miR-1915-3 p showed promise as additional markers for evaluating disease activity in patients with RA. Prospective investigation of hsa-miR-1915-3 p may facilitate development of new diagnostic tools to assess disease activity and prognosis in RA and other autoimmune diseases.

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**THU0088 MONOCYTE DOWNREGULATION OF MITOCHONDRIAL TRANSLOCATOR PROTEIN MAY BE A CONTRIBUTORY MECHANISM TO INFLAMMATION IN RA**

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**Background:** The translocator protein is an 18 kDa mitochondrial transporter, increasingly thought to play a critical role in cholesterol efflux in macrophages. Recent work demonstrates that macrophages engineered to over-express TSPO, exhibit increased cholesterol efflux, and reduced ability to form a pro-inflammatory ('M1') phenotype, with significant reduction in the ability to produce TNF- $\alpha$ . Additionally, there is growing data to demonstrate a difference in TSPO expression in monocytes in those with inflammatory disease compared with healthy, as exemplified by studies of multiple sclerosis, suggesting a role for TSPO in the generation of inflammation.

**Objectives:** In this study, we investigate the expression of TSPO in healthy and RA peripheral blood monocytes, and in monocyte derived macrophages (MDM), differentiated to an M1 (pro-inflammatory), and M2 (reparative) phenotype.

**Methods:** Using positive magnetic-activated cell sorting, we use peripheral blood mononuclear cells from 24 RA patients with active disease (as determined by clinical examination, and DAS28 CRP score), and 24 healthy controls, to isolate peripheral blood monocyte mRNA and protein, to ascertain any differences in TSPO expression at monocyte level. MDM were generated *in vitro* through differentiation of monocytes with 100 ng/ml M-CSF for 7 days, followed by activation to an M1 phenotype using LPS and IFN- $\gamma$ , and a reparative 'M2' phenotype using IL-4, TGF- $\beta$  or glucocorticoid, followed by quantification of TSPO mRNA utilising real-time PCR, and TSPO protein, utilising western blotting and radioligand binding.

**Results:** Our data establishes that both healthy and RA peripheral blood monocyte derived macrophages (MDM) exhibit a statistically significant downregulation of TSPO at mRNA and protein level, when activated to a pro-inflammatory 'M1' macrophage phenotype, with no change in TSPO expression in MDM activated to a reparative 'M2' phenotype. Our mRNA data also suggests that M1 macrophages from both healthy and RA donors, exhibit a significant reduction in expression of key cell components promoting cholesterol efflux in macrophages, including CYP27A1, and ABCA1. Our data additionally demonstrates a significant reduction in expression of TSPO between healthy and RA monocytes, at both mRNA and protein level (mean fold change TSPO mRNA of 1.00 for healthy monocytes, and 0.47 $\pm$ 0.24, p<0.001 for RA monocytes and mean TSPO optical densitometry of 1.01 $\pm$ 0.10 for healthy monocytes and 0.85 $\pm$ 0.02 p<0.05 for RA monocytes relative to  $\beta$ -actin).

**Conclusions:** Our findings indicate that pro-inflammatory activation of both healthy and RA monocyte-derived macrophages downregulates TSPO, and is also associated with reduction in key components of the cholesterol efflux pathway, in line with pre-existing studies of TSPO silencing and over-expression in human macrophages. Furthermore, we demonstrate that RA peripheral blood monocytes themselves may have a predisposition to a pro-inflammatory phenotype through downregulation of TSPO expression, which could indicate an as yet uninvestigated cellular mechanism contributing to synovial inflammation in RA.

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**THU0089** **IL-17A+GM-CSF+ NEUTROPHILS ARE THE MAJOR INFILTRATING CELLS IN INTERSTITIAL LUNG DISEASE IN AN AUTOIMMUNE ARTHRITIS MODEL**

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**Background:** Interstitial lung disease (ILD) is a common extra-articular manifestation of rheumatoid arthritis (RA). Discrepancy in the effect of biologic agents on synovial and lung inflammation exists, indicating that the nature of inflammation in the synovium and lung may be different in RA.

**Objectives:** To gain a better understanding of the pathogenesis of rheumatoid arthritis-associated interstitial lung disease (ILD), we sought to identify the characteristics of lung-infiltrating cells in SKG mice with ILD.

**Methods:** We injected curdlan in SKG mice at 8 weeks of age, and identified the presence of ILD by PET-MRI at 20 weeks post-injection and histological analysis at 22 weeks post-injection. Lung-infiltrating cells were examined by flow cytometry. Analysis of serum cytokines by the Luminex multiplex cytokine assay was performed at 14 and 22 weeks post-injection, and cytokine profiles before and after the development of ILD were compared. Opal multiplexed immunofluorescent staining of lung tissue was also performed.

**Results:** At 20 weeks post-injection, curdlan-treated SKG mice developed not only arthritis but also lung inflammation combined with fibrosis, which was identified by PET-MRI and histological analysis. The majority of inflammatory cells that accumulated in the lungs of curdlan-treated SKG mice were CD11b<sup>+</sup>Gr1<sup>+</sup> neutrophils, which co-express IL-17A and GM-CSF, rather than TNF- $\alpha$ . Compared with 14 weeks post-injection, serum levels of GM-CSF, MCP1, IL-17A, IL-23, TSLP, and IL-7R $\alpha$  had increased at 22 weeks post-injection, whereas those of IFN- $\gamma$ , IL-22, IL-6, and TNF- $\alpha$  remained unchanged. Furthermore, IL-23, CXCL5, IL-17A, and GM-CSF, but not TNF- $\alpha$ , were observed in immunofluorescent-stained lung tissue.

**Conclusions:** We found that IL-17A<sup>+</sup>GM-CSF<sup>+</sup> neutrophils represented the major inflammatory cells in the lungs of curdlan-treated SKG mice. In addition, GM-CSF and IL-17A appear to play a more important role than TNF- $\alpha$  in ILD development.

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**THU0090** **PREVALENCE AND CLINICAL PHENOTYPE OF ANTI-CARBAMYLATED PROTEIN ANTIBODIES IN PALINDROMIC RHEUMATISM**

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**Background:** Anti-carbamylated protein antibodies (anti-CarP) are a newly-identified antibody family present in the sera of rheumatoid arthritis (RA) patients whose specificity is close to that of ACPA but whose sensitivity is lower. Palindromic rheumatism (PR) is an intermittent form of arthritis that may progress to RA. Patients with PR may present the characteristic autoantibody profile seen in RA, even in the absence of evolution to RA. There are no studies on the presence of anti-CarP antibodies in PR.

**Objectives:** To analyse the prevalence of anti-CarP in patients with PR and evaluate their clinical phenotype and relationship with ACPA.

**Methods:** Patients diagnosed with PR attended by the Arthritis Unit, Rheumatology Service, Hospital Clínic de Barcelona were included according to the criteria of Guerne et al. Only patients considered as pure PR (patients without evidence of RA or other chronic rheumatic disease at the time of the first determination of anti-CarP) were analysed. An established RA control group was included. Anti-CarP were analysed by a home-made ELISA using a fibrin/chimeric flaggrin homocitrullinated peptide as antigen. IgG, IgA and IgM isotypes were measured. ACPA were analysed with a commercial CCP2 test. The clinical and therapeutic characteristics were compared according to anti-

CarP positivity/negativity and to the clinical evolution, including the progression to RA during the follow-up.

**Results:** Anti-CarP were analysed in 54 patients with pure PR and 53 RA patients. Anti-CarP were detected in 16.7% and 37.7% (p: NS) of patients with PR and RA, respectively. All PR patients positive for anti-CarP were ACPA positive and had higher ACPA titers. IgG was the predominant isotype (100%), only one patient presented IgA (11.1%) and none IgM. In the RA group, the percentages of IgG, IgA and IgM were 55%, 50% and 40%, respectively, in anti-CarP positive patients. More anti-CarP positive patients developed RA (33.3% vs. 13.6%), although the difference was not significant, during a mean follow-up of 3.8 $\pm$ 1.1 years. Remission at the last follow-up visit was more frequent in patients who were anti-CarP negative (22% vs. 60.5% p<0.05). Anti-CarP positive patients were receiving DMARD more frequently than anti-CarP negative patients (100% vs. 60% p<0.05).

**Conclusions:** This is the first study to demonstrate the presence of anti-CarP in patients with pure PR. Anti-CarP was associated with ACPA positivity and higher ACPA titers. Anti-CarP isotypes differed between PR and RA, with lower isotype use in PR. Anti-CarP positivity in PR patients could indicate a more refractory disease, with lower rates of remission and greater predisposition to evolve to RA.

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**THU0091** **TIE2 INDUCES AN INFLAMMATORY PHENOTYPE IN RHEUMATOID ARTHRITIS AND PSORIATIC ARTHRITIS PATIENTS DRIVEN BY ANGIOPOIETIN-2**

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**Background:** Several studies have shown that angiopoietin signalling to Tie2 may play a role in the initiation and perpetuation of disease rheumatoid arthritis (RA) and psoriatic arthritis (PsA). However, the cell type(s) involved in this process, as well as the specific role of Tie2 signalling in the synovium of arthritis patients, remain unclear.

**Objectives:** To examine the role Tie2 signalling in macrophages and fibroblast-like synoviocytes (FLS) within the context of the synovial microenvironment of arthritic patients.

**Methods:** Peripheral blood (PB) monocytes from healthy donors (HD) were differentiated with synovial fluid (SF) of RA and PsA patients. PB and SF monocytes from RA and PsA patients were differentiated into pro-inflammatory macrophages with IFN- $\gamma$ . Tie2 expression was analysed by flow cytometry and quantitative PCR. Macrophages, RA FLS and synovial tissue explants were stimulated with Ang-1 or Ang-2 (200 ng/ml) alone or in combination with TNF (10 ng/ml) for 4 hour or 24 hour. mRNA and protein expression of inflammatory mediators was analysed by quantitative PCR and ELISA and luminex, respectively. Arthritis was induced in wild type (WT) and Tie2 over-expressing (Tie2-TG) mice by intraperitoneal injection of 100 ml of K/BxN serum on day 0 and day 2. Mice were sacrificed on day 14 after serum transfer.

**Results:** Tie2 expression was observed IFN- $\gamma$ -differentiated macrophages, from RA and PsA patients, as well as HD macrophages differentiated with RA and PsA SF. In all cases, both Ang-1 and Ang-2 stimulation significantly enhanced TNF-induced expression of pro-inflammatory cytokines (IL-6, IL-12B) and chemokines (IL-8, CCL-3 and CXCL-6). Tie2 activation also enhanced TNF-mediated production of these inflammatory mediators in RA FLS. The clinical severity of serum-induced arthritis was significantly higher in Tie2-TG mice compared to WT mice, associated with enhanced synovial expression of IL-6, IL12B, iNOS, CCL-2 and CXCL-10.

Finally, we found that Ang-2, and to a lower extent Ang-1, induced the production of IL-6, IL-12B, IL-8, and CCL-3 in the synovial tissue explants of RA and PsA patients. Importantly, Ang-2 blockade with a specific neutralising anti-Ang2 antibody suppressed the production of IL-6 and IL-8 in synovial tissue of RA patients.

**Conclusions:** These results suggest that Tie2 signalling, even within the complex microenvironment of affected synovial tissue, has an important pro-

inflammatory role in the pathology of RA and PsA. As this effect can be reversed by Ang-2 neutralisation, interfering with Tie2 activity may be a promising therapeutic target in arthritic diseases.

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#### THU0092 INTRA-CYTOPLASMIC CYTOKINES IN CD20 POSITIVE LYMPHOCYTE SUBPOPULATIONS IN RHEUMATOID ARTHRITIS (RA) PATIENTS

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**Background:** The administration of biological drugs inactivating various elements of the immune system such as cytokines and immune cells, induces a significant ameliorating effect on rheumatoid arthritis (RA) patients. The mechanisms involved in the pathogenesis of RA are unclear, and the precise role of different cellular elements of the immune system in its pathogenesis remain to be elucidated.

**Objectives:** In the present study we concentrated on one cellular target for a biologic treatment in RA (Rituximab), the CD20 positive lymphocytes. Various types of lymphocytes are positive to CD20. Based on its expression, these lymphocytes include dim and bright CD20 +types. These cells' capacity to secrete various cytokines was determined among lymphocytes of healthy controls (HC) and RA patients.

**Methods:** Peripheral blood lymphocytes (PBL) of RA patients (n=20) and HC (n=15) were isolated using Ficoll Hypaque gradient columns. To  $5 \times 10^5$  cells in 0.5 ml RPMI-1640 medium, 1.25 ng PMA, 0.5  $\mu$ g Ionomycin and 5  $\mu$ g Brefeldin were added for 5 hours of activation after which cells were incubated for 30 min at 4°C with Phycoerythrin-(PE) conjugated anti-CD20 monoclonal antibody (mab). Thereafter, suspensions were incubated in fixation buffer for 45 min, washed and re-suspended in 100  $\mu$ l of permeabilization buffer and 20  $\mu$ l of fluorescent (FITC) conjugated anti-cytokine mabs, and were incubated at 4°C for 30 min. A t-test for independent samples, was performed.

**Results:** Intra-cytoplasmic detection of various key-role cytokines, such interleukins 4 (IL-4), 17 (IL-17), 10 (IL-10) and interferon gamma (INF- $\gamma$ ) was determined. The percentage of IL-4 positive lymphocytes among CD20 +cells in HC was higher in CD20 +dim cells (4.5%) than in CD20 +bright cells (1.2%) (p value 0.0001). Among lymphocytes of RA patients the proportion of IL-4 positive cells was much higher than in HC (p<0.0002) and was comparable between dim (54.5%) and bright (48.6%) CD20 +lymphocytes. The proportion of IL-10 positive cells among both dim and bright CD20 +lymphocyte subpopulations was significantly lower in RA patients than in HC (p<0.0002). While in HC, 56% of CD20 +dim and 61% of CD20 +bright lymphocytes, showed IL-10 positivity, among RA lymphocytes it constituted only 17.8% and 9.3% of the CD20 +dim and bright lymphocytes, respectively.

Staining with anti-IL-17 mab yielded in low proportions of IL-17 positive cells in all CD20 +populations tested, in both HC and RA. Among dim CD20 +lymphocytes, IL-17 positive cells constituted 1.4% (HC) and 3.6% (RA). IL-17 staining appeared on only 0.74% of CD20 +bright lymphocytes in HC and similarly in RA (0.54%). While the proportion of INF- $\gamma$  positive lymphocytes was similar in HC and RA, it was significantly higher among dim (11.8% HC, 9.5% RA) than in bright CD20+ (1% HC, 1.4% RA) indicating a different cell pattern (p=0.0001).

**Conclusions:** The present study demonstrates that CD20 +lymphocytes, targeted in RA treatment, expressing different levels of CD20, in RA differ from HC in their capacity to produce various cytokines. Although there was no difference in IL-17 and INF- $\gamma$  they may modulate the immune response in RA due to higher levels of IL-4 and reduced IL-10 levels produced by both CD20 +cell populations; dim and bright lymphocytes.

**Disclosure of Interest:** None declared

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#### THU0093 NADPH OXIDASES ASSOCIATED PRODUCTION OF REACTIVE OXYGEN SPECIES IN RHEUMATOID ARTHRITIS

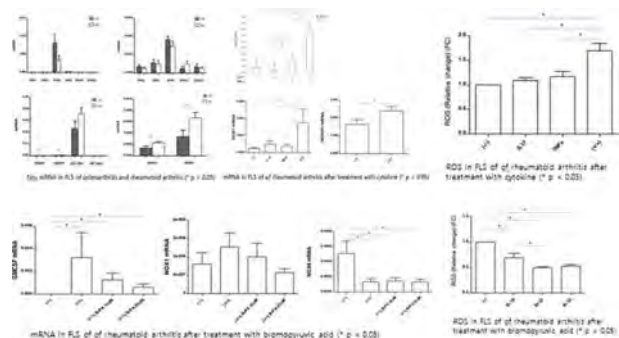
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**Background:** Reactive oxygen species (ROS) is produced during metabolism of Oxygen. ROS is important in cell signalling and homeostasis. Production of ROS can be elevated in stressful condition. Oxidative stress has been known to be related with the disease like infection and malignancy. NADPH oxidases (Nox) are membrane proteins which produce ROS.

**Objectives:** In this study we aimed to investigate the role of Nox in rheumatoid arthritis (RA) associated with production of ROS.

**Methods:** Nox and Granulocyte macrophage colony-stimulating factor (GM-CSF) messenger ribonucleic acid (mRNA) were analysed in fibroblast like synoviocyte (FLS) of patients with RA and osteoarthritis (OA) by reverse transcription polymerase chain reaction. Amount of ROS which is produced in FLS of patients with RA and OA is determined using the cell permeant fluorophore 5-(and-6)-chloromethyl-2',7'-dichlorodihydrofluorescein diacetate acetyl ester (CM-H2DCFDA) by flowcytometry. Same experiments were performed after treatment with cytokine, interleukin (IL)-17 and tumour necrosis factor- $\alpha$  (TNF- $\alpha$ ).

**Results:** Among Nox subunits (Nox1, Nox2, Nox4, Nox5, DUOX1, DUOX2, NOXA1, NOXO1), NOXA1 and NOXO1 mRNA were expressed higher in RA FLS than in OA FLS. After treatment with IL-17 and TNF- $\alpha$  for 24 hours GM-CSF, Nox1 and NOXO1 mRNA in RA FLS were elevated. Amount of ROS production was also elevated after treatment with IL-17 and TNF- $\alpha$ . When RA FLS were treated with bromopyruvic acid (BrPa), glycolysis inhibitor by inhibition of hexokinase II, GM-CSF mRNA and ROS were decreased and Nox1 and Nox4 mRNA showed no difference.



**Conclusions:** Several factors may be involved between ROS and Nox in RA FLS. Both ROS and Nox were elevated in inflammatory condition in RA FLS. From this result we expect that Nox-targeted therapy may be effective for treatment with RA.

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**Disclosure of Interest:** None declared

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**THU0094** **ROLE OF SPHINGOSINE-1-PHOSPHATE RECEPTOR 3 SIGNALLING IN COLLAGEN-INDUCED ARTHRITIS**

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**Background:** Sphingosine-1-phosphate (S1P) is a biologically active phospholipid, which is derived from membrane lipid. It binds to the receptors, named S1P1–5, and regulates several signalling pathways involved in inflammation, cell survival, angiogenesis and cell migration. Concentration of S1P and expression of S1P receptors can vary according to local tissue conditions. RA is a chronic inflammatory disorder of joints and the concentration of S1P in synovial fluid is higher in RA patient than in OA patient. *In vitro*, S1P3 expression in RA synovio-cyte is upregulated by TNF $\alpha$  treatment. On the other hand, it is not clarified whether S1P/S1P3 signalling pathway contributes to arthritis in RA.

**Objectives:** The objective of this study is to investigate the role of S1P/S1P3 signalling in inflammatory arthritis.

**Methods:** Collagen-induced arthritis (CIA) was induced by subcutaneous injection of bovine type II collagen emulsified in complete Freund's adjuvant in wild-type (WT) or S1P3-knock-out (S1P3-KO) 7–9 week-old DBA/1J mice. Arthritis severity were evaluated by visual scoring and histological analysis. The severity was assessed over time by using the arthritis score, in which each paw was scored on a scale of 0–4 and the scores of all four paws were cumulated, resulting in a maximum possible score of 16 per mouse. For histopathological examination, mice were sacrificed on the 42nd day and the hindlimbs were removed and fixed in 4% buffered formaldehyde. Paraffin embedded sections of the knee joints stained with hematoxylin and eosin were systematically scanned in a microscope and scored based on cell infiltration, cartilage destruction and bone erosion parameters. S1P3 mRNA expression was examined by realtime PCR method with total RNA extracted from knee joint capsules of CIA or normal WT mice. Murine primary fibroblast like synoviocytes (FLS) were obtained from CIA mice. We examined S1P3 expression after TNF $\alpha$  treatment and measured cytokine produced after S1P treatment with or without TNF $\alpha$  pretreatment in FLS.

**Results:** S1P3 deficiency resulted in modest symptoms of arthritis and a significant reduction in synovial inflammation and bone erosions in histological analysis. S1P3 mRNA expression in knee joint capsule in CIA mice was about five times as high as that in normal mice. TNF $\alpha$  treatment upregulated S1P3 expression and S1P treatment enhanced IL-6 production in WT-FLS significantly. TNF $\alpha$ -priming enhanced S1P-induced IL-6 production, which is significantly higher in WT-FLS than in KO-FLS. This effect was not observed in MCP-1 production of WT-FLS.

**Conclusions:** S1P3-KO reduced severity of arthritis, inflammation and bone erosions in CIA. S1P3 mRNA was upregulated in inflamed joint capsule. S1P induces IL-6 production via S1P3 upregulation by TNF $\alpha$  in CIA-FLS. S1P3 inhibition could be a good target of the therapy for arthritis.

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**Disclosure of Interest:** None declared

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**THU0095** **DIFFERENTIAL COMPLEMENT ACTIVATION IN RHEUMATOID ARTHRITIS PATIENTS**

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**Background:** An atypical subgroup of patients with seropositive rheumatoid arthritis (RA) has been identified with active disease but normal levels of the acute phase protein C-reactive protein (CRP), considered an accurate marker of disease activity. Previously we identified that patients with normal CRP (nCRP) during flares of RA had an altered immunological profile, had diagnostic delays and seemed to respond less well to conventional treatment compared to RA patients who mounted an appropriately high CRP (hCRP) response. Activation of the complement pathway has been associated with disease activity in RA patients and it is suggested both the presence of autoantibodies and activation of complement are required during the inflammatory processes that lead to joint damage. CRP plays a crucial role in the regulation of complement activation via both the alternative and classical pathways, either through interaction with C4 binding protein or degrading C3 fragment-C3b to C3i via factor H. However, it is not known whether these pathways are altered in RA patients with nCRP compared with hCRP during active flares.

**Objectives:** To investigate how altered CRP response may differentially regulate C3 cleavage in RA patients with nCRP compared to hCRP levels during flares of RA.

**Methods:** 24 RA patients with active synovitis were recruited, defined by  $\geq 1$  joint with Power Doppler detected by US, 15 had normal (n)CRP ( $\leq 5$  mg/L) and 9 had high (h)CRP ( $> 5$  mg/L) levels. Serum and detailed clinical data were collected. 18 age and sex matched healthy donors (HCs) were also analysed. Serum was subjected to SOMAscan Proteomic Assay. Complement components were analysed by Western blot following 1:400 serum dilution and assessed for C3/C3a and albumin expression. Densitometric analysis was applied to the Western blots and the C3a values were normalised against albumin, resultant values were expressed as fold change from HC. Results were correlated with clinical and disease features using linear regression curves in Prism.

**Results:** Proteomics identified differential expression of complement components in serum from hCRP compared to nCRP patients; specifically a significant upregulation of alternative complement pathway factors (eg Factors I, H and B) was seen in hCRP patients and a downregulation of kallistatin, an inhibitor of the classical pathway in nCRP patients. Average C3 cleavage product was 4.8 (0.18–14.4) for hCRP and 3.05 (0.28–6.6) for nCRP, both significantly higher compared to HCs ( $p < 0.01$  HC vs nCRP,  $p < 0.05$  HC vs hCRP). The levels of C3 cleavage were then correlated against ESR, CRP and anti-anti-cyclic citrullinated peptide (CCP) levels in both sets of patients. In hCRP patients, strong correlations ( $R^2 > 0.5$ ) were observed for C3 vs ESR ( $p < 0.05$ ), C3 vs CRP ( $p < 0.03$ ) and ESR vs CRP ( $p < 0.0003$ ) but no correlation was found between C3 and levels of anti-CCP antibodies ( $R^2 = 0.208$ ,  $p = 0.255$ ). In contrast nCRP patients demonstrated a strong correlation between C3 levels vs anti-CCP antibodies ( $R^2 = 0.53$ ,  $p < 0.05$ ) whilst no correlation was seen with CRP or ESR levels ( $R^2 = 0.0004$ ,  $p = 0.236$ ).

**Abstract THU0095 – Table 1.** A table of proteins related to complement and coagulation found differentially expressed between hCRP and nCRP patients by SOMAscan proteomics.

hCRP	nCRP
Factor H	Kallistatin
Factor B	IL17F
Factor I	
C3b	
F1xab	
C5a	
C9	
F Xa	
F IX	

**Conclusions:** Cleavage of complement factor C3 appears to be driven by a different mechanism in hCRP compared to nCRP patients suggesting that complement is activated via different pathways. This supports the hypothesis that nCRP and hCRP patients have an altered disease pathogenesis.

**Disclosure of Interest:** None declared

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**THU0096** **A MAPK ACTIVATED KINASE 2 INHIBITOR ATTENUATES INFLAMMATORY AND DESTRUCTIVE ARTHRITIS IN HUMAN EX VIVO MODELS**

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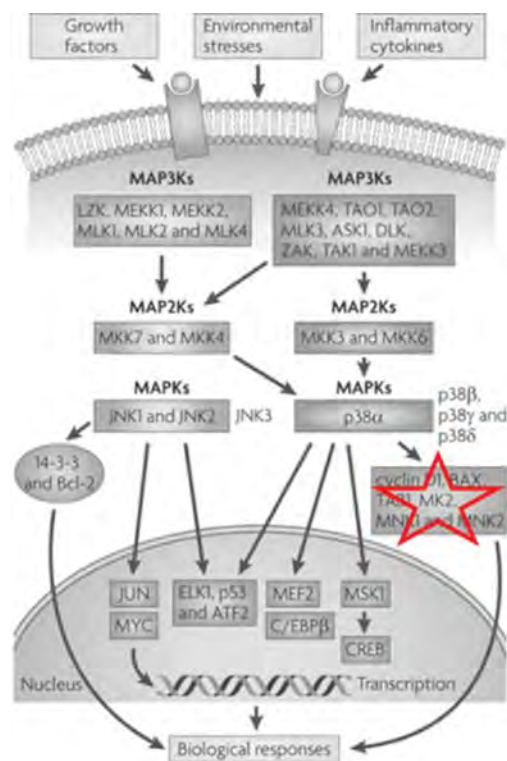
**Background:** Targeting intracellular pathways with oral small molecules is an attractive therapeutic approach for treating immune mediated inflammatory diseases. The mitogen-activated protein kinase (MAPK) pathway is activated by environmental stressors, growth factors and inflammatory cytokines. However, the inhibition of central MAPK proteins has so far had undesirable side effects. The MAPK-activated protein kinase 2 (MK2) is a downstream mediator in the MAPK signalling pathway and could therefore be inhibited without the same side effects (see figure 1).

**Objectives:** The objective of this study was to study the effects of a small molecule inhibiting MK2 on inflammation and structural changes in *ex vivo* models of immune mediated inflammatory arthritis.



**Methods:** Synovial fluid mononuclear cells (SFMCs), fibroblast like synovial cells (FLSs) and peripheral blood mononuclear cells (PBMCs) were obtained from a study population consisting of patients with active RA or peripheral SpA with at least one swollen joint (for obtaining synovial fluid) (n=14). SFMCs were cultured for 48 hours with and without addition of a MK2 inhibitor (Celgene) at 1000 nM, 333 nM and 111 nM and supernatants were analysed by the Olink proseek multiplex interferon panel and commercially available ELISA assays. Because FLSs are only found in small amounts among SFMCs, autologous co-cultures of FLS and PBMCs and SFMCs were also used. SFMCs cultured for 21 days were used to study inflammatory macrophage differentiation and osteoclastogenesis.

**Results:** In SFMCs cultured for 48 hours, the MK2 inhibitor decreased the production of CXCL9 ( $p<0.001$ ), CXCL10 ( $p<0.01$ ), HGF ( $p<0.01$ ), CXCL11 ( $p<0.01$ ), TWEAK ( $p<0.05$ ), and IL-12B ( $p<0.05$ ) and increased the production of CXCL5 ( $p<0.0001$ ), CXCL1 ( $p<0.0001$ ), CXCL6 ( $p<0.001$ ), TGF $\alpha$  ( $p=0.01$ ), MCP-3 ( $p<0.01$ ), LAP TGF $\beta$  ( $p<0.05$ ) dose-dependently after Bonferroni correction (all corrected P values). At the highest concentration, the MK2 inhibitor also decreased MCP-1 production ( $p<0.05$ ). In FLS-SFMC co-cultures, the MK2 inhibitor decreased MCP-1 production ( $p<0.05$ ) but did not change the production of DKK1 and MMP3. In FLS-PBMC co-cultures, the MK2 inhibitor decreased the production of MCP-1 ( $p<0.0001$ ), increased MMP3 production ( $p<0.05$ ) but did not change DKK1 production. In SFMCs cultured for 21 days as a model of inflammatory macrophage differentiation and osteoclastogenesis, the MK2 inhibitor decreased the production of MCP-1 ( $p<0.05$ ) and tartrate-resistant acid phosphatase (TRAP) ( $p<0.05$ ) but did not change the production of IL-10.



**Abstract THU0096 – Figure 1.** Modified from Wagner & Nebreda, *Nature Review Cancer*, 2009.

**Conclusions:** This study reveals the effects of a MK2 inhibitor in *ex vivo* models of immune mediated inflammatory arthritis. The MK2 inhibitor changed the secretory profile of SFMCs and decreased inflammatory osteoclastogenesis. Taken together, this points to a role of this MK2 inhibitor in attenuating inflammatory and destructive arthritis.

**Disclosure of Interest:** T. Kragstrup: None declared, A. Mellekjær: None declared, M. Nielsen: None declared, L. Hefdal: None declared, P. Schafer Shareholder of: Celgene, Employee of: Celgene, B. Deleuran: None declared

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#### THU0097 PHOSPHODIESTERASES 4 (PDE4) INHIBITOR AMELIORATES EXPERIMENTAL ARTHRITIS

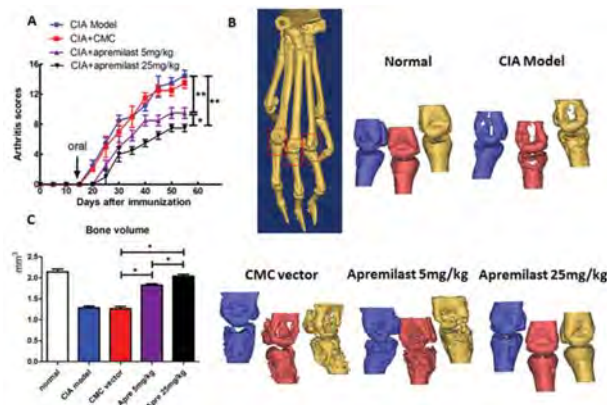
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**Background:** Rheumatoid arthritis (RA) is a chronic inflammatory bone-destructive disorder with autoimmune features. Apremilast is a novel phosphodiesterases 4 (PDE4) inhibitor suppressing immune and inflammatory responses.

**Objectives:** We assessed the anti-inflammatory and bone protection effects of apremilast in collagen CII induced arthritis (CIA) models.

**Methods:** Apremilast was given starting from day 14 after immunisation, we investigated whether apremilast (5 mg/kg or 25 mg/kg) can ameliorate arthritis onset. Bone erosion was measured by histological and micro-computed tomographic analysis. Anti-mouse type II collagen (CII) antibody levels were measured by enzyme-linked immunosorbent assay. Human cartilage and rheumatoid arthritis (RA) synovial fibroblasts (RASFs) implantation in the severe combined immunodeficiency (SCID) mouse model of RA were used to study the role of apremilast in suppression of RASFs destroying cartilage *in vivo*.

**Results:** We found that apremilast therapy delayed arthritis onset and reduced arthritis scores in CIA model at a different dose, compared to CIA model and blank vector (figure 1A). Total serum IgG, IgG1, IgG2a, and IgG2b were all decreased in apremilast groups. Furthermore, apremilast can prevent CIA mice from bone erosion by CT analysis. High dose of apremilast (25 mg/kg) was superior to low dose (5 mg/kg) in treating CIA (figure 1B, C). Apremilast treatment can inhibit destroy and migratory ability of RASFs to cartilages. Compared to the model group, Apremilast treatment significantly reduced the invasion scores in both primary implant and contralateral implant.



**Conclusions:** Our data suggest that apremilast was effective in preventing arthritis and bone erosion in CIA model, implicating a potential promise of therapy on rheumatoid arthritis.

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**Disclosure of Interest:** None declared

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#### THU0098 COMBINATION THERAPY OF RAPAMYCIN AND A GLUTAMINE ANTAGONIST FACILITATES THE EXPANSION OF MYELOID-DERIVED SUPPRESSOR CELLS AND AMELIORATES ARTHRITIS IN SKG MICE

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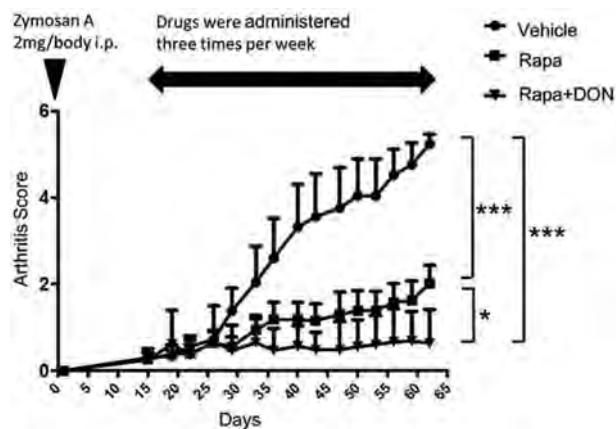
**Background:** Myeloid-derived suppressor cells (MDSCs) are a heterogeneous population of immature cells that increase in the pathological state such as tumour or inflammation and have the immunosuppressive ability. MDSCs have been

reported to ameliorate arthritis in several mice models. Mechanistic target of rapamycin (mTOR) pathway and glutaminolysis activate cooperatively in the differentiation from myeloid progenitors to mature myeloid cells such as dendritic cells, macrophages, or osteoclasts as well as the activation of effector T cells and the differentiation of Th1 and Th17 cells. Although rapamycin has reported to facilitate the expansion of MDSCs and their immunosuppressive ability, the effect of the inhibitor of glutaminolysis on MDSCs is still unknown.

**Objectives:** The aim of this study is to evaluate the facilitative effects of the inhibition of mTOR pathway and glutaminolysis on MDSCs in a mouse model of rheumatoid arthritis.

**Methods:** Bone marrow (BM) cells from untreated Balb/c mice were cultured for 5 days under granulocyte-macrophage colony-stimulating factor (GM-CSF) stimulation with four patterns of drugs; 1) DMSO (control), 2) rapamycin (Rapa), 3) 6-Diazo-5-oxo-L-norleucine (DON; a glutamine antagonist), or 4) the combination of rapamycin and DON (Rapa +DON). Cultured BM cells were analysed by flow cytometry. Cultured MDSCs were isolated by manual MACS and analysed their immunosuppressive characters by co-culture with CFSE-dyed CD4<sup>+</sup> T cells. Rapa or Rapa +DON were administered intraperitoneally to arthritic SKG mice induced by Zymosan A injection.

**Results:** We found that DON suppressed the differentiation of dendritic cells (DC) in a dose-dependent manner and the addition of Rapa on DON inhibited the differentiation of macrophages *in vitro*. The proportions of the phenotype of MDSCs were increased with administrations of Rapa or DON, and large part of them were Ly6G<sup>+</sup> cells (the phenotype of polymorphonuclear MDSCs; PMN-MDSCs). Rapa ±DON significantly increased the expressions of TGF-β and PD-L1 and the inhibitory capacity of Ly6G<sup>+</sup> PMN-MDSCs. Rapa +DON significantly suppressed arthritis more efficiently in SKG mice than Rapa *in vivo*. (see figure 1)



**Conclusions:** The combination of rapamycin and a glutamine antagonist facilitates the expansion of PMN-MDSCs *in vitro* and ameliorates arthritis in SKG mice *in vivo*.

**Disclosure of Interest:** None declared

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THU0099

#### MYELOID SIRTUIN 6 DEFICIENCY ACCELERATES EXPERIMENTAL AND HUMAN ARTHRITIS BY INCREASING MACROPHAGE INFILTRATION INTO SYNOVIUM

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**Background:** Rheumatoid arthritis (RA) is an autoimmune inflammatory disease of the joints and is characterised by immune cell infiltration, synovial hyperplasia, and destruction of cartilage and underlying bone<sup>1</sup>. Myeloid derived monocytes and macrophages secrete a variety of cytokines such as tumour necrosis factor-α (TNF-α), interleukin (IL)-1β and IL-6, all of which perpetuate and amplify the vicious cycle of chronic inflammatory pathways<sup>2</sup>. Indeed, macrophage numbers in the synovium and serum levels of monocyte-derived cytokines correlate well with clinical symptoms and degree of joint damage in RA<sup>3</sup>.

**Objectives:** We recently reported that myeloid sirtuin 6 (Sirt6) is a critical determinant of phenotypic switching and the migratory responses of macrophages<sup>4</sup>.

Given the prominent role of macrophages in rheumatoid arthritis (RA) pathogenesis<sup>5</sup>, we tested whether myeloid Sirt6 deficiency affects the development and exacerbation of RA.

**Methods:** Arthritis was induced in wild type and myeloid Sirt6 KO (mS6KO) mice using collagen-induced and K/BxN serum transfer models. Peripheral blood mononuclear cells (PBMC) and synovial fluid macrophages were obtained from patients with RA and osteoarthritis and used for comparisons of Sirt6 expression and inflammatory activities.

**Results:** Based on clinical scores, ankle thickness, pathology and radiology, arthritis was more severe in mS6KO mice relative to wild type with a greater accumulation of macrophages in the synovium. Consistently, myeloid Sirt6 deficiency increased the migration potential of macrophages toward synovioctes-derived chemoattractants. Mechanistically, Sirt6 deacetylates forkhead box protein O1 to trigger its nuclear export and proteasomal degradation. Lastly, PBMC and macrophages isolated from RA patients exhibited lower Sirt6 expression compared with those from osteoarthritis patients or healthy subjects and their Sirt6 activity was inversely correlated with disease severity of the patients.

**Conclusions:** Our data identify a role of myeloid Sirt6 in clinical and experimental RA and suggest that myeloid Sirt6 may be an intriguing therapeutic target.

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**Disclosure of Interest:** None declared

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THURSDAY, 14 JUNE 2018

#### Rheumatoid arthritis – prognosis, predictors and outcome

THU0100

#### WORK IMPAIRMENT IN RHEUMATOID ARTHRITIS IS HIGHLY CORRELATED WITH DEPRESSION

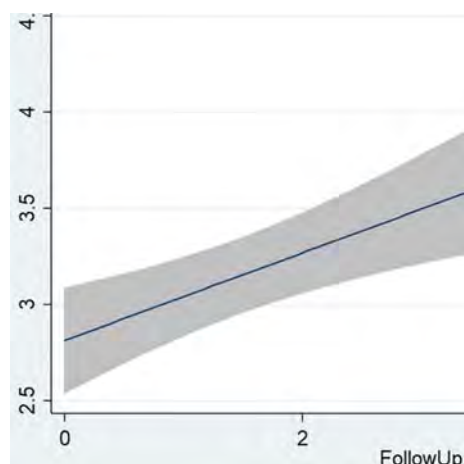
A.D. Houssien, J. Galloway. *Academic Rheumatology department, King's College London, London, UK*

**Background:** Work outcomes are highly relevant in rheumatoid arthritis. Almost a third of people are no longer in employment by 2 years after diagnosis. Remaining in the workforce has positive attributes in terms of health outcome and quality of life.

**Objectives:** We set out to study the relationship between work and depression in rheumatoid arthritis.

**Methods:** We used routinely collected data from a hospital rheumatoid arthritis cohort that has systematically collected longitudinal data on disease measures, mental health, and work impairment. The Work and Social Adjustment Scale was used to estimate work impact, and we used question 2 (scale 0–8, above 6 indicating severe impairment) for analyses. Mood was assessed using the PHQ2. Cross sectional analyses were used to describe the relationship between work impairment and depression, adjusting for disease severity factors. We then analysed the temporal relationship between work impairment and mood.

**Results:** In total 283 patients had data available for analysis. Mean age was 53 years (SD 15), 81% were female, median disease duration 6 years (IQR 0 to 10). 74% were seropositive (RF or CCP), mean baseline DAS28 score 3.8 (SD 1.7), baseline HAQ 1.2 (SD 0.9). At baseline 69% reported no depression, 13% reported some symptoms, 18% had probable major depression. 72% of patients reported some degree of work impairment, 14% reported severe impairment. There was a strong relationship between baseline depressive symptoms and work impairment: coefficient 2.4, 95% CI 1.7 to 3.0, p<0.001. Adjusting for age, gender, DAS28, HAQ: 1.3, 95% CI 0.5 to 2.0, p=0.004. Over time work impairment increased (linear regression coefficient: 0.2 per year 95% CI 0.1 to 0.4), see figure 1. People with baseline low mood had an accelerated worsening of work impairment.



**Conclusions:** Work impairment is highly prevalent in contemporary rheumatoid arthritis patients. It is significantly correlated with mental health, even after adjusting for disease severity factors. Baseline mental health also predicts progression of work impairment. The relationship is likely bidirectional, and future research is justified to evaluate whether mental health interventions could improve work outcomes.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.5395

#### THU0101 TISSUE METABOLITE OF TYPE I COLLAGEN, C1M, AND CRP PREDICTS STRUCTURAL PROGRESSION OF RHEUMATOID ARTHRITIS

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**Background:** Biomarkers of rheumatoid arthritis (RA) disease activity typically measure inflammation or autoimmunity (e.g. CRP, rheumatoid factor (RF)). Another class of biomarkers are structural proteins of the joint. C1M and C3M, metabolites of type I and III collagen, are such biomarkers. These biomarkers have previously been documented to provide additional value as compared to standard inflammation biomarkers, for prognosis and prediction of response to treatment<sup>1</sup>.

**Objectives:** We investigated the relationship of high serum levels of C1M or C3M to radiographic progression, and benchmarked to CRP levels and RF status, demonstrated to be associated with structural progression<sup>2</sup>.

**Methods:** Placebo treated patients of the OSK123 studies (Ph3 clinical trials testing efficacy of fostamatinib) with baseline serum biomarkers C1M, C3M, CRP and RF were included ( $n_{BL}=474$ ). Van der Heijde mTSS was calculated at baseline and 24 week ( $n_{24}=264$ ). Progression was defined as moderate or rapid ( $\geq 0.5$  or  $\geq 5$  mTSS units/y). Patients were divided into subgroups; low, high or very high C1M, C3M and CRP (above/below median and highest quartile), or RF negative, positive and high positive ( $\geq 110$  U/L)<sup>2</sup>. Difference in clinical parameters were analysed by Mann-Whitney/Chi-squared tests, and multivariate predictive calculations by *Classification And Regression Tree* analysis including covariates (age, BMI, gender and disease activity assessment scores).

**Results:** High C1M, C3M and CRP levels were significantly associated with measures of disease activity ( $p<0.05$ ) and patient reported scores ( $p<0.05$ ). RF<sub>pos</sub> was also associated with disease active scores ( $p<0.05$ ). RF<sub>pos</sub> and CRP ( $p<0.001$ ), as well as C1M and C3M ( $p<0.05$ ), were significantly associated with mTSS at baseline. For prognostic measures, there were 2.5 and 4-fold as many rapid progressors in the C1M<sub>high</sub> and CRP<sub>high</sub> ( $p<0.05$ ), and in the C1M<sub>veryhigh</sub> and CRP<sub>veryhigh</sub> groups ( $p<0.001$ ) compared C1M<sub>low</sub> and CRP<sub>low</sub>, respectively. C1M and CRP performed similarly in the predictive analysis with AUCs of 0.67 and 0.69 (table 1). The best model involving C1M in predicting rapid progressor included BMI, SJC and HAQ (AUC 0.85), whereas the best model for CRP included CRP, BMI, SJC and HAQ (AUC 0.85). C3M and RF did not provide prognostic value.

Model description	Progressors (delta mTSS $\geq 0.5$ units per year)			Rapid progressors (delta mTSS $\geq 5$ units per year)		
	AUC	Specificity	Model parameters	AUC	Specificity	Model parameters
C1M alone	0.600	Sensitivity	C1Mveryhigh	0.672	Sensitivity	C1Mveryhigh
	59.7	Correctly identified	C1Mhigh	83.1	Correctly identified	C1Mhigh
C1M with demo, clinical ass., and X-ray	53.8			45.8		
	56.7			64.3		
CRP alone	0.712		C1Mveryhigh	0.849		C1Mveryhigh
	87.8		Age	78.4		BMI
CRP with demo, clinical ass., and X-ray	40.5		BMI	73.9		Disease duration
	64.1		Disease duration	76.2		HAQ
CRP alone	0.594		HAQ			
	85.1		CRPveryhigh	0.687		CRPveryhigh
CRP with demo, clinical ass., and X-ray	28.8		CRPhigh	84.0		CRPhigh
	56.9			50		
CRP alone	0.717		CRPhigh	67.0		
	76.1		Age	84.7		CRPhigh
CRP with demo, clinical ass., and X-ray	51.9		BMI	53.4		BMI
	64.0		Disease duration	95.7		SJC
			SJC	74.2		HAQ
			HAQ			

**Conclusions:** Of the four markers analysed only C1M and CRP were associated with structural progression. They seem to perform equally well, but reflect two different aspects of disease pathogenesis (tissue turnover vs. inflammation), thus may provide individual, but supplementary, information. These simple measures may be important for enrichment of clinical trials with structural progressors.

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**Disclosure of Interest:** A. Bay-Jensen Shareholder of: Nordic Bioscience, Employee of: Nordic Bioscience, A. Platt Shareholder of: AstraZeneca, Employee of: AstraZeneca, M. Jenkins Employee of: AstraZeneca, M. Weinblatt: None declared, I. Byrjalsen Employee of: Nordic Bioscience, K. Musa Employee of: Nordic Bioscience, M. Genovese: None declared, M. Karsdal Shareholder of: Nordic Bioscience, Employee of: Nordic Bioscience

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#### THU0102 HIGH RATES OF RESIDUAL DISEASE ACTIVITY DESPITE CURRENT THERAPIES IN A REAL LIFE RHEUMATOID ARTHRITIS COHORT: DATA FROM 1096 PATIENTS

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**Background:** It is unclear if the widespread use of biologic DMARDs (bDMARDs) and the implementation of the treat to target approach have led to better disease control in patients with rheumatoid arthritis (RA) in daily clinical practice.

**Objectives:** To study the longitudinal changes in disease activity in a large, real life, longitudinal RA cohort.

**Methods:** Multicenter (11 hospitals, 3 private offices), prospective, RA epidemiological study in Greece. Demographics, disease characteristics, treatments and co-morbidities were collected via a web-based platform in registered patients at baseline and one year after their 1st visit.

**Results:** 1.096 RA patients with available paired evaluations one year apart (mean interval: 13.4 $\pm$ 3.6 months) were included (women: 78%, mean age: 62.8 years, mean disease duration: 11 years, RF and/or anti-CCP positive: 60%, mean HAQ: 0.44 $\pm$ 0.56). At baseline, 50% (n=548) of patients were on conventional DMARDs (csDMARDs) alone, 35% on cs- and b-DMARD combination (n=379) and 11% on bDMARD monotherapy (n=124). Among bDMARD treated patients, 60% were



receiving tumour necrosis factor inhibitors (TNFi) while 40% were on corticosteroids (mean daily dose: 4.7 mg). Despite these therapies, 43% of patients had active disease (DAS28-ESR>3.2); 34% moderate (MDA, DAS28-ESR=3.2–5.1) and 9% high (HDA, DAS28-ESR>5.1) disease activity. During the 1 year observation period, among the group of patients with MDA who were only on csDMARDs, 15% started a bDMARD while among those on bDMARDs, 11% switched to another bDMARD. The respective rates of starting a bDMARD (in those on csDMARDs) or switching to another bDMARD (in those on bDMARDs), were much higher for patients in the HDA group (41% and 32% respectively,  $p<0.001$  for both groups). At the end of the 1st year, the proportion of patients on TNFi and corticosteroids was 57% and 32%, respectively. Overall, despite a decrease in the DAS28-ESR score (from  $3.2\pm 1.2$  to  $2.9\pm 1.3$ ,  $p<0.001$ ), 37% of patients had still active disease (6% improvement after 1 year; MDA: 30%, HDA: 7%).

**Conclusions:** In a large, real life, RA cohort with almost half of patients on bDMARD-based therapies, more than one third of patients had still active disease at the end of the 1st year of follow-up. These findings could be explained in part by the low rate of bDMARD initiation or switching in this cohort or they could indicate the limitations of current therapeutic approaches in RA patients with longstanding disease in Greece.

**Acknowledgements:** Supported by grants from the Greek Rheumatology Society and Professional Association of Rheumatologists.

**Disclosure of Interest:** None declared

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### THU0103 EVALUATION OF SERUM B-2 MICROGLOBULIN LEVELS AND ITS RELATIONSHIP WITH DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS

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**Background:**  $\beta$ -2 microglobulin ( $\beta$ 2MG) is produced and secreted from T and B lymphocytes. In autoimmune diseases, due to lymphocyte activation and proliferation, serum  $\beta$ 2MG level is expected to be higher than normal. In a few studies, increased serum and synovial fluid  $\beta$ 2MG levels in rheumatoid arthritis (RA) were reported.

**Objectives:** The aim of this study was to evaluate the concentration of  $\beta$ 2MG in peripheral blood in RA patients and to show its relationship with disease activity.

**Methods:** In this study, 121 RA patients and 50 sex and age matched healthy controls were enrolled. Patients who had other inflammatory diseases or any kind of malignancy were excluded.

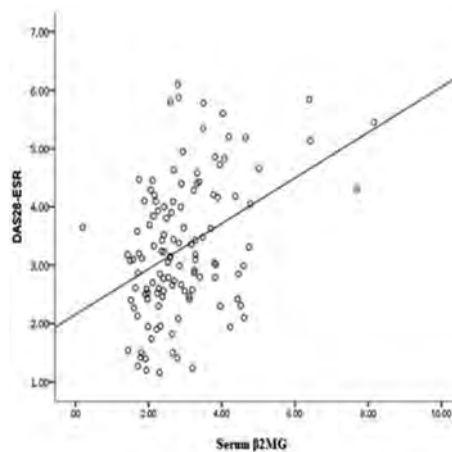
**Results:** The mean age of RA patients (97 female and 24 male) were 55 years ( $\pm 10.9$  years) and mean disease duration was 9 years (min: 6 months, max: 42 years). The demographic data of patients and healthy controls are shown in table 1. There was a statistically significant difference between haemoglobin, erythrocyte sedimentation rate and C-reactive protein levels between two groups ( $p<0.001$ ,  $p<0.001$ ,  $p=0.001$  respectively). Serum  $\beta$ 2MG levels were higher in RA group than healthy controls ( $p<0.001$ ). When RA patients were grouped according to disease activity as remission to low disease activity (DAS28-ESR<3.2) ( $n=65$ ) and moderate to severe disease activity (DAS28-ESR $\geq$ 3.2) ( $n=56$ ), the serum  $\beta$ 2MG levels were higher in DAS28-ESR $\geq$ 3.2 group than in DAS28-ESR<3.2 group ( $p=0.003$ ). The difference between serum  $\beta$ 2MG levels were statistically significant in low and high disease activity groups when grouped both according to DAS-ESR and DAS-CRP ( $p=0.003$  and  $p=0.006$ , respectively). The seropositivity between two groups were similar ( $p=0.385$ ), although serum ESR, CRP levels and the rate of morning stiffness were significantly higher in high disease activity group. The results were shown in table 2. According to Spearman correlation test, the serum  $\beta$ 2MG level and DAS-ESR and DAS-CRP were positively correlated which were both statistically significant. ( $r=0.378$ ,  $p<0.001$  and  $r=0.324$ ,  $p<0.001$  respectively).

**Abstract THU0103 – Table 1.** Baseline characteristics of RA patients and healthy controls

Characteristics	RA(n=121)	Control (n=50)	p value
Female Sex, n (%)	97 (80.2)	35 (70.0)	0.150
Age, years	55.0 $\pm$ 10.9	52.6 $\pm$ 10.6	0.183
WBC	7736 $\pm$ 3177	7170 $\pm$ 1759	0.139
Hb	12.6 $\pm$ 1.5	14.1 $\pm$ 1.7	<0.001
Thrombocyte	290.4 $\pm$ 88.9	279.7 $\pm$ 65.2	0.441
ESR	24.3 $\pm$ 17.0	12.2 $\pm$ 8.2	<0.001
CRP (IQR)	2.5 (4.7)	6.1 (10.7)	0.001
$\beta$ 2-microglobulin	2.93 $\pm$ 1.20	2.21 $\pm$ 0.54	<0.001
DAS28-ESR	3.30 $\pm$ 1.16		
DAS28-CRP	3.60 $\pm$ 1.39		

**Abstract THU0103 – Table 2.** Baseline characteristics of RA patients

	DAS28-ESR $\leq$ 3.2 (n=65)	DAS28-ESR>3.2 (n=56)	p value
Female Sex, n (%)	48 (73.8)	29 (87.5)	0.060
Age, years	53.4 $\pm$ 11.3	56.9 $\pm$ 10.1	0.079
ESR	17.8 $\pm$ 12.3	31.9 $\pm$ 18.6	<0.001
CRP (IQR)	4.0 (7.9)	10.2 (12.6)	<0.001
B2-microglobulin	2.62 $\pm$ 0.87	3.29 $\pm$ 1.42	0.003
DAS28-ESR	2.42 $\pm$ 0.59	4.31 $\pm$ 0.78	<0.001
DAS28-CRP	2.67 $\pm$ 0.61	4.67 $\pm$ 2.26	<0.001
Morning stiffness, n (%)	13 (20)	24 (42.9)	0.007



**Abstract THU0103 – Figure 1.** The figure that shows the relationship of serum  $\beta$ 2MG with DAS28-ESR

**Conclusions:** Our results show that serum  $\beta$ 2MG concentration increase in RA and is higher in active patients. It can be concluded that serum  $\beta$ 2MG may be an appropriate parameter to monitor disease activity in rheumatoid arthritis.

**Disclosure of Interest:** None declared

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### THU0104 THE TEMPORAL PROFILE OF ANTIBODIES DIRECTED AGAINST POST-TRANSLATIONAL MODIFICATIONS VARIES ACCORDING TO ISOTYPE AND TARGET IN PATIENTS WITH NEW-ONSET RHEUMATOID ARTHRITIS

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**Background:** Autoantibodies directed against antigens with post-translational modifications (PTMs), such as citrullination (ACPA), are a hallmark of rheumatoid arthritis (RA)<sup>1</sup>. ACPA titres increase prior to disease onset, but are thought to be relatively stable after symptomatic inflammation is established<sup>2</sup>. The temporal profile of antibodies against acetylated (AAPA) and carbamylated (ACarPA) peptides has not been so comprehensively characterised following the onset of joint swelling<sup>3</sup>.

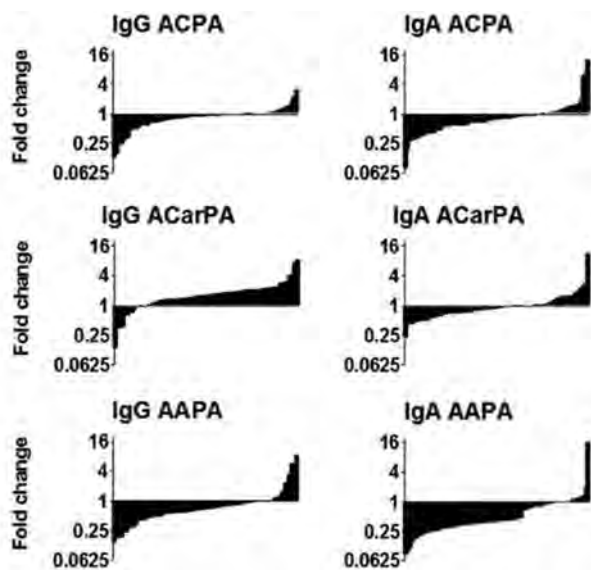
**Objectives:** We aimed to track serum levels of anti-PTM antibodies over 18 months in patients with newly-presenting RA in our prospective observational cohort.

**Methods:** Patients with treatment-naïve inflammatory arthritis donated serum at baseline, 6 and 18 months. 103 patients satisfying ACR<sup>EULAR 2010</sup> criteria for RA underwent testing for IgG and IgA antibodies against peptides with citrulline (ACPA), carbamylated lysine (ACarPA), and acetylated lysine (AAPA) PTMs using ELISA as previously described<sup>4</sup>.

**Results:** 57% of participants were female, and 48% and 50% patients were anti-CCP2 or rheumatoid factor positive respectively. Mean age was 56 years (s.d. 15.2), symptom duration 55 days (s.d. 22.4), and DAS28CRP 4.4 (s.d. 1.3) at enrolment.

Comparing baseline and 18 month median antibody levels measured by optical density, a decrease was observed over time for IgG (0.26 vs 0.17,  $p<0.0001$ ) and IgA AAPA (0.23 vs 0.09,  $p<0.0001$ ), as well as both IgG and IgA antibodies against citrullinated peptides (0.47 vs 0.40,  $p<0.0001$  and 0.16 vs 0.12,  $p<0.0001$  respectively). Significant reductions occurred between baseline and 6 months for both IgG ( $p<0.0001$ ) and IgA ( $p<0.0001$ ) AAPA antibodies, but not between 6 and

18 month timepoints after correction for multiple testing. A similar pattern was observed for IgA ACPA antibody levels, although IgG ACPA levels did not vary significantly comparing baseline with 6, and 6 with 18 month timepoints. Antibody levels were not influenced by exposure to therapy. Patients seropositive for anti-CCP2 at baseline demonstrated less labile antibody levels, with the exception of sustained increases in IgG ACPA reactivity compared with seronegative individuals. **Abstract THU0104 – figure 1.** demonstrates bidirectional changes in anti-PTM antibody reactivity at the patient level.



**Abstract THU0104 – Figure 1.** Fold change in anti-PTM autoantibody levels between baseline and 18 months in patients with newly-presenting rheumatoid arthritis (n=130)

**Conclusions:** Median ACPA and, to a lesser extent, ACPA levels fell over time, regardless of therapy. This was most marked for the IgA isotype. Differential isotype effects may represent maturation of the autoantibody repertoire from mucosal IgA antibodies involved in the breach of tolerance. Lability of ACPA levels may reflect the relative reversibility of acetylation of a lysine amino acid residue by comparison with citrullination and carbamylation modifications. By contrast, and as observed previously<sup>3</sup>, IgG ACPA levels increased over time, perhaps reflecting the tendency of the human proteome to accrue carbamylation modifications due to ageing, and metabolic or inflammatory stress.

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THU0105

#### RELATIONSHIP BETWEEN DAS28 CATEGORIES AND RAID PATIENT REPORTED OUTCOME IN RHEUMATOID ARTHRITIS; SIGNIFICANT ADVANTAGE OF TARGETING DAS REMISSION

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**Background:** EULAR/ACR guidelines recommend remission or low DAS28 as the treat to target goal for patients with rheumatoid arthritis (RA). The DAS28 is a composite score derived from objective (swollen joint count and ESR/CRP) and subjective (tender joint count and patient global) measures of disease activity, restricted to 28 joints. It has been criticised as not being representative of the whole patient or completely allied to patient experience. Alternative patient reported outcomes (PROM) have been developed, including the rheumatoid arthritis impact of disease (RAID) which is a self-reported index which assesses seven domains by visual analogue scale: pain, disability, fatigue, sleep, coping,

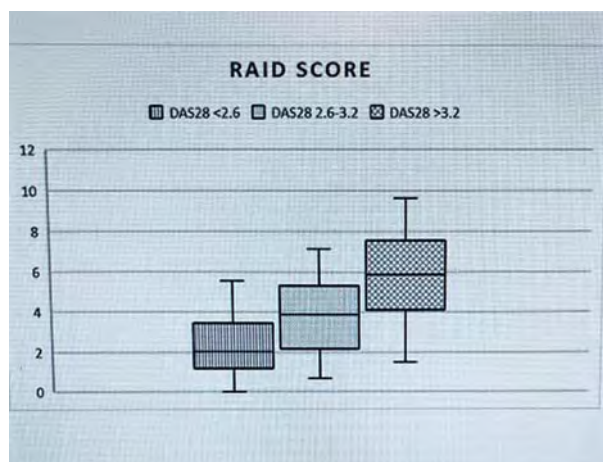
physical and emotional well-being. Responses are weighted differently producing a final score from 0–10 and a score <2 is considered a patient-acceptable status.

**Objectives:** Given uncertainty over the necessity to aim for DAS remission (RDAS) as opposed to low DAS (LDAS) as a treatment target, we sought to explore the relation between DAS outcomes and RAID scores in routine clinical practice.

**Methods:** RA patients attending for routine review in the outpatient clinic at St George's Hospital were assessed by a physician associate between June 2016 and September 2017. DAS28 CRP and ESR scores were recorded and RAID questionnaires completed by patients and calculated using the on-line EULAR tool. Data were analysed on Excel for summary statistics and Spearman correlation coefficient and socscistatistics.com for Mann-Whitney U tests.

**Results:** 117 RA patients were assessed, 84% female, mean age 59.6 years, 77% RF positive and 85% ACPA positive. The prevalence of DAS28 ESR categories was RDAS ( $\leq 2.6$ ) n=57 (49%), LDAS (2.6–3.2) n=17 (14.5%), moderate (MDAS 3.21–5.1) n=35 (30%), high (HDAS  $\geq 5.1$ ) n=8 (6.5%). RAID scores correlated strongly with patient global (r=0.62), DAS28 CRP (r=0.58) and DAS28 ESR (r=0.54) but poorly with tender joint count (r=0.32), swollen joint count (r=0.10), ESR (r=0.13) and CRP (r=0.09). The mean RAID score in DAS28 ESR categories was RDAS 2.49, LDAS 3.77, M+HDAS 5.92, see figure 1, box and whisker plots. RAID scores were significantly different (Mann-Whitney U) between M+HDAS versus RDAS (p<0.0001), M+HDAS versus LDAS (p=0.0048) and also between RDAS versus LDAS (p 0.013). Similar significant differences in RAID scores were found with DAS28 CRP categories. There were no significant differences in RAID scores between RF positive versus negative or ACPA positive versus negative patients.

Of 30 patients with RAID <2, DAS28 ESR was <2.6 in 27 (90%) and <3.2 in 29 (97%). Of 74 patients with DAS28 ESR <3.2, RAID was >2 in 45 (61%) with fatigue followed by sleep being the worst scoring domains.



**Conclusions:** RAID scores strongly correlate with patient global and total DAS28 (ESR or CRP) scores, and are significantly different between all DAS categories, including RDAS versus LDAS. Patients with RAID <2 are almost all at LDAS target, but high numbers at LDAS have unacceptable RAID, largely driven by high fatigue and sleep scores. This suggests that achieving RDAS has significant benefit over LDAS from a PROM perspective, and attention should be paid to fatigue and sleep if RAID is unacceptable in LDAS patients.

**Disclosure of Interest:** None declared

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THU0106

#### CONVERTING PATIENT-REPORTED OUTCOME MEASURES OF FATIGUE AND PAIN TO PROMIS SCORES: DATA FROM PHASE 3 BARICITINIB RHEUMATOID ARTHRITIS TRIALS

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**Background:** Fatigue and pain in patients (pts) with RA are often measured with the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) and the Medical Outcomes Study Short-Form-36 (SF-36). Patient-Reported Outcomes Measurement Information System (PROMIS) was developed using a population-calibrated T-score metric (Mean 50, SD 10). Crosswalk tables were developed linking legacy instruments to PROMIS instruments, including Fatigue and Pain

Interference (PI). Comparisons to the general population can be made from PROMIS scores.<sup>1-2</sup>

**Objectives:** To convert FACIT-F and SF-36 Bodily Pain (BP) scores to PROMIS Fatigue and PI scores to determine how PROMIS performs in 2 phase 3 baricitinib (bari) RA trials.

**Methods:** In RA-BEAM, pts with inadequate response (IR) to MTX were randomised 3:3:2 to placebo (PBO) once daily (QD), bari-4 mg QD, or adalimumab (ADA) 40 mg biweekly.<sup>3</sup> In RA-BEACON, pts with IR to bDMARDs were randomised 1:1:1 to receive PBO or bari 2 mg or 4 mg QD.<sup>4</sup> FACIT-F assessed fatigue and SF-36 BP, pain. Pt-level PROMIS scores were converted from FACIT-F/SF-36 BP using validated crosswalk tables.<sup>1-2</sup> Analysis of covariance was conducted on PROMIS score conversions to compare bari to all treatment arms.

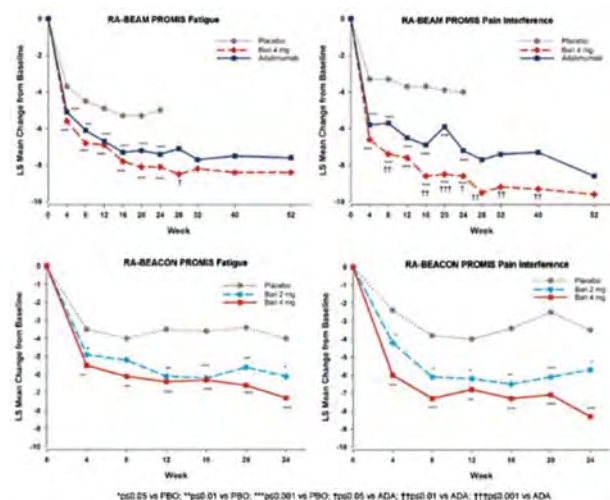
**Results:** Pts had considerable baseline fatigue/pain; mean scores approached or exceeded 1 SD (10 points on the metric) from population norms. Bari was associated with clinically relevant improvements (exceeding 0.5 SD/5 points on the T-score metric) vs PBO for PROMIS fatigue/PI scores (table 1). PROMIS fatigue/PI scores in RA-BEAM reached population norms (<55) by week 12 for bari and ADA (table 1). Bari remained associated with significant improvements in PROMIS fatigue/PI vs PBO through 24 weeks in both studies and vs ADA for PI in RA-BEAM (figure 1).

Data are mean (SD)

<sup>a</sup>Higher PROMIS scores mean more fatigue/pain

<sup>b</sup>BEACON was a 24 week study

ADA=adalimumab; bari=baricitinib; PBO=placebo



**Abstract THU0106 – Figure 1.** Change from baseline for PROMIS Fatigue and Pain Interference in RA-BEAM and RA-BEACON

**Conclusions:** While PROMIS was not used in the studies directly, pt-level crosswalk tables provide an estimate of effect that may be demonstrated when using PROMIS in clinical trials. These results provide preliminary evidence of the ability of PROMIS to demonstrate treatment benefit.

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**Abstract THU0106 – Table 1.** PROMIS Patient-Reported Outcome scores<sup>a</sup> in RA-BEAM and RA-BEACON

	RA-BEAM		ADA (n=330)	RA-BEACON <sup>b</sup>		
	PBO (n=488)	Bari-4 mg (n=487)		PBO (n=176)	Bari-2 mg (n=174)	Bari-4 mg (n=177)
<b>PROMIS Fatigue converted from FACIT-F</b>						
Baseline	58.1 (7.8)	58.6 (7.6)	59.0 (8.4)	62.8 (7.5)	62.4 (7.0)	61.9 (8.2)
Week 4	54.5 (7.6)	52.9 (7.5)	53.5 (7.9)	59.3 (8.0)	57.7 (8.5)	56.7 (8.5)
Week 12	53.2 (8.0)	51.4 (8.3)	51.7 (8.6)	58.7 (8.7)	56.0 (9.5)	55.3 (9.3)
Week 24	53.1 (8.5)	50.2 (8.7)	51.1 (9.0)	58.2 (8.7)	56.0 (9.4)	54.4 (10.3)
Week 52	–	50.1 (8.6)	51.0 (9.2)	–	–	–
<b>PROMIS Pain Interference converted from SF-36 Bodily Pain score</b>						
Baseline	61.3 (7.9)	61.9 (7.4)	61.9 (8.3)	65.2 (7.3)	63.7 (7.1)	64.8 (7.8)
Week 4	58.3 (7.8)	55.2 (7.4)	55.9 (7.9)	61.6 (7.1)	59.3 (8.3)	57.8 (7.9)
Week 12	57.5 (8.1)	53.7 (8.6)	54.8 (8.6)	60.2 (8.7)	57.6 (9.1)	57.2 (9.4)
Week 24	57.2 (8.4)	52.7 (8.9)	54.0 (8.8)	60.8 (8.3)	58.1 (8.8)	55.8 (9.8)
Week 52	–	52.0 (9.4)	53.1 (9.8)	–	–	–

#### THU0107 EVALUATION OF CARDIOVASCULAR RISK IN PATIENTS WITH RHEUMATOID ARTHRITIS AND ANTI-TNF-ALPHA THERAPY

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**Background:** Rheumatoid arthritis is a chronic inflammatory autoimmune disease that causes systemic inflammation associated with increased risk of coronary, cerebral and peripheral ischaemic accidents. Biological therapy, by decreasing systemic inflammation, implicitly reduces cardiovascular risk in patients with rheumatoid arthritis. The assessment of carotid atheromatosis in Doppler ultrasound examination can be a useful element in the diagnosis of patients with cardiovascular risk.

**Objectives:** We followed the cardiovascular risk as well as the development of the carotid artery plaque by carotid Doppler ultrasound, lipid profile and arterial hypertension in patients with rheumatoid arthritis who have undergone biological treatment with anti-TNF-alpha. We also studied the correlation of the intima-medium thickness index in the carotids with the activity of rheumatic disease (DAS28, CRP, VSH) and the evolution of these parameters under biological therapy.

**Methods:** Our study included 37 patients with rheumatoid arthritis in treatment with DMARD's (group 1) and 50 patients with rheumatoid arthritis in treatment with anti-TNF-alpha (etanercept, adalimumab, infliximab) biological therapy (group 2). The following parameters were assessed in all patients: DAS28, lipid profile (total cholesterol, LDL, HDL, triglycerides), which were followed at 0, 6, and 12 months. The Intima-Medium Thickness Index was measured by Mode B sonography at the level of the common carotid artery, bifurcation of both arteries and the external carotid artery. The value of the index above 0.7 mm was considered pathological.

**Results:** In lot 1, after the carotid Doppler ultrasound, of the 37 patients, 21 presented the carotid artery plaque, and in lot 2 of the 50 patients, 34 showed these changes. A full evaluation (DAS28, lipid profile, arterial tension, carotid ultrasound) of all patients was performed at the start of the study. At 6 months, inflammatory markers and DAS28 showed a decrease in baseline values in both groups, more significant in the biological therapy group. Reduction of the intima-medium thickness index and blood pressure was observed in both groups, with no significant differences. At 12 months, CRP and DAS28 in the DMARD-treated group corresponded to disease remission values in 33 patients (89%), and in the group treated with biological therapy, the same remission rates of the disease were recorded in 49 patients (97.7%). The intima-medium thickness index in the DMARD-treated group decreased from the 6 month values. In patients with biological therapy, the reduction in the mid-thickness index recorded a progressive decrease from the previous assessment.



**Conclusions:** There is a direct correlation between the markers of inflammation and the evolution of carotid atheromatosis in patients with rheumatoid arthritis. The intima-medium thickness index is a paraclinical feature useful in assessing cardiovascular risk in patients with rheumatoid arthritis.

Biological therapy, by controlling the underlying disease, also improves cardiovascular prognosis. Treatment with anti-TNF-alpha makes good control, together with lipid-lowering and antihypertensive medication of associated cardiovascular pathology, in patients with rheumatoid arthritis.

**Disclosure of Interest:** None declared

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#### THU0108 PATIENT REPORTED OUTCOME MEASURES FOLLOWING KNEE AND HIP REPLACEMENT FOR INDIVIDUALS WITH RHEUMATOID ARTHRITIS: EVIDENCE FROM ROUTINELY-COLLECTED DATA

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**Background:** Most estimates of patient-reported outcome measures (PROMs) following total knee replacement (TKR) and total hip replacement (THR) are from individuals with osteoarthritis (OA). It is not well-known whether individuals with rheumatoid arthritis (RA) achieve similar results.

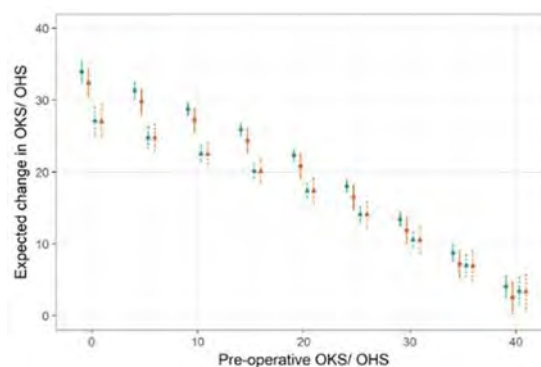
**Objectives:** To assess the association between RA, relative to OA, with 1) post-operative PROMs and 2) the change between pre- and post-operative PROMs for TKR and THR.

**Methods:** PROMs for TKR and THR between 2009 and 2015 identified using Hospital Episode Statistics (HES), with diagnosis of RA or OA identified in the Clinical Practice Research Datalink (CPRD). The condition-specific Oxford Knee Score/Oxford Hip Score (OKS/OHS), with pain and function subscales, and Euro-Qol 5-dimension (EQ-5D) overall quality of life were collected prior to and six months following surgery. OKS/OHS ranges from 0 to 48, OKS/OHS function from 0 to 20, OKS/OHS pain from 0 to 28, and EQ-5D from -0.5 to 1, with higher scores being better for each. The effect of RA, relative to OA, on post-operative PROMs was estimated using multivariable linear regressions, which adjusted for age, gender, comorbidities (measured by the Charlson score) and socioeconomic status (measured by IMD Quintile). The effect of RA, relative to OA, on change in PROMs was assessed by adding pre-operative scores as an explanatory factor in the models.

**Results:** 2212 (2,070 OA and 142 RA) and 2128 (2,030 OA and 98 RA) individuals informed the analyses of TKR and THR, respectively. A diagnosis of RA, relative to OA, was associated with a one-point lower post-operative OKS and a 3-point lower OHS, although only the latter difference was significant. These lower estimates of post-operative OKS/OHS were primarily due to significantly lower scores on the function subscales. The estimated change in OKS/OHS, after accounting for pre-operative scores, was similar for those with RA and OA. RA was also associated with a 0.1 lower post-operative EQ-5D, which was significant for both TKR and THR. The expected change in EQ-5D remained significantly lower for those with RA. The effect of diagnosis from the models is summarised in table 1, with estimated change in OKS/OHS shown in figure 1.

**Abstract THU0108 – Table 1.** Effect of RA, relative to OA, on 1) total post-operative scores and 2) change in scores. Estimated coefficients with 95% confidence intervals. Significant differences in bold.

	TKR		THR	
	Total	Change	Total	Change
OKS/OHS (0 to 48)	-1.33 (-2.92 to 0.27)	-0.07 (-1.59 to 1.46)	<b>-2.80 (-4.43 to -1.18)</b>	-1.57 (-3.15 to 0.01)
OKS/OHS function (0 to 20)	<b>-1.22 (-1.90 to -0.54)</b>	-0.50 (-1.13 to 0.14)	<b>-1.91 (-2.75 to -1.07)</b>	<b>-0.97 (-1.76 to -0.18)</b>
OKS/OHS pain (0 to 28)	-0.13 (-1.12 to 0.87)	0.34 (-0.63 to 1.30)	-0.89 (-1.80 to 0.02)	-0.66 (-1.56 to 0.25)
EQ-5D (-0.5 to 1)	<b>-0.12 (-0.16 to -0.08)</b>	<b>-0.09 (-0.13 to -0.06)</b>	<b>-0.12 (-0.17 to -0.08)</b>	<b>-0.08 (-0.13 to -0.04)</b>



**Abstract THU0108 – Figure 1.** Estimated effect of diagnosis on expected change in OKS/OHS by pre-operative score

**Conclusions:** Individuals with RA undergoing TKR and THR appear to achieve similar improvements in condition-specific scores as those with OA, although the gain in function may be slightly less. The gain in overall quality of life is less for those with RA, however, which is likely due to the systemic nature of the disease.

**Disclosure of Interest:** E. Burn: None declared, N. Arden Consultant for: Freshfields Bruckhaus Deringer, Bioventus, Flexion, Merck, and Regeneron, C. Edwards: None declared, C. Cooper: None declared, D. Murray Grant/research support from: Zimmer Biomet, Consultant for: Zimmer Biomet, R. Pinedo-Villanueva: None declared, D. Prieto-Alhambra Grant/research support from: Amgen, Servier and UCB Biopharma, and non-financial support from Amgen

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#### THU0109 AUTOANTIBODY PROFILING FOR RESPONSE TO BARICITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS AND NO OR LIMITED EXPOSURE TO METHOTREXATE

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**Background:** Posttranslational antigen modification plays a role in the pathogenesis of rheumatoid arthritis (RA). The associated autoantibodies are considered unfavourable prognostic factors with respect to disease severity and radiographic outcome. Limited information is available for different serotypes and prediction of treatment response to Janus kinase inhibitors including baricitinib (BARI).

**Objectives:** To clarify whether fine profiling of baseline autoantibodies against different modified isoforms of vimentin correlate with clinical or radiographic outcome in patients (pts) with active RA and no or limited prior DMARD treatment who initiate treatment with BARI.

**Methods:** Baseline sera samples from DMARD-naïve pts participating in the randomised, active comparator-controlled Ph3 trial RA-BEGIN<sup>1</sup> [methotrexate (MTX) n=210, BARI 4 mg (mono) n=159 and BARI 4-mg+MTX (combo) n=215] were investigated for autoantibody class (IgG, IgM and IgA) reactivity towards vimentin (V), modified by citrullination (MCV), carbamylation (Carb) or acetylation (Acct), using enzyme-linked immunosorbent assay. Pts were stratified according to negative (<20 U/ml), low-positive (20–60 U/ml) and high-positive (>60 U/ml, 3-fold above the ULN) antibody titre or with respect to the antibody titre tertiles. Change in clinical outcomes (DAS28-CRP, CDAI) and radiographic progression (modified Total Sharp Score) were analysed from baseline to Week 24 using modified last observation carried forward and linear extrapolation, respectively, by baseline autoantibody subclass and titre.

**Results:** Comparison of least squares mean difference in clinical scores showed more consistent improvement in pts treated with BARI combo vs MTX irrespective of baseline autoantibody subclass and titre. In general, pts with low-titre anti-CarbV, AcctV and MCV subclass antibodies showed numerically less improvement in most of the analyses under BARI mono vs MTX compared to BARI combo vs MTX although for anti-CarbV subclass seronegative pts, no significant differences were found in the clinical response between BARI mono vs MTX. Furthermore, anti-MCV IgA and IgM as well as anti-CarbV IgA negative status was also associated with significant reduction of radiographic progression in pts treated with BARI combo vs MTX. For seropositive pts, response to treatment with BARI mono or combination therapy was higher in pts with highest titres of anti-MCV and anti-CarbV. However, a significant difference with respect to radiographic progression was detectable only for BARI combo vs MTX. By stratifying pts according to their antibody profile, these observed radiographic differences were achieved in the anti-MCV and anti-CarbV IgG high-positive as well as anti-CarbV IgM low-positive pts.

**Conclusions:** In these exploratory analyses, seropositive pts with high titres of anti-MCV and anti-CarbV at baseline showed better responses to BARI mono or combo vs MTX for composite scores, and to BARI combo in structural progression outcomes.

#### REFERENCE:

[1] Fleischmann R, et al. *Arthritis Rheumatol* 2017;69(3):506–517.

**Disclosure of Interest:** L. Martinez Gamboa Grant/research support from: Eli Lilly and Company, H. Bang: None declared, M. Issa Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, S. Zuckerman Employee of: Former employee of Eli Lilly and Company, A. Cardoso Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, T. Holzkaemper Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, F. De Leonardi Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, I. de la Torre Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Y. Tanaka Grant/research support from: Mitsubishi-Tanabe, Takeda, Bristol-Myers, Chugai, Astellas, Abbvie, MSD, Daiichi-Sankyo, Pfizer, Kyowa- Kirin, Eisai, Ono, Speakers bureau: Daiichi-Sankyo, Astellas, Pfizer, Mitsubishi-Tanabe, Bristol-Myers, Chugai, YL Biologics, Eli Lilly and Company, Sanofi, Janssen, UCB, E. Feist Grant/research support from: Eli Lilly and Company, Novartis, Roche, BMS, Consultant for: Eli Lilly and Company, Novartis, Roche, Pfizer, Abbvie, BMS, MSD, Sanofi, Speakers bureau: Eli Lilly and Company, Novartis, Roche, Pfizer, Abbvie, BMS, MSD, Sanofi

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THU0110

#### EARLY TREATMENT AND LOW DOSE CORTICOSTEROIDS MIGHT DECREASE MORTALITY IN EARLY ARTHRITIS: RESULTS FROM THE RECORD LINKAGE OF CLINICAL AND ADMINISTRATIVE DATABASES

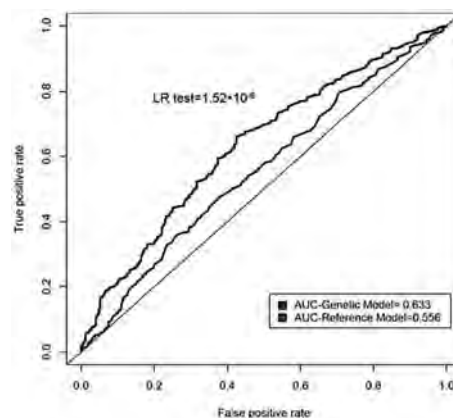
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**Background:** In patients with rheumatoid arthritis (RA) increased mortality, especially for cardiovascular (CV) events, is still described, despite the advances in RA management.

**Objectives:** To evaluate the impact of early diagnosis and treatment with disease modifying anti-rheumatic drugs (DMARDs) on mortality in patients with early RA and undifferentiated arthritis (UA) through record linkage between clinical and administrative databases.

**Methods:** Consecutive patients with RA or UA from an early arthritis clinic (2005–2016), treated with tight control to achieve DAS28 <3.2, were included. Health assessment Questionnaire (HAQ) and date of symptom onset were recorded at baseline. Data on mortality, cause of death and drug prescription derived from administrative healthcare databases, linked to the clinical database. Cox regression models were used to evaluate the impact of the interval from symptom onset to diagnosis (categorised <3 months, 3–6 months, >6 months), from diagnosis to treatment (<3 months, >3 months, never) and from onset to treatment (<3 months, 3–6 months, >6 months, never) on overall mortality. Analyses were adjusted for age, gender, ACPA positivity, Charlson comorbidity index, HAQ and median daily prednisone dose. Results were presented as hazard ratios (HR) with 95% CI. Secondary analyses categorising prednisone in low dose (≤5 mg/day) or medium-high dose (>5 mg/day) were performed, as well as analyses evaluating CV mortality as outcome. Moreover, analyses excluding patients not receiving DMARDs and patients dying in the first year of observation were conducted.

**Results:** A total of 857 patients (62% RA, 73% female, median (IQR) age 59,<sup>47–71</sup> mean (sd) baseline DAS28 3.08 (0.97)) were included. After a median (IQR) follow-up of 80<sup>51–109</sup> months, 77 patients died (2 in the first year); of the 41 patients with known cause of death, 9 were for CV causes. An interval >3 months between diagnosis and introduction of DMARDs or never introducing DMARDs related to higher mortality (table 1). The mean daily prednisone dose was not a significant predictor of mortality, while in all secondary analyses patients receiving low-dose prednisone, compared to those never receiving corticosteroids, had a lower mortality (eg. HR (95% CI) 0.45 (0.26,0.78) in the model including time between symptom onset and diagnosis). Patients not starting DMARDs, compared to these starting within 3 months from diagnosis, had a higher CV mortality, while the intervals between onset and diagnosis and onset and treatment were not significant predictors. Analyses limited to patients receiving DMARDs and with the exclusion of patients dying in the first year yielded to similar results.



**Conclusions:** In patients with early RA and UA treatment delay significantly increases mortality, while low-dose corticosteroids seem to decrease mortality. These results support strategies aiming at early access to treatment and the use of low dose corticosteroids in the initial treatment strategy.

**Disclosure of Interest:** None declared

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THU0111

#### FREQUENCY AND PREDICTORS OF SUSTAINED REMISSION IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS TREATED WITH CONVENTIONAL SYNTHETIC DISEASE MODIFYING DRUGS

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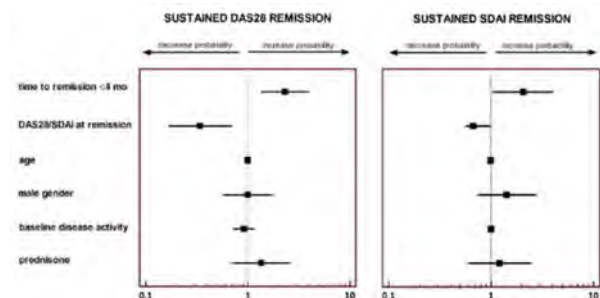
**Background:** The management of patients with early rheumatoid arthritis (RA) should be aimed at reaching the target of disease remission as soon as possible. In order to prevent joint damage and disability, and eventually allow treatment withdrawal, the state of disease remission should be also maintained. Whilst point remission is frequently achieved in early RA, the sustainability of remission in clinical practice remains poorly investigated.

**Objectives:** To investigate the prevalence and predictors of sustained remission in patients with early RA treated with conventional synthetic disease anti-rheumatic drugs (csDMARDs).

**Methods:** We evaluated 533 RA patients from the Pavia early arthritis inception cohort not in remission at baseline with at least 24 months of follow-up. Patients had arthritis of short duration (<12 months of symptoms) and were treatment-naïve at presentation. After diagnosis, patients were initiated a treat-to-target regimen with methotrexate aiming at low disease activity according to the 28-joint disease activity score (DAS28 ≤3.2), and were seen at regular intervals (2 months in the first 6 months, then trimestraly). Point remission was defined as the achievement of DAS28 remission (<2.6) or SDAI (simplified disease activity index) remission (≤3.3) at any time point within the first 12 months. Sustained remission was defined as mean DAS28 <2.6 and mean SDAI ≤3.3 in the 3 visits following first remission. The frequency and predictors of point remission and sustained remission were analysed by Cox and binary regression respectively.

**Results:** 287/533 (53.9%) patients achieved point DAS28 remission and 234/533 (43.9%) point SDAI remission. Independent predictors of point DAS28 remission were male gender (HR [95% CI] 1.84 [1.36–2.50]), shorter symptoms' duration (HR [95% CI] 0.99 [0.98–0.99]), a lower tender joint count at baseline (HR [95% CI] 0.97 [0.94–0.99]), better functional status (HR [95% CI]

0.74 [0.59–0.94]), absence of radiographic erosions (HR [95% CI] 1.52 [1.06–2.20]) and use of prednisone (HR [95% CI] 1.51 [1.36–1.74]). The same predictors were confirmed for point SDAI remission. Irrespective of the criterion, remission was maintained by only half of the patients at follow-up, resulting in sustained remission rates of 28% for DAS28 and 19% for SDAI in the entire cohort. At multivariate analysis, independent predictors of sustained remission according to either the DAS28 or the SDAI were lower time to achieve remission and deeper remission, whilst demographic factors, baseline disease activity and use of prednisone were not significant (figure 1). Using ROC curve analysis, the best discriminative ability for sustained remission were time to remission  $\leq 4$  months, DAS28 at remission  $\leq 2.2$  and SDAI at remission  $\leq 1$ .



**Conclusions:** Despite early diagnosis and prompt institution of goal-steered treatment strategies with csDMARDs, only a minority of RA patients experience sustained remission. Remission is more likely to be maintained if the target is attained rapidly after treatment institution and if joint and systemic inflammation are effectively suppressed.

**Disclosure of Interest:** None declared

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#### THU0112 THE INFLUENCE OF AGE AND SEX ON THE PROGRESSION OF RHEUMATOID ARTHRITIS

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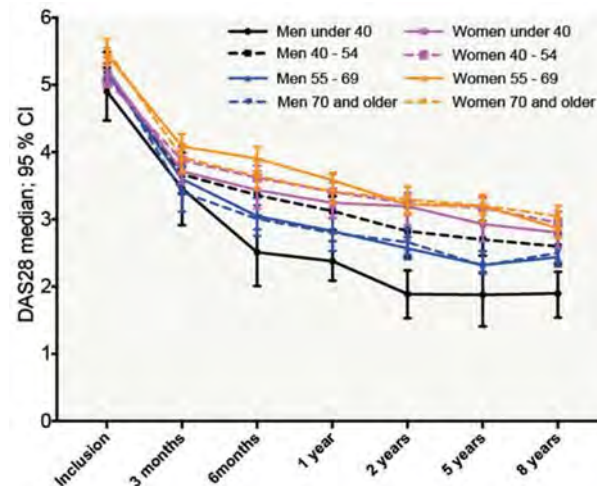
**Background:** In Europe, life expectancy is increasing and so does the incidence rheumatoid arthritis (RA), which peaks for both men and women at 70–79 years of age. Further, more than 50% of patients with RA are >65 years of age. To correctly treat and handle all patients with RA irrespective of age there is a need to study the outcome and progression of the disease depending on age of onset as this, to our knowledge, is largely unknown.

**Objectives:** To study how age at onset of RA influence the course of disease in men and women.

**Methods:** This study included 2825 patients, 68% females, from the BARFOT (Better Anti-Rheumatic Pharmacotherapy) early RA cohort. Patients were divided into males and females and into the following age groups: <40 years (yr) n=415, 40–54 year n=658, 55–69 year n=986 and  $\geq 70$  year n=766 at onset of disease and inclusion in the study. They were assessed at 3, 6 months and 1, 2, 5, 8 years. The following parameters were analysed: DAS28 (disease activity), VAS pain, VAS global health, 28 joint count of tender and swollen joints, respectively, ESR, rheumatoid factor (RF), antibodies to citrullinated proteins (APCA) and Health Assessment Questionnaire (HAQ). The median and 95% bootstrap confidence interval were calculated in MATLAB R2015a using the bias corrected and accelerated percentile method with 2000 bootstrap samples. Mann-Whitney U-test and Wilcoxon Rank test were used to compare groups,  $p < 0.01$  was considered as significant due to multiple comparisons.

**Results:** At inclusion, there were no significant differences in DAS28, VAS global health, VAS pain or tender and swollen joint counts in any of the groups. From 3 months and onward, the DAS28 score were significantly lower for men compared to women in the age groups <40 year, 55–69 year and  $\geq 70$  year, whereas in the age group 40–54 year there were no significant differences between the sex groups (figure 1). The lowest DAS28 score, at each assessment point, was seen for RF and ACPA positive men <40 year and this group had a significantly lower DAS28 score at 8 years compared to all other groups except RF and ACPA negative men and women  $\geq 70$  year. At the same time, the worst outcome was seen for RF positive women and for men  $\geq 70$  year irrespective of RF, compared to all other groups.

In the age groups <40 year, 55–69 year and  $\geq 70$  year, both VAS pain and VAS global health were significantly lower in men compared to women from 3–6 month and onward. However, no differences were obtained between the sexes in the age group 40–54 year. As expected, HAQ was significantly higher among women than men in all age groups.



**Conclusions:** Depending on age at onset, the course of disease, measured as DAS28, differs significantly where seropositive men <40 year have the most favourable prognosis compared to both men and women  $\geq 70$  year the worst. No differences in DAS28, VAS global health or pain was found between men and women aged 40–54 year, which is in contrast to previous studies<sup>1</sup> comparing men and women without considering the age of onset. The causes for these findings need to be further investigated.

#### REFERENCE:

- [1] Patients with Early Rheumatoid Arthritis in the 2000s Have Equal Disability and Pain Despite Less Disease Activity Compared with the 1990s: Data from the BARFOT Study over 8 Years. *J Rheumatol* 2017 Jun;44(6):723–731.

**Disclosure of Interest:** None declared

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#### THU0113 LINKING SYSTEMIC ANGIOGENIC MARKERS TO SYNOVIAL VASCULARISATION IN RHEUMATOID ARTHRITIS

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**Background:** Neoangiogenesis is a crucial event to promote the development of the hyperplastic proliferative pathologic synovium in Rheumatoid arthritis (RA). Ultrasound (US) is sensitive for detection of power Doppler (PD) vascularisation.

**Objectives:** To explore the associations between a set of complementary circulating angiogenic markers reflecting different angiogenic processes and a comprehensive US assessment in patients with RA.

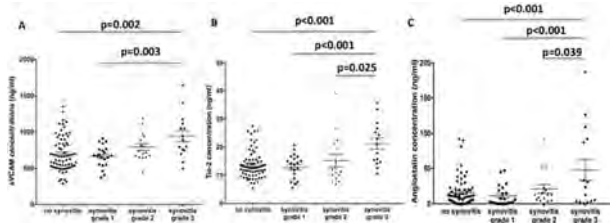
**Methods:** Serum levels of eight angiogenic markers (Vascular Endothelial Growth Factor (VEGF), Placenta Growth Factor (PlGF), Tie-2, Angiopoietin-1, soluble Vascular Cell Adhesion Molecule-1 (sVCAM-1), Interleukin-8 (IL-8, CXCL8), CYR61 (CCN1) and Angiostatin), reflecting endothelial cell activation, proliferation, survival, growth and migration, as well as vessel maturation and stabilisation, were measured by quantitative ELISAs in a total of 125 patients with RA, who were all systematically assessed in parallel by PDUS, performed on 32 joints.

**Results:** Synovitis was detected in 84 patients with RA (67.2%). Among these patients, 53 patients (42.4%) had positive Doppler signal, including 31 with moderate to marked hyperemia. Serum levels of soluble Vascular Cell Adhesion Molecule-1 (sVCAM-1) ( $808 \pm 293$  ng/mL vs.  $697 \pm 240$  ng/mL,  $p = 0.022$ ) and Tie-2 ( $16.2 \pm 7.5$  ng/mL vs.  $13.8 \pm 4.9$  ng/mL,  $p = 0.038$ ), were more likely to be increased in patients with synovial hyperemia detected on at least one joint (Power Doppler grade  $\geq 1$ ). sVCAM-1, Tie-2 and Angiostatin concentrations gradually increased together with the grade of the semiquantitative PDUS scale (figure 1A-C) and concentrations of these three markers were markedly increased in patients with



moderate to marked hyperemia (Power Doppler grade 2 and 3). Levels of sVCAM-1 ( $r=0.20$ ,  $p=0.028$ ), Tie-2 ( $r=0.28$ ,  $p=0.001$ ), and Angiostatin ( $r=0.25$ ,  $p=0.006$ ) correlated with a global arthritis sum score, defined by the sum of the semiquantitative PDUS scores for all joints examined.

Among the 81 patients with a DAS28-CRP $\leq 3.2$ , 22 patients had synovial hyperemia detected on at least one joint (Power Doppler grade 1 in 13 patients, grade 2 in 6 patients and grade 3 in 3 patients). Patients with synovial hyperemia on at least one joint were more likely to have significantly increased levels of PIGF ( $18.9 \pm 11.2$  pg/mL vs.  $13.1 \pm 9.5$  pg/mL,  $p=0.022$ ) and Tie-2 ( $15.7 \pm 5.8$  ng/mL vs.  $12.6 \pm 3.4$  ng/mL,  $p=0.004$ ) than patients with absence of synovial hyperemia.



**Conclusions:** Serum levels of the angiogenic markers Tie-2, sVCAM-1 and Angiostatin were strongly associated with synovial vascularisation and inflammation assessed by PDUS among patients with established RA. Moreover, Tie-2 and PIGF were associated with persistent disease activity in RA patients in low disease activity. These findings suggest that it may be possible to find surrogate serum angiogenic biomarkers of active synovitis that might replace PDUS examination, in case of further confirmation of their pertinence.

**Disclosure of Interest:** A. Leblond: None declared, S. Pezet: None declared, A. P. Trouvin: None declared, M. Elhai: None declared, V. Gonzalez: None declared, Y. Allanore: Grant/research support from: Pfizer, J. Avouac: None declared  
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**THU0114 INFLUENCE OF AUTOANTIBODY STATUS IN TIME TO INITIATE DMARDS IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS**

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**Background:** Factors contributing to an early referral to Rheumatologist and DMARDs initiation following symptom onset in rheumatoid arthritis (RA) patients are unclear. Recent data suggest that ACPA/RF double seropositivity is associated with delayed presentation to primary care and DMARDs initiation. Identification of these factors is mandatory to facilitate an early diagnosis and treatment of RA patients.

**Objectives:** To determine whether time to DMARDs initiation and time to first visit at early arthritis clinic (EAC) following symptoms onset differs between RA patients according to autoantibody status.

**Methods:** A prospective analysis of an EAC cohort including 1377 referred patients from 1993 to 2017 was undertaken for this study. Patients diagnosed of RA (according to physician's diagnosis) were selected. Based on the serological status, we classified patients in 4 groups: RF+/ACPA+, RF-/ACPA+, RF+/ACPA-, RF-/ACPA-. A baseline clinical assessment was completed including time (months) from symptoms onset to first assessment at EAC and to DMARD initiation. First, differences between serotypes were tested using chi-squared and student-t tests. Second, univariable and multivariable logistic regression models taking into account confounding factors (age, smoking and baseline DAS28) were employed to evaluate the association between autoantibody status and both periods: time to first visit at EAC and to DMARDs initiation.

**Results:** A total of 463 RA patients were included for analysis, of whom 292 (63.1%) were RF/ACPA double-seropositive (RF+/ACPA+), 35 (7.6%) RF-/ACPA+, 39 (8.4%) RF+/ACPA- and 92 (19.9%) RF-/ACPA-. Demographic and clinical data are shown in table 1. In the univariate analysis, statistically significant differences were observed for both periods when patients were stratified by autoantibody serotype, where RF+/ACPA+ individuals experienced the longer delay to presentation at EAC compared with RF-/ACPA- ( $5.0 \pm 4.6$  vs  $3.5 \pm 3.4$  months;  $p < 0.05$ ). RF+/ACPA+ patients experienced also significantly longer symptom duration before DMARD initiation than RF-/ACPA- ( $7.4 \pm 11.2$  vs  $4.9 \pm 5$  months;  $p < 0.05$ ). In the univariable analysis, autoantibody status (double seropositive and RF-/ACPA+ vs RF-/ACPA-) was significantly associated with time to DMARDs initiation. However, after adjusting by confounding factors in the multivariable analysis, the autoantibody status did not remain significantly associated with time to initiate DMARDs (RF+/ACPA-;  $\beta$  0.186;  $p=0.1$ , RF-/ACPA+;  $\beta$  0.112;  $p=0.3$ , RF+/ACPA+;  $\beta$  0.228;  $p=0.1$ )

	Beta	95% C.I.	
		Lower	Upper
<b>Non adjusted</b>			
RF positive	.035	-2,462	4944
ACPA positive	.104	.038	7736
Double-seropositive	.120	.157	4791
<b>Adjusted</b>			
RF positive	.186	-4,952	26 414
ACPA positive	.112	-14,512	37 175
Double-seropositive	.228	-2,520	20 308
DAS 28	-.239	-7,575	.144
Age	-.073	-.384	.207
Smoker	-.066	-14,996	9118
Former smoker	-.081	-19,051	10 942

**Abstract THU0114 – Table 1.** Baseline characteristics of patients, stratified by autoantibody status

	Total n= 463	RF+/ACPA+ n=292	RF-/ACPA+ n=35	RF+/ACPA- n=39	RF-/ACPA- n=92	p
<b>Age</b>	58.3(10.5)	59.0(9.2)	47.0(14.1)	60.2(10.9)	57.0(11.0)	<0.001
<b>Sex</b>	1224(26.7%)	79(22.7%)	3(12.8%)	14(11.8%)	26(24.3%)	>0.5
<b>Race</b>	594(21.2%)	198(64.3%)	11(33.8%)	14(77.7%)	31(33.2%)	<0.001
<b>Smoking</b>	118(23.3%)	74(24.7%)	7(16.9%)	12(27.3%)	16(16.8%)	<0.001
<b>Smoker</b>	108(21.3%)	85(26.9%)	3(24.9%)	7(15.9%)	9(9.5%)	<0.001
<b>Never smoker</b>	226(45.1%)	142(46.1%)	11(31.9%)	14(31.5%)	21(22.2%)	<0.001
<b>Systemic</b>	40(16.4%)	29(9.4%)	2(7.4%)	4(9.7%)	10(10.7%)	<0.001
<b>Arteriosclerotic</b>	16(4.3%)	6(1.9%)	1(2.7%)	2(4.9%)	1(1.0%)	<0.001
<b>Diabetes</b>	8(1.5%)	4(1.3%)	0(0.0%)	0(0.0%)	0(0.0%)	<0.001
<b>Cardiovascular</b>	3(0.5%)	2(0.6%)	0(0.0%)	0(0.0%)	0(0.0%)	<0.001
<b>Polycystic ovary syndrome</b>	4(0.8%)	3(0.9%)	0(0.0%)	0(0.0%)	0(0.0%)	<0.001
<b>Hypertension</b>	1(0.2%)	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)	<0.001
<b>Time (months) from symptoms onset to DMARD initiation</b>	6.0±5.8	7.4±11.2	6.0±9.6	6.2±7.2	4.9±5	<b>0.005</b>
<b>Time (months) from presentation at EAC to DMARD initiation</b>	2.0±1.1	2.3±1.0	2.3±0.5	2.0±1.0	1.8±1.0	<b>0.7</b>
<b>Time (months) from symptoms onset to presentation at EAC</b>	4.7±4.4	5±6	6.6±4.9	4.3±3.7	3.5±3.4	<b>0.019</b>
<b>Pharmacological Assessment</b>	31,7(26.2)	10,6(26.1)	5(14.9%)	31,2(27.8)	34,9(23.3)	<b>NS</b>
<b>Phases Global Assessment (0-100)</b>	33,6(23.8)	38,5(23.7)	34,2(23.7)	35,6(25.3)	34,6(24.4)	<b>NS</b>
<b>HAQ</b>	0.8±0.7	0.9±0.7	0.6±0.2	0.8±0.6	0.7±0.5	<0.005
<b>33 Tendons Joint Count</b>	3.6±6.5	4±6.2	5.1±5.7	16.7±7.5	9.4±6.7	<0.001
<b>33 Swollen Joint Count</b>	6.1±6.2	8.1±5.1	4±3.8	8±6.2	6±6.6	<0.001
<b>DAS 28</b>	5.2±1.6	5.2±1.42	4.5±1.33	5.7±1.3	5.0±1.3	<0.001
<b>ESR (mm/h)</b>	36.1±24.3	37.8±26.1	25.7±21	40.3±31.2	32.6±26.2	<0.001

**Conclusions:** In our EAC cohort, time to EAC presentation and DMARD initiation following symptom onset in early RA does not differ according to patients' autoantibody status. However, more studies with greater sample size are necessary to confirm these results.

**Disclosure of Interest:** None declared  
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**THU0115 PSYCHOLOGICAL AND FUNCTIONAL STATES PREDICT DISEASE FLARE FOLLOWING TNF INHIBITOR TAPERING IN PATIENTS WITH RHEUMATOID ARTHRITIS: A POST-HOC ANALYSIS OF DATA FROM THE OPTIMISING TNF TAPERING IN RA (OPTTIRA) COHORT**

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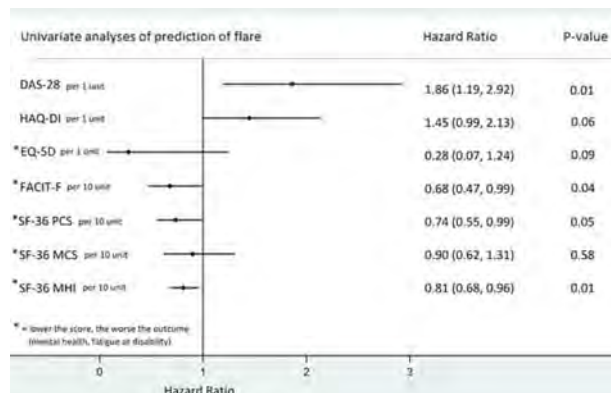
**Background:** Tapering or discontinuation of anti-TNF therapy appears to be feasible, safe and effective in a selected proportion of Rheumatoid Arthritis (RA) patients. Depression is highly prevalent in RA and may impact on flare incidence through a number of mechanisms. It is an independent predictor for flare in patients with active disease and is negatively associated with remission.<sup>1</sup> To date, there are no studies directly addressing the role of depression, anxiety or low mood in predicting flares in patients tapering their biological therapy.

**Objectives:** To investigate if psychological and functional states predict flare in RA patients with low disease activity (LDA) or in remission who undergo treatment tapering of their anti-TNF agents.

**Methods:** This study is a post-hoc analysis of the OPTTIRA trial,<sup>2</sup> a multi-centre, prospective, randomised, open label study investigating anti-TNF tapering in established RA patients in sustained LDA. Baseline patient-reported outcomes including HAQ-DI, EQ-5D, FACIT-F, and SF-36 including the Mental Health Index (MHI) component were collected. The MHI has been validated as a screening tool for depression in RA patients.<sup>3</sup> The primary outcome was flare, defined as an increase in DAS28  $\geq 0.6$ , and at least one additional swollen joint. Logistic regression was used to identify patient-reported outcomes that predict flare, adjusting for baseline covariates (age, gender, treatment arm, DAS28 and BMI).

**Results:** 97 were randomised into a tapering arm, either by 33% or 66% of their anti-TNF dose. The majority of patients were on methotrexate in combination with their anti-TNF therapy (n=67, 69%) and the median disease duration was 11 years [IQR: 7–17]. Seventy three (75%) fulfilled DAS28 remission criteria (DAS28 < 2.6). The median SF36 MHI score was 84. A score of  $\leq 56$ , the cut off used to detect depression was observed in 11% of patients. Forty one patients (42%) flared. Baseline DAS28 score was associated with flare, remaining significant after

adjusting for covariates [HR 1.96 (95% CI: 1.18, 3.24)  $p=0.01$ ]. Disability (SF-36 physical component), fatigue (FACIT-F) and mental health (SF-36 MHI) predicted flare in univariate models (figure 1). In multivariate analyses, only MHI score remained a statistically significant independent predictor of flare [HR per 10 units 0.74 (95% CI: 0.60, 0.93)  $p=0.01$ ].



**Conclusions:** Baseline DAS28 and mental health predict flare events in patients in LDA who taper their anti-TNF agents. Other psychological and functional states, measured by patient-reported outcome do predict flare events although the effect size is small and does not persist when adjusting for known predictors. Based on these findings, an assessment of functional and mental health states should be considered prior to biologic tapering.

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**Disclosure of Interest:** None declared

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#### THU0116 LIPID PROFILE AND CARDIOVASCULAR RISK IN SUBJECTS AT RISK FOR DEVELOPING RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is a systemic inflammatory autoimmune disease associated with an increased cardiovascular (CV) risk that is already present at the time of diagnosis. However, it is unclear at what point in the period before diagnosis of RA the CV risk increases. Therefore, we assessed the 10 year risk of CV morbidity and mortality in a cohort of subjects at risk for RA and analysed associations with anti-citrullinated protein antibody (ACPA) status and arthritis development.

**Methods:** In a cohort of 594 consecutive arthralgia patients with positivity for rheumatoid factor (RF) and/or ACPA, demographics, medical history, medication use and comorbidities were assessed. Lipid profile was determined and blood pressure was measured in a subset of patients. The 10 year CV risk score according to the Dutch CV risk management guideline (Dutch Systematic Coronary Risk Evaluations (SCORE)) was calculated for patients of whom data were complete.

**Results:** ACPA positive subjects ( $n=382$ ) were younger (mean age 48.6 vs 51.6,  $p=0.003$ ), more often smokers (31.8% vs 23.9%,  $p=0.045$ ) and had lower cholesterol (mean level 5.2 vs 5.5,  $p=0.001$ ) and HDL (mean level 1.1 vs 1.2,  $p=0.004$ ) than ACPA negative subjects. Subjects who developed arthritis ( $n=205$ ) had lower cholesterol (mean level 5.2 vs 5.4,  $p=0.008$ ) and HDL levels (mean level 1.0 vs 1.2,  $p=0.001$ ) and a higher TC/HDL ratio (median ratio 5.2 vs 4.8,  $p=0.047$ ) compared to subjects who did not develop arthritis. Lower cholesterol (OR 1.24, CI 1.04–1.48), lower HDL (OR 2.01, CI 1.29–3.13) and higher TC/HDL ratio (OR 1.07, CI 1.000–1.138) predicted arthritis development.

The Dutch SCORE was calculated in 177 subjects (median 2, IQR 1–9). 76.4% had a low risk (SCORE <10%), 12.5% a medium risk (SCORE 10–<20%) and 11.4% had a high 10 year risk (SCORE >20%) of cardiovascular morbidity and mortality. The score was not associated with ACPA status or arthritis development.

**Conclusions:** Dyslipidemia as known in RA patients with active disease was also present in seropositive arthralgia patients at risk for RA, and predicted development of RA. However, arthralgia subjects who developed arthritis did not have a higher CV risk score than those who did not develop arthritis. Also, despite differences in lipid profile and smoking, the CV risk score does not differ between ACPA positive and ACPA negative subjects at risk for RA. Overall, differences in lipid profile predicted development of RA but were too small to have an effect on the 10 year risk of CV morbidity and mortality as calculated by the Dutch CV risk score.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.3936

#### THU0117 CHEMOKINE CCL18 ENRICHED IN SYNOVIAL FLUID IS INVOLVED IN JOINT DESTRUCTION THROUGH PROMOTING MIGRATION OF FIBROBLAST-LIKE SYNOVIOCYTES IN RHEUMATOID ARTHRITIS

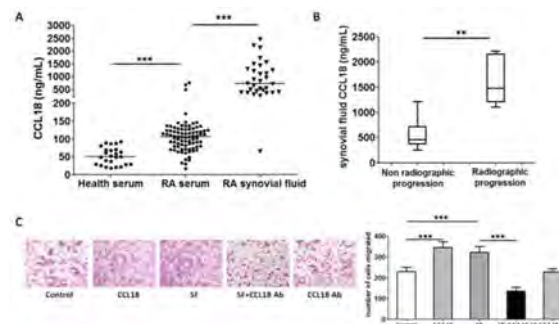
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**Background:** CC chemokine ligand 18 (CCL18) which is either constitutively expressed or induced in monocytes/macrophages and dendritic cells has been reported to be highly expressed in peripheral blood and synovial fluid of rheumatoid arthritis (RA) patients compared with healthy controls, indicating the possible role of CCL18 in the development and pathogenesis of RA.

**Objectives:** To explore the association of serum and synovial fluid CCL18 with clinical and radiographic outcome in RA patients and its potential effect on RA fibroblast-like synoviocytes (FLS).

**Methods:** Consecutive patients with active RA (DAS28-CRP>2.6) were recruited. Synovial fluid was collected from inflamed joints if available. Demographic and clinical data were collected according to the 2017 EULAR recommendation. Serum and synovial fluid CCL18 was detected by ELISA. RA-FLS was cultured *in vitro* with RA synovial fluid and neutralising antibody to CCL18. Migration/invasion ability was analysed by Transwell assay.

**Results:** (1) Among 83 RA patients, age (median and IQR, similarly hereinafter) was 50 (41~58) years old and 65 patients (78%) were female, with median disease duration 36 (12~102) months, median DAS28-CRP 5.0 (4.6~6.1). (2) Serum CCL18 was 107 (80~126) ng/mL, which was significantly higher than healthy controls [ $n=25$ , 51 (29~70) ng/mL,  $p<0.001$ , figure 1A]. Serum CCL18 correlated slightly but significantly with CRP ( $r=0.385$ ,  $p<0.001$ ), ESR ( $r=0.239$ ,  $p=0.03$ ), PrGA ( $r=0.249$ ,  $p=0.03$ ), DAS28-CRP ( $r=0.368$ ,  $p=0.001$ ), DAS28-ESR ( $r=0.336$ ,  $p=0.003$ ), SDAI ( $r=0.360$ ,  $p=0.001$ ), CDAI ( $r=0.328$ ,  $p=0.004$ ) and HAQ ( $r=0.325$ ,  $p=0.004$ ). (3) Synovial fluid CCL18 of 31 patients was 719 (415~1271) ng/mL, which was significantly higher than corresponding serum level (Paired test,  $p<0.001$ , figure 1A). Among them, 13 patients who were treated according to treat to target strategy received X-ray assessment of hand/wrist both at baseline and month 12. Six patients who had one-year radiographic progression (a change of the Sharp/van der Heijde modified sharp score  $\geq 0.5$  units) showed higher synovial fluid CCL18 than other 7 patients without radiographic progression [1481 (1244~2034) ng/mL vs. 458 (405~681) ng/mL,  $p=0.004$ , figure 1B). (4) When incubated with RA synovial fluid, the migration ability of RA-FLS was significantly increased; but this effect was inhibited by neutralising antibody to CCL18 (figure 1C).



**Abstract THU0117 – Figure 1.** Chemokine CCL18 which was enriched in RA synovial fluid promoted migration of fibroblast-like synoviocytes in Rheumatoid Arthritis (RA), but was inhibited by neutralising antibody to CCL18. A: Comparison of RA synovial fluid CCL18 with serum CCL18 of RA patients and health controls. B: Comparison of RA synovial fluid CCL18 between patients with and without one-year radiographic progression. C: Transwell assay, crystal violet staining for RA-FLS (purple), with original magnification of  $\times 100$ .

\*\* $p<0.001$ , \*\*\* $p<0.0001$

**Conclusions:** CCL18 elevates especially in synovial fluid of RA patients, which may correlate with one-year radiographic progression through promoting migration of RA-FLS.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.6704

THU0118

### PATIENT-AND PHYSICIAN-REPORTED BARRIERS TO ACHIEVING RHEUMATOID ARTHRITIS (RA) DISEASE CONTROL

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**Background:** Many patients with RA do not achieve guideline-recommended treat-to-target (T2T) goals in clinical practice. Little is known about the challenges that patients and rheumatologists face when attempting to achieve better control of RA disease activity.

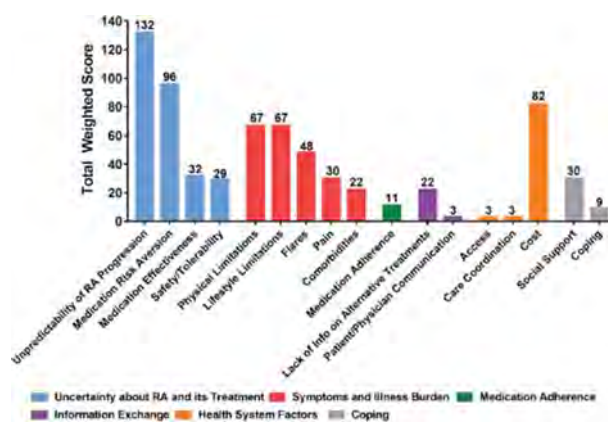
**Objectives:** To identify and prioritise patient- and rheumatologist-perceived barriers to achieving RA disease activity control.

**Methods:** Participants were recruited from the Consortium of Rheumatology Researchers of North America (Corrona) registry and invited to participate in nominal groups (NGs), 4 with patients and 3 with rheumatologists. Each group generated a list of barriers to reaching RA disease control (patients) and T2T goals (rheumatologists). Two separate lists containing the generated items were created and were subjected to a card sort procedure to create common themes. A random sample of Corrona RA patients were invited by email to complete a compensated online survey and asked to rank their top 3 barriers. A weighted score was assigned for each barrier by considering the number of respondents who ranked it and the priority rank they assigned. The barriers/themes were sorted into domains. The patient survey also included knowledge items about T2T strategy and attitudes about RA treatment.

**Results:** Nominal groups with 37 RA patients identified 17 themes to achieving control of RA activity. Similarly, 8 themes emerged from the physician NGs, 7 of which were also found in the patient NGs (table 1). Cost of RA care was ranked highest by both patients and physicians, while medication risk aversion ranked second and third among the physician- and patient-generated barriers, respectively. We sent 1694 invitations to complete the survey and 450 patients with RA for whom clinical data was available responded within 3 weeks. There were no differences in age, sex, or disease duration between survey-respondents and non-respondents. A higher proportion of respondents were college-educated. A total of 344 (77%) respondents considered RA to be a high priority for their health, 225 (51%) reported being familiar with T2T as a treatment strategy, and 312 (85%) displayed core beliefs favouring medications. Among the challenges to controlling RA disease activity, the domain that received the highest score was unpredictability of RA and its treatment (figure 1). Symptoms and illness burden domain received the second highest score, followed by the health system factors domain (figure 1).

**Abstract THU0118 – Table 1.** Common Patient- and Physician- Reported Barriers to Achieving RA Control Identified by Nominal Groups (NGs)

Barriers (Themes)	Proportion of Total Votes	
	Patient NGs	Physician NGs
Cost/Administrative	13.0%	27.0%
Medication Effectiveness	7.4%	3.0%
Medical Risk Aversion	6.5%	20.0%
Access to Care	4.6%	8.0%
Medication Adherence	1.9%	9.0%
Patient-Physician Communication	1.9%	12.0%
Education	0.9%	5% (Physician)



**Figure 1.** Patient-prioritised Barriers to Achieving RA Control in Corrona Registry

**Conclusions:** There are common patient- and physician-perceived barriers to achieving RA disease control. From the patient perspective important barriers are unpredictability of how RA may progress, medication risk aversion and cost of RA care. Addressing these barriers, when possible, may improve goal-directed RA care.

**Acknowledgements:** Pfizer IGLC, Corrona

**Disclosure of Interest:** None declared

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THU0119

### SMOKING IS NEGATIVELY ASSOCIATED WITH CLINICAL RESPONSE TO CONCOMITANT PREDNISONE USE IN EARLY RHEUMATOID ARTHRITIS

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**Background:** Smoking and overweight increase the risk of development of rheumatoid arthritis (RA) and have been associated with a reduced clinical response to several biological disease modifying anti-rheumatic drugs (bDMARDs) and methotrexate (MTX).<sup>1-6</sup> The effect of smoking and overweight on clinical response to prednisone (pred) has not been investigated

**Objectives:** To determine whether smoking and overweight are negatively associated with clinical response to pred in RA, as assessed by the disease activity score using 28 joints (DAS28). Second, to similarly determine the effect of smoking and overweight on the four individual components of DAS28.

**Methods:** In the second Computer Assisted Management in Early Rheumatoid Arthritis trial (CAMERA-II), patients with early, DMARD naïve RA were randomised to an MTX based treatment strategy with addition of 10 mg pred or placebo daily for 2 years. We used data from the patients concomitantly treated with pred, n=127. We performed linear mixed model analyses with DAS28 over the 2 year trial period as outcome variable and smoking status (current yes/no) and BMI (in mg/kg<sup>2</sup>) as predictor variables, corrected for baseline DAS28, gender, rheumatoid factor (RF-test negative or positive), MTX administration route (subcutaneous or oral), MTX dosage (mg/week) and bDMARD use (yes/no), time (in months) and time<sup>2</sup>. For the second aim, we performed an extended mixed model analysis with a multivariate outcome, consisting of the individual components of the DAS28 (tender joint count 28, swollen joint count 28, erythrocyte sedimentation rate and VAS general health) and as predictor variables smoking status and BMI, correcting for important confounders.

**Results:** Smoking data was available of 104/127 patients. Smoking was significantly associated with higher DAS28 over time, corrected for baseline DAS28, compared to non-smoking (table 1). No significant associations were found between BMI and response to pred, nor between smoking or BMI and any of the individual components of DAS28.

Table 1 The association between smoking and DAS28 in patients treated with concomitant prednisone for 2 years



Parameter	Estimate (95% CI)	P-value
Smoking (vs non-smoking)	0.60 (0.19 to 1.00)	0.01
Subcutaneous MTX administration route (vs oral)	-0.17 (-0.40 to 0.05)	0.13
MTX dose (mg/week)	-0.01 (-0.02 to -0.00)	0.00
bDMARD use (vs no bDMARD use)	0.45 (0.19 to 0.70)	0.00
DAS28 at baseline	0.36 (0.22 to 0.50)	0.00
Time	-0.25 (-0.27 to -0.23)	0.00
Time <sup>2</sup>	0.01 (0.01 to 0.01)	0.00
BMI (mg/kg <sup>2</sup> )	0.03 (-0.02 to 0.07)	0.26
Female gender (vs male)	-0.48 (-0.86 to -0.10)	0.02
Negative RF test status (vs positive)	-0.22 (-0.60 to -0.16)	0.25

Outcome measure: DAS28 over 2 years; CI: confidence interval; MTX: methotrexate; bDMARD: biological disease modifying anti-rheumatic drug; BMI: body mass index; RF: rheumatoid factor. A positive estimate reflects a higher DAS28 over time, corrected for baseline DAS28, and thus a lesser effect of the concomitant prednisone therapy

**Conclusions:** To our knowledge, this is the first time that smoking is shown to be a negative predictor for clinical response to pred in RA patients. Cessation of smoking needs to be encouraged in patients initiating bDMARDs, MTX and pred and in those already on these drugs

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#### THU0120 VITAMIN D IN INDIVIDUALS BEFORE ONSET OF RHEUMATOID ARTHRITIS – RELATION TO VITAMIN D BINDING PROTEIN AND ITS ASSOCIATED GENETIC VARIANTS

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**Background:** Vitamin D has been implicated as being involved in the aetio-pathogenesis of several autoimmune diseases including rheumatoid arthritis (RA). Previous studies present contradictory results. Vitamin D binding protein (DBP), the major transport protein, is also involved in various inflammatory processes.

**Objectives:** The aim of this study was to investigate the relationship between circulating levels of 25-hydroxyvitamin D [25(OH) D], DBP and polymorphisms in group-specific component (GC) in pre-symptomatic individuals and matched controls within prospective cohorts of the Northern Sweden.

**Methods:** Blood samples donated to the Medical Biobank prior to the onset of symptoms of RA (n=515, mean [SD] time before the onset of symptoms 6.2 [9.3] years) and from matched (2:1) population-based controls (n=267) were used. Plasma 25(OH) vitamin D levels were analysed using liquid chromatography tandem-mass spectrometry and DBP levels were analysed using enzyme-linked immunosorbent assay. GC polymorphisms (rs4588 and rs7041) were analysed with TaqMan assays (Applied Biosystems).

**Results:** Levels of 25(OH) D or DBP were not statistically different between pre-symptomatic individuals and controls in a crude, or a multiple-adjusted logistic regression model. However, an increased risk for future RA was found in females of DBP (OR 1.0001 [95%CI 1.000–1.0003]), adjusted for carriage of the minor allele of rs4588, in a multiple-adjusted model (p<0.05).

**Conclusions:** This study indicated that vitamin D is not associated with the future risk of RA although increasing levels of DBP were however, associated with an increased risk of disease in females carrying the minor allele of a DBP encoding SNP.

**Acknowledgements:** Samples and data for the cohort were obtained through the Västerbotten Intervention Program, the Northern Sweden MONICA Study,

and the mammary screening program of Västerbotten. Staff of the Department of Biobank Research, Umeå University, aided in acquisition of samples and data.

**Disclosure of Interest:** None declared

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#### THU0121 MORTALITY RATE AND PREVALENCE OF CARDIOVASCULAR DISEASE IN RHEUMATOID ARTHRITIS: 5-YEAR KARRA PROSPECTIVE STUDY

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**Background:** Rheumatoid arthritis (RA), which is an autoimmune chronic arthritis, leads to elevated rates of disability and mortality.

The main causes of mortality identified among RA patients are increased incidences of cardiovascular (CV) disease, which accounts for one-third to one-half of the premature deaths, infection and cancer.

In our previous study, we identified that cumulative inflammatory burden contributes to the development of carotid atherosclerosis through a synergistic interaction with conventional CV risk factors in patients with RA.

During the 2 years follow-up period, the mortality rate was 2.4% (10/412), and the main causes of death were infection (4/10) and CV disease (3/10).

**Objectives:** To investigate the incidences of mortality and CV disease in patients with RA in the 5 year Kyungpook National University Hospital Atherosclerosis Risk in Rheumatoid Arthritis (KARRA) prospective study.

**Methods:** A total of 372 patients with RA and 162 healthy controls were followed up for 5 years or until deaths in a prospective KARRA cohort study (412 patients and 221 controls at baseline).

To detect the presence and progression of carotid atherosclerosis, we performed carotid ultrasound at baseline and 5 year.

We analysed the incidence of CVD, conventional CV risk factors, RA disease activity and severity markers, medication histories, mortality rate, and causes of death.

**Results:** During 5 year follow-up period, the mortality rate was 10.7% (44/412) in RA patients and 1.4% (3/221) in healthy controls (p<0.001), while the incidence of CVD were 11.4% (47/412) in RA patients and 0.9% (2/221) in healthy controls (p<0.001).

Among CVD in RA patients, cerebrovascular accident (CVA) and cardiovascular event (CVE) were 17 (36.2%) and 30 (63.8%) events, respectively.

Major causes of death included infection (21/44, 47.7%), CVD (12/44, 27.3%), and others (11/44, 25%).

The mean age, presence and number of carotid plaques, functional class, modified Korean version of the HAQ (mKHAQ), tender joint count (TJC), swollen joint count (SJC), ESR and CRP, and conventional CV risk factors at baseline and cumulative ESR (ESR area under the curve), DAS28-ESR and DAS28-CRP at year 5 were significantly associated with mortality in RA patients.

Multivariate logistic regression analysis showed that the presence of carotid plaque (OR 6.22 [95% CI 1.08–24.99; p=0.031]), mKHAQ (OR 1.04 [95% CI 1.01–1.12; p=0.014]), and ESR (OR 1.09 [95% CI 1.03–1.16; p<0.001]) at baseline and cumulative ESR (ESR area under the curve) (OR 1.047 [95% CI 1.01–1.13; p=0.048]) and DAS28-ESR (OR 1.55 [95% CI 1.08–2.21; p=0.016]) at year 5 were independent risk factors for mortality of RA patients.

**Conclusions:** During the follow-up period of 5 years, the mortality rate and prevalence of CV disease were significantly increased in RA patients, compared to the controls. Furthermore, main causes of death were infectious disease and CV disease. Furthermore the risk factor for CVD and mortality is carotid plaque which is determined by disease activity and CV risk factors.

**Disclosure of Interest:** None declared

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#### THU0122 IMAGING CHARACTERISATION OF REMISSION IN RHEUMATOID ARTHRITIS

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**Background:** Remission in rheumatoid arthritis (RA) is now achievable in a significant proportion of patients using a combination of a treat to target strategy and biologic therapy. A number of clinical assessment tools exist for assessing remission. Several reports have shown that ultrasound (US) may have a role in better characterising this group of patients suggesting that subclinical synovitis increases the risk of erosive disease and flares in patients in DAS28 remission.<sup>1–3</sup>

These observations hint at a stratum of patients where remission is incomplete and may require a more tailored approach to therapy.

**Objectives:** In an early RA cohort we examine the relationship between US imaging and histological synovitis in the context of clinical remission and examine the predictive value of US to confirm synovial inflammation.

**Methods:** A prospective, observational study of 122 DMARD naïve, early RA patients classified according to the 1987 ACR criteria, with a maximum disease duration of 12 months (MRC PEAC study [www.peacmrc.mds.qmul.ac.uk](http://www.peacmrc.mds.qmul.ac.uk)). One hundred and three synovial biopsies were analysed at baseline and 75 at 6 months, with 85 paired US 12 joint scores (US 12: 10 metacarpophalangeal joints (MCPJ) and 2 wrists). US images were analysed using a semi-quantitative score for synovial thickness (ST) and power Doppler (PD).<sup>4</sup> Synovial inflammation was assessed using the Krenn synovitis scoring system. Fisher exact statistical test and Spearman's rank was used to determine the association and correlations.

**Results:** Demographics of this cohort are listed in table 1. There was a good correlation between US ST and PD scores with the Krenn histology score at the level of the single biopsied joint (ST:  $r=0.47$ ,  $p<0.001$ , PD:  $r=0.5$ ,  $p<0.001$ ). An association continued to be demonstrated when extending the US data set to 12 joints (ST  $r=0.27$   $p<0.01$ , PD  $r=0.28$   $p<0.01$ ).

Twenty-two patients with paired histology and ultrasound data were in DAS28 remission at 6 months and were eligible for analysis. A significant association between low PD ( $\leq 3/36$ ) signal (but not ST) and low Krenn score ( $\leq 4$ ) was demonstrated (Fisher exact test  $p<0.03$ ) with a predictive value of 90%. This reduced to 80% in patients not in DAS remission at 6 months ( $n=42$ ). Lastly, a clear relationship was noted between patients with US PD score recorded after 6 months of DMARD therapy ( $n=62$ , flares  $n=19$ ). No subsequent flares were recorded during the course of the follow up period of 6 months with a low US PD score ( $p<0.002$ , negative predictive value 76%) and a high US PD score had a 86% positive predictive value for disease flare within this time course.

**Conclusions:** This study demonstrates that there is considerable validity in the use of US to assess disease activity, which reflects histological synovitis in patients in low disease activity states and remission. Ultrasound imaging may demonstrate a distinct clinical and histological remission cohort of patients and may be a useful predictive tool in terms of predicting subsequent clinical disease activity.

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#### THU0123 MEDICATION ADHERENCE AND COST-RELATED MEDICATION NON-ADHERENCE IN PATIENTS WITH RHEUMATOID ARTHRITIS, A MIXED METHOD STUDY IN IRAN

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**Background:** Rheumatoid arthritis (RA) is a chronic inflammatory disease that often requires long term treatment with multiple medications. Medication adherence is essential in patients with RA to manage the disease.

**Objectives:** This study aimed to assess medication adherence and cost-related medication non-adherence (CRN) among patients with RA in Shiraz, Iran from the perspective of patients and rheumatologists.

**Methods:** A convergent parallel mixed method study was employed. A survey targeted RA patients attending the outpatient clinics in Shiraz. The survey collected demographic information followed by an assessment of adherence using the Compliance Questionnaire Rheumatology (CQR)<sup>1</sup> and featured 4 questions on CRN.<sup>2</sup> The cut-off point of 80% was used to identify patients as adherent or non-adherent. Semi-structured interviews were conducted with rheumatologists exploring their experiences in regard to medication adherence and its determinants. Descriptive data analysis of the surveys was undertaken using SPSS version 24. Interviews were transcribed and analysed using thematic analysis.

**Results:** A total of 308 surveys were collected and 10 interviews were conducted. The majority of patients were female (86%), married (79.7%), living in urban areas (66.2%), housewives (73.1%), with no income (68.2%) and illiterate (41.9%). Six of the interviewed rheumatologists were male and participants had a mean of 8.6 years of experience as a physician. According to the CQR questionnaire; 59.7% of patients were considered non-adherent. In terms of cost, 26.3% of patients had

not refilled their prescription; 52.1% had delayed refilling their prescription; 18.2% had skipped doses; or 18.5% had taken less medication to make the medication last longer. In contrast, the rheumatologists considered that the majority of their patients were adherent to their prescribed medication. However, they saw medication side effects, poor patient-doctor relationship and high costs of biologics as barriers of adherence. Surveys found that only 19.9% of patients were using biologic agents. This is in concordance with rheumatologists' discussion about high costs of biologics and they will not prescribe biologics because they know that the majority of patients cannot afford the medication.

**Conclusions:** Although the findings of the survey suggested that medication adherence is sub-optimal among Iranian patients with RA, rheumatologists consider the majority of their patients as adherent. The high costs of the medication was found to contribute to medication non-adherence. Therefore, health policy makers should consider this issue while identifying the medication prices.

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#### THU0124 LOW INFLAMMATION ON MAGNETIC RESONANCE IMAGING IN PATIENTS WITH RHEUMATOID ARTHRITIS THAT ACHIEVED SUSTAINED CLINICAL REMISSION ON ADALIMUMAB: DATA FROM THE PREDICTRA STUDY

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**Background:** ACR and EULAR recommend bDMARD tapering in patients (pts) with rheumatoid arthritis (RA) who achieved stable clinical remission. However, there are limited systematically collected data on objective magnetic resonance imaging (MRI)-assessed levels of musculoskeletal inflammation, especially tenosynovitis, in RA pts in stable clinical remission with previous data derived from a range of cohorts with differing definitions of clinical remission.

**Objectives:** To evaluate within the PREDICTRA study, the extent of disease control, in particular MRI inflammation, in RA patients in DAS28-based stable clinical remission, attained on adalimumab (ADA) at the standard dosing of 40 mg every other week (eow).

**Methods:** PREDICTRA is a multicenter, randomised, double-blind study generating data on pt and disease characteristics that may predict the clinical course of ADA dose-tapering for RA pts in stable clinical remission. RA pts with DAS28-CRP or -ESR $<2.6$  for  $\geq 6$  months following treatment with originator ADA 40 mg eow for  $\geq 12$  months in clinical practice were eligible to enter a 4 week (wk) lead-in study period with continued standard ADA dosing. Pts must have had confirmed DAS28-ESR $<2.6$  at the beginning and end of the lead-in period and quality-verified MRI of the most affected or, if both equally affected, the dominant hand to be eligible for randomization. Study assessments included multiple measures of disease activity (SJC28 and 68, TJC28 and 68, DAS28, CDAI, SDAI, patient's and physician's global assessment of disease activity), physical function (HAQ-DI, SF-36 PCS), and OMERACT RAMRIS scores for synovitis, tenosynovitis, bone marrow oedema, and erosions. Data of the randomised pts at the end of the lead-in period are presented.

**Results:** Of the 149 pts that entered the lead-in period, 122 (82%) were randomised. The randomised pts were 75% female, mean age of  $59.7 \pm 10.3$  years, RA duration of  $12.8 \pm 9.8$  years, prior ADA exposure for  $5.1 \pm 3.0$  years, and DAS28 remission duration of  $2.2 \pm 2.1$  years. Most pts received concomitant methotrexate (83.6%; mean dose 13.2 mg) and few received concomitant corticosteroids (9.8%; mean dose 3.2 mg). All the clinical disease activity measures showed very low disease activity. There was very low disease activity also in terms of the MRI inflammation scores (synovitis [ $3.5 \pm 3.13$ ], osteitis [ $1.0 \pm 2.01$ ], tenosynovitis [ $2.7 \pm 2.7$ ]). The mean MRI erosion score was low given the disease duration and the physical function scores were within normal levels (table 1).

Abstract THU0124 – Table 1. Summary of Patient Characteristics

Patient Characteristic (N=122)	Mean (SD)*
Duration of prior adalimumab, years	5.1 (3.0)
Duration of remission, years	2.2 (2.0)
Concomitant csDMARDs dose, mg	
Methotrexate (weekly)	13.2 (5.5)
Hydroxychloroquine (daily)	228.6 (75.6)
Sulfasalazine (daily)	750.0 (288.7)
Concomitant oral corticosteroids dose, mg (daily)	3.2 (1.7)
Anti-cyclic citrullinated peptide (ACCP), Unit	286.6 (206.4)
ACCP positive, n (%)	63 (52.9)
Rheumatoid factor (RF), IU/L	139.5 (395.4)
RF positive, n (%)	90 (76.3)
C-reactive protein (CRP), mg/L	5.3 (28.0)
Erythrocyte sedimentation rate (ESR), mm/hr	11.4 (8.4)
Tender joint count (TJC) 66	0.3 (0.6)
Swollen joint count (SJC) 66	0.1 (0.3)
DAS28 (ESR)	1.7 (0.6)
Clinical Disease Activity Index (CDAI)	1.3 (1.4)
Simplified Disease Activity Index (SDAI)	1.6 (3.0)
Patient's Global Assessment of Disease Activity –VAS, 0-100 mm	6.4 (8.9)
Physician's Global Assessment of Disease Activity –VAS, 0-100 mm	3.7 (5.0)
Pain –VAS, 0-100 mm	8.5 (11.5)
HAQ-DI	0.3 (0.4)
SF-36 MCS	54.4 (7.7)
SF-36 PCS	50.1 (7.8)
MRI OMERACT scores	
Synovitis, Range 0-24	3.5 (3.1)
Osteitis, Range 0-75	1.0 (2.0)
Tenosynovitis, Range 0-30	2.7 (2.7)
Erosion, Range 0-250	21.4 (26.9)

\* All values are Mean (SD), unless otherwise specified.  
 ACCP = Anticyclic citrullinated peptide; CRP = C-reactive protein; ESR = Erythrocyte sedimentation rate; EAM = extra-articular manifestations; HAQ-DI = Health Assessment Questionnaire – Disability Index; IBD = inflammatory bowel disease; MCS = mental component summary; OMERACT = Outcome Measures in Rheumatology; PCS = physical component summary; Pts = patients; RF = rheumatoid factor; SD = standard deviation; SF-36=Short form 36-item health survey; VAS = Visual Analogue Scale.

**Conclusions:** Pts with long-standing RA randomised to the tapering phase of the PREDICTRA study based on sustained DAS28-based clinical remission on prior standard dose ADA therapy showed very low levels of clinical disease activity and normal physical function. This concurred with low MRI inflammation scores, especially for osteitis and tenosynovitis, the latter pathology being reported for the first time in RA clinical remission pts.

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## THU0125 PREVENTION OF THE PROGRESSIVE BIOCHEMICAL CARTILAGE DESTRUCTION UNDER METHOTREXATE THERAPY IN EARLY RHEUMATOID ARTHRITIS

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**Background:** Can methotrexate (MTX) stop cartilage loss measured by Delayed gadolinium-enhanced MRI of the cartilage (dGEMRIC) in patients with early rheumatoid arthritis (eRA)?

**Objectives:** Objective of the study was to investigate biochemical cartilage composition under MTX therapy and to intra-individually assess the impact of inflammation severity on cartilage composition by using dGEMRIC MRI in patients with eRA.

**Methods:** dGEMRIC of MCP joints of the index and middle finger of 28 patients from the AthroMark cohort were examined prior to MTX-therapy as well as after 3 and 6 months. OMERACT RA MRI score and clinical parameters (CRP and DAS28) were registered at any time point. Each patient's second and third MCP joints were dichotomized into the joint with more severe synovitis versus the joint with less severe synovitis according to the RAMRIS synovitis subscore.

**Results:** MCP joints with more severe synovitis ('bad joints') demonstrated significantly lower dGEMRIC values compared to MCP joints with less severe synovitis ('good joints') at time-points 0 and 3 months (p=0.002; p=0.019, respectively). After 6 months of MTX therapy no significant difference of dGEMRIC index was found between good and bad joint (p=0.086).

**Conclusions:** Under MTX therapy, biochemical cartilage integrity remains stable; no further cartilage destruction occurred if patients are treated early in the course of the disease. In addition, six months of MTX therapy triggered an alignment of

dGEMRIC index of MCP joints with initially severe synovitis and less severe synovitis in an intra-individual assessment. This underlines the importance of an early treatment in eRA to reduce further cartilage damage of the inflamed joints.

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**Disclosure of Interest:** None declared

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## THU0126 IMPACT OF RESIDENTIAL AREA ON THE PROFILE OF RHEUMATOID ARTHRITIS PATIENTS INITIATING THEIR FIRST BIOLOGIC DMARD: RESULTS FROM THE ONTARIO BEST PRACTICES RESEARCH INITIATIVE (OBRI)

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**Background:** Access to care and management of Rheumatoid Arthritis (RA) patients may differ based on residential area which, in turn, can affect the real-world effectiveness of anti-rheumatic medications.

**Objectives:** We aimed to describe differences in the profile of patients initiating their first biologic disease modifying antirheumatic drug (bDMARD) based on their residence in urban vs. rural areas.

**Methods:** RA patients enrolled in the OBRI initiating their first bDMARD within 30 days prior to or anytime following enrolment were included in the analysis. Patients excluded if they had less than 2 years of follow-up and less than 2 visits during this period of time. Patients characteristics included sociodemographics (age, gender, race, education level, marital status, smoking status, annual household income, health insurance coverage), disease duration, disease severity parameters (Disease Activity Score (DAS), Clinical Disease Activity Index (CDAI), Swollen and Tender Joints (SJC28, TJC28), Physician Global Assessment (PhGA), Patient Global Assessment (PGA), Health Assessment Questionnaire – Disability Index (HAQ-DI), presence of erosion), bDMARD type, and concomitant anti-rheumatic medications including conventional synthetic disease modifying antirheumatic drug (csDMARDs), non-steroidal anti-inflammatory drugs (NSAIDs), and oral steroids.

**Results:** A total of 629 RA patients were included of whom 522 (83%) resided in urban areas and 107 (17%) in rural areas. Other than marital status (urban vs. rural: 64.6% vs. 82.2% married; p<0.001) and race (urban vs. rural: 78.0% vs. 95.3% Caucasian; p=0.001) no significant differences in sociodemographics were observed between groups. However, patients from urban areas were less likely to have an erosion (46.6% vs. 50.5%; p=0.23), had lower TJC28 (7.2 vs. 7.9; p=0.43), and lower SJC28 (6.6 vs. 7.1; p=0.42) at bDMARD initiation. Type of bDMARD (anti-TNF vs. other mechanism of action) was comparable between groups (87.9% on anti-TNF) as was concomitant treatment with csDMARDs (84.9% on csDMARDs), and NSAIDs (19.6% on NSAIDs). Concomitant use of oral steroids was significantly lower in patients from urban areas (21.5% vs 29.9%; p=0.04).

**Conclusions:** Important differences may exist in the profiles of RA patients initiating their first bDMARD, and residing in rural versus urban areas. The implications on treatment outcomes should be assessed.

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THU0127

### THE SEVERITY OF KERATOCONJUNCTIVITIS SICCA IN RHEUMATOID ARTHRITIS CORRELATES WITH THE MEDICAL OUTCOME STUDY 36-ITEM SHORT FORM HEALTH SURVEY (SF-36) SCORE BUT NOT THE DISABILITY INDEX (HAQ-DI)

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**Background:** Keratoconjunctivitis sicca (KCS) is the most frequent ocular manifestation of rheumatoid arthritis (RA). It is highly heterogeneous and exhibits a considerable variability of presentation. Whereas a significant proportion of patients with KCS may be asymptomatic; it is unknown if the degree of dryness of the eyes, irrespective of symptomatology, has an association with the overall quality of life and functional ability.

**Objectives:** To determine the correlation between the Schirmer's score and the Medical Outcome Study 36-Item Short Form Health Survey (SF-36) score as well as the disability index measured by the Health Assessment Questionnaire-Disability Index (HAQ-DI).

**Methods:** A total of 50 Nigerian patients satisfying the 2010 American College of Rheumatology/European League Against Rheumatism classification criteria for RA were studied. Tear production was measured by unstimulated 5 min Schirmer's test (using 5 mm by 35 mm Whatman filter paper) and ocular staining with fluorescein stain. Each patient also completed the SF-36 and HAQ-DI questionnaires.

**Results:** The mean age of the patients was 47.2±12.5 years. Among them, 42 (84%) were females, giving a female-to-male ratio of 5.25:1. Rheumatoid factor and anti-citrullinated protein antibody were positive in 38 (76%) and 30 (60%) patients respectively. KCS was found in 15 (30%) patients among whom only 6 patients were symptomatic for dry eyes. The mean visual acuity [LogMAR (Snellen equivalent)] among the patients with and without KCS were 0.70 (6/30) and 0.10 (6/7.5). Among all patients, there was a positive correlation between the mean Schirmer's score (between each patients two eyes) and the Physical Component Summary ( $r=0.292$ ,  $p=0.008$ ) as well as the Mental Component Summary ( $r=0.228$ ,  $p=0.030$ ) of the SF-36. There is however no significant correlation between the mean Schirmer's score and the HAQ-DI ( $r=0.148$ ,  $p=0.188$ ).

**Conclusions:** Ocular manifestation is very common in RA and KCS is particularly rampant. Even in asymptomatic patients, the degree of xerophthalmia may give a reliable insight into both the physical and mental quality of life but not into the degree of functional disability.

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THU0128

### DO BIOLOGICAL DMARDS PREVENT LONG TERM ARTICULAR DAMAGE BY RHEUMATOID ARTHRITIS IN ROUTINE CLINICAL CARE?

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**Background:** Treatment of rheumatoid arthritis is primarily aimed to achieve remission and thereby reduce the risk of permanent joint damage. Preventing disabling joint damage is an important long term goal for patients. Effectiveness of bDMARDs on disease activity has been proven in randomised controlled studies; however studies on long term joint damage are scarce and show conflicting results.<sup>1,2</sup>

**Objectives:** To compare joint damage more than 5 years after RA diagnosis in patients who have never used bDMARDs and in patients treated with bDMARDs. Joint damage is measured with the Rheumatoid Arthritis Articular Damage (RAAD) score, a clinical method comprising all joints that may be affected by RA.<sup>3</sup>

**Methods:** Retrospective cohort study in RA patients in a Dutch teaching hospital diagnosed between 2006 and 2011. Inclusion criteria were receiving a DMARD for at least 12 months and availability of a RAAD-score after a disease duration of 5 years or more. Exclusion criteria was receiving a DMARD for an other indication than RA. The exposure of interest was the type of treatment (sDMARD or bDMARD).

**Results:** Among 305 patients included, 101 used a bDMARD (table 1). Baseline characteristics were not significantly different in terms of prognostic factors for

joint damage progression, with the exception of patients in the bDMARD group being younger. During follow up, the highest DAS28 was higher in the bDMARD group 5.0 vs 4.3,  $p<0.001$ . After 8.5 years, more than half of the patients in bDMARD (55.4%) and sDMARD (57.4%) groups had no joint damage (RAAD-score 0). No significant differences in long term joint damage were observed, even after adjusting for potential confounders ( $b=-0.26$ , 95% CI  $-1.9-1.4$ ,  $p=0.76$ ).

Table	bDMARD n=101	sDMARD n=204
Values as median (IQR) unless indicated otherwise;		
Age yrs mean (SD)	49 (13)	57 (14)*
Female n (%)	63 (62.4)	129 (63.2)
ESR	22.0 (14.0-37.5)	27.5 (13.2-43.7)
CRP	10.0 (3.0-21.0)	15.0 (4.0-36.0)
≥6 ACR2010 criteria n%	79 (78.2)	158 (78.2)
Rheumatoid factor n%	81 (81.0)	145 (71.1)
ACPA n%	54 (76.1)	90 (70.9)
Bone erosions	17 (16.8)	46 (22.9)
DAS28	4.9 (4.3-5.60)	4.7 (3.8-5.5)
Disease duration yrs mean (SD)	8.5 (1.9)	8.5 (2.2)
Prednisolone use n%	57 (56.0)	63 (30.0)*
Highest measured DAS	5.0 (4.2-5.8)	4.3 (2.9-5.1)*
RAAD-score	0.0 (0.0-2.0)	0.0 (0.0-2.0)
HAQ	0.3 (0.0-0.9)	0.1 (0.0-0.4)*

**Conclusions:** In this cohort joint damage is not significantly different between patients treated with sDMARD(s) alone and those also using a bDMARD. Given the higher disease activity in the bDMARD group it is possible that this treatment prevented long-term joint damage by RA. Since there was limited joint damage in these groups this analysis should be repeated after longer disease duration and preferably in randomised cohorts.

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THU0129

### PREDICTIVE VALUE OF CD19 SERUM LEVELS FOR LONG TERM THERAPEUTIC RESPONSE AND UTILITY AS BIOMARKER FOR OPTIMISATION, IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH RITUXIMAB

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**Background:** Rituximab (RTX) is a chimeric monoclonal antibody directed against CD20 antigens in B lymphocytes (BL) surface, producing selective depletion of BL, without affecting mature plasmatic cells. Current guidelines recommend optimisation of biologic therapy once remission has achieved in rheumatoid arthritis (RA) patients. A serum biomarker able to predict what patients would maintain remission after optimisation in RTX treated RA patients is lacking.

**Objectives:** To analyse the predictive value of CD19 serum level prior to RTX infusion for the long term maintenance of therapeutic response, and it's utility as a biomarker for optimisation in RA patients treated with RTX.

**Methods:** all RA patients treated with RTX in our centre during 2016 and 2017 for at least 6 months, and with 12 months follow-up, were included. Demographic data, clinical data related to RA, including activity parameters (DAS28, HAQ, ESR, RCP), number of infections, optimisation and serum levels of lymphocytic subpopulations (CD19, CD3 and CD56) and immunoglobulins (Ig) prior to each RTX cycle were collected. Optimisation was defined as any dose decrease (lower dose for cycle and/or increase interval between cycles). Recurrent infections were defined as three or more infections in one year. Descriptive statistics, correlation between basal levels of CD19, CD3 or CD56, and activity parameters or Ig levels at 6 and 12 months, and association studies between lymphocyte subpopulations and optimisation or recurrent infections were performed.

**Results:** Thirty patients (25 females, 60±12 year) with RA (24 RF/aCCP +, 17 ±11 years from disease onset), treated with RTX during 52±40 months, with an accumulated dose of 13±10 g were included. At study inclusion, DAS28 was 3,77 ±1,65, HAQ was 1,28±0,78 and 22 had been optimised. CD19 levels were lower

than 2% in 22 patients (79%), including 10 with undetectable levels. CD19 levels (cells/mm<sup>3</sup>) were lower in optimised patients (73 vs 14,  $p=,03$ ), and were correlated with DAS28 at 6 months ( $r=0,5$ ;  $p=,007$ ) and 12 months ( $r=0,44$ ;  $p=,03$ ), and with ESR at 6 m ( $r=0,6$ ;  $p=,002$ ). CD19 levels did not correlate with IgG levels, and were not associated with recurrent infections. CD3 and CD56 levels did not show any relevant association or correlation.

**Conclusions:** In RA patients treated with RTX for more than 6 months, CD19 levels correlate with long term therapeutic response, being low or undetectable levels predictors of good outcome, without association with Ig levels or increased infections. Our results suggest that CD19 levels before every RTX cycle might be a useful biomarker to select candidate patients for optimisation with this therapy.

**Disclosure of Interest:** None declared

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#### THU0130 EXPLORING THE MINIMUM PAIRED JOINT SET OF ULTRASONOGRAPHY TO PREDICT CLINICALLY SIGNIFICANT RESIDUAL SYNOVITIS IN RHEUMATOID ARTHRITIS PATIENTS WITH REMISSION

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**Background:** Patients with rheumatoid arthritis (RA) who achieved clinical remission sometimes have synovitis detected by joint ultrasonography (US) <sup>(1)</sup>. This residual synovitis has been shown to be predictive of insidious radiographic progression, flares after tapering or cessation of DMARDs. Since it is difficult to examine all joints by US in daily clinical practice, several joint combinations have been proposed for optimal and/or feasible assessments of joint inflammation in patients with RA.

**Objectives:** To find the minimum number of paired joint set for US to predict clinically significant residual synovitis.

**Methods:** A comprehensive US assessment of joints was performed in 109 RA patients who achieved DAS28-CRP remission or low disease activity. Totally 40 (20 pairs) of joints including metacarpophalangeal (MCP) 1 to 5, proximal interphalangeal (PIP) 1 to 5, wrist, elbow, shoulder, knee, ankle, metatarsophalangeal (MTP) 1 to 5 joints were evaluated according to the EULAR recommendation <sup>(2)</sup>. Residual synovitis was defined as synovial hypertrophy with grey scale (GS) score greater than 1 or GS score 1 with any power Doppler (PD) signal, using semi quantitative scoring system (scale 0 to 3).

**Results:** 73 of 109 patients (67%) had at least one residual synovitis, and 39 of 73 patients (53.4%) had residual synovitis at least two different joints. As shown in table 1, residual synovitis at wrist and knee joints were found in 54.8% and 53.4% of 73 patients respectively, while for residual synovitis of another joints were less than 20% of patients. Solitary residual synovitis was most frequent in wrist and knee joints. By adding and combining joints which frequently found to have residual synovitis, we found that combination of wrist, knee, ankle, elbow, MCP1, and MCP2 joints (6 pairs) could detect residual synovitis in 94.5% of patients (table 2). Using the fact that one patients can have more than one residual synovitis at different joints and the tendency of residual synovitis to be found at some particular joints, we might find minimum pairs set of joint ultrasonography to detect residual ultrasound-defined synovitis. This could minimise the efforts needed to perform thorough joint US, while keeping the sensitivity high enough to detect any residual synovitis.

**Abstract THU0130 – Table 1.** Residual synovitis distribution

	n (%) total 73		n (%) total 73
Wrist	40 (54.8)	MTP 5	7 (9.6)
Knee	39 (53.4)	MCP 5	6 (8.2)
Ankle	14 (19.2)	PIP 3	4 (5.5)
Elbow	12 (16.4)	MCP 4	4 (5.5)
MCP 2	9 (12.3)	MTP 1	4 (5.5)
MCP 3	8 (10.9)	PIP 4	3 (4.1)
MCP 1	8 (10.9)	MTP 3	3 (4.1)

**Abstract THU0130 – Table 2.** Detectability of residual synovitis with each paired joint set.

Combination of Joints	Detectability (%)
wrist	40 (54.8)
wrist+knee	59 (80.8)
wrist+knee+ankle	63 (86.3)
wrist+knee+ ankle+elbow	66 (90.4)
wrist+knee+ankle+elbow+MCP1	68 (93.2)
wrist+knee+ankle+elbow+MCP1+MCP2	69 (94.5)

**Conclusions:** Patients achieved DAS28-CRP remission often had residual synovitis. The residual synovitis had tendency to be distributed at wrist, knee, ankle, elbow, MCP1, and MCP2, joints frequently used in activities of daily life. We propose this combination of joints as the minimum paired joint set to predict ultrasonographic remission.

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#### THU0131 LEVELS OF CXCL13 AND sICAM1 CORRELATE WITH DISEASE ACTIVITY SCORE IN RHEUMATOID ARTHRITIS (RA) PATIENTS TREATED WITH TOCILIZUMAB (TCZ)

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**Background:** The biomarkers CXCL13 and sICAM1 have been associated with outcomes in patients with RA treated with TCZ.

**Objectives:** To determine the association of CXCL13 and sICAM1 with response to TCZ and disease activity in early RA and DMARD-IR patients.

**Methods:** Patient subsets from the FUNCTION (early RA) and LITHE (DMARD-IR) clinical trials were selected based on baseline and Week 24 sample availability; serum CXCL13 and sICAM1 levels were measured. Correlations between CXCL13 and sICAM1 levels and DAS28-ESR at baseline, and between change in CXCL13 and sICAM1 levels and change in DAS28-ESR at Week 24, were determined. Changes in CXCL13 and sICAM1 levels from baseline to Week 24 were compared between treatment arms using Welch *t* test. The effect of treatment, baseline DAS28-ESR and baseline CXCL13 and sICAM1 levels on the likelihood of DAS28-ESR remission and ACR50 response at Week 24 was determined via logistic regression. DAS28-ESR remission and ACR50 rates were compared against CXCL13 and sICAM1 status (high vs low based on median values) within each trial arm using a Cochran-Mantel-Haenszel test.

**Results:** Overall, 458 of 872 patients from FUNCTION (TCZ +MTX, n=60; TCZ monotherapy [TCZ-mono], n=157; placebo [PBO]+MTX, n=141) and 287 of 791 patients from LITHE (TCZ +MTX, n=137; PBO+MTX, n=150) were included. In these patient subsets, mean disease duration in FUNCTION was significantly shorter than in LITHE (0.45 vs 8.65 years). At baseline, correlation of serum CXCL13 levels with DAS28-ESR was moderate in the early RA population and weak in the DMARD-IR population (table 1). Correlation between baseline serum sICAM1 levels and DAS28-ESR was low in both populations. Serum levels of CXCL13 decreased significantly at Week 24 in all treatment arms in both populations, with greater reductions in the TCZ +MTX and TCZ-mono arms; sICAM1 levels decreased significantly at Week 24 in the TCZ-mono arm in patients with early RA and the TCZ +MTX arms in both populations but not in the PBO+MTX arms. Change in CXCL13 levels correlated moderately with change in DAS28-ESR at Week 24 in both populations (table 1). Change in sICAM1 levels correlated moderately with change in DAS28-ESR at Week 24 in the DMARD-IR population but weakly in the early RA population. Although the treatment arm had a significant effect on the likelihood of DAS28-ESR remission and achievement of ACR50, the effect of baseline levels of CXCL13 and sICAM1 were not significant. DAS28-ESR remission and ACR50 response rates at Week 24 within each treatment arm of the early RA and DMARD-IR populations were not significantly different between patients with high vs low baseline CXCL13 and sICAM1 levels.

**Abstract THU0131 – Table 1.** Correlation Between Serum CXCL13 and sICAM1 Levels and DAS28-ESR

	Baseline						Week 24*					
	CXCL13			sICAM1			ΔCXCL13			ΔsICAM1		
	n	r	P value	n	r	P value	n	r	P value	n	r	P value
FUNCTION (early RA)	458	0.38	<0.0001	458	0.14	0.0029	458	0.33	<0.0001	458	0.16	0.0005
LITHE (DMARD-IR)	287	0.21	0.0002	287	0.17	0.0045	287	0.33	<0.0001	287	0.26	0.0002

CXCL13, C-X-C motif chemokine ligand 13; DAS28-ESR, Disease Activity Score in 28 joints per erythrocyte sedimentation rate; DMARD-IR, inadequate response to disease-modifying antirheumatic drugs; RA, rheumatoid arthritis; sICAM1, soluble intercellular adhesion molecule 1.

\* Correlation between change in CXCL13 and sICAM1 levels from baseline to Week 24 and change in DAS28-ESR from baseline to Week 24; all patients combined.

**Conclusions:** The association of baseline CXCL13 levels with RA disease activity was stronger in the early RA population than in the DMARD-IR population. Changes in CXCL13 and sICAM1 correlated significantly with changes in DAS28-ESR at Week 24. However, baseline levels of CXCL13 and sICAM1 did not predict response to TCZ at Week 24, suggesting that although these biomarkers are associated with disease activity, they do not predict response to TCZ in all RA populations.

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**THU0132 THE PATIENT GLOBAL ASSESSMENT RATING VARIES MINIMALLY IF USING ARTHRITIS OR GLOBAL HEALTH CONDITION AND AGREEMENT IS HIGH BETWEEN COMMON COMPOSITE DISEASE ACTIVITY MEASURES AND REMISSION CLASSIFICATION USING EITHER: RESULTS FROM A NATIONAL EARLY RA COHORT STUDY**

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**Background:** The patient global assessment (PtGA) is a core domain in several RA composite disease activity (CDA) measures for trials, treat-to-target paradigms and practice, and can be asked differently, either referring to the patient's global health or condition (PtGA-GH), or specifically to arthritis disease activity (PtGA-AR).

**Objectives:** To assess agreement between PtGA-GH vs. PtGA-AR ratings and commonly used CDA indices calculated using both versions of the PtGA.

**Methods:** We included classifiable RA patients enrolled in CATCH (Canadian Early Inflammatory Arthritis Cohort) between 2011 and 2017 who simultaneously completed both PtGA-GH and PtGA-AR using a 10 cm VAS (scored 0–10) at each of baseline, 6- and 12 months visits. Differences in descriptive statistics were compared using Wilcoxon-sign rank tests and chi-square tests for baseline characteristics, PtGA ratings and CDA indices. Agreement was assessed using Intraclass correlation coefficients (ICC) for continuous measures and weighted kappa coefficients for categorical measures. Stratified analyses were also performed by age (older >65) and sex.

**Results:** Of 571 eligible early RA patients, 71% were female, 83% were white, 17% were current smokers, 17% had erosions, and 60% had completed high-school. Baseline mean(SD) age was 55<sup>(15)</sup> symptom duration was 5 (3) months and there were 2 (2) comorbid conditions. Agreement between PtGA ratings, composite CDA measures and remission classification by PtGA-GH and PtGA-AR are summarised in table 1. Mean(SD) PtGA-GH ratings were only marginally higher than PtGA-AR ratings and agreement was high between PtGA ratings at baseline and over the first year follow up (all ICCs>0.8). Agreement in CDA scores calculated with either PtGA was higher at baseline and over time (all ICCs>0.95). Concordance in classification of remission using either PtGA was also high at all time points (Kappa's>0.85). Results of stratified analyses showed that relative to men, women tended to report slightly higher differences in PtGA-GH vs. PtGA-AR (all p's<0.0001) but overall agreement in PtGA ratings, CDA scores and remission classification was high and similar in both sexes. Age stratified analyses were similar to those in the whole sample.

**Conclusions:** Results from this large longitudinal study of early RA patients followed in routine practice settings, showed patients rated the PtGA-GH marginally higher than PtGA-AR but differences had minimal impact on commonly used CDA indices and remission classification. These findings suggest that common composite measures of RA disease activity can be calculated using either the PtGA-GH or PtGA-AR.

**Table 1.** Agreement in Patient Global Assessment, RA Composite Disease Activity Indices and Classification of Remission calculated using PtGA-GH vs PtGA-AR

Variable	Baseline (N = 571)		6-Months (N = 571)		12-Months (N = 571)	
	PtGA - GH	PtGA - AR	PtGA - GH	PtGA - AR	PtGA - GH	PtGA - AR
<b>Patient Global Assessment (VAS 0-10cm)</b>						
Mean (SD)	5.7 (2.8)	5.2 (2.8)	3.0 (2.7)	2.8 (2.6)	2.7 (2.6)	2.4 (2.5)
Intraclass correlation coefficient	0.80		0.88		0.88	
<b>Composite Disease Activity (CDA) indices</b>						
<b>DAS28-ESR</b>						
Mean (SD)	5.0 (1.3)	4.9 (1.3)	2.9 (1.4)	2.9 (1.4)	2.6 (1.4)	2.6 (1.4)
Intraclass correlation coefficient	0.98		0.99		0.99	
Remission, Frequency (%)	23 (4%)	23 (4%)	193 (34%)	196 (34%)	243 (43%)	247 (43%)
Kappa (95% CI)	0.93 (0.91, 0.95)		0.97 (0.96, 0.98)		0.98 (0.97, 0.98)	
<b>SDAI</b>						
Mean (SD)	38.7 (14.4)	28.1 (14.4)	10.5 (10.4)	10.2 (10.4)	8.2 (9.8)	7.9 (9.7)
Intraclass correlation coefficient	0.99		0.99		0.99	
Remission, Frequency (%)	6 (1%)	6 (1%)	143 (25%)	155 (27%)	192 (34%)	203 (36%)
Kappa (95% CI)	0.95 (0.93, 0.97)		0.95 (0.94, 0.97)		0.95 (0.94, 0.97)	
<b>CDAI</b>						
Mean (SD)	27.1 (13.7)	26.6 (13.7)	9.7 (10.3)	9.5 (10.3)	7.3 (9.2)	7.0 (9.1)
Intraclass correlation coefficient	0.99		0.99		0.99	
Remission, Frequency (%)	5 (1%)	6 (1%)	158 (28%)	173 (30%)	210 (37%)	215 (38%)
Kappa (95% CI)	0.93 (0.909, 0.96)		0.92 (0.901, 0.94)		0.92 (0.90, 0.94)	
<b>RAPID III</b>						
Mean (SD)	4.6 (2.4)	4.5 (2.5)	2.5 (2.2)	2.4 (2.2)	2.2 (2.1)	2.1 (2.1)
Intraclass correlation coefficient	0.97		0.98		0.98	
Remission, Frequency (%)	52 (9%)	53 (9%)	199 (35%)	206 (36%)	231 (41%)	237 (42%)
Kappa (95% CI)	0.85 (0.81, 0.89)		0.86 (0.83, 0.90)		0.85 (0.815, 0.89)	
<b>Boolean Remission</b>						
N, % Remission (REM)	6 (1%)	7 (1%)	114 (23%)	123 (25%)	159 (33%)	167 (34%)
Kappa (95% CI)	0.99 (0.97, 1.00)		0.95 (0.93, 0.98)		0.94 (0.91, 0.96)	

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**THU0134 ULTRASOUND DETECTED TENOSYNOVITIS PREDICTS ARTHRITIS ONSET IN INDIVIDUALS AT RISK OF DEVELOPING RHEUMATOID ARTHRITIS**

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**Background:** The pathophysiological processes leading from musculoskeletal (MSK) complaints to clinically manifest rheumatoid arthritis (RA) are not fully understood. The urgency for imaging and serological markers that predict arthritis development in individuals at risk of RA is of clinical importance.

**Objectives:** To identify ultrasound (US) markers that can predict arthritis development.

**Methods:** Patients presenting with MSK complaints and a positive Anti-Citrullinated Protein Antibody (ACPA) test were referred from primary care units to the Rheumatology Unit. Those lacking clinical signs of arthritis, confirmed by absence of synovial hypertrophy with Doppler activity on US examination, were recruited into the Risk-RA prospective program. A total of 66 patients with complete US records were included between years 2015 up to December 2016. Hands and feet, including symptomatic joints were US-evaluated for synovitis, hyperemia and bone erosions. The presence of wrist (compartments 1–6) and finger (flexor and extensor) tenosynovitis, according to OMERACT guidelines were also recorded in all patients. Serum samples from inclusion were analysed on a multiplex immunoassay

**Results:** 66 Risk-RA patients (85% female, median age 50 years, range 22–82) were included and followed up to arthritis onset (median 8 months, range 1–27), or to the end of year 2017 (median 25 months, range 11–43). 27 patients (41%, 86% female, median age 52 years, range 22–74) developed arthritis. Of these 7 had tenosynovitis detected by US at inclusion and 7 more developed tenosynovitis at follow-up visits (in total n=14). At the time of diagnosis, 20 out of 27 patients presented with both tenosynovitis and synovitis.

A large majority of patients with tenosynovitis (12 out of 14, 86%) and a minority without tenosynovitis (15 out of 52, 29%) developed arthritis, resulting in an increased relative risk of 3.0 (95% CI 1.8–4.8) to develop arthritis for patients presenting with tenosynovitis at baseline or follow-up visits (p=0.001).

Concentrations of the anti-CCP antibodies, anti-CEP antibodies and anti-citrullinated vimentin<sup>60–75</sup> antibodies tended to be higher in patients with tenosynovitis developing arthritis (n=12, median of 70 AU/ml, range 2–175 for anti-CCP, median of 68 AU/ml, range 0–673 for anti-CEP, median of 53, range 0–644 for anti-vim) than those without tenosynovitis developing arthritis (n=15, median of 35 AU/ml, range 1–100 for anti CCP, median of 12, range of 0–1179 for anti-CEP, median of 29, range 0–332 for anti-vimentin). Same trend was observed when comparing



patients with tenosynovitis developing arthritis to those without-tenosynovitis not-developing arthritis. The 2 patients with tenosynovitis not developing arthritis, had lower levels of the antibodies as compared to those with tenosynovitis developing arthritis. No significant differences in other patient baseline characteristics were seen between those with, and those without tenosynovitis (86 vs 85% female, median (range) 54 years<sup>29-71</sup> vs 50 years,<sup>22-82</sup> mean visual analogue scale pain 34 vs 31, mean c-reactive protein 2.7 vs 3.2; tender joint count 1.2 vs 0.7).

**Conclusions:** Ultrasound detected tenosynovitis in the context of ACPA positivity is a good clinical predictor of rapid arthritis onset in individuals at risk of developing RA.

**Disclosure of Interest:** None declared

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THURSDAY, 14 JUNE 2018

## Rheumatoid arthritis – comorbidity and clinical aspects

### THU0135 USING FRAX® AND PERIPHERAL BONE MINERAL DENSITY FOR IDENTIFYING POTENTIAL CANDIDATES FOR OSTEOPOROSIS THERAPY AMONG RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Rheumatoid arthritis (RA) and glucocorticoids (GC) therapy are proven risk factors (RF) for osteoporosis (OP) and osteoporotic fractures (OPF). Along with these factors, patients with RA have other diseases and conditions that can affect the increase of the risk of OPF.

**Objectives:** To determine the frequency of RA in the epidemiological random sample of persons aged  $\geq 50$  years and to identify among them patients who need the prevention of OPF.

**Methods:** The epidemiological sample included 18 018 people (13 941 women and 4 077 men, mean age  $62 \pm 10$  years). A survey was conducted using a unified questionnaire that included possible risk factors for osteoporosis (age, body mass index, individual or family history of fragility fracture, smoking, alcohol misuse, confirmed diagnosis of RA, long-term use of GC, premature menopause, physical inactivity, disorder strongly associated with osteoporosis) and daily calcium intake with food. The 10 year probability of fracture was calculated using the FRAX. Bone mineral density (BMD) was measured in the distal forearm using Osteometer Meditech DTX-200 as a screening method.

**Results:** The prevalence of RA in the epidemiological sample was 1.7% (1.9% for women and 1.2% for men,  $p=0.0047$ ). The mean FRAX values for the major OPF in RA patients were significantly higher than those without RA:  $18.4\% \pm 10\%$  and  $13.2\% \pm 7.9\%$ , respectively ( $p < 0.0001$ ) for women and  $8.9 \pm 6.4$  and  $6.2 \pm 3.7$ , respectively ( $p < 0.0001$ ) for men. Forty-two percent of RA patients had a high risk of OPF: 48% of women and 8% of men. The percentage of women with RA who had FRAX above the threshold of therapeutic intervention was significantly higher than among those without RA (31%),  $p=0.00001$ . At the same time, in men, the frequency of high fracture risk was the same in patients with RA and without RA (8% and 7%, respectively,  $p > 0.05$ ). Among the most common RF OP and OPF in RA patients were previous fractures (33%), causes of secondary OP (30%) and taking GC (18%), for men an additional factor - smoking (33%). Women with RA had significantly more concomitant diseases and other secondary causes of OP and OPF (33%) than those without RA (23%),  $p=0.0004$ . More of them used GC compared to control (17% and 8%, respectively,  $p < 0.0001$ ). Among men significant differences were obtained only for the using of GC: 20% in RA patients and 5% in control group ( $p < 0.0001$ ). Other RF were found with the same frequency. The average calcium intake with food was  $683 \pm 231$  mg per day among women and  $635 \pm 276$  mg per day in men without statistical differences between RA patients and control. 20% of men and 16% of women had less than half of daily calcium intake norm ( $p=0.53$ ). OP in the distal forearm was diagnosed in 47% RA women and 20% RA men compared to control: in 22% women ( $p < 0.0001$ ) and 19% men ( $p > 0.05$ ). Among RA patients, 13% of women and 20% of men had low FRAX and OP in the distal forearm.

**Conclusions:** Every third woman with RA had at least one more comorbid disease or condition associated with an increased risk of OPF and about every second - low BMD. 48% of women and 8% of men with RA had a high risk of OPF and needed prevention of OP. Additionally, among RA patients, 13% of women and 20% of men with low BMD in the distal forearm require axial densitometry.

**Disclosure of Interest:** None declared

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### THU0136 MAJOR CARDIOVASCULAR EVENTS IN 434 RHEUMATOID ARTHRITIS PATIENTS TREATED WITH RITUXIMAB FROM A SINGLE-CENTRE

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**Background:** Increased cardiovascular (CV) risk due to excess atherosclerosis in rheumatoid arthritis (RA) is attributed to systemic inflammation. Effective disease modifying drugs have been associated with reduced CV burden. Pre-clinical models of atherosclerosis suggest atheroprotective IgM and atherogenic IgG B-cell populations; with reduced atherosclerosis in murine models treated with depleting anti-CD20 monoclonal antibody suggesting relative preservation of protective B-cell population. The specific impact of rituximab (RTX) on the development of CV disease in RA has not been evaluated thus far.

**Objectives:** To determine the incidence of major cardiovascular events (MACE) in RA patients treated with rituximab and factors associated with any increased risk.

**Methods:** This was a single-centre, cohort study of patients with RA treated with  $\geq 1$  RTX cycle recruited prospectively. MACE outcomes were retrospectively identified as myocardial infarction, cerebrovascular accident, or death due to CV disease. Patients with and without MACE were compared for age, sex, CV risk factors (diabetes mellitus, hypertension, hyperlipidaemia, smoking, prior CV disease), disease characteristics (disease duration, ACPA, RF, methotrexate use, DAS28) and immunoglobulin levels. Association between the proportion of MACE and these variables of interest was analysed using the Student T test or Chi squared test as appropriate.

**Results:** A total of 434 patients were studied (mean age 58 years [SD 13], 80% females). Total follow-up was 3211 patient-years (PY). Of these, 32/434 (7.4%) had a MACE (incidence rate 10 per 1000 PY). Forty-three deaths (any cause; 9.9%) were recorded, 6/43 and 26/391 deaths respectively in patients with and without MACE (14% vs 7%,  $p=0.114$ ). Patients with MACE were older (64 [SD 9] vs 58 [SD 13] years,  $p=0.001$ ), more likely to be diabetics (22% vs 6%,  $p=0.001$ ), smokers (11% vs 5%,  $p=0.027$ ), and were treated less frequently with methotrexate (4% vs 13%,  $p=0.002$ ), but did not differ for hypertension, hyperlipidaemia, prior CV disease nor RA characteristics. Data on immunoglobulins at baseline and after the first cycle were available in the first instance in 287/434 patients. There were no significant differences in baseline immunoglobulin levels between patients with MACE and those without. However, the proportion of patients with MACE was significantly lower among those who had a reduction in their IgM levels from baseline (5% vs 21%,  $p=0.006$ ), but not for IgG or IgA. No significant differences in the clinical profile of patients with decreased IgM and those without were observed.

**Conclusions:** These preliminary data suggest decrease of IgM is associated with decreased risk of MACE in RA patients treated with RTX. Planned analysis on serial Ig with cumulative RTX exposure will clarify this initial observation. Whether and how any such association is related to a specific RTX-mediated effect and/or the overall reduction in the inflammatory burden deserves further investigation.

**Disclosure of Interest:** None declared

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### THU0137 RHEUMATOID ARTHRITIS AS AN EMERGENCY DEPARTMENT RISK FACTOR FOR ACUTE CORONARY SYNDROME

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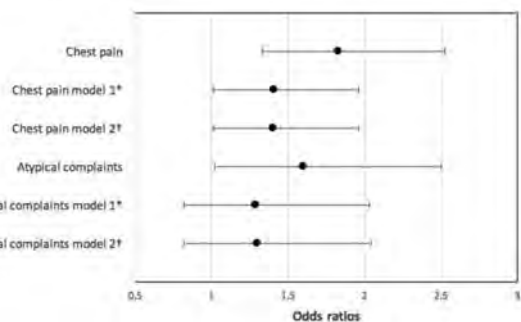
**Background:** In rheumatoid arthritis (RA), the risk of myocardial infarction (MI) is 1.5–2.0 times higher than for the general population. However, it is unknown whether RA is a risk factor also in high-risk populations, such as among patients subjected to a cardiac diagnostic work-up at the emergency department (ED).

**Objectives:** To study 1) whether RA is a risk factor for acute coronary syndrome (ACS) in a population-based sample of individuals seen in the ED, and 2) how any association with RA relates to the presence of chest pain.

**Methods:** A total of 96 220 patients (of whom 1 312 had RA) seen in the ED of the four hospitals in the larger Stockholm area, due to chest pain and/or tested for

troponin T, were identified through records of ED visits and cross-referenced to other registers. The outcome measure was ACS, defined as a discharge diagnosis of MI, unstable angina requiring urgent revascularisation, or death within 30 days (for directly discharged only). The association between RA and the outcome was assessed using logistic regression.

**Results:** ACS was more common in patients with RA (4.7%) than in subjects without RA (3.3%) – but this difference was largely attributable to RA patients being older and, upon taking age and gender into account, not statistically significant ( $p=0.13$ ). Overall and across all individuals with chest pain and/or a troponin T test taken, RA was not associated with ACS when adjusting for age, demographics and comorbidity, odds ratio (OR) 1.24, 95% confidence interval (CI): 0.95–1.61. In analyses restricted to patients presenting with chest pain (irrespective of troponin T test status,  $n=49$  283), a significant association between RA and ACS was observed (adjusted OR 1.40 95% CI 1.01–1.96).



**Figure 1 Odds ratios for myocardial infarction (MI) in rheumatoid arthritis (RA) patients compared with unexposed.** Patients with suspected MI in the emergency department (ED) grouped by presence of chest pain. Other chief complaints than chest pain labelled as atypical complaints. MI refers to combined outcome of MI or 30 day major cardiac event (MACE). \* Model 1: adjusted for age, gender, hospital, year of ED visit. † Model 2: adjusted for age, gender, hospital, year of ED visit, smoking, estimated glomerular filtration rate (eGFR), hypertension, hyperlipidaemia, diabetes mellitus, obesity, atrial fibrillation, heart failure and previous cardiovascular disease. Previous cardiovascular disease meant having one of the following diagnoses: previous stroke or MI, angina pectoris or peripheral vascular disease.

**Conclusions:** Although RA was not an independent risk factor for ACS among all patients subjected to a cardiac diagnostic work-up in the ED, RA was an independent risk factor among patients presenting with chest pain as chief complaint, an association that was not readily explained by traditional cardiovascular risk factors. The combination of RA and chest pain should thus increase the suspicion of ACS.

**Disclosure of Interest:** None declared

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#### THU0138 OCCURRENCE OF IN-STENT RESTENOSIS AFTER CORONARY DRUG-ELUTING STENT IMPLANTATION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is associated with increased risk of cardiovascular events. Thus, patients with RA have a greater chance of undergoing coronary drug-eluting stent (DES) implantation. However, it is not known whether the rate of in-stent restenosis (ISR) is also increased in RA patients.

**Objectives:** To investigate characteristics of in-stent restenosis (ISR) after drug-eluting stent (DES) implantation in patients with rheumatoid arthritis (RA), and to evaluate the effect of disease modifying anti-rheumatic drugs (DMARDs) on ISR.

**Methods:** Patients with RA who underwent DES implantation between January, 2005 and March, 2017 were included. Characteristics of the patients and the vessel lesions were reviewed retrospectively. To evaluate the effect of DMARDs on ISR, previously known ISR risk factors and ISR incidence were compared between the treated vessels of patients who did and did not receive specific DMARDs.

**Results:** In total, 30 RA patients (43 vessel lesions) were included. 4 treated vessel lesions developed ISR (4/43, 9.3%) in median 106.8 (81.1–109.0) months after DES implantation. Compared with the previous data in general population (occurrence of ISR: 3%–20%, mean time of ISR occurrence: 13 months), the

**Abstract THU0138 – Table 1.** Comparison between treated vessels in the MTX group and treated vessels in the non-MTX group

	Treated vessels in the MTX group (n=31)	Treated vessel in the non-MTX group (n=12)	p-value
<b>General characteristics</b>			
Female, n (%)	16 (51.6)	5 (41.7)	0.558
HTN, n (%)	19 (61.3)	5 (41.7)	0.245
Smoking, n (%)	Current smoker, 4 (12.9)	Current smoker, 1 (8.3)	0.615
Statin, n (%)	27 (87.1)	12 (100.0)	0.563
Other csDMARDs, n (%)	26 (83.9)	12 (100.0)	0.300
DAS28-CRP	1.54 (1.36–1.90)	1.51 (1.25–1.93)	0.547
<b>Risk factors of ISR</b>			
Age (year)	68.0 (60.0–71.0)	65.5 (59.0–73.0)	0.820
DM, n (%)	13 (41.9)	5 (41.7)	0.987
Vessel disease, n (%)	1-vessel disease, 13 (41.9) 2-vessel disease, 13 (41.9) 3-vessel disease, 5 (17.2)	1-vessel disease, 2 (16.7) 2-vessel disease, 8 (66.7) 3-vessel disease, 2 (16.7)	0.305
Ostial lesion, n (%)	3 (9.7)	2 (16.7)	0.608
LAD involvement, n (%)	18 (58.1)	4 (33.3)	0.146
Multiple lesions, n (%)	10 (32.3)	7 (58.3)	0.168
Type of DES, n (%)	Zotarolimus, 9 (29.0) Everolimus, 8 (25.8) Sirolimus, 12 (38.7) Paclitaxel+Cilostazol, 1 (3.2) Biolimus, 1 (3.2)	Zotarolimus, 1 (8.3) Everolimus, 6 (50.0) Sirolimus, 3 (25.0) Paclitaxel+Cilostazol, 2 (16.7) Biolimus, 0 (0.0)	0.161
Diameter (mm)	3.00 (3.00–3.50)	3.00 (2.81–3.00)	0.243
Length (mm)	29.0 (24.0–48.0)	21.0 (15.0–30.3)	0.018
ISR, n (%)	0 (0.0)	4 (33.3)	0.004

incidence was similar, but the time to ISR occurrence was much longer. In the comparison of patients receiving MTX ( $n=31$  vessel lesions) and those not receiving MTX ( $n=12$  vessel lesions), the ISR incidence was significantly different [0/31 (0.0%) vs. 4/12 (33.3%),  $p=0.004$ ].

**Conclusions:** ISR after DES implantation in RA patients occurs in a similar rate, but after a much longer period of time than in the general population. Administration of MTX in patients with RA might have potential benefit to prevent ISR after DES implantation.

**Acknowledgements:** None.

**Disclosure of Interest:** None declared

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#### THU0139 INCREASED HOMOCYSTEINE LEVEL FOR 7 YEARS IN PATIENTS WITH RHEUMATOID ARTHRITIS: TOMORROW STUDY

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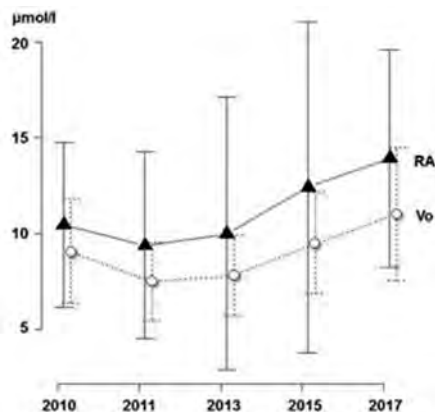
**Background:** Osteoporosis is a disease in which not only bone density but also bone quality is low. Patients with rheumatoid arthritis (RA) are at higher proven risk of osteoporosis. Increased homocysteine (Hcy), one of the main markers of bone quality, is caused by insufficiency of folate or vitamin B. Elevation of Hcy inhibits physiological crosslink of collagen, which yields worse bone quality.

**Objectives:** In this study, we evaluated Hcy level as a bone quality marker in patients with RA for a period of 7 years and compared Hcy in RA patients with that in healthy volunteers (Vo).

**Methods:** We used the data for 7 years from a prospective cohort study (TOMORROW Study: UMIN000003876), which started in 2010 and compares data from RA patients with age- and sex-matched volunteer controls (Vo) recruited through mass media. Laboratory data were collected for all participants, including bone metabolic markers (urinary pentosidine, Hcy, collagen type 1 crosslinked N-telopeptide (NTX), and osteocalcin) and anthropometric parameters. Bone mineral density (BMD) of the lower leg was determined using whole-body dual-energy X-ray absorptiometry (DXA). Their parameters were compared with those of healthy controls, and multiple regression analysis was carried out

only in the RA population. In RA patients, treatment regimen and Disease Activity Score 28 were recorded.

**Results:** There were 413 participants (208 RA patients and 205 in the Vo group; mean age, 58 years) enrolled in the study, 349 of whom were female. In RA patients (mean disease duration, 13 years), bone density was significantly lower ( $p < 0.001$ , repeated-measures ANOVA) and Hcy ( $p < 0.0001$ , repeated-measures ANOVA) was higher in comparison with the Vo group during the 7 year study period. In the analysis of change in Hcy level over 7 years, "RA" and "time" were found to interact with each other ( $p = 2.58e-7$ , repeated-measures ANOVA) (figure 1). Multiple linear regression analysis in the RA population revealed a relationship between the level of Hcy and MTX dose at baseline ( $p = 0.048$ ), but no relationship between the level of Hcy and MCV ( $p = 0.165$ ).



**Abstract THU0139 – Figure 1.** Homocysteine level during the study period in the patients with rheumatoid arthritis (RA) and healthy volunteer (Vo)

**Conclusions:** MTX intake leads to folate deficiency, which is thought to cause elevation of the Hcy level. Ageing is another significant factor related to Hcy increase.

**Acknowledgements:** We thank Atsuko Kamiyama and Tomoko Nakatsuka for serving as research coordinators in terms of recruiting participants, collecting data and managing the quality of the data.

**Disclosure of Interest:** None declared

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#### THU0140 EFFECTS OF STATIN-TREATMENT ON CORONARY PLAQUES IN PATIENTS WITH INFLAMMATORY JOINT DISEASES

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**Background:** Statins have an established preventive effect on coronary artery disease in the general population. The effect of statins on coronary plaque progression and characteristics in patients with inflammatory joint diseases (IJD) is unknown.

**Objectives:** Our aim was to evaluate the change in coronary atherosclerosis in long-term statin-treated patients with IJD.

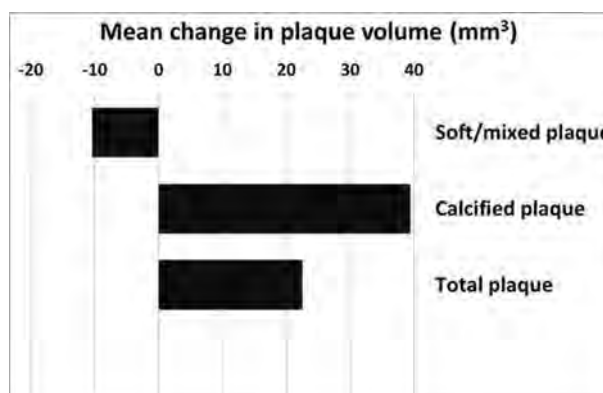
**Methods:** Sixty-eight patients with IJD and carotid artery plaque, underwent coronary computed tomography angiography before and after 4.7 (range 4.0–6.0) years of statin treatment. The treatment target for low density lipoprotein cholesterol (LDL-c) was  $\leq 1.8$  mmol/L. Changes in coronary artery calcification (CAC) and coronary artery plaque volume (calcified, mixed/soft and total) from baseline to follow-up were assessed using the 17-segment model of the American Heart Association. Linear regression analysis was used to identify predictors of atherosclerotic progression.

**Results:** Coronary plaques were present in 42% of the patients at baseline and in 51% at follow up. Mean CAC score increased with  $173 \pm 284$ , calcified plaque volume with  $39.4 \pm 78.3$  mm<sup>3</sup> and total plaque volume with  $22.8 \pm 54.6$  mm<sup>3</sup> ( $p \leq 0.01$ , for all) (figure 1). Mean mixed/soft plaque volume decreased with  $-10.4 \pm 27.5$  mm<sup>3</sup> ( $p \leq 0.01$ ). At follow-up, 51% of the patients had obtained LDL-c treatment target. Compared to patients above LDL-c target, patients with an LDL-c  $\leq 1.8$  mmol/L experienced reduced median progression of both CAC ( $21^{2-143}$  vs.  $69$  [ $16-423$ ],

$p < 0.01$ ) and total plaque volume ( $0.08$  [ $-1.0-13.9$ ] vs.  $13.0$  [ $0.0-60.8$ ],  $p = 0.02$ ) (table 1).

	LDL $\leq$ 1.8 mmol/L n=34	LDL $>$ 1.8 mmol/L n=34	p-value*
LDL-c level baseline, mean $\pm$ SD	3.7 $\pm$ 0.9	4.4 $\pm$ 1.0	<0.01
LDL-c level follow-up, mean $\pm$ SD	1.5 $\pm$ 0.2	2.4 $\pm$ 0.7	<0.01
Change LDL-c level, mean $\pm$ SD	-2.2 $\pm$ 0.9	-1.9 $\pm$ 1.3	0.38
Change in CAC, median (IQR)	21 (2-143)	69 (16-423)	<0.01
Change in soft/mixed plaque volume, median (IQR)	0 (-3.5-0.0)	0 (-15.7-0.0)	0.71
Change in calcified plaque volume, median (IQR)	1.7 (0.0-17.3)	13.4 (1.5-107.6)	0.02
Change in total plaque volume, median (IQR)	0.08 (-1.0-13.9)	13.0 (0.0-60.8)	0.02

\*independent samples t-test



**Abstract THU0140 – Figure 1.** Mean change in plaque volume (mm<sup>3</sup>)

**Conclusions:** We revealed a progression of atherosclerotic plaque volume in statin-treated patients with IJD, mainly due to calcifications. However, soft, unstable plaques were reduced, probably as a result of an alteration in plaque composition from mixed/soft plaques into calcified plaques. Patients with recommended LDL-c levels at follow-up experienced a reduced atherosclerotic progression compared to patients with LDL-c levels above the treatment target. Our results support the importance of treatment to guideline recommended lipid targets in IJD patients.

**Disclosure of Interest:** None declared

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#### THU0141 LONG-TERM EFFECTS ON BONE MINERAL DENSITY AFTER FOUR YEARS OF TREATMENT WITH TWO INTENSIVE COMBINATION STRATEGIES, INCLUDING INITIALLY HIGH DOSE PREDNISOLONE, IN EARLY RHEUMATOID ARTHRITIS PATIENTS: THE COBRA-LIGHT TRIAL

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**Background:** Combinatie therapie Bij Reumatoïde Artritis (COBRA)-light therapy (methotrexate and initially 30 mg/day prednisolone) has proven to be non-inferior to COBRA therapy (methotrexate, sulfasalazine and initially 60 mg/day prednisolone) in the first year of treatment of early rheumatoid arthritis (RA) patients.

**Objectives:** This study assessed changes in bone mineral density (BMD) after four years in early RA patients initially randomised to one year of COBRA or COBRA-light therapy.

**Methods:** In the open-label, randomised, non-inferiority trial patients were assigned to COBRA or COBRA-light therapy. After one year, treatment was at the discretion of the treating rheumatologists. BMD in g/cm<sup>2</sup> was measured at baseline, after one, two and four years at total hip, femoral neck, and lumbar spine with dual-energy X-ray absorptiometry (DXA).

**Results:** Of the 164 original patients, 154 could be assessed after a follow-up of four years (range 34 to 74 months); 68% were female; mean (SD) age at follow-up 52<sup>13</sup> years. In the COBRA-light group, 11% of the patients used bisphosphonates after four years; the mean cumulative prednisolone dosage was 2.6 g (inter quartiles: 1.9; 5.9) and 49% of the patients had minimal disease activity (DAS44 <1.6).



**Abstract THU0141 – Table 1.** BMD values and changes in BMD during four years of treatment

	Baseline	COBRA-Light		Baseline	COBRA		Mean difference	GEE analyses CI	P
		Bone Loss			Bone Loss				
		Absolute	% of baseline		Absolute	% of baseline			
Lumbar Spine	1.10 (0.15)	-0.01 (0.08)	-0.5	1.12 (0.18)	-0.01 (0.08)	-1.0	-0.01	-0.03–0.02	0.56
Total Hip	0.96 (0.13)	-0.03 (0.05)	-3.3	0.95 (0.15)	-0.02 (0.05)	-1.7	-0.01	-0.03–0.02	0.56
Femoral Neck	0.88 (0.12)	-0.03 (0.05)	-3.7	0.90 (0.16)	-0.03 (0.06)	-3.0	-0.01	-0.03–0.02	0.59
								0.00–0.02	0.05+
								-0.02–0.00	0.05+
								-0.03–0.00	0.02+
								-0.04–0.02	0.38
								-0.04–0.01	0.37
								-0.04–0.01	0.29

In the COBRA group, these numbers were 10%, 3.2 g (2.5; 6.2) and 49%, respectively. At the lumbar spine, both groups showed no significant decline in BMD over four years and no difference between treatment groups in BMD change (table 1). At the hips, 1.7% to 3.7% BMD loss over four years was found with slightly but significantly more loss in the COBRA-light group (table 1).

Outcomes are mean (SD) unless stated otherwise. BMD in g/cm<sup>2</sup>. +Significant difference between COBRA-light and COBRA on average over time. \*Adjusted for bisphosphonate usage (yes vs no). \*\*Adjusted for bisphosphonate usage (yes vs no), cumulative prednisolone usage, age, gender and disease activity based on DAS44 (DAS44 <1.6 in remission vs DAS44 ≥1.6 not). CI, confidence interval; GEE, Generalised Estimating Equations; T4, measurement after four years; SD, Standard Deviation.

**Conclusions:** In modern treat-to-target management of RA, including bone surveillance, a high starting dose of prednisolone, either 30 or 60 mg/day, was not associated with a dramatically increased bone loss at the lumbar spine, and minor losses at the hip over four years.

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#### THU0142 THE PROGNOSIS OF HEART FAILURE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Heart failure (HF) is a condition with high rates of hospital admission and mortality. The impact of rheumatoid arthritis (RA) and its treatment on the prognosis of prevalent HF has been insufficiently studied.

**Objectives:** To evaluate deterioration of HF and mortality in patients with RA and concomitant HF.

**Methods:** The prospectively followed cohort of the German register RABBIT continuously includes RA patients with a new start of a DMARD after at least one csDMARD failure. Among all patients enrolled between 05/2001 and 10/2017 (n=15,037) patients with prevalent HF were selected (n=393). HF patients were followed until their end of observation or death. Deterioration of HF requiring hospital admission, and death were analysed as composite outcome. Incidence rates (IR) were calculated for current treatment at time of event (9 months risk window after last infusion of rituximab). Generalised estimation equations (GEE) were used to investigate risk factors for the composite outcome. To avoid uncertainties when allocating therapies, only treatment episodes >6 months were included in the GEE analysis. Missing values (DAS28, CRP, physical function) were addressed by multiple imputations.

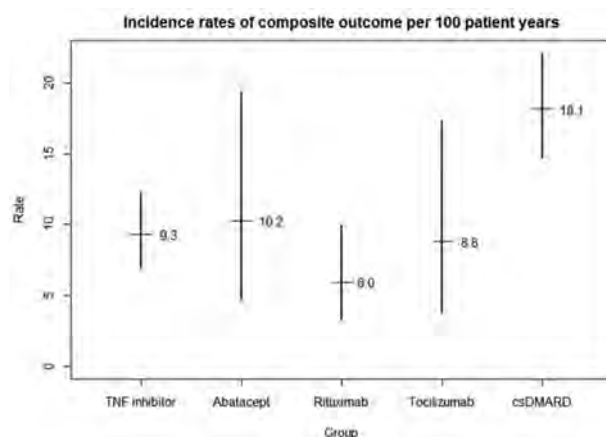
**Results:** Of the 393 patients with prevalent HF and 1490 patient years (PY) of follow-up, a total of 131 patients had at least one outcome (19 HF deteriorations, 123 deaths). Infections (30%) and cardiovascular events (25%) were most frequently

reported as causes of death. The mean time until deterioration/death was 30/35 months. At baseline, patients with an event were older (69 vs. 67 years), more often male (43 vs. 32%), rheumatoid factor positive (80 vs. 74%), had higher CRP-values (39 vs. 23 mg/L) and a worse FFbH (% of physical function: 43 vs. 50) than patients without event. All HF patients had high numbers of comorbidities (mean of 7/6 in patients with/without event).

Crude IR were highest in patients under csDMARD only exposure (figure 1). IR were similar during the first 3 or 6 months after start of treatment and thereafter (data not shown). Biologic treatment was not associated with the outcome (table 1). Male gender, higher age, a higher glucocorticoid dose, worse physical function and elevated CRP under treatment were significantly associated with hospitalisation due to HF or a fatal outcome.

**Abstract THU0142 – Table 1.** Adjusted relative risk of HF deterioration or death in RA patients with underlying HF. CRP, FFbH and glucocorticoid doses were averaged for the time of a therapy episode.

	Relative risk	95% Confidence interval	
csDMARD	Ref.		
TNF inhibitors	0.7	0.4	1.3
Abatacept	0.8	0.3	2.3
Rituximab	0.5	0.2	1.1
Tocilizumab	0.9	0.3	2.6
Baseline age per 5 years	1.3	1.1	1.5
Male vs. female	2.4	1.4	3.9
CRP per 5 mg/L	1.03	1.004	1.1
% of physical function per 10 points	0.9	0.8	0.999
Sum of baseline comorbidities	1.1	0.96	1.3
Glucocorticoids per 5 mg/d	1.4	1.03	1.8
Smoker vs non-smoker	1.7	1.02	3.0



**Abstract THU0142 – Figure 1.** Incidence rates of composite outcome per 100 patient years

**Conclusions:** Patients with RA and HF have an unfavourable prognosis. One third of them were hospitalised for HF or died during follow-up. In addition to patient characteristics, smoking, insufficiently controlled inflammation and treatment with glucocorticoids significantly increased the risk of hospitalisation or death.

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**THU0143 VASCULAR WALL INFLAMMATION IN RHEUMATOID ARTHRITIS PATIENTS DECREASES AFTER 6 MONTHS OF ANTI-INFLAMMATORY THERAPY WITH METHOTREXATE OR ADALIMUMAB AS MEASURED BY 18F-FDG-PET/CT**

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**Background:** Patients with rheumatoid arthritis (RA) have an elevated cardiovascular (CV) disease risk, mostly explained by both an increased prevalence of traditional CV risk factors and the presence of systemic inflammation that accelerates atherosclerosis. There is accumulating evidence that anti-inflammatory treatment for RA reduces this CV risk. A non-invasive tool for detecting vascular wall inflammation in atherosclerosis is 18F-Fluorodeoxyglucose-Positron Emission Tomography/Computed Tomography (18F-FDG-PET/CT).

**Objectives:** To study the effect of anti-inflammatory treatment with methotrexate (MTX) or adalimumab on vascular wall inflammation in RA assessed by 18F-FDG-PET/CT.

**Methods:** 18F-FDG-PET/CT was done in patients with active early RA starting MTX (n=25) and active established RA starting adalimumab (n=24) before and after 6 months of therapy, and in osteoarthritis controls (OA; n=29). 18F-FDG uptake in arterial wall was determined by standardised uptake values (SUV). Volumes of interest covering the arterial segment with the highest 18F-FDG were defined to derive the maximum SUV (SUVmax) in the ascending, descending and abdominal aorta and the aortic arch. Global arterial uptake was estimated using the mean SUVmax of the four arterial segments.

**Results:** Mean age was 65±9 for early RA, 61±7 for established RA and 63±5 years for OA controls. Median disease duration was 2.1 (interquartile range (IQR) 1.3–3.3) weeks for early RA and 6.9 (IQR 1.8–13.9) years for established RA. DAS28 was 4.9±1.0 and 4.4±1.0 at baseline and declined to 3.1±1.3 and 2.8±1.4 after 6 months therapy, respectively.

At baseline mean SUVmax was 1.86±0.38 for early RA, 1.68±0.43 for established RA and 1.56±0.41 for OA controls. SUVmax tended to decline more in early RA patients when compared to established RA (1.86±0.38 to 1.79±0.43 (-3.7%) and 1.68±0.43 to 1.63±0.43 (-3.0%), respectively). SUVmax in most arterial segments declined after 6 months of therapy (table 1). The most prominent decline in SUVmax was in the abdominal aorta in established RA patients (-9.8%).

**Conclusions:** A decline in global arterial SUVmax and in most of arterial segments was found in both early and established RA patients after 6 months of MTX and/or adalimumab, suggesting that anti-inflammatory therapy with either MTX and/or adalimumab decreases arterial wall inflammation and thus CV risk in RA.

**Disclosure of Interest:** None declared

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**Abstract THU0143 – Table 1.** Arterial 18F-FDG uptake in RA patients before and after 6 months of therapy

	OA		Early RA 6 months MTX		Established RA 6 months adalimumab		
	Baseline	Baseline			Baseline		
SUVmax ascending aorta	1.55±0.44	1.82±0.38	1.77±0.38	-2.7%	1.69±0.61	1.60±0.44	-5.3%
SUVmax descending aorta	1.57±0.42	1.93±0.53	1.81±0.47	-6.2%	1.65±0.39	1.71±0.47	+3.6%
SUVmax abdominal aorta	1.62±0.43	1.84±0.44	1.81±0.58	-1.6%	1.73±0.61	1.56±0.45	-9.8%
SUVmax aortic arch	1.51±0.48	1.85±0.48	1.76±0.45	-4.9%	1.66±0.40	1.64±0.59	-1.2%
Mean SUVmax over 4 segments	1.56±0.42	1.86±0.38	1.79±0.43	-3.7%	1.68±0.43	1.63±0.43	-3.0%

**THU0144 PERFORMANCE OF THE ERS-RA CARDIOVASCULAR RISK PREDICTION TOOL: EXTERNAL VALIDATION IN A LARGE SWEDISH COHORT WITH RA**

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**Background:** Risk prediction tools developed for the general population tend to underestimate the risk of cardiovascular (CV) disease in patients with RA<sup>1</sup>. An accurate and RA-specific CV risk prediction tool would ideally be integrated as a routine part of clinical practice in rheumatology, to identify patients with increased CV risks. For example, 10 year CV risks above 7.5%, or 10%, could warrant specific preventive measures<sup>2,3</sup>. The ERS-RA was derived and internally validated in the US Corona RA registry<sup>4</sup>. ERS-RA estimates the 10 year CV risk using dichotomous clinical variables, and includes variables on RA disease severity and activity.

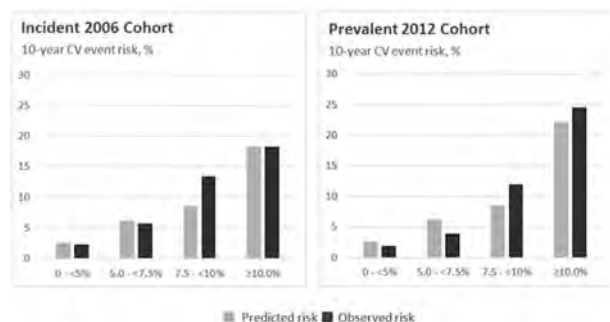
**Objectives:** To assess the external validity of the ERS-RA in Swedish cohorts of patients with RA, with focus on the risk intervals of main clinical interest.

**Methods:** We identified two cohorts of patients with RA: (i) an "incident 2006 cohort" with RA patients in the Swedish Rheumatology Register from Jan 1, 2006 – Dec 31, 2011 who were also in the EIRA case-control study (n=2047, mean age 55±13 years, 72% women), and (ii) a "prevalent 2012 cohort" that included all RA patients in the Swedish Rheumatology Register between Jan 1, 2012 – Dec 31, 2015 (n=14485, mean age 61±14 years, 74% women). The 10 year CV risk was estimated using ERS-RA. Patients with a history of myocardial infarction or stroke were excluded. All patients were followed for the first of any of the following: a CV event (myocardial infarction, stroke, cardiovascular death), death, 10 years of follow-up, or Dec 31, 2015. Ten-year CV rates were expressed using the Kaplan-Meier method. In the prevalent 2012 cohort, the 10 year event rates were extrapolated from the observed (maximally four-year) rates.<sup>5</sup> The C-statistic was estimated to assess discrimination. A measure of model calibration, the observed event rates were compared with the mean predicted 10 year risks.

**Results:** The C-statistic was 0.75 for both cohorts. Most patients had an estimated CV risk <5% or of >10% (See table 1). An accurate risk prediction was observed for estimated risks in the intervals <5%, and 5.0 to <7.5%. ERS-RA underestimated risk in the interval 7.5 to <10% (see table 1 and figure 1).

**Abstract THU0144 – table 1.** and figure 1. Comparisons of the mean estimated and the observed 10-year CV risks within groups of estimated risk levels.

	Groups of estimated 10 year risk	N patients (%)	Mean estimated 10 year risk (%)	Observed 10 year rate (%)	Difference Observed rate – Mean estimated risk
<b>Incident 2006 Cohort</b>	<5%	884 (48)	2.5	2.3	-0.2
	5.0 to <7.5%	282 (15)	6.2	5.7	-0.5
	7.5 to <10%	43 (2)	8.6	13.4	4.8
<b>Prevalent 2012 Cohort</b>	≥10.0%	638 (35)	18.3	18.3	0
	<5%	4691 (32)	2.7	1.9	-0.8
	5.0 to <7.5%	1604 (11)	6.2	4.0	-2.2
	7.5 to <10%	1485 (10)	8.6	12.0	3.4
	≥10.0%	6705 (46)	22.2	24.5	2.3



**Conclusions:** In a Swedish population with RA, ERS-RA performed well in identifying patients with a very low and very high CV 10 year CV risk. In clinical routine practice, ERS-RA could be used to identify low and high risk individuals, who might be considered for additional CV risk factor evaluation and subsequent intervention.

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THU0145

#### CHANGES IN BONE METABOLISM AND TRABECULAR BONE SCORE IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is a systemic inflammatory disease which can lead to bone and joint damage including local bone erosion and general osteoporosis. Dual X-ray Absorptiometry (DXA) is the established standard for measuring Bone Mineral Density (BMD), but it does not provide any informations about the bone microarchitecture, which is an essential parameter to define bone strength. The Trabecular Bone Score (TBS) is a new structural parameter that can be obtained by DXA scanning and it is related to bone microarchitecture and provides data on bone quality irrespective of bone density.

**Objectives:** The aim of this study is to evaluate the changes of BMD, TBS and bone remodelling parameters in subjects with recent-onset rheumatoid arthritis, treated or not with high doses of glucocorticoid, compared to age and sex matched healthy controls

**Methods:** The study included 42 subjects (31F, 11M), fulfilling the 2010 EULAR/ACR diagnostic criteria for RA and recent onset of joint symptoms (<6 months of synovitis) (Early RA), which were treated according to the current EULAR guidelines. As control group, 25 sex and age matched healthy subjects (21F, 4 M) were recruited. Post-menopausal women were excluded from the study. Lumbar spine and femoral BMD and TBS were evaluated at recruitment and after 12 months. The following parameters of bone remodelling and regulatory cytokines were measured at recruitment and every 3 months for 12 months: type I N-terminal propeptide (P1NP), osteocalcin, alkaline phosphatase, sclerostin, dickkopf-1 (DKK1), osteoprotegerin (OPG), Receptor Activator of Nuclear Factor Kappa-B ligand (RANKL). The clinical and demographic characteristics, including disease activity index and quality of life, were also evaluated

**Results:** No difference in BMD (spine and hip) and TBS values were detected between Early RA and control group at recruitment time (0,893 g/cm<sup>2</sup> vs 0,972 g/cm<sup>2</sup>; 0,790 g/cm<sup>2</sup> vs 0,770 g/cm<sup>2</sup>; 1598 vs 1521 respectively). After 12 months, the BMD at spine and hip and TBS values were significantly lower in patients with Early RA compared to healthy controls (0,601 g/cm<sup>2</sup> vs 1,011 g/cm<sup>2</sup>; 0,560 g/cm<sup>2</sup> vs 0,981 g/cm<sup>2</sup>; 1335 vs 1488 respectively). After 12 months, patients treated with high-dose of corticosteroids showed lower mean TBS values compared to patients untreated or treated with low-dose of corticosteroids (1,210 vs 1,430), whereas BMD values were similar. No differences were observed in osteocalcin and ALP between Early RA patients and healthy subjects at any time. Compared to healthy subjects, Early RA patients showed a significantly higher RANKL/OPG ratio and DKK1 serum levels, beginning from 6 month of observation, that correlated with disease activity (DAS28)

**Conclusions:** These preliminary data confirm that even in the early stages of disease, RA exert a negative effect on bone metabolism, whose pathogenesis is very complex and involves regulatory cytokines of bone homeostasis. This lead to a reduction of BMD and to changes of parameters of bone quality (TBS), that are more pronounced in patients treated with higher doses of corticosteroids compared to patients treated with lower corticosteroid doses

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**Disclosure of Interest:** None declared

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THU0146

#### GLYCEMIC PROFILE AND INSULIN RESISTANCE IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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**Background:** In established rheumatoid arthritis (RA) there is a high incidence of patients with increased insulin resistance, which can favour the development of Diabetes Mellitus (DM) and the appearance of cardiovascular complications. These aspects, however, have not been studied in depth in patients with early rheumatoid arthritis.

**Objectives:** To describe the glycemic profile and insulin resistance (IR) in patients with early diagnosis of RA who had not received any background treatment or steroids.

**Methods:** Observational study in which patients were included 18 years old, diagnosed with RA according to criteria <sup>ACR 1987</sup> and/or <sup>ACR-EULAR 2010</sup> from the service of Arthritis of Recent Beginning of the Hospital Universitario Central de Asturias, between December 2016 and December 2017. In the basal visit, values of insulin, glucose, fasting glycosylated haemoglobin (HbA1c), body mass index (BMI) and abdominal perimeter were collected. In addition, RI and beta cell dysfunction were estimated with HOMA-IR and HOMA-B respectively.

**Results:** 66 patients were collected, of which 4 were excluded because they were known to be DM and 17 because they had not completed the analytical studies. Of the 45 that were finally studied, 80% (36 patients) are women, the mean age of 54.13±12.9 years, the progression of the disease to diagnosis is 22.8±15.3 weeks, 46.7% (21 patients) are FR and ACPA positive, and the mean disease activity measured by SDAI is 28.03±12.2.

Eighteen patients (45%) and 71.1% (31.5 patients) had HOMA-IR, with both 17 patients (37.7%) showing a statistically significant association of SDAI>11 (p=0.001), BMI >24 (p=0.03) and an increased abdominal perimeter (p=0.013).

Based on the WHO's diagnostic criteria for DM, 2 patients (4.4%) were diagnosed with DM (all based on a previously unknown HbA1c>6.5%) and 21 (46.7%) as pre-diabetic (14 with glucose between 100–125, 16 with HbA1c>5.7 and 9 patients with both alterations). In this subgroup the mean of HOMA-IR and HOMA-B was higher than the mean of the complete sample, 3.4 and 139 respectively. These patients compared with the rest of the sample had a statistically significant association with BMI >24 (p=0.07), SDAI >11 (p=0.01).

No correlations were found between these metabolic alterations and the sex, age or positivity for RH.

**Conclusions:** In patients with AR of less than one year of evolution and who have not received previous treatment with FAME or steroids, a high percentage of RI, pancreatic B cell dysfunction and alterations of the glycemic profile are detected. These alterations are significantly correlated with the presence of overweight and obesity, as well as with the high degree of activity of the disease. Follow-up of these patients is necessary to determine the effect of therapy for rheumatoid arthritis on these metabolic alterations.

**Disclosure of Interest:** None declared

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THU0147

#### TREATMENT RESPONSE IN ANTIDEPRESSANTS-TREATED RA PATIENTS WITH DEPRESSIVE AND ANXIETY DISORDERS RECEIVING DMARDS AND BIOLOGICS ON A FIVE-YEAR FOLLOW-UP

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**Background:** Anxiety and depressive disorders (ADD) significantly affect disease activity and prognosis, treatment compliance and response in rheumatoid



arthritis (RA) patients (pts). Personalised antidepressant treatment of ADD could be beneficial in managing of RA in this group of patients.

**Objectives:** To compare treatment response and remission rates in 4 groups of RA patients with ADD treated with DMARDs, biologics and antidepressants at the endpoint of a prospective 5 years study.

**Methods:** 128 RA-pts were enrolled in pilot study. All of them met the full ACR criteria for RA classification. 86% RA-pts were women with a mean age of 47.4±1.0 (M±m) yrs. RA activity was evaluated with DAS28 and SDAI, remission was defined according to DAS28 (<2,6) and ACR/<sup>EULAR 2011</sup> (SDAI <3,3) remission criteria, response to treatment was classified according to EULAR and ACR/<sup>EULAR 2011</sup> (SDAI) response criteria. Average DAS28 and SDAI scores at baseline were high and moderate (5.25±0.16 and 33.5±1.38 (M±m)). 62.6% RA-pts were taking prednisone (9 (5; 10) mg/day (Me (25%; 75%)), 75,1% - DMARDs, 32% - biologics (rituximab – 12,5%, anti-TNF-α – 11%, anti-IL6 – 6,2%). ADD were diagnosed in 123 (96,1%) of RA-pts by psychiatrist in accordance with ICD-10 in semi-structured interview. Severity of anxiety and depression was evaluated with Montgomery–Asberg Depression Rating Scale (MADRS) and Hamilton Anxiety Rating Scale (HAM-A). RA-pts with ADD were divided into the following treatment groups: 1 – DMARDs (n=39), 2 – DMARDs+antidepressants (sertraline or mianserine) (n=43), 3 – DMARDs+biologics (n=32), 4 – DMARDs+biologics+ antidepressants (sertraline or mianserine) (n=9). Biologics treatment duration varied from 1 to 6 years, antidepressants – from 6 to 96 weeks. Differences in baseline disease activity scores were significant only in DAS28 for group 1 versus group 4 (4.95 ±0.24 vs 6.45±0.52; p=0,026).

**Results:** The RA-treatment efficacy was evaluated at 5 years endpoint in 83 RA-pts. The percentage of patients who achieved good response according to EULAR (DAS28) criteria was higher (p<0,05) in groups 2 (41,4%) and 3 (28,6%) vs DMARDs (4,2%) group. In biologics groups (3 and 4) good response according to SDAI criteria was more (p<0,05) prevalent (52,4% and 88,8% respectively) than in group 2 (25%), and vice versa for moderate response. In addition, patients in biologics groups achieved good response significantly more often than moderate (p<0,05). EULAR and SDAI nonresponse rates were significantly lower in 2–4 vs DMARDs groups. Patients treated with DMARDs+antidepressants achieved remission significantly more often (p=0,024) than ones receiving DMARDs only. Remission by ACR/<sup>EULAR 2011</sup> criteria was reached exclusively by DMARDs+antidepressants patients.

**Conclusions:** our findings demonstrate that successful treatment of ADD with antidepressants provides more significant positive influence on treatment response to DMARDs and biologics in rheumatoid arthritis patients on a five-year follow-up. Diagnosis and treatment of ADD would potentially play an important role in individualised management of RA patients

**Disclosure of Interest:** None declared

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#### THU0148 SCREENING SYSTEM FOR EARLY ARTHRITIS WITH HEALTH PROFESSIONAL ASSISTANTS – A PROJECT OF THE T2T INITIATIVE IN GERMANY

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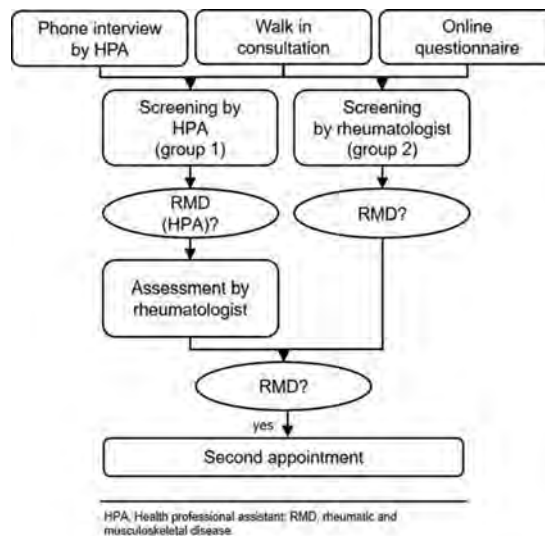
**Background:** Early stages of rheumatic diseases are still difficult to diagnose and treatment is delayed often due to the lack of practicing rheumatologists. Therefore, novel ways of diagnostic strategies are urgently needed.

**Objectives:** Evaluation of a structured screening system for selecting and treating patients (pts) with rheumatoid arthritis (RA) or rheumatic and musculoskeletal diseases (RMD) with health professional assistants (HPA, trained specialist nurses).

**Methods:** 177 pts visited a screening appointment for early arthritis (EA) between February 2015 and July 2016 in a specialised EA clinic. Inclusion criterion was arthritis in ≥one joint for less than one year. Pts had three options for accessing the screening: phone call with qualified HPAs, online questionnaire or attending a walk in clinic (figure 1). Upon screening, all pts filled in a digital questionnaire about their symptoms and comorbidities. In group 1 an HPA performed the joint count and analysed the questionnaire for 116 pts before giving a suspected diagnosis. Subsequently, a rheumatologist saw these pts and also made a suspected diagnosis. 61 pts in group 2 were examined directly by a rheumatologist. In case of a suspected RMD or abnormal laboratory parameters, pts received a new appointment for completing diagnostics, or in acute cases, treatment was started immediately. All pts had the opportunity of a new appointment in case of persistency or worsening of the symptoms.

**Results:** Pts had a mean age of 50.9±15.2 years and 135 (76.3%) pts were female. 160 (90.4%) pts had access to the screening by phone call. 10 (5.7%) pts used the online questionnaire, and 7 (3.9%) pts used the walk-in consultation. Pts waited 3.1±1.8 weeks for a screening appointment. According to the digital questionnaire pts had symptoms for 58.1±90.5 weeks at the screening appointment.

34 (56.7%) pts with RMD visited the screening clinic within six months after symptom onset. 2 (1.7%) pts had an RMD that had not been suspected by the HPA upon screening in group 1 and subsequently received conventional disease modifying antirheumatic drugs (cDMARDs) and glucocorticoids (GC). In group 2, 3 (4.9%) pts received cDMARDs although in the screening an RMD had not been initially suspected by the rheumatologist. In total 69 (39.0%) pts finally had an RMD, whereof 43 (24.3%) pts had an RA. 44 (24.9%) pts received therapy with a cDMARDs and 6 (3.4%) had the recommendation for a therapy with cDMARDs but refused treatment. Therapy with cDMARDs started 44.8±41.9 days after screening. 21 (11.9%) pts could already start with GC at the screening appointment. 27 (15.2%) pts without a diagnosed RMD visited the rheumatologist at least twice.



**Abstract THU0148 – Figure 1.** HPA, Health professional assistant; RMD, rheumatic and musculoskeletal disease.

**Conclusions:** HPAs can select pts with RMDs efficiently in a structured screening system which leads to treating RMDs at an early stage in times of limited resources.

**Acknowledgements:** Abbvie supported the project within the T2T Initiative Germany.

**Disclosure of Interest:** None declared

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#### THU0149 TRENDS IN THE INCIDENCE OF INFECTION IN PATIENTS WITH RHEUMATOID ARTHRITIS IN SPAIN: AN OBSERVATIONAL COHORT STUDY OF HOSPITAL DISCHARGES FROM 1999 TO 2015 (TREND-AR STUDY)

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**Background:** Rheumatoid Arthritis (RA) patients are at an increased risk of infection compared with healthy individuals, related to immune dysfunction. New treatments have revolutionised RA management; however, serious infection especially in elderly remains a concern.

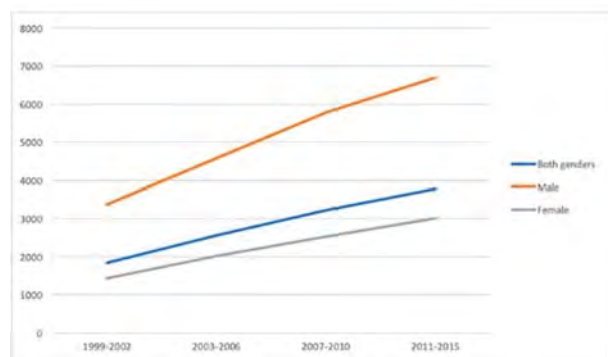
**Objectives:** To analyse the incidence and trend of hospital admissions for all infections in patients with RA in Spain during the period between 1999 and 2015.

**Methods:** This is a national retrospective population based study. We analysed a national administrative database that includes a Minimum Basic Data Set (MBDS) in all hospital admissions of patients with RA. Period: 1999 to 2015. Cases were identified by the presence of ICD9 codes. The population at risk was estimated through the population census of the National Institute of Statistics. The adjusted rates of infection were calculated, by sex and age. The trend was analysed by Generalised Linear Models (GLM). Statistical analysis was made using SPSS statistical package version 20 (SPSS Inc, Chicago, IL).

**Results:** 338.343 RA hospital admissions were detected in the study period, being 81.468 (24,07%) due to infections. The main clinical-demographic characteristics are shown in table 1:

	Women	Men	Total	1999–2002	2003–2006	2007–2010	2010–2015
<b>N (%)</b>	53 528 (65.7%)	27 939 (34.3%)	81 467 (100)	10 518	15 644	21 280	34 025
<b>Mean Age (SD)</b>	71.38 (13.3)	70.62 (12.47)	71.12 (13.02)	68.39 (12.73)	69.65 (12.93)	71.21 (13.12)	72.60 (12.89)
<b>Dead during admission, n (%)</b>	5139 (9.6)	2957 (10.5)	8096 (9.93)	ND	ND	ND	ND
<b>Mean Charlson Index (SD)</b>	2.05 (1.5)	2.45 (1.8)	2.19 (1.63)	1.90 (1.40)	2.0 (1.51)	2.18 (1.60)	2.37 (1.75)
<b>Average length of stay (SD)</b>	13.86 (16.3)	14.14 (15.5)	13.9 (16.1)	15.94 (18.84)	15.36 (17.23)	14.43 (16.77)	12.42 (13.93)

The annual age-adjusted rate of infections increased during the study period, especially in men (fig 1). The annual trend of infections age-adjusted increased during the study period 5.29%, women 5.08% and men 5.92%. For age groups the annual increase was 3.51% for 20–40 years, 3.2% for 40–60 years, 4.5% for 60–80 years and 9.27% for >80 years.



**Conclusions:** Rate of infection in RA hospitalised patients in Spain has increased during study period. The patients are progressively elderly and has more comorbidities. However the average hospital stay decrease.

**Disclosure of Interest:** None declared

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**THU0150 IMPACT OF COMORBIDITY BURDEN AND OBESITY ON THE EFFECTIVENESS OF TOCILIZUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS**

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**Background:** Few real-world studies have evaluated the impact of comorbidity burden or obesity on the effectiveness of tocilizumab (TCZ) for the improvement of rheumatoid arthritis (RA) disease activity.

**Objectives:** To compare the effectiveness of TCZ in treating RA in patients with high vs low comorbidity burden and in obese vs nonobese patients in US clinical practice.

**Methods:** Patients in the Corrona RA registry who initiated TCZ and had follow-up visits at 6 and 12 months after initiation were included. To assess the impact of comorbidity burden on TCZ effectiveness, outcomes were stratified by patients with low Charlson Comorbidity Index (CCI=1) vs high (CCI ≥2). To assess the impact of obesity, outcomes were stratified by patients with BMI <30 (nonobese) vs ≥30 (obese). The primary outcome was mean change in CDAI at 6 and 12 months. Secondary outcomes were mean change in HAQ, the proportions of patients with change ≥ the minimum clinically important difference (MCID) in CDAI and HAQ and the proportion who achieved low disease activity (LDA; CDAI≤10). Baseline demographics, clinical characteristics, disease activity and treatment history in the comorbidity and BMI cohorts were compared separately using standardised differences; characteristics with |standardised difference|>0.1 were identified as covariates for inclusion in adjusted comparisons. Outcomes were compared between cohorts using two-sample t-tests or  $\chi^2$  tests in unadjusted analyses and linear or logistic regression models to adjust for covariates.

**Results:** Of 770 patients who initiated TCZ and had CCI data available at baseline (93.8% treated with intravenous [IV] TCZ and 6.2% with subcutaneous [SC]

TCZ), 575 (74.7%) had a low CCI and 195 (25.3%) a high CCI. Patients with a high CCI were older (mean [SD] age, 61.5 [12.3] vs 56.9 [13.1] years), were more likely to be obese (52.8% vs 41.7%), had a longer disease duration (mean [SD], 12.8 [9.9] vs 11.6 [8.9] years) and had higher mean (SD) baseline CDAI (25.7 [13.4] vs 23.9 [13.9]) and HAQ (0.71 [0.57] vs 0.57 [0.51]) scores than those with a low CCI.

Of the 805 TCZ initiators with BMI data available at baseline (93.9% treated with IV TCZ and 6.1% with SC TCZ), 449 (55.8%) were not obese and 356 (44.2%) were obese. Obese patients were younger (56.7 [12.0] vs 59.0 [13.7] years), had shorter disease duration (11.4 [8.6] vs 12.6 [9.7] years) and had higher baseline CDAI (25.4 [14.3] vs 23.6 [13.4]) and HAQ (0.65 [0.53] vs 0.57 [0.53]) scores than nonobese patients.

Patients in all cohorts had improvement from baseline in CDAI at 6 and 12 months, with no significant differences between those with a low vs high CCI or between obese vs nonobese patients (table 1). Secondary outcomes yielded similar results (table 1).

**Abstract THU0150 – Table 1.** Study Outcomes at 6 and 12 Months in Patient With RA Who Initiated TCZ, Stratified by Comorbidity Burden and Obesity Status

	Comorbidity Burden				Obesity			
	Low* (CCI = 1) [n = 575]	High (CCI ≥ 2) [n = 195]	Unadjusted Difference†	Adjusted Difference‡	Nonobese* (BMI < 30) [n = 449]	Obese (BMI ≥ 30) [n = 356]	Unadjusted Difference†	Adjusted Difference‡
<b>Outcomes at 6 Months†</b>								
Change in CDAI, mean (SD)	-7.57 (13.05)	-7.72 (13.62)	-0.15 (-2.37, 2.07)	0.22 (-1.82, 2.36)	-7.77 (13.12)	-7.38 (14.05)	0.38 (-1.48, 2.26)	1.29 (0.94, 2.06)
Change in HAQ, mean (SD)	-0.05 (0.41)	-0.09 (0.43)	-0.04 (-0.11, 0.36)	0.01 (-0.09, 0.10)	-0.06 (0.41)	-0.05 (0.42)	-0.05 (-0.06, 0.06)	0.03 (-0.62, 0.29)
Change in CDAI > MCID, % patients§	51.1	44.8	0.77 (0.56, 1.07)	0.79 (0.45, 1.40)	51.2	46.8	0.83 (0.63, 1.10)	0.83 (0.61, 1.16)
Change in HAQ > MCID, % patients§	30.4	31.8	1.07 (0.75, 1.51)	0.47 (0.23, 0.98)	30.7	30.3	0.75 (0.73, 1.33)	0.86 (0.59, 1.27)
Achievement of LDA, % patients¶	24.7	21.5	0.84 (0.57, 1.24)	0.85 (0.45, 1.62)	27.0	19.7	0.66 (0.47, 0.92)	0.75 (0.48, 1.01)
<b>Outcomes at 12 Months†</b>								
Change in CDAI, mean (SD)	-8.42 (14.24)	-7.82 (14.52)	0.59 (-1.74, 2.92)	1.22 (-4.22, 1.77)	-8.24 (13.39)	-8.09 (13.27)	0.15 (-1.84, 2.14)	1.53 (-0.32, 3.39)
Change in HAQ, mean (SD)	-0.05 (0.40)	-0.11 (0.42)	-0.06 (-0.13, 0.01)	-0.06 (-0.15, 0.03)	-0.07 (0.40)	-0.04 (0.42)	-0.04 (-0.02, 0.09)	0.07 (0.01, 0.13)
Change in CDAI > MCID, % patients§	52.7	49.7	0.89 (0.64, 1.23)	0.86 (0.60, 2.13)	53.5	49.4	1.21 (0.94, 1.42)	0.72 (0.52, 1.01)
Change in HAQ > MCID, % patients§	27.7	26.7	1.11 (0.77, 1.58)	0.86 (0.42, 1.78)	27.8	26.1	1.01 (0.74, 1.38)	0.83 (0.56, 1.24)
Achievement of LDA, % patients¶	30.4	31.3	1.54 (0.73, 2.35)	1.52 (0.65, 2.71)	32.1	27.5	0.80 (0.59, 1.09)	0.75 (0.53, 1.06)

BMI, body mass index; CCI, Charlson Comorbidity Index; CDAI, Clinical Disease Activity Index; eCDAI, e-comorbidity-adjusted CDAI; HAQ, Health Assessment Questionnaire; LDA, low disease activity; MCID, minimum clinically important difference; OR, odds ratio.  
 \* Reference group.  
 † The CCI used for this analysis is a modified CCI and is the sum of prior reported comorbid conditions that are reported in Canada in the final 4th digit position, including myocardial infarction, congestive heart failure, cerebral vascular disease, cardiovascular disease, chronic obstructive pulmonary disease, specific liver disease, diabetes mellitus, leukemia, lymphoma, solid tumor cancer (excluding non-melanoma of the skin) and liver disease. The CCI also includes cardiovascular disease, which was added as 1 to account for misclassification.  
 ‡ Adjusted for age, duration of RA, race, college education, smoking status, alcohol consumption, BMI, work status, insurance type, comorbidity burden category at initiation, number of prior eCDAI use, number of prior biologics used, CCI at initiation, HAQ at initiation, patient-reported fatigue at initiation and patient-reported pain at initiation.  
 § The 6-month visit occurred in a window of 4 to 8 months; the 12-month visit occurred in a window of 10 to 14 months.  
 ¶ CDAI ≤ 10 at baseline; MCID = 2; CDAI = 19 or ≥ 22 at baseline; MCID = 8; CDAI = 22 at baseline; MCID = 11.  
 \*\* LDA, CDAI ≤ 10.

**Conclusions:** In this real-world analysis, the effectiveness of TCZ for the improvement of RA disease activity was comparable among patients regardless of comorbidity burden or obesity.

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**THU0151 ASSESSMENT OF COMPLIANCE OF RHEUMATOID ARTHRITIS PATIENTS IN COGNITIVE DYSFUNCTION**

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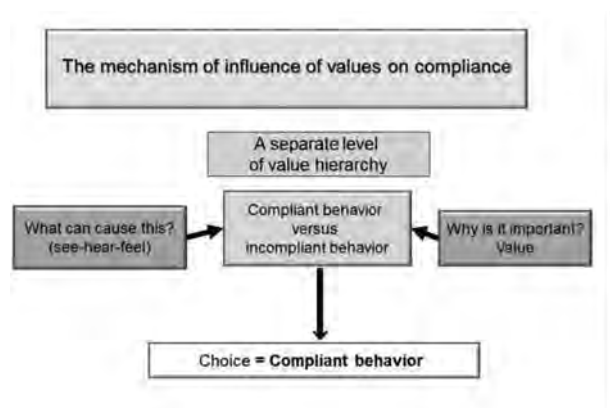
**Background:** Compliance decline may result in a decrease of treatment effectiveness in rheumatoid arthritis. RA patients had global cognitive impairment, which was associated with disease activity and immune changes.<sup>1</sup> Cognitive dysfunction may have a negative effect on the results of traditional methods of compliance assessment.

**Objectives:** Our aim was to develop the method of structured and algorithms interview to assess compliance and cognitive functions in patients with rheumatoid arthritis.

**Methods:** 240 patients fulfilling EULAR 2010 classification criteria for rheumatoid arthritis were examined. Pain in the joints was assessed using a visual analogue scale, the clock-drawing test was used, the structured and algorithms interview with clear determination of at least 3 levels of patient values was performed.<sup>2</sup>

Each patient chose the subject of the interview: compliance, pain or side effects of drugs. Subjective values that determine the choice and behaviour of the patient with dichotomy, for example, taking or missing drugs were revealed.

**Results:** 162 patients chose the theme of the interview concerning of pain, 50 patients chose the theme compliance with drug therapy, 38 patients - side effects of drugs. The criteria of cognitive dysfunction were the following: inability for the patient to determine subjective values influencing the process of decision-making, repeating one value with inability to build a value hierarchy, a limited number of the levels of the value hierarchy. The indirect criterion was the duration of the structured interview as the measure of patient's and interviewer's efforts. Cognitive dysfunction determined by the method of the structured interview was connected with the low score of the clock-drawing test. Compliance decline was noticed in the presence as well as in the absence of cognitive dysfunction. Determining values and their hierarchy may lead to the increase of patients' compliance.



**Conclusions:** The method of the structured and algorithms interview with the assessment of the hierarchy of values is used to assess compliance and cognitive functions in patients with rheumatoid arthritis as well as to reveal the ways to increase compliance.

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**Disclosure of Interest:** None declared

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#### THU0152 SERUM PRESEPSIN AS A NOVEL BIOMARKER FOR BACTERIAL INFECTION IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH TOCILIZUMAB

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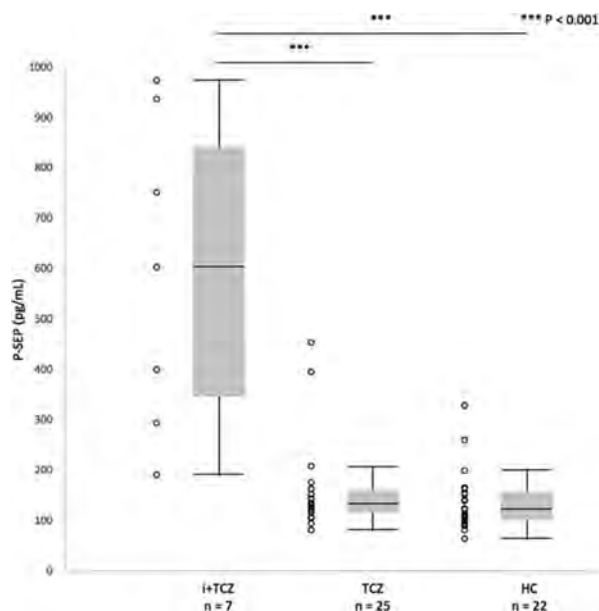
**Background:** Tocilizumab (TCZ), an inhibitor of interleukin-6 (IL-6), has been widely used to treat rheumatic diseases such as rheumatoid arthritis (RA) and juvenile idiopathic arthritis. Recently, TCZ was approved for use in patients with giant cell aortitis and Takayasu aortitis. However, TCZ treatment sometimes obscures changes in the conventional biomarkers for infection such as serum levels of C-reactive protein (CRP) and procalcitonin (PCT). Presepsin (P-SEP), a subtype of soluble CD14, has been recently identified as a biomarker for sepsis. In addition, we have reported the usefulness of P-SEP for the diagnosis of bacterial infection in RA patients because it is less affected by the disease activity.

**Objectives:** To examine the usefulness of P-SEP in RA patients complicated with bacterial infections during TCZ treatment.

**Methods:** In this study, 49 RA patients with bacterial infections (i-RA), 76 RA patients without bacterial infections (RA) and 23 healthy controls (HC) were enrolled. The presence of infection was strictly diagnosed by bacteriological examinations, typical clinical characteristics such as fever (38.0°C) and/or CRP elevation and/or increased white blood cell count, and improvements of these manifestations with antibiotics. Serum P-SEP levels were measured by an immunoassay. The CRP and PCT levels were measured simultaneously.

**Results:** The median serum P-SEP levels were 186.0 [interquartile range (IQR), 134.0-236.0], 691.0 [IQR, 345.5-842.0], 154.5 [IQR, 145.8-165.5] l,

and 161.0 [IQR, 146.5-166.0] pg/mL for TCZ (n=25), i+TCZ (pre-antibacterial treatment; n=7), i+TCZ (post-antibacterial treatment; n=7) and the HC group, respectively. The P-SEP levels of the i+TCZ group were significantly elevated compared with those of the TCZ group (p<0.001). The i+TCZ group displayed elevated P-SEP levels despite normal CRP and PCT levels. After antibacterial treatment, P-SEP levels of the i+TCZ group were significantly decreased (p=0.016).



**Conclusions:** These results suggest that serum P-SEP levels are less affected by TCZ treatment compared with other conventional inflammatory biomarkers such as CRP and PCT. Moreover, P-SEP levels are useful for the assessment of bacterial infections in RA patients treated with TCZ.

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**Disclosure of Interest:** None declared

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#### THU0153 THE EFFECT OF 5-YEARS B-DMARDS TREATMENT ON DIFFERENT 10-YEARS CARDIOVASCULAR RISK SCORES APPLIED IN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Patients with rheumatoid arthritis (RA) have an excess risk of cardiovascular (CV) disease.

**Objectives:** We aimed to assess whether 5 years treatment with biologic DMARDs can impact on the 10 year CV risk assessed with different scores.

**Methods:** In this monocentric study we retrospectively evaluated data available at 2012 and 2017 to calculate the CV scores according to the Italian CV risk score Cuore project,<sup>1</sup> QRISK2-2017 score<sup>2</sup> and the score proposed by Solomon DH et al.<sup>3</sup> Moreover, RA characteristics were registered and correlated to the risk scores at baseline and after 60 months of treatment with RA approved biologic agents. Any CV event was registered.

**Results:** 110 patients with RA treated for the first time with a bDMARDs, and no prior CV events were included (mean age 52±11.3 years; 80% women; median disease duration 36 months). During the evaluated period 47 (42%) patients switched to a different bDMARD, 10 (9%) patients stopped the treatment for side effects and 3 (2.7%) patients with high CV risk scores at baseline presented a CV event within 4 years (2 myocardial infarction and 1 stroke). At baseline we observed a mean CV risk of 3.69 (95% confidence interval [CI], 2.70-4.68) assessed as moderate by the Cuore project, 10.64 (95%CI 8.48-12.8) and 10.43 (95%CI 8.61-12.24) considered as high risk according to the QRISK2-2017 and Solomon's scores, respectively. After 5 years we recorded a significant increase in CV risk assessed by the Cuore project and the QRISK2-2017 score [4.20 (95% CI 3.23-5.18) and 13.12 (95%CI 10.72-15.53), respectively; p<0.001 vs



baseline]. In comparison with baseline the change in the Solomon's score did not reach the statistical significance [10.68 (95%CI 8.78–12.58);  $p=0.66$ ]. In 38 (39.2%) patients that achieved persistent CDAI remission/low disease activity during the entire 5 years follow-up we observed a statistically significant reduction in the Cuore project score [4.1 (95%CI 2.1–6) vs 3.8 (95%CI 2.3–5.3);  $p=0.02$ ] and in the Solomon's score [9.3 (95%CI 5.6–13) vs 7.8 (95%CI 5.2–10.5);  $p=0.04$ ]. No statistical significance was found in CV risk scores stratifying patients for disease duration, RA specific disease characteristics, and mechanism of action and/or number of switch in bDMARD treatment.

**Conclusions:** RA patients are at moderate/high CV risk as assess by the different CV risk scores used, more consistent if inflammatory or disease specific items are considered in the score. Sustained CDAI remission obtained with bDMARDs can invert CV risk progression for 5 years estimated by Cuore project and Solomon's score, despite ageing.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.3870

#### THU0154 A PROGRAM FOR SCREENING AND TREATMENT OF CARDIOVASCULAR RISK FACTORS IN PATIENTS WITH CHRONIC ARTHRITIS: 2-YEAR RESULTS

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**Objectives:** Assess the efficacy of a program for the screening and management of cardiovascular risk factors (CVRF) in patients with chronic arthritis at 2 year follow-up.

**Methods:** Longitudinal and prospective study of patients included in a program aimed at the screening and improvement of the management of CVRF. Patients diagnosed with rheumatoid arthritis (RA), spondyloarthritis (SpA) and psoriatic arthritis (PsA) were included in the program. In the baseline and follow-up visits, CVRF were recorded, as was their treatment and whether treatment targets were achieved. SCORE index was calculated and modified according to EULAR 2010 recommendations. Tailored education was performed by the nurse and (if needed) referral to the rheumatologist or GP was performed for CVRF drug treatment.

For this analysis, we selected patients who completed baseline assessment and the 2 year follow-up. Prevalence and degree of control of CVRF were compared at both time points.

**Results:** Out of a total of 416 patients included in the program, 123 have completed both the baseline visit and the 2 year follow-up: 79 (64%) women with a mean age of 59.3±10 years. Patients with RA (n=85), SpA (n=14) and PsA (n=24) were included.

	BASELINE		2 YEAR FOLLOW UP	
	N (%)	Poor control N (%)	N (%)	Poor control N (%)
DM	14 (11%)	4 (3%)	14 (11%)	4 (3%)
Hypertension	77 (63%)	54 (44%)	84 (68%)	42 (34%)
Hypercholesterolemia (CT>220 mg/dL)	66 (54%)	37 (31%)	83 (67%)*	20 (16%)*
Smoker	28 (23%)	—	20 (16%)	—
Obesity (BMI>30)	47 (38%)	—	45 (37%)	—
CV events	6 (5%)	—	6 (5%)	—

\* $p<0.05$  comparison baseline – 2 year follow-up

The mean modified SCORE index was 4.6±4 at baseline and 4.6±4 at follow-up. Risk stratification (according to European guidelines) was 73 patients with intermediate risk, 20 with high risk and 20 with very high risk. Meanwhile, at 2 year follow-up, 74 patients showed an intermediate risk, 25 a high risk and 19 a very high risk.

**Conclusions:** A specific program aimed at detecting CVRF increases the proportion of patients with a CVRF diagnosis. However, it is also associated with an

increase rate of well-controlled hypercholesterolemic patients, with a trend observed in hypertensive patients and smokers. In case the improvement in CVRF control is confirmed, programs such as this could improve the CV prognosis of patients with chronic arthritis.

**Disclosure of Interest:** None declared

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#### THU0155 CUSTOMISED CONSTRUCTION OF DEVICES AS INTEGRATION OF OCCUPATIONAL THERAPY INTERVENTION IN RHEUMATOLOGY BY 3D PRINTING TECHNOLOGY AND CO-DESIGN: FURTHER DEVELOPMENT AND VERIFICATION OF LONG-TERM EFFECTIVENESS

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**Background:** In our previous study<sup>1</sup> we have analysed the potentiality to create customised personalised aids through the 3D printing technique for patients with chronic physically and psycho-socially progressively disabling rheumatic diseases. It has been shown that the active involvement of the patient in the aid prototyping process through co-design sessions allows a greater acceptance of the aid itself in daily activities.

**Objectives:** To confirm the effectiveness of custom co-designed aids made with 3D printing technique. To check long-term patient's satisfaction in their daily use. To demonstrate that a client-centred intervention leads to aids greater acceptance, reduces social stigma and improves self-esteem.

**Methods:** 9 patients affected by long term rheumatoid arthritis were enrolled overall. They expressed their specific needs regarding the aid devices and therefore subsequent meetings were organised that have allowed us to produce and deliver customised objects.

Tools: Autodesk Fusion360 and Dassault Systemes SolidWorks for object modelling; Ultimaker Care for slicing; 3D printing DeltaWASP 20 40

Following a co-design approach, 6 aid devices were customised: hand grip holder for chalk, tablespoon, aid to open the moka coffee machine (2 different models), cans opener, zip puller. For the collection of the design features the product analysis of the USERfit tool was used. The psycho-social impact assessment of the assistance by PIADS (Psychosocial Impact of Assistive Devices Scale) and the patient's satisfaction by QUEST (Quebec User Evaluation of Satisfaction with Technical Aids, scale 1–5) were analysed after 1 week and after 1 year

**Results:** After 1 year all co-designed aids are still in use and the patients' satisfaction remains unchanged. The psychosocial assessment of delivered aid devices, collected through PIADS (– scale –3+3), showed an overall positive outcome (mean competence +1.92; adaptability:+1.590; self-esteem:+1.70). The assessment of patient satisfaction through QUEST, was good (scale 1–5: satisfaction aid: 4.65; service satisfaction: 4.9). There are no significant changes between scores after 1 week and 1 year except for a reduction in the self-esteem score ( $p=0.006$ )

**Conclusions:** This work shows that an interactive co-design, made possible by 3D printing, allows patients with long-established strategies in the activities of daily life to change habits, satisfactorily. The decrease of self-esteem scores could be probably due to a lower patient's emotional involvement with respect to an object that has become a regular part of his life.

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#### THU0156 DEPRESSION AMELIORATED BY ORTHOPAEDIC SURGICAL INTERVENTION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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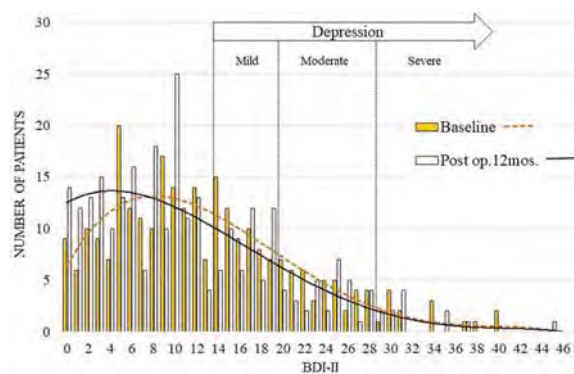
**Background:** Depression is the most frequently seen comorbidity in the patients with rheumatoid arthritis (RA) <sup>1</sup>. Inflammatory mediators, including TNF- $\alpha$ ,

interleukin-1 and interleukin-6, affect serotonin transporters in the brain and promote low stress tolerance and depression<sup>2</sup>.

**Objectives:** To investigate the effect of orthopaedic surgery on the mental condition of patients with RA by assessing the Beck depression inventory II (BDI-II) and to investigate the factors associated with changes in the BDI-II.

**Methods:** A prospective cohort study was performed in 294 sites of primary elective surgery in 276 patients with structural damage due to RA. The average (range) age was 64<sup>19–89</sup> years old, and the average (range) disease duration was 16<sup>1–60</sup> years. The surgical site was the shoulder in 6 patients, elbow in 26, wrist in 74, hand in 63 (with wrist in 18), hip in 13, knee in 50, ankle in 12, and forefoot in 50. The BDI-II, EuroQol 5 dimensions (EQ-5D), Japanese version of the Stanford Health Assessment Questionnaire (J-HAQ), and disease activity score 28 using C-reactive protein<sup>4</sup> (DAS28-CRP<sup>4</sup>) were assessed at the baseline and at 12 months after surgery. During the observational period, the number of patients using methotrexate (MTX), prednisolone (PSL), and biological disease-modifying anti-rheumatic drugs (bDMARDs) did not change significantly. The mean dose of MTX and PSL was reduced by 0.4 mg/w and 0.2 mg/d, respectively, at 12 months after surgery.

**Results:** In total, the mean BDI-II significantly improved from 13.0 to 11.5 at 12 months after surgery ( $p < 0.01$ ). The number of patients with depression (BDI-II  $\geq 14$ ) decreased from 42.8% to 34.8% (figure 1). A significant improvement in the BDI-II was noted in the elbow, wrist, hand, and forefoot surgeries ( $p < 0.05$ ). EQ-5D, J-HAQ, and DAS28-CRP<sup>4</sup> also improved significantly ( $p < 0.01$ )<sup>3</sup>. A multiple regression analysis showed that the magnitude of decrease in the BDI-II ( $\Delta$ BDI-II) was independently related to the Steinbrocker's stage (95% confidence interval [CI]: 0.42, 2.39,  $p = 0.005$ ) and pain-visual analogue scale (VAS) (95% CI: 0.01, 0.10,  $p = 0.02$ ) at baseline and inversely related to matrix metalloproteinase-3 (MMP-3) (95% CI:  $-0.01, -0.001$ ,  $p = 0.03$ ) at baseline. The BDI-II was correlated with the EQ-5D ( $\gamma = -0.049$ ,  $p < 0.01$ ) and J-HAQ ( $\gamma = 0.387$ ,  $p < 0.01$ ) at 12 months after surgery.



Abstract THU0156 – Figure 1. Distribution of BDI-II at baseline and a postop. 12mos.

**Conclusions:** Depression was ameliorated by surgical intervention in patients with RA. The mental condition is associated with the quality of life and physical function.

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**Disclosure of Interest:** None declared

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### THU0157 ALTERED DNA-METHYLATION IN CHILDREN BORN TO MOTHERS WITH RHEUMATOID ARTHRITIS DURING PREGNANCY

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**Background:** Exposures during early life are associated with later-life health, which is referred to as the Developmental Origins of Health and Disease hypothesis<sup>1</sup>. Epigenetic processes are thought to be one of the mechanisms underlying this hypothesis. DNA-methylation is the best studied and understood epigenetic modification. DNA-methylation of the fetus *in utero* may be influenced by multiple factors, including maternal disease<sup>2</sup>.

**Objectives:** To determine whether the DNA-methylation profile of children born to women with RA is different from children born to women from the general

population. Furthermore to determine which pathways are associated with the significantly differentially methylated CpG sites.

**Methods:** For the current study, blood from 80 children with a mean age of 6.82 (SD=1.28) born to women with RA, who were followed prospectively during pregnancy and postpartum in the PARA-study<sup>3</sup>, was used to measure genome-wide DNA-methylation using the Infinium Illumina Human-Methylation 450 k BeadChip. DNA from 345 children with a mean age of 6.04 (SD=0.39) born to women from the population-based Generation R study<sup>4</sup> were used as controls, also followed prospectively during pregnancy and postpartum. Linear mixed models were used to analyse differences in methylation between these groups. The models were corrected for age, BMI(SDS) and sex of the child, gestational age at delivery, maternal age, folic acid use during pregnancy, socioeconomic status, maternal smoking during pregnancy, white blood cell subtypes and technical batch.

**Results:** In total 770 CpGs were significantly different between the 2 groups at Bonferroni threshold  $p = 1.08 \times 10^{-7}$  (see table 1. for top 10 sites). In addition, pathway analysis resulted in 4 statistically significant enriched pathways. The top 2 pathways were the FOXO signalling pathway consisting of 16 genes ( $p = 3.39 \times 10^{-4}$ ) and mTOR signalling pathway consisting of 17 genes ( $p = 5.65 \times 10^{-4}$ ). These pathways are known for regulating the glucose and lipid metabolism, respectively.

Table 1 Top 10 methylation sites from the linear mixed model

CpG	P-value	Beta	SE	Nearby gene ( $\pm$ bp)	Chr	Bp	Location*
(Effect size)							
cg07786668	$4.75 \times 10^{-11}$	0.027	0.002	ZFXJ(-10142)	16	73092391	-
cg06642177	$1.29 \times 10^{-28}$	0.028	0.002	SLC2A12(-122529) SGK1(+142878)	6	134496341	-
cg08867893	$5.68 \times 10^{-21}$	0.017	0.001	ZNF365(+221)	10	64134160	-
cg20116574	$4.89 \times 10^{-23}$	0.024	0.002	NCOA5(+435)	20	44718168	Promoter
cg06778273	$9.33 \times 10^{-25}$	0.021	0.002	TNFRSF18(+4995) RLL10(+27808)	1	1137117	-
cg21160472	$8.45 \times 10^{-21}$	0.015	0.001	ATF3(+119)	1	212782112	Promoter
cg01067849	$4.09 \times 10^{-22}$	0.011	0.001	WRNIP1(-102)	6	2765587	Promoter
cg06656994	$5.88 \times 10^{-18}$	0.051	0.005	FAM163A(+903)	1	179713176	Enhancer
cg14810343	$1.36 \times 10^{-28}$	0.013	0.001	CXXC5(-327)	5	139028149	-
cg01458961	$3.47 \times 10^{-14}$	0.032	0.003	PPP3CA(-822)	4	102269425	-

\* Location in promoter, gene, enhancer or other/unknown (-)  
SE= standard error; bp=base pair; Chr= chromosome

**Conclusions:** This study demonstrates that children born to women with RA have a different methylation profile compared with children born to mothers from the general population.

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**Disclosure of Interest:** None declared

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### THU0158 INCREASED PROGRESSION OF ATHEROSCLEROSIS IN PATIENTS WITH RHEUMATOID ARTHRITIS IS PARTIALLY REFLECTED BY DISEASE SEVERITY AT THE TIME OF DIAGNOSIS- 11-YEAR PROSPECTIVE FOLLOW-UP

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**Background:** Patients with Rheumatoid arthritis (RA) have increased mortality and morbidity due to cardiovascular disease (CVD) compared to general population. While it has been established that atherosclerosis is increased, there is much yet to reveal about the underlying cause. Contributing factors, such as

inflammation, traditional CVD risk factors and metabolic disease have been suggested, but no full explanation is currently present.

**Objectives:** In this prospective case-control study, we investigated how the progression of subclinical atherosclerosis is associated with CVD risk factors and parameters of inflammation in patients with RA compared with matched controls.

**Methods:** By the time of diagnosis, patients from northern Sweden diagnosed with early RA are consecutively recruited into an ongoing prospective study. From these, a subgroup aged  $\leq 60$  years was consecutively included for ultrasound measurements of intima media thickness (IMT) of a. carotis communis at inclusion (T0) (n=79), after 5 years (T5) (n=71) and after 11 years (T11) (n=55). 44 age-sex-matched controls were included and 31 could be reevaluated at T11. Pharmacological treatment, previous CVD, markers of inflammation, lipid status, blood pressure, body mass index as well as measurements of disease activity were registered. Any previous CV events were verified by medical records. European Systematic Coronary Risk Evaluation (SCORE) and Reynolds Risk Score were calculated and Larsen score (of hands and feet) were registered. IMT progression rate ( $\Delta$ IMT T0-T11) was calculated by subtracting baseline values from IMT after eleven years follow up.

**Results:** IMT increased significantly between T0 and T11 among patients with RA (IMT T0: 0.51 (0.12) T11: 0.68 (0.16)  $p < 0.0001$ ) and controls (IMT T0: 0.54 (0.12) T11: 0.63 (0.13)  $p < 0.0001$ ). There was a higher progression rate between T0 and T11 in the RA group compared with the controls ( $p < 0.05$ ). In simple regression models, IMT T11 was significantly associated with several traditional CVD risk factors as well as Larsen score at T0 among RA patients (table 1). Moreover, in simple regression models  $\Delta$ IMT T0-T11 was significantly associated with Larsen score and age at T0 (both  $p < 0.01$ ) among patients with RA. A multiple regression model, with  $\Delta$ IMT T0-T11 as dependent variable, including traditional CVD risk factors at T0 (age, systolic blood pressure (BP), cholesterol and smoking), resulted in a  $R^2$  of 0.32 where age and cholesterol ( $p < 0.01$  for both) were significantly associated with  $\Delta$ IMT T0-T11. When also adding CRP and Larsen score the  $R^2$  increased to 0.50 and age ( $p < 0.05$ ) and Larsen score ( $p < 0.01$ ) were significantly associated with IMT T11.

**Abstract THU0158 – Table 1.** Simple regression models among 55 patients with RA with IMT after 11 years of follow up as the dependent variables.

Variable	IMT T11		
	$\beta$	95% CI	p
Age, T0	0.104/year	0.071–0.136	<0.001
Systolic BP, T0	0.035/ mmHg	0.009–0.061	0.009
SCORE, T0	0.534/unit	0.261–0.807	<0.001
Reynolds risk score, T0	0.182/unit	0.048–0.315	0.009
Larsen score, T0	0.122/unit	0.004–0.239	0.043
DAS 28, T0	-0.236/unit	-0.771– 0.298	0.364

**Conclusions:** In this prospective study, we found that there was an increased progression of atherosclerosis among RA patients, compared with controls, eleven years after diagnosis, and that this increase is associated with Larsen score and age at baseline.

**Disclosure of Interest:** None declared

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#### THU0159 BARRIERS TO RHEUMATOID ARTHRITIS TREATMENT OPTIMISATION: REAL-WORLD DATA FROM THE ARTHRITISPOWER REGISTRY

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**Background:** Few research studies have investigated treatment (Tx) goals in rheumatoid arthritis (RA) from the patients' (pts) perspective, including factors preventing achievement of Tx targets and reasons why pts tolerate sub-optimal disease control.

**Objectives:** To identify barriers to Tx optimisation, using real-world data from the ArthritisPower registry. Secondary objectives were to understand pts' Tx goals and why pts tolerate active disease.

**Methods:** This was an observational, cross-sectional sub-study of pts in the ArthritisPower registry. Pts were aged  $\geq 19$  years, had physician-diagnosed RA, no change to Tx within 3 months of baseline, and had access to a computer/smartphone. Pt-reported outcomes (PROs) included pain, fatigue, sleep, physical function, and general health. Pts also completed an online survey on barriers to Tx escalation, and were classified into 3 groups based on physician and pt attitudes to Tx change (change not offered, change offered and accepted, change offered

and rejected). Disease activity was reported using Routine Assessment of Patient Index Data 3 (RAPID3) scores.

**Results:** 257 pts met the inclusion criteria (table 1). 195/257 (76%) pts were treated with DMARDs (non-biologic or biologic). 180/257 (70%) pts had high disease activity by RAPID3 (median 18.0 on 0–30 scale), of which only 67/180 (37%) were offered a Tx change at their last physician visit. Most of these pts accepted the Tx change (48/67 [72%]). There were few differentiating factors in demographics, RA-related features, and background therapy among pts who were offered a Tx change versus not. Most pts (33/44 [75%]) who intensified Tx did so because their symptoms remained bad or worsened, whereas only 16/44 (36%) changed because they did not reach pre-defined Tx goals. The most common reason (21/32 [66%]) for deciding not to change therapy was the rheumatologist's satisfaction with the current therapy; pt concerns related to safety of the new therapy were less common (8/32 [25%]). There was a weak correlation between the RAPID3 score and pts' self-reported perception of their own disease activity. The majority of pts (176/257 [69%]) valued being actively involved in making decisions with their doctor about Tx.

**Abstract THU0159 – Table 1.** Patient demographics at baseline

	Demographics		
	Survey participants (N=257)	High disease activity (n=180)	Moderate or low disease activity, or near remission (n=77)
Age, mean years (SD)	51.9 (11.0)	51.1 (10.8)	53.7 (11.3)
Females, n(%)	236 (91.8)	187 (92.8)	69 (89.6)
Ethnicity, n (% white)	231 (89.9)	157 (87.2)*	74 (96.1)*
Years since diagnosis, mean (SD)	11.4 (9.9)	10.9 (9.2)	12.4 (11.3)
PRO scores, median (IQR)			
RAPID3	15.0 (12.0–19.0)	18.0 (15.0–20.0)*	9.0 (6.0–11.0)*
Pain	53.2 (50.0–58.9)	55.7 (52.7–57.6)*	58.7 (54.5–61.5)*
Fatigue	54.0 (50.7–60.0)	54.0 (52.3–59.3)*	57.1 (50.7–62.5)*
Physical function	37.3 (33.9–40.7)	36.3 (32.5–39.6)*	42.6 (36.8–45.9)*
Sleep	59.4 (54.3–63.0)	61.2 (55.8–64.8)*	55.8 (50.4–61.9)*

\*Statistical significance between patient groups,  $p < 0.05$ ; p values were nominal in nature and should be interpreted in an exploratory manner. Chi square tests were used to compare patient groups. IQR: interquartile range; PRO: patient reported outcome; RAPID3: Routine Assessment of Patient Index Data 3; SD: standard deviation.

**Conclusions:** Despite treat-to-target recommendations,<sup>1</sup> about two-thirds of RA pts with high disease activity in this sample were not offered a Tx change by their rheumatologist. Only a minority changed because they had not met predefined targets for disease control. Pts commonly followed their rheumatologist's decision that no Tx change was needed and placed greater importance on their doctor's Tx goals than their own. These findings suggest that pts may be more deferential to their physicians' satisfaction with poor RA disease control than is appropriate. Encouraging pts (not just physicians) to overcome the status quo by changing medications and striving for low disease activity/remission may be worthwhile, but traditional metrics (e.g. RAPID3) may not reflect the most relevant target for pts' goals for therapy.

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#### THU0160 JUXTA-ARTICULAR BONE HEALTH AFFECTS NEW CAROTID PLAQUE FORMATION INDEPENDENT WITH GLUCOCORTICOID THERAPY IN POSTMENOPAUSAL PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is a chronic and systemic inflammatory disease.

The incidence of cardiovascular (CV) disease is increased in patients with RA, compared with the general population, which is related to the fact that atherosclerosis has an inflammatory etiology.



Several studies revealed that RA is associated with systemic bone loss, and long-term glucocorticoid therapy is also known to affect CV events as well as bone health such as osteoporosis.

Especially in postmenopausal women, the prevalence of osteoporosis and its complications are important medical issues.

**Objectives:** In the present study, we investigated the bone mineral density (BMD) for the carotid plaque formation in RA patients in the Kyungpook National University Hospital Atherosclerosis Risk in Rheumatoid Arthritis (KARRA) cohort study.

**Methods:** After a baseline evaluation for KARRA enrollment, RA patients were prospectively followed up for 5 years or until deaths.

We analysed the demographic findings, conventional CV risk factors and RA disease activity.

Carotid ultrasound at baseline and year 5 was performed to evaluation of the intima-medial thickness (IMT) and presence and progression of carotid plaque.

A total 323 patients (272 female) with RA, who performed dual-photon x-ray absorptiometry and carotid ultrasound, were included.

We assessed disease activity of RA, risk factors for atherosclerosis including hypertension, diabetes mellitus and dyslipidemia, presence of carotid plaque, BMD and cumulative glucocorticoid doses.

**Results:** A total of 417 RA patients were included in the baseline KARRA cohort, and 327 patients with RA were followed for the 5 year period.

Of the 417 baseline RA patients, 212 patients had no carotid plaque. At year 5, new carotid plaque formation was found in 91 of 214 patients who underwent BMD examination.

The BMD in the l-spine, femur, and radius was significantly lower in patients with carotid plaques (n=154), compared to patients without plaques (n=172) (1.016 g/cm<sup>2</sup>±0.22 vs. 1.066±0.18, p=0.013 for l-spine; 0.817±0.15 vs. 0.865±0.14, p<0.001 for femur; 0.542±0.14 vs. 0.605±0.13, p<0.001 for radius).

In postmenopausal patients, the BMD was significantly lower in carotid plaque group (n=93) than non-plaque group (n=109) (0.962±0.171 vs. 1.056±0.174, p<0.001 for L spine; 0.780±0.14 vs. 0.857±0.12, p<0.001 for femur; 0.502±0.110 vs. 0.593±0.112, p<0.001 for radius).

The cumulative steroid dose was confirmed in postmenopausal female patients, and the glucocorticoid dose was correlated with new carotid plaque formation. (r=0.334, p=0.04). Multivariate logistic regression analysis revealed that but radius BMD (p=0.04) was independent risk factors for new carotid plaque formation during the 5 year followed period after correlation with cumulative glucocorticoid dose, but l-spine (p=0.06) and femur BMD (p=0.07) were not statistically significant.

**Conclusions:** This study shows formation of new plaques after long-term follow-up depends on the juxta-articular bone health in postmenopausal RA patients.

**Disclosure of Interest:** None declared

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#### THU0161 TRENDS IN THE INCIDENCE OF AMYLOIDOSIS IN PATIENTS WITH RHEUMATOID ARTHRITIS IN SPAIN: AN OBSERVATIONAL COHORT STUDY OF HOSPITAL DISCHARGES FROM 1999 TO 2015 (TREND-AR STUDY)

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**Background:** Treatment and evolution of Rheumatoid Arthritis (RA) have had an important change in the last years. However the trend of amyloidosis, habitually related to long-standing and active RA, in Spain is unknown.

**Objectives:** To analyse the incidence and trend of hospital admissions for amyloidosis in RA patients in Spain from 1999 to 2015.

**Methods:** We performed an observational retrospective population study analysing the Spanish administrative database that includes a Minimum Basic Data Set (MBDS) of hospital admissions of RA patients from 1999 to 2015. We selected the MBDSs for amyloidosis. Cases were identified by the presence in primary and secondary diagnosis of its ICD9 code. The population at risk was estimated with an estimated prevalence of RA of 0.5% (0.8% women and 0.2% men). Crude and adjusted rates were calculated, and the trend was analysed using the Generalised Linear Model (GLM) with the year as the analysis variable. SPSS version 20 (SPSS Inc, Chicago, IL) was used.

**Results:** 338.343 RA hospital admissions were detected, being 3085 (0.9%) due to amyloidosis with 2298 (74.5%) women and 787 (25.5%) men. Mean age 65.42 (SD 13.08). There were 366 (11.9%) deaths. Age-adjusted rate during the period was 122.87/10<sup>5</sup> inhab. per year (98.96 women and 146.79 men). Amyloidosis age-adjusted rate decreased from 138.88/10<sup>5</sup> inhab. per year in 1999 to 71.47 in 2015, both women (128.18 in 1999 to 61.35 in 2015) and men (162.36 in 1999 to 107.95 in 2015). An annual decrease in the amyloidosis rate of 4.6% is estimated (RRI 0.953; CI 95% 0.939–0.968).

**Conclusions:** In Spain from 1999 to 2015 amyloidosis hospital admissions in patients with RA decreased, with an estimation of 4.6% annual reduction. This finding concurs with a greater knowledge of RA and its treatment advances with "treat-to-target" strategies.

**Disclosure of Interest:** None declared

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#### THU0162 RESIDUAL SYNOVITIS IN ANKLES AND FEET DETECTED BY ULTRASONOGRAPHY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Twenty eight joints that are usually evaluated for disease activity score of rheumatoid arthritis (RA) do not include ankles and metatarsophalangeal joints. Although foot synovitis of patients in remission is clinically important in that it associates to relapse and worse physical function,<sup>1</sup> composite markers without an assessment of foot have demonstrated poor performance in detecting foot synovitis.<sup>2</sup>

**Objectives:** The aim of this study was to investigate the frequency and impact of residual synovitis in ankles and feet in patients with RA.

**Methods:** Patients with RA who underwent both physical examination and ultrasonography (US) on 44 joints including hands, fingers, ankles, and metatarsophalangeal joints between April 2016 and January 2018 in Keio University Hospital were enrolled. We compared patients with swollen joints of feet and ankles and those without, and then analysed those who did not have swollen joints by physical examination but were detected to have synovitis by US.

**Results:** Sixty one patients were enrolled in the study. The mean age was 58.5 years old, the disease duration was 7.1 years, and 85% were female. Among them, 21 patients had joint swelling in feet and ankles and 40 patients did not by physical examination. The patients in the former group showed significantly higher disease activity (DAS28 4.0 vs 2.4, p<0.05), higher doctor visual analogue scale (VAS, 33 vs 8 mm, p<0.05) and higher serum matrix metalloproteinase (MMP)-3 (165 vs 51 mg/dL, p<0.05). In the 40 patients with no swollen joints in ankles and feet by physical examination, 24 (60%) had active synovitis detected by US in those joints (US positive group) and the other 16 patients showed no synovitis in ankles and feet by US (US negative group). Whereas age and disease duration were not different between two groups, body mass index tended to be higher in the US positive group than the US negative group. Although the majority of both groups were in remission according to DAS28, fewer patients in the US positive group achieved remission according to Boolean criteria (29% vs 63%, p<0.05). The residual disease activity in ankles and feet was reflected in pain visual analogue scale most sensitively (33 mm vs 9 mm, p<0.05). The discordance in global assessments between patient and estimator of more than 30 mm was significantly frequent in the US positive group than the US negative group (33% vs 6%, p<0.05).

**Conclusions:** The residual synovitis in ankles and feet did not reflect in remission criteria by DAS28 but did by Boolean criteria. It caused a discordance in global assessments between patient and estimator.

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THU0163

**EXTRA-ARTICULAR MANIFESTATIONS IN RHEUMATOID ARTHRITIS: A COMPREHENSIVE ANALYSIS IN A LARGE COHORT**

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**Background:** Although Rheumatoid Arthritis (RA) extra-articular manifestations (ExRA) occurrence have been decreasing over time, they are still a major mortality risk factor for patients, and also a challenge for rheumatologists.

**Objectives:** To determine the prevalence of ExRA in a large cohort, and its association with several clinical data.

**Methods:** A cross-sectional and observational study, based on a multi-centric database from a prospective cohort (The REAL – RA in real life in Brazil), in which 11 public rheumatology centres enrolled RA patients (1987 ARA or 2010 ACR-EULAR). Data collection began in 08–2015, using a single online electronic medical record, and included demographic, socioeconomic, clinical and therapeutic characteristics.

**Results:** 1116 patients from 11 centres were included: 89% women, age [mean ±SD] 58.2±11.5 year, disease duration 14.5±12.2 year, positive Rheumatoid Factor (RF) in 77%. Regarding ExRA, 334 occurrences (detailed in table 1) were registered in 261 patients, summing for an overall prevalence of 23.4% in our cohort. Comparison among ExRA and No-ExRA groups reveals significant higher age, disease duration, Clinical Disease Activity Index (CDAI), Health Assessment Questionnaire (HAQ) and Disease Activity Index (DAS 28) in ExRA group (table 2). Unexpectedly, some well-known factors associated with ExRA, such as Rheumatoid factor (RF) and tobacco use, were similar among the two groups.

Abstract THU0163 – Table 1. - ExRA

Subcutaneous nodules	92		
Anaemia	78		
Sicca Syndrome	65		
Interstitial lung disease	45		
Peripheral neuropathy	15		
Vasculitis	14		
Scleritis/Episcleritis	12		
Pleuritis/Pericarditis	12		
Glomerulonephritis	1		
Table 2	ExRA (n=261)	No-ExRA (n=855)	p
n=1116			
Age [mean±SD] yr	60.4±10.1	57.5±11.8	<b>0.0003</b>
Sex (female) [n,%]	236 (90%)	762 (89%)	0.645
RF positive [n,%]	204 (78%)	659 (77%)	0.7363
Disease duration [mean±SD] yr	17.5±10.3	13.7±9.1	<b>0.0001</b>
Smoker, ever [n,%]	110 (42%)	331 (39%)	0.3471
Smoker, current [n,%]	25 (9%)	96 (11%)	0.496
CDAI; DAS28 [mean±SD]	18.2±16; 4.3±1.6	11.5±10.6; 3.4±1.4	<b>&lt;0.0001</b>
HAQ [mean±SD]	1.15±0.8	0.87±0.7	<b>&lt;0.0001</b>

**Conclusions:** ExRA still shows an expressive occurrence that should not be underestimated. Our findings reinforce that long-term disease, associated with significant disability and persistent inflammatory activity, are the key factors related to ExRA development. Early aggressive treatment with effective therapies should lower the risk and severity of ExRA.

**Disclosure of Interest:** None declared

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THU0164

**EFFICACY OF BIOLOGIC DMARDS IN DEPRESSIVE SYMPTOMS IN PATIENTS WITH RHEUMATOID ARTHRITIS**

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**Background:** Rheumatoid arthritis (RA) affects people both physically and psychologically. Comorbid depression is common, with a prevalence of 13%–42%.<sup>1</sup> According to 2015 ACR Guideline, RA patients should be treated with conventional synthetic or biologic Disease Modifying Anti-Rheumatic Drugs (csDMARDs or bDMARDs) according to their disease activity.<sup>2</sup> Correlating depression with RA disease activity, it is thought that patients with lower disease activity are less likely to be depressed.<sup>1</sup> A study comprising 83 RA patients revealed lower frequency of depressive disorders in anti-TNF group regardless of disease activity, however the data is limited by small case number.<sup>3</sup> A review of inflammation in depression in 2016 reported IL-1β, IL-6, TNF and CRP as the most reliable biomarkers of inflammation in depression.<sup>4</sup> Thus, chronic inflammatory status in RA might contribute to a high risk of depression.

**Objectives:** This aim of this study was to investigate the independent effect of the use of bDMARDs on the risk of depression in RA patients.

**Methods:** Using a cross-sectional study design, patients with definitive diagnosis of RA were recruited during regular outpatient follow-up in a regional hospital in southern Taiwan. Data was ascertained by questionnaires, laboratory measurements, and medical records. RA disease activity and depressive symptoms were recorded with the Disease Activity Score 28 (DAS 28) and the depression subscale of the Hospital Anxiety and Depression Scale (HADS-D), respectively. Patients were considered to be depressive cases if their HADS-D score >11. Patients who were prescribed with csDMARDs were considered as the non-biologic group, and those who were under bDMARDs or combination of csDMARDs and bDMARDs were considered as the biologic group.

**Results:** A total of 378 RA patients were recruited with 60 patients in the non-biologic group and 318 patients in the biologic group. Baseline characteristics including sex, educational level, marital status, socioeconomic status, working status, vegetarian dietary habit, and religion were similar between two groups. 4.1% of the biologic patients and 13.3% of the non-biologic patients were classified as depressive. Results from the multiple logistic regression analysis adjusted for the possible confounders including disease activity showed that biologic treatment was significantly associated a lower risk of depression (odds ratio=10.11, 95% CI=2.72–37.64, p=0.001).

**Conclusions:** Patients receiving bDMARDs showed a significant lower risk of depression, despite their higher RA disease activity. Further studies on the association between the use of bDMARDs and risk of depression are warranted.

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THU0165

### OBESITY AS ONE OF THE COMMODITIES WAS THE ROBUSTEST PREDICTION FACTORS FOR POST THERAPEUTIC CLINICAL REMISSION OF RHEUMATOID ARTHRITIS WITH SHORT DISEASE DURATION – RESULTS FROM KANSAI CONSORTIUM FOR WELL-BEING OF RHEUMATOID DISEASE PATIENTS

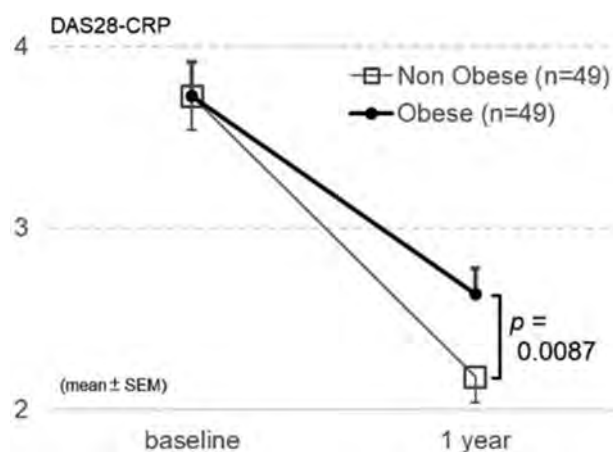
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**Background:** A part of rheumatoid arthritis (RA) patients are resistant to clinical remission (CR) irrespective of therapies. In addition to known risk factors, systemic organ complications are assumed to interfere with CR.

**Objectives:** To extract the predictive comorbidities of clinical response of disease activities.

**Methods:** In Kansai consortium for well-being of rheumatic disease patients (ANSWER) cohort, which was the real world cohort of clinical database of rheumatic diseases, RA patients within 3 years of disease duration were included and followed. Using logistic regression analysis, background factors at the initial visit were extracted in order to predict CR after 1 year (1 year-non CR).

**Results:** 651 patients met in the inclusion criteria were under the analysis. Of those, 245 (37.6%) cases were resulted in 1 year-non CR. The average scores of DAS28-CRP at first visit and one year later was 3.51 and 2.02, respectively. Logistic regression analysis revealed that DAS28-CRP at first visit (OR 1.42/unit, 95% CI 1.24–1.63), concomitant use of methotrexate (MTX) or biologic disease modifying rheumatic drugs (bDMARDs) (OR 2.04, 95% CI 1.41–2.96) and body mass index (BMI) (OR 1.07/unit, 95% CI 1.02–1.12) were significant predictive factors of 1 year-non CR, but not in the case with gender, age, disease duration, hypertension, diabetes, dyslipidemia, lung diseases, heart diseases, digestive tissue diseases, history of malignancy nor concomitant autoimmune diseases. Using propensity score matching (1:1) stratified by gender, age, disease duration, concomitant use of MTX or bDMARDs and DAS28-CRP at baseline, the 49 pairs were matched between obese (defined as body mass index (BMI) over than 28) and non-obese patients. In these cohort, mean score of DAS28-CRP after 1 year was significantly higher in obese patients than in non-obese patients (2.63 and 2.18, respectively, see the figure 1).



**Conclusions:** In these early arthritis cohort, obese patients tend to remain higher disease activities even considering with gender, age and therapeutic management, although validation studies should be added to confirm these findings.

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**Disclosure of Interest:** None declared

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THU0166

### THE DIASTOLIC DYSFUNCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis is autoimmune rheumatic disease characterised by injury not only the joints but also other organs, including the heart. It is known that the presence of rheumatoid arthritis increases the risk of fatal cardiovascular complications by 1.5 times compared to the general population.

**Objectives:** to identify features of development of diastolic dysfunction in patients with rheumatoid arthritis.

**Methods:** we examined 180 patients with rheumatoid arthritis. The activity of disease was defined according to the scale of the DAS-28. By echocardiography in 101 patients (group 1) were identified diastolic dysfunction of the left or both ventricles and in 79 patients (group 2) it was absent. Both groups were matched for age and sex. We determined the following echocardiographic parameters: mitral E/A, tricuspid E/A, end-diastolic dimension of left ventricle. In addition to echocardiography, patients underwent the vectorcardiography with the assessment of electrophysiological parameters: the squares of loops P, QRS, T, maximum vector (MV), MV-azimuth and MV- ascent. To compare two independent groups on quantitative grounds used nonparametric methods, the rank correlation and Mann-Whitney test. Differences were considered to be valid when  $p < 0.05$ .

**Results:** when comparing the groups revealed that in the 1st group, DAS-28 was higher than in the 2nd ( $p < 0.05$ ): 5.57<sup>5,17</sup>; 6.15 and 5.32<sup>4,8</sup>; 5.8 respectively. In the 1st group, the square of loop QRS and the MV- ascent directly correlated with E/A of mitral valve ( $p < 0.05$ ), whereas in the 2nd group, we have established a direct relationship with end-diastolic dimension ( $p < 0.05$ ).

**Conclusions:** the results indicate that increased activity of rheumatoid arthritis contributes to the development of diastolic dysfunction of the myocardium. In addition, the decrease in E/A observed in diastolic dysfunction, accompanied by electrophysiological remodelling and reduction in electrical activity of the myocardium of the left ventricle, diagnosed during registration of vectorcardiogram. Moreover, even in the absence of diastolic dysfunction, a tendency to its development in the presence of electrophysiological remodelling. This demonstrates the relationship between early electrophysiological, structural-geometric changes in patients with rheumatoid arthritis. Early diagnosis allows for timely start prevention of remodelling in patients with rheumatologic diseases.

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THU0167

### FALLS IN RHEUMATOID ARTHRITIS (RA) AND ITS RELATION TO DISEASE ACTIVITY, DISABILITY AND PHYSICAL PERFORMANCE TESTS

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**Background:** Rheumatoid patients(RA)are known to have an increased falls incidence with a threefold increased risk of hip fracture. Few studies have been conducted to evaluate the relation between falls, disease activity, disability and physical functioning.

**Objectives:** To evaluate the prevalence of falls in RA and its relation with disease activity, disability and physical performance tests.

**Methods:** 113 RA patients were evaluated from the outpatient clinic of the Rheumatology Division of the State University of Campinas/Unicamp. Patients were assessed for occurrence of falls in last year, fear of falling, sociodemographic and clinical data (medication, visual impairment, vertigo, physical activity, body mass index, disease duration, rheumatoid factor, lower limb swollen and tender joints, foot tactile sensitivity, disease activity-CDAI and disability-HAQ). Subjects were submitted to Berg Balance Scale-BBS, the Timed Up and Go Test-TUG and 5-Time Sit Down-to-Stand Up Test-SST5 and were divided in "Fallers" and "Non-Fallers" groups. For comparison of groups the chi-squared test, Fisher's exact test and Mann-Whitney were used. Univariate linear regression and multivariate analysis were used to analyse the relation between sociodemographic, clinical data and physical tests with the occurrence of falls. Kruskal-Wallis test was used for analysis of the association of BBS, TUG and SST5 with CDAI and HAQ. The data were analysed with a 5% level of significance.

**Results:** 52.21% reported the occurrence of falls in the past 12 months and 62.8%were fearful of falling. Comparing "Fallers" and "Non-Fallers", significant differences were noted for HAQ( $p=0.0242$ ), fear of falling( $p=0.0196$ ) and BBS ( $p=0.0120$ ). After univariate logistic regression there was association of falls with income(OR 1.05), HAQ(OR 1.945), fear of falling(OR 2.586) and TUG (OR 1.09). In multivariate model, income was independently linked to falls(OR 1.07). BBS, TUG, SST5 were correlated with CDAI and HAQ( $p < 0.05$ ).



**Conclusions:** RA patients have high prevalence of falls and fear of falling. Income was an independent fall risk factor. BBS seems to be higher among fallers and TUG can be considered a fall risk predictor. BBS, TUG and SST5 are related to CDAI and HAQ. CDAI does not seem to be a good instrument to predict falls due to its variability over time. In clinical practice, HAQ can be a valuable tool to recognise patients with an increased risk of falls.

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THU0168

#### RELATIONSHIPS BETWEEN BODY FAT COMPOSITION ASSESSED WITH BIOELECTRICAL IMPEDANCE ANALYSIS, SERUM ADIPOKINES AND DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

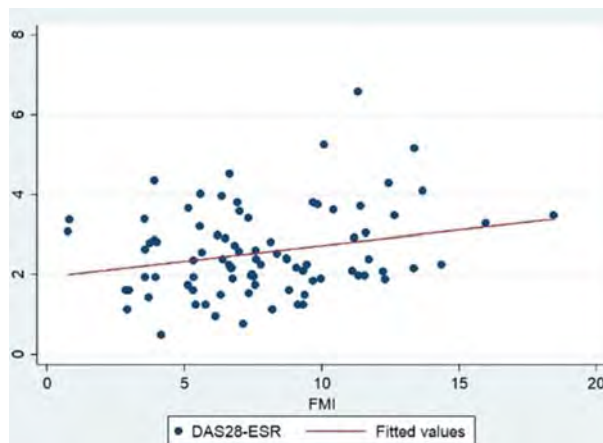
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**Background:** High-grade inflammation in patients affected with Rheumatoid Arthritis (RA) leads to an imbalanced body composition characterised by increased fat mass and decreased lean mass, with stable or increased body weight, resulting in little or no change in body mass index (BMI).<sup>1</sup> This condition, known as rheumatoid cachexia, is proven to be reversible once inflammatory process has been shut down. BMI and waist-to-hip ratio (WHR) are used as indirect measurements of visceral fat even if not capable of discriminating it from subcutaneous fat tissue. An alternative method proposed for assessment of fat composition, indicating nutritional status, is bioelectrical impedance analysis (BIA).

**Objectives:** To analyse body fat composition of patients with RA assessed using either BIA and anthropometric measures, investigating relationships between the related indices, serum adipokines and disease activity.

**Methods:** The body composition of 87 consecutive patients (72 female, 82.76%) affected with RA according to 2010 ACR/EULAR classification criteria, mean age of 52.42±13.29, mean disease duration of 10.71±8.58 years, treated with DMARDs and/or biologics, was assessed during their visit to our outpatient department. Data including demographic characteristics clinical manifestations, disease activity indices (DAS28-ESR, DAS28-CRP, CDAI, SDAI), Health Assessment Questionnaire (HAQ), lipid profile, as well as radiological findings were collected. Patients underwent to anthropometric measures (WHR and BMI) and BIA for the evaluation of fat-free mass (FFM), fat mass (FM) and the derived indices (fat-free mass index (FFMI) and fat mass index (FMI)). In addition for each patient blood samples were collected to determine serum levels of several adipokines (leptin, adiponectin, visfatin, resistin). Statistical tests as well as linear and logistic regression analysis were carried out.

**Results:** DAS28-ESR was found to be related to FMI ( $p=0.02$ ;  $r=0.22$ ) and to BMI ( $p=0.03$ ;  $r=0.22$ ). In addition, in patients in whom DAS28-ESR remission was not achieved, FMI but not BMI was found to be related to the latter disease activity index ( $p=0.007$ ,  $r=0.37$ ). FMI was shown to correlate to HAQ ( $p=0.01$ ,  $r=0.31$ ). Higher serum levels of leptin were found to predict higher FMI and BMI ( $p<0.0001$  for both,  $r=0.68$  and  $r=0.57$ , respectively) with DAS28 being also related to the latter adipokine ( $p=0.02$ ;  $r=0.24$ ). FFMI was inversely related to adiponectin serum levels ( $p=0.0003$ ;  $r=-0.40$ ). Both male and female patients classified as underweight for BMI were found to have a normal mean FFMI, with both groups presenting a mean DAS28-ESR score indicating remission.



**Conclusions:** Either body fat composition assessed with BIA-related indices and serum leptin have been noticed to predict disease activity. Moreover nutritional status of patients in remission according to DAS28-ESR may be better assessed by determining indices brought by BIA along with BMI, in order to rule out rheumatoid cachexia on the basis of FMI and FFMI.

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THU0169

#### RELATIONSHIP OF FRAILTY AND DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS: DATA FROM THE CHIKARA STUDY

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**Background:** Frailty is defined as degradation of physical and cognition function in elderly adult<sup>1</sup>. The characteristics of frailty include not only physical problems as co-morbidity and disability, but also mental and social problems. It is unclear of relationship between frailty and disease activity of patients with rheumatoid arthritis (RA).

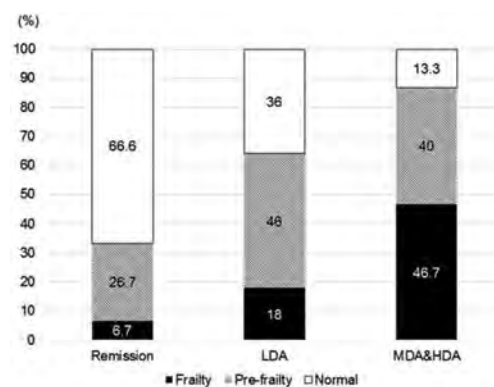
**Objectives:** We investigated the relative factors about frailty in patients with RA from a prospective observational study.

**Methods:** 95 from 100 patients entered the CHIKARA study (Correlation research of sarcopenia, skeletal muscle and disease Activity in Rheumatoid Arthritis) were investigated by frailty check list (maximal score is 25). According to reported article, frailty was defined from 8 to 25 and pre-frailty was from 4 to 7, and normal was from 0 to 3. We investigated relationship of disease activity in frailty, pre-frailty and normal groups, and analysed the relative factors for frailty.

**Results:** The prevalence of frailty, pre-frailty, and normal was 19%, 39% and 42%, respectively. The character of groups indicated at table 1. Frailty group was the oldest of three groups. Disease activity score 28 erythrocyte sedimentation rate (DAS28ESR) and matrix metalloproteinase 3 (MMP3) of frailty group was higher than those of pre-frailty and normal groups. Whereas, modified health assessment questionnaire (mHAQ) of frailty group was lower than those of pre-frailty and normal groups. Normal was 66.6% and frailty was 6.7% in remission patients. However, Normal was 13.3% and frailty was 46.7% in moderate and high disease activity patients (figure 1). The prevalence of frailty was increased with disease activity. The relative factors for frailty were age, locomotive syndrome, DAS28ESR, mHAQ, and Steinbrocker class, positively and leg muscle score and grip strength, negatively by univariate analysis. Steinbrocker class (odds ratio: 3.25 95% CI: 1.11–9.51,  $p=0.031$ ) and mHAQ (odds ratio: 1.29, 95% CI: 1.13–1.46,  $p<0.001$ ) were independent relative factors by multivariate analysis.

**Abstract THU0169 – Table 1.** The character of frailty, pre-frailty, and normal in patients with RA

	Frailty	Pre-frailty	Normal	P value
Age, years	72.5±10.3	68.6 ±11.3	60.7 ±16.4	0.01
Leg muscle score	84.9±5.9	86.2±6.4	93.2±9.7	<0.001
Grip, kg	12.6±6.9	17.7±7.1	18.1±6.2	0.013
Locomotive 5 score	11.1±5.8	6.4±4.9	2.6±4.0	<0.001
MMP3, ng/dl	143.7 ±122.0	95.9 ±66.0	88.6 ±52.0	0.033
DAS28ESR	3.62±0.97	3.27 ±1.02	2.83 ±0.96	0.015
mHAQ	0.9±0.7	0.4±0.2	0.1±0.1	<0.001
Sarcopenia,%	39	41	18	0.063



**Conclusions:** It was revealed that frailty involved disease activity and physical function in patients with RA. Control of disease activity is important to prevent not only disease progression, but also frailty.

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**Disclosure of Interest:** None declared

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### THU0170 RISK FACTOR FOR SERIOUS PULMONARY COMPLICATION IN PATIENTS WITH PRE-EXISTING LUNG DISEASE IN RHEUMATOID ARTHRITIS

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**Background:** Lung diseases, such as airway disease and interstitial lung disease (ILD), are often complicated in patients with rheumatoid arthritis (RA). The presence of those pre-existing lung diseases is one of the poor prognostic factors and risk factors for infectious pneumonia in patients with RA. There have been several concerned issues regarding pulmonary complications in RA patients with pre-existing lung diseases during treatment with disease-modifying antirheumatic drugs (DMARDs) because of infectious pneumonia or acute exacerbation in ILD, occasionally resulting in fatal outcome.

**Objectives:** We identified risk factors for serious pulmonary complications in patients with pre-existing lung disease during treatment with DMARDs in RA.

**Methods:** This study enrolled consecutive 487 RA patients at our hospital from 2005 to 2016 retrospectively. 110 of those 487 patients had pre-existing lung disease at the first visit to our hospital. At first, we divided those 110 patients into two subsets, one with development of serious pulmonary complication and the other without that during observational periods. We defined hospitalisation due to lung disease as a serious pulmonary complication regardless of the causes. Demographic and clinical data at enrollment as well as treatment regimens were collected by review of medical charts. We conducted a univariate analysis to compare the differences of clinical characteristics between the subsets. In multivariate analysis, the Cox proportional hazard model was employed to identify factors independently associated with serious pulmonary complication. The explanatory variables were chosen based on candidates ( $p < 0.25$ ) identified by the univariate analysis. In addition, we focused on 42 RA patients during treatment

with biological DMARD (bDMARD), and identified their risk factors by the same procedure mentioned above.

**Results:** In 110 RA patients with pre-existing lung disease, the median age and disease duration at enrollment was 70 and 3 years, and 71% were female. Rheumatoid factor and anti-cyclic citrullinated protein antibody (anti-CCP) were detected in 97 (88%) and 95 (86%) patients. Methotrexate (MTX), sulfasalazine (SSZ), bDMARDs and corticosteroid were prescribed in 37 (34%), 48 (44%), 42 (38%) and 65 (59%) patients. During the median observation periods of 11 months, 17 (15%) patients had serious pulmonary complications due to pulmonary infection in 11, exacerbation of ILD in 5, and drug-induced pneumonia in 1. The univariate analysis identified candidate variables for serious pulmonary complications as follows: use of MTX and bDMARDs, and no use of SSZ. In multivariate analysis, use of bDMARDs (HR 2.9, 95% CI 0.99–9.0;  $p = 0.05$ ) was identified as the independent risk factor. In 42 patients during treatment with bDMARDs, the univariate analysis identified candidate variables as follows: elder age, male, higher levels of anti-CCP, use of MTX, and no use of SSZ. In multivariate analysis, the higher levels of anti-CCP (HR 1.002, 95% CI 1.0003–1.004;  $p = 0.0007$ ) and no use of SSZ (HR 441.8, 95% CI 1.1–4658460.2;  $p = 0.04$ ) were identified as the independent risk factors.

**Conclusions:** Serious pulmonary complications should be more careful for RA patients with pre-existing lung disease during treatment with bDMARDs, particularly those with higher levels of anti-CCP or no use of SSZ.

**Disclosure of Interest:** None declared

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### THU0171 IDENTIFICATION OF METHOTREXATE-INDUCED PULMONARY TOXICITY CASES IN A FULLY SEARCHABLE ROUTINE CLINICAL DATABASE

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**Background:** Methotrexate (MTX) remains the favoured disease-modifying anti-rheumatic drug for the treatment of rheumatoid arthritis (RA) and is frequently used in other inflammatory conditions. However, side effects are frequent and toxicity is of concern, especially since MTX-induced pulmonary side effects, including pneumonitis, are potentially fatal. Estimates of MTX-induced pneumonitis in the literature range from 0.3% to 7.5% of exposed cases (Barrera et al., 1994 Kremer et al., 1997).

**Objectives:** We aimed to identify and characterise MTX-induced lung injury in patients exposed to low-dose MTX at the Rheumatology Division of the Kantonsspital Aarau, Switzerland.

**Methods:** The revised diagnostic criteria for adverse pulmonary events due to MTX treatment as defined by Kremer et al 1997 were used to categorise MTX-induced lung injury. The electronic patient files of the Rheumatology Division are stored in a NoSQL-database (MongoDB), which is fully addressable by the Solr search platform (Apache Lucene). The entire database was searched for terms associated with methotrexate exposure and potential pulmonary side effects.

**Results:** Of 9'550 cases, 11 fulfilled the criteria for definite MTX-induced pulmonary injury, while three additional patients could be classified as suffering from probable MTX-induced pulmonary side effects. To determine the number of exposed cases, the case files were queried for the mention of MTX and related terms. 1'947 case files contained a reference to MTX. In a random sample of 395 of these cases, an exposure to MTX was verified in 328 (83%). Assuming a calculated exposure of 1'639 cases, MTX-induced lung injury was present in 0.85%.

**Conclusions:** In a comprehensive survey of patients exposed to MTX in a fully searchable routine clinical database, MTX-induced pulmonary injury occurred in a low frequency.

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### THU0172 SLEEP QUALITY IN ELDERLY PATIENTS WITH RHEUMATOID ARTHRITIS SHOULD BE KEPT IN MIND

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**Background:** Sleep disturbance is one of the most important geriatric syndromes and its evaluation is part of the routine comprehensive geriatric assessment (CGA). Elderly patients with poor sleep quality are at risk of worse clinical outcomes such as falling, impairment of activities of daily living, depression and anxiety. Rheumatoid arthritis (RA) is an inflammatory disorder characterised by joint pain and may worsen sleep quality. Previous clinical trials in the literature have shown that elderly patients with RA have poorer sleep quality compared to younger patients. However, there is lack of data on sleep quality of elderly patients with RA.

**Objectives:** We aimed to investigate sleep quality of elderly patients with and without RA and also explore the effects of sleep quality on quality of life (QoL) and its association with disease activity.

**Methods:** This study was conducted in the Geriatric and Rheumatology outpatient clinics at a tertiary University Hospital. Fifty elderly RA patients diagnosed according to the ACR criteria and 30 age-matched controls without inflammatory arthritis were included in the study. All patients underwent CGA including evaluation of Basic Activities of Daily Living (ADL), Instrumental ADL, Yesavage Depression Scale (YDS), Mini-Mental State Examination, handgrip strength and Mini-Nutritional Assessment-Short Form. Sleep quality was assessed by Pittsburg Sleep Quality Index (PSQI), disease activity with Disease Activity Score 28 (DAS28-CRP) and QoL with RA QoL questionnaire (RAQoL).

**Results:** The median age was 70 years (min-max: 65–86) and 62.5% was female. Age, gender and co-morbidities, such as hypertension, coronary artery disease, osteoporosis, urinary incontinence, depression and chronic obstructive pulmonary disease, and comprehensive geriatric assessment parameters were similar between two groups. Diabetes mellitus frequency was higher in the control group compared to RA patients (43.3% vs. 22.0%,  $p=0.044$ ). Median PSQI global score was higher in elderly patients with RA compared to controls [9 (min-max: 1–20) vs. 5 (min-max: 1–13),  $p=0.029$ ], indicating poorer sleep quality. In elderly patients with RA, DAS28-CRP score significantly correlated with PSQI global ( $r=0.514$ ,  $p<0.001$ ) and RAQoL scores ( $r=0.493$ ,  $p<0.001$ ). PSQI global score also significantly correlated with RAQoL score ( $r=0.689$ ,  $p<0.001$ ), number of medication ( $r=0.324$ ,  $p=0.022$ ), handgrip strength ( $r=-0.370$ ,  $p=0.017$ ) and YDS score ( $r=0.417$ ,  $p=0.005$ ).

**Conclusions:** Our results suggest that elderly patients with RA may have poorer sleep quality compared to elderly control patients. Disease activity of RA had adverse effects on both sleep quality and QoL. In daily practice, when evaluating an elderly RA patient, sleep quality should also be assessed. Further studies are needed to investigate if management of sleep disturbances improve quality of life in elderly patients with RA.

**Disclosure of Interest:** None declared

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### THU0173 TRENDS IN HIP FRACTURE INCIDENCE IN RHEUMATOID ARTHRITIS: A NATIONAL OBSERVATIONAL COHORT STUDY

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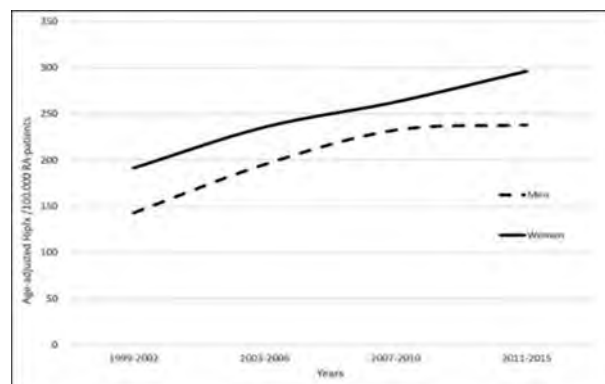
**Background:** During the last 20 years there have been significant changes in the treatment of patients with rheumatoid arthritis (RA) and in the prevention and treatment of osteoporosis. The potential impact of these strategies on important outcomes as the incidence of hip fracture in RA is unknown.

**Objectives:** To analyse the incidence and trend of hospital admissions for hip fracture in patients with RA, in Spain, during the period between 1999 and 2015.

**Methods:** This is a retrospective population based study. We analysed a national administrative database that includes a Minimum Basic Data Set (MBDS) of hospital admissions of patients with RA. Period: 1999 to 2015. The hip fracture cases were identified by the presence in primary and secondary diagnosis of ICD 9 codes. The population at risk was estimated through the population census of the

National Institute of Statistics, with an estimated prevalence of RA of 0.5%. The crude and adjusted rates of hip fracture were calculated. The trend was analysed using Generalised Linear Models (GLM) using the year variable as the analysis variable.

**Results:** Of a total of 338.343 admissions of patients with RA, 6.656 (2%) was due to hip fracture, 5.608 (84.2%) in women and 1.048 (15.7%) in men. The mean age was 77.54 (SD 9.6). Mean age increased linearly during the study period (from 75,3 years in 1999 to 79,9 in 2015). There was a total of 326 (4.9%) deaths during admission. The fracture age-adjusted rate during the study period was 243,66/100.000 RA-patients\*year (245,24 in women and 198,05 in men). The fracture age-adjusted rate increased from 150.11/100.000\*year in 1999, to 303.12 in 2015 (in both sex). In women from 134.71 in 1999 to 304.83 in 2015) and in men from 99.63 in 1999 to 268.5 in 2015). An annual increase in the fracture rate of 3.1% is estimated.



**Conclusions:** In Spain, during the period from 1999 to 2015, although the mean age has increased, the incidence of hip fracture has not been reduced. We estimate an annual increase of 3.1%.

**Disclosure of Interest:** None declared

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### THU0174 SEXUAL FUNCTION OF WOMEN WITH RHEUMATOID ARTHRITIS IN COMPARISON WITH HEALTHY VOLUNTEERS

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**Background:** Rheumatoid Arthritis (RA) is one of the first diseases where quality of life (QoL) measurements are considered as a therapeutic goal. Sexual health is an important part of a quality of life. Persons with RA often experience decreased sexual health, due to pain, fatigue and physical disability.

**Objectives:** To assess the prevalence of sexual dysfunction in married women with RA and to compare it with a control group.

**Methods:** We conducted a cross-sectional study including seventy one married women with RA (ACR/EULAR Criteria), having sexual activity and seventy one, healthy volunteers women matched for socio-demographic characteristics. Sexual function was assessed by a self-reported questionnaire the Index of Female Sexual Function (FSFI).

The comparison of qualitative variables was performed with the Chi square test and the comparison of qualitative variable and quantitative ones was performed with the Student's test. The significance level was set at 0.05.

**Results:** The prevalence of female sexual dysfunction in women with RA and in controls was 49% and 23,9% respectively. There was a significant difference in the total FSFI score between patients and controls (24±6,7 versus 27,05±5,34;  $p=0,002$ ). We found statistically significant differences between the two groups in dimensions of sexual function: desire ( $p=0,050$ ), arousal ( $p=0,038$ ) and satisfaction ( $p=0,024$ ). However, no significant differences were found for pain ( $p=0,757$ ), lubrication ( $p=0,069$ ) and orgasm ( $p=0,083$ ).

**Conclusions:** Our findings showed that RA adversely affects women's sexual function. The FSFI, easy and quick to use, could be proposed for the assessment of female sexual function to optimise the management of patients with RA.

**Disclosure of Interest:** None declared

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THU0175

### ASSESSMENT OF INSULIN RESISTANCE IN A RHEUMATOID ARTHRITIS INCEPTION COHORT: NESTED CASE-CONTROL STUDY

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**Objectives:** To assess insulin resistance (IR) in patients with rheumatoid arthritis (RA) and compare it with healthy controls and to analyse the association between the accumulated inflammatory burden in patients with RA and IR

**Methods:** **Design:** Nested case-control study. **Population:** consecutive RA-patients (ACR/EULAR 2010 criteria), >16 years, selected from a prospective inception cohort (diagnosis of RA between 2007 and 2011). Patients with Diabetes Mellitus (according to ADA 2010 criteria) were excluded. **Controls:** sex- age and BMI -matched controls were collected from a health centre in our hospital area. **Protocol:** Cases and controls were evaluated by a rheumatologist. Clinical data of disease activity (RA patients), analytical values and oral glucose tolerance test (OGTT) were determined. **Main outcome:** IR measured by the homeostasis model for insulin resistance (HOMA-IR) (IR >2.29µU\*mmol/ml). **Secondary outcome:** RI measured by quantitative insulin sensitivity check index (QUICKI) (<0.337µU \*mmol/ml) and by the homeostatic model assessment of β-cell function (HOMA β). **Variables:** Demographic, clinical-analytical variables, Disease Activity Score of 28 joints (DAS28-ESR), Health Assessment Questionnaire (HAQ), BMI (OMS classification) and glucose and insulin before and after OGTT values. **Statistical analysis:** Descriptive and paired T-test or Chi-square test followed by Multivariate linear regression in RA patients (Dependent variable: HOMA-IR)

**Results:** One hundred and fifty six subjects were studied, 4 of them were excluded after OGTT (2 diabetics and their respective controls). Finally, 1522 subjects were included; 89 RA and 63 controls. The mean age of patients with RA was 56.6 (10.9%) years. Most of them were women (76.4%), with seropositive (FR 83.1% y ACPA 79.1%) and erosive (62%) RA. The mean duration of the disease was 86 (±23) months and mean DAS28 index at the cut-off date of 2.8 (±1.1). Differences between clinical characteristics and in relation to IR between cases and controls are shown in table 1. No significant differences in the proportion of subject with IR in cases and controls were observed and 28.7% of patients with RA had IR. Of the 25 patients with IR, 75% had an average of DAS28 ≥3.2. In multivariate analysis, the independent variables associated with IR in patients with RA were: Obesity (β=1.7494 [p=0.003]), diagnosis delay (β=0.034 [p=0.003]) and disease activity (β=1.045 [p=0.058]). This model would explain 23% of the variability of the IR (R<sup>2</sup>=0.23).

VARIABLE	CASES n=89	CONTROLS n=63	P- VALUE
Age, years; mean(±SD)	56.6 (10.9)	56.1 (11.0)	0.756
Sex, women; n(%)	68(76.4)	52(82.5)	0.361
<b>Comorbidities</b>			
BMI > 30 (obesity) n(%)	30(34.1)	17(27.4)	0.386
BMI, mean(±SD)	28.2 (5.0)	27.2 (5.0)	0.205
Dyslipemia, n(%)	20 (22.7)	11 (18.6)	0.552
Hypertension, n(%)	23 (25.5)	16(25.8)	0.996
<b>Insulin Resistance Indexes</b>			
HOMA-IR>2.25, n(%)	25 (28.7)	17 (27.9)	0.908
HOMA-IR, mean(±SD)	25 (28.7)	17 (27.9)	0.908
HOMA-β, mean(±SD)	2.24 (2.6)	2.05 (1.5)	0.578
QUICKI, mean(±SD)	46.7 (32.3)	45.1 (32.1)	0.848

**Conclusions:** We did not find an increased IR in patients with RA compared with healthy controls, which may be due to adequate treatment and good control of inflammatory activity in the most of patients with RA. Obesity, diagnosis delay and inflammatory activity (measured by mean DAS28 index since the onset of the disease), were the predictors of IR in patients with RA in our study

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THU0176

### THE EFFECT OF METHOTREXATE ON GASTROINTESTINAL SYMPTOMS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Methotrexate (MTX) can cause gastrointestinal (GI) symptom in patients with rheumatoid arthritis (RA); however, it is uncertain how much dose of MTX affects GI symptoms. RA patients may receive various drugs besides MTX. NSAIDs are known to be a risk factor for GI disorders, and folic acid has been reported to reduce GI side effects of MTX. Moreover, obesity is a risk factor for reflux. Therefore, it is necessary to evaluate comprehensively the causes of GI symptoms in RA patients.

**Objectives:** To compare prevalence of GI symptoms for the patients with RA treated with low and high dose MTX, and investigate factors associated with GI symptoms.

**Methods:** A total of 529 patients with RA treated with MTX were included in this cross-sectional study. GI Symptom Rating Scale (GSRS) was used to evaluate GI symptoms. The GSRS has five subscales (Reflux, Abdominal pain, Indigestion, Diarrhoea and Constipation) and a seven-point graded Likert-type scale. Symptomatic was defined as a score of ≥2 on GSRS subscale. Patients were divided into two categories according to their MTX dosage: low dose (≤8 mg/week) and high dose (>8 mg/week). Prevalence was compared by two groups with the chi-square test, and factors associated with GI symptoms were assessed with multivariate logistic regression analysis.

**Results:** Patient characteristics are shown in table 1. Of all patients, 313 (59%) received low dose MTX at a mean (SD) dose of 6.2 (1.7) mg/week, whereas 216 (41%) received high dose MTX at a mean (SD) dose of 11.8 (1.8) mg/week. Relative to patients receiving low dose MTX, those receiving high dose MTX had a higher prevalence of reflux (24% vs 32%, p=0.047) and abdominal pain (18% vs 28%, p=0.008) (figure 1). Multivariate analysis revealed that higher dose MTX was independently associated reflux (OR: 1.62, 95% CI: 1.07–2.43) and abdominal pain (OR: 1.70, 95% CI: 1.12–2.59) (table 2). The odds ratio of reflux or abdominal pain in patients receiving high dose MTX was similar to that in patient receiving NSAIDs.

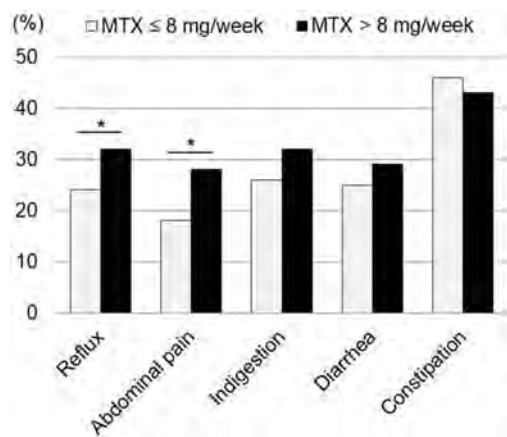
**Abstract THU0176 – Table 1.** Demographic and clinical characteristics of patients

	MTX≤8 mg/w (n=313)	MTX>8 mg/w (n=216)	P value
Age, years	64±12	60±15	<0.001
Gender, female, n (%)	258 (82)	170 (79)	0.312
Body mass index	22±3	22±3	0.604
Disease duration, years	14±11	11±9	<0.001
MTX dose, mg/week	6.2±1.7	11.8±1.8	<0.001
DAS28-CRP	1.95±0.82	2.24±0.99	<0.001
Folic acid, n (%)	264 (84)	201 (93)	0.003
csDMARD other than MTX, n (%)	32 (10)	50 (23)	<0.001
bDMARD, n (%)	108 (35)	44 (20)	<0.001
Glucocorticoid, n (%)	66 (21)	59 (27)	0.118
NSAID, n (%)	95 (30)	84 (39)	0.050
Proton pump inhibitor, n (%)	49 (16)	47 (22)	0.085

**Abstract THU0176 – Table 2.** Factors associated with score of ≥2 on GSRS subscales

Reflux	OR (95% CI)	Abdominal pain	OR (95% CI)
Female	1.94 (1.11–3.39)	MTX≤8 mg/week (ref.)	1.00
NSAID	1.71 (1.13–2.68)	MTX>8 mg/week	1.70 (1.12–2.59)
MTX≤8 mg/week (ref.)	1.00	NSAID	1.67 (1.09–2.55)
MTX>8 mg/week	1.62 (1.07–2.43)		
Body mass index*	1.12 (1.06–1.19)		
Disease duration, year*	1.02 (1.01–1.04)		

\* Odds ratio for 1-unit increase in each item.



Abstract THU0176 – Figure 1. Percentage of patients with GSRS score  $\geq 2$ .

**Conclusions:** MTX more than 8 mg/week is associated with upper GI symptoms as much as NSAIDs in Japanese patients with RA.

**Disclosure of Interest:** None declared

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#### THU0177 CAN SIMPLE EDUCATIONAL FLASHCARDS CHANGE ATTITUDES TO VACCINATION IN AN UNDER-VACCINATED RHEUMATOID ARTHRITIS COHORT?

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**Background:** There is increased infection risk in RA which relates to immune system dysregulation, comorbidities and immunosuppression.<sup>1,2</sup> Therefore, there is a need to improve currently suboptimal vaccination rates reported globally.<sup>3</sup>

**Objectives:** To re-examine vaccination rates and to determine if educational flashcards with messages targeted to patient perceptions can change attitudes towards vaccination in a tertiary hospital RA clinic cohort.

**Methods:** Vaccination status and attitudes were examined in 126 consecutive rheumatoid arthritis clinic patients (data collection ongoing). Patients were then shown two simple educational flashcards and any shift in attitude to vaccination was recorded. Insights gleaned from a 2016 study on attitudes to vaccination in the same cohort were used to design the flashcards based on unvaccinated patients' main concerns.<sup>4</sup>

**Results:** The RA cohort was representative of a typical RA population. 67% of patients were female with a mean age of 57 years (range 18 to 88 years). 40% of patients were on biologic medication and 34% were on prednisolone. 13% of patients were previously hospitalised for influenza or pneumonia and 15% had a close contact hospitalised for these infections. 37% of patients had not received the influenza vaccine. In patients over 65 years old, 51% had not received the pneumococcal vaccine within the last 5 years, and of those, 80% had never been vaccinated against pneumococcal. Reasons reported for not being vaccinated included "I forgot", "I worry about the side effects of vaccine", "I don't think I need the vaccine as I don't get the flu", and "I had the vaccine and it made me sick". 33% of patients were not aware of the hospital's free vaccination service, and of those that were aware of this service 13% cited this as their main reason for getting the vaccine.

After reading the education flashcards 49% of currently unvaccinated patients reported "I feel more informed and am more likely to get the vaccine next year". Rates of vaccination, infection and attitudes both pre and post flashcards did not differ between patients on biologics and not on biologics (all p-values > 0.05).

##### Reasons reported for not vaccinating (in order of frequency)

1	I forgot
2	I am worried about the side effects of the vaccine.
3	I don't think I need the vaccine as I don't get the flu.
4	I had the vaccine and it made me sick.
5	I don't think the vaccine will work.,
6	I have received it before so I don't need it or want it this year.
7	I am afraid of needles

#### Vaccine Education Flashcards



**Conclusions:** This at-risk RA cohort continues to be under-vaccinated in studies over the past two years. Simple flashcards showed potential to change attitudes in unvaccinated patients who were previously comfortable to express resistance. Insights from this study could be used to refine and reiterate this educational intervention for implementation in a larger cohort to measure impact on vaccination rates in subsequent years.

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**Disclosure of Interest:** None declared

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#### THU0178 CLINICAL SIGNIFICANCE OF PERIODONTITIS IN RHEUMATOID ARTHRITIS PATIENTS: ASSOCIATION WITH DISEASE ACTIVITY, FUNCTIONAL STATUS AND RADIOLOGRAPHIC SCORE

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##### Background:

**Objectives:** To evaluate frequency of periodontitis (PD) in rheumatoid arthritis (RA) patients and relate it with clinical characteristics, disease activity, functional status, anti-cyclic citrullinated peptide (anti-CCP) and radiographic scores.

**Methods:** The study included 60 RA patients and 30 controls. Clinical Disease activity index (CDAI), Modified Health Assessment Questionnaire (MHAQ), visual analogue scale of pain and Scott's modification to Larsen scoring method were assessed. Rheumatoid factor (RF) positivity and antiCCP titer were measured. Periodontal examination was performed and relevant indices calculated

**Results:** The mean age of the patients was 49.1±13 years and they were 52 females and 8 males. PD was present in 71.7% of RA patients versus 46.7% in control (p=0.02). PD was predominantly generalised (p=0.004) and moderate-severe degree (p=0.01). Age (p=0.007), disease duration (p<0.0001), morning stiffness (p=0.01), CDAI (p<0.0001), MHAQ (p=0.02), CRP (p=0.02), anti-CCP titer (p=0.01) and methotrexate treatment (p=0.005) were significantly higher in RA-PD versus RA. However, gender, smoking, oral hygiene, erythrocyte sedimentation rate, RF, anti-CCP positivity and radiographic scoring were insignificantly different. PD positivity was 96.3%, predominant generalised in 92.6%, moderate (40.7%) and severe degree (37%) in early RA versus (51.5%, 24.2%, 24.2%, 12.1% respectively) in late RA patients. All PD indices were higher in early patients (p≤0.05) while teeth loss (p=0.03) was higher in late cases. CDAI, VAS and ACPA titer all significantly correlated with PD indices (p<0.05).

**Conclusions:** Periodontitis is frequent in RA patients' especially in early cases and is remarkably associated to disease activity and reduced functional status.

**Disclosure of Interest:** None declared

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**THU0179** **MIR-382-5P TARGETING IL-33 GENE AS BIOMARKER TO PREDICT SUBCLINICAL ATHEROSCLEROSIS PROGRESSION IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS**

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**Background:** Patients with rheumatoid arthritis(RA) had increased risk of cardiovascular disease(CVD). IL-33, a member of the IL-1 family, plays an important role in the pathogenesis of RA and development of CVD. Yet, plasma IL-33 level was not detectable in most subjects which limits its utility as a biomarker for CVD. Meanwhile, microRNAs(miRNAs) targeting IL-33 gene expression might play a role.

**Objectives:** To ascertain if dysregulated miRNAs targeting *IL-33* gene expression in early RA patients were associated with subclinical atherosclerosis progression

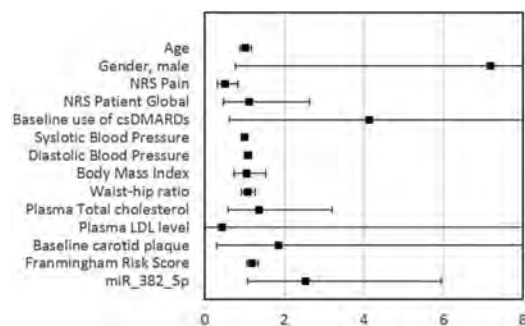
**Methods:** 73 ERA patients were recruited for this 1 year cohort study. Potential miRNAs binding to *IL-33* gene were predicted by miRanda. 10 miRNAs with the highest possibility of targeting functional sites of *IL-33* gene were quantified in cell free plasma samples. cel-miR-39 was used as spike-in control. Carotid plaque (CP) was identified using high-resolution ultrasound annually. Plaque progression (PP) was defined as an increased region harbouring plaque.

**Results:** CPs were identified in 25 (34%) and 31 (43%) subjects at baseline and month 12 respectively. 16 (22%) subject had plaque progression(PP +group). At baseline, subjects in PP +group were older, with lower pain and patient global scores, a higher proportion on conventional synthetic DMARDs, and higher cardiovascular risk compared to patients without plaque progression (PP-) (table 1). Plasma level of miR-382-5 p in the PP +group was significantly higher than that in the PP- group after adjusting for baseline difference (table 1). Using multivariate logistic regression, miRNA-382-5 p was an independent predictor for plaque progression(OR:2.534, 95%CI=1.079-5.952, p=0.033) after adjustment of baseline characteristics. [AUC:0.66,95% CI:0.51-0.81,p=0.048]. Other independent predictor included higher baseline Framingham risk score, diastolic BP and lower pain score.

**Abstract THU0179 – Table 1.** Characteristics of patients with and without plaque progression

	No plaque progression (n=57)	Plaque progression (n=16)	p	p*
Age	50±12	56±7	0.011	
Gender, male	11 (19.3%)	6 (37.5%)	0.128	
Framingham Risk Score	6.1±7.9	14.2±11.6	0.017	
log miRNA				
miR_9_5 p	-1.14±1.48	-1.23±0.97	0.825	0.947
miR_382_5 p	0.79±0.66	1.38±1.29	0.094	0.011
miR_377_3 p	0.75±0.65	0.96±0.85	0.285	0.783
miR_590_3 p	0.2±0.46	0.13±0.16	0.517	0.472
miR_499a_5 p	-1.65±0.67	-1.48±0.88	0.418	0.370
miR_145_5 p	2.43±1.35	3.26±2.08	0.060	0.169
miR_542_3 p	-1.95±0.55	-1.85±0.99	0.615	0.750
miR_186_5 p	2.67±1.42	2.77±1.69	0.811	0.556
miR_214_3 p	-0.68±1.29	-0.8±1.02	0.730	0.849
miR_496	-1.65±0.9	-1.68±0.83	0.917	0.538

\*adjusted for age, sex, baseline NRS pain, patient global score, wrist to hip ratio, plasma LDL level and Framingham risk score



**Abstract THU0179 – Figure 1.** Multivariate regression analysis for plaque progression

**Conclusions:** miR-382-5 p was an independent predictor for progression of sub-clinical atherosclerosis and may serve as a novel biomarker for cardiovascular risk assessment in ERA patients.

**Acknowledgements:** Acknowledgement to Hong Kong Society of Rheumatology Project Fund for supporting this project.

**Disclosure of Interest:** None declared

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**THU0180** **SHOULD WE INCLUDE ULTRASOUND IN THE 1987 ACR AND 2010 ACR/EULAR CLASSIFICATION CRITERIA FOR RHEUMATOID ARTHRITIS?**

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**Background:** Ultrasound imaging (US) is actually considered as a crucial element of the diagnostic process in rheumatic diseases and could be the method of choice in imaging peripheral synovitis, typical feature during rheumatoid arthritis (RA). The 2010 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) classification criteria focused on early-stage RA, and were designed to remedy the deficiencies in the 1987 ACR criteria, but still lacking sensitivity.

**Objectives:** We undertook this study to investigate whether including the ultrasonographic data in calculating the 1987 ACR and 2010 ACR/EULAR criteria is useful in diagnosing RA.

**Methods:** We performed a cross-sectional study of one hundred patients with inflammatory joint pain or synovitis for more than 6 weeks and less than 2 years.

An experienced radiologist performed the MSUS scan of 22 joints (2 wrists, 10 metacarpophalangeal joints MCP and 10 proximal interphalangeal joints PIP) unaware of clinical and biological findings. After US assessment, patients were classified as having RA according to ACR/ EULAR 2010 criteria using clinical, biologic and radiographic data (clinical ACR87 or clinical ACR/EULAR2010). Then we calculate those criteria using US data: US-ACR87 including erosion detected in US as a criterion and US-ACR/EULAR2010 including the number of synovitis detected in US as a criterion.

**Results:** One hundred RA patients were included (77 women and 23 men) with a mean age of 51.8 years. <sup>16-77</sup> The mean disease duration was 10.96. <sup>24</sup> Rheumatoid factor and antibodies against cyclic citrullinated peptides were positive in 53% and 25% cases respectively. Sixty-five patients (65%) accomplished the clinical ACR87 criteria and 55 patients (55%) fulfilled the clinical ACR/EULAR2010 criteria for the diagnosis of RA. Using US data eighty patients (80%) accomplished the US-ACR87 criteria and 68 patients (68%) fulfilled the US-ACR/EULAR2010 criteria for the diagnosis of RA. A good correlation was found between clinical and US ACR/EULAR criteria (k=0.684, p=0.000). US score showed a very good sensitivity of 100%, specificity of 67.5%, positive predictive value of 76.9% and negative predictive value of 100% compared to clinical score. In table 1 we summarise correlation between clinical and US ACR/EULAR criteria.

**Abstract THU0180 – Table 1.** Correlation between clinical and US ACR/EULAR criteria

	Clinical ACR/EULAR2010			
	Yes	No	Total	
US-ACR/EULAR2010	Yes	50	18	68
	No	5	27	32
	Total	55	45	100

**Conclusions:** Our study showed that including US data in the classification criteria of RA, will improve diagnostic impact of those criteria during RA management.

**Disclosure of Interest:** None declared

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**THU0181** **GLUCOCORTICOID USE IS AN INDEPENDENT RISK FACTOR FOR SARCOPENIA IN PATIENTS WITH RHEUMATOID ARTHRITIS – FROM THE CHIKARA STUDY -**

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**Background:** Patients with rheumatoid arthritis (RA) are at higher risk of sarcopenia due to joint dysfunction and chronic inflammation. The prospective observational CHIKARA study (Correlation research of sarcopenia, skeletal muscle and disease activity in rheumatoid arthritis; registration number UMIN000023744) was



started in 2016 to clarify the correlation between RA disease activity and sarcopenia.

**Objectives:** We investigated risk factors for developing sarcopenia in patients with RA.

**Methods:** We analysed baseline and 1 year data from the CHIKARA study. The body composition (body weight, muscle mass, fat mass, predicted bone mass, etc.) of 100 patients (78% women; mean age, 68 years) enrolled in this study was examined using a body composition analyzer (MC-780A; TANITA, Tokyo, Japan). Grip strength and walking speed were also measured. Laboratory data, disease activity, Health Assessment Questionnaire (HAQ) and treatment were investigated. Sarcopenia was diagnosed using the criteria of the Asia Working Group on Sarcopenia. Patients with sarcopenia onset at 1 year were detected and their characteristics were analysed. Predictors for development of sarcopenia were also investigated by uni- and multivariate analyses.

**Results:** Nine patients developed sarcopenia during 1 year. Glucocorticoid (GC) use was significantly more frequent among patients with sarcopenia onset (55.6%) than among those without sarcopenia onset (22.1%,  $p=0.029$ ). Univariate analysis revealed that GC dosage ( $r=0.217$ ,  $p=0.035$ ), body fat mass at baseline ( $r=-0.211$ ,  $p=0.040$ ) and change in CRP at 1 year ( $r=-0.205$ ,  $p=0.046$ ) were significantly associated with sarcopenia onset. GC use  $>2$  mg/day (Odds ratio (OR) 8.0, 95% confidence interval (CI) 1.2–54.8,  $p=0.034$ ) and body fat mass (OR 0.78, 95% CI 0.61–0.98,  $p=0.037$ ) were detected as significant factors by multivariate analysis. (table 1)

**Abstract THU0181 – Table 1.** Risk factors for developing sarcopenia in patients with rheumatoid arthritis

		Univariate		Multivariate		
		R value	p value	Odds ratio	95% CI	P value
GC	Dosage $>2$ mg/day	0.217	0.035	8.0	1.2–54.8	0.034
		-	-	-	-	-
Body fat mass		-0.211	0.040	0.78	0.61–0.98	0.037
		-	-	-	-	-
$\Delta$ CRP		-0.205	0.046	-	-	-

GC: glucocorticoids, CI: confidence interval,  $\Delta$ : change from baseline to 1 year

**Conclusions:** RA patients using GC at  $>2$  mg/day or with low fat mass were more likely to develop sarcopenia.

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THURSDAY, 14 JUNE 2018

## Rheumatoid arthritis – biological DMARDs

THU0182

### A COMPARATIVE CLINICAL STUDY OF PF-06410293, A CANDIDATE ADALIMUMAB BIOSIMILAR, AND REFERENCE ADALIMUMAB FOR THE TREATMENT OF ACTIVE RHEUMATOID ARTHRITIS

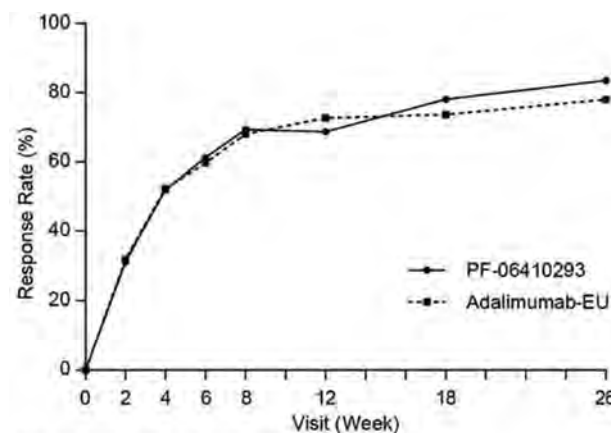
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**Background:** To confirm the efficacy, safety and immunogenicity of biosimilars, a comparative clinical study is typically required.

**Objectives:** This double-blind, randomised, 78 week (wk) study compared the efficacy, safety and immunogenicity of PF-06410293, a candidate adalimumab biosimilar, with reference adalimumab sourced from the EU (ADA-EU), in biologic-naïve patients (pts) with active rheumatoid arthritis (RA) despite methotrexate (MTX; 10–25 mg/wk).

**Methods:** Pts with active RA ( $n=597$ ) were stratified by region and randomised (1:1) to PF-06410293 or ADA-EU (40 mg subcutaneous injection every 2 wks), with continued MTX. The primary endpoint was American College of Rheumatology 20% improvement (ACR20) at Wk 12. Therapeutic equivalence was concluded if the 2-sided 95% confidence interval (CI) for the difference in Wk 12 ACR20 between arms was within the symmetric equivalence margin of  $\pm 14\%$ . Additionally, a 2-sided 90% CI was requested by the US Food and Drug Administration, using the asymmetric equivalence margin of  $-12\%$  to  $+15\%$ . Secondary efficacy endpoints to Wk 26 included ACR20/50/70, change from baseline Disease Activity Score in 28 joints [DAS28(CRP)], European League Against Rheumatism (EULAR) response, achievement of DAS28(CRP)  $<2.6$ , and ACR/EULAR remission. QuantiFERON-TB testing was performed at Screening and Wk 26.

**Results:** Pts (78.7% female, 81.6% seropositive) had a mean age of 52.5 years, and mean RA duration of 6.8 years. Mean baseline DAS28(CRP) was 5.9 (PF-06410293) and 6.1 (ADA-EU). The observed Wk 12 ACR20 was 68.7% (PF-06410293) and 72.7% (ADA-EU) in the intent-to-treat population (figure 1). Using non-responder imputation ( $n=19$ ; 3.2%), the treatment difference in Wk 12 ACR20 was  $-2.98\%$ , and the corresponding CIs [95% CI ( $-10.38\%$ ,  $+4.44\%$ ); 90% CI ( $-9.25\%$ ,  $+3.28\%$ )] were entirely contained within both equivalence margins (symmetric and asymmetric). The ACR20 difference ranged from  $-3.98\%$  to  $+5.50\%$  (Wks 2–26). Mean DAS28(CRP) change from baseline at Wk 26 was  $-2.7$  and  $-2.8$  in the PF-06410293 and ADA-EU arms, respectively. ACR50/70, EULAR response, DAS28(CRP)  $<2.6$  and ACR/EULAR remission were similar between arms at each visit. Incidence of treatment-emergent adverse events (AEs) was 48.1% vs 47.8%, serious AEs were 4.0% vs 4.3% (with a fatal myocardial infarction in the ADA-EU arm) and serious infections were 0.7% vs 1.3% for PF-06410293 and ADA-EU, respectively. Injection site reactions occurred at 1.7% vs 2.0%, hypersensitivity events at 4.4% vs 8.4%, pneumonia at 0.7% vs 2.0%, and latent tuberculosis (based on specialist consultation for Wk 26 QuantiFERON-TB+) at 1.7% vs 0.3% for PF-06410293 and ADA-EU, respectively. Post-dose anti-drug antibody rates to Wk 26 were 44.4% (PF-06410293) and 50.5% (ADA-EU).



ACR=American College of Rheumatology; ITT=Intent-to-treat.

Figure 1. ACR20 response rates (ITT population)

**Conclusions:** The efficacy, safety and immunogenicity of PF-06410293 and ADA-EU were similar up to Wk 26 in pts with active RA on MTX. At Wk 26, pts on ADA-EU were blindly re-randomised (1:1) to continue ADA-EU or transition to PF-06410293 for ongoing treatment in the study.

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THU0183

### LESS PAIN OVER 2 YEARS WITH BIOLOGICAL COMPARED TO CONVENTIONAL COMBINATION THERAPY IN EARLY RHEUMATOID ARTHRITIS: RESULTS FROM THE RANDOMISED CONTROLLED SWEFOT TRIAL

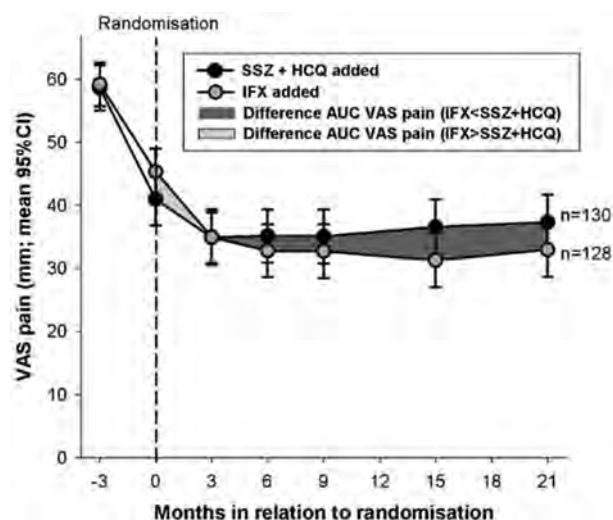
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**Background:** Pain is a common and debilitating feature of rheumatoid arthritis (RA) and a level >40 mm on a Visual Analogue Scale (VAS) of pain (scale 0–100 mm) has been suggested as a measure of unacceptable pain.<sup>1</sup> While many studies have focused on the effect on inflammation of different pharmacological options, few earlier reports have directly compared pain outcomes between common treatment strategies.

**Objectives:** The aim of this study was to investigate pain development and unacceptable pain over 2 years after start of biological as compared to conventional combination therapy in early RA patients.

**Methods:** The multicentre SWEFOT (SWEdish FarmacOTherapy) trial was designed as a randomised, active-controlled, open-label study, enrolling new-onset (<1 year) patients fulfilling 1987 American College of Rheumatology criteria for RA Oct 2002 to Dec 2005. After a 3 month run-in period on methotrexate (MTX), patients who did not reach low disease activity (Disease Activity Score using 28-joint count; DAS28 ≤3.2) were randomised to addition of infliximab (IFX) or sulfasalazine +hydroxychloroquine (SSZ +HCQ). Results for disease activity, radiographic data and health-related quality-of-life have been published earlier.<sup>2,3</sup> Here, unacceptable pain (VAS pain >40 mm) at 2 years follow-up and area under the curve (AUC) for VAS pain were used as outcome measures. We used intention-to-treat with last observation carried forward in case of protocol breach as study approach. Statistical analyses were performed by logistic regression for unacceptable pain and analysis of covariance for AUC for VAS pain, adjusting for age, sex, and VAS pain at randomisation.

**Results:** 487 RA patients were enrolled of whom 258 (who did not respond sufficiently to MTX) were randomly allocated to either addition of IFX (n=128) or SSZ +HCQ (n=130). Baseline characteristics were similar between the two groups. Of patients assigned to IFX, 32% had unacceptable pain at 2 years follow-up (21 months after randomisation), while the same figure for SSZ+HCQ (n=130) was 45% (adjusted odds ratio 0.41 [95%CI 0.23–0.73]; p=0.003). Serial VAS pain measurements are displayed in figure 1. An AUC analysis for mean VAS pain levels from randomisation to 2 years follow-up confirmed significantly lower levels for patients randomised to IFX compared to SSZ+HCQ (p=0.01).



**Conclusions:** Despite early active treatment, a large share of new-onset RA patients showed unacceptable pain after 2 years. Interestingly, both the fraction of patients with unacceptable pain and assessment of pain over time were substantially lower for patients randomised to addition of IFX compared to SSZ+HCQ, contrasting to earlier SWEFOT reports where significant between-group differences at 2 years follow-up for disease activity and health-related quality-of-life were not seen.<sup>2,3</sup> This suggests a better effect on long term pain for the biological therapy, which could be taken into account when choosing treatment strategy in patients responding insufficiently to MTX.

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THU0184

### IMPACT OF IMMUNOGENICITY ON CLINICAL EFFICACY AND ADMINISTRATION RELATED REACTION IN TNF INHIBITORS: A POOLED-ANALYSIS FROM THREE BIOSIMILAR STUDIES IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** SB4, SB2, and SB5 are biosimilars of reference etanercept, infliximab, and adalimumab, respectively. The phase III randomised, double-blind clinical studies comparing the efficacy and safety of each biosimilar with its reference product had similar study designs, patient demographics, and the same primary endpoint of the ACR20 response rate. In each study immunogenicity was measured using a validated ECL assay tagged with the biosimilar.

**Objectives:** To assess the immunogenicity of three TNFi and examine the potential impact of anti-drug antibodies (ADAb) on efficacy and injection site reactions (ISR) or infusion related reactions (IRR) by a pooled analysis of three biosimilar studies.<sup>1–3</sup> Data to the time of the primary endpoint for each study (week 24 for etanercept and adalimumab studies and week 30 for infliximab study) are presented.

**Methods:** Data from patients who had immunogenicity results from each phase III study were pooled. Efficacy (ACR responses, clinical response [defined as good or moderate EULAR response], change in disease activity [DAS28, SDAI, CDAI]) and ISR/IRR were evaluated in relation to the presence of ADAb (at least one ADAb positive result up to when the primary endpoint was measured).

**Results:** The analysis included 1710 patients and the incidence of ADAb by treatment group is presented in the table 1.

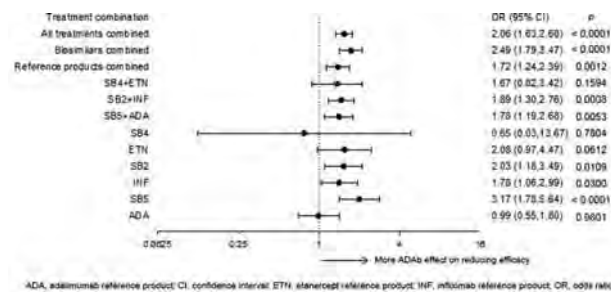
Across treatment groups, efficacy was greater in patients without ADAb compared to those with ADAb. In all treatments combined, the ACR20 response rate was lower in the presence of ADAb (OR 2.06, 95% CI: 1.63–2.60, p<0.0001) (figure 1) and the mean improvement in DAS28 was significantly greater in patients without ADAb (estimated difference: 0.383, 95% CI: 0.24–0.52, p<0.0001). The ADAb effect on reducing ACR20 response rates as well as other efficacy parameters was similarly observed in other treatment groups.

In all treatments combined, the presence of ADAb was associated with increased ISR/IRR (OR 1.73, 95% CI: 1.02–2.96, p=0.043), predominantly with the infliximab combined (OR 2.67, 95% CI: 1.04–6.89, p=0.041) rather than the etanercept combined (OR 1.72, 95% CI: 0.38–7.77, p=0.478) and adalimumab combined (OR 1.00, 95% CI: 0.35–2.88, p=0.998).

Abstract THU0184 – Table 1. Incidence of Anti-drug Antibody (n/n)

Treatment	SB4	ETN	SB2	INF	SB5	ADA
ADAb	2/299	39/297	158/287	145/292	88/266	86/269
Incidence	(0.7%)	(13.1%)	(55.1%)	(49.7%)	(33.1%)	(32.0%)
Treatment	SB4 +ETN	SB2+INF	SB5 +ADA	Biosimilars combined	RP combined	All treatments combined
ADAb	41/596	303/579	174/535	248/852	270/858	518/1710
Incidence	(6.9%)	(52.3%)	(32.5%)	(29.1%)	(31.5%)	(30.3%)

ADA, adalimumab reference product; ADAb, anti-drug antibody; ETN, etanercept reference product; INF, infliximab reference product; RP: reference product



Abstract THU0184 – Figure 1. Effect of Anti-drug Antibody on ACR20 Response Rates

**Conclusions:** In a pooled analysis, the development of ADABs to TNFi is associated with reduced clinical efficacy and increased incidence of ISR/IRR in patients with RA.

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**THU0185 THE VALUE OF ADALIMUMAB TROUGH LEVELS AND CLINICAL ASSESSMENTS IN PREDICTING CLINICAL RESPONSE IN PATIENTS WITH ESTABLISHED RHEUMATOID ARTHRITIS AND AN INADEQUATE RESPONSE TO METHOTREXATE**

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**Background:** Low trough levels of the tumour necrosis factor inhibitor, adalimumab (ADL), and anti-ADL antibodies (AAA) were reported to be correlated with lack of response at later time points in patients (pts) with rheumatoid arthritis (RA).<sup>1</sup>

**Objectives:** To assess the ability of ADL trough levels and clinical assessments at Week 12 to predict clinical remission (REM) after 24 weeks (wks) of treatment with ADL ±methotrexate (MTX) in established RA pts.

**Methods:** Data from MTX inadequate responders (MTX-IR) pts with established RA with available measurement of ADL trough levels and clinical assessments at Wks 12 and 24 from several clinical trials were pooled: for pts who received ADL +MTX combination therapy from DE009, DE019, M10–261 and M13–390; for pts who received ADL monotherapy from DE011, M10–261 and M13–390. Efficacy endpoints at Wk 24 were DAS28-CRP<2.6 and DAS28-CRP low disease activity (LDA,<3.2), remission (REM) and LDA by simplified disease activity index (SDAI)≤3.3 and≤11 respectively; REM and LDA by clinical disease activity index (CDAI)≤2.8 and≤10 respectively). Each of the pooled datasets was randomly and equally split into training and testing sets. Predictive modelling was performed on

the training set, and the best-performing model was selected and validated in the testing set. The performance of the final model was reported based on the testing set.

**Results:** Based on the cutoffs selected by the predictive model, ADL concentrations at Wk 12 were only slightly predictive for Wk 24 clinical assessment in the ADL monotherapy group, but not in the ADL+MTX group (table 1). However, based on achievement of the specified CDAI, SDAI or DAS28-CRP score at Wk 12 (selected by the model), pts were correctly predicted to reach Wk 24 REM or LDA with an accuracy of 80%–90% and area under the receiver operating characteristic curve (AUC) of 75%–90% (table 2). As an example, pts on ADL monotherapy with DAS28 <3.3 at Wk 12 had 60% and 70% chance of reaching Wk 24 DAS28-CRP<2.6 and LDA respectively, whereas pts with DAS28 ≥3.3 had 0% and 7% chance of achieving Wk 24 DAS28-CRP<2.6 and LDA, respectively (table 1). Pts on ADL+MTX with Wk 12 SDAI<12.5 had a 25% and 77% chance of achieving SDAI REM and LDA at Wk 24, respectively.

Abstract THU0185 – Table 1

Ability of Week 12 Drug Concentration to Predict Disease Control at Week 24 in Patients Treated with ADL / MTX											
Week 24 Endpoints	Week 12 conc (µg/ml)	High conc resp rate (n)	Low conc resp rate (n)	Sensitivity	Specificity	PPV	NPV	AUC			
<b>ADL Monotherapy</b>											
DAS28 <2.6	>7.62	0.36 (11)	0.05 (42)	0.67	0.85	0.36	0.95	0.76			
CDAI REM	>7.82	0.27 (11)	0.05 (42)	0.60	0.83	0.27	0.95	0.72			
SDAI REM	>7.62	0.27 (11)	0.05 (42)	0.60	0.81	0.27	0.95	0.72			
DAS28 LDA	<6.51	0.42 (12)	0.122 (43)	0.50	0.84	0.42	0.88	0.77			
SDAI LDA	>7.27	0.46 (11)	0.148 (42)	0.46	0.88	0.46	0.86	0.77			
CDAI LDA	<6.806	0.42 (12)	0.171 (43)	0.42	0.83	0.42	0.82	0.74			
<b>ADL + MTX Combination Therapy</b>											
DAS28 <3.2	>9.03	0.24 (46)	0.34 (88)	0.34	0.65	0.24	0.76	0.50			
CDAI REM	>7.43	0.10 (68)	0.11 (84)	0.5	0.48	0.10	0.89	0.48			
SDAI REM	>7.03	0.11 (70)	0.10 (82)	0.57	0.48	0.11	0.90	0.52			
DAS28 LDA	<8.87	0.41 (49)	0.42 (83)	0.36	0.82	0.41	0.58	0.52			
CDAI LDA	<4.50	0.42 (100)	0.44 (113)	0.75	0.24	0.42	0.56	0.46			
SDAI LDA	<9.00	0.48 (46)	0.47 (86)	0.34	0.85	0.48	0.54	0.51			
Ability of Selected Week 12 Clinical Scores to Predict Disease Control at Week 24 in Patients Treated with ADL / MTX											
Week 24 Endpoints	Week 12 Cutoff	Pts missing		n	resp. rate	Sens. rate	Specificity	PPV	NPV	Accu. rate	AUC
		missing	not missing								
<b>ADL Monotherapy</b>											
DAS28 <2.6	DAS28 <3.3	10	0.60	43	0.0	1.00	0.92	0.80	1.00	0.81	0.96
CDAI REM	CDAI <3.6	8	0.63	45	0.0	1.00	0.94	0.63	1.00	0.94	0.97
SDAI REM	SDAI <11.3	10	0.50	41	0.0	1.00	0.90	0.50	1.00	0.91	0.95
DAS28 LDA	DAS28 <3.9	10	0.70	41	0.07	0.70	0.93	0.70	0.91	0.89	0.82
CDAI LDA	CDAI <11.8	10	0.70	41	0.09	0.64	0.91	0.70	0.91	0.87	0.78
SDAI LDA	SDAI <12.7	10	0.80	41	0.09	0.67	0.90	0.80	0.91	0.89	0.81
<b>ADL + MTX Combination Therapy</b>											
DAS28 <2.6	DAS28 <3.3	11	0.49	95	0.15	0.56	0.81	0.49	0.83	0.75	0.69
CDAI REM	CDAI <7.0	29	0.41	103	0.02	0.86	0.86	0.41	0.96	0.86	0.56
SDAI REM	SDAI <7.9	22	0.38	100	0.02	0.80	0.83	0.38	0.96	0.83	0.64
DAS28 LDA	DAS28 <3.5	61	0.72	71	0.16	0.80	0.78	0.72	0.85	0.79	0.79
CDAI LDA	CDAI <12.2	57	0.74	79	0.19	0.75	0.80	0.74	0.81	0.78	0.78
SDAI LDA	SDAI <12.5	57	0.77	75	0.23	0.72	0.82	0.77	0.77	0.77	0.77

**Conclusions:** The ADL concentrations at Week 12 selected by the prediction model were weak predictors of disease control at 6 months, especially for pts on ADL+MTX combination therapy. However, using the model-selected cutoffs of composite clinical endpoints at Wk 12, disease control after 6 months of ADL ±MTX treatment could be correctly predicted in 70%–80% of pts.

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THU0186

### RHEUMATOID ARTHRITIS AND INTERSTITIAL LUNG DISEASE. MULTICENTRIC RETROSPECTIVE STUDY OF 118 PATIENTS TREATED WITH BIOLOGICAL NO ANTI TNF

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**Background:** Interstitial lung disease (ILD) associated with Rheumatoid Arthritis (RA) has a poor prognosis. Treatments such as anti-TNF, have been implicated in the exacerbation of an ILD.

**Objectives:** Our objective is to evaluate and compare the evolution of ILD in patients with RA treated with Abatacept (ABA), Rituximab (RTX) and Tocilizumab (TCZ) after 1 year of treatment.

**Methods:** Retrospective multicentre study of patients with ILD and AR treated with ABA, RTX and TCZ at standard doses. The ILD was diagnosed by CT. The efficacy was evaluated with the following measures: i) Dyspnea by modified scale of the Medical Research Council (mMRC); considering variations of 1 point. ii) Respiratory function tests; considering variations in FVC and DLCO  $\geq 10\%$ . iii) Imaging test (CT).

**Results:** We included 118 (72 women/46 men) patients, mean age of 62.27  $\pm$  10.55 years. The ILD had a median evolution of 12 12–37 months. The RA was ACPA+in 102 cases (86.4%). At diagnosis, the mean DLCO onset of biological treatment was 65.63 $\pm$ 19.38. Table 1 shows the characteristics by subgroups. The Figure expresses the evolution in the cases available at 12 months. There is an improvement in CT in 36.4% of patients with ABA, 28.6% of patients with RTX and only 8.3% of patients with TCZ.

Abstract THU0186 – Table 1

	ABA	RITU	TCZ	p
AGE median years	65 (57–70)	64 (54,75–72)	60 (48–68,5)	0.187
SEX M/F	36/27	21/9	15/10	0.490
SMOKER OR EX-SMOKER Si/No	25/38	13/17	11/14	0.909
APCC+	85,7	90	84	0.776
BIOLOGICAL DMARD BEFORE%	44,4	30	60	0.084
DLCO Onset	64.76	67.52	65.58	0.854
	$\pm 15.93$	$\pm 23.4142$	$\pm 22.700$	
CT	29/34	14/16	11/14	0.677
UIP/OTHERS				
FVC at star	87.09	87.83 $\pm$ 23.14	80.38	0.178
	$\pm 15.56$		$\pm 27.79$	
MONTHS OF EVOLUTION OF PNEUMONITIS	12 (12–36,75)	15 (5,75–37,75)	10 (3–10)	0.875

\*p significant &lt;0,05



**Conclusions:** There seems to be a trend towards a better radiological response in patients treated with RTX and ABA. It would be necessary prospective studies.

**Disclosure of Interest:** None declared

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THU0187

### CIRCULATING AUTOANTIBODIES AS INDICATORS TO PREDICT THE CLINICAL RESPONSE TO INFLIXIMAB IN RHEUMATOID ARTHRITIS

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**Background:** Approximately a third of Rheumatoid Arthritis (RA) patients treated with tumour necrosis factor (TNF)- $\alpha$  inhibitors such as Infliximab (IFX) fail to respond. This has prompted a widespread interest in the finding of measures for predictors of response to TNF $\alpha$  inhibitors.

**Objectives:** To search for serum autoantibodies that aid to identify RA patients most likely to benefit from IFX.

**Methods:** We analysed serum of 170 biologic-naïve RA patients at baseline assigned to receive IFX plus methotrexate. The serum samples were distributed in 3 independent samples sets that were provided by 3 different sources: 1 discovery sample set (n=24) collected from Hospital Clínico Universitario de Santiago de Compostela (Spain) and 2 validation sample sets collected from Hospital Universitario de A Coruña (Spain), (n=61); and the Swedish Pharmacotherapy (SWEFOT) trial (Sweden), (n=85). The European League Against Rheumatism (EULAR) criteria were used to assess the clinical response at six months of follow-up: good response (GR, n=60), moderate (MR, n=60) and non-response (NR, n=50). A suspension bead array platform built on protein fragments within Human Protein Atlas and selected from an initial screening using an array containing 42 000 antigens was employed to identify the IgG and IgA autoantibodies in the discovery sample set and validate the results within the 2 validation sets. Thresholds for autoantibodies were calculated by Receiver Operating Characteristics (ROC) curve analysis performed with SPSS 24.

**Results:** Our data revealed a more prevalent IgG reactivity and higher IgG autoantibody levels against the antigen Centromere Protein F (CENPF) in GR when compared with NR, showing an overall reactivity of 31% vs 0%, 45% vs. 26% and 17% vs 4% in the three sample sets analysed respectively. The area under the ROC curve was 0,649 [p-value=0.049; IC 95% (0.510–0.789)]. CENPF is a proliferation-associated and cell cycle-dependent centromere autoantigen that might be involved in the increased or abnormal cell proliferation that occurs during RA process. Interestingly, our results also showed that IgA autoantibodies levels toward the antigen Solute Carrier family 39 member 2 (SLC39A2), a zinc transporter protein, were decreased in GR when compared with MR in the discovery sample set and this trend was significantly validated (p=0.018) in the SWEFOT cohort. The area under the ROC curve was 0,681 [p-value=0,019; IC95% (0,543–0,818)].

**Conclusions:** We have identified two autoantibodies in RA that associate with IFX response. Our findings could potentially be useful to guide the treatment decisions for IFX and lead to further studies focusing on the role of the autoantibodies against CENPF and SLC39A2 within RA.

**Disclosure of Interest:** None declared

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THU0188

### EFFICACY OF INFLIXIMAB FOR SUPPRESSING RADIOGRAPHIC PROGRESSION OF CERVICAL LESIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS COMPARISON WITH METHOTREXATE; THREE YEARS OF FOLLOW-UP – A MULTICENTER REGISTRY STUDY ~

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**Background:** Cervical lesions are known to occur at high frequency as a complication of rheumatoid arthritis (RA). Treatment with biological agents are more clinically effective than the DMARDs that were in use previously, in particular, with their efficacy in suppressing joint destruction having been emphasised. We reported the efficacy of infliximab (IFX), anti-tumour necrosis factor antibodies for suppressing the radiographic progression of RA cervical lesions at ACR2009, EULAR2010, 11, 12, 13, 14 and 16. However there is still few studies of efficacy of against RA cervical lesions of IFX comparison with methotrexate (MTX).

**Objectives:** To evaluate the efficacy of IFX for suppressing the radiographic progression of RA cervical lesions comparison with MTX for 3 years.

**Methods:** We used MTX or MTX +IFX for treating Japanese patients with active RA who fulfilled the ACR criteria in 1987. The final study cohort of each 64 and 70 patients received continuous MTX and IFX treatment for at least 3 years. MTX was used in all patients receiving IFX. For evaluation of cervical lesions, the atlanto-dental interval (ADI), the space available for the spinal cord (SAC), and the Ranawat value were measured by plain lateral radiographs in the flexion position, at initiation, Year 1, 2 and 3.

**Results:** In the patients receiving MTX (n=64) and IFX (n=70), the number of female were each 46 (72%) and 60 (86%) cases (p=0.049). The mean age was 63.4±11.0 and 54.2±12.8 years old (p<0.001); disease duration was 8.5±9.8 and 10.5±9.3 years (p=0.027) and the mean dose of MTX was 7.9±2.8 and 7.5±1.7 mg/w (p=0.607). Clinical findings related to RA were as follows; CRP 1.5±2.1 and 3.3±3.0 mg/dl (p<0.001); ESR 29.9±21.1 and 54.9±23.9 mm/h (p<0.001); MMP3 223±373 and 355±328 ng/ml (p<0.001); DAS28 4.21±1.35 and 5.43±1.29 (p<0.001); ADI 2.7±1.6 and 3.4±1.7 mm (p=0.005); SAC 20.7±2.6 and 18.4±2.5 mm (p<0.001) and Ranawat value 15.9±1.5 and 14.5±2.3 mm (p<0.001). The respective changes in cervical lesion parameters after 3 years were as follows: ADI: 0.70±0.77 and 0.47±0.74 mm (p=0.042); SAC: -0.69±0.85 and -0.44±0.79 mm (p=0.043); and Ranawat value: -0.48±0.69 and -0.34±0.51 mm (p=0.359) between MTX and IFX patients (figure 1). The numbers of patients who did not showed progression in ADI, SAC and Ranawat value were each 30 (47%) vs 45 (64%) cases (p=0.043); 33 (52%) vs 48 (69%) cases (p=0.044) and 40 (63%) vs 47 (67%) cases (p=0.574) after 3 years. Also the number who was able to suppress progression in all three parameters were each 30 cases (47%) receiving MTX and 39 cases (56%) receiving IFX (p=0.307) after 3 years (figure 2).

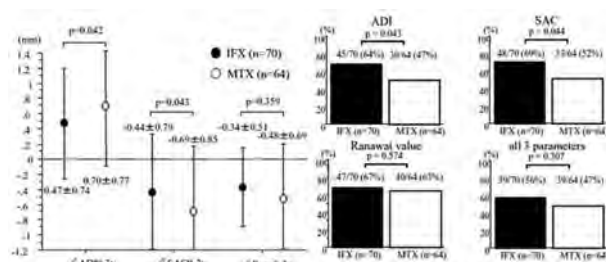


Figure 1: Respective changes in ADI, SAC and Ranawat value from Year 0 to Year 3 between MTX and IFX patients

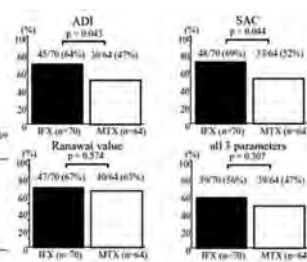


Figure 2: The rate of patients who did not showed progression in ADI, SAC, Ranawat value and all three parameters after 3 years

**Abstract THU0188 – Figure 1.** Respective changes in ADI, SAC and Ranawat value from Year 0 to Year 3 between MTX and IFX patients. **Abstract THU0188 – Figure 2.** The rate of patients who did not showed progression in ADI, SAC, Ranawat value and all three parameters after 3 years

**Conclusions:** This study suggested that IFX treatment can be used to suppress the progression of RA cervical lesions more than MTX treatment.

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THU0189

### ONE-YEAR TREATMENT RETENTION AFTER A NATIONWIDE NON-MEDICAL SWITCH FROM ORIGINATOR TO BIOSIMILAR ETANERCEPT IN 2,061 PATIENTS WITH INFLAMMATORY ARTHRITIS FOLLOWED IN THE DANBIO REGISTRY

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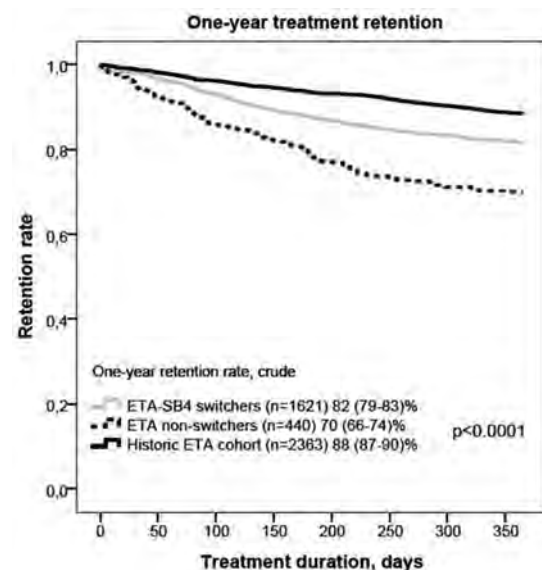
**Background:** In Denmark, rheumatoid arthritis (RA), psoriatic arthritis (PsA) and axial spondyloarthritis (AxSpA) patients (pts) treated with originator etanercept (ETA) 50 mg SC conducted a mandatory non-medical switch to biosimilar Etanercept (SB4) in April 2016 (switchers). Pts treated with 25 mg ETA or 50 mg powder solution were not mandated to switch (non-switchers).

**Objectives:** To characterise switchers and non-switchers, and to compare 1 year treatment retention in switchers with non-switchers and a historic cohort of ETA treated pts.

**Methods:** Pt data were retrieved from the DANBIO registry and national registries. We applied Chi-square/Mann-Whitney for comparisons and Kaplan-Meier/Cox regression analyses (crude, adjusted for gender/age/MTX/remission/comorbidities/ETA-start-year) for drug retention. The historic cohort encompassed pts treated with ETA by Jan 1st 2015.

**Results:** Of 2,061 ETA treated pts by April 2016, 79% switched to SB4 (933RA/351PsA/337AxSpA), whereas 21% (286RA/56PsA/98AxSpA) continued ETA. In RA, compared to switchers, non-switchers more often received 25 mg ETA, had higher disease activity and HAQ (table 1). Similar patterns were seen for PsA and AxSpA. Median (IQR) follow-up was 383 (314–414) days. In all 3 cohorts, withdrawals were mainly due to lack of effect. Retention rate was lowest in non-switchers (figure 1). 1 year adjusted rates were 83% (95% CI 79–87) in switchers, 77% (72–82) in non-switchers and 90% (88–92) in historic cohort. Pts not in remission had poorer retention than pts in remission both in switchers (hazard ratio 1.7 (1.3–2.2) and non-switchers (2.4 (1.7–3.6)).

Numbers are medians (IQR) unless otherwise stated. \* DAS28 <2.6 (RA, PsA), ASDAS <1.3 (AxSpA)



**Conclusions:** Of >2000 ETA treated pts, ≈80% switched to SB4. Non-switchers had higher disease activity and more often received 25 mg ETA. Switchers had poorer retention rate than a historic ETA-cohort, but better than non-switchers. Withdrawal was most common in pts not in remission. These real-world data indicate that a switching-to-biosimilar option facilitated clinical decision making in

Abstract THU0189 – Table 1. Baseline characteristics

	Switchers n=1621			Non-switchers n=440			p-value		
	RA n=933 (58%)	PsA n=351 (22%)	AxSpA n=337 (21%)	RA n=286 (65%)	PsA n=56 (13%)	AxSpA n=98 (22%)	RA	PsA	AxSpA
Female, %	74	46	34	76	55	35	0.5	0.2	0.9
Age, yrs	61 <sup>(49–70)</sup>	52 <sup>(43–61)</sup>	48 <sup>(39–57)</sup>	62 <sup>(48–70)</sup>	52 <sup>(43–58)</sup>	48 <sup>(40–57)</sup>	0.8	0.8	0.8
Concomitant MTX, %	60	48	15	49	30	18	<0.01	0.02	0.4
In remission, %*	65	70	28	55	73	21	<0.01	0.6	0.2
Pt global <30 mm, %	52	51	51	45	43	42	0.03	0.3	0.1
DAS28	2.1 (1.6–3.0)	2.0 (1.6–2.8)	-	2.5 (1.8–3.3)	2.0 (1.8–2.8)	-	<0.01	0.5	-
HAQ	0.8 (0.3–1.3)	0.5 (0.0–1.0)	0.4 (0.0–0.8)	0.9 (0.4–1.5)	0.8 (0.6–1.3)	0.4 (0–0.9)	<0.01	0.07	0.3
Received 25 mg ETA/inj, %	1	1	1	44	19	39	<0.01	<0.01	<0.01
Prior ETA duration, yrs	6.0 (3.6–8.6)	4.3 (2.9–7.3)	4.6 (2.8–6.8)	5.3 (2.4–8.6)	3.4 (1.6–6.0)	4.7 (2.9–9.0)	0.01	0.02	0.3

standard care, leading to withdrawal from ineffective therapy in both switchers and non-switchers.

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THU0190

**CLINICAL OUTCOMES AMONG RHEUMATOID ARTHRITIS PATIENTS RECEIVING ADALIMUMAB WHO DID OR DID NOT PARTICIPATE IN THE PATIENT SUPPORT PROGRAM: A SUBANALYSIS OF THE PASSION STUDY**

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**Background:** The AbbVie Patient (pt) Support Program (PSP) is offered to pts prescribed adalimumab (ADA) for rheumatoid arthritis (RA) and other indications.

**Objectives:** This subanalysis evaluated the impact of ADA in achieving clinical, functional, and pt-reported outcome treatment targets and sustained responses by PSP use.

**Methods:** PASSION was a 78-wk postmarketing, multinational, observational study enrolling pts with moderate to severe RA receiving ADA in routine clinical care. Pts with an insufficient response to  $\geq 1$  disease modifying antirheumatic drug (DMARD; 1 prior biologic DMARD was allowed) and newly initiating ADA were enrolled. Pts were divided into 2 groups based on PSP participation: ever (PSP users) vs never (PSP non-users). Outcome measures included proportion of pts with low disease activity (LDA)/remission defined by Clinical Disease Activity Index (CDAI)  $\leq 10$ , Simplified Disease Activity Index (SDAI)  $\leq 11$ , and Disease Activity Score (DAS)28(C-reactive protein [CRP])  $\leq 3.2$ ; proportion with mild to moderate disability (Health Assessment Questionnaire Disease Index [HAQ-DI] 0 to 1); and proportion with 20%/50%/70% improvement from baseline (BL) in ACR components (table 1). Missing values were imputed using last observation carried forward, and differences in proportions between PSP users and PSP non-users were compared with Chi-square tests.

**Results:** Of 1025 pts treated with ADA in the study, 499 were PSP users and 526 were PSP non-users. A significantly greater proportion of PSP users vs PSP non-users had LDA/remission as defined by CDAI at wks 24, 52, and 78 and as

defined by SDAI or DAS28(CRP) at weeks 52 and 78 ( $p < 0.05$  for all). A significantly greater proportion of PSP users vs PSP non-users also had mild to moderate disability defined by HAQ-DI at wk 78 ( $p = 0.0239$ ). Compared with PSP non-users, a significantly greater proportion of PSP users had 70% improvement from BL in PtGA, pain, and CRP at wks 24, 52, and 78; SJC28 at wks 52 and 78; and TJC28 and PhGA at wk 78 (table 1). At wks 24, 52, and 78, a significantly greater proportion of PSP users vs PSP non-users had 20% and 50% improvements from BL in all ACR components (all  $p < 0.05$ ), except for 50% improvement from BL in TJC28 at wks 24 and 78 and PhGA at wk 24.

Abstract THU0190 – Table 1. Proportion of Patients With 70% Improvement in ACR Individual Components (LOCF) by PSP Utilisation Category by Visit (Intent-To-Treat Population)

	Visit	PSP User n/N (%)	PSP Non-user n/N (%)	P-value
TJC28 70% improvement from baseline	Week 24	278/482 (57.7)	270/508 (53.2)	0.1521
	Week 52	281/482 (58.3)	266/508 (52.4)	0.0604
	Week 78	296/482 (61.4)	277/508 (54.5)	0.0284*
SJC28 70% improvement from baseline	Week 24	313/482 (64.9)	300/508 (59.1)	0.0568
	Week 52	326/482 (67.6)	306/508 (60.2)	0.0154*
	Week 78	327/482 (67.8)	299/508 (58.9)	0.0034**
PtGA 70% improvement from baseline	Week 24	154/497 (31.0)	100/518 (19.3)	<0.0001***
	Week 52	171/497 (34.4)	119/518 (23.0)	<0.0001***
	Week 78	187/497 (37.6)	125/518 (24.1)	<0.0001***
PhGA 70% improvement from baseline	Week 24	183/461 (39.7)	202/512 (39.5)	0.9383
	Week 52	209/461 (45.3)	207/512 (40.4)	0.1224
	Week 78	229/461 (49.7)	210/512 (41.0)	0.0677**
Pain 70% improvement from baseline	Week 24	151/497 (30.4)	95/519 (18.3)	<0.0001***
	Week 52	172/497 (34.6)	119/519 (22.5)	<0.0001***
	Week 78	190/497 (38.2)	132/519 (25.4)	<0.0001***
CRP 70% improvement from baseline	Week 24	173/455 (38.0)	129/494 (26.1)	<0.0001***
	Week 52	166/455 (36.5)	134/494 (27.1)	0.0022**
	Week 78	173/455 (38.0)	150/494 (30.4)	0.0129*

The intent-to-treat (ITT) population includes patients who received  $\geq 1$  dose of study drug. n=number of patients in the ITT population; N=number of patients with non-missing values at each visit. \*\*\*, \*\*, \*, statistically significant at  $P = 0.001$ , 0.01, and 0.05 levels, respectively. P-values derived from Chi-square test.

Missing data were imputed for each efficacy endpoint using LOCF. The differences between groups in efficacy endpoints at wk 24, 52, and 78 were based on ANCOVA models adjusting for baseline and demographic variables (sex, race, ethnicity, age [years], PSP participation [ever (PSP users) vs never (PSP non-users)], diagnosis RA duration [years]).

ANCOVA, analysis of covariance; CRP, C-reactive protein; LOCF, last observation carried forward; Pain, Patient Global Assessment of Pain; PhGA, Physician Global Assessment of Disease Activity; PtGA, Patient Global Assessment of Disease Activity; PSP, patient support program; SJC28, Swollen 28-Joint Count; TJC28, Tender 28-Joint Count.

**Conclusions:** Among pts with moderate to severe RA initiating ADA treatment, participation in the PSP resulted in significantly greater improvements in clinical, functional, and pt-reported outcomes at wks 24, 52, and 78 in comparison to the PSP non-users.

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THU0191

### NOVEL FORMULATION OF CT-P13 FOR SUBCUTANEOUS ADMINISTRATION IN PATIENTS WITH RHEUMATOID ARTHRITIS: INITIAL RESULTS FROM A PHASE I/III RANDOMISED CONTROLLED TRIAL

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**Background:** While the treatment with intravenous (IV) CT-P13, an infliximab biosimilar, is effective and well tolerated, a new subcutaneous (SC) CT-P13 formulation (CT-P13 SC) is developed to provide additional, more convenient treatment options and opportunity for self-injection.

**Objectives:** To find the optimal dose of CT-P13 SC and to evaluate efficacy, PK and safety over the first 30 weeks in patients with rheumatoid arthritis.

**Methods:** This study consists of 1 cohort with CT-P13 IV, and 3 cohorts with 3 different doses of CT-P13 SC injected biweekly. All enrolled patients initially received CT-P13 IV at Weeks 0 and 2 and patients who received 2 full doses and displayed no safety concerns were randomly assigned to receive either CT-P13 SC or IV at Week 6. Using part 1 result, PK-PD modelling was conducted for the 3 regimens.

**Results:** A total of 50 patients were enrolled, of whom 48 patients were randomly assigned into 4 cohorts.

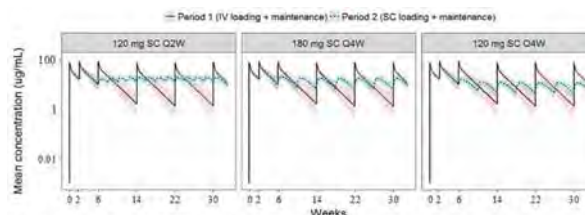
Overall, the efficacy results of CT-P13 SC up to Week 30 were comparable to those of CT-P13 IV. Disease improvement by DAS28 and ACR20 were comparable across all 4 cohorts, regardless of the route of administration or dosage of CT-P13 (table 1).

The safety profiles in CT-P13 SC cohorts were generally comparable to CT-P13 IV. One of the 2 patients who experienced a hypersensitivity reaction became anti-drug antibody (ADA) positive at Week 6 and experienced hypersensitivity from Week 2 to 8. All injection site reactions were grade 1 or 2. The proportion of ADA (positive) was lower in the SC cohorts.

In PK-PD modelling, bioavailability was 59% (95% CI, 52%–67%). The dose linearity in SC regimens was confirmed based on Weeks 22 to 30  $C_{trough}$ ,  $AUC_{0-24}$ , and  $C_{max, ss}$  (figure 1).  $C_{trough}$  were greater (above 4  $\mu\text{g/mL}$ ) than the target exposure (1  $\mu\text{g/mL}$ )<sup>[1][2]</sup> in all SC regimens. There was a trend towards slightly lower DAS28 score in all SC regimens, which was consistent with the higher  $C_{trough}$  comparing with CT-P13 IV. Based on the exposure-response safety analyses, there was no correlation between PK ( $AUC_{0-24}$  or  $C_{max, ss}$ ) and safety (IRRs or infections).

Abstract THU0191 – Table 1. Efficacy and safety up to Week 30

		Cohort 1 IV 3 mg/ kg (n=13)	Cohort 2 SC 90 mg (n=11)	Cohort 3 SC 120 mg (n=12)	Cohort 4 SC 180 mg (n=12)
DAS28 (CRP), mean ±SD	Week 0	5.4±0.8	6.3±0.8	5.7±0.9	5.5±0.8
	Week 6	3.9±1.5	4.6±1.1	3.9±1.2	3.4±1.2
	Week 22	3.9±1.6	3.7±1.0	3.3±1.4	2.8±1.3
Week 30 ACR20, n (%)	Week 6	3.3±1.3	3.0±1.1	3.1±1.0	2.7±1.0
	Week 22	8 (61.5)	8 (72.7)	7 (58.3)	7 (58.3)
	Week 30	8 (61.5)	8 (72.7)	9 (75.0)	11 (91.7)
Safety, n (%)	Week 30	11 (84.6)	10 (83.3)	10 (83.3)	12 (100)
	Hypersensitivity/ IRR	0	1 (9.1)	1 (8.3)	0
	Injection site reactions	0	2 (18.2)	0	2 (16.7)
	Infections	4 (30.8)	2 (18.2)	0	4 (33.3)
	ADA	9 (69.2)	3 (27.3)	4 (33.3)	1 (8.3)



Solid line = Period 1 (IV reference regimen: IV loading + IV maintenance dose)  
Dashed line = Period 2 (SC test regimen: IV loading + SC maintenance dose)

**Abstract THU0191 – Figure 1.** Mean (± SD) Simulated CT-P13 Serum Concentration vs Time Profiles for the Simulated Fixed Dose SC Maintenance Dosing Regimens with Overlaid IV Maintenance Reference Treatment (Semi-Logarithmic Scale). Solid line=Period 1 (IV reference regimen: IV loading+IV maintenance dose). Dashed line=Period 2 (SC test regimen: IV loading+SC maintenance dose)

Abstract THU0191 – Table 2. Summary of Steady State Median (Prediction Interval 5<sup>th</sup>-95<sup>th</sup> percentile) CT-P13 Exposure Results

Simulated Dose Regimen	$C_{trough}$ ( $\mu\text{g/mL}$ )	$AUC_{0-24}$ ( $\text{h}\cdot\mu\text{g/mL}$ )	$C_{max}$ ( $\mu\text{g/mL}$ )
3 mg/kg IV every 8 weeks	1.53 (0.18 - 5.2)	16725.64 (9328.94 - 26297.08)	76.01 (52.73 - 103.21)
120 mg SC every 2 weeks	13.66 (6.66 - 24.25)	22717.66 (12849.49 - 37845.41)	18.95 (11.38 - 30.81)
180 mg SC every 4 weeks	6.66 (2.55 - 13.7)	17060.69 (9660.52 - 28442.43)	17.47 (11.13 - 26.76)
120 mg SC every 4 weeks	4.44 (1.7 - 9.14)	11375.19 (6440.93 - 18976.74)	11.65 (7.42 - 17.84)

Treatment continuation in patients enrolled with SB4 or oETN who were bionative until enrollment.

**Conclusions:** CT-P13 SC showed comparable efficacy and safety with CT-P13 IV. The preliminary results suggest CT-P13 SC as a future alternative treatment of infliximab.

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THU0192

### RETENTION RATES FOR ETANERCEPT: COMPARING THE ORIGINAL WITH A BIOSIMILAR

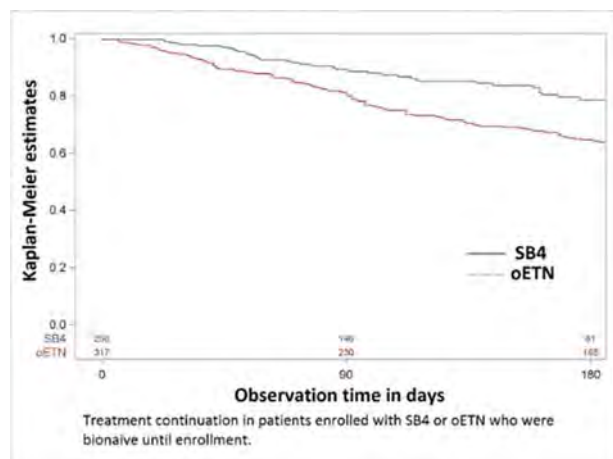
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**Background:** Since the first approval of a biosimilar in 2015, the number of biosimilars approved for the treatment of rheumatoid arthritis (RA) in Germany has been increasing. Until now, there are just a few analyses investigating retention rates of biosimilars and the respective originators.

**Objectives:** To compare treatment survival on SB4 to the originator etanercept (oETN) using real-world data.

**Methods:** We used data gathered until December 2017 from the prospective, longitudinal RABBIT (Rheumatoid Arthritis: Observation of biologic therapy) cohort. RA patients are enrolled in RABBIT when they start a biologic, biosimilar or new csDMARD treatment. For comparative analyses, patients starting SB4 either at enrollment or during follow-up were compared to patients enrolled with oETN since 2015. The drug survival rates during the first six months were analysed in biologic naive patients prior to enrollment using Kaplan-Meier curves.

**Results:** Overall, 283 patients were included in the register starting SB4 and 369 with oETN. Another 355 patients who had already been enrolled in RABBIT switched to SB4 during follow up. Compared to oETN patients, those enrolled with SB4 had slightly lower disease duration (8 vs. 9 years) and significantly fewer patients had three or more comorbidities (40% vs. 47%,  $p=0.04$ ). 88% ( $n=250$ ) of patients enrolled with SB4 and 86% ( $n=317$ ) enrolled with oETN were bionative. Out of all patients who started SB4 during follow up, 40% had been treated with oETN, and 39% with another biologic before switching. 21% had received csDMARD or no drug treatment before treatment start. Kaplan-Meier curves show comparable retention rates over 6 months for SB4 and oETN (figure 1). Adjusting the curves for disease duration and comorbidities had no significant influence on the results. 8% ( $n=20$ ) of bionative SB4 patients and 17% ( $n=54$ ) of bionative oETN patients stopped treatment during the first 90 days. Additional 6% ( $n=14$ , SB4)/15% ( $n=46$ , oETN) stopped the treatment within 180 days after enrolment. The reasons for discontinuation of both treatments were adverse events (AE) in 59% ( $n=20$ , SB4)/49% ( $n=49$ , oETN) and loss of response in 26% ( $n=9$ , SB4)/31% ( $n=31$ , oETN). The most common cause for discontinuation within 180 days due to AE were skin reactions at the injection site in 35% (7 of 20) of SB4, and 49% (24 of 49) of oETN patients).



**Abstract THU0192 – Figure 1.** Treatment continuation in patients enrolled with SB4 or oETN who were bionative until enrollment.

**Conclusions:** The retention rates for bionative patients starting either the biosimilar SB4 or the originator oETN were similar. The distribution of adverse events was also comparable. A selection bias cannot fully be ruled out since patients on oETN had more comorbidities.

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#### THU0193 EFFICACY AND SAFETY OF BCD-055 (INFLIXIMAB BIOSIMILAR) IN RHEUMATOID ARTHRITIS. RESULTS OF BCD-055-3/LIRA PHASE 3 CLINICAL STUDY

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**Background:** Equivalent efficacy of BCD-055 and infliximab (INF) innovator has been previously established (the primary endpoint: ACR20 at Wk14)<sup>1</sup>.

**Objectives:** The impact of BCD-055 and INF innovator on RA activity has been analysed within 14 week study period. DAS28-CRP,<sup>4</sup> CDAI and SDAI were evaluated. Additionally, safety data has been collected.

**Methods:** The study was conducted as international multicenter randomised double-blind placebo controlled study. The study enrolled 426 adults with active RA. Patients were randomised into 2 study arms in 2:1 ratio to receive BCD-055 or INF innovator in dose of 3 mg/kg. In the analysed period of the study, patients received the iv infusions on Wk0, Wk2, Wk6, Wk14.

**Results:** Efficacy: BCD-055 and INF innovator showed similar impact on RA activity: in both groups significant decline of DAS28-CRP<sup>4</sup> was observed (figure 1). This result corresponds to positive CDAI and SDAI dynamics (table 2). Medians of CDAI/SDAI on screening indicated high RA activity, while on Wk 14 – moderate activity. Analyses of inflammatory markers (ESR and C-reactive protein) revealed pronounced decline in ESR and CRP levels by Wk 2. No further elevation has been observed.

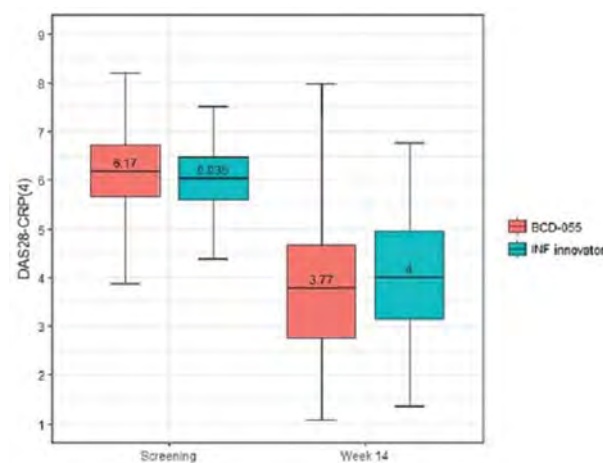
**Safety:** No differences in safety profiles of BCD-055 and INF innovator has been shown. One of the most frequent AEs were arterial hypertension, anaemia, neutropenia and increase of transaminases. Number of patients with binding and neutralising antibodies also did not differ between groups. Babs were detected in 6.83% patients in BCD-055 arm and in 7.81% in INF innovator arm ( $p=0.888$ ), Nab were observed in 1.61% and 0.78% patients in same arms ( $p=0.666$ ).

**Abstract THU0193 – Table 1.** SDAI, CDAI dynamics.

		Screening	Wk14	p-value
SDAI	BCD-055 (n=280)	42.46 [35.15–51.11]	16.22 [8.45–25.03]	<0.00000
	INF innovator (n=138)	41.22 [34.21–47.52]	16.15 [9.06–27.11]	<0.00000
CDAI	BCD-055 (n=280)	39.15 [31.50–46.00]	15.40 [8.00–24.00]	<0.00000
	INF innovator (n=138)	36.85 [31.90–42.00]	15.55 [8.30–25.50]	<0.00000

**Abstract THU0193 – Table 2.** Summarised safety data

Percentage of patients with	Arm		p-value
	BCD-055 (n=280)	INF innovator (n=138)	
Any AE/SAE	53.57% (150)	44.93% (62)	0.119
Therapy-related AEs	26.43% (74)	24.64% <sup>34</sup>	0.784
Any SAE	2.14% <sup>6</sup>	1.45% <sup>2</sup>	1.00
Grade 3–4 AEs	10.00% <sup>28</sup>	5.80% <sup>8</sup>	0.966
Therapy-related grade 3–4 AEs	5.71% <sup>16</sup>	4.35% <sup>6</sup>	0.722
Therapy-discontinuation due to AE	2.50% <sup>7</sup>	2.90% <sup>4</sup>	0.757



**Conclusions:** Treatment with BCD-055 and INF innovator leads to significant decline in RA activity and inflammatory markers by Wk14, which corresponds with previous results of ACR20 assessment<sup>1</sup>. Both drugs are well tolerated with no differences in safety profiles. The frequency of ADA formation is also comparable.

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#### THU0194 CD4+ T CELLS, IMMUNOGLOBULINS AND RISK OF INFECTION IN PATIENTS WITH RHEUMATOID ARTHRITIS OVER MULTIPLE CYCLES OF RITUXIMAB

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**Background:** Rituximab (RTX) may be responsible for infectious event in RA patients. Immunological markers may be associated with the occurrence of infections.

**Objectives:** To evaluate lymphocyte counts and immunoglobulin concentrations over multiple cycles of RTX in RA patients, and to analyse the relationship between these markers and the occurrence of infections.

**Methods:** Retrospective monocentric study on 94 RA patients treated with RTX. At baseline and during follow up, lymphocyte phenotyping (CD4+, CD3+, CD19 +cells), gammaglobulin, IgG, IgM and IgA concentration were assessed. Patients were dichotomized according to the absence or presence of infectious events. A student's test was used to compare the continuous variables and a Chi2 test or the Fisher test was used for the dichotomous variables.

**Results:** A total of 119 infectious events occurred during follow-up, of which only 11 were serious, with respective incidences of 65 per 100 patient-years and 6 per 100 patient-years. Low IgM concentration at RTX initiation and low IgG concentration (<5 g/L) throughout follow-up were associated with an increased risk of infection. Both gammaglobulin and IgG concentrations decreased along with successive cycles of RTX in patients with infection, while they remained stable in patients without infection. Twelve patients had a CD4 +cell count<200/mm<sup>3</sup> during follow up, of which one with a CD4 +cell count 233/mm<sup>3</sup> at baseline, who subsequently presented an opportunistic infection.

**Conclusions:** Gammaglobulin, IgM and IgG concentrations and CD4 +cell count are valuable before RTX initiation in RA patients. IgG or gammaglobulin concentration should also be monitored before each cycle. CD4 +lymphocytes monitoring should be considered in patients with low value at initiation.

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#### THU0195 PREVALENCE OF OCCULT HEPATITIS B CARRIER STATUS AND ITS ASSOCIATED FACTORS IN PATIENTS WITH RHEUMATIC DISEASES UNDERGOING BIOLOGICAL THERAPIES

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**Objectives:** To study the prevalence of occult hepatitis B carrier status and its associated factors in patients with rheumatic diseases undergoing biological therapies

**Methods:** Consecutive adult patients with various rheumatic diseases who were currently receiving biological therapies between November 2016 and April 2017 were recruited in this cross-sectional study. Blood was taken for evidence of hepatitis B infection (HBsAg, anti-HBs, anti-HBc-IgG). For patients tested positive for HBsAg or anti-HBc-IgG, assay of serum HBV-DNA level was also performed. Occult hepatitis B carrier was defined as patients who were HBsAg negative but anti-HBc-IgG positive. Logistic regression was performed to study factors independently associated with occult hepatitis B carrier status in these patients.

**Results:** 310 Chinese patients were studied (60% women, age at biological therapy 44.0±13.0 years). The underlying rheumatic diseases requiring biological therapies were rheumatoid arthritis (46%), spondyloarthritis (31%), psoriatic

arthritis (12%) and systemic lupus erythematosus (8.1%). The biologics being used were the TNF inhibitors (66%), tocilizumab (16%), abatacept (2.9%), rituximab (7.7%), belimumab (5.8%) and tofacitinib (1.3%). Hepatitis B carrier (HBsAg +) status was detected in 11 (3.5%) patients and they were all put on preemptive anti-viral therapy (entecavir). A total of 105 patients (34%) were occult hepatitis B carriers (HBsAg- but anti-HBc-IgG+). Anti-HBs was present in 83/105 (79%) of these patients. Occult hepatitis B carriers were significantly older than the non-carriers (49.9±11.1 vs 40.9±13.3 years; p<0.001), and were more frequently identified in rheumatoid arthritis than other rheumatic diseases (45% vs 25%; p<0.001). However, there was no gender difference in the prevalence of the occult hepatitis B carrier status (37% in women vs 28% in men; p=0.10). Logistic regression revealed that older age (RR 1.05 [1.03–1.08] per year; p<0.001) was the only independent factor significantly associated with occult hepatitis B infection. Rheumatoid arthritis was not significantly associated with occult hepatitis B carrier status after adjustment for age and sex. Of the occult hepatitis B carriers, 9 (8.6%) had detectable HBV-DNA levels but all were very low titers (<100 IU/ml). Five (56%) patients with detectable HBV-DNA levels received entecavir treatment during biological therapies, while 19 (20%) patients without detectable HBV-DNA were put on preemptive entecavir treatment (including all patients who were receiving rituximab). None of the overt (HBsAg+) or occult hepatitis B (HBsAg-anti-HBc-IgG+) carrier patients developed clinical reactivation of hepatitis B during a mean of 5.0±3.7 years of biological therapies.

**Conclusions:** Occult hepatitis B carrier status was present in one-third of Hong Kong Chinese patients with various rheumatic diseases undergoing biological therapies. Older age was the only independent factor associated with occult hepatitis B infection. Despite the relatively low rate of preemptive anti-viral treatment in these patients, clinical reactivation of hepatitis B was not reported over 5 years of biological therapies.

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#### THU0196 DO CONTEXTUAL FACTORS INFLUENCE SURVIVAL ONDRUG OF BIOSIMILARS IN CLINICAL PRACTICE?

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**Background:** The introduction of biosimilars has been linked to concerns regarding their effectiveness and safety compared to their originator products. Whilst randomized controlled trials may address their relative efficacy, the outcome of biosimilars in clinical practice may be influenced by contextual factors, such as the treating rheumatology unit's experience with biosimilars and non-medical switching.

**Objectives:** To analyze whether contextual factors, such as department size and use of biosimilars, and calendar period of treatment start, influence time until treatment discontinuation (i.e. drug survival) of biosimilars as compared to corresponding originator products.

**Methods:** We used data from the Swedish Rheumatology Quality register to identify all patients with rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, or other spondyloarthropathies who started infliximab between March 1st 2015 and Sept 30th 2017 or etanercept between April 1st 2016 and Sept 30th 2017, as their first ever biologic. Kaplan-Meier curves and Cox models were used to assess the association between drug survival and the size of the rheumatology unit, its use of biosimilars (extent of biosimilar use above/below national median at teach time point), and whether the treatment start occurred soon after biosimilar introduction (infliximab: first 12 months, etanercept: 6 months counting from first date of availability of the biosimilar in question). To avoid artefacts, patients were censored if switching from the originator to a biosimilar (or vice versa).

**Results:** During the study period, 368 and 738 patients started infliximab originator or biosimilar, and 125 and 2079 started etanercept originator or biosimilar, as first ever biological treatment. Overall, the hazard ratio (HR) of discontinuing treatment (comparing the biosimilar vs its originator) was 1.21 (95% CI: 0.96–1.51) for infliximab and 0.88 (95% CI: 0.57–1.35) for etanercept, adjusted for indication, age (quartiles), gender, region, and HAQ (quartiles), DAS28 (quartiles) and global health (quartiles) at treatment start. Patients treated in large clinics (more than 1695 patients (75th percentile) at the end of the study period) were at a lower risk of drug discontinuation (table 1). We noted no association between overall biosimilar use in the rheumatology clinic in question and survival on drug (neither originator nor biosimilar). By contrast, those who started infliximab biosimilar later had a lower risk of discontinuing (HR: 0.65 (95% CI: 0.50–0.85)) compared to those who started in the first year of availability. For etanercept biosimilar, no such association was noted.



**Abstract THU0196 – Table 1.** Hazardratios among patients starting their first biologic treatment during the studyperiod according to contextual factors

	Infliximab- originator	Infliximab biosimilar	Etanercept originator	Etanercept biosimilar
Number of patients	368	738	125	2079
Number of discontinuations	165	265	23	392
Dept. size				
Low [quartile I & II]	0.88 (0.37-2.13)	1.47 (0.88-2.46)	30.66 (6.16-152.68)	1.69 (1.12-2.55)
Medium [quartile III]	1.29 (0.81-2.08)	1.90 (1.36-2.65)	19.96 (2.13-56.49)	1.80 (1.08-1.82)
High [quartile IV]	Ref	Ref	Ref	Ref
Dept. use of biosimilars				
Low	Ref	Ref	Ref	Ref
High	0.88 (0.58-1.34)	1.30 (0.82-1.75)	1.90 (0.64-5.70)	1.90 (0.77-1.29)
Period of biologic start*				
Early period	Ref	Ref	Ref	Ref
Later period	0.98 (0.67-1.42)	0.65 (0.50-0.85)	0.06 (0.01-0.53)	0.94 (0.76-1.17)

\*Additionally adjusted for department size and use of biosimilar;  
§ Only 2 discontinuation in the later period of etanercept originator

**Conclusions:** Contextual factors, presumably related to expectations and differences in clinical monitoring, influence the observed survival on drug of biologics, including biosimilars, and must be considered when the comparative effectiveness of biosimilars is evaluated.

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THU0197

#### EFFECTS OF TOCILIZUMAB, AN ANTI-INTERLEUKIN-6 RECEPTOR ANTIBODY, ON SERUM LIPID AND ADIPOKINE LEVELS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Patients with rheumatoid arthritis (RA) are at increased risk of cardiovascular disease.<sup>1</sup> Dyslipidemia is a known adverse reaction to tocilizumab (TCZ), the anti-interleukin-6 receptor antibody, used in RA treatment.

**Objectives:** To assess the effect of TCZ on lipid and adipokine levels in the serum of RA patients

**Methods:** Forty RA patients with active disease initiating TCZ treatment and 40 healthy matched controls were included. Height, weight, disease activity score (DAS28), lipid profile and atherogenic indices (AI) were measured before and four months after TCZ treatment initiation. Serum concentrations of leptin, adiponectin, resistin, interleukin-6 and high sensitivity CRP were measured by ELISA in both study groups.

Statistical analysis: The differences in clinical and laboratory data of RA patients between baseline and follow up were assessed by paired t-test and by linear mixed models with repeated measures for adipokines levels after adjustment to BMI, statin treatment and disease duration. To compare the adipokines levels between RA and control groups adjusted to baseline BMI and statin treatment we used ANCOVA models. HsCRP and IL-6 were compared between the two groups by two-tailed Mann Whitney test. The results were considered statistically significant when  $p \leq 0.05$ .

**Results:** The average age of the study population was  $57.5 \pm 11$  years, 82.5% were women, with a disease duration of  $8.7 \pm 5.6$  years. The majority of the patients responded to TCZ and reduced their diseases activity from DAS28 score of  $5.45 \pm 1.06$  to  $3.46 \pm 1.37$  ( $p < 0.0001$ ). Following treatment, a significant elevation of total cholesterol ( $199 \pm 52$  to  $221 \pm 53$  mg/dl,  $p < 0.01$ ), HDL ( $55 \pm 19$  to  $59 \pm 23$  mg/dl,  $p < 0.01$ ) and triglycerides ( $140 \pm 69$  to  $168 \pm 107$ ,  $p = 0.04$ ), and no significant changes in weight, BMI, low density lipoprotein (LDL) and AI were found. Significantly higher adiponectin levels ( $5.59 \pm 2.39$  vs.  $3.75 \pm 1.63$  ng/ml,  $p < 0.0001$ ), lower resistin levels ( $16.25 \pm 7.17$  vs.  $21.53 \pm 8.19$  pg/ml,  $p = 0.007$ ) and leptin/adiponectin ratio ( $6.44 \pm 6.44$  vs.  $5.52 \pm 6.08$ ,  $p = 0.03$ ) were measured in the RA group compared to controls after adjustment to BMI and statin treatment. Four months after TCZ treatment a statistically significant decrease in adiponectin ( $4.53 \pm 2.12$  ng/ml  $p < 0.0001$ ), resistin levels ( $20.42 \pm 8.06$  pg/ml,  $p = 0.01$ ) and leptin/adiponectin ratio ( $7.99 \pm 7.84$ ,  $p = 0.002$ ) were measured after adjustment to BMI, statin treatment and disease duration. The levels of hsCRP decreased significantly

( $3.37 \pm 2.0$  vs  $0.74 \pm 1.36$  mg/dl,  $p < 0.001$ ) and IL-6 increased significantly ( $13.15 \pm 25.43$  vs  $99.80 \pm 97.97$  pg/ml,  $p < 0.001$ ) following treatment.

**Conclusions:** The impact of TCZ treatment on lipid metabolism is complex. The elevation in HDL without change in AI, and the tendency toward normalisation of the adipokine profile observed, suggests a protective role of TCZ treatment against the cardiovascular burden in RA patients.

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THU0198

#### IMMUNOGENICITY ASSOCIATED WITH A TRANSITION FROM ADALIMUMAB REFERENCE PRODUCT TO ABP 501 IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** In clinical practice, patients treated with an originator product may be transitioned to a biosimilar. Therefore, it is important to ensure that such transition is safe and is not associated with increased immunogenicity.

**Objectives:** To study the incidence of binding anti-drug antibodies (bADAs) and neutralising anti-drug antibodies (nADAs) after patients with rheumatoid arthritis (RA) are transitioned from adalimumab reference product (RP) to ABP 501, an approved biosimilar for adalimumab.

**Methods:** We analysed data from the open-label extension (OLE) of a randomised 26 week phase 3 study (NCT 01970475) comparing ABP 501 and adalimumab. In this OLE study (NCT02114931), patients originally randomised to ABP 501 in the parent study continued on ABP 501 while patients originally randomised to adalimumab (RP) were switched to ABP 501 so that all patients received ABP 501. Specifically, we studied the incidence of new ADAs in patients who were ADA negative at the time of entry into the OLE study. The incidence after excluding transiently elevated ADAs was also examined.

**Results:** The Table summarises the incidence of ADAs.

**Abstract THU0198 – Table 1**

Original randomization arm	ABP 501/ ABP 501	Adalimumab RP/ ABP 501
Number of patients with negative bADA at OLE baseline	147	149
New cases of +bADA post OLE baseline	50	35
New cases of +nADA post OLE baseline	20	12
Transient cases of +bADA	33	13
Transient cases of +nADA	8	2
Overall incidence of new cases of +bADA	34.0%	23.5%
Overall incidence of new cases of +nADA	13.6%	8.1%
Incidence of non-transient cases of +bADA	11.6%	14.8%
Incidence of non-transient cases of +nADA	8.2%	6.7%

**Conclusions:** Transitioning from adalimumab reference product to ABP 501 was not associated with increased immunogenicity over the observational period of 72 weeks.

**Disclosure of Interest:** E. Krishnan Shareholder of: Amgen Inc., Employee of: Amgen Inc., D. Mytych Shareholder of: Amgen Inc., Employee of: Amgen Inc., N. Zhang Shareholder of: Amgen Inc., Employee of: Amgen Inc., H. Wang Shareholder of: Amgen Inc., Employee of: Amgen Inc., A. Kaliyaperumal Shareholder of: Amgen Inc., Employee of: Amgen Inc.

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THU0199

#### A PILOT STUDY TO ASSESS THE RELATIONSHIP BETWEEN SMOKING AND DRUG INEFFECTIVITY IN RHEUMATOID ARTHRITIS – PART OF A QUALITY IMPROVEMENT PROJECT AIMED AT SMOKING CESSATION

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**Background:** It has long been known that patients with rheumatoid arthritis who smoke have more severe disease. This results in greater joint destruction and disability, and further increase in cardiovascular risk<sup>1</sup>. Patients' disease may be more difficult to control with disease modifying anti-rheumatic drugs (DMARDs) and biologic drugs. Smoking may also interfere with the pharmacokinetics of biologic

drugs<sup>2</sup>. Clinicians could then cycle through more of these expensive drugs because of inefficacy. As a modifiable risk factor smoking should be targeted to improve outcomes for patients.

**Objectives:** To complete a pilot study examining for an association between smoking and drug inefficacy in rheumatoid arthritis. This baseline data was used in a quality improvement project aimed at reducing the prevalence of smoking in our rheumatology patients.

**Methods:** We identified patients using a dataset and a database including all patients currently receiving biologics in Musgrave park hospital. Each patient had a diagnosis of rheumatoid arthritis and was being treated with a biologic. We randomly selected 100 patients with rheumatoid arthritis, 50 of whom were current smokers and 50 non-smokers. We then performed a search on Northern Ireland's electronic care record for each patient and identified how many DMARDs and biologics were discontinued due to inefficacy. Inefficacy was defined as ongoing synovitis despite receiving the drug at adequate dosage for 3–6 months resulting in the drug being discontinued. We also identified patients who received rituximab and the number of patients for which it was stopped due to inefficacy.

**Results:** DMARDs and inefficacy: non-smokers had on average 0.98 stopped and smokers had on average 2.2 stopped. Biologics and inefficacy: non-smokers had on average 0.5 stopped and smokers had on average 0.82 stopped. Twenty smokers and twenty non-smokers were treated with rituximab. Non-smokers: 4 out of 20 had rituximab discontinued due to inefficacy. Smokers: 8 out of 20 had rituximab discontinued due to inefficacy.

**Conclusions:** In this small sample of patients, we found that smokers had greater DMARD and biologic inefficacy, particularly with rituximab where smokers had double the rate of inefficacy compared to non-smokers. Our quality improvement project aims to reduce the prevalence of smoking in our rheumatology patients which could result in better disease control, reduction in cardiovascular risk, and less drugs being cycled through. Aiming to achieve this, steps have been taken to set up a rheumatology smoking cessation clinic in our health trust.

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THU0200

#### SUBCUTANEOUS TOCILIZUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS; A HIGH NUMBER OF PATIENTS ACHIEVE DOPPLER REMISSION AFTER 24 WEEKS

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**Background:** Clinical remission in rheumatoid arthritis (RA) is evaluated by Composite Disease Activity Scores (CDAS) including DAS28 and CDAI. Ultrasound (US) is more sensitive than clinical examination for detection of synovitis and assessed by use of Grey Scale (GS) and vascularisation by power/colour Doppler.

**Objectives:** To explore the number of patients reaching Doppler compared to CDAS remission in moderate to severe biologically naïve RA patients (pts) treated with subcutaneous tocilizumab (TCZ-SC) over 24 weeks and to evaluate the safety of TCZ-SC.

**Methods:** A regional multi-country (Denmark, Finland, Norway, Sweden) open-label, single-arm study (part of TOZURA<sup>1</sup>), enrolled pts with inadequate response to csDMARDs. Pts received TCZ-SC 162 mg qw for 24 weeks as monotherapy or in combination with a csDMARD. Stable oral NSAIDs and corticosteroids (CS) ( $\leq 10$  mg/day prednisone or equivalent), were allowed. Clinical (tender and swollen joints), laboratory tests, safety assessments as well as US examination (36 joints and 4 tendons, scored according to the Norwegian US atlas<sup>2</sup>) were performed at baseline, 4, 12 and 24 weeks. US reliability between centres was assessed prior to the study. There is no consensus on definitions of Doppler remission, and Doppler sum scores of 0 to 3 were presently explored as definitions of US remission. CDAS and EULAR/ACR Boolean remission were calculated.

**Results:** 133 pts were included, and 110 pts were followed with US assessments (83% female, mean (SD) age 55.6 (12.1) years and RA duration 8.7 (9.5) years, 81% anti-CCP positive and 62% with erosive disease). All clinical, laboratory and US variables decreased significantly, already after 4 weeks ( $p < 0.001$ ) (table 1). Table 2 illustrates the high percentages of patients reaching remission, especially for DAS28(ESR) and Doppler. Fourteen serious AE were reported in 12 pts and 15 AEs led to permanent withdrawal of treatment.

	Baseline Median (IQR) n=110	4 weeks Median (IQR) n=102	12 weeks Median (IQR) n=95	24 weeks Median (IQR) n=91
DAS28(ESR)	5.0 (4.3–5.8)	3.1 (2.1–3.8)	2.1 (1.5–2.9)	1.6 (1.1–2.4)
CDAI	23.8 (17.1–31.2)	12.9 (7.3–21.9)	7.2 (3.6–11.4)	4.3 (1.8–9.8)
CRP	5.5 (2.6–13.1)	0.2 (0.2–0.4)	0.2 (0.2–0.6)	0.2 (0.2–0.4)
ESR	21 (12–34)	4 (2–7)	3 (2–5)	3 (2–5)
Patient's global VAS (0–100)	55 (36–70)	32 (18–49)	16 (7–31)	12 (4–28)
Assessor's global VAS (0–100)	35 (25–49)	17 (11–31)	10 (5–18)	5 (2–11)
Tender joint count	8 (5–12)	4 (1–9)	2 (0–5)	1 (0–3)
Swollen joint count	6 (2–10)	2 (0.5–6)	1 (0–2.5)	0 (0–2)
Sum score GS	21 (13–36)	16 (8–30)	12 (5–21)	9 (3–19)
Sum score PD	8 (2–20)	4 (1–10)	1 (0–4)	0 (0–2)
<b>Remission criteria</b>		<b>Percentages of Pts in remission at 12 weeks</b>	<b>Percentages of Pts in remission at 24 weeks</b>	
CDAI		19.2	34.7	
DAS28(ESR)		64.6	83.5	
Boolean		14.0	27.4	
PD sum score=0		42.6	53.3	
PD sum score $\leq 1/\leq 2/\leq 3$		60.6/68.1/73.4	65.6/75.6/78.9	

**Conclusions:** This open label study showed TCZ-SC to significantly reduce inflammation assessed by both CDAS and Doppler US. A high number of pts (53%–79%) obtained Doppler remission at 24 weeks using the different definitions. The safety profile was similar to what has previously been reported.

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THU0201

#### A POOLED ANALYSIS OF THREE TNF-A INHIBITOR BIOSIMILAR STUDIES IN PATIENTS WITH RHEUMATOID ARTHRITIS COMPARING RADIOGRAPHIC PROGRESSION BY DISEASE ACTIVITY STATES

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**Background:** SB4, SB2, and SB5 are biosimilars of the reference etanercept (ETN), infliximab (INF), and adalimumab (ADA), respectively. Radiographic progression using the modified Total Sharp Score (mTSS) at week 0 and final week (week 52 for etanercept and adalimumab and week 54 for infliximab) was measured in phase III randomised, double-blind studies comparing efficacy and safety of biosimilar to its reference product.

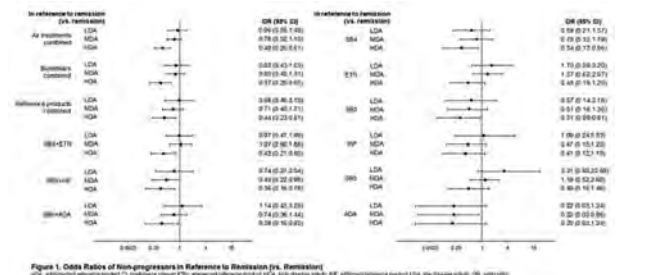
**Objectives:** Assess and compare radiographic progression by disease activity states at week 24 (for etanercept and adalimumab) or week 30 (for infliximab) in terms of DAS28 from a pooled analysis of three biosimilar studies.<sup>1–3</sup>

**Methods:** Patients with radiographic data from each phase III study were pooled and grouped based on their disease activity state (remission, low disease activity [LDA], moderate disease activity [MDA], and high disease activity [HDA]) at week 24 or 30 in terms of DAS28. The mean change in mTSS and the proportion of radiographic non-progressors of higher disease activity groups (LDA, MDA, and HDA) in reference to remission were summarised descriptively and odds ratios (OR) were compared using 95% confidence interval (CI) obtained from logistic model with baseline DAS28.

**Results:** A total of 1263 patients from phase III studies had radiographic assessment available and the results are summarised in table 1. Across all treatment groups, radiographic progression was the highest in HDA followed by MDA, LDA, and remission. In all treatments combined, the mean change in mTSS was 0.03, 0.38, 0.27, and 1.27 and the proportion of non-progressors was 79.7% (181/227), 78.1% (125/160), 74.1% (473/638), 58.4% (139/238) in remission, LDA, MDA, and HDA groups, respectively. In all treatments combined, compared to remission group, the estimated difference in mTSS was greater in HDA (1.15, 95% CI: 0.63–1.66) than MDA (0.20, 95% CI: –0.22–0.62) and LDA (0.36, 95% CI: –0.20–0.91) groups and the OR of the proportion of the non-progressors was the smallest in HDA (OR 0.40, 95% CI: 0.26–0.61) followed by MDA (OR 0.76, 95% CI: 0.52–1.10) and LDA (OR 0.90, 95% CI: 0.55–1.49) (figure 1). This trend was similarly observed in other treatment groups.

**Abstract THU0201 – Table 1.** Summary of Change in Mean mTSS and a Proportion of Non-progressors

Treatment	Change in mTSS Mean±SD	Non-progressors n/n (%)
All Treatments Combined	0.43±2.78	918/1263 (72.7%)
Biosimilars Combined	0.33±2.40	523/702 (74.5%)
Reference Products Combined:	0.55±3.18	395/561 (70.4%)
SB4+ETN	0.59±2.94	324/477 (67.9%)
SB2+INF	0.38±2.83	313/422 (74.2%)
SB5+ADA	0.28±2.46	281/364 (77.2%)
SB4	0.45±2.50	174/249 (69.9%)
ETN	0.74±3.36	150/228 (65.8%)
SB2	0.38±2.15	157/213 (73.7%)
INF	0.37±3.39	156/209 (74.6%)
SB5	0.17±2.49	192/240 (80.0%)
ADA	0.50±2.40	89/124 (71.8%)



**Abstract THU0201 – Figure 1.** Odds Ratios of Non-progressors in Reference to Remission (vs. Remission)

**Conclusions:** A pooled radiographic assessment data from three different biosimilar studies showed that radiographic progression was greater as disease activity worsened.

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THU0202

**COMPARATIVE EFFECTIVENESS OF TOCILIZUMAB AS MONOTHERAPY VERSUS TNF INHIBITORS IN COMBINATION WITH CONVENTIONAL SYNTHETIC DISEASE MODIFYING ANTIRHEUMATIC DRUGS IN BIO-NAÏVE PATIENTS WITH RHEUMATOID ARTHRITIS**

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**Background:** Tocilizumab (TCZ) as monotherapy was more efficacious than the TNF inhibitor (TNFi) adalimumab as monotherapy for treatment of rheumatoid arthritis (RA) patients refractory to methotrexate (MTX) or in whom MTX was deemed inappropriate (ADACTA study).<sup>1</sup> However, data are lacking regarding the comparative real life effectiveness of TCZ as monotherapy versus TNFi combined with conventional synthetic DMARDs (csDMARDs).

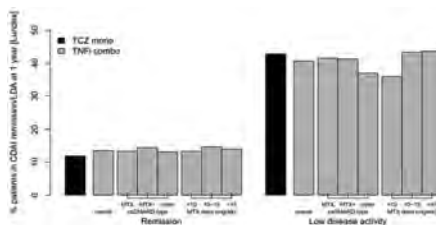
**Objectives:** To analyse treatment effectiveness by comparing drug retention rates and disease activity level in RA patients naïve to biological DMARDs (bDMARDs) treated with TCZ as monotherapy (TCZ mono) or TNFi combined with csDMARDs (TNFi combo).

**Methods:** We included patients with RA across 10 European registries (TOCERRA collaboration) who were naïve to bDMARDs and received treatment with either TCZ mono or TNFi combo from 2009 to 2016. Drug retention rate was analysed using a Kaplan–Meier model. The proportions of patients reaching CDAI low disease activity (LDA) and remission after one year were adjusted for attrition with the LUNDEX index.<sup>2</sup>

**Results:** A total of 6315 patients were eligible, 253 on TCZ mono and 6062 on TNFi combo. Patients with TCZ mono were younger, smoked less, and used less glucocorticoids at baseline compared with TNFi combo patients (table 1). The crude median retention was 2.8 years (95% CI: 2.0–3.3) and 2.0 years (95% CI: 1.8–2.1) for TCZ mono and TNFi combo, respectively (p=0.21). At 1 year, the rates of LUNDEX corrected CDAI LDA (CAI ≤10) and remission (CAI ≤2.8) were similar between both groups (figure 1). The results were unchanged when considering the type of combination with csDMARDs and the dosage of MTX.

**Abstract THU0202 – Table 1.** Baseline characteristics

	TCZmono (n=253)	TNFi combo (n=6062)	p
Age, yr (median [IQR])	54.7 [45.1; 62.6]	59.1 [48.0; 66.0]	<0.001
Female gender, n (%)	202 (80.2%)	4715 (77.8%)	0.42
Ever smoker, n (%)	23 (15.8%)	1254 (26.3%)	0.006
Disease duration, yr (median [IQR])	5.6 [2.1; 12.5]	5.4 [1.9; 11.4]	0.44
Seropositivity (RF and/or ACPA), n (%)	158 (80.2%)	4158 (81.5%)	0.72
Glucocorticoids, n (%)	56 (22.1%)	2932 (48.4%)	<0.001
GC dose mg/day	5.0 [5.0; 7.5]	5.0 [5.0; 10.0]	0.02
Concomitant csDMARD, n (%)			
MTX		3528 (58.2%)	
MTX+other csDMARDs		1377 (22.7%)	
Other csDMARDs than MTX		1157 (19.1%)	
Route of administration, n (%)			<0.001
Intravenous	154 (80.6%)	441 (13.3%)	
Subcutaneous	37 (19.4%)	2870 (86.7%)	



**Abstract THU0202 – Figure 1.** Patients in LUNDEX corrected CDAI or low disease activity (LDA) at 1 year



**Conclusions:** In routine care across 10 European countries, the retention and proportion of RA patients in LUNDEX corrected CDAI LDA and remission at 1 year were similar if treated with TCZ mono or TNFi combo.

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#### THU0203 COMPARISON OF THE RETENTION RATE OF BIOLOGICAL DMARDS ~ THE DATA FROM PATIENTS WITH RA WHO WERE FOLLOWED UP FOR OVER 10 YEARS

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**Background:** The use of biological disease modifying anti-rheumatic drugs (bDMARDs) or synthetic DMARDs for the treatment of rheumatoid arthritis (RA) has improved the management of RA and prevented patients with RA from joint destruction. However, there are some cases in which it is difficult to continue the treatment with these medicines due to insufficient therapeutic effect or complications. In Japan, 8 of bDMARDs and 2 of synthetic DMARDs can be used for the treatment of RA. Among them, infliximab (INF) and etanercept (ETN) were applied for RA treatment in 2003 and 2005, respectively, and have been utilised for more than 10 years. Although adalimumab (ADA) and tocilizumab (TCZ) were applied in 2008, RA treatment by ADA and TCZ had been conducted by clinical trials since 2003, and they have also been utilised for more than 10 years.

**Objectives:** In this study, we evaluated the retention rate of these 4 bDMARDs (INF, ETN, ADA, and TCZ) for over 10 years.

**Methods:** RA patients who started the treatment with INF, ETN, ADA, or TCZ before 2007 in Matsubara mayflower hospital and were observed for over 10 years were included in this study. INF was used in the treatment for 111 patients with RA, and 95 out of them were observed for over 10 years (INF group). 95 out of 119 RA patients treated with ETN (ETN group), 24 out of 27 RA patients treated with ADA (ADA group), and 21 out of 25 RA patients treated with TCZ (TCZ group) were included in this study. Kaplan-Meier analysis was applied to determine the differences in the retention rate of these bDMARDs.

**Results:** Kaplan-Meier analysis showed no statistically significant difference in the retention rate of these bDMARDs. The retention rate of INF group and TCZ group decreased with time and was 10.5% and 33.3% at the final survey in November 2017, respectively. That of ETN group and ADA group plateaued at 9 years after the start of treatment and was 22.1% and 8.33% at the final survey, respectively.

**Conclusions:** In this study, there was no statistically significant difference in the retention rate of these bDMARDs. The retention rate of over 10 years was the highest in TCZ group and the lowest in ADA group. The rate of INF group and TCZ group continued to decrease, and that of ETN group and ADA group was almost constant after 9 years from the start of treatment.

**Disclosure of Interest:** None declared

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#### THU0204 REAL WORLD EXPERIENCE OF BIOSIMILAR SWITCHING AT THE NORFOLK & NORWICH UNIVERSITY HOSPITAL, UNITED KINGDOM

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**Background:** Tumour Necrosis Factor (TNF) inhibitors are routinely used in managing rheumatoid arthritis (RA), psoriatic arthritis (PsA) and spondyloarthritis (SpA). In 2012 and 2015, the patents for the Etanercept (ETN) and Infliximab (IFX) originator molecules expired in Europe respectively and the use of biosimilar ETN and IFX was approved for use in England.

**Objectives:** To determine the proportion of rheumatology patients who experienced a flare of their disease following a switch from originator to biosimilar IFX or ETN and in those who flared, to determine whether disease control can be re-captured following reverting to the originator product.

**Methods:** This was a retrospective study of all patients switched from their originator IFX or ETN to their corresponding biosimilar product between July 2016 and July 2017 at a UK tertiary rheumatology centre. A total of 475 patients were identified by our Biologics team. Seventeen patients experienced a flare defined by: an increase in Disease Activity Score (DAS)28 > 1.2 points in RA, worsening of any of the Psoriatic Arthritis Response Criteria (PsARC) in PsA, an increase in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) of at least 1 unit in SpA, and worsening of swollen and tender joint count in our patient with adulthood juvenile idiopathic arthritis (JIA). Follow-up at 3 months determined disease re-capture, defined by an improvement in DAS28 score > 1.2 units, improvement in at least two of the PsARC, one to be tender or swollen joint score, an improvement of BASDAI score and improved swollen and tender joint count in our patient with adulthood JIA.

#### Results:

	Diagnosis	Flare	Re-capture of disease control following switch back to originator	Side effects
<b>INFLIXIMAB</b>				
	RA	4/63 (6.3%)	1/4 (25.0%)	1/63 (1.6%)
	PsA	2/15 (13.3%)	0/2	0
	SpA	2/19 (10.5%)	1/2 (50.0%)	1/19 (5.3%)
	JIA	1/1 (100%)	1/1 (100%)	0
<b>ETANERCEPT</b>				
	RA	4/238 (1.7%)	4/4 (100%)	6/238 (2.5%)
	PsA	1/55 (1.8%)	1/1 (100%)	2/55 (3.6%)
	SpA	3/84 (3.6%)	2/3 (66.7%)	2/84 (2.4%)

Nine patients (9.2%) who switched to biosimilar IFX flared: four with RA, two with PsA, two with SpA and one with JIA. Of those, three patients (33.3%) were able to re-capture disease control on switching back to originator IFX. Two patients (2.0%) experienced side effects on switching to biosimilar IFX.

Eight patients (2.1%) experienced a flare on switching to biosimilar ETN: four with RA, one with PsA and three with SpA. Of those, seven patients (87.5%) re-captured disease control on switching back to originator ETN. Ten patients (2.7%) experienced side effects on switching to biosimilar ETN.

**Conclusions:** The majority of our patients did well following the switch to biosimilar IFX and ETN.

Patients who did flare on biosimilar ETN are more likely to re-capture their disease control than those who flared on biosimilar IFX.

This adds to real-world evidence to support the European League Against Rheumatism recommendations to utilise biosimilar therapy in rheumatology practice, which is likely to include patients who differ from those enrolled in clinical trials; important when considering health economy implications.

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**THU0205 THE EFFECT OF CERTOLIZUMAB DRUG CONCENTRATION AND ANTI-DRUG ANTIBODIES ON TNF NEUTRALISATION**

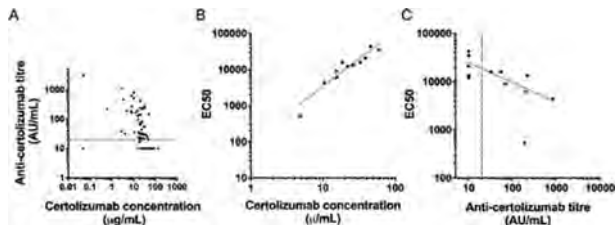
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**Background:** Although tumour necrosis factor- (TNF) inhibitors have proven to be a successful treatment option for patients with rheumatoid arthritis (RA), TNF-inhibitors, including certolizumab, elicit an immunogenic response leading to the formation of anti-drug antibodies (ADAs) (reported range ~5%–39% of the patients).

**Objectives:** We sought to investigate the relationship between certolizumab concentrations, ADAs, and the effective TNF neutralising capacity in sera of RA patients. TNF neutralising capacity of certolizumab was compared to the neutralising capacity of adalimumab.

**Methods:** Blood was collected of 35 consecutive certolizumab-treated RA patients at baseline and 4, 16, 28 and 52 weeks after treatment initiation. Certolizumab and ADA levels were quantified using a certolizumab bridging enzyme-linked immunosorbent assay (ELISA) and a drug-tolerant radioimmunoassay (RIA), respectively. TNF neutralisation of certolizumab and adalimumab in patient sera, in presence or absence of ADAs, was analysed using the TNF-sensitive WEHI bioassay.

**Results:** Despite a high incidence of ADAs during one year of follow-up (69%; 24/35 patients), certolizumab levels of ~>10 µg/mL were measured in most patients (Spearman's  $r = -0.7155$ ,  $p < 0.0001$  ( $n = 118$ ); **figure 1A**). Furthermore, TNF neutralisation, expressed by EC50 values, was highly correlated with certolizumab serum concentration, while there was no association with ADAs (Pearson  $r = 0.9087$ ,  $p < 0.0001$  ( $n = 12$ ) and Pearson  $r = -0.4712$ ,  $p = 0.1220$  ( $n = 12$ ); **figure 1B and C**, respectively). Grey lines indicate log-log linear fit, weight by  $1/Y^2$ ). Similar results were obtained for adalimumab, although TNF neutralisation by adalimumab was less potent; the relative *in vitro* neutralising potency was 43 times higher for certolizumab compared to the neutralising potency of adalimumab.



**Conclusions:** Our study shows that certolizumab is highly immunogenic. In most cases where ADAs are detected, certolizumab is also present in high amounts, and can still potently neutralise TNF. Furthermore, TNF neutralisation is highly correlated with certolizumab concentrations. Therefore, measurement of certolizumab concentrations is the relevant parameter to assess clinically relevant immunogenicity.

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**THU0206 ADD-ON SHORT-COURSE TOCILIZUMAB ACCELERATES DOSE TAPERING OF GLUCOCORTICOIDS IN RHEUMATOID ARTHRITIS: RESULTS FROM A CHINESE PROSPECTIVE COHORT STUDY**

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**Background:** In real-world clinical practice, self-paid and expensive price limit the application of bDMARDs and only a few patients especially in developing countries could afford long-term use. Only 9.1%>11% of Chinese rheumatoid arthritis (RA) patients were treated with bDMARDs with mean course no more than 6 months. Such short course of bDMARDs had always been raised doubt about their efficacy and benefit for rare reported evidence.

**Objectives:** To explore the efficacy of additional short-course of Tocilizumab (TCZ) combined with csDMARDs in real-world RA management.

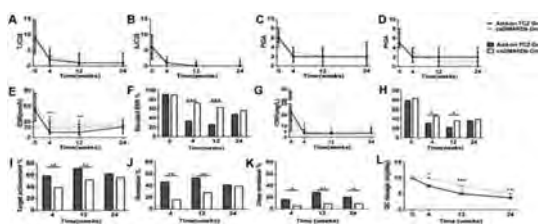
**Methods:** Consecutive patients with active RA (DAS28-ESR>2.6) who had completed 6 month follow-up were retrospectively recruited from a prospective RA cohort ( $n = 582$ ). All patients were treated according to the treat-to-target strategy and patient's willingness especially biologics use. RA patients who finished at least 3 infusions of TCZ (8 mg/Kg/4 weeks) were included as add-on TCZ group, and matched RA patients without any bDMARDs by age, sex and disease activity at baseline with the ratio of 1:1 were included as csDMARDs group. Clinical data were collected according to the 2017 EULAR recommendation at baseline and regular visits at week 4, 12 and 24.

**Results:** (1) The baseline characteristics of 101 paired RA patients showed no significant difference except for lower csDMARDs-naïve percentage between two groups (table 1). (2) During 24 week follow up, there were significantly higher percentage of patients in add-on TCZ group achieving therapeutic target (DAS28-ESR<3.2, at Week 4: 59% vs. 39%,  $p = 0.005$ ; at Week 12: 71% vs. 52%,  $p = 0.006$ , figure 1) or remission (DAS28-ESR<2.6, at Week 4: 46% vs. 16%,  $p < 0.001$ ; at Week 12: 53% vs. 28%,  $p < 0.001$ ) than those in csDMARDs group. Furthermore, there were significantly higher percentage of patients in add-on TCZ group achieving deep remission (DAS28-ESR<1.98, at Week 4: 16% vs. 5%,  $p = 0.015$ ; at Week 12: 28% vs. 9%,  $p = 0.001$ ; at Week 24: 20% vs. 9%,  $p = 0.046$ ). (3) There were 76% RA patients in add-on TCZ group with glucocorticoids (GC) therapy which is significantly lower than that in csDMARDs group (92%,  $p = 0.002$ ). Among patients with GC therapy, the GC dosage per day was tapered more rapidly at each visit and the cumulative dose at week 24 was significantly lower in add-on TCZ group than that in csDMARDs group ( $826 \pm 616$  vs.  $1128 \pm 519$  mg,  $p < 0.001$ ).

**Table 1.** Baseline characteristics of RA patients in add-on TCZ group or csDMARDs group

	Total (n=102)	Add-on TCZ group (n=51)	csDMARDs Group (n=51)	P
Age, years	51.08 (8)	48.27 (8)	51.60 (5)	0.81
Female, n (%)	167 (81)	82 (81)	85 (80)	0.88
Disease duration, months	88 (52.04)	88 (86.23)	89 (52.84)	0.242
SF36	8.08 (4)	9.18 (7)	8.18 (3)	0.882
ESR	3.52 (8)	4.02 (8)	4.02 (8)	0.211
ESR, mm/h	33 (52-41)	33 (52-44)	33 (51-40)	0.817
CRP, mg/L	18.81 (4-44.4)	22.82 (9-51.3)	13.4 (8-30.8)	0.204
RF positive rate, n (%)	334 (76)	74 (71)	86 (76)	0.321
ACPA positive rate, n (%)	532 (77)	78 (71)	78 (71)	0.890
DAS28-ESR	5.12 (18.18-10.2)	5.12 (18.18-10.2)	5.12 (18.28-7.9)	0.518
DAS28-ESR	3.78 (2.88-4.68)	3.78 (2.88-4.6)	3.78 (3.04-4.6)	0.708
CD41	26 (18-36)	34 (18-39)	36 (18-34)	0.758
CD41	28.2 (18.3-38.8)	30.3 (18.8-43.8)	37.3 (18.9-37.1)	0.888
Previous medication				
csDMARDs-naïve, n (%)	111 (75)	47 (86)	49 (97)	0.881
Glucocorticoid, n (%)	176 (84)	49 (88)	36 (68)	0.313
Double csDMARDs, n (%)	63 (51)	38 (88)	27 (57)	0.272
Triple csDMARDs, n (%)	11 (1)	7 (1)	8 (8)	0.287

**Conclusions:** Add-on short-course TCZ may be an alternative induction strategy for RA patients in developing countries which can quickly achieve target and accelerate dose tapering of GC.



**Abstract THU0206 – Figure 1.** Dynamic changes of therapy indexes between add-on TCZ group and csDMARDs group. (A-H) Comparison of disease activity indexes at baseline and week 4, 12 and 24. (I-K) Comparison of therapeutic effect. (L) Comparison of glucocorticoid dosage per day. Therapeutic target, remission and deep remission were defined as DAS28-ESR<3.2, <2.6 and <1.98, respectively. \*P<0.05. \*\*P<0.01. \*\*\*P<0.001.

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**THU0207 FINDING THE OPTIMAL TREATMENT STRATEGY FOR DISEASE ACTIVITY-GUIDED DOSE REDUCTION OF ADALIMUMAB AND ETANERCEPT IN RHEUMATOID ARTHRITIS: A MODELLING STUDY**

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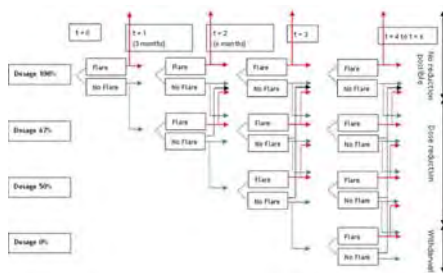
**Background:** Several studies have shown that disease activity-guided dose reduction without deterioration of disease activity is possible, while saving costs in patients with stable and low disease activity.<sup>(1)</sup> Despite these positive results, questions remain on the optimal tapering strategy. Different strategies are conceivable, with varying results regarding the balance between number of flares, utilities and costs.

**Objectives:** The objective of this study was to investigate the most cost-effective TNFi dose reduction strategy for RA patients using a modelling design.

**Methods:** In a cost-utility analysis using Markov modelling based on data from the DRESS study, STRASS study, and the RA Nijmegen cohort, the following strategies were tested against continuation: 1. Four-step DRESS tapering (figure 1: 100%–67%–50%–0%); 2. Tapering with an extra dosage step of 33%; 3. Tapering without withdrawal; 4. Use of a stricter flare criterion (DAS >2.6); and 5. Use of a predictor (biomarker: 80% specific, 80% sensitive, € 100 per test) for successful tapering. Scenario analyses with 30% and 50% drug price discount and no discounting were executed. Also, it was examined how well a biomarker should be able to predict to become cost-effective compared to the other strategies.

**Results:** All examined tapering strategies were found to be cost saving but yielded more short-lived flares compared to continuation (table 1). The change in utilities was minimal and not clinically relevant. Strategy 1 was cost-effective compared to all other strategies (highest incremental Net Monetary Benefit (iNMB)). However, there was a large overlap in credible intervals, especially between strategy 1 and 2. Scenario analyses showed that 50% reduction of drug prices would result in the highest iNMB for strategy 2. A biomarker only becomes cost-effective when it has a sensitivity and specificity of at least 86%.

Data is mean values per patient over 1.5 years (95% credible intervals). \*Stricter flare criterion (DAS28 >2.6). \*\* NMB=QALYs \* WTP/WTA – costs; iNMBs are given at a WTP/WTA of € 80 000.



**Conclusions:** All dose reduction strategies dominated the continuation strategy regarding cost-effectiveness. Because our study showed a comparable iNMB for tapering in four or five steps, we recommend a choice between these strategies, based on shared decision making.

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**THU0208 EFFECTIVENESS AND SAFETY OF CERTOLIZUMAB PEGOL IN RHEUMATOID ARTHRITIS PATIENTS AFTER FAILURE TO ANTITNF OR NAÏVE PATIENTS IN REAL WORLD SETTING. ONE YEAR FOLLOW-UP EXPERIENCE**

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**Background:** Between 30%–40% of patients with rheumatoid arthritis (RA) dis- continue at their first line biological therapy due to inadequate response or adverse events. There is currently a great controversy about using a second anti- TNF, after failure to the first one, or a therapeutic target change, due to the avail- ability of a wide pharmacological arsenal for patients with RA.

**Objectives:** The objective of this study is to determine the effectiveness and safety during one year of Certolizumab pegol (CZP) in patients with RA in second line (after failed to a previous antiTNF) and compare it with those who received this therapy as first line (bio-naïve).

**Methods:** National, observational, prospective, longitudinal and multicenter study in patients with RA who received CZP as the first line of biological treatment or fail- ure to a previous anti-TNF for lack of efficacy, during one year of follow-up. Demo- graphic and clinical variables were collected (gender, age, disease duration, TJC, SJC, ESR, CRP, DAS28, HAQ), at baseline visit, 3 and 12 months of treatment. As response variables, DAS28 remission, low disease activity by DAS28 (LDA) and EULAR response, were used. The Student t test and the Mann-Whitney U test were used for the statistical analysis and a survival analysis (Kaplan-Meier) was performed

**Results:** A total of 360 patients were included, of which 272 (75.6%) were bio- naïve and 88 (24.4%) previous anti-TNF failure. Baseline characteristics of both groups are shown in table 1. Clinical variables of effectiveness at 3 and 12 months are summarised in table 2. Statistically significant differences in DAS28, HAQ and % patients with corticosteroids were observed in both groups at year of treatment comparing with baseline, even though bio-naïve group had a statistically lower DAS28 and a higher percentage response than the antiTNF failure group. Accord- ing to Kaplan-Meier analysis, similar retention rates were observed independently if CZP were used as first (77.2%) or second line (73.9%). No differences were found in terms of safety at one year of treatment between both groups.

**Conclusions:** This study, derived from the experience of national clinical practice with CZP, demonstrates the effectiveness and safety of this drug in patients with RA regardless of its use in the first line or after failure to a previous antiTNF, with better response scores in bio-naïve patients. No differences were observed in the retention rate in both groups.

**Abstract THU0207 – Table 1.** Main outcomes of each strategy

Outcome measure	0. Continuation (comparator)	1. DRESS strategy (four-step tapering)	2. Five-step tapering	3. No withdrawal	4. Stricter flare criterion	5. Predictor
<b>Costs (€)</b>	21 071 (20,563–21,383)	13 198 (12,469–13,988)	13 794 (13,150–14,496)	14 266 (13,685–14,856)	15 943 (15,115–16,793)	14 327 (13,281–15,359)
<b>QALYs</b>	1.182 (1.165–1.199)	1.177 (1.160–1.193)	1.181 (1.165–1.197)	1.182 (1.166–1.198)	1.189 (1.173–1.205)	1.185 (1.168–1.200)
<b>Mean number of short-lived flares</b>	0.53 (0.35–0.73)	0.97 (0.83–1.12)	0.74 (0.58–0.93)	0.69 (0.52–0.87)	2.08* (1.80–2.41)	0.55 (0.53–0.56)
<b>iNMB**</b>	-	7434 (6,514–8,302)	7176 (6,307–8,000)	6798 (5,977–7,539)	5650 (3,598–7,625)	6938 (5,863–8,040)



Abstract THU0208 – Table 1. Baseline characteristics

	Bionaive	Bioexperience (after antiTNF failure)	P
Gender, female %	78.3	73.9	NS
Age, years, mean (Q1-Q3)	52.8 (18-82)	54.8 (19-82)	NS
Disease duration, years, mean (Q1-Q3)	5.8 (0-37)	8.0 (1-33)	<0.001
> 2 yr	58.2	89.0	<0.001
Never smoker %	68.4	69.2	NS
Seropositivity, %	73.9	73.6	NS
Erosions, %	47.6	61.9	0.023
Comorbidities (yes), %	32.7	40.9	NS
Corticosteroids (yes), %	72.8	63.6	NS
Prior Biologic Treatment %	-	Etanercept 46.6 Adalimumab 39.8 Infliximab 11.4 Golimumab 2.3	
CZP monotherapy, %	14.3	19.3	NS
>1 concomitant csDMARD, %	8.5	2.3	0.047
TJC, mean (SD)	9.3 (±6.2)	9.6 (±6.4)	NS
SJC, mean (SD)	6.7 (±4.7)	7.2 (±5.8)	NS
CRP, mg/L, mean (SD)	6.6 (±15.8)	9.2 (±14.7)	NS
ESR, mean (SD)	29.6 (±22.8)	30.1 (±24.5)	NS
HAQ, mean (SD)	1.2 (±0.7)	1.2 (±0.7)	NS
DAS28, mean (SD)	4.7 (±1.1)	4.7 (±1.1)	NS

Disclosure of Interest: None declared

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#### THU0209 4 YEARS FOLLOW-UP OF A COHORT OF PATIENTS WITH RHEUMATOID ARTHRITIS IN SUSTAINED CLINICAL REMISSION AND OPTIMISATION OF BIOLOGICAL THERAPY

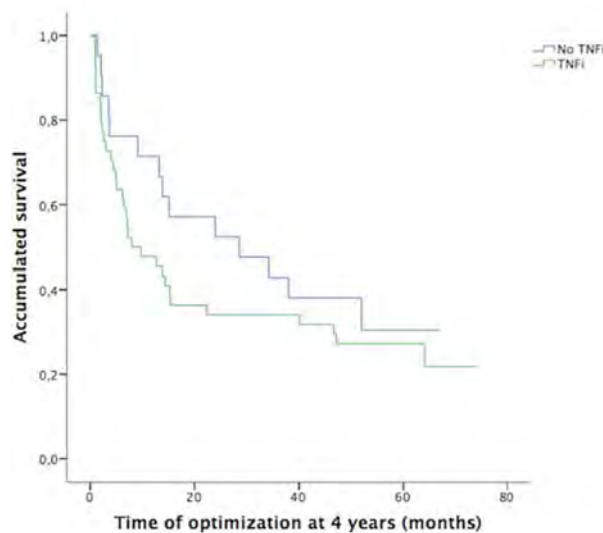
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**Background:** The objectives of Rheumatoid Arthritis (RA) treatment comprise achieving persistent Clinical Remission (CR) or sustained low clinical activity. Nowadays management follows a “treat to target” strategy based on adjustment of treatment in accordance with protocols. In patients with persistent disease activity after treatment with at least two of the classic disease-modifying antirheumatic drugs the use of biological therapy is recommended. Once sustained CR is achieved, the most efficient strategy is optimisation, by tapering the dose of the biological therapy or by increasing administration intervals. Searching for the lowest effective dose for each patient could minimise the risk of adverse effects and improve the cost-effectiveness of RA treatment.

**Objectives:** To prove that the performance of an optimisation strategy in patients with RA and sustained CR under biological treatment maintains the proportion of patients with DAS28 ≤2.6 after 4 years, to assess the maintenance of the effectiveness of the optimisation at 4 years in terms of clinical manifestations, and to analyse the time until relapse.

**Methods:** An open observational prospective study that included 70 patients with RA (CREATE registry) in CR at least for 6 months, under treatment with tapered dose of biological therapy (TNFi, abatacept or tocilizumab). Treatment effectiveness was assessed with the main variable DAS28 ≤2.6. Statistical analysis included a descriptive study of variables and a confidence interval of 95% (95% CI) was estimated. For bivariate analysis, we used Student t-test for independent samples, repeated measures analysis of variance and mixed analysis of variance, and as a post-hoc contrast, Sidak adjustment. The log-rank test was used to compare the time until relapse according to the biological therapy.

**Results:** The mean age of the patients was 56,9 (13,7) years, 78,6% were women, 68,8% were rheumatoid factor (RF) positive and 66,7% ACPA positive; the mean DAS28 at the beginning of the optimisation was 2,24 (0,73). After 4 years, 27,7% (95%CI:16,82%–38,58%) of patients maintained CR with the optimised dose, with a DAS28 2,15 (0,81). Through the first year, the percentage of relapses was 15,71%, in the second year, 7,35% and 4,61% relapsed during the third year. The median time of optimisation until relapse was 13,83<sup>3,18</sup> months (95% CI:7,6–20,06). No significative differences were found at comparing the survival curves of the optimised patients until relapse for 4 years according to the biological therapy (TNFi vs no TNFi) (log-rank test:0,865, p:0,352) (graphic).



**Conclusions:** After 4 years, all of the patients maintained DAS28 levels of low disease activity, including those who had suffered a previous relapse and had turned back to the previous dose of biological treatment. In view of this outcomes, optimisation strategy in clinical practice is possible and effective in patients with persistently controlled RA.

Disclosure of Interest: None declared

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#### THU0210 SAFETY, TOLERABILITY AND EFFICACY OF SUBCUTANEOUS TOCILIZUMAB ADMINISTERED AS MONOTHERAPY OR IN COMBINATION WITH CSDMARDS IN RHEUMATOID ARTHRITIS: RESULTS FROM THE OSCAR STUDY

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**Background:** Efficacy and safety of intravenously (IV) administered tocilizumab (TCZ) in rheumatoid arthritis (RA) has been shown. Recently, efficacy and safety was confirmed for subcutaneous (SC) administration of TCZ.<sup>1</sup> The possible effects of SC TCZ upon tapering of GCs/NSAIDs has not been investigated.

**Objectives:** First, to establish the safety and efficacy of SC TCZ monotherapy or in combination with csDMARDs in DMARD-IR RA. Second, to assess GC/NSAID dose reduction and/or discontinuation under SC TCZ treatment.

**Methods:** The OSCAR study was a Dutch multicenter, open-label, single arm phase IV study within the phase 4 TOZURA program.<sup>1</sup> RA patients with an inadequate response (IR) to csDMARDs and 1 bDMARD were treated with weekly SC

Abstract THU0208 – Table 2. Effectiveness of CZP. Comparing at 12 months bionaive and bioexperience groups

	Baseline		3 months		12 months		P
	Bionaive	Bioexperience (after antiTNF failure)	Bionaive	Bioexperience (after antiTNF failure)	Bionaive	Bioexperience (after antiTNF failure)	
HAQ, mean (SD)	1.2 (±0.7)	1.2 (±0.7)	1.1 (±0.7)	1.1 (±0.7)	0.9 (±0.6)	0.9 (±0.7)	0.925
DAS28, mean (SD)	4.7 (±1.1)	4.7 (±1.1)	3.5 (±1.3)	3.7 (±1.2)	3.0 (±1.3)	3.4 (±1.3)	0.011
Corticosteroids (yes), %	72.8	63.6	61.8	56.8	43.8	45.5	0.780
DAS28 remission,%	-	-	25.2	17.9	45.5	32.1	0.031
DAS28 LDA,%	-	-	43.6	31.0	61.7	45.2	0.008
EULAR Response,%	-	-	60.2	54.8	77.1	64.3	0.020

injections of TCZ monotherapy or in combination with csDMARDs up to 24 weeks. From week 16 onwards dose reduction and/or discontinuation of glucocorticoids (GC) and NSAIDs was allowed. Primary endpoints were occurrence of adverse events (AEs), serious AEs (SAEs) and AEs of special interest (AESI). Secondary endpoints were time to GC/NSAID dose reduction and/or discontinuation, and DAS28 (remission), ACR 50 response, EULAR response, SDAI, CDAI and HAQ-DI. Occurrence of AEs was analysed using descriptive statistics. Changes over time in efficacy endpoints and response rates were analysed using Wilcoxon test. **Results:** Of the 150 patients 121 (81%) patients completed the treatment period. In 91% of the patients there was  $\geq 1$  AE, in 9% an SAE, and in 4% an AESI. Most AEs were mild or moderate in intensity and resolved without sequelae. Permanent TCZ treatment discontinuations due to AEs occurred in 7% of the 150 patients; of these, five patients were prematurely withdrawn from the study due to AEs. From week 16 onwards, 8 (5.3%) and 13 (8.7%) patients discontinued or reduced (for any reason) the dose of NSAIDs or GCs, respectively. Between weeks 16 and 20, 2 (1.3%) patients discontinued or reduced the dose of NSAIDs due to safety and other reasons. The dose of GCs was discontinued or reduced in 3 patients (2.0%) between weeks 16 and 20, and in another 3 between weeks 20 and 24 (2.0%), in all 6 patients mainly due to safety reasons (1.3%), while NSAIDs dosage remained stable. The safety profile observed in this trial was in line with the known TCZ safety profile. Efficacy parameters improved over time for all of the endpoints. A selection of these results is shown in table 1.

Abstract THU0210 – Table 1. Efficacy results

Table. Efficacy results.

Efficacy parameter		P-value
<b>Change from BL in DAS28, median (min, max)</b>		P<0.0001
Week 4	1.9 (1.10, -4.54)	
Week 12	-3.0 (0.89, -6.00)	
Week 24	3.2 (-0.06, -7.57)	
<b>DAS28 remission, % (n/N)</b>		
Week 4	52.1 (75/144)	
Week 12	77.4 (103/133)	
Week 24	86.8 (105/121)	
<b>ACR 50 response rate, %</b>		P<0.0001
Week 4	21.5	
Week 12	45.1	
Week 24	66.1	
<b>EULAR good response, % (n/N)</b>		P<0.0001
Week 4	59.7 (86/144)	
Week 12	85.0 (113/133)	
Week 24	85.0 (113/133)	
<b>Change from BL in SDAI, median (min, max)</b>		P<0.0001
Week 4	-11.0 (-30.9,8.2)	
Week 12	17.1 (-46.5,16.9)	
Week 24	-19.7 (-53.3,-0.07)	
<b>Change from BL in CDAI, median (min, max)</b>		P<0.0001
Week 4	-9.1 (-30.8,8.3)	
Week 12	-15.1 (-45.1,6.9)	
Week 24	17.3 (-60.2,0.1)	
<b>Change from BL in HAQ-DI, median (min, max)</b>		P<0.0001
Week 4	-0.25 (-1.25,1.13)	
Week 12	-0.38 (-2.13,0.38)	
Week 24	-0.50 (-2.38,0.88)	

DAS28: disease activity score of 28 joints; ACR: American College of Rheumatology; EULAR: European League Against Rheumatism; BL: baseline; SDAI: simple disease activity index; CDAI: clinical disease activity index; HAQ-DI: health assessment questionnaire disease activity; P-values refer to the differences between baseline and week 4, week 12 and week 24 measured per parameter.

The median time of follow-up of the studied population was 822 days, IQR 429–727 days.

**Conclusions:** The OSCAR study showed that SC TCZ is safe, well-tolerated and effective in RA patients with an inadequate response to csDMARDs and max 1 bDMARD. Importantly, a subset of patients could reduce GC and/or NSAID use during SC TCZ treatment. These findings support the notion that SC TCZ can be safely used in clinical practice.

#### REFERENCE:

[1] Choy E, et al. *Rheumatology* 2017. doi:10.1093/rheumatology/kex443

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THU0211

#### SIX MONTHS AFTER TREATMENT DISCONTINUATION TNF IS STILL IN COMPLEX WITH ADALIMUMAB

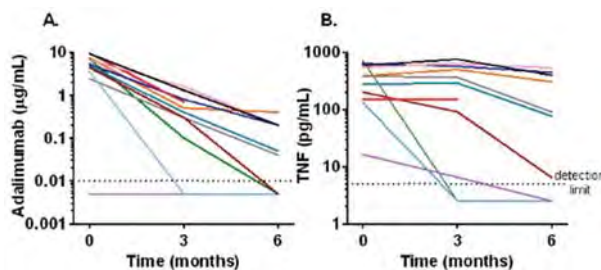
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**Background:** Many patients with rheumatoid arthritis (RA) are successfully treated with tumour necrosis factor inhibitors (TNFi). We recently developed a novel assay that can quantify TNF in the presence of large amounts of TNFi, i.e. a 'drug-tolerant' assay. We showed in RA patients that TNF levels increased and stabilised during adalimumab treatment due to complex forming between TNF and adalimumab. In the presence of adalimumab, all TNF was in complex and biologically inactive. Once in remission, some patients can discontinue the TNFi for a prolonged period. It is unclear how long adalimumab levels are detectable and TNF complexes are formed after the last adalimumab administration.

**Objectives:** To investigate adalimumab levels and complexed TNF levels 6 months after the last adalimumab administration.

**Methods:** TNF and adalimumab levels were measured using a novel drug-tolerant competition enzyme-linked immunosorbent assay (ELISA), and a regular ELISA, respectively, in 11 consecutive RA patients with stable low disease activity (disease activity score of 28 joints < 3.2) who discontinued adalimumab for 6 months (prior dose: 40 mg every 2 weeks). Blood samples were drawn prior to adalimumab discontinuation and 3 and 6 months thereafter.

**Results:** After the last adalimumab administration, mean adalimumab level decreased from 5.5 (SD 2.9) to 0.55 (0.52) and 0.11 (0.13)  $\mu\text{g/mL}$  at 3 and 6 months after treatment discontinuation, respectively (figure 1A). In contrast, complexed TNF levels remained stable for prolonged periods of time: in 8 patients TNF levels at 3 months were indistinguishable from levels seen at baseline, on standard-dose adalimumab (figure 1B). After 6 months, TNF still remained stable in patients with adalimumab concentrations above 0.1  $\mu\text{g/mL}$  (n=4). Overall, mean TNF levels decreased from median 381 (inner quartiles 16; 707) to 290<sup>2</sup>:<sup>755</sup> and 83<sup>2</sup>:<sup>532</sup>  $\text{pg/mL}$  at 3 and 6 months after treatment discontinuation, respectively. In 5 patients, TNF levels decreased significantly. In those patients, adalimumab levels dropped to, or below the detection limit.



**Conclusions:** This is the first study showing that TNF is still in complex with adalimumab in the majority of patients 6 months after the last administration. Therefore, one may wonder at which point in time a patient has truly discontinued adalimumab treatment.

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### THU0212 REINVESTMENT OF BIOSIMILAR SAVINGS: WHAT ARE THE BEST OPTIONS?

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**Background:** Biosimilars are becoming available for many of the biologic compounds in rheumatoid arthritis (RA). Biosimilars provide similar benefit at a reduced cost, therefore generating potential savings to the health care system.

**Objectives:** To investigate whether it is most beneficial to reinvest biosimilar savings to treat additional RA patients or whether this same budget would be more beneficially spent on alternative treatments from a UK payer perspective.

**Methods:** We developed a model to first estimate the savings obtained from using biosimilars from a UK National Health Service (NHS) perspective. Then we identified five treatment alternatives, in addition to RA: melanoma, hepatitis C (HepC), multiple sclerosis (MS), Duchenne's disease (MD), and non-small cell lung cancer (NSCLC). These indications were considered because of their burden of illness, high cost but high efficacy treatments being available which are associated with investment pressures. The treatments selected were: ataluren (MD), natalizumab (MS), pembrolizumab (melanoma), crizotinib (NSCLC), sofosbuvir + ribavirin (HepC), and etanercept biosimilar. We estimated the health gain (expressed as QALYs) that could be obtained from treating the patients in the four indications of interest using the available savings to identify the most cost-effective way to spend the savings. Data on QALY gains were obtained from published sources, mostly HTA assessments.

**Results:** Based on a biologics expenditure of ~£430 million, we estimated that ~£5 million in savings would be generated over a 5 year period.

Based on the outcome of QALY maximisation, over a 5 year period, biosimilar savings in the UK are best spent on treatments in hepatitis C, followed by NSCLC and melanoma. Re-investment in an RA biosimilar only came in 5th place, before cystic fibrosis.

**Conclusions:** In a country like the UK, where patients have ready access to biologics, the savings from prescribing biosimilars can be better spent, if QALY maximisation is desired, on non-RA therapies where over a 5 year period more QALYs are generated. On the basis of the research, payers should consider the potential to reinvest biosimilar savings in disease areas with higher QALY yields.

**Disclosure of Interest:** None declared

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### THU0213 ADHERENCE AND PERSISTENCE TO DISEASE MODIFYING ANTI RHEUMATIC DRUGS IN COLOMBIAN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Adherence in the treatment of rheumatoid arthritis (RA) ranges 20% to 70% in worldwide population.<sup>1</sup> In Colombia there are no studies comparing adherence and persistence to conventional and biological treatment.

**Objectives:** To determine adherence and persistence and associated factors to the treatment of conventional disease-modifying anti-rheumatic drugs (cDMARD) and biological DMARD (bDMARD) in patients with RA under real world data.

**Methods:** We conducted an observational, analytical retrospective cohort study from January 2015 to December 2016. The study population was 552 RA patients older than 18 years who received any cDMARD treatment in monotherapy or combined with two or more cDMARD and bDMARD (Rituximab and Tofacitinib were excluded). Clinical information was obtained from electronic clinical records and Morisky-Green test was performed during the follow-up. Univariate analysis (proportions and medians), bivariate analysis [relative risk (RR)] and multivariate analysis (logistic regression and Kaplan-Meier survival curve) were developed.

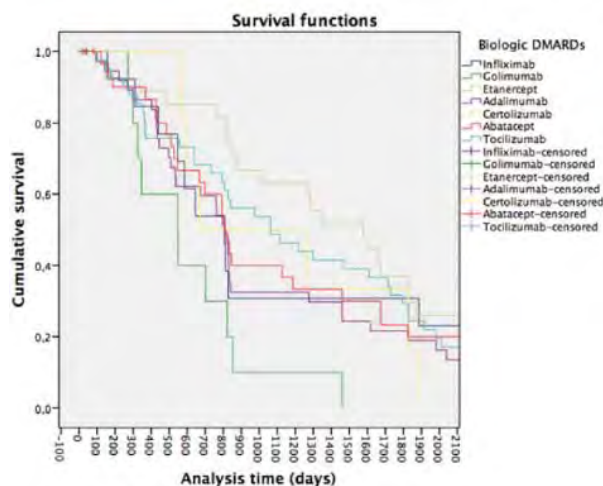
**Results:** Eighty nine percent were women, the median age was 59 years, 50% have  $\geq 12$  years of duration of disease. Adherence for cDMARD was 61% and for bDMARD 56%. There was an association between adherence and high degree education level (adjusted RR=2.1; **CI: 1.09–4.14**) and non-adherence with clinical factors such as high disease activity (adjusted RR=0.41; **CI: 0.22–0.75**); in the cDMARD group the greatest persistence was leflunomide (mean: 631 days) followed by methotrexate (mean: 526 days) and in the bDMARD group was etanercept (mean 1577 days) and tocilizumab (mean 1064 days). Patients with social support had greater persistence in the treatment with cDMARD (adjusted HR=2.1; **CI: 1.11–4.28**).

**Abstract THU0213 – Table 1.** Sociodemographic, clinical and therapeutic characteristics in 552 Colombian patients with rheumatoid arthritis

Characteristics	n	(%)
Rheumatoid factor	415	81
ACPA	150	71

DAS-28	<2,6	267	49
	2,6–3,2	68	12
	3,2–4,9	129	23
	>5	88	16
	Methotrexate	281	55
cDMARD	Leflunomide	130	25
	Sulfasalazine	71	14
	Chloroquine	30	6
bDMARD	Tocilizumab	41	24
	Adalimumab	38	22
	Abatacept	32	19
	Etanercept	29	17
	Infliximab	14	8,2
	Golimumab	11	6,4
	Certolizumab	6	3,5

IQR: interquartile range, ACPA: anti-cyclic citrullinated protein/peptide antibodies



**Abstract THU0213 – Figure 1.** The median time of follow-up of the studied population was 822 days, IQR 429–727 days.

**Conclusions:** In real world data, education level and disease activity significantly impact adherence level in RA patients. Social support positively impacts the persistence of the treatment of RA patients, which suggest the implementation of care programs taking this aspect into consideration in order to improve outcomes.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.6091

### THU0214 PREDICTIVE FACTORS FOR ACHIEVEMENT OF LOW DISEASE ACTIVITY AT 52 WEEKS ARE DIFFERENT BETWEEN YOUNG AND ELDERLY RHEUMATOID ARTHRITIS PATIENTS TREATED WITH ABATACEPT

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**Background:** Japanese post-marketing survey (PMS) data demonstrated that the clinical efficacy of abatacept was similar between the young and elderly rheumatoid arthritis (RA) patients, while they have quite different characteristics including age, disease duration, and concomitant drugs. We hypothesised that the predictive factors for clinical outcomes of abatacept were different between the young and elderly patients.

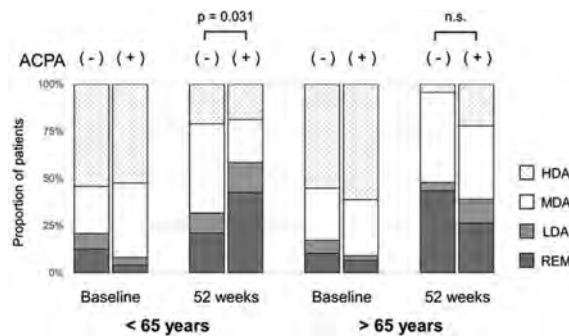
**Objectives:** We studied the predictive factors for good clinical response of abatacept in the young and elderly patients, respectively, in this study.

**Methods:** Participants were consecutive 463 RA patients treated with abatacept and observed for longer than 52 weeks in the TBCR, a Japanese multicenter registry system for RA patients treated with biologics. Univariate and multivariate logistic regression analysis was used to study predictive factors for achievement



of low disease activity (LDA) at 52 weeks, separately in the young (<65 years, n=215) and the elderly (>65 years, n=248) group.

**Results:** Mean age was 55.3/74.0 years (young/elderly), disease duration was 10.2/12.8 years, DAS28-CRP was 4.34/4.40 at baseline, concomitant MTX was used in 55.4/37.1%, concomitant steroid was used in 51.0/49.6%, and proportion of bio-naïve was 49.3/63.3%. As shown in table 1, multivariate analysis revealed that no history of previous biologics and lower DAS28 score at baseline was the independent positive predictors in both young and elderly group. Interestingly, ACPA positivity was significant predictor only in the young group. The ACPA positive patients showed the significantly higher proportion of LDA achievement at 52 weeks, only in the young group (figure 1).



**Conclusions:** It has been reported that lower proportion of the elderly onset RA (EORA) patients has ACPA positivity, and some reports have previously demonstrated that the ACPA negative was negatively associated with good clinical outcomes of abatacept. Our current results suggested that the effect of ACPA positivity on the clinical results of abatacept treatment was different between ages. Abatacept would be a valuable treatment option in the ACPA negative elderly RA patients.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.3382

**Abstract THU0214 – Table 1.** Logistic regression analysis to study predictive factors for LDA achievement at 52 weeks.

	Univariate		Multivariate	
	OR (95% CI)	p-value	OR (95% CI)	p-value
<65 years				
Male	0.944 (0.438–2.036)	0.884		
Disease duration,<10 years	1.454 (0.771–2.742)	0.248		
ACPA positive	3.044 (1.070–8.656)	0.037	4.544 (1.049–19.689)	0.043
No previous biological DMARDs	2.458 (1.336–4.524)	0.004	3.386 (1.119–10.244)	0.031
Concomitant MTX	1.879 (1.022–3.453)	0.042		
Concomitant PSL	0.693 (0.380–1.265)	0.232		
mHAQ,<0.5	2.756 (1.373–5.531)	0.004		
DAS28-CRP at baseline	0.631 (0.489–0.814)	<0.001	0.457 (0.260–0.803)	0.006
>65 years				
Male	1.205 (0.601–2.418)	0.599		
Disease duration,<10 years	2.154 (1.120–4.141)	0.021		
ACPA positive	0.697 (0.284–1.711)	0.431		
No previous biological DMARDs	3.040 (1.564–5.912)	0.001	3.678 (1.370–9.876)	0.010
Concomitant MTX	1.357 (0.746–2.467)	0.318		
Concomitant PSL	0.469 (0.256–0.857)	0.014		
mHAQ,<0.5	3.224 (1.670–6.224)	<0.001		
DAS28-CRP at baseline	0.571 (0.444–0.736)	<0.001	0.638 (0.433–0.942)	0.024

**THU0215 EFFICACY OF SARILUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS WITH AND WITHOUT PREVIOUS RESPONSE TO TOCILIZUMAB**

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**Background:** Sarilumab is an IL-6R inhibitor recently approved for the treatment of rheumatoid arthritis (RA). To help clinical decision making, we studied the response rate on open-label sarilumab treatment in patients previously treated with tocilizumab, the other IL-6R inhibitor approved for RA. In the ASCERTAIN trial (NCT01768572), patients were randomised 1:1:2 to 24 weeks of sarilumab 150 mg sc every 2 weeks (q2w; n=49), sarilumab 200 mg sc q2w (n=51), or tocilizumab 4 mg/kg iv q4w (n=102) increased to 8 mg/kg at investigator's discretion if clinically indicated as per the US label; each added to conventional synthetic disease-modifying antirheumatic drug (csDMARD) background therapy. Patients who completed ASCERTAIN were eligible to enrol in an open-label extension study of sarilumab 200 mg sc q2w (EXTEND, NCT01146652), with csDMARDs as specified in the previous study.

**Objectives:** To examine outcomes for patients who switched from tocilizumab in ASCERTAIN to open-label sarilumab in EXTEND.

**Methods:** In this post-hoc analysis, patients were recorded as responders or non-responders at the end of ASCERTAIN and at Weeks 12 and 24 of EXTEND according to each of: clinical disease activity index (CDAI)≤2.8, CDAI≤10.0, disease activity score (DAS)-28 CRP <2.6, DAS-28 CRP <3.2, and American College of Rheumatology (ACR)20/50/70 response criteria.

**Results:** A total of 168 patients entered EXTEND from ASCERTAIN, of whom 93 had been in the tocilizumab group (last tocilizumab dose 4 mg/kg in 37 patients and 8 mg/kg in 56 patients). After switch to sarilumab, response was achieved in an additional number of patients who were non-responders on tocilizumab at the end of ASCERTAIN (table 1). The reverse, response loss in tocilizumab responders, was infrequent. Patients who switched from tocilizumab 4 mg/kg or 8 mg/kg achieved similar response rates.

Last tocilizumab dose, mg/kg	Week in EXTEND	CDAI		DAS28-CRP		ACR20	ACR50	ACR70
		<2.8	≤10	<2.6	<3.2			
Non-responders at the end of ASCERTAIN with response in EXTEND (%) <sup>a,b</sup>								
4	12	3/27 <sup>11</sup>	7/18 <sup>39</sup>	8/23 <sup>35</sup>	8/18 <sup>44</sup>	3/5 (60)	8/19 <sup>42</sup>	7/25 <sup>28</sup>
	24	4/25 <sup>16</sup>	7/16 <sup>44</sup>	9/22 <sup>41</sup>	10/17 (59)	3/4 (75)	6/17 <sup>35</sup>	5/22 <sup>23</sup>
8	12	7/48 <sup>15</sup>	9/31 <sup>29</sup>	13/36 <sup>36</sup>	8/21 <sup>38</sup>	2/11 <sup>18</sup>	14/30 <sup>47</sup>	9/43 <sup>21</sup>
	24	10/46 <sup>22</sup>	13/29 <sup>45</sup>	16/35 <sup>46</sup>	7/20 <sup>35</sup>	6/10 (60)	13/28 <sup>46</sup>	13/41 <sup>32</sup>
Responders at the end of ASCERTAIN with response in EXTEND (%) <sup>a,b</sup>								
4	12	8/89 (89)	15/83 (83)	11/100 (100)	16/100 (100)	28/90 (90)	16/94 (94)	10/91 (91)
	24	6/75 (8)	15/88 (88)	9/90 (90)	14/93 (93)	27/93 (93)	27/94 (94)	9/90 (90)
8	12	4/57 (7)	21/88 (88)	13/76 (76)	26/81 (90)	38/90 (90)	19/83 (83)	7/64 (64)
	24	5/71 (7)	20/83 (83)	14/78 (78)	28/85 (85)	39/91 (91)	19/79 (79)	9/75 (75)

<sup>a</sup>responder status according to measure listed in column heading; <sup>b</sup>subjects with missing measurements are excluded from numerator and denominator

**Conclusions:** These results may indicate that clinical improvements can be attained in a relevant proportion of tocilizumab non-responders with switch to sarilumab, irrespective of previous tocilizumab dose, and the majority of patients responding to tocilizumab maintain response when switching to sarilumab.

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Dutch Healthcare Insurance companies, Consultant for: Boehringer Ingelheim, Amgen, Employee of: Sint Maartenskliniek the Netherlands

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**THU0216 SERUM CXCL16 LEVELS IN RF+/ACPA+RHEUMATOID ARTHRITIS PATIENTS BEFORE AND AFTER TREATMENT WITH DMARDS**

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**Background:** Rheumatoid arthritis (RA) is characterised by profound mononuclear cell (MNC) recruitment into synovial tissue (ST). Studies have shown that chemokine CXCL16 is a premier MNC recruiter in RA. CXCL16 contributes to chronic inflammation, since it is highly expressed in RA synovial fluid (SF), is a potent chemoattractant for mononuclear cells (MNCs) *in vitro*, and is chemotactic for peripheral blood mononuclear cells (PBMCs) to RA ST *in vivo*. Hence treatment for RA will reflect change in serum CXCL16 levels

**Objectives:** The aim of this study was to analyse the change of serum chemokine level of CXCL16, in patients with either RF +or ACPA +rheumatoid arthritis (RA), by DMARDs treatment.

**Methods:** This was a prospective interventional study done in a tertiary care centre. 31 patients with RA were recruited for a period of 12 months. Serum CXCL16 levels were assayed in them along with other baseline investigations. The patients were treated with DMARDs. CXCL16 levels post treatment were measured after 6 months. For comparison another group of age and sex matched controls was taken (n=18) and their serum CXCL16 was also recorded. The serum CXCL16 levels were correlated with disease activity.

**Results:** After treatment with conventional DMARDs 26 patients showed lowering of mean serum CXCL16 levels from 56.07 pg/ml to 21.79 pg/ml (62% reduction) after 6 months. The patients who showed inadequate response to conventional DMARD treatment (n=5) underwent therapy with biological DMARDs (TNF- $\alpha$  blocker) which reduced their CXCL16 levels from 63.81 pg/ml to 12.36 pg/ml (80.6% reduction) in subsequent 6 months. There was a corresponding improvement in the disease activity of RA. Lowering of CXCL16 was found to correlate positively with improvement of symptoms and lowering of disease activity

**Conclusions:** DMARDs treatment significantly lowered the serum levels of CXCL16 in patients with RA. CXCL16 is one of the crucial chemokines regulated by DMARDs treatment

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**THU0217 SIMILAR EFFICACY AND SAFETY OF SARILUMAB 150 MG OR 200 MG Q2W REGARDLESS OF PRIMARY (1°) OR SECONDARY (2°) FAILURE WITH TNF INHIBITORS**

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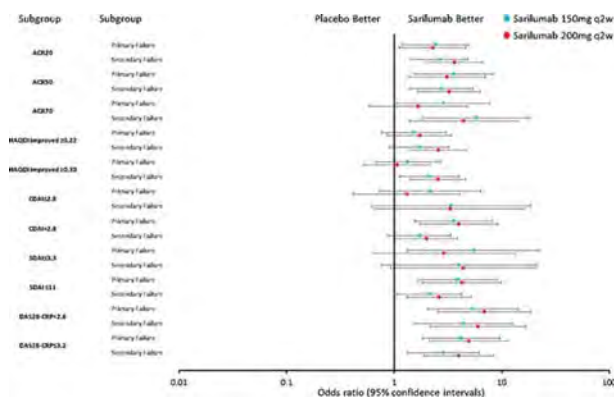
**Background:** Sarilumab (150 or 200 mg subcutaneously [SC] every 2 wks [q2w]) +csDMARDs demonstrated efficacy in adults with moderate-to-severely active

rheumatoid arthritis (RA) with intolerance or inadequate response to prior TNFi treatment in TARGET (NCT01709578). Patients with an initial refractory response (1° failure) to TNFi may respond differently to subsequent treatment vs those who initially respond but lose TNFi effectiveness (2° failure).

**Objectives:** This post hoc analysis examined efficacy and safety of sarilumab +csDMARDs in patients who had previously demonstrated 1° vs 2° TNFi failure.

**Methods:** TNFi failure (1° vs 2°) was investigator-determined on enrolment to TARGET. Patients who experienced 1° or 2° failure were randomised to placebo (pbo; n=75 and n=99), sarilumab 150 mg (n=72; n=91), or sarilumab 200 mg q2w (n=64; n=103), respectively. Disease activity, physical function (HAQ-DI), and safety were assessed at Wk 24.

**Results:** By Wk 24, ACR20/50/70 response rates and improvements in LS mean HAQ-DI were similar in both sarilumab dose groups and superior to pbo, irrespective of 1° vs 2° TNFi failure (table 1). Odds ratios for the benefit of sarilumab over pbo according to ACR response rates, HAQ-DI, DAS28-CRP, CDAI and SDAI (figure 1) showed no differences between patients with 1° vs 2° failures. No significant treatment by subgroup (1° vs 2° failure) interactions were observed. In the 1° failure group, treatment emergent adverse events (TEAEs; table 1) occurred in 59.7%, 65.6% vs 45.3% (sarilumab 150, 200 mg vs pbo, respectively) of patients; and in 73.6% and 63.1% vs 52.5% with sarilumab 150, 200 mg vs pbo, respectively, in the 2° failure group. There was only one TEAE leading to death (pbo group) and one case each of venous thrombosis (200 mg sarilumab q2w, 2°) and pulmonary embolism (150 mg sarilumab q2w, 2°).



**Conclusions:** Key efficacy and safety measures were similar in patients treated with sarilumab +csDMARDs, regardless of previous 1° or 2° failure with TNFis.

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**Disclosure of Interest:** R. Fleischmann Grant/research support from: AbbVie, Amgen, AstraZeneca, Bristol-Myers Squibb, Celgene, EMD-Serono, Eli Lilly, Merck, Novartis, Pfizer, Roche, Sanofi-Genzyme, UCB, Consultant for: AbbVie, ACEA, Amgen, Bristol-Myers Squibb, GSK, Eli Lilly, Novartis, Pfizer, Sanofi-Genzyme, UCB, A. Spindler: None declared, A. Kivitz Shareholder of: Novartis, Consultant for: AbbVie, Janssen, Pfizer, UCB, Genzyme, Sanofi, Regeneron, Boehringer Ingelheim, Sun Pharma, Speakers bureau: Celgene, Genentech, Merck, Novartis, Pfizer, Genzyme, Sanofi, Regeneron, Horizon, D. Ching Grant/research support from: Sanofi, Lilly, Celgene, Pfizer, Galapagos, Gilead and AbbVie, Consultant for: AbbVie, E. Mangan Shareholder of: Regeneron, Pfizer, Employee of: Regeneron, T. Kimura Shareholder of: Regeneron, Employee of: Regeneron, M. Iglesias-Rodriguez Employee of: Sanofi, G. Burmester Grant/research support from: AbbVie, Pfizer, UCB, Roche, Consultant for: AbbVie, Lilly, Merck Sharpe and Dohme, Pfizer, Sanofi, Roche, UCB, Speakers bureau: AbbVie, Lilly, Merck Sharpe and Dohme, Pfizer, Sanofi, Roche, UCB

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**Abstract THU0217 – Table 1.** Efficacy responses and percentage of patients experiencing AEs ( $\geq 5\%$  in any subgroup) at Wk 24

	Primary failure			Secondary failure		
	Placebo (n=75)	Sarilumab 150 mg q2w (n=72)	Sarilumab 200 mg q2w (n=64)	Placebo (n=99)	Sarilumab 150 mg q2w (n=91)	Sarilumab 200 mg q2w (n=103)
<b>Efficacy parameters</b>						
ACR20/50/70,% Responders	33.3/18.7/12.0	51.4/37.5/23.6	51.6/37.5/15.6	35.4/ 18.2/4.0	59.3/39.6/19.8	66.0/41.7/15.5
CDAI, LS mean $\Delta$ from baseline (SE)	-15.28 (1.9)	-23.73 (1.9)	-22.73 (2.0)	-17.89 (1.6)	-24.42 (1.6)	-27.43 (1.5)
<b>TEAEs (%)</b>						
Neutropenia	1.3	12.5	10.9	0.0	13.2	12.6
UTI	6.7	1.4	7.8	7.1	5.5	6.8
Increased ALT	1.3	5.6	7.8	0.0	1.1	3.9
uRTI	5.3	1.4	4.7	2.0	3.3	2.9
Hypertriglyceridemia	1.3	8.3	6.3	2.0	3.3	1.0
Accidental overdose	4.0	1.4	6.3	2.0	6.6	2.9
Hypertension	0.0	0.0	6.3	4.0	1.1	2.9
Hypercholesterolemia	0.0	5.6	4.7	0.0	2.2	1.0
Diarrhoea	5.3	0.0	4.7	2.0	1.1	1.9
RA	4.0	0.0	0.0	5.1	3.3	2.9
Injection site erythema	0.0	4.2	4.7	0.0	7.7	1.9
Nasopharyngitis	4.0	4.2	1.6	5.1	7.7	4.9

THU0218

### THE EFFICACY AND DRUG SURVIVAL OF THE BIOSIMILAR INFLIXIMAB (CT-P13) COMPARED TO THE ORIGINAL REFERENCE INFLIXIMAB IN INFLAMMATORY RHEUMATIC DISEASES; RESULTS FROM THE TURKBIO REGISTRY

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**Background:** Biosimilar infliximab (CT-P13) has been used to treat patients with rheumatoid arthritis (RA), ankylosing spondylitis (AS) and psoriatic arthritis (PsA) in Turkey since 2013.

**Objectives:** The aim of this study was to examine its efficacy, drug survival and compare it to the original reference infliximab (inf) in patients with inflammatory rheumatic diseases based on the database from the TURKBIO registry.

**Methods:** All patients with RA, SpA, PsA, and other diseases receiving CT-P13 and inf registered in the TURKBIO database between the dates of June 2013 and January 2017 were included in the study. Demographic information, laboratory parameters and disease indices were collected (at baseline, and months 6 and 12). We used Kaplan Meier survival curves to examine drug survival patterns.

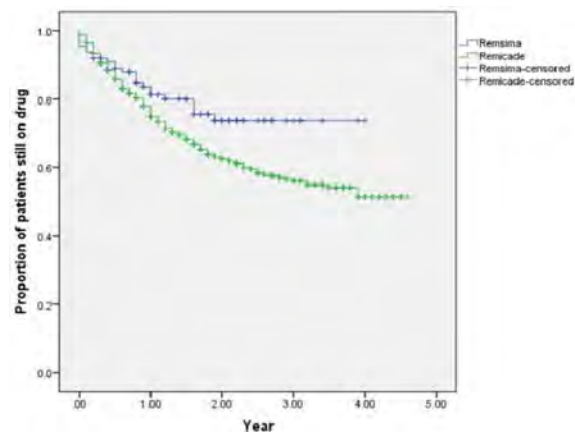
**Results:** Data collected from a total number of 614 patients were analysed (table 1). The analysis of each treatment group was made according to gender, age, and diagnosis. In both groups most of the patients were diagnosed as having axial SpA, followed by RA, PsA and other diseases. CT-P13 group had female predominance. In patients with RA and PsA, baseline DAS28 scores were found to be higher in CT-P13 group. Baseline values of ASDAS-CRP in SpA patients and CRP in all patients were similar for both groups (table 2). Mean CRP levels at month 6 and ASDAS scores at month 12 were found to be higher in inf group. The ratio of males was higher in axial SpA patients receiving inf, but did not statistically affect the 12th month ASDAS results. The results of the database analysis showed that the drug survival rate of CT-P13(78,4%) is higher than inf(63,6%) at year 4 (figure 1). At 4 year follow-up, drug withdrawal was observed in both groups due to ineffectiveness (CT P13;n=13 54,16%, inf;n=89 41,58%) and side effects (CT-P13;n=8 33,33%, inf;n=43 20,09%). In CT-P13 group, six patients had switched from inf to biosimilar and other 20 had used  $\geq 1$  previous biologicals. Of the 503 patients who used inf, 164 had used  $\geq 1$  biologicals previously.

**Abstract THU0218 – Table 1.** Baseline characteristics of CT-P13 and original infliximab, by diagnostic group

	CT-P13 (n=111)	infliximab (n=503)	P value
Age, mean	44.37	45.68	0.350
F, n%	74 (65.49)	241 (47.25)	<0.001
RA, n%	17 (15.32)	54 (10.74)	0.229
F, n%	14 (82)	44 (81)	1.000
AS+NraxSpa, n%	8 (72.07)	334 (66.40)	0.297
F, n%	50 (63)	140 (42)	0.001
PsA, n%	7 (6.31)	39 (7.75)	0.745
F, n%	4 (57)	25 (64)	1.000
Other, n%	7 (6.31)	76 (15.11)	0.021
F, n%	4 (57)	29 (38)	0.563

**Abstract THU0218 – Table 2.** Disease activity follow-up

	CT-P13	infliximab	P value
<b>DAS28, mean</b>	3.95	3.47	0.007
Baseline	2.54	2.27	0.385
Month 6	2.18	2.17	0.959
Month 12			
<b>CRP, (mg/L)</b>	21.00	21.82	0.818
Baseline	4.06	13.09	<0.001
Month 6	10.52	9.97	0.889
Month 12			
<b>ASDAS, mean</b>	3.47	3.31	0.280
Baseline	1.57	1.90	0.093
Month 6	1.23	1.87	0.008
Month 12			

**Abstract THU0218 – Figure 1.** Kaplan-Meier survival curve of biosimilar infliximab and original reference infliximab ( $p < 0.05$ )

**Conclusions:** The results of this study demonstrated long term higher drug survival rate of biosimilar CT-P13. The study also suggested that efficacy of CT-P13 on disease activity was similar to original infliximab in patients with inflammatory rheumatic diseases.

**Disclosure of Interest:** None declared

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### THU0219 BENEFICIAL EFFECT OF ANTI-IL-6 BLOCKADE ON INSULIN RESISTANCE AND INSULIN SENSITIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Systemic inflammation, insulin resistance (IR), and endothelial dysfunction have been implicated in the development of cardiovascular disease in rheumatoid arthritis (RA).<sup>1-3</sup> In this regard, it has been described that the blockade of IL-6, a cytokine involved in the pathogenesis of both RA and atherosclerosis, yields a rapid improvement of endothelial function in RA.<sup>4</sup> However, there are no studies on the role of anti-IL-6 treatment on IR in patients with RA.

**Objectives:** To assess whether IL-6 blockade may result in a reduction of insulin serum levels and an improvement of IR in patients with RA.

**Methods:** 50 Spanish patients on treatment with anti-IL-6 monoclonal antibody-Tocilizumab who fulfilled the 2010 classification criteria for RA<sup>5</sup> were recruited. Patients with diabetes mellitus or plasma glucose >110 mg/dl were excluded. Fasting blood samples were taken for determination of plasma glucose and serum insulin levels immediately prior to (time 0) and after (time 60 min) Tocilizumab infusion. IR was assessed by the homeostasis model assessment (HOMA) and insulin sensitivity was evaluated by the quantitative insulin sensitivity check index (QUICKI).

**Results:** A marked reduction in the serum insulin levels was observed following Tocilizumab infusion (mean ±standard deviation (SD): 10.60±5.80 μU/ml versus 7.61±5.08 μU/ml, p<0.0001). In addition, a decrease in the insulin/glucose index was observed in patients with RA after Tocilizumab dose (mean ±SD: 0.12 ±0.06 versus 0.08±0.05, p<0.0001). Finally, our results disclosed a significant improvement of insulin resistance (HOMA: mean ±SD: 2.61±2.05 versus 1.65 ±1.14, p=0.0003) and insulin sensitivity (QUICKI: mean ±SD: 0.34±0.003 versus 0.37±0.04, p<0.0001) following Tocilizumab infusion.

**Conclusions:** Our study confirms a rapid beneficial effect of Tocilizumab on IR and insulin sensitivity in RA patients treated with this drug. It may support the long-term use of drugs that act blocking IL-6 function to reduce the mechanisms implicated in the development of atherosclerosis in RA patients.

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**Disclosure of Interest:** None declared

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### THU0220 DISCONTINUATION OF BIOLOGIC DMARDs IN A REAL-LIFE POPULATION OF PATIENTS IN REMISSION: OUTCOME AND PREDICTORS

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**Background:** Data from randomised controlled trials have shown that in patients with sustained remission discontinuation of bDMARD therapy is feasible. However, the criteria for selecting patients that will successfully remain in remission after bDMARD discontinuation remain to be defined.

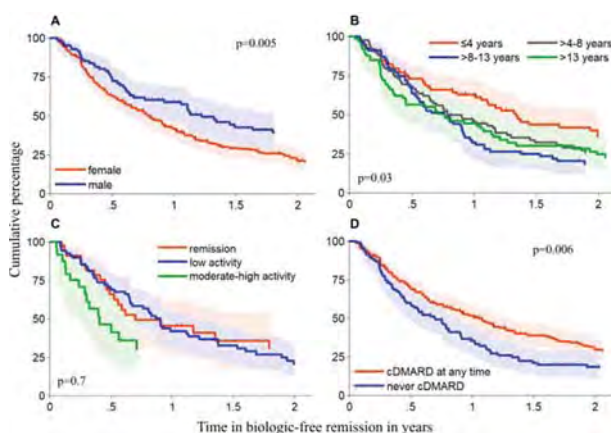
**Objectives:** To assess the rate of loss of remission after discontinuation of bDMARDs in a real life setting and to identify predictors in a large cohort of patients.

**Methods:** Adult RA patients in bDMARD-free remission from the Swiss clinical quality management in rheumatic diseases registry (SCQM) were included. bDMARD-free remission was defined as a discontinuation of the bDMARD and a DAS28 ≤2.6 at a clinical visit within 90 days prior to 30 days after the bDMARD discontinuation. Loss of remission was defined as a DAS28 >2.6 or restart of a bDMARD. Patients treated with rituximab were excluded. Kaplan-Meier methods were applied and cox regression was used for multivariable analyses (adjusted for sex, anti-CCP, RF, DAS28, bDMARD Type, CDAI, therapy with conventional DMARDs, number of previous bDMARDs). Missing data were imputed using multiple imputation.

**Results:** Between 1997 and 2017, 318 patients achieved a bDMARD-free remission (table1). Median observation time was 2.8 years (IQR 1.2–4.9). 241 patients lost remission (76%), 54% of those re-started a bDMARD. 34% experienced a DAS28 flare and 12% did both. The median time to loss of remission was 0.9 years (95% CI 0.7–1.0). 76% discontinued a TNFα-inhibitor, 6% stopped abatacept, 14% tocilizumab and 4% tofacitinib. Women lost remission faster than men (figure 1A; p=0.005); this was also seen in multivariable analysis (HR 1.4, p=0.03). Longer disease duration was associated with a faster loss of remission (figure 1B; p=0.03) also in multivariable analysis (HR[4–8 years] 1.6, p=0.03, HR [8–13 years] 1.6, p=0.01, HR[>13 years] 1.5, p=0.035 vs 0–4 years disease duration). Remission was lost faster by patients who discontinued tofacitinib compared to those who stopped a TNFα-inhibitor (HR 2.3, p=0.01) also after adjustment (HR 2.0, p=0.047). There was a trend for a faster loss of remission in patients with a higher disease activity as measured by the CDAI at baseline (figure 1C; p=0.7); this association was significant in multivariable analysis (HR[CDAI low disease activity] 1.6, p=0.03, HR[CDAI moderate/high disease activity] 2.5, p=0.003, both vs CDAI remission). Patients who received MTX/leflunomide during the observation period lost remission less rapidly (figure 1D; p=0.006) also in multivariable analysis (HR 0.8, p=0.046).

**Abstract THU0220 – Table 1.** Baseline demographic and disease characteristics of patients with bDMARD-free remission

Characteristics	% or median (IQR)
Male sex	26
Age	57 (46–66)
Disease duration in years	8 (4–13)
Number of previous bDMARDs	0 1–2 ≥3
cDMARD any time during Remission	68 27 5
Anti-CCP/RF positive	64/72
DAS28	2.0 (1.5–2.3)
HAQ	0.4 (0–1.0)
CDAI	Remission Low Activity Moderate-High Activity
	27 54 19



**Abstract THU0220 – Figure 1.** Kaplan-Meier for time in biologic-free remission according to sex (A), disease duration (B), CDAI (C), conventional DMARD therapy (D)

**Conclusions:** In a large real-life cohort of RA patients that achieved DAS28 remission and stopped therapy with bDMARD the majority lost remission within less than a year. Predictors for loss of remission included female sex, longer disease duration, a higher CDAI score and absence of cDMARD therapy. This

suggests that discontinuation of bDMARD should be considered in patients on cDMARD therapy, fulfilling the more stringent remission criteria by CDAI.

**Disclosure of Interest:** None declared

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THU0221

### CLINICAL OUTCOMES OF ABATACEPT VERSUS TNF INHIBITORS IN ACPA-POSITIVE PATIENTS WITH RHEUMATOID ARTHRITIS: DATA FROM THE BIOLOGIC REGISTER KOBIO

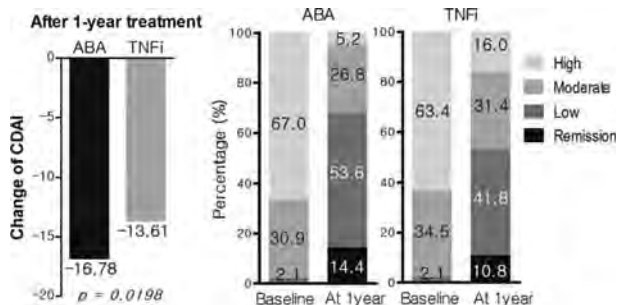
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**Background:** Determining the optimal, patient-tailored biologic agent is a new challenge for future guidelines in rheumatoid arthritis (RA) management. Recent studies demonstrated that anti-citrullinated protein antibody (ACPA) -positive patients have better disease activity improvement with abatacept (ABA), yet validation studies are in need.

**Objectives:** To investigate disease activity changes after treatment with ABA versus TNF inhibitors (TNFi) in Korean ACPA-positive, RA patients.

**Methods:** Data of RA patients were obtained from the Korean College of Rheumatology Biologics Registry (KOBIO). ACPA-positive patients who were treated with ABA and TNFi were selected through propensity score matching (1:2, calliper=0.2\*SD). Clinical outcomes including CDAI changes at the first year of therapy were evaluated, and adjusted drug survival in each group was analysed.

**Results:** The baseline characteristics of the ABA (n=97) and TNFi (n=194) groups were comparable. The CDAI reduction after 1 year treatment was significant in the ABA group compared with patients who received TNFi (-13.61 versus -13.61, p=0.0198) [figure 1]. This was confined when used as the first-line agent (p=0.0213). Proportion of remission and low disease activity in ABA was significant as well (p=0.041). Patients with the lower tertile of ACPA titers treated with ABA had the most significant CDAI reduction compared with the TNFi group (p=0.0201). Drug retention rate (median follow-up 48 months) of ACPA-positive ABA users was also notable compared with TNFi yet did not meet statistical significance (adjusted hazard ratio 0.774, p=0.086).



**Conclusions:** Our data further support that ACPA could also be an important marker to help determine first-line biologic agent of choice among the armamentarium of biologic therapy for RA patients.

**Acknowledgements:** We would like to thank Song Wha Chae and Evo Alemao for their input and support.

**Disclosure of Interest:** None declared

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THU0222

### MULTISWITCHING – FROM REFERENCE PRODUCT ETANERCEPT TO BIOSIMILAR AND BACK AGAIN – REAL-WORLD DATA FROM A CLINIC-WIDE MULTISWITCH EXPERIENCE

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**Background:** The etanercept (ETN) biosimilar SB4 was introduced in Sweden in 2016 at a lower price than the reference product etanercept (RPE). Now the reverse is true, as the price of RPE dropped. Switching ETN-treated patients to the lowest priced ETN available is economically favourable. The safety of multiple switches between RPE and biosimilar has been addressed in a psoriasis trial,<sup>1</sup> finding no indications of harm. No reports on outcomes of multiswitching in a rheumatology setting are available.

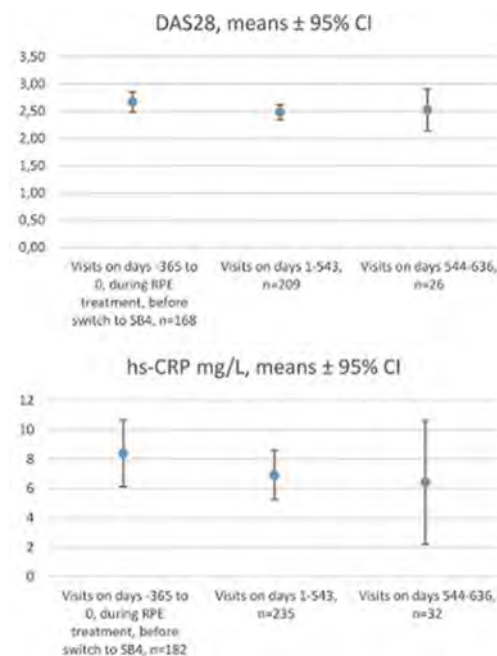
**Objectives:** To describe the impact of a clinic-wide switch from RPE to SB4 and then back to RPE on disease activity and drug-survival, relating outcomes to a historical cohort of RPE-treated patients.

**Methods:** Observational study of 145 patients switched from RPE to SB4 (day 0=20/4/2016) and back to RPE (day 544=16/10/2017) for economical reasons. Letters were mailed to patients on day 0 and 544, informing them that prescriptions had been changed from RPE to SB4 and from SB4 to RPE respectively. During days 1–543, clinicians were allowed to switch patients back to RPE if requested by the patient or if medically indicated. Disease activity data was entered into the Swedish Rheumatology Quality Register (SRQ) at visits. The SRQ was searched retrospectively for data from day –365 to 771 (May 31, 2018). Visits were categorised into visits occurring a) on days –365 to day 0, b) on days 1–543 and c) on days 544–771. A reference cohort of all RPE-treated patients on April 20, 2013 at the clinic was used for comparison.

**Results:** Numbers and proportions of patients discontinuing SB4 during days 1–543 in the switching cohort and RPE in the historical cohort are shown in the table 1. On day 544, the 97 patients still treated with SB4 were switched back to RPE. In the switching cohort, DAS28 and CRP did not change significantly when comparing data from visits occurring before the switch from RPE to SB4 to data from visits that occurred on days 1–543 and days 544–636 (figure 1). Data from 5 months of additional follow-up, up until day 771 will be presented at the congress. Among the 24 patients that discontinued SB4 during days 1–543 and went back to RPE, no worsening of disease activity parameters was seen during SB4 treatment.

	Switching cohort, n=145	Historical RPE-treated cohort, n=98	p
Discontinued SB4/RPE, total*	48 (33)	15 (15)	0.002
‡Back to RPE	24 (17)	Not applicable	N/A
‡No biologic	14 (10)	6 (6)	0.32
‡Non ETN biologic	10 (7)	9 (9)	0.52
On ETN (SB4 or RPE) at day 544	121 (83)	83 (85)	0.80

\*During days 1–543 ‡ Treatment after discontinuation of SB4/RPE



**Abstract THU0222 – Figure 1.** Mean DAS28 and CRP with 95% CI for 145 patients in the switching cohort according to timepoint of visit...n.s refer to number of visits contributing to data during each period.

**Conclusions:** The strategy of multiswitching ETN-treated patients has thus far not impacted disease activity negatively in our population. An additional 5 months of follow-up data after the second switch will be presented at the congress. A high proportion of patients discontinued SB4 after the initial switch, as no worsening in disease activity measures was seen in the data we believe this to have been due to nocebo effects.

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Disclosure of Interest: None declared

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**THU0223 IMPACT OF TREATMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS AND DEPRESSIVE SYMPTOMS IN THE MONARCH PHASE 3 TRIAL OF SARILUMAB**

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**Background:** In the MONARCH Phase 3 randomised controlled trial (RCT) [NCT02332590], sarilumab subcutaneous (SC) 200 mg every 2 weeks (q2w) improved clinical outcomes and multiple aspects of health status/health-related quality of life (HRQoL), as measured by the Medical Outcomes Survey Short Form (SF-36) questionnaire, to levels greater than adalimumab SC 40 mg q2w. Both treatments were administered as monotherapy in patients with active rheumatoid arthritis (RA) who had discontinued treatment with methotrexate. Depression/mood disorder is a common co-morbidity in people with RA.

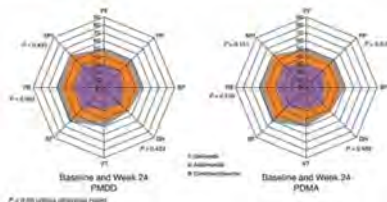
**Objectives:** To explore whether observed differences in health status/HRQoL following treatment with sarilumab compared with adalimumab are also seen in the subgroup of patients in the MONARCH trial with probable depressive symptoms.

**Methods :** Post-hoc statistical analyses were performed. Patients were categorised as having probable major depressive disorder<sup>1</sup> (PMDD; SF-36 mental health (MH) domain score ≤56) or probable depressed mood and anhedonia<sup>2</sup> (PDMA; score ≤10 on both items of the MH domain: "Have You Felt Downhearted and Depressed" and "Have You Felt So down in the Dumps that nothing could cheer you up"). Least squares mean (LSM) differences in changes from baseline (CFB) in SF-36 domains at Week 24 were calculated for sarilumab PMDD/PDMA versus adalimumab PMDD/PDMA. Sensitivity analysis included adjustment for Disease Activity Score 28 C-reactive protein (DAS28-CRP) at baseline.

**Results:** Of the 369 patients from MONARCH, 250 (67.78%) were categorised with PMDD (mean age 52 years, 85% female) and 194 (52.6%) with PDMA (mean age 52 years, 87% female). Disease duration, DAS-28 CRP, tender and swollen joint counts (table 1) and SF-36 domain scores (figure 1) were similar between sarilumab and adalimumab within the PMDD and PDMA subpopulations at baseline. LSM differences in CFB in SF-36 domains were greater for sarilumab versus adalimumab at Week 24 in physical functioning (PF), bodily pain (BP), vitality (VT) and social functioning (SF) domains in both the PMDD and PDMA subgroups, and role-physical (RP) in the PMDD subgroup (nominal p<0.05) (figure 1). Sensitivity analysis showed similar results.

Abstract THU0223 – Table 1

Table Baseline characteristics in MONARCH patients with PMDD or PDMA	PMDD: SF-36 MH domain score ≤56 (N=250)		PDMA: ≤10 on both items of SF-36 MH domain (N=194)	
	Sarilumab 200mg q2w (n=128)	Adalimumab 40mg q2w (n=122)	Sarilumab 200mg q2w (n=98)	Adalimumab 40mg q2w (n=96)
Duration of RA since diagnosis, (years, mean (SD))	8.29 (8.13)	7.01 (8.51)	7.92 (7.50)	7.46 (8.47)
SAS28 CRP, mean (SD)	6.13 (0.85)	6.18 (0.88)	6.17 (0.96)	6.18 (0.83)
Tender joint count (0-68), mean (SD)	29.03 (14.05)	28.36 (14.71)	28.99 (14.34)	28.69 (14.46)
Swollen joint count (0-66), mean (SD)	19.20 (11.87)	19.89 (10.74)	19.68 (11.78)	19.53 (11.09)



**Conclusions:** Among patients with RA and probable depressive symptoms, sarilumab SC 200 mg q2w monotherapy was more effective than adalimumab SC 40 mg q2w monotherapy in demonstrating clinically meaningful improvements in some domains of health status/HRQoL. This may be a function of the different

target of sarilumab (soluble IL-6 receptor [sIL-6R]) and associated improvements in disease activity versus adalimumab (tumour necrosis factor [TNFα]).

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**Disclosure of Interest:** V. Strand Consultant for: AbbVie, Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, Celltrion, Corrona, Crescendo Bioscience, Eli Lilly, Genentech/Roche, GlaxoSmithKline, Horizon, Janssen, Merck, Novartis, Pfizer, Regeneron Pharmaceuticals, Samsung, Sandoz, Sanofi and UCB, O. Hagino Shareholder of: Sanofi, Employee of: Sanofi, S. Guillonnet Shareholder of: Sanofi, Employee of: Sanofi, S. Boklage Shareholder of: Regeneron Pharmaceuticals, Inc., Employee of: Regeneron Pharmaceuticals, Inc., M. Reaney Shareholder of: Sanofi, Employee of: Sanofi, J. Sadeh Shareholder of: Sanofi, Employee of: Sanofi, N. Narcisse Consultant for: Sanofi, E. Mangan Shareholder of: Regeneron Pharmaceuticals, Inc., Employee of: Regeneron Pharmaceuticals, Inc., T. Kimura Shareholder of: Regeneron Pharmaceuticals, Inc., Employee of: Regeneron Pharmaceuticals, Inc.

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**THU0224 RENACER STUDY: EFFICACY AND SAFETY ASSESSMENT OF CZP THERAPY IN THE TREATMENT OF 501 PATIENTS WITH RHEUMATOID ARTHRITIS(RA) AMONG SPANISH POPULATION IN CLINICAL PRACTICE**

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**Background:** Certolizumab PEGol (CZP) differs from other anti-TNFs in that it is monovalent and it lacks the Fc region found in monoclonal antibodies. CZP is also PEGylated. Its efficacy in patients with rheumatoid arthritis (RA) has been evaluated in previous clinical trials.

**Objectives:** The purpose of the current study is to assess effectiveness, safety and survival rate in patients with RA after 12 months of treatment and also within specific subgroups, in clinical practice settings.

**Methods:** Observational longitudinal prospective study of RA patients from 40 sites in Spain. Variables (baseline, 3- and 12 month assessment): socio-demographics, smoking status, previous synthetic DMARD (sDMARD) and biological DMARD (bDMARD) use; TJC, SJC, ESR, CRP, DAS28. Response variables EULAR Moderate/Good Response and DAS28 remission and Safety were assessed. Descriptive, comparative and Logistic regression analyses were performed. Kaplan-Meier survival curve was performed.

**Results:** A total of 501 patients were included: 78.6% women, mean age 53.6 year (±13.2 SD) and 77% were aged <65 year Mean disease duration 7.5 year (±7.3 SD) and 27.7% having early RA. Baseline features are shown in table 1. Mean number of prior sDMARD 1.5 (±1.1 SD). Mean number of prior bDMARD was 0.8 (±1.2 SD). Mean duration of exposure to CZP was 9.8 months (±3.4 SD); Concomitant steroids intake 12.6%, sDMARD 24.2% and sDMARD plus steroids 54.9%; Smoking status: 69.8% never smoked, 12.9% former smoker and 17.3% current smoker.

Baseline predictors of response: lower prior number sDMARD; low number prior bDMARD; higher CRP, ESR, TJC, SJC and DAS28 (p<0.05) scores.

Patients<65 year had shown better DAS28 Remission rates as well as those who had previously received <2 sDMARDs, those who were "bionaive" at CZP initiation and those who used CZP in combination.

CZP survival rates are shown in *Figures 1 and 2*.

Adverse effects from treatment were reported in 65 patients (13%), mostly mild.

**Conclusions:** CZP showed benefit in active RA patients, with clear improvement in all clinical parameters, mostly in <65 yo patients and those who had received low number of previous sDMARD and bDMARD. Survival rate at 12 month assessment was high, demonstrating a reasonable safety profile.

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**Disclosure of Interest:** None declared  
**DOI:** 10.1136/annrheumdis-2018-eular.1186

**THU0225 THE PROGRESSION OF LUNG INVOLVEMENT IN RHEUMATOID ARTHRITIS PATIENTS RECEIVING BIOLOGICAL THERAPIES**

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**Background:** Lung involvement is one of the extra-articular manifestations that is shown to be related to morbidity and mortality in Rheumatoid arthritis (RA).

**Objectives:** We evaluated the progression of lung involvement in RA patients receiving biological treatment.

**Methods:** Eighty RA patients fulfilling ACR/EULAR classification criteria (2010) receiving biologics who had high-resolution computerised tomography (HRCT) of chest within 6 months of respiratory symptoms (cough/dyspnea) and/or any pathology in chest radiography were included. Warrick score, evaluating alveolitis and fibrosis, was calculated in RA patients by using HRCT of chest.

**Results:** The demographics and clinical findings were summarised in table 1. In 29 RA patients with interstitial findings in HRCT of chest; 7 (24%) were regressed and 1 (4%) was progressed with biologic drugs. Findings of alveolitis and fibrosis were completely regressed in 2, only alveolitis component was completely regressed in 3 and partially in 2 patients. The patient who progressed had new findings of alveolitis (table 2). Twenty-one patients in whom Warrick scores did not change, 5 received rituximab (RTX) and 10 received TNF inhibitors (TNF-inh). The mean Warrick scores was improved after biologics (11,3±9 (3–30) vs 10,3±9 (0–30), p=0,035). The improvement in alveolitis scores was significant (2,1 ±1,6 vs 1,5±1,6, p=0,031) while fibrosis scores were not (9,2±7,7 vs 8,8±8). Initial and control Warrick scores were higher in RTX receivers (16±9 vs 9,2±8, p=0034 and 14,8±10,1 vs 8,4±8,1), but the improvement after biologics was not different.

**Abstract THU0225 – Table 1.** Demographics in Rheumatoid Arthritis Patients

	n=80
Age(year)	53±12
Gender(F/M)	61/19
Disease duration(year)	12±9
Smoking(%)	26%
RF(+)	64 (80%)
AntiCCP(+)	50 (63%)
DAS28-ESR-after biologics	3,3 ±1,1

Scores	Initial Warrick-Alveolitis	Initial Warrick-Fibrosis	Initial Warrick-Total	Control Warrick-Alveolitis	Control Warrick-Fibrosis	Control Warrick-Total	Current Therapy
Case 1	3	8	11	0	0	0	RTX+MTX.seropositive
Case 2	3	5	8	0	0	0	TNFi+MTX.seropositive
Case 3	3	8	11	2	8	10	RTX.seropositive
Case 4	4	17	21	3	17	20	RTX.seropositive
Case 5	3	0	3	0	0	0	TNFi+MTX.seropositive
Case 6	3	0	3	0	0	0	TNFi+MTX.seronegative
Case 7	3	4	7	0	4	4	TNFi+MTX.seronegative
Case 8	0	3	3	2	3	5	RTX+MTX.seropositive

**Abstract THU0225 – Table 2.** Progression of Warrick Scores in Cases After Biologics

**Conclusions:** This study revealed an improvement in alveolitis after biologic drugs in RA patients. Fibrosis was not found to be effected by therapy. Lung lesions were improved in both RTX and TNF-inh groups.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.5823

**THU0226 SERIAL INTERFERON-GAMMA RELEASE ASSAYS IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH BIOLOGIC AGENTS**

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**Background:** It is increasing attention about the risk of latent tuberculosis infection (LTBI) reactivation during the treatment of biologic agents for patients with rheumatoid arthritis. Taiwan rheumatology association recommend performing at least annual interferon-gamma release assays (IGARs) testing during biologic treatment course because of the moderate prevalence of tuberculosis in Taiwan. [1] Although several studies have reported the risk of active tuberculosis infection in patients with rheumatoid arthritis (RA), the long-term serial IGARs testing in patients with RA is limited.

**Objectives:** The aims of this study is to use serial interferon-gamma release assays(IGRAs) as a screening tool in patients with rheumatoid arthritis treated with different biologic agents in Taiwan.

**Methods:** We retrospectively collected 189 patients with rheumatoid arthritis receiving biologic agents between 2013 to 2017 in Chang Gung Memorial hospital in Taiwan. All RA patients underwent semi-annual IGRA test during biologic agents treatment.

**Results:** The seroconversion rate of IGAR in patients with rheumatoid arthritis after biologic treatment is 6.9%. The median seroconversion period is 19 months. Out of the 13 patients with seroconversion, 8 (61.5%) patients were treated with TNF block and 5 (38.5%) patients were treated with non-TNF blocker. All the patients with seroconversion evaluate the possible active TB infection and 69.2% (9/13) received chemoprophylactic therapy by isoniazid. There is no active tuberculosis infection during serial IGAR tests. The risk factor included high baseline TBAg-nil/nil (OR 3.44, CI 6.64–1.78), leflunomide(OR 11.51, CI 61.34–2.16).

**Abstract THU0226 – Table 1**

	Total (n=189)	Seroconversion (n=13)	Non-seroconversion (n=176)	p-value
Female	162(14.3%)	10(76.9%)	152(86.4%)	0.348
Age (Mean± standard deviation)	54.7±12.2	60.0±13.6	54.3±12.1	0.104
Disease duration (Mean± standard deviation)	4.9±1.4	4.6±1.4	4.9±1.4	0.591
Prednisolone Mean dose (mg/day)	132/189(69.8%)	9/13(69.2%)	123/176(69.88%)	0.873
	8.8±9.5	8.3±3.5	8.8±9.8	
Methotrexate	146(77.2%)	9(69.2%)	137(77.8%)	0.475
Sulfasalazine	99(52.4%)	9(69.2%)	90(51.1%)	0.207
Leflunomide	24(12.7%)	5(38.5%)	19(10.8%)	0.015*
Hydroxychloroquine	104(55%)	11(84.6%)	93(52.8%)	0.026*
TNF blocker	143(75.7%)	8(61.5%)	135(76.7%)	0.219
Non-TNF blocker	46(24.3%)	5(38.5%)	41(23.3%)	0.219
TB Ag-nil	0.02±0.12	0.14±0.12	0.01±0.12	<0.001*
Mitogen-nil	6.66±5.2	8.16±4.84	6.52±5.23	0.278
DAS28	6.06±1.09	6.42±0.91	6.03±1.1	0.261
Characteristics	OR(95%CI)		p value	
Age	1.02 (1.09, 0.95)		0.474	
Disease duration	1.31 (2.36, 0.72)		0.366	
TB Ag-nil/nil	3.44 (6.64, 1.78)		<0.001*	
Leflunomide	11.51 (61.34, 2.16)		0.004*	
Hydroxychloroquine	6.49 (43.88, 0.96)		0.055	

**Conclusions:** Our study revealed patients with rheumatoid arthritis receiving long-term biologic therapy had a low rate IGAR seroconversion rate (6.9%). Patients with background Leflunomide had higher odds ratio of seroconversion. However, the clinical importance of IGAR seroconversion remain controversial and further long-term large scale investigation is needed.

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**Disclosure of Interest:** None declared

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THURSDAY, 14 JUNE 2018

## Spondyloarthritis – clinical aspects (other than treatment)

### THU0227 SPINAL FRACTURE RISK IN ANKYLOSING SPONDYLITIS IN WESTERN AUSTRALIA

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**Background:** In Ankylosing Spondylitis (AS) chronic spinal inflammation contributes to spinal osteoporosis and rigidity. Large scale studies on vertebral fractures in AS patients are scarce with rates reported between 0.4% and 32%<sup>1-3</sup>. While biological therapy for AS has been associated with better clinical outcomes, the long-term effect on spinal osteoporosis remains uncertain.

**Objectives:** To longitudinally investigate population wide spinal fracture rates in AS patients and compare the risk, disease burden and survival rates between AS and age/gender matched controls.

**Methods:** A case-control study sourced from linked health data on Emergency Department visits, Hospital Morbidity and Mortality Registry data for the period 1980–2015. Vertebral fractures prevalence (ICD-9: 733.13, 805X and 806X, ICD-10: M48.4X, M48.5X, M80.0X, S12.X, S22.X, S32.X), burden of disease and mortality were compared between AS patients (ICD-9: 720.0, ICD-10: M45X or M08.1) with up to 5 controls matched for age, gender, Indigenous status and event date.

**Results:** We included 1285 AS patients (70% males) with mean age of 42.87 ± 18.4 years at first event, followed for a median of 24 years.<sup>19, 30</sup> Spinal fractures were more frequent in AS patients than controls (52, 2.8% vs. 39, 0.6%,  $p < 0.0001$ , respectively), and among the AS patients, 27 (2%) had a single and 9 (0.7%) had multiple fractures. Thoracic fractures were most common (17, 33%), followed by cervical (10, 19%), lumbar (9, 17%), sacral and coccyx (4, 8%) and one unspecified vertebral fracture.

Overall AS participants were at greater risk (OR: 4.78; 2.9, 7.7 CI) for spinal fractures than controls. The risk remained relatively consistent; ranging from OR: 4.72 (2.75, 8.08 CI) during 1980–89 to OR: 4.90 (1.68, 14.25 CI) throughout 1990–99. However, during 2000–2013, all 4 newly AS diagnosed patients experienced a total of 7 fractures compared to none in controls. Greater age at first hospital contact among AS patients increased the risk in having a vertebral fracture (OR: 1.035; 1.01, 1.05 CI), while presence of psoriasis and inflammatory bowel disease were not risk factors.

Survival rates following vertebral fractures at end of follow-up (35 years) were significantly lower for AS patients, (92%, vs. 98.5%,  $p < 0.0001$ ) compared to controls.

**Conclusions:** The absolute risk for spinal fractures in AS patients is 2.8%, which is nearly 5 times the risk in controls. The risk has not improved in the era of TNFi therapy and the associated increased mortality indicates that spinal fractures remain a severe complication of AS.

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### THU0229 ABSOLUTE REGULATORY OF PERIPHERAL CD4+CD25+FOXP3+T REGULATORY CELLS IN PATIENTS WITH SPONDYLOARTHROPATHY-RELATED OCULOPTHY

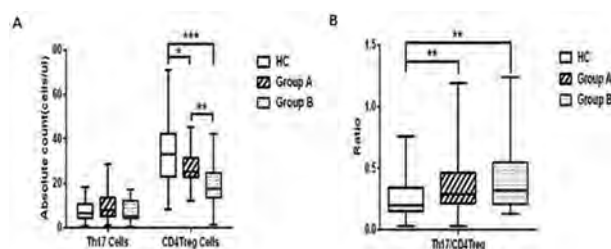
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**Background:** Spondyloarthritis is a group of systemic chronic autoimmune diseases, which is characterised by the spine, peripheral joint, joint tissue inflammation and high morbidity. And ocular inflammatory disorders are the most common and important extra-articular manifestations with unclear pathogenesis. The imbalance of T help 17 cells (Th17)/regulatory T cells is considered to be a pivotal cause of autoimmune diseases, their roles in spondyloarthritis, especially the related oculoopathy, are rare studied.

**Objectives:** To explore the status of both absolute number and percentage of CD4 +CD25+Foxp3+T regulatory (CD4Treg) cells and Th17 cells in peripheral blood (PB) of patients with spondyloarthritis-related oculoopathy.

**Methods:** Ninety six patients were enrolled, including fifty spondyloarthritis without related oculoopathy (Group A), mean age of 43.23±11.49 years, and forty six spondyloarthritis-related oculoopathy (Group B), mean age of 43.50±13.51 years. BD Trucount tubes with the lyophilized pellet of a known number of internal counting beads were used for determining absolute counts of total CD4 +T cells in PB and then calculating the absolute number of Th17 cells and CD4Treg. Ninety three healthy volunteers, matched for patients' age and gender, were also included for the estimation of CD4 +T cell subsets.

**Results:** As compared to healthy controls (median of CD4Treg cells: 33.06 cells/ul), the frequencies of circulating CD4Treg cells were significantly decreased in both spondyloarthritis without related oculoopathy (median: 25.07 cells/ul,  $p < 0.05$ ) and spondyloarthritis-related oculoopathy (median: 17.65 cells/ul,  $p < 0.001$ ). The median ratios of Th17/CD4Treg cells in each group of patients were greatly higher than those of healthy volunteers [Group A: 0.29 (0.22, 0.47) vs. 0.21 (0.15, 0.34),  $p < 0.01$ ; Group B: 0.32 (0.21, 0.55) vs. 0.21 (0.15, 0.34),  $p < 0.01$ ]. Nevertheless, there were not significantly different in circulating Th17 cell changes among the three groups. Moreover, there was more absolute reduction of peripheral CD4Treg cells in Group B than Group A ( $p = 0.006$ ), while greater increase in the ratio of Th17/CD4Treg despite no statistical significance ( $p > 0.05$ ).



**Abstract THU0229 – Figure 1.** The numbers of different CD4+ T cells were compared between various groups and healthy controls. (A) The absolute counts of CD4Treg and Th17 cells were compared among various groups; (B) The ratios of Th17/CD4Treg cells were compared among various groups. HC: Healthy Controls, Group A: Spondyloarthritis Without Related Oculoopathy, Group B: Spondyloarthritis-related Oculoopathy. \*  $P < 0.05$ , \*\*  $P < 0.01$ , \*\*\*  $P < 0.001$ .

**Conclusions:** The reduction of CD4Treg but not the elevation of Th17 cells may be the major reason for imbalance of Th17/CD4Treg. It is speculated that spondyloarthritis-related oculoopathy is an autoimmune disease triggered by the defect of immunotolerance. More importantly, the recovery of CD4Treg may be a potential target treatment for patients with spondyloarthritis-related oculoopathy.

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THU0230

**PERFORMANCE OF AN ONLINE SELF-REFERRAL QUESTIONNAIRE COMPARED TO A PHYSICIAN-BASED REFERRAL APPROACH TO IDENTIFY PATIENTS WITH A HIGH PROBABILITY OF AXIAL SPONDYLOARTHRITIS: RESULTS FROM THE OPTIREF STUDY**

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**Background:** The diagnostic delay in axial spondyloarthritis (axSpA) has been reported to be 9 years and still remains unacceptably high. One of the major reasons for this delay is a late referral of patients with suspicion of axSpA by primary care (PC) physicians dealing with patients with chronic back pain (CBP). Physician-based referral programs have performed well in recognition of patients with high probability of axSpA among CBP patients. However, there is still an unmet need for patients who do not receive a referral to a rheumatologist because of lack of awareness on PC level.

**Objectives:** To develop and evaluate an online self-referral tool for CBP patients and suspicion of axSpA.

**Methods:** Patients with CBP were included in the Identification of the Optimal Referral Strategy for Early Diagnosis of Axial Spondyloarthritis (OptiRef) Study and assessed by a rheumatologist if they either 1) were referred by a physician using the Berlin referral tool (CBP >3 months and CBP onset <45 years of age +at least 1 of the following 3 parameters: inflammatory back pain (IBP), HLA-B27 positivity, sacroiliitis on imaging), or 2) completed an online referral tool (www.bechterew-check.de) and indicated the presence of CBP >3 months with CBP onset <45 years of age +at least 1 additional SpA parameter (IBPsymptoms, good response to NSAID's, peripheral symptoms suggestive of arthritis/enthesitis, HLA-B27 positivity, elevated CRP, psoriasis, inflammatory bowel disease, uveitis, familyhistory). Rheumatologist then performed a structured assessment of SpA features and made the diagnosis of axSpA/non-axSpA.

**Results:** A total of 339 patients were included in the study: 162 patients (47.8%) were referred by a physician and 177 (52.2%) entered the study via the online self-referral tool. A total of 60 patients (37%) in the physician-referral group and 33 (18.6%) in the self-referral group were finally diagnosed with axSpA (p<0.001). The main patient characteristics are shown in table 1. Patients who were included via the online referral tool had a longer symptom duration, were more often females, less often HLA-B27 positive and had less often elevated CRP as compared to physician-referred patients. Furthermore, the physician global assessment of disease activity done by a rheumatologist was significantly lower in the self-referred group. In patients diagnosed with axSpA there were no significant differences concerning demographics, clinical features or disease activity parameters between the two groups, except of HLA-B27, which was significantly more often positive in subjects referred by a physician (p<0.001).

**Abstract THU0230 – Table 1.** Characteristics of patients with CBP and suspicion of axSpA referred by a physician or by a self-referral online tool.

Characteristics	Referral by a physician N=162	Self-referral N=177	p-value*
Diagnosis of axSpA, n (%)	60 (37.0%)	33 (18.6%)	<0.001
Age, years (mean±SD)	37.3 ± 11.8	36.6 ± 9.2	0.99
Female sex, n (%)	71 (43.8%)	101 (57.1%)	0.02
Back pain duration, (mean±SD)	6.2 ± 6.6	9.3 ± 8.0	<0.001
HLA-B27 positivity, n (%)	90 (55.6%)	36 (20.3%)	<0.001
Elevated CRP (>5 mg/l), n (%)	28 (17.3%)	16 (9.2%)	0.02
Good response to NSAIDs, n (%)	85 (52.5%)	85 (48%)	0.45
Peripheral arthritis, current, n (%)	5 (3.1%)	4 (2.3%)	0.74
Enthesitis, current, n (%)	12 (7.4%)	13 (7.3%)	1.00
Psoriasis, ever, n (%)	13 (8%)	21 (11.9%)	0.28
Inflammatory bowel disease, ever, n (%)	2 (1.2%)	4 (2.3%)	0.69
Uveitis, ever, n (%)	14 (8.6%)	9 (5.1%)	0.20
Family history of SpA, n (%)	19 (11.7%)	21 (11.9%)	1.00
BASDAI, 0-10 (mean±SD)	4.2 ± 2.0	4.2 ± 1.8	0.90
BASFI, 0-10 (mean±SD)	2.5 ± 2.2	2.4 ± 1.8	0.87
Patient global (0-10), mean±SD	5.3 ± 2.7	4.8 ± 2.5	0.07
Physician global (0-10), mean±SD	3.9 ± 2.3	2.5 ± 2.2	<0.001

\*Mann-Whitney U-test or Fisher's exact test, whatever appropriate.

axSpA=axial spondyloarthritis; BASDAI=the Bath Ankylosing Spondylitis Disease Activity Index; BASFI=the Bath Ankylosing Spondylitis Functional Index; CBP=chronic back pain; CRP=C-reactive protein; SD=standard deviation.

**Conclusions:** The self-referral strategy resulted in the diagnosis of axSpA in 19% of the patients as compared to 37% with a referral done by a physician. However, the proportion of axSpA among self-referred patients was clearly higher than the expected 5% prevalence of axSpA in patients with CBP. The online self-referral tool can be used, therefore, in addition to a physician based referral program to improve the early diagnosis and to increase awareness of axSpA.

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THU0231

**DO DEGREE OF FAMILY RELATIONSHIP AND ETHNICITY IMPACT THE ASSOCIATION BETWEEN A POSITIVE FAMILY HISTORY FOR SPONDYLOARTHRITIS AND PRESENCE OF HLA-B27? RESULTS FROM THE WORLDWIDE ASAS COHORT**

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**Background:** The ASAS definition of a positive family history (PFH) of spondyloarthritis (SpA) consists of the following diseases in first (FDR)- or second-degree relatives (SDR): ankylosing spondylitis (AS), acute anterior uveitis (AAU), reactive arthritis (ReA), inflammatory bowel disease (IBD), and psoriasis. In two European cohorts (SPACE and DESIR) a PFH of AS and AAU, but not a PFH of ReA, IBD, and psoriasis, were associated with HLA-B27 carriership in patients suspected of axSpA<sup>1</sup>. However, it is unknown what the role of the degree of family relationship or ethnicity is.

**Objectives:** To investigate the impact of the degree of family relationship and ethnicity on the association between the current ASAS definition of a PFH and the presence of HLA-B27 in an international cohort of patients suspected of axSpA.

**Methods:** Baseline data from patients suspected of axSpA in the worldwide ASAS cohort were analysed. Univariable analyses were performed. Each disease (AS, AAU, psoriasis, IBD, ReA) in a PFH according to ASAS expert opinion was a determinant in separate models with HLA-B27 carriership as outcome. Analyses were stratified for FDR, SDR, and self-reported ethnicities (white, Asian, and other). Analyses were repeated in multivariable models.

**Results:** In total, 594 patients suspected of axSpA were analysed. Patients had a mean age (SD) of 33.7 (11.7) years, 46% were male, had a mean symptom duration of 7.1 (9.0) years, had 3.5 (2.2) SpA features including HLA-B27 and imaging, 52% were HLA-B27 positive, 20% had sacroiliitis according to the mNY criteria, and 32% had active inflammation on MRI-SI. Sixty-two percent of the patients were diagnosed as axSpA and of these diagnosed patients 83% fulfilled the ASAS axSpA criteria. A PFH was reported by 23% of the patients; a PFH of AS was the most (15%) and PFH of AAU (1%) the least often reported family history among all patients. Any PFH was associated with HLA-B27 carriership in patients with a PFH in FDR, whites, and Asians but not in SDR. A PFH of AS was positively associated with HLA-B27 carriership in all subgroups (table 1). A PFH of AAU, ReA, IBD, or psoriasis was never positively associated with HLA-B27 carriership. In the multivariate analysis, similar results were found.

**Abstract THU0231 – Table 1.** Univariable associations between each disease of a positive family history and HLA-B27 carriership in chronic back pain patients suspected of axSpA included in the ASAS cohort (n=594)

	HLA-B27+ n=310	HLA-B27- n=284	OR (95% CI)	p-value
<b>Any positive family history</b>				
<i>Stratified by degree of family relationship</i>				
First-degree relatives	79	31	2.9 (1.8-4.5)	<0.001
Only second-degree relatives	15	10	1.7 (0.7-3.8)	0.212
<i>Stratified by self-reported ethnicity</i>				
white	54	26	2.3 (1.4-3.9)	0.001
Asian	38	14	3.1 (1.6-5.8)	0.001
Other ethnicities*	2	1	2.3 (0.2-25.0)	0.509
<b>Family history of ankylosing spondylitis</b>				
<i>Stratified by degree of family relationship</i>				
First-degree relatives	61	9	7.8 (3.8-16.0)	<0.001
Only second-degree relatives	13	4	3.7 (1.2-11.6)	0.023
<i>Stratified by self-reported ethnicity</i>				
white	37	6	7.1 (2.9-17.1)	<0.001
Asian	35	7	5.7 (2.5-13.2)	<0.001
Other ethnicities*	2	0	n.a.	n.a.

Statistically significant results are printed in bold.

\* Self-reported ethnicity was missing for 5 patients, who are included in this category, and other ethnicities are black, East-Indian, Hispanic/Latino, mixed, or Turkish).

**Conclusions:** In the international ASAS cohort, a PFH of AS, but not of AAU, ReA, IBD, or psoriasis, was associated with HLA-B27 carriership in both first- and second-degree of family members and self-reported white and Asian ethnicity in patients suspected of axSpA. These data, in combination with data from two European cohorts, show that a PFH of AS and possibly also a PFH of AAU could be valuable in the general practice or other low SpA prevalence settings for identifying patients who are HLA-B27 positive and therefore have an increased risk of axSpA.



## REFERENCE:

[1] Ez-Zaitouni, et al. AR&T 2017;19(1):118.

**Disclosure of Interest:** None declared

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THU0232

### IS A POSITIVE FAMILY HISTORY OF SPONDYLOARTHRITIS RELEVANT FOR DIAGNOSING AXIAL SPONDYLOARTHRITIS ONCE HLA-B27 STATUS IS KNOWN? DATA FROM THE ASAS, DESIR AND SPACE COHORTS

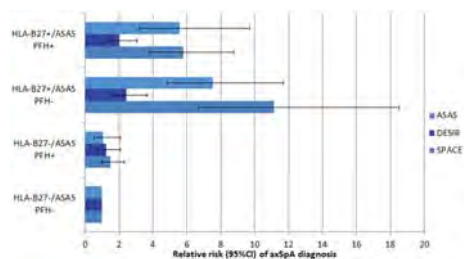
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**Background:** Knowledge of a positive family history (according to the ASAS definition (ASAS PFH)) for spondyloarthritis (SpA), in particular a PFH of ankylosing spondylitis (AS) or acute anterior uveitis (AAU), is considered valuable in making a diagnosis of axSpA but clusters with HLA-B27 positivity<sup>1</sup>. So a relevant clinical question is if a PFH is still important for making a diagnosis of axSpA if HLA-B27 status is known.

**Objectives:** To investigate in three independent axSpA cohorts if an ASAS PFH, a PFH of AS or a PFH of AAU contributes to a diagnosis of axSpA in patients with known HLA-B27 status.

**Methods:** Baseline data of patients suspected of axSpA in the ASAS, DESIR and SPACE cohorts were analysed. In each cohort, univariable logistic regression models were performed with HLA-B27 status and ASAS PFH as determinants and a clinical axSpA diagnosis as outcome. The analyses were repeated in multivariable models with both determinants. Relative risks for axSpA diagnosis were calculated stratified on both HLA-B27 status and ASAS PFH (HLA-B27-/ASAS PFH- as reference). Analyses were repeated with a PFH of AS and a PFH of AAU.

**Results:** In total, 1964 patients suspected of axSpA were analysed (ASAS n=594, DESIR n=647, SPACE n=723). ASAS, DESIR and SPACE patients had a mean (SD) symptom duration of 85.7 (108.4), 18.2 (10.5) and 13.3 (7.0) months; 54%, 47% and 38% were male; 52%, 58% and 44% were HLA-B27+; 44%, 40% and 35% had sacroiliitis on imaging (MRI and/or radiographs); 62%, 45% and 53% received a clinical diagnosis of axSpA; an ASAS PFH was reported in 23%, 39% and 43%, respectively. In the univariable analysis, HLA-B27 status was significantly associated with an axSpA diagnosis in all three cohorts; ASAS: OR 6.7 (95%CI 4.7–9.8), DESIR: OR 2.1 (95%CI 1.5–2.9), SPACE: OR 6.6 (95%CI 4.7–9.2). An ASAS PFH was univariately associated with an axSpA diagnosis in SPACE (OR 1.5 (95%CI 1.01–2.0)), but not in ASAS (OR 1.4 (95%CI 0.9–2.0)) and DESIR (OR 1.0 (95%CI 0.7–1.4)). In the multivariable models, HLA-B27 status was independently associated with a diagnosis of axSpA but such an independent association was not found for ASAS PFH in any cohort (ASAS: HLA-B27 OR 6.9 (95%CI 4.7–10.2), ASAS PFH OR 0.9 (95%CI 0.6–1.4); DESIR: HLA-B27 OR 2.1 (95%CI 1.5–2.9), ASAS PFH OR 1.0 (95%CI 0.7–1.3); SPACE: HLA-B27 OR 6.6 (95%CI 4.7–9.3), ASAS PFH OR 1.0 (95%CI 0.7–1.4)). In all cohorts, the relative risk of an axSpA diagnosis was highest in HLA-B27+/ASAS PFH- patients (**Abstract THU0232 – figure 1**). Similar results were found for a PFH of AS and AAU (data not shown).



**Abstract THU0232 – Figure 1.** Relative risks of axSpA diagnosis in patients suspected of axSpA stratified on HLA-B27 status and a positive family history according to the current ASAS definition (ASAS PFH) per cohort. HLA-B27-/ASAS PFH- is the reference category (RR=1).

**Conclusions:** A PFH does not contribute to the likelihood of an axSpA diagnosis in back pain patients with a known HLA-B27 status. This suggests that asking for a PFH of SpA in patients presenting with back pain is redundant if HLA-B27 status is known.

## REFERENCE:

[1] Ez-Zaitouni, et al. AR&T 2017;19(1):118.

**Disclosure of Interest:** None declared

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THU0233

### SICK LEAVE AND ITS PREDICTORS IN ANKYLOSING SPONDYLITIS: LONG-TERM RESULTS FROM THE OUTCOME IN ANKYLOSING SPONDYLITIS INTERNATIONAL STUDY

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**Background:** Sick leave (SL) among patients with ankylosing spondylitis (AS) is a relevant outcome for individuals and for society. Disease related factors, contextual factors, but also SL itself may be risk factors for future adverse work outcome. To reveal predictors of SL over time, longitudinal studies are necessary. If SL itself is an independent predictor for further SL, this further underpins initiatives in clinical care to support worker participation.

**Objectives:** To investigate the occurrence of AS-related SL over 12 years and to explore which factors predict or explain SL.

**Methods:** Data from employed patients from the Outcome in Ankylosing Spondylitis International Study were used. At each visit, patients indicated the occurrence of SL (yes/no) in the previous inter-assessment period. Cox regressions were used to predict the hazard for a first episode of SL using baseline predictors. Generalised estimating equations (GEE) were used to investigate the association between SL and (time-lagged) predictors. To investigate whether SL predicts future SL, SL in the first year was included as covariate in a separate GEE analysis. Due to collinearity between ASDAS, BASDAI and BASFI, separate multivariable models were computed.

**Results:** 139 patients (76% males, mean [SD] age 38.7 [10.0] years) were at risk for SL during a mean (SD) period of 7.9 (3.9) years. Among the 88 patients (63%) who ever reported SL, 62 (70%) reported SL at more than 1 assessment. In separate multivariable Cox baseline predictors models, baseline ASDAS (HR 1.67 [95%CI 1.23–2.28]), BASDAI (HR 1.33 [95%CI 1.18–1.51]) and BASFI (HR 1.17 [95%CI 1.02–1.34]) were associated with increased hazard of SL, but only in male patients with a low level of education. In separate multivariable time-varying GEE models, 1 year time-lagged ASDAS (OR 1.48 [95%CI 1.07–2.03]), BASDAI (OR 1.31 [95%CI 1.15–1.49]) and BASFI (OR 1.31 [95%CI 1.16–1.47]) were associated with SL, but only in patients with a low level of education. Further adjustment for job type did not lead to different results, and job type itself was not significantly associated with SL. SL during the first year predicted SL over time (OR: 2.62–8.37 in different models, all p<0.05), independently of educational level, disease activity or physical function.

**Conclusions:** Disease activity and physical function predict and explain variation in SL, but only in patients with a low level of education. Prior SL results in future SL, and SL should be considered an actionable factor for support to prevent future adverse work outcome. Research into which SL is beneficial with regard to recovery and which SL is a risk for work disability is needed.

**Disclosure of Interest:** None declared

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THU0234

### BMI DOES NOT AFFECT CLINICAL OUTCOME IN PSORIATIC ARTHRITIS PATIENTS TREATED WITH TIGHT CONTROL STRATEGY

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**Background:** Psoriatic arthritis (PsA) is characterised by several comorbidities; among these obesity and overweight have a major impact on patients' quality of

life and on disease treatment. Obesity increases the risk of developing psoriatic arthritis in the general population compared to normal-weight subjects. Obesity increases the risk of developing arthritis in patients with psoriasis, especially for HLA B27 negative and late onset forms.

**Objectives:** Aim of the study was to evaluate the incidence of overweight and obesity in a cohort of PsA patients, the differences between disease phenotypes and therapeutic response between patients with normal weight and overweight/obesity.

**Methods:** In this retrospective observational study 332 PsA patients, afferent to our unit between 2010 and 2017, were assessed. At each visit data on disease characteristics, BMI, ongoing treatment, joint count and clinimetric indexes were collected.

The baseline was defined as the onset of the disease in bio-naive patients or the start of the last bDMARD therapy for patients previously treated with cs or bDMARDs, while the last follow-up is considered the last visit at our unit

**Results:** The 332 patients had a mean age of 52.5±7.3 years;35% of the patients were normal weight, 39.5% were overweight and 25.5% obese. No differences were observed in terms of disease characteristics according to BMI category at baseline and during follow-up, with comparable percentages of peripheral arthritis, enthesitis, dactylitis, axial arthritis or uveitis, as well as cutaneous psoriasis among the groups.

At baseline, obese patients had more tender(4.4±5.2 vs 2.3±3.6 p=0.003)and swollen joints(mean value 2.3 vs 1 p=0.03)and higher activity indexes, as for DAS28(3.3±1.2 vs 2.7±1.2 p=0.002)and DAPSA(15.6±9.9 vs 11.5±9 p=0.004) compared to normal weight patients. The same difference was observed between normal-weight and overweight patients, with higher values of DAS28(3.04±1.4 vs 2.7±1.2,p=0.17)and DAPSA(13.6±11 vs 11.5±9, p=0.025)in overweight patients. No significant difference was observed in patients treated with NSAIDs, csDMARDs or bDMARDs according to BMI category.

In 190 patients followed according to the tight control strategy, with evaluations every 3 months, the disease activity indexes after two years of follow-up became similar in obese patients compared to normal weight patients.

Among the normal-weight patients, 69.4% took csDMARDs,48.7% were treated with bDMARDs. 74.7% of obese patients took csDMARDs, while 36.1% took bDMARDs, with no statistically significant differences between the two groups (p=ns).

In particular low-disease activity according to DAPSA was achieved in 76% of normal weight patients, compared with 68.9% of obese patients (p=ns), and also the percentage of patients reaching Minimal Disease Activity in the two groups was comparable (28.4% vs 22.7%, p=ns).

**Conclusions:** Clinical manifestations of psoriatic disease do not seem to differ according to BMI category;however, at the first evaluation, obese patients appear to have more disease activity than non-obese patients.

At the same treatment intensity, obese patients seem to achieve a percentage of remission comparable to normal weight patients, suggesting that the an intensive treatment strategy allows to obtain optimal results also in a more challenging group of patients.

**Disclosure of Interest:** None declared

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**THU0235 ANKYLOSING SPONDYLITIS AND RHEUMATOID ARTHRITIS HOSPITALISATION TRENDS IN THE US: DATA FROM NATIONAL INPATIENT SAMPLE**

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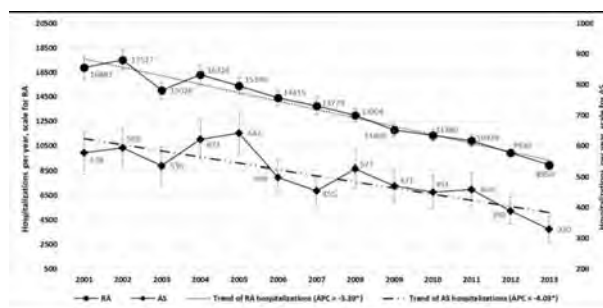
**Background:** Ankylosing spondylitis (AS) imposes significant morbidity and disability in the affected population. Hospitalisation trends provide an insight as to

burden of disease and long-term data is lacking. We evaluated AS related hospitalisation trends in the US from 2001–13, comparing it to the more common inflammatory arthritis- rheumatoid arthritis (RA).

**Objectives:** To evaluate AS related hospitalisation trends in the US in comparison to the more common inflammatory arthritis- RA

**Methods:** Using the Nationwide Inpatient Sample (NIS) data from 2009–2011, we identified patients ≥18 years with AS and RA at primary diagnosis positions based on ICD-9 codes 720.0 and 714.0, 714.2, 714.30–714.33 respectively. We also excluded patients with psoriatic arthritis and inflammatory bowel disease to improve the specificity of codes used. We used the trend weight (contained in the variable TRENDWT) supplied by HCUP to study the annual trends of hospitalizations in AS and RA (2001–13). We used Stata version 13.0 (College Station, TX) and Joinpoint regression analysis software to calculate yearly trends.

**Results:** NIS database from 2001–2013 contained 36 883 (weighted count, n=175,356) patients with RA and 1377 (weighted count- 6,554) patients with AS. A decreasing trend in AS and RA hospitalizations was noted with an annual percentage change (APC) of 5.35 and 4.28 respectively (p<0.05) (table 1 and figure 1).



**Conclusions:** While recent studies have shown a rise in incidence of AS, the hospitalisation rates have declined similar to RA. Our study findings may reflect increased recognition of inflammatory back pain in the primary care setting and prompt referral and diagnosis due to improved imaging techniques of the spine and pelvis. Furthermore, the use of biologics, such as TNF and IL-6 inhibitors have significantly improved outcomes.

**Disclosure of Interest:** None declared

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**THU0236 ANKYLOSING SPONDYLITIS RELATED FACTORS PREDICT THE PRESENCE OF CARDIAC CONDUCTION DISTURBANCES – A SWEDISH LONGITUDINAL COHORT STUDY**

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**Background:** Despite a well-known association between ankylosing spondylitis (AS) and cardiac conduction disturbances (from here CCD), it's not clear which factors that predict their presence.

Year	RA, n	RA, N	SE, N	RA, per 1,000,000	SE, per 1,000,000	AS, n	AS, N	SE, N	AS, per 1,000,000	SE, per 1,000,000
2001	3473	16 883	927	564	29	120	578	66	19	2
2002	3797	17 527	842	579	26	131	593	66	20	2
2003	3206	15 028	648	490	18	115	536	60	18	2
2004	3469	16 328	853	527	26	133	622	66	20	2
2005	3256	15 390	646	497	18	132	642	72	21	2
2006	3073	14 415	631	456	17	106	499	54	16	2
2007	2892	13 779	713	437	20	95	455	49	14	2
2008	2759	13 004	574	406	15	112	527	62	16	2
2009	2419	11 803	517	373	14	97	471	55	15	2
2010	2377	11 380	471	363	14	93	451	56	14	2
2011	2386	10 939	488	348	13	99	460	54	15	2
2012	1986	9930	223	323	7	78	390	44	13	1.4
2013	1790	8950	291	299	9	66	330	42	11	1.4
<b>TOTAL</b>	<b>36 883</b>	<b>1 75 356</b>		<b>5662</b>		<b>1377</b>	<b>6554</b>		<b>212</b>	
<b>APR</b>		<b>(-5.39)*</b>		<b>(-5.35)*</b>			<b>(-4.03)</b>		<b>(-4.28)*</b>	

**Objectives:** To describe electrocardiographic (ECG) alterations in a cohort of patients with AS and if AS related factors at baseline predict the presence of CCD at 5 year follow-up.

**Methods:** In total 210 patients diagnosed with AS at 3 rheumatology clinics from Western Sweden participated 2009 in an observational longitudinal cohort study with a planned follow-up after 5 years. At follow-up 2014 physical examination, ECG, questionnaires, laboratory tests and radiographic examinations were repeated in 172 patients (82%). CCD was defined in the presence of AV block I (PQ duration  $\geq 220$  ms), AV block Ix (PQ duration 200–219 ms), AV block II-III, right and left bundle branch block (RBBB and LBBB), left anterior and posterior fascicular block (LAFB and LPFB) and pacemaker. Descriptive statistics and logistic regression analyses were performed in order to find predictors at baseline for the presence of CCD at follow-up. Baseline characteristics with a p-value $<0.2$  in univariate analyses (dependent variable *present CCD* (yes=1, no=0)) were included as independent variables in a forward stepwise multiple logistic regression analysis.

**Results:** In total 23 of the 172 patients (13.4%) had CCD at 5 year follow-up. Eight had developed a new CCD out of which 2 had required pacemaker implantation, 3 had a more aggravated CCD, whereas 10 patient had an unchanged and 2 a less pronounced. CCD compared with 2009 CCD and some of the patient characteristics are presented in table 1. (None had LPFB or AV block II-III). According to multiple logistic regression analysis, male sex (Odds ratio (OR) (95% CI) 4.7 (1.1–20.6)), increasing age (OR 1.1 (1.0–1.1) per 1 year), a history of anterior uveitis (OR 6.4 (1.1–36.2)), higher ASDAS-CRP (OR 3.6 (1.6–7.9)) and existing CCD at baseline (OR 42.4 (8.9–202.2)) were predictors for the presence of CCD at follow-up.

Abstract THU0236 – Table 1

	Patients without CCD (n=149)	Patients with CCD (n=23)
<b>BASELINE CHARACTERISTICS 2009</b>		
Male sex	74 (49.7)	19 (82.6)
Age, years	48.5 $\pm$ 12.3	58.7 $\pm$ 11.4
Symptom duration, years	22.5 $\pm$ 12.3	33.5 $\pm$ 14.3
HLA-B27	127 (85.2)	22 (95.7)
ASDAS-CRP	2.0 $\pm$ 0.8	2.7 $\pm$ 1.0
History of anterior uveitis	69 (46.3)	19 (82.6)
Aortic regurgitation <sup>#</sup>	20 (13.4)	6 (26.1)
At least one syndesmophyte	63 (42.3)	17 (73.9)
<b>Reported comorbidity</b>	36 (24.2)	11 (47.8)
1. Hypertension	5 (3.4)	0 (0.0)
2. Diabetes	7 (4.7)	4 (17.4)
3. Hyperlipidemia		
<b>Medications</b>	6 (4.0)	8 (34.8)
1. Anticoagulation	22 (14.8)	11 (47.8)
2. Potential antihypertensive	7 (4.7)	3 (13.0)
3. Lipid modulators	55 (36.9)	5 (21.7)
4. DMARDs		
<b>CCD 2014</b>		10 (43.5)
1. AV block Ix		7 (30.4)
2. AV block I		3 (13.0)
3. LAFB		1 (4.3)
4. RBBB		2 (8.7)
5. LBBB		3 (13.0)
6. Pacemaker		

Data are expressed as mean  $\pm$ SD or number (%). <sup>#</sup> Missing data in 13 patients (10 without CCD and 3 with CCD) who did not underwent echocardiography at

baseline. DMARDs; disease-modifying anti-rheumatic drugs. ASDAS-CRP; ankylosing spondylitis disease activity score using C-reactive protein.

**Conclusions:** The presence of CCD in AS is dynamic. AS related factors, represented by baseline ASDAS-CRP and a history of anterior uveitis, predicted their presence at 5 year follow-up.

**Disclosure of Interest:** None declared

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### THU0237 INFLAMMATORY LESIONS OF THE SACROILIAC JOINTS, BUT NOT OF THE SPINE, ARE OF HIGH UTILITY FOR AXSPA RECOGNITION: RESULTS OF THE ILOS-DESIR STUDY

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**Objectives:** To evaluate the performance of MRI inflammatory lesions suggestive of axSpA for the axSpA recognition

**Methods:** Observational cross-sectional national multicentre study. **Patients:** a) Recent onset axSpA patients: first, a sample of 100 patients representative in terms of imaging abnormalities of the global DESIR recent onset axSpA cohort were selected. b) Recent onset CBP patients: consecutive in- and outpatients consulting for recent (>3 months but <5 years) mechanical CBP, initiating before the age of 45 y and with a maximum age of 50 y, in four tertiary care Hospitals were included in the study. **Imaging:** MRI scans (T2-STIR and T1 sequences) of the SIJ and full spine were performed in both groups with identical protocol. **Central reading:** an experienced reader (AM) centrally read all MRI scans, blinded for clinical diagnosis. **Statistical analysis:** Sensitivity, specificity and positive likelihood ratio of each lesion were calculated.

**Results:** A total of 98 patients with recent onset CBP were included, and compared to 100 recent onset axSpA patients. Age and gender were comparable (mean (SD) 36.2 (9.9) vs. 32.2 (8.7)y, and 41.8% and 45% males, in the CBP vs. axSpA groups, respectively). MRI inflammatory lesions of the SIJ were quite frequent in the CBP group (25% patients with at least one inflammatory lesion) but were significantly more frequently observed in the axSpA group (table 1), with a mean SIJ - SPARCC score of 4.9 (8.8) vs. 0.6 (1.3), p<0.001. The ASAS definition of MRI sacroiliitis presented a high specificity and a good positive likelihood ratio. Conversely, prevalence of inflammatory lesions of the spine was very frequent in the CBP group and not significantly lower compared to the axSpA group (SPARCC spine 5.6 (13.5) vs. 3.3 (5.8), NS, in the axSpA vs. CBP groups, respectively). Regardless the definition of a positive MRI for the spine applied, performances were not good

**Conclusions:** ASAS definition of a positive MRI-sacroiliitis performed very well for axSpA recognition; however, definitions proposed for a positive MRI-spine suggestive of axSpA did not seem to perform adequately in this recent disease stage. This supports the idea of not including a positive MRI of the spine in the ASAS classification criteria.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.4142

		CBP n=98	SpA n=100	p	Se	SpE	LR+
SIJ-MRI	At least one inflammatory lesion of the SIJ	24 (25.3%) n=95	40 (40.0%)	0.028	0.4 (0.3– 0.5)	0.8 (0.7– 0.8)	1.6 (1.0– 2.4)
	ASAS definition of positive MRI sacroiliitis	8 (8.4%) n=95	35 (35.0%)	<0.001	0.4 (0.3– 0.5)	0.9 (0.8– 0.9)	4.2 (2.0– 8.5)
Spine-MRI	At least one inflammatory lesions of the spine	44 (44.9%)	52 (52.5%)	NS	0.5 (0.4– 0.6)	0.6 (0.5– 0.7)	1.2 (0.9– 1.6)
	ASAS definition of positive MRI spine ( <sup>3</sup> inflammatory lesions)	33 (33.7%)	44 (44.4%) n=99	NS	0.4 (0.3– 0.6)	0.7 (0.6– 0.8)	1.4 (0.9– 1.9)
	SPACE ( <sup>3</sup> ) definition of positive MRI spine ( <sup>5</sup> inflammatory lesions)	25 (25.5%)	30 (30.3%) n=99	NS	0.3 (0.2– 0.4)	0.7 (0.7– 0.8)	1.2 (0.8– 1.9)



THU0238

### ULTRASONOGRAPHIC EVALUATION OF DISTAL PATELLAR ENTHESIS IN PATIENTS AFFECTED BY ENTEROPATHIC SPONDILOARTHRITIS

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**Background:** Enteropathic arthritis (EA) belongs to the spondyloarthritis (SpA) spectrum of diseases and occurs in patients affected by inflammatory bowel diseases (IBD). Several works demonstrated that ultrasonography (US) is a feasible, reliable and easily accessible tool for detecting chronic and active enthesal abnormalities even in a subclinical contest in SpA patients.<sup>1,2</sup>

**Objectives:** To evaluate the prevalence of US enthesal involvement of the distal insertion of patellar ligament in patients affected by EA.

**Methods:** Twenty-two consecutive AE patients (12 with Crohn's disease and 10 with ulcerative colitis; 8 females and 14 males; mean age 44.7 years, range 18–72 years; mean AE duration 10.1 years range 4–21 years) and 18 healthy age- and gender-matched controls (8 females and 10 males; mean age 48 years, range 24–68 years) underwent an US examination (ESAOTE MyLAB 70 6–18 MHz linear array transducer) according to the validated Madrid Sonographic Enthesis Index (MASEI). Clinical and clinimetric variables were assessed in both groups according with daily clinical practice.

**Results:** Focusing on the 44 distal patellar entheses we identified a higher prevalence of all the elementary lesion analysed. In 34 entheses we identify a dishomogeneous echostructure (77.3% vs 33.3%;  $p=0.0001$ ), in 38 structural thickness (86.4% vs 66.7%;  $p=0.03$ ), in 16 power Doppler positivity (36.3% vs 16.7%;  $p=0.04$ ), in 17 presence of calcifications (38.6% vs 16.7%;  $p=0.03$ ) and in 8 entheses the presence of erosions (18.8% vs 0%;  $p=0.007$ ). In the 45% of the examined patients we detected a simultaneous presence of dishomogeneous echostructure, structural thickness and power Doppler positivity suggestive for US active enthesitis at the level of the same entheses.

**Conclusions:** US detectable signs of enthesopathy and enthesitis are very frequent in EA patients even when we analyse the distal entheses of the patellar ligament alone. Further studies involving a larger number of patients are needed to confirm these preliminary data.

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**Disclosure of Interest:** None declared

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THU0239

### PROGRESSION OF STRUCTURAL DAMAGE ON MRI OF THE SPINE AND SACROILIAC JOINTS IN PATIENTS WITH AXIAL SPONDILOARTHRITIS IS LIMITED: THE 5 – YEAR RESULTS IN THE DESIR COHORT

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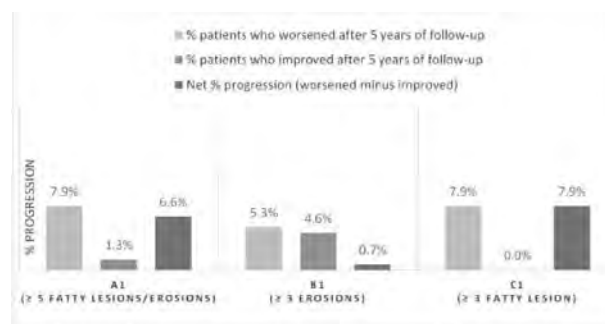
**Background:** Reliably detecting radiographic structural change in patients with axial spondyloarthritis (axSpA), especially in the sacroiliac joints (SIJ), is notoriously difficult. Magnetic resonance imaging (MRI) is an alternative for radiographs to assess structural damage. However, so far the utility of MRI in capturing change in structural damage over time has been poorly studied.

**Objectives:** We aimed to evaluate the change over time of structural lesions on MRI of the SIJ and spine in patients with axSpA.

**Methods:** Patients with recent onset ( $\leq 3$  years) axSpA (according to the treating rheumatologist) from the DESIR cohort were included. MRI of the SIJ (MRI-SIJ) and spine (MRI-spine) were obtained at baseline and 5 years and scored by 3 trained central readers unaware of the chronology. Structural damage in the SIJ (MRI-SIJ-STR) and in the spine (MRI-spine-STR) was defined according to 3 binary rules (A1:  $\geq 5$  fatty lesions and/or erosions; B1:  $\geq 3$  erosions; and C1:  $\geq 3$  fatty lesions) and 3 continuous scores (A2: number of fatty lesions/erosions; B2: number of erosions; and C2: number of fatty lesions). For binary outcomes, structural damage was defined by the agreement of at least 2 out of 3 readers and the % of net progression by subtracting the number of patients that 'improved' from those that 'worsened' divided by the total number of patients with complete

baseline and 5 year data. For continuous outcomes, the mean of the 3 readers was used and the difference between year 5 and baseline was calculated.

**Results:** In total, 151 and 145 patients had complete MRI-SIJ and MRI-spine data available from 3 readers, respectively. The percentages of net progression at SIJ level are summarised in the figure 1. These were 6.6%, 0.7% and 7.9% for the binary outcomes A1, B1 and C1 respectively. Notably, the percentage of 'improvement' (4.6%) was almost as high as the percentage of 'worsening' (5.3%) for definition B1 ( $\geq 3$  erosions); while no 'improvements' were seen by the 3 readers for definition C1 ( $\geq 3$  fatty lesions). Similar differences were seen for the mean (standard deviation) change of the 3 MRI-SIJ-STR continuous outcomes (A2: 1.02 (2.60); B2: 0.20 (1.39); and C2: 0.83 (2.20);  $p<0.01$  for all). MRI-spine-STR net change over time was almost absent (A1:  $-0.7\%$ ; B1: 0.0%; C1: 0.7%) considering the binary outcomes, and small (though statistically significant) considering definition A2 (0.18 (0.52);  $p<0.01$ ) and C2 (0.14 (0.48);  $p<0.01$ ) but absent for definition B2 (0.03 (0.24);  $p=0.109$ ).



**Abstract THU0239 – Figure 1.** Changes in different binary MRI-SIJ-STR outcome measures. All outcomes are assessed according to the '2 out of 3' definition in the completers population (N=151). MRI-SIJ-STR, structural damage on magnetic resonance imaging of the sacroiliac joints

**Conclusions:** These results suggest that patients with early axSpA only show modest structural progression in the MRI of the SIJ and that fatty lesions are more sensitive to change compared to erosions. In this early axSpA population, MRI-detected structural progression in the spine is very limited/absent.

**Disclosure of Interest:** None declared

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THU0240

### THE SIZE AND FREQUENCY OF BONE MARROW OEDEMA ON SACROILIAC JOINT MRI DIFFERS IN A CLUSTER-WISE COMPARISON OF PATIENTS WITH FINDINGS SUGGESTIVE OF AXIAL SPONDILOARTHRITIS

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**Background:** Multiple correspondence analysis (MCA) is a statistical method that allows for the translation of data from multiple categorical variables into single coordinates per individual. When combined with cluster analysis, individuals that share phenotypic characteristics can be grouped together. The Assessment of Axial Spondyloarthritis international Society (ASAS) published classification criteria for axial spondyloarthritis (axSpA) in 2009<sup>1</sup> that included active sacroiliitis on magnet resonance imaging (MRI) of the sacroiliac joints (SIJ) defined as bone marrow oedema (BME) present in either as 2 lesions on one slice, or 1 lesion on 2 consecutive slices.<sup>2</sup> It has been shown that extent of BME is associated with risk of radiographic progression.<sup>3</sup>

**Objectives:** To identify phenotypes in low back pain (LBP) patients recruited from primary care with findings suggestive of early axSpA and to assess differences in size and frequency of BME lesions on SIJ MRI.

**Methods:** Age, gender and the ASAS SpA features (SIJ BME on MRI, HLA-B27, inflammatory back pain, arthritis, heel enthesitis, uveitis, psoriasis, inflammatory bowel disease, good response to NSAIDs, family history of SpA, but not dactylitis (not observed) or radiographic sacroiliitis) of 134 LBP patients who either met or were one feature short of meeting the ASAS classification criteria for axSpA were analysed by MCA and subsequent k-means cluster analysis in order to identify various clinical phenotypes. The above listed SpA features, and if present, the

size and frequency of SIJ BME as defined by the Aarhus scoring module,<sup>4</sup> were compared across clusters.

**Results:** MCA and cluster analysis revealed 3 clusters. Cluster 1 was predominantly HLA-B27 positive (96.7%) with SIJ BME in half of the cases. Cluster 2 and 3 had SIJ BME in all cases. Cluster 3 had fewer features suggestive of axSpA than clusters 1 and 2. There were significant differences in frequency (3.0 vs 2.0 vs 1.0) and extent of BME (4.0 vs 2.0 vs 1.0) across clusters 1, 2 and 3.

**Abstract THU0240 – Table 1.** Cluster-wise comparison of the construction variables, frequency and size of sacroiliac joint bone marrow oedema\*

Characteristic	All (n=134)	Cluster 1 (n=30)	Cluster 2 (n=45)	Cluster 3 (n=59)	p-value†
Male	42.5	53.3	40.0	39.0	NS
Age category (years)					
≤25	18.7	26.7	6.7	23.7	<0.05 <sup>‡</sup>
26-32	29.9	23.3	40.0	25.4	NS
≥33	51.5	50.0	53.3	50.8	NS
SIJ BME	86.8	50.0	100.0	100.0	<0.001 <sup>§</sup>
HLA-B27 positive	30.6	96.7	17.8	5.8	<0.001 <sup>§</sup>
Inflammatory back pain	58.2	73.3	95.6	22.0	<0.01 <sup>§</sup> , <0.001 <sup>§</sup>
Arthritis	20.1	46.7	26.7	1.7	<0.001 <sup>§</sup>
Heel enthesitis	19.4	26.7	35.6	3.4	<0.01 <sup>§</sup> , <0.001 <sup>§</sup>
Uveitis	2.2	3.3	4.4	0.0	NS
Psoriasis	4.5	3.3	8.9	1.7	NS
Inflammatory bowel disease	1.5	6.7	0.0	0.0	NS
Good response to NSAIDs	35.1	63.3	48.9	30.2	<0.001 <sup>§</sup>
Family history of SpA <sup>‡</sup>	18.9	40.0	28.9	0.0	<0.001 <sup>§</sup>
Elevated CRP	13.4	30.0	4.4	11.9	<0.01 <sup>§</sup> , <0.05 <sup>§</sup>
Among patients with SIJ BME					
Frequency of BME (1-4) <sup>‡</sup>	2.0 (2.0)	3.0 (5.0)	2.0 (2.0)	1.0 (1.0)	<0.01 <sup>§</sup> , <0.001 <sup>§</sup> , <0.05 <sup>§</sup>
Size of BME (1-24) <sup>‡</sup>	2.0 (2.0)	4.0 (7.0)	2.0 (3.0)	1.0 (1.0)	<0.01 <sup>§</sup> , <0.001 <sup>§</sup> , <0.05 <sup>§</sup>

\* Values are percent of patients or medians with interquartile ranges; †Kruskal-Wallis and Dunn's test for multiple comparisons; ‡Cluster 1 vs Cluster 2; ‡Cluster 1 vs Cluster 3; ‡Cluster 2 vs Cluster 3; ‡missing in 2 patients; ‡Frequency of BME was defined as the total count of lesions, i.e. 4 locations per joint; ‡Size of BME was graded as slight (<25%), moderate (25% to <50%), or severe (≥50%) extent of BME in the cartilaginous and ligamentous part of the corresponding sacral and iliac subcortical bone area, i.e. 4 locations per joint, and combined into a total score.

Abbreviations: SIJ, sacroiliac joints; BME, bone marrow oedema; MRI, magnet resonance imaging; HLA-B27, Human Leukocyte Antigen B27; NS, not significant; NSAIDs, non-steroidal anti-inflammatory drugs; CRP, C-reactive protein; NS, not significant

**Conclusions:** Three clusters were identified among LBP patients with findings suggestive of axSpA: 1 predominantly HLA-B27 positive cluster with SIJ BME in half of the subjects, and 2 clusters having less features suggestive of SpA and with SIJ BME in all subjects. The predominantly HLA-B27 positive cluster had more and larger BME lesions than the other 2, which may indicate individuals at risk for progression.

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#### THU0241 MUSCULOSKELETAL INVOLVEMENT IN INFLAMMATORY BOWEL DISEASE'S PATIENTS: A MONO CENTRIC EXPERIENCE

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**Background:** Musculoskeletal symptoms are frequently reported by patients with inflammatory bowel diseases (IBD). Those symptoms may vary from arthralgia to arthritis, involving peripheral or axial joints, with a prevalence ranging from 17% to 62% when considering any SpA manifestation (with a similar range for axial or peripheral involvement from 5% to 30%) and a definite SpA diagnosis up to 46%.<sup>1–10</sup> To date, a more comprehensive approach is needed, also because the use of DMARDs or biologics could improve both gastrointestinal and musculoskeletal symptoms.

**Objectives:** To evaluate the rate of MSK involvement in a mono centric cohort of IBD patients.

**Methods:** A questionnaire based on the features of SpA was used in the IBD out-patient clinic from January 1st to December 31st 2017. When there was a positivity for any feature, the patients were evaluated by a rheumatologist (with more than 18 years of experience in SpA). All the visits were performed in 2–3 weeks from the moment the questionnaire was performed (varying according to the seasonal time for holidays). When there were some doubts about the diagnosis, further examinations were requested.

**Results:** A total of 403 patients were visited in the out-patient clinic (220 affected by CD, 172 affected by UC and 11 with a not defined IBD). Fifty-nine patients were sent to the rheumatologist (33 CD, 24 UC and 2 not defined IBD). Eleven patients had 2 or more rheumatologic visits (to follow-up the disease and check the results

of the exams requested). To allow a diagnosis, 4 sacroiliac joints MRI and 1 ultrasound assessment of the feet were requested. A diagnosis of peripheral SpA was given in 9 patients while axial SpA was diagnosed in 7 subjects. The diagnosis was fibromyalgia, osteoarthritis and arthralgia in 1, 2 and 40 patients, respectively. Therapy was modified in 16/59 patients after the rheumatologic assessment (DMARDs were prescribed in 12 subjects while anti-TNFa in 4 of them). In 1 patient (with absolute contraindication for biologic therapy), two courses of SI joint injection were performed, improving local pain.

**Conclusions:** The results of our study confirm the already published prevalence of musculoskeletal involvement in IBD patients (15% of our IBD population complained musculoskeletal pain and 27% of the patients sent to the rheumatologist were given an enteropathic arthritis diagnosis). As for the already existing literature, we did not notice any evident difference in the prevalence of axial and peripheral involvement. An established collaboration between gastroenterologists and rheumatologists is necessary to provide an integrated and more comprehensive management of IBD, improving the quality of life of the patients.<sup>11–12</sup>

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#### THU0242 PREGNANCY OUTCOMES AND DISEASE ACTIVITY IN WOMEN WITH AXIAL SPONDYLOARTHRITIS: A SYSTEMATIC LITERATURE REVIEW

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**Background:** Women with axial spondyloarthritis (axSpA) are often affected by the disease during their reproductive years,<sup>1</sup> but reports on disease activity and pregnancy outcomes in these patients (pts) are sparse. In women with ankylosing spondylitis (AS), also currently termed as radiographic axSpA, a higher risk of disease activity flares and prevalence of adverse pregnancy outcomes have been reported vs healthy controls; however, in non-radiographic (nr)-axSpA pts, such data are virtually non-existent.<sup>2,3</sup>

**Objectives:** To review the available evidence on the relationship between axSpA disease activity and pregnancy, including foetal outcomes.

**Methods:** A systematic literature review was conducted in October 2017 by searching EMBASE, MEDLINE<sup>®</sup>, the Cochrane Database of Systematic Reviews, and the Database of Abstracts of Reviews of Effects. Publications were systematically screened for English language articles on observational studies of axSpA pts reporting pregnancy outcomes or disease activity during pregnancy. Studies utilising agents contraindicated in pregnancy were excluded. Supplementary searches of selected, 2016–17 conference proceedings and bibliographies of relevant review articles were also conducted.

**Results:** 2216 publications were reviewed, with 20 publications on 15 unique studies meeting the inclusion criteria. When utilising the verified disease activity measurement instruments, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) or Ankylosing Spondylitis Disease Activity Score C-Reactive Protein (ASDAS-CRP), 5 studies (3 prospective, 2 retrospective) reported active disease (as described by individual studies; table 1) both during pregnancy and postpartum in most pts. Pregnancy outcomes in axSpA pts were compared with healthy controls in 6 studies (3 retrospective, 2 prospective, 1 case-control), the 3 largest of which (including 1 prospective) revealed higher risk or odds of preterm births in axSpA pts. Higher rates or risk of low birth weight/small-for-gestational-age neonates were shown in pts vs controls in 2/5 studies reporting such outcomes. Stillbirths, miscarriages or foetal loss/abortion were found to occur at similar rates in both populations.

**Conclusions:** Robust, prospective data on disease activity during pregnancies of women with axSpA are limited. Within the samples reported here, available data suggest that there may be a small increase in pre-term births; no signal for increased pregnancy loss was detected. Further research is needed to investigate relationships between maternal disease activity and pregnancy outcomes in axSpA.

**Abstract THU0242 – Table 1.** Maternal disease activity and pregnancy outcomes in axSpA patients

Maternal axSpA disease activity during pregnancy and postpartum				
Study	Population(s)	Instrument	Activity during pregnancy (a)	Activity postpartum (b)
Urnäs 2017 [c][d]	axSpA: 181/168	BASDAI	Stable, low disease activity (2 <sup>nd</sup> trimester: BASDAI=3.97)	Stable, low disease activity (6 weeks pp: BASDAI=3.46)
Förger 2009 [e]	AS [f]: 10	BASDAI	Moderate disease activity	Increased by 50% (8/10)
Förger 2005 [e]	AS [f]: 10	BASDAI	Clinical improvement (4/10)	Not reported
van den Brandt 2017 [e]	axSpA [g]: 37	ASDAS-CRP	‘Persistent high activity’ [h]	‘Persistent high activity’ [h]
Timur 2016 [d]	AS [f]: 20	ASDAS-CRP	‘Decreased score’ (14/20) ‘Unchanged score’ (6/20)	‘Decreased score’ (2/20) ‘Increased score’ (15/20)

Pregnancy outcomes of axSpA patients and healthy controls				
Study	Populations (a)	Incidence per pregnancies vs controls (p value)		
Fang 2017 [c][d]	AS: 2492 Controls: 2,347,847	Preterm birth: 148/2492 vs 106,014/2,347,847 (aOR) 1.18 [1.00–1.38] [i] (<0.05)	Birth weight <2500 g: 173/2492 vs 151,048/2,347,847 (aOR) 1.06 [0.91–1.22] NS [j]	SGA: 221/2492 vs 227,984/2,347,847 (aOR) 0.97 [0.85–1.11] NS
Förger 2017 [c][d]	axSpA: 78/70 Controls: 70	Preterm birth: ‘higher risk’ SGA: ‘higher risk’		
Park 2017 [c][d]	AS: 27/20 Controls: 108	Preterm birth: Data not reported (NS) Low birth weight: 22.2% vs 8.3% (0.024)	SGA: 5/199 vs 6/477 (aOR) 1.34 [0.37–4.85] NS for untreated patients; 4.47 [0.95–20.6] NS for NSAID-treated patients	Abortion: 0.2±0.4 vs 0.2±0.4 (1,000)
Timur 2016 [d]	AS [f]: 20 Controls: 40	Preterm birth: 3/20 vs 3/40 (0.390) Birth weight <2500 g: 5/20 vs 3/40 (0.150)	SGA: 5/199 vs 6/477 (aOR) 1.34 [0.37–4.85] NS for untreated patients; 4.47 [0.95–20.6] NS for NSAID-treated patients	
Jakobsson 2016 [d]	AS [f]: 199 Controls: 477	Preterm birth: 22/199 vs 21/477 (aOR) 2.62 [1.27–5.39] for untreated patients; 1.79 [0.55–5.82] NS for NSAID-treated patients	SGA: 5/199 vs 6/477 (aOR) 1.34 [0.37–4.85] NS for untreated patients; 4.47 [0.95–20.6] NS for NSAID-treated patients	
Ostensen and Husby 1983 [d]	AS [f]: 13 Controls: 31	Preterm birth: 1/13 vs 0/31 Miscarriage: 0/13 vs 1/31	SGA: 5/199 vs 6/477 (aOR) 1.34 [0.37–4.85] NS for untreated patients; 4.47 [0.95–20.6] NS for NSAID-treated patients	Stillbirth: 0/13 vs 1/31

[a] Pregnancies/Women (if not equal); [b] Cases per total pregnancies (n/N); [c] Congress abstract; [d] Retrospective data; [e] Prospective data; [f] modified New York criteria; [g] ASAS classification criteria; [h] ASDAS-CRP 2.1–5.3; [i] aOR [95% confidence interval]; [j] Crude odds ratio significant at 1.19 (1.03–1.38); [k] Case-control study; [l] ICD-10 M45. aOR: adjusted odds ratio; AS: ankylosing spondylitis; ASDAS-CRP: ankylosing spondylitis disease activity score-C-reactive protein; axSpA: axial spondyloarthritis; BASDAI: Bath ankylosing spondylitis disease activity index; NS: not significant; NSAID: non-steroidal anti-inflammatory drug; pp: postpartum; SGA: small-for-gestational-age.

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**THU0243 CASE FATALITY OVER 365 DAYS AFTER FIRST ACUTE CORONARY SYNDROME IN PATIENTS WITH ANKYLOSING SPONDYLITIS**

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**Background:** Ankylosing spondylitis (AS) is characterised by systemic and local inflammation of the axial skeleton, joints, and entheses. Studies have suggested a higher risk of acute coronary syndrome (ACS) among patients with AS compared with the general population, but whether patients with AS also have an increased fatality following ACS is not known.

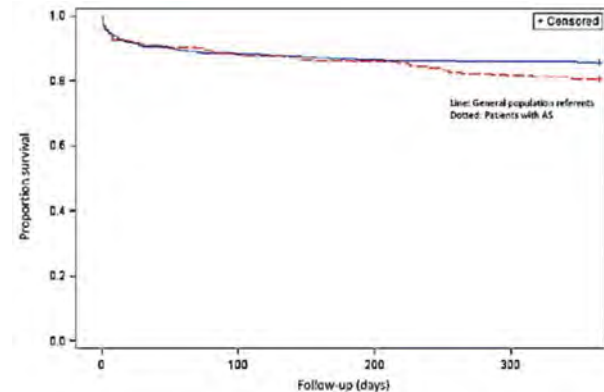
**Objectives:** Is AS associated with an increased case fatality after a first-time ACS compared with the general population?

**Abstract THU0243 – Table 1.** Mortality and hazard ratios (HR) for patients with AS and general population referents during 365 days of follow up after a first ACS

	Start		At 30 days follow up		At 365 days follow up		
	Individuals at risk	Individuals at risk	n deaths	HR (95% CI) day 0–30	Individuals at risk	n deaths	HR (95% CI) day 31–365
AS	292	273	26	0.9 (0.6;1.5)	266	56	2.0 (1.3;3.1)
General population comparator	1276	1204	118	ref	1158	184	ref

**Methods:** From the Swedish National Patient Register (NPR) we identified all patients registered with AS Jan 2001 through Dec 2014 and a later registration of a first time ACS between Jan 2006 and Dec 2014 (n=292). As a general population comparator, we identified up to 5 individuals per index-patient (n=1276), matched on year of first ACS and birth, gender, and place of living. The follow-up period began at the date of admission for ACS and extended until death, emigration, 365 days of follow-up or 31 December 2014, whichever occurred first. Hazard ratios (HR) for death in the AS group vs. the general population comparator was assessed using Cox regression. We assessed HRs for death in two intervals: 30 day mortality (day 1 through 30), and mortality day 31 through 365.

**Results:** During the 365 days following the ACS, 56 (19%) of the 292 AS patients and 184 (14%) of the 1276 population controls died (table 1). Whereas the 30 day mortality in the AS group was not elevated (HR=0.9), the mortality day 31 through 365 was doubled compared with the general population (HR=2.2, table 1 and figure 1).



**Abstract THU0243 – Figure 1.** Kaplan-Meier curves showing survival after first ACS in patients with AS and general population referents during 365 days follow up.

**Conclusions:** Patients with AS were at increased risk of death during the first year, though not during the first month, following ACS. It is yet not clear whether this could be due to factors associated with the AS disease *per se*, or differences in ACS characteristics or treatment.

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**THU0244 HIGH PREVALENCE OF CLINICAL SPONDYLOARTHRITIS FEATURES IN PATIENTS WITH HIDRADENITIS SUPPURATIVA**

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**Background:** Hidradenitis suppurativa (HS) is a chronic debilitating inflammatory skin disease and is associated with several comorbidities. HS and spondyloarthritis (SpA) share several pathophysiological and clinical features, such as elevated cytokine levels of TNF-α and IL-17 and the association with inflammatory bowel



disease. Recognition of clinical axial and peripheral SpA features might help to identify patients with a higher chance of having SpA.

**Objectives:** To investigate the prevalence of self-reported clinical SpA features in HS patients and to identify HS patient characteristics associated with the presence of these features.

**Methods:** In this cross-sectional study, a questionnaire concerning clinical SpA features was sent to all patients with a billing code of HS (between 2010 and 2016) in two tertiary HS referral centres in the Netherlands. First, questions were formulated based on the ASAS definitions for axial and peripheral SpA entry classification criteria: "back pain for  $\geq 3$  months with age of onset  $< 45$  years" and "peripheral arthritis, enthesitis or dactylitis" in past or present, respectively. Additionally, questions concerning other clinical SpA features (table 1) in past or present were asked. Questions were provided with proto-typical coloured pictures of SpA features for clarification. Prevalence of self-reported SpA features was calculated and comparative analysis was performed.

**Results:** Overall, 47.2% (620/1313) of questionnaires were eligible for analyses. Included patients had a mean age of  $43 \pm 14$  years, 70% were female, mean BMI was  $28.0 \pm 5.8$ , 84% were ex- or current smokers, and 25% had no HS symptoms at the time of the survey.

In total, 67.1% (416/620) of HS patients fulfilled  $\geq 1$  of the four ASAS entry criteria. The entry criteria for axial and peripheral SpA were reported by 72.8% (303/416) and 27.2% (113/416), respectively. The large majority of patients (87%) reported  $\geq 1$  clinical SpA features in addition to the entry criteria: one feature by 137 (32.9%) patients, two by 121 (29.1%), three by 67 (16.1%), and  $\geq 4$  by 37 (8.9%). An overview and percentage of the clinical SpA features is presented in table 1.

In comparison to patients without self-reported SpA entry criteria features (n=204), patients fulfilling the ASAS entry criteria were more frequently female (p<0.001), had higher BMI (p<0.001), more often positive smoking history (p=0.001), longer HS disease duration (p=0.012), and showed more active HS symptoms at time of the survey (p<0.001).

**Abstract THU0244 – Table 1.** Overview of self-reported clinical SpA features in patients with HS fulfilling the axial or peripheral ASAS entry criteria (n=416).

Self-reported clinical SpA features	Number of patients (%)
Inflammatory back pain	84 (20.2)
Good response to NSAIDs on back pain	63 (22.0)
Peripheral arthritis (swollen joints)	248 (59.6)
Enthesitis (Achilles tendon)	66 (15.9)
Dactylitis	83 (20.0)
Inflammatory bowel disease	31 (7.6)
Psoriasis	39 (9.4)
Uveitis	13 (3.2)
Positive family history of SpA	125 (30.0)

**Conclusions:** Clinical axial and peripheral SpA features are common in HS patients, especially in the 'classic' HS patient (female, overweight, smoker), with longer HS disease duration and symptoms of active HS.

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#### THU0245 RELATIVE RISK CHART SCORE FOR THE ASSESSMENT OF THE CARDIOVASCULAR RISK IN YOUNG PATIENTS WITH ANKYLOSING SPONDYLITIS

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**Background:** Ankylosing spondylitis (AS) is associated with increased rates of cardiovascular (CV) mortality. CV events can be prevented by identifying patients with high CV risk who can benefit from strict primary prevention measures. The systematic coronary risk evaluation (SCORE) is the predictive model recommended in Europe, but it underestimates the CV risk in individuals under 50 years old.

**Objectives:** To determine if the use of the relative risk (RR) chart score (figure 1) may help to identify young AS patients at high risk of CV disease.

**Methods:** A set of 73 AS patients younger than 50 years old without history of CV events, diabetes mellitus or chronic kidney disease was assessed. CV risk was calculated according to the total cholesterol systematic coronary risk evaluation (TC-SCORE) and the RR chart score. A value of C-reactive protein (CRP)  $> 3$  mg/L at diagnosis, cut-off point associated with an increased risk of CV events, and carotid ultrasound data performed at the time of the assessment were also analysed.

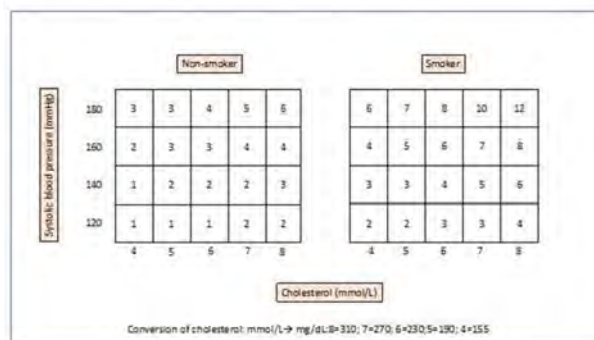
**Results:** Twenty (27.4%) of 73 patients exhibited carotid plaques and, consequently, they were classified into the category of very high CV risk. CRP  $> 3$  mg/L at disease diagnosis was associated with the presence of carotid plaques after adjustment for confounding factors (odds ratio 5.66, 95% confidence interval 1.11–28.77; p=0.03). None of these young patients were included in the category of high/very high CV according to the TC-SCORE. Whereas only 5 (14.2%) of the 35 patients with RR=1 had carotid plaques, 15 (39.5%) of 38 with RR  $> 1$  showed plaques. A model that included the performance of carotid US in patients with RR  $> 1$  who had CRP  $> 3$  mg/L at disease diagnosis allowed us to identify 60% of young AS with very high CV risk, with a specificity of 77.4% (area under the curve [AUC]: 0.69). The performance of carotid US in young AS patients with RR  $> 1$  regardless of CRP data at diagnosis increased the sensitivity up to 75% at the expense of a significant decline in the specificity to 56.6% (AUC: 0.66) (table 1).

**Abstract THU0245 – Table 1.** Study of 73 AS patients between 35 and 50 years without cardiovascular events, diabetes mellitus or chronic kidney disease to establish the presence of high/very high cardiovascular risk.

	Sensitivity	Specificity	Correctly classified	ROC [95% CI]
<b>Model 1.</b> TC-SCORE $\geq 5\%$ OR TC-SCORE $\geq 1\%$ $< 5\%$ plus carotid US (presence of plaques)	40%	88.7%	75.3%	0.64 [0.53–0.76]
<b>Model 2.</b> RR $> 1$ and CRP $> 3$ mg/L at time of disease diagnosis plus carotid US (presence of plaques)	60.0%	77.4%	72.6%	0.69 [0.56–0.81]
<b>Model 3.</b> RR $> 1$ plus carotid US (presence of plaques)	75.0%	56.6%	61.6%	0.66 [0.53–0.78]

TC-SCORE: Total Cholesterol systematic coronary risk evaluation, US: ultrasound, RR: relative risk, CRP: C-reactive protein.

The gold standard used to define high/very high cardiovascular risk was the presence of TC-SCORE  $\geq 5\%$  or carotid plaques.



Based on the ESC 2016 guidelines

**Abstract THU0245 – Figure 1.** Relative Risk chart, derived from SCORE. Based on the ESC 2016 guidelines

**Conclusions:** RR chart score assessment may help to identify young AS at high risk who are underdiagnosed as having very high CV risk by the SCORE.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrhumdis-2018-eular.3906

THU0246

### CAN DISEASE ACTIVITY IN PATIENTS WITH PSORIATIC ARTHRITIS BE ADEQUATELY ASSESSED BY A MODIFIED DISEASE ACTIVITY INDEX FOR PSORIATIC ARTHRITIS (DAPSA) BASED ON 28 JOINTS?

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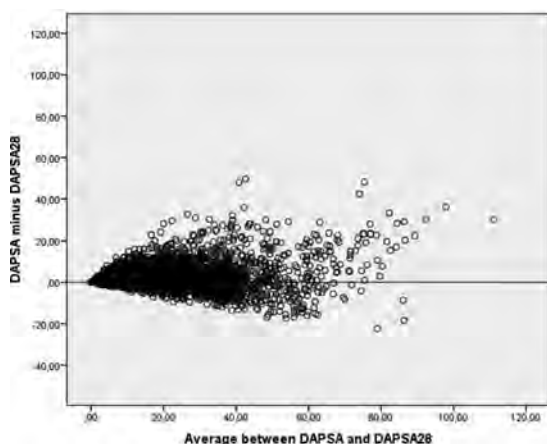
**Background:** 66/68 vs. 28 joint count has higher face validity in PsA. However, many databases/registries routinely collect only 28-joint count. It is not known if these data can be used to provide sufficient information on disease activity and response to therapy.

**Objectives:** To compute and test the potential validity of a simplified Disease Activity index for Psoriatic Arthritis (DAPSA) using 28 instead of 66/68 joint count.

**Methods:** We included PsA patients from the Danish national quality registry DANBIO, divided into examination (n=3157 patients, 24160 visits) and validation cohorts (n=3154 patients, 24160 visits) according to odd/even IDs. We defined: DAPSA28=(28TJCxconversion factor<sub>1</sub>)+(28SJCxconversion factor<sub>2</sub>)+patient global[0–10VAS]+pain[0–10VAS]+CRP[mg/dL]. Identification of conversion factors was performed by Generalised Estimating Equations (GEE, multiple visits per patient) in the examination cohort, and criterion, correlational and construct validity explored in the validation cohort.

**Results:** Mean(SD) age: 52.0 (13.8) years, 54.4% females. GEE: Conversion factor<sub>1</sub>=1.6, 95% CI(1.6–1.7), conversion factor<sub>2</sub>=1.6, 95% CI(1.5–1.6), leading to: DAPSA28=(28TJC+28 SJC)x1.6+patient global[0–10VAS]+pain[0–10VAS]+CRP[mg/dL]. Criterion validity: Physician global and DAPSA/DAPSA28 were similarly correlated (r=0.63/r=0.61, p<0.001). DAPSA/DAPSA28 had comparable discriminative power, expressed as standardised mean difference (DAPSA,0.90; DAPSA28,0.93) to distinguish between patients in high (starting bDMARD) and low (not starting/changing s/bDMARD for ≥60 days) disease activity. Agreement between DAPSA/DAPSA28 disease activity states was best for remission/low disease activity (table 1).

Kappa with quadratic weighting of DAPSA/DAPSA28 disease activity states indicated very good agreement; 0.92 95% CI (0.92–0.92). Standardised response means for DAPSA/DAPSA28 were –0.96/–0.92 (n=572) for visits after start of bDMARD. Correlational validity: Baseline DAPSA/DAPSA28 had strong correlation with DAS28CRP (r=0.87/r=0.93), SDAI (r=0.92/r=0.99), p<0.001. Bland-Altman plot showed better agreement between DAPSA/DAPSA28 for low than high disease activity (figure 1). Construct validity: DAPSA/DAPSA28 were similarly correlated to HAQ; r=0.60/0.62, p<0.001. DAPSA/DAPSA28 discriminated patients reporting their symptom state as acceptable (n=1140) vs. not acceptable (n=1045) equally well: mean(SD) 9.1 (8.7)/8.4 (8.0) and 24.2 (14.9)/22.5 (13.8), respectively.



**Conclusions:** DAPSA28 showed good criterion, correlational and construct validity, and sensitivity to change. However, agreement between DAPSA and

DAPSA28 was better for low than high disease activity levels. We recommend that 66/68 joint count should be performed and the original DAPSA should be preferred in PsA. However, our study suggests that data sets with only 28-joint counts available can use DAPSA28, especially in patients with low disease activity.

**Disclosure of Interest:** B. Michelsen: None declared, J. Sexton: None declared, J. Smolen: None declared, D. Aletaha: None declared, N. Krogh: None declared, D. van der Heijde: None declared, T. Kvien: None declared, M. Hetland Consultant for: Abbvie, Biogen, BMS, CellTrion, MSD, Novartis, Orion, Pfizer, Samsung, UCB.

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THU0247

### SPA-NET: A DISEASE-SPECIFIC INTEGRATED EHEALTH SYSTEM AND QUALITY REGISTRY FOR SPONDYLOARTHRITIS IN DAILY PRACTICE IN THE NETHERLANDS

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**Background:** Regular and personalised monitoring of disease activity, physical activity, medication use and side effects is essential to improve and maintain patients' health-related quality of life in spondyloarthritis (SpA). Transparency on outcomes, safety, practice variation and efficiency of care are increasingly demanded. Furthermore, patient empowerment and shared decision making are advocated. An integrated eHealth system including an electronic patient medical record (EMR) and real-time quality management system could provide a solution to meet these demands.

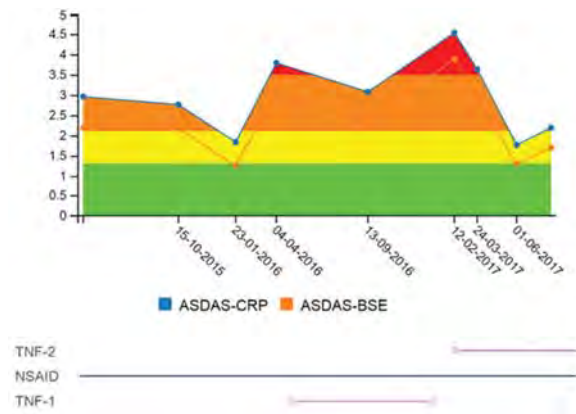
**Objectives:** To develop and test the feasibility of a disease-specific integrated eHealth system and quality registry for SpA in the Netherlands ('SpA-Net'), in order to 1) improve the quality of care for the individual patient, 2) provide transparency on treatment results, practice variation and costs and 3) to produce data for scientific research.

**Methods:** The eHealth system was developed in four phases. First, the content and design were discussed with experts in the field of SpA and patients (pts). Second, the database, EMR and quality management system were developed. Third, multiple rounds of internal and external testing were performed in collaboration with IT specialists, care providers and pts. Fourth, the eHealth system was implemented in practice and feasibility was tested among pts and care providers through semi-structured focus interviews.

**Results:** SpA-Net was designed and developed in 2015 and implemented into practice in May 2016. All pts entered into SpA-Net have a diagnosis of SpA according to their treating rheumatologist. There are no inclusion or exclusion criteria towards the subtype of SpA or treatment. Information prospectively collected at routine outpatient consultations on diagnosis, demographics, specific SpA manifestations, patient reported outcome measures, clinical outcomes, comorbidities, medication use and safety, supplemented with data from the hospital information system, is directly stored in a database. The comprehensive individual patient data are readily available to the physician and an excerpt of this can be accessed by the patient. Prior to each visit, pts complete online questionnaires. The information is presented in graphs wherever possible (figure 1).

In December 2017, 1078 pts participated in SpA-Net (mean [SD] age 53.7 [14.3] years, 46.6% females), and inclusion is ongoing. Focus group interviews were held with 16 pts, 9 rheumatologists, and 5 nurses. Pts considered the layout of SpA-Net as clear, accessible and intuitive. They felt the use of questionnaires resulted in better quality of care and communication, and appreciated having access to their EMR with lay-term explanations. Points of improvement were the login process and providing more details about the care provider's notes. Care providers appreciated the additional information for (preparing) consultations. Barriers against use of SpA-Net were the initial time required to adopt the EMR and the quantity of data entry.

DAPSA28 (n=6421)	DAPSA(n=6421) n(%) stratified by DAPSA disease activity states			
	DAPSA≤4	DAPSA>4 and≤14	DAPSA>14 and≤28	DAPSA>28
DAPSA28≤4	1135 (98.4)	126 (5.6)	4 (0.2)	0 (0)
DAPSA28>4 and≤14	18 (1.6)	2073 (91.5)	345 (17.8)	14 (1.3)
DAPSA28>14 and≤28	0 (0)	66 (2.9)	1509 (77.9)	248 (23.3)
DAPSA28>28	0 (0)	80 (4.1)	803 (75.4)	



Abstract THU0247 – Figure 1. Example of graph in SpA-Net reporting the evolution of ASDAS in relation to medication use over time

**Conclusions:** SpA-Net enables regular monitoring of pts with SpA and can serve as a first step to optimise knowledge and communication between pts and care providers. Both pts and care providers thought SpA-Net improves quality of care in daily practice.

**Disclosure of Interest:** C. Webers: None declared, E. Beckers: None declared, Y. van Eijk: None declared, H. Vonkeman: None declared, M. van de Laar: None declared, P. van Riel: None declared, M. Efdé: None declared, A. Boonen: None declared, A. van Tubergen Grant/research support from: AbbVie, Celgene, Janssen-Cilag, MSD, Novartis, Pfizer, UCB

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THU0248

#### ASSOCIATION OF KINESIOPHOBIA, AEROBIC EXERCISE, FUNCTIONAL IMPAIRMENT AND DISEASE ACTIVITY OF PATIENTS WITH RHEUMATOID ARTHRITIS AND SPONDYLOARTHRITIS

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**Background:** Rheumatoid arthritis (RA) and spondyloarthritis (SA) are the most common chronic inflammatory rheumatism, leading to functional disability, but also cardiovascular mortality. Aerobic exercise (AE) is one of the most effective non-pharmacological resources for cardiovascular rehabilitation while the patients RA and SA have difficulty to join the practice of physical exercise. It can be explained by the presence of kinesiophobia, fear that the movement exacerbates the pain and disease.

**Objectives:** To compare the level of AE of patients with RA and SA with healthy subjects and to verify the association between kinesiophobia, the level of activity of the disease and the functional disability

**Methods:** Fifty RA patients and fifty SA patients followed by the rheumatology department of the University Hospital of Besançon and fifty healthy age-matched subjects were included. The main inclusion criteria: between 18 and 80 years old and without orthopaedic surgery <1 year. The disease activity (DAS-28 and ASDAS), the functional disability (HAQ and BASFI), the level of AE (SQUASH questionnaire) and kinesiophobia (TSK questionnaire) were evaluated. The control group answered to the SQUASH questionnaire. The t-test was used to compare inflammatory rheumatism groups with the control group (healthy subjects). The Pearson Correlation Test for each group (RA and SA) was used to verify the associations between variables.

**Results:** The level of AE is significantly higher in healthy subjects ( $p=0.022$ ). In the RA group, kinesiophobia is associated with disease activity, functional disability and level of AE. In the SA group, kinesiophobia is associated only with the functional disability. Patients have a low level of AE compared to healthy subjects. However, only the RA group has an association between kinesiophobia and AE. In the SA group, functional disability appears to be a factor limiting the practice of AE.

Abstract THU0248 – Table 1. Results of pearson correlation test between variables

	Aerobic Exercise	Kinesiophobie	Functional Disability	Disease Activity
RA				
Aerobic Exercise	-	$r = -0.280^*$	$r = -0.414^{**}$	$r = -0.149$
Kinesiophobie	$r = -0.280^*$	-	$r = 0.522^{**}$	$r = 0.327^*$
Functional Disability	$r = -0.414^{**}$	$r = 0.522^{**}$	-	$r = 0.531^*$
SA				
Aerobic Exercise	-	$r = -0.165$	$r = -0.40$	$r = -0.064$
Kinesiophobie	$r = -0.165$	-	$r = 0.345^*$	$r = 0.224$
Functional Disability	$r = -0.040$	$r = 0.345^*$	-	$r = 0.737^{**}$

\*  $p < 0.005$ ; \*\*  $p < 0,005$

**Conclusions:** RA and SA patients need to be encouraged and better informed about the benefits of physical exercise.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.6741

THU0249

#### MORE THAN 60% PATIENTS WITH SPONDYLOARTHRITIS REPORT PERIPHERAL MANIFESTATIONS: AN ANCILLARY ANALYSIS OF THE ASAS-COMOSPA STUDY

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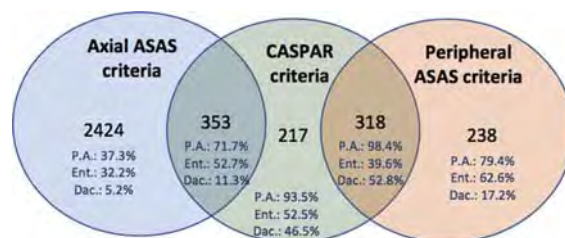
**Background:** Peripheral manifestations (arthritis, enthesitis and dactylitis) can be observed in patients with Spondyloarthritis (SpA)<sup>1</sup>, but the factors associated with their presence are not well known. Studies are needed in order to thoroughly evaluate these symptoms.

**Objectives:** a) To describe the prevalence of peripheral manifestations in patients with SpA in a world-wide population; and b) to determine the factors associated with the presence of these manifestations.

**Methods:** Data from the ASAS-COMOSPA study were analysed. The prevalence of each peripheral manifestation was evaluated with regard to the criteria fulfilled by the patient (ASAS axial, ASAS peripheral, CASPAR) and with regard to the time of occurrence of axial symptoms (before/concomitant/after). Factors associated with the presence of these peripheral manifestations were also explored by univariate and multivariate logistic regression.

**Results:** Out of the 3984 patients included in ASAS-COMOSPA, 2562 (64.3%) reported, at least, one peripheral manifestation. Among these, 2051 patients (51.5% from the total database) had current or past history of peripheral arthritis, being more frequent among patients who met CASPAR and Peripheral ASAS criteria (see figure 1). Involvement was more frequently oligoarticular (40.2%) and appearing after axial symptom onset (48.9%). Multivariate analysis showed that patients from South America [OR 2.45, (95%CI 1.93–3.11)], the presence of enthesitis [OR 2.46, (95%CI 2.11–2.86)], dactylitis [OR 6.46, (95%CI 4.78–8.71)], skin psoriasis [OR 2.46, (95%CI 1.79–3.37)], HLAB27+ [OR 0.83, (95%CI 0.72–0.97)] and inflammatory back pain (IBP) [OR 0.37, (95%CI 0.29–0.47)] were associated with peripheral arthritis.

A total of 1506 (37.8%) and 618 (15.6%) patients reported enthesitis and dactylitis, respectively. Both occurred after axial symptoms onset in 58.3% and 60.8% of the patients, respectively. Similar results than peripheral arthritis were obtained in the multivariate analysis regarding these two peripheral manifestations, with exception of IBP and HLAB27+, which were not associated with enthesitis.



\*434 patients fulfil neither axial ASAS, nor peripheral ASAS, nor CASPAR criteria.

(P.A. 43.8%, Ent. 34.8%, Dac. 11.3%).

P.A.: Peripheral Arthritis, Ent.: Enthesitis, Dac.: Dactylitis.

Abstract THU0249 – Figure 1. \*434 patients fulfil neither axial ASAS, nor peripheral ASAS, nor CASPAR criteria.



**Conclusions:** Peripheral manifestations appear in 64% of patients with SpA and in more than 50% after axial symptoms onset. Peripheral arthritis, were more frequently mono- or oligo- rather than poly-articular, and the presence of psoriasis or any of the three peripheral manifestations acts as risk factor for the development of other peripheral symptoms.

#### REFERENCE:

[1] Dougados M, d'Agostino MA, Banessiano J, et al. *Joint Bone Spine* 2011 Dec;78(6):589–603. doi:10.1016/j.jbspin.2011.01.013

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.5309

#### THU0250 IMPACT OF GUT INVOLVEMENT IN EARLY SPONDYLOARTHRITIS. THE DESIR COHORT

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**Background:** Inflammatory bowel disease (IBD) is a well-known extra articular feature of spondyloarthritis (SpA), with increasing evidence of a pathophysiological relationship.

**Objectives:** The aims of this study were to evaluate in the DESIR cohort a) the prevalence of IBD at baseline and M60, and b) the incidence of IBD over the first 5 years of follow-up, c) factors (epidemiological, clinical, imaging, biological data available in the database) associated with IBD, a on the prevalent cases at baseline and at year 5 and also on the incident cases.

**Methods:** DESIR is a prospective observational cohort of patients with recent onset (<3 years) inflammatory back pain, suggestive of axial SpA. All available factors in the database were compared between patients with and without past or present IBD at baseline and at M60, and with and without incident cases of IBD over the 5 years of follow-up, by uni and multivariate analysis.

**Results:** At baseline, 706 patients were analysed, 35 had a past history or a concomitant IBD: prevalence 4.94% [CI 95%: 3.3–6.5]. IBD was significantly associated (univariate) with family history of IBD, DMARD use, steroid use, history of uveitis, elevated ESR and negatively associated with psoriasis, HLA-B27 and NSAID score. In multivariate analysis IBD was positively and independently associated with history of uveitis; OR 3.62 [1.95–6.74], levels of DKK-1: OR 1.03 [1.02–1.05] and TNF serum levels: OR 1.17 [1.08–1.26]. IBD was not associated with phenotypic presentation (peripheral arthritis, enthesitis, dactylitis, uveitis) or baseline serum levels of other cytokines (IL-6, IL-17 A, IL-17 F, IL-23, IL-23).

At M60, 480 patients were analysed, 58 with IBD: prevalence 12.1% [9.17–14.99]. In univariate analysis on prevalent cases, IBD was associated with lower NSAID score, worse activity and function indexes (ASDAS-CRP, BASFI, SF-36, HAQ, ASQoL), use of DMARD anti TNF, more sick leave. In multivariate analysis, IBD was associated with fulfilment of modified New York criteria: OR 4.85 [2.23–10.57], sick leave: OR 1.01 [1.005–1.014], BASDAI: OR 1.10 [1.05–1.16], and with smoking: OR 2.79 [1.53–5.07]. No association with MRI scores, enthesitis, psoriasis, BMD.

After a 5 year follow-up period, 23 new incident cases of IBD were recorded, giving an estimated occurrence rate of 0.95/100 [0.57–1.35] patient-years in this population. Incidence of IBD was independently associated (multivariate) with: HLA B27: OR 0.36 [0.22–0.59], fulfilment of modified New York criteria at M0: OR 3.35 [1.85–6.08], family history of IBD: OR 3.31 [1.62–6.77].

**Conclusions:** In early SpA, IBD occurs with an incidence of around 1/100 patient-years, and is associated with poor outcome at 5 years, family history of IBD, absence of HLA-B27, fulfilment of modified New York criteria.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.3205

#### THU0251 CHARACTERISTICS OF NEWLY DIAGNOSED AXIAL SPONDYLOARTHRITIS PATIENTS IN RHEUMATOLOGY PRACTICES ACROSS GERMANY

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**Background:** There is still limited knowledge about early axial spondyloarthritis (axSpA) patients in primary rheumatology care.

**Methods:** Rheumatologist from n=70 study centres across Germany recruited patients with spondyloarthritis (SpA) diagnosed for the first time (time since diagnosis <1 year) over three consecutive years. Patients were evaluated and

documented regarding clinical, laboratory and imaging characteristics, fulfilment of ASAS classification criteria and treatment. In addition, participating centres (n=36) documented the frequency of newly diagnosed SpA among all patients seen for the first time in their practice in one week.

**Results:** A total of 427 newly diagnosed SpA patients were recruited. 342 patients (mean age 38.9 years, range 18–73; 55.3% males) had a new diagnosis of axSpA (mean symptom duration 81.5 months (range 0–599)) and are presented here in more detail. 36.5% were classified as radiographic axSpA according to the modified New York criteria and 19.3% were imaging (magnetic resonance imaging and X-rays) negative. The laboratory, clinical and imaging characteristics of these patients are shown in the table 1. 85.4% of these patients diagnosed as axSpA by the rheumatologist fulfilled the ASAS classification criteria. 69.9% were treated with NSAIDs, 3.8% with conventional DMARDs and 1.2% with biologics when seen for the first time by the rheumatologist. The therapy has been continued or changed as follows by the rheumatologist at first visit after making the diagnosis of axSpA: NSAIDs in 80.7%, conventional DMARDs in 8.8% and biologics in 10.5%. However, additional treatment with biologics might be initiated at follow-up visits.

The proportion of SpA patients among all newly diagnosed patients with rheumatic conditions documented in one week was 17.5% (10.1% axSpA and 7.4% peripheral SpA).

**Abstract THU0251 – Table 1.** Clinical, laboratory and clinical characteristics of patients with axial SpA (n=342)

Parameter	Prevalence,%
Inflammatory back pain, current	74.9
Arthritis, current	14.6
Enthesitis, current	10.5
Positive family history	18.1
Uveitis, ever	12.0
Psoriasis, ever	10.5
Inflammatory bowel disease, current	1.8
HLA-B27 positiv	69.6
CRP positive, current	37.7
MRI sacroiliac joints positive, current	60.8
MRI spine positive, current	11.7
Definite radiographic sacroiliitis (X-ray positive)	29.5
MRI and X-ray negative	19.3

**Conclusions:** The characteristics of axSpA patients seen in primary rheumatology practices are comparable to what has been reported. The majority of patients are still in the stage of non-radiographic axSpA when diagnosed first and the majority of patients have active MRI inflammation in the sacroiliac joints but not in the spine. In about 10% of patients a TNF-blocker was started already at first visit.

**Disclosure of Interest:** D. Poddubnyy Grant/research support from: AbbVie, MSD, Novartis., Consultant for: AbbVie, BMS, Boehringer, MSD, Novartis, Pfizer, and UCB., Speakers bureau: AbbVie, BMS, Janssen, MSD, Novartis, Pfizer, and UCB., E. Edelmann Consultant for: AbbVie, Boehringer-Ingelheim, Lilly, Mundipharma, MSD, Novartis, Pfizer, Roche, UCB., V. Rios Rodriguez Consultant for: Abbvie, MSD and Novartis., S. Saringen Shareholder of: AbbVie Inc., Employee of: AbbVie Deutschland GmbH and Co. KG., T. Mosch Shareholder of: AbbVie Inc., Employee of: AbbVie Deutschland GmbH and Co. KG., J. Sieper Grant/research support from: AbbVie, Merck, and Pfizer., Consultant for: AbbVie, Janssen, Lilly, Merck, Novartis, Pfizer, and UCB., Speakers bureau: AbbVie, Janssen, Merck, Novartis, Pfizer, Roche, and UCB.

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#### THU0252 THE RATE OF US VERIFIED HIP INVOLVEMENT IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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**Background:** Hip joint (HJ) involvement is one of the most common extra-axial manifestations of ankylosing spondylitis (AS).

**Objectives:** To correlate clinical manifestations of coxitis with the ultra-sound findings in AS patients.

**Methods:** 224 consecutive AS patients (mean age 33.2±14.2 y) meeting 1984 modified N-Y criteria and hospitalised in V.A. Nasonova Research Institute of Rheumatology with hip pain were evaluated. Patients' mean age at the onset of the disease was 26.3±20.3 y., 93% of them were HLA-B27-positive. Median AS duration was 57 [12–444] months, the BASDAI score was 5.7±3.1. The diagnosis of coxitis was based on clinical signs and symptoms, such as inguinal pain and/or limitation in the range of hip motion (ROM) at the time of patients' admission to the clinic. All patients (regardless current complaints) were subjected to ultrasound

(US) examination of the HJ (Sono Diagnost 360 (Philips)) using linear (7,5 MHz) and convex (5,0 MHz) transducers. A neck capsular pattern (NCP – the distance between the signals from inner surface of the femoral neck and the joint capsule) more than 7 mm was used as the US criterion, verifying the clinical diagnosis of coxitis.

**Results:** The US criterion of coxitis was found in 119 (53%) out of 224 patients, and two groups of pts were analysed based on NCP values with 7 mm threshold.

Parameters	P		
	Group <sup>1</sup> without US signs of coxitis (n=105)	Group <sup>2</sup> US confirmed coxitis (n=119)	
Gender(f/m), n	79/26	77/40	<b>0,01</b>
AS duration, mo, Me[25%; 75%;]	43 <sup>19;80</sup>	102 <sup>24;120</sup>	<b>0,0006</b>
BASDAI, Me <sup>25;75</sup>	4,1 <sup>2;6;</sup> 5,5	5,2 <sup>4;2;</sup> 6,7	<b>0,0001</b>
BASFI, Me <sup>25;75</sup>	2,4 <sup>2;0;</sup> 3,8	3,4 <sup>2;0;</sup> 5,4	<b>0,0001</b>
HLA-B27, n (%)	96 (91%)	113 (95%)	<b>0,4</b>
ASDAS (?RP) ?? <sup>[25;75]</sup>	2,8 <sup>2;0;</sup> 3,8	3,5 <sup>2;6;</sup> 3,8	0002
ESR, mm/h, Me [25%; 75%]	10 <sup>5;</sup> 25	25 <sup>8;</sup> 35	0001
CRP, mg/mL, Me [25%; 75%]	10,5 <sup>3;8;</sup> 28,5	23,0 <sup>4;9;</sup> 43,5	<b>0,06</b>
Peripheral arthritis%	38 (36%)	28 (30%)	<b>0,06</b>

**Conclusions:** US criterion of coxitis, i.e, increased NCP, was found in 53% of patients with clinical AS manifestations. Patients with US-confirmed coxitis demonstrate more active disease with greater functional impairment and longer history of AS, as compared to AS population without US signs of hip involvement.

**Disclosure of Interest:** None declared

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THU0253

#### THE CHRONIC SPINAL PAIN IN SPONDYLOARTHROPATHIES, OSTEOARTHRITIS, AND FIBROMYALGIA: THE ROLE OF CENTRAL SENSITISATION

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**Background:** Central sensitisation (CS) is a new phenomenon associated with several medical diagnoses, including post-cancer pain, low back pain, osteoarthritis (OA), whiplash, and fibromyalgia (FMS).<sup>1</sup> Central sensitisation inventory (CSI) suggest the tool generates reliable and valid data that quantify the severity of several symptoms of CS.<sup>2</sup>

**Objectives:** To the best of our knowledge, there is no study to evaluate CS pain in patients with Spondylarthritis (SpA). The aim of this study was to show the role of CS pain in patients with painful spine of SpA, OA, and FMS.

**Methods:** Totally 137 patients with chronic spinal pain (42 SpA, 45 OA and 50 FMS) were included. CSI consists of 2 parts<sup>1,2</sup>: CSI-A and CSI-B (restless leg, chronic fatigue, FMS, temporomandibular disorders, migraine/tension type headache, irritable bowel, multiple chemical sensitivity, whiplash, anxiety/panic attack, and depression).

**Results:** Only 4 patients (9.52%) had active SpA (BASDAI $\geq$ 4). Twelve patients (28.57%) have used anti-TNF drugs. Age, BASDAI and VAS-pain scores were not related with SS-A or SS-P positivity. Spine in patients with SpA was less painful compared with them of OA and FMS (p=0.001). The CS pain was detected in most with FMS, compared with OA, and SpA patients (p<0.001). Similarly, CSI-A score was the highest in patients with FMS group (p<0.001) and similar in both OA and SpA groups (p=0.197). CS-related syndromes (CSI-B) were also detected similarly in both SpA and OA groups, but less than FMS group (p<0.001). The numbers of CS syndromes were also similar in both SpA and OA (p=0.551) and lower than FMS group (p=0.003). Table 1 shows the clinical parameters in all groups.

**Abstract THU0253 – Table 1.** The comparisons of clinical characteristics

	1. SpA	2. OA	3.FMS	P1-3	P2-3
Age	41,0 $\pm$ 10,03	61,2 $\pm$ 9,67	45,22 $\pm$ 8,6	0233	0000
Female%	%38,09	%88,88	% 94	0001	0370
BASDAI	2,42 $\pm$ 1,18				
VAS	3,48 $\pm$ 2,17	6,78 $\pm$ 1,70	8,00 $\pm$ 1,8	0000	0001
CSI-A%	%45,23	%62,22	%94	0000	0000
CSI-Ascore	36,26 $\pm$ 18,5	43,6 $\pm$ 13,1	58,92 $\pm$ 14,78	0000	0000
CSI-B%	%40,47	%28,88	%100	0000	0000
CSI-Bscore	0,93 $\pm$ 1,3	0,51 $\pm$ 1,05	1,98 $\pm$ 1,2	0000	0000
Restless leg	%9,52	%4,44	%8,00	0796	0477
Chr.fatigue	%7,14	%2,22	%6	0825	0360
Fibromyalgia	%7,14	%2,22	%100	0000	0000
TMD	%11,90	%17,77	%0	0012	0002
Migraine/TTH	%14,28	%2,22	%30	0086	0231
Irrit.bowel	%9,52	%2,22	%5	0285	0621
Multi-chem s.	%0	%0	%5	0190	0175
Whiplash	%2,38	%0	%2	0901	0340
Anxiety/panic	%14,28	%2,22	%18	0779	0030
Depression	%16,22	%15,55	%28	0222	0215

**Conclusions:** Central sensitisation should be considered in patients with chronic persistent pain, not only having FMS, but also half of the patients having SpA and OA. It is not a rare phenomenon and if it exists, effective pain management strategies could be needed in addition to the specific pharmacologic treatment.

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THU0254

#### RELATION BETWEEN SUBCLINICAL ULTRASONOGRAPHIC CHANGES OF THE ANTERIOR CHEST WALL JOINTS AND PULMONARY FUNCTION TESTS IN ANKYLOSING SPONDYLITIS PATIENTS

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**Background:** Ultrasonography can detect subclinical changes in anterior chest wall (ACW) joints of patients with ankylosing spondylitis (AS).<sup>1</sup> Pulmonary functions may be affected during the course of AS.<sup>2</sup>

Up to the best of our knowledge, there are no previous studies of the relationship between ultrasound detected subclinical changes in ACW and the pulmonary functions in AS patients.

**Objectives:** To detect the relation between ultrasonographic changes of asymptomatic ACW joints and pulmonary function tests (PFTs) in patients with AS.

**Methods:** The study included 88 sternoclavicular joints (SCJ) and 44 manubri-sternal joints (MSJ) in 44 subjects (22 AS and 22 control). None of the participants had a history of respiratory complaints such as dyspnea, chronic cough, or chest pain. High resolution Computed Tomography (HRCT) was done on the chest to exclude interstitial lung problem that may affect chest expansion and PFTs.

Ultrasound (US) assessments were performed to detect synovitis, erosions, ankylosis, osteophytes, or Doppler signals. Chest expansion was measured. PFTs was done and included measurement of the forced expiratory volume in 1 s (FEV1), forced vital capacity (FVC), and the ratio of forced expiratory volume in 1 s to the forced vital capacity (FEV1/FVC). In AS group, Ankylosing Spondylitis Disease Activity Score (ASDAS), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Bath Ankylosing Spondylitis Functional Index (BASFI) were recorded.

**Results:** US detected subclinical changes of ACW joints in (77.3%) of AS patient with significant difference between total US changes in AS(77.3%) and control (21.2%) (p<0.001). MSJ ankylosing was highly associated with limited chest

expansion in AS group ( $p < 0.001$ ). PFTs were found to be restrictive in 14 AS patient (63.6%) with mean of FVC ( $70.3 \pm 9\%$ ),  $FEV1$  ( $55.2 \pm 15.9\%$ ),  $FEV1/FVC$  ( $80.1 \pm 2$ ) and these restrictive PFTs were associated with SCJ synovitis ( $p = 0.03$ ), SCJ PD activity ( $p = 0.03$ ), SCJ erosions (0.05) and highly associated with MSJ ankylosing ( $p < 0.001$ ). All AS patients (100%) with ankylosed MSJ by US had limited chest expansion and restrictive PFTs.

In AS group, ultrasonographic changes and restrictive PFTs were found to be higher with older age, male sex, smoking, longer disease duration and high BASDAI and BASFI.

**Conclusions:** Our study demonstrated that ultrasound detected subclinical changes in ACW joints is associated with restrictive pattern of PFTs in AS patients.

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#### THU0255 LOW BONE MINERAL DENSITY IS COMMON IN AXIAL SPONDYLOARTHROPATHY

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**Background:** Osteoporosis is a known consequence of inflammatory arthritis (IA). In the general population and IA such as rheumatoid arthritis, the impact of osteoporosis is well outlined. However, it is often ignored in axial spondyloarthritis (axSpA), a form of IA centred on sacroiliac joints and the spine, as axSpA predominantly affects men, in whom osteoporosis is often not considered. As a result, osteoporosis prevalence figures are unclear, with wide variation in the literature. Accurate epidemiology regarding bone mineral density (BMD) in axSpA is crucial to begin understanding the impact of low BMD in this cohort.

**Objectives:** 1. Investigate the prevalence of low BMD in a well-characterised axSpA cohort

2. Explore relationships (demographic, disease-related, laboratory) between BMD and axSpA.

**Methods:** A detailed assessment was performed on axSpA patients, including demographics, clinical characteristics and laboratory investigations. Disease severity was assessed with tools validated in axSpA: ASDAS-CRP and BASDAI (disease activity), BASMI (spinal mobility) and BASFI (function). BMD was assessed using DXA of the spine, hip and radius. Lateral vertebral assessment (LVA) was also performed. The WHO criteria were used to classify low BMD. SPSS was used for statistical analysis.

**Results:** One hundred and four patients with axSpA were consecutively recruited: 77.9% (n=81) male, 98.1% (n=102) Caucasian, mean (SD) age 51<sup>12</sup> years, disease duration 26<sup>13</sup> years. The mean (SD) ASDAS-CRP was 2.3 (1), BASDAI was 3.9 (2.2), BASMI was 4.3 (1.9) and BASFI was 3.8 (2.5), reflecting mild to moderate disease burden. A history of fracture was present in 42.3% (n=44) of the cohort, with only 3 fragility fractures reported.

Of the cohort, 42.3% (n=44) had osteopenia and 16.3% (n=17) had osteoporosis. Low BMD was most prevalent at the spine, with 44% of the cohort affected, followed by the femoral neck (30.1%, n=22). Low BMD at the radius was uncommon (<10% of the cohort). Only 6.4% of the cohort had a prior diagnosis of osteoporosis and only 39.4% had a previous DXA.

Three vertebral fractures were detected on LVA – all patients were unaware of these fractures prior to the study.

Female gender, higher BASFI, lower BMI and lower urate levels were significantly associated with bone loss at both the spine and the hip. ASDAS-CRP and BASDAI had no impact on low BMD. Additionally, longer disease duration was associated with spine BMD loss. Non-obese patients were more likely to have low BMD at any site than obese patients (62.3% v 40%, OR 2.5,  $p = 0.04$ ). The use of biologics didn't influence BMD.

**Conclusions:** Low BMD is common in this axSpA cohort, with over 50% of patients affected. Most cases of low BMD were undiagnosed prior to this study and less than half of the cohort had ever had a DXA, suggesting a continued low awareness of the risk of osteoporosis in a male-dominated disease.

**Disclosure of Interest:** None declared

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#### THU0256 HIGH DISEASE ACTIVITY, REDUCED PHYSICAL FUNCTION, LONG DISEASE DURATION, FATIGUE AND LIVING WITHOUT A PARTNER ARE FACTORS RELATED TO WORSE HEALTH RELATED QUALITY OF LIFE IN ANKYLOSING SPONDYLITIS

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**Background:** Ankylosing spondylitis (AS) begins early in life. The disease often leads to reduced physical function and also reduced health related quality of life (HRQoL). Knowledge is limited about factors related to HRQoL and how it develops over time.

**Objectives:** To assess HRQoL by SF-36 in a cohort of patients with AS compared with controls and to explore associations between HRQoL and spinal radiographic damage, physical function, disease activity and demographic data.

**Methods:** A cohort of patients with AS from Western Sweden were assessed at baseline and after 5 years with; x-ray of the spine for mSASSS, clinical examination and questionnaires, including BASMI, BASFI, ASDAS, BASDAI and SF-36. In this abstract we report the baseline results. Each patient's SF-36 results were compared with 5 age- and sex matched persons (n=1055) from the SF-36 Swedish normative population database. Associations between SF-36 mental component summary (MCS) and physical component summary (PCS) scores and disease related and demographic factors were investigated. Univariate logistic regression analyses were assessed with PCS and MCS below/above their respective median values (below median=1 and above median=0) as dependent variables and disease related and demographic variables as covariates. Variables with  $p$ -values  $\leq 0.2$  in the univariate analyses were entered as covariates in multivariate models after checking for multicollinearity.

**Results:** 210 patients, age (median, IQR) 49.0 (40.0, 61.2) years, symptom duration 24.0 (13.0, 34.0) years, men 58%, HLAB27 87% were included. AS patients scored significantly lower ( $p < 0.001$ ) compared to controls in all SF-36 domains and component summaries. AS women scored significantly lower compared to AS men in three domains, Physical Function, Vitality and Mental Health. Both men and women scored significantly lower in PCS compared with MCS. The results of the multiple logistic regressions are shown in the table 1.

Variables	PCS below median 42.4 (1)			MCS below median 48.0 (1)		
	OR	95% CI	P-value	OR	95% CI	P-value
Civil state, single	2.19	0.95–5.02	0.065	3.12	1.40–6.97	0.006
VAS global fatigue, >median				7.05	3.50–14.20	<0.001
Duration of symptoms, decades	1.59	1.16–2.17	0.004			
BASFI	1.98	1.51–2.58	<0.001			
ASDAS-CRP <sub>≥2.1</sub>	3.37	1.58–7.20	0.002	3.85	1.95–7.60	<0.001

**Conclusions:** Patients with AS had significantly lower HRQoL compared with controls. Women with AS scored lower in some domains compared to men and PCS was more affected compared to MCS in both sexes. Both demographic and disease related factors were associated with HRQoL, partly overlapping for PCS and MCS. By modifying factors, such as ASDAS and fatigue, HRQoL may potentially be improved. The development of SF-36 over 5 years will be investigated.

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#### THU0257 ASSOCIATIONS BETWEEN TRABECULAR BONE SCORE AND VERTEBRAL FRACTURES IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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**Background:** The bone tissue directly exposed to inflammation in axSpA is the trabecular bone of the vertebrae, and consequently, vertebral osteoporosis and resorption of trabecular bone are increased in axial spondyloarthritis. The trabecular bone score (TBS) is a novel tool used to evaluate bone microarchitecture. AxSpA patients showed poor bone quality compared with matched controls.

**Objectives:** This study aims to compare TBS between axSpA patients with and without vertebral fractures and investigate associations between TBS and vertebral fractures.



**Methods:** Two hundred and fifty-five patients fulfilling the imaging arm of the Assessment of SpondyloArthritis International Society axSpA criteria were enrolled. TBS and bone mineral density (BMD) were assessed using dual-energy X-ray absorptiometry. Vertebral fracture of the thoracic and lumbar spine was defined according to the Genant criteria. Osteoporosis risk factors, inflammatory markers, disease activity scores, and spinal structural damage were also assessed. Multivariate logistic regression analysis was performed to identify factors associated with vertebral fractures.

**Results:** Of 255 axSpA patients, 28 (11%) had 31 vertebral fractures. The mean TBS was 1.39±0.11 and 1.30±0.13 in patients without and with vertebral fractures, respectively (<0.001). BMD in the femoral neck was lower in patients with vertebral fractures (p=0.027), but BMDs in the lumbar spine and total hip were not. In the multivariate analyses, low TBS and the presence of syndesmophytes were significantly associated with vertebral fractures, independently of BMD (OR [95% CI]=3.6 [1.2–11.1] and 3.3 [1.0–10.7], respectively). For the total hip, TBS has a better discriminatory value than BMD for prediction of vertebral fractures in axSpA patients (p=0.034).

**Conclusions:** TBS values are lower in axSpA patients with vertebral fractures. Low TBS and syndesmophytes were independently associated with prevalent vertebral fractures. TBS has better predictive value to BMD for the discrimination of vertebral fractures and could help to detect axSpA patients with vertebral fractures.

**Disclosure of Interest:** None declared

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**THU0258** **DIAGNOSTIC VALUE OF ANTI-CD74 AUTOANTIBODIES IN AXIAL SPONDYLOARTHRITIS AND AXIAL PSORIATIC ARTHRITIS. RESULTS OF OPEN-LABEL, CROSS-SECTIONAL, CONTROLLED, MULTICENTER PROGRESS STUDY**

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**Background:** The problem of axial spondyloarthritis (axSpA) differential diagnostics is not solved, especially in the early stages of the axSpA. Therefore, new diagnostic markers for axSpA are needed.

**Objectives:** of the study were to evaluate the prevalence, sensitivity and specificity of anti-CD74 autoantibodies (anti-CD74-AB) in HLA-B27 associated axSpA in comparison with HLA-B27 associated axial Psoriatic arthritis (axPsA) and with healthy controls.

**Methods:** Anti-CD74-AB (quantitative ELISA) were measured in serum of 114 HLA-B27-positive patients with axSpA, and in 26 age- and sex – matched HLA-B27 positive patients with axPsA, and in 37 healthy controls without HLA-B27. 68 axSpA patients had ankylosing spondylitis (AS) according mNew-York criteria (1984), 46 axSpA persons had non-radiographic axSpA (nr-axSpA) due to ASAS criteria for axSpA (2009). AxPsA patients had psoriatic arthritis with axial involvement and fulfilled both <sup>CASPAR</sup> (2006) and ASAS axSpA criteria (2009). Disease activity in axSpA and axPsA patients was measured according ASAS recommendations.<sup>1</sup>

**Results:** Patients with AS, nr-axSpA and axPsA were comparable in SpA activity: differences in BASDAI, ASDAS indices and C-reactive protein levels were not significant, p≥0.05 for all. Nr-axSpA patients had shorter disease duration as compared with AS and axPsA patients (p<0.001).

The concentration of anti-CD74-AB in patients with axSpA was 3.5±3.0 U/ml (3.1 ±3.0 U/ml in AS and 3.8±2.9 U/ml in nr-axSpA patients), 2.1±1.4 U/ml in patients with axPsA (p≥0.05 compared to controls and ax-SpA) and 1.3±1.4 U/ml in healthy controls (p<0.05 for the difference with ax-SpA, AS and nr-axSpA). Diagnostic values of anti-CD74-AB in axSpA (ROC-analyse results) are presented in table 1.

**Abstract THU0258 – Table 1.** Diagnostic values of anti-CD74 autoantibodies in patients with axial spondyloarthritis

**(ROC-analyse):**

	AUC (95% CI)	Sensitivity of the test, %	Specificity of the test, %	+LR	Upper cut-off value for reference interval, U/ml	p
axSpA	0,74 (0,67–0,82)	64,4	89,2	5,9	>2,0	<0,0001
AS	0,68 (0,59–0,79)	60,3	89,2	5,6	>2,0	0001

nr-axSpA	0,78 (0,58–0,83)	73,1	84,0	4,5	>1,73	<0,0001
axPsA	0,7 (0,69–0,89)	96,1	45,9	1,8	0,7	0005

AS - ankylosing spondylitis, axSpA - axial spondyloarthritis, axPsA – axial psoriatic arthritis, nr-axSpA - non-radiographic axial spondyloarthritis, CI - confidence interval, +LR – positive likelihood ratio.

Cut-off value of anti-CD74-AB>2.0 U/ml in patients with axSpA showed the diagnostic sensitivity of 64.4%, specificity of 89.2%, the positive LR of 5.9, whereas in patients with nr-axSpA at concentrations of 1.7 U/ml - sensitivity 73.1%, specificity 84% and positive LR 4.5.

**Conclusions:** Anti-CD74-AB are strongly associated with nr-axSpA and less – axPsA. The measurement of anti-CD74-AB can be considered as candidate biomarker in the diagnostics of axSpA and in differential diagnostics between HLA-B27 positive ax-SpA and axPsA, especially in early stages of the diseases. Further studies are needed for the evaluation of anti-CD74-AB diagnostic capacity.

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**THU0259** **FREQUENCY AND PATTERN OF THE UVEITIS IN SPONDYLOARTHRITIS WITH BIOLOGICAL THERAPY**

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**Background:** Uveitis is the most frequent extra-articular manifestation (EAM) of spondyloarthritis (SpA). Its prevalence is approximately 30% and increases with the duration of the SpA. The characteristic pattern is anterior, acute, recurrent and unilateral uveitis. However, the frequency and characteristics of uveitis in SpA treated with biological therapy (BT) are unknown.

**Objectives:** The main target is to describe the frequency and characteristics of uveitis in SpA with BT in a single centre.

**Methods:** Descriptive and retrospective study (January 2003-December 2017) of SpA that develops uveitis in a reference hospital. The epidemiological variables, type of SpA, presence of uveitis and its characteristics, presence of BT at the time of onset and treatment received are collected. For the analysis, frequencies and percentages were used in qualitative variables, and mean and standard deviation (SD) for quantitative variables. Statistical analysis was performed with IBM SPSS v.23.

**Results:** We studied 246 patients with SpA. The subtypes of SpA were: ankylosing spondylitis (AS) (n=125, 50.8%), psoriatic arthritis (PsA) (n=101, 41.1%), undifferentiated SpA (n=13, 5.3%), non-radiographic axial SpA (n=3, 1.2%), enteropathic arthropathy (n=3, 1.2%) and reactive arthritis (n=1, 0.4%).

Uveitis was observed in 41 patients (16.7%) after an average time of development of 109.47 (73.9) months of the SpA. The incidence rate was 5.5 cases of uveitis/100 patients-year of follow-up. 70.7% were men and the mean age(SD) was 47.4 (12.06) years. 87.8% of the cases were HLAB27 positive and had a family history of SpA 41.5%.

Uveitis was observed in 33 patients (80.5%) with AS, in 6 (14.6%) with PsA, in 1 (2.4%) with non-Rx axial SpA and in 1 (2.4%) with undifferentiated SpA. (table 1)

The uveitis pattern was anterior (100%), acute (92.7%), unilateral (87.8%) and in 12.2% bilateral (80% in PsA). At the time of onset of uveitis, the mean ESR was 30.11 mm1<sup>st</sup>h, CRP 3.56 mg/dL, DAS28 3.66 and BASDAI 3.21.

Regarding the diagnosis of SpA, uveitis was after (85.4%), before (12.2%) and simultaneous (2.4%).

At the time of the onset of uveitis, 14 patients (34.1%) were with BT (35.7% etanercept, 28.6% infliximab, 21.4% adalimumab, 7.1% golimumab and 7.1% certolizumab). BT was modified in 3 of the cases.

The treatment of uveitis was topical (78%), corticoids in oral regimen (57.5%), conventional DMARDs (12.5%), with methotrexate predominating in 60% of cases and BT (15%). The most used biologics were adalimumab (50%), infliximab (33.3%) and sekukinumab (16.7%).

Abstract THU0259 – Table 1. Characteristics of the UVEITIS in SpA subtypes

	MEN/ WOMEN	AGE TO THE DIAG. OF UVEITIS (range in years)	HLA B27*	ANT/ POST	ACUTE/ CHRONIC	UNILATERAL/ BILATERAL	RECURRENT/ NON RECURRENT	INCIDENCE RATE (men/women at follow-up)	BT AT THE DIAG. OF UVEITIS	ETN/ MONOCL. CL.
AS (n=41)	23/18	47.4	32	13/0	11/2	12/1	15/0	5.48	11	4/7
PsA (n=4)	3/1	48.7	3	4/0	3/1	2/0	1/2	1.25	3	0/2
uSpA (n=1)	0/1	58	0	1/0	1/0	1/0	1/0	0.55	0	0
nr-uSpA (n=1)	1/0	35	1	1/0	1/0	1/0	0/1	3.54	1	1/0
TOTAL 43	27/12	47.5	36	18/3	18/3	16/5	19/12	3.3	14	5/9
	(70.9%/29.1%)		(81.4%)	(41.9%)	(42.7%/27.3%)	(47.4%/12.5%)	(76.9%/26.9%)		(34.1%)	(105.9%/34.3%)

AS: ankylosing spondylitis; PsA: psoriatic arthritis; uSpA: undifferentiated spondylarthritis; nr-uSpA: non-radiographic axial spondylarthritis; DIAG: diagnosis; ANT: anterior; POST: posterior; BT: biological therapy; ETN: etanercept; MONOCL. CL.: monoclonal antibody

**Conclusions:** In our series, uveitis was observed in 16.7% of patients with SpA of which 80.5% were AS and 14.6% PsA. The most frequent uveitis was anterior, unilateral, acute and recurrent. In PsA, the association with HLA B27 was less frequent and was more bilateral. In most cases, the diagnosis was later than the SpA.

**Disclosure of Interest:** None declared

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**THU0260 THE UVEITIS IMPACT STUDY: A SURVEY BY THE SPONDYLITIS ASSOCIATION OF AMERICA**

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**Background:** Uveitis is the most common clinically apparent concomitant of ankylosing spondylitis. The implications of developing uveitis in association with AS could help to understand this association and assist both clinicians and patients.

**Objectives:** To compare survey responses from patients with AS and no history of uveitis to those with AS and a history of uveitis.

**Methods:** Patients associated with the Spondylitis Association of America (SAA) participated in a web based survey with telephone follow-up performed for a subset.

**Results:** 716 respondents replied that a physician had made a diagnosis of AS. 30.4% of these patients had a history of uveitis. Patients with a history of uveitis tended to be older (median age 31 versus 23 years) and the median age for onset of uveitis was 18 years. Although patients with uveitis did not differ from patients without uveitis on many measures of function, medication, or disability, patients with uveitis were more likely to have heel pain (56% v.45%, p<0.005), rib pain (60% v. 50%, p=0.02), gut inflammation (37% v 23%, p=0.0001), hypertension (42% v 33%, p=0.02), fibromyalgia (18% v 12%, p=0.03), psoriatic arthritis (11% v 6%, p=0.02), or acid reflux (57% v 48%, p=0.03). Patients with uveitis were more like to be negatively impacted in the past week for the ability to concentrate (18% v 12%, very limited, p=0.03); the ability to read, listen, or watch TV (15% v 9%, very limited, p=0.01); and the ability to enjoy family life or friends (6% v 2%, totally limited, p=0.005). Prednisone was more commonly used by those with uveitis (16% v 7%, p=0.0002); and while sulfasalazine was more commonly used previously (41% v 24%, p<0.001), it was less commonly used currently (7% v. 10%). Etanercept, which is less effective in preventing uveitis than monoclonal anti-TNF inhibitors, was used equally in the two groups (11% v 12%).

**Conclusions:** This survey suggests associations between uveitis and clinical manifestations such as heel pain, bowel disease, and skin disease. It is one of the first reports to suggest that uveitis affects quality of life such as the ability to enjoy family or friends. Although medications differentially affect uveitis, our study did not indicate an impact on therapy resulting from uveitis except for the current use of prednisone and a prior history of the use of sulfasalazine.

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**THU0261 CARDIOVASCULAR RISK STRATIFICATION IN ANKYLOSING SPONDYLITIS: LATERAL LUMBAR RADIOGRAPHY IS USEFUL TO DETECT HIGH-CARDIOVASCULAR RISK PATIENTS**

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**Background:** Ankylosing spondylitis (AS) is associated with increased rates of cardiovascular (CV) disease. CV events in these patients can be prevented by identifying patients at high risk who can benefit from appropriate primary prevention measures. The systematic coronary risk evaluation (SCORE) is the predictive model recommended in Europe, but it underestimates the CV risk in AS.

**Objectives:** To determine if a lateral lumbar radiography, which is available in most of AS patients, may help to identify AS patients at high risk of CV disease.

**Methods:** 125 AS patients older than 35 years old without history of CV events, diabetes mellitus or chronic kidney disease were recruited. All patients underwent a carotid ultrasound (US) and lateral lumbar spine radiography and a multi-detector coronary tomography (MDCT) was also performed in a subgroup of 43 AS patients. Carotid plaques were defined according to the Mannheim consensus and the presence of AAC as calcific densities visible in an area parallel to the lumbar spine and anterior to the lower part of the spine. A Coronary Artery Calcification Score (CACS) superior to 100 were considered as a surrogate marker of coronary atherosclerosis. CV risk was calculated according to the total cholesterol systematic coronary risk evaluation (TC-SCORE).

**Results:** CV risk was categorised according to the TC-SCORE as low (<1%; n=64), moderate (≥1% and <5%; n=54) and high/very high risk (≥5%; n=7). Most patients with low TC-SCORE did not show CAA, which was only present in 3 patients (4,68%). In contrast, 38,9% of patients included in the moderate-risk group had CAA. The lateral lumbar radiography showed a sensitivity to detect subclinical atherosclerosis lower than that observed by carotid US, which found plaques in 61% of patients with moderate TC-SCORE, but superior to the MDCT (61,9% Vs 28,6% in the subgroup of 43 patients). 89% of patients with AAC also had carotid plaques (r=0.49, p<0,0001). We set up a predictive model to disclose the largest number of AS with high/very high CV risk, defined by the presence of carotid plaques or a TC-SCORE ≥5% (table 1). A model including patients with a chart TC-SCORE ≥5% along with the presence of AAC showed a sensitivity of 50,9% (model 4). The combination of a TC-SCORE ≥5% and the performance of carotid US in patients with a moderate SCORE showed the highest sensitivity to detect patients at high/very high risk (72,7%, model 2). Nevertheless, model 4 showed greater specificity than model 2 (70% Vs 95,7%), leading to a higher global diagnostic accuracy (area under curve: 0,73 Vs 0,71).

Abstract THU0261 – Table 1

	Sensitivity	Specificity	Correctly classified	ROC [95% CI]
<b>Model 1.</b> TC-SCORE ≥5%	12.7%	100%	61.6%	0.56 [0.52 - 0.61]
<b>Model 2.</b> TC-SCORE ≥1% OR TC-SCORE ≥1% <5% plus carotid US (presence of plaques)	72.7%	70.0%	71.2%	0.71 [0.63 - 0.79]
<b>Model 3.</b> TC-SCORE ≥5% OR TC-SCORE ≥1% and <5% plus lateral lumbar X-ray (presence of AAC)	45.5%	95.7%	73.6%	0.71 [0.64 - 0.78]
<b>Model 4</b> TC-SCORE ≥5% or TC-SCORE <5% plus lateral lumbar X-ray (presence of AAC)	50.9%	95.7%	76.0%	0.73 [0.66 - 0.8]

The gold standard used to define high/very high cardiovascular risk was the presence of TC-SCORE ≥5% or carotid plaques.

**Conclusions:** Several AS patients at high CV risk who are underdiagnosed as having very high CV risk by the SCORE can be detected by a lateral lumbar radiography.

**Disclosure of Interest:** None declared  
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THU0262

### IDENTIFYING PATIENTS WITH AXIAL SPONDYLOARTHRITIS FROM A COHORT OF PATIENTS WITH CHRONIC BACK PAIN IN ORTHOPAEDICS CARE (AWARE STUDY)

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**Background:** Making an early diagnosis of axial spondyloarthritis (axSpA) has remained a challenge. The combination of clinical items suggestive of inflammatory back pain has proved useful for early identification of patients with axSpA in a pilot study in primary care.<sup>1</sup> It has been shown that at least three of five features have a high prognostic impact.

**Objectives:** To evaluate the performance of these 5 clinical items (called AWARE criteria) to identify patients with axSpA from a large cohort of patients with chronic back pain in orthopaedics care.

**Methods:** In adult patients with chronic back pain (>3 months) and age at onset of symptoms <45 years, who were concerned for referral to rheumatologists, the AWARE criteria were assessed and documented prior referring to the rheumatologists.

**Results:** A total of 1306 patients (pts) first seen by orthopaedic surgeons were included. Of those, 500 pts were also seen by rheumatologists, and 188 (37.6%) were diagnosed as axSpA, and, amongst others, 52.2% with non-specific back pain by clinical judgment. A total of 87 cases (17.4%) were diagnosed with ankylosing spondylitis (AS) and 101 (20.2%) with non-radiographic axSpA. A total of 206 pts fulfilled the ASAS classification criteria. The mean age of patients with axSpA was 38±11.5 years, 46.2% were male, the mean duration of back pain was 94.1±103.6 months. The AWARE criteria had a sensitivity and specificity of 93.6% and 17.0% if ≥3 criteria were chosen, and 6.3% and 83.0% with <3 criteria. In axSpA vs. non-axSpA pts, imaging (MRI or x-ray) was positive in 90.6% vs 9.4%, HLA B27 in 69.4% vs 30.6%, 57.6% vs. 42.1% had a good response to NSAIDs, and an elevated CRP in 70.1% vs. 29.9%. A minority of axSpA patients had arthritis (5.6%), enthesitis (6.2%), dactylitis (1%), uveitis (3.8%), psoriasis (4.8%) and IBD (3.6%). Positive imaging (MRI or x-ray) resulted in the highest likelihood ratio (LR) for a diagnosis of axSpA. In combination with HLA B27 +the LR was highest (127.1).

**Conclusions:** Even though the procedure of how patients were preselected in this study caused a selection bias for statistical analyses we think that this study confirms the usefulness of the original AWARE criteria to improve the identification of young patients with chronic back pain in primary care. The important role of imaging and HLA B27 was confirmed. In future studies the two-step approach with three clinical question first and then HLA B27 testing if necessary will be further investigated.

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THU0263

### ANALYSIS ON CHARACTERISTICS OF 82 PATIENTS WITH ANKYLOSING SPONDYLITIS IN JAPAN

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**Background:** Ankylosing spondylitis (AS) is the prototype of spondyloarthritis, which affects sacroiliac joints, spine, peripheral joints and entheses. HLA-B27 is known to be related with AS and there is a considerable number of patients

suffering from AS among other rheumatic diseases. In Japan, however, the prevalence of AS was reported to be less than 0.1% much lower than western countries and also other East Asian countries<sup>1) 2) 3)</sup>. This is due to the low frequency of HLA-B27 in Japanese (0.3%) compared to 5%–10% in the countries mentioned above. Because of small number of AS patients, clinical features and HLA-B27 positivity has not been well investigated in Japanese patients with AS. Since our hospital has an outpatient specialising in AS and there are many patients, we conducted a survey on AS

**Objectives:** In this study, we examined the characteristics of patients with AS in our hospital and compared the data of patients with AS in Japan and overseas.

**Methods:** We conducted a questionnaire survey on patients fulfilling the modified New York criteria for AS. A questionnaire included demographic data and histories. We also retrospectively investigated the data of blood test, radiographs and the presence of inflammatory back pain (IBP), HLA-B27, enthesitis, dactylitis, radiographic sacroiliitis and extra-articular manifestation.

**Results:** A total of 82 patients (82.9% male) including Japanese (68), Chinese,<sup>9</sup> Korean<sup>5</sup> with AS who fulfilled the modified New York criteria were enrolled from May in 2013 to April in 2016. Of 68 patients with HLA-B27 test result, 61 patients (89.7%) were HLA-B27 positive. Of 54 Japanese patients, 48 patients (88.9%) were HLA-B27 positive. IBP, enthesitis, dactylitis, bamboo spine and uveitis were found in 67 patients (81.7%), 31 patients (37.8%), 5 patients (6.1%), 44 patients (53.7%) and 30 patients (36.6%), respectively.

**Conclusions:** In Japanese AS patients, the prevalence of HLA-B27 was high (almost 90%) and other characteristics were similar with those of Western countries. In Japan where the frequency of HLA-B27 is very low, B27 positivity is considered to have high diagnostic value.

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THU0264

### IMPACT OF EXTRA-ARTICULAR MANIFESTATIONS ON PATIENT-REPORTED OUTCOMES IN ANKYLOSING SPONDYLITIS AND PSORIATIC ARTHRITIS: INTERIM RESULTS FROM THE COMPLETE STUDIES

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**Background:** Extra-articular manifestations (EAMs) in rheumatic diseases have been previously found to negatively impact health outcomes including quality of life and work capacity. Even though EAMs may be directly associated with worse response to treatment, differences in patient-reported outcomes (PROs) based on the presence of EAMs could be an important contributory variable.

**Objectives:** To assess the impact of EAMs on PROs among patients with active AS or PsA followed in Canadian routine clinical care.

**Methods:** Patients eligible for the COMPLETE studies are anti-TNFα naïve adults, with active AS or PsA per the judgment of the treating physician, who require change in their treatment regimen. In the current analysis patients enrolled between July/2011 - June/2017 were included. EAMs were defined as the presence of the following at baseline: enthesitis, uveitis, inflammatory bowel disease (IBD) or psoriasis (EAM<sub>AS1</sub> for AS); enthesitis, uveitis, or IBD (EAM<sub>AS2</sub> for AS); enthesitis or dactylitis (EAM<sub>PsA</sub> for PsA). PROs included the Short Form Health Survey (SF-12), Work Limitations Questionnaire (WLQ) and Beck's Depression Inventory (BDI). PROs were compared between patients with and without EAMs using the independent samples t-test. The independent association between presence of EAMs and PROs at baseline was assessed with multivariate generalised linear models adjusting for disease state (high/very high vs. inactive/low/moderate disease based on the BASDAI for AS and the DAS28 for PsA), disease type, and ever smoking.

**Results:** A total of 609 AS and 406 PsA patients were included with a mean (SD) age of 43.1 (13.4) and 51.3 (12.3) years, respectively. EAM<sub>AS1</sub> and EAM<sub>AS2</sub> prevalence among AS patients was 33.9% and 25%, respectively, while among PsA patients EAM<sub>PsA</sub> prevalence was 45.4%.



In univariate analysis, presence of EAMs in AS was associated with significantly higher disease activity, BDI total score, WLQ mental interpersonal demands (only for EAM<sub>AS1</sub>), WLQ physical demands, WLQ time demands, SF-12 physical function, SF-12 role physical, SF-12 bodily pain, SF-12 vitality, SF-12 mental health (only for EAM<sub>AS1</sub>), and the SF-12 physical component summary score (PCS). Among PsA patients, patients with EAM<sub>PsA</sub> had higher disease activity but no significant association was observed between EAM<sub>PsA</sub> and PROs.

Upon adjusting for disease state, disease type, and ever smoking, presence of EAM<sub>AS1</sub>/EAM<sub>PsA</sub> for AS/PsA patients was associated with significantly higher BDI total score (14.0 vs. 12.6,  $p=0.046$ ) and lower SF-12 physical function (38.4 vs. 44.8,  $p=0.047$ ). When evaluating the impact of EAM<sub>AS2</sub>/EAM<sub>PsA</sub> for AS/PsA patients no significant differences were observed in PROs; however, BDI was notably higher among patients with EAMs (14.1 vs. 12.7,  $p=0.056$ ).

**Conclusions:** In a Canadian routine clinical care setting, a substantial proportion of AS and PsA patients requiring a change in treatment report EAMs. Presence of EAMs, particularly psoriasis for AS patients, was found to be a significant independent predictor of depressive symptoms and reduced quality of life due to worse physical functioning.

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#### THU0265 PATIENTS WITH AXIAL SPONDYLOARTHRITIS RARELY HAVE 1 OR 2 INFLAMMATORY BACK PAIN PARAMETERS

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**Background:** The Berlin Algorithm is a tool that assists clinicians in diagnosing axial spondyloarthritis (axSpA). In the modified Berlin Algorithm inflammatory back pain (IBP) is excluded as entry criterion. Although the modified Berlin Algorithm is used in clinical practice some argue that this modification insufficiently emphasises the inflammatory character of axSpA.

**Objectives:** The study aim was to provide an overview of the IBP parameters present in axSpA patients included in the Be-Giant cohort.

**Methods:** Data of an observational multicentre cohort study was used. Patients aged  $\geq 18$  years with a new axSpA diagnosis and fulfilling the ASAS axSpA criteria were included in the Belgian inflammatory arthritis and spondylitis cohort (Be-Giant). All 5 IBP parameters used in the ASAS axSA classification criteria were collected during the clinical visit to the outpatient clinic. IBP parameters collected were: 1) Age at onset  $< 40$  years, 2) insidious onset, 3) improvement with exercise, 4) no improvement with rest and 5) pain at night. IBP is defined when  $\geq 4$  of these parameters are present. Besides these 5 parameters also 'alternating buttock pain' and 'morning stiffness' are reported as these parameters are part of other IBP criteria then the ASAS criteria. All descriptive data was presented as n (%) or means ( $\pm$ SD).

**Results:** All IBP parameters were collected from 228 patients and 49.6% ( $n=113$ ) was male with mean age of 34.7 years (SD 9.7). Individual parameters were present in  $>75\%$  of the patients; the parameter 'age at onset  $< 40$  years' was present in 95.2%, 'insidious onset' in 89%, 'improvement with exercise' in 86%, 'no improvement with rest' in 81.6% and 'pain at night' in 75.9% of the patients. There were 83 patients (36.4%) with alternating buttock pain and 173 patients (75.9%) with morning stiffness.

More than 80% of the patients (183/228) had IBP according to the ASAS criteria as they had  $\geq 4$  IBP parameters. Patients rarely had 1 or 2 IBP parameters; 2 (0.9%) patients with 1 parameter and 12 (5.3%) patients with 2 parameters (table 1).

**Abstract THU0265 – Table 1.** Total number of ASAS-IBP parameters in patients with axSpA diagnosis and classified according to the ASAS criteria in the Be-Giant cohort.

	Be-Giant cohort n=228
0 IBP parameters	0
1 IBP parameters	2 (0.9%)
2 IBP parameters	12 (5.3%)
3 IBP parameters	31 (13.6%)
4 IBP parameters	59 (25.9%)
5 IBP parameters	124 (54.4%)

IBP, inflammatory back pain.

IBP parameters: Age onset back pain  $< 40$  years, insidious onset of back pain, improvement with exercise, no improvement with rest, pain at night.

**Conclusions:** The majority of early axSpA patients had  $\geq 4$  IBP parameters and therefore fulfilled the ASAS IBP criteria. A minority shows 1 or none IBP parameter. Hence, the inflammatory character of axSpA does not seem to subverted now that IBP is not a mandatory feature in classification of axSpA.

**Disclosure of Interest:** None declared

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#### THU0266 THE VALUE OF BELONGING TO PATIENTS' ASSOCIATION FOR AXIAL SPONDYLOARTHRITIS: RESULTS FROM THE ATLAS-2017

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**Background:** International guidelines suggest that patients with axial spondyloarthritis (axSpA) become members of patient associations and self-help groups. However, the scientific evidence for this advice is limited and poor.

**Objectives:** To assess the relationship between membership of axSpA patient associations with regard to physical and psychological outcomes of the disease.

**Methods:** A sample of 680 axSpA patients was interviewed as part of the Spanish-2017 Atlas, which aimed to promote early referral, improve healthcare, and the use of effective treatments in patients with axSpA. By means of an online survey, the following self-reported data were collected: sociodemographic, smoking habits, degree of functional limitation in 18 daily activities (graded from 0–3 as none, little, some, moderate), spinal stiffness level at cervical, thoracic, and lumbar spine (0–3 none, little, some, moderate), disease activity through BASDAI (0–10), risk of severe psychiatric illness using General Health Questionnaire – GHQ-12 (0–12), and treatment received (NSAIDs and biological therapy). Differences for all these variables between associated-patients and non-associated patients were tested, using Mann-Whitney or Chi-square tests.

**Results:** Out of 680 patients, 301 (44.3%) were members of patient associations. Compared to non-associated patients, those associated were older, more frequently male, married, and few smoked (table 1). Additionally, despite having longer disease duration and receiving similar treatment, associated patients had lower disease activity (BASDAI 5.1 vs 5.8;  $p=0.001$ ), less functional limitation (26.5 vs 28.7;  $p<0.05$ ), and less risk of severe psychiatric illness (GHQ-12 4.9 vs 6.5;  $p<0.001$ ).

**Abstract THU0266 – Table 1.** Characteristics stratified by patient association membership status

	Associated (mean $\pm$ SD or %)	Non-Associated (mean $\pm$ SD or %)	P
Age (years)	49.7 $\pm$ 11.2	42.4 $\pm$ 9.4	$<0.001$
Gender (Male)	57.8%	39.3%	$<0.001$
Education Level (University)	34.6%	38.8%	0.3
Marital Status (Married)	79.1%	65.4%	$<0.001$
Smoker	32.6%	41.6%	$<0.01$
Disease duration (years) (n=555)	26.0 $\pm$ 12.4	17.0 $\pm$ 10.3	$<0.001$
HLA-B27 (Positive) (n=558)	79.7%	74.9%	0.097
Treatment			
- NSAIDs (without biology)	28.6%	30.9%	0.5
- Biological (monotherapy or with NSAIDs)	39.2%	34.0%	0.2
BASDAI (0–10) (n=442)	5.1 $\pm$ 2.1	5.8 $\pm$ 2.1	0.001
Stiffness			$<0.01$
-Without Stiffness - low	10.2%	11.2%	
- mild			
- high	17.6%	20.0%	
Functional Limitation (0–54) (n=605)	26.5 $\pm$ 13.4	28.7 $\pm$ 12.9	0.038
GHQ-12 (0–12) (n=474)	4.9 $\pm$ 4.5	6.5 $\pm$ 4.4	$<0.001$

**Conclusions:** In axSpA, belonging to patient associations is related to better physical and psychological outcomes. Accordingly, rheumatologists should encourage patients to join these groups. However, further data on longitudinal studies is required to confirm these results.

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THU0267

### GASTROINTESTINAL INVOLVEMENT IN SPONDYLOARTHRITIS IS NOT ALL IBD: INCREASED RISK OF DIVERTICULITIS WITH LONGER DISEASE DURATION IN THE ASAS-COMOSPA COHORT

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**Background:** Inflammatory bowel disease (IBD) is an established extra-articular manifestation of Spondyloarthritis (SpA). The association of SpA with other gastrointestinal and hepatic comorbidities is less well known.

**Objectives:** To examine the relationship between SpA disease duration and gastrointestinal comorbidities other than IBD.

**Methods:** ASAS-COMOSPA is a large global cross-sectional study comprising 3984 patients with SpA. We evaluated the association between "SpA disease duration" (defined in 5 year blocks) and upper gastrointestinal ulcers, hepatitis B (HBV), hepatitis C (HCV) and diverticulitis. Binary logistic regression models were created, adjusted for age, sex, BMI, smoking, alcohol, NSAIDs, DMARDs, biologics, steroids and IBD history. Subgroup analysis was performed, stratified by peripheral and/or axial joint involvement.

**Results:** The data of 3923 patients (64.9% male) were available for analysis, 5.3% of whom had a history of IBD. The self-reported prevalence of other gastrointestinal conditions was: upper gastrointestinal ulcers 10.7%; viral hepatitis 4.7% and diverticulitis 1.5%, with significant geographic variation. "SpA disease duration" was not associated with the occurrence of the upper gastrointestinal ulcers (OR=0.98, 95% CI: 0.92–1.05), HBV (OR=0.43, 95% CI: 0.28–0.67) or HCV (OR=0.27, 95% CI: 0.11–0.62). In contrast, the risk of diverticulitis was significantly increased by "SpA disease duration" (OR=1.14, 95% CI: 1.01–1.29); increased risk of 14% for every 5 years of disease duration) across the entire cohort, after adjustment for potential confounders, including age. Confounding variables showing significant association with diverticulitis were current age (OR=1.06, 95% CI: 1.04–1.08) and high alcohol (≥3 units/day) intake (OR=3.84, 95% CI: 1.62–9.07) but not medication history (table 1). Subgroup analyses revealed stronger association of SpA disease duration with diverticulitis in those with axial (OR=1.24, 95% CI: 1.08–1.42) than those with peripheral (OR=1.12, 95% CI: 0.98–1.29) SpA disease.

Abstract THU0267 – Table 1. Association between diverticulitis and SpA disease duration

	p value	OR	95% CI for OR
<b>SpA Disease Duration (5 y blocks)</b>	<b>0.032</b>	<b>1.14</b>	<b>1.01–1.29</b>
Delay in SpA Diagnosis	0.477	1.01	0.98–1.04
Age (year)	<0.001	1.06	1.04–1.08
Gender (ref: Female)	0.062	0.57	0.31–1.03
Current BMI	0.965	1.00	0.95–1.05
Smoking (pack-year)	0.354	1.01	0.99–1.02
Alcohol (ref: Never)	0.022		
Ex-drinker	0.731	1.25	0.35–4.51
Current, <3 Units	0.132	1.66	0.86–3.23
Current, ≥3 Units	0.002	3.84	1.62–9.07
Ever use of NSAIDs	0.816	0.90	0.37–2.21
Ever use of Steroids	0.380	1.30	0.73–2.31
Ever use of DMARDs	0.805	0.93	0.51–1.69
Ever use of Biologics	0.613	1.16	0.66–2.04
History of IBD	0.904	1.07	0.37–3.12

**Conclusions:** Patients with SpA have a number of gastrointestinal comorbidities, including increased risk of diverticulitis with increased SpA disease duration, highest in those with axial disease. The reasons for this association are unclear and warrant further investigation. Diverticulitis should be considered, in addition to IBD, when patients with SpA present with lower gastrointestinal symptoms.

**Disclosure of Interest:** None declared

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THU0268

### THE FREQUENCY OF JUVENILE SPONDYLOARTHROPATHIES IN CHILDHOOD FAMILIAL MEDITERRANEAN FEVER

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**Background:** Familial Mediterranean fever (FMF) is the most common monogenic autoinflammatory disease characterised with fever, recurrent episodes of self-limiting polyserositis and arthritis. FMF arthritis is generally acute monoarthritis especially in the larger joints of the lower extremities, healing without a sequelae. However some of the patients develop different type of chronic arthritis, predominantly oligoarticular juvenile idiopathic arthritis (JIA) and juvenile spondyloarthropathies (JSpA). Studies on JSpA among childhood FMF patients are sparse.

**Objectives:** To evaluate frequency of JSpA in a large childhood FMF cohort. Furthermore, we aimed to define main characteristics of JSpA among childhood FMF patients.

**Methods:** A total of 320 juvenile FMF patients were blindly questioned according to recently proposed criteria for JSpA by 3 researchers (EO, DS, ET) that were previously educated for FMF and JSpA. A standardised case report form was prepared and completed for each patient. This form was including demographic data, clinical features, MEFV mutation and treatment. Patients fulfilled the JSpA criteria and were classified as probable JSpA. Afterwards, an expert in paediatric rheumatology (OK) reevaluated the classified patients and some of them were reconfirmed to be a definite while some of them were accepted as potential JSpA patients.

**Results:** As a result, 37 patients (11.5%) were initially classified as potential JSpA. Furthermore, 32 (10%) of them were accepted as definite and 5 (1.5%) patients as probable JSpA in childhood FMF. Demographic, clinical and treatment data of definitive JSpA patients are shown in Table I. The most frequent MEFV mutation among JSpA patients was M694V (63.33%).

Table I. Demographic, clinical and genetic features of childhood FMF patients.

	FMF + Definite JSpA	FMF + Probable JSpA	FMF patients without JIA and JSpA	FMF+JIA (except ERA or JSpA)
Patients, n	32	5	268	15
Female, n (%)	10 (31.25%)	1 (20%)	148 (55.22%)	10 (66.66%)
Age of disease onset, mean±SD years	7.19 ±3.68	5.60 ±4.93	4.91±3.40	4.93±3.32
Age at study, mean ±SD years	14.84 ±3.70	13.40 ±1.67	12.51±4.43	10.73±3.57
Family History of FMF, n (%)	15 (46.87%)	1 (20%)	132 (49.25%)	6 (40%)
Colchicine resistance in FMF patients, n(%)	2 (6.25%)	0	14 (5.22%)	1 (6.66%)
M694V mutation n(%)	19/30 (63.33%)	3 (60%)	148/245 (60.40%)	11 (73.33%)
Homozygote, n(%)	7 (26.31%)	2 (66.66%)	51 (34.45%)	8 (72.72%)
Heterozygote, n(%)	36.84%	1 (33.33%)	43 (29.05%)	2 (18.18%)
Compound heterozygote, n(%)	5 (36.84%)	0	23 (8.58%)	1 (9.09%)
NA, n(%)	7 (26.31%)	0	0	0
Disease onset over 6 years, n (%)	26 (81.25%)	5 (100%)		6 (40%)
Oligoarthritits, n(%)	21 (65.62%)	1 (20%)		14 (93.33%)
Inflammatory back pain, n(%)	17/32 (53.12%)	3/5 (60%)		0
Enthesopathy	22/32 (68.75%)	3/5 (60%)		0
Sacroiliitis	14/21 (66.66%)	0/1 (0)		0/5 (0)

**Conclusions:** Articular involvement compatible with JSpA could be seen in childhood FMF patients. Spondyloarthropathy was detected in 10% of childhood FMF cases. The M694V mutation is the most common MEFV mutation among JSpA patients with FMF. JSpA should be considered in childhood FMF patients, especially in those chronic arthritis, axial involvement and enthesopathy.

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THU0269

### DEVELOPMENT OF ANKYLOSING SPONDYLITIS IN PATIENTS WITH REACTIVE ARTHRITIS AND PERIPHERAL SPONDYLOARTHROPATHY: HOSPITAL BASED STUDY IN NORTH INDIA

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**Background:** Reactive arthritis (ReA) is a seronegative spondyloarthropathy (SpA) that is precipitated by urogenital or gastrointestinal infection. Undifferentiated Peripheral spondyloarthropathy (UpSpA) may be indistinguishable from ReA except known preceding infection. It is stated that two-thirds of ReA resolve within three months while a third develop chronic or recurrent course. However, there is a paucity of data on the long-term outcome. Thus, it is difficult to justify treatment decisions like the use of biologicals in ReA

**Objectives:** To determine the outcome of ReA/upSpA patients attending a referral rheumatology centre in North India.

**Methods:** ReA was classified as per Braun's criteria, while UpSpA were included as meeting ASAS criteria but not criteria for psoriatic arthritis or inflammatory bowel disease associated arthritis. Data on this retrospective cohort was updated with telephonic interviews. Follow-up of less than 1 year were excluded. Patients with persistent inflammatory back pain (IBP) were reviewed in the clinic. Radiographs assessed progression to AS (modified New York criteria).

**Results:** Follow-up data on 85 patients (63 ReA; 22 pSpA) was obtained. Median (IQR) age at presentation was 24.5 (20–33) years. 14 (16.5%) were female. At presentation, 23 (30%) had monoarthritis, 44 (57%) had oligoarthritis, 10 (13%) had polyarthritis (data missing for eight). Enthesitis and dactylitis were documented in 20 and 5 respectively. Keratoderma and balanitis were seen in one each. 40 (80%) out of 50 were positive for HLA-B27.

Median (IQR) follow-up was 2 (1–5.25) years. 22 had monophasic illness of which 13 had acute arthritis (<12 weeks). Seven had two episodes, 27 had polycyclic course while 29 had persistent arthritis. 26 had inflammatory back pain (IBP) at any time and eight had persistent symptoms. Out of these, three (3.5%) met criteria for AS (disease duration: 1, 3 and 10 years) while two had unilateral grade 2 sacroiliitis. Three patients without IBP also had sacroiliitis on radiographs. Logistic regression revealed no significant parameter that could predict progression to AS

**Conclusions:** In contrast to general opinion that two thirds attend remission, this study showed that one third undergo drug free remission. Of the remaining, half develop recurrent and half persistent arthritis. 3.5% progressed to AS. As duration of follow-up increases, a greater proportion may progress to AS.

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THU0270

### THE PROPENSITY TO FAT METAPLASIA OF SACROILIAC JOINT IN SPONDYLOARTHROPATHY: RESULTS FROM THE SINGLE REGIONAL CENTRE COHORT

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**Background:** The predictor of radiographic spinal progression is the presence of syndesmophytes at baseline in axial spondyloarthritis (axSpA) and fat metaplasia on spine may predict the formation of new syndesmophytes. Some studies suggest that fat metaplasia may be a potential starting point for new bone formation

and have a general systemic effect on new bone formation in spine, rather than results from local inflammation. Recent studies suggest that fat metaplasia on sacroiliac joint (SIJ) MRI at baseline is associated with spinal radiographic progression in axSpA patients.

**Objectives:** So in this study, we investigated for propensity to fat metaplasia on SIJ in axSpA patients.

**Methods:** The 357 patients who fulfilled the ASAS axSpA criteria were enrolled. All underwent MRI on SIJ with T2 MR image, T1 fat suppressed with enhanced and short τ inversion recovery (STIR) image at baseline and lumbar spine radiographs at baseline and after 2 years. Inflammatory and structural lesions on SIJ MRI was scored using the SPondylo Arthritis Research Consortium of Canada (SPARCC) method. Spinal radiographs were scored using the Stoke AS Spinal Score (SASSS). Multivariate logistic regression analysis was performed to identify for propensity to fat metaplasia on SIJ in axSpA patients.

**Results:** Among the 357 patients on baseline SIJ MRI finding, 182 patients showed fat metaplasia on SIJ, 148 patients showed erosion and 27 patients showed ankylosis. Propensity to fat metaplasia in axSpA patients showed the male, HLA-B27 negative, smoking, back pain onset time within 6–12 months at time of diagnosis, uveitis, peripheral arthritis, compared to erosion and ankylosis on SIJ in axSpA patients. The patient with fat metaplasia or ankylosis on SIJ at baseline showed increased SASSS but there was no significant change in SPARCC over 2 years. univariate logistic regression analysis showed back pain onset time within 6–12 months at time of diagnosis and uveitis as a significant predictors of fat metaplasia. multivariate logistic analysis showed back pain onset time within 6–12 months at time of diagnosis as an affecting factor for fat metaplasia on SIJ (OR,5.67; 95% CI 4.71–17.95).

**Abstract THU0270 – Table 1.** The radiographic spinal progression over 2 years according to structural lesion in the sacroiliac joints observed on baseline MRI

	Fat metaplasia	Erosion	Ankylosis
Baseline SASSS	8.5±11.5	24±4.1	18.5±11.8
Change in SASSS over 2 years	0.7±1.7	0.4±0.6	0.8±1.7

OR: odd ratio CI: confidence interval

**Abstract THU0270 – Table 2.** Univariate and multivariate analysis of affecting factor for fat metaplasia on SIJ

variables	univariate analysis		Multivariate analysis	
	OR(95% CI)	p-value	OR(95% CI)	p-value
Age at time of diagnosis (years)	1.10(1.05-1.15)	0.04		
HLA-B27 positive	0.28(0.09-0.84)	0.07		
Smoking	0.38(0.15-0.96)	0.06		
Back pain within 6-12months at time of diagnosis	1.12(0.89-10.91)	0.02	5.67(4.71-17.95)	0.03
Uveitis	2.59(1.04-6.44)	0.03	2.00(0.47-8.62)	0.07
BAGSMA	1.45(0.69-2.78)	0.05		
Peripheral arthritis	0.32(0.10-1.00)	0.06		
Elevated ESR	2.59(1.04-6.44)	0.06		
Elevated CRP	2.48(1.00-6.19)	0.06		

OR: odd ratio CI: confidence interval

**Conclusions:** The back pain onset time within 6–12 months at time of diagnosis was affecting factor for propensity to fat metaplasia on SIJ in axSpA patients statistically and fat metaplasia on SIJ was associated with radiographic spinal progression in axSpA patients. so the early detection of fat metaplasia on SIJ in axSpA patients was important to protection of radiographic spinal progression.

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Place of study, year of publication	Subjects	Female: male	Follow up	Remission	Chronic arthritis	HLA B27	Radiological sacroiliitis (including asymptomatic)
France, 20 161	62 ReA	10:52	45 pt; 34 months	54%	44% SpA; 4% PsA	64.3%	NA
Finland, 19 972	63 reactive salmonella arthritis	28:35	50 pt; mean 11 years	Drug free: 31.7%	28.5%	88%	13.6%
Helsinki, 2009 <sup>3</sup>	60 ReA	26:34	40 at 32 years	HAQ 0 in 15%	NA	85%	15%
Current study	61 ReA/14 uSpA	14:71	85 pt; median 2 years	Drug free: 35%	34%	80%	8.23%



THU0271

### EMERGENCE OF SEVERE SPONDYLOARTHROPATHY RELATED ENTHESEAL PATHOLOGY FOLLOWING VEDOLIZUMAB THERAPY FOR INFLAMMATORY BOWEL DISEASE

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**Background:** The Spondyloarthritides (SpA) and inflammatory bowel disease (IBD) share common aetiopathogenetic and clinical manifestations. Vedolizumab, a humanised IgG1 monoclonal antibody to  $\alpha 4\beta 7$  integrin, has been approved for the treatment of inflammatory bowel disease (IBD) and inhibits  $\alpha 4\beta 7$  integrin at the gut level. Vedolizumab therapy for IBD has been associated with mild SpA related features including sacroiliitis and synovitis. Herein, we report the emergence of severe SpA under therapy with Vedolizumab.

**Objectives:** We conducted a clinical evaluation of 7 vedolizumab treated patients with IBD that developed severe active SpA and/or enthesopathy with the aim of characterising the vedolizumab associated SpA/enthesal flares.



**Methods:** Vedolizumab treated IBD patients with SpA/enthesopathy were identified across four hospitals. We identified clinical, biochemical and imaging characteristics within routine case records as part of a clinical evaluation.

**Results:** We identified 6/7 subjects that developed *de novo* SpA/enthesopathy and 1/7 (subject 1) with a severe flare of pre-existing SpA. There were 3/7 patients hospitalised due to the severity of skeletal disease. The median time from vedolizumab initiation to flare was 10 weeks (table 1 below). Subject 4 developed new-onset SpA with severe spinal vertebral end-plate oedema (T6–12) and inflammatory Romanus lesions (L3–4) (image below). Acute sacroiliitis was identified on MRI in 3 subjects, one of which showed evidence of radiographic bilateral grade 2 sacroiliitis. In at least 4 cases the IBD disease activity was considered to be low or well controlled. Following vedolizumab discontinuation, so far 3 patients have switched to alternative biologic therapies including certolizumab pegol, golimumab, and 1 subject to sulphasalazine.

cpd=cigarettes per day, MTX=methotrexate, AZA=azathioprine, OC=oral corticosteroid, Pred=prednisolone, nr=non radiographic, MRI+ve= MRI positive, XR+ve = radiograph positive, NA=not available.

**Conclusions:** This case series demonstrates severe vedolizumab associated SpA/enthesopathy that resulted in hospitalised cases. The severity of vedolizumab related SpA flares is relatively severe disease in comparison to the literature. We recognise that vedolizumab is efficacious in IBD, however our observations highlight the need to monitor symptoms to identify patients that develop axial or peripheral SpA several weeks from commencing vedolizumab.

**Disclosure of Interest:** None declared

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THU0272

### WHICH SCORING METHOD DEPICTS SPINAL RADIOGRAPHIC DAMAGE IN (EARLY) AXIAL SPONDYLOARTHRITIS BEST? FIVE-YEAR RESULTS FROM THE DESIR COHORT

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**Background:** Scores capturing spinal radiographic damage have been proposed and compared in r-axSpA. In early phases of the disease, it is still unknown how these perform.

**Objectives:** To compare the performance of different radiographic scores of the spine in patients with early axial spondyloarthritis (axSpA).

**Methods:** Five-year follow-up data (baseline, 2 and 5 years) from the DESIR cohort, including patients with early axSpA, have been used. Spine (cervical, thoracic and lumbar), sacro-iliac joints (SI), and hips were scored on radiographs centrally and independently by 3 readers (scores averaged) for the calculation of different radiographic methods (table 1). Following the OMERACT filter, scores were compared with regard to truth, discrimination (sensitivity to change and reliability) and feasibility. Baseline status scores, and 2- and 5 year change scores were calculated for each of the methods, as well as the proportion of patients with a net change (number of patients with a positive change minus number of patients with a negative change divided by all patients) above the smallest detectable change (SDC). The proportion of total variance explained by the patient ('true variance') was calculated for the change scores of the different instruments and their components using ANOVA, as a measure of reliability.

**Results:** In total, 699 patients (mean age 34 (SD 9) years, 47% males) had at least one radiograph available. Mean baseline and 5 year change scores were: mSASS 0.4(SD 1.5) and 0.4 (1.8), RASSS 0.5 (1.6) and 0.6 (2.2), SASSS 0.2 (0.7) and 0.3 (1.1), BASRI spine 1.0 (1.2) and 0.2 (0.6), BASRI spine with thoracic spine: 1.1 (1.4) and 0.3 (0.7), BASRI total 1.0 (1.3) and 0.3 (0.6) and BASRI total with thoracic spine 1.2 (1.4) and 0.3 (0.7), respectively. SDCs and proportion of 2- and 5 year change, including net change, are presented in the table 1. The

Subject number	1	2	3	4	5	6	7
Age, M/F	28, M	48, M	33, F	50, M	35, F	40, F	21, F
Hospitalised	Y	N	N	N	Y	Y	N
Vedolizumab exposure (weeks)	14	20	20	6	8	10	5
SpA type	per+axSpA (MRI+ve, perifacetal spinal vertebral oedema)	per+axSpA (acute sacroiliitis MRI+ve)	axSpA (MRI +ve sacroiliitis)	nr-axSpA (MRI+ve, extensive thoracolumbar vertebral oedema/osteitis and inflammatory corner lesions)	nr-axSpA	Enthesitis/periostitis distal tibio-fibular (MRI+ve)	per+axSpA (MRI +ve and XR +ve sacroiliitis)
HLA-B27	N	NA	NA	N	Y	NA	N
Smoker (cpd)	15	NA	NA	25	N	NA	N
EIMs (Uveitis, PsO)	N	N	PsO	N	PsO	N	N
IBD activity	Low	NA	NA	High	Low	Low	Low/well controlled
CRP at flare (mg/l)	216	<5	<5	24	24	28	55
Concomitant immunosuppressive therapy	MTX 15 mg s/c/week	AZA 150 mg/day	OC (Pred 0.5 mg/day)	Nil	Nil	OC (4 mg Pred)	Nil

mSASSS and the RASSS performed the best in terms of capturing the signal (i.e. positive change) despite the noise (i.e. negative change), which is taken into account in the net change calculation.

The proportion of variance explained by the patient for the radiographic scores was highest for the mSASSS and RASSS, both for status and progression scores (e.g. 70% for mSASSS 69% for RASSS 2 year progression). However, the proportion of patient variance in the thoracic segment of the RASSS was unsatisfactory (36% for 2 year progression, compared to 54% lumbar segment and 73% cervical segment).

In what concerns feasibility, all scores seemed feasible, but the thoracic segment was missing in up to 7% of the cases, thus not allowing computation of BASRI modifications to include that segment.

**Abstract THU0272 – Table 1.** Two- and 5-year change, above the smallest detectable change, across the different radiographic scores

	2-year Change > SDC				5-year Change > SDC					
	N	SDC	Positive change N (%)	Negative change N (%)	Net change N (%)	N	SDC	Positive change N (%)	Negative change N (%)	Net change N (%)
mSASSS (0-72)	488	0.9	29 (6)	6 (1)	23 (5)	372	1.1	41 (11)	3 (1)	38 (10)
RASSS (0-84)	484	1.0	26 (5)	2 (0.4)	24 (5)	370	1.2	54 (15)	1 (0.3)	53 (14)
SASSS (0-72)	499	0.8	13 (3)	0 (0)	13 (3)	389	1.2	36 (9)	0 (0)	36 (9)
BASRI spine (0-12)	484	0.6	40 (8)	22 (5)	18 (4)	371	0.7	39 (11)	2 (0.5)	37 (10)
BASRI spine with thoracic (0-16)	360	0.6	35 (10)	17 (5)	18 (5)	267	0.9	31 (12)	2 (1)	29 (11)
BASRI total (0-16)	480	0.6	41 (9)	22 (6)	19 (4)	368	0.8	41 (11)	2 (0.5)	39 (11)
BASRI total with thoracic (0-20)	358	0.7	19 (4)	4 (1)	15 (3)	266	0.9	32 (12)	2 (1)	30 (11)

SDC, smallest detectable change; mSASSS, modified Stoke in Ankylosing Spondylitis Spine Score; RASSS, Radiographic Ankylosing Spondylitis Spinal Score; SASSS, Stoke Ankylosing Spondylitis Spine Score; BASRI, Bath Ankylosing Spondylitis Radiology Index.

**Conclusions:** The existing scoring methods to assess spinal radiographic damage performed well in early phases of axSpA. The mSASSS and RASSS captured most change. There was no clear gain in additionally scoring the thoracic spine for the RASSS while an increased noise was introduced. The mSASSS remains the most sensitive and valid scoring method in axSpA, including early phases of the disease.

**Disclosure of Interest:** None declared

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#### THU0273 PREVALENCE OF VERTEBRAL FRACTURES IN ANKYLOSING SPONDYLITIS: A META-ANALYSIS

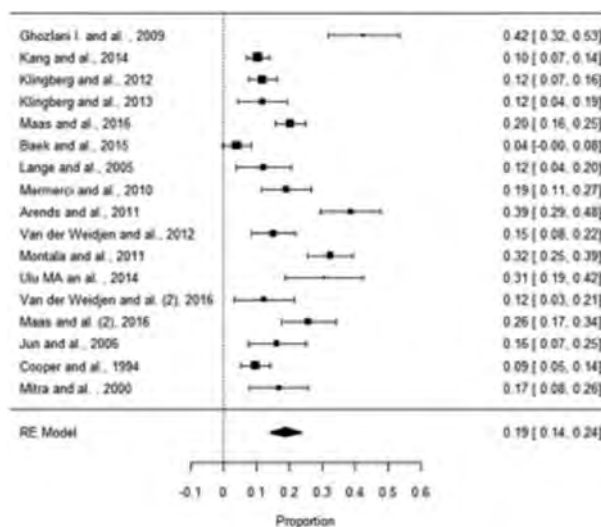
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**Background:** Osteoporosis is a well-recognised feature of ankylosing spondylitis (AS). Patients with AS have an increased risk of vertebral fractures (VF) but prevalence of VF is variable across studies from 4% to 42%. The diagnosis of VF is still problematic because frequently asymptomatic and sometimes difficult to differentiate from vertebral deformities which are not fractures.

**Objectives:** The aim of our study was to determine the prevalence of VF in AS and the risk factors associated.

**Methods:** Two independent investigators conducted a search in Medline and Cochrane databases, including cohorts, cross-sectional, and case-control studies that had assessed the prevalence of VF in patients with AS fulfilling the modified New York criteria. We collected data about study design, demographics, disease activity and severity (HLA B27 antigen status, BASDAI, BASFI, ASDAS, mSASSS, CRP, ESR, treatment history), bone mineral density, method of VF assessment (method of X-rays reading, number of readers) and characteristics of VF (number, prevalence, grade).

**Results:** Among 434 screened studies, 17 were eligible for meta-analysis. The pooled VF prevalence in patients with AS was 19% (95% CI 14%>24%, I<sup>2</sup>90.5%) (figure 1). The CRP (p<0.001) and mSASSS (p=0.046) scores were associated with a higher risk of VF. When focusing only on moderate to severe VF, HLA B27 antigen (p=0.046), lumbar spine osteoporosis (p=0.018) and osteopenia (p=0.024), hip BMD (p=0.024), CRP (p=0.004), ESR (p<0.001), and Genant method (p=0.009) were associated with higher risk of VF.



**Conclusions:** Despite a large heterogeneity among studies, the prevalence of VF in AS patients is high. CRP and mSASSS scores were associated with the prevalence of all VF. Classical VF risk factors, such as osteoporosis, were associated only with moderate and severe VF.

**Disclosure of Interest:** None declared

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#### THU0274 ASSESSMENT OF RADIOGRAPHIC SACROILIITIS ON ANTERO-POSTERIOR LUMBAR RADIOGRAPHS AS COMPARED TO CONVENTIONAL PELVIC RADIOGRAPHS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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**Background:** EULAR guidelines consider conventional radiography of sacroiliac joints (SIJs) as the first recommended imaging method in case of suspected axial spondyloarthritis (axSpA).<sup>1</sup> However, it is not clear whether sacroiliac joints can be reliably assessed on anteroposterior (AP) lumbar radiographs, which are often performed as a part of the diagnostic work-up in patients presented with back pain.

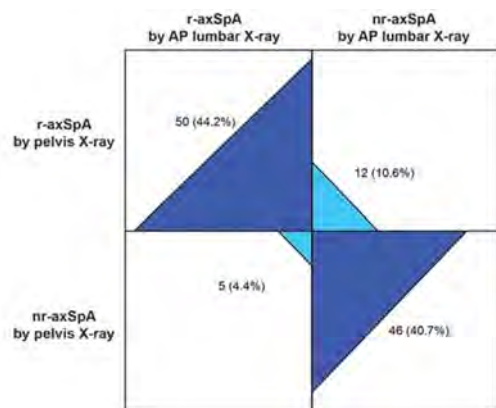
**Objectives:** To investigate reliability and validity of radiographic sacroiliitis assessment on AP lumbar radiographs as compared to conventional pelvic X-rays in patients with axSpA.

**Methods:** Patients from the GERman SPondyloarthritis Inception Cohort (GESPIC) were selected based on the availability of sets of pelvic and AP lumbar radiographs with visible SIJs at baseline and after 2 years of follow-up. Two trained readers (ML and VR) scored the images independently and in a random order according to the radiographic system of the modified New York (mNY) criteria (grade 0 to 4). The sacroiliitis sum score (0–8) was calculated as a sum of the mean grades of 2 readers for the right and left SIJ. We assessed intra- and inter-reader reliability using intraclass correlation coefficients (ICC) of the sacroiliitis sum scores. Patients were classified as having radiographic axSpA (r-axSpA) when both readers agreed on the presence of definite radiographic sacroiliitis according to the mNY criteria, and non-radiographic axSpA (nr-axSpA) otherwise.

**Results:** A total of 226 sets radiographs were scored from the 113 patients included in the present study. Intra-observer agreement was good to excellent for

the sacroiliitis sum score of pelvic vs. AP lumbar radiographs. Inter-observer agreement for pelvic and AP lumbar radiographs was also good to excellent: ICC at baseline: 0.81 and 0.73, respectively, at year 2: 0.76 and 0.79, respectively. A total of 62 (54.9%) and 55 (48.7%) patients were classified as r-axSpA at baseline based on evaluation of pelvic and AP lumbar radiographs, respectively. The absolute agreement on the classification was 84.9% (figure 1). A total of 17 patients (12 (10.6%) with nr-axSpA and 5 (4.4%) with r-axSpA) were classified differently based on assessment of AP lumbar as compared to conventional pelvic radiographs (figure 1).

After 2 years of follow-up, progression from nr- to r-axSpA occurred in 7 patients (6.2%) and 8 patients (7.1%) classified as nr-axSpA at baseline based on pelvic or AP lumbar radiographs assessment, respectively. Regression from r- to nr-axSpA occurred in 4 patients (3.5%) and 3 patients (2.7%) on pelvic or AP lumbar radiographs, respectively, giving a respective net progression rates of 2.7% and 4.4%.



**Abstract THU0274 – Figure 1.** Classification as non-radiographic or radiographic axial spondyloarthritis based on sacroiliitis assessment on conventional pelvic and anteroposterior lumbar radiographs.

**Conclusions:** Radiographic sacroiliitis can be assessed on AP lumbar radiographs with a similar reliability as on conventional pelvic radiographs.

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THU0275

#### THE RELATIONSHIP BETWEEN MAASTRICHT ANKYLOSING SPONDYLITIS ENTHESITIS SCORE AND THE SPONDYLOARTHRITIS RESEARCH CONSORTIUM OF CANADA ENTHESITIS INDEX IN ANKYLOSING SPONDYLITIS: FRIENDS OR ENEMIES?

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**Background:** The enthesitis screening is critical for the diagnosis and for monitoring the disease activity in axial spondyloarthritis (AS). Several indices have been developed for the clinical evaluation of enthesitis, including the Maastricht Ankylosing Spondylitis Enthesitis Score (MASES) in 2003 and the Spondyloarthritis Research Consortium of Canada (SPARCC) in 2008. Each of them has advantages and limitations, but could they be complementary?

**Objectives:** The objective of our study was to compare the abilities of MASES and SPARCC in detecting enthesitis and to look for possible correlations between these two scores.

**Methods:** We designed this prospective study in 60 patients meeting modified New York criteria for AS and seen at the rheumatology department. All patients underwent a clinical evaluation, in which scores of MASES (range 0–13) SPARCC (range 0–16) and visual analogue scale (VAS) for enthesial pain were recorded. Ultrasound scans were taken for five entheses sites on both sides in lower limbs (proximal and distal insertions of the patellar tendon, patellar insertion of the quadriceps tendon, and calcaneal insertions of the Achilles tendon and superficial plantar fascia).

**Results:** Sixty AS patients were enrolled (48 men and 12 women) with a mean age of 36 years<sup>20–74</sup> and mean disease duration of 8.8 years [0.5–25]. Biological inflammation was detected in 51 patients with mean erythrocyte sedimentation rate (ESR) of 33<sup>2–98</sup> and mean C reactive protein of 16.9 mg/L [0–240]. Physical examination found 77/600 painful entheses sites (12.8%), of which quadriceps and calcaneum entheses were the most painful in 16% and 15.8% cases respectively. The mean MASES was 3.4 [0–13] and the mean SPARCC was 2.98 [0–16]. A null MASES and SPARCC scores were recorded in 18 (30%) and 23 (38%) patients respectively. US imaging of the entheses showed peritendinous oedema and bursitis mainly at distal insertions of the patellar tendon in 51% and 55% respectively. Erosions were more likely detected at Achilles tendon site (95.8%). MASES and SPARCC scores were both significantly correlated with VAS for enthesial pain ( $r=0.52$ ;  $r=0.46$ ;  $p<0.0001$  respectively), with the BASDAI ( $r=0.39$ ;  $r=0.40$ ;  $p<0.0001$  respectively), with BASFI ( $r=0.45$ ;  $r=0.39$ ;  $p<0.0001$ ), with VAS for global pain ( $r=0.55$ ;  $r=0.51$ ;  $p<0.0001$  respectively) and with ESR ( $r=0.23$ ;  $p=0.012$  for both). The sonographic score for acute enthesitis correlated only with the MASES, however overall sonographic score correlated only with the SPARCC (table 1). The MASES and SPARCC scores were positively correlated ( $r=0.768$ ;  $p<0.0001$ ).

**Abstract THU0275 – Table 1.** Correlations among clinical and sonographic scores.

Enthesitis indices	Sonographic score for acute enthesitis	Overall sonographic score	Sonographic score for chronic enthesitis	Doppler score
MASES	$r=0.24$ $p=0.008$	$r=0.114$ $p=0.2$	$r=0.14$ $p=0.12$	$r=0.1$ $p=0.27$
SPARCC	$r=0.15$ $p=0.09$	$r=0.198$ $p=0.030$	$r=0.17$ $p=0.05$	$r=0.12$ $p=0.18$

**Conclusions:** Good correlations were found between the 2 enthesitis indices in AS with special sonographic features for each, attesting their complementary relationship.

**Disclosure of Interest:** None declared

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THU0276

#### MRI LESION DEFINITIONS IN AXIAL SPONDYLOARTHRITIS: A CONSENSUS REAPPRAISAL FROM THE ASSESSMENTS IN SPONDYLOARTHRITIS INTERNATIONAL SOCIETY (ASAS)

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**Background:** There has been substantial progress in the characterisation of MRI lesions in the sacroiliac joints (SIJ) and spine in axial spondyloarthritis (axSpA) since the last consensus-based descriptive reports from ASAS<sup>1,2</sup>. There is as yet a lack of international consensus on standardised definitions of all the lesions reported to date. Consequently, the ASAS MRI group was convened to generate a consensus update.



**Objectives:** To evaluate the literature describing the spectrum of MRI lesions in axSpA and to generate a consensus update on standardised definitions.

**Methods:** The literature pertaining to MRI lesion definitions in axSpA was discussed at 3 meetings of the ASAS MRI group attended by 26 investigators. The group reviewed the literature for MRI lesion definitions and decided by consensus which definitions would be retained, which required modification, and which required a new definition.

**Results:** For definitions denoting signs of activity in the SIJ, there are no revisions to the most current ASAS definition of a positive MRI<sup>1</sup>. Definitions for capsulitis and enthesitis are revised. A new definition, *joint space enhancement*, denotes increased signal on contrast-enhanced images in the joint space of the cartilaginous portion of the SIJ. This replaces the term 'synovitis' and a separate definition describes what constitutes joint space fluid. For structural change in the SIJ, the definition for sclerosis is unchanged. Revised definition for a fatty lesion incorporates characteristics typical of axSpA, and for erosion requires both loss of cortical bone as well as adjacent marrow matrix. A new definition, *fat metaplasia in the joint space ('backfill')*, denotes the reparative change on a T1W image at the site of erosion when signs of activity recede. The new definition for ankylosis stresses the continuity of bright marrow signal across the joint space. Spinal lesion definitions are divided into those that occur in defined central and lateral sagittal slices. The revised definition of a vertebral corner inflammatory lesion divides this into a regular (type A) and dimorphic (type B) lesion. A new definition for corner erosion requires both loss of cortical bone as well as adjacent marrow matrix. New definitions for new bone growth require bright signal on T1W images extending from the vertebral corner marrow or endplate, which may (ankylosis) or may not (bone spur) be continuous with the adjacent vertebra.

**Conclusions:** The ASAS MRI group has generated a consensus based update on MRI lesions in axSpA.

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THU0277

#### WHICH MRI LESIONS IN THE SACROILIAC JOINT ARE ASSOCIATED WITH THE DIAGNOSIS OF AXIAL SPONDYLOARTHRITIS AFTER 2 YEARS FOLLOW UP IN THE ECHOGRAPHY IN SPONDYLOARTHRITIS COHORT (ECHOSPA)?

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**Background:** MRI of the sacroiliac joint (SIJ) is emerging as an important prognostic tool for assessment of patients presenting with SA and this may have consequences for early treatment. A major challenge in early SA is establishing the diagnosis and this requires prospective follow up to determine which cases have developed SA with more certainty. In addition, it is unclear which MRI lesions have prognostic capacity

**Objectives:** To assess the baseline distribution and prognostic capacity of MRI lesions in the SIJ of patients diagnosed with axSpA after 2 years follow up in the ECHOSPA cohort.

**Methods:** Consecutive outpatients with age <50 years and symptoms >3 months suggestive of SpA (inflammatory back pain, peripheral arthritis or inflammatory arthralgia, enthesitis or dactylitis, uveitis with B27 positivity, a family history of SpA) were enrolled in the prospective French ECHOSPA cohort study. The diagnosis of SpA was ascertained by an expert committee, blind to MRI evaluation, after at least 2 years of follow-up. MRI scans from 223 cases were available for evaluation by 2 readers and an adjudicator who assessed MRI lesions in the SIJ according to updated consensus definitions from the ASAS-MRI group. These were recorded in an ASAS consensus-derived eCRF that comprises global assessment (active and/or structural lesion typical of axSpA present/absent) and detailed scoring of individual lesions (SPARCC SIJ inflammation, SPARCC SIJ structural). Clinical, lab, and imaging variables associated with the diagnosis of axSpA at 2 years were first identified by univariate regression. A base model of all clinical/lab variables associated with axSpA was included as a group in multivariate logistic regression models that tested the independent association with MRI lesions.

**Results:** Mean age of the 223 cases was 39.6 (10.5) years, mean symptom duration was 2.5 (4.1) years, 49.5% were HLA-B27 + and 63.7% were female. Primary inclusion criterion was IBP in 53%, IA in 27%, ED in 9%, B27 +U in 8% and Fam in

4%. At 2 years follow up, 165 (74%) were deemed to have axSpA. In group comparisons (table 1) and univariate regression, both active and structural MRI lesions were associated with diagnosis of axSpA at 2 years (p=0.03, p=0.01, respectively). Age, B27, and psoriasis were the clinical variables associated with diagnosis of axSpA at 2 years in univariate analysis (all p<0.0001) and were included together with gender in multivariate analyses. Active and structural lesions typical of axSpA and SPARCC BME score ≥2 were each independently associated with diagnosis of axSpA at 2 years (OR(95% CI)- 6.8 (1.4–34.1) (p=0.02); 17.9 (2.2–146.6) (p=0.007); 4.9 (1.3–18.4) (p=0.02). With all variables simultaneously added to the model, only structural lesions were significantly associated.

**Abstract THU0277 – Table 1.** Distribution of MRI lesions at baseline according to diagnosis of axSpA after 2 years

MRI Lesion	AxSpA n=165 (74.0%)	NOT SpA n=58 (26.0%)	P value
Active lesion typical for axSpA	26 (16.0%)	2 (3.6%)	0.019
Active lesion typical for axSpA (confidence ≥3, 0-4 scale)	18 (11.9%)	1 (1.8%)	0.027
ASAS MRI positivity	24 (14.6%)	1 (1.7%)	0.006
ASAS MRI positivity (confidence ≥3, 0-4 scale)	17 (10.8%)	1 (1.7%)	0.048
Structural lesion typical for axSpA	32 (19.6%)	1 (1.8%)	0.0004
Structural lesions typical for axSpA (confidence ≥3, 0-4 scale)	27 (17.3%)	0 (0%)	0.0002
Active AND structural lesion typical for axSpA	19 (11.7%)	0 (0%)	0.004
Active OR structural lesion typical for axSpA	39 (23.9%)	3 (5.4%)	0.001
Only active lesion typical of axSpA	7 (4.3%)	2 (3.6%)	1.0
Only structural lesion typical of axSpA	13 (8.0%)	1 (1.8%)	0.12

**Conclusions:** Assessment of both active and structural lesions on MRI may help determine which patients have axSpA with higher diagnostic certainty over time.

**Disclosure of Interest:** None declared

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THU0278

#### SERUM CALPROTECTIN IS CORRELATED WITH DISEASE ACTIVITY IN EARLY AXIAL SPONDYLOARTHRITIS BUT DOES NOT PREDICT RADIOGRAPHIC PROGRESSION AT 2 YEARS: RESULTS FROM THE DESIR COHORT

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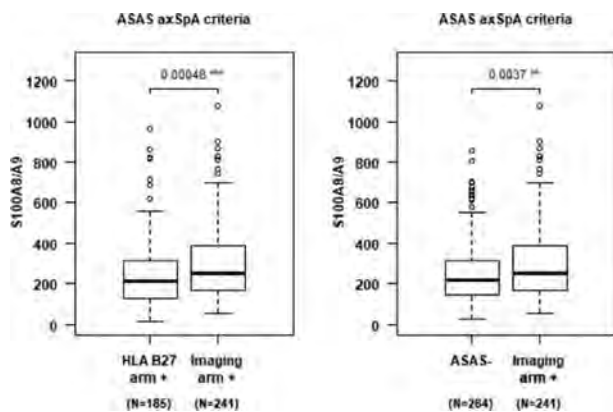
**Background:** Calprotectin (S100A8/A9), a protein secreted by activated neutrophils and monocytes in inflammatory conditions, is upregulated in active spondyloarthritis and associated with radiographic spinal progression in axial spondyloarthritis (axSpA)<sup>2</sup>

**Objectives:** To determine if serum calprotectin level at baseline can predict the radiographic progression of structural damage in spine at 2 years in the early axSpA cohort DESIR (DEvenir des Spondyloarthrites Indifférenciées Récentes) and to compare the association with spine and sacroiliac joint (SIJ) inflammation on magnetic resonance imaging (MRI).

**Methods:** Patients presenting with inflammatory back pain suggestive of axSpA for less than 3 years from the DESIR cohort were analysed. axSpA patient were defined as patients who fulfilled the Assessment in SpondyloArthritis Society (ASAS) criteria for axSpA at baseline. Calprotectin was assessed in the serum at baseline with ELISA kit (Hycult Biotech, the Netherlands). Spine radiographs, SIJ and spine MRI were centrally scored. Radiographic spinal progression was defined as worsening by ≥2 units of the mSASSS 2 years after the inclusion. Level of MRI spine and SIJ inflammation at baseline and 2 years was evaluated with BERLIN and SPARCC score. The associations between calprotectin level and mSASSS worsening were tested with Wilcoxon test, Berlin and SPARCC score were tested by Spearman's correlation tests.

**Results:** Of all, 426 had a calprotectin dosage and an early axSpA according to the ASAS criteria. Among them, 211 patients have had a mSASSS scoring at baseline and M24. A total of 399 patients have had spinal and SIJ MRI scoring at baseline. Only 15 patients had a radiographic progression with a variation of mSASSS ≥2. We showed a correlation between baseline calprotectin and MRI inflammation in SIJ or spine (Berlin score (r=0.15, p=0.003), SPARCC Sacroiliac score (r=0.12, p=0.012) and SPARCC Spine score (r=0.16, p=0.002)). Calprotectin baseline level was significantly higher in patients who fulfilled axSpA ASAS sacroiliitis arm criteria versus those who fulfilled ASAS HLA B27 arm criteria without any signs of sacroiliitis or versus patients did not fulfil ASAS criteria

(respectively  $p < 0.001$ ,  $p = 0.004$ ). Calprotectin level was correlated with baseline disease activity index (BASDAI ( $r = 0.16$ ,  $p = 0.001$ ), ASDAS-CRP ( $r = 0.26$ ,  $p < 0.001$ )) and disability score (BASFI ( $r = 0.14$ ,  $p = 0.003$ ), ASQoL ( $r = 0.16$ ,  $p = 0.001$ )). Interestingly, calprotectin at baseline did not predict radiographic progression at M24 (mSASSS worsening  $0.27 \mu\text{g/mL} \pm 0.14$  vs without mSASSS worsening  $0.29 \mu\text{g/mL} \pm 0.19$  (mean  $\pm$  SD)). There was also no correlation between calprotectin level and number of syndesmophytes.



**Conclusions:** Calprotectin do not seem to be a helpful biomarker predicting clinically relevant radiographic progression at 2 years although calprotectin levels at baseline are moderately correlated with disease activity in early axSpA.

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**Disclosure of Interest:** None declared

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#### THU0279 GENDER DIFFERENCE IN PSYCHOLOGICAL STATUS AND SLEEP QUALITY IN THE PATIENTS WITH ANKYLOSING SPONDYLITIS

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**Background:** Ankylosing spondylitis (AS) is a chronic inflammatory disease which mainly involves the spine and sacroiliac joints. Anxiety and depression, are common among people with arthritis and interplay independently and synergistically with clinical outcomes such as pain and disability.<sup>1</sup> Psychological variables can be found either within the body functions or within the personal factors.<sup>2</sup> Meanwhile, AS patients may suffer from various sleep problems. Pain intensity, anxiety, and depression correlated significantly with poorer sleep quality.<sup>3</sup> Whether gender difference exists in psychological status and sleep disturbance in AS patients remains unknown.

**Objectives:** Our aim was to investigate the prevalence of psychological disorders and sleep disturbance in Chinese patients with AS and then to explore gender difference in psychological status and sleep quality in the patients with AS.

**Methods:** Patients fulfilling modified New York criteria were enrolled from several rheumatology centres in China. Participants were required to complete a set of questionnaires and examinations, including demographic and clinical information, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI), Zung self-rating anxiety scale (SAS), Zung self-rating depression scale (SDS) and the Pittsburgh Sleep Quality Index questionnaire (PSQI). Independent T test was performed to compare patients with different gender.

**Results:** Totally 3117 patients were included in the study. 2501 were males, and mean age were  $27.20 \pm 9.13$  years. While 616 were female patients' whose mean age were  $28.84 \pm 9.21$  years. 32.3% of the patients had anxiety. 62.2% had depression according to SDS. 63.4% had sleep disturbance. Male patients had an earlier age of disease onset than females ( $p < 0.01$ ). Although female patients had a shorter disease duration, they had higher scores of SAS and SDS ( $p < 0.05$ ). There was no significant difference in sleep quality between male and female patients.

**Conclusions:** A large number of AS patients were found to have anxiety, depression, sleep disturbance. Male AS patients tend to have an earlier age of disease onset, while female patients are more likely to have psychological disorders. Clinicians should take these factors into account during the assessment of the patients.

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**Disclosure of Interest:** None declared

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THURSDAY, 14 JUNE 2018:

#### Psoriatic arthritis

#### THU0280 EARLY AND LONG-TERM TREATMENT RESPONSE AS WELL AS HIGH TOLERABILITY LEAD TO HIGH TREATMENT SATISFACTION OF A THERAPY WITH USTEKINUMAB IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS – RESULTS OF THE NON-INTERVENTIONAL STUDY SUSTAIN

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**Background:** SUSTAIN is a prospective, multi-centre non-interventional study in Germany to observe long term efficacy and safety, quality of life and further patient reported outcomes in patients with active psoriatic arthritis under treatment with ustekinumab in routine clinical care.

**Methods:** In this study nearly 400 patients were planned to be documented at 75 centres for 160 weeks with documentation intervals at week 0 and 4 and then every 12 weeks. The treatment with Ustekinumab is according to the label (Stelara®). Besides demographic data, the following data will be documented: Number of swollen and tender joints, tender entheses, amount of skin symptoms (BSA and PASI), patient reported outcome concerning disease activity and pain, Health Assessment Questionnaire (HAQ), quality of life (SF-12), sleep quality (VAS), satisfaction with therapy of patient and physician, safety (adverse events [AE]/serious adverse events [SAE]), pharmacoeconomic aspects, number of patients with "Minimal Disease Activity" (MDA), number of patients with MDA at week 28 and 52. For the present second interim analysis baseline data of all 336 patients and results of the documented visits up to week 76 were analysed.

**Results:** For the present analysis 336 patients (57% women) at 75 centres were observed. The visit at week 4 was documented for 290 patients, at week 16 for 305 patients, at week 28 for 262 patients, and at week 76 for 100 patients. At baseline, the patients had a mean age of 54 years<sup>22-85</sup> and BMI of 30 kg/m<sup>2</sup>.<sup>19-52</sup> 53.9% of the patients had as prior medication a TNF inhibitor and stopped because of inadequate response. Only 38% of the patients used MTX as concomitant medication. The patients showed arthritis at small (73.2%) and/or large (52.1%) joints, spinal involvement (16.7%) and enthesitis (13.1%). Number of tender joints improved from a mean of 10.0 (CI 95% 8.6/11.3) at baseline to 6.4 (5.4/7.3) at week 4 and 2.1 (1.4/2.9) at week 76. Number of swollen joints improved from 4.1 (3.4/4.9) at baseline to 2.6 (2.1/3.1) at week 4 and to 0.7 (0.4/1.0) at week 76. Efficacy of the therapy with ustekinumab was assessed as "very good" or "good" by 76.2% of the treating physicians at week 16 and by 89.9% at week 76. The patients assessed the efficacy as "very good" or "good" by 71.2% at week 16 and by 90.7% at week 76. Until data cut off point (32 months after study start), 67 SAEs have been documented, of which only 13 were related to ustekinumab. All in all, safety of therapy with ustekinumab was assessed as "very good" or "good" by 96.0% of the treating physicians after 16 weeks and by 98% after 76 weeks. The patients assessed the safety as "very good" or "good" by 93.3% at week 16 and by 98.0% at week 76.

**Conclusions:** The non-interventional study SUSTAIN showed relevant improvements with high therapy satisfaction and good safety in patients with active psoriatic arthritis treated with Ustekinumab after 4 weeks up to 76 weeks in daily practice life.

**Disclosure of Interest:** J. Wendler Consultant for: Janssen-Cilag GmbH., E. Movshovich Employee of: Janssen-Cilag GmbH., J. Behrens Employee of: Janssen-Cilag GmbH., F. Hamann: None declared, P. Wagener: None declared, F. Behrens: None declared

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THU0281

### DO IMPROVEMENTS IN HEALTH-RELATED QUALITY OF LIFE DURING DMARD TREATMENT DIFFER BETWEEN PSORIATIC AND RHEUMATOID ARTHRITIS PATIENTS? DATA FROM THE PROSPECTIVE OBSERVATIONAL NOR-DMARD STUDY, INCLUDING BASELINE COMPARISONS WITH NORWEGIAN GENERAL POPULATION CONTROLS

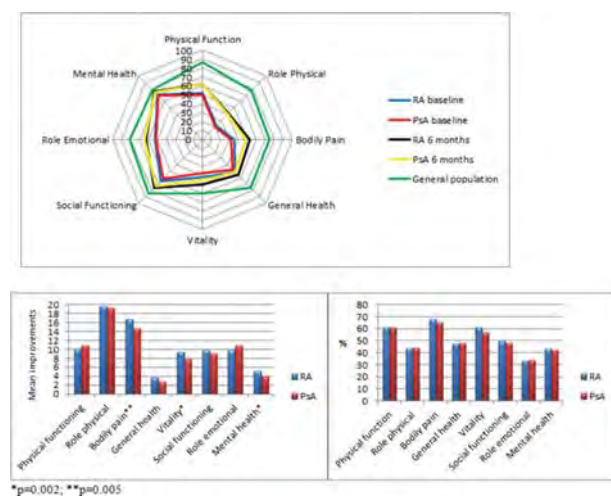
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**Background:** Only few longitudinal observational studies exist on the comparison of Health-related quality of life (HRQoL) between PsA and RA patients using the Medical Outcomes Survey Short Form-36 (SF-36), as well as with general population controls.

**Objectives:** The aims were 1) to explore if improvements in SF-36 scale scores differ between PsA and RA patients, 2) to compare proportions of PsA and RA patients achieving Minimum Clinically Important Improvements (MCII) in scale scores at 6 months follow-up<sup>1</sup>, 3) to compare HRQoL between RA, PsA patients and Norwegian general population controls.

**Methods:** We included first-time enrolled PsA and RA patients from the prospective observational multicenter NORwegian-Disease Modifying Anti-Rheumatic Drug (NOR-DMARD) study, starting conventional synthetic and/or biologic (cs/b) DMARDs between year 2000 and, 2012 as well as data from Norwegian general population controls.<sup>2</sup> Continuous variables were compared using independent t-test or Mann-Whitney U test as appropriate. Prespecified ANCOVA analyses adjusted for age and gender were performed to compare changes in scale scores from baseline to 6 months follow-up between PsA and RA patients. Radar diagram was made to visualise changes in scale scores (0 worst, 100 best) and bar charts to visualise improvements from baseline to 6 months as well as proportions of patients fulfilling MCII ( $\geq 5$ ) in scale scores at 6 months.

**Results:** A total of 1515 PsA and 3898 RA patients as well as 2323 Norwegian general population controls<sup>2</sup> were included (mean (SD) age 48.1 (12.6)/55.9 (31.6)/44.9 (16.5) years, 50.3%/71.4%/51.3% women, respectively; median (25th-75th percentile) disease duration RA; 2.0 (0.1–9.6), PsA: 1.9 (0.1–11.0) years). Mean (SD) DAS28 was lower in PsA vs. RA patients at baseline (4.2 (1.3)/4.9 (1.4)) and at 6 months ((3.1 (1.3)/3.5 (1.5)), as well as median (25th-75th percentile) 28 swollen joint count at baseline (2 (1–5)/6 (3–10)) and at 6 months (0 (0–2)/2 (0–4) follow-up, all  $p < 0.001$ . All scale scores were worse in PsA and RA compared with the general population ( $p \leq 0.001$ ), but improved during cs/bDMARD treatment (figure 1a). The improvements were marginally better in RA versus PsA patients for bodily pain, vitality and mental health (figure 1b). Similar percentages of RA and PsA patients achieved MCII  $\geq 5$  in scale scores from baseline until 6 months.



**Abstract THU0281 – Figure 1a.** Estimated marginal means of scale scores in RA and PsA patients as well as Norwegian general population controls, adjusted for age and gender. **Abstract THU0281 – Figure 1b.** Mean improvements in SF-36 scale scores from baseline to 6 months, adjusted for age, gender and the respective baseline values. **Abstract THU0281 – Figure 1c.** Similar proportions of RA and PsA patients achieved MCII  $\geq 5$  in scale scores from baseline to 6 months follow-up. \* $p = 0.002$ ; \*\* $p = 0.005$

**Conclusions:** These findings indicate that PsA patients have at least as high disease burden in terms of HRQoL as RA patients, in spite of higher levels of joint inflammation in the RA patients. Improvements during treatment were overall similar, except for somewhat larger improvements in bodily pain, vitality and mental health in RA patients. Similar proportions of PsA and RA patients achieved MCII at 6 months.

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**Disclosure of Interest:** None declared

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THU0282

### THE IMPACT OF COMORBIDITIES ON PHYSICAL FUNCTION IN PATIENTS WITH ANKYLOSING SPONDYLITIS (AS) AND PSORIATIC ARTHRITIS (PSA) ATTENDING RHEUMATOLOGY CLINICS

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**Background:** Regardless of disease activity, functional status gets worse in patients with rheumatoid arthritis (RA) with comorbidities. However, the impact of comorbidities on physical function in ankylosing spondylitis (AS) and psoriatic arthritis (PsA) is less known.

**Objectives:** To assess the impact of comorbidities on physical function (PF) in patients with AS and PsA.

**Methods:** Analysis of the baseline visit from the ongoing multicentric, observational, prospective, CARMA study. Data from patients with AS and PsA were analysed. Two different adjusted multivariate models were performed, where PF was the dependent variable (BASFI in AS and HAQ in PsA) and the following independent variables: comorbidities, a proxy for the Charlson index (ChI) (minimum 0; maximum 11), sociodemographic, disease activity (ESR, CRP and BASDAI in AS; while SJC, TJC, CRP, ESR, DAS, dactylitis count and PASI in PsA) and duration, radiographic damage and treatments. Results are presented as  $\beta$  coefficients and p-values.

**Results:** 738 patients with AS and 721 with PsA included (mean age at inclusion 48.1  $\pm$  11.7 and 51.8  $\pm$  12 years, respectively). AS patients: median BASFI 3.1 [interquartile range (IQR): 1.3–5.2], BASDAI 3.5 [IQR: 1.7–5.3], mean ChI 1.32  $\pm$  0.73. PsA patients: HAQ 0.4 [IQR: 0.0–0.9], DAS28 2.9 [IQR: 2.0–3.8], mean ChI 1.30  $\pm$  0.66. A ChI  $> 1$  found in 21% of the patients. Hypertension in 25.7% and 29.5%; hypercholesterolemia in 27% and 35.6% and diabetes in 7.6% and 9.2% of the patients with AS and PsA, respectively. Cardiovascular events occurred in 7.6% AS and 7.2% PsA, in most cases after the rheumatic disease diagnosis. Only patients with PsA with higher ChI showed worse adjusted physical function ( $\beta$ : 0.09;  $p = 0.03$ ). Also female sex ( $\beta$ : 0.03;  $p = 0.001$ ), obesity ( $\beta$ : 0.09;  $p = 0.04$ ), disease duration ( $\beta$ : 0.01;  $p = 0.009$ ), NSAIDs ( $\beta$ : 0.1;  $p = 0.02$ ), corticosteroids ( $\beta$ : 0.12;  $p = 0.02$ ) and biologics ( $\beta$ : 0.15;  $p = 0.07$ ) were associated with worse function in patients with PsA. In contrast, a higher educational level was associated with less disability. In patients with AS, thyroid disease ( $\beta$ : 1.19,  $p = 0.002$ ) and raised ESR ( $\beta$ : 0.01,  $p = 0.010$ ) were independently associated with function.

**Conclusions:** The presence of comorbidities in patients with PsA is independently associated with worse physical function, similar to what happens in RA. Early detection and control may yield an integral management of the disease and better final outcomes.

**Disclosure of Interest:** None declared

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THU0283

### PATIENTS WITH PSORIATIC ARTHRITIS WHO ARE NOT ELIGIBLE FOR RANDOMISED CLINICAL TRIALS FOR TNF INHIBITORS HAVE SIMILAR TREATMENT RESPONSE AND DRUG SURVIVAL. RESULTS FROM THE ICEBIO REGISTRY

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**Background:** We have recently reported that a majority of patients with psoriatic arthritis who are being treated with TNF inhibitors in Iceland would not have been



eligible for the randomised clinical trials (RCTs) performed leading up to registration of the respective pharmaceutical product.<sup>1</sup>

**Objectives:** To determine whether patients with psoriatic arthritis who did not fulfil the inclusion criteria (group B) in RCTs receive similar benefits and drug survival from TNF inhibitors as those patients who would have fulfilled the inclusion criteria (group A).

**Methods:** All patients with rheumatic disorders who are treated with biologic DMARDs in Iceland are registered in ICEBIO. ICEBIO is based on the Danish Registry for biologic therapies in rheumatology<sup>2</sup> and has data about approximately 98% of all patients with psoriatic arthritis treated with biologic DMARDs in Iceland. On February 1st 2016 there was information on 1058 individuals in ICEBIO. 231 patients with psoriatic arthritis received their first-line treatment and could be classified according to inclusion criteria of respective pharmaceutical RCT.<sup>1</sup> Information on disease activity at baseline was collected and we estimate the treatment response at 6 and 18 months according to ACR20 and DAS28CRP and drug survival.

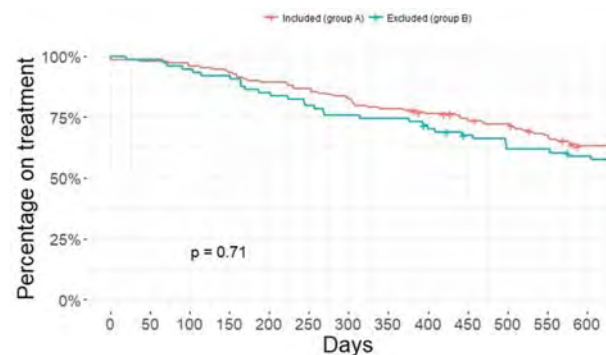
**Results:** The groups were similar at baseline (table 1), although Group A predictably had higher SJC (5.5 vs 3.8) and subsequently higher DAS28CRP (4.6 vs 4.2). Out of 231 patients we have sufficient data to determine ACR20 and DAS28CRP response in 92 and 91 patients respectively. Treatment response is outlined in table 2, with better response in group A in regards to HAQ and SJC. There was similar drug survival between the groups (figure 1).

	Group A	Group B	p value
VAS pain	65±17	64±22	0.705
VAS global	71±21	66±24	0.222
TJC	6.3±3.8	5.4±4.4	0.198
SJC	5.5±3.3	3.8±3.6	0.003
HAQ	1.2±0.69	1.0±0.65	0.114
DAS28CRP	4.6±0.8	4.2±0.9	0.012

**Abstract THU0283 – Table 1.** Group characteristics, mean values±SD.

Improvement in clinical parameters:	Included in RCTs	Not included in RCTs	p value
HAQ at 6 months	-0.8±0.7	-0.3±0.6	0.008
HAQ at 18 months	-0.6±0.7	-0.3±0.6	0.051
SJC at 6 months	-4.3±2.7	-2.2±2.7	0.001
SJC at 18 months	-4.4±3.4	-2.2±3.6	0.007
TJC at 6 months	-4.2±3.8	-2.8±5.1	0.163
TJC at 18 months	-4.0±4.9	-3.9±4.1	0.889
ACR20 at 6 months	77%	60%	0.207
ACR20 at 18 months	69%	59%	0.545
DAS28CRP at 6 months	77%	71%	0.749
DAS28CRP at 18 months	81%	67%	0.304

**Abstract THU0283 – Table 2.** Response to first-line TNF $\alpha$  inhibitors, mean values and percentage achieving response by ACR20 or decrease in disease activity by DAS28CRP.



**Abstract THU0283 – Figure 1.** First-line TNF inhibitor drug survival

**Conclusions:** Patients with psoriatic arthritis that would not have fulfilled the inclusion criteria in RCTs seem to respond to treatment effectively and have similar drug survival. Thus, treatment outcomes for psoriatic arthritis from RCTs may probably be applied to daily clinical practice, whether patients would have fulfilled RCT criterias or not. However, more detailed studies are needed.

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**Disclosure of Interest:** None declared

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## THU0284 HAQ IN PSORIATIC ARTHRITIS IS DRIVEN BY GENDER, INFLAMMATION AND AGEING: OBSERVATIONAL DATA FROM COHORT STUDIES IN UK, DENMARK, ICELAND AND SWEDEN

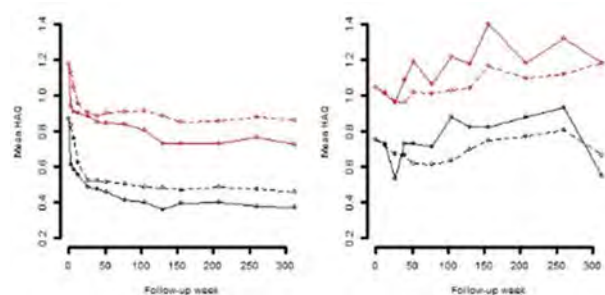
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**Background:** Psoriatic arthritis (PsA) is a chronic inflammatory disorder associated with skin and joint involvement, pain and impaired function. HAQ has been widely used but components contributing to HAQ and changes thereof have been sparsely studied.

**Objectives:** The objective of this multinational population-based cohort study was to investigate factors associated with longitudinal changes in HAQ in patients with PsA in independent settings.

**Methods:** Data on PsA patient characteristics, disease activity components and HAQ was obtained from the DANBIO (Denmark), ICEBIO (Iceland), SSATG (southern Sweden) and BATH (UK) cohort registries. Farewell's linear increments model for missing data was used to fit each longitudinal response by regressing the observed increments onto lagged values of the response variables (HAQ, CRP and VAS pain) while also adjusting for other covariates (gender, age and disease duration). Due to homogeneity of the nature of registries, the Nordic data was pooled for patients initiating first course of biologics (anti-TNF therapy, secukinumab or ustekinumab), whereas UK data represents an ongoing cohort with different treatments.

**Results:** In the period 2006 through 2016, we identified 1473 patients from DANBIO, 168 from ICEBIO, 469 from BATH, and 716 from SSATG eligible for analyses. Mean age in years (SD) and percentage of females for the populations were 46 (SD ±12), 55% for DANBIO, 46 (SD ±12), 61% for ICEBIO, 47 (SD ±11), 51% for SSATG, and 58 (SD ±13) 49% for BATH; respectively. The figure displays observed HAQ values (solid lines) and Farewell modelled (broken lines) curves divided on gender for the development of HAQ after initiation of biologic therapy for pooled Nordic data (A) and for the ongoing UK cohort (B). It should be noted, that Farewell modelling inflates HAQ-values in the Nordic registries reflecting a correction for channelling bias due to drop out during biologic treatment. Whereas the modelled HAQ values for the BATH cohort are deflated possibly due to extra visits during flares in this ongoing observational cohort. At all time points and cohorts female HAQ values are higher than males (p<0.001). After initiation of biologic therapy there is a significant decline in the HAQ scores in the Nordic registers of 0.23 (95% CI 0.21–0.25) at 6 months. Changes in CRP, VAS-pain nor disease duration did not appear to affect HAQ during follow-up. However, ageing seemed to have a tendency to increase HAQ over time. The same consistent pattern was present when analyses were done separated by country (data not shown).



**Conclusions:** In PsA, across independent European cohorts, HAQ is higher for women, and significantly decreases for both genders when anti-inflammatory treatment is initiated. HAQ does not depend on CRP, VAS-pain or disease duration during longitudinal follow-up. However, a significant increasing trend was identified with ageing.

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**Disclosure of Interest:** L. E. Kristensen Speakers bureau: Pfizer, AbbVie, Amgen, UCB, Celgene, BMS, MSD, Novartis, Eli Lilly, Janssen Pharmaceuticals, T. S. Jørgensen Speakers bureau: AbbVie, Roche, UCB, Novartis, Pfizer, Biogen and Eli Lilly, L. Coates: None declared, P. Frederiksen: None declared, B. Gudbjornsson: None declared, J. Wallman Consultant for: AbbVie, Celgene, Eli Lilly, Novartis, UCB, N. McHugh Grant/research support from: Pfizer, Celgene and AbbVie, Speakers bureau: Eli Lilly, Pfizer and AbbVie, M. Kapetanovic: None declared, L. Dreyer Speakers bureau: UCB, MSD, Janssen, W. Tillett Speakers bureau: AbbVie, Celgene, Eli Lilly, Janssen, Novartis, Pfizer, UCB  
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#### THU0285 THE EFFECT OF FAMILY HISTORY ON DISEASE PHENOTYPES IN 1393 PSORIATIC ARTHRITIS PATIENTS

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**Background:** Psoriatic arthritis (PsA) has a genetic background, approximately 40% of patients having a family history of psoriasis or PsA in first-degree relatives, which may impact the disease features.

**Objectives:** The aim of this study was to evaluate the effects of family history of psoriasis or PsA on the disease phenotypes.

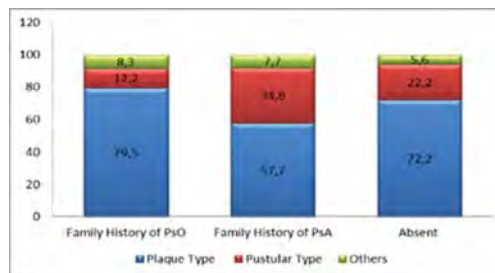
**Methods:** The demographic and clinical data were retrieved from the longitudinal, multicenter PsArt-ID (Psoriatic Arthritis-International Database). Family history of psoriasis and PsA were investigated for 1st and 2nd degree relatives separately. The effect of the family history of psoriasis and/or PsA on disease phenotypes and severity were analysed, calculating the relative risks (RR).

**Results:** 1393 patients had the data for family history, 444 (31.9%) of whom was positive for psoriasis and/or PsA. The majority of the family history was only psoriasis (333/444; 75%) and 58.5% (260/444) of the patients had first-degree relatives affected. There was no differences in maternal or parental transmission rates however women had more psoriasis and/or PsA in their family (67.3% vs 32.7% p: 0.028). Patients with a family history had an earlier onset of age for psoriasis (29±14.8 vs 31±14.9 p: 0.007), more frequent nail involvement (50.7% vs 29.6% p: 0.032), more frequent enthesitis (28.2% vs 17.7% p<0.001) and deformities (25.2% vs 19.9% p: 0.05) and were able to achieve minimal disease activity (MDA) less often. (38.6% vs 49.5% p: 0.045). Plaque psoriasis was more common if the family history was positive for psoriasis whereas pustular psoriasis was more frequent when the family history was positive for PsA (figure 1). Family history of psoriasis were found as a risk factor for a younger onset (RR: 1.138), for nail disease (RR: 1.179), for enthesitis (RR: 1.504) and for not achieving MDA (RR: 1.246) whereas family history of PsA was a risk factor for having deformities (RR: 1.215) (table 1).

**Abstract THU0285 – Table 1.** Relative Risks in patients with or without family history of psoriasis or PsA

	Family history	p	RR	95% CI
Onset of psoriasis before 40 years age	Psoriasis	<0.05	1.138	1.063–1.219
	PsA	>0.05	1.023	0.879–1.191
Nail involvement (ever)	Psoriasis	<0.05	1.179	1.04–1.335
	PsA	>0.05	1.157	0.917–1.461
Enthesitis (ever)	Psoriasis	<0.05	1.504	1.192–1.898
	PsA	>0.05	1.350	0.871–2.092
Not achieving MDA	Psoriasis	<0.05	1.246	1.003–1.547
	PsA	>0.05	1.044	0.655–1.666
Presence of deformities	Psoriasis	>0.05	1.215	0.928–1.592
	PsA	<0.05	1.786	1.170–2.727

PsA: Psoriatic Arthritis; MDA: Minimal Disease Activity



**Figure:** Distribution of skin lesions according to the family history in patients with PsA. Numbers are given as percentages. PsO: Psoriasis; PsA: Psoriatic Arthritis

**Conclusions:** The family history of psoriasis and PsA has impacts on skin phenotypes, musculoskeletal features and the disease severity. The differences between family history of psoriasis and PsA and pustular vs plaque phenotypes may point out to a different genetic background and pathogenic mechanisms in these subsets.

**Disclosure of Interest:** None declared

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#### THU0286 PREDICTORS FOR ORTHOPAEDIC SURGERY IN PATIENTS WITH PSORIATIC ARTHRITIS. RESULTS FROM A RETROSPECTIVE COHORT STUDY OF 590 PATIENTS DIAGNOSED 1954–2011, AND FOLLOWED UP UNTIL 2017

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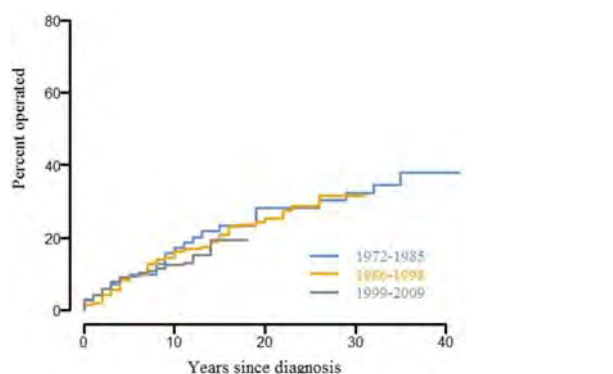
**Background:** Psoriatic arthritis with peripheral joint affection is a progressive disease in most patients, and erosions are seen in 47% within the first two years.<sup>1</sup> Synthetic disease modifying anti rheumatic drugs (DMARDs) are generally prescribed, to inhibit inflammation, but have not been proven to slow or prevent radiographic changes. Biologic treatment is recommended when other agents are not efficient, and has been shown to give better control of structural damage.<sup>2</sup> Orthopaedic corrective surgery has been a necessary part of treating patients with psoriatic arthritis, when medication fails to prevent joint destruction. Surgery can be considered a proxy for joint damage, and studying time trends in orthopaedic surgery thus gives valuable information regarding the prognosis of patients with inflammatory arthritis. In patients with rheumatoid arthritis there has, over time, been a declining incidence of orthopaedic interventions. The change in available medical treatment is believed to be responsible for this.<sup>3</sup> As synthetic

DMARDs may be less efficient in patients with psoriatic arthritis, it is uncertain whether a decline of the same magnitude can be expected among these patients.

**Objectives:** We wished to investigate trends in the incidence of orthopaedic procedures in patients with psoriatic arthritis, and to explore how patient characteristics, time of diagnosis and treatment affect the need for surgery.

**Methods:** We reviewed the medical history of 1432 patients with possible psoriatic arthritis at Haukeland University Hospital in Bergen, Norway from 1954–2011, of which 590 (mean age 49, 52% women) had a confirmed diagnosis of psoriatic arthritis, and sufficient journal information, and were included in the present study. Relevant orthopaedic procedures were obtained from the Norwegian Arthroplasty Register and the hospital's administrative patient records. 171 procedures (25% joint synovectomies, 15% arthrodeses and 53% prostheses) were performed in 117 patients. Survival analyses were completed to evaluate the impact of different factors such as year of diagnosis, age, sex, radiographic changes, disease activity and treatment, on the risk of undergoing surgery.

**Results:** Female sex, older age ( $\geq 70$ ) and maximum ESR 30–59 significantly increased the risk of surgery whereas time period of diagnosis had no effect on the outcome. Anti-rheumatic treatment changed significantly over time.



**Abstract THU0286 – Figure 1.** Cumulative percent operated depending three separate time periods of diagnosis

**Conclusions:** 20% of patients with psoriatic arthritis needed surgery during disease course. In our material, the prognosis of patients with psoriatic arthritis has not changed, with regard to the risk of orthopaedic surgery, despite significant changes in treatment. This is contrary to what is seen for patients with rheumatoid arthritis.

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**Disclosure of Interest:** None declared

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#### THU0287 THE PREVALENCE OF REMISSION IN A REAL-LIFE COHORT OF PSORIATIC ARTHRITIS PATIENTS TREATED WITH SYNTHETIC OR BIOLOGIC DISEASE MODIFYING DRUGS

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**Background:** The treat-to-target (T2T) strategy for the management of psoriatic arthritis (PsA) recently proposed by EULAR recommendations suggests to ideally achieve remission/Low Disease Activity (LDA) in all treated patients, but nowadays data on remission/LDA rate in a real-world setting are still lacking.

**Objectives:** To evaluate the disease activity state in a real-life cohort of PsA patients treated with synthetic and/or biologic disease modifying drugs (DMARDs).

**Methods:** We undertook a cross-sectional analysis of all PsA consecutive patients enrolled in a large Italian multicentric registry including 7 Italian tertiary rheumatology centres. Disease activity defined as number of swollen (SJ) and

tender (TJ) joints, Leeds Enthesis Index (LEI), number of dactylitis, Body Surface Area (BSA), patient global assessment (PGA), patient pain (PP), Health Assessment Questionnaire Disability Index (HAQ-DI), and C-reactive protein (CRP, mg/L) were computed and the rates of patients achieving Disease Activity in Psoriatic Arthritis (DAPSA) remission/LDA and Minimal Disease Activity (MDA) were calculated. Subanalysis after stratification according to ongoing treatment (sDMARDs or bDMARDs) were also performed.

**Results:** The study population included 362 PsA patients (56.6% men; mean  $\pm$  standard deviation, SD) age  $53.3 \pm 12.4$  years; mean  $[\pm$ SD] disease duration  $9.4 \pm 8.2$  years), treated with sDMARDs (15.8%, mainly methotrexate [66.6%]) or bDMARDs (79.6%, mainly anti-TNF agents [72.9%]), as monotherapy [78.1%] or in combination with sDMARDs [21.9%]. Oligoarthritis (32%), polyarthritis (42%), axial involvement (11.9%), enthesitis (10.5%), and dactylitis (3.6%) were the reported predominant subsets of PsA. In the overall population the mean values  $[\pm$ SD] of disease activity measures were: SJ count  $1.4 \pm 2.6$ , TJ count  $1.9 \pm 3$ , LEI  $0.5 \pm 1.1$ , number of dactylitis  $0.1 \pm 0.3$ , BSA  $2.6 \pm 6.9$ , PGA  $1.4 \pm 2.6$ , PP  $3 \pm 2.6$ , HAQ-DI  $0.4 \pm 0.5$ , CRP level  $3.4 \pm 8$ , and DAPSA  $9.3 \pm 9.2$ . The rates of DAPSA LDA and remission were 46.9% and 31.7%, respectively. We found 51.6% of patients achieving MDA, without significant difference according to ongoing treatment (53.4% and 51% in bDMARD versus sDMARD treated patients, respectively;  $p=0.87$ ).

**Conclusions:** In our real-life cross-sectional analysis, an acceptable comprehensive disease control was reported only in half of patients, irrespectively of ongoing therapy. These findings suggest the need to further improve the real-world application of T2T strategy for the management of PsA.

**Disclosure of Interest:** None declared

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#### THU0288 IMPLEMENTATION OF THE TREAT TO TARGET CONCEPT IN EVALUATION OF PSORIATIC ARTHRITIS PATIENTS

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**Background:** Minimal disease activity (MDA) in psoriatic arthritis (PsA) is a composite outcome measure that represents the multifaceted domains of psoriatic disease including the joints, enthesitis and skin, as well as patient's reported outcomes (PRO). MDA is currently used as a goal of treatment in the "treat-to-target" (T2T) approach in PsA management.<sup>1</sup>

**Objectives:** To assess the implementation of the T2T concept in PsA patients.

**Methods:** A retrospective analysis of all the patients included in a PsA registry during 2016–2017 was performed. Medical charts were reviewed by an independent rheumatologist and the following data were collected: patient demographics, duration of PsA and psoriasis, alcohol and tobacco use, treatment changes, as well as items that constitute the MDA including the tender and swollen joint count, enthesitis, psoriasis area skin score (PASI), physician and patient evaluation of disease activity and pain and the health assessment questionnaire (HAQ) score. Medical records were reviewed to assess whether T2T concept was indeed followed by the treating rheumatologist to determine whether MDA was achieved and medication changes were made. The associations between T2T concept implementation and categorical and continuous variables were assessed by Chi square test, or t-test as appropriate. The association between the physician's assessment at each visit with each of the MDA parameters (active versus inactive) was assessed by Chi square test.

**Results:** The records of 117 consecutive patients were evaluated, one patient was excluded due to lack of data. The mean age was  $58.4 \pm 13$  years, of whom 76 (65.5%) were women. The T2T approach was implemented in 76 (65.5%) patients. There was no correlation between the T2T implementation and patient age, gender, alcohol and tobacco use, disease activity parameters at the patient's visit and the various treatment regimens. The physician assessment of disease activity did not correlate with the MDA score in 40 (34.5%) patients. In most cases 30 (75%), this discrepancy occurred because physicians labelled patients as having inactive disease while disregarding the PRO category of the MDA score, including 29 patients who reported a high VAS pain score, 22 patients reporting a high patient global disease activity and 25 patients reporting a high HAQ- score. In the other 10 (25%) of cases, the treating rheumatologists made treatment changes because they considered patients as having active disease based on one tender or swollen joint or enthesitis, despite these patients actually meeting MDA criteria.

**Conclusions:** In our cohort, the T2T concept was implemented in 65.5% of the visits in accordance with other PsA studies. The main obstacle that we encountered in implementation of MDA concept was in physicians' overlooking the PRO components of the score. Efforts are needed to increase the accurate use of the MDA score and treat to target concept in daily practice.



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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.5634

THU0289

### BURDEN OF PSORIATIC ARTHRITIS IN DIFFERENT DEFINITIONS OF DISEASE ACTIVITY: COMPARING MINIMAL DISEASE ACTIVITY AND DISEASE ACTIVITY INDEX FOR PSORIATIC ARTHRITIS

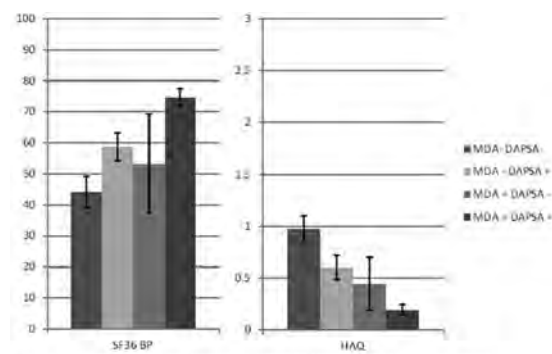
<sup>1</sup>K. Wervers, M. Vis<sup>1</sup>, I. Tchetcherikov<sup>2</sup>, A.H. Gerards<sup>3</sup>, M.R. Kok<sup>4</sup>, C.W. Appels<sup>5</sup>, W. L. van der Graaff<sup>6</sup>, J.H. van Groenendaal<sup>7</sup>, L.A. Korswagen<sup>8</sup>, J.J. Veris-Van Dieren<sup>9</sup>, J.M. Hazes<sup>1</sup>, J.J. Luime<sup>1</sup>, on behalf of Cicero. <sup>1</sup>Rheumatology, ERASMUS MC, Rotterdam; <sup>2</sup>Rheumatology, Albert Schweitzer Hospital, Dordrecht; <sup>3</sup>Rheumatology, Sint Franciscus Vlietland Group, Schiedam; <sup>4</sup>Rheumatology, Maasstad Hospital, Rotterdam; <sup>5</sup>Rheumatology, Amphia Hospital, Breda; <sup>6</sup>Rheumatology, Rivas Hospital, Gorinchem; <sup>7</sup>Rheumatology, Reumazorg Zuid West Nederland, Roosendaal; <sup>8</sup>Rheumatology, Sint Franciscus Vlietland Group, Rotterdam; <sup>9</sup>Rheumatology, Reumazorg Zuid West Nederland, Goes, Netherlands

**Background:** Treat-to-target strategies have improved outcomes in rheumatic diseases. In psoriatic arthritis (PsA), the proposed targets are the multidimensional target Minimal Disease Activity (MDA) and the articular target Disease Activity index for PsA (DAPSA).

**Objectives:** We aimed to compare burden of PsA in patients with low disease activity according to the two definitions MDA and DAPSA-Low Disease Activity (DAPSA-LDA), one year after diagnosis.

**Methods:** We obtained data on MDA, DAPSA-LDA and disease burden one year after diagnosis from patients included in the Dutch southwest early PsA cohort. Disease burden was assessed in two domains: 'Body Functions', including Short Form 36 Bodily Pain (SF36-BP), and 'Activity', including Health Assessment Questionnaire (HAQ).

**Results:** Of the 292 patients included, 48% achieved MDA and 64% DAPSA-LDA. Average 'Body Functions' and 'Activity' were similar in patients in MDA and patients in DAPSA-LDA. However the scores were significantly better in the 44% of patients in both MDA and DAPSA-LDA than in the 20% of patients only in DAPSA-LDA. The average SF36-BP was higher in patients achieving both targets (74.7, 95% CI 72.0–77.4) than in patients only in DAPSA-LDA (58.7, 95% CI 54.8–62.6). Similarly, mean HAQ scores measuring 'Activity' were 0.19 (95%CI 0.14–0.25) and 0.61 (95%CI 0.48–0.73) respectively.



SF36-BP: Short Form 36 Bodily Pain, HAQ: Health Assessment Questionnaire, MDA: Minimal Disease Activity, DAPSA: Disease Activity Index for Psoriatic Arthritis, MDA - not in MDA, MDA + : in MDA, DAPSA - : not in DAPSA-Low Disease Activity (DAPSA-LDA), DAPSA + : in DAPSA-LDA

**Abstract THU0289 – Figure 1.** SF36-BP and HAQ scores in MDA and DAPSA subgroups.

**Conclusions:** Of patients newly diagnosed with PsA, 48% achieved MDA and 64% DAPSA-LDA after one year receiving usual care. Average disease burden was similar in patients in MDA and in patients in DAPSA-LDA. However, those that only achieved DAPSA-LDA reported worse outcomes than those also achieving MDA.

**Disclosure of Interest:** None declared

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THU0290

### EFFECTS OF BIOLOGIC DMARDs ON PHYSICAL FUNCTION IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS: RESULTS OF NETWORK META-ANALYSES

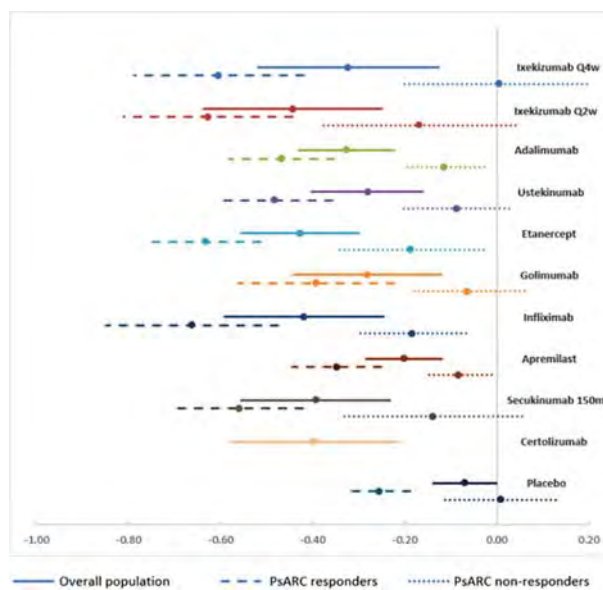
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**Background:** Psoriatic arthritis (PsA) is a chronic inflammatory rheumatic disease associated with psoriasis and characterised by pain, stiffness, swelling of joints, joints ankylosing and low patient quality of life.<sup>1</sup> The economic burden of PsA is substantial<sup>2</sup>, and biologic treatments for PsA are increasingly scrutinised in health technology assessments. The most commonly used economic model framework for assessing biologics in PsA is the York Assessment Group model developed as part of a NICE appraisal (the "York model").<sup>3</sup> In this model improvement in Health Assessment Questionnaire- Disability Index (HAQ-DI) reflects physical function, and is linked to initial treatment response measured by joint improvement assessed by PsARC.

**Objectives:** To assess the effectiveness of biologic DMARDs on HAQ-DI among active biologic-naïve PsA patients through Bayesian network meta-analyses (NMAs) and to understand the relationship to PsARC response.

**Methods:** Data for the NMA was identified through a systematic literature review of published and grey literature (1990-May 2017) in EMBASE/MEDLINE. Bayesian NMAs were conducted in line with NICE guidelines<sup>4</sup> to assess the mean HAQ-DI scores change from baseline for ixekizumab, adalimumab, ustekinumab, etanercept, golimumab, infliximab, apremilast, secukinumab, certolizumab pegol, and placebo in the biologic-naïve overall population as well as in PsARC responders and non-responders. Results were expressed as absolute mean change from baseline and associated standard deviations, and 95% credibility intervals.

**Results:** Overall, 42 publications reporting 19 randomised clinical trials were included for the NMAs, most of these evaluated outcomes at 12 and 24 weeks. Mean changes in HAQ-DI score (overall and by PsARC response) from baseline are shown in figure 1. Among PsARC responders, the greatest mean changes were observed for infliximab, etanercept, ixekizumab, and secukinumab. Among PsARC non-responders, those values were greatest for infliximab, etanercept, ixekizumab Q2W, secukinumab, and adalimumab. The relatively wide 95% credibility intervals reflect the scarcity of available evidence.



**Abstract THU0290 – Figure 1.** Mean changes in HAQ-DI in patients on different biologic DMARD treatments

**Conclusions:** The results of the NMAs suggest that among the biologic DMARDs infliximab, etanercept, ixekizumab Q2W, secukinumab 150 mg, and certolizumab had the highest HAQ-DI improvements in biologic-naïve patients with active PsA. Changes in HAQ-DI were strongly associated with PsARC response for each treatment.

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**Disclosure of Interest:** A. Ruysen-Witrand: None declared, C. Sapin Employee of: Eli Lilly and Company, S. Hartz Employee of: Eli Lilly and Company, S. Liu Leage Employee of: Eli Lilly and Company

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**THU0291** **INCIDENCE OF SERIOUS GASTROINTESTINAL EVENTS AND INFLAMMATORY BOWEL DISEASE AMONG TILDRAKIZUMAB-TREATED PATIENTS WITH MODERATE TO SEVERE PLAQUE PSORIASIS: DATA FROM 3 LARGE RANDOMISED CLINICAL TRIALS**

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**Background:** Tildrakizumab, is a high-affinity, humanised, anti-IL-23p19 monoclonal antibody for the treatment of chronic plaque psoriasis.

**Objectives:** Here, we evaluated gastrointestinal (GI) adverse events (AE) and, specifically, cases of inflammatory bowel disease (IBD; ie, Crohn's disease or ulcerative colitis) in the clinical development program for tildrakizumab.

**Methods:** Patients with moderate to severe plaque psoriasis were randomised in 3 large, clinical trials: P05495 (phase 2; NCT01225731), reSURFACE 1 (phase 3; NCT01722331), and reSURFACE 2 (phase 3; NCT01729754).<sup>1,2</sup> In this analysis, we identified serious GI AEs and new-onset or exacerbation of pre-existing IBD from a pooled dataset of tildrakizumab-treated patients from these 3 studies. Doses of tildrakizumab included 5 mg, 25 mg, 100 mg, and 200 mg in P05495 and 100 mg and 200 mg in the reSURFACE studies.

**Results:** In this analysis, we pooled 1911 patients from the 3 trials who received either tildrakizumab 100 or 200 mg. There were no new cases of IBD reported; among 6 patients with a history of IBD randomised to tildrakizumab, none experienced an exacerbation. The numbers (rate per 100 patient-years) of patients with serious GI AEs in the pooled dataset were 8 (0.80) for tildrakizumab 100 mg and 4 (0.43) for tildrakizumab 200 mg. These serious GI AEs included abdominal pain, constipation, diverticulum, dyspepsia, gastritis, thrombosed haemorrhoids, esophageal polyp, pancreatitis (1 patient each) among tildrakizumab 100 mg patients and abdominal hernia, upper abdominal pain, acute pancreatitis, and salivary gland enlargement (1 patient each) among tildrakizumab 200 mg patients.

**Conclusions:** In this post-hoc analysis of patients from 3 large randomised clinical trials, serious GI AEs were infrequent and there were no new cases of IBD or exacerbations of IBD.

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**Acknowledgements:** This study was funded by Merck and Co., Inc. Editorial support for abstract submission was provided by Fishawack Communications and funded by Sun Pharmaceutical Industries, Inc. Analyses were previously presented at the American Academy of Dermatology. Annual Meeting, San Diego, California, USA, 2018

**Disclosure of Interest:** M. Gooderham Grant/research support from: Abbvie Inc., Akros Pharma Inc., AMGEN Inc., Boehringer Ingelheim International GmbH, Bristol-Myers Squibb Company, Celgene, Dermira Inc. Eli Lilly and Company, Galderma SA GlaxoSmithKline Janssen Inc. LEO Pharma MedImmune Merck and Co. Novartis, Pfizer Inc., Regeneron Pharmaceuticals Inc. Roche Laboratories Sanofi Genzyme UCB Valeant Pharmaceuticals Inc., Consultant for: Akros Pharma Inc., AMGEN Inc., Boehringer Ingelheim International GmbH, Celgene, Eli Lilly and Company, Janssen Inc. Novartis, Sanofi Genzyme, Valeant

Pharmaceuticals Inc., Speakers bureau: Abbvie Inc. Actelion Pharmaceuticals, AMGEN Inc., Boehringer Ingelheim International GmbH, Celgene, Eli Lilly and Company, Galderma SA, Janssen Inc., LEO Pharma, Novartis, Pfizer Inc., Regeneron Pharmaceuticals Inc., Sanofi Genzyme Valeant Pharmaceuticals Inc., B. Elewski Grant/research support from: Abbvie, Boehringer Ingelheim, Celgene, Incyte, Lilly, Merck, Novartis, Pfizer, Regeneron, Sun Pharma, Viamed, Valeant Pharmaceuticals, Consultant for: Celgene, Lilly, Novartis, Pfizer, Sun Pharma, Valeant; all funds derived from her participation have been paid to her university, D. Pariser Grant/research support from: Abbott Laboratories, Amgen, Asana Biosciences, Bickel Biotechnology, Celgene, Dermavant Sciences, Eli Lilly, LEO Pharma US, Merck and Co., Inc., Novartis, Novo Nordisk, Ortho Dermatologics, Peplin Inc., Pfizer Inc., Photocure ASA, Promius Pharmaceuticals, Regeneron, Stiefel a GSK company, and Valeant Pharmaceuticals, Consultant for: Bickel Biotechnology, Biofrontera AG, Celgene Corporation, Dermira, DUSA Pharmaceuticals, LEO Pharma US, Novartis, Promius Pharmaceuticals, Regeneron, Sanofi, TheraVida, and Valeant Pharmaceuticals, H. Sofen Grant/research support from: Amgen, Boehringer Ingelheim, Janssen, Lilly, Merck and Co., Inc. Novartis, Pfizer, Consultant for: Janssen, Lilly, Novartis, Speakers bureau: Janssen, Lilly, Novartis, A. Mendelsohn Employee of: Sun Pharmaceutical Industries, Inc., N. Cichanowitz Shareholder of: Merck and Co., Inc., Employee of: Merck Sharp and Dohme Corp., a subsidiary of Merck and Co., Inc., Kenilworth, NJ, USA, Q. Li Employee of: Merck Sharp and Dohme Corp., a subsidiary of Merck and Co., Inc., Kenilworth, NJ, USA, C. La Rosa Employee of: Merck Sharp and Dohme Corp., a subsidiary of Merck and Co., Inc., Kenilworth, NJ, USA

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**THU0292** **DIAGNOSTIC EXPERIENCES OF PATIENTS WITH PSORIATIC ARTHRITIS: MISDIAGNOSIS IS COMMON**

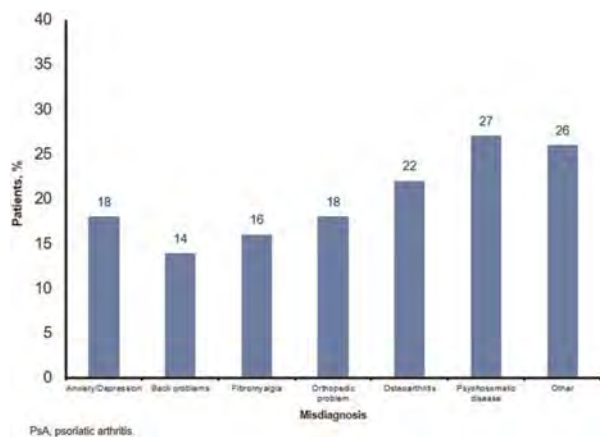
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**Background:** Psoriatic arthritis (PsA) is a heterogeneous, chronic, immune-mediated disease characterised by a range of musculoskeletal conditions including joint pain, swelling, enthesitis and dactylitis as well as skin and nail manifestations. Early diagnosis of PsA is important as shorter time to treatment may improve outcomes.<sup>1</sup> However, PsA is often undiagnosed or misdiagnosed.<sup>2</sup> There is limited information on the diagnostic experiences of patients with PsA, including medical care sought and potential barriers to diagnosis.

**Objectives:** To determine patients' experiences related to the diagnosis of PsA including initial symptoms experienced, medical care sought, and time to diagnosis.

**Methods:** US patients aged  $\geq 18$  years with a self-reported diagnosis of PsA were recruited through CreakyJoints ([www.Creakyjoints.org](http://www.Creakyjoints.org)), an online patient support community comprising patients with arthritis and arthritis-related diseases and their caregivers, and outreach through social media. Participants completed an online survey designed to collect data on socio-demographics, clinical symptoms, disease burden, and diagnosis history, including initial PsA symptoms experienced, types of health care providers seen, misdiagnoses received before a diagnosis of PsA, and time to PsA diagnosis. Survey questions were developed following analysis of qualitative interviews of patients with PsA and clinical experts, as well as a targeted literature review.

**Results:** Of the 203 patients included in the study, 172 (85%) were female, with a mean (SD) age of 51.6 (10.8) years; 132 patients (65%) had private insurance, 61 (30%) Medicare, and 25 (12%) Medicaid. The most common initial symptoms that led patients to seek medical attention were joint pain (142 patients [70%]), stiffness (109 [54%]), swollen joints (101 [50%]), skin rash/psoriasis (97 [48%]), and fatigue (96 [47%]). Most patients (153 [75%]) sought medical treatment within 2 years of symptom onset. During the diagnosis process, patients most commonly sought care from a general practitioner (162 [80%]), rheumatologist (135 [66%]), dermatologist (67 [33%]), orthopedist (44 [22%]), and/or podiatrist (25 [12%]). Only 8 patients (4%) reported that they had never received a misdiagnosis; common misdiagnoses were psychosomatic disease, osteoarthritis, and anxiety/depression (figure 1). Patients reported median (IQR) time since diagnosis of 6.0 (2–11.5) years. Many patients (94 [51%]) received a diagnosis of PsA  $\leq 1$  year after seeking medical attention; however, 25 (17%) and 31 (15%) patients received a PsA diagnosis  $\geq 5$  and  $> 10$  years after seeking medical attention for the first time, respectively.



**Abstract THU0292 – Figure 1.** Misdiagnoses Received Before Diagnosis of PsA (N=203). PsA, psoriatic arthritis

**Conclusions:** This study showed that patients often had substantial delays and misdiagnoses before they received a PsA diagnosis. Increased understanding of the diagnostic barriers may lead to earlier diagnosis and appropriate treatment that may improve outcomes.

#### REFERENCES:

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#### THU0293 THE TRAJECTORY OF RADIOGRAPHIC PROGRESSION SLOWS AMONGST PATIENTS WITH PSORIATIC ARTHRITIS TREATED WITH ANTI-TNF

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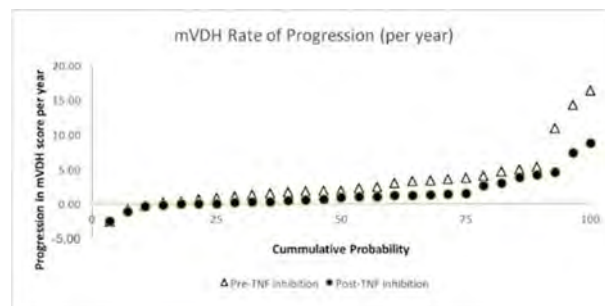
**Background:** Radiographic damage is an important outcome in psoriatic arthritis (PsA) but the natural history of radiographic progression has not been well described. Randomised Controlled Trials (RCTs) of treatment with anti-TNF have shown reduced damage progression in the short term but long term real world data is lacking.

**Objectives:** We set out to describe the long term radiographic progression amongst patients with PsA who transitioned from conventional synthetic Disease Modifying Drugs (csDMARDs) to anti-Tumour Necrosis Factor alpha inhibitors (anti-TNF) in routine care.

**Methods:** A retrospective sample of 28 patients (CASPAR criteria for PsA) was taken from the Bath longitudinal cohort. All patients had radiographs of the hands and feet taken at approximately 3 time points; 5 years before [T<sub>0</sub>], at the time of [T<sub>1</sub>] and 5 years post [T<sub>2</sub>] commencing anti-TNF treatment. 84 radiographs were scored using the Sharp-van der Heijde modified method (VDH) and osteoproliferation was scored using the psoriatic arthritis Rating score (PARS) method, by three assessors (AA, AA and WT). The assessors were blinded to the patient details and the order of the x-rays. Inter- and intra-rater reliability was assessed using intra-class correlation coefficients (ICC). Cumulative probability plots were used to describe radiographic progression on csDMARDs (T<sub>0</sub> to T<sub>1</sub>) compared with subsequent anti-TNF treatment (T<sub>1</sub> to T<sub>2</sub>). Change between probability plots was determined using the two-sample Kolmogorov-Smirnov test (K-S test). This sample size was calculated to ensure 90% power to determine the smallest detectable difference of the VDH (6.25) to 5% significance level.

**Results:** Of the 28 patients 15 were male, the mean age was 61 years (SD 13.4) and mean disease duration at T<sub>0</sub> was 11.2 years (SD 11.14). The mean study follow up period was 10.2 years (SD 2.76). Inter- and intra-rater reliability was >0.9. The median VDH score at baseline was 8.5 (IQR 1.75–27.5). The median scores for erosions, joint space narrowing and proliferation at baseline were 1.5 (IQR 0–8.5), 4.5 (IQR 1–15) and 7 (SD1–13.5) respectively.

The median change in VDH score on csDMARDs was 11.00 (IQR 3–19.5) and on anti-TNF was 4.00 (IQR 0.75–11.5). The median rate of change in VDH score per year was 2.29 (IQR 0.95–3.81) on csDMARDs and on anti-TNF was 1.04 (IQR 0.16) p=0.012 (figure 1). These scores correlate with observed improvements in clinical disease outcome measures including tender joint count, swollen joint count and nail score (data not shown).



**Abstract THU0293 – Figure 1.** mVDH rate of progression (per year). Δpre-TNF inhibition •post-TNF inhibition

**Conclusions:** In this real world observational cohort study the rate of radiographic progression slows following commencement of anti-TNF therapy. The overall rate of damage progression was low over long term follow up of more than ten years even amongst this group of more severe patients selected on the basis they progressed to anti-TNF therapy.

**Disclosure of Interest:** None declared

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#### THU0294 5-YEAR EFFICACY AND SAFETY OF APREMILAST TREATMENT IN SUBJECTS WITH PSORIATIC ARTHRITIS: POOLED ANALYSIS OF THE PALACE STUDIES

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**Background:** Apremilast (APR) is an oral phosphodiesterase 4 inhibitor for the treatment of adult patients with active psoriatic arthritis (PsA).

**Objectives:** The long-term efficacy and safety of APR treatment were evaluated for up to 5 years in subjects with active PsA from the phase 3 PALACE 1, 2, and 3 studies.

**Methods:** Subjects were randomised at baseline (BL) (1:1:1) to receive placebo (PBO), APR 30 mg BID (APR30), or APR 20 mg BID (APR20). PBO subjects were re-randomised (1:1) to APR30 or APR20 at Week 16 (early escape) or Week 24. Double-blind APR treatment continued to Week 52; subjects could continue APR during an open-label, long-term treatment phase for up to 5 years. Safety was assessed at each visit throughout the study.

**Results:** A total of 1493 subjects were randomised and received ≥1 dose of study medication (PBO: n=495; APR30: n=497; APR20: n=501). Of those randomised to APR30 at BL, 66.6% (331/497) completed 260 weeks of treatment. At Week 52, modified ACR20, ACR50, and ACR70 responses were achieved by 55.3%, 26.1%, and 11.9% of APR30 subjects, respectively, regardless of when APR was started (BL, Week 16, or Week 24). Sustained response rates were observed with continued APR30 treatment at Week 260 (table 1). Marked SJC improvements were seen, with mean percent reduction of 82.3% at Week 260; TJC reduction was 72.7%. At Week 260, 62.4% (136/218) of APR30 subjects with BL enthesitis achieved a MASES of 0; 80.9% (114/141) with BL dactylitis achieved a dactylitis count of 0. A total of 52.6% of APR30 subjects achieved HAQ-DI MCID ≥0.35 at Week 260, and low disease activity and remission, as defined by the cDAPSA (score ≤13), were achieved by 60.4% of APR30 subjects. Sustained responses in psoriatic skin involvement were observed with continued treatment at Week 260 in APR30 subjects who had ≥3% BL psoriasis body



surface area involvement, with PASI-50 and PASI-75 response rates of 65.8% (98/149) and 43.6% (65/149), respectively. Results were similar for subjects receiving APR20 (data not shown). Consistent efficacy results were seen across the 3 individual trials. No new safety concerns were identified with APR up to 260 weeks. For APR30 subjects entering the 5th year of APR exposure, adverse events (AEs) occurring in  $\geq 5\%$  were nasopharyngitis (6.6%) and upper respiratory tract infections (5.8%); most AEs were mild or moderate in severity. Among APR30-exposed subjects, serious AEs occurred in 5.8% in Weeks $>208$  to $\leq 260$ ; 5 subjects discontinued due to an AE.

**Table 1:**

	Outcomes at Week 260	
	APR30 n=329*	
ACR20, n/m <sup>†</sup> (%)	215/320 (67.2)	
ACR50, n/m <sup>†</sup> (%)	144/324 (44.4)	
ACR70, n/m <sup>†</sup> (%)	89/325 (27.4)	
SJC (0-76), mean % change from BL	-82.3	
TJC (0-78), mean % change from BL	-72.7	
MASES=0, n/m <sup>†</sup> (%)	136/218 (62.4)	
Dactylitis count=0, n/m <sup>†</sup> (%)	114/141 (80.9)	
cDAPSA (0-154) $\leq 13$ , n/m (%)	198/328 (60.4)	
HAQ-DI (0-3), mean change from BL	-0.42	
HAQ-DI MCID $\geq 0.35$ , n/m (%)	173/329 (52.6)	
PASI-50, n/m <sup>†</sup> (%)	98/149 (65.8)	
PASI-75, n/m <sup>†</sup> (%)	65/149 (43.6)	

Data as observed.  
\*The n reflects the number of subjects with data available at Week 260, regardless of when subjects started taking APR30 (BL, Week 16, or Week 24); actual number of subjects having data available for each end point may vary. †Denominators vary slightly due to availability of sufficient data for each level of ACR response assessment. ‡Examined among subjects with enthesitis at BL and having data at Week 260. §Examined among subjects with dactylitis at BL and having data at Week 260. ¶Examined among subjects with psoriasis involvement of the body surface area  $\geq 3\%$  at BL and data at Week 260. ACR20/50/70= $\geq 20\%/25\%/27\%$  improvement in American College of Rheumatology response criteria. n/m=number of responders/number of subjects with sufficient data for evaluation. SJC=swollen joint count. TJC=tender joint count. MASES=Maastricht Ankylosing Spondylitis Enthesitis Score. cDAPSA=Clinical Disease Activity in Psoriatic Arthritis. HAQ-DI=Health Assessment Questionnaire-Disability Index. MCID=minimal clinically important difference. PASI-50/75= $\geq 50\%/27\%$  reduction from BL Psoriasis Area and Severity Index score.

**Conclusions:** APR demonstrated sustained, clinically meaningful improvements in PsA signs and symptoms, physical function, and associated psoriasis in the population of subjects continuing treatment over 5 years. APR continued to demonstrate a favourable safety profile and was generally well tolerated at 5 years.

**Disclosure of Interest:** A. Kavanaugh Grant/research support from: Abbott, Amgen, AstraZeneca, BMS, Celgene Corporation, Centocor-Janssen, Pfizer, Roche, and UCB, D. Gladman Grant/research support from: AbbVie, Amgen, BMS, Celgene Corporation, Janssen, Novartis, Pfizer, and UCB, Consultant for: AbbVie, Amgen, BMS, Celgene Corporation, Janssen, Novartis, Pfizer, and UCB, C. Edwards Grant/research support from: Celgene Corporation; Pfizer, Roche, Samsung, Consultant for: Celgene Corporation, Pfizer, Roche, Samsung, Speakers bureau: Abbott, GSK, Pfizer, Roche, G. Schett Grant/research support from: Abbott, Celgene Corporation, Roche, UCB, Consultant for: Abbott, Celgene Corporation, Roche, UCB, B. Guertel Employee of: Celgene Corporation, N. Delev Employee of: Celgene Corporation, L. Teng Employee of: Celgene Corporation, M. Paris Employee of: Celgene Corporation, P. Mease Grant/research support from: Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Genentech, Janssen, Eli Lilly, Novartis, Pfizer, Roche, UCB, Consultant for: Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Genentech, Janssen, Eli Lilly, Novartis, Pfizer, Roche, UCB, Speakers bureau: Abbott, Amgen, Biogen Idec, BMS, Genentech, Janssen, Eli Lilly, Pfizer, UCB

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#### THU0295 FACTORS ASSOCIATED WITH PATIENT-PHYSICIAN DISCORDANCE IN A PROSPECTIVE COHORT OF PATIENTS WITH PSORIATIC ARTHRITIS: AN ASIAN PERSPECTIVE

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**Background:** Psoriatic arthritis (PsA) is a chronic inflammatory articular disease with diverse clinical manifestations. Few biomarkers are available to assess disease activity in PsA. Hence, both the patient's and the physician's assessment of disease activity is vital in ensuring optimal treatment outcomes. Understanding factors associated with patient and physician discordance can facilitate shared decision making and treatment management between patient and physician. There is limited data on factors associated with patient and physician discordance in psoriatic arthritis; none of which exist in the Asian population.

**Objectives:** To identify the factors associated with patient-physician discordance in a multi-ethnic Asian cohort of Psoriatic arthritis (PsA) patients.

**Methods:** Data was obtained from a prospective cohort of consecutive patients with psoriatic arthritis, who fulfil the CASPAR criteria recruited from a single centre in Singapore. Sociodemographic, clinical data and patient reported outcomes

were collected using a standardised protocol at baseline, 4 months, 8 months, 1 year and 2 years. Patient-physician discordance was defined as patient global assessment minus physician global assessment (PGA - PhGA). We evaluated factors associated with patient-physician using generalised linear regression to control for within-subject effect.

**Results:** From 126 patients (50.4% male, 67.5% Chinese, age: 51 $\pm$ 13.8 years, duration of illness: 5.6 $\pm$ 6.1 years) recruited at baseline, paired data for patient and physician global assessments were available for 224 visits over a median follow up of 10 (range 0–15) months. In univariable analysis, gender, duration of illness, fatigue, pain score, number of tender joint/swollen joint/dactylitis, mental health subscale of SF36 and physical function by Health Assessment Questionnaire (HAQ) were significantly associated with patient-physician discordance. In multivariable analysis, higher level of fatigue, higher pain score, poorer mental health were associated with PGA-PhGA; while higher swollen joint and dactylitis count were negatively associated with PGA-PhGA (table 1).

**Abstract THU0295 – Table 1.** Multivariable analysis for factors associated with patient-physician discordance

Factors	$\beta$	95% Confidence Interval	p-value
Age	0.211	(-0.029, 0.452)	0.085
Gender	-3.687	(-8.830, 1.457)	0.160
Female	Ref	-	-
Male			
Ethnicity	-1.085	(-6.654, 4.484)	0.703
Chinese	Ref	-	-
Non-Chinese			
Education	- 6.105	(-12.2,-0.012)	0.050
Secondary or below	Ref	-	-
Post-secondary (>10 years)			
Duration of illness (years)	0.252	(-0.187, 0.692)	0.261
Fatigue <sup>a</sup>	1.964	(0.577-3.350)	0.005
Pain <sup>a</sup>	0.456	(0.312-0.601)	<0.001
Tender joint count	-1.006	(-2.197, 0.184)	0.098
Swollen joint count	-3.312	(-5.095,-1.528)	<0.001
Dactylitis count	-3.059	(-5.594,-0.523)	0.018
HAQ <sup>a</sup>	-2.265	(-8.619, 4.090)	0.485
SF36-mental health domain <sup>a</sup>	0.958	(0.169-1.747)	0.017

#### REFERENCE:

[1] A Higher score represents poorer status

**Abbreviations:** HAQ: Physical function by Health Assessment Questionnaire; SF36: Medical Outcome Short Form 36

**Conclusions:** Higher pain score, higher level of fatigue and poorer mental health may explain underestimation of patient global assessment by physicians. Higher swollen joint and dactylitis count may explain overestimation of physician global assessment.

**Disclosure of Interest:** None declared

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#### THU0296 CLINICAL RESULTS OF PATIENTS WITH PERIPHERAL PSORIATIC ARTHRITIS NOT RECEIVING BIOLOGICAL THERAPY IN A MULTIDISCIPLINARY UNIT

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**Background:** We consider multidisciplinary management necessary, especially in a subgroup of patients with Psoriatic Arthritis (PsA) for complexity, cutaneous and/or joint involvement. Despite the limited evidence of efficacy of methotrexate (MTX) and other classical synthetic DMARDs (csDMARDs) in these patients, they are commonly prescribed in our multidisciplinary unit (following the recommendations of experts, in peripheral PsA).

**Objectives:** To assess joint and cutaneous involvement in patients with peripheral psoriatic arthritis not receiving biologics in our multidisciplinary unit (visited for at least 6 months).

**Methods:** We review clinical the records of 199 PsA patients visited in our multidisciplinary unit and select 74 patients with the above mentioned criteria; we collect epidemiological and clinical data, and joint and skin activity evaluation by DAPSA, PASI, BSA and PGA (in plaque psoriasis) and proportion of patients that achieve MDA (minimum disease activity) as a therapeutic goal. Data were analysed using SPSSv23.

**Results:** 74 patients, 63.5% males, aged mean(SD) 54.8 (14.0) years. 56 peripheral PsA and 18 mixed (peripheral predominance); with mean 94.9 (92.4) months of disease; 35.1% with previous clinical enthesitis and 37.8% previous dactylitis. Cutaneous disease consisted mainly (82.4%) in plaque psoriasis, 9.5% affecting folds, 4.1% onychopathy. 52.7% have received a previous DMARD of (31.1% MTX, 9.5% leflunomide) and 23.0% PUVA; 4.1% have received previous biological treatment. Current treatment: 83.8% DMARDs (68.9% MTX and 5.4% leflunomide) with a mean follow-up of 60.6 (55.0) months.

**Disease activity:**

Skin plaque psoriasis was mainly controlled: 73.4% low PASI level (23.4% moderate) median PASI 3.0 [1.5–5.0]; 50.0% mild BSA, median BSA 3.0 [1.0–6.0]. 73.1% PGA of very mild or mild-moderate disease 87.0% of patients met DAPSA criteria of remission-low disease activity (DAPSA median 3.15 [1.34–6.71]; 55.9% achieved DAPSA<4); 75.7% were in low activity/remission according to medical judgement.

Overall 63.9% of patients achieved MDA.

15.3% (10 patients) had "relative contraindications" to biological therapy (6 cases of recent cancer, 2 HBV infection).

**Conclusions:** Over half of PsA patients from our multidisciplinary unit achieve low cutaneous and articular disease activity under csDMARDs, mainly Methotrexate. The use of targeted DMARDs such as apremilast in this scenario, before biological therapies, may improve disease outcomes in a subgroup of patients, corresponding with the efficacy shown in different domains of the psoriatic disease. Further research is needed to compare clinical results between csDMARDs and apremilast.

**Disclosure of Interest:** None declared

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THU0297

#### EVALUATION OF CARDIOVASCULAR RISK FACTORS AMONG PATIENTS WITH PSORIASIS, PSORIATIC ARTHRITIS AND PERIPHERAL SPONDYLOARTHRITIS

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**Background:** It is well known that the prevalence of Cardiovascular Risk Factors (CVRF) in patients with Psoriatic Arthritis (PsA) is higher than in the general population<sup>1</sup>. However, there is a lack of studies comparing PsA against Psoriasis without arthritis, and also against peripheral Spondyloarthritis (SpA).

**Objectives:** a) To compare the prevalence of CVRF among patients with PsA, Psoriasis without arthritis and peripheral SpA without Psoriasis; and b) to evaluate the association between CVRF and the presence of arthritis and/or Psoriasis.

**Methods:** A cross-sectional, observational and unicenter study in which clinical, analytical and demographic data from 300 patients were analysed. Patients were divided into four groups: PsA, Psoriasis without arthritis, peripheral SpA without Psoriasis and controls. Patients with PsA and peripheral SpA met CASPAR and peripheral ASAS criteria, respectively. Hypertension, Diabetes (T2DM) and Dyslipidemia were evaluated among the four groups by using the chi-square test. In order to evaluate whether CVRF could be explained by the presence of arthritis or Psoriasis, we divided patients (by excluding control groups) in arthritis/no arthritis and Psoriasis/no Psoriasis. Univariate and multivariate logistic regressions adjusted by sex and age were performed in order to determine variables independently associated with the presence of these three CVRF.

**Results:** Among the 300 patients included in the analysis, 89 (29.7%), 35 (11.7%) and 87 (29%) patients reported Hypertension, T2DM and Dyslipidemia, respectively. Regarding classification, 61 (20.3%) patients, 100 (33.3%), 100 (33.3%) and 39 (13.0%) patients were classified as control group, Peripheral SpA without Psoriasis, PsA and Psoriasis without arthritis, respectively. Patients from the control group showed significantly lower prevalence of Hypertension and Dyslipidemia against the other three groups (p<0.05); however, there were no differences between Peripheral SpA group, PsA and Psoriasis without arthritis regarding CVRF.

Patients with arthritis showed similar prevalence of CVRF than those without arthritis, as well as patients with Psoriasis vs. no Psoriasis.

Univariate analysis showed that Hypertension is significantly associated (p<0.05) to AINEs intake [OR 1.79 (95%CI 1.06–2.99)] as well as with disease duration [OR 1.02 (95%CI 1.01–1.05)]; however, the multivariate analysis adjusted by age and sex did not show significant differences. Regarding T2DM and dyslipidemia, the presence of arthritis or Psoriasis was not associated with the development of these comorbidities.

**Conclusions:** Our data suggest that the prevalence of CVRF among patients with Psoriasis, PsA and peripheral SpA are similar, although it is higher than in the general population. The presence of Hypertension in these patients is associated

with the use of NSAIDs; however, greater new studies would be necessary in order to determine specific associations.

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**Disclosure of Interest:** None declared

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THU0298

#### PERITENON EXTENSOR TENDON INFLAMMATION, SYNOVITIS AND ENTHESOPATHY IN PSORIATIC ARTHRITIS: WHAT IS THE CONNEXION?

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**Background:** Metacarpophalangeal joint (MCPJ) swelling in Psoriatic Arthritis (PsA) can be produced both by intra-articular synovitis (IAS) and peritenon extensor tendon inflammation (PTI). This last lesion has been reported as an enthesitis-like lesion.

**Objectives:** To evaluate if PTI is a synovitis or enthesitis related lesion using MASEI (Madrid Sonographic Enthesis Index) to analyse the existence of association with IAS and PTI.

**Methods:** 27 consecutive non selected PsA patients were included. An expert rheumatologist obtained the US images from the dorsal aspect of 2nd to 5th MCPJ of both hands evaluating IAS and PTI, and also performed the MASEI examination. In addition to the PD item of MASEI (defined as signal in bone profile or intra-tendon or bursa at the enthesitis), PD OMERACT was evaluated as present or absent (defined as signal in the enthesitis ≤2 mm to the bone profile). We used a MyLab 70 XVG machine, Esaote, Genova, Italy, with a greyscale (GS) 13 MHz probe and 7.1 MHz power Doppler (PD) frequency, PRF 750 Hz and 60 Gain. 3–5 s videos of each MCPJ and enthesitis were obtained in transverse and longitudinal views for further reliability analysis. Reliability of IAS and PTI was performed by 5 readers (true US result was the consensus of at least three) and MASEI's reliability was performed by 3 readers (true US result was the consensus of at least two). For reliability analysis, mean Cohen kappa was used for IAS and PTI, and intraclass correlation coefficient (ICC) for MASEI based on a mean-rating three readers, absolute-agreement, two-way mixed effect model. Statistical association between IAS, PTI and MASEI was analysed with T student test. SPSS statistical package version 20 (SPSS Inc, Chicago, IL) was used.

**Results:** Eighteen patients had PTI PD (66.7%), same for SIA PD. Inter-reader reliability for PTI and SIA was 0.685 and 0.680 kappa values respectively. Inter-reader reliability for MASEI was excellent ICC 0.922 (IC 95% 0.852–0.962), similar to PD MASEI ICC 0.921 (IC 95% 0.851–0.962) and PD OMERACT ICC 0.895 (IC 95% 0.802–0.949). Association data are shown in table 1.

**Abstract THU0298 – Table 1.** Association between IAS and PTI with MASEI and different PD subgroups.

	PTI		p value	IAS		p value
	Present	Absent		Present	Absent	
Mean MASEI±SD	32,44 ±15,62	27±9,33	0270	32±6,16	27,89 ±7,72	0380
Mean PD MASEI±SD	8±6	3,67 ±3,28	0023	6,83 ±6,15	6±4,5	0694
Mean PD OMERACT ±SD	1,61±1,33	0,56 ±1,01	0033	1,39 ±1,46	1±1	0426

**Conclusions:** In PsA, IAS at MCPJ didn't show any association with enthesitis. However, PTI showed a significant statistically association with active enthesitis (PD MASEI and PD OMERACT). This finding reinforces the idea that PTI at MCPJ level is related with the swelling of the functional enthesitis related to the retinaculum pulley structure.

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THU0299

**AN INTEGRATED ANALYSIS OF CHANGES IN LIPID LEVELS AND INCIDENCE OF CARDIOVASCULAR EVENTS FOLLOWING TOFACITINIB TREATMENT IN PATIENTS WITH PSORIATIC ARTHRITIS ACROSS PHASE 3 AND LONG-TERM EXTENSION STUDIES**

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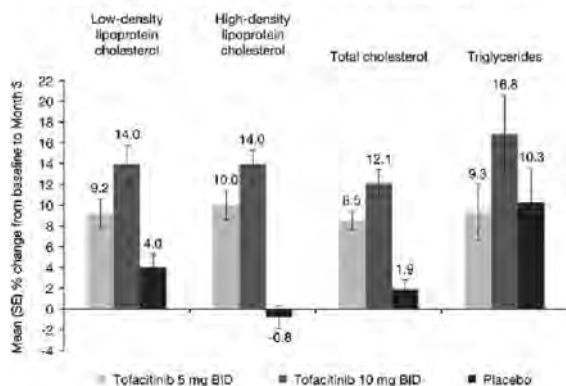
**Background:** Cardiovascular (CV) disease and cardiometabolic syndrome are common comorbidities/causes of mortality in patients (pts) with psoriatic arthritis (PsA). Tofacitinib is an oral JAK inhibitor for the treatment of PsA.

**Objectives:** To investigate changes in lipid levels and incidence of CV events in pts with PsA treated with tofacitinib in Phase (P) 3 and long-term extension (LTE) studies.

**Methods:** Data were analysed for pts who received  $\geq 1$  dose of tofacitinib 5 or 10 mg BID or placebo (PBO), integrated across 2 P3 studies (OPAL Broaden [12 months (m); NCT01877668, including adalimumab control]; OPAL Beyond [6 m; NCT01882439]) and 1 LTE study (OPAL Balance [data cut-off May 2016; ongoing, database not locked; NCT01976364]). Lipid levels were assessed throughout P3 and LTE studies; this analysis included data from the PBO-controlled period (M0–3) of P3 studies. Blood pressure, hypertension events (standardised MedDRA query [narrow]) and adjudicated (independent/blinded to treatment) major adverse cardiovascular events (MACE) are reported for all pts who received  $\geq 1$  dose of tofacitinib (pooled across doses for hypertension and MACE). Incidence rates (IR; pts with events/100 pt-years [PY]) and 95% CI are reported.

**Results:** Overall, 783 pts (776 PY of tofacitinib exposure) were included in P3 and LTE studies; treatment duration was 1–927 days. After 3 m of tofacitinib treatment in P3 studies, dose-dependent increases in lipid levels were observed with tofacitinib; minimal changes were observed with PBO, except for triglycerides (figure 1). Concurrent increases in high-density and low-density lipoprotein (HDL/LDL) and no change in the total cholesterol/HDL ratio were shown. Across P3 and LTE studies, no clinically significant changes in mean systolic or diastolic blood pressure were seen to 24 m. Hypertension events were reported in 38 (4.9%) pts: IR 4.93 [95% CI 3.49, 6.77]. Of these events, 4 led to pt discontinuation and 2 were serious adverse events. MACE were reported for 3 (0.4%) pts receiving tofacitinib (IR 0.38 [95% CI 0.08, 1.11]) and included sudden cardiac death (57 days of exposure at time of event), myocardial infarction (197 days) and ischaemic stroke (80 days). This is within the range reported in tofacitinib studies in pts with psoriasis (IR 0.24 [0.15, 0.37]; 8,759 PY of exposure) and rheumatoid arthritis (RA) (IR 0.38 [0.30, 0.47]; 21,286 PY of exposure). No dose-dependent effects on blood pressure were apparent.

**Figure.** Mean % change from baseline in lipid levels to Month 3 integrated across Phase 3 studies



BID, twice daily; SE, standard error

**Abstract THU0299 – Figure 1.** Mean% change from baseline in lipid levels to Month 3 integrated across Phase 3 studies. BID, twice daily; SE, standard error

**Conclusions:** In pts with PsA, the magnitude and dose dependency of increases in lipid levels to M3 were consistent with findings in tofacitinib studies in pts with psoriasis and RA. In P3 and LTE studies, no clinically significant changes were seen in blood pressure or incidence of hypertension. Incidence of MACE was within the range reported in prior tofacitinib studies in psoriasis and RA; however, the long latency of MACE requires longer-term observation.

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THU0300

**NETWORK META-ANALYSIS OF TOFACITINIB VS bDMARDS OR APREMILAST FOR THE TREATMENT OF TNF INHIBITOR-NAIVE PATIENTS WITH PSORIATIC ARTHRITIS**

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**Background:** Tofacitinib is an oral JAK inhibitor for the treatment of psoriatic arthritis (PsA).

**Objectives:** To perform a systematic literature review (SLR) and network meta-analysis (NMA) to evaluate the efficacy of tofacitinib 5 and 10 mg BID relative to biologic disease-modifying antirheumatic drugs (bDMARDs) or a targeted synthetic DMARD (apremilast [APR]) in tumour necrosis factor inhibitor-naïve (TNFi-N) patients with active PsA.

**Methods:** The SLR identified randomised controlled clinical trials (RCTs) evaluating tofacitinib, bDMARDs or APR to treat patients with active PsA who were TNFi-N. Outcomes included American College of Rheumatology (ACR)20 response and change from baseline in Health Assessment Questionnaire-Disability Index ( $\Delta$ HAQ-DI), Dactylitis Severity Score ( $\Delta$ DSS) and Leeds Enthesitis Index ( $\Delta$ LEI). Treatment effects were only evaluated during placebo (PBO)-controlled trial phases. The Bayesian NMA (with non-informative priors) was conducted using WinBUGS. The binomial logit model was used for ACR20.  $\Delta$ HAQ-DI,  $\Delta$ DSS and  $\Delta$ LEI were analysed using the normal identify link model. A fixed-effect model was fitted to the data. Median treatment rankings represent data from each iteration of the model from which inferences are based, following model convergence.

**Results:** The SLR identified 25 RCTs and 21 were included in the NMA (see treatments in table 1). All trials allowed methotrexate use. PBO-controlled treatment durations ranged from 12–24 weeks. In general, patient characteristics were similar across trials. All treatments were associated with improvements in ACR20 and  $\Delta$ HAQ-DI vs PBO. Tofacitinib 5 mg BID was associated with substantially decreased odds ratios (ORs) for ACR20 vs golimumab 50 and 100 mg Q4W, etanercept 25 mg BW, infliximab 5 mg/kg and secukinumab 150 mg QW-Q4W (table 1); ORs for all remaining comparators were not substantially different. Tofacitinib 10 mg BID was associated with a substantially increased OR for ACR20 vs APR 20 mg BID. Etanercept was associated with an improvement in  $\Delta$ HAQ-DI vs tofacitinib 5 and 10 mg BID. There was no difference in  $\Delta$ HAQ-DI for tofacitinib vs other bDMARDs. For ACR20, tofacitinib 5 and 10 mg BID were median ranked 14 (95% credible interval: 8, 17) and 9,<sup>5, 14</sup> respectively, among 18 comparators. For  $\Delta$ HAQ-DI, tofacitinib 5 and 10 mg BID were median ranked 11,<sup>4, 13</sup> and 8,<sup>2, 13</sup> respectively, among 14 comparators. Two studies evaluated  $\Delta$ DSS and  $\Delta$ LEI; there were no substantial differences in  $\Delta$ DSS and  $\Delta$ LEI for tofacitinib 5 and 10 mg BID vs adalimumab 40 mg Q2W and ixekizumab 80 mg Q2W and Q4W.



**Abstract THU0300 – Table 1.** Fixed-effect NMA data for ACR20 and ΔHAQ-DI in TNFi-N patients with PsA – comparison of bDMARDs or apremilast vs tofacitinib 5 and 10 mg BID<sup>a</sup>

Treatment	ACR20, OR (95% CrI) <sup>b,c</sup>		Difference in ΔHAQ-DI (95% CrI) <sup>d,e</sup>	
	vs tofacitinib 5 mg BID	vs tofacitinib 10 mg BID	vs tofacitinib 5 mg BID	vs tofacitinib 10 mg BID
Akatorcept 125 mg	1.0 (0.4, 2.4)	0.7 (0.3, 1.6)	NA	NA
Alectinib 40 mg Q2W	1.4 (0.8, 2.2)	0.9 (0.5, 1.3)	-0.1 (-0.2, 0.1)	0.0 (-0.1, 0.1)
Apremilast 30 mg BID	0.9 (0.5, 1.6)	0.6 (0.3, 1.0)	0.04 (-0.1, 0.2)	0.1 (-0.1, 0.3)
Apremilast 50 mg BID	0.7 (0.4, 1.3)	0.5 (0.3, 0.9)	NA	NA
Ceritinib 450 mg Q1W + 200 mg Q2W	1.6 (0.8, 3.2)	1.1 (0.5, 2.1)	NA	NA
Enasoprevir 25 mg BW	1.7 (1.2, 2.4)	2.4 (1.7, 3.3)	-0.8 (-1.1, -0.6)	-0.9 (-1.2, -0.5)
Gedintinib 50 mg Q4W	4.8 (2.7, 18.4)	2.7 (1.6, 6.9)	-0.1 (-0.2, 0.1)	-0.0 (-0.2, 0.1)
Gedintinib 100 mg Q4W	1.3 (1.4, 8.4)	2.1 (0.9, 5.3)	-0.2 (-0.3, 0.02)	-0.1 (-0.3, 0.1)
Infliximab 5 mg/kg	1.6 (1.7, 7.5)	2.4 (1.1, 5.9)	NA	NA
Infliximab 80 mg Q4W	1.4 (0.7, 2.7)	0.9 (0.5, 1.4)	-0.1 (-0.2, 0.1)	-0.0 (-0.2, 0.2)
Evritinib 50 mg Q2W	1.6 (0.8, 3.1)	1.0 (0.5, 2.1)	-0.2 (-0.3, 0.01)	-0.1 (-0.3, 0.1)
Secukinumab 150 mg Q1W then Q4W	2.3 (1.2, 4.9)	1.4 (0.8, 2.3)	-0.01 (-0.2, 0.2)	0.04 (-0.2, 0.5)
Secukinumab 300 mg Q1W then Q4W	2.2 (1.0, 5.0)	1.3 (0.6, 3.3)	-0.1 (-0.3, 0.2)	0.0 (-0.2, 0.2)
Trilokinib 45 mg Q12W	1.0 (0.5, 1.8)	0.6 (0.3, 1.2)	-0.03 (-0.2, 0.1)	0.02 (-0.1, 0.2)
Trilokinib 90 mg Q12W	1.2 (0.6, 2.3)	0.8 (0.4, 1.5)	-0.1 (-0.2, 0.1)	-0.02 (-0.2, 0.1)

<sup>a</sup>Results which do not include the null value are bold and italicized.  
<sup>b</sup>OR, odds ratio; CI, confidence interval; NA, not available.  
<sup>c</sup>95% CrI, 95% credible interval; OR, odds ratio; CI, confidence interval; NA, not available.  
<sup>d</sup>ΔHAQ-DI, change in Health Assessment Questionnaire Disability Index; OR, odds ratio; CI, confidence interval; NA, not available.  
<sup>e</sup>CrI, 95% credible interval; OR, odds ratio; CI, confidence interval; NA, not available.

**Conclusions:** Based on the NMA of published RCTs in TNFi-N patients with PsA, tofacitinib 5 and 10 mg BID had similar efficacy vs many, but not all, bDMARDs and APR in improving ACR20 and ΔHAQ-DI.

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**THU0301 A NOVEL ROLE FOR THE PSORIATIC ARTHRITIS IMPACT OF DISEASE QUESTIONNAIRE (PSAID)**

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**Background:** Psoriatic arthritis (PsA) is an inflammatory arthritis that occurs in about 30% of patients with Psoriasis (Ps). Recently, a new Patient Reported Outcome Measure (PROM), Psoriatic Arthritis Impact of Disease (PsAID) was specifically developed for PsA Patients. The two versions of the PsAID, PsAID-9 and PsAID-12, are scored on a Numeric Rating Scale (NRS) of 0–10. The Minimal Disease Activity (MDA) is a composite outcome measure for PsA patients, which uses the Health Assessment Questionnaire (HAQ) as one criterion. However, the HAQ does not correlate well with measures of disease activity as PsA disease duration increases, and its use in the assessment of disease activity has been questioned.

**Objectives:** Our objectives were to 1) validate the PsAID within our patient cohort, 2) determine if the PsAID can replace any of the other PROMs administered in the clinic, and 3) determine if the PsAID can replace the HAQ in the MDA.

**Methods:** Patients were recruited from a large psoriatic arthritis clinic. All patients completed the PsAID and 10 other PROMs. Various measures of disease activity were recorded by a physician at each visit. Descriptive statistics (mean, median, SD, min, max) were calculated for all PROMs. PsAID cut-offs for use in the MDA were generated based on Remission (REM) and Low Disease Activity (LDA) disease states in the Clinical Disease Activity for Psoriatic Arthritis Index (cdAPSA).

**Results:** 115 patients completed the PsAID. There were 70 males, 45 females, with a mean PsA duration of 18.7 (±11.6) years. Mean scores of PsAID-9 and PsAID-12 were 3.4 (±2.4) and 3.2 (±2.3) respectively. The PsAID correlated moderately well with 9 of the PROMs administered in the clinic (R<sup>2</sup>=0.51–0.78). Four

PsAID cutoffs were generated for use in the MDA: REM PsAID-9, REM PsAID-12, LDA PsAID-9, and LDA PsAID-12. All four versions of the PsAID MDAs had a sensitivity greater than 85% with the HAQ MDA, and three versions of the PsAID MDA had a specificity greater than 85% with the HAQ MDA.

**Conclusions:** Our cohort had lower mean PsAID scores than previously reported series suggesting that our patients are monitored carefully. The only moderate correlations with other PROMs suggest that the PsAID cannot replace any of these PROMs. The high sensitivity and specificity of the PsAID MDA with the HAQ MDA suggest that the PsAID is an effective replacement for the HAQ in the MDA.

**Disclosure of Interest:** None declared

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**THU0302 SURVIVAL OF DISEASE-MODIFYING DRUGS (DMARD) IN PATIENTS WITH RECENT DIAGNOSIS OF PSORIATIC ARTHRITIS IN DAILY CLINICAL PRACTICE**

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**Background:** Psoriatic arthritis (PsA) is a chronic inflammatory disease that benefits from DMARDs, in this regard knowing more about these therapies is a great step forward in the management of these patients in daily clinical practice.

**Objectives:** To evaluate the survival of DMARDs used in recent diagnose PsA patients as well as the causes of discontinuation and to analyse the possible associated factors.

**Methods:** Retrospective longitudinal observational study. **Subjects:** Inception cohort of patients from January 2010 to , December 2014 and followed up to December 2016, diagnosed with PsA according to ICD-10 code. **Main outcome:** discontinuation of conventional synthetic DMARDs (csDMARDs) and biological originator DMARDs (boDMARDs) due to: Adverse drug reactions (ADRs); Improvement or remission; Inefficacy; Patient's decision and Physician's decision. **Covariables:** sociodemographic and clinical. **Statistical analysis:** To estimate DMARDs discontinuation rates, survival techniques were used, expressing the incidence rate (IR) per 100 patients\*year with their respective CI at 95%. Multivariate Cox regression models were performed to analyse the factors associated with DMARDs discontinuation and the results were expressed in Hazard ratio (HR) and 95% CI.

**Results:** 191 patients with recent diagnosis of PsA were included, with a 379.70 Patients\*year follow-up. 50.3% were male, the mean age at diagnosis was 50 ±14.6 years old. 46.6% of the patients had a history of cutaneous psoriasis. The HLA-B27 was positive in 20% of patients. 50% of the patients started a DMARDs at the first visit. Throughout the follow-up, all patients received csDMARDs and 23 used boDMARDs. The median DMARD per patient was 2<sup>1-3</sup>. Methotrexate (MTX) was the most used drug 69.7%. According to the treatment regimen, 30% were on combination therapy, the most frequent was antiTNF +MTX (33%). 103 discontinuations were recorded with a IR 27.13 [22.36–32.90] within these, 44 were related with ADRs (IR 11.59 [8.62–15.57]), 24 (IR 6.32 [3.58–11.13]) were due to inefficiency, 9 (IR 2.37 [1.23–4.55]) were registered after remission, 12 (IR 3.16 [1.79–5.56]) by decision of the patient and 12 (IR 3.16 [1.79–5.56]) by doctor's decision. The DMARDs median survival was 1.8 years [1.4–2.7]. Table 1 shows the discontinuation rates for each type of DMARDs and the multivariate analysis for the factors associated with DMARDs discontinuation is in table 2.

**Table 1:**

Table 1	Patients*year	Events(n)	IR	95%CI
MTX orally	243.46	53	21.77	16.63–28.49
Sc MTX	49.90	18	36.07	22.73–57.25
Salazopyrine	84.80	30	35.37	24.73–50.59
Leflunomide	21.83	10	45.80	24.64–85.13
Antimalarials	25.34	8	31.56	15.78–63.12
boDMARDs	57.56	25	43.43	29.35–64.28

Table 2	HR	95% CI	P
Women	1.51	0.61–3.09	0.436
Age at diagnosis	0.97	0.97–1.01	0.267
Distress level	1.87	1.00–3.48	0.049
C Reactive protein≥1.05gr/dL	1.85	0.99–3.48	0.055
Combination therapy	2.36	1.46–3.80	0.000
boDMARDs	1.05	0.52–2.11	0.886
MTX vs rest DMARDs	0.53	0.31–0.91	0.021

**Conclusions:** In our study, the DMARD discontinuation rate was 27.13, mainly related with ADRs. We have also found some psychological, clinical and therapy regimen factors that can modify the DMARDs survival on PsA. We observed that MTX, presented the longest survival independent of the rest of the factors.

**Disclosure of Interest:** None declared

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THU0303

### THE EARLY PSORIATIC ARTHRITIS SCREENING QUESTIONNAIRE IDENTIFIES PATIENTS WITH PSORIATIC ARTHRITIS AMONGST TREATED PATIENTS WITH PSORIASIS

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**Background:** Studies suggest a high prevalence (approximately 15%) of undetected psoriatic arthritis (PsA) amongst patients with psoriasis<sup>1</sup>. A number of screening questionnaires have been designed to allow detection of such patients. This includes the Early Psoriatic Arthritis Screening Questionnaire (EARP) which detects early PsA in untreated patients with psoriasis, with a sensitivity of 85.2% and specificity of 91.6%<sup>2</sup>. Little is known about whether such questionnaires are also able to detect PsA in treated patients with psoriasis.

**Objectives:** To determine the case finding ability of EARP in a tertiary centre cohort of treated psoriasis patients.

**Methods:** All patients attending a tertiary centre psoriasis clinic were invited to complete the EARP. EARP comprises a 10 point patient reported questionnaire regarding symptoms of joint disease. Scores of 3 or more are considered positive. All patients who completed the questionnaire and received a positive score were assessed by a rheumatologist. Diagnosis of PsA was made by clinician impression and CASPAR criteria. Disease activity was assessed using psoriasis area severity index (PASI), 66/68 swollen and tender joint count, SPARCC enthesitis index, CRP and Health associated quality of life disability index (HAQ-DI). The composite disease activity measure DAPSA and the OMERACT definition of minimal disease activity were determined.

**Results:** 133 patients were invited to complete the EARP questionnaire and 119 participated. Fifty patients had a positive result (42%). Of these, 8 were known to have PsA and under rheumatologic care. A further 21 attended for formal rheumatologic assessment. Thirteen of the 21 patients (61.9%) were found to have psoriatic arthritis and were not under the care of a rheumatologist. This represents 10% of the initial 133 patients screened. Ten of those patients were further assessed. The average age was 52.8 and BMI 33.2. Seven patients were male. All 10 were on biologic agents but only 3 on concurrent conventional DMARDs. Average tender joint count was 16, swollen joint count 3.6, SPARCC 6.2 and PASI score 3.42. Only 1 patient was in minimal disease activity.

**Conclusions:** The EARP tool can identify patients with active PsA amongst patients with psoriasis, even those on treatment with biologic agents. Such a tool may be useful in identifying patients who may benefit from rheumatology care.

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THU0304

### ASSOCIATION OF ANXIETY, DEPRESSION AND FATIGUE WITH DISEASE ACTIVITY, JOINTS EROSION AND SKIN LESION SEVERITY IN EARLY PSORIATIC ARTHRITIS PATIENTS

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**Background:** Depression is one of the precursors of psoriasis and psoriatic arthritis (PsA) development. It was found that depression and anxiety negatively affect the achievement of remission in PsA. B. Michelsen 2017] Interrelation of anxiety, depression and fatigue (according to patient-reported outcomes) with disease activity, erosive arthritis and skin lesion severity in early PsA hadn't been sufficiently studied.

**Objectives:** To study anxiety, depression and fatigue disorders (according to patient-reported outcomes) and their correlation with disease activity, erosive arthritis and severity of psoriasis in early PsA patients (pts).

**Methods:** 78 pts (M/F=39/39) with early PsA according to CASPAR criteria were included; all pts had peripheral arthritis for  $\leq 2$  years; mean age 36.5 $\pm$ 10.7 years, disease duration 12.2 $\pm$ 10.3 mo. It was a treatment naïve cohort. All pts underwent

standard clinical examination of PsA activity. Mean disease activity indexes (DAS)=4.0 $\pm$ 1.4, DAS28=4.2 $\pm$ 1.1. 78 patients were studied for fatigue (according to FACIT), patient global disease activity (PGA), patients pain measured by VAS, and Health Assessment Questionnaire (HAQ); 66 patients (M/F=33/33) were studied for anxiety and depression (according to HADS). At HADS score  $\geq 8$  patients had anxiety and depression disorders. Higher scores for FACIT scales indicate better quality of life (less fatigue). Skin lesion severity was evaluated in terms of body surface area (BSA) affected and Psoriasis Area Severity Index (PASI). When BSA was  $\geq 3\%$ , PASI was calculated. PASI $\geq 11$  indicates moderate and severe psoriasis. Descriptive statistics was used, M $\pm$ SD, Me [Q25;Q75], U-test were performed; p<0.05 was considered to indicate statistical significance.

**Results:** Mean FACIT score was low amounting to 35.3 $\pm$ 9.6, testifying increased fatigue; mean anxiety index was 5.7 $\pm$ 3.1, depression index was 3.8 $\pm$ 3.0. Anxiety disorders were detected in 16 out of 66 (24.2%) pts, depression disorders in 9 out of 66 (13.0%) pts. Negative correlation was found between FACIT score and DAS (r=-0.26), DAS28 (r=-0.26), CRP (r=-0.27), PGA (r=-0.35); and pain VAS (r=-0.25). Depression was more pronounced in pts with erosive arthritis in hands and/or feet (r=0.31). Negative correlation of FACIT score (r=-0.54), correlation of anxiety (r=0.26) and depression (r=0.33) indexes was found with health-related functional indexes according to HAQ. HADS indexes (anxiety and depression) are cross-correlating (r=0.51) and are negatively correlating with FACIT scores (r=-0.49 and r=-0.48, accordingly). An association was found of anxiety and depression indexes with the severity of psoriasis PASI index (r=0.38 and r=0.31, accordingly).

**Conclusions:** In early treatment-naïve PsA patients, increased fatigue and in a quarter of cases anxiety disorders, in 13% of patients depression disorders had been found. Psychological disorders are associated with PsA activity, the severity of psoriasis and joints erosion. Fatigue, anxiety and depression in early PsA patients result in the reduction of their functional capacity.

**Disclosure of Interest:** None declared

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THU0305

### MINIMAL DISEASE ACTIVITY (MDA) ATTAINMENT AFTER STARTING BIOLOGICAL (B) DMARDs AND NON-BDMARDs TREATMENT IN PSORIATIC ARTHRITIS PATIENTS (PTS) IN ROUTINE CARE: RUSSIAN PSORIATIC ARTHRITIS REGISTRY (RU-PSART) DATA

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**Background:** MDA is a valid instrument for evaluating PsA treatment results. There is limited data about MDA attainment after starting bDMARDs and non-bDMARDs in routine care. RU-PsART collected data from 25 rheumatology clinics in the Russian Federation.

**Objectives:** evaluate MDA attainment after starting bDMARDs and non-bDMARDs treatment in PsA pts in routine care.

**Methods:** 294 (M/F=133/161) pts with PsA, diagnosed according to CASPAR criteria, mean age 41.2 $\pm$ 1.9 (Min 21 – Max 72) years (yrs.), PsA duration 6.1 $\pm$ 5.3 (Min 0 – Max 31) yrs., psoriasis duration 13.6 $\pm$ 10.7 (Min 0.2 – Max 54.8) yrs. were included in the RU-PsART after signing consent participation forms. The present analysis included 274 pts who have data concerning PsA activity, treatment and MDA. The number of pts who reached MDA at least once were calculated. At the time of evaluation 81 out of 274 pts (29.6%) were taking bDMARDs $\pm$ sDMARDs (Infliximab (25 pts), Etanercept (16 pts), Adalimumab (14pts), Ustekinumab (8pts), Golimumab (5pts), Sekukinumab (2pts)). 193 out of 274 pts (70.4%) were taking other types of treatment - sDMARDs $\pm$ NSAID, mostly methotrexate (74.2%), sulfasalazine (12%), leflunomide (3.6%), hydroxychloroquine (0.4%); steroids (9.8%). All pts underwent evaluation of PsA activity by DAS28, CRP, Pt/Physician GA, Pain GA by VAS (0–100 mm), swollen/tender joints count (SJC/TJC), DAPSA and considered REM $\leq 4$ /LDA $\leq 14$ . M $\pm$ SD, Me [Q25; Q75], Min-Max, %, U-test, ORs with 95% CI were performed. All CI >1, p $\leq$ 0.05 were considered to indicate statistical significance.

**Results:** At time of evaluation 60 out of 274 pts (21%) reached MDA at least once. Mean duration of sDMARDs and bDMARDs $\pm$ sDMARDs was 11<sup>6/17</sup>/Min 3 - Max 204 months and 9<sup>15</sup>/Min 2 - Max 82 months accordingly. 28 out of 193 pts (10.4%) taking sDMARDs achieved MDA. Among 81 pts taking bDMARDs  $\pm$ sDMARDs MDA was seen in significantly more cases - 32 pts (30.8%), OR=3.85 [CI 95% 2.11–7.01]. REM/LDA by DAPSA was found in significantly more cases compared to pts taking other therapies - in 50 out of 81 pts (61.7%) and in 56 out of 193 pts (29%) accordingly (p $\leq$ 0.05, U-test). Pts who had ever



taken bDMARDs±sDMARDs had significantly less PsA activity compared to those who had taken other types of treatment (table 1).

Abstract THU0305 – Table 1

Parameters	bDMARDs	other therapy
DAS28	1.8 [1.8;4.2]*	3.4 [2.8;5.1]
CRP	1.3 [0.9;7.9]*	6 [2.5;17.8]
Pain, VAS	20 [13;50]*	30 [30;60]
PGA, VAS	30 [17;60]*	40 [30;60]
PhGA, VAS	30 [10;50]*	38 [30;60]
SJC	1 [0;5]*	1 [0;8]
TJC	1 [0;2]*	1 [0;6]

\* p<0.05, U-test

**Conclusions:** MDA was seen in 21% of PsA pts in routine care but starting bDMARDs has a significantly higher probability of reaching MDA in most cases despite duration of treatment.

**Disclosure of Interest:** None declared

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THU0306

### CLINICAL SPECIALTY SETTING AS A DETERMINANT FOR DISEASE MANAGEMENT IN PATIENTS WITH PSORIATIC ARTHRITIS: RESULTS FROM LOOP, A CROSS-SECTIONAL, MULTI-COUNTRY, OBSERVATIONAL STUDY

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**Background:** Evidence suggests that timely and effective management can improve long-term outcomes in patients (pts) with psoriatic arthritis (PsA); however factors influencing treatment management decisions are not well understood.

**Objectives:** To evaluate the association between the clinical specialty setting and time from inflammatory musculoskeletal symptom onset to PsA diagnosis and to different management steps in pts with a diagnosis of PsA.

**Methods:** LOOP is a large cross-sectional, multi-centre, observational study conducted in 17 countries across Western and Eastern Europe, Latin America, and Asia. Adult pts (≥18 years) with a suspected or an established diagnosis of PsA routinely visiting a rheumatologist (rheum), dermatologist (derm) or non-rheum/non-derm site were eligible to participate in this study. Each enrolled patient in the study was assessed by both rheum and derm. Main endpoints assessed were time from inflammatory musculoskeletal symptom onset to PsA diagnosis, time from PsA diagnosis to first csDMARD and to first bDMARD, and time from first csDMARD to first bDMARD.

**Results:** Of the 1483 pts enrolled in this study, 1273 pts with a confirmed diagnosis of PsA were included in this analysis. A majority of pts were recruited by rheums (671, 52.7%), followed by derms (541, 42.5%), physiatrists (36, 2.8%), and other specialties (25, 2.0%). PsA was first suspected by a rheum in 726 (57.0%) pts and by a derm in 541 pts (42.5%). Pt demographics and disease characteristics were mostly comparable between rheum and derm settings. Current disease activity and disease burden of patients with PsA categorised by clinical specialty are shown in **table 1**. Disease activity was higher in PsA pts in derm setting compared with rheum setting. The timing of different disease management steps by clinical specialty is reported in **table 2**. The mean time from symptom onset to PsA diagnosis was 24 months (mo) in rheum setting and 1 mo longer for derms. In rheum and derm settings, the mean time from PsA diagnosis to first csDMARD were 11 and 25 mo, respectively; whereas the mean time to first bDMARD were 52 and 55 mo, respectively. The mean time from first csDMARD to first bDMARD was 42 mo for rheums; while it was 3 months shorter for derms.

Abstract THU0306 – Table 1. Baseline Characteristics and Current Disease Activity and Disease Burden by Clinical Specialty in Patients with PsA from LOOP Study

Characteristic/Measure <sup>a</sup>	Rheum (N=726)	Derm (N=541)	P-value <sup>b</sup>
Age, years	51.1 (12.9)	50.7 (13.1)	.645
Gender, male, n (%)	375 (51.7)	270 (49.9)	.570
Weight, kg	77.3 (16.4)	77.7 (17.1)	.708
BMI, kg/m <sup>2</sup>	27.4 (5.5) <sup>c</sup>	27.4 (5.3)	.902
TJC66	6.0 (10.1) <sup>d</sup>	8.5 (12.6) <sup>e</sup>	<.001
SJC66	2.2 (4.3) <sup>f</sup>	3.2 (6.2) <sup>g</sup>	.001
Dactylitis count	0.4 (1.3) <sup>h</sup>	0.8 (2.6) <sup>i</sup>	<.001
Tender enthesal points	0.8 (1.7) <sup>j</sup>	1.5 (2.6) <sup>k</sup>	<.001
DAPSA	18.4 (24.0)	23.9 (30.9) <sup>l</sup>	.017
DAS28	2.8 (1.3) <sup>m</sup>	2.9 (1.5) <sup>n</sup>	.066
MDA, n (%)	309 (46.7) <sup>o</sup>	186 (39.2) <sup>p</sup>	.012
PGA	3.3 (2.6) <sup>q</sup>	4.4 (2.7) <sup>r</sup>	<.001
BSA (%)	6.6 (11.3) <sup>s</sup>	13.1 (19.7) <sup>t</sup>	<.001
Psoriatic nail count	4.0 (5.5) <sup>u</sup>	5.3 (6.3) <sup>v</sup>	<.001
HAQ-DI	0.7 (0.7) <sup>w</sup>	0.7 (0.7) <sup>x</sup>	.783
SF12-PCS	43.0 (10.6) <sup>y</sup>	42.6 (10.1) <sup>z</sup>	.544
SF12v2-MCS	44.9 (10.5) <sup>aa</sup>	44.6 (12.1) <sup>ab</sup>	.803
WPAI-PsA-TWPI (%)	30.1 (30.9) <sup>ac</sup>	29.5 (31.7) <sup>ad</sup>	.824
WPAI-PsA-TAI (%)	25.0 (29.8) <sup>ae</sup>	26.5 (31.4) <sup>af</sup>	.017
DLQI	5.3 (6.2) <sup>ag</sup>	7.6 (7.2) <sup>ah</sup>	<.001

<sup>a</sup>P-value from simple linear regression: Rheumatologist vs Dermatologist. All data are presented as mean (SD) unless otherwise specified. <sup>b</sup>WPAI-PsA-TWPI = work productivity and activity impairment questionnaire. <sup>c</sup>WPAI-PsA-TAI = total activity impairment. <sup>d</sup>TJC66 = tender joint count, 66 joints. <sup>e</sup>SJC66 = swollen joint count, 66 joints. <sup>f</sup>TJC = total active joint count. <sup>g</sup>SJC = swollen joint count. <sup>h</sup>HAQ-DI = health assessment questionnaire – disability index. <sup>i</sup>MCS = mental component score. <sup>j</sup>MDA = minimal disease activity. <sup>k</sup>PCS = physical component score. <sup>l</sup>PGA = physician global assessment. <sup>m</sup>PsA = psoriatic arthritis. <sup>n</sup>Rheum = rheumatologist. <sup>o</sup>SF12v2 = Short form 12-item health survey version 2. <sup>p</sup>SD = standard deviation. <sup>q</sup>SJC66 = swollen joint count, 66 joints. <sup>r</sup>TAI = total activity impairment. <sup>s</sup>TJC66 = tender joint count, 66 joints. <sup>t</sup>TWPI = total work productivity impairment. <sup>u</sup>WPAI-PsA = Work productivity and activity impairment questionnaire. <sup>v</sup>PsA = psoriatic arthritis. <sup>w</sup>Rheum = rheumatologist. <sup>x</sup>SD = standard deviation.

Abstract THU0306 – Table 2. Timing of Disease Management Steps by Clinical Specialty in Patients with PsA from LOOP Study

Duration in months, Mean (SD)	Rheum	Derm	P-value <sup>a</sup>
Time from inflammatory musculoskeletal symptom onset to PsA diagnosis <sup>b</sup>	23.6 (70.7)	24.9 (72.1)	.747
Time from PsA diagnosis to first csDMARD <sup>c</sup>	10.7 (59.4)	25.2 (33.9)	.004
Time from PsA diagnosis to first bDMARD <sup>d</sup>	52.3 (81.0)	54.7 (91.0)	.715
Time from first csDMARD to first bDMARD <sup>e</sup>	42.4 (82.7)	39.1 (83.5)	.556

<sup>a</sup>P-value from simple linear regression: Rheumatologist vs Dermatologist. <sup>b</sup>Rheum, N=631; Derm, N=527. <sup>c</sup>Rheum, N=428; Derm, N=264. <sup>d</sup>Rheum, N=372; Derm, N=178. <sup>e</sup>csDMARD = biologic disease modifying antirheumatic drug; csDMARD = nonbiologic synthetic disease modifying antirheumatic drug; Derm = dermatologist; PsA = psoriatic arthritis; Rheum = rheumatologist; SD = standard deviation.

**Conclusions:** Although the duration from symptom onset to PsA diagnosis was similar between rheum and derm setting, there were differences in the timing of introduction of different DMARD classes. Notably, mean time to first csDMARD was significantly shorter in rheum setting. PsA pts in derm setting had significantly higher disease activity. These data lend further support to the need for rheum-derm collaborative approach to optimise management of pts with PsA.

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THU0307

### QT INTERVAL AND ITS CORRELATIONS WITH TRADITIONAL RISK FACTORS OF DEVELOPMENT OF CARDIOVASCULAR DISEASES IN PATIENTS WITH ACTIVE EARLY PSORIATIC ARTHRITIS

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**Background:** Cardiovascular diseases (CVD) are leading cause of morbidity and mortality in patients (pts) with psoriatic arthritis (PsA). An abnormally prolonged and shorted QT interval are associate with an increased risk of ventricular arrhythmias and sudden cardiac death.

**Objectives:** to evaluate QT interval during Holter monitoring and cardiovascular (CV) risk assessment using SCORE (Systematic COronary Risk Evaluation) in early PsA (EPsA) pts.

**Methods:** We included data of 48 (F.-23) DMARD-naive EPsA pts (according to the CASPAR criteria) with no history of CVD: mean age - 36<sup>[26; 47]</sup> years, EPsA duration - 6,9<sup>[4; 12]</sup> months, DAS - 3.97 [3.27; 4.1], C-reactive protein - 19.4 [8.8; 37.6]mg/l. Controls subjects were matched by age, sex (n=48). All pts were assessed for traditional risk factors of CVD, ESC guidelines, 2016 24 hour (24 hour) ECG monitoring were analysed for QT interval corrected for heart rate (QTc). Prolonged QTc was defined as  $\geq 460$  ms in women and  $\geq 450$  ms in men, short QTc  $< 330$  ms. Ten-year risk of CV death was estimated using SCORE algorithms, ESC guidelines, 2016 categorised as low (<1%), intermediate (1% to <5%), high ( $\geq 5\%$  to <10%) or very high ( $\geq 10\%$ ). Intima-media thickness of the carotid artery (c-IMT) was measured using a high-resolution B-mode ultrasound machine.

**Results:** QTc interval during the 24 hours was significantly prolonged in EPsA pts when compared to the control group (table 1). We didn't find short or prolong QTc interval in EPsA pts and control group.

**Abstract THU0307 – Table 1.** QTc interval in EPsA pts and control group

Parameters	EPsA pts	Controls
QTc (ms), day	397[376; 404]	387.5[370.5; 396]*
QTc (ms), night	396[377; 408]	390[367; 396.5]*
QTc (ms), 24 hour	395[378; 406]	387[370; 396]*

Data are present in median values and interquartile range, \*p<0,05 (nonparametric paired Mann-Whitney U-test).

62.5% of patients with EPsA were classified as being at low risk 10 year risk of CV death using the SCORE algorithm, 6.25% pts - intermediate risk, 29.2% pts - high risk, 2.1% pts - very high risk. Increased cIMT was found in 11 (22.9%), atherosclerotic plaques - in 15 (31.3%). We found significant correlations between age and QTc duration during the 24 hours (R=0.48), as well as in both day (R=0.46) and night periods (R=0.45), for all p<0.05. We didn't find correlations between QTc duration and traditional risk factors of CVD, disease activity of EPsA. Significantly correlations were observed between SCORE level and abdominal obesity (R=0.43, p<0.05), BMI (R=0.41, p<0.0001), c-IMT (R=0.41, p<0.05).

**Conclusions:** QT interval was significantly prolonged in EPsA pts when compared to the control group. The age of pts was associated with increase of the QTc interval. 29.2% of patients were classified as being at high risk 10 year risk of CV death using the SCORE algorithm. The increase level of SCORE associated with a subclinical atherosclerosis. Combination of prolonged QT interval and carotid atherosclerosis confirms presence of high cardiovascular risk in EPsA pts.

**Disclosure of Interest:** None declared

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THU0308

### CALPROTECTIN AS A MARKER OF DISEASE ACTIVITY IN PATIENTS WITH NEW ONSET PSORIATIC AND RHEUMATOID ARTHRITIS: CORRELATION WITH ULTRASONOGRAPHIC SYNOVITIS

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**Background:** Serum Calprotectin has been tested as a marker of disease activity in psoriatic (PsA) and rheumatoid (RA) arthritis. In RA and in PsA on TNF inhibitors in remission calprotectin correlates with power-Doppler (PD) positive ultrasonographic (US) synovitis, while there is no data on untreated patients with new-onset PsA.

**Objectives:** To investigate the correlation and association between calprotectin and US synovitis in patients with new-onset PsA and in a control group of RA.

**Methods:** Consecutive patients with PsA and a group of age and gender-matched patients with RA, referred to an early arthritis clinic (2005–2014) were

included. Demographic and clinical features, including a 44 joint count for tenderness and swelling (TJC, SJC) and C-reactive protein (CRP) were recorded. US of wrists (radiocarpal, intracarpal and ulnocarpal) and MCP joints with grey scale (GS) and PD synovitis scored 0–3 at each site, with a total score from the sum of each site, was available at the same time, as well as serum samples to measure calprotectin concentration. Serum levels of calprotectin were compared by Mann Whitney test in PsA and RA. The correlation between calprotectin, TJC, SJC, CRP and US PD and GS was evaluated by Spearman's correlation coefficient, while the association of calprotectin concentrations and PD synovitis by regression analysis. Secondary analyses separating poliarticular and oligoarticular (SJC  $\leq 4$ ) PsA and using different definitions of synovitis (GS >1, PD >1) were performed.

**Results:** 156 patients (78 PsA and 78 RA) were included (RA: male 28.2%, mean (sd) age 51.9 (13.3); PsA male 32%; mean age 51.7 (13.5)). Patients with RA had significantly higher CRP (median, IQR) (0.6, 0.3–2.1 vs 0.36, 0.3–1, p 0.04), SJC (7, 5–12 vs 6, 3–9, p 0.008), GS (6, 4–11 vs 5, 2–7, p 0.01) and PD (2, 0–9 vs 1, 0–3, p 0.003) scores. Calprotectin (ng/ml, median, IQR) did not significantly differ in PsA (3123, 2063–4669) and RA (2556, 1615–4441), also when separating poliarticular and oligoarticular PsA. In patients with PsA, calprotectin significantly correlated with GS score (rho 0.340, p 0.007), PD score (rho 0.290, p 0.02) and with the presence of PD (categorical variable) (rho 0.263, p 0.04), while in RA there were no statistically significant correlations. When separating poliarticular and oligoarticular PsA, a significant correlation between calprotectin and GS score (rho 0.369, p 0.01) and PD score (rho 0.363, p 0.02) was confirmed in poliarticular but not oligoarticular disease. In both RA and PsA SJC and TJC did not significantly correlate with calprotectin. Calprotectin showed a statistically significant correlation with CRP in both PsA (rho 0.273, p 0.01) and RA (rho 0.27, p 0.01), showing concurrent validity. In regression analysis, calprotectin levels did not associate with the presence of PD in PsA also when using a more stringent cut-off. Similar results were achieved in RA.

**Conclusions:** In untreated patients with early onset PsA, but not in RA, calprotectin correlates with US PD-positive synovitis, especially in poliarticular disease. Prospective studies are needed to confirm the use of calprotectin as a biomarker in early inflammatory arthritis.

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THU0309

### TEN YEARS FOLLOW-UP STUDY OF CLINICAL DISEASE STATUS AND TREATMENT IN PSORIATIC ARTHRITIS PATIENTS FROM AN OUTPATIENT CLINIC IN SOUTHERN NORWAY

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**Background:** In the new millennium remission has become an obtainable treatment goal for chronic inflammatory joint disorders, shown in particular for rheumatoid arthritis (RA). This has been attributed to new treatment strategies (early intervention and treat-to-target) and new drugs e.g. biologic Disease Modifying Anti-Rheumatic Drugs (bDMARDs).<sup>1</sup> For psoriatic arthritis (PsA) there is a lack of longitudinal long term clinical data illuminating potential changes that may have occurred over the years.

**Objectives:** To explore long term changes in clinical disease status and treatment in PsA patients monitored in an ordinary Norwegian outpatient clinic in the period 2008–2017.

**Methods:** For each year we collected data from last patient visit recorded in the hospital clinical computer system GoTreatIT Rheuma. Included patients had to fulfil the CASPAR criteria and have peripheral arthritis. Standard clinical data collection included demographic data, clinical measures of disease activity (Disease Activity Score with 28 joint counts [DAS28], Clinical Disease Activity Index [CDAI] and Assessors Global Assessments (AGA) on Visual Analogue Scale 0–100 mm (VAS)) laboratory measures of disease activity (Erythrocyte Sedimentation Rate (ESR), C-Reactive Protein (CRP) and Patient-Reported Outcomes Measures (PROMs) of physical function (MHAQ), morning stiffness and VAS scores for joint pain, fatigue and Patient Global Assessment (PGA). Treatment with prednisolone, synthetic DMARDs (sDMARDs) or bDMARDs, was recorded.

**Results:** Over the 10 years mean annual number of PsA patients monitored was 331, mean age 58.4 years, disease duration 9.6 years, BMI 27.6 kg/m<sup>2</sup>, females 49% and current smokers 17.6%. A statistically significant decrease for measures of disease activity for the period 2008–2017 was seen (all p<0.01): ESR 15.8–10.9 mm/hr, CRP 7.6–4.1 mg/dl, 28 swollen joints 1.5–0.6, 28 tender joints 3.3–1.6, DAS28 3.32–2.46, CDAI 10.1–6.8 and AGA 14.5–8.6 mm. No statistically significant changes in PROMs was seen. Mean values for the period was: MHAQ 0.46, joint pain 36.3 mm, fatigue 44.2 mm, PGA 38.8 mm and morning stiffness 0.95 hour. From 2008 to 2017 the percentage of patients treated with bDMARDs and/or sDMARDs and/or prednisolone increased from 72.6% to 80.9%. For the

10 year period the annual proportion of patients did not significantly change neither for treatment with prednisolone (14.9%), synthetic DMARDs (53.0%, Methotrexate 38.5%) or biologics (29.9%), this both for TNF (28.1%) and non-TNF inhibitors (1.8%).

**Conclusions:** Despite obvious limitations using disease activity measures (28 joint count, DAS28 and CDAI) designed for use in RA, our study indicate that disease activity decreased in our PsA outpatients over the 10 year period. This despite no significant change in proportions of patients treated with sDMARDs and bDMARDs. For PROMs no significant changes was seen. With new available outcome measures designed for use in PsA and more treatment options available e.g. secukinumab (IL17 inhibition) and ustekinumab (IL12/23) and tofacitinib (JAK inhibitor) further improvements in clinical outcomes both for disease activity and patient perception can be expected.

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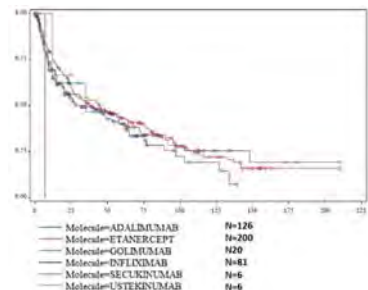
#### THU0310 BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS IN PSORIATIC ARTHRITIS: A REAL-WORLD COHORT OF 439 PATIENTS

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**Background:** For more than 15 years, severe psoriatic arthritis (PsA) has been treated only by TNF inhibitors. Two new Biologic Disease-modifying Antirheumatic Drugs (bDMARDs) have recently arrived on the market with different targets: IL12–23 for ustekinumab and IL 17 for secukinumab. Few studies exist with a large number of patients and with required hindsight.

**Objectives:** The objective was to assess drug survival in an observational cohort of 630 PsA depending on the line of treatment and to analyse the reasons of discontinuation.

**Methods:** This is a retrospective, multicentric observational study based on the data of the registry RIC Nord de France, from patients suffering from PsA (CASPAR criteria) and treated by bDMARDs from January 2000 to August 2017. Drug survival is defined as the time from initiation to discontinuation (stop/switch) of biologic therapy on the registry. The number of patients who discontinued each treatment and the duration of therapy were recorded. Using Kaplan-Meier survival curves and Cox-regression analyses [hazard ratios (HR) and 95% confidence intervals (CIs)], time to discontinuation was compared across cohorts undergoing first-, second- or third-line treatment.



Abstract THU0310 – Figure 1. Drug survival of biotherapies at first-line treatment

**Results:** Out of 630 PsA, 439 were included with a mean follow up greater than or equal to 6 months. The sex ratio was balanced with 47% of women. The mean age was 54.5 years old and the body mass index (BMI) was 28.7 kg/m<sup>2</sup>. The disease duration was 14.25 years. 51.6% of patients did not smoke. The DAS-28

CRP was 3.99 at the initiation of the biotherapy. The drug survival of the TNF inhibitors was similar at first-line treatment (n=439 patients) (figure 1) and at second-line treatment (n=238 patients). The drug survival of infliximab was statistically longer at third-line treatment (n=209) (p<0.0001), as the drug survival of TNF inhibitors compared to non TNF inhibitor biotherapies (ustekinumab and secukinumab) (p0.011). There was no impact of the age, the sex or the BMI on the drug survival. The discontinuation was mainly due to primary and secondary failure at first-line (respectively 33.33% and 33.71%) and to adverse events at second- and third-line (respectively 30.22% and 44.55%).

**Conclusions:** The results of the large observational study confirm those of the clinical trials, especially for the patients with failing initial TNF inhibitor therapy.

**Disclosure of Interest:** None declared

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#### THU0311 IMPACT OF SECUKINUMAB TREATMENT ON PSORIATIC ARTHRITIS PATIENTS WITH OR WITHOUT ENTHESITIS AT BASELINE: POOLED DATA FROM TWO PHASE 3 STUDIES (FUTURE 2 AND FUTURE 3)

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**Background:** Enthesitis is a common phenotypic manifestation of psoriatic arthritis (PsA) affecting approximately 70% of patients (pts) and may be associated with worse outcomes. <sup>1</sup>Secukinumab (SEC), a fully human monoclonal antibody that selectively neutralises IL-17A, provided significant and sustained improvement in the signs and symptoms of active PsA, with sustained resolution of enthesitis in Phase 3 studies.<sup>2,3</sup>

**Objectives:** To report the impact of SEC treatment on efficacy outcome measures in active PsA pts with or without baseline (BL) enthesitis (defined by Leeds Enthesitis Index) using pooled data from the FUTURE 2 (NCT01752634) and FUTURE 3 (NCT01989468) studies over 2 years.

**Methods:** SEC and placebo (PBO) were administered weekly during the first 4 weeks (wks) followed by subcutaneous maintenance dosing every 4 wks thereafter (PBO until Wk 16/24). The results are reported only for SEC 300 and 150 mg (approved doses). Efficacy outcomes (ACR20/50/70, PASI 90, HAQ-DI, SF-36 PCS and DAS28-CRP) were analysed *post-hoc* in pts with enthesitis at BL (BLE; n=466) or without enthesitis at BL (No BLE; n=246). Observed data are presented for binary variables and least-square (LS) means from analysis of covariance for continuous variables.

**Results:** A total of 65% of pts had BLE. BL demographics were balanced between the BLE and No BLE groups except for a higher proportion of females and numerically higher tender joint count, disability (HAQ-DI) and lower physical function (SF-36 PCS) in BLE pts than No BLE pts. At Wk 16, improvements in ACR and PASI responses, HAQ-DI, SF-36 PCS and DAS28-CRP were similar in both groups treated with SEC 300 mg, but were lower (except for PASI) in BLE pts treated with SEC 150 mg (table 1). Improvements in these outcomes followed a similar trend to Wk 104 in SEC-treated pts (table 1).

Abstract THU0311 – Table 1. Summary of Results with Secukinumab

	Wk	BLE			No BLE		
		300 mg	150 mg	PBO	300 mg	150 mg	
ACR20 <sup>a</sup>	16	53.5	46.5	19.6	53.7	64.6	18.1
	104	56.8	52.4	-	62.6	62.9	-
ACR50 <sup>a</sup>	16	31.3	21.4	6.7	35.8	35.4	5.6
	104	44.7	24.8	-	47.3	34.3	-
ACR70 <sup>a</sup>	16	16.0	8.2	1.8	21.1	16.5	1.4
	104	26.5	15.2	-	34.1	21.4	-
PASI 90 <sup>b,c</sup>	16	50.0	36.6	7.9	42.1	37.0	6.7
	104	67.9	59.7	-	73.5	44.4	-
HAQ-DI <sup>d</sup>	16	-0.5	-0.3	-0.2	-0.5	-0.5	-0.2
	104	-0.5	-0.4	-	-0.5	-0.6	-
SF-36 PCS <sup>d</sup>	16	6.4	3.7	2.5	6.5	7.4	2.6
	104	7.4	4.3	-	6.6	6.9	-
DAS28-CRP <sup>d</sup>	16	-1.5	-1.05	-0.5	-1.35	-1.6	-0.5
	104	-1.7	-1.6	-	-2.0	-1.9	-

<sup>a</sup>Response,%; <sup>b</sup>At Wk 16/104, n=144/132 (SEC 300), 159/145 (SEC 150) and 163 (PBO) with enthesitis and n=95/91 (SEC 300), 79/70 (SEC 150) and 72 (PBO) without enthesitis at BL; <sup>c</sup>At Wk 16/104, n=66/56 (SEC 300), 82/62 (SEC 150) and 63 (PBO) with enthesitis and n=38/34 (SEC 300), 46/36 (SEC 150) and 30 (PBO) without enthesitis at BL (psoriasis subset); <sup>d</sup>LS mean

**Conclusions:** Although pts with BLE had more severe BL clinical characteristics than pts with No BLE, SEC showed higher efficacy than PBO at Wk 16 and sustained efficacy over 104 wks in both groups with greater magnitude of improvement in pts treated with SEC 300 mg than 150 mg.

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#### THU0312 RISK OF INFECTION IN PATIENTS WITH PSORIASIS/ PSORIATIC ARTHRITIS: A POPULATION-BASED STUDY IN THE PROVINCE OF BRITISH COLUMBIA

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**Background:** Psoriasis (PsO) is a chronic autoimmune disease of the skin with a third of patients (pts) also developing inflammatory arthritis (PsA), which can lead to joint destruction. Research suggests that pts with PsA have an increased risk of complications (e.g. cardiovascular disease). There are limited data on the risk of infections among pts with PsO/PsA.

**Objectives:** To assess the risk of mild and severe infections in pts with newly diagnosed PsO/PsA in a general population.

**Methods:** Using administrative health data from British Columbia (Canada) we developed an incident cohort of pts diagnosed with PsO/PsA between 1996 and 2013, with equal control pts matched on sex, age and calendar year. PsO/PsA cases were determined by: a) one International Classification of Diseases code (696.X) for PsO/PsA assessed by a rheumatologist or dermatologist; b)  $\geq 2$  diagnostic codes for PsO/PsA,  $\geq 2$  months apart in a 2 year period assessed by a non-rheumatologist or dermatologist; c)  $\geq 1$  hospitalisation with a diagnostic code for

PsO/PsA. Individuals with a history of HIV or tuberculosis were excluded. Outcomes were mild infections (requiring a physician visit and antibiotics) or serious infections (requiring hospitalisation). Adjusted risks of these infections were estimated using generalised estimating equation extensions of multivariate Poisson regression models.

**Results:** We identified 84 616 newly diagnosed pts with PsO/PsA (51.6% female; mean age 49.5 years [SD: 18.2]) who were matched with an equal non-PsO/PsA cohort. Pts with PsO/PsA had a higher risk of developing mild infections during follow-up, including HIV (2.6-fold) and mycosis (2-fold), compared with the general population. PsO/PsA also increased the risk of severe infections including *Chlamydia* (1.7-fold) and viral diseases with exanthema (2.6-fold) (table 1).

P-Y=patient years

**Conclusions:** This large epidemiological study demonstrates that pts with PsO/PsA are at significantly higher risk of acquiring infections. The role of therapy for PsO/PsA on the risk of these infections needs to be evaluated.

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#### THU0313 IXEKIZUMAB IMPROVES NAIL AND SKIN LESIONS THROUGH 52 WEEKS IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS AND INADEQUATE RESPONSE TO TUMOUR NECROSIS FACTOR INHIBITORS

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**Background:** Ixekizumab (IXE) is a high-affinity monoclonal antibody selectively targeting interleukin-17A. Compared to placebo (PBO), IXE resulted in significantly greater reduction and clearance of fingernail and skin lesions at Wk 24 in patients (pts) with active psoriatic arthritis (PsA) and inadequate response (IR) to tumour necrosis factor inhibitors (TNF-i).<sup>1</sup>

**Objectives:** This analysis examined the persistence of effect at 1 year.

**Methods:** In this Phase 3, double-blind trial (SPIRIT-P2; NCT02349295), pts with active PsA who were TNF-i-IR were randomised to PBO or 80 mg IXE SC every 2 or 4 Wks (IXEQ2W, IXEQ4W), after a 160 mg starting dose.<sup>2</sup> At Wk 16, pts with IR to treatment (ERB supplement defined) received rescue therapy and pts on PBO

**Abstract THU0312 – Table 1.** Incidence Rate (IR) and Rate Ratio (RR) of Mild and Severe Infections Among PsO/PsA Pts Compared With the General Population

Outcomes	Mild infections				RR (95% CI)	Severe infections				RR (95% CI)
	PsO/PsA cohort		Non-PsO/PsA cohort			PsO/PsA cohort		Non-PsO/PsA cohort		
	n	IR (per 100K P-Y)	n	IR (per 100K P-Y)	n	IR (per 100K P-Y)	n	IR (per 100K P-Y)		
Viral diseases with exanthema	5612	912.7	3735	611.3	1.49 (1.43–1.56)	47	7.3	18	2.9	2.56 (1.49–4.40)
HIV-related infections	119	18.6	41	6.5	2.63 (1.91–3.63)	–	–	–	–	–
Intestinal infections	3659	587	2420	392.5	1.50 (1.42–1.57)	835	130.6	508	81	1.61 (1.44–1.80)
Mycoses	5318	867.9	2520	409.3	2.12 (2.02–2.22)	–	–	–	–	–
Poliomyelitis	78	12.2	48	7.6	1.59 (1.11–2.28)	–	–	–	–	–
Syphilis venereal	514	80.4	391	62.4	1.29 (1.13–1.47)	–	–	–	–	–
Tuberculosis	340	53.1	212	33.8	1.52 (1.29–1.79)	–	–	–	–	–
<i>Chlamydia</i>	3580	575.8	2140	346.8	1.66 (1.57–1.75)	113	17.6	67	10.7	1.65 (1.22–2.23)
Zoonotic	73	11.4	48	7.6	1.49 (1.03–2.14)	–	–	–	–	–
Pneumonia	9622	1613.1	6306	1053.4	1.53 (1.48–1.58)	1685	264.8	1236	198	1.34 (1.24–1.44)
Intracranial abscess	37	5.8	18	2.9	2.01 (1.15–3.53)	–	–	–	–	–
Rickettsioses	140	21.8	97	15.5	1.41 (1.09–1.83)	–	–	–	–	–
Helminthiasis	110	17.2	77	12.3	1.40 (1.05–1.87)	–	–	–	–	–



were re-randomised to IXEQ2W or IXEQ4W. The primary objective was ACR20 at Wk 24, and an extension from Wks 24 to 156 is on-going. In this analysis, efficacy was assessed at Wk 52 for the intent-to-treat (ITT) population of pts randomised to IXE at Wk 0 by Nail Psoriasis Severity Index (NAPSI) scores in pts with baseline fingernail psoriasis (IXEQ4W, n=89; IXEQ2W, n=74), PASI 75/90/100 response rates in pts with baseline BSA  $\geq 3$  (IXEQ4W, n=68; IXEQ2W, n=68), and the rate of Static Physician Global Assessment (sPGA) of psoriasis scores of 0 or 1 (0=cleared, 1=minimal) in pts with baseline sPGA  $\geq 3$  (IXEQ4W, n=60, IXEQ2W, n=62). For categorical variables, nonresponder imputation was used for missing data. Percent change from baseline was calculated using modified baseline observation carried forward.

**Results:** At Wk 52, NAPSI total score (observed cases; mean (SD)) was 5.0 (12.7), 4.4 (7.6), IXEQ4W, IXEQ2W, respectively, with a mean percent change from baseline of -15.2 (19.7), -14.4 (19.0), IXEQ4W, IXEQ2W, respectively. The percentage of pts achieving a NAPSI score of 0 (0=cleared) was 46.1% (n=41), 32.4% (n=24), IXEQ4W, IXEQ2W, respectively. The percentage of pts achieving PASI responses was 60.3% (n=41), 54.4% (n=37) for PASI 75; 50.0% (n=34), 39.7% (n=27) for PASI 90; and 39.7% (n=27), 35.3% (n=24) for PASI 100, IXEQ4W, IXEQ2W, respectively. The percentage of pts achieving sPGA 0 or 1 was 61.7% (n=37), 66.1% (n=41), IXEQ4W, IXEQ2W, respectively. Safety was consistent with the larger study population.

**Conclusions:** In patients with active PsA, an inadequate response to TNF-inhibitors, and baseline fingernail or skin lesions, treatment with ixekizumab resulted in persistent<sup>1</sup> reduction and clearance of nail and skin lesions after 1 year.

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**THU0314 IXEKIZUMAB MAKES VERY LOW DISEASE ACTIVITY AND REMISSION WITH PSORIATIC ARTHRITIS DISEASE ACTIVITY SCORE POSSIBLE IN ACTIVE PSORIATIC ARTHRITIS PATIENTS FOR UP TO 1 YEAR: SPIRIT-P1 AND SPIRIT-P2 TRIALS**

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**Background:** Treatment goals in psoriatic arthritis (PsA) are moving toward attainment of absolute therapeutic thresholds rather than relative improvement. Minimal disease activity (MDA) and very low disease activity (VLDA); Disease Activity in Psoriatic Arthritis (DAPSA) LDA and DAPSA Remission; and Psoriatic Arthritis Disease Activity Score (PASDAS) LDA and PASDAS VLDA are validated composite indices used to measure disease activity states in PsA.

**Objectives:** The effect of ixekizumab (IXE), as assessed by composite endpoints that incorporate multiple disease domains, was explored up to 52 weeks for the SPIRIT-P1<sup>1</sup> and SPIRIT-P2<sup>2</sup> trials.

**Methods:** Data were analysed from 2 double-blind, phase III SPIRIT trials investigating the efficacy and safety of IXE, a high-affinity monoclonal antibody selectively targeting interleukin-17A, for patients with active PsA. For SPIRIT-1 (NCT01695239), patients who were biologic disease-modifying antirheumatic drug (DMARD)-naïve were randomised to placebo (n=106) or 80 mg IXE every 4 weeks (Q4W, n=107) or every 2 weeks (Q2W, n=103) after a 160 mg starting dose. For SPIRIT-2 (NCT02349295), patients who had an inadequate response or were intolerant to tumour necrosis factor inhibitors (TNFi) were randomised to placebo (n=118) or 80 mg IXE every 4 weeks (Q4W, n=122) or every 2 weeks (Q2W, n=123) after a 160 mg starting dose. MDA, MDA VLDA, DAPSA LDA, DAPSA Remission, PASDAS LDA, and PASDAS VLDA composite endpoints were evaluated. Imputation for categorical responses was non-responder

imputation. Treatment comparisons (with respect to placebo up to Week 24) based on the intent-to-treat population were made using a logistic regression model. Data up to Week 52 are summarised descriptively.

**Results:** The therapeutic threshold results are summarised in table 1. At Week 24, the percentage of patients achieving MDA, MDA VLDA, DAPSA LDA, DAPSA Remission, PASDAS LDA, and PASDAS VLDA was greater with IXE Q4W and IXE Q2W compared with placebo. In patients who continued treatment with IXE through Week 52, response rates of these therapeutic thresholds were either sustained or further improved.

**Abstract THU0314 – Table 1.** Summary of MDA, DAPSA, and PASDAS Composite Endpoints (NRI) for the SPIRIT-1 and SPIRIT-2 Trials (ITT Population)

	SPIRIT-1 <sup>1</sup>				SPIRIT-2 <sup>2</sup>			
	PBO (n=106)	IXE Q4W (n=107)	IXE Q2W (n=103)	OR (95% CI) P Value	PBO (n=118)	IXE Q4W (n=122)	IXE Q2W (n=123)	OR (95% CI) P Value
<b>MDA (n%)</b>								
Week 24	16 (15.1)	32 (29.9)	42 (40.8)	2.7 (1.8, 3.9) <0.001	4 (3.4)	34 (27.9)	24 (19.5)	2.0 (1.2, 3.4) <0.01
Week 52	NA	42 (39.2)	38 (36.9)	NA	NA	42 (34.4)	29 (23.6)	NA
<b>MDA VLDA (7/9) (n%)</b>								
Week 24	7 (6.6)	11 (10.3)	12 (11.6)	1.7 (1.1, 2.7) 0.019	1 (0.8)	15 (12.3)	4 (3.2)	2.4 (1.1, 5.4) 0.028
Week 52	NA	15 (14.0)	16 (15.5)	NA	NA	15 (12.3)	8 (6.4)	NA
<b>DAPSA LDA (n%)</b>								
Week 24	19 (17.9)	34 (31.8)	35 (34.0)	2.2 (1.5, 3.3) <0.001	13 (11.1)	31 (25.4)	14 (11.3)	2.4 (1.6, 3.8) <0.001
Week 52	NA	31 (29.0)	30 (29.1)	NA	NA	42 (34.4)	23 (18.8)	NA
<b>DAPSA Remission (n%)</b>								
Week 24	2 (1.9)	17 (15.9)	25 (24.3)	11.2 (3.2, 39.2) <0.001	1 (0.8)	18 (14.8)	9 (7.3)	8.3 (3.6, 18.4) <0.001
Week 52	NA	34 (32.4)	30 (29.1)	NA	NA	29 (23.8)	16 (12.7)	NA
<b>PASDAS LDA (n%)</b>								
Week 24	20 (18.8)	45 (42.1)	42 (40.8)	2.3 (1.6, 3.3) <0.001	11 (9.3)	48 (39.3)	22 (17.6)	2.2 (1.5, 3.3) <0.001
Week 52	NA	46 (43.9)	42 (40.8)	NA	NA	38 (31.1)	26 (20.3)	NA
<b>PASDAS VLDA (n%)</b>								
Week 24	1 (1.0)	12 (11.2)	21 (20.4)	13.5 (2.8, 62.7) <0.001	0 (0.0)	16 (13.1)	9 (7.3)	7.3 (2.7, 19.9) <0.001
Week 52	NA	19 (17.8)	18 (17.3)	NA	NA	21 (17.2)	12 (9.4)	NA

Abbreviations: CI, confidence interval; DAPSA, Disease Activity in Psoriatic Arthritis; LDA, low disease activity; MDA, minimal disease activity; NRI, non-responder imputation; PASDAS, Psoriatic Arthritis Disease Activity Score; PBO, placebo; VLDA, very low disease activity. ORs for absolute thresholds compared across SPIRIT-1 and SPIRIT-2 are presented using the unadjusted treatment effect estimates from logistic regression models. P-values from a logistic regression model using the unadjusted treatment effect estimates are presented in parentheses. NA, not applicable. <sup>1</sup>Patients from a logistic regression model using the unadjusted treatment effect estimates are presented in parentheses. <sup>2</sup>Patients from a logistic regression model using the unadjusted treatment effect estimates are presented in parentheses. <sup>3</sup>Patients from a logistic regression model using the unadjusted treatment effect estimates are presented in parentheses. <sup>4</sup>Patients from a logistic regression model using the unadjusted treatment effect estimates are presented in parentheses. <sup>5</sup>Patients from a logistic regression model using the unadjusted treatment effect estimates are presented in parentheses. <sup>6</sup>Patients from a logistic regression model using the unadjusted treatment effect estimates are presented in parentheses. <sup>7</sup>Patients from a logistic regression model using the unadjusted treatment effect estimates are presented in parentheses. <sup>8</sup>Patients from a logistic regression model 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using the unadjusted treatment effect estimates are presented in parentheses. <sup>99</sup>Patients from a logistic regression model using the unadjusted treatment effect estimates are presented in parentheses. <sup>100</sup>Patients from a logistic regression model using the unadjusted treatment effect estimates are presented in parentheses.

**Conclusions:** Regardless of previous TNFi exposure, in patients with active PsA, a higher proportion of IXE-treated compared with placebo-treated patients achieved MDA and MDA VLDA, DAPSA LDA and DAPSA Remission, and PASDAS LDA and PASDAS VLDA at Week 24. At Week 52, the extent of IXE clinical response was sustained or further improved.

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**THU0315 PATIENT-PERCEIVED INVOLVEMENT IN DISEASE MANAGEMENT DRIVES PATIENT-PHYSICIAN ALIGNMENT IN SATISFACTION WITH DISEASE CONTROL IN PSORIATIC ARTHRITIS**

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**Background:** Previous analyses have indicated misalignment between Psoriatic Arthritis (PsA) patients and their physicians can be frequent, and can result in worse disease severity and health-related quality of life<sup>1,2</sup>. Factors associated with this misalignment have not been determined.

**Objectives:** To assess patient-physician misalignment regarding satisfaction with PsA disease control and identify factors associated with this misalignment.

**Methods:** Data were drawn from the Adelphi PsA Disease Specific Programme, a real-world survey conducted in 2015 across the US, France, Germany, Italy, Spain, UK. Patients had physician-confirmed PsA and had to have been receiving their current synthetic-DMARD (biologic naïve) or biologic therapy for at least 6 months.

Physicians and patients independently provided information on satisfaction with disease control on a 5-point scale (very satisfied/satisfied/neither/dissatisfied/very dissatisfied). Physician and patient reports of satisfaction were compared to assess levels of misalignment. Physicians also provided information on demographics and disease history/severity. Patients provided information on involvement in treatment decisions, EuroQol-5D Visual Analogue Scale (EQ-5D), Work Productivity and Activity Impairment (WPAI) and Health Assessment Questionnaire Disability Index (HAQ-DI). Factors associated with misalignment were analysed by a multivariate logistic regression modelled using predictors identified as significant in univariate logistic regression. Data entered in the analyses included demographics, time diagnosed, treatment history, disease severity, flaring, pain, patient-reported involvement in treatment decisions, EQ-5D, WPAI, HAQ-DI.

**Results:** 519 physicians (331 rheums, 188 derms) provided data for 2467 PsA patients, 656 meeting all inclusion criteria. Mean age was 49.9 (SD 12.1) years, mean disease duration 6.7 (6.2) years, 53.8% patients were male and 66.1% employed. Satisfaction with disease control was generally high amongst both patients (78.3%) and physicians (91.9%) with alignment in 79.4% of cases. In 16.8% of cases there was misalignment where patients were dissatisfied but physicians satisfied.

Multivariate logistic regression showed that worse HAQ-DI (OR [95% CI]: 0.54 [0.38–0.77],  $p=0.001$ ), worse EQ-VAS (OR 1.03 [1.02–1.04],  $p<0.001$ ), lack of involvement in treatment decisions (OR 1.26 [1.07–1.50],  $p=0.007$ ) and physician-reported severe disease as opposed to mild (OR 0.20 [0.05–0.78],  $p=0.020$ ) were all independently associated with misalignment.

**Conclusions:** Satisfaction with disease control was generally high for both patients and physicians; however, misalignment was not rare. Patients had higher levels of symptoms/increased impact on activities where there was misalignment. An independent factor associated with misalignment was patient-perceived involvement in condition management. Improving patient-physician engagement in overall disease management may lead to greater patient satisfaction and patient-physician alignment.

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THU0316

#### GENDER DIFFERENCES IN BIOLOGIC TREATMENT OUTCOMES – A STUDY OF 1750 PATIENTS WITH PSORIATIC ARTHRITIS USING DANISH HEALTH CARE REGISTERS

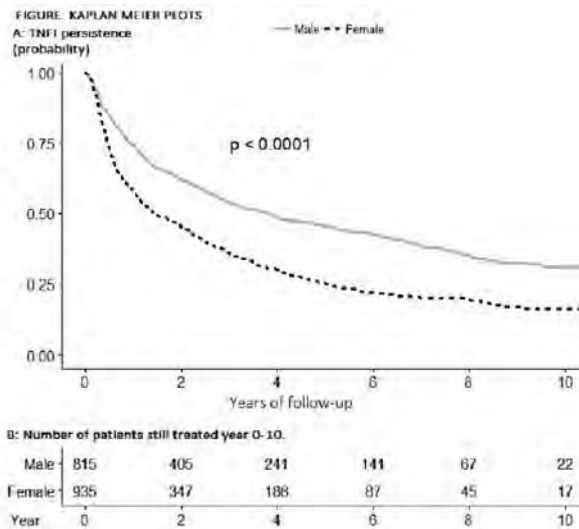
P. Højgaard<sup>1,2</sup>, C. Ballegaard<sup>1,2</sup>, R. Cordtz<sup>1</sup>, K. Zebbe<sup>1,2</sup>, M. Clausen<sup>1</sup>, L. E. Kristensen<sup>2</sup>, B. Glinthorg<sup>1,3</sup>, <sup>4,5</sup>L. Dreyer. <sup>1</sup>Center for Rheumatology and Spine diseases, Rigshospitalet Gentofte, Hellerup; <sup>2</sup>The Parker Institute, Bispebjerg and Frederiksberg Hospital, Frederiksberg; <sup>3</sup>Center for Arthritis Research COPECARE, Rigshospitalet Glostrup, Glostrup; <sup>4</sup>Center for Rheumatology and Spine diseases, Rigshospitalet Gentofte, Copenhagen; <sup>5</sup>Department of Rheumatology, Aalborg University Hospital, Aalborg, Denmark

**Background:** Previous studies have shown conflicting findings on the impact of gender on effectiveness of tumour necrosis factor alpha inhibitor (TNFi) treatment in patients with psoriatic arthritis (PsA).

**Objectives:** To investigate gender differences in disease manifestations, patient-reported outcomes, comorbidities and treatment effectiveness among patients with PsA treated with their first TNFi

**Methods:** In this observational cohort study, the nationwide DANBIO register provided prospectively collected data on disease activity and treatment outcomes for PsA patients who initiated their first TNFi in 2000–2015. Data on comorbidities, diagnosed in hospital departments, were obtained by cross-linkage to the Danish National Patient Register. Treatment response was evaluated according to EULAR and ACR criteria at 3- and 6 months. Cox- and logistic regression models analysed the impact of gender on TNFi persistence and response, respectively, while adjusting for a priori selected confounders including clinical-, laboratory- and patient-reported factors, comorbidities and lifestyle characteristics

**Results:** A total of 1750 PsA patients (53% females) were included. At baseline, women were older (49 years/47 years), more often smokers (32%/26%), had worse patient-reported scores (e.g. global score 71 mm/65 mm) and higher frequencies of hospital-diagnosed anxiety or depression (7%/4%) and chronic pulmonary disease (7%/3%), than men (all  $p<0.01$ ). Median TNFi persistence was 3.8 years (95% CI 3.0–5.7) in men versus 1.4 (1.1–1.8) in women ( $p<0.001$ ), figure 1. Men had higher odds of achieving response according to all response criteria, e.g. adjusted odds ratio=3.2 (1.6–6.1) for EULAR good/moderate response at 6 months (vs. women).



Abstract THU0316 – Figure 1. Kaplan meier plots

**Conclusions:** Male patients had better TNFi treatment outcomes. Adjustment for baseline risk factors including patient-reported outcomes, disease activity, comorbidities and lifestyle factors did not influence this relationship, which suggests a role of biological factors.

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THU0317

#### CREATING A EUROPEAN DATABASE OF PSORIATIC ARTHRITIS PATIENTS TREATED IN ROUTINE CARE – FIRST, PRELIMINARY RESULTS FROM THE EUROSPA RESEARCH NETWORK COLLABORATION

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**Background:** A research network collaboration of 15 European registries collecting data on patients with spondyloarthritis (SpA), "EuroSpA", has recently been created to strengthen research capabilities in the real world setting<sup>1</sup>. Here we present initial findings from the collaboration.

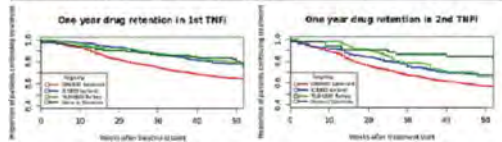
**Objectives:** To investigate the feasibility of creating a common database within the EuroSpA collaboration and to conduct proof-of-concept analyses by investigation of baseline characteristics, disease activity at baseline and after 6 months and 12 months' TNFi retention rate in patients with psoriatic arthritis (PsA) initiating Tumour Necrosis Factor inhibitors (TNFi).

**Methods:** A common data model for PsA was agreed upon by the EuroSpA Scientific Committee. Virtual meetings between the EuroSpA and registry data managers clarified data availability and structure. This was followed by upload of anonymized data through the secure Virtual Private Network pipelines to the EuroSpA server. Baseline characteristics and disease activity at baseline and after 6 months were investigated with non-parametric descriptive statistics. Kaplan-Meier estimation was used to investigate TNFi retention rates.

**Results:** : By January 8th 2018, four of the 15 registries participating in EuroSpA had completed data upload to the EuroSpA database resulting in 3172 patients with PsA in a pooled dataset. Baseline characteristics of the participating registry populations at initiation of first TNFi are shown in table 1. Crude 12 month TNFi retention rates varied from 65%–80% for 1st TNFi and 57%–82% for 2nd TNFi (see figure 1). For the pooled dataset crude 12 months TNFi retention rates were 68% and 60% for the 1st and 2nd TNFi, respectively.

**Abstract THU0317 – Table 1.** Baseline demographic and disease characteristics of patients with PsA registered in four EuroSpA registries

	HAEMO (EurosA) N= 2378	BioRx (EurosA) N= 878	TNF- $\alpha$ (EurosA) N= 81	CBR (EurosA) N= 138
Age, years	49 (29-56)	49 (25-57)	51 (20-61)	51 (28-59)
Male, n(%)	1488 (63)	202 (23)	11 (14)	139 (100)
CRP (mg/L)	1.96 (0.71)	2.78 (1.7)	3.9 (3.0)	1.73 (0.7)
Disease duration, years	11 (3-15)	8 (2-12)	11 (3-16)	11 (3-16)
Swelling status, n(%)	184 (7)	24 (3)	14 (17)	18 (13)
First TNFi, n(%)				
+ DMARD	615 (26)	11 (13)	16 (20)	161 (117)
+ NSA	1973 (84)	76 (9)	65 (80)	121 (88)
+ ADA	174 (7)	19 (2)	1 (1)	11 (8)
+ CCB	178 (7)	17 (2)	1 (1)	1 (1)
+ COX	127 (5)	19 (2)	1 (1)	1 (1)
First TNFi, n(%)				
+ Biologics	423 (18)	28 (3)	18 (22)	31 (22)
+ TNFi	1955 (82)	181 (21)	63 (78)	107 (78)
+ 2017-2018	1630 (69)	239 (27)	11 (14)	108 (78)
	Baseline	6 months	Baseline	6 months
DMARD-CRP	1.6 (2.4-1.3)	2.7 (1.3-3.4)	1.4 (1.3-1.4)	2.7 (1.2-3.6)
CRP (mg/L)	1.7 (1.3)	2.1 (1.6)	1.8 (1.3)	2.1 (1.6)
CRP (mg/L) post	1.8 (1.3)	1.1 (0.7)	1.8 (1.3)	1.1 (0.7)
TNF post, n(%)	41 (1.7)	28 (3.2)	19 (23)	28 (20)



**Conclusions:** Preliminary analyses showed differences across European registries regarding baseline characteristics and crude retention rates in PsA patients initiating TNFi. These initial, preliminary analyses demonstrate that the creation of a large European database of PsA patients treated in routine care based on a common data model is feasible, offering important opportunities for future research.

**REFERENCE:**  
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**THU0318 TREATING PSORIATIC ARTHRITIS TO TARGET: COMORBIDITIES, NON-ADHERENCE AND FACTORS RELATED TO THE HEALTH SYSTEM PREVENT ESCALATION OF THERAPY IN REAL LIFE**

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**Background:** Although the treat-to-target (T2T) strategy in psoriatic arthritis (PsA) clinical trials resulted in better outcomes in domains such as joints, skin, function and quality of life compared to standard care, in real life several factors affect such a strategy<sup>1</sup>.

**Objectives:** To determine the prevalence of patients achieving minimal disease activity (MDA) in our PsA clinic and the reasons why therapy in patients not achieving MDA was not optimised.

**Methods:** An observational, retrospective cross-sectional study nested in a cohort study was conducted; medical records of patients attending PsA clinic in a public university hospital were reviewed. Demographic data, current treatment and components of the MDA score were collected. When patients were not in MDA but the treatment was not optimised, the reasons for the non-escalation of therapy were recorded.

**Results:** MDA score was available in 113 visits, corresponding to 69 patients. Mean age of patients was 57.4±10.6, 53.6% (n=37) were females and 40.6% (n=28) were treated with biological drugs. MDA was reached in 31.0% (n=35) of visits; 36.2% (n=25) of the patients achieved MDA in at least one visit during the 8 months follow-up. There was no statistical difference in the proportion of patients achieving MDA according to treatment prescribed (biological DMARDs versus synthetic conventional DMARDs) (p=0.979). Although MDA was not achieved in 69.0% (n=78) of visits, optimisation of therapy was done in only 42.3% (n=33) of those visits. The main reasons which prevented treatment escalation were: physician impression of clinical remission and MDA overestimated by comorbidities and chronic deformities (57.7%, n=26), non-adherence to previous prescription (17.8%, n=8), delay to receive drugs from health insurance (17.8%, n=8), adverse events (11.1%, n=5), patient low cognitive level (6.7%, n=3) and patient refusal to escalate therapy (4.4%, n=2). In visits with impression of remission by rheumatologist, the skin and the swollen joint components of the MDA score were achieved in more than 80% of this visits (80.8%, n=21).

**Conclusions:** Rheumatologists are reluctant to escalate therapy in PsA even if patients are not in MDA if “objective” components of the MDA score such as skin and swollen joint counts are reached. Comorbid conditions, patients non-adherence to therapy and factors related to the health system influence a tight control strategy in the real life clinical practice.

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**THU0319 OVERALL SAFETY OF 7-WEEK SECUKINUMAB EXPOSURE DURING PREGNANCY IN WOMEN WITH PSORIATIC ARTHRITIS**

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**Background:** Psoriatic arthritis (PsA) often affects women of reproductive age. Secukinumab (SEC), a monoclonal antibody against interleukin-17A is effective in contrasting the progression of articular and cutaneous manifestations of PsA but has not been extensively studied in pregnancy, despite 84 cases of accidental exposure reported with reassuring safety outcomes.

**Objectives:** To evaluate the maternal and fetal outcomes in women with PsA exposed to SEC during pregnancy.

**Methods:** During a 10 months observational period, we enrolled 6 patients, treated by SEC 150 mg subcutaneously every month after weekly induction. All of them stopped the treatment by the time pregnancy test turned positive. All women had previously been counselled about contraceptive methods adoption and the potential risk of becoming pregnant during SEC administration, signing an informed consent. We collected demographic and clinical data of both patients



and babies, with a peculiar focus on maternal-fetal safety issues. APGAR scores at 1 min (APGAR1) and 5 min (APGAR5) from delivery were recorded.

**Results:** We observed 6 pregnancies from 6 mothers (4 of European, 1 Asian and 1 Latin-American ethnicity). Patient mean age at conception was 336±131 months; disease duration, 62±27 months; pre-conceptual exposure, 46±9 weeks; the (estimated) post-conceptual exposure 7±2 weeks. No major gestational complications were reported. One mother consulted the Emergency Department for a syncopal episode, but after a routine evaluation and an observation of 6 hours, was discharged; her pregnancy was otherwise unremarkable. Four girls (mean weight: 3170±200 g) and 2 boys (mean weight: 3460±60) were born. Mean gestational age was 38±2 weeks; 3 vaginal deliveries (1 oxytocine-induced for scarce dilation) and 3 caesarean sections were observed. The APGAR scores were above 8, excepting for an APGAR1 of 6 (born with caesarean section), then turned on 10 at APGAR5. Results are summarised on table 1. DAPSA, for the whole population, was under 4 (remission) at conception, and remained stable after delivery.

Abstract THU0319 – Table 1

Observed pregnancies	6					
Gestational age (weeks+days)	38±2					
Sex	M (4)			F (2)		
Birth weight (g)	3460±60			3170±200		
APGAR						
1 minute	6	10	9	9	8	10
5 minute	10	10	10	10	10	10
Delivery modality						
Vaginal spontaneous		1		1		1
Vaginal induced					1	
Caesarean section	1		1			1
Complications	-	-	-	-	-	ED
Malformations	-	-	-	-	-	-
Growth restrictions (SGA, IUGR)	-	-	-	-	-	-
Maternal age at conception (months)	336±131					
PsA duration at conception (months)	62±27					
PsA activity at conception (DAPSA)	<4	<4	<4	<4	<4	<4
Pre-conceptual exposure (weeks)	46±9					
Post-conceptual exposure (weeks)	7±2					
PsA activity postpartum (DAPSA)	<4	<4	<4	<4	<4	<4

APGAR, Appearance-Pulse-Grinace-Activity-Respiratory Score, SGA, Small for Gestational Age; IUGR, Intra-Uterine Growth Restriction; PsA, Psoriatic arthritis; DAPSA, Disease Activity in Psoriatic Arthritis; ED, Emergency Department (access).

**Conclusions:** The present study, despite the limited number of observations, represents the first report on pre-conceptual exposure to SEC. The available data, due to the lack of controlled studies, place the drug's use on FDA "B" category. Of note, SEC failed to cause teratogenicity, when administered throughout the whole pregnancy in a study conducted on primates (*Cynomolgus* monkeys). The limited knowledge on human beings suggests, nevertheless, not to administer SEC during pregnancy, unless a clear benefit overwhelm the potential risk. SEC, in conclusion, seems to have an acceptable safety profile, even when accidentally taken in the very first pregnancy phase. Reporting the cases of pregnancy exposures, as recommended by the ongoing Producer's policy, is the only way that would allow to confirm, or reject, this statement. A long-term follow-up of the mother and the offspring health, similarly, is needed.

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#### THU0320 A SHORT, EASILY READABLE, ONLY 3-ITEM TOOL – BRISTOL RHEUMATOID ARTHRITIS FATIGUE SCALE (BRAFF) – IS VALID IN PATIENTS WITH PSORIATIC ARTHRITIS

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**Background:** Fatigue in Psoriatic arthritis is very little studied. Recently, an instrument, the Functional Assessment of Chronic Illness Therapy (FACIT), has been validated in PsA, which is a relatively long, 13-item, instrument. An alternative instrument, the Bristol Rheumatoid Arthritis Fatigue Numerical Rating Scales (BRAFF-NRS), is an easily readable, much shorter, 3-item tool. The BRAFF-NRS

has been studied and validated in rheumatoid arthritis population; however, this has not been validated in patients with PsA.

**Objectives:** The purpose of this study was firstly to determine the internal consistency, test-retest reliability, criterion validity of the BRAFF-NRS in patients with PsA. Secondly, we also examined the potential clinical associations of worse fatigue in patients with established PsA.

**Methods:** Two independent cohorts fulfilling CASPAR criteria were enrolled.

STUDY PHASE 1: BRAFF-NRS SCALE VALIDATION COHORT (n=70)

A consecutive cohort of 70 PsA patients completed the 3-item BRAFF-NRS scale and 13 items of the FACIT-F scale, alongside laboratory testing and disease activity assessments. Moreover, all these patients completed BRAFF-NRS questionnaires twice, one day apart. Internal consistency was measured by Cronbach's alpha; test-retest reliability by the intra class correlation coefficient (ICC); and validity by the correlation of the BRAFF-NRS results with validated FACIT-F measures.

STUDY PHASE-2: IDENTIFYING THE POTENTIAL CLINICAL ASSOCIATIONS OF FATIGUE BY USING BRAFF-NRS (n=283)

Following informed consent, patients underwent a detailed skin and rheumatologic assessment including disease activity measures, and whether patient has achieved minimal disease activity (MDA). Moreover, we measured comorbidity using the Charlson Comorbidity Index (CCI). The factors predicting worse fatigue as measured by the BRAFF-NRS score were determined using univariate and multivariate linear regression analysis.

**Results:** STUDY PHASE 1: BRAFF-NRS SCALE VALIDATION COHORT (n=70): 67 patients had the complete assessments [mean age 52±9 years, 54% female, mean PsA duration of 5±3 years]. The internal consistency of the 3 items BRAFF-NRS questionnaire as measured by Cronbach's alpha was 0.92. Test-retest reliability as measured by the intraclass correlation coefficient between the first and repeat questionnaires was 0.98. The BRAFF-NRS scores were compared with the FACIT fatigue scores. There was an excellent correlation between the BRAFF-NRS and FACIT fatigue (r=-0.83 (p<0.001).

STUDY PHASE-2: IDENTIFYING THE POTENTIAL CLINICAL ASSOCIATIONS OF FATIGUE BY USING BRAFF-NRS (n=283)

On multiple linear regression analysis, the model predicted the significant association of low education status (p=0.03), number of deformed joints (p=0.01), not achieving MDA (p<0.001), higher CCI scores and worse HAQ (p<0.001) with worse fatigue scores.

**Conclusions:** BRAFF-NRS provides a reliable, reproducible and valid instrument of measuring fatigue in PsA. Fatigue is associated with low education status, higher number of deformed joints and comorbidities, not achieving remission and worse functional index. This short assessment tool can be especially valuable in the context of a busy clinic, and also in large epidemiological studies when other core domains warrant assessment.

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#### THU0321 ACUTE PHASE MARKERS IN PSORIATIC ARTHRITIS IDENTIFY PATIENTS WITH A MORE SEVERE PHENOTYPE

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**Background:** CRP and ESR are the most commonly and probably the most studied inflammatory markers among patients with inflammatory arthritis. In contrast to rheumatoid arthritis, however, these markers are raised in less than 50% of people with psoriatic arthritis (PsA). Little is known about the long term significance of elevated inflammatory markers during the course of PsA disease.

**Objectives:** In a well characterised PsA cohort with a long term follow up, we examined the association of CRP and ESR over the disease course with demographics, clinical and radiographic features, patient reported outcome measures and the number of comorbid conditions.

**Methods:** A cohort of 283 PsA patients all meeting CASPAR criteria and attending rheumatology clinics were evaluated. All underwent detailed skin and rheumatologic assessments, along with cardiovascular risk factor evaluation. Moreover, we documented the presence/absence of comorbidities using the Charlson Comorbidity Index (CCI). All of these patients had CRP and ESR laboratory values assessed along with the other routine laboratory parameters during the disease course. For each patient, we documented CRP and ESR values at 3 different time points: firstly, at the time of the initial diagnosis; secondly, the highest value of CRP and ESR recorded during the disease course; and thirdly at the time of full assessment for this study. Cumulative inflammation over time was

represented by the cumulative averages of CRP (ca-CRP) and ESR (ca-ESR) which were calculated from the AUC (Area Under the Curve) of the 3 documented measurements divided by the total number of months of follow-up. Variables significantly associated at a Bonferroni-corrected p-value were included in the multiple linear regression modelling CRP and ESR.

**Results:** A total of 283 PsA patients [mean age 54.6±12 years; 52% female; mean PsA duration of 19±9 years; 25% with sacroiliitis; 44.5% with peripheral joint erosions; 60% of patients requiring TNFi for PsA] attended for detailed assessments. The median (IQR) and mean (SD) Ca-CRP was 8.8 (4.6–14.8) and 11.72 (10.52), respectively. The median (IQR) and mean (SD) Ca-ESR was 13.8 (7.8–20.1) and 15.78 (10.46). The variables were also checked for multicollinearity. On multiple linear regression, erosions, sacroiliitis, and the CCI were most significantly associated with Ca-CRP (unstandardised coefficient B=6.4, 2.9, 1.05, respectively, p<0.01), when controlled for all other variables in the model [(F=77.6, p<0.001), 72% (R-square)]. There was borderline significant association with the higher number of DMARDs and TNFi used (p=0.09, 0.08, respectively). Moreover, on multiple linear regression analysis, the erosions, extent of joint involvement (oligoarthritis/polyarthritis), number of TNFi used and the CCI were most significantly associated with Ca-ESR (unstandardised coefficient B=3.8, 1.8, 1.8, 0.76, respectively) when controlled for all other variables in the model [(F=130, p<0.001), 77% (R-square)].

**Conclusions:** PsA is a heterogeneous disease with <50% of patients developing radiographic damage. Elevated inflammatory markers, CRP and ESR, can help identify patients with a severe PsA phenotype. Such patients experience more radiographic damage, they have more comorbidities and their disease is more resistant to DMARDs and TNFi.

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THU0322

#### SECUKINUMAB PROVIDES SUSTAINED IMPROVEMENTS IN THE SIGNS AND SYMPTOMS OF ACTIVE PSORIATIC ARTHRITIS: 3-YEAR RESULTS FROM THE PHASE 3 FUTURE 2 STUDY

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**Background:** Secukinumab, a fully human monoclonal antibody that selectively neutralises IL-17A, provided significant and sustained improvement in the signs and symptoms of active psoriatic arthritis (PsA) over 2 years in the FUTURE 2 study (NCT01752634).<sup>1</sup>

**Objectives:** To report 3 year efficacy and safety results from the FUTURE 2 study.

**Methods:** Overall, 397 patients (pts) with active PsA were randomised to receive subcutaneous secukinumab (300, 150 or 75 mg) or placebo at baseline, Weeks (Wks) 1, 2, 3 and 4, and every 4 wks thereafter.<sup>1</sup> Assessments at Wk 156 are from pts originally randomised to secukinumab and included ACR20/50, PASI 75, HAQ-DI, and resolution of dactylitis and enthesitis. Analyses by prior anti-TNF use (naïve/inadequate response [IR]) and with/without concomitant methotrexate (MTX) were assessed. Data are reported as observed for secukinumab 300 and 150 mg (approved doses). Safety analysis included all pts who received ≥1 dose of secukinumab.

**Results:** In total, 73/100 (73.0%) and 72/100 (72.0%) pts in the secukinumab 300 and 150 mg groups, respectively, completed 156 wks of treatment. Sustained clinical improvements were observed in those continuing with secukinumab across all endpoints through Wk 156 (table 1). ACR20 response rates at Wk 156 in anti-TNF-naïve pts were 85.2% and 76.5% with secukinumab 300 and 150 mg respectively; corresponding rates in anti-TNF-IR pts were 55.6% and 54.5%. ACR20 response rates in pts receiving concomitant MTX were 73.0% and 77.1% with secukinumab 300 and 150 mg, respectively; rates in pts without concomitant MTX use were 77.3% and 63.2%. Over the study (mean secukinumab exposure of 991.3 days) the type, incidence and severity of adverse events (AEs) were consistent with that reported previously. Exposure adjusted incidence rates with secukinumab for selected AEs of interest were: serious infections (1.8), candida infections (1.8), inflammatory bowel disease (0.1), major adverse cardiovascular event (0.2) and malignant/unspecified tumours (1.2).

**Abstract THU0322 – Table 1.** Summary of Efficacy Results at Wk 156

Variable % responders (n), unless stated	Secukinumab 300 mg s.c. (n=100)	Secukinumab 150 mg s.c. (n=100) <sup>†</sup>
ACR20	75.3 (81)	69.9 (73)
ACR50	54.3 (81)	38.4 (73)
<sup>a</sup> PASI 75	74.3 (35)	81.8 (44)
HAQ-DI, mean change from BL (n)	-0.63 (81)	-0.47 (74)
<sup>b</sup> Resolution of enthesitis	68.9 (45)	70.8 (48)
<sup>c</sup> Resolution of dactylitis	82.1 (39)	80.0 (25)

<sup>a</sup>PASI responses assessed in pts with psoriasis affecting ≥3% body surface area at BL (300 mg: n=41; 150 mg: n=58)

<sup>b</sup>Assessed in pts (n=56 [300 mg] and 64 [150 mg]) with this symptom at BL

<sup>c</sup>Assessed in pts (n=46 [300 mg] and 32 [150 mg]) with this symptom at BL

<sup>†</sup>Secukinumab 150 mg arm includes 42 pts who were up-titrated to 300 mg starting at Wk 128

BL, baseline; HAQ-DI, health assessment questionnaire-disability index; PASI, psoriasis area and severity index

N, number of pts randomised; n, number of pts with evaluation

**Conclusions:** Secukinumab 300 and 150 mg provided sustained improvements in signs and symptoms of active PsA through 3 years. Secukinumab was well tolerated, with a safety profile consistent with that reported previously.<sup>1</sup>

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THU0323

#### TOFACITINIB IMPROVES COMPOSITE ENDPOINT MEASURES OF DISEASE IN PATIENTS WITH PSORIATIC ARTHRITIS

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**Background:** Tofacitinib is an oral Janus kinase inhibitor for the treatment of psoriatic arthritis (PsA). PsA is a heterogeneous disease and composite endpoints allow assessment of multiple clinical outcomes in one instrument.

**Objectives:** To examine the effects of tofacitinib treatment on several composite endpoints in patients (pts) with PsA.

**Methods:** In 2 placebo (PBO)-controlled, double-blind, multicentre, global Phase 3 studies, pts had active PsA and either had an inadequate response (IR) to ≥1 conventional synthetic disease-modifying antirheumatic drug (csDMARD) and were tumour necrosis factor inhibitor (TNFi)-naïve (OPAL Broaden [n=422;



12 months; NCT01877668]), or had an IR to  $\geq 1$  TNFi (OPAL Beyond [n=394; 6 months; NCT01882439]). Pts were randomised to receive tofacitinib 5 mg twice daily (BID), tofacitinib 10 mg BID, adalimumab 40 mg subcutaneous injection once every 2 weeks (OPAL Broaden only) or PBO (advancing to tofacitinib 5 or 10 mg BID at Month 3, OPAL Broaden and OPAL Beyond), in addition to continuing on a single, stable csDMARD. Composite endpoints assessed: Psoriatic Arthritis Disease Activity Score (PASDAS), Disease Activity Score using 28 joints with C-reactive protein, Disease Activity Index for Reactive Arthritis/Psoriatic Arthritis (DAREA/DAPSA) and Composite Psoriatic Disease Activity Index (CPDAI).

**Results:** Demographics and baseline disease characteristics were generally similar between treatment groups within the 2 studies, except for duration of PsA disease (longer in OPAL Beyond) and geographic distribution (OPAL Broaden having more Eastern EU pts). Baseline values for composite endpoints were generally similar across treatment groups and studies (table 1). Both doses of tofacitinib showed improvements in composite endpoints vs PBO at Month 3 in both studies (table 1). In OPAL Broaden, the effects of adalimumab were similar to both doses of tofacitinib across composite endpoints. Effect size for the composite endpoints (using a subpopulation of pts who had all available data for all endpoints) was highest for PASDAS and typically lowest for DAREA/DAPSA; this rank order of effect size was similar across treatment arms and studies. At Month 3, effect sizes in pts receiving active treatment ranged from 0.90 (DAREA/DAPSA for tofacitinib 5 mg BID) to 2.40 (PASDAS for tofacitinib 10 mg BID) in OPAL Broaden, and 0.81 (DAREA/DAPSA for tofacitinib 5 mg BID) to 1.84 (PASDAS for tofacitinib 10 mg BID) in OPAL Beyond (table 1). Standardised response means generally followed the same pattern as effect size across studies with both doses of tofacitinib (table 1).

**Abstract THU0323 – Table 1.** Summary of mean at baseline, LS mean change from baseline, effect size and standardised response mean at Month 3 for composite endpoints (PASDAS, DAS28-3(CRP), DAREA/DAPSA, CPDAI) in OPAL Broaden and OPAL Beyond studies

	OPAL Broaden			OPAL Beyond			
	Tofacitinib 5 mg BID N=107	Tofacitinib 10 mg BID N=104	Adalimumab 40 mg SC Q2W N=106	Placebo N=105	Tofacitinib 5 mg BID N=141	Tofacitinib 10 mg BID N=142	Placebo N=141
<b>Baseline mean (SD) [95% CI]</b>							
PASDAS	6.03 (1.15) [1.05]	6.01 (1.06) [1.00]	5.92 (1.06) [1.00]	6.03 (1.15) [1.05]	5.09 (1.24) [1.24]	6.43 (1.21) [1.21]	5.97 (1.26) [1.26]
DAS28-3(CRP)	4.56 (0.92) [1.07]	4.48 (0.87) [1.04]	4.35 (1.00) [1.06]	4.50 (1.05) [1.05]	4.51 (0.94) [1.17]	4.67 (1.17) [1.32]	4.40 (1.03) [1.31]
DAREA/DAPSA	45.55 (20.33) [1.77]	43.89 (19.11) [1.91]	38.22 (18.17) [1.93]	43.88 (22.46) [1.93]	45.53 (23.51) [1.91]	51.54 (27.80) [1.91]	46.64 (26.59) [1.91]
CPDAI*	9.9 (2.30) [1.1]	10.0 (2.26) [1.0]	9.7 (2.28) [1.7]	9.9 (2.45) [1.1]	10.1 (2.58) [1.9]	0.7 (2.56) [1.9]	9.6 (2.66) [1.9]
<b>LS mean change from baseline at Month 3 (SE) [95% CI]</b>							
PASDAS	-1.90*** (0.14) [1.04]	-2.30*** (0.14) [1.02]	-2.17*** (0.14) [1.06]	-1.21 (0.14) [1.01]	-1.91*** (0.14) [1.21]	-2.14*** (0.14) [1.24]	-1.83 (0.14) [1.26]
DAS28-3(CRP)	-1.33*** (0.10) [1.17]	-1.23*** (0.10) [1.07]	-1.51*** (0.10) [1.06]	-0.77 (0.11) [1.04]	-1.38*** (0.10) [1.30]	-1.23*** (0.10) [1.32]	-1.01 (0.10) [1.31]
DAREA/DAPSA	-3.05*** (1.72) [1.91]	-2.49*** (1.53) [1.09]	-1.93*** (1.77) [1.09]	-1.93*** (1.82) [1.09]	-2.46*** (1.67) [1.29]	-3.04*** (1.70) [1.52]	-1.80 (1.69) [1.51]
CPDAI*	-2.9 (0.34) [1.1]	-4.24*** (0.36) [1.0]	-3.1* (0.34) [1.7]	-2.2 (0.36) [1.0]	-3.3*** (0.31) [1.7]	-3.4*** (0.31) [1.7]	-1.8 (0.31) [1.2]
<b>Effect size at Month 3</b>							
	N3=68	N3=62	N3=66	N3=77	N3=64	N3=62	N3=73
PASDAS	1.74	2.40	1.60	1.01	1.74	1.84	0.74
DAS28-3(CRP)	1.47	1.77	1.37	0.73	1.07	1.16	0.62
DAREA/DAPSA	0.90	1.15	1.09	0.36	0.81	0.84	0.31
CPDAI	1.74	1.73	1.05	0.60	1.41	1.45	0.50
<b>Standardised response mean at Month 3</b>							
PASDAS	1.42	1.75	1.73	1.19	1.26	1.55	0.65
DAS28-3(CRP)	1.25	1.46	1.53	0.79	1.14	1.29	0.61
DAREA/DAPSA	1.05	1.25	1.47	0.78	0.94	1.15	0.58
CPDAI	0.89	1.27	1.11	0.80	1.11	1.49	0.63

**Conclusions:** In 2 Phase 3 studies, tofacitinib 5 mg and 10 mg BID improved composite endpoint scores vs PBO over 3 months in pts with PsA. The largest effect size and standardised response means were observed for PASDAS. Effect sizes and standardised response means varied across endpoints but were consistent across studies.

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**THU0324 DISEASE ACTIVITY AND PATIENT CHARACTERISTICS BY COMORBIDITY AMONG PSORIATIC ARTHRITIS (PSA) PATIENTS IN A US REGISTRY**

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**Background:** PsA patients have greater prevalence of cardiovascular disease (CVD), metabolic syndrome (MetS), and cancer than patients without PsA.

**Objectives:** To examine patient characteristics and disease activity by comorbidity profile among PsA patients.

**Methods:** This analysis included adults with PsA enrolled in the US Corrona PsA/spondyloarthritis Registry from March 2013-March 2017 and followed for  $\geq 6$  months. Prevalence (at registry entry) and incidence rate (time to new events after registry entry) of CVD, MetS, and cancer were determined. Patient characteristics and disease activity were described by prevalent comorbidity, with t-tests for means despite skewed data and chi-squared tests for percentages.

**Results:** The analysis included 1493 patients and 3564 patient-years of follow-up. Incidences (95% confidence interval) per 1000 patient-years were 9.4 (6.5–13.5), 1.0 (0.3–3.1), and 11.4 (8.2–15.8) for CVD, MetS, and cancer (6.8 [4.5–10.2] nonmelanoma skin cancer), respectively. PsA patients with (vs without) prevalent CVD, MetS, or cancer were older, and fewer had full-time jobs or private insurance. Patients with (vs without) CVD had higher swollen joint count and mean body surface area, and tended to have higher rates of obesity. Patients with (vs without) MetS tended to have greater disease activity. Patients with (vs without) comorbidities reported less disease activity on patient global assessment. Data are mean or %

$\geq 3$  of 4 conditions: hypertension, hyperlipidemia, diabetes mellitus, or obesity  
<sup>b</sup>P value across all categories for employment or body mass index

**Conclusions:** PsA patients with (vs without) CVD had greater disease activity and those with (vs without) MetS tended to have greater disease activity by physician-derived measures, but PsA patients with (vs without) CVD or MetS reported lower global assessment of disease activity. Patient perception of PsA may mask the effect of comorbid CVD or MetS on disease activity.

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**Abstract THU0324 – Table 1.** Patient Characteristics by Prevalent Comorbidity at Registry Entry

	Yes (n=201)	CVD No (n=1292)	P	Yes (n=227)	MetS <sup>a</sup> No (n=1266)	P	Yes (n=177)	Cancer No (n=1316)	P
Women	44.3%	52.7%	0.03	50.7%	51.8%	0.8	55.7%	51.0%	0.3
Age, y	62.5	53.0	<0.001	61.8	52.9	<0.001	61.9	53.2	<0.001
Employed full-time <sup>b</sup>	33.5%	58.6%	<0.001	36.2%	58.6%	<0.001	39.4%	57.3%	<0.001
Private insurance	61.9%	81.4%	<0.001	60.6%	82.0%	<0.001	68.6%	80.1%	<0.001
Obese <sup>b</sup>	61.0%	52.8%	0.1	92.0%	46.8%	<0.001	51.2%	54.3%	0.7
Clinical disease activity index	11.8	11.7	0.9	11.9	11.7	0.7	11.1	11.8	0.4
Tender joint count	4.42	4.37	0.9	5.16	4.23	0.1	4.33	4.38	0.9
Swollen joint count	2.58	1.96	0.045	2.50	1.96	0.07	1.76	2.08	0.3
Physician global assessment	17.7	16.4	0.4	16.7	16.5	0.9	15.7	16.6	0.5
Patient global assessment	51.7	57.8	0.01	50.7	58.1	<0.001	52.3	57.6	0.03
% body surface area	7.1	5.1	0.02	6.6	5.1	0.07	5.3	5.4	0.9
Enthesitis	26.4%	26.9%	0.9	26.9%	26.8%	0.9	28.3%	26.6%	0.6
Dactylitis	14.9%	12.9%	0.4	17.2%	12.5%	0.054	9.0%	13.8%	0.08
Nail visual analogue scale	8.0	7.1	0.5	7.3	7.2	0.9	6.4	7.3	0.5

THU0325

**SECUKINUMAB DEMONSTRATES A CONSISTENT SAFETY PROFILE WITH UP TO 5 YEARS TREATMENT IN PATIENTS WITH PSORIATIC ARTHRITIS AND MODERATE TO SEVERE PLAQUE PSORIASIS: UPDATED POOLED SAFETY ANALYSES**

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**Background:** Pooled safety data from secukinumab (SEC) studies in psoriasis and psoriatic arthritis (PsA) have been reported previously.<sup>1</sup>

**Objectives:** To report updated longer-term safety data with up to 5 years of SEC treatment from psoriasis and PsA studies.

**Methods:** The moderate to severe plaque psoriasis and active PsA data pool consisted of 15 and 3 Phase III studies, respectively. Different SEC doses in the studies included intravenous (up to 10 mg/kg) or subcutaneous (s.c.; 75–300 mg) loading, followed by s.c. maintenance dosing (300, 150 or 75 mg). Placebo patients were re-randomised to SEC at 12–24 weeks depending on study design. Adverse events (AEs) were reported as exposure adjusted incident rates (EAIR) per 100 patient-years and analyses included all patients who received ≥1 dose of SEC.

**Results:** A total of 5181 and 1380 patients from psoriasis and PsA studies representing an exposure of 10416.9 and 3866.9 patient years, respectively, were included in this study. The most frequently reported AE was viral upper respiratory tract infection (table 1). EAIRs for serious infections, *Candida* infections, inflammatory bowel disease (IBD) and major adverse cardiac events (MACE) were low and similar in both psoriasis and PsA indications (table 1). No cases of tuberculosis were reported.

**Abstract THU0325 – Table 1.** Summary of Secukinumab Safety across Psoriasis and PsA studies: Entire Safety Period

	Psoriasis Any secukinumab n=5181	PsA Any secukinumab n=1380
Total exposure, patient-years	10416.9	3866.9
Min–max exposure (days)	1–1825	8–1827
Exposure (days), mean (SD)	734.4 (562.9)	1023.5 (472.3)
Death, n (%)	9 (0.2)	11 (0.8)
<b>EAIR per 100 Patient-years (95% CI)</b>		
Any AE	204.4 (198.4, 210.5)	147.0 (138.9, 155.5)
Any serious AE	6.9 (6.3, 7.4)	7.9 (7.0–8.9)
<b>Most Common AEs<sup>1</sup></b>		
Viral upper respiratory tract infection	21.0 (19.9–22.0)	12.1 (10.9–13.4)
Headache	6.2 (5.8, 6.8)	3.8 (3.2, 4.5)

Upper respiratory tract infection	5.4 (4.9, 5.9)	9.1 (8.1, 10.2)
<b>AEs of Selected Interest</b>		
Serious infections <sup>2</sup>	1.4 (1.2, 1.6)	1.9 (1.5, 2.4)
<i>Candida</i> infections <sup>3</sup>	2.2 (1.9, 2.5)	1.5 (1.1, 2.0)
IBD <sup>4</sup>	0.01 (0.0–0.05)	0.05 (0.01–0.19)
Crohn's disease <sup>4</sup>	0.05 (0.02–0.11)	0.08 (0.02–0.23)
Ulcerative colitis <sup>4</sup>	0.13 (0.07–0.23)	0.08 (0.02–0.23)
MACE <sup>5</sup>	0.3 (0.2, 0.5)	0.4 (0.3–0.7)

<sup>1</sup>AEs in the SEC group that occurred with an EAIR of ≥5 during the entire safety period in either of the pooled groups; <sup>2</sup>Rates are for system organ class; <sup>3</sup>Rates are for high level term; <sup>4</sup>Rates are for PT (IBD PT data are reported for unspecified IBD); <sup>5</sup>Rates are for Novartis MedDRA Query term; EAIR, exposure adjusted incidence rate per 100 patient-years; N, number of patients in the analysis; SD, standard deviation

**Conclusions:** SEC demonstrated a favourable safety profile during long-term treatment (up to 5 years) in patients with moderate to severe plaque psoriasis or PsA, hence, supporting long-term use. The safety profile was consistent with previous reports and comparable across psoriasis and PsA patients.

**REFERENCE:**

[1] Mease, et al. *Arthritis Rheumatol* 2017; 69(suppl 10):A606.

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**THU0326 DISCONTINUATION AND SWITCHING PATTERNS OF TUMOUR NECROSIS FACTOR INHIBITOR (TNFI) THERAPY IN TNFI-NAIVE AND TNFI-EXPERIENCED PATIENTS WITH PSORIATIC ARTHRITIS IN THE US CORRONA PSORIATIC ARTHRITIS/ SPONDYLOARTHRTIS (PSA/SPA) REGISTRY**

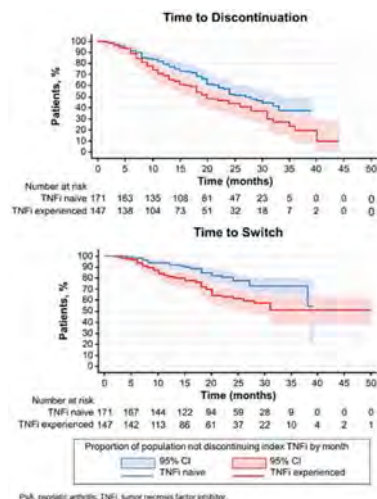
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**Background:** To better inform treatment decisions for patients with psoriatic arthritis (PsA), it is important to understand outcomes in patients who initiate a first line vs a subsequent line of TNFi therapy. Limited studies have evaluated persistence and switching of TNFi therapy in TNFi-naive vs TNFi-experienced US patients with PsA.

**Objectives:** To examine discontinuation and switching of TNFis in TNFi-naive and -experienced patients with PsA in the US Corrona PsA/SpA Registry.

**Methods:** All patients aged ≥18 years in the Corrona PsA/SpA Registry who were diagnosed with PsA, initiated a TNFi (index therapy) between March 2013 and , January 2017 and had ≥1 follow-up visit after TNFi initiation were included. Patients were stratified by prior TNFi use (TNFi naive: no prior TNFi or other biologic; TNFi experienced: ≥1 prior TNFi). Patient demographics and clinical and disease characteristics were assessed at the time of TNFi initiation (baseline). Time to discontinuation of the index TNFi (with or without switching) and time to switch to another biologic were assessed by Kaplan-Meier analysis. Log-rank tests were used to assess differences in persistence and switching between the TNFi-naive and -experienced cohorts. Provider-reported reasons for discontinuation of the index TNFi were summarised descriptively.

**Results:** 318 patients with PsA were included (TNFi naive, n=171; TNFi experienced, n=147), with a total follow-up of 579.2 person-years. Experienced patients had a longer mean (SD) disease duration (13.3 [10.0] vs 9.5 [9.7] years; p<0.01) and a higher proportion had a history of prednisone use (27.9% vs 17.5%; p=0.03) compared with naive patients. A total of 75 naive (43.9%) and 80 experienced patients (54.4%) discontinued their index TNFi, including 33 (19.3%) and 48 (32.7%), respectively, who switched to a new biologic. The median (95% CI) time to discontinuation of the index TNFi in naive vs experienced patients was 27 (22 to 33) vs 20 (18 to 28) months, respectively (figure 1). Among those who discontinued their TNFi, the mean (SD) time to discontinuation was 14.5 (8.0) months in naive patients vs 14.0 (8.9) months in experienced patients. Due to the low number of switching events, the median time to switch of the index TNFi could not be estimated. Among those who switched to a new biologic, the mean (SD) time to switch was 16.0 (8.1) vs 13.5 (7.5) months in naive and experienced patients, respectively. TNFi-naive patients had greater persistence with their index TNFi (p=0.03) and were less likely to switch to another biologic (p=0.002) compared with TNFi-experienced patients. Provider-reported reasons for discontinuation included lack of effect (naive, 71%; experienced, 62%), side effects (10%; 23%), social reasons (6%; 3%), doing well (3%; 0%), and other (10%; 12%).



**Abstract THU0326 – Figure 1.** Time to Discontinuation (With or Without Switching) and Time to Switch of Index TNFi in TNFi-Naive and TNFi-Experienced Patients With PsA. PsA, psoriatic arthritis; TNFi, tumour necrosis factor inhibitor.

**Conclusions:** In this real-world analysis of US patients with PsA, TNFi-experienced patients were more likely to discontinue and switch their index TNFi and had a shorter time to discontinuation compared with TNFi-naive patients. These results may help inform treatment decisions when selecting later lines of TNFi therapy in patients with PsA.

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**THU0327 REAL WORLD (RW) EXPERIENCE WITH AN ANTI-IL-17A INHIBITOR IN BIOLOGIC NAÏVE AND BIOLOGIC EXPERIENCED PSORIATIC ARTHRITIS (PSA) PATIENTS**

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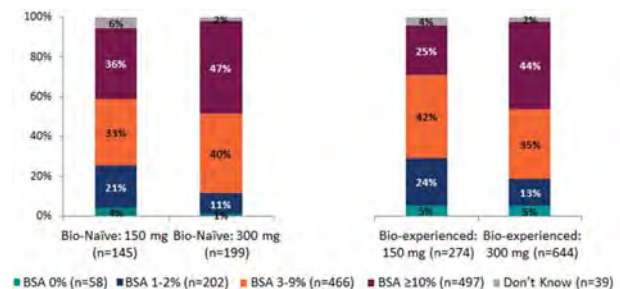
**Background:** Two IL-17A inhibitors are approved for the treatment of PsA, ixekizumab and secukinumab. At the time of this survey, real world evidence was only available for secukinumab, which was approved for PsA in 2016 in EU, Australia and Switzerland. Secukinumab label dose for PsA patients with either concomitant moderate to severe plaque psoriasis or anti-TNFα inadequate responders is 300 mg. For other patients, the recommended dose is 150 mg. All patients receive a loading dose regimen by S.C. injection at Weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dose. Little data are published on the RW utilisation of secukinumab in PsA.

**Objectives:** Describe RW dose utilisation of an anti-IL-17A inhibitor, among biologic naïve and biologic experienced PsA patients.

**Methods:** Data from a chart review study conducted in 2017 across France, Germany, Italy, Spain, UK, Australia and Switzerland where secukinumab is reimbursed were used. Specialists were recruited by field-based interviewers, and provided information on demographics, Body Surface Area (BSA), time since diagnosis and treatment for their adult PsA patients currently receiving secukinumab.

**Results:** 212 rheumatologists, 89 dermatologists, 1 orthopedist provided data for 1451 patients. Mean age 50.6 years, 47% female, mean time since PsA diagnosis 5.9 years and 86% had concomitant psoriasis. 96% received prior csDMARD(s) and 8% prior apremilast. 29% (425) were biologic naïve and 71% (1024) biologic experienced (limited differences between specialists: 74% rheumatologists; 63% dermatologists). 34%, 24%, and 13% received, 1, 2, and 3+prior biologics respectively.

Among biologic naïve patients on 150 mg, 36% (52/145) had a BSA ≥10%, where the recommended dose is 300 mg at secukinumab initiation. 29% (274/930) of biologic experienced patients received secukinumab at 150 mg, not the recommended 300 mg dose (figure 1)



**Abstract THU0327 – Figure 1.** Secukinumab Dosing: Current Dose (Loading or Maintenance). \*For this analysis, moderate to severe psoriasis was defined as BSA ≥10

**Conclusions:** In the RW, secukinumab is prescribed mainly in biologic experienced patients (71%) and is not universally prescribed at the recommended dose for PsA. Specifically, of those who are biologic naïve (29%), 36% of patients on 150 mg had moderate to severe psoriasis, which is outside the recommended dose. Further RW experience is needed for ixekizumab.

**Acknowledgements:** Acknowledgements: This chart review study was designed and run by Adelphi Real World. The study was supported by a number of

pharmaceutical companies, including Eli Lilly and Company. This specific analysis and abstract was supported by Eli Lilly and Company.

**Disclosure of Interest:** R. Moon: None declared, J. Hill Grant/research support from: Eli Lilly and Company, Employee of: Eli Lilly and Company, N. Booth: None declared, S. Lobosco: None declared

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#### THU0328 MIR-499 POLYMORPHISM IS ASSOCIATED WITH SUSCEPTIBILITY TO PSORIATIC ARTHRITIS – PRELIMINARY STUDY

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**Background:** Polymorphism within the miR-499 has been reported to be associated with susceptibility to rheumatoid arthritis (RA) in various populations.

**Objectives:** Our study aimed to find out whether similar association could be observed also in Polish population in both RA and psoriatic arthritis (PsA) patients.

**Methods:** For this purpose 359 individuals were studied, including 111 RA patients, 86 patients with PsA and 162 healthy blood donors that served as a control group.

Genotyping for miR-499 rs3746444 T/C was performed using a LightSNIP assay. **Results:** Distribution of the miRNA-499 alleles and genotypes was similar in RA patients and controls. Among RA patients those carrying the CC homozygous genotype presented with lower DAS28 at diagnosis (0.027) but higher CRP levels after 12 weeks of anti-TNF treatment (p=0.042).

Interestingly, the TT genotype (rs3746444) was overexpressed in patients with PsA as compared to controls (OR=1.85, p=0.034) but its frequency was not significantly different when compared to RA cases. This polymorphism was also not found to be associated with clinical parameters in PsA patients.

**Conclusions:** These results show that miR-499 rs3746444 T/C polymorphism may constitute a risk factor for psoriatic arthritis development.

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#### THU0329 AN ITALIAN OBSERVATIONAL PROSPECTIVE STUDY ON PREDICTORS OF CLINICAL RESPONSE TO GOLIMUMAB AT 6 MONTHS IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS

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**Background:** The identification of markers of response to biologic agents in the treatment of active psoriatic arthritis (PsA) may help in predicting the outcome and hence in optimising therapy.

**Objectives:** To evaluate the ability of a panel of candidate factors to predict the clinical response, defined as the achievement of minimal disease activity (MDA) following 6 month therapy with golimumab.

**Methods:** This Italian 6 month observational study included 149 PsA patients (53.7% males, mean age 49 years (SD 11) inadequate responders to conventional therapies who started the anti-tumour necrosis factor- $\alpha$  golimumab. Estimated factors included demographic data and baseline characteristics of the disease, measures of disease activity and functional disability, and biomarkers.

**Results:** At 6 months, a high rate of treatment persistency (80%) was observed. MDA was achieved in 44.3% of patients. Multivariate analysis showed Disease Activity in Psoriatic Arthritis (DAPSA) score, high-sensitivity C-reactive protein (hs-CRP), age, and disease duration as baseline factors correlating with MDA achievement at 6 months (table 1). A higher hs-CRP value and the absence of comorbidities were predictive factors for MDA at 6 months in biomarker-enhanced prediction models.

Golimumab was effective in improving disease and functional parameters and was well tolerated.

**Conclusions:** The availability of predictive factors of treatment response identified in this study may be helpful in driving the selection of PsA patients that are most likely to benefit of the therapy with golimumab.

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#### THU0330 OBESITY IN PSORIATIC ARTHRITIS: COMPARATIVE PREVALENCE WITH SKIN PSORIASIS AND ASSOCIATED FACTORS

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**Background:** Obesity (BMI  $\geq 30$  kg/m<sup>2</sup>) is a common cardiovascular risk factor in psoriatic disease<sup>1</sup>. Although the prevalence of obesity is high, the factors associated with it in psoriatic arthritis (PsA) are poorly understood.

**Objectives:** We aimed to evaluate the prevalence and obesity-associated factors in patients with PsA.

**Methods:** Retrospective cross-sectional study that included 205 consecutive patients with PsA according to CASPAR criteria. The prevalence of obesity was compared with that of 310 patients with skin psoriasis of similar age ( $\pm 3$  years). The factors associated with obesity were first analysed by a conditional logistic regression. The significant factors in this first model were then introduced in a multivariate model using a backward step approach (p-values < 0.05 were considered significant).

**Results:** One-hundred twelve men and 94 women were included, with a mean age of 53  $\pm$  13 years. Obesity was more prevalent among psoriatics (36.5%) compared to PsA patients (24%), OR 1.6 (1.1–2.3), p < 0.05. The factors associated with obesity in the univariate analysis (p < 0.05) were: onset of psoriasis > 40 years (OR 2.4), onset of arthritis > 40 years (OR 2.1), PsA family history (OR 3.1), polyarticular presentation (OR 1.9), axial presentation (OR 2.5), polyarticular evolution (OR 2.4), axial evolution (OR 4.2), diabetes (OR 3.6), HBP (OR 3.9), and dyslipidemia (OR 3.5). After correcting for age, sex, disease duration and other confounders, independent associations with obesity found in the multivariate model (p < 0.05) were: PsA family history (OR 3.6, IC95%: 1.1–14.4), axial evolution (OR 4.4, IC95%: 1.0–22.4) and dyslipidemia (OR 3.5, IC95%: 1.5–8.6).

Used model	Parameter	Item considered	Odds Ratio	95% confidence interval	P value
Univariate logistic model (ULM)	Gender	Female	0.3197	0.1531–0.6677	0.0024
		Continuous	0.9570	0.9252–0.9899	0.0109
	Baseline DAPSA score	Continuous	0.9287	0.8967–0.9618	<0.0001
	Baseline HAQ total score	Continuous	0.2937	0.1423–0.6063	0.0009
	Baseline Pain	Continuous	0.9833	0.9684–0.9984	0.0299
	Baseline BASDAI	Continuous	0.7036	0.5733–0.8635	0.0008
Multivariate logistic model (MLM)	Comorbidities	Presence	0.3258	0.1465–0.7241	0.0059
		Continuous	0.9542	0.9112–0.9993	0.0465
	Age	Continuous	1.0015	1.0002–1.0028	0.0241
	Baseline hs-CRP	Continuous	0.9255	0.8879–0.9647	0.0003
	Baseline DAPSA score	Continuous	1.0057	1.0007–1.0107	0.0260
	Disease duration	Continuous	1.0688	1.008–1.1334	0.0261
Biomarker-enhanced ULM	Baseline hs-CRP	Continuous	1.0688	1.008–1.1334	0.0261
Biomarker-enhanced MLM	Comorbidities	Presence	0.2645	0.0881–0.7941	0.0177
		Baseline DAPSA score	Continuous	0.9231	0.8850–0.9628



**Conclusions:** Obesity was more common among our patients with cutaneous psoriasis than in those with arthritis. The model that best explains obesity in this PsA series combines genetic factors (PsA family history), together with factors specific to the metabolic syndrome (dyslipidemia), with others owned to arthritis (axial evolution).

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**THU0331 RELATIONSHIP BETWEEN THE NAIL ULTRASONOGRAPHIC EVALUATIONS AND CLINICAL FEATURES IN PATIENTS WITH PSORIATIC ARTHRITIS**

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**Background:** Nail ultrasonography (US) is a favourable visualisation method to evaluate the subunits of the nail. Little is known about the relation between the properties of nail structures and the clinical characteristics of patients with psoriatic arthritis (PsA).<sup>1</sup>

**Objectives:** To show the relationship between the clinical features and ultrasonographic evaluations of the nail in patients with PsA.

**Methods:** Patients with PsA according to the CASPAR criteria were recruited into the study. All of the hand nails and toenails were examined by grayscale and power Doppler techniques. The relations between the characteristics of the patients and the sonographic findings of the nail structures were assessed. Concerning to patient characteristics, subtypes of PsA, gender, age, height, BMI, working status, smoking, PsA duration, psoriasis duration, history of dactylitis, history of uveitis, number of tender and swollen joints, Maastricht Ankylosing Spondylitis Enthesitis Score, CRP, disease activity, haemoglobin, sacroiliitis, inspectional nail involvement (INI), Nail Psoriasis Severity Index (NAPSI), PASI, HAQ, quality of life, and the biologic treatment were recorded. The nail plate thickness (NPT), number of nails with trilaminar irregularity (NTI), nail bed thickness (NBT), and the doppler activity score (DAS) were recorded as the sonographic nail findings. The Kruskal Wallis analysis, Spearman's correlation, and Man Whitney U tests were used in statistical analysis. p<0.05 was accepted as significant.

**Results:** 63 patients (756 nails) were evaluated. Among the PsA subtypes, 38% of patients were asymmetrical oligoarticular arthritis, 38% were symmetrical polyarthritis, 7.9% distal interphalangeal arthropathy, and 15.8% predominant spondylitis. All of the ultrasonographic nail parameters were independent of the PsA subtypes (p>0.05). The mean of NPT was higher in males and correlated with age, height, and the haemoglobin levels. The NTI score was higher in patients with INI and correlated with the NAPSI score. The mean of NBT was only correlated with the haemoglobin levels. The DAS was higher in workers and correlated with age and the NAPSI score. The other clinical parameters were not associated with the sonographic findings.

**Abstract THU0331 – Table 1.** Relationships between the patients' characteristics and the ultrasonographic parameters\*

US nail parameters	Gender	Worker	INI	Age	Height	NAPSI	Hemoglobin
NPT (mm)	p=0.002			p=0.001 rho:0.396	p=0.021 rho:0.290		p=0.021 rho:0.292
NTI (0-12)			p<0.0001			p<0.0001 rho:0.668	
NBT (mm)							p=0.012 rho:0.316
DAS (0-48)		p=0.042		p=0.001 rho:-0.407		p=0.006 rho:0.344	

(US: ultrasonography, INI: inspectional nail involvement, NAPSI: nail psoriasis severity index, NPT: nail plate thickness, NTI: nails with trilaminar irregularity, NBT: nail bed thickness, DAS: doppler activity score. \*Only parameters which have statistical significant relations by Mann Whitney U test and Spearman's correlation)

**Conclusions:** The ultrasonographic findings of the nail structures were determined in PsA. These findings did not differ among the subtypes of the disease. Although the sonographic nail findings were not associated with the most of the clinical parameters; they had significant relations with some demographics, inspectional nail involvements, and haemoglobin levels in PsA.

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**Disclosure of Interest:** S. Acer: None declared, H. S. Baklacioğlu: None declared, D. Erdem: None declared, M. T. Duruöz Grant/research support from: Abbvie, Consultant for: Novartis, Speakers bureau: Abdi Ibrahim

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**THU0332 FATIGUE REMAINS A DOMINANT SYMPTOM DESPITE TUMOUR NECROSIS FACTOR INHIBITOR THERAPY IN PSORIATIC ARTHRITIS: A POPULATION-BASED COHORT STUDY**

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**Background:** Psoriatic arthritis (PsA) is a chronic inflammatory disorder associated with fatigue, pain and impaired function. Tumour necrosis factor inhibitor (TNFi) therapy fails among half of patients with PsA treated in routine care.

**Objectives:** The objective of this population-based cohort study was to investigate the association of fatigue with disease activity and adherence to therapy in PsA patients receiving their first TNFi.

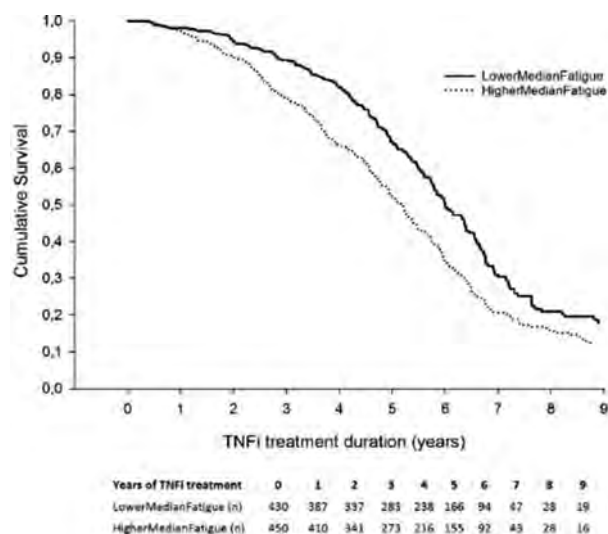
**Methods:** Data on patient characteristics, disease activity and treatment adherence were obtained from the DANBIO register. Information on comorbidities according to the Charlson Comorbidity Index (CCI) and psychiatric comorbidities was obtained through linkage with the Danish National Patient Register. We performed Kaplan-Meier plots and univariate Cox proportional hazard regression analysis. Percentages of patients achieving relevant clinical responses were calculated.

**Results:** From 2006 thru 2016, we identified 880 patients eligible for analyses. Patients with upper median fatigue scores had statistically significantly higher disease activity measures, higher pain and HAQ scores, more comorbidities and current smoking status at baseline compared with patients with lower median fatigue scores (table 1). After treatment initiation the mean VAS fatigue score decreased from 62 mm (SD 25) to 44 mm (SD 30) at six months (p<0.001). Kaplan-Meier curves showed shorter adherence to treatment in patients with higher baseline fatigue scores compared with patients with lower fatigue scores (HR 1.43 [1.2 to 1.7], p<0.001) (figure 1). ACR20, 50 and 70 responses at six months were 49%, 35% and 18% respectively. VASfatigue20, 50 and 70 responses were 57%, 39% and 20%, respectively. The kappa value between ACR20, 50, 70 and VASfatigue responses were 0.37, 0.40 and 0.48 (p<0.001), respectively.

**Abstract THU0332 – Table 1.** Baseline characteristics according to median fatigue stratification

	Lower median VAS fatigue (n=430)	Upper median VAS fatigue (n=450)	p value
Age, years	47.8 (39.4–57.3)	49.0 (40.0–56.1)	p=0.905
Male gender	51%	40%	p<0.001
DAS28-CRP (0–10)	4.0 (3.2–3.7)	4.8 (3.9–5.5)	p<0.001
HAQ score (0–3)	0.75 (0.38–1.13)	1.38 (0.88–1.75)	p<0.001
VAS patient pain (0–100)	45 (29–62)	74 (63–84)	p<0.001
BMI	26.8 (23.7–30.7)	27.7 (24.3–31.2)	p=0.118
Current smoking	28%	36%	p=0.034
Comorbidities (%)	66%	61%	p=0.049
CCI=0	27%	27%	
CCI=1	7%	12%	
CCI≥2			
Depression treated in hospital, n (%)	18 (4.2)	31 (6.8)	p=0.105

Values are the mean and SD except where stated otherwise. Comparisons were assessed by X<sup>2</sup>/Mann-Whitney test. Lower median fatigue <64 mm, higher median fatigue ≥64 mm



**Conclusions:** Fatigue remains a dominating symptom after TNFi treatment, and is associated with higher baseline disease activity, more comorbidities, smoking, higher pain and HAQ scores, and increased risk of TNFi treatment discontinuation in a cohort of Danish patients with PsA. The agreement between ACR responses and VASfatigue responses is weak to moderate suggesting heterogeneity between experienced fatigue and joint inflammation.

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### THU0333 EFFICACY AND SAFETY OF IXEKIZUMAB IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS: THREE YEAR RESULTS FROM A PHASE 3 STUDY (SPIRIT-P1)

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**Background:** Ixekizumab (IXE) is a high affinity monoclonal antibody that selectively targets interleukin-17A. IXE, every 4 (Q4W) or 2 (Q2W) weeks, was superior to placebo (PBO) in improving the signs and symptoms of psoriatic arthritis (PsA) at Week 24 in biologic-naïve patients (pts).

**Objectives:** To determine the efficacy and safety of IXE treatment up to 3 years in biologic-naïve pts with PsA.

**Methods:** In SPIRIT-P1 (NCT01695239), 381 pts entered the extension period (EP; Weeks 24–156). Pts failing to demonstrate  $\geq 20\%$  improvement in both tender and swollen joint counts at Week 32, or any subsequent visit, were discontinued (mandatory discontinuation criteria). Ad-hoc efficacy data are presented for intent-to-treat (ITT) pts initially randomised to IXE at Week 0. Modified non-responder imputation (mNRI; missing data treated as non-response for pts discontinued due to lack of efficacy or adverse events [AEs]; multiple imputation (MI) for all other missing data) was applied to categorical measures. Modified baseline observation carried forward (mBOCF) was applied to continuous efficacy measures. Safety assessments are presented for all pts who entered the EP; baseline was the first IXE dose during the EP.

**Results:** Of the 210 pts initially randomised to IXE at Week 0 (ITT), 125 (60%) pts completed 156 weeks of treatment; 27 pts discontinued due to AEs, and 26 pts met the mandatory discontinuation criteria. Efficacy results are summarised (table 1). Improvements in ACR (American College of Rheumatology) and PASI (Psoriasis Area and Severity Index) responses, resolution in enthesitis and dactylitis, and improvements from baseline HAQ-DI (Health Assessment Questionnaire Disability Index), enthesitis, and dactylitis persisted up to Week 156. Safety

assessments for all pts who entered the EP are summarised (table 2). Frequencies of treatment-emergent AEs (TEAEs) were similar between IXE Q4W and Q2W. The majority of TEAEs were mild or moderate in severity; serious AEs occurred in 47 pts.

Abstract THU0333 – Table 1. Efficacy Overview at Week 156 (ITT Population)

	IXE Q4W (n=107)	IXE Q2W (n=103)
<b>Responder Rates (n/Nx [%]): mNRI</b>		
ACR20	74/107 (69%)	64/103 (62%)
ACR50	55/107 (51%)	58/103 (56%)
ACR70	35/107 (33%)	45/102 (44%)
PASI75 <sup>a</sup>	46/73 (63%)	41/59 (69%)
PASI90 <sup>a</sup>	37/73 (51%)	38/59 (65%)
PASI100 <sup>a</sup>	32/73 (44%)	36/59 (61%)
LEI=0 <sup>b</sup>	32/68 (47%)	23/57 (40%)
LDI-B=0 <sup>c</sup>	23/37 (62%)	17/25 (68%)
<b>Mean Change from Baseline (SD): mBOCF</b>		
HAQ-DI	-0.4 (0.6)	-0.5 (0.6)
LEI <sup>b</sup>	-1.7 (1.8)	-1.7 (1.7)
LDI-B <sup>c</sup>	-51.2 (91.0)	-55.4 (61.3)

LEI=Leeds Enthesitis Index; LDI-B=Leeds Dactylitis Index-Basic; Nx=pts with non-missing data; n=responders. With mNRI, missing data were treated as non-response for pts discontinued due to lack of efficacy or AEs. All other missing data were imputed with MI. With MI analysis, 32 patients were considered ACR20 responders. <sup>a</sup>Pts with psoriatic lesions  $\geq 3\%$  of body surface area at baseline. <sup>b</sup>Pts with LEI >0 at baseline. <sup>c</sup>Pts with LDI-B >0 at baseline.

Abstract THU0333 – Table 2. Safety Outcome Measures (Weeks 24–156)

	Total IXE Q4W (N=191)	Total IXE Q2W (N=190)
TEAEs	146 (76%)	144 (76%)
Serious AEs	28 (15%)	19 (10%)
Serious infections	5 (3%)	1 (<1%)
Discontinued due to AE	16 (8%)	21 (11%)
Death	1* (<1%)	0
Infections	92 (48%)	94 (49%)
Injection-Site Reactions	21 (11%)	23 (12%)
Hypersensitivities	8 (4%)	11 (6%)

n=pts with  $\geq 1$  designated AE. Data presented as n (%). For safety analyses, baseline was defined as the time of first study drug injection during the EP (Weeks 24–156). \*Pt experienced a cerebrocardiovascular accident.

**Conclusions:** In pts treated with IXE, improvements in the signs and symptoms of PsA persisted up to 3 years. No unexpected safety signals were observed, and the safety profile was consistent with previous studies of IXE.

**Disclosure of Interest:** V. Chandran Grant/research support from: Abbvie, Consultant for: Abbvie, Amgen, Celgene, Eli Lilly and Company, Janssen, Novartis, Pfizer, UCB, R. Fleischmann Consultant for: AbbVie, Acea, Amgen, Bristol-Myers Squibb, Eli Lilly and Company, Novartis, Pfizer, Sanofi-Aventis, and UCB, E. Lespessailles Grant/research support from: Novartis, Eli Lilly and Company, Servier, and Amgen, Speakers bureau: Novartis, Eli Lilly and Company, P. Helliwell Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Janssen, Merck, Novartis, and UCB, O. Benichou Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, J. Erickson Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, C. Shuler Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company

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THURSDAY, 14 JUNE 2018

### SLE, Sjögren's and APS – clinical aspects (other than treatment)

#### THU0334 PATTERNS OF ASPIRIN USE IN SLE PREGNANCIES WITHIN A MULTINATIONAL INCEPTION COHORT AND RELATIONSHIP TO PREECLAMPSIA RISK FACTORS

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**Background:** Aspirin reduces the risk of preeclampsia in pregnancies at high risk, and is recommended in pregnant women with  $\geq 1$  risk factors for preeclampsia, including systemic lupus erythematosus (SLE).

**Objectives:** To assess the prevalence of aspirin use in SLE pregnancies within a multinational inception cohort and compare aspirin use among those with and without additional preeclampsia risk factors.

**Methods:** Premenopausal women aged 18–45 enrolled in the Systemic Lupus International Collaborating Clinics (SLICC) Registry (2000–2017) within 15

months of SLE onset were evaluated with yearly visits to update co-morbidities, pregnancy status, and medications. Study visits with a current pregnancy were assessed for aspirin use and preeclampsia risk factors. Aspirin use was compared over time and among those with and without traditional risk factors for preeclampsia (i.e. hypertension, renal disease, diabetes, nulliparity, BMI $\geq$ 35, age  $>$ 40), as well as known disease-specific risk factors (i.e. antiphospholipid antibodies [+aPL], nephritis).

**Results:** We identified 297 women who had 479 pregnancies over the study period. Mean age during pregnancy was 31 (SD 4.9) years and 30% were nulliparous. Half of the pregnancies experienced  $\geq$ 1 traditional preeclampsia risk factors in addition to SLE, while a third had +aPL. We observed aspirin use in 121/475 (25% of pregnancies (95% CI 22,29) versus 22% (95%CI 19,25) of visits before and after pregnancy among the same women. Aspirin use was similar among pregnancies with and without  $\geq$ 1 traditional risk factor for preeclampsia [25% (95%CI 20,31) versus 26% (95%CI 21,32)], while we observed a higher prevalence of aspirin use in those with +aPL (38%, 95% CI 24,55) versus those without (23%, 95% CI 15,34). There was a significant difference in aspirin use based on maternal race/ethnicity, with 67/205 (33%, 95% CI 26,39) aspirin use in Caucasians versus 9/88 (10%, 95% CI 5,18) for black women. Prevalence of aspirin use in pregnancy varied across regions (12% $>$ 37%), and did not increase over time.

**Abstract THU0334 – Table 1.** Prevalence of preeclampsia (PE) risk factors among pregnant SLE visits and prevalence of ASA use among women with and without PE risk factors

Risk factor	Overall prevalence n=475 n (%)	Prevalence of ASA use (%; 95% CI)	
		With risk factor	Without risk factor
Age $>$ 40	14 (3)	2/14 (14%, 4–40)	119/461 (26%, 22–30)
BMI $\geq$ 35	33/437 <sup>o</sup>	8/33 (24%, 13–41)	113/404 (28%, 24–33)
Nulliparous	136/461 <sup>oo</sup>	37/136 (27%, 20–35)	80/325 (25%, 20–30)
Renal disease	83 (17)	17/83 (20%, 13–30)	104/392 (27%, 22–31)
Nephritis	53 (11)	11/53 (21%, 12–23)	109/422 (26%, 22–30)
Hypertension	79 (17)	24/79 (30%, 21–41)	97/396 (24%, 21–29)
Diabetes	2 (0)	0/2 (0%, 0–1)	121/473 (26%, 22–30)
$\geq$ 1 traditional PE risk factor	234 (49)	58/234 (25%, 20–31)	63/241 (26%, 21–32)
aPL +	34/104 <sup>oo</sup>	13/34 (38%, 24–55)	16/70 (23%, 15–34)

**Conclusions:** In this cohort including 479 SLE pregnancies, most pregnant women were not on aspirin and half had preeclampsia risk factors in addition to SLE. It is possible that aspirin was introduced at/or following the study visit when the pregnancy was documented, highlighting the importance of the treating rheumatologist in reviewing aspirin use and initiating it in pregnant SLE women. Our findings suggest black SLE women as a potentially vulnerable group during pregnancy, having the lowest prevalence of aspirin use.

**Disclosure of Interest:** None declared

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#### THU0335 FACTORS ASSOCIATED WITH DEVELOPMENT AND MORTALITY OF PULMONARY HYPERTENSION IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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**Background:** Pulmonary hypertension (PH) is a major cause of death in patients with systemic lupus erythematosus (SLE). In recent years, SLE with PH has become more common in the past few decades, and novel therapies has been developed to improve the prognosis of PH in SLE patients. Therefore, it is necessary to investigate further to identify serological and clinical factors for the development and mortality of PH in SLE patients.

**Objectives:** This study aims to estimate the prevalence of PH in SLE patients and identify the factors associated with the development of and mortality from PH in SLE patients.

**Methods:** We conducted a prospective study of SLE patients with fulfilling the American College of Rheumatology criteria (ACR) in a single tertiary centre from February 1998 to December 2013. PH was defined as a systolic pulmonary

arterial pressure (sPAP)  $\geq$ 30 mmHg at rest on transthoracic echocardiography (TTE). We assessed potential associated factors contributing to the development and mortality of PH in SLE patients using univariate and multivariable logistic regression models.

**Results:** Of 1110 patients with SLE, 48 patients were identified to have PH. Multivariable analysis indicated that pleuritis or pericarditis (odds ratio (OR)=4.62, 95% confidence interval (CI)=2.46 to 8.70, p<0.01), anti-RNP antibody (OR=2.42, 95% CI=1.21 to 4.82, p=0.01), interstitial lung disease (ILD) (OR=8.34, 95% CI=2.21 to 31.54, p<0.01), and cerebro-cardiovascular disease (OR=13.37, 95% CI=3.56 to 50.21, p<0.01) were independently associated with the development of PH in SLE. Subgroup analysis among patients with PH demonstrated that there were no statistically significant factors associated with PH mortality in SLE.

**Abstract THU0335 – Table 1.** Factors associated with pulmonary hypertension development in systemic lupus erythematosus

	Univariate		Multivariable	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Sex: female	1.92 (0.46 to 8.07)	0.37	4.44 (0.54 to 36.76)	0.17
Age at diagnosis of SLE	0.99 (0.97 to 1.02)	0.59	0.99 (0.96 to 1.02)	0.49
Disease duration*	1.00 (1.00 to 1.00)	0.87	1.00 (0.99 to 1.00)	0.48
Ever smoker	0.52 (0.18 to 1.47)	0.23		
Pleuritis or pericarditis	4.62 (2.55 to 8.29)	<0.01	4.62 (2.46 to 8.70)	<0.01
Raynaud phenomenon	1.48 (0.79 to 2.77)	0.22		
Anti-Sm	1.65 (0.81 to 3.39)	0.17	0.89 (0.38 to 2.11)	0.79
Anti-RNP	2.48 (1.36 to 4.51)	<0.01	2.42 (1.21 to 4.82)	0.01
ACL	1.10 (0.55 to 2.19)	0.79		
LAC	0.83 (0.32 to 2.12)	0.69		
SLEDAI score at enrollment	1.03 (0.96 to 1.09)	0.42		
ILD (pulmonary, pleural fibrosis)	8.34 (2.89 to 31.69)	<0.01	8.34 (2.21 to 31.54)	<0.01
Cerebro-cardiovascular disease	13.37 (3.56 to 50.21)	<0.01	13.37 (3.56 to 50.21)	<0.01

OR: odds ratio; CI: confidence interval; SLE: systemic lupus erythematosus; Anti-Sm: Anti-Smith; Anti-RNP: Anti-ribonucleoprotein; ILD: interstitial lung disease.

\*From diagnosis of SLE to last follow-up.

**Conclusions:** The prevalence of PH was 4.3% in our cohort. There were significant associations with pleuritis or pericarditis, ILD, cerebro-cardiovascular disease, and anti-RNP antibody in SLE, which may contribute to the development of PH. However, there were no statistically significant factors correlating PH mortality in SLE.

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#### THU0336 PREDICTORS OF SUBCLINICAL CAROTID ATHEROMATOSIS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: RELEVANCE OF ACTIVITY, DAMAGE AND SEVERITY INDEXES

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**Background:** The prevalence of subclinical atheromatosis in patients with systemic lupus erythematosus (SLE) is double that observed in the general population. The mechanisms of this accelerated atherosclerosis are unknown, but they may include factors related to the disease, as well as the interaction of these with classic cardiovascular risk factors (CVRF).

**Objectives:** We analyse wich predictors of subclinical carotid atheromatosis exist in a large series of patients with SLE, with special emphasis on the role of the activity, damage and severity indexes.

**Methods:** Cross-sectional study that included 276 patients with SLE. Lipid serum levels, autoimmunity profile and the activity (SLEDAI), severity (Katz) and damage (SLICC) indexes were determined. The thickness of the carotid intima-media (cIMT) and the presence of plaques were determined by radiofrequency US. The cardiovascular risk was estimated through SCORE. Multivariate regression analysis was performed to assess the relationship of the indexes with CVRF, cIMT and



carotid plaque. Predictive capacity for the presence of plaque by comparing the AUC of the different models was performed through the DeLong method

**Results:** 106 (38%), 85 (31%), 47 (17%) and 21 (8%) patients showed respectively SLEDAI null, low, moderate and high, 197 (71%) had a SLICC >1 and 104 (38%) a Katz>3. In 36% (99) of the patients carotid plaques were detected, with an average cIMT of 0.631±0.108 mm. SLEDAI showed a positive relationship with hypertension; the Katz with hypertension and dyslipidemia; and the SLICC with these and also with age, body mass index and abdominal waist. The relationship of the latter with the CVRF was maintained after subtracting its items related to cardiovascular risk. SLICC was univariately related to plaque (OR 1.29 [95% CI 1.13–1.48], p=0.000) and a SLICC >1 showed a tendency to be associated with a higher cIMT (beta coefficient 0.03 [95% CI 0.00–0.06], p=0.053). No univariate relationships were found between Katz or SLEDAI with subclinical atherosclerosis. The relationship of SLICC with plaque was maintained after adjusting for age, sex and CVRF (OR 1.19 [95% CI 1.00–1.42], p=0.047). Similarly, SLICC (even without its vascular damage items) (beta coefficient 0.26 [95% CI 0.12–0.41], p=0.000), but not Katz and SLEDAI, correlated significantly with SCORE. The predictive capacity of SCORE for the presence of plaque was AUC 0.788 (95% CI 0.735–0.842). Analogously SLICC showed an AUC 0.659 (95% CI 0.594–0.724) for plaque; the AUC of Katz and SLEDAI did not reach statistical significance. The AUC of the SCORE +SLICC versus SCORE did not show statistically significant differences (p=0.31). The statistical significance of the reclassification indexes were net reclassification index p=0.61, and integrated discrimination improvement p=0.01.

**Conclusions:** SLICC is independently related to the presence of plaque. SLE activity, severity and damage indexes are related to CVRF but they have little impact on the predictive capacity of SCORE for the presence of carotid plaque.

**Disclosure of Interest:** None declared

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### THU0337 NONBACTERIAL THROMBOTIC ENDOCARDITIS (NBTE) IN SLE: PREVALENCE, CLINICAL CHARACTERISTICS AND SEROLOGICAL PROFILE

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**Background:** SLE is characterised by excessive production of various autoantibodies and correlation of these antibodies with organ involvement may help to evaluate disease severity and long term prognosis. NBTE is a rare cardiac manifestation of SLE with prevalence rate varying from 6%–11%. Many, but no all, studies have shown association of NBTE with anti phospholipid antibodies, but, except this association, data regarding clinical, laboratory and serological characteristics of NBTE is sketchy. We designed this study to evaluate profile of patients having NBTE in SLE.

**Objectives:** 1. To study the prevalence of NBTE in SLE patients.

2. To study association of NBTE with clinical and laboratory characteristics and serological profile.

**Methods:** All consecutive SLE inpatients and outpatients attending the department of Rheumatology from September 2015 to December 2017 were enrolled. Patients subjected to 2D Echo were included and their demographic, clinical, laboratory and serological profile were recorded. Serological profile was studied with Blue diver kit which is an immunodot blot assay measuring autoantibodies against 25 ENA. Anti cardiolipin and anti beta 2 glycoprotein antibody were tested by ELISA. Study was approved by an independent ethics committee [ECR/282].

**Results:** Total number of patients enrolled in study were 355 out of which 213 had undergone 2DEcho. NBTE was found in 33 (15.49%) patients. Among all autoantibodies studied, we found that the presence of **anti-Nucleosome antibody, LAC, ACL and B2GP1** were significantly associated with NBTE (p<0.05). **Myocarditis, valvular lesions and Pulmonary Hypertension** were more common in NBTE group (p value: 0.012, <0.0001 and 0.013 respectively).

We also noticed that there is a statistically significant association between presence of NBTE with **APLA syndrome** and **Thrombotic events** (p value<0.0001 and 0.005 respectively).

Tab.1 Significant Serological association of SLE patients with NBTE.

Antibodies	SLE With NBTE-33 (15.49%)	SLE without NBTE- 180	P value
Anti-nucleosome	27 (81.8)	32 (17.7)	<0.0001
LAC	16/30 (53.3)	31/149 (20.8)	0.0002
ACL (Ig M and IgG)	9/30 <sup>ns</sup>	13/128 (10.1)	0.004
B2GP-1(Ig M and IgG)	6/22 <sup>ns</sup>	9/103 (8.73)	0.033

APLA profile was available in 30 patients of NBTE and 147 patients not having NBTE. Out of this, positivity for APLA antibodies were seen in 17 (56.6%) and 36 (24.4%) patients respectively [p:0.005]. 82.3% patients with Anti phospholipid antibodies had APLA syndrome in NBTE group while in NBTE group 48.5%

patients having Anti phospholipid antibodies had APLA syndrome. Thus, presence of NBTE increased the possibility of developing APLA syndrome in patients having positive serology for anti phospholipid antibodies

Tab.2 Significant Clinical and laboratory characteristic of SLE patients with NBTE.

Organ involvement	SLE with NBTE- 33	SLE without NBTE- 180	p- value
Myocarditis	11	27	0.012
Valvulopathy	10	4	<0.0001
PAH	9	21	0.013
Thrombotic events	8	16	0.005
APLA syndrome	14	17	<0.0001

**Conclusions:** Presence of Anti nucleosome antibody, LAC, Anti cardiolipin and anti beta 2 glycoprotein antibodies may predict presence or future development of NBTE in SLE patients. Presence of NBTE increases probability of developing APLA syndrome in patients with anti phospholipid antibodies. We have found association of NBTE with myocarditis, valvulopathy and PAH and thus propose that such patients with NBTE should be treated early and aggressively.

**Disclosure of Interest:** None declared

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### THU0338 OUTCOME OF STROKE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A NESTED CASE-CONTROL STUDY

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**Objectives:** To evaluate the outcome of stroke in patients with systemic lupus erythematosus (SLE) in comparison with matched non-SLE patients.

**Methods:** Patients who fulfilled ≥4 ACR criteria for SLE and had a history of stroke were identified from our SLE database. The outcome of stroke in these patients was evaluated retrospectively and compared with a group of randomly selected age/gender-matched non-SLE patients (in a 1:3 ratio) admitted to our stroke unit within the same time period. The type and extent of stroke, atherosclerotic risk factors (hypertension, smoking, diabetes mellitus, dyslipidemia, atrial fibrillation, valvular lesions) and previous stroke were compared between the two groups of patients. The primary outcome of interest was the 90 day functional outcome as assessed by the modified Rankin scale (mRS) (score 0–2: functional independence; score 3–6: functional dependence). Secondary outcomes included all-cause mortality, 30 day stroke mortality, stroke recurrence and stroke complications. Factors independently associated with a poor functional outcome was studied by logistic regression.

**Results:** A total of 40 SLE patients (age 53.7±11.5, 88% women) with stroke were identified from our database (stroke prevalence 0.39/100 patient-year). A control group of 120 non-SLE patients (age 52.8±14.8, 87.5% women) with stroke were randomly selected from our stroke database. All were ethnic Chinese. The prevalence of atherosclerotic risk factors was similar between the two groups, except SLE patients had a higher atherogenic index (Log serum [triglyceride/HDL-cholesterol]) (1.51±0.47 vs 1.32±0.31; p=0.005.) In SLE patients, the median time to stroke since diagnosis was 24 months. Ischaemic stroke was more common in SLE than non-SLE patients (90% vs 63%; p=0.001). Among patients with ischaemic stroke, SLE patients had more extensive infarction than controls on CAT scan (multiple infarct 65.7% vs 18.7%; p<0.001). The 90 day mRS score was significantly higher in SLE patients than controls (1.70±1.97 vs 0.88±1.36; p=0.004). Significantly more SLE patients had functional dependence (mRS score 3–6) at 90 days post-stroke than controls (32.5 vs 8.3%; p<0.001). Logistic regression showed that SLE was an independent risk factor for a poor stroke outcome after adjustment for age, sex, history of stroke, various atherosclerotic risk factors and the type of stroke (ischaemic vs haemorrhagic) (OR 12.2 [2.97–49.9]). Subgroup analysis of patients with ischaemic stroke showed that SLE was also independently associated with a poorer functional outcome after adjustment for the same confounding covariates and the extent of stroke (solitary vs multiple infarcts) (OR 12.4 [1.02–150]; p=0.048). There was no significant difference in the 30 day stroke mortality between SLE and non-SLE patients (5% vs 2.5%; p=0.43). However, SLE patients had a higher incidence of post-stroke epilepsy than controls (22.5% vs 3.3%; p=0.001). Upon a mean follow-up time of 7.5±5.2 years, SLE patients had a lower stroke recurrence free survival (59.5% vs 85.7%; p<0.001) and a higher rate of all-cause mortality (34.6% vs 15.1%; p<0.001).

**Conclusions:** Stroke in SLE patients is more likely to be ischaemic in origin and more extensive than matched controls. Short-term functional outcome of stroke is poorer in SLE patients. Over 7.5 years, stroke recurrence, post-stroke epilepsy and all-cause mortality is significantly more frequent in SLE than non-SLE patients.

**Disclosure of Interest:** None declared

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THU0339 **IMPACT OF CAROTID ULTRASOUND ON THE CARDIOVASCULAR RISK STRATIFICATION OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS**

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**Background:** Autoimmune rheumatic diseases, including systemic lupus erythematosus (SLE), are associated with a significant increase in cardiovascular morbidity and mortality. The risk stratification instruments used in the general population underestimate the true risk of events in these patients. Carotid ultrasonography, through the detection of subclinical atherosclerosis, is a powerful predictor of future cardiovascular events. The available evidence, endorsed in the official Prevention Guidelines, supports the use of this technique for the adequate identification of those patients of "very high risk", candidates for preventive interventions of greater intensity.

**Objectives:** To analyse the cardiovascular risk profile, the prevalence of subclinical atherosclerosis detected by carotid echography, and its implications in the prevention strategy in patients with SLE.

**Methods:** A cross-sectional study of 276 patients diagnosed with SLE. The clinical characteristics and risk profile were analysed by SCORE. The presence of plaques and intima-media thickness (cIMT) was determined by carotid ultrasound and the cIMT percentiles were calculated according to tables adjusted for age and sex. Differences in risk stratification before and after carotid ultrasonography were determined by univariate regression analysis. The therapeutic implications after reclassification were evaluated according to the 2016 European Prevention Guides.

**Results:** Risk stratification using SCORE was: low in 187 (67%), moderate in 73 (26%), and high or very high in 16 (6%). The median percentiles for cIMT were not statistically different from the p50 of healthy general population ( $p=0.54$ ). Ultrasound showed the presence of plaque or cIMT  $>p75$  or cIMT  $>0.90$  mm in 60% (166) of the patients evaluated. The presence of this finding by risk categories was: low 102/187 (55%), moderate 55/73 (75%), high 7/9 (78%) and very high 6/7 (86%). According to the published guidelines, the detection of plaque carried out the re-stratification to a very high risk in 35% of patients. These patients whose reclassification was achieved showed a higher SLICC index compared to those that did not change of category (mean difference 0.9 points,  $p=0.000$ ). This difference remained statistically significant when the items related to cardiovascular risk that SLICC possesses were eliminated. SLEDAI and Katz were not statistically different between both groups. The SCORE of patients who were reclassified was also statistically higher (mean difference 0.7 points,  $p=0.021$ ). Ninety percent of patients were re-classified to a very high risk had out-of-target LDL cholesterol levels for their new risk category (LDL  $<70$  mg/dl). Similarly, only 46% of them were on statin therapy. Therefore, the indication or intensification of lipid-lowering treatment was followed only in 30% of the total evaluated.

**Conclusions:** The reclassification of cardiovascular risk through the use of ultrasonography in SLE occurs in one third of patients. Our data suggests that this may be consequence of the damage produced by the disease. One in three candidates needed preventive interventions of greater intensity that had not been taken.

**Disclosure of Interest:** None declared

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THU0340 **PROLONGED REMISSION IS ASSOCIATED WITH A REDUCED RISK OF CARDIOVASCULAR DISEASE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS**

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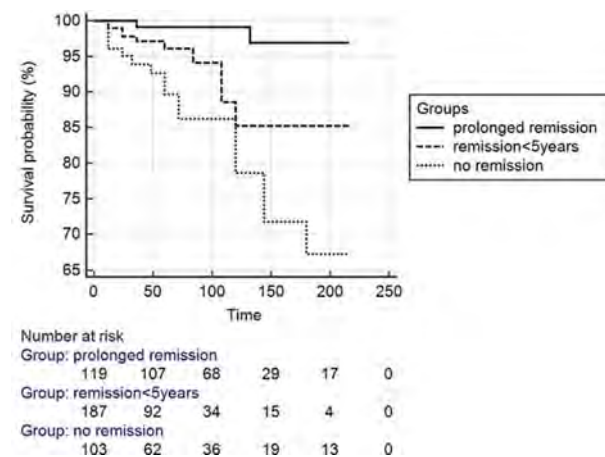
**Background:** Cardiovascular disease (CVD) has emerged as one of the most important causes of mortality in systemic lupus erythematosus (SLE)<sup>1</sup>. In previous studies, disease activity, as assessed by SLEDAI (at the first visit or as mean annual value registered during follow-up), did not result to have any predictive role on the subsequent occurrence of CVD<sup>2-3</sup>.

**Objectives:** To investigate the relationship between prolonged remission and the occurrence of a subsequent first CV event in patients with SLE.

**Methods:** Out of 452 patients consecutively admitted to two tertiary Italian centres from November 1st 2000 to December 31st 2016, the 409 patients, who, at admission, had not experienced any CV event, had not received any anticoagulation therapy and had been visited at least biannually during follow-up, were considered for the present study. Prolonged remission was defined as a 5 year consecutive period of no disease activity based on SLEDAI-2K<sup>3</sup>. Patients with

prolonged remission were furtherly subdivided according to Zen et al<sup>4</sup> into 3 groups: complete remission, clinical off-corticosteroids remission (offCR), clinical on-corticosteroids remission (onCR). Kaplan-Meier curves and the log-rank test were used to analyse differences in event-free survival between groups. Cox regression analysis was used to investigate disease and therapeutic features associated with the development of a first CV event.

**Results:** During 72 months median follow-up time, 29 (7.0%) CV events occurred (two events in patients who had undergone prolonged remission). Out of the 409 patients, 28 patients (6.8%) achieved a prolonged complete remission, 13 (3.1%) prolonged clinical offCR and 64 (15.5%) prolonged clinical onCR. Kaplan-Meier analysis revealed a greater overall CV event-free rate in patients achieving a prolonged remission compared to those in remission but for less than 5 years and patients not in remission (logrank test  $\chi^2=19.82$ ;  $p=0.0001$ ; figure 1). However, at Kaplan-Meier analysis, CV outcome was similar among patients in prolonged remission, irrespective of the type of remission achieved ( $p>0.05$ ). At multivariate analysis, treatment with hydroxychloroquine for more than 5 years and prolonged remission were protective (HR 0.38; 95% CI 0.16–0.90; HR 0.08, 95% CI 0.01–0.53) while antiphospholipid syndrome increased the risk of a first CV event (HR 3.80; 95% CI 1.68–8.61). No differences were found between patients treated or not with aspirin. Nevertheless, among patients from Rome cohort, aspirin was only prescribed to patients with high traditional CV risk score.



**Conclusions:** A prolonged remission, whichever the subtype, is associated with a better CV outcome and should be considered as a treat-to-target goal in the CV risk management of the lupus patient.

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**Disclosure of Interest:** None declared

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THU0341 **LOW VITAMIN D IS ASSOCIATED WITH THROMBOSIS IN SYSTEMIC LUPUS ERYTHEMATOSUS**

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**Background:** Low vitamin D is common in systemic lupus erythematosus (SLE). It is also found in antiphospholipid syndrome. Vitamin D has effects on tissue factor, PAI-1, thrombomodulin and platelet aggregation that suggest it has an anti-thrombotic role. We asked whether low vitamin D was associated with thrombosis in SLE, adjusting for lupus anticoagulant.

**Objectives:** We asked whether low vitamin D was associated with thrombosis in SLE, adjusting for lupus anticoagulant.

**Methods:** A total of 1,392 SLE patients were included in the analysis. At the first visit when vitamin D was measured, 76.7% had levels of 25-hydroxyvitamin D  $<40$  ng/mL. The SLE patients were: 92% female, mean age 42.9 years, and ethnicity 50% Caucasian, 41% African American. 27% patients had a history of thrombosis; 7% stroke, 4% MI and 14% DVT.

**Results:** Vitamin D, measured either as a continuous variable or as "low" ( $<40$  ng/mL) vs. normal, was associated with any thrombosis and with DVT.

**Abstract THU0341 – Table 1.** Associations of First Vitamin D Measurement with Thrombosis

	Positive for Thrombotic Event		No Thrombotic Event		P-value
	Mean (SD)	N (%)	Mean (SD)	N (%)	
<b>Any Thrombotic Event</b>					
Vitamin D (ng/ml) (Mean/SD)	27.6 (15.1)		30.6 (14.6)		0.0008
Vitamin D<40 ng/ml (N%)		299 (80.4)		759 (75.4)	0.064
<b>Stroke</b>					
Vitamin D (ng/ml) (Mean/SD)	28.9 (15.2)		29.9 (14.7)		0.5408
Vitamin D<40 ng/ml (N%)		79 (75.2)		988 (76.9)	0.7914
<b>Myocardial Infarction (MI)</b>					
Vitamin D (ng/ml) (Mean/SD)	30.2 (16.9)		29.8 (14.7)		0.883
Vitamin D<40 ng/ml (N%)		35(70)		1032(77)	0.3258
<b>DVT</b>					
Vitamin D (ng/ml) (Mean/SD)	25.9 (13.4)		30.4 (14.9)		<0.0001
Vitamin D<40 ng/ml (N%)		171 (87.2)		895(75)	0.0002

We next adjusted for race, age, sex and lupus anticoagulant. Low vitamin D remained associated with DVT.

**Abstract THU0341 – Table 2.** Summary of Adjusted Odds Ratio for Low Vitamin D (<40 ng/ml)

Dependent Variables	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Any Thrombosis	1.33 (0.99,1.79)	1.36 (0.99,1.86)
Stroke	0.91 (0.58,1.45)	0.92 (0.57,1.48)
MI	0.7 (0.38,1.29)	0.8 (0.42,1.53)
DVT	2.28 (1.47,3.54)	2.31 (1.47,3.65)

We next looked prospectively: this analysis excluded thrombotic events before the first vitamin D measurement. It allowed for vitamin D to be a time-varying variable, as replacement therapy was given if it was low. After adjustment for race, age and sex, the adjusted hazard ratio remained significant for any thrombosis: 1.75 (1.04,2.92).

**Conclusions:** Low vitamin D was significantly associated with any thrombosis and with DVT (even after adjustment for lupus anticoagulant). In prospective models it remained significantly associated with any thrombosis. As supplementation with vitamin D was proven to reduce thrombosis in an oncology randomised clinical trial, vitamin D replacement should become routine in SLE patients at risk for thrombosis.

**Disclosure of Interest:** None declared

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### THU0342 THE LUPUS FOUNDATION OF AMERICA RAPID EVALUATION OF ACTIVITY IN LUPUS (LFA-REAL) PROVIDES A SIMPLE BUT RELIABLE MEASUREMENT OF SLE DISEASE ACTIVITY

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**Background:** Clinical trial evaluations in SLE are problematic, in part due to glossary-based outcome measures with imperfect granular relevance. Visual analogue scales (VAS) allow real world scaling of disease severity, but may be inconsistent when used over time or by different raters. The SELENA SLEDAI Physician's Global Assessment (SSPGA) is a VAS with severity anchors and instructions to promote consistent, transitional scoring. The Rapid Evaluation of Activity in Lupus (LFA-REAL<sup>TM</sup>) extends the SSPGA by scoring each active feature separately, allowing additive impact of each manifestation within organs, and a global score with meaningful weighting of multiple symptoms. It differs from previous constructions that combine PGA with component scoring<sup>1</sup> by incorporating all manifestations of lupus and refining scaling of the SSPGA<sup>2</sup>.

**Objectives:** To compare performance of SSPGA and LFA-REAL<sup>TM</sup> to accepted SLE trial outcome measures during an ongoing trial in SLE, using a strict protocol for transitional scoring.

**Methods:** Disease activity, SLEDAI, BILAG 2004 CLASI, SSPGA and LFA-REAL<sup>TM</sup> was evaluated at monthly visits in an investigator-initiated, double-blind, placebo controlled study of abatacept (trial results pending). Validation of total scores and change in SSPGA and REAL vs SLEDAI and BILAG were examined by Spearman Correlation. ROC curve analysis compared changes in SSPGA and LFA-REAL<sup>TM</sup> to the dichotomous SLE trial endpoints, SRI-4 and BICLA.

**Results:** 50 adult SLE patients, 47 female, were assessed at 528 visits. Changes in disease activity compared to screening were examined in 478 visit pairs. Total SSPGA and REAL scores strongly correlated to each other (r=0.932), as well as to total SLEDAI and BILAG [SSPGA: r=0.742 (SLEDAI), r=0.776 (BILAG); REAL:

r=0.776 (SLEDAI), r=0.813 (BILAG); all p<0.0001]. Changes in SSPGA and LFA-REAL<sup>TM</sup> at each visit compared to screening correlated to each other (r=0.857) as well as to changes in SLEDAI and BILAG (all p<0.0001) (table 1). Changes in SSPGA and LFA-REAL<sup>TM</sup> were very strongly related to the dichotomous SRI-4 and BICLA endpoints by ROC analysis (all p<0.0001) (table 2). LFA-REAL<sup>TM</sup> musculoskeletal correlated to BILAG musculoskeletal, SLEDAI arthritis, and tender and swollen joint counts (r=0.842, 0.817, 0.634 and 0.784 respectively, all p<0.0001). LFA-REAL<sup>TM</sup> mucocutaneous also correlated to BILAG mucocutaneous, the sum of SLEDAI mucocutaneous features as well as CLASI activity (r=0.826, 0.798 and 0.789 respectively, all p<0.0001).

**Abstract THU0342 – Table 1.** Change in LFA-REAL<sup>TM</sup> and SSPGA in relation to change in SLEDAI and BILAG.

	ΔSLEDAI	ΔBILAG
ΔLFA-REAL <sup>TM</sup>	0.701	0.700
ΔSSPGA	0.681	0.624

**Abstract THU0342 – Table 2.** AUC of change in LFA-REAL<sup>TM</sup> and SSPGA in relation to SRI-4 and BICLA.

	SRI-4	BICLA
ΔLFA-REAL <sup>TM</sup>	0.876	0.852
ΔSSPGA	0.895	0.913

**Conclusions:** Both the SSPGA and LFA-REAL<sup>TM</sup> are reliable surrogates of commonly used endpoints in SLE trials. Both instruments are easy to score and understand, and could be employed as continuous or dichotomous endpoints. The LFA-REAL<sup>TM</sup> allows individualised scoring at the symptom or organ level, and each symptom contributes its exact severity to a global score. The simplicity of PGA scoring is accompanied by gains in versatility.

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**Disclosure of Interest:** None declared

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### THU0343 HOW PATIENTS ABILITY BELIEFS ABOUT MATH MATTER TO SLE PATIENTS DISEASE

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**Background:** Systemic lupus erythematosus (SLE) is a heterogeneous disease with high morbidity and mortality; requiring complex treatment plans which can be daunting especially to SLE patients with neuropsychiatric deficits. Numeracy is the "ability to use and understand numbers in daily life" and a key component for effective shared-decision making between physician and patient to ensure the best patient outcomes. Numeracy skills are needed for decisions about health care risk stratification when understanding treatments, understanding potential harm and benefits of therapy and for counting pills and taking medications as prescribed.

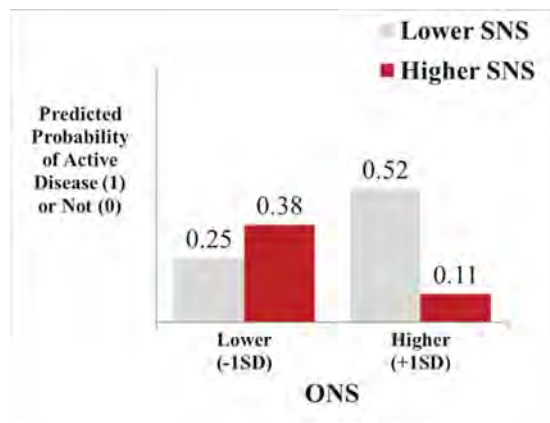
**Objectives:** As there is a lack of information within the lupus patient population, this proposal explores the relationship between patients' numeric ability (both actual and perceived ability) and clinical outcomes fulfilling a gap in our current knowledge of how to support physician communication with patients to ensure patient understanding.

**Methods:** Patients>18 recruited from IRB approved The Ohio State University Lupus, Vasculitis, Glomerulonephritis Registry. 112 patients had finished subjective numeracy (SNS) which measures patients' perception of their math ability, objective numeracy (ONS) which measures patients' actual math ability. We conducted regression analyses with ONS, SNS, and demographics as predictors of disease activity (measured by SLEDAI). We used backwards-stepwise regression, removing nonsignificant variables one at a time from the model.

**Results:** Logistic regression analysis revealed a significant interaction between ONS and SNS in predicting whether patients had the active disease or not (interaction b(SE)=-0.70 (0.33), p=0.03; ONS b(SE)=-0.13 (0.30), p=0.68; SNS b(SE)=-0.40 (0.32), p=0.21). Patients higher in both numeric competencies were least likely to have the active disease. Specifically, among those higher in ONS



(+1 SD), the predicted probability of having the active disease was 11% vs. 52% for those higher vs. lower in SNS ( $\pm 1$  SD), respectively. In comparison, among those lower in ONS ( $-1$  SD), the likelihood of active disease was 38% vs 25% for those higher vs. lower in SNS, respectively. Thus, among patients with greater math abilities, having greater beliefs in one's abilities appeared beneficial; however, among patients with lower math abilities, greater ability beliefs appeared harmful.



**Conclusions:** Patients with greater math ability, coupled with greater beliefs in one's numeric ability, were least likely to have the active disease. This is consistent with psychological theory about actual math ability and perceived math ability as an outcome predictor. Patients that are overconfident and more active in their health and numeric tasks may make decisions that lead them to worse outcomes. The SNS and ONS may be an efficient screening tool to identify high risk SLE patients that may require extra health care needs.

**Disclosure of Interest:** None declared

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#### THU0344 ASSESSMENT OF THE PSYCHOMETRIC PROPERTIES OF PATIENT-REPORTED OUTCOMES OF DEPRESSION IN SLE

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**Background:** Mood disorders, including depression, are amongst the most common manifestations of neuro-psychiatric SLE. Currently, the screening and diagnosis for depression in ambulatory settings are delayed and often missed due to the lack of standardised valid questionnaires for assessing depression in patients with SLE.

**Objectives:** This study aims to: 1) Determine the prevalence of depression in SLE patients using the Centre for Epidemiological Studies-Depression Scale [CES-D] and Hospital Anxiety and Depression Scale [HADS] questionnaires. 2) Study the criterion validity and interpretability of CES-D and HADS, and 3) evaluate their diagnostic accuracy when compared to the assessment of an independent psychiatric assessment using the Mini-International Neuropsychiatric Interview (MINI), based on the DSM-5, as the gold standard.

**Methods:** A cross-sectional study of consecutive consenting SLE patients (n=227), aged 18–65 and attending the Toronto Lupus Clinic between June 2017–September 2017, was performed. Participants were screened for depression using the CES-D and HADS, and underwent the MINI on the same date of their clinic visit. Conventional cut-off scores were used to indicate the prevalence of depression: CES-D  $\geq 16$  and HADS-D  $\geq 8$ . Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were evaluated against the MINI. Receiver operator characteristic (ROC) curves and the Youden Index were utilised to determine the optimal cut-off scores for CES-D and HADS-D.

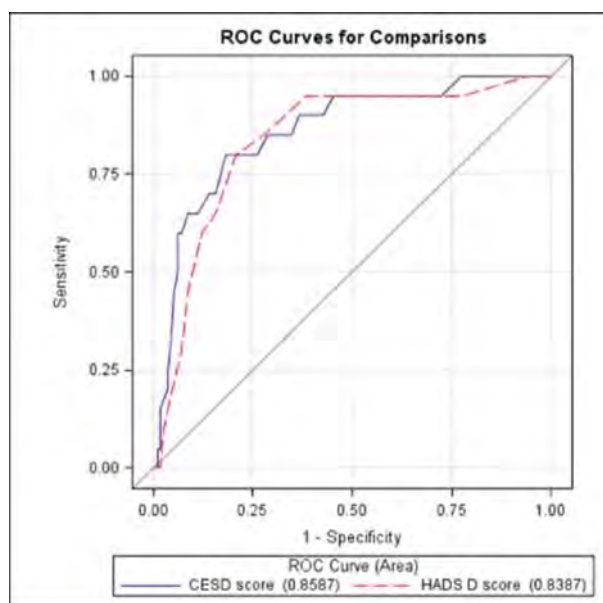
**Results:** Among 227 patients, the prevalence of depression ranged from 27.8% (HADS-D) to 46.3% (CES-D). ROC curves showed that the CES-D (AUC 0.86, 95% CI: 0.78–0.95) slightly outperformed HADS-D (AUC 0.84, 95% CI: 0.75–0.93), when compared to the MINI. The sensitivity, specificity, PPV, and NPV for CES-D at the optimal cut-off of 26 was 80%, 82%, 43%, and 96%, respectively. The Youden index exhibited optimal cut-offs for CES-D at 26 and HADS-D at 8 that optimised their sensitivity and specificity as screening metrics for depression in SLE patients. The performance of the CES-D and HADS-D at various cut-offs are displayed in table 1 below.

**Abstract THU0344 – Table 1.** Cut-offs to predict depression by Youden Index

Cutoffs	Sensitivity	Specificity	PPV	NPV
<b>CES-D</b>				
26*	0.80	0.82	0.43	0.96
24	0.80	0.77	0.37	0.96
21†	0.85	0.71	0.34	0.97
16†	0.95	0.55	0.27	0.98
<b>HADS-D</b>				
8*†	0.80	0.79	0.40	0.96
7	0.85	0.72	0.35	0.97
6	0.95	0.62	0.30	0.99

\*Optimal cutoff as determined by the Youden Index

†Conventional cutoffs found in literature



**Abstract THU0344 – Figure 1.** ROC curves for comparisons

**Conclusions:** This study assessed the criterion validity and interpretability of patient-reported outcome tools HADS, and CES-D for depression screening in SLE patients. Compared to the gold standard, CES-D outperformed HADS-D. These results suggest that SLE-specific cut-offs may improve diagnostic accuracy of current screening metrics in lupus.

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**Disclosure of Interest:** None declared

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#### THU0345 SENSITIVITY AND SPECIFICITY OF ANTIBODIES AGAINST CARBAMYLATED PROTEINS IN A MONOCENTRIC COHORT OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND RHEUMATOID ARTHRITIS

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**Background:** Systemic lupus erythematosus (SLE) is a chronic systemic autoimmune disease characterised by numerous organ involvement. In SLE, autoantibody development against nucleic acids and their binding proteins plays an important role in disease pathogenesis.

**Objectives:** Purpose of this study is the determination of the diagnostic value of anti-carbamyl antibody in patients with Systemic Lupus Erythematosus and rheumatoid arthritis and the relationship with disease prognosis.

**Methods:** Fifty-seven SLE patients (F/M 50/7; median age 40.9 $\pm$ 13.7; median disease duration 2 years) were included in the study according to the 2012 SLICC SLE diagnostic criteria. 46 RA patients (F/M 38/8, median age 54.2 $\pm$ 12.4 years,

the median duration of disease 2 years) selected according to 2010 ACR/EULAR diagnostic criteria were included. 30 healthy control groups were selected. Anti carP antibody Anti-carbamylated Protein Human anti-carbamylated Protein Antibody (ACP-Ab) ELISA Kit (SunRedBio, China) was used for measurement of antibodies against carbamylated proteins.

**Results:** The study population consisted of 133 subjects, 30 controls, 57 SLEs and 46 RAs. The mean age of SLE patients was lower than that of RA patients. (40.9±13.7 versus 54.2±12.4;  $p<0.001$ ). The proportion of active smokers was found to be higher in RA patients compared to SLE patients (19.6% versus 5.3%,  $p=0.005$ ). The frequency of anti carP antibody positivity was 3.3% in the healthy control group. In contrast, the frequency of anti carP antibody positivity was found as high as 17.4% in patients with RA. ( $p<0.001$ ). And this frequency was 54.4% in the SLE patient group ( $p<0.001$ ). Anti carP antibody predicted SLE patients with 54.4% sensitivity and 96.7% specificity compared to the healthy control group. (AUC: 0.755,  $p<0.001$ ) Anti carP antibody predicted RA patients with 17.4% sensitivity and 96.7% specificity compared to the healthy control group (AUC: 0.570,  $p=0.032$ ). Anti carP antibody predicted SLE patients with 54.5% sensitivity and 82.6% specificity compared to healthy RA group (AUC: 0.685,  $p<0.001$ ). AnticarP antibodies were found to be positive in all of the SLE patient groups with anti-CCP positivity. There was no significant difference in terms of organ involvement between anti-carP antibody positive or negative SLE patients. Anti-carP antibody positivity was assessed by ROC Curve analysis for the prediction of diagnostic performance in SLE patients compared to RA patients. Accordingly, Anti carP antibody positivity, ANA positivity, were found to have similar diagnostic performance. (AUC: 0.639)

**Abstract THU0345 – Table 1.** Anti carbamylated protein antibody positivity distribution across groups

Variables	control n=30	SLE n=57	RA n=46	p
Anti carP antibody				
Negative	29(96.7)	26(45.6)	38(82.6)	$<0.001$
Positive	1(3.3)	31(54.4)	8(17.4)	

Categorical variables were expressed as number (%) (carP:carbamylated protein SLE:systemic lupus erythematosus RA: rheumatoid arthritis)

**Conclusions:** Antibody positivity was found to be 54.4% in SLE patient group. It is significantly higher in SLE compared to healthy control and RA patient group. In the SLE group, it is still a more significant diagnostic prognostic than the healthy control and RA group. Both SLE and RA patients have significant sensitivity and specificity compared to the healthy control group.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.4882

#### THU0346 DETERMINANTS OF SONOGRAPHIC GLANDULAR DAMAGE IN A LARGE COHORT OF PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME AND ITS IMPACT ON SALIVARY GLAND DYSFUNCTION

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**Background:** Salivary gland ultrasonography (SGUS) has increasingly appeared as a valid tool to characterise major salivary glands involvement in primary Sjögren's syndrome (pSS). An international score based on the number and location of the hypoechoic areas in the gland has been proposed for diagnostic purposes. Recently, a specific interest in using SGUS to estimate major salivary gland damage has also arisen in order to individualise patients treatment.

**Objectives:** a) to investigate frequency and severity of salivary gland damage in a large monocentric cohort of pSS patients; b) to explore determinants that could be associated with salivary gland damage accrual.

**Methods:** Sonographic data from a monocentric cohort of 311 pSS patients were collected from 2012 to 2017. SGUS had been performed according to a standard protocol that evaluated the echostructure of each gland graded on a 5-point scale (0–4). Salivary gland damage was defined by the presence of hyperechoic bands in more than 50% of the glandular parenchyma and on the basis of the size of the four glands.

**Results:** We included in the study 311 patients. The median age of the patients was 58 years (IQR, 49–68) and the median disease duration was 3 years (IQR, 0–9). Out of the cohort, 163 (52.4%) patients underwent SGUS examination within 3 years from the diagnosis, 91 (29.3%) within 4 to 10 years and 57 (18.3%) 10 years or more after the diagnosis. At SGUS evaluation 134/311 (43.1%) pSS patients did not present any findings of damage, whereas 177/311 (56.9%) presented at least one element of damage. SGUS damage inversely correlated with USFR ( $r=-0.382$ ,  $p$ -value=0.001). At the univariate analysis SGUS damage was associated to disease duration, number and location of the hypo-anechoic areas, focus score, ESSDAI score, hypergammaglobulinemia, and positivity for anti-Ro/SSA, anti-La/SSB, Rheumatoid Factor (RF) and cryoglobulins. In the linear

regression, duration of the follow-up, number and location of the hypo-anechoic areas and presence of cryoglobulins remained independently associated with SGUS damage. In 138/311 (44.4%) patients, SGUS was repeated prospectively at least twice during a median follow-up of 24 months (IQR, 12–36). Notably, 23/138 (16.7%) patients presented a damage progression. Presence of hyperechoic bands in the submandibular glands at the baseline evaluation was an independent risk factor for damage progression, whereas pSS low disease activity (ESSDAI <5) was protective against damage accrual.

**Conclusions:** Ultrasonographic damage resulted quite frequent in pSS patients and significantly associated with salivary gland dysfunction. Notably, pSS patients with normal echostructure of their glands were those less prone to develop SGUS damage during the disease course, whereas those presenting localised, diffuse or scattered hypo-anechoic areas were at higher risk of damage accrual.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.5843

#### THU0347 AQUAPORIN-4 IMMUNOGLOBULIN G ANTIBODY POSITIVE NEUROMYELITIS OPTICA SPECTRUM DISORDER AND SYSTEMIC AUTOIMMUNE DISEASES OVERLAP SYNDROME: A SINGLE CENTRE EXPERIENCE

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**Background:** The coexistence of neuromyelitis optica spectrum disorder (NMOSD) with other systemic autoimmune diseases is well recognised, especially with systemic lupus erythematosus (SLE) and Sjögren syndrome (SS). However literature is scarce, limited to case reports and multicentric case series.

**Objectives:** To describe the clinical and radiological characteristics and outcomes of patients with AQP4-IgG seropositive NMOSD coexisting with SLE and SS in a single centre.

**Methods:** This was a retrospective study that included patients with concurrent diagnosis of AQP4-IgG seropositive NMOSD according to the 2015 International Consensus Diagnostic Criteria, and SLE according to the ACR revised criteria or SS according to the AECG criteria who regularly attended a tertiary referral centre in Mexico City (2003–2018). We collected demographics, clinical (neurological events, number of relapses, remission, treatment, follow-up [date of last visit to a rheumatologist and/or neurologist] and disability according to the Expanded Disability Status Scale [EDSS]), laboratory (cerebrospinal fluid (CSF) analysis) and imaging data of NMOSD, as well as clinical and serological data of the overlapping autoimmune disease. We assessed disease activity in SLE and SS using SLEDAI-2K and ESSDAI respectively, and accrual damage with the SLICC/ACR-DI and SSSDI respectively.

**Results:** We included 11 patients, 10 (90.9%) women with a mean age at diagnosis of 36±15 years. Seven (63.6%) had SLE and 4 (36.6%) primary SS. Five (45.5%) patients had also another systemic or organ-specific autoimmune disease. In 8 (72.7%) patients NMOSD followed SLE/SS onset, 3 (27.3%) had a simultaneous presentation, and in 1 (9.1%) NMOSD preceded SS diagnosis. The mean time from diagnosis of SLE/SS to the first neurological event was 54.6 months. The mean SLEDAI-2K and ESSDAI at first neurological event was 3.1 (mainly hypocomplementemia and high anti-dsDNA) and 14.3 points (mainly renal and peripheral nerve involvement) respectively. During follow-up, 10 patients (90.9%) experienced myelitis, 5 (45.5%) optic neuritis, 2 (18.2%) each experienced area postrema syndrome, acute brainstem syndrome and cerebral syndrome; being the median number of neurological events 4.<sup>1-8</sup> Three patients (27.3%) had antiphospholipid antibodies. None of the patients had pleocytosis or low CSF glucose and 3 had high CSF proteins. All patients had longitudinally extensive transverse myelitis on MRI, 3 (27.3%) optic nerve findings and 6 (54.5%) NMOSD-typical brain lesion patterns. Nine (81.8%) patients went into either total or partial NMOSD remission at a mean follow up of 6.5±5.3 years. At last follow up the median EDSS, SLICC/ACR-DI and SSSDI was 2.5 (1–10), 2 (0–7) and 2 (0–3) points respectively; 4 (36.4%) patients had sequelae and 1 patient was death.

**Conclusions:** Patients with SLE or SS with clinical features of NMOSD should be tested for AQP4-IgG. In our cohort, AQP4-IgG seropositive NMOSD arose in the context of low SLE activity and in the context of SS with extraglandular features, and the disability and accrual damage at last follow up appeared to be mild.

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**THU0348 TIME ON DIALYSIS ADVERSELY AFFECTS RENAL TRANSPLANT OUTCOME IN LUPUS NEPHRITIS**

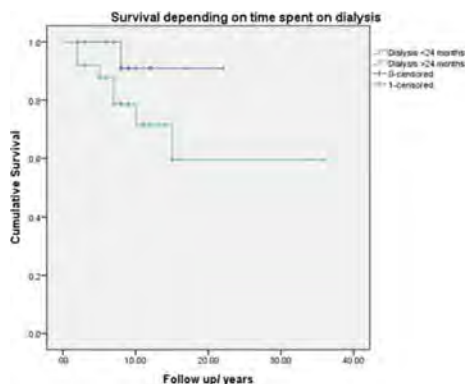
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**Background:** Lupus nephritis (LN) is an important cause of morbidity and mortality in patients with systemic lupus erythematosus (SLE) often leading to end stage renal failure (ESRF) and necessitating renal transplantation. However, the optimal timing of transplantation in SLE patients with ESRF is uncertain and could potentially affect survival.

**Objectives:** We investigated time spent on dialysis before renal transplantation and survival following the transplantation in a cohort of SLE patients.

**Methods:** Retrospective analysis of all adult SLE patients undergoing renal transplantation over a 40 year period (1975–2015) in two tertiary UK centres followed up until 2017. Cox proportional hazard regression and receiver operator curves (ROC) were used to determine the risk associated with time on dialysis before the transplantation and other potential predictors.

**Results:** Forty patients (age 35±11 years, 34 female, 15 Caucasian, 15 Afro Caribbean and 10 South Asian) underwent transplantation. During a median follow up of 104 months (IQR 80,145), 8 (20%) patients died and the five year survival was 95%. Univariate analysis identified time on dialysis prior to transplantation as the only potentially modifiable risk predictor of survival with a Hazard Ratio of 1.013 for each additional month spent on dialysis (95% CI=1.001–1.026, p=0.03). ROC curve demonstrated that >24 months on dialysis had an adverse effect with sensitivity of 0.875 and specificity 0.500 for death. No other modifiable predictors were significantly associated with mortality, indicating that time on dialysis had an independent effect.



**Abstract THU0348 – Figure 1.** Kaplan-Meier estimator plot between patients who had less than 24 months of dialysis (blue line) or more than 24 months (green line), suggesting a trend of almost threefold risk of survival in those spending longer time on dialysis, HR 2.84 log rank p=0.15.

**Conclusions:** Increased time on dialysis pre-transplantation is an independent modifiable risk factor of mortality in this cohort of patients with lupus nephritis and should be one of the factors considered for patient selection to transplantation.

**Disclosure of Interest:** None declared

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**THU0349 ANTIBODIES TO PHOSPHATIDYLSENERE-PROTHROMBIN COMPLEX AND ANNEXIN V AS RISK FACTORS FOR THE DEVELOPMENT OF THROMBOTIC COMPLICATIONS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS**

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**Background:** Seronegative antiphospholipid syndrome (APS) is a type of APS where the diagnostic levels of "classical" antiphospholipid antibodies (aPL) are not detected, though antibodies to the phosphatidylserine-prothrombin complex (aPS-PT) and anti-annexin V antibodies can be present. The role of these antibodies in the diagnosis of APS needs to be clarified.

**Objectives:** To study the prevalence of aPS-PT and anti-annexin V antibodies and their role in the development of thrombotic complications.

**Methods:** 79 SLE patients were enrolled in the study (M/F 7/72; mean age 11.0 years, range<sup>18,0,78,0</sup>). The main group consisted of 38 SLE patients with thrombotic complications and/or obstetric complications (mentioned in the classificational criteria for APS), a comparison group consisted of 41 SLE patients without thrombotic/obstetric complications. The groups were comparable in age, duration and SLE activity.

ELISA was used to test for aPL: anticardiolipin (aCL) IgG and IgM, anti-β<sub>2</sub>-glycoprotein-1 antibodies IgGAM (anti-β<sub>2</sub>GPI), antibodies to phosphatidylserine-prothrombin complex (anti-PS/PT) IgG/M, anti-annexin V antibodies IgG/IgM. Lupus anticoagulant (LA) was evaluated using the DRVV test method.

**Results:** In 11 patients (29%) of the main group "classical" aPL were not detected, although one SLE patient with thrombosis had elevated levels of antibodies to annexin V IgG (>5 U/ml).

Sensitivity and specificity of aPL for the diagnosis of APS in patients with SLE were 19% and 96% for anti-PS/PT, 11% and 94% for anti-annexin V antibodies IgG, 11% and 88% for anti-annexin V antibodies IgM respectively.

When comparing two groups using rank test, significant differences were revealed for aCL IgG, anti-β<sub>2</sub>GPI IgGAM levels (p<0.05); there were no significant differences between the main group and the comparison group (p>0.05) for levels of aCL IgM, aPS-PT and anti-annexin V antibodies. A positive correlation was revealed between the level of aPS-PT and the following aPL: LA (r=0.45, p=0.0006), aCL IgM and IgG (r=0.4 and r=0.45, p<0.001), anti-annexin V antibodies IgM and IgG (r=0.72 and r=0.47, p<0.001).

In a subgroup with elevated aPS-PT levels (>16 U/ml, 6 patients) thrombotic complications, venous thrombosis and its recurrence developed significantly more often than in a subgroup with a normal aPS-PT levels (OR=3.4, p=0.02, OR=4.1, p=0.02, OR=1.5, p=0.01, respectively).

**Conclusions:** 1. Anti-annexin V antibodies IgG and IgM have high specificity (94% and 88% respectively), but low sensitivity (11% and 11% respectively) for diagnosis of APS in SLE patients. 2. A level of aPS-PT has a positive correlation with both "classical" aPL and anti-annexin V antibodies, and has a sensitivity of 19% and a specificity of 96% for the diagnosis of APS in SLE patients. 3. Elevated levels of aPS-PT (>16 U/ml) increase the incidence of thrombotic complications in patients with SLE.

**Disclosure of Interest:** None declared

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**THU0350 TIME DEPENDENT ASSOCIATION OF ACTIVE RENAL DISEASE WITH IRREVERSIBLE ORGAN DAMAGE ACCRUAL IN SYSTEMIC LUPUS ERYTHEMATOSUS**

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**Background:** Lupus nephritis (LN) is a common feature of systemic lupus erythematosus (SLE). While LN is considered a contributor to irreversible organ damage in SLE, the magnitude of impact of active renal disease relative to other contributors to damage accrual is unknown.

**Objectives:** To determine the time-dependent association of active lupus nephritis (LN) with organ damage accrual in SLE.

**Methods:** This study was performed on patients from the Asia Pacific Lupus Collaboration (APLC) cohort. SLE Disease Activity Index-2000 (SLEDAI-2k) is collected per-visit and SLICC-ACR Damage Index (SDI) annually. Analysis was restricted to patients with ≥2 SDI scores. Active LN was defined if patients had urinary casts, proteinuria, haematuria or pyuria as indicated in the SLEDAI-2k descriptor. Organ damage accrual was defined as a change of SDI (ΔSDI>0) between baseline and final visit. Glucocorticoid (GC) categories were defined according to cumulative GC exposure at each visit as either no GC (cum.GC=0); low GC (cum.GC ≤median) or high GC (cum.GC >median). Cox regression analyses were performed.

**Results:** 1735 patients and 5593 visits were included in the analysis. 93% of patients was female with a median ([inter-quartile range (IQR), (range)] age of 40 years.<sup>31, 51, 18, 77</sup> Median study observation period was 853 days [621, 1094].<sup>96, 1443</sup> 36% were Chinese; 20% Thai and 10% Caucasian ethnicity. 82% of patients were



**Abstract THU0348 – Table 1.** Univariate Cox proportional hazard modelling investigating the association of various parameters and mortality showing that only one modifiable risk factor associated with prognosis (time on dialysis, the longer on dialysis the worse the prognosis) and one non-modifiable (rTp taking place after 2000 associated with better survival). SLE- Systemic Lupus Erythematosus, LN- Lupus Nephritis, ESRF- End Stage Renal Failure, rTp- renal transplantation, PD- Peritoneal Dialysis, HD- Haemodialysis, APLS- Antiphospholipid syndrome, MI- Myocardial Infarction, TIA- Transient Ischaemic Attack.

Factor	P value	HR	95% CI
Time on Dialysis/per month	0.031	1.013	1.001–1.026
Gender/male	0.442	0.038	0.001–161.3
Ethnicity	0.987	0.995	0.537–1.844
Age at SLE diagnosis	0.552	1.021	0.953–1.094
Age of LN	0.941	1.003	0.920–1.092
Age at rTp	0.431	1.026	0.963–1.092
Dialysis PD (vs HD)	0.764	0.706	0.073–6.862
Time between LN and Dialysis	0.540	0.999	0.994–1.003
LN Duration before Dialysis	0.152	1.066	0.977–1.164
Type IV LN	0.398	2.533	0.294–21.82
Dialysis Decade	0.712	0.872	0.420–1.807
Diabetes Mellitus	0.561	0.038	0.001–2319
Hypertension	0.323	0.329	0.360–2.987
Dyslipidaemia	0.905	0.872	0.092–8.234
APLS	0.508	0.036	0.000–672.6
Cardiac disease (MI, stroke, TIA)	0.873	1.071	0.463–2.476
Donor source living	0.353	0.459	0.089–2.372
Graft Failure post rTp	0.314	2.073	0.501–8.567

exposed to glucocorticoids. 40% had active renal disease at least once during the study period, and active renal disease was observed in 22% of visits (n=1238 visits). 41% of patients had organ damage at baseline and 14% accrued organ damage (272 damage accrual episodes in 250 patients). Active renal disease was significantly associated with damage accrual; after adjusting for confounders, patients with active renal disease were 66% more likely to accrue organ damage compared to those without active renal disease (adjusted hazard ratio=1.66 (95% CI: 1.26, 2.19), p-value<0.01 (table 1). High cumulative GC and age were also significantly associated with damage accrual.

	Univariable Cox regression analysis			Multivariable Cox regression analysis		
	HR	(95% CI)	p-value	HR	(95% CI)	p-value
Age at baseline (years)	1.02	(1.01,1.03)	<0.01	1.02	(1.01,1.03)	<0.01
Asian ethnicity	0.74	(0.52,1.05)	0.09	0.72	(0.50,1.04)	0.08
Cumulative glucocorticoid (GC) categories						
No GC	1.00	(1.00,1.00)		1.00	(1.00,1.00)	
Low GC (<median PNL)	1.42	(0.94,2.14)	0.1	1.47	(0.97,2.23)	0.07
High GC (>median PNL)	1.51	(1.04,2.18)	0.03	1.46	(0.99,2.16)	0.05
Baseline organ damage present	1.56	(1.22,2.00)	<0.01	1.27	(0.97,2.23)	0.09
Active lupus nephritis	1.66	(1.29,2.14)	<0.01	1.66	(1.26,2.19)	<0.01

**Conclusions:** Active LN is an independent risk factor for damage accrual in SLE. The concomitant independent association of GC exposure with damage accrual suggests non-GC treatments to reduce active LN are needed to reduce damage burden in SLE.

**Disclosure of Interest:** None declared

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THU0351

### SUSCEPTIBILITY TO CEREBRAL ISCHEMIA IN EARLY LUPUS PATIENTS: A PILOT STUDY OF CO-REGISTRATION WITH CONVENTIONAL BRAIN MRI, DIFFUSION- AND PERFUSION-WEIGHTED IMAGING

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**Background:** Conventional brain Magnetic Resonance Imaging (cMRI) has a limited usefulness in patients with early diagnosis of Systemic Lupus Erythematosus (SLE), showing not specific abnormalities in up to half of the patients. No data are available about cMRI combined with advanced MRI techniques in early SLE patients.

**Objectives:** To evaluate differences between early SLE patients, even without overt neuropsychiatric (NP) manifestations, and healthy controls (HCs) in a mono-centric cohort, using data derived from cMRI, diffusion-weighted imaging (DWI) and perfusion-imaging (PWI).

**Methods:** Patients referred to a single tertiary rheumatologic centre with early diagnosis of SLE (less than 24 months), aged less than 55, were consecutively enrolled (01/05/2013–31/12/2017) and imaged with cMRI, DWI and PWI (1.5 Tesla Philips "Signa Achieva" scanner). Data were analysed with a semi-automated measuring system (Diffusion/Perfusion Project Suite, developed in Multiple Sclerosis patients) to co-register apparent diffusion coefficient (ADC), cerebral blood flow (CBF) and volume (CBV), mean transit time (MTT) in normal appearing grey (NAGM) and white matter (NAWM), deep GM (putamen, pallidus, caudate, thalamus) and lesions. Demographic, clinical, serological and treatment information were collected as well as NP events at baseline attributed to SLE according to a validated algorithm. Statistical analysis were performed by comparing median (interquartile range, IQR) values for skewed variables between SLE and HCs and with quantile regression adjusted for cardiovascular comorbidities (hypertension, diabetes, previous coronary heart disease, hyperlipidaemia, obesity).

**Results:** 30 patients with early SLE (mean age 37.0 years, standard deviation SD 10.7, 27 females) and 8 HCs (mean age 40.6, SD 11.2, 6 females) were enrolled. MRI was performed after a mean period of 259 days from diagnosis; mean (SD) Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2k) was 8.87 (3.85) while mean (SD) Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SDI) was 0.40 (0.72); 3 patients were classified as NPSLE at diagnosis. Median (IQR) values of ADC in NAGM and NAWM were  $1.15 \times 10^{-3} \text{ mm}^2/\text{s}$  (1.12–1.16) and 0.86 (0.85–0.88) in SLE, 1.28 (1.16–1.33) and 0.97 (0.87–0.98) in HCs respectively (table 1). After adjusting for comorbidities, median differences between ADC values remained significant (p<0.001). SLE patients had lower median ADC values at bilateral putamen and pallidus. No differences were found in perfusion parameters in all the regions of interest (ROI) and lesions. A trend towards lower CBV and CBF and higher MTT values for NAGM-NAWM in NPSLE compared to non-NPSLE was found.

**Abstract THU0351 – Table 1.** Differences in diffusion and perfusion parameters at normal appearing GM and WM level in SLE patients and HCs.

ROI	NAGM ADC	NAWM ADC	NAGM CBF	NAWM CBF	NAGM CBV	NAWM CBV	NAGM MTT	NAWM MTT
SLE (30), median (IQR)	1.15 (1.12-1.16)	0.86 (0.85-0.88)	37.09 (30.97-47.21)	29.42 (26.00-37.48)	2.43 (2.20-2.58)	1.95 (1.80-2.26)	4.31 (3.80-5.23)	4.87 (4.12-5.85)
HCs (8), median (IQR)	1.28 (1.16-1.33)	0.97 (0.87-0.98)	33.89 (25.38-47.79)	26.54 (20.16-39.79)	2.57 (2.19-3.07)	2.11 (1.77-2.54)	5.11 (4.11-6.18)	5.78 (4.58-6.72)
p	0.004	0.009	0.591	0.519	0.283	0.452	0.123	0.124

Unit of measurement: ADC ( $\times 10^{-3} \text{ mm}^2/\text{s}$ ); CBF (ml/100g/min); CBV (ml/100g); MTT (s).

**Conclusions:** Lower ADC values in normal appearing GM and WM in early SLE patients could reflect susceptibility to cerebral ischemia, partially confirmed analysing perfusion data in NPSLE patients. Further prospective studies with higher sample size are necessary to confirm these findings.

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THU0352

### ASSOCIATION BETWEEN MEMORY B-CELLS AND PHENOTYPIC FEATURES OF SJÖGREN'S SYNDROME

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**Background:** B-cell disturbances are a hallmark of pSS and play a pivotal role in the disease pathogenesis and clinical evolution, and may as well have a potential role in diagnosis. In pSS, an increase of the naïve subset and a decrease of memory B-cells have been reported. A decreased frequency of memory cells has also been identified in patients with Sicca syndrome without criteria for pSS.

**Objectives:** Our study aims to evaluate the distribution of B-lymphocyte subpopulations in pSS and Sicca patients and to establish cut-off points for pSS classification in relation to healthy controls. Moreover, we aim to evaluate the relation between lymphocyte subpopulations and phenotypic features in pSS.

**Methods:** Fifty-seven pSS patients, 68 non-Sjögren Sicca patients and 24 healthy controls were included. Circulating B-cell frequencies were determined by flow cytometry, and the naïve and memory (switched and unswitched) subsets were characterised based on surface marker expression of the following monoclonal antibodies: CD19, CD24, CD27, Anti-IgD and Anti-IgM.

Kruskal-Wallis test was applied for groups' comparison. ROC curves were used to establish cut-off points in the B-cells subset levels and to estimate corresponding sensitivity and specificity. Data analysis was performed with R software.

**Results:** Absolute numbers of lymphocytes in pSS were lower compared to controls, with Sicca presenting intermediate levels.

Significant differences were found between pSS and controls in absolute counts of all memory populations: total memory (TMem) (CD19<sup>+</sup>CD27<sup>+</sup>), switched (SwM) (CD19<sup>+</sup>IgD<sup>+</sup>CD27<sup>+</sup>) and unswitched memory (UnSwM) (p<0.001 for all). Comparing pSS with controls, we found lower percentages of TMem in patients (p=0.078) and more significant differences in the UnSwM subset (p=0.043). Percentages of memory B-cells in Sicca were not significantly different from pSS and controls. Absolute memory B-cells numbers in Sicca were intermediate between those of pSS and controls.

Through ROC curves, the B-cell subsets that better discriminate between pSS and controls were TMem and SwM. A cut-off of equal to 58 TMem cells/μl yielded a specificity of 0.88 and a sensitivity of 0.60 for pSS, and was met by 59.6% of pSS, 12.5% of controls and 38.8% of Sicca, and a cut-off of equal to 23.5 SwM cells/μl yielded a specificity of 0.88 and a sensitivity of 0.54 and was met by 54.4% of pSS, 12.5% of controls and 37.3% of Sicca.

pSS patients with lower values than the established cut-off points had longer disease duration, higher disease activity (ESSDAI), and were more likely to present auto-antibodies and positive biopsy. Several Sicca patients also presented memory B-cell subsets counts lower than the pSS cut-off, but no consistent differences in clinical profile were identified.

**Conclusions:** Decreased numbers of memory B-cell subsets clearly discriminate pSS from healthy controls. Lower memory B-cells counts are associated with more active pSS disease profile. It remains to be clarified whether Sicca patients with decreased memory B-cells represent pSS and if B-cell profiling could help in the diagnosis of pSS.

**Disclosure of Interest:** None declared

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THU0353

### LUNG ULTRASOUND OF PLEURAL IRREGULARITIES (PI-US) IN PRIMARY SJÖGREN'S SYNDROME (PSS)-ASSOCIATED INTERSTITIAL LUNG DISEASE (ILD): CLINICAL, FUNCTIONAL, RADIOGRAPHIC AND ULTRASONOGRAPHIC SHORT-TERM FOLLOW-UP

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**Background:** Ultrasound of Pleural Irregularities (PI-US) has recently been suggested as a useful tool for the diagnosis and the assessment of interstitial lung disease (ILD) in primary Sjögren's Syndrome (pSS). However, no data are available regarding its role in the post-therapy evaluation of pSS-ILD.

**Objectives:** Aim of this study was to describe the post-therapeutic changes of the pleural profile in a monocentric cohort of pSS-ILD patients analysing clinical, functional, US and radiographic features.

**Methods:** Eighteen patients with pSS-ILD were included in the study. PI-US, HRCT and pulmonary function test (PFT) were performed in each patient at baseline. In 15/18 patients who had been treated according to international guidelines for ILD, clinical assessment, PFT and PI-US were repeated after 6 months. PI-US was performed by a single operator using a MyLab-25 (Esaote), 10 MHz, 5 cm linear probe. PI was defined as the loss of normal hyperechoic linear pleural contour

(score 0–2: normal, minimal and major changes at each intercostal space). PI-US total score represented the sum of partial scores assigned to 6 lung fields (2 for the anterior, 2 for postero-superior and 2 for postero-inferior chest surface). HRCT- abnormal findings, distinguishing C-NSIP, F-NSIP and UIP pattern, were quantified using the Warrick score system.

**Results:** Eighteen pSS-ILD patients (14 F:4 M, mean age=68.8±9.9 years) were included in the study. The median PI-US score was 45 (range 25.5–73.5). Both PI-US total score and partial postero-inferior PI-US score strongly correlated with the Warrick HRCT score (r=0.813, p=0.000 and r=0.914, p=0.000) and inversely correlated with FVC (r=-0.849, p=0.000 and r=-0.836, p=0.000), TLC (r=-0.895, p=0.000 and r=-0.829, p=0.000), and DLCO (r=-0.953, p=0.000 and r=-0.883, p=0.001). Both PI-US score and PI-US of the poster-inferior field directly correlated with FEV1/SVC (r=0.701, p=0.004 and r=0.619, p=0.01) and with FEV1/FVC (r=0.600, p=0.02 and r=0.501, p=0.05). After 6 months of therapy, 15 patients (12F:3M, mean age 65.3 years) presenting at HRCT different ILD pattern distributions (4 C-NSIP, 7 F-NSIP, 4 UIP), were re-evaluated after appropriate medical treatment. Out of these 15 patients, 5 had been treated with glucocorticoids (GC) alone, 2 with azathioprine, 4 with hydroxychloroquine, 2 with Mycophenolate Mofetil, 1 with Rituximab and 1 with abatacept. Clinical, radiographic and functional evaluation showed stability of all parameters in the majority of the patients (13/15), maintaining unchanged the correlations with PI-US scores. Moreover, 2/15 patients with active C-NSIP pattern, showed a significant improvement in clinical, radiographic and functional parameters. In these patients a significant reduction of the PI-US scores was also observed (PI-US score from 22 to 10 and from 57 to 30).

**Conclusions:** This study confirms the usefulness of PI-US evaluation for the diagnosis and assessment of pSS-ILD, demonstrating a strong correlation between PI-US and both HRCT findings and PFT. Furthermore, the significant reduction of PI-US score in patients with clinical, radiographic and functional improvement suggests that this tool may play a role in the follow-up of treated patients with active pSS-ILD.

**Disclosure of Interest:** None declared

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THU0354

### IMPACT OF BIOLOGIC THERAPY IN SJÖGREN'S SYNDROME PATIENTS WITH OVERLAPPING AUTOIMMUNE DISEASES OR EXTRAGLANDULAR MANIFESTATIONS. A SYSTEMATIC REVIEW OF LITERATURE

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**Background:** Treatment of Sjögren's syndrome (SS) has traditionally focused on conventional synthetic DMARDs (csDMARDs), with encouraging evidence on the benefit of biologic therapies emerging, mainly for treatment of SS extraglandular manifestations. Overlapping autoimmune diseases in SS are poorly studied; yet evidence primarily from case reports suggest a beneficial effect with biologics.

**Objectives:** To systematically review the literature on the treatment of SS with biologics, taking a focus on case reports and overlapping autoimmune conditions or extraglandular manifestations (defined here as those described in the EULAR SS disease activity index - ESSDAI).

**Methods:** A literature review was performed independently by two reviewers, using Pubmed and the following search terms: "Sjogren" or "Sjogren's" AND any of the following: "biologics", "Etanercept", "Adalimumab", "Infliximab", "Golimumab", "Certolizumab", "Tocilizumab", "Abatacept", "Rituximab", "Belimumab", "Secukinumab", "Ustekinumab" and "Anakinra". Inclusion criteria were: articles in English; published until January 2018; case reports of patients with primary or secondary SS. Initial screening was based on title/abstract, followed by full-text review for articles fulfilling inclusion criteria. For articles written in a different language, information was obtained from abstract if available, otherwise excluded. Concordance in article screening was 95% across the two reviewers. Data extraction focused on reporting overlapping autoimmune diseases and extraglandular manifestations, treatment and response data.

**Results:** Out of 679 papers screened, 39 articles were included. 22 overlapping autoimmune conditions were reported in 22 SS patients (table 1). Most of the patients were treated with Rituximab (63.6%), while TNF-inhibitors (22.7%), Tocilizumab (9.1%) and Ustekinumab (4.5%) were also used. Concurrent treatment with csDMARDs and steroids was used in 28.6% and 42.9% of the cases, respectively. 61.9% and 13.6% of the patients were csDMARDs- and biologic- experienced, respectively. Good response of overlapping condition was seen in 86.4% of them, while in 13.6%, control or partial response was reported. Although, most of the studies do not mention the effect of biologic treatment on SS, general

'improvement' was mentioned in 4 cases, while arthritis was improved in 6 patients, 4 of which had secondary SS.

In terms of extraglandular manifestations (e.g cryoglobulinemic vasculitis, interstitial nephritis) 18 were reported. 16 (88.8%) patients received Rituximab (one of them in combination with Belimumab), while 2 (11.1%) were treated with TNF-inhibitors. 11.1% and 61.1% of them received concurrent treatment with csDMARDs and steroids, respectively. 55.5% and 11.1% of the patients were csDMARDs- and biologics- experienced, respectively. Extraglandular manifestations responded well in the majority (83.3%) of the patients, with the remaining having partial or late response. SS and arthritis 'improvement' was mentioned in 5 and 1 patients, respectively.

**Table 1** Biologic treatments used for overlapping autoimmune conditions in SS patients. csDMARDs: conventional synthetic Disease Modifying Antirheumatic Drugs, NA: Not Applicable, Joints: improvement of arthritis. ^SS response was defined as clinical improvement of sicca symptomatology or improvement in ESS-DAL. Improvement of arthritis was reported separately. † cases of secondary Sjogren's syndrome (3 cases co-existing with RA and one case with SLE)

Biologic Drug	Overlapping condition	Response of overlapping condition	SS-response <sup>†</sup>	csDMARDs (concurrent)	csDMARDs (past)	Steroids (concurrent)	First Biologic
Adalimumab	Crohn's disease	Good	Yes	No	Yes	No	Yes
Etanercept	Autoimmune hepatitis	Good	No (joints)	No	Yes	No	Yes
Infliximab	Psoriasis	Good	NA	Yes	Yes	No	Yes
Infliximab	gangrenous Sweet syndrome	Good	NA	No	Yes	Yes	Yes
Infliximab	Amphibias	Stable	NA (joints)	Yes	Yes	No	Yes
Tocilizumab <sup>†</sup>	Sarcoidosis	Good	NA (joints)	Yes	No	No	Yes
Tocilizumab	Organizing pneumonia	Good	Yes (joints)	Yes	No	Yes	No
Ustekinumab	Psoriasis	Good	NA (joints)	No	Yes	Yes	No
Rituximab	Psoriasis/dermatitis	Good	NA	No	Yes	No	Yes
Rituximab	Shrinking lung syndrome	Good	NA (joints)	Yes	Yes	Yes	Yes
Rituximab	Protein lung enteropathy	Good	NA	No	Yes	Yes	Yes
Rituximab	Angiodema	Partial	NA	No	No	Yes	Yes
Rituximab	Coeliac	Good	NA	No	Yes	No	Yes
Rituximab	Anterior scleritis	Good	NA	Yes	Yes	No	No
Rituximab	TTP	Good	NA	No	No	Yes	Yes
Rituximab	Acquired demyelinating neuropathy	Good	Yes	No	No	No	Yes
Rituximab	Werner's syndrome	Good	Yes	NA	NA	NA	Yes
Rituximab	Esophagitis	Good	NA	No	No	No	Yes
Rituximab	Acquired factor viii inhibitor	Good	NA	No	No	Yes	Yes
Rituximab	Anti-GAD ataxia	Stable	NA	No	No	No	Yes
Rituximab	ANCA-vasculitis	Good	NA	No	No	Yes	Yes
Rituximab	Shrinking lung syndrome	Good	NA	No	Yes	No	Yes

**Conclusions:** Treatment with biologic DMARDs, sometimes accompanied by steroids, appears to be beneficial also in treating overlapping autoimmune diseases as well as some extraglandular manifestations in SS patients.

**Disclosure of Interest:** None declared

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**THU0355 DAMAGE ACCRUAL AND MORTALITY RATES AMONG DIFFERENT AGE GROUPS IN A COHORT OF PATIENTS WITH LUPUS**

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**Background:** Systemic lupus erythematosus (SLE) is a chronic, multi-system autoimmune disease, characterised by relapses and remissions, which eventually can lead to progressive, irreversible organ damage accrual. SLE-related damage implies increased morbidity and impaired quality of life. In addition, it constitutes itself a risk factor for the development of further damage and associates with early mortality. Age at disease onset has been postulated to affect the presenting clinical phenotype, the rate and likelihood of accruing damage and eventually mortality risk. Early-onset SLE patients have been reported to present with a more aggressive disease, especially in the first years after diagnosis. However, long-term data from large cohorts are scanty.

**Objectives:** To assess retrospectively the mortality and damage accrual rates in a large cohort of patients with SLE.

**Methods:** Demographic, clinical and laboratory data from 692 consecutive patients with SLE (631 females, 61 males), diagnosed according to the revised American College of Rheumatology (ACR) criteria in a single tertiary referral centre, were retrospectively analysed focusing on age of diagnosis. Damage accrual was assessed according to the Systemic Lupus Erythematosus

International Collaborating Clinics (SLICC)/ACR damage index (SDI). Cox's regression analysis, chi-square test, Kruskal-Wallis test and ANOVA were employed as appropriate.

**Results:** Thirty-three out of 692 patients were diagnosed with SLE before the age of 12, 172 between 12 and 20, 443 between 21 and 50 and 44 after 50 years of age. As previously reported, a female preponderance was more evident in the central part of the age spectrum (p=0.015). Nephritis and decreased complement were more frequent in patients with early-onset SLE (p=0.001 and p=0.033 respectively), serositis in the central age groups (p=0.025), and arthritis in late-onset patients (p=0.002). Neuropsychiatric manifestations were less frequent in patients aged >50 years (p=0.013; table 1). The global incidence rate for any damage was 48.36 per 1000 persons-years, whereas the death incidence rate was 8.54 per 1000 persons-years. Late-onset SLE associated with a higher risk of damage accrual (HR=1.63, p=0.024) and of death (HR=6.22, p<0.001). However, there were no significant differences in the time to first damage, to death after diagnosis and to death after the development of the first damage item, according to the age of diagnosis.

**Conclusions:** Younger patients with SLE show a distinct clinical phenotype, but share an accelerated accrual of morbidity and a higher risk of early mortality with patients of older age. Identifying age-specific predictors of disease severity will be of outstanding importance to improve long-term survival rates and patients' quality of life.

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**THU0356 SYNERGISTIC EFFECT OF CUMULATIVE CORTICOSTEROID DOSE AND IMMUNOSUPPRESSANTS ON AVASCULAR NECROSIS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS**

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**Background:** Avascular necrosis (AVN) is one of the most common organ damage in patients with systemic lupus erythematosus (SLE) and often causes serious physical disability.

**Objectives:** The aims of this study were to investigate clinical risk factors associated with symptomatic AVN and to analyse their synergistic effects in a large SLE cohort in Korea.

**Methods:** Patients with SLE were enrolled and followed from 1998 to 2014 in the Hanyang BAE Lupus cohort, in whom damage was measured annually according to the Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index. AVN was confirmed by imaging study if patients had symptoms. To determine risk factors for AVN, clinical, laboratory, and therapeutic variables were analysed by logistic regression. Relative excess risk due to interaction (RERI), attributable proportion (AP), and synergy index (S) were calculated to measure interactions between significant variables.

**Results:** Among 1,219 SLE patients, symptomatic AVN was the most common type of musculoskeletal damage (10.8%, n=132). SLE patients with AVN showed an earlier onset age, demonstrated AVN more commonly in conjunction with certain other clinical manifestations such as renal and neuropsychiatric disorders, and received significantly higher total cumulative corticosteroid dose and immunosuppressive agents than did patients without AVN. However, in multivariable analysis, only two variables including use of a cumulative corticosteroid dose greater than 20 g (odds ratio (OR) 3.08, p=0.005) and use of immunosuppressants including cyclophosphamide or mycophenolate mofetil (OR 4.34, p=0.002) remained as significant risk factors for AVN. Patients with cumulative corticosteroid dose >20 g and immunosuppressants use had a

Age group (years)	N	Females (%)	Nephritis (%)	Neurological inv. (%)	Arthritis (%)	Rash (%)	Photosensitivity (%)	Oral ulcers (%)	Serositis (%)	antiDNA (%)	Reduced complement (%)
<12	33	78.8	48.5	27.3	72.7	81.8	42.4	27.3	18.2	72.7	51.5
12-20	172	89.5	41.9	32.1	87.2	65.7	39.0	30.2	37.8	66.9	55.0
21-50	443	93.2	33.4	22.6	91.9	66.8	41.8	26.0	41.1	61.2	46.0
>50	44	86.4	11.4	6.8	93.2	54.5	27.3	22.7	27.3	63.6	31.8



15.44-fold increased risk for AVN, compared with patients without these risk factors ( $p < 0.001$ ). RERI, AP, and S, which define the strength of interactions between two risk factors, were 9.01 (95% confidence interval (CI) 1.30–16.73), 0.58 (95% CI 0.36–0.81), and 2.66 (95% CI 1.42–4.99), respectively, supporting the presence of synergistic interactions in the development of symptomatic AVN in our Korean lupus cohort.

**Abstract THU0356 – Table 1.** Synergistic effect of total cumulative steroid dose and use of immunosuppressants in development of AVN in SLE patients

	No. patients with AVN	No. patients without AVN	OR <sup>a</sup> (95% CI)	p-value
Total cumulative steroid dose $\leq 20$ g and immunosuppressants (-)	11	314	1.00	
Total cumulative steroid dose $> 20$ g and immunosuppressants (-)	17	168	3.08 (1.40–6.81)	0.005
Total cumulative steroid dose $\leq 20$ g and immunosuppressants (+)	18	121	4.34 (1.99–9.49)	$< 0.001$
Total cumulative steroid dose $> 20$ g and immunosuppressants (+)	64	134	15.44 (7.64–31.19)	$< 0.001$
RERI			9.01 (1.30–16.73)	
AP			0.58 (0.36–0.81)	
S			2.66 (1.42–4.99)	

AVN: avascular necrosis; SLE: systemic lupus erythematosus; OR: odds ratio; CI: confidence interval; RERI: relative excess risk due to interaction; AP: attributable proportion; S: synergy index

a. Odds ratios were adjusted for sex, age and disease duration.

**Conclusions:** An individual risk assessment for AVN development should be made prior to and during treatment for SLE, especially in patients with high-dose corticosteroid and immunosuppressant use regardless of clinical manifestations and disease activity.

**Disclosure of Interest:** None declared

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#### THU0357 FEATURES ASSOCIATED WITH LOSS TO FOLLOW-UP IN THE YEAR PRIOR TO DEATH IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A RETROSPECTIVE ANALYSIS FROM A NATIONAL REFERRAL CENTRE

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**Background:** Loss to follow-up in the year prior to death may lead to underrecognition and underreporting of systemic lupus erythematosus (SLE) as a cause of death of lupus patients.

**Objectives:** We aimed to assess the extent and features associated with loss to follow-up in the year prior to death in a group of 90 deceased SLE patients from our tertiary centre.

**Methods:** We retrospectively analysed 90 SLE patients (68 females) followed-up at our centre, deceased from 2002 to 2011. Patients were  $\geq 18$  years of age at death and fulfilled  $\geq 4$  classification criteria of the American College of Rheumatology (ACR). The cause and place of death were identified by matching patient data from our department's SLE registry with data from the National Death Database. Patients were considered lost to follow-up in the year prior to death (LTF) if the time span between the last visit to our centre and death exceeded 1 year. Other patients were considered to be under regular follow-up (RGF).

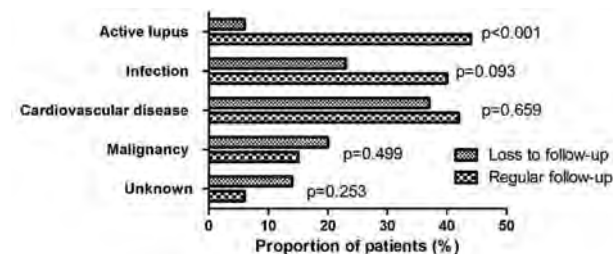
An extensive set of parameters was compared between the LTF and RGF groups: demographics, ACR classification criteria, cumulative damage according to the Systemic Lupus International Collaborative Clinics (SLICC)/ACR index, as well as causes of death. Frequencies were compared using the chi-square and Fisher's exact test, and continuous variables using the t-test and Mann-Whitney U-test.

**Results:** We identified 35/90 patients in the LTF group (29 females). The time span between the last visit to our centre and death of LTF patients ranged from  $> 1$  to 3 years. Compared to the RGF group, LTF patients were diagnosed at a later age (mean  $\pm$  SD:  $54 \pm 15$  vs.  $44 \pm 17$  years,  $p = 0.006$ ), while there was no difference in disease duration (median of 11 years, IQR of 5–15 years in the RGF group vs. median of 7 years, IQR of 5–15 years in the LTF group,  $p = 0.285$ ). The

LTF and RGF groups did not differ in the count of ACR criteria (median of 5, IQR of 4–6 vs. median of 6, IQR of 5–7,  $p = 0.053$ ) and cumulative damage (median damage of 3, IQR of 2–5 vs. median of 5, IQR of 3–8,  $p = 0.068$ ).

Compared to the RGF group, LTF patients had a lower cumulative proportion of pericarditis (1/35 vs. 16/55), proteinuria (10/35 vs. 30/55), hemolytic anaemia (1/35 vs. 10/55), thrombocytopenia (5/35 vs. 21/55) and Hughes syndrome (2/35 vs. 13/55) ( $p < 0.05$ ). Pulmonary damage and peripheral vascular damage were observed only in RGF patients (9/55 vs. 0/35,  $p = 0.011$ ; and 8/55 vs. 0/35,  $p = 0.021$ , respectively). LTF patients also had a lower proportion of cardiomyopathy (7/35 vs. 24/55,  $p = 0.021$ )

RGF patients died more frequently from active lupus compared to their LTF counterparts (24/55 vs. 2/35,  $p < 0.001$ ), while no difference was observed between the proportions of death from infections, cardiovascular diseases, malignancies and unknown causes (figure 1). SLE was reported in death certificates of 30/55 RGF patients compared to only 11/35 LTF patients ( $p = 0.032$ ). Compared to the RGF group, a lesser proportion of LTF patients died in the hospital (17/35 vs. 46/55,  $p = 0.004$ ).



**Abstract THU0357 – Figure 1.** Causes of death according to follow-up status

**Conclusions:** A lower proportion of LTF patients exhibited features of active SLE over their disease course. This may have led to underrecognition of SLE as a contributor to death.

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#### THU0358 USEFULNESS OF 18F-FDG POSITRON EMISSION TOMOGRAPHY (PET) FOR LYMPHOMA DIAGNOSIS IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME

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**Background:** Primary Sjögren's syndrome (pSS) is the autoimmune disease having the highest risk of lymphoma. The differential diagnosis between benign and malignant lymphoproliferation is sometimes difficult. Among imaging procedures, 18F-FDG PET could be useful for that purpose.

**Objectives:** To compare 18F-FDG PET results between patients with and without lymphoma to identify PET pattern associated with lymphomas in pSS

**Methods:** Retrospective study conducted in 2 centres including pSS patients (according to ACR/EULAR 2016 criteria) who undergo 18F-FDG PET. We compared PET abnormalities in patients with and without lymphoma, the PET having been done before any chemotherapy. Two independent readers analysed PET blind to lymphoma diagnosis. ESSDAI-PET score previously described by Cohen *et al.*<sup>1</sup> was calculated.

**Results:** 45 patients were included; 15 had lymphoma: MALT (n=12), nodal marginal zone with plasmacytic differentiation (n=2), diffuse large B-cell (n=1). Patients with lymphoma had more frequently parotid gland swelling (67% vs 20%,  $p = 0.003$ ) and higher ESSDAI score (24 [13.5–29] vs 9,  $p = 0.03$ ), even after exclusion of lymphoma item (19<sup>11–27</sup> vs 9,  $p = 0.03$ ).

Compared to non-lymphoma patients, mean size ( $45.5^{38–56}$  mm vs.  $40^{37–41}$  mm;  $p = 0.048$ ) and maximum standardised uptake value (SUVmax) of the parotid glands (5.6 [5–6.9] vs 3.8 [3.2–4.4];  $p = 0.001$ ) were higher in lymphoma patients. 53.3% of patients with lymphoma and 43.3% without lymphoma had lymph node FDG uptake, but neither their number nor their repartition or mean SUV differ between them.

Pulmonary uptake was observed in 6 (40%) patients with lymphoma and 6 (20%) without lymphoma ( $p=0.17$ ). But in lymphoma patients, this uptake was focal in 5 (33.3%) patients (nodules or condensation) and in only one (3.3%) patient without lymphoma ( $p=0.01$ ). Remaining patients had interstitial FDG uptake. Mean PET score ( $4^{-2}$  vs.  $2^{-3}$   $p=0.04$ ) and SUVmax at any site (6.3 [5.6–7.3] vs. 4.2 [3.7–5.9]  $p=0.02$ ) were significantly higher in lymphoma group. 20 patients had PET guided biopsy of a hypermetabolic lesion that conducted to lymphoma diagnosis in 7 cases (46.6%). After chemotherapy for lymphoma, PET was available for 10 patients: complete regression of hypermetabolic lesions was observed in 6 patients (60%), and decreased uptake intensity in the 4 remaining patients.

**Conclusions:** Some of the systemic manifestation of pSS (lung, lymph nodes and salivary glands) can be assessed by 18F-FDG PET. Lymph nodes hypermetabolism is frequent and not associated with lymphoma. The 18F-FDG PET abnormalities associated with lymphoma diagnosis are SUV max at any site  $>6$ , SUV max of parotid glands  $>5$  and focal nodular hypermetabolic lung lesions. Finally, PET can be helpful to guide biopsy toward the most hypermetabolic structure for diagnosing lymphoma.

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#### THU0359 RELATIONSHIP BETWEEN DAMAGE CLUSTERING AND MORTALITY IN JUVENILE SYSTEMIC LUPUS ERYTHEMATOSUS: CLUSTER ANALYSES IN A LARGE COHORT FROM THE SPANISH SOCIETY OF RHEUMATOLOGY LUPUS REGISTRY

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**Objectives:** Identify patterns (clusters) of damage manifestations within a large cohort of patients with juvenile-onset SLE (jSLE) and evaluate their potential association with mortality.

**Methods:** Multicenter, descriptive and cross-sectional study of a cohort of 345 patients with jSLE (age at SLE diagnosis  $<18$  years) from the Lupus Registry of the Spanish Society of Rheumatology (RELESSER). Organ damage was determined by using the SLICC/ACR damage index (SDI). By using cluster analysis, groups of patients with similar patterns of damage manifestations were identified and compared among them.

**Results:** Mean age (years) $\pm$ S.D. at diagnosis was  $14.2\pm 2.89$ , 88.7% were female and 93.4% were Caucasian. Mean SLICC/ACR DI $\pm$ S.D. was  $1.27\pm 1.63$ . A total of 12 (3.5%) patients died. Three damage clusters were identified: Cluster 1 (72.7% of patients) presented a lower amount of individuals with damage (22.3% vs 100% in clusters 2 and 3,  $p<0.001$ ). Cluster 2 (14.5% of patients) was featured by renal damage in 60% of patients, significantly more frequent than clusters 1 and 3 ( $p<0.001$ ), alongside more ocular, cardiovascular and gonadal damage. Cluster 3 (12.7%) was the only group with musculoskeletal damage (100%), significantly higher than in clusters 1 and 2 ( $p<0.001$ ). The overall mortality rate in cluster 2 was 2.2 times higher than that in cluster 3 and 5 times higher than that in cluster 1 ( $p<0.017$  for both comparisons).

**Conclusions:** In a large cohort of jSLE patients, renal and musculoskeletal damage manifestations were the two dominant forms of damage to sort patients into clinically meaningful clusters. We found two clusters of jSLE with important clinical damage that were associated to higher rates of mortality, especially for the cluster of patients with predominant renal damage. Physicians should pay special attention to the early prevention of damage in this particular subset of jSLE patients with kidney involvement.

**Disclosure of Interest:** None declared

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#### THU0360 A VALIDATION STUDY OF THE GLOBAL ANTIPHOSPHOLIPID SYNDROME SCORE (GAPSS) IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND PREGNANCY MORBIDITY

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**Background:** Systemic lupus erythematosus (SLE) and antiphospholipid antibodies (aPL) are associated with pregnancy complications.

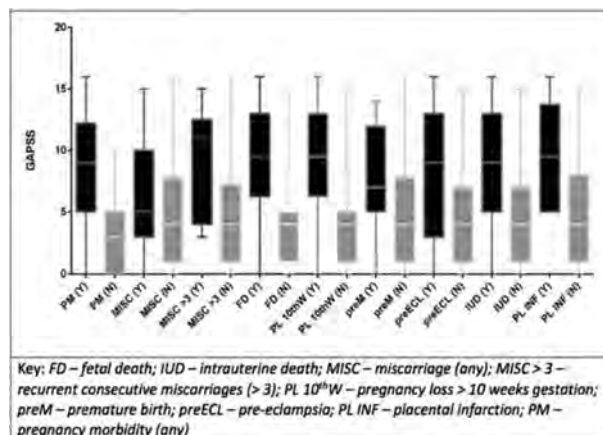
**Objectives:** To validate the global antiphospholipid syndrome score (GAPSS) in a cohort of women with SLE.

**Methods:** 143 women ever pregnant with SLE who presented in our outpatient clinic were included (table 1). Data on cardiovascular risk factors and aPL positivity were retrospectively collected. The individual GAPSS was calculated for each patient by calculating the sum of each risk factor score, which is based on a linear transformation derived from the  $\beta$  regression coefficient as follows: 3 for hyperlipidaemia, 1 for arterial hypertension, 5 for aCL IgG/IgM, 4 for anti-b2 glycoprotein I IgG/IgM, 3 for aPS/PT IgG/M and 4 for lupus anticoagulant (LA)<sup>1</sup>.

**Results:** Significantly higher GAPSS values were seen in patients with a history of pregnancy complications compared to those without a history pregnancy complications. Results are outlined in table 1 and figure 1.

**Abstract THU0360 – Table 1.** Patient demographics

Patients Characteristics	All (n=143)	%
Age, mean (S.D.), years	43.6 (SD 10.8)	
Disease duration, mean (S.D.), years	13.4 (9.3)	
Ethnicity (White:Black:afro-carib:Columbian: Asian)	119:6:11:1:1:4	
Cardiovascular risk factor (any), n	84	58%
Smoking, n	39	27%
Arterial Hypertension	44	31%
Hyperlipidemia, n	31	22%
Diabetes, n	4	3%
Pregnancies, n	382	
Pregnancy morbidity (any), n	54	14%
Consecutive early miscarriages (>3), n	9	2%
Any miscarriage, n	39	10%
Fetal death, n	25	7%
Prematurity, n	15	4%
Pre-eclampsia, n	19	5%
Intrauterine death, n	10	3%
Placental infarction, n	5	1%



**Abstract THU0360 – Figure 1.** Graphic illustration of the global antiphospholipid syndrome scores (GAPSS) in women with and without pregnancy morbidity.

**Conclusions:** Higher GAPSS values are found in women with SLE and aPL with previous pregnancy complications compared to those without pregnancy complications. The clinical utility of the GAPSS score in pregnancy seem promising and should be validated in a prospective cohort.

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**Disclosure of Interest:** None declared

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#### THU0361 CHARACTERISATION OF NOVEL AUTOANTIBODIES TO AHNK1 SPECIFICALLY PRESENTED IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Aberrant activation of T cells has been considered to play important roles for pathogenesis of SLE. In T cells activation, calcium signalling is essential for the process. Interestingly, T cells of SLE patients have been reported to show several abnormalities of calcium signalling. In the present study, we postulated that patients with SLE may target calcium signaling-related molecules as autoantigen as autoantibodies to these molecules are potentially capable of interfering with calcium signalling through binding to these molecules localised at the plasma membrane eventually resulting in abnormal T cells activation in SLE. Regarding to the calcium signaling-related molecules, recent studies have shown that AHNK1 is predominantly expressed in CD4 +T cells of cell membrane and cytoplasm. Moreover, AHNK1 is known to play significant roles for regulating of calcium signalling at T cells activation through its ability to localise calcium channels properly at the plasma membrane as scaffold protein. Therefore, we verify whether autoimmune response to AHNK1 is elicited in SLE.

**Objectives:** The present study was conducted to clarify whether autoantibodies to AHNK-1 are produced in SLE compared with other connective tissue diseases and normal healthy controls (NHCs).

**Methods:** The Patients sera consisting of SLE (n=59), other connective tissue diseases (PM/DM; n=40, SSc; n=40, SS; n=30, MCTD; n=30, and RA; n=30) and NHCs (n=115) were used in the present study. Immunoreactivity against AHNK1 recombinant antigens was evaluated by ELISA. AHNK1 mRNA expression in peripheral blood mononuclear cells (PBMCs) was evaluated by quantitative RT-PCR. Indirect immunofluorescence (IIF) staining using monoclonal anti-AHNK1 antibodies in combination with the patient's sera containing anti-AHNK1 antibodies was evaluated using HEp-2 substrate. The experimental data were statistically analysed using the Mann-Whitney U-test or Chi-square test, and differences with P-values<0.05 were considered to be significant.

**Results:** Immunoreactivity against AHNK1 was significantly elevated in SLE patients compared to both NHCs and other connective tissue diseases. Significant elevation of AHNK1 mRNA expression was observed in PBMC of SLE patients compared to NHCs. Among 17 SLE patients with anti AHNK1 antibodies positive sera, 4 patients revealed reduction of anti- AHNK1 antibodies level after the treatment like glucocorticoid or immune suppressive reagents, however, the remaining 13 patients did not show the reduction of serum level of anti-AHNK1 antibodies. In clinical profile, lymphopenia was frequently observed in these SLE patients. IIF analysis showed that AHNK-1 is localised at cell membrane and cytoplasm rather than nucleus.

**Conclusions:** In the present study, we found that autoantibodies to AHNK1 were significantly observed in sera with SLE compared to both NHCs and other connective tissue diseases. Furthermore, AHNK1 were enriched in PBMC of SLE patients suggesting antigen driven system may play an important role for this autoantibodies production. Anti-AHNK1 antibodies may be pathological and play an important role for pathogenesis of SLE because it may possibly alter physiological calcium signalling of T cells through binding to AHNK1 on cell membrane eventually resulting in aberrant T cells activation in SLE.

**Disclosure of Interest:** None declared

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#### THU0362 INCIDENCE OF MAJOR INFECTIONS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Major infections are one of the leading causes of morbidity and mortality in patients with systemic lupus erythematosus (SLE), and one of key concerns when considering the risk of immunosuppressive therapy. Previous studies have limited information on the relationship of infections and disease characteristics.

**Objectives:** To examine the incidence of major infections and describe the types of infections that occur in a cohort of well-characterised SLE patients

**Methods:** The study included 192 SLE patients who attended the Monash Lupus Clinic at Monash Health and enrolled in the Australian Lupus Registry and Bio-bank (ALRB) between 1st of July 2009 to 31st Dec 2016. Major infections were defined as any serious infections resulting in hospitalisation, reactivation of major viral infection, latent or active tuberculosis or any opportunistic infections. Patient and disease characteristics were examined in patients with or without major infections, and comparison was also made with 86 rheumatoid arthritis (RA) patients who are on similar level of immunosuppression. Associations between a number of patient and disease variables and infection were examined using Wilcoxon rank-sum tests (continuous variables) and Person's chi-squared tests (binary/categorical variables).

**Results:** 57 (30%) SLE patients reported 97 episodes of infection during the observation period (974 person-years). The median age of patients and observation period and other demographics were similar in patients who have experienced a major infection. In contrast, 15 (17%) RA patients reported 28 infection events during the study period. RA patients who reported infections were significantly older than SLE patients with infections events, median age (IQR) 68 years<sup>53</sup> vs 42 years<sup>33, 54</sup> (p<0.001) respectively. 61% of SLE patients and 54% of RA patients were on prednisolone. Comparing lupus with RA patients, the type of pathogens identified was significantly different (p<0.001), with no organism identified being the most common in lupus whereas in RA multiple pathogens are common (table 1). VZV reactivation causing shingles was the most common skin and soft tissue infection in lupus patients, and occurred more frequently than the RA patients. Among all of serious infections requiring hospitalisation, infection site did not differ between SLE and RA patients, and lower respiratory and urinary tracts were most commonly involved. In patients who experienced major infection they had a significantly higher SLEDAI (p 0.04), higher ESR (p 0.005) and lower haemoglobin (p 0.003).

Pathogen_type	SLE n=97	RA n=28	<0.001
CMV, EBV	4 (3.2%)	0 (0%)	
E coli, Salmonella	6 (5%)	7 (25%)	
HSV	9 (9%)	1 (4%)	
Influenza	2 (2%)	0 (0%)	
Multiple	7 (7%)	14 (50%)	
Unknown	30 (31%)	2 (7%)	
Pneumocystis jirovecii	1 (1%)	0 (0%)	
Staphylococcus,	12 (10%)	0 (0%)	
Streptococcus			
VZV	10 (10%)	2 (7%)	

**Conclusions:** Our data suggests that major infections occur commonly in SLE patients, and the likelihood of infection is higher in SLE, when compared to RA patients on a similar level of immunosuppression. Higher disease activity measures were associated with increased likelihood of infection. Medication exposure such as prednisolone use was similar in SLE and RA patients, suggesting other factors other than medication use plays an important role in driving infections.

**Disclosure of Interest:** None declared

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#### THU0363 ASSOCIATION OF DEPRESSION WITH SOCIOECONOMIC STATUS, ANTICARDIOLIPIN ANTIBODIES, AND ORGAN DAMAGE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: RESULTS FROM THE KORNET REGISTRY

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**Objectives:** Depression is more common in patients with systemic lupus erythematosus (SLE) compared to the general population. However, few studies have



investigated risk factors of depression in SLE patients, and the results are inconsistent. This study evaluated the prevalence of, and risk factors for, depression in ethnically homogeneous Korean SLE patients.

**Methods:** In this study, 505 consecutive SLE patients were enrolled from the Korean Lupus Network registry. Demographic variables, clinical manifestations, laboratory findings, physician global assessment, and SLEDAI-2000 and SLICC damage index were recorded at enrollment. Patients were identified as having depressive symptoms using the Korean version of the Beck Depression Inventory (BDI) with a cut-off  $\geq 16$ , and categorised into four groups. Multivariable logistic regression analyses were performed to identify independent risk factors for depression defined as a BDI score  $\geq 16$ .

**Results:** Of the 505 patients, 97 (19.2%) were diagnosed with depression. Patients with a higher BDI score were older, more likely to be a current smoker, and had a SLICC score  $>1$ . Conversely, they had lower income and educational levels. Regarding the serologic findings, patients with a higher BDI score had lower anti-double-stranded DNA positivity and higher anticholinergic (aCL) positivity. On multivariate analysis, the following factors were associated with depression: current smoking status (OR 2.533,  $p=0.049$ ), aCL-positivity (OR 2.009,  $p=0.035$ ), and a SLICC damage index score  $>1$  (OR 2.781,  $p=0.039$ ). On the other hand, high-level education (OR 0.253,  $p=0.024$ ) and a high income (OR 0.228,  $p=0.008$ ) were negatively associated with depression.

**Conclusions:** Our results show that depression is prevalent in patients with SLE and multiple factors are associated with depression in SLE. These data could help guide target programs for those at high risk of depression in SLE.

**Disclosure of Interest:** None declared

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#### THU0364 RELATIONSHIP BETWEEN DISEASE ACTIVITY INDEX SCORES AND PHYSICIAN GLOBAL ASSESSMENT IN EARLY AND NON-EARLY SYSTEMIC LUPUS ERYTHEMATOSUS

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**Objectives:** To evaluate the disease activity and to compare it to physician's global assessment in patients with early (early SLE) and non-early systemic lupus erythematosus

**Methods:** Performed case-control study included SLE patients that fulfilled SLICC classification criteria, 2012. The research included two groups: patients with early SLE – first group (disease duration less than 24 months) and non-early SLE – second group (disease duration more than 24 months). The disease activity was assessed by SLEDAI-2K and SLAM. Physician global assessment (PhGA) was rated by 0–100 numeric score. We correlated disease activity indices with physician global assessment by Pearson coefficient.

**Results:** A total of 96 SLE patients were analysed. First group included 45 patients with female:male ratio 14:1. The second group included 51 patients, female:male ratio 1:49. The disease activity indices: SLEDAI and SLAM denoted high disease activity level in both groups. PhGA didn't correlate with SLEDAI ( $r=0.28$ ,  $p>0.05$ ) in the first group, while a statistically significant correlation was determined with SLAM index ( $r=0.39$ ,  $p=0.007$ ). In the second group we found a moderate statistical significant correlation of PhGA with SLAM ( $r=0.53$ ,  $p=0.0001$ ) and weak, but also statistical significant relationship with SLEDAI ( $r=0.35$ ,  $p=0.01$ ). There is a better correlation of PhGA assessment and SLAM in both study groups, which can be explained by the presence of subjective components in appreciation of this index. Patient's better appreciation of their condition in the group with longer disease duration (statistical significant correlation of PhGA and both indices:SLAM and SLEDAI), probably, is because this patients know better to appreciate their disease, and patients with early SLE tend to underestimate their general condition.

Parameters of the disease	Gr I, Nr 45	Gr II, Nr 51
Age at study entry $\pm$ SD (range), years	41.18 $\pm$ 14.0 (20–75)	43.51 $\pm$ 12.3 (22–67)
Disease duration $\pm$ SD (range), month	10.14 $\pm$ 9.10 (0.1–24)	159.71 $\pm$ 94.53 (31–432)
SLAM $\pm$ SD (range), points	9.31 $\pm$ 4.87 <sup>-24</sup>	8.08 $\pm$ 4.38 <sup>-22</sup>
SLEDAI $\pm$ SD (range), points	11.13 $\pm$ 7.58 <sup>-34</sup>	7.33 $\pm$ 5.54 (0–23)
PhGA $\pm$ SD (range), points	44.02 $\pm$ 18.75 <sup>10-80</sup>	47.73 $\pm$ 22.63 <sup>5-92</sup>

**Conclusions:** In patients with early SLE PhGA correlated with SLAM, while in patients with non-early lupus PhGA correlated with both indices - SLAM and SLEDAI-2K. A better correlation of PhGA with SLAM can be explained by the presence of multiple components in this tool and also subjective data as fatigue or cognitive dysfunction.

**Disclosure of Interest:** None declared

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#### THU0365 POTENTIAL PREDICTIVE FACTORS INFLUENCING ESSDAI OF PRIMARY SJÖGREN'S SYNDROME PATIENTS

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**Background:** The useful tool to assessing disease activity in primary Sjögren's syndrome (pSS) is an EULAR Sjögren's syndrome disease activity index (ESSDAI)<sup>1,2</sup>.

**Objectives:** The aim of this study was indication of laboratory and clinical factors affecting the ESSDAI in pSS patients.

**Methods:** 75 pSS patients were included; 65 (87%) female, 10 (13%) men; mean age 50 years SD  $\pm 15$ . The tests included: basic laboratory tests, rheumatoid factor (RF), erythrocyte sedimentation rate, CRP, gammaglobulins serum concentration, C4 and C3 component of complement, antinuclear antibodies (ANA) - IF test HEp-2000, anti-SS-A and anti-SS-B antibodies evaluation with semi-quantitative immunoblotting, standard ELISA assays for serum cytokines levels (BAFF, APRIL, FLT-3L, TNF- $\beta$ , IL-21) and  $\beta 2$ -microglobulin. Biopsy of minor salivary gland with the histopathological evaluation (focus score-FS) and the immunocytochemistry was also performed with the CD3+, CD4+, CD19+, CD21+, CD35+ cells presence assessment. The Schirmer's test and ocular staining score (OSS) were performed. The Bioethics Committee approval was obtained. Statistics: U Mann-Whitney (continuous variables) tests, Spearman correlation coefficient (correlations between quantitative variables) with statistical significance set at  $p<0.05$ .

**Results:** ESSDAI depends on FS, the presence of CD4+, CD3+ cells in the minor salivary glands infiltrates, RF and cryoglobulins ( $p<0.05$ ). The division of pSS subjects into two subgroups (ESSDAI  $>5$ ;  $<5$ ) revealed, that the autoantibodies as anti-SS-A and anti-SS-B, influence the severity of the disease ( $p=0.046$ ;  $p=0.015$  respectively). ESSDAI positively correlated with OSS, but not with the Schirmer's test, other tested cytokines, ESR, CRP and gammaglobulins concentration - yet interestingly ESSDAI correlates negatively with IgG4 ( $\rho=-0.435$ ).

**Conclusions:** The results confirm, that organ-related complications are influenced by inflammatory activity. This activity is expressed by mononuclear cell infiltrates (FS), which consist primarily of T-lymphocytes (indicators of active and early stage inflammation). However, contrary to other observations,<sup>3</sup> no correlation between ESSDAI and cytokines or  $\beta 2$ -microglobulin was found. The correlation of ESSDAI with the presence of pSS marker autoantibodies (anti-SS-A, anti-SS-B antibodies), as well as with non-specific ones (RF or cryoglobulins), indicates the immunological disease activity and overactivity of B lymphocytes as suspected. The reduction of IgG4 concentration in pSS patients correlating with higher ESSDAI can be associated with breaking the autotolerance and lack of stimulation of IgG4 production. But the role and importance of IgG4 in immunological processes both as an activator of dependent autoimmune diseases and, on the other hand, the marker of induction of immune tolerance requires further research.

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#### THU0366 STUDY OF THE ROLE OF MICRO-RNA 20A EXPRESSION IN SYSTEMIC LUPUS ERYTHEMATOSUS IN AN EGYPTIAN COHORT

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**Background:** Micro-RNAs are small noncoding RNAs that act as cytoplasmic post-transcriptional gene expression regulators by targeting their complementary messenger RNA. They regulate several inflammatory, immunologic and oncogenic pathways.<sup>(1)</sup> MicroRNAs are differentially expressed in patients with systemic lupus erythematosus (SLE), especially in association with lupus nephritis.<sup>(2,3)</sup> The positive miRNA list in SLE patients in different studies presents relatively

limited overlap. The heterogeneity of patient ethnicity and variety in detection method may in part explain some of the discrepancies.<sup>(4)</sup>

**Objectives:** to study the role of micro-RNA 20a expression in SLE in an Egyptian cohort and its role as a potential biomarker of lupus nephritis.

**Methods:** Expression levels of micro-RNA-20a extracted from peripheral blood mono-nuclear cells determined using quantitative reverse transcription-polymerase chain reaction assay. A total of 90 plasma samples were obtained from 30 SLE patients without clinical and laboratory evidence of lupus nephritis, 30 SLE patients with lupus nephritis and 30 healthy control subjects.

**Results:** The expression of micro-RNA-20a in SLE patients was significantly lower than the expression in normal healthy control,  $p < 0.001$ . In addition the Roc curve of micro-RNA-20a showed that micro-RNA-20a expression levels can significantly discriminate between lupus patients with and without lupus nephritis at a cut off level  $\leq 9.3 \times 10^{-6}$  with a specificity of 76.67% and sensitivity of 96.67%. We also found a significant correlation between micro-RNA-20a expression levels and the pathological activity index of renal biopsy, while there was no significant correlation between micro-RNA-20a expression level and the pathological chronicity index.

**Conclusions:** The expression level of micro-RNA-20a could be considered a diagnostic marker of SLE. Also, the expression level of micro-RNA-20a could be considered a potential biomarker for recognition of renal involvement in SLE patients.

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THU0367

#### PREVALENCE AND SIGNIFICANCE OF ANTI-PHOSPHATIDYL SERINE ANTIBODIES: A POOLED ANALYSIS IN 5992 PATIENTS

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**Background:** The current classification criteria for antiphospholipid syndrome (APS) include three laboratory tests: lupus anticoagulant, anti-cardiolipin, and anti-b2 glycoprotein-I.<sup>1</sup>

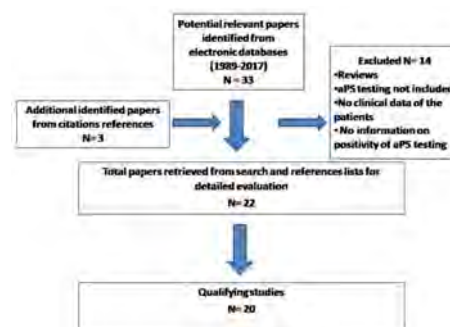
Among the so-called 'extra-criteria' aPL tests, anti-phosphatidylserine (aPS) antibodies have been proposed as an additional tool to be considered when patient is suspected for having APS. However the exact prevalence of aPS antibodies, and their independent role as risk factor for developing clinical manifestations of APS, is uncertain.

**Objectives:** To estimate the prevalence of aPS antibodies in patients with clinical manifestations of APS, by systematically reviewing the literature.

**Methods:** A detailed literature search was applied *a priori* to Ovid MEDLINE, In-Process and Other Non-Indexed Citation 1989 to present and to abstracts from EULAR and ACR/ARHP Annual Meetings (2011–2017) (figure 1).

**Results:** Data from 5992 patients from 20 studies were analysed (table 1). In APS patients, we report an overall estimated median prevalence of aPS antibodies of 55% [S.D.±21.1, range 29%–87%] and 35% [S.D.±17.9, 16–65%] for IgG and IgM, respectively. aPS antibodies were more frequently found in patients with known APS, when compared to patients with thrombosis/pregnancy loss or SLE (IgG mean 55%±28.9, 30±19.6, 22±13; IgM 35±4.3, 1±2.8, 14±8.3, respectively,  $p < 0.05$ ). In detail, patients were distributed as follow: 366 APS patients in 7 studies [55% aPS IgG/37% aPS IgM-positive; in more detail, 78 primary APS in 2 studies (64% aPS IgG/48% aPS IgM-positive), 29 secondary APS in 2 studies (37% aPS IgG/24% aPS IgM-positive) and 259 not specified], 787 SLE patients in 7 studies (22% aPS IgG/14% aPS IgM-positive), 24 aPL asymptomatic carriers in one study (21% aPS IgG/25% aPS IgM-positive), 3565 patients with cardiovascular accidents in 4 studies (18% aPS IgG/7% aPS IgM-positive), 1250 patients with pregnancy morbidity in 6 studies (30% aPS IgG/1% aPS IgM-positive) and 952 healthy controls.

DIAGNOSIS	Number of patients included in the analysis	% of positive patients for anti aPS IgG antibodies	% of positive patients for anti aPS IgM antibodies	Studies included in the analysis
APS*	366	55	37	Roggenbuck et al. 2016 Khoger et al. 2014 Jaskowski et al. 2009 Lopes et al. 2004 Musial et al. 2003 Ware Branch et al. 1997
PAPS	78	64	48	Roggenbuck et al. 2016 Musial et al. 2003
Secondary APS	29	37	24	Roggenbuck et al. 2016 Bertolaccini et al. 1998
SLE	787	22	14	Nojima et al. 2014 Fialova et al. 2003 Musial et al. 2003 Amoroso et al. 2003 Palomo et al. 2002 Bertolaccini et al. 1998 Toschi et al. 1993
aPL+, asymptomatic	24	21	25	Roggenbuck et al. 2016 Carmel-Neiderman et al. 2017 Bu et al. 2016 Saidi et al. 2009 Khales et al. 2005
Cardiovascular accidents**	3565	21	7	Ching et al. 2013 Sater et al. 2012 Jaskowski et al. 2009 Aljotas-Reig et al. 2010 Ulcova-Gallova et al. 2005 Ware Branch et al. 1997
Pregnancy Morbidity**	1250	30	1	



**Conclusions:** While aPS are frequently detected in patients with known APS, their added diagnostic value and clinical role in patients with thrombosis/pregnancy loss and/or concomitant autoimmune disease remain uncertain.

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**Disclosure of Interest:** None declared

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THU0368

### ARE ANTI-PHOSPHATIDYLSERINE PROTHROMBIN ANTIBODIES A USEFUL SCREENING TOOL FOR THE LUPUS ANTICOAGULANT?

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**Background:** Anti-phosphatidylserine prothrombin antibodies (PSPT) have been reported to be strongly associated with the lupus anticoagulant (LAC) in established antiphospholipid syndrome (APS) and autoimmune cohorts. However, there is a paucity of similar studies assessing clinical utility on an all-comer patient population undergoing evaluation for suspicions of APS.

**Objectives:** To determine the sensitivity and specificity of IgG and IgM PSPT to the LAC in patients undergoing evaluation for APS.

**Methods:** Patients from June 2017 to December 2017 undergoing evaluation for APS had blood draws for the LAC, anti-cardiolipin (aCL), anti-β2 glycoprotein-1 (β2GP1), and PSPT. Both IgG and IgM isotypes were tested for each antibody. Presence of the LAC was determined by trained haematologists interpreting a number of mixing and neutralisation studies. Demographic details were abstracted from the medical record and cases meeting the SLICC criteria for systemic lupus erythematosus (SLE) and the revised Sapporo criteria for APS were enumerated.

**Results:** Fifty six eligible patients were identified. Mean age was 50±18 years. 68% were female, 20% with SLE, and 20% with APS. At time of testing, 18% were on warfarin, 7% on direct factor Xa inhibitors and 2% on low-molecular weight heparin. The LAC was negative in 45% (25/56) of those tested. In LAC negative cases, the IgG and IgM PSPT were negative in 100% and 92% of cases, respectively. In LAC positive cases, IgG PSPT was positive in 35% and IgM PSPT was positive in 61%. Compared to the LAC, IgG PSPT was 100% (95% CI: 72%, 100%) sensitive but was only 56% (40%, 70%) specific. Similarly, the IgM isotype of PSPT showed 90% (70%, 99%) sensitivity but only 66% (48%, 81%) specificity. Overall, 38% (21/56) of the cases possessed an isolated, singly positive LAC with concurrent negative IgG/M aCL and β2GP1 antibodies. In this isolated LAC positive-only group, further testing with IgG and IgM PSPT was positive in 38% and 57% of the cases, respectively.

**Conclusions:** In this study, IgG and IgM PSPT were found to be highly sensitive to the LAC and may be a useful tool in the screening of and the interpretation of the LAC.

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THU0369

### CREATION OF A WEIGHTED SLICC SLE CLASSIFICATION CRITERIA AND COMPARISON WITH PROPOSED EULAR/ACR SLE CLASSIFICATION CRITERIA

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**Background:** In previous validation work, the SLICC 2012 SLE classification criteria were more sensitive than the revised ACR-11 criteria, while both criteria had similar agreement with physician diagnoses. Both of these classification rules count each SLE manifestation equally.

**Objectives:** Our objective was to derive and test a classification rule which differentially weights the variable used in the SLICC classification rule. We also compared this rule to a recently proposed EULAR/ACR classification rule that also uses a weighted approach.

**Methods:** The physician-rated patient scenarios used to develop the 2012 SLICC classification criteria were re-employed to devise a weighted classification rule. A multiple linear regression model was constructed with the 2012 SLICC criteria variables as predictors and the binary outcome (physician classification of SLE) as the outcome. To generate the weights for each criteria, we then multiplied each criteria's coefficient by 100 and rounded to the nearest integer. The 'Direct Coombs' criteria (coefficient <1) was deleted for simplicity. The weights for the remaining manifestations were: acute cutaneous, 26 chronic cutaneous, 12 oral ulcers, 16 arthritis, 9 serositis, 16 renal without biopsy, 9 neurologic, 9 hemolytic anaemia, leukopenia or lymphopenia, 14 thrombocytopenia, 15 alopecia, 9 ANA, 11 anti-dsDNA, 19 anti-Sm, 16 antiphospholipid antibodies, 9 low complement. 11 A cutoff for classification was chosen as the score that maximised overall agreement (i.e., the sum of sensitivity and specificity) of the new weighted criteria with physician diagnosis. Patients with lupus nephritis or the new weighted classification rule of 56 or more with at least one clinical component and one immunologic component were classified as SLE. We evaluated the performance of this revised SLICC criteria, on an independent set of patient scenarios, and compared this to the performance of the older revised ACR criteria, the previous <sup>SLICC 2012</sup> criteria, and the newly proposed EULAR/ACR criteria.

**Results:** Table 1 shows the performance of the four classification rules. There was no statistically significant difference (at the 0.05-level) between any pair of rules with respect to overall agreement with the physician diagnosis.

**Abstract THU0369 – Table 1.** Sensitivity and specificity of four different SLE classification rules based on physician diagnoses of patient scenarios

Classification Rule	Sensitivity (n=349)	Specificity (n=341)	Overall Agreement (n=690)
Revised ACR-11	290 (83%)	326 (96%)	616 (89%)
SLICC 2012	340 (97%)	288 (84%)	628 (91%)
Proposed EULAR/ACR	317 (89%)	302 (90%)	619 (90%)
Weighted SLICC 2012 criteria	310 (88%)	304 (89%)	614 (89%)

**Conclusions:** The two newly derived weighted classification rules did not perform better than the existing list-based rules in terms of over-all agreement. Given that the list-based rules are easy to calculate, they may be preferred in most clinical settings.

**Disclosure of Interest:** None declared

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THU0370

### THE SIGNIFICANCE OF NON-MYDRIATIC FUNDUS EXAMINATION OPERATED BY RHEUMATOLOGISTS IN SCREENING FOR RETINOPATHY OF SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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**Background:** Retinopathy is a common fundus lesion in SLE patients. Non-mydriatic Fundus Camera images directly and objectively and avoids the mydriatic drug-induced glaucoma attack, which can not only reduce the suffering of patients but also save time and costs.

**Objectives:** To understand the significance of non-mydriatic fundus examination operated by rheumatologists in screening for retinopathy of SLE.



**Methods:** After professional training, rheumatologists use non-mydratric fundus camera to take fundus photography of inpatients in our department and record the clinical features and laboratory test results of the patients. The results of fundus photography are interpreted by both ophthalmologists and rheumatologists. The fundus results of SLE patients from July 2016 to June 2017 were analysed. 35 cases (62 eyes) of retinopathy were defined as experimental group, and 35 cases (70 eyes) without retinopathy were randomly selected as the control group.

**Results:** A total of 203 patients with SLE with an average age of 38.4±11.6 years acquired bilateral fundus results, including 28 males and 175 females (86.2%). Ocular lesions were found in 51 (25.1%) cases, of which 35 (62.6%) were common retinopathy. There were 5 cases of retinal atrophy and pigmented degeneration (4 binocular, 1 monocular), 9 cotton spots (6 binocular, 3 monocular), 7 flaming bleeding (7 binocular), 14 choroiditis with drusen (9 binocular, 5 monocular), arteries tortuous or occluded in 5 (3 binocular, 2 monocular). The SLEDAI score, anti-dsDNA level and C3 decline rate of the experimental group were significantly higher than those of the control group ( $p<0.05$  or  $p<0.01$ ), while the titer of antinuclear antibody, the positive rate of anti-SM antibody, the positive rate of anti-phospholipid antibodies, and the erythrocyte sedimentation rate had no significant difference ( $p>0.05$ ). Subsequently, we followed up 16 patients with retinopathy and SLEDAI score  $\geq 10$  and achieved remission (SLEDAI score  $\leq 4$ ) with glucocorticoid and immunosuppressive agents with an average duration of 6.5 ±4.5 months. The second examination showed that retinal lesions were improved in 9 cases (56.25%), 3 cases (18.75%) were unable to judge due to the appearance of optical media change which may caused by glucocorticoid, and 4 cases (25%) showed no obvious changes.

**Conclusions:** Non-mydratric fundus examination performed by rheumatologists may assist rheumatologists in screening for retinopathy in SLE patients, assessment of disease activity and treatment outcome.

**Disclosure of Interest:** None declared

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#### THU0371 CORRELATION BETWEEN IRREGULAR MENSTRUATION AND DISEASE ACTIVITY OF SYSTEMIC LUPUS ERYTHEMATOSUS :1 YEAR COHORT STUDY

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**Background:** Systemic lupus erythematosus (SLE) often occurs to young women of reproductive age. Not only the disease but the treatment itself could affect the capability of getting pregnant. In clinical scene, we often experience SLE patients having menstrual irregularity before their relapse. Reports about correlation between menstrual irregularity and disease activity of SLE was very limited.

**Objectives:** We started this study, that this study could be a suggestion for clinician to use the symptom as a warning sign for relapse.

**Methods:** The study design was prospective cohort. 67 patients who fulfilled  $\geq 4$  of the American College of Rheumatology (ACR) criteria for the classification of SLE whose age was 20 to 45 years old and treated as outpatient at Showa University Hospital from Feb 2016 to Jan 2017 were recruited. At the initial point, patients' disease were not active and were receiving maintenance therapy. Loss to follow up was eliminated. We set the main exposure as menstrual irregularity and the primary outcome as whether they would have relapse within 1 year from the registration. We defined the menstrual irregularity as deviation from the normal menstruation, which is 'flow occur every 25 to 35 days and last three to seven days'. We had questionnaire formed from each patient. Definition of relapse was the doctor's decision, to intensify the patients' treatment. We set the confounding as age, Japan Perceived Stress Scale (JPSS), current smoking, history of treatment with IVCY and logistic regression analysis was performed.

**Results:** The mean age was 35.7 years old. Irregular menstruation patients were 11 (16.4%). The relapse group was 12 (17.9%) and those of normal group was 59 (89%). There was no significant difference in patients' background between both groups. Adjusted with the cited confounding variable there was no significant difference between the both groups (Odds ratio 2.25; 95% Confidence Interval (CI) 0.24 to 20.7;  $p=0.47$ ).

**Abstract THU0371 – Table 1.** Abstract THU0371 – Table 2. Logistic regression analysis. Adjusted with age, history of treatment with IVCY, current smoking, and JPSS.

	Total	Normal menstruation group	Irregular menstruation group	p value
Number	67	36	11	
Age median [IQR]	35 [31-41]	38 [31-41]	37 [29-41]	0.26
0 month SLEDAI median [IQR]	32 [6]	30 [6]	42 [6]	0.04
JPSS median [IQR]	13 [11-18.8]	13 [11-18.5]	13 [9-29]	0.51
Current smoking (%)	8 (11.9)	6 (16.7)	2 (18.2)	0.4
History of IVCY (%)	10 (14.9)	6 (16.7)	4 (36.4)	0.74
0 month PSL dose median [IQR]	5.3 [4-10]	5.7 [4.3-9.6]	5 [3-11]	0.73
0 month Immune-Suppressing drug (%)	40 (59.7)	26 (72.2)	14 (127)	0.29

IQR: interquartile range; SLEDAI: Systemic Lupus Erythematosus Disease Activity Index; JPSS: Japan Perceived Stress Scale; IVCY: immunosuppressive drug; PSL: prednisolone.

	Coefficient ( $\beta$ )	SE	Wald $\chi^2$	p value	Odds ratio	95%CI
Irregular Menstruation Group	0.40	0.56	0.51	0.47	2.25	0.24-20.7

Adjusted with age, history of treatment with IVCY, current smoking, and JPSS

**Conclusions:** We investigate that whether menstrual irregularity could be the predictor for the disease relapse, but we could not prove the significant relation.

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#### THU0372 ULTRASONOGRAPHIC SCORING OF THE MAJOR SALIVARY GLANDS: IS THERE A RELATIONSHIP WITH DISEASE ACTIVITY AND FUNCTIONAL STATUS OF THE GLANDS ?

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**Background:** Ultrasonography (USG) of major salivary glands (SG-USG) is a non-invasive tool that has been used to evaluate salivary glands in primary and secondary Sjogren's syndrome (SjS).

**Objectives:** We aimed to investigate relation between the ultrasonographic scoring of major salivary glands and systemic disease activity or salivary secretion in patients with primary SjS.

**Methods:** Seventy-five SjS patients (F/M:73/2) with the mean age of 52±12 and duration of follow-up period of 58±54 months fulfilling ACR-EULAR classification criteria (2002) were included. Disease activity indexes (Sjögren's Syndrome Patients Reported Index (ESSPRI), Visual Analogue Scale (VAS), EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI)) were recorded. Simultaneously, sialometric evaluation of the salivary glands was performed. Major salivary glands (bilateral parotid and submandibular glands) were scored according to two different scoring systems [Hocevar A. (0–48) and Milic VD. (0–12)] and elastography was recorded as well.

**Results:** Demographics, clinical characteristics, disease activity indexes and SG-USG scores were summarised in table 1 and table 2. Forty-one (55%) and 45 (60%) patients had the cut-off values of  $\geq 17$  (Hocevar) and  $\geq 6$  (Milic USG). The patients with the scores of  $\geq 17$  (Hocevar) were found to have higher scores of ESSPRI-total (16±6 vs 13±7,  $p=0.045$ ) and lower sialometry (4.6±4.7 vs 8.4±4.6 ml,  $p=0.002$ ). Scores of Hocevar and Milic-USG were negatively correlated with sialometry ( $r=-.430$ ,  $p=0.001$  and  $r=-.430$ ,  $p=0.001$ ). Hocevar, Milic and

elastography-USG scores were shown to be higher in patients with sialometry of  $\leq 1.5$  ml ( $n=7$ ) ( $28\pm 3$  vs  $17\pm 10$ ,  $p=0.010$ ,  $8\pm 1$  vs  $5\pm 3$ ,  $p=0.006$  and  $9\pm 1$  vs  $5\pm 2$ ,  $p=0.028$ ) and anti-Ro positivity ( $n=24$ ) ( $24\pm 10$  vs  $13\pm 8$ ,  $7\pm 3$  vs  $4\pm 2$ ,  $p<0.001$  and  $7\pm 2$  vs  $3\pm 2$ ,  $p=0.003$ ). The patients with severe parotid involvement (inhomogeneity/hypoechoic areas  $\geq 2$ ) had more frequent anti-Ro and anti-La positivity (80 vs 42%,  $p=0.004$  and 48 vs 17%,  $p=0.011$ )

**Abstract THU0372 – Table 1.** Demographics and Clinical Characteristics of SjS patients.

	n=75
Sicca symptoms	69(92%)
Arthralgia/arthritis	62(83%)
Parotitis	20(27%)
Raynaud Phenomenon	12(16%)
Leucocytoclastic vasculitis	5(7%)
Peripheral neuropathy	7(9%)
Interstitial lung disease	3(4%)
Lymphadenopathy	12(16%)
Congenital heart block	2(3%)
ANA	62 (82%)
Anti-Ro/La	35(47%)
ESR(mm/h)	32±20
CRP(mg/l)	4,8±6,1

**Abstract THU0372 – Table 2.** Disease Activity Indexes and SG-USG Scores of SjS Patients

	n=75
ESSPRI-total	14,8±6,5
-dryness	5,4±2,5
-fatigue	4,8±2,8
-pain	4,6±3
VAS	50±22
ESSDAI-total	2,1±3,5
Hocevar-USG Score	19±5
Milic-USG Score	6±3
Sialometry (ml) (n=45)	6,4±5
Elastography (n=32)	5,3±2,6

**Conclusions:** Hocevar scoring system of major salivary glands was found to be related to patient reported activity in SjS. USG scores were associated with reduced saliva secretion and anti-Ro positivity. Severe parotid involvement was shown to be related to anti-Ro and La positivity. Evaluation of SG-USG including different scoring systems and elastography might reflect function of the salivary glands.

**Disclosure of Interest:** None declared

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#### THU0373 THE MARKERS USEFUL IN PREDICTING LUPUS NEPHRITIS IN CLINICAL PRACTICE

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**Background:** Lupus nephritis (LN) is one of the most severe clinical manifestations of systemic lupus erythematosus (SLE). LN can be found in approximately 50% of SLE patients. The renal biopsy remains the gold diagnostic standard. However non-invasive and clinically practical laboratory markers of kidney damage in this disease are sought.

**Objectives:** The aim of the study was to assess the utility of biomarkers like inflammable indicators, complement system components and albuminuria in a single urine sample for prediction of kidney involvement and disease activity in patients with SLE.

**Methods:** A prospective study included 33 patients (81.8% women) with SLE criteria according to SLICC (Systemic Lupus International Collaborating Clinics) in age of  $39.0\pm 14.3$  years. Disease-duration ranged 6–60 months. We performed full physician examination and we excluded patients with active infection. The

disease activity based on the SELENA-SLEDAI scale was assessed and divided into groups: low activity (L) $<6$ , moderate (M) 7–12, high (H) $>12$  points.

In the blood samples complement components (C3, C4) (g/L), C-reactive protein CRP (mg/L), interleukin 6 (IL-6) (pg/mL), serum creatinine concentration (sCr) (mg/g), ESR (mm/h), glomerular filtration rate (eGFR) according to CKD-EPI (ml/min/1.73 m<sup>2</sup>) were determined. The concentration of albumin (uAlb) (mg/dl) and creatinine sCr (g/dL) from the morning urine sample was measured and the albumin/creatinine index (uACR) (mg/g) was calculated. Based on the obtained results, patients were divided into stages of chronic kidney disease (CKD) according to .KDIGO 2012. A daily proteinuria (DP) (g/24 hour) was performed. In the assessment of statistical significance, Kruskal-Wallis or Mann-Whitney U-tests were used.

**Results:** In our study the SLE activity was as follows (%): L-24 (72.7), M-6 (18.2), H-3 (9.1). The average values (range) of biomarkers of renal function were: Cr= $0.81\pm 0.27$  (0.55–1.65), eGFR= $99.6\pm 24.4$  (46–131), uAlb= $13.6\pm 34.4$  (0.04–161.0), uACR= $121.3\pm 356.3$  (4.8–1905.3), DP= $0.32\pm 0.92$  (0.015–5.3), and other biomarkers: OB= $26.1\pm 25.9$  (4.0–99.0); CRP= $10.3\pm 28.1$  (0.2–148.7); IL-6= $7.8\pm 14.7$  (0–78.3); C3= $1.08\pm 0.36$  (0.33–2.25); C4= $0.16\pm 0.09$  (0.02–0.43). The study group met the CKD criteria: G1 n=21 (63.6%), G2 n=9 (27.3%), G3 n=3 (9.1%); A1 n=26 (78.8%), A2 n=3 (9.1%), A3 n=4 (12.1%).

We showed a negative relationship between the eGFR and: CRP (R=–0.49,  $p=0.005$ ), IL-6 (R=–0.48,  $p=0.005$ ) and C4 (R=–0.43,  $p=0.01$ ). There was also a significant dependence of the SLEDAI SLE activity with: uAlb (L, H) ( $p=0.04$ ), DP (M, H) ( $p=0.03$ ), uACR in the whole study group ( $p=0.04$ ) and between uACR and DP ( $p=0.0003$ ).

**Conclusions:** Our studies showed that the risk of kidney damage in SLE may depend on the concentration of CRP, IL-6, C4. In addition albuminuria (uAlb, uACR) correlates with the value of DP and SLE activity, what indicates the dominant glomerular lesion in the etiopathogenesis of proteinuria in LN.

**Disclosure of Interest:** None declared

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#### THU0374 FACTORS ASSOCIATED WITH HIGH-DOSE CORTICOSTEROID USE IN SLE PATIENTS POST INITIATION OF SLE THERAPY

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**Background:** Systemic lupus erythematosus (SLE) therapies include non-steroidal anti-inflammatory drugs, antimalarials, systemic immunosuppressants, and biologics with corticosteroids as necessary. The majority of these current therapies are only partially effective in disease control. Despite treatment, patients may experience flares of disease activity, which can lead to progressive end-organ damage. Severe flares may require intensive immunosuppression, including with high-dose corticosteroids, with risk including end-organ damage.

**Objectives:** To understand the unmet need in SLE by quantifying use of high-dose ( $\geq 40$  mg/day) corticosteroids and determining factors associated with its use.

**Methods:** This study utilized the Truven Marketscan commercial claims database. Patients were indexed on first use of antimalarial, oral immunosuppressant or biologic during 2012–2013 (first use determined based on no claims for the 3 drug classes during the 1 year pre-index). Included patients had 2 recorded SLE diagnoses, were 18–50 years of age and had continuous medical and prescription enrollment from baseline through the 2 year follow-up. Patients with other pre-specified autoimmune disorders or cancers during the study period (baseline through follow-up) were excluded. During follow-up, fill of at least 1 high-dose corticosteroid prescription was assessed and associative logistic regression modeling performed.

**Results:** 1401 patients (93% female; mean age 38.4 years) met the study criteria; 79% were indexed on an antimalarial, 15% on an oral immunosuppressive, 1% on a biologic and 5% on a combination of at least 2 of the aforementioned classes. 16% patients received a diagnosis code for nephritis or chronic kidney disease (CKD), 3% for myocarditis or pericarditis, and 13% for thrombocytopenia or leukopenia. During baseline, 56% of patients had at least 1 visit to a rheumatologist and 13% filled at least 1 high-dose corticosteroid prescription. During follow-up, 22% of patients had at least 1 high-dose corticosteroid prescription. Factors significantly associated ( $p<0.05$ ) with high-dose corticosteroids during follow-up included: baseline rheumatologist visit (OR=0.62; 95% CI=0.47–0.82), number of SLE medication classes received during follow-up (OR=1.85, 95% CI=1.36–2.51), receipt of high dose corticosteroid during baseline (OR=5.21, 95% CI=3.60–7.53), nephritis or CKD (OR=1.85, 95% CI=1.29–2.64), myocarditis/pericarditis (OR=3.38, 95% CI=1.75–6.55), and thrombocytopenia/leukopenia (OR=1.70, 95% CI=1.17–2.48).

**Conclusions:** A number of baseline factors were associated with high-dose corticosteroid treatment during the follow-up period; one notable factor is the high percentage of patients using high-dose corticosteroids ( $\geq 40$  mg/day). This indicates

that important subsets of patients experience inadequate disease control with current therapies. This study reveals high-dose corticosteroid use is prevalent in SLE management broadly, underscoring the unmet need in this population.

**Disclosure of Interest:** K. Schroeder Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, J. Paik Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, R. Hoffman Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, S. Gelwicks: None declared  
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THU0375

### QUALITY OF LIFE IN INDIAN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN DURABLE REMISSION: PSYCHOSOCIAL AND DEMOGRAPHIC FACTORS

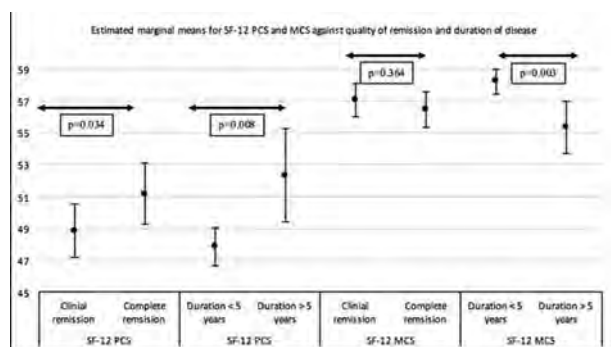
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**Background:** Remission in systemic lupus erythematosus (SLE) is uncommon. Detrimental effect of disease activity on quality of life (QoL) is reported but literature on QoL in lupus patients in durable remission is scant.

**Objectives:** To study QoL in Indian SLE patients in durable remission

**Methods:** We retrospectively included female SLE patients fulfilling  $\geq 4$  SLICC Classification Criteria, followed regularly at our clinic, who were in durable remission as determined by European consensus criteria (complete/clinical remission  $\pm$  immunosuppressive drugs). QoL was assessed with Medical Outcomes Study Short-Form-12 (SF-12). We also collected data on demographics (age, duration of disease, years of education), duration and quality (complete versus clinical) of remission and patient reported fatigue through fatigue severity scale (FSS). A structured interview with a clinical psychologist using ICD-10 Diagnostic Criteria for Research (DCR) was performed to diagnose depression. Age matched female control subjects were also included and underwent similar exercises. Association of physical and mental component summary scores (PCS and MCS) of SF-12 with depression, quality and duration of remission, duration of disease, years of education and FSS were tested with generalised linear models using Gamma regression with log-link function.

**Results:** We included 106 female SLE patients (age:  $28.9 \pm 7.6$  years; duration of disease:  $45.1 \pm 34.8$  months; years of education:  $9.6 \pm 5.2$ ; depression present in 41 (38.7%) and 98 female controls (age:  $30.4 \pm 7$  years; years of education:  $10.8 \pm 6.2$ ; depression present in 32 (32.7%). At last visit, clinical remission was present in 68 (64.2%) and complete remission in 38 (35.2%). Duration of remission achieved were:  $<1$  year in 17 (16%), 1–2 years in 40 (37.7%), 2–3 years in 18 (17%) and  $>3$  years in 31 (29.2%). Steroid-free remission was present in 64 (60.37%) and the rest 42 (39.62%) were on  $\leq 5$  mg/d prednisolone. All were on hydroxychloroquine. A stable dose of 2nd immunosuppressive drug was present in 54 (50.94%) with 3 on stable dose of mycophenolate and 51 on azathioprine. SLE patients had comparable SF-12 PCS ( $48.4 \pm 8.1$  vs  $47.1 \pm 7$ ,  $p=0.098$ ) and MCS ( $57.7 \pm 3.4$  vs  $56.6 \pm 5.6$ ,  $p=0.199$ ) as compared to controls. Among lupus patients, both PCS ( $r=-0.616$ ,  $p<0.001$ ) and MCS ( $r=-0.298$ ,  $p<0.001$ ) were correlated with FSS and years of education (with PCS,  $r=-0.215$ ,  $p=0.027$ ; with MCS,  $r=-0.269$ ,  $p=0.005$ ). Independent predictors of PCS were: clinical remission (Odds ratio (OR) 0.95, 95% confidence interval (CI) 0.92–0.99,  $p=0.033$ ), FSS (OR 0.90, 95% CI 0.89–0.92,  $p<0.001$ ) and disease duration  $<5$  years (OR 0.92, 95% CI 0.86–0.97,  $p=0.006$ ). Independent predictors of MCS were: FSS (OR 0.991, 95% CI 0.983–0.999,  $p=0.025$ ), years of education (OR 0.998, 95% CI: 0.995–0.999,  $p=0.028$ ) and disease duration  $<5$  years (OR 1.053, 95% CI 1.018–1.089,  $p=0.003$ ). Estimated marginal means of PCS and MCS against quality of remission and duration of disease are plotted in figure 1.



**Abstract THU0375 – Figure 1.** Estimated marginal means for SF-12 PCS and MCS against quality of remission and duration of disease

**Conclusions:** Indian lupus patients in durable remission had similar physical and mental QoL compared to healthy controls. Physical QoL was better in patients with complete remission, longer disease duration and low fatigue. Mental QoL was better in patients with low fatigue, less education and longer disease duration.

**Disclosure of Interest:** None declared

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THU0376

### CHARACTERISTICS OF PRIMARY SJÖGREN'S SYNDROME PATIENTS WITH MORPHOLOGICAL CHANGES OF THE PAROTID GLANDS IN MR IMAGING

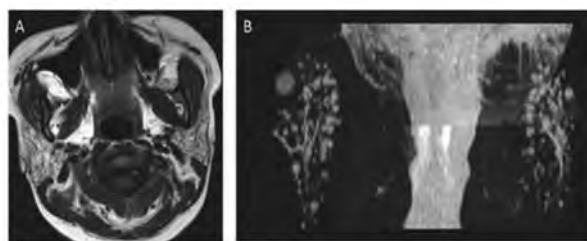
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**Background:** Primary Sjögren's syndrome (pSS) is a chronic autoimmune disease characterised by injury of exocrine glands, and a considerable proportion of pSS patients develop extraglandular involvement. The parotid glands are the most frequently involved glands in pSS. Conventional parotid examinations, such as X-Ray sialography and 99mTechnetium (<sup>99mTc</sup>) pertechnetate scintigraphy, played an important role in the diagnosis of pSS. However, X-Ray sialography only shows the abnormality of parotid ductal system and there is exposure to radionuclides with 99mTechnetium. Both examinations are invasive, while MR imaging is noninvasive, radiation-free, and sensitive to the morphological and signal changes of the parotid glands. MR sialography could be used to evaluate the parotid ductal system without the need for a contrast agent. But the clinical application value of parotid grand MR imaging in pSS patients has not been verified.

**Objectives:** The purpose of this study was to investigate the morphological changes of the parotid glands in MR imaging in patients with pSS and the correlations between morphological changes and the clinical manifestations.

**Methods:** Ninety-nine pSS patients who underwent parotid 3.0 Tesla MR imaging (T1, T2 and T2 STIR) were enrolled in this study. The morphological changes of the parotid glands (grades 0–3) and ducts (grades 0–4) were rated according to our previous studies.<sup>1</sup> Patients were divided into normal parotid MR group (both glands grade and ducts grade were 0) and abnormal parotid MR group. The correlations between morphological changes of the parotid glands and clinical or serological characteristics were analysed by chi-square test.

**Results:** There were 93 females (93.9%) and 6 males (6.1%) in this study. The mean age and median disease duration were 47.4 years and 24 months. There were 50 (50.5%) pSS patients in parotid grand grade 0, 27 (27.3%) in grade 1, 15 (15.2%) in grade 2 and 6 (6.1%) in grade 3 (Fig 1A), and there were 53 (53.5%) pSS patients in parotid duct grade 0, 15 (15.2%) in grade 1, 17 (17.2%) in grade 2, 4 (4.0%) in grade 3, and 10 (10.1%) in grade 4 (Fig 1B). We found that patients in abnormal parotid MR group presented lower positive rates of myasthenia and higher positive rates of xerostomia, Schimer's test, serum anti-SSA antibodies, anti-Ro-52 antibodies, antinuclear antibodies (ANA), rheumatoid factor (RF), plasma globulin, immunoglobulin G (IgG), and Hashimoto thyroiditis ( $p<0.05$ ). But no significant difference was observed between two groups in the incidence of salivary gland enlargement, articular involvement, dermatological involvement, interstitial lung disease, tubulointerstitial nephritis and primary biliary cirrhosis.



**Abstract THU0376 – Figure 1.** A: Axial T1-weighted image shows homogenous signal intensity of bilateral parotid glands with obvious hyperintense nodules (grade 3). B: MR sialography shows duct dilation of bilateral parotid glands (grade 4).

**Conclusions:** The results indicated that parotid MR imaging is a noninvasive, radiation-free examination with a potential role in diagnosing pSS. pSS patients with morphological changes of the parotid glands in MR imaging were more likely to have xerostomia, hyperglobulinemia and thyroid involvement.



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THU0377

### INFLUENCE OF UNDIAGNOSED VERTEBRAL FRACTURES ON ORGAN DAMAGE IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Objectives:** To investigate the influence of asymptomatic vertebral fractures on organ damage and to identify risk factors associated with critical organ damage in women with systemic lupus erythematosus (SLE).

**Methods:** 197 women with SLE were included in this study. Bone mineral density (BMD) measurements of the hip and spine were performed using the dual energy X-ray absorptiometry (DXA). Vertebral fracture assessment (VFA) was done for detection vertebral fractures using a method described by Genant. Accumulated damage was scored using the SLICC/ACR damage index (SDI). Critical organ damage was defined as SDI>3.

**Results:** Vertebral fractures were developed in 55 (27.9%) women with SLE. Half of all women with SLE (n=31, 15.7%) had asymptomatic vertebral fractures which were diagnosed for the first time in this study. 131 (66.5%) women with SLE had critical organ damage (SDI>3). Average SDI before and after morphometry was 4.4±2.2 and 5.3±2.6 respectively. Multivariate analysis showed age (p=0.01), cumulative dose of glucocorticoids (p=0.00005), previous therapy with cyclophosphamide (p=0.04) were significantly associated with critical damage in women with SLE.

**Conclusions:** Detection of vertebral fractures helps in counting accumulated organ damage correctly. VFA in the combination with DXA in women with SLE is an effective method for diagnostic asymptomatic vertebral fractures.

**Disclosure of Interest:** None declared

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THU0378

### WIRE-LOOP LESION IS ASSOCIATED WITH SEROLOGICAL IMMUNE ABNORMALITY, BUT NOT RENAL PROGNOSIS IN LUPUS NEPHRITIS

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**Background:** International Society of Nephrology/Renal Pathology Society (ISN/RPS) 2003 Classification of Lupus Nephritis (LN) defines wire-loop lesion (WL) as an active lesion (AL). In it, LN patients with WL are classified as class III or IV, which are associated with a poor prognosis and recommended to be treated by intense immunosuppressive therapy including corticosteroid, cyclophosphamide, mycophenolate mofetil and other immunosuppressants.<sup>1</sup> However, among AL, few reports have focused on the clinicopathological impact of WL on serological immune abnormality and renal prognosis.

**Objectives:** To identify clinicopathological characteristics associated with WL, and to clarify whether WL predicts renal prognosis of LN.

**Methods:** We enrolled 117 Japanese LN patients subjected to renal biopsy in 11 hospitals from 2000 to 2017. We measured clinical findings at the time of renal biopsy, including creatinine (Cr), estimated glomerular filtration rate (eGFR), total protein (TP), IgG, IgA, IgM, C3, C4, CH50, anti-nuclear antibodies (Abs), anti-double strand DNA (dsDNA) Abs, anti-Sm Abs, anti-RNP Abs in the sera, urinalysis, and presence of comorbidities (antiphospholipid antibody syndrome, hypertension, hyperlipidemia, diabetes mellitus, and hyperuricemia). Renal biopsy findings were classified by ISN/RPS classification including AL and chronic lesions (CL). Immune deposit was evaluated by immunofluorescence. We also measured Cr and eGFR at the last patient visit, and recorded medications prescribed for LN. Chronic kidney disease (CKD) was defined as eGFR <60 ml/min/1.73 m<sup>2</sup>. In class III or IV patients, we retrospectively compared these clinical and histological findings between those with WL (WL +group) and without WL (WL- group).

**Results:** Of 117 patients, 94 (81.2%) were classified as class III or IV (78 females; mean age 41.3 years; observational period 5.8±5.2 years). WL was found in 27 of them (28.7%). Although there was no significant difference in renal function (eGFR; 81.1±31.4 vs 80.6±34.4 ml/min/1.73 m<sup>2</sup>, p=0.91), WL +group had higher

titer of serum anti-dsDNA Abs (median values; 205 vs 67 IU/ml, p=0.011) and lower level of TP (5.7±1.2 vs 6.3±1.0 g/dl, p=0.025) than WL- group. There were no significant differences in any other clinical findings. In histological findings, most WL (96.3%) were accompanied by other ALs such as endocapillary proliferation and/or crescent formation. WL +group had a higher frequency of class IV, AL and IgM deposit, while CL did not differ between the two groups. Linear regression analysis revealed associations between anti-dsDNA Abs and IgM deposit and WL (β=0.48, p<0.01; β=0.26, p=0.016, respectively). There was no difference in the latest renal function (eGFR; 76.9±27.5 vs 74.0±29.5 ml/min/1.73 m<sup>2</sup>, p=0.72) between the two groups. Cox regression analysis revealed significant associations between AL such as necrosis, CL, initial eGFR, HT, HL and medication for LN with CKD at the last visit, but not with WL (p=0.13).

**Conclusions:** WL was associated with serum anti-dsDNA Abs, but not with renal prognosis, suggesting that WL reflects immune abnormality, but is not an independent factor predictive of the renal prognosis of LN. Although WL is defined as an AL in the present classification, this may need to be revised to better reflect its clinical impact.

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THU0379

### CORONARY ARTERY DISEASE IN SLE: A CASE-CONTROLLED ANGIOGRAPHIC STUDY

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**Background:** Coronary artery disease (CAD) is a major cause of morbidity and mortality in systemic lupus erythematosus (SLE) patients.<sup>1</sup> Whether SLE is a cardiovascular risk factor *per se* remains controversial.

**Objectives:** This study was conducted to determine the clinical and angiographic characteristics of SLE patients with CAD and to compare them to those of control non-SLE patients with CAD.

**Methods:** All SLE patients who underwent a coronary angiography procedure in our tertiary centre between 2005 and 2016 were enrolled in the study. Those without significant atherosclerosis (stenosis >50%) were excluded. Each SLE patient was matched by sex and age at catheterization with seven non-SLE controls with significant CAD. Angiographic characteristics were reviewed by two independent cardiologists.

**Results:** Among the 73 SLE patients who underwent coronary angiography, 28 patients had at least one significant coronary atherosclerotic lesion. The SLE patients were predominantly female (75%, median age of 55.7 years) with a long-standing disease duration (median SLE duration of 20.5 years). Ten patients (35%) had renal involvement, and 9 patients (32%) had antiphospholipid syndrome. The patients with SLE had fewer cardiovascular risk factors (1.6 vs 2.1, p=0.01) than the controls, including lower body mass index (23.8 kg/m<sup>2</sup> vs 24.98 kg/m<sup>2</sup>, p=0.03), less frequent family history of coronary artery disease (3.5% vs 18%, p=0.049) and less diabetes (7% vs 22%, p=0.07) than controls. However, SLE patients were more likely to have chronic kidney failure (35% vs 20%, p=0.07) and to need hemodialysis (17% vs 2%, p=0.001). The SLE patients more often had multivessel disease (50%).

**Conclusions:** While they have fewer cardiovascular risk factors, patients with SLE experience more severe CAD than non-SLE patients, suggesting that SLE, associated conditions or the treatments themselves play key roles in the development of atherosclerosis.<sup>2</sup>

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**Disclosure of Interest:** None declared

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**THU0380** **DIAGNOSTIC UTILITY OF ANTI-DFS-70 AUTOANTIBODIES IN A UNIVERSITY RHEUMATOLOGY CENTRE**

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**Background:** The detection of antinuclear autoantibodies by immunofluorescence (ANA-IFT) supports the diagnosis of many different autoimmune and rheumatological diseases (ARE). In combination with the detection of specific autoantibodies against known extracted nuclear antigens (ENA) ANAs have high diagnostic sensitivity and specificity. However, positive ANA-IFT may also occur in disease states not related to ARE and even in healthy individuals. Especially in the latter group this may lead to unnecessary and repeated hospital visits, as well as avoidable diagnostic and therapeutic interventions. Anti-DFS70 autoantibodies were introduced as a biomarker for the exclusion of ARE in ANA-IFT +patients without additional ENAs and non-specific clinical history.

**Objectives:** To evaluate if the diagnostic pathway for suspected or established ARE patients in our centre benefits from the addition of anti-DFS70 autoantibodies to an existing ENA test profile.

**Methods:** Serum from patients was tested for anti-DFS70 autoantibodies by the ANA-Profil 3 plus DFS70 line blot (Euroimmun, Lübeck Germany).

**Results:** In 2017 the Freiburg university rheumatology centre tested 671 patients, referred to for diagnosis or follow up of ARE, for anti-DFS70 and 126 patients were found positive. Descriptive statistics of the anti-DFS70 positive vs negative cohorts are summarised in table 1. Of the 126 anti-DFS70 positive patients, 53 (42%) had one or more additional ENAs positively tested (4 snRNP/Sm, 1 Sm, 15 SS-A/Ro, 15 Ro-52, 2 SS-B/La, 4 Scl-70, 8 PM-Scl, 2 PM-Scl75, 1 SRP, 2 Ku, 1 Jo-1, 4 Centromer, 2 PCNA, 2 Nucleosomes, 9 Histones, 1 ribos-P-Prot, 2 AMA-M2, 6 ds-DNA) and 3 (2%) patients had anti-DFS70 in conjunction with anti CCP autoantibodies. 70 (56%) patients were tested single positive for anti-DFS70. 81 (64%) of anti-DFS70 positive patients either had an established diagnosis of ARE or were newly diagnosed with ARE based on clinical criteria and laboratory results. The majority of these patients had additional ENAs or other autoantibodies tested positive, as described above. A diagnosis of ARE was excluded or revised with help of the anti-DFS70 result in 45 (36%) patients, all of these were anti-DFS70 positive only. In 10 of these patients (20%) preexisting therapies were discontinued (9 Hydroxychloroquin, 1 MTX/sulfasalazine).

	Anti-DFS70 positive (n=126)	Anti-DFS70 negative (n=544)	p-value
Male, n (%)	19 (15.1)	111 (20.4)	n.s.
Mean age, years (min-max)	47 (18–77)	52 (14–88)	n.s.
DFS70 +++, n (%)	82 (65.1)	NA	NA
DFS70 ++, n (%)	13 (10.3)	NA	NA
DFS70 +, n (%)	10 (7.9)	NA	NA
DFS70 (+), n (%)	21 (16.7)	NA	NA

**Abstract THU0380 – Table 1.** Descriptive statistics of the patient cohorts tested for anti-DFS70-antibodies

**Conclusions:** We found a high added diagnostical value of anti-DFS70 autoantibodies testing, since they were helpful to rule out or revise a previously suspected diagnosis of ARE in more than a third all patients tested anti-DFS70 positive at our centre. However, patients referred to a university rheumatology centre are a highly selected cohort and have a higher probability being finally diagnosed with ARE, and thus consideration of clinical criteria and thorough testing for additional autoantibodies is recommended in such a setting since also many patients with confirmed ARE will test positive for anti-DFS70.

**Disclosure of Interest:** None declared

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**THU0381** **HIGH LEVELS OF CIRCULATING TYPE I, II AND III INTERFERONS DEFINE DISTINCT PATIENT SUBSETS WITH ACTIVE SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)**

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**Background:** Interferons (IFN) play a major role in SLE pathogenesis.<sup>1</sup> IFNs type I (predominately IFN- $\alpha$ s) are of major importance,<sup>2</sup> but IFN type II (IFN- $\gamma$ ) and IFNs type III ( $\lambda$ ) have also important roles.<sup>3,4</sup> How the levels of circulating IFNs type I, type II and type III relate to each other, and if they associate with any particular SLE disease manifestations is not known.

**Objectives:** We investigated serum levels of type I, type II, and type III IFNs and explored how these measurements relate to each other and to specific organ manifestations in patients with SLE.

**Methods:** We studied 497 well-characterised SLE patients and 322 controls. Functional type I IFN-activity (IFN-activity) was measured by WISH cell assay. IFN- $\alpha$  and IFN- $\lambda$ 1 were measured by ELISA, and IFN- $\gamma$  by MSD 30-plex assay. High IFN-activity/levels were defined as value over 3rd quartile of the measurement.

**Results:** SLE patients had higher levels of all investigated IFNs. IFN-activity correlated with IFN- $\alpha$  and IFN- $\gamma$ . High functional IFN-activity associated with active SLE in most domains: weight loss, fatigue, fever, rash, lymphadenopathy, arthritis and nephritis. The IFN- $\gamma$  high group had active disease with higher rates of nephritis, arthritis, leuko-, lymphopenia and Sm, SmRNP, RNP68, Ro52 and Ro60 autoantibodies. A higher proportion of the IFN- $\alpha$  high group had active rash, lymphadenopathy, Ro52 and La autoantibodies, while rates of antiphospholipid antibodies/syndrome, vascular events and renal affection were lower. High IFN- $\lambda$ 1 associated with anti-nucleosome autoantibodies and lymphopenia.

**Conclusions:** High type I IFN functional activity is associated with active SLE in the majority domains. A severe SLE phenotype, including active nephritis, arthritis and anti-Sm/SmRNP autoantibodies is associated with high IFN- $\gamma$ , while rash and a benign cardiovascular profile are linked to high serum IFN- $\alpha$ . Isolated increase in IFN- $\lambda$ 1 is only coupled to lymphopenia and antinucleosome antibodies. Our findings demonstrate that several IFNs can be elevated at the same time in SLE and the importance of IFN- $\gamma$  has so far been underscored. Sub-setting of SLE patients might be important when planning future clinical trials.

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**THU0382** **FATIGUE IN CHINESE PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: CONTRIBUTING FACTORS AND EFFECTS ON THE QUALITY OF LIFE**

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**Background:** Fatigue is a very common symptom in Systemic Lupus Erythematosus (SLE), affecting more than 90% of patients<sup>1</sup>. Fatigue can lead to a decline in the quality of life<sup>2</sup>. Fatigue in SLE patients is associated with adverse demographic, clinical, and psychological characteristics<sup>3,4</sup>. However, there is no systematic study of SLE fatigue in China.

**Objectives:** This cross-sectional study aims to evaluate the contributors of fatigue and the effects of fatigue on the quality of life in Chinese SLE patients.

**Methods:** A self-report survey was administered to 119 SLE patients and 105 healthy individuals using the Fatigue Severity Scale (FSS) to assess the severity of fatigue. SLE patients completed the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) for disease activity, the Hospital Anxiety and Depression Scale (HADS) for anxiety and depression, the Pittsburgh Sleep Quality Index (PSQI) for sleep quality and the Short Form 36 health survey for the quality of life. Meanwhile, healthy individuals completed the Hospital Anxiety and Depression Scale (HADS) and the Pittsburgh Sleep Quality Index (PSQI). We used independent samples t-tests, Chi square analysis and logistic regression modelling to analyse these data.

**Results:** Our results found that the FSS score of patients with SLE was higher than that of the controls ( $4.33 \pm 1.66$  versus  $3.41 \pm 1.39$ ;  $p < 0.001$ ). The SLE patients were significantly different from the control group in terms of anxiety, depression and quality of life. There were significant correlations among course of disease, anxiety, depression, subjective sleep quality, sleep disorders and fatigue in SLE patients. Meanwhile, logistic regression models identified depression and

sleep disorders as predictors of fatigue. In SLE patients, fatigued patients had lower quality of life than those who were non-fatigued.

**Conclusions:** This is the first known evaluation of the contributors of fatigue and the effects of fatigue on SLE patients' quality of life in China. The majority of Chinese SLE patients suffer from fatigue, which significantly impairs their quality of life. The results emphasise the need for holistic assessment and targeted intervention/management of SLE patients to relieve the symptoms of fatigue and finally improve their quality of life.

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#### THU0383 PERFORMANCE OF MUSCULOSKELETAL INVOLVEMENT OF SYSTEMIC LUPUS ERYTHEMATOSIS: AN ULTRASOUND STUDY IN 114 PATIENTS

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**Background:** Joints are commonly involved in systemic lupus erythematosus (SLE). Ultrasound (US) has been widely used in rheumatoid arthritis (RA), however rarely applied and studied in SLE.

**Objectives:** To investigate the ultrasonic changes of the symptomatic joints and their correlations with clinical manifestations in SLE patients.

**Methods:** 114 SLE patients who complained of arthralgia or arthritis from May 2014 to Aug 2017 and 15 Rhupus patients due to overlapping with RA were recruited for ultrasound evaluation. Ultrasound scan of the symptomatic joint areas was completed. The correlation between ultrasonographic changes and clinical characteristics was analysed. Besides that, US changes of bilateral wrists and hands of Rhupus patients were compared with those of the SLE patients.

**Results:** In a total of 1866 joints scanned, synovial hyperplasia, tenosynovitis, erosion and osteophytes were all observed. Synovial hyperplasia was more often observed in knees in 28.6% patients (12/42), ankles in 25% patients (7/28), wrists in 23.3% patients (23/69) and elbows in 20% patients (5/25). Tenosynovitis and erosion were most commonly found in shoulders in 35% (7/20) and 65% (13/20) patients. Osteophytes were more common in proximal interphalangeal (PIP) joints, elbows and knees. Among 69 patients with 22 joints (bilateral wrists and hands) scanned, synovial hyperplasia was observed in 25 patients (36.2%) and erosion in 22 patients (31.8%). The agreement between synovial hyperplasia and swollen joints in PIP was fair ( $\kappa=0.633$ ,  $p<0.01$ ), however poor in wrists ( $\kappa=0.089$ ,  $p=0.584$ ). 18.4% patients with synovial hyperplasia had no tenderness or swollen clinically, while 15.7% patients with tenderness or swollen had no synovial hyperplasia on ultrasound. No correlation was found between ultrasound changes with SLE disease activity index. Both synovial hyperplasia and erosion were more common in Rhupus patients (73.3% vs. 36.2%,  $p=0.08$ ; 66.7% vs. 26.0%,  $p=0.03$ ) with significantly higher GS score ( $7.4\pm 6.4$  vs.  $1.6\pm 4.1$ ,  $p=0.04$ ) than SLE alone patients.

**Conclusions:** Variety of changes can be observed by ultrasound at different joints in SLE patients. The ultrasonographic changes and clinical manifestations did not always correspond to each other. Synovial hyperplasia and erosion was more common in Rhupus patients.

**Disclosure of Interest:** None declared

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#### THU0384 SALIVARY GLAND ULTRASONOGRAPHY AND STIMULATED SALIVARY FLOW CORRELATED WITH SALIVARY GLAND BIOPSY AMONG PATIENTS WITH SJÖGREN SYNDROME AND SICCA SYMPTOMS: EXPERIENCE FROM A SINGLE MEDICAL CENTRE IN TAIWAN

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**Background:** Sjögren's syndrome is an autoimmune disease that involves several organs. In the latest classification criteria, salivary minor gland is one of the major factor contributing to the diagnosis. Ultrasonography is a non-invasive, easy accessible tool in evaluation the contour and structure of salivary glands, which have been shown to have efficacy in monitoring the disease status of Sjögren's syndrome as well as in diagnosis the disease. Otherwise, salivary flow rate is another component of classification criteria, and its association with disease activity remains to be elucidated.

**Objectives:** To investigate the efficacy of salivary gland ultrasonography and salivary flow rate in patients with Sjögren's syndrome and Sicca symptoms.

**Methods:** Total 97 patients of primary or secondary Sjögren's syndrome, and patients with sicca symptoms were enrolled. Ultrasonography was performed at parotid and submandibular glands with 13–16MHz linear probe. Each gland was scored from 0 to 4. Minor salivary gland biopsy results were examined by pathologist with Chisholm-Mason grade. Unstimulated salivary flow rate was recorded first, and stimulated salivary flow rate was tested after 5 min of sugar-free chewing gum stimulation. Patients' symptoms were recorded by ESSPRI questionnaires.

**Results:** Total 56 primary Sjögren's Syndrome, 10 secondary Sjögren's Syndrome, and 31 patients with sicca symptoms were enrolled. Significant correlations were noted between unstimulated salivary flow rate and minor gland biopsy ( $p=0.029$ ), stimulated salivary flow rate and biopsy ( $p=0.006$ ), salivary gland ultrasonography and minor gland biopsy ( $p<0.001$ ), and minor gland biopsy with serum anti-SSB (La) level ( $p=0.009$ ). The correlations between minor gland biopsy and serum anti-SSA (Ro) level was not significant. The stimulated salivary flow rate also correlated with self-reported dryness in ESSPRI questionnaires ( $p=0.018$ ). The salivary gland ultrasonography also correlated with ESSPRI ( $p<0.001$ ) and the three factors in ESSPRI (dryness,  $p<0.001$ ; pain,  $p=0.039$ ; fatigue,  $p=0.002$ ).

**Conclusions:** Both salivary gland ultrasonography and salivary flow rate correlated with the severity of salivary minor gland biopsy. The stimulated salivary flow rate had better correlations with the biopsy result than unstimulated flow, and it also correlated with patients' self-reported dryness symptoms. Salivary gland ultrasonography had correlations with symptoms of patient. These non-invasive methods may play roles in evaluation of the disease activity.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.6445

#### THU0385 URINARY INFLAMMATORY CELLS REFLECT HISTOPATHOLOGICAL KIDNEY INJURY IN PATIENTS WITH LUPUS NEPHRITIS

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**Background:** Lupus nephritis (LN) is one of the common manifestations of systemic lupus erythematosus (SLE), and is considered to be a very important factor influencing the course of the disease. Although kidney biopsy is the gold standard for defining the histopathologic class of LN, it is an invasive procedure sometimes associated with a risk of bleeding and thrombotic events; furthermore, repeated biopsies are not always applicable in clinical practice. We have already reported that, in patients with glomerulonephritis, inflammatory cells such as T cells and macrophages appear in the urine when there are accompanying signs of active cellular infiltration such as cellular crescent formation and diffuse interstitial cell infiltration, but not when active inflammatory lesions are absent.

**Objectives:** To assess the utility of urinary inflammatory cell analysis in patients with LN by examining the correlations between the numbers of urinary inflammatory cells and renal histopathological findings.



**Methods:** Twenty-six patients with SLE, who had been referred to Niigata University Hospital between 2004 and 2017 and diagnosed as having LN by percutaneous kidney biopsy, were recruited for this study. Flow-cytometric analysis of urinary inflammatory cells was performed for each subject at the time of admission for kidney biopsy. Numbers of urinary T cells or macrophages were determined by multiplying the number of viable cells in the gated mononuclear cell region in each sample by the percentage of urinary CD3-positive or CD14-positive cells in the population, respectively. The histopathological findings of kidney biopsy specimens for each subject were classified according to the 2003 International Society of Nephrology/Renal Pathology Society (ISN/RPS) classification of LN. In addition, they were also evaluated for glomerular and interstitial lesions such as mesangial cell/matrix proliferation, endocapillary hypercellularity, crescent formation, and interstitial cell infiltration and fibrosis. The severity of each lesion was scored from 0 to 4, and the numbers of urinary inflammatory cells were analysed by Spearman's rank correlation coefficient to determine the relationships among these scores. Next, the patients were divided into two groups according to whether the total number of urinary inflammatory cells was significantly increased (more than 120 cells/ml; positive group, n=12) or not (negative group, n=14), and the severities of the histopathological lesions were compared between the two groups.

**Results:** Disease severity in terms of the ISN/RPS classifications was positively correlated with the severity of mesangial cell and matrix proliferation, cellular crescent formation, and duplication of the glomerular basement membrane. In addition to these four factors, the numbers of CD3-positive and CD14-positive cells were also positively correlated with adhesion, endocapillary hypercellularity, interstitial inflammatory cell infiltration, and interstitial fibrosis. The severity scores for adhesion, endocapillary hypercellularity, cellular and fibrous crescent formation, duplication, and interstitial cell infiltration were significantly higher in the positive group than in the negative group.

**Conclusions:** Analysis of urinary immune cells reflects the histopathological features of kidney biopsy specimens from patients with LN.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.1313

THU0386

#### DIFFERENCE OF IMAGE FEATURES ON COMPUTED TOMOGRAPHY BETWEEN LUPUS ENTERITIS AND MESENTERIC VASCULITIS OF OTHER CONNECTIVE TISSUE DISEASES

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**Background:** Lupus enteritis (LE), lupus mesenteric vasculitis, occurs occasionally in systemic lupus erythematosus (SLE). Not only LE but also other mesenteric vasculitis can lead to bowel haemorrhage or perforation and will be fatal, but it is difficult to demonstrate histologically-proven vasculitis on endoscopic biopsy.<sup>1</sup> Although several computed tomography (CT) features of LE are reported, we have little knowledge about whether they differ from those of other mesenteric vasculitis.

**Objectives:** To clarify the imaging pattern on CT which can distinguish LE from other mesenteric vasculitis.

**Methods:** Patients diagnosed with LE and non-LE at our hospital were consecutively registered from January 2009 to August 2017. The diagnosis of LE was made by the criteria of <sup>BILAG</sup> 2004 which is defined as either vasculitis or inflammation of small or large bowel with supportive imaging and/or biopsy findings.<sup>2</sup> Non-LE was defined as mesenteric vasculitis of other connective tissue diseases (CTDs). We compared the contrast-enhanced CT patterns of LE with non-LE. Statistical analyses were performed using XLSTAT.

**Results:** A total of 8 patients were diagnosed with LE and enrolled in this study. The mean age was 41.1 years old, range 23–53, and 7 were females. CT exams of all 8 patients demonstrated small bowel wall thickening, dilatation of intestine and comb sign (indicating engorgement of mesenteric vessels). Severe bowel wall thickening (>8 mm) was observed in 87.5% (n=7), ascites in 75.0% (n=6) and target sign (indicating abnormal bowel wall enhancement) in 62.5% (n=5). 5 patients were enrolled in non-LE (1 eosinophilic granulomatosis with polyangiitis, 1 IgA vasculitis and 3 Behcet's disease). Comparison of CT findings between LE patients and non-LE patients were summarised on table 1. Bowel wall thickness and comb sign were common in both groups, however the prevalence of dilatation of intestine in LE patients was significantly higher than in non-LE patients. Although not significant, complication of large bowel involvement was shown only in LE patients.

Abstract THU0386 – Table 1

	LE (n=8)	non-LE* (n=5)	p-value
Thickening bowel wall	100%	100%	—
Large bowel involvement	50.0%	0%	0.10
Asymmetrical patterns of involvement	12.5%	60.0%	0.21
Dilatation of intestine	100%	20.0%	0.0070
Ascites	75.0%	40.0%	0.29
Target sign	62.5%	40.0%	0.59
Comb sign	100%	100%	—

\*non-LE : 1 Eosinophilic granulomatosis with polyangiitis, 1 IgA-vasculitis, 3 Behcet's disease

\*non-LE : 1 Eosinophilic granulomatosis with polyangiitis, 1 IgA-vasculitis, 3 Behcet's disease

**Conclusions:** Dilatation of intestine on CT is significant to distinguish LE from mesenteric vasculitis of other CTDs.

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- [1] Janssens P, et al: *Orphanet J Rare Dis* 2013;8:67.  
[2] Isenberg DA, et al: *Rheumatology (Oxford)*. 2005;44:902–6.

**Disclosure of Interest:** Y. Yoshida Speakers bureau: Bristol-Myers Squibb, Chugai, Sanofi, T. Kondo: None declared, K. Yukawa: None declared, T. Tokunaga: None declared, T. Kuranobu: None declared, K. Oi: None declared, T. Nojima: None declared, S. Hirata Grant/research support from: Eli Lilly, UCB, Consultant for: Bristol-Myers Squibb, UCB, Paid instructor for: AbbVie, Eisai, Tanabe-Mitsubishi, Speakers bureau: AbbVie, Astellas, Ayumi, Bristol-Myers Squibb, Chugai, Eisai, Eli Lilly, Jansen, Kissei, Pfizer, Sanofi, Takeda, Tanabe-Mitsubishi, UCB, E. Sugiyama Grant/research support from: AbbVie, Astellas, Ayumi, Bristol-Myers Squibb, Chugai, Eisai, Eli Lilly, Kissei, Pfizer, Sanofi, Takeda, Tanabe-Mitsubishi, Speakers bureau: AbbVie, Astellas, Ayumi, Bristol-Myers Squibb, Chugai, Eli Lilly, Kissei, Pfizer, Sanofi, Tanabe-Mitsubishi, Actelion  
**DOI:** 10.1136/annrheumdis-2018-eular.2654

THURSDAY, 14 JUNE 2018:

#### Scleroderma, myositis and related syndromes

THU0387

#### HIGH-THROUGHPUT QUANTITATIVE HISTOLOGY IN SYSTEMIC SCLEROSIS SKIN DISEASE USING COMPUTER VISION

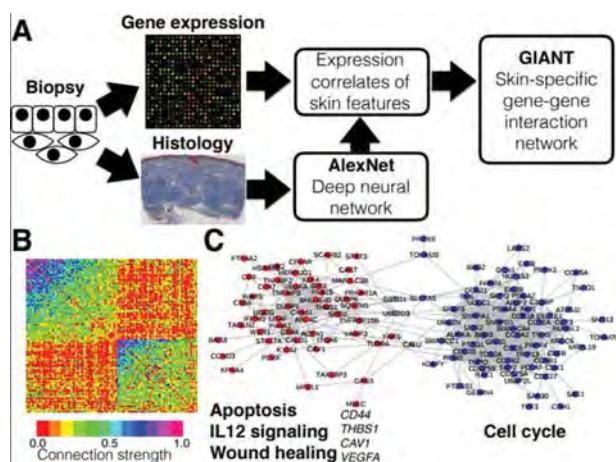
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**Background:** There are no validated systems to quantify dermal architecture of skin biopsy sections in systemic sclerosis (SSc). Significant advances in computer vision, called deep neural networks (DNNs), have demonstrated human-level pattern recognition abilities using mathematical transformations of images into millions of quantitative features.<sup>1</sup> Publicly available DNN algorithms have the potential to radically augment current histological analyses via robust, reproducible, and high-throughput image quantification.

**Objectives:** Apply publicly available DNN algorithms to trichrome-stained sections of dermal biopsies from patients with SSc to identify quantitative features of images that correlate with clinical skin fibrosis assessment via the validated modified Rodnan skin score (mRSS) and skin gene expression.<sup>2</sup>

**Methods:** One rheumatologist performed local mRSS (lmRSS) assessments (0–3) and two dermal punch biopsies for 7 patients with SSc and one healthy control at baseline and 6, 12, 24, and 36 months. One biopsy was paraffin embedded, sectioned, stained with trichrome, and photomicrographed. Images were transformed into high-level quantitative features using AlexNet and the Matlab Neural Network Toolbox.<sup>3</sup> Correlations between quantitative features and lmRSS were determined with Bonferroni-Holm correction. One biopsy underwent gene expression profiling by DNA microarray. The degree of correlation between each gene and lmRSS was assessed and a functional gene network was determined using the GIANT database.<sup>4</sup>

**Results:** We identified 90 quantitative features that correlated significantly with local skin score (p<0.05, Bonferroni-Holm correction). Using these features, biopsies sorted into three clusters corresponding to low (mean=0.13), intermediate (mean=0.91), and high (mean=1.7) lmRSS. Gene expression for 488 genes in the biopsies correlated significantly with quantitative features (p<0.05, Bonferroni-Holm correction). Among these 488 genes, 185 genes formed a large functional network in the GIANT database including genes associated with the cell cycle, apoptosis, IL12 signalling, and wound healing such as CD44, THBS1, CAV1, and VEGFA.



**Conclusions:** This proof-of-principal study demonstrates that DNN processing of stained dermal biopsy sections are sensitive to clinically relevant features of SSc skin. These results suggest that DNNs dramatically expand the quantifiable SSc phenome and that histological samples can now be incorporated into models of SSc. Moreover, our results indicate that the gene expression underlying SSc may be driving histological differences in SSc skin.

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**Acknowledgements:** NIH NIAMS P30 AR057216; NIAMS K23 AR059763I, L30 AR054311 and Scleroderma Research Foundation. Chase Correia is supported in part by Grant Number T32 AR007611–13 from the National Institute of Arthritis and Musculoskeletal and Skin Diseases.

**Disclosure of Interest:** None declared

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#### THU0388 DIFFERENCES IN CLINICAL COURSES AND SERUM MARKERS OF INTERSTITIAL LUNG DISEASE ASSOCIATED WITH ANTI-AMINOACYL-TRANSFER RNA SYNTHETASE ANTIBODY AND ANTI-MELANOMA DIFFERENTIATION-ASSOCIATED GENE 5 ANTIBODY-POSITIVE POLYMYOSITIS/DERMATOMYOSITIS

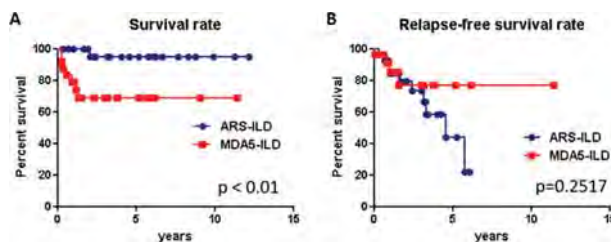
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**Background:** Polymyositis/dermatomyositis (PM/DM) is a chronic autoimmune disease that is often complicated by interstitial lung disease (ILD). Anti-aminoacyl-transfer RNA synthetase antibody (ARS-Ab) and anti-melanoma differentiation-associated gene 5 antibody (MDA5-Ab) are highly detected in PM/DM with ILD. It was reported that ARS-Ab-positive-ILD (ARS-ILD) is often recurrent<sup>1</sup>, and patients with MDA5-Ab-positive-ILD (MDA5-ILD) develop fatal rapidly progressive ILD<sup>2</sup>.

**Objectives:** To evaluate the differences in clinical courses between ARS-ILD and MDA5-ILD, including the changes in serum ILD markers.

**Methods:** We retrospectively investigated 25 patients with ARS-ILD and 26 patients with MDA5-ILD who received induction therapy between April 2002 and September 2017 at Kobe University Hospital. The survival rate and relapse-free survival rate were analysed with Kaplan-Meier estimation and the log-rank test. The differences in serum ILD markers between patients with ARS-ILD and MDA5-ILD were evaluated with the Student's t-test.

**Results:** Disease subtypes at diagnosis with PM/DM-associated ILD were as follows: Eleven ARS-ILD and no MDA5-ILD patients had PM, 10 ARS-ILD and 5 MDA5-ILD patients had DM, and 4 ARS and 21 MDA5 patients had amyopathic DM. The survival rate for MDA5-ILD was significantly lower than that for ARS-ILD ( $p < 0.01$ , figure 1A). On the other hand, there was no significant difference in the relapse-free survival rate between ARS-ILD and MDA5-ILD ( $p = 0.25$ , figure 1B). The serum level of Krebs von den Lungen-6 was not significantly different between ARS-ILD and MDA5-ILD (1044.3 ± 768.1 U/ml in ARS-ILD vs 1044.863.1 ± 566.5 U/ml in MDA5-ILD,  $p = 0.33$ ), but the serum level of ferritin was significantly higher in MDA5-ILD than in ARS-ILD (286.4 ± 422.3 ng/ml in ARS-ILD vs 696.2 ± 839.5 ng/ml in MDA5-ILD,  $p = 0.04$ ). Although the serum level of surfactant protein D (SP-D) in ARS-ILD was high, the SP-D level in MDA5-ILD was normal (158.9 ± 82.1 ng/ml in ARS-ILD vs 46.3 ± 22.1 ng/ml,  $p < 0.01$ ).



**Conclusions:** MDA5-ILD patients should be monitored for both rapidly progressive disease and relapsing disease. A normal SP-D level is a feature of MDA5-ILD.

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**Acknowledgements:** none.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.1975

#### THU0389 BORDERLINE PULMONARY HYPERTENSION WAS ASSOCIATED WITH REDUCED CARDIAC OUTPUT DURING EXERCISE IN PATIENTS WITH CONNECTIVE TISSUE DISEASES

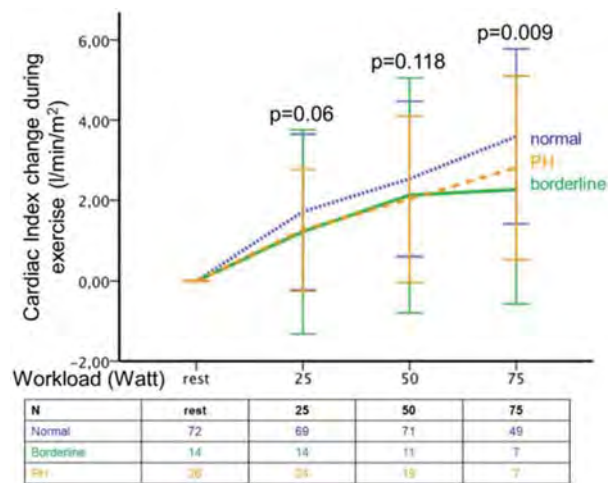
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**Background:** In patients with systemic sclerosis (SSc) borderline mean pulmonary arterial pressures (mPAP; 21–24 mmHg at rest) are a frequent finding and could represent an intermediate stage between normal pulmonary pressures and manifest pulmonary hypertension (PH).<sup>1</sup>

**Objectives:** The objective of this prospective study was to compare right ventricular function and pulmonary arterial compliance (PAC) at rest and during exercise between systemic sclerosis (SSc)-patients with normal and borderline mean pulmonary artery pressures, respectively.

**Methods:** SSc-patients (n=112) underwent clinical assessment, including right heart catheterization at rest and during exercise and were divided in three groups according to their resting mPAP values: normal mPAP (≤20 mmHg), borderline mPAP (21–24 mmHg) and manifest pulmonary hypertension (PH, mPAP ≥25 mmHg). Results were compared between groups by ANOVA followed by post-hoc student's t-test.

**Results:** SSc Patients with borderline PAP showed significantly lower cardiac index (CI) increase during exercise and higher PVR values than SSc patients with normal PAP at rest. Six-Minute-walking distance (6MWD) and PAC (stroke volume/(systolicPAP-diastolicPAP)) were significantly lower in the borderline PAP group compared to patients with normal PAP.



**Conclusions:** The results of this study suggest that impaired 6MWD in SSc patients with borderline PAP (and normal RV function at rest) might be caused by reduced RV contractile reserve (reduced RV output) and reduced PAC during exercise rather than by elevated pressures in the borderline range alone. These findings give further evidence for borderline PAP being an early stage of pulmonary vascular disease.

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**Acknowledgements:** Special thanks to the patients that participated in this research.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.4106

#### THU0390 PATIENTS WITH SYSTEMIC SCLEROSIS DEVELOP FOCAL FIBROSIS OVER TIME, AND INCREASED ECV DIFFUSE FIBROSIS SEEN IN POOR PROGNOSTIC GROUP – A FIRST LONGITUDINAL CARDIAC MRI STUDY

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**Background:** Subclinical SSc-cardiomyopathy is described in up to 2/3 of the patients when sensitive methods such as cardiac MRI (CMR) are used. The prognostic implications and the natural history of these findings is unknown.

**Objectives:** To evaluate in SSc patients, free of cardiovascular (CV) risk factors and CV disease (CVD) the prevalence, clinical association and natural history of CMR abnormalities over 3 years.

**Methods:** 35 SSc patients, fulfilling the ACR/EULAR criteria, with no CVD, diabetes and  $\leq 1$  CV risk factor had 2 CMRs, 3 years apart. A 3T CMR with late gadolinium enhancement (LGE), T1 mapping for extracellular volume (ECV) quantification and stress perfusion (data available later) was undertaken. Initial CMR was compared with CMR results of 30 healthy controls (HC).

**Results:** 35 pts had an initial CMR: 26 (74%) female, mean (SD) age 55 (15) (43%) dcSSc, 11 (31%) ACA+, 12 (34%) Scl70+, 15 with (43%) interstitial lung disease (ILD) and 13 (37%) with history of digital ulcers (DU). 21 (60%) received any DMARD over the 3 year period and 10 (29%) prior treatment with cyclophosphamide. The first CMR (CMR1) of SSc pts vs HC showed higher ECV% values and comparable left ventricle (LV) volumes (table 1). LGE was present in 9/22 pts vs 1/30 HC. 22/35 pts had a second CMR (CMR2) at year 3 (Y3). A further 5 pts had evidence of LGE, total of 14 (40%): 7/14 had dcSSc, 6/14 males, 2 ACA positive, 6 Scl70 positive. LGE distributed in the basal and mid segments, mainly in a linear or patchy pattern. Of those with LGE at CMR1 (5/9 pts with LGE on CMR1 had CMR2) no change in the LGE pattern at CMR2 was observed. None of the initial CMR measures associated with LGE development at Y3 ( $p > 0.05$ ). Whilst ECV had an overall decrease, ECV increased in patients with ILD [mean diff. (CI) 3 (-

1,6),  $p = 0.14$ ] and in those with higher mRSS at baseline ( $r = 0.455$ ,  $p = 0.04$ ). A significant decrease over the 3 years was observed in LV end-diastolic volume (LVEDV/BSA), LV end-systolic volume (LVESV/BSA) and left ventricular stroke volume (LVSV/BSA) (table 1). A decrease in LVEDV/BSA was noticed for those with a history of DU [mean diff. (CI)  $-5$  (-12.2),  $p = 0.1$ ], ILD [mean diff. (CI)  $-6$  (-12.0, 5),  $p = 0.07$ ] and shorter disease duration ( $r = -0.504$ ,  $p = 0.02$ ).

**Abstract THU0390 – Table 1**

CMR variable	HC Mean (SD)	SSc patients Mean (SD)	SSc patients Mean (SD)	Change (95% CI) in CMR between SSc patients	P value
LGE	3% (1/30)	21% (9/35)	22% (10/22)	23%	McNemar 0.063
ECV%	25(3)	30(4)	29(3)	-0.1 (-0.3, 0.1)	0.2
T1 native	1202 (35)	1199 (58)	1243 (67)	47 (-1, 94)	0.053
LVEDV/BSA (ml/m <sup>2</sup> )	80 (11)	78(16)	71(15)	-7(-10,-3)	<0.001
LVESV/BSA (ml/m <sup>2</sup> )	31(6)	30(9)	26(9)	-4(-6, 2)	0.001
LVSV/BSA (ml/m <sup>2</sup> )	49(7)	48(9)	45(8)	-3(-6,-0)	0.028
Lvmass/BSA (g/m <sup>2</sup> )	49(8)	44(13)	50(21)	6 (-2, 13)	0.129
LVEF(%)	62(5)	62(5)	64(6)	2 (-0, 4)	0.08
Distensibility (10-3mmHg <sup>-1</sup> )	5 (2)	4 (2)	5 (3)	0 (-1, 2)	0.491
Torsion	15(4)	13(4)	13(5)	0 (-2, 3)	0.828

**Conclusions:** This longitudinal CMR study in SSc demonstrates that CMR is sensitive to change over time. More individuals developed LGE (of focal fibrosis) despite immunosuppressive treatment, and ECV% (diffuse fibrosis) appeared to worsen in a poor prognostic group. Functional changes were also observed. These data justify larger studies to inform stratification strategy for CMR in SSc, and also provide new insights for further investigation.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.7442

#### THU0391 CLINICAL VALUE OF COMPUTED TOMOGRAPHY FOR THE DIAGNOSIS OF ESOPHAGEAL DYSMOTILITY IN SYSTEMIC SCLEROSIS

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**Background:** Esophageal dysmotility is common in Systemic Sclerosis (SSc), affecting 50%–80% of patients, usually associated with poor prognosis. SSc leads to atrophy and fibrosis of the smooth muscle of the oesophagus, modifying peristaltic contractions and motility. Manometry is considered the gold standard for the diagnosis of esophageal motility disorders, but dilatation can also be observed with computed tomography (CT), even if its diagnostic validity is still unknown.

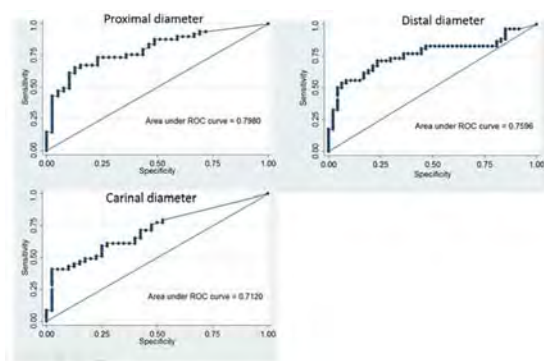
**Objectives:** To compare esophageal dilatation observed with CT to manometry, in patients with SSc and to confirm whether CT can be used in the assessment of esophageal dysmotility.

**Methods:** Forty six patients meeting the 2013 ACR/EULAR Classification Criteria for SSc, and 53 healthy controls were included and retrospectively studied. Patients with overlapping syndromes, active infections or with longstanding diabetes were excluded. Epidemiological and clinical data were collected from medical records. All patients and controls had undergone at least one manometry and one CT, requested in daily clinical practice for another purpose. The most recent exams were selected for the study. Esophageal involvement was assessed using manometry (aperistalsis, inefficient peristalsis, nonspecific dysmotility and normal peristalsis) and compared with the largest coronal esophageal luminal diameters proximally, near the carina, and distally observed by CT. Data analysis was performed by STATA. All patients signed written informed consent, approved by the Research Ethics Committee.

**Results:** The sample included 76 women (10 dcSSc, 28 lcSSc, 3 MCTD, 35 controls) and 23 men (3 dcSSc, 2 lcSSc, 18 controls). Esophageal dysmotility was seen in 40/46 patients with SSc (87%) by manometry (defined as inefficient peristalsis or aperistalsis). Esophageal dilatation ( $\geq 10$  mm) was present proximally in 23/44 patients (52.3%), distally in 35/46 patients (76.1%), and near the carina in 26/44 patients (59.1%). Esophageal dilatation at any level was statistically associated with esophageal dysmotility ( $p < 0.05$ ). The areas under the ROC curves (figure 1) suggest that the esophageal proximal diameter in the coronal plane is good for detecting esophageal dysmotility (0.798, 95% CI 0.705–0.890), with the distal diameter (0.759, 95% CI 0.661–0.857) and the carinal diameter (0.712, 95% CI



0.607–0.816), being slightly lower. A proximal diameter  $\geq 7.5$  mm provides a specificity of 87.2% (95% CI: 76.7–96.7) and a sensitivity of 65.3% (95% CI: 51.9–78.6) for esophageal dysmotility, enabling correct classification of 75% of the patients. A distal diameter  $\geq 12.9$  mm provides a specificity of 76.6% (95% CI: 64.5–88.7) and a sensitivity of 71.2% (95% CI: 58.8–83.5), correctly classifying 73% of the patients.



**Abstract THU0391 – Figure 1.** ROC curves of the diameters for esophageal dysmotility detected by manometry.

**Conclusions:** CT, a less invasive technique than manometry, can be an acceptable diagnostic tool for esophageal dysmotility in SSc, when the maximum proximal or distal esophageal diameter are  $\geq 7.5$  mm and 12.9 mm, respectively. CT done in the daily clinical practice could be exploited when manometry is not preferred in selected patients with SSc. More studies need to be carried out to confirm this results.

**Disclosure of Interest:** None declared

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THU0392

#### SYSTEMIC SCLEROSIS AND PRIMARY BILIARY CHOLANGITIS: AN OVERLAP SYNDROME? PRELIMINARY DATA FROM A MULTICENTRE EUSTAR STUDY

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**Background:** The association between systemic sclerosis (SSc) and primary biliary cholangitis (PBC) is well known. However, classifications criteria of the 2 diseases have been recently revised and may change the relationships. Furthermore, the specific outcomes with regards to organ involvement and also of liver aspects have been only scarcely investigated.

**Objectives:** To describe clinical characteristics of SSc-PBC patients compared to SSc using a large series

**Methods:** A multicentre EUSTAR study collection data of SSc patients with known PBC or with PBC-specific antibodies (abs) and of SSc controls matched for disease duration and cutaneous subset. Data were recorded at baseline and at the last available visit.

**Results:** 229 patients were enrolled (85 SSc-PBC and 144 SSc). The mean age of the population at the SSc diagnosis was of  $53 \pm 12.8$ . **Baseline characteristics.** The limited cutaneous subset was the most common. Anticentromere abs (ACA) were present in 82.9% of SSc-PBC patients (vs 68.5% in SSc,  $p$ -value=0.01) while anti-topoisomerase I abs were less frequently (1.2% vs 9.7%),  $p$ -value=0.02. Out of 85 SSc-PBC patients, antimitochondrial abs (AMA) were present in 80%, only 9.4% presented anti-gp210 abs and 7.1% anti-sp100 abs. The two populations did not differ for fibrosis at HRCT, lung function tests, the value of creatinine and for pulmonary arterial hypertension. A trend towards statistical significance was found in the prevalence of digital ulcers (DUs) as patients that have never suffered from past or current DUs were greater in the SSc-PBC group (78.6% vs 66%,  $p$ -value=0.051). Regarding other autoimmune associated diseases, a greater prevalence of Hashimoto thyroiditis was found in SSc-PBC ( $p$ -value=0.03). At baseline, transaminase, alkaline phosphatase and  $\gamma$ GT levels were all higher in PBC-SSc ( $p$ -value<0.001) (see Fig 1). **Outcomes of organ**

**involvements.** The mean follow-up was of  $10.5 \pm 6.8$  years. During the follow-up the percentage of patients presenting ILD (defined as new appearance of fibrosis at control HRCT scan) was greater in SSc vs SSc-PBC (12.9% vs 2.8%,  $p$ -value=0.02) and PAH percentage of new cases was of 9.9% in SSc while it was not present in SSc-PBC ( $p$ -value=0.003).

	SSc-PBC population	SSc controls	p-value
Cutaneous subset			
Limited cutaneous subset	77 (30.6%)	132 (91.7%)	0.73
Diffuse cutaneous subset	2 (2.4%)	5 (3.5%)	
Unclassified cutaneous subset	6 (7.1%)	7 (4.8%)	
CT fibrosis	15 (17.6%)	28 (19.4%)	0.69
PVC (forced vital capacity) [mean±SD]	104 (321.5)	103 (217.1)	0.72
DLD (diffusing capacity for carbon monoxide) [mean±SD]	78 (218.5)	76 (217.5)	0.50
Portal hypertension	4 (4.7%)	-	
Arrhythmia	4 (4.7%)	4 (2.8%)	0.55
Conduction block	7 (8.2%)	7 (4.9%)	0.28
PAH	5 (5.9%)	2 (1.4%)	0.20
Never DU	66 (77.6%)	85 (58%)	0.052
GI symptoms			
GERD	44 (51.8%)	90 (62.5%)	0.24
Malabsorption	2 (2.4%)	3 (1.9%)	>0.99
Anorectal incontinence	1 (1.2%)	4 (2.8%)	0.55
Thyroid disease			
Basedow	1 (1.2%)	1 (0.7%)	>0.99
Hashimoto	10 (11.8%)	8 (5.6%)	0.034
SSc specific abs			
Anti-topoisomerase I	1 (1.2%)	14 (9.7%)	0.022
ACA	63 (80%)	85 (65.1%)	0.012
PBC specific abs			
AMA	68 (80%)	-	
gp210	8 (9.4%)	-	
sp100	6 (7.1%)	-	
Therapy			
Immunosuppressant therapy	18 (21.2%)	43 (29.9%)	NS
Steroid therapy	19 (22.4%)	27 (18.8%)	NS
Deoplastic acid	50 (66.2%)	-	
Creatinine [median(IQ)]	70 (61-81.3)	70 (61-79.5)	0.99
Alkaline transaminase [median(IQ)]	34.5 (26-59.25)	20 (15-26)	<0.001
Aspartate transaminase [median(IQ)]	38 (26-54.25)	21 (19-27)	<0.001
Alkaline phosphatase (AP) [median(IQ)]	147 (94-296)	71 (56-90)	<0.001
vGT [median(IQ)]	143 (59.5-251.5)	18 (11-31.25)	<0.001

**Abstract THU0392 – Figure 1.** Clinical features at baseline

**Conclusions:** PBC is more present in ACA positive IcSSc; SSc-PBC patients have a higher risk of polyautoimmunity. Of the most interest, SSc-PBC patients seem to have a milder SSc phenotype with less severe organ involvement and progression. Regarding PBC phenotype, only 4 patients presented portal hypertension and nobody was subjected to liver transplantation. At baseline, the SSc-PBC group had higher cholestatic liver enzymes and more than 60% were treated with deoxycholic acid. In the future, it will be useful to evaluate the PBC phenotype during the follow-up enrolling a greater number of patients.

**Disclosure of Interest:** None declared

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THU0393

#### THE PREDICTOR OF MALNUTRITION IN SYSTEMIC SCLEROSIS (PREMASS) SCORE: A VALIDATED COMBINED INDEX PREDICTIVE OF FUTURE WEIGHT LOSS IN SYSTEMIC SCLEROSIS

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**Background:** Malnutrition and severe gastrointestinal dysfunction are the cause of mortality in 4%–15% of systemic sclerosis (SSc) patients whereas overall gastrointestinal involvement is observed in 75%–90% of cases.<sup>1</sup> Hence, a reliable tool for stratification of risk for malnutrition would be of great value in the clinical management of SSc.

**Objectives:** Here we set out to identify a combined index predictive of significant weight loss at 12 months employing Malnutrition Universal Screening Tool (MUST) and serum adiponectin to leptin ratio (A/L) already used in other conditions.

**Methods:** This was an international, multicentre, longitudinal study employing 180 SSc patients in two independent cohorts: a study cohort (110 consecutive SSc patients) enrolled from University of Messina (60) and University of Padova,<sup>50</sup> and a validation cohort (70) at the University of Leeds. Serum A/L ratio was measured by ELISA. MUST score, which includes BMI and weight loss reported by the patient in the last 3–6 months, was calculated as described: 0=no, 1=mild, >2= moderate/severe risk of malnutrition. End point of the study was weight loss >10% of baseline weight at 12 months.

**Results:** The two cohorts showed no significant differences in demographic and clinical features. Overall, median BMI decreased over time in both study and validation cohorts (23.5 vs 22.35 and 23.44 vs 22.49, respectively;  $p$ <0.0001). A/L

ratio correlated significantly with BMI in both cohorts ( $r^2=0.19$  for study cohort,  $r^2=0.25$  for validation cohort;  $p<0.0001$ ). MUST score had only moderate value in predicting weight loss in the study cohort (AUC 0.7; 95% CI: 0.58–0.82). Specifically, 46.5% of SSc patients lost >10% wt despite having “no” or “mild” MUST scores. Logistic regression analysis identified the combination of BMI and A/L as the best PREDICTOR of MAInutrition in Systemic Sclerosis (PREMASS). The formula  $12.18-(0.63 \times \text{BMI})+(1.51 \times \text{A/L})$  predicted the end point with AUC=0.91 (95% CI: 0.77–0.84). A PREMASS score >0.23 showed 91.3% sensitivity (95% CI: 79.79–100) and 80.46% specificity (95% CI: 72.13–88.79) for >10% wt loss with an overall 55.26% positive predictive value (PPV) (95% CI: 39.45–71.07) and 97.22% negative predictive value (NPV) (95% CI: 93.43–100) and a relative risk (RR) of 19.90 (95% CI: 4.93–80.37). In the validation cohort, PREMASS showed 76.47% sensitivity (95% CI: 56.31–96.63) and 75.47% specificity (95% CI: 63.89–87.06) with an overall 50% PPV (95% CI: 30.78–69.22) and 90.91% NPV (95% CI: 82.41–99.4) and a RR of 5.5 (95% CI: 2–15.10).

**Conclusions:** PREMASS is the first validated index for weight loss risk stratification in the following 12 months in SSc. Prediction of future weight loss in SSc could aid both in clinical management and stratification/enrichment in clinical trials.

**Disclosure of Interest:** None declared

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### THU0394 ENTHESTITIS IN SYSTEMIC SCLEROSIS (SSC): AN ULTRASOUND (US) PILOT STUDY

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**Background:** Articular involvement is frequently encountered in SSc and previous US studies suggest that synovitis is the commonest manifestation. Recently, it has been reported that SSc patients may show typical “hall-marks” of spondyloarthritis (SpA). Apart from tendon involvement which is a common event, sacroiliitis has been estimated to have a prevalence of 23%.

**Objectives:** To estimate the prevalence of enthesal and Synovio-Enthesal Complex (SEC) modifications in SSc

**Methods:** 30 SSc patients (2013 ACR/EULAR classification criteria) without a history of articular involvement (4 male, 26 female, mean age 53.3±16.6 years) were included in this pilot cross sectional US study. 12 healthy subjects (2 male, 10 female, mean age 46.9±5.8 years) were used as controls. The enthesal sites were the lateral epicondylar common extensor tendons (CET), and sites of the Glasgow Ultrasound Enthesis Scoring System. The GUESS score was also calculated as a soft tissue score (GUESS soft tissue) and as a bone score (GUESS bone). US assessment was performed with a MyLab 70XVG scanner equipped with a 6–18 MHz linear transducer (Esaote). Only the epicondylar region was evaluated with PowerDoppler US (PDUS), using semi-quantitative graded from 0 to 3. Involvement of SEC was evaluated at the epicondylar region in SSc patients who presented a PDUS signals  $\geq 1$  in the CET closer than 2 mm from the bony surface. SEC involvement was defined as the presence of a PDUS signal  $\geq 2$  in the elbow epicondylar synovial fold proximal to the annular ligament (AL), inferior to the bone insertion of CET and to the radial collateral ligament (RCL). Statistical analyses were carried out using Mann-Whitney U, Spearman correlation and Chi-square tests. Results were considered significant if  $p<0.05$

**Results:** In SSc, the GUESS and GUESS soft tissue scores were significantly higher ( $5.67 \pm 0.87$  and  $3.43 \pm 0.44$ , respectively) than in controls ( $1.25 \pm 0.41$  and  $0.92 \pm 0.29$ , respectively) ( $p<0.0001$ ) as was the GUESS bone score (SSc  $2.23 \pm 0.55$  vs controls  $0.33 \pm 0.22$ ;  $p<0.05$ ). The CET entheses of SSc patients showed significantly more US B-mode alterations than controls (hypoechoogenicity  $\chi^2=5.95$ ,  $p=0.015$ , cortical irregularity  $\chi^2=7.90$ ,  $p=0.005$ , calcification/enthesophytes  $\chi^2=3.78$ ,  $p=0.05$ ). A PD signal in the CET enthesis was found in 18/60 sites in SSc and in 1/24 in controls. The PD signal of the CET enthesis was significantly higher in SSc patients than in healthy controls ( $0.47 \pm 0.10$  and  $0.08 \pm 0.08$  respectively,  $p=0.018$ ) as was the presence of SEC inflammation ( $\chi^2=4.54$ ,  $p=0.033$ ). In SSc, there was a strong correlation between the presence of PD signal at CET entheses and concomitant SEC inflammation ( $\rho=0.655$ ,  $p<0.0001$ ) but there were no correlations between GUESS score or CET enthesitis and disease subset, disease duration, antibodies, DLCO, FVC, DLCO/VA.

**Conclusions:** Our data show that SSc patients frequently present the usual US features of enthesitis. Moreover, CET enthesitis were correlated with SEC inflammation suggesting that enthesal inflammation in SSc may share same microanatomical targets as SpA.

**Disclosure of Interest:** None declared

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### THU0395 INFLUENCE OF SETTING AN UPPER LIMIT OF THE MRSS AS AN INCLUSION CRITERION IN SSC CLINICAL TRIALS ON THE RATIO OF SKIN FIBROSIS PROGRESSION VS. IMPROVEMENT – AN ANALYSIS OF THE GENISOS COHORT

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**Background:** Skin involvement is a main domain in the assessment of patients with systemic sclerosis (SSc), and the modified Rodnan skin score (mRSS) is a primary outcome measurement in SSc clinical trials. Recent studies on large SSc cohorts have shown that lowering the upper threshold of mRSS as a study inclusion criterion leads to cohort enrichment with patients with progressive skin disease. Limitations of these studies were lack of racial diversity and low proportion of patients with anti-RNA-Polymerase III (Pol3) antibodies.

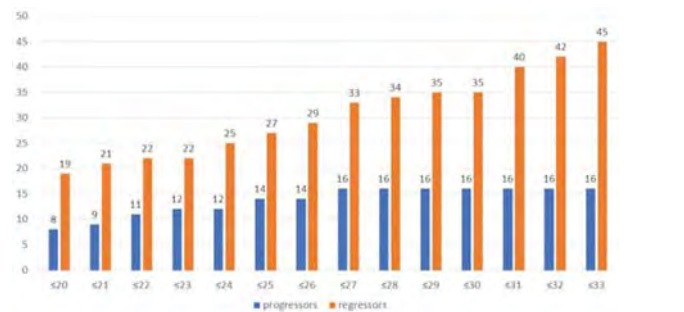
**Objectives:** As the Texas-based GENISOS is an ethnically diverse cohort and includes a large proportion of Pol3-positive patients, this study aimed to assess the effect of different mRSS cut-off values at baseline on progression of skin fibrosis after one year of follow-up.

**Methods:** We extracted data from GENISOS for patients fulfilling the 1980 ACR criteria for SSc and the Le Roy criteria for diffuse cutaneous SSc, who had a mRSS  $\geq 7$  at inclusion and a follow-up visit with documented mRSS at 12±2 months. Progressors were defined as having an increase in mRSS >5 points and  $\geq 25\%$  from the baseline to 2nd visit, while regressors were defined as having a decrease in mRSS of >5 points and  $\geq 25\%$ . To identify the optimal cut-off of baseline mRSS that yields the highest sensitivity for progressive skin fibrosis, we developed ROC curves and logistic regression models with “progression” as outcome variable and a binary variable of baseline mRSS cut-off point as predictor.

**Results:** We identified 152 patients (age and disease duration [median, Q1-Q3, years] 49.5, 40.2–57.3 and 2.2, 1.1–3.3 respectively, 22.4% males) who matched the inclusion criteria. The proportion of patients of African American ethnicity was 31/152 and 50/152 were Pol3-positive patients, both substantially higher than in European cohorts.

After one year, 17 patients (11.2%) classified as progressors and 51 (33.6%) as regressors. Progressors were more frequently positive for anti-topoisomerase antibodies (37.5% vs. 15.3%,  $p=0.028$ ), negative for anti-Pol3 antibodies (93.8% vs. 62.3%,  $p<0.012$ ), had a shorter disease duration (median, Q1-Q3: 1.3, 0.5–2.2 vs. 2.4, 1.1–3.5 years,  $p<0.005$ ) and lower mRSS (median, Q1-Q3: 21, 11–25 vs. 24, 16–31,  $p<0.012$ ) than non-progressors.

Sixteen of 17 progressors, but only 33 of 51 regressors had a baseline mRSS  $\leq 27$ . The mRSS cut-off of  $\leq 27$  had the highest probability of progression (odds ratio 9.1, 95% confidence interval 1.2–70.9,  $p<0.035$ , area under the curve 0.652). Using this cut-off as an inclusion criterion (vs. no cut-off) would have included 94% of all progressors, but only 65% of all regressors and 67% of all patients. The figure 1 displays absolute numbers of progressors and regressors at 1 year for each mRSS cut-off.



**Conclusions:** This analysis reconfirmed, in a population rich in patients of African American origin and with high prevalence of Pol3 antibodies, that setting a lower upper threshold of mRSS at study inclusion increases the proportion of progressors and reduces the absolute number of regressors. This confirms that this recruitment strategy should be used for clinical trial design in early diffuse SSc.

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### THU0396 COMBINED POSITRON EMISSION TOMOGRAPHY AND MAGNETIC RESONANCE IMAGING FOR THE ASSESSMENT OF SYSTEMIC SCLEROSIS GASTROINTESTINAL INVOLVEMENT

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**Background:** The gastrointestinal (GI) tract is affected in 90% of patients with systemic sclerosis (SSc), a disease characterised by excessive fibrosis. Baseline GI involvement is an independent predictor of 2 year mortality in patients with early diffuse cutaneous SSc. There is an urgent need to develop non-invasive methods of assessing SSc GI involvement for early diagnosis and monitoring. Novel non-invasive tools such as fluorodeoxyglucose-positron emission tomography (FDG-PET) and magnetic resonance imaging (MRI) have been used in oncology. Development of a new MRI sequence, T1 MOLLI (modified look-locker inversion recovery) mapping, has been used in cardiac imaging for detection and quantification of diffuse fibrosis.

**Objectives:** In this pilot study comparing SSc patients with healthy controls, we investigated whether FDG-PET-MRI is able to detect fibrosis and inflammation associated with SSc GI tract involvement.

**Methods:** We recruited 16 patients fulfilling the 2013 ACR/EULAR criteria for SSc and 15 healthy age-matched (within 5 years) controls. Severity of GI involvement was determined by the total Gastrointestinal Tract score (GIT, from University of California Los Angeles Scleroderma Clinical Trials Consortium).

All subjects fasted 6 hours prior and had non-spicy low-residue diet 3 days prior. Subjects were injected with FDG (6mCi) 1 hour prior and 10 mg hyoscine butylbromide (to reduce peristalsis) immediately before scanning. Breath-hold native T1 MOLLI mapping was acquired. FDG uptake was quantified by specific uptake value (SUV). All SSc patients and 5 controls underwent PET-MRI protocol. The remaining 10 controls only had MRI scanning. Student t-test was performed and statistical significance was taken to be  $p < 0.05$ .

**Results:** Demographics and clinical features of our study cohort are shown in table 1. Mean T1 values on MRI for the large and small bowels were significantly higher in SSc patients than healthy controls (large bowel:  $1113 \pm 189$  ms vs  $856 \pm 182$  ms respectively,  $p = 0.0006$ ; small bowel:  $1331 \pm 246$  ms vs  $1169 \pm 123$  ms respectively,  $p = 0.0296$ ), indicating the presence of GI fibrosis.

Mean PET SUV values for the large bowels were also higher in SSc patients than healthy controls ( $1.12 \pm 0.23$  vs  $0.82 \pm 0.23$  respectively,  $p = 0.0217$ ).

Abstract THU0396 – Table 1. Demographics and clinical features

	SSc patients (n=16)	Controls (n=15)
Limited/Diffuse SSc, n	11/5	Not applicable
Female, n (%)	14 (87.5%)	11 (73.3%)
Age, years	49.2±13.9	45.3±14.4
Mean disease duration from Raynaud's phenomenon onset, years	6.1±7.3	Not applicable
Mean disease duration from non-Raynaud's phenomenon onset, years	6.6±7.4	Not applicable
Mean GIT score	0.43±0.31	0

**Conclusions:** MRI T1-MOLLI mapping demonstrated evidence of bowel fibrosis in SSc patients. FDG-PET showed increased large bowel inflammation in patients. FDG-PET-MRI may potentially be a useful diagnostic and monitoring tool for SSc GIT disease.

**Disclosure of Interest:** None declared

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### THU0397 THE PROGNOSTIC VALUE OF AUTOANTIBODIES IN SYSTEMIC SCLEROSIS AND A TWO-YEAR FOLLOW-UP OF FORCED VITAL CAPACITY

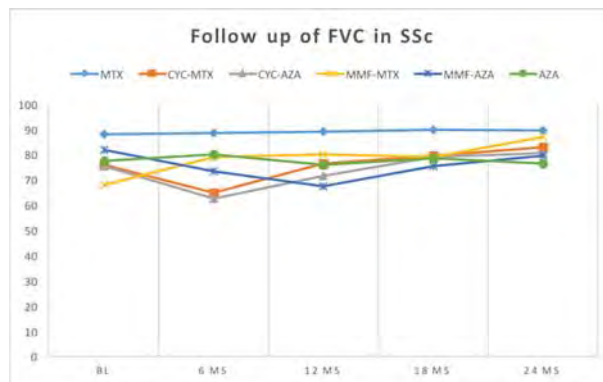
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**Background:** Systemic sclerosis (SSc) is a connective tissue disease involving the skin and internal organs of the body. Affection of the lungs and the vascular system significantly increases the morbidity and mortality. Controlling disease progression represents a challenge in clinical practice.

**Objectives:** We aimed to address prognostic factors of disease activity and study the progress of interstitial lung disease (ILD) under conventional disease modifying anti-rheumatic drugs (DMARDs) therapy.

**Methods:** Data of SSc patients (limited or diffuse) followed up in the Rheumatology Department Clinics throughout the past 2 years were collected for a retrospective study. The positivity of Antinuclear (ANA), Anti-centromere (ACA) and Anti-Scl70 antibodies was gathered from patients' data. Disease activity was assessed by the European Scleroderma Study Group (EScSG) activity index. Forced vital capacity (FVC) was used to mark the progress of ILD. Friedman and Wilcoxon signed rank tests were used for comparison of paired data as appropriated. Mann-Whitney U test, Kruskal-Wallis test and Chi-Square test were used to compare between two or more groups.

**Results:** The data of 42 SSc patients (59.5% limited SSc and 40.5% diffuse SSc) with a mean age  $40 \pm 12$  years were enrolled. 83.3% of the patients showed ANA positivity. ACA was positive in 28.6% of the patients and Anti-Scl70 in 23.8% while 47.6% of the patients were negative for both. DMARDs were indicated according to organ involvement, and changes were made according to breakthrough events. Low scores of EScSG were noticed in the ACA +ve group compared to intermediate scores in the Scl70 +ve group and high scores in the negative group at baseline ( $p = 0.082$ ) and 24 month follow-up ( $p = 0.045$ ). The frequency of pitting digital ulcers at baseline was lowest in the ACA +ve group compared to the highest frequency in the negative group ( $p = 0.026$ ), however, there was no difference between the groups at the 24 month follow-up. ANA did not affect the activity throughout the studied period. Follow up of FVC in the two years with different DMARDs is illustrated in figure 1. Patients followed on methotrexate (MTX) after cyclophosphamide (CYC) or mycophenolate (MMF) had raised FVC ( $p = 0.033$  and  $p = 0.054$  respectively) comparable to azathioprine (AZA) after CYC or MMF ( $p = 0.031$  and  $p = 0.27$  respectively).



**Conclusions:** ACA is proposed to be a marker of low disease activity and good response to therapy. Despite the risk of inducing ILD, MTX maintained a favourable effect on FVC throughout a follow-up period.

**Disclosure of Interest:** None declared

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### THU0398 UNEXPLAINED IRON DEFICIENCY IS FREQUENT IN SYSTEMIC SCLEROSIS

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**Background:** Prevalence of iron deficiency (ID) in systemic sclerosis (SSc) is unclear and can occur related to several causes.

**Objectives:** This cross sectional study aims to analyse association between ID and disease characteristics in SSc patients who does not have an overt cause for ID.

**Methods:** We identified 227 consecutive SSc patients who had iron laboratory studies (serum iron, total iron binding capacity and ferritin) with concurrent full blood count and serum C-reactive protein (CRP) measurement between May



2015 and November 2017. Exclusion criteria were as follows: not having serum CRP levels within 1 month of iron studies, chronic kidney disease (eGFR <60 ml/min), haemoglobinopathies, major surgery within one year, overt gastrointestinal (GI) or genitourinary blood loss, active GI cancer and vascular lesions of GI (GAVE, intestinal telangiectasia). Patients who have ferritin levels below cut-off values or were already on iron replacement were considered as iron deficient. To define iron deficient status, threshold levels of serum ferritin 30 ng/mL and 100 ng/mL were used to denote those with normal and high CRP levels (>5 mg/L) respectively. WHO classification system was used to determine the presence and severity of anaemia. Relationship between demographic and disease characteristics and serum iron status was analysed using Fisher's exact and Mann-Whitney U test.

**Results:** 178 patients (76.4% female) were eligible for final analysis. Clinical characteristics are reported in table 1. Median age and disease duration (interquartile range, IQR) were 54.6 (44.8–66.1) and 4.9 (2.1–4.8) years, respectively. ID was present in 43.2% of the patients and 41.6% of these patients was not anaemic. Iron deficient patients were more frequently female and had longer disease duration. Among female patients, ID was significantly more prevalent before the age of 50 (77.6% vs 0%,  $p < 0.001$ ).

**Abstract THU0398 – Table 1.** Comparison of demographics and disease characteristics between iron deficient and iron replete patients

	Iron replete (n=101)	Iron deficient (n=77)	p
Age, years, median (min-max)	58.8 (48.9–66.2)	52.9 (35.7–65.9)	0.06
Female, n (%)	70 (69.3)	66 (85.7)	0.01
Disease duration, years, median (min-max)	3.6 (1.7–8.1)	6.1 (3.0–24.6)	<0.01
Diffuse disease, n (%)	87 (86.3)	46 (59.7)	0.06
Anaemia, n (%) <sup>1</sup>	39 (38.6)	45 (58.4)	0.01
Moderate/severe anaemia, n (%) <sup>2</sup>	11 (10.9)	24 (31.2)	<0.01
* GI involvement, n (%) <sup>3</sup>	8 (8.0)	3 (3.9)	0.73
* Digital ulcer (DU), n (%)	23 (22.8)	20 (26.0)	0.62
* Severe DU, n (%) <sup>4</sup>	14 (13.9)	12 (15.6)	0.74
* PAH, n (%)	2 (2.0)	3 (4.5)	0.85
ILO, n (%)	29 (28.7)	28 (36.3)	0.43
Proton pump inhibitor use, n (%)	51 (50.5)	64 (83.0)	0.34
Antibody specificity			
Scl-70, n (%)	11 (10.9)	11 (14.3)	0.25
Centromere, n (%)	20 (19.8)	13 (16.9)	0.67
RNA polymerase III, n (%)	16 (15.8)	9 (11.6)	0.48

\* Diagnosed between May 2015 and November 2017  
<sup>1</sup> Serum haemoglobin level of <13 mg/dL for men and <12 mg/dL for women  
<sup>2</sup> Serum haemoglobin level of <11 mg/dL for both sexes  
<sup>3</sup> Required antibiotics or bosentan, critical digital ischaemia, gangrene  
<sup>4</sup> Intestinal pseudo-obstruction requiring hospitalisation, >2 courses of small bacterial overgrowth, PEG insertion or parenteral nutrition

**Conclusions:** Unexplained iron deficiency is frequent in scleroderma patients and a significant number of these patients do not have frank anaemia. Female sex and longer disease duration is associated with iron deficiency. Increased frequency in young female patients can be related to menstrual blood loss and further study to evaluate this association is required.

**Disclosure of Interest:** None declared

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#### THU0399 FEMALE SEXUAL DYSFUNCTION IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES

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**Background:** Idiopathic inflammatory myopathies (IIM) are characterised by inflammation and atrophy of skeletal muscles, pulmonary and articular involvement, which leads to functional impairment, reduced quality of life including sexual life.

**Objectives:** To assess sexual functions/quality of life and pelvic floor function in female IIM patients compared to age-/sex-matched healthy controls (HC).

**Methods:** In total, 22 women with IIM [mean age: 55.1, disease duration: 7.9 years, dermatomyositis (DM, 8)/polymyositis (PM, 10)/necrotizing myopathy (IMNM, 3)/inclusion body myositis (IBM, 1)], who fulfilled the Bohan/Peter 1975 criteria for DM/PM, and 22 healthy controls (mean age: 55.1 years) without rheumatic diseases filled in 12 well-established and validated questionnaires assessing sexual function/quality of life, pelvic floor function, fatigue, physical activity and depression. Data are presented as mean  $\pm$  SEM.

**Results:** Compared to HC, patients with IIM had significantly higher prevalence and greater severity of sexual dysfunction (FSFI, BISF-W: in all subscales as well as total scores), dysfunction of pelvic floor (PISQ-12), and worse sexual quality of life (SQoL-F) (table 1). Worse scores in IIM patients were associated with elevated muscle enzyme levels [lactate dehydrogenase: FSFI ( $r = -0.524, p = 0.0123$ ), BISFW ( $r = -0.528, p = 0.0115$ )], greater fatigue [FIS: FSFI ( $r = -0.434, p = 0.0438$ ), BISF-W ( $r = 0.488, p = 0.0211$ ), SQoL-F ( $r = -0.488, p = 0.0070$ ), PISQ-12 ( $r = 0.643, p = 0.0013$ )], more severe depression [BDI-II: PISQ-12 ( $r = 0.474, p = 0.0258$ )], deteriorated quality of life [HAQ: PISQ-12 ( $r = 0.476, p = 0.0252$ )], and worse ability to perform physical activities [HAP: FSFI ( $r = 0.437, p = 0.0417$ ), BISF-W ( $r = 0.451, p = 0.0351$ ), PISQ-12 ( $r = -0.494, p = 0.0195$ )].

Questionnaire: score range	Idiopathic inflammatory myopathies (n=22)	Healthy controls (n=22)	p-value
FSFI: Female Sexual Function Index: 2 (worst)–36(best)	14.2 $\pm$ 2.7	23.5 $\pm$ 2.5	$p = 0.0146$
BISF-W: Brief Index of Sexual Function for Women: –16(worst)–75(best)	15.5 $\pm$ 3.9	28.9 $\pm$ 3.8	$p = 0.0193$
PISQ-12: Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire short form: 0(best)–48(worst)	13.8 $\pm$ 1.1	8.0 $\pm$ 1.0	$p = 0.0003$
PFIQ7: Pelvic Floor Distress Inventory Questionnaire – short form 7: 0(best)–300(worst)	15.8 $\pm$ 4.5	5.6 $\pm$ 2.3	$p = 0.1450$
SQoL-F: Sexual Quality of Life Questionnaire – Female: 0(worst)–100 (best)	54.9 $\pm$ 6.0	83.1 $\pm$ 3.4	$p = 0.0006$
FSS: Fatigue Severity Scale: 9(best)–63 (worst)	46.9 $\pm$ 2.8	26.7 $\pm$ 2.5	$p < 0.0001$
FIS: Fatigue Impact Scale: 0(best)–160 (worst)	60.6 $\pm$ 6.9	29.0 $\pm$ 4.2	$p = 0.0003$
MAF: Multidimensional Assessment of Fatigue Scale: 1(best)–50(worst)	26.1 $\pm$ 2.3	17.8 $\pm$ 1.4	$p = 0.0129$
BDI-II: Beck's Depression Inventory II: 0 (best)–63(worst)	14.5 $\pm$ 2.2	5.3 $\pm$ 1.1	$p = 0.0003$
HAP: Human Activity Profile – adjusted activity score: 0(worst)–94(best)	53.7 $\pm$ 4.3	81.1 $\pm$ 1.5	$p < 0.0001$
HAQ: Health Assessment Questionnaire: 0 (best)–3(worst)	1.0 $\pm$ 0.2	0.0 $\pm$ 0.0	$p < 0.0001$

**Conclusions:** Women with IIM reported significantly impaired sexual function, sexual quality of life and pelvic floor function than age-matched healthy controls. Worse scores in IIM were associated with disease activity, physical activity, fatigue, depression and quality of life.

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**Disclosure of Interest:** None declared

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**THU0400** **INCIDENCE AND RISK FACTORS FOR GANGRENE IN PATIENTS WITH SYSTEMIC SCLEROSIS FROM THE EUSTAR COHORT**

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**Background:** Digital ulcers (DUs) affect about half of systemic sclerosis (SSc) patients during disease course. In some patients, peripheral vasculopathy can promote critical ischemia and gangrene, severe complications with potential life threatening consequences. Recently the DUO registry suggested a 18% prevalence of gangrene in DU-SSc patients, with smoking and a high number of DUs being predictive factors. However, little is known about gangrene in unselected SSc patients.

**Objectives:** To investigate the prevalence, incidence and risk factors for gangrene in the EUSTAR cohort.

**Methods:** We included patients from the EUSTAR database satisfying the <sup>ACR</sup> 1980 or the ACR/EULAR 2013 classification criteria for SSc, with at least one visit recording data on gangrene. We extracted from this database data regarding the reporting of DUs, DUs history and digital gangrene. Centres were asked for supplementary data on traditional cardiovascular (CV) risk factors. We analysed by uni- and multivariable logistic regression the cross-sectional relationship between gangrene and its potential risk factors such as history of DUs, cutaneous subset, disease duration, autoantibodies, traditional CV risk factors. Furthermore, longitudinal data were analysed by Cox proportional hazards regression.

**Results:** 1757 patients matched the inclusion criteria (age at inclusion 55.9±14.5 years, disease duration since first non-Raynaud's symptom 7.9±10.3 years and from onset of Raynaud's phenomenon (RP) 11.1±11.0 years, male sex 16.7%, 24.6% diffuse cutaneous subset (DcSSc). At inclusion, 8.9% of patients had either current or previous digital gangrene, 15.7% had current DUs and a further 25.8% had previously had DUs. Among the potential risk factors, older age, a history of DUs and the DcSSc subset were statistically significant risk factors in the cross-sectional multivariable model.

For the longitudinal part, during the entire follow-up (median [Q1,Q3] 13.1 [9.6, 19.3] months), 16/771 patients had incident gangrene (2.1%), accounting for an incidence of 1.73/100 patient-years. All 16 patients who developed incident gangrene had previously had DUs and gangrene. Further risk factors for incident gangrene were the DcSSc subset and longer disease duration: hazard ratio [95% confidence interval]: 8.97 [2.90–27.71] and 1.08 [1.04–1.13] respectively, both p<0.001.

**Conclusions:** In unselected SSc patients, gangrene still occurs in about 9% of SSc patients. Of the most importance, a history of DUs and, to a lesser extent, the DcSSc subset are strongly and independently associated with gangrene, while traditional CV risk factors were not identified as risk factors. Our results confirm that gangrene is still a concern in SSc. They emphasise the importance of microvascular SSc-associated disease in the pathogenesis of gangrene and suggest that the DcSSc subset should be prioritised for risk-stratification of the patients.

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**THU0401** **GLOBAL LONGITUDINAL STRAIN AS EARLY PREDICTOR OF SYSTOLIC DYSFUNCTION IN SYSTEMIC SCLEROSIS**

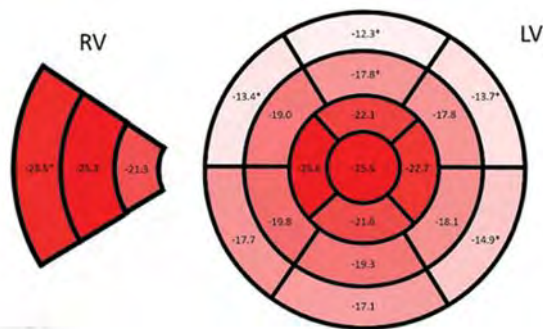
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**Background:** Systemic sclerosis (SSc) is a chronic autoimmune disease of unknown etiology, characterised by microvascular abnormalities, immune abnormalities and progressive cutaneous and internal organs fibrosis. Subclinical heart disease in SSc patients is common but difficult to detect through conventional imaging.

**Objectives:** We sought to evaluate speckle-tracking derived global longitudinal strain (GLS) as an early marker of subclinical systolic dysfunction in patients with SSc.

**Methods:** We enrolled 52 patients with SSc and 52 age and gender matched controls. Patients with structural heart disease, heart failure, atrial fibrillation or pulmonary hypertension were excluded. An echocardiographic exam was performed for all patients, and standard and speckle-tracking derived variables for the systolic and diastolic function of the left ventricle (LV) and right ventricle (RV) were acquired. SSc variant, antibodies pattern, cardiovascular risk factors and involvement of other organ systems were recorded.

**Results:** Common parameters of left and right systolic function did not differ between SSc patients and controls and were on average well above the cut-off for normality (all p=NS). LV and RV GLS were significantly impaired in patients with SSc when compared to healthy controls (-19.2% vs. -21.1%; p=0.009 and -18.2% vs. -22.3%; p=0.012 respectively). In patients with SSc, GLS impairment was greater in basal segments when compared to midventricular and apical ones and homogeneous between the endo-, meso-, or epicardial layers of the RV, while LV showed an eccentric pattern with the epicardial layers mostly impaired. Using -20% as a cut-off for GLS, SSc patients had a 2.5-fold increased risk of subclinical LV systolic impairment (OR 2.5; 95% CI 1.1–5.5; p=0.027) and a 3.3-fold increased risk of subclinical RV systolic impairment when compared to age and gender matched controls (OR 3.3; 95% CI 1.4–7.7; p=0.004).



**Conclusions:** While traditional parameters are ineffective in detecting subclinical systolic impairment, a reduced GLS is common in patients with SSc and is significant for both LV and RV. While GLS impairment recognises a basal-apical gradient, transmural heart involvement seems different between RV and LV, suggesting a different mechanism of disease between the two ventricles.

**Disclosure of Interest:** None declared

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### THU0402 DO WE HAVE GOOD INSTRUMENTS TO PREDICT MAJOR CARDIOVASCULAR EVENTS IN SYSTEMIC SCLEROSIS PATIENTS?

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**Background:** While macrovascular disease and higher cardiovascular (CV) risk are well documented in other systemic rheumatic diseases, the risk for major cardiovascular events for patients with systemic sclerosis (SSc) is yet to be established.

**Objectives:** The aim of the study was to determine the ability of different cardiovascular risk indices to predict major cardiovascular events (MACE) in systemic sclerosis.

**Methods:** The study included 144 patients followed in EUSTAR centre 096, but only patients with a follow-up for more than 10 years were selected for statistical analyses. Cardiovascular risk was estimated using QRiskII, systemic coronary risk evaluation (SCORE) and ACC/AHA risk indices. MACE were defined as: myocardial infarctions, strokes, peripheral vascular disease and cardiovascular related death. Data were compared by non-parametric tests.

**Results:** 32 patients, 31 females, 12 diffuse SSc subsets were included. The control group included 30 age and sex matched patients without autoimmune diseases. Mean age of the group was 52 years±SD 9.7, mean disease duration was 8 years±SD 9. The prevalence of traditional risk factors was: 13% smokers, significant family history 38%, obesity 16%, dyslipidemia 32%, older age 13%, hypertension 16%. There were no significant differences from the control group.

Major cardiovascular events were: 13% myocardial infarction, 9% peripheral vascular disease, 9% CV related deaths. Concerning CV risk indices of the 32 SSc patients, 4 (13%) were classified as having high CV risk according to QRiskII/SCORE/ACC risk.

In SSc patients, we could not identify any correlation between the above mentioned risk indices and MACE, including death of cardiovascular causes, except for a slight correlation between the SCORE and cardiovascular related death ( $p=0.04$ ).

**Conclusions:** In our study, the main prediction indices were not correlated with the 10 year risk for CV events in SSc patients suggesting that we need better risk prediction tools. Both traditional risk factors and endothelial dysfunction have been proposed to participate at the onset and progression of vascular disease in SSc. Special attention should be paid to correct the traditional risk factors in combination with specific treatment for SSc.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.7005

### THU0403 SERUM LEVELS OF MACROPHAGE MIGRATION INHIBITORY FACTOR AND INTERLEUKIN-1 FAMILY CYTOKINES ARE ELEVATED IN SYSTEMIC SCLEROSIS

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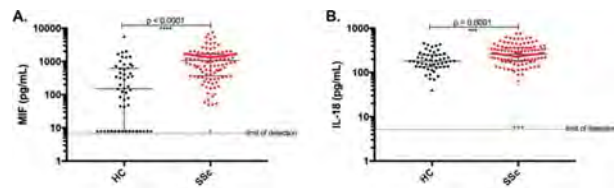
**Background:** Systemic sclerosis (SSc) is an autoimmune connective tissue disorder, the pathogenesis of which remains unknown. Recent evidence suggests dysregulation of the innate immune system, particularly interleukin-(IL)-1 family cytokines. Given the emerging role of macrophage migration inhibitory factor (MIF) in pathways of IL-1 family cytokine secretion, the role of MIF, IL-1 $\alpha$ , IL-1 $\beta$  and IL-18 in SSc is of interest.

**Objectives:** To examine associations between MIF and IL-1 cytokines (IL-1 $\alpha$ , IL-1 $\beta$ , IL-18), in SSc, and associations with clinical features.

**Methods:** 115 SSc patients (2013 ACR/EULAR criteria) attending Monash Scleroderma Clinic and 52 healthy controls were recruited between August 2015 and August 2017. Serum MIF, IL-1 $\alpha$ , IL-1 $\beta$  and IL-18 levels were quantified using ELISA and analysed alongside concurrent clinical and laboratory data from the Australian Scleroderma Cohort Study database

**Results:** Compared to controls, SSc patients had significantly elevated serum MIF and IL-18 (figure 1). A weak positive correlation was observed between MIF

and SScHAQ score ( $R=0.2107$ ,  $p=0.0437$ ) which was stronger in the diffuse cutaneous (dcSSc) subgroup ( $R=0.457$ ,  $p=0.0373$ ). Patients with elevated IL-18 levels were more likely to have active disease (EUSTAR score  $\geq 3$ ) however IL-18 was lower in patients with pulp atrophy and sclerodactyly. IL-1 $\beta$  was elevated in dcSSc patients with pulmonary fibrosis and correlated with mRSS ( $R=0.213$ ,  $p=0.0254$ ) in all SSc patients. IL-1 $\alpha$  was elevated in patients with joint contractures and pulp atrophy. Positive correlations were found between concentrations of MIF and both IL-1 $\alpha$  and IL-1 $\beta$ . However, there was no significant correlation between MIF and IL-18.



**Abstract THU0403 – Figure 1.** Serum cytokines in SSc patients and healthy controls. Serum cytokines (A) MIF and (B) IL-18 were measured by ELISA in healthy controls ( $n=52$ ) and SSc patients ( $n=115$ ). Data is presented as median  $\pm$  interquartile range. Analysis was performed in Prism using the Mann-Whitney test.

**Conclusions:** MIF and IL-18 were significantly elevated in SSc compared to health controls, and IL-1 family cytokines were variably associated with clinical manifestations of SSc. A relationship between MIF and IL-1 $\beta$  was confirmed. Further investigation into the roles of MIF and IL-1 family cytokines in SSc is justified.

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**Disclosure of Interest:** None declared

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### THU0404 ESOPHAGEAL INVOLVEMENT PREDICTS PULMONARY FUNCTION DETERIORATION IN PATIENTS WITH SYSTEMIC SCLEROSIS

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**Background:** Interstitial lung disease (ILD) is the leading cause of death in systemic sclerosis (SSc) but its pathogenesis and the risk factors of pulmonary function deterioration are not fully understood. Esophageal disease is high frequent in SSc and motor activity abnormalities with occult micro-aspiration of both acid and non-acid gastro oesophageal reflux has been implicated in the pathogenesis of ILD. DLCO reduction is considered the earliest sign of microaspiration-induced lung damage<sup>1</sup>. Cross-sectional studies have demonstrated an association of SSc-ILD and esophageal abnormalities on 24 hours intraoesophageal pH-monitoring and esophageal manometry but prospective evaluation of lung deterioration is lacking<sup>2,3</sup>. Esophagogram was proposed as a useful tool to evaluate disease severity of upper gastrointestinal tract involvement in SSc<sup>4</sup>.

**Objectives:** To assess the role of esophagogram in predicting pulmonary function test deterioration in SSc-patients.

**Methods:** We retrospectively evaluated 160 consecutive SSc patients who underwent esophagogram because of suspected upper gastro-intestinal involvement. All patients underwent baseline pulmonary function tests and global clinical evaluation. Eighty-five patients underwent a High Resolution CT within 3 months from esophagogram because of suspected lung involvement. One hundred twenty three patients underwent pulmonary function test every 6 months up to 24 months.

**Results:** Seventy five patients (46.9%) presented abnormalities of peristaltic waves, 50 patients (31.2%) showed structural changes (hypotonic oesophagus or dilatation) while indirect signs of cardiac incontinence (patent cardia or gastro-esophageal reflux) were present in 36 patients (22.5%). A reduced peristaltic activity with a prolongation of transit time was associated to reduced DLCO (50.16% $\pm$ 19.80% vs 60.36% $\pm$ 22.69%,  $p=0.002$ ) and TLC (87.05% $\pm$ 20.43% vs 95.09% $\pm$ 20.59%,  $p=0.017$ ). An hypotonic oesophagus was reported in 25.2% of patients and it was associated to ILD on CT (72.0% vs 28.0%,  $p=0.033$ ). Patients



with hypotonic oesophagus presented a reduced FVC (84.63%±22.86% vs 102.93±21.40%,  $p<0.0001$ ), TLC (79.85%±19.62% vs 95.29±19.80,  $p<0.0001$ ) and DLCO (42.88%±20.00% vs 59.89±20.78%,  $p<0.0001$ ) at baseline and to a faster deterioration of DLCO median values (5.10%±20.61% vs -4.77±14.23%,  $p=0.012$ ) at follow-up. Patients with hypotonic oesophagus have a higher prevalence of diffuse skin disease and ongoing immunosuppressive treatment, but were comparable in term of age, sex, BMI, smoking habits, disease duration and prevalence of autoantibodies to the patients without this alteration.

**Conclusions:** The esophagogram is wide available, well tolerated and inexpensive tool to assess upper gastro-intestinal tract involvement and its abnormalities are associated to SSc-ILD severity. Because of a faster deterioration of lung function is associated to esophagogram abnormalities, a complete gastro-intestinal evaluation in ILD-SSc patients is mandatory.

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THU0405

#### THE ASSOCIATION BETWEEN BASELINE SERUM RESISTIN LEVELS AND THE DEVELOPMENT OF NEW DIGITAL ULCERS IN PATIENTS AFFECTED BY SYSTEMIC SCLEROSIS

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**Background:** Resistin is a soluble factor produced by adipose tissue, implicated in the regulation of inflammatory processes and in microvascular damage.<sup>1</sup> When incubated with resistin, endothelial cells respond by a greater production of endothelin-1, a potent endothelium-derived vasoactive factor that engenders endothelial dysfunction (ED) in many cardiovascular and autoimmune diseases, such as Systemic Sclerosis (SSc).<sup>2</sup> SSc is a complex connective tissue disease, whose pathogenesis results from the variable interaction of three main processes: microvascular damage, autoimmunity-mediated inflammation and fibroblast activation.<sup>3</sup> ED is at the base of the development of painful ischaemic events due to chronic hypoxia, namely digital ulcers (DUs),<sup>4</sup> considered a prognostic marker of disease severity.<sup>5</sup>

**Objectives:** To evaluate the association between baseline serum resistin levels and the development of new DUs in a cohort of patients with SSc.

**Methods:** We conducted a one-year prospective cohort study. Patients with SSc and healthy controls (HC) were consecutively enrolled. Baseline serum resistin was assessed by commercial ELISA kit. The development of new DUs was prospectively evaluated during the follow-up after the cross-sectional point in which the resistin levels were measured.

**Results:** We enrolled 70 SSc patients and 26 HC matched by gender and vital parameters. Mean basal resistin levels were increased in SSc patients compared to HC (6.58±5.48 vs 2.56±0.95,  $p=0.0004$ ). In SSc group, resistin was higher among patients with active DUs ( $p=0.0007$ ), infected DUs ( $p=0.0009$ ) and active pattern at nailfold videocapillaroscopy ( $p=0.01$ ). During one-year follow-up, 27 (38%) SSc patients presented new skin ulcers. Baseline resistin was increased in patients who developed new DUs (8.4±6.4 vs 5.4±4.5,  $p=0.026$ ). In multiple logistic regression, the development of new DUs was associated to basal serum resistin concentration (OR 2.1, 95% CI 1.1–3.9), to the presence of active DUs at

baseline (OR 3.4, 95% CI 1.0–11.9), and to basal Disease Activity Score (DAI) according to European Scleroderma Study Group<sup>6</sup> (OR 1.3, 95% CI 1.0–1.6). In proportional Cox regression, the time to new DUs was associated to basal resistin concentration (HR 1.7, 95% CI 1.1–2.8) and DAI (HR 1.2, 95% CI 1.0–1.4).

**Conclusions:** Serum resistin seems to be associated to the presence and to the development of DUs, suggesting a possible involvement in micro-vascular dysfunction in patients affected by SSc.

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THU0406

#### IV CYCLOPHOSPHAMIDE VS. RITUXIMAB FOR THE TREATMENT OF EARLY DIFFUSE SCLERODERMA LUNG DISEASE: OPEN LABEL, RANDOMISED, CONTROLLED TRIAL

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**Background:** Systemic sclerosis is characterised by fibrotic changes in the skin and lung, and the mainstay of treatment has been cyclophosphamide. B cell involvement suggests that rituximab may also be of therapeutic benefit. In this study, we compared the safety and efficacy of rituximab compared to cyclophosphamide in the treatment of skin and lung manifestations of systemic sclerosis.

**Objectives:** The aims of the study were to assess the efficacy and safety of IV Rituximab compared to IV cyclophosphamide in the primary therapy of systemic sclerosis, with particular emphasis on pulmonary and dermatological manifestations.

**Methods:** We randomly assigned 60 patients of systemic sclerosis, age 18–70 years with skin and lung involvement, to monthly pulses of cyclophosphamide 500 mg/sq. m or rituximab 1000 mg x 2 doses at 0, 15 days. Primary outcomes were forced vital capacity (FVC) percent predicted at six months. Secondary outcomes were: absolute change in litres (FVC-L) at 6 months; modified Rodnan Skin Scores at 6 months, six-minute walk test (6MWT), and Medsger's score

**Results:** The FVC (%mean ±SD) in Rituximab group improved from 61.30 (±11.28) to 67.52 (±13.59) while in Cyclophosphamide group, it declined from 59.25 (±12.96) to 58.06 (±11.23) at 6 months ( $p=0.003$ ). The change of FVC was 1.51 (±0.45) L to 1.65 (±0.47) L in Rituximab group compared to 1.42 (±0.49) to 1.42 (±0.46) L in Cyclophosphamide group. The mRSS changed from 21.77 (±9.86) to 12.10 (±10.14) in RTX group and 23.83 (±9.28) to 18.33 (±7.69) in Cyclophosphamide group after 6 months. Serious adverse events were more common in the cyclophosphamide group.

	Rituximab (n=30)			Cyclophosphamide (n=30)			Difference at 6 months Mean (95% CI)	p-value
	Baseline (mean (SD))	6 months (mean (SD))	p-value	Baseline (mean (SD))	6 months (mean (SD))	p-value		
Forced vital capacity (%)	61.30 (11.28)	67.52 (13.59)	0.002 <sup>a</sup>	59.25 (12.96)	58.06 (11.23)	0.496 <sup>a</sup>	9.46 (3.01 to 15.90)*	0.003 <sup>b</sup>
Forced vital capacity (L)	1.51 (0.45)	1.65 (0.47)	<0.001	1.42 (0.49)	1.42 (0.46)	0.356	0.23 (-0.013 to 0.47)**	0.091 <sup>b</sup>
Modified Rodnan Skin Score at baseline	21.77 (9.86)	12.10 (10.14)	<0.001	23.83 (9.28)	18.33 (7.69)	<0.001	-6.23 (-10.88 to -1.58)***	0.001 <sup>b</sup>
Medsger's Severity Scale	8.33 (3.04)	4.67 (2.35)	<0.001	9.60 (2.44)	5.96 (2.81)	<0.001	-1.30 (-2.64 to 0.04)#	0.036 <sup>b</sup>
6 min walking test (metres)	359.63 (65.95)	409.60 (69.29)	<0.001	335.90 (89.30)	349.14 (99.75)	0.428	60.46 (16.07 to 104.84) ****	0.001 <sup>b</sup>
Pulmonary hypertension present	4 (13%)	5 (16%)		5 (16%)	5 (16%)		##	

a Statistical comparison for FVC (%) before and after therapy for each group were done with paired-t test. For all other outcome variables same analysis was run with Wilcoxon signed rank test and reported p-values are 2-tailed only.

b Denoted comparison of outcome variables at 6 month between the two treatment groups i.e., rituximab versus cyclophosphamide. P-values were calculated by Mann-Whitney U test and reported p-values are 2-tailed only.

\* $p=0.005$  \*\* $p=0.063$  \*\*\* $p=0.01$  \*\*\*\* $p=0.008$  #  $p=0.057$  ## $p=1$

**Conclusions:** Rituximab is a safe and effective alternative to cyclophosphamide in the primary therapy of skin and lung manifestations of scleroderma.

**Disclosure of Interest:** None declared

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#### THU0407 EVALUATION OF SOLUBLE AND MEMBRANE HLA-G IN PATIENTS WITH SYSTEMIC SCLEROSIS AND ROLE OF THESE MOLECULES IN THE PATHOGENESIS OF THE DISEASE

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**Background:** Systemic sclerosis (SSc) is a complex disease characterised by immune abnormalities, vascular damage and fibrosis. Human leukocyte antigen-G (HLA-G) is a non-classic class I major histocompatibility complex (MHC) molecule expressed on different cell lineages in both physiological and pathological conditions and detectable in soluble forms (sHLA-G1 and HLA-G5 shed and secreted isoform, respectively). Several immunomodulatory functions have been attributed to both membrane-bound and soluble HLA-G molecules. HLA-G is expressed on extravillous cytotrophoblast, in placenta but also in a few normal tissues, solid tumours, transplanted organs and virally infected cells. Soluble form (sHLA-G) derives from shedding of cleaved surface isoforms (sHLA-G1) or secretion of soluble isoforms (HLA-G5). Immunosuppressive functions have been attributed to both membrane HLA-G (mHLA-G) and sHLA-G.

**Objectives:** The aims of the present study were: 1) to determine the serum levels of sHLA-G molecules in a cohort of SSc patients with the limited or diffuse form of the disease; 2) to correlate sHLA-G levels with TGF- $\beta$ ; 3) to evaluate the expression of HLA-G in peripheral blood mononuclear cells (PBMC).

**Methods:** Thirtyfive patients (28 females/7 males, age 40–89 years) with diffuse SSc (dSSc, n. 12) or limited SSc (lSSc, n. 23) and 40 healthy sex and age matched controls were enrolled. Plasma sHLA-G, sHLA-G1 and HLA-G5 levels were determined by immunoenzymatic assays. mHLA-G expression in peripheral blood mononuclear cells (PBMC) was evaluated by flow cytometry.

**Results:** The plasma levels of sHLA-G were higher in SSc patients (444.27  $\pm$  304.84 U/ml) compared to controls (16.74  $\pm$  20.58 U/ml) ( $p < 0.0001$ ). The plasma levels of TGF- $\beta$  were higher in SSc patients (18937  $\pm$  15217 pg/ml) compared to controls (11099  $\pm$  6081 pg/ml);  $p = 0.003$  and a significant correlation was found between TGF- $\beta$  and the plasma levels of total sHLA-G ( $r: 0.65$ ;  $p < 0.01$ ), sHLA-G1 ( $r: 0.60$ ;  $p = 0.003$ ) and HLA-G5 ( $r: 0.47$ ;  $p = 0.02$ ). The percentage of HLA-G-positive monocytes (0.98  $\pm$  1.72), CD4+ (0.37  $\pm$  0.68), CD8+ (2.05  $\pm$  3.74) and CD4+CD8+ double positive cells (14.53  $\pm$  16.88) was higher in SSc patients than in controls (0.11  $\pm$  0.08, 0.01  $\pm$  0.01, 0.01  $\pm$  0.01 and 0.39  $\pm$  0.40, respectively) ( $p < 0.0001$ ). A high percentage of HLA-G+ cells (30.47  $\pm$  26.75) was detectable on CD4<sup>dim</sup>CD8<sup>high</sup> cells from SSc patients only.

**Conclusions:** These data indicate that in SSc secretion and/or shedding of sHLA-G and mHLA-G are clearly elevated and involved in immune dysregulation.

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#### THU0408 CHARACTERISTICS OF MILD TO MODERATE LUNG DISEASE IN SYSTEMIC SCLEROSIS AND IMPACT OF SURVIVAL; DATA FROM THE POPULATION-BASED, NATIONWIDE NORWEGIAN COHORT

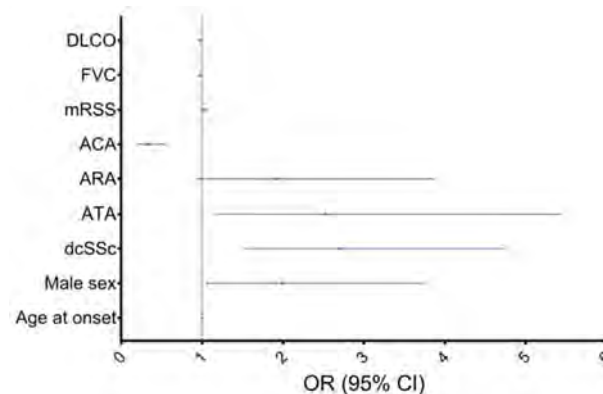
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**Background:** In systemic sclerosis (SSc) it is well-documented that severe interstitial lung disease (ILD), defined as an extent of lung fibrosis >20% on high resolution computed tomography (HRCT) is strongly associated with male gender, anti-topoisomerase antibody (ATA), diffuse cutaneous (dc) form of disease and decreased survival. Much less is, however, known about the disease characteristics and impact of less lung involvement. A possible explanation might be the selected nature of many hitherto investigated SSc cohorts. In an era with novel treatment options, and multiple ongoing clinical trials, it is important to gain natural history knowledge on the whole spectre of lung involvement in systemic sclerosis.

**Objectives:** Characterise the SSc patients with mild to moderate ILD, defined as 1%–10% extent of lung fibrosis on HRCT in the population based nationwide Norwegian SSc cohort and assess the impact of this ILD form on survival.

**Methods:** The Norwegian, nationwide SSc (Nor-SSc) study cohort included all adult SSc patients who were resident in Norway between 01.01.2000–01.01.2013 and met the classification criteria for SSc. Detailed electronic patient journal review was performed in all patients to assess demographic, clinical and ILD features at baseline. Pulmonary function tests (PFTs) and lung HRCT images were analysed and the extent of lung fibrosis was expressed as percentage of total lung volumes. We defined mild-moderate ILD as 1%–10% fibrosis on HRCT and severe disease as >20% fibrosis. Ground glass opacities, bronchiectasis and honeycombing were registered if present. Vital status and causes of deaths were available in all patients at study end (January 2018). Descriptive statistics and regression analysis were applied.

**Results:** The Nor-SSc cohort included 815 patients. Baseline lung HRCT images were available in 416 patients (51%), whereof 226 (54.3%) had signs compatible with ILD. Mild to moderate ILD, defined as 1%–10% lung fibrosis were present in 149 (65.9%), while 48 (21.2%) had extensive lung fibrosis defined as >20%. Patients with mild-moderate ILD were 55.2 years at SSc onset and characterised by female gender (81.9%) and limited cutaneous SSc (70.5%). Their antibody profile was dominated by anti-centromere Ab (ACA) in 48.3%, followed by anti-polymerase III, ATA, and anti-RNP, in 14.1%, 13.4% and 5.4%, respectively. The mean modified Rodnan skin score (mRSS) was 9.3 (9.3%), baseline FVC was 93.4% and DLCO 66.5%. Univariable associations of clinical characteristics and mild-moderate ILD are shown in figure 1. After a mean observation time of 8.2 years, 49 (32.9%) of patients with mild-moderate ILD had died. The 5- and 10 year survival was 76% and 62% compared to 83% and 76% in patients with no ILD ( $p = 0.03$ ). In univariable cox regression analyses, mild-moderate ILD was associated with mortality (HR 1.6, 95% CI 1.03–2.40,  $p = 0.034$ ).



**Abstract THU0408 – Figure 1.** Associations of clinical characteristics and mild-moderate ILD at baseline

**Conclusions:** In this population based, nationwide study, mild-moderate ILD was frequent and had a considerably impact on survival in SSc patients.

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THU0409

### MANAGEMENT OF SYSTEMIC SCLEROSIS (SSC) RELATED DIGITAL ULCERS (DU) IN EXPERT TERTIARY CENTRES: RESULTS FROM THE ANALYSIS OF THE MULTICENTRE OBSERVATIONAL REAL-LIFE DESSCIPHER/EUSTAR STUDY

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**Background:** In SSC, the management of DU is a real clinical challenge. It includes the use of vasoactive and vasodilating drugs, but no comparative studies between agents are available. DeSScipher was the first European multicentre observational study with the aim to decipher the optimal management of SSC.

**Objectives:** To assess in expert centres the current therapeutic strategy for the management of SSC related DU.

**Methods:** Baseline demographic and clinical characteristics of patients enrolled in the DeSScipher/EUSTAR ulcer study and detailed data regarding DU were analysed.

**Results:** There were 1823 patients enrolled in this study. 277 (15.2%) presented DU at the enrolment visit, 628 (34.4%) had previous DU and 918 (50.4%) had never experienced DU. Patients with DU (current or previous) were more frequently anti-Scl70 positive, had more frequently the diffuse cutaneous subset (40.8% vs 26.7% ( $p<0.000$ )), gastro-esophageal symptoms (70% vs 63.4% ( $p=0.002$ )) and lung fibrosis on lung Rx or HRCT (65.7% vs 54% ( $p=0.001$ )) compared to patients without DU. There were no significant differences in the prevalence of pulmonary hypertension (7.3% patients with DU vs 5.3% patients without DU,  $p=0.87$ ). Treatment of patients with and without DU is shown in table 1.

**Abstract THU0409 – Table 1.** Treatment of patients with and without DU

	Patients with DU (current or previous) 905 patients	Patients without DU (never developed) 918 patients
Calcium channel blockers	601 (66.4%)	704 (76.9%)* ( $p<0.000$ )
Bosentan	199 (22%)	41 (4.5%)* ( $p<0.000$ )
Sildenafil	120 (13.3%)	57 (6.2%)* ( $p<0.000$ )
Bosentan+Sildenafil	85 (9.4%)	15 (1.6%)* ( $p<0.000$ )
Iloprost iv in the last 3 months	306 (33.8%)	74 (8.1%)* ( $p<0.000$ )
No vasodilating therapy	48 (5.3%)	97 (10.6%)* ( $p<0.000$ )
Immunosuppressants	482 (53.3%)	560 (61%)

Information on recurrent DU were available for 779 (86.1%) of patients with DU. Treatment of patients with and without recurrent DU is shown in table 2.

**Abstract THU0409 – Table 2.** Treatment of patients with and without recurrent DU

	Patients with recurrent DU (428)	Patients without recurrent DU (351)
Calcium channel blockers	258 (60.3%)	255 (72.7%)* ( $p<0.000$ )
Bosentan	105 (24.5%)	70 (19.9%)
Sildenafil	58 (13.6%)	45 (12.8%)
Bosentan+Sildenafil	323 (75.5%)	87 (24.7%)* ( $p<0.000$ )
Iloprost iv in the last 3 months	212 (49.5%)	77 (22%)* ( $p<0.000$ )
No vasodilating therapy <sup>a</sup>	27 (6.3%)	14 (3.9%)
Immunosuppressants	222 (51.9%)	226 (64.3%)

**Conclusions:** 90% of SSC patients were on vasodilating and/or vasoactive treatment regardless of the history/presence of DU. Recurrent DU were treated

aggressively, using in 75% of cases Bosentan and Sildenafil combination therapy. Our data indicate frequent use of Sildenafil and Bosentan for DU management in specialised centres, especially for recurrent DU.

**Disclosure of Interest:** None declared

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THU0410

### SURVIVAL OF PATIENTS WITH MUSCLE BIOPSY PROVEN IDIOPATHIC INFLAMMATORY MYOPATHY BASED ON A STUDY IN A TERTIARY UNIVERSITY CENTRE

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**Background:** Idiopathic inflammatory myopathies (IIM) are characterised by muscle weakness due to muscle inflammation, various organ involvements and the presence of certain specific autoantibodies.

**Objectives:** To assess survival and characterise subsets based on muscle biopsy and myositis specific autoantibodies.

**Methods:** Eighty-two patients with muscle biopsy proven IIM were included in the study. Muscle biopsy was reevaluated and categorized by the same investigator (EP). All cases had myositis specific (MSA) and myositis associated (MAA) antibody tests. The MSAs and MAAs (Jo-1, PL-7, PL-12, Mi-2, SRP, Pm-Scl, Ku, ribosomal, AMA-M2) were tested with Western-blot.

Dermatomyositis/DM/, polymyositis/PM/, juvenile PM/DM, inclusion body myositis/IBM/, overlap myositis/OM/ and immune mediated necrotizing myopathy/IMNM/were identified based on clinical data, immunoserology and muscle biopsy. Patients were treated with glucocorticoids/cytostatics, interstitial lung disease was treated with pulse cyclophosphamide in 15/43 cases. Survival analysis was performed by Kaplan Meier test.

**Results:** Fifty-nine women and 23 men with a mean age of 49.3±14.6 years were included. Mean follow-up of the patients was 7.5±4.5 years. Interstitial lung disease (ILD) (51.2%), arthritis (51.2%), Raynaud's phenomenon (42.7%), skin symptoms (45.1%), dysphagia (24.4%) and significant cardiac involvement (15.9%) were the most prevalent disease manifestations. 15 cases were associated with malignancies.

The distribution of myositis subsets is as follows: 26.8% (n=22) PM, 30.5% (n=25) DM, 1.2% (n=1) juvenile PM/DM, 8.5% (n=7) IBM, 22% (n=18) OM, and 11% (n=9) IMNM.

Malignancy was most frequently associated with IMNM (7 out of 9 patients).

Altogether 18 patients died from which 15 deaths can be connected to myositis related events. Eight patients died of malignancies (4 in the IMNM, 2 in the PM and 2 in the DM group), 5 patients due to cardiac events (heart failure, arrhythmia), 2 due to lung fibrosis and 3 by unknown causes. The worst prognosis with a 10 year survival of 31% was in the IMNM subgroup ( $p<0.01$ ), followed by patients with PM (68%), IBM (84%) OM (85.1%) and DM (85.3%). Mi-2 positive patients had a favourable prognosis with a 10 year survival of 100. Patients with muscle histology corresponding with IMNM had the worst prognosis (10 year survival of 31.1%), followed by PM (76%), DM and IBM (85.7% each). Non specific muscle changes unclassifiable to any of the previous groups were associated with a relatively favourable prognosis (5 year survival of 80%) ( $p<0.01$ ).

Patients with antisynthetase antibody-positivity had worse prognosis compared with patients with other antibodies or no identifiable antibodies (10 year survival of 55%, n=16) ( $p<0.05$ ). When comparing patients with MSA or MAA, the worst prognosis was seen in patients with both MSA and MAA positivity (10 year survival of 35.6%, n=10).

**Conclusions:** The worst survivals were seen in the IMNM and PM groups, due to the high frequency of the underlying malignancies and cardiac manifestations. Although ILD was the most frequent involvement, it was not a major determinant of outcome.

**Disclosure of Interest:** None declared

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THU0411

### MYASTHENIA GRAVIS WITHOUT THYMIC PATHOLOGY AND POLYMYOSITIS: A RARE ASSOCIATION

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**Background:** Myasthenia gravis(MG) is an autoimmune disease frequently associated with antibodies against the acetyl-choline receptor. These antibodies contribute to the characteristic defects in neuromuscular transmission. Inflammatory myopathies, as polymyositis(PM), are immune-mediated neuromuscular



diseases. PM and MG present both with muscle weakness and other similar features; electrophysiological and laboratory features of each of them are distinct. In Literature there are only few reports about PM and MG association

**Objectives:** To evaluate the prevalence of MG in patients with PM in our case series

**Methods:** We enrolled patients with PM/DM visited in our Centre in past 10 years; diagnoses of PM/DM were based on Bohan and Peter criteria. The follow-up was conducted until December 2017

**Results:** We made 17 PM/DM diagnosis:14 F and only 3 M aged 41–85 years (mean 65 y). We found 6 patients (42,8%) with association of PM and MG. They are all F, aged 51–78 years (mean 61 y) who developed inflammatory myositis confirmed by increasing of CK, EMG, autoantibodies pattern positivity and deltoid biopsy. Paraneoplastic, post-infectious or post-vaccinal syndromes was excluded. At the onset all presented progressive proximal muscle weakness and pain and asthenia. After initial treatment with oral corticosteroids (0.5–1 mg/kg/day methylprednisolone) a minimal response was observed only as improvement of asthenia and decreasing of CK levels. After one month of therapy 2 patients developed a bilateral palpebral ptosis, one dysphagia and mild dyspnea, one a severe intestinal pseudo-obstruction, 2 a mild dysarthria, ipovision and a worsening of muscular tone. Pyridostigmine test was positive in all patients; antiAChR antibodies levels were high. We started high doses corticosteroids (methylprednisolone 500–1000 mg/day for 5 days) and pyridostigmine (180–240 mg/day) with smart improvement. After this we introduced an immunosuppressant: azathioprine in 3 patients, mycophenolate mofetil in 4 patients. At the same time, because of the severity of the disease, monthly cycles of high doses IgV (20 g/kg in 5 days) were performed in 5 patients. A stable remission was achieved and maintained in all patients

**Conclusions:** This is one of the largest case series of patients with PM/DM-MG overlap. Our findings suggest that this association is not so rare and that patients affected by PM presenting palpebral ptosis, diplopia, gastrointestinal or oral symptoms, bulbar symptoms, weakness, asthenia, should be evaluated to exclude a concomitant MG, despite the absence of thymic pathology. A patient with PM-MG overlap should allow us for proper management of both conditions. This may include a more adequate therapy providing simultaneous association between immunosuppressant, pyridostigmine and, if necessary, a short time of high doses IgV therapy

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THU0412

#### ABSOLUTE REDUCTION OF PERIPHERAL CD4 + REGULATORY T CELL SUBSET OF PATIENTS WITH SYSTEMIC SCLEROSIS AND ITS RESTORATION BY SHORT-TERM AND LOW DOSE IL-2 TREATMENT

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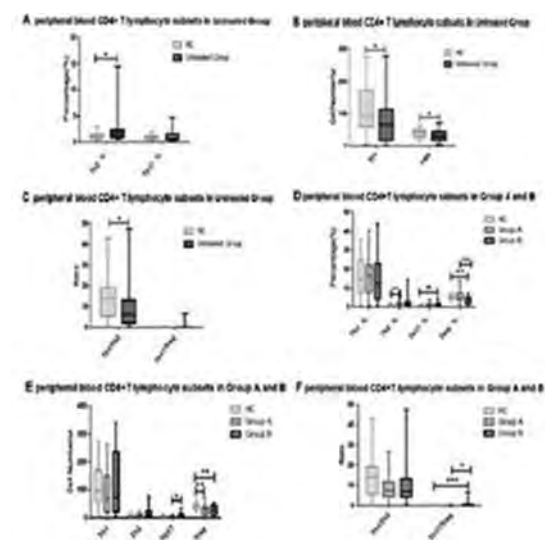
**Background:** Systemic sclerosis (SSc) is a chronic inflammatory disease with complex pathogenesis. The role of regulatory T cells (Tregs) in the development of SSc has started being studied during the last decade with new aspects being disclosed continuously. Although there is a general agreement in the medical literature regarding the decreased functional capacity of circulating Tregs in SSc, the alteration of absolute number of Treg cells as well as other CD4 + T lymphocyte subsets in SSc is still unclear.

**Objectives:** The aim of the present study was to explore the absolute number status of CD4 + T subsets in peripheral blood of patients with SSc using our modified flow cytometric method and investigate whether the imbalance of Th17 and Treg cells can be corrected by supplementing low dose interleukin -2 (IL-2).

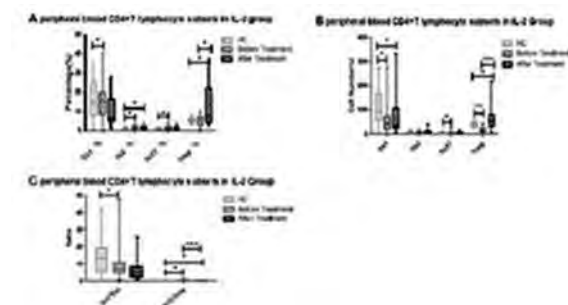
**Methods:** The peripheral CD4 + T subsets from 54 patients with SSc and 30 healthy control subjects were analysed. The patients were divided into the untreated group (n=29) and treated group (n=25). The patients were also divided into group A (n=28) who only used low-dose glucocorticoids (GCS), and group B (n=26) who also used immunosuppressant cyclophosphamide (CYC), methotrexate (MTX), leflunomide (LEF) or mycophenolate mofetil (MMF). In addition, 21 patients from 54 patients, given a small dose of IL-2 (50WIU) treatment for a 5 day

course, divided into pre-treatment group and post-treatment group. Directly using the results from flow cytometry combined with internal standard beads, absolute number of peripheral CD4 + T subsets from the subjects in each group were calculated.

**Results:** Although there were some changes among CD4 + T cell subsets in peripheral blood from these SSc patients, the major alteration was the reductions of Treg cell absolute number. Compared with the normal controls, the number of CD4 + CD25 + FOXP3 + Treg cells were significantly decreased in all patients (p=0.001), in untreated group (p=0.029), in treated group (p=0.029), in group A (p=0.006) and in group B (p=0.004). The ratio of Th17/Treg in total patients (p=0.008) and group B (p=0.001) were significantly higher than that in normal control group, and the group B was significantly higher than the group A (p=0.032). Moreover, the number of Th17 cells in group B was significantly higher than that in group A (p=0.023). After IL-2 treatment, the absolute number of CD4 + CD25 + FOXP3 + Treg cells (p<0.001) were significantly increased, while the number of Th1, Th2 and Th17 cells were slightly higher than those before treatment with IL-2 (p>0.05). Since Th17 cells increases significantly lower than Treg cells, so their ratio decreases significantly (p=0.001) to get re-balance.



**Abstract THU0412 – Figure 1.** Comparison of the levels of CD4+ T lymphocyte subgroups among different groups. (A and D) The percentage of Th2 cells were significantly increased in untreated group and Group A compared with healthy controls. (B and E) The number of CD4+CD25+FOXP3+Treg cells decreased in patients with SSc, whether or not they use immunosuppressive agents. (C and F) The ratio of Th17/Treg cells was found to be significantly increased in Group A, as well as between Group B and Group A. \*P<0.05; \*\*P<0.01; \*\*\*P<0.001.



**Abstract THU0412 – Figure 2.** Comparison of the levels of CD4+ T lymphocyte subgroups among different groups as well as before and after IL-2 treatments. (A) The percentage of Th2 cell were significantly increased before and after IL-2 treatment compared with healthy controls, and the percentage of Treg cells significantly increased after IL-2 treatment. (B) The number of CD4+CD25+FOXP3+Treg cells decreased in patients before IL-2 treatment, but increased significantly after IL-2 treatment (p<0.05); while Th1, Th2 and Th17 cells after IL-2 treatment were slightly higher than those before treatment (p>0.05). (C) The ratio of Th17/Treg cells were found to be significantly increased after IL-2 treatment. \*P<0.05, \*\*P<0.01, \*\*\*P<0.001.

**Conclusions:** The absolute number of peripheral CD4 +CD25+FOXP3+Treg cells decreased in untreated patients, indicating that this reduction arising from the disease itself. Our findings suggest that SSc progression is associated with the absolute decrease of peripheral Treg cells. Although there was no statistically

significant different, absolute number of the Treg cells trended to decrease in patients treated with immunosuppressive agents. The use of IL-2 can effectively up-regulate Treg cells as well as increase Th17 to a certain extent, which restores the balance of Th17/Treg cells, but the long-term effect needs further investigation.

**Disclosure of Interest:** None declared

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#### THU0413 NORMALISATION OF NAILFOLD MICROVASCULATURE AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION IN SEVERE SYSTEMIC SCLEROSIS

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**Background:** Microangiopathy in Systemic Sclerosis (SSc), as visualised by nailfold capillary microscopy (NCM), is a dynamic and sequential process. Uncontrolled case-reports and a case-series report possible improvement of nailfold microangiopathy after hematopoietic stem cell transplantation (HSCT).

**Objectives:** To evaluate differences in nailfold microvasculature in patients with severe SSc treated with HSCT and those treated otherwise.

**Methods:** Severe SSc was defined as fulfilling criteria of the ASTIS trial.<sup>1</sup> For included patients two treatment groups were defined: 1. Patients treated with HSCT, 2. Patients treated otherwise (including cyclophosphamide, methotrexate, mycophenolate mofetil and rituximab). All available capillaroscopy images collected prior to and after treatment were scored independently by two trained observers, blinded for treatment. Scoring included categorical scores (0=no changes to 3≥66% alterations per millimetre) for capillary loss, neoangiogenesis, haemorrhages, dilatations, giants, disorganisation, together with a qualitative pattern and a VAS score for overall severity of microangiopathy.

**Results:** In total 55 patients were included, of whom 33 were female, mean age was 50±13 years and median mRSS of 20.<sup>15-28</sup> Twenty-nine patients were treated with HSCT. After treatment categorical score of capillary loss was lower with HSCT (median score 1.0 vs. 2.0, p=0.04) and VAS scores for severity of microangiopathy were better with HSCT (50.0 vs. 67.3, p=0.03). Compared to controls, a typical SSc pattern was less frequent in patients treated with HSCT (n=12/22, 55%, vs. n=18/20, 90% p=0.01).

In 25 patients (HSCT n=11, control n=14) images prior to treatment were available. Improvement in capillary loss (HSCT -0.5 [IQR -1 to 0] vs. control +0.3 [IQR -1.0 to 1.0] p=0.01;), dilatation (HSCT -1.5 [IQR -2.0 to -1.0] vs. control 0.0 [IQR -1.0 to 0.5] p<0.01) and VAS scores (HSCT median -32.5 [IQR -80.5 to -4.5] vs. - controls +2.0 [IQR -35.5 to +46.0] p<0.01;) improved significantly more in the HSCT group.

**Conclusions:** In patients with severe SSc, microangiopathy as reflected by nailfold capillaroscopy images, is less severe after treatment with HSCT and shows more improvement over time compared to patients with severe SSc treated otherwise. In specific, improvement seems to be characterised by normalisation of the capillary diameter and capillary density. To our knowledge, this is the first study to report on changes in microangiopathy after HSCT in a controlled study design.

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**Disclosure of Interest:** None declared

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#### THU0414 ASSOCIATION OF THE ESOPHAGEAL DILATION AND INTERSTITIAL LUNG DISEASE ON CHEST HIGH-RESOLUTION COMPUTED TOMOGRAPHY IN PATIENTS WITH IN SYSTEMIC SCLEROSIS: A CROSS-SECTIONAL STUDY

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**Background:** Esophageal dilation and dysfunction has been implicated in the pathogenesis of interstitial lung disease (ILD) in systemic sclerosis (SSc).

**Objectives:** The aims of this were to explore the association of the esophageal dilation and ILD on chest high-resolution computed tomography (HRCT) in patients with SSc and to establish a cut-off point for the esophageal dilation suggestive for the presence of a significant SSc-ILD.

**Methods:** The widest esophageal diameter (WED) was obtained on axial HRCT images. The parenchymal abnormalities on HRCT were coded and scored according to Warrick method. Patient-centred measures, pulmonary function tests (PFTs) and the single breath carbon monoxide diffusing capacity of the lung (DLco) were also obtained. Multivariate regression analyses were performed to identify factors associated with esophageal diameter on HRCT.

**Results:** 126 subjects with SSc were included in the analysis. The mean (±SD) WED was 13.5 (±4.2) mm, and in 76 (60.3%) participants WED was ≥11 mm. ILD was diagnosed in 86 SSc patients (Warrick score ≥7), while in 40 subjects the lung findings were normal. SSc patients with ILD had larger mean esophageal diameter than those without lung disease (19.4 mm vs. 14.1 mm, p<0.001). We observed a high correlation between WED and Gastroesophageal reflux disease questionnaire (GerdQ) (r=0.886, p<0.001), Borg score (r=0.705, p<0.001), Warrick score (r=0.614, p<0.001). WED negatively correlated with DLco (r=-0.508, p<0.001). Multivariate analysis demonstrated positive associations between mean esophageal diameter and GerdQ (p<0.0001), Borg index (p<0.0005), and total Warrick score (p=0.019).

**Conclusions:** In patients with SSc, an increased esophageal diameter (>11 mm) on chest HRCT is associated with pulmonary and esophageal symptoms, more severe ILD, and lower DLco.

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**Disclosure of Interest:** None declared

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#### THU0415 ANTI-PM/SCL ANTIBODY CLINICAL ASSOCIATIONS IN PATIENTS WITH SYSTEMIC SCLEROSIS. ANALYSIS OF THE MULTICENTER EUSTAR COHORT

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**Background:** Antibodies to the PM/ScI complex are found in patients with Systemic Sclerosis (SSc), but also with Polymyositis, Dermatomyositis and overlap syndromes. Historically, the main clinical association of anti-PM/ScI antibodies in SSc, which include calcinosis, articular and muscle involvement, and interstitial lung diseases, were described by some large single-centre studies, or by multicenter studies which recruited a relatively small number of positive patients. Therefore, some unresolved issue deserves further research. In particular, scleroderma renal crisis was recently identified in a sizeable number of anti-PM/ScI +SSc patients in a large monocentric British cohort (4 out of 70; 5.7%), a somewhat unexpected finding since this antibody type is generally considered not to be associated with renal crisis.<sup>1</sup>

**Objectives:** To evaluate clinical associations of anti-PM/ScI in patients with SSc in the large multicenter EUSTAR database, with specific focus on scleroderma renal crisis.

**Methods:** Patients from the EUSTAR database were included when the item anti-PM/ScI was fulfilled in at least one visit; clinical data were collected from the last visit available.

**Results:** Anti-PM/ScI status was available in 8,287 SSc patients from EUSTAR database: 295 were anti-PM/ScI +. After exclusion of 145 patients with multiple autoantibody positivity, 150 anti-PM/ScI+ patients were compared with 7992 anti-PM/ScI -negative patients. Among these, 2530 were positive for anticentromere, 1933 for anti-topoisomerase I, 186 for anti-RNA polymerase III, and 220 for anti-U1Rnp antibodies.

Renal crisis was identified in 8 of 150 anti-PM/ScI+SSc patients (5.3%), and was significantly more frequent than in anti-PM/ScI-negative SSc patients (1.6%; p=0.0015). Positivity for anti-PM/ScI was also associated with male sex, diffuse cutaneous subsets, joint and muscle involvement, lung fibrosis at chest X-rays, heart conduction blocks, stomach and intestinal symptoms (table 1). However, in multivariate analysis, adjusted for age at disease onset, sex, and disease duration, the association of anti-PM/ScI with renal crisis was not significant, whereas

the associations with joint and muscle involvement, lung fibrosis, and intestinal symptoms were confirmed (table 1).

**Table 1** Results of the univariable and multivariable analysis adjusted on sex, age at disease onset and disease duration (n=8142 patients). Results are presented as number/number available data (%) unless stated otherwise.

Characteristics	Univariable analysis			Multivariable analysis		
	Anti-PM/Scl -	Anti-PM/Scl +	p Value	N available data (%)	OR (95% CI)	p Value
Age at disease onset (years, mean (SD) (n available))	46.7 (14.5) (6883)	44.7 (15.1) (1461)	0.081	7025 (86.3)	0.98 (0.90 to 0.99)	0.0015
Disease duration (months, mean (SD) (n available))	152.3 (107.6) (8874)	128.5 (99.8) (1398)	0.051	7013 (86.1)	0.997 (0.995 to 0.999)	0.0136
Male sex	11407/9997 (14.2)	31/150 (20.7)	0.036	8342 (100.0)	1.001 (1.006 to 1.004)	0.4095
Caucasian ethnicity	6462/7992 (80.9)	126/140 (90.0)	0.152	8142 (100.0)		
Raynaud's phenomenon	8904/7548 (91.5)	146/150 (97.3)	0.016	7699 (94.6)		
Oesophageal symptoms	4317/766 (56.4)	91/150 (61.0)	0.180	7811 (95.9)		
Stomach symptoms	1593/7317 (21.2)	49/150 (32.7)	0.099	7461 (92.0)		
Intestinal symptoms	1803/7587 (23.6)	63/150 (42.0)	<0.0001	7737 (95.0)	2.894 (1.890 to 4.450)	<0.0001
Scleroderma renal crisis	128/7605 (1.6)	8/150 (5.3)	0.0015	7755 (95.2)	1.488 (0.423 to 5.219)	0.4640
Diffuse cutaneous subtype	2390/7412 (32.1)	33/148 (22.3)	0.022	7580 (92.9)	0.825 (0.625 to 1.096)	0.4033
Active digital ulcers ever	2597/9471 (27.4)	84/156 (53.8)	0.37	8095 (92.4)		
Joint synovitis	734/7411 (9.9)	34/149 (22.8)	<0.0001	7680 (92.9)	2.963 (1.159 to 7.215)	0.0072
Joint contractures	2191/7152 (30.6)	64/149 (43.0)	<0.0001	7301 (89.7)		
Tendon friction rubs	404/7007 (5.8)	24/149 (16.1)	<0.0001	7236 (88.9)		
Muscle weakness	1177/7512 (15.7)	59/149 (39.6)	<0.0001	7640 (94.1)		
Muscle atrophy	468/7184 (6.5)	37/148 (25.0)	<0.0001	7142 (91.3)		
CK elevation	380/6258 (6.1)	47/140 (33.6)	<0.0001	3389 (78.6)	8.699 (4.181 to 10.720)	<0.0001
Conduction blocks	880/8333 (10.6)	35/151 (23.2)	0.028	8464 (87.1)	1.468 (0.995 to 2.180)	0.1199
Elevated sPAP (ECHO)	376/8882 (4.2)	18/137 (13.9)	0.33	5729 (70.4)		
Lung fibrosis on plain X-rays	64/117 (54.7)	1342/4537 (29.6)	10.0001	4664 (57.0)	2.812 (1.429 to 5.872)	<0.0001

**Conclusions:** In the largest series of anti-PM-Scl positive patients so far reported, well-known clinical associations were confirmed. Moreover, scleroderma renal crisis was more frequent than in the antibody-negative patient controls (which included a majority of anticentromere-positive patients, and a relatively small number of anti-RNA polymerase III-positive patients). However, this association was probably explained by covariates, such as joint and muscle involvement, or lung fibrosis. A possible role of corticosteroid therapy might therefore be suspected.

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THU0416

#### VERTEBRAL FRACTURE PREVALENCE AND MEASUREMENT OF THE SCANOGRAPHIC BONE ATTENUATION COEFFICIENT ON CT SCAN IN 70 PATIENTS WITH SYSTEMIC SCLERODERMA

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**Background:** Osteoporosis screening is not systematic in scleroderma patients but some studies demonstrated a similar risk between rheumatoid arthritis and systemic scleroderma.<sup>1,2,3</sup> Thoracic and/or TAP (thoraco-abdomino-pelvic) CT (Computed Tomography) scans are classically performed in the follow-up of scleroderma, mainly to evaluate lung involvement.

**Objectives:** To study vertebral fracture (VF) prevalence and the scanographic bone attenuation coefficient of the first lumbar vertebra (SBAC-L1) on CT scans in systemic scleroderma patients. Secondary objectives are to study specific risk factors of SBAC-L1 ≤145 Hounsfield Units (HU) and to evaluate SBAC-L1 measurements reliability.

**Methods:** This monocentric retrospective study included patients followed from 2000 to 2014 and fulfilling ACR/EULAR 2013 criteria for systemic scleroderma and who underwent a thoracic or TAP CT scan. Osteoporotic risk factors, Dual Energy X-ray Absorptiometry (DXA) measurements and clinical characteristics were collected. For CT scan, the VFs were determined according to Genant's

classification on sagittal sections. The SBAC-L1 was measured in Hounsfield Units (HU) on axial section of L1 in a Region of Interest drawn in trabecular bone. Intra- and inter-reader reliabilities for SBAC-L1 were calculated. An SBAC-L1 ≤145 HU (fracture threshold) was used to define patients at risk of VF.<sup>4</sup> Predictive factors for VF or SBAC-L1 ≤145 HU were studied.

**Results:** A total of 70 patients were included (mean age: 62.3 (±15.6) years, women 88.5%, diffuse scleroderma 22.9% (n=16)) in the study. Sixty patients (85.7%) presented with at least one clinical risk factor for osteoporosis. Eighteen patients (25.7%) received vitaminocalcic supplementation and 10 (14.3%) received antiresorptive therapy. DXA was only performed on 30 patients (42.8%), and 5 (16.7%) of them presented a T-score ≤ -2.5 DS. 3 VFs were detected in 3 patients (4.3%). The mean SBAC-L1 was 157.26 HU (±52.1), and 35 patients (50%) presented a SBAC-L1 ≤145 HU. SBAC-L1 measurements were highly reliable (Kappa >0.9 for both intra- and inter-reader reliability). For the univariate analysis, a SBAC-L1 ≤145 HU was significantly associated with age (OR=1.09, CI 95%: 1.04–1.13), calcinosis (OR=6.3, CI 95%: 1.61–24.75) and periarticular calcifications (OR=3.22, CI 95%: 1.06–9.77). For the multivariate analysis, age (especially patients older than 63 years), calcinosis and acro-osteolysis were independently associated with a SBAC-L1 ≤145 HU.

**Conclusions:** On a large sample of scleroderma patients with clinical risks of osteoporosis, only 42.8% were screened for DXA and 16.7% of them were osteoporotic. The VF prevalence on CT scan was 4.3% and the SBAC-L1 measurement identified 50% of the population at the fracture threshold. The presence of calcinosis, periarticular calcifications or acro-osteolysis should lead to an osteoporosis screening, especially for patients under 63 years old.

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THU0417

#### WHOLE BODY DISTRIBUTION AND CLINICAL ASSOCIATIONS OF TELANGIECTASIA IN SYSTEMIC SCLEROSIS: A CROSS-SECTIONAL STUDY

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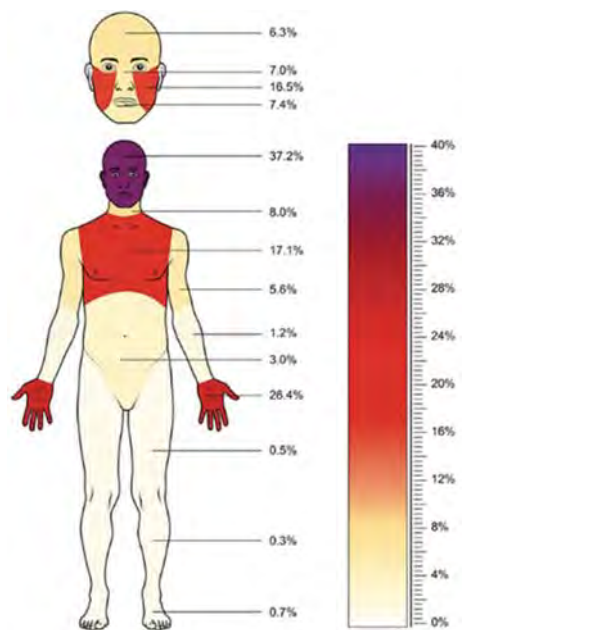
**Background:** Telangiectasia (TA), one of the diagnostic criteria for systemic sclerosis (SSc), could be a clinical marker for the severity of vasculopathy, including pulmonary hypertension (PH).

**Objectives:** We designed a cross-sectional study: (i) to describe the whole-body distribution of TA, (ii) to assess the associations between the whole-body number of TA and the characteristics of patients, (iii) to determine whether the number of TA may be useful to discriminate SSc-PH patients.

**Methods:** Patients were included in the National Referral Centre for Rare Systemic And Autoimmune Diseases if they fulfilled the 2013 ACR/EULAR criteria for SSc. They were excluded if they had received laser treatment. The whole-body number and distribution of TA were recorded at inclusion. The associations were studied using univariate, adjusted and multiple linear regressions.

**Results:** 106 patients were enrolled, including 12 with PH. The median (interquartile range) number of TA was 30 (82.7). Their distribution was: 37.2% on the face, 33.2% on the upper limbs including 26.4% on the hands, 28.1% on the trunk including 17.1% for the upper part of the trunk, and 1.5% on the lower limbs. Using multivariate linear regression model, the whole-body telangiectasia number was independently associated with male gender (percentage change (95% CI)= +144.4% (7.5; 455.9), p=0.033), pulmonary hypertension (+162.8% (5.6; 553.8), p=0.038), history of pulmonary embolism (+336.4% (39.0; 1270.1), p=0.012), glomerular filtration rate (-1.6% (-3.2; -0.1) per 1 ml/min/1.73m<sup>2</sup> increase, p=0.038) and soluble endoglin (+28.2% (1.2; 62.5) per 1 ng/ml increase, p=0.039). The ROC analyses assessing the ability of telangiectasia to discriminate the presence of pulmonary hypertension revealed that the area under the curve was significant for the telangiectasia number on the whole body (0.77 (0.57; 0.88)), on the hands and face (0.81 (0.57; 0.91)) and on the hands (0.77 (0.57; 0.89)).





**Conclusions:** In SSc-patients, TA were predominantly located on the face, hands and the upper part of the trunk. They may reflect the vasculopathy of SSc and could represent a clinical biomarker for vascular disease, particularly for PH, one of the most severe vascular complications of the disease.

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THU0418

#### LONG-TERM EFFICACY AND SAFETY OF MONOTHERAPY VERSUS COMBINATION THERAPY IN SYSTEMIC SCLEROSIS-ASSOCIATED PULMONARY ARTERIAL HYPERTENSION (PAH): A RETROSPECTIVE COHORT STUDY FROM THE NATIONWIDE SPANISH SCLERODERMA REGISTRY (RESCLE)

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**Background:** Monotherapy with endotelin antagonist receptors (ERA) an phosphodiesterase 5 (PDE5) inhibitors is a first choice treatment for PAH in functional class (FC) II-III, with the same grade of evidence and recommendation than combination therapy. Recently, studies have proven superiority of combination therapy against monotherapy in combined morbi-mortality endpoints.

**Objectives:** To demonstrate superiority of combination therapy against monotherapy in a single mortality endpoint in SSc-associated PAH.

**Methods:** Retrospective cohort study including patients from the Spanish Scleroderma Registry (RESCLE) diagnosed with SSc-associated-PAH by right heart catheterization (RHC). Patients were divided in 3 groups: monotherapy vs. sequential combination therapy (>12 weeks between first and second treatment)

vs. upfront combination therapy (<12 weeks between treatments). Primary endpoint was mortality from any cause.

**Results:** Seventy-six patients with PAH out of 1817 participants were included. Thirty-four (45%) were receiving monotherapy [with ERA (22 patients, 29%) or PDE5 inhibitors (12 patients, 16%)], 25 patients (33%) sequential combination therapy and 17 patients (22%) upfront combination therapy.

Baseline demographic, clinical and complementary tests were similar among groups. ILD (mainly moderate) was more frequent in both combination groups in 58% vs. 80% vs. 76.4%, without statistical significance. A worse FVC/DLco in the sequential combination group was reported (2.9±1.1 vs. 1.8±0.4 vs. 2.3±0.8, global p=0.085 but p=0.043 comparing monotherapy with sequential combination) and also a worse mPAP in both sequential and upfront combination groups (37.2±8.7 mmHg vs. 40.8±8.8 vs. 46±15.9, p=0.026).

The treatment regimen prescribed (p=0.017) and FC at baseline (p=0.007) were found predictors of mortality. Sequential combination therapy was found a protective factor [HR=0.11 (95%CI 0.03–0.51), p=0.004] and the upfront combination therapy showed a tendency of protection [HR=0.68 (95%CI 0.23–1.97), p=0.476]. Survival rates from diagnosis of PAH among groups were: 78% vs. 95.8% vs. 94.1% at 1 year, 40.7% vs. 81.5% vs. 51.8% at 3 years and 31.6% vs. 56.5% vs. 34.5% at 5 years (p=0.007).

Side effects were not significantly different among groups.

**Conclusions:** Combined sequential therapy improves survival in SSc-PAH patients, even with moderate ILD.

Upfront combination therapy may improve survival, but did not reach statistical significance due to study limitations.

Treatment regimen and FC were found as prognostic factors for survival: sequential combination therapy was a protective factor and FC was a risk factor.

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THU0419

#### ASSOCIATION OF INFLAMMATORY MARKERS C-REACTIVE PROTEIN AND ERYTHROCYTE SEDIMENTATION RATE WITH PULMONARY FUNCTION TESTS AND EUROPEAN SCLERODERMA STUDY GROUP ACTIVITY INDEX (ESCSG-AI) IN SYSTEMIC SCLEROSIS – ASSOCIATED INTERSTITIAL LUNG DISEASE IN FOLLOW UP STUDY

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**Background:** inflammatory markers are very important to assess severity and activity of SSc-ILD, but it's role needs further investigation.

**Objectives:** to assess inflammatory markers of SSc such as hsCRP and ESR and compare with lung function test and ESCSG-AI in the long-term follow up study.

**Methods:** It was a longitudinal study involving 77 pts with SSc-ILD (mean age was 46,2±13,4; 69% have limited subset of the disease; 93% were female). The mean duration of follow up was 58,9±11,4 months. Pts. were investigated with HRCT twice (at first visit and at the end of the study) and according the CT-changes were divided into 3 groups: the 1st group (16 pts) with improvement; 2nd group (39 pts) without any changes and 3rd group (22 pts) with worsening of fibrosis. Other data collected including biological results (high-sensitivity C-reactive protein (hsCRP) and erythrocyte sedimentation rate (ESR)), PFT (forced vital capacity (FVC,% of predicted) and diffusing capacity of the lung for carbon monoxide (DLCO,% of predicted), composite score (ESCSG-AI).

**Results:** there were no significant differences between groups related to sex, frequency of diffuse form and duration disease. Mean levels of hsCRP and ESR didn't change significantly during the follow up. In all pts the mean levels of hsCRP and ESR correlated directly with each other at first visit and at the end of the study (R=0,45 and R=0,4 (p<0,001) accordingly). We compared the mean levels of hsCRP and ESR with mean dates of FVC, DLCO and ESCSG-AI score in first visit and the end of follow up. Mean levels of hsCRP inversely correlated with mean dates of DLCO at the first visit and at the end of the study (R=-0,39 and R=-0,42 (p<0,05) accordingly); in groups 2 and 3 (R=-0,34 and R=-0,47 (p<0,05) accordingly) at the end of the study; with mean dates of FVC in all pts and group 2 (R=-0,42 and R=-0,47 (p<0,05) accordingly) only at the end of the study; correlated directly with ESCSG-AI score in all pts and groups 2,3 (R=0,58 (p<0,0001), R=0,46 (p<0,01) and R=0,77 (p<0,001) accordingly) at the end of the study. While mean levels of ESR inversely correlated with mean dates of DLCO only in all pts and groups 1,2 (R=-0,43, R=-0,66 and R=-0,39 (p<0,05) accordingly) at first visit; correlated directly with ESCSG-AI score in all pts. (R=0,309 (p<0,01) at the end of the study. Mean levels of hsCRP inversely correlated with DLCO, FVC and directly correlated with ESCSG-AI and these correlations were more evident than with mean levels of ESR.

**Conclusions:** In our group of pts. the hsCRP has proven to be an accurate reflection of disease severity especially in pts with progression of ILD.

**Disclosure of Interest:** None declared  
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THU0420

### AN EXTENT OF INTERSTITIAL LUNG DISEASE IS A POTENTIAL PREDICTOR OF RESPONSE TO A-B-CELL THERAPY IN THE PATIENTS WITH SSC

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**Background:** Systemic sclerosis (SSc) is a connective tissue disease associated with chronic polyclonal B-lymphocytic activation and immunological tolerance disturbance. Several research and clinical studies showed that B-cell depletion is potentially efficacious in SSc treatment. However, neither strong evidence of RTX efficacy for treatment of interstitial lung disease (ILD) associated with SSc, no potential predictor of response to a-B-cell therapy.

**Objectives:** To evaluate rituximab (RTX) therapy efficacy in the patients with systemic sclerosis (SSc) differing in extent of interstitial lung disease (ILD) based on multispiral computed tomography (MSCT) findings.

**Methods:** 42 patients (average age 48±2 years; male/female 1/6, diffuse/limited disease 15/1 (25 and 17), disease duration since the first non-Raynaud syndrome – 6.6±5.9 years) with definitely diagnosed SSc and ILD signs evidenced by MSCT were enrolled into the study. During the observation period 29±15.3 months the patients received rituximab (RTX) total dose of 2.5±1.3 grams in combination with glucocorticoids at average dose of 11.7±3.9 mg. 10 (24%) patients concurrently took immunosuppressants. The therapy efficacy was evaluated both in the general study population and in the patient subgroups with interstitial lesion extent up to 20% (Group A, n=13) and greater than 20% (Group B, n=29) of total pulmonary tissue area.<sup>1</sup>

**Results:** In the general patient population significant FVC increase from 73.2±18.8% to 82±21.8% (p=0.000031) and stabilisation of DLCO (42.6%±15.7% vs 44.7±14.6%. p=0.2) were observed. Median FVC increment was 6% (25th% >3.3%; 75th%>16%). FVC-based parameters increased by ≥10% in 16 (38%) patients and decreased in 3 (7%) patients.

Average FVC values in Group A were significantly higher compared with Group B both at the baseline (88.8%±18.6% vs 65.4±14.5%, p=0.0002) and after the treatment (103.3%±15.9% vs 74.1±18.5%, p=0.0009) with statistically significant FVC increase in both groups during the treatment period (p=0.016 and p=0.0014, respectively). Median FVC increment in Group A and Group B was 10.2% (25th% >4.7%; 75th%>21.9%) and 5.9% (25th%>2.75%; 75th%>14.7%), p>0.05, respectively. FVC-based parameters increased by ≥10% in 6 (46%) patients in Group A, and in 10 (34%) patients in Group B, and decreased in 1 (8%) and 2 (7%) patients, respectively.

Average DLCO values were also significantly higher in Group A compared to Group B both before and after treatment (58.4%±16.4% vs 36.3±10.1%. p=0.025; 59.3±15.2% vs 38.9±9.7%. p=0.005); DLCO values did not change over time during RTX therapy.

**Conclusions:** RTX therapy resulted in significant FVC increase. FVC increment in the patient group with ILD extent up to 20% achieved clinical significance level in contrast to the patients with ILD extent greater than 20%, where FVC increment was 5.9%. Obtained data suggest that initial lung lesion area is a potential predictor of response to a-B-cell therapy in the patients with SSc.

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THU0421

### PREVALENCE AND CLINICAL CORRELATES OF SMALL AIRWAY OBSTRUCTION IN PATIENTS WITH SYSTEMIC SCLEROSIS

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**Background:** Small airways are usually defined as non-cartilaginous airways with an internal diameter <2 mm. Small airway obstruction (SAO) may be result of a primary bronchiolar disorder, or secondary to a disease that also affects large airways (like asthma or chronic obstructive pulmonary disease - COPD), or related to an interstitial lung disease with bronchiolar involvement.

**Objectives:** To assess prevalence and clinical correlates of SAO in patients with systemic sclerosis (SSc).

**Methods:** 69 consecutive patients with SSc (63 women and 6 men) were included in this study. Patients with previously diagnosed bronchiectasis, COPD or asthma were excluded. Forty two (60.9%) patients had limited cutaneous SSc, whilst 27 (39.1%) of patients had diffuse form of the disease. Seventeen patients (24.6%) were tobacco-smokers, 52 (75.4%) were nonsmokers. Lung function tests, including assessment of lung diffusing capacity, were performed in all patients. Patients were considered to have small airway obstruction (SAO) when Maximum Expiratory Flow at 25% of the forced vital capacity (MEF<sub>25</sub>) was lower than 60% as predicted. We assessed the relationship of SAO in our patients with large airway obstruction, decreased lung diffusing capacity, disease duration, disease subtype, scleroderma-specific antibodies and smoking.

**Results:** SAO was noticed in 46/69 (66.6%) of patients with SSc. Restrictive lung disease was found in 4/69 (5.8%), obstruction of large airways in 18/69 (26.1%) and decreased lung diffusing capacity in 47/69 (68.1%) of patients. No difference in gender, age, disease duration, disease form and scleroderma-specific antibodies was found between patients with and without SAO. 18/46 (39.1%) patients with SAO had decreased FEV<sub>1</sub> and FEV<sub>1</sub>/FVC, indicating presence of coexistent large airway obstruction. Indeed, all patients with signs of obstructive lung disease on spirometry, had associated SAO. Moreover, MEF<sub>25</sub> correlated significantly with FEV<sub>1</sub> (ρ=0.54, p<0.001), FEV<sub>1</sub>/FVC (ρ=0.74, p<0.001), PEF (ρ=0.29, p=0.02) and MEF<sub>50</sub> (ρ=0.80, p<0.001) in our patients with SSc. However, 28/46 (60.9%) SSc patients with SAO did not have signs of concomitant large airway obstruction. 20/46 (43.5%) patients had associated decreased lung diffusing capacity, whilst 8/46 (17.4%) of patients had isolated SAO. We have found that tobacco-smokers among SSc patients with SAO have more common associated obstructive lung disease on spirometry (58.8% vs 15.4%, p=0.004), and have a significantly lower mean value of MEF<sub>25</sub> compared to non-smokers (32.1%±7.1% vs. 45.4±11.6%, p=0.001). On the other hand, isolated SAO, and SAO associated with impaired diffusing capacity was equally frequent among smokers and non-smokers.

**Conclusions:** Patients with SSc have commonly SAO. It can be considered as clinical feature of undiagnosed asthma or COPD, if associated with large airway obstruction, especially in tobacco-smokers. On the other hand, isolated SAO or associated with decreased lung diffusing capacity was found to be not related to smoking, and may indicate a possible prominent bronchiolar involvement within SSc related interstitial lung disease.

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THU0422

### PERFORMANCE OF EULAR/ACR 2017 IDIOPATHIC INFLAMMATORY MYOPATHIES CLASIFICATION CRITERIA IN A REAL WORLD COHORT

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**Background:** Idiopathic Inflammatory Myopathies (IIM) are a heterogeneous group of multisystemic diseases. It includes Polymyositis (PM), Dermatomyositis (DM) with its clinically amioopathic variant (CADM), the antisynthetase syndrome (ASS), the inclusion body myositis (IBM), Immune-mediated necrotising myopathy (IMNM), the juvenile variants of DM/PM and the connective tissue disease-myositis overlap (CTD-OM).

Distinction between subtypes is made on grounds of clinical features, histologic findings at muscle biopsy and presence of certain autoantibodies.

Multiple classification criteria had been proposed through time, EULAR/ACR been the most recent. However, their performance in patients from common practice in Latin America had not been widely evaluated.

In our practice, access to muscle biopsy and electromyogram (EMG) is not always available

**Objectives:** To evaluate the performance of the EULAR/ACR 2017 IIM classification criteria in a real world cohort and compare it with the performance of other classification criteria

**Methods:** Retrospective study. IIM patients defined by expert opinion followed in our centre between October 2007 and November 2017 were included.

The patients were classified clinically in DM, CADM, PM, ASS and CTD-OM. Patients with positive antisynthetase antibodies were reclassified as ASS.

Availability of EMG, muscle biopsy and anti Jo-1 antibodies was evaluated. Bohan & Peter (1975) Tanimoto (1995) y EULAR/ACR (2017) criteria were applied to the population

**Results:** 60 patients were included. DM 20 (33.3%), CADM 4 (6.66%), PM 4 (6.66%), ASS 10 (16.66%) y CTD-OM 22 (36.66%). Muscle biopsy available 14/60 (23.33%), EMG available 33/60 (55%) and anti Jo-1 determination available in 57/60 (95%).

In general, 12/60 (20%) classified as defined disease by Bohan and Peter criteria, 29/60 (48.3%) by Tanimoto criteria and 34/60 (56.6%) by EULAR/ACR 2017 criteria.



Extending the classification to probable besides defined, 38/60 (63.3%) met Bohan and Peter criteria and 51/60 (85%) met EULAR/ACR criteria.

Table 1 shows percentage of patients meeting each criteria set by clinical subtype.

Patients with available muscle biopsy (n=14) were subanalyzed: 11/14 (78.6%) muscle biopsy were compatible with IIM (3 not compatible, but previously treated). DM 3/11 (28.6%), ASS 1/11 (7.14%) y CTD-OM 7/11 (50%). 7/11 (50%) met Bohan and Peter criteria, 8/11 (78.6%) met Tanimoto criteria and 8/11 met EULAR/ACR criteria. If extended to probable cases, 11/11 (100%) met Bohan and Peter criteria and 10/11 (91%) EULAR/ACR criteria.

Table 1 Fulfillment of different criteria set by IIM subtype

	Bohan & Peter (%)			Tanimoto (%)	EULAR/ACR (%)		
	Probable	Definite	Total		Probable	Definite	Total
DM (n=20)	60	25	85	35	10	85	95
CADM (n=4)	0	0	0	0	25	75	100
PM (n=4)	75	0	75	50	50	0	50
ASS (n=10)	50	10	60	80	30	70	100
CTD-OM (n=22)	27,3	27,3	54,6	54,50%	41	31,8	72,8
DM/CTD-OM (n=4)	25	50	75	75	0	100	100
PM/CTD-OM (n=18)	27,8	22,2	50	55,5	50	18,6	66,6

**Conclusions:** EULAR/ACR<sup>2017</sup> performed especially well for DM, and were the only criteria set met by CADM patients.

PM patients failed to meet Bohan and Peter and EULAR/ACR criteria for definite disease, probably due to low availability of EMG and muscle biopsy. This was similar for pure PM and PM/CTD-OM.

Tanimoto criteria were the most sensitive for classification of ASS patients, which could be explained because they consider arthritis among clinical features.

When considering probable and defined cases, EULAR/ACR criteria were highly sensitive in this real world cohort

**Disclosure of Interest:** None declared

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#### THU0423 EPIDEMIOLOGY AND SURVIVAL OF SYSTEMIC SCLEROSIS-SYSTEMIC LUPUS ERYTHEMATOSUS OVERLAP SYNDROME

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**Background:** Systemic sclerosis (SSc) is an immune disorder characterised by vasculopathy and fibrosis that may overlap with another disease such as systemic lupus erythematosus (SLE). Little is known about the epidemiology, clinical characteristics, and survival of SSc-SLE overlap (also called lupoderma). We evaluated the prevalence of SSc-SLE overlap syndrome, differences in SSc clinical characteristics and survival compared with SSc without SLE.

**Methods:** A cohort study was conducted including subjects who fulfilled the ACR-EULAR classification criteria for SSc and/or the ACR criteria for SLE. The primary outcome was the time from diagnosis to death from all causes. Survival was evaluated using Kaplan Meier curves and Cox Proportional Hazard models.

**Results:** We identified 1252 subjects (SSc n=1166, SSc-SLE n=86) with a SSc-SLE prevalence of 6.8%. SSc-SLE were younger at diagnosis (37.9 years versus 47.9 years, p<0.001), more frequently had lupus anticoagulant (6% versus 0.3%, p<0.001), anticardiolipin antibody (6% versus 0.9%, p<0.001), and pulmonary arterial hypertension (PAH) (52% versus 31%, p<0.001). SSc-SLE less frequently had calcinosis (13% versus 27%, p=0.007), telangiectasia (49% versus 75%, p<0.001) and diffuse subtype (12% versus 35%, p<0.001). There were no significant differences in the occurrence of renal crisis (7% versus 7%), interstitial lung disease (40% versus 34%), and digital ulcers (38% versus 32%). SSc-SLE had better survival (median 26.1 versus 22.4 years), but this was not statistically significant (log rank p=0.06). Female sex and diffuse subtype attenuated survival differences between groups (Hazard Ratio 0.70, 95% CI 0.45, 1.11).

**Conclusions:** SSc-SLE are younger at diagnosis, more frequently have PAH, and less frequently have cutaneous manifestations of SSc. SSc-SLE patients should be monitored for pulmonary hypertension, interstitial lung disease, renal crisis and digital ulcers.

**Disclosure of Interest:** None declared

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#### THU0424 ARTICULAR INVOLVEMENT IN SYSTEMIC SCLEROSIS: COMPARISON OF CLINICAL, RADIOGRAPHIC AND SONOGRAPHIC FINDINGS

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**Background:** Joint involvement in Systemic Sclerosis (SSc) is frequent and varied.<sup>1,2</sup>

**Objectives:** We study US synovitis and its correlation with clinical synovitis, radiological erosions and organ involvement.

**Methods:** In a prospective cohort of SSc patients, tender and swollen joint counts, DAS28-CRP, hand US sonographies, X-ray hand views, as well as respiratory, cardiac, cutaneous and renal characteristics were assessed.

**Results:** 54 patients were included with a median age of 59 years,<sup>27-81</sup> 45 women (83%), with a diffuse cutaneous subtype in 13 patients (24%). 23 patients (52%) presented with arthralgia, 9 had clinical synovitis (16%) and DAS28-CRP of 3.7 (2.98-5.90). US sonography (34 patients) found at least one synovitis in 23 patients: 14 patients with grade 1 (66%), 6 patients grade 2 (29%), 1 patient grade 3 (5%), with a positive power Doppler signal in one case (3%). Among the patients having US-synovitis, 4 had clinical synovitis (17%), and 4 had X-ray erosions (17%). Radiological erosions were present in 8 patients (15%), without any correlation with clinical or US synovitis. Articular involvement (defined as clinical synovitis, US-synovitis and/or articular erosions) were found more frequently in limited SSc (n=28, 72%) than in diffuse SSc (n=4, 31%) (p<0.001), with a more frequent positivity of anti-centromere antibodies (n=23, 60% versus n=3, 20%). No correlation was found with disease severity or other organ impairment.

**Conclusions:** US synovitis were found more frequently than clinical synovitis, which are merely active, and did not correlate with articular destruction.

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#### THU0425 18F-FLUORODEOXYGLUCOSE POSITRON EMISSION TOMOGRAPHY/COMPUTED TOMOGRAPHY AND LUNG INVOLVEMENT IN SYSTEMIC SCLEROSIS

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**Background:** At early stages, SSc lung involvement is characterised by Ground Glass Opacities (GGO) at High Resolution Computed Tomography (HRCT). However, HRCT scan is not able to provide functional information and to discriminate between an "active inflammatory" and an "established fibrotic" GGO. 18Fluoro-Deoxy-d-Glucose (18F-FDG) Positron Emission Tomography/Computed Tomography (PET/CT) is able to detect metabolic activity picking up inflammation and provides both morphologic and metabolic data.

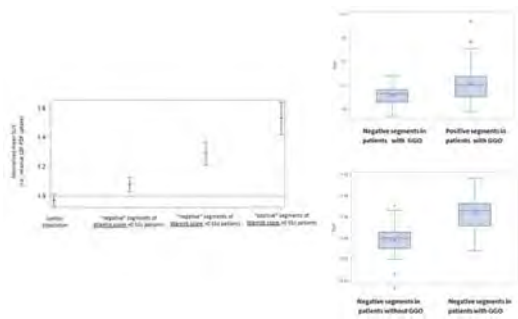
**Objectives:** The aim of this study was to evaluate, if 18F-FDG PET/CT scan may identify the inflammatory component of GGO in SSc interstitial lung disease.

**Methods:** Seven patients with SSc (1 male and 6 females; mean age 59.56 y ±9.15 SD; median disease duration 5 years,<sup>2-11</sup> who underwent 18F-FDG PET/CT scan because of cancer screening, were retrospectively analysed. HRCT



images analysis led to classification of pulmonary segments as "negative" (normal morphology) and "positive" (GGO). Furthermore, the "Warrick score" was used as a staging tool for SSc-ILD. Mean Standardised Uptake Value (mSUV) of segmental parenchyma was normalised (nmSUV) by comparison with the values of selected control subjects.

**Results:** No SSc patient was affected by cancer. Three patients had a Warrick Score >0, while 4 patients did not have any lung involvement (Warrick Score=0). The 3 patients with a Warrick Score >0 had also skin involvement with a median mRSS 6 (2–7) and pathological lung FDG uptake. In "positive" segments of SSc patients, nmSUV was significantly higher than in the lung segments of the control population (mean estimation 1.53; C.I. 1.42–1.65,  $p<0.0001$ ). In "negative" segments of SSc patients, with a Warrick score >0, the nmSUV was significantly higher than in segments of the control population (mean estimation 1.29; C.I. 1.22–1.37,  $p<0.0001$ ). Lung segments with GGO showed an nmSUV higher (21%) than "negative" segments (C.I. 0.13–0.28,  $p<0.0001$ ) of patients with Warrick score >0. "Negative" lung segments of patients with Warrick Score >0 showed a 32% higher 18F-FDG uptake than "negative" lung segments of patients with Warrick Score=0. (C.I. 0.17–0.48,  $p<0.0001$ ). (figure 1)



**Abstract THU0425 – Figure 1.** a) Differences in 18F-FDG uptake between "positive" segments of Warrick score >0 SSc patients, "negative" segments of Warrick score >0 SSc patients and "negative" segments of Warrick score=0 SSc patients vs attended normalised control value (=1); b) Differences in 18F-FDG uptake between "positive" lung segments of SSc patients with Warrick score>0 vs "negative" segments of the same patients; c) Differences in 18F-FDG uptake "negative" lung segments of patients with Warrick Score>0 vs "negative" lung segments of patients with Warrick Score=0

**Conclusions:** Morphologically "positive" GGO segments show an increased 18F-FDG uptake suggesting the existence of a metabolically active (inflammatory) GGO. However, in patients with GGO, negative lung segments showed a higher nmSUV than negative lung segments in patients without GGO. This may suggest that PET/CT may disclose an underlying inflammatory process, which cannot yet be evidenced by HRCT. Further studies on a larger population are warranted to confirm these data and possibly provide a prognostic significance of PET/CT positivity in SSc patients.

**Disclosure of Interest:** None declared

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#### THU0426 ETHNIC VARIATION IN SYSTEMIC SCLEROSIS MORBIDITY AND MORTALITY

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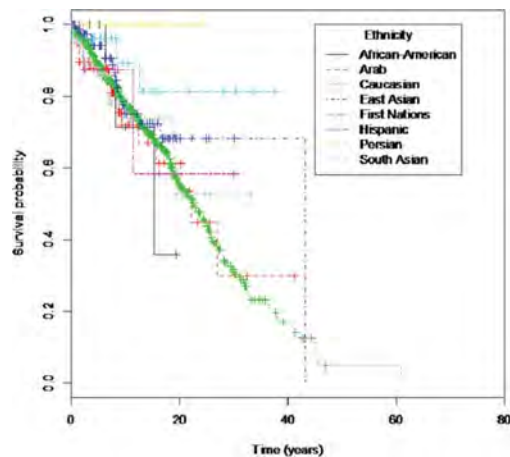
**Background:** Systemic sclerosis (SSc) is an uncommon connective tissue disease characterised by pathological skin thickening and can involve multiple internal organs. Ethnic variations in SSc have been reported in clinical manifestations, severity of the disease as well as survival.

**Objectives:** Our aim was to compare the survival and disease manifestations across ethnicity among SSc patients.

**Methods:** The Toronto Scleroderma Program is the largest single-centre, multi-ethnic, longitudinal SSc cohort in Canada. Patients are followed every 6 to 12 months using a standardised protocol. Patients who fulfilled the American College of Rheumatology-European League Against Rheumatism classification criteria for SSc and are 16 years of age or older were included in our retrospective cohort study. The study period was 1970–2017. Ethnicity was self-reported and was categorised as: Caucasian, African-American, Hispanic, Arab, East-Asian, First Nations or Persian. The primary outcome was the time from diagnosis to death from all causes. Secondary outcomes were differences in disease duration, SSc subtype, clinical manifestations, and serology. Survival probabilities and median survival times were determined using Kaplan-Meier survival curves. Cox proportional hazard models were used to estimate adjusted survival.

**Results:** 1005 subjects were evaluated, the majority of whom were Caucasian ( $n=745$  (74%), African-American  $n=58$  (6%), South Asian ( $n=69$  (7%)), and East Asian ( $n=80$  (8%)). Compared to Caucasians, East Asians less frequently had calcinosis (29% versus 9%,  $p=0.002$ ), and esophageal dysmotility (88% versus 69%,  $p=0.002$ ); African-Americans more frequently had interstitial lung disease (31% versus 53%,  $p=0.007$ ); and First Nation subjects more frequently had diffuse cutaneous disease (35% versus 56%,  $p=0.02$ ) and diabetes (5% versus 33%,  $p=0.03$ ). There were no differences across ethnicities in the prevalence of pulmonary hypertension, renal crisis, or digital ulcers.

We found no difference in the short-term survival across ethnicities. However, in the long-term, there was trend for Hispanic subject to have better survival (81.3% (95%CI 63, 100), while First Nations (58.3% (95%CI 25, 100) and South Asian subjects (52.6% (95%CI 32, 87) had worst survival at 15 years and 20 years, respectively. East Asians appear to have the longest median survival time 43.3 years.



**Conclusions:** Ethnic variations in disease SSc disease manifestations are observed. However, in the setting of a universal health care system, this does not result in significant differences in survival.

**Disclosure of Interest:** None declared

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#### THU0427 COMPARABLE CARDIOVASCULAR DISEASE AND NEOPLASM RATES BUT HIGHER FREQUENCY OF DEPRESSION IN SYSTEMIC SCLEROSIS VERSUS RHEUMATOID ARTHRITIS: A MULTICENTRE COMPARATIVE STUDY OF COMORBIDITIES

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**Background:** An increased burden of comorbid conditions negatively impacts patients' outcomes, leads to increased mortality and seems to characterise all chronic systemic connective tissue diseases. Systemic Sclerosis (SSc) is associated with the highest mortality rate comparing to other diseases, whereas data regarding epidemiology and clinical expression of SSc comorbidities is limited. In contrast, comorbidities of rheumatoid arthritis (RA), and especially the increased rate of cardiovascular disease, are better established.

**Objectives:** To compare the prevalence of common comorbidities in SSc versus RA in a large multicentre case-control study from 5 academic centres in Greece.

**Methods:** Between 2016 and 2017 consecutive SSc patients ( $n=408$ , mean age: 58.6 years, 88% women) were matched 1:1 for age and gender with 408 RA patients. Evaluated comorbidities were dyslipidemia, diabetes mellitus, arterial hypertension, coronary artery disease, stroke, chronic obstructive pulmonary disease, osteoporosis, neoplasms and depression. Differences were examined by  $\chi^2$  test.

**Results:** The prevalence of dyslipidemia (18.4% vs 30.1%,  $p=0.001$ ) and diabetes mellitus (5.6% vs 11.8%,  $p=0.007$ ) was lower in SSc than RA patients and there was no difference regarding arterial hypertension (31.8% vs 30.6%, respectively,  $p=0.742$ ) between the two groups. Disease duration, smoking and alcohol consumption were comparable between SSc and RA groups. While there was a trend for lower prevalence of ischaemic strokes in SSc than RA (0.4% vs 2.2%,  $p=0.085$ ), comparable rates of coronary artery disease were noted (2.7% vs 3.7%,  $p=0.445$ ). No differences were found between SSc and RA patients regarding chronic obstructive pulmonary disease (5.2% vs 3.7%, respectively,  $p=0.326$ ), osteoporosis (24% vs 22%,  $p=0.668$ ) and neoplasms (1.1% vs 1.7%,  $p=0.534$ ). Depression requiring treatment was more prevalent in SSc compared to RA patients (22% vs 12%,  $p=0.001$ ).

**Conclusions:** Despite almost half prevalence of dyslipidemia and diabetes mellitus in SSc versus RA patients, the cardiovascular comorbidity burden appears to be similar between the two diseases. SSc has no higher prevalence of neoplasms than RA but a greater negative impact on quality of life, as clearly more SSc patients develop depression compared to RA patients. Acquisition of prospective data is currently underway.

**Disclosure of Interest:** None declared

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#### THU0428 SKIN SCORE CHANGES IN EARLY DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS (dcSSc) PATIENTS ARE ASSOCIATED WITH OVERALL DISEASE SEVERITY

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**Objectives:** To determine if skin changes over 2 years are associated with changes in organ involvement in early diffuse cutaneous systemic sclerosis (dcSSc).

**Methods:** dcSSc with  $\leq 5$  years disease duration followed for 2 years from the Canadian Scleroderma Research Group (CSRG) registry were studied for organ involvement using the Medsger Disease Severity Score (DSS) with  $\geq 1$  point changes (decrease or increase) considered improvement or progression, correspondingly. Other disease measures were assessed including pulmonary function, patient and physician globals, functional disability and quality of life. Modified Rodnan Skin Score (mRSS) improvement was defined as a decrease of  $\geq 5$  points and/or  $\geq 25\%$  reduction. Adjusted regression analysis, ANOVA, chi-square, t-test and Pearson's tests were used.

**Results:** Of the 128 patients, mRSS improved for 50% from 22.6 to 18.1 ( $p=0.0001$ ). More skin-improvers improved in severity of lung (39% vs 17%,  $p=0.006$ ), joint/tendon (50% vs 21%,  $p=0.017$ ), and any visceral organ involvement (renal, cardiac, pulmonary or gastrointestinal) (60% vs 27%,  $p=0.031$ ) compared to mRSS non-improvers. Skin-improvers less often developed new skin ulcers (0% vs 11%,  $p=0.015$ ) and GI disease (5% vs 18%,  $p=0.023$ ), as well as progression of joint/tendon involvement (7% vs 29%,  $p=0.02$ ). Improving mRSS correlated with changes in total Medsger's severity score (without skin domain), severity of lung, GI, and peripheral vascular disease (table 1). FVC% stabilised in skin-improvers vs. worsened by 6.5% in non-improvers,  $p=0.026$ . Physician global assessments (severity, activity, damage) HAQ-DI, and SF-36 PCS improved more with improved mRSS ( $p<0.003$ ,  $p=0.001$ ,  $p=0.005$  respectively). Improvement in Forced Vital Capacity% predicted correlated with skin improvement ( $r=0.33$ ,  $p=0.004$ ).

**Abstract THU0428 – Table 1.** Relationship between change in disease measures and change in skin score

Outcome measure	Skin-improver (n=64)	Skin non-improver (n=64)	P-value Improvers vs. Non-improvers
Total Medsger's severity score without skin domain (negative is improvement)	-2.57 $\pm$ 3.11	0.42 $\pm$ 2.98	0.002
Patient global score	-0.70 $\pm$ 2.69	0.15 $\pm$ 2.61	0.088
Physician global score:	-1.97 $\pm$ 2.50	-0.61 $\pm$ 2.63	0.003
Activity	-1.33 $\pm$ 2.54	-0.03 $\pm$ 2.04	0.002
Severity	-0.72 $\pm$ 1.87	0.77 $\pm$ 1.98	0.000
Damage			
HAQ-DI	-0.19 $\pm$ 0.64	0.18 $\pm$ 0.47	0.001

SHAQ Numeric Rating Scales:	-0.29 $\pm$ 2.59	0.00 $\pm$ 2.55	0.552
Pain	0.29 $\pm$ 2.93	0.66 $\pm$ 2.30	0.445
RP	0.32 $\pm$ 1.96	0.16 $\pm$ 2.32	0.681
Finger ulcers	-0.21 $\pm$ 3.02	0.54 $\pm$ 2.97	0.178
Gastrointestinal	0.02 $\pm$ 2.32	0.05 $\pm$ 3.34	0.950
Breathing	-0.70 $\pm$ 2.70	-0.22 $\pm$ 2.62	0.340
Overall			
SF-36 PCS	3.08 $\pm$ 9.03	-1.55 $\pm$ 8.33	0.005

**Conclusions:** Over two years, improving skin scores in dcSSc were associated with an improvement in lung disease, joint/tendon, physician global assessments, HAQ-DI, SF-36 PCS, and overall visceral organ improvement. Improvement in mRSS as a primary outcome in drug trials is likely to be concordant with improvement in organ involvement and several other disease measurement domains in early dcSSc.

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#### THU0429 NAILFOLD VIDEO CAPILLAROSCOPY AND DETERIORATION OF SKIN INVOLVEMENT AND LUNG FUNCTION TESTS IN SYSTEMIC SCLEROSIS: A 3-YEAR PROSPECTIVE STUDY

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**Background:** Nailfold video-capillaroscopy(NVC) is a non-invasive method to assess peripheral microangiopathy. Abnormal capillaroscopic patterns are almost universally found in patients with Systemic Sclerosis (SSc) and assist the diagnosis of SSc. However, little is known about the prognostic value of NVC in skin and lung involvement progression in these patients.

**Objectives:** To test the hypothesis that baseline capillaroscopic indices, as well as possible changes in capillaroscopic indices over time, correlate with deterioration in skin thickening and lung function tests in a prospective SSc cohort.

**Methods:** Fifty-five consecutive SSc patients from a tertiary care university centre (49 women, 29 limited cutaneous SSc, mean age: 50.84 $\pm$ 14.88 years, mean disease duration 6.74 $\pm$ 6.25 years) were evaluated by NVC at baseline and after a median of 3.1 years. Qualitative assessment of NVC findings permitted categorization of patients to a predominantly normal, early, active or late capillaroscopic pattern. Capillary loss, capillary dilatation, giant or ramified capillaries and microhemorrhages were further assessed using a semi-quantitative rating scale (score 0–3), derived as the mean of three fields in each of the 2nd, 3rd, 4th and 5th finger of both hands. Scoring was performed by two different assessors. Skin thickening was measured using the modified Rodnan Skin Score (mRSS). FVC and DLCO were performed within 6 months from the NVC. Deterioration in FVC and DLCO was considered clinically significant when  $>10\%$ . Between baseline and follow-up evaluation 36% of patients had been receiving both major antiproliferative and vasodilator therapy, while 15% and 29% had been receiving only antiproliferative or vasodilator therapy, respectively.

**Results:** Intraclass correlation coefficient (ICC) for interrater reliability analyses was very good for all semi-quantitative capillaroscopy scores [ICC: 0.97 (0.74–0.99) for capillary loss score, 0.94 (0.85–0.98) for dilatation score, 0.98 (0.97–0.99) for giant score, 0.94 (0.84–0.97) for microhemorrhages score], except for the ramification score [ICC: 0.52 (-0.2, -0.81)] which was excluded from all analyses. Linear regression, adjusted for age and gender, showed no association between either baseline capillaroscopy scores or of their changes and changes in mRSS over time. FVC and DLCO deteriorated in 13 and 11 patients, respectively. Binary logistic regression analysis adjusted for age and gender showed no association either baseline capillaroscopy scores or of their changes with deterioration in FVC or DLCO, with the exception of the change in microhemorrhages score, which correlated inversely with deterioration in FVC [ $p=0.013$ , Odds Ratio=0.051 (CI: 0.005–0.534)]. Regarding qualitative analysis of capillaroscopic findings, the baseline capillaroscopy pattern remained unchanged in 35, deteriorated in 15 and improved in 5 patients. No difference was found between these 3 groups regarding change in mRSS (ANOVA,  $p=0.634$ ), deterioration in FVC ( $\chi^2$  test,  $p=0.502$ ) or deterioration in DLCO ( $\chi^2$  test,  $p=1.00$ ).

**Conclusions:** Although a possible confounding effect of treatment cannot be excluded, NVC seems to have poor prognostic value for the progression of skin thickening and interstitial lung disease in rigorously treated SSc patients.

**Disclosure of Interest:** None declared

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**THU0430 DESCRIPTION AND PROGNOSIS FACTORS OF SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE OUTCOME ON SERIAL HRCT**

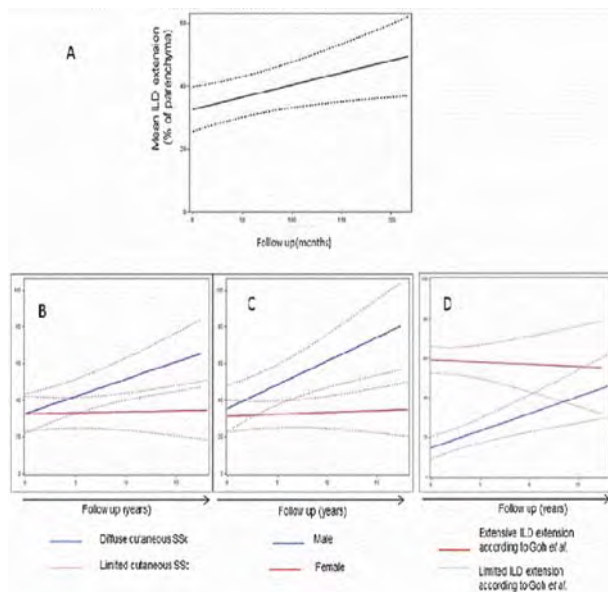
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**Background:** Interstitial lung disease (ILD) is a leading cause of morbidity and mortality in systemic sclerosis (SSc). While factors associated with the presence of ILD in SSc (SSc-ILD) are identified, those associated with ILD outcome are still debated and studies assessing the evolution of SSc-ILD on HRCT are scarce. Yet, it is important to identify patients at risk of SSc-ILD worsening because those patients are thought to benefit the most from immunosuppressants.

**Objectives:** Thus, the aims of our study were: to describe the evolution of HRCT extension and patterns of SSc-ILD, to identify baseline prognosis factors of ILD outcome on serial HRCT and to investigate whether the evolution of pulmonary function tests (PFTs) parameters correlated with the evolution on HRCT.

**Methods:** We included 58 SSc patients with HRCT proven ILD, with at least two available HRCT, and collected clinical, biological data and PFT at baseline. We collected all HRCT and PFTs available during follow-up. We modeled PFTs and HRCT evolution using linear mixed model with random coefficients.

**Results:** Mean ILD extension at baseline was 32.3%±28.7%. During a mean follow-up of 5.3±4.9 years, we found a significant mean progression of ILD extension of 0.92%±0.36% per year (p=0.018). Male sex, anti-topoisomerase 1 antibodies, diffuse cutaneous SSc were associated with faster progression of ILD extension. Limited ILD according to Goh *et al.* staging system, and a coarseness score at zero (meaning 100% of ground glass opacification) were associated with a faster progression of ILD extension. We also found a significant decline of DLCO, FVC and TLC during follow-up. There was a significant correlation between the progression of ILD extension on HRCT and the decline of DLCO, but not with the evolution of FVC.



**Conclusions:** Male patients, patients with diffuse SSc/antitopoisomerase 1, patients with less severe and less extensive ILD at baseline were more likely to experience a faster progression of ILD extension on serial HRCT. To our knowledge, this is the first study that clearly highlighted the diffuse form of SSc/presence of antitopoisomerase 1 as a worsening factor of SSc-ILD on HRCT. FVC might not be the best mirror of ILD progression while DLCO significantly correlated with change in ILD extension. Our study helps to define the profile of patients who are going to experience a progression of ILD on HRCT during follow up.

**Disclosure of Interest:** None declared

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**THU0431 ARE EXTREMITY TELANGIECTASES RELATED TO SEVERE DISEASE IN SYSTEMIC SCLEROSIS ?**

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**Background:** The number and morphology of telangiectases (T) have been studied in terms of severity and organ involvement in systemic sclerosis (SSc). T are located more frequently on face and trunk than extremities.

**Objectives:** We aimed to evaluate the impact of the localisation of T on different skin areas in addition to number on disease severity of SSc.

**Methods:** SSc patients fulfilling ACR/EULAR classification criteria (2013) who had the manifestation T were included. The number of T were calculated by using telangiectasia score (TS) (Shah A, et al) and localisation was classified according to presence of T on extremities or not. Simultaneously; early, active and late scleroderma patterns (Cutolo et al.) were determined qualitatively and capillary number (CN) was calculated per linear mm at distal row quantitatively by using nail fold video-capillaroscopy (NVC) in all patients.

**Results:** In 113 (106 female) SSc patients with T; the mean age was 52±12, the duration of follow-up 57±62 months, Raynaud and non-Raynaud symptom 10 ±8 and 7±7 years. Limited cutaneous form was found to be in 77 (%68), ANA positivity in 102 (%90) ve anti-Scl70 positivity in 33 (%29) patients. In SSc patients with TS score ≥6 or extremity T; the duration of non-Raynaud symptom was found to be longer (p=0010 or 0,009), MRSS and activity scores were higher (p=0004 or 0012 and p=0010 or 0,009) and severity scores of general, peripheral vascular involvement and skin were higher (p=0022 or 0,014, p=0030 or 0025 and p=0006 or 0,02), digital ulcers and flexion contractures were more frequent (p=0008 or 0035 and p=0027 or 0,032), late NVC pattern was more frequent and CN was lower (p=0001 or 0003 and p=0001 or 0,007). When patients were classified in 3 groups according to TS and presence of extremity T, differences in terms of organ involvement, disease activity and severity scores and NVC findings were summarised in table 1.

**Abstract THU0431 – Table 1.** The scores of disease activity, severity and capillaroscopy in SSc patients grouped according to TS and localisation of T.

	All patients N=113	TS ≤ 6 Extremity T(-) N=77	TS ≤ 6 Extremity T(+) N=11	TS > 6 Extremity T(-) N=25	P*
Duration of non-Raynaud's (year)	6±7	6±6	8±5	10±9	P=0,008
MRSS	7,7±6,5	6±6	9±6	11±9	P=0,013
Disease activity score (Valentin)	1,4±1,2	0,7±0,9	1,2±1,0	1,6±1,4	P=0,015
Disease severity score (Medinger)	5,6±3,7	5,3±4,1	5,9±2,6	6,4±2,7	P=0,024
severity-general	0,6±0,7	0,5±0,6	0,7±0,7	1±0,8	P=0,050
severity-PVI	1,5±0,8	1,4±0,8	1,6±0,5	1,8±0,8	P=0,023
severity-skin	1,1±0,5	1±0,5	1,2±0,4	1,3±0,6	P=0,012
Clinical findings					
digital ulcer	52(%46)	29(%38)	7(%64)	16(%64)	P=0,033
Flex contr.	16(%14)	7(%9)	2(%18)	7(%28)	NS
renal crisis	1(%1)	0(%0)	1(%9)	0(%0)	P=0,010
Low DLCO	55(%49)	33(%44)	7(%70)	15(%60)	NS
Fibrosis	48(%43)	28(%38)	7(%70)	13(%52)	P=0,028
high PAB	20(%18)	10(%13)	2(%20)	8(%32)	P=0,034
IS receivers	64(%57)	39(%54)	8(%80)	17(%68)	NS
ERA receivers	30(%27)	15(%21)	3(%33)	12(%50)	P=0,028
NVC					
Normal	7(%6)	6(%9)	0(%0)	0(%0)	NS
Early	23 (%20)	19(%25)	2(%18)	2(%8)	NS
Active	22(%19)	19(%25)	1(%9)	2(%8)	NS
Late	62(%54)	33(%43)	9(%82)	21(%84)	P<0,001
Capillary number	5,8±2,0	6,4±2,1	5±2	4,9±1,8	P<0,001

NS=not significant, MRSS=modified Rodnan skin score, PVI=peripheral involvement, IS=Immunosuppressives, ERA=endothelin receptor antagonists, \*Kruskal-Wallis H/Chi-Square tests

**Conclusions:** Disease duration was shown to be long, disease activity and severity were high and NVC findings were severe in patients with high scores of TS and extremity T. In patients with lower TS the presence of T on extremities was found to be related to severe disease. The number and localisation of T was emphasised as they are easy to evaluate in clinical practice and may be useful in determining severe patients with SSc.

**Disclosure of Interest:** None declared

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**THU0432 PERICARDIAL EFFUSION IS AN INDEPENDENT FACTOR PREDICTIVE OF SCLERODERMA RENAL CRISIS**

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**Background:** Scleroderma renal crisis (SRC) adversely affects renal and patient survival in systemic sclerosis (SSc).<sup>1, 2</sup> The survival rate of SRC has been



improved dramatically by angiotensin-converting enzyme inhibitor therapy, but SRC still has a poor prognosis.<sup>3</sup> Factors predictive of SRC include early diffuse skin involvement, rapid skin thickening, anti-RNA polymerase (RNAP) III antibodies, arthralgia/synovitis, and high glucocorticoid dosage.<sup>4</sup> Although classical data have implicated pericardial effusion as another predictive factor of SRC,<sup>5</sup> its role in SRC has not been well established.

**Objectives:** To clarify the clinical impact of pericardial effusion as a predictor of SRC.

**Methods:** Ninety-five patients diagnosed with SSc at our hospital between January 2003 and December 2017 were enrolled in the study. They were divided into a pericardial effusion group (n=21) and non-pericardial effusion group (n=74), and their clinical features retrospectively compared. Cox-regression analysis was performed to identify factors predictive of SRC.

**Results:** The patients comprised 14 men and 81 women with an average age of 57.4 years (range, 14 to 82) and the mean observation period was 65 months (range, 1 to 125). Pericardial effusion was detected in 21 of 95 (22.1%) cases. In the pericardial effusion group, SRC, modified Rodnan's total skin thickness score (mRSS), C-reactive protein, maximum glucocorticoid dose, proteinuria, finger apex ulcers, and interstitial pneumonia were significantly more prevalent compared to the non-pericardial effusion group. Cox regression analysis indicated that pericardial effusion (hazard ratio; HR 11.8 [95% CI 1.6–84.6], p=0.014) and anti-RNAP III antibodies (HR 11.1 [95% CI 2.0–59.6], p=0.005) were independent risk factors for SRC, while mRSS (HR 1.0 [95% CI 0.9–1.1], p=0.12), finger apex ulcers (HR 0.57 [95% CI 0.073–4.2], p=0.57), max glucocorticoid dose (HR 1.0 [95% CI 0.9–1.0, p=0.89]), and interstitial pneumonia (HR 0.9 [95% CI 0.2–3.7], p=0.96) were not. In the Kaplan-Meier method, SRC was significantly increased in the pericardial effusion group compared to non-pericardial effusion group (p<0.0001 by log rank test).

**Conclusions:** Pericardial effusion is another independent factor predictive of SRC in addition to anti-RNAP III antibodies.

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THURSDAY, 14 JUNE 2018

## Vasculitis

### THU0433 THE PREVALENCE OF SPONDYLOARTHROPATHY IN PATIENTS WITH TAKAYASU ARTERITIS

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**Background:** Takayasu arteritis (TA) is characterised by inflammation of large arteries causing stenosis, occlusion, dilatation and/or aneurysm of affected vessels. TA is most commonly seen in younger women between 20–30 ages. Etiopathogenesis of TA is largely unknown although evidence suggest complex interplay between environmental and genetic factors such as HLA (human leukocyte antigen) groups. The coexistence of TA with spondyloarthropathies (SPA) has been reported in limited case series, raising hypotheses about shared pathogenetic mechanisms.

**Objectives:** To determine prevalence of spondyloarthropathy in patients with TA.

**Methods:** Detailed clinical and demographic features of TA patients were recorded and all were screened for the presence of SPA following recommendations of (ASAS). Patients were questioned for inflammatory back pain, enthesitis, uveitis, inflammatory bowel disease, peripheral arthritis, and investigated accordingly with HLA-B27, plain X-rays of pelvis and sacroiliac magnetic resonance imaging. Radiographic spondyloarthritis was reported in case of bilateral grade  $\geq 2$  or unilateral grade  $\geq 3$  sacroiliitis.

**Results:** There were 65 patients (61 female, 4 male) in the cohort. Mean age was 43±13 years and age at the diagnosis of TA was 35±13 years. Inflammatory bowel disease, psoriasis and psoriatic arthritis were observed in four, three and one patients. Chronic axial pain was reported by 26 (40%) patients but inflammatory back pain was evident in 13 (20%) patients. Chronic arthritis was observed in 4 patients. HLA-B27 was positive in three patients. Six patients were diagnosed as radiographic SPA and 3 were diagnosed as non-radiographic SPA. In sum nine patients were diagnosed as SPA (14.2%).

**Conclusions:** Our study demonstrated that SPA is common in patients with Takayasu arteritis suggesting shared pathogenetic mechanisms.

**Disclosure of Interest:** None declared

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### THU0434 PREDICTORS OF LONG-TERM GLUCOCORTICOID THERAPY IN POLYMYALGIA RHEUMATICA: DISCONTINUATION IS MORE COMMON FOR PATIENTS TREATED WITH AMINOBISPHOSPHONATES

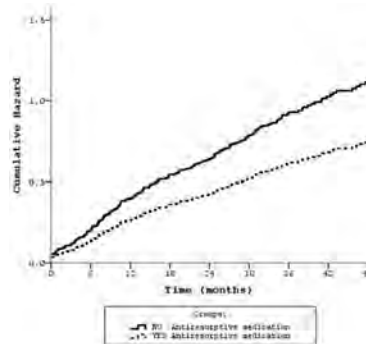
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**Background:** Glucocorticoids (GCs) are the cornerstone of polymyalgia rheumatica (PMR) therapy. Although guidelines for PMR generally recommend tapering GCs after 12–24 months, most patients are unable to discontinue GCs within the recommended time-frame. However, glucocorticoid-related adverse events can occur in up to 85% of treated cases. Patients treated with GCs should receive aminobisphosphonates (N-BPs) for the prevention of GCs-induced osteoporosis.

**Objectives:** In this retrospective observational study, we aimed to establish: 1) the proportion of patients with PMR who do not discontinue GCs, and 2) whether the use of N-BPs may be associated with a discontinuation of GCs.

**Methods:** Data were collected from electronic medical records of Rheumatology Unit at Azienda Ospedaliera Universitaria Integrata (AOUI) Verona, Italy. Patients were eligible for inclusion if they fulfilled the 2012 EULAR/ACR classification criteria for PMR. The following exclusion criteria were applied: a history of large vessel vasculitis and other diagnoses that could explain the symptoms. The main outcome was the long-term use of GCs, defined as a patient still receiving active treatment with GCs at the last evaluation available. Putative predictors included age, sex, dosage of prednisone, inflammatory markers (ESR and CRP), haemoglobin, peripheral joint involvement, use of DMARDs, number of relapses, osteoporosis and use of N-BPs. Univariable and multivariable Cox regression analyses were used to examine the association between several predictors and the outcome.

**Results:** 385/467 patients screened were eligible (median age 72 years [IQR 66–78], 64% females). Peripheral joint involvement was detected in 29%; 22% received DMARDs. The initial prednisone dose (median daily dose 20 mg<sup>13–25</sup>) was correlated with age, haemoglobin, CRP and ESR. More than 60% of patients were treated with N-BPs, of whom only 26% were diagnosed with osteoporosis. The median follow up time was 38 months [IQR 9–57]. Disease relapse occurred in 307/467 patients (80%). GCs were discontinued in 47% after a median time of 20 months [IQR 14–27], but were restarted in 39%. At the last evaluation, 276 patients (72%) were still receiving active treatment with GCs (median daily dose 5 mg [IQR 0–8]). Multiple Cox regression analysis showed that older age (HR 1.02, 95% CI 1.00–1.04, p=0.006) and higher CRP at baseline (HR 1.24, 95% CI 1.10–1.40, p=0.001) were associated with the long-term use of GCs, whereas significant predictors of a shorter treatment duration were the use of N-BPs (HR 0.66, 95% CI 0.50–0.88, p=0.004; figure 1) and a higher initial prednisone dose (HR 0.98, 95% CI 0.96–0.99, p=0.002).



**Abstract THU0434 – Figure 1.** Risk function of long-term GC use for the use of antiresorptive medications.

Adjusted HR 0.66 (95% CI: 0.50, 0.88), p=0.004.

**Conclusions:** Unlike current guidelines, in clinical practice a long-term treatment with GCs is often necessary in PMR. There is need to investigate novel treatments for PMR. This preliminary data suggests that aminobisphosphonates may have a role in the management of PMR.

**Disclosure of Interest:** None declared

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**THU0435** **LONG-TERM OUTCOME AND PROGNOSIS FACTORS OF COMPLICATIONS IN THROMBOANGIITIS OBLITERANS (BUERGER'S DISEASE): A MULTICENTER STUDY OF 224 PATIENTS**

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**Background:** Buerger's disease or thromboangiitis obliterans (TAO) is a non-atherosclerotic arteritis of distal extremities. Data regarding long term outcome of patients with Buerger's disease or thromboangiitis obliterans (TAO) are lacking and most series come from Middle-East and Far-East.

**Objectives:** We aim report clinical presentation and assess long-term outcome and prognosis factors in a large cohort of TAO.

**Methods:** Retrospective multicenter study of characteristics and outcomes of 224 TAO patients fulfilling Papa's and/or 5 Shinoya's criteria were analysed. Factors associated with vascular event free survival and amputation free survival were identified.

**Results:** The median age at diagnosis was 38.5<sup>32-46</sup> years, 51 (28.5%) patients were female and 81.5% were Caucasians. All but 3 were smokers with a median of 22 pack-year and 22.8% were also addict to cannabis. At diagnosis, 53% had claudication, 73% trophic disorders and 8.8% an infection. Lower extremities and upper extremities were affected in 54% and 28% respectively. Superficial vein thrombosis, Raynaud's phenomenon and arthralgia occurred in 18%, 41% and 8%, respectively.

Ethnic group (non-Caucasian) and ischaemic ulcers or necrosis were independent factors of vascular events HR=7.67 [3.1-19.2] p=0.005 and 2.28 [1.3-4] p<0.001. At 15 years, amputation-free survival and major amputation-free survival were 66% and 91%, respectively. Infection was the only independent predictive factor of amputation HR=4.6[1.9-11], p<0.001. Age, sex and cannabis addiction were not associated with events or amputation. Patient who stopped their tobacco consumption had lower vascular event (p=0.029) and amputation rate (p=0.001) than those who continued. Three patients died during follow-up.

**Conclusions:** This nationwide study shows that 34% of TAO patients will experience an amputation within 15 years from diagnosis. We identified specific characteristics that identified those at highest risk for subsequent vascular complications.

**Disclosure of Interest:** None declared

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**THU0436** **INCIDENCE, PREVALENCE, MORTALITY AND CHRONIC RENAL DAMAGE OF ANCA-ASSOCIATED GLOMERULONEPHRITIS IN A 20 YEAR POPULATION-BASED COHORT**

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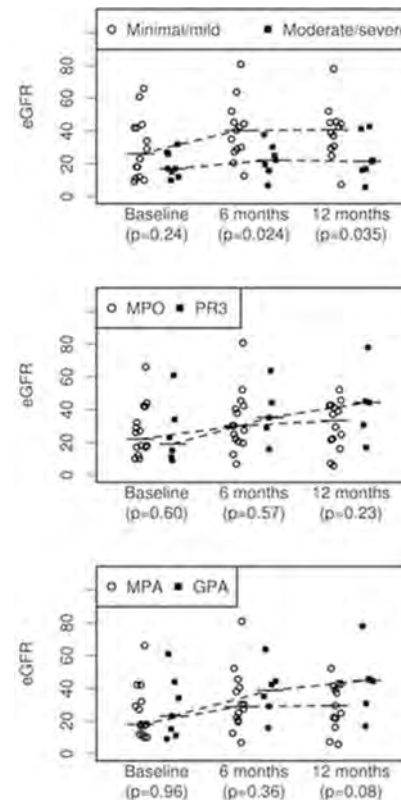
**Background:** True population-based incidence rates of ANCA-associated glomerulonephritis (AAGN) are lacking.

**Objectives:** We aimed to estimate incidence, prevalence and mortality of AAGN, and to assess if the grade of chronic renal damage at presentation predicts renal and non-renal outcomes.

**Methods:** A population-based incident cohort of 57 Olmsted County residents diagnosed with ANCA-associated vasculitis (AAV) in 1996-2015 was identified

by medical record review. AAGN was defined as an increase in creatinine >30% and/or a decrease in estimated glomerular filtration rate >25%, and/or the presence of urine red cell casts or hematuria and/or biopsy-proven necrotizing and/or crescentic glomerulonephritis. Incidence rates were age- and sex-adjusted to the 2010 US white population. Age- and sex-adjusted prevalence was calculated for January 1, 2015. Survival rates were compared with expected rates in Minnesota population. Chronic renal damage was assessed by chronicity score (CS) on biopsies performed at diagnosis.

**Results:** Thirty-four (60%) patients had AAGN. Of these, 65% had microscopic polyangiitis (MPA), and 74% were myeloperoxidase (MPO)-ANCA-positive. The annual incidence of AAGN was 2.0/100,000 population (95% CI:1.3-2.7), the overall prevalence was 35/100,000 (95%CI:24-47). Mortality for AAGN was increased (p<0.001), whereas mortality for AAV without glomerulonephritis did not differ from the general population. Minimal/mild CS predicted recovery of renal function at 1 year (p=0.035; **figure 1A**); clinical diagnosis (granulomatosis with polyangiitis (GPA) versus MPA) and ANCA-specificity (proteinase 3(PR3)-AAV versus MPO-AAV) did not (**figure 1B-C**).



**Conclusions:** Annual incidence and prevalence of AAGN in Minnesota are 2.0/100,000 and 35/100,000, respectively. Mortality is worse compared to AAV patients without glomerulonephritis. More advanced renal damage at diagnosis predicts less renal recovery.

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**Disclosure of Interest:** None declared

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THU0437

**ILLNESS PERCEPTION AND ITS CORRELATES IN PATIENTS WITH IN ANCA-ASSOCIATED VASCULITIS – PRELIMINARY REPORT**

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**Background:** Illness perception (IP) is one of the most important factors related to health related quality of life, psychological and physical functioning and medical adherence.<sup>1,2</sup>

**Objectives:** To explore illness perception and its relationship with chosen clinical, socio-demographic and psychological variables in patients with granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA).

**Methods:** 38 patients (57.9% women; median age 57 years; range 18–85; median disease duration: 11.5, range: 1–248 months) with GPA (28 patients) and MPA (10 patients). Inpatients recruited in 3 clinical centres were asked to complete Brief-Illness Perception Questionnaire (B-IPQ),<sup>3</sup> Hospital Anxiety and Depression Scale-Modified (HADS-M) and Multidimensional Fatigue Inventory-20 (MFI-20). Socio-demographic variables included age, sex, education and marital status. Medical files were reviewed to gather data on disease duration and its activity (assessed using Birmingham Vasculitis Activity Score version 3, BVASv3). p<0.05 was considered significant.

**Results:** 63% of patients had active disease as defined by BVASv3. Median total score of B-IPQ was 48.5 points (range 24–64). There were no significant differences in illness perception (B-IPQ total score) between groups according to sex, education and marital status. No significant relationships between IP and age, disease duration and its activity were noted. Significant positive correlations were observed between B-IPQ total score and MFI-20 total score, general, physical and mental fatigue as well as depression, anxiety and irritability (table 1).

**Abstract THU0437 – Table 1.** Correlation coefficients between studied variables and B-IPQ results.

Variable	Spearman's r correlations
Age	0.06
Disease duration	-0.02
BVASv3	0.00
MFI-20 total	0.48*
General fatigue	0.48*
Physical fatigue	0.38*
Reduced activity	0.26
Reduced motivation	0.25
Mental fatigue	0.34*
Depression	0.54*
Anxiety	0.53*
Irritability	0.35*

\* statistically significant p<0,05

**Conclusions:** In the studied group illness perception was not related to clinical and socio-demographic factors. More negative illness perception was related to higher levels of fatigue, depression, anxiety and irritability. The results suggest that psychotherapeutic interventions seem vital for improving illness perception in this population.

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**Disclosure of Interest:** None declared

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THU0438

**COMPARATIVE STUDY OF INFlixIMAB VERSUS ADALIMUMAB IN REFRACTORY UVEITIS ASSOCIATED TO CYSTOID MACULAR OEDEMA DUE TO BEHÇET'S DISEASE. MULTICENTER STUDY OF 40 CASES**

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**Objectives:** To compare the efficacy of infliximab (IFX) versus adalimumab (ADA) as first biologic drug in refractory uveitis with cystoid macular oedema (CME) associated to BD.

**Methods:** Multicenter study of 40 patients with BD-associated uveitis with CME refractory or intolerant to standard treatment (corticosteroids and at least one conventional immunosuppressive agent). CME was considered if macular thickness was greater than 300 µm. Comparative outcome measures were macular thickness, improvement of visual acuity (VA), activity of anterior chamber inflammation and vitritis. Results were expressed as mean ±SD for variables with a normal distribution, or as median [25th-75th interquartile range- IQR] when not normally distributed. The comparison of continuous variables among time-periods was performed with the Wilcoxon signed rank test.

**Results:** We selected patients with CME from a cohort of 177 patients with refractory BD-related uveitis (n=40). IFX was used in 15 cases and ADA in 25. No significant differences at baseline were observed between IFX vs ADA groups in sex (♂/♀ 8/7 vs 13/12, p=0.93), mean age (38±9 vs 41±10 years, p=0.53), HLA-B51 + (10 vs 19, p=0.87), uveitis pattern (panuveitis 67% vs 80%, posterior uveitis 33% vs 20%, p=0.34), previous conventional treatment (intravenous pulses of methylprednisolone 60% vs 52%, p=0.62, oral corticosteroids 93% vs 72%, p=0.1, methotrexate 53% vs 52%, p=0.93, cyclosporin A 73% vs 88%, p=0.23, azathioprine 53% vs 56%, p=0.86, other drugs 47% vs 68%, p=0.18), and combined treatment (67% vs 64%, p=0.86). After 1 year of therapy, ocular remission was achieved in 60% of cases with IFX and in 76% of cases with ADA (p=0.28). Regarding CME, 65% of patients with IFX reached a macular thickness <250 µm vs 87% of patients with ADA, with no statistically significant differences (p=0.07). Evolution of ocular parameters is shown in the table 1. Only 2 adverse effects were observed, both in ADA group (local rash and bacteremia).

**TABLE 1.** Rapid and maintained improvement following the onset of anti-TNF agents. Data are expressed as mean±SD or median [IQR].

	IFX	ADA	p
<b>Basal</b>			
VA	0.32±0.24	0.40±0.28	0.27
Anterior chamber cells	1 [0-1]	2 [0-3]	0.17
Vitritis	1 [0-2]	3 [0-3]	0.38
CCT	484.20±130.87	481.52±120.58	0.97
<b>1 week</b>			
VA	0.37±0.22	0.43±0.24	0.69
Anterior chamber cells	0 [0-1]	2 [0-5]	0.29
Vitritis	1 [0-2]	2 [0-3]	0.71
CCT	466.30±121.39	470.77±125.77	0.80
<b>2 weeks</b>			
VA	0.46±0.25	0.49±0.23	0.50
Anterior chamber cells	0 [0-1]	1 [0-2]	0.38
Vitritis	1 [0-1]	1 [0-1]	0.38
CCT	438.00±115.78	426.03±95.18	0.43
<b>1 month</b>			
VA	0.55±0.28	0.51±0.24	0.37
Anterior chamber cells	0 [0-0]	0 [0-1]	<0.05
Vitritis	0 [0-0]	1 [0-2]	0.76
CCT	366.30±117.69	354.03±85.57	0.11
<b>3 months</b>			
VA	0.65±0.30	0.57±0.29	0.48
Anterior chamber cells	0 [0-0]	0 [0-1]	1.00
Vitritis	0 [0-0]	0 [0-1]	<0.05
CCT	336.22±118.88	318.87±100.38	<0.05
<b>6 months</b>			
VA	0.59±0.30	0.59±0.29	0.88
Anterior chamber cells	0 [0-0]	0 [0-0]	1.00
Vitritis	0 [0-0]	0 [0-1]	1.00
CCT	284.60±102.30	278.25±87.31	<0.05
<b>1 year</b>			
VA	0.56±0.30	0.73±0.28	0.12
Anterior chamber cells	0 [0-0]	0 [0-0]	1.00
Vitritis	0 [0-0]	0 [0-0]	1.00
CCT	292.73±104.40	246.70±84.89	<0.05

Abbreviations: ADA, adalimumab; IFX, infliximab; CCT, optical coherence tomography; VA, visual acuity.

**Conclusions:** IFX and ADA show a similar efficacy in the treatment of CME in BD-related refractory uveitis.



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**THU0439** TOCILIZUMAB IN GIANT CELL ARTERITIS. NATIONAL MULTICENTER STUDY OF 134 PATIENTS OF CLINICAL PRACTICE

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**Background:** Giant cell arteritis (GCA) can be refractory to corticosteroids<sup>1-3</sup>. Tocilizumab (TCZ) demonstrated to be effective in two short-term clinical trials.

**Objectives:** To assess efficacy of TCZ in refractory GCA or with side effects to corticosteroids in clinical practice.

**Methods:** Multicenter study on 134 patients with GCA in treatment with TCZ due to lack of efficacy and/or unacceptable adverse events of previous therapy.

**Results:** 134 patients (101 w/33 m); mean age of 73.0±8.8 years. Main clinical features at TCZ onset were: PMR (n=73), constitutional syndrome (n=31), headache (n=70), visual (n=28) and jaw (n=14) affection. Besides steroids, 98 patients also received immunosuppressive agents. table 1 shows evolution during follow-up period. After a median follow-up of 12 [3.7–24] months, it was observed a decrease in: **a)**CRP from 1.7 [0.4–3.2] to 0.1 [0.0–0.3] mg/dL **b)**ESR from 33 [14.5–61] to 4<sup>2-9</sup> mm/1st hour and **c)** Prednisone dose from 15<sup>10-30</sup> to 5 [0–7.5] mg/day. Outcome of patients was: **a)**discontinuation of TCZ (n=15) due to sustained remission, **b)**dose reduction due to improvement (n=17) or side effects (n=11), **c)**withdrawal of TCZ because of side effects (n=12) and **d)**same dose that at onset (n=73). TCZ had to be discontinued due to: infections, haematological and cardiovascular alterations, neoplasms and hepatic toxicity among the most frequent.

Table 1:

	Baseline n=134	Month 1 n=132	Month 3 n=122	Month 6 n=99	Month 12 n=71	Month 24 n=39
Clinical improvement % (n#)		93.9% (124/132)	94.2% (115/122)	94.9% (94/99)	92.9% (66/71)	100% (38/39)
Laboratory markers, median [IQR]						
ESR (mm/1 <sup>st</sup> h)	33 [14.5-61]**	8 [2-12]** (102)	4 [2-7]** (116)	4 [2-6]** (98)	4 [2-6]** (71)	5 [2-16]** (39)
CRP (mg/dl)	1.7 [0.4-3.2]**	0.1 [0.0-0.3]** (98)	0.1 [0.0-0.3]** (116)	0.1 [0.0-0.2]** (92)	0.1 [0.0-0.2]** (67)	0.1 [0.0-0.1]** (38)
Hemoglobin (g/dl)	12.3 [11.4-13.2]**	11.2 [12.3-14]** (104)	13.5 [12.5-14.2]** (107)	13.8 [12.8-14.1]** (88)	13.3 [12.6-14]** (64)	13.1 [12.3-13.8]** (36)
Dose of corticosteroids (mg/day), median [IQR]	15 [10-30]** (134)	8.7 [7.5-20]** (116)	6.1 [5-12.8]** (120)	5 [2.5-7.8]** (97)	2.9 [2.6]** (71)	0 [0-5]** (38)

# Improvement in at least one of the clinical features. \* p<0.001 \*\* p<0.0001 (test de Wilcoxon).

**Conclusions:** TCZ leads to a rapid and maintained improvement in patients with refractory GCA and/or with unacceptable side effects related to corticosteroids. However, the risk of neutropenia and infection should be kept in mind.

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**THU0440** SOLUBLE CTLA-4 IS ELEVATED IN PATIENTS WITH POLYMYALGIA RHEUMATICA AND CORRELATES WITH VASCULAR INFLAMMATION DETECTED BY PET/CT

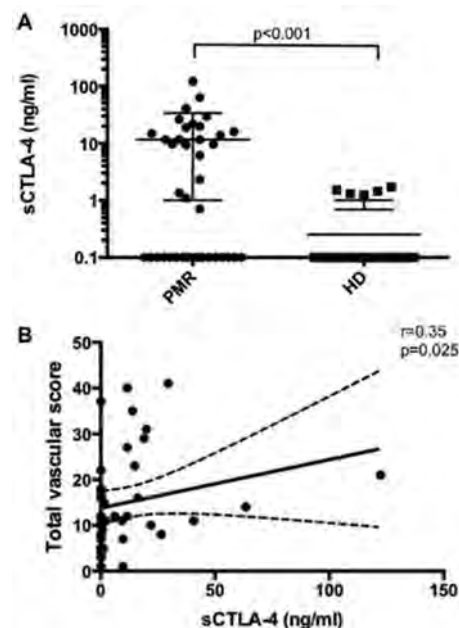
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**Background:** Positron emission tomography has shown the presence of large vessel vasculitis (LVV) in 30%–40% of patients with apparently isolated polymyalgia rheumatica (PMR)<sup>[1]</sup>, but biomarkers associated with the presence of LVV in PMR patients are still lacking. Anti-cytotoxic T lymphocyte antigen-4 (CTLA-4) and its soluble (s) form, resulting from alternative splicing, are well-known immune checkpoint receptors<sup>[2]</sup> and have shown to play a role both in neoplastic<sup>[3]</sup> and autoimmune diseases<sup>[4]</sup>. The rationale for studying the involvement of CTLA-4 in PMR is provided by the evidence of drug-induced PMR/giant cell arteritis (GCA) in patients treated with ipilimumab, an anti-CTLA-4 antibody<sup>[5]</sup>.

**Objectives:** To evaluate the concentration of sCTLA-4 in PMR patients and to correlate it with vascular and joint inflammation.

**Methods:** Forty consecutive patients with of PMR, of whom 9 also had also GCA, underwent a standardised clinical examination and a PET/CT scan. Arterial and joint uptake of FDG were scored relative to liver and then summed up to obtain a total vascular score (TVS) and a total joint score (TJS). Patients were further subdivided into three groups for the analysis of the correlation with joint and vascular uptake: "vasculitic patients" (with grade-3 uptake in at least one vascular district), patients with intermediate uptake (excluded from this set of analyses), and patients without vasculitis. sCTLA-4, was evaluated by ELISA. Patients without autoimmune diseases served as controls.

**Results:** sCTLA-4 serum levels were significantly higher in PMR patients than in controls (p<0.001, figure 1), although their concentrations did not significantly differ between patients with and without vasculitis. However, sCTLA-4 showed a positive correlation with TVS (r=0.35, p=0.025), figure 1. Panel A: comparison of serum level of sCTLA-4 in patients with PMR and controls (HD: healthy donors). Panel B: correlation between sCTLA-4 and total vascular score.



**Conclusions:** The present study provides the first evidence that serum sCTLA-4 concentration is elevated in PMR patients, and that it correlates with TVS. Although the exact mechanisms underlying the upregulation of sCTLA-4 remain

elusive, we feel that aberrant production of cytokines, or abnormal activation of intercellular signalling pathways can be involved.

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#### THU0441 ENDOTHELIAL DYSFUNCTION IN POLYMYALGIA RHEUMATICA

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**Background:** Polymyalgia Rheumatica (PMR) is an inflammatory disease that affects people over 50 years old, characterised by pain and functional limitation of shoulder and hip, acute phase reactant elevation and a dramatic response to low doses of steroids.

Atherosclerosis is a chronic inflammatory process that affects the arterial vessels of multiple districts. Endothelial dysfunction is an early event of the atherogenic process. Chronic inflammatory diseases have an increased risk of accelerated atherosclerosis and cardiovascular disease.

A study on 41 subjects with giant cell arteritis with and without PMR showed an increased mean-intimal thickness, suggesting a pro-atherogenic role of PMR. However there are no studies that evaluated endothelial dysfunction which is a more precocious marker of subclinical atherosclerosis in PMR patients

**Objectives:** Aim of the study was to compare endothelial function among PMR patients to a control population. Moreover, the trend of endothelial dysfunction was evaluated over time in relationship to the improvement of clinical, laboratory and instrumental parameters.

**Methods:** The study involved 16 treatment-naive patients with a new PMR diagnosis.

Every 3 months routine visits were performed; at each visit laboratory and clinical data and the endothelial function at the brachial artery were evaluated.

The endothelial function was evaluated at the brachial artery level after 15 min of rest; the brachial artery diameter and the basal flow was measured at baseline and after the positioning of sphygmomanometer for 5 min to induce the forearm ischemia. The flow was measured again 15 s after deflation of the sleeve and 60–90 s after the diameter of the artery reassessed to obtain flow-mediated dilatation (FMD). The FMD, which represents endothelium-dependent vasodilatation was expressed as percentage increase to the starting diameter after stimulation

**Results:** 16 PMR patients (mean age 73.9±5.8, 7 Female) were compared with a population of 16 healthy controls age-matched (70.8±8.1, p=ns).

The two groups differed for the values of Erythrocyte Sedimentation Rate (ESR) (61.1±28 vs 19.3±16 mm/h, p<0.001) and C-Reactive Protein (CRP) (35.6±28.1 mg/L vs 2.4±0.4 mg/L, p<0.001).

At the sixth month of follow-up ESR was 31.2±29.9 mm/h while CRP was 8±5.9 mg/L; at the twelve month of follow-up ESR was 22.7±13.6 and CRP was 9.1±8.2 mg/L

In PMR patients group 11 patients had hypertension, 5 dyslipidemia, 1 diabetes and 5 patients were smokers, while in control group 9 had hypertension, 10 dyslipidemia, 6 were smokers and no one had diabetes. Healthy subjects matched by age, sex and comorbidity were chosen as controls.

At baseline FMD of patients was lower than controls (6.6±3.4 vs 10.7±2.3, p<0.001). After 6 months of steroid therapy the difference between the two groups remained significant (6.1±2.7 vs 10.7±2.3 p=0.001), while at the twelfth month the two groups achieved comparable FMD values (8.7±3.6 vs 10.7±2.3, p=0.067). The FMD values show an inverse correlation with values of ESR (R=-0.42 p=0.019) and CRP (R=-0.56 p=0.001) at baseline.

**Conclusions:** Endothelial dysfunction in patients with PMR appears early during the course of the disease and is related to levels of acute phase reactant; steroid therapy gradually improves these values; only after a year of therapy comparable values are observed between patients and healthy controls.

**Disclosure of Interest:** None declared

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#### THU0442 IS BEHCET'S SYNDROME GETTING Milder? A RETROSPECTIVE ANALYSIS OF INITIAL PRESENTATION FINDINGS THROUGHOUT 4 DECADES

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**Background:** There is some evidence that incident Behcet's syndrome (BS) might be becoming less severe.<sup>1</sup>

**Objectives:** We compared clinical findings at presentation of BS patients registered in a large, long standing dedicated multidisciplinary outpatient clinic at 4 time points during a 40 years period.

**Methods:** There were 4 groups. Group 1 included patients registered in 1979–1981, Group 2 those registered in 1990, Group 3 in 2000 and Group 4 in 2010. Only demographic and clinical findings at initial presentation were recorded.

**Results:** As shown in table 1, over 4 decades, male/female ratio decreases gradually. While mean age at presentation does not change, the median disease duration got shorter. Almost all clinical manifestations except genital ulcers and neurological involvement tended to decrease in frequency. This was also true when genders were separately analysed. Importantly the severity of vascular and eye disease decreased (table 1,2). The slope of vascular disease was more obvious.

**Abstract THU0442 – Table 1.** Initial demographic and clinical characteristics of cohorts

	Group 1 1979–81 cohort n=211	Group 2 1990 cohort n=170	Group 3 2000 cohort n=225	Group 4 2010 cohort n=270	P
Male/Female	140/71	110/60	142/83	150/120	0.069
Male/Female ratio	1.97	1.83	1.71	1.25	
Mean age at disease onset	31.5±8.3	30.9±9.0	30.7±9.3	32.3±9.6	NS
Median disease duration	2.5 [1.0–6.0]	2.0 [1.0–5.0]	1 [0.5–3]	1 [0.6–4]	0.06
Mucocutaneous inv., n (%)					
Genital ulceration	187 (88.6)	137 (80.6)	184 (81.7)	220 (81.4)	NS
Papulopustular lesion	174 (82.5)	130 (76.5)	187 (83)	185 (68.5)	<0.001
Erythema nodosum	132 (62.6)	88 (51.8)	101 (44.8)	112 (41.4)	<0.001
Ocular involvement, n (%)	107 (50.7)	107 (62.4)	97 (43.1)	129 (47.7)	0.001
Vascular involvement, n (%)	49 (23.2)	29 (17.0)	41 (18.2)	31 (11)	0.008
Large vessel involvement, n (%)	21 (42.9)	11 (38.0)	13 (31.7)	7 (22.5)	<0.001
Neurologic involvement, n (%)	7 (3.3)	6 (3.5)	5 (2.2)	10 (3.7)	NS
Arthritis, n (%)	79 (37.4)	37 (21.8)	53 (23.6)	56 (20.7)	<0.001

**Abstract THU0442 – Table 2.** Severity of ocular involvement at presentation

Ocular involvement	Group 1 1979–81 cohort n=107	Group 2 1990 cohort n=106	Group 3 2000 cohort n=97	Group 4 2010 cohort n=129	p
Visual acuity<0.1 in bilateral eyes, n (%)	17 (15.7)	8 (7.5)	6 (6.5)	9 (6.9)	0.03*
Visual acuity<0.1 in unilateral eye, n (%)	23 (21.3)	19 (17.9)	18 (19.7)	22 (17)	
Visual acuity>0.5 in bilateral eyes	39 (36.1)	54 (55.6)	55 (60.4)	73 (56.6)	

\*Group 1 vs 4 and Group 1 vs 3

**Conclusions:** Our observations support the notion that incident BS might be getting milder. There might be a list of explanations for this observation. 1. It might be a biological phenomenon due to changing environmental causes. In this line the significant decrease in papulopustular lesions could be due to a more sanitary environment while the rather unchanging frequency of neurologic involvement might be its possible independence from the environment. 2. It might be that the awareness of BS is increasing and we are recognising less severe cases. 3. Another explanation might be the more effective treatment these patients received before they were referred which was not specifically sought in this survey.

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**Disclosure of Interest:** None declared

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#### THU0443 A PROBABILITY SCORE FROM A FAST TRACK CLINIC TO AID THE MANAGEMENT OF SUSPECTED GIANT CELL ARTERITIS

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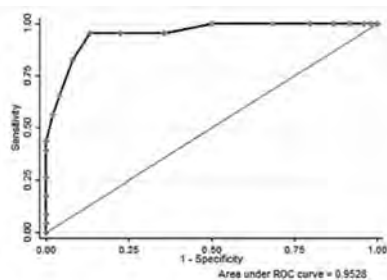
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**Background:** Diagnosis of Giant Cell Arteritis(GCA) is difficult since its manifestations are protean<sup>1</sup>. Under-diagnosis is associated with ischaemic complications whereas over diagnosis is associated with inappropriate glucocorticoids (GC)<sup>2</sup>. GCA is diagnosed by different specialties, including family physicians, who would benefit from a clinical prediction score. A fast track pathway also requires clinical triage in terms of probability of disease. We evaluated all referred patients (08/16–08/17) to develop a pre-test probability score(PTBS) to support a diagnostic pathway and decision-making.

**Methods:** The PTBS was generated from long standing clinical experience. Information collected at initial assessment was given varying positive weightage. This included baseline demographics (age-gender), symptomatology at presentation (onset, headache and scalp tenderness, ischaemic symptoms, constitutional symptoms, polymyalgia), C-Reactive protein(CRP) and examination findings (ischaemic ophthalmic complications, temporal artery abnormalities, extra-cranial abnormalities, cranial nerve palsies). Negative weightage was given for competing diagnoses (infection, cancer, head and neck pathology, systemic rheumatological diseases). The PTBS was compared with the final diagnosis as GCA or non-GCA 6 months after the initial assessment. Analysis was performed in Stata SE, version 13.1.

**Results:** 122 PTBS were collected of which CRP was missing in 1 case which was excluded from the analysis. 23 had a final diagnosis of GCA at 6 months follow up. The rest consist our control group(99 patients). The area under the ROC curve for the 121 cases was 0.953 (figure 1). Using the bootstrap method gave an estimated area under the ROC curve (95% confidence interval) of 0.953 (0.911, 0.994). At the point of inflection, corresponding to a cut point of 9.5, sensitivity was 95.7%, and specificity was 86.7%; the likelihood ratio for a positive test was 7.2 and the likelihood ratio for a negative test, 0.050. At this cut point, 88.4% cases were correctly classified.



**Conclusions:** This single centre retrospective study suggests that PTBS is a useful standardised assessment tool for rating pre-test probability for GCA with high levels of sensitivity and specificity. PTBS may reduce variation in clinical assessment and aid decision making. A patient with low probability score(<9.5) can be managed with colour doppler ultrasound examination(US) which if

negative will exclude the disease and the clinician can reassure patient. A patient with high PTBS and positive US can safely have the diagnosis confirmed and treated with GC. With intermediate scores, conflicting PTBS and US findings, equivocal US, additional investigations including TA biopsy and/or other imaging scans may be needed. Our results need validation in a prospective study and in internal and external validation cohorts. PTBS has the potential for forming the basis for education programme for the correct and early diagnosis of GCA and limit inappropriate GC in non GCA mimics.

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**Disclosure of Interest:** None declared

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#### THU0444 AORTIC DILATATION IN PATIENTS WITH LARGE VESSEL VASCULITIS: A LONGITUDINAL CASE CONTROL STUDY USING POSITRON EMISSION TOMOGRAPHY/COMPUTED TOMOGRAPHY

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**Objectives:** To evaluate aortic diameter and predictors of aortic dilatation using FDG-PET/CT in a longitudinally followed cohort of patients with large vessel vasculitis (LVV) compared with controls.

**Methods:** All consecutive patients with LVV who underwent at least 2 PET/CT scans between January 2008 and May 2015 were included. The first and last PET/CT study of each patient was independently evaluated by a radiologist and a nuclear medicine physician. The diameter of the aorta was measured at 3 different levels: ascending, descending thoracic and infrarenal aorta. Aortic dilatation was defined as a diameter of >4 cm in the ascending, ≥4 cm in the descending thoracic and ≥3 cm in the infrarenal aorta. Aortic FDG uptake was graded at the same levels using a 0–3 semiquantitative scale and was reported as negative (score 0 or 1) or positive (score 2 and 3). Patients younger than 50 years at symptoms' onset were classified as Takayasu arteritis (TAK), while those older than 50 years as giant cell arteritis (GCA). 29 age- and sex-matched patients with lymphoma who underwent at least 2 PET/CT in the same time interval without evidence of aortic FDG uptake were selected as controls.

**Results:** 93 patients with LVV were included in the study. 53% of patients were newly-diagnosed; the remaining 47% had a median disease duration of 34 months. At first PET/CT, the mean (SD) diameter of descending thoracic aorta was significantly higher in LVV patients compared with controls [28.07 (4.40) vs 25.60 (3.59) mm, p=0.012]. At last PET/CT, after a median time of 31 months, patients with LVV compared with controls had higher diameter of ascending [35.41 (5.54) vs 32.97 (4.11) mm, p=0.029] and descending thoracic aorta [28.42 (4.82) vs 25.72 (3.55) mm, p=0.007] and more frequently had aortic dilatation [19% vs 3%, p=0.023]. Significant predictors of aortic dilatation were male sex [OR 7.27, p=0.001], and the diameter of ascending [OR 2.03, p<0.001], descending thoracic [OR 1.57, p<0.001] and infrarenal [OR 1.25, p=0.005] aorta at first PET/CT study. Positive aortic FDG uptake, disease activity and elevated inflammatory markers at first PET/CT were not associated with an increased risk of aortic dilatation. The results remained unchanged when the analysis were restricted to the 48 newly-diagnosed LVV patients.

According to age at symptoms onset, 56% of patients were classified as GCA and 44% as TAK. Compared with TAK, GCA patients had higher aortic diameter at all 3 levels evaluated in both first and last PET/CT study. However there were no differences in the proportion of patients with aortic dilatation (at last PET/CT 23% in GCA vs 15% in TAK, p=0.306). The results remained unchanged when the analysis were restricted to the newly-diagnosed patients.

**Conclusions:** Patients with large vessel vasculitis are at increased risk of aortic dilatation compared with age- and sex-matched controls. Significant predictors of aortic dilatation are male sex and aortic diameter at first imaging study. Positive aortic FDG uptake at first PET/CT is not associated with increased risk of aortic dilatation.

**Disclosure of Interest:** None declared

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THU0445

### PRIMARY DIAGNOSIS OF LARGE VESSEL VASCULITIS BY TISSUE HISTOLOGY AFTER SURGERY OF AORTIC VALVE AND ASCENDING AORTA

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**Background:** Large vessel vasculitis showed different histological patterns, ranging from well-formed granulomas and lymphoplasmacytic pattern to giant cell pattern. Most of entities of large vessel vasculitis belong to rheumatic diseases such as the giant cell arteritis (GCA). The clinical feature is very variable depending on the GCA manifestations.

**Objectives:** Here we present an observation study of non-vasculitis patients, which had to undergo surgery of aortic valve and/or ascending aorta with a tissue histology of aortic inflammation.

**Methods:** In the department of thoracic surgery of the University Medical School of Saarland, Germany, 1474 patients (in 2014 n=806, in 2015 n=668) underwent thoracic surgery of aortic valve or ascending aorta due to different indications such as any entity of aortic aneurysm, dissection, aortic stenosis and/or insufficiency. Patients with bacterial endocarditis were excluded from analysis. All surgical specimens were pathologically analysed according standard procedure. All specimens (n=19 in 2014, n=17 in 2015) with histological inflammation signs of aortitis being negative for tbc, mycosis, or lues were underwent further investigation searching for IgG4 +plasmacells, giant cells, and granuloma; all patients (n=36) were re-evaluated by a rheumatologist (immediately during the hospitalisation or within 3 weeks with outpatient presentation) including laboratory tests for RF, ANA, ANCA, ACCP, IgG subclasses, complement, ESR, CRP. Furthermore, all aortitis patients were investigated with MRI of aorta (n=15) or PET scan (n=17) or both (n=4) between 4 to 12 weeks after surgery to exclude persistent aortitis in native vessels. All patients which were diagnosed for aortitis through MRI and/or PET received immunosuppressive treatment containing glucocorticosteroids with or without synthetic or biological DMARDs.

**Results:** Patients after thoracic surgery of aortic valve and/or ascending aorta were positive tested for aortitis in 2014 with the frequency of 2.36% (n=19/806) and in 2015 2.54% (n=17/668). The mean age of the 36 cases were 61 (range 39–80), of them were male 55.5% (n=20). The pathologic findings described 14 cases typical for GCA, 6 with granuloma, one with IgG4 +plasmacells, and one with predominant lymphocytic infiltration, 14 with unspecific inflammation. Rheumatologic consultation in all 36 cases could evaluated in 6 patients a preexisting rheumatologic disorder (RA n=2, polymyalgia rheumatica (PMR) n=4) without treatment. One patient were positive for significant elevated serum levels of IgG4. MRI and/or PET scan documented aortitis spots in the native aorta with or without concerning iliac arteries and/or supra-aortic vessels. All imaging-positive aortitis patients (n=12) were treated with glucocorticosteroids according to the protocol for giant cell arteritis (prednisolone 1 mg/Kg/body weight), six patients additionally with methotrexate, one with tocilizumab and one with rituximab.

**Conclusions:** Only a small fraction of thoracic surgery patients with aortic aneurysm, dissection, aortic stenosis and/or insufficiency show histologic signs of aortitis. However, a third of them could be diagnosed via histological findings for active large vessel vasculitis after surgery.

**Disclosure of Interest:** None declared

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THU0446

### USEFULNESS OF COLOUR DOPPLER ULTRASONOGRAPHY IN FOLLOW UP OF GIANT CELL ARTERITIS

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**Background:** Colour doppler ultrasonography (CDU) in temporal arteries (TA) is useful for diagnosis and follow-up of giant cell arteritis (GCA).<sup>1</sup> However, the usefulness of CDU in carotid arteries (CA) for follow-up of GCA is not fully understood.<sup>2</sup>

**Objectives:** We investigated retrospectively relationship between clinical features and vessel wall thickness of TA and CA on CDU at baseline and during follow-up.

**Methods:** We recruited patients with newly diagnosed GCA in our hospital from January in 2004 to July in 2017. Among 35 patients, both of TA and CA were evaluated by CDU before and after treatment in 14 patients (four male and 10 female). Trained ultrasonographers and rheumatologists evaluated the CDU findings. Vessel wall thickness was evaluated at thickest portion of parietal or frontal ramus of TA, where biopsy was often performed. Intima-media thickness (IMT) of CA was also evaluated at thickest portion in each carotid artery.

**Results:** Average age was 73.2±11.3 years old. Follow-up periods after starting treatment were 244±149 weeks. All patients were diagnosed as GCA according to ACR criteria (1990) or temporal artery biopsy. Twelve patients were complicated with polymyalgia rheumatica (PMR) meeting EULAR/ACR classification criteria

(2012). All patients were treated with oral glucocorticoids (0.2 to 1.0 mg/kg prednisolone, 0.886 mg/kg on average). Immunosuppressants were added in four patients (methotrexate; n=3, tacrolimus; n=1). Aspirin was prescribed in nine patients.

Eleven patients (78.6%) had circumferential hypoechoic vessel wall thickness (halo sign) of TA at baseline, and halo signs disappeared in eight patients during follow-up. Average of vessel wall thickness significantly decreased from 0.665 mm to 0.311 mm (p=0.0016). The vessel wall thickness apparently increased in two patients out of three on clinical relapse, but it didn't increase in those who kept remission.

Graphical changes consistent with vasculitis in CA were observed in six patients, who showed hypoechoic thick intima and media on ultrasound or integration of FDG on PET/CT. Average of IMT in CA decreased from 1.167 mm to 0.883 mm (p=0.090) during follow-up in patients with vasculitis on CA. IMT changed little in patients without vasculitis on CA. Improvement rate was significantly higher in CA-involved patients than in CA-non-involved patients (p=0.043). IMT increased during follow-up in two CA-non-involved patients.

**Abstract THU0446 – Table 1.** Time-dependent change in vessel wall thickness of TA (mm)

	Baseline	Follow-up	Relapse
Patient 1	0.30	0.30	0.30
Patient 2	0.63	0.30	0.60
Patient 3	0.63	0.10	0.60

**Abstract THU0446 – Table 2.** Improvement rate of IMT in CA involved and non-involved patients

	IMT (mm)		Rate(B/A)	Median follow-up period (months)
	Baseline [A]	Follow-up [B]		
All (n=14)	0.964	0.843	0.874	30.0
CA involved (n=6)	1.167	0.883	0.757	34.0
CA non-involved (n=8)	0.813	0.813	1.000	27.6

Difference in B/A between CA involved and non-involved: p=0.043 (Mann-Whitney U test)

**Conclusions:** CDU of temporal arteries is useful for follow-up of GCA. CDU of carotid arteries has limited usefulness only in CA-involved patients.

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**Disclosure of Interest:** None declared

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THU0447

### NO ADVANTAGE OF METHOTREXATE IN THE TREATMENT OF GIANT CELL ARTERITIS

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**Background:** The high-dose glucocorticoids (GCs) are the mainstay of treatment in Giant Cell Arteritis (GCA). Patients treated with greater GCs dosages are at the greatest risk of morbidity. Immunosuppressive agents have been trialled in an effort to reduce toxicity from GCs and to improve efficacy of treatment. The results of one meta-analysis with the three trials that included methotrexate (MTX) showed a weak benefit in those patients receiving MTX, but the results were heterogeneous, with one trial showing significant benefit, while the other two did not.<sup>1</sup>

**Objectives:** To study the efficacy and safety of MTX adjunct to GCs in the treatment of GCA.

**Methods:** New-onset giant-cell arteritis initiating treatment of the disease was included in a retrospective observational study to compare treatment efficacy and safety. According to the treatment received the patients were divided two groups: GCs alone (group 1) and MTX and GCs (group 2). To avoid bias, we defined a subgroup of patients in which only patients who started MTX in the first trimester of treatment were included (group 3). As efficacy outcome the number of relapses and the cumulative dose of GCs at 6, 12 and 24 months were collected. For safety,

the number of emergency room visits, hospitalisation admissions and infections were investigated in the follow-up.

**Results:** One hundred twenty-three patients were included, 74 (60.2%) women, the mean age was 79.41 years old. Fifty-six (45.53%) received GCs alone (group 1) and 67 (54.48%) received GCs and MTX as an adjuvant treatment at some time during follow-up (group 2). 30 of these 83 patients (24.39% of total patients) received MTX in the first trimester after diagnosis (group 3). The cumulative doses of GCs, number of patients with relapses, visits to the emergency room and hospitalisation admissions are shown in the table 1. In none of these variables there were statistically significant differences among the three groups, except for the number of patients with relapses, which was greater in group 2 than in group 1 ( $p=0.03$ ). The number of relapses in patients who received MTX early (group 3) was 56.7%, in the rest of patients (who only received GCs and those who started MTX after the first trimester) was 52.69%–33.3% of the patients in group 3% and 21.5% of the rest of the patients presented infections.

	Group 1: GCs alone	Grupo 2: GCs+MTX at some moment during the follow-up	Group 3: GCs and MTX since 1st trimester	P group 3 vs (1 +2)	P group 1 vs 2
Cumulative GCs doses at 6 month (mg±SD)	6193 ±6820	7028±11 230	5942,50±1827	0.629	0.646
Cumulative GCs doses at 12 months (mg ±SD)	7772 ±7154	8976±11 148	7987±2360	0.759	0.897
Cumulative GCs doses at 24 months (mg ±SD)	9340 ±7886	10814±11 150	9383±2522	0.608	0.903
N° of patients with relapses (35.71%)	20/56	42/67 (62.69%)	17/30 (56.7%)	0.430	0.003
N° of patients with emergency room visits	20 (35%)	22 (32.8%)	12 (24%)	0.508	0.849
N° of patients hospitalisation admissions	16 (28.57%)	21 (31.34%)	11 (36.7%)	0.370	0.844

**Conclusions:** Whilst MTX have been used in an effort to reduce toxicity from GCs and to improve efficacy of treatment our observational study shows that there is no benefit from adjunct MTX in GCA either in terms of efficacy or toxicity.

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**Disclosure of Interest:** None declared

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#### THU0448 IS THERE AN ASSOCIATION BETWEEN ADULT IGA VASCULITIS AND CANCER?

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**Background:** An increased incidence rate of cancer has been reported in adult patients with IgA vasculitis (IgAV). These conclusions are mostly based on observations in severely ill, hospitalised subgroup of patients. Most of the studies allowed for a wide time interval between IgAV and cancer appearance, not necessarily reflecting a causative link.

**Objectives:** The aim of our study was to look for the potential association between IgAV and cancer in an unselected adult IgAV population.

**Methods:** We analysed medical records of prospectively followed, histologically proven adult IgAV cases at our secondary/tertiary rheumatology centre between 1 January 2010 and 30 June 2017, who were followed until 31 December 2017 and lived in a well-defined referral region. We identified cancer as concurrent with IgAV, if the patients had afferent cancer or a relapse of cancer or newly-diagnosed cancer diagnosed up to 6 months prior or 6 months after IgAV diagnosis. Cancers developing after 6 months of follow up were labelled as unrelated to IgAV. We used appropriate descriptive statistical methods, and the Fisher's exact and Mann-Whitney U tests to assess differences of clinical characteristics in acute phase of IgAV, between the cancer and non-cancer groups. The national prevalence and age adjusted incidence rates of cancer from a well-defined referral region were obtained from National cancer registry (NCR).

**Results:** During the 90 months of observation we identified 196 new IgAV cases. 2 patients died in the acute disease phase due to vasculitis, and 8 during the first 6 months of follow-up for reasons other than IgAV or cancer. 20 patients were lost to

follow-up. The remaining 166 patients (55% male, median (IQR) age 63<sup>43–76</sup> years) were followed for a median (IQR) of 20<sup>11–32</sup> months. At the time of IgAV diagnosis, 6/166 (3.6%) had active, previously diagnosed malignant disease (prostatic cancer in 4, among which one also had cancer of urinary bladder, and sarcoma in 2 patients). In 2/166 patients (1.2%) a new cancer was diagnosed at presentation and in 2/166 (1.2%) during follow-up. One of the patients with an active cancer of urinary bladder, was treated with antibiotics for urinary tract infection prior to IgAV diagnosis, and was also on chemotherapy. The patients with cancer were older (median age (IQR) 80<sup>77–83</sup> vs. 64<sup>44–77</sup> years;  $p=0.002$ ) but their presenting features of IgAV, and the initial IgAV treatment did not significantly differ from those without cancer. At the end of the observation period, the prevalence of cancer in our cohort was 6.0%, compared to the 4.8% prevalence of cancer in our general population and the relative risk of cancer in our IgAV cohort was 1.25 (95% CI 0.687–2.29;  $p=0.461$ ). The age adjusted incidence rate of cancer was 11.4 per 1000 patients per year. The annual age adjusted incidence rate of cancer in our citizens, acquired from NCR, was 8.9 per 1000 adults and the standardised incidence ratio for our IgAV cohort was 1.62 (CI 0.441–4.15;  $p=0.472$ ).

**Conclusions:** In our cohort of unselected adult IgAV cases, we did not confirm the previous observations of the association of IgAV, and cancer.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2018-eular.5359

#### THU0449 DIAGNOSTIC PERFORMANCE OF ANTINEUTROPHIL CYTOPLASMIC ANTIBODIES IN A COHORT OF UNSELECTED SPANISH PATIENTS

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**Background:** Antineutrophil cytoplasmic antibodies (ANCA) are the serological marker of some idiopathic systemic vasculitides, predominantly involving small and medium-sized blood vessels, such as granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) and eosinophilic granulomatosis with polyangiitis (EGPA), which are known as the ANCA-associated vasculitis (AAV). Nevertheless, ANCA have been reported in a number of other conditions.

**Objectives:** To retrospectively evaluate ANCA diagnostic accuracy in a cohort of unselected patients.

**Methods:** From January 2014 to December 2016 a total of 6781 serum samples with a test request for ANCA were submitted to the Immunology Department of a 1.000-bed tertiary teaching hospital from Barcelona (Spain), from both inpatients and outpatients.

Indirect immunofluorescence (IIF) was performed for all requests using a commercially available "Granulocyte Mosaic 13" (EUROIMMUN). IIF allowed recognition of three staining patterns: cytoplasmic (cANCA), perinuclear (pANCA) and atypical (xANCA). For the detection of antibodies against myeloperoxidase (MPO) and proteinase 3 (PR3) a chemiluminescent immuno-assay (CLIA) using commercially available "QUANTA Flash MPO/PR3" (INOVA diagnostics) was performed in patients with positive IIF.

We reviewed the clinical charts of patients that underwent ANCA testing and collected patients' diagnoses, as established by their treating physician one year after sampling. In the event of multiple ANCA test in a single patient we include only the first test request (we excluded 1323 tests performed in 661 patients). We also excluded 184 patients with insufficient information and 306 ANCA tests with no diagnostic purpose. Therefore the study population includes 4968 patients.

Statistical analysis was performed with Stata 14.2 (College Station, TX, USA). Diagnostic performance was assessed using sensitivity, specificity, positive likelihood ratio (LR+), positive and negative predictive values (PPV and NPV) and global efficiency. Confidence Intervals (CI) were calculated using Wilson method.

**Results:** Only 34 patients (0.68%) received a diagnosis of AAV: 25 MPA, 6 GPA and 3 EGPA.

	Sensitivity [CI 95%]	Specificity [CI 95%]	LR+ [CI 95%]	PPV [CI 95%]	NPV [CI 95%]	Efficiency [CI 95%]
<b>Positive IIF</b>	94.1% [80.9– 98.4]	87.6% [86.7– 88.5]	7.6 [6.8– 8.5]	5% [3.5– 6.9]	99.95% [99.83– 99.99]	87.7% [86.7– 88.5]
<b>IIF Typical pattern</b>	91.2% [77–97]	96.9% [96.3– 97.3]	29 [24.1– 35]	16.7% [12– 22.7]	99.94% [99.82– 99.98]	96.8% [96.3– 97.3]
<b>cANCA/PR3 or pANCA/MPO</b>	76.5% [60–87.6]	99.1% [98.8– 99.3]	83.8 [59.3– 118.4]	36.6% [26.4– 48.2]	99.84% [99.68– 99.92]	98.9% [98.6– 99.2]

The majority (87.1%) of patients had a negative ANCA test and only 12.9% were found positive by IIF. Among 643 positive patients IIF pattern distribution was: 457 (71.1%) atypical, 108 (16.8%) perinuclear and 78 (12.1%) cytoplasmic pattern.

Among patients with positive ANCA 32 (5%) had an AAV. Two patients with AAV had negative ANCA (one GPA and one EGPA).

Data of diagnostic accuracy of ANCA for AAV are showed in table 1:

**Conclusions:** ANCA testing with commonly commercially available methods has an excellent diagnostic performance for AAV in routine clinical practice, especially if a typical pattern is associated with proper antigenic specificity (cANCA with PR3 or pANCA with MPO).

**Disclosure of Interest:** None declared

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#### THU0450 DIAGNOSTIC RELEVANCE OF ORGAN BIOPSIES IN ANCA ASSOCIATED VASCULITIS

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**Background:** The diagnostic workup of ANCA-associated vasculitis (AAV) is a challenge due to the possible multi-organ involvement and the wide range of differential diagnosis. Before classification, vasculitis needs to be proofed by clinical or histopathologic signs.

**Objectives:** We aimed to evaluate specific histopathologic features of organ biopsies and their contribution to the diagnosis of vasculitis and to the classification of specific AAV subgroups.

**Methods:** Retrospective, single-centre cohort study in patients with granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) and eosinophilic granulomatosis with polyangiitis (EGPA), classified by ACR-criteria, who have received at least one organ biopsy. Characteristic histopathologic features were analysed and compared between AAV subgroups, organ systems and ANCA-status (Chi-square-test).

**Results:** 306 patients (GPA n=154, MPA n=58, EGPA n=94) diagnosed between 1990–2017 were included. All biopsies were taken at active stage of GPA, MPA or EGPA at initial diagnosis (n=415) or during flair of the disease (n=36). 168 patients had a renal biopsy, 185 patients had 283 non-renal biopsies (1 biopsy in 102 pts, 2 different organ biopsies in 68 pts, >2 in 15 pts). In kidney biopsies glomerulonephritis was described in 78.6%, unspecific inflammation in 26.8% and normal tissue in 1.2%. In non-renal biopsies vasculitis, granuloma, tissue eosinophilia, unspecific inflammation or normal tissue were reported in patients with GPA 32.9/29.4/21.2/71.8/9.4%, MPA 27.3/9.1/27.3/90.9/9.1% and EGPA 20.2/10.1/67.4/73.0/20.2%; p<0.0001 (lung n=103, 13.6/13.6/37.9/71.8/3.9%; skin n=35, 42.8/11.4/40.0/51.4/1.4%; upper respiratory tract n=98, 19.3/16.3/37.7/72.4/8.2%; peripheral nerves n=7, 14.3/14.3/0/14.3/42.8%; p<0.0001). According to the ANCA status the distribution was 31.1/25.2/28.3/68.9/10.7% in ANCA+patients and 20.8/11.1/62.5/79.2/19.4% in ANCA- patients (p<0.0001). Diagnosis of vasculitis was based on biopsy result in 2% of GPA, none of MPA and 8% of EGPA patients, but ACR criteria were only fulfilled including a characteristic biopsy in 6.6% of GPA and 35.5% of EGPA patients. Assignment to GPA, MPA and EGPA by application of the EMA algorithm were only possible in consideration of a characteristic non-renal biopsy in 2.8/0/21.9% and of a characteristic non-renal and/or renal biopsy in 4.7/14.6/28.1% of all patients.

**Conclusions:** Histologic proof of vasculitis remains the gold standard of AAV diagnostic, however the diagnostic value is most prominent for renal biopsies. Distribution of various histopathologic features is different among AAV subgroups (GPA, MPA, EGPA) and varies between different organ biopsies. While classification of GPA and MPA is only in a few cases based on histopathology, in EGPA a characteristic histopathology is necessary for classification in almost one third of patients.

**Disclosure of Interest:** None declared

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#### THU0451 CAUSE OF DEATH IN PATIENTS DIAGNOSED WITH GIANT CELL ARTERITIS IN WESTERN NORWAY 1972–2012

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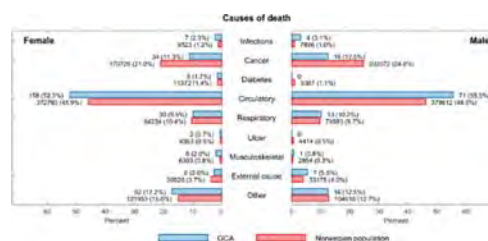
**Background:** Giant cell arteritis (GCA) is the most common systemic vasculitis in adults.

**Objectives:** To determine the causes of death in GCA patients during a 41 year period.

**Methods:** Hospital-based retrospective cohort study including patients diagnosed with GCA in Bergen Health Area during 1972–2012. Patients were

identified through computerised hospital records using the International Classification of Diseases (ICD)-coding system. Clinical information was extracted from patients' medical journals. We excluded patients if data were unavailable, if the reviewing rheumatologist found GCA to be an implausible diagnosis or if the American College of Rheumatology (ACR) 1990 classification criteria for GCA were not fulfilled. Information on cause of death was obtained from the Norwegian Cause of Death Registry (NCoDR). We grouped causes of death according to the European Shortlist for Causes of Death 2012-version (COD-SL-2012). Statistics Norway (www.ssb.no) provided background population data (all deaths during 1972–2012 in the Norwegian population ≥50 years of age). Statistical comparison was performed using mid-p values.

**Results:** The patient inclusion process and patient characteristics have been published previously.<sup>1</sup> A total of 792 patients were included, 566 (71.5%) females (mean age 73.5 years, SD 8) and 226 (28.5%) males (mean age 72.1, SD 9). 432 patients (54.5%) died during the study period (1 January 1972 – 31 December 2012). NCoDR had data on the cause of death for 431 of these. During the study period (1972–2012) there were 1635979 registered deaths in the general Norwegian population aged ≥50 years. The most frequent underlying causes of death in the overall study population were diseases of the circulatory system (53.4%), cancer (11.6%) and diseases of the respiratory system (10.0%). The most frequent causes of death in the general population were also diseases of the circulatory system (46.0%), cancer (22.8%) and diseases of the respiratory system (10.0%). The distribution of causes of death differed significantly between GCA-patients and the general Norwegian population (mid-p-value<0.001 both overall and stratified by sex). Absolute numbers of deaths and corresponding percentages of all causes of death stratified by sex are presented in figure 1.



**Conclusions:** The most frequent causes of death in our cohort of GCA-patients were diseases of the circulatory system, cancer and diseases of the respiratory system (including influenza and pneumonia). These were also the most frequent causes of death in the general Norwegian population aged ≥50 years, but the distribution of death causes differed significantly between GCA-patients and the general population. However, this might reflect differences in the composition of the populations that we were not able to adjust for. We aim to analyse this further by comparing our GCA-cohort with randomly selected age-, sex- and geographically matched control subjects.

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#### THU0452 ANTI-INTERLEUKIN-6 (TOCILIZUMAB) EXPERIENCE IN TAKAYASU'S ARTERITIS PATIENTS

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**Background:** Targeted therapies such as tumour necrosis factor inhibitors (TNFi) and anti-interleukin 6 (anti-IL-6) are increasingly being used in Takayasu's Arteritis (TA) patients who are unresponsive to corticosteroids±conventional immunosuppressives.

**Objectives:** The aim of this study was to evaluate the indications and efficacy of anti-IL-6 (tocilizumab) therapy in a case series of TA patients.

**Methods:** In the prospective database of the Hacettepe University Vasculitis Centre (HUVAM), 105 TA patients meeting the 1990 modified American College of Rheumatology (ACR) criteria were registered at the end of July 2017. Total 28



(26.7%) patients were treated with biological therapy and 22 (21.0%) of them were taking tocilizumab. Patients were assessed using a combination of clinical, laboratory and radiological evaluation before and after Tocilizumab therapy. The demographic and clinical characteristics of the patients, the pre-tocilizumab and end of the follow-up acute phase values (Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP)), visual analogue scales (VAS) (Pain, Fatigue, Patient Global), and concomitant therapies were recorded. Other clinical, imaging and laboratory results of the TA patients were obtained from hospital files. The comparative imaging (Computed Tomography and Magnetic Resonance Imaging) results of the patients just before the Tocilizumab therapy and during follow-up were recorded from the hospital data system.

**Results:** Twenty-two patients (86.4% female) were included in to the analysis. The median (minimum-maximum) age of the patients was 40<sup>24-63</sup> years and the median disease duration (from diagnosis) was 48<sup>12-168</sup> months. Before tocilizumab therapy; cyclophosphamide (8 patients (36.4%), conventional immunosuppressives (21 patients, 95.4%) and TNFi (7 patients, 31.8%) were used in addition to corticosteroid therapy. Main indications for tocilizumab therapy was as follows; radiological progression in 9 patients (acute phase was normal in 2 of them), acute phase elevation in 8 patients (4 of them radiologically stable, 4 of them had no radiologic evaluation), physician's decision and clinical symptoms in 3 patients (acute phase normal; 2 of them radiologically stable, one had no radiologic evaluation), in two patients tocilizumab therapy was started out of our centre and data before tocilizumab was not available. Fifteen patients (median follow-up time 15<sup>3-42</sup> months) were evaluated for response to tocilizumab treatment. There was a significant decrease in ESR, CRP, and VAS-patient-global of patients after tocilizumab therapy; median (min-max) ESR (26<sup>5-119</sup> vs. 3 (2-49) mm/s, p=0.02), CRP (39.8 (2.4-149.0) vs. 7.9 (0-92.9) mg/L, p=0.017), VAS-patient-global (50 (0-90) vs. 30 (0-60), p=0.027), respectively. Total of 9 patients had follow-up imaging; 8 of them was radiologically stable and regression was seen in one patient (figure 1).

**Table 1:**

Patient No	Age/Sex	Age at diagnosis	Disease Duration (months)	Previous treatments	Before Tocilizumab Therapy Steroid dosage	ESR mm/h	CRP mg/L	VAS (Pain/Fatigue/Patient Global)	Imaging
1	52F	35	43	MTX	Pred. 15 mg/day	36	42.8	8/2/20	Stable
2	44MF	31	72	CYC, MTX, SGC, P.E., ADA	Pred. 18 mg/day	75	81.7	8/2/20	Stable
3	47F	37	96	CYC, SGC, MTX, P.E., ETH	Mpred. 32 mg/day	24	19.8	8/7/30	Progression
4	53F	30	26	CYC, MTX, LEF, P.E., ADA	Pred. 30 mg/day	11	42.7	8/7/30	Stable
5	50F	53	17	MMF	Mpred. 18 mg/day	68	78.1	-	Stable
6	48F	28	12	MTX, P.E., PFC	Pred. 40 mg/day	28	28.0	-	Stable
7	50F	37	12	MTX, P.E., PFC	Pred. 40 mg/day	119	188.5	7/5/27	Progression
8	43F	61	12	MTX	-	-	-	-	Tocilizumab was started out of our center
9	78F	23	48	MTX, P.E.	P.E. 500 mg/month	103	85.1	8/8	-
10	43F	30	168	CYC, MTX	Pred. 40 mg/day	25	62.7	10/2/18	-
11	43F	40	38	CYC, MTX	-	12	18.7	8/8/30	Progression
12	34F	26	72	MTX, PFC	Pred. 50 mg/day	30	3.2	8/2/24	Progression
13	55F	39	36	AZT, MTX	Pred. 10 mg/day	7	1.8	8/8/37	Stable
14	54MF	13	72	MTX, P.E.	Pred. 5 mg/day	-	-	-	Tocilizumab was started out of our center
15	51F	23	84	CYC, MTX	Pred. 20 mg/day	6	2.7	8/8/28	Progression
16	51F	29	34	AZT, MTX	Pred. 30 mg/day	7	2.4	8/7/30	Stable
17	58F	38	13	CYC	Pred. 5 mg/day	42	28.8	7/9/27	Stable
18	68F	48	12	MMF	Mpred. 18 mg/day	2	8.8	8/8/20	Progression
19	52MF	20	24	CYC, MTX	Pred. 40 mg/day	18	31.7	8/10	Progression
20	53F	23	12	-	Mpred. 4 mg/day	14	3.5	8/8/30	Progression
21	68F	58	132	AZT	-	2	2.7	8/9/30	-
22	43F	34	60	MTX	Pred. 10 mg/day	10	1.8	8/7/30	Progression

**Conclusions:** The use of biological therapies in more than a quarter of TA patients suggests that the role of conventional therapies in TA is limited. Although imaging modalities and acute phase elevations are the main factors in the decision of change in treatment, presence of symptoms and physician opinion are also important. Significant response was obtained with the treatment of tocilizumab.

**Disclosure of Interest:** None declared

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**THU0453 EFFICACY OF AB INITIO OR VERY EARLY INTRODUCTION OF IMMUNOSUPPRESSIVE THERAPY IN GIANT CELL ARTERITIS: A MULTICENTER RETROSPECTIVE OBSERVATIONAL STUDY**

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**Background:** Glucocorticoids (GC) remain the mainstay of treatment of giant cell arteritis (GCA). However, relapses occur in up to 50% of patients when GC are tapered and prolonged courses of GC are associated with serious side effects. In this setting, the outcome is frequently determined by GC-related adverse events

(AEs). Thus, several studies have been conducted on the effectiveness of a GC-sparing immunosuppressive therapy (IT), with conflicting results.

**Objectives:** To evaluate the effectiveness of IT in a series of GCA patients, in: 1) reducing the risk of GCA relapse; 2) lowering the exposure to GC therapy; 3) minimising the occurrence of steroid-induced AEs.

**Methods:** We performed a multicenter retrospective observational study including 69 patients (75.4% females; mean age  $\pm$ SD 68,7 $\pm$ 7,8 y; median follow-up time 40 months [range 26-65]) diagnosed with GCA, all receiving an adjunctive IT given ab initio (71%) or within 3 months from the start of GC. All but 17 patients (with extracranial involvement) fulfilled the GCA ACR classification criteria. Risk of first relapse of GCA, GC exposure and main AEs were retrospectively analysed. Results were compared with those reported in other studies, all characterised by a lower use of IT.

**Results:** all patients received GC plus IT: methotrexate up to 20 mg/week in 63 patients, cyclophosphamide in 22, tocilizumab in 12. In the follow-up, a first relapse of GCA occurred in 14 (20.3%) of patients. The rates of first relapse at 12, 24, 36 and 48 weeks were 4.3%, 11.6%, 15.9% and 15.9%, respectively, in comparison with rates of 24.3%, 41.6%, 61%, 64.9%, respectively, in the GC monotherapy arm in the meta-analysis by Mahr,<sup>1</sup> where similar data were available. The median daily prednisone dose at beginning was 50 mg, and decreased to 10 mg at 3 months and to 5 mg at 6 months. The median time required to reduce prednisone to 7.5 mg/day and 5 mg/ was 3 and 5 months respectively (vs. 6.5 and 7.5 months in series by Proven,<sup>2</sup> where similar data were available). In our cohort, lower cumulative GC use was accompanied by a reduction of AEs, without further toxicity (tab.1).

	Present work	Proven 20032	Mahr 20071	Souza 20143	Alba 20144	Labarca 20165
Number of patients	69	120	77	45	106	286
% use of IT	100%	2%	0%	55.6%	14.2%	0%
Follow up, months	40	120	13,7	54,9	93,6	61,2
Fragility fractures	11,6%	38%	8%	NA	NA	27%
Diabetes	4,3%	9%	12%	33,4%	8,5%	NA
Hypertension	8,7%	22%	NA	66,7%	51%	1,7%
Infections	10,1% (2,9% hospitalisation)	31%	NA	23%	NA	17% (all needing hospitalisation)

**Conclusions:** The use of IT ab initio or very early in the treatment of GCA appears to be effective and safe, lowering the risk of relapses, reducing GC dose and the rate of GC-related AEs. Therefore, the present data support the early introduction of IT in the treatment of GCA.

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**Disclosure of Interest:** None declared

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**THU0454 INCREASED FDG UPTAKE OF THE MUSCLES IN POLYMYALGIA RHEUMATICA (PMR)**

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**Background:** PMR is an inflammatory disease affecting the shoulder and pelvic girdles of elderly patients. Its causes, development mechanisms and anatomical targets of inflammatory damage are still elusive. Synovitis, vasculitis, and bursitis have all been demonstrated in PMR but data on muscles are scanty.

**Objectives:** Our study evaluated muscular uptake at FDG-PET/CT in patients with PMR.

**Methods:** Fifty patients with PMR diagnosed according to Bird et al criteria and 50 age- and sex-matched control patients without inflammatory disorders, who underwent FDG-PET/CT to rule out malignancy, were studied. Standard FDG-

PET/CT examination was performed and its results were evaluated by both qualitative scoring, on a 5-grade scale from 0 (no uptake) to 4 (clearly higher than liver uptake), and analysis of the standardised uptake value (SUV max and mean) in a ROI placed on the deltoid, biceps, gluteus and quadriceps muscles. A ROI of the joints and bursae was also designed and the SUV calculated. The muscle ROIs were positioned distant from the corresponding joints to avoid interference from possible articular or periarticular uptake. Demographic, clinical and laboratory data were collected.

**Results:** PMR patients showed an uptake higher than that of controls in the deltoid ( $p=0.0004$ ), gluteus ( $p=0.015$ ), and quadriceps ( $p=0.009$ ), but not in the biceps ( $p=0.06$ ) muscles. The semiquantitative SUV evaluation was consistent for the deltoid (SUV mean,  $p=0.047$ ) and gluteus (SUV mean,  $p=0.01$ ; SUV max,  $p=0.006$ ) muscles. There was no correlation between muscle uptake and that of the adjoining joint. Similarly, no correlation was found between muscle uptake and demographic, clinical and laboratory (CRP, ESR) findings.

**Conclusions:** PMR show muscular inflammation at FDG-PET/CT, which does not derive from the nearby joints or periarticular tissues. A clearly defined myositis is not probable, because creatine kinase concentrations are normal in PMR. However, muscle inflammation may contribute to the global inflammatory burden and symptoms of patients with PMR.

**Disclosure of Interest:** None declared

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#### THU0455 AGE IS MORE CLOSELY ASSOCIATED WITH POSITIVE TEMPORAL ARTERY BIOPSY OVER BIOPSY LENGTH IN LARGE VETERANS ADMINISTRATION DATABASE STUDY

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**Background:** Giant cell arteritis (GCA) is a granulomatous vasculitis with a predilection for older women. While American College of Rheumatology (ACR) diagnostic guidelines exist, temporal artery biopsy (TAB) remains an essential tool often used independently to substantiate long-term steroid use and/or immunosuppression. No consensus exists regarding the ideal length of biopsy to optimise pathological yield. The influence of demographic factors such as age, race, and gender on the yield of biopsies is not defined.

**Objectives:** To determine if length of TAB and patient's race, gender, or age at biopsy influenced TAB results using the Veteran's Administration (VA) national database.

**Methods:** Patients with a procedure code for TAB between 1999–2017 were queried through the VA national database. The biopsy length and result (positive, negative, or indeterminate) were recorded. Demographic information including subject age, gender, and race was also extracted. Logistic regression models were run using Stata to identify independent determinants of a positive TAB.

**Results:** 2136 biopsies have been randomly reviewed to date. The average length of TAB was 12.15 mm. TAB results were 9% positive, 89% negative, and 2% indeterminate. There was no statistically significant association between biopsy length and a positive result; however, when compared to the reference group (>10 mm–<15 mm), the odds ratio for positive results increased with specimen length >20 mm to 30 mm in length. Conversely, there was a trend towards negative biopsy results for samples <10 mm in length when compared to the reference length group. There was no correlation between TAB result and race or gender; however, age correlated with a positive biopsy which was statistically significant. None of the subjects <50 years of age had a positive TAB. Younger age groups (age categories 50–59 and 60–69) were less likely to have a positive TAB (OR of 0.32 CI 0.17–0.61 and OR 0.53 CI 0.38–0.74, respectively) when compared to the reference age group (age 70–79). Conversely, older populations aged 90 and above demonstrated a statistically significant increased likelihood of a positive biopsy result with an OR of 2.25, CI 1.05–4.85.

**Conclusions:** The incidence of positive TAB among patients with suspected temporal arteritis in the VA national database was surprisingly low. The effect of other factors, such as the referring specialty or pre-biopsy steroid use, on TAB result may be insightful in understanding the low yield. Age remains a helpful tool given its association with increased likelihood of a positive biopsy, and the decision to pursue TAB in patients <50 years old should be approached judiciously. Length of biopsy was not associated with a positive result; however, the trends we note suggest a biopsy between 10 mm and 25 mm could optimise the yield. Gender and race were not helpful predictors for biopsy yield in this population.

**Disclosure of Interest:** None declared

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#### THU0456 THE CLINICO-HISTOPATHOLOGICAL ALGORITHM FOR DIFFERENTIAL DIAGNOSIS OF BUERGER'S DISEASE, TAKAYASU ARTERITIS AND ATHEROSCLEROTIC OCCLUSIVE DISEASE

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**Background:** Arterial occlusive disease is a significant cause of the disability due to lower limbs amputations. In addition to atherosclerosis, systemic vasculitides can present with progressive critical limb ischemia and could be misdiagnosed as atherosclerotic occlusive disease.

**Objectives:** To investigate the pathological findings in vessels of the lower limbs amputated due to Takayasu arteritis (TAK), Buerger's disease (BD) in comparison to atherosclerotic occlusive disease (AOD) and diabetic angiopathy (DA). Additionally, to develop an algorithm for clinico-histopathological differential diagnosis.

**Methods:** The specimens of vessels segments were obtained from the nine anatomical levels of amputated lower extremities in 132 patients, of which 30 were with TAK, 42 with BD, 30 with AOD and 30 with DA.

**Results:** In cases of BD, the exudative-productive endo-mesoarteritis with intimal hyperplasia from stenosis to complete obliteration have been found in the lower leg and foot arteries. No morphological abnormalities were observed in proximal arteries above knee. The pathologic hallmark of BD was panphlebitis with intimal hyperplasia, most often in anterior and posterior tibial veins, vena dorsalis pedis and superficial vein. The most remarkable finding in cases of TAK was mesoarteritis and luminal narrowing due to the reactive intimal hyperplasia in proximal arterial segments. In approximately half of the cases, TAK was not diagnosed clinically and identified only based on the pathological examination. The most common incorrect clinical diagnosis was atherosclerotic occlusive disease. In seven cases of TAK, concomitant premature atherosclerosis of varying severity was observed. Interestingly, in our series of cases of TAK, males were most frequently affected. The correct clinical diagnosis of TAK was made in all females' cases. It seems to be a trend to miss the clinical diagnosis of TAK in men. In cases of AOD, pathological examination revealed stenotic atherosclerotic plaques occurred most prominently in the tunica intima of femoral and popliteal arteries. The most common morphologic features in cases of DA were media calcinosis and fibrous lipid plaques both distal and proximal arterial segments. The algorithm for clinico-histopathological differential diagnosis of TAK, BD, AOD and DA consists of the following: a) the best diagnostic performance can be obtained with four-five specimens of the magistral vessels from the proximal and distal parts of the amputated limb and the superficial vein at the level of the upper third of the shin; b) using routine and special staining techniques (H and E, Masson's trichrome stain for collagen fibres, Hart's elastin stain); c) analysis of the demographic and clinical data; d) interpretation of pathologic changes in vessels of the lower limbs; e) making a pathologic diagnosis.

**Conclusions:** The current findings could contribute to the improving the differential diagnosis of Takayasu arteritis, Buerger's disease, atherosclerotic occlusive disease and diabetic angiopathy.

**Disclosure of Interest:** None declared

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#### THU0457 INTERLEUKIN-6 EXPRESSION IN INFLAMED AND NON-INFLAMED TEMPORAL ARTERIES FROM PATIENTS WITH GIANT CELL ARTERITIS

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**Objectives:** To evaluate if interleukin-6 (IL-6) expression in the temporal artery biopsy (TAB) specimens may differentiate patients with giant cell arteritis (GCA) from those without.

**Methods:** 63 consecutive formalin-fixed, paraffin-embedded (FFPE) TABs performed between 2009 and 2012 from 32 patients with transmural biopsy-proven GCA, 8 patients with biopsy-negative GCA and 23 controls were retrieved. Demographic, clinical, and laboratory data at presentation and at each follow-up visit were collected. A pathologist reviewed all TABs. Immunohistochemistry was performed on 4 µm FFPE tissue sections with a 1:400 dilution of rabbit polyclonal anti-human IL-6 antibody (NOVUS Biologicals Littleton, Co.) for 60' at 37°. Slides of TAB specimens were independently assessed by five readers. IL-6 expression was graded as 0 (absent), 1 (mild), 2 (moderate) and 3 (marked). Inter-reader differences were resolved by consensus. Anti-IL6 staining was considered positive if staining was grade 2 or 3, since grade 1 was faint, sometimes difficult to differentiate from background, and showed the least degree of agreement between readers.

**Results:** TAB specimens from patients with biopsy-proven GCA, biopsy-negative GCA and controls were positive for anti-IL-6 staining in 59%, 13% and 48% of cases, respectively, the difference between biopsy-proven and biopsy-negative GCA patients being significant ( $p=0.04$ ). In non-inflamed TABs, IL-6 was mainly expressed by mesenchymal cells in media and intima layers, while in inflamed TABs IL-6 was mainly expressed by mononuclear inflammatory infiltrating cells. IL-6 grade 2–3 expression was observed in all 6 patients with visual loss compared to 25 (43.9%) of 57 patients without ( $p=0.011$ ). Blindness was recorded in 2 patients with biopsy-proven GCA and 4 controls (all with a final diagnosis of non-arteritic ischaemic optic neuropathy). No associations were found between IL-6 expression and demographic characteristics, GCA signs/symptoms, laboratory and histopathological TAB findings. However, there was a statistical trend ( $p=0.055$ ) of increased frequency of the halo sign at temporal artery CDS in patients with IL-6 expression grade 2–3 compared to those with IL-6 expression grade 0–1. No significant differences for the expression of IL-6 were observed between patients with and without PMR (5/8%–62.5% - versus 6/15%–40% -,  $p=0.400$ ) and between patients with isolated PMR and those with TAB positive GCA (62.5% vs 59%,  $p=1.000$ ).

**Conclusions:** Our study provides evidence that IL-6 expression does not increase the sensitivity of TAB in patients with morphologically uninfamed arteries. A search for further markers that may increase the sensitivity of TAB is warranted.

**Disclosure of Interest:** None declared

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**THU0458 INVESTIGATION OF THE ROLE OF M-TOR PATHWAY IN KIDNEY NEEDLE BIOPSIES OF PATIENTS WITH ANTINEUTROPHIL CYTOPLASMIC AUTOANTIBODY-ASSOCIATED VASCULITIS**

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**Background:** Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) frequently affect the kidneys and renal involvement is an important factor regarding morbidity and mortality. Kidney lesion in AAV is characterised by necrotizing and crescentic glomerulonephritis by little or no immune deposition, and hence it was called pauci-immune glomerulonephritis (PIGN). The underlying mechanisms in the formation or progression of crescent formation need further investigations. Mammalian target of rapamycin (mTOR) is a serine/threonine kinase and plays role in the regulation of cell growth and proliferation.

**Objectives:** We aimed to evaluate the role of mTOR, which might be a potential therapeutic target, in kidney biopsies of patients with AAV.

**Methods:** The patients diagnosed as PIGN at an outpatient nephrology clinics of a tertiary hospital, between May 2009 and June 2016, were retrospectively reviewed and those patients who had a renal biopsy before receiving an immunosuppressive treatment were included in the study. Renal biopsy specimens were immunohistochemically stained with antibodies of mTOR, phosphatase and tensin homolog (PTEN) and transforming growth factor- $\beta$  (TGF- $\beta$ ) and scored by an experienced renal pathologist.

**Results:** In total 54 patients with AAV (52% female) were included in the study. Twenty-five (46%) patients were diagnosed as granulomatosis with polyangiitis, 6 (11%) patients as microscopic polyangiitis, 16 (30%) patients as renal-limited disease, one (2%) patient as eosinophilic granulomatosis with polyangiitis. Six (11%) patients with PIGN could not be classified definitely. According to the histopathologic examination; 22% of the biopsies were classified as focal, 33% crescentic, 22% mixed and 22% as sclerotic. The mTOR was expressed in substantial percentages of glomeruli of patients with PIGN. However we observed PTEN expression in all samples and mTOR in all tubulointerstitial areas. mTOR expression was found to be related with the presence of crescentic and sclerotic changes observed in glomeruli and the degree of fibrosis in interstitial areas. In our study serum creatinine level or response to treatment were not found to be associated with mTOR pathway expression

**Conclusions:** Our study showed that glomerular or interstitial expression of PI3K/Akt/mTOR pathway may play a role in the pathogenesis of PIGN and mTORC1 inhibitors might provide a viable alternative for this disease.

**Disclosure of Interest:** None declared

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**THU0459 SURVIVAL OF BIOPSY PROVEN GIANT CELL ARTERITIS IN NORTHERN ITALY: CORRELATION WITH CLINICAL, LABORATORY AND HISTOPATHOLOGICAL FINDINGS**

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**Objectives:** To correlate survival with clinical, laboratory and histopathological findings in a population based cohort of patients with biopsy-proven giant cell arteritis (GCA) living in the Reggio Emilia area during a 26 years period.

**Methods:** In this population-based study, all patients living in the Reggio Emilia area who underwent temporal artery biopsy (TAB) for suspected GCA from January 1, 1986 to December 31, 2012 were identified. A pathologist with expertise in vasculitis and blinded to clinical data and final diagnosis reviewed all TABs. Based on the localization of the inflammation, positive TABs were classified into 4 categories: small vessel vasculitis (SVV), with inflammation limited to small periadventitial vessels devoid of muscular coat; vasa vasorum vasculitis (VVV), with inflammation surrounding the adventitial vasa vasorum; inflammation limited to adventitia (ILA), with inflammation spreading from vasa vasorum to the adventitia without extension to the media; transmural inflammation (TMI), with external elastic lamina disruption and extension of the inflammation to the media. Histopathologic features evaluated were: the severity of inflammation and intimal hyperplasia, both graded on a semiquantitative scale (mild=1, moderate=2 severe=3), the presence of intraluminal acute thrombosis, calcifications, giant cells, fibrinoid necrosis and laminar necrosis. Information about clinical manifestations, laboratory findings, treatment and disease course were collected. Patients were followed from GCA diagnosis to death, migration or December 2013.

**Results:** 281 patients (206 female, 73.3%) with biopsy-proven GCA were identified in the study period. 120 patients (84 female, 70%) died during a median follow-up period of 96 (IQR 55, 143) months. At univariate analysis, the presence of polymyalgia rheumatica (PMR) (HR 0.54, 95% CI 0.37–0.79,  $p=0.002$ ), higher level of haemoglobin (HR 0.84, 95% CI 0.74–0.96,  $p=0.011$ ) at disease onset, long-term remission (HR 0.47, 95% CI 0.26–0.86,  $p=0.015$ ) and ILA or VVV at TAB (HR 0.48, 95% CI 0.24–0.97,  $p=0.041$ ) were associated with lower mortality, while the evidence of large vessel involvement at imaging studies performed at diagnosis was associated with increased mortality (HR 5.84, 95% CI 1.57–21.8,  $p=0.009$ ). Multivariate analysis confirmed the association between lower mortality and PMR (HR 0.54, 95% CI 0.36–0.81,  $p=0.003$ ), higher level of haemoglobin (HR 0.83, 95% CI 0.69–0.99,  $p=0.049$ ) at disease onset, and ILA or VVV at TAB (HR 0.38, 95% CI 0.17–0.82,  $p=0.014$ ), and between increased mortality and large vessel involvement at imaging studies performed at diagnosis (HR 5.31, 95% CI 1.39–20.26,  $p=0.014$ ).

**Conclusions:** PMR at diagnosis and only adventitial inflammation at TAB seem to identify subsets of biopsy-proven GCA patients with more benign disease, while large vessel involvement at diagnosis a subset with reduced survival.

**Disclosure of Interest:** None declared

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**THU0460 FULLY INTEGRATED 18F-FDG PET/MR IN LARGE VESSEL VASCULITIS**

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**Background:** Positron emission tomography (PET) is a non-invasive imaging method that detects <sup>18</sup>F-fluorodeoxyglucose (FDG) uptake in vessel's walls. Its simultaneous combination with magnetic resonance (MR) would offer not only a more detailed morphological analysis of the vessels but also a reduction of the radiation, simplifying the clinical workflow and being logistically easier for the patient.

**Objectives:** To evaluate, for the first time up to now, the usefulness of a fully integrated 18F-FDG PET/MR in a series of large vessels vasculitides (LVV) patients.

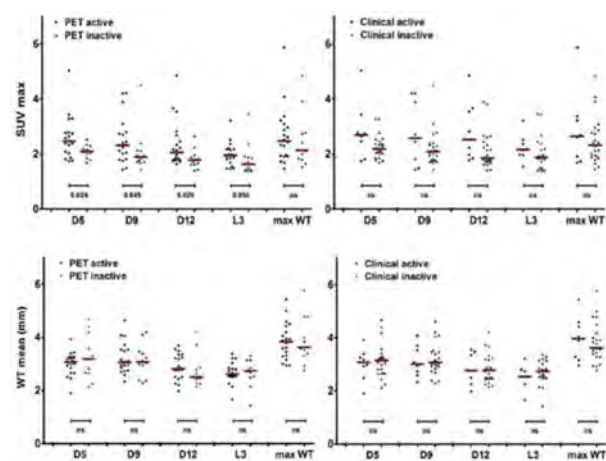
**Methods:** We performed a controlled non-randomised prospective study. Images were acquired on a fully integrated PET/MR scanner (Siemens Biograph mMR), consisting in a complete MR protocol and FDG-PET whole body imaging. We evaluated vessel's standard uptake value (SUV) maximum and wall thickness (WT), defined as the mean of 4 measures (at 12, 3, 6 and 9 o'clock) at the inferior margin of D5, D9, D12, L3 and at thickest point (max WT).



	All (n 23)	GCA (n 13)	TAK (n 8)	p
Female, n (%)	19 (82.6)	12 (92.3)	6 (75)	ns
Age at diagnosis	63 (51–68)	68 (63–73)	43.5 (30.5–57)	0.003
Diagnostic latency (months)	4.5 (2–12)	3 (2–10)	8 (3.5–12)	ns
ESR at disease onset (mm/h)	49 (38–68)	52.5 (45.5–59.7)	42 (40–61.5)	ns
CRP at disease onset (mg/L)	61.8 (13–132.5)	89 (32.5–106)	60.5 (9.3–132.5)	ns
Disease duration at PET/MR (months)	27 (18–36)	24 (13–29.5)	36.5 (14.75–129.3)	ns
ESR at examination (mm/h)	18 (9–35)	16 (7–31)	20.5 (11–44.5)	ns
CRP at examination (mg/L)	4.5 (2.55–8.9)	3.9 (3.48–4.72)	4.55 (2.05–10.4)	ns

**Results:** 23 LVV patients were included, 56.5% GCA, 34.8% TAK and 8.7% isolated aortitis, all Caucasian, mostly females (82%). We considered 55 PET scans, 32/55 in LVV group (from min. 1 to max. 3 scans/patient) mainly during follow-up (29/32 scans), and 23/55 in control group. Considering patients with abdominal aorta involvement, we found higher SUV max compared to controls, in all sites, regardless of disease activity. Mean WT resulted higher in patients than controls, but did not significantly differ between PET active or inactive patients (figure 1). Mean WT positively correlated with age in both cohorts, inversely correlated to disease duration in LVV patients, while no correlation with SUV max was observed. Despite clinical assessment was suggestive of remission in 24 (75%) cases before PET/MR acquisition, a normal uptake was present only in 12 (50%) of them. On the contrary, all patient with active disease at clinical examination (8, 25%) had also a positive PET/MR. Cohen's K coefficient between clinical assessment and imaging was poor (K Cohen=0, 33, 0.11–0.55). Finally, we found no significant correlation between SUV max and acute phase reactants.

Demographic and clinical data of LVV patients.



**Conclusions:** PET/MR is a safe imaging technique capable of detecting vasculitic inflammation, similar to PET/CT, but with a greater anatomical definition. The low radiological exposure represents a valid alternative to PET/CT for disease monitoring, especially in young women.

**Disclosure of Interest:** None declared

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THU0461

#### COMPARISON BETWEEN CLINICAL PROFILE AND OUTCOME OF PATIENTS WITH JUVENILE ONSET AND ADULT ONSET TAKAYASU ARTERITIS

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**Background:** There is a paucity of data comparing juvenile onset Takayasu arteritis (jTA) and adult onset TA (aTA).

**Objectives:** We aimed to compare differences in clinical profile and outcome of patients with jTA and aTA attending our centre during 1998–2017.

**Methods:** Details of demography, clinical presentation, laboratory results, angiography and treatment response were collected prospectively for 252 and retrospectively for the rest of patients with TA. Disease activity was defined by Indian Takayasu Activity Score- A (ITAS-A)(CRP).<sup>1</sup> Complete remission (CR) was defined as ITAS-A=0 with no angiographic progression. Patients with onset of disease at ≤16 years of age were classified as jTA while the rest as aTA.

**Results:** Among 602 patients with TA during this period, 119 (19.8%) were jTA, while 483 were aTA. Female predominance was less striking in jTA (71.4%) than aTA (79%), p=0.047. Patients with jTA had presented more commonly with fever (29% vs 17.4%, p=0.002), headache (31% vs 18%, p=0.002), pain abdomen (11% vs 5.6%, p=0.031), systolic hypertension (66.4% vs 48.4%, p<0.001), cardiomyopathy (15.1% vs 5.4%, p<0.001) and raised creatinine (16% vs 4.7%, p<0.001) while claudication as presenting symptom was less common in jTA (39%) as compared to aTA (55%), p=0.003. Pulse abnormality tended to be commoner in aTA. Angiographically, type-I disease (5.1% vs 22.6%, p<0.001) and coronary involvement (8.3% vs 20.6%, p=0.016) was less common while type-IV disease occurred more frequently (25% vs 14.3%, p=0.004) in jTA than in aTA. Logistic regression showed similar results after adjustment for gender. Median ITAS<sup>2010</sup> score was higher in jTA [7 (2–14)] than aTA [5 (2–11)].

Follow up was available for 77 and 287 patients with jTA and aTA respectively. Median follow up duration was 32<sup>10–61</sup> months for jTA and 27<sup>10–59</sup> months for aTA. CR was attained more frequently in jTA (n=67; 87%) than aTA (n=190; 66.2%), p=0.001. Another, 7 (9%) and 55 (19.2%) of patients with jTA and aTA respectively achieved partial response with immunosuppression. Among patients with initial CR, relapse of active disease during further follow up was observed more frequently in jTA [n=20, (29.9%)] as compared to aTA [n=50, (26.6%)], p=0.029. Altogether, persistently stable disease course was more common in jTA (62.3%) than aTA (47.5%), p=0.029.

**Conclusions:** In our large cohort of TA treated with uniform immunosuppression protocol, systemic features, hypertension, cardiomyopathy, renal dysfunction and type IV disease are more commonly observed in jTA while claudication, pulse abnormality, coronary involvement and type I disease are more frequent in aTA. Patients with jTA respond better to immunosuppression but relapse more frequently than aTA. Persistent stable disease course is commoner in jTA patients.

#### REFERENCE:

- [1] Ruchika Goel, Debashish Danda, et al. Long term outcome of 251 patients with Takayasu Arteritis on combination immunosuppressant therapy: single centre experience from a large tertiary care teaching hospital in southern India. *Seminars in Arthritis and Rheumatism*, <http://dx.doi.org/10.1016/j.semarthrit.2017.09.014>

**Disclosure of Interest:** None declared

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THU0462

#### LONG TERM FOLLOW-UP RESULTS OF TAKAYASU ARTERITIS COHORT: A TERTIARY-SINGLE CENTRE STUDY

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**Objectives:** To assess the clinical characteristics and long term follow-up outcomes of patients with Takayasu's arteritis (TAK) in a tertiary referral centre.

**Methods:** In this retrospective study, 107 (F/M: 96/11) patients fulfilling ACR<sup>1990</sup> criteria for Takayasu Arteritis and referred to our centre between 2004 and 2017 were investigated. All clinical and demographic data during first diagnosis and longitudinal follow-up were abstracted from medical records. Relapse was defined according to the physician's global assessment (PGA).

**Results:** The median age was 30<sup>14–67</sup> years at symptom onset and 33<sup>14–68</sup> years at diagnosis. Median follow-up duration was 72 (6–264) months. According to Hata Angiographic Classification, Type 5 (51.8%) and Type 1 (38.8%) were the most common patterns with the most frequently affected vessel subclavian artery (82.2%). At diagnosis 0.5–1 mg/kg/day corticosteroid treatment was started in 94.6% patients and a steroid-sparing immunosuppressive (IS) agent in 96.3% of the patients. An initial pulse steroid (1 g/day) therapy was chosen for 8 patients. Before diagnosis 24% patients had a history of a revascularisation procedure. After IS treatments, 24% of the patients were undergone a new revascularisation procedure. During follow-up, biologic agents were chosen for 13.8% of the

patients (5 infliximab and certolizumab each, 2 adalimumab and 2 tocilizumab). Remission was observed in 84% of the patients. At least one relapse was occurred in 43% and >1 relapse in 14 patients. At the last visit 26% were determined to have an active disease. A >4 mg of methylprednisolone dose was required in only 8.4%. Mortality rate was 3.7% (4 patients).

Table 1 Clinical characteristics and outcomes of patients

Gender (F)	96 (89.8%)
Takayasu Arteritis Type	
1	42 (38.8%)
2	8 (7.4%)
3	0 (0%)
4	2 (1.8%)
5	51 (47.8%)
Age at symptom onset	39 (14.4)
Age at diagnosis	39 (14.4)
Time for diagnosis delay (months)	12 (0-130)
Follow-up time (months)	72 (6-264)
Cardiovascular risk factors (Baseline)	
Hypertension	41 (38.3)
Diabetes	6 (5.6)
Dyslipidemia	25 (23.4)
Coronary artery disease	15 (14.1)
Congestive heart failure	4 (3.7%)
peripheral artery disease	13 (12.1%)
Stroke	10 (9.3%)
Smoking	
Current	30 (28%)
Former	6 (5.6%)
Family history of atherosclerosis	28 (26.2%)
Laboratory findings (Baseline)	
ESR (mm/h)	45.8±27.9
CRP (mg/L)	18.3±22.6
Treatment at last visit n (%)	
Immunosuppressives	100 (95.4%)
Methotrexate	16 (15%)
Azathioprine	49 (45.8)
Leflunomide	20 (18.7%)
Infliximab	2 (1.9%)
Adalimumab	1 (0.9%)
Certolizumab	3 (2.8%)
Tocilizumab	2 (1.8%)
Certolizumab + Azathioprine	1 (0.9%)
Certolizumab + methotrexate	1 (0.9%)
Infliximab + azathioprine	3 (2.8%)
Adalimumab + Leflunomide	1 (0.9%)
Glucocorticoids*	51 (47.7%)
≤ 4 mg	42 (39.2%)
> 4 mg	9 (8.4%)
Cumulative glucocorticoid dose (g)	7.3 (0-31.9)
Damage Scores	
VDI**	5.6±2.3
TADS***	8.3±3.1

\*methylprednisolone \*\* Visualized Damage Index \*\*\* Takayasu arteritis damage score

**Conclusions:** We have defined the long-term follow-up results of our Takayasu's arteritis cohort. Comparing with European and Asia series published recently, requirement for a surgical intervention was lower under immunosuppressive treatments in our series. However, disease activity and relapse rate were still high under conventional ISS, suggesting a need for better therapeutic options.

**Disclosure of Interest:** None declared

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#### THU0463 COMPLEMENT FACTORS OF THE ALTERNATIVE PATHWAY IN GPA AND MPA

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**Background:** In antineutrophil cytoplasm autoantibody (ANCA)-associated vasculitis (AAV), involvement of complements, especially alternative pathway of complement, has been reported in researches using mouse models. In human, while some studies have identified levels of C3 as a renal prognostic factor, entire complement factors in alternative pathway have not been evaluated.

**Objectives:** To evaluate complement profiles of AAV patients at diagnosis and at 6 months after treatments (Month 6).

**Methods:** In total, 91 incident cases of granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA) based on the European Medicines Agency algorithm were enrolled. They are a part of participants of the Japanese nationwide, prospective, inception cohort study from 22 tertiary Japanese institutions (RemIT-JAV-RPGN). Multiplex complement bead assays to measure levels of C1q, C2, C3, C3b/iC3b, C4, C4b, C5, C5a, C9, Factor D, Factor I, MBL, factor B, factor H, and properdin were performed using preserved sera at diagnosis and at Month 6. We compared complement levels at diagnosis of AAV patients with those of age- and sex-matched healthy donors, and compared those of the AAV patients at diagnosis and Month 6.

**Results:** Seventy-two of 91 patients had serum both at baseline and Month 6. Compared with healthy donors, GPA patients had significantly higher levels of C2, C5a, and Factor B, and significantly lower levels of C3b/iC3b, C4b, and properdin. MPA patients had significantly higher levels of C2 and Factor D, and significantly

lower levels of C3b/iC3b, C4, C5, Factor H, and properdin (table 1). At baseline, GPA had significantly higher levels of C4, Factor B and Factor H, and had significantly lower levels of C4b and Factor D compared to MPA. There are no significant differences in levels of C3, C5, Factor D, MBL, and properdin using Wilcoxon signed-rank test between at diagnosis and Month 6 both in GPA and MPA. Factor I significantly decreased at Month 6 only in GPA. Other complement factors significantly decreased at Month 6 both in GPA and MPA.

**Abstract THU0463 – Table 1.** Complement profiles of patients with AAV at baseline and healthy donors

	GPA (median)	MPA (median)	HD (median)	GPA vs. MPA	GPA vs. HD	MPA vs. HD
C1q, ng/mL	1 04 220	96 890	1 08 242	N.S.	N.S.	N.S.
C2, ng/mL	50 181	54 422	18 610	N.S.	p<0.05	p<0.05
C3, ng/mL	1265500	1371550	1416900	N.S.	N.S.	N.S.
C3b/iC3b, ng/ mL	10433000	11066000	17364500	N.S.	p<0.05	p<0.05
C4, pg/mL	3 10 020	2 66 554	3 08 085	p<0.05	N.S.	p<0.05
C4b, ng/mL	18 064	27 740	31 287	p<0.05	p<0.05	N.S.
C5, ng/mL	30 014	27 805	32 015	N.S.	N.S.	p<0.05
C5a, pg/mL	7783	6592	4836	N.S.	p<0.05	N.S.
C9, ng/mL	6934	5905	6742	N.S.	N.S.	N.S.
Factor D, ng/ mL	5335	7706	5658	p<0.05	N.S.	p<0.05
Factor I, ng/ mL	29 917	25 633	25 653	N.S.	N.S.	N.S.
MBL, ng/mL	3583	3638	3023	N.S.	N.S.	N.S.
Factor B, ng/ mL	2 54 961	1 80 045	2 12 153	p<0.05	p<0.05	N.S.
Factor H, ng/ mL	2 58 187	2 28 238	2 95 480	p<0.05	N.S.	p<0.05
Properdin, ng/mL	18 794	19 665	32 521	N.S.	p<0.05	p<0.05

GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis; HD, healthy donor.

**Conclusions:** We found some differences in complement factors among GPA, MPA, and healthy donors. There were no differences of levels of C3, C5, Factor D, and properdin, which suggested involvements of alternative pathway, both in GPA and MPA between at diagnosis and Month 6.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.3384

#### THU0464 INCREASED FREQUENCY OF OBSTRUCTIVE SLEEP APNEA SYNDROME IN BEHÇET'S SYNDROME PATIENTS WITH VENA CAVA SUPERIOR THROMBOSIS

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**Background:** Superior vena cava syndrome (SVCS), is a medical emergency and can also be seen in Behçet's syndrome (BS). Contrary to the severe outcome seen in malign conditions, SVCS in BS usually has a benign course, complicated rarely by hemoptysis, pleural effusion, and a chylothorax. We had noted that BS patients with SVCS frequently complained of sleep disturbances, snoring and sleep apnea, suggesting an obstructive sleep apnea (OSA) disorder.

**Objectives:** We formally surveyed the degree of risk for OSA among BS patients with SVCS and suitable controls using the Berlin questionnaire, a screening questionnaire for OSA with a high sensitivity and modest specificity.<sup>1</sup>

**Methods:** Because of the lower frequency of female patients with VCSS (n=2), only males were included. We studied 28 BS patients with SVCS (Group 1), 80 BS patients with vascular involvement without a SVCS (Group 2), and 59 BS patients with no vascular involvement (Group 3). Also, 80 apparently healthy individuals (Group 4) of similar age and gender to BS patients were studied. Polysomnography was performed in patients at high risk for OSA according to the Berlin questionnaire.

**Results:** There were no differences regarding demographic characteristics, disease duration, and variables associated with OSA among the groups (table 1). The Berlin questionnaire categorised 57.1% (16/28) of the BS patients with SVCS (Group 1) as having a high risk for OSA and this was significantly higher compared to that found in the control groups. The frequency of those at high risk for OSA was 15%, 8.5%, 11.3% in Group 2, 3 and 4, respectively (p>0.05). Until now, polysomnography was performed in 12 subjects (5 patients with SVCS, 1 patient with vascular involvement without a SVCS and 6 healthy controls). OSA was detected

in 3/5 patients with SVCS and 1/1 patient with vascular involvement without a SVCS and 4/6 healthy controls.

**Abstract THU0464 – Table 1.** Demographic characteristics and variables associated with obstructive sleep apnea

	Group 1 (BS patients with SVCS) (n=28)	Group 2 (BS patients with vascular involvement without SVCS) (n=80)	Group 3 (BS patients with no vascular involvement) (n=59)	Group 4 (Healthy controls) (n=80)	<i>p</i> value
Age, mean ±SD, years	44.3±9.7	42.1±7.8	41.9±5.9	42.7±9.7	0.051
Disease duration, mean±SD, years	18.7±9.4	14.6±7.7	12.5±6.5		<b>0.001</b>
Hypertension, n (%)	4 (14.3)	6 (7.5)	2 (3.4)	4 (5)	NS
BMI, mean ±SD	26.8±4.7	26.4±3.9	26.2±3.3	27.0±3.5	NS
High risk for OSA, n (%)	16 (57.1)	12 (15)	5 (8.5)	9 (11.3)	<0001

**Conclusions:** This study shows that BS patients with a history of VCSS are at high risk of OSA. This is probably due to the external pressure of the significant venous collaterals on the upper airways.

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**Disclosure of Interest:** None declared

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#### THU0465 A LONGITUDINAL STUDY OF NEUTROPHIL PHENOTYPE CHANGES IN GIANT CELL ARTERITIS

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**Background:** Neutrophils with differential surface protein expression were recently implicated in pathogenesis of Giant Cell Arteritis (GCA)<sup>1</sup>. However, data are lacking with regard to treatment-naïve GCA and their long-term follow-up.

**Objectives:** To determine the expression of I-selectin (CD62L) and integrin  $\alpha$ M (CD11b) on CD16<sup>+</sup> neutrophils in peripheral blood of newly diagnosed, treatment-naïve GCA cases, at the time of diagnosis (time 0) and during follow-up - at week 1, 4, 12, 24 and 48. In parallel, we aimed to measure also sera levels of serum amyloid A (SAA) and interleukin-6 (IL-6).

**Methods:** Peripheral blood from 33 treatment-naïve GCA patients and 16 healthy blood donors (HBD) was stained, lysed, fixed and analysed by flow cytometry (Miltenyi). SAA and IL-6 were measured by nephelometry and ELISA, respectively. 3/33 GCA patients experienced relapse and were analysed separately during follow-up, at the time of relapse and 12 weeks after relapse. At the time of diagnosis, all patients received steroid treatment and therapy tapering started after 4 weeks. At week 12, some of the patients (14/22) received leflunomide, in addition to steroid therapy.

**Results:** Expression of CD62L, but not CD11b, was significantly higher on CD16<sup>+</sup> neutrophils in treatment-naïve GCA patients (median; IQR: 72.5; 56.2–100.7), as compared to HBD (55.9; 44.5–70.6,  $p=0.017$ ). Longitudinally, the expression of CD62L significantly decreased in GCA patients from day 0 to week 4 ( $p=0.005$ ). At week 12 there was an elevation in CD62L which escalated also at week 24. Patients receiving steroids only showed a marked increase at week 48, while patients receiving also leflunomide exhibited a decrease (Fig 1). Expression of CD11b declined from day 0 to week 4, but substantially increased throughout week 12, 24 and 48, regardless of therapy used. SAA and IL-6 declined sharply from day 0 to week 1 and 4, with gradual elevation of both at week 12. There was a decline in SAA levels observed in all patients at week 24, while IL-6 increased in patients receiving only steroids. These patients exhibited further elevation of both markers at week 48, while patients receiving steroids, in combination with leflunomide, showed a decrease. In 2/3 patients who experienced a relapse, we could observe an increase in the expression of CD62L at the time of relapse, which was found to be decreased again 12 weeks later. A similar trend was observed for IL-6.

**Conclusions:** Neutrophil CD62L could represent a good surface marker for detection of relapse in GCA. A distinct dichotomy was found for CD62L, as well as SAA and IL-6 in GCA during long term follow-up, with the combination of steroids with leflunomide showing more optimal results.

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#### THU0466 SEXUAL DYSFUNCTION AND DEPRESSION IN BEHCET'S DISEASE – ARE THERE DIFFERENCES REGARDING PATIENT'S ORIGIN

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**Background:** Behcet's disease (BD) is a systemic vasculitis of veins and arteries characterised by oral and genital ulcers (aphthae), skin lesions and uveitis. BD is more common in Middle Eastern countries and Asia but also occurs in Caucasian people.

**Objectives:** Aim of this study was to evaluate the prevalence of sexual dysfunction (SD) in patients with BD as well as analysing differences between patients from different origins. Additionally we investigated the prevalence of depression in both ethnic groups.

**Methods:** This prospective, monocentric study included 106 patients with BD. The International Index of Erectile Function (IIEF) and the Female Sexual Function Index (FSFI) were used for assessing sexual dysfunction and the Beck Depression Inventory (BDI) was used for depression assessment.

**Results:** The mean age of our group was 40.5 years. Half of the patients had Middle Eastern and half Caucasian origin. SD was found in 24.5% of all subjects. Only 6.9% of the male patient's group showed signs of SD, while half of the women's group was suffering from SD ( $p<0.001$ ). The prevalence for SD was significantly higher in women with Middle Eastern origin compared to women with Caucasian origin (75% vs. 33.3%,  $p=0.024$ ). Genital ulcers affected 73.6% of all patients. Depression was found in 36.7% of all subjects. Both SD and depression correlated positively in males ( $p=0.017$ ) and females ( $p=0.013$ ).

**Conclusions:** SD and depression are very common problems in BD and should be addressed by the treating physician. Both manifestations are intensifying each other.

**Disclosure of Interest:** None declared

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#### THU0467 EFFICACY AND PATENCY OF REVASCULARISATION IN PATIENTS WITH THROMBOANGIITIS OBLITERANS (BUERGER'S DISEASE)

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**Background:** The cornerstone of therapy in thromboangiitis obliterans (TAO) is complete abstinence from tobacco. In addition to discontinuation of cigarette smoking, very few pharmacological and surgical options of controversial efficacy are available to date. TAO is associated with a high amputation rate because of tobacco continuation, medical therapy failure, and desert foot with no revascularisation option. Endovascular or bypass revascularisation patency and efficacy are poorly described in the literature.

**Objectives:** To describe the results of the French National Reference Centre on TAO on revascularisation modalities, their patency and efficacy.

**Methods:** Among the 198 patients followed in our centre, we retrieved data from 19 patients for who a revascularisation procedure has been attempted. Patency was assessed on angioCT scan and Duplex ultrasounds performed during follow-up. Efficacy was assessed according to clinicians in charge of the patient, and if



an amputation had been performed or not despite a primary successful procedure.

**Results:** In this cohort of 19 patients, 16 were male (84%), all were tobacco active users, and 21% cannabis users. Median follow-up was 19.9 months [11.0–36.9]. Iloprost infusion had been tested for 84.2% of the patients before revascularisation, and 63.2% had a dihydropyridine, 73.3% a statin and 100% at least aspirin. Endovascular procedure was exclusive for 14 patients, and bypass surgery for 1 patient. Four patients had combined procedures. Globally, 44 procedures including 7 bypasses (15.9%) and 37 endovascular surgeries (84.1%), due to multiple procedures for some patients. Primary patency of endovascular procedures was 89.4% and their patency duration was  $221 \pm 173$  days. For bypass surgery, the patency duration was higher  $827 \pm 408$  days ( $p=0.273$ ). Looking at the territory, aorto-iliac revascularizations gave better results on long term 1830 days followed by upper limb  $751 \pm 402$  days, femoro-popliteal procedures  $347 \pm 196$  days and finally infra-popliteal ones with  $178 \pm 134$  days.

Stability or improvement was observed after 52.3% of the revascularizations. Among the failures, 21.2% were associated with a minor amputation, and 11.3% with a major amputation. No predicting factors of failure could have been determined.

**Conclusions:** We report the largest series of revascularization in TAO. As expected, proximal artery revascularisation of lower limbs were associated with a higher and a longer patency rate than femoro-popliteal procedures and even more than infra-popliteal revascularisations. Surprisingly, upper limb revascularisation had a better outcome than for lower limbs. Efficacy of revascularizations are difficult to assess because such procedures are often proposed as a salvage option. However, it is worth to note that more than 50% of the patients had a benefit from the revascularisation.

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#### THU0468 SERUM ANGIOGENESIS BIOMARKERS PREDICT DISEASE OUTCOME IN GIANT CELL ARTERITIS

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**Background:** Giant cell arteritis (GCA) is characterised by inflammation of the medium and large vessels. Two forms of GCA are described, C(cranial)-GCA and LV(large vessel)-GCA, which can be present either separately or co-exist in a patient. Clinical features, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels are used for disease diagnosis and monitoring, but are not disease specific. Relapses are common during and after treatment, therefore new biomarkers are needed for diagnosis and disease course prediction.

**Objectives:** As the majority of infiltrating cells in the vessels of GCA patients are macrophages the aim of this project was to identify and compare levels of macrophage products in the serum of GCA patients as potential biomarkers.

**Methods:** Forty-one newly diagnosed GCA patients (temporal artery biopsy proven C-GCA and FDG-PET scan-positive LV-GCA) were recruited before start of glucocorticoids. Disease course was monitored and time to glucocorticoid treatment free remission was documented. Thirty age- and sex matched healthy controls (HCs) and 13 infection controls (bladder or lung infection) were also included. Serum concentrations of interleukin (IL)-6, serum amyloid A (SAA), soluble CD163 (sCD163), calprotectin, YKL-40 (human cartilage glycoprotein-39), vascular endothelial growth factor (VEGF), and angiopoietin-1 and 2 were determined by ELISA or Luminex assay.

**Results:** IL-6, SAA, sCD163, calprotectin, YKL-40, VEGF and angiopoietin-2 levels are increased in GCA and infection controls compared to HCs. IL-6 levels correlated strongly with CRP, ESR and SAA, all markers of the Acute Phase Response (APR), in GCA. Interestingly, YKL-40, angiopoietin-2 and calprotectin levels showed only weak or no correlation with APR biomarkers, while they were strongly correlated with the APR in infection controls. Monocytes in peripheral blood correlated with APR biomarkers in GCA, whereas neutrophils correlated with the APR in infection controls. Patients with overlapping C-GCA and LV-GCA displayed a significantly stronger APR than patients with C-GCA or LV-GCA alone. High VEGF and angiopoietin-1, but low angiopoietin-2 levels at baseline predicted a shorter time to treatment free remission. This is in contrast to markers of the APR, which did not significantly predict time to treatment free remission.

**Conclusions:** In this study, we show that markers of angiogenesis are better predictors of disease outcome than APR biomarkers. It appears that levels of calprotectin, YKL40 and angiopoietin-2 are increased through other than APR pathways during GCA compared to acute infection. Monocytes rather than neutrophils appear to drive the APR in GCA. This response is stronger in GCA patients with both cranial and systemic symptoms.

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THURSDAY, 14 JUNE 2018

## Osteoporosis

#### THU0469 QUANTIFYING THE TREATMENT WITH GLUCOCORTICOID AS A RISK FACTOR FOR THE OCCURRENCE OF OSTEOPOROSIS AND FRACTURES IN PATIENTS WITH RA

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**Background:** Rheumatoid arthritis (RA) is associated with increased systemic bone loss, leading to a high risk for fragility fractures. The etiology of increased fracture risk in RA is multifactorial and comprises next to general risk factors also RA-specific risks, most prominently chronic inflammation, seropositivity and glucocorticoid (GC) use<sup>1</sup>. Yet, there is evidence that GCs may, by adequately suppressing systemic inflammation, also have a positive effect on BMD and fracture risk in RA<sup>2</sup>.

**Objectives:** The purpose of this study was to investigate the prevalence of osteoporosis and fragility fractures in RA patients and to characterise, among other risk factors, the role of GC dose, cumulative dose (GCCD) and duration as well DMARD treatment on bone health.

**Methods:** Rh-GIOP is an ongoing prospective observational study collecting and analysing disease- and bone-related data from patients with chronic rheumatic diseases treated with GCs. In this cross-sectional analysis, we evaluated the initial visit of 238 patients with RA. Descriptive analyses were performed, with values displayed as mean/standard deviation and median/range for continuous variables. For subgroup analyses, non-parametric tests were used.

**Results:** Of 238 patients with RA (79.4% women, mean age:  $63.6 \pm 12.5$  years), 155 were seropositive and 83 seronegative. Seronegative patients were numerically older ( $66.8 \pm 12.1$  vs  $61.8 \pm 12.1$  years) and more often in menopause (78.3% vs 61.8%, ns) than seropositive, while the latter had longer disease duration (median:  $4.0 \pm 20$  vs  $11.0$  years,  $p=0.03$ ). Overall, osteoporotic BMD was more frequent at femoral sites, with 21% of patients having T-Scores  $< -2.5$ . Osteoporotic BMD was more common in seronegative patients (ns), although no difference in the frequency of fragility fractures ( $n=18; 24.1\%$  vs  $n=28; 23.2\%$ ) was found.

All patients received GCs (mean dose:  $5.0 \pm 6.8$  mg, mean GCCD  $15.1 \pm 19.3$  g, mean duration  $7.7 \pm 8.2$  years) with seropositive patients having numerically higher GCCD, longer duration of GC therapy and more often current GC doses above  $>10$  g/day. Biological DMARDs were more frequently used in seropositive patients ( $n=20; 24.1\%$  vs  $n=67; 43.2\%$ ,  $p=0.02$ ). Anti-osteoporotic therapies between both groups did not differ.

Neither current GC doses nor GCCD nor DMARD therapy had a statistically significant and independent effect on BMD or fragility fractures in either RA group.

**Conclusions:** Osteoporosis and fragility fractures remain a challenge in the management of RA, being determined by multiple interacting factors. Our data confirm that GCs may not *per se* increase fracture risk and decrease BMD in RA but rather, that optimal management of disease activity with or without GCs may be beneficial to bone health. Interestingly however, despite higher cumulative GC doses and duration, seropositive RA patients did not have lower BMD or higher prevalence of fragility fractures compared to seronegative patients. Further prospective data is warranted to better characterise the role of GCs and DMARDs in regard to osteoporosis and fracture risk in RA patients.

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**THU0470 NON-CLONAL ELEVATION OF SERUM IMMUNOGLOBULIN FREE LIGHT CHAINS IS PREDICTIVE OF HIP FRACTURE IN BOTH WOMEN AND MEN**

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**Background:** Proinflammatory cytokines favour uncoupling of bone turnover and decreased bone density and strength, leading to increased fracture risk. Non-clonal elevation of serum immunoglobulin free light chains (sum of kappa and lambda chains) ( $\Sigma$ FLC) may be a global marker of generalised immune stimulation, and has been associated with chronic co-morbidities<sup>1</sup> as well as increased mortality<sup>2</sup>.

**Objectives:** We examined whether elevated  $\Sigma$ FLC is associated with an increased risk for hip fractures in a population-based cohort.

**Methods:** We studied Olmsted County, Minnesota, USA residents, age  $\geq 50$  years, in whom  $\Sigma$ FLC was measured between March 1995 and November 2003 and research authorisation was available. Anyone with a known plasma cell disorder was excluded. Using the Rochester Epidemiology Project, a unique medical records linkage system that allows access to all (inpatient and outpatient) community medical records for Olmsted County residents, we identified all hip fractures that occurred in subjects following their  $\Sigma$ FLC measurement to their last available follow-up or the end of 2015. All available medical records were reviewed by trained nurse abstractors to validate hip fractures identified and to determine their antecedent cause (pathological process [e.g., malignancy], severe trauma [e.g., motor vehicle accidents] and those due to no more than moderate trauma [by convention, equivalent to a fall from standing height or less]). Charlson comorbidity index (CCI) was determined at the time of baseline  $\Sigma$ FLC measurement. We used a Cox proportional hazards model, stratified by sex, adjusting for age, serum creatinine and CCI, to examine whether a  $\Sigma$ FLC  $\geq 4.72$  mg/dl (levels previously associated with increased mortality in this population<sup>1</sup>) is associated with an increased risk for hip fracture.

**Results:** We studied 15 814 residents [mean age (SD), 64<sup>10</sup> yrs; 8722 women, 7092 men] of whom 796 (9.1%) women and 781 (11.0%) men had a  $\Sigma$ FLC  $\geq 4.72$  mg/dl. Women and men with an elevated  $\Sigma$ FLC  $\geq 4.72$  mg/dl had higher CCI [median (IQR) 2 (0,4) vs 0 (0,2); same results for both sexes]. We identified 687 women and 255 men with a hip fracture from any cause (628 women and 220 men had a moderate trauma hip fracture), over 1 12 171 person-years (p-y) and 89 269 p-y of follow-up, respectively. We found that both women and men with  $\Sigma$ FLC  $\geq 4.72$  mg/dl had an increased risk for hip fracture due to any cause: hazard ratio (HR) [95% CI] 1.31 [1.00, 1.73] in women, HR 1.97 [1.37, 2.83] in men; as well as for moderate trauma hip fractures: HR 1.39 [1.05, 1.84] in women, HR 2.12 [1.46, 3.09] in men.

**Conclusions:** We found that  $\Sigma$ FLC  $\geq 4.72$  mg/dl is associated with an increased risk for hip fracture in both women and men, independent of age and chronic co-morbidities. Elevated  $\Sigma$ FLC may be a marker of proinflammatory cytokines detrimental to bone health and warrants further study.

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**THU0471 RISK FACTORS OF LOW BONE MINERAL DENSITY IN PATIENTS WITH SYSTEMIC SCLEROSIS**

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**Background:** Systemic sclerosis (SSc) is a multisystem autoimmune disease, characterised by diffuse fibrosis, degenerative changes, and vascular

abnormalities in the skin, joints, and internal organs. The effect of systemic sclerosis on bone density is not well understood.

**Objectives:** The aim of this study is to evaluate the risk factors of low bone mineral density (BMD) and occurrence of fracture and fracture-related mortality in patients with SSc.

**Methods:** Demographics, disease manifestations of SSc, biological inflammatory parameters, functional disability, scleroderma health assessment questionnaire, immunological status, BMD (lumbar spine and femoral neck), risk factors for low BMD, fractures, and fracture-related mortality were collected in patients with SSc. BMD was measured by using a dual-energy X-ray absorptiometry in lumbar spine (L1-L4) and femoral neck. Fisher's Exact and Student's t-tests were used to evaluate differences between women with and without low BMD. Logistic regression was used for multivariate analysis.

**Results:** Forty eight consecutive unselected SSc women were approached. The mean age of women was 48,32 $\pm$ 15,56 years, the mean disease duration was 10,12 $\pm$ 4,78 years. Twenty-nine women (60,42%) had low BMD, of those 11 (37,93%) had osteoporosis, mean BMD in lumbar spine was  $-2,86\pm 0,38$  and in femoral neck was  $-2,22\pm 0,26$ . Twenty three (47,92%) women with SSc were postmenopausal. In correlation analysis and in multiple regression models, there were correlations between BMD and longer duration of SSc (p<0,01), family history of osteoporosis (p<0,05), age (p<0,01), menopause (p<0,01), low body mass index (p<0,02), presence of internal organ involvement (p<0,05), malabsorption syndrome (p<0,05), joint involvement (severe joint pain and erosive arthropathy) (p<0,05), and immunological status (positivity of anti-DNA topoisomerase I antibodies) (p<0,05). 4 women (4/29) with low BMD had a fracture, compared to 2 without low BMD. Fracture-related mortality did not occur in any patients.

**Conclusions:** Our data suggest that women with SSc are at risk of low BMD and fracture, especially when other risk factors for osteoporosis are present. A number of clinically relevant factors (longer duration of SSc, presence of internal organ involvement, joint involvement, immunological status) are associated with low BMD.

**Disclosure of Interest:** None declared

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**THU0472 FACTORS ASSOCIATED WITH READINESS FOR ADOPTING OSTEOPOROSIS TREATMENT CHANGE**

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**Background:** Understanding factors associated with the readiness for adopting osteoporosis treatment change may inform the design of behavioural interventions to improve osteoporosis treatment uptake in women at high risk for fracture.

**Objectives:** To examine the factors associated with the readiness for adopting osteoporosis treatment change among US women with prior fractures.

**Methods:** US women in the Global Longitudinal Study of Osteoporosis (GLOW) with prior self-reported fractures who were not currently using osteoporosis therapy were eligible to participate in the Activating Patients at Risk for Osteoporosis (APROPOS) Study. Participants' readiness for behaviour change was assessed using a modified form of the Weinstein Precaution Adoption Process Model (PAPM). We defined pre-contemplative participants as those who self-classified in the unaware and unengaged stages of PAPM. Contemplative participants were defined by the undecided, decided not to act, and decided to act stages of PAPM. Bivariate tests and stepwise multivariable logistic regression evaluated the following factors associated with these two levels of readiness for behaviour change: sociodemographic characteristics, health literacy, self-reported history of depression and dementia, previous treatment for osteoporosis, whether participants had been told they had osteoporosis/osteopenia, and whether they had concerns about osteoporosis.

**Results:** A total of 2684 women were enrolled in APROPOS. Participants were 95% Caucasian, with a mean (SD) age 74.9 (8.0) years and 77% had some college education. Overall, 25% (n=544) self-classified in the contemplative stage of behaviour change. Compared to women who self-classified as pre-contemplative, contemplative women were more likely to be concerned about osteoporosis (adjusted OR [aOR]=3.2, 95% CI 2.3-4.4) and to report prior osteoporosis treatment (aOR 4.3, 95% CI 3.1-6.0). Participants who were told they had osteoporosis had a 12.4 fold odds to be in the contemplative group (95% CI 8.5-18.1), while those who were told they had osteopenia had 4.1 fold odds to be in the contemplative group (95% CI 2.9-5.9).

	Age>75	Sex M vs F	Residence	Hepatic Disease	CRF	OCFA	Dementia	CHF	Diabetes mellitus	Charlson i. >2
HR	1.05	1.32	1.48	3.25	1.87	1.46	1.46	2.50	1.11	1.98
IC	(1.04–1.06)	(1.21–1.44)	(1.36–1.60)	(2.17–4.86)	(1.60–2.18)	(1.30–1.62)	(1.30–1.62)	(2.07–3.00)	(1.02–1.22)	(1.73–2.26)

**Conclusions:** Among women with high risk of future fracture, having been told by a health care provider that they had osteoporosis/osteopenia was independently associated with considering taking medications for osteoporosis. Our results suggest that in considering osteoporosis intervention design efficiency and effectiveness, women's recognition of a diagnosis of osteoporosis/osteopenia are critical components to be considered when attempting to influence stage of behaviour transitions.

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#### THU0473 TREND OF MORTALITY AFTER OSTEOPOROTIC HIP FRACTURE IN A PERIOD OF 17 YEARS

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**Background:** It is known that the mortality after a hip fracture is increased with respect to the general population. However, the trend of mortality is a controversial issue.

**Objectives:** The objective of this study is to analyse the incidence, trend and factors associated with mortality in patients with osteoporotic hip fracture.

**Methods:** This is a retrospective cohort study using the Minimum Basic Data Set (MBDS) of our hospital that collects a minimum data set at hospital discharge. We identified patients older than 45 years who suffered an osteoporotic hip fracture during the period from 1999 to 2015. (3992 hip fractures). The demographic data and comorbidities were obtained from the exploitation of the MBDS and the Income Nursing Assessment Form (subgroup of 810 patients). The identification of the deceased was obtained by consulting the MBDS and the INDEF (National Death Index facilitated by the Ministry of Health). A survival analysis was performed (regression of Cox and Kaplan-Meier). The incidence rate, standardised mortality index (SMI) was calculated with respect to the mortality of the general population of Madrid (mortality data of the general population obtained INE), trend (Poisson regression) and risk (Hazard Ratio) for the different clinical and demographic variables.

**Results:** The cumulative incidence of mortality was 72.69% in the study period. The crude mortality rate at 1, 3, 6 months and 1 and 3 years was 9.2%, 17.4%, 24.6%, 33% and 56%, respectively. In men it was 13.7%, 25%, 32.7%, 43.3% and 65.6% and in women 7.9%, 15.7%, 22.3%, 30%, 53.2%. The median overall survival was 886 days (95% CI: 836–951), with 576 for men and 998 for women. A statistically significant reduction in median survival was observed throughout the study period. The IME was 8.3 (95% CI: 7.98–8.59); (similar values in men and women). The clinical-demographic variables that showed a statistically significant association with mortality are shown in the following table 1 (HR and p-value):

Other variables that showed statistical association were: presence of auditory and visual alterations, incontinence (urinary and faecal) and the total score on the Norton scale and the Downton scale.

**Conclusions:** We found an increase in mortality (or decrease in median survival) of patients with hip fracture during the last 17 years. An increase in mortality has been observed in patients with hip fracture related to age, male sex, diabetes, hepatic disease and living in a nursing home.

**Disclosure of Interest:** None declared

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#### THU0474 UTILISATION OF ANTI-OSTEOPOROTIC DRUGS IN REAL-WORLD DATA: AN ANALYSIS OF PERSISTENCE TO THERAPY AND RISK OF FRACTURE

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**Background:** Osteoporosis is a chronic progressive disease characterised by low bone mass and deterioration of bone structure, leading to an increase risk of fractures. It is a major public health problem, affecting hundreds of millions of people worldwide. The primary aim of pharmaceutical therapy is to reduce the risk of osteoporotic fractures. However, long-term adherence to therapy is requisite for optimal therapeutic benefit for patients with osteoporosis. Poor adherence is considered to be one primary reason for suboptimal clinical benefit.

**Objectives:** The aim of this study was to investigate the determinants of non-persistence and impact of persistence on the risk of fractures by using administrative databases.

**Methods:** We conducted a retrospective cohort study using administrative data from four local health authorities in the Abruzzo Region (Central Italy), which comprise about 9 000 000 inhabitants (68% of the overall regional population). The final cohort consisted of a total of 7862 patients, aged ≥60 years, identified through records of filled prescriptions for an antiosteoporotic drug between January 1, 2006 to December 31, 2006. The primary outcome of this study was persistence at one year. Persistence was defined as the length of time (in days) from the date of the index prescription to the date of discontinuation therapy.

**Results:** Kaplan – Meier analysis showed that 3733 patients (47.5%) were persistent with antiosteoporotic drugs after 1 year. An adjusted analysis showed that there is a big difference in persistence between women and men: women are more likely to be non-persistent than men (HR:1.94). Switcher patients were more likely to be non-persistent (HR:1.22). The odds of fracture were significantly higher for patients with previous fractures in comparison with those without previous fractures [OR, 1.70, (95% CI, 1.12–2.59)] (table 1)

**Table 1** Logistic regression model: impact of persistence and other factors on the risk fracture

Characteristics	Unadjusted OR (95%CI)	p-value	Adjusted OR (95%CI)	p-value
<b>Gender</b>				
Male	Reference			
Female	1.31 (0.93-1.85)	0.119	1.28 (0.91-1.82)	0.159
<b>Age</b>				
60-69	Reference			
70-79	1.54 (1.14-2.06)	0.005	1.52 (1.13-2.06)	0.006
≥80	2.56 (1.89-3.45)	< 0.001	2.49 (1.83-3.39)	< 0.001
<b>Previous fractures</b>				
No	Reference			
Yes	1.71 (1.58-1.84)	< 0.01	1.70 (1.12-2.59)	0.013
<b>Persistence</b>				
No	Reference			
Yes	0.78 (0.63-0.97)	0.022	0.79 (0.63-0.97)	0.026
<b>ACCI</b>				
Zero score [0]	Reference			
Mild score [1-4]	0.86 (0.32-2.36)	0.772	1.35 (0.49-3.78)	0.562
Severe score [≥5]	1.50 (1.06-2.12)	0.022	1.33 (0.94-1.90)	0.112

**Conclusions:** Persistence with antiosteoporotic drugs is a significant predictor of incurring a fracture. For these reason, improving osteoporosis treatment compliance and persistence represents one of a major challenge for the future.

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THU0475

### INCIDENCE AND DETERMINANTS OF VERTEBRAL AND PERIPHERAL FRACTURES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A PROSPECTIVE LONGITUDINAL COHORT STUDY

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**Background:** Systemic lupus erythematosus (SLE) is associated with an increased risk of fractures<sup>1</sup>. However, data on the incidence of vertebral and peripheral fractures are limited. In particular, data on (morphometric) vertebral fracture incidence and determinants of such fractures are scarce and show conflicting results.

**Objectives:** To assess the incidence of fractures in a population of patients with SLE, and to identify determinants that predict incident vertebral and peripheral fractures.

**Methods:** A prospective longitudinal cohort study in 145 patients with SLE was performed. Serial bone mineral density (BMD) measurements using dual x-ray absorptiometry, and radiographs of the thoracic and lumbar spine were performed at inclusion and after a median of 5 years (IQR 3–5) follow-up. Demographic and clinical data were also collected. Vertebral fractures were scored according to the semi-quantitative method by Genant *et al.* Reported peripheral fractures were confirmed by x-rays. Analyses were performed with logistic regression (forward selection procedure, p-value of 0.05 as cut-off level). The outcome measures were incident fracture in general (yes/no), vertebral fracture (yes/no), and peripheral fracture (yes/no).

**Results:** Of the 145 included patients, 131 (90%) were females and 100 (69%) Caucasian. The mean age was 41 years (SD 12) at baseline, and median follow-up was 7.2 years (IQR 6–12). A total of 42 incident fractures (vertebral and peripheral) occurred during 998 patient years. The incidence rate of vertebral and peripheral fractures was 2.0 per 100 patient years (95% CI 1.30–3.13), and 2.20 per 100 patient years (95% CI 1.45–3.35), respectively.

Any fracture (both vertebral and peripheral) was predicted by postmenopausal status and Caucasian ethnicity. Vertebral fractures were predicted by age, in which the older the SLE patient, the higher the odds of getting vertebral fractures. Peripheral fractures were predicted by history of stroke, postmenopausal status and moderate alcohol use (1–12 units per week). Use of higher dosages of alcohol (>13 units per week) did not reduce peripheral fracture occurrence. Table 1 shows the final prediction models.

**Conclusions:** The results of our study suggest a twofold increased risk of both vertebral and peripheral fractures in SLE patients compared to the general population<sup>1,2</sup>. Age, Caucasian ethnicity and postmenopausal status are important risk factors for incident fractures in SLE. In addition, special attention should be paid to SLE patients with a history of stroke since this subgroup of patients is at high risk of peripheral fractures.

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THU0476

### SPONTANEOUS VERTEBRAL FRACTURES AFTER DENOSUMAB DISCONTINUATION: A REPORT OF 6 CASES

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**Background:** Denosumab (Dmab) is an antiresorptive treatment with demonstrated efficacy in osteoporosis. However, discontinuation of Dmab has been associated with rapid bone loss, and recently, the development of vertebral fractures (VF) in some patients. It is essential to identify the risk factors for these adverse events and follow its evolution.

**Objectives:** To analyse the clinical characteristics, parameters of bone metabolism and evolution of patients developing VF after Dmab discontinuation.

**Methods:** Six women with spontaneous VF after Dmab discontinuation were included (median age 66 years<sup>56–75</sup>). The clinical history, cause of osteoporosis, treatments received, fractures, Dmab treatment duration and discontinuation period were reviewed. Additionally, the clinical and densitometric evolution, and bone mineral parameters were also analysed after Dmab discontinuation.

**Results:** All the patients had postmenopausal osteoporosis, and one was receiving glucocorticoid treatment; 3/6 patients had previous fractures (2 VF and 1 calcaneus); 4/6 had previously received antiosteoporotic treatment (hormone replacement therapy, risedronate, alendronate, zoledronate [once or consecutively]) during 1–23 years. All had received Dmab for 24–53 months (median 37). The reasons for treatment discontinuation were: dental indication (1 patient), BMD improvement (T-score –1.2) (1 patient), poor adherence,<sup>1</sup> prescription problems and/or delay in administration.<sup>3</sup> The median bone mineral density T-scores prior to VF were –2.6 (–1.2/–4) at the lumbar spine and –3.0 (–0.6/–3.7) at the femoral neck. The mean time between the last Dmab dose and VF was 9.5 months,<sup>8–20</sup> with a median of 5 VFs/patient.<sup>2–8</sup> No patient showed 25-OH vitamin D <20 ng/ml. After Dmab discontinuation, bone turnover markers increased (median increase +364% in PINP and +287% in NTx); one patient presented hypercalcaemia (Ca 11.3 mg/dL); and BMD decreased 1%–21% in the lumbar spine and 2%–6% in total hip at 8–19 months. After VF, 3 patients restarted Dmab, 1 received zoledronate and 2 alendronate. No new fractures occurred during follow-up.

**Conclusions:** Discontinuation of Dmab is associated with an increase in bone turnover markers and bone loss which can be associated with the development of spontaneous VF. Previous bisphosphonate therapy does not seem to decrease this risk. Further studies are needed to assess the optimal antiresorptive treatment and its duration after Dmab discontinuation.

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THU0477

### FACTORS ASSOCIATED WITH THE INITIATION OF TREATMENT AFTER FRAGILITY FRACTURE IN A FRACTURE LIAISON SERVICE

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**Background:** Adherence to treatment in osteoporosis (OP) is not adequate, so that in the first year the percentage of suspensions is between 30% and 50%, up to an adherence of 20% at 3 years. In 2012, we started in Gran Canaria a Fracture Liaison Service (FLS).

**Abstract THU0475 – Table 1.** Multivariate logistic regression analyses of independent explanatory variables that predict incident fracture, showing OR and 95% CI

Variables	Any fracture			Vertebral fractures			Peripheral fractures		
	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P
Age				1.0	1.0–1.1	0.017			
Caucasian ethnicity	13.3	1.7–104.3	0.014						
Postmenopausal status	4.0	1.6–10.1	0.004				3.2	0.86–11.6	0.084
Past stroke							15.5	1.1–212.2	0.040
Alcohol use							Ref	Ref	Ref
- No							0.06	0.01–	0.019
- Moderate							1.9	0.62	0.634
- Heavy								0.14–24.9	

**Objectives:** To describe the factors associated to an effective initiation of treatment after the baseline visit to our FLS.

**Methods:** Prospective observational study that consists of: 1) training of primary care physicians (GP), 2) capture of patients; 3) baseline visit: questionnaire including FRAX; 4) Bone densitometry; 5) patient education by a Nurse with special attention to adherence; 6) referral to GP with a report with management recommendations; those with multiple fractures or who require parenteral therapy were referred to rheumatology; and 7) follow-up by telephone survey to check whether the treatment was taking and confirmation of the prescription in the electronic records (both of which are necessary to consider an effective start of treatment). The variables included were: sex, age, type of fracture, use of previous bisphosphonate, type of prescribed treatment, prescribing physician and causes of non-adherence.

**Results:** Up to December 2017, the adherence of 887 patients with fragility fractures to whom a bisphosphonate or equivalent was prescribed, was recorded. Treatment was initiated in the following 3 months by 74% (n=656) of patients. The following variables were associated with the initiation of treatment: female sex, previous treatment with antiresorptives, prescription of denosumab vs bisphosphonate and treatment prescribed by a rheumatologist vs GP (table 1). The causes of not initiating or withdrawing the treatment at 3 months are shown in table 2. In the regression analysis, we found a significant association with the effective initiation of treatment with a previous treatment with bisphosphonate (p<0.01), initiation of treatment by the rheumatologist (p=0.01) and prescription of denosumab vs bisphosphonate (p<0.01)

**Abstract THU0477 – Table 1.** Factors associated to start of treatment at 3 months \*p<0,01

	Patients that initiate treatment (n=656)	Patients who did not initiate or stop treatment (n=231)
Female/Male, n(%)	577 (76)/79 (63)*	185 (24)/46 <sup>37</sup>
Age, mean (SD)	76 (9)	76 (9)
Type of fracture, n (%) Wrist/Hip	191 (29)/213 <sup>32</sup>	71 (31)/68 <sup>29</sup>
Previous treatment with	178 (91)/478 (69)*	18 (9)/213 <sup>31</sup>
Bisphosphonate, n (%) Yes/No		
Prescription of Bisphosphonate/denosumab n (%)	446 (70,5)/203 (80)*	186 (29,5)/
Prescription by Primary Care/Rheumatology, n (%)	412 (69,5)/230 (82)*	180 (30,5)/51 <sup>18</sup>

**Abstract THU0477 – Table 2.** Causes of no start or stop treatment, N (%)

No prescription/suspension by GP	115 (50)
Patient related causes	93 (40)
Patient does not want the treatment	39 (17)
Polipharmacy	20 (9)
Don't know/Did not visit the GP	20 (9)
Drug intolerance	14 (6)
Other causes	23 (10)

**Conclusions:** 74% of patients seen in the FLS start treatment within 3 months of the baseline visit. The factors associated with the initiation of therapy were prior antiresorptive treatment, denosumab prescription and initial prescription by the rheumatologist. The reason of non adherence in half of the cases is the GP's refusal to initiate or continue the FLS recommendation.

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#### THU0478 BEFORE AND AFTER MENOPAUSE, OSTEOPOROSIS RISK FACTORS ARE DIFFERENT IN WOMEN WITH RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is an autoimmune disease characterised by systemic inflammation, involving not only the juxta-articular bone erosion, but generalised bone loss.<sup>1</sup> Sex hormone activates RA disease activity and induced bone resorption, but hormone replacement therapy increases bone mass and density. The ambiguous role of sex hormone on bone remodelling is confusing in RA patients. Under the impact of sex hormone, risk factors for osteoporosis might be different at pre- and post-menopausal stage.

**Objectives:** To investigate the different clinical risk factors of osteoporosis in pre- and post-menopausal women with RA.

**Methods:** A cross-sectional study was performed during 2014 to 2017, enrolling female participants fulfilled 2010 RA criteria.<sup>2</sup> We recorded demographic data,

risk factors for osteoporosis and blood test. Osteoporosis is defined if one of hip, distal forearm, and lumbar spine bone mineral density less than -2.5 by T-score for post-menopausal women, or less than -2.0 by Z-score for pre-menopausal women. Data was analysed by Student's t test and Chi-square test for continuous and categorical variables, respectively. Multivariate logistic regression was applied to detect association of osteoporosis and selected variables.

**Results:** A total of 451 participants were enrolled in the study, including 89 pre- and 362 post-menopausal women. The prevalence of osteoporosis is 14.6% and 36.7% for pre- and post-menopausal women with RA, respectively. At pre-menopause, low body weight is the only significant risk factors for osteoporosis, while old age, low body height, low body weight, positive anti-cyclic citrullinated peptide antibody (anti-CCP), previous fracture history, elevated white blood cell and platelet count, and lower calcium level are potential risk factors for post-menopausal women developing osteoporosis (table 1). Multivariate stepwise logistic regression analysis (table 2) showed body weight remains the leading risk factors in pre-menopausal women (Odds ratio[OR]=0.84, 95% confidence interval [CI]=0.76-0.94, P-value=0.002), while body weight and previous fracture history are significant risk factors in post-menopausal women (body weight OR=0.91, 95% CI=0.88-0.94, P-value<0.001, previous fracture OR=2.03, 95% CI 1.13-3.64, P-value 0.02).

**Conclusions:** Risk factors of osteoporosis are different in pre- and post-menopausal women with RA. For pre-menopausal women, Low body weight is a leading risk factor, while low body weight and previous fracture history are important for post-menopausal women. Without protection of sex hormone, there are Potential roles of anti-CCP and white blood cell participating in osteoporosis pathogenesis and need more survey for confirmation.

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#### THU0479 THE ANTI-OSTEOPOROTIC TREATMENT IS SCARCE AMONG PATIENTS WITH VERTEBRAL FRACTURE REFLECTED IN THE RADIOLOGICAL REPORT: DATA FROM A FRACTURE UNIT-FLS

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**Background:** A relevant number of patients with vertebral fracture (VF) do not receive specific treatment for osteoporosis and remain as invisible fractures. The objective of the Fracture Units-FLS is to detect patients with fracture, to perform an adequate diagnostic evaluation, initiate treatment and try to prevent new fractures.

**Objectives:** To know the characteristics of the patients and attitude of the referring service, in which the radiological report identifies the presence of VF.

**Methods:** Observational study carried out from January 1 to June 30, 2017, of consecutive patients in which the radiological report after performing simple radiology or CT, reflects the presence of dorsal, lumbar or both VF. The attitude of the service requesting the radiological test was reviewed 3 months after the radiological report.

The following variables were collected: general data of the patients (age, gender), the service requesting the imaging test (specialty, request from hospitalisation or ambulant, diagnosis and/or previous treatment for osteoporosis, attitude towards the VF) and the radiological test (type of test and location of the VF).

**Results:** 91 patients were included, of which 62% were women, with a mean age of 72±11.56 years. In 46% of the patients, the image test was requested by one of the Internal Medicine Services (gastroenterology: 31%, oncology-haematology: 17%, rheumatology: 14%, neumology: 12%, cardiology: 10%), 36% by Primary Care Physicians, 15% from the Emergency Department of the Hospital and the remaining 2% from a Surgical Service.

In 77%, the radiological test was given to ambulatory patients. In 56%, the imaging test was simple radiology (chest X-ray: 56%, dorsal-lumbar spine: 41% and the

remaining 4% bone series study) and 44% CT. In 61%, the fracture was located in dorsal spine, in 28% in lumbar spine and the remaining 11% in the dorsal and lumbar spine. Previously, 44% were diagnosed with osteoporosis and 38% were undergoing specific treatment (oral bisphosphonate: 23%, bisphosphonate iv: 20%, denosumab: 20%, SERM: 8%, PTH: 6% and only calcium +vitamin supplements D: 23%).

Three months after the identification of the VF, 66% did not receive specific treatment for osteoporosis, 11% were referred to Rheumatology (initiating treatment in all) and 3% to Traumatology. Three (3%) of the patients had died and 2 (2%) had moved away.

**Conclusions:** Despite being reflected in the radiological report, a significant number of patients with vertebral fracture do not receive antiosteoporotic treatment, 3 months later.

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#### THU0480 MULTI-DISCIPLINARY FRACTURE LIAISON SERVICE IN THE NORTH AREA OF GRAN CANARIA; 6 YEARS EXPERIENCE

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**Background:** in March 2012 was implemented a FLS Unit coordinated by Rheumatology

**Objectives:** communicate the results of the unit in the 2012–2017 period.

**Methods:** Patients >50 years with fragility fracture. The program consists of: 1) training of primary care doctors (GP), 2) recruitment from the emergency room or admitted with hip fracture; 3) Bone densitometry; 4) patient education by a nurse; 6) report to GP with recommendations of managing; and 7) follow-up of persistence of treatment (telephonic survey plus prescription in the electronic records) at 3, 6, 12 and 24 months.

**Results:** The FLS has attended 1739 patients: mean age 73 y, 81% women. The location of fractures was forearm (32%), hip (24%), humerus (21%), vertebra (10%) and other locations (12%). Previous treatment with bisphosphonate 17%, 10% of them at baseline.

After the baseline visit, 75% of patients were sent to GP and 25% to rheumatology. Treatment with bisphosphonate or equivalent was recommended to 1264 patients (72%). Persistence of treatment (analysed at 3, 6, 12 and 24 months in 1,051, 823, 622 and 351 patients, respectively) was 74%, 72%, 75% and 69%, respectively.

Risk factors (FRAX), n (%)

Previous fracture	323 (18)
Parent's hip fracture	190 (11)
Glucocorticoids	148 (8)
Somking	186 (10)
Alcohol	68 (4)
Secondary Osteoporosis	287 (16)
BMI<18.5	31 (2)
Rheumatoid arthritis	40 (2)
Bone Densitometry, n (%)	
Normal	159 (13)
Osteopenia	551 (45)
Osteoporosis	517 (42)
FRAX, mean (DE)	
Major Fracture	13,2 (9)
Hip Fracture	6 (7)

**Conclusions:** Our FLS is effective in terms of beginning and persistence of anti-fracture treatment in the medium term.

**Disclosure of Interest:** None declared

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#### THU0481 PHYSICAL PERFORMANCE FACTORS INFLUENCING GAIT SPEED IN PATIENTS SURGICALLY TREATED FOR OSTEOPOROTIC HIP FRACTURES

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**Objectives:** This study was undertaken to determine physical performance factors associative of gait speed in patients surgically treated for hip fractures.

**Methods:** Fifty eight patients (16 males and 42 females; average age 79.1±9.1 years) who underwent a hip surgery due to hip fractures participated in this study. Patients completed 10 metre walk test (10MWT) to assess gait speed. Additional physical performance tests included Timed up and go test (TUG), Berg balance scale (BBS), one repetitive maximum (1RM) of leg extension, leg curl, hip abduction of surgical and nonsurgical sides, and instrumental gait analysis for spatio-temporal parameters.

**Results:** In the bivariate analyses, postoperative 10MWT had a significant positive correlation with the postoperative TUG ( $r=0.85$ ,  $p<0.01$ ), age ( $r=0.57$ ,  $p<0.01$ ), swing phase duration ( $r=0.35$ ,  $p<0.01$ ), gait cycle duration ( $r=0.49$ ,  $p<0.01$ ) and significant negative correlation with the postoperative BBS ( $r=-0.69$ ,  $p<0.01$ ), 1RM of surgical leg extension ( $r=-0.35$ ,  $p=0.01$ ), 1RM of nonsurgical leg extension ( $r=-0.40$ ,  $p<0.01$ ), 1RM of surgical leg curl ( $r=-0.44$ ,  $p<0.01$ ), 1RM of nonsurgical leg curl ( $r=-0.41$ ,  $p<0.01$ ), 1RM of hip abduction ( $r=-0.32$ ,  $p=0.02$ ), cadence ( $r=-0.53$ ,  $p<0.01$ ), stance phase duration ( $r=-0.26$ ,  $p=0.04$ ). In addition, a presence of dementia was significantly correlated with 10MWT (44.2 s vs 22.4 s,  $p=0.02$ ). In the linear regression analyses, the postoperative TUG ( $\beta=0.85$ ,  $p<0.01$ ) was a factor associative of the postoperative 10MWT.

**Conclusions:** This study revealed that the presence of dementia, the postoperative balance ability, muscle strength of surgical and nonsurgical legs were significantly associated with postoperative gait speed 1 month after hip surgery due to hip fractures. Therefore, these results could be importance in planning various postoperative rehabilitative programs to improve gait speed early after hip surgery due to hip fractures.

**Disclosure of Interest:** None declared

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#### THU0482 RELATIONSHIP BETWEEN MILD VERTEBRAL BODY DEFORMITY AND KELLGREN-LAWRENCE'S OSTEOARTHRITIS LEVEL WITH THE PREVALENCE OF NON-TRAUMATIC DORSAL AND LUMBAR BACK PAIN IN FEMALE PATIENTS WITH RISK OF OSTEOPOROTIC VERTEBRAL COLLAPSE

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**Background:** There is a lack of information about the meaning of mild vertebral body deformities and its relationship with back pain. Many patients with this kind of wedges are sent to rheumatology clinics to assess the possibility to start treatment for secondary prevention of osteoporosis fractures.

**Objectives:** The present study aims to determine the relationship of the number of medical consultations due to dorsal or lumbar pain and two categorical variables: Presence or absence of mild vertebral wedge (Genant's first level of classification) and Kellgren-Lawrence's osteoarthritis classification levels I-II and III-IV.

**Methods:** We conducted a retrospective follow-up of 1131 patients with and without mild vertebral body deformities along three years to compare the frequency of axial pain episodes assessed in emergency units and their chance to evolve to moderate or severe wedges.

**Results:** In the group without deformities, the cumulative incidence of dorsal or lumbar pain episodes was 7.2% per year, and the incidence density was 7805 cases per 100 patients-year. In the group with mild deformities, the cumulative incidence of dorsal or lumbar pain episodes was 7.0% per year, and the incidence density was 7318 cases per 100 patient-year ( $p=0.77$  and  $0.58$ , respectively). We grouped patients according to their osteoarthritis severity. The cumulative incidence of dorsal and lumbar pain episodes along the period of observation, in patients with a spinal Kellgren-Lawrence's osteoarthritis degree I-II and III-IV were 19.8% (CI95% 12.10%>27.49%) and 31.5% (CI95% 18.27%>44.72%), respectively ( $p<0.0001$ ). The density of incidence for both groups was 6.18 cases per 100 patients-year and 11.3 cases per 100 patients-year, respectively ( $p<0.0001$ ). The difference in proportions of patients who developed a moderate or severe Genant's vertebral deformities was not statistically significant among patients with or without mild vertebral wedges.

**Conclusions:** Our results point that back pain incidence is not related to the presence of mild vertebral wedges but the severity of axial osteoarthritis. Also, the behaviour of starting a secondary osteoporosis prevention treatment after the detection of a mild vertebral wedge is not supported by our results.

**Disclosure of Interest:** None declared

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THU0483

### BONE MINERAL DENSITY AND PREVALENCE OF OSTEOPOROSIS IN HIV-INFECTED PATIENTS IN COMPARISON WITH A REFERENCE SPANISH POPULATION: THE IMPORTANCE OF LOCAL NORMATIVE RANGES

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**Background:** HIV-infected patients have less bone mineral density (BMD) than non-HIV population. According to current guidelines, the normal BMD reference range is that derived from the US NHANES III (National Health and Nutrition Examination Survey) and from BMDCS-Hologic. However, local variations of BMD could change the interpretation of bone loss and the prevalence of osteoporosis (OP) in this population.

**Objectives:** To compare the BMD in HIVinfected Spanish patients with values from healthy Spanish population and to estimate the prevalence of OP in this patients, based on the local data.

**Methods:** This was a cross-sectional study in a homogenous cohort of HIV-infected patients (RyC cohort, EC 009/17). Data of femoral neck and spine BMD were obtained by DXA (Dual-Energy X-ray Absorptiometry) from 949 patients (241 women, 25%) and compared with the results of a nationally representative Spanish cohort (14 centres) including 2442 subjects (1305 women, 53%) aged 20–80 years.

**Results:** Overall, mean age was 45.4 years (women, 46.5 years). The Spanish reference cohort showed a reduced BMD (–7%, 3%–12%) in comparison with NHANES, especially in middle aged women. HIVinfected patients had a lower BMD than Spanish cohort in both spine and femoral neck localizations for the different age strata ( $p < 0.001$ ), not significant in femoral neck for males aged 30–39 ( $n = 152$  patients, 0.848 vs 0.869 gr/cm<sup>2</sup>;  $p = 0.07$ ). Using NHANES data, the prevalence of OP was 26% in women in the Spanish cohort and 41% in our HIV population. By contrast, if the Spanish data are used as normative range, the prevalence of OP decreased in HIV females, significant between 40–60 years (from 26.5% to 23.5% in spine,  $p < 0.01$ ). Although OP in spine was less frequent in males by using Spanish data ( $p < 0.01$ , OP decrease from 17.8% to 6.5%), there was more OP in femoral neck in males older than 40 years (from 13.5% to 21% in 60–69;  $p < 0.01$ ).

**Conclusions:** Our data demonstrate that HIV-infected patients had a significantly reduced BMD in comparison with both US and Spanish reference data for all the age strata. However, the prevalence of osteoporosis could change if local representative cohorts are used as normative data, with almost 30% of patients being reclassified.

**Disclosure of Interest:** None declared

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THU0484

### REBOUND-ASSOCIATED MULTIPLE VERTEBRAL FRACTURES AFTER DISCONTINUATION OF DENOSUMAB: NINE CASES REPORT

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**Background:** Denosumab (DNB) is an IgG monoclonal antibody with high affinity for RANKL that transiently decreases bone resorption. It increases bone mineral density (BMD) and decreases turnover markers, reducing fracture risk in patients with osteoporosis (OP). Several cases of rapid loss of BMD, severe bone turnover rebound (BTR) and associated fractures have been reported after DNB discontinuation. A clinical alert has been generated from these findings.

**Objectives:** To evaluate the clinical and demographic features in a case series of patients with multiple vertebral fractures after discontinuation of denosumab.

**Methods:** An observational descriptive study analysing data from nine patients with multiple vertebral fractures after DNB discontinuation that were admitted to our Rheumatology service between 2015 and 2017.

**Results:** Nine women with postmenopausal OP that received treatment with DNB were included (table 1). Mean age at treatment onset was 66.9±8.0 SD years. Four of them had previous fragility fractures, and one of them had risk factors for secondary OP (treatment with aromatase inhibitors, case 8). Eight patients (88.9%) had already received treatment other than DNB. Mean DNB received doses was 6±1.6 SD. Mean T-score before treatment was –2.6±0.6 SD for femoral neck (FN) and –3.0±1.3 SD for lumbar spine. Mean T-score ±SD after 6 months or more of DNB discontinuation was –3.5±0.8 and –3.3±1.8, respectively. Bone turnover markers (BTM) remained elevated (CTX mean 0.143 ±0.663 SD ng/ml and P1NP 152.1±122.4 SD ng/ml). There were a total of 47 fractures, and all occurred spontaneously. Most affected vertebrae were D9, D12, L3 y L5. Two patients underwent vertebroplasty, suffering both of them vertebral fractures after surgery.

**Table 1** Clinical features of the patients

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9
Age*	72	37	59	87	64	61	11	76	65
DNB†	24	24.2	25.5	22.2	26	26	30.2	19.1	15.1
FRAX‡	NR	Major Fr 7.1%, Hip Fr 2.3%	Major Fr 40%, Hip Fr 14%	NR	Major Fr 10%, Hip Fr 2.5%	NR	NR	Major Fr 16%, Hip Fr 9.8%	Major Fr 6.3%, Hip Fr 2.1%
Previous Fr	Right iliac crest, several vertebrae	No	D12	No	C6/5	No	No	No	D12, L1, L3, L4
DNB dose	4	4	4	4	4	7	7	7	6
Time last dose-§	18	3	10	12	11	9	8	12	8
Number of Fr after DNB end	10	3	3	4	2	7	3	3	8
Fr localization	D8, D7, D10, D11, D12, L1, L5	D10, D11, L3, L3, L5	D6, D6, D11	D5, D7, D9, L1, L5	D7, D9, D12, L1, L3, L4, L5	D6, D9, D12	D6, D9, D10, L3	D1, D6, D9, D10, D11, L3, L5	D1, D6, D9, D10, D11, L3, L5
End time cases	Oral	Max	Max	Max	Max	Low Fr risk	Oral	Max	Max
Previous T-scores*	FN -2.6, LS -3.9	FN -2.2, LS -3.9	FN -3.5, LS -3.2	FN -3.4, LS -4.0	FN -2.4, LS -3.4	FN -3.2, LS -3.0	FN -1.5, LS -2.8	NR	FN -1.9, LS -4.3
Post DNB T-scores*	FN -3.2, LS -4.1	FN -3.0, LS -4.7	FN -2.5, LS 0.4	FN -3.4, LS -4.0	FN -4.1, LS NR	FN -4.1, LS -4.0	NR	FN -4.7, LS -3.7	NR
CTX after 6m	1.89	1.40	1.45	1.44	NR	1.07	0.95	NR	NR
P1NP after 6m	387.4	220.6	92.3	114.2	NR	196.0	142.6	NR	NR
Tm after 6m	Temporale, Deconsomab	Temporale, Deconsomab	Zolendronic Acid	Zolendronic Acid	Denosumab	Temporale	Temporale, Denosumab	Temporale, Denosumab	Alendronic Acid, Denosumab

BMI: Body Mass Index; Fr: fracture; Tm: treatment; CTX: collagen telopeptide; P1NP: collagen propenide; FN: femoral neck; LS: lumbar spine; NR: Not reported.  
 \*At onset of DNB treatment.  
 †Time last DNB until first fracture, in months.  
 ‡T-score before DNB.  
 §T-score 6 months or later from DNB discontinuation.  
 ¶Bone turnover markers after treatment discontinuation, at least 10 months later.

**Conclusions:** This report of nine cases suffering multiple vertebral fractures early after the interruption of the DNB highlights the emerging concern on the subject in the scientific community and the need to clarify its pathogenic mechanism ("rebound effect") and support in solid evidence the new recommendations on its management.

**Disclosure of Interest:** None declared

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THU0485

### PREDICTING 1-YEAR MORTALITY AFTER A FRAGILITY HIP FRACTURE – THE EXPERIENCE OF A FRACTURE LIAISON SERVICE

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**Background:** Hip fractures are the most serious outcome of osteoporosis and are a leading public health concern due to the associated increase in morbidity and mortality, loss of independence and financial burden.

**Objectives:** The aim of this study was to investigate possible predictive factors of 1 year mortality in patients with fragility proximal femur fracture referred to a fracture liaison service (FLS).

**Methods:** Patients aged ≥65 years admitted in Orthopaedics department with a fragility hip fracture were evaluated and referred to the Rheumatology outpatient clinic. In this setting patients were evaluated with laboratory and imagiological workup and afterwards anti-osteoporotic therapy was started. We retrospectively collected information regarding patients hospitalised from March 2015 to March 2017 and conducted univariate and multivariate analysis to determine possible predictive factors of 1 year mortality.

**Results:** 522 patients were included, with a median age of 84 years (range 65–104), 416 (79.7%) females. The median time to intervention was 2 days (range 0–44) and median hospital stay 10 days (range 0–175). Median Charlson Comorbidity Index (CCI) score was 5 (range 2–13). In-hospital mortality was 6.3% and overall 1 year mortality was 16.7%.

In the univariate analysis, the factors significantly associated with death in one year time were male gender, CCI score >5, previous physical limitation in daily activities, walking disability previously and 2 months after the fracture, longer time to surgery (>48 hour), conservative treatment and previous osteoporosis diagnosis. In multivariate analysis previous physical limitation in daily activities (OR 2.1, CI 1.22–3.62;  $p = 0.007$ ) and walking disability 2 months after the fracture (OR 4.23, CI 1.73–10.37;  $p = 0.002$ ) were independent predictors of 1 year mortality.

**Conclusions:** In this study, in-hospital mortality was similar to what has been described in literature but 1 year mortality was slightly lower. Previous physical limitation and walking disability 2 months after the fracture were independent risk factors for 1 year mortality. These findings should be confirmed in larger, prospective studies with a control group.

**Disclosure of Interest:** None declared

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**THU0486 THE VITAMIN D RECEPTOR EXPRESSION IN SKELETAL MUSCLE OF WOMEN WITH DISTAL RADIUS FRACTURE**

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**Background:** A distal radius fracture (DRF) is the most common upper extremity fracture in old women. Since DRFs typically occur earlier than hip fractures by an average of 15 years, they can reflect early changes of bone such as osteoporosis and muscle frailty for instance, the loss of muscle mass.

**Objectives:** We aimed to evaluate the relationship between the vitamin D receptor (VDR) expression in the muscle cell and the muscle mass in women with a DRF.

**Methods:** This research was conducted as a part of the Study on Ageing Radial fracture Cohort (SARCO) which is an ongoing longitudinal, population-based cohort investigation of patients with a DRF which began in November 2015. For the current study, we prospectively recruited 45 women over 50 years of age (mean age, 66 years) with DRF and acquired biopsy of the forearm flexor muscle. The muscle cross-sectional area (CSA) and VDR expression were measured using immunohistochemistry staining. The clinical parameters including grip strength, gait speed, body mass index (BMI), bone mineral density (BMD), and serum vitamin D levels were compared between patients grouped by appendicular lean mass index and were correlated with the VDR expression.

**Results:** Twelve patients (27%) showed a decreased appendicular lean mass index, less than the cut-off value of 5.4 kg/m<sup>2</sup> which was suggested by the Asian Working Group for Sarcopenia. Patients with a low appendicular lean mass index had significantly lower muscle CSA ( $p=0.037$ ), but a higher VDR expression ( $p=0.045$ ) than those with higher indices. VDR expression was negatively correlated with BMI ( $r=-0.417$ ,  $p=0.004$ ) and appendicular lean mass index ( $r=-0.316$ ,  $p=0.044$ ).

**Conclusions:** DRF patients with low appendicular lean mass index presented high VDR expression and low CSA in forearm muscle cells. This suggests that the VDR expression might be up-regulated in the attempt to compensate for the decreasing muscle mass. Further studies are necessary to explore the role of VDR in the progression of sarcopenia.

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**THU0487 AN AUDIT OF THE USE OF PERCUTANEOUS VERTEBROPLASTY FOR OSTEOPOROTIC VERTEBRAL FRACTURES IN A UK RHEUMATOLOGY CLINIC**

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**Background:** University Hospital, Coventry, UK (UHCW), offers percutaneous vertebroplasty (PVP) to patients with painful osteoporotic vertebral fractures. The National Institute for Health and Care Excellence (NICE) Technology Appraisal 279 (TA279) (2013) restricts the use of PVP to patients with severe ongoing pain despite optimal pain management, where the pain corresponds to the level of fracture on examination and imaging.<sup>1</sup>

**Objectives:** To audit the use of PVP by Rheumatology at UHCW against NICE TA279.<sup>1</sup>

To assess the clinical outcomes of PVP for our patients.

**Methods:** The records of all UHCW Rheumatology patients who received PVP from MD<sup>3</sup> (Interventional Radiologist) between September 2007 and August 2014 were retrospectively assessed against NICE TA279.<sup>1</sup>

We defined a 'recent' fracture as occurring 6–12 weeks prior to PVP as this allows time for natural bone healing whilst minimising therapeutic delay.<sup>1</sup> 'Optimal pain

management' was defined as analgesia in addition to, or stronger than, paracetamol.

**Results:** 57 of the 221 PVP performed by MD were for Rheumatology patients. 38 patients were female and 19 were male. They were aged 42–95 years (median 73), and 95% were Caucasian. 26 had taken corticosteroids for more than 6 months.

7 patients received PVP 6–12 weeks after their fracture. 10 patients had PVP within 6 weeks. 39 patients waited 12 weeks or longer due to late patient presentation, slow referral processes, and the time taken to optimise analgesia.

38 (67%) patients received optimal analgesia before PVP.

46 (81%) patients had pain that correlated with the level of vertebral fracture.<sup>1</sup>

Following PVP back pain was gone for 9 (16%) patients, improved for 38 (66%), not changed for 4 (7%), and worse for 1 (2%) patient.

Complications included leakage of cement locally (57%) or into local veins (5%). 2 patients had pulmonary cement emboli. One presented with breathlessness and the second was found incidentally. Both recovered with conservative therapy.

**Conclusions:** In line with NICE TA279, most patients had pain at the level of their fracture and received optimal pain management prior to receiving PVP.

10 patients received PVP earlier than our standard of 6 weeks. However, recent randomised trials suggest that PVP may be beneficial in this group.<sup>2</sup>

Most (68%) patients received PVP later than 12 weeks but they often found benefit. The VERTOS V trial may help determine the role of PVP for chronic fractures.<sup>3</sup>

Introducing an osteoporotic vertebral fracture pathway at UHCW will help ensure appropriate management, timely review and, when necessary, prompt PVP.

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**THU0488 AGE AT THE TIME OF HIP FRACTURE IN PATIENTS WITH RHEUMATOID ARTHRITIS IS GREATER THAN IT WAS 10 YEARS AGO, BUT IS STILL YOUNGER THAN THAT OF THE GENERAL POPULATION**

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**Background:** Niigata Prefectural Central Hospital (NPCH) is the principal hospital of Joetsu and Myoko cities in Niigata Prefecture, Japan. It serves a population of 230,186, of whom 70,205 (30.5%) were aged  $\geq 65$  years in 2015. About 90% of patients with hip fractures underwent surgery within 48 working hours after admission in NPCH. Between 50% and 60% of all hip fractures in our region are treated at the NPCH, which employs two rheumatologists and treats 500 rheumatoid arthritis (RA) patients.

**Objectives:** We sought to identify the characteristics of RA patients with hip fractures, as compared to those of the general population and of RA patients treated 10 years previously.<sup>1</sup>

**Methods:** Between 2012 and 2015, 789 hip fractures were treated at the NPCH. The mean age of these patients was 84 $\pm$ 8.0 years. RA patients with such fractures were compared with fracture patients from the general population. We recorded the neck/trochanter (n/t) ratio, age at fracture, disease duration, steroid and anti-osteoporosis drug-use rates, secondary fracture rate, walking capacity after operation, 1 year and 30 day mortality rates, and infection rate, in both current RA patients and those treated 10 years previously.

**Results:** Eleven RA cases had hip fractures (mean age: 76 $\pm$ 7.0 years; all females); 8 had been treated for RA at NPCH. RA patients constitute 1.4% of the general population, and 1.6% of all RA patients treated at the NPCH. Mean RA duration was 23 $\pm$ 20 years. The n/t ratio was 1.2. Three cases aged 60–69 years were of the mutilated type and mean RA duration was 35 $\pm$ 18 years. Five cases

aged 70–79 years featured amyloidosis associated with hemodialysis (1 case), severe interstitial pneumonia,<sup>1</sup> Parkinson's disease,<sup>1</sup> total knee arthroplasty triggered by RA,<sup>2</sup> and mean RA duration was 17±11 years. Of 3 cases aged 80–89 years, RA onset was after age 80 years in two. At the time of fracture, 7 were receiving anti-osteoporosis treatment; 2 were on teriparatide, 4 on bisphosphonate, and 3 on activated vitamin D. Some patients discontinued anti-osteoporotic medication because of renal failure or side effects; 84% of patients had taken anti-osteoporotic medications prior to fracture. Seven patients were taking steroids (mean prednisolone dose 3.9±2.1 mg/day). Secondary fractures occurred in 2 cases; one had RA of the mutilated type with renal failure; a secondary fracture occurred 4 months later. The 2nd case was taking anti-osteoporotic medication but the secondary fracture occurred 32 months later. At 3 months after surgery, the walking abilities of all patients were the same as prior to fracture. No mortality was recorded at either 30 days or 1 year. No infective complication was noted.

**Conclusions:** Hip fracture in patients with RA occurs in 1.4% of the general population in Joetsu and Myoko, Japan, ranging from 0.93% in Taiwan<sup>2</sup> to 1.6% in Sweden<sup>3</sup>, and 1.6% of all RA patients, ranging 3.3% in Taiwan<sup>2</sup> to 6.5% in Sweden<sup>3</sup>. The mean age at hip fracture was 76±7.0 years, thus about 8 years younger than that of fracture patients from the general population, but was 72±4.5 years 10 years ago<sup>1</sup>. Among all patients, 64% were on steroids (83% 10 years ago<sup>1</sup>), 84% were on anti-osteoporosis drugs (31% 10 years ago<sup>1</sup>) and the n/ratio was 1.2 (3.2 10 years ago<sup>1</sup>).

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#### THU0489 THE IMPACT OF CALCIUM INTAKE AND PHYSICAL EXERCISE ON PEAK BONE MINERAL DENSITY

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**Background:** Regular exercise and adequate nutrition are frequently prescribed as strategies to optimise peak bone mass and maintain bone and muscle health throughout life.

**Objectives:** The aim of our work was to determine the relationship of clinically assessed milk intake and physical exercise with bone mineral density (BMD) in young adults.

**Methods:** This cross-sectional study included members of the general population aged between 20 and 30 years from the Portuguese cohort SAOL (individuals aged 18+years randomly selected from a local county of Coimbra, Portugal). No exclusion criteria were applied. Individuals were asked to describe their milk intake (up to 2 glass/day and 2+glass/day, corresponding to up to and more than 480 mg/day), regular physical activity (categorised as none-to-moderate and at least intense physical activity) and strenuous sports practice (up to 2 hour/week and 2+hour/week) from the age of 10 to 25. They underwent a Dual-energy x-ray absorptiometry (DEXA) of the lumbar spine (LS) and proximal femur (PF). Categorical data is presented as proportions/percentages and continuous variable as median ±standard deviation. Differences between groups were assessed by Mann–Whitney U test. Potential predictors of a higher BMD of PF and LS were identified using multiple linear regression analysis. P-values<0.05 were considered statistically significant.

**Results:** We included 259 individuals (mean age of 24.7±2.7 years, 60.6% being female). The majority (82.6%), described having a moderate regular physical activity (equivalent to working as a mailman), practicing strenuous sports at least 2 hours per week (81.1%) and ingesting at least two glasses of milk per day (83.4%). The current BMD of the PF and LS were 0.8±0.13 and 0.99±0.11, respectively. On univariate analysis, the only significant association related the PF BMD and milk intake (p=0.008). Multiple linear regression analysis showed that while physical activity and sports practice did not predict BMD values, milk intake persisted as a predictor of a higher BMD of PF (p=0.022), even after including other explanatory variables. No statistically significant predictors were found for BMD of the LS.

**Conclusions:** Our study showed that clinically assessed milk intake between the ages of 10 and 25 years, but not physical exercise, is a significant predictor of higher bone mineral density assessed by DEXA at the PF. These results do not exclude a positive impact of exercise upon peak bone mass, but suggest that its retrospective evaluation in a clinical setting should not be taken as reassurance that a good peak bone mass was achieved in early adulthood.

**Disclosure of Interest:** None declared

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#### THU0490 TEMPORAL INCREASES IN SIDE EFFECT CONCERNS OF OSTEOPOROSIS MEDICATIONS AMONG WOMEN WITH PREVIOUS FRACTURES

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**Background:** High-consequence, albeit rare, adverse side effects of osteoporosis medication raise patients' risk perceptions and contribute to non-adherence. In the past decade, fears of osteonecrosis of the jaw (ONJ) and atypical femoral fractures (AFF) have been increasingly reported as barriers to both the initiation of and adherence to osteoporosis medications.

**Objectives:** To examine the temporal prevalence of self-reported concern about ONJ and AFF as reason for discontinuation of osteoporosis medication.

**Methods:** Activating Patients at Risk for Osteoporosis (APROPOS) enrolled US women from the Global Longitudinal Study of Osteoporosis (GLOW) with previous self-reported fractures and no current use of osteoporosis medication. Using mailed surveys in 2010 (T1), 2012 (T2) and 2013 (T3), women were asked whether they discontinued osteoporosis medication in the prior year because of concerns about ONJ at three time points (T1, T2, T3) and AFF at two time points (T2, T3). We calculated the proportion of women reporting fears of ONJ and AFF among those who discontinued osteoporosis medication, and compared the proportions using chi-square tests.

**Results:** A total of 833 women discontinued osteoporosis treatment at three time points, T1 (n=255), T2 (n=471), and T3 (n=107), respectively. There were no differences in the demographic characteristics between groups. The proportion of women reporting concerns of ONJ was 18.4% (T1), 26.7% (T2) and 64.5% (T3), while 23.5% (T2) and 60.7% (T3) reported fear of AFF as reason to discontinue osteoporosis treatment. These differences were statistically significant (p<0.0001) for all comparisons.

**Conclusions:** The proportion of women reporting concerns of ONJ and AFF increased over time among those women who discontinue osteoporosis medications. Strategies are needed to help patients balance risks and benefits given a significant and temporally growing concern of rare bisphosphonate side effects.

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#### THU0491 FACTORS ASSOCIATED WITH ANNUAL PERCENTAGE CHANGES IN BONE MINERAL DENSITY: A-14 YEARS PROSPECTIVE POPULATION-BASED STUDY

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**Background:** Gradual bone loss is expected with advancing age and gender differences were reported in the rate of annual loss of bone. Ideally, the decision to introduce interventions designed to prevent bone loss would be informed by reliable algorithms to identify fast bone losers. However, these are not readily available.

**Objectives:** In this analysis of 14 years prospective population-based data, we aim to identify predictors of the bone mineral density (BMD) loss in the perimenopausal and elderly population.

**Methods:** This study included members of the general population aged 40+years from the longitudinal cohort SAOL (individuals aged 18+years randomly selected from a local county of Coimbra, Portugal). The included individuals answered validated self-reported questionnaires at baseline (1997–2000) comprising questions on osteoporosis risk factors and medication use and underwent a Dual-energy x-ray absorptiometry (DXA) of the proximal femur (PF) and lumbar spine (LS). These procedures were repeated at follow-up (2011–2014). Demographic characteristics and DXA BMD details were descriptively summarised at baseline.



Annual percentage changes of total BMD ( $\text{g}/\text{cm}^2$ ) in the PF and LS were computed (annual  $\Delta\text{BMD}$ ). The relationship between annual  $\Delta\text{BMD}$  and potential predictors was assessed by independent-samples t-test or Pearson correlations, according to the categorical or continuous nature of the independent variable. The baseline independent variables included were: age (years); gender; body mass index ( $\text{kg}/\text{m}^2$ ); smoking, alcohol intake, rheumatoid arthritis, glucocorticoid treatment and secondary osteoporosis according to FRAX algorithm definitions. The follow-up reported calcium/vitamin D supplementation and treatment with bisphosphonates, for at least 1 year (yes/no), were also considered as independent variables. We used linear regression models (enter method) to estimate the possible association between socio-demographic/clinical variables and the BMD changes of PF and LS. The predictor variables included in the model were selected *a priori* based on variables that were associated with annual  $\Delta\text{BMD}$  on univariate analysis. Results were considered significant when  $p < 0.05$ .

**Results:** This analysis included data from 636 individuals (mean ( $\pm\text{SD}$ ) age of 53  $\pm 8$  years, 76% female). The mean ( $\pm\text{SD}$ ) follow-up period was 13.6  $\pm 1.1$  years. Baseline mean ( $\pm\text{SD}$ ) BMD of the PF and LS were 0.77  $\pm 0.004$  and 0.94  $\pm 0.132$ , respectively. The mean ( $\pm\text{SD}$ ) percentage of annual bone loss was: -0.19  $\pm 1.02$  for PF and -0.06  $\pm 0.84$  for LS. On univariate analysis,  $\Delta\text{BMD}$  at both the PF and LS was significantly associated with gender ( $p < 0.001$ ). Annual  $\Delta\text{BMD}$  was also associated with vitamin D supplements ( $p = 0.014$ ) at PF, and with calcium supplements ( $p = 0.002$ ) and bisphosphonate treatment ( $p = 0.027$ ) at LS. On multiple linear regression analysis, female gender persisted as a predictor of faster BMD loss in both PF ( $p < 0.001$ ) and LS ( $p = 0.006$ ). While bisphosphonate treatment didn't predict the annual bone loss, vitamin D and calcium supplementation persisted as predictors of lower annual  $\Delta\text{BMD}$  at PF ( $p = 0.034$ ) and LS ( $p = 0.033$ ), respectively.

**Conclusions:** Our results confirm that the rate of BMD loss at PF and LS over 14 years is significantly associated with gender. Vitamin D and calcium supplementation appeared to have a role in the prevention of bone loss in this general population cohort.

**Disclosure of Interest:** None declared

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#### THU0492 PRELIMINARY STUDY OF THE BONE MASS IN LUNG TRANSPLANTED PATIENTS IN TREATMENT WITH DENOSUMAB

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**Background:** Osteoporosis (OP) is a known complication before and after a lung transplant. In addition to altering bone mass, treatment with glucocorticoids alters the bone microarchitecture, conditioning an increased risk of fracture in these patients. Denosumab (Dmab) is a monoclonal antibody approved for the treatment of postmenopausal OP and its use for corticoid OP is pending approval.

**Objectives:** To describe the subcohort of lung transplant patients who have been treated with Dmab. To study the evolution of bone mass in patients with lung transplantation, with OP induced by glucocorticoids, treated with Dmab.

**Methods:** We included 19 lung transplant patients between 1995 and 2017 controlled in rheumatology for OP and in treatment with Dmab. Of these 19 patients, the evolution of bone mass of the 9 patients who have completed a minimum of 12 months of treatment is shown. Bone densitometry (DXA) was performed on a General Electric Healthcare Lunar Prodigy Advance 15 version densitometer, before and after treatment with Dmab. Demographic data of the patients were collected, the diagnosis of the disease that motivated the transplant, the glucocorticoid doses before and after the transplant, as well as the immunosuppressive treatment. In the 9 patients with DXA follow-up, the 3D-SHAPER software was applied in the DXA before and after the transplant.

**Results:** We included 19 patients (10 women) with a mean age of 58.6 years  $\pm 11.4$ . The diagnosis of the disease that led to the transplant was in 4 COPD patients, 6 patients with pulmonary fibrosis or diffuse interstitial disease, 2 with bronchiectasis, 2 patients with cystic fibrosis, 1 with histiocytosis X, 2 with lymphangioleiomyomatosis, 1 with bronchiolitis obliterans and 1 patient with pulmonary hypertension. Before transplantation, 8 patients (42.1%) had required high doses of glucocorticoids. The prevalence of OP prior to start Dmab treatment in the 19 lung transplant patients was 94.7%. The means of BMD in  $\text{g}/\text{cm}^2$  and T-score before treatment with Dmab and the results of the 3D-SHAPER are shown in table 1.

	DMO $\text{g}/\text{cm}^2$	T-score
Lumbar spine	0,909 $\pm 0,13$	-2,40 $\pm 1,08$
Femoral Neck	0,708 $\pm 0,94$	-2,50 $\pm 0,77$
Total Hip	0,702 $\pm 0,86$	-2,73 $\pm 0,59$
Cortical Density ( $\text{g}/\text{cm}^2$ )	109,3 $\pm 7,7$	-2,9 $\pm 0,3$ ‡
Trabecular vBMD ( $\text{g}/\text{cm}^3$ )	85,7 $\pm 21,4$	-2,9 $\pm 0,8$ ‡
Integral vBMD ( $\text{g}/\text{cm}^3$ )	198,7 $\pm 19$	-3,3 $\pm 0,5$ ‡

The mean time in which the DXA was performed prior to the treatment with Dmab with respect to the transplant date was 4.31  $\pm 5.83$  years. The mean time in which the DXA was performed after the start of Dmab was 19  $\pm 4.17$  months. The results of the evolutionary BMD, the 3D-SHAPER study and its percentage of change are shown in table 2. Of these 9 patients, 88.9% had received osteoactive treatment before Dmab, 5 with oral bisphosphonates and 3 with endovenous bisphosphonates. The mean time of treatment with bisphosphonates until the onset of Dmab was 5.4 years. There were no significant differences in BMD evolution between patients treated for OP prior to Dmab and those not treated, nor for 3D-SHAPER.

		Tx (9)	
OP pre-Dmab		8 (88,9%)	
OP post-Dmab		8 (88,9%)	
DMO post-Dmab (mean)		$\text{g}/\text{cm}^2$	T-score
-	L1-L4	0,949 $\pm 0,13$	-2,05 $\pm 1,07$
-	CF	0,722 $\pm 0,12$	-1,86 $\pm 2,22$
-	FT	0,696 $\pm 0,06$	-2,76 $\pm 0,49$
% change DMO			
-	L1-L4	8,42 $\pm 6,64$ *	
-	CF	2,21 $\pm 6,55$ *	
-	FT	2,80 $\pm 3,56$ *	
High GC dose pre-Transplant		2 (22,2%)	
3D-SHAPER (mean):			
-	Cortical Density ( $\text{g}/\text{cm}^2$ )	113,7 $\pm 10$	
-	Trabecular vBMD ( $\text{g}/\text{cm}^3$ )	88,5 $\pm 23,7$	
-	Integral vBMD ( $\text{g}/\text{cm}^3$ )	203,7 $\pm 24,4$	
% change 3D-SHAPER:			
-	Cortical Density	4,13 $\pm 4,5$	
-	Trabecular vBMD	3,4 $\pm 10,9$	
-	Integral vBMD	2,6 $\pm 7,7$	

**Conclusions:** All patients who started treatment with Dmab had a diagnosis of OP except one patient with osteopenia. The mean increase in BMD in patients treated with Dmab was significant in all the regions assessed, being higher in the lumbar spine. There was an increase in cortical density, trabecular volumetric BMD and integral volumetric BMD after Dmab treatment, although this increase was not significant for any of the three parameters.

**Disclosure of Interest:** None declared

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#### THU0493 ARE BISPHOSPHONATES SOLELY RESPONSIBLE FOR ATYPICAL FEMORAL FRACTURES? A CASE SERIES

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**Background:** Atypical femoral fracture (AFF) is an uncommon but important type of fracture. It is concerning because of the associated morbidity, bilateral nature of the condition and delay in healing which has significant implications on the health of the patients.

**Objectives:** To identify other risk factors contributing to development of atypical femoral fractures in our cohort of patients presenting to the fracture liaison service.

**Methods:** We identified a case series of 18 cases were retrospectively from June 2006 to January 2018 through the cohort of patients presenting to the fracture liaison service at Yeovil District Hospital NHS foundation trust, with features suggestive of Atypical femoral fractures. Individual patient cases were evaluated and notes and images reviewed. Atypical femoral fractures were diagnosed according to the 2013 American society of mineral and bone research (ASMBR) criteria. Demographic and co morbidity status was investigated from case notes. Blood results and dual energy x-ray absorptiometry (DEXA) images were accessed through electronic patient records. The results were compiled with Microsoft excel.

**Results:** There were total 22 patient episodes, of which 4 patients had bilateral symptoms. Female to male ratio was 21:1. Median age of presentation was 71. The incidence of AFF was more in shaft fractures. 54% cases had prodromal symptoms lasting from 1-3 months. 9 cases had radiographic evidence of stress fractures of whom 6 were not identified until they fractured. 86% cases had either concurrent or previous bisphosphonate therapy. Duration of Bisphosphonate therapy was variable from 12 months to 30 years. 54% were taking Proton pump inhibitors and 41% were on long term glucocorticoids. 9% were active smokers. 50% episodes were in patients having two or more risk factors. 3 patients had no risk factors identified.

Conclusions: Exposure to Bisphosphonates remains a major risk factor for development of AFF but our case series has shown that other risk factors do play an important part eg. prolonged courses of glucocorticoids and Proton pump inhibitor therapy. It is plausible that bisphosphonates are given for prolonged courses in patients on glucocorticoids and this combination seems to be a particular risk. The risk appears to be greater with multiple risk factors. The temporal relationship of fractures with relation to bisphosphonate therapy cannot be determined as it can happen even after the cessation of therapy. Further longitudinal and larger studies are required to identify whether Bisphosphonate would play a role to reduce the risk of Atypical Femoral fractures.

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#### THU0494 THE EFFICACY OF DENOSUMAB IN GLUCOCORTICOID-INDUCED OSTEOPOROSIS DID NOT DEPEND ON PRIOR TREATMENT BUT WAS AFFECTED BY THE DOSAGE OF GLUCOCORTICOID

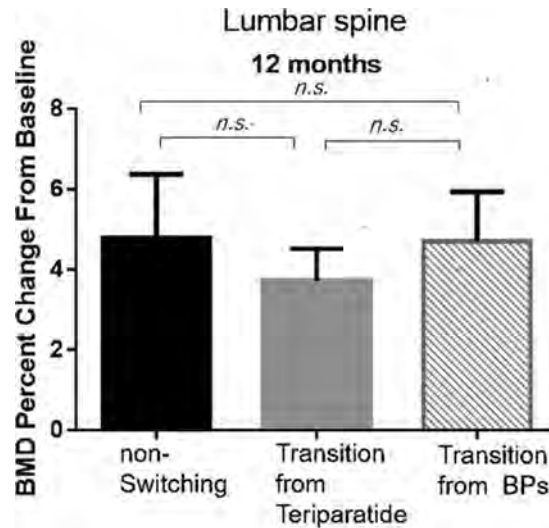
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**Background:** Despite of the good clinical efficacy of denosumab for primary osteoporosis, 2017 American College of Rheumatology guideline for treatment of glucocorticoid-induced osteoporosis (GIOP) placed denosumab as second-line treatment because of lack of clinical experiences with concomitantly use of immunosuppressive agents. Moreover, recently large phase 3 study in primary osteoporosis revealed that transition from teriparatide to denosumab continuously increased bone mineral density (BMD)<sup>1</sup> However, there is still remain unclear whether prior treatment affect to the efficacy of denosumab in GIOP.

**Objectives:** The aim of this study is to compare the therapeutic effect of denosumab in GIOP between previous anti-osteoporotic treatments, and to investigate the factor that influence the efficacy of denosumab in GIOP.

**Methods:** Sixty-six patients for whom treated by denosumab, were enrolled. All patients were receiving several dosages of prednisolone (PSL) (2–20 mg) for RA and connective tissue diseases at initiation of denosumab. 23 patients had been treated with daily teriparatide and 27 patients had been treated with bisphosphonate (BPs) prior to denosumab. The rest 16 patients had not been treated by anti-osteoporosis medication at initiation of denosumab. We evaluated BMD at lumbar spine and bone turnover markers (NTX, BAP and P1NP) every 6 months for 12 months. The changes in BMD was compared among these 3 groups at 6 months and at 12 months. To assess the factors which influences clinical response of denosumab in GIOP, univariate and multivariable ordinal logistic regression analyses were used.

**Results:** Mean percentage change in BMD of lumbar spine from baseline to 6 and 12 months were significant (2.85% increased;  $p < 0.0001$  and 4.40% increased;  $p < 0.0001$ , respectively) Gains higher than 3% were observed in 68.2%. Whereas, the subjects who showed decrement of BMD at 12 months were few (16.67%). All bone turnover markers determined in this study were decreased at 6 months. Transition from BPs to denosumab further increase BMD at 12 months as compared to transition from teriparatide to denosumab (4.71% increased, 3.71% increased, respectively). However, difference among these 2 groups was not significant and furthermore, the changes in BMD in patients who did no transition from anti-osteoporosis medication to denosumab also showed no significant difference (figure 1). Univariate analysis showed that dosage/duration of PSL, body weight and gender were associated with BMD increase higher than 3% at 12 months. Among these candidates, multivariable logistic analysis showed that dose of PSL was independently associated with clinical response of denosumab (OR 1.36, 95% CI 1.045–1.761  $P < 0.01$ ). No hypocalcemia and osteonecrosis of the jaw was observed during the study period.



**Conclusions:** Our present study demonstrated that denosumab increased BMD in GIOP regardless of prior anti-osteoporotic treatment in 'real-world' settings. We should consider denosumab treatment for GIOP, especially who are treated by much dose of glucocorticoids or at the time when the efficacy of BPs is diminished.

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**Disclosure of Interest:** None declared

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#### THU0495 INDICES OF VERTEBRAL PAIN SYNDROME, PHYSICAL PERFORMANCE AND QUALITY OF LIFE IN OLDER AGE WOMEN WITH VERTEBRAL FRACTURES DEPENDING ON THEIR QUANTITY AND LOCALIZATION

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**Background:** Nowadays, vertebral fractures (VF) are one of the frequent and severe complications of systemic osteoporosis, which lead to severe spine pain, restriction of physical activity, increased disability and mortality, however, the data about their particularities depending on their quantity and localization are limited. The purpose was to study the indices of vertebral pain syndrome, physical performance, disability and quality of life in women of older age groups with VF depending on their number and localization.

**Objectives:** We examined 230 women aged 50–89 years old, which were divided into 2 groups: I – patients without any history of osteoporotic fractures (n=151), II – women with VF at thoracic and/or lumbar spine (n=79). Subsequently, the persons of the second group were divided into subgroups depending on the number (1 or 2 and more) and localization (thoracic, lumbar spine or combined) VF.

**Methods:** The presence and intensity of pain in the thoracic and lumbar spine were evaluated using the 11-component visual analogue scale (VAS), the level of physical performance was evaluated using static and dynamic functional tests (FT) (Thomayer, Schober tests, chest excursion, lateral trunk lean, 3-, 4-, 15-metre tests, "stand up from the chair", static balancing); disturbance of life was determined using Roland-Morris questionnaire, quality of life - EuroQol-5D questionnaire.

**Results:** It was demonstrated that the intensity of vertebral pain (pain at the time of investigation, the most common level of pain, pain in the best periods of the disease) is significantly worse in women with VF than corresponding parameters in persons without fractures. It was found that women with 2 and more VF have worse values of majority of measured FT (results of Schober test, lateral trunk lean, chest excursion, breath holding, hand grip strength, 15-metre test) in comparison with control group, while in women with 1 VF only results of Schober test and breath holding were significantly worse than same ones in control group. It was shown that for women with VF at the thoracic spine, results of breath holding

and 15-metre tests were significantly worse compared with control, whereas in persons with VF at lumbar spine results of Schober index, lateral trunk lean, hand grip strength and test "stand up from the chair" were worse. In patients with combined VF most of the FT (lateral trunk lean, chest excursion, hand grip strength and 15-metre test) were significantly worse in comparison with control group. The Roland-Morris questionnaire score was significantly higher in women with 2 or more VF compared to controls, unlike the women with 1 VF. We did not find any differences in EQ-5D questionnaire score depending on the number and location of VF.

**Conclusions:** Indices of pain assessment and physical performance in women of older age groups have own peculiarities depending on the number and location of VF, which should be taken into account while assessing of physical abilities and developing of rehabilitation programs for people with VF.

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**Disclosure of Interest:** None declared

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#### THU0496 SKELETAL DEFICIT DUE TO ALTERED BONE QUALITY IN TYPE 1 DIABETES MELLITUS

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**Background:** Diabetes mellitus (DM) is associated with osteoporosis and increase fracture risk<sup>1</sup>. Increase fractures in type 1 DM are linked to decrease bone mineral density (BMD) but BMD alone does not explain the increase fracture rate seen in diabetics. Alterations in bone quality which entails bone microarchitecture, material and composition of bone tissue also contributes to diabetic osteopathy<sup>2</sup>. Chronic state of hyperglycaemia, hypoinsulinemia, inflammation, low levels of insulin growth factor-1 (IGF-1), increased marrow adiposity, altered adipokine and endocrine factors, increased cell death and accumulation of advanced glycation products that compromise matrix properties impairs normal bone metabolism in type 1 DM<sup>3</sup>. While BMD is detected clinically using a dual-energy X-ray absorptiometry (DEXA) scan, methods to detect changes in bone quality are limited. Estimating bone markers in serum and urine are used in assessing bone quality. An imbalance in bone remodelling as measured by various bone markers is observed in type I DM. But due to discrepancy in results of various studies the exact mechanisms is still elusive.

**Objectives:** To investigate the underlying mechanism of altered bone quality in type 1 diabetes:

1. By measuring the bone formations and resorption markers.
2. By measuring the advanced glycation end products.
3. By analysing the changes at cellular level in type I diabetes

**Methods:** Experimental diabetes mellitus was induced in 24 Wistar rats by injecting streptozotocin 60 mg/kg body weight intraperitoneally. Rats were sacrificed at 6th, 8th and 12th week of developing diabetes. Blood and bone specimens were collected. Serum levels of osteocalcin, bone alkaline phosphatase, C-terminal cross-linked telopeptide of type-I collagen (CTX) and pentosidine were measured using ELISA to investigate bone turnover in type I DM. The bone specimens were fixed, processed, sectioned and stained for bone histomorphometry<sup>3</sup>. Histological analysis was carried out using an 'Olympus Research Inverted Microscope Model IX53' complete with fluorescent attachment equipped with a DP73 camera (Olympus). Statistical analysis was carried out using sigmastat 4.0.

**Results:** Low levels of osteocalcin and bone alkaline phosphatase and increased levels of pentosidine and CTx levels in serum were found in 6th and 12th week duration of diabetes. Additionally increase number of mast cells  $p < 0.05$  were observed in diabetic bones as compared to control specimens

**Conclusions:** Chronic hyperglycaemic state in type I DM impairs bone remodelling by decreasing bone formation and increasing bone resorption. Increase in advanced glycation end products and mast cells also contribute to diabetic osteopathy.

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#### THU0497 IS THE SECONDARY OSTEOPOROSIS SOMETHING SECONDARY? EXPERIENCE OF A SECONDARY OSTEOPOROSIS CONSULTATION

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**Background:** There are many pathologies and drugs that favour the development of Osteoporosis (OP). Although the prevalence of this secondary OP is very high, sometimes assuming a high risk of fracture, it remains an underdiagnosed and undertreated pathology.

**Objectives:** To assess the characteristics of the patients and bone metabolic pathology referred to a secondary OP consultation.

**Methods:** In order to optimise the management of bone metabolic pathology associated with Rheumatoid Arthritis (RA) and other inflammatory articular diseases, an inflammatory op consultation was founded in april/2012. Faced with the growing demand from other medical specialities, it became a secondary OP Consultation in 2014, 2 days per week. Sociodemographic, clinical, biochemical and densitometric data were collected.

**Results:** 418 patients with a mean age of 58.7±11.3 years were evaluated, 78.9% were women, 15.4% premenopausal. 57.4% of patients had densitometric OP and 25.8% Osteopenia. 22.4% had a fragility fracture (60.6% vertebral, 26.5% peripheral, 1.1% hip, 8.5% peripheral/vertebral). Vitamin D level was deficient in 71% of patients.

The most frequent medical specialities who referred patients to our consultation were Rheumatology (18.9% from early RA Unit and 18.2% from Consultation or Rheumatol. Day Hospital), Gynaecology (12.7%) and Neumology (11.2%). But also, there were patient from Oncology, Endocrinology, Nephrology, Haematology and several more medical specialities.

The most frequent underlying diseases were: breast cancer (22.5%), 77.6% in treatment with aromatase inhibitors, early RA (12.4%) and pulmonary disease (11.5%), 41.6% of them were sarcoidosis, other diseases are shown in table 1.

The glucocorticoid-induced OP represented 30.1% of the sample, with a main age of 60.2±11.4 years, being 73% women, 20.6% premenopausal. The most frequent reasons for the use of corticosteroids were: early RA and pulmonary disease (23% respectively), rheumatic diseases (autoimmune dis.(13.5%), established RA (12%), other inflammatory articular disease(7.9%), multifactorial (8.7%), haematological conditions and kidney transplantation(4% respectively). 42.8% of these patients had densitometric OP and 29.3% osteopenia We found 33 fragility fractures (26.1% of patients), 25 were vertebral (75.7%), peripheral 5 (15.1%) and 3 (9.1%) vertebral and peripheral. In 21.2% of cases, these fractures presented with BMD in the osteopenic range and in 6% with a normal BMD.

DISORDER	N (%)
Breast Cancer	94 (22.5%)
Early RA	52 (12.4%)
Endocrinopathies	31 (7.4%)
Pulmonary dis.	48 (11.5%)
Other inflamm. articular dis.	28 (6.7%)
Autoimmune dis.	27 (6.4%)
Multifactorial	27 (6.4%)
Stablished RA	25 (6%)
Digestive dis.	22 (5.3%)
Haematological condition	17 (4%)
Kidney transpl.	12 (2.9%)
Abnormal bone architecture	6 (1.4%)
Nutritional dis.	5 (1.2%)
Prostate Cancer androgenic supp.	5 (1.2%)
Other (HIV, neurological dis,...)	19 (4.5%)

**Conclusions:** There are multiple processes that can associate bone metabolic pathology or a secondary OP, with a high prevalence of fragility fracture in these patients, being the rheumatologist a reference for the management of this comorbidity. A monographic consultation of secondary OP has been useful for other medical specialities and to optimise the management of OP associated with inflammatory/autoimmune diseases in Rheumatology

**Disclosure of Interest:** None declared

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THU0498

### CORE ENDURANCE AND POSTURAL STABILITY IMPAIRMENTS IN OSTEOPOROTIC WOMEN: A CASE-CONTROL STUDY

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**Background:** Crosstalk between bone and muscle has been focused, lately.<sup>1</sup> Any impairment in bone quality may affect core muscle endurance and whole postural control.<sup>2,3</sup>

**Objectives:** This study aimed to compare core muscle endurance and postural stability in women with and without osteoporosis.

**Methods:** Women with (n: 40, age: 59.16±6.83 years, body mass index (BMI): 31.46±5.44 kg/m<sup>2</sup>) and without osteoporosis (Controls, n: 36, age: 56.10±7.17 years, BMI: 33.81±5.32 kg/m<sup>2</sup>) were recruited. Core endurance was assessed with McGill's trunk muscle endurance tests in seconds.<sup>4</sup> Postural stability were evaluated with Biodex Balance System SD in static-dynamic, eyes-open and closed conditions. Independent sample *t* and Mann Whitney U tests were used for analysis.

**Results:** The ages and BMI of the groups were similar (*p*>0.05). The following scores were found respectively in osteoporotic women and controls: the endurance of trunk flexor [15.0 (20.0)/17.5 (15.2) s]; back extensor [9.0 (16.0)/12.5 (22.2) s], right lateral [0.0 (7.0)/6.5 (20.0) s] and left lateral muscles [0.0 (8.0)/5.0 (20.0) s], static eyes-open [1.93±0.80/1.44±0.86] and eyes-closed [2.46±1.71/1.68±0.73], dynamic eyes-open [3.08±1.95/2.86±1.39] and eyes-closed [6.31±2.31/5.40±1.24] postural stability. Lateral trunk muscle endurance decreased, static and dynamic eyes-closed instability increased in women with osteoporosis in comparison to women without osteoporosis (*p*<0.05). No differences were found in trunk flexor and back extensor muscle endurance, and static and dynamic eyes open stability scores (*p*>0.05).

**Conclusions:** Lateral core muscle endurance and static and dynamic eyes-closed postural stability impairments were observed in osteoporotic women. It might be appropriate to be aware of these deficits for prevention programs.

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THU0499

### THE EFFECT OF CONCOMITANT TYPE OF VITAMIN D, BIOLOGICAL DMARDS AND DISEASE ACTIVITY FOR THERAPEUTIC EFFECT OF DENOSUMAB IN OSTEOPOROTIC PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Osteoporosis is one of the major comorbidity in patients with rheumatoid arthritis (RA). There are a lot of evidence that denosumab increase bone mineral density (BMD) in patients with osteoporosis. However, there are few reports investigated the influence of denosumab in patients with RA.

**Objectives:** We evaluated the BMD change in patients with RA treated denosumab and assessed the effect of various factors, such as the type of vitamin D, biological disease-modifying anti-rheumatic drugs (bDMARDs) use, and disease activity.

**Methods:** This study included 100 RA patients (96 female, mean age 69.9±9.3 years) treated with denosumab. BMD at the lumbar spine and proximal femoral were evaluated by dual energy X-ray absorptiometry (DXA) at baseline and

1 year after treatment. We evaluated the influence of the type of vitamin D, bDMARDs and disease activity for BMD change.

**Results:** In all patients, BMD at the lumbar spine, proximal femoral and femoral neck were significantly increased in one years (6.2%: *p*<0.01, 4.0%: *p*<0.01, 2.2%: *p*=0.04, respectively). There were no significant differences in improvement ratio of BMD between 10 patients taking active form vitamin D and 71 patients taking native form vitamin D (7.7 vs 4.4%: *p*=0.55, 4.3 vs 4.0%: *p*=0.83, 1.4 vs 4.2%: *p*=0.52), between 30 patients treated with bDMARDs and 57 patients treated without bDMARDs (6.4 vs 6.2%: *p*=0.3, 2.7 vs 4.5%: *p*=0.95, 1.1 vs 2.5%: *p*=0.2), between 61 patients in remission or low disease activity and 26 patients in moderate or high disease activity (7.2 vs 4.0%: *p*=0.25, 3.3 vs 5.0%: *p*=0.87, 1.6 vs 3.8%: *p*=0.98) (figure 1).

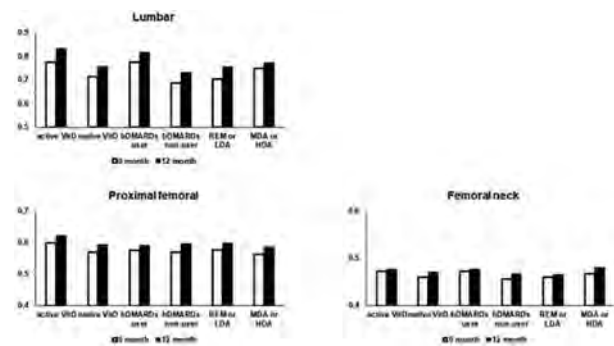


Figure 1. BMD change

**Conclusions:** Denosumab improved BMD in patients with RA independently regardless of the type of vitamin D, bDMARDs use, disease activity.

**Disclosure of Interest:** None declared

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THU0500

### EFFECTS OF LONG-TERM USE OF UNFRACTIONATED HEPARIN (UFH) OR LOW-MOLECULAR-WEIGHT HEPARIN (LMWH) ON BONE MINERAL DENSITY (BMD) IN PATIENTS WITH NEPHROTIC SYNDROME

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**Background:** Osteoporosis is a systemic skeletal disease characterised by decreased bone mass and micro- and macroarchitectural tissue alterations, resulting in bone fragility and increased fracture risk. Generalised osteoporosis is a result of different causes and pathogenic mechanisms, which often combine forces to become clinically relevant. Among the different exogenous factors, several drugs have been associated with increased risk of osteoporosis, when used chronically.

**Objectives:** The aim of this study is to determine the effects of UFH or LMWH therapy of at least 1 year duration on bone mineral density BMD in patients with nephrotic syndrome (NS).

**Methods:** All patients undergoing native renal biopsy for NS between 2006 and 2017 yielding a diagnosis of primary glomerulonephritis were identified. Baseline serum albumin, proteinuria, estimated glomerular filtration rate, date of biopsy and histological diagnosis were recorded. 465 (238 male, 227 female) patients with nephrotic syndrome received the prophylactic anticoagulation regimen were included. Mean age at biopsy was 43,8±19,2 years. Median follow-up was 5,3±2,4 years. In addition to the prophylactic anticoagulation regimen, patients received treatment for their underlying glomerulopathy. This included optimising blood pressure control, renin-angiotensin system blockade, and prescribing immunosuppressive therapy if indicated. Patients received corticosteroid treatment or with renal failure were excluded from the study. 312 patients (67,1%) received treatment with UFH and 153 - with LMWH at some point in the course of their disease. There was no difference in mean age, sex, or disease duration between both groups. 276 patients were switched from UFH or LMWH to acenocoumarol as a result of protracted hypoalbuminemia (serum albumin <2.0 g/dl) at a median time of 24,3±9,3 weeks' treatment. The anticoagulant control achieved in these patients was good. Bone mineral density (BMD) was measured at the lumbar spine and total hip region with dual x-ray absorptiometry.

**Results:** Results of Poisson regression analysis showed that LMWH therapy was associated with a lower risk of osteoporosis compared with UFH (0,7 vs 1,1 per 100 person-years). No statistically significant increase in the risk of fractures at 12 months was found for patients (RR = 1, 03; 95% CI: 0,27-3,34). UFH for 24

months decreased mean BMD by 2.6–3.5% (depending on the BMD site) compared to mean BMD decreases of 1.9–2.9% with LMWH. BMD of the spine and hip is significantly lower in patients with LMWH therapy than in subjects with UFH therapy, which is independent of age, sex, menopause, low BMI and altered body composition.

**Conclusions:** LMWH most likely have less effect on bone turnover when compared to UFH. LMWH for 6 months may not increase the risk of osteoporosis, but longer exposure for up to 24 months may adversely affect BMD. Clinicians should consider monitoring BMD in adults on long-term heparin therapy who are at increased risk of bone loss or fracture.

**Disclosure of Interest:** None declared

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#### THU0501 WHAT DOES TRABECULAR BONE SCORE CONTRIBUTE TO A FRACTURE LIAISON SERVICE?

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**Background:** The utility of the trabecular bone score (TBS) is controversial.

**Objectives:** To analyse the clinical usefulness of FRAX-TBS in patients with fragility fracture seen in a Fracture Liaison Service (FLS) compared to FRAX without TBS.

**Methods:** Consecutive outpatients >50 y seen in our FLS were included, excluding patients admitted with hip fracture. The variables included were: age, sex, type of fracture, risk factors for FRAX, FRAX for major and hip fractures with and without TBS, bone densitometry (DXA) and indication of treatment to prevent new fractures.

**Results:** We included 251 patients, mean age 69 y, 86% women. The most frequent type of fracture was the forearm (n=122) followed by the humerus (n=64). The DXA scan results (taking the lowest value of column/hip) was osteoporosis in 41%. The average TBS was 1.307 (SD 0.103, range 0.961–1.550): forearm fracture 1.313 (SD 0.102), vertebra 1.281 (SD 0.131) and hip 1.291 (SD 0.103). 32% presented normal TBS result 53% partially degraded and 15% degraded (table 1). The results of FRAX with and without TBS were similar, with an average for major/hip fracture of 10.7/4.2 with DXA and 10.6/4.0 with TBS respectively (p>0.05). A high risk of hip fracture (FRAX ≥3) was observed in 43% of patients using FRAX-DXA and 41% using FRAX-TBS. A high risk of major fracture (FRAX ≥10) in 40% of patients using FRAX-DXA and 41% using FRAX-TBS. In 241 cases (96%) there was concordance in level of risk for FRAX-DXA and FRAX-TBS, while the 10 discordant cases for high risk of fracture were distributed as follows: in 6 cases FRAX-DXA was high and FRAX-TBS was normal, and in 4 cases FRAX-DXA was normal and FRAX-TBS was elevated. In our FLS, a bisphosphonate was prescribed to 169 patients (67%). Regarding patients with a low FRAX risk (n=82), in one patient FRAX-TBS was in favour of treatment. Thus, in 1/251 fractures FRAX-TBS could have influenced the treatment indication compared to FRAX-DXA.

	TBS≥1.350 Normal	TBS<1.350 y≥1.200 partially degraded	TBS<1.200 Degraded
Number of patients	80	134	37
Age, mean (SD)	67 (11)	70 (10)	71 (10)
Sex, women, n (%)	65 (81)	124 (92)	33 (92)
<b>Risk factors, n (%)</b>			
BMI, mean	27	29	31
Previous fracture	8 (10)	34 (25)	7 (19)
Parent's hip fracture	8 (10)	21 (16)	2 (5)
Glucocorticoids	6 (8)	5 (4)	5 (13)
Smoking	9 (11)	20 (15)	6 (16)
Alcohol	2 (3)	4 (3)	1 (3)
Rheumatoid arthritis	3 (4)	2 (1)	0
Secondary osteoporosis	13 (16)	22 (18)	10 (28)
<b>Bone Densitometry, n (%)</b>			
Normal	24 (30)	7 (5)	3 (8)
Osteopenia	37 (46)	65 (49)	12 (32)
Osteoporosis	19 (24)	62 (46)	22 (60)

**Conclusions:** In our FLS unit, TBS does not help to classify patients' risk. The values of FRAX-TBS are similar to those of FRAX-DXA, not offering advantages when classifying patients with high risk who are candidates for treatment.

**Disclosure of Interest:** None declared

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#### THU0502 ASSESSMENT OF SEVERITY OF ATHEROSCLEROTIC LESIONS OF CAROTID ARTERIES IN MEN WITH CORONARY HEART DISEASE DEPENDING ON BONE MINERAL DENSITY AND RISK OF OSTEOPOROTIC FRACTURES

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**Objectives:** To assess severity of atherosclerotic lesions of carotid arteries (CA) in men with coronary heart disease (CHD) depending on bone mineral density (BMD) and risk of osteoporotic fractures according to FRAX scale.

**Methods:** The study involved 102 men aged 51–75 years (median age of 61<sup>55</sup>; 65 with CHD, verified by coronary angiography method. All patients underwent dual energy X-ray absorptiometry of lumbar vertebral bodies L1-LIV and femoral neck and colour duplex scanning of extracranial arteries. Assessment of severity of carotid atherosclerosis was carried out by presence of atherosclerotic plaques (ASP) and stenosis of CA, thickness of intima-media (TIM) CA. Threshold TIM for men over age of 50 was considered 0.9 mm (recommendations of American Society of Echocardiography, 2008 Based on results of densitometry value of T-criterion (recommendations ISCD, 2007 men were divided into three groups: 33 patients with osteoporosis (OP, T-criterion ≤2.5), 48 patients with osteopenia (OPE, T-criterion of –1 to –2.5) and 21 men with normal BMD (NBMD, T-criterion ≥–1). On the basis of information on the presence of clinical risk factors of osteoporotic fractures and densitometry data at all included in the study patients FRAX calculator was used to quantify probability of major osteoporotic fractures and hip fracture in next 10 years.

**Results:** It was found that 86.3% of patients value TIM exceeds threshold value (0.9 mm). Thickening of intima-media complex was in men with OP in 88.0% of cases, with OPE – in 87.5%, with NBMD – in 81.0% without statistically significant differences (p>0.05). In a comparative analysis of atherosclerotic lesions CA found that men with OP significantly were more likely to have ASP in CA (75.8%) compared to patients with OPE (43.7%, p=0.010) and NBMD (38.1%, p=0.016). Stenosis of CA in all investigated men was discovered in 54 cases (53%). Comparative analysis showed that in patients with OP percentage of patients with stenosis of CA was 2 times more than men with NBMD (75.8% vs 38.1%, p=0.006) and was significantly higher than proportion of such patients in the group with OPE (44.0%, p=0.004). In all included the study patients 10 year absolute risk of major osteoporotic fracture by FRAX was equal to 9.88±7.22, risk of hip fracture – 3.97 ±6.27. There was inverse correlation of TIM with T-criterion (r=–0.21, p=0.035) and with BMD (r=–0.20, p=0.045) at level of hip and reliable direct correlation between TIM and risk of hip fracture by FRAX (r=0.21, p=0.035).

**Conclusions:** In men with CHD aged over 50 years low BMD (T-criterion is less than 2.5) is associated with more severe carotid atherosclerosis, and thickening of intima-media CA – with an increased risk of hip fracture.

**Disclosure of Interest:** None declared

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#### THU0503 COST ANALYSIS OF ANTI-OSTEOPOROTIC DRUGS IN REAL-WORLD CLINICAL PRACTICE

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**Background:** Nonadherence can reduce treatment effectiveness and can negatively affect healthcare costs and thus the treatments' cost-effectiveness. Adherence in the setting of osteoporosis has been shown to be just as problematic, if not worse, than that in other chronic diseases. Economic evaluations based on modelling are commonly used to compare alternative treatment strategies in osteoporosis, to support decision-makers and to inform treatment guidelines.

**Objectives:** The aim of this study is to analyse healthcare costs of osteoporosis and to build a economic model cost-effectiveness of pharmacological interventions based on real world data.

**Methods:** The data of the analysed subjects were drawn from the administrative databases of four Local Health Authorities in the Abruzzo Region. Patients 60 years of age or older were included if at least one prescription for any

antiosteoporosis drugs had been filled in between January 1, 2006 and December 31, 2006. The patients were classified as exposed or not exposed to osteoporotic fracture. For each group, compliance with antiosteoporosis drugs was calculated. Patients were considered compliant if their Medication Possession Ratio (MPR) was  $\geq 80\%$ . The cost analysis was conducted taking each healthcare service into account, i.e. drug therapy, diagnostic tests and hospitalisation admissions, during the study period. A hypothetical scenario based on the real-life available evidence was constructed. The mean level of adherence to populate the hypothetical scenario of "full adherence" was set at  $MPR > 80\%$ . The model built by adding a step value, constrained by a normal random variable, to the real-world adherence of each subject so that the subject shifted to the hypothetical scenario of full adherence, in order to quantify the clinical outcome (number of fractures) achievable in the hypothetical scenario. Cost-effectiveness of full adherence compared to real world adherence was expressed in terms of Incremental Cost Effectiveness Ratio (ICER) and the number of fractures avoided was set as an effectiveness unit of measure.

**Results:** The mean annual healthcare cost per fracture avoided was € 247.44, of which medical treatments and diagnostic tests accounted for € 103.60 (41.9%) and € 143.84 (58.1%), respectively. The mean annual healthcare cost per fractured patient was € 1,044.85, of which medical treatments, diagnostic tests and hospitalizations for osteoporotic fracture accounted for € 88.73 (8.5%), € 169.48 (16.2%) and € 786.65 (75.3%), respectively.

**Conclusions:** Costs per fractured patients resulted to be about four times greater than those of not fractured patients. Therefore, only enhancing adherence to medication may lead to reductions in the number of patients requiring hospitalisation.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.6620

#### THU0504 UTILISATION OF ANTI-OSTEOPOROTIC DRUGS IN REAL-WORLD DATA: A STUDY OF GENDER-RELATED DIFFERENCES

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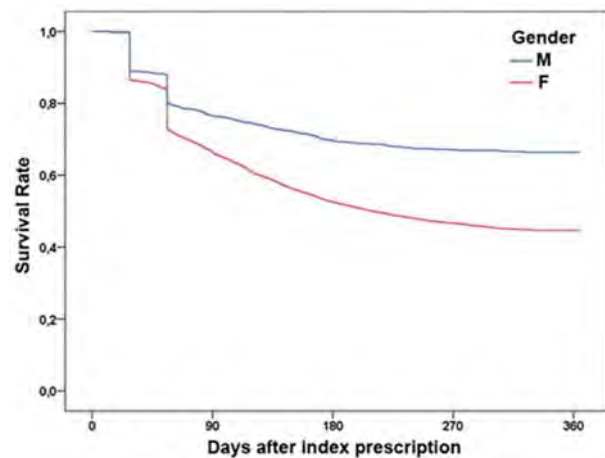
**Background:** Osteoporosis is mostly defined as the disease of women, because the prevalence and fracture rates are much higher in postmenopausal women than in older men. However, there has been increasing recognition that male osteoporosis also represents an important burden as a common cause of morbidity, mortality and health care expenditure. Also, men are more likely than women to have osteoporosis that is undiagnosed and undertreated.

Moreover, bone fracture are important factors of high mortality and morbidity rates in osteoporotic patients. Lack of persistence is common among subjects using oral anti-osteoporotic drugs, and leads to increased risk of fragility fracture.

**Objectives:** The aim of this study is to perform gender specific analysis regarding the persistence to antiosteoporosis drugs.

**Methods:** We conducted a retrospective cohort study using administrative data from four local health authorities in the Abruzzo Region (Central Italy), which comprise about 9 00 000 inhabitants (68% of the overall regional population). Patients 60 years of age or older were included if at least one prescription for any antiosteoporosis drugs had been filled in between January 1, 2006 and December 31, 2006. Persistence estimates over time (discontinuation rates were assessed at 365 days) were derived using Kaplan–Meier survival analysis, stratifying for gender, considering treatment discontinuation as failure event and comparing differences using Log-rank test (1 degree of freedom).

**Results:** The final cohort consisted of a total of 7867 patients (87.2% women). The mean patient age for both genders at the index date was 74.5 years. The crude analysis of long-term gender persistence showed a significant difference between women and men: the relative number of persistence patients after 1 year was 66.4% in men and 44.7% in women. The Kaplan Meier plots of time to persistence start to differ for men vs women approximately 60 days after treatment start (figure 1).



**Conclusions:** The results showed that gender influences adherence to therapy and this is an issue that could be taken in strong consideration in tailor intervention to improve adherence.

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#### THU0505 INFLUENCE OF ORAL PREDNISOLONE ON EFFECT OF DENOSUMAB ON OSTEOPOROSIS IN PATIENTS WITH JAPANESE RHEUMATOID ARTHRITIS; 36 MONTHS OF FOLLOW-UP –A MULTICENTER REGISTRY STUDY–

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**Background:** Denosumab (DMB) is a fully human monoclonal antibody to the receptor activator of nuclear factor-kappaB ligand (RANKL) that blocks its binding RANK, inhibiting the development and activity of osteoclasts, decreasing bone resorption, increasing bone density and reducing fracture risk. Osteoporosis(OP) is more frequent in patients with rheumatoid arthritis(RA) than in the general population due to active systemic inflammation as well as the use of glucocorticoid and immobility. We investigated the influence of oral prednisolone on effect of DMB in patients with Japanese RA from initiation to 36 months at this time.

**Objectives:** This prospective study investigated the efficacy of DMB for 36 months on glucocorticoid-induced OP in RA patients.

**Methods:** Patients with a diagnosis of RA according to the 2010 ACR/EULAR criteria who had been prescribed DMB from Tsurumi Biologics Communication Registry (TBCR)-BONE between October 2013 and October 2014 were enrolled. The final study cohort of 56 patients received continuous DMB therapy more than 36 months. The DMB dose was 60 mg at once every 6 months. In all cases native or activated vitamin D has been used. We reviewed the results for 36 months about the increase and decrease of bone mineral density(BMD) of lumbar spine (LS) and total hip (TH) by DEXA and bone turnover markers, intact n-terminal propeptide type I procollagen(PINP) and tartrate-resistant acid phosphatase form 5b (TRACP-5b).

**Results:** In the patients receiving oral prednisolone group(n=20, GC+) and not receiving group(n=36, GC-), the number of female was each 18 (90%) and 35 (98%) cases(p=0.288). The mean age was 69.5±7.0 and 70.5±6.6 years old (p=0.700); disease duration was 15.9±9.5 and 16.3±13.7 years (p=0.688); the body mass index was 20.6±3.5 and 19.5±3.0 (p=0.225) and the FRAX was 33.8



±19.1 and 23.5±13.7 (p=0.024). Clinical findings related to RA and OP at baseline were as follows; CRP 1.2±1.4 and 0.4±1.0 mg/dl(p=0.012); DAS-CRP 3.14 ±1.24 and 2.40±1.24(p=0.019); m-HAQ 1.27±0.81 and 0.70±0.73(p=0.018); P1NP 59.7±41.3 and 53.0±26.2 µg/L(p=0.694); TRACP-5b 528±269 and 493 ±192 mU/dL (p=0.986); LS-BMD 0.86±0.20 and 0.81±0.16 g/cm<sup>2</sup>(p=0.285) and TH-BMD 0.60±0.12 and 0.60±0.08 g/cm<sup>2</sup> (p=0.899). The rate of decreased P1NP from baseline to 6, 12, 24 and 36 months were each -20.6% vs -40.0% (p=0.110) at 6 month, -3.5% vs -42.0% (p=0.046) at 12 month, -8.7% vs -32.4% (p=0.113) at 24 month and -16.8% vs -33.7% (p=0.215) at 36 month and TRAC-5b were -25.9% vs -39.6% (p=0.847) at 6 month, -17.5% vs -36.4% (p=0.111) at 12 month, -19.5% vs -30.3% (p=0.521) at 24 month and -20.2% vs -29.5% (p=0.513) at 36 month in the GS +vs GS- group. The rate of increased LS-BMD from baseline to 6, 12, 24 and 36 months were each 4.1% (p=0.753) at 6 month, 5.5% vs 6.7% (p=0.587) at 12 month, 10.4% vs 7.3% (p=0.043) at 24 month and 12.3% vs 12.6% (p=0.738) at 36 month and TH-BMD were 3.3% vs 3.2% (p=0.892) at 6 month, 1.3% vs 4.3% (p=0.751) at 12 month, 6.2% vs 5.0% (p=0.838) at 24 month and 8.4% vs 6.0% (p=0.889) at 36 month in the GS +vs GS- group (figure1 and 2).

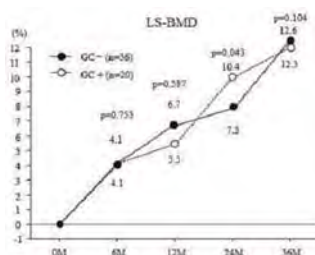


Figure 1. The rate of increased LS-BMD from baseline to 36 month

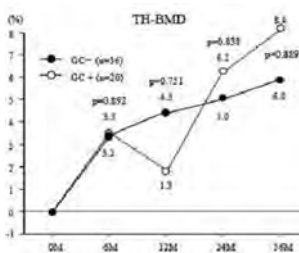


Figure 2. The rate of increased TH-BMD from baseline to 36 month

**Conclusions:** DMB was effective in OP of RA patients. Oral prednisolone use did not influence the efficacy of DMB for 36 months.

**Disclosure of Interest:** Y. Kanayama: None declared, Y. Hirano Speakers bureau: Abbvie Japan, Eisai, Mitsubishi Tanabe Pharma, Pfizer, Chugai Pharmaceutical, and Bristol-Myers Squibb., N. Takahashi Speakers bureau: Abbvie Japan Co. Ltd, Eisai Co. Ltd, UCB Japan Co. Ltd, Mitsubishi Tanabe Pharma Corporation, Takeda Pharmaceutical Company Ltd, Pfizer Co. Ltd, Chugai Pharmaceutical Co. Ltd, Janssen Pharmaceutical K.K., and Bristol-Myers Squibb Co. Ltd., S. Asai: None declared, N. Ishiguro Grant/research support from: Daiichi Sankyo, Takeda Pharmaceutical, Kaken Pharmaceutical, Eisai, Janssen Pharmaceutical, Bristol-Myers Squibb, AbbVie, Chugai Pharmaceutical, Mitsubishi Tanabe Pharmaceutical, Astellas Pharma, and Pfizer Japan, Speakers bureau: Daiichi Sankyo, Takeda Pharmaceutical, Hisamitsu Pharmaceutical, Otsuka Pharmaceutical, Taisho Toyama Pharmaceutical, Kaken Pharmaceutical, Eisai, Janssen Pharmaceutical, Bristol-Myers Squibb, AbbVie, Chugai Pharmaceutical, Mitsubishi Tanabe Pharmaceutical, Astellas Pharma, and Pfizer Japan., T. Kojima Speakers bureau: Mitsubishi Tanabe Pharma, Takeda Pharma, Eisai Pharma, AbbVie, Bristol-Myers Squibb, and Pfizer, Janssenn Pharmaceutical Companies, Astellas Pharma and Chugai Pharma.

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THURSDAY, 14 JUNE 2018

## Fibromyalgia

### THU0506 CROSS-SECTIONAL ANALYSIS OF THE ASSOCIATIONS BETWEEN FIBROMYALGIA AND CANCER

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**Background:** Fibromyalgia syndrome (FMS) is defined as chronic widespread musculoskeletal pain and tenderness with concomitant mood and cognitive dysfunction. Several comorbidities have been reported to be associated with FMS. However, these studies are mostly based on small populations and lack solid evidence.

**Objectives:** To evaluate the association of FMS with Cancer diagnoses.

**Methods:** This cross-sectional study used the database of the largest Health Maintenance Organisation in Israel, Clalit Health Services, serving more than 4 million members. FMS patients were compared to age- and sex-matched controls regarding comorbid Cancer diagnoses. Chi-square and t-tests were used for univariate analysis.

**Results:** Our study utilised data from 14,296 FMS patients and 71 324 age- and sex-matched controls. FMS patients compared to controls had a higher proportion of the following types of cancer: Cervix and Uteri, Connective Tissue Sarcoma, Thyroid, Non Hodgkin Lymphoma (NHL) and Benign brain tumours (OR=1.39, 1.60, 1.68, 1.26, 1.87 respectively, P value<0.005) – See table 1.

Characteristics	Fibromyalgia N=14,296	No Fibromyalgia N=71,324	Odds ratio	P-value
Age	55.2±13.9	56.0±13.7	1.00 [0.99,1.00]	<0.001
Females	13210 (92.4%)	65910 (92.4%)	1.00 [0.93,1.07]	0.978
BMI	29.1±6.20	28.0±6.01	1.03 [1.03,1.03]	<0.001
Smoking	4679 (32.7%)	19987 (28.0%)	1.25 [1.20,1.30]	0.000
SES				
Low	6669 (46.8%)	27747 (39.2%)	Ref.	Ref.
Medium	5397 (37.9%)	27499 (38.8%)	0.82 [0.78,0.85]	0.000
High	2192 (15.3%)	15554 (22.0%)	0.58 [0.55,0.61]	0.000
Malignancy diagnosis				
Cervix / Uteri	50 (0.35%)	180 (0.25%)	1.39 [1.01,1.89]	0.046
Connective Tissue Sarcoma	32 (0.22%)	100 (0.14%)	1.60 [1.06,2.36]	0.026
Thyroid	150 (1.05%)	448 (0.63%)	1.68 [1.39,2.02]	<0.001
Non Hodgkin Lymphoma (NHL)	99 (0.69%)	394 (0.55%)	1.26 [1.00,1.56]	0.048
Benign Brain Tumor	182 (1.27%)	490 (0.69%)	1.87 [1.57,2.21]	<0.001

Adjusted for age, sex, SES, smoking and BMI  
 BMI: Body mass index, kg/m<sup>2</sup>; SES: Socioeconomic status

Figure 1. BMI: Body mass index, kg/m<sup>2</sup>; SES: Socioeconomic status

**Conclusions:** Study results show a higher proportion of malignancy diagnoses amongst FMS patients compared to matched controls. Accordingly, in treating FMS patients, physicians should bear in mind the likelihood of concomitant tumour as it might explain various FMS symptoms, and more importantly, shorten a patients' time for diagnosis and treatment of the oncological condition.

**Disclosure of Interest:** None declared

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THU0507

### HETEROGENITY OF FIBROMYALGIA: PSYCHOPATHOLOGICAL CHARACTERISTICS OF DIFFERENT SUBTYPES AND EFFICACY OF THERAPY

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**Background:** fibromyalgia (FM) is one of the most complicated diseases in the rheumatology and therapeutic practice. Despite the relative success in diagnosing pathology and developing new diagnostic criteria, the treatment of FM remains uncertain. This, in particular, may be due to the presence of various subtypes of disease, which differ in their pathogenesis and, therefore, require differentiated therapy.

**Objectives:** to identify the subtypes of FM, to determine their basic psychopathological characteristics and adherence to therapy.

**Methods:** the study included 104 patients with FM according to 2010/2011 diagnostic criteria. All patients were questioned about their attitudes towards employment and sports, and determined the level of anxiety and depression by the HADS scale, as well as therapy compliance 2 months later.

**Results:** the results obtained support the presence of five subtypes of FM. Patients with a high level of anxiety (10.57±2.87) and minimal widespread pain index (WPI) (6.30±6.04) were included in Group 1. This group consisted of 40.35% of the total number of patients with the minimum average age (45 years) and the highest ratio of men/women (8/38). Group 1 was also characterised by the greatest employment (34 of 46 patients) and a relatively rare abandonment of physical exercises (14 of 46 patients). The second group of patients was conditionally called anxious-depressive because of the frequent detection of both anxiety and depression (11.33±4.64 and 11.67±3.64, respectively) with a moderate number of WPI (10.78±4.09). They differed from the Group 1 by mainly female sex and more frequent avoidance of physical exercises (8 of 18 patients). Group 3 (the proposed name is hysteroid) consisted of women with the maximum number of WPI (14.33±4.22) and low levels of anxiety and depression. Despite the average working age, they were mostly unemployed with the lowest level of adherence to physical activity (4 of 24 patients). The fourth subtype of FM consisted of patients with concomitant chronic diseases. They were expected to be the oldest (68 years on average) with a high number of painful areas (13.44±5.0), low levels of anxiety and depression. All of them refused to perform physical exercises and were unemployed. Finally, Group 5 included patients without concomitant affective and somatic disorders. This group has taken the middle position for all indicators, except the lowest level of anxiety and depression among all groups.

The lowest rates of therapy compliance were demonstrated in Group 3. At the same time, the time of communication with these patients was the maximum.

**Conclusions:** patients with FM are a heterogeneous group, differing in their psychopathological characteristics. Younger patients are more likely to exhibit an elevated level of anxiety and depression and are prone to catastrophize their sensations, while older patients usually have a severe somatic pathology. They are often found in therapeutic practice, which makes it necessary to conduct educational programs on FM diagnostic and management for general practitioners. We consider it very important to identify the hysteroid subtype of FM, since these patients are not inclined to seek recovery and represent a huge difficulty for the treating doctors. We proposed that they use their disease to attract the attention of others.

**Disclosure of Interest:** None declared

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THU0508

### EVALUATION OF TISSUE SPECIFIC AUTOANTIBODIES IN FIBROMYALGIA PATIENTS WITH SICCA AND/OR XEROSTOMIA

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**Background:** A significant proportion of patients with fibromyalgia complain of dry eyes and mouth. The 2010 preliminary criteria for fibromyalgia even includes dry eyes and mouth as part of the somatic symptoms severity complex used to diagnose this condition. A significant proportion of Sjögren's syndrome patients also complain of fibromyalgia symptoms, and there is literature that suggests that there is interplay between these two disorders. Recently, the presence of novel tissue specific autoantibodies (TSAs), SP-1, CA6, and PSP, has been observed in the early stages of Sjögren's syndrome (SS). These early markers present themselves before the classic autoantibodies, such as SSA/Ro, SSB/La, ANA, and RF.

**Objectives:** This study aims to examine the relationship between SS and fibromyalgia by testing patients with fibromyalgia, that also complain of xerostomia and sicca symptoms, for Sjögren's related biomarkers SSA/Ro, SSB/La, SP-1, CA6, and PSP.

**Methods:** Over the past 5 years, we identified a cohort of 310 patients that presented with symptoms of fibromyalgia and fulfilled both the 1990 and 2010

preliminary diagnostic criteria. These patients were further questioned about xerostomia and sicca symptoms. Patients that admitted to using artificial tears at least biweekly, drinking water excessively to relieve dry mouth, or have previously experienced a blocked tear duct, but did not meet the strict diagnostic criteria for SS and did not have elevated inflammatory markers ESR or CRP, were selected for this study. Serum from study patients was sent to a tertiary lab, Immco Diagnostics, for testing of the classic autoantibodies (SSA/Ro, SSB/La, ANA and RF) and Tissue Specific Autoantibodies (SP-1, CA6, PSP). Patients testing positive for the TSA markers were provided with literature on the disease and offered appropriate treatment options, such as hydroxychloroquine.

**Results:** As of November, 2017 310 patients were selected for this study and tested for the SS markers. 91.0% of the patients were female and 8.6% of the patients were male. The average patient age was 56.5 years. 271 of the study patients were tested for both the TSAs and classic autoantibodies, while 39 were tested for only TSAs. Of the patients that were evaluated for both the TSAs and classic Sjögren's autoantibodies, 29.8% (81) tested positive for SS. 22.8% (71) of the patients were positive for TSAs, 9.4%<sup>29</sup> were positive for the classic Sjögren's markers, and 2.3%<sup>7</sup> were positive for both the TSA and classic Sjögren's autoantibodies. Further analysis of all the patients that tested positive for the TSAs (n=71), found 74.5% (53) were positive for SP-1, 8.5%<sup>6</sup> were positive for CA6% and 44.7%<sup>32</sup> were positive for PSP. 68.1%<sup>48</sup> of these patients were positive for only one of the TSA and 23 (31.9%) were positive for more than one TSA.

**Conclusions:** In this cohort of 310 fibromyalgia patients, about 1/3 of patients that were tested for both the TSAs and classic Sjögren's markers tested positive for SS, with the majority of those patients being positive for one or more of the TSAs. This suggests that autoimmunity, specifically early-stage Sjögren's syndrome, may be a confounding variable in the pathophysiology of fibromyalgia.

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**Disclosure of Interest:** None declared

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THU0509

### THE ROLE OF THIOL-DISULFIDE HOMEOSTASIS IN THE ETIOPATHOGENESIS OF FIBROMYALGIA

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**Background:** Fibromyalgia syndrome (FMS) is a chronic disease with unknown etiology, characterised by widespread pain, fatigue, sleep disturbance, cognitive dysfunction and anxiety. Oxidative stress has also been implicated in etiopathogenesis in recent years.

**Objectives:** In this study we aimed to investigate the role of thiol-disulfide balance in the etiopathogenesis of fibromyalgia, as an indicator of oxidative stress.

**Methods:** 98 female patients with fibromyalgia, 61 of whom were newly diagnosed and 37 were presently ongoing treatment and 82 healthy female controls were included in the study. Fibromyalgia impact questionnaire, pain visual analogue scale, Pittsburgh sleep quality index, fatigue severity scale, short form-36, tender point count, Beck depression inventory and Beck anxiety inventory were evaluated in both groups. To determine the oxidative balance, the thiol/disulfide balance was investigated by the new automatic measurement method developed by Erel and Neselioglu.

**Results:** Serum native thiol levels were 394.43±52.43 μmol/L and 418.12±49.95 μmol/L (p=0.002), total thiol levels were 429.55<sup>53.5</sup> μmol/L and 440.95<sup>58.7</sup> μmol/L (p=0.052) and serum disulphide levels were 17.5 (9.8) μmol/L and 14.8 (10.3) μmol/L in the FMS and control groups, respectively (p=0.002). In the FMS group, disulphide/native thiol percent ratios (p<0.001) and disulphide/total thiol percent ratios (p<0.001) were statistically significantly higher while native/total thiol percent ratios (p<0.001) were statistically significantly lower than those of the control group. Serum native thiol levels (p=0.008) were 384.2 (76.7) μmol/L, 387.6 (65.05) μmol/L and 416.55<sup>53.4</sup> μmol/L; disulfide levels were measured as 17.2 (7.5) μmol/L, 18.3 (14.55) μmol/L and 14.8 (10.3) μmol/L newly diagnosed patients, treated patients and control groups, respectively. Serum native thiol values at the thiol-disulfide balance did not improve disulfide in spite of being slightly approaching the control group in the treated patients. When the ratio of disulfide/native thiol was examined, it was seen that both newly diagnosed and treated patients remained in a balanced disulfide state. There were statistically significantly correlations between tender points (respectively p=0.02, r=-0.241; p=0.039, r=-0.213; p=0.039, r=-0.213; p=0.039, r=0.213), SF-36 pain subscale (respectively p=0.032, r=0.216, p=0.041, r=0.206, p=0.042, r=0.206, p=0.041, r=0.207) and Beck anxiety inventory scores (respectively p=0.009, r=-0.216, p=0.027, r=-0.225, p=0.026, r=-0.225, p=0.026, r=0.225) with disulphide levels, disulphide/native thiol, disulphide total thiol and native thiol/total thiol ratio.

**Conclusions:** The disulfide shift of the thiol-disulfide balance and the correlation between the clinical parameters and the thiol-disulfide balance components suggesting the presence of oxidative stress in FMS patients suggests that the role of thiol-disulfide balance in the etiopathogenesis of FMS.

**Disclosure of Interest:** None declared

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#### THU0510 HYPERSENSITIVITY, ALEXITHYMIA AND DISEASE CHARACTERISTICS OF PATIENTS PRESENTING WITH SYMPTOMS OF FIBROMYALGIA

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**Background:** Fibromyalgia (FM) is characterised by chronic widespread pain and other symptoms such as fatigue, sleep disturbances and cognitive problems. Psychosocial factors and personality traits may be present in a variable degree and may play a role in the perception, coping and treatment of FM.

**Objectives:** We looked for symptoms of hyperventilation, depression, anxiety and burn-out as well as for personality traits such as hypersensitivity and alexithymia in a large sample of patients. We looked at differences in prevalence of these symptoms in the population when selected by the 1990 FM classification criteria and by the 2010 diagnostic FM criteria.

**Methods:** A large group of patients presenting on the Unit of Physical Medicine between 2014 and 2017 with chronic widespread pain was analysed and grouped depending on the 1990 ACR classification criteria for FM on one hand and the 2010 ACR diagnostic criteria for FM on the other hand. Self-administered tools used were the Nijmegen questionnaire (hyperventilation), the Aron questionnaire (hypersensitivity), the HADS questionnaire (anxiety and depression), the BMS-10 questionnaire (burn-out) and the TAS alexithymia questionnaire.

**Results:** Out of 1085 patients, 828 (76%) fulfilled the 1990 ACR classification criteria for FM. Hyperventilation (score  $\geq 12$ ) was found in 97% and hypersensitivity (score  $\geq 12$ ) in 75%. Symptoms of anxiety and depression (scores  $\geq 11$ ) were observed in 59% and 36% respectively. Burn-out (score  $\geq 4.5$ ) was seen in 40% of patients while a high TAS score ( $\geq 8$ ) was found in 70% of patients. Overall, 906 patients fulfilled the 2010 ACR diagnostic criteria for FM. The distributions of disease characteristics and personality traits in this population were very similar. Only 38 out of these 906 patients had a wide spread pain index (WPI) of 3 to 6.

**Conclusions:** A significant number of patients demonstrated high levels of anxiety, more than depression. Hypersensitivity and alexithymia were also found to be highly prevalent. There was a substantial level of hyperventilation. It may be useful to consider all these characteristics in the development of treatment programs for FM patients. Results were similar when groups were selected by 1990 ACR classification criteria for FM or by the 2010 ACR diagnostic criteria for FM. Only a minority of patients had a WPI of 3 to 6.

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**Disclosure of Interest:** None declared

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#### THU0511 EFFECTS OF ADD-ON TRANSCRANIAL DIRECT CURRENT STIMULATION ON PAIN IN KOREAN PATIENTS WITH FIBROMYALGIA

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**Objectives:** Despite promising preliminary results of transcranial direct current stimulation (tDCS) treatment in patients with fibromyalgia (FM), several issues need to be addressed, including its limited efficacy, low response rate, and poor tolerability. We investigated the efficacy and safety of tDCS as an add-on treatment for chronic widespread pain in Korean patients with FM.

**Methods:** This study enrolled 38 patients, who were refractory to pain medications, seen at Chonnam National University Hospital from May 2016 to December 2016. A conventional tDCS device was used to supply 2 mA of current for 20 min on 5 consecutive days. The anode was placed over the primary motor cortex (M1)

and the cathode was located contralateral supraorbital area. The primary end point was a change in visual analogue scale (VAS) pain score at the end of treatment and secondary end points included changes in Fibromyalgia Impact Questionnaire (FIQ), Brief Pain Inventory (BPI), Brief Fatigue Inventory (BFI), Beck Depression Inventory (BDI), State-Trait Anxiety Inventory (STAI), and Medical Outcomes Study Sleep Scale scores.

**Results:** After tDCS, 38 patients showed clinical improvements in the VAS pain score on days 6, 13 and 36 compared with day 0 ( $p < 0.001$ ). However, improvement of FIQ scores was only seen at day 36. The BPI and BDI were significantly decreased on days 6 and 13, while BFI and STAI-I were significantly improved only at day 6. The most of improved indices were not maintained until day 36. There were no significant improvements in Sleep Scale scores after tDCS at days 6, 13, and 36. No serious adverse event was observed.

**Conclusions:** Our results suggest that tDCS has the potential to produce significant pain relief in FM patients, and may constitute an effective add-on treatment for these patients.

**Disclosure of Interest:** None declared

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#### THU0512 HYPERBARIC OXYGEN THERAPY (HBOT) TREATMENT IN FIBROMYALGIA

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**Background:** Chronic pain conditions, such as fibromyalgia (FM), are among the most common health problems managed by general practitioners, rheumatologists, clinical psychologists. FM is characterised by multifocal pain, fatigue, non-restorative sleep, cognitive complaints high levels of distress, associated with greater affect intensity. There's evidence from randomised controlled trials that some treatments like pharmacotherapy, patient education, behavioural therapy and physiotherapy are effective in reducing symptoms; however the majority of the patients aren't satisfied with the current treatments. HBOT showed some clinical effects that may induce a significant improvement of the FM symptoms.

**Objectives:** The goal of this work was to evaluate the effect of HBOT on FM symptoms.

**Methods:** 33 female patients aged 29–63 y, with FM were included in this work. Patients initially pharmacologically treated (Pregabalin 150 mg/die, Duloxetine 60 mg/die) with unsatisfactory clinical improvement, were enrolled at the Rheumatology Unit San Cesario-Italy. The HBOT protocol comprised 20 sessions, 3d/w, 90 min, 100% oxygen at 2.5ATA. Patients were randomly assigned to treated and control groups and evaluated every month for the next 4 months: patients in group A were treated with 20 sessions of HBOT in the first 2 months and evaluated for the following 2 months; patients in group B used the pharmacological treatment for the first 2 months and then were treated with 20 sessions of HBOT in the last 2 months. During HBOT no pharmacological treatment was allowed. The treated group patients were evaluated at baseline and after 10 and 20 HBOT sessions. Evaluations consisted of physical examination, including tender point count, and socio-demographic and clinimetric questionnaires: Fibromyalgia Impact Questionnaire (FIQ), Functional Assessment of Chronic Illness Therapy, Pittsburgh Sleep Quality Index, Quality of life, Beck Depression Inventory, State Trait Anxiety Inventory, Pain Catastrophizing Scale.

**Results:** 5 patients withdrew from the HBOT treatment for claustrophobia. HBOT led to significant amelioration of all FM symptoms, with significant improvement in life quality. HBOT leads to a reduction in the number of tender points in the 2 groups. This reduction occurs in the group A without changing during the following 2 months of observation. In the group B the improvement is more related to the HBOT than to the therapy. The FIQ score improves in group A. No improvement was observed in the control group.

**Conclusions:** The analgesic effects of HBOT have been studied in nociceptive, in inflammatory and neuropathic pain models, and may be useful for the treatment of various chronic pain syndromes. Excessive pain in FM may be due to hyperexcitability of the pain processing pathways and under-activity of the pain inhibiting pathways in the brain. It has been shown that HBOT increases cell metabolism, reduces apoptosis, alleviates oxidative stress, increases neurotrophin and nitric oxide levels by enhancing mitochondrial function in neurons and glial cells, it may even promote the neurogenesis of endogenous neural stem cells. HBOT-induced neuroplasticity also leads to the repair of chronically impaired brain functions. Our data confirm the efficacy of HBOT in treating FM. Further studies are required to evaluate the protocol and to understand the duration of the clinical effect.

**Disclosure of Interest:** None declared

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### THU0513 IS THERE A ROLE OF SERUM NESFATIN-1 LEVEL IN FIBROMYALGIA?

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**Background:** Fibromyalgia (FM) is characterised by chronic widespread pain, sleep disturbances, affective disorders, fatigue, cognitive dysfunction, anxiety and depressive episodes and its pathogenesis is still unclear.<sup>1</sup> Nesfatin-1 is a recently identified anorexigenic hypothalamic polypeptide which plays role on mood, stress, sleep, anxiety, eating behaviour, and metabolic regulation.<sup>2, 3</sup> Serum level of nesfatin-1 may be associated with the physiopathology and clinical symptoms of FM.

**Objectives:** The aim of the present study was to compare serum nesfatin-1 level in patients with FM with healthy controls, and to investigate its relationship with demographic features and clinical parameters such as pain severity, disease activity, fatigue, emotional status, and sleep quality in FM patients.

**Methods:** Forty-six female patients with FM and 46 healthy female controls were included in the study. Demographic characteristics of participants were recorded. Severity of Pain by Visual Analogue Scale (VAS), disease activity by Fibromyalgia Impact Questionnaire (FIQ) were evaluated in patients with FM. Fatigue by Multidimensional Assessment of Fatigue (MAF), sleep quality by Pittsburgh Sleep Quality Index (PSQI), emotional status by Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI) were performed in both groups. Serum nesfatin-1 concentrations were measured in all participants.

**Results:** Serum nesfatin-1 concentrations were significantly low in patients with FM compared to the healthy subjects ( $p<0.05$ ). When compared to the FM patients without anxiety, serum nesfatin-1 concentrations were significantly increased in FM patients with anxiety ( $p<0.05$ ). Serum nesfatin-1 concentrations were positive correlated with BAI scores in patients with FM ( $p<0.05$ ) whereas no statistically significant correlations were found between serum nesfatin-1 concentrations and age, BMI, and other clinical parameters in the patient and control group ( $p>0.05$ ).

**Conclusions:** According to the results of this study, it can be suggested that decreased nesfatin-1 plays a role in the FM pathogenesis and nesfatin-1 may mediate anxiety-related responses in FM patients.

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### THU0514 FAT BUT FIT. THE COMBINED ASSOCIATION OF BODY MASS INDEX AND CARDIORESPIRATORY FITNESS WITH THE FIBROMYALGIA SEVERITY AND TENDERNESS: THE AL-ÁNDALUS PROJECT

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**Background:** Since fibromyalgia is a complex widespread pain condition with large impact on physical and psychological health,<sup>1</sup> it is imperative to focus on modifiable factors that might decrease the impact of the disease on patients' lives. Accordingly, obesity and cardiorespiratory fitness (CRF) have been proposed as possible targets related to lower fibromyalgia severity and tenderness.<sup>2, 3</sup> However, based on the Fat but Fit Paradigm,<sup>4</sup> no previous studies have examined if women with adverse body mass index (BMI) but high CRF, might present lower fibromyalgia severity and tenderness than those with non-adverse BMI and low CRF.

**Objectives:** To examine the combined association of BMI and CRF with fibromyalgia severity and tenderness in women with fibromyalgia.

**Methods:** A total of 433 women with fibromyalgia (51.8±7.5 years old) were included in this cross-sectional study. BMI was calculated and CRF was assessed with the 6 min walk test (6-MWT). The fibromyalgia severity and its components (function, overall impact and symptom severity) along with tenderness were assessed with the Revised Fibromyalgia Impact Questionnaire (FIQR) and algometry, respectively. BMI groups were stratified according to international criteria.

Fit and unfit cut-offs were established according to the median value (fit  $\geq 489$  m, unfit  $<489$  m in the 6-MWT). Analyses of covariance and Bonferroni post-hoc analyses were used to assess the combined association of BMI and CRF with FIQR variables and tenderness, and the differences of these outcomes variables between the groups created from the combination of the different levels of BMI and CRF, respectively. The potential confounders were age, occupational status, medication for relaxing or sleeping, and antidepressants.

**Results:** Normal-weight and fit women showed better function, and lower overall impact and fibromyalgia severity than obese and unfit women (all,  $p\leq 0.05$ ). Overweight but fit women showed better function, and lower overall impact and fibromyalgia severity than normal-weight and unfit women (all,  $p<0.01$ ) or obese and unfit women (all,  $p<0.001$ ). Additionally, overweight but fit women showed lower symptom severity than obese and unfit women ( $p<0.001$ ). Obese but fit women experienced lower tenderness than normal-weight and unfit women ( $p=0.038$ ). For the remaining analyses, differences of outcomes variables between groups were not statistically significant ( $p>0.05$ ).

**Conclusions:** The combination of BMI and CRF was significantly associated with the fibromyalgia severity and tenderness. Since overweight and obese fit women showed lower fibromyalgia severity and tenderness, it seems that the "Fat but Fit" paradigm might play an important role on fibromyalgia. These findings suggest that fitness might be able to counteract the adverse influence of obesity on fibromyalgia severity and tenderness. However, future physical exercise and dietary interventions are warranted to ascertain these findings.

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### THU0515 SOMATOSENSORY TEMPORAL DISCRIMINATION IS IMPAIRED IN FIBROMYALGIA

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**Background:** Fibromyalgia is the prototypical central sensitivity syndrome which is associated with increased sensitivity to pain and other stimuli. Somatosensory temporal discrimination (STD) is the perception of two discrete stimuli applied at short intervals as separate. The evaluation of STD ability essentially provides information about central processing of sensory stimuli.<sup>1</sup>

**Objectives:** In this study, we aimed to evaluate whether STD ability, which requires an intact central sensory processing, is altered in patients with fibromyalgia.

**Methods:** Fifteen patients with fibromyalgia and 15 healthy subjects participated in the study. Demographic characteristics of participants and severity for fatigue, sleep quality, cognitive symptoms, somatic symptoms and health-related quality of life in fibromyalgia patients were recorded. STD thresholds were measured from the dorsum of the dominant hands of the participants by using a constant current stimulator.<sup>2</sup>

**Results:** Patients with fibromyalgia had higher STD thresholds than healthy subjects (table 1). There were significant correlations between STD thresholds and pain intensity, fibromyalgia impact questionnaire scores and symptom severity scale scores in fibromyalgia group ( $p=0.006$ ,  $r=0.68$ ;  $p=0.037$ ,  $r=0.54$ ;  $p=0.017$ ,  $r=0.61$  respectively).

**Table 1 STD measures and clinical characteristics of study participants**

	Fibromyalgia group (n:15) mean±SD	Control group (n:15) mean±SD	Mean difference (95% CI)	p
Pain (VAS), cm	7.3±1.1			
FIQ score	58.8±5.5			
SSSS	7.7±1.4			
STDT, ms	69.1±8.6	33.4±4.6	35.7 (30.6– 40.8)	<0.001

VAS: Visual analogue scale, FIQ: Fibromyalgia impact questionnaire, SSSS: Symptom severity scale score, STDT: Somatosensory temporal discrimination threshold, SD: Standard deviation, CI: Confidence interval

**Conclusions:** Somatosensory temporal discrimination ability is impaired in fibromyalgia patients compared to healthy subjects. Disrupted somatosensory temporal discrimination ability correlates with increased widespread pain and severity of

other symptoms including fatigue, sleep quality, cognitive symptoms, somatic symptoms and decreased functional status. The impaired somatosensory temporal discrimination ability indicates an alteration in higher cognitive sensory processing in fibromyalgia.

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THU0516

#### EFFICACY AND SAFETY OF VITAMIN D3 IN PATIENTS WITH FIBROMYALGIA. RANDOMISED, DOUBLE BLIND, PLACEBO-CONTROLLED TRIAL

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**Background:** fibromyalgia (FM) is a disease characterised by widespread pain, sometimes fatigue, memory problems and sleep disturbances. It has been suggested that low blood levels of vitamin D correlate with increased pain scores in patients with FM. A recent meta-analysis indicated that vitamin D may decrease pain scores in patients with FM, but with a low quality trials.

**Objectives:** to assess the efficacy and safety of vitamin D3 in Fibromyalgia patients.

**Methods:** a 12 week randomised, double blind, placebo-controlled trial in eighty FM patients according to the criteria of the American College of Rheumatology (ACR) 2010 who were randomised into two groups, the treatment group (n=40) received 50,000 IU of oral vitamin D3 weekly, the second group (n=40) received placebo for 12 weeks. The primary outcome was to assess the change in the Spanish version of Fibromyalgia Impact Questionnaire (S-FIQ) and Visual Analogue Scale (VAS 0–10) from baseline to week 12. Baseline serum calcium levels were measured in all subjects. Vitamin D levels were measured by chemiluminescence considering normal ranges between 30 and 100 ng/ml, insufficiency between 10 and 30 ng/ml and deficiency less than 10 ng/ml, baseline and after 12 weeks.

**Results:** of the total, 61/80 (76%) had vitamin D insufficiency, 8/80 (10%) deficiency and 11/80 (14%) normal levels, the mean overall level of vitamin D was 21.2±9.0. There was no statistically significant reduction in S-FIQ scores in patients in the treatment group compared with placebo (47.0±23.3 vs 43.9±25.0, p=0.56) after 12 weeks; there was also no statistically significant decrease in VAS scores (6±5 vs 4±4.5, p=0.57). There was no improvement in the perception of pain when normalising vitamin D levels. No serious adverse events were reported in both groups.

**Table 1 Baseline characteristics:**

	Treatment (n=40)	Placebo (n=40)	p
Age, mean (SD), years	50.3 (11.9)	51.4 (9.5)	0.6
BMI median (IQR)	26.8 (7.3)	27.2 (5.29)	0.7
Primary FM n (%)	18 (48.6)	19 (51.4)	0.8
Secondary FM n (%)	22 (51.2)	21 (48.8)	0.8
Tender Points median (IQR)	12.5 (4.4)	14 (7)	0.2
Basal Vitamin D median (IQR)	20.1 (14.5)	12.6 (13.4)	0.2
Vitamin D (%)			0.24
Normal	7 (17.5)	4 (10)	
Insufficiency	31 (77.5)	30 (75)	
Deficiency	2 (5)	6 (15)	
Baseline FIQ mean (SD)	64.51 (15.25)	61.88 (18.21)	0.48
Baseline VAS median (IQR)	6 (3)	6 (3.5)	0.36
<b>Primary outcomes</b>			
Final FIQ mean (SD)	47.09 (23.37)	43.9 (25.02)	0.56
Final VAS median (IQR)	6 (5)	4 (4.5)	0.57
Delta FIQ median (IQR)	-16.39 (35.28)	-18.94 (105.13)	0.59
Control Vitamin D median (IQR)	50.8 (24.9)	20.7 (5.84)	0.0001

**Conclusions:** at 12 weeks of treatment with vitamin D3 50,000 IU versus placebo in patients with fibromyalgia had no statistically significant differences in the FIQ and VAS. It may be possible to find greater benefit from vitamin D if this period is extended.

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THU0517

#### IDENTIFICATION OF CANDIDATE GENES ASSOCIATED WITH FIBROMYALGIA SUSCEPTIBILITY IN SOUTHERN SPANISH WOMEN: THE AL-ÁNDALUS PROJECT

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**Background:** Family aggregation suggests genetic susceptibility to fibromyalgia. Candidate-gene studies on fibromyalgia susceptibility often include a small number of SNPs,<sup>2,3</sup> which is a limitation.<sup>4</sup> Additionally, there is a paucity of evidence in Europe.

**Objectives:** To compare genotype frequencies of candidate single nucleotide polymorphisms (SNPs) in a well-characterised sample of Spanish women with fibromyalgia and healthy non-fibromyalgia women.

**Methods:** Three hundred and fourteen women with a diagnosis of fibromyalgia (cases) and 112 non-fibromyalgia healthy (controls) women participated in the present candidate-gene study. Buccal swabs were collected for DNA extraction. Using TaqMan OpenArray, we analysed 63 single nucleotide polymorphisms (SNPs) of 33 genes related to fibromyalgia susceptibility, symptoms, or potential mechanisms.

**Results:** The rs841 and rs1799971 GG genotype was more frequently observed in fibromyalgia than in controls (p=0.04 and p=0.02, respectively). The rs2097903 AT/TT genotypes were also more often present in the fibromyalgia participants than in their control peers (p=0.04).

**Conclusions:** We identified, for the first time, associations of the rs841 (guanosine triphosphate cyclohydrolase 1 gene) and rs2097903 (catechol-O-methyltransferase gene) SNPs with higher risk of fibromyalgia susceptibility. We also confirmed that the rs1799971 SNP (opioid receptor μ1 gene) might confer genetic risk of fibromyalgia. Further studies are needed to confirm or refute the present findings.

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THU0518

#### THE DIAGNOSTIC VALUE OF SELECTED MICRORNAS IN PATIENTS WITH FIBROMYALGIA ASSOCIATED WITH RHEUMATOID ARTHRITIS: A PILOT STUDY

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**Background:** Fibromyalgia (FM) is present in a significant proportion of patients with rheumatoid arthritis (RA).<sup>1</sup> Diagnosis and management of patients with rheumatoid arthritis and associated fibromyalgia (FRA) is challenging.<sup>1</sup> MicroRNAs (miRNA) are small noncoding RNAs that target mRNA and repress protein production. Recent studies have identified specific patterns of microRNA (miRNA) expression in FM patients.<sup>3</sup>

**Objectives:** Our objectives were to determine if there are differences in expression levels of miR let-7a, miR-21–5 p, miR –143 and miR-103a-3p in the blood of

FRA, RA and FM patients and to determine if any of the aforementioned miR could differentiate between FRA and RA.

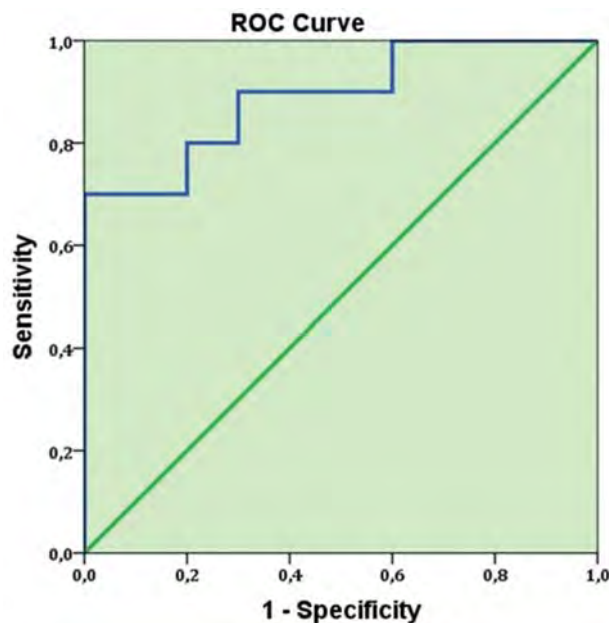
**Methods:** We performed a case control study on 10 FRA patients compared to 10 FM, 10 RA patients with pain of at least 50 mm on VAS, and 10 healthy controls. All patients underwent clinical and laboratory examinations. Cell lysate from peripheral blood was used for the extraction of total RNA with TriReagent; miRNA reverse transcription was performed with the miScriptII Reverse Transcription kit (Qiagen) according to manufacturer's instructions. cDNAs obtained were further amplified by quantitative PCR (qPCR) with the miScript SYBR Green PCR kit. miRNA relative expression was quantified using the  $2^{-\Delta\Delta Ct}$  method. Relative miRNA levels are expressed as fold change (Fc). Data are expressed as median (interquartile range).

**Results:** There were no significant differences in terms of baseline characteristics between the groups. Clinical characteristics of included patients are listed in table 1. Patients with RA had higher SJC values and higher ESR and CRP levels as compared to FRA and FM patients. However, the mean DAS28 scores of RA and FRA patients were not significantly different, due to higher TJC values and higher pain levels in the FRA group.

Expression levels for miR let-7a, miR-21-5 p3 and miR-103a-3p were similar between the groups. miR-143 was downregulated in FRA, with a median Fc of 0.6 (IQR 0.3) and FM patients with a median Fc=0.5 (IQR 1.6) and upregulated in RA patients with a median Fc of 1.4 (IQR 0.5). miR-143 expression levels correlated negatively with TJC ( $r=-0.7$ ;  $p<0.05$ ) and with the Fibromyalgia Impact Questionnaire score ( $-0.8$ ,  $p<0.01$ ) in patients with FRA. ROC analysis showed that the AUC to identify FRA from RA patients was 0.89 (95%CI 0.7–1),  $p=0.03$  (Fig 1). A cut-off value for miR-143 Fc of  $>1.04$  had a sensitivity of 90% and specificity of 70% in differentiating FRA from RA.

Abstract THU0518 – Table 1. Demographic and clinical data of patients

Variable	FRA n=10	RA n=10	FM n=10	Controls n=10	p
Age (years)	54 <sup>(14)</sup>	55.5 (11)	55 <sup>(14)</sup>	46.5 (9)	0.1
TJC	17 <sup>(12)</sup>	9 (7)	7 (11)	0	0.006
SJC	4 (10)	7 (3;9)	0	0	<0.001
Pain on VAS(mm)	75 <sup>(32)</sup>	70 <sup>(30)</sup>	70 <sup>(25)</sup>	0	0.01
ESR(mm/h)	25 <sup>(33)</sup>	54 <sup>(46)</sup>	9 (7)	5 (9)	0.002
CRP(g/dl)	6 (21.4)	24.6 (41.1)	1.3 (1.2)	1.3 (4.3)	0.001
DAS28ESR	5.9 (1.9)	5.5 (2)	3.8 (1.4)	-	0.001
DAS28CRP	5.5 (2)	5.5 (2)	3.8 (0.8)	-	<0.001
HAQ	1.8 (0.9)	1.8 (0.7)	1.1 (1.4)	0	0.001
Tender point count	16 <sup>(6)</sup>	6 (7)	15 <sup>(5)</sup>	0 (1)	<0.001



**Conclusions:** miR-143 is downregulated in patients with FRA and may discriminate between patients with FRA and RA. Further studies are needed in order to validate these results.

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THURSDAY, 14 JUNE 2018

## Epidemiology, risk factors for disease or disease progression

### THU0519 PREDICTION OF PERSISTENT KNEE PAIN BY PRESSURE PAIN DETECTION THRESHOLDS: RESULTS FROM THE KNEE PAIN IN THE COMMUNITY COHORT (KPIC)

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**Background:** Knee pain results from a combination of nociceptive input from the joint, and processing of that input by the central nervous system. Pressure pain detection thresholds (PPTs) are lower and pain is more severe in people with greater central sensitisation.

**Objectives:** We hypothesised that lower PPTs predicted worse pain prognosis in people with knee pain.

**Methods:** KPIC participants were people aged  $>40$  years recruited from Nottingham, UK. Participants were mailed questionnaires at baseline and 1 year. This study reports the sample of responders who attended baseline and 1 year clinical assessment, had self-reported knee pain (within the last 4 weeks) and underwent PPT. PPT was measured at the knee, anterior tibia and the sternum. Radiographic knee OA was classified using an atlas. Questionnaires measured ICOAP (constant and intermittent knee pain), painDETECT (neuropathic-like) and average knee pain severity over 4 weeks (0–10).

The presence of pain at baseline and 1 year (persistent pain), or pain severity were predicted from baseline anterior tibia PPT. Additional analyses adjusted for baseline pain score, age, sex, BMI, or for radiographic knee OA. Pain persistence (Yes/No) was analysed using t tests, odds ratios (OR) and logistic regression. Pain severity was analysed using linear regression.

**Results:** The sample for this study contained  $n=419$  people at baseline, of whom  $n=182$  people reported knee pain persistent over both time points. The mean (SD) values for those with persistent knee pain at 1 year, were age 61<sup>9</sup> years, BMI 30.1 (5.8)  $\text{kg m}^{-2}$ , 59% female, and 36% fulfilled radiographic OA criteria at the index knee.

In univariate analysis, persistent knee pain was associated with a lower PPT at baseline (461 vs 424 kPa; OR (95% CI) 0.58 (0.34–0.97)  $p=0.020$ ). Adjustments for age, sex and BMI removed the significance from the association (adjusted OR (95% CI) 0.64 (0.36–1.13)  $p=0.120$ ).

In those with persistent pain, worse 1 year ICOAP-constant, ICOAP-intermittent, painDETECT and knee pain severity were correlated with lower baseline anterior tibia PPT ( $r=-0.28$  to  $-0.24$ ;  $p<0.004$ ). After adjustment for baseline pain, 1 year ICOAP-constant pain scale was significantly predicted by baseline PPT (B (95% CI),  $-1.05$  ( $-1.91$  to  $-0.20$ )  $p=0.016$ ). Linear regression with adjustments for age, sex and BMI also indicated that baseline PPT predicted worse ICOAP-constant pain (B (95% CI)  $-0.99$  ( $-1.94$  to  $-0.04$ )  $p=0.041$ ).

The presence of radiographic OA at baseline predicted pain at 1 year, but was not significantly associated with PPT at baseline. Adjustment for baseline radiographic OA did not remove the association between baseline PPT and ICOAP-constant at 1 year (anterior tibia PPT  $-1.04$  ( $-1.89$  to  $-0.18$ )  $p=0.018$ ). PPT at joint lines or sternum displayed similar patterns of association with 1 year pain as did PPT at the anterior tibia.

**Conclusions:** Pressure pain detection thresholds suggestive of central sensitisation at baseline were associated with knee pain prognosis at 1 year, in particular with constant knee pain. The presence of radiographic OA also predicts 1 year pain prognosis, but does not explain its prediction by PPT.

**Disclosure of Interest:** None declared

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THURSDAY, 14 JUNE 2018

## Fibromyalgia

THU0520

## ASSESSMENT OF CARDIOVASCULAR RISK IN PATIENTS WITH FIBROMYALGIA BY CAROTID-FEMORAL PULSE WAVE VELOCITY – RESULTS OF A PROSPECTIVE STUDY

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**Background:** Autonomic dysfunction, a basic element of fibromyalgia (FM), has been in some cases related to increased risk of cardiovascular (CV) disease. CV risk associates with aortic stiffness, which can be reliably assessed by carotid-femoral pulse wave velocity (cfPWV).

**Objectives:** Aims of this study were to test the hypothesis of increased cfPWV in a group of patients with FM and to examine its association with FM associated parameters and selected traditional CV risk factors.

**Methods:** We performed measurements of cfPWV in 99 FM patients and 102 healthy controls. The difference between cfPWV values in the two groups after controlling for possible confounding factors was evaluated through multiple regression analysis. The associations of cfPWV with FM related parameters such as pain severity on the EuroQol visual analogue scale (EQ-VAS) and FM tender points were also analysed. Finally, we explored the relationship of cfPWV with various laboratory parameters (patients' group) and traditional CV risk factors (both groups).

**Results:** Adjusted statistical analyses for confounding factors showed significantly higher cfPWV values in FM patients in comparison to controls ( $p_{adj}=0.044$ ). cfPWV associated significantly with age in both the patients and the control group ( $\rho=0.614$ ,  $p<0.001$  and  $\rho=0.678$ ,  $p<0.001$  accordingly). Moreover, cfPWV correlated in the control group with systolic, diastolic and mean arterial pressure ( $p<0.001$ ,  $p=0.013$  and  $p<0.001$  accordingly) as well as with Body Mass Index ( $p=0.003$ ).

Abstract THU0520 – Table 1. Descriptive characteristics by group.

	Controls (n=102)	Patients (n=99)	Significance (p)
cfPWV (m/s)	7.50 (6.78–8.40)	8.00 (7.20–9.30)	0.004*
Age (years)	50 (38.25–56.25)	53 (46.00–59.00)	0.025*
Gender (female)	92 (90.2%)	93 (93.9%)	0.436
Nicotin (smokers)	21 (20.6%)	28 (28.6%)	0.250
Antihypertensive drugs	16 (15.2%)	35 (36.1%)	0.001*
BMI	23.74 (21.08–27.05)	26.50 (23.80–30.81)	<0.001*
MAP (mmHg)	92.33 <sup>85–100</sup>	93 (83.33–96.67)	0.586
Heart rate (/min)	66.00 (59.00–73.0)	72.00 (66.00–90.0)	0.001*
Cholesteroline (mg/dl)	-	222.8±44.4	-
HDL (mg/dl)	-	65 (54–77.5)	-
LDL (mg/dl)	-	140 (108.50–173.50)	-
Triglycerides (mg/dl)	-	105 (74.50–156.00)	-
Tender points (18/18 positive)	-	52 (52.5%)	-
CRP (mg/l)	-	1.67 (1.00–4.62)	-
ESR (mm/h)	-	13.50 <sup>9–18</sup>	-
RF (positive)	-	11 (11.1%)	-
ANA (>1:80)	-	5 (5.1%)	-
EQ-VAS (%)	-	45 (35–60)	-

\*p&lt;0.05

**Conclusions:** Our data reveal that patients with FM have higher aortic stiffness than healthy controls, even after adjusting for confounding factors of cfPWV. Therefore, FM may be associated with an increased CV risk. To our knowledge, this is the largest study to examine the gold standard assessment method of aortic stiffness in patients with FM and the first one to find increased cfPWV-values in comparison to healthy subjects.

**Disclosure of Interest:** None declared

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THU0521

## A SIMPLE INDEX BASED ON SCORES ON A MULTIDIMENSIONAL HEALTH ASSESSMENT QUESTIONNAIRE (MDHAQ) PROVIDES INFORMATION QUITE SIMILAR TO ACR CRITERIA FOR FIBROMYALGIA IN ROUTINE CARE

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**Background:** Fibromyalgia (FM) is common in the general population, easily identified in many patients, but subtle in some, particularly when patients meet criteria for rheumatic diseases such as rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), osteoarthritis (OA), and others. American College of Rheumatology (ACR) FM criteria were reported in 1990 (Arth Rheum 33:160, 1990) and 2010 (Arth Care Res 62:600, 2010) as "preliminary diagnostic criteria," modified for patient self-report in 2011 (Ann Med 43:495, 2011), and in 2016 as the "2016 revisions to the 2010/2011 fibromyalgia diagnostic criteria" (Sem Arth Rheum 46:319, 2016). These FM criteria are not used in most routine care settings. A multidimensional health assessment questionnaire (MDHAQ) is more widely used in the USA (Arth Care Res 64:640, 2012), and is informative in RA, OA, SLE, and most rheumatic diseases (J Clin Rheumatol 19:169, 2013). MDHAQ may provide clues to primary and secondary FM in routine care, EULAR 2016, 2017

**Objectives:** To compare 2 indices of MDHAQ scales to the 2011 and 2016 FM criteria to identify patients with possible primary or secondary FM in routine care.

**Methods:** All patients with all diagnoses seen at an academic rheumatology clinic complete an MDHAQ at each visit. The modified FM criteria questionnaire was added from April-July 2017. Two MDHAQ scales were studied: MDHAQ-FM3 includes a 0–10 pain visual analogue scale (VAS), 0–48 self-report rheumatoid arthritis disease activity index (RADAI) painful joint count, and 0–60 symptom checklist; one point each is scored for pain  $\geq 6/10$ , RADAI  $\geq 16/48$ , symptom checklist  $\geq 16/60$  – total=0–3. MDHAQ-FM4 adds a MDHAQ fatigue VAS; 6/10 is scored 1 (Total 0–4). Both MDHAQ indices were compared to both modified 2011 and 2016 FM criteria using kappa statistics and the proportion correctly classified ("Correct").

**Results:** We studied 502 patients; primary diagnoses (ICD10 in the medical record) included FM in 49, OA in 74, RA in 78, SLE in 88, others in 213. Overall, 131 patients (26.1%) met 2011 modified FM criteria and 112 (22.3%) 2010 modified FM criteria. Agreement between physician diagnosis of FM and 2016 modified criteria was 80.9% (kappa 0.44,  $p<0.001$ ), and with 2011 modified criteria was 80.3% (kappa 0.45,  $p<0.001$ ). Agreement of MDHAQ-FM3 score  $\geq 2$  with 2011 modified FM criteria was 84.3% (kappa 0.63,  $p\leq 0.001$ ), and with 2016 FM criteria 81.7% (kappa 0.56,  $p\leq 0.0001$ ). MDHAQ-FM4 increased the level of agreement only slightly (table 1).

Abstract THU0521 – Table 1. Prevalence and agreement of criteria and FAST3 and FAST4 versions in 502 university rheumatology clinic attendees

FM criteria status	FM2011		FM2016	
	Criteria Positive	Criteria Negative	Criteria Positive	Criteria Negative
<b>MDHAQ-FM3</b> (n=502)				
Screening positive	112 (85.5%)	60 (16.2%)	96 (55.8%)	16 (4.8%)
Screening negative	19 (14.5%)	311 (83.8%)	76 (44.2%)	314 (95.1%)
	Correct 84.3% Kappa 0.63 (0.56–0.70)*		Correct 81.7% Kappa 0.56 (0.48–0.63)*	
<b>MDHAQ-FM4</b> (n=464)				
Screening positive	93 (73.8%)	32 (9.5%)	81 (64.3%)	27 (7.9%)
Screening negative	33 (26.2%)	306 (90.5%)	45 (35.7%)	311 (92.0%)
	Correct 85.9% Kappa 0.64 (0.57–0.72)*		Correct 84.5% Kappa 0.59 (0.50–0.67)*	

**Conclusions:** Two indices derived from MDHAQ variables for pain, painful joints, somatic symptoms, and fatigue, provide a useful clue to FM in routine rheumatology care.

**Disclosure of Interest:** J. Schmekler: None declared, I. Castrejon: None declared, T. Pincus Shareholder of: Dr. Pincus holds a copyright and trademark for MDHAQ and RAPID3 for which he receives royalties and license fees. All revenue is used to support further development of quantitative questionnaire measures for patients and doctors in clinical rheumatology care.

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THURSDAY, 14 JUNE 2018

## Back pain, mechanical musculoskeletal problems, local soft tissue disorders

### THU0522 EXPERIMENTAL TENDINOPATHY TREATMENT WITH SM04755, A TOPICAL SMALL MOLECULE INHIBITOR OF THE WNT PATHWAY

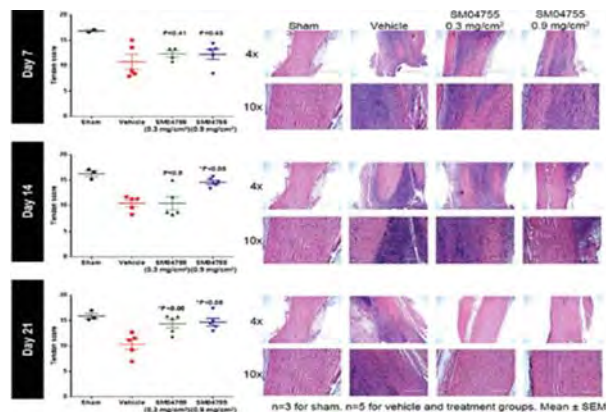
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**Background:** Tendinopathy is an inflammatory and degenerative disorder caused by injuries and overuse. Affected tendons become fibrotic, with micro tears that can lead to pain and rupture. Current therapeutic options treat symptoms and not underlying causes. The Wnt pathway is upregulated in chronic tendinopathy and involved in inflammation, tenocyte differentiation and fibrosis.

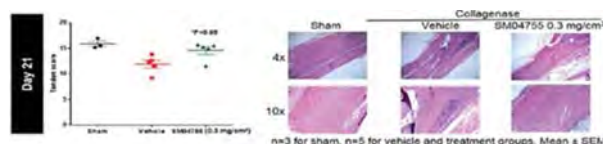
**Objectives:** SM04755, a novel, topical, small molecule Wnt pathway inhibitor, has previously been shown to inhibit inflammation, reduce fibrosis and increase tenocyte differentiation in nonclinical models<sup>1</sup>. Two further experiments are presented: 1. SM04755 treatment in an acute dose response tendinopathy model and 2. SM04755 treatment in a repeat injury/delayed treatment (RIDT) tendinopathy model. These models simulate acute and acute-on-chronic clinical tendinopathy, respectively.

**Methods:** SM04755 was assessed in rodent Achilles tendinopathy models, induced by intra-tendon collagenase injection (500 µg). In the acute dose response model, a single injection of collagenase or sham per animal on Day -4 was followed on Day 0 by daily topical vehicle, or 0.3 mg/cm<sup>2</sup> or 0.9 mg/cm<sup>2</sup> SM04755. Achilles tendons were harvested on Days 7, 14, and 21. In the RIDT model, collagenase injections were given at Days -28 and -14, followed on Day 0 with daily topical vehicle or 0.3 mg/cm<sup>2</sup> SM04755. Achilles tendons were harvested on Days 7, 14, 21 and 28. Blinded histology analyses scored tendon health based on linearity, tendon cell shape, tendon cell density, inflammation, and haemorrhage (range 5–20). Statistical analyses used one-way ANOVA for multiple group comparisons and t-tests for comparison between two groups.

**Results:** In the acute dose response model, SM04755 improved tendon health from baseline compared to vehicle as assessed by tendon histology scores. Vehicle scores were 10.77 [±1.46] at Day 7, 10.44 [±0.66] at Day 14, and 10.31 [±1.02] at Day 21. SM04755 0.3 mg/cm<sup>2</sup> dose group scores were 12.30 [±0.62] at Day 7 (NS), 10.45 [±1.29] at Day 14 (NS), and 14.37 [±0.82] at Day 21 (p<0.05). SM04755 0.9 mg/cm<sup>2</sup> dose group scores were 12.22 [±1.02] at Day 7 (NS), 14.57 [±0.41] at Day 14 (p<0.05), and 14.67 [±0.76] at Day 21 (p<0.05) (figure 1). In the RIDT model, vehicle scores were 12.35 [±0.30] at Day 7, 10.09 [±0.76] at Day 14, 11.92 [±0.77] at Day 21 and 13.72 [±0.35] at Day 28. SM04755 0.3 mg/cm<sup>2</sup> dose group scores were 11.86 [±2.13] at Day 7 (NS), 9.44 [±0.48] at Day 14 (NS), 14.61 [±0.77] at Day 21 (p<0.05), and 14.93 [±0.46] at Day 28 (NS) (figure 2).



**Abstract THU0522 – Figure 1.** Progression of tendon health scores after SM04755 treatment in the acute treatment collagenase model.



**Abstract THU0522 – Figure 2** Treatment with SM04755 in the delayed treatment collagenase model

**Conclusions:** In the acute dose response model, SM04755 0.3 mg/cm<sup>2</sup> dose showed statistically significant improvements in tendon scores compared to vehicle at Day 21. The 0.9 mg/cm<sup>2</sup> dose achieved significance at Days 14 and 21, indicating faster response at higher SM04755 dose. In the RIDT model of repeat collagenase injections and delayed intervention, SM04755 0.3 mg/cm<sup>2</sup> dose promoted accelerated tendon healing compared to vehicle. Therefore, SM04755 demonstrated accelerated improvement of tendon histology in acute and RIDT models compared to vehicle and has potential as a tendinopathy therapy. Clinical studies are planned.

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**Disclosure of Interest:** V. Deshmukh Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, T. Seo Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Y. Yazici Shareholder of: Samumed, LLC, Employee of: Samumed, LLC

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### THU0523 DO WE NEED STEROID INJECTION AFTER ULTRASOUND GUIDED PERCUTANEOUS LAVAGE OF A ROTATOR CUFF CALCIFICATION ? RESULTS AT 3 MONTHS OF A DOUBLE BLINDED RANDOMISED CONTROLLED STUDY

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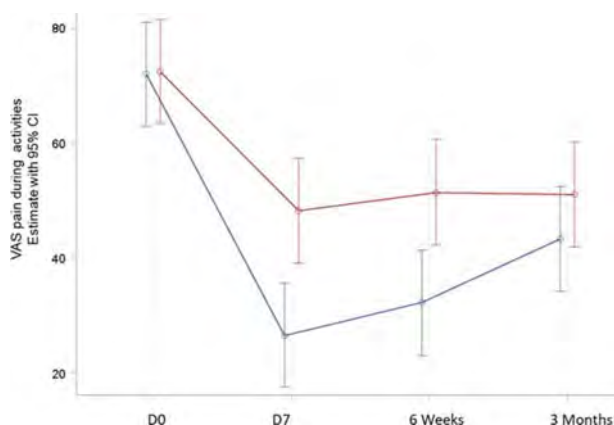
**Background:** Rotator cuff calcific tendinopathy is a common condition causing up to 20% of the painful shoulder. Ultrasound guided percutaneous lavage (UGPL) is indicated after failure of conservative treatments. Steroids injections in the subacromial bursa (SAB) are usually performed after the lavage to prevent the pain induced by the procedure. However, some suggested that this injection could prevent the inflammatory reaction leading to the disappearance of the calcific deposit. Moreover, its efficacy to prevent post-procedure pain has never been demonstrated.

**Objectives:** The goal of this study was to evaluate the effect of a steroid injection in the SAB after UGPL on the pain and the radiographic evolution of the calcification.

**Methods:** This was a multicentric prospective double blinded randomised controlled study. We included patients with shoulder pain for more than 3 months and a type A or B calcification >5 mm on X-Ray. Patients were treated with UGPL using a single needle technic. At the end of the procedure, they received a blind injection of either 2 mL of methylprednisolone acetate or 2 mL of serum saline. The primary outcome was the maximal VAS pain (0–100) the first week following UGPL. Secondary outcomes were the evolution of VAS pain at 7 days, 6 weeks and 3 months and the radiographic changes of the calcification at 3 months.

**Results:** We included 134 patients, mean age 49.8 (±9.7) years, 89 females (67.4%). Calcifications involved the supraspinatus, infraspinatus and subscapularis in 114 (85%), 14 (10%) and 6 patients (5%) respectively. Calcifications were type A and type B in 42,5% and 57,5% of the cases respectively and mean size of the calcification was 1,5 cm (±0,5). Backflow of calcific material was obtained in 107 patients (81.1%). Maximum pain during the first week following UGPL was 71.5 [CI95%:63.9–79.20] in the serum saline group versus 59.8 [CI95%:52.2–67.41] in the steroid group with a mean difference of 11.7 [CI95%:3.7–19.7]. More patients in the placebo group needed to take NSAID (12.1% versus 6.1%) and paracetamol (16.7% versus 9.1%) during the first week. VAS pain at rest and during activities decreased significantly more in the steroid group compared to the placebo: VAS pain during activity was 72.02 [62.98–81.06], 26.63 [17.60–35.67], 32.30 [23.11–41.49] and 43.27 [34.18–52.37] in the steroid group versus 72.46 [63.41–81.51], 48.22 [39.14–57.31], 51.44 [42.26–60.62] and 51.09 [41.95–60.24] in the placebo group at day 0, 7, 6 weeks and 3 months respectively (figure

1). At 3 months no difference was found in the radiographic evolution: 62.1% of the patients treated with steroid and 64.8% treated with serum saline had more than 50% of resorption of their calcification.



**Conclusions:** Our study shows that steroid injection in the SAB leads to a significant decrease of maximal pain the following week. This treatment also decreases significantly the pain during the 3 first months after UGPL. Importantly, we found no difference between the 2 groups in the radiographic evolution of the calcification at 3 months. Overall, steroids injections in the SAB can be recommended after UGPL.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.7349

#### THU0524 IS THERE ANY EFFECT OF KINESIOTAPING ON RADIAL NERVE IN PATIENTS WITH UNILATERAL LATERAL EPICONDYLITIS? A RANDOMIZED-SINGLE BLIND STUDY

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**Objectives:** Lateral epicondylitis is characterised by pain in the lateral epicondyle of the humerus and common extensor tendon (CET). It was reported that radial nerve cross-sectional area were increased in refractory lateral epicondylitis measuring with ultrasonography, although nerve conduction studies were normal. In literature, it is indicated that kinesiotaping is effective at the treatment of lateral epicondylitis. In this study, we aimed to evaluate the effect of kinesiotaping with the larger sample size and using ultrasonography in addition to clinical parameters with patients lateral epicondylitis.

**Methods:** Eighty-five patients with unilateral lateral epicondylitis who completed the inclusion criteria were randomised into two groups. The non-steroidal anti-inflammatory drug (NSAID) was administered to the control group (CON) twice daily for 10 days, while kinesiotaping (KT) was performed 3 times a week for 2 weeks, in addition to the same NSAIDs. Clinical and ultrasonographic evaluation was performed before treatment, at 2 weeks (at the end of treatment) and at 6 weeks. Visual analogue scale (VAS), Nirschl grading, and PRTEE (Patient Based Tennis Elbow Evaluation Test) were used for clinical evaluation. The radial nerve cross-sectional area (RNCSA) were measured at two level: spiral groove, just before bifurcation and CET thickness was calculated by ultrasonography. Clinical evaluation, ultrasonographic evaluation and management of treatment were performed by blind investigators.

**Results:** The study was completed with 80 patients and there were 40 patients in both groups. There were no significant difference age, gender, education, occupation, symptom duration and body mass index in both groups. The improvement of VAS was significant in CON at 2nd week ( $p < 0.05$ ), but not at 6th weeks. In KT group, improvement of VAS was significant both at the 2nd and at 6th weeks ( $p = 0.00$ ). Significant improvement was observed in spiral groove RNCSA and CET thickness in both groups. In the KT group, RNCSA at the level of pre-bifurcation was decreased significantly at the 2nd and 6th weeks ( $p = 0.00$ ), but there was no descreation in the CON. When the groups were compared, significant differences were observed in clinical parameters, CET thickness, and bifurcation RNCSA values at 2 and 6 weeks in the KT group ( $p < 0.01$ ).

**Conclusions:** Kinesiotaping improves clinical parameters and decreases ultrasonographic parameters such as CET thickness and radial nerve cross-sectional area. Therefore, kinesiotaping may be an alternative method that can be used in the treatment of lateral epicondylitis.

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**Disclosure of Interest:** None declared

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#### THU0525 EFFECT OF LOCAL INSULIN INJECTION IN THE TREATMENT OF MILD TO MODERATE CARPAL TUNNEL SYNDROME IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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**Background:** Carpal tunnel syndrome (CTS) is the most common focal nerve entrapment and is a significant cause of morbidity; this syndrome has a higher incidence in diabetic patients. It has been suggested that insulin influences nerve regeneration in a similar way to that of nerve growth factor.

**Objectives:** Aim: The aim of the study was to compare the effectiveness of local insulin injection, with that of local steroid injection and of local steroid followed by insulin injections in treating mild to moderate carpal tunnel syndrome in patients with type 2 diabetes mellitus.

**Methods:** Patients and methods: The study included 60 type 2 diabetic patients with electrophysiologic evidence of mild to moderate CTS. They were randomly assigned to three groups: group I received insulin injection of 10 IU Neutral Protamine Hagedorn insulin (NPH insulin) locally into the affected carpal tunnel at the first visit and a similar dose of insulin after 2 weeks; group II received a single injection of 40 mg methylprednisolone acetate injection into the carpal tunnel. And group III received a steroid injection into the carpal tunnel then followed by insulin injection twice after 2 and 4 weeks from the steroid injection. Clinical, electrophysiologic and ultrasonographic evaluations were carried out at the start of the study and at 10 weeks after treatment.

**Results:** Results: In all groups, there was significant improvement in symptoms, signs and assessment questionnaires (SS score, FD score, and VAS) after receiving the injection. Also, there was a statistically highly significant improvement in DML, SNCV, PSL, and a statistically significant improvement in Samp in the insulin group. While in steroid group there was a statistically highly significant improvement in PSL, and a statistically significant improvement in SNCV. In the third group (steroid followed by insulin), there was a statistically highly significant improvement in DML, SNCV and PSL. As for ultrasonographic assessment, there was a statistically significant improvement in CSA and PD in all groups. The third group (steroid followed by insulin) showed the best improvement as regard the CSA.

**Conclusions:** Conclusion: Local insulin injection was found to be as effective as steroid in reducing the symptoms of CTS and improving electrophysiological and ultrasonographic findings, being a safer alternative for diabetic patients. Our findings suggest that local insulin injection after local steroid injection may be of additional benefit in improving median nerve ultrasonographic parameters in mild to moderate diabetic CTS. **Keywords:** Type 2 diabetes mellitus, carpal tunnel syndrome, local insulin injection.

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**Disclosure of Interest:** None declared

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**THU0526 ACUTE PARASPINAL MUSCLE NECROSIS WITH CRACK COCAINE AND HEROIN; A CASE REPORT**

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<sup>1</sup>Rheumatology, Guys and St Thomas Hospital Trust; <sup>2</sup>Clinical Neuropathology, Kings College Hospital, London, UK

**Background:** Cocaine can cause serious muscle injury ranging from asymptomatic creatine phosphokinase (CK) elevation to massive rhabdomyolysis with acute renal failure. Muscle injury is more common after intravenous use or after smoking the alkaloid freebase (crack cocaine) because of the more rapid effect and higher blood levels of the drug achieved via those routes. The onset of symptoms is acute and can even happen with one time drug use.

**Objectives:** to broaden the knowledge about severe focal myositis as a consequence of crack cocaine abuse

**Methods:** We report a case of Acute Paraspinal myositis and Rhabdomyolysis in a previously healthy African gentleman after smoking crack cocaine and heroin.

**Results:** 35 years old gentleman, previously well, presented to the emergency with 12 hour history of severe lower back pain and stiffness in the absence of any trauma or systemic symptoms. On admission he was conscious and alert with tenderness and stiffness of paraspinal muscles, urinary retention requiring catheterization but no muscle weakness. Serum Creatinine was elevated at 597 µmol/L and Creatine Kinase was 66000 U/L. Urinalysis showed haematoproteinuria (3 +blood, 4+protein). Patient reported smoking crack cocaine and snorting heroin, as well as drinking alcohol 12 hours before the onset of symptoms. Drug screen was positive for cocaine and benzodiazepines while autoimmune serology was negative for ANA, muscle specific antibodies anti-GBM and ANCA-antibody. Infection screen was negative and Urine and blood cultures were sterile. STIR images on MR scan revealed ill-defined areas in the paraspinal muscles consistent with Myositis. The muscle biopsy showed necrosis and focal intense infiltration by sheets of macrophages associated with proliferation of myoblast forming multinucleated giant cells but no evidence of granuloma formation the overall appearances being consistent with focal myositis. Serum Creatinine and CK improved progressively. He was treated with a tapering dose of steroids for 8 weeks while clinical and biochemical markers continued to improve.



**Conclusions:** Drug induced Rhabdomyolysis can occur with cocaine, heroin and alcohol but it is the first reported case of focal myopathy affecting Paraspinal Muscles alone. There is one case report in the literature suggesting isolated myopathy with cocaine in the absence of central nervous system manifestations. One of the main differentials in such a scenario is Pyomyositis which requires early identification and prompt treatment to prevent systemic complications.

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**THU0527 EFFECTS OF MANUAL THERAPY, SACROILIAC AND LUMBAR EXERCISES IN PATIENTS WITH SACROILIAC JOINT DYSFUNCTION SYNDROME**

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**Objectives:** The aim of this study was to determine the effects of sacroiliac joint (SIJ) manipulation, sacroiliac and lumbar home exercises on pain, sacroiliac mobilisation levels and functional status in patients with sacroiliac joint dysfunction syndrome (SIJDS).

**Methods:** In a prospective, randomised interventional trial 69 eligible women were assigned to SIJ manual therapy +sacroiliac home exercise group (Group 1, n=23), SIJ manual therapy +lumbar home exercise group (Group 2, n=23) (n=19), or lumbar home exercise group (Group 3, n=23). All the patients who were included in the study were evaluated on the 0 th, 28 th day and 90 th day of the treatment. Specific tests (motion palpation and pain provocation tests) for SIJ were performed. Activity and rest pain was assessed by using the Visual Analogue Scale (VAS). Functional status and quality of life were assessed using the Modified Oswestry Disability Index (MODI) and Short Form-36 (SF-36), respectively.

**Results:** The VAS scores significantly decreased in all three groups (p<0,05). Gillet test, Vorlauf test, Posterior Shear Test (POSH), Irritation point test and Compression test showed significant decrease after treatment in both training groups (p<0.05). A significant improvement was determined in functional disability score (MODI), quality of life scores, Short Form-36 (SF-36) and neuropathic pain in all three groups (p<0.05). However, a more significant improvement was detected with manual therapy and sacroiliac home exercise program compared to patients in group 2 and group 3.

**Conclusions:** Our data suggest that manual therapy, sacroiliac and lumbar exercises programs can be effective in patients with sacroiliac joint dysfunction syndrome. In SIJDS, a pathology that should be considered in patients with low back pain, it is necessary to know that special SIE exercises and SIE manipulation therapy can be applied in combination with lumbar exercises and SIE manipulation therapy, or that exercises alone can be given but the benefit expected from exercise alone is less than combined treatment revealed.

**Disclosure of Interest:** None declared

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**THU0528 THE RELIEF OF CHRONIC LOW BACK PAIN (CLBP) IMMEDIATELY AFTER ONE SESSION OF LOW LEVEL LASER ACUPUNCTURE THERAPY (LLLAT)**

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**Background:** Low-level Laser acupuncture therapy (LLLAT) is defined as the stimulation of acupuncture points with low-intensity, laser irradiation and is widely used in treating musculoskeletal pain.

**Objectives:** To determine whether the use of a single session of LLLAT for Chronic Low Back Pain (CLBP) will result in better outcome than using acupuncture alone.

**Methods:** 40 patients with CLBP were randomly assigned to two treatment groups: G1 (Acupuncture; 20 patients) and G2 (laser acupuncture; 20 patients). All patients received a single session only. The Acupuncturists inserted a stainless steel needle in local low back (Du3,4, UB23,5,6), distal (UB36, 40,54,7,8,60, GB30,1,4, Li4) and auricular points. laser-acupuncture treatment with a 20 Hz 200 mW 820 nm Gallium Aluminium Arsenide diode laser was used the same previous points. Pain intensity was assessed on a 100 mm visual analogue scale (VAS). The lumbar range of motion was measured by fingertip-to-floor method. A

physiotherapist, who was blinded to treatment assignment, evaluated the patients immediately before and after treatment as well as 4, 12 and 24 weeks later.

**Results:** Immediately after the completion of treatment, the mean VAS dropped from 78 to 66 mm in the acupuncture group (G1) but increased at the follow up visits to 76 mm after 24 weeks. In contrast, VAS scores decreased from 80 to 48 mm in the laser acupuncture group. Although it increased in the follow up visits 60 mm after 24 weeks, it remained significantly better (24 mm  $P < 0.0001$ ) than at the initial assessment. The mean of fingertips and floor distance decreased significantly in G2 from 41 cm to 15 cm immediately after the completion of the first session (the difference from baseline was 26 cm) compared to a decrease from 44 to 35 after the first session in G1. Forward flexion of the lumbar spine improvement remained stable between the first assessment and the other four assessments in patients exposed to prayers with the difference between the baseline and 24 week assessments highly significant ( $p < 0.0001$ ) compared to G1 ( $p > 0.05$ ).

**Conclusions:** Both measures were decreased in both groups but laser acupuncture resulted in a significant improvement in functional and symptomatic outcomes in this group of patients with CLBP even after 24 weeks follow up.

**Disclosure of Interest:** None declared

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#### THU0529 THE COMPARISON OF PHYSICAL ACTIVITY LEVEL IN PREGNANT WOMEN WITH AND WITHOUT LOW BACK PAIN

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**Background:** Low back pain (LBP) is one of the most common musculoskeletal problems during pregnancy that occurs due to a combination of mechanical, hormonal, circulatory and psychological factors. The changes in the load, body mechanics and centre of gravity, increased levels of relaxin, and decreased venous circulation in the pelvic and lumbar region may contribute to LBP in pregnant women.<sup>1,2</sup> It has been reported that the prevalence of LBP ranges between 50% and 80%. Pregnant women suffer from LBP may experience significant physical, psychological and social problems which adversely affect their quality of life.<sup>3</sup>

**Objectives:** The aim of the study was to compare the physical activity level of pregnant women with and without LBP.

**Methods:** A total of 151 pregnant women without obstetric and medical complications were included in this study. Sociodemographic and obstetric characteristics of the participants were assessed with a standart questionnaire. The presence of LBP was recorded as "yes" and "no". The level of physical activity was assessed with the Pregnancy Physical Activity Questionnaire (PPAQ). The PPAQ is self-administered and asks respondents to report the time spent participating in 32 activities including household/caregiving, occupational, sports/exercise, transportation and inactivity. Independent samples t test was used to determine whether there was a difference in physical activity level between two independent groups (Group 1: Pregnant women with LBP, Group 2: Pregnant women without LBP).

**Results:** 77 pregnant women (mean age: 29.28±5.14 years, mean body mass index (BMI): 25.95±3.86 kg/m<sup>2</sup>) had no LBP. However, 74 pregnant women (mean age: 29.22±4.90 years, BMI: 26.85±2.78 kg/m<sup>2</sup>) have experienced LBP. There was no statistically significant difference in gestational week between two groups ( $p > 0.05$ ). Exercise-sports activity (mean: 5.69±7.29 MET-h.week<sup>-1</sup>) and vigorous activity (mean: 2.39±3.80 MET-h.week<sup>-1</sup>) scores of PPAQ were significantly lower in the pregnant with LBP than in those without LBP. Other activity scores were similar between groups ( $p > 0.05$ ).

**Conclusions:** The presence of LBP during pregnancy causes decreased levels of sports and exercise activities in the pregnant women while household/caregiving and occupational activities are being carried out. LBP can be a barrier to perform physical activities and exercises for pregnant women. Therefore, it should be treated with appropriate methods and pregnant women should be encouraged to regularly participate to exercise programs.

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#### THU0530 CHRONIC LOW BACK PAIN AND DEPRESSION: SIGNIFICANT DECREASE WITH GLUCOSAMINE-CHONDROITIN SULFATE TREATMENT IN A LARGE, COMMUNITY-BASED, PILOT, OPEN PROSPECTIVE INTERVENTIONAL STUDY

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**Background:** Low back pain (LBP) is the leading cause of Years Lived with Disability worldwide.<sup>1</sup> The number of people suffering from LBP grew more than 50% from 1990 to 2013, to 651 million.<sup>1</sup> Chronic low back pain can often lead to depression. Data on 1 90 593 community-dwelling adults aged ≥18 years from the World Health Survey (WHS) 2002–2004 in 43 Low and middle-income countries show a strong correlation between chronic back pain and depression.<sup>2</sup> Glucosamine-chondroitin sulfate (GCS) combination is widely used in the treatment of OA; however, there are few prospective scientific investigations of its therapeutic merits in severe LBP.

**Objectives:** To study the efficacy of GCS in the decreasing depression in patients with chronic low back pain in a large open pilot prospective observational study.

**Methods:** We enrolled patients between 40 and 65 years of age who had LBP for at least 12 weeks with a pain intensity >3 on a 0–10-point visual analogue scale (VAS) in a single-arm, open-label prospective interventional study. Major exclusion criteria were the presence of fibromyalgia, degenerative spondylolisthesis, and alcohol and/or drug abuse. All patients were treated with a combination of glucosamine hydrochloride 500 mg and chondroitin sulfate 500 mg in tablet form (Unipharm Inc.) at a dose of 1 tablet bid for the first month and then 1 tablet daily for the next two months. The primary endpoint was pain intensity (at rest and movement) as measured on a 0–10 point VAS. Depression was measured by the 13-questionnaire Beck's Depression Inventory (BDI). There are 13 questions in this score with highest possible score of 39 (5–7 is mild depression; 8–15 moderate depression, 16 and over severe depression).<sup>3</sup>

**Results:** A total of 8598 subjects (mean age 52.1 years, 67.3% women, mean BMI 27.4) were enrolled in the study, and formed the intent-to-treat (ITT) population. All but 95 subjects (1.1%) completed the study. Previously-reported ITT analysis with worst observation carried forward (WOCF) showed an improvement in pain at rest from mean (±SD) of 5.2±1.9 at study entry to 1.4±1.6 at 3 months ( $p < 0.0001$ ). Pain at movement decreased from 6.8±1.6 to 2.2±1.8 ( $p < 0.0001$ ). Baseline BDI scores showed a highly significant correlation with baseline pain scores at rest and movement ( $p < 0.0001$  for both). After 12 weeks of GCS treatment, the mean BDI score dropped from 8.7 (95% CI 8.6 to 8.9) to 2.9 (95% CI 2.8–3.0) (paired-test  $p < 0.0001$ ). An adverse event (AE) was reported by 604 (7.0%) patients (mostly gastrointestinal in origin, such as nausea, abdominal pain and dry mouth) but only 85 (1.0%) patients deemed it severe enough to discontinue therapy.

**Conclusions:** Although open and uncontrolled, this large pilot community-based study shows dramatic reductions in pain and depression in patients with LBP treated with GCS. With its benign safety profile, GCS therapy deserves serious evaluation in the management of LBP in a prospective randomised double-blinded clinical trial.

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#### THU0531 COMPARISON OF THREE DIFFERENT TRIGGER POINT TREATMENT IN THE MANAGEMENT OF LOW BACK PAIN: A PILOT STUDY

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**Background:** Low-back pain is a common health problem worldwide. In the majority of cases, the pathoanatomical source of an individual's pain cannot be identified and are therefore defined as non-specific in nature. Although there are many potential contributing factors to low back pain, one area that has received

scientific emphasis is the trigger point (TrP). TrP is defined as hyperirritable areas within taut bands of skeletal muscle and classified as either active or latent. Although many methods have been proposed for use in the treatment of TrP, there has been no study investigating which method is more effective.

**Objectives:** The aim of our study is to compare the different trigger point techniques used in the treatment of low back pain.

**Methods:** 28 cases with low back pain with trigger point origin were included in the study. The subjects were randomly divided into 3 groups. Strain-Counter Strain (SCS) technique was applied to Group 1 (n=16), Integrated Neuromuscular Inhibition Technique (INIT) for Group 2 (n=16), and Ischaemic Compression Technique (ICT) for Group 3 (n=16). The duration of treatment was a maximum of 6 weeks (12 sessions) in both three groups. Visual Analogue Scale (VAS) was used for pain severity, algometer examination was used to measure pain threshold, and Oswestry Disability Index was used to assess disability score. In addition, the Beck Depression Scale was used to assess the psychosocial status of the cases, and the STAI (State Trait Anxiety Inventory)- I and STAI-II scales were used to assess emotion-state and continuity. The evaluations were made before the treatment, after the 1st session of the treatment and at the end of the treatment (after 6 weeks). The data were analysed by using Kruskal-Wallis Test.

**Results:** Mean age and body mass index (BMI) of our study group were, respectively, 38.6±12.3 years and 26.6±6.2 kg/m<sup>2</sup> in the SCS group, 34.2±10.1 years and 26.3±5.9 kg/m<sup>2</sup> in the INIT group and 34.8±14.2 years and 24.5±5.2 kg/m<sup>2</sup> in the ICT group. There was no significant difference among groups in respect of age, BMI, depression and anxiety score (p>0.05) before the treatment. Three groups had significant decreases in pain according to the VAS and algometer (p<0.05). The ROM values and function level significantly improved within three groups after treatment (p<0.05). There was no statistically significant difference in pain (p=0.13), lumbar flexion (p=0.77), lumbar extension ROM (p=0.43) and disability score (p=0.65) among the three groups before and after the treatment.

**Conclusions:** The results indicate that patients with low back pain gain clinically benefit from trigger point treatment on pain, ROM and function. Therefore, we suggest that physiotherapist either can apply SCS, INIT or ICT based on their clinical experience in the management of low back pain. This work was supported by Istanbul University, Scientific Research Projects (Number: TYL-2017-24209)

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#### THU0532 TO ASSESS WHETHER THERE IS AN ASSOCIATION BETWEEN HYPERMOBILITY AND SPORTS INJURY

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**Background:** Joint Hypermobility (JH) is an extremely heritable condition in which joints have a range of motion beyond normal limits. This is frequently seen in healthy individuals.<sup>1</sup> It is important to differentiate this from Joint Hypermobility Syndrome (JHS).<sup>2</sup> (JH is diagnosed as a Beighton score of four or more).<sup>3</sup>

**Objectives:** The objective of this project was to determine whether there is an association between hypermobility and sports injury.

**Methods:** A quantitative observational approach using a cross sectional survey was adopted. A pilot study and initial focus group was arranged, involving 10 university students. Individuals were identified as hypermobile or not using the Beighton score. All participants were asked to complete two questionnaires; the first asking demographic information; the second questionnaire was injury specific. Fisher's exact test was used for statistical analysis.

**Results:** A total of 114 individuals participated in the study. 62 were women and 52 men. 26% of participants were found to be hypermobile. There was no significant association between hypermobility and sports injury (p=0.6596). There was a significant increase in joint and ligament sprain amongst the non-hypermobile (NH) group covering all sports studied (p=0.0269). Results showed that joint dislocation was found exclusively amongst hypermobile individuals. Duration of injury in hypermobile individuals was higher than NH. The use of oral painkillers or anti-inflammatories in the semi professional group was greater than the general population.

Table 1 Prevalence of hypermobility in each sport

Sport	Total Participants	H	NH	H (%)
Running	26	8	18	30.8
Football	24	6	18	25
Cycling	5	2	3	40
Squash	2	0	2	0
Swimming	1	1	0	100
Rugby	16	2	14	12.5
Hockey	19	6	13	31.6
Tennis	4	1	3	25
Netball	17	4	13	23.5
Total	114	30	84	26.3

**Conclusions:** Hypermobility is relatively common amongst individuals and there is a lot of anecdotal evidence associating it with increased rates of injuries. This

project finds that NH individuals are more likely to sustain a ligament or joint sprain in sports. This is thought to be due to increased joint laxity and flexibility preventing injury.

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#### THU0533 PREVALENCE OF LOW BACK PAIN AND KINESIOPHOBIA IN ELDERLY RESIDENTS OF SAO PAULO CITY: A CROSS-SECTIONAL PRELIMINARY DATA

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**Background:** Low back pain (LBP) is an important health problem around the world associated with disability, high costs for the health system and work absenteeism. A recent systematic review estimated that in Brazil, the point prevalence of LBP in the elderly is 25%, superior to knee osteoarthritis and rheumatoid arthritis, being considered one of the most relevant health conditions in the elderly.

**Objectives:** To measure the prevalence of LBP and kinesiophobia in the elderly, following the existing guidelines on conducting specific prevalence studies about LBP and to investigate the factors associated.

**Methods:** This is a cross-sectional study and the total sample to be recruited is 513 individuals of both genders, over 60 years old. Pain was investigated at two different times: current and last year, and pain intensity was measured by Numerical Pain Rating Scale (NPRS). Disability was measured using the Roland Morris Disability Questionnaire - Brazil version (RMDQ - BRA) and kinesiophobia was measured by the Tampa Scale for Kinesiophobia (TSK).

**Results:** Until now, 387 elderly were interviewed, of which 77% were women and the mean age was 71.98 (±7.70). The prevalence of LBP was 76.23%, with a punctual prevalence of 72.54% and a 12 months prevalence of 93.22%. The mean NPRS score was 7.52 (±2.16), the mean RMDQ - BRA score was 11.32 (±5.35), and the mean of the TSK score was 43.78 (±7.50).

**Conclusions:** Preliminary data indicate that the prevalence of LBP and kinesiophobia are high in this population. However, the level of functional disability due is moderate. There are few studies that approach these symptoms in the elderly population, and will serve as the basis for the creation of health policies.

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#### THU0534 THE EFFECT OF LUMBER STABILISATION EXERCISE ON THE BALANCE AND CLINICAL HEALTH

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**Objectives:** The aim of this study is to investigate the effects of lumbar stabilisation exercises on chronic low back pain in term of pain, functioning, quality of life, balance and trophic improvement of lumbar multifidus muscles.



**Methods:** 66 patients with chronic low back pain were enrolled in this study. The patients were randomised and divided into two groups. Lomber stabilisation exercises, TENS and Hotpack treatments were given to the first group (n: 28) while the second group (n: 37) were treated with only TENS and Hotpack. Patients' evaluations have been carried out before and after 8 weeks following the exercises. Visual Analogue Scale (VAS) were used to determine the pain as a numeric scale during the rest and physical activity. Modified Oswestry Questionnaire Survey and Roland Morris Scale were used to evaluate of functional disability. The Short Form-36 (SF36) applied to measure of quality of life. Tetrax device has been used to evaluation the body balance. 7–15 MHZ Ultrasound has been used to evaluate the change of trophic changes of multifidus muscle's cross-sectional areas.

**Results:** Except falling risk, in all parameters we have observed significant improvement in group 1. Cross-sectional area of the multifidus muscles, physical role of SF-36, mental health and energy/vitality sub parameters were found significantly better in group 1 when compared to the other group. There was no significant difference between the groups when the fall index, VAS scores, Roland Morris Questionnaire and Oswestry Disability Index were considered.

**Conclusions:** As a result, lomber stabilisation exercises have positive effect on pain relief, improve the functional capacity and quality of life. Additionally the exercises also had benefit and increased cross-sectional areas of multifidus muscles.

**Disclosure of Interest:** None declared

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**THU0535 TITLE: SAFETY AND EFFICACY OF PLATELET-RICH PLASMA IN TREATMENT OF CARPAL TUNNEL SYNDROME; A RANDOMISED CONTROLLED TRIAL**

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**Background:** Carpal tunnel syndrome is the most common peripheral entrapment neuropathy, for which conservative treatments are the first measures taken but they are not usually sufficient.

**Objectives:** Recently major attention has been drawn to platelet-rich plasma, for its possible effects on axon regeneration and neurological recovery. Although few studies have evaluated the effects of this treatment in carpal tunnel syndrome, further investigations are required to reach concrete conclusion.

**Methods:** In this randomised controlled trial, women referring to the physical medicine and rehabilitation clinic at Shahid Modarres Hospital during 2016 with a diagnosis of mild and moderate idiopathic carpal tunnel syndrome were included and randomly assigned to two groups of control, only using a wrist splint, and platelet-rich plasma that received wrist splints along with a single local injection of platelet-rich plasma. The outcome measures were assessed via Visual Analogue Scale, the Boston Carpal Tunnel Syndrome Questionnaire and electrophysiological findings including the peak latency of sensory nerve action potential and the onset latency of the compound muscle action potential.

**Results:** A total of 41 women were included and randomly assigned to two groups of control (20 wrists) and platelet-rich plasma (21 wrists). Before treatment there were no significant differences between the two groups except for the median peak latency of sensory nerve action potential which was significantly higher among the patients in the platelet-rich plasma group ( $p=0.03$ ). All the measured variables significantly decreased in both groups after 10 weeks of treatment except for the median onset latency of the compound muscle action potential ( $p=0.472$ ). Finally, the changes in neither of the outcome measures evaluated were found to significantly differ between the two groups, even when the analyses were adjusted for age of the patients.

**Conclusions:** The findings of this study showed that in a relatively short period of time after treatment, a single injection of platelet-rich plasma in the wrist does not add significantly to the effects of conservative treatment with wrist splints, in regards to the women pain and symptom severity, functional status and electrophysiological parameters.

**Disclosure of Interest:** None declared

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**THU0536 KNOWLEDGE OF AND EXPECTATIONS ABOUT FUNCTIONAL RESTORATION PROGRAM FOR CHRONIC LOW BACK PAIN ARE OFTEN FALSE: A MIRROR SURVEY OF 40 PATIENTS AND 59 PHYSICIANS IN 2017**

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**Background:** Functional restoration programs (FRP) are multi-disciplinary programs that have demonstrated their effectiveness in chronic low back pain (CLBP) but they appear to be little known by patients and/or physicians.

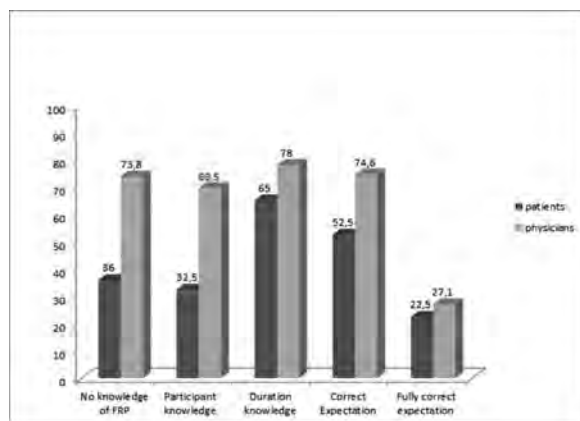
**Objectives:** To assess the knowledge and expectations of CLBP patients and physicians about FRP.

**Methods:** Multicenter cross-sectional study in 2017 in 6 tertiary-care hospitals in France. Consecutive patients with CLBP (more than 6 weeks) who were seen for their CLBP were included. Physicians (rheumatologists or general practitioners, GPs) who had referred at least 5 patients to the tertiary-care centres were sent a survey. Patients and physicians were asked about their knowledge and expectations of a FRP. Results were scored as 'correct' regarding health professionals involved in the FRP, if both doctors and (physiotherapists or physical activity coach) were ticked; and 'correct' for duration if 3 to 6 weeks. Expectations regarding the FRP were rated on a list of potential expectations on a scale of 0–10. Expectations were scored 'correct' if return to work was scored  $\geq 7/10$ , and 'fully correct' if physical activity and pain management, but not 'healing' were also expected. Responses were then compared between patients and physicians by Chi 2 test.

**Results:** Of 172 patients, median age 48 years (IQR 38–58), median CLBP duration 5 years (IQR 2–10), 60.0% women: 110 (64.0%) had no knowledge of FRP; 22 had already participated in an FRP. The remaining 40 patients were compared to physicians (figure 1). Of 80 physicians, 42.5% GPs and 53.7% rheumatologists, 57.5% women: 21 (26.2%) had no knowledge of FRP ( $p$  value $<0.0001$  vs patients). The remaining 59 were compared to the 40 patients.

Knowledge of FRP health professionals was 'correct' for 13/40 (32.5%) patients vs 41/59 (69.5%) physicians ( $p=0.0003$ ); and knowledge of duration was 'correct' for 26/40 (65.0%) vs 46/59 (78.0%) physicians ( $p=0.15$ ).

Expectations were 'correct' for 21/40 (52.5%) patients vs 44/59 (74.6%) for physicians ( $p=0.02$ ), and 'fully correct' for 9/40 (22.5%) patients vs 16/59 (27.1%) for physicians ( $p=0.6$ ).



**Conclusions:** FRP was largely unknown to patients with CLBP. Even those who were aware of the FRP did not know what to expect. While physicians' knowledge and perception of the FRP was better, there was still a lack of knowledge and therefore a likely underutilization or misuse of the FRP. Information campaigns are needed.

**Disclosure of Interest:** None declared

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THU0537

### ASSOCIATION BETWEEN BIG FIVE PERSONALITY TRAITS AND RESPONSE TO MULTIDISCIPLINARY PROGRAM IN PATIENTS WITH CHRONIC LOW BACK PAIN: A PROSPECTIVE STUDY

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**Background:** Chronic back pain is a multifactorial condition, which cannot be thoroughly addressed without understanding the psychological factors that influence its onset, maintenance and the response to its management. Patient attitudes and personality traits often determine how they experience pain, how they adjust to it, and their response to the different management strategies.

**Objectives:** This study aimed to identify whether patients with specific Big Five personality traits are more likely to seek medical care, and to uncover whether there is an association between personality and the patient's response to multidisciplinary functional rehabilitation program.

**Methods:** 97 patients (57% male) aged 41.1 (10.1) with chronic low back pain, enrolling in an intensive 4 week multidisciplinary functional rehabilitation program, completed the NEO Personality Inventory-Revised (NEO PI-R) at baseline. Outcome was assessed at treatment admission and discharge, and at 6 months follow up, including Core Outcome Measure Index (COMI), Tampa Scale for Kinesiophobia (TSK), Oswestry Disability Index (ODI) and Hospital Anxiety and Depression Scale (HADS).

**Results:** Both men and women had significantly lower scores in the Openness to Experience domain and significantly higher scores in the Conscientiousness domain than the average general population. At baseline, Neuroticism was found to correlate positively with TSK and HADS. Low Openness to Experience, and low Extraversion correlated with high HADS at baseline as well. Analysis of the follow up data showed a significant reduction in the COMI, ODI, HADS and TSK at the end of the program, and at 6 months follow up. There was no correlation between the improvement in COMI, ODI or TSK scores after 6 months and any of the 5 domains of the NEO PI-R

**Conclusions:** Low Openness to Experience and high Conscientiousness seem to be key factors of chronicity in patients with low back pain. Significant decrease in pain, disability as well as depressive and anxious moods showed that these patients were effectively treated by the multidisciplinary functional rehabilitation program regardless of their personality traits.

**Disclosure of Interest:** None declared

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THU0538

### PATIENTS WITH CHRONIC LOW BACK PAIN ORIENTED TO FUNCTIONAL RESTORATION PROGRAM ARE YOUNGER, WITH HIGHER SMOKING AND LONGER SICK LEAVE: A CROSS-SECTIONAL STUDY OF 166 PATIENTS

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**Background:** Functional Restoration Programs (FRP) are multi-disciplinary programs that have demonstrated effectiveness to promote functional status and return to work in patients with chronic low back pain (cLBP)<sup>1, 2, 3</sup> and moderate or high disability.

**Objectives:** To explore the characteristics of cLBP patients oriented or not towards a FRP.

**Methods:** This was an observational cross-sectional, multi-centric study in France in 2017. Consecutive patients with cLBP (>6 weeks) with or without radiculalgia, aged 18–66 years and visiting the rheumatologist for cLBP were included. Patient and disease characteristics were collected. Patients oriented or not towards a FRP were compared in particular for demographic characteristics, duration of sick leave over the past 12 months, smoking, ongoing aerobic physical activity (patient-reported as <or at least 30 min sessions twice a week), anxiety or

depression (Hospital Anxiety and Depression Scale $\geq$ 11), disability (Oswestry >40%) and kinesiophobia (Tampa Kinesiophobia Scale $\geq$ 40).

**Results:** In all, 166 patients were analysed: median age 48 years, median cLBP duration 5 years, and 100 (60%) were females. Overall, 62 (37%) were proposed for a FRP. Patients oriented towards a FRP, versus not, were more frequently male (50% vs 44%,  $p=0.04$ ), younger (median 46 vs 52 years,  $p=0.02$ ), and had lower pain levels (median 6 vs 7 of 0–10 numeric scale,  $p=0.006$ ). They had longer sick leave (mean 18 vs 10 weeks/year,  $p=0.006$ ), were more frequently smokers (33% vs 23%,  $p=0.02$ ), had similar pain duration (60 month vs 72,  $p=0.32$ ), functional disabilities (39% vs 49%,  $p=0.22$ ), kinesiophobia (62% vs 55%,  $p=0.65$ ), anxiety (52% vs 55%,  $p=0.60$ ) and depression score (40% vs 35%,  $p=0.54$ ), but less physical activity practice (38% vs 54%,  $p=0.04$ ).

**Conclusions:** Patients oriented towards a FRP were younger and more often males, with higher smoking and longer sick leave. It appears that kinesiophobia, functional status and duration of low back pain didn't influence the orientation toward a FRP. More comprehensive assessments of patients with cLBP are needed; multifactorial questionnaires such as StartBack or BP2 may be useful to orient patients towards FRPs.

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THU0539

### MECHANICAL TRACTION FOR LUMBAR RADICULAR PAIN: SUPINE OR PRONE? A RANDOMISED CONTROLLED TRIAL

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**Background:** Mechanical lumbar traction has been used to treat spinal disorders and low back pain for centuries, since Hippocrates.<sup>2,3</sup> Although the supine position is generally preferred, the patient may also be positioned prone during traction treatment.<sup>4,5</sup> However, to the best of our knowledge, no studies have compared the effects of lumbar traction in these two different positions for patients with chronic LBP.

**Objectives:** To compare the effects of mechanical lumbar traction either in the supine or prone position with conventional physical therapy (PT) in patients with chronic low back pain (LBP) and lumbosacral nerve root involvement in terms of disability, pain, and mobility.

**Methods:** Participants ( $n=125$ ) were randomly assigned to receive 15 sessions of PT with additional mechanical lumbar traction either in the supine position (supine traction group), or in the prone position (prone traction group), or only PT without traction (PT only group). Patients were assessed at baseline and at the end of the PT sessions in terms of disability, pain, and mobility. Disability was assessed using the modified Oswestry Disability Index (ODI); pain was assessed using a visual analogue scale (VAS); and lumbar mobility was assessed using the modified lumbar Schober test (mLST).

**Results:** 118 patients completed the trial. All groups improved significantly in the ODI, VAS, and mLST ( $p<0.05$ ) (table 1). In the between-group analysis, improvements of ODI and VAS were found significantly better in the prone traction group compared with the PT only group (adjusted  $p=0.031$  and  $0.006$ , respectively).

**Conclusions:** Addition of traction in prone position to other modalities resulted in larger immediate improvements in terms of pain and disability, and the results suggest that when using traction, prone traction might be first-choice. Further research is needed to confirm the benefits of lumbar traction in the prone position.

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Abstract THU0539 – Table 1

	Supine traction group (n=39)			Prone traction group (n=39)			Only PT group (n=40)		
	preintervention	postintervention	P	preintervention	postintervention	P	preintervention	postintervention	P
ODI	50.4±22.5	33.2±15.5	.001	53.8±15.1	35.9±15.9	.001	49.5±15.1	40.9±17.6	.002
VAS	8.0±1.6	4.3±2.2	.001	8.0±1.7	3.7±2.7	.001	7.7±1.5	5.2±2.3	.001
mLST	19.4±1.9	20.7±1.8	.001	18.8±1.8	20.5±1.3	.001	19.7±1.9	20.8±1.7	.001

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THU0540

#### INCREASED WORK CAPACITY IN CHRONIC LOW BACK PAIN PATIENTS AFTER A MULTIDIMENSIONAL PROGRAM ASSOCIATED WITH DECREASE IN FEAR AND APPREHENSION

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**Background:** Chronic low back pain has a high burden in our society. Almost 85% of the population would be affected from low back pain. Less than 10% would be chronic but they have an important economic impact since they have the highest costs. According to Vlayen, the kinesiophobia (avoidance of movement) is the most important prognostic factor when evaluating the return to work

**Objectives:** To study the importance of kinesiophobia, fear and anxiety in the chronic low back (CLB) pain patient and their relationship to workability after a multidimensional intensive treatment program.

**Methods:** We included 850 patients who had followed an outpatient program of functional restoration during 3 weeks. The program was composed of physical exercises, occupational therapy and psychological group discussions. They were followed over 1 year. Using different questionnaires (TSK -Tampa scale of Kinesiophobia, FABQ, Pact -subjective work capacity-, Phoda, SF 36), physical performances tests (muscular endurance: Shirado, Biering-Sörensen, Bruce; lumbar mobility, Pile lifting test) we analysed the important factors for their work capacity.

**Results:** There were a clear relationship between a decrease in kinesiophobia and an increase of work capacity. Globally, the work capacity increased from 41.2% to 79%. There were no long standing increases in muscular performances, but the important change appeared in the decrease in the physical part of FABQ (14 to 9/24) and the SF36 limitations physical health/emotional problems (19.4% to 51.8%/36 to 65.7%).

**Conclusions:** A multidimensional intensive program including approaches on fear and apprehension has an important impact on work capacity. This observation is important to take into account in creating functional restoration programs

**Disclosure of Interest:** None declared

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THU0541

#### THE EFFECT OF PHYSICAL THERAPY ON CLINICAL AND QUALITY OF LIFE IN CHRONIC NECK PAIN PATIENTS: A RANDOMISED CONTROLLED TRIAL

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**Background:** In the treatment of chronic neck pain (CNP), education, medical treatment, exercise and physical therapy (PT) modalities are in place. However, there are not enough studies on the efficacy of PT modalities in CNP

**Objectives:** To evaluate the effectiveness of the addition of PT modalities to exercise and medical treatment in relieving pain and improving the functional status of patient with CNP

**Methods:** 80 patients with CNP were included in a randomised, controlled trial. Patients were assigned in two groups randomly. Treatment group (TG) received conventional PT (hot pack (HP), ultrasound (US), Transcutaneous Electrical Nerve Stimulation (TENS)) treatment in addition. PT was applied ten sessions. HP treatment was applied in 20 min. US treatment was applied with 1,5watt/cm<sup>2</sup> dose and continuous type in 10 min. TENS treatment was applied with conventional type in 30 min. All patients were informed about correct posture and daily life activities. Both groups received home-based exercises program and analgesic medical treatment if it is necessary. Patients were evaluated before and after therapy and 3th month later by Visual Analogue Scale (VAS), cervical range of motion (ROM), Beck Depression Scale (BDS) and short form-36 (SF-36)

**Results:** In both groups there is significant improvement in VAS, cervical ROM, SF 36 and BDS after treatment (p<0.01). In TG significant improvement was seen on 3th month follow up. But the significant improvement was not seen on 3th month in control group (CG).

There is no significant difference between groups for VAS, SF-36 parameters and BDS before and after treatment (p>0.05). There was a significant improvement in VAS, SF-36 parameters and BDS in the TG compared with the CG at the end of therapy and 3 months post-treatment (p < 0.01)

**Conclusions:** Medical treatment and exercise with HP, US and TENS therapy was effective on both pain and disability during the treatment. This improvement kept on 3th month follow up. Also same improvement was seen on mood and life quality. Exercise has better effects on after treatment, but these good effects decrease on 3th month follow up. So we think physical medicine modalities should be used in CNP with disability

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THU0542

#### EVALUATION OF THE EFFECTIVENESS OF ULTRASOUND GUIDED EPIDURAL CORTICOSTEROID INJECTION AND PULSED ELECTROMAGNETIC FIELD STIMULATION IN CHRONIC LOW BACK PAIN

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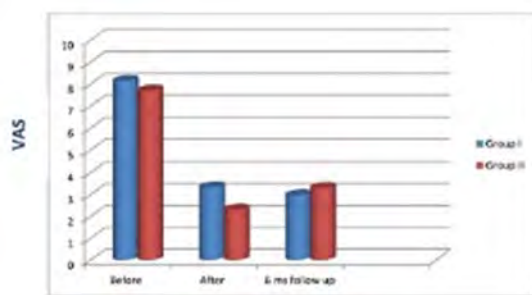
**Background:** Epidural injections are one of the most common nonsurgical interventions for managing chronic low back pain. They have been used to treat radicular pain from herniated discs, spinal stenosis, and axial spinal pain. Pulsed electromagnetic field stimulation therapy (PEMFs) provides a noninvasive and safe method to treat the site of injury, the source of pain, inflammation by modulating factors involved in pain signalling and the inflammatory response.

**Objectives:** To assess the improvement in patients with chronic low back pain treated with epidural steroid injection or Pulsed electromagnetic field stimulation. To compare the efficacy of epidural steroid injection and pulsed electromagnetic field stimulation in treatment of patients with chronic low back pain.

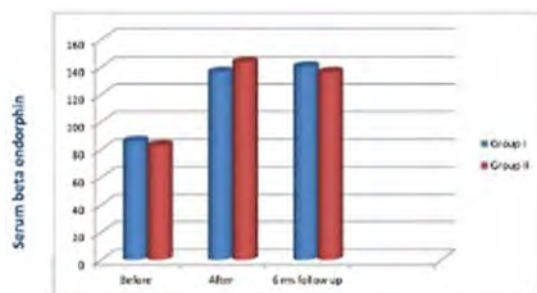
**Methods:** In this study; sixty patients with chronic discogenic low back pain (diagnosed clinically and by magnetic resonant imaging of lumbosacral region) with or without radicular pain of at least 6 months duration were selected. We excluded patients with other causes of back pain as spondylololthesis, inflammatory, infective, neoplastic, traumatic causes. Patients were randomly divided into two equal groups (30 patients each); after informed consent; group I treated by ultrasound guided caudal epidural injection of 40 mg methylprednisolone and 2 ml 2% lidocaine and 20 ml of 9% NaCl twice one week in between and group II received PEMFs daily for 4 weeks. And all patients will be instructed to follow an exercise program. All patients were assessed clinically, functionally by Oswestry Disability Index (ODI) and by measuring serum level of beta-endorphin by ELIZA before, at the end treatment and six months after the end of treatment.

**Results:** In both groups; there was highly significant improvement in pain after treatment (P1 <0.0001) the mean value of the (VAS) was 8.13+0.63, 7.70 +1.34 respectively before treatment and 3.33+2.63, 2.30+2.32 respectively after treatment. Still further significant improvement at the end follow up (P1 <0.0001) in group I. There was highly significant improvement (p<0.0001) of functional status in both groups after treatment and at follow up period as compared to before treatment but there was significant decrease of functional status at follow up period as compared to after treatment in group II. There was significant improvement of serum level of beta endorphin (p>0.05) in both groups after treatment and follow up period as compared to before treatment but there was insignificant difference at follow up period as compared to after treatment. Our result showed insignificant difference between two groups in clinical, functional or laboratory parameters.





**Figure 1.** Comparison regarding low back pain as measured by VAS before, after treatment and at 6 months follow up



**Figure 2.** Comparison regarding serum beta endorphin before, after treatment and at 6 months follow up

**Conclusions:** Epidural corticosteroid injection and Pulsed electromagnetic field stimulation are effective tools in management of chronic low back pain

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**Disclosure of Interest:** None declared

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THU0543

#### COMPARISON OF THE EFFECTIVENESS OF LOW LEVEL LASER THERAPY AND STEROID INJECTION IN MODERATE CARPAL TUNNEL SYNDROME: A RANDOMISED CONTROLLED TRIAL

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**Background:** Recent studies have reported that low-level laser therapy (LLLT) reduces pain and improves function in carpal tunnel syndrome (CTS). However, to the best of our knowledge, there exist no studies that compares the effectiveness of LLLT and steroid injections in moderate CTS.

**Objectives:** Is to evaluate the effectiveness of LLLT and steroid injection in moderate CTS, by comparing the symptoms, the electrophysiologic and the Magnetic Resonance Imaging (MRI) findings of the patients.

**Methods:** 87 patients with moderate CTS were included in the study. 87 patients were randomised to the steroid or LLLT groups. LLLT was applied to the carpal tunnel area (6 joules/5 min) five times per week, for a total of 10 sessions. Steroid injections were performed once after randomization. Numbness and pain of the patients were assessed using a Visual Analogue Scale (VAS), disability was assessed using the Quick arm-shoulder-hand (Quick DASH) disability questionnaire. Rough and fine grasping strength tests, Tinel and Phalen tests and

electrophysiological test were performed. All the patients were evaluated by MRI in terms of median nerve cross-sectional area, median nerve intensity and intensity rate, and median nerve palmary spring rate. All tests were performed before the treatment, and 1. month and 6. months after the treatment, except the MRI evaluations, which were done before and after 6. months of the treatment.

**Results:** The study was completed with 80 patients, 133 wrists at the end of six months. There were no significant differences between the groups in terms of demographic and baseline clinic characteristics, electrophysiologic and MRI findings of the patients ( $p>0,05$ ). While the VAS scores of numbness and pain and Quick Dash symptom scores were better in the steroid group in the first month, there were no significant differences between the groups in the sixth month. In both groups, there were similar significant improvements in the Phalen and Tinel tests, rough and fine grasping forces, median nerve motor distal latency value in the first and sixth months after the treatment in comparison to pretreatment values ( $p<0,05$ ). Median nerve sensory distal latency and median sensory NCV showed significant improvements in the 1st and the 6th months after treatment in comparison to pretreatment only in the steroid group ( $p<0,05$ ). In both groups, there were similar significant improvements in the median nerve intensity rate in the radioulnar plane and median nerve palmary spring rate on the MRI after the treatment. Median nerve intensity rate was improved in both groups also at the pisiform plane but this improvement was significant only in the steroid group.

**Conclusions:** It is possible to conclude that LLLT reduces the signs and symptoms of the patients who has moderate CTS as well as the steroid treatment. Our study offers a data regarding LLLT's efficiency in short-intermediate terms. Further studies are needed to make comments about long-term efficiency of LLLT. LLLT is a noninvasive treatment option in moderate CTS and with a similar efficacy as steroid treatment.

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THU0544

#### STUDY OF THE EFFECTS OF OZONE VERSUS STEROID INJECTION ON PATIENTS WITH RECALCITRANT TENNIS ELBOW; A CLINICAL TRIAL

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**Background:** Tennis elbow is a prevalent musculoskeletal disorder. In recent years ozone injection has been proposed as a treatment for many musculoskeletal disorders. This study aims to compare the effect of ozone injection with steroid in patients with recalcitrant tennis elbow.

**Objectives:** The aim of this study is to compare the effect of ozone with the standard treatment of steroid injection in patients with tennis elbow, resistant to conservative treatments. This comparison is made according to VAS score, Pressure pain threshold (PPT) and modified Mayo clinic performance index for elbow.

**Methods:** In this study 64 patients with tennis elbow, which have had the symptoms for more than 3 months and were resistant to conservative treatments, were randomised to two groups. In steroid injection group 40 mg of methylprednisolone acetate and in ozone injection group 4 ml of ozone with concentration of 15mcg/ml was injected. 32 patients in steroid and 29 patients in ozone injection group finished this study. Data were gathered before injection and 2 and 6 months after that by VAS score, modified Mayo clinic performance index for elbow and PPT (measured by the means of an algometer). Variables were compared between the two groups and also the changes in each group have been measured in reference to baseline data.

**Results:** In both groups VAS score, Mayo clinic performance index and PPT improved significantly in 2 and 6 month follow up. Steroid injection was significantly better than ozone injection in improving 2 and 6 months pressure pain threshold and 6 months Mayo clinic performance index. Other data didn't show significant difference between the two groups.

**Conclusions:** Both steroid and ozone injection improved pain and function in patients with recalcitrant tennis elbow for at least 6 months. Steroid injection was superior to ozone injection in improving PPT during the 2 and 6 month follow up and function improvement in steroid group was significantly more than ozone group after 6 month.

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THU0545

### CHARACTERISING A MOUSE MODEL OF TEMPOROMANDIBULAR JOINT (TMJ) ARTHRITIS TO STUDY OROFACIAL PAIN AND INFLAMMATION

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**Background:** The temporomandibular joints (TMJ) encompass the jawbones (mandibular condyle) and the skull region (temporal bone)<sup>1</sup>. Dysfunctions in these joints and surrounding muscles result in a condition known as TMJ disorder (TMD), which include mastication-related pain. 16%–59% of patients reported painful symptoms while 33%–86% of these patients showed clinical signs<sup>1</sup>. Currently, the etiology of TMD is unknown, although lavage samples from patients showed signs of synovitis, which may lead to the development of degenerative disorders, such as TMJ arthritis<sup>2</sup>. There are only a few murine models available, as the most commonly used animal model is TMJ arthritis in rats.

**Objectives:** We aimed to characterise a mouse model of TMJ arthritis by mimicking the formation of synovitis using zymosan. We sought to characterise the development of orofacial pain by performing various behavioural measurements and measure joint inflammation.

**Methods:** All *in vivo* procedures were carried out according to the UK Home Office Animals (Scientific Procedure) Act 1986. Male CD1 mice (6–8 weeks) were anaesthetised transiently using 2% isoflurane. Zymosan (10, 30, or 100 µg; 10 µl), or saline was administered unilaterally into the TMJ as previously described<sup>3</sup>. Spontaneous pain behaviours were observed by counting the number of unilateral cheek wipes. All studies were terminated by cervical dislocation and the tissue was collected for *ex vivo* analyses. Mean ±SEM was calculated and data were analysed by unpaired Student's T-test or 2-way repeated measures ANOVA with Bonferroni's *post hoc* test.  $p < 0.05$  was accepted as statistically significant.

**Results:** A dose response study showed that 30 µg, but not 10 µg and 100 µg of zymosan, resulted in a maximal wiping response at 2 hours, which was maintained at 4 hours (table 1; \*\*\* $p < 0.001$  zymosan ipsi vs saline ipsi; ##  $p < 0.01$  zymosan ipsi vs contra). Hind paw scratching was negligible. Hence, 30 µg was used for subsequent experiments. Increased neutrophils (measured by MPO assay) was observed in zymosan-treated joints (table 1 \*\* $p < 0.01$  saline ipsi vs zymosan ipsi), while a similar trend was also observed in 3-nitrotyrosine protein expression, a marker of protein nitrosylation ( $p = 0.053$ ). Preliminary studies are being undertaken to characterise other inflammatory markers in addition to the development of *in vivo* orofacial mechanical hyperalgesia using the Von Frey filaments.

Table 1 A summary of zymosan-mediated spontaneous orofacial pain behaviours and inflammation.

	Saline (n=4)		Zymosan					
			10 µg (n=6)		30 µg (n=5)		100 µg (n=6)	
	Ipsi	Contra	Ipsi	Contra	Ipsi	Contra	Ipsi	Contra
Unilateral cheek wipe (no. of events)	5.0 ±1.0	5.5 ±1.9	5.7 ±2.6	6.0 ±1.2	22.0 ±4.4	8.2 ±2.6	5.3 ±3.3	3.1 ±1.2
					*** ##			
Unilateral hind paw scratching (no. of events)	0.5 ±0.5	0.0 ±0.0	1.0 ±0.7	4.5 ±2.6	3.4 ±0.8	2.1 ±1.0	0.4 ±0.2	0.4 ±0.2
MPO (U/mg of protein)		0.01±0.003		N/A	0.08±0.01	**		N/A
3-nitrotyrosine/GAPDH		2.3±0.4			3.8±0.5			

**Conclusions:** We have established a mouse model of TMJ arthritis, which showed significant orofacial pain responses *in vivo*. Our data highlights an inflammatory profile typical of zymosan and shows a potential use for this model to investigate novel TMD treatments.

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**Disclosure of Interest:** None declared

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THURSDAY, 14 JUNE 2018

### Paediatric rheumatology

THU0546

### CHILDREN WITH PSORIASIS ALSO SHOW ENTHESOPATHY SIGNS RELATED TO SKIN DISEASE ACTIVITY

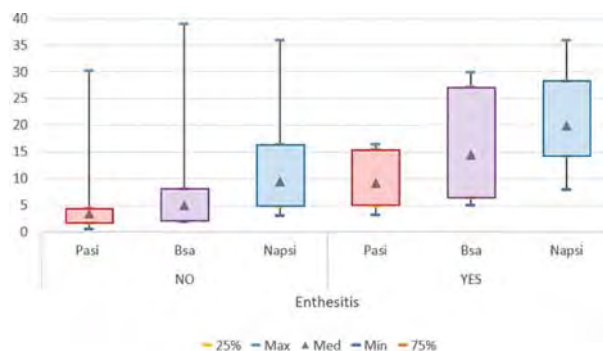
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**Background:** Many recent evidences shows the role of enthesopathy in psoriatic disease and the high prevalence of musculoskeletal widespread pain in patients with psoriasis and psoriatic arthritis. It may be very difficult to distinguish between inflammatory disease activity and fibromyalgia. Limited data are available about the prevalence of rheumatological findings in children with psoriasis.

**Objectives:** To determine the prevalence of musculoskeletal pain complaints, enthesitis and tender points in a population of children and adolescents with psoriasis and correlate it to the skin disease activity and quality of life.

**Methods:** 26 children and adolescents with psoriasis were included in this cross sectional study and assigned a written informed consent. Patients and parents were interviewed about musculoskeletal complaints, personal and familiar history of rheumatic diseases. A paediatric rheumatologist performed the physical examination, which included evaluation of active joint count, palpation of entheses and tender points of fibromyalgia. A paediatric dermatologist performed PASI score and BSA to assess skin disease activity. Nails involvement were assessed by NAPS. The functional capacity was assessed by CHAQ. The quality of life was assessed by CDLQI.

**Results:** Participants were 69% female, with a mean age of 10.1±3.0 years at observation. The median of age at the beginning of skin disease was 3 (0.5–12) years. PASI median was 4 (0.6–30.2), BSA 6 (2–39) and NAPS 12.<sup>3–36</sup> A severe PASI above 5 were present in 38.5%. Complaints of any kind of musculoskeletal recurrent pain were seen in 46.1% of the patients and lumbar pain in 15.4%. Pain, limit on motion or joint oedema were seen in 26.9% whereas tenderness on palpation of any site of entheses was found in 30.7% and tenderness on palpation of sacroiliac joint was found in 19.2% of the patients. The median of fibromyalgia tender points was 5 (0–16). The presence of enthesitis was associated to the skin disease activity scores of PASI ( $p < 0.006$ ), BSA ( $p < 0.016$ ) and nail index NAPS ( $p < 0.05$ ) (figure 1). As expected, the presence of enthesitis was associated to the number of tender points ( $p < 0.001$ ). For those with a severe PASI>5, we found a higher number of tender points (Med 0 versus 10;  $p < 0.03$ ), a worst functional capacity by CHAQ (Med 0 versus 0.12;  $p < 0.03$ ) and worst quality of life by CDLQI (Med 1 versus 9;  $p < 0.05$ ).



**Conclusions:** High prevalence of musculoskeletal pain symptoms, enthesitis and fibromyalgia tender points was observed in this sample of children and adolescents with psoriasis. Differently from adults, we do not expect to have age-related degenerative changes in entheses in this population, what reinforce the inflammatory origin of these rheumatologic findings. Otherwise, the association with the severity of psoriasis increases the need for vigilance against the appearance of psoriatic spondyloarthropathy in this group.

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THURSDAY, 14 JUNE 2018

## Rheumatoid arthritis – biological DMARDs

THU0547

### REAL-WORLD EFFECTIVENESS OF EARLY AGGRESSIVE TREATMENT WITH BIOLOGICAL DISEASE-MODIFYING ANTIRHEUMATIC DRUGS FOR THE TREATMENT OF NEWLY DIAGNOSED POLYARTICULAR FORM OF JUVENILE IDIOPATHIC ARTHRITIS

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**Background:** Limited evidence from randomised clinical trial suggested early aggressive treatment with biological disease modifying antirheumatic drugs (DMARDs) maybe a better treatment strategy in children with polyarticular form of Juvenile idiopathic arthritis (pJIA).<sup>1</sup> Three consensus treatment plans (CTP) were recommended for treating children with newly onset of pJIA.<sup>2</sup> The real-world effectiveness is unknown.

**Objectives:** Evaluate the comparative effectiveness of early combination CTP vs. the step-up CTP, in treating children with newly diagnosed pJIA, utilising electronic health records (EHR) data collected from routine clinical care.

**Methods:** This inception cohort is derived from data captured in a single institute EHR from January 2009 to July 2017. Eligible patients are 2–16 years of age, newly (<6 m) diagnosed with pJIA and treated on DMARD. The first clinical encounter initiate DMARDs is identified as the baseline. The primary end point is clinical Juvenile Arthritis Disease Activity Score (cJADAS) 6 months after the treatment.

**Results:** Out of 1834 pJIA patients captured in EHR, 432 are eligible for the study. Most patients (362, 84%) initiated DMARD within 6 month of diagnosis: 105 (29%) on early combination and 257 (71%) on step-up plan. Three months following the initial DMARD assignment, 98 (93%) and 244 (95%) remained on the initial early combination and step-up plan respectively, thus are used in this study. Patients on early combination had significantly higher cJADAS score at the baseline (15.5±6.6 vs. 12.5±5.9; Student P value<0.01), and higher rate of RF (18% vs. 7%, Chisq p<0.01). After 6 months of treatment, their cJADAS scores are more comparable (mean ±SD of 6.9±5.4 in early combination, and 7.1±6.1 in step-up; Student T p=0.7). After statistically adjusting for treatment selection bias, causal inference methods suggest lower cJADAS is expected had the patient been treated on early combination than on the step-up plan, mean and 95% confidence interval of averaged treatment effect is 2.90 (0.89, 4.91).

**Conclusions:** The early combination approach improves clinical outcomes at 6 months more effectively than the step-up strategy in children with newly onset pJIA.

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**Disclosure of Interest:** None declared

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## Diagnostics and imaging procedures

THU0548

### STANDARDISED PROCEDURES FOR ULTRASOUND IMAGING IN PAEDIATRIC RHEUMATOLOGY: PROGRESS OF EULAR/PRES TASK FORCE

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**Background:** Musculoskeletal ultrasound (MSUS) is dependent on sensitivity of the machine used and the skills of the operator. Additional specificities are unique features of the growing skeleton, which include age-related variation of the thickness of the articular cartilage (due to incomplete ossification) and the presence of physiologically detected vascularisation even in healthy children.

**Objectives:** EULAR/PRES task force objective was to develop EULAR/PRES Standardised Procedures for Ultrasound Imaging in Paediatric Rheumatology through a consensus process among rheumatologists, paediatric rheumatologists, and radiologists highly experienced in the performance, teaching and research in paediatric MSUS in rheumatic diseases.

**Methods:** In the first phase we performed a systematic literature review (SLR) on guidelines for MSUS for children endorsed by international societies and articles on how to perform MSUS scanning in children. Based on the SLR results, project conveners formulated a Delphi survey by selecting the items to be included (i.e. musculoskeletal anatomic structures evaluable by US, scanning technique, and their lesions/abnormalities detectable by US at the principal joint areas). The Delphi survey was distributed among a broad panel of experts in MSUS, selected for their high experience in the performance, teaching and research in MSUS in children. Based on the Delphi results the main anatomical structures (for definitions, photo and video recordings) were selected to be analysed in the final phase organised as an exercise on live healthy children models. The meeting involved: 16 project participants (13 paediatric US experts, fellow, as well as, AHP and PARE representatives), 16 healthy children models (representing four different age groups) accompanied by their parents (who had signed informed consent to participate), 4 photo/imaging technicians, 2 expert technicians in US machines.

**Results:** Structures from 8 musculoskeletal areas (i.e. shoulder, elbow, wrist and hand, hip, knee, ankle and foot) in 4 age groups of children were selected. Detailed scanning procedures (i.e. patient position, probe placement, scanning method and bony/other landmarks) were defined. We recorded the reference photo (live and US image) and video (procedure video clip and US video record) of the scanning procedures. As a result, we obtained photo and video image library with a detailed description of the standardised US procedures in children which can be used as EULAR/PRES web-based educational application.

**Conclusions:** This task force has produced a consensus-based comprehensive and practical framework on standardised procedures for MSUS imaging in paediatric rheumatology.

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THURSDAY, 14 JUNE 2018

## Paediatric rheumatology

THU0549

### ABSENCE OF ASSOCIATION BETWEEN DRUG EXPOSURE AND INFECTION IN PATIENTS WITH POLYARTICULAR-COURSE JUVENILE IDIOPATHIC ARTHRITIS AND INADEQUATE RESPONSE TO BIOLOGIC OR NON-BIOLOGIC DMARDs TREATED WITH SC AND IV ABACEPT

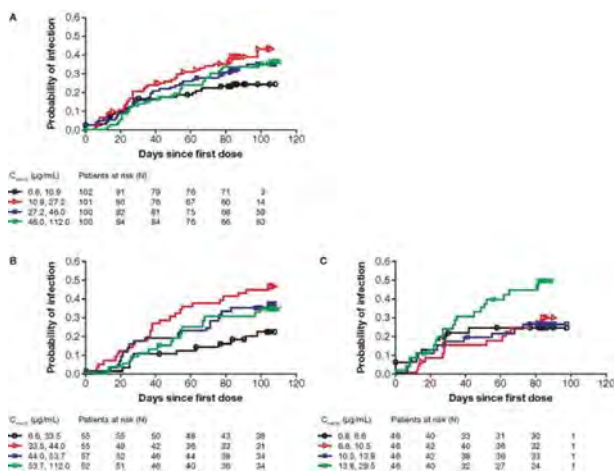
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**Background:** Infections are the most common expected AEs linked to biologic (b) DMARDs in paediatric patients (pts) with juvenile idiopathic arthritis (JIA). Blood concentrations achieved with bDMARDs vary greatly between individual pts. It is not known if higher abatacept (ABA) exposure is linked to higher infection risk in paediatric populations.

**Objectives:** To assess the relationship between the incidence of infection and SC (50–125 mg weekly) and IV (10 mg/kg monthly) ABA exposure in pts with polyarticular-course JIA (pJIA).

**Methods:** Data from the 4 month open-label periods of a Phase III SC ABA study (NCT01844518; weight-tiered ABA: 10–<25 kg [50 mg], 25–<50 kg [87.5 mg], ≥50 kg [125 mg]; 219 pts aged 2–17 years) and an IV ABA study (NCT0095173; ABA 10 mg/kg monthly; 184 pts aged 6–17 years) in pts with pJIA were analysed. The association between serum ABA exposure measures (steady-state trough [ $C_{\min ss}$ ], maximum [ $C_{\max ss}$ ] and time-averaged [ $C_{\text{avgss}}$ ] concentrations) estimated by population pharmacokinetic analysis and time to first infection (regardless of seriousness) was assessed. Kaplan–Meier (KM) plots of infection probability versus time to first infection by ABA exposure quartiles were created and log-rank test was performed to test the differences in distribution of time to first infection across exposure quartiles. Box plots of ABA exposure measures over time to Month 4 were generated, stratified by first infection occurrence (yes/no). Data for SC and IV ABA were assessed separately and pooled.

**Results:** Baseline demographic and clinical characteristics were comparable in the SC and IV studies.<sup>1,2</sup> Overall, 135/403 pts (33.5%) had ≥1 infection over 4 months: 77/219 (35.2%) with SC ABA and 58/184 (31.5%) with IV ABA. KM plots for pooled SC and IV ABA showed no statistically significant difference in infection probability across four quartiles of ABA  $C_{\min ss}$  (Fig A;  $p=0.2317$ ; log-rank test),  $C_{\max ss}$  ( $p=0.5501$ ) or  $C_{\text{avgss}}$  ( $p=0.3808$ ). Consistent results were seen for individually studied SC and IV ABA  $C_{\min ss}$  (Fig B, C),  $C_{\max ss}$  and  $C_{\text{avgss}}$  (not shown). In addition, there was no difference in median ABA exposure measures by infection occurrence (yes/no) in pooled and separate SC and IV analyses.



**Abstract THU0549 – Figure 1.** Kaplan–Meier Plots of Probability of First Infection, Regardless of Seriousness, Versus Days From First Dose to Infection by Abatacept  $C_{\min ss}$  Quartiles and Route of Administration: Pooled SC and IV (A); SC (B); IV (C)

**Conclusions:** In pts with pJIA who received SC or IV abatacept, higher relative abatacept exposure was not associated with a higher risk of infections for 4 months.

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THU0550

### NEW IL10 RECEPTOR GENE MUTATION ASSOCIATED TO A SPECTRUM OF INFLAMMATORY APHTHOSIS AND CROHN'S DISEASE

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**Background:** IL-10 is defined as an anti-inflammatory cytokine. Its activity is mediated by interaction with a cell surface receptor composed of 2 subunits: alpha (IL-10RA) and beta (IL-10RB). Homozygous mutations of IL-10RA gene have been linked to Very Early Onset Inflammatory Bowel Disease (VEO-IBD) in children with a total of 28 mutations identified till present.

**Objectives:** We report a Lebanese family presenting with a new exonic mutation in the IL-10RA gene variably associated to inflammatory aphthosis and adult onset IBD.

**Methods:** The proband is a boy born to consanguineous parents who presented to our attention at the age of 9. He suffered from persistent severe oral aphthosis, recurrent fever and intermittent diarrhoea since the age of 2 months, and anal aphthosis since the age of 7.

His Familial history is notable for moderate oral aphthosis in the father and adult onset Crohn's disease in a paternal uncle.

He was diagnosed with Behçet disease and received colchicine since the age of 8 with no efficiency.

His physical exam was normal except for severe oral and anal ulcers. No history of genital ulcers.

Laboratory tests revealed normal inflammatory markers. ANA titers, anti-DNA and anti-ENA were negative with normal complement level. Pathergy test and HLA B51 were negative as well as pANCA and cANCA. Iron, Zinc, vitamin and immune deficiencies were ruled out.

Yearly ophthalmologic screening revealed no signs of inflammation.

Repeated gastroscopy and colonoscopy and enteric MRI showed no pathologic findings.

**Results:** A genomic sequencing study for recurrent fever was performed. A novel heterozygous exonic mutation of the IL-10RA gene (c.G172A G>A, p.E58K) was identified. The child's father and his uncle were found to have the same mutation at homozygous state, however with different phenotypic presentations.

The child was started on Infliximab with favourable outcome after 3 months.

**Conclusions:** In this Lebanese family, the previously unreported IL-10RA gene mutation (c.G172A G>A, p.E58K) is associated to a variable spectrum from

benign oral aphthosis to IBD, both in homozygous and heterozygous forms. Our finding suggests that the presence of this mutation is a risk factor for inflammatory aphthosis. Whether this mutation will eventually lead to IBD is uncertain. Other unknown environmental and genetic factors might have a role in the final phenotype of the disease.

As bipolar aphthosis and recurrent fever can be misdiagnosed as Behçet disease, pro-inflammatory genetic mutations such as IL-10RA mutations should be considered in the setting of incomplete Behçet disease.

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**Disclosure of Interest:** None declared

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#### THU0551 TREATMENT STRATEGY STUDY IN NEW ONSET DMARD NAIVE JUVENILE IDIOPATHIC ARTHRITIS FIRST RESULTS ON 24 MONTHS CLINICAL OUTCOME

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**Background:** In rheumatoid arthritis treatment, targeted treatment has shown to improve disease outcomes including the option of drug tapering and discontinuation. In non-systemic juvenile idiopathic arthritis (nsJIA) this has not been tried in a trial.

**Objectives:** To investigate which of three treatment strategies, targeting at drug-free inactive disease, is most effective and safe in recent onset DMARD-naive nsJIA.

**Methods:** We conducted a randomised, multicenter, treatment strategy study with 24 months of follow up. Patients, 2–16 years old with symptom duration <18 months were randomised to 1) Sequential DMARD-mono therapy (sulfasalazine (SSZ) or methotrexate (MTX), 2) Combination therapy MTX +6 weeks prednisolone, 3) Combination therapy MTX +etanercept. Treatment to target entailed three-monthly treatment intensifications in case of persistent disease activity. DMARDs were tapered to nil in case of inactive disease for at least 3 (in oligoarticular) or 6 (in polyarticular) months. After 24 months, primary outcomes were time-to-inactive-disease and time-to-flare after DMARD discontinuation. Secondary outcomes were adapted ACRPedi30/50/70/90 scores, functional ability and toxicity. Missing data were imputed.

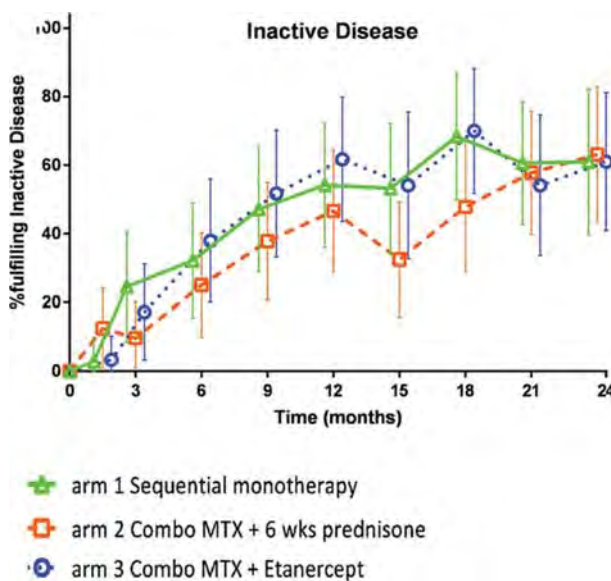
**Results:** 94 children (67% girls) with a median (InterQuartile Range) age of 9.1 (4.6–12.9) years were enrolled: 32 in arms 1 and 2, 30 in arm 3. Eleven had oligoarticular JIA, n=73 polyarticular JIA and n=8 juvenile psoriatic arthritis, 37% were ANA positive. At baseline VAS physician was median (IQR) 50<sup>39–58</sup> mm, VAS patient 54<sup>37–70</sup> mm, ESR 6 (2–14) mm/hr, active joints 8, <sup>5–12</sup> limited joints 2.5 (1–5), and CHAQ score 0.9 (0.6–1.5).

After 24 months 61% (arm 1), 63% (arm 2) and 61% (arm 3) of patients had inactive disease and 45% (arm 1) 31% (arm 2) and 38% (arm 3) had stopped all DMARD(s). Time to inactive disease (median 9.0 (6.0–12.0) months) was not significantly different between arms, nor was time to flare (18.0 (15.0–21.0) months). Adapted ACRPedi-scores were comparably high between arms. Functional ability

improved and remained almost normal. Toxicity reports showed mild events in similar rates across all arms.

	Arm 1 n=31	Arm 2 n=32	Arm 3 n=29
ACRPedi50 (%) (CI)	85.5 (72.4–98.6)	83.8 (70.1–97.4)	93.1 (83.7–102.4)
ACRPedi70 (%) (CI)	69.0 (52.1–85.9)	68.8 (51.6–85.9)	82.8 (68.8–96.8)
ACRPedi90 (%) (CI)	58.4 (40.6–76.1)	55.3 (37.3–73.3)	69.0 (51.8–86.1)
Inactive disease (%)	61.0 (39.7–82.3)	63.1 (43.6–82.7)	61.0 (40.9–81.2)

Results after 24 months by GEE.



**Conclusions:** Treatment to target drug free inactive disease is feasible in recent onset non-systemic JIA, resulting, regardless of initial treatment, in over 60% of patients in inactive disease and 38% drug free.

**Disclosure of Interest:** None declared

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#### THU0552 ARTICULAR AND EXTRA-ARTICULAR DAMAGE IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS – RESULTS FROM THE INCEPTION COHORT OF NEWLY DIAGNOSED PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS (ICON)

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**Background:** Juvenile idiopathic arthritis (JIA) may lead to disability and damage, preventing both is an important therapeutic goal. The frequency of damage in children and adolescents with JIA and the question of whether the damage increases with the duration of the disease also in the biologic treatment era have hardly been investigated.

**Objectives:** To assess the prevalence and accrual of damage in patients with JIA over six years and to analyse damage association with disease activity, quality of life and functional limitations.

**Methods:** We analysed data of patients with JIA who were enrolled in ICON. Clinical characteristics such as disease activity (e.g. JIA core set criteria) and details on current treatment as well as patient's quality of life (PedsQL) and functional limitations (CHAQ) were assessed quarterly during the first 12 months in ICON and half-yearly thereafter. The Juvenile Arthritis Damage Index (JADI, range 0–89, best=0) was reported by the physician at the 3 year, 4 year and 6-year-FU, respectively. The JADI is composed of two sub-scores, the JADI-A scores joint

damage (in 36 joints or joint groups) and the JADI-E extraarticular damage (in 5 different organs/systems: ocular, musculoskeletal excluding joints, cutaneous, endocrine, any organ/system).

**Results:** A total of 953 patients (67.2% female, mean age 7.9 years (SD 4.8)) with JIA were included in ICON after a median disease duration of 6 months (IQR: 3.0–11.1). About half of the patients (46%) had oligoarthritis, followed by rheumatoid factor-negative polyarthritis (RF-PA) (26%) and enthesitis-related arthritis (11%). The mean disease activity score cJADAS10 was 9.8 (6.2) and the mean CHAQ was 0.57 (0.69) at enrolment. Any damage was reported for 58 patients (8.6%) at the 3-year-Follow-up (FU) (mean JADI-A 0.17, mean JADI-E 0.06, JADI-A >0: 6.1%, JADI-E >0: 3.1%). At the 4 year (mean JADI-A 0.17, mean JADI-E 0.07) and 6-year-FU (mean JADI-A 0.13, mean JADI-E 0.12), 8.6% and 10.7% of patients had any damage. The number of patients with articular damage did not change during FU (6-year-FU: 6.5%), whereas the proportion of patients with extra-articular damage slightly increased (6-year-FU: 5.0%). At the 6-year-FU, the most frequently scored joints were the knee joints, followed by the wrist. JADI-E was dominated by eye damage. Among the JIA categories, patients with RF-PA showed most frequently damage (16.7%), followed by patients with enthesitis-related arthritis (15.4%) and extended oligoarthritis (14.3%) at the 6 year FU. The JADI-A score significantly correlated ( $r=0.27$ ,  $p<0.001$ ) with the number of active joints and JADI-E with the cJADAS10 ( $r=0.14$ ,  $p=0.041$ ) However, there was no significant association between the JADI scores and quality of life (PedsQL), and functional limitations (CHAQ, all  $r<0.05$ ).

**Conclusions:** About one in ten patients with JIA has developed any damage three, four and six years after disease onset. Thus, a relevant increase in damage over time does not occur under current therapeutic conditions. Articular and extra-articular damage is similarly frequent.

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**Disclosure of Interest:** None declared

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THU0553

#### TNF-INHIBITOR AND LEFLUNOMIDE COMBINATION THERAPY IN POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS IN CLINICAL PRACTICE – LESSONS FROM THE GERMAN BIOLOGICS JIA REGISTRY (BIKER)

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**Background:** Leflunomide has been shown to be a safe and effective therapy for adult rheumatoid arthritis.

**Objectives:** Safety and efficacy of combination of TNF inhibitors with leflunomide versus methotrexate for treatment of polyarticular-course juvenile idiopathic arthritis (pcJIA) were assessed in the prospective BIKER registry 2000–2016.

**Methods:** 3 cohorts of pcJIA patients ageing 3–17 years were analysed: Patients receiving leflunomide starting a TNF inhibitor,<sup>1</sup> a TNF inhibitor starting leflunomide,<sup>2</sup> methotrexate starting a TNF inhibitor.<sup>3</sup> Efficacy was determined using the JADAS response criteria, JADAS-10 minimal disease activity (MDA) and remission. Safety assessments were based on adverse events reports from the responsible physician.

**Results:** We identified 94 patients treated with Leflunomid-TNF-inhibitor in combination. 44 started a TNF-inhibitor on background Leflunomide, 50 started Leflunomide on background TNF inhibitor. 1361 patients starting a TNF-inhibitor on background Methotrexate served as control group. Differences in patients' characteristics at baseline limit direct comparison. Patients of cohort 3 had higher CRP, patients of cohort 2, already treated with a biologic, had lower disease activity parameters such as mean active joint count, physician and patient global disease activity judgement and JADAS10. At month 6, upon MTX +TNFi 54.6%/41.7%/19.6% and upon LEF +TNFi 35.0%/36.2%/13.8% reached JADAS improvement/JADAs minimal disease activity/JADAs remission. Thus significantly more patients with MTX +TNFi reached JADAS improvement (OR 2.22 [1.44–3.44];  $p<0.001$ ) while there comparable rates of patients reached JADAS-MDA and JADAS-remission. In the LEF cohorts, there were 95 adverse events in 54 patients (58%) compared to 1845 events in 626 (46%) on MTX (OR 1.6 [1.0–12.4]  $p=0.031$ ). No differences were noted for the number of infections, nausea or elevated transaminases.

**Abstract THU0553 – Table 1.** Baseline patients' and disease characteristics

	Cohort 1 (n=44) LEF+TNFi	Cohort 2 (n=50) TNFi+LEF	Cohort 3 (n=1361) MTX+TNFi
Female	28 (64%)	40 (80%)	937 (68.8%)
Age at disease onset, median (IQR)	6.9 (2.1;11.3)	6.2 (1.8;9.6)	7.4 (2.9;11.5)
Disease duration, median (IQR)	6.3 (3.0;8.5)	5.1 (2.0;7.2)	4.1 (1.3;6.0)
ANA positive, n (%)	19 (43%)	28 (56%)	647 (47.5%)
CRP, median (IQR)	14.8 (3;22)	9.5 (0.6;4;.5)	20.8 (1.4;23)

Active joint count, median (IQR)	6.2 (2;7.8)	3.5 (0;5.3)	7.3 (2;9)
Physician global, median (IQR)	5.3 (3.6;7.0)	2.6 (4.3;3.2)	5.4 (3.2;7.6)
Patient global, median (IQR)	4.4 (1.7;6.7)	2.9 (0.6;5.0)	4.4 (2.0;6.5)
CHAQ-DI, median (IQR)	0.59 (0;1)	0.5 (0;0.8)	0.7 (0.1;1.1)
JADAS10, median (IQR)	17 (13.1;19.2)	9.7 (12.5;3.5)	15.2 (11.5;22.5)

**Abstract THU0553 – Table 2.** Improvement at month 6 and tolerability

	Cohort 1 +2 LEF+TNFi	Cohort 3 MTX +TNFi	OR (Cohort 3 vs. 1+2)	P
JADAS improvement	35.1%	54.6%	2.2 [1.4–3.4]	<0.001
JADAS MDA ( $\leq 3.8$ )/ remission ( $\leq 1$ )	36.2%/13.8%	41.7%/19.6%		n.s.
AE (rate)	160 (57.4%)	1845 (46%)	0.63 [0.41–0.96]	0.031
Infections (rate)	37 (23.4%)	410 (22.2%)		n.s.
Nausea (rate)	9 (5.3%)	156 (8.5%)		n.s.
Elevated transaminases (rate)	8 (5.3%)	112 (6.1%)		n.s.

**Conclusions:** Combination with both leflunomide and methotrexate to treatment with TNF-inhibitors resulted in clinically meaningful improvements with a comparable rate of patients reaching JADAS-MDA and JADAS-remission at month 6 of treatment. Leflunomide turned out to be a well-tolerated alternative to methotrexate for polyarticular JIA.

**Disclosure of Interest:** None declared

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THU0554

#### RITUXIMAB (RTX) IN PAEDIATRIC DISEASES: DESCRIBING ITS PHARMACODYNAMICS WITH A FOCUS ON B-CELL DEPLETION AND REPOPULATION, INFECTIONS AND ANTI-DRUG ANTIBODIES

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**Background:** Rituximab (RTX) is increasingly used in rheumatologic,<sup>1,2</sup> hematologic<sup>3</sup> and renal diseases.<sup>4</sup> The induced B cell depletion can lead to hypogammaglobulinemia and thus an increased risk of infection.<sup>5</sup> B cell depletion is not always achieved, and this has a negative effect on therapeutic response.<sup>6</sup> Anaphylaxis is a frequent side effect of RTX and has been associated with the occurrence of anti-drug antibodies (ADA) against RTX.<sup>7</sup>

**Objectives:** To describe in different paediatric patient groups the pharmacodynamics of RTX in children by outcome variables, i.e. success of B-cell depletion and time of B cell repopulation, as well as the risk factors for severe infections and anaphylaxis.

**Methods:** Patient data of children who received RTX between 2008 and 2017 at our centre were retrospectively collected. Three patient subgroups were defined: autoimmune diseases (AID), immune dysregulation (ID) and renal diseases (RD). B cell repopulation was defined as a number above the cut-off value of B cell depletion ( $=0.050 \times 10^6/l$  or  $<2\%$  of the total amount of lymphocytes).

**Results:** B cell measurements were performed in 53/55 patients. B cell depletion was not achieved in 9 patients. In the 35 patients with B cell repopulation, median time until repopulation was 155 days (IQR 105–222): in the AID group (n=12) 129 days (IQR 77.5–243,  $p=0.363$ ), in the ID group (n=5) 172 days (IQR 154–181,  $p=0.574$ ) and in the RD group (n=18) 163 days (IQR 121–229,  $p=0.847$ ). After RTX treatment, in 36 patients IgG levels were measured of which 14 (39%) had low IgG levels on at least one occasion (median 7 g/L [range 0.6–38.1 g/L]). Severe infections leading to hospitalisation occurred in 15 (27%) cases. An allergic reaction during or directly after RTX infusion was observed in 27 patients (49%). Anaphylaxis, defined as a systemic allergic reaction, characterised by impairment of airway, breathing, circulation or consciousness, occurred in 10 of these patients (18% of total cohort). Seven patients were tested for anti-RTX antibodies of whom 6 tested positive: 5 patients in the AID-group and one patient with renal disease. Allergic reactions occurred in all 6 while RTX failed to induce B cell depletion in 4 of these.

**Conclusions:** Time-to-B-cell-repopulation after RTX did not significantly differ between different paediatric patients groups. Severe infections were common (27%) in the cohorts studied. It is unclear from our data whether this is merely related to RTX treatment. Presence of ADA against RTX seems to predict failure of B-cell depletion and/or anaphylaxis after RTX treatment.

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**Disclosure of Interest:** None declared

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**THU0555** **GUIDELINES FOR JUVENILE IDIOPATHIC ARTHRITIS MANAGEMENT: IS THERE A ROOM FOR COMBINED METHOTREXATE AND LEFLUNOMIDE THERAPY IN THE TREATMENT RECOMMENDATIONS**

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**Objectives:** To set recommendations for the management of children and adolescents living with JIA and assess whether there is a room for combined methotrexate and leflunomide therapy, adopting treat to target approach.

**Methods:** the treatment guidelines were developed based on systematic review, local studies, formal consensus and feedback. Initiation of methotrexate or leflunomide was recommended for polyarticular JIA children who, after 3 month of treatment, did not respond to methotrexate or leflunomide monotherapy, or those whose DMARD dose could not be optimised; a new management step was introduced where a combination of both medications was administered. This was a multicentre study including 76 JIA patients who had been treated with the combination of methotrexate plus leflunomide. All patients were classified according to the International League of Associations for Rheumatology (ILAR) criteria. Recorded data included: demographics, JIA subtype, reason for starting combined treatment, treatment duration, withdrawals, causes of discontinuation, efficacy and safety. Patients were classified as “responders” or “non-responders”. Responders were those patients with articular improvement  $\geq$ ACR-Paediatric 30 and/or ocular improvement according to the Standardisation of Uveitis Nomenclature Working Group (SUN) definitions. Efficacy was assessed at 3, 6- and 12 month and outcomes were compared to methotrexate monotherapy.

**Results:** Out of the 76 children there were, oligoarthritis (34%), polyarthritis (31%), systemic JIA with synovitis (>4 joints) (20%), and psoriatic arthritis (15%). Mean age at initiation of combined therapy 10.2 $\pm$ 3.4 years, mean disease duration is 9.4 $\pm$ 4.8 months. The combined therapy was superior to methotrexate alone and did not significantly increase the rate of adverse events. ACR-Ped 30 was achieved in 64% at 3 months, 75% at 6 months. This was superior to methotrexate alone (37.3% and 53.8%;  $p < 0.01$  at 3- and 6 months respectively). At 1 year, 81% reached Ped 30, 74.5% reached ACR-Ped 50, 64% achieved ACR-Ped 70 whereas 51% met ACR-Ped 90 criteria. There were no serious adverse events. One of the two DMARDs was stopped in 51% of the children; of them: 25% were due to adverse events, clinical remission in 25% whereas 21% were switched to anti-TNF therapy according to guidelines due to inefficacy or loss of efficacy. All patients who had had uveitis responded well and achieved clinical remission.

**Conclusions:** For the children with polyarticular JIA who did not respond to monotherapy with methotrexate, combination of methotrexate and leflunomide treatment appeared to be efficacious and maintain a durable response. The current recommendation would be to use combined methotrexate and leflunomide in children with polyarticular JIA who are either intolerant to higher methotrexate doses or who did not have a satisfactory response to methotrexate. The combination should be considered prior to the use of a biologic agent.

**Disclosure of Interest:** None declared

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**THU0556** **IMPACT OF METHOTREXATE ON GROWTH IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS**

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**Background:** Juvenile idiopathic arthritis (JIA) is a heterogeneous group of chronic inflammatory disease which could be responsible for functional impairment and severe growth disturbance. Conventional disease-modifying antirheumatic drugs, such as methotrexate (MTX), may improve growth velocity especially by regulating systemic inflammation.

**Objectives:** The objective of this study was to evaluate the effect of MTX on growth parameters in pre-pubertal children with JIA and to determine the factors affecting the growth velocity.

**Methods:** We assessed height and changes in the height standard deviation score (SDS) at disease onset, at the onset of MTX and at the last follow-up visit in a cross-sectional study of JIA children. All patients were pre-pubertal when MTX began and were followed for at least 6 months afterward. We compared growth parameters (height, growth rate, weight and body mass index (BMI)) in responders and non-responders to MTX. The growth rate was defined as the number of millimetres of height acquired during 1 year. Associations between changes in the height SDS and discrete variables were evaluated using chi-square or Fisher's exact tests. The significance level was set at 0.05.

**Results:** We enrolled 36 pre-pubertal children with JIA (24 boys and 12 girls) who had been treated with MTX orally. Median patient age was 6.2 years<sup>4–13</sup> at the onset of MTX and 8.4 years [6.1–14.9] at the latest follow-up. The median disease duration was 2.7 years [2.5–5.3]. Twenty-one patients (58.3%) had oligoarticular JIA, 2 patients (5.5%) had systemic JIA, 10 (27.7%) had polyarticular JIA and 3 (8.3%) had enthesitis-related arthritis. Nineteen children (52.7%) had received corticosteroids during an average period of 1.7 years [0.6–3] with a mean of 10 mg/day of prednisone or equivalent. The median duration of MTX at the latest follow-up was 3.1 years [0.62–5.5] with a mean MTX dose of 10 mg/m<sup>2</sup>/week.<sup>10–15</sup> Twenty-eight patients responded to MTX treatment and 8 did not. There were no significant differences between the responders and non-responders for age at treatment initiation, disease duration and mean MTX dose. At MTX onset, no significant differences between the two groups in terms of height ( $p = 0.52$ ), growth rate ( $p = 0.08$ ), weight ( $p = 0.74$ ) and BMI ( $p = 0.9$ ) were found. One year after MTX therapy, mean height (0.2 versus  $-1.1$ ;  $p = 0.03$ ), mean growth rate (0.5 versus  $-2.9$  SDS;  $p = 0.01$ ), mean weight (0.4 versus  $-2.3$  SDS;  $p = 0.01$ ) and mean BMI (0.6 versus  $-1.9$ ;  $p = 0.04$ ) were significantly higher in the responder group than in non responders, respectively. At the latest follow-up, this increase was significantly maintained for growth rate ( $p = 0.001$ ) and height ( $p = 0.002$ ) in the responder group. In the multivariate analysis, patients who required more than 10mg/m<sup>2</sup>/week of MTX, systemic JIA and patients with reliance on steroids had a significantly lower growth velocity after the onset of MTX ( $p < 0.01$ ,  $p = 0.02$ ,  $p = 0.02$  respectively).

**Conclusions:** In our study, the increase in growth parameters in pre-pubertal children with JIA was associated with a better control of the disease activity under MTX therapy.

**Disclosure of Interest:** None declared

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**THU0557** **THERAPEUTIC DRUG MONITORING OF BIOLOGICALS IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS (JIA): AN OVERVIEW OF CURRENT PRACTICE IN ANTI-TNF THERAPY**

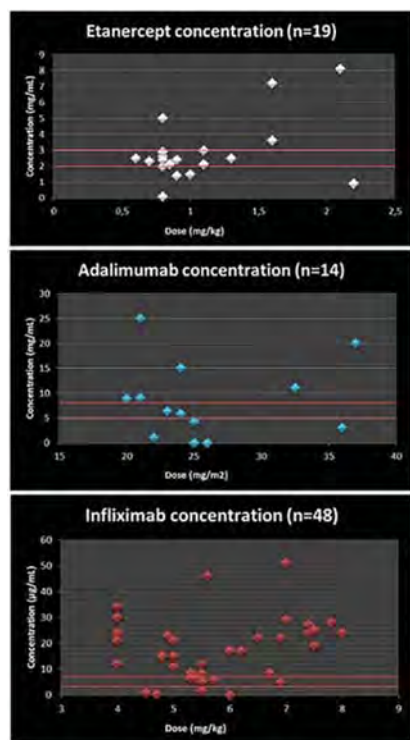
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**Background:** Juvenile idiopathic arthritis (JIA) is the most prevalent paediatric rheumatic disease.<sup>1</sup> Long term complications include physical disability and a decreased quality of life.<sup>2,3</sup> Since the introduction of anti-TNF drugs for JIA, its prognosis has improved significantly.<sup>1</sup> Personalised medicine is the next step to improve treatment in JIA. Anti-TNF trough levels and demonstration of the presence of anti-drug antibodies (ADA) could help individualise treatment decisions in JIA patients, but evidence supporting this is missing.

**Objectives:** To describe cross-sectional data of anti-TNF trough levels and ADA, combined with decision effects, in children with JIA.

**Methods:** Patients' records in children with JIA using etanercept, adalimumab or infliximab were retrospectively checked for measurements of anti-TNF trough levels and ADA. Anti-TNF trough concentrations and ADA were measured using an enzyme-linked immunosorbent assay (ELISA) and antigen-binding test. Data on age, sex, JIA subtype, reason for testing and the decision effect of trough level or presence of ADA on the current therapy were collected.

**Results:** Eighty-one anti-TNF trough levels were measured in 45 children with JIA. A wide variety of anti-TNF trough levels was found. Therapeutic drug concentrations, according to adult ranges in RA and IBD<sup>4,5,6</sup> were found in 11 (58%) patients on etanercept (n=19), 2 (14%) on adalimumab (n=14) and 8 (17%) on infliximab (n=48). Four patients on adalimumab and one patient on infliximab showed ADA. All of these five patients had non-detectable drug trough levels. Reasons for testing trough level and/or presence of ADA were loss of response (20%), partial or no response (40%), measurement after dosage increase (2%), remission (17%), uveitis flare (9%) and allergic reaction (11%). Treatment decisions were influenced by trough levels in 70/81 (86.4%) of measurements and in 5/5 (100%) of patients with ADA.



Abstract THU0557 – Figure 1. Dose vs Concentration (etanercept, adalimumab, infliximab)

**Conclusions:** Measuring anti-TNF trough levels and ADA was a valuable tool in making personalised treatment decisions in JIA. Treatment changes included dose/frequency increase, or stopping and switching treatment in the presence of ADA combined with undetectable drug levels. More data are needed to access optimal therapeutic drug levels in anti-TNF treatment in JIA and to implement this strategy more widely.

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THU0558

#### INCREASED FREQUENCY OF FEBRILE SEIZURES IN TWO PERIODIC FEVER SYNDROMES: FAMILIAL MEDITERRANEAN FEVER AND PFAPA SYNDROME

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**Background:** Fever and the fear of febrile seizure risk in parents are a common reason that lead parents to seek care in childhood emergency departments. The most frequently seen periodic fever syndromes in Turkey are periodic fever, aphthous stomatitis, pharyngitis, cervical adenitis (PFAPA) syndrome and familial Mediterranean fever (FMF). There is lack of data regarding the frequency of febrile seizures in periodic fever syndromes.

**Objectives:** To document the frequency of febrile seizure in patients with Familial Mediterranean Fever and PFAPA syndrome.

**Methods:** Patients with FMF and PFAPA, who were diagnosed according to Turkish paediatric FMF diagnostic criteria and Marshall criteria, were enrolled to the study. Past medical history of all subjects from postnatal six months to 6 years of age were assessed in terms of febrile seizure. Clinical, demographic and laboratory data of both patient groups were obtained from patient files. The frequency of febrile seizure in both disease groups was compared with the prevalence in healthy children of a previous Turkish study.

**Results:** A total of 417 FMF and 157 PFAPA subjects were recruited to the study with a female frequency of 49.9% and 42.8%, respectively. The mean age of the FMF and PFAPA patients at study time was 12.4±4.5 years and 5.3±2.1 years, respectively. The mean age at disease onset was 5.1±3.8 (IQR: 2–7) years in FMF group, whereas it was 21±16.5 months (IQR: 10–30) in PFAPA group. The frequency of febrile seizure in FMF and PFAPA syndrome was similar (8.4% versus 8.6%, p>0.05). Among the subjects with febrile seizure, 42.9% (n=15) in FMF group and 30.8% (n=4) in PFAPA group underwent electroencephalography. The EEG result of all subjects were reported to be normal. While 8 subjects with febrile seizure (22.9%) in FMF group required anticonvulsant therapy, 2 patients (15.4%) in PFAPA group used anticonvulsant treatment. Among the PFAPA subjects with febrile seizure (n=13), 53.9% (n=7) underwent tonsillectomy. Thereafter, 85.7% (n=6) of the patients with tonsillectomy never experienced a febrile seizure.

Both the FMF and PFAPA syndrome group were found to have a higher frequency of febrile seizure compared with the healthy subjects of the previous Turkish study (FMF versus healthy children: 8.4% versus 3.2%) (PFAPA syndrome versus healthy children: 8.6% versus 3.2%); and this was statistically significant (p<0.001). However, the frequency of febrile seizure in FMF did not differ from the patients with PFAPA syndrome (8.4% versus 8.6%, p>0.05).

**Conclusions:** Compared to the healthy children, the frequency of febrile seizure in FMF and PFAPA syndrome was significantly increased. The recurrent fever, which is the main shared manifestation of these two diseases, is possibly a trigger for febrile seizure. This increased frequency of febrile seizure in both periodic syndrome seems to be a result of recurrent fever, other than a neurologic involvement of the FMF itself.

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THU0559

#### THE PERFORMANCE OF THE NEWLY PROPOSED EULAR/ACR CLASSIFICATION CRITERIA IN JUVENILE-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS-A PRELIMINARY STUDY

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**Background:** The sensitivity and specificity of the ACR-1997 and SLICC-2012 classification criteria in juvenile-onset systemic lupus erythematosus (SLE) are already studied. In previous reports, the main limitations of the ACR-1997 and

SLICC-2012 were low sensitivity and low specificity, respectively. To avoid misclassifications, a new set of classification criteria have been developed by the collaboration of the European League Against Rheumatism (EULAR) and the American College of Rheumatology (ACR) and the draft was presented at the 2017 ACR/ARHP Annual Meeting in San Diego, California. After application on 500 SLE patients and 500 controls, the sensitivity and specificity were found as 98% and 97%, respectively.

**Objectives:** To compare the sensitivity of the new EULAR/ACR criteria with those of the 1997 American College of Rheumatology (ACR) criteria and 2012 Systemic Lupus International Collaborating Clinics criteria in juvenile-onset SLE patients.

**Methods:** Patients initially were evaluated by ACR-1997, SLICC-2012 and EULAR/ACR classification criteria at baseline, when the diagnosis for the first time had been established by an expert paediatric rheumatologist (OK). All data were obtained from patient records. The diagnostic sensitivity of the three sets of classification criteria were further tested within 1 year of diagnosis and at last patient visit, longitudinally.

**Results:** A total of 104 juvenile-onset SLE patients were enrolled for the sensitivity performance of classification criteria at diagnosis. Since the follow-up period was less than 1 year, 12 subjects excluded after baseline evaluation. Finally, 92 subjects were eligible for sensitivity evaluation within 1 year of diagnosis and at last visit. The median age at diagnosis of clinician was 13.0 years (range 3.1–17.9 years, interquartile range (IQR) 11.1–16.5 years) with a median disease duration of 5.0 years (IQR 3.0–8.0 years). The female-to-male ratio was 4.7:1. The newly developed EULAR/ACR classification criteria were more sensitive than SLICC-2012 and ACR-1997 at diagnosis (93.3% versus 91.3% and 85.6%, respectively), and at first year (95.7% versus 94.6% and 90.2%, respectively ( $p>0.05$ )). At last visit the sensitivity of the new set of criteria and SLICC-2012 were same (97.8%), but higher compared to ACR-1997 criteria (95.7%).

**Conclusions:** Juvenile-onset systemic lupus erythematosus was classified by the newly proposed EULAR/ACR criteria with higher sensitivity compared with SLICC-2012 and ACR-1997 at disease onset and within one year of diagnosis. However, last visit assessment demonstrated equal sensitivity between new EULAR/ACR criteria and SLICC-2012. Although the difference was not significant, the new set of criteria seem to be capable of recruiting more children with juvenile SLE to clinical trials.

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**Disclosure of Interest:** None declared

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#### THU0560 CHRONIC RECURRENT MULTIFOCAL OSTEOMYELITIS: FOUR TERTIARY SPANISH HOSPITALS EXPERIENCE. A MULTICENTRIC STUDY

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**Background:** Chronic recurrent multifocal osteomyelitis (CRMO) is a rare autoinflammatory polygenic bone disease characterised by aseptic bone inflammation in paediatric population. Its management, clinical, radiological findings and treatment have not yet been standardised.

**Objectives:** Retrospective, descriptive multicentric study of patients diagnosed of CRMO in four tertiary level hospitals' paediatric rheumatology section. There were 16 patients included. The clinical, radiological characteristics were analysed as well as response to treatment options.

**Results:** The median age at diagnosis was 10.5 years, female:male ratio 62.5:37.5%. The delay in the diagnosis had a median of 4.5 months, being less than one year in 11 patients. Bone pain was the first symptom in 100% of the patients accompanied by fever in 25% of them. A single patient presented perilesional arthritis. A slight-moderate increase on acute phase reactants was observed at the debut of the disease: median ESR 47.5 mm/h.

The median number of locations at debut was 2.5 (range 1–14), with multifocal involvement in 75%. The most frequent location was tibia (56%), followed by pelvis (44%) and vertebrae (31.25%). Other locations less frequent were: carpus (12.5%), femur (12.5%) mandible (6%) and sternum (6%).

Biopsy was performed in 14/16 patients and bone scintigraphy with Tc99 in 12/16 patients, with pathological uptake observed in 91.6% of cases. MRI was the radiological test of suspected diagnosis in 15/16 patients.

NSAIDs were the initial treatment. 5 patients received different antibiotic therapy regimens, without clinical or radiological improvement. 56.25% of patients required other treatments. Systemic corticosteroids were used in 12.5% of patients and bisphosphonates in 43.75% (100% of patients with axial involvement). After 6 months of treatment with bisphosphonates, 57.14% had complete remission, 28.57% partial remission and 14.28% worsening. 12.5% of the patients had a torpid evolution, receiving sequential therapies with multiple synthetic or biological DMARDs (Anakinra, Canakinumab, Etanercept), and another 12.5% required surgery.

**Conclusions:** The diagnosis of CRMO is a challenge in the absence of pathognomonic features which leads to delay in diagnosis and the initiation of treatment. In our centres the bisphosphonates were the treatment strategy used in patients with spinal involvement with 85.67% response at 6 months.

**Disclosure of Interest:** None declared

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#### THU0561 ANAKINRA FIRST- OR SECOND-LINE IN SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS PATIENTS

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**Background:** Treatment of systemic juvenile idiopathic arthritis (sJIA) still remains a challenge.

**Objectives:** Patients newly starting treatment with Anakinra (ANA) as first-line biologic were compared to ANA second-line users regarding efficacy and safety.

**Methods:** ANA treatment courses are documented by the German Biologics registry (BiKeR). Demographics, clinical characteristics, disease activity parameters as well as efficacy and safety parameters were compared in pts using ANA as first biologic with those previously treated with other biologics. For efficacy analyses ACR inactive disease, JADAS minimal disease activity (MDA), JADAS remission (REM) and active joint count as well as functional ability assessment (CHAQ) were used. "Intention to treat" (ITT) and "as observed" (AO) analyses was performed. Safety assessments were based on adverse events (AE) reports.

**Results:** 47 pts started treatment with ANA, 33 pts were pretreated with other biologics (Etanercept n=29, Tocilizumab n=4, Infliximab and Canakinumab n=1). ANA first line pts had significantly shorter disease duration and had received DMARDs and i.a. steroids significantly less frequent than second line users. At baseline, ANA first-line users had higher disease systemic activity indicators (fever, rash, ESR), functional disability (CHAQ) and impaired parent/patient global assessment of overall well-being significantly more often, while there were no significant differences in Physician global assessment of disease activity, active joint count and JADAS 10. At last follow-up 43%>66% of pts in both groups reached ACR inactive disease, 43%>63% JADAS MDA, 29%–50% JADAS REM and 43%>69% reached status of no functional disability. Rates did not differ between the 2 cohorts (table 1). 13 pts experienced adverse events (AE) with a rate of 53/100PY, 5 pts experienced serious AE (9/100PY) and in 11pts infections were reported (33/100PY). Macrophage activation syndrome was reported once in each group. One case of AML was reported in a patient one year after last exposure to ANA. No deaths were reported.

**Conclusions:** Anakinra is a feasible first-line biologic for treatment of sJIA. In the BiKeR cohort ANA treated pts showed a marked treatment response, as first or consecutive biologic. Rates of AE, SAE and infectious AE seem acceptable.

**Disclosure of Interest:** None declared

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#### THU0562 EVOLUTION OF SERUM CALPROTECTIN IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS IN CLINICAL PRACTICE

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**Background:** Serum Calprotectin (MPR8/MPR14) is a promising biomarker in the management of juvenile idiopathic arthritis (JIA), mainly as a predictor of flare, especially in treatment de-escalation

**Objectives:** To describe the evolution of serum Calprotectin in patients with JIA, their clinical evolution and its impact on therapeutic decisions



Abstract THU0562 – Table 1 ND=Not Done

Subtype	Sex	Age (years)	Calpro1 (µg/mL)	RCP(mg/dl)	ESR (mmHg)	Disease Activity	Decision	Outcome	Calpro2 (µg/mL)	Decision	Outcome
Oligo JIA	Fem	3	2.25	0.7	9	No	Same treatment	Flare	3.6	Escalate	Remission
	Fem	11	2.2	0.7	20	Yes	Start MTX	Gets better	5.28	Escalate	Remission
	Mas	11	5.01	1.5	3	Yes	Start MTX	Remission	2.01	Same treat.	Equal (remission)
	Fem	7	2.17	ND	34	No	Same treatment	Equal (remission)	1.37	Same treat.	Equal (remission)
	Mas	6	1.56	0.8	15	No	De-escalate	Equal (remission)	3.14	No de-escalate	Equal (remission)
	Fem	18	2.27	0.7	12	No	De-escalate	Equal (remission)	2.09	Same treat.	Equal (remission)
	Fem	22	1.16	0.9	6	No	Same treatment	Equal (remission)	ND		
Sis JIA	Fem	12	1.73	0.7	3	No	De-escalate	Equal (remission)	2.74	No de-escalate	Equal (remission)
Poli JIA	Fem	8	3.78	ND	8	No	No De-escalate	Equal (remission)	4.47	No de-escalate	Equal (remission)
	Fem	9	2.75	0.7	6	Yes	Same treatment	Flare	ND		
ERA JIA	Mas	15	3.61	5.7	8	Yes	Escalate	Gets better	3.02	Escalate	Gets better
	Mas	13	3.39	9.2	51	Yes	Start MTX	Gets better	3.08	Same treat.	Remission
	Mas	11	0.78	4.6	8	No	Same treatment	Equal (remission)	ND		
	Fem	12	3.3	1.9	8	No	Same treatment	Equal (remission)	1.81	Same treat.	Equal (remission)
Psor JIA	Fem	11	1.95	2.2	6	No	Same treatment	Equal (remission)	ND		

**Methods:** Demographic, clinical and inflammatory activity data (RCP and ESR) were retrospectively collected in patients with JIA of any subtype in whom serum Calprotectin had been determined at least once

**Results:** We present the data of 15 children, 7 with Oligoarticular subtype JIA, 1 Systemic, 3 Polyarticular, 1 Psoriatic and 3 Entesitis Related Arthritis (ERA)

The average age was 11 years, 66% female. The characteristics of each patient can be seen in table 1, together with the first determination of serum Calprotectin, CRP and ESR. It also shows the physician's decision, and the outcome, obtained from the assessment in the next visit

Considering the cutoff point of serum Calprotectin in our sample of: 2.2 µg/mL (80% sensitivity and 69% specificity), 9 of 15 patients presented high values, 2 of them presented a flare (1 Oligo and 1 Poly), both had maintained the same treatment, because they were considered inactive. There were no flares in patients with negative Calprotectin

The evolution of serum Calprotectin, together with the clinical decisions (based on clinical and analytical assessment) are described in table 1

In most of stable patients in whom serum calprotectin was high, it was decided not to lower treatment, and only in one case it was de-escalated. There were no flares in any of them

**Conclusions:** Serum Calprotectin is a useful biomarker in routine clinical practice, together with other markers such as CRP and ESR, and our clinical judgment, it helps us to make therapeutic decisions

**Disclosure of Interest:** None declared

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#### THU0563 ULTRASOUND CHANGES IN JOINTS INDUCED BY INTRA-ARTICULAR CORTICOSTEROID INJECTION IN JUVENILE IDIOPATHIC ARTHRITIS

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**Background:** Ultrasonography (US) studies carried out on joints of juvenile idiopathic arthritis (JIA) patients in clinical remission demonstrate the presence of subclinical synovitis. The significance of subclinical synovitis and the positive power Doppler (PD) signal on US in JIA.

**Objectives:** The objectives of this study were to assess whether the changes detected by US induced by intra-articular corticosteroid injection in JIA patients.

**Methods:** We evaluated 49 joints (47 knees, 1 tibiotalar and 1 elbow) of 32 patients who diagnosed JIA. We used grey-scale US by high frequency transducer (7.5–10) MHz at study entry and after a therapeutic intervention. Each joint was scored for grey-scale (GS) and power Doppler (PD) abnormalities according to a 4-point semiquantitative scale. Pre- and post-treatment US scores were compared and the sensitivity to change of GSUS and PDUS was estimated. US assessment was performed separately, immediately after the clinical evaluation, by an experienced paediatric rheumatologist (BS) with certificated by EULAR. Medical records were reviewed for JIA subtype and state of disease. Clinical examination, including routine joint examination was carried. Clinical response was assessed using the ACR paediatric (pedi ACR) response criteria

**Results:** Five patients had polyarthritis, 5 had entesitis-related arthritis, 22 had oligoarthritis. Nine patients (28%) underwent intra-articular corticosteroid injection (IACI) only, 23 (71.9%) were given IACI and systemic medications. The medication used were methotrexate (22 patients), Sulfasalazine (2 patients), and methotrexate and biologic (5 patient). Synovial hyperplasia, joint effusion, PD signal and tenosynovitis in at least one joint were detected in 77.4%, 100%, 33.3% and 15% of patients, respectively. Both GSUS and PDUS scores improved significantly ( $p < 0.0001$ ) from baseline to follow-up. At the follow-up visit, 18/49 (36.7%) joints complete resolution among these patients 2 had minimal synovial hyperplasia. Although, 31/49 (63.3%) joints residual US abnormalities were judged in remission on clinical grounds.

**Conclusions:** US is a sensitive tool to assess therapeutic response in patients with JIA. Subclinical disease on US is common in joints with clinically-defined

	1 st Biologic n=14 (29.8%)	2nd Biologic n=33 (70.2%)	p
Age baseline, mean (SD), years	7.1 (4.7)	9.4 (4.8)	n.s.
Disease duration, mean (SD), years	1.2 (2.5)	4.9 (3.8)	0.002
Pretreatment	12 (85.7)	31 (93.9)	n.s.
- Systemic Steroids, n (%)			
- MTX, n (%)	4 (33.3)	32 (94.7)	<0.0001
Disease activity parameters at baseline	1.2 (2.0)	3.2 (4.7)	n.s.
- Active joints mean (SD)			
- Phys VAS mean (SD)	58.7 (35.0)	40.8 (33.5)	n.s.
- Pat VAS mean (SD)	66.0 (39.0)	28.0 (25.7)	0.0003
- CHAQ mean (SD)	1.75 (1.1)	0.66 (0.89)	0.0008
- ESR, mm/h mean (SD)	53.7 (26.1)	30.7 (24.5)	0.006
- JADAS10 mean (SD)	13.8 (9.8)	11.0 (9.3)	n.s.
- Fever, n (%)	9 (64.3)	4 (12.1)	0.0006
- Rash, n (%)	7 (50)	1 (3.0)	0.001
Efficacy parameters at last follow-up	n=10	n=22	n.s.
- ACR inactive disease, n (%ITT;%AO)	6 (43; 60)	15 (45;68)	
- No active joint, n (%ITT;%AO)	10 (71;100)	17 (52;77)	n.s.
- CHAQ=0, n (%ITT;%AO)	6 (43; 60)	16 (48;73)	n.s.
- JADAS MDA, n (%ITT;%AO)	6 (43;60)	14 (42;64)	n.s.
- JADAS remission, n (%ITT;%AO)	4 (29;40)	12 (36;55)	n.s.

remission.. Further studies are needed to establish the impact of US on therapeutic decision-making in JIA.

**Disclosure of Interest:** None declared

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THU0564

#### EFFICIENCY AND SAFETY EVALUATION OF BIOSIMILAR INFILIXIMAB FOR TREATMENT OF PAEDIATRIC NON-INFECTIOUS UVEITIS IN SINGLE CENTRE

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**Background:** Biosimilar infliximab (Remsima) has been introduced in our country, together with other European countries in 2014. Information regarding the use in child age group is limited but it is reported that its therapeutic efficiency and safety is similar to the reference molecule regarding the paediatric Chron disease

**Objectives:** In this study, our aim was to report the efficiency and safety of BI used for children with non-infectious uveitis

**Methods:** In this study, there were 13 subjects (9 boys, and 4 girls) diagnosed with non-infectious uveitis.

BI (Remsima) treatment had been given in 5 mg/kg in 0.,2.,4 th week and then every 8th week. Ophthalmic assessment of disease activity and ocular complications were measured throughout the trial with the use of slit-lamp biomicroscopy for uveitis activity, according to the SUN criteria. The Drug exposure has been evaluated by calculated of patient year (HY), adverse event (AE) was assessed using the CTCAE criteria. The median values due to the small number of patients are considered

**Results:** The patients who were include the study, 5 had diagnosed extended oligo JIA, 2 with enthesitis-related arthritis (ERA), 2 with persistent oligo JIA, 2 with pars planitis and one of them Behcet's disease. At the time of evaluation, the median age was 10 years,<sup>3-13</sup> age at diagnosis of their disease 8 years,<sup>1-13</sup> respectively. The median age of uveitis diagnosis was 8 years. The median disease duration before BI was 10 months. All of the patients had methotrexate therapy with BI and BI before.

Only one patient used a different biological agent prior to BI, and revealed they were determined that considered unresponsive.

Other patients (n=12) had biosimilar infliximab as first biologic drug due to the activation of disease after using the drug methotrexate.

After therapy of BI, in all of the patients, joint and eye symptoms were improvement.

The systemic steroid therapy was cut down in the first month in all patients, 2 of them continue prophylactic topical steroids.

The median duration of BI therapy was 10 months. There was one case of anaphylaxis in all the patients, whereas five of them frequent upper respiratory tract infection have been observed as side effect

**Conclusions:** In this preliminary report, This biosimilar infliximab treatment appears to be safe and effective in paediatric age group on the paediatric patients with non-infectious uveitis. These results must be supported by multicenter studies and registries.

**Disclosure of Interest:** None declared

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THU0565

#### NEEDS ASSESSMENT OF TRAINING IN PAEDIATRIC RHEUMATOLOGY AMONG SPANISH PAEDIATRICIANS. MULTICENTER DESCRIPTIVE STUDY

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**Background:** There is a perception that care for paediatric patients with pathology

Rheumatic is heterogeneous, as several previous publications have shown. Likewise, in Spain we do not have the recognition of a specialisation in Rheumatology Paediatric, for which it is possible that the training in this field is not sufficiently specific. This could be detrimental to the best care received on the part of the patients.

Paediatric rheumatology has some specific characteristics that make it unique, but there is yet no recognised specialisation in some countries.

**Objectives:** To examine the needs assessment for specific training in paediatric rheumatology among paediatricians and paediatricians in training from different countries using a specific questionnaire.

**Methods:** An online anonymous questionnaire was sent to paediatricians and paediatricians in training from different centres in Spain, London and Mexico. Data on working place, city, and perception of the state of training in paediatric rheumatology in their workplace were collected.

**Results:** A total of 447 questionnaires were answered: 287 by senior paediatricians (64.5%) and 125 by paediatric trainees (28.1%); 96.4% in different Spanish cities and 3.6%<sup>16</sup> a in other countries.

For 54.7% (254) of the respondents there is no specialisation in paediatric rheumatology in their workplace. The main responsible of children with rheumatic pathology is a paediatric rheumatologist in 59.7% (257) cases, with or without recognised specialisation, a general paediatrician in 21.2% (91) cases and an adult rheumatologist in 19.1% (82) cases.

96.8% of the respondents believe that there should be an accredited training in paediatric rheumatology. The formative aspects that were believed to be more important were the knowledge in paediatric rheumatology, general paediatrics and immunology, and the most valued capacities were the physical exploration, arthrocentesis and infiltration and the performance of musculoskeletal ultrasound.

**Conclusions:** The majority of paediatricians reached believe there is a lack of recognised specialisation in paediatric rheumatology in Spain, and a need for accredited training. The attention to children with rheumatic diseases in Spain is heterogeneous. This survey reinforces the perception that training in paediatric rheumatology in our country should be improved.

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THU0566

#### ASSESSMENT OF BEHAVIOURAL DISORDERS IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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**Background:** Juvenile Idiopathic Arthritis(JIA) is the most frequent paediatric rheumatologic disease which, because of its chronic, winding evolution, long-term treatment and dreadful complications, has a powerful impact on the somatic and psycho-social development of the children affected by it.

**Methods:** A number of 49 children with Juvenile Idiopathic Arthritis followed-up in the District Emergency University Hospital in Craiova and aged between 6 and 18, and a control group consisting in 49 healthy children of similar age and sex, were examined using the Child Behaviour Checklist (CBCL).

**Results:** Our results showed that 57.1% of the patients with JIA were classified as borderline and 6.12% as clinical behaviour, compared to the control group in which just 16.3% presented Internalising and Externalising problems. Thus, the majority of children with progressing forms of JIA presented social adjustment disorders, anxiety/depression, attention deficit, and 3 of them, males, presented verbal/physical aggressiveness and Rule-Breaking Behaviour. While among the patients with JIA it was mostly the feminine gender that presented behavioural disorders, in the control group all children with Internalising and Externalising problems were males.

**Conclusions:** Children with JIA must be carefully kept under observation for an early detection and treatment of behavioural deviations. Further studies are necessary, on large groups of patients, in order to identify the manner in which Juvenile Arthritis affects the patient and his or her family.

**Acknowledgements:** The authors declare that they have no conflict of interests.

**Disclosure of Interest:** None declared

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**THU0567 TESTING PERFORMANCE MEASURES IDENTIFIES GAPS IN JUVENILE IDIOPATHIC ARTHRITIS (JIA) CARE**

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**Background:** JIA is the most prevalent type of childhood inflammatory arthritis. Timely diagnosis, treatment and ongoing care by a paediatric rheumatologist are associated with improved outcomes.

**Objectives:** To test the Arthritis Alliance of Canada's JIA Performance Measures: i) The percentage of patients with new onset JIA with at least one visit to a paediatric rheumatologist in the first year of diagnosis; ii) The percentage of patients with JIA under rheumatology care seen in follow-up by a paediatric rheumatologist at least once per year.

**Methods:** Validated JIA case ascertainment algorithms were used to identify cases from provincial health administrative databases in Manitoba, Canada in patients <16 years of age with ≥6 months of health insurance coverage in the population registry between 01/04/2005 and 31/03/2015. Cases were identified by either 1 hospitalisation separation with an International Classification of Disease (ICD)-10 code for JIA (M05.X, M06.X, M08.X, M45.X) or ≥2 physician billing claims (ICD-9 codes: 714.x or 720.x) for JIA ≥8 weeks apart within 2 years. A 3 year washout period prior to the first code was used to determine the percentage of incident JIA patients with ≥1 visit to a paediatric rheumatologist in the first year. For reporting the percentage of JIA patients seen in yearly follow-up, once a patient is seen at least twice by a paediatric rheumatologist they are considered under rheumatology care. The measure was computed by comparing yearly observed and expected follow-ups. The proportion of patients with gaps in care of >12 and >14 months between consecutive rheumatologist visits was also calculated. As there is no paediatric rheumatologist identifier in Manitoba administrative datasets, a physician was identified as a paediatric rheumatologist if they had ≥40 visits for individuals ≤16 years in a year and at least 50% of those visits in a year were JIA. This identified 5 physicians.

**Results:** 194 incident cases of JIA were diagnosed between 01/04/2008 and 03/31/2015. The median age at diagnosis was 9.1 years (Q1 5.5, Q3 12.8) and 71% were female. Table 1 describes the number of JIA cases who saw a paediatric rheumatologist within a year of diagnosis (between 51% and 81%). Table 2 describes the percentage of patients seen on a yearly basis with no significant changes seen over time (p=0.47). A single gap of >12 months was seen in 52% (n=144) and ≥2 gaps of >12 months were seen in 11% (n=28). One gap of >14 months was seen in 34% of cases, and only 5% had ≥2 gaps >14 months.

**Abstract THU0567 – Table 1.** Number of incident JIA cases that have seen a paediatric rheumatologist within the first year

Fiscal Years (Some year combined due to small sample sizes, n<5)	Number of incident JIA cases	Percentage seen by a paediatric rheumatologist within a year
2008/2010	50	80%
2010/2012	54	81%
2012/2014	55	78%
2014/2015	35	51%

**Abstract THU0567 – Table 2.** Proportion of JIA follow-up visits by a paediatric rheumatologist using fixed 12-month intervals

	2008/ 09	2009/ 10	2010/ 11	2011/ 12	2012/ 13	2013/ 14	2014/ 15
Observed	74	94	82	72	70	66	68
Expected	101	120	114	116	123	116	118
Percent	73	78	72	62	57	57	58

**Conclusions:** Many JIA patients are not seen by a paediatric rheumatologist within a year of diagnosis, and up to half of those followed have at least 1 gap in care of >12 months. Such gaps may lead to a delay in diagnosis, timely treatment and ongoing care that could impact outcomes.

**Disclosure of Interest:** None declared

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**THU0568 BIOSIMILAR USE IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS IN A REAL-WORLD SETTING IN THE UNITED KINGDOM**

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**Background:** Although biosimilars are routinely used in adults with musculoskeletal diseases, there are limited data regarding the use of biosimilars in patients with juvenile idiopathic arthritis (JIA).

**Objectives:** To describe the characteristics of patients with JIA starting biosimilars in the United Kingdom (UK) following their approval in the UK with musculoskeletal diseases.

**Methods:** Patients were selected from the Biologics for Children with Rheumatic Diseases (BCRD) study, launched in 2010, an ongoing prospective UK study of biologic therapies other than the etanercept originator (followed in a separate parallel study) in JIA. Baseline information is collected via questionnaires completed by the treating physician or affiliated clinical research nurse. Follow-up data including disease activity measures and changes in drug therapy are collected at 6 months, 1 year and annually thereafter. From 30-Sept-2015, data has been captured on 3 biosimilars available in the UK: 2 infliximab and 1 etanercept biosimilar.

**Results:** To 12-Dec-2017, 58 patients were identified in the BCRD study starting a biosimilar; 48 (84%) infliximab and 10 (17%) etanercept biosimilars (table 1). Of these, 36 (62%) started a biosimilar as their first biologic therapy. Seventeen (29%) switched to a biosimilar from a non-originator biologic. Five patients switched from their originator. Follow-up data ranging from 6 months to 2 years were available in 14 patients. Four patients switched to another biologic in this period, 3 switching from an infliximab biosimilar to tocilizumab, and 1 etanercept biosimilar patient to adalimumab. Two serious adverse events in a 90 day exposure window were reported, both cases of recurrent uveitis in patients on an infliximab biosimilar switching from a non-originator biologic.

**Abstract THU0568 – Table 1**

Patients who are	Biological naive	Switched from a non-originator	Switched from originator
<b>Number</b>	36	17	5
<b>Biosimilar</b>			
Infliximab biosimilars	28 (77%)	17 (100%)	3 (60%)
etanercept biosimilar	8 (22%)	0 (0%)	2 (40%)
<b>ILAR class</b>			
Persistent Oligoarthritis	4 (11%)	4 (24%)	0 (0%)
Extended Oligoarthritis	8 (22%)	5 (29%)	1 (20%)
RF Negative Polyarthritis	13 (36%)	4 (24%)	1 (20%)
RF Positive Polyarthritis	0 (0%)	0 (0%)	0 (0%)
Psoriatic Arthritis	2 (6%)	3 (18%)	3 (60%)
Enthesitis Related Arthritis	8 (22%)	1 (6%)	0 (0%)
Unknown	1 (3%)	0 (0%)	0 (0%)
<b>Active uveitis at start of therapy</b>	4 (11%)	7 (41%)	2 (40%)
<b>Female</b>	22 (61%)	12 (71%)	2 (40%)
<b>Age (years)</b>	13 (9-15)	14 (11-15)	13 (12-16)
<b>Disease duration (years)</b>	2 (1-5)	6 (3-10)	7 (6-13)
<b>Active Joints (71 joints)</b>	2 (1-4)	0 (0-2)	0 (0-0)
<b>Limited Joints (71 joints)</b>	2 (1-4)	2 (0-4)	0 (0-1)
<b>Physician Global (0-10cm)</b>	2 (2-4)	1 (0-2)	0 (0-0)
<b>Patient Global (0-10cm)</b>	5 (1-7)	2 (0-4)	2 (0-4)
<b>Pain VAS (0-10cm)</b>	4 (1-7)	4 (2-5)	1 (0-1)
<b>CHAQ (0-3)</b>	1 (0-1)	0 (0-2)	0 (0-1)

All data presented are number (percentages) or median (interquartile range). International League of Associations for Rheumatology (ILAR), Rheumatoid Factor (RF), Visual Analog Scale (VAS), Childhood Health Assessment Questionnaire (CHAQ).

**Conclusions:** Biosimilars in children and young people are used as both first-line and subsequent-line biologic therapy, although currently few UK children have been switched directly from an originator product. Whether a move towards switching all children receiving originator products to biosimilar products, as has been seen in rheumatoid arthritis, will occur is currently unknown but it is imperative that the safety of these treatment decisions are captured in patient registers.

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THU0569

### A RANDOMISED, DOUBLE-BLIND, PARALLEL STUDY TO COMPARE RATES OF REMISSION (INACTIVE DISEASE) IN PATIENTS WITH JIA ON MTX TREATMENT ALONE VERSUS A COMBINATION OF MTX AND ETANERCEPT

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**Background:** Remission is the major goal of treatment of juvenile idiopathic arthritis (JIA). Advances in treatment options allowed achievement of remission to come into reach. Timing for initiating intensive treatment in a treat to target approach to early reach remission is still a debate.

**Objectives:** Multi-centre, double-blind, randomised study in polyarticular JIA patients (pts) receiving either Etanercept+Methotrexate (cohort 1) or Placebo +Methotrexate (cohort 2) for 24 weeks followed by 24 week open label phase. Escape to open-label ETN and MTX for pts not achieving paedACR30 at week 12 or not achieving inactive disease at week 24.

**Results:** 35 pts were randomised to cohort 1 and 33 to cohort 2. Baseline demographic and clinical characteristics were comparable between the groups except mean tender joint count, physician assessment of global disease activity and JADAS10 which all were higher in cohort 1. At week 12, 12 pts randomised to cohort 2 did not reach paedACR30. At week 24, further 10 pts of cohort 2 not reaching inactive disease escaped to ETA and MTX. 5 pts of cohort 1 and 4 pts of cohort 2 dropped out. At week 12, significantly more pts on ETA and MTX (33 (94%)/27 (79%)) than on PLC and MTX (17 (52%)/15 (47%)) reached paedACR30/50 (p<0.001/0.01). At week 24, inactive disease was reached by 10 pts on ETA and MTX vs. 6 on PLC and MTX. Inactive disease at week 48 was achieved by 5 pts of cohort 2 on MTX alone while 22 patients (67%) escaped to open label ETA and MTX. 15 (43%) pts of cohort 1 and 16 (49%) of cohort 2 reached inactive disease at week 48. At week 48, paedACR30/50/70/90 was reached by 100%/97%/97%/77% in cohort 1 compared to (97%/93%/93%/73%) in cohort 2. The number of visits with inactive disease in cohort 1 (87 (24%)) was comparable to that of cohort 2 (79 (21%)) while the number of visits with no active joint was significantly higher in cohort 1 (178(48%) vs. 146 (39%); OR 1.45 (1.08–1.94); p=0.012). 44 (74/100 y) adverse events (AE) were noted leading to discontinuation in 6 patients. 3 serious AE occurred, two first uveitis events and one diagnosis of dermatomyositis, all in the placebo group. No new safety signal arose from our observation.

**Conclusions:** Early combination of ETA and MTX proved to be highly effective with a high rate of patients reaching high paediatric ACR response and 50% reaching inactive disease. Pre-defined targets to treat to, paediatric ACR30 at week 12, defining minimal response or inactive disease at week 24/48 were more often reached upon ETA and MTX than with MTX alone. Compared to immediate intense anti-rheumatic combination treatment with ETA and MTX, a comparable rate of patients on targeted therapy reached the final endpoint of inactive disease at week 48 but numbers of visits with active arthritis were higher in patients receiving delayed combination therapy.

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THU0570

### LONG-TERM EFFICACY AND SAFETY OF CANAKINUMAB IN PATIENTS WITH COLCHICINE-RESISTANT FMF (CRFMF), TRAPS AND HIDS/MKD: RESULTS FROM THE PIVOTAL PHASE 3 CLUSTER TRIAL

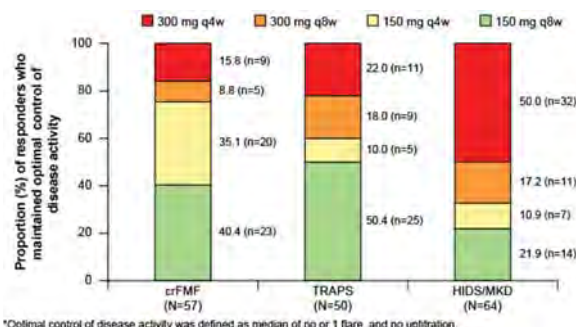
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**Background:** Canakinumab (CAN), a selective, human anti-interleukin (IL)–1 $\beta$  mAb, has demonstrated efficacy and safety in patients (pts) with colchicine-resistant familial Mediterranean fever (crFMF), TNF receptor-associated periodic syndrome (TRAPS), and hyper-IgD syndrome (HIDS)/mevalonate kinase deficiency (MKD) in the epoch 2 and 3 (E2 and E3) of the CLUSTER study (NCT02059291).<sup>1</sup>

**Objectives:** To evaluate the long-term maintenance of optimal control of disease activity (median of no or 1 flare, and no up-titration) and safety on every 4 weeks (q4w) and every 8 weeks (q8w) dosing regimens of CAN in pts with crFMF, TRAPS or HIDS/MKD from the epoch 4 (E4; 112 weeks) of the CLUSTER study.

**Methods:** The study comprised 4 epochs (E1–E4). Study design for E2 and E3 have been reported earlier.<sup>1</sup> After lead-in E1, in E2, a 16 wk randomised, double-blind, placebo (PBO)-controlled epoch, efficacy of CAN 150/300 mg q4w to induce complete response (absence of flares) was assessed. E3 (24 wks) evaluated whether responders to CAN 150/300 mg q4w in E2 could maintain clinical efficacy on 150/300 mg q8w or PBO. In E4, a 72 wk, open-label epoch, the long-term maintenance of efficacy and safety of CAN 150/300 mg q4w or q8w in pts with crFMF, TRAPS or HIDS/MKD was evaluated. Pts who did not maintain clinical response on q8w could be up-titrated to 150/300 mg q4w. Safety assessments included adverse events (AEs) and serious AEs.

**Results:** At the end of E4 (Wk 112), a substantial proportion of pts maintained optimal control of disease activity following treatment with 150/300 mg q4w or q8w in all 3 cohorts (figure 1). HIDS/MKD pts more often required up-titration to 300 mg q4w. Majority of pts in all 3 cohorts had 1 or no new flare (crFMF: 96.6%, TRAPS: 94.3%, HIDS/MKD: 83.3%) and physician global assessment <2 (no or minimal disease activity). In all 3 cohorts, the median SAA levels decreased rapidly from baseline and remained suppressed through E4 (crFMF: 618 to 21 mg/L, TRAPS: 243 to 12 mg/L and HIDS/MKD: 2061 to 16 mg/L). No new safety findings were reported in CAN-treated pts through E4.



**Abstract THU0570 – Figure 1** Proportion of responders who maintained optimal control of disease activity\* at the end of epoch 4 (Week 112); following treatment with canakinumab 150/300 mg q4w or q8w)

**Conclusions:** Epoch 4 of the CLUSTER study demonstrated that optimal control of disease activity in the crFMF, TRAPS and HIDS/MKD patients can be maintained following long-term treatment with canakinumab 150/300 mg q4w. For all 3 cohorts, patients requiring 150/300 mg q8w in epoch 3 to maintain disease control were less likely to control disease during epoch 4 and therefore a substantial number of these patients were uptitrated to q4w regimen by the end of epoch 4. No new or unexpected safety issues were reported over 112 weeks of canakinumab treatment.

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#### THU0571 PROTEOMIC IDENTIFICATION OF SYSTEMIC-ONSET JUVENILE IDIOPATHIC ARTHRITIS PHENOTYPIC BIOMARKERS

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**Background:** Systemic juvenile idiopathic arthritis (SJIA) is a childhood rheumatic auto-inflammatory disorder of largely unknown pathogenesis. The presence of fever, rash and arthritis support a diagnosis of SJIA, though early in disease arthritis may be minimal, complicating the exclusion of alternative diagnoses such as infection. Furthermore, two clinical phenotypes of SJIA can be identified, a chronic articular-dominant (ART\_SJIA) and a classical auto-inflammatory phenotype (AID\_SJIA).

**Objectives:** To identify novel serum protein biomarkers that may discriminate ART\_SJIA from AID\_SJIA and distinguish AID\_SJIA from infection.

**Methods:** Patients with active SJIA (joint activity plus or minus fever and elevated laboratory inflammation markers) were sub-grouped into the two clinical phenotypes (ART\_SJIA and AID\_SJIA). Serum from patients with SJIA or confirmed infection was analysed for the standard laboratory markers: C-reactive protein (CRP), white cell count (WCC) and erythrocyte sedimentation rate (ESR). A "discovery cohort" (n=10 per group) of patient serum samples was subjected to unbiased label-free proteomics using liquid chromatography mass spectrometry (LC-MS/MS) and in a separate "verification cohort" (AID\_SJIA, n=48; ART\_SJIA, n=29; infection, n=32) candidate biomarkers were measured by multiple reaction monitoring MS (MRM-MS; Agilent 6490 and 6495) and microsphere bead-based immunoassay (Luminex). Serum concentrations of S100A12 and MRP8/14 were also measured in all samples using enzyme linked immunoabsorbant assays (ELISAs).

**Results:** The routine laboratory markers CRP, WCC, ESR, as well as ELISA-measured S100A12 and MRP8/14 serum concentrations were highest in AID\_SJIA, followed by infection and were lowest in patients with ART\_SJIA. Proteins identified and quantified by LC-MS/MS could differentiate patients with ART\_SJIA from those with AID\_SJIA (area under the curve, AUC: 0.97). The discrimination between AID\_SJIA and infection performed less well, AUC: 0.58. Targeted MRM measurement of novel protein candidate biomarkers verified the discovery cohort data. A combined biomarker panel consisting of MRM, ELISA and Luminex analysis which was evaluated using a Random forest model, indicated the correct

overall identification of the clinical groups to be as follows: ART\_SJIA: 24/29 (83%), AID\_SJIA: 37/45 (82%) and infection: 20/32 (63%).

**Conclusions:** Significant differences in the serum protein signature between two phenotypes of SJIA suggest that different immunological processes may underlie these phenotypes. Serum protein profiles also distinguished patients with SJIA and infection. Distinguishing these two groups remains an important goal of research and therefore this study could help inform future prospective studies.

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#### THU0572 ORGANISED SPORTS IN CHILDREN AND ADOLESCENTS WITH JUVENILE IDIOPATHIC ARTHRITIS (JIA): A COMPARISON OF PATIENT AND GENERAL POPULATION PARTICIPATION

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**Background:** Despite the well-established physical, social and mental health benefits of physical activity (PA) in childhood, a substantial proportion of children and adolescents with JIA seem to be not active enough to achieve their age-appropriate fitness level.<sup>1</sup> Previous research revealed that organised sports (OS)<sup>1</sup> is associated with greater health benefits compared to non-organised sporting activities, as intensity and net exercise duration are usually higher,<sup>2</sup> has a strong predictive value in improving leisure time PA, and<sup>3</sup> has a positive influence on mental well-being and life satisfaction.<sup>2</sup>

**Objectives:** This study was aimed at comparing OS prevalence in JIA with the general population and at determining correlates associated with OS participation.

**Methods:** Data from the German National Paediatric Rheumatologic Database (NPRD) were considered for the analyses. The outcome variable 'OS participation' was analysed in patients aged 3 to 17 and compared to a population-based nationwide sample (German Health Interview and Examination Survey for Children and Adolescents; KiGGS). Correlates of OS participation were analysed using data of the year 2014.

**Results:** 5,056 children and adolescents with JIA (mean disease duration 4.5 ±3.6 years) provided information about their exercise habits, of which 36% stated to be involved in OS (34% of girls, 41% of boys). The prevalence was higher in the age groups 7 to 10 and 11 to 13 years with almost 50% than in the age groups 3 to 6 and 14 to 17 years with 35% and 42%, respectively. In KiGGS participants, almost 60% reported to be physically active in OS (54% aged 3 to 6, 65% aged 7 to 10, 60% aged 11 to 13% and 49% aged 14 to 17). Non-participation in OS was associated with active disease status (cJADAS), functional disability (C-HAQ), low parental education, higher body mass index (BMI) and worse patient-reported pain, fatigue and overall well-being.

**Conclusions:** The prevalence of OS participation in JIA was considerably lower compared to the general population and varied with increasing age, parental education and functional ability. Considering that low levels of PA might even be more dangerous for young patients with JIA, as they also have signs of inflammation, it is all the more important to create opportunities and incentives in the future to improve young rheumatic's exercise habits.

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THU0573

### 15-YEAR TRENDS AND CORRELATES OF SCHOOL SPORTS ATTENDANCE AMONG CHILDREN AND ADOLESCENTS WITH JIA ENROLLED IN THE GERMAN NATIONAL PAEDIATRIC RHEUMATOLOGIC DATABASE

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**Background:** Besides leisure-based physical activities (PA), the school-setting is described as one of the most effective areas for providing opportunities for PA, collectively reaching school-aged children vulnerable to sedentary behaviours.<sup>1</sup> In this context, regular participation in school sports can help children and adolescents achieve a part of the recommended amount of daily physical activity and help gain the knowledge and attitudes they need to engage in lifelong active lifestyle.

**Objectives:** Since adolescents with juvenile idiopathic arthritis (JIA) are less involved in physical and social activities compared to their healthy peers, the objectives were as follows:<sup>1</sup> to describe the extent to which school sports attendance among patients with JIA changed over time, and<sup>2</sup> to determine correlates associated with exemption from school sports.

**Methods:** Data of school-aged children and adolescents with JIA recorded in the National Paediatric Rheumatologic Database (NPRD) in the years 2000 to 2015 were considered for the analyses. Whether school sports participation had changed between 2000 and 2015 was determined using linear mixed models. Data from 2015 were inspected to analyse correlates of school sports absenteeism.

**Results:** During the observation period, participation rates in school sports were determined in 23,016 patients. The proportion of patients who participated always steadily increased from 31% in 2000 to 64% in 2015 ( $\beta=0.017$ , 95% confidence interval (CI) 0.015, 0.020), whereas the exemption rate simultaneously decreased from 44% in 2000 to 16% in 2015 [ $\beta=-0.009$ , 95% CI  $-0.011$ ,  $-0.007$ ]. In 2015, data from 5879 patients (mean age 13.1 $\pm$ 3.3 years, disease duration 5.9 $\pm$ 4.0 years, persistent oligoarthritis 37%) were available for evaluation. Fully exemption was associated with functional limitations, disease activity and any use of DMARDs, intra-articular glucocorticoid injection or physiotherapy.

**Conclusions:** School sports attendance among children and adolescents with JIA has increased significantly over the last 15 years. Possible explanations may

include improved functional ability, probably due to earlier and more frequent use of DMARDs. Considering the impact of JIA on daily life, the sedentary habits that come with it, and the potentially favourable effect of PA, it is important to promote an active lifestyle in children with JIA. In order to encourage patients to attend more frequently, it will be necessary to provide comprehensive information among teachers, parents and physicians regarding opportunities and risks of school sports.

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THU0574

### LONG TERM PHARMACOVIGILANCE OF BIOLOGICS FOR JUVENILE IDIOPATHIC ARTHRITIS: THE BIKER-REGISTRY

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**Background:** Long-term surveillance of biologics drugs is particularly important in paediatric patients (pts)

**Objectives:** To evaluate long-term rates of serious adverse events (AE) and AEs of special interest (AESI) in clinical practice in pts with juvenile idiopathic arthritis (JIA)

**Methods:** Safety data from pts registered in the BIKER registry were analysed. Rates of 25 AESI were analysed from first dose through 70 days after last dose and compared by Wald test

	ETA	ADA	GOL	INF	ABA	TOC	ANA	CAN
Patients,n	2481	845	67	69	98	295	57	45
Exposure, years	5376.0[KM1]	1333.6	71.7[KM2]	98.6	109.3	434.8	96.6	71.3
AE all*	1878 (34.9)	748 (56.1)	214(298)	100(101)	61 (55.8)	452(104)	39 (40.4)	94(131)
SAE	252 (4.7)	78 (5.8)	10 (13.9)	14 (14.2)	6 (5.4)	75 (17.3)	9 (9.3)	17 (23.8)
AESi all	320 (6.0)	143 (10.7)	16 (22.3)	23 (23.3)	10 (9.1)	96 (22.1)	7 (7.2)	14 (19.6)
Uveitis	106 (2.0)	70 (5.2)	5 (7.0)	9 (9.1)	2 (1.8)	2 (0.5)	0	0
	RR2.01 [1.52–2.67]; p<0.0001	RR2.64 [1.98–3.54] p<0.0001	RR2,78 [1.13–7,14] p=0.025	3.68 [1.89–7.19] p=0.0001				
Infection	90 (1.7)	32 (2.4)	6 (8.4)	3 (3.0)	1 (0.9)	18 (4.1)	4 (4.1)	1 (1.4)
	RR0.57 [0.41–0.78]; p=0.0005		RR4.21 [1.86–9.51] p=0.0005			RR2.17 [1.32–3.54] p=0.002		
Cytopenia	30 (0.6)	1 (0.1)	0	1 (1.0)	0	22 (5.1)	2 (2.1)	6 (8.4)
	RR0.39 [0.23–0.64] p=0.0002					RR9.07 [5.3–15.3] p<0.0001		RR11.34 [4.89–26.3] p<0.0001
Hepatic event	17 (0.3)	6 (0.4)	0	1 (1.0)	1 (0.9)	13 (3.0)	0	1 (1.4)
	RR0.32 [0.17–0.60] p=0.0004					RR8.25 [4.23–16.0] p<0.0001		
Anaphylaxis	3 (0.1)	3 (0.2)	1 (1.4)	5 (5.1)	2 (1.8)	15 (3.5)	0	1 (1.4)
	RR0.05 [0.01–0.15] p<0.0001			RR15.1[5.79–39.5] p<0.0001		RR16.49 [8.06–33.7] p<0.0001		
Autoimmuno-pathy	8 (0.1)	10 (0.7)	1 (1.4)	1 (1.0)	2 (1.8)	3 (0.7)	0	0
	RR0.19 [0.08–0.45] p=0.0001				5.97 [1.41–25.3] p=0.015			
CED	19 (0.4)	2 (0.1)	0	2 (2.0)	0	0	0	0
				RR7.21 [1.69–30.7] p=0.008				
Depression	12 (0.2)	2 (0.1)	0	0	1 (0.9)	1 (0.2)	0	1 (1.4)
MAS	2 (0.0)	0	0	0	0	6 (1.4)	1 (1.0)	3 (4.2)
	RR0.08 [0.02–0.38] p=0.001					RR16.49 [5.32–51.13] p<0.0001		RR 35.3 [9.56–130] p<0.0001
Malignancy	6 (0.1)	0	0	1 (1.0)	0	1 (0.2)	0	0
Hypertension	4 (0.1)	4 (0.3)	0	0	0	0	0	0
		RR4.69 [1.17–18.8] p=0.02						



**Results:** A total of 3975 courses of biologics with a total exposure of 7592 PY were identified with Etanercept (5376PY) followed by Adalimumab (1334PY), Tocilizumab (435PY), Abatacept (109PY), Infliximab (99PY), Anakinra (96 PY), Canakinumab (71PY) and Golimumab (67PY). Differences in JIA category distribution and concomitant treatment were noted. A total of 3586 AE (47.2/100PY), 461 (6.1) SAE and 629 (8.3) AESI were reported. The most common AESI were uveitis (194 (2.6)) followed by medically important infections (155 (2.0)), cytopenias (62 (0.8)), hepatic events 39 (0.5), anaphylaxis (28 (0.4)), other autoimmune-pathies (25 (0.3)), chronic inflammatory bowel disease (23 (0.3)), depression (17 (0.2)), macrophage activation syndrome (12 (0.2)), malignancies (8 (0.1)) and pregnancies (8 (0.1)). There were marked differences in the rate of AESI with different biologics. Uveitis was most common in TNF-antibody treated cohorts, infections upon GOL, TOC, ANA, cytopenias upon TOC, CAN, hepatic events upon TOC, anaphylaxis upon INF, TOC, CED upon ETA, INF (table 1). One case of latent TB but no further opportunistic infections were reported. There was a single death due to sepsis.

[KM1]Vorn 2481

[KM2]Vorn 67?

**Conclusions:** Surveillance of pharmacotherapy as provided by BIKER is an important approach especially for long term treatment of children. Overall, tolerance is acceptable. Differences between several biologics were noted and should be considered in daily patient care

**Disclosure of Interest:** None declared

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#### THU0575 ANAKINRA FOR FIRST LINE STEROID FREE TREATMENT IN SYSTEMIC ONSET JUVENILE IDIOPATHIC ARTHRITIS

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**Background:** Systemic juvenile idiopathic arthritis (sJIA) is characterised by arthritis accompanied or preceded by systemic autoinflammation. High-dose steroids has been the mainstay of therapy with proven effectiveness but also with side-effects. In many patients a chronic course with destructive arthritis long-term cannot be prevented.

**Objectives:** In patients naïve for steroids, a steroid-free treatment may allow reconstitution of an impaired NK-cell function and probably remission of sJIA.

**Methods:** First experience with first line Anakinra without steroids in 9 consecutive patients is reported.

**Results:** All patients presented with ongoing spiking fever and rash and further features of sJIA, high CRP, S100 and IL18 (table 1). Daily sq. injections of Anakinra 2 mg/kg for 3 months resulted in complete remission in 4 and partial response in two children presenting with an oligoarticular involvement. One patient with typical sJIA and very high S100 (MRP8/9) levels did not respond to Anakinra nor to Canakinumab. Two patients presented with polyarthritis. One had no response, the other showed a minor response but improved on steroids and was later treated with tocilizumab. One of the oligoarticular patients with an initial partial response had a flare upon anakinra captured by increased dosing (4 mg/kg) but finally developed macrophage activation syndrome. Anakinra was discontinued after 3 months in 3 of the 4 responders. Two remained in drug free remission while the remainder flared several months later and retreatment was instituted. The patients with polyarticular involvement first received corticosteroids and were later both treated successfully with the IL-6 inhibitor.

**Conclusions:** Experience with first line steroid free treatment with Anakinra for sJIA is presented. A complete remission was reached in 4 cases with oligoarticular

involvement. In 3 further cases improvement was observed and 2 had no response including one who also failed Canakinumab. A toddler with a particular response to Anakinra later on developed MAS. One patient did not respond to both IL-1 inhibitors. Thus, steroid free treatment regimen with Anakinra is feasible and resulted into remission in most but not all patients. Aside, unwarranted effects of long lasting steroid application were avoided.

**Disclosure of Interest:** None declared

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#### THU0576 CARDIOVASCULAR RISK IN LONG-TERM JUVENILE IDIOPATHIC ARTHRITIS

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**Background:** Juvenile Idiopathic Arthritis (JIA) is one of the more common chronic diseases of childhood that often persists into adulthood and can result in significant long-term morbidity, including physical disability. The long-term risk of cardiovascular disease for individuals with Juvenile Idiopathic Arthritis (JIA) remains uncertain.

**Objectives:** This study aims to determine whether adults with JIA in remission and medium-long duration of the disease have an increased risk of cardiovascular disease.

**Methods:** This is a cross-sectional study including 25 patients (14 females and 11 males) diagnosed with JIA according to the International League of Associations for Rheumatology criteria ILAR 2001 were compared to 20 age- and sex-matched controls. Remission was determined by JADAS27 <1 and according to Wallace criteria. An extensive clinical analysis including body index mass, lipid profile, HOMA-IR and intra-arterial blood pressure was performed. Intima media thickness of the common carotid artery (CIMT) was measured as a marker of sub-clinical atherosclerosis. Different proinflammatory cytokines (TNF $\alpha$ , IL1b and IL6), molecules involved in the endothelium dysfunction (VEGF and E-Selectin) and adipokines (resistin and visfatin) were analysed on serum by ELISA.

**Results:** Mean duration of the disease was 13.31 $\pm$ 1.14 years. Mean age was 27.21 $\pm$ 0.68. Time in remission was 3.52 $\pm$ 0.84 years. Metabolic comorbidities such as obesity and metabolic syndrome were more prevalent in our cohort of JIA patients compared to controls. Levels of cholesterol were significantly elevated in patients. However, HOMA-IR values and intra-arterial pressure were not significantly increased in JIA patients. CIMT was higher in JIA patients compared to controls (0.44 $\pm$ 0.009 vs 0.41 $\pm$ 0.017, p=0.078), although it did not reach the statistical significance. Serum levels of cytokines (including TNF $\alpha$ , IL6 and IL1b), adipokines (such as resistin and visfatin), and VEGF were significantly augmented in the cases vs healthy donors. In addition, IMT values significantly correlated with the disease duration (r=0.439, p=0.046) and serum VEGF levels (r=0.498, p=0.030).

**Conclusions:** In our cohort of JIA patients the increased CIMT was not associated with inflammatory markers, but disease duration. Although patients were in clinical remission, the serum levels of inflammatory cytokines, adipokines and VEGF were elevated, molecules with a relevant role in the onset and progression of endothelial dysfunction and atherosclerosis. These results might suggest that long-term JIA patients could have higher cardiovascular risk, although they are in sustained remission.

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Age, gender	Clinical features	CRP, mg/l	S100 (MRP8/9)	IL18, pg/ml	Initial response	Outcome
11, m	spiking fever, rash, arthralgia	95.6	1910	2483	complete response	remission off treatment
2, m	spiking fever, rash, organomegaly, arthralgia	101.7	14 110	>10 000	complete response	remission off treatment
1, f	spiking fever, rash, organomegaly, oligoarthritis	158.3	820	>5000	partial response	increase of dosage upon flare, discontinued with MAS
8, f	spiking fever, rash, polyarthritis	224.5	4040	>10 000	no response	remission upon Tocilizumab
15, f	spiking fever, rash, polyarthritis	329.6	4780	>10 000	partial response	remission upon Tocilizumab
5, m	spiking fever, rash, organomegaly, arthralgia	20.5	22 650	3820	minor response	improvement with corticosteroids, remission on Tocilizumab
11, w	spiking fever, rash, organomegaly, arthralgia	145.8	20 775	6000	complete response	remission off treatment
4, m	spiking fever, rash, pericarditis, splenomegaly, arthralgia	203.8	3 04 850	>10 000	no response	switch to Canakinumab with no response, remission on steroids
5, m	spiking fever, rash, arthralgia	237.7	1 61 700	2830	complete response, switch to Canakinumab after 7 days	remission off treatment

THU0577

### DO RAYNAUD PHENOMENON NEGATIVE JUVENILE SYSTEMIC SCLERODERMA PATIENTS HAVE A DIFFERENT PATTERN OF ORGAN INVOLVEMENT AS RAYNAUD PHENOMENON POSITIVE PATIENTS?

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**Background:** Juvenile systemic sclerosis (jSSc) is an orphan disease, with an estimated prevalence of 3 per 1000 000 children. Most jSSc patients primarily present with Raynaud phenomenon (RP). We investigated in our patient of the juvenile scleroderma inception cohort, how fare patients with (RP+) and without (RP-) RP differed in their clinical presentation at enrolment.

**Methods:** The jSSc is a prospective cohort of jSSc patients. Patients were enrolled who were diagnosed with jSSc, had a jSSc onset age under 16 years and were younger as age of 18 years at the time of inclusion. The patients are prospectively assessed every 6 months according to a standardised protocol. We reviewed the organ involvement pattern of our patients currently followed in the cohort.

**Results:** 100 patients are currently followed in the cohort and 89 (89%) of them had RP. The female/male ratio was lower in the RP +group, 3.7:1 compared to 4.5:1 (p=0.808). Diffuse subtype was more common in the RP +group, 72% compared to 63%. Mean age of onset of first non-Raynaud symptomatic was 10.4 years in both groups. Mean disease duration was slightly higher in the RP +group, 3.4 compared to 2.2 years. ANA positivity was higher in the RP +group, 88% compared to 70% (p=0.48). Anti-Sc170 was 34% in the RP +and 20% in the RP-group (p=0.34). Interestingly 7% of RP +but none of the RP +were anti-centromere positive. The mean modified skin score was lower in RP +group (mean of 14.8 compared to 17.0). There were significantly more nailfold capillary changes (70% compared to 18%, p=0.001) and a higher rate of history of ulceration in the RP +group (49% compared to 20%, p=0.083). Decreased DLCO and FVC <80% was higher in the RP-negative group with 45%/50% compared to 37.5%/31% respectively. Pulmonary hypertension occurred in 7% in the RP +group and there was no case in the RP- group (p=0.335). RP- group had a higher rate of urinary sediment changes 18% compared to 4.5% in the RP +group (p=0.07). No renal crisis or hypertension was reported in neither groups. Gastrointestinal involvement was similar between the two groups with around 35%. Occurrence of swollen joints was similar in both groups as the frequency of muscle weakness with around 20%. The tendon friction rub occurred around 10% in both groups. In the patient related outcomes, there was only a difference in rating of Raynauds activity.

**Conclusions:** The RP- group differed from RP +group in the clinical presentation at enrolment. The absence of Raynaud phenomenon was associated with a decreased rate of history of ulceration, no occurrence of pulmonary hypertension. Interestingly higher rate of urinary sedimentary changes and no anticentromere positivity was observed in RP- patients.

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THU0578

### PATIENTS AND PHYSICIAN RELATED OUTCOMES IMPROVE SIGNIFICANTLY OVER 12 MONTHS FOLLOW UP IN PATIENTS WITH JUVENILE SYSTEMIC SCLEROSIS. RESULTS FROM THE JUVENILE SCLERODERMA INCEPTION COHORT. WWW.JUVENILE-SCLERODERMA.COM

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**Background:** Juvenile systemic sclerosis (jSSc) is an orphan disease with an estimated prevalence of around 3 per 1 000 000 children. There are no studies which evaluated prospectively the patient related outcomes in these patients. We report the data from juvenile scleroderma inception cohort (jSSc) regarding organ involvement and patient related outcomes.

**Methods:** The jSSc is a prospective cohort of jSSc patients. Patients were enrolled who were diagnosed with jSSc, had a jSSc onset age under 16 years and were younger as age of 18 years at the time of inclusion. The patients are prospectively assessed every 6 months according to a standardised protocol. Patients with available 12 months follow up data were included in the analyses.

**Results:** Currently 100 patients are followed in the jSSc cohort. 51 of them had available 12 months follow up data. Among those patients 37 (72.5%) had diffuse and 14 (27.5%) limited subtype. Mean age of onset of disease was 9.5 (±4.1) years and the mean disease duration at time of inclusion was 3.1 years (±3.2). The proportion of patients treated with DMARD increased from 74.5% to 88% at 12 months follow up. 86% were ANA positive at both assessments. Anti-scl70 positivity increased from 38% to 42%. Anticentromere antibody positivity was 2.4% at both assessments. Mean modified skin score decreased from 17.7 to 14.3 (p=0.151) Raynaud phenomenon occurred in 86% at enrolment and increased up to 88% at 12 months follow up. Nailfold capillary changes occurred around 70% at both assessments, but number of patients with active ulceration decreased from 28% to 16% (p=0.148). The number of patients with decreased FVC (FVC under 80%) decreased from 40.5% to 32% (p=0.497). The number of patients with pulmonary hypertension remained around 10%. No renal crisis or hypertension were reported. The gastrointestinal involvement was around 40% at both assessments. The number of patients with swollen joints decreased from 24% to 10% (p=0.06). The number of patients with muscle weakness decreased significantly from 33% to 9% (p=0.016), parallel to the number of patients with elevated CK values which decreased from 27% to 12% (p=0.074). All patient related outcomes, like global disease activity (p=0.048), global disease damage (p=0.05), Raynaud activity (p=0.003) and ulceration activity (p=0.001) improved significantly over 12 months. Physician assessed global disease activity (p=0.003) and ulceration activity (p=0.001) also improved significantly.

**Conclusions:** Our data show, that jSSc patients over a 12 months disease course stayed quite stable or improved regarding organ involvement. But patient and physician related outcomes regarding activity assessment improved significantly.

**Disclosure of Interest:** None declared

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THU0579

### VALIDATION OF CONTRAST-ENHANCED MRI SCORES ON (TENOSYNOVITIS OF THE WRIST IN JUVENILE IDIOPATHIC ARTHRITIS) PATIENTS BY COMPARISON WITH CHILDREN UNAFFECTED BY CLINICAL ARTHRITIS

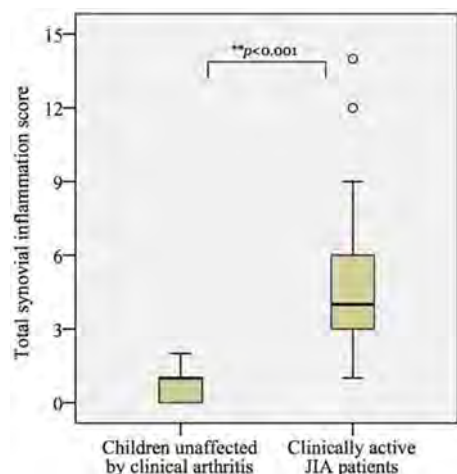
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**Background:** Delayed and/or inappropriate treatment of juvenile idiopathic arthritis (JIA) may lead to permanent loss of joint functionality.<sup>1</sup> Contrast-enhanced MRI is increasingly being accepted as a sensitive tool for detecting JIA disease activity in an early stage.<sup>2</sup>

**Objectives:** The aim of this study was to assess the validity of two reliable contrast-enhanced MRI scores for the assessment of synovitis and tenosynovitis in the wrist of clinically active JIA patients by a comparison with children unaffected by clinical arthritis.

**Methods:** An axial T1-weighted MRI sequence with contrast-enhancement and fat-saturation was performed on the wrist of 25 children who had no signs of joint inflammation at clinical examination and who were already subjected to contrast-enhanced MR enterography. Wrist MRI scans of 25 clinically active JIA patients were matched based on time-interval between contrast injection and start of the MRI sequence. After being blinded for clinical status, two radiologists scored synovitis and tenosynovitis in consensus. Synovitis was scored at 5 locations by degrees of synovial enhancement (0–2 scale) and synovial inflammation (0–3 scale). Tenosynovitis was scored at the extensor tendons (compartments II, IV and VI) and flexor tendons by degree of inflammation based on a 0–3 scale.<sup>3,4</sup>

**Results:** Children unaffected by clinical arthritis had significantly lower total synovial enhancement (median=1 vs 4, p<0.001) and total synovial inflammation (median=1 vs 4, p<0.001) scores compared to clinically active JIA patients (graph). No significant difference in total tenosynovitis score was found between both groups (median=0 vs 0, p=0.220). Fifteen out of 25 (60%) clinically active JIA patients were given a total tenosynovitis score of 0.



**Conclusions:** The contrast-enhanced MRI scores for the assessment of synovial enhancement and synovial inflammation in the wrist of clinically active JIA patients appear valid. Due to a low incidence of wrist tenosynovitis in this cohort, the validity of the tenosynovitis score could not be assessed. These findings further establish contrast-enhanced MRI as a diagnostic tool with synovitis as the primary target of disease in the wrist of JIA patients.

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#### THU0580 THE ACR RECOMMENDATIONS FOR JIA IN DAILY CLINICAL PRACTICE: ARE THEY FOLLOWED OR WOULD TREAT-TO-TARGET THERAPY LEAD TO BETTER RESULTS?

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**Background:** What factors drive the physician decision to escalate to anti-TNF therapy 3 and 6 months after start of methotrexate (MTX) in both persisting oligoarthritis (OJIA) and polyarticular course (PJIA) juvenile idiopathic arthritis.

**Objectives:** Are the escalation-decisions in accordance with the ACR JIA treatment recommendations (ACR-CPG)<sup>1</sup> and if not, what factors drive these decisions. How does it perform as a "prognostic" test to predict failure when not escalated. Could the clinical Juvenile Arthritis Disease Activity Score (cJADAS) be used instead. What is the value of the patient-VAS in the ACR-CPG, the physician decision and in the cJADAS.

**Methods:** Monocentric retrospective cohort study analysing all OJIA and PJIA patients starting MTX for the first time between 2011 and 2016.

**Results:** The ACR-CPG is mostly not followed and implementation would increase the anti-TNF-use from 12.0% to 65.1%. However, the physician decision not to escalate was now correct in 70%–75%, therefore implementation results in an overuse of anti-TNF. Some items of the ACR-CPG were non-discriminatory. The use of cJADAS in predicting failure if not escalated outperformed the ACR-CPG with a much higher sensitivity and specificity for the OJIA and PJIA group respectively. The omission of the patient-VAS-scores resulted in a substantial decrease of the identification of patients failing to respond without escalation.

**Conclusions:** The ACR-CPG not only is too complicated to be applicable in clinical practice, it also fails to identify those patients really in need of escalation to

anti-TNF. The cJADAS can be used instead since this is user-friendly, does not require waiting for ESR results and performs better than the ACR-CPG. The patient-VAS is a critical item for the decision to escalate.

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#### THU0581 USE OF BIOLOGICAL THERAPIES IN ADULT PATIENTS DIAGNOSED WITH JUVENILE IDIOPATHIC ARTHRITIS: RESULTS FROM BIOBADASER, THE SPANISH REGISTRY OF ADVERSE EVENTS WITH BIOLOGIC THERAPIES

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**Background:** Juvenile idiopathic arthritis (JIA) is the most frequent chronic rheumatic disease in childhood. The early disease recognition and treatment is critical to prevent long-term complications and disability in childhood. During the last decade the arrivals of biologics has dramatically changed the prognosis of these patients. A number of well-designed clinical trials, as well as cohort studies have demonstrated that biologics are an effective option for JIA patients who do not respond or cannot tolerate treatment with synthetic disease modifying drugs (DMARDs).

JIA is not confined to childhood, and a 41% had active disease are on medication after 30 years and 28% had a high symptom state.

**Objectives:** The aim of this work was to study the pattern of use, drug survival and adverse events of biologic therapy in JIA patients during the transition period from the diagnostic to the adulthood.

**Methods:** Information was obtained from BIOBADASER, a safety multicenter prospective registry. All patients included in the registry diagnosed of JIA between 2000 and 2015 were analysed. Proportions, means and standard deviations (SD) were used to describe population. Incidence rates and 95% confidence intervals were calculated to assess adverse events. Kaplan-Meier analysis was used to compare the drug survival.

**Results:** 469 patients, 46.1% women were included in this study. Age at diagnosis was 9.4 (SD=5.3) and years of disease evolution 24.1 (SD=14.1). The age at biological treatment initiation was 23.9 years (SD=13.9). The pattern of use of biologics in JIA patients in the paediatric age shows a linear increase from 24% in 2000 to 65% in 2014. Interestingly, the biologic suspension for disease remission was higher in patients who initiated its use under 16 years (25.7%) than in those who began at 16 years or later (7.9%,  $p < 0.0001$ ). Serious adverse events showed a total incidence rate of 41.4 (35.2–48.7) (1000 patients/year) without differences between patients younger or older than 16 years old. However, patients younger than 16 years old showed a significant increment in infection and infection ( $p < 0.001$ ).

**Conclusions:** The biologic survival and suspension by remission was higher when the biologic therapy started before 16 years old in JIA patients. The incidence rate severe adverse events in the childhood and adulthood in JIA patients treated with biologics was similar, however, a significant increment of infection was observed in patients under 16 years old.

**Disclosure of Interest:** None declared

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**THU0582 A SYSTEMATIC REVIEW OF EMPLOYMENT OUTCOMES OF ADULTS WITH CHILDHOOD-ONSET SYSTEMIC AUTOIMMUNE RHEUMATIC DISEASES**

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**Background:** Childhood-onset systemic autoimmune rheumatic diseases (ChildCRD) include: systemic lupus erythematosus (SLE), Sjogren's syndrome, systemic sclerosis, inflammatory myositis, and chronic systemic vasculitides (Takayasu arteritis, polyarteritis nodosa, anti-neutrophil cytoplasmic antibodies (ANCA) associated systemic vasculitides). These conditions had mortality rates of up to 50%, but most patients now live into adulthood. Employment is an important milestone in adulthood: it has direct effects on one's socioeconomic status and access to health insurance, which could in turn affect disease outcomes.

**Objectives:** To perform a systematic review of the employment outcomes of ChildCRD individuals. To identify gaps of knowledge and methodological issues in this field so as to inform future studies.

**Methods:** ChildCRD patients have disease-onset <18 years old and adulthood outcomes reported at ≥18 years old. We developed a search strategy for employment outcomes of ChildCRD with an academic librarian; this was iteratively refined and finalised after peer-review by other librarians. We included English language articles published from Jan 1990 Oct 2017 in MEDLINE, EMBASE, and Scopus. Case reports, case series, editorials, letters, or short reports were excluded. We supplemented our search by hand-searching references in review articles. Information on outcomes, prognostic factors, and study designs was recorded. Studies were graded independently by 2 reviewers (after prior training for agreement) using the Quality in Prognosis Studies (QUIPS) risk-of-bias tool which examines quality in 6 study domains. Authors were contacted as necessary for further information or clarification.

**Results:** Of 2109 studies, we identified 3 publications (G1) studying SLE patients. None studied other ChildCRD. Two papers were from a single study and studied both SLE and juvenile arthritis; we only used SLE patients' information. Three additional manuscripts (G2) studied childhood- and adult-onset patients but did not report outcomes separately. All G1 publications were from North America (2 Canada, 1 USA). 193 patients in 2 studies were examined; 1 study had longitudinal (non-inception) design. Only G1 studies have data for report. Patients' disease durations were a mean of 7.6–15 years and the mean ages at study were 23–29 years. Half of the patients were employed. Lower disease activity, better physical function, and higher education were associated with longitudinal employment in 1 study; greater independence and social support were associated with employment in another. One study showed psychosocial and work context factors to be associated with absenteeism, disease activity with job disruptions, and fatigue and work context factors with lost productivity. Of QUIPS-graded G1 publications, study populations and confounding were at moderate-high risk-of-bias. Study outcomes, prognostic factors, and statistical analyses were at low-moderate risks-of-bias. Attrition was low in the longitudinal study.

**Conclusions:** Currently, there is minimal information on employment outcomes in ChildCRD adults except for few studies on SLE; information about other ChildCRD is needed. Study populations and confounding are at moderate-high risks-of-bias, limiting the generalizability. More information on employment outcomes, the specific aspects of employment, disease and non-disease related prognostic factors affecting employment are needed.

**Disclosure of Interest:** None declared

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**THU0583 PAIN INTERFERENCE ASSOCIATED FACTORS IN A COHORT OF FINNISH YOUNG ADULTS WITH JUVENILE IDIOPATHIC ARTHRITIS**

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**Background:** Pain is one of the most distressing and persisting features of JIA and frequently interferes with everyday life.

**Objectives:** This study was conducted to find out the factors associated with pain interference in young adults (aged 18 to 30 years) with JIA.

**Methods:** 195 adult patients with JIA were eligible for the study. Associations between patients reported outcome data and pain interference were examined. Sociodemographic and clinical data were analysed. Pain interference was measured by a single item from the RAND 36 questionnaire. Five response categories were coded into different groups: patients reporting "extremely" and "quite a bit" or "moderate" were classified having significant pain interference; "a little bit" as having minor pain interference; and "not at all" as having no pain interference. Functional disability was measured by HAQ, depressive symptoms were measured by Beck Depression Inventory-II, self-esteem was assessed by Rosenberg Self-

Esteem Scale, and anxiety was assessed by PASS-20. Leisure time physical activity (LTPA) metabolic equivalent (MET) score was calculated.

**Results:** Pain intensity scores were higher in patients expressing significant pain interference (mean 5.3, SD 2.1) and minor pain interference (mean 2.8, SD 2.09);  $p$  for linearity <0.001, thus the mean pain intensity for the whole study group was quite low (mean 2.3, SD 2.3). Of the 195 patients 98 (50.3%) reported no pain interference, 59 (30.3%) reported minor pain interference, and 39 (20%) reported significant pain interference. We found that pain interference was associated with older age ( $p=0.029$ ), female gender ( $p=0.028$ ) and receiving antirheumatic treatment ( $p=0.032$ ), analgesics ( $p<0.001$ ), antidepressants ( $p=0.008$ ), and opioids ( $p<0.001$ ). Also cohabiting ( $p=0.003$ ), LTPA MET ( $p=0.032$ ), smoking (0.006), being more disabled ( $p<0.001$ ), having fewer leisure time activities ( $p<0.001$ ) or having co-morbidities ( $p=0.006$ ), and headache ( $p<0.001$ ) were associated with having pain interference. Higher anxiety scores were associated with more pain interference ( $p<0.001$ ). When controlling for gender, age, depression, LTPA MET, disability, life situation, disease remission, analgesics, antidepressants, and pain intensity, all subscales in PASS-20 were significantly associated with higher pain interference levels: cognitive anxiety ( $p=0.004$ ), escape/avoidance ( $p<0.001$ ), fear ( $p=0.001$ ), psychological anxiety ( $p=0.016$ ).

**Conclusions:** Half of the JIA patients reported pain interference, and they also expressed higher pain scores. Age, gender, using antirheumatic drugs, antidepressants, analgesics or opioids, cohabiting, lower LTPA MET score, disability, smoking, co-morbidities, lack of activities, and suffering anxiety were most significantly related to pain interference. Our study highlights the need to develop better strategies for pain-relieving interventions and for supporting patients' health-behaviour in order to achieve better pain outcome in young adults with JIA.

**Disclosure of Interest:** None declared

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**THU0584 VITAMIN D STATUS IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS AND ITS ASSOCIATION WITH DISEASE ACTIVITY AND PROGRESSION – RESULTS FROM THE INCEPTION COHORT ICON**

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**Background:** Vitamin D has been shown to have immunomodulatory properties in addition to its well-established role in the maintenance of mineral homeostasis and bone health. Conflicting data have been available regarding vitamin D status in children and adolescents with juvenile idiopathic arthritis (JIA) and its influence on the disease.

**Objectives:** To determine 25–0 hour-vitamin D3 (25-OHD) levels in patients with JIA, and to evaluate whether 25-OHD levels are associated with disease activity and disease course.

**Methods:** Serum 25-OHD levels were determined in a pair of serum samples from patients with JIA who were enrolled in the JIA inception cohort study ICON and prospectively followed for three years. The frequencies of 25-OHD deficiency (defined as <20 ng/ml) and 25-OHD sufficiency (≥30 ng/ml) were determined and compared with those of the age-, sex- and ethnicity-matched general population (KIGGS study). The association of 25-OHD levels and the likelihood for uveitis were analysed by a Cox-proportional hazard model. Logistic regression analysis was used to investigate the predictive value of 25-OHD in terms of disease progression into extended oligoarthritis (OA).

**Results:** In 360 patients with early JIA (48% OA, 27% rheumatoid-factor negative polyarthritis), 25-OHD levels were determined twice: after a median disease duration of 6.6 and of 13.0 months. The mean 25-OHD level of all JIA samples was insufficient (22.1 ng/ml, SD 7.8), but significantly higher than that of the control population (18.4 ng/ml, SD 10,  $p<0.001$ ). Vitamin D levels decreased with age in patients and controls, but did not differ between males and females.

An insufficient mean 25-OHD level was found in 40% of JIA patients and in 25% in both samples each, sufficient levels in 13% and 7%, respectively. There were no significant differences in 25-OHD levels among the JIA categories. Disease activity, measured by the cJADAS-10, was inversely correlated with the first 25-OHD level ( $\beta=-0.20$ , 95% CI  $-0.37,-0.03$ ,  $p=0.018$ ), especially in 141 DMARD-naïve patients ( $\beta=-0.26$ , 95% CI  $-0.44,-0.01$ ,  $p=0.041$ ). Up to the 3-year-follow-up, 17% (61/360) developed uveitis, and 30% (52/173) of OA patients an extended OA. While 20% (17/87) of those with 25-OHD deficiency at both measurements were affected by uveitis, this applied to only 9% (2/23) in those with sufficient levels. Multivariable regression analysis revealed that the 25-OHD level was significantly associated with the risk to develop uveitis (Hazard ratio 0.95, 95% CI 0.91,0.99,  $p=0.008$ ). Twelve out of 29 (41%) patients with OA and two deficient

vitamin D levels, but only 2 of 14 (14%) with two sufficient 25-OHD levels developed extended OA during the first 3 years ( $p=0.034$ ).

**Conclusions:** Overall, vitamin D levels were higher in JIA patients than in matched controls. JIA patients with higher disease activity had lower 25-OHD levels. In particular, complicated courses with uveitis or the development of polyarthritis seem to be associated with lower 25-OHD levels. Further studies are needed to substantiate these results.

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#### THU0585 PERSONALISED TREATMENT IN JUVENILE IDIOPATHIC ARTHRITIS – FUTURE OR FICTION? PRELIMINARY RESULTS OF USING S100A8A9, S100A12 AND VASCULAR ENDOTHELIAL CADHERIN AS DIAGNOSTIC AND PROGNOSTIC BIOMARKERS

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**Background:** Serological biomarkers with ability to predict outcome and therapeutic response of patients might be helpful in introducing the concept of treat-to-target into management of juvenile idiopathic arthritis (JIA). Among others, calprotectin (S100A8A9) and calgranulin C (S100A12) are considered to be valuable markers of disease activity and risk factors for flare after withdrawal of treatment. Vascular endothelial cadherin (VE-cadherin) is a marker of endothelial permeability which has been postulated to predict response to methotrexate therapy in rheumatoid arthritis (RA) patients.

**Objectives:** The aim of the study was to assess the clinical significance of measuring serum concentrations of S100A8A9, S100A12 and VE-cadherin in patients with freshly diagnosed JIA and those with exacerbated course of the disease.

**Methods:** Serum levels of the listed biomarkers were determined in 30 patients diagnosed with JIA and 21 age- and sex-matched healthy controls. In the study group blood samples were obtained in two time points in order to evaluate dynamics of concentrations of markers.

**Results:** S100A8A9 and S100A12 serum concentrations at baseline were positively correlated with ESR at second time point ( $r=0.378$  and  $0.425$ ,  $p=0.0397$  and  $0.0193$ , respectively). S100A12 had equal correlation with CRP at second time point ( $r=0.391$ ,  $p=0.0329$ ). Patients freshly diagnosed with JIA had higher levels of S100A12 ( $8.49\pm 4.92$  ng/ml vs.  $5.49\pm 2.21$  ng/ml,  $p=0.007$ ) and VE-cadherin ( $5.31\pm 1.13$  ng/ml vs.  $3.50\pm 0.58$  ng/ml,  $p<0.001$ ) when compared to healthy controls. VE-cadherin level was elevated in JIA patients at second time point as well ( $4.10\pm 0.93$  ng/ml,  $p=0.0194$ ). Patients who underwent arthrocentesis at baseline had higher concentrations of S100A12 at second time point ( $6.69\pm 3.56$  ng/ml vs.  $3.84\pm 2.58$  ng/ml,  $p=0.0168$ ). Levels of markers were independent of sex and age.

**Abstract THU0585 – Table 1.** General characteristics of the study group

No. of patients (%)	30 (100.0%)
Age at diagnosis of JIA $\pm$ standard deviation	9.6 $\pm$ 4.8 years
Female (%)	23 (76.7%)
Oligoarticular JIA (%)	24 (80.0%)
Enthesitis-related JIA (%)	2 (6.7%)
Polyarticular RF-negative JIA (%)	3 (10.0%)
Polyarticular RF-positive JIA (%)	1 (3.3%)
Freshly-diagnosed JIA at 1st time point (%)	10 (33.3%)
Exacerbated course of the disease at 1st time point (%)	15 (50.0%)
Minimal disease activity at 1st time point (%)	5 (16.7%)
Arthrocentesis performed at 1st time point (%)	16 (53.3%)
Duration of period between time points $\pm$ standard deviation	99.1 $\pm$ 27.7 days
Exacerbated course of the disease at 2nd time point (%)	9 (30.0%)

**Abstract THU0585 – Table 2.** Serum concentrations of assessed biomarkers (values presented as mean $\pm$ standard deviation)

Marker	Study group – 1st time point (n=30)	Study group – 2nd time point (n=30)	Control group (n=21)
S100A8A9 [ug/ml]	2.56 $\pm$ 2.15	1.69 $\pm$ 1.42	1.47 $\pm$ 0.68
S100A12 [ng/ml]	9.08 $\pm$ 5.25	5.36 $\pm$ 3.41	5.49 $\pm$ 2.21
VE-Cadherin [ng/ml]	4.85 $\pm$ 0.93	4.10 $\pm$ 0.93	3.50 $\pm$ 0.58

**Conclusions:** Presented study group needs to be expanded with more patients, especially with minimal disease activity, in order to validate demonstrated preliminary results. VE-cadherin may be considered as a future diagnostic biomarker, however its specificity requires detailed assessment. S100A8A9 and S100A12 merit further evaluation as potential prognostic biomarkers for more aggressive course of the disease.

**Disclosure of Interest:** None declared

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#### THU0586 METHOTREXATE DRUG SURVIVAL AND ADVERSE EFFECTS IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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**Background:** Methotrexate is usually the first-line disease modifying anti-rheumatic drug (DMARD) for patients with juvenile idiopathic arthritis (JIA), due to its efficacy, the low-cost and favourable safety profile in patients. However, one of the most reported adverse effects of interest (AEIs) of methotrexate is nausea.

**Objectives:** The objectives of this analysis were to (i) calculate methotrexate monotherapy drug survival, (ii) describe AEIs over the first two years of treatment, and (iii) investigate factors associated with occurrence of AEIs among children with JIA.

**Methods:** Patients with all forms of JIA starting methotrexate monotherapy from both the UK BSPAR Etanercept Cohort Study (BSPAR-ETN) and Biologics for Children with Rheumatic Diseases study (BCRD) were included. Patient characteristics and anti-rheumatic therapy details were collected at treatment start. Follow-up data were collected at six months, one year, and annually thereafter, on changes to anti-rheumatic therapy and any adverse events. AEIs were grouped into gastrointestinal-related (nausea, vomiting, abdominal pain), raised liver enzymes, leukopenia, drug hypersensitivity (injection site reaction), rash, needle phobia, and any other event leading to permanent discontinuation of methotrexate. All person time was included from methotrexate start date until first methotrexate stop date, start of biologic therapy, last patient follow-up date, or 30-June-2017 (study cut-off date), whichever came first. Survival analysis was used to assess time on methotrexate monotherapy and time to first AEI on methotrexate monotherapy. Multivariable logistic regression was used to assess baseline characteristics associated with experiencing an AEI, and a gastrointestinal-related AEI only.

**Results:** Of 505 patients starting methotrexate between 01-January-2010 and 30-June-2015 (to allow at least two years of follow-up for all children), median time on monotherapy was 1.5 years (IQR 0.7, 2.3). At two years, 274 (54%) patients were no longer on methotrexate monotherapy. Reasons included: inefficacy ( $n=174$ ; 64%) mostly due to start of biologic therapy ( $n=161$ ), adverse events ( $n=54$ ; 20%), remission ( $n=24$ ; 9%), and patient/family decision ( $n=9$ ; 3%). Within the first two years of methotrexate monotherapy, 181 (36%) patients experienced at least one AEI; the most common were gastrointestinal problems ( $n=116$ ; 53%) and liver enzyme abnormalities ( $n=42$ ; 19%). No clinical factors were associated with occurrence of any AEI, nor a gastrointestinal-related AEI.

**Conclusions:** After two years, over half of the patients were no longer on methotrexate monotherapy, whilst one-third experienced at least one AEI, most commonly gastrointestinal-related problems. Further research focussing on identifying which children will respond and/or experience an AEI with methotrexate is crucial, such that AEIs can be minimised or prevented and treatment benefit maximised.

**Disclosure of Interest:** None declared

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THU0587

### CLINICAL AND THERAPEUTIC ASPECTS OF A SOUTH ASIAN POPULATION OF SYSTEMIC ONSET JUVENILE IDIOPATHIC ARTHRITIS IN A TERTIARY CARE PEDIATRIC RHEUMATOLOGY CENTRE IN SRI LANKA

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**Background:** Systemic onset juvenile idiopathic arthritis is a rare multisystem inflammatory disease of childhood associated with significant morbidity and mortality. Sri Lanka is a country situated in south Asia. Disease characteristics of systemic onset juvenile idiopathic arthritis is not well studied in this geographical region. Sri Lanka offers public funded free universal healthcare for all citizens including biological disease modifying drugs. Lady Ridgway hospital for children is the national centre for tertiary paediatric care and draws patients from wider geographical territory of Sri Lanka.

**Objectives:** To describe the demographic parameters, clinical features, disease activity and therapeutic aspects of systemic onset juvenile idiopathic arthritis among a population of Sri Lankan patients.

**Methods:** A descriptive cross sectional study was conducted at the department of rheumatology at Lady Ridgway hospital for children. Systemic onset juvenile idiopathic arthritis patients of 1–16 years of age, with minimum 6 months follow up in the study centre were recruited. Patients' demographic, clinical and laboratory data were collected.

**Results:** Data of 32 patients were analysed. Eleven (34.4%) were males and 21 (65.6%) were females. Mean age was 9.3 years (SD=4.19) while mean age at diagnosis was 5.95 years (SD=3.35). Majority n=17 (55%) had polyarthritis at the onset while n=12 and n=2 showed oligo-arthritis and mono-arthritis respectively. Mean inflammatory joint count at presentation was 5.4 (SD=3.7). Fifteen (46.9%) patients had persistent disease while 11 (34.4%) showed monocyclic and 6 (18.7%) had polycyclic disease pattern. Mean erythrocyte sedimentation rate of the study population at diagnosis was 104.02 mm/1st hour, dramatically reduced to 43.9 mm/1st hour after 6 months of treatment. All patients received corticosteroids for variable durations and doses during the disease course. Methotrexate was given to majority of patients (n=25, 78.1%). Thirteen patients (40.6%) received Tocilizumab. Disease remission was achieved by majority of 18 (56.2%) patients. All eligible patients received biological disease modifying drugs when indicated. Mean JDAS 10 score of the population was 4.4.

**Conclusions:** The above study revealed important demographic data, clinical features and therapeutic aspects of a population of systemic onset juvenile idiopathic arthritis in a tertiary care paediatric rheumatology centre in a south Asian population in Sri Lanka. Majority of patients were able to achieve remission or low disease activity with treatments.

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THU0588

### REDUCTION IN THE UTILISATION OF PREDNISON AND/OR METHOTREXATE FOLLOWING THE INITIATION OF ETANERCEPT IN PAEDIATRIC PATIENTS

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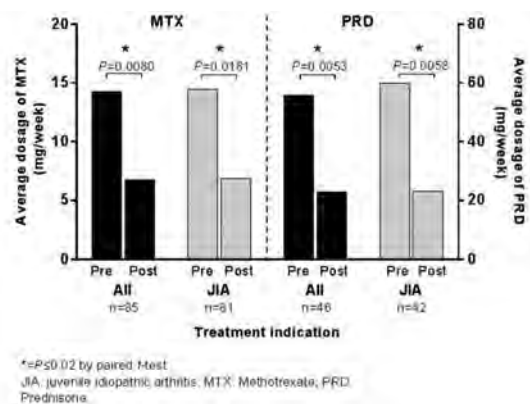
**Background:** In Canada, the paediatric indications of the soluble TNF $\alpha$  receptor etanercept (ETN) are active ankylosing spondylitis (AS) and moderate to severely active juvenile idiopathic arthritis (JIA); in those who have had an inadequate response to  $\geq 1$  disease-modifying anti-rheumatic drugs and are  $\geq 4$  years of

age). A previous analysis of Canadian claims data for children demonstrated a 78% yearly retention rate over Year 1 for ETN, which remained high over Years 2–6 (80%–90% per year). However, at this time, the changes in co-medication during ETN treatment in paediatric patients have rarely been evaluated in the real-world setting.

**Objectives:** To evaluate co-treatment utilisation and ETN costs in Canadian paediatric patients initiating ETN therapy.

**Methods:** A retrospective cohort study was conducted using longitudinal prescription drug claims data from the IQVIA Private Drug Plan (PDP), Ontario Public Drug Plan (OPDP), and Quebec Public Drug Plan database (RAMQ). Biologic-naïve paediatric patients (<18 years, with no biologic treatment in the preceding 12 months) were included if they initiated ETN during the selection period Jan 2008–Jan 2016). Disease indications were inferred through patient drug history. Analyses of ETN doses and co-treatments were conducted in patients <17 years at index and with no missing data or drug histories indicative of conditions other than JIA, AS, or psoriatic arthritis (PSA). Weekly ETN dose was estimated for patients who completed 12 month continuous ETN therapy (7 x [mg dispensed/days between claims]). Co-treatments were captured for the 6 months preceding and 12 months following index. Drug costs of ETN (manufacturing plus wholesale and pharmacy mark-up) were estimated for all those <18 years who initiated ETN therapy.

**Results:** The study identified 391 patients <18 years old who initiated ETN and who had not received treatment with a biologic in the preceding 12 months. From this group 330 patients provided data for the evaluation of ETN doses and co-treatments (67% female, 39% aged 10–14 years). The majority were from Quebec (36%) or Ontario (33%), insured on PDP (87%). Drug history was consistent with JIA (96%), PSA (3%), and AS (1%). Among the 316 patients who completed 12 months of continuous ETN therapy, the average weekly ETN dose was 31 mg (range 29–35 mg), but varied with age. Overall, 103 of 330 patients (31%) used methotrexate (MTX) before initiating ETN, with 85/103 (83%) continuing this through the first 12 months of treatment; 28% of patients (n=92) used prednisone (PRD) before initiating ETN, with 46/92 (50%) continuing PRD during the first 12 months of ETN treatment. In patients continuing co-treatment, weekly dosages were significantly reduced ( $p \leq 0.008$  by paired *t*-test; figure 1). The average yearly cost of ETN among the 330 paediatric patients indexed was \$13 671 (Canadian \$ per year).



**Abstract THU0588 – Figure 1** Average. dose of methotrexate or prednisone pre- and post-initiation of etanercept in paediatric patients with continuing co-treatment

**Conclusions:** This evaluation of Canadian claims data demonstrated that less than a third of paediatric patients initiating ETN were co-treated with MTX or PRD. Many patients discontinued their co-therapies, and among those who continued therapy with these agents, weekly dosages of MTX or PRD were significantly lower within the first year of initiating treatment with ETN.

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**THU0589 PHYSICAL ACTIVITY IN CHILDREN AND ADOLESCENTS WITH JUVENILE IDIOPATHIC ARTHRITIS**

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**Background:** Juvenile Idiopathic Arthritis (JIA) is the most common rheumatic disease of childhood which may cause physical dysfunction and inactive sedentary lifestyle. Physical activity (PA), known to maintain optimal metabolic function and normal development could be impaired during JIA.

**Objectives:** The aim of this study was to assess PA in children and adolescents with JIA compared with a healthy population and to analyse associations between PA, functional ability and disease activity.

**Methods:** This is a cross-sectional study including patients with JIA (ILAR criteria) and age and gender-matched healthy Tunisian schoolchildren. Disease activity was evaluated by Juvenile Arthritis Disease Activity Score (JADAS) and functional ability by the Childhood Health Assessment Questionnaire (CHAQ). PA was assessed by children's physical activity questionnaire (CPAQ) for children and for adolescents (APAQ) and expressed as physical activity level (PAL). Moderate to vigorous PA (MVPA) (hours/day) and sedentary time (hours/day) were determined.

**Results:** A total of 55 patients (38 boys and 17 girls) with JIA and 60 healthy schoolchildren were included. No significant differences for age, height, weight, and body mass index between JIA patients and controls were observed. A quarter of children lived in poor socio-economic conditions. Subtypes of JIA were: oligoarticular (52.7%), rheumatoid factor-negative (16.3%) or positive (10.9%) polyarthritis, systemic JIA (9%), and enthesitis-related arthritis (7.2%). The mean disease duration was 3.2 years.<sup>2-6</sup> Twelve patients had active disease (21.8%), 25 patients had inactive disease (45.4%) and 18 patients were in remission (32.7%). The mean average of CHAQ was 0.98. Seventy six percent of the JIA group spent most of the time (average of 15 hours/week) on the two lowest categories: sleeping and sitting compared with the control group (average of 8 hours/week). Only 11 children with JIA (20%) played sport regularly with an average of 40 minutes/week which was significantly lower compared with controls (120 minutes/week;  $p=0.01$ ). Children with JIA spent less time in MVPA compared with the control group ( $0.5\pm 0.6$  versus  $1.9\pm 0.9$  hours/day;  $p<0.01$ ). Only 34.5% of JIA patients met public health recommendations to perform  $\geq 1$  hour daily MVPA compared with 66.6% in the control group ( $p<0.01$ ). No associations were found between PA level, disease duration and disease activity. However, lower PAL in children with JIA was significantly associated with young age ( $p=0.03$ ), worse well-being ( $p=0.01$ ) and CHAQ  $>1$  ( $p<0.001$ ). A higher CHAQ score was associated with less time spend in MVPA ( $p<0.001$ ) and poor willingness to practice PA ( $p=0.001$ ). Sedentary time was associated with higher body mass index ( $p=0.02$ ).

**Conclusions:** In our study, children and adolescents with JIA were less physically active than the healthy peers and less active than recommended for general health. This population needs more attention in achieving normal PA.

**Disclosure of Interest:** None declared

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**THU0590 THE ROLE OF STAT4 RS7574865 G/T AND IFR5 RS2004640 G/T GENE POLYMORPHISM IN JUVENILE IDIOPATHIC ARTHRITIS SUSCEPTIBILITY AMONG RUSSIAN PAEDIATRIC POPULATION**

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**Background:** Juvenile idiopathic arthritis (JIA) is the common chronic condition in paediatric population aged under 16 y.o. JIA is an autoimmune disorder with the potential contribution from genetic factors and environmental exposures. Signal transduction and activation of transcription 4 (STAT4) gene and interferon regulatory factor 5 (IRF5) are the common set of susceptibility genes in many autoimmune disorders.

**Objectives:** To study STAT4 rs7574865 G/T and IFR5 rs2004640G/T gene polymorphisms impact on JIA susceptibility among Russian children.

**Methods:** The study included 177 subjects, 66 JIA cases and 111 healthy volunteers (the control group). Mean age of JIA patients was  $11.7\pm 4.2$  y (3–17 y), mean disease duration was  $4.8\pm 3.8$  y. All JIA patients were on the record at V. A. Nasonova Research Institute of Rheumatology, meeting ILAR-2001 criteria for JIA diagnosis. JIA group was comprised of 30 (45%) patients with oligoarthritis (oligo-JIA), 20 (30%) patients with polyarthritis (poly-JIA) and 16 (24%) patients with systemic onset arthritis (SoJIA). Oligo-JIA subgroup included 20 (67%) HLA-B27-seropositive patients (JIA-B27), and 10 (34%) patients with anterior uveitis (JIA-uveitis). The variables used for patients classification were: sex (44 girls and 22 boys); disease duration:  $\leq 4$  years - 34 (51%) patients and  $>4$  years - 32 (49%) patients; the number of joints involved:  $\leq 4$  - 29 (44.0%) and  $>4$  - 37 (56.0%);

positive antibody titers to nuclear antigens (ANA) - 26 (39%) patients. STAT4 and IFR5 genes polymorphism was studied using real time PCR.

**Results:** There was no significant difference between JIA and healthy volunteers in the incidence of various genotypes and alleles in the studied range of polymorphisms. The only significant difference was found between the rates of T STAT4 allele in oligo-JIA group and T allele in the control group (38% and 20.4%, respectively,  $p=0.006$ ). Similar differences with the controls in T allele rates were observed in JIA-B27 and JIA-uveitis subgroups (35% and 45% vs 20.4%  $p=0.044$  and  $p=0.021$ , respectively). Therefore, carriers of T STAT4 allele demonstrate high JIA susceptibility as compared to healthy subjects (OR 2.43 95% CI (1.23–4.70),  $p=0.007$ ). The risk in JIA-B27 and JIA-uveitis was (OR 2.10 95% CI (0.38–4.60),  $p=0.070$  and OR 3.19 95% CI (1.09–9.06),  $p=0.021$ , respectively). There was no specific association between studied gene polymorphisms and increased JIA susceptibility depending on sex, disease duration, number of joints involved and ANA status.

**Conclusions:** Obtained data confirm the specific role of STAT4 rs7574865 G/T polymorphism as the susceptibility factor to oligo-JIA associated with uveitis, HLA-B27 in Russian paediatric population.

**Disclosure of Interest:** None declared

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**THU0591 SERUM 25 OH VITAMIN D IN PAEDIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS: IN RELATION TO DISEASE ACTIVITY, DURATION AND BONE MINERAL DENSITY**

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**Background:** Vitamin D has immunomodulatory effects and is commonly deficient in Paediatric SLE (pSLE) so associated with the disease activity and low bone density<sup>1,2</sup>

**Objectives:** To assess serum level of 25(OH)vitamin D in paediatric lupus patients and correlate it with disease activity, duration and bone density

**Methods:** A retrospective cohort study conducted on 90 patients with pSLE classified into three groups (30 patients in each) according to disease activity and duration. Group I (Initial active patients), group II (relapsing active patients) and group III (inactive patients), compared with 60 healthy children as controls (group IV). Disease and drugs duration, present steroid dose, medications' history and SLEADI for disease activity were evaluated. CBC, serum C3, C4, 24 hour urinary proteins, anti-dsDNA, Ca, P, PTH, 25(OH) D levels and lumbar spine BMD Z score were measured. Vitamin D levels were correlated with clinical, laboratory and radiological parameters.

**Results:** There were significant differences in mean 25(OH) D concentration between the patients' groups (I= $15.37\pm 5.72$ , II= $17.70\pm 4.88$ , III= $26.98\pm 6.59$  ng/ml) and controls= $35.90\pm 9.66$  ng/ml ( $p<0.05$ ), with significant difference between active groups (I, II) and inactive group III ( $p<0.05$ ). Lumbar spine Z-score was significantly different between groups (I:  $-0.39\pm 0.81$ , II:  $-1.58\pm 1.12$ , III:  $-0.99\pm 0.89$ , IV:  $0.58\pm 0.71$ ). There were significant negative correlations between serum 25(OH) D and SLEADI ( $r = -0.545$ ,  $p = 0.001$ ), steroid dose ( $r = -0.561$ ,  $p = 0.001$ ), anti-dsDNA ( $r = -0.685$ ,  $p = 0.006$ ), 24 hr-proteinuria ( $r = -0.738$ ,  $p = 0.001$ ) and PTH ( $r = -0.335$ ,  $p = 0.001$ ), significant positive correlations between 25(OH) D and C3 ( $r = 0.617$ ,  $p = 0.001$ ), C4 ( $r = 0.544$ ,  $p = 0.001$ ) and serum Ca ( $r = 0.424$ ,  $p = 0.001$ ) with non-significant correlations between 25(OH) D and disease duration, steroids' duration, serum P and Z scores ( $p>0.05$ ).

**Abstract THU0591 – Table 1.** different correlations in this study

Pearson Correlation	25(OH) Vit D	
	(r)	(P value)
SLEADI	-0.545	0.001*
Steroid dose	-0.561	0.001*
Anti-dsDNA	-0.685	0.006*
24 hr-proteinuria	-0.738	0.001*
PTH	-0.335	0.001*
C3	0.617	0.001*
C4	0.544	0.001*
Ca	0.424	0.001*
Disease duration	-0.215	0.080
Steroid duration	-0.089	0.363
Z-score	0.084	0.431
P	0.154	0.092

**Conclusions:** Vitamin D deficiency is common in pSLE and is considered a risk factor for the disease occurrence as it is correlated significantly with the disease activity not duration.

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**Disclosure of Interest:** None declared

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**THU0592** PUBERTAL DELAY DESPITE INTENSIVE TREATMENT OF JUVENILE IDIOPATHIC ARTHRITIS: RESULTS OF A LONGITUDINAL STUDY

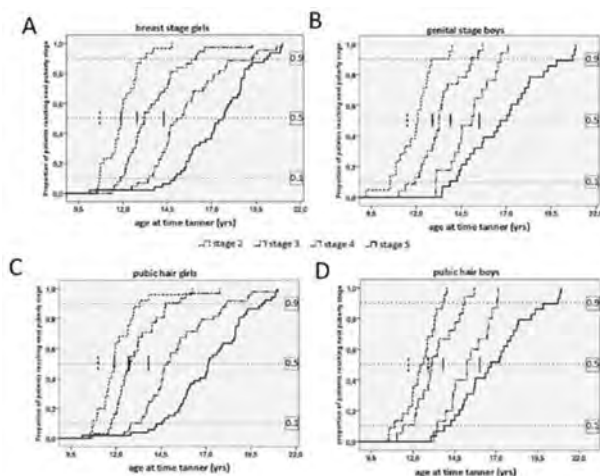
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**Background:** Delayed puberty and reduced adult height have been reported in JIA before the era of biologicals. Long-term consequences of delayed puberty are among others growth disturbances, low bone mineral mass and decreased fertility. Treatment with anti-TNF restores growth, but data on puberty are unknown

**Objectives:** We evaluated onset and course of puberty and growth, in JIA-patients who are treated intensively, including the possibility of biologicals, and identified variables related with puberty and growth

**Methods:** In a longitudinal JIA-cohort, all consecutive patients (10–21 years) were followed for three years. Annual examinations were performed regarding demographic and disease-related items as well as Tanner pubertal stages and anthropometric measurements. Median ages at reaching each stage were estimated by Kaplan-Meier curves. Parametric tests were used to determine differences between patients and healthy controls, non-parametric tests between patient-groups. Univariate analyses and mixed models were used to identify associated variables

**Results:** 138 patients were included (66% girls). Median disease-duration was 7,8 years (IQR 3.7–10.5), median JADAS-27 3,7 (IQR 1,3–8,0), DAS-28 2,16.<sup>1,5–2,8</sup> Puberty onset was 1,2 years delayed in girls (p<0,01), in boys 0,6 years (ns). The progression was also delayed: end-stage (Tanner-5) in girls was 3,3 years delayed (p<0,01), in boys 1,7 years (p<0,01). A positive association was found for longer disease-duration and a lower BMI. Biological-use was not associated. Both for girls and boys, standardised height was not different at the onset and at the end of puberty



**Abstract THU0592 – Figure 1** Vertical. lines indicate median age of healthy population of Tanner stages

**Conclusions:** In contrast to normalised longitudinal growth, we found in JIA-patients in disease remission or with low disease activity a delayed onset and progression of puberty despite intensive treatment including biologicals. Eventually, puberty was completed and normal adult height was reached. The effects on bone mass and fertility will have to be evaluated in cohort studies

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Statistical support was provided by Reinier Timman and Kees A.G.M.van Montfort, department of biostatistics, Erasmus University Rotterdam.

**Disclosure of Interest:** None declared

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**THU0593** MULTICENTRIC OSTEOLYSIS WITH NODULOSIS AND ARTHROPATHY (MONA): REPORT OF THE FIRST LEBANESE FAMILY

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**Background:** “Multicentric Osteolysis with Nodulosis and Arthropathy” (MONA) also known as Winchester-Torg syndrome is a rare chronic skeleton disorder caused by matrix metalloproteinase 2 (MMP2) deficiency. It is characterised by facial dysmorphism, subcutaneous fibrocollagenous nodules, carpal and tarsal osteolysis and interphalangeal joint erosions. Short stature and Osteopenia are frequent and heart defects have been described. As children first present with joint pain, swelling and stiffness, MONA is often misdiagnosed as Juvenile Idiopathic Arthritis (JIA).

**Objectives:** We report the first Lebanese family with 3 siblings presenting MONA, two of which were diagnosed at first as JIA.

**Methods:** The proband is the eldest boy born of consanguineous parents. At birth, a ventricular septal defect (VSD) was noted. At the age of 5 bone erosions and nodules in his hands and feet, and cuneiform vertebrae of unknown cause appeared. He was diagnosed with JIA. His pain partially improved with methotrexate and TNF agonist treatment; steroid injections were performed in wrists and permitted a gain in range of motion. Secondly, Osteopenia was detected.

The middle boy was examined at the age of 7; he had wrist arthritis and metacarpal tenosynovitis. He was known to have psoriasis. He was treated first with steroid injections then with NSAID and methotrexate with a good response but his condition slowly progressed to deviated fingers.

The youngest boy suffered from foot pain and Kohler disease was diagnosed at the age of 4. Soon after he developed global stiffness of the foot with erosions and nodules. He had failure to thrive and a VSD was detected.

**Results:** This family history along with the progressive coarsening of face features in the 3 siblings raised the possibility of a genetic disorder. Exome sequencing for skeletal dysplasia in the eldest boy detected a mutation in the MMP2 gene (NM\_001127891:exon2:c.8A>G:p.Y3C). The same mutation was found in the 2 other siblings.



**Conclusions:** These cases are to add to the 44 individuals coming from 27 different families, with molecularly proven MONA reported in the medical literature. This diagnosis should be raised in front of patients having resistant articular erosions with hand and feet nodules, despite anti-rheumatic drugs. Till date, no specific therapy is available and management is only supportive. In this described family, steroid injections were efficient when children presented with swelling and stiffness of joints and seemed to slow progression to erosion.

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**THU0594 SHIARI-JAVADI CRITERIA FOR THE DIAGNOSIS OF GENERALISED JOINT HYPERMOBILITY IN CHILDREN**

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**Background:** Benign joint hypermobility syndrome (BJHS) is the occurrence of musculoskeletal symptoms in hypermobile individuals in the absence of systemic rheumatologic disease.<sup>1–3</sup> One of the most common criteria for the evaluation of generalised joint hypermobility is Beighton's criteria. However, Beighton criteria were designed for all ages not specifically for children group (according to the children physiological and growth characteristics). Inability to identify limited hypermobility, failure to differentiate generalised joint hypermobility from joint hypermobility syndrome and BJHS and the restrictions on the use of epidemiological studies are further limitations.<sup>4, 5</sup>

**Objectives:** Because of the disadvantages of the existing criteria and the high prevalence of generalised joint hypermobility in children, we decided to propose further modifications to Beighton criteria for the diagnosis of joint hypermobility.

**Methods:** A case-control study was designed with 200 participants from 3 to 16 years of age with 100 children with BJH (according to Beighton criteria) in case group and 100 age-sex matched children as control group. Cases were selected from outpatients Clinic of Rheumatology and the control group was selected from the emergency department of hospital. The case group consisted of children who had musculoskeletal pain complaints or were suspected to be hypermobile. The Beighton criteria were used as the gold standard, and all of cases fulfilled the Beighton criteria. In addition, the participants in the control group should be free of chronic disease or musculoskeletal complaints. For the determination of new criteria we performed literature review on the range of motion in different age and gender paediatric groups, studied the various existing criteria and their differences, and utilised our own clinical observations. Eight manoeuvres were set for examination (Fig 1). All were bilateral, except the neck hyperextension.

**Results:** There were 42 (42%) male children in each group. The mean age was 6.8 years. Table 2 compares the results of the new and Beighton criteria in both cases and controls. All cases were hypermobile, and two of the 100 controls were hypermobile with the new criteria. Based on these results, new proposed criteria had the sensitivity, specificity, positive predictive value and negative predictive value of 100%, 98%, 100% and 98% respectively.



**Conclusions:** Shiri-Javadi criteria appears to be useful for detecting hypermobility. In addition, they have also overcome many of the disadvantages of the Beighton criteria, and are easier, more practical and more comprehensive to be used in children. However, further studies are required to validate this criteria.

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**THU0595 CLINICAL AND THERAPEUTICAL DIFFERENCES BETWEEN ADULTS AND CHILDREN IN A COLOMBIAN COHORT WITH INFLAMMATORY IDIOPATHIC MYOPATHY**

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**Background:** Age-related autoimmunity is a key differentiating factor with diverse presentations in different age groups possibly depending on immune regulatory mechanisms. Even patients with the same diagnostic category may have different presentations according to age and other factors. Inflammatory Idiopathic Myopathies (IIM) are not the exception with important clinical and prognostic differences between adults and children.

**Objectives:** To describe the clinical and therapeutical differences between adults and children (younger than 18 m years old) in a cohort with IIM

**Methods:** A cross-section retrospective research was done with data collected between 2014 and 2017 from a population diagnosed with IIM according to Peter and Bohan criteria and followed up for at least six months. Statistical association was evaluated by means of Chi-square and Fisher's tests.

**Results:** Out a total of 149 patients, 112 were adults and 37 were children. There was significant difference between the clinical presentation of symmetrical muscle weakness 98% in adults vs 73% in children (p: 0,0001), Gottron's papules 32% vs 89% (p: 0,0001), Heliotrope rash 31% vs 62% (p: 0,0016), Calcinosis cutis 1% vs 37% (p: 0,0001), Dermatological involvement 47% vs 94% (p: 0,0001), Myopathic changes in the electromyogram 41% vs 25% (p: 0,0001), and Myopathy proven biopsy 41% vs 25% (p: 0,0001). Therapeutical options showed a significant difference in the use of steroid therapy 93% vs. 84% (p: 0,045), Methotrexate (58% vs 91% p: 0,0001), Azatioprine (62% vs 27% p: 0,0002) and Cloroquine (31% vs 73% p: 0,0001). Other therapies like Cyclophosphamide (19% vs 5% p: 0,04) and Inmunoglobulins (23% vs 5% p: 0,01) were significantly different between adults and children.

**Abstract THU0595 – Table 1.** Clinical characteristics of Colombian Patients with Inflammatory Idiopathic Myopath (Adults and Children)

	Juvenile n=37		Adults n=112		p-value
	N	%	N	%	
Female	28	75,7	76	67,9	0,42
<b>Clinical characteristics</b>					
Symmetrical muscle weakness	27	73	110	98,2	<,0001
Gottron's papules	33	89,2	49	32,9	<,0001
Heliotrope rash	23	62,2	35	31,3	0,0016
Calcinosis cutis	14	37,8	2	1,8	<,0001
Dermatological involvement	35	94,6	53	47,3	<,0001
Myopathic changes (EMG)	9/23	39,1	68/81	84,0	<,0001
Biopsy-proven myopathy (Positive)	4/16	25	46/54	41,1	<,0001
ANA(+)	14/27	51,9	65/89	73,0	0,0580

EMG, electromyogram

**Conclusions:** Several differences in the clinical and therapeutical characteristics were found between adults and children with IIM. Adults had more frequently symmetrical weakness, myopathic changes in EMG and biopsy proven myopathy. In contrast children had higher skin involvement. Calcinosis constituted an important manifestation of IIM in children. These results suggest that paediatric IIM is a distinct sub-phenotype related to the early age at onset and possibly mediated by different immune interplay key factors.



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THU0596

### MEASUREMENT OF SERUM CALPROTECTIN MRP8/14 IN PAEDIATRIC PATIENTS DIAGNOSED WITH JUVENILE IDIOPATHIC ARTHRITIS AND AUTOINFLAMMATORY DISEASES

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**Background:** There is evidence of the correlation between serum levels of calprotectin MRP8/14 and disease activity in Juvenile Idiopathic Arthritis (JIA), but the same correlation with other rheumatic diseases in children such as autoinflammatory diseases has not been studied as much.

**Objectives:** To analyse calprotectin MRP8/14 in serum of patients with juvenile idiopathic arthritis (JIA) and various autoinflammatory diseases with different degrees of activity. To check if there is a correlation between serum MRP8/14 and disease activity.

**Methods:** Study in two phases: **1)** Initial, transversal, in JIA and/or autoinflammatory disease patients, determining serum MRP8/14 (by ELISA test) and collecting clinical data: number of active joints, Visual Analogue Scale parents/patients (VASp), VAS physician (VASph); and analytical: C-Reactive Protein (CRP) and white cells blood count (WBC) (among others). **2)** Second prospective phase, repeating the same analysis 3–6 months later. Disease activity was assessed by Juvenile Arthritis Disease Activity Score (JADAS) in AIJ; and by VASp, VASph and CRP in autoinflammatory diseases.

**Results:** The sample included 90 patients (25 males) between the ages of 1 and 21 years (median 11.1); 61 diagnosed with JIA (excluding systemic category), and 29 with different autoinflammatory diseases (including systemic JIA). 69 patients (20 males, with median age 11.2, 48 AIJ, 21 autoinflammatory) participated in the prospective phase. The main results are shown in table 1.

MRP=myeloid related proteins. JADAS=Juvenile arthritis disease activity score. ACJ=active joints count. VASm=visual analogue scale–physician. VASp=visual analogue scale–parents/patient. CRP=C reactive Protein.

**Conclusions:** In patients with non-systemic JIA, a positive correlation was found between serum MRP8/14 and JADAS, VASph, VASp, CRP, WBC, neutrophilia and (inversely) haemoglobin.

In autoinflammatory diseases positive correlation has been found with VASm, CRP, leukocytosis, neutrophilia, thrombocytosis and (inversely) haemoglobin. MRP8/14 seems to behave as a marker of activity in both JIA and autoinflammatory diseases, although with a stronger association in the latter.

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THU0597

### PULMONARY MANIFESTATIONS IN MIXED CONNECTIVE TISSUE DISEASE WITH JUVENILE AND ADULT ONSET – ARE THERE ANY DIFFERENCES?

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**Background:** Mixed connective tissue disease (MCTD) presents in childhood in 7%–23% of cases, but there is limited knowledge about the comparability of juvenile and adult onset of the disease. A common and serious manifestation is interstitial lung disease (ILD), possibly more common in adult MCTD according to a retrospective report<sup>1</sup>.

**Objectives:** To compare disease variables in juvenile and adult onset MCTD, particularly regarding pulmonary manifestations, after long-term follow-up.

**Methods:** Two cohorts consisting of, respectively, 52 patients with juvenile onset MCTD and 90 patients with adult onset MCTD from all regions of Norway were compared. Inclusion criteria were fulfilment of the Kasukawa- or the Alarcon-Segovia criteria. Patients with onset of symptoms before the age of 18 years were considered to have juvenile onset. All patients were clinically examined, including high resolution CT and pulmonary function tests.

**Results:** Mean age at examination was 28.0 (SD 10.3) in juvenile onset, and 54.3 (SD 13.0) in adult onset MCTD (p<0.001). Age at disease onset was 14.4 (SD4.4) and 37.9 (SD 15.1) years, respectively. Patient and disease characteristics are shown in table 1.

	Juvenile onset	Adult onset	p-value
Male gender, n (%)	8 (15)	28 (24)	0.192
Disease duration from symptom onset, mean (SD)	16.2 (10.3)	17.0 (8.9)	0.766
Anti-RNP levels, median (IQR)	180 (36.0–240.0)	44.0 (7.0–237.0)	0.002
ESR, median (IQR)	8.0 (5.0 to 16.0)	11.0 (7.0–18.5)	0.048
CRP, median (IQR)	0.7 (0.5–2.5)	2.0 (0.7–4.9)	<0.001
ILD, n (%)	14 (27)	39 (43)	0.051
ILD% of TLV, median (IQR)	4.0 (1.0–8.3)	5.0 (1.8–20.0)	0.258
ILD in >20% of TLV, n (%)	1 (2)	10 (11)	0.048
DLCO% pred, mean (SD)	73.0 (12.5)	72.0 (19.4)	0.598
FVC% pred, mean (SD)	89.2 (14.7)	89.2 (20.8)	0.711
FEV1% pred, mean (SD)	89.4 (13.7)	81.2 (20.0)	0.016

Juvenile patients had higher levels of anti-RNP, but lower ESR and CRP compared to adult onset patients. ILD was found in 27% of juvenile and 43% of adult patients (p=0.051), and more adult onset patients had ILD in >20% of total lung volume (TLV). Adult onset patients had lower forced expiratory volume in 1 s (FEV1), but similar diffusing capacity (DLCO) and forced vital capacity (FVC) as the juvenile patients.

**Conclusions:** ILD tended to be more frequent in patients with adult onset MCTD than in those with juvenile onset, although not statistically significant. More patients with adult onset had affection of >20% of TLV. Juvenile and adult patients

	JIA (n=61)		Autoinflammatory diseases (n=29)	
	1 st determination (n=61)	2nd determination (n=48)	1 st determination (n=29)	2nd determination (n=21)
JADAS	r=0.270* p=0.035	r=0.054 p=0.717		
ACJ	r=0.053 p=0.685	r=0.042 p=0.779		
VASph	r=0.308* p=0.016	r=0.041 p=0.784	r=0.304 p=0.108	r=0.622** p=0.003
VASp	r=0.329** p=0.010	r=-0.023 p=0.877	r=0.341 p=0.082	r=0.341 p=0.141
CRP	r=0.212 p=0.107	r=0.349* p=0.018	r=0.579** p=0.001	r=0.102 p=0.688
WBC	r=0.296* p=0.022	r=-0.071 p=0.633	r=0.749** p=0.000	r=0.693** p=0.000
Neutrophiles	r=0.389** p=0.002	r=0.421** p=0.002	r=0.281 p=0.140	r=0.710** p=0.000
Haemoglobin	r=-0.255* p=0.049	r=-0.023 p=0.828	r=-0.454* p=0.013	r=-0.552** p=0.009
Platelets	r=-0.033 p=0.802	r=0.001 p=0.993	r=0.659** p=0.000	r=0.208 p=0.366

with similar disease duration had comparable degree of ILD. Juvenile MCTD patients showed higher levels of anti-RNP, but lower ESR and CRP than patients with adult MCTD.

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THU0598

#### SAFETY OF TOCILIZUMAB IN PATIENTS AGED <2 YEARS WITH ACTIVE SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS TREATED FOR ONE YEAR

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**Background:** Intravenous (IV) tocilizumab (TCZ) was approved in the, US (2011), EU (2013) and other countries for the treatment of systemic juvenile idiopathic arthritis (sJIA) patients (pts) ≥2 years of age, based on a phase 3 study WA18221.<sup>1</sup> US Food and Drug Administration approval resulted in postmarketing requirement to investigate TCZ in pts with sJIA <2 years of age (study NP25737; ClinicalTrials.gov, NCT01455701). Results from the 12 week main evaluation period (MEP) have been reported.<sup>2</sup>

**Objectives:** Report safety results after completion of the optional extension period (OEP) of NP25737 (until 52 weeks from baseline or 2 years of age, whichever was longer).

**Methods:** NP25737 was a multicenter, open-label, single-arm study to evaluate the pharmacokinetics and safety of IV TCZ, 12 mg/kg every 2 weeks, for 12 weeks in pts aged <2 years with active sJIA for ≥1 month who failed corticosteroid and nonsteroidal anti-inflammatory drug treatment and received stable background therapy during the MEP. After the 12 week MEP, pts could participate in the OEP and continue TCZ treatment (without requirement for stable background therapy). Cumulative adverse events (AEs) over the entire study period are reported.

**Results:** Seven of 11 pts enrolled in the MEP continued to the OEP and received ≥1 dose of TCZ. Over the entire study period (n=11), the median number of TCZ doses was 11 (range, 2–26) and the median duration of TCZ exposure was 22 weeks (range, 4–58). Most pts (10/11; 91%) had ≥1 AE; most were mild or moderate in intensity and unrelated to study drug. The most common AEs were upper respiratory tract infection (6/11 pts, 55%), hypersensitivity, neutropenia, rash, viral upper respiratory tract infection, and vomiting (each in 3/11 pts; 27%). Seven serious AEs occurred in 5 of 11 pts (46%): 2 in the OEP (transaminases increased and histiocytosis hematophagic), 3 in the MEP (3 hypersensitivity events), and 2 in the safety follow-up of the MEP (sJIA flare and hand-foot-and-mouth disease). AEs leading to dose modification occurred in 5 of 11 pts (1 in the MEP, 4 in the OEP) mostly because of infections, neutropenia, and elevated liver enzymes, all mild or moderate in intensity. AEs leading to withdrawal occurred in 5 of 11 pts (46%): 1 in the OEP because of serious increased transaminases, 3 in the MEP because of serious hypersensitivity reactions to TCZ, and 1 in the MEP because of thrombocytopenia. No deaths were reported during the study. AE rates per 100 pt-years of exposure are reported in the table 1.

Abstract THU0598 – Table 1. Rates of AEs

Table: Rates of AEs	TCZ 12 mg/kg IV Every 2 Weeks		
	Main Evaluation Period n = 11	Optional Extension Period n = 7	Entire Study Period n = 11
Total patient-years at risk	2.3	8.1	7.4
Number of events (AE rate per 100 patient-years at risk)			
Ave. AE	32 (1396.5)	47 (579.3)	79 (1072.7)
Serious AE	5 (216.3)	3 (370.4)	7 (945.1)
AE with fatal outcome	0	0	0
AE leading to withdrawal	4 (174.0)	1 (119.7)	5 (67.9)
AE leading to dose interruption	1 (43.6)	12 (146.5)	13 (176.5)

**Conclusions:** During the OEP of the study, long-term treatment with TCZ was well tolerated in sJIA pts aged <2 years, and no additional safety signals were reported in the OEP beyond those reported in the MEP or observed previously for pts with sJIA aged ≥2 years.

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THU0599

#### EVALUATION OF EFFICACY AND SAFETY OF CANAKINUMAB IN JAPANESE PATIENTS WITH SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS IN PHASE III CLINICAL TRIAL, COMPOSED PREDOMINANTLY OF PATIENTS WITH PRIOR USE OF TOCILIZUMAB

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**Background:** Systemic juvenile idiopathic arthritis (SJIA) is a distinct form of juvenile idiopathic arthritis (JIA), accounting for approximately 4% to 17% of JIA<sup>1</sup>. In Japan, a higher frequency of SJIA, 41.7% of JIA<sup>2</sup> has been reported compared to Europe and United States. Tocilizumab (TCZ) is the only approved biologic for SJIA treatment in Japan. However, some patients (pts) demonstrate persistently high disease activity and/or drug intolerance. Therefore, new treatment options are required. Here, we evaluated the efficacy and safety of canakinumab (CAN), a human anti-interleukin-1β monoclonal antibody, in Japanese SJIA pts.

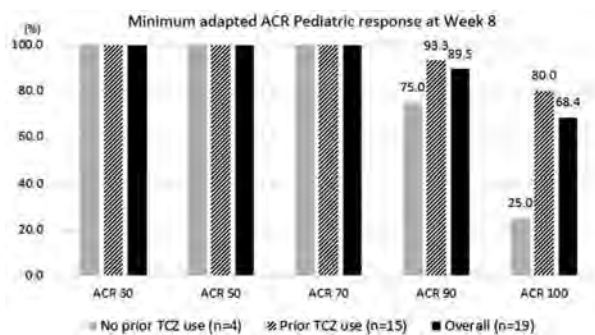
**Objectives:** To report the results of a 28 week (Wk) interim whole analysis of Phase III data (NCT02396212) of CAN, and the subgroup analysis of pts with or without prior use of TCZ.

**Methods:** Patients (age ≥2-<20 years) received open-labelled CAN 4 mg/kg (max 300 mg) every 4Wks (q4w) subcutaneously (s.c.). The primary objective was to evaluate the proportion of pts who achieved 30% improvement from baseline of adapted ACR Paediatric criteria (aACR 30) at Wk8 and who achieved corticosteroid tapering at Wk28. Steroid reduction was allowed from Wk8. We also analysed the data with or without prior use of TCZ.

**Results:** The trial enrolled 19 pts who had insufficient response to prior treatment; the majority (15/19, 78.9%) had received TCZ (table 1). Of the 19 pts, 3 discontinued CAN due to lack of efficacy or adverse events (AE) by Wk28 and 16 completed the assessment of Wk28. All pts (19/19) achieved aACR 30/50/70 at Wk8 (figure 1). Overall, 73.7% (14/19) pts achieved corticosteroid tapering at Wk28 and 2 pts (10.5%) achieved "steroid free". Of 15 pts with prior use of TCZ, 12 pts (80.0%) achieved aACR 100 at Wk8 and 11 pts (73.7%) achieved corticosteroid tapering (26.3%, 5/19). Serious AE (SAE) was seen in 41.1% (8/19) pts, and the most frequent SAE was JIA (flare or worsening of SJIA, 21.1%, 4/19). One macrophage activation syndrome (MAS) but no death was reported.

Abstract THU0599 – Table 1. Patient Characteristics

Characteristic	G1301 trial n=19
Male (%)	6 (31.6)
Age (mean)	9.9
BMI (kg/m <sup>2</sup> ) (mean)	19.59
Time from SJIA diagnosis to study entry (years) (mean)	6.1
CRP at baseline (standardised in mg/L) (mean)	357.79
Oral prednisone equivalent dose (mg/kg/day) (mean)	0.309
Oral steroid use at baseline - n(%)	19 (100)
Number of active joints (mean)	6.3
Number of joints with limitation of motion (mean)	4.4
Prior use of tocilizumab (%)	15 (78.9)



**Abstract THU0599** – Figure 1 Efficacy of canakinumab with adapted ACR Paediatric criteria in SJA patients with/without prior use of tocilizumab (TCZ)

**Conclusions:** CAN 4 mg/kg q4w s.c. provided improvement in disease activity and a reduction of oral steroid dose in Japanese SJA pts, including those who were not well-controlled with TCZ. No new safety concerns were reported.

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THU0600

#### HIGH VACCINE COVERAGE RATES ARE NOT ENOUGH: VACCINATION DELAY AND RISK FOR VACCINE-PREVENTABLE DISEASES IN PAEDIATRIC PATIENTS WITH RHEUMATIC DISEASES WITH AND WITHOUT IMMUNOSUPPRESSIVE THERAPY

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**Background:** Paediatric patients with rheumatic diseases (PedRD) are more susceptible to invasive infectious diseases, due to their underlying disease, high disease activity and immunosuppressive therapy (IT).<sup>1,2</sup> In Switzerland, specially indicated (SI) vaccinations for PedRD patients against pneumococcus, varicella zoster, hepatitis B, influenza and human papilloma virus should be administered as early as possible. On-time and complete coverage reduces the risk of vaccine-preventable infections<sup>3</sup> and its associated morbidity. Information about on-time vaccination is scarce, especially in PedRD patients.

**Objectives:** To assess the relationship of vaccine coverage and on-time vaccination in PedRD patients in Switzerland with and without IT.

**Methods:** Multicenter retrospective prevalence study based on the Juvenile Inflammatory Rheumatism (JIR) cohort, an international registry for rheumatic diseases. Patients treated in Swiss paediatric rheumatology centres (Basel, Geneva, Lausanne, Lucerne, Zurich) were included. Vaccine coverage and timeliness of administered vaccines were assessed for routine and for SI vaccinations according to the Swiss Federal Office of Public Health.

**Results:** 239 patients were included. 93 (39%) received IT during a median observation period of 2.7 years (IQR 1.1–5.4). Median age was 6.7 years (IQR 2.9–10.3) at diagnosis, 10.9 years (IQR 7–14.3) at reference date (12th April 2016). At diagnosis, 185 patients (77%) had complete routine vaccine coverage; 76 (32%) fulfilled Swiss on-time immunisation criteria. At reference date, the routine vaccine coverage rate decreased to 74% with on-time vaccination achieved in 29% of PedRD patients without IT and in 23% with IT, respectively. Completeness of SI vaccinations was documented in 19 PedRD patients (13%) without IT and 6 patients (6.5%) with IT. On-time vaccination for SI vaccination was fulfilled in 7 patients without IT; no patient with IT was vaccinated on-time. Only 23 (9.6%)

patients showed complete and thereof 4 (1.6%) on-time vaccination status for routine and SI vaccinations.

**Conclusions:** Despite moderate to high routine vaccination coverage in Switzerland, vaccinations particularly recommended for PedRD patients to prevent from complications, are incompletely administered. Moreover, the high frequency of delayed vaccination implicates a potential increase of vaccine-preventable disease. Close surveillance of vaccination status improves standard of care for this susceptible population.

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THU0601

#### CARRIER RATE OF FAMILIAL MEDITERRANEAN GENE (MEFV) MUTATION IN PARENTS OF CHILDREN WITH FAMILIAL MEDITERRANEAN FEVER

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**Background:** Familial Mediterranean Fever (FMF) is one of the most prevalent periodic fever syndromes, MEFV, the responsible gene for the disease is in the short arm of chromosome 16. In the considerable count of the FMF patients, only one mutation is found in the MEFV, and parents who was the obligatory carriers for that mutation, were asymptomatic.

**Objectives:** The aim of this study was to evaluate these asymptomatic parents in regard to mutation in MEFV gene and similarity between parents and offspring patients.

**Methods:** In this cross sectional study, asymptomatic parents of FMF patients enrolled the study, which were referred to periodic fever clinic or paediatric rheumatology clinic of Tehran University of medical sciences. The patients should have at least one mutation in MEFV gene and none of them had any family history of auto inflammatory disease. Twelve mutations in MEFV gene was assessed in the parents by Vienna Lab FMF Strip Assay kit by MAS PCR/Reverses hybridization.

**Results:** Forty three patients and their parents participated in the study. Sixty three percent<sup>27</sup> of patients were male. Onset of disease symptoms in 31 patients (72%) were before 4 years of old. Nine (21%) of the patients were homozygote, 16 (37%) compound heterozygote and 17 (40%) heterozygote for MEFV mutation, there was a case of complex alleles mutations (2%). M694V/M694V in 4 patients (9%) was the most homozygote genotype, M694V/R761H in 4 (9%) and E148Q in 7 (16%) were the most compound heterozygote and heterozygote genotype, respectively. M694V, M680I and E148Q were the most mutation in the parents. Overall, 41 patients, had mutations similar to their parents' mutation, except in 2, which parents had not mutation, but patient did.

**Conclusions:** It seems that occurrence of new mutations in offspring is not prevalent among FMF patients, and there are other reasons for different clinical presentation in similar mutation carriers. On the other hand, in ethnicities with high prevalence of FMF, new mutation in descendant may occurs, infrequently.

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THU0602

### TARGETING GENERATION Z: DEVELOPMENT AND VALIDATION OF AN ILLUSTRATED TRANSITION READINESS QUESTIONNAIRE FOR ADOLESCENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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**Objectives:** To develop, validate and implement a transition readiness assessment tool to be completed by adolescents living with juvenile idiopathic arthritis.

**Methods:** Cross sectional, quantitative multicenter study. Patients with juvenile idiopathic arthritis aged 14 years or older were included. The assessment tool, designed to be self-administered, is divided into 4 domains: medical, psychosocial, emotional/cognitive, and academic. The medical domain assesses managing medications, booking appointments, disease literacy, self-management, and organ screening. The psychosocial domain assesses the adolescents' understanding of information related to adult rights, talking to providers as well as child motivation. Emotional concerns related to transition, self-advocacy skills, and completion of a personal health record. The academic domain assesses whether the adolescent is meeting school graduation requirements, able to verbalise an educational/job training plan and on track with future planning (eg, completed required testing). Items within each domain have equal value (ie, each question on the checklist is worth 1 point) and the sum of points yields the quantifiable assessment of how well patients are performing in each area of their health. Assessment meetings occur monthly when eligible patients are discussed. The questions are supported with illustrations explaining every answer. The tool was available in both paper and electronic formats. The children were also asked to rate the comprehensibility of the questionnaire on 0–10 numeric VAS. Sociodemographic, clinical as well as motivation scores were recorded.

**Results:** A total of 104 patients participated. The majority of patients (95.8%) understood the questionnaire and completed it correctly, in self-administered modality. Mean comprehensibility score was 9.3±0.2. Mean completion time was 6.2 min, with little or no help (78%). Children from low income families or those who had lower education level for their age needed more help. Internal consistency (Cronbach's alpha) for each domain score were 0.872, 0.861, 0.892, and 0.884 respectively. Construct validity was demonstrated by testing different hypotheses ( $p < 0.01$ ).

**Conclusions:** The developed illustrated questionnaire was a valid, patient-centred questionnaire which can be used by the paediatricians/rheumatologists to assess the level of preparedness of adolescents with JIA during planning for adult transition. The questionnaire gives information regarding the adolescents' ability to make appointments, attend their consultations, understand their treatment and to develop other skills required for transition to adult care. The questionnaire can be used to identify aspects in which the adolescent need education or training to achieve independence in transition-relevant skills. The questionnaire can be used also to set goals for the achievement of skills that will help adolescents manage their health and health care into adulthood. Implementing the questionnaire in the standard practice has the potential to improve transition assessment and support as well as improve health outcomes during healthcare transition for adolescents with inflammatory arthritic conditions.

**Disclosure of Interest:** None declared

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THU0603

### DISEASE MODIFYING ANTI-RHEUMATIC DRUGS IN JUVENILE IDIOPATHIC ARTHRITIS: MOVING TOWARDS TARGETED INDIVIDUALISED TREATMENT STRATEGY

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**Background:** Despite the expansion in the number of medications available in the treatment of juvenile idiopathic arthritis (JIA), inter-individual variation in therapeutic response and drug-associated toxicities continue to be a major concern and has driven efforts towards individualised therapy. Recent advances in paediatric treatment strategies and guidelines, as well as innovative approaches to identify a priori predictors of drug response, hold the promise for an individualised approach to therapy that will yield the highest efficacy and safety potential for each JIA patient.

**Objectives:** To determine whether baseline demographic, clinical, articular, laboratory variables and adherence to therapy may act as predictors of good response to DMARDs therapy in JIA.

**Methods:** Patients with JIA treated with DMARDs (methotrexate (MTX), leflunomide (LEF) or combination of MTX and LEF) were recruited for this study. Juvenile arthritis disease activity score (JADAS-27) was calculated at 3, 6 and 12 months. Multivariate logistic regression analysis was used to identify predictors of good response according to JADAS-27 score, development of deformities and extra-articular manifestations (uveitis).

**Results:** A total of 114 children were included in this study. The majority of patients were females 91 (79.8%). Mean age was 11.97±3.26 years; mean age at disease onset was 8.19±3.46 years whereas mean disease duration was 3.68±2.89 years. The most common ILAR subtype was polyarthritis RF negative (50.9%), Polyarticular RF positive (21%), oligoarticular extended (14.9%), oligoarticular persistent (7.9%) and systemic type (5.3%). Over half of the patients were on MTX (55.3%), and (34.2%) were using combined MTX and LEF while (10.5%) of patients were on LEF monotherapy. Mean MTX dose was 12.9±3.4 mg/week, and mean LEF dose was 16.67±4.78 mg/day. Prevalence of positive RF was 24/114 (21.05%). Anti-nuclear antibody (ANA) was detected in 20/114 (17.5%) of patients. 10.5% of patients had chronic anterior uveitis. At baseline, joint deformities were present in (13.1%) of patients. After one-year follow up (45.6%) of patients achieved remission while (27.1%) reached a state of low disease activity. Multivariate logistic regression analysis revealed that the most important predictors of JADAS-27 remission/low disease activity status were: Short disease duration <6.1±0.4 months (OR 1.93), polyarticular disease subtype, Childhood Health Assessment Questionnaire (CHAQ) disability index <2.125 (OR 1.75), absence of joint damage/deformities (OR 1.92). A short duration of NSAIDs therapy (<3 months) before moving to MTX therapy as well as from MTX to combination of MTX and LEF therapy (<4 months) were associated with the targeted disease activity status (OR 1.76 and 1.95 respectively). Adherence to therapy was also a predictor of good response (OR 1.86). 15.4% of patients did not achieve the disease activity target and received biologic therapy.

**Conclusions:** The subgroup of JIA patients with polyarticular disease onset, shorter disease duration, rapid optimisation/escalation of DMARDs therapy as well as those who were adherent to therapy were significantly associated with a good response to DMARDs therapy.

**Disclosure of Interest:** None declared

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THU0604

### JUVENILE INFLAMMATORY ARTHRITIS: THE DEVELOPMENT AND VALIDATION OF AN ILLUSTRATED QUESTIONNAIRE TO MEASURE CHILDREN'S MOTIVATION

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**Background:** Self-determination theory (SDT) is a macro theory of human motivation and personality that concerns people's inherent growth tendencies and innate psychological needs. SDT is concerned with the motivation behind choices people make without external influence and interference. JIA disrupts a child's sense of normality and impairs his or her motivation capacity. Children with JIA have a sense of being misunderstood and stigmatised, and they feel perpetually caught between having hope and control over their bodies and overwhelming pain and despair. To increase their confidence and the ability to manage pain, children need ongoing information about treatments, lifestyle management, and active involvement in their own health decision making.

**Objectives:** To develop a questionnaire for evaluating the "motivation" amongst children living with inflammatory arthritic conditions and assess the psychometric properties of that measure.

**Methods:** Based on content analysis and semi structured group discussion as well as Rasch analysis, ten domains were identified and used as a frame for an expert consensus and patient focus groups. The questionnaire was developed including: 10-items scale (0–10 on VAS scale). A mean score is calculated across all items. The total score ranged from 0–10. Each item was supported by illustrations explaining both ends of the measure. The questionnaire was formatted, one copy for adolescents and another copy was directed for the parents of younger children. Construct validity was assessed by correlating the score of the questionnaire to disease activity scores (JADAS-27, SLEDAI-2K, ASDAS-CRP);

measures of functional disability, quality of life, patient self-helplessness measure as well as the patients' adherence to therapy. Reliability and comprehensibility and sensitivity to change were also assessed.

**Results:** The questionnaire was assessed in 71 children with JIA, 32 with enthesitis related arthritis and 34 with cSLE. Results revealed that the developed illustrated questionnaire mean score correlated significantly with disease activity measures: JADAS-27:  $r=-0.87$ ; ASDAS-CRP:  $r=-0.85$ , SLEDAI-2K:  $r=-0.86$  reflecting its validity. It also correlated significantly with the scores of functional disability:  $r=-0.89$ , QoL:  $r=-0.88$  as well as patient self-helplessness  $r=-0.91$ . The questionnaire was reliable (Cronbach's alpha 0.926 and had no misfitting items. The illustrations were well received and this was reflected on the questionnaire comprehensibility (9.5) and sensitivity to change ( $p<0.01$ ). The patient motivation score showed significant ( $p<0.01$ ) correlation with adherence to therapy.

**Conclusions:** The illustrated children motivation measure, is a patient-centred unidimensional scale that is valid, reliable and comprehensible. The measure has good psychometric properties indicating that it can be used at the individual child's level to tailor management and monitor changes in response to therapy. The illustrations enhanced the questionnaire perception by the children as well as the parents.

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#### THU0605 FACILITATING PATIENT CENTRED CARE: THE DEVELOPMENT OF ILLUSTRATED MULTIDIMENSIONAL PATIENT REPORTED OUTCOME MEASURE FOR CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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**Background:** The advances in paediatric rheumatology management have mandated a drastic change in the way children with juvenile arthritis are assessed and monitored. As a consequence, there has been a call for new outcome measures that reflect a more holistic approach to day to day standard management. Such an emphasis reflects contemporary views about the relation between mind and body, and acknowledges the critical link between physical and psychological health as well as adherence to therapy amongst the children living with inflammatory arthritis.

**Objectives:** To assess validity; reliability and responsiveness to change of an illustrated child/parent Multidimensional Patient Reported Outcome Measures questionnaire which can assess construct outcome measures of children with juvenile inflammatory arthritis.

**Methods:** 106 children with juvenile inflammatory arthritis were included in this work in a multicentre study. The questionnaire was developed by integrating information obtained from children living with JIA as well as their parents. The questionnaire included 5 main categories which are patient-centred: 1. Health related quality of life: functional ability (children health assessment questionnaire) and quality of life (10-items reflecting psychological, social, school and behavioural issues as well as the patient's own perception). 2. Disease activity measure: pain intensity, the child's overall well-being, measure of fatigue and morning stiffness using (0–10 numerical visual analogue scale), 3. self-reported joint tenderness and swelling. 4. Current medication, side effects as well as adherence to therapy (2 questions using 0–10 numerical visual analogue scale); 4. Comorbidities as well as 5. Patient motivation. All the items were supported by illustrations to explain the question and make it easier to understand. The questionnaire has parent and patient versions. The disease activity status was assessed using JADAS-27.

**Results:** The questionnaire was reliable as demonstrated by a high-standardised alpha (0.890–0.978). The questionnaire items correlated significantly ( $p<0.01$ ) with clinical parameters of disease activity. The patient reported tender joints correlated significantly with the physician's scores (0.842). Changes in functional disability, quality of life as well as the motivation score showed significant variation ( $p<0.01$ ) with diseases activity status in response to therapy. The illustrated PROMs questionnaire showed also a high degree of comprehensibility (9.6).

**Conclusions:** Integrating patient reported outcome measures into standard clinical practice is feasible and applicable. This version of illustrated multidimensional questionnaire was found to be valid and reliable. It provides informative quantitative measure for the disease activity core set data, and in the meantime, facilitates

assessing the children's health related quality of life measure, adherence to therapy, comorbidities as well as motivation on individual basis.

**Disclosure of Interest:** None declared

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THURSDAY, 14 JUNE 2018

#### Other orphan diseases

#### THU0606 EFFECT OF INTERLEUKIN-1 ANTAGONISTS ON THE QUALITY OF LIFE IN FAMILIAL MEDITERRANEAN FEVER PATIENTS

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**Background:** Familial Mediterranean Fever (FMF) is characterised by febrile inflammatory painful attacks of peritonitis, pleuritis, arthritis and erythema. Colchicine is the mainstay of treatment in FMF but about 10% of patients do not respond well to colchicine. IL-1 antagonists have been shown to be effective in the prevention of attacks in colchicine resistant FMF (crFMF) patients. Herein we investigated effect of these agents on quality of life of crFMF patients.

**Objectives:** to investigate effect of IL-1 antagonists on quality of life of crFMF patients.

**Methods:** Data is derived from Gazi FMF cohort which was established in year 2010. Since then data of patients with FMF who were diagnosed according to the Tel Hashomer criteria were registered. Co-morbidities, detailed attack characteristics, treatments, laboratory parameters and impact of FMF on their life in terms of quality of life were recorded. A retrospective cohort analysis was made from records of patients who were treated with IL-1 inhibitors. SF-36 form was filled before and 3 months after the IL-1 antagonist treatment. Wilcoxon test was used for the analyses and a p value equal or less than 0.05 is considered as statistically significant.

**Results:** there were 41 patients (24 women and 17 men). Anakinra was used in 33 patients and 8 patients received canakinumab. There was a statistically significant reduction in the frequency, severity and the duration of attacks after treatment with IL-1 antagonists ( $p<0.001$ , for each). A statistically significant improvement was observed in all domains of SF-36 (figure 1).

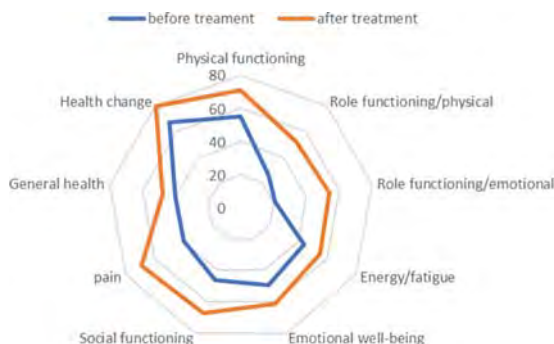


Figure. The change of SF-36 parameters before and after treatment

**Conclusions:** IL-1 inhibitor therapy reduces frequency, severity and duration of attacks and significantly improves the quality of life of crFMF patients.

**Disclosure of Interest:** None declared

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#### THU0607 AUTOINFLAMMATORY SYNDROMES: CLINICAL AND GENETIC CHARACTERISATION OF A COHORT OF ADULT PATIENTS IN A SINGLE REFERENCE CENTRE

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**Background:** Autoinflammatory syndromes are diseases that are characterised by increased inflammation mediated by cells and molecules of the innate immune system. Currently, new techniques have been developed that allow earlier diagnosis and treatment of these pathologies.

**Objectives:** Describe the clinical characteristics, genetic variants of different autoinflammatory diseases of a cohort of adult patients with follow-up in a 3rd level hospital

**Methods:** We carried out a descriptive cross-sectional study of adult patients with follow-up in reference hospital consultations with suspicion and/or diagnosis of autoinflammatory disease. Clinical, demographic, and treatment variables were characterised. A descriptive analysis was carried out by subgroup of pathology. The qualitative variables were expressed in frequency and percentages and the quantitative variables in median and interquartile range (IQR). The statistical software IBM SPSS v.18 was used for the analysis

**Results:** A total of 51 patients were included, 31 women (60.8%). Overall, the median age at diagnosis was 28 years (RI 15–40). The most used treatment was colchicine (60.8%), steroids (43.1%), FAMES (21.6%), anti IL-1 (17.6%). By subgroup of pathologies the most prevalent with 31 cases (60.78%), 16 women (51.6%) was familial Mediterranean fever (FMF) presenting 15 patients (48.4%) pathogenic mutations, 8 patients (25, 8%) low penetrance mutations and the rest (25.8%) genetic polymorphisms. The median age at diagnosis was 30.6 years (IQR16–44). The most common symptoms were fatigue (80.6%), acute phase reactants (APR) elevation (71%), fever and myalgias (67.7%), arthralgias (64%), abdominal pain (48.4%), rash (31%), arthritis (29%), lymphadenopathy (29%), serositis (12.9%)

With regard to TRAPS, 10 patients were diagnosed (19.6%), 7 women (70%), with a median age at diagnosis of 26.5 years (IQR 15–31.5). The most common symptoms were arthralgias, fatigue and myalgias (90%) with elevated APR, fever (80%), abdominal pain (70%), rash (60%) and arthritis (50%). There were 2 cases of women (4%) with Schnitzler syndrome, with arthritis symptoms, elevated APR and chest pain (in 1 case). There were 6 cases (11.8%) of disease associated with NOD 2 gene with a median age at diagnosis of 30 years (IQR 12.5–40), 4 were women (66.7%). The most common symptoms were arthralgias, fever and myalgias (83.3%) with increased APR, arthritis (66.7%), abdominal pain, oral thrush and rash (66.7%).

In the disease associated with NLRP12 gene there were 2 cases (3.9%), both cases were women. The most common symptoms were arthralgias, arthritis, fever, fatigue, increased APR and serositis (in one case). There was a case of sickness associated with the NLRP3 gene (cryopyrinopathy) (2%) in a woman with fever and refractory pyoderma gangrenosum and another woman with a diagnosis of Muckle-Wells (2%) with clinical signs of deafness since childhood, conjunctivitis, fever and arthritis. There was a case of PFAPA (2%) in a woman with fever, pharyngitis, rash and lymphadenopathy.

**Conclusions:** In our series, the most frequent pathology was FMF followed by TRAPS. The most prevalent symptoms were systemic manifestations (fever, fatigue, APR elevation) and musculoskeletal manifestations.

**Disclosure of Interest:** None declared

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THU0608

#### THE RELATIONSHIP BETWEEN SERUM SOLUBLE KLOTHO, FGF-23 LEVELS AND FLOW-MEDIATED DILATATION (FMD) IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER (FMF)

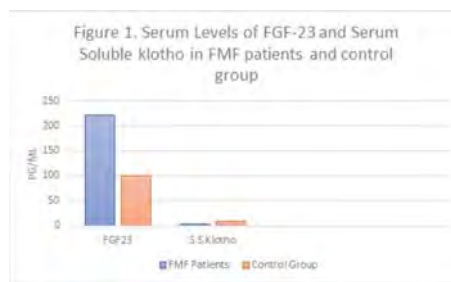
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**Background:** Familial Mediterranean fever (FMF) is a disease having inflammatory attacks.<sup>1</sup> Systemic inflammation has an important role in the etiology of endothelial dysfunction. Fibroblast Growth Factor 23 (FGF-23) is expressed by osteoblasts and needs serum soluble klotho. FGF-23 provides phosphate regulation. Increased FGF-23 is associated endothelial dysfunction.<sup>2</sup> An invasive way of measuring endothelial dysfunction is Flow-Mediated dilatation (FMD).<sup>3</sup>

**Objectives:** To investigate the possible relationship between FGF23, serum soluble klotho levels and FMD in patients with FMF and healthy subjects.

**Methods:** Between March 2017 - September 2017, sixty -FMF patients that following-up at Cumhuriyet University Medical Faculty Rheumatology-Internal Medicine Department and thirty healthy volunteers were included into the study. Blood samples were taken from all participants and serum soluble klotho, FGF23 values were measured. Clinical findings of all patients were recorded. Blood tests were examined by Elisa method in Cumhuriyet University Department of Biochemistry. FMD assessed by Doppler ultrasound in all participants.

**Results:** Mean serum FGF 23 level was measured as 221.01 pg/ml pg in FMF group and 99.4 pg/ml in healthy control (HC) group. There was statistically significant difference between two groups (p<0.05). The mean serum levels of serum soluble Klotho was measured as 3.0 pg/ml FMF group and 8.25 pg/ml in the HC group. There was statistically significant difference between the two groups (p<0.05) (figure 1). The mean percentage of FMD was measured as 10.1 in FMF group and 13.6 in the HC group. There was statistically significant difference between the two groups (p<0.05).



**Abstract THU0608 – Figure 1** Serum. Levels of FGF-23 and Serum Soluble klotho in FMF patients and control group

**Conclusions:** We found that high FGF 23 levels in FMF patients caused a significant decrease in FMD. In addition, FGF23 may be a parameter for the early diagnosis and prognosis of possible cardiovascular events showing significant change in FMD which demonstrates endothelial dysfunction indirectly.

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THU0609

#### CLINICAL CHARACTERISTICS AND OUTCOME OF SPANISH PATIENTS WITH ACUTE MYELITIS ASSOCIATED WITH AUTOIMMUNE DISEASES

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**Background:** Acute myelitis (AM) is a focal inflammatory disorder of the spinal cord characterised by motor, sensory, and autonomic dysfunctions that usually develop during a short period (several hours to days) and may resolve over several weeks to months. Acute has been reported as an unusual complication of autoimmune diseases (AD), mainly in systemic lupus erythematosus (SLE) and Sjögren's syndrome (SS).

**Objectives:** To analyse the frequency of concomitant AD in patients with patients with AM seen in a Spanish tertiary centre and to compare their clinical characteristics and outcome with those of AM patients without other AD.

**Methods:** We performed a retrospective study including all the patients diagnosed with AM in our centre between January 1989 and December 2017. Patients with previous history of spinal disease (multiple sclerosis [MS], compression, trauma, arteriovenous malformation, radiotherapy) and children were excluded. Demographics, clinical, laboratory, imaging, therapeutic and outcome data were obtained from their medical records.

**Results:** During the study period 144 cases of AM were identified, 76 of them had complete data and were analysed. Most of the patient were women (47, 62%), with a mean age at diagnosis 42±17 years. The main causes of AM in our series were MS (35%), AD (18%), postviral myelitis (9%) and idiopathic (34%). The AD diagnosed in these patients were: SLE,<sup>4</sup> SS,<sup>3</sup> undifferentiated connective tissue disease,<sup>2</sup> Graves' disease,<sup>1</sup> ulcerative colitis,<sup>1</sup> polymyalgia rheumatica,<sup>1</sup> cryoglobulinemic vasculitis<sup>1</sup> and sarcoidosis.<sup>1</sup> A patient with MS had concomitantly another AD (inflammatory myopathy). Most of the patients with AD (12, 80%) were diagnosed of these disorders before the AM episode (median 48 months, range: 24–120). No differences regarding to sex, age and anatomical extension of AM were detected between AD and non-AD patients. The recurrence of AM was more frequent in non-AD patients (7% vs 54%, p<0.001) and a tendency to less severe clinical course was found in AD patients (67% vs 41%, p=0.08).

**Conclusions:** AD were an important cause of AM in our series and this usually occurred after diagnose of AD, so it is important to consider AM when these patients develop neurological dysfunctions that suggest spinal cord damage. The outcome of AM seem to be better in patients with concomitant AD.



**Disclosure of Interest:** None declared  
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**THU0610** **SERUM CALPROTECTIN LEVELS IN BEHÇET'S DISEASE: RELATIONSHIPS BETWEEN DISEASE ACTIVITY AND CLINICAL PARAMETERS**

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**Background:** Behçet's disease (BD) is an inflammatory disease with chronic systemic vasculitis. The disease is characterised by attacks of oral and genital ulcers, skin lesions, arthritis, uveitis and deep vein thrombosis. The main histopathologic feature is known to be vascular inflammatory changes. Calprotectin is expressed by granulocytes, monocytes and endothelial cells, and produce an inflammatory response in human microvascular endothelial cells.

**Objectives:** The aim of this study was to evaluate serum calprotectin levels and their relationships with disease-related variables in patients with BD.

**Methods:** Forty-eight patients diagnosed with BD according to International Study Group of BD classification criteria and 22 demographically matched healthy control subjects participated in this study. Calprotectin levels were measured in blood samples from patients and controls. The disease durations of the patients were between 1 and 28 years. The Behçet's Disease Current Activity Form (BDCAF), that scores the history of clinical features presenting during four weeks prior to the day of assessment, and *Behçet's Syndrome Activity Scale (BSAS)* were used for the evaluation of disease activity.

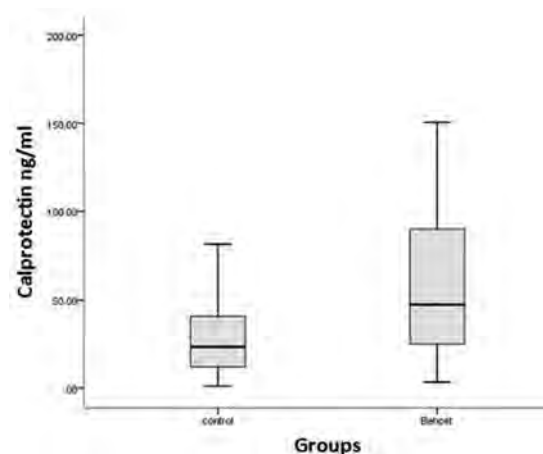
**Results:** Mean serum calprotectin levels were significantly higher in patients with BD compared to the control group (60.6±43.8, 37.6±37.5, respectively; p=0.037) (Figure 1). Distribution of age (years; 40.6±12.9, 46.6±11.4, respectively; p=0.075) and sex (male; 62.5%, 45.5%, respectively, p=0.191) between these groups were similar. In the comparison of the calprotectin levels of the patients with or without the components of BD, we found significantly higher levels of calprotectin in patients with oral and genital ulceration versus without these involvements (table 1). Since there were only 2 uveitis patients in this patient group, no calculations were made on uveitis. Serum calprotectin was significantly associated with BDCAF, BSAS, patient's impression of disease activity, clinician's impression of disease activity, ESR (Erythrocyte sedimentation rate) and CRP (C-reactive protein) (table 2).

**Abstract THU0610 – Table 1.** Comparison of calprotectin levels of patients with or without the components of disease activity

	(n)	Calprotectin (ng/ml)	P value
Oral ulceration	yes <sup>29</sup> no <sup>19</sup>	73.2±46.2	0.007
		41.4±32.3	
Genital ulceration	yes <sup>9</sup> no <sup>39</sup>	94.5±45.6	0.009
		52.8±40.0	
Erythema nodosum	yes <sup>5</sup> no <sup>43</sup>	82.9±45.1	0.23
		58.0±43.5	
Skin pustules	yes <sup>18</sup> no <sup>30</sup>	66.0±48.7	0.51
		57.3±41.1	
Arthritis	yes <sup>15</sup> no <sup>33</sup>	57.5±43.1	0.74
		62.1±44.7	
Vascular activation	yes <sup>9</sup> no <sup>39</sup>	59.5±52.3	0.93
		60.9±42.4	

**Abstract THU0610 – Table 2.** Correlation between calprotectin level and disease characteristics in patients with BD

	Calprotectin	p
BSAS	0.409	0.004
BDCAF	0.375	0.009
Patient's impression of disease activity	0.401	0.005
Clinician's impression of disease activity	0.385	0.007
ESR	0.440	0.002
CRP	0.312	0.031



**Abstract THU0610 – Figure 1** Serum calprotectin levels in BD and control groups

**Conclusions:** Our study demonstrated that serum calprotectin levels were significantly higher in patients with BD relative to the control group, and were significantly correlated with disease activity scores. The presence of a newly-developed genital and oral ulceration may be associated with higher levels of calprotectin. It can be concluded that serum calprotectin level seems to be useful marker to monitor disease activity in BD.

**Disclosure of Interest:** None declared

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**THU0611** **ANAKINRA TREATMENT IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER: A SINGLE-CENTRE EXPERIENCE**

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**Background:** Approximately 5 to 10% of FMF patients do not respond to colchicine treatment and/or intolerant to colchicine due to side effects. Several case reports and case series have pointed out the efficacy of IL-1 blockade in colchicine resistant FMF subgroup.

**Objectives:** To review the patients followed in our centre with FMF who received anakinra, an anti-IL-1 receptor antagonist, because of insufficient colchicine response.

**Methods:** FMF patients who were treated with anakinra were retrospectively reviewed with regard to indication, effect on disease activity and acute phase response, adverse events. Patient global assessment was recorded before and after anakinra treatment.

**Results:** There were 48 FMF patients with FMF who were treated with anakinra for various indications (colchicine resistant recurrent febrile attacks in 42, colchicine related side effects in 6). The mean age of the group was 31.8±9.2 years. The mean duration of the disease was 12.3±7.9 years. There were various co-existing pathologies among this study group like multiple sclerosis,<sup>1</sup> ankylosing spondylitis,<sup>1</sup> SLE,<sup>1</sup> Behçet's disease,<sup>1</sup> low grade lymphoma,<sup>1</sup> psoriasis,<sup>2</sup> vasculitis<sup>2</sup> and PAN.<sup>2</sup> The mean colchicine dose was 2,13±0,51 mg/d. The mean duration of anakinra treatment was 14.47±10.8 months. Twenty seven patients reported no attacks after anakinra treatment whereas 10 patients reported at least 50% decrease in the attack frequency. There are 4 patients who were primarily irresponsive to the therapy, whereas in 5 patients response to therapy ameliorated during the course of the treatment. Mean patient global assessment decreased from 8.58±1.2 to 2.72±3.16 under anakinra treatment (p=0.001). Four patients had severe allergic reactions (severe disseminated rash in 1 patient and severe injection site reaction in 3 patients) and therefore the drug was stopped. Two patients had infections (one had genital warts and urinary tract infection, the other had sinusitis and folliculitis) and the treatment was terminated.

One of our patients reported that her psoriatic lesions got worse on anakinra. Forty one patients reported no adverse events during the treatment.

**Conclusions:** Anakinra was effective in controlling the symptoms in colchicine-resistant FMF cases. It was also effective in FMF related amyloidosis. The major cause of treatment termination was injection site reactions. Anakinra seems to be an effective alternative in patients who have insufficient response to colchicine.

**Disclosure of Interest:** None declared

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#### THU0612 BONE SARCOIDOSIS: A RETROSPECTIVE MULTICENTER STUDY OF 27 CASES

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**Background:** Studies on bone involvement of sarcoidosis (BS) are scarce.

**Objectives:** To analyse in depth main features, treatments and follow up of patients presenting a BS.

**Methods:** Among 926 patients with a proved sarcoidosis from four tertiary hospitals in Paris (France) seen between 2000 and 2015, all cases of BS were retrospectively analysed for demography, clinical features, biological tests and imaging results. Inclusion criteria were a) a bone biopsy with epithelioid granuloma and no casein necrosis, or b) radiological evidence of BS, after exclusion of other diagnoses.

**Results:** 27 out 926 (2.9%) sarcoidosis patients fulfilled inclusion criteria for BS. Most patients were caucasian (56%), M/F sex ratio 1.5, 30% were active smokers, mean age at sarcoidosis diagnosis was 39±12 years and at BS diagnosis 43 ±11 years. Extra-osseous involvement of sarcoidosis was found in lymph nodes (93%), lungs (78%), skin (52%), CNS (33%), ENT (33%), and heart (19%). BS was symptomatic in 15/27 (56%) patients i.e. bone pain (15/15), local inflammation (5/15), bone deformation (3/15), arthritis (4/15), and myalgia (5/15). BS was never the revealing symptom of sarcoidosis. BS was more frequently symptomatic when it was a Perthes-Jüngling osteitis and an appendicular skeleton involvement.

On imaging exams, BS lesions were found at the spine skeleton alone (14/27, 52%), appendicular skeleton alone (10/27, 37%) or both (3/27, 11%). BS lesions had an aspect of pseudo-metastasis (59%), micro-cysts (Perthes-Jungling, 37%) or Paget disease (4%). Bone lesion was unique in 22% and 26% of patients had more than 10 lesions. When a bone biopsy was done it always confirmed the diagnosis (n=9); in all other cases extra-osseous biopsies confirmed the diagnosis of sarcoidosis.

Nine patients received a treatment for BS, i.e. prednisone (n=8, 0.25–1 mg/kg/day), hydroxychloroquine (n=8), and methotrexate (n=5). Response to treatment was complete (n=3), partial (n=4) or nul (n=2). Of note, 21 out of 27 patients received an immunosuppressant for a severe form of systemic sarcoidosis (n=11) or for a steroid-sparing effect (n=10). A relapse of BS was noted in 13 patients, with a mean number of relapse of 2.1–24. After a mean follow up of 49 months, BS was in complete remission (8/27, 30%), partial remission (16/27, 59%) or remained active (3/27, 11%).

**Conclusions:** Bone involvement remains a rare manifestation of sarcoidosis. It was symptomatic in 56% of patients, mainly when Perthes-Jüngling osteitis and appendicular skeleton involvement were present. Extra-osseous involvement of sarcoidosis were always present at the time of BS diagnosis. Treatment remains difficult with frequent relapses.

**Disclosure of Interest:** None declared

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#### THU0613 THE FREQUENCY AND CHARACTERISTICS OF HEADACHE IN BEHCET'S DISEASE AND ITS EVALUATION BY TRANSCRANIAL DOPPLER ULTRASONOGRAPHY

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**Background:** Behcet's disease (BD) is a multisystem vasculitic disease and the most often neurologic manifestation of BD is headache. Transcranial Doppler ultrasonography (TCD) is a test which used for evaluating the changes in blood flow velocity developed against visual stimulation. It is not well known TCD findings in BD patients who suffered from headache.

**Objectives:** To evaluate the frequency and the types of headache and to investigate cerebral reactivity by TCD in BD patients.

**Methods:** 113 patients with BD diagnosed based on diagnostic criteria of BD by ISG and 40 healthy individuals were included in the study. The patients with BD

who had neurological involvement were not included to the study. Headache type was specified by a specialist neurologist according to International classification of headache disorders society criteria. TCD was applied to 62 patients with BD and 40 healthy individuals. TCD results were evaluated by a specialist neurologist.

**Results:** Headache was determined in 89 (78.8%) patients with BD. It was statistically significant compared to HC group (60%, p<0.03). 48 of 89 BD patients had tension type of headache and 33 of them had migrainous type. No significant difference was found between BD patients and HC group in terms of cerebral reactivity by TCD. Low pulsatility index for both the right side and the left side were noted in BD patients suffering from headache compared to BD patients not having headache (p<0.006, p<0.003). No significant differences were found between tension type and migrainous type of headache in terms of TCD parameters.

**Conclusions:** Headache is common in BD patients, but cerebral reactivity is maintained.

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**Disclosure of Interest:** None declared

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#### THU0614 INTERSTITIAL LUNG DISEASE IN PATIENTS WITH ANTISYNTHEASE SYNDROME AND ANTI-RO52 ANTIBODIES POSITIVE

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**Background:** Antisynthetase syndrome (ASS) is characterised by the presence of myositis, arthritis, interstitial lung disease (ILD), fever, Raynaud's phenomenon and mechanical's hand, in the presence of antisynthetase autoantibodies (AA), the most frequent being anti-Jo1, anti-PL7 and anti-PL12. An association between ASS and anti-Ro52 with increased ILD has been described and it is believed that the presence of both antibodies is accompanied by a more severe ILD.

**Objectives:** To describe the clinical and analytical characteristics of a cohort of patients with ASS. To analyse the lung involvement in this type of patient and to determine the possible relationship between the different subtypes of ILD and the presence of anti-Ro52.

**Methods:** Retrospective descriptive study of patients treated in our Hospital (2006–2017), with AA and at least 2 clinical characteristics. The data was obtained through the review of medical records.

Variables analysed: age, sex, age, smoking, clinical presentation, diagnosis of ASS, associated neoplasia and paraneoplastic syndrome (PS) (neoplasia 3 years before or after the diagnosis of ASS), muscle enzymes (CK and aldolase), autoimmunity, glucocorticoids (GC), immunosuppressants (IS), diagnosis of ILD, HRCT pattern (High Resolution Computed Tomography) and respiratory function tests (RFT) at the beginning of ILD.

**Results:** We included 27 patients (20 women), mean age 61±13 years. 7.4% smokers and 18.5% ex-smokers. 88.8% were anti-Jo1, 7.4% anti-PL12% and 3.7% anti-PL7. Anti-Ro52 present in 18 patients. The most common clinical presentation: ILD 88% (59% had Ro52), followed by myositis 85% (40% are dermatomyositis), arthritis 81%, mechanic's hand 51%, fever 37% and Raynaud's phenomenon 25%. The classic triad (arthritis, myositis, ILD) was present in 16 patients. Three patients presented neoplasia in the course of the disease, being identified as PS. Elevation of CK in 70% and aldolase in 74%. 96% of patients have been treated with GC and IS.

The HRCT patterns were: non-specific interstitial pneumonia (NSIP) (66%), usual interstitial pneumonia (UIP) (29%), organised cryptogenic pneumonia (OP) (4%), baseline RFT were performed in 19 patients. Diagnosis of ASS and ILD, both entities appear at the same time in 6 patients, in 3 patients the ILD appears before and in 14 after. In these, the median duration (range) of the ASS until the diagnosis of ILD was 1 year (0–1).

There is no relationship between the HRCT and anti-Ro52 patterns (chi-square considering the exact distribution p=0.892), nor between the ILD and anti-Ro52 (Fisher exact test p=0.999).

**Conclusions:** Our results, in general, agree with what is published in the literature. Three patients have an uncommon presentation of ASS, with a diagnosis of ILD prior to myopathy (in most of the published cases, myositis precedes or coincides with the onset of ILD), and it is important to include ASS in the differential diagnosis of ILD. In our cohort, the association between ILD and anti-Ro52 has not been demonstrated, nor among the different subtypes of ILD to Ro52. Therefore, prospective studies with a greater number of patients are necessary to define Ro52's role in the development of ILD in ASS.

**Disclosure of Interest:** None declared

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**THU0615 IMMUNE RELATED ADVERSE EVENTS (IRAES) ASSOCIATED WITH CHECKPOINT INHIBITORS: 12 CASES FROM A SINGLE CENTRE**

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**Background:** Immune checkpoint inhibitors (ICI) have made a significant impact on the treatment of many advanced malignancies. There is little data on the rheumatologic complications of these treatments.

**Objectives:** We describe 12 cases of rheumatologic IRAEs following ICI treatment to further characterise the spectrum of disease and treatment responses.

**Methods:** We report patients evaluated in a general Rheumatology outpatient clinic from 2014 to 2017. Cases were defined as those with new rheumatologic symptoms following treatment with an ICI. Alternative explanations for the presenting syndrome were excluded clinically. Clinical data was extracted by retrospective chart review.

**Results:** This case series includes 12 patients (6 female, 6 male) with a mean age at IRAE onset of 63.9 years (range 33–79). Multiple cancers were represented including melanoma (n=9), Hodgkin's lymphoma (n=1), squamous cell lung cancer (n=1), and adenocarcinoma of the lung (n=1). 5/12 patients received Nivolumab, 8/12 received Pembrolizumab, and 2/9 received Ipilimumab. ICI exposure was associated with various rheumatologic IRAEs including PMR-like syndrome (n=4), symmetric polyarthritis (n=6), psoriatic arthritis (n=1), oligoarthritis (n=1), and erythema nodosum (n=1). Other IRAEs were also noted including vitiligo (n=1), pulmonary capillaritis (n=1), ulcerative colitis flare (n=1), inflammatory seborrheic keratosis and psoriasis (n=1). The mean time of onset of the IRAE from the first exposure to an ICI was 6.8 months (range 0–21 months). In 7 cases, rheumatologic symptoms worsened with each ICI dose. Laboratory investigations demonstrated elevated CRP in 7 cases (mean 75.6; range 3.7–290.1), RF positivity in 2 cases, weak positive ANAs in 4 cases (1:80), SSA positivity in 2 cases, and a single case where a pre-existing anti-CCP antibody was identified. Steroids were used in 11 cases at a mean starting dose of 36 mg (range 10–50 mg) by mouth daily for an average duration of 6.1 months (range 1–12 months). Other DMARDs were necessary in some cases (Hydroxychloroquine n=1; Methotrexate n=5). While 6 patients experienced rapid improvement, 4 experienced gradual improvement. Most patients achieved partial resolution of symptoms (n=6) while only 4 achieved complete resolution. Tumour response was observed in all 12 patients.

**Conclusions:** This case series of IRAEs associated with ICI treatment suggest that symmetric polyarthritis and PMR-like syndromes are the most common rheumatologic IRAEs, although the spectrum is broad. IRAEs seem to develop around 6 months after first exposure, worsen with ongoing doses of ICI administration, and respond to treatment with corticosteroids. Treatment doses and duration were higher than expected for phenotype, with few patients achieving significant improvement with short courses. Those with IRAEs tend to have good tumour response, despite concurrent use of immunosuppressants. MTX and HCQ appear to be safe and effective, but more experience with these and other DMARDs/biologics is required in these patients.

**Disclosure of Interest:** None declared

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**THU0616 ELEVATED THYROID STIMULATING HORMONE AS A POTENTIAL BIOMARKER FOR RHEUMATIC IMMUNE-RELATED ADVERSE EVENTS FOLLOWING PD-1 INHIBITOR THERAPY**

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**Background:** Programmed cell death protein (PD-1) inhibitor immunotherapy is being increasingly used in oncology, but may cause immune-related adverse events (irAEs) resembling classical rheumatic and non-rheumatic autoimmune diseases. While oncological response to therapy has been associated with the development of rheumatic irAEs, no biomarker to predict the development of rheumatic irAEs has yet been identified. Thyroid stimulating hormone (TSH) is readily available in clinical practice and is frequently tested prior to the administration of PD-1 inhibitors to screen for existing thyroid disease.

**Objectives:** To investigate whether thyroid stimulating hormone, or changes to it, are associated with the development of immune-related adverse events (irAEs) following PD-1 inhibitor therapy for cancer.

**Methods:** This was a retrospective chart review of all patients at a single centre who had a TSH level performed in the institutional laboratory prior to the patient being dispensed nivolumab or pembrolizumab before January 1, 2017, with follow-up until July 1, 2017. TSH levels before and during PD-1 inhibitor therapy were recorded. Patients with any diagnosis of a rheumatic irAE or any non-

cutaneous irAE were identified. Linear regression was performed to determine the relationship between TSH and the development of irAEs. Youden's index was used to derive the optimal cut-off point. Recursive partitioning methods with imbalanced prior probabilities were used to create a decision tree model.

**Results:** There were 213 episodes of therapy which met criteria, of which a non-cutaneous irAE occurred in 62 episodes (29.1%), thyroid irAEs occurred in 22 episodes (10.3%) and rheumatic irAEs were diagnosed in 16 episodes (7.5%). Even when corrected for duration of exposure to PD-1 inhibitor therapy, elevated TSH levels (>4.2 mU/L) were statistically significantly associated with the development of rheumatic irAEs (adjusted OR 6.08, 1.53–24.22), and this was not weakened by excluding patients who went on to develop thyroid irAEs. There was no significant association between elevated TSH levels and the development of any non-cutaneous irAE. Change in TSH levels with PD-1 inhibitor therapy was also not associated with the development of non-cutaneous irAEs or rheumatic irAEs specifically. Using a TSH level >2.4 to predict rheumatic irAEs led to a positive predictive value of 25% and a negative predictive value of 93% in our cohort. A decision tree model to predict rheumatic irAEs combining a pre-PD-1 inhibitor TSH level >2.4 and an oncological response to therapy led to a positive predictive value of 50% and a negative predictive value of 94% in our cohort.

**Conclusions:** Elevated TSH levels may be a potential biomarker for the development of rheumatic irAEs. In particular, a pre-PD-1 inhibitor TSH level of >2.4 mU/L, in combination with oncological response to therapy, may identify patients at risk of rheumatic irAEs. Associations observed in this cohort should be examined in larger cohorts to determine the clinical utility of TSH in predicting rheumatic irAEs.

**Disclosure of Interest:** None declared

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**THU0617 IS THE NUMBER OF IGG4+ PLASMA CELLS SEEN BY IMMUNOSTAINING USEFUL BEYOND ITS DIAGNOSTIC UTILITY IN IGG4-RELATED DISEASE?**

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**Background:** The histopathological findings in IgG4-related disease (IgG4-RD) includes the presence of marked IgG4 +plasma cell infiltration seen by immunostaining and it has been used in clinical practice only as a diagnostic tool. Whether the number of IgG4 +plasma cells in tissue is associated with any clinical or serological feature of the disease has not been previously evaluated.

**Objectives:** To evaluate if the number of IgG4 +plasma cell infiltration is associated with any clinical or serological outcome.

**Methods:** We included 30 patients with biopsy proven IgG4-RD according to the Comprehensive Diagnostic Criteria for IgG4-RD who regularly attended a tertiary referral centre in Mexico City (2000–2017). We collected demographics, clinical (organ involvement, relapses and the disease activity assessed by the IgG4-RD Responder Index [IgG4-RD RI] at baseline) as well as baseline laboratory data (C3, C4, total eosinophil count, IgG4 levels). Patients were divided in three groups according to the number of IgG4 +plasma cells seen by immunostaining as follows: <50 IgG4 +plasma cells/HPF, 50–100 IgG4 +plasma cells/HPF, and >100 IgG4 +plasma cells/HPF.

**Results:** We included 30 patients, 17 (56.6%) women, mean age 53±13.9 years and median disease duration 13 months. The biopsies were from the following tissues: lacrimal gland (n=6), pancreas (n=5), orbit (n=4), kidney (n=4), lymph node (n=3), mediastinum (n=2), salivary gland (n=2) and other tissues (n=4). Eleven patients (36.6%) had <50 IgG4 +plasma cells/HPF, 9 patients (30%) 50–100 IgG4 +plasma cells/HPF and 10 (33.3%) patients >100 IgG4 +plasma cells/HPF. We did not find any difference regarding age, gender, time of follow up, number of involved organs and relapses. The median basal IgG4-RD RI was 9, 6 and 15, for the <50 IgG4 +plasma cells/HPF, 50–100 IgG4 +plasma cells/HPF, and >100 IgG4 +plasma cells/HPF groups respectively, however, they did not reach statistical significance. The group with >100 IgG4 +plasma cells/HPF had more frequently lymphadenopathy when compared with the other groups (36.4%, 66.7% and 80%, p=0.02; respectively) while the proportion of involvement of the other anatomic sites were similar. We found a statistical difference in serum C3 levels (99.5 mg/dl, 159 mg/dl, 78.5 mg/dl, p=0.04) and a tendency for serum C4 levels (20 mg/dl, 27 mg/dl, and 6 mg/dl, p=0.08) among the groups, whereas the levels of serum IgG4 (60.8 mg/dl, 196 mg/dl, 245 mg/dl, p=0.35) and the eosinophil count (284/mm<sup>3</sup>, 189/mm<sup>3</sup>, 283/mm<sup>3</sup>, p=0.46) were similar. The C3 and C4 serum levels negatively correlated with the basal IgG4-RD RI ( $\tau=-0.48$ , p=0.005 and  $\tau=-0.58$ , p=0.001).

**Conclusions:** Our results show that the number of IgG4 +plasma cells seen by immunostaining in IgG4-RD may be of value in identifying a subset of patients with hypocomplementemia, lymphadenopathy and probably higher basal disease activity. The finding of an association between hypocomplementemia and higher tissue infiltration by IgG4 +plasma cells expands the evidence that complement activation may contribute to the pathogenesis of IgG4-RD.



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**Disclosure of Interest:** None declared

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### THU0618 HYPHOPHOSPHATASIA IN FRENCH TERTIARY CARE HOSPITALS

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**Background:** Hypophosphatasia is a rare heritable metabolic disorder. Its prevalence is estimated at 1: 1 00 000. Its diagnosis can only be established after genetic confirmation. A low serum total alkaline phosphatase (ALP) level is the hallmark for the diagnosis of hypophosphatasia. Its prevalence is 0.05% in the general population and may be associated with symptoms similar to those of adult forms of hypophosphatasia: excess of joint pathology (chondrocalcinosis, osteoarthritis), periarticular disorders (calcifications, tendinopathies enthesopathies), and disorders of bone mineralization (risk of fracture).

**Objectives:** The aim of this study was to assess the recognition of persistent low ALP in 3 tertiary care hospitals in France.

**Methods:** All of the ALP assays of 3 tertiary care hospitals measured in 2013 were reviewed. Persistent hypophosphatasemia was defined by at least one assay <30 IU/L without any assay >40 IU/L. Selected records were analysed to eliminate secondary causes of hypophosphatasemia. A telephone questionnaire was conducted with included patients from the rheumatology and internal medicine departments.

**Results:** In 2013, 288,851 PAL assays were performed in 1 24 044 patients. Excluding emergency and intensive care unit services, 216,817 PAL assays were performed in 83 657 patients. 716 patients had a value ≤30 IU/L. Of these, 174 had 1 single dosage, 542 multiple dosages, of which 186 never had value >40. 31 patients were excluded due to secondary hypophosphatasemia: severe caloric restriction (n=10), massive surgery (n=6), cancer/hemopathy (n=8), acute pathology -sepsis/voluntary drug intoxication (n=4), high-dose corticosteroid therapy (n=3). 155 patients were selected; the prevalence of hypophosphatasemia in hospitals is therefore 0.124%. Hypophosphatasemia was noticed in the summary discharge in 1,3%. 4 patients received bisphosphonates despite low PAL (before treatment) and 2 patients had a fracture under treatment. Of the 155, 38 were followed in the rheumatology and internal medicine departments and 33 answered a standardised telephone questionnaire (78% women, average age 43.8 years). 11 patients reported a history of fracture, 2 patients had a history of rickets in childhood, and 1 had known hypophosphatasia in the family. 9 patients had tooth enamel disorders, 7 had gingival recession, 3 had spontaneous tooth loss, and 1 had lost their deciduous teeth by the age of 3 years.

**Conclusions:** The prevalence of hypophosphatasemia is higher in hospitals than in the general population. This biological anomaly is almost never recorded in the files. However, the existence of hypophosphatasemia should be systematically reported as it is a contraindication to anti-resorptive therapy because of the risk of atypical femoral fracture.

**Disclosure of Interest:** None declared

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### THU0619 THE FREQUENCY OF EXON-10 MUTATIONS IN MEFV GENE IN "PROBABLE" DIAGNOSED FMF PATIENTS ACCORDING TO TEL HASHOMER CRITERIA

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**Background:** Familial Mediterranean Fever (FMF) is characterised with recurrent inflammatory attacks with serosal inflammation. The clinical findings of FMF is seen in a large spectrum. Tel Hashomer criteria are widely used for classifying FMF. According to this criteria set FMF is classified as 'definite' and 'probable' disease.

**Objectives:** We aimed in this study to investigate the frequency of exon-10 MEFV mutations in 'probable' FMF patients according to Tel Hashomer criteria.

**Methods:** The study group consisted of 117 patients (79 male, 38 female, median age:31±11, <sup>12-69</sup> which is classified as 'probable' FMF according to Tel-Hashomer criteria. The 12 frequently seen mutations in Turkey analysed in all blood samples and compared with the previous reported 'definite' FMF data from Turkey.

**Results:** We found in probable FMF group single mutation in 36 patients (%30,8), two mutations in 56 patients (%47,9), 3 mutations in 5 patients (%4,3) and no

mutations in 20 patients (%17,1). The distribution of exon 10 mutations showed single exon-10 mutation in 46 patients (%39,3) and two exon-10 mutations only in 23 patients (%19,7). The detailed distribution of MEFV mutations in 'probable' FMF group is shown in table 1.

**Abstract THU0619 – Table 1.** The Distribution of MEFV gene mutations in 'probable' FMF group

	Homozygout	Heterozygout	Negative
M694V	5 (4,3%)	42 (35,9%)	70 (59,8%)
M680I	2 (1,7%)	18 (15,5%)	82,8 (96%)
V726A	1 (0,9%)	12 (10,3%)	104 (88,9%)
M694I	-	3 (2,6%)	114 (97,4%)
R202Q	2 (1,7%)	35 (29,9%)	80 (68,4%)
E148Q	1 (0,9%)	15 (12,8%)	101 (86,3%)
P369S	-	3 (2,6%)	114 (97,4%)
R761H	1 (0,9%)	6 (5,1%)	110 (94%)
K695R	-	2 (1,7%)	115 (98,3%)
A744S	-	2 (1,7%)	115 (98,3%)

**Conclusions:** We found decreased frequency of exon 10 mutations in the MEFV gene in "probable FMF" group according to Tel-Hashomer criteria in comparison previous reported MEFV mutations data. The distribution of non-exon 10 mutations were similar in the definite FMF group. It is needed more clinical studies with large patient group for the clinical significance of non-exon 10 mutations in "probable" FMF patients.

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### THU0620 ON DEMAND USE OF ANAKINRA FOR THE ATTACKS OF FAMILIAL MEDITERRANEAN FEVER (FMF)

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**Background:** IL-1 blocking agents have been shown to be effective in the prevention of attacks in colchicine-resistant FMF (crFMF) patients by their regular use. However, their high cost, side effects and treatment noncompliance limit their use which might be overwhelmed by on-demand use of them which has not been reported in FMF patients. Herein, we evaluated the efficacy of on demand use of anakinra in crFMF patients.

**Methods:** Data were derived from Gazi FMF cohort which was established in the year 2010. From that date patients with FMF who were diagnosed according to the Tel Hashomer criteria were registered. Co-morbidities, detailed attack characteristics, type, duration, severity, treatments, laboratory parameters and impact of FMF on their life in terms of quality of life and work productivity were recorded either by FMF diary or a mobile phone application (FMF AIDD free to download from AppStore and Android market). A retrospective cohort analysis was made from records of patients who have ever been treated with IL-1 inhibitors.

**Results:** A total of 60 patients were treated with anakinra in our cohort and 15 patients were identified who were received on demand anakinra protocol. Rationale for on demand use of anakinra was prominent prodrome or trigger for attacks and patients' personal claim. Six patients were switched from regular use and 9 were directly started as on demand use. All were using background colchicine in maximum tolerated doses. None of patients had evidence of persistently elevated acute phase reactants or proteinuria. The median duration of on demand anakinra use was 6 (min 3- max 36) months. Pre- and post- on demand anakinra periods were compared (table 1). Patient reported attack severity (p=0.002), duration (p=0.001), absenteeism (p=0.001) and presenteeism (p=0.002) were significantly

improved but C-reactive protein (CRP) remained in the same levels. On demand anakinra prevented progression of prodromes to full-blown attacks which was demonstrated by decrease in the rate of attack/prodrome ratio ( $p=0.002$ ). On demand anakinra can be continued in 10 subjects on long-term but continuous treatment was required in 5 subjects.

**Abstract THU0620 – Table 1.** Comparison of attack characteristics before and after on demand anakinra protocol

	Colchicine period	Colchicine plus On-Demand Anakinra period	p
Attack severity, VAS	10 (2)	6 (3)	0.002
Duration, days	3 (2)	1.5 (1)	0.001
Frequency*, number	4 (1.5)	1.5 (1.75)	0.001
CRP (mg/L)	5.1 (6.1)	4.1 (5.9)	0.58
AIDAI	18 (22.5)	4 (5)	0.001
Attack/prodrom ratio, (n=10)	1	0.6 (0.4)	0.002
Absenteeism, days	7 (8)	2 (2.5)	0.001
Presenteeism, days	9 (7.5)	2.5 (3)	0.002

Attack frequency and work productivity parameters are adjusted for 3 months intervals. VAS: visual analogue scale, CRP: C-reactive protein, AIDAI: autoinflammatory disease activity index

**Conclusions:** On demand anakinra significantly improved FMF attacks which suggest this approach would be of benefit in daily practice in selected patients.

**Disclosure of Interest:** None declared

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**THU0621** **PERSISTENT PRURITIC SKIN LESIONS WITH DYSKERATOTIC CELLS IN UPPER LAYER OF EPIDERMIS ARE SPECIFIC AND ASSOCIATED WITH HIGH LEVELS OF SERUM IL-18 IN ADULT-ONSET STILL'S DISEASE**

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**Background:** Adult-onset Still's disease (AOSD) is an acute and systemic inflammatory disorder that is characterised by high spiking fever, evanescent rash, arthralgia/arthritis and hyperferritinemia. However, recent reports showed that not only typical evanescent salmon-coloured rash but also atypical skin lesions, persistent pruritic papules and plaques, could be associated with AOSD.

**Objectives:** To assess the clinical significance of dyskeratotic cells (DCs) in skin lesions of AOSD.

**Methods:** We assessed histology of skin lesions including persistent pruritic skin lesions in Japanese patients with AOSD (n=15). Moreover, we compared histology of AOSD with dermatomyositis (DM) (n=6), drug eruptions (DE) (n=7), and graft versus host disease (GVHD) (n=6).

**Results:** AOSD with persistent pruritic skin lesions (n=10) histologically showed DCs only in upper layer of epidermis and horny layer without inflammatory cells infiltrations, indicating dyskeratosis. AOSD with evanescent rash (n=5) histologically showed no DCs. DCs were positive by ssDNA staining, suggesting apoptotic cells. Serum IL-18 showed significantly higher in AOSD patients with dyskeratosis (n=10) than without dyskeratosis (n=5). In contrast to AOSD with DCs, the histology of DM, DE and GVHD demonstrated that DCs existed in all layers of epidermis with inflammatory cells infiltrations.

**Conclusions:** Persistent pruritic skin lesions in AOSD are specific by prominent epidermal apoptosis involving the upper layers of epidermis. Moreover, hyper IL-18 might be related with dyskeratosis.

**Disclosure of Interest:** None declared

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**THU0622** **HISTOPATHOLOGY AND EXPRESSIONS OF CHEMOKINES, CXCL10, CXCL13, AND CXCR3, AND AN ENDOGENOUS LIGAND S100A8/A9 IN LYMPH NODES OF PATIENTS WITH ADULT-ONSET STILL'S DISEASE**

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**Background:** Adult-onset still's disease (AOSD) is a rare systemic inflammatory disease with several symptoms, such as a persistent high spiking fever, typical rash, and lymphadenopathy. Endogenous factors related to interleukin (IL)-1,

such as S100A8/A9 and several chemokines including CXCL10, CXCL13 and CXCR3, could play a potential role in the pathogenesis of AOSD.

**Objectives:** We aimed to find out typical histopathologic features, expressed pattern of chemokines in lymph nodes (LN) of AOSD patients.

**Methods:** Formalin-fixed paraffin-embedded excisional LN tissues from 48 AOSD patients and 6 nonspecific reactive hyperplasia were histologically reviewed. The immunohistochemical stain for CXCL10, CXCL13, CXCR3 and S100A8/A9 were done. The clinical and laboratory data of the patients who underwent LN biopsies were reviewed.

**Results:** The LN specimens were categorised according to four distinctive patterns: follicular (n=2, 4.2%), paracortical (n=19, 39.6%), diffuse (n=9, 18.8%) hyperplasia, or mixed pattern (n=18, 37.5%). The other examined histologic features were presence of necrosis, karyorrhexis, immunoblastic, histiocytic and vascular proliferation. Most of the cases were required to take into differential diagnosis such as dermatopathic lymphadenitis (n=16, 33.3%), lymphoma (n=11, 22.9%) and histiocytic necrotizing lymphadenitis (n=9, 18.8%). The expression of chemokines and S100A8/A9 were higher than that of nonspecific reactive hyperplasia. The expression of chemokines and S100A8/A9 were higher than that of nonspecific reactive hyperplasia.

**Conclusions:** Histopathologic findings of LN in AOSD patients are diverse enough to be included various differential diagnosis. Because the several chemokines and S100A8/A9 were more expressed in AOSD patients than those of reactive hyperplasia, they may serve as a pathogenesis of AOSD.

**Disclosure of Interest:** None declared

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**THU0623** **SERUM IGG4 LEVELS AT DIAGNOSIS CAN PREDICT THE OUTCOMES OF UNTREATED PATIENTS WITH IGG4-RELATED DISEASE: A RETROSPECTIVE STUDY**

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**Background:** IgG4-related disease (IgG4-RD) is a recently recognised systemic fibro-inflammatory disorder that can affect many organs.<sup>1</sup> In IgG4-RD, spontaneous, or at least temporary, remissions without treatment have been reported, and watchful waiting may be appropriate in certain patients with asymptomatic and inactive disease.<sup>2</sup> However, the outcomes of patients with IgG4-RD who do not undergo treatment are still unclear.

**Objectives:** This study aimed to clarify the outcomes of untreated patients with IgG4-RD and the factors related to the outcomes.

**Methods:** We retrospectively reviewed the medical records of 107 patients with IgG4-RD, who were followed up for more than 6 months, at a single centre in Japan. Among them, 27 patients were followed up without treatment after the initial diagnosis. We compared the clinical features of these 27 patients with those of the 80 patients who underwent treatment. The outcomes of untreated patients were investigated, and logistic regression analysis was performed to assess factors related to the outcomes. Deterioration of IgG4-RD was defined as symptomatic, radiological, or functional exacerbation of the organ involved or new organ involvement.

**Results:** The patients comprised 73 men and 34 women (mean age 65.7 years). The follow-up periods were 7–252 (mean, 64.1) months, and the serum IgG4 levels at diagnosis were 10.7–3610 (mean, 706) mg/dL. The 27 untreated patients had significantly fewer affected organs ( $1.9 \pm 1.2$  vs  $3.0 \pm 1.6$ ,  $p=0.001$ ), lower IgG4-RD responder index ( $10.8 \pm 5.1$  vs  $13.8 \pm 6.8$ ,  $p=0.048$ ), and lower frequency of ophthalmic and renal parenchymal lesions ( $25.9\%$  vs  $53.8\%$ ,  $p=0.015$ , and  $3.7\%$  vs  $26.3\%$ ,  $p=0.012$ , respectively) than did the 80 patients who underwent treatment. Of these 27 patients, 8 experienced deterioration of IgG4-RD 3–232 months (mean, 62.8) after the diagnosis. New organ involvement was observed in all 8 patients, 2 of whom concurrently suffered exacerbation of the organs involved. In age- and sex-adjusted logistic regression analysis, serum IgG4 elevation (per 100 mg/dL, odds ratio 1.194, 95% confidence interval 1.017–1.402,  $p=0.030$ ) was the only significant factor related to deterioration of disease in untreated patients with IgG4-RD.

**Conclusions:** The present study suggests that serum IgG4 levels may be useful to predict the outcomes of untreated patients with IgG4-RD, who tend to have fewer affected organs and lower IgG4-RD responder index.

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**Disclosure of Interest:** None declared

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### THU0624 COLCHICINE: AN EFFECTIVE TREATMENT OPTION FOR UNCLASSIFIED AUTOINFLAMMATORY DISEASES IN CHILDREN

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**Background:** Children and adults with clinically and genetically defined autoinflammatory diseases (AID) including CAPS, TRAPS and HIDS can receive expensive Interleukin-1 (IL-1) inhibitors in many countries around the world. However, patients suffering from unclassified autoinflammatory conditions characterised by recurrent fevers and organ dysfunction and the absence of a known pathogenic mutation commonly have no access to these treatment options.

**Objectives:** The aim of this study was to explore the efficacy and safety of colchicine treatment in children and adults with autoinflammatory diseases without pathogenic mutations.

**Methods:** Consecutive children and adults with autoinflammatory diseases without pathogenic mutations treated with colchicine were included in this single centre study and observed for a median of 12.94 months (range 1.25–66.73). Clinical features, autoinflammatory disease activity indices (AIDAI), inflammatory markers ESR, CRP, SAA and S100, frequency and duration of flares and physician global assessment of disease activity (VAS) were recorded serially and compared at baseline and while receiving Colchicine therapy.

**Results:** A total of 39 patients were included in the study. These were 16 girls and 23 boys, median age at start of colchicine therapy was 4 years (range 1–54). The diagnoses included PFAPA in 15, mutation-negative FMF in 11, autoinflammation with low-penetrance variants in nine (all *NLRP3*) and other unclassified AID in four patients. Recurrent fever was the leading symptom, mostly associated with arthralgia and myalgia. The mean disease activity decreased from 4.4 at baseline to 2.2 on colchicine. Mean SAA-levels decreased from 159 to 63.3 mg/L, CRP levels from 6.4 to 2.3 mg/dl. Flare frequency was reduced in 72% and remained unchanged in 28% of patients. Flare duration was reduced in 82%, unchanged in 14% and increased in only 4% of patients. Most common adverse events were abdominal pain and nausea in 50% of patients and appeared to be dose dependent.

**Conclusions:** Children and adults with unclassified autoinflammatory diseases may benefit significantly for colchicine therapy. Control of clinical disease activity and improved inflammatory markers were documented in 59% of patients. Colchicine should be considered in patients with active inflammatory disease with no access to IL-1 inhibitors. Controlled trials are needed to further explore this approach.

**Disclosure of Interest:** None declared

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### THU0625 IGG4-RELATED DISEASE MANIFESTATIONS DIFFER BETWEEN ASIAN AND NON-ASIAN SUBJECTS

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**Background:** IgG4-related disease (IgG4-RD) is a multi-system immune-mediated condition that can affect nearly any organ. No study has evaluated differences in disease manifestations according to race. We evaluated this in a large cohort of IgG4-RD subjects submitted by an international group of investigators.

**Objectives:** To evaluate racial differences in manifestations of IgG4-RD.

**Methods:** To validate the ACR/EULAR IgG4-RD Classification Criteria, 76 investigators from North America, South America, Europe, and Asia submitted cases they considered to be IgG4-RD in either the preliminary phase or the validation phase. For each case, investigators included details related to diagnostic certainty, age at disease onset and diagnosis, race, organ involvement, biopsy findings, and laboratory results. Based on reported race, we dichotomized subjects into either Asian or non-Asian categories; subjects of South Asian (n=14) descent (e.g., India, Pakistan), all of whom resided in North America or Europe were grouped with non-Asian subjects. We compared the distribution of disease features according to race using t-tests, Wilcoxon tests, and Chi square tests, where appropriate, as well as in multivariable-adjusted models.

**Results:** In the validation phase, there were 493 cases of IgG4-RD submitted by 23 investigators who practice in Asia and 29 investigators who practice in North America or Europe. There was no significant difference in the distribution of specialists (e.g., rheumatology, gastroenterology) between Asian and non-Asian investigators (p=0.3). The majority of IgG4-RD subjects, both Asian (n=208) and non-Asian (n=285), were male (61% and 69%, respectively). Asian subjects were significantly older both at symptom onset and diagnosis (61.2±13.2 years and 62.6±12.8 years, respectively) compared to non-Asian subjects (55.1±14.9 years and 57.2±14.4 years, respectively, p<0.0001 for both comparisons). There was a significantly shorter diagnostic delay among Asian subjects compared to non-Asian subjects (1.4±2.7 years vs 2.2±3.7 years, p=0.01). Head/neck involvement was more common in Asians (52% vs 27%, p<0.0001) whereas hepatobiliary involvement was more common in non-Asians (52% vs. 42%, p=0.04). Asian subjects had a significantly higher median serum IgG4 concentration (666 mg/dL, IQR 320.5–1230 vs 240.5, IQR 100–505, p<0.0001) and were more likely to have a serum IgG4 concentration greater than five times the upper limit of normal (48% vs 20%, p<0.0001). In multivariable-adjusted models, differences in age and serum IgG4 concentration according to race remained strongly significant (p<0.001 for both comparisons).

**Conclusions:** Asian and non-Asian subjects differed regarding the age of disease onset and diagnosis, the distribution of organ involvement, and baseline serum IgG4 concentrations. There was a significantly shorter diagnostic delay among Asian subjects compared to non-Asian subjects. The etiology(ies) of these observed differences in the respective presentation of IgG4-RD in Asian and non-Asian subjects requires further investigation, but could include differences in diagnostic approach, environmental factors, and genetic predisposition.

**Disclosure of Interest:** None declared

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### THU0626 CORRELATION AMONG SERUM AMYLOID A LEVELS, CLINICAL MANIFESTATIONS, TREATMENT AND DISEASE ACTIVITY IN PATIENTS WITH BEHÇET'S DISEASE

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**Background:** Behçet's disease (BD) is an inflammatory disorder potentially leading to life- and sight-threatening complications: no laboratory marker correlating with disease activity or predicting the occurrence of disease manifestations is currently available in the clinical practice.

**Objectives:** To search for a correlation between serum amyloid-A (SAA) levels and disease activity evaluated via BD current activity form (BDCAF), to assess disease activity in relationship with different SAA thresholds, to examine the association between single organ involvements and the overall major organ involvement with different SAA thresholds, and to assess the influence of biologic therapy on SAA levels.

**Methods:** Ninety-five serum samples were collected from 64 BD patients, and their related demographic, clinical and therapeutic data were retrospectively collected.

**Results:** No correlation was identified between SAA levels and BD disease activity (Spearman  $\rho=0.085$ ; p=0.411), while a significant difference was found in the mean BDCAF score between patients presenting SAA levels<200 mg/L and those with SAA levels>200 mg/L (p=0.027). SAA levels higher than 200 mg/L were significantly associated with major organ involvement (p=0.008). A significant association was found between SAA levels>150 mg/dl and ocular (p=0.008), skin (p=0.002) and mucosal manifestations (p=0.012). Patients undergoing biologic therapies were significantly associated with SAA levels<200 mg/L compared with patients who were not treated with biologics (p=0.012).

**Conclusions:** SAA level does not represent *per se* a biomarker of disease activity, but might be useful as a predictor of major organ involvement and ocular disease relapse at certain thresholds in patients with BD.

**Disclosure of Interest:** None declared

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### THU0627 DEMOGRAPHICS AND PRESENTING ORGAN INVOLVEMENT IN A COHORT OF PATIENTS WITH SARCOIDOSIS

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**Background:** Sarcoidosis is a multisystem disorder of unknown etiology characterised pathologically by non-caseating granulomas in involved organs. Although mortality is reported in only 1%–5% of patients, there is data suggesting it might



be increasing and there is little information about the clinical and epidemiological characteristics of this group of patients.

**Objectives:** To compare basic demographics of a cohort of deceased sarcoid patients with a non-deceased sarcoid population, and to describe the presenting organ involvement among the deceased sarcoid population.

**Methods:** Patients seen at the Stanford University Hospital and Clinics from 2009–2017 who were >18 years of age with at least one ICD-9 or 10 diagnosis of sarcoidosis and at least one clinical note with the term "sarcoidosis" were identified by EMR. After determining the demographics of this cohort, deceased patients were identified and an extensive chart review of these subset of patients was conducted. The project was approved by Stanford's Institutional Review Board.

**Results:** 1190 adult patients with an ICD code for sarcoidosis were identified. Demographic comparison between the non-deceased and deceased population is summarised in the table 1 below.

	Non-deceased sarcoid patients	Deceased sarcoid patients
Total patients	1086	104
Gender:	660 (60.8%)	59 (56.7%)
Females	426 (39.2%)	45 (43.3%)
Males		
Race:		1 (0.9%)
Asian	67 (6.2%)	26 (25%)
Black	197 (18.1%)	45 (43.2%)
White	596 (54.9%)	0 (0%)
Native American	6 (0.6%)	18 (17.4%)
Others	128 (11.8%)	14 (13.5%)
Unknown	91 (8.4%)	
Ethnicity	918 (84.5%)	80 (76.9%)
Non-Hispanic	67 (6.2%)	11 (0.5%)
Hispanic/Latino	101 (9.3%)	13 (12.6%)
Unknown		

In comparison with non-deceased patients with sarcoidosis, the proportion of African American population was higher in the deceased population, whereas the proportion of Asians and whites was lower in the deceased population. The percentage of male patients in the deceased subset was slightly higher than the non-deceased population. 65 (62.5%) of the 104 deceased patients were symptomatic at diagnosis, 6 (5.8%) were asymptomatic and information was not available for 33 (31.7%) patients. Of the 65 symptomatic patients, presenting organ involvement was either pulmonary (34, 52.3%), cardiac (11, 16.9%), cutaneous (8, 12.3%), neurological (4, 6.2%), ocular (3, 4.6%), constitutional (5, 7.7%), unknown (1, 1.5%), musculoskeletal (1, 1.5%), renal–calcium related (1, 1.5%), hepatic (2, 3%), laryngeal (1, 1.5%), nasal and sinus (2, 3%), parotid gland (1, 1.5%), gastrointestinal (1, 1.5%), or others (5, 7.6%).

**Conclusions:** This study compares the demographics of subset of deceased sarcoid patients with a population of non-deceased sarcoid patients, and describes the presenting organ involvement among the deceased sarcoid population. African American males had a higher mortality rate compared to Asians and Caucasians. Pulmonary and cardiac disease represented 69.2% of organ involvement in the deceased. Our study showed a mortality rate of 8.7% in the sarcoid population which is in keeping with the newer studies that mortality in patients with sarcoid might be on the rise. With further study of this population, we aim to compare the characteristics of non-deceased sarcoid patients with the deceased patients, including presenting organ involvement, diagnostic workup and treatment regimen and hope to gain a better understanding of the possible reasons for increasing mortality in patients with sarcoidosis.

**Disclosure of Interest:** None declared

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#### THU0628 DIFFERENCES IN CLINICAL MANIFESTATIONS OF BEHCET'S SYNDROME BY GENDER: CROSS-SECTIONAL ANALYSIS IN A UK COHORT

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**Background:** Geographical variations in genotype and phenotype of Behçet's syndrome (BS) are reported.<sup>1,2</sup> Previous meta-analysis of international cohorts has highlighted differences in clinical manifestations of BS by gender.<sup>3</sup> A comparison of BS clinical manifestations by gender has not been analysed previously in a large UK BS cohort.

**Objectives:** 1) To compare the clinical manifestations of BS in a UK cohort by gender and 2) to compare this to published international data.

**Methods:** A retrospective cross sectional analysis was performed using clinical databases at the Liverpool and Birmingham BS Centres of Excellence. Patients with a multi-disciplinary diagnosis of BS or International Study Group (ISG) diagnostic criteria were included. Clinical manifestations and HLA-B51 positivity were compared by gender. T-tests and chi-squared tests were used for continuous and categorical data respectively and a p value of 0.05 or less was considered statistically significant.

**Results:** 433 patients met inclusion criteria (140 males, 32.3%). Male patients were younger and had significantly higher rates of ocular and vascular involvement, papulopustular skin rash and HLA-B51 positivity. Female patients had significantly higher rates of genital aphthosis and arthralgia.

	Male (n=140)	Female (n=293)	p value
Age (years), mean (s.d.)*	41.2 (12.5)	44.1 (11.9)	0.02
Recurrent oral aphthosis, n (%)	139 (99.3)	291 (99.3)	0.97
Genital aphthosis, n (%)*	111 (79.3)	278 (94.9)	<0.01
Papulopustular skin rash, n (%)*	69 (49.3)	107 (36.5)	0.01
Erythema nodosum, n (%)	29 (20.7)	56 (19.1)	0.70
Skin aphthosis (n,%)	7 (5.0)	8 (2.7)	0.23
Uveitis, n (%)*	81 (57.9)	99 (33.8)	<0.01
Retinal vasculitis, n (%)*	39 (27.9)	36 (12.3)	<0.01
Central nervous system involvement, n (%)	16 (11.4)	20 (6.8)	0.11
Large vein thrombosis, n (%)*	22 (15.7)	19 (6.5)	<0.01
Arterial thrombosis or aneurysm, n (%)	4 (2.9)	7 (2.4)	0.77
Thrombophlebitis, n (%)*	10 (7.1)	5 (1.7)	<0.01
Gastro-intestinal involvement, n (%)	8 (5.7)	25 (8.5)	0.30
Arthralgia, n (%)*	68 (48.6)	180 (61.4)	0.01
Ethnicity (British or White), n (%)*	90 (64.3)	238 (85.9)	<0.01
	(n=126)	(n=277)	
HLA-B51 positive, n (%)*	14 (58.3)	9 (20.0)	<0.01
	(n=27)	(n=45)	

\*statistically significant

**Conclusions:** Similar to published international cohorts, male patients with BS in the UK have higher rates of ocular and venous involvement, papulopustular skin rash and HLA-B51 positivity and lower rates of genital aphthosis and arthralgia in comparison to female patients. However, the extent to which these differences are attributable to ethnicity is unclear.

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#### THU0629 A STUDY OF WBMRI IN ESTIMATING DISEASE ACTIVITY OF PM/DM AND THE FOLLOWING DISEASES DIAGNOSIS

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**Background:** IM is a group of disease characterised by chronic symmetrical myasthenia, muscle fatigue and monocyte infiltrating skeletal muscle. This disease usually associates with the muscle of trunk and proximal limbs, skin lesions accompanied or not. Dermatomyositis (DM) and polymyositis (PM) account for the major part of IM clinically. The diagnose of these diseases mainly rely on clinical manifestation, biopsy, ECG and serum creatase. Whole-body magnetic resonance imaging (WBMRI) has been reported succeeding in diagnosing PM/DM through short tau inversion recovery (STIR) sequence, but the ability to estimate disease activity hasn't been reported.

**Objectives:** To evaluate the value in WBMRI through STIR sequence in evaluating the disease activity of polymyositis (PM) and dermatomyositis (DM) and screening interstitial lung disease (ILD) and osteonecrosis.

**Methods:** PM/DM patients meeting the Bohan and Peter diagnostic criteria from the First Affiliated Hospital of Zhengzhou University were admitted between 2015 August to 2017 December. A retrospective analysis of the WBMRI imaging data, serum creatine kinase, electromyography and muscle biopsy were performed. The WBMRI images were estimated by semiquantitative score and the disease activity was estimated by MDAAT. SPSS 20.0 was utilised to analyse the statistical significance.

**Results:** This study includes 61 patients, including 41 DM cases and 20 PM cases, all of these shows typical pathological feature and inflammatory muscle in WBMRI. Significant statistical correlation was found between the grade of muscle oedema estimated by WBMRI and the clinical assessment through MDAAT for muscle disease activity (DM  $r=0.57$ ,  $p=0.006$ ; PM  $r=0.84$ ,  $p=0.001$ ). The positive rate of serum creatine kinase test was 63% (39/61). Besides muscular changes, we also detected 35 cases in interstitial lung disease, 2 cases in osteonecrosis, 1 case in bone marrow oedema.

**Conclusions:** WBMRI is a sensitive, noninvasive method to evaluate the disease activity, which is better than serum creatine kinase. And it is of great value to screen the complication or concomitant diseases such as ILD and osteonecrosis.

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#### THU0630 IMMUNE-RELATED ADVERSE EVENTS ASSOCIATED WITH IMMUNE CHECKPOINT INHIBITORS IN SPANISH PATIENTS

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**Background:** Immune checkpoint inhibitors (ICI), a type of immunotherapy which block negative co-stimulation of T-cells, have surfaced as an important alternative of treatment for advanced malignancies. Unfortunately, these agents have been associated with immune-related adverse events (irAE).

**Objectives:** To analyse the frequency, type and outcome of irAE in Spanish patients treated with ICI.

**Methods:** We carried out a retrospective, observational and longitudinal study, including adult patients diagnosed with cancer and treated with ICI followed in our centre (Spanish university hospital) from October 2012 to December 2017. Demographics, clinical, therapeutic and outcome data were collected from their medical records.

**Results:** We included 125 patients, 66.4% males, all them Caucasians, with a mean age at diagnosis 63 years (range:42-81). The most common types of cancers were lung carcinoma (61.6%) and melanoma (12.8%). The ICI most frequently used was nivolumab (29.6%), followed by pembrolizumab (8.8%) and atezolizumab (8.8%), as monotherapy. It was also common, combinations, or the use of consecutive way with different drugs. Occurrence of irAE was reported in 51 patients (table 1) and the systems more frequently involved were gastrointestinal tract, endocrine glands and skin. Most of these cases were treated steroids at high doses but a case of colitis required infliximab. Withdrawal of immunotherapy was required in almost half of the adverse events (45%). During the follow-up period there were 5 deaths associated with irAE.

**Conclusions:** The frequency and type of irAE associated ICI in our series were similar to those reported in previous studies, except for rheumatological events, being arthritis and sicca syndrome the most frequently reported in other series. These adverse events are not rare and may be a potential cause of morbidity in these patients, so it is important to recognise them early and treat properly, with the rheumatologist being one of the specialists involved.

**Disclosure of Interest:** None declared

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#### THU0631 REFRACTORY AND SEVERE UVEITIC CYSTOID MACULAR OEDEMA IMPROVES WITH TOCILIZUMAB IN DIFFERENT IMMUNE-MEDIATED INFLAMMATORY DISEASES

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**Background:** Cystoid macular oedema (CME) represents the leading cause of blindness in uveitis of different immune-mediated inflammatory diseases (IMIDs).

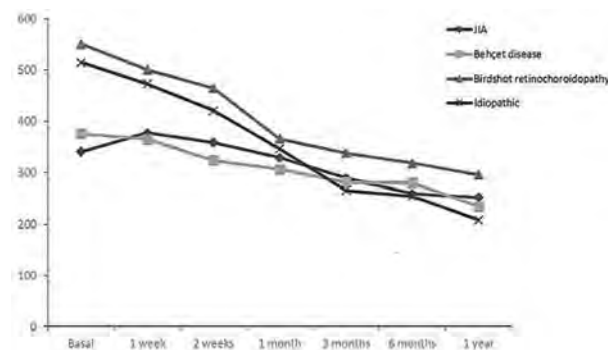
**Objectives:** Our aim was to evaluate the efficacy of Tocilizumab (TCZ) in different IMIDs with refractory CME.

**Methods:** Multicentre study of 24 patients with CME due to uveitis of different IMIDs refractory to traditional treatment with systemic corticosteroids and at least one conventional immunosuppressive drug including in most cases biological therapy (n=21). CME was defined by (OCT >300 µm). We studied CME with TCZ in 4 different IMID: juvenile idiopathic arthritis (JiA), Behçet's disease (BD), Birdshot retinochoroidopathy (BR) and idiopathic.

The main outcome was the improvement of macular thickness. Other variables assessed were inflammation of the anterior chamber and vitreous and best corrected visual acuity (BCVA)

**Results:** We studied 16 ♀/8 ♂, mean age 35.2±19.3 years. The associated diseases were: JiA (n=9), BD, BR<sup>4</sup> and idiopathic.<sup>4</sup> The ocular patterns were: panuveitis,<sup>9</sup> anterior uveitis,<sup>6</sup> posterior uveitis<sup>5</sup> and intermediate uveitis.<sup>4</sup> Most patients had bilateral involvement.<sup>22</sup> The biological therapy used before the administration of TCZ were infliximab,<sup>8</sup> adalimumab,<sup>18</sup> etanercept,<sup>2</sup> golimumab,<sup>2</sup> rituximab,<sup>2</sup> abatacept,<sup>3</sup> anakinra<sup>1</sup> and daclizumab.<sup>1</sup>

TCZ administration schedule was 8 mg/kg/4 weeks iv.<sup>23</sup> or every 2 weeks.<sup>1</sup> TCZ was used in monotherapy<sup>12</sup> or combined with conventional immunosuppressive drugs.<sup>12</sup> OCT values improved considerably in 12 months: in JiA from 340.6±134.1 µm to 252.5±30 µm, in BD from 375.1±117 µm to 235±7.1 µm, in BR from 550.7±214.4 µm to 295.5±43.2 µm and in idiopathic from 515±219.6 µm to 208.3±46.7 µm (figure 1). Inflammation in anterior chamber and vitritis and BCVA also improved in the 4 subtypes. No minor side effects were observed, so no patient had to stop treatment.



**Conclusions:** TCZ seems a rapid effective treatment in severe and refractory uveitic CME, regardless of the underlying IMIDs.

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iRAEs	n	frequency	Time (months)	Treatment	Discontinuation of immunotherapy	Response to treatment
Gastrointestinal tract	17	13.6%	4	23% steroid	58% no	17% steroid
Colitis	8			5% Infliximab	29.4% definitive	83% improvement
Intestinal perforation	1			72% nothing	11.7% temporary	
Hepatitis	8					
Endocrine glands	11	8.8%	4	18% steroid	90% no	63% stable
Hypophysitis	1			82% Other	10% definitive	37% improvement
Hypothyroidism	7					
Adrenal insufficiency	2					
Other	1					
Skin	10	8%	4	20% steroid	60% no	100% improvement
Rash/Prurito	7			20% topic treatment	30% definitive	
Vitiligo	1			60% other	10% temporal	
Other	2					
Rheumatological	7	5.6%	5	20% steroid	72% no	100% improvement
Arthralgias	3			20% local treatment	28% definitive	
Polymyalgia rheumatic	1			60% other		
Sicca syndrome	1					
Inflammatory myopathy	1					
Tenosynovitis	1					
Haematological	4	3.2%	Not available	25% steroid	50% no	25% death
Thrombocytopenia	2				25% definitive	75% improvement
Neutropenia	1				25% temporal	
Pancytopenia	1					
Lung (Pneumonitis)	3	2.4%	12	100% steroid	66% definitive	33% stable: 33% improvement; 33% death
					33% temporary	
Ophthalmologic	1	0.8%	Not available	Not available	Not available	Not available
Neuropathy	1	0.8%	2	steroid	Not available	Improvement
Cardiac	1	0.8%	Not available	Not available	Not available	Not available

THU0632

#### IDENTIFICATION OF ABERRANT T-CELL PHENOTYPE IN EPISODIC ANGIOEDEMA WITH HYPEREOSINOPHILIA (GLEICH SYNDROME) IN 30 PATIENTS: FREQUENCY, CLINICAL IMPLICATION AND PROGNOSIS

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**Background:** Gleich's syndrome or "Episodic Angioedema with eosinophilia" (EAE) is a rare disorder characterised by recurrent episodes of angioedema, concomitant hyper eosinophilia and frequent elevated serum Immunoglobulin M (IgM) levels. So far, no series were reported in literature.

**Objectives:** In this retrospective French study we report the clinical spectrum and therapeutic management of patients with EAE in a large French nationwide retrospective multicenter cohort study, with a particular focus on lymphoid variant of hyper eosinophilic syndromes-related EAE.

**Results:** Thirty patients were included with a median age at diagnosis of 41 years<sup>5-84</sup> and a median follow up duration of 53 months.<sup>31-99</sup> The median time between two angioedema crises was 30 days<sup>7-192</sup> and the median duration of each crisis was 5.5 days<sup>1-90</sup> with swelling affected the face, the neck, the upper limbs, and the lower limbs. Twelve patients (40%) had an abdominal. The median blood eosinophil count at diagnosis was 6.9 G/L [1.44-53.5] and total serum IgM levels were increased in 20 patients (67%). Abnormal T-cell immunophenotypes were detected in 12 patients (40%): CD3-CD4+ in 8 patients, CD3 +CD4+CD7 in 2, CD3-CD3ic+CD4 CD8-CD5+CD7 in 1 patient and CD3 +4-8-2+5+7+TCR γδ in 1 patients with presence of clonal TCR γ gene rearrangement in 5 cases (17%). Fourteen patients (47%) had bone marrow cytology and/or histology revealing high eosinophil counts and/or infiltration by non-dystrophic eosinophils in all cases. Eosinophilic perivascular infiltration (without vasculitis) was reported in 2 patients (7%) in which a skin biopsy was performed. An eosinophilic infiltrate was also found in various organs (stomach, gallbladder, liver, ileon, and colon) that were biopsied and/or surgically removed.

All 30 patients were initially treated with glucocorticoid with a median initial dose of 40 mg of daily prednisone.<sup>5-80</sup> After first line treatment and a median time of 15.2 months (95% CI: 9.4-50.1), disease was considered as uncontrolled in 24 patients (80%) with relapses in 15 patients (50%) or glucocorticoid's dependence in 9 (30%).

Glucocorticoid-sparing agents were used in 14 cases (47%) for relapses (n=8) or glucocorticoid- dependence (n=6). Associated treatments consisted of interferon-α (n=8, 27%), mepolizumab (n=2, 7%), ciclosporin A (n=5, 17%), methotrexate (n=4, 13%), hydroxycarbamide (n=2, 7%).

The presence of an abnormal T-cell population was the sole factor associated with a shorter time to relapse (hazard ratio 4.15 [CI 95% 1.18-14.66; p=0.02]).

Two deaths occurred during follow-up (7%) due to lymphoma evolution for one and unexplained sudden death for the other.

**Conclusions:** EAE could be classified as a lymphoid variant of hyper eosinophilic syndrome but that it is an heterogeneous condition. Although patients usually respond well to glucocorticoids, those with a circulating T-cell clonal population are at higher risk of both relapse and lymphoma suggesting necessity to long-term treatment and close monitoring.

**Disclosure of Interest:** None declared

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THU0633

#### ACUTE FORM OF SARCOIDOSIS (LÖFGREN SYNDROME) IN RHEUMATOLOGY PRACTICE

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**Background :** Löfgren syndrome (LS) is the acute form of sarcoidosis, characterised by erythema nodosum (EN), joints involvement, fever and intrathoracic lymphadenopathy. LS clinical polymorphism leads to diagnostic errors.

**Objectives:** To study the clinical, laboratory and radiological features of early stages of sarcoidosis in a cohort of patients referred to rheumatology centre.

**Methods:** The study included 125 patients (104 females and 21 males, mean age 42±12 y) with clinical and radiological features of LS. All patients were referred to rheumatology centre with EN diagnosis. The median duration of disease was 1 (0,5-2,0) months. All patients were subjected to comprehensive clinical and laboratory-instrumental examination, including biochemical panel and immunological parameters, chest X-ray or CT, as well as (15 cases) histopathology examination of nodular biopsy specimens of the skin and subcutaneous fat.

**Results:** In 97% pts EN involved the lower legs, mostly the anterior surface, in 35% - the hips, in 25% - the upper limbs and in 3% - the trunk. Symmetric lesions were documented in 50% of patients. Confluence of nodules forming conglomerates was registered in 48% pts. The involvement of more than 50% of lower leg surface (68%) was directly associated with the number of nodules (p<0.001; r=0.60) and C-reactive protein level (p=0.006; r=0.38). There was a direct correlation between the number of nodules and EN duration (p=0.04; r=0.20), and also the tendency to nodules confluence (p<0.001; r=0.39). Joint involvement was documented in 106 (85%) patients, with predominantly ankle (66,4%) and knee (40%) joints affected. Asymmetry of joint involvement was documented in 8% pts. Articular manifestations preceded the emergence of EN in 35 (28%) patients by mean 12±9 days. There was a significant direct correlation between the duration of articular syndrome and appearance of nodules and their number (p=0.02; r=0.45). Joint involvement after EN manifestation - in an average 12±7 days - was documented in 10% of cases. Male gender (odds ratio (OR) 6.5; confidence



interval (CI) 1.2–35;  $p=0.026$ ) and presence of nodular conglomerates (OR 4.8; CI 1.4–16.1;  $p=0.01$ ) were the key predictors of ground glass opacity (GGO) CT phenomenon. In 90% of patients EN did not relapse, and articular syndrome almost completely regressed during 1 year follow-up.

**Conclusions:** Patients with an acute form of sarcoidosis require coordinated action of different medical specialties, including rheumatologists, to determine the scope of further examination and adequate therapeutic regimen.

**Disclosure of Interest:** None declared

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**THU0634 RISK OF SUDDEN CARDIAC DEATH IN PATIENTS WITH SARCOIDOSIS: A POPULATION-BASED RETROSPECTIVE COHORT STUDY**

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**Background:** Sarcoidosis is an inflammatory, non-caseating, granulomatous disorder of unknown etiology which can affect any body system including the heart and can be associated with increased risk of cardiovascular disease including sudden cardiac death (SCD). However, the risk and incidence of SCD are unknown.

**Objectives:** We sought to determine whether the risk of SCD in patients with sarcoidosis is higher than in the general population.

**Methods:** A population-based cohort of 345 incident cases of sarcoidosis (50% female; 90% Caucasian, 5% African-American; mean age 45.6 years) among Olmsted County, Minnesota residents in 1976–2013 was identified from a comprehensive medical record-linkage system. Medical records of those cases were individually reviewed to confirm the diagnosis of sarcoidosis which required physician diagnosis supported by histopathology, compatible clinical presentation and exclusion of other granulomatous diseases. A total of 345 sex and age-matched comparators (50% female; 95% Caucasian, 1% African-American; mean age 45.4 years) were also identified from the same underlying population. Mortality, including time, place and cause of death of cases and comparators were individually reviewed for SCD events. SCD incidence rates are reported per 1 00 000 person-years and Cox proportional hazards models were used for comparisons between groups.

**Results:** The median length of follow-up was 12.9 (6.0–23.4) years and 15.8 (6.8–25.5) for cases and comparators, respectively. Of the 58 deaths in patients with sarcoidosis, 10 were due to definite/probable SCD, versus 57 all-cause and 9 definite/probable SCDs in comparators. Incidence rate of SCD in sarcoidosis was 192 per 1 00 000 person-years (PY) (95% confidence interval (CI), 92–352) versus 155 per 100,000 PY (95% CI, 71–294) in comparators, corresponding to the hazard ratio of 1.28 (95% CI, 0.52–3.17,  $p=0.59$ ). Analysis by time of SCD, sex, age, calendar year of incidence/index date also did not reveal a significantly different rate of SCD between the 2 groups as demonstrated in table 1.

Category	Number of deaths in sarcoidosis/non-sarcoidosis	Rate per 100,000 PY in sarcoidosis (95% CI)	Rate per 100,000 PY in non-sarcoidosis (95% CI)	Hazard Ratio (95% CI)	p-value
SCD at night (22:00–06:00)	3/1	57 (12–168)	17 (0.4–95)	3.76 (0.39–36.47)	0.25
SCD at day	6/6	115 (42–250)	103 (38–224)	1.16 (0.37–3.60)	0.80
SCD an unknown time	1/2	NA	NA	NA	
Females	6/6	217 (79–471)	205 (75–447)	1.12 (0.37–3.47)	0.85
Males	4/3	163 (44–418)	103 (21–302)	1.49 (0.33–6.69)	0.60
Age: 18–39 years	0/0	0	0	NA	
Age: 40–59 years	2/0	76 (9–275)	0	NA	
Age: 60+ years	8/9	450 (194–886)	470 (215–895)	NA	
1976–1994	3/3	259 (54–756)	228 (47–666)	NA	

1995–2004	1/2	62 (2–345)	110 (13–397)	NA
2005+	6/4	244 (90–532)	149 (41–382)	NA

**Conclusions:** In this first ever population-based evaluation of SCD in sarcoidosis, patients are not at increased risk for SCD (all sub-types). These findings may reflect actual risk, but estimates may be affected by low statistical power. Future studies may further elucidate the risk and nature of cardiac death among patients with sarcoidosis.

**Disclosure of Interest:** None declared

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**THU0635 PREGNANCY OUTCOMES IN MIXED CONNECTIVE TISSUE DISEASE: RESULTS FROM A MULTICENTRE COHORT STUDY**

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**Background:** Mixed connective tissue disease (MCTD) is characterised by signs and symptoms of a combination of disorders, primarily systemic lupus erythematosus (SLE), scleroderma and polymyositis and is characterised by the presence of high titre antibodies to U1-ribonucleoprotein (RNP).

When planning a pregnancy in patients with connective tissue diseases, ENA profiling is suggested but generally refers to testing for maternal antibodies specifically to components of the SSA/Ro-SSB/La ribonucleoprotein complex since these have been associated with foetal cardiac conduction abnormalities and neonatal skin rashes. Nevertheless, little is known about the maternal and foetal pregnancy outcomes in women with the presence of anti-U1RNP antibodies absent reactivity to SSA/Ro-SSB/La.

**Objectives:** We aimed to investigate foetal and maternal pregnancy outcomes from a large multicentre cohort of MCTD women.

**Methods:** Data was retrospectively collected from S. Giovanni Bosco Hospital and Sant' Anna University Hospital, Turin, Italy, the Lupus Unit, Department of Rheumatology at St Thomas' Hospital, London, UK, Hospital das Clínicas da Faculdade de Medicina da Universidade de Sao Paulo, Sao Paulo, Brazil, Hospital Reina Sofia de Córdoba, Spain, ASST Spedali Civili di Brescia, Brescia, Italy.

**Inclusion criteria included:** Women ever pregnant who fulfilled the established criteria of MCTD with confirmed anti-U1RNP positivity.

**Results:** This multicentre retrospective cohort study describes the foetal and maternal outcomes of 203 pregnancies in 94 consecutive women ever pregnant (mean age at data collection 45.1 years old, S.D. 10.9; mean disease duration at data collection 12.9 years, S.D. 8.5). Demographic, clinical and laboratory characteristics are summarised in table 1. Of the 203 pregnancies analysed the foetal outcomes were as follows: 146 (71.9%) resulted in live births, 38 (18.7%) in miscarriages, 18 (8.9%) in stillbirths (after 20 weeks gestation) and eleven (5.4%) cases showed intrauterine growth restriction (IUGR). Maternal pregnancy outcomes were as follows: eight (3.9%) cases developed pre-eclampsia, two (0.9%) cases developed eclampsia, 31 (15.3%) women developed gestational hypertension and three (1.5%) cases were diagnosed with gestational diabetes. Moreover, we report a case of complete congenital heart block (0.45%) and a case of skin rash in consecutive offspring born to a mother with anti U1RNP antibodies in the absence of anti-Ro/SSA-SSB/La antibodies.

Patients Characteristics	# (n)	%
Age at data collection, mean (S.D.), years	45.1 (10.9)	
Ethnicity		
Caucasian, n	148	72.9
Black, n	8	3.9
Asian, n	4	2.0
Other, n	13	6.4
Diagnosis		
MCTD, n	148	100
Disease duration at data collection, mean (S.D.), years	12.9 (8.5)	
MCTD and aPL, n	13	1.6
MCTD and aPL, n	6	0.8
Clinical manifestations		
Hemostatic, n	36	17.9
SLE, n	17	8.4
Sjögren, n	15	7.4
Scleroderma, n	10	5.0
Raynaud, n	9	4.4
Myositis, n	3	1.5
Keratomy, n	6	3.0
Rheumatism, n	27	13.2
Neurological, n	6	2.9
Cardiovascular risk factors		
History of smoking, n	10	5.0
Arterial Hypertension, n	13	6.4
Hyperlipidemia, n	13	6.4
Diabetes, n	2	1.0
Laboratory testing		
Hypocomplementemia (C3), n	28	13.8
Hypocomplementemia (C4), n	25	12.3
anti-dsDNA positive, n	12	5.9
Hypogammaglobulinemia, n	47	23.2

**Conclusions:** The observed live-birth-rate was as high as 72%, with poorer foetal outcomes observed in MCTD women with antiphospholipid antibodies and

pulmonary or muscular involvement. While the true frequency of heart block associated with anti-U1RNP remains to be determined, this study raises the consideration of echocardiographic surveillance in this setting. Women with MCTD should receive a specific counselling when planning a pregnancy, as it is currently done in women with SLE.

**Disclosure of Interest:** None declared

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**THU0636 CANAKINUMAB TREATMENT IN ADULT-ONSET STILL'S DISEASE: CASE SERIES**

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**Background:** In Adult-onset Still's disease (AOSD), cases refractory to typical DMARDs. Canakinumab (an anti-IL-1 $\beta$  monoclonal antibody) has been reported to be effective in a limited number of refractory cases.<sup>1</sup>

**Objectives:** The aim of this retrospective study was to represent AOSD patients treated with Canakinumab in 3 centres.

**Methods:** The follow up data of 10 AOSD patients (8 female, 2 male), who were followed up in outpatient clinics of 3 tertiary centres were reviewed retrospectively. The initial characteristics and follow up findings were reported.

**Results:** The mean timespan between the initial diagnosis and Canakinumab treatment 45.2 $\pm$ 29 months (mean  $\pm$ SD). Before the onset of Canakinumab therapy, all patients were exposed to methotrexate, 1 to leflunomide, 8 to Tocilizumab and 8 to Anakinra. As for the biologic agents, 3 patients were also treated beforehand with Infliximab, 2 with Adalimumab, 2 with Etanercept and 2 with Rituximab. Canakinumab therapy was initiated in all patients with the indication of refractory disease under other medications, except for the one in whom neutropenia became evident under anakinra. The mean number of Canakinumab injections was 9.3 $\pm$ 8. The mean follow-up period of patients treated with Canakinumab was 43.1 $\pm$ 33 months. Seven out of 10 patients are still being treated with Canakinumab of 150 mg/month and one of 150 mg/every 2 months. One patient had a single injection and was fully controlled. The mean ferritin measure of 9 patients was reduced from 1292.3 $\pm$ 1530 ng/ml to 354 $\pm$ 530.2 ng/ml following the Canakinumab therapy (p=0.035). The mean of patient-reported global visual analogue scale (PG-VAS) scores was reduced from 7.4 $\pm$ 2.4 to 2.3 $\pm$ 2.2 with Canakinumab (p<0.001). Mean Erythrocyte sedimentation rate (ESR) was reduced from 44.2  $\pm$ 35.1 to 22.7 $\pm$ 26.5 with the help of Canakinumab therapy (p=0.005). Six patients are still on prednisolone at a maximum dose of 10 mg/day. The indication of therapy termination in the remaining 1 patient was the diagnosis of tuberculosis at 9th month of the treatment despite isoniazid prophylaxis. The patient was also treated with multiple biological agents beforehand, therefore it is not easy to conclude that treatment with Canakinumab induces tuberculosis flares.

**Conclusions:** Canakinumab treatment seems to be effective in refractory AOSD patients who were previously treated with various agents. We state that an IL-1 blocking agent, Canakinumab is a relatively safe and effective alternative in managing refractory AOSD cases. On the other hand, randomised controlled trials are needed to further investigate the role of Canakinumab in these cases as well as its use as the first choice of biologic agents.

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**THU0637 EVALUATIONS OF COMPLEMENT PATHWAYS IN IGG4 RELATED DISEASE**

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**Background:** In IgG4 related disease (IgG4-RD), hypocomplementemia is known to be seen. Complement pathways consist of three pathways, classical,

alternative, and lectin pathways. Although IgG1 and IgG3 have ability to activate complement, IgG4 is known to be ineffective at activating complement.

**Objectives:** We attempted to elucidate which complement pathway is mainly associated with IgG4-RD.

**Methods:** Levels of complement elements and complement-associated elements, C1q, C2, C3, C3b/iC3b, C4, C4b, C5, C5a, C9, Factor D, Factor I, mannose-binding lectin (MBL), Factor B, Factor H, and properdin in preserved sera of patients with IgG4-RD at diagnosis and at remission were measured using multiplex bead-based assay. We compared complement levels at diagnosis of IgG4-RD patients with those of sex-matched healthy donors.

**Results:** This study included 28 IgG4-RD patients and sex-matched 28 healthy donors. The median age at diagnosis and healthy donors' age were 65 [interquartile range (IQR): 55–70] and 64 (IQR:56–73), respectively. Patients with IgG4-RD at diagnosis had significantly higher levels of C5 and C5a [33347 ng/mL vs. 30375 ng/mL (median), p=0.0293, 16417 pg/mL vs. 7083 pg/mL, p<0.0001, respectively] and significantly lower levels of C4, C4b, and Factor D (219671 ng/mL vs. 325596 ng/mL, p=0.0140, 8784 ng/mL vs. 16285 ng/mL, p=0.0101, 4569 ng/mL vs. 5482 ng/mL, p=0.0299, respectively) compared to healthy donors. Levels of C5, C5a, C4, C4b, and Factor D were not different in two groups which were divided by clinical manifestations at diagnosis except for lower C4b levels in patients with lymphadenopathy compared with patients without lymphadenopathy. There were no differences in MBL, which was associated with the lectin pathway. In remission after the administrations of prednisolone, levels of C5a significantly decreased compared to levels of C5a at diagnosis (16305 pg/mL to 10029 pg/mL, p=0.0043). Other complement factors did not change significantly.

**Conclusions:** The classical complement pathway may be associated with IgG4-RD rather than the alternative pathway and the lectin pathway based on results except for Factor D.

**Disclosure of Interest:** None declared

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**THU0638 CLINICAL CHARACTERISTIC OF A GROUP OF PATIENTS WITH PSTPIP1-ASSOCIATED MYELOID-RELATED PROTEINEMIA INFLAMMATORY SYNDROME (PAMI)**

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**Background:** PSTPIP1-gene associated autoinflammatory diseases is a group of clinically diverse syndromes predominantly manifested by various skin conditions (pyoderma gangrenosum, acne, hidradenitis suppurativa, necrotizing fasciitis). Yet one of them – PAMI – manifests mainly with haematologic abnormalities and autoinflammation with or without purulent features, presenting diagnostic difficulties for treating physicians – mainly haematologists. PAMI treatment is also challenging as IL-1 inhibitors alleviate inflammatory symptoms but cytopenias usually require additional therapeutic agents.

**Methods:** We describe five PAMI patients from 3 families: (2 girls, 2 boys, and affected mother of two patients). c.748G>A(p.E250K) heterozygous mutation in PSTPIP1 was detected in all patients via targeted panel next generation sequencing and confirmed by Sanger sequencing.

**Results:** The median age of disease onset was 2 years (varied from at-birth onset to 7 years), the adult patient manifested at the age of 3. As described all patients manifested with cytopenias: thrombocytopenia in three, severe anaemia in five, neutropenia in three. All patients had elevated CRP and zinc levels, as previously described. Splenomegaly was noted in five, lymphadenopathy in one, colitis in one, severe arthritis in one (adult patient) and arthropathy in two patients. Mild pyoderma was noted only in one patient, two patients had skin vasculitis. One patient developed myelodysplastic syndrome and underwent successful hematopoietic stem cell transplantation (HSCT).

All patients received various immunosuppression prior to diagnosis with partial effect. After PAMI diagnosis rituximab was effective in two out of three, tocilizumab in one out of two, high dose anakinra in one patient. The girl who underwent HSCT is currently well, with full donor chimerism.

**Conclusions:** Haematologists need to be aware of the PAMI phenotype and include it in the diagnostic algorithm. Treatment still remains challenging and requires further investigation in larger groups of patients.

**Disclosure of Interest:** None declared

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**THU0639 CHINESE EXPERIENCE WITH METHOTREXATE AS MAINTENANCE THERAPY IN IGG4-RELATED DISEASE**

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**Background:** So far, for IgG4-related disease, no randomised clinical trials concerning therapy are published. Corticosteroids are considered the first-line treatment and most patients respond promptly to steroids. However, recurrent or refractory cases are common. Various immunosuppressive agents such as azathioprine (AZA), methotrexate or mycophenolate mofetil (MMF) have been introduced as corticosteroid-sparing treatment on small case series.<sup>1</sup> High cost of MMF and occasional severe bone marrow toxicity of Aza have limited their use in Chinese patients. Efficacious therapies with less toxicity and more cost-effectiveness were required to be identified and thus modify the immunotherapeutic strategies. Methotrexate (MTX) was commonly used in many other autoimmune disease. In the present study, we retrospectively reviewed 84 IgG4-RD patients who received MMF, Aza or MTX as maintenance regimens, compared the efficacy among these three groups and observed side effects of the medication.

**Objectives:** To assess the efficacy, safety and tolerability of methotrexate as maintenance therapy in the treatment of IgG4-related disease.

**Methods:** We retrospectively reviewed 84 IgG4-RD patients refractory or recurrent to steroids in south China from January 2012 to December 2015 who received MMF, Aza or MTX as maintenance regimen. MMF was administered daily to a maximum of 3 g/day. Aza was given at a dose maximum of 200 mg/day. MTX was given at a dose of 10–20 mg/week. Steroids were continued at the lowest effective dose. Details of the clinical presentation, serological, immunological variables and side effects were collected.

**Results:** Of the 84 patients, no significance of demographic variables was found among MMF group (22 cases), Aza group (29 cases), and MTX group (33 cases). The 2 year overall, the three groups had similar rates of remaining remission, which was 87.9% (29/33) in MTX group, 86.2% (25/29) in Aza group and 86.3 (19/22) in MMF group. Of the 11 recurrent cases despite immunosuppressive therapies, 2 cases were related to thyroid gland, 4 cases were related to pancreas, 3 cases were related to nose, and 2 cases were related to brain. All cases but the 2 patients with brain lesions achieved remission again after we changed the immunosuppressives. One case on Aza had severe bone marrow toxicity and 2 cases on MMF had severe infection. None of the cases on MTX had side effects affecting the treatment course. It's only associated with reversible liver dysfunction in our study.

**Conclusions:** MTX was as efficacious as MMF and Aza in maintaining remission in IgG4-related diseases, but with lower price and less severe side effects. IgG4-related brain lesions may be refractory and probably need to be treated with more aggressive agents.

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THURSDAY, 14 JUNE 2018

**Public health, health services research and health economics**
**THU0640 PHARMACOLOGICAL TREATMENT AMONG NEWLY DIAGNOSED PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS IN THE UNITED STATES**

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**Background:** Juvenile idiopathic arthritis (JIA) is a chronic condition affecting approximately 3 000 000 children and adolescents in the United States, yet little is documented about its real-world burden or treatment patterns.<sup>1</sup>

**Objectives:** To describe treatment patterns among JIA patients (pts) who initiated biological and non-biologic DMARDs.

**Methods:** Truven Health Analytics MarketScan<sup>®</sup> Commercial Database was used to identify pts aged 2–17 years with a new JIA diagnosis (index date; 2008–2016) and 12 months of continuous enrolment pre- and post-diagnosis. Pts with other rheumatic or autoimmune conditions were excluded. Receipt of a biologic and/or non-biologic was evaluated on or after the new JIA diagnosis. JIA-related

healthcare resource utilisation was defined as the presence of JIA diagnosis on a medical claim.

**Results:** A total of 3815 pts newly diagnosed with JIA met study selection criteria (mean [SD] age 10.0 [4.5] years, 69.0% female). Pts with 12 months of continuous enrolment post-treatment initiation (n=2014) were classified as non-biologic only (n=734), biologic only (n=873), and both biologic and non-biologic (n=407) users. Among all three cohorts, baseline corticosteroid use was 48.8%–60.4%, prescription NSAID use 69.6%–85.3% and opioid use 24.5%–29.0%. Mean (SD) number of JIA-related outpatient office visits was 4.9 (3.2) in non-biologic-only users, 6.0 (3.8) in biologic and non-biologic users, and 5.0 (4.4) in biologic-only users. The most commonly used non-biologic was MTX and biologic was etanercept (table 1). In the year following diagnosis, total JIA-related costs were highest among pts who used only biologics (mean \$27,292; SD \$32,833; median \$20,782) vs biologic and non-biologic agents (mean \$15,808; SD \$16,086; median \$11,925) and vs only non-biologics (mean \$4094; SD \$9292; median \$1918) (all p<0.001). Mean prescription costs in the year following biologic initiation were \$17 985 (SD \$11,188) for etanercept, \$26 217 (SD \$15,039) for adalimumab and \$38 260 (SD \$42,260) for infliximab. Of pts treated with a biologic only, TNF inhibitors (TNFi) comprised 87.1% of their treatment costs.

**Abstract THU0640 – Table 1.** JIA Treatment Frequency

	First agent used	Biologic-only users (n=873)	Biologic and non-biologic users (n=407)	Non-biologic-only users (n=734)	All treated patients (n=2014)	
<b>Biologics</b>	Abatacept	15 (1.7)	6 (1.5)		21 (1.0)	
	Adalimumab	188 (21.0)	106 (25.7)		294 (14.4)	
	Anakinra	43 (4.8)	9 (2.2)		52 (2.5)	
	Etanercept	523 (58.4)	259 (62.7)		782 (38.3)	
	Infliximab	71 (7.9)	20 (4.8)		91 (4.5)	
	Intravenous immunoglobulin	17 (1.9)	1 (0.2)		18 (0.9)	
	Tocilizumab	16 (1.8)	6 (1.5)		22 (1.1)	
	<b>Non-biologics</b>	Hydroxychloroquine		31 (7.5)	149 (20.2)	180 (8.8)
		MTX		341 (82.6)	506 (68.8)	847 (41.4)
		Sulfasalazine		42 (10.2)	75 (10.2)	117 (5.7)
Other (azathioprine, leflunomide)			5 (1.2)	15 (2.0)	20 (1.0)	

Data are n (%)

**Conclusions:** Initial JIA treatment is driven by etanercept, MTX and adalimumab, with the majority of biologic costs coming from TNFi. Receipt of other supportive medications (corticosteroids and NSAIDs) was common and JIA-related costs varied substantially by treatment cohort.

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**Disclosure of Interest:** A. Marshall Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, K. Gupta Employee of: Bristol-Myers Squibb, M. Pazirandeh Employee of: Bristol-Myers Squibb, M. Bonafede Grant/research support from: Bristol-Myers Squibb, Employee of: Truven Health Analytics (IBM), D. McMorrow Grant/research support from: Bristol-Myers Squibb, Employee of: Truven Health Analytics (IBM)

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**THU0641 MUSCULOSKELETAL DISEASE CLINIC MANAGED BY A RHEUMATOLOGY DEPARTMENT**

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**Background:** Medical pathology of the Locomotor Apparatus (LA) is highly prevalent in the general population, tends to chronicity, generates an important temporary or definitive disability with great impact on the quality of life and functionality of the patient and entails high indirect and direct costs for the System National Health Classically, the medical pathology of LA has been managed by Traumatology departments.

**Objectives:** To analyse the characteristics of an LA clinic managed by the Rheumatology department and compare the data with the Traumatology department in the health area of the north of Tenerife (Reference population: 4 30 021 inhabitants).



**Methods:** We present the data collected from the Rheumatology clinic aimed to treat the medical pathology of the LA during the first 3 months, October to December 2017 and we compared the results with the same period of 2016, when this consultation was in charge of Traumatology department. Patients are referred from Primary Care (PC). We recorded the epidemiological characteristics of the patients, reason for consultation and final diagnosis, ability to resolve the consultation, need to request additional tests, treatment prescribed at discharge and referrals to other specialties.

**Results:** We treated 744 patients, with an average age of 55.26 years ( $\pm 15.02$ ), mainly women (62.6%). The most frequent referral consultation were: gonalgia (30.6%), polyarthralgia (14.5%) and low back pain (13.7%). Peripheral Osteoarthritis (26.6%) and soft tissue diseases (24.2%) were the most frequent processes. In 11.6% of the cases, no organic cause was found that justified the referred clinic ("nonspecific mechanical pathology") and 4.3% were asymptomatic when assessed. They provided complementary tests in the first consultation 85.2% of patients: 92.43% simple radiographs and 10.72% magnetic resonances. We requested: 7.2% MRI (54), 7.8% X-Ray (58), 7.1% Ultrasound (53), 5% Analysis,<sup>37</sup> 4.2% neurophysiological study,<sup>31</sup> 1.2% scintigraphy.<sup>9</sup> Discharged at the first consultation 72.4% and at the second visit 5%, leaving 22.6% of patients still in follow-up. 23.1% of the patients were referred to another specialty, mainly to Traumatology (15.3%). During the same period of time, October-December 2016, Traumatology treated 3730 patients and requested 506 MRI (13.5%).

**Conclusions:** The management of a locomotor apparatus clinic carried out by rheumatologists is more efficient: high resolution capacity in the first consultation, less number of complementary tests requested, mainly MRI (7.2% vs. 13.5%), and little referral to other specialties. It is necessary to create referral protocols from Primary Care to Rheumatology and to enhance the Rheumatology as the medical specialty of reference of the locomotor apparatus musculoskeletal diseases.

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**THU0642 LIVING IN IMMIGRANT COMMUNITIES DOES NOT IMPACT TOTAL KNEE ARTHROPLASTY OUTCOMES: EXPERIENCE FROM A HIGH-VOLUME CENTRE IN THE UNITED STATES**

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**Background:** Social factors affect TKA outcomes in osteoarthritis, both at the individual and neighbourhood level.<sup>1</sup> However, prior studies have not evaluated the influence of the proportion of immigrants within a neighbourhood, as reported for other high-volume and high-cost procedures.<sup>2</sup>

**Objectives:** Our objective was to determine the association of neighbourhood immigrant proportion (IP) on Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain and function scores at baseline and 2 years after elective TKA, and to examine if this is different between sexes.

**Methods:** Individual patient-level variables were obtained from a single institution TKA registry between May 2007 and February 2011, including demographics, baseline and 2 year WOMAC pain and function (0–100; 100 best), and geocodable US addresses. We only included patients living in the tri-state area - i.e. New York, Connecticut and New Jersey which is the catchment area for the hospital. Individual patient level variables were then linked to US Census Bureau data at the census tract level. Data was analysed using univariate and multivariable linear mixed effects models, with census tracts variables treated as random effects. A separate linear mixed-effects model was used to assess the interaction between neighbourhood IP and gender.

**Results:** Table 1 describes the 3,898 TKA cases analysed. In multivariable analyses, patients from neighbourhoods with low IP (<10%) had slightly higher baseline and 2 year WOMAC pain and function scores than those with high IP ( $\geq 40\%$ ), but these differences were not statistically significant (table 2). While women had

worse baseline and 2 year WOMAC pain and function scores (all  $p \leq 0.04$ ), this difference was not significantly influenced by neighbourhood IP (all  $p_{\text{interaction}} \text{ NS}$ ).

**Abstract THU0642 – Table 1.** Baseline characteristics

Characteristic	IP* <10% (n=1032)	IP* $\geq 10$ - <40% (n=1527)	IP* $\geq 40\%$ (n=339)	p-value ( $\leq 10\%$ v. $\geq 40\%$ )
<b>Patient demographics</b>				
Age at surgery (years) mean $\pm$ SD	57.6 $\pm$ 9.2	56.1 $\pm$ 9.6	61.3 $\pm$ 9.8	0.18
Sex: female, n (%)	568 (55.0%)	1538 (60.9%)	246 (70.8%)	<0.001
BMI (kg m <sup>2</sup> ) mean $\pm$ SD	30.1 $\pm$ 5.7	29.9 $\pm$ 6.0	31.0 $\pm$ 6.6	0.03
<b>Race, n (%)</b>				
White	1612 (99.1%)	2597 (90.9%)	259 (76.4%)	
Black	3 (0.3%)	128 (5.1%)	41 (12.1%)	
Asian	9 (0.9%)	47 (1.9%)	18 (5.3%)	
Other	5 (0.3%)	33 (1.4%)	16 (4.7%)	
Unknown	1 (0.1%)	20 (0.8%)	5 (1.5%)	
<b>Ethnicity, n (%)</b>				
Hispanic	3 (0.3%)	35 (1.4%)	16 (4.7%)	<0.001
<b>Patient status</b>				
ASA class				0.81
I-II	678 (80.2%)	2026 (80.2%)	270 (79.7%)	
III-IV	203 (19.7%)	301 (19.8%)	69 (20.4%)	
One or more comorbidities	267 (25.9%)	674 (26.7%)	116 (34.2%)	0.003
<b>Sociodemographic characteristics</b>				
Education level (highest), n (%)				<0.001
Some high school, high school graduate or some college	359 (36.0%)	449 (35.1%)	158 (49.4%)	
College graduate or Masters, professional or doctorate degree	639 (64.6%)	1069 (64.9%)	182 (50.6%)	
<b>Lives alone, n (%)</b>				
No	863 (84.4%)	1891 (73.9%)	229 (69.0%)	<0.001
Yes	159 (15.6%)	536 (21.1%)	105 (31.0%)	
<b>Census tract characteristics</b>				
Poverty, n (%)				<0.001
< 10%	815 (94.3%)	2078 (81.2%)	122 (36.0%)	
10% - <20%	48 (4.7%)	100 (11.9%)	161 (48.1%)	
$\geq 20\%$	9 (0.9%)	149 (5.9%)	54 (15.9%)	
<b>Patient-reported outcomes</b>				
<b>Baseline survey results, mean<math>\pm</math>SD</b>				
WOMAC** pain	54.9 $\pm$ 17.6	54.7 $\pm$ 17.3	51.6 $\pm$ 16.9	<0.001
WOMAC** function	54.2 $\pm$ 16.9	54.1 $\pm$ 17.7	49.1 $\pm$ 17.3	<0.001
<b>2-year survey results</b>				
WOMAC** pain, mean $\pm$ SD	49.3 $\pm$ 14.7	47.3 $\pm$ 15.7	46.5 $\pm$ 17.3	0.01
WOMAC** function, mean $\pm$ SD	46.7 $\pm$ 14.9	45.4 $\pm$ 16.2	43.6 $\pm$ 17.9	0.005

Timepoint	WOMAC** pain estimate $\pm$ SD	p-value	WOMAC** function estimate $\pm$ SD	p-value
Baseline		0.36		0.24
IP* $\geq 10\%$	52.30 $\pm$ 3.26		51.71 $\pm$ 3.28	
IP* $\geq 40\%$	51.19 $\pm$ 3.33		50.31 $\pm$ 3.36	
2-year		0.80		0.87
IP* $\geq 10\%$	45.08 $\pm$ 3.02		45.93 $\pm$ 3.11	
IP* $\geq 40\%$	44.81 $\pm$ 3.09		45.90 $\pm$ 3.18	

Table 2 Impact of neighbourhood immigrant proportion (IP) on WOMAC pain and function.

**Conclusions:** Patients coming from high (>40%) IP neighbourhoods present with worse baseline pain and function. Two years later, worse pain and function persist; however, the difference is not significant. Although sex differences favouring males are notable, these differences are not associated with IP. Social factor contributions to healthcare disparities are multidimensional, and future studies examining immigration-related neighbourhood characteristics may be warranted.

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**THU0643 IMPACT OF SHOULDER ULTRASOUND IN QUALITY OF CARE INDICATORS IN PATIENTS WITH RECENT ONSET OF PAIN**

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**Background:** Ultrasound is a technique that has demonstrated diagnostic accuracy in the periarticular pathology of the shoulder. Although its value is not questioned, any diagnostic or therapeutic instrument must also demonstrate a beneficial impact for the patient in terms of quality of care. The quality of care can be measured by direct indicators (satisfaction surveys, waiting times) or indirect ones (referral rate, need for new consultations). We do not have studies that measure the impact of ultrasound in the assessment of hyperacute shoulder pain or of recent onset (less than a week) pain.

**Objectives:** Our purpose is to determine to what extent its use modifies three indicators of quality of care in relation to hyperacute omalgia of non-traumatic origin.

**Methods:** We conducted an analysis of three indirect indicators of quality of care: Need for reassessment due to pain (NRD), specialised referral rate (TDE) and length of stay in the emergency room (TDU). Records of patients treated for acute omalgia between 2014 and 2016 were reviewed and classified according to whether or not ultrasound was used as a diagnostic tool. For the statistical analysis we used the Student's T test, Fisher's exact test and survival curve (for TDU, TDE and NRD, respectively). The design used was that of a retrospective descriptive study. The information on waiting times was obtained from the CAJAL registry, information on new consults and specialised referral registration were obtained from the HORUS program and CAJAL registry. A comparative retrospective study was carried out based on the usual clinical practice. We examined the records of patients treated between 2015–2016 in the rheumatological emergency unit, who were known diabetics and who underwent an ultrasound-guided infiltration. Using the HORUS program we reviewed the patient's files of the immediate outcome after infiltration and the follow up consults.

**Results:** We included 1433 records of patient. Of these, 547 (38.1%) were examined with ultrasound assistance (Group-ECO) from which 2 were performed by a radiologist and the rest by a trained physician (Rheumatologist or Family Physician). The rest of the assessments, 886 (61.8%) were made without using the ultrasound (Control group), although in 540 cases a different imaging test was used. At 30 days after the first assessment, 90 patients (10.1%) in the control group had consulted again (56 due to emergencies and 34 per AP), while in the ECO-Group 14 (2.5%) consulted again at least once (12 for emergencies and 2 for AP) ( $p<0.001$ ). The referral rate to the specialist in the Control-Group was 36.5%, while in the ECO-Group was 6.21% ( $p<0.0001$ ). The average stay time was 94.5 DE 34.3 min in the Control Group and 105.4 DE 40.1 min in the ECO-Group ( $p<0.0001$ ).

**Conclusions:** The use of ultrasound as a diagnostic tool reduces the need for re-evaluations of patients and the rate of referrals to the specialist in a significant way. On the contrary, it increases the patient's stay time in the emergency room, probably due to delays in the availability of the equipment to perform the diagnostic procedure. Globally, our results show that most quality health care indexes improve in patients assessed by using ultrasonography.

**Disclosure of Interest:** None declared

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#### THU0644 PERCEPTIONS OF BIOSIMILARS AMONG PRACTICING RHEUMATOLOGISTS: RESULTS FROM A MULTICOUNTRY STUDY IN EUROPE

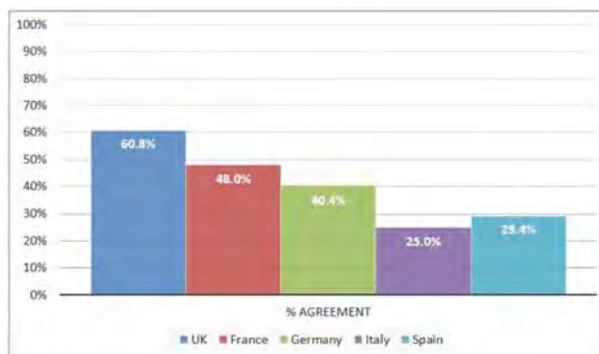
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**Background:** In recent years, a substantial number of biosimilar (BioSm) products have come into the market for the treatment of rheumatic disorders, that might potentially improve patient access to treatment, resulting in cost savings and improved outcomes. However, given the limited regulatory evidence, clinical decision making continues to be a challenge.

**Objectives:** The objective of the study was to assess perceptions of prescribing biosimilars among rheumatologists and gain insights on barriers to access in the EU5 countries (United Kingdom (UK), France (FR), Italy (IT), Spain (SP) and Germany (DE)).

**Methods:** A cross-sectional survey was conducted in Q4 2016 in the EU5 among national, regional and hospital physicians who had been practicing between 3–30 years. Respondents completed a Physician Biosimilar Perceptual Questionnaire, which assessed the overall perception of anti-TNF biosimilars, specific barriers to prescribing them and cost factors influencing the current use and adoption of biosimilars. Data was analysed using descriptive statistics.

**Results:** A total of 256 rheumatologists in the EU5 were recruited as part of the study (with almost equal number of rheumatologists representing each EU5 country). Treating rheumatologists were practicing for an average of 16 years, mainly practicing in teaching hospitals (52%), and urban hospitals (21.9%). Overall, 83% of rheumatologists had awareness of biosimilars (range: 70% in DE and IT to 92% in UK). Among the different domains queried, only one in four rheumatologists trusted BioSm as much as branded biologics (range: 17.3% in IT to 39.2% in UK) and about 30% were comfortable with the safety profiles, and reported that long term efficacy and safety was of great importance for prescribing BioSm. Comparing perceptions of BioSm across countries, only 25% of rheumatologists in IT felt that BioSm offered equivalent efficacy to branded biologics, whereas 60.8% in the UK agreed with the same statement (figure 1). There was a consensus among respondents in all five countries regarding the lower cost of BioSm (range: 56.9% in SP to 72.5% in UK). Over 35% of the rheumatologists anticipated that clinical guidelines would require them to prescribe biosimilars. Data also showed that 63% chose BioSm for cost and 49% for formulary placement in clinical practice.



**Abstract THU0644 – Figure 1** Perceptions of Physicians in EU5: Equivalent efficacy as branded biologics

**Conclusions:** Overall, rheumatologists expressed the greatest level of awareness of biosimilars, even though differences were seen among the countries. Long term safety and efficacy data was of key importance; however, cost and formulary coverage did impact the prescribing pattern.

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#### THU0645 IMPACT OF SECOND-LINE THERAPY WITH ABATACEPT VERSUS OTHER TARGETED DMARDS ON THE RISK FOR INFECTION-RELATED HOSPITALIZATIONS AND ASSOCIATED COSTS AMONG RA PATIENTS IN THE UNITED STATES

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**Background:** Abatacept is a targeted DMARD (tDMARD) with a unique mechanism of action that has demonstrated a lower risk of infection-related hospitalizations as a second-line (2L) therapy compared with other tDMARDs among patients (pts) with RA. The cost savings in the United States associated with this reduced risk of infection-related hospitalizations is not well understood.

**Objectives:** To compare infection-related hospitalisation risk and associated healthcare costs of RA pts who were treated at 2L with abatacept versus other tDMARDs, including TNF- $\alpha$  inhibitors (TNFis) and non-TNFis.

**Methods:** Pts prescribed a 2L tDMARD (index date) who had  $\geq 1$  inpatient diagnosis or  $\geq 2$  outpatient diagnoses of RA in the 12 months prior to the index date were identified from the MarketScan<sup>®</sup> Commercial and Medicare claims databases between 1 January 2010 and 30 September 2015. Pts were required to have 12 months of continuous insurance coverage prior to the index date (baseline period) and throughout the follow-up period ( $\geq 12$  and up to 36 months). All pts were treated with a TNFi in first line. Infection-related hospitalizations and associated costs (on a per-pt per-month [PPPM] basis) were evaluated during baseline and follow-up periods. Multivariable regression analyses were used to evaluate the impact of index drugs on the risk of infection-related hospitalisation, as well as infection-related medical cost change from baseline to follow-up periods, while controlling for differences in baseline pt characteristics.

##### Unadjusted Comparison of Medical Cost, PPPM

	Abatacept	TNFis	Non-TNFis	p-value
Baseline medical costs	\$121	\$48	\$39	0.02
Follow-up medical costs	\$30	\$69	\$102	0.16
Medical cost difference (follow-up – baseline)	–\$91	\$21	\$63	0.005

##### Regression Adjusted Comparison of Difference of Medical Cost, PPPM

	Cost difference, PPPM	p-value
TNFi vs abatacept	\$51	0.09
Non-TNFi vs abatacept	\$76	0.04

**Results:** Among the study population, 285 pts (mean age 55 years; 85% female) were treated with abatacept, 954 with TNFis (mean age 52 years; 82% female) and 288 with non-TNFis (mean age 55 years; 76% female). After controlling for differences in pts' characteristics, Cox regression showed that the risk for an infection-related hospitalisation was significantly greater among those treated with TNFis (hazard ratio [HR] 2.8; 95% CI 1.2, 6.7;  $p=0.02$ ) and higher, although not

significant, among those treated with other non-TNFis (HR 2.4; 95% CI 0.9, 6.3;  $p=0.08$ ) compared with those treated with abatacept. Infection-related medical costs were lower for abatacept compared with other non-TNFis as shown in the table 1.

**Conclusions:** In the real-world setting in the United States, pts treated with abatacept versus other tDMARDs tended to have a lower risk for infection-related hospitalisation and lower infection-related medical costs.

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#### THU0646 EVALUATING THE QUALITY OF CARE FOR RHEUMATOID ARTHRITIS

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**Background:** The Arthritis Alliance of Canada (AAC) has developed performance measures (PMs) to evaluate RA care quality.

**Objectives:** To operationalize and report on 4 PMs using administrative data for British Columbia (BC), Canada: PM1) percentage of patients with new onset RA with at least one visit to a rheumatologist in the first year after diagnosis, PM2) percentage of RA patients under the care of a rheumatologist seen in follow-up at least once per year, PM3) percentage of RA patients dispensed a disease modifying anti-rheumatic drug (DMARD) during the measurement year, PM4) time to DMARD therapy in new onset RA.

**Methods:** All patients with RA visits between 01/01/1997 and 31/12/2009 in BC were identified using health administrative data and followed until December 2014. Cases were identified by  $\geq 2$  physician billing codes for RA  $\geq 8$  weeks but  $\leq 5$  years apart. For this study, only cases age  $>18$  who were seen by a rheumatologist at some point over follow-up were included. PM1: The percentage of incident RA cases with at least one visit to a rheumatologist within one year of their first RA visit was evaluated. PM2: The proportion of prevalent RA cases having at least one visit per year was calculated for those under rheumatology care. PM3: The percentage of prevalent RA patients dispensed a DMARD (including biologic agents and small molecule inhibitors) was calculated. PM4: time from RA onset (defined as first RA visit) to DMARD therapy was reported (in the calendar year of RA incidence), using median and 90th percentile wait time, as well as the proportion meeting the benchmark of 14 days.

**Results:** The cohort included 18 976 incident and 29 639 prevalent RA cases. The percentage of patients seen by a rheumatologist within 1 year from RA diagnosis increased over time, while the percentage of RA patients under the care of a rheumatologist seen in yearly follow-up declined steadily overtime. Further analysis (data not shown) suggests this is due to having more people with longer follow-up in the latter years, and lost to follow-up increasing over time, rather than a true

calendar year effect. The percentage of RA patients dispensed a DMARD was suboptimal (56% $>$ 65%). Of note, patients were not necessarily seen by a rheumatologist during the measurement year. The median time to DMARD improved over time to 23 days in 2009, with roughly one third receiving a DMARD within the benchmark of 14 days.

**Conclusions:** The present study represents the first time the AAC's PMs have been tested in administrative data and highlights where the measures are being met and potential gaps in care which require further examination.

**Disclosure of Interest:** None declared

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#### THU0647 LONGITUDINAL STUDY OF LONG-TERM POVERTY AND PERSISTENT DEPRESSIVE SYMPTOMS IN SLE

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**Background:** A prior study found that persons with SLE in long-term poverty have greater accumulation of disease damage over 6 years than those exiting poverty or never in poverty<sup>1</sup>. The present study evaluates the effect of long-term poverty status on depressive symptoms over the same duration of time.

**Objectives:** Analyse the impact of long-term poverty on prevalent and incident persistent depression after accounting for other risk factors for depression among persons with SLE.

**Methods:** Data are from the UCSF Lupus Outcomes Study in which persons with SLE were recruited in 2003 throughout the U.S. and interviewed annually through 2015. In each year we characterised respondents' poverty status based on household income and family size and administered the CESD measure of depressive symptoms, defining a high level of depressive symptoms using a validated SLE-specific cutpoint ( $\geq 24$ ) associated with a formal diagnosis of depression<sup>2</sup>. Prevalent persistent depression was defined as having high levels of depressive symptoms for  $\geq 3$  years between 2009 and 2015. Incident persistent depression used the same criteria, measured only among those who had low levels of depressive symptoms between 2006 and 2009. Logistic regression was used to estimate the impact of being poor in every year from 2003–2009, permanently leaving poverty by 2009, or never being poor on prevalent and incident persistent depression, with and without adjustment for gender, age, marital status, race/ethnicity, education, disease duration, extent of accumulated damage by 2009 using the Brief Index of Lupus Damage<sup>3</sup>, smoking status, and BMI.

**Results:** 535 persons with SLE were interviewed in each year from 2003 to 2015 (94% female, 65% non-Hispanic whites, mean age in 2003 50 years, range 20–83, mean disease duration 17 years, range 1–51). Between 2003 and 2009, 81% were never poor, 8% exited poverty, and 11% were poor in every year. 89 of the 535 (16.6%) met the study definition of prevalent persistent depression; 23 (7.4%) of the 312 free of high levels of depressive symptoms from 2006–2009 had incident persistent depression as of 2015. Table 1, below, indicates that those who were poor in every year had significantly higher rates of prevalent and incident persistent depression than those exiting poverty or never poor.

Abstract THU0646 – Table 1. Results of Four Performance Measures for RA.

Measurement Year <sup>1</sup>	Prevalent RA cases	Incident RA cases	PM1: Patients seeing rheumatologist within 1 year of RA onset	PM2:% of Patients under rheum care with yearly rheumatology visits	PM3: % Patients dispensed a DMARD	PM4: Median (90th percentile) days to DMARD	PM4: % with DMARD within 14 days of onset
2004	17 472	1647	80%	57%	59%	31 (825)	27%
2005	19 097	1614	82%	56%	60%	26 (579)	30%
2006	20 612	1704	85%	54%	60%	23 (411)	31%
2007	21 764	1430	83%	53%	60%	29 (399)	28%
2008	22 721	1305	86%	50%	60%	26 (339)	29%
2009	23 386	921	92%	49%	61%	23 (188)	34%
2010	23 122	-	-	46%	60%	-	-
2011	22 781	-	-	44%	56%	-	-
2012	22 370	-	-	42%	56%	-	-
2013	21 966	-	-	41%	57%	-	-
2014	21 412	-	-	41%	57%	-	-

<sup>1</sup>PMs reported on a prevalent cohort until 2014, and on an incident cohort reported until 2009



**Abstract THU0647 – Table 1.** Odds Ratios (95% CI) for Effect of Poverty Status between 2003 and 2009 on Prevalent and Incident Persistent Depression. CESD Score  $\geq 24$  in 3 or More Years), between 2009 and 2015, with and without Adjustment

Outcome	Poor Every Year	Exited Poverty	Never Poor
<b>Prevalent Persistent Depression (n=535)</b>			
Unadjusted	3.9 (2.1, 7.2) *	1.0 (0.4, 2.2)	Ref.
Adjusted†	2.9 (1.4, 6.1) *	0.8 (0.3, 1.8)	Ref.
<b>Incident Persistent Depression (n=312)‡</b>			
Unadjusted	4.5 (1.3, 15.4) *	0.9 (0.2, 3.9)	Ref.
Adjusted†	4.1 (0.9, 19.1)	0.7 (0.1, 3.7)	Ref.

\*  $p < .01$

† Adjusted for gender, age, marital status, race/ethnicity, education, disease duration, extent of accumulated damage in 2009, smoking status, and BMI

‡ Excludes persons with high levels of depressive symptoms 2006–2009

**Conclusions:** Public policy to help persons with SLE stay out of poverty or to exit poverty may lower their rates of prevalent and incident persistent depression. Attention to the economic status of persons with SLE should be part of an overall treatment strategy including treatment for depression since such attention may help reduce accumulation of damage as well as reduce the prevalence and incidence of persistent depression.

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#### THU0648 “AS A PRACTITIONER I FEEL ENRICHED”: RHEUMATOLOGY TUTORS' EXPERIENCES OF DELIVERING A MANUALISED GROUP COGNITIVE-BEHAVIOURAL FATIGUE PROGRAMME TO PATIENTS WITH RHEUMATOID ARTHRITIS (RA)

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**Background:** Reducing Arthritis Fatigue by clinical Teams using cognitive-behavioural approaches (RAFT) is a 7-centre RCT of a manualised group cognitive-behavioural (CB) programme to reduce fatigue impact.<sup>1</sup> After four days training plus a delivery observed by clinical supervisors, tutor pairs (rheumatology nurses and occupational therapists (OTs)) delivered the programme four times to patients with RA. Quality assurance observations confirmed tutors used CB approaches and RAFT results show the programme reduced patients' fatigue impact at 26 weeks.<sup>2</sup>

**Objectives:** The aim of the current study was to understand tutors' experiences of RAFT training and delivery to inform future programme roll out.

**Methods:** 14 RAFT tutors (9 nurses; 5 OTs) participated in one-to-one interviews, which were audio-recorded and transcribed. Data were analysed by ED, SH, and AH using inductive thematic analysis.

**Results:** Four main themes were identified.

Theme 1: “It's quite daunting” - Delivering a complex programme that was “quite different to what any of us had done before” required time and effort (“I couldn't really make sense of it without actually doing a lot of work around it”). Initially, training with clinical supervisors (“experts”) who are “so good at what they do” challenged tutors' confidence (“the anxiety is are we going to deliver it the way they did?”).

Theme 2: “Most useful was actually getting to practice the sessions” - Tutors valued watching clinical supervisors demonstrate programme sessions during training (“professionals who have shown us how to do it”) plus the opportunity to practice themselves (“role playing the sessions was really helpful”).

Theme 3: “Putting it in a way that was still true to the message” - The RAFT manual was “very valuable” and “it had to be adhered to”; however, tutors wrote individual crib notes (“our own manual in our own words”) to consolidate information, deepen understanding, and gain confidence. The process was supported by “positive and constructive criticism” in the observed delivery (“the supervisor kept putting us back on track”).

Theme 4: “As a practitioner I feel enriched” - CB skills acquired during RAFT impacted tutors' wider work (“making a massive difference to my clinical practice”), and enhanced the self-management support they offered patients, including

“the particular ability to draw things out from people” and “learning when to listen and stand back and try and get the patients to find the answers”.

**Conclusions:** Initially, RAFT training and delivery were a challenge for tutors because the CB approach was a new way of working. Individually adapting RAFT manual wording plus feedback from supervisors increased tutors' confidence. Tutors believed the CB skills acquired during RAFT enhanced their wider clinical practice and the self-management support they offered patients. Future training should include RAFT session demonstrations and skills practice for tutors, with feedback from clinical supervisors.

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#### THU0649 UNDERSTANDING ETHNIC DIFFERENCES IN THE UTILISATION OF EXERCISE FOR OSTEOARTHRITIS

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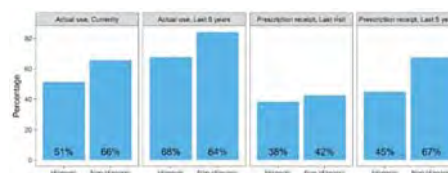
**Background:** According to a US survey, the prevalence of arthritis-attributable activity limitation, work limitation and severe pain are all significantly higher among Hispanics than among non-Hispanics (NHs). Ethnic differences in osteoarthritis (OA) patients' experience of pain may be related to marked disparities in the use of OA treatments. According to EULAR OA guidelines, exercise should be an integral part of the management of knee and hip OA. Whether or not exercise is underutilised and why it may be underutilised by Hispanics to treat OA is unclear.

**Objectives:** The objective of this study was to determine if there are ethnic differences in the history and current use of exercise as therapy for patients with knee or hip OA. The secondary objective was to compare Hispanic and NH patients with lower extremity OA with respect to their familiarity and perceptions of the efficacy and risk of exercise as treatment for OA.

**Methods:** Research participants  $\geq 50$  years of age with chronic and frequent pain due to knee or hip OA were recruited from a university medical centre. Structured interviews were conducted to determine patient sociodemographic characteristics, clinical information, self-reported actual use/prescription receipt of exercise for OA treatment (currently, last 5 years), and familiarity with exercise (3 items, yes/no response). Perceptions of the benefits (4 items) and risks (3 items) of exercise, and willingness to exercise to treat OA were also evaluated; each question in these measures has a five-category ordinal response scale. Fisher's exact or Wilcoxon-Mann-Whitney tests were conducted to determine if knowledge and perceptions about exercise were associated with ethnicity (Hispanic vs NH).

**Results:** In our cohort of patients with knee or hip OA, Hispanics (n=119), in comparison to NHs (n=201), were younger (mean age 61.5 vs. 65.3) and less likely to have an annual income of  $\geq \$50,000$  (13.5% vs. 39.1%). A lower proportion of Hispanics than NHs reported using exercise to treat OA at present (51% vs. 66%,  $p=0.0165$ ) and in the last five years (68% vs. 84%,  $p=0.0010$ ) or receiving a prescription for exercise in the last five years (45% vs. 67%,  $p<0.0001$ ) (figure 1).

Hispanics, compared to NHs, were also less likely to report ever hearing about exercise to treat OA (71.43% vs. 91.83%,  $p<0.0001$ ), having family/friends that received it for treatment (33.33% vs. 51.20%,  $p=0.0023$ ), or having a good understanding of it as a treatment for OA (66.96% vs. 79.33%,  $p=0.0161$ ). A lower proportion of Hispanics than NHs believe that exercise is beneficial (or very beneficial) for arthritis (49.12% vs. 69.09%,  $p<0.0001$ ) and that exercise is helpful (or very helpful) for them (60.52% vs. 75.61%,  $p=0.0056$ ). No ethnic differences in the perceptions of risk of exercise were observed. Hispanics were also less willing to exercise to treat OA than NHs (67.83% vs. 82.61%,  $p=0.0018$ ).



**Abstract THU0649 – Figure 1** Proportion who reported use of or prescription receipt for exercise to treat OA by ethnicity **Conclusions:** Among patients with knee or hip OA, Hispanics were less likely than NHs to utilise exercise as treatment for arthritis.

They were also less familiar with its use for OA treatment, less likely to believe in its efficacy, and less willing to use it as treatment for OA. Improving patient knowledge and attitudes about exercise may increase utilisation of this OA treatment and help reduce ethnic differences in OA outcomes.

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#### THU0650 EARLY HELP SEEKING OR SELF-MANAGEMENT: A QUANTITATIVE ASSESSMENT IN THE CONTEXT OF RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) should be treated with DMARDs in its earliest stages to reduce the likelihood of permanent joint damage and disability<sup>1</sup>. This therapeutic window is often missed. One important cause is delayed help seeking by patients themselves<sup>2</sup>. Qualitative work with members of the public has previously identified a number of potential causes for this delay<sup>3</sup>.

**Objectives:** To quantify and extend the findings of existing qualitative research investigating factors which impact on speedy help seeking for symptoms of RA.

**Methods:** A survey of members of the public without a diagnosis of inflammatory arthritis assessed the speed with which they would seek medical attention if they were to experience symptoms of RA (stiffness, pain and joint swelling). It explored factors which might impact on the speed with which help would be sought, including: self-management of symptoms; barriers to and drivers of help seeking and information seeking.

**Results:** 1088 people (788 females; 9 undisclosed) aged between 18 and 96 years completed the survey. 48% indicated that they would seek help quickly for RA symptoms, however 63% would delay seeing their GP in order to try to self-manage the symptoms. Most intended to self-manage with over the counter medication (e.g. ibuprofen), massaging the joint or exercising. Barriers endorsed included difficulty getting a GP appointment (39%); fear of wasting the GP's time (34%) and being busy with family/work (37%). Drivers (>90%) included worsening of symptoms, inability to work, struggling to do usual activities, symptoms spreading to other parts of the body or inability to self-manage symptoms. Most participants would seek out information prior to seeking medical attention for the symptoms. Sources of information frequently endorsed were: Internet (74%); relatives/friends (49%); someone with a joint problem (41%) and pharmacists (37%).

**Conclusions:** Less than half of the current sample would seek help quickly for the symptoms of RA. Several barriers and drivers identified in qualitative research<sup>3</sup> were endorsed by the survey sample making them valid targets for interventions. Most participants would further seek out information about the symptoms prior to seeking medical attention and their preferred sources of information such as the internet or the pharmacist should be used in these targeted interventions.

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#### THU0651 THE INFLUENCE OF AGE, GENDER, EMPLOYMENT STATUS, OR EDUCATION ON THE CHOICE OF BIO-SIMILAR VS. BIO-ORIGINAL VARIANT OF THE SAME BDMARD IN PATIENTS WITH RA OR AS STARTING BIOLOGICAL THERAPY – REAL LIFE DATA FROM THE CZECH BIOLOGICS REGISTRY ATTRA

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**Background:** Perceptions on bio-originator (bo) and bio-similar (bs) biologics among HCPs and pts, as well administrative regulations or economic incentives may influence their utilisation in clinical practice. The ATTRA registry captures more than 95% of pts with RA and AS treated with biologics in the Czech Republic (CZ). Access to biological therapy in CZ is limited to about 30 authorised centres. Bs infliximab (INF) has been prescribed in CZ since 11/2013, and bs etanercept (ETA) since 1/2016 concurrently with bo INF and ETA. There has been no administrative regulation concerning the use of bs or bo in CZ.

**Objectives:** To explore whether age, gender, employment status, or level of education influence the choice of bs vs. bo variant of the same bDMARD in pts with RA or AS starting bDMARD in CZ.

**Methods:** Data from the ATTRA registry on pts with RA or AS starting their first bDMARD between 11/2013 and 10/2017 were used. The start of bo vs. bs ETA, or bo vs. bs INF as the first bDMARD was the main outcome of interest. Multivariate logistic regression analysis was used to explore the impact of education, employment status, age and gender on the start of a first bDMARD after adjustment for disease characteristics, and the bDMARD molecule.

**Results:** 560 pts started ETA (22.6% bo, 14.2% bs) or INF (9.7% bo, 53.5% bs) in the study time frame. In the multivariate model (table 1) pts starting ETA (ref. INF) had lower odds to receive a bs (OR 0.11, CI95% 0.07–0.17), and pts with primary education (vs. secondary or tertiary) had higher odds to receive any bs (OR 1.84, CI95% 1.08–3.13). When we performed separate analyses for pts treated in academic/public hospitals (n=314), the adjusted OR for pts with primary education was 0.78 (CI95% 0.37–1.64), while in private centres (n=246) the OR was 5.32 (CI 95% 2.32–12.16). When we introduced an interaction term for type of practice x level of education, the adjusted OR for pts with primary education in private centres was 2.26 (CI95%, 1.14–4.46, p=0.019).

Abstract THU0651 – Table 1.

Parameters	OR (95% CI)	p-value
HDA vs. REM+LDA+ MDA (acc to DAS28/ASDAS)	0.94 (0.50; 1.77)	0.859
CRP [mg/l]	1.00 (0.99; 1.01)	0.770
HAQ	1.16 (0.75; 1.78)	0.513
AS (vs. RA)	1.40 (0.81; 2.40)	0.229
ETA (vs. INF)	0.11 (0.07; 0.17)	<0.001
Age at start of 1st bDMARD	1.01 (0.99; 1.04)	0.271
Disease duration	1.01 (0.98; 1.04)	0.693
Female	0.78 (0.48; 1.26)	0.316
Primary education (vs. Secondary or Tertiary)	1.84 (1.08; 3.13)	0.024
Sick leave (vs. employed)	1.61 (0.68; 3.82)	0.283
Disability pension (vs. employed)	0.74 (0.36; 1.54)	0.421
Old age pension (vs. employed)	0.61 (0.28; 1.31)	0.205
Unemployed (vs. employed)	1.08 (0.48; 2.42)	0.845
Maternity leave/student (vs. employed)	1.48 (0.43; 5.08)	0.529

**Conclusions:** We found that in private centres providing biological therapy in CZ, pts with primary education had higher adjusted odds to obtain bs as the first bDMARD. We cannot exclude that different pt characteristics and residual confounding may have been involved. The interpretation is complex and related not only to perception of bs by HCPs and pts, but also to unmeasured economic incentives and other factors.

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**Disclosure of Interest:** None declared

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THU0652

### COMPARATIVE COST PER RESPONSE FOR FOUR CLINICAL OUTCOMES OF TOCILIZUMAB MONOTHERAPY VERSUS ADALIMUMAB MONOTHERAPY IN A HEAD-TO-HEAD RANDOMISED DOUBLE-BLIND SUPERIORITY TRIAL (ADACTA) IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** The cost-effectiveness of different biologic therapies is an important component in guiding treatment decisions for patients with rheumatoid arthritis (RA).

**Objectives:** To compare drug and adverse event costs and cost per successful clinical response with tocilizumab (TCZ) monotherapy vs adalimumab (ADA) monotherapy in patients with RA.

**Methods:** Patients in the ADACTA trial<sup>1</sup> were randomised to either TCZ 8 mg/kg intravenously every 4 weeks or ADA 40 mg subcutaneously every 2 weeks as monotherapy for 24 weeks. Drug costs of \$397.71/80 mg vial for TCZ (plus \$136 administration cost per infusion) and \$2220.62/40 mg for ADA were based on Wholesale Acquisition Costs (WAC) drug prices (July 2017). Outcomes included patient-level drug costs and cost of hospitalisation due to adverse events, and cost per response. Cost per response was calculated by dividing the mean drug plus administration cost by the proportion of patients achieving Disease Activity Score-28 joints (DAS28) <2.6 (remission) or American College of Rheumatology response criteria 20%/50%/70% (ACR20/ACR50/ACR70). The proportions of patients achieving DAS28 <2.6, ACR 20, ACR50 and ACR70 were 39.9%, 65.0%, 47.2% and 32.5% for TCZ, respectively, and 10.5%, 49.4%, 27.8% and 17.9% for ADA, respectively; p<0.0001, p=0.0038, p=0.0002, p=0.0023 for TCZ vs ADA, respectively. Hospitalisation costs were calculated using the daily hospital cost of \$2433 (2017) and number of hospital days.

**Results:** Among the 163 patients treated with TCZ and 162 with ADA, mean total drug and administration costs per patient over 24 weeks were \$16,674.74 and \$23,357.63, respectively. Mean drug and administration costs were lower per each clinical response achieved with TCZ compared with ADA (DAS28 <2.6: \$41 791 vs \$222,454; ACR20: \$25 653 vs \$47,283; ACR50: \$35 328 vs \$84,020; ACR70: \$51 307 vs \$130,490). The total hospital days/costs were 32/\$77 856 for TCZ and 43/\$1 04 619 for ADA.

**Conclusions:** In this comprehensive comparative assessment, the cost to achieve all four clinical responses was lower for patients receiving TCZ than for ADA.

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**Disclosure of Interest:** J. Best Shareholder of: Genentech, Inc., Employee of: Genentech, Inc., J. Pei Shareholder of: Genentech, Inc., Employee of: Genentech, Inc.

**DOI:** 10.1136/annrheumdis-2018-eular.2009

THU0653

### CHANGES IN RHEUMATOLOGY PROVISION AND PRACTICE IN A PUBLICLY-FUNDED SINGLE PAYER HEALTHCARE SYSTEM

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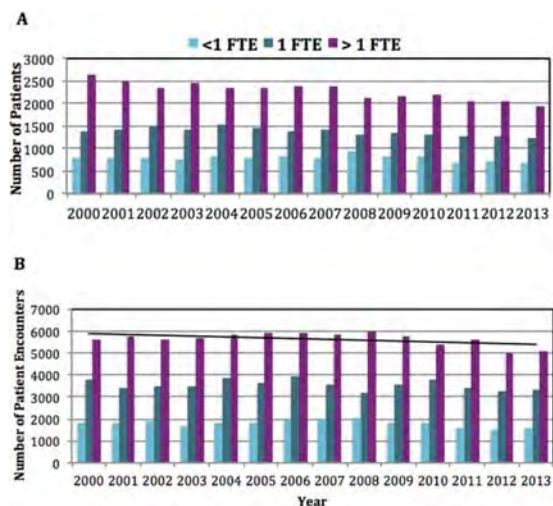
**Background:** The global shortage of rheumatologists is an increasing concern. Statistics from physician surveys have projected changes in the workforce composition (ageing, feminization, and generational trends), which have implications for the workforce clinical activity. In order to adequately document the issues and potential solutions, more detailed information is needed regarding clinical activity, demographic changes and the implications of these, in a population-based sample.

**Objectives:** To describe changes in the number, demographics and clinical activity of Ontario rheumatologists over the past decade.

**Methods:** We analysed administrative health data from 2000 to 2013 in Ontario, Canada, where all 13 million residents are covered by a publicly funded health-care system. Rheumatologists, and their characteristics, were identified using a validated physician registry. We used fee-for-service billing claims to quantify clinical activity levels expressed as full-time equivalents (FTE). Physicians below the 40th percentile of total billings were classified as providing less clinical activity

(<1 FTE i.e. professor/scientist); 40–60th percentile were classified as 1 FTE; and >60 th percentile as >1 FTE (i.e. high volume community practice).

**Results:** In 2000, there were 146 rheumatologists in Ontario (88 of whom worked  $\geq 1$  FTEs); this increased to 187 rheumatologists (114  $\geq 1$  FTEs) in 2013. Despite the increase, due to an increase in the Ontario population over this time, the proportion of Ontarians seen by a rheumatologist annually remained constant (2.7%) as was the overall provincial per capita supply (1.2 rheumatologists per 75 000 population, 0.7 FTEs/75,000). In 2000, 34% of rheumatologists were female compared to 48% in 2013. During this time, the proportion of rheumatologists aged >60 + years increased (16% to 26%). The annual median (IQR) number of days of clinical service decreased from 220<sup>178–243</sup> days in 2000 to 176<sup>138–213</sup> days in 2013. The percentage of rheumatologists with patient encounters on at least 209 days/year (an alternative FTE benchmark) showed a downward trend from 46% in 2000 to 22% in 2013. Male rheumatologists had more patient encounters each year, and a higher proportion of male rheumatologists worked as  $\geq 1$  FTE. Average practice sizes declined over time (figure 1A), as did the median number of patient encounters per rheumatologist per year (figure 1B).



**Abstract THU0653 – Figure 1.** A) Average Rheumatology Practice/Panel Size (Number of Unique Patients per Rheumatologist) According to FTE Classification; B) Average Number of Patient Encounters per Rheumatologist According to FTE Classification

**Conclusions:** Although there has been an increase in the number of rheumatologists, the per capita supply and access to rheumatologists have remained unchanged. We observed changing workforce demographics and declining clinical activity over time. Factors affecting clinical activity (including an ageing and greater feminization of the workforce, clinic saturation, increasing care complexity, models of care, greater demands for continuing medical education and research activity) warrants further study.

**Disclosure of Interest:** None declared

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THU0654

### ABSTRACT WITHDRAWN

THU0655

### PATIENTS' EVALUATION OF DUTCH HEALTH CARE IN SYSTEMIC SCLEROSIS: UNMET NEEDS AND PREFERENCES

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**Background:** Systemic sclerosis (SSc) is a chronic, heterogeneous autoimmune disease with a large impact on quality of life. To optimise health care, more insight is needed in patients' experiences of the currently provided care.

**Objectives:** To identify unmet needs and preferences from a patient point of view regarding health care in the Netherlands

**Methods:** 2093 patients with SSc, from both regional (n=7) and university hospitals (n=6) in the Netherlands, were invited through their rheumatologist for an online, anonymous questionnaire comprising multiple choice, multiple response

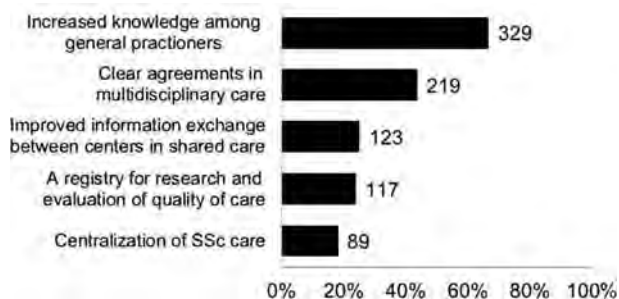


and open questions about health care needs, quality of care (CQ index), and additional sociodemographic characteristics. Questions were based on results from a literature study and three semi-structured multicenter focusgroup interviews with 23 patients. Eight themes were identified (table 1).

**Results:** 493 patients, median age was 60 years and 73% were women, completed the questionnaire at the 10th of January 2018. Inclusion is still ongoing. Patients had been diagnosed for a median period of four years, 38% and 23% reported having been diagnosed with limited or diffuse cutaneous SSc, respectively. Interestingly, 39% did not know the subtype. 50% received care in a centre of expertise and 32% in  $\geq$ two centres. 32% had to travel >one hour for each visit. Themes containing the most important unmet needs were:<sup>1</sup> multidisciplinary collaboration;<sup>2</sup> education of caregivers;<sup>3</sup> patient information;<sup>4</sup> the role of the patient and;<sup>5</sup> non-pharmacological care. Multidisciplinary collaboration was rated 68 out of 100 and information exchange among physicians 66 out of 100. The lack of knowledge about the disease among health professionals (40%) and difficulty finding experts in SSc (25%) were most reported hurdles. 10% of patients did not receive any information from the rheumatologist at time of diagnosis, but when provided 97% thought this information was clear. Although most of the patients were involved in treatment decisions (83%), 12% did not receive the care they needed in their opinion. 60% was referred to a specialised nurse for non-pharmacological support. During hospital visits, more focus was preferred on fatigue (45%, n=227), Raynaud's phenomenon (31%, n=155), physical disabilities (29%, n=147), impaired hand function (26%, n=129) and coping with the unpredictable course of the disease (25%, n=124). Highest priority was given to improved knowledge among general practitioners (67%), multidisciplinary collaboration (43%) and information exchange among health care providers (25%) (figure 1)

Abstract THU0655 – Table 1. Identified health care themes from focusgroup interviews

Themes
Multidisciplinary collaboration
Education of caregivers
Patient information
Role of the patient
Shared care; regional and university hospitals
Information exchange among caregivers
Organization of health care services
Non-pharmacological support



Abstract THU0655 – Figure 1 Top. five prioritised points for improvement

**Conclusions:** SSc patients mainly prefer more attention to symptoms during doctor's visits and wish for improved collaboration and information exchange among health care providers. This knowledge will guide the nation-wide initiative to optimise health care for patients with SSc in The Netherlands.

**Disclosure of Interest:** None declared

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## THU0656 SYSTEMIC LUPUS ERYTHEMATOSUS IN COLOMBIA: A BIBLIOMETRIC ANALYSIS

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**Background:** Systemic lupus erythematosus (SLE) is a chronic autoimmune disease with a high burden of disease on individuals and healthcare systems.<sup>1</sup>

Bibliometric analyses assess scientific literature on a given topic, and allow the identification of novel research trends, based on statistical data of scientific literature and their indicators.<sup>2,3</sup> In Colombia, few efforts have addressed at Rheumatology or Autoimmunity.

**Objectives:** To perform a bibliometric study on the scientific production on SLE in Colombia that describes its distribution, development trends, national and international collaboration trends, and its impact on the scientific community.

**Methods:** A descriptive bibliometric study was performed using three databases (Web of Science, SCOPUS and Scielo). Annual national research output, number of articles, city and institution of origin, national and international collaboration, scientific journals, publication language, and citations number were assessed. VOS-viewer was used to illustrate collaboration networks.

**Results:** SCOPUS disclosed 307 articles, Web of Science 270, and Scielo 90. The highest number of citations per item (19.8) and the maximum national H index<sup>41</sup> were found in SCOPUS. More than 80% of articles, regardless of the database, were published during the last 10 years. 'Universidad del Rosario' and 'Universidad de Antioquia' showed the highest research output. Bogotá and Antioquia, followed by Valle del Cauca, presented the highest number of articles. An important number of national and international collaborations were observed, which differed in each database.

Production per institution in WoS, Scielo and SCOPUS

Item	WoS	SCOPUS	Scielo
Number of articles	270	307	90
Number of registries <sup>a</sup>	376	469	150
Articles in the last 10 years (%)	86	87	91
Mean historic number of publications (SD)	5.9 (9.7)	6.7 (11)	1.9 (3.4)
Annual mean number of publications in the last 10 years (SD)	21.2 (7.5)	24.2 (9.6)	7.4 (2.5)
Original articles (%)	62	73	74
National H index for the last 10 years	32	41	3
Total number of cites	5260	6093	39
Total number of cites adjusted by auto-citation	4953	4987	24
Mean cites per element	19.5	19.8	0.43
Most frequent journals (% of grand total)	'Annals of the rheumatic diseases'(10) and 'Arthritis and rheumatism' (8)	'Revista Colombiana de Reumatología' <sup>18</sup> (7)	'Revista Colombiana de Reumatología' (68) and 'Acta Médica Colombiana' (7)

<sup>a</sup> Defined as the number of positive results in each database, which may differ due to co-authors as both sum up for both institutions.

Abbreviations: WoS Web of Science, SD Standard deviation

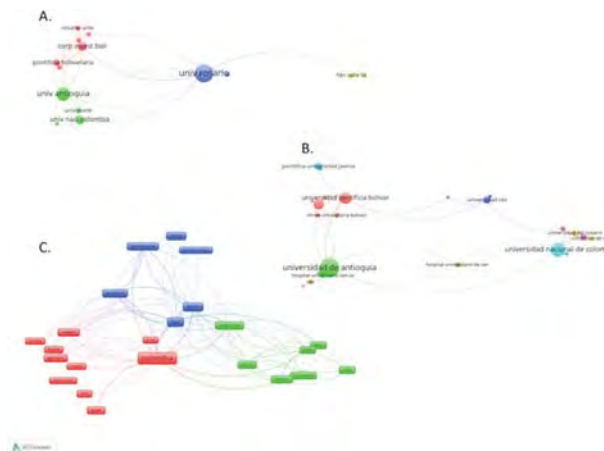


Figure. National and international collaboration networks on SLE research in Colombia. A. National (WoS) B. National (Scielo) C. International (WoS)

**Conclusions:** A significant growth of the research on SLE in Colombia was observed, however, its impact is far from being meaningful. Strategies aimed at strengthening the interest in Rheumatology and research in undergraduate

students must be encouraged, particularly supporting research seedbeds and young researchers.

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**Disclosure of Interest:** None declared

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#### THU0657 EFFECTS OF ADALIMUMAB INITIATION ON CORTICOSTEROID UTILISATION AND MEDICAL COSTS AMONG PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Treatment guidelines recommend low dose corticosteroids (steroids) as a short-term (<3 months) therapy among rheumatoid arthritis (RA) patients to 'bridge' patients until benefits of disease modifying anti-rheumatic drugs (DMARDs) are observed.<sup>1</sup> However, for many patients it may be difficult to wean/eliminate steroids once they are initiated. Initiation of more effective therapies such as biologics may help promote reduction in steroid use.

**Objectives:** This study examined the impact of initiating adalimumab (ADA) on steroid utilisation and medical costs among patients with RA.

**Methods:** A retrospective analysis was conducted among adult RA patients initiating ADA as the initial biologic in the MarketScan Database (2012–2016). Study outcomes included whether oral/injectable steroids were used, daily dose, dosage categories (<5 and ≥5 mg/day), number of steroid injections, and medical costs. Outcomes were compared 6 months pre- and post ADA initiation using Chi-square tests for categorical variables and paired t-tests and Wilcoxon rank sum tests for continuous variables. Because various types of variables were used for study outcomes, mixed effects logistic, classical linear, multinomial logistic models, and linear model with a log link and gamma distribution were used to adjust for patient demographic and health characteristics such as age, gender, health plan type, census region, and Charlson Comorbidity Index.

**Results:** The study sample included 6,214 ADA initiators. As compared to the 6 months prior to ADA initiation, there was a reduction in proportions of patients using oral steroids (from 72% to 59.5%) and injectable steroids (from 34.9% to 26.9%), average daily dose of oral steroids (from 3.3 mg/day to 2.5 mg/day), patients with dose ≥5 mg/day (from 22.3% to 15.1%), number of steroid injections (from 0.63 to 0.47), and medical costs (from \$5,233.5 to \$4,807.9) ( $p < 0.01$  for all comparisons). Multivariate analysis produced similar patterns. In the 6 months post-ADA initiation, patients were less likely to use oral steroids (Odds Ratio (OR): 0.40; 95% Confidence Interval (CI): 0.36–0.45) or steroid injections (OR: 0.59; 95% CI: 0.54–0.65). Coefficient estimate for daily dose reduction was  $-0.87$  (95% CI:  $-1.00$ – $-0.74$ ). Post-ADA relative risk ratios for dosage categories <5 mg/day and ≥5 mg/day compared to zero were 0.48 (95% CI: 0.43–0.53) and 0.36 (95% CI: 0.32–0.41), respectively. Post-ADA incidence rate ratio for number of steroid injections was 0.72 (95% CI: 0.69–0.76). Ratio estimate for medical costs was 0.84 (95% CI: 0.79–0.89). All multivariate results reported were significant ( $p < 0.01$ ).

**Conclusions:** Among patients with RA, following ADA initiation, there is a reduction in steroid utilisation and its dose, and patients' medical costs. Prospective studies should be conducted to confirm this relationship in the future.

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**Acknowledgements:** Financial support for the study was provided by AbbVie. AbbVie participated in the interpretation of data, review, and approval of the abstract.

**Disclosure of Interest:** Y. Qiao Grant/research support from: AbbVie, K. Winthrop Grant/research support from: AbbVie, Consultant for: AbbVie, J. Griffith Shareholder of: AbbVie, Employee of: AbbVie, C. Kaplan Grant/research support from: AbbVie, C. Spivey Grant/research support from: AbbVie, A. Postlethwaite Grant/research support from: AbbVie, J. Wang Grant/research support from: AbbVie

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#### THU0658 RECOMMENDATIONS FOR THE ASSESSMENT AND OPTIMISATION OF ADHERENCE TO DISEASE-MODIFYING DRUGS IN CHRONIC INFLAMMATORY RHEUMATIC DISEASES: A PROCESS BASED ON LITERATURE REVIEWS AND CONSENSUS

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**Background:** In chronic inflammatory rheumatic diseases including rheumatoid arthritis (RA), spondyloarthritis (SpA), psoriatic arthritis (PsA) and connective tissue diseases (CTD), adherence to disease-modifying drugs is only moderate over the long term and non-adherence may lead to complications, unnecessary treatment switches and heightened costs.

**Objectives:** To develop recommendations to facilitate in daily practice, the measurement of non-adherence, the individualised assessment of risk of non-adherence and the management of non-adherence with the objective to optimise adherence to treatments in patients with chronic inflammatory rheumatic diseases.

**Methods:** The project scope was limited to chronic inflammatory rheumatic diseases (i.e., RA, SpA, PsA, CTD, crystal-induced arthritis, vasculitis and auto-inflammatory diseases), and to disease-modifying drugs (i.e., mainly conventional DMARDs, biologics and targeted synthetic DMARDs). The process comprised (a) systematic literature reviews of data from 3 key databases and several websites, of methods (including questionnaires) to measure non-adherence, risk factors for non-adherence and management options for non-adherence with their reported efficacy. (b) a consensus of 104 rheumatologist and nurse experts during a 2 day face-to-face meeting. (c) Final recommendations were anonymously evaluated by the participants for agreement and ease of applicability (1–5 were 5 is highest).

**Results:** (a) After screening 1131 publications and 194 other documents, 231 relevant papers were analysed. (b) The consensus process led to 5 overarching principles and 10 recommendations regarding adherence. In summary, adherence is important, imperfect, and multi-factorial. Patient-physician interactions play an important role, as do patient beliefs. Adherence should be assessed at each outpatient visit, at least using an open question. Questionnaires and hydroxychloroquine blood level assessments may also be useful. People who are younger, worried of side effects, do not see the necessity of the treatment, and are in psychological distress are more prone to non-adherence. Patient information and education, and patient/physician shared decision, are key to optimise adherence. Other techniques such as formalised education sessions, motivational interviewing and cognitive behavioural therapy may be useful. All health professionals can get involved and e-health may be a support. (c) The agreement with the recommendations was high (range of means, 3.88–4.47) but ease of applicability was lower (2.69–4.38).

**Conclusions:** Using an evidence-based approach followed by expert consensus, this initiative should improve the assessment and optimisation of adherence in chronic inflammatory rheumatic disorders. Next steps include dissemination and implementation.

**Acknowledgements:** AbbVie France funded this initiative but played no role in the recommendations.

**Disclosure of Interest:** None declared

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#### THU0659 EUORRHEUMAVISION: ARE THE LARGEST EUROPEAN RHEUMATOLOGY SOCIETIES THE ONES WITH THE MOST ORAL COMMUNICATIONS?

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**Background:** Between June 14 and 17, 2017, coinciding with the 70th anniversary of its foundation, the annual EULAR congress took place in Madrid. With 14,000 participants from 130 countries, 4845 accepted abstracts, 2300 posters and more than 800 oral communications, it became a record congress in the history of European rheumatology.

Now, EULAR is formed, among others, by 45 national rheumatology societies. Are the various countries proportionally represented at a scientific level? Those with the greatest number of rheumatologists have a greater weight in communications to the congress?

**Objectives:** To assess the scientific weight of the different European rheumatological societies in the EULAR congress

**Secondary objective:** To analyse the characteristics of these societies in terms of the number of rheumatologists, specialists for 100,000 inhabitants and percentage with the total number of doctors

**Methods:** The scientific communications of the 2017 EULAR congress (Madrid) are analysed, according to the country of origin of the speakers.

The number of rheumatologists in each country is assessed, their specific weight with respect to the total of European rheumatologists and in relation to the total number of doctors in their respective countries.

**Results:** Results: The countries with the highest number of rheumatologists in Western Europe are France 2,600, Italy (1800), Spain (1155), UK (950), Germany (800) and Netherlands (775). However, in number of communications The order changes, so the UK is the most productive (121), followed by the Netherlands (101), Germany (91), France (74), Italy (51), Sweden<sup>37</sup> and Spain.<sup>36</sup>

In proportion, the Dutch presented 1 communication for every 7.6 rheumatologists, 1 German for every 8.7, 1 for every 7.8 British. The Mediterranean countries are far away, with 1 communication for every 32 Spanish rheumatologists and 1 for every 35 in the case of France and Italy

#### Oral Communications EULAR Madrid 2017

UNITED KINGDOM	121
GERMANY	91
FRANCE	74
ITALY	51
SPAIN	36
NETHERLANDS	101
REST OF EU	250 (37 Swe, 17 Port., Swith, Denma, Norw, Bel, Irel.)
REST OF THE WORLD	156

Country	N° of rheumatologist (N° of communications x rheumatologist)
UK	950 (1 com x 7,82reum)
GER	800 (1 com x 8,79 reum)
FRA	2600 (1 com x 35,1 reum)
ITA	1800 (1 com x 35,29 reum)
SPA	1155 (1 com x 32 reum)
NETHE	775 (1 com x 7,6 reum)

#### REPRESENTATION AT A SCALE OF COUNTRIES BY EULAR ACADEMIC POWER



**Conclusions:** There is a marked disparity between the number of rheumatologists by country and number of oral communications. While the Netherlands, United Kingdom and Germany are protagonists of more than a third of the oral communications, nations such as Spain, France or Italy only contribute, together, to the 18% although nearly 5600 rheumatologists work in their countries. Therefore, with twice as many specialists, they present half of communications.

**Disclosure of Interest:** None declared

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THU0660

#### GOLIMUMAB IMPROVES SOCIO- AND HEALTH ECONOMIC PARAMETERS IN PATIENTS WITH RA, PSA AND AS: REAL WORLD-DATA FROM A NON-INTERVENTIONAL CLINICAL STUDY IN GERMANY

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**Background:** Golimumab (GLM) has shown its efficacy and safety in various clinical trials. Data from socio- and health economic parameters in daily clinical practice in Germany are rare.

**Objectives:** Our objective was to describe effects on socio- and health economic parameters and on health care resource use in patients in Germany with rheumatoid arthritis (RA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS) who were initiated on subcutaneous GLM.

**Methods:** Descriptive post-hoc analysis of socio- and health-economic parameters of the non-interventional, multicenter, prospective GO-NICE study (n=1458) at baseline (BL) compared to the situation at 24 months (M24) (n=664, 45.5%) to explore the impact of GLM on days of sick leave/absenteeism, and days of impaired capability/presentism, as well as the work productivity, quality of work and normal course of life (in the past 30 days and 6 months) using. Further gather the number of consultations, ambulatory treatments, alternative treatments days of hospitalizations and rehabilitation measures in the past 6 months.

**Results:** The mean number of sick leave days in the previous 30 days decreased from baseline (BL) 4.0 to 0.9, and in the past 6 months from BL 13.7 to 3.3 at M24. The improvement was greatest in patients with RA. The mean number of days with impaired capability in the previous 30 days decreased from BL 14.9 to 4.5, in the previous 6 months from BL 65.8 to 19.8 at M24. The improvement was greatest in patients with AS. On a numeric rating scale (range: 1=no limitation to 10=very strong limitation), the patients' mean ratings on the impact of disease during the previous 6 months of work productivity decreased from BL 5.5 to 2.5 points, on quality of work from 4.8 to 2.2 points, and on the normal course of life from 5.3 to 2.4 points at M24, respectively. The decrease in the mean scores BL to M24 was comparable in patients with RA, PsA and AS. Intersubject variability was high. On retrospective evaluation for the past 6 months, the percentage of patients with physician consultations declined from BL to M24: with general practitioners in patients with PsA -19.7%, AS by -17.8%, RA -6.8% in patients with RA. A marked decline was also observed in the percentage of patients with PsA having dermatologist consultations (-15.0%). The percentage of patients receiving physiotherapy, massages, occupational therapy and packs declined from BL to M24, primarily the application of physiotherapy (-16.9%, -10.9% and -9.1%) in patients with AS, PsA and RA. The frequency of hospitalizations decreased from 10.4/7.6/14.0% at BL to 1.7/2.2/0.8%, and the frequency of rehabilitation decreased from 3.3/3.7/7.5% at BL to 0.6/1.8/2.1% at M24 in patients with RA, PsA, and AS

**Conclusions:** This evaluation showed remarkable improvements in socio- and health-economic parameters. On GLM treatment, there was a reduction in the days of absenteeism from work, impaired capability/presentism and the days with limited productivity, while the quality of work increased, in a very similar manner across the three indications.

The proportion of patients requiring physician consultations, days of hospitalisation and furthermore the need for rehabilitation measures decreased on GLM 50 mg treatment.

**Disclosure of Interest:** K. Krüger Consultant for: AbbVie, BMS, Celgene, Janssen Biologics, Lilly, MSD, Pfizer, Roche, and Sanofi-Aventis, and UCB, G. Burmester Consultant for: AbbVie, BMS, MSD, Pfizer, Roche, and UCB, M. Thomas Employee of: MSD Sharp and Dohme GmbH Germany, S. Wassenberg Consultant for: AbbVie, Chugai, Janssen Biologics, MSD, Novartis, Pfizer, Roche, and UCB

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THU0661

#### OSTEOPOROSIS SCREENING, PRIMARY PREVENTION, AND TREATMENT IN GLUCOCORTICOID TREATED INDIVIDUALS WITH RHEUMATOLOGIC DISEASE

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**Background:** Glucocorticoids are commonly used in a wide variety of inflammatory conditions treated by rheumatologists. Bone loss from glucocorticoids is known to occur early and with relatively small doses. The American College of Rheumatology outlines that Glucocorticoid-Induced Osteoporosis (GIOF) is under screened and undertreated. The ACR guidelines suggest standard clinical care to



obtain a baseline DEXA in any individual with anticipated long-term steroid use, primary prevention with calcium, and vitamin D initiation and medical therapy when appropriate based on fracture risk assessments.

**Objectives:** The objective of this study was to determine how successfully the ACR GIOP guidelines are implemented in daily rheumatologic practice. The study investigates the prevalence of osteoporosis screening, prevention, and treatment in patients with rheumatologic diseases over a 2 year period at a large medical centre.

**Methods:** A retrospective cohort study of patients who received rheumatology care between 2014 and 2015 at a large medical centre was performed. Patients were included if they were older than 18 years of age, had a diagnosis of rheumatoid arthritis, systemic lupus, vasculitis, polymyalgia rheumatica, or gout and were receiving  $\geq 5$  mg prednisone daily for  $\geq 90$  days. Electronic medical records were reviewed and medication history was evaluated. Screening was defined as bone mineral density testing with DEXA within one year of glucocorticoid initiation. Primary prevention and treatment were derived from ACR GIOP criteria and included the initiation of appropriate doses of calcium and vitamin D and initiation of medical therapy to prevent bone loss. The prevalence of screening and treatment was assessed and the relationships with age, gender, and ethnicity were evaluated using Chi Squared analyses and independent samples t-tests.

**Results:** Of the 600 patients reviewed, 61 met criteria of new long-term glucocorticoid initiations. Overall 61% received BMD testing and 48% received osteoporosis primary prevention. Of those who qualified for treatment by ACR GIOP criteria, only 19% received treatment. Patients who received a baseline DEXA were older than those who did not ( $65 \pm 15$  vs  $57 \pm 16$  years,  $p=0.046$ ). Age did not influence treatment. More women compared to men received screening DEXA (68% F vs 41% M,  $p=0.053$ ) and primary prevention (55% F vs 29% M,  $p=0.078$ ). Patients who received a longer duration of steroid treatment were more likely to receive primary prevention ( $16 \pm 10$  months vs  $10 \pm 8$  months,  $p=0.015$ ). There was no association between ethnicity or disease status on screening, prevention, or treatment.

**Conclusions:** Glucocorticoid-induced osteoporosis in the setting of a rheumatology practice is a common and manageable condition that should be screened, prevented, and treated. These results from one large academic medical centre in the United States suggest that rheumatologists may not be following ACR guidelines for the assessment and management of patients on chronic steroids. Quality improvement initiatives may be necessary in order provide optimal care for patients.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.4288

THU0662

#### IMPACT OF THE INTERVENTION OF A MULTIDISCIPLINARY ADHERENCE TEAM IN CLINICAL OUTCOMES OF PATIENTS WITH RHEUMATOID ARTHRITIS AND SPONDYLOARTHROPATHIES IN COLOMBIA

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**Background:** The multidisciplinary adherence team (MAT) is a interprofessional health care group conformed by a general practitioner, a pharmaceutical chemist and a psychologist, which evaluate the patient to provide a simultaneous multidisciplinary approach focused on promoting strategies to improve adherence to treatment in patients with high disease activity of autoimmune or autoinflammatory pathologies

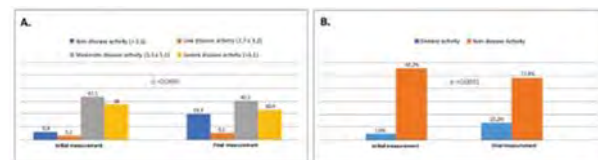
**Objectives:** To determine the impact of the MAT group intervention on the disease activity and therapeutic adherence of Colombian patients with rheumatoid arthritis (RA) and seronegative spondyloarthropathies (SpA).

**Methods:** A quasi-experimental analytical study was performed where 4.921 RA and 756 SpA patients were analysed, of which 395 and 90 respectively presented high persistent disease activity (from moderate to severe persistent), despite of conventional strategies implemented; therefore they underwent intervention by the MAT group between January and December of 2016. Clinical disease activity according to each disease (DAS28 and BASDAI measurements respectively) and adherence level (categories through the Morisky-Green test: no adherence, partial adherence, total adherence) were measured before and after the MAT intervention. The impact on disease activity and adherence level was determined through the McNemar test for independent samples

**Results:** A significant increase in the proportion of patients in total adherence level was found for both diseases when comparing the initial and final measurements after the intervention by the MAT (table 1). Furthermore, statistical significant differences in the disease activity level were found, identifying a reduction in the proportion of patients with moderate to severe disease activity (Graph 1, A and B) after the MAT intervention

**Abstract THU0662 – Table 1.** Impact in adherence in patients with RA and SpA underwent by the MAT group intervention

Treatment adherence (Morisky-Green test)	AR n=395			SpA n=90		
	Initial (%)	Final (%)	P-value	Initial (%)	Final (%)	P-value
No adherence	9,1	8,1	<0001	7,8	2,2	0002
Partial Adherence	40,8	32,9		37,8	40	
Total Adherence	50,1	59		54,4	57,8	



**Figure 1** A) Disease Activity in patients with RA (DAS28); B) Disease Activity in patients with SpA (BASDAI)

**Conclusions:** The intervention by the MAT interprofessional group is an efficient strategy impacting the disease activity and therapeutic adherence of RA and SpA patients, improving their clinical outcomes and the natural history of the disease. These findings are relevant and may highlight the potential benefits for the implementation of this approach in patients with devastating autoimmune diseases.

**Disclosure of Interest:** None declared

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THU0663

#### RHEUMATOLOGY ADOLESCENT AND YOUNG ADULT CARE: REAL WORLD CHALLENGES AND OPPORTUNITIES

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**Background:** Adolescents and young adults (AYA) form one sixth of the world's population and account for 6% of the world's global burden of disease. Those with chronic illness are particularly vulnerable. Globally, significant improvements in healthcare related morbidity and mortality have been seen, but not within the 10–24 year old group. Adolescence is a rapidly changing, formative phase of human development; opportunities exist to impact this through restructuring care pathways and patient empowerment.

**Objectives:** Establish awareness of current national guidance and identify unmet needs in existing rheumatology AYA systems.

**Methods:** Interested parties from South East England (South London, Kent, Surrey and Sussex) formed a multi-disciplinary, patient based, co-design initiative (RAYA collaborative) which included representatives from primary/secondary/tertiary care, allied health professionals and a youth worker/patient from the charity sector. Our discussions and an anonymous survey to hospitals in the region, formed the basis of a qualitative and quantitative analysis, which helped gain a holistic insight into the challenges and opportunities in delivering AYA care in our region.

**Results:** 15/20 centres, covering an 8 million population, responded; 4 tertiary care hospitals, 11 district general hospitals with 32 responses (19 consultants, 13 senior registrars).

31 (97%) of responders felt that AYA cohort (16–25 years old) required an approach different to that of older adults. 25 (78%) felt there was a need for dedicated AYA services. 23 (72%) and 17 (53%) were aware of UK national guidelines<sup>CCC 2014</sup>/NICE NG43 2016 respectively) for transitional/integrated and coordinated care.

Barriers to developing dedicated AYA services (% of responders): Not a priority for NHS managers,<sup>31</sup> other clinical priorities,<sup>31</sup> insufficient patient numbers,<sup>22</sup> not cost effective,<sup>19</sup> unlikely to be commissioned,<sup>19</sup> more research required,<sup>13</sup> cohort by diagnosis,<sup>13</sup> other ways to deliver care,<sup>13</sup> only focus on transitioning patients from paediatrics<sup>13</sup>

Responders would like assistance in future care delivery through: Clinical toolkit: 63% n=20, Service commissioning toolkit: 43% n=14, Training: 43% n=14, Workshops: 47% n=15.

Potential low cost/neutral approaches to systems change, cultural change, education and sharing of resource were discussed (see image).

Questions	Comments/Objections	Potential Solutions	Potential Outcomes/Actions
1. How to fund additional activity or support staff required for AYA services?	<ul style="list-style-type: none"> <li>These patients are already being seen in the service so no additional activity needs to be accounted for</li> <li>Restructuring the service allows for a more streamlined and efficient use of services</li> </ul>	<ul style="list-style-type: none"> <li>Restructuring the clinics into specialist matched subjects</li> <li>Slightly longer time slots (45mins for, 30mins follow up)</li> <li>Support services - physiotherapy/ psychology run in parallel for "One stop shop clinics"</li> <li>A key worker (nurse/young worker) has demonstrated significant improvements through helping to sign base to relevant support services</li> </ul>	<ul style="list-style-type: none"> <li>Improve patient engagement, self management and self advocacy</li> <li>Should reduce follow up/acute admissions/disease flares / non-attendance rates</li> <li>Encourage this to be cost neutral over current need and increasing population base to address</li> </ul>
2. How do we structure our departments and managers there is a need for age appropriate care?	<ul style="list-style-type: none"> <li>District General Hospital - Not enough patients to colour a whole clinic</li> <li>Problems with out patient capacity</li> <li>Treat need incentive from commissioners</li> <li>Continative appointments do not allow flexibility (patients have care or last minute appointments/ exams/work / social commitments)</li> </ul>	<ul style="list-style-type: none"> <li>Dedicate the first hour (2-3 patients) of a clinic to AYA cohort</li> <li>Bring or work out clinics to accommodate additional priority</li> <li>Follow up coordinator. One center has reduced non-attendance rates by 19% as this allows flexibility/urgent appointments to be re-scheduled without excessively overbooking clinics</li> </ul>	<ul style="list-style-type: none"> <li>Engage in dialogue with commissioners/ community agencies early on (Lambeth &amp; Southwark commissioners are moving towards population based commissioning model)</li> <li>Business case for a patient pathway coordinator</li> </ul>
3. What resources are available to support clinicians / direct patients?	<ul style="list-style-type: none"> <li>General lack of recognition within organisations about importance of supporting young adults through the process of a chronic health condition</li> <li>Importance of sharing resource throughout the RAYA network</li> </ul>	<ul style="list-style-type: none"> <li>Improve training and understanding of age appropriate care</li> <li>Modification of registrar training curriculum to encompass age appropriate care</li> <li>Regional website to share resource</li> <li>Collaboration with existing AYA networks</li> </ul>	<ul style="list-style-type: none"> <li>Summary of resources and training modules</li> <li>Website / app would require a web master to manage and update regularly (Could this be patient led)</li> <li>Shape of training: Curriculum wording has been modified to encompass age appropriate care and admitted to training body</li> </ul>
4. What is the benchmark standard of good practice for AYA patients we should be aspiring to?	<ul style="list-style-type: none"> <li>Models of care will need to be flexible and based on local needs</li> </ul>	<ul style="list-style-type: none"> <li>Complex patients may need referral to a tertiary center or a Hub and Spoke model may work better for more district general hospitals.</li> </ul>	<ul style="list-style-type: none"> <li>NICE, QIC and JRCAR guidance are useful resources</li> <li>Future RAYA meetings could be a platform for peer review and complex case discussion</li> </ul>

**Conclusions:** Improving outcomes for AYA patients through delivering age appropriate care and self advocacy has driven global strategy and guidelines. Our survey identifies that the majority of rheumatologists agree with this, however there is room for improvement regarding awareness and implementation of current guidance.

Financial constraints and whole population healthcare delivery has limited change. A systematic, unified approach within regions may help to effect change. There is a demand for the development of clinical and commissioning toolkits and training/workshops to help facilitate this.

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THU0664

#### TREATMENT ADHERENCE TO CONVENTIONAL AND BIOLOGIC DISEASE MODIFYING ANTIRHEUMATIC DRUGS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** While treatment with conventional or biologic disease-modifying antirheumatic drugs (DMARDs) is highly effective in preventing radiographic progression and improving long-term functional outcome among patients with rheumatoid arthritis (RA), patient adherence to DMARD treatment is required for these positive effects. Suboptimal medication adherence has been repeatedly noted in patients with chronic medical conditions including RA.

**Objectives:** To examine patient adherence to different DMARDs for RA in a real-world setting.

**Methods:** We conducted a population-based cohort study using claims data from a US commercial health plan (Optum Clinformatics™ Datamart 2004–2015) and Medicaid (2000–2010). Eligible patients were those aged between 18 and 65 years and had at least two visits, 7–365 days apart, coded for RA (ICD-9: 714.xx). We then identified patients who newly started a conventional or biologic DMARD. The index date was the first dispensing date of conventional or biologic DMARDs after a 12 month continuous enrollment period. We examined patient demographics, clinical characteristics and health care utilisation factors specific to DMARDs types and their adherence to conventional or biologic DMARDs. All patients were required to be continuously enrolled for at least 1 year after the index date. Patients' adherence to each DMARD was measured using the proportion of days covered (PDC) calculated as the number of days supplied divided by 365 days post-index.

**Results:** We identified a total of 77,999 RA patients (37 018 in Optum and 40 981 in Medicaid) who started a conventional or biologic DMARD. Of those, 28 332 initiated methotrexate, 27 157 hydroxychloroquine, 6505 sulfasalazine, 2773 leflunomide and 19 381 biologic DMARDs. Table 1 shows patients' adherence specific to DMARD types. Overall, adherence was better in patients enrolled in Optum (i.

e., a commercial health plan) than Medicaid. Except for infliximab given only intravenously, the PDC for the 1 year after initiating a conventional or biologic DMARD ranged from 30.99% (sulfasalazine in Medicaid) to 60.84% (abatacept in Optum).

**Abstract THU0664 – Table 1.** Adherence to DMARDs in patients with RA: Proportion of days covered for 1 year

	Optum	Medicaid
Mean (SD) in percentage		
<b>Conventional DMARDs</b>		
Methotrexate	58.13 (31.39)	44.00 (29.58)
Hydroxychloroquine	50.87 (31.72)	39.79 (28.71)
Sulfasalazine	36.59 (29.46)	30.99 (25.65)
Leflunomide	48.54 (32.09)	41.72 (30.62)
<b>Biologic DMARDs</b>		
Abatacept	60.84 (30.36)	49.70 (31.51)
Adalimumab	53.02 (29.60)	49.09 (29.01)
Certolizumab	49.53 (29.10)	39.54 (27.91)
Etanercept	52.71 (29.37)	50.00 (29.25)
Golimumab	51.10 (28.92)	48.36 (26.82)
Infliximab *	74.39 (28.65)	60.69 (30.63)
Tocilizumab	57.95 (27.77)	-

\*assumed infliximab was given every 8 weeks.

**Conclusions:** In this large population-based cohort of RA patients enrolled in a commercial health plan or Medicaid, the 1 year medication adherence is generally low regardless of type of DMARDs. While adherence is better in the commercial health plan cohort than Medicaid, other factors predicting medication adherence need to be determined further. There is a strong need for future research examining the impact of medication adherence on long-term RA-related clinical outcomes.

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THU0665

#### PHARMACOVIGILANCE SURVEILLANCE OF AUTOIMMUNE DISEASES INDUCED BY BIOLOGICAL AGENTS: A REVIEW OF 16123 CASES (AEBIOGEAS-SEMI REGISTRY)

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**Objectives:** The increasing use of biological agents has been linked with the paradoxical development of autoimmune processes. The scenario has dramatically change in recent years due to the increased number of biologics used in daily practice and the emerging use of biologics in patients with solid cancers.

**Methods:** In 2006, the Study Group on Autoimmune Diseases (GEAS) of the Spanish Society of Internal Medicine created the BIOGEAS project, a multicenter study devoted to collecting data on the use and safety of biological agents in adult patients. The aeBIOGEAS Registry (autoimmune events) was designed to collect data on autoimmune diseases secondary to the use of biologic agents, with the aim of formulating a standardised, consensual protocol for these patients, through a systematic and yearly MEDLINE search. We present the updated results of the aeBIOGEAS Registry (cases collected until Dec 31, 2017).

**Results:** The aeBIOGEAS Registry currently includes 16 123 cases of more than 50 different systemic and organ-specific triggered autoimmune diseases related to the administration of 46 different biological molecules in patients with inflammatory diseases (9907 cases, overwhelmingly rheumatic diseases in 8639) and cancer (6216 cases, overwhelmingly solid neoplasia in 5955). The main biological agents identified consisted of anti-TNF agents in 9514 cases (mainly adalimumab in 4147, infliximab in 3028 and etanercept in 1648), checkpoint inhibitors in 5264 (overwhelmingly the CTL4 inhibitor ipilimumab in 4980 cases), tyrosine kinase inhibitors in 952 (mainly imatinib in 377 cases) and B-cell targeted therapies in

298 cases. Organ-specific classification of triggered autoimmune diseases included cutaneous (n=7140), digestive (n=2323), endocrine (n=1701), pulmonary (n=1683), systemic/rheumatic (n=1230), neurological (n=1172), ocular (n=349), cardiac (n=322), haematological (n=106) and renal (n=96) diseases. The most frequently reported induced individual autoimmune diseases were psoriasis (n=6401), enterocolitis (n=1947), interstitial lung diseases (n=1680), thyroiditis (n=1076), hypophysitis (n=492), demyelinating CNS diseases (n=452), peripheral neuropathies (n=431), lupus (n=371), vasculitis (n=339), uveitis (n=298), vitiligo (n=256) and sarcoidosis (n=185).

**Conclusions:** The number and diversity of induced autoimmune disorders is increasing exponentially in parallel with the increased use of biological therapies in neoplastic diseases, which are currently representing 40% of reported cases. Management of these biologic-induced autoimmune diseases will be an increasing multidisciplinary clinical challenge in the daily practice in the next years.

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#### THU0666 COSTS ASSOCIATED WITH SWITCHING SUBCUTANEOUS TUMOUR NECROSIS FACTOR- $\alpha$ INHIBITOR IN THE TREATMENT OF IMMUNE-MEDIATED RHEUMATIC DISEASE

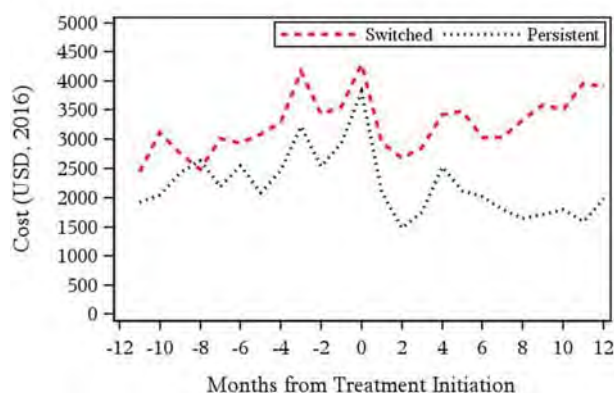
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**Background:** Few studies have investigated the costs associated with switching subcutaneous tumour necrosis factor- $\alpha$  inhibitor (SC-TNFi) in the treatment of immune-mediated rheumatic disease (IMRD; rheumatoid arthritis, ankylosing spondylitis, and psoriatic arthritis),<sup>1-2</sup> and to our knowledge no studies have been performed in a European setting.

**Objectives:** The objective of this retrospective observational study was to explore costs of health care resource utilisation (HCRU) associated with switching SC-TNFi in patients with IMRD in Sweden.

**Methods:** Using data from Swedish Health Data Registers, adult, treatment naïve IMRD patients filling prescriptions between May 1st 2010 and December 31st 2015 for any of the currently available SC-TNFi (adalimumab, etanercept, certolizumab, and golimumab) were included. Prescriber specialty and department were used to exclude patients with SC-TNFi treatment unrelated to IMRD. A switch was defined as a filled prescription for a subsequent SC-TNFi within 60 days of first line discontinuation. HCRU, including non-DMARD medication, inpatient and specialised outpatient care, was captured 12 months pre- and post-treatment initiation. Eligible patients had at least 12 months follow-up, and were either persistent throughout or switched treatment during the follow-up period. The analysis was performed on a propensity score matched (PSM) cohort.

Figure 1. Total Cost of Health Care Resource Utilization



Abstract THU0666 – Figure 1 Total. cost of health care resource utilisation

**Results:** In total, 6213 eligible patients were identified, of which 5092 were persistent with their index therapy throughout the follow-up period while 1120 patients switched SC-TNFi. The PSM cohort was derived as “Persistent” vs. “Switched” with a total of 1120 matched pairs. Patients switching therapy had higher total

HCRU costs during the baseline period and maintained their average cost during the follow-up period (figure 1), whereas persistent patients decreased their average costs from the baseline period to the follow-up period. The average yearly cost during baseline and follow-up was USD 4,512 vs USD 4,690 for patients switching SC-TNFi, and USD 3,630 vs USD 2,662 for persistent patients. This corresponds to a difference in difference of USD 1,146 (p<0.001).

**Conclusions:** Similar to previous findings,<sup>3-4</sup> patients switching maintained their higher costs, while persistent patients decreased their costs from baseline to the follow-up period. This further highlights the notion that persistence may not only serve as a marker for drug effectiveness, safety, and treatment satisfaction, but also for reduced HCRU and costs.

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**Disclosure of Interest:** J. Dalén Employee of: Mapi, A. Svedbom Employee of: Mapi, K. Luttropp Employee of: Mapi, S. Kachroo Shareholder of: Merck and Co., Inc., Employee of: Merck and Co., Inc.

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#### THU0667 DISEASE, WORK AND PERSONAL RELATED FACTORS ASSOCIATED WITH PRESENTEEISM IN PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS FROM THE NATIONAL RHEUMATOID ARTHRITIS SOCIETY SURVEY (NRAS)

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**Background:** At-work productivity loss (i.e. presenteeism) is a major problem for patients with rheumatoid arthritis (RA) and employers and could be a marker of long-term absenteeism. To develop interventions to prevent presenteeism, a better understanding of which factors are associated with presenteeism is needed.

**Objectives:** To assess the association between disease and work related factors with presenteeism.

**Methods:** A large survey about employment amongst patients with RA was conducted in the UK using an online platform and inviting NRAS members and non-members to participate. Patients completed the multi-item Workplace Activity Limitation Scale (WALS; range 0–36 worst score), a measure of presenteeism. Other job related questions included: occupation (NS-SEC coding), job demand questions, help from colleagues (categorised into: always/often, sometimes, rarely/never) and a patient acceptable state questionnaire about work (PASS). Patients also completed the disease specific RAID questionnaire (score 0–10=worst score). Univariable and multivariable linear regression analyses were performed to assess the association between the disease and job related factors and presenteeism, adjusting for age and gender.

**Results:** 891 respondents were in paid work at the time of the survey (51.5% working for others, 33.1% self-employed and 15.4% on temporary sick leave). The majority of participants were women (91.5%) and 4.9% were aged 16–30, 69.2% 31–54 and 25.8% aged 55–74 years. Over half (51.5%) had a higher managerial, administrative or professional occupations, 33.1% an intermediate occupation, and 15.4% a routine/manual occupation. Mean (SD) RAID score was 5.2 (2.2). 58.2% rated their current job performance somewhat/much worse than before the onset of their arthritis. In univariable regression analyses greater disease activity, less control, lower support from colleagues and being in a unacceptable disease state (PASS) were associated with higher levels of presenteeism. In multivariable analysis, disease activity, ability to influence work and a unacceptable disease state remained statistically significantly associated with presenteeism.



Abstract THU0667 – Table 1

	N (%) or mean (SD)	Univariable analysis R (95%CI)*	Multivariable analysis R (95%CI)*
<b>RAID users</b>	5.3 (2.2)	<b>1.96 (1.80, 2.12)</b>	<b>1.59 (1.43, 1.78)</b>
RAID requires using a lot of force, e.g. lifting, pulling or use of tools and machines using a lot of force:			
• Never/Rarely	328/865 (62%)	1	
• Sometimes	366/865 (19%)	0.81 (-0.3, 1.03)	
• Often/Always	359/865 (19%)	<b>2.48 (1.26, 3.70)</b>	
RAID requires a lot of standing:			
• Never/Rarely	385/865 (45%)	1	
• Sometimes	142/865 (17%)	0.44 (-0.88, 1.73)	
• Often/Always	337/865 (39%)	<b>1.90 (0.90, 2.91)</b>	
RAID requires use of computer for more than 4 hours:			
• Never/Rarely	225/865 (26%)	1	
• Sometimes	93/86 (11%)	0.67 (0.98, 2.33)	
• Often/Always	535/865 (63%)	<b>-0.20 (-1.26, 0.86)</b>	
Able to influence work:			
• Never/Rarely	218/865 (25%)	1	
• Sometimes	244/865 (29%)	<b>-2.13 (-3.33, -0.94)</b>	<b>-1.02 (-2.02, -0.03)</b>
• Often/Always	398/865 (46%)	<b>-4.33 (-5.42, -3.24)</b>	<b>-1.87 (-2.95, -0.80)</b>
Able to take time off, small breaks, when needed:			
• Never/Rarely	268/865 (31%)	1	
• Sometimes	213/865 (25%)	<b>-1.78 (-2.92, -0.54)</b>	
• Often/Always	372/865 (44%)	<b>-3.22 (-4.27, -2.17)</b>	
How often do you get help and support from colleagues:			
• Never (reference)	67/773 (9%)	1	
• Sometimes	305/773 (42%)	<b>-1.94 (-3.65, -0.19)</b>	
• Often/Always	341/773 (45%)	<b>-2.94 (-4.71, -1.17)</b>	
<b>PASS</b>			
• Acceptable	187/786 (24%)	1	
• Not acceptable	399/786 (51%)	<b>7.10 (6.84, 7.46)</b>	<b>2.65 (1.78, 3.52)</b>

**Conclusions:** In this large national survey in patients with RA we found that not only disease activity, but also having control, especially the flexibility to influence work and take breaks when needed, were associated with levels of presenteeism. Preventing presenteeism should therefore be aimed at managing the disease, but also toward adapting work circumstances and finding the right balance between work requirements and personal needs.

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THU0668

**CHOICE OF INITIAL BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUG IMPACTS HEALTHCARE RESOURCE USE AMONG PATIENTS WITH RAPIDLY PROGRESSING RHEUMATOID ARTHRITIS**

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**Background:** Current management of rheumatoid arthritis (RA) in the United States is often directed by payer medical policy, typically requiring a tumour necrosis factor- $\alpha$  inhibitor (TNFi) as a first-line (1L) biologic disease-modifying antirheumatic drug (bDMARD). Recent studies<sup>1</sup> suggest clinical subsets of patients with RA may benefit from early intervention with a non-TNFi bDMARD.

**Objectives:** To characterise 6 month healthcare resource utilisation (HRU) for patients with RA in the United States when treated with different 1L bDMARDs (1L TNFi or 1L abatacept) and assess the impact of initial bDMARD selection on 6 month HRU.

**Methods:** Early, rapidly progressive RA (eRRA) is a recognised clinical entity comprising a constellation of clinical and biomarker features: anti-cyclic citrullinated peptide-2 positivity (ACCP+), DAS28 (CRP)  $\geq 3.2$ , symptomatic synovitis in  $\geq 2$  joints for  $\geq 8$  weeks and onset of symptoms  $\leq 2$  years. Physicians with adult RA patients meeting these criteria for eRRA used patient medical records to provide patient data via an electronic case report form. Patients received either abatacept or TNFi in 1L. Patient characteristics and HRU in the first 6 months of bDMARD treatment were summarised and compared across treatment groups. Odds ratios (OR) of HRU were estimated using multivariable logistic regression to adjust for baseline indicators of disease severity and patient mix (age, sex, race, ethnicity, region, payer type, time from RA diagnosis to bDMARD start, baseline concomitant medication use, baseline swollen joint count [SJC], tender joint count [TJC], Clinical Disease Activity Index [CDAI], extra-articular manifestations).

**Results:** There were 60 abatacept and 192 TNFi patients in 1L. Mean ages at bDMARD start were 49.1 and 49.9 years, and mean times from RA diagnosis to bDMARD initiation were 1.5 and 6.4 months for abatacept and TNFi users, respectively (all  $p > 0.05$ ). At bDMARD start, patients with eRRA treated with abatacept or TNFi, respectively, had mean SJC of 6.8 and 7.3, TJC of 10.4 and 10.2, ESR of 39.8 and 44.0 mm/h, CRP of 8.1 and 8.2 mg/L and numbers of bony erosions of 1.2 and 1.7 (all  $p > 0.05$ ). 45% and 47% ( $p > 0.05$ ) of abatacept and TNFi users, respectively, had concomitant oral corticosteroids at bDMARD start. A lower proportion of patients treated with abatacept had hospitalizations (72 vs 88%), emergency department (ED) visits (75 vs 90%) and MRI (65 vs 82%) (all  $p < 0.05$ ), while use of ultrasound (82 vs 88%) and radiography (88 vs 93%) during the first 6 months of bDMARD treatment was similar. After adjusting for patient

characteristics, those treated with 1L abatacept had significantly lower odds of hospitalisation (OR 0.42; 95% CI 0.18, 0.95), ED visits (OR 0.39; 95% CI 0.16, 0.93) and MRI (OR 0.45; 95% CI 0.21, 0.97) compared with 1L TNFi (all  $p < 0.05$ ). Adjusted odds of achieving CDAI low disease activity within 100 days of bDMARD favoured 1L abatacept vs 1L TNFi (OR 3.26; 95% CI 1.32, 8.07;  $p < 0.05$ ).

**Conclusions:** After adjusting for baseline disease severity, patients treated with 1L abatacept were less likely to have hospitalizations, ED visits and MRIs during the first 6 months of bDMARD treatment compared with those who received a 1L TNFi.

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**Disclosure of Interest:** A. Klink Consultant for: Bristol-Myers Squibb, Janssen, Celgene, EMD Serono, Ipsen, Kite, Merck, Novartis, Vertex, Amgen, Astellas, Heron, AbbVie, Array, Seattle Genetics, Employee of: Cardinal Health, K. Tuell Employee of: Bristol-Myers Squibb, R. Szymialis Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, T. Curtice Employee of: Bristol-Myers Squibb, K. Gupta: None declared, D. Nero Consultant for: Bristol-Myers Squibb, Employee of: Cardinal Health, B. Feinberg: None declared

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THU0669

**A SELF-REPORT SYMPTOM CHECKLIST ON A MULTIDIMENSIONAL HEALTH ASSESSMENT QUESTIONNAIRE (MDHAQ) TO CAPTURE A “POSITIVE REVIEW OF SYSTEMS” AS A STANDARD, QUANTITATIVE, AND INFORMATIVE “SCIENTIFIC” CLUE TO FIBROMYALGIA SIMILAR TO MODIFIED CRITERIA FOR FIBROMYALGIA**

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**Background:** The scientific method is based on recording information as quantitative standard data rather than as narrative descriptions, to test possible value in diagnosis, management, and outcomes. This approach generally is applied to laboratory tests and other data from high technology sources. However, information from a patient history and physical examination can be analysed for scientific validity if collected in as standard, quantitative and reproducible data. A symptom checklist of 60 items was initially designed as a review of systems to screen for symptoms and possible adverse events of medications, for which it has been helpful. It has also been observed that patients who report a large number of symptoms may provide a clue to the presence of fibromyalgia (FM); Clin Exp Rheumatol. 2004. 22:453–61).

**Objectives:** To compare results of a 60-item symptom checklist on a multidimensional health assessment questionnaire (MDHAQ) vs the modified 2016 revised preliminary diagnostic criteria for fibromyalgia (Sem Arth Rheum 46:319–329, 2016).

**Methods:** All patients seen at an academic rheumatology clinic complete an MDHAQ; J Rheumatol 2005 32:1432–9) at each visit, which includes a 60-item symptom checklist. In April-July 2017, patients also completed a questionnaire to identify the 2016 revised preliminary diagnostic criteria for FM. The likelihood of reporting each symptom by a patient with RA who did not have FM was compared to patients who met 2016 criteria for FM using a chi-square test. Receiver operator characteristic (ROC) curves were performed of the 60 symptom checklist as well as the 10 most discriminatory symptoms vs the FM criteria.

**Abstract THU0669 – Table 1.** Proportion of patients with rheumatoid arthritis (RA) who did not meet fibromyalgia criteria versus patients with primary or secondary fibromyalgia to meet fibromyalgia criteria who responded positively regarding the 10 most discriminatory symptoms on a symptom checklist

Symptom	RA (84)	FM (110)	Chi2*
Muscle pain, aches, or cramps	30 (35)	100 (31)	65.6367
Muscle weakness	16 (19)	82 (75)	58.6852
Dizziness	11 (13)	65 (59)	42.2875
Headaches	25 (30)	84 (76)	42.0177
Problems with thinking	7 (8)	57 (52)	40.7405
Problems with memory	12 (14)	65 (59)	39.9442
Neck pain	29 (35)	87 (79)	39.3505
Problems with sleeping	30 (36)	88 (80)	39.2017
Numbness or tingling of arms or legs	16 (19)	70 (64)	38.3709
Unusual fatigue	23 (27)	79 (72)	37.7207

\*all  $p < 0.001$

**Results:** We studied 84 patients with RA who did not meet FM criteria vs 110 patients who met FM criteria – no differences were seen between patients with primary or secondary FM who met criteria. Patients who met FM criteria were more likely to report each of the 60 symptoms. The 10 symptoms that were most discriminatory of RA vs FM are illustrated in the table 1. A ROC curve for the 60 symptoms vs the FM Criteria had an area of 0.896 (Confidence interval 0.872–0.925), and for the 10 most discriminatory symptoms of 0.8975 (Confidence interval 0.8667–0.928).

**Conclusions:** A simple MDHAQ symptom checklist may be informative in routine rheumatology care to identify possible primary and secondary FM in agreement with FM criteria. The MDHAQ may provide a useful and feasible alternative to FM Criteria for busy clinical settings.

**Disclosure of Interest:** T. Pincus Shareholder of: Dr. Pincus holds a copyright and trademark on MDHAQ and RAPID3 for which he receives royalties and license fees. All revenue is used to support further development of quantitative questionnaire measures for patients and doctors in clinical rheumatology care., S. Jamal: None declared, I. Castrejon: None declared

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#### THU0670 A REUMATOLOGIST'S EVALUATION OF HOW EFFICIENCIES IN THE MANAGEMENT OF PAINFUL LUMBAR SYNDROME IN WORK DISABILITY CREATES BENEFITS & SAVINGS

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**Background:** Musculoskeletal disorders are the most important cause of sick leave in the world.<sup>1</sup> Lumbar pain is the main cause of temporary incapacity which significant socio-economic impact.

**Objectives:** Test efficiency of Healthcare approach by rheumatologist as savings in indirect costs e.g days off work and in direct costs derived from medical assistance in controlled patient group on sick leave diagnosed with lumbar pain.

**Methods:** 2 year quasi-experimental bi-directional analytical design trial. Retrospective cohort in Control Group- CG and prospective cohort for intervention group -IG. Two groups, IG and CG respectively contain 150 (56% women aged 47.5 years±10) and 172 (48.8% women aged 44.2 years±10) working age patients with lumbar pain. Study made by Program for the Management of Temporary Disability implemented by Rheumatology Service of University Hospital of the Canary Islands. Study included early intervention, protocol in diagnostic tests and treatment. This study was evaluated by the Ethics Committee of the research of the University Hospital of Canary Islands fulfilling the requirements of suitability.

**Results:** 24% of patients of IG fit to return to work after first appointment. Maximum efficiency of study between 30th and 45th day of sick leave. At 45 days 8% IG and 18,6% CG remained on sick leave. Average reduction 26 days of sick leave respect to CG, a total saving of 6.182 days of sick leave over 1 year, with efficiency of 62,2%. Saving in direct costs in IG over CG: medicaments, complementary tests, inter-consultations, follow up 48%. Absolute saving of 38.891€, or equivalent 256.680€ for 1.000 patients. National Institute of Social Security Indirect sick leave costs 67,1%. Absolute saving of 129.883€, or equivalent of 857.227€ for 1.000 patients. Indirect costs savings for Employers for intervention 50%. Absolute saving 108.649€, or equivalent to 717.083€ for 1.000 patients. Workers in program saved 50% in salary loss. Average saving 605€/worker. Total saved by implementation of program to State, to worker, to Employer-360.142€. Program Cost effective, producing average annual saving per patient of 259€ and average reduction of sick leave days of 41,2. Program cost efficiencies produced. Every day of disability saved equivalent to implementation cost of 5,06€. Cost-benefit program produced for State saving of 6,44€ for every € invested in implementation 137.248€. Program had 93,8% patient acceptance expressing maximum satisfaction.

**Conclusions:** Management of disability by rheumatologist highly profitable given low program implementation cost compared to savings generated for State and Employer.

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**Disclosure of Interest:** None declared

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THURSDAY, 14 JUNE 2018

## Epidemiology, risk factors for disease or disease progression

#### THU0671 STANDARDISED MORTALITY RATES FOR SYSTEMIC LUPUS ERYTHEMATOSUS IN WESTERN AUSTRALIA FROM 1980 TO 2015

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**Background:** Patients with Systemic Lupus Erythematosus (SLE) are at increased risk of premature mortality. However, population-level mortality rates for SLE have not yet been reported in Australia.

**Objectives:** Calculate the standardised mortality rates (SMR) for SLE patients in Western Australia (WA) from 1980 to 2015, overall and by age and gender.

**Methods:** Utilising whole-population linked hospital admission, cancer registration and death data for WA from 1980 to 2015, we compared characteristics and calculated SMRs (95% CI) for patients with SLE (ICD-9-CM 695.4, 710.0, ICD-10-AM L93.0, M32.0) against controls (5:1) free of rheumatic disease after matching for age, gender, Aboriginality and year of first SLE event.

**Results:** SLE patients (n=2,868) and controls (n=12,785) recorded 1335 and 4400 deaths with crude mortality rates of 56.3/1,000 vs 37.1/1,000 person-years, respectively. SLE patients were approximately 10 years younger (71 vs 81 years) and 2.2-times more likely hospitalised at death (p<0.001). The age-adjusted SMR (per 1,000) for SLE patients was 4.4 (95%CI 3.0, 5.8), and higher in females 5.4 (95%CI 3.5, 7.4) than in males 3.4 (95%CI 1.5, 5.4). Five-year period SMRs were 8.6 (95%CI 5.0, 12.2) between 1990–1994, 9.3 (95%CI 4.4, 14.2) between 1995–1999, 7.6 (95%CI 3.1, 12.1) between 2000–2004, 4.5 (95%CI 0.2, 8.7) between 2005–2009, and 4.9 (95%CI 1.32, 8.5) between 2010–2015.

**Conclusions:** SLE patients in WA experienced a decline in SMRs over time, but remain at increased risk of premature mortality. Within the limitations of administrative linked data, SLE in WA associates with an average reduction in life span of 10 years.

**Acknowledgements:** The authors wish to thank the staff at the Western Australian Data Linkage Branch and Emergency Department Data Collection, Hospital Morbidity Data Collection, WA Cancer Registry and Death Registrations.

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**Disclosure of Interest:** None declared

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#### THU0672 IMPACT OF PREGNANCY ON PHYSICAL FUNCTION AND HEALTH-RELATED QUALITY OF LIFE IN WOMEN WITH AXIAL SPONDYLOARTHRITIS

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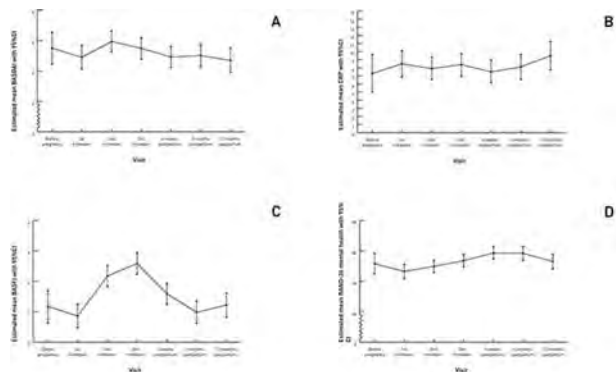
**Background:** The only previous study exploring the impact of pregnancy on health-related quality of life in women with axial spondyloarthritis (axSpA), included only ten women.<sup>1</sup>

**Objectives:** To prospectively study physical function and health-related quality of life in a large cohort of women with axSpA during and after pregnancy, using Bath Ankylosing Spondylitis Functional Index (BASFI) and three of the dimensions of RAND 36-Item Health Survey (RAND-36): Physical functioning, bodily pain and mental health.

**Methods:** RevNatus is a Norwegian nationwide register designed for the follow-up of pregnant women with rheumatic diseases. Our study comprised 179 pregnancies in 166 women with axSpA included in RevNatus between 2006 - 2016. The women had seven visits at a rheumatology unit; before pregnancy, in each trimester, and six weeks, six months and twelve months postpartum. BASFI-scores and scores of RAND-36 physical functioning, bodily pain and mental health from each visit were analysed in a linear mixed model. BASFI has an overall index score between 0 ("no functional impairment") and 10 ("maximal functional

impairment").<sup>2</sup> The dimensions of RAND-36 have scores between 0–100 (where 100="best possible health").<sup>3</sup>

**Results:** BASFI-scores were highest in third trimester, significantly higher than six weeks postpartum (mean BASFI 3.6 vs. 2.6,  $p<0.001$ ). In line with this result, scores of RAND-36 physical functioning was significantly lower in third trimester compared to six weeks postpartum (mean physical function 54.5 vs. 71.0,  $p<0.001$ ). The women reported considerable pain throughout the study period, with worst reported pain in second trimester, when scores of RAND-36 bodily pain were significantly lower than six weeks after postpartum (mean bodily pain 44.3 vs. 49.6,  $p=0.01$ ). Scores of RAND-36 mental health were high and stable throughout the study period, with best reported mental health six weeks after delivery, when mental health was significantly better than in all time points in pregnancy.



**Abstract THU0672 – figure 1.** shows changes in functionality and mental health from preconception to one year after delivery, and disease activity and CRP in the same time period.

**Conclusions:** Even though women with axSpA reported considerable pain and gradually worsening of physical function in pregnancy, they experienced good and stable mental health from preconception to one year after delivery.

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**Disclosure of Interest:** None declared

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#### THU0673 DISEASE ACTIVITY DURING AND AFTER PREGNANCY IN WOMEN WITH PSORIATIC ARTHRITIS

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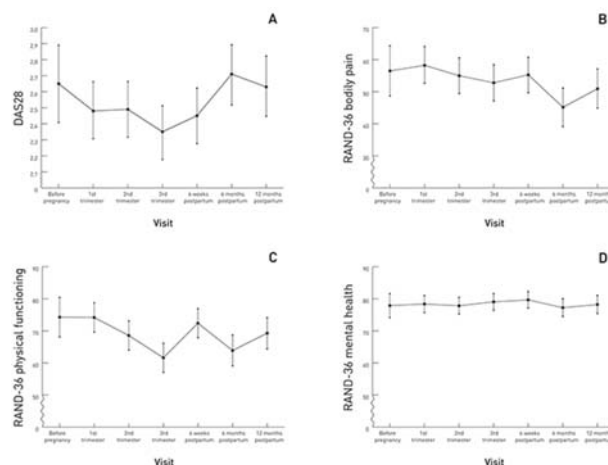
**Background:** The few previous studies on disease activity of psoriatic arthritis in pregnancy have shown diverging results.<sup>1–3</sup> None of the studies used validated disease activity measures and the only prospective study was conducted before the widespread use of biological DMARDs.

**Objectives:** The aim of this project was to prospectively study disease activity in women with psoriatic arthritis before, during and after pregnancy with DAS28-CRP-3 as disease activity measure.

**Methods:** RevNatus is a Norwegian nationwide register designed for the follow-up of pregnant women with rheumatic diseases. Our study comprised 108 pregnancies in 103 women with psoriatic arthritis with mainly peripheral involvement, included in RevNatus between 2006 - 2017. The women had seven visits at a rheumatology unit; before pregnancy, in each trimester, and six weeks, six months and twelve months postpartum. DAS28-CRP-3-scores from each visit

were analysed in a linear mixed model. We did additional analyses with "tumour necrosis factor inhibitor (TNFi) in pregnancy (yes/no)" as covariate.

**Results:** Altogether, our study demonstrated stable, low disease activity during and after pregnancy in women with psoriatic arthritis. However, as shown in figure 1, disease activity decreased in pregnancy and increased within six months postpartum, with disease activity six months postpartum significantly higher than six weeks postpartum (estimated mean DAS28 2.71 vs. 2.45,  $p=0.016$ ). Women using TNFi in pregnancy had significantly lower disease activity than women not using TNFi (estimated mean DAS28 six weeks postpartum 1.97 vs. 2.48,  $p=0.039$ ).



**Abstract THU0673 – Figure 1.** also shows self-reported pain, physical functioning and mental health throughout the study period.

**Conclusions:** Studying women with psoriatic arthritis, we found that disease activity was highest six months postpartum, but altogether stable in the period from planning pregnancy to one year after delivery. Women using TNFi in pregnancy had significantly lower disease activity.

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**Disclosure of Interest:** None declared

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#### THU0674 RHEUMATIC DISEASES AND PREGNANCY: A SINGLE CENTRE DEDICATED CLINIC EXPERIENCE

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**Background:** Pregnancy causes immune and endocrine systems alterations, therefore it can change the course of the rheumatic diseases. On the other hand, rheumatic diseases can negatively influence pregnancy outcome. Therefore, in the past pregnancy has been discouraged in patients with rheumatic diseases, for high maternal-fetal risks. Nowadays we are aware that counselling, planning of pregnancy, multidisciplinary management and follow up in a dedicated clinic are mandatory for a good maternal-fetal outcome.

**Objectives:** To assess the impact of close multidisciplinary rheumatological-obstetrical management on high risk pregnancies.

**Methods:** We considered patients diagnosed with a rheumatic disease before pregnancy who had at least one pregnancy prospectively followed at our dedicated clinic. Each patient underwent a monthly rheumatological and obstetrical evaluation during the all pregnancy. All obstetrical complications were recorded and a final pregnancy outcome was assessed: favourable outcome (delivery) or



unfavourable outcome (spontaneous abortion/stillbirth/induced abortion). We then compared prospective versus anamnestic pregnancy outcomes.  
**Results:** Between 2005 and 2016, 862 women were evaluated. We included in the study 201 patients followed prospectively during 261 pregnancies. The patients were affected by 19 different rheumatic diseases, alone or in association. The most represented diagnoses were undifferentiated connective tissue disease (UCTD) (72 patients, 33.03%), rheumatoid arthritis (33, 15.14%), systemic lupus erythematosus (LES) (22, 10.09%), ankylosing spondylitis (14, 6.42%), psoriatic arthropathy (12, 5.5%), antiphospholipid antibody syndrome (APS) (10, 4.59%). Maternal age at conception was 34 years (range 18.3–45.7); 19 patients underwent medically assisted reproductive techniques. The most frequent obstetric complications were fluximetric changes, premature rupture of membranes, hypertension and related disorders, gestational diabetes, hypothyroidism and intrauterine growth retardation. The average gestational age at delivery was 38.24 weeks (range 26.71–41.29) with higher frequency of prematurity in patients with APS (55%), LES (39%) and UCTD (19%), as well as in the two pregnancies of patients with mixed connective tissue disease and systemic sclerosis. The comparison between favourable outcomes of prospective versus anamnestic pregnancies showed a significant difference ( $p < 0.001$ ) for prospectively followed pregnancies, regardless of maternal diagnosis.

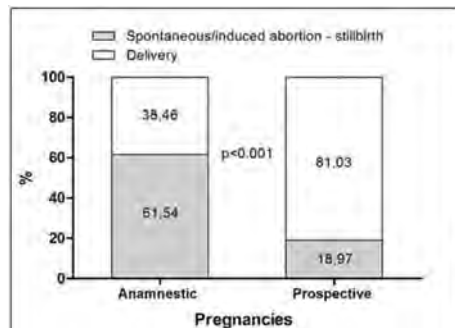


Figure 1: Outcome of anamnestic vs prospective pregnancies in patients followed in our dedicated clinic.

**Abstract THU0674 – Figure 1** Outcome of anamnestic vs prospective pregnancies in patients followed in our dedicated clinic.

**Conclusions:** Pre-conception counselling and close multidisciplinary follow-up during pregnancy are essential for a better maternal-fetal outcome in patients with rheumatic diseases.

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**Disclosure of Interest:** None declared  
**DOI:** 10.1136/annrheumdis-2018-eular.6481

**THU0675 THE IMPACT OF AUTOIMMUNE RHEUMATIC DISEASES ON BIRTH OUTCOMES IN AN ETHNICALLY DIVERSE COHORT OF WOMEN IN THE UNITED STATES**

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**Background:** Autoimmune rheumatic diseases (ARDs) often affect women of childbearing age and have been associated with adverse pregnancy outcomes. Most of the literature on the impact of ARDs on birth outcomes to date has focused on the burden of common ARDs (e.g., rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE)) within Caucasian populations. The effect of race/

ethnicity on birth outcomes among women with ARDs is not well understood. Identification of groups who are at highest risk of adverse birth outcomes may aid in increased prenatal surveillance and prevention of maternal and fetal morbidity.

**Objectives:** To evaluate the impact of ARD on adverse birth outcomes, specifically preterm birth (PTB), congenital anomalies, and low birth weight (LBW), in a large, ethnically diverse cohort.

**Methods:** We conducted a matched cohort analysis of retrospective data from all singleton live births in California occurring between 2007 and 2012. Data on ARD diagnosis, including RA, SLE, antiphospholipid syndrome (APS), psoriatic arthritis (PsA), ankylosing spondylitis (AS), or juvenile idiopathic arthritis (JIA), and birth outcomes were derived from birth certificate records linked to hospital/discharge ICD9 codes present anytime at or one year prior to delivery. Women without any of the previously mentioned rheumatic diseases were age- and ethnicity-matched in 2:1 ratio to women with ARD; their characteristics were compared using conditional logistic regression. We also examined the association between specific ARD diagnoses and birth outcomes stratified by race/ethnicity.

**Results:** We identified 10 975 women with a recorded ARD diagnosis (RA: 3129 (26%), SLE: 3863 (33%), APS: 4180 (35%), PsA: 173 (2%), AS: 144 (1%), and JIA: 354 (3%). The odds of PTB were increased for women with any ARD (aOR 1.90 (95% CI 1.76–2.05)) and among those with RA (aOR 1.65 (95% CI 1.47–1.85)), SLE (aOR 2.25 (95% CI 2.05–2.47)), APS (aOR 1.82 (95% CI 1.64–2.01)), and JIA (aOR 1.76 (95% CI 1.32–2.35)) compared to women without ARD. After stratifying by race/ethnicity, the odds of PTB and congenital anomalies were highest among Asian women and the odds of LBW were highest among Hispanic women compared to other race/ethnicity-matched controls (table 1). Further sub-analyses revealed that it was predominantly women with SLE who were contributing to the adverse outcomes seen in the combined ARD group.

**Abstract THU0675 – Table 1.** Odd of adverse birth outcomes among women with autoimmune rheumatic disease (ARD) compared with women without a recorded ARD by race/ethnicity.

Outcome	Total Population		White		Black		Hispanic		Asian	
	No. ARD	OR (95% CI)	No. ARD	OR (95% CI)	No. ARD	OR (95% CI)	No. ARD	OR (95% CI)	No. ARD	OR (95% CI)
Preterm birth	1,989 (18.0)	1.90 (1.76-2.05)	1,989 (18.0)	1.90 (1.76-2.05)	1,989 (18.0)	1.90 (1.76-2.05)	1,989 (18.0)	1.90 (1.76-2.05)	1,989 (18.0)	1.90 (1.76-2.05)
Low birth weight	1,989 (18.0)	1.90 (1.76-2.05)	1,989 (18.0)	1.90 (1.76-2.05)	1,989 (18.0)	1.90 (1.76-2.05)	1,989 (18.0)	1.90 (1.76-2.05)	1,989 (18.0)	1.90 (1.76-2.05)
Stillbirth	1,989 (18.0)	1.90 (1.76-2.05)	1,989 (18.0)	1.90 (1.76-2.05)	1,989 (18.0)	1.90 (1.76-2.05)	1,989 (18.0)	1.90 (1.76-2.05)	1,989 (18.0)	1.90 (1.76-2.05)

OR, Odds Ratio; CI, Confidence Interval; ARD, autoimmune rheumatic disease; PTB, preterm birth; LBW, low birth weight.

**Conclusions:** Consistent with prior literature, we found that women with ARDs tend to be more likely to have PTB and infants of LBW. To our knowledge, this is the largest study to date to analyse these associations in Asian women. Our results suggest that Asian and Hispanic women with ARDs may disproportionately benefit from additional monitoring throughout pregnancy. Our study raises the need for public health initiatives that can help improve pregnancy outcomes in women with autoimmune rheumatic diseases across all races and ethnicities.

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THU0676

### A SYSTEMATIC REVIEW AND META-ANALYSIS OF VIRAL EXPOSURES AS A RISK FACTOR FOR RHEUMATOID ARTHRITIS

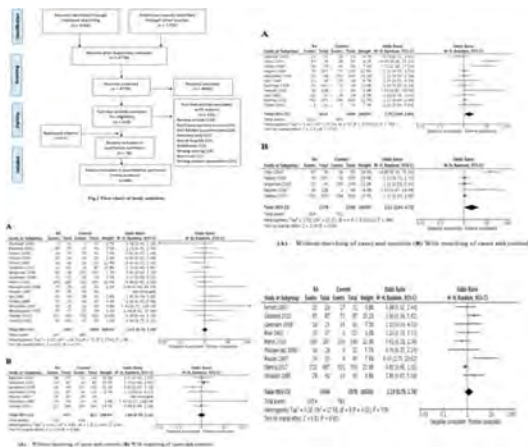
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**Background:** Rheumatoid arthritis (RA) is an autoimmune disease with a complex and poorly understood etiology. Development of autoimmune disease stems from a combination of immune, genetic, hormonal and environmental factors. Infections are viewed as triggers of some autoimmune disorders, including RA.

**Objectives:** Different viral exposures have been implicated in the etiology of RA via several mechanisms of immune activation, such as molecular mimicry. The purpose of this systematic review was to summarise the evidence relating to the association between putative viral exposures and the development of RA

**Methods:** A systematic literature search was conducted using MEDLINE-OVID, EMBASE-OVID, PUBMED and Cochrane library databases. Articles were included if they were case-controls, cross-sectional or cohort studies and were published in English. Case-series were included if there was a lack of other study designs.

**Results:** Of 6724 citations, 78 studies were selected for review, and 48 were included in meta-analysis. Studies had poor quality. Based on the IgG antibodies (n=12 studies) and viral DNA detection (n=3 studies), the odds of parvovirus B19 (PBV19) infection were increased in RA patients than in controls (odds ratio (OR) (95% CI)=1.77 (1.11; 2.80), p=0.02, OR (95% CI)=3.53 (1.00; 12.53), p=0.05 for PVB19 IgG and DNA, respectively). For Epstein-Barr virus (EBV), patients with RA had not significant OR of anti-Epstein-Barr nuclear antigen (EBNA) (n=17 studies, OR (95% CI)=1.05 (0.79; 1.39), p=0.75), but significant OR of anti-viral capsid antigen (VCA) (n=18 studies, OR (95% CI)=1.5 (1.07; 2.10), p=0.02) and anti-early antigen (EA) (n=11 studies, OR (95% CI)=2.74 (1.27; 5.94), p=0.01). Cytomegalovirus (CMV) was not associated with RA (n=13 studies, OR (95% CI)=1.24 (0.78; 1.95), p=0.36). Chronic hepatitis B (HBV) was not associated with RA in 5 case-control (OR (95% CI)=1.37 (0.83; 2.25), p=0.22) and 1 cohort studies (HR 1.09 (0.74, 1.63), p>0.05). Chronic hepatitis C (HCV) was associated with increased risk of RA in 7 case-control (OR (95% CI)=2.82 (1.35; 5.90), p=0.006) and 1 cohort studies (HR 2.03 (1.27, 3.22), p<0.01). There seem to be a risk of persistent arthritis after Chikungunya fever (CHIKV) (n=2 studies, OR (95% CI)=90 (15.2; 134.3).



**Abstract THU0676 – Figure 1.** Flow chart of study selection. Abstract THU0676 – Figure 2. Forest plots for cumulative odds ratio (95%CI) of serum IgG anti-PVB19 antibodies in RA cases and controls. (A) Without matching of cases and controls (B) With matching of cases and controls. Abstract THU0676 – Figure 3. Forest plot for cumulative odds ratio (95% CI) of serum anti-EBNA IgG in RA cases and controls. (A) Without matching of cases and controls (B) With matching of cases and controls. Abstract THU0676 – Figure 4. Forest plot for cumulative odds ratio (95% CI) of serum anti-CMV IgG in RA patients and controls.

**Conclusions:** Studies about the risk of RA after viral exposures suffer from inconsistent methodological quality. There is a risk of RA after Parvo B19 infection and possibly HCV but not EBV or HBV. There seems not to be a risk of RA after EBV infection. CHIKV is associated with the persistent inflammatory arthritis. There is not enough evidence to support an association between some viruses and RA development, but they probably lead to RA in genetically susceptible individuals.

**Disclosure of Interest:** None declared

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THU0677

### PNEUMOCOCCAL ANTIBODY PROTECTION IN RHEUMATOLOGICAL PATIENTS RECEIVING BDMARD THERAPY – A CROSS-SECTIONAL STUDY

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**Background:** Severe pneumococcal infections contribute to increased mortality in patients with rheumatic diseases, and is preventable by vaccination against *Streptococcus pneumoniae*. EULAR recommends that pneumococcal vaccination should be strongly considered in patients with rheumatic diseases, however, need and timing of revaccination for this patient group remains unknown<sup>1</sup>. Since 2009, rheumatological patients from our department have been vaccinated against *S. pneumoniae* prior to initiation of bDMARD therapy, by use of the 23-valent pneumococcal polysaccharide vaccine (PPV23). To our knowledge, we are the only centre in Denmark to vaccinate these patients routinely.

**Objectives:** The aim of the study was to determine the prevalence of rheumatological patients receiving bDMARD therapy with a protective level of antibodies against *S. pneumoniae*, and to identify possible factors of relevance affecting antibody production.

**Methods:** Antibodies against 12 pneumococcal serotypes were measured in the period of June to December 2017 in patients receiving bDMARD therapy initiated before March 1st 2017. A geometric mean level of all serotypes above 1 µg/ml was considered a protective antibody level. The patients had been diagnosed with rheumatoid arthritis, spondyloarthritis, psoriatic arthritis or juvenile idiopathic arthritis. The study group consisted of both vaccinated and unvaccinated individuals, where unvaccinated individuals initiated bDMARD therapy before vaccination occurred routinely.

Differences in protection between vaccinated and unvaccinated patients were evaluated using the  $\chi^2$  test. We included the following variables in a logistic regression model, to analyse factors of possible significance to the protective level of antibodies: age, sex, diagnosis, methotrexate (MTX) and/or prednisolone treatment at time of vaccination, and years since vaccination.

**Results:** A total of 319 patients were included in the study: 186 (58%) vaccinated and 133 (42%) unvaccinated patients. Among the vaccinated patients, 30% had a protective antibody level versus 0% of the unvaccinated patients (p<0.0001).

Logistic regression analysis showed that a significantly smaller proportion of patients treated with MTX at time of vaccination had a protective antibody level compared with patients not treated with MTX (p=0.03; odds ratio: 2.3; 95% CI [1.1;4.7]). The same applied for advanced age at time of vaccination (p=0.04), whereas years since vaccination did not decrease antibody protection significantly (p=0.12).

**Conclusions:** Only one third of PPV23 vaccinated rheumatological patients treated with bDMARD were observed with a GML of pneumococcal antibodies above 1 µg/ml. This suggests that a majority of these patients are not protected adequately against pneumococcal disease in spite of vaccination. MTX treatment at time of vaccination and advanced age were both independently associated with lack of protective antibody level.

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**Disclosure of Interest:** None declared

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THU0678

### TREND OF VENOUS THROMBOEMBOLISM AMONG SELECT RHEUMATOLOGIC DISEASES: AN AUDIT OF LARGE NATIONAL US DATABASE

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**Background:** Venous thromboembolism (VTE) is 3rd commonest cause of cardiovascular deaths and encompasses deep-venous thrombosis (DVT) and pulmonary embolism (PE). Rheumatologic diseases have been found to be associated with an increased risk of VTE among hospitalised patients.

**Objectives:** To describe the trend of VTE among select rheumatologic diseases over 15 years.

**Methods:** We used National Inpatient Sample (NIS) database for years 2000–2014 to identify adults ≥18 years with select rheumatologic diseases and VTE based on ICD-9 codes. Prevalence was age-sex adjusted against US census population data. STATA was used for querying database and Joinpoint regression

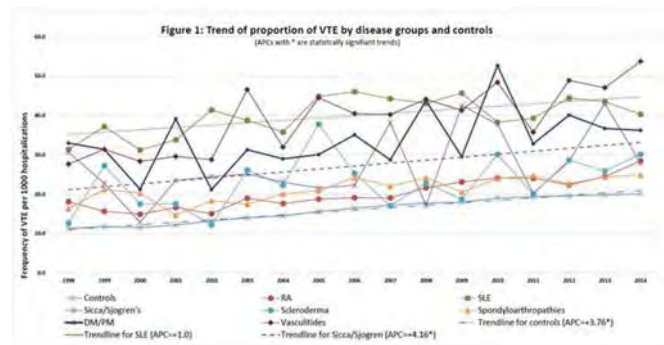
	Totals	Controls	RA	SLE	Sicca/Sjogren's	Scleroderma	Spondyloarthropathies	DM/PM	Vasculitides	VTE
<b>Counts (% of hospitalizations)</b>										
Overall	461089203 (100)	451761667 (97.98)	5609502 (1.22)	1980776 (0.43)	2 74 106 (0.06)	3 35 926 (0.07)	4 36 702 (0.09)	1 82 420 (0.04)	5 08 104 (0.11)	8822456 (1.91)
2000/ 2002	89251049 (100)	87822413 (98.4)	8 29 687 (0.93)	3 24 117 (0.36)	32 618 (0.04)	60 004 (0.07)	56 851 (0.06)	32 495 (0.04)	92 863 (0.1)	1292852 (1.45)
2003/ 2005	92374203 (100)	90738381 (98.23)	9 50 197 (1.03)	3 74 136 (0.41)	40 013 (0.04)	66 331 (0.07)	67 450 (0.07)	36 482 (0.04)	1 01 213 (0.11)	1582058 (1.71)
2006/ 2008	95006960 (100)	1847533 (98.05)	28 589 (1.16)	14 668 (0.43)	1334 (0.05)	1745 (0.07)	2126 (0.09)	1536 (0.04)	4302 (0.11)	1901832 <sup>2</sup>
2009/ 2011	94195026 (100)	1961465 (97.73)	37 829 (1.4)	14 408 (0.46)	1903 (0.08)	1920 (0.08)	2619 (0.11)	1603 (0.04)	4767 (0.11)	2026514 (2.15)
2012/ 2014	90261964 (100)	1948300 (97.48)	40 800 (1.56)	15 635 (0.5)	2330 (0.09)	2145 (0.08)	3670 (0.14)	1630 (0.04)	4690 (0.12)	2019200 (2.24)
<b>VTE%</b>										
Overall	1.91	1.89	2.62	3.38	2.65	2.58	2.49	3.89	4.08	-
2000/ 2002	1.45	1.43	2.1	2.98	2.65	1.96	1.89	3.17	3.29	-
2003/ 2005	1.71	1.7	2.34	3.35	2.09	2.56	2.03	3.57	3.85	-
2006/ 2008	2	1.98	2.59	3.63	2.64	2.55	2.58	4.09	4.19	-
2009/ 2011	2.15	2.13	2.88	3.35	2.69	2.65	2.6	4.14	4.45	-
2012/ 2014	2.24	2.21	2.89	3.48	2.9	3.12	2.84	4.39	4.5	-
<b>Adjusted odds of VTE association (p-value, 95% CI)</b>										
Overall	-	1	1.24 (<0.0001, 1.22–1.3)	2.2 (<0.0002, 2.17–2.3)	1.3 (<0.0003, 1.28–1.4)	1.4 (<0.0004, 1.3–1.45)	1.3 (<0.0005, 1.2–1.33)	2 (<0.0006, 1.9–2.2)	1.8 (<0.0007, 1.76–1.9)	-

was used to analyse annual trends of prevalence in terms of annual percentage change (APC). Logistic regression with survey command was used to derive adjusted odds of VTE association for all years combined.

**Results:** We included a total of 461,089,203 hospitalizations among which 8,822,456 (1.91%) had VTE (table 1). An upward trend in the prevalence of VTE (APCs 2.45–4.16) (and PE subset) was noted in most of the rheumatologic disease groups (figure 1). DVT, however, had a decreasing or non-significant increasing trend among most disease groups (data for DVT and PE not shown). The adjusted odds of VTE association was highest among SLE group (aOR=2.2, CI=2.17–2.3) followed by DM/PM (aOR=2.0, CI=1.9–2.2) (table 1).

Table 1 Frequency counts of rheumatologic diseases and controls; prevalence of VTE and adjusted regression analysis of VTE association

**Abstract THU0678 – Figure 1** Trend of proportion of VTE by disease groups and controls (APCs with \* are statistically significant trends)



**Conclusions:** Inflammatory rheumatologic diseases seem to be associated with higher prevalence and odds of having VTE among hospitalised patients and the overall trend is rising. This might indicate some lag in following of guidelines for VTE prophylaxis. Closer look into the implications of stricter prophylaxis among rheumatologic patients is a matter of further studies.

**Disclosure of Interest:** None declared

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THURSDAY, 14 JUNE 2018

**Public health, health services research and health economics**

**THU0679 INCREASED HOSPITALISATION RATES FOLLOWING HEART FAILURE DIAGNOSIS IN RHEUMATOID ARTHRITIS**

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**Background:** There is a 2-fold increased risk of heart failure (HF) in rheumatoid arthritis (RA) compared to the general population. Little is known about hospitalisation rates in patients with RA and HF.

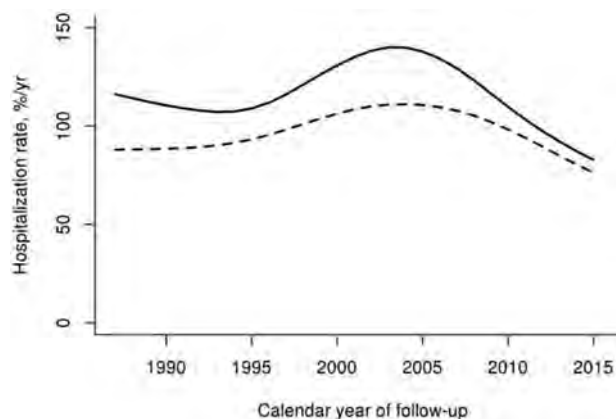
**Objectives:** We aimed to compare the frequency of and trends in hospitalizations after HF diagnosis in patients with and without RA during 1987–2015 and to assess risk factors for hospitalizations following HF in RA.

**Methods:** The study included a retrospectively identified population-based cohort of patients with incident HF and prior RA (age ≥18 years, 1987 ACR criteria) and a cohort of incident HF patients without RA matched 3:1 on age, sex, and year of HF diagnosis. Hospitalizations at the time of HF diagnosis were excluded. All subjects were followed until death, migration, or 12/31/2015. Person-years methods and rate ratios (RR) from Poisson regression models were used to compare hospitalisation rates (number of hospitalizations divided by person-years of follow-up) between the groups. Conditional frailty models were used to examine risk factors for hospitalisation.

**Results:** The study included 212 patients with RA (mean age at HF diagnosis 78.3 years; 68% female) and 636 non-RA patients (mean age at HF diagnosis 78.6 years; 68% female). The hospitalisation rate after HF diagnosis was higher in RA vs non-RA (RR 1.16; 95% CI 1.08–1.25). This difference may be decreasing after 2010 (figure 1). The magnitude of the increase was similar in both sexes and across all ages. In a subset with available echocardiography (n=68 RA and 449 non-RA), HF with preserved ejection fraction (HFpEF) was similarly prevalent in RA (57%) vs non-RA (51%; p=0.3). Among those with HF with reduced ejection fraction (HFrEF) RA patients had more hospitalizations than non-RA subjects (RR



1.65; 95% CI 1.29–2.09); this was not observed in HFpEF (RR 0.80; 95% CI 0.63–1.01). Following HF diagnosis, RA patients were more likely to be hospitalised for non-cardiovascular causes (RR 1.26; 95% CI 1.14–1.39), but not for HF (RR 0.96; 95% CI 0.76–1.21) or other cardiovascular causes (RR 0.99; 95% CI 0.81–1.20) compared to the non-RA patients. Readmission rates within 30 days of prior discharge were similar in RA and non-RA ( $p=0.14$ ). Smoking (current or former), prior myocardial infarction (MI) and higher score on Charlson comorbidity index were associated with increased risk for hospitalisation: hazard ratio (HR) 1.33, 95% CI 1.06–1.68; HR 1.37, 95% CI 1.03–1.82; and HR 1.10, 95% CI 1.06–1.14, respectively.



**Conclusions:** Hospitalisation rate following HF diagnosis was 16% higher in RA than in non-RA patients regardless of sex and age. This difference was particularly apparent between 1990 and 2010. Increased hospitalisation risk was mostly among patients with RA who had HFpEF rather than HF, and was predominantly due to non-cardiovascular causes. Smoking, prior MI and Charlson comorbidity index were associated with increased risk of hospitalisation suggesting that increased complexity of management of patients with comorbid RA may play a role in more frequent hospitalizations in the RA cohort.

**Disclosure of Interest:** None declared

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## Epidemiology, risk factors for disease or disease progression

THU0680

### SURVIVAL ANALYSIS OF PATIENTS WITH CONNECTIVE TISSUE DISEASE ASSOCIATED INTERSTITIAL LUNG DISEASE

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**Background:** Interstitial lung disease (ILD) is common in connective tissue diseases (CTDs) and can lead to significant shortened survival. Although the various CTDs associated with ILD are often considered as a whole because of their sharing the same autoimmune nature, there are substantial differences in the natural course in each specific CTD. Still, there is little research comparing the mortalities in different underlying CTDs and investigated the risk factors.

**Objectives:** We aimed to examine mortality in patients with ILD secondary to dermatomyositis and polymyositis (DM/PM), systemic sclerosis (SSc), rheumatoid arthritis (RA), primary Sjögren syndrome (pSS), and systemic lupus erythematosus (SLE), to test whether the survival was associated with ILD imaging subtypes, as well as to identify independent risk factors for CTD-ILDs.

**Methods:** We retrospectively reviewed the medical records of patients with newly diagnosed CTD-ILD. The high-resolution computed tomography of lung images was reviewed by two expert pulmonary radiologists. According to imaging manifestations, ILD was categorised into three subtypes, i.e., usual interstitial pneumonia (UIP), nonspecific interstitial pneumonia (NSIP) and indeterminate, respectively. The extensity of ILD lesions was also evaluated as grade 1, 2, 3. The primary outcome assessed was all-cause mortality. We examined survival after stratifying on each specific CTD, or lung-CT imaging subtypes, respectively. We used Cox proportional hazards model to identify independent predictors of survival.

**Results:** Three hundred and twenty-five patients were included with a median follow-up time of 54 months. Eighty-four (25.8%) had DM/PM, 73 (22.5%) had SSc,

63 (19.4%) had RA, 58 (17.8%) had pSS, 47 (14.5%) had SLE. Overall, 98 (30.2%) patients died. The survival rate of pSS-ILD (85.1%) and SLE-ILD (79.3%) were significantly higher than other CTD-ILDs [SSc-ILD (68.5%), RA-ILD (66.7%), DM/PM-ILD (58.6%),  $p=0.009$ ]. However, after categorised into three different ILD imaging subtypes, it showed no statistical differences in survival rates (64.5%, 73.6%, 69.5% of the UIP group, NSIP group, indeterminate group, respectively,  $p=0.558$ ). Multivariable analysis revealed that compared with DM/PM-ILD, the mortality rate was significantly lower in pSS-ILD (RR=0.321,  $p=0.001$ ), RA-ILD (RR=0.466,  $p=0.016$ ), SSc-ILD (RR=0.566,  $p=0.045$ ), and SLE-ILD patients (RR=0.363,  $p=0.018$ ), and old age (RR=1.028,  $p=0.002$ ), long course of disease (RR=1.004,  $p=0.005$ ), extended ILD lesions (RR=1.854,  $p=0.025$ ) were independent predictors of mortality in all types of CTD-ILD. The present study shows DM/PM-ILD patients had the worst prognosis then pSS-ILD, RA-ILD, SSc-ILD, and SLE-ILD patients. Age, disease course, intensity of ILD lesions at baseline is also critical for the survival of CTD-ILD patients.

**Conclusions:** The present study shows DM/PM-ILD patients had the worst prognosis then pSS-ILD, RA-ILD, SSc-ILD, and SLE-ILD patients. Age, disease course, intensity of ILD lesions at baseline is also critical for the survival of CTD-ILD patients.

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**Disclosure of Interest:** None declared

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THU0681

### ESTABLISHING THE BATH ANKYLOSING SPONDYLITIS METROLOGY INDEX (BASMI) NORMATIVE VALUES IN A MALAYSIAN POPULATION: THE IMPORTANCE OF SEX AND AGE FACTORS

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**Background:** Ankylosing spondylitis (AS) is a chronic spinal inflammatory disorder which leads to progressive fusion and deformity. The loss of spinal mobility is recognised as an important clinical sign. The BASMI, a composite index of spinal mobility is used internationally in clinical practice and research. However, the interpretation of BASMI has been impeded by the absence of normative values.

**Objectives:** We aimed to attain the normative values for BASMI in Malaysian healthy individuals.

**Methods:** BASMI data of 142 healthy individuals and 187 AS patients were analysed. Each BASMI component was assessed, using the 10-point scoring system, where zero is no mobility and 10 is very severe limitation. Measurements were performed by the rheumatologists and trained researchers following a designated protocol. Data were summarised and analysed according to sex and age groups.

**Results:** The total BASMI scores ranged from 0.2 to 4.2 and 0.6 to 9.6 in the healthy individuals and the AS cases, respectively. There was no significant difference for the BASMI median score between healthy men and women (men=1.2, women=1.6,  $p>0.05$ ). The estimated median score for healthy individuals aged 15–19 years was 1.2, increasing with age to 2.7 for healthy individuals aged  $\geq 60$

years. In AS cases, the estimated median score was 5.4 and 5.8 for men and women, respectively ( $p > 0.05$ ). We observed significant increase of estimated median score between AS patients aged 15–19 years (BASMI score=2.0) and AS patients aged  $\geq 60$  years (BASMI score=6.4) ( $p < 0.05$ ).

**Conclusions:** Our data suggest that it is uncommon for healthy individuals to score zero on the BASMI. The magnitude of increase in BASMI score is apparent with increasing age, but not sex in the healthy individuals. Establishment of normative values may aid baseline measurement and monitor change of spinal mobility in AS patients over time, as well as help assess the impact of clinical interventions.

**Disclosure of Interest:** None declared

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#### THU0682 HUMAN HISTOCOMPATIBILITY ANTIGENS (HLA) CLASS I IN ANTERIOR UVEITIS PATIENTS WITH AND WITHOUT SPONDYLOARTHRITIS

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**Background:** Anterior uveitis (AU) and spondyloarthritis (SpA) are associated with HLA-B27. Previous genetic studies in different populations demonstrated other associations, in particular, HLA, both common and different for AU and SpA

**Objectives:** To assess the relationship of HLA class I antigens with AU depending on the presence or absence of SpA

**Methods:** 148 pts with AU were typed. All pts were divided into 2 groups: 1–52 pts with confirmed diagnosis of SpA (AU +SpA), 96 pts – with other forms of AU (52 – idiopathic AU, 29 – viral AU, 2- multiple sclerosis, 2 - toxoplasmosis, 1- sarcoidosis, 1- tuberculosis, 3- chlamydial AU, 2 - Behcet's disease, 3 - juvenile chronic arthritis, 1 - Fuchs's heterochromic iridocyclitis). 150 healthy donors formed control group. Analysis of the distribution of HLA- class I antigens (loci A, B, Cw) was performed comparing 2 groups of patients with AU and each group with control.

**Results:** HLA-27 in the group of pts AU +SpA identified in 96.1% (50/52), in the group AU – in 40.6% (39/96), in control – in 7.3% (11/150). If HLA-27 was present in the genotype, the risk of developing of common pathology (AU +SpA) was OR=315.9 [95% CI 61.9–2176.7],  $p < 0.0000001$ , the risk of AU - OR=8.7 [95% CI 3.9–19.4],  $p < 0.000001$ . Among locus C antigens high frequency of Cw2 was identified in the groups AU +SpA and AU compared with control (64.0%, 36.3% and 10.0%, respectively): AU +SpA vs control -  $p < 0.000001$ , AU vs control, -  $p < 0.0001$ . The occurrence of Cw7 was significantly lower in the group AU +SpA in comparison with control: 12.8% and 38.7%,  $p = 0.002$ . In the group AU the occurrence of this antigen was not significantly different from the control group and the group AU +SpA.

**Conclusions:** The analysis of the distribution of HLA class I antigens confirmed association of HLA- B27 with AU in Russian population. Other associations, except Cw2, were not identified. Such significant increase of Cw2 in two groups of pts with high frequency of B27 is natural due to the phenomenon of linkage disequilibrium for HLA-B27 and Cw2 antigens. Cw7 antigen can play a "protective" role in relation to SpA, because the frequency of this gene in the group AU was not reduced compared to control.

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#### THU0683 PREDICTORS FOR PRETERM DELIVERY AMONG PREGNANT WOMEN WITH RHEUMATOID ARTHRITIS AND JUVENILE IDIOPATHIC ARTHRITIS

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**Background:** It has previously been shown that pregnant women with inflammatory arthritis are at an increased risk for preterm delivery (PTD), yet it remains unclear what underlying maternal factors may drive this excess risk.

**Objectives:** The aim of our study is to identify overall predictors for PTD among women with rheumatoid arthritis (RA) and juvenile idiopathic arthritis (JIA) and to

analyse the contribution of maternal disease activity, medication use, and comorbid pregnancy conditions on the risk for PTD in this population.

**Methods:** Data were obtained from the Organisation of Teratology Information Specialists (OTIS) Autoimmune Disease in Pregnancy Project, a prospective cohort study among pregnant women in the U.S. and Canada. Women who enrolled between 2004 and 2017 prior to 19 weeks' gestation, had not enrolled with a previous pregnancy, and delivered at least one live born infant were considered eligible for analysis. All data were obtained by maternal report via telephone interviews and confirmed in the medical record when available. For our statistical analysis, Poisson regression with robust standard errors was used to estimate multivariable adjusted risk ratios.

**Results:** Mothers with RA and JIA had a higher risk of PTD, preterm labour, early term delivery, and caesarian section versus comparison women. Women with RA additionally had a higher risk of gestational diabetes mellitus (GDM), and women with JIA had a higher risk of preeclampsia versus the comparison group. Active disease (defined as patient activity scale (PAS) score  $> 3.70$ ) was associated with PTD among women with RA both at intake and anytime during pregnancy, and this association remained after adjustment for corticosteroid (CS) use (aRR 1.60, 95% CI 1.12–2.30; aRR 1.54, 95% CI 1.08–2.20, respectively). CS use in all three trimesters was associated with PTD among women with both RA and JIA, an association that remained after multivariable adjustment for maternal factors including disease activity. Use of non-steroidal anti-inflammatory drugs (NSAIDs) in the first trimester was associated with PTD in women with JIA (aRR 2.31, 95% CI 1.04–5.14). Additional analysis showed that preeclampsia was associated with a higher risk of PTD among both RA and JIA women (aRR 1.92, 95% CI 1.12–3.31; aRR 3.01, 95% CI 1.10–8.23, respectively) but not in the comparison group. GDM and caesarian section were associated with a higher risk of PTD exclusively among RA women (aRR 1.84, 95% CI 1.07–3.15 and aRR 1.58, 95% CI 1.09–2.28, respectively) and fever during pregnancy increased the risk for PTD exclusively among women with JIA (aRR 3.45, 95% CI 1.47–8.08).

**Conclusions:** Women with RA and JIA are at risk for preterm delivery. Maternal disease activity and medication use, particularly corticosteroid use, may explain much of this excess risk.

**Disclosure of Interest:** None declared

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#### THU0684 PREVALENCE OF RHEUMATIC DISEASES IN ADULT POPULATION IN SPAIN. EPISER 2016 STUDY

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**Background:** Prevalence of rheumatic diseases was first studied in Spain in 2000 (EPISER 2000 study<sup>1</sup>). Sociodemographic and lifestyle changes during the last 16 years and their possible influence in prevalence figures justify a new study.

**Objectives:** To estimate the prevalence of rheumatoid arthritis (RA), psoriatic arthritis (PsA), ankylosing spondylitis (AS), systemic lupus erythematosus (SLE), Sjögren syndrome, symptomatic osteoarthritis (knee, hip, hands, cervical and lumbar spine), fibromyalgia, gout and symptomatic osteoporotic fracture in adult population in Spain.

Disease	Prevalence	95% CI
Cervical osteoarthritis	10.1%	9.1–11.2
Lumbar osteoarthritis	15.5%	14.3–16.8
Hand osteoarthritis	7.9%	7.0–8.9
Hip osteoarthritis	5.2%	4.4–6.0
Knee osteoarthritis	13.9%	12.7–15.1
RA	0.9%	0.7–1.3
PsA	0.6%	0.4–0.8
AS	0.4%	0.3–0.7
Gout	2.5%	2.0–3.1
SLE	0.2%	0.1–0.4
Sjögren syndrome	0.3%	0.2–0.5
Fibromyalgia	2.4%	2.1–2.9
Symptomatic osteoporotic fracture	1.8%	1.4–2.4

**Methods:** Population-based multicenter cross-sectional study, with the participation of 78 municipalities in the 17 Spanish autonomous communities. The reference population are adults aged 20 and above residing in Spain. All participants gave their informed consent. CATI system (Computer Assisted Telephone Interview) was used for initial data collection and screening questionnaire. Diagnostic suspicions and diagnosis referred by the participants were studied by rheumatologists in the referral hospital for the selected municipalities. Statistical analysis: the prevalence of the rheumatic diseases were calculated using estimators and their

95% confidence intervals. Weights were calculated in each of the sampling stages in accordance with the probability of selection. The distribution of population in Spain obtained from the National Statistics Institute was taken into account.

**Results:** 4916 subjects were included in the study. 4753 completed their participation. Prevalence of rheumatic diseases were the following: The negative predictive value (NPV) of the initial screening questionnaire was 93.8%. The lower NPV corresponded to knee osteoarthritis (95.1%).

**Conclusions:** Prevalence of RA, PsA, AS, gout and SLE seems to be higher than previously published in other European countries.

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**Acknowledgements:** This study was funded by Celgene, Gebro Pharma, MSD, Novartis, Hopira/Pfizer and Sanofi Genzyme.

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#### THU0685 CARDIOVASCULAR RISK ESTIMATION IN SLE PATIENTS: A COMPARISON OF THREE ALGORITHMS

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**Background:** Cardiovascular (CV) disease is a major cause of mortality and morbidity in SLE patients; several instruments have been developed to estimate the 10 years risk of major CV events in the general population according to the presence of traditional CV risk factors. However, it is well known that traditional CV risk factors cannot fully explain the increased CV disease in SLE. Recently, a new version of the Qrisk algorithm was released (QRISK3) incorporating new variables associated with increased risk of CV disease, including SLE diagnosis and the GC use.

**Objectives:** To assess the 10 years CV risk in a cohort of SLE patients by comparing three different algorithms.

**Methods:** Consecutive patients with a diagnosis of SLE according to the ACR criteria were recruited from the inpatients and outpatients clinics of our Unit. Previous major CV events (myocardial infarction and stroke) were considered exclusion criteria. Traditional CV risk factors, disease activity and damage as well as therapies and comorbidities were evaluated. Disease activity was assessed with the SLEDAI score, organ damage with the SLICC/DI. Three algorithms to estimate the 10 years risk of major events were applied: the Framingham score, the ACC/AHA score and the QRISK3. This latter incorporates new variables associated with increased risk of cardiovascular disease, including SLE and GC use.

Abstract THU0685 – Table 1

Cumulative organ involvement (%)	
Renal	45%
Articular	75%
Hematological	52%
Cutaneous	52%
Neuropsychiatric	10%
Serositis	20%
Ongoing therapies (%)	
Antimalarials	80%
Glucocorticoids	60%
Immunosuppressants	45%
Traditional CV risk factors (%)	
BMI > 30	5.8%
BMI > 25	12.5%
Sedentary life style	46%
Hypertension	33%
Diabetes	4%
Family history of CV events	15%
Actual smoking	20%
Dyslipidemia	35%
Metabolic syndrome	12%

**Results:** 115 SLE patients (90.5%) without previous major CV events were included in this analysis. They were predominantly females (93%), Caucasian (96.5%) with a mean age at enrollment of 42.8±12.5 and a mean disease duration

of 13.4±9.2 years. The prevalence of organ involvement and traditional risk factors are reported in table 1. Disease activity at enrollment was low (median SLE-DAI 2, IQR 0–4) while 39.1% was presenting at least one organ damage.

The median Framingham risk score resulted 4.5% (IQR 2.4–8.6), the ACC/AHA resulted 1.2% (0.5–3.2), the QRISK3 resulted 5.4% (2.4–9.6). According to the three methods, there was a significant difference in the risk stratification: 10% of patients at medium-high CV risk according to the Framingham score, 5% with the ACC/AHA score and 21% with the QRISK3. The median “healthy heart age” of our cohort (the age at which a healthy subject has the same CV risk) provided by the QRISK3 resulted 62 years.<sup>52–68</sup>

**Conclusions:** These data show that by applying the QRISK3 algorithm a significant percentage of patients would be reclassified at high risk of CV events with respect to the traditional CV risk scores. Longitudinal data are necessary to validate the QRISK3 accuracy against the traditional scores in the identification of SLE patients at higher risk of CV events.

**Disclosure of Interest:** None declared

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#### THU0686 CHANGES IN HEALTH-RELATED QUALITY OF LIFE OVER 5 TO 8 YEARS IN 1347 PATIENTS WITH EARLY ARTHRITIS OR EARLY INFLAMMATORY BACK PAIN

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**Background:** Health-related quality of life (HRQoL) is a priority for patients.

**Objectives:** The objectives were to describe the changes in HRQoL over 5–8 years in patients with early arthritis (EA) or early inflammatory back pain (IBP), and to explore factors associated with HRQoL.

**Methods:** In 2 prospective observational French cohorts (ESPOIR for EA patients and DESIR for early IBP patients), HRQoL was assessed every 6 months during the first 24 months and then every year over 5–8 years, using the SF36 physical composite score (PCS) and mental composite score (MCS) (range 0–100, US population norm: 50). Disease activity was assessed by DAS28-ESR and ASDAS-CRP. Univariate and multivariate linear mixed-effect models, and trajectory-based mapping (k-means) were applied.

Figure: Evolution of SF36-MCS and PCS over follow-up in EA and early IBP

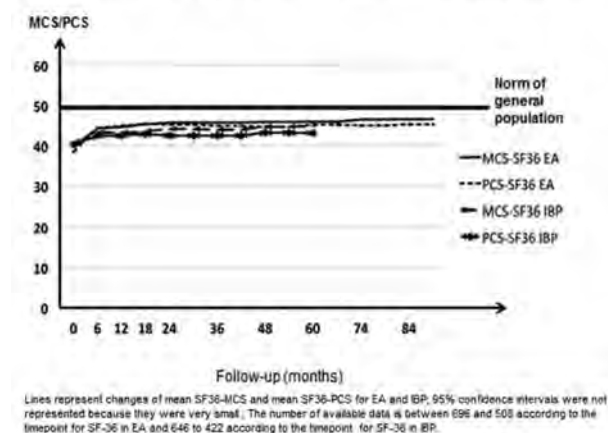


Figure 1 Evolution of SF36-MCS and PCS over follow-up in EA and early IBP

**Results:** In all, 1 347 patients (701 EA and 646 early IBP) were analysed: mean age 48.4±12.2 and 33.9±8.7 years respectively; mean disease duration 3.4±1.7 and 18.2±10.8 months, 76.3% and 55.0% females. At baseline, in EA, mean PCS and MCS were respectively 40.2±9.1 and 40.4±11.2, and in early IBP respectively 38.5±8.5 and 39.8±10.9. Over follow-up, HRQoL mean levels and trajectories improved mostly over the first 6 months (p<0.001). Overall, 54%–61% of patients reached levels of HRQoL close to population norms. DAS28-ESR and ASDAS-CRP over time were related to PCS (range of explained variance: 9% >43%, p<0.001 in the mixed models) but not to MCS.



Lines represent changes of mean SF36-MCS and mean SF36-PCS for EA and IBP; 95% confidence intervals were not represented because they were very small; The number of available data is between 696 and 508 according to the timepoint for SF-36 in EA and 646 to 422 according to the timepoint for SF-36 in IBP.

**Conclusions:** HRQoL was altered similarly for both physical and mental aspects in EA and early IBP. More than half the patients reached levels of HRQoL close to the general population. Disease activity only partly explained HRQoL: the drivers of HRQoL should be further explored.

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**Acknowledgements:** DESIR was financially supported by unrestricted grants from both the French Society of Rheumatology (FSR) and Pfizer-Wyeth Ltd France. ESPOIR was financially supported by an unrestricted grant from Merck Sharp and Dohme for the first 5 years. Part of the biological database was supported by two additional grants from Institut National de la Santé et de la Recherche Médicale (INSERM). The ESPOIR cohort study was supported by the FSR, AbbVie, Pfizer and Roche Chugai.

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#### THU0687 THE IMPACT OF URATE-LOWERING THERAPY ON KIDNEY FUNCTION (IMPULSKF): PRELIMINARY RESULTS

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**Background:** The extended 2016 EULAR updated report states that for patients on ULT, SUA level should be monitored and maintained to <6 mg/dL (360 μmol/L). SUA level <3 mg/dL (180 μmol/L) is not recommended in the long term. And among EULAR proposals for future research is mentioned the optimal duration for prophylaxis of acute attacks when starting ULT, long-term impact of very low urate levels on the central nervous system, impact of ULT on kidney function.

**Objectives:** This project aims to investigate the impact of two target levels urate-lowering therapy (ULT) caused by hyperuricemia (HU) on kidney function and CKD progression measured by eGFR and albuminuria (A).

This trial had been formulated by 2016 updated EULAR evidence-based recommendations for the management of gout as a perspective proposal task for future research.

The key points are: 1) an unknown target HU level and 2) the time duration of ULT resulting in preserved kidney function in two subject groups a) with gout and b) without gout but highly elevated uricemia and CKD.

**Methods:** The trial has a POEM design with 36 months duration. IMPULSKF is a Clinical Randomised Prospective Controlled Open Multicenter trial that randomly (by chance) assigns 180 participants in parallel groups. These patients with high SUA level (>8 mg/dL; 480 μmol/L) were divided into 2 arms (90+90) 1) with gout (EULAR's criteria) and 2) without gout but with presence of CKD 1–4) and 2 target SUA levels in each group as 5 mg/dL (300 μmol/L) and ultralow SUA <3 mg/dL (180 μmol/L) achieved either with allopurinol or febuxostat. The data obtained will be compared with control group (45 with gout without CKD and 45 with CKD).

**Results:** Retrospective analysis and 6 mothes in trial results has been shown that treatment with febuxostat improves GFR and BP control in patients with asymptomatic HU in non-diabetic CKD 2–3.<sup>2</sup>

Febuxostat treatment led to the most beneficial decrease in the level of uric acid (–223±16 μmol/l, p<0,01 with control and p<0,05 with allopurinol group), increased GFR (+10±2 ml/min, p<0,01 with control and p<0,05 with allopurinol group), blood pressure decrease (- 7±2/–3±1 mm hg, p<0,05 with control and p=0,93 with allopurinol group), albuminuria (–131±19 mg, p<0,01 with control and p<0,05 with allopurinol group. Potential benefits of febuxostat were better tolerability compared with allopurinol group with target levels of uricemia less 180 μmol/l in 32% of people.

**Conclusions:** Treatment with febuxostat (better than allopurinol) improves GFR and BP in patients with asymptomatic hyperuricemia in non-diabetic CKD 2–3. Ultralow SUA levels seems to be safe in majority of patients but its effect on CKD function is not yet clear.

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#### THU0688 DO CERTAIN DMARDS INCREASE RISK OF NEW-ONSET TYPE 2 DIABETES? EVALUATION OF PATIENTS' BASELINE CHARACTERISTICS

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**Background:** The risk of cardiovascular morbidities is higher in patients (pts) with RA and is exacerbated with type 2 diabetes (T2D).<sup>1</sup> Recent analysis showed that abatacept (ABA), a biologic (b)DMARD, has a lower incidence of T2D in pts with RA in clinical practice.<sup>2</sup>

**Objectives:** To compare baseline characteristics of pts with RA on DMARDs and evaluate incidence of T2D among these pts based on DMARD exposure.

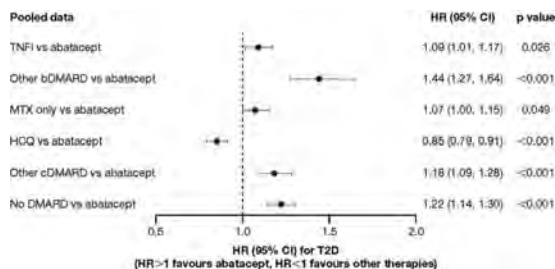
**Methods:** Administrative claims data (2006–2016) from Optum Clinformatics (database A), QuintilesIMS PharMetrics Plus (database B) and Truven Market-Scan® (database C). Inclusion criteria were: 2 RA diagnosis codes+1 DMARD prescription; age ≥18 years; ≥3 months baseline (pre-index date); and 3 months of follow-up (post-index date). Mutually exclusive treatment groups (grp) were created based on the first prescription (index date) using a hierarchy of ABA, non-ABA bDMARDs (TNF inhibitors [TNFi] and non-TNFi [excluding ABA]) and conventional DMARDs (cDMARD; MTX or hydroxychloroquine [HCQ]). Also, an RA grp without DMARD use (NoDMARD) was identified. The index date for NoDMARD was first diagnosis date. Incident T2D was identified as those without T2D prior to index using one International Classification of Disease (ICD)–9 or ICD-10 diagnosis code for T2D. Assessment of T2D risk between treatment grps was based on regression and disease risk score (DRS) models. Adjusted incidence rate for T2D was based on a Cox model (stratified by DRS grps and categorised into 4 equal grps using quartile scores) with treatment as the independent variable.

**Results:** In databases A, B and C, 84,875, 2 07 811 and 1 94 819 pts with RA were identified, respectively (table 1). The combined proportions of pts in each treatment grp were: 3%–4% ABA; 12%–16% non-ABA bDMARD; and 41%–45% cDMARDs. Pts treated with ABA were older compared with those on non-ABA bDMARDs and a greater proportion had T2D risk factors of obesity, hypertension, dyslipidaemia and heart failure (table 1). The adjusted hazard ratios for T2D were significantly higher for non-bDMARD grps of TNFi and other bDMARDs vs ABA (figure 1).

**Abstract THU0688 – Table 1.** Baseline Risk Factors for T2D in Pts With RA by DMARD Grps

	ABA	TNFi	Non-TNFi	MTX only	HCQ	cDMARD – others	NoDMARD
<b>Database A (N)</b>	2825	9569	632	12 676	18 233	4368	36 572
Age≥55 years	52.5	38.8	60.3	63.3	53.4	62.6	61.3
Smoking	11.3	9.8	8.7	11.2	11.2	11.7	14.1
Obesity	9.7	7.1	6.2	7.4	7.9	8.2	10.0
Hypertension	39.9	30.5	36.2	44.1	40.7	46.7	54.8
Dyslipidaemia	35.9	28.4	29.1	41.2	39.9	43.9	52.2
<b>Database B (N)</b>	6497	30 329	1664	29 821	49 652	10 358	79 490
Age≥55 years	45.5	34.1	39.6	49.7	41.7	48.9	45.0
Smoking	9.4	8.4	8.0	9.3	8.9	9.3	11.7
Obesity	8.4	6.4	5.1	6.5	7.5	7.1	9.3
Hypertension	36.1	25.2	27.2	34.4	31.9	35.8	42.4
Dyslipidaemia	31.2	24.4	23.1	33.6	32.6	36.7	42.0
<b>Database C (N)</b>	8853	29 671	1714	30 669	47 850	10 891	65 171
Age≥55 years	50.7	36.0	43.3	54.9	46.1	54.5	53.1
Smoking	4.7	5.0	5.5	5.4	5.2	5.3	6.8
Obesity	5.4	4.6	5.0	4.8	5.2	4.8	6.4
Hypertension	37.7	26.2	29.2	36.1	33.5	37.8	43.8
Dyslipidaemia	28.9	23.4	23.1	31.1	30.2	33.7	38.4

All data are% unless indicated otherwise



**Abstract THU0688 – Figure 1** Hazard Ratios for Incidence of T2D in Pts With RA on Different DMARDs.

(HR>1 favours abatacept, HR<1 favours other therapies)

**Conclusions:** Pts with RA treated with abatacept had greater risk factors for T2D at baseline. However, the adjusted risk of new-onset T2D was lower among abatacept pts versus other bDMARDs.

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#### THU0689 VARIABILITY OF PAIN LEVELS IS EXPLAINED BY SELF-REPORTED DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS AND AXIAL SPONDYLOARTHRITIS: A 3-MONTHS PROSPECTIVE STUDY OF 165 PATIENTS

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**Background:** Pain is a central characteristic of rheumatoid arthritis (RA) and axial spondyloarthritis (axSpA), but it is multifactorial. Some patients describe high fluctuation of pain intensity, but fluctuation of pain and its association with disease activity has been little investigated.

**Objectives:** To compare the variability of pain and of self-reported disease activity in patients with RA or axSpA through repeated assessments, and to describe clinical characteristics of patients with high variability of pain.

**Methods:** Data were extracted from a prospective cohort study (ActConnect) including patients with clinician-confirmed RA or axSpA owning a smartphone.<sup>1</sup> Baseline characteristics were collected. Over 3 months, weekly self-assessments of pain and patient global assessment of disease activity on 0–10 points numerical rating scales (NRS) were obtained. For each patient, the mean of the inter-assessment differences of NRS (average of absolute change – AAC) of pain and disease activity were calculated. RA and AxSpA patients were compared by t-test. High variability was defined as the upper tercile of AAC. Pearson's correlation was used to evaluate the correlation between variability of pain and of self-reported disease activity. Univariate and multivariate logistic regression compared patients with high vs low variability of pain, without imputation of missing data, on R, including weekly self-reported flare over follow-up.

**Results:** Eighty-six patients with RA and 79 with axSpA were included, mean age was respectively 48.7 (SD 12.7) and 41.7 (SD 10.2) years, mean disease duration was 8 (SD 8.8) and 8.6 (SD 8.6) respectively years, 81% and 44% respectively were female. Mean DAS28 and BASDAI were respectively 2.27 (SD 1.18) and 3.21 (SD 2.06) at baseline; 44% and 62% respectively of patients were receiving a biologic.

Mean levels of pain and patient global assessment of disease activity were non-significantly higher in AxSpA than RA patients (table 1) and variability of pain and disease activity were also higher in AxSpA (table 1). Correlation between AAC of pain and activity was 72% in RA, and 84% in AxSpA. In multivariate analyses, self-reported flares were the only determinant of pain AAC (Odds ratio 2.25 [1.27–4.38] p=0.01 and 3.26 [1.67–6.35] p<0.001 respectively for RA and axSpA).

#### Abstract THU0689 – Table 1

	RA	AxSpA	p value
Baseline pain	2.90 (SD 2.36)	3.40 (SD 2.30)	0.16
AAC of pain	1.02 (SD 0.74)	1.20 (SD 0.70)	0.10
Baseline PGA of disease activity	3.09 (SD 2.27)	3.73 (SD 2.48)	0.08
AAC of PGA of disease activity	0.98 (SD 0.67)	1.22 (SD 0.70)	0.02

**Conclusions:** In this population of overall well-controlled patients, close repeated assessments of pain showed relatively low fluctuations of pain in RA and axSpA (around 1 point on a 0–10 scale). Patients with axSpA reported slightly more pain, self-reported disease activity and fluctuations of these outcomes, than patients with RA. Fluctuations in pain were highly correlated to fluctuations in patient global assessment of disease activity, indicating significant overall between these 2 patient-reported outcomes. Self-reported flares were the main element explaining fluctuations in pain, confirming the validity of self-reported flares.

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#### THU0690 RETROSPECTIVE ANALYSIS OF TEMPORAL ARTERY BIOPSY AND ITS IMPACT IN THE MANAGEMENT OF GIANT CELL ARTERITIS

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**Background:** Prevalence of Giant cell arteritis (GCA) as per primary care data is 17/10000 for patients >55 years of age<sup>1</sup>. British society of rheumatology (BSR) guidelines recommend that suspected cases of GCA should be started on treatment with high dose corticosteroids immediately and then referred for temporal artery biopsy<sup>2</sup>. Temporal artery biopsy has diagnostic yield around 13%<sup>3</sup>. We have done a retrospective analysis of patients who had temporal artery biopsy in order to assess the compliance with BSR guidelines and assess the diagnostic yield.

**Objectives:** To assess the yield of temporal artery biopsy and its impact in the management of Giant cell arteritis

**Methods:** The medical records of patients who had temporal artery biopsy from September 2015 to August 2017 were retrospectively reviewed. We documented demographics, management pre and post biopsy, and timeframes between referral, treatment and biopsy. Data was searched through the clinic letters, referral letters and pathology results.

**Results:** Total number of patients identified was 45. Among them 23 (51%) patients had typical clinical features of GCA and 21 (49%) had atypical features as per the referral letter. Age distribution found was as following: 50 years and below-3; 51 to 60 years-7; 61 to 70 years-15; 71 to 80 years-12; 81 to 90 years-7 and above 90 years-1. Timeframe between biopsy referral and biopsy was as following: within 1 week-27; between 1–2 weeks-10; between 2–3 weeks-6 and more than 3 weeks-1. Ophthalmologists performed biopsy for 37 patient and vascular surgeons for 8 patients. Referral was made by primary care for 7 patients, acute medicine for 12 patients, neurology for 3 patients and by rheumatologist for 23 patients. Treatment was initiated in 37 (82%) patients prior to biopsy. Biopsy was positive in 11 (25%) patients, negative in 30 (66%) patients and 4 (8%) showed healed inflammatory changes (HIC). Age distribution of biopsy positive patients was as following - age 61 to 70 years - 4; age 71 to 80 years - 4; age 81 to 90 years - 3. Out of the 11 biopsy positive patients 7 were started on treatment prior to the biopsy and remaining 4 were initiated on treatment after the results. The distribution of duration of treatment before biopsy was as following - within 1 week - 2; between 1 to 2 weeks - 3; between 2 to 3 weeks - 2.

**Conclusions:** - Majority of the patients (80%) had temporal artery biopsy done within 2 weeks of referral

- Diagnostic yield of temporal artery biopsy was found nearly twice the existing data

- Biopsy was positive in the age group between 61 to 90 years
- Positive biopsy was seen up to 3 weeks of treatment with high dose corticosteroids
- Duration of treatment pre biopsy and age group appear to impact the diagnostic yield of temporal artery biopsy.

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Department of pathology, Heart of England NHS trust

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THU0691

### ASSOCIATION BETWEEN PERIODONTITIS AND CLINICAL RESPONSE IN RHEUMATOID ARTHRITIS PATIENTS UNDER BIOLOGICAL TREATMENT

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**Background:** Previous studies showed that periodontitis (PD) was a propagation factor for the severity of rheumatoid arthritis (RA) and our previous epidemiological study revealed that PD was associated with discontinuation risk of etanercept.

**Objectives:** To investigate the association between PD and the risk of 3 month clinical non-response using the Disease Activity Score (DAS)-based European League Against Rheumatism (EULAR) response criteria in RA patients under biological therapy.

**Methods:** We enrolled 111 RA patients treated with biologics, including etanercept (n=16), adalimumab (n=44), golimumab (n=7), tocilizumab (n=23), abatacept (n=14), and rituximab (n=7). A qualified periodontist performed the periodontal assessment, and the 3 month clinical response was determined DAS-based EULAR response criteria. We quantified the association between PD and the risk of non-response by calculating odds ratios (ORs) with 95% confidence intervals (CIs) using the logistic regression analysis, after adjusting for confounders including age, sex, tobacco use, RA disease duration, biologic treatment duration, rheumatoid factor and anti-citrullinated peptide antibody, erythrocyte sedimentation rate and C-reactive protein, concurrent medication, and diabetes.

**Results:** Of 111 RA patients, 83 (74.8%) had PD. 37 (44.6%) of PD patients received periodontal treatment within three months. After adjusting for potential confounders, PD patients had a higher risk of non-response to treatment than non-PD patients (OR, 4.20; 95% CI, 1.06–16.68; p=0.041). Compared with non-PD patients, the risk of non-response was significantly greater in PD patients who did not receive periodontal therapy (OR, 5.12; 95% CI, 1.16–22.56; p=0.031), but not in PD patients who received periodontal therapy (OR, 3.28; 95% CI, 0.72–15.06; p=0.126). Among those who were under tumour necrosis factor inhibitor therapy (n=67), the risk of clinical non-response was markedly higher in those with PD (OR, 9.65; 95% CI, 1.33–70.04; p=0.025), particularly in those who did not receive periodontal therapy (OR, 14.39; 95% CI, 1.59–130.38; p=0.018).

Significant predictor of 3 month non-response	Univariable analysis OR (95% CI)	Multivariable	
		Model A OR (95% CI)	Model B OR (95% CI)
Periodontitis			
No	Reference:	Reference:	Reference:
Yes	1.39 (0.56–3.45)	4.20 (1.06–16.68)	
Not treated	1.77 (0.66–4.74)		5.12 (1.16–22.56)
Treated	1.01 (0.36–2.90)		3.28 (0.72–15.06)
RA duration, incremental year	1.03 (1.00–1.06)	1.13 (1.04–1.24)	1.13 (1.03–1.23)
Baseline DAS28	1.00 (0.86–1.15)	1.64 (0.99–2.73)	1.69 (1.01–2.82)
Baseline ESR	1.06 (1.02–1.09)	1.06 (1.004–1.11)	1.06 (1.003–1.11)

**Conclusions:** In RA patients under biological therapy, an increased risk of clinical non-response to treatment was observed in patients with PD, especially among those who did not receive periodontal treatment.

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THU0692

### RISK OF END-STAGE RENAL DISEASE REQUIRING DIALYSIS IN ANKYLOSING SPONDYLITIS PATIENTS STARTING MEDICAL THERAPY: A NATIONWIDE, POPULATION-BASED, COHORT STUDY

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**Background:** From the year 2000 Taiwan has had the highest incidence and prevalence of end-stage renal disease (ESRD) among the regions investigated by the US Renal Data System. Also, previous studies had suggested a possible association between IgA nephropathy and ankylosing spondylitis (AS) because an increased prevalence of microscopic hematuria and a higher proportion of elevated serum IgA levels were found in AS patients. However, whether the risk of ESRD was increased in treated AS patients or not is still unknown.

**Objectives:** To examine the risk of ESRD requiring dialysis in patients with AS who started medical therapy.

**Methods:** Using 2003–2012 claims data from the Taiwanese National Health Insurance Research Database, we identified 38,259 AS patients who received at least 3 courses of AS-related medical therapy (i.e., non-steroidal anti-inflammatory drugs, methotrexate, salazopyrine or corticosteroid) and started therapy from 2005 to 2012. The first date of medical therapy was defined as the index date. After excluding those who had a history of chronic renal disease (ICD9-CM 585, 586) or receiving dialysis before the index date, we identified 37 070 newly-treated AS cases. We randomly selected 3 70 700 non-AS individuals matching (1:10) AS cases for age, sex and the year of the index date without a history of chronic renal failure or dialysis before the index date. After adjusting for age, sex, moderate to severe renal disease, diabetes mellitus, hypertension, and annual cumulative defined daily dose (cDDDs) of traditional non-steroidal anti-inflammatory drugs (NSAIDs), selective cyclooxygenase-2 inhibitors (COX2i), and preferential COX2i, we calculated the adjusted hazard ratios (aHRs) with 95% confidence intervals (CIs) using the Cox proportional hazard model to quantify the risk of ESRD in AS patients compared with non-AS controls. We re-selected 6,621 AS patients and 6621 non-AS subjects by further matching (1:1) for cDDDs of three groups of NSAIDs to re-estimate the aHRs for ESRD.

**Results:** 51 (0.14%) of 37,070 AS patients and 1,17 (0.38%) of non-AS individuals developed ESRD after a follow-up of 1 58 846 and 1,707,757 person-years respectively. The aHR for ESRD was 0.4 (0.30–0.54) in AS patients compared with non-AS individuals. However, after further matching for cDDDs of NSAIDs, the aHR of ESRD was 0.80 (0.34–1.86). Significant risk factors included diabetes mellitus, hypertension, renal disease, and use of COX2i.

**Conclusions:** The risk of ESRD was not significantly different between treated AS patients and age, sex, index date, and NSAIDs use matched non-AS individuals.

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**Disclosure of Interest:** None declared

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**THU0693 GOUT AND THE RISK OF PARKINSON'S DISEASE IN THE ELDERLY**

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**Background:** A recent systematic review and meta-analysis, based on two cohort studies and three case-control studies, reported a pooled risk ratio of subsequent Parkinson's disease (PD) in patients with gout was 0.93 (95% CI, 0.79 to 1.09), a non-significant result. However, statistical heterogeneity was high at 87%–96%, indicating that studies differed from each other. Thus, it is not clear that gout is associated with PD and if so, what is the direction and magnitude of the risk of PD with gout.

**Objectives:** To assess the association of gout with the risk of incident Parkinson's disease.

**Methods:** We used the 5% Medicare sample from 2006–2012 to assess whether a diagnosis of gout was associated with the risk of incident Parkinson's disease in the elderly. Multivariable Cox regression model adjusted for demographics, Charlson-Romano comorbidity index, common medications, allopurinol and febuxostat use, was used to obtain hazard ratios (HR) and 95% confidence interval (CI).

**Results:** The mean cohort age was 73 years (standard deviation [SD], 6.5), mean Charlson-Romano comorbidity index score was 1.2 (SD, 1.9), 58% were female, 86% were White and 30% had Charlson-Romano comorbidity index score of  $\geq 2$  (n=15,675). The crude incidence rates of incident PD of 3.3 vs. 1.7 per 1000 person-years in those with gout vs. without gout. Gout was associated with a higher risk of PD in the main analysis, 1.18 (95% CI, 1.10, 1.27). Older age, male gender, White race, higher Charlson-Romano comorbidity index score were associated with higher risk of PD. Sensitivity analyses confirmed main findings. No gender or race differences were noted, but the risk differed by the age: ages 65–<75, 75–<85 and  $\geq 85$  years were associated with hazard ratios of incident PD with gout of 1.27, 1.12 and 0.98, respectively.

**Conclusions:** Gout was associated with a higher risk of incident PD in the elderly. The risk of PD with gout was highest in the age group 65–75 years. Mechanisms of this increased risk need to be evaluated in future studies.

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**THU0694 THE EXCESS RISK OF DISABILITY IN PEOPLE WITH NEUROPATHIC PAIN WHEN COMPARED TO THOSE WITH NOCICEPTIVE PAIN IS EXPLAINED BY PAIN CATASTROPHISING AND PHYSICAL INACTIVITY**

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**Background:** Neuropathic pain (NP) is associated with worse patient outcomes including poorer quality of life and increased disability and mortality when compared to persons with pain that is predominantly nociceptive (NCP). It is not known if the higher rate of co-morbid psychosocial factors (e.g. depression, fatigue) in persons with NP explains the increased risk of poor outcomes.

**Objectives:** To test the hypotheses that pain predominantly of NP origin would be associated with higher levels of disability when compared to NCP, and the excess risk would be independent of putative confounders.

**Methods:** 1587 participants in a population based prospective study completed a baseline and follow up questionnaire 12 months later. Participants were asked about the presence, location and duration of musculoskeletal pain and they completed the Douleur Neuropathique 4 (scores  $\geq 3$  indicating NP). Participants were classified according to their pain reports as having no pain (NP), some pain with (SPn) and without (SP) NP, and chronic widespread pain American College of Rheumatology 1990 criteria) with (CWPn) and without (CWP) NP. The primary outcome was the Stanford Health Assessment Questionnaire (HAQ) from which

the Standard Disability Index (HAQ-DI) was calculated. Participants also completed the Hospital Anxiety and Depression Scale (HADS), Chalder Fatigue scale (CF); the Pain Catastrophising Scale (PCS); Rapid Assessment of Physical Activity (RAPA); Social Support scale (SS); Joint Hypermobility scale (JH); Jenkins Sleep Scale (JSS). Ordered logistic regression tested the relationship between pain status at baseline and HAQ-DI at follow up with results expressed as odds ratios (OR) with 95% confidence intervals (CI).

**Results:** 1235 (77%) participants provided complete data and formed the cohort for this analysis. At 12 month follow up the mean (standard deviation) HAQ-DI score was 0.31 (0.62), with higher scores in women and older participants. After adjusting for age and sex, when compared to those with NP at baseline participants with SP were 3 times (OR=2.9, 95% CI (2.2, 3.9)) and those with SPn almost 9 times (8.7 (5.4, 14.0)) more likely to have higher HAQ-DI scores at follow up. Those with CWP were 8 (7.8 (5.7, 10.8)) and those with CWPn 38 (38.1 (23.3, 62.5)) times more likely to have higher HAQ-DI scores. When these associations were adjusted for putative confounders and baseline HAQ-DI scores having pain remained associated with increased HAQ-DI scores at follow up although the relationships were significantly attenuated, and the 95% CIs were similar across pain groups: SP 1.8 (1.3, 2.5); SPn 2.6 (1.4, 4.8); CWP 2.3 (1.6, 3.4); 3.3 (1.9, 6.0). The PCS helplessness scale (1.07 (1.01, 1.13)) and RAPA (0.93 (0.87, 0.99)) were significantly associated with 12 month HAQ-DI scores.

**Conclusions:** The increased risk of disability in persons with NP was not independent of common pain co-morbidities. Screening and targeting treatment for pain-related helplessness and physical inactivity has the potential to significantly improve disability outcomes for persons with NP.

**Disclosure of Interest:** None declared

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**THU0695 DOES HORMONE REPLACEMENT THERAPY PREVENT UNDIFFERENTIATED ARTHRITIS PROGRESSING TO RHEUMATOID ARTHRITIS**

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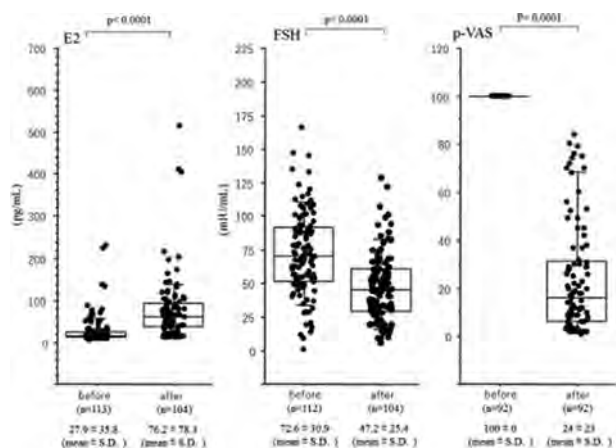
**Background:** Oral contraceptive (OC) and hormone replacement therapy (HRT) have been reported to have a protective and preventive effect on the progression of rheumatoid arthritis (RA). Although these observations are controversial, progression of undifferentiated arthritis (UA) to RA in pre- and post-menopausal women is largely unreported.

**Objectives:** Over a 10 year period, we followed patients with undifferentiated arthritis (UA) who were referred to rheumatologists and did not fulfil classification or diagnostic criteria for RA or other connective tissue disease. We studied the efficacy of hormone replacement therapy (HRT) in this setting. In this study, the primary objective was to determine whether HRT reduces joint pain and/or decreased the progression of UA to RA.

**Methods:** From 2007 to 2016, 1076 patients (male:60, female:1016) classified as UA were referred to one of two clinics because of complaints of joint pains and were enrolled in this study. Beginning in 2012, premenstrual, perimenstrual and postmenstrual women with UA were prescribed ultra-low dose tocopherol (600 mg/day) and HRT. A reduction of over 70% joint pain on a p-visual analogue scale (p-VAS) was set as the criterion of a favourable outcome. Each patient was assigned into one primary disease category. For example, primary SjS was regarded as a disease category but if a patient had secondary SjS, they were assigned to the primary (RA, SLE, SSc) disease category.

**Results:** During the 5 year observation period, 213/343 (62.1%) had postmenopausal arthralgia (PoMA), 46/112 (41.1%) with perimenopausal arthralgia (PeMA), 17/25 (68%) with premenopausal arthralgia (PrMA). In the RA patients, 10.2% had RF alone, 73.1% (250/342) had ACPA and/RF or ACPA alone and 16.7% had neither ACPA or RF. The specificity of ACPA was 93.2%. Regarding efficacy of HRT, the incidence of RA in RF positive individuals was 9.1% (5/55) in patients undergoing HRT (current and past user), which was significantly lower ( $p < 0.01$ ) than the 48.4% (30/62) in those never treated with HRT. Likely due to low numbers in the cohort, the incidence of RA in ACPA positive females was 22.2% (2/9) in those receiving HRT was not statistically significantly lower than the 70% (7/10) in those with without HRT.

Figure 1 Postmenopausal women responded to conventional HRT in 2013–2015



**Conclusions:** The progression of UA to RA is apparently ameliorated in RF positive females who received conventional HRT and oral E3 treatment. Although the numbers were smaller, a significant protective effect was not observed in ACPA positive UA females, because they developed RA before menopause. Our observations suggest that HRT in peri- and post-menopausal and oestrogen (E3) in pre-menopausal females with RF and ACPA positive UA may be important in ameliorating the progression of UA to RA.

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**Disclosure of Interest:** None declared

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#### THU0696 IS AUTOIMMUNITY RELATED TO NAILFOLD VIDEOCAPILLAROSCOPY PATTERNS PROGRESSION? DATA FROM A TERTIARY CENTRE

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**Background:** Nailfold videocapillaroscopy (NVC) is a non-invasive technique that allows to evaluate the structure and distribution of capillaries in the nail microcirculation.

**Objectives:** Our objective was to investigate the relation between the autoantibodies (Ab) detected in the patients who undergo follow-up NVCs and the progression from lower to higher severity of the NVCs patterns.

**Methods:** Longitudinal, observational and descriptive study that includes patients with at least two NVCs, between June 2012 and December 2016 in the Rheumatology service of a tertiary centre. We collected demographics data, number of NVCs performed, Ab positivity, as well as the NVCs patterns. The relationship between the basal autoimmunity and the progression of the NVCs patterns during the follow-up period, defining progression from non-specific patterns to patterns of scleroderma to late scleroderma.

**Results:** 473 patients were included, 115 had two or more NVCs performed, 104 women (90.51%). Of these, 40 (34.78%) had a third NVC, 9 (7.82%) a fourth and only two patients a fifth. Regarding the Ab registered in patients before the first NVC, 27 patients did not present positivity to any Ab (23.47%), 28 had isolated ANA + (24.34%), 33 Anticentromere+with or without ANA (28.69%), 7 patients Anti-scl70 +with or without ANA (6.08%), 10 patients Anti-Ro or Anti-La with or without ANA (8.69) and 10 patients presented other types of antibodies than those mentioned (11.3%). The most frequent pattern in the first NVC was non-specific mild alterations (49 cases) in 42.6%, followed by normal pattern<sup>20</sup> in 17.39%, early scleroderma<sup>19</sup> in 16.52%, non-specific moderate lesions<sup>17</sup> and pattern of late scleroderma<sup>10</sup>. There was a progression from lower to higher severity in 25 NVCs,

88 maintained a similar pattern and 2 NVCs presented significant regression (table 2).

**Abstract THU0696 – Table 1.** Baseline diagnosis before first NVC.

Baseline diagnosis	n:	%
	<b>115</b>	
Primary Raynaud Phenomenom	56	48.27
Systemic scleroderma	27	23.27
Systemic Lupus Erythematosus	8	6.89
Undifferentiated connective tissue	8	6.89
Mixed Connective Tissue	4	4.31
Diseasee		
Dermatomyositis	2	1.72
Others	10	8.62

**Abstract THU0696 – Table 2.** Patients whose NVC progresses, patterns and related autoantibodies.

n:25 (%)	Autoantibodies	Progression
2 (8%)	Ninguno	1/2: NMI to ES, 1/2: NML to LS
4 (16%)	ANA+	2/4: NMI to AS, 1/4: NML to AS, 1/4: NMI to ES
10 (40%)	ANA ±Anticentrómero	3/10: AS to LS, 3/10: ES to LS, 2/10: NML to ES, 1/10: NMI to ES, 1/10: NMI to AS
3 (12%)	ANA±AntiScl70 +	1/3: NML to AS, 1/3: AS to LS, 1/3: ES to AS
3 (12%)	ANA±Anti-Ro/ Anti-La+	2/3: NML to ES, 1/3: ES to LS
3 (12%)	Otros	2/3: ES to LS, 1/3: NMI to LS

**NVC patterns:** Normal (N), non-specific mild alterations (NMI), non-specific moderate lesions (NML), Early scleroderma (ES), Active scleroderma (AS) y Late scleroderma (LS)

**Conclusions:** Autoimmunity does not seem to influence on the degree of progression of NVCs patterns. The association between positive ANA with anticentrome + or not, it is the most frequently combination related to the progression of such patterns.

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**Disclosure of Interest:** None declared

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#### THU0697 RISK OF MAJOR CONGENITAL MALFORMATIONS ASSOCIATED WITH EXPOSURE TO CONVENTIONAL SYNTHETIC DISEASE MODIFYING ANTIRHEUMATIC DRUGS IN WOMEN WITH INFLAMMATORY ARTHRITIS: A POPULATION-BASED COHORT STUDY

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**Background:** Prior studies of perinatal exposure to conventional synthetic disease modifying antirheumatic drugs (csDMARDs) and risk of major congenital malformations (MCM) have often lacked comparator groups and specific timing of medication exposure.

**Objectives:** To evaluate the association between csDMARD use before and during pregnancy and risk of MCM.

**Methods:** We conducted a population-based, retrospective cohort study using British Columbia administrative data from 01/01/2002 and 12/31/2012 on all physician visits, hospital admissions, and dispensed medications, linked to a perinatal registry with valid information on date of conception. We created a pregnancy cohort of women with inflammatory arthritis (IA) using a case definition of 2 ICD9 codes  $\geq 2$  months and  $\leq 2$  years apart for rheumatoid arthritis, systemic autoimmune rheumatic diseases, ankylosing spondylitis, juvenile idiopathic arthritis, and psoriatic arthritis. We categorised csDMARDs according to accepted safety profiles: Group 1 - antimalarials, cyclosporine-A, gold, and sulfasalazine; and Group 2 - methotrexate, leflunomide, cyclophosphamide, azathioprine, chlorambucil, penicillamine, mycophenolate mofetil, and minocycline. We defined exposure over two periods: binary use (yes/no) during the 90 days preconception and first trimester of pregnancy. The outcome was occurrence of  $\geq 1$  MCM identified

at birth. We used logistic regression models fitted with generalised estimating equations.

**Results:** There were 598 pregnancies in 503 women (32±5 years), and 5651 pregnancies in 4086 women (31±5 years) in the csDMARDs exposed and unexposed groups, respectively. The adjusted odds ratio (OR) for exposure to csDMARDs preconception and during pregnancy and risk of MCM was 1.60 (95% CI, 1.19, 2.14) (table 1). In subgroup analyses, risk of MCM births was highest in those exposed to Group 2 csDMARDs during pregnancy (OR 3.63, 95% CI, 1.21, 10.92). For methotrexate specifically, we observed an OR of 1.62 (95% CI, 0.53, 4.91).

**Abstract THU0697 – Table 1.** Association of csDMARD exposure preconception and/or during pregnancy and risk of MCM

Models*	Exposure period	OR	95% Confidence Interval
Model 1	Preconception only vs. unexposed	1.37	0.84–2.24
All csDMARDs	During pregnancy only vs. unexposed	2.39	1.20–4.77
	Preconception AND during pregnancy vs. unexposed	1.60	1.19–2.14
Model 2	Preconception only vs. unexposed	1.04	0.55–1.99
Group 1 csDMARDs	During pregnancy only vs. unexposed	2.16	1.02–4.61
	Preconception AND during pregnancy vs. unexposed	1.49	1.09–2.05
Model 3	Preconception only vs. unexposed	1.43	0.73–2.77
Group 2 csDMARDs	During pregnancy only vs. unexposed	3.63	1.21–10.92
	Preconception AND during pregnancy vs. unexposed	1.71	1.06–2.76
Model 4	Preconception only vs. unexposed	1.19	0.49–2.87
Methotrexate only	During pregnancy only vs. unexposed	3.06	0.55–16.90
	Preconception AND during pregnancy vs. unexposed	1.62	0.53–4.91

\*All models were adjusted for baseline covariates including maternal characteristics, obstetrical history, comorbidities, and medication use before/during pregnancy.

**Conclusions:** We found associations with exposure to csDMARDs before and during pregnancy, namely the first trimester, with MCMs. These have implications for informing women with IA who are pregnant or planning to become pregnant.

**Disclosure of Interest:** None declared

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#### THU0698 CLINICAL OUTCOME OF ULTRASONOGRAPHIC DETECTED UNDIFFERENTIATED SYNOVITIS IN PATIENTS WITH POLYARTHRALGIA

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**Background:** Ultrasonography (US) has better sensitivity than clinical evaluation for the detection of synovitis in early inflammatory arthritis. The clinical importance and fate of undifferentiated synovitis in patients with polyarthralgia are still unknown.<sup>1</sup>

**Objectives:** To identify clinical outcome of undifferentiated synovitis detected by ultrasound in patients with polyarthralgia and to identify variables that can predict differentiation into specific type of arthritis.

**Methods:** New patients with polyarthralgia and undifferentiated synovitis were followed by clinical and ultrasound examination in the period between June 2015 to June 2017. Undifferentiated synovitis was defined as ultrasound detected synovial hypertrophy in cases in which no definitive diagnosis can be made.

Baseline assessments included: clinical examinations of complaining joints, laboratory investigations (CBC, ESR, CRP, RF, ACPA, ANA) and ultrasonographic evaluation of fifty joints (DIPs, PIPs, MCPs, wrists, elbows, shoulders, hips, knees, ankles and MTPs)

Follow ups were every 6–8 weeks until remission of synovitis or a definite clinical diagnosis was reached. Remission was defined as absence of a previously US detected synovitis in two consecutive follow-ups eight weeks apart.

Patients were received treatment according to the opinion of the treated rheumatologist who had a full data about clinical, laboratory and ultrasonographic data. Multivariate logistic regression analysis was used to identify predictors of remission, RA, PsA and continuation as undifferentiated synovitis.

**Results:** 174 patients (88.6% women, mean age 43.2±14.2 years (range 17–75)) were included.

Duration of follow up period ranged from 3 to 38 months (mean 11.4 months)

Final diagnoses were as follow; complete remission in 73 (41.7%) cases, rheumatoid arthritis (RA) in 20 cases (11.4%), psoriatic arthritis (PsA) in 10 cases (5.7%), spondyloarthropathy (SPA) in 11 cases (6.1%), sarcoidosis in 4 cases (2.3%), osteoarthritis (OA) in 10 cases (5.7%) and 46 cases (26.4%) continued as undifferentiated synovitis up to the end of the follow up period.

Remission of undifferentiated synovitis was associated with significantly older mean age, acute onset and absence of PD activity (OR 1.92, 1.95 and 1.86 respectively).

Development of RA was associated with chronic onset, positive rheumatoid factor, positive ACPA and US detected synovitis in more than three joints (OR 1.91, 1.75, 1.92 and 1.79 respectively). All patients with final diagnosis of RA had US detected synovitis in wrist joint with increased PD activity. PsA was associated with chronic onset, PD activity, bilateral knee synovitis, negative RF and ACPA (OR 1.84, 1.83, 1.94, 1.88 and 1.79 respectively). Cases with significantly younger mean age and shorter disease duration completed with undifferentiated synovitis (OR 1.92 and 1.87).

**Conclusions:** In our study, more than half of cases of ultrasound detected undifferentiated synovitis in patients with polyarthralgia differentiated into specific type of arthritis during the follow up period. older age and acute onset of symptoms are associated with remission while positive rheumatoid factor, positive ACPA, US detected synovitis in more than 3 joints including wrist joints are associated with development of RA. Bilateral knee synovitis are in favour of PsA and OA.

#### REFERENCE:

[1] Zufferey P, et al. *Joint Bone Spine* 2017 May;84(3):299–303. doi:10.1016/j.jbspin.2016.05.011

**Disclosure of Interest:** None declared

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#### THU0699 PREDICTORS OF FRACTURE AND LOW BONE MINERAL DENSITY IN PATIENTS WITH HISTORY OF PARENTAL FRACTURE

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**Background:** Predictors of fragility fracture (FF) risk and low bone mineral density (BMD) in the general population are well-documented. Previous studies have shown strong familial association between parental and offspring BMD and hip fracture, varying according to factors including body mass index and corticosteroids. Little data exists on predictors of FF and BMD in patients with a family history of fracture, despite this increasing fracture risk.

**Objectives:** We aimed to evaluate predictors of FF and low BMD in patients attending for dual energy X-ray absorptiometry scanning.

**Methods:** Patients referred for BMD estimation, between 2004 and 2016, with a history of parental fracture, were included. Parameters recorded: femoral and vertebral BMD, height, weight, fat mass, age, smoking, alcohol, corticosteroids, aromatase inhibitors, Depo-Provera, hormone replacement therapy (HRT), rheumatoid arthritis (RA), polymyalgia rheumatica (PMR), breast or prostate cancer, and coeliac disease.

Logistic regression was used to model fracture risk, and linear regression was used to model the impact of each factor on vertebral and femoral BMD.

**Results:** 6053 patients (5513 female) were included. 2094 patients (34.6%) had sustained at least one fracture. Smoking, alcoholism, corticosteroid, increased age, height, and fat mass significantly increased fracture risk. Coeliac disease, HRT, and aromatase inhibitors were protective. Cancer, aromatase inhibitor use, and female gender significantly decreased vertebral BMD. Corticosteroids, RA, and PMR significantly decreased L1–2 BMD. Increased age and height, and decreased weight, fat mass, and tissue thickness decreased vertebral and right femoral BMD; this significantly increased FF risk. Corticosteroids, RA, PMR, Depo-Provera, female gender, and aromatase inhibitors decreased BMD; in the left femur, alcohol, corticosteroid use, increased age, height, and decreased weight decreased BMD.

**Conclusions:** Similar to studies in the general population, smoking, alcohol, and corticosteroid therapy increase fracture risk, while HRT decreases it. Chronic aromatase inhibitor use increases fracture risk, suggesting a dose-dependent effect. Coeliac disease was found to be protective; previous studies have shown coeliac disease to decrease BMD, with a variable impact on fracture. Concurrent with previous studies, a differential effect of BMD in the dominant and non-dominant hip was found, with decreased right femoral BMD significant for fracture risk. Limitations of this study include lack of dose and duration of medications and lack of comparative data before and after fracture in a single patient.

Our study confirms the effect of the above factors on spinal BMD, but suggests a differential effect of smoking and alcohol on L1–2, with corticosteroids, RA and PMR affecting the lower lumbar spine. Our results also suggests a differential effect of the studied factors on the right femur compared to the left, suggesting the dominant femur is more susceptible to factors decreasing BMD. Limitations of this study include the large proportion of female subjects and lack of data on dose and duration of medications studied.

**Disclosure of Interest:** None declared

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THU0700

### PERINATAL EXPOSURE TO DISEASE MODIFYING ANTIRHEUMATIC DRUGS IN WOMEN WITH INFLAMMATORY ARTHRITIS AND THE RISK OF SMALL-FOR-GESTATIONAL-AGE NEWBORNS: A POPULATION-BASED COHORT STUDY

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**Background:** Currently there exists limited data on pregnancy outcomes among women with inflammatory arthritis (IA) using conventional synthetic DMARDs (csDMARDs), and the risk of small-for-gestational-age (SGA) births.

**Objectives:** To investigate the association between csDMARD use before and during pregnancy and SGA births.

**Methods:** We linked population-based health data in British Columbia, Canada over a 10 year study period (01/01/2002 – 12/31/2012) on all physician visits, hospital admissions, and dispensed medications with a perinatal registry containing valid information on date of conception. We created a pregnancy cohort of women with IA using a case definition of 2 outpatient physician ICD9 codes  $\geq 2$  months and  $\leq 2$  years apart for rheumatoid arthritis, systemic autoimmune rheumatic diseases, ankylosing spondylitis, juvenile idiopathic arthritis, and psoriatic arthritis. We categorised csDMARDs according to accepted safety profiles - antimalarials, cyclosporine-A, gold, and sulfasalazine (Group 1); and methotrexate, leflunomide, azathioprine, cyclophosphamide, chlorambucil, penicillamine, mycophenolate mofetil, and minocycline (Group 2). We determined exposure as binary use (yes/no) during the 90 days preconception; and during pregnancy from date of conception until date of delivery. The SGA outcome was defined as  $< 10$  th percentile of sex- and gestational-age specific weights for singleton births or with ICD9/10 codes. We used logistic regression models fitted with generalised estimating equations and adjusted for baseline covariates.

**Results:** There were 611 pregnancies in 513 women ( $32 \pm 5$  years), and 5638 pregnancies in 4077 women ( $31 \pm 5$  years) in the csDMARDs exposed and unexposed groups, respectively. We identified 13%, 18%, and 42% of newborns as SGA in unexposed pregnancies and exposed to Group 1 and 2 csDMARDs, respectively. The adjusted odds ratio (OR) for exposure to Group 1 csDMARDs preconception and during pregnancy and risk of SGA births was 1.49 (95%CI 1.12, 1.97) (table 1). The risk of SGA births was higher in those exposed to Group 2 csDMARDs (OR 1.78, 95% CI 1.14, 2.78). With respect to specific csDMARDs, we observed an OR of 1.25 (95% CI, 0.41, 3.82) for methotrexate.

**Abstract THU0700 – Table 1.** Association of csDMARD exposure preconception and/or during pregnancy and risk of SGA births

Models*	Exposure period	OR	95% Confidence Interval
Model 1	Preconception only vs. unexposed	0.79	0.42–1.50
Group 1	During pregnancy only vs. unexposed	1.57	0.83–2.99
csDMARDs	Preconception AND during pregnancy vs. unexposed	1.49	1.12–1.97
Model 2	Preconception only vs. unexposed	0.85	0.42–1.72
Group 2	During pregnancy only vs. unexposed	2.65	0.95–7.37
csDMARDs	Preconception AND during pregnancy vs. unexposed	1.78	1.14–2.78
Model 3	Preconception only vs. unexposed	0.77	0.31–1.88
Methotrexate	During pregnancy only vs. unexposed	2.24	0.48–10.48
	Preconception AND during pregnancy vs. unexposed	1.25	0.41–3.82

\*All models were adjusted for baseline covariates including maternal characteristics, obstetrical history, comorbidities, and medication use before/during pregnancy.

**Conclusions:** Our findings suggesting a risk of SGA births with exposure to csDMARDs preconception and during pregnancy have implications for informing women with inflammatory arthritis who are pregnant or planning to become pregnant.

**Disclosure of Interest:** None declared

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THU0701

### UPDATED INCIDENCE AND COSTS OF HIP FRACTURES IN ELDERLY ITALIAN POPULATION

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**Background:** It had already been evaluated the hospitalisation rate of femoral neck fractures in the elderly Italian population over ten years, showing that incidence of hip fractures in Italy are continuously increasing, although women aged 65–74 years old started showing a decreasing trend.

**Objectives:** To update our previous researches about the burden of hip fractures in elderly Italian population.

**Methods:** We analysed national hospitalizations records from 2007 to 2014 to compute age- and sex-specific standardised rates.

**Results:** 7 41 633 hospitalizations were observed in people  $\geq 65$  (women: 568,203; men: 173,430), with an overall increase of 5.50% over the 8 year period (females:+3.36; males:+12.9%). About 43.75% of total hip fractures were suffered by patients aged  $\geq 85$  years old. Women aged  $\geq 85$  accounted for 34.49% ( $n=255,763$ ) of total fractures. The incidence rate per 10 000 inhabitants in people aged 65–74 decreased from 28.65 to 25.31 in women ( $-13.02\%$ ) and from 13.41 to 11.65 in men ( $-13.12\%$ ). Incidence per 10 000 in people 75–84 decreased from 121.6 to 105.2 in women ( $-13.49\%$ ) and from 55.8 to 47.5 in men ( $-14.87\%$ ). Paradoxically, also in people aged  $\geq 85$ , the incidence per 10 000 declined from 300.99 to 268.72 in women ( $-10.72\%$ ) and from 174.59 to 171.17 in men ( $-1.96\%$ ) because the number of subjects aged  $\geq 85$  is growing faster than the number of fractures occurring in this latter age group. Direct hospitalisation costs and rehabilitation costs increased from 433 to 457 million Euros and from 478 to 504 million Euros over the 8 year period, respectively. Overall costs of hip fractures in people aged  $\geq 65$  years old raised from 911 to 961 million Euros from 2007 to 2014.

**Abstract THU0701 – Table 1**

Year	2007	2008	2009	2010	2011	2012	2013	2014
Hospitalizations due to hip fractures (female) (n/1000)	88,801	92,532	93,169	92,549	91,733	92,408	94,116	94,525
Overall hospitalizations due to hip fractures (€)	433,210,977	447,402,694	450,482,661	447,484,891	443,339,438	451,038,253	450,061,513	457,039,074
Overall rehabilitation costs (€)	478,324,281	493,971,382	497,371,926	494,662,138	489,706,016	488,647,810	502,427,386	504,610,782
Overall direct costs estimation (€)	911,535,258	941,374,076	947,854,587	942,147,028	933,045,454	939,686,063	952,488,909	961,649,856

**Conclusions:** The number of hip fractures and related hospitalizations costs in Italian elderly population is still increasing due to the fractures occurring in people  $\geq 85$  years old, although incidence rates are decreasing in all the age groups.

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THU0702

### SECULAR TRENDS OF HIP FRACTURES IN FRANCE BETWEEN 2002 AND 2013: IMPACT OF THE REFERENCE VALUES

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**Background:** Hip fractures are a societal burden because of their high related morbidity and mortality, and the cost they generate. With the ageing of the population, worries grow about an increase of the incidence and incidence rate of hip fracture in the next years. Numerous studies have shown an increase in the incidence whilst a decrease in the incidence rates of hip fracture in the majority of Europe countries and North America. These data come from heterogeneous studies regarding the reference population used, and thus their interpretations remain controversial.

**Objectives:** The aim of our study was to assess the impact of the choice of the reference population in the interpretation of incidence rates data, using country-based data of French population.

**Methods:** We used data related to the hospitalizations for hip fracture in France between 2002 and 2013 in patients over 59 years, extracted from the French National Hospital Database. Data were based on the whole French population and were classified by sex and age (60–74, 75–84, over 84 years, over 59 years). We first calculated the crude incidence rates of hip fracture by dividing the number of hospitalizations for hip fracture by the corresponding populations. To assess the impact of the choice of the reference population, we then calculated the crude and adjusted incidence rates using direct standardisation on age with three different reference populations (2002, 2013, mean population of 2002–2013).

**Results:** Between 2002 and 2013 in France, the incidence of hip fracture raised of 4.8% in women (from 49 287 to 51,661) and 21.8% in men (from 12 716 to 15,482), aged 59 years and over. In the meantime, French population over 59 years increased more with a rise of 21.3% in women and 28.7% in men, which explained a decrease in the crude incidence rates of 13.6% in women and 5.4% in men. However, this decrease was even more obvious after direct standardisation

whatever population of reference was used in women: 24.9%, 25.6% and 26.1% and men 18.2%, 19.2%, 19.8% with respectively 2002, 20013, and 2002–2013 as population of reference.

**Conclusions:** The incidence rates of hip fracture decreased in France between 2002 and 2013 in men and women aged 60 years and over. The decrease is more important after direct standardisation whatever population used as a reference as a results of a difference in age-structure of the population that can be erased by the process of direct standardisation. In conclusion, the incidence of hip fractures continues to grow despite a reduced incidence rate throughout a 12 year-period.

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**Disclosure of Interest:** None declared

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### THU0703 IDENTIFYING CLINICAL, PSYCHOLOGICAL AND WORK RELATED FACTORS ASSOCIATED WITH PRESENTEEISM: THE INTERNATIONAL EULAR-PRO AT-WORK PRODUCTIVITY STUDY

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**Background:** Worker productivity loss, including presenteeism, is an important outcome for patients with inflammatory (IA) diseases and osteoarthritis (OA) and is frequently seen as a health outcome in clinical studies. It is important to understand which factors are related with this patient reported outcome in order to inform future work related interventions.

**Objectives:** To assess the association between disease related, psychological and work related factors with presenteeism.

**Methods:** In a large international study evaluating measures of presenteeism we recruited patients with IA and OA from UK, Fr, NL, Es, Se, Ro, It, Pt, and Ca. Absence rates and presenteeism levels (range 0–10=worst score) were measured using the Work Productivity and Activity Impairment (WPAI) questionnaire. Other job related questions were about demands and satisfaction, help from colleagues and opportunities to postpone or organise ones work. Disease related variables included HAQ, EQ-5D, VAS health status. The Hospital Anxiety and Depression Scale (HADS) was also completed. Cross-sectional univariable and multivariable Zinb regression models were applied to assess the association between these disease related, psychological, and work related factors and presenteeism, adjusting for age, gender and country. Due to high co-linearity only HAQ and HAD-anxiety were included in the multivariable model.

**Results:** A total of 544 patients (AS=138, OA=43, PsA=97, RA=266) were recruited with a mean (SD) age of 47<sup>10</sup> yrs and a median symptom duration [IQR] of 10<sup>5–18</sup> yrs; 62% were women. 17% had a manual occupation. 111/544 (20.4%) reported being absent during the previous 7 days. Mean (SD) presenteeism score was 2.9 (2.7). In univariable analyses, worse self-reported disease activity and high levels of depression and anxiety were significantly associated with presenteeism in both the count and inflate part of the model (table 1). Less consistent results were observed for work related factors. In the multivariable model (β, 95% CI), worse functional disability was associated with presenteeism in both the count and excess zero part of the model (0.63; 0.49, 0.78: -2.70, -3.73, -1.66, resp). In addition, higher HAD-anxiety score (-0.09; -0.18; -0.00) was associated with a decreased likelihood of excessive zeros whilst not receiving help from colleagues (1.47; 0.64, 2.30) was associated with an increased likelihood of

excessive zeros. There was a trend towards an association between very demanding jobs (-0.79; -1.63, 0.05) and presenteeism.

**Abstract THU0703 – Table 1**

	Value: N (%) / Mean (SD)	Univariable analyses	
		Count part Zinb model β (95%CI)	Inflate part Zinb model β (95%CI)
Age	47.7 (10.1)		
Gender	337/544 (62%)		
VAS health status	39.1 (25.8)	0.013 (0.01, 0.16)	-0.13 (-0.20, -0.06)
HAD-score	0.50 (0.50)	0.66 (0.52, 0.80)	-4.61 (-7.11, -2.11)
EQ-5D score	0.63 (0.65)	-0.82 (-1.04, -0.60)	7.53 (5.81, 9.76)
HAD Anxiety	6.2 (5.9)	0.02 (0.01, 0.03)	-0.21 (-0.32, -0.11)
HAD Depression	4.7 (3.7)	0.05 (0.03, 0.07)	-0.29 (-0.46, -0.12)
PASS, satisfied	154/543 (28%)	-0.54 (-0.68, -0.40)	1.40 (0.68, 2.11)
Job demands:			
- a bit/not demanding	137/541 (25%)	ref	ref
- demanding	218/541 (40%)	-0.01 (-0.22, 1.20)	-0.72 (-1.43, -0.01)
- very/extremely demanding	186/541 (34%)	0.19 (-0.03, 0.41)	-0.70 (-1.42, 0.02)
Job satisfaction:			
- (very) satisfied	390/542 (72%)	ref	ref
- neither satisfied nor unsatisfied	82/542 (15%)	0.10 (-0.08, 0.29)	-1.71 (-3.05, -0.34)
- (very)unsatisfied	70/542 (13%)	0.14 (-0.08, 0.35)	-0.36 (-1.17, 0.45)
Help colleagues:			
- often/always	159/541 (29%)	ref	ref
- sometimes	278/541 (52%)	0.05 (-0.13, 0.23)	-0.09 (-0.87, 0.69)
- never	103/541 (19%)	0.09 (-0.16, 0.34)	1.65 (0.83, 0.46)
Ability to postpone tasks:			
- often/always	92/542 (17%)	ref	ref
- sometimes	319/542 (59%)	0.06 (-0.15, 0.27)	-0.08 (-0.86, 0.69)
- never	131/542 (24%)	0.33 (0.09, 0.57)	0.49 (-0.34, 1.33)
Ability to organise own work:			
- often/always	353/542 (65%)	ref	ref
- sometimes	147/542 (27%)	0.11 (-0.06, 0.29)	-0.12 (-0.72, 0.48)
- never	42/542 (8%)	0.30 (0.04, 0.55)	-0.37 (-1.34, 0.60)

VAS=visual analogue scale (0–100 worst score); EQ-5D=EuroQol-5D (-0.11–1=perfect health); HAD=Hospital Anxiety Scale (0–21=abnormal); PASS=do you feel your current condition is satisfactory, when you take your general functioning and your current pain into account (satisfactory/unsatisfactory). Count part=score in those with a score >0; inflate part=estimate of excess zero scores.

**Conclusions:** In this large international study of patients with IA and OA having a median symptom duration of 10 years, worse functional ability was the main factor associated with presenteeism.

**Disclosure of Interest:** None declared

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### THU0704 A NEW ASSESSMENT TOOL FOR ULNAR DRIFT IN PATIENTS WITH RHEUMATOID ARTHRITIS USING PATHOPHYSIOLOGICAL PARAMETERS OF THE METACARPOPHALANGEAL JOINT

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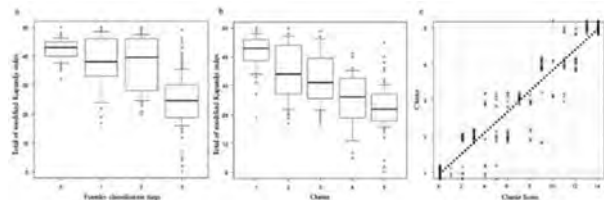
**Background:** Ulnar drift (UD) in rheumatoid arthritis (RA) is the most common and difficult to manage deformity in the rheumatoid hand; it is reported that 44% of patients develop UD within the first 10 years. Nevertheless, the assessment of UD is challenging; the Fearnley classification method, first reported in 1951, is still used for evaluation. However, it is sometimes difficult to determine the best surgical procedure simply based on the Fearnley classification, which only evaluates reducibility. Therefore, we have been using both the Fearnley classification as a 'gold standard' and an original scoring method that enables us to easily treat the deteriorated condition contributing to UD.

**Objectives:** To establish and verify a new assessment tool for UD in rheumatoid hand.

**Methods:** We established an observational cohort of 67 patients (134 rheumatoid hands) beginning in 2004, among the RA outpatients who had any apparent finger deformity in either hand. Fifty-two patients (100 hands) had follow-up in 2009, and thirty-seven patients (63 hands) completed follow-up in 2015. For evaluation of UD, we used both the Fearnley classification as a 'gold standard' and an original scoring method which assesses four parameters of the metacarpophalangeal joint. Cluster analysis using UD parameters divided hands into groups. For functional assessment, we used the modified Kapandji index (MKI). The MKI enables us to assess unilateral hand functional mobility within a few minutes. Changes in UD over time, correlation of the Fearnley stage and cluster with MKI, and reliability of the parameters with clustering were analysed.

**Results:** The 10 year follow-up rate was 55.2%, and UD increased and worsened over time (p<0.001). A dendrogram indicated five clusters would be appropriate. Twenty-six hands in total changed to a higher cluster number during the follow-up period. Both the Fearnley classification and cluster were associated with MKI

significantly. Though the Fearnley classification showed a floor effect, our method related to function more linearly (R-squared: 0.42). Each parameter of our method showed statistical significance for the clusters by regression analysis. And the ratio of the partial regression coefficient of each parameter was around 1:1:3:2, so we calculated a 'cluster score' using a weighted score for each parameter. A regression analysis has shown a strong correlation ( $r=0.95$ ,  $p<0.001$ ); however, its scatter plot also suggested that it is difficult to classify the cluster using CS only. We found one type of hand in which bone destruction precedes the joint dislocation and one type in which joint dislocation progresses with little deviation during UD progression. It is considered that two patterns of pathological findings and included some suggested indications for operative therapy to recover disability due to UD.



**Conclusions:** Our UD evaluation method is quite simple but is closely related to function. Additionally, it enables dividing UD hands into five stages. Thus, our assessment should be beneficial compared to the Fearnley classification in considering treatments of UD.

**Acknowledgements:** The authors thank all the researchers involved in this 10 year observational study.

**Disclosure of Interest:** None declared

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#### THU0705 OCCURRENCE OF ANKYLOSING SPONDYLITIS (AS) AMONG RELATIVES OF PROBANDS WITH RADIOGRAPHIC AS AND NON-RADIOGRAPHIC AS/ AXIAL SPONDYLOARTHRITIS (SPA)

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**Background:** The occurrence of AS in families as it relates to the presence or absence of HLA-B27 and radiographic sacroiliitis is not well-known.

**Objectives:** To assess among relatives the occurrence of AS and its association with HLA-B27 and presence of sacroiliitis among AS probands. AS is broader than just radiographic (classical) AS by modified New York criteria (mNY). We asked whether the likelihood of having a relative with classical AS is comparable for probands with radiographic AS by mNY criteria, and probands with non-radiographic AS/axSpA.

**Methods:** Re-analysis of the 1985–86 Swiss AS Family Study: 1178 subjects (363 clinically defined AS probands, 806 first-degree relatives, and 9 spouses) had participated. The AS patients were members of the Swiss AS patient society. The invited and consenting participants underwent physical exam of the spine and joints, completed questionnaires dealing with musculoskeletal problems, had pelvic radiographs taken, and provided blood samples for HLA-A,B,C typing. Radiographs were blindly read twice by each of up to 4 experienced readers. They scored sacroiliac joints according to NY criteria for sacroiliitis (bilateral grade  $\geq 2$  or unilateral grade  $\geq 3$ ). The study had been approved by the ethical committee of the University of Bern, Switzerland.

**Results:** Among 358 AS probands, 308 (86%) were HLA-B27(+) and 50 (14%) lacked this gene. The radiographic NY criteria were met by 81% of the 308 HLA-B27(+) probands versus only 44% of the 50 HLA-B27(-) probands. AS, as defined by NY criteria, was observed only among relatives of HLA-B27(+) probands; and all 14 of these relatives were also HLA-B27(+). Note: The probands in 12 of these 14 cases met the NY criteria, while 2 did not. Two of 59 HLA-B27(+) relatives from AS probands not-fulfilling the mNY criteria met the NY criteria, compared with 12 of 245 HLA-B27(+) relatives from AS probands fulfilling the mNY criteria ( $p=0.62$ ). Interestingly, inflammatory back pain (by Calin criteria) occurred among 46 of 286 (16.1%) HLA-B27(+) relatives of HLA-B27(+) probands, but in only 27 of 272 (9.9%) HLA-B27(-) relatives of HLA-B27(+) probands ( $p=0.031$ ).

**Conclusions:** AS among relatives was only observed in families of HLA-B27(+) AS/axSpA probands. The risk for HLA-B27(+) relatives to develop AS by NY criteria seems not to be influenced by the presence of sacroiliitis in the HLA-B27(+) AS/axSpA probands. HLA-B27(+) relatives who do not show radiographic

sacroiliitis are at higher risk to demonstrate symptoms of non-radiological AS/axSpA as they seem more prone to have inflammatory back pain.

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**Disclosure of Interest:** None declared

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#### THU0706 PRESENCE OF EXTRACTABLE NUCLEAR ANTIGENS (ENA) ANTIBODIES IN A LARGE POPULATION-BASED COHORT FROM THE NETHERLANDS

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**Background:** Previous studies have demonstrated that years before the clinical onset of auto-immune diseases, auto-antibodies can already be present in the blood of these patients. However, it is also known that some individuals can have these auto-antibodies and will never develop an auto-immune disease. So far, little information is available on the presence of Extractable Nuclear Antigens antibodies (anti-ENA) in the general population in relation to the risk of developing an auto-immune disease.

**Objectives:** To estimate the prevalence of anti-ENA and their association with the presence of known risk factors of Systemic Lupus Erythematosus (SLE) and Sjögren Syndrome (SS) in the general Dutch population.

**Methods:** Lifelines is a prospective population-based cohort study in the Netherlands. Cross-sectional data from 40 135 participants were analysed. The detection of anti-ENA was performed using the ENA-CTD (connective tissue disease) screen on the Phadia-250 analyser with a ratio  $>1.0$  are considered positive. An extensive questionnaire was taken on demographic and clinical information (e.g. early musculoskeletal symptoms). Furthermore, some general blood parameters were available. SLE and SS were defined by a combination of self-reported SLE or SS, specific medication use and visiting a medical specialist within the last year. Characteristics were compared between 3 groups: SLE/SS patients, anti-ENA positive, and anti-ENA negative participants (without defined SLE/SS).

**Results:** Of the total 40 135 consecutive individuals, 41 were detected as having defined SLE or SS of whom 48% were anti-ENA positive SLE/SS patients were older and more often female. Of the remaining individuals, <sup>40,094</sup> 1089 (2.7%) were anti-ENA positive and anti-ENA positivity was also significantly associated with older age and female gender in this population. No significant associations were found for smoking and alcohol intake. As might be expected, SLE/SS patients reported more often complaints concerning fatigue, joint pain and joint stiffness. But also anti-ENA-positive participants reported significantly more often joint stiffness compared to anti-ENA-negative participants. Interestingly, levels of haemoglobin, leucocytes and lymphocytes were significantly decreased in anti-ENA-positive participants compared to anti-ENA-negative participants.

**Conclusions:** In this large population-based study, the prevalence of anti-ENA-positivity was 2.8% for the total group and 2.7% when excluding patients with SLE or SS. Older age, female gender, joint complaints and lower levels of haemoglobin, leucocytes and lymphocytes were more frequently present in anti-ENA-positive participants. Longitudinal studies are performed up to 15 years to investigate which individuals might develop SLE or SS to be able to develop prediction models.

**Disclosure of Interest:** None declared

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#### THU0707 ANALYSIS OF ANTINUCLEAR ANTIBODIES IN BREAST CANCER PATIENTS

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**Background:** Analysis of antinuclear antibodies (ANA) may be found in malignant diseases

**Objectives:** To study the prevalence of ANA in breast cancer patients and its association with tumour characteristics.

**Methods:** Ninety one patients with breast mass detected by image studies and assigned to do diagnostic biopsy and eventual surgical treatment were studied for demographical, tumour data and presence of ANA. Serum of positive ANA patients was submitted to examination of ENA (extractable nuclear antigens)



profile. As comparison 91 healthy individuals paired for age and from same geographical area had ANA determination.

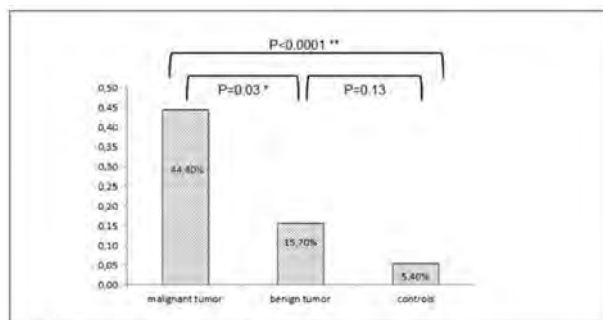
**Results:** In this sample 72/91 (79.1%) had malignant lesions (83% ductal infiltrative carcinoma). Ana was positive in 44.4% of malignant tumour patients, in 15.7% of benign lesions ( $p=0.03$ ) and in 5.4% of controls ( $p<0.0001$ ). The most common immunofluorescence pattern was fine dense speckled pattern. In the ANA positive patients with malignant lesions, 7 had positivity for ENA profile (3 for anti-RNP and anti-Sm, 1 for just anti-RNP, 2 for anti-Ro and anti-LA e 2 for just anti-La). It was not possible to associate ANA positivity with tumour histological characteristics or staging, neither with patient's age. A negative association of ANA with hormonal receptor status was found ( $p=0.01$ ).

**Abstract THU0707 – Table 1.** Comparison of malignant breast lesions characteristics according to positivity of antinuclear antibody (ANA)

	Positive ANA n=32	Negative ANA n=40	P
Ethnic background	Caucasians=32/32–100%	Caucasians –38/40–95% Afro descendentes - 2/40%–5%	0.49
Female gender	32/32%–100%	39/40%–97.5%	1.00
Mean age (years)	53.1±14.74	55.10±14.44	0.57
Histology	Ductal invator –26/32–81.2% Others - 6/32%–18.7%	Ductal invator –34/40–85% Others- 6/40%–15%	0.30
Stage IV	10/27%–37.0%	11/30%–36.6%	0.97
Luminal A	5/25%–20%	7/30%–23.3%	0.76
Luminal B	10/25%–40%	16/30%–53.3%	0.32
HER-2 positive	4/25%–16%	3/30%–10%	0.68
Triple negative	6/25%–24%	4/30%–13.3%	0.48
Hormonal receptor +	16/28%–57.1%	26/30%–86.6%	0.01*
Smoking	2/16%–12.5%	2/26%–7.6%	0.62
Body mass index (kg/m <sup>2</sup> )	29.18±6.13	25.99±3.28	0.09

(\* ) OR=4.8 (95%CI=1.33–17.7)

Figure 1 Prevalence of ANA in patients with breast tumours and controls



(\* ) Malignant vs benign - OR=4.26; 95%CI= 1.34-15.92.  
(\*\*) Malignant vs controls - OR=13.76; 95% CI = 4.98-37.95.

**Conclusions:** In this sample there was a high prevalence of ANA positivity in breast cancer patients with a negative association with the presence of hormone receptors.

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**Disclosure of Interest:** None declared

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THU0708

#### DISPARITY IN OSTEOARTHRITIS KNEE PREVALENCE- A TALE OF TWO CITIES IN IRAN (TEHRAN) AND INDIA (PUNE): FINDINGS FROM WHO ILAR COPCORD POPULATION SURVEY (STAGE I)

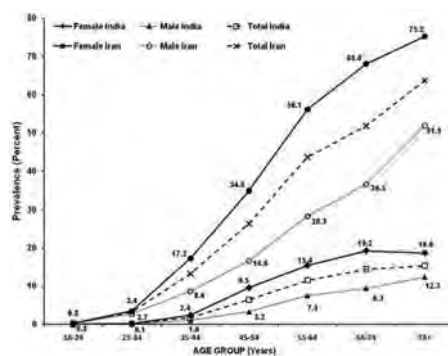
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**Background:** Radiographs are a major deterrent in population surveys. COPCORD (community oriented program for control of rheumatic diseases), a low infrastructure low cost model. advocates clinical approach ([www.copcord.org](http://www.copcord.org)). Iran and India completed COPCORD surveys during 2000–2010. Tehran (dominantly Muslim Shia ethnic) is 35° N, 51° E, altitude 3907' and Pune (dominantly Hindu Maratha ethnic) is 18° N, 73° E altitude 1817'. Tehran and Pune represent distinct culture and ethnicity but people in both communities sit and squat (ground). Early reports showed an adjusted prevalence of OA knee was 15.3 in Tehran and 3.4 in Pune.

**Objectives:** To determine and compare the age gender specific prevalence of knee OA in an urban survey in Iran and India

**Methods:** 8145 population (51% women) in Pune and 10 107 population (53% women) in Tehran were screened (convenience sampling). House to house survey (Phase 1) identified respondents with past(last 3 months) and/or current musculoskeletal (MSK) pain (last 7 days). Trained community volunteers interviewed respondents to map MSK pain and disability (Phase 2). Concurrently, rheumatologists examined cases to make a clinical diagnosis (phase 3). 8.1% in Iran and 16.6% in Pune population were aged 65+years. The age-gender structure in both surveys (phase 1) was similar to the respective national census. Current data pertains to clinically diagnosed symptomatic OA knees (No X-Rays). Crude prevalence (95% confidence intervals) rate is shown.

**Results:** The prevalence was 15.1 (14.5, 15.9) in Tehran and 5.6 (5.1, 6.1) in Pune (OR=3.15, 95% confidence interval 2.83, 3.52,  $p<0.001$ , ANOVA); knee was the commonest affliction amongst OA sites- 93% in Tehran and 87% in Pune (data not shown). The age gender specific prevalence (percent) is shown in the figure 1. The prevalence was exceptionally high in Iran, both men and women, compared to Pune (Men: OR=2.84,  $P$ -value<0.001; Women: OR=2.56,  $P$ -value<0.001). The odds ratio remained more or less unchanged for each of the age group by gender. Presentation will include probable risk factors (culture) and global comparisons.



**Conclusions:** Based on a unique community model, urban surveys in Iran and India showed an enormous burden of OA knee. Women suffered more. The burden was strikingly high and unprecedented in Iran. Further research of life styles and risk factors is required to improve understanding of OA in the community.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.3090

**THU0709 REUMAHEART – A PORTUGUESE POPULATION BASED STUDY ON CARDIOVASCULAR RISK FACTORS**

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**Background:** Individuals diagnosed with rheumatic diseases have shown an increased risk of developing several comorbid conditions, of which cardiovascular (CV) comorbidities are the most common and have the greatest effect on mortality.

**Objectives:** Our global aim is to assess the impact of Inflammatory Rheumatic Diseases (IRD) in the development of cardiovascular diseases controlling for traditional CV risk factors in a Portuguese national-wide population-based cohort.

**Methods:** This study used data from a population-based longitudinal cohort study – the EpiDOC cohort. IRD participants were selected according to Rheumatoid Arthritis (RA), Systemic Lupus Erythematosus (SLE), Ankylosing Spondylitis (SpA) and polymyalgia rheumatic (PMR) diagnosis criteria fulfilment. Outcome was defined as a composite of myocardial infarction or angor pectoris (ischaemic heart disease), arrhythmias, valvular disease, stroke or transient ischaemic attack and peripheral artery disease. Multivariate logistic regression models were used to assess predictors of CV events in IRD participants. Calibration and discrimination of

a predictive model were assessed by goodness-of-fit and area under receiver operating characteristic curve.

**Results:** In a national cohort of 10 661 people, patients with RA (n=61), SLE (n=13), SpA (n=92), PMR (n=8) were identified. Patients with IRD had similar age as non-IRD (mean age 55 vs 53 years-old; 72,1% female), with a predominance of dyslipidaemia diagnosis (40.7% vs 31.4%; p=0,033) and sedentary lifestyle (exercise practise 22.7% vs 33%; p=0,016). IRD participants were followed by a median follow-up of 2.6 years compared with 2.4 years in the non-IRD group (p<0,01). Cardiovascular events were proportional in both populations, leading ischaemic heart disease on IRD group (34.6%) and arrhythmias in controls (29.4%). After adjustment for risk factors, the odd of cardiovascular event is high (OR 1.64, 95% CI: 1.04–2.58; p=0.03). A stepwise approach to find the best predictive model attained that gender, age, history of hypertension, body mass index, IRD and follow-up time are the most important predictive variables of CV event, with an area under ROC of 0,80.

**Conclusions:** We report an increase odd of major CV events in inflammatory rheumatic disease in Portugal adjusting for potential modifiers. This study brings forward a contemporary awareness of physicians and patients with IRD for a premature identification and control of higher risk patients among this population.

**Disclosure of Interest:** None declared

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FRIDAY, 15 JUNE 2018

**Basic science in paediatric rheumatology**

FRI0001

**EXTENDED OLIGOARTICULAR AND POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS PATIENTS HAVE A SIMILAR B CELL PHENOTYPE WHEN COMPARED TO ESTABLISHED RHEUMATOID ARTHRITIS**

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**Background:** Our group has recently described that the majority of polyarticular juvenile idiopathic arthritis (pJIA) and a large fraction of extended oligoarticular JIA (oJIA) patients fulfil classification criteria for rheumatoid arthritis (RA) in adulthood. B cells play several important roles in RA pathogenesis, but it is still unclear if the pattern of B cell involvement in pJIA and extended oJIA follows what has been described for adults with RA.

**Objectives:** The main goal of this study was to characterise peripheral blood B cell phenotype and cellular activation in pJIA and extended oJIA patients when compared to established RA.

**Methods:** Blood samples were collected from JIA patients (n=10; mean age 10±4 years), established RA patients treated with synthetic DMARDs (n=10; mean age 72±7 years) and two corresponding groups of age- and sex-matched healthy donors. B cell phenotype was characterised by flow cytometry and B cell apoptosis was assessed after 48 hour of *in vitro* cell culture.

**Results:** JIA patients recruited in this study were either classified as extended oJIA (n=6) or pJIA (n=4). Seven JIA patients (4 extended oJIA and 3 pJIA) were treated with methotrexate and three patients (2 extended oJIA and 1 pJIA) were untreated. We found that JIA patients had similar CD19 +B cell levels in circulation when compared to controls, but significantly higher CD19 +B cell frequencies in comparison to established RA. In addition, increased frequencies of transitional (IgD +CD38++) and naïve (IgD +CD27+) B cell subpopulations were observed in JIA patients when compared to RA. However, established RA patients had significantly higher levels of CD21<sup>low</sup>CD38<sup>low</sup>, post-switch (IgD-CD27+) and IgD-CD27-memory B cell subsets when compared not only to controls, but also to JIA patients. No significant differences were detected in pre-switch (IgD +CD27+) memory and plasmablasts (IgD-CD38++) levels in JIA patients when compared to both controls and RA. Furthermore, the frequency of CD5 +B cells, CD5 median fluorescence intensity (MFI), CD40 MFI and CXCR5 MFI B cell expression levels were significantly increased in JIA patients when compared to established RA, but not to controls. No significant differences were observed between JIA and established RA patients in BAFF-R, FcγRIIB, CD21, CD23, CD38, CD86, CD95, HLA-DR, TLR9 and RANKL expression on B cells. After 48 hour of *in vitro* cell culture a significantly higher B cell death was found in JIA in comparison to RA patients.

**Conclusions:** The increased frequencies of transitional, naïve and CD5 +B cells in circulation and reduced levels of memory B cell subpopulations in JIA patients when compared to established RA are probably related to an immature immune system present in children when compared to adults. Nevertheless, the similarity in B cell phenotype found between extended oJIA, pJIA and established RA patients suggests an early B cell involvement in the pathogenesis of these two categories of JIA.

**Disclosure of Interest:** None declared

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FRI0002

**ANALYSIS OF B CELLS AND T CELLS SUBPOPULATIONS AND COLLAGEN SPECIFIC T CELL REPERTOIRE IN JUVENILE IDIOPATHIC ARTHRITIS PATIENTS**

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**Background:** The cause of the breach in immune tolerance in the arthritic joint is not fully understood; many associations between subsets of JIA and HLA and non-HLA molecules have been described.<sup>1</sup> An important role is played by T cell population, that is driven also by its specific T cell receptor (TCR) repertoire; it has been previously observed that synovial T cells exhibit oligoclonal TCR repertoires.<sup>2</sup>

**Objectives:** To examine frequency and distribution of human Collagen<sub>261–273</sub>-specific T cells and the phenotypes of B and T cells subpopulations and the role of DR alleles in JIA, in order to find new biomarker for management of JIA.

**Methods:** HLA genotyping and CDR3 TRBV-TRBJ spectratyping (TCR repertoire Immunoscope analysis)<sup>3</sup> were performed on Peripheral blood mononuclear cells (PBMCs) on a total of 40 Juvenile Idiopathic arthritis (JIA) patients (and in 2 cases also in samples of Synovial fluids) and 6 Healthy Controls. The enrolled patients were mainly affected by polyarticular arthritis (26 out 40) and were free of CS (38 out 40) and cDMARDs (24 out 40) treatments. The mean disease duration was 37 months. All the patients were ACPA and RF negative and the mean ESR and PCR values were respectively 39.5±32.4 mm/h and 17.5±37.4 mg/L. B cells and T cells subpopulations were analysed by flow cytometry assays.

**Results:** In our cohort 4 patients were DR4+ (10%) and 8 were DR1+ (20%). In the entire cohort no differences were found in terms of B cells subpopulations, but dividing the cohort on the basis of the age of disease onset it was possible to identify a upregulation of Switched B cells compartment in younger patients more than the JIA with an exordium after 12 years, confirming the data recently published.<sup>4</sup> We checked for the presence of collagen specific TRBV25-TRBJ2.2 T cells, whom the expansion were significantly associated with disease activity and modulated by therapy in RA patients, as described in our previous work.<sup>3</sup> Our preliminary results in a so small cohort of patients indicate that the same expansion in JIA patients seems to associate with JADAS and DR4/DR1 positivity, independently from any conventional and biological treatment. Moreover our T cells subpopulation analysis allowed to find interesting correlation between Tregs and switched memory, Tregs and double negative (IgD<sup>neg</sup>/CD27<sup>neg</sup>) B cells (r=0.476, p=0.04) and Tregs and DR4/1 positivity (0.432 p=0,03) and between CD27<sup>high</sup>/CD38<sup>high</sup> cells and Il17a producing cells (r=0.414, p=0.04); these correlations are more significant in JIA patients with a disease onset at a young age (age <6 years).

**Conclusions:** These preliminary results suggest that the analysis of collagen specific T cells repertoire, T and B cells subpopulations and HLA-DR haplotype can provide useful information to characterise peculiar details of each JIA patient

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**Disclosure of Interest:** None declared

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FRI0003

**EPIGENETIC ALTERATIONS LEADING TO SPECIFIC EXPRESSION PATTERNS OF IMMUNE RESPONSE REGULATING GENE MIGHT BE RESPONSIBLE FOR DISTINCTIVE MICROBIOTA COMPOSITION AND DISEASE DEVELOPMENT IN JUVENILE SPONDYLOARTHRITIS PATIENTS**

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**Background:** Juvenile spondyloarthritis (jSpA) is a diverse group of related syndromes with shared symptoms and pathogenic mechanisms in which both extrinsic environmental factors and intrinsic genetic background perpetuate inflammatory response through immune system alterations. Recently obtained gene signatures in jSpA patients revealed TLR4 and CXCR4 gene had increased, while NLRP3 and PTPN12 had decreased expression.<sup>1</sup> Although gene expression is regulated by various mechanisms, the increasing numbers of studies is showing the importance of epigenetic mechanisms in this fundamental biological process.

**Objectives:** To investigate the possible mechanistic role of DNA promoter region methylation and several non-coding micro RNA (miR-150, miR-146a, miR-181a, miR-223) in jSpA patients regarding the expression of genes with previously observed alterations.

**Methods:** The expression of specific microRNAs was analysed in 8 jSpA patients and 5 matched controls using RT-PCR with predeveloped microRNA assays. Methylated DNA Immunoprecipitation (MeDIP) was performed in 19 patients and 7 controls. Enrichment in MeDIP fraction was determined by qRT-PCR using the AriaMx.

**Results:** The difference in fold enrichment of immunoprecipitated DNA was significant only for NLRP3 promoter site (p=0.0220). Expression analysis of selected



miRNAs showed no significant difference in fold change between jSpA patients and healthy controls.

**Table 1.** Results of DNA promoter methylation and previously performed gene expression analysis in juvenile spondyloarthritis patients<sup>1</sup>

GENES	Fold Enrichment of Immunoprecipitated DNA		Fold Change of Expression <sup>1</sup>		
	Controls (n=19)	p	Fold Change	p	
TLR4	0213	0153	0,5759	+3,91	<0,01
NLRP3	11,24	5412	0,0220	-5,00	<0,01
CXCR4	0303	0170	0,2658	+1,87	<0,01
PTPN12	0338	0202	0,3768	-2,63	<0,01

**Conclusions:** Our study indicated epigenetic modifications are probably responsible for some of the expression alterations in jSpA patients in the initial phase of the disease. Since NLRP3 has a crucial role in inflammasome assembly and inflammasomes have been shown to shape microbiota, it is reasonable to assume dysbiosis in jSpA patients can at least partially be explained by reduced NLRP3 expression due to hypermethylation, stressing for the first time the epigenetic contribution to jSpA pathophysiology. While it is still not clear if these epigenetic alterations are caused by genetic mutations in epigenetic factors or exposure to certain environmental factors that mediate the occurrence of aberrant epigenetic profiles, the discovery of DNA methylation-based signature of the NLRP3 gene could have important implications in addressing extrinsic and intrinsic contribution to jSpA pathophysiology, whereas the possibility of reverting epigenetic modifications opens whole new prospects for therapeutic treatment of this complex disease.

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**Disclosure of Interest:** None declared

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FRI0004

#### GRANULOCYTE MACROPHAGE COLONY STIMULATING FACTOR IS SECRETED AT HIGHER LEVELS FROM STIMULATED MONOCYTE-DERIVED MACROPHAGES FROM PATIENTS WITH ENTHESITIS RELATED ARTHRITIS AND IS SIGNIFICANTLY ENHANCED BY THE UNFOLDED PROTEIN RESPONSE

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**Background:** Enthesitis related arthritis (ERA) is a subtype of juvenile idiopathic arthritis exhibiting many similarities to the adult spondyloarthropathies (SpA). The innate immune system and intracellular stress responses, including the unfolded protein response (UPR), have been implicated in the pathogenesis of SpA. Granulocyte macrophage colony stimulating factor (GMCSF), as well as being a haemopoietic growth factor, plays a central role in regulating innate immunity and has recently been implicated in the pathogenesis of SpA<sup>1</sup> but has not been studied in ERA.

**Objectives:** To compare levels of GMCSF produced by monocyte-derived macrophages (MDMs) from patients with ERA and healthy controls and to observe the effect of inducing the UPR on those levels.

**Methods:** Peripheral blood monocytes were isolated from 39 patients with ERA (68% HLA B27 positive, 84% male, median age 16 years 4 months, median disease duration 3 years 10 months) and 21 age and gender-matched healthy controls and differentiated *in vitro* with macrophage-colony stimulating factor. Cells were treated with interferon gamma for 24 hours to upregulate HLA B, washed and then stimulated with lipopolysaccharide (LPS) alone (50 ng/mL) or LPS and tunicamycin (TM) (5 µg/mL), an inducer of the unfolded protein response. GMCSF was measured from the cell culture supernatants after 24 hours culture by luminex assay.

**Results:** Levels of GMCSF at baseline were similar in patients and healthy controls [median 121.3 pg/mL (IQR 96.6–194.0 pg/mL) vs 157.1 pg/mL (124.2–203.3 pg/mL), p=0.1]. However, with LPS stimulation, MDMs from patients secreted significantly higher levels of GMCSF [median 1853 pg/mL (IQR 1206–3061 pg/mL) vs 1342 pg/mL (IQR 713.3–1797 pg/mL), p=0.0057]. On stimulation with TM in addition to LPS, GMCSF production was further enhanced in both patients and healthy controls [median 9027 pg/mL (IQR 4746–13961 pg/mL) vs

3834 pg/mL (IQR 1603–9158 pg/mL)] and remained significantly higher in patients (p=0.0096). To investigate the effect of the UPR, fold change in GMCSF was calculated for each sample between MDMs stimulated with LPS alone and MDMs stimulated with both LPS and TM. Median fold change in patients was 3.95 (IQR 1.54–5.47) and 2.36 (IQR 0.49–4.69) in healthy controls. Interestingly, MDMs from patients who were HLA B27 positive exhibited significantly higher median fold change in GMCSF with UPR induction compared to HLA B27 negative patients [4.14 (IQR 2.22–6.10) vs 1.33 (IQR 0.36–3.91), p=0.0098]. No associations were seen with different treatment regimes in the patient group.

**Conclusions:** MDMs from patients with ERA produce significantly higher levels of GMCSF after stimulation compared to healthy controls and this is further enhanced by the UPR, especially in HLA B27 positive patients. These results potentially implicate GMCSF in the pathogenesis of ERA and thus further support the concept of GMCSF as a novel target for treatment in certain subgroups of patients.

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**Disclosure of Interest:** None declared

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FRI0005

#### THE RELATIONSHIP BETWEEN JUVENILE SYSTEMIC LUPUS ERYTHEMATOSUS AND THE TRANSCRIPTION FACTORS NF-KAPPAB AND PPAR-GAMMA

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**Background:** Systemic lupus erythematosus (SLE) is an autoimmune disease characterised by high-levels of autoantibodies mainly targeting nuclear antigens and loss of self-tolerance. Peroxisome-proliferator activated receptor gamma (PPAR $\gamma$ ) and nuclear factor-kappa beta (NF- $\kappa$ B) are transcription factors, which, within normal levels, have shown to be crucial in immunomodulation namely, activation and development of normal lymphocytes, negative and positive selection of T and B cells. High-levels of NF- $\kappa$ B has inflammatory properties such as release of autoreactive T cells. On the contrary, PPAR $\gamma$  has anti-inflammatory effects, which has been demonstrated to be effective when used early in prevention of disease in murine models of systemic lupus erythematosus.

**Objectives:** Herein, we investigated whether NF- $\kappa$ B and PPAR $\gamma$  could exert opposite effects in the immune response and the possible implications in immunomodulation of juvenile systemic lupus erythematosus.

**Methods:** Serum NF- $\kappa$ B and PPAR $\gamma$  levels were measured in 42 juvenile systemic lupus erythematosus. In addition, 19 juvenile systemic sclerosis and 25 age-matched healthy children were selected for patient control and healthy control, respectively. We have also assessed the relation of these transcription factors with disease activity and anti-ds DNA.

**Results:** The control group did not differ from the juvenile SLE and juvenile systemic sclerosis patients for age (p>0.05). According to our study, serum NF- $\kappa$ B levels of juvenile SLE and juvenile systemic sclerosis patients were significantly higher (1.87±1.0 and 2.17±1.0 versus 1.25±0.7), while serum PPAR $\gamma$  levels were significantly lower than that of healthy controls (1.58±0.6 and 1.52±0.5 versus 2.03±0.9). The difference was not significant between juvenile systemic lupus erythematosus and juvenile systemic sclerosis. In patients with juvenile systemic sclerosis serum NF- $\kappa$ B levels negatively correlated with serum PPAR $\gamma$  levels (R=-0.49; p=0.032); however, this relationship was not observed in juvenile SLE patients and healthy controls.

**Conclusions:** Increased serum NF- $\kappa$ B levels represent upregulated signalling cascades, so it is associated with increased levels of pro-inflammatory cytokines. Since juvenile systemic sclerosis and juvenile systemic lupus erythematosus are autoimmune diseases, patients had high levels of NF- $\kappa$ B and low levels of PPAR than controls, as expected. Previous studies revealed that PPAR $\gamma$  activation inhibits NF- $\kappa$ B transcriptional activity. Correlation results in juvenile systemic sclerosis cohort are compatible with this finding, however not in juvenile systemic lupus erythematosus patients. This could be due to the limited number of patients. Further studies with large number of patients are needed to better elucidate the implication of these transcription factors in therapeutic pathways.

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**Disclosure of Interest:** None declared

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**FRI0006** **ASSOCIATION BETWEEN INTERLEUKIN-10 POLYMORPHISMS AND JUVENILE IDIOPATHIC ARTHRITIS: A META-ANALYSIS**

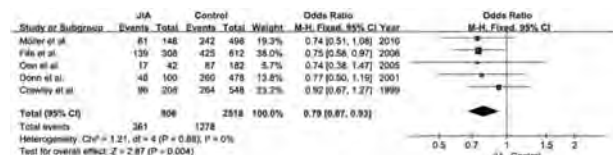
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**Background:** Juvenile idiopathic arthritis (JIA) is the most common chronic arthritis in children. JIA is a heterogeneous group of complex diseases and the result of a combination of genetic and environmental factors. Multiple genes contribute to the risk of developing JIA. Interleukin-10 (IL-10) is an anti-inflammatory cytokine that is associated with inflammatory diseases. IL-10 is considered a candidate gene for JIA based on its chromosomal location and functional relevance.

**Objectives:** IL-10 genetic polymorphisms associated with JIA were previously identified, especially in haplotypes studies. However, results from different studies have been inconsistent. Thus, we investigated whether IL-10 polymorphisms were associated with susceptibility to JIA.

**Methods:** A meta-analysis was conducted of the associations between the IL-10-1082G/A, -819 C/T, and -592 C/A polymorphisms and JIA. A total of eight studies involving 1495 patients and 1670 controls were considered in the meta-analysis. This meta-analysis was conducted based on the Preferred Reporting Items for Systemic Reviews and Meta-Analyses (PRISMA) guidelines.

**Results:** There was no association between the IL-10-1082G/A, -819 C/T, and -592 C/A polymorphisms and JIA in allele contrast and any of the genetic models (allele contrast: OR=0.90, 95% CI=0.79–1.02, p=0.09; OR=0.97, 95% CI=0.83–1.13, p=0.68; OR=0.92, 95% CI=0.81–1.06, p=0.24, respectively). Subgroup analyses revealed a significant association between the IL-10-1082 G allele and systemic JIA (OR=0.80, 95% CI=0.67–0.96, p=0.02). Meta-analysis of the IL-10 haplotype revealed no association between GCC, ACC, and ATA haplotypes and JIA.



**Abstract FRI0006 – Figure 1.** ORs and 95% CIs of the individual studies and pooled data for the associations between the IL-10 -1082 G allele and systemic JIA

**Conclusions:** This meta-analysis indicated lack of associations between IL-10 polymorphisms and susceptibility to JIA. However, there was a significant association between IL-10-1082 G allele and systemic JIA.

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**Disclosure of Interest:** None declared

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FRIDAY, 15 JUNE 2018

**Rheumatoid arthritis – prognosis, predictors and outcome**

**FRI0007** **PERFORMANCE OF MUSCULOSKELETAL ULTRASONOGRAPHY (MSUS) AND OPTIMAL CUTOFF CRITERIA FOR PATIENTS AT RISK FOR RHEUMATOID ARTHRITIS: A META-ANALYSIS**

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**Background:** The identification of patients with rheumatoid arthritis (RA) in the early stages of the disease leads to early treatment and improved outcomes. MSUS is a relatively easy, accessible and low cost method, which has been proven more sensitive in detecting findings suggestive of inflammatory arthritis than clinical or radiographic exams. Evidence shows that MSUS seems to bring additional knowledge when assessing the joints on patients with suspected RA, however, there is still controversy whether it can improve substantial discriminatory value for early arthritis.

**Objectives:** To assess the diagnostic value of MSUS and optimal cutoff criteria for the diagnosis of RA in patients with arthralgia and non-classified arthritis.

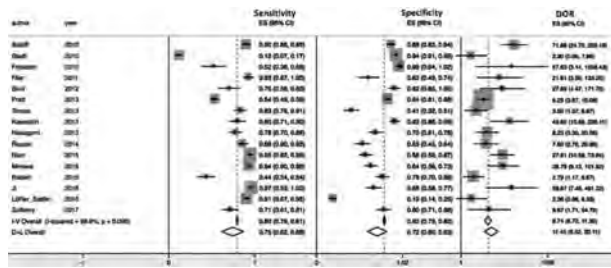
**Methods:** We conducted a meta-analysis for original studies evaluating ultrasound on patients with arthralgias and non-classified arthritis, published in Pubmed, EMBASE and Cochrane databases until December 2017. Statistical analysis included i) the calculation of sensitivity and specificity for ultrasound ii) summary receiver operating characteristic (SROC) curves for a linear regression model iii) I squared test for heterogeneity.

**Results:** Sixteen studies were included in the review. The overall sensitivity and specificity were 0.75 (95% CI 0.62, 0.88) and 0.72 (95% CI 0.60, 0.83) respectively. The overall diagnostic odds ratio (DOR) was 11.45 (95% CI 6.52, 20.11). The relative DOR for studies performed in Asia (10.43, p=0.002), published before 2013 (15.71, p=0.001) and involving MCP (11.27, p=0.003) and MTP (2.78,

**Abstract FRI0007 – Table 1**

	N	Summary Random Effect Model		DOR Random Effect Model			Adjusted RDOR Random Effect Model		
		Sensitivity	Specificity	DOR	IC 95%	p	RDOR	IC 95%	p
<b>Total</b>	16	0.75	0.72	11.5	(6.5–20.1)	<0.001	1.15	(0.9–1.4)	0.117
Year before 2013	5	0.64	0.89	20.6	(4.5–94.4)	0.001	15.7	(4.8–51.8)	0.001
2013 and after	11	0.80	0.65	9.2	(5.2–16.2)	<0.001	1.0		
Countries in Asia	4	0.88	0.74	23.6	(8.8–63.5)	0.098	10.4	(3.2–33.7)	0.002
Countries in Europe	12	0.70	0.71	8.9	(4.7–17.5)	<0.001	1.0		
<b>Joint included</b>									
MCP	12	0.79	0.74	16.0	(8.1–31.9)	<0.001	11.3	(3.0–41.9)	0.003
MTP	4	0.78	0.67	9.6	(5.1–18.2)	<0.001	2.8	(1.2–6.3)	0.021
Wrist	11	0.82	0.73	18.6	(8.4–40.9)	<0.001	1.0		
<b>Cutoff criteria</b>									
GS <sub>≥</sub> 1	6	0.86	0.57	16.5	(9.6–28.3)	0.503	6.0	(1.6–22.5)	0.009
GS <sub>≥</sub> 2	5	0.66	0.69	5.6	(2.9–10.5)	0.025	2.4	(0.7–7.6)	0.139
GS <sub>≥</sub> 3	3	0.74	0.79	12.9	(5.6–29.9)	0.314	3.1	(0.7–14.1)	0.132
PD <sub>≥</sub> 1	9	0.67	0.72	7.9	(4.3–14.9)	0.003	3.9	(1.3–11.7)	0.018
PD <sub>≥</sub> 2	7	0.73	0.77	9.6	(4.1–22.5)	<0.001	3.3	(0.9–11.8)	0.059
PD <sub>≥</sub> 3	6	0.38	0.84	4.5	(5.2–9.4)	<0.001	2.0	(0.29–14.4)	0.462
Tenosynovitis	3	0.27	0.65	0.73	(0.01–82.8)	<0.001	1.0		
Erosions	6	0.40	0.84	3.3	(1.7–6.2)	0.242	1.0		

p=0.021) exhibited higher diagnostic performance. Meta-regression after adjusting for country, year, and type of joint involved, showed that Grey Scale (GS)  $\geq 1$  RDOR 6.0 (95% CI 1.6, 22.5; p=0.009) and Power Doppler (PD)  $\geq 1$  RDOR 3.9 (95% CI 1.3, 11.7, p=0.018) had greater diagnostic accuracy when compared to higher cutoff values.



**Conclusions:** MSUS is a valuable diagnostic tool when used in patients with arthralgia and at risk for RA. GS  $\geq 1$  and PD  $\geq 1$  combined have better discriminative ability for diagnosing RA due that the overall specificity is greater than for either alone.

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**Disclosure of Interest:** None declared

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**FRI0008 TISSUES ARE DIFFERENTLY MODULATED BY TOCILIZUMAB AND METHOTREXATE; ASSESSMENT OF CONNECTIVE TISSUE METABOLITES IN THE AMBITION STUDY**

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**Background:** Response to any treatment in rheumatoid arthritis (RA) is assessed by symptomatic changes, such as swollen joint count. Such assessments does not provide information regarding the effect of the treatment at tissue level. Chronic inflammation has a detrimental effect resulting in elevated levels of tissue remodelling and the release of extracellular matrix (ECM) metabolites into the circulation. The tissues consist mainly of interstitial matrix, basement membrane and cells, which are all affected by auto-immune disorders. Tissue metabolites can be measured in serum as biomarkers of tissue remodelling.

**Objectives:** The purpose was to investigate if tissue remodelling is differently modulated by tocilizumab (TCZ) and methotrexate (MTX).

**Methods:** The AMBITION study, a phase III RCT with tocilizumab vs. Methotrexate in which TCZ monotherapy (8 mg/kg every 4 weeks) was compared to methotrexate monotherapy over 24 weeks in patients with moderate-severe RA (AMBITION, NCT00109408). TCZ is a compound that inhibits the IL-6 receptor. Tissue metabolites were measured in baseline and 8 weeks sera (n=319) by ECM specific ELISAs: Connective tissue remodelling was measured by C3M (type III collagen degradation), basement membrane remodelling by C4M (type IV collagen), inflammation by C-reactive protein (CRP) and its metabolite CRPM. Comparison between groups were done by ANCOVA adjusting for age, gender, BMI and disease duration.

**Results:** Tissue remodelling was increased by 10% in the placebo group and significantly (p<0.001) inhibited by both MTX and TCZ compared to placebo. Inhibition with TCZ was 14% greater than that of MTX (p=0.0005). Basement membrane remodelling was likewise inhibited by both MTX and TCZ; the effect of TCZ was 20% greater than MTX (p<0.0001). MTX had limited effect on CRP and its metabolite CRPM compared to placebo or baseline. TCZ reduced the level to 27% and 73% of baseline, respectively. Although the effect of TCZ was much greater when assessing CRP, this was the least significant response marker, due to the huge placebo modulation, as well as the general high variation in response. Only changes in CRP was correlated to 8 week changes in DAS (rho=0.27, p=0.001) in the TCZ group. In the MTX group all changes in markers were correlated to change in DAS (rho=0.28 to 0.41, p<0.001). Only changes in C4M and CRP in the TCZ treatment arms were significantly correlated with DAS changes (rho=0.31, p<0.05).

**Abstract FRI0008 – Table 1**

Table	Mean change baseline (%)	8-week from	Lower 95%-CI	Upper 95%-CI	8 week change difference	P value
<b>Connective tissue metabolite (C3M)</b>						
PLACEBO	111		101	120	TCZ vs PLACEBO	<0.0001
MTX	88		83	94	MTX vs PLACEBO	0.0001
TCZ	74		69	79	TCZ vs MTX	0.0005
<b>Basement membrane remodeling metabolite (C4M)</b>						
PLACEBO	107		98	116	TCZ vs PLACEBO	<0.0001
MTX	87		82	93	MTX vs PLACEBO	0.0007
TCZ	67		62	72	TCZ vs MTX	<0.0001
<b>C-reactive protein metabolite (CRPM)</b>						
PLACEBO	112		91	133	TCZ vs PLACEBO	0.005
MTX	99		87	111	MTX vs PLACEBO	ns
TCZ	73		61	85	TCZ vs MTX	0.0091
<b>C-reactive protein (CRP)</b>						
PLACEBO	450		214	686	TCZ vs PLACEBO	0.007
MTX	102		-36	240	MTX vs PLACEBO	0.034
TCZ	27		-110	164	TCZ vs MTX	ns

**Conclusions:** Chronic inflammation results in an increased amount of tissue remodelling. There was a significant difference in the magnitude of effect MTX and TCZ on tissue remodelling. In addition there was a disconnect between tissue remodelling and change in disease activity, which was treatment dependent.

**Disclosure of Interest:** A. Bay-Jensen Shareholder of: Nordic Bioscience, Employee of: Nordic Bioscience, A. S. Siebuhr Employee of: Nordic Bioscience, C. Thudium Employee of: Nordic Bioscience, M. Karsdal Shareholder of: Nordic Bioscience, Employee of: Nordic Bioscience

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**FRI0009 A COMPARISON OF THE JOINT SYNOVITIS AND TENOSYNOVITIS USING ULTRASONOGRAPHY AND HISTOPATHOLOGICAL FINDINGS IN PATIENTS WITH RHEUMATOID ARTHRITIS**

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**Background:** In the treatment of rheumatoid arthritis (RA), the early diagnosis and early medical treatment via tight control have become increasingly important with the advent of biological therapy. In addition, the existence of inflammation without bone destruction on magnetic resonance imaging has been found to be significantly associated with symptoms in the patient standpoint type inspection of early RA patients.

**Objectives:** This study was conducted to clarify the differences between the joint synovium and tendon sheath synovium, local disease activity using ultrasonography (US) and the findings on a synovial histopathological evaluation.

**Methods:** Between March 2011 and November 2017, 663 synovectomies were surgically treated, and synovial biopsies were performed at the time of surgery. Among them, 75 tendon sheath synovia and 588 joint synovia were investigated. A total of 81 men and 582 women were examined, with an average age of 64 years old. We examined the finger in 312 cases (39 tendons, 273 joints), wrist in 323 cases (33 tendons, 290 joints) and ankle in 28 cases (3 tendons, 25 joints). There were no cases with both tendon sheath synovium and joint synovium. Just before surgery, the US probe was placed on the dorsal and palmar/plantar aspect of the joint or the tendon sheath to evaluate the activity of local synovitis. The maximum grade of power Doppler (PD) signal was determined, ranging from 0 to 3. The serum C reactive protein (CRP), matrix metalloproteinase-3 (MMP-3) and DAS28 values were also examined just before surgery. A histopathological examination of the gathered synovium at the surgical site was performed using the Rooney score (RS).

**Results:** For the tendon sheath synovium, PD0, 14 cases; PD1, 32 cases; PD2, 19 cases and PD3, 10 cases were observed, with an average score of 1.33. For the joint synovium, PD0, 114 cases; PD1, 179 cases; PD2, 209 cases and PD3, 86 cases were observed, with an average score of 1.45. Regarding the DAS28, for the tendon sheath synovium, the average score was 3.59, and for the joint synovium, the average score was 3.61. Regarding the CRP, for the tendon sheath synovium, the average score was 0.64, and for the joint synovium, the average score was 0.66. Regarding the MMP-3, for the tendon sheath synovium, the average score was 113, and for the joint synovium, the average score was 123. There were no marked differences in the grade of PD, DAS28, CRP or MMP-3 between the synovia. The rate of synoviocytes hyperplasia did not differ between the synovia, but the rates of fibrosis and proliferating blood vessels were significantly high in the tendon sheath synovium, perivascular infiltrates of lymphocytes, focal aggregates of lymphocytes, diffuse infiltrates of lymphocytes was significantly high in joint synovium.



**Conclusions:** There was no marked difference in the US findings and the disease activity between the tendon sheath synovium and the joint synovium. However, there were differences in the local disease activities between the synovia. These results show that the tendon sheath synovium lacked acute inflammation.

**Disclosure of Interest:** None declared

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#### FRI0010 PREDICTION OF RADIOGRAPHIC PROGRESSION IN PATIENTS WITH RHEUMATOID ARTHRITIS BY BOTH MAGNETIC RESONANCE IMAGING AND ULTRASOUND

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**Background:** Magnetic resonance imaging (MRI) and ultrasound (US) are both useful modality to monitor disease status of RA whereas combination analysis of disease course by both modalities are quite few.

**Objectives:** To clarify the predictors of radiographic progression in patients with RA examined by both MRI and US.

**Methods:** Thirty-three patients with active RA, managed with a treat-to-target strategy and checked disease activity score every three months along with examination of both MRI and US, were enrolled from June 2010 to June 2016 and observed for 12 months. US of wrist and finger joints was examined every three months, MRI and radiograph were done every six months. US were evaluated by synovitis score of semi-quantitative manner by gray-scale (GS) and power Doppler (PD) proposed from EULAR. In MRI, synovitis, bone oedema and bone erosion were assessed by the Rheumatoid Arthritis Magnetic Resonance Imaging Scoring system (RAMRIS). Radiographic bone erosion and joint space narrowing (JSN) were scored by Genant-modified Sharp Score (GSS). Radiographic progression was defined as delta radiographic score >0.5. Multivariate analysis was employed to clarify independent predictors for radiographic progression at 12 month.

**Results:** Thirteen patients were treated with methotrexate monotherapy and eighteen were received combination of methotrexate and biologics. Three were given biologic monotherapy. Median of age was 57.0 years and that of disease duration was 9 months. Female was 84.8%, positive rate of RF was 87.1% and that of ACPA was 79.3%. DAS28-CRP was 4.20, total GS score 6.0, total PD score 4.0, MRI synovitis score 6.0, MRI bone oedema score 3.0, MRI bone erosion score 3.0, and GSS score 1.0 at baseline. Radiographic progression was found in 12 patients. Multivariate analysis revealed that high MRI bone oedema score at baseline, high MRI bone oedema score and PD ≥ grade 2 articular synovitis at any joints at 6 month were associated with radiographic progression at 12 months. Clinical indices of DAS28-CRP at any point did not predict radiographic progression compared with MRI or US.

	odds ratio	95% CI	p-value
MRI bone edema score at 0m	1.52	1.06-2.17	0.02
CRP at 0m	4.75	0.29-77.74	0.28
GSS JSN at 0m	1.05	0.80-1.38	0.72

MRI bone edema score at 6m	1.37	1.04-1.81	0.03
CRP at 6m	7.00	0.96-51.15	0.06

PD ≥ grade 2 at 6m	13.84	1.84-104.03	0.01
CRP at 6m	8.24	0.59-115.45	0.12

**Conclusions:** During treat-to-target strategy, the presence of MRI bone oedema as well as PD ≥ grade 2 articular synovitis are found to be important to predict radiographic outcome in active RA patients. These imaging indices may be more sensitive to monitor radiographic progression as compared with clinical indices.

**Disclosure of Interest:** None declared

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#### FRI0011 ULTRASONOGRAPHIC CRITERIA FOR THE DIAGNOSIS OF EROSIIVE RHEUMATOID ARTHRITIS DISEASE USING OSTEOARTHRITIC PATIENTS AS CONTROLS COMPARED TO VALIDATED RADIOGRAPHIC CRITERIA

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**Background:** Rheumatoid arthritis (RA) is the most prevalent chronic inflammatory joint disease<sup>1,2</sup> responsible for structural damage. Radiography (RX) is considered as the gold standard for visualising and quantifying bone lesions in RA.<sup>3</sup> Musculoskeletal ultrasound (US) is booming in clinical practice for the diagnosis of RA. US can detect more erosions than RX at the joint level, especially at an early stage of the disease.<sup>4</sup>

**Objectives:** To determine thresholds for the diagnosis of erosive RA by US in RA and osteoarthritic (OA) patients and to compare these US thresholds with RX ACR/EULAR 2013 criteria for erosive RA.

**Methods:** Patients fulfilling ACR 1987 and/or ACR/EULAR 2010 criteria for RA or hand OA criteria were prospectively included. A modified Sharp erosion score was assessed by two blinded readers and one adjudicator for discordant cases (number of eroded joints ≤ three). Erosions in US were scored on six bilateral joints (MCP2-3, 5; MTP2-3, 5) with a four-grade scale to calculate total US score for erosions (USSE).

**Results:** A total of 168 patients were included: 122 RA (32 early RA <2 years; 90 late RA ≥2 years); 46 OA patients. On RX: 42 RA patients (6 early; 36 late) and 5 OA patients were eroded according to ACR/EULAR 2013 criteria with sensitivity at 34.4% and specificity at 89.1%. On US, 95 RA patients (21 early; 78 late) and 12 OA patients were eroded. Considering at least two joint facets eroded or at least one joint facet eroded at grade 2 on US, sensitivities were good (68%–72.1%) and specificities excellent (89.1%–100%). Agreement between RX and US was excellent (90%–92%). US diagnosed two times more patients than RX as erosive disease in both early and late RA patients.

**Conclusions:** USSE can differentiate RA from OA in erosive disease and detect two times more patients with erosive RA than RX with excellent specificity and agreement, according to two different criteria (number of facets eroded and severity of erosion at the joint facet level).

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#### FRI0012 SHARING THE BURDEN OF RHEUMATOID ARTHRITIS THROUGH REMOTE MONITORING OF RHEUMATOID ARTHRITIS (REMORA): IMPLICATIONS FOR PATIENTS AND CLINICIANS

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**Background:** People living with rheumatoid arthritis (RA) experience continuous, daily symptoms that fluctuate over time. Clinical decisions made by healthcare

professionals at intermittent consultations rely upon history taking, which is subject to pitfalls including recall bias, variable help-seeking behaviours and difficulty in summarising fluctuating symptoms.

**Objectives:** REMote MONitoring in Rheumatoid Arthritis (REMORA) was a pilot study to design, implement and evaluate a system of remote data collection for RA patients, for health and research purposes. A unique feature was its aim to integrate patient-generated data from a smartphone app into the electronic health record (EHR).

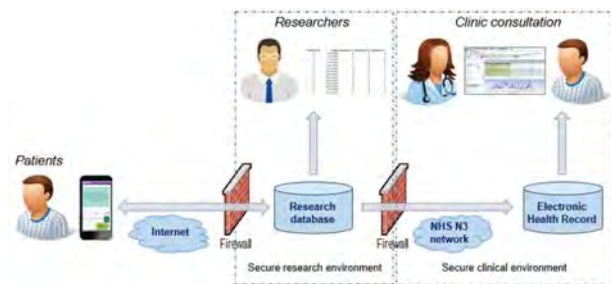
**Methods:** Semi-structured interviews with key stakeholders informed project design and evaluation, comprising three stages: 1) co-design of smartphone app prototype and integration into the electronic patient record (EHR); 2) end-to-end prototype testing (1 month); 3) evaluation of feasibility and acceptability (3 months).

Qualitative data from audio-recorded interviews and 'routine' consultations, following app use, were coded using *a priori* and emergent themes, and triangulated.

**Results:** Daily, weekly and monthly question sets were developed. Patients tracked daily symptoms for one month (n=8) and three months (n=20). Patients submitted daily scores on most days (median 91% of days; IQR 78%-95%) with 4/20 patients submitting on <60% days. Further detail on feasibility has been reported elsewhere.<sup>1</sup> REMORA data were successfully integrated into the EHR (figure 1).

Data from interviews with 16 patients, 2 clinician-researchers (WD and CAS) and 17 clinical consultations were analysed. Patients and clinicians found remote monitoring acceptable and easy to use.

Three themes emerged with REMORA data providing the 'bigger picture' by highlighting episodes that might otherwise have been missed, for example short-lived flares and gradual changes in disease; **empowering patients** through increased self-awareness and improved understanding of RA; and **changing the nature of consultations** with graphs integrated into the EHR facilitating shared conversations and leading to more personalised care.



**Conclusions:** This study demonstrates the acceptability and feasibility of the REMORA system. Novel integration of patient-generated data into the EHR positively impacted consultations and was felt to empower patients. The system generated a unique, temporally-rich research dataset. The next challenge is to scale-up and spread the adoption of this innovation across a range of clinical contexts.

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FRI0013

**CONVERTING PATIENT-REPORTED PHYSICAL FUNCTION OUTCOMES SCORES TO PROMIS METRIC SCORES IN PHASE 3 TRIALS OF BARICITINIB IN RHEUMATOID ARTHRITIS**

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**Background:** In patients (pts) with RA, physical function (PF) can be measured with the Health Assessment Questionnaire-Disability Index (HAQ-DI). Patient-Reported Outcomes Measurement Information System (PROMIS) was developed by the National Institutes of Health using a population-calibrated T-score metric (Mean 50, SD 10). Crosswalk tables that link legacy instruments to PROMIS instruments, including PF, have been developed. Comparisons to the general population can also be made from PROMIS scores.<sup>1-2</sup>

**Objectives:** To convert HAQ-DI scores to PROMIS PF scores to determine how the PROMIS metric performs in 2 phase 3 baricitinib (bari) clinical trials in pts with RA.

**Methods:** In RA-BEAM, pts with inadequate response (IR) to methotrexate were randomised 3:3:2 to placebo (PBO) once daily (QD), bari 4 mg QD, or adalimumab (ADA) 40 mg biweekly.<sup>3</sup> In RA-BEACON, pts with IR to bDMARDs were randomised 1:1:1 to receive PBO or bari 2 mg or 4 mg QD.<sup>4</sup> In both studies, PF was assessed using HAQ-DI. Patient-level HAQ-DI scores were converted to PROMIS PF scores using a validated crosswalk table.<sup>1</sup> Analysis of covariance was conducted on the PROMIS PF score conversions to compare bari to all treatment arms in both studies. Missing data were imputed using modified last observation carried forward.

**Results:** Pts had considerable PF impairment at baseline; mean scores exceeded 2 SD (20 points on the T-score metric) from population means (table 1). Treatment with bari was associated with clinically relevant improvements approaching or exceeding 0.5 SD (5 points on the T-score metric) by week 24 (minimally important difference for PROMIS PF: 0.2 SD or 2 points<sup>5</sup>) vs PBO in HAQ-DI converted to PROMIS PF scores (table 1). Using the converted PROMIS scores, bari remained associated with significant improvements in PF vs PBO through 24 weeks in both studies and vs ADA through 52 weeks in RA-BEAM (figure 1).

**Abstract FRI0013 – Table 1.** PROMIS Physical Function scores<sup>a</sup> converted from HAQ-DI in RA-BEAM and RA-BEACON

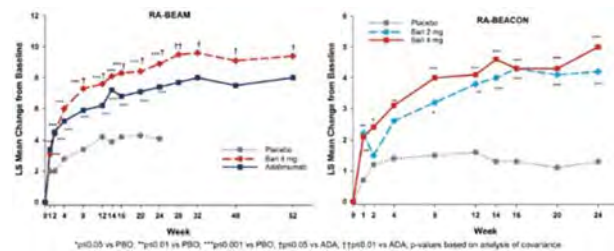
	RA-BEAM			RA-BEACON <sup>b</sup>		
	PBO (n=488)	Bari-4 mg (n=487)	ADA (n=330)	PBO (n=176)	Bari-2 mg (n=174)	Bari-4 mg (n=177)
Baseline	31.9 (6.8)	31.9 (6.6)	31.7 (7.5)	30.0 (5.3)	30.7 (5.7)	30.3 (6.1)
Week 1	33.8 (7.0)	35.0 (7.5)	35.0 (8.0)	30.7 (5.6)	32.8 (6.3)	32.4 (7.6)
Week 4	34.5 (7.7)	37.6 (8.8)	36.7 (8.3)	31.6 (6.2)	33.5 (6.9)	33.7 (8.8)
Week 12	35.9 (8.6)	39.4 (9.5)	37.8 (9.0)	32.1 (6.8)	34.9 (8.5)	35.1 (8.5)
Week 24	36.0 (8.7)	40.8 (10.3)	39.1 (9.7)	31.6 (6.4)	35.2 (9.0)	35.7 (10.2)
Week 52		41.2 (10.2)	39.6 (10.1)			

Data are mean (SD)

<sup>a</sup>Higher PROMIS Physical Function score means better physical function.

<sup>b</sup>RA-BEACON was a 24 week study

ADA=adalimumab; bari=baricitinib; PBO=placebo



**Abstract FRI0013 – Figure 1.** Change from baseline for PROMS Physical Function converted from HAQ-DI in RA-BEAM and RA-BEACON

**Conclusions:** While RA-BEAM and RA-BEACON did not use the PROMIS instrument directly, these results indicate PROMIS PF has the potential to show responsiveness and differentiate between active treatments in clinical trials.

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C. Gaich Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, A. DeLozier Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, A. Quebe Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, L. Sun Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, S. Otawa Employee of: Eli Lilly and Company, J. Pope Grant/research support from: Amgen, Bayer, BMS, GSK, Merck, Novartis, Pfizer, Roche, UCB, Consultant for: AbbVie, Amgen, Bayer, BMS, Celtrion, Lilly, Merck, Novartis, Pfizer, Roche, UCB

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FRI0014

#### LOW-DOSE ASPIRIN MAY HAVE A ROLE AS PRIMARY PROPHYLAXIS OF CARDIOVASCULAR EVENTS IN RHEUMATOID ARTHRITIS: EVIDENCE FROM AN ITALIAN MULTICENTRIC RETROSPECTIVE STUDY

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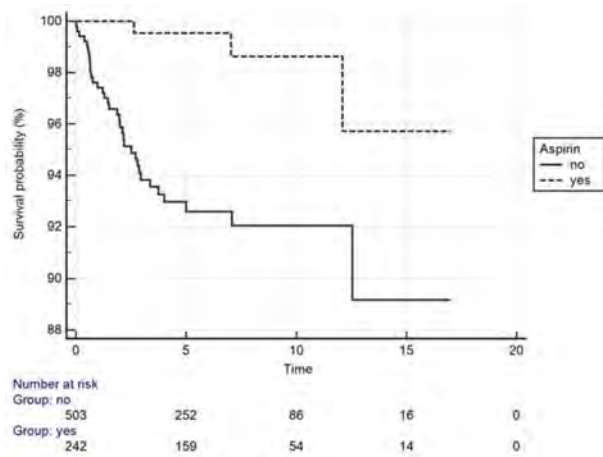
**Background:** Cardiovascular (CV) morbidity and mortality are significantly greater in Rheumatoid Arthritis (RA) patients than in the general population. Acetylsalicylic acid (ASA) is known to be associated with a significant decrease in the incidence of CV events in patients at high CV risk, as we have recently demonstrated in patients with Systemic Lupus Erythematosus, but its effectiveness as primary prophylaxis in RA patients has not yet been addressed.

**Objectives:** To investigate the role of ASA in reducing the incidence of CV events in an Italian multicentre RA cohort from the GIRRCS (*Gruppo Italiano di Ricerca in Reumatologia Clinica e Sperimentale*).

**Methods:** The clinical charts of RA patients consecutively admitted to 4 GIRRCS centres for their 1<sup>st</sup> visit from November 1<sup>st</sup> 2000 to December 31<sup>st</sup> 2015, who, at admission, satisfied 2010 ACR/EULAR criteria for RA and had not experienced any CV event, were analysed. The incidence of CV events during follow-up was recorded at December 2016. Kaplan Meier curve and log-rank test were used to investigate differences in event-free survival. Cox regression analysis served to identify factors associated with CV event occurrence.

**Results:** Seven hundred and forty-six consecutive RA patients were enrolled and followed up for a median of 5.6 years (range 2.9–8.9 years). The incidence rate (IR) of CV events was 7.8/1000 person-years (pys) in the overall cohort. Patients were subdivided into two groups, namely ASA- (242 patients) and non-ASA-treated (504 patients). The IR of CV events was significantly lower in the ASA-treated with respect to the non-ASA-treated group (IR 1.7 vs 11.5/1000 pys;  $p=0.0002$ ). Furthermore, the CV event-free rate was longer in ASA-treated than in non-ASA-treated patients (log-rank test 12.3;  $p=0.0004$ ). Figure 1.

At multivariate analysis hypertension and metabolic syndrome (HR 5.6, 95% CI:1.2–26.3;  $p=0.03$  and HR 3.7, 95% CI:1.3–9.8;  $p=0.009$ ) resulted to be the only positive predictors; ASA treatment (HR 0.04, 95% CI:0.06–0.33;  $p=0.02$ ) the only negative one.



**Conclusions:** The incidence rate of CV events in our Italian multicentric cohort was lower than that reported in other European and non-European cohorts. Low-dose ASA may have a role in the primary prophylaxis of CV events in RA patients.

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**Disclosure of Interest:** None declared

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FRI0015

#### TREATING RHEUMATOID ARTHRITIS TO TARGET: IS LOW DISEASE ACTIVITY GOOD ENOUGH?

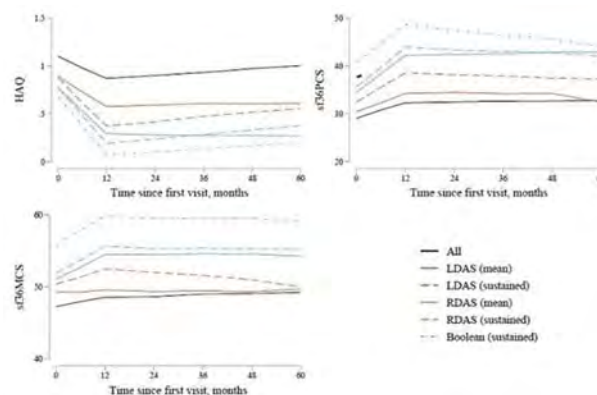
E. Nikiphorou<sup>1</sup>, S. Norton<sup>1</sup>, A. Young<sup>2</sup>, L. Carpenter<sup>1</sup>, J. Dixey<sup>3</sup>, D. Walsh<sup>4</sup>, P. Kiely<sup>5</sup>, on behalf of ERAS-ERAN working group. <sup>1</sup>Academic Rheumatology, King's College London, London; <sup>2</sup>Life Sciences, University of Hertfordshire, Hertfordshire; <sup>3</sup>Rheumatology, The Royal Wolverhampton, Wolverhampton; <sup>4</sup>Rheumatology, The University of Nottingham, Nottingham; <sup>5</sup>Rheumatology, St George's Hospital, London, UK

**Background:** Treat-to-target (T2T) principles in rheumatoid arthritis (RA) are now widely recognised as effective in achieving optimal disease outcomes.

**Objectives:** To examine for differences in outcomes between low (LDAS) and remission (RDAS) disease activity score (DAS) categories, addressing the question: is LDAS a 'good enough' treatment target in RA?

**Methods:** Data from two consecutive UK multi-centre RA inception cohorts with similar design were used: the Early RA Study (ERAS) and Early RA Network (ERAN). Recruitment figures/median follow up for ERAS and ERAN were 1465/10 years (maximum 25 years), and 1236/6 years (maximum 10 years) respectively. Standard demographic and clinical variables were recorded at baseline and then annually until the end of study follow up. Disease activity was categorised by mean DAS28 score between years 1–5 as remission [mRDAS <2.6] or low [mLDAS 2.6–3.2]; as sustained low/remission DAS (sLDAS/sRDAS) based on DAS persisting in each of the two categories at years 1–2 and as Boolean remission (years 1–2). Change in HAQ and SF36 (physical [PCS] and mental [MCS] components) for each disease activity category were modelled using linear mixed models with time incorporated as a linear spline with change-point at 12 months. Year of onset, age, gender and use of steroids or conventional DMARDs at first visit were included as covariates.

**Results:** Out of 2701 patients, 468 (17%) were in mRDAS, 284 (11%) in mLDAS in the first five years of disease. Lower proportions had achieved sRDAS (8%), sLDAS (6%) and Boolean (2%) remission. Mean age was similar across categories; more women were in low vs remission DAS. Compared to mLDAS or sLDAS, inflammatory markers, DAS, functional (HAQ, PCS) and mental (MCS) scores tended to be better in the mRDAS, sRDAS or Boolean remission categories (figure 1). Significant differences ( $p<0.05$ ) were noted between the mRDAS and mLDAS between years 1–5 for all outcomes; for sRDAS compared to sLDAS, the difference was significant at one year but not by five years.



**Conclusions:** The results demonstrate striking differences between remission and low DAS categories, suggesting worse functional and SF36 outcomes over



time in the low DAS categories. This supports that remission should be the primary T2T goal in RA.

**Disclosure of Interest:** None declared

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#### FRI0016 NO RELATIONSHIPS BETWEEN ACPA AND PERIODONTITIS IN EARLY RHEUMATOID ARTHRITIS

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**Background:** Proteins citrullination contributes to generate anticitrullinated peptide antibodies (ACPA) in rheumatoid arthritis (RA). Porphyromonas gingivalis (Pg) is one of main germs incriminated in the development of periodontitis (PD), it has an enzyme called peptidyl arginine deiminase which is able to citrullinate the host proteins

**Objectives:** The aim of this study was to seek for a possible association between ACPA and periodontitis

**Methods:** We conducted a case-control study of 69 patients with early rheumatoid arthritis ( $\leq 2$  years), naive of biotherapy and 138 age- and sex matched healthy controls. Smokers, diabetics, and subjects who received dental care and those who used antibiotics in the previous 6 months were not included. Demographic data and ACPA were determined. A periodontal examination was performed to all participants. Subgingival plaque samples were analysed to seek for Porphyromonas gingivalis (Pg) in both population in the case of periodontitis.

**Results:** The mean age of our patients was  $40.75 \pm 12.04$ , the mean duration of the illness was  $14.30 \pm 6.76$  months (extremes: 1–24 months). ACPA was detected in 88% of patients and the mean titre was  $255.57 \pm 409.78$ . PD frequency was higher in patient with PR compared with healthy controls (43% versus 29%) and a significant association was found between PR and PD ( $p < 10^{-3}$ ). Patients with RA had 2.46 (CI 1.12 to 5.39) higher odds of having PD compared with healthy controls. In early RA, ACPA titre and rate was not associated with PD ( $p = 0.06, p = 0.44$  respectively). Regarding the frequency of Porphyromonas gingivalis, there was no significant difference between the PR group and the control group ( $p = 0.45$ ). In addition, there was no significant difference between RA group and controls ( $p = 0.68$ ) concerning Porphyromonas gingivalis and ACPA

**Conclusions:** Periodontitis is a risk factor for the occurrence of rheumatoid arthritis. The ACPA does not seem to be related to periodontitis. In addition there was no association between ACPA and the presence of porphyromonas gingivalis.

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#### FRI0017 AN EXPLORATORY STUDY ON THE ROLE OF VITAMIN D SUPPLEMENTATION IN IMPROVING PAIN AND DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS

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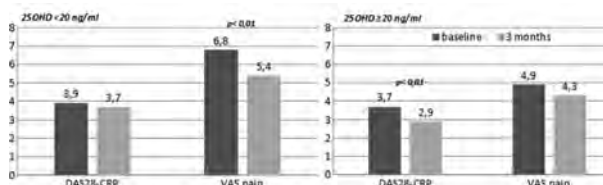
**Background:** Lower serum vitamin D levels have been associated with various autoimmune disorders. Especially in patients affected by Rheumatoid Arthritis

(RA), has been observed an inverse correlation between serum levels of 25-hydroxyvitamin D (25OHD), pain and disease activity, but the cause-effect relationship is not clear.

**Objectives:** The aim of this exploratory study is to investigate the effects of supplementation with cholecalciferol (vitD3) in improving pain and disease activity in RA patients with or without vitamin D deficiency ( $25\text{OHD} < 20$  ng/ml).

**Methods:** In this prospective open-label intervention study, patients fulfilling the EULAR/ACR 2010 criteria for diagnosis of RA, in non-remission ( $\text{DAS28-CRP} > 2.6$ ), on stable disease-modifying antirheumatic drugs, and whose treatment was not expected to be changed over a 3 month period following inclusion, were recruited. DAS28-CRP, VAS pain and serum levels of 25OHD, were evaluated at the baseline and after 3 months of supplementation with oral 100,000 IU/monthly of vitD3.

**Results:** A sample composed by 61 patients (47 females), with an average age (SD) of 58.12 years within 26–86 years range were included. At baseline the mean (SD) 25OHD levels were 22.10 ng/mL. 57% of the patients were found to have vitamin D deficiency ( $< 20$  ng/mL). Mean serum 25OHD levels improved from  $13 \pm 5$  to  $32 \pm 12$  and from  $29 \pm 7$  to  $41 \pm 10$  ng/mL in patients with or without vitamin D deficiency, respectively. At baseline, mean VAS pain was significantly higher in patients with vitamin D deficiency. In the figure are shown DAS28-CRP and VAS pain at baseline and after 3 months of vitD3 supplementation both in patients with or without vitamin D deficiency. After large doses of VitD3, VAS pain significantly decreased in patients with vitamin D deficiency, while DAS28-CRP significantly improved only in patients without vitamin D deficiency at baseline.



**Conclusions:** VitD3 supplementation appears to be associated with significant and different effects on pain and disease activity in RA patients dependent on 25OHD serum levels. Vitamin D deficiency ( $< 20$  ng/mL) seems to be mainly correlated with pain, while higher levels of 25OHD might have immunomodulatory effects. A randomised, double-blind, low versus high vitD3 dose, placebo-controlled trial is recommended.

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#### FRI0018 THE ABILITY OF DISEASE ACTIVITY MEASURES TO PREDICT MAJOR THERAPEUTIC CHANGE IN US VETERANS WITH RHEUMATOID ARTHRITIS

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**Background:** Current rheumatoid arthritis (RA) treatment guidelines recommend the use of disease activity measures (DAMs) to guide RA therapy. These guidelines recommend considering escalation of therapy in RA patients with high or moderate disease activity. Recent work by our group has demonstrated that many RA patients with high/moderate RA by Disease Activity Score with 28 joints (DAS28) did not have therapy escalated despite active disease ( $\text{DAS28} \geq 3.2$ ).

**Objectives:** 1) To determine if the rate of major therapeutic change (MTC) for RA patients with high/moderate disease activity based on DAS28 was similar when measured using two other common DAMs; 2) to compare the ability of different DAMs to predict MTC across the full spectrum of RA disease activity.

**Methods:** US Veterans enrolled in the VA Rheumatoid Arthritis (VARA) registry with 1) a complete set of DAMs (DAS28, Clinical Disease Activity Index [CDAI], Routine Assessment of Patient Index Data 3 [RAPID3]) recorded (index date), 2) two other visits during the preceding 18 months separated by at least 60 days, and 3) clinical data available for 18 months prior to through 30 days following index date were eligible. Each patient was assessed for MTC within 1 week before and 30 days after index date. MTC was defined as any of the following: 1) initiation of new biologic or nonbiologic DMARD, 2) escalation of DMARD dose by  $\geq 25\%$ , 3) initiation of prednisone (as new agent or after 90 day gap during baseline), or 4) increase in monthly average prednisone dose by 25% and/or 5) injection of 2 or more joints with corticosteroids. MTC was analysed by DAM severity thresholds of 1) high, moderate, low, and remission, and 2) high, high/moderate, and high/moderate/low levels. Analyses of the latter thresholds included sensitivity, specificity, predictive values, and accuracy estimations for MTC at each DAM level.

**Results:** Of 1776 eligible patients, 89% were male, mean age was 63.4 years, mean disease duration was 13.4 years, 79% tested positive for rheumatoid factor,

and 63% positive for anti-cyclic citrullinated peptide antibodies. Overall, 33.1% (591/1776) of patients had an MTC. A markedly larger percentage of patients with high disease activity had MTC (range 55.1%–43.5%) compared to patients with moderate disease (range 38.7%–27.8%) (table 1). Sensitivity, specificity, predictive values, and accuracy at each DAM threshold level varied markedly by DAM, with RAPID3 having a higher sensitivity, lower specificity, and less accuracy than DAS28 or CDAI (table 2).

**Abstract FRI0018 – Table 1.** Rates of MTC Stratified by DAM

	Patients with MTC, n/N (%)		
	DAS28	CDAI	RAPID3
High	165/313 (52.7%)	231/419 (55.1%)	346/795 (43.5%)
Moderate	285/737 (38.7%)	219/601 (36.4%)	155/568 (27.8%)
Low	72/283 (25.4%)	105/547 (19.2%)	47/217 (21.7%)
Remission	69/443 (15.6%)	36/209 (17.2%)	43/206 (20.9%)

n, number of patients with MTC; N, number of patients with level of disease severity

**Abstract FRI0018 – Table 2.** Performance of DAMs for Prediction of MTC

		Positive Threshold		
		High	High/Moderate	High/Moderate/Low
Sensitivity	DAS28	27.9%	76.1%	88.3%
	CDAI	39.1%	76.1%	94.9%
	RAPID3	58.5%	84.8%	92.7%
Specificity	DAS28	87.5%	49.4%	31.6%
	CDAI	84.1%	51.9%	14.6%
	RAPID3	62.1%	28.1%	13.8%
Positive Predictive Value	DAS28	52.7%	42.9%	39.2%
	CDAI	55.1%	44.1%	35.4%
	RAPID3	43.5%	37.0%	34.9%
Negative Predictive Value	DAS28	70.9%	80.6%	84.4%
	CDAI	73.5%	81.3%	82.8%
	RAPID3	75.0%	78.7%	79.1%
Accuracy	DAS28	67.7%	58.3%	50.5%
	CDAI	69.1%	60.0%	41.0%
	RAPID3	60.9%	47.0%	40.0%

**Conclusions:** Most patients with high/moderate disease activity did not have a MTC. This observation was consistent regardless of which DAM was utilised. MTC increased with disease activity with all DAMs; however, DAS28 and CDAI appeared to have greater accuracy than RAPID3 at predicting MTC at all disease severity thresholds. There is need for continued evaluation of DAM thresholds for defining disease activity for MTC decisions, better DAMs, and/or better application of DAMs in clinical practice to improve the treatment of patients with active RA.

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**FRI0019** **ARE DISEASE ACTIVITY, DISABILITY OR PSYCHOLOGICAL FACTORS MOST ASSOCIATED WITH PATIENTS WITH RHEUMATOID ARTHRITIS BEING SATISFIED WITH THEIR CONDITION AFTER 12 MONTHS FOLLOWING TREATMENT ONSET?**

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**Background:** An important treatment goal in the management of patients with rheumatoid arthritis (RA) is patients being satisfied with their condition, the patient acceptable symptom state (PASS). It is unclear whether reduction in disease activity, the main therapeutic aim of RA treatment, is associated with reaching PASS, or whether reductions in other factors are also important.

**Objectives:** To analyse change over one year of disease activity, patient reported outcomes (PROs) and psychological factors and their association with PASS at one year.

**Methods:** The Rheumatoid Arthritis Medication Study (RAMS) is a prospective cohort of patients with RA starting MTX for the first time in the United Kingdom. At baseline and one year, patients reported demographics and completed pain and fatigue visual analogue scales (VAS-pain/VAS-fatigue), the Hospital Anxiety and Depression Scale (HADS-A, HADS-D) and the Health Assessment Questionnaire (HAQ). A research nurse performed a 28 swollen and tender joint count (SJC28/TJC28) and the disease activity score (DAS28) was calculated. Patients answered the question "Is your current condition satisfactory, when you take your general functioning and your current pain into consideration?" at baseline and at one year. Only patients not in PASS at baseline are included in this analysis. Change in disease related factors (SJC28, TJC28, DAS28), PROs (HAQ, VAS-pain, VAS-fatigue), and psychological factors (HADS-A, HADS-D) from baseline to one year were calculated (see table 1). Predictors of PASS at one year were assessed using multivariable logistic regression, adjusting for age and gender. The discriminative power of disease activity, PROs and psychological factors were assessed by comparing the area under the curve (AUC) of the receiver operating characteristic curve.

**Results:** Of 358 not in PASS at baseline (mean (SD) age: 58.1 (13.0) years; 244 (68.2%) women), 241 (67.3%) were in PASS after one year. The only independent predictors of PASS were change in HAQ, VAS-pain and HADS-D (OR (95% CI) per unit change from baseline: HAQ 0.38 (0.16, 0.91); VAS-pain 0.96 (0.95, 0.98); HADS-D 0.86 (0.75, 0.99)). The model containing PROs had significantly greater AUC compared to a disease activity model (0.91 vs. 0.84, p=0.004) and a psychological factors model (0.91 vs. 0.81, p<0.0001).

**Abstract FRI0019 – Table 1.** Baseline, one year and change scores stratified by whether patients were in PASS at one year

Variable	Median (IQR) baseline score		Median (IQR) one year score		Median (IQR) Change		
	PASS at one year	Not-PASS at one year	PASS at one year	Not-PASS at one year	PASS at one year	Not-PASS at one year	
Disease activity	SJC28	6.5 (2.5, 11.0)	6.0 (3.0, 12.0)	0.0 (0.0, 2.0)	3.0 (0.0, 7.0)†	-5 (-9, -2)†	-2 (-6, 1)†
	TJC28	6.0 (3.0, 12.0)	9.0 (5.0, 17.0)†	1.0 (0.0, 4.0)	6.0 (2.0, 14.0)†	-4 (-9, -1)†	-2 (-6, 3)†
	DAS28	4.6 (3.8, 5.4)	4.9 (4.2, 5.8)	2.7 (2.1, 3.5)	4.3 (3.5, 5.3)†	-1.6 (-2.9, -0.8)†	-0.6 (-1.6, 0.4)†
PROs	HAQ	1.3 (0.8, 1.8)	1.4 (1.0, 1.9)	0.6 (0.1, 1.1)	1.5 (1.0, 1.9)†	-0.5 (-1.0, -0.1)†	0.0 (-0.4, 0.3)†
	VAS-Pain	63 (46, 75)	58 (50, 80)	18 (7, 33)	60 (41, 76)†	-38 (-55, -18)†	-5 (-24, 9)†
	VAS-Fatigue	62 (37, 74)	72 (57, 85)†	29 (13, 54)	70 (55, 83)†	-24 (-43, -1)†	-1 (-17, 12)†
Psychological	HADS-D	7 (4, 10)	8 (5, 10)	3 (1, 6)	8 (5, 11)†	-2 (-5, 0)	1 (-1, 2)†
	HADS-A	6 (4, 10)	8 (4, 12)†	4 (2, 8)	8 (4, 11)†	-2 (-4, 0)	0 (-2, 2)†

† p<0.05, † p<0.01 – PA09 groups compared using logistic regression.  
DAS28 = Disease Activity Score 28, HADS-A = Hospital Anxiety and Depression Scale (Anxiety), HADS-D = Hospital Anxiety and Depression Scale (Depression), HAQ = Health Assessment Questionnaire, IQR = interquartile range, PASS = Patient acceptable symptom state, PROs = Patient Reported Outcomes, SJC28 = swollen joint count (28), TJC28 = tender joint count (28), VAS = visual analogue scale.

**Conclusions:** Change in PROs have a greater association with attaining PASS at one year compared to disease related or psychological factors and should be taken into account when designing treatment strategies.

**Disclosure of Interest:** None declared

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**FRI0020** **ANTI-CEP-1 ANTIBODIES AND OTHER AUTOANTIBODIES IN EARLY ARTHRITIS**

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**Background:** As it is very important to identify patients with a high risk of developing rheumatoid arthritis (RA), new, diagnostic methods, evaluating the possibility of progression from undifferentiated arthritis (UA) to RA are needed.

**Objectives:** The aim of this work was the evaluation of the frequency of rheumatoid factor, anti-cyclic citrullinated peptide (anti-CCP) antibodies, mutated citrullinated vimentin antibodies (a-Sa), anti-CEP-1 antibodies, anti-filaggrin antibodies (AFA), heterogeneous nuclear ribonucleoprotein compies/anti-RA33-antibody (HnRNPI/RA33), anti-CarP antibodies (a-Carp) in patients with early arthritis.

**Methods:** 74 patients with early arthritis and 20 healthy volunteers were enrolled to the study. 51 patients were diagnosed with RA, 23 with UA. Exclusion criteria were the application of disease-modifying antirheumatic drugs or glucocorticosteroids. In all patients the following laboratory tests were performed: inflammatory markers, rheumatoid factor (RF) and antibodies mentioned above, together with necessary diagnostic that enables diagnosis.

**Results:** In patients with early arthritis the sensitivity and specificity of the presence of RF was 69% and 95%, respectively, and of anti-CCP was 67% and 97%. In patients with early arthritis we observed significantly higher concentration of CEP-1 (65.8±111.6) than in the healthy group (2.0±0.0). In RF(+) RA patients we

observed higher concentration of antibodies a-Sa and CEP-1 than in other groups.

Antibodies a-Sa were positive in 69% of RF(+) RA patients, in 37% of RF(-) RA patients, in 26% of UA patients and in 10% of healthy people. In 8 aCCP (-) and RF(-) patients we observed the presence of a-Sa; 3 of them were diagnosed with RF(-) RA with and 5 with UA. Anti-CEP-1 antibodies were positive in 77% of RF(+) RA patients, in 56% of RF(-) RA patients, in 4,5% of UA patients, but their presence were not observed in the healthy people. In 8 aCAPP (-) and RF (-) patients we observed positive anti-CEP-1 antibodies; 6 of them were diagnosed with RA, 2 of them with UA. Anti-CEP-1 antibodies were positive in 50% of RF(-) RA patients, in whom there was no aCCP nor RF, and only in 4,5% of UA patients.

In case of marking a-Car-P, positive values were present in: the group of RF(+) RA in 40% of patients, in patients diagnosed with RF(-) RA in 6%, in case of UA in 22% of patients. In patients with RF(+) RA, positive anti-CarP antibodies are present statistically significantly more often than in the group of RF (-) RA patients ( $p < 0,05$ ).

In case of marking hnRNP/RA33 and AFA no statistically significant differences between RF(+) RA, RF(-) RA and UA in their occurrence were observed. In patients with arthritis no correlation between smoking and analysed autoantibodies was observed. In smokers higher CRP concentration and ESR values was observed.

**Conclusions:** Our results suggest that a-Sa and CEP-1 parameters allow to differentiate RF(+) RA, RF(-) RA and UA, but do not differentiate UA from RF(-) RA. Marking CEP-1 in patients with early arthritis may help in differentiation between RF(-) RA and UA. Marking CEP-1 and a-Sa may be useful in diagnosing early arthritis patients. The presence of Anti-CarP antibodies in UA patients is probably considerable risk factor in RA development. Smoking cessation may contribute to decrease RA activity.

**Disclosure of Interest:** None declared

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FRI0021

#### PREDICTORS OF RHEUMATOID ARTHRITIS DEVELOPMENT IN PATIENTS WITH EARLY UNDIFFERENTIATED ARTHRITIS: A 2-YEARS FOLLOW-UP STUDY

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**Background:** Early treatment of rheumatoid arthritis (RA) improves longterm outcomes<sup>(1)</sup>. However, at the beginning of the disease, some patients with RA fall within undifferentiated arthritis (UA) patients. Several studies have shown that almost half of patients with UA may experience spontaneous remission<sup>(2)</sup>. So, in order to prevent overtreatment and poor outcomes, the identification of predictors of RA development is desirable.

**Objectives:** To determine the frequency of patients with UA evolving into RA after 2 years of follow-up and the factors contributing to predict this outcome.

**Methods:** A prospective analysis of an early arthritis cohort of 1377 patients from 1993 to 2017 was undertaken. For this study, 2 years follow-up data of patients who presented with UA were analysed. A detailed baseline assessment was completed including clinical features, physical examination and laboratory tests. Patients were stratified in two groups based on progression to RA (according to physician's diagnosis) or to another disease (non-RA). First, differences between groups were tested using chi-squared and Student-t tests in the univariate analysis. Second, multivariate logistic regression models were employed to investigate the association between possible predictive factors and RA development.

**Results:** A total of 471 UA patients were included for analysis. Mean age was 48.7±17.5 years, 352 (74.9%) were females, and mean symptoms duration was 13.9±13.9 weeks. After 2 years of follow-up, 93 (19.7%) of UA patients evolved into RA. Meanwhile, 175 (37.2%) remained undifferentiated and 203 (43.1%) developed into other musculoskeletal diseases. In the univariate analysis, the presence of rheumatoid factor (RF) and anti-citrullinated peptides antibodies (ACPA), tender and swollen joint count, duration of morning stiffness, smoking, symmetry and ESR values were significantly associated with RA development. In the multivariate analysis, RF (OR=5,899; 95% CI 1,795–19,382), ACPA (OR=123,238; 95% CI 29,353–517,410) and swollen joint count (OR=1,233; 95% CI 1,048–1,450), remained significantly associated with RA development (table 1).

**Abstract FRI0021 – Table 1.** Independent predictors of RA development based on logistic regression model

	Odds ratio	95% C.I.	
		Lower	Upper
Physician Global Assessment (0–100)	1016	,983	1051
28 Tender Joint Count	,949	,852	1057
28 Swollen Joint Count	1233	1048	1450
ESR(mm/h)	1018	,992	1044
Race	,633	,021	19 250
Smoking	,851	,223	3245
Symmetry	,568	,145	2225
RF(IU/mL)	5899	1795	19 382
ACPA(IU/mL)	1 23 238	29 353	5 17 410

**Conclusions:** Approximately, 1 out of 5 patients with UA evolves into RA after 2 years of follow-up. Swollen joint count, and the presence of rheumatoid factor (RF) and anti-citrullinated peptides antibodies (ACPA) are independent predictors for the development of RA, supporting the early DMARDs initiation in such patients.

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FRI0022

#### RAPID AND SUSTAINED REMISSION CONTRIBUTES TO IMPROVED PSYCHOSOCIAL OUTCOMES AFTER 1 YEAR OF TREATMENT IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS: DATA FROM THE CARERA TRIAL

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**Background:** The goal of early rheumatoid arthritis (RA) treatment is to reach remission as soon as possible, as this initial treatment response is a strong predictor of long-term clinical outcomes. Rapidly reaching remission is not only clinically meaningful, it also matters from the patient's perspective.<sup>1</sup> Yet, the influence of an initial response on patients' future psychosocial functioning remains understudied in early RA.

**Objectives:** To explore the association between the initial clinical response of patients with early RA and their psychosocial functioning after 1 year of treatment.

**Methods:** We included patients with early RA (disease duration  $\leq 1$  year) who started first-time treatment within the Care in early RA (CareRA) trial.<sup>2</sup> Based on the speed of response defined as the response at week 16, and the stability of response evaluated from week 16 onwards until week 52 of treatment, we created 4 profiles of initial clinical response relevant to patients: persistent responders, secondary failures, delayed responders and non-responders (table 1). Having a response was defined as a disease activity score (DAS28CRP) < 2.6 indicating remission. Psychosocial functioning was operationalized using relevant subscales of the Short-form 36 (SF-36) and the Revised Illness Perception Questionnaire (IPQ-R) (table 2). We built multiple linear regression models for each psychosocial outcome separately adjusted for confounding variables. Imputation using the Expectation-Maximisation method was performed for missing SF-36 and IPQ-R scores (range 22.2% > 23.1%) only at week 52.



**Results:** The 333 included patients shared typical characteristics of an early RA population (69.5% being woman, mean(SD) age of 52.3 (13.0) years), with no differences in demographics between patients for the different response profiles. In almost all regression models, the initial clinical response profiles were identified as significant predictors for each psychosocial outcome at week 52 (table 2). A rapid and sustained response, when compared to having a relapse after initial response or a delayed response or no response at all, resulted in higher vitality, less interference with normal social activities, less problems with work or other daily activities because of emotional problems, an improved mental health, more positive beliefs about disease consequences, a higher belief in the effect of treatment, and a more coherent illness understanding.

**Abstract FRI0022 – Table 1.** Definitions of the self-created profiles of initial clinical response throughout the first year of treatment in patients with early rheumatoid arthritis.

Clinical response* profiles	Group size	Definition of the profiles
Persistent responders	n=140	Early response at week 16 and stability of this response over year 1
Secondary failures	n=92	Early response, but relapse between week 16 and week 52 of treatment
Delayed responders	n=71	Late response, between week 16 and week 52 of treatment
Non-responders	n=30	No response to treatment throughout year 1

\* Having a response was defined as a disease activity score (DAS28CRP) <2.6 indicating remission.

**Abstract FRI0022 – Table 2.** The contribution of the initial clinical response to psychological outcomes (patient-reported) after 1 year of early RA treatment.

Psychosocial outcome at year 1	Number of patients	Persistent responders	Secondary failures	Delayed responders	Non-responders	Adjusted R square of the model
Vitality (SF-36)	n=326	REF	$\beta = -.169^{**}$ (-10.86, 2.85)	$\beta = -.177^{**}$ (-12.46, -3.16)	$\beta = -.270^{**}$ (-23.70, 11.41)	34.6%
Social functioning (SF-36)	n=327	REF	$\beta = -.121^{*}$ (-10.64, 0.78)	$\beta = -.170^{**}$ (-14.41, -3.15)	$\beta = -.325^{**}$ (-32.28, 17.13)	27.0%
Role emotional (SF-36)	n=324	REF	$\beta = -.137^{*}$ (-20.04, 2.49)	$\beta = -.229^{**}$ (-30.32, 10.57)	$\beta = -.199^{**}$ (-40.23, 12.96)	23.8%
Mental health (SF-36)	n=327	REF	$\beta = -.168^{**}$ (-9.71, -2.65)	$\beta = -.112^{*}$ (-8.53, -0.47)	$\beta = -.198^{**}$ (-17.13, -6.25)	37.5%
Consequences (IPQ-R)	n=325	REF	$\beta = .202^{**}$ (1.06, 2.98)	$\beta = .241^{**}$ (1.54, 3.74)	$\beta = .319^{**}$ (3.68, 6.70)	37.4%
Treatment control (IPQ-R)	n=326	REF	$\beta = -.202^{**}$ (-1.65, -0.46)	$\beta = -.221^{**}$ (-1.94, -0.57)	$\beta = -.196^{**}$ (-2.55, -0.71)	10.6%
Illness coherence (IPQ-R)	n=325	REF	$\beta = -.130^{**}$ (-1.83, -0.27)	$\beta = -.111^{*}$ (-1.87, -0.08)	$\beta = -.083$ (-2.27, 0.14)	36.6%

Note: SF-36: Short Form-36 items; IPQ-R: Revised Illness Perception Questionnaire; REF: Reference category; the beta values show the relative difference between each group and the persistent responders group (i.e., the group we chose as the reference category);  $\beta$ : standardized beta coefficient with 95% Confidence Interval; Regression analyses (enter method) were adjusted for age, gender, baseline disease activity, presence of depression, baseline value of the outcome and treatment strategy; Significant results in bold (\*\* p < 0.01, \* p < 0.05).

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FRI0023

## FIVE-YEAR PROGRESSION OF RHEUMATOID ARTHRITIS DISEASE ACTIVITY AND QUALITY OF LIFE IN 2002 AND 2011. HAVE REDUCTIONS IN DISEASE ACTIVITY IN RECENT YEARS RESULTED IN IMPROVEMENTS IN QUALITY OF LIFE?

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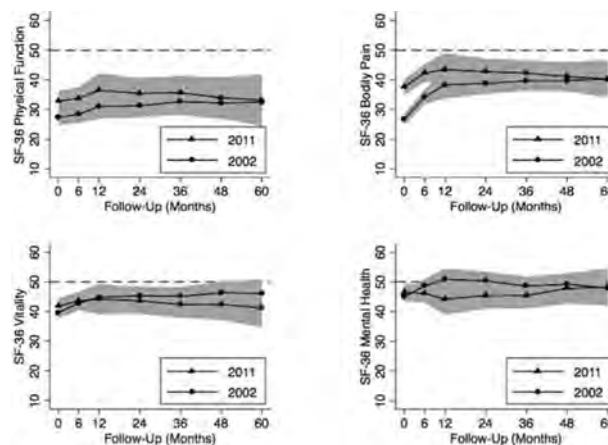
**Background:** The treat-to-target (T2T) approach, with earlier, aggressive treatment has resulted in improvements in rheumatoid arthritis (RA) outcomes<sup>1,2</sup>. Whether these improvements have translated into improvements in patient reported outcomes is less clear. Studies have indicated declines in pain and function as well as depression and anxiety. However, these studies are limited to short

follow-up periods or were restricted to cross-sectional, rather than longitudinal analyses.

**Objectives:** To assess changes in 5 year progression rates for disease activity and patient reported outcomes in a prospective cohort of early RA patients between 2002 and 2011.

**Methods:** The Early RA Network (ERAN) is a longitudinal prospective cohort study that recruited 1236 early RA patients from 2002 to 2011. DAS-28 and SF-36 were measured at baseline, 6 months, 12 months and then yearly. Multi-level linear regression were used to model 5 year progression rates of both DAS-28 and SF-36 in patients recruited between 2002–2011. Models controlled for sex and age and seropositivity at baseline. DMARD use at baseline was controlled for using propensity score weighting. Year of diagnosis was entered as a continuous variable, allowing for the mean of the outcome variables to be estimated for 2002 and 2011. Restricted cubic splines were used to account for non-linear progression over time.

**Results:** Disease activity for patients diagnosed in 2011 demonstrated a statistically significant decrease at year 5 compared to patients diagnosed in 2002 (5 year estimated mean difference –0.35; 95% CI 0.22–0.49, p<0.001). Using the SF-36 measure, Physical Function, Bodily Pain, Vitality (indicating fatigue) and Mental Health indicated similar levels at year-5 between those patients diagnosed in 2011 to those diagnosed in 2002 (p>0.05). Mental health was similar to the normalised population mean of 50, irrespective of year diagnosed. However, levels of vitality/fatigue, function and pain remain less favourable for all early RA patients over the first 5 years.



**Conclusions:** Although disease activity has shown a marked decline at 5 years between 2002 and 2011, there is little evidence that this has led to improvements of an equivalent magnitude in function, pain, fatigue and mental health. Treatment should also focus on improved function, pain management, fatigue and mental health as part of the T2T protocol.

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FRI0024

## DO AGE AND EDUCATION INFLUENCE THE DISEASE ACTIVITY SCORE? AN EXPLORATIVE ANALYSIS IN THE NORWEGIAN COHORT STUDY NOR-DMARD

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**Background:** While ageing influences auto-immune inflammation and the structure of the joints, knowledge about its influence on appraisal of disease outcomes is more limited.

**Objectives:** To examine the effect of age and education on the components of the 28-joint Disease Activity Score (DAS28-ESR) in patients with rheumatoid arthritis (RA).

**Methods:** Baseline data of Disease Modifying Anti-Rheumatic Drug (DMARD)-naive patients with RA from the Norwegian Register of DMARDs (NOR-DMARD) were used. Linear regression models, adjusted for gender and education (low, intermediate and high level), were used to investigate the strength of the association between age (<45, 45–65 and >65 years) and each DAS28-component (Erythrocyte Sedimentation Rate (ESR), 28-tender joint count (28-TJC), 28-swollen joint count (28-SJC), and patient global assessment of disease activity (PGA)). Adjusted scores for components of DAS28 and total DAS28-ESR were computed and relative change across age categories was explored. Interactions between age and gender and age and education were also tested.

**Results:** Baseline data from 2037 patients (mean (SD) age 55.2 (14.0) years, 68% female) were available. Regression models were stratified for gender ( $p$  – interaction <0.05); education was a significant covariate in all regression analyses. Older males (>65 years) with an intermediate level of education would have a 21% higher ESR and 14% higher 28-SJC, as compared to their younger counterparts (<45 years). For females in the intermediate education category, the corresponding differences were 16% and 15%, respectively. Conversely, differences in 28-TJC and the PGA between the highest and lowest age group were negligible in both males and females (table 1). In absolute effects on DAS28, this means that in male patients the adjusted DAS28 for those >65 years was 4.8 compared to 4.3 in patients <45 years (females 5.0 compared to 4.6). For low and high levels of education, the results were comparable in terms of relative contribution to each DAS28-component.

**Abstract FRI0024 – Table 1.** Effect of age on DAS28 (ESR) for patients with an intermediate educational level.

Component	< 45 years (reference) n = 181 (25%)	45 – 65 years n = 419 (58%)	> 65 years n = 123 (17%)	Difference between highest and lowest age group (%)
<b>Males</b>				
28-TJC	1.32	1.33	1.34	2%
28-SJC	0.62	0.66	0.71	14%*
PGA	0.57	0.59	0.58	2%
ESR	1.83	2.00	2.22	21%*
DAS28-ESR	4.34	4.58	4.83	11%
<b>Females</b>				
28-TJC	1.32	1.39	1.33	1%
28-SJC	0.59	0.63	0.68	15%*
PGA	0.67	0.68	0.68	1%
ESR	1.99	2.14	2.31	16%*
DAS28-ESR	4.57	4.84	5.00	9%

Abbreviations: TJC, tender joint count; SJC, swollen joint count; PGA, patient global assessment; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; DAS28, 28-joint Disease Activity Score.

\*Difference in scores is significant ( $p < 0.05$ ).

**Conclusions:** As expected, DAS28 increases with age. However, the components of DAS28 increase at different rates. The age-related increase in ESR and 28-SJC without a simultaneous increase in 28-TJC and PGA might imply that age-related processes (e.g. osteoarthritis and physiological increase in ESR) drive the DAS28 in older patients. The observed patterns were largely comparable between males and females. The age effect on DAS28 is relevant in a treat-to-target strategy and may be considered when identifying a defined target in individual patients.

**Disclosure of Interest:** None declared

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### FRI0025 SERUM MEDIATED PEPTIDYLARGININE DEIMINASE (PAD) ACTIVATION IN EARLY RHEUMATOID ARTHRITIS

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**Background:** Peptidylarginine deiminases (PADs) are a family of enzymes catalysing the conversion of arginine residues to citrulline, a post translational modification which has been recognised in the generation of neo-epitopes due to anti-citrullinated protein antibodies (ACPAs) in rheumatoid arthritis (RA). ACPAs are

included in the classification criteria for RA, and may be present before disease onset and predictive of disease progression.

**Objectives:** To investigate whether serum of patients with early RA have the capacity to significantly increase the citrullination performed by PAD enzymes, and the possible role of increased enzyme activation as a mechanism preceding the production of ACPAs.

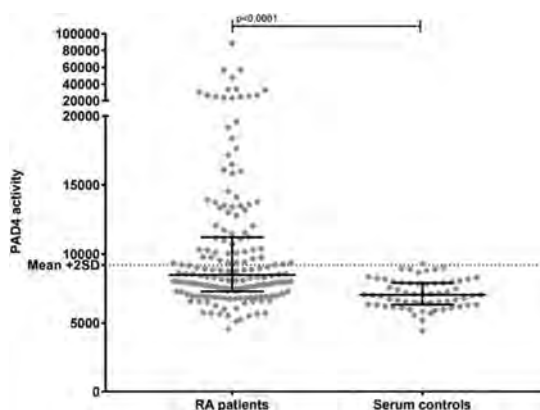
**Methods:** Serum from DMARD-naive, early RA patients from the ARCTIC trial<sup>1</sup> classified according to the 2010 ACR/EULAR criteria were analysed for PAD4 activating capacities using HPLC fluorometric method. A sample was defined as positive if above mean +2 SD of the healthy controls. Patient characteristics and subgroups with PAD activity were assessed using Mann-Whitney U-test and chi-square test as appropriate.

**Results:** A total of 225 patients and 63 controls were included in the study. Patient characteristics and measures of disease activity and radiographic damage are presented in the table 1. Median PAD activity levels were higher in patients than in healthy controls (8768 [7491,11393] vs. 7046 [6347,7905],  $p < 0.0001$ ; figure 1). ACPA and rheumatoid factor (RF) positive patients had higher PAD activity than ACPA and RF negative patients (9104 [7739,13213] vs. 7281 [6764,9010],  $p < 0.0001$ , and 8871 [7715,12259] vs. 8407 [6867,10062],  $p = 0.048$ , respectively). PAD positivity occurred in 42% (n=95) of the patients and was more prevalent in ACPA positive compared to ACPA negative patients (47 vs. 20%,  $p = 0.002$ ), but not in RF positive vs. RF negative patients (44 vs. 38%,  $p = 0.49$ ). Disease Activity Score was numerically higher in patients positive for PAD than patients who were PAD negative (3.6 (1.1) vs. 3.3 (1.2),  $p = 0.08$ ).

**Abstract FRI0025 – Table 1.** Baseline characteristics in subgroups of RA patients and healthy controls

	All patients (n=225)	PAD4+ (n=95)	PAD4- (n=130)	Healthy controls (n=63)
Age <sup>1</sup> , years	51.3 (13.8)	48.7 (13.5)	53.2 (13.7)	53.7 (9.0)
Female <sup>2</sup>	137(61)	56(59)	81(62)	30 (48)
ACPA positivity <sup>2</sup>	184(82)	87(92)	97(75)	0
RF positivity <sup>2</sup>	160(71)	70(74)	90(69)	NA
Disease duration <sup>1</sup> , months	7.1 (5.4)	8.3 (6.1)	6.2 (4.7)	NA
Ever-smoker <sup>2</sup>	149(66)	63(66)	86(66)	NA
ESR <sup>3</sup>	19 [11,32]	18 [11,30]	21 [11,32]	NA
SJC4 <sup>3</sup>	9 [4,14]	10 [5,15]	8 [4,14]	NA
Ultrasound grey scale	18 [10,28]	20 [11,28]	17 [10,26]	NA
Ultrasound power Doppler <sup>3</sup>	7 [3,14]	7 [3,14]	6 [2,13]	NA
Disease Activity Score <sup>1</sup>	3.4 (1.2)	3.6 (1.1)	3.3 (1.2)	NA
vdHS total score <sup>3</sup>	4 [1.5,8.5]	4 [1.5,7.5]	4.5 [2,9]	NA
PAD activity level <sup>3</sup>	8768 [7491,11393]	13175 [10370,19374]	7659 [6865– 8316]	7046 [6347,7906]

<sup>1</sup>Mean(SD), <sup>2</sup>n(%), <sup>3</sup>Median[25,75 percentile] Abbreviations: PAD, peptidylarginine deiminase; ACPA, anti-citrullinated protein antibody; RF, rheumatoid factor; ESR, erythrocyte sedimentation rate; SJC, swollen joint count; vdHS, van der Heijde modified Sharp



**Abstract FRI0025 – Figure 1.** PAD4 activity in patients and controls. Centre bar indicates median PAD4 activity level and error bars 25 and 75 percentile. The dashed line represents the cut-off value for increased PAD4 activity, defined as the mean plus two times the SD of the healthy controls.

**Conclusions:** Serum capacity to activate PAD4 was associated with ACPA and RF positivity in patients with early RA, but no distinct relationship was seen for Disease Activity Score.

#### REFERENCE:

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FRI0026

### U-ACT-EARLY TRIAL 3 YEARS FOLLOW-UP. THE LONGER EFFECTIVENESS OF TREAT-TO-TARGET STRATEGIES IN EARLY RA WITH TOCILIZUMAB, METHOTREXATE, OR THEIR COMBINATION

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**Background:** The U-Act-Early trial was a 2 year placebo controlled, double-blind randomised controlled trial in early (DMARD-naïve) RA patients treated to the target of sustained remission (SR), starting with tocilizumab (TCZ), methotrexate (MTX) or their combination (TCZ +MTX)<sup>1</sup>. When the treatment target was achieved, medication was tapered and stopped, if patients remained in remission. During the trial period, the strategies starting with TCZ were more effective than the strategy initiating MTX only. Subsequently, patients were followed for 3 years, during which treatment was open and according to usual care.

**Objectives:** To establish the effectiveness of step-up strategies starting with MTX, TCZ or their combination in early RA over a 5 year period.

**Methods:** 226 of the 317 patients starting in the U-Act-Early trial (initial strategy: 75 TCZ +MTX, 79 TCZ, 72 MTX) participated in the 3 year follow-up phase.

DAS28 was collected every 3 months during the first year and every 6 months thereafter.

The primary endpoint, was SR, defined as DAS28 <2.6 AND 28 joint count ≤4 for >24 weeks. Secondary endpoints were sustained drug free remission (sDFR), defined as remission for ≥3 months after tapering and stopping all medication during SR, and DAS28 over 5 years.

Differences between the randomised strategies in proportions of patients achieving SR and sDFR and durations of SR and sDFR were tested with Cochran-Mantel-Haenszel and Kruskal-Wallis tests, respectively.

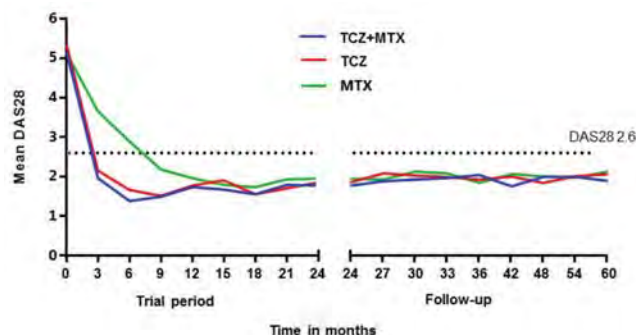
A mixed model analysis was used to compare DAS28 over time, with a random intercept and fixed effects for: treatment, visit-week, the interaction visit-week\* treatment, and it was corrected for gender, age, and for DAS28, RA-duration, CRP and RF-positivity at baseline.

**Results:** Baseline characteristics at the start of U-Act-Early of the patients included in this 3 year follow-up study were not significantly different from those of all patients included in U-Act-Early trial. Over 5 years, SR was achieved in 224/226 (99%) patients without significant differences (p=0.15) between the initial treatment strategies in proportions of patients achieving it, nor in durations (p=0.96) of these endpoints (table 1). Neither between-group significant differences were found for sDFR (proportion; p=0.10, duration; p=0.27), only a tendency for longer duration in TCZ +MTX. The mean DAS28 over 5 years was not significantly different between initial strategy groups (figure 1), but it was on average 0.15 (95% CI -0.12 to 0.42) units higher in the TCZ+(MTX) groups, compared to MTX initiation group.

**Abstract FRI0026 – Table 1.** Outcome for sustained (drug free) remission over 5 years

	Initial treatment strategy group			p-value
	TCZ+MTX	TCZ+placebo	MTX+placebo	
<b>Sustained remission</b>				
Proportion achieving, n/N (%)	75/75 (100)	77/79 (97.5)	72/72 (100)	0.15 <sup>1</sup>
Duration weeks, Median (IQR)	49 (37 - 81)	52 (40 - 71)	46 (36 - 114)	0.96 <sup>2</sup>
<b>Sustained drug free remission</b>				
Proportion achieving, n/N (%)	26/75 (34.7)	19/79 (24.1)	14/72 (19.4)	0.10 <sup>1</sup>
Duration weeks, Median (IQR)	106 (72 - 157)	83 (31 - 156)	71 (30 - 147)	0.27 <sup>2</sup>

<sup>1</sup>= Cochran-Mantel-Haenszel test. <sup>2</sup>=Kruskal-Wallis test



**Abstract FRI0026 – Figure 1.** DAS28 over time stratified for initial treatment strategy

**Conclusions:** On the short term, initiation of TCZ-based strategies yields the most benefit, but on longer term, no difference in important clinical outcomes was found anymore between initial strategy groups, probably due to continuation of the treat-to-target principle<sup>2</sup>. Almost all patients achieved SR over 5 years, with a tendency for longer duration of sDFR in the TCZ+MTX strategy.

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FRI0027

### PATIENT-BASED DISEASE ACTIVITY SCORE PREDICTS FLARE BETTER THAN IMPROVEMENT – BLOOD TEST PROVIDES INSIGNIFICANT CONTRIBUTION

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**Background:** Patient-derived Disease Activity Score (PDAS) was developed to allow rheumatoid arthritis (RA) patients to self-assess without the need of evaluator. Two versions, PDAS1 with ESR (erythrocyte sedimentation rate) and PDAS2 without, had been validated and shown to correlate well with DAS28 and display responsiveness to change in patients put on disease-modifying drugs. PDAS has the potential to inform disease activity change between evaluator's assessments and/or blood tests. This would be a useful monitoring tool to deliver treat-to-target tight RA control.

**PDAS1**=0.019×(PGA out of 100)+0.842×ln(ESR +2)+0.432×ln(patient 50 TJC +2)+0.271×HAQ



$PDAS2=2.667+0.021 \times (PGA \text{ out of } 100)+0.483 \times HAQ +0.033 \times (\text{patient } 28 \text{ SJC}) +0.002 \times (EMS \text{ in minutes})$  whereas PGA=patient global assessment, TJC=tender joint count; SJC=swollen joint count; HAQ=Health Assessment Questionnaire; EMS=early morning stiffness

**Objectives:** To assess whether PDAS is sensitive to change for an evaluator-based flare and improvement and whether PDAS1 (with ESR) is better than PDAS2.

**Methods:** A prospective cohort of 92 RA patients completed PDAS1 and 2 scores at the first and second clinic visits in a tertiary referral rheumatology centre. **Flare** was taken as increased RA activity from Simplified Disease Activity Index (SDAI) (remission or low activity) at the 1st visit → (moderate or high activity) at the 2nd visit, while **improvement** was the reverse change. Overall changes ( $\Delta$ ) of SDAI and PDAS1 and 2, in both directions, between these two visits were correlated using Spearman correlation coefficients. Further subgroup analysis (flare and improvement) was done by comparing the magnitude of changes between SDAI and PDAS1 and 2 using Mann-Whitney U test.

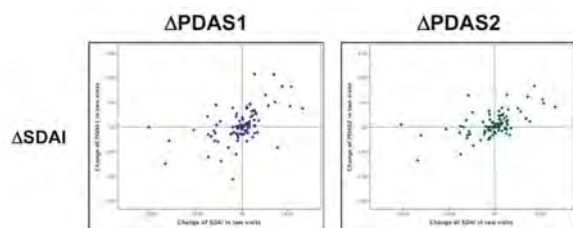
**Results:** Mean age of the cohort was 60 years, mean RA duration 14 years, 90% female, 71% sero-positive, 64% in remission/low disease activity at the 1st visit and follow-up interval was 17.5 weeks (standard deviation 9.4 weeks). At the 2nd visit, 11 out of 59 patients had a flare while 10 out of 33 patients improved. The Spearman correlation coefficients of  $\Delta SDAI$  with  $\Delta PDAS1$  and  $\Delta PDAS2$  were 0.55 and 0.54 respectively (both  $p \leq 0.001$ ). Data distributions were depicted in the scatterplot.

For the subgroup of flare, both  $\Delta PDAS1$  and 2 were significantly associated with the corresponding  $\Delta SDAI$  (all  $p < 0.02$ ). However, this association was not significant in the subgroup of improvement (See table 1). PDAS1 did not appear to perform better than PDAS2 in both groups of flare and improvement.

Abstract FRI0027 – Table 1

Flare (n=59)			
	Flare (11/59)	No flare (48/59)	P-value
$\Delta SDAI$	+6.90 (8.20)	0.12 (0.16)	<0.001
$\Delta PDAS1$	+0.75 (1.40)	0.01 (0.59)	0.016
$\Delta PDAS2$	+0.52 (0.74)	0.00 (0.32)	<0.001
Improvement (n=33)			
	Improved (10/33)	Not improved (23/33)	P-value
$\Delta SDAI$	-6.80 (7.20)	0.40 (6.90)	<0.001
$\Delta PDAS1$	-1.40 (0.96)	0.06 (0.49)	0.20
$\Delta PDAS2$	-0.16 (0.35)	0.00 (0.54)	0.25

Values are median (interquartile range). P-values are results of Mann-Whitney U test.



**Conclusions:** Overall PDAS1 and 2 are sensitive to change, but both predicted flare better than improvement. Clinically signalling flare has a far greater utility than documenting improvement. PDAS2 was as sensitive as PDAS1 in predicting flare yet without the need of a blood test for ESR. Hence, PDAS2 is suitable to serve as a purely patient-based home monitoring tool to detect a flare.

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**Disclosure of Interest:** None declared

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FRI0028

**DEVELOPMENT AND IMPLEMENTATION OF AN EDUCATIONAL VIDEO THAT INSTRUCTS PATIENTS WITH RHEUMATOID ARTHRITIS FOR SELF-ASSESSMENT OF DISEASE ACTIVITY: METHODOLOGY OF THE AUTO-DAS IN MIDDLE EASTERN ARAB COUNTRIES STUDY**

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**Background:** Using a treatment target in rheumatoid arthritis (RA), such as DAS-28 and involving patients in their disease management can improve prognosis.

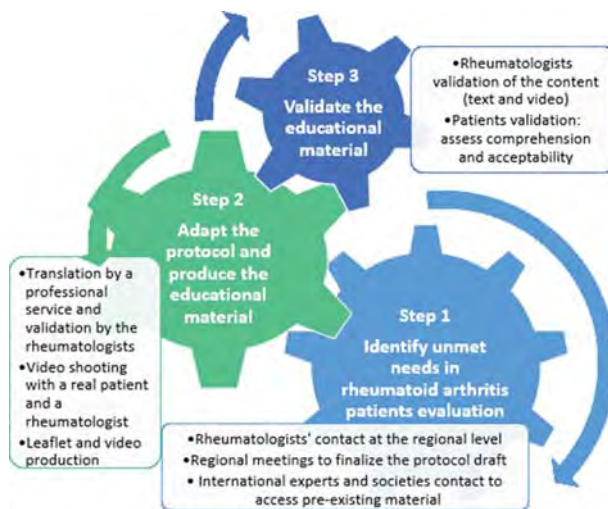
**Objectives:** To develop and implement an educational video that instructs patients with RA for self-assessment of disease activity using DAS-28.

**Methods :** *Step 1:Initiation.* Rheumatologists from some Middle Eastern Arab countries were invited to participate in this study. International experts and societies were contacted to access pre-existing educational material.

*Step 2: Development.* Different material sources were synthesized and translated into Arabic and validated by the rheumatologists. The educational video was shot by a professional team with a real patient and a rheumatologist on set.

*Step 3. Validation.* The final products (leaflets and video) were validated by the rheumatologists and tested with patients (figure 1). Obstacles were noted at the various study levels.

**Results:** 23 rheumatologists from 7 Middle Eastern Arab countries participated in the study. A one-page educational leaflet was developed in Arabic and English languages. An educational video presenting the treat-to-target concept and the basics of DAS performance was produced in Arabic language with English subtitles. Obstacles at the rheumatologist, patient, cultural and logistic levels were identified and the potential solutions were addressed by the study team.



Abstract FRI0028 – Table 1

Rheumatologist	Patient	Cultural	Logistics
DAS as target	Patient empowerment	Uniform text	Multiple IRB
Patient empowerment	Video understanding	Acceptable video	Funding
Patient adherence	Confidence in performance	Cultural mix	Computerised data

**Conclusions:** Collaboration between several countries sharing the same language and similar cultural backgrounds was possible and able to produce an

educational video aiming at the empowerment of RA patients for the self-assessment of their disease activity. The video will serve for future studies in the Arabic-speaking countries and will be available later for clinical use according to the rheumatologist's clinical judgment.

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#### FRI0029 CLINICAL SIGNIFICANCE OF 14–3–3ETA PROTEIN LEVELS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** 14–3–3 $\eta$  is a protein that is overexpressed in serum and joint fluid of patients with rheumatoid arthritis (RA) and may represent a diagnostic biomarker for RA.

**Objectives:** We assessed the prevalence and serum levels of 14–3–3 $\eta$  in patients with RA and with other rheumatic diseases.

**Methods:** Serum levels of 14–3–3 $\eta$  were measured in 96 patients with RA, in 101 patients with other rheumatic diseases and in 66 healthy subjects. The RA group consisted of 51 patients with well-established RA who were treated with different DMARDs, and 45 patients with early untreated disease (onset of less than 1 year). The disease control group included 33 patients with systemic lupus erythematosus (SLE), 44 patients with ankylosing spondylitis (AS) and 24 psoriatic arthritis (PsA) patients. All of the sera samples were evaluated by JOINT stat 14–3–3 $\eta$  ELISA test kits (Augurex Life Sciences Corp.). The cut-off was defined as 0.19 ng/ml.

**Results:** Median (IQR) 14–3–3 $\eta$  levels were significantly higher in the early RA group [0.25 ng/ml (0.075–3.11)] and in established RA patients [0.15 ng/ml (0.08–1.26)] in comparison with healthy subjects [0 ng/ml (0–0)] and disease controls: SLE [0.01 ng/ml (0–0.055)], AS [0.05 ng/ml (0–0.255)] and PsA [0.01 ng/ml (0–0.065)].

The prevalence of 14–3–3 $\eta$  positivity in early RA patients was 58%, significantly higher than in the disease control group (SLE: 9%,  $p < 0.001$ ; AS: 27%,  $p < 0.002$ , PsA: 12.5%,  $p < 0.001$ ) and in the healthy subjects group (5%,  $p < 0.001$ ). In established-RA patients, this prevalence was 43%, and it was significantly higher than in disease control and healthy subjects groups ( $p < 0.05$ ), excluding the AS group ( $p = 0.054$ ).

**Conclusions:** The concentration of 14–3–3 $\eta$  protein may be used to distinguish between patients with early RA and patients with other rheumatic diseases and serve as an additional biomarker in the diagnosis of RA.

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#### FRI0030 COMPARISON OF CLINICAL AND ULTRASOUND MEASURES OF DISEASE ACTIVITY IN A LARGE NATIONAL 'REAL LIFE' COHORT OF RA PATIENTS

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**Background:** Several studies have demonstrated that the clinical measures of disease activity, such as the DAS-score and ultrasound (US) scores can sometimes yield discordant results. Little research has attempted to understand the reasons for the discordances and how frequently these discordances occur in real life. **Objectives:** The objectives of this study were to determine the percentage of patients presenting discordances between DAS and US assessments in a real-life cohort, to describe associated factors and to evaluate the evolution of both measures of disease activity over time.

**Methods:** All patients with at least one concomitant US assessment and DAS score, performed since the introduction of validated US scoring in the Swiss registry for inflammatory arthritis SCQM registry between 2009 and 2017 were included. Disease activity was categorised as remission, low, moderate and high activity based on previously established cut-offs (for clinical: DAS categories and for US: on cutoffs of SONAR score established in previous testing among RA patients and asymptomatic subjects<sup>1,2</sup>). A search for potential clinical and US predictors of discordance was performed. Finally a longitudinal analysis was done in all patients with at least 2 subsequent visits. Discordances were analysed using successively DAS and US categories as references (see table 1)

**Results:** 1196 out of 2367 assessments were found discordant (50.4%). The proportion discordant assessments did not significantly differ by clinical disease status or when US categories were considered as the reference. Disease activity was equally frequently over-estimated by DAS compared to US-score (26.9%) and by US-score compared to DAS (23.5%). Factors associated with the presence of discordant results were all the components of the DAS when US categories were the reference. The presence of tenosynovitis was a significant factor when DAS was the reference. For 1181 patients with several DAS and US assessments, the proportion of discordances during follow up remained similar to the initial evaluation. Initial discordance/concordances could however change status without obvious reason in up to 30% of cases.

Abstract FRI0030 – Table 1

DAS	Remission (<2.6)	Low/moderate activity (DAS $\geq$ 2.6 and $\leq$ 5.2)	High activity (>5.1)	Total
Discordance: n (%)	449/893 (50.3%)	547/1138 (48.1%)	200/341 (58.7%)	1196/2372 (50.4%)
US > DAS n (%)	449/893 (50.3%)	189/1138 (16.6%)	0	638/2369 (26.9%)
US $\leq$ DAS n (%)	0	358/1138 (31.5%)	200/341 (58.7%)	558/2369 (23.5%)
US	Remission	Low or moderate disease	Very active disease	Total
Discordance:	393/837 (47.0%)	559/1149 (48.7%)	245/386 (63.5%)	1196/2372 (50.4%)
US > DAS n (%)	0	393/1149 (34.2%)	245/386 (63.5%)	638/2372 (26.9%)
US $\leq$ DAS n (%)	393/837 (47.0%)	165/1149 (14.4%)	0	558/2372 (23.5%)

**Conclusions:** Discordances between DAS and US assessments appear to be higher than expected in real life. Both outcome measures could lead to over- or under-estimations of the disease activity.

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FRI0031

**CHANGE IN FUNCTIONAL DISABILITY IN ACPA-POSITIVE ARTHRALGIA PATIENTS PRIOR TO PROGRESSION TO INFLAMMATORY ARTHRITIS**

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**Background:** Only one study<sup>1</sup> has assessed functional limitation in the pre-clinical phase of rheumatoid arthritis. Finding that functional limitations already exist during the symptomatic pre-arthritis phase. It is unclear if patient reported outcomes (PROs) are associated with progression to inflammatory arthritis (IA).

**Objectives:** To assess baseline and change in PROs in the lead up to progression to IA and its association with progression to IA.

**Methods:** From June 2008 to August 2016, 205 CCP positive patients without clinical synovitis were observed 3 monthly for 12 months and then as clinically indicated. The end point was development of IA within 12 months. PROs including HAQ, fatigue VAS, disease activity (DA) VAS and pain VAS were recorded at each visit. Cox regression was used to assess the association of each PRO at baseline with progression, then latent growth curves (LGC) were constructed to model change in PRO over time. The LGC were added as covariates in the cox regression models to determine whether changes in PROs over 12 months were associated with progression.

**Results:** 204 anti-CCP positive cases were included (one case excluded as had only baseline data). Of these, 50 developed IA within 12 months. Estimated mean baseline HAQ was 0.53 (Standard Error, SE 0.04) and mean increase in HAQ 0.06 per 12 months (SE 0.04). Mean baseline fatigue and pain VAS were 32 mm and 28 mm, respectively (SE 1.8 and 1.6, respectively). Mean increases in fatigue and pain per 12 months were 3.9 mm (SE 2.6) and 3.5 mm (SE 2.1), respectively. Table 1 shows how hazard ratios for progression IA relate to baseline and change in HAQ and VAS. Hazards for progression to IA were increased with greater baseline fatigue VAS, and greater rate of increase in reported functional impairment, fatigue and pain.

**Abstract FRI0031 – Table 1.** Hazards for progression to inflammatory arthritis in relation to reported baseline and changes in function, fatigue and pain

	HR for progression to IA	95% CI	p
<b>Covariate at baseline</b>			
HAQ	1.38	(0.95–3.38)	0.070
Fatigue	1.01	(1.01–1.04)	0.003
Pain	1.01	(0.99–1.03)	0.434
<b>Rate of change in covariate over 12 months</b>			
HAQ	2.07	(1.81–31.34)	0.005
Fatigue	1.01	(1.01–1.07)	0.002
Pain	1.03	(1.02–1.08)	<0.001

CI, confidence interval; IA, inflammatory arthritis; HAQ, Health Assessment Questionnaire; HR, hazard ratio; p, (statistical) probability. Each covariate was included in a separate model; all were controlled for age and gender.

**Conclusions:** Greater rates of increase in HAQ, fatigue and pain VAS were associated with small, but statistically significant increases in hazards of progression. Therefore, patient reported measures may be helpful for risk stratification in patients with positive anti-CCP.

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FRI0032

**ROLE OF ULTRASOUND IN ASSESSING DISEASE ACTIVITY IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS TREATED BY TWO TREAT-TO-TARGET STRATEGIES**

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**Background:** Ultrasound (US) is a sensitive tool for detecting joints and tendon inflammation in patients with rheumatoid arthritis (RA). Subclinical inflammation is often found in patients with RA in composite score remission. We hypothesise that achieving the ACR/EULAR remission, which reflects a more rigorous control of disease inflammation than the DAS28-based definition, may be associated with less subclinical inflammation detected by US.

**Objectives:** To determine the effect of two treat-to-target (T2T) strategies aiming at the Simplified Disease Activity Index (SDAI) remission (SDAI  $\leq$ 3.3) and DAS28 remission (DAS28-CRP <2.6) on US outcomes in patients with early RA.

**Methods:** This is a sub-study of the Hong Kong Early RA Vascular Study.<sup>1</sup> Fifty-five patients were randomised to receive 1 year of tight-control treatment with an aim to achieve either SDAI  $\leq$ 3.3 (group 1, n=21) or DAS28 <2.6 (group 2, n=34). Both wrists, 1 st to 5th metacarpophalangeal joints, 2nd to 5th proximal interphalangeal joints and the thumb inter-phalangeal joints were evaluated for synovial hypertrophy (SH) by greyscale and power Doppler (PD), scored 0–3. Global indexes for SH and PD (SH- and PD- index) and the Global OMERACT-EULAR Synovitis Score (GLOESS) were calculated. A post-hoc analysis was performed to ascertain whether achieving sustained DAS28 remission (SDR) from month 6 to 12 could improve the US outcomes which included the change in SH- and PD-index, and GLOESS between baseline and 1 year.

**Results:** At baseline, SH and PD signal were found at both wrists and the MCP joints (SH: 79.9%; PD: 82.6%) with moderate grade (SH: 58.3%; PD: 65.8%). Both groups demonstrated significant improvements in clinical and laboratory markers of inflammation. The SH-index, PD-index and GLOESS (median [IQR]: change: group 1: –8 [–22,–4], –6 [–15,–4], –8 [–22,–4]; group 2: –7 [–11,–3], –5 [–8,–2], –7 [–11,–3]) also improved in both groups to a similar extent (p=0.224, 0.297, 0.306 respectively). In view of the lack of differences in all outcomes in both groups, the results of all 55 patients were combined for a post-hoc analysis. Twenty-four patients achieved SDR from month 6 to month 12. After 12 months, the SDR group had a significantly greater improvement in swollen joint count, erythrocyte sedimentation rate, pain, patient global assessment, physician global assessment and Health Assessment Questionnaire. Significant improvements in SH-index, PD-index and GLOESS (–8 [–16,–5], –6.5 [–14,–5], –8 [–16,–6]) were observed in the SDR group and the non-SDR group (–6 [–11,–2], –4 [–10, 0], –6 [–11,–3]). Nonetheless, the SDR group had a significantly greater improvement in the PD-index (p=0.017) compared to that in the non-SDR group; while the SH-index (p=0.179) and GLOESS (p=0.094) were similar between the two groups.

**Conclusions:** In early RA, a SDAI remission-driven T2T strategy led to more intensive treatment but was not associated with significantly better clinical or US outcomes than a DAS28-driven strategy. However, patients who achieved SDR had a significantly greater clinical improvement and reduction in PD index compared to those who could not achieve SDR.

**REFERENCE:**

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FRI0033

### TRENDS IN THE INCIDENCE OF ORTHOPAEDIC SURGERY IN PATIENTS WITH RHEUMATOID ARTHRITIS IN SPAIN. A NATIONAL OBSERVATIONAL COHORT STUDY

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**Background:** The need of orthopaedic surgery (OS) is a marker of disease severity in RA. During the last 20 years, the treatment in RA has changed, incorporating strategies based on "treat-to-target" and biological therapies. But, have these new strategies modified the incidence of OS in RA?

**Objectives:** To analyse the incidence and trend of hospital admissions for OS in patients with RA, in Spain, during the period between 1999 and 2015.

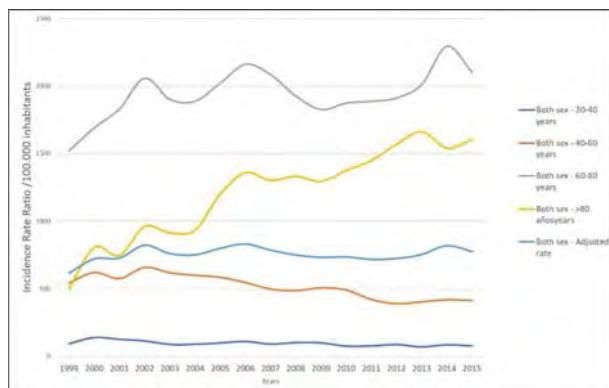
**Methods:** This is a national retrospective population based study. We analysed a national administrative database that includes a Minimum Basic Data Set (MBDS) of all hospital admissions of patients with RA. Period: 1999 to 2015. The OS were identified by the presence of ICD9 codes for arthrodesis, Total Hip Arthroplasty -THA-, Total Knee Arthroplasty -TKA-, Total Superior Limb Arthroplasty -TSLA. The population at risk was estimated through the population census of the National Institute of Statistics. The adjusted rates of hip fracture were calculated, by sex and age. The trend was analysed by Generalised Linear Models (GLM).

**Results:** Of a total of 338.343 hospital admissions, 21.088 (6,62%) were for OS. The main clinical-demographic characteristics are shown in the next table 1.

Table

	OS	THA	TKA	Arthrodesis	TSLA
N (% of total admissions)	21.088 (6.2)	8.709 (2.6)	9.006 (2.7)	1.372 (0.4)	2.230 (0.7)
Females (% of OS)	16.432 (100)	6.545 (39.83)	7.117 (43.31)	1.118 (6.8)	1.846 (11.23)
Age (SD)	65.02 (13.26)	66.57 (14.78)	65.97 (10.9)	55.90 (13.12)	59.93 (12.5)
Stay (SD)	10.97 (12.55)	13.48 (13.5)	10.73 (11.2)	6.69 (18.6)	4.54 (4.69)
In-hospital exitus	125 (0.6)	104 (1.2)	20 (0.2)	1 (0)	1 (0)

The mean age of OS increased 6 years during the study period ( $p < 0.001$ ). The OS age-adjusted rate during the study period was 752,9/10<sup>5</sup> inhab-year. The global fracture age-adjusted remained stable during the study period (IRR 1,002; IC95% 0,9–1,01). In RA patients >60 the rate increase while in RA <60 years the rate decrease (figure 1).



**Conclusions:** In Spain, during the period from 1999 to 2015, the global incidence rate of orthopaedic surgery in patients with RA has remained stable. In RA patients >60 years the rate increase while in RA <60 years the rate decrease. The mean age of OS increased 6 years.

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FRI0034

### EFFICACY OF ETANERCEPT BY BODY MASS INDEX IN WOMEN AND MEN WITH RHEUMATOID ARTHRITIS: A POST HOC ANALYSIS OF THREE RANDOMISED TRIALS

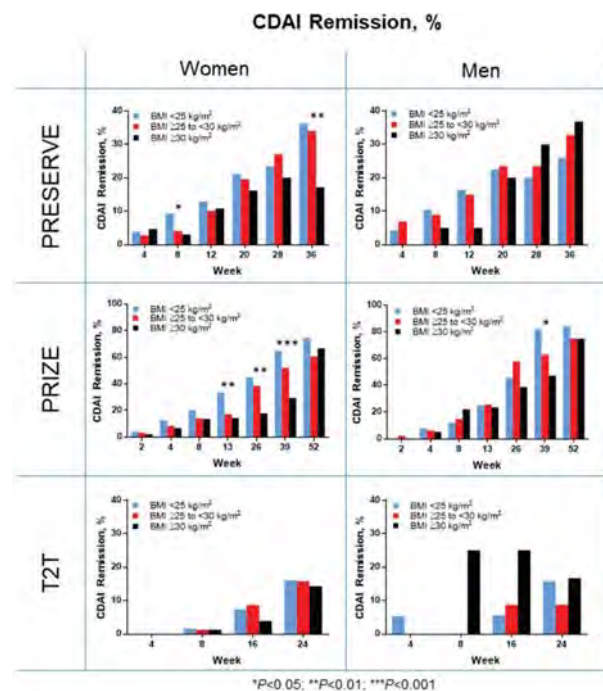
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**Background:** In patients with rheumatoid arthritis (RA) treated with tumour necrosis factor  $\alpha$  (TNF $\alpha$ ) inhibitors, a higher body mass index (BMI) has been associated with lower odds of achieving disease remission.

**Objectives:** To evaluate the effect of BMI on response to etanercept (ETN) therapy in women and men with RA, (a) during open-label treatment and (b) following dose reduction or dosing off in patients who achieved low disease activity (LDA) or remission.

**Methods:** In this post hoc analysis, data were collected from three randomised trials (PRESERVE, n=834; PRIZE, n=306; T2T, n=489) in which patients with RA were assigned to an open-label treatment with ETN (50 mg) and MTX for 24–52 weeks, followed by randomised double-blind treatment with ETN (25 mg or 50 mg)+MTX, placebo +MTX, or placebo for 28–52 weeks in those who achieved LDA or remission. Data (observed cases) were analysed by BMI (<25 kg/m<sup>2</sup>,  $\geq 25$  and <30 kg/m<sup>2</sup>, or  $\geq 30$  kg/m<sup>2</sup>) for women and men separately, using a one-way ANCOVA model with baseline value and BMI category for continuous variables and a logistic regression model with BMI as factor for categorical variables. The parameters analysed included changes from baseline in Clinical Disease Activity Index (CDAI), 28-joint Disease Activity Score with C-reactive protein level (DAS28 CRP) or erythrocyte sedimentation rate (DAS28 ESR), and Health Assessment Questionnaire – Disability Index (HAQ-DI), as well as the percentages of patients who achieved CDAI remission (CDAI  $\leq 2.8$ ) or LDA (CDAI >2.8 and  $\leq 10$ ).

**Results:** In the open label periods of all three studies, there was no significant BMI effect on treatment response to ETN in male patients, except for CDAI remission at a single visit in PRIZE (figure 1). In open-label periods of the PRIZE and T2T trials, a significantly smaller decrease in DAS28 CRP and DAS28 ESR in women with BMI  $\geq 30$  kg/m<sup>2</sup>, compared with the other two BMI categories, was observed at most visits. In addition, in PRIZE trial (but not in PRESERVE or T2T), women, but not men, with BMI  $\geq 30$  kg/m<sup>2</sup> had a significantly smaller decrease in CDAI and HAQ-DI scores and lower rates of CDAI LDA at most visits, compared with their counterparts with BMI <30 kg/m<sup>2</sup>. For CDAI remission, there was evidence of the effect of BMI  $\geq 30$  kg/m<sup>2</sup> in women in both PRIZE and PRESERVE (figure 1). Overall, these nominally significant differences between women with BMI  $\geq 30$  kg/m<sup>2</sup> and <30 kg/m<sup>2</sup> were transient: most of them diminished or were no longer significant toward the end of the open-label periods. In randomised, double-blind periods, there were no discernible trends attributable to BMI category in either women or men.



Abstract FRI0034 – Figure 1

**Conclusions:** Results of this post hoc analysis suggest that, in men with RA, there was no impact of BMI on ETN efficacy. In women, there was evidence of a transient negative impact of BMI  $\geq 30$  kg/m<sup>2</sup> on ETN efficacy in open-label periods, but it diminished by the end of the induction period and was not consistent across trials. There was no evidence of BMI effect in men or women during the double-blind periods.

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### FRI0035 DISEASE REMISSION IS MORE COMMON BUT LESS STRINGENT IN ANTI-CITRULLINATED PROTEIN ANTIBODY-POSITIVE PATIENTS WITH EARLY RHEUMATOID ARTHRITIS TREATED WITH CONVENTIONAL SYNTHETIC DISEASE MODIFYING DRUGS

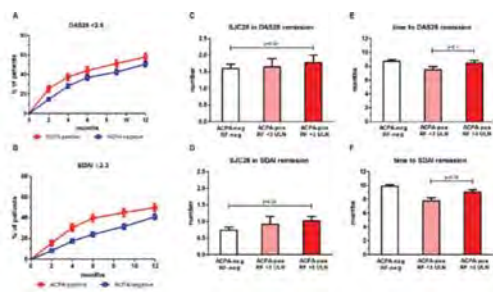
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**Background:** Early diagnosis and goal-steered treatment strategies allow the achievement of disease remission in a significant proportion of patients with early rheumatoid arthritis (RA). Autoantibodies such as anti-citrullinated protein autoantibodies (ACPA) identify a subset of patients with a common pathogenetic background and more severe course of the disease. However, whether autoantibodies also impact the response to conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs) remains object of debate.

**Objectives:** To investigate the frequency and the characteristics of disease remission in relation to the autoantibody status in patients with early RA treated with csDMARDs.

**Methods:** The study population consisted of 578 early RA patients (<12 months of symptoms) consecutively recruited at our Early Arthritis Clinic, treatment-naïve at inclusion and prospectively followed-up at regular intervals upon initiation of therapy with methotrexate (MTX) aimed at the achievement of low disease activity (28-joints disease activity score [DAS28]  $\leq 3.2$ ). ACPA and rheumatoid factor (RF) were centrally determined on baseline sera. The frequency of remission according to the DAS28 (<2.6) and to the simplified disease activity index (SDAI  $\leq 3.3$ ) over the first 12 months stratified by the autoantibody status was assessed by Cox regression. The following characteristics were further analysed: time to remission, swollen and tender joint count, and acute phase reactants at remission.

**Results:** 533/578 (92.2%) patients completed a follow-up of at least 12 months. Patients fulfilled the 2010 classification criteria for RA (81% also fulfilled the 1987 criteria) and had short disease duration at inclusion (median [IQR] 15.6 [9.4–27.8] weeks). Collectively, 53.9% and 44% of the patients achieved DAS28 and SDAI remission, respectively, at least once over the first 12 months of treatment. After adjusting for age, gender, symptoms' duration, baseline disease activity, MTX starting dose and prednisone co-medication, ACPA positivity was associated with slightly increased hazards of achieving both DAS28 (HR [95% CI] 1.24 [1.01–1.63]) and SDAI remission (HR [95% CI] 1.36 [1.01–1.85]) (figure 1A, B). However, irrespective of the remission criterion, ACPA-positive patients had higher numbers of residual swollen joints while being in remission, particularly in association with high levels of RF (>3 ULN) (figure 1C, D). Furthermore, remission was delayed in RF-high ACPA-positive patients compared to RF-low (figure 1E, F). Other features such as joint tenderness and acute phase reactants did not show significant differences among different serological subgroups.



Abstract FRI0035 – Figure 1

**Conclusions:** Early diagnosis and initial treatment with MTX result in high remission percentages in RA patients regardless of autoantibody positivity. However, remission appears less stringent in ACPA-positive patients, particularly when RF is also high. These findings indicate that current treatment approaches may be insufficient at effectively suppressing joint inflammation in autoantibody-positive patients.

**Disclosure of Interest:** None declared

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### FRI0036 SUSTAINED REMISSION RELATED FACTORS IN PATIENTS WITH RHEUMATOID ARTHRITIS: IS IT POSSIBLE TO PREDICT SUSTAINED REMISSION?

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**Background:** The management of RA have been changed during past decades and sustained remission (SR) is the ultimate goal to halt joint damage and prevent the accrual of disability. Factors predicting SR are essential to individualise treatment and recognise patients that have an opportunity to taper medications in daily practice.

**Objectives:** To determine baseline predictors of sustained remission and comparison of its predictability by different remission criteria.

**Methods:** A total of 428 consecutive patients with RA visiting our outpatient clinic routinely between September 2012–2013 were evaluated. Seventy seven of these patients satisfying the DAS28 remission (<2.6) within the time frame were enrolled and followed-up prospectively for 62.2±9.9 months. Of these fulfilling the DAS28 remission  $\geq 6$  months (sustained remission) and shorter (non-sustained remission:N-SR) were compared in terms of baseline demographic and clinical data and the presence of anxiety, depression, fibromyalgia and fatigue to determine possible predictors of SR. At enrollment, first and fifth years, the DAS28, SDAI and Boolean remission rates of patients were determined and compared with regard to DAS28 remission visit counts throughout the follow-up. We also assessed the difference between the SDAI and Boolean remission rates at initial, first and fifth years' visits.

**Results:** Of these 77 patients, 63 were in SR and 14 were in N-SR. Lower baseline DAS28 and HAQ scores ( $p=0.045$ ;  $p=0.026$ , respectively) and anti-CCP positivity ( $p=0.035$ ) were positive predictors of SR. Although the presence of anxiety, depression, fibromyalgia and fatigue were lower in SR group, there was no statistical significance.

DAS28 remission visit counts of patients in Boolean ( $n=32$ ) and DAS28 ( $n=77$ ) remission at enrollment ( $5.7\pm 3.2$  vs  $5.4\pm 3.1$ ;  $p=0.995$ ) were not different. Similarly, no difference was found between patients in SDAI ( $n=38$ ) and DAS28 remission ( $5.6\pm 3.3$  vs  $5.4\pm 3.1$ ;  $p=0.769$ ). Patients meeting the DAS28 criteria ( $n=77$ , 100%) reduced 64% ( $n=50$ ) at first and 42.6% ( $n=29$ ) at fifth years. Patients satisfying SDAI and Boolean criteria were 49%, 44% vs 32.4% ( $n=22$ ) and 41%, 28% vs 20.6% ( $n=14$ ), respectively.

If the duration of SR is considered as 6 months, the remission rates of SDAI were not different between patients at inclusion and fifth years but Boolean remission rates differed significantly and if it is accepted as  $\geq 12$  months, the SDAI and Boolean remission rates were not different than at fifth year visit.

**Conclusions:** Low DAS28 and HAQ score at baseline and anti-CCP positivity were positive predictors of SR. Although the presence of anxiety, depression, fibromyalgia and fatigue were lower in SR group, there was no statistical significance. Compared to the DAS28, remission determined by the Boolean and especially SDAI criteria continued consistently in long term.

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**FRI0037 CHARACTERISTICS OF RECENT ELDERLY-ONSET RHEUMATOID ARTHRITIS PATIENTS**

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**Background:** Elderly-onset rheumatoid arthritis (EORA) has been increasing along with the ageing society. EORA is believed to be different from young-onset RA (YORA) in clinical characteristics, however, it is unknown whether the characteristics of recent EORA are similar with those in the past.

**Objectives:** To elucidate recent characteristics of recent EORA patients.

**Methods:** Consecutive patients who were newly diagnosed with RA in our institution from November 2015 until May 2017 (group 1), and those from February 2011 until December 2012 (group 2) were enrolled. Each group was divided into EORA and YORA according to the onset age of 65 years old. Clinical data were collected from their medical records and compared.

**Results:** In group 1, 176 patients with newly diagnosed RA were identified; EORA 37% and YORA 63%. The mean age was 74.0±1.5 and 46.3±2.4 years old, and female was 73.9% and 84.7%, respectively. The duration from onset to first visit was significantly shorter in the EORA compared to the YORA (4.7±3.0 to 13.9±5.9 months;  $p=0.038$ ). Disease activity was significantly higher in EORA than the YORA (DAS28-CRP; 4.47±0.35 vs 3.49±0.27,  $p<0.001$ ; CDAI, 20.5±3.6 vs 15.1±2.2,  $p=0.009$ ). Inflammatory biomarkers at the first visit were also significantly higher in the EORA than the YORA; CRP (2.6±0.7 vs 1.2±0.5 mg/dl,  $p<0.001$ ), ESR (68±9 vs 38±6 mm/hr,  $p<0.001$ ), and serum ferritin (173.3±36.7 vs 102.3±18.8 ng/ml,  $p<0.001$ ). RF and anti-CCP antibody were less positive in EORA than in YORA (RF 55.4 vs 72.1%,  $p=0.024$ ; anti-CCP 40.0 vs 63.1%,  $p=0.003$ ). Large joints were more involved in EORA, but small joint involvement was not different between EORA and YORA. In group 2, 255 patients with newly diagnosed RA were enrolled, EORA 44% and YORA 56%, and female was 85.3% and 84.6%, respectively. The mean age at onset of RA was not different between group 1 and group 2 (58.3±2.4 vs 58.9±2.0,  $p=0.512$ ).

**Conclusions:** EORA developed more rapidly and showed severer inflammatory signs with more large joints involved. Conflicting with previous reports, the age at onset of RA did not increase between the patients in 2015–2017 and in 2011–2012.

**Disclosure of Interest:** None declared

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**FRI0038 CORRELATION BETWEEN CLINICAL AND ULTRASONOGRAPHIC REMISSION? THE EFFECT OF NON-INFLAMMATORY PATIENT-BASED FACTORS ON DIFFERENT REMISSION DEFINITIONS**

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**Objectives:** In this study, we aimed to investigate the concordance of ultrasonographic remission with other remission criteria and to show the influence of non-inflammatory patient-induced factors such as depression, anxiety, fibromyalgia and fatigue on both clinical and ultrasonographic remission.

**Methods:** Fifty consecutive patients with clinical remission (DAS-28-ESR<2.6) who were diagnosed according to the 2010 ACR/EULAR criteria were recruited to this study.

Patients were also assessed whether they met the Boolean and SDAI remission criteria. 28 joint grey scale (GS) and power Doppler (PD) ultrasonography were performed. Patients' depression and anxiety were assessed by The Hospital Anxiety and Depression Scale (HADS), and their fatigue was assessed by multidimensional Assessment of Fatigue (MAF) scores and patients' fibromyalgia was assessed by widespread pain index (WPI) and symptom severity score (SS).

**Results:** Patients were divided into 4 groups according to different remission definitions by ultrasonography. (Group1: PD=0 and GS=0, Group2: PD=0 and GS≥0, Group3: PD=1 or 0 and GS=1 or 0, Group4: PD=1 or 0 and GS≥0).

Although it is not statistically significant, the highest agreement with all the clinical remission criteria was found in the USG remission group 4 (table 1).

Patients with ultrasonographic remissions at their first visit in 2011 were reevaluated with clinical remission criteria at the end of 5 years. The highest remission rates were found in patients with USG remission group 3 (DAS28 58%, Boolean 29%, SDAI 47%). There was no significant difference between fatigue, fibromyalgia, depression and anxiety measures between remission and non-remission in all USG remission groups. In contrast, depression ( $p<0.05$ ) and anxiety ( $p<0.03$ ) were significantly higher in patients without SDAI remission. Depression ( $p<0.008$ ) and anxiety ( $p<0.014$ ) were also significantly higher in patients without Boolean remission.

**Abstract FRI0038 – Table 1.** The concordance between Ultrasound remission and other remission criteria

		Das28 (n=50)	SDAI (n=23)	Boolean (n=22)
Group 1: PD=0 GS=0	n (%)	13 (% 26)	8(%34,7)	5 (%22,7)
Group 2: PD=0 GS≥0	n (%)	22 (% 44)	10 (%43,4)	8(%36,3)
Group 3: PD=1 or 0 and GS=1 or 0	n (%)	17 (%34)	8 (%34,7)	7 (%31,8)
Group 4: PD=1 or 0 and GS≥0	n (%)	28 (%56)	13(%56,5)	11 (%50)

**Conclusions:** Clinical and ultrasonographic remission was found to be compatible in half of the patients.

The compliance of the USG remission in Group 4 with the clinical remission definitions was good, and clinical remission continuity was higher in the group meeting the definition of group 3. In contrast the ultrasound remission, the high levels of depression and anxiety in patients without SDAI and Boolean remission suggest that non-inflammatory patient-derived measures have less influence on the ultrasound remission.

**Disclosure of Interest:** None declared

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**FRI0039 MEASURING HEALTH RELATED QUALITY OF LIFE (EQ-5D) IN PATIENTS WITH RHEUMATOID ARTHRITIS AFTER ONE YEAR TREATMENT WITH csDMARDS AND BIOLOGIC DMARDS**

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**Background:** Health-related quality of life (HRQoL) is a multi-dimensional concept that includes domains related to physical, mental, emotional, and social functioning. It goes beyond direct measures of patients' health, and focuses on the impact health status has on quality of life.

**Objectives:** To measure the QoL (EuroQoL – 5D) of patients with RA and analyse their change after one year treatment with csDMARDS and biologic DMARDS (bDMARDS).

**Methods:** For the purpose of the study were selected 220 patients: 29 males (13%) and 86 women (87%) meet the classification criteria for RA by ACR 1987 Patient's age is between 18–85 years (mean age for DMARDS – 54.8, biologic DMARDS – 55.3 years). The duration of the disease is between 0.5–44 years. In our study 96 patients are treated with DMARDS and 124 with bDMARDS. Patients with significant comorbidity, infectious diseases, congestive heart failure (NYHA class III or IV), malignant hypertension, psychiatric illness, a history of lymphoproliferative disease or neoplasia were excluded from the study. All of the patients completed the questionnaire EuroQoL-5D on baseline, 6th and 12th month of treatment. The results were calculated via licensed calculator

**Results:** On Baseline, first part of EQ-5D mean values in patients with biologic therapy were significantly lower than those in the csDMARDS group ( $p=0.001$ ). During the follow-up period patients on biologic DMARDS experienced significant improvement in this indicator in both time intervals (6th month – 63.24±16.52 SD, 12th month – 76.38±14.85). After 6 months of treatment the group on bDMARDS have higher mean values for EQ-5D than the patients on csDMARDS (57.64±20.2 SD), which shows significantly higher Quality of life ( $p=0.0025$ ). During the following period from 6th to 12th month the patients on csDMARDS didn't have significant improvement in QoL (58.65±22.41 SD) ( $p=0.214$ ). On the 12th month of the treatment the patients on bDMARDS have significantly higher QoL than the group on csDMARDS ( $p=0.000$ ). Analysing the data from the second part of the questionnaire, we found similar results with the data obtained from the first. Patients on biological therapy experienced a significant improvement in quality of life during the entire follow-up period. In contrast, patients on csDMARDS had significant improvement in the mean values of the EQ-5D – 0.51±0.2 3SD to 6th month, after which there was a non-significant reduction of EQ-5D=0.49±0.23 SD to 12th month ( $p=0.266$ ).

**Conclusions:** The patients on biologic DMARDS have significantly higher QoL than the patients on csDMARDS on the 6th and 12th month of treatment period.

**Disclosure of Interest:** None declared

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FRI0040

### DEVELOPMENT AND VALIDATION OF CLINICAL PREDICTORS FOR INADEQUATE RESPONSE TO TREAT-TO-TARGET METHOTREXATE THERAPY IN NEWLY DIAGNOSED RA PATIENTS

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**Background:** In new-onset rheumatoid arthritis (RA), therapy should be aimed at achieving sustained remission according to current guidelines, in which methotrexate (MTX) is recommended to be included in the initial treatment strategy. However, a large proportion (~30%) eventually need additional treatment to control inflammation making it necessary to find predictors which helps clinicians in choosing the optimal initial therapy to further improve the long-term outcome of early RA patients.

**Objectives:** To identify and validate clinical baseline predictors associated with inadequate response (IR) to MTX therapy in disease modifying anti-rheumatic drug (DMARD)-naïve early RA patients.

**Methods:** For identifying clinical predictors, data was used from the U-Act-Early trial of newly diagnosed RA patients treated-to-target with a MTX strategy (n=108, development sample). MTX (oral) was started at 10 mg/week and increased in monthly steps up to 30 mg/week or maximum tolerable dose until remission. If no remission, hydroxychloroquine (HCQ) was added and, if the target, remission, thereafter still was not achieved, HCQ was replaced by tocilizumab. Patients in the tREACH trial who initiated MTX (25 mg/week) in combination with a prednisone tapering scheme were used as validation sample (n=83). In tREACH, if disease activity score (DAS) was  $\geq 2.4$  after three months, etanercept was added. When three months thereafter the target still was not achieved, patients switched to another tumour necrosis factor alpha inhibitor. In both studies, the definition of IR to MTX, (designated here "MTX+" therapy), was met if patients needed a biological DMARD within the first year. Clinical predictors were identified using logistic regression with backward selection ( $p \leq 0.10$ ).

**Results:** In the development sample, the following predictors for IR to "MTX+" therapy were identified: DAS assessing 28 joints (DAS28), adjusted odds ratio (OR<sub>adj</sub>) 2.1, 95% CI 1.4–3.1;  $p < 0.001$ ; current smoking, OR<sub>adj</sub> 3.0, 95% CI 1.1–8.0;  $p = 0.027$ ; and alcohol consumption, OR<sub>adj</sub> 0.3, 95% CI 0.1–0.9;  $p = 0.021$ . A risk matrix, categorised by these predictors, shows nearly a twelve and a half fold risk difference in predicted probabilities (figure 1). The area under the receiver operating characteristic curve (AUROC) of the model is 0.75 (95% CI 0.66–0.84); no statistically significant difference ( $p = 0.96$ ) was found between the observed and predicted probabilities (i.e. calibration). When using a negative predictive value (NPV), i.e. predicted chance of not failing "MTX+" therapy, of  $> 80\%$  as cut off in the development sample, the positive predictive value (PPV) was 65% (sensitivity: 0.89, specificity: 0.52). The AUROC of the model in the validation sample was 0.67 (95% CI 0.55–0.79) with no significant difference ( $p = 0.28$ ) between observed and predicted probabilities, indicating good calibration. In the validation sample, a cut-off of NPV  $> 80\%$ , the PPV was 54% (sensitivity: 0.88, specificity: 0.38).



Alcohol consumption, yes:  $\geq 1$  unit per week. DAS28 = disease activity assessing 28 joints; LDA = low disease activity (DAS28  $2.6 < 3.2$ ); MDA = moderate disease activity (DAS28  $3.2 < 5.1$ ); HDA = high disease activity (DAS28  $\geq 5.1$ ); NS = not specified, insufficient data to calculate predicted probability; IR = inadequate response.

**Abstract FRI0040 – Figure 1.** Risk matrix of predicted probability (%) of IR to "MTX+" therapy.

**Conclusions:** Higher DAS28, current smoking and no alcohol consumption were associated with an increased risk of IR to "MTX+" therapy in newly diagnosed RA patients.

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Welsing: None declared, P. de Jong: None declared, J. Hazes: None declared, A. Weel: None declared, A. Pethö-Schramm Employee of: AP-S is an employee of F Hoffmann-La Roche, M. Borm Employee of: MEAB is an employee of Roche Nederland BV, J. van Laar Grant/research support from: JMWL received fees from Arthrogeen, MSD, Pfizer, Eli Lilly, and BMS and research grants from Astra Zeneca, Roche-Genentech., F. Lafeber Grant/research support from: FPJGL reports grants from Roche, J. Bijlsma Grant/research support from: JWJB reported grants and fees from Roche, AbbVie, Bristol-Myers Squibb, Merck Sharp and Dohme, Pfizer, and UCB

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FRI0041

### ASSOCIATIONS BETWEEN TYMS POLYMORPHISMS AND RESPONSIVENESS TO OR TOXICITY OF METHOTREXATE IN RHEUMATOID ARTHRITIS

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**Background:** Thymidylate synthase (TYMS) is a key protein in the *de novo* synthesis of pyrimidines, and is essential for DNA replication and cell proliferation. MTX is polyglutamylated to form MTX polyglutamates after entering cells, and directly inhibits TYMS. TYMS is an important target for MTX, and over-expression of the TYMS gene is associated with resistance to TYMS-targeted drugs.

**Objectives:** The aim of this study was to investigate whether the thymidylate synthase (TYMS) 2R/3R and 6 bp I/D polymorphisms can predict the response to or toxicity of methotrexate (MTX) in patients with rheumatoid arthritis (RA).

**Methods:** We conducted a meta-analysis of studies on the association between the TYMS 2R/3R and 6 bp I/D polymorphisms and non-responsiveness to or toxicity of MTX in RA patients.

**Results:** A total of 11 studies involving 1613 patients were considered. Meta-analysis showed no association between the TYMS 2R/3R 3R allele and non-responsiveness to MTX therapy (OR=1.087 CI=0.682–1.731,  $p=0.726$ ). The meta-analysis indicated that there was no association between the TYMS 6 bp I/D D allele and non-responsiveness to MTX therapy (OR=0.688, 95% CI=0.281–1.683,  $p=0.413$ ). Meta-analysis revealed no association between the overall toxicity of MTX treatment in RA and the TYMS 2R/3R 3R allele. However, meta-analysis revealed that MTX toxicity was associated with the TYMS 2R/3R polymorphism in RA patients when a co-dominant model (3 R2R vs. 3 R3R +2R2R) was used, indicating that heterozygotes (3 R2R) for the polymorphism had a higher risk of developing MTX toxicity than homozygotes (3 R3R+2R2R). Stratification by ethnicity indicated an association between the TYMS 2R/3R 3R allele and non-responsiveness to MTX in Caucasians, but not in non-Caucasians. In contrast, meta-analysis revealed no association between the overall toxicity of MTX and the TYMS 6 bp I/D D allele.

**Conclusions:** This meta-analysis demonstrates that the TYMS 2R/3R and 6 bp I/D polymorphisms may not be associated with non-responsiveness to MTX therapy, but that the TYMS 2R/3R polymorphism may be associated with MTX toxicity in RA, particularly in Caucasians.

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FRI0042

### TENDER JOINTS HAVE LOW AGREEMENT WITH PATIENT'S EVALUATION OF SPONTANEOUS JOINT PAIN, JOINT SWELLING AND ULTRASOUND VERIFIED SYNOVITIS IN PATIENTS WITH ESTABLISHED RHEUMATOID ARTHRITIS

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**Background:** Tender joint count is included in the clinical composite scores (CDAI, SDAI, DAS28) which serves as a proxy for inflammatory activity. However, there may be several causes of joint tenderness, including both nociception and central sensitisation. Ultrasonography (US) is sensitive for evaluation of joint inflammation (synovitis (grey scale, GS) and vascularisation (power Doppler, PD)).

**Objectives:** In patients with rheumatoid arthritis (RA) to explore the agreement at a joint level between tenderness, spontaneous patient reported joint pain, swelling and US synovitis.

**Methods:** 174 patients with established RA (mean (SD) age 52<sup>13</sup> years, disease duration 10<sup>9</sup> years, 82% women, 79% anti-CCP positive were assessed when they initiated bDMARD treatment and after 1, 2, 3, 6 and 12 months. An experienced study nurse assessed presence/absence of joint tenderness and swelling (wrist, MCP1–5, PIP2–3, elbow, knee, ankle and MTP1–5 bilaterally). The same 32 joints were assessed by use of a manikin for Patient Reported Spontaneous Joint Pain (PRSJP) the last day as well as US (GS and PD, both scored 0–3) by an experienced sonographer (HBH). Agreement at joint level was explored between categorical variables using Cohens kappa (US scores transformed to presence (PD score 1–3/GS score 2–3) versus absence (PD score 0/GS score 0–1), and in addition agreement between presence of tenderness/swelling and the different US scores were explored.

**Results:** A total of 4091 (baseline) and 22 885 (all visits) joints were assessed. Tender joints had moderate agreement with PRSJP and swollen joints, and lower with US synovitis. Swollen joints had high agreement with US synovitis (table 1), and US synovitis was found in 75% of swollen joints. There were no differences in agreement between results at baseline and all visits, or if subgroup analyses were performed of only finger joints. A clear relationship was found between increasing GS/PD scores and percentages of joints being swollen, but this association was not found for tender joints (table 2).

**Abstract FRI0042 – Table 1. Kappa values for agreement between categorical variables at baseline (4091 joints)/all visits (22885 joints)**

	PRSJP	Swollen joint	GS US	PD US
Tender joint	0.34/0.40	0.32/0.32	0.21/0.21	0.20/0.20
PRSJP		0.25/0.26	0.23/0.24	0.25/0.23
Swollen joint			0.57/0.56	0.56/0.54

**Abstract FRI0042 – Table 2. At joint level; percentages of agreement between joints being tender and/or swollen and US synovitis (all visits, number of joints in parenthesis)**

	GS=0 (n=13874)/PD=0 (n=18656)	GS=1 (n=4077)/ PD=1 (n=1888)	GS=2 (n=3079)/ PD=2 (n=1791)	GS=3 (n=1855)/ PD=3 (n=550)
Swollen joints	3.8%/7.9%	16.3%/45.7%	47.1%/70.1%	77.7%/86.7%
Swollen, but not tender joints	2.1%/4.4%	8.8%/28.2%	26.7%/42.0%	49.4%/51.8%
Tender joints	9.7%/12.7%	20.4%/27.5%	29.7%/33.1%	32.7%/39.3%
Tender, but not swollen joints	8.0%/9.1%	12.8%/10.0%	9.3%/4.8%	4.4%/3.8%

**Conclusions:** Tender joints had weak agreement with presence of US synovitis, while swollen joints had strong agreement. PRSJP had moderate/weak agreement with all the other assessments. Presence of swelling was highly associated with the degree of US synovitis, while this association was not found for tenderness. Our results raise questions regarding the prominent role of tender joint count in RA clinical composite scores for disease activity.

**Disclosure of Interest:** None declared

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**FRI0043 TRENDS IN ALL-CAUSE AND CARDIOVASCULAR MORTALITY IN PATIENTS WITH RHEUMATOID ARTHRITIS. A 10- TO 20-YEAR FOLLOW-UP STUDY IN 3 CONSECUTIVE INCIDENCE COHORTS**

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**Background:** The mortality rate in patients with rheumatoid arthritis (RA) has been estimated to be 1.5–1.6 compared to the general public. Moreover, RA patients are still not benefitting fully from the declining mortality rate that the general population has enjoyed and cardiovascular disease (CVD) continues to be a major concern.

**Objectives:** To examine the all-cause and CVD mortality in 3 consecutive cohorts of patients with incident RA, compared to population controls

**Methods: The Oslo RA register (ORAR)** was established in 1994. The inclusion criteria were a diagnosis of RA according to the 1987 ACR criteria and residency in Oslo. The register was updated annually until 2009, and validated for completeness.<sup>1</sup> In January 2012, 3328 patients were registered in ORAR. We grouped patients into 3 successive incidence cohorts; 1996(1994–1998), 2001 (1999–

2003) and 2006(2004–2008). For each patient we identified 5 historical population controls matched according to age at disease incidence, gender and postal code of residence. Patients and controls were linked to the Norwegian Cause of Death Registry. Counts were compared using chi<sup>2</sup> tests. The hazard ratio (HR) for survival was calculated using stratified cox-regression models adjusted for highest achieved level of education.

**Results:** 422, 477 and 459 patients in the 1996, 2001 and 2006 cohorts were matched to 2110, 2385 and 2295 controls respectively. 20, 15 and 10 years follow-up for 1996, 2001 and 2006 cohorts were available in 201, 292 and 311 patients respectively. Results are presented in the table 1.

	1996		2001		2006	
	ORAR	Controls	ORAR	Controls	ORAR	Controls
Age years mean (SE)	55.9 (0.8)	55.9 (0.4)	54.1 (0.7)	54.1 (0.3)	54.7 (0.7)	54.7 (0.3)
Female gender n (%)	308 (73.0)	1540 (73.0)	358 (75.1)	1790 (75.1)	328 (71.5)	1640 (71.5)
Deaths at 5 years n(%)	37 (8.8)	180 (8.5)	30 (6.3)	130 (5.5)	25 (5.5)	104 (4.5)
Deaths at 10 years n (%)	95 (22.5)	371 (17.6)*	78 (16.4)	297 (12.5)*	38 (12.2)	257 (11.2)
Deaths at 15 years n (%)	147 (34.8)	586 (27.8)*	82 (28.1)	482 (20.2)*		
Deaths at 20 years n(%)	88 (43.8)	801 (38.9)				
CVD deaths 5 years n(%)	20 (4.7)	57 (2.7)*	8 (1.7)	30 (1.3)	6 (1.3)	26 (1.1)
CVD deaths 10 years n (%)	39 (9.2)	128 (6.1)	28 (5.9)	74 (3.1)*	9 (2.8)	59 (2.6)
CVD deaths 15 years n (%)	57 (13.5)	210 (10.0)*	27 (9.2)	138 (5.8)		
CVD deaths 20 years n (%)	43 (21.4)	290 (13.7)*				
HR 5 year all-cause mortality (95% CI)	1.01 (0.71–1.44)		1.01 (0.67–1.51)		1.17 (0.75–1.81)	
HR 10 year all-cause mortality (95% CI)	1.27 (1.01–1.61)*		1.18 (0.91–1.52)		0.98 (0.69–1.40)	
HR 15 year all-cause mortality (95% CI)	1.39 (1.15–1.69)*		1.41 (1.10–1.83)*		-	
HR 20 year all-cause mortality (95% CI)	1.49 (1.16–1.90)*		-		-	
HR 5 year CVD mortality (95% CI)	1.68 (1.00–2.82)		1.13 (0.51–2.51)		1.20 (0.49–2.95)	
HR 10 year CVD mortality (95% CI)	1.49 (1.03–2.16)*		1.69 (1.07–2.69)*		0.97 (0.47–2.02)	
HR 15 year CVD mortality (95% CI)	1.55 (1.13–2.12)*		1.67 (1.05–2.65)*		-	
HR 20 year CVD mortality (95% CI)	2.27 (1.56–3.31)**		-		-	

\*p<0.05.

**Conclusions:** RA patients with disease incidence in the period 1994–2003 had increased all-cause and CVD related mortality after 10–15 years of disease duration, compared to the population of Oslo. The increased mortality was not observed in the 2004–2008 cohort. Improved survival in recent years may be related to more effective therapies and earlier diagnosis, but further analyses are warranted.

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**FRI0044 EXCEEDING PREDEFINED THRESHOLDS FOR MRI BONE OEDEMA AND EROSION AND HAQ-DI CAN PREDICT RELAPSE AFTER WITHDRAWAL OF ALL TREATMENT IN MTX-NAÏVE PATIENTS WITH RA IN REMISSION AFTER 12 MONTHS OF ABATACEPT THERAPY IN THE AVERT TRIAL**

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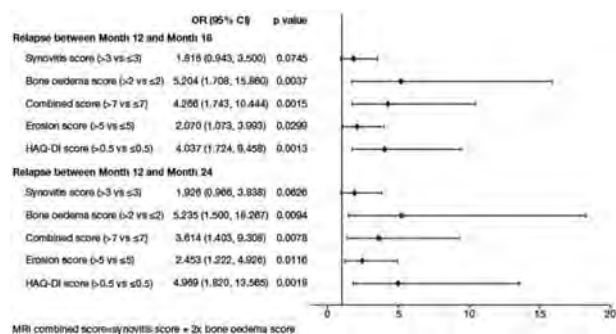
**Background:** To assist in clinical decision making it is important to understand the factors, and their thresholds, that might predict relapse following treatment

withdrawal in patients with RA in remission. In a previous *post hoc* analysis of the AVERT trial (NCT01142726), in which several potential factors were assessed, erosions, synovitis and bone oedema scores on MRI and HAQ-DI scores in patients with DAS28 (CRP) <2.6 were associated with clinical relapse 6 and 12 months after complete drug withdrawal following 12 months of blinded treatment with abatacept +MTX or abatacept or MTX alone.<sup>1,2</sup> Knowledge of the thresholds for these measures, above which relapse is more likely to occur, may aid clinical decisions about when to withdraw treatment in patients who have achieved remission.

**Objectives:** To evaluate *post hoc* the association between different thresholds of MRI and HAQ-DI scores at Month 12 and the risk of relapse at Months 18 and 24 in AVERT.

**Methods:** This analysis compared relapse event rates at Months 18 and 24 in patients with DAS28 (CRP) <2.6 but with differing severities of synovitis, bone oedema and erosion (assessed by MRI individual and combined scores) and HAQ-DI scores at Month 12. A relapse event was defined by the doubling of TJC28 and SJC28 and an increase in DAS28 (CRP)  $\geq 1.2$  relative to the Month 12 visit. Synovitis, bone oedema and erosion in the dominant hand and wrist MRI were scored using the OMERACT RAMRIS. Severity of each score was defined by cut-offs of >3 for synovitis, >2 for bone oedema, >7 for (weighted) combined synovitis and bone oedema, >5 for erosion and >0.5 for HAQ-DI. Univariate logistic models were conducted for comparisons and odds ratios (OR) with 95% CI and associated p values.

**Results:** All randomised and treated patients with DAS28 (CRP) <2.6 at Month 12 and relapse status available at Months 18 and 24 (n=155) were included. Among the overall study cohort at Month 12, 70 (45.2%) patients with DAS28 (CRP) <2.6 had a higher synovitis score (>3), 28 (18.1%) had a higher bone oedema score (>2), 39 (25.2%) had a higher combined score (>7), 73 (47.1%) had a higher erosion score (>5) and 42 (27.1%) had a higher HAQ-DI score (>0.5). Relapse events at Months 18 and 24 were significantly associated with supra-threshold MRI bone oedema, erosion and combined scores and with supra-threshold HAQ-DI score at Month 12 (figure 1). There was a trend toward association of relapse at Months 18 and 24 with high synovitis score (figure 1).



**Abstract FRI0044 – Figure 1.** Association Between Month 12 MRI and HAQ-DI Scores and Relapse Status at Months 18 and 24

**Conclusions:** It was possible to define MRI and HAQ-DI scores in patients with DAS28 (CRP) remission that were predictive of relapse 6 and 12 months after complete drug withdrawal in AVERT. Assessment of imaging and physical function, using predefined thresholds, in patients achieving remission may aid clinical decisions on when to withdraw therapy in MTX-naïve patients with RA.

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#### FRI0045 EVALUATION OF SERUM PROTEIN LEVELS AT BASELINE AS PREDICTORS OF RESPONSE TO METHOTREXATE IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS: RESULTS FROM SWEFOT TRIAL POPULATION

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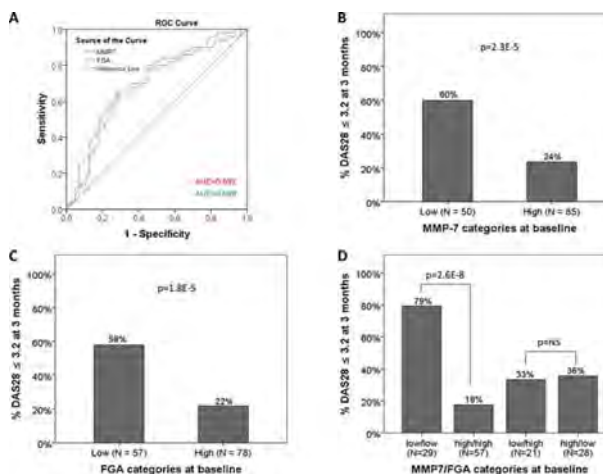
**Background:** Methotrexate (MTX) is a standard first-line therapy option for patients with early rheumatoid arthritis (eRA). However, a substantial proportion of patients still do not respond to MTX.

**Objectives:** To identify biomarkers for prediction of response to MTX.

**Methods:** We analysed a group of patients (n=135) with eRA from the Swedish Pharmacotherapy (SWEFOT) trial population. Baseline serum levels of 177 proteins were profiled using 380 antibodies in a suspension bead array format. Median fluorescent intensity (MFI) levels of the proteins were subsequently analysed for association with achievement of low 28-joint disease activity score (DAS28  $\leq 3.2$ ) after 3 months of MTX therapy (primary outcome). Proteins that remained significant in multivariate model were analysed using receiver operating characteristic (ROC) curve analysis for cut-off definition of MFI and categorisation into high and low categories. Proportion of patients with primary outcome between the generated categories were compared using Chi-squared test.

**Results:** In multivariate analysis, serum levels of two of the 177 proteins at baseline, matrix metalloproteinase 7 (MMP-7) and alpha-chain of fibrinogen (FGA) were significantly different among patients who achieved or not achieved low DAS28 at 3 months. ROC curve analysis revealed AUC of 0.692 for MMP-7 and 0.699 for FGA (p<0.001; figure 1A). ROC curve-based dichotomisation indicated that of patients with low versus high levels of either MMP-7 or FGA, 60% versus 24% and 58% versus 22%, respectively, achieved low DAS28 (p<0.001; figure 1B and C). Among patients with low categories of both proteins, 79% achieved low DAS28 at 3 months, while only 18% of those in high categories for both proteins (p<0.001; figure 1D).

Validation in the COMBINE cohort with available MMP-7 data (whose concentration was measured by different method) did not confirm results from the SWEFOT trial.



**Abstract FRI0045 – Figure 1.** Assessment of baseline levels of MMP-7 and FGA as predictors of LDA at 3 months. Receiver operating characteristic curve analysis and area under the curve of MMP-7 and FGA (A), proportion of patients achieving low DAS28 among groups dichotomised by MMP-7 (B), FGA (C) or using combination of MMP-7 and FGA (D).



**Conclusions:** Low levels of MMP-7 and FGA at baseline were associated with better clinical outcome in eRA patients. Following further characterisation, such biomarkers would be of high clinical relevance for the optimisation of treatment of RA.

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**FRI0046 PATIENTS PRESENTING WITH NEW MUSCULOSKELETAL SYMPTOMS IN THE WRISTS, HANDS AND FEET ENRICHES DETECTION OF ANTI-CCP ANTIBODIES IN PRIMARY CARE – A NATIONAL COHORT STUDY**

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**Background:** Selecting patients with new non-specific musculoskeletal complaints can enrich the prevalence of anti-cyclic citrullinated peptide (anti-CCP) antibodies compared with the general population.<sup>1</sup> Patients with rheumatoid arthritis (RA) frequently present with involvement of the wrist, hands and feet. Patients with elderly onset RA have a higher frequency of polymyalgic onset. However, it is unknown if elderly patients with shoulder complaints are more likely to be CCP positive.

**Objectives:** To confirm the proportion of individuals with new-onset, non-specific MSK symptoms who were anti-CCP positive (CCP+) across a national cohort and investigate the initial presenting complaint of all individuals, as this may help determine whether there is a symptom complex that would prompt antibody testing. In addition to determine if the risk of being CCP + is increased in older patients presenting with shoulder symptoms.

**Methods:** Individuals aged  $\geq 18$  years with new musculoskeletal complaints without synovitis from primary care were recruited prospectively. Participants completed a questionnaire on baseline musculoskeletal symptoms and provided a blood sample for anti-CCP antibody (Phadia CCP-2) testing. CCP+ individuals were invited to attend follow-up in the rheumatology department, Leeds. The association between CCP status, smoking and shared epitope status was also assessed.

**Results:** 4257 individuals were recruited, 2.9% (125/4257) were CCP+, a significantly higher proportion compared with the general population (1% (95% CI 2.4% >3.5%  $p < 0.001$ )). Patients who presented with pain in the wrists, hands (RR 2.2 (1.5–2.9),  $p < 0.001$ ) or feet (RR 1.72 (1.2–2.4),  $p < 0.001$ ) had an increased relative risk of being CCP+. Patients who were older than 60 years who presented with shoulder symptoms (4.8% (7/146)) were no more likely to be CCP + than those who did not have shoulder symptoms (3.2% (31/1007), chi square  $p = 0.313$ ) and had the same prevalence of CCP + as those <60 years (3.5% (13/370), chi square  $p = 0.461$ ). A significantly higher proportion of ever smokers were CCP+ (14.2% (48/337)) compared with never smokers (3.3% (64/1926); chi square  $p < 0.001$ ). Ever smokers were also more likely than never smokers to be shared epitope positive in CCP + individuals (62.2% (23/37) cf 37.8% (14/37);  $p < 0.007$ ).

**Conclusions:** Selecting individuals with new non-specific MSK symptoms without synovitis enriched the prevalence of anti-CCP positivity to 2.9%. Patients presenting with symptoms localising to the wrists, hands and feet were more likely to be CCP + which could prompt anti-CCP testing in these patients in primary care. Patients with shoulder complaints were no more likely to be CCP + than those without shoulder symptoms and had the same prevalence of CCP + as those <60 years.

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**FRI0047 MRI INTEROSSEOUS TENDON INFLAMMATION OCCURS IN ANTI-CCP POSITIVE AT-RISK INDIVIDUALS AND MAY PRECEDE THE DEVELOPMENT OF SYNOVITIS**

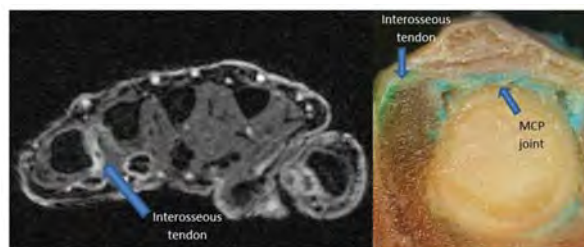
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**Background:** Tenosynovitis (TSV) occurs in individuals at-risk of developing RA and could explain pain and stiffness in the absence of synovitis. TSV of the wrist and finger flexor tendons has been described in at-risk individuals but involvement of other hand tendons has not been well investigated. The hand interossei are crucial to hand function and can become inflamed in RA.<sup>1</sup> Whether the interosseous tendons (IT) are sites of inflammation in at-risk individuals, and how this relates to joint inflammation and clinical features is unknown.

**Objectives:** To describe the anatomy, prevalence, pattern and clinical associations of IT inflammation in anti-CCP positive at-risk individuals.

**Methods:** Anti-CCP positive individuals with no synovitis (CCP+), healthy controls (HC), DMARD-naïve early RA patients (ERA) and treated 'late' RA patients (LRA) were recruited. All subjects underwent clinical and MRI assessment. 1.5T or 3T unilateral hand MRI scans were consensus scored for RAMRIS, TSV and IT inflammation by two radiologists. IT inflammation was defined as enhancing tissue around the tendon evident in two planes. For RAMRIS and tenosynovitis, scores were adjusted for 193 age-matched controls.<sup>2</sup> To understand the anatomical basis for MRI IT inflammation, a cadaveric study was performed on 20 fresh hand specimens; coloured dyes were injected along the first dorsal IT and into the adjacent second MCP joint and specimens were frozen and sectioned.

**Results:** 93 CCP+, 20 HC, 47 ERA and 28 LRA were recruited. Frequency of swollen and tender joints, MRI inflammation (synovitis, BME, erosions, TSV) and CRP level increased along the RA continuum with increasing disease duration. The proportion of patients with IT inflammation increased along the RA continuum. No HC, 18/93 (19%) CCP+, 23/47 (49%) ERA and 16/28 (57%) LRA patients had inflammation of  $\geq 1$  IT ( $p < 0.001$ ). The number of affected ITs increased along the RA continuum ( $p < 0.001$ ) and tendons associated with MCPJs 2 and 5 were most commonly affected. IT inflammation and MRI synovitis were associated with MCPJ swelling [OR 2.7 (0.9, 8.1) and OR 3.1 (1.0, 9.8) respectively] but IT inflammation was the only feature independently associated with MCPJ tenderness [OR 3.1 (1.4, 6.8)  $p = 0.004$ ]. In CCP+, 99/372 (27%) MCPJs had only one MRI abnormality; in 68% of these the abnormality was extra-capsular (57% TSV and 11% IT inflammation). No IT sheath was identified in the cadaveric specimens suggesting the MRI findings represent peri-tendonitis rather than TSV. Dye studies indicated no clear communication between the IT and the adjacent joint (figure 1).



Axial MRI showing inflammation of the 3<sup>rd</sup> palmar interosseous tendon and frozen section showing green dye around the interosseous tendon and blue dye within the MCP joint

**Abstract FRI0047 – Figure 1.** Axial MRI showing inflammation of the 3<sup>rd</sup> palmar interosseous tendon and frozen section showing green dye around the interosseous tendon and blue dye within the MCP joint

**Conclusions:** IT inflammation represents a peri-tendonitis and is present in anti-CCP +at risk individuals and RA patients where it is associated with MCPJ swelling and tenderness. IT inflammation can occur as the lone MRI abnormality in CCP +at risk individuals suggesting the interossei may be an early extra-capsular target in the development of RA.

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FRI0048

#### MORTALITY AND MORBIDITY OF RHEUMATOID ARTHRITIS-ASSOCIATED LUNG DISEASE DURING A 10-YEAR PERIOD: A LONGITUDINAL COHORT STUDY OF 103 JAPANESE PATIENTS

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**Background:** Subclinical and overt lung diseases associated with rheumatoid arthritis (RA-LD) are present in 30%–50% of the patients. Early and effective intervention improved joint prognosis in RA. By contrast, lung complications are still the primary contributors to premature deaths in patients with RA. Lung complication in RA can be due to a variety of conditions. However, the individual mortality and progression of pulmonary manifestations have not been established.

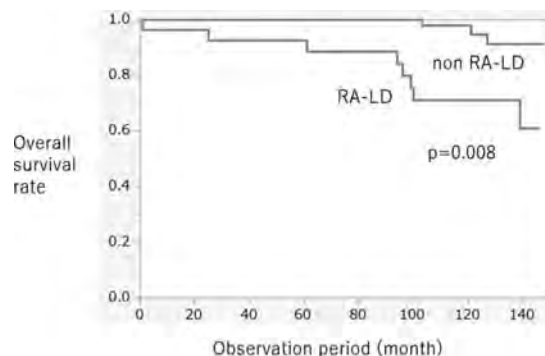
**Objectives:** To clarify the prognostic factors of patients with RA-LD.

**Methods:** This cohort study comprised RA patients examined with lung high resolution CT (HRCT) scan regardless of respiratory symptoms from 2005 to 2009. Respiratory diagnoses were certified by pulmonologists. The patients were reassessed by one follow-up CT scan after 10 years. All patients were evaluated for the events defined as death, serious infections and others (admission due to bone fracture, and ischaemic heart disease) from 2005 to 2017. Mortality risks were assessed using Kaplan-Meier method.

**Results:** Clinical features of 103 (82 females) patients are shown in table 1. Thirty-one (30%) had RA-LD including 18 interstitial pneumonia and 13 bronchiolitis at the start of observation. Mean observation period was 110 months. During observation, patients without RA-LD (non RA-LD) never developed new lung complications. The 10 year survival rate (SR) was 92% (mortality rate was 1.3 per 100 patient-years) and the 10 year event free survival rate (EFS) 69% (event rate was 4.8 per 100 patient-years). SR in RA-LD was significantly low compared with non RA-LD ( $p=0.008$ ) (figure 1). EFS in RA-LD was significantly lower than in non RA-LD ( $p=0.03$ ). Types of lung complication didn't correlate with high mortality. The causes of death comprised infection (55%), malignant tumour (27%), interstitial pneumonia (9%), and the others (9%). The adverse events included infection (41%), malignant tumour (21%), bone fracture (15%), cardiac disease (10%), and severe drug eruption including Steven-Johnson syndrome (13%). Univariate analysis showed that infection ( $p<0.001$ , HR 26.7) and acute exacerbation of RA-LD ( $p<0.001$ , HR 57.3, 95% CI 13–287) were strong risk factors for deaths.

**Abstract FRI0048 – Table 1.** Characteristics of RA patients with and without LD at the start of observation

	RA-LD(n=31)	non RA-LD(n=72)
Female (%)	80	80
age(y)	74±10	68±13
age at RA diagnosis(y)	54±14	48±13
RF positive (n,%)	20(65)	48(67)
ACPA positive (n,%)	19(61)	45(63)
DAS28	4.3±1.4	4.4±1.5
Stage (n,%)	6 (20)	15(21)
Stage (n,%)	10(32)	21(29)
Stage (n,%)	5 (16)	16(22)
Stage (n,%)	10(32)	20(28)



**Conclusions:** RA-LD is a serious complication in RA, and related with a high mortality.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.2884

FRI0049

#### SIGNIFICANT IMPROVEMENT OF RHEUMATOID ARTHRITIS (RA) OUTCOME WITH REPEATED SELF-ASSESSMENT APPLYING SMART SYSTEM OF DISEASE MANAGEMENT (SSDM) MOBILE TOOLS: A COHORT STUDY OF RA PATIENTS EMPOWERING

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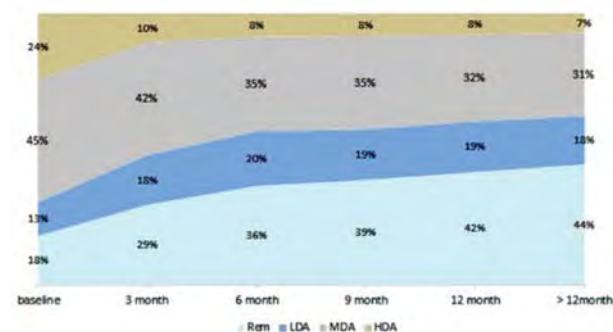
**Background:** Treat-to-Target (T2T) strategy are critical for the treatment of RA, but the Chinese rheumatologists can hardly provide patients with a complete assessment in the clinic due to limited time. The SSDM includes interfaces of both physicians' and patients' application. After inputting lab test records, treatment regimens, and executing DAS28 assessment by patients themselves, all data can be synchronised automatically to the authorised physicians' mobile tool. The rheumatologists can adjust treatment regimens base on patients' profile. Our previous study showed that patients in China can master the application of SSDM for accurately evaluating DAS28 and health assessment questionnaire (HAQ) after training.

**Objectives:** The objective of this study is to explore the effectiveness of applying SSDM in improvement of disease activity after repeated self-assessment in Chinese RA patients.

**Methods:** Patients were trained to do DAS28 evaluation with SSDM and asked to repeat the self-assessment once a month. Descriptive statistics were performed

for patient and disease characteristics. According to DAS28 scores, disease activity, the cohort was divided into four groups: remission (Rem), low disease activity (LDA), moderate disease activity (MDA) and high disease activity (HDA). T2T, achieving a DAS28 score lower than 2.6 (Rem) or below 3.2 (LDA), is the main management strategy recommended by ACR and EULAR.

**Results:** From Jun 2014 to Jan 2018, a total of 24,731 RA patients from 486 centres in China participated in the study. The mean age was  $49.28 \pm 16.08$  (18 to 99) years and the median disease duration was 18.30 months. All patients performed self-assessment of DAS28, HAQ and morning stiffness time totally for 30 358 times. Proportion of patients in Rem, LDA, MDA and HDA was 18%, 13%, 45% and 24% respectively at baseline. Of which, 3492 patients performed repeated assessment for 11 251 times. Proportion of patients in Rem, LDA, MDA and HDA changed into 44%, 18%, 31% and 7% at the last assessment. The proportion of T2T at the last assessment was significantly higher than that of baseline significantly ( $p < 0.001$ ). According to the assessments, the rate of T2T from baseline to 3 months, 6 months, 9 months, 12 months and over 12 months were 31%, 47%, 56%, 58%, 61% and 62% (see figure 1). With the increase of the times of self-assessment, the T2T rate was significantly improved ( $p < 0.001$ ).



**Abstract FRI0049 – Figure 1.** The times of repeated self-assessment and the proportion of DAS28 stratification

**Conclusions:** Under repeated self-assessment of DAS28 using SSDM, RA patients can achieve better T2T result. Though empowering patients, SSDM can assist rheumatologist to rationally adjust treatment for RA patients.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.6412

### FRI0050 TOCILIZUMAB ACHIEVES BETTER REPAIR OF FOCAL BONE EROSIONS THAN TUMOUR NECROSIS FACTOR INHIBITION IN RA PATIENTS – DATA FROM THE PROSPECTIVE REBONE STUDY ON EROSION REPAIR

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**Background:** Focal bone erosions are considered as markers for irreversible structural damage in patients with rheumatoid arthritis (RA). Several studies have suggested that limited repair of focal bone erosion can occur but no study has so far compared the effect of different biological disease modifying anti-rheumatic drugs (bDMARDs) on erosion repair.

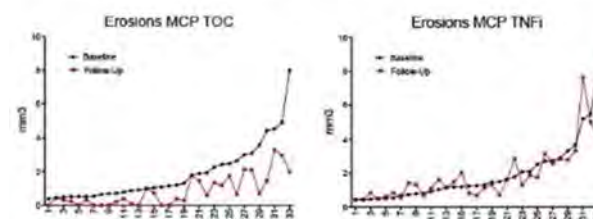
**Objectives:** To compare focal bone erosion repair in RA patients treated with interleukin-6 receptor inhibitor (tocilizumab, TOC) with patients receiving tumour necrosis factor inhibitors (TNFi)

**Methods:** Prospective non-randomised observational study in 66 erosive RA patients with active disease (DAS28-ESR > 3.2) and inadequate response to methotrexate receiving treatment with TOC monotherapy (n=33) or TNFi in combination with methotrexate (n=33) for 52 weeks. Patients received high-resolution peripheral quantitative computed tomography (HR-pQCT) of the MCP and wrist joints of the dominant hand at baseline and after 52 weeks. Volume (in mm<sup>3</sup>) of the largest (“sentinel”) erosion in the MCP joints and in the wrist was assessed by two readers blinded for treatments and for the sequence of the images. Demographic (sex, age, body mass index, smoking, Charlson comorbidity index) and disease specific parameters (disease duration, ACPA and RF status) were assessed at baseline and activity scores (DAS28, SDAI, CDAI, HAQ) at baseline and every three months thereafter.

**Results:** Groups were balanced for age, sex, BMI and comorbidities as well as disease duration, disease activity, functional state, autoantibody status and bone damage at baseline. TOC (DAS28-ESR: baseline:  $6.2 \pm 0.5$ ; 52wk:  $2.3 \pm 1.0$ ) and TNFi (DAS28-ESR: baseline:  $6.3 \pm 0.6$ ; 52wk:  $2.8 \pm 1.2$ ) significantly reduced

disease activity to a similar extent, achieving DAS28 remission in 22/33 and 19/33 patients, respectively, after 52 weeks. Volumes of the sentinel erosions significantly decreased in the MCP joints of TOC patients ( $-1.0 \pm 1.1$  mm<sup>3</sup>), while remaining stable in TNFi treated patients ( $-0.05 \pm 0.9$  mm<sup>3</sup>) (TOC vs. TNFi:  $p < 0.001$ ). Similar effects were observed in the wrist (TOC:  $-2.9 \pm 5.6$  mm<sup>3</sup>;  $-0.08 \pm 4.1$  mm<sup>3</sup>) with significant differences between the two groups ( $p = 0.0017$ ). Erosion repair was particularly frequent in RA patients reaching fast remission within the first 3 months of treatment.

### Erosion repair in the metacarpophalangeal joints of tocilizumab treated RA patients after 52 weeks



Y axis shows the volume of the sentinel erosion at baseline (black circles) and 52-weeks follow-up (red squares), x-axis the patient numbers (N=33)

**Abstract FRI0050 – Figure 1.** Erosion repair in the metacarpophalangeal joints of tocilizumab treated RA patients after 52 weeks

Y axis shows the volume of the sentinel erosion at baseline (black circles) and 52 weeks follow-up (red squares), x-axis the patient numbers (n=33)

**Conclusions:** The REBONE study shows that TOC has higher efficacy than TNFi to repair existing bone erosions in patients with RA. In contrast, the effects of TOC and TNFi on the inflammatory symptoms of RA are comparable. These data suggest that IL-6 is the central factor for the disturbed homeostasis between bone resorption and bone formation in the joints of RA patients.

**Acknowledgements:** The RE-BONE study was supported by Chugai Pharmaceutical Co., Ltd.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.3188

### FRI0051 THE RISK OF ASEPTIC ARTHROPLASTY LOOSENING IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Total joint arthroplasty (TJA) of the hip (THA) and knee (TKA) are well-established operations for end stage degenerative or inflammatory joint disease, and has excellent outcomes. In rheumatoid arthritis (RA), it is performed in about 25% of the patients.<sup>1</sup> According to registry data septic complications after TJA are more frequent in RA than in osteoarthritis (OA), which is likely linked to the immunomodulatory therapy that RA patients receive.<sup>2</sup> However, aseptic prosthesis loosening (APL) is the most common complication and it remains unclear whether RA *per se* is also a risk factor for non-infectious complications, e.g. by the presence of higher levels of systemic inflammation.

**Objectives:** To compare the rates of APL between OA and RA patients, and to investigate the influence of disease activity levels on the risk for APL in RA patients.

**Methods:** We identified all patients who underwent THA and TKA between 2002 and 2015 at our academic centre, and linked them with an existing prospective RA database to identify documented RA patients. Age and sex-matched OA patients were used as controls. Our primary endpoint were radiographic signs of APL as previously established.<sup>3,4</sup> Radiographs were evaluated by two independent observers blinded to the clinical diagnosis.

To explore the effects of systemic inflammation, we compared the time integrated level of disease activity by the Simplified Disease Activity Index (SDAI) during the year before an x-ray indicated loosening (for those with loosening) with the respective levels over one year before the last available x-ray (for those without loosening).

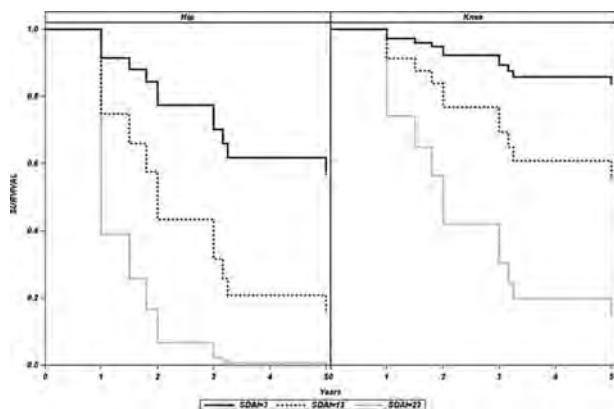
We used nonparametric tests and the chi-square test to compare rates of loosening between RA and OA patients and to compare AUC SDAI between patients with and without APL. Additionally, we calculated a Cox proportional hazard



regression to estimate the risk of loosening with increasing SDAI, stratified for TKA and THA.

**Results:** Data of 49 RA patients and 88 OA patients were available for analysis. The rate of APL was 36.7% in the RA and 13.6% in the OA group ( $p=0.002$ ). This was explained by a much higher rate of APL in the TKA group (RA: 34.4%; OA: 6.5%;  $p=0.001$ ), while the rates in the THA group were only numerically different (RA: 41.2%; OA: 30.8%;  $p=0.528$ ).

In the RA group one year time integrated SDAI was significantly higher prior to loosening than in controls without loosening ( $p=0.043$ ). In the Cox model, SDAI was also significantly related to time to APL with a Hazard ratio of 1.125 (95% CI 1.021–1.241) ( $p=0.018$ ). Figure 1 depicts cox regression adjusted for AUC SDAI 3, 13 and 26 separately for TKA and THA.



**Conclusions:** RA is not only a risk factor for infectious complications after TJA, but also for APL after THA or TKA. This effect might—at least partly—be explained by systemic and local inflammation in RA patients as depicted by higher levels of disease activity in RA patients with APL. In the context of treatment-to-target of RA, the presence of an arthroplasty should be considered as an indication for even more stringent control of disease activity.

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**Disclosure of Interest:** None declared

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FRIDAY, 15 JUNE 2018

## Rheumatoid arthritis – comorbidity and clinical aspects

### FRI0052 HIGHER URIC ACID IS ASSOCIATED WITH A LOWER DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** An association between serum uric acid (UA) and disease activity in rheumatoid arthritis (RA) patients has not been well studied.

**Objectives:** We describe RA patients with high and normal UA and study its association with RA activity.

**Methods:** Adult RA patients from The Kuwait Registry for Rheumatic Diseases (KRRD) who satisfied the ACR classification criteria for RA from four major hospitals were studied from February 2013 through April 2017. Patients with recorded

UA were identified. Visits with documented UA levels were included. UA of  $\geq 357$   $\mu\text{mol/L}$  (6 mg/dL) was considered high. Statistical correlations were made.

**Results:** A total of 564 RA patients with 2710 hospital visits and available UA were identified, 353 (62.6%) females. Mean age  $50.8 \pm 11.5$  years and disease duration  $10.5 \pm 2.9$  years. Mean DAS28 was  $2.9 \pm 1.2$  and mean HAQ-DI  $0.77 \pm 0.67$ . Rheumatoid factor (RF) was positive in 431/564 (76.4%) and anti-cyclic citrullinated peptide antibodies (ACPA) in 374/564 (66.3%).

Mean UA was  $271 \pm 78$   $\mu\text{mol/L}$  with 12.7% readings being high. There were more males among patients with high UA than with normal UA (56% vs 36%,  $p < 0.01$ ) with no difference in age.

UA was negatively correlated with DAS28 ( $p < 0.001$ ), CDAI ( $p < 0.001$ ), SDAI ( $p = 0.038$ ), ESR ( $p = 0.034$ ), VAS pain ( $p = 0.049$ ), morning stiffness ( $p = 0.033$ ), patient's global assessment ( $p = 0.006$ ), physician's global assessment ( $p = 0.033$ ), number of tender joints ( $p < 0.001$ ) and number of swollen joints ( $p < 0.001$ ). There was no significant correlation with RF, ACPA or HAQ. The use of steroid, synthetic and biologic antirheumatic drugs, either individually or as a class, was similar among patients with high and normal UA.

**Conclusions:** RA patients with a higher UA had a lower disease activity despite using similar antirheumatic drugs. Reasons behind such association need to be further studied.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.5638

### FRI0053 THE CHANGING FACE OF RHEUMATOID ARTHRITIS AT THE END OF THE 20TH CENTURY – A COMPARATIVE POSTMORTEM CLINICOPATHOLOGIC STUDY OF 237 RHEUMATOID ARTHRITIS PATIENTS WITH AA AMYLOIDOSIS AND SYSTEMIC VASCULITIS

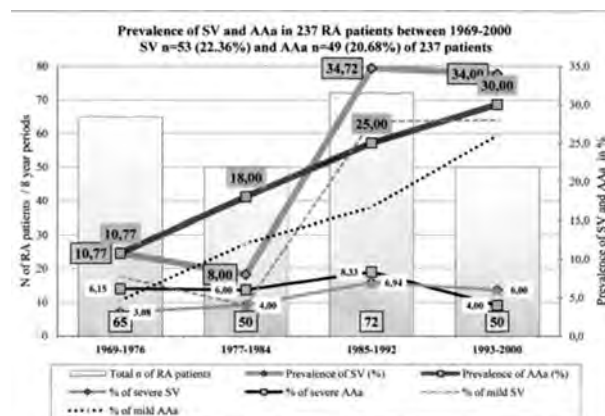
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**Objectives:** Most clinicians accept that the course of rheumatoid arthritis (RA) has changed in the last decades. The aim of this study was to verify this clinical impression characterised by systemic vasculitis (SV) and AA amyloidosis (AAa).

**Methods:** At the National Institute of Rheumatology 12 138 patients died between 1969 and 2000; among them 237 with RA, who were autopsied.

RA was complicated in 53 (22.36%) by SV, and in 49 (20.68%) of 237 patients by AAa. RA was confirmed clinically according to the criteria of the American College of Rheumatology.<sup>1</sup> The presence of SV and of AAa was determined histologically. The "severity" of vasculitis and the extent of amyloid A deposition/patient was evaluated by semi-quantitative visual estimation on a 0 to 3 plus scale.<sup>2</sup> The average prevalence of SV and AAa was calculated in percentage of the number of RA patients, who died during four periods of time (8–8–8–8 years) covering 32 years (between 1969 and 2000).

**Results:** During these four periods of time (from 1969 to 2000) the average age of RA patients with SV continuously increased from 57.00 to 68.00 years, and with AAa from 56.71 to 64.08 years. The prevalence of SV and AAa and the proportion of severe cases in % of RA patients are demonstrated on figure 1.



**Conclusions:** According to our data RA became more aggressive with higher prevalence of SV and AAa at the end of the last century.

The longer life spans (longer duration of the immune processes) with repeated exacerbations of vasculitis may have contributed to the increased prevalence of SV at death. The increased prevalence of SV (including fourfold mild and double severe cases) in 32 years supports the changing face of RA.

The increased prevalence of AAa may be related to the longer duration of the inflammation as well. The changing trend (inverse proportion) of severe and mild amyloid deposition, i.e. the increase of mild and decrease of severe cases could likely have been related to the introduction of more effective immunosuppressive therapy.

The longer disease duration and later death of RA patients with SV or AAa point to more effective therapy.

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**Disclosure of Interest:** None declared

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#### FRI0054 RISK FACTORS FOR POSTPARTUM FLARE IN RHEUMATOID ARTHRITIS – A ROMANIAN COHORT

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**Background:** Patients diagnosed with rheumatoid arthritis (RA) before pregnancy may experience a postpartum flare. This event may occur independently of the patient treatment, according to recent guidelines.<sup>1</sup>

**Objectives:** The aim of this study was to identify possible risk factors of postpartum RA flares.

**Methods:** We analysed pregnant RA patients treated with b DMARDs pre-conception/during pregnancy which delivered children. Data analysis was performed in a combined manner: prospectively and retrospectively. Data collection was focused on 5 distinct periods of time: pre-conception, 1 st, 2nd, 3rd pregnancy trimesters, postpartum period before 12 weeks and after 12 weeks. Following parameters were analysed: demographic data (type of pregnancy- planned/unplanned), immunology (RF and ACPA positivity), disease activity score DAS-CRP,<sup>2</sup> type of medication and duration. Subfertility status and postpartum flares were registered. The retrospective analysis was represented by interview collected data. Flare was defined as early (<12 weeks postpartum) or late >12 weeks)

**Results:** Among 96 pregnant patients, 54 (56%) patients delivered 57 children. Out of 54 patients, 17 (31.5%) were analysed prospectively and 37, 68.5% retrospectively. The patients were exposed to 3 types of b DMARDs: TNF blockers,<sup>9</sup> Rituximab<sup>5</sup> and Tocilizumab.<sup>1</sup> Rituximab was stopped before pregnancy in 4 out of 5 patients (1 continued therapy during the 1 st trimester- unplanned pregnancy) and all presented a postpartum flare. Out of 9 patients with TNF blocker therapy, 2 of them stopped the drug before pregnancy and the other 7 used the medication until pregnancy test positivity or until the end of the 2nd trimester. In this group, 6 of 9 patients presented a postpartum flare. One patient was treated with Tocilizumab before pregnancy and experienced an early flare. table 1 presents the analysis of a set of collected parameters. Overall, the majority of the patients (77.8%) experienced a postpartum flare. An early postpartum flare was identified in 53.7% and late one in 24.1%, with a mean value of 11.59±9.45 weeks. The prospective group experienced more frequently an early flare in comparison to group 2 (0.244 (95% CI 0.62–0.965) but without statistic significance. A positive correlation was found between active disease during the 2<sup>nd</sup> and 3<sup>rd</sup> trimester and postpartum early flare occurrence (p=0.044). No correlation was found between postpartum flare, fertility status or therapy type and duration.

**Table 1.** Risk factors for early postpartum RA flare

Variable	Early flare	p
Prospective	87%	0.044
Planned pregnancy	55%	0.534
Active disease during third trimester	100%	0.044
Active disease during second trimester	87.5%	0.044
Active disease during first trimester	77.8%	0.117
Active disease during preconception	73.8%	0.629
Subfertility	44.4%	0.371
Seropositivity	87%	0.593

**Conclusions:** RA pregnant patients treated with b DMARDs experience a postpartum flare in the majority of the cases. Persistent active disease during the second and third trimester was identified as a risk factor for postpartum disease flare. Larger prospective studies are needed in order to make a better analysis of all evaluated parameters.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.7155

#### FRI0055 SAFETY OF ETANERCEPT IN ELDERLY PATIENTS WITH RHEUMATOID ARTHRITIS: A POOLED ANALYSIS

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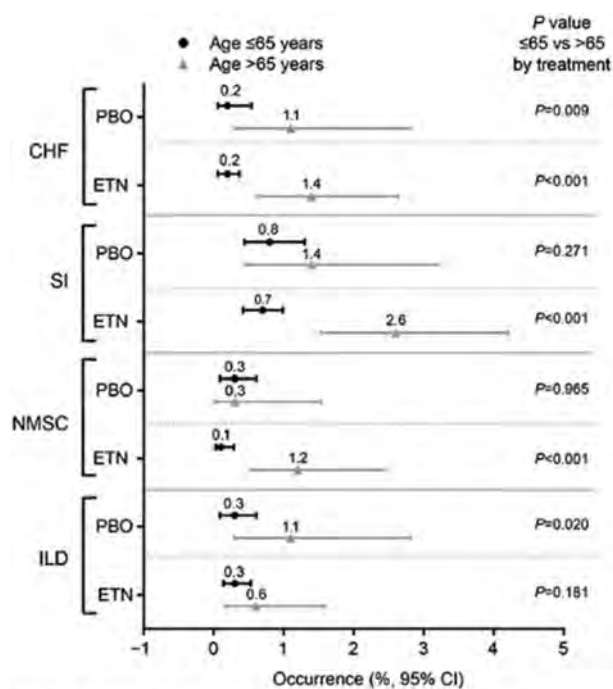
**Background:** Both ageing and rheumatoid arthritis (RA) are associated with a higher risk of comorbidities, some of which may be increased by current therapies. However, failure to control RA can lead to a particularly rapid loss of function and independence in the elderly population.

**Objectives:** To assess the safety of etanercept (ETN) in older (aged >65 years) vs younger (aged ≤65 years) patients with RA.

**Methods:** Patient-level data were pooled from the double-blind, placebo (PBO)-controlled phases of all completed, randomised, Pfizer- or Amgen-sponsored ETN studies in patients with RA. The occurrence of adverse events (AEs,%) in PBO- and ETN-treated patients was analysed by age (≤65 years vs >65 years), using the exact Poisson method to calculate 95% confidence intervals (CI). Fisher's Exact tests and Breslow Day tests for interaction were used to assess statistical differences.

**Results:** Data on 6418 patients were collected from 19 studies (≤65 years: PBO, n=1910; ETN, n=3497;>65 years: PBO, n=364; ETN, n=647). In PBO-treated patients, the occurrence of congestive heart failure (CHF), interstitial lung disease (ILD), and angioedema was significantly higher in older than younger patients (CHF and ILD: figure 1; angioedema: 0.82%, 95% CI 0.17–2.41% and 0%, 95% CI 0–0.19, respectively, p<0.0001). In patients treated with ETN, the occurrence of CHF, serious infections (SI), and non-melanoma skin cancers (NMSC) was significantly higher in older than younger patients (all p<0.0001, figure 1), as was the occurrence of anaphylactic reactions (p=0.02), central nervous system and peripheral demyelinating events (both p=0.001), and seizures (p=0.02). In contrast, the occurrence of non-serious infections and injection site reactions (ISRs) was significantly lower in older than younger ETN-treated patients (infections: 43.12%, 95% CI 38.21–48.49% and 48.27%, 95% CI 45.99–50.63,

respectively,  $p=0.016$ ; ISRs: 17.31%, 95% CI 14.25–20.83% and 22.36%, 95% CI 20.82–23.99, respectively,  $p=0.004$ ). The difference between PBO- and ETN-treated patients was statistically significant in the 2 age groups combined (Breslow Day interaction) for angioedema ( $p=0.003$ ), ISRs ( $p=0.042$ ), and NMSC ( $p=0.042$ ). Older, but not younger, patients had greater (but not statistically significant) occurrence of CHF, SI, and NMSC when taking ETN vs PBO. There was an interesting, non-significant, reduction of ILD occurrence in older, but not younger ETN-treated vs PBO-treated patients (figure 1). There were no significant age-related increases in the occurrence of other AEs of interest such as uveitis, opportunistic infections (invasive fungal, protozoal, bacterial, and atypical mycobacterial infections and Legionella), tuberculosis, lymphoma, melanoma, or leukaemia. The smaller number of patients in the older cohort was a study limitation, and further stratification of the data in the higher age brackets may provide key information on the age at which the risk of particular AEs increases.



SI included pneumonia, cellulitis, septic arthritis, sepsis, and parasitic infection.

**Abstract FRI0055 – Figure 1.** Occurrence of AEs with notable age-related differences in patients with RA

SI included pneumonia, cellulitis, septic arthritis, sepsis, and parasitic infection.

**Conclusions:** The occurrence of CHF, SI, and NMSC was higher in older vs younger patients taking ETN. While the analysis suggests an overall acceptable safety profile of ETN, the relative risks and benefits need to be considered when treating older patients.

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#### FRI0056 CLINICAL FEATURES AT THE ONSET OF LYMPHOPROLIFERATIVE DISORDER IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is intrinsically associated with an increased incidence of lymphoproliferative disorders (LPDs). Furthermore, treatment with immunosuppressing agents, such as methotrexate (MTX) sometimes

leads to the development of immunosuppressing agents related LPDs. Thus the development of LPDs is an increasingly important issue. However, previous studies focused on the pathological features and regression of LPDs after ceasing MTX administration, and evidence that could allow for the early diagnosis of LPDs in patients with RA is lacking.

**Objectives:** We surveyed the clinical course of patients with RA who developed LPDs at our hospital, with a focus on the clinical course and laboratory findings leading to their development.

**Methods:** Patients with RA who were treated at Niigata Rheumatic Centre between April 2011 and December 2017 were analysed. Patient data were obtained retrospectively from medical records. Twenty-nine patients (14 men, 15 women) developed a LPD (LPD group). We compared them with 87 patients without LPD (non-LPD group), who were matched for age, sex, and RA duration among 2628 patients with RA who attended our outpatient department in 2017. Data indicated are median (IQR<sub>1/4–3/4</sub>) values.

**Results:** The median patient age was 71.0 (64.0–74.0) years, and the duration of RA was 16.0 (10.0–22.0) years in both groups. Twelve patients were diagnosed with diffuse large B cell lymphoma, 5 with Hodgkin lymphoma, and 4 with T cell lymphoma; 8 patients had other diagnosis.

Of 29 patients, 23 were treated with MTX, 10 with tacrolimus, 8 with biological disease-modifying antirheumatic drugs (bDMARD). Twenty-two patients had Steinbrocker stage-IV RA. Multivariate analysis showed that Steinbrocker stage IV and MTX treatment were risk factors for the development of LPDs, with hazard ratios of 4.65 and 3.32, respectively.

In the LPDs group, although the C-reactive protein level (CRP) level and lactate dehydrogenase (LDH) level significantly rose (CRP, 0.10 [0.090–0.20] mg/dL 6 months before LPD diagnosis to 1.9 [1.1–3.8] mg/dL at LPD diagnosis, LDH, 198.0 [184.0–230] to 310 [210–489] IU/L), neither the tender joint count (TJC) and swollen joint count (SJC), nor matrix metalloproteinase-3 (MMP-3) level showed any significant change. On the contrary, CRP and LDH levels, as well as TJC, SJC, and MMP-3 level did not change significantly at the 6 month follow-up in non-LPDs group. LDH, MMP, and CRP ratios were calculated as the ratio of them at LPD diagnosis to those at 6 months before diagnosis. CRP and LDH ratios were significantly higher in the LPD group (CRP, 1.00 [0.65–1.75] in the non-LPD group vs 9.50 [2.40–23.0] in the LPD group; LDH, 1.00 [0.93–1.09] in the non-LPD group vs 1.46 [1.17–2.04] in the LPD group). However, the MMP-3 ratio was not different significantly between the non-LPD and LPD groups (1.00 [0.88–1.12] vs 0.98 [0.85–1.21]). MMP-3 ratio/CRP ratio was significantly lower in the LPD group than in the non-LPD group (0.0979 [0.036–0.384] vs 1.00 [0.54–1.67]). The receiver operating characteristic curve suggested that MMP-3 ratio/CRP ratio <0.476 was the best cut-off point for the prediction of LPD development, with a sensitivity of 90.9%, specificity of 79.0%, and an area under the curve of 0.894.

**Conclusions:** LDH elevation, and CRP elevation that is disproportionate to TJC, SJC, and MMP-3 level might indicate underlying LPD.

**Disclosure of Interest:** None declared

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#### FRI0057 EFFECTS OF ANTI-TNF THERAPY ON VASCULAR BIOMARKER LEVELS IN RHEUMATOID ARTHRITIS

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**Background:** Previous studies have shown an increased risk of cardiovascular disease in rheumatoid arthritis (RA), due to RA-associated inflammation. Different vascular biomarkers, such as anti-hsp65 antibodies, asymmetric dimethylarginine (ADMA) and B-type natriuretic peptide (BNP) have been associated with atherosclerosis and RA. Anti-hsp65 antibodies are also linked also to autoimmunity, inflammation and atherosclerosis. ADMA is an endogenous competitive inhibitor of NOS and consequential can lead to increased nitrosative and oxidative stress. ADMA has been implicated with atherosclerosis, and in RA. BNP is also involved in cardiovascular diseases.

**Objectives:** The aim of this study was to assess the effects of anti-TNF therapy on different vascular biomarkers, such as anti-hsp65, ADMA and BNP in patients with RA and their correlation with different laboratory and clinical markers.

**Methods:** Altogether 36 RA patients were recruited and treated with either etanercept (ETN) or certolizumab pegol (CZP) in this 12 months follow-up study. Assessments were performed at baseline, at month 6 and 12. Amounts of IgG antibodies reacting with recombinant M. bovis hsp65 (Lionex, Braunschweig, Germany) were measured by ELISA. Asymmetric dimethylarginine (ADMA) was assessed by HPLC with fluorescent detection. BNP fragments were assessed by commercially available ELISA kit (Biomedica, Vienna). In addition, disease activity



(DAS28), age, disease duration, CRP, IgM rheumatoid factor, anti-CCP and plasma lipid levels were also measured. Arterial flow-mediated vasodilation (FMD), carotid intima-media thickness (cIMT) and arterial pulse-wave velocity (PWV) were assessed by ultrasound.

**Results:** There were no significant changes in the levels of anti-hsp60, ADMA and BNP due to anti-TNF therapy. However, baseline level of BNP is strongly correlated with the levels of rheumatoid factor (RF) ( $R=0.479$ ,  $p=0.004$ ) and cyclic citrullinated peptid (CCP) ( $R=0.591$ ,  $p<0.001$ ). Serum BNP levels at baseline and at month 6 were significantly increased in RF positive compared to RF negative patients ( $680.60\pm 381.64$  versus  $292.94\pm 198.27$  pmol/L;  $p=0.007$  and  $668.95\pm 346.51$  versus  $312.20\pm 207.01$  pmol/L;  $p=0.001$ ) and also in CCP positive compared to CCP negative patients ( $670.61\pm 323.04$  versus  $137.98\pm 436.41$  pmol/L;  $p=0.030$  and  $652.93\pm 283.21$  versus  $456.48\pm 423.11$  pmol/L;  $p=0.021$ ). Furthermore we found the following correlations between baseline values: anti-hsp60 level correlated with ADMA ( $R=0.900$ ,  $p=0.037$ ), triglyceride (TG) ( $R=0.462$ ,  $p=0.040$ ) and PWV ( $R=0.564$ ,  $p=0.040$ ). Baseline level of ADMA positively correlated with body mass index (BMI) score ( $R=0.720$ ,  $p=0.040$ ) and also with HDL levels (high density lipoprotein) of patients ( $R=0.473$ ,  $p=0.047$ ). Baseline level of BNP also correlated with triglyceride (TG) level ( $R=0.377$ ,  $p=0.036$ ).

**Conclusions:** BNP levels were significantly higher in RF +compared to RF- patients, which imply that BNP may associate with RF positivity. Specific biomarkers, such as ADMA, anti-hsp60 and BNP may play important role cardiovascular disease in RA.

**Disclosure of Interest:** None declared

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### FRI0058 SERUM AND SYNOVIAL SURVIVIN ARE ASSOCIATED WITH EROSIIVE NOT ACTIVE RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is a progressive debilitating autoimmune disease leading to cartilage and bone destruction caused by insufficient apoptosis in the inflamed RA synovium. Survivin is a proto-oncogene biomarker known for its anti-apoptotic and cell cycle regulating properties and has been linked linked to inflammation, presumably contributing to the decreased apoptosis in the T cells in non cancerous processes.

**Objectives:** The aim of this study is to measure the serum and synovial levels of survivin and clarify their relations to disease activity, functional capacity and radiographic damage in RA patients.

**Methods:** This study was carried out on 50 RA patients (F:M=39:11) had a mean age of ( $46.4\pm 10.94$ ) years and 30 subjects of matched age and sex with a mean age of ( $46.03\pm 10.53$ ) years and F:M (23/7) as a control group. All patients were subjected to full history taking, thorough clinical examination, assessment of disease activity by DAS-28 score and functional capacity and using Health assessment Questionnaire (HAQ). Plain x- ray radiographs of both hands and feet were done, scored and graded by Larsen score. Survivin levels in all studied subjects' sera and the synovial fluid aspirated from 18 RA patients presented with knee effusion at the time of examination were measured by enzyme- linked immunosorbent assay (ELISA).

**Results:** The mean serum survivin level was highly significantly elevated ( $p<0.001$ ) in the RA patients sera than in the controls' being  $479.61\pm 52.68$  (pg/ml) and  $239.1\pm 115.15$  (pg/ml) respectively. Synovial survivin levels ranged between  $420-575$  (pg/ml) with a mean of  $479.61\pm 52.68$  (pg/ml) and was significantly higher than in the RA patients' sera ( $p<0.001$ ). RA patients were divided into survivin -ve group included 21/50 (42%) and survivin +ve group included 29/50 (58%), the serum survivin cut off point ( $167.63$  pg/ml) was selected at the mean plus 3 SD for the control group. Survivin+ve RA patients group have significantly longer mean disease duration and higher HAQ and larsen scores ( $p<0.001$ ) than survivin -ve RA patients group. 9/13 (69%) of the RA patients with Sjogren's syndrome, 8/10 (80%) of the patients with pleural effusion, 3/6 (50%) patients with Raynaud's phenomenon, all patients with sc nodules (5, 100%), episcleritis (2, 100%) and vasculitis (1, 100%) were survivin +ve. RA patients who had Larsen score grading  $\geq 2$  (27/50, 52%) were considered to have an erosive RA disease. There were no statistically significant differences between RA patients according to the presence of erosion regarding age, sex, VAS, DAS score, the presence of RF abs, Anti- CCP abs, mean HB%, WBCs count, PLTs count, ESR 1 st hr value or CRP level.

All RA patients with erosive disease were survivin +ve and had statistically significantly elevated mean serum and synovial survivin levels than the RA patients with non erosive disease ( $337.37\pm 55.19$  pg/ml vs  $126.78\pm 24.33$  pg/ml and  $422.5\pm 3.53$  pg/ml vs  $486.75\pm 51.52$  pg/ml respectively)

**Conclusions:** High levels of survivin are detected in the blood and synovial fluid of RA patients and are associated with erosive joint damage and poor functional outcomes but not related to disease activity.

### REFERENCE:

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### FRI0059 INTERSTITIAL LUNG DISEASE IN PATIENTS WITH RHEUMATOID ARTHRITIS OF A COHORT TREATED WITH METHOTREXATE MONOTHERAPY

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**Background:** Diffuse interstitial lung disease (ILD) is a common extra-articular manifestation of rheumatoid arthritis (RA) and an important cause of morbidity and mortality in this patient population. The predisposing and prognostic factors of this complication are a matter of debate.

**Objectives:** To determine the characteristics associated with the development of ILD in a cohort of patients with RA who received Methotrexate (MTX) monotherapy.

**Methods:** Case-control study in a cohort of patients with RA who had received MTX monotherapy, being cases those who developed ILD and controls, those who did not develop it.

**Results:** The cohort consisted of 301 patients (67% women), with a mean age of 49.6 ( $\pm 13.2$ ) years and a follow-up of 135.8 ( $\pm 93.5$ ) months. There were 15 (5%) cases of ILD, classified by high resolution chest CT as usual interstitial pneumonitis 7, nonspecific interstitial pneumonitis 7 and interstitial bronchiolitis 1. The distribution by sex was 8 ILD among 202 women (3.9%) and 7 ILD among the 99 men (7.1%). They all had RF and/or ACPA positive. ILD was associated with longer duration of the disease ( $p<0.05$ ), exposure to DMARDs prior to MTX ( $OR=3.3$ ,  $p<0.05$ ), history of chronic lung disease ( $OR=6.5$ ;  $p<0.01$ ) and coexistence with secondary Sjögren syndrome ( $OR=3.2$ ,  $p<0.05$ ). We did not find significant differences in mean values of age, RF, ACPA, baseline CRP and DAS28, dose, route and time of exposure to MTX, smoking, functional capacity, presence of erosions, MTX response and toxicity. The predictive factors in the logistic regression were the history of chronic pneumopathy, extra-articular involvement, time of evolution and basal biological activity (CRP) of the disease. Of the 15 patients with ILD, 5 (33.3%) had good response (DAS28-CRP  $< 3.2$ ) with MTX and remained on monotherapy, another 3 continued with MTX combined with another DMARD and 7 (46.7%) discontinued MTX. In addition, 8 of these 10 patients received a biological therapy. Eleven patients died during follow-up, 3 (20%) cases (ILD) and 8 (2.8%) controls ( $p<0.01$ ).

Clinical characteristics of the cohort

	Total (301)	ILD(15)	No ILD (286)	p
Age, years, mean(SD)	49,6 (13,2)	53,5 (13,9)	49,3 (13,2)	0,23
Women, n(%)	202 (67,1)	8 (53,3)	194 (67,8)	0,24
RA Duration, months, mean(SD)	135,8 (93,5)	105,0 (27,1)	92,4 (5,5)	0,04
Smoker, n(%)	183 (60,8)	8 (53,3)	175 (61,2)	0,54
Previous chronic lung disease, n (%)	51(16,9)	8 (53,3)	43 (15,0)	0001
Sjogren síndrome, n(%)	33 (11,0)	4 (26,7)	29 (10,1)	0,04
Previous FAME, n(%)	81(26,9)	8 (53,3)	73 (25,5)	0,02
CRP, mg/l, mean(SD)	17,8 (21,3)	32,3 (31,9)	17,0 (20,4)	0,09
DAS28-CRP, mean(SD)	4,5 (0,8)	4,6 (0,8)	4,5 (0,8)	0,54
RF, mean (SD)	141,7 (212,3)	226,0 (314,1)	137,2 (205,4)	0,30
ACPA, mean (SD)	156,4 (156,7)	198,3 (161,5)	154,2 (156,5)	0,31
MTX, mg/week, mean (SD)	16,5 (3,7)	16,2 (3,9)	16,5 (3,7)	0,74
MTX Response, n(%)	149 (49,5)	5 (33,3)	144 (50,3)	0,20
Withdrawal of MTX, n(%)	71 (23,6)	7 (46,7)	64 (22,4)	0,03
Deaths, n(%)	11 (3,6)	3 (20,0)	8 (2,8)	0001

**Conclusions:** ILD is a frequent and serious complication in RA. It appears more frequently in patients with previous pneumopathy and long-term disease and with extra-articular involvement of RA.

**Disclosure of Interest:** None declared

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**FRI0060 ARE OLDER RA PATIENTS FRAIL, OR LONELY AND DEPRESSED?**

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**Background:** The average rheumatoid arthritis (RA) patient has approximately 2 comorbidities, and this number increases with age. Both comorbidity and ageing are considered risk factors for frailty, a physiological syndrome characterised by reduced functional reserves and resistance to 'stressors' due to a cumulative decline of physiological and psychosocial systems. Frailty results in adverse health outcomes including hospitalisation and increased risk of mortality. The extent to which frailty is a relevant problem in elderly RA patients remains unknown.

**Objectives:** (1) To assess the prevalence of frailty and (2) to identify which factors are associated with frailty in elderly patients with RA.

**Methods:** Consecutive patients of the outpatient clinic were invited to participate in a study on ageing while ensuring equal representation of patients in three pre-defined age groups: 55–64, 65–74, and ≥75 years. Rheumatologists recorded the number of comorbidities. Patients rated their overall health on a visual analogue scale (0–100; 100 very bad health) and completed the validated Groningen Frailty Indicator (GFI), which contains 15 questions on the loss of functions and resources across 4 domains: physical (mobility functions, multiple health problems, physical fatigue, vision, hearing), cognitive (cognitive dysfunction), social (emotional isolation), and psychological (depressed mood and feelings of anxiety). Scores on items are dichotomized, "1"; indicating a problem or dependency. Prevalence of problems/dependency was compared among the 3 age-groups using a Kruskal-Wallis test. Characteristics of patients classified as frail (GFI score ≥4) or non-frail (GFI score <4) were compared using a chi-square test for categorical data or the independent samples t-test for continuous data.

**Results:** The prevalence of frailty across age groups was respectively 43.3%, 40.0% and 43.4%. Frail RA patients were more often female, had a lower subjective health status. Remarkable, patients classified as frail identified problems in the social and psychosocial domains. Of interest, there were no differences regarding age, polypharmacy, number of comorbidities, and cognitive domain (figure 1).

**Table 1** Comparison of demographics, clinical characteristics, and number of patients with problems/dependency per frailty domain between frail and non-frail elderly rheumatoid arthritis patients.

	Frail (n=38)	Non-frail (n=52)	p-value
<b>DEMOGRAPHICAL CHARACTERISTICS</b>			
Male	8 (21)	23 (42)	0.035
Age, mean (SD)	69.9 (9)	69.6 (7)	0.878
<b>CLINICAL CHARACTERISTICS</b>			
Patient global health (0–100), mean (SD)	45.7 (20)	34.5 (16)	0.004
Comorbidities, mean number (SD)	0.6 (1)	0.5 (1)	0.862
<b>FRAILTY DOMAIN SCORES</b>			
<b>Physical domain GFI; problem or dependency: n (%)</b>			
Grocery shopping	5 (13)	2 (4)	0.103
Walk outside the house	3 (8)	0 (0)	0.039
Getting (un)dressed	3 (5)	0 (0)	0.094
Visiting restroom	1 (3)	0 (0)	0.239
Vision	5 (13)	2 (4)	0.103
Hearing	6 (16)	6 (12)	0.558
Nutrition	6 (16)	1 (2)	0.015
Use of 4+ medication types	30 (79)	38 (73)	0.522
Subjective physical fitness	23 (61)	13 (25)	0.001
<b>Cognitive domain GFI; problem or dependency: n (%)</b>			
Memory complaints	10 (26)	6 (12)	0.070
<b>Social domain GFI; problem or dependency: n (%)</b>			
Emptiness	24 (63)	2 (4)	<0.001
Missing the presence of people around	25 (66)	4 (8)	<0.001
Feelings of loneliness	23 (55)	0 (0)	<0.001
<b>Psychosocial domain GFI; problem or dependency: n (%)</b>			
Feelings of depression	28 (74)	4 (12)	<0.001
Nervous or anxious feelings	22 (58)	8 (15)	<0.001

Data are presented as number (percentage) of patients unless stated otherwise.

**Conclusions:** Using validated questionnaires, frailty is highly prevalent in all RA patients older than 55 years and seems to be a distinctive health construct which is not necessarily related to increasing age, polypharmacy and comorbidity in patients with RA. An alternative explanation of our findings is that rheumatologists seem to miss symptoms of depression and loneliness among RA patients.

**Disclosure of Interest:** None declared

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**FRI0061 CARDIOVASCULAR RISK FACTOR AND DISEASE BURDEN IN BELGIAN PATIENTS WITH RHEUMATOID AND MUSCULOSKELETAL DISEASES OF NORTH AFRICAN COMPARED TO EUROPEAN DESCENT**

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**Background:** Patients with rheumatic and musculoskeletal diseases (RMDs) from developed populations often experience increased atherosclerotic cardiovascular disease (ACVD) risk. In European countries, increasing proportions of inhabitants originate in developing countries and are therefore reportedly at an earlier epidemiological transition stage, which is associated with reduced ACVD.<sup>1</sup>

**Objectives:** This study aimed to determine whether population origin specific cardiovascular risk management is indicated in Belgian patients with RMDs.

**Methods:** We recorded major conventional cardiovascular risk factors included in the Systematic Coronary Risk Evaluation (SCORE) or/and Framingham score equation, other conventional and non-conventional cardiovascular risk factor profiles and the prevalence of subclinical ACVD comprising arterial stiffness (pulse pressure >60 mmHg) and established ACVD (coronary artery disease, ischaemic cerebrovascular disease or/and peripheral artery disease) in 673 consecutive patients with RMDs; 126 and 547 were of North-African and European ancestry, respectively. Cardiovascular risk factors and disease were compared between patients of North African and European descent in multivariable logistic and linear regression models.

**Results:** Patients of North African descent tended to have less frequently inflammatory RMDs (OR (95% CI)=0.69 (0.45–1.04)) including rheumatoid arthritis (RA) (OR (95% CI)=0.46 (0.19–1.09)), and had more often fibromyalgia (OR (95% CI)=2.93 (1.84–4.65)). Patients of North African descent were younger than their European descent counterparts (mean (SD)=47.5 (14.7) vs 55.7 (16.5) years, p<0.0001). In age, sex and inflammatory RMD adjusted analysis, North African descent patients had less prevalent hypertension (OR (95% CI)=0.54 (0.33–0.87)) and more frequent diabetes (OR (95% CI)=3.69 (2.00–6.80)); North African descent patients exercised ((OR (95% CI)=0.34 (0.20–0.57)) and used alcohol (OR (95% CI)=0.05 (0.02–0.12)) less often, and had a less frequent family history of ACVD (OR (95% CI)=0.64 (0.41–0.99)), smaller body height (mean (SD)=1.64 (0.09) vs 1.66 (0.11) m, p<0.0001) and larger the Arthritis Impact Measurement Scales Depression score (mean (SD)=4.4 (1.9) vs 3.7 (2.0), p=0.009). These findings translated into a frequencies of having ≥1 major cardiovascular risk factor, overall 10 year high risk for any (Framingham score ≥20) and fatal (SCORE ≥5) ACVD, and prevalence of subclinical and established ACVD that were as large in RMD patients from North African compared to European descent. European League Against Rheumatism multiplier<sup>2</sup> application in patients with RA did not alter these findings.

**Conclusions:** Consistent disparities exist in ACVD risk factor profiles between RMD patients of North-African and European descent. However, the overall cardiovascular risk factor and disease burden is currently as large in RMD patients of North African compared to European ancestry. Adequate ACVD risk management in RMD patients should be performed irrespective of population origin.

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**FRI0062 CORTICOSTEROID INJECTION FOR PLANTAR HEEL PAIN: A SYSTEMATIC REVIEW AND META-ANALYSIS**

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**Background:** Plantar heel pain is one of the most common conditions affecting the foot in adults, with prevalence estimates between 4% and 7%.<sup>1,2</sup> Corticosteroid injection is a common intervention used to treat plantar heel pain,<sup>3</sup> however there is limited high quality evidence to support this practise. Because corticosteroid injection is frequently used for plantar heel pain, it is important that health professionals understand whether the evidence-base supports the use of this intervention.

**Objectives:** To conduct a systematic review and meta-analysis of the effectiveness of corticosteroid injection for pain and function in people with plantar heel pain.

**Methods:** Databases searched include Medline, CINAHL, SPORTDiscus, Embase and the Cochrane Library. Included studies had to be randomised trials that evaluated the effectiveness of corticosteroid injection on pain or function for plantar heel pain. The primary outcomes were pain (including 'first step' pain) and function, categorised as short (0 to 6 weeks), medium (7 to 12 weeks) or longer term (13 to 52 weeks). A secondary outcome was plantar fascia thickness. Mean differences or standardised mean differences and 95% confidence intervals were calculated. The Cochrane Collaboration tool for assessing risk of bias was used to assess trial quality, and the GRADE approach was used to assess the strength of evidence.

**Results:** A total of 37 trials (2200 participants) were included. In the short term, corticosteroid injection was more effective for reducing pain than autologous blood injection (SMD  $-0.56$  [ $-0.86, -0.26$ ]) and orthotic devices (SMD  $-1.20$  [ $-2.30, -0.11$ ]). There were no significant findings in the medium term. In the longer term, corticosteroid injection was less effective than platelet-rich plasma injection (SMD  $0.87$  [ $0.30, 1.45$ ]). For function, corticosteroid injection was more effective than physical therapy in the short term only (SMD  $-0.69$  [ $-1.31, -0.07$ ]). Notably, corticosteroid injection was not more effective than placebo injection for reducing pain in the short (SMD  $-0.98$  [ $-2.06, 0.11$ ]) and medium (SMD  $-0.86$  [ $-1.90, 0.19$ ]) terms. When trials considered to have high risk of bias were excluded, there were no significant findings.

**Conclusions:** Our review found that corticosteroid injection is more effective for reducing pain than some comparators, and more effective for improving function than physical therapy in the short term. Corticosteroid injection is more effective than platelet-rich plasma injection in the longer term. Corticosteroid injection is *not* more effective than placebo injection for reducing pain or improving function.

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**Disclosure of Interest:** None declared

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#### FRI0063 RAPAMYCIN INDUCES REMISSION IN PATIENTS WITH REFRACTORY RHEUMATOID ARTHRITIS

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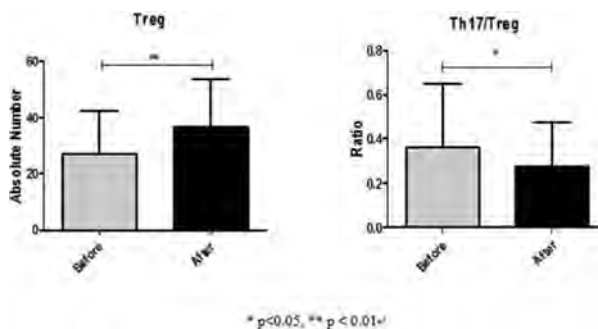
**Background:** Rheumatoid arthritis (RA) is a chronic inflammatory disease that results in destruction of joint cartilage and bone. However, many patients do not achieve satisfactory disease control by current therapy with high risk of adverse reactions. We have reported that absolute number of peripheral regulatory T (Treg) cells reduced in RA patients (EULAR Abstract). Moreover, rapamycin has been reported to inhibit differentiation of Th17 and promote growth of FoxP3 +Treg cells by inhibiting mTOR pathway<sup>[1]</sup>.

**Objectives:** To observe the therapeutic efficacy of rapamycin on the reduction of disease activity, increase in Tregs and decrease in Th17 to restore balance of Th17/Treg cells in RA patients with high disease activity (DAS28  $\geq 2.6$ ).

**Methods:** Fifty RA patients who treated with two kinds of DMARDs for more than half a year did not achieve remission (DAS28  $\geq 2.6$ ) were enrolled and were treated with rapamycin at a dose of 0.5 mg every 2 days for 24 weeks. The absolute number of CD4 +T cell subsets in peripheral blood from these patients were assessed by flow cytometry combined with internal standard beads before the treatment as baseline and at week 24 after treatment. Meantime, the DAS28, the dosage of corticosteroids and immunosuppressant were also recorded.

**Results:** Rapamycin treatment reduced the disease activity and induced remission (DAS28 < 2.6) in 44.9% of active RA patients. Their DAS28 was reduced from a median 2.9 (at week 0) to 1.9 (at week 24) ( $P < 0.001$ ) and the absolute number of peripheral Treg cells was increased from  $27.14 \pm 15.11$  cells/ $\mu$ l (at week 0) to  $36.59 \pm 17.23$  cells/ $\mu$ l (at week 24) ( $p = 0.002$ ). The ratios of Th17/Treg cells also had a significant decrease from  $0.36 \pm 0.29$  at baseline to  $0.27 \pm 0.20$  at week 24 ( $P < 0.041$ ). In contrast, the decrease in the absolute number of Th17 cells was not

statistically significant ( $p = 0.846$ ). After the treatment, the proportion of patients taking glucocorticoids decreased from 66.0% to 64.0% and the mean dosage of prednisone decreased from 9.89 mg/d to 7.70 mg/d. And the usages of DMARDs were also reduced ( $P < 0.001$ ).



**Conclusions:** Rapamycin combined with low level of conventional therapy effectively reduced disease activity and induced remission among RA patients who received long-term conventional treatment without remission (DAS28  $\geq 2.6$ ) by increasing the absolute number of Treg cells and restoring the balance of Th17 cells and Treg cells. As the research progresses, rapamycin is likely to become a promising therapeutic candidate.

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**Disclosure of Interest:** None declared

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#### FRI0064 RIGHT VENTRICLE DIASTOLIC DYSFUNCTION IN EARLY RHEUMATOID ARTHRITIS PATIENTS: RISK FACTORS AND THE EFFECT OF ANTIRHEUMATIC THERAPY

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**Objectives:** To determine the frequency of diastolic dysfunction of the right ventricle (RVDD) in patients (pts) with early rheumatoid arthritis (RA) prior to therapy with basic anti-inflammatory drugs (DMARDs), examine its relationship with traditional risk factors of cardiovascular disease and markers of inflammation, to study the effect of antirheumatic therapy administered in accordance with "treat to target" (T2T) principles on RVDD in early RA pts during 18 month follow-up.

**Methods:** A total of 66 pts with early RA (ACR/EULAR criteria, 2010) were included: 71% of women, age  $56^{46;61}$  years, disease duration  $6^{4;8}$  months; DAS28  $5.3$  [ $5.0;6.2$ ], positive for ACCP (100%)/RF (87%), without prior administration of DMARDs and glucocorticoides. All pts underwent blood pressure monitoring (BP), echocardiography, tissue Doppler imaging. Methotrexate (MT) therapy was started in all pts with an escalation of the dose up to 30 mg/week subcutaneously. In case of no remission 3 months later, MT was added with biologic therapy (BT): Adalimumab, Certolizumab pegol, Abatacept, Rituximab. After 18 months 29 (44%) pts achieved remission. Antihypertensive therapy was administered in 51 (77%) pts: ACE inhibitors, ARBs, beta-blockers, calcium antagonists, diuretics.

**Results:** At baseline RVDD was detected in 16 (24%) pts. RVDD related factors that remained associated on a multivariable forward stepwise linear regression analysis were body mass index (BMI) ( $\beta$ -coefficient (95% CI)  $0.3$  ( $-0.003; -0.008$ ), SDAI  $0.2$  ( $-0.009; -0.001$ ), carotid atherosclerosis (CA)  $0.2$  ( $-0.3; 0.01$ ), disease duration  $0.2$  ( $-0.02; 0.001$ ). Multiple coefficient of determination ( $R^2$ ) was 38% ( $p = 0.03$ ). After 18 months the incidence rate of RVDD decreased from 24% to 18%,  $p > 0.05$ . The dynamics of diastolic function was multidirectional. RVDD was normalised in 10 (63%) of 16 RA pts with RVDD ( $p = 0.02$ ). All of them had effective control of BP and achieved remission. 67% of pts with normalised RVDD received MT+BT. 5 (31%) pts with new cases of RVDD and 6 pts with preserved RVDD did not reach the target values of BP and RA remission.

**Conclusions:** Presence of CA, higher BMI, SDAI and disease duration strongly associated with the incidence rate of RVDD. A significant decrease of RVDD in case of achieved targeted BP values and RA remission was observed during 18 month therapy of early RA pts in accordance with "T2T" principles

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FRI0065

### DHCR7 AND GENETIC POLYMORPHISMS IN THE ASSOCIATION BETWEEN VITAMIN D AND LIPID PROFILE IN RA: NEW PLAYERS IN CARDIOVASCULAR DISEASE?

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**Background:** rheumatoid arthritis (RA) is associated with increased cardiovascular (CV) risk. Although vitamin D deficiency has been linked to CV disease in other conditions, studies in RA have yielded contradictory results and pointed to the involvement of additional factors. On the one hand, several genetic polymorphisms have been linked to vitamin D levels. Moreover, emerging evidence suggests a role for the enzyme DHCR7 in the crosstalk between cholesterol and vitamin D synthesis.

**Objectives:** to evaluate the effect of genetic polymorphisms and DHCR7 levels in the interaction between vitamin D and lipid profile in RA.

**Methods:** serum levels of vitamin D and DHCR7 were measured in 212 RA patients (2010 EULAR/ACR criteria) and 104 matched healthy controls (HC) by chemiluminescence and immunoassays, respectively. VDR rs2228750 and DHCR7 rs12785878 SNPs were studied by TaqMan Assays. The effect of vitamin D deficiency on clinical features was assessed by linear regression analyses adjusting for age, gender, seasonality, vitamin D supplementation and DMARD usage.

**Results:** decreased vitamin D was found in RA compared to HC ( $p < 0.001$ ), vitamin D deficiency ( $< 20$  ng/ml) being more prevalent in winter/spring (58/151, 38.4%) than in summer/autumn (12/61, 19.6%;  $p = 0.010$ ). Vitamin D levels were positively correlated to those of HDL ( $r = 0.217$ ,  $p < 0.001$ ), this association being restricted to patients with the rs2228750 AG/AA genotype ( $r = 0.287$ ,  $p = 0.003$ ) but not in those with the GG one ( $r = 0.082$ ,  $p = 0.531$ ). Equivalent results were obtained for total/HDL-cholesterol ratio. Vitamin D deficiency was associated with lower HDL ( $p = 0.040$ ), higher tender joint count ( $p = 0.003$ ), swollen joint count ( $p = 0.005$ ), DAS28 ( $p = 0.028$ ) and HAQ ( $p = 0.030$ ) in AG/AA-patients but not in those with the GG status (all  $p > 0.050$ ). Decreased DHCR7 levels were found between RA and HC in winter/spring ( $p = 0.008$ ) but not in summer/autumn ( $p = 0.116$ ). RA patients with CV disease exhibited lower DHCR7 levels ( $p = 0.012$ ) than their CV-free counterparts. Moreover, the associations among DHCR7, vitamin D and HDL levels followed a seasonal pattern: DHCR7 was correlated to vitamin D levels in summer/autumn ( $r = 0.441$ ,  $p = 0.004$ ), where vitamin D was associated with both HDL levels ( $r = 0.354$ ,  $p = 0.009$ ) and total/HDL ratio ( $r = -0.393$ ,  $p = 0.003$ ). A DHCR7 rs12785878-driven effect was observed for these associations. On the contrary, a weak correlation between HDL and vitamin D was found in winter/spring ( $r = 0.215$ ,  $p = 0.014$ ), where decreased DHCR7 was associated with age at onset ( $r = -0.285$ ,  $p = 0.006$ ) and RF titre ( $r = -0.326$ ,  $p = 0.013$ ).

**Conclusions:** the effect of vitamin D on the lipid profile is dependent on genetic polymorphisms. DHCR7 has a pivotal role in the interaction between vitamin D and lipid profile in RA. Seasonality and DHCR7-HDL axis may be novel mediators in the CV disease in RA.

**Disclosure of Interest:** None declared

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FRI0066

### IMPACT OF SERUM ADIPOKINES IN EARLY STAGES OF RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is a systemic chronic inflammatory disease. Adipose tissue is regarded as an active endocrine organ producing adipokines such as leptin and adiponectin, and some proinflammatory cytokines which have proinflammatory properties that account for chronic low-grade systemic inflammation

**Objectives:** To investigate the levels of adipokines in eRA and establish their association with the state of rheumatic condition

**Methods:** Cross sectional study was conducted. 51 patients with eRA according to the ACR/EULAR 2010 criteria and 51 healthy controls matched by age and gender, were included. A complete medical history was obtained. Adiponectin levels measured by Luminex technology, IL6 by chemiluminescence and Iptin by Enzyme-linked immunosorbent assay. Serum markers of RA such as rheumatoid factor, erythrocyte sedimentation rate(ESR), C reactive protein(CRP), and anticitrullinated protein antibodies-APCA IgG/IgA. Disease activity was evaluated by

DAS28CRP, DAS28ESR, CDAI, SDAI and RAPID3, the functional status using Multidimensional health assessment questionnaire(MDHAQ) and radiological status by Simple Erosion Narrowing Score(SENS). An association analysis was made to evaluate the relationship between adipokines levels and rheumatologic conditions using X2 test, Mann Whitney and logistic regression model was performed to confirm this associations. All the results were performed with a level of significance of 95%

**Results:** In the eRA group, 80.39% were women, the mean age was 48.54  $\pm$  10.93 years. 37.25% had overweight and 13.72% had obesity Among the controls, 80.39% were women, with the mean age of 48.55  $\pm$  11.07 years. 27.45% had overweight and 5.88% had obesity. 45.09% moderate activity and 17.64% high activity by DAS28ESR. High leptin levels were found in 64.7% vs 23.5% in healthy controls ( $p = 0.001$ ). High adiponectin levels was found associated to BMI  $< 25$  ( $p = 0.017$ ) and high leptin level to BMI  $> 25$  ( $p = 0.038$ ) and disease activity by RAPID3 ( $p = 0.039$ ). The presence of joint space narrowing in hands was associated with low adiponectin levels ( $p = 0.044$ ). The association of leptin levels  $> 1.67$  ng/mL with the diagnosis of RA was maintained in the model adjusted for the presence of *P. gingivalis*, DAS28-ESR, CRP  $> 3$  mg/L, economic status and BMI  $> 30$ , OR = 2.79 95% CI (1.54–5.07). The presence of high leptin and IL6 levels and low level adiponectin at the same time were more frequently found in the female gender ( $p = 0.047$ ), primary schooling ( $p = 0.050$ ), BMI  $> 30$  ( $p = 0.023$ ), patients with radiological damage SENS  $> 3$  ( $p = 0.047$ ) and were found associated at the same time to MDHAQ  $> 3$ , BMI  $> 25$  and RAPID3  $> 12$  (OR 5.03 95% CI 1.05–24) adjusted to clinical variables

**Conclusions:** The role of adipokines as the leptin could be considered to be the bridge between immune tolerance, metabolic function and autoimmunity and suggests the possibility to use circulating levels of adipokines as potential biomarkers of disease activity and functional status in early stage of rheumatoid arthritis

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**Disclosure of Interest:** None declared

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FRI0067

### TRENDS IN THE INCIDENCE OF FELTY'S SYNDROME IN PATIENTS WITH RHEUMATOID ARTHRITIS IN SPAIN: AN OBSERVATIONAL COHORT STUDY OF HOSPITAL DISCHARGES FROM 1999 TO 2015 (TREND-AR STUDY)

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**Background:** Felty's syndrome (FS) is an infrequent entity related to Rheumatoid Arthritis (RA) but it's unknown the trend of FS in Spain.

**Objectives:** To analyse the incidence and trend of hospital admissions for FS in RA patients in Spain from 1999 to 2015.

**Methods:** We performed an observational retrospective population study analysing the spanish administrative database that includes a Minimum Basic Data Set (MBDS) of hospital admissions of RA patients from 1999 to 2015. We selected the MBDSs for FS. Cases were identified by the presence in primary and secondary diagnosis of its ICD9 code. The population at risk was estimated with an estimated prevalence of RA of 0,5% (0,8% women and 0,2% men). Crude and adjusted rates were calculated, and the trend was analysed using the Generalised Linear Model (GLM) with the year as the analysis variable. SPSS version 20 (SPSS Inc, Chicago, IL) was used.

**Results:** 338.343 RA hospital admissions were detected, being 802 (0,2%) due to FS, 455 (56,7%) women and 347 (43,3%) men. Mean age was 67,94(SD 13,76). There were 61 (7,6%) deaths. Age-adjusted rate during the period was 42,19/10<sup>5</sup> inhab. per year (19,76 women and 64,61 men). FS age-adjusted rate decreased from 25,90/10<sup>5</sup> inhab. per year in 1999 to 17,20 in 2015, both women (12,85 in 1999 to 11,75 in 2015) and men (80,15 in 1999 to 38,75 in 2015). An annual decrease in the FS rate of 0,5% is estimated (RRI 0,995; CI 95% 0,976–1,014).

**Conclusions:** In Spain FS hospital admissions in patients with RA decreased between 1999–2015 with an estimation of 0,5% annual reduction not statistically significant.

**Disclosure of Interest:** None declared

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### FRI0068 ULTRASONOGRAPHIC SUBCLINICAL CARDIOVASCULAR FINDINGS IN HISPANIC RA PATIENTS: A CASE-CONTROL STUDY

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**Background:** Patients with RA have a 1.5–2.0 fold increased risk of developing coronary artery disease (CAD) compared with the general population. Patients with RA are typically managed by several physicians, and coordination of care may be suboptimal.<sup>1</sup> The leading cause of death in RA-patients is atherosclerotic cardiovascular disease (ASCVD).<sup>2</sup> Carotid artery and heart evaluation by ultrasound is a useful tool for detection of cardiovascular conditions.

**Objectives:** To compare the presence of subclinical cardiovascular conditions among Mexican-mestizo RA patients and matched controls.

**Methods:** Design: Observational, cross-sectional, case-control study. Patients of 40 to 75 years old who fulfilled the 2010 ACR/EULAR and/or the 1987 ACR classification criteria for RA were consecutively enrolled. Patients with previous ASCVD or any other rheumatic disease were excluded. Two board-certified radiologist performed and assessed all carotid ultrasounds (cUS) and two board-certified cardiologist performed and assessed transthoracic echocardiography (TTE) according to guidelines of the American Society of Echocardiography. ASE, 2016

**Results:** The RA patients showed higher prevalence of cardiovascular risk conditions with respect to control population, such as concentric remodelling/hypertrophy, diastolic dysfunction, valve regurgitation and Carotid intima media thickness (CIMT) (See table 1).

**Abstract FRI0068 – Table 1.** Ecographic cardiovascular pathological conditions among RA patients.

Ecographic findings	RA n=50 (%)	Controls n=50 (%)	P	O.R. (C.I. 95%)
Valve regurgitation, n (%)	42 (84)	32 (64)	0.023	2.93 (1.14-7.64)
Aortic, n (%)	4 (8)	3 (6)	0.999*	1.36 (0.28-6.42)
Tricuspid, n (%)	41 (82)	29 (58)	0.009	3.29 (1.32-8.23)
Mitral, n (%)	37 (74)	29 (58)	0.091	2.06 (0.88-4.80)
Moderate, n (%)	4 (8)	0 (0)	0.126*	0.92 (0.84-0.99)
Mitral, n (%)	28 (56)	6 (12)	0.0001	9.30 (3.36-25.87)
Pulmonary, n (%)	4 (8)	2 (4)	0.046	4.57 (0.91-22.73)
Diastolic dysfunction, n (%)	24 (48)	16 (32)	0.002	3.46 (1.52-7.90)
LVEF, n (%)	13 (26)	6 (12)	0.074	2.50 (0.89-7.44)
LVH, n (%)	5 (10)	1 (2)	0.092	5.40 (0.61-48.39)
LVEF/LVH, n (%)	18 (36)	8 (16)	0.017	3.09 (1.19-7.99)
Mass index (kg/m <sup>2</sup> ), mean ± SD	66.73 ± 17.40	75.11 ± 22.49	0.132	1.01 (-1.67-1.93)
LVEF (%), mean ± SD	60.14 ± 12	63.42 ± 67	0.004	1.12 (-5.49-1.06)
GLS (%), mean ± SD	-20.73 ± 9.0	-21.02 ± 4.8	0.639	0.96 (-0.96-1.56)
TAPSE (mm), mean ± SD	23.01 ± 4.1	24.06 ± 12	0.193	1.05 (-2.6-0.34)
CAWH, n (%)	21 (42)	10 (20)	0.017	2.80 (1.16-7.05)
Carotid plaque, n (%)	11 (22)	10 (20)	0.806	1.12 (0.43-2.95)

P (P value) O.R. (Odds ratio) C.I. (Confidence interval) LVCR (Left ventricle concentric remodeling) LVH (Left Ventricle hypertrophy) LVEF (Left ventricle ejection fraction) GLS (Global longitudinal strain) TAPSE (Tricuspid annular plane systolic excursion) CAWH (Carotid artery wall hypertrophy) SD (Standard deviation) \* (Yates continuity correction)

**Conclusions:** This study reinforces the usefulness of cUS and TTE as a tool in the evaluation of cardiovascular conditions in RA patients. A systematic search of extra-articular and cardiovascular comorbidities should be mandatory in all RA patients.

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### FRI0069 DIFFERENCE OF CLINICAL IMPLICATION REGARDING THE NUMBERS OF AUTOANTIBODIES AT PRESENTATION IN KOREAN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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**Background:** Epitope spreading occurs prior to the clinical diagnosis of rheumatoid arthritis (RA), the number of peptide recognised and its titer increases remarkably as becoming close to the clinical diagnosis. However, the effect of multiple autoantibodies on the clinical outcome is not well known.

**Objectives:** This study is to investigate the association between the number of autoantibodies at presentation and the clinical aspects in Korean patients with early RA.

**Methods:** The number of baseline autoantibody (rheumatoid factor, anticitrullinated peptide antibodies (ACPA), and anti-carbamylated protein antibodies (anti-CarP)) was analysed in the Korean Intensive Management of Early Rheumatoid Arthritis (KIMERA) cohort. All patients were disease-modifying antirheumatic drug (DMARD)-naïve RA patients with symptom duration less than 1 year. They were intensively treated by adjusting medications every 4 weeks, and treated to target as DAS28 of <2.6. Patients were classified regarding the number of autoantibodies and clinical characteristics were compared between the groups.

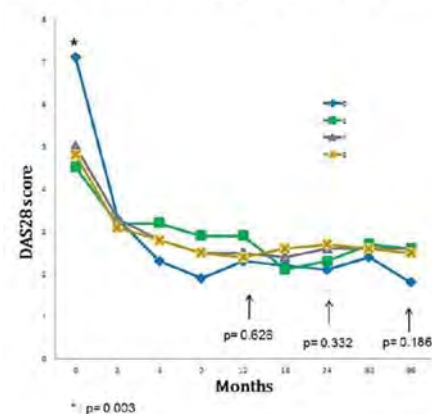
**Results:** A total of 128 patients were included, seronegative patients showed higher baseline physician global VAS (7.3 vs 4.7 vs 4.6 vs 4.4, p=0.005) and DAS28-ESR (7.1 vs 4.5 vs 5.0 vs 4.7, p=0.003) than patients with 1, 2, and 3 autoantibodies. Also seronegative patients showed a trend to have higher baseline HAQ score and pain VAS. After intensive treatment, there were no differences in remission rate and DAS28-ESR at 12, 24, and 36 months.

**Abstract FRI0069 – Table 1.** Disease characteristics regarding number of autoantibodies

Variables	0 (n=5)	1 (n=13)	2 (n=58)	3 (n=52)	p-value
Age, years	58.2±16.2	46.4±12.4	52.8±12.9	48.2±13.5	0.104
Female sex, N (%)	5 (100%)	7 (53.8%)	44 (75.9%)	44 (84.6%)	0.062
Symptom duration, days	7.0±4.8	10.2±12.1	10.5±16.0	8.1±7.5	0.736
BMI (kg/m <sup>2</sup> )	24.1±4.2	21.7±1.9	23.0±2.9	23.0±3.1	0.508
ESR (mm/hour)	59.0±15.8	44.4±17.6	56.8±32.0	57.9±32.2	0.543
CRP (mg/L)	20.9±17.3	13.6±26.9	19.0±29.4	12.9±15.7	0.559
HAQ score	1.4±0.5	0.6±0.6	0.7±0.6	0.7±0.6	0.092
Pain VAS	7.6±0.9	4.0±2.0	4.5±2.7	4.4±2.9	0.073
Patient global VAS	7.3±1.7	4.7±2.2	4.6±2.5	4.4±2.7	0.127
Physician global VAS	7.0±0.9	4.9±1.1	5.5±1.2	4.5±1.6	0.005
DAS28-ESR	7.1±0.6	4.5±1.2	5.0±1.4	4.7±1.4	0.003

Values are expressed as means±standard deviation or N (%). BMI, body mass index; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; HAQ: health assessment questionnaire; VAS, visual analogue scale; DAS, disease activity score

### Changes in DAS28 according to number of autoantibodies



**Conclusions:** Seronegative patients showed higher levels of baseline inflammation than seropositive patients. However, they had favourable treatment response with rapid improvement which resulted in excellent clinical outcome.

**Disclosure of Interest:** None declared

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FRI0070

### COST-EFFECTIVENESS OF BIOLOGIC AGENTS FOR RHEUMATOID ARTHRITIS WAS SUPERIOR TO TRADITIONAL/CONVENTIONAL DMARDs WHEN ANALYSED WITH NUMBER NEEDED TO TREAT(NNT) METHOD

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**Background:** Recently biologic agents are widely used for patients with rheumatoid arthritis (RA). Biologic agents are reported to have higher effectiveness than other disease-modifying anti-rheumatic drugs (DMARDs) including methotrexate (MTX), however, those new agents are more expensive.

**Objectives:** This study evaluated the cost-effectiveness of biologic agents for RA using number needed to treat (NNT) method. NNT is an index for determining the number of patients who need to be treated in order to reach a patient toward to clinical goal when a new treatment is introduced.

**Methods:** Fifty-three patients with RA was included in this study. These patients were introduced biologic agents between September 2012 to <sup>March 2017</sup> and continued same agent up to 24 weeks. NNT was calculated based on disease activity score (DAS28-ESR) and clinical disease activity index (CDAI) at 24 weeks. Ninety-four patients were investigated as a control group who treated with DMARDs. In addition, actual healthcare cost including doctor's fee, laboratory examination, prescription fee, and cost of biologic agents in each patient were calculated based on hospital's medical receipt, then averaged and compared between two groups.

**Results:** In biologic group, tocilizumab (TCZ) were used for 20 patients, golimumab (GLM) for 14 patients, etanercept (ETN) for 13 patients, and other biologics for six patients. In control group, 66 patients administered MTX and/or conventional DMARDs (csDMARDs), and 28 patients administered only csDMARDs. In biologic group, 53 patients (79.2%) achieved remission in DAS28-ESR, and 24 patients (45.2%) achieved remission in CDAI. On the other hand, the rate of remission was 61.7% and 23.4% respectively in control group. NNT was 1.26 (DAS28) and 2.21 (CDAI) in biologic group, and 1.62 and 4.27 respectively in control group. In biologic group, NNT based on DAS28-ESR of each agent was 1.11 of TCZ, 1.30 of ETN, 1.40 of GLM, and 1.50 of others (table 1). The total actual healthcare cost in the study period was 7,812.5 Euro (1044066 JPY; 1 Euro=133.6 JPY, in December 2017) in biologic group and 583.8 Euro (78020 JPY) in control group.

	Number	Ave. DAS28-ESR	Remission	ARR	NNT
Biologic group	53	1.92	42	0.79	1.26
TCZ	20	1.58	18	0.90	1.11
GLM	14	2.10	10	0.71	1.40
ETN	13	2.05	10	0.77	1.30
others	6	2.56	4	0.67	1.50
Control group	97	2.39	58	0.62	1.62
MTX	66	2.30	41	0.61	1.61
csDMARDs	28	2.63	17	0.61	1.65

	Number	Ave. CDAI	Remission	ARR	NNT
Biologic group	53	4.31	24	0.45	2.21
TCZ	20	2.94	11	0.55	1.82
GLM	14	5.10	5	0.36	2.80
ETN	13	4.52	7	0.54	1.86
others	6	6.58	1	0.17	6.00
Control group	94	5.43	22	0.23	4.27
MTX	66	5.19	16	0.24	4.13
csDMARDs	28	6.00	6	0.21	4.67

**Conclusions:** The total actual health care cost of biologic group was much higher than DMARDs group, however, the cost-effectiveness of biologics was superior to DMARDs from the stand point of NNT.

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FRI0071

### OUTCOMES FROM RHEUMATOLOGY AND REPRODUCTIVE HEALTH CLINIC 2013–2016

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**Background:** A multidisciplinary approach to pregnancy in women with rheumatic diseases will ensure best outcomes for mother and baby.<sup>1</sup>

**Objectives:** In 2013, we developed a dedicated nurse-led multidisciplinary Rheumatology Reproductive Health Clinic (RRHC) in order to provide a multidisciplinary service.

**Methods:** 98 women attended the RRHC from January 2013–16. They were prospectively assessed for age, diagnosis, medications, use of assisted reproductive technology (ART) and pregnancy outcomes.

**Results:** The mean (range) age was 35 years.<sup>19–48</sup> The majority of patients had rheumatoid or psoriatic arthritis. The characteristics of the patients is summarised in table 1 and their outcomes in table 2. 24 women were on a biologic DMARD therapy at the time of conception. 10 discontinued in the first semester and 5 in the second trimester. 9 continued throughout their pregnancies. 90% of women surveyed were "very satisfied" with the physical and emotional support received in the clinic.

Abstract FRI0071 – Table 1. Patient Characteristics

Diagnosis	Number of Patients
Rheumatoid Arthritis	41
Psoriatic Arthritis	16
Ankylosing Spondylitis	3
Systemic Lupus Erythematosus	2
Juvenile Idiopathic Arthritis	2
Chronic Regional Pain Syndrome	2
Giant Cell Arteritis	1
Reactive Arthritis	2
Behcet's Disease	2
Sicca Syndrome	2
Takayasu's Arteritis	2
Raynaud's Syndrome	2
Fibromyalgia Syndrome	2
Sarcoidosis	1
Mixed Connective Tissue Disease	1
Systemic Sclerosis	1
Total	98

Abstract FRI0071 – Table 2. Outcomes

Outcome	Number of Patients
Information gathering only	10
Pregnancy achieved	62
Using Assisted Reproductive Technology	3
Actively trying to conceive	26
Total number of pregnancies	68
Births	76
Mothers who had one birth only	49
Mothers who had two births (including one set of twins)	27
1st trimester pregnancy loss	11
2nd trimester pregnancy loss	1
Neonatal death (fetal aplasia diagnosed in utero)	1
Breastfeeding continued to 6 week postpartum review	21
Total number of women	98

**Conclusions:** This is the first report of results from a multidisciplinary RRHC. These data show high levels of successful pregnancy outcomes and patient satisfaction.

The majority of patients had an inflammatory arthritis. Successful pregnancy outcomes were achieved in 70% of women actively trying to conceive. 38% of



patients on biologic DMARDs continued these throughout pregnancy. There were comparable miscarriage rates observed when compared with the general population (14% versus 20%).<sup>2</sup> Breastfeeding rates were low at 28% compared to the figure of 55% for the general population in Ireland.<sup>3</sup> Most patients were "very satisfied" with the service.

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**FRI0072 THE IMPACT OF ANTI-TNF-THERAPY ON ENDOTHELIAL FUNCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS OR ANKYLOSING SPONDYLITIS**

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**Background:** Increased mortality in chronic rheumatic diseases is mostly attributed to cardiovascular events (CVE). Assessment of endothelial dysfunction can help to identify patients at risk for major CVE. Studies have shown that the underlying endothelial dysfunction in rheumatoid arthritis is closely associated with inflammation. Only limited information is available whether the blockade of TNF $\alpha$  can restore endothelial function.

**Objectives:** To investigate parameters of endothelial function before and after initiation of immunosuppressive therapy (anti-TNF-therapy or methotrexate) in patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) or ankylosing spondylitis in an open-label, prospective study.

**Methods:** Patients with active RA, PsA or SpA were eligible for inclusion with active disease and when new treatment with sDMARD (methotrexate) or bDMARD (anti-TNF-therapy) was started. Study visits were performed at baseline, at 3 and at 12 months. Clinical disease activity and inflammation marker were obtained. Systemic Coronary Risk Evaluation (SCORE) and measurement of intima media thickness (IMT) were performed to assess baseline cardiovascular (CV) risk. Endothelial function was measured as arterial dilatation (artFD), arterial constriction (artFIC) and venous dilatation (venFD) in response to flicker light by dynamic vessel analysis (DVA; IMEDOS) and by peripheral arterial tonometry (EndoPAT) as reactive hyperemia index (RHI). For the primary endpoint, we analysed the endothelial function before and during treatment (month 12). Secondary endpoints were ACR20/50 response for RA and PsA and ASAS20 response for SpA. A comparison was made for changes in endothelial function in responder and non-responder to immunosuppressive treatment.

**Results:** 62 patients (37 RA, 13 PsA, 14 SpA) were included (mean age 51.3  $\pm$  14.9 years, 46.8% females). The mean ten-year risk of fatal cardiovascular disease (SCORE) was estimated with 2.2% (95%CI: 1.5–3.0). Mean IMT was 0.59  $\pm$  0.13 mm. Treatment was initiated with etanercept (n=21), certolizumab (n=10), infliximab (n=2), adalimumab (n=13), golimumab (n=4) or methotrexate (n=12). Response to treatment after 3 (n=57) and 12 months (n=32) measured by ACR20/50 (RA and PsA) and ASAS20 (SpA) was found in 33.3/16.7% and 57.2% (month 3) and 29.2/20.8% and 50.0% (month 12). ArtFD increased (3.1% $\pm$ 2.8% to 4.0  $\pm$ 3.2%; p<0.05), while artFIC and venFD remained unchanged (-0.3 $\pm$ 1.6% to -0.2 $\pm$ 2.1%; p=0.613, 3.7 $\pm$ 3.0% to 3.9% $\pm$ 2.2%; p=0.383). RHI did not change (1.9% $\pm$ 0.5% to 1.8 $\pm$ 0.5%; p=0.166). There were no differences in changes of endothelial function between responder and non-responder to immunosuppressive therapy or between anti-TNF-therapy and methotrexate.

**Conclusions:** Our data indicate, that patients with active RA, PsA or SpA are at risk for cardiovascular events. Immunosuppressive treatment can improve endothelial function at retinal arteries but has no effect on reactive hyperemia index at peripheral arteries. The effect of immunosuppressive treatment on parameters of endothelial function was not different in responders or non-responders and did not depend on whether the patients were treated with anti-TNF-therapy or methotrexate.

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**FRI0073 CHANGES OF BONE MINERAL DENSITY OVER 10 YEARS IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS**

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**Background:** Patients with Rheumatoid Arthritis (RA) have been shown to have an increased risk of osteoporosis and fractures. Most studies on RA and osteoporosis are cross-sectional. There are very few studies on changes in bone mineral density (BMD) over time.

**Objectives:** To study changes in BMD in men and women with early RA over a period of ten years.

**Methods:** An inception cohort of consecutive patients with early RA (n=233, symptom duration <12 months), recruited 1995–2005, was investigated. Patients were followed according to a structured program, including dual-energy X-ray absorptiometry (DXA) of the left femoral neck and the lumbar spine (L2-L4) at inclusion and after 2, 5 and 10 years. Z-scores (standard deviations above or below the mean BMD for the given age and sex) were calculated using a cohort of healthy individuals from the same area as a reference population. The mean Z-score over the study period was estimated using mixed linear effect models. Changes in Z-scores between follow-up visits were analysed using the paired T-test. Data are presented as mean (95% confidence interval (CI)).

**Results:** At inclusion, 219 patients were examined with DXA. The corresponding numbers at 2, 5 and 10 years were 196, 172 and 121. Among those with baseline DXA data, mean age was 60 years, mean symptom duration 7.4 months and 70% were women. Men were older (mean age 63 vs 59 years) and more often treated with corticosteroids (49% vs 35%) than women at inclusion. The majority of men and women were on disease modifying anti-rheumatic drugs (86% vs 81%). More women were treated for osteoporosis (bisphosphonates and/or calcium and vitamin D) and of the women, 16% were on oestrogen at inclusion.

At the femoral neck, the mean Z-score over 10 years of time was -0.07 (-0.22; 0.08) in women and -0.33 (-0.57; -0.08) in men. Men had significantly lower BMD at the femoral neck than expected by age at inclusion (estimated by the intercept Z-score value -0.35; 95% CI -0.61; -0.09), whereas there was no significant overall change in Z-score over time in men or women. At the lumbar spine, the mean Z-score for women was 0.06 (-0.10; 0.21) and for men -0.05 (-0.29; 0.19). There was a significant increase in Z-scores at the lumbar spine over time in both groups (change/year 0.04 (0.03; 0.05) in women and 0.02 (0.00; 0.05) in men).

The paired comparisons of BMD at different follow-up visits are shown in table 1. In the femoral neck, Z-scores for men decreased significantly from inclusion to the 5 year follow-up visit. After 5 years, no further reduction was seen. Lumbar spine BMD Z-scores increased in both men and women over the study period.

**Abstract FRI0073 – Table 1.** Bone mineral density (femoral neck and lumbar spine – L2-L4) in the early RA cohort, by sex. Pairwise comparisons of different follow-up visits.

L2-L4	Comparison	Patients with data at follow-up 2 years		Patients with data at 5 years		Patients with data at 10 years		Patients with data at inclusion and 2 years		Patients with data at inclusion and 5 years		Patients with data at inclusion and 10 years	
		n	CI	n	CI	n	CI	n	CI	n	CI	n	CI
Women	Z score mean	0.04	0.00	0.12	0.26	0.42	0.80	0.00	0.20	0.29	0.56	0.00	0.16
	95% CI	-0.13; 0.21	-0.07; 0.13	-0.08; 0.30	0.07; 0.45	0.13; 0.62	0.39; 0.85	-0.11; 0.27	0.09; 0.49	0.02; 0.42	0.34; 0.77	-0.11; 0.27	0.09; 0.49
	Mean change (95% CI)	0.01 (-0.01; 0.11)		0.14 (0.02; 0.25)		0.18 (0.01; 0.34)		0.20 (0.04; 0.31)		0.20 (0.11; 0.29)		0.20 (0.11; 0.29)	
Men	Z score mean	-0.12	-0.08	-0.19	-0.33	-0.33	-0.61	-0.18	-0.11	-0.48	-0.6	-0.18	-0.48
	95% CI	-0.19; 0.11	-0.17; 0.15	-0.41; 0.09	-0.47; 0.14	-0.67; 0.01	-0.41; 0.38	-0.46; 0.14	-0.41; 0.19	-0.83; -0.32	-0.42; 0.01	-0.46; 0.14	-0.41; 0.19
	Mean change (95% CI)	-0.08 (-0.24; 0.12)		-0.09 (-0.25; 0.07)		-0.23 (-0.39; 0.01)		-0.23 (-0.39; 0.01)		-0.47 (-0.58; -0.34)		-0.47 (-0.58; -0.34)	
NECK	Z score mean	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	95% CI	-0.19; 0.11	-0.19; 0.11	-0.19; 0.11	-0.19; 0.11	-0.19; 0.11	-0.19; 0.11	-0.19; 0.11	-0.19; 0.11	-0.19; 0.11	-0.19; 0.11	-0.19; 0.11	-0.19; 0.11
	Mean change (95% CI)	-0.08 (-0.24; 0.12)		-0.08 (-0.24; 0.12)		-0.08 (-0.24; 0.12)		-0.08 (-0.24; 0.12)		-0.08 (-0.24; 0.12)		-0.08 (-0.24; 0.12)	
Men	Z score mean	-0.13	-0.12	-0.12	-0.12	-0.11	-0.10	-0.11	-0.11	-0.11	-0.11	-0.11	-0.11
	95% CI	-0.21; 0.01	-0.19; 0.01	-0.20; 0.01	-0.19; 0.01	-0.19; 0.01	-0.19; 0.01	-0.19; 0.01	-0.19; 0.01	-0.19; 0.01	-0.19; 0.01	-0.19; 0.01	-0.19; 0.01
	Mean change (95% CI)	-0.04 (-0.20; 0.11)		-0.04 (-0.20; 0.11)		0.11 (-0.07; 0.30)		0.11 (-0.07; 0.30)		0.11 (-0.07; 0.30)		0.11 (-0.07; 0.30)	

**Conclusions:** In this study of patients with early RA, men had low femoral neck BMD at study start and kept losing bone mass during the first 5 years of follow up. Lumbar spine BMD Z-scores in both women and men increased significantly over the study period. Potential explanations for the low femoral neck BMD in men include exposures that may predispose to both RA and low BMD, such as smoking and low androgen levels. The increasing lumbar spine BMD could be due to more extensive anti-osteoporotic treatment compared to the reference population, and possibly more artefacts, such as extensive aortic calcification or degenerative spinal changes, in patients with RA.

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FRI0074

### FACTORS ASSOCIATED WITH THE DEVELOPEMENT OF SEVERE RESPIRATORY INFECTIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS INCLUDED IN A VACCINATION PROGRAM

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**Background:** Rheumatoid arthritis (RA) patients are at increased risk of severe infections. Besides the disease itself, the immunosuppressive treatment appears to play an important role in the risk of infections. Vaccination programs are designed to decrease the risk of infections in these patients.

**Objectives:** Our aim was to assess the incidence of severe respiratory infections in patients with RA and to determine the underlying risk factors for the development of these complications.

**Methods:** Retrospective study of 401 patients diagnosed with RA who were invited to participate in a vaccination program from October 2011 to October 2016. The follow-up was made until June 2017 with a minimum follow-up period of 8 months and maximum of 5.5 years.

Information on severe respiratory infection episodes was retrieved from the hospital medical records. Serious infections were defined as those that required hospitalisation or at least one dose of intravenous antibiotic treatment at the emergency room.

Only 7 patients refused vaccination (2%). Information was not obtained in 4 of the remaining 394 patients. Therefore, these 4 patients were not included in the assessment.

**Results:** 390 patients (307♀/83 ♂) average age 61.28±12.9 years were vaccinated a followed-up. The main features at the time of vaccination were: median disease duration (4 years), positive rheumatoid factor (56.7%), subcutaneous nodules (4.9%), erosive arthritis (36.9%), pulmonary fibrosis (3.8%), Sjögren syndrome (5.1%) other extraarticular manifestations (14.6%) and rheumatoid vasculitis (5.6%). Most patients had received immunosuppressive drugs before the vaccination program. The most frequently used were systemic corticosteroids (n=228), methotrexate (n=362) and biologic agents (40.3%).

During the follow-up, 42 patients (10.7%) had required hospital admissions due to infections, 17 of them were severe respiratory infections (4.35%) The remaining 25 admissions were in the setting of urinary tract infections (n=12), intraabdominal infections (n=7), skin and soft tissues (n=12) and articular (n=1). Also 12 of these patients had a zoster herpes.

The presence of anti-citrullinated protein antibodies (ACPA) was associated with an increased frequency of admissions due to these infections. It was also the case for the presence of a history of biologic therapy prior to vaccination. No association of severe respiratory infection with rheumatoid factor, erosions or pulmonary fibrosis was found. (table 1).

Abstract FRI0074 – Table 1

Admission for severe respiratory infections (CI 95%)	Crude OR (CI 95%)	p	Adjusted OR* (CI 95%)	p
RF positivity	2.13 (0.67-6.83)	0.2011	2.26 (0.69-7.84)	0.1799
ACPA positivity	3.73 (1.04-13.43)	0.0441	4.49 (1.2-16.83)	0.0259
Erosions	2 (0.71-5.64)	0.1896	2.16 (0.75-6.25)	0.1573
Rheumatoid vasculitis	1.48 (0.40-5.42)	0.5527	1.38 (0.37-5.22)	0.6336
Pulmonary fibrosis	4.27 (0.87-20.91)	0.2932	2.45 (0.46-13.05)	0.2932
Biologic treatment before vaccination	3.02 (1.01-9.02)	0.0476	2.61 (0.85-8.07)	0.0947

\*adjusted by age and sex

**Conclusions:** Vaccinated patients with RA present a low incidence of severe respiratory infections. Positivity for ACPA and the use of biologics prior to vaccination are associated with increased risk of severe respiratory infections in these patients. Therefore, vaccination should be performed prior to the onset of biologic treatment.

**Disclosure of Interest:** None declared

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FRI0075

### RISK OF HEPATITIS B INFECTION REACTIVATION IN RHEUMATIC DISEASES PATIENTS TREATED WITH ANTI-CD20 THERAPY

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**Background:** It has been widely established that the risk of hepatitis B reactivation is high in haematological patients receiving ANTI-CD20 therapy. For these patients the use of prophylaxis with antiretroviral drugs is recommended, and the same approach is also advocated in patients affected with rheumatic diseases, although the real risk seems to be lower.

**Objectives:** To evaluate the risk of HBV infection reactivation in patients with rheumatic diseases undergoing treatment with ANTI-CD20 therapy.

**Methods:** Retrieved data including demographical, therapeutic and clinical features as well as serological data were collected in 92 patients with different rheumatic diseases who underwent treatment with ANTI-CD20 from January 2009 to December 2016. Occult HBV infection at baseline (HBsAg negative, anti-HBcAg positive with or without anti-HBsAg and undetectable HBV-DNA) was observed in 25 patients (18 rheumatoid arthritis, 4 vasculitis, 2 systemic sclerosis and 1 dermatomyositis), none of them was treated with antiretroviral prophylaxis. HBV-DNA value was recorded at least every year, whereas HBsAg together with anti-HBsAg every six months and ALT every three months.

**Results:** During the whole observation period (mean time 39.28±26.6 months) none of the 25 patients (mean age 58.64±8.58 years; 68% women) had hepatitis B reactivation or HBsAg seroreversion. During the evaluated period 2 patients dropped out therapy, 1 stopped treatment for adverse event and 1 for ineffectiveness. After 70 months of therapy 1 patient presented low fluctuation of HBV-DNA title (13 IU/ml), that spontaneously returned negative after 3 months without therapeutic changes. In addition 1 patients shown an ALT increase unrelated to HBV reactivation.

**Conclusions:** In line with previous data, our experience suggests that the risk of hepatitis B reactivation in rheumatic patients undergoing treatment with ANTI-CD20 combined with sDMARD is very low. The regular monitoring of transaminases and hepatitis markers (HBsAg, antiHBsAg and HBV-DNA) during treatment has to be preferred to universal prophylaxis.

**Disclosure of Interest:** None declared

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FRI0076

### CHRONIC WIDESPREAD PAIN IN PATIENTS WITH RHEUMATOID ARTHRITIS: A SEVEN YEAR FOLLOW-UP OF PAIN DISTRIBUTION AND FACTORS FOR IMPROVEMENT

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**Background:** The knowledge of chronic widespread pain and factors associated to improvement of pain in patients with RA is sparse, in particular regarding longitudinal studies.

**Objectives:** To describe the change of pain distribution reports over time and to identify factors that predict improvement from chronic widespread pain in patients with RA.

**Methods:** Two postal questionnaires were sent out to patients included in the BARFOT (Better anti-rheumatic pharmacotherapy) study, the first in 2010 and the second in 2017. The questionnaire included a pain mannequin, NRS scales of pain, patient global assessment (PatGA) and fatigue, health assessment questionnaire (HAQ), health related quality of life measured by EQ-5D and patient reported BMI and 28-joint count of tender (TJC) and swollen joints (SJC). The responders to both questionnaires were divided into 3 groups according to the reported pain duration and distribution at each time point— patients having no chronic pain (NCP), chronic widespread pain (CWP), and chronic regional pain (CRP).

**Results:** 1525 (73%) patients answered the pain questions in 2010 and 1046 (68%) in 2017. In all 950 of the patients answered the questions at both time points and were included in the study. One third (324) of the patients had reported <sup>CWP</sup> in 2010 and 140 (43%) of the patients with CWP in 2010 had improved in 2017. The patients, who improved, had lower BMI,  $p=0.045$ , less tender joint counts,  $p=0.007$ , less pain,  $p=0.005$ , less fatigue,  $p<0.001$  and less painful regions,  $p<0.001$ , better PatGA,  $p=0.002$ , better HAQ,  $p<0.001$  and better EQ-5D,  $p=0.003$ . Fifty-five percent of the patients who improved were treated with DMARD, compared to 52% of those not improving, the rate treated with biologics were 32% vs. 26%. There were, however, no statistical significant difference in medical treatment between the groups,  $p=0.088$ .

Age and sex adjusted logistic regression models showed an increased chance for improvement from CWP in patients with normal BMI, less TJC, pain, fatigue and tender regions and better PatGA, HAQ and EQ-5D, table 1. Biologic treatment also increased the chances to improve from CWP. The most common biologic treatment was anti-TNF treatment. Of the patients, who were treated with biologics, 86% in the group, who improved from CWP and 74% in the group, who did not improve, were treated with anti-TNF treatment. Age, gender, smoking habits, SJC and glucocorticoid treatment were not associated with improvement in the model.

**Abstract FRI0076 – Table 1.** A crude logistic regression model were the data were age and sex adjusted, except age, which was adjusted for sex and sex, adjusted for age.

	OR	95% CI	
Age 2010	1.011	0.992-1.031	
Gender			
women	0.960	0.542-1.702	
Smoking habits 2010			
Smoker	0.580	0.282-1.195	
Previous smoker	0.793	0.479-1.311	
BMI 2010			
<18,5	0.320	0.037-2.930	
18,5-24,9	2.146	1.121-4.106	
25-29,9	1.294	0.708-2.365	
TJC 2010	<7	1.798	1.148-2.815
SJC 2010	<4	1.477	0.943-2.312
PatGA 2010	<4	1.806	1.146-2.848
Pain 2010	<5	1.836	1.164-2.898
Fatigue 2010	<6	3.249	2.013-5.246
EQSD 2010	≥0.725	2.092	1.318-3.3821
HAQ 2010	<0.75	1.988	1.246-3.173
Total pain regions 2010	<8	2.987	1.888-4.727
Medical treatment 2010			
DMARD	1.779	0.940-3.366	
Biologics	2.202	1.099-4.413	
Prednisolone treatment 2010			
Pred	0.753	0.448-1.265	

**Conclusions:** Lower scores in pain related variables and fatigue, normal BMI, better physical function and health-related quality of life, and biologic treatment were associated to improvement from CWP in patients with RA. Knowledge of factors associated to improvement from CWP could be helpful when treating RA patients with CWP. More studies with focus on improvement from chronic pain in patients with RA are needed.

**Disclosure of Interest:** None declared

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FRI0077

#### HEPATITIS B VIRUS REACTIVATION IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH BARICITINIB: POST-HOC ANALYSIS FROM CLINICAL TRIALS

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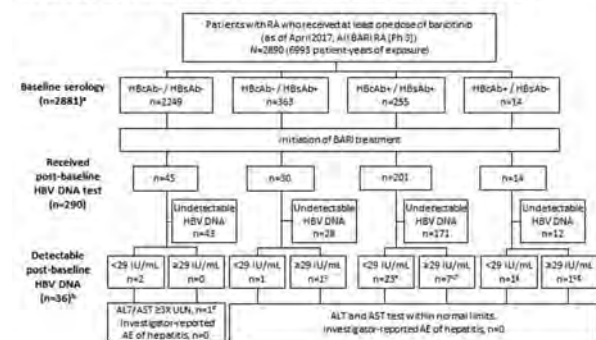
**Background:** Baricitinib (BARI) is an oral selective Janus kinase (JAK)1 and JAK2 inhibitor approved in the EU, Japan, and other countries for treatment of moderately to severely active rheumatoid arthritis (RA) in adults. RA therapies may increase risk of hepatitis B virus (HBV) infection<sup>1</sup>. HBV reactivation is a concern in previously infected patients (pts), including those with serologic evidence of resolution. HBV exposure is common in many Asian countries.<sup>2</sup> Limited data exist on HBV reactivation among pts with RA treated with JAK inhibitors.

**Objectives:** To assess HBV reactivation in pts with RA treated with BARI during Phase (Ph) 3 trials.

**Methods:** At screening, all pts were tested for HBV surface antigen (HBsAg), core antibody (HBcAb) and surface antibody (HBsAb). In Japan and elsewhere if required, pts had screening HBV DNA tests. Pts were excluded if they had 1) HBsAg+, 2) HBcAb+/HBsAb- (in Japan, could enrol if HBV DNA-), or 3) HBsAb +and HBV DNA+. Routine HBV DNA monitoring was performed in Japan for pts with HBcAb +and/or HBsAb +at screening, and was later instituted globally for HBcAb +pts. Pts with post-baseline HBV DNA+ (≥29 IU/mL) were discontinued from the study and referred to a hepatologist. In select cases, investigators continued study drug following a HBV DNA +test in consultation with the sponsor and in accordance with HBV management guidelines. Data were integrated from 4 completed Ph 3 trials and 1 ongoing long-term extension (LTE) (data to April 2017).

**Results:** Of 2890 pts with ≥1 dose of BARI (6993 pt-years exposure), 2679 pts had baseline serology suggestive of prior infection (HBcAb+/HBsAb+, n=255; HBcAb+/HBsAb-, n=14) (figure 1). Post-baseline HBV DNA tests were performed for 290 pts (including some pts without a baseline HBV DNA result). After BARI initiation, 7 of 201 pts (3%) with HBcAb+/HBsAb+ at baseline had quantifiable HBV DNA +levels (≥29 IU/mL; median 256, range 31–1547 IU/mL). An additional 23 (11%) had qualitative HBV DNA +results below the lower limit of detection (LLD) (<29 IU/mL). Of these 30 HBcAb+/HBsAb+ pts with HBV DNA +tests post-baseline, 22 had HBV DNA- tests at baseline. Among 14 pts with HBcAb+/HBsAb-, all had HBV DNA- tests at baseline; repeat HBV DNA test results post-baseline were quantifiable (1 at 36 IU/mL), below the LLD,<sup>1</sup> and undetectable.<sup>1,2</sup> Of pts with quantifiable HBV DNA, adverse events (AE) of detectable HBV DNA resulted in discontinuation of 4 of 8 pts of whom 3 received antivirals. 4 of 8 pts continued BARI in the LTE and have not received antivirals. All pts with quantifiable HBV DNA had alanine transaminase (ALT) or aspartate transaminase (AST) within normal limits, and none had an investigator-reported AE of hepatitis.

#### HBV serology and DNA detectability in patients treated with baricitinib in Phase 3 trials



\*Total number of patients with baseline serology is n=2881 due to missing data for 9 patients (8 missing surface antibody and 1 missing core antibody data).  
<sup>1</sup>Patients with detectable post-baseline HBV DNA were from China (11), Japan (9), Taiwan (6), Israel (2), Greece (2), Russia (2), United States (2), Argentina (1), and South Korea (1).  
<sup>2</sup>Nine patients had quantifiable HBV DNA levels of 31, 36, 60, 76, 92, 256, 257, 859, and 1547 IU/mL.  
<sup>3</sup>Patient with ALT/AST ≥3xULN was discontinued from study due to abnormal liver function test. Patient had a single detectable HBV DNA test result <29 IU/mL. At last available observation, ALT and AST were <5xULN and <2xULN, respectively.  
<sup>4</sup>Baseline HBV DNA not detected (5), not tested (5).  
<sup>5</sup>Baseline HBV DNA not detected (5), not tested (2).  
<sup>6</sup>Baseline HBV DNA not detected.  
 Abbreviations: AE=adverse event, ALT=alanine transaminase, AST=aspartate transaminase, BARI=baricitinib, HBcAb=hepatitis B virus core antibody, HBsAb=hepatitis B virus surface antibody, HBV=hepatitis B virus, DNA=deoxyribonucleic acid, Ph=phase, RA=rheumatoid arthritis, ULN=upper limit of normal.

**Abstract FRI0077 – Figure 1.** HBV serology and DNA detectability in patients treated with baricitinib in Phase 3 trials

**Conclusions:** Approximately 12% of BARI-treated pts with prior HBV infection later tested HBV DNA+ (3% were above the LLD), although no pts developed clinical evidence of hepatitis and in most cases antiviral therapy was not used.

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FRI0078

### PROSPECTIVE FOLLOW-UP OF A COHORT OF PATIENTS WITH INTERSTITIAL LUNG DISEASE ASSOCIATED WITH RHEUMATOID ARTHRITIS IN TREATMENT WITH DMARD

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**Objectives:** To describe prospectively the evolution of interstitial lung disease (ILD) in RA treated with modifying antirheumatic drugs (DMARDs) in clinical practice.

**Methods:** **Design:** Multicenter prospective observational cohort. **Patients:** Patients with RA (ACR<sup>EULAR</sup> 2010 criteria) and ILD (American Thoracic Society) from different centres of Málaga, Valme Hospital of Sevilla and Virgen Nieves of Granada were included. **Protocol:** All patients with RA and ILD who visited clinic from 2015 to 2017 were recruited. They were reviewed according to a predetermined protocol for data collection. Resolution Computed Tomography (HRCT), Pulmonary function test (PFT) and echocardiogram were requested for all patients who did not have it in the last year. This visit was marked as v0 (index date). At 12 months (v12) the joint assessment (DAS28), echocardiogram, PTF and HRCT were again evaluated. HRCT's were assessed by the same radiologist. **Outcomes:** At v12: (1) improvement (ie improvement in FVC  $\geq$ 10% or DLCO  $\geq$ 15% and no radiological progression), (2) non-progression (stabilisation or improvement in FVC  $\leq$ 10% or DLCO  $<$ 15% and no radiological progression), (3) progression (worsening of FVC  $>$ 10% or DLCO  $>$ 15% and radiological progression), or (4) death due to ILD. **Variables:** Description of ILD type and lung function by PTF, HRCT. Presence of PTH by echocardiogram and dyspnoea. Disease activity by DAS28-ESR; Adverse events during the follow-up period. **Statistical analysis:** Descriptive analysis and Wilcoxon or T test between the v0 and v12. One factor ANOVA between sDMARD, bDMARD and combination therapy groups.

**Results:** The main characteristics at V0 of the patients (n=41) are shown in the table 1. Nine patients (21.9%) received a sDMARDs with a bDMARDs; 25 patients (60.9%) monotherapy with sDMARD and 7 (17.0%) monotherapy with bDMARDs (table 1). Nine patients (21.9%) had improvement (2 with MTX, 1 with MTX +HCQ, 2 with RTX, 2 HCQ +RTX, 1 MMF +RTX and 1 with ABA); 24 patients (58.5%) remained stable (6 with MTX, 6 with LFN, 3 with HCQ, 1 AZA, 1 SSZ, 1 MMF, 1 TCZ, 2 ABA, 1 MTX +ETN, 1 HCQ +RTX, 1 HCQ +ADA, 1 RTX +MMF); and 7 (17.0%) got worse of ILD (2 with MTX developed lung nodules not known, 2 with LFN, 1 with LFN +IFX, 1 with ETN +MTX and 1 with SSZ). One patient died due to respiratory infection (with RTX). Two patients developed PPH. We did not find significant differences between Vo DAS28 and v12 (2.61 [0.74] vs 2.54 [1.12]; p=0.684) or in HAQ (1.12 [0.89] vs 1.23 [0.73], p=0.368). There were no significant differences in PTF, HRCT or DAS28 between sDMARD, bDMARD and combination therapy groups. During the follow-up period 27 patients had infections, the majority (53.7%) respiratory infection.

VARIABLES	Patients
Sex (male), n (%)	21 (51.2)
Age (years), mean (DE)	67.9 (7.8)
Smoker, n (%)	8 (19.5)
Ex-smoker, n (%)	32 (78)
Body mass index (BMI), mean (SD)	28.7 (5.3)
Disease duration (months), median (p25-p75)	138.1 (77.7-285.3)
ILD duration (months), median (p25-p75)	41.4 (10.1-79.2)
Rheumatoid factor, n (%)	39 (95.1)
Anti-cyclic citrullinated peptide, n (%)	35 (85.4)
Erosions, n (%)	27 (66)
DAS28, mean (DE)	2.8 (0.8)
HAQ, mean (DE)	1.2 (0.8)
Treatment	
sDMARD, n (%)	34 (82.9)
Methotrexate, n (%)	13 (31.7)
Leflunomide, n (%)	9 (22.0)
Sulfasalazine, n (%)	2 (4.9)
Hydroxychloroquine, n (%)	6 (14.6)
Azathioprine	1 (2.4)
Mycophenolato	3 (7.3)
MTX+HCQ	2 (4.9)
bDMARDs, n (%)	16 (39.0)
Rituximab, n (%)	7 (17.1)
Abatacept, n (%)	3 (7.3)
Etanercept, n (%)	3 (7.3)
Infliximab, n (%)	1 (2.4)
Adalimumab, n (%)	1 (2.4)
Tocilizumab, n (%)	1 (2.4)

**Conclusions:** Most patients with RA and ILD who are receiving treatment with DMARD (80.5%) remained stable or improved after at least one year of both synthetic and biological DMARD treatment. More prospective studies are necessary to identify the influence of DMARDs in this evolution.

**Disclosure of Interest:** None declared

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FRI0079

### ADIPONECTIN LEVEL, INSULIN RESISTANCE, ENDOTHELIAL DYSFUNCTION IN FEMALES WITH RHEUMATOID ARTHRITIS AND COMORBID HYPERTENSION

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**Background :** Rheumatoid arthritis (RA) associates with accelerated atherosclerosis and high cardiovascular mortality. Cardiovascular risk assessment in RA pts with comorbid hypertension (HT) is do not fully reflected by traditional risk scales, thus additional factors searching is required.

**Objectives:** We aimed to estimate the adiponectin level, insulin resistance, endothelial function in RA females with comorbid HT and its relationship with subclinical manifestations of atherosclerosis.

**Methods:** The study included 82 RA females with low disease activity and comorbid HT (mean age of 54.6 [49.7; 62.5] years) and 40 HT females without RA (control group). All pts received stable therapy of RA more than 6 months. Pts with coronary artery disease were excluded. The risk of fatal cardiovascular disease was calculated using mSCORE. RA disease activity was measured using DAS28 scale. Carotid ultrasound detection and endothelial-dependent flow mediated vasodilatation (EDVD) by Celermajer method were performed. The levels of adiponectin, insulin were measured using ELISA kit test, insulin resistance was estimated using HOMA2 index.

**Results:** Endothelial dysfunction was established in the majority of main group patients – 61 (74.4%), insulin resistance – in 70 (85.4%), elevated levels of adiponectin – in 35 (42.7%). Hypertensive females with RA had significantly higher adiponectin, insulin, insulin resistance levels compare to control (p<0.05). Subclinical manifestations of atherosclerosis were established in 64 (78.0%) HT females with RA and 10 (50%) control group pts. While the median cardiovascular risk level was 4.2 [2.7; 6.5] matched by mSCORE. The presence of atherosclerotic plaques in HT females with RA was associated with age (OR=1.242, p=0.004, 95% CI 1.007–1.78), glucocorticosteroid therapy >3 months (OR=1.56, p=0.001, 95% CI 1.22–2.45), endothelial dysfunction (OR=3.584, p=0.001, 95% CI 1.71–4.723), insulin resistance (OR=1.684, p=0.011, 95% CI 1.22–2.74), abnormal adiponectin level (OR=1.71, p=0.028, 95% CI 1.17–2.43). AUROC index for prognostic role of adiponectin and HOMA2 in subclinical atherosclerosis develop were 0.79 (95% CI 0.64–0.95; p<0.05) and 0.76 (95% CI 0.61–0.92; p<0.05) respectively, that indicate a good quality of diagnostic models.

**Conclusions:** Hypertensive females with rheumatoid arthritis are characterised by higher frequency of insulin resistance, endothelial dysfunction, adiponectin level changes which associates with subclinical atherosclerosis manifestations.  
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**DOI:** 10.1136/annrheumdis-2018-eular.2341

**FRI0080 THE ROLE OF PAIN IN RHEUMATOID ARTHRITIS (RA) PATIENTS' ASSESSMENTS OF THEIR HEALTH**

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**Background:** Patients often describe pain as the most important symptom of RA. Despite advances in RA therapy to improve disease control, some patients continue to have significant pain<sup>1,2</sup>. The relative impact of pain on RA patients' evaluations of overall health and RA-specific global assessments is unknown.

**Objectives:** Determine the relative role of pain in RA patients' health assessments.

**Methods:** Data derived from the Forward (The National Databank for Rheumatic Diseases) longitudinal cohort, collected January-May 2017. Respondents (n=5471) have rheumatologist-confirmed RA. Two health assessments were examined:<sup>1</sup> overall satisfaction with health (SAT) measured by the item: "How satisfied are you with your health now?" with responses of very unsatisfied to very satisfied; and<sup>2</sup> patient global assessments of RA impact (GBL) measured using a numeric rating scale (NRS): "Considering all the ways that your RA affects you, rate how you are doing on a scale of 0-10, where 0=very well and 10=very poor." For regression analyses, SAT was dichotomized as "very satisfied" or "somewhat satisfied" vs. other responses. Current pain severity was rated on an NRS from 0 (no pain) to 10 (extreme pain). Spearman correlations examined the association of pain with SAT and GBL. Initial multiple regression analyses (table 1, Model 1) examined the following as predictors of SAT and GBL: age, sex, education, disease duration, obesity (BMI >30), conventional and biologic DMARD use, Rheumatic Disease Comorbidity Index<sup>3</sup> (RDCI), self-report of depression, fatigue, and functional limitations (Health Assessment Questionnaire [HAQ] score). Follow-up models (Model 2) added pain to determine its relative independent role in health assessments.

**Results:** The sample was 84% female, mean age 65 years, mean RA duration 22 years. 53% were satisfied with their health, and mean GBL was 3.6±2.5. Mean pain severity rating was 3.8±2.8. Correlations of pain with SAT and GBL were 0.58 and 0.71, respectively (each p<0.0001). Regression models predicting both SAT and GBL improved with the addition of pain (table 1). Pain was significantly and independently associated with both health assessments.

	Model 1 (excluding pain)	Model 2 (adding pain)
Satisfied with health		0.81 (0.79, 0.84)*
Pain		0.40
Model R <sup>2</sup>	0.37	0.40
Global assessment of RA		0.33 (<0.0001)†
Pain		0.57
Model R <sup>2</sup>	0.51	0.57

\*Odds ratio (95% CI)

† b (p-value)

Regression models included age, sex\*, education, disease duration, obesity, medications, RDCI, depression, fatigue\*, and HAQ\*. Variables noted with asterisk were also statistically significant (p<0.05) in both final models.

**Conclusions:** Pain plays a critical role in RA patients' assessments of general and RA-specific health. Analyses suggest that pain may be more important to RA global assessments than to overall health satisfaction, though the clinical relevance of this difference is not known. RA global assessments are included in some indices of disease activity. Future research should focus on distinguishing between non-inflammatory and inflammatory causes, which may lead to more accurate assessment of RA disease activity.

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**FRI0081 THE IMPORTANCE OF TRANSFERRIN SATURATION, SERUM FERRITIN, LOG FERRITIN AND TRANSFERRIN/LOG FERRITIN IN DIFFERENTIATING IRON DEFICIENCY ANAEMIA FROM ANAEMIA OF CHRONIC DISEASE IN RHEUMATOID ARTHRITIS PATIENTS**

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**Background:** The most common types of anaemia in rheumatoid arthritis (RA) are iron deficiency anaemia (IDA) and anaemia of chronic disease (ACD). The differentiation between both is very important and challenging.

**Objectives:** is to select the most simple, cheap, accurate method differentiate IDA from ACD in RA patients.

**Methods:** This case control study was carried out on 80 RA patients. Group I 40 RA patients with anaemia Group II 40 RA patients without anaemia, complete blood count, assessment of disease activity using DAS 28 score, serum iron, total iron binding capacity (TIBC) "transferrin level", transferrin saturation (TSAT), serum ferritin, log ferritin and transferrin/log ferritin were tested, then we divided the patients in group 1 into 2 subgroups according to TSAT : group Ia (RA patients with anaemia and low TSAT) and group Ib (RA patients with anaemia and normal TSAT) and we compared the parameters.

**Results:** There was a statistically significant difference between anaemic and non anaemic RA patients as regard serum iron level and transferrin saturation and there was no significant difference as regard serum ferritin, log ferritin, transferrin and transferrin/log ferritin. Among the anaemic group (67.5%) had low TSAT (IDA) and only (32.5%) had normal TSAT (ACD). In these 2 subgroups there was no significant differences as regard DAS28 score, blood indices, serum ferritin and transferrin/log ferritin) except Log ferritin and there was positive correlation between TSAT and (ferritin and log ferritin) and significant negative correlation between TSAT and transferrin/log ferritin.

**Abstract FRI0081 – Table 1.** Clinical and laboratory parameters in both groups

Characteristic	Group I <sup>40</sup> RA +anaemia	Group II <sup>40</sup> RA without anaemia	P
DAS-28	2.99±1.07	2.35±0.77	0.002*
Hb (g/dl)	9.62±0.96	12.95±0.64	<0.0001*
MCV (fl)	79.71±7.29	83.0±9.34	0.083
MCH (pg/cell)	26.06±4.05	28.05±2.66	0.006*
MCHC (g/dl)	31.1±2.21	31.23±2.38	0.8
Serum iron (µg/ml)	0.66±0.37	0.89±0.38	0.0076*
Serum ferritin (ng/ml)	83.02±93.08	84.87±86.82	0.927
TIBC (µg/ml)	3.94±1.06	3.71±0.59	0.23
TSAT (%)	17.7±10.6	24.73±11.36	0.0054*
Log ferritin	1.61±0.75	1.7±0.46	0.52
Transferrin/Log ferritin	3.23±3.8	2.41±0.9	0.18

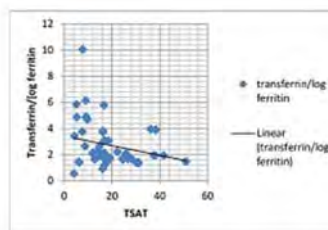
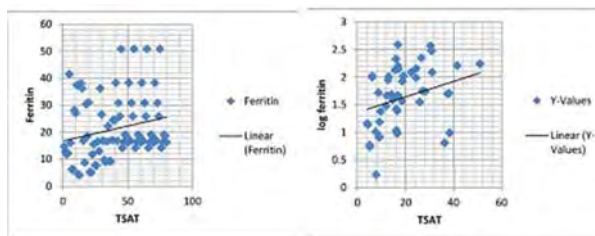


Figure 1 Correlation between TSAT and (serum ferritin, log ferritin and Transferrin/Log ferritin)

**Conclusions:** Iron deficiency anaemia is prevalent in RA patients. A combination use of serum ferritin and TSAT is the most simple, accurate parameter now to differentiate both. log ferritin, transferrin/log ferritin may be promising new parameters in diagnosis of IDA in general population but their use in inflammatory diseases like RA still has a limitation so we suggest further large studies to be done in order to assess their accuracy.

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#### FRI0082 PREDICTORS OF FATIGUE AND PERSISTENT FATIGUE IN EARLY RHEUMATOID ARTHRITIS: A LONGITUDINAL OBSERVATIONAL STUDY

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**Background:** Fatigue is a multifactorial and persistent symptom reported by patients with rheumatoid arthritis (RA). It is considered as frequent as pain. It would be of value to identify potential predictive factors of fatigue that can influence on its evolution.

**Objectives:** To identify predictive factors of fatigue and of persistent fatigue in a large prospective cohort of early RA patients.

**Methods:** *The Etude de Suivi des polyarthrites Indifférenciées Récentes (ESPOIR)* is a multicenter French cohort of patients with early arthritis. We selected patients fulfilling the 2010 ACR/EULAR criteria for RA during the first year of follow-up. We recorded sociodemographic and clinical characteristics, the SF-36 vitality score, Health Assessment Questionnaire (HAQ) score and 28-joint Disease Activity Score (DAS28) at baseline and every 6 months up to 5 years. The association of fatigue (SF vitality score  $\leq 40$ ) or persistent fatigue (SF vitality score  $\leq 40$  at the end of the study and at least in 50% of visits in the 5 years follow up) with other characteristics were evaluated by bivariate logistic regression models/tests (chi-squared test for qualitative variables and t-test/Mann-Whitney test for quantitative variables). A multivariate logistic regression model was used to determine independent predictors of persistent fatigue.

**Results:** We included 677 patients (73.4% women, mean  $\pm$ SD age 48.6 $\pm$ 12 years); 46.5%, 28% and 22% of RA patients presented fatigue at baseline, 6 months and 5 years of follow up respectively. At baseline, fatigue was independently and significantly associated with single patients (OR=2.5 95% CI [0.30–0.70]  $p < 0.001$ ), higher BMI (OR=1.1 95% CI [1.01–1.10]  $p = 0.007$ ), higher DAS28 (OR=1.3 95% CI [1.08–1.60]  $p = 0.006$ ), higher severity of morning stiffness (scored 0–10) (OR=1.0 95% CI [1.00–1.01]  $p = 0.012$ ), higher HAQ (OR=2.4 95% CI [1.70–3.44]  $p < 0.001$ ), negativity of FR (OR=1.5 95% CI [1.09–2.29]  $p = 0.016$ ) and history of depression or anxiety (OR=6.1 95% CI [3.90–9.83]  $p < 0.001$ ). A 14.9% of patients presented persistent fatigue. Independent predictors of persistent fatigue at 5 years of follow-up were HAQ (OR=2.5 95% CI [1.63–3.67]  $p < 0.001$ ), history of depression/anxiety (OR=3.7 95% CI [1.53–9.15]  $p = 0.004$ ),  $> 3$  comorbidity (OR=2.1 95% CI [1.23–3.73]  $p = 0.007$ ), dry syndrome (OR=2.4 95% CI [1.39–4.17]  $p = 0.002$ ), and negativity in RF (OR=1.85 95% CI [1.07–3.21]  $p = 0.027$ ).

**Conclusions:** Fatigue was frequent in this cohort of early RA patient, its presence decreased at 6 months and remained stable over time. Baseline fatigue and persistent fatigue were both predicted by functional impairment, negativity of RF and history of depression or anxiety. Disease activity measured by DAS28 was strongly associated to fatigue at baseline but it was not a predictor of persistent fatigue.

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#### FRI0083 ADJUSTMENT OF THE THRESHOLD MAY IMPROVE CARDIOVASCULAR RISK STRATIFICATION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is associated with increased cardiovascular (CV) risk. Besides monitoring of the disease activity, identification of high CV risk patients is of great importance<sup>1,2</sup>.

**Objectives:** The aim of the study was to assess the abilities of 3 risk models (SCORE, QRisk2 and 10 year ASCVD) in detecting high CV risk RA patients.

**Methods:** 56 patients with RA (ACR/EULAR<sup>2010</sup> without known CV disease were examined (84% females, age 58.4 $\pm$ 14.1 (M $\pm$ SD) years, BMI 26.1 $\pm$ 5.4 kg/m<sup>2</sup>, smokers 9%, arterial hypertension (AH) 64%, dyslipidemia 57%, diabetes 7%). Median duration of RA was 7 years (IQR 2–14). Seropositive RA was diagnosed in 73% of patients. Median hsCRP was 7.8 mg/dl (IQR 2;21.4), rheumatoid factor (RF) – 61.2 IU/ml (IQR 18.5;179.2), mean DAS-28(CRP) – 3,7 $\pm$ 1,2. All patients received disease-modifying antirheumatic drugs. SCORE, QRisk2 and 2013 ACC/AHA 10 year ASCVD risk and EULAR recommended modified versions were calculated. Patients with SCORE  $\geq 5\%$ , QRisk2  $\geq 20\%$  and ASCVD risk  $\geq 7.5\%$  were classified as having high CV risk. Carotid intima-media thickness (CIMT)  $\geq 0,9$  mm and/or carotid plaques detected by ultrasonography were used as the gold standard test for high CV risk.  $p < 0.05$  was considered significant.

**Results:** The median SCORE, QRisk2 and ASCVD were 2.2% (IQR 0.6;4.9), 10.2% (3.4;19.2) and 4.9% (1.5;12.8) respectively. The proportion of high-risk patients was as follows: 14 (25%), 13 (23%), 24 (43%) for SCORE, QRisk2 and ASCVD. Mean CIMT was 0.76 $\pm$ 0.24 mm. US criteria for subclinical atherosclerosis (US+) were found in 27 (48%) pts. Discriminating capacities for the indexes were as follows: AUC 0.723 (CI 95% 0.626–0.821) for SCORE, AUC 0.705 (CI 95% 0.606–0.804) for QRisk2 and AUC 0.837 (CI 95% 0.757–0.917) for ASCVD. The percentages of high-risk patients in US+group were as follows: 13 (48%), 12 (44%) and 21 (78%), respectively, ( $p < 0.05$  compared to ASCVD). After multiplying by 1.5 EULAR 2016 mASCVD reclassified 2 (7.4%) and mSCORE – 4 (14.8%) pts from moderate to high risk. Use of lower cut-off values for risk indices (SCORE  $\geq 1\%$ , QRisk2  $\geq 10\%$  and ASCVD  $\geq 5\%$ ) resulted in better detection of US+pts (100%, 85% and 85% respectively).

**Conclusions:** The 2013 ACC/AHA 10 year ASCVD risk estimator is better than the SCORE and QRisk2 indices for the detection of high CV risk RA patients. Adjustment of the threshold may be a better modification of risk scales than use of the EULAR multiplier factor.

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#### FRI0084 INTENSE AEROBIC AND RESISTANCE EXERCISE REDUCES THE FREQUENCY OF PERIPHERAL BLOOD REGULATORY CELL POPULATIONS IN ELDERLY PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** RA is an autoimmune joint disease driven by complex immune dysregulation. Exercise can improve immune health and is beneficial for physical function in elderly patients with RA, but the immunological mechanisms are largely unknown.

**Objectives:** We evaluated the effect of a person-centred randomised controlled exercise programme on regulatory immune cell populations in aged persons with RA.

**Methods:** Aged persons with RA were randomised to either a 20 week of aerobic and resistance exercise intervention of moderate-to high intensity (n=24) or to an active control group performing low-intensity home exercise (n=25). Blood samples were collected at baseline and after 20 weeks. The frequency of the adaptive regulatory populations Foxp3 +CD25+CD127<sup>+</sup>CD4<sup>+</sup>T cells and CD24hiCD38hi B



cells and the CD33 +CD11b+myeloid derived suppressor cells were assessed using flow cytometry.

**Results:** After 20 weeks of exercise intervention there was a decrease in the frequency of Foxp3 +CD25+CD127 regulatory T cells and CD24hiCD38hi B cells but no change was observed in the active control group. The reduction in Tregs by exercise was most pronounced in the female participants. Despite lower levels of adaptive immune cell populations the disease activity did not increase.

**Conclusions:** Aerobic and resistance exercise in elderly patients with rheumatoid arthritis lead to a decreased number of regulatory Foxp3 +CD25+CD127 regulatory T cells and CD24hiCD38hi B cells. This decrease was not associated with an increased disease activity score or increased inflammation.

**Disclosure of Interest:** None declared

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#### FRI0085 A STUDY OF THE RELATIONSHIP BETWEEN SERUM VITAMIN D LEVEL AND DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Vitamin D is an essential component of our body. Approximately 3% of the human genome is directly or indirectly regulated by the Vitamin D endocrine system, which supports the idea that Vitamin D insufficiency has widespread adverse consequences for human health.<sup>[1]</sup>Till date several studies have been done regarding the relation of Vitamin D and Rheumatoid Arthritis but there are limited studies in Eastern India. Hence this study is being done to examine the relation of serum 25 hydroxy Vitamin D level and Disease Activity in Rheumatoid Arthritis patients.

#### Objectives:

- To examine the relationship between Serum 25 Hydroxy Vitamin D level and SDAI (Simplified Disease Activity Index) in Rheumatoid Arthritis patients.
- To examine the relationship between Serum 25 Hydroxy Vitamin D level and Tender Joint Count(TJC), Swollen Joint count(SJC) and CRP in Rheumatoid Arthritis patients.
- To evaluate the relation of serum vitamin D level with various socio demographic factors like Gender, Diet, Occupation, Season, Height, Weight, BMI in Rheumatoid Arthritis Patients.

**Methods:** Ninety six RA patients attending The Rheumatology clinic of Out Patient Department of An Urban Tertiary care hospital (Latitude of KOLKATA is 22°32'N) from October 2013 to September 2014, fulfilling the ACR –EULAR 2010 criteria for classification of RA, were included in the study. 25(OH)vitamin D levels were measured. Disease activity of RA was assessed by SDAI score.

**Results:** More than Ninety Percent of the RA patients were found to have either Vitamin D deficiency or insufficiency. The mean serum vitamin D level of these RA patients was 20.02 (±8.92) ng/ml. The RA patients with High Disease Activity (SDAI between 26.1 and 86) had significantly low ( $p < 0.0001$ ) mean serum vitamin D level [11.11 (±6.08) ng/ml] than those with Moderate (SDAI between 11.1 and 26) or Low Disease Activity (SDAI between 3.4 and 11.0) whose serum vitamin D level was 21.15 (±7.47) ng/ml and 25.58 (±7.30) ng/ml respectively. There is a significant negative correlation between the Serum Vitamin D level and SDAI score ( $r = -0.669$ ,  $p < 0.0001$ ) in the whole group of the study population. However On analysing the data separately in RA patients with Vitamin D deficiency, insufficiency and sufficiency, this significant relation is separately evident only in the RA patients with Vitamin D deficiency (serum vitamin D level  $< 20$  ng/ml) but not in those who were in the insufficient or sufficient groups. There is an independent negative impact of Simplified Disease Activity Index (SDAI) on Serum Vitamin D level (Adjusted  $R^2 = 0.464$ ,  $p < 0.0001$ ).

**Conclusions:** RA patients having high disease activity in terms of SDAI Score had significantly low vitamin D level compared to patients of RA having low or moderate disease activity. Lower levels of serum vitamin D was associated with increased disease activity in RA patients. On subgroup analysis, there is significant negative correlation separately evident only in the RA patients with Vitamin D deficiency (serum vitamin D level  $< 20$  ng/ml) but not in those who were in the insufficient or sufficient groups.

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**Disclosure of Interest:** None declared

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#### FRI0086 IS THE DISCORDANCE BETWEEN THE DOCTOR AND THE PATIENT A DETERMINANT OF ADHERENCE?

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**Background:** Adherence is a critical factor in the therapeutic response in rheumatoid arthritis (RA), which may be influenced by the doctor-patient relationship. In the ARCO study, we previously reported a percentage of lack of adherence to the subcutaneous biologic of 14.3% during the first 14 months of treatment, and that the adherence was better in patients without induction and with a monthly administration schedule.<sup>1</sup> In this *post hoc* analysis, we explored whether doctor-patient disagreements may be related to lower adherence rates.

**Objectives:** To analyse the percentage of patients with discrepancies in the evaluation of the activity of the disease between doctors and patients and a possible association between the existence of disagreement and adherence to subcutaneous biological drugs.

**Methods:** The ARCO study was a multicenter, cross-sectional study in which patients with RA were included according to EULAR-ACR 2010 criteria, who had been prescribed a subcutaneous biological drug in the previous 12–18 months. As part of the evaluation of the disease, patients and doctors were asked to rate the disease on a visual analogue scale (VAS), with values ranging from 0 to 10; with higher values indicating worst symptoms. Disagreement was defined as a difference of  $\geq 3$  points between the absolute values. Adherence was assessed retrospectively by means of the Medication Possession Ratio (MPR), considering adherence those patients with MPR  $> 80\%$ . The association between adherence and disagreement was studied using bi and multivariate logistic regression models with covariates-adjustments.

**Results:** We included 360 patients (77.5% women, mean age:  $55 \pm 0.6$  years). Disagreement was detected in 56 (15.5%). In patients with disagreement, the mean VAS score of the patient was  $5.75 \pm 1.8$  versus  $2.7 \pm 2.2$  in the group without disagreement ( $p < 0.001$ ), and there were no differences in terms of the doctors VAS (group with disagreement =  $2.7 \pm 1.8$  versus  $2.2 \pm 2.0$  in the group without disagreement,  $p = 0.110$ ). The two groups of patients presented differences in terms of age (5 years more than average in the group with disagreement,  $p = 0.010$ ), presence of comorbidity (14% more frequent in the group with disagreement,  $p = 0.030$ ) and the value of the mean DAS28 (0.6 points higher in the group with disagreement,  $p < 0.001$ ). Among the patients who presented a VAS disagreement, the percentage of non-adherence was 10.7%, and of 14.5% among those who had a VAS similar to the doctor ( $p = 0.45$ ). The regression analysis showed no difference in the association between adherence and disagreement; by introducing into the models covariates associated with adherence (induction, frequency of administration and age) or with disagreement (age, comorbidity and DAS28).

**Conclusions:** We observed a disagreement between patients and doctor VAS scores in 15.5% of cases, with higher values coming from patients. We did not observe an association between this disagreement and adherence to subcutaneous biological drugs.

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#### FRI0087 REGIONAL AGE- AND SEX-SPECIFIC INTIMA-MEDIA THICKNESS CRITERIA IN YOUNG PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is associated with early progression of cardiovascular (CV) diseases. The CV risk calculators had been verified on a specific population<sup>1</sup> and should be applied predominantly for them. Systematic Coronary Risk Evaluation (SCORE) was recommended by EULAR for use in RA patients with multiplying coefficient 1.5.<sup>2</sup> Nevertheless, SCORE don't consider RA-specific factors and couldn't be used in young patient. For timely prevention

additional criteria is needed to evaluate CV risk in RA-patients. A presence of atherosclerotic plaque (API) or intima-media thickening, assessed by carotid ultrasonography, may be used as a high CV risk marker after adjustment by age and sex factors.

**Objectives:** To investigate the prevalence of carotid intima-media thickening, using regional age- and sex-specific criteria.

**Methods:** One hundred forty eight Caucasian patients with RA (age – 53 years;<sup>40;</sup> <sup>60</sup> DAS28 5.01 [3.91; 5.90]) without (API) were included in our study. Patients had ACR-defined RA (1987 classification criteria). All patients gave written informed consent before enrollment. SCORE with multiplying coefficient 1.5 was used for the CV risk determining. Range of atherosclerotic progression was assessed by ultrasonography with measurement of carotid intima-media thickness (IMT). IMT measured had been compared with ranges followed: <35/35–44/45–54/55–64/65–74/>75 age – 0,55/0,72/0,72/0,80/0,86/1,0 mm for the right artery and 0,53/0,65/0,73/0,85/0,89/1,0 mm for the left one (men); 0,47/0,51/0,71/0,78/0,87/0,87/0,87 mm for the right artery and 0,50/0,55/0,71/0,80/0,91/0,98 for the left one (women), respectively.<sup>3</sup> Descriptive statistics, Chi-squared test, Spearman rank correlation coefficient were used for data analysis. Results are presented as median and 25th/75th percentiles (Me [25th percentile; 75th percentile]).

**Results:** IMT significantly correlated with age ( $p=0,63$ ;  $p<0,001$ ), systolic blood pressure ( $p=0,22$ ;  $p=0,017$ ), but not with other parameters (sex, smoking, cholesterol, etc). Risk was evaluated by SCORE for 109 RA patients elder than 40 years (age – 57 years<sup>50;</sup> <sup>63</sup>) and was 0%>15% (1.95%–3%) [0.75; 3.15]. An intima-media thickening had been revealed in 86 from 109 (78,9%) patients and correlated with SCORE value ( $p=0,42$ ;  $p<0,001$ ). 34 patients (23,0%) were younger than 40 years (age – 30.5 years<sup>28,0;</sup> <sup>36,0</sup>), therefore the relative CV risk scale had been used for ones. Risk evaluated was medium (1.5%–3%) for all young patient. An intima-media thickening had been revealed in 31 from 34 (91,2%) patients and didn't correlate with SCORE value ( $p=0,37$ ;  $p=0,104$ ). Number of patients with carotid thickening between two groups didn't significantly difference ( $p=0,13$ ).

**Conclusions:** Using age- and sex-specific criteria for the IMT evaluation may be useful in young patients with RA.

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#### FRI0088 PSYCHOLOGICAL IMPACT IN RHEUMATOID ARTHRITIS: ROLE OF SPECIFIC TREATMENT AND ASSOCIATED MEASURES

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**Background:** Psychological issues in rheumatoid arthritis (RA) are often spontaneously mentioned by patients or identified by rheumatologists. Besides classic follow up parameters like DAS28, we have to consider those issues to improve our patients psychological well-being.

**Objectives:** Explore reasons of psychological impact in RA. Analyse in a quantitative way symptoms of discontent and their repercussions. Evaluate consequences of disease treatment on those symptoms and propose recommendations for rheumatologists.

**Methods:** RA cases were collected by a group of 20 private practice rheumatologists in the Paris area. Basic informations about the patient and his disease were provided by his rheumatologist. Questionnaire including 14 items about psychological and life quality involvement was filled in by the patient.

**Results:** 167 cases collected : 82% women, mean age 57 years, 56% moderate and 14% severe disease, 76% ACPA positive, 73% structural damage. Initial DAS28 4.7. Post treatment DAS28 2.7. Drugs: classic DMARDs 95%, corticosteroids 73%, biological DMARDs 22%, combination therapy 76%.

In 82% of the cases, the rheumatologist recommends more than only specific RA drug treatment: rest (47%), physiotherapy, ergotherapy, balneotherapy (42%), adapting professional activity and environment, help for housework (33%), psychological support or psychoactive drugs (19%), yoga or other relaxation exercises (11%), balneology...

Psychological repercussions are spontaneously mentioned by 71% of the patients.

Psychological state is altered by : disease announcement, pain (85%), physical fatigue (71%), handicap (58%), other people's attitude.

Are limited : housework (51%), getting about (44%), do-it-yourself (55%), sports (61%), artistic activities (41%), professional activity (29%).

Social life is affected by : lack of being listened to (72%), lack of being understood (68%), lack of empathy (49%).

RA treatment reduces all those factors by at least one third, except impact on family relations.

Before treatment, RA patients report: sleeping trouble (70%), anxiety (57%), lack of motivation (55%), dependency (49%), frustration (42%), lack of self-esteem (37%), concentration problems (35%), disillusion (31%), depression (30%), family tension (29%), isolation (27%) and libido decrease (23%).

After treatment, all those factors are 41%–55% less frequent, except libido decrease (–28%).

55% sleep better, 49% aren't depressed anymore, concentration problems diminish by 48% and social life is improved by 50%.

**Conclusions:** There is a major psychological impact in RA patients, with repercussions on their well-being and life quality. This can be improved by specific anti RA treatment, but we must also consider other measures and, if necessary, psychological support and/or psychoactive drugs. All chosen items are improved, except impact on family relations.

**Disclosure of Interest:** None declared

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#### FRI0089 ASSESSMENT OF COGNITIVE FUNCTION IN RHEUMATOID ARTHRITIS

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**Background:** For long, rheumatoid arthritis (RA) was thought not to associate with central nervous system (CNS) involvement. In recent years some studies suggest that cognitive function is impaired in RA patients. Accelerated atherosclerosis and reduced function of intracranial vessels in RA can be associated with vascular dementia.

**Objectives:** We assessed RA patients and healthy controls by neuropsychological tests, cognitive function such as attention, intelligence, memory tests and also by anxiety and depression tests. We wished to explore the prevalence of neuropsychiatric manifestations and cognitive impairment in patients with RA. Intracerebral vascular lesions were investigated by brain MRI.

**Methods:** Sixty RA female patients were included. Among them, 20 were MTX-treated, biologic-free, 40 patients received biologics. The controls included 39 non-RA healthy women. The following standardised tests were used: the Montreal Cognitive Assessment (MoCa) Test, the Victoria Stroop Test (VST), the Spielberger State-Trait Anxiety Inventory (STAI), the Benton Visual Retention Test (BVRT), the Beck Depression Inventory (BDI), the Brigg's and Nebe's Test, the Trail Making Test (TMT) A and B, the Word fluency with the letter (WF-L) and with category naming tests (WF-C), the Rey-Osterreich Auditory Verbal Learning Test (RAVLT), the Weschler Adult Intelligence Scale (WAIS). We also performed brain MRI in all patients in order to associate cognitive function with MRI changes.

**Results:** The MoCa total score was significantly lower in RA patients (23.3±3.8) especially in biologic-treated group (22.6±4.3) compared to controls (25.6±2.4) ( $p=0,002$ ;  $0,001$ ). The attention MoCa test score was significantly lower in biologic- (4.5±1.6) compared to MTX-treated patients (5.7±0.6)( $p=0,001$ ). The STAI scores were significantly higher in RA (STAI-S: 45.5±8.5; STAI-T: 48.0±11.0) compared to controls (STAI-S: 36.9±9.1; STAI-T: 41.1±9.0)( $p<0,001$ ;  $0,002$ ). The BDI score was significantly higher in RA (13.2±8.8) and in biologic-treated patients (13.7±8.7) than in controls (8.9±6.5)( $p<0,05$ ). The TMT scores were significantly higher in RA (TMT-A: 69.0±26.3; TMT-B:100.2±48.5) compared to controls (TMT-A: 53.1±14.3; TMT-B: 53.1±22.7)( $p<0,05$ ). The VST scores were also significantly higher in RA vs controls. The WAIS and Benton scores were significantly lower in

RA and in biologic-treated patients than in controls ( $p=0.005$ ). On brain MRI scans, there were significantly more vascular lesions both in the left and the right side in RA patients (55,1%>53,1%) than in controls (23,5%>20,1%) ( $p<0,05$ ), the cerebral atrophy is much more common in RA (0,26 vs. 0,03; $p=0,005$ ).

**Conclusions:** These findings suggest that the presence of neuropsychiatric manifestations and cognitive impairment in RA patients is significant. Biologic-treated patients may represent a more severe RA subset thus having cognitive dysfunction more commonly. Brain atrophy, emollition and vascular lesions are more often in RA patients than controls.

**Disclosure of Interest:** None declared

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#### FRI0090 ASSOCIATION OF BODY COMPOSITION WITH DISEASE ACTIVITY AND DISABILITY IN RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is a chronic form of inflammatory arthritis characterised by multiple joint involvement and significant disability. Previous studies showed that RA is associated with considerable changes in body composition, lipid profile, adipokines and insulin sensitivity

**Objectives:** To explore the association of body composition with pain, disease activity and disability in rheumatoid arthritis (RA)

**Methods:** Three hundred thirty five patients with RA visiting the Hallym University Sacred Hospital underwent body composition measurement with inbody analyzer and examined the disease activity score (DAS28). The association of body mass index (BMI), body fat mass and skeletal muscle mass with DAS28, DAS28-P (an index derived to measure subjective component of DAS28), pain VAS and disability measured with the health assessment questionnaire (HAQ) was explored. Obesity was defined as BMI  $\geq 25$  kg/m<sup>2</sup>. Pain VAS was dichotomized as  $\leq 40$  and  $>40$ . Low HAQ score was defined as  $\leq 0.5$ . Logistic regression was divided in female versus male.

**Results:** Mean age of patients was  $56 \pm 11.9$  years and 84.8% were female. The median(IQR) disease durations was 6 (3.5–9) years and mean DAS28 score was  $3.55 \pm 1.14$ . Mean BMI was  $23.6 \pm 3.7$  kg/m<sup>2</sup> and 109 patients (32.5%) were obese. Obese patients had higher CRP level (1.68 ml/dL vs 0 ml/dL,  $p=0.013$ ), ESR level (25 mm/hr vs 18 mm/hr,  $p=0.032$ ), pain VAS score (40 vs 35,  $p=0.045$ ), and higher DAS28-ESR score ( $3.75 \pm 1.18$  vs  $3.46 \pm 1.11$ ,  $p=0.031$ ), than non obese patients. In multivariable regression analysis, DAS28 score in female was positively associated with current steroid dose, HAQ and body fat mass. In univariable logistic regression, higher pain VAS category in female was associated with older age, higher BMI and higher body fat mass. In multivariable logistic regression analysis, higher HAQ score in female was associated with older age, higher DAS28, higher body fat/skeletal muscle ration and lower skeletal muscle mass. In multivariable regression analysis, DAS28-P score in female was positively associated with higher body fat/skeletal muscle ratio and negatively associated with positivity of anti-CCP.

**Conclusions:** Body compositions such as body fat mass and skeletal muscle mass are significantly associated with pain and disability in RA patients

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#### FRI0091 SOMATOSENSORY DYSFUNCTION IN RHEUMATOID ARTHRITIS – A QUANTITATIVE SENSORY TESTING ASSESSMENT

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**Background:** Significant pain persists in a substantial proportion of Rheumatoid Arthritis (RA) patients and features suggestive of neuropathic pain (NP) were described. Few studies applied quantitative sensory testing (QST) to evaluate the somatosensory phenotype of RA pain.

**Objectives:** To explore the sensory abnormalities in RA and study its association with clinical and disease activity parameters.

**Methods:** Cross-sectional study was performed with RA patients followed at our rheumatology department. QST was performed in patients classified with NP (according to LANSS and/or pain DETECT scores) in both the most painful and non-painful contralateral joint areas. The evaluation followed the protocol of the German Research Network on Neuropathic Pain. Patients with diagnosed neuropathy or non-RA risk factors for NP were excluded. Proportions of abnormal detection/pain thresholds were calculated after z-transformation of QST data

based on gender, age and site reference values. Correlations were studied (Spearman correlation coefficient) and comparison between groups was performed (Mann-Whitney and  $\chi^2$  tests).

**Results:** From 112 evaluated RA patients, 47% were classified with NP and 39 performed QST. Thirty four (87%) were women, with a mean age of  $53.5 \pm 11.8$  years and median disease duration of 11 years; <sup>2-31</sup> 74% were seropositive for Rheumatoid Factor and/or ACPA; 90% were treated with conventional synthetic Disease-Modifying Antirheumatic Drugs (DMARDs) and 39% with biological DMARDs (bDMARDs). Mean DAS28 CRP was  $3.44 \pm 0.7$ . For non-nociceptive parameters, 23 (59%) patients exhibited sensory loss (Lo), 6 to thermal stimuli (L1), 10 to mechanical stimuli (L2) and the reminder for both (L3). Concerning nociceptive parameters, hyperalgesia (Ga) was noted in almost all the patients (97%), 1 to thermal (G1), 20 to mechanical (G2) and 17 for both stimuli (G3). Twenty two (60%) patients presented both Lo and Ga findings. Higher proportion of Lo was noted in bDMARDs group (86% vs 46%,  $p=0.02$ ). Lo patients had significant lower median CRP and ESR levels, but no differences were observed concerning disease activity scores. Thermal Lo (L1 and L3) was also more frequent in the bDMARDs group (57% vs 21%,  $p=0.04$ ) and cold Lo in hydroxychloroquine (HCQ) treated patients (90% vs 21%  $p=0.02$ ). Cold Ga was more frequent in patients under methotrexate (MTX) (48% vs 6%,  $p=0.04$ ) and less frequent in the bDMARDs group (7% vs 46%,  $p<0.05$ ). A weak correlation of Z cold detection and Z warm detection values with CRP and ESR levels was noted ( $r=0.34$  and  $r=0.35$ ,  $p=0.04$ ). Time exposure to HCQ, MTX and bDMARDs was negatively correlated with Z cold detection ( $r=-0.34$ ,  $p=0.03$ ), Z pressure pain ( $r=-0.33$ ,  $p=0.04$ ) and Z vibration detection ( $r=-0.32$ ,  $p=0.04$ ), respectively.

**Conclusions:** Almost all patients presented hyperalgesia, but a sizable proportion also had sensory loss, frequently involving A $\beta$  fibres. CRP and ESR levels possibly influence small fibre function, but no association with disease activity scores was found. Possible association of bDMARDs and HCQ treatment with sensory detection loss and of MTX with lower pain thresholds was pointed.

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#### FRI0092 THE ASSOCIATION OF PSYCHOLOGICAL STRESS WITH INFLAMMATION IN PATIENTS WITH CLINICALLY SUSPECT ARTHRALGIA – A STUDY DURING RHEUMATOID ARTHRITIS DEVELOPMENT

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**Background:** Within established Rheumatoid Arthritis (RA), stress can have pro-inflammatory effects by activating the immune system via the hypothalamic-pituitary-adrenal axis and the autonomic nervous system. It is unknown if stress-levels promote also inflammation during RA-development.

**Objectives:** We studied whether the psychological stress response was increased in Clinically Suspect Arthralgia (CSA) and if this associated with inflammation at presentation with arthralgia and with progression to clinical arthritis.

**Methods:** In 241 CSA-patients, psychological stress was measured by the Mental Health Inventory (MHI-5) and the Perceived Stress Scale (PSS-10) at first presentation and during follow-up. Systemic inflammation was measured by C-reactive protein (CRP) and joint inflammation by 1.5T-MRI of wrist-, MCP- and MTP-joints.

**Results:** At baseline, 10% of CSA-patients had a high psychological stress-response according to the MHI-5. This was not different for patients presenting with or without an elevated CRP, with or without subclinical MRI-detected inflammation and for patients who did or did not develop arthritis. Similar findings were obtained with the PSS-10. When developing clinical arthritis, the percentage of patients with 'high psychological stress' increased to 31% ( $p=0.025$ ); during the first year of treatment this decreased to 8% ( $p=0.020$ ). 'High psychological stress' in non-progressors remained infrequent over time (range 7%–13%). Stress was associated with fatigue ( $p=0.003$ ) and wellbeing ( $p<0.001$ ).



**Conclusions:** Psychological stress was not increased in the phase of arthralgia, raised at the time of diagnoses and decreased thereafter. This temporal-relationship, and the lack of association with inflammation in arthralgia, argue against psychological stress having a significant contribution to inflammatory arthritis development.

**Disclosure of Interest:** None declared

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**FRI0093** **DON'T MISS THE DEPRESSION! COMORBIDITIES IN PATIENTS WITH RHEUMATOID ARTHRITIS AND THEIR IMPACT ON PATIENT-REPORTED OUTCOMES: RESULTS OF CLAIMS DATA LINKED TO A QUESTIONNAIRE SURVEY**

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**Background:** Comorbidities are increasingly acknowledged as important clinical manifestation in patients with rheumatoid arthritis (RA).

**Objectives:** To investigate the prevalence of comorbidities in RA and their association with patient-reported outcomes.

**Methods:** Data of 96 921 persons with RA and 4 84 605 age- and sex-matched controls of a German statutory health fund were studied on the presence of selected comorbidities in 2015. Diagnoses and therapies were assigned to the provider (general practitioner, rheumatologist or another specialist). A self-reported questionnaire, comprising joint counts (TJC, SJC), functional status (FFbH), impact of the disease (RAID) and well-being (WHO-5) was sent to a random sample of 6195 persons with RA of whom 3184 responded. For respondents who confirmed their RA (n=2,535), the association between comorbidities and patient-reported outcomes were analysed by multivariable linear regression analyses.

**Results:** Compared to controls, persons with RA (mean age 63 years, 80% female) had higher prevalences of all comorbidities, the most common were depression and osteoporosis besides cardiovascular risk factors (table 1). The diagnosis of depression was provided in 50% of cases by general practitioners, in 13% by rheumatologists and in 48% by other specialists while the diagnosis of osteoporosis was made in 76% by general practitioners, in 48% by rheumatologists and in 46% by other specialists. Among the survey respondents, increasing numbers of comorbidities were associated with worse TJC, SJC, function and WHO-5 values. Depression, obesity and osteoporosis had the highest impact on functional status and TJCs. The percentage of patients in rheumatologic care decreased from 73% with 0–1 comorbidity to 62% with ≥8 comorbidities (age-adjusted).

**Abstract FRI0093 – Table 1.** Prevalence of selected comorbidities in cases and controls

	RA patients n=96 921 % (95% CI)	Controls n=4 84 605 % (95% CI)
<b>Cardiovascular risk factors</b>		
Hypertension	61.8 (61.5–62.1)	48.0 (47.8–48.1)
Hyperlipidemia	39.4 (39.1–39.7)	32.4 (32.2–32.5)
Obesity	17.7 (17.5–18.0)	12.3 (12.2–12.3)
<b>Comorbid disorders</b>		
Depression	31.4 (31.1–31.7)	20.4 (20.3–20.5)
Osteoporosis	25.7 (25.4–26.0)	9.7 (9.6–9.8)
Diabetes	21.5 (21.2–21.7)	15.3 (15.2–15.4)
Cardiac arrhythmia	18.8 (18.5–19.0)	13.2 (13.1–13.3)
Hypothyroidism	17.9 (17.6–18.1)	12.8 (12.7–12.9)
Coronary heart disease	15.2 (15.0–15.4)	9.6 (9.5–9.7)
Liver disease	13.8 (13.6–14.0)	9.1 (9.0–9.1)
Vascular diseases	12.9 (12.7–13.1)	8.5 (8.4–8.6)
Asthma	12.3 (12.1–12.5)	7.4 (7.3–7.4)
COPD	11.3 (11.0–11.4)	6.6 (6.5–6.6)

**Conclusions:** Osteoporosis and depression are amongst the most common disorders in persons with RA. While osteoporosis is usually taken into account by the rheumatologist, more attention should be paid to depression as both disorders strongly affect patient-reported outcomes.

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**Disclosure of Interest:** None declared

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**FRI0094** **DOES SUBCLINICAL INFLAMMATION EXPLAIN JOINT PAIN IN PATIENTS WITH ARTHRALGIA SUSPICIOUS FOR PROGRESSION TO RHEUMATOID ARTHRITIS? – RESULTS OF A CROSS-SECTIONAL MRI-STUDY**

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**Background:** The development of Rheumatoid Arthritis (RA) is often preceded by a symptomatic phase of arthralgia. The etiology of symptoms in this phase is unclear.

**Objectives:** Since subclinical joint inflammation is expected to be causally related to pain, we aimed to determine associations between subclinical MRI-detected inflammation and pain in patients with arthralgia suspicious for progression to RA.

**Methods:** Unilateral MRIs of the wrist, MCP(2–5)- and MTP(1–5)-joints of 325 patients who fulfilled the EULAR definition of arthralgia suspicious for progression to RA were made and scored by two readers on subclinical inflammation (synovitis, bone marrow oedema (BME) and tenosynovitis). Associations between MRI-detected inflammation and overall pain severity at patient level (measured using the visual analogue scale (VAS)), and local tenderness at joint palpation, were studied in all patients, in ACPA-positive and ACPA-negative patients separately, and in the subgroup of patients that progressed to inflammatory arthritis.

**Results:** At patient level, synovitis ( $\beta=0.10$ ,  $p=0.048$ ) and tenosynovitis ( $\beta=0.11$ ,  $p=0.026$ ) associated with the VAS-pain. Of the 1620 imaged joints, 447 (28%) were tender. Subclinical inflammation was present in 32% of tender joints and in 25% of non-tender joints. MRI-detected synovitis associated independently with joint tenderness (OR 1.74,  $p<0.001$ ). In ACPA-negative patients synovitis associated independently with joint tenderness (OR 1.96,  $p<0.001$ ), while BME was independently associated with joint tenderness in ACPA-positive patients (OR 2.39,  $p=0.005$ ). Sensitivity analyses in patients who developed arthritis during follow-up (n=61) revealed similar associations.

**Conclusions:** In patients with arthralgia suspicious for progression to RA, joint tenderness and pain are associated with MRI-detected subclinical inflammation. The association is incomplete, indicating that subclinical inflammation is not the sole explanation of the arthralgia.

**Disclosure of Interest:** None declared

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**FRI0095** **ANTI-TNFA VERSUS RITUXIMAB IN REFRACTORY PERIPHERAL ULCERATIVE KERATITIS ASSOCIATED TO RHEUMATIC DISEASES. MULTICENTER STUDY OF 24 PATIENTS**

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**Background:** This study shows that treatment with biologic drugs, including anti-TNF drugs, in NION associated to IMIDs, refractory to conventional treatment, seems to be effective. These results must be confirmed in prospective and randomised trials.

**Objectives:** Our aim was to compare anti-TNF $\alpha$  vs Rituximab (RTX) in refractory PUK.

**Methods:** Multicenter study of 24 patients with PUK. All of them presented inadequate response to corticosteroids and at least 1 systemic traditional immunosuppressive drug.

Anti-TNF $\alpha$  were used in 17 patients: Adalimumab (n=9) 40 mg/sc every 1–2 weeks, infliximab (IFX) (n=7) 3–5 mg/kg iv/4–6 weeks, etanercept (n=1) 50 mg/week. RTX was used in 7 patients 1–2 g i.v. every 6 or 12 months.

The main outcomes were Best Corrected Visual Acuity (BCVA), signs of inflammation (scleritis and episcleritis), progression to corneal thinning, central keratolysis and ocular perforation.

Abstract FRI0095 – Table 1

	anti-TNF $\alpha$ n=17	RTX n= 7	P
<b>General features</b>			
Sex ( $\bar{x}/\bar{z}$ )	4/2	13/5	0.79
Mean age (years)	59.1 $\pm$ 18.3	54.28 $\pm$ 10.7	0.49
Ocular bilateral involvement #	23.53	57.14	0.13
Duration of underlying diseases (days)	183.06 $\pm$ 18.3	138.85 $\pm$ 77.68	0.59
<b>Basal</b>			
BCVA*	0.58 $\pm$ 0.38	0.56 $\pm$ 0.34	0.68
Peripheral thinning #	18	9	0.77
Central keratolysis #*	4	1	0.59
Ocular perforation #	2	1	0.89
Scleritis #	3	8	0.001
Episcleritis #	3	4	0.15
Uveitis #	3	2	0.77
<b>1<sup>st</sup> month</b>			
BCVA*	0.67 $\pm$ 0.31	0.56 $\pm$ 0.27	0.67
Peripheral thinning #	5	6	0.032
Central keratolysis #*	-	-	-
Ocular perforation #	-	-	-
Scleritis #	1	1	0.54
Episcleritis #	1	0	0.45
Uveitis #	1	2	0.23
<b>6<sup>th</sup> month</b>			
BCVA*	0.7 $\pm$ 0.25	0.73 $\pm$ 0.29	0.67
Peripheral thinning #	9	3	0.14
Central keratolysis #*	0	3	0.028
Ocular perforation #	-	-	-
Scleritis #	-	-	-
Episcleritis #	-	+	-
Uveitis #	1	0	0.38
<b>1st year</b>			
BCVA*	0.75 $\pm$ 0.22	0.70 $\pm$ 0.24	0.77
Peripheral thinning #	7	3	0.25
Central keratolysis #*	1	1	0.89
Ocular perforation #	0	1	0.30
Scleritis #	-	-	-
Episcleritis #	-	-	-
Uveitis #	1	0	0.35

Comparisons were made between baseline and 1<sup>st</sup> month, 6<sup>th</sup> month and 1<sup>st</sup> year (STATISTICA, StatSoft Inc. Tulsa, Oklahoma, USA). Quantitative variables were expressed as mean  $\pm$ SD or median [IQR], accordingly to its distribution. They were compared with the Student t or the Mann-Whitney U test respectively. Dichotomous variables were expressed as percentages and compared by the chi-square test.

**Results:** We studied 24 patients/32 affected eyes. The underlying diseases in the anti-TNF $\alpha$  group were Rheumatoid Arthritis (RA) (n=14), Psoriatic Arthritis (n=2) and Behçet Disease (n=1); and in the RTX group: RA (n=5), granulomatous polyangiitis (n=1) and microscopic polyangiitis (n=1).

At baseline there were no significant differences between both groups in general features or in ocular involvement (table 1). Before biologic therapy they had received the following systemic drugs (anti-TNF $\alpha$  vs RTX) i.v. methylprednisolone (2 vs 4), doxycycline (7 vs 1), ascorbic acid (2 vs 0), MTX (11 vs 4), AZA (1 vs 2) and others (7 vs 3). In addition, 10 patients, in both groups, had required surgery: amniotic membrane (n=5), penetrating keratoplasty (n=2), conjunctival resection (n=2), tissue adhesives (n=2), conjunctival flap (n=1) and lamellar keratoplasty (n=1).

Once the treatment was initiated the ocular outcome was similar (table 1). After a mean follow-up of 22.53 $\pm$ 22.60 (anti-TNF $\alpha$ ) and 22.28 $\pm$ 8.28 months with RTX the following severe side effects were observed: supraventricular tachycardia (n=1) with RTX and pulmonary tuberculosis (n=1) with IFX.

**Conclusions:** In this study, anti-TNF $\alpha$  therapy and RTX were equally effective for the treatment of peripheral ulcerative keratitis associated to rheumatic diseases refractory to conventional treatment.

**Disclosure of Interest:** None declared

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#### FRI0096 IS SIDE EFFECTS AND TREATMENT RESPONSE TO METHOTREXATE ASSOCIATED TO COMORBIDITY IN EARLY RHEUMATOID ARTHRITIS

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**Background:** In Denmark approximately 0.7% (35.000) of the population is diagnosed with rheumatoid arthritis (RA). RA is a risk factor in development of comorbidity, and comorbidities are not well managed in RA patients. In addition of being first line treatment of early RA, methotrexate (MTX) gives a 70% reduction in cardiovascular disease caused mortalities, and if treatment exceeds a year, the general mortality risks are lowered by 60%. Discontinuation of MTX is therefore a bad outcome for RA. It remains unclear whether side effects and treatment response to MTX is associated to comorbidity in early RA.

**Objectives:** To evaluate the association between comorbidity and persistence to MTX treatment and side effects for RA patients.

**Methods:** Patient files from three centres were evaluated retrospectively. Inclusion criteria were: diagnosis obtained according to ACR/EULAR 2010 criteria for RA in the period 01/01/2010 to present, and MTX as first line of treatment. Medical records were reviewed for side effects, dose changes of MTX, formulation changes and persistence. Comorbidities and comedication was evaluated by usage of the Danish National Patient Registry (DNPR), and the Odense Pharmacoepidemiological Database (OPED). Comorbidities were scored according to the Charlson Comorbidity Index (CCI), and analysed by the cox proportional hazards model for discontinuation of MTX treatment and dose reduction.

**Results:** 501 patients were screened, 177 were eligible and analysed at baseline for disease characteristics, medication besides MTX and comorbidities in a 5 year window before RA diagnosis baseline. The highest risk of MTX discontinuation was a CCI of 3–4, they had crude 4.18 (95% CI 1.67–10.45) increased risk compared to the reference group (RA with no comorbidities). Risk of dosage reduction was highest at CCI 1–2: 1.38 (95% CI 0.72–2.62). A CCI of 5 or higher gave a –4.83 mg (95% CI –10.24– –0.59) adjusted difference in maximum weekly tolerable MTX dosage. Side effects occurred for 23.7%. Most likely dosage causing side effect was 20 mg (IQR 15–20 mg). Nausea occurred in 29% and hepatic events 21%.

**Conclusions:** Patients with CCI in the range of 3–4 had an increased risk for discontinuing MTX treatment.

**Disclosure of Interest:** None declared

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#### FRI0097 EXPRESSION OF UNCOUPLING PROTEIN-1 IN SUBCUTANEOUS FAT REDUCES THE TOTAL CHOLESTEROL LEVEL AND CARDIOVASCULAR RISK IN FEMALE RA PATIENTS

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**Objectives:** To improve understanding of fat-related molecular mechanisms behind the increased cardiovascular (CV) morbidity in patients with rheumatoid arthritis (RA).

**Methods:** Transcription of uncoupling protein 1 (UCP1) was measured in the subcutaneous fat tissue and serum levels of lipoproteins, adipokines, and inflammation markers in 185 middle-aged female patients (mean age 51 years) with RA and compared between the groups stratified by the total cholesterol (TC) levels and the body mass index (BMI). The risk of dying of CV disease within 5 years was calculated electronically using the strategy proposed by Pocock et al.<sup>1</sup>

**Results:** CVR was highest (risk score 27.76, 5 year CVR 0.67%) in the patients combining high TC (>5.1 mmol/L) and high BMI (>25 kg/m<sup>2</sup>), while those with low levels of TC and BMI had lowest CVR (risk score 10.82, CVR 0.11%). CVR was significantly decreased if either TC (TC<sup>0</sup>BMI<sup>hi</sup>) or BMI (TC<sup>hi</sup>BMI<sup>lo</sup>) was low (p=0.017 and p=0.014, respectively). With the exception of TC<sup>lo</sup>BMI<sup>lo</sup> group, these groups had no difference with respect to age, disease duration, inflammation defined by serum IL6 and IL1, and disease activity measured by DAS28. TC<sup>lo</sup>BMI<sup>hi</sup> patients had an overall increase in fat expression of UCP1 (p=0.047) that has the cholesterol lowering capacity and may explain low TC levels in this

group. In contrast, TC<sup>hi</sup>BMI<sup>lo</sup> patients had high prevalence of cases with unmeasurable UCP1 expression and higher levels of serum adiponectin (p=0.053) and HDL (p<10<sup>-5</sup>).

Measurable expression of UCP1 was found in 79%. In total cohort, the patients with measurable UCP1 had higher inflammation and RA activity presented by IL-6 (p=0.0001), IL1b (p=0.037) and DAS28 (p=0.0086), compared to those with no UCP1 expression. TC<sup>lo</sup>BMI<sup>hi</sup> patients had an overall increase in fat expression of UCP1 (p=0.047) and lowest prevalence of cases with no UCP1 expression (6.2%).

**Conclusions:** The study shows that UCP-1 expression in subcutaneous fat may be a CV protective mechanism in RA patients. The inflammation seems to be the driving force of UCP1 expression in RA.

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FRI0098

#### HEPATIC SAFETY IN PATIENTS WITH RHEUMATOID ARTHRITIS WHO RECEIVED ISONIAZID FOR LATENT TUBERCULOSIS: POST-HOC ANALYSIS FROM PHASE 3 BARICITINIB STUDIES

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**Background:** Baricitinib (BARI) is an oral selective Janus kinase (JAK 1/2)<sup>1</sup> inhibitor approved in the EU, Japan, and other countries for treatment (tx) of moderately to severely active rheumatoid arthritis (RA) in adults. RA therapies may increase risk of tuberculosis (TB).<sup>2</sup> The use of isoniazid (INH) plays a vital role to control TB. However, INH may result in hepatic adverse events (AEs)<sup>3</sup>. Limited data exist on hepatic safety in TB patients (pts) with RA treated with JAK inhibitors and INH.

**Objectives:** To evaluate the hepatic safety in pts with RA, who were receiving INH for latent TB (LTBI) in BARI phase 3 trials.

**Methods:** This is a descriptive post-hoc analysis of three phase 3 studies: RA-BEAM, RA-BUILD, and RA-BEACON. All pts were screened for LTBI prior to randomisation. Pts with untreated LTBI and without documentation of prior completed tx, received INH at least for 4 weeks (wk) prior to randomisation and during the clinical trial period. Changes in ALT levels ( $\geq 1X$ ,  $\geq 3X$ ,  $\geq 5X$ , and  $\geq 10X$  of ULN) from baseline up to 24 wk were analysed by tx groups (BARI 4 mg, BARI 2 mg, adalimumab [ADA], and placebo [PBO]).

**Results:** In total, 2516 pts were included in this analysis. Of these, 891 pts were treated with BARI 4 mg, 403 with BARI 2 mg, 330 with ADA, and 892 with PBO. Background csDMARDs, mainly methotrexate (MTX) were continued. Overall, 246 pts reported LTBI at screening across all tx groups. Of these, 169 with confirmed lab data received INH as LTBI tx. At wk 24, ALT $\geq 1X$  was reported in 24 (41.4%) pts receiving BARI 4-mg+INH. None of the pts in BARI 4-mg+INH reported ALT level of  $\geq 3X$ ,  $\geq 5X$ , and  $\geq 10X$  ULN. For BARI 2-mg+INH, ALT $\geq 1X$  reported in 9 (33.3%) pts, ALT $\geq 3X$  in 2 (7.4%), ALT $\geq 5X$  in 1 (3.7%), and ALT $\geq 10X$  in 1 (3.7%) of the pts. Among pts treated with ADA +INH, ALT $\geq 1X$  was reported in 12 (44.4%), ALT $\geq 3X$  in 2 (7.4%), ALT $\geq 5X$  in 1 (3.7%), and ALT $\geq 10X$  in none of pts. Among pts treated with PBO+INH, ALT $\geq 1X$  was reported in 21 (36.8%), ALT $\geq 3X$  and ALT $\geq 5X$  levels were reported in 2 (3.5%, for both) of the pts. None of the pts reported ALT $\geq 10X$ . One pt receiving INH in RA-BEAM PBO arm had temporary interruption of tx due to abnormal hepatic lab results. No study tx interruption or discontinuation was reported in INH users in BARI or ADA groups due to abnormal hepatic lab results.

**Abstract FRI0098 – Table 1.** Changes in ALT level from baseline to week 24 in patients receiving BARI, ADA, and PBO

	BARI 4-mg (RA-BEAM, RA-BUILD, RA-BEACON) N=891		BARI 2-mg (RA-BUILD, RA- BEACON) N=403		ADA (RA-BEAM) N=330		PBO (RA-BEAM, RA-BUILD, RA-BEACON) N=892	
	INH (n=58)	No INH (n=833)	INH (n=27)	No INH (n=376)	INH (n=27)	No INH (n=303)	INH (n=57)	No INH (n=835)
ALT $\geq 1X$ ULN	24 (41.4%)	260 (31.2%)	9 (33.3%)	82 (21.8%)	12 (44.4%)	91 (30.0%)	21 (36.8%)	183 (21.9%)
ALT $\geq 3X$ ULN	0	13 (1.6%)	2 (7.4%)	6 (1.6%)	2 (7.4%)	9 (3.0%)	2 (3.5%)	13 (1.6%)
ALT $\geq 5X$ ULN	0	5 (0.6%)	1 (3.7%)	1 (0.3%)	1 (3.7%)	3 (1.0%)	2 (3.5%)	3 (0.4%)
ALT $\geq 10X$ ULN	0	2 (0.2%)	1 (3.7%)	0	0	1 (0.3%)	0	0

ALT=alanine transaminase; ULN=upper limit of normal; INH=isoniazid.

All pts were on concomitant use of csDMARDs, mainly MTX.

**Conclusions:** The percentage of pts with  $\geq 1X$  ULN ALT was numerically higher in INH group vs no INH and was consistent across PBO, BARI and ADA tx groups. The data do not suggest an increased hepatic safety risk in pts treated with BARI who were receiving concomitant INH.

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FRI0099

#### LIVER ENZYME ABNORMALITIES AFTER TOFACITINIB TREATMENT IN PATIENTS WITH HEPATIC STEATOSIS FROM THE RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS AND PSORIASIS CLINICAL PROGRAMMES

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**Background:** Non-alcoholic fatty liver disease, characterised by hepatic steatosis (HS), is a major cause of chronic liver disease in many countries. Limited data are available on liver enzyme elevation in patients (pts) with HS who are receiving medications for inflammatory conditions, such as rheumatoid arthritis (RA), psoriatic arthritis (PsA) and psoriasis (PsO). Tofacitinib is an oral Janus kinase inhibitor for the treatment of RA and PsA, and has also been studied in PsO.

**Objectives:** To describe baseline characteristics and liver enzyme abnormalities in pts from the tofacitinib RA, PsA and PsO clinical programmes with/without HS at baseline.

**Methods:** Pts randomised to the tofacitinib (5 or 10 mg twice daily; doses pooled) and placebo arms of 25 studies in the RA, PsA and PsO programmes were



included in this pooled post hoc analysis. Most studies allowed or mandated concomitant treatment with disease-modifying antirheumatic drugs. HS was determined by the investigator and captured per the Medical Dictionary for Regulatory Activities term at baseline. Baseline characteristics, incidence of elevated total bilirubin, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) >1 x and >3 x the upper limit of normal (ULN) up to Month (M) 3, and change from baseline in C-reactive protein (CRP) at M3 – all by HS at baseline – are reported.

**Results:** A total of 10 212 pts were in the analysis. The prevalence of HS was 1.6% across indications (RA: 87/6729 [1.3%]; PsA: 277/10 [3.8%]; PsO: 45/2773 [1.6%]). Baseline characteristics were generally similar in pts with or without HS (table 1). However, baseline obesity, diabetes, triglycerides and liver enzymes were numerically higher, and CRP was numerically lower, in pts with HS than in those without HS (table 1). In both tofacitinib- and placebo-treated pts, incidence of elevated total bilirubin, AST and ALT >1 x ULN up to M3 was higher in pts with HS than in those without HS, across indications (table 1). Incidence of elevated total bilirubin, AST and ALT >3 x ULN up to M3 was low across indications, irrespective of HS (table 1). Among tofacitinib-treated pts, CRP was reduced at M3 in pts with or without HS, but to a lesser extent in those with HS, across indications. Among placebo-treated pts, changes in CRP were small, irrespective of HS (table 1).

**Abstract FRI0099 – Table 1.** Baseline characteristics and liver function up to Month 3, by HS at baseline

	No HS at baseline, all indications (N=6180)*				HS at baseline, all indications (N=167)			
Age, mean (SD), years	59.2 (10.9)				61.0 (10.6)			
Female, n (%)	972 (15.6)				91 (53.9)			
RAE, mean (SD), mg/L	27.1 (6.6)				23.0 (6.8)			
HAQ, mean (SD), n (%)	1.7 (1.0)				1.8 (1.0)			
Alcohol use, n (%)	2012 (32.6)				67 (40.1)			
Diabetes, n (%)	101 (1.6)				7 (4.2)			
CRP, mean (SD), mg/L	2.2 (2.4)				1.6 (1.7)			
Comorbidities, n (%)	2038 (33.0)				89 (53.3)			
Cardiovascular, n (%)	1018 (16.5)				34 (20.4)			
LDL, mean (SD), mg/dL	113.7 (31.6)				117.1 (34.1)			
HDL, mean (SD), mg/dL	60.1 (19.6)				55.4 (17.2)			
Triglycerides, mean (SD), mg/dL	131.2 (38.3)				152.8 (46.6)			
ALT, mean (SD), U/L	31.0 (15.1)				37.4 (13.6)			
ALT, mean (SD), U/L	25.0 (12.4)				34.4 (12.6)			
Gamma-GT, mean (SD), U/L	137.0 (45.6)				143.0 (37.7)			
ALT or GGT, mean (SD), U/L	172.2 (47.2)				87 (51.5)			

Indication	RA		PsA		PsO		RA		PsA		PsO	
	(N=4881)	(N=499)	(N=116)	(N=113)	(N=5)	(N=11)	(N=11)	(N=7)	(N=11)	(N=1)	(N=1)	(N=1)
CRP, mean (SD), mg/L*	12.1 (24.0)	4.8 (12.4)	4.4 (11.9)	11.1 (24.2)	4.9 (14.6)	2.4 (7.3)	2.1 (11.5)	2.1 (11.5)	2.1 (11.5)	2.1 (11.5)	2.1 (11.5)	2.1 (11.5)
Tot bilirubin >= 1.5 x ULN, n (%)	129 (2.7)	42 (8.5)	13 (11.3)	17 (15.1)	4 (8.0)	1 (7.7)	1 (9.1)	1 (9.1)	1 (9.1)	1 (100)	1 (100)	1 (100)
Tot bilirubin >= 3 x ULN, n (%)	4 (0.1)	1 (0.2)	1 (0.9)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ALT >= 1.5 x ULN, n (%)	416 (8.5)	141 (28.4)	20 (17.2)	25 (22.1)	6 (12.0)	1 (9.1)	1 (9.1)	1 (9.1)	1 (9.1)	1 (100)	1 (100)	1 (100)
ALT >= 3 x ULN, n (%)	18 (0.4)	6 (1.2)	1 (0.9)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ALT or GGT >= 1.5 x ULN, n (%)	1016 (20.8)	323 (64.7)	30 (26.3)	30 (26.5)	6 (12.0)	1 (9.1)	1 (9.1)	1 (9.1)	1 (9.1)	1 (100)	1 (100)	1 (100)
ALT or GGT >= 3 x ULN, n (%)	7 (0.1)	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Indication	RA		PsA		PsO		RA		PsA		PsO	
	(N=111)	(N=22)	(N=8)	(N=8)	(N=1)	(N=1)	(N=1)	(N=1)	(N=1)	(N=1)	(N=1)	(N=1)
CRP, mean (SD), mg/L*	2.8 (2.1)	0.7 (1.5)	1.4 (1.4)	1.3 (1.4)	0.3 (0.4)	0.3 (0.4)	0.3 (0.4)	0.3 (0.4)	0.3 (0.4)	0.3 (0.4)	0.3 (0.4)	0.3 (0.4)
Tot bilirubin >= 1.5 x ULN, n (%)	1 (0.9)	1 (4.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Tot bilirubin >= 3 x ULN, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ALT >= 1.5 x ULN, n (%)	11 (10.0)	4 (18.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ALT >= 3 x ULN, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ALT or GGT >= 1.5 x ULN, n (%)	11 (10.0)	4 (18.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ALT or GGT >= 3 x ULN, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

**Conclusions:** In this exploratory analysis, prevalence of HS at baseline was 1.6% across the tofacitinib RA, PsA and PsO programmes. After up to 3 months of tofacitinib treatment, incidence of mildly elevated liver enzymes was higher in pts with HS than in those without HS. Incidence of severely elevated liver enzymes was low overall, and similar in pts with or without HS. Further studies are needed to evaluate the effects of tofacitinib on CRP and liver enzymes, and the potential impact on clinical response, in pts with RA, PsA or PsO who have comorbid HS.

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FRIDAY, 15 JUNE 2018

**Rheumatoid arthritis – biological DMARDs**

**FRI0100 MULTI-OMICS ANALYSIS IDENTIFIES A GENE SIGNATURE ASSOCIATED WITH THE CLINICAL RESPONSE TO ANTI-TNF THERAPY IN RHEUMATOID ARTHRITIS**

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**Background:** Tumour Necrosis Factor (TNF) inhibitors have improved the management of many patients with rheumatoid arthritis (RA). However, ~30% of anti-TNF treated patients do not show a significant clinical improvement. To date, little is known on the biological mechanisms underlying the differential response to anti-TNF agents.

**Objectives:** We sought to identify genetic variation associated with the anti-TNF response in RA using a sequential multi-omics approach.

**Methods:** First, we aimed to identify gene coexpression modules (GCMs) associated with anti-TNF response. For this objective, we extracted the RNA from synovial biopsies of 13 RA patients starting anti-TNF therapy and determined the expression profiles using Illumina microarrays. GCMs were identified using the WGCNA approach. The association between GCMs and anti-TNF response was performed using the eigengene of each GCM. Clinical response was defined using the EULAR criteria at week 14. To analyse the association of GCMs with anti-TNF response at the genetic level, we used 348 anti-TNF treated RA patients from Spain. The statistical analysis was performed using GWAS data and the set-based test in PLINK. The GCMs that were significantly associated with anti-TNF response were subsequently tested for validation in an independent cohort of 2706 anti-TNF treated RA patients. The functional implication of the validated GCMs was studied via pathway and cell type epigenetic enrichment analyses.

**Results:** We identified 148 GCMs in the RA synovium. From these, 15 GCMs were found to be associated with anti-TNF response (p<0.05). At the genetic level, we found two of the 15 GCMs to be associated with the adalimumab (ADL) and infliximab response (p<0.05) in the Spain cohort. In the independent cohort, we replicated the association of the GCM associated with ADL response (p=0.01). The validated GCM was found to be enriched in genes that participate in the nucleotides metabolism (p=2.41e-5). The epigenetic analysis revealed that ADL-associated variants are enriched in epigenetic marks from immune cell types like Tregs (p=0.04).

**Conclusions:** Our study shows the existence of a drug-specific genetic basis for the anti-TNF response. Therefore, this molecular diversity should be considered for biomarker research in RA.

**Disclosure of Interest:** None declared

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**FRI0101 UNMET NEEDS IN THE TREATMENT OF RHEUMATOID ARTHRITIS. AN OBSERVATIONAL STUDY AND A REAL-LIFE EXPERIENCE FROM A SINGLE UNIVERSITY CENTRE**

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**Background:** Despite the progress in the treatment of rheumatoid arthritis (RA), a significant number of patients does not achieve low disease activity (LDA).

**Objectives:** The purpose of this study was to estimate the size of unmet needs in the treatment of RA, using all the conventional synthetic disease modifying antirheumatic drugs (csDMARDs) and/or biological DMARDs (bDMARDs) in a long-term observational study.

**Methods:** Between January 2006 and December 2017, 538 patients with early RA were followed up in the outpatient rheumatology clinic. All patients fulfilled the 2010 ACR/EULAR classification criteria, had disease duration less than 1 year and were csDMARDs and bDMARDs naive. The patients were treated according to EULAR and ACR recommendations and strategies for RA. The following

csDMARDs were introduced: methotrexate (MTX), leflunomide (LFN), sulfasalazine (SSZ) and hydroxychloroquine (HCQ). In addition, the following bDMARDs were used: abatacept, adalimumab (ADA), certolizumab, etanercept (ETN), golimumab, infliximab (INF), rituximab and tocilizumab. Finally, small doses of steroids were used. During follow-up the clinical, laboratory findings as well as the treatment decisions and strategies were all recorded. In addition, the adverse drug reactions, the reason of termination or changing strategies, disease complications and comorbidities were all recorded. Finally, disease activity was measured with the 28 joint count, Disease Activity score-28 (DAS-28) using the erythrocyte sedimentation rate.

**Results:** All patients have received one csDMARD, at least for 6 months. The csDMARD of first choice was MTX (58%), followed by LFN (32%), HCQ (8%), and SSZ (2%) with or without small doses of steroids. The bDMARD of first choice was INF (37%) followed by ETN (32%) and ADA (31%). During the follow up period, 14 patients were lost. In addition, 7 patients never received bDMARDs due to various comorbidities. Thus, the final results are referred to 517 patients. Among those patients, 324 (66%) were treated with csDMARDs as monotherapy or in combination therapy with or without the use of steroids with significant clinical improvement and sustained LDA. However, eleven patients (3,2%) from this group neither achieved LDA, nor received bDMARDs, due to comorbidities. On the other hand, 175 patients (34%) were treated with bDMARDs with or without csDMARDs or/and steroids. The majority of them demonstrated sustained LDA for a long period of time. From this group 31 patients (17,7%) never achieved LDA, despite that they switched and received all bDMARDs. Thus a total of 20,9% of our patients never achieved LDA.

**Conclusions:** Using the EULAR and ACR recommendations for RA therapy we successfully treated the majority of our patients. However, we found that the size of gap and the unmet needs for RA treatment is about twenty per cent. This is the first study aiming to estimate the gap and the size of unmet needs for RA treatment in a large patient population followed-up in a tertiary university centre.

**Disclosure of Interest:** None declared

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FRI0102

#### REDUCTION OF ANTIDRUG ANTIBODY LEVELS AFTER SWITCHING TO RITUXIMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS WITH PREVIOUS FAILURE TO INFILIXIMAB OR ADALIMUMAB

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**Background:** Rituximab (Rtx), a monoclonal antibody against CD20+, induces transient depletion of B cells and was approved for the treatment of patients with active rheumatoid arthritis (RA). Previous data<sup>1</sup> showed that Rtx is particularly effective on autoimmune diseases in which auto-antibodies (auto-Ab) are produced. Based on this, it is hypothesised that auto-Ab produced by short-lived plasma cells expressing CD20 are targets of Rtx. Given this scenario, the immunogenicity related to the use of Infliximab (Ifx) or Adalimumab (Ada) could be cleared by Rtx.

**Objectives:** First, to analyse the persistence of anti-drug antibodies (ADA) after switching to either a 2nd biological therapy (TNFi or Rtx) after 12 months of follow-up. Second, to evaluate whether the reduction of ADA levels are influenced by the mechanism of action of the second biological therapy (BT).

**Methods:** Dataset from a prospective cohort including all patients with RA starting BT at the Unit of Complex Therapy in a tertiary hospital was used. For this study, data from 21 patients who had experienced previous failure to Ifx (57%) or Ada (43%) related to ADA detection and then switched to a 2nd TNFi (Ifx, Ada, Etanercept or Certolizumab) or to Rtx was analysed. Additionally, patients should have both determinations of ADA levels: at the end of the first BT and 12 months after switching. ADA were determined by a bridging ELISA. The proportion of patients with ADA positive levels at 12 months was determined. Also, the relative reduction (in median) of ADA levels between patients switching to a 2nd TNFi vs Rtx in both visits was compared.

**Results:** Out of 21 ADA positive patients with RA, 15 (71%) switched to a 2nd TNFi and 6 (29%) to Rtx. Demographic characteristics of patients are shown in table 1.

ADA remained positive in 80% of patients at 12 months after switching BT. The percentage of patients with undetectable ADA levels at 12 months was higher in

the group of patients treated with Rtx compared with patients receiving a 2nd TNFi (33% vs 13%, respectively). The median ADA levels (AU/ml) values at baseline and at 12 months were 536 and 123 for Rtx and 3625 and 1842 for TNFi. The relative reduction of median ADA levels between baseline and 12 months visits was higher in patients with Rtx than in patients treated with TNFi (-78% vs -50%, respectively).

**Abstract FRI0102 – Table 1.** Demographics characteristics of the 21 patients according to the second biological.

Switch to:	TNFI(n=15)	RTX(n=6)
Women, n(%)	13 (87%)	6 (100%)
Age, years, median(IQR)	47 <sup>(37–56)</sup>	50.5 (42.5–65.5)
Smoking status, n(%)	2 (13%)	1 (17%)
IMC, Kg/m <sup>2</sup> , median(IQR)	23.6 (19.3–28.6)	34.1 (25.2–32.5)

**Conclusions:** Despite discontinuing TNFi, ADA titers remain positive in a high proportion of patients with RA after one year. Over time, ADA levels decrease in patients who switch to a second BT, being this effect more pronounced in patients receiving Rtx than a 2nd TNFi. This effect could be explained by the intrinsic action mechanism of Rtx on plasmatic CD20+ cells.

#### REFERENCE:

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**Disclosure of Interest:** None declared

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FRI0103

#### ONE-YEAR FOLLOW-UP OF A NATIONWIDE COHORT OF PATIENTS WITH INFLAMMATORY ARTHRITIS, WHO SWITCHED FROM ORIGINATOR TO BIOSIMILAR ETANERCEPT, FOCUSING ON PATIENTS WHO SWITCHED BACK TO ORIGINATOR. AN OBSERVATIONAL DANBIO STUDY

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**Background:** In Denmark, patients (pts) treated with originator etanercept (ETA) 50 mg SC conducted a mandatory non-medical switch to biosimilar SB4 in April 2016 (*switchers*). Pts treated with 25 mg ETA or 50 mg powder-solution were not mandated to switch (*non-switchers*). Some switchers resumed ETA during follow-up (*back-switchers*).

**Objectives:** To investigate the frequency of *back-switching* after the non-medical switch from ETA to SB4, and in *back-switchers* to study, 1) baseline characteristics at the time of initial switch (ETA->SB4), 2) reasons for SB4 withdrawal, 3) changes in disease activity during treatment with SB4 and after *back-switching*.

**Methods:** Patient data were retrieved from the DANBIO registry (censored August 2017). For *back-switchers*, disease activity at the start of SB4 (=baseline) and at the time of *back-switching* to ETA were compared, and changes in disease activity between the two time points were calculated (=delta values), stratified by indication (RA/PsA/AxSpA). Baseline characteristics of *back-switchers* were compared to the rest of the switch population (Chi-sq, Mann-Whitney U-test). Abbreviations are shown in table 1.

**Results:** 1641 pts switched from ETA to SB4. Of these, 299 (18%) withdrew SB4 therapy during 1 year follow-up and either switched back to ETA (n=120, 7%), started another bDMARD (n=104), died (n=9), were lost to follow-up (n=1) or did not re-start bDMARDs (n=65).

Among the 120 *back-switchers*, SB4 was withdrawn due to LOE (52%), AE (39%), or other/unknown reasons (9%). The reasons for withdrawal of SB4 in *back-switchers* are listed in table 1. No major safety events occurred. The median time on SB4 before *back-switching* was 120 (IQR 73–193) days, and the time

between stop of SB4 and re-start of ETA was  $1^{1-1}$  days. Baseline characteristics of back-switchers vs the rest of the switch population were similar (all  $p>0.05$ ). Among back-switchers who stopped SB4 due to LOE, PGA increased during SB4 treatment, whereas CRP and SJC were largely unchanged (table 1). At the date of censoring, 104/120 back-switchers (87%) were still treated with originator ETA (median treatment duration 236 (155–302) days).

**Abstract FRI0103 – Table 1.** Description of ETA-SB4-ETA back-switchers (n=120)

	RA, n=80	PsA, n=20	AxSpA, n=20
<b>Characteristics upon start of SB4, n=120</b>			
Female, %	73	55	35
Age, years	59 (52-70)	45 (36-56)	43 (38-56)
SJC, n	0 (0-1)	0 (0-0)	-
CRP, mg/L	3 (1-8)	1 (1-5)	3 (1-6)
PGA, mm	27 (12-54)	25 (13-63)	23 (13-44)
<b>Characteristics upon re-start of ETA in pts who back-switched due to LOE, n=62</b>			
Pt number, n	38	11	13
SJC, n	2 (0-5)	0 (0-2)	-
CRP, mg/L	3 (2-11)	3 (2-7)	4 (1-6)
PGA, mm	64 (50-76)	78 (18-90)	42 (35-63)
<b>Delta-values among pts who stopped due to LOE and back-switched, n=62**</b>			
Delta-SJC, n	1 (0-4)	0 (0-0)	-
Delta-CRP, mg/L	0 (-1-5)	1 (0-2)	0 (0-4)
Delta-PGA, mm	30 (12-52)	15 (7-77)	25 (19-35)
Pts stopped due to AE, n=47: Arthralgia 1 pt, bladder dysfunction 1, blurred vision 1, diarrhea 4, dizziness 2, dyspnea 2, erectile dysfunction 1, hair loss 1, headache/migraine 4, hyperhidrosis 2, hypertension 1, hypotension 1, infections 2, leg cramps 1, local injection problems 3, myalgia 1, nausea 2, neuropathies 1, psoriasis/pustulosis 1, rash/itching 9, not stated 21 (total =62 events)			
Numbers are medians (IQR) unless otherwise stated, *DAS28<2.6 (RA, PsA), ASDAS<1.3 (AxSpA)			
** Disease activity at time of re-start ETA minus SB4 start			
<b>Abbreviations:</b> AE: adverse event, CRP: C-reactive protein, ETA: originator etanercept, LOE: lack of effect, PGA: patient global score, SB4: biosimilar etanercept, SJC: swollen joint count			

**Conclusions:** In a nationwide cohort of 1621 arthritis patients that were switched from ETA to SB4, 7% switched back to ETA. Back-switchers had no distinct clinical or disease characteristics upon start of SB4. AEs prior to back-switching were largely unspecific. In pts who withdrew SB4 due to LOE, PGA had increased. Reasons for back-switching appeared to be predominantly subjective rather than objective (nocebo effect). Originator drug was still available (25 mg or 50 mg powder-solution), which may have encouraged back-switching.

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FRI0104

#### PREDICTORS FOR THE RESPONSE TO ANTI-TNF THERAPY AND THE IMPACT OF SMOKING IN RHEUMATOID ARTHRITIS- RESULTS ON A GROUP OF PATIENTS IN ROMANIA

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**Background:** 20%–40% of the patients are declared nonresponders to at least one of the biologic agents.

**Objectives:** to test the possible predictive role of RF type IgM and IgA, anti-CCP, anti-MCV, 14–3–3eta protein and COMP on a group of patients treated with anti-TNF $\alpha$  agents. We also followed the evolution of serum titres of these biomarkers under biologic therapy and the impact of smoking regarding response to treatment.

**Methods:** prospective and observational study including 64 patients followed 12 months with active RA, uncontrolled by csDMARDs. Clinical assessment was performed at 0,6 and 12 months according to ACR criteria and evaluation of treatment response according to EULAR criteria (good/moderate/nonresponder).

**Results:** Following baseline immunological parameters titres and the response at 6 months, tests for identifying differences between the groups showed that lower titres of both RF isotypes, anti-CCP, 14–3–3eta protein and COMP had predictive value on achieving a good EULAR response at 6 months. Grouping patients in 2 categories (responders/nonresponders), just 14–3–3eta protein and anti-CCP maintained their predictive value for the response at 6 months.

For the visit at 12 months, lower baseline titres for RF type IgM (92.93 $\pm$ 120.22 U/ml,  $p=0.010$ ) and IgA (49.96 $\pm$ 98.08 U/ml,  $p=0.002$ ) had predictive value for achieving a good response at 12 months. We didn't obtain other informations grouping patients in 2 categories.

The status pretreatment influenced the good response for COMP at 6 months ( $p=0.001$ ) and RF IgA at 12 months ( $p=0.004$ ).

Using multivariate logistic regression methods we obtained a statistical model for predicting the response at 6 months including normal values for 14–3–3eta protein, anti-CCP and COMP (Hosmer and Lemeshow according test  $\lambda^2=5.795$ ,  $p=0.670 \geq 0.05$  with a predictive response accuracy of 89.1%).

Smoking had a negative impact on the EULAR response as well as on 2 groups response at 6 months of treatment ( $p=0.017$ ).

	6 Months response nonresponders	6 Months response moderate	6 Months response good
<b>Smoking</b>	2/7 (28.6%)	29/38 (76.3%)	17/19 (89.5%)
No	0/6 (0.0%)	3/38 (7.9%)	1/19 (5.3%)
Past	5/7 (71.4%)	6/38 (15.8%)	1/19 (5.3%)
Yes			

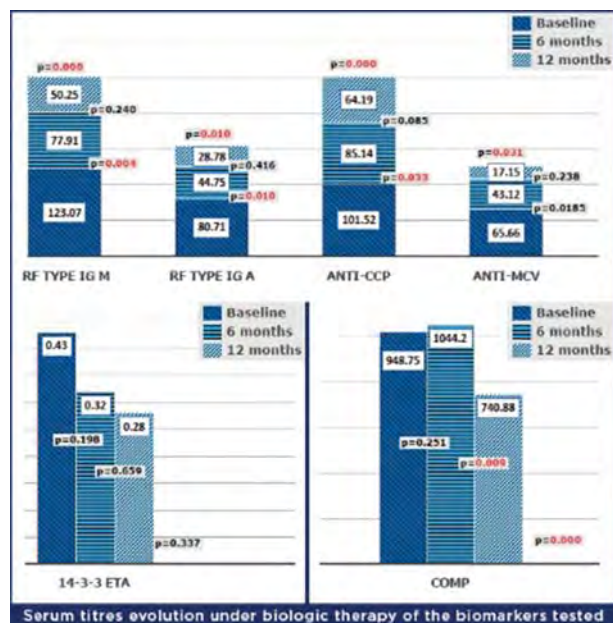
0.046 (Likelihood Ratio corrected Bonferroni)

Following the evolution of serum levels, we noticed a reduction for all biomarkers tested, statistically significant at 6 and/or 12 months from baseline.

**Abstract FRI0104 – Table 1.** Description of ETA-SB4-ETA back-switchers (n=120)

	Nonresponder	Moderate response	Good response	p value	Nonresponder	Responder	p value
No.	7	38	19		7	57	
RF type Ig M	132.35 $\pm$ 99.602	157.22 $\pm$ 131.47	51.36 $\pm$ 95.359	<b>0.016</b>	132.35 $\pm$ 99.602	121.93 $\pm$ 129.92	0.571
RF type Ig A	122.81 $\pm$ 99.876	102.08 $\pm$ 128.33	22.45 $\pm$ 61.256	<b>0.033</b>	122.81 $\pm$ 99.87	75.54 $\pm$ 116.282	0.307
Anti-MCV	74.04 $\pm$ 47.951	80.06 $\pm$ 149.543	33.77 $\pm$ 113.069	0.459	74.04 $\pm$ 47.951	64.63 $\pm$ 139.174	0.860
14–3–3 eta protein	0.99 $\pm$ 0.888	0.28 $\pm$ 0.469	0.51 $\pm$ 0.580	<b>0.045</b>	0.99 $\pm$ 0.888	0.36 $\pm$ 0.515	<b>0.040</b>
Anti-CCP	146.16 $\pm$ 41.688	113.65 $\pm$ 50.448	60.82 $\pm$ 26.331	<b>0.000</b>	146.16 $\pm$ 41.68	96.04 $\pm$ 50.355	<b>0.028</b>
COMP	1042.2 $\pm$ 181.71	1032.8 $\pm$ 188.67	746.04 $\pm$ 130.09	<b>0.000</b>	1042.2 $\pm$ 181.717	937.27 $\pm$ 218.10	0.227





**Conclusions:** in the future a version using multiple biomarkers could increase accuracy for identifying pretreatment patients who will respond to anti-TNF therapy. Smoking has a negative impact on the response to biologic treatment.

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#### FRI0105

#### CONCOMITANT USE OF CORTICOSTEROIDS AT THE BASELINE DOES NOT AFFECT THE DRUG SURVIVAL OF ABATACEPT IN RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is a chronic inflammatory disease leading to deformities and disabilities. In the treatment of RA glucocorticoids are selected sometimes to relieve symptoms and to increase compliance for treatment.

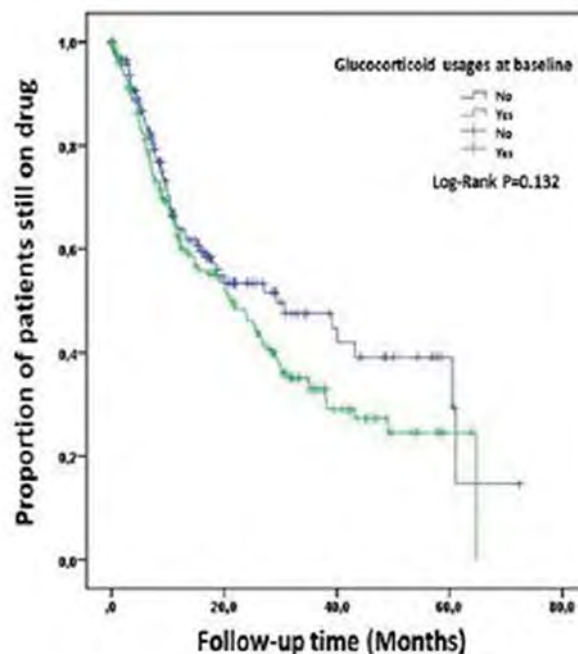
**Objectives:** The purpose of our study is to investigate whether concomitant glucocorticoid treatment at the baseline affects drug survival for abatacept treatment in RA.

**Methods:** Data on patient characteristics, diagnosis, previous treatment and outcomes have been collected since 2011 in Turkish Biologic (TURKBIO) Registry. By the end of December 2017, 338 RA patients, received abatacept from the TURKBIO registry, were included in the analysis. Patients were divided into groups according to the use of glucocorticoid when abatacept therapy was started. Demographic and clinical data including age, sex, disease type, disease duration, and previous or current treatment with DMARDs and biological drug durations are recorded in the database. Kaplan-Meier survival analysis was performed to estimate the drug survival. Subgroups were compared by log-rank.

**Results:** There were no significant differences in age, gender, seropositivity, tender and swollen joint counts at baseline in the study groups. The disease duration was higher in the glucocorticoid users ( $p=0.001$ ). Abatacept was the first choice bDMARDs in the 44.5% of glucocorticoid users while it was 68.6% in the glucocorticoid non-users ( $p<0.001$ ). In addition to abatacept, use of sDMARDs were 96.7% and 53.8% in the glucocorticoid users and non-users, respectively. Baseline VAS-pain and ESR were higher in the glucocorticoid non-users ( $p=0.047$ ,  $p=0.009$ , respectively), but other baseline parameters were similar in glucocorticoid users and non-users. There was no difference between groups in terms of drug survival rates for abatacept (figure 1).

**Abstract FRI0105 – Table 1.** Clinical and laboratory characteristics

	Glucocorticoid non-users (n=156)	Glucocorticoid users (n=182)	p
Age, year	56 (47–64)	57 (47–63)	0.827
Gender (Females), n (%)	135 (86.5)	151 (82.9)	0.390
Disease duration, years	10 (5–15)	13 (8–18)	0.001
1 st choice bDMARDs is abatacept,%	68.6%	44.5%	<0.001
Concomitant sDMARD usage,%	53.8%	96.7%	<0.001
RF positivity, n (%)	68.1	65.8	0.735
CCP positivity, n (%)	61.8	66.7	0.485
Baseline ESR, mm/h	38 (24–55)	28 (18–44)	0.009
12th month ESR, mm/h	33 (20–50)	27 (16–39)	0.155
Baseline CRP, mg/dl	12 (5–21)	12 (4.89–30.9)	0.870
12th month CRP, mg/dl	4 (3–8)	9 (3–19)	0.020
Baseline DAS28-CRP	4.95 (4.2–5.4)	4.8 (3.9–5.35)	0.123
12th month DAS28-CRP	2.05 (1.7–2.9)	2.6 (2.1–3.9)	0.002
Baseline CDAI	22 (13.8–28.3)	19.8 (13.2–27)	0.278
12th month CDAI	3.2 (2–7.95)	6.3 (3–10.7)	0.061



**Abstract FRI0105 – Figure 1.** Drug survival curve in glucocorticoid user and non-user patients

**Conclusions:** When abatacept treatment started, concomitant use of glucocorticoid at the baseline could not significantly alter drug survival for abatacept in the RA.

**Disclosure of Interest:** None declared

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#### FRI0106

#### IMPACT OF BIOLOGICAL AND TARGETED SYNTHETIC DMARDs ON WORK IN PATIENTS WITH CHRONIC INFLAMMATORY ARTHRITIS : A META ANALYSIS OF RANDOMISED CONTROLLED TRIALS AND CONTROLLED COHORTS

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**Background:** The addition of biological (b) and new targeted synthetic (ts) DMARDs agents in chronic inflammatory arthritis (CIAs) therapeutic strategies

has improved the possibility of controlling disease activity and slowing the progression of joint damage. However their impact on work participation is unclear.

**Objectives:** To assess the effect of biological and tsDMARDs versus conventional treatments in patients with CIAs on work outcomes: employment, presenteeism and absenteeism.

**Methods:** A systematic review of the literature using Pubmed-Medline and the Cochrane library was performed until January 2017. All randomised controlled trials (RCT) and controlled cohorts (CC) comparing work outcomes in patients with rheumatic diseases such as rheumatic arthritis (RA), ankylosing spondylarthritis (AS) and psoriatic arthritis (PsA) treated with biological or tsDMARDs versus conventional therapies were selected. Statistical analysis determined in each study effect size (ES) or odds-ratios (OR) as appropriate to assess the magnitude of treatment effect. Pooled ES and OR were computed by meta-analysis. A random effect model was used in case of heterogeneity.

**Results:** Thirty six RCTs and eight CCs were analysed ie 12 769 patients with conventional treatment and 19 875 patients with bDMARD or tsDMARD (4619 Infliximab, 4629 Etanercept, 3872 Adalimumab, 670 Golimumab, 2101 Certolizumab, 691 Abatacept, 444 Sirukumab, 1668 Baricitinib, 672 Tofacitinib, 365 Sarilumab, 444 Sirukumab etc); 34 studies included 30 423 patients with RA, 7 studies included 1496 patients with AS and 3 studies included 725 patients with PsA.

This meta-analysis showed in patients treated by bDMARD vs conventional treatment:

- a significant decrease of accumulated missed workdays at week 24: ES  $-0.34$  IC95% $[-0.6; -0.08]$  and at week 52: ES  $-0.04$  IC95% $[-0.29; 0.2]$ ,

- a significant decrease of patients losing hours due to CIAs: RR 0.63 IC95% $[0.48; 0.83]$ ,

- a significant improvement in VAS productivity: ES  $-1.81$  IC95% $[-2.61; -1.01]$ ,

- For the employment loss, the positive effect of bDMARDs was nearly significant: OR 0.60 IC95% $[0.33; 1.09]$ .

**Conclusions:** Despite the heterogeneity of the data, this meta-analysis showed the beneficial effect of bDMARDs on both absenteeism and presenteeism in CIAs. Thus the high cost of biologic agents could be partly balanced with savings in indirect costs.

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#### FRI0107 FIVE SUCCESSFUL PREGNANCIES WITH ANTENATAL ANAKINRA EXPOSURE

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**Background:** Current recommendations are to discontinue the interleukin-1 (IL-1) inhibitor anakinra prior to pregnancy given lack of safety evidence.<sup>1</sup> A total of 39 previous exposed pregnancies have been documented in the literature, and two resulting cases of fetal renal agenesis have been described.<sup>2,3</sup>

**Objectives:** Our aim is to add to the limited existing data on IL-1 inhibitor use in pregnancy.

**Methods:** Data were obtained from the Organisation of Teratology Information Specialists (OTIS) Autoimmune Disease in Pregnancy Project, a prospective cohort study of pregnancy outcomes in the U.S. and Canada. Eligible women enrolled prior to 19 weeks' gestation between 2004 and 2017. Women who consented to participate were interviewed two to three times during pregnancy with a standard questionnaire regarding medical history, exposures during pregnancy, and demographic characteristics. Outcomes were obtained by maternal interview and medical record abstraction.

**Results:** Five pregnancies with anakinra exposure were identified, all resulting in full-term singleton live births, mean gestational age at delivery of 38.9 weeks, with no major or long-term infant complications. Three maternal subjects used anakinra for adult-onset Still's disease (AOSD) and two for juvenile idiopathic arthritis (JIA). One mother was diagnosed with AOSD during pregnancy, and anakinra was started at 20 weeks' gestation. All other subjects had a known diagnosis prior to pregnancy, and four subjects used the medication into the third trimester. All maternal subjects used 100 mg dosing of anakinra, four with daily use, one with weekly use. For all subjects who discontinued anakinra, some amount of steroid medication was necessary for treatment of disease flare. Two subjects developed oligohydramnios, one also with pregnancy-induced hypertension. Two women

had caesarian sections, one medically-indicated and one scheduled. One infant had low birth weight, but follow-up records indicated normal adjusted weight at one year. Three women successfully breastfed their infants, at least two of whom continued anakinra while breastfeeding.

**Conclusions:** Anakinra was used successfully in five full term pregnancies. Two subjects developed oligohydramnios, however. With the two previous reported cases of fetal renal agenesis, a process leading to low fluid levels, and the fact that maternal hyperthermia has been previously linked to fetal renal anomalies,<sup>4</sup> it is worth further exploring the potential link between anakinra use, uncontrolled maternal febrile disease, and fetal outcomes. These data add to the limited knowledge regarding antenatal anakinra use and support its use in pregnant women without access to effective alternative therapies that have a larger volume of reassuring safety data.

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**Disclosure of Interest:** None declared

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#### FRI0108 GOLIMUMAB IMPROVES WORK PRODUCTIVITY AND ACTIVITY AND QUALITY OF LIFE IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA), PSORIASIS ARTHRITIS (PSA) AND AXIAL SPONDYLOARTHRITIS (AXSPA): INTERIM RESULTS FROM A NON-INTERVENTIONAL STUDY IN AUSTRIA (GO ACTIVE)

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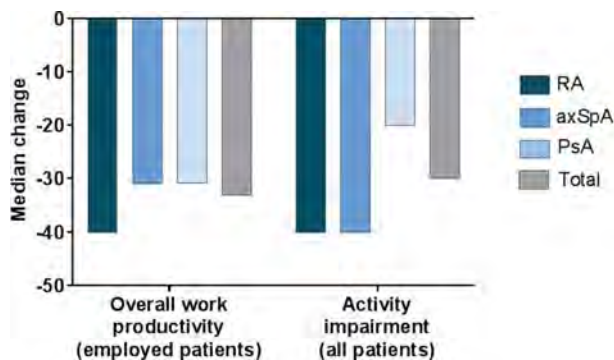
**Background:** Golimumab has shown clinical efficacy and tolerability within its clinical trial program. No systemic outcome data regarding patient-reported outcomes and health economic parameters reflecting the real world use of golimumab in Austria are currently available.

**Methods:** Go Active is a prospective, non-interventional, multi-centre study in Austria. The impact of golimumab therapy on work productivity and activity (WPAI) and quality of life (RAQoL for RA patients, AsQoL for axSpA patients, PsAQoL for PsA patients) is assessed by using patient reported outcomes. Patients (target recruitment: n=320) are followed up to 2 years. For the current interim analysis (data cut-off: 18DEC2017) changes in the primary endpoint from baseline to month 3 were analysed in 167 patients.

**Results:** 167 patients are included in the current analysis (74 patients with RA, 49 patients with axSpA, and 44 patients with PsA). At study entry, most patients were biological-naïve and employed.

Median age at registration was 52 years (patients with RA: 57 years, patients with axSpA: 41 years, and patients with PsA: 44 years). Almost 2/3 of patients were female (84% of patients with RA, 37% patients with axSpA, and 55% of patients with PsA). Most patients were biological-naïve at study entry (77% of all patients, 73% of patients with RA, 80% of patients with axSpA, and 82% of patients with PsA). 42% of patients were not employed (58% of patients with RA, 29% of patients with axSpA, and 30% of patients with SpA); 14% due to incapacity for work (12% of patients with RA, 21% of patients with axSpA, and 16% of patients with SpA) and 54% due to age-related pension (60% of patients with RA, 21% of patients with axSpA, and 69% of patients with SpA). Most of the patients, who worked for pay, worked full time. 159 of all patients and 66 of employed patients completed the WPAI questionnaire at baseline and after 3 months. Overall work productivity improved by  $-33$  ( $-40$  for patients with RA, and  $-31$  for patients with axSpA and PsA) and activity impairment by  $-30$  ( $-40$  for patients with RA and

axSpA, and  $-20$  for patients with PsA; figure 1). Quality of life improved by  $-5$  for patients with axSpA and PsA, and by  $-7$  for patients with RA.



Abstract FRI0108 – Figure 1. WPAI questionnaire – Changes from baseline after 3 months of golimumab treatment

**Conclusions:** This interim analysis shows that golimumab treatment is effective in improving work productivity, daily activities as well as quality of life already within the first 3 months of treatment in RA, axSpA and PsA patients.

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#### FRI0109 DRUG IMMUNOGENICITY AND THE DEVELOPMENT OF PARADOXICAL ADVERSE EVENTS WITH BIOLOGIC THERAPIES

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**Background:** Defined as *de novo* or exacerbation of pathologies that usually responds to biologic agents, paradoxical reactions encompass for a wide spectrum of manifestations (cutaneous, intestinal, ocular) reported during biological therapy (TNF and non-TNF medications) regardless of the underlying rheumatic or non-rheumatic disorder.

**Objectives:** To assess drug levels (DL) and anti-drug antibodies (ADA) in patients with paradoxical reactions (*de novo* or exacerbation of psoriasis, uveitis, Crohn's disease) induced by biological drugs (bDMARS) in Rheumatoid Arthritis (RA), Ankylosing Spondylitis (AS) and Psoriatic Arthritis (PsA).

**Methods:** We performed a retrospective observational study in cohorts of consecutive RA (267), PSA (65) and AS (145) undergoing TNF (i-TNF) or non-TNF biologics according to the local recommendations for initiation and monitoring, attending a single academic rheumatology department.

All patients were assessed at every 24 weeks months for disease activity and outcomes; supplementary, drug immunogenicity (ADA and DL) was systematically evaluated in patients developing paradoxical adverse events.

DL and ADA were measured with an ELISA assay and antibody binding test, respectively. Serum drug levels were considered positive for infliximab if  $>0.035$   $\mu\text{g/mL}$ , for adalimumab  $>0.024$   $\mu\text{g/mL}$ , for etanercept  $>0.035$   $\mu\text{g/mL}$ , rituximab  $>0.75$   $\mu\text{g/mL}$ , while the cut-offs for ADA positivity to infliximab was established at 5AU/ml, for adalimumab at 10AU/ml, etanercept at 142 AU/ml, rituximab 140 AU/mL (ELISA, Progenika)

**Results:** 42 patients with paradoxical psoriasis (30 with *de novo* lesions, 18 with palmo-plantar pustulosis, 12 with exacerbation of pre-existent lesions), 12 with paradoxical uveitis (5 with a new onset uveitis) and 3 with paradoxical Crohn's were included in the final analysis. Paradoxical events related to abatacept, certolizumab (one *de novo* psoriasis per agent) or golimumab (2 new onset uveitis, one flare of Chron's disease) were excluded from the final analysis as no immunogenicity lab tests were provided.

Drug induced paradoxical events were described not only with all TNF inhibitors but also with rituximab. DL was in normal range in all these patients; in addition,

ADA were either negative, or, if present, had no impact on drug concentration. Furthermore, we found no significant differences in drug levels of TNF inhibitors for RA, PsA and AS.

Moreover, no statistical significant differences were observed in the detection of ADA between the three groups.

**Conclusions:** Patients who develop either true or borderline paradoxical AE have adequate drug levels, with normal ADA concentrations.

**Disclosure of Interest:** None declared

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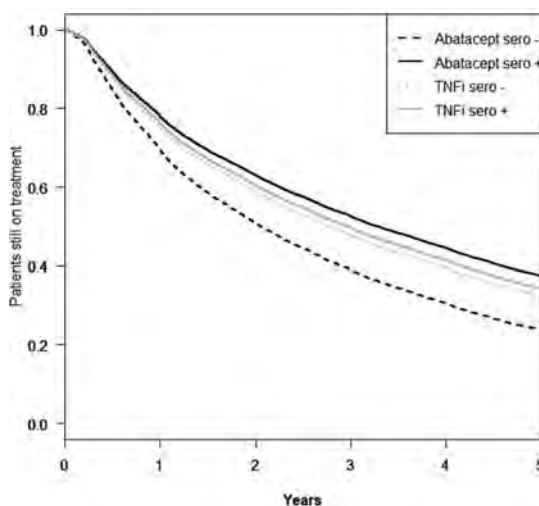
#### FRI0110 THE IMPACT OF SEROPOSITIVITY ON THE EFFECTIVENESS OF ABATACEPT VERSUS TNF INHIBITORS IN RHEUMATOID ARTHRITIS. REAL LIFE DATA FROM SEVERAL EUROPEAN REGISTRIES (THE PAN-ABA STUDY)

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**Background:** Rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA) are used as diagnostic tools, but may also be used as prognostic factors, as these biomarkers have been associated with better clinical responses to some biologic agents in rheumatoid arthritis (RA).

**Objectives:** To compare the impact of seropositivity on drug discontinuation and effectiveness for abatacept (ABA) and TNF inhibitors (TNFi) in patients (pts) with RA.

**Methods:** Pooled analysis of 13 observational RA registries from countries (FR, IT, CZ, DK, NO, PT, RO, ES, SE, CH, NL, JP, CA) where both ABA and TNFi were available concomitantly. Inclusion criteria were RA diagnosis, treatment with ABA or TNFi, and available RF or ACPA status. Main exposure was seropositivity: positive if RF or ACPA were positive, negative if both were negative, and missing if one was missing and the other was negative. Primary endpoint was drug discontinuation, analysed using Cox models, including treatment, seropositivity, and their interaction, adjusting for patient-, treatment-, and disease-characteristics, using strata terms for country and calendar year. We first tested for effect modification by country by additionally including an interaction term between treatment, seropositivity and country. Since we found no effect modification, we took out the interaction term. Effectiveness was analysed using DAS28 remission and low disease activity (LDA) at 1 year, corrected for attrition using Lundex<sup>1</sup>.



**Results:** Using data from 39 266 treatment-courses, in crude analyses, seronegativity was associated with higher drug discontinuation for pts on ABA but not on TNFi ( $p$  interaction  $<0.001$ ), with a hazard ratio (HR) for seropositive vs seronegative of 0.74 (95%CI: 0.66–0.82) for pts on ABA and 0.96 (95%CI: 0.92–1.01) for



pts on TNFi. On average, pts on ABA were older and had more prior bDMARDs. Adjusting for potential confounding factors did not modify the results qualitatively (figure 1), with significantly longer time before discontinuation in seropositive vs seronegative pts on ABA (adj. HR: 0.74 (95% CI: 0.67–0.84) but not on TNFi (adj. HR: 0.99 (95% CI: 0.94–1.04)).

The proportion of pts reaching DAS28 remission or LDA at 1 year was significantly higher for seropositive vs seronegative pts on ABA (difference in proportion: remission: 5.0%; LDA: 9.7%), but similar for seropositive vs seronegative pts on TNFi (difference in proportion: remission: –2.7%; LDA: –2.3%).

**Conclusions:** Data from this large pooled registry suggests that seropositivity in RA pts is associated with increased drug retention and effectiveness for ABA but not for TNFi.

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[1] Kristensen, et al. *A&R* 2006;(54):600–6.

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#### FRI0111 ANALYSIS OF REAL-LIFE INFLIXIMAB AND ADALIMUMAB DATA: DRUG SWITCHING AND FATE OF ANTIDRUG ANTIBODIES AND TROUGH LEVELS OVER TIME

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**Background:** Infliximab (IFX) and adalimumab (ADL) are biological drugs used in the treatment of rheumatoid arthritis (RA), spondyloarthritis (SpA), and juvenile idiopathic arthritis (JIA). Development of antidrug antibodies (ADAb) may lead to increased drug clearance and loss of therapeutic drug trough levels (TL). Switching to another drug may be necessary after ADAb development.

**Objectives:** To use real-life data from a large Finnish rheumatology patient cohort to determine the association between drug switching and ADAbs and the fate of ADAbs and TLs after ADAb development.

**Methods:** Serum samples for IFX or ADL ADAb and TL measurements from 1345 (567 RA, 479 SpA, and 299 JIA) rheumatology patients were taken on a clinical basis in daily practice in 20 Finnish referral hospitals. ADAb analyses were performed at Sanquin laboratories (Amsterdam, The Netherlands) using radioimmunoassays; TL analyses were performed at United Medix Laboratories (Helsinki, Finland) using commercial methods (Promonitor ELISA, Progenika Biopharma). Samples were collected and analysed from January 2012 until September 2017. ADAb values  $\geq 12$  AU/ml were considered positive; ADAb values were classified as low (12–30 AU/ml), intermediate (30–100 AU/ml) and high ( $\geq 100$  AU/ml).

**Results:** On the basis of TL data, we identified 67 patients (5%) who switched drugs. Of these patients, 47 (70.2%) provided ADAb measurements for the first drug; 33 (49.3%) patients were ADAb positive. Most (22 patients, 63.6%) had high ADAbs. Forty-nine (73.1%) patients provided ADAb measurements for the second drug. Of these patients, 11 (16.4%) were ADAb positive against the second drug; seven (63.6%) had high ADAbs. We identified 48 (3.6%) ADAb-positive patients who provided at least one follow-up ADAb measurement. Of these patients, 32 (66.7%) experienced ADAb loss; most (24 patients, 50%) experienced complete ADAb loss (most recent ADAb value  $\leq 12$  AU/ml). Twenty-five

patients that experienced ADAb loss had available TL measurements both before and after ADAb loss; 23 (92%) had increased TL after ADAb loss. Of the 16 patients that experienced ADAb gain, only 3/11 (27.3%) patients that had available TL measurements both before and after ADAb gain had increased TL after ADAb gain.

**Conclusions:** ADAb positivity is associated with drug switching; ADAb development against a second biologic drug is common. A significant proportion of ADAb-positive patients lose ADAbs over time. ADAb loss is associated with TL increase.

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#### FRI0112 PERSISTENCE ON TUMOUR NECROSIS FACTOR INHIBITOR (TNFI) MONOTHERAPY AFTER ACHIEVING REMISSION OR LOW DISEASE ACTIVITY (LDA) ON COMBINATION THERAPY AMONG PATIENTS WITH RHEUMATOID ARTHRITIS (RA)

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**Background:** Combination therapy with TNFis and conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) is standard for moderate to severe RA.

**Objectives:** To estimate persistence with etanercept (ETN) or other TNFi monotherapy among RA patients who achieved remission/LDA on combination TNFi +csDMARD therapy and then discontinued the csDMARD.

**Methods:** Data from RA patients in the Corrona registry during 10/1/2001–8/31/2017 were analysed. All patients had to be treated with TNFi +csDMARD combination therapy and to have reached Clinical Disease Activity Index remission/LDA and then discontinued the csDMARD (index date). ETN (fusion protein comprising TNF receptor and human IgG1 Fc) and other TNFi therapies (monoclonal antibodies: adalimumab, certolizumab pegol, golimumab, and infliximab) were analysed separately. Outcomes were percentages of patients persistent on index TNFi monotherapy, discontinued index TNFi, switched (to another biologic or to csDMARD monotherapy), or added csDMARD therapy (to receive combination therapy) at 6 months (primary analysis) and 12 months post-index.

**Results:** Data from 617 patients were analysed (182 ETN, 435 other TNFi); mean age (standard deviation [SD]) was 57.4 (13.3) years, 73% were female. Mean time (SD) in remission/LDA before csDMARD discontinuation was 17.0 (24.3) months. Rates of monotherapy persistence at 6 months were 56% for ETN and 45% for other TNFi (table 1). Patients with  $\geq 6$  month persistence on monotherapy had mean duration (SD) of 28.2 (22.1) months on ETN monotherapy or 27.8 (23.3) months on other TNFi monotherapy. Rates of persistence for all patients at 12 months were 46% for ETN and 33% for other TNFi. Patients with  $\geq 12$  month persistence had mean duration (SD) of 35.9 (22.6) months on ETN monotherapy or 39.3 (24.4) months on other TNFi monotherapy. For a subset of patients with  $< 6$  months in remission/LDA before index date (44% of patients), rates of monotherapy persistence at 6 months were 60% for ETN and 42% for other TNFi.

	Treatment pattern, n (%)			
	Persistent on index TNFi monotherapy	Not persistent on index TNFi monotherapy		
		Discontinued index TNFi	Switched to new biologic or csDMARD	
<b>6 months</b>				
ETN (n=182)	102 (56)	6 (3)	10 (6)	64
Other TNFi (n=435)	195 (45)	21 (5)	23 (5)	(35) 196 (45)
<b>12 months</b>				
ETN (n=120)	55 (46)	1 (1)	8 (7)	56
Other TNFi (n=307)	102 (33)	22 (7)	19 (7)	(47) 164 (53)

**Conclusions:** Monotherapy with ETN or other TNFi is an option for patients in remission/LDA;  $> 50\%$  of patients on ETN remained on monotherapy 6 months after discontinuing their csDMARD.

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#### FRI0113 SWITCHING TO ANTI-IL-6 BIOLOGICS AFTER ANTI-TNF THERAPY IN CHILDREN WITH JIA

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**Background:** Development of biologics gives rise to novel classes of drugs, offering more options for treating children with primary or secondary failure of anti-TNF therapy. However, the question of whether or not previous exposure to biologic therapy and the number of previously administered biologics influence the efficacy of current treatment still needs to be solved.

**Objectives:** To compare tocilizumab efficacy in biologics-naïve and biologics-switched patients with JIA.

**Methods:** Comparative analysis involved patients who had initiated TOC treatment at the National Medical Research Centre of Children's Health (Moscow) depending on previous history of biologics therapy. Treatment efficacy was evaluated according to the dynamics of clinical and laboratory signs using the ACR-Pedi criteria. The Wallace criteria were used to evaluate whether or not remission had been achieved.

**Results:** Thirty-two patients were biologics-naïve and 43 patients switched to TOC were previously treated with ETA (n=10), ADA (n=34), certolizumab (n=2), and infliximab (n=1). Children in the biologics-naïve group differed from the switchers in a number of important baseline parameters: shorter disease duration (2.13 [1.25:5.34] and 7.42 [3:10.75] years, respectively; p<0.001) and lower arthritis severity indices (the number of joints affected, the CHAQ and JADAS scores). Therapy with TOC in children was found very effective. The CHAQ and JADAS disease activity scores, the CRP and ESR laboratory values, morning stiffness duration, and the VAS score (assessed by both patient and physician), and the number of affected joints (swollen or painful joints, joints with the limited range of motion and with active arthritis) significantly decreased after 4 week therapy in all patients (p<0.01). The percentages of biologics-naïve patients and switchers who achieved ACR90 after the first 12 months of therapy were 31.25% and 25.6%, respectively (p=0.613). A smaller percentage of children achieved stable remission: 4.65% of switchers and 6.25% of biologics-naïve patients (p>0.999).

**Conclusions:** Tocilizumab therapy is highly efficient both as the first and subsequent biologic agent. Children with history of therapy with at least one biologic agent have lower chances for achieving remission during the first 12 months of therapy. However, this difference is most likely caused by the longer and more severe arthritis course in children allocated to the group of biologics-switched patients compared to biologics-naïve ones. Further matched large-cohort study is needed to identify predictors of response to therapy.

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#### FRI0114 EFFICACY AND RETENTION RATE OF CERTOLIZUMAB PEGOL IN RHEUMATOID ARTHRITIS: DATA FROM A LARGE REAL-LIFE MULTICENTRE RETROSPECTIVE COHORT

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**Background:** Even though certolizumab pegol (CZP) has been licensed for the treatment of rheumatoid arthritis (RA) since longtime, observational data in a real-life setting are still lacking.

**Objectives:** To retrospectively evaluate the use of CZP in a multicentric observational cohort of Northern Italy (the LORHEN registry), calculating both clinical response and retention rate. To explore the effectiveness of CZP in childbearing age female.

**Methods:** Data were retrospectively extracted from the LORHEN registry which includes all RA patients treated with CZP as first or second-line biologic agent between December 2010 and April 2017. The 2 year clinical response was evaluated as EULAR response and proportion of patients achieving Disease Activity Score 28 (DAS28-ESR) remission. The 5 year retention rate was calculated by Kaplan-Meier method. Cox proportional hazard models were developed to examine potential predictors of CZP persistence, including sex, line of CZP treatment (naïve vs switchers), childbearing age, and concomitant MTX as categorical variables, whereas age, disease duration, and baseline DAS28-ESR as continuous variables.

**Results:** The overall study population included 242 RA patients (78.9% female; mean [±standard deviation, SD] age 54.2±13.8 years; mean disease duration 10 ±13.1 years; baseline DAS28-ESR 4.58±1.39), who received CZP as first- (64%) or second-line (36%) biologic agent, as monotherapy (40.9%) or in combination with methotrexate (MTX, 59.1%). Two-year EULAR good +moderate response and remission rates were similar in first- and second-line patients (66% vs 60.7% [p=0.65] and 39.6% vs 32.1% [p=0.52], respectively). The overall 5 year retention rate was 42.5%, with no difference between first- and second-line therapy (43.5% vs 40.5%, respectively; p=0.98), but with a clear trend in favour of childbearing subpopulation versus older women (62.8% vs 32.3%, respectively; p=0.07). Concomitant MTX was a predictor of CZP persistence (Hazard Ratio [HR] 1.79, 95% confidence interval [95% CI] 1.08–2.95; p=0.02), whereas sex (HR 1.35, 95% CI 0.71–2.54, p=0.35), age (HR 1.01, 95% CI 0.99–1.03; p=0.14), mean disease duration (HR 0.99, 95% CI 0.97–1.02; p=0.87), and baseline DAS28-ESR (HR 1.15, 95% CI 0.96–1.38; p=0.12) were not associated with CZP retention rate. The most frequent reason for discontinuation was inefficacy (60%), whereas only 21% of patients stopped the drug because of adverse events.

**Conclusions:** In our real-life experience, CZP showed a very good clinical response, with more than one third of patients achieving 2 year clinical remission and more than 40% persisting on treatment after 5 years. Unexpectedly, no significant difference was found between first and second line of treatment. The use of CZP in childbearing women seems to be associated with a higher retention rate.

**Disclosure of Interest:** None declared

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#### FRI0115 INDIRECT STANDARDISED ASSESSMENT OF INJECTION SITE PAIN FOLLOWING SUBCUTANEOUS ADMINISTRATION OF CITRATE-FREE FORMULATION OF ADALIMUMAB AND ITS BIOSIMILAR ABP 501

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**Background:** In randomised double-blind studies in patients with rheumatoid arthritis (RA) and psoriasis (PsO), ABP 501, an approved adalimumab biosimilar, had significantly lower injection site pain (ISP) perception compared with the citrate-containing formulation (CCF) of adalimumab reference product (RP) (40 mg/0.8 mL); however, there have been no direct or indirect comparisons of ISP perception between ABP 501 and the CFF of the RP (40 mg/0.4 mL).

**Objectives:** To demonstrate that pain perception after injection of both the ABP 501 formulation and the CFF-RP formulation was lower than after CCF-RP.

**Methods:** We analysed ISP perception data after injection from two ABP 501 phase 3 studies, one in patients with RA (NCT01970475) and another in patients with PsO (NCT01970488) and 2 citrate-free RP formulation studies (NCT01561313, NCT01502423) where the "control" group received the CCF-RP. In all studies, patients were equally randomised between the 2 treatment arms. Patients were asked to rate the ISP perception on a visual analogue scale (VAS) on which the current pain level was marked from 0 cm (no pain) to 10 cm (worst possible pain). We calculated Cohen's d-statistic for difference in ISP perception with ABP 501 compared with CCF-RP for the 2 ABP 501 studies. Similar comparisons were performed between the ISP perception associated with CFF-RF and CCF-RF. These measures were subsequently compared in a descriptive manner.

**Results:** Both ABP 501 and CFF-RF were associated with lower ISP perception after injection with maximum reduction observed immediately post-injection. The 95% confidence intervals of relative reduction in ISP perception for ABP 501 formulation and the CFF-RP (table 1) were provided descriptively.



**Abstract FRI0115 – Table 1.** Cross-sectional indirect comparison of ISP after injection between adalimumab CFF and ABP 501.

Time point of pain assessment	Within 2 minutes		Within 5 minutes		15 minutes after injection	
Investigational products	CFF-RP vs. CCF-RP		ABP 501 vs. CCF-RP		CFF-RP vs. CCF-RP	
Study	Study 1	Study 2	RA study baseline visit	PsO study baseline visit	Study 1	Study 2
Overall number of subjects	62	60	576	343	62	60
Mean (SD) [n] ISP VAS score for CCF-RP (cm)	3.3 (2.2) [62]	4.2 (2.8) [60]	2.1 (2.3) [262]	1.9 (2.0) [173]	1.0 (1.52) [62]	1.0 (1.61) [60]
Mean (SD) [n] ISP VAS score for ABP 501/CCF-RP (cm)	1.6 (2.1) [62]	0.9 (1.1) [60]	1.0 (1.6) [264]	0.5 (0.8) [170]	0.9 (1.66) [62]	0.4 (1.08) [60]
Difference in mean VAS score (cm)	1.7	3.3	1.1	1.4	0.1	0.6
Cohen's d statistic (95% confidence interval)	0.80 (0.42, 1.17)	1.56 (1.19, 1.94)	0.56 (0.39, 0.73)	0.92 (0.76, 1.08)	0.06 (-0.22, 0.34)	0.44 (0.20, 0.69)

**Conclusions:** Compared with CCF-RP, both ABP 501 and CFF-RP were associated with lower injection site pain perception.

#### REFERENCE:

[1] Nash P, et al. *Rheumatol Ther* 2016;3(2):257–270.

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#### FRI0116

#### IMPACT OF PRIOR BIOLOGIC USE ON TREATMENT RESPONSE IN PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING ADALIMUMAB IN ROUTINE CLINICAL CARE: RESULTS FROM THE PASSION STUDY

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**Background:** It is recognised that early diagnosis and treatment are important in maximising long-term quality of life in patients (pts) with rheumatoid arthritis (RA). Prior biologic disease modifying antirheumatic drug (bDMARD) use has been shown to affect treatment response to further biologic therapy including adalimumab (ADA).

**Objectives:** To evaluate the impact of prior bDMARD use on clinical and pt-reported outcomes in pts enrolled in the PASSION study.

**Methods:** PASSION was a 78-wk postmarketing, multinational, observational study that assessed the effectiveness of ADA in pts with moderate to severe RA receiving ADA in routine clinical care in the context of participation in the voluntary AbbVie pt support program. Pts with an insufficient response to  $\geq 1$  DMARD (1 prior bDMARD was allowed) and newly initiating ADA were enrolled and categorised as bDMARD-naïve or bDMARD-experienced. For the present analysis, ADA treatment response was determined by evaluating least squares (LS) mean change from baseline for multiple clinical and pt-reported outcomes (table 1). Missing data for each efficacy endpoint were imputed using last observation carried forward, and differences between groups for efficacy endpoints at wks 24, 52, and 78 were based on ANCOVA models adjusting for baseline and demographic variables (table 1). Additionally, the percentages of pts at each time point (observed population) who achieved HAQ-DI minimal clinically important difference (MCID; improvement from baseline of  $\geq 0.22$ ) were assessed.

**Results:** Of 1025 pts included in the intent-to-treat population, 182 were bDMARD-experienced and 843 were bDMARD-naïve at baseline. There were no significant differences between groups in sex, race, ethnicity, weight, height, body mass index, TJC28, SJC28, and pain at baseline. However, bDMARD-

experienced pts were significantly older, had longer RA duration, and had lower values for HAQ-DI, DAS28(CRP), CDAI, SDAI, PtGA, and PhGA than bDMARD-naïve pts at baseline ( $p < 0.05$  for all). ADA treatment response was significantly higher for bDMARD-naïve vs bDMARD-experienced pts at all timepoints for HAQ-DI, DAS28(CRP), CDAI, PtGA, and pain, at wks 24 and 52 for SDAI, and at wk 24 for TJC28 and SJC28 (table 1). In the observed population, a large percentage of bDMARD-naïve and bDMARD-experienced pts achieved HAQ-DI MCID at wk 24 (67% and 60%), wk 52 (71% and 65%), and wk 78 (74% and 59%).

**Abstract FRI0116 – Table 1.** Least Squares Mean Change from Baseline in Efficacy Measures by Prior bDMARD Use at Each Study Visit (Intent-to-Treat Population, LOCF)

Measure	Visit	bDMARD-Naïve		bDMARD-Experienced		P-value
		N	LS Mean Change (SE)	N	LS Mean Change (SE)	
TJC28	Week 24	787	-6.05 (1.064)	164	-4.87 (1.136)	0.013*
	Week 52	795	-4.75 (1.122)	166	-3.99 (1.198)	0.139
	Week 78	797	-7.02 (1.190)	167	-6.03 (1.271)	0.066
SJC28	Week 24	787	-4.75 (0.750)	163	-3.96 (0.800)	0.019*
	Week 52	795	-4.23 (0.781)	167	-3.65 (0.833)	0.099
	Week 78	797	-5.87 (0.846)	168	-5.28 (0.903)	0.124
HAQ-DI	Week 24	799	-0.44 (0.107)	168	-0.29 (0.114)	0.001**
	Week 52	807	-0.52 (0.116)	171	-0.31 (0.124)	<0.001***
	Week 78	808	-0.49 (0.120)	171	-0.31 (0.128)	<0.001***
DAS28(CRP)	Week 24	721	-1.83 (0.263)	148	-1.34 (0.283)	<0.001***
	Week 52	748	-1.62 (0.275)	154	-1.27 (0.296)	0.007**
	Week 78	755	-2.05 (0.288)	154	-1.67 (0.310)	0.005**
CDAI	Week 24	743	-16.77 (2.299)	159	-13.65 (2.458)	0.003**
	Week 52	753	-14.48 (2.401)	161	-12.10 (2.568)	0.030*
	Week 78	756	-20.14 (2.570)	161	-17.18 (2.749)	0.011*
SDAI	Week 24	703	-18.27 (2.539)	147	-14.45 (2.731)	0.001**
	Week 52	729	-16.16 (2.613)	152	-13.42 (2.807)	0.025*
	Week 78	734	-21.59 (2.756)	152	-19.09 (2.960)	0.052
Pt Pain	Week 24	799	-22.21 (4.940)	168	-17.04 (5.283)	0.019*
	Week 52	806	-19.50 (5.124)	171	-14.27 (5.473)	0.022*
	Week 78	807	-32.40 (5.281)	171	-26.87 (5.642)	0.019*
PtGA	Week 24	799	-21.22 (4.819)	168	-13.31 (5.159)	<0.001***
	Week 52	807	-20.34 (4.998)	171	-14.01 (5.346)	0.005**
	Week 78	808	-28.60 (5.132)	171	-21.60 (5.490)	0.002**
PhGA	Week 24	763	-50.49 (4.482)	161	-27.25 (4.824)	0.118
	Week 52	771	-28.40 (4.616)	162	-26.00 (4.966)	0.260
	Week 78	774	-34.24 (4.855)	163	-30.24 (5.223)	0.074

\*\*\*, \*\*, \* statistically significant at  $P < 0.001$ , 0.01, and 0.05 levels, respectively for LS mean difference. Missing data were imputed for each efficacy endpoint using LOCF. The difference between two groups in efficacy endpoints at week 24, 52 and 78 were based on ANCOVA models adjusting for baseline and demographic variables (sex, race, ethnicity, age [years], PSP participation [ever (PSP users) vs never (PSP non-users)], diagnosis RA duration [years]).

ANCOVA, analysis of covariance; bDMARD, biologic disease modifying antirheumatic drug; CDAI, Clinical Disease Activity Index; DAS28(CRP), 28-joint Disease Activity Score C-Reactive Protein; HAQ-DI, Health Assessment Questionnaire Disability Index; LOCF, last observation carried forward; PtGA, physician global assessment of disease activity; PSP, Patient Support Program; PtGA, patient global assessment of disease activity; SDAI, Simplified Disease Activity Index; SJC28, Swollen 28-Joint Count; TJC28, Tender 28-Joint Count.

**Conclusions:** Among pts with moderate to severe RA that initiated ADA treatment in the PASSION study, bDMARD-naïve pts achieved significantly larger improvements from baseline to wk 78 in a variety of clinical and pt-reported outcomes compared with bDMARD-experienced pts. A large proportion of both bDMARD-naïve and bDMARD-experienced pts achieved HAQ-DI MCID with ADA treatment.

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FRI0117

### TOCILIZUMAB USE DIRECTLY AFTER sDMARD FAILURE SHOWS HIGHER RESPONSE RATES AND A LONGER TREATMENT DURATION

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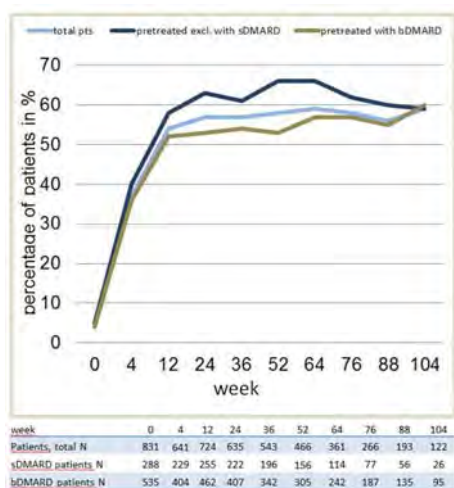
**Background:** The non-interventional study (NIS) ARATA (NCT02251860) observes the clinical effectiveness and safety of subcutaneous Tocilizumab (TCZ) s.c. treatment under routine conditions over a 2 year period.

**Objectives:** In this interim analysis, the patients were subgrouped according to their pretreatment: (I) pretreated exclusively with sDMARD or (II) also pretreated with bDMARD.

**Methods:** TCZ-naïve patients (Pts) ( $\geq 18$  years) with RA, who receive TCZ s.c. treatment, could be included in the study since 2014. Demographic and disease-specific characteristics, the progression of the disease (rheumatoid activity scores), concomitant medications, adverse events (AE) and patient questionnaires were documented.

**Results:** In this interim analysis (reporting date 01-FEB-2017), the data of 912 Pts were evaluated. 319 Pts (35%) were pretreated exclusively with sDMARD and 585 Pts (64.8%) were also pretreated with bDMARD. The main reason for a switch to TCZ s.c. was lacking effectiveness of the pretreatment.

In comparison, patients exclusively pretreated with sDMARD demonstrated a shorter median disease duration (6 vs. 9 years), TCZ s.c. was applied at BL more rarely in combination with MTX (23.5% vs. 35.6%) and more rarely with glucocorticoids (59.2% vs. 69.5%). The comorbidity rates were comparable in both groups. However, patients exclusively pretreated with sDMARD suffered half as often from osteoporosis (9.1% vs. 21.2%). Patients Exclusively pretreated with sDMARD had a longer median treatment duration (380.5 vs. 341.0 days) and a higher retention rate to week 52 (78.9% vs. 70.5%). The effectiveness of the TCZ s.c. treatment was examined with 831 patients. More patients with exclusively sDMARD pretreatment achieved a DAS28 remission and remained in remission (figure 1). The change from BL for the CDAI and Dcrt response was higher in the sDMARD subgroup. No new safety signals and no differences between the subgroups for all safety parameters were observed.



**Abstract FRI0117 – Figure 1.** Clinical remission (DAS28-ESR <2.6) after pretreatment (N=831). DAS28-ESR, Disease activity score 28-erythrocyte sedimentation rate.

**Conclusions:** The results of the third interim analysis of the NIS ARATA confirm the efficacy of TCZ s.c. observed in the approval trials in clinical practice. A fast and effective reduction of disease activity in the treated RA patients as well as a lasting improvement in all RA progression parameters collected was observed. In case of the earlier application of TCZ s.c., directly after sDMARD failure, higher response rates and a longer retention of the treatment were observed.

**Disclosure of Interest:** F. Behrens Grant/research support from: Abbvie, Pfizer, Roche, Chugai, Janssen, Novartis, Consultant for: Abbvie, Pfizer, Roche, Chugai, UCB, BMS, Celgene, MSD, Novartis, Biotest, Janssen, Genzyme, Lilly, Boehringer, Sandoz, W. A. Biewer: None declared, G.-R. Burmester Consultant for: Lilly, Pfizer, Sanofi, Roche, M. Feuchtenberger Consultant for: MSD, Roche, Abbvie, Chugai, Pfizer, UCB, J.-P. Flacke Employee of: Roche Pharma AG, M. Hofmann Employee of: Chugai Pharma Europe Ltd., P. Kästner: None declared, H. Kellner Consultant for: Roche, T. Klopsch: None declared, C. Kühne Consultant for: Celgene, Roche, Pfizer, Novartis, BMS, H.-P. Tony Consultant for: Roche Pharma, Abbvie, BMS, Chugai, Janssen, Novartis, Sanofi, Lilly, Speakers bureau: Roche Pharma, Abbvie, BMS, Chugai, Janssen, Novartis, Sanofi, Lilly, C. Amberger Consultant for: Chugai, AbbVie, Celgene, MSD, Pfizer, BMS, Hexal  
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FRI0118

### DEKAVIL (F8IL10) – UPDATE ON THE RESULTS OF CLINICAL TRIALS INVESTIGATING THE IMMUNOCYTOKINE IN PATIENTS WITH RHEUMATOID ARTHRITIS

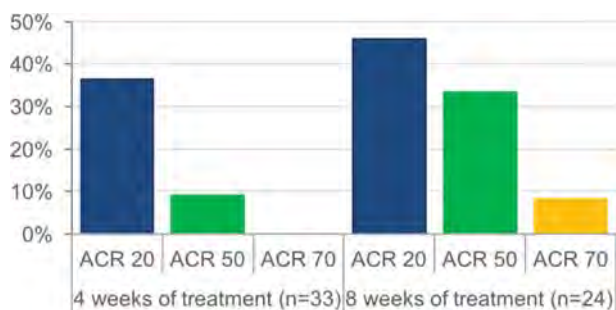
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**Background:** The targeted pharmacodelivery of cytokines by means of antibody-fusion proteins aims at selective accumulation of the active compound at the site of disease while sparing healthy tissues. Dekavil (F8IL10) is a fully human fusion protein composed of the vascular targeting antibody F8 fused to the cytokine interleukin-10. A phase 1 dose escalation study in patients with rheumatoid arthritis (RA) has recently been completed. Dekavil is currently under investigation in a phase 2 clinical study for the treatment of RA.

**Objectives:** The phase 1 study investigated safety, tolerability and the maximum tolerated dose of Dekavil when administered in combination with methotrexate (MTX). The currently ongoing phase 2 (in patients with active RA despite MTX therapy who had failed anti-TNF treatment) measures the mean change from baseline in DAS28-CRP between F8IL10 and placebo arms as primary endpoint.

**Methods:** The target population of both RA studies comprises patients with active RA despite MTX therapy who had failed anti-TNF treatment. Dekavil is administered once weekly for 8 consecutive weeks by s.c. injection in combination with a fixed dose of MTX (10–25 mg). The recently completed phase 1 study investigated escalating doses of Dekavil (6–600 µg/kg +MTX). The ongoing randomised multicenter, double-blind, placebo-controlled phase 2 trial assesses therapeutic activity in two treatment groups (Dekavil 30 or 160 µg/kg plus MTX) and one placebo group (placebo plus MTX).

**Results:** Dekavil was well tolerated up to the highest investigated dose (600 µg/kg) and an MTD was not reached. In 34 out of 35 patients treated in the phase 1 study no SAEs and no SUSARs were reported. One subject (cohort 9, 450 µg/kg) experienced a DLT (G2 purpura), which was accompanied by an SAE (G2 dyspnea, not drug related). The patient fully recovered within one week following corticosteroid administration. The most frequently observed adverse event was mild (G1) injection site reaction and occurred in 60% of the patients. Furthermore, two cases of drug related anaemia (G3 and G2; 160 µg/kg and 450 µg/kg, respectively) were reported in this study. All adverse reactions resolved completely. After 4 cycles of treatment, 36.4% of patients (12/33) exhibited ACR responses. The fraction of responses increased to 45.8% (11/24) after 8 cycles. Two patients achieved an ACR70 for more than 12 months after the last drug administration. As of January 2018, 25 patients have been treated in the phase 2 clinical study and neither SUSARs nor treatment-related deaths were recorded. Immunogenicity assessment is completed for the first 20 study subjects did not reveal an antibody response specific to F8IL10. An interim read-out after 45 patients will provide a more thorough understanding of the therapeutic activity of F8IL10.



**Abstract FRI0118 – Figure 1.** ACR responses after 4 and after 8 weeks of Dekavil treatment in the phase 1 study population including all dose levels (6 – 600µg/kg)

**Conclusions:** The data obtained in the population studied to date suggest that Dekavil may be a safe and well tolerated novel therapeutic for the potential treatment of RA.

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#### FRI0119 EFFECT OF DISCONTINUING TNF INHIBITORS DURING PREGNANCY ON THE COURSE OF RHEUMATOID ARTHRITIS AND JUVENILE IDIOPATHIC ARTHRITIS

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**Background:** Treatment changes at early pregnancy can be followed by a disease worsening.<sup>1</sup>

**Objectives:** To investigate whether the discontinuation of tumour necrosis factor inhibitors (TNFi) use during pregnancy is associated with any changes of disease activity at the third trimester in women with rheumatoid arthritis (RA) and juvenile idiopathic arthritis (JIA).

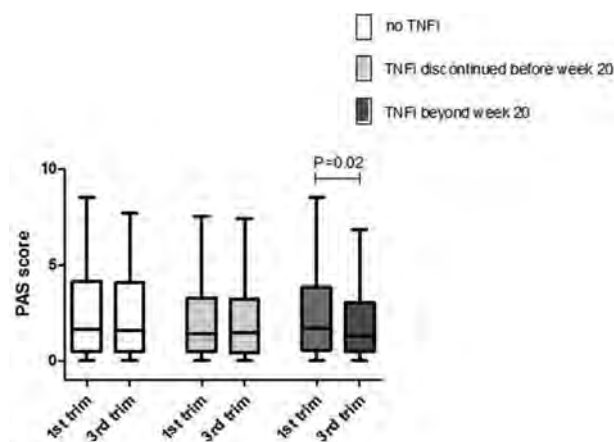
**Methods:** A prospective cohort study was conducted using the Organisation of Teratology Information Specialists (OTIS) Autoimmune Diseases in Pregnancy Project in the U.S. and Canada. Pregnant women with RA and JIA were enrolled between 2005 and 2017. Information about medication and disease activity were collected by telephone-based interviews prior to gestational week 20 and at gestational week 32. Disease activity was assessed by the Health Assessment Questionnaire Disability Index (HAQ-DI), the patient's pain scale and the patient's global scale. The composite tool Patient Activity Scale (PAS) was calculated in retrospect.

**Results:** In the OTIS cohort, data were available for 490 women of whom 397 had RA and 93 had JIA. Of all patients, 323 (65.9%) used TNFi during pregnancy of whom 122 (24.9%) patients discontinued TNFi before gestational week 20 (the mean time of discontinuation was gestational week 6 (SD ±5.03)) and 201 (41.0%) used TNFi beyond week 20. There were 167 (34.1%) patients not taking TNFi during pregnancy. At the time of enrollment, disease activity was low to minimal in 357 (72.9%) patients as defined by PAS scores below 3.7.

From the first to the third trimester, women using TNFi beyond week 20 showed a decrease of the PAS scores ( $p=0.02$ , figure 1) whereas women not using TNFi and those discontinuing TNFi before gestational week remained stable.

The univariate regression analysis, but not the adjusted model, revealed that TNFi use beyond week 20 was associated with improved HAQ scores at the third trimester (coefficient B  $-0.142$ , 95% CI  $-0.258$  to  $-0.026$ ) and with improved PAS scores (coefficient B  $-0.423$ , 95% CI  $-0.843$  to  $-0.002$ ). However, the various TNFi treatment modes during pregnancy were not associated with any minimum clinically important difference at the third trimester.

When selecting for 58 patients with active disease (PAS score  $\geq 3.71$ ) at the first trimester, the discontinuation of TNFi before gestational week 20 was not associated with any clinically important worsening of the disease at the third trimester.



**Conclusions:** In patients with RA and JIA who enter pregnancy with well controlled disease, the discontinuation of TNFi before gestational week 20 is possible without a risk of disease flares at the third trimester.

#### REFERENCE:

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**Disclosure of Interest:** None declared

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#### FRI0120 EVALUATION OF RITUXIMAB, TOCILIZUMAB AND ABATACEPT IN A FRENCH MULTICENTER RHUPUS COHORT

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**Background:** Rhupus, a combination of Rheumatoid Arthritis (RA) and Systemic Lupus Erythematosus, is a rare entity. Existing epidemiological and therapeutic data are limited.

**Objectives:** The aim of this study was to describe the therapeutic impact and safety of three biologic therapies: Rituximab, Tocilizumab and Abatacept in a french Rhupus cohort.

**Methods:** We have set up a transverse observational retrospective and multicentric study. To be included in the cohort, patients had to present an overlap syndrome fulfilling criterias for rheumatoid arthritis and lupus, and to be treated at least by one of these three therapies. Enrollment has been made with a file available on the CRI website and the analysis of the French RA registers (AIR, REGATE and ORA). Primary endpoint was the median time in therapeutic maintenance for each biological agent.

**Results:** Forty patients from fifteen rheumatologic centres were included. The main demographic data for these patients are given in table 1. Thirty of them received a treatment with Rituximab, twelve with Tocilizumab and seven with Abatacept. Nine patients received 2 biologics at two different times of the disease. The medians of therapeutic maintenance were 82 months with Rituximab, 48 with Tocilizumab and 55 with Abatacept. The detailed analysis of clinical and biologic parameters revealed differences in effectiveness between therapies: corticosteroid doses decreased more in Rituximab group, VAS activity decreased more in Abatacept group, CRP decreased more in Tocilizumab group. Safety of biologics was similar to the data in literature for RA patients.

	RITUXIMAB (n=30)	TOCILIZUMAB (n=12)	ABATACEPT (n=7)
Disease duration (years)	4.8	8.3	11.9
Median of therapeutic maintenance (month)	82	48	55
Average duration of treatment (month)	44.8 [5.8;83.8]	27.0 [4.3;49.7]	26.0 [-0.79;52.93]
DAS 28 CRP evolution	-1.03 [-2.73;0.67]	-1.88 [-3.36;-0.38]	-1.97 [-3.55;-0.41]
Prednisone evolution (mg/d)	-8.45 [-23.15;9.25]	-5.15 [-10.95;0.65]	-2.71 [-5.00;-0.43]
VAS evolution (/100)	-5.40 [-32.70;21.90]	-18.50 [-35.3;35.04]	-30.43 [-65.27;4.41]
CRP evolution (mg/L)	-14.46 [-46.46;17.54]	-21.75 [-53.41;9.91]	-12.86 [-25.95;0.26]

**Conclusions:** This study provides original data on the effectiveness and safety of non-TNF biologics, mostly rituximab, in a large cohort of patients with rhupus. We have not enough patients treated with Tocilizumab and Abatacept to conclude but the therapeutic maintenance of Rituximab in Rhupus is similar to the one usually observed in RA.

**Disclosure of Interest:** None declared

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FRI0121

### CHARACTERISTICS OF PATIENTS WITH EARLY RHEUMATOID ARTHRITIS WHO HAVE A DELAYED RESPONSE TO TREATMENT WITH METHOTREXATE IN MONOTHERAPY OR IN COMBINATION WITH ADALIMUMAB

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**Background:** In patients (pts) with rheumatoid arthritis (RA), treat-to-target recommendations call for adjustment of treatment if a target is not met within 3–6 months of initiation. While some pts continue therapy beyond 3–6 months despite not achieving the target, it's unclear if they still can achieve the target, and how the timing of target attainment impacts long-term outcomes.

**Objectives:** To evaluate clinical, functional, and radiographic outcomes on the basis of initial time to low disease activity (LDA) attainment among early RA pts who are naïve to MTX, or are MTX-insufficient responders (MTX-IR).

**Methods:** This post hoc analysis included pts receiving MTX in monotherapy or in combination with adalimumab (ADA) in 2 randomised, controlled trials (RCTs) of MTX-naïve pts with early RA: PREMIER included a 104 week (wk) RCT<sup>1</sup>; OPTIMA included a 26 wk RCT followed by treatment adjustments based on a target of LDA at wks 22 and 26<sup>2</sup>. Pts not achieving stable LDA received open-label (OL) ADA +MTX for an additional 52 wks (MTX-inadequate responders, IR). Pts were subgrouped by treatment and time to first LDA event [SDAI ≤11: 0-3 months (mths), 3-6 mths, >6-12 mths]. The following were summarised for each subgroup: mean values and change from baseline in SDAI, HAQ-DI and modified total Sharp score (mTSS). The proportions of pts achieving SDAI remission (REM) at 1 year (yr) were assessed.

**Results:** Roughly equal proportions of pts on MTX alone experienced their first LDA response between 0-3 mths (21%), 3-6 mths (21%), and >6-12 mths (17%). More pts on ADA+MTX experienced LDA within 3 mths (0-3: 45% and 56% for MTX-naïve and MTX-IR backgrounds, respectively), with smaller proportions in the 3-6 mths (19% for both MTX-naïve and -IR backgrounds), and >6-12 mths groups (14% and 4% for MTX-naïve and MTX-IR backgrounds). Approximately 50% of the 0-3 mth group across treatments achieved SDAI REM at 1 year. Interestingly, 10%, 14%, and 8% of the MTX, ADA+MTX (MTX-naïve), and ADA+MTX (MTX-IR) pts who first experienced LDA after 6 mths were in SDAI REM at 1 year.

Among MTX-naïve pts, pts on ADA+MTX had greater ΔHAQ and smaller ΔmTSS than pts on MTX alone at Wks 26 and 52 (table 1). Regardless of their time to first SDAI LDA response, pts on MTX monotherapy or ADA+MTX experienced comparable improvements in SDAI, HAQ-DI and comparable ΔmTSS at Wks 26 and 52.

Table 1 Mean Values at Baseline and Change From Baseline in Clinical, Functional, and Structural Parameters in Patients with Early RA Receiving MTX or ADA+MTX, on the Basis of First Achievement of Low Disease Activity by SDAI.

	MTX N=256			ADA+MTX, naïve N=631			ADA+MTX <sup>0</sup> MTX-IR N=347		
Achievement of low disease activity at months									
Months	0 to <3	3 to ≤6	6 to ≤12	0 to <3	3 to ≤6	6 to ≤12	0 to <3	3 to ≤6	6 to ≤12
Mean (SE) SDAI at BL									
	40.4 (1.5)	44.8 (1.6)	49.9 (1.8)	39.8 (0.8)	49.0 (1.1)	52.8 (1.8)	18.7 (0.8)	27.3 (1.6)	29.2 (3.3)
Mean Change (SE) from BL in SDAI									
Wk 26	-32.0 (2.2)	-30.3 (1.8)	-32.5 (1.8)	-32.4 (0.9)	-39.9 (1.3)	-30.4 (2.1)	-11.2 (0.9)	-17.2 (1.9)	-14.0 (3.9)
Wk 52	-33.1 (2.2)	-36.9 (2.2)	-35.9 (2.2)	-34.2 (0.9)	-41.7 (1.4)	-43.4 (2.1)	-12.6 (0.9)	-18.1 (2.2)	-19.3 (4.1)
Mean (SE) HAQ-DI at BL									
	1.1 (0.1)	1.5 (0.1)	1.5 (0.1)	1.4 (0.0)	1.6 (0.1)	1.8 (0.1)	0.9 (0.0)	1.3 (0.1)	1.2 (0.1)
Mean Change (SE) from BL in HAQ-DI									
Wk 26	-0.8 (0.1)	-1.0 (0.1)	-0.8 (0.1)	-1.0 (0.0)	-1.1 (0.1)	-0.7 (0.1)	-0.3 (0.0)	-0.4 (0.0)	-0.4 (0.0)
Wk 52	-0.8 (0.1)	-1.1 (0.1)	-0.8 (0.1)	-1.0 (0.0)	-1.2 (0.1)	-1.0 (0.1)	-0.4 (0.0)	-0.4 (0.1)	-0.4 (0.1)
Mean (SE) mTSS at BL									
	16.6 (3.1)	21.7 (2.2)	19.7 (3.0)	12.4 (1.0)	16.5 (2.4)	14.6 (2.4)	12.0 (1.3)	11.6 (1.8)	14.1 (4.3)
Mean Change (SE) from BL in mTSS									
Wk 26	1.9 (0.5)	1.5 (0.4)	2.5 (0.5)	0.3 (0.1)	0.4 (0.2)	0.3 (0.2)	0.0 (0.2)	0.1 (0.2)	0.0 (0.2)
Wk 52	3.0 (0.7)	2.6 (0.6)	3.4 (0.7)	0.5 (0.1)	0.5 (0.2)	0.5 (0.2)	0.0 (0.1)	0.0 (0.2)	-0.1 (0.1)

<sup>1</sup> Timing of LDA outcome from time of ADA addition.

BL, baseline; Wk, week; SDAI, simplified disease activity index; HAQ-DI, health assessment questionnaire-disability index; mTSS, modified total Sharp score

**Conclusions:** Pts on ADA+MTX achieved a first SDAI LDA response earlier than pts on MTX monotherapy, regardless of whether they were MTX-naïve or MTX-IR. More pts with a very early response went on to achieve SDAI REM at 1 year. However, pts with a longer time (>6 mths) to their first SDAI LDA response had comparable clinical, functional and radiographic outcomes compared to pts who responded earlier (within 3 or 6 mths). Therefore, achieving a clinical response in the direction of the treatment target, even if not yet achieving it, may be sufficient to continue therapy in appropriate pts.

### REFERENCES:

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- [2] Smolen, et al. Lancet 2014;383:321.

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**Disclosure of Interest:** J. Smolen Grant/research support from: AbbVie, Consultant for: AbbVie, X. Bu Shareholder of: AbbVie, Employee of: AbbVie, X. Wang Shareholder of: AbbVie, Employee of: AbbVie, J. Suboticki Shareholder of: AbbVie, Employee of: AbbVie, A. Kavanaugh Grant/research support from: AbbVie Inc., Amgen, Astra-Zeneca, BMS, Celgene, Centocor-Janssen, Pfizer, Roche, and UCB., Consultant for: expert advice to AbbVie Inc., Amgen, Astra-Zeneca, BMS, Celgene, Centocor-Janssen, Pfizer, Roche, and UCB

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FRI0122

### DRUG SURVIVAL OF ADALIMUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS, ANKYLOSING SPONDYLITIS AND PSORIATIC ARTHRITIS OVER 10 YEARS IN REAL-WORLD SETTING OF CZECH REGISTRY ATTRA

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**Background:** Drug survival in real clinical practice is reflecting both efficacy and safety of the drug. It is valuable outcome measure complementary to data from RCT.

**Objectives:** To evaluate 10 years efficacy and survival of adalimumab (ADA) in Czech registry ATTRA. To analyse reasons for drug discontinuation and analyse baseline demographic and clinical characteristics predictive for drug discontinuation. We also aimed to compare survival of ADA between 3 different diagnosis (RA, AS, SpA). Finally we aimed to compare survival between different anti TNF drugs.

**Methods:** All patients fulfilled criteria of Czech Rheum. Soc. for indication of anti TNF therapy and were included in registry. They were followed each 3 month first

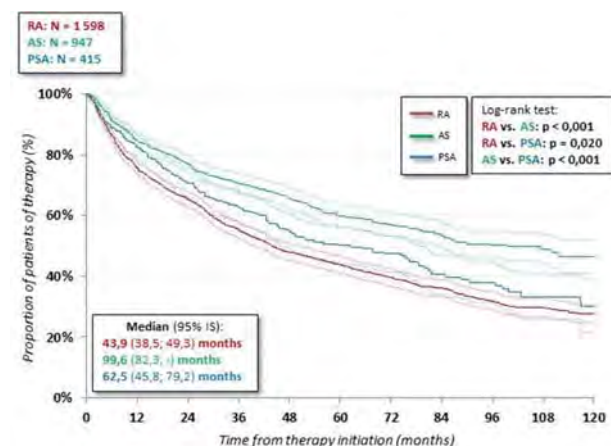


year and than each 6 month. The main outcome measures in RA were DAS 28, HAQ, EuroQuol, SF36, CRP, in AS BASDAI, HAQ and ASDAS. Reasons for drug discontinuation were reported as primary failure, secondary failure, adverse event, remission and others. Statistics – survival on therapy was estimated by Kaplan-Meier analysis. The search for outcome predictors was performed by log-rank test (continuous predictors were appropriately categorized).

**Results:** Altogether 3159 patients with RA, 1785 with AS and 723 with PsA were included.

1598 patients with RA were treated with adalimumab and retention was 75,8 % in one year, 43,8 % in 5 years and 27,7 % in 10 years. The reasons for drug discontinuation were: primary failure 24,9 %, secondary failure 30,5 %, and adverse events (19,8 %)

Predictive factors for adalimumab retention in rheumatoid arthritis were: younger age < 50 years, failure of  $\leq 1$  csDMARDs in past, combination therapy with csDMARDs at baseline. Sex, RF and anti CCP were not predictive. Drug retention was longest in AS (median 99,6 m), than PsA (median 62,5 m) and shortest in RA (median 43,9 m) (graph 1). Drug survival in rheumatoid arthritis was longer on etanercept than on infliximab ( $p < 0,001$ ), longer on adalimumab than infliximab ( $p < 0,001$ ) and equal between adalimumab and etanercept ( $p = 0,85$ ).



**Conclusions:** Adalimumab retention in registry ATTRA was comparable to other European registries. Predictors of drug retention in RA were: younger age (< 50 years),  $\leq 1$  csDMARDs in past and in combination with csDMARDs. Survival on adalimumab was longer in AS, than PsA and RA and the same was true for all three anti TNF drugs. Survival on drug in rheumatoid arthritis was longer in adalimumab and etanercept compared to infliximab.

**References:** Key words: biologic therapy, registry ATTRA

**Disclosure of Interest:** None declared

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### FRI0123 COMPARATIVE EFFECTIVENESS OF SUBCUTANEOUS VERSUS INTRAVENOUS TOCILIZUMAB IN A PAN-EUROPEAN COLLABORATION OF REGISTRIES

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**Background:** In randomised controlled trials, subcutaneous tocilizumab (TCZ sc) has been found non-inferior to intravenous TCZ (TCZ iv) for the treatment of rheumatoid arthritis (RA) patients. However, to our knowledge, there are no observational studies comparing these two different routes of administration in routine care.

**Objectives:** To compare the real-world effectiveness of TCZ sc and TCZ iv in RA patients.

**Methods:** We included RA patients treated with TCZ from 8 European registries. We compared drug retention using Kaplan-Meier and Cox models. The proportions of patients achieving CDAI remission and low disease activity (LDA) at

1 year were compared using LUNDEX correction with computation of confidence intervals by bootstrapping.<sup>1</sup>

**Results:** 2896 patients were retrieved from the collaborative registries before January 2017, including 2469 TCZ iv and 427 TCZ sc. Baseline demographics were similar between both groups, but patients in the TCZ iv group had a more severe disease activity, with higher DAS28, CDAI, tender joint count (TJC), swollen joint count (SJC), ESR and physician global assessment values (table 1). Crude median retention was 2.14 years (95% CI 2.03–2.33) for TCZ iv and 1.00 year for TCZ sc (95% CI 0.83–1.10),  $p < 0.001$ . However, in a covariate-adjusted analysis, stratified by country- and year of treatment initiation, we found that hazards of discontinuation were similar among patients on TCZ iv compared to patients on TCZ sc (hazard ratio: 0.92, CI 95% 0.77–1.09). The average adjusted CDAI change at 1 year was  $-1.15$  for TCZ iv, and  $-1.06$  for TCZ sc patients ( $p$ -value of interaction between treatment group and time: 0.68). The average adjusted DAS28 change at 1 year was also similar between groups ( $-0.28$  for TCZ iv and  $-0.09$  for TCZ sc,  $p$  value of interaction: 0.21). CDAI remission and LDA at 1 year (LUNDEX corrected) were similar between TCZ sc and TCZ iv patients (CDAI remission: 9.5% in TCZ iv vs. 9.4% in TCZ sc (difference:  $-0.1\%$ , bootstrap 95% CI:  $-3.8\%$ – $3.8\%$ ); CDAI LDA: 37.3% in TCZ iv vs. 33.7% in TCZ sc (difference:  $-3.6\%$ ; bootstrap 95% CI:  $-9.4\%$ ; 2.5%)). Likewise, DAS28 remission and LDA at 1 year (LUNDEX corrected) were comparable between TCZ sc and TCZ iv (difference in DAS28 remission:  $-2.7\%$ ; bootstrap 95% CI:  $-8.8\%$ ; 3.5%; difference in DAS28 LDA:  $-5.8\%$ ; bootstrap 95% CI:  $-11.9\%$ ; 0.4%).

Abstract FRI0123 – Table 1. Baseline characteristics

N = 2896	TCZ i.v. (n=2469)	TCZ s.c. (n=427)	p
Number of visits (median [IQR])	2 [1-5]	2 [1-3]	
Total patient-years	5099.16	379.11	
Age, yr (median [IQR])	56.2 [48.0, 64.0]	55.6 [47.1, 63.6]	0.30
Female gender, n (%)	2004 (81.2)	345 (80.8)	0.91
Ever smoker, n (%)	319 (21.7)	68 (22.1)	0.94
BMI (median [IQR])	25.3 [22.4, 28.6]	25.2 [22.7, 28.5]	0.73
Disease duration, yr (median [IQR])	7.8 [3.4, 14.7]	8.0 [3.4, 15.7]	0.52
Seropositivity (RF and/or ACPA), n (%)	1799 (83.1)	291 (81.5)	0.52
Previous bDMARDs, n (%)	1750 (75.0)	302 (73.5)	0.54
Previous csDMARDs, n (%)	1939 (89.4)	345 (90.1)	0.76
Glucocorticoids, n (%)	1276 (51.7)	237 (55.5)	0.16
Glucocorticoids dose, mg/day (median, IQR)	5.0 [5.0, 10.0]	5.0 [5.0, 8.0]	0.17
Concomitant csDMARD			0.40
None	680 (27.6)	131 (30.7)	
MTX	977 (39.6)	152 (35.6)	
MTX + other csDMARDs	348 (14.1)	60 (14.1)	
Other csDMARDs than MTX	462 (18.7)	84 (19.7)	
DAS28 (median [IQR])	4.6 [3.2, 5.6]	4.2 [2.6, 5.1]	<0.001
CDAI (median, [IQR])	25.0 [14.0, 37.3]	20.6 [10.3, 31.6]	<0.001
HAQ (median, [IQR])	1.4 [0.9, 1.9]	1.3 [0.8, 1.9]	0.17
TJC (over 28 joints) (median, [IQR])	8.0 [3.0, 14.0]	5.0 [2.0, 11.0]	<0.001
SJC (over 28 joints) (median, [IQR])	6.0 [2.0, 11.0]	4.0 [0.0, 8.0]	<0.001
ESR (mm/hour) (median, [IQR])	26.0 [9.0, 46.8]	20.0 [8.0, 40.0]	0.049
CRP (mg/L) (median, [IQR])	6.0 [1.1, 22.0]	5.0 [1.0, 19.0]	0.11
Patient global assessment (median, [IQR])	6.0 [4.0, 8.0]	6.0 [3.9, 7.5]	0.40
Physician global assessment (median, [IQR])	5.0 [3.0, 7.0]	4.4 [2.0, 6.3]	0.002

**Conclusions:** Drug retention and clinical effectiveness, assessed by CDAI and DAS28 changes and responses, were similar in both groups of patients, treated with TCZ sc or TCZ iv.

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**FRI0124 PREVENTION OF EXTENSIVE BONE MARROW OEDEMA AND CONSEQUENT RAPID RADIOGRAPHIC PROGRESSION BY SHORT TERM USAGE OF BIOLOGICS IN DRARDS RESISTANT PATIENTS WITH EARLY DESTRUCTIVE RHEUMATOID ARTHRITIS**

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**Objectives:** To investigate possible preventive effect of radiographic joint damage, especially RRP by short term treatment with biologics in non-biological disease-modifying ant-rheumatic drugs(non-bio DMARDs) resistant early RA (Clinical registration number; UMIN-CTR 000013614).

**Methods:** Fifty early RA patients with extensive BE by hand MRI test despite treatment with non-bio DMARDs were recruited. Among these, 44 patients were diagnosed as RRP. Twenty three patients (male 5, female 18) were treated with combination of non-bio DMARD and biologic DMARDs (Bio group) and 26 patients were treated with enhanced DMARDs therapy using MTX with or without other DMARDs (enhanced DMARDs group). Baseline demographics of both groups were not significantly different (Data not shown). In the Bio group, the following biologics were added: Adalimumab (13 cases), Tocilizumab (3 cases), Abatacept (3 cases), Infliximab (2 cases), Certolizumab (1 case), Golimumab (1 case). In enhanced DMARDs group, mean MTX dose was increased from 7.3 mg/w to 11.3 mg/w or other DMARDs were added. Bone destruction was determined before and 3 or 6 months after treatment by modified total Sharp scoring (mTSS) using by conventional radiography, and expressed as yearly progression of mTSS ( $\Delta$ mTSS/y). BE score was measured by RAMRIS method using T1 or STIR image of hand MRI (HITACHI, Elis, 0.5T).

**Results:** Significant reduction in DAS28-ESR values after 3 or 6 months treatment were observed: from 4.2 to 3.3(p=0.0004) in the enhanced DMARDs group, and 4.37 to 3.0(p<0.0001) in the Bio groups. Similarly, improvement of BE: 7 out of 26 (26.9%) and 14 out of 23 patients (60.9%), mean  $\Delta$ mTSS/y: 5.8 and 2.4, incidence of RRP: 9 (34.6%) and 9 (34.6%), and structural remission: 5 (21.7%) and 16 patients (69.6%), in the enhanced DMARDs and the Bio group, respectively. Accordingly, improvement of BE and incidence of structural remission was higher, whereas mean  $\Delta$ mTSS/y value was significantly lower (p<0.05) in the Bio group compared to in the enhanced DMARDs group (table 1, figure 1).

**Abstract FRI0124 – Table 1.** Comparison between the Enhanced DMARDs group and the Bio group

	Enhanced DMARDs group (n=23)	Bio group (n=26)	P
$\Delta$ mTSS/y	5.8	2.4	0.0142*
% RRP	34.6% (9/26)	21.7% (5/23)	n.s
% Structural remission (%)	34.6% (9/26)	69.6% (16/23)	0.0146*
% BE improvement	26.9% (7/26)	60.9% (14/23)	0.0166*

\*: significant

Enhanced DMARDs group						Bio group					
BE (0-6)	BE (>6)	Improve	mTSS/y	$\Delta$ mTSS/y	Structural Remission (9 cases)	BE (0-6)	BE (>6)	Improve	mTSS/y	$\Delta$ mTSS/y	Structural Remission (16 cases)
36	2	O	46	6.8		21	2	O	8	-4.8	
27	18	X	14.1	0		28	5	O	30	0	
11	4	O	8	0		28	17	X	3.4	0	
17	15	X	12	0		23	0	O	6.4	0	
22	3	O	11.1	0		29	6	O	8.2	0	
29	13	X	48	0		29	0	O	8.4	0	
19	1	O	30	0		35	8	O	42	0	
15	0	O	12	0		31	9	O	30.8	0	
34	34	X	62.4	0.86		28	8	O	15.1	0	
38	3	O	15	1.2		16	15	X	21.8	0	
19	13	O	66	1.5		27	5	O	31.2	0	
32	18	X	24	1.8		26	15	X	20	0	
25	1	O	2	2.7		27	7	O	33	0	
14	2	O	1.8	2.9		36	37	X	14.6	0	
29	30	X	15.9	3.3		22	6	O	10	0	
22	29	X	12	4.4		21	3	O	15	0	
18	12	X	4.3	8		28	3	O	11.7	1	
12	16	X	11	4		20	4	O	18.7	2	
29	14	X	5	6.3		18	18	X	12	5.3	
39	32	X	2.8	7.2		26	30	X	32	5	
39	36	X	24	13		24	17	X	8.4	10	
33	30	X	13	17		22	34	X	4	12	
27	11	X	28.1	26.3		42	42	X	37.7	20.6	
38	27	X	35	29							
13	26	X	36	33.6							
25.8	16.2		22.5	5.8		26.4	12.6		18.4	2.4	

**Abstract FRI0124 – Figure 1.** Radiographic data

**Conclusions:** Results of this study indicated that short term (3 or 6 months) treatment with biologics is effective in the reducing BE, and consequently prevent further progression of the disease into RRP status in 80% of early destructive RA despite extensive DMARDs therapy. The effect of withdrawal of biologics in RA improving BE are currently under investigation (figure 1). We consider that a short-term treatment with biologics for early RA patients, who are resistant to

DMARDs and at high risk to transit to RRP, will be an effective and economical treatment strategy.

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**FRI0125 QUANTIFICATION OF TUMOUR NECROSIS FACTOR IN ANKYLOSING SPONDYLITIS PATIENTS DURING ADALIMUMAB TREATMENT**

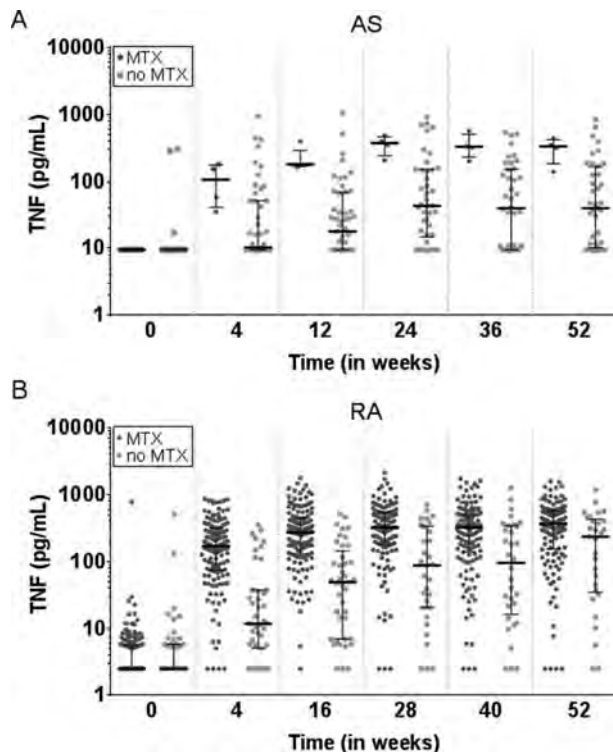
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**Background:** Tumour necrosis factor- (TNF) inhibitors, including adalimumab, are widely used in the treatment of inflammatory autoimmune diseases. Longitudinal (drug-bound) TNF levels in rheumatoid arthritis (RA) patients increased upon adalimumab treatment, and remained stable over two years follow-up. Low TNF levels at week four were associated with a significantly higher frequency of anti-drug antibodies (ADAs) at subsequent time points, significantly less methotrexate (MTX) use at baseline and a significantly reduced clinical response after 52 weeks (unpublished data).

**Objectives:** To investigate TNF levels during adalimumab treatment in ankylosing spondylitis (AS) patients and to compare this with TNF levels measured in RA patients.

**Methods:** Longitudinal TNF levels were quantified in 76 consecutive AS patients during adalimumab treatment, using a competition enzyme-linked immunosorbent assay (ELISA). This ELISA is drug-tolerant, which enables the quantification of TNF in the presence of large amounts of TNF-inhibitor. The relationship between TNF levels, drug levels and ADA detection was evaluated.

**Results:** At baseline, TNF levels were close to the detection limit, but levels increased during adalimumab treatment (figure 1A; stratified to concomitant MTX use; black lines represent median TNF (IQR)). The increase in TNF was more gradual in patients treated with adalimumab monotherapy, compared to the increase in TNF levels in patients concomitantly treated with MTX (only 9% of the patients). Similar results were found for adalimumab-treated RA patients, stratified to concomitant MTX use (figure 1B; Black lines show median (IQR)). Furthermore, at week four, low TNF levels in AS patients tended to associate with a higher frequency of ADAs after 24 weeks.



**Conclusions:** This is the first study describing an increase in TNF levels in AS patients during one year of adalimumab treatment. The dynamics in TNF levels is different for patients concomitantly treated with MTX, compared to patients treated with adalimumab monotherapy. Low TNF levels at week four tended to associate with a higher frequency of ADAs, which is potentially associated with the low frequency of MTX use at baseline.



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**FRI0126 PATIENTS' CONCERNS ABOUT AND PERCEPTION OF BIOSIMILARS IN RHEUMATOLOGY : A FRENCH SURVEY**

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**Background:** Patient adherence to biosimilars DMARDs have become a big medico-economic issue. Indeed, savings will depend on penetration rate of biosimilars on the biologics market. Like generics, biosimilars are unknown by the general population and patients reluctance appears to be an obstacle to the diffusion of these therapeutics.

**Objectives:** To assess patients' knowledge, information and concerns about biosimilars and to identify levers and obstacles to adherence to biosimilars prescription.

**Methods:** National cross-sectional study assessing information, knowledge and concerns about biosimilars of french patients treated for a rheumatism (whether they were treated by a bDMARDs or not). The data were collected from march to july 2017 by an online assessment.

**Results:** 629 patients answered the assessment. 43% knew the definition of biosimilars. 65% felt insufficiently informed about biosimilars. The principal sources of information were the rheumatologist and the patient associations. 44% of patients treated with a biosimilar were not informed before they received a biosimilar. Patients concerns focused on molecular structure (46%), efficacy (60%) and tolerance (57%) comparatively to originator bDMARDs.

Receiving information about biosimilars and understanding the definition of biosimilarity were two characteristics associated with better adherence to biosimilars. The rheumatologist was considered the most influent source of information about biosimilar. Patients trust him concerning the decision to switch from the originator biologic to its biosimilar. Patient were reluctant to substitution by the pharmacist (2%).

**Conclusions:** Biosimilars are largely unknown by french patients at present. Information seems to be instrumental in patient adherence to biosimilars and in the preservation of the therapeutic relationship.

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**FRI0127 OPEN-LABEL NON-MANDATORY TRANSITIONING FROM ORIGINATOR ETANERCEPT TO BIOSIMILAR SB4: 6-MONTH RESULTS FROM A CONTROLLED COHORT STUDY**

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**Background:** Open-label mandatory transitioning to a biosimilar has no impact on disease activity in inflammatory rheumatic diseases.<sup>1</sup> In light of shared treatment decision-making between patients and physicians, non-mandatory transitioning might be preferable above mandatory transitioning. First attempts with non-mandatory transitioning unfortunately showed suboptimal acceptance and persistence rates to a biosimilar.<sup>2</sup>

**Objectives:** To evaluate the effects of non-mandatory transitioning from originator etanercept (ENB) to biosimilar etanercept (SB4) on drug survival and effectiveness in a controlled cohort study of patients with an inflammatory rheumatic disease.

**Methods:** In 2016, 642 ENB treated patients were asked to transition to SB4 by a structured communication strategy with opt-out option. Consenting patients were eligible for the current study [BIO-SPAN]. ENB treated patients in 2014 were recruited as historical cohort. Drug survival was compared by Cox regression analyses adjusting for age, gender, diagnosis, ENB treatment duration, ENB dose interval, csDMARD and CRP, using a robust variance estimator to account for repeated subjects. Adjusted differences in CRP, DAS28-CRP and BASDAI change over 6 months were assessed.

**Results:** 635 (99%) patients agreed to transition to SB4 of whom 625 patients (433 RA, 128 PsA, 64 axSpA) were included in the transition cohort. Additionally, 600 patients were included in the historical cohort. Crude 6 months retention rates of SB4 in the transition cohort and ENB in the historical cohort were: 90% (95%CI 88%-93%) vs 92% (95%CI 90%-94%). The transition cohort had a significantly higher relative risk of discontinuation (adjusted HR 1.57, 95% CI 1.05-2.36). Reasons for discontinuing SB4 (n=60) and ENB (n=46) were: lack of effect (43% vs 61%), adverse events (47% vs 28%), malignancy (3% vs 4%), pregnancy (4% vs 4%), other (3% vs 3%). In the transition cohort, 17 patients restarted ENB, 32 patients switched to another biologic and 11 patients maintained biologic-free. DAS28-CRP, BASDAI and CRP were similar between baseline and month 6. Compared with the historical cohort, the transition cohort had a smaller decrease in CRP (adjusted diff 1.8 (95%CI 0.3-3.2)) and DAS28-CRP (adjusted diff 0.15 (95%CI 0.05-0.25)) over 6 months.

**Conclusions:** Open-label non-mandatory transitioning from ENB to SB4 using a structured communication strategy showed a slightly lower persistence rate and smaller decreases in disease activity compared with a historical cohort, but these differences were considered as not being clinically relevant. The acceptance and persistence rates of SB4 in our transition cohort were similar to those of mandatory transitioning. Since mandatory transitioning is not acceptable in many countries, the use of a communication strategy which might optimise acceptance and persistence rates of non-mandatory transitioning seems attractive.

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**FRI0128 INTEGRATED SAFETY DATA ANALYSIS ACROSS PHASE 3 CLINICAL STUDIES FOR INTRAVENOUS GOLIMUMAB IN RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS, AND ANKYLOSING SPONDYLITIS**

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**Background:** Intravenous golimumab (IV GLM) is approved for treatment of adults w/rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS).

**Objectives:** To present the integrated safety data from three Phase 3 studies of IV GLM in patients (pts) w/RA, PsA and AS up to 24 weeks (wks). Safety outcomes in pts receiving concomitant methotrexate (MTX) and low-dose oral corticosteroids (CS) were assessed when used in treatment of the indicated disease.

**Methods:** Integrated safety data from Phase 3 double-blind placebo-controlled trials (RA [GO-FURTHER], PsA [GO-VIBRANT] and AS [GO-ALIVE]) were analysed up to wk24. In general, pts received either IV PBO or IV GLM (2 mg/kg) at 0, 4, 12, and 20 wks. PBO pts crossed over to GLM at wk24 except RA pts randomised to PBO who met early escape criteria crossed over at wk16 and AS pts randomised to PBO, who crossed-over at wk16. Data before crossover are presented. Infusion reactions, infections, serious infections, serious adverse events (SAEs), death, and antidrug antibodies (ADAs) were evaluated.



**Results:** Overall, 740 and 539 pts were randomised to IV GLM and PBO groups, respectively. The % of IV GLM vs PBO pts reported the following across studies: infusion reactions (2.8 vs 0.2); SAEs (3.8 vs 2.4); infections (23.8 vs 17.3); serious infections (0.8 vs 0.4) and malignancies (0.1 vs 0.4). No deaths occurred in IV GLM group through wk24. Pts on IV GLM (n=574) vs PBO (n=391) w/concomitant MTX had similar proportions of serious infections (0.9 vs. 0.6). In IV GLM (n=349) vs PBO (n=224) pts who received CS, serious infections were 1.1% vs 0.9%; in pts who did not receive CS, serious infections were 0.5% vs 0%. In IV GLM pts w/ normal ALT at baseline, 30% had postbaseline ALT elevation w/concomitant MTX vs 28% w/o. CS use had inconsistent effect on ALT elevations. Overall incidence of ADAs via drug tolerant assay was 20% (19% w/ MTX and 25% w/o MTX) through wk20 across RA, PSA and AS studies.

	RA		PsA		AS		ALL	
	IV GLM	PBO	IV GLM	PBO	IV GLM	PBO	IV GLM	PBO
Treated Pts	395	197	240	239	105	103	740	539
Age in years, Mean (Range)	51.9 (18-83)	51.4 (19-78)	45.7 (19-69)	46.7 (18-79)	38.4 (19-64)	39.2 (20-67)		
Disease Duration in Years, Mean (SD)	6.9 (7.00)	7.0 (7.24)	6.2 (6.03)	5.3 (5.92)	5.6 (6.57)	5.5 (5.93)		
Avg duration of follow-up (wks)	23.6	20.9	23.9	23.2	16.1	16.0	22.6	21.0
Pts w/≥1 infusion reaction, n (%)	14 (3.5)	1 (0.5)	4 (1.7)	0	3 (2.9)	0	21 (2.8)	1 (0.2)
Pts w/≥1 SAE, n (%)	19 (4.8)	5 (2.5)	7 (2.9)	8 (3.3)	2 (1.9)	0	28 (3.8)	13 (2.4)
Pts w/≥1 infection, n (%)	119 (30.1)	48 (24.4)	45 (18.8)	37 (15.5)	12 (11.4)	8 (7.8)	176 (23.8)	93 (17.3)
Pts w/≥1 serious infection, n (%)	4 (1.0)	0	1 (0.4)	2 (0.8)	1 (1.0)	0	6 (0.8)	2 (0.4)
Pts w/≥1 malignancy, n (%)	1 (0.3)	0	0	2 (0.8)	0	0	1 (0.1)	2 (0.4)
Deaths, n (%)	0	1 (0.5)	0	2 (0.8)	0	0	0	3 (0.6)
% ADA positive*	21		20		19		20	

\*w/drug tolerant assay

**Conclusions:** IV GLM demonstrates the expected safety profile across RA, PSA and AS clinical trials in the PBO-controlled period. Differences between studies may be related to age, use of concomitant medications and disease indication.

**Disclosure of Interest:** M. Husni: None declared, S. Schwartzman: None declared, A. Deodhar: None declared, S. Kafka Employee of: Janssen Scientific Affairs, LLC, S. Chakravarty: None declared, E. Hsia: None declared, D. Harrison: None declared, J. Leu: None declared, Y. Zhou: None declared, K. Lo: None declared, A. Kavanaugh: None declared

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### FRI0129 SWITCH BETWEEN REFERENCE ETANERCEPT (ETN) AND GP2015, AN ETANERCEPT BIOSIMILAR, DID NOT IMPACT EFFICACY AND SAFETY IN PATIENTS WITH MODERATE-TO-SEVERE RHEUMATOID ARTHRITIS: 48-WEEK RESULTS FROM THE PHASE 3 EQUIRA STUDY

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**Background:** GP2015 is an etanercept biosimilar. It has shown an equivalent efficacy, and comparable safety and immunogenicity to ETN in patients with chronic plaque-type psoriasis.<sup>1</sup>

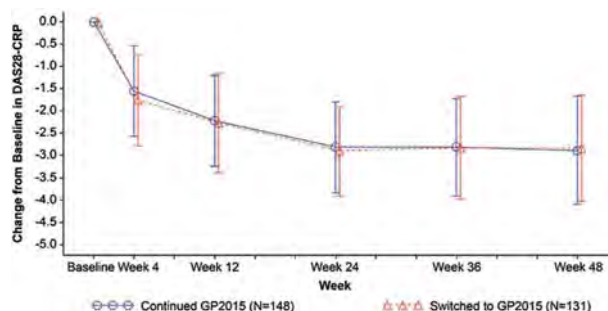
**Objectives:** To compare the efficacy and safety of GP2015 versus ETN in patients with moderate-to-severe rheumatoid arthritis (RA) and evaluate the effects of switching from ETN to GP2015.

**Methods:** EQUIRA was a 48 week, randomised, double-blind, Phase 3 study. The primary endpoint was equivalent change from baseline (BL) in DAS28-CRP at Week 24. Patients ≥18 years with active RA ACR 1987 or ACR<sup>EULAR 2010</sup> criteria for ≥6 months before BL and active disease defined as DAS28-CRP ≥3.2 and CRP >5 mg/L or ESR ≥28 mm/h and inadequate response to methotrexate (MTX) were randomised 1:1 to 50 mg GP2015 or ETN subcutaneously once weekly for 24 weeks (Treatment period 1). Patients with at least moderate EULAR response at Week 24 either continued GP2015 treatment or, in the ETN group, were switched to receive 50 mg GP2015 up to 48 weeks (Treatment period 2 [TP2]). All patients continued to receive concomitant MTX (10–25 mg/week) at a stable dose and folic acid. Efficacy outcome measures included change in DAS28-CRP, EULAR and ACR20/50/70 responses.

**Results:** Baseline characteristics were comparable between the GP2015 (n=186) and ETN (n=190) groups. The primary endpoint for equivalence was met.<sup>2</sup> The mean change in DAS28-CRP from BL to Week 48 was comparable between the continued and switched to GP2015 groups (TP2 per-protocol set; figure 1). At Week 48, the EULAR and ACR 20/50/70 response rates were comparable between the two groups (table 1). In TP2, treatment-emergent adverse events (AEs) occurred in 42.9% vs 38.0% patients in the continued GP2015 (n=175) vs the switched (n=166) groups; serious AEs occurred in 2.3% vs 2.4% patients (TP2 safety set). Injection site reactions occurred in 6 (3.6%) patients in the switched group but none in the continued GP2015 group. In TP2, 4 (2.4%) patients in the continued GP2015 group had single-event, very low titer, non-neutralising antidrug antibodies detected.

**Abstract FRI0129 – Table 1.** Efficacy response over 48 weeks, TP2 per-protocol set (W=week)

Variables	Time	Continued GP2015 n=148	Switched to GP2015 n=131
EULAR good response, n (%)	W48	80 (54.4)	67 (51.9)
EULAR moderate response, n (%)	W48	61 (41.5)	57 (44.2)
ACR20 response, n (%)	W4	70 (47.9)	70 (53.8)
	W12	114 (78.1)	100 (76.9)
	W24	132 (89.8)	122 (93.1)
	W36	128 (87.7)	114 (87.0)
	W48	131 (89.1)	108 (82.4)
ACR50 response, n (%)	W4	19 (13.0)	26 (20.0)
	W12	48 (32.9)	61 (46.9)
	W24	93 (63.3)	96 (73.3)
	W36	90 (61.6)	83 (63.4)
	W48	93 (63.3)	86 (65.6)
ACR70 response, n (%)	W4	6 (4.1)	6 (4.6)
	W12	18 (12.3)	24 (18.5)
	W24	50 (34.0)	60 (45.8)
	W36	47 (32.2)	50 (38.2)
	W48	54 (36.7)	55 (42.0)



**Abstract FRI0129 – Figure 1.** Change from Baseline in DAS28-CRP up to Week 48 (TP2 per-protocol set)

**Conclusions:** The efficacy of GP2015 was comparable to that of ETN. Moreover, the switch from ETN to GP2015 did not impact on efficacy and safety of etanercept in patients with moderate-to-severe RA.

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**FRI0130** **CERTOLIZUMAB PEGOL EXPOSURE DURING PREGNANCY IN WOMEN WITH RHEUMATOID ARTHRITIS: EVALUATION OF THE LONG-TERM NEWBORN OUTCOMES**

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**Background:** Increased TNF alpha (TNF $\alpha$ ) levels have been associated to pregnancy complications such as intra-uterine growth retardation and fetal loss. Even if pregnancy has classically been considered as having a positive impact on RA, disease flares potentially leading to poor obstetrical outcomes are not uncommon, raising the challenge of RA management in the early stages of pregnancy. Among TNF $\alpha$  inhibitors indicated for rheumatoid arthritis (RA), the use of certolizumab pegol (CTZ) has been reported as safe during pregnancy. As such, CTZ is allowed during pregnancy as provided by the factory-issued product's sheet.

**Objectives:** To assess the CTZ use safety during RA pregnancies, including maternal-fetal outcomes.

**Methods:** We retrospectively evaluated twelve women with RA, fulfilling the 2010 ACR/EULAR criteria, who had been exposed to CTZ throughout pregnancy. All women had signed an informed consent prior to treatment initiation.

**Results:** All cases were free from any potentially teratogenic drug, stopped at least 6 months before conceiving. Due to the underlying disease activity, and thanks to the approval for CTZ to be continued throughout the whole pregnancy, we carried on the treatment. Mean maternal age at conception was 31.6 $\pm$ 4.0 months; mean disease duration dated of 51 $\pm$ 26 months. All patients were on low-dose daily oral prednisone ranging from 2.5 to 5 mg; four subjects were on sulfasalazine 500 mg TID and four others on hydroxychloroquine 200 mg TID. We observed 12 singleton pregnancies; 8/12 mothers were primiparous. Mean gestational duration was 37 $\pm$ 3 weeks and mean birth weight 3.037 $\pm$ 0.58 grams. No stillbirths or fetal deaths were recorded. Five patients experienced elective caesarean section, while the others had vaginal delivery (four labour were induced by intravenous oxytocin; no dystocic births were reported). Mean APGAR scores after 1, 5 and 10 min from delivery were, respectively, 8 $\pm$ 2; 8 $\pm$ 1 and 9 $\pm$ 1. No obstetric, perinatal or neonatal complications were observed. Eight/12 newborns were breastfed. After a 12 months observational gap, all babies were healthy and the development index above the 75th percentile. All children underwent the Italian scheduled vaccine program, without complications. Their antibody vaccine response is nowadays being investigated by our Research team.

**Conclusions:** The data from our case series confirm the safety of CTZ administration during pregnancy in women with RA, regarding both the mothers and the offspring. No infection rate increase, neither major maternal-fetal issue were reported. The higher caesarean section rate in our patients, in comparison to the average of northern Italy (20%), could have a iatrogenic explanation, as suggested by the fact that all had been scheduled ahead of time. Similarly, the relative low rate of breastfeeding could be justified by the lack of information given to mothers. Further large data collection and perspective, controlled studies are needed to confirm this statement.

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**FRI0131** **POTENTIAL FACTORS ASSOCIATED WITH LONG-TERM CONTINUATION OF ETANERCEPT**

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**Background:** With the advent of biologic agents, it has become possible to prevent progression of symptoms and joint destruction in rheumatoid arthritis (RA). However, less than half of patients achieve remission. The patient subgroup that benefits from a specific biologic agent remains unclear. Etanercept has been repeatedly reported to have a high long-term continuation rate, and can also be tapered once the therapeutic goal has been achieved. Identification of a patient

subgroup that benefits from long-term use of etanercept would not only benefit the patients but would also reduce healthcare costs.

**Objectives:** The purpose of this study was to evaluate the characteristics of patients who benefited from long-term use of etanercept and patients who discontinued the drug due to loss of efficacy using our hospital records, and evaluated factors that may predict the difference in efficacy.

**Methods:** We compared RA patients who continued etanercept treatment for at least 3 years, without interruption for 3 months or longer for reasons other than remission, including patients who switched from other biologics (continuation group), and patients who discontinued treatment within 3 years of treatment initiation due to loss of efficacy (discontinuation group). All patients were treated at our hospital before October 31, 2017. Multiple regression analysis was used to determine factors that may predict long-term etanercept efficacy, using 10 patient background characteristics, including age at initiation of etanercept and DAS28ESR, as explanatory variables.

**Results:** At the time of evaluation, the 3 year continuation rate of etanercept by the Kaplan-Meier method was 49.7%. Reasons for discontinuation included adverse events (33.3%), loss of efficacy (50%), and patient preference (17.3%). The continuation group comprised 87 cases, including 5 cases where etanercept was discontinued due to remission. Initial dose was 50 mg, and relative dose intensity was 0.78 (95% confidence interval 0.66–0.89). The discontinuation group included 51 cases. Regarding patient characteristics at the time of etanercept initiation, age (continuation group 60.1 vs. discontinuation group 66.7, p=0.019), number of previously used biologics (continuation group 1.24 vs. discontinuation group 1.45, p=0.016), and disease duration (continuation group 110.2 months vs. discontinuation group 74.2 months, p=0.035) were statistically significant with  $\alpha=0.05$ , suggesting potential utility in predicting long-term response. In contrast, combination therapy with methotrexate (p=0.259), rheumatoid factor, or anti-cyclic citrullinated peptide antibody positivity (p=0.086), and DAS28ESR (p=0.056) were not statistically significant.

**Conclusions:** Although this was a retrospective study, the results showed that young RA patients who have previously used few biologics, with long disease duration, may be more likely to benefit long-term from etanercept without loss of efficacy.

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**FRI0132** **FACTORS INFLUENCING SATISFACTION IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH TOCILIZUMAB**

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**Background:** Biologics are effective for improving disease activity in patients with rheumatoid arthritis (RA). However, improved disease activity of RA alone does not always lead to high patient satisfaction.

**Objectives:** We evaluate which factors among items of disease activity and health status are correlated with improvement of patient satisfaction in patients with RA treated with biological agent.

**Methods:** Patients with RA who were planning to be treated with tocilizumab (TCZ) were enrolled in this study. Satisfaction, disease activity, and health status were assessed at week 0 and week 24 of TCZ therapy. Disease activity was evaluated using SJC, TJC, PGA, EGA and CDAl. Pain was also assessed using Visual Analogue Scale (VAS). Satisfaction and health status were assessed using the patient satisfaction score and the 5 components of the Arthritis Impact Measurement Scale 2 (AIMS-2).

Multiple linear regression analysis was used to assess the correlation between changes in satisfaction, disease activity and health status adjusted for CDAl at week 0. Also, Wilcoxon signed rank test was used to evaluate effect of TCZ on satisfaction, disease activity, and health status.

**Results:** Nineteen patients (male/female: 4/15) were evaluated. Patients' data at baseline were as follows: mean of age (51.3), disease duration (7.6 years), SJC (12.2), TJC (9.6), PGA (47.9 mm), EGA (51.4 mm), CRP (2.9 mg/dl) and CDAl (10.2), respectively. SJC, TJC, PGA, CDAl and RA-pain showed a statistically significant decrease at week 24 compared to the baseline (p<0.001, for each of all items). Out of the 5 components of AIMS-2, "physical", "symptom", "role" and "affect" improved statistically significantly at week 24 compared to the baseline (p<0.0001, p=0.0179, p<0.0005, p=0.0056, respectively), while there was no statistically significant improvement for "social interaction". Patient satisfaction was also statistically significantly higher compared to the baseline (p=0.00038).

After adjusting for CDAl at week 0, the change in satisfaction from week 0 to week 24 showed statistically significant correlation with changes in PGA and pain-VAS (all p-values<0.05), but not with changes in TJC, SJC EGA. Regarding

health status, the change in patient satisfaction adjusted for CDAI at week 0 was statistically significantly correlated with changes in "symptom" and "affect" (all  $p$ -values  $< 0.05$ ). However, there were no statistically significant correlations between change in patient satisfaction and change in "physical", "role", and "social interaction".

**Conclusions:** Satisfaction was correlated with pain, PGA and psychological state in patients with RA treated with tocilizumab. On the other hand, satisfaction was not correlated with TJC, SJC and EGA. In other words, it appears that patient satisfaction is more closely linked with how symptoms are experienced physically and mentally. Further research into specific factors influencing the patients' experience could shed more light on conditions for improving patients' satisfaction and QOL.

**Disclosure of Interest:** None declared

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### FRI0133 CENTRAL ROLE OF TOCILIZUMAB IN FIBROBLAST DOMINATED MODELS OF INFLAMMATORY AUTOIMMUNE ARTHRITIS

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**Background:** Immune mediated inflammatory arthritis including rheumatoid arthritis (RA), psoriatic arthritis (PsA) and spondyloarthritis (SpA) all characterised by joint synovitis. Disease-modifying antirheumatic drugs (bDMARDs) targeting specific components of the pathogenesis have radically improved the treatment of the diseases. However, a fair proportion of patients are non-responders.

Today, the first choice of DMARD is dependent on market pricing, regardless of the immunological target. This is due to the rather similar efficacy profile of the different DMARDs. Therefore, there is a need for stratification of patients suffering from Immune mediated inflammatory arthritis in order to reduce the fraction of DMARD non-responders.

**Objectives:** The objective of this study was to study the effects of various DMARDs on different synovial cell subsets using several human *ex vivo* models of immune mediated inflammatory arthritis. This could potentially guide future studies of personalising DMARDs in these diseases.

**Methods:** Synovial fluid was obtained from a study population of patients with active rheumatoid arthritis (RA) or peripheral spondyloarthritis (SpA). Synovial fluid mononuclear cells (SFMCs) containing primarily synovial monocytes and lymphocytes cultured for 48 hours ("Macrophage and Lymphocyte model") were used to study the effect of different biological agents on secretion of monocyte chemoattractant protein-1 (MCP-1) ( $n=14$ ). Further, fibroblast-like synovial cells (FLSs) were co-cultured with autologous PBMCs ("FLS model") to study the effects of the same biological agents ( $n=6$ ) in cultures dominated by synovial FLSs. Finally, SFMCs cultured for 21 days ("Osteoclast model") were studied to assess the effects on inflammatory osteoclastogenesis ( $n=10$ ) measured by tartrate-resistant acid phosphatase (TRAP). The DMARDs investigated are shown in table 1.

**Results:** "Macrophage and Lymphocyte model"; In SFMCs cultured for 48 hours, all DMARDs included, except anakinra, had the ability to decrease the production of MCP-1. The two TNF inhibitors (adalimumab and etanercept) ( $p < 0.05$  and  $p < 0.01$ ) and baricitinib ( $p < 0.05$ ) had the most pronounced effects and reduced the production of MCP-1 by approximately 25%. Tocilizumab had in this culture a non-significant reduction of MCP-1 production.

"FLS model"; In the FLS+PBMCs cultured for 48 hours, tocilizumab ( $p < 0.001$ ) and the two JAK inhibitors (tofacitinib and baricitinib,  $p < 0.05$  and  $p < 0.05$ ) were exclusive in decreasing the cytokine production of MCP-1 by around 50%.

"Osteoclast model"; In SFMCs cultured for 21 days, only the two TNF inhibitors, adalimumab and etanercept were able to significantly reduce the secretion of TRAP from adherent macrophage like synovial cells by roughly 25% ( $p < 0.01$ ,  $p < 0.001$ ).

#### Abstract FRI0133 – Table 1

##### Generic name:

Adalimumab  
Etanercept  
Tocilizumab  
Anakinra  
Ustekinumab  
Secukinumab  
Tofacitinib  
Baricitinib

**Conclusions:** This study reveals that most DMARDs have effects in the "Macrophage and Lymphocyte model" whereas tocilizumab, tofacitinib and baricitinib were superior in the "FLS model" and only the two TNF inhibitors were effective in

the "Osteoclast model". The findings in the "FLS model" reveals a possible beneficial effect of tocilizumab and JAK inhibitors to patients with fibroblast dominated arthritis. This study could potentially guide future studies of personalising DMARDs to treat immune mediated inflammatory arthritis.

**Disclosure of Interest:** None declared

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### FRI0134 IS THERE ANY DIFFERENCE IN RA PATIENTS FOR METHOTREXATE USE VS. LEFLUNOMIDE USE AS A CONCOMITANT TREATMENT WITH BIOLOGICAL AND TARGETED SYNTHETIC DMARDs IN TURKIBIO REGISTRY?

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**Background:** TURKIBIO registry is the Turkish version of Danish DANBIO rheumatologic database which has been established in 2011. Demographics and previous or current treatment with conventional (csDMARD) and targeted synthetic (tsDMARD), and biological DMARDs (bDMARDs) were collected.

**Objectives:** We aimed to investigate the efficacy and safety status of methotrexate (MTX) vs. leflunomide (LEF) use as a concomitant treatment with bDMARDs and tsDMARD in this registry.

**Methods:** Frequencies of achievement of remission or remission +low disease activity (LDA) at the 6th month of bDMARD or tsDMARD treatment were compared between patients who were on these medications with MTX vs. LEF as a concomitant treatment. Drug survival and switch rates of bDMARDs and tsDMARD treatments either with MTX or LEF were compared. The adverse effects with MTX and LEF concomitant use were evaluated as well.

**Results:** The study included 725 bDMARD or tsDMARD receiving RA patients from 8 participating centres of the TURKIBIO registry. Of these patients, 462 (63.7%) were receiving concomitant MTX and 263 (36.3%) LEF. Demographic findings are given in the table 1. Achievement of remission and remission +LDA at the 6th month of bDMARD or tsDMARD initiation was similar in concomitant MTX vs LEF groups (51.4% vs. 53%,  $p=0.683$ ). When each bDMARD and tsDMARD was evaluated separately, achievement of remission were again similar in MTX and LEF concomitant users (TNFi: 53% vs. 54%; ABA: 50% vs. 59%; RTX: 53% vs. 61%; TCZ: 42% vs. 35%;  $p > 0.05$  for all). For TOFA, although remission +LDA rate was numerically higher in MTX concomitant group than LEF group (42% vs. 21%), the difference was not statistically significant due to the smaller sample size of TOFA ( $n=33$ ). The results were similar for all DMARD groups when remission was evaluated alone. Drug survival ( $17 \pm 12$  vs.  $16 \pm 11$  months,  $p > 0.05$ ) and drug discontinuation (42,2 vs 38,  $p > 0.05$ ) rates of bDMARDs or tsDMARD were also not different in MTX vs. LEF concomitant users. Adverse effects rate (19.5% vs 20.5%,  $p > 0.05$ ) were similar between MTX vs. LEF concomitant users as well.

#### Abstract FRI0134 – Table 1. Demographic findings of patients.

Sex, n (%)	Female	596 (82,2)
	Male	129 (17,8)
Age, Median (Q1-Q3)		55 (45-62)
Age, Mean±SD		54±13
Disease duration, Orttan (Q1-Q3)		12 (8-17)
Disease duration, Ortt±SD		13±8
Biological and targeted synthetic drugs, n (%)	TNFi*	354 (48,8)
	RITUXIMAB	144 (19,9)
	ABATACEPT	127 (17,5)
	TOCILIZUMAB	61 (8,4)
	TOFACITINIB	36 (5,0)
	ANAKINRA	3 (0,4)
Biological+MTX, n (%)		462 (63,7)
Biological+LEF, n (%)		263 (36,3)

\*TNFi: ETANERCEPT, ADALIMUMAB, CERTOLIZUMAB, GOLIMUMAB, INFILIXIMAB, REMSIMA.

**Conclusions:** Achievement of remission or remission +LDA was not different with the concomitant use of MTX vs. LEF with any bDMARD or tsDMARD treatment in RA patients with a similar safety profile. LEF might be an alternative as a concomitant DMARD in MTX-intolerant RA patients initiating bDMARDs or tsDMARD.

**Disclosure of Interest:** None declared



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### FRI0135 HAVE PREVALENCE OF JOINT SURGERY DECREASED WITH THE USE OF BIOTHERAPY IN RHEUMATOID ARTHRITIS?

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**Background:** Biological response modifiers have greatly expanded therapeutic arsenal of rheumatoid arthritis (RA) leading to a better control of inflammation, a reduced long-term complications and a prevention of joint damage.

**Objectives:** Our objective was to assess the impact of use of biologics on joint surgery during RA.

**Methods:** This is a retrospective study including patients with RA according to American College of Rheumatology (1987) followed- over 15 years period [2000–2014]. We excluded patients who underwent joint surgery without direct relevance to RA. The significance level was set at 0.05.

**Results:** A total of 500 RA patients (422 women and 78 men) were enrolled in this period. The mean age was 53.3 years (21–83) and the mean disease duration was 12 years (2–40). Rheumatoid factor was positive in 71.4% cases. A high disease activity was noted at diagnosis with a mean disease activity score of 5.90 ± 1.38. The mean Health Assessment Questionnaire index was 1.62 [0.2 à 3]. All patients received at least 2 conventional disease-modifying antirheumatic drugs, one of which was methotrexate. Twenty seven per cent of RA patients (135 patients) received biologics: 35 patients received Rituximab (7%) and 100 patients (20%) received anti TNF  $\alpha$  (infliximab, etanercept and adalimumab in 10%, 6.8% and 3.2% respectively). The trend curve of biologics use showed a linear increase with spikes of use in 2008, 2011 and 2014. A surgical act was considered necessary in 59 cases (11.8%) mainly total knee arthroplasty (56%). The mean duration between the onset of RA and surgery was 7.02 (1–33). Patients who received biologics had less joint surgery without significant association ( $p=0.350$ ). The joint surgery showed a decrease in the number of procedures from 2004, concomitantly with promoting biologics.

**Conclusions:** Our study concluded that joint surgery was less frequent in RA patients who received biologics without a significant association.

**Disclosure of Interest:** None declared

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### FRI0136 PERSISTENCE OF MONOTHERAPY OR COMBINATION THERAPY WITH DISEASE-MODIFYING AGENTS IN PATIENTS WITH PSORIATIC ARTHRITIS IN A REAL-WORLD SETTING

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**Background:** Until recently, treatment for moderate to severe psoriatic arthritis (PsA) mainly focused on conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) and tumour necrosis factor inhibitors (TNFi). However, the persistence of TNFi alone or in combination with csDMARDs is not well understood.

**Objectives:** To assess real-world treatment patterns among patients with PsA receiving TNFi monotherapy, csDMARD monotherapy, or TNFi and csDMARD combination therapy.

**Methods:** This retrospective study utilised data from patients with PsA aged  $\geq 18$  years, enrolled in the Corrona PsA registry between March 21, 2013, and July 31, 2017, treated with a TNFi and/or csDMARD (index therapy), and with  $\geq 6$  months of follow-up time. Patients were stratified by prevalent (initiation before enrollment) or incident (initiation after enrollment) therapy use; cohorts were based on index therapy: TNFi monotherapy, csDMARD monotherapy, or combination therapy. Outcomes of interest were the percentage of patients who were persistent on their index therapy or had a therapy change (discontinued, switched, or restarted) 12 months after the index visit.

**Results:** There were 1266 patients in this study: 1144 prevalent and 122 incident (table 1). Patient characteristics at the index date were similar among patients; however, csDMARD monotherapy patients had higher disease activity than either TNFi group. Among prevalent patients, TNFi monotherapy patients were likely to be female (59%) and younger (51.9 years), nearly all patients had psoriasis, and BSA was similar and  $\leq 5$ . At month 12, among patients with a follow-up visit within the 9–15-month window, the vast majority of prevalent patients and half of incident patients were persistent on their index therapy, and one quarter to one third of incident patients discontinued or switched therapy (table 1).

Characteristic at index date	Prevalent TNFi mono N=421	Prevalent csDMARD mono N=347	Prevalent combi N=375	Incident TNFi mono N=43	Incident csDMARD mono N=56	Incident combi N=23
Sex (female), n (%)	244 (58)	158 (46)	165 (50)	15 (44)	24 (43)	11 (48)
Age, mean (SD)	51.9 (12.3)	57.7 (13.3)	53.9 (11.3)	50.7 (14.0)	55.8 (14.1)	53.3 (13.5)
BMI (obese), n (%)	202 (51)	182 (54)	204 (66)	18 (46)	37 (70)	8 (47)
Current psoriasis, n (%)	366 (93)	300 (90)	312 (90)	35 (93)	48 (94)	15 (88)
HASQ, mean (SD)	0.2 (0.4)	0.3 (0.4)	0.3 (0.4)	0.3 (0.4)	0.3 (0.3)	0.4 (0.5)
CDAI, mean (SD)	9.7 (5.6)	11.6 (9.2)	11.7 (6.4)	12.6 (7.3)	16.2 (8.5)	15.7 (13.9)
DAS28 CRP, mean (SD)	2.4 (0.9)	2.7 (1.0)	2.8 (1.0)	3.0 (0.7)	3.4 (0.8)	2.8 (1.4)
Enthesitis, n (%)	74 (18)	52 (15)	75 (20)	14 (32)	8 (14)	3 (13)
Dactylitis, n (%)	27 (6)	25 (7)	12 (3)	7 (16)	14 (25)	4 (17)
BSA (%), mean (SD)	4.9 (8.7)	4.8 (9.3)	5.0 (11.1)	6.2 (8.8)	5.4 (8.9)	1.3 (2.1)
Psoriasis VAS, mean (SD)	5.6 (12.4)	8.1 (22.6)	7.2 (14.3)	11.9 (18.8)	5.9 (15.2)	10.3 (23.3)
History of biologic, n (%)	421 (100)	0	375 (100)	2 (5)	0	0
History of csDMARD, n (%)	132 (46)	347 (100)	369 (98)	13 (30)	0	13 (57)
Treatment pattern, n (%)						
Persistent						
patients with a follow-up visit within 9-15 month window	733/251 (92.8)	196/225 (87.1)	186/214 (86.9)	13/26 (50.0)	15/25 (42.9)	8/15 (53.3)
Time on drug (mo), mean (SD)	88.8 (46.4)	82.5 (78.1)	49.8 (37.7)	15.9 (5.4)	16.9 (8.7)	16.0 (5.0)
Discontinuation	3 (1.2)	8 (3.6)	17 (7.9)	5 (19.2)	9 (25.7)	4 (28.7)
Switch (to another biologic)	2 (0.8)	2 (0.9)	4 (1.9)	1 (3.8)	4 (11.4)	2 (13.3)
Restart	0	3 (1.3)	1 (0.5)	0	0	0

**Conclusions:** Most patients who were prevalent on therapy at the time of enrollment in Corrona remained persistent on their therapy for 12 months in this study, while roughly half of patients initiating therapy after enrollment remained persistent over the same period. Young, female patients were more likely to receive TNFi monotherapy; the TNFi monotherapy cohort was associated with the least disease activity. The incident group was not different from the prevalent group. Although the prevalent group is more likely to have patients who responded to treatment, the data suggest that most therapy changes occur within the first year of PsA treatment.

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### FRI0137 EFFICACY, SAFETY AND IMMUNOGENICITY FROM WEEK 30 TO WEEK 54 IN A RANDOMISED, DOUBLE-BLIND PHASE III STUDY COMPARING A PROPOSED INFLIXIMAB BIOSIMILAR (PF-06438179/GP1111) WITH REFERENCE INFLIXIMAB

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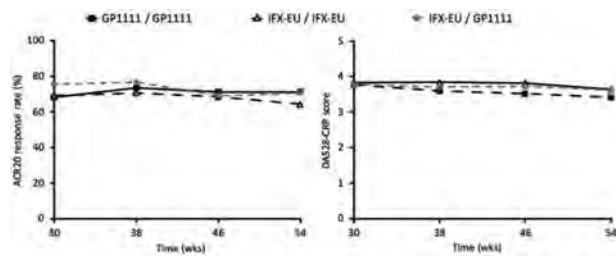
**Background:** PF-06438179/GP1111 (GP1111) is an infliximab (IFX) biosimilar in development for the treatment of immune-mediated inflammatory diseases, including rheumatoid arthritis (RA). The efficacy, safety and immunogenicity of GP1111 and European reference IFX (IFX-EU) have been reported to be similar over 30 weeks (Wks).

**Objectives:** To evaluate the efficacy, safety and immunogenicity of GP1111 and IFX-EU with longer-term treatment, and after treatment transition from IFX-EU to GP1111.

**Methods:** A randomised, double-blind, parallel-group study compared GP1111 with IFX-EU in biologic-naïve, adult patients with moderate-to-severe active RA on a stable dose of methotrexate (MTX). Patients were randomised (1:1) to GP1111 or IFX-EU (3 mg/kg IV at Wks 0, 2, 6, and then every 8 wks, with one dose escalation to 5 mg/kg allowed at or after Wk 14 for inadequate responders)

for 30 weeks (treatment period 1). The primary endpoint was a  $\geq 20\%$  improvement in ACR response (ACR20) at Wk 14. At Wk 30 (treatment period 2 [TP2]), patients receiving IFX-EU were blindly re-randomised (1:1) to remain on IFX-EU or transition to GP1111 for 24 wks. Here we report longer-term efficacy, safety and immunogenicity data from Wks 30–54.

**Results:** 650 patients were randomised initially (GP1111, n=324; IFX-EU, n=326). At Wk 30, 566 patients entered TP2 (continued GP1111, n=280; continued IFX-EU, n=143; switched from IFX-EU to GP1111, n=143). ACR20 rates and DAS28-CRP scores were comparable between groups at all TP2 visits after re-randomisation in the TP2 population (figure 1). Incidences of TP2 treatment-emergent adverse events (AEs) (36.8%, 33.6%, and 37.8%), serious AEs (4.6%, 7.7% and 2.8%) and infusion-related reactions (3.2%, 8.4% and 4.2%) were comparable between the GP1111/GP1111, IFX-EU/IFX-EU, and IFX-EU/GP1111 groups, respectively. Pre-dose ADA rates at Wk 30 (TP2) were 47.1%, 53.8% and 45.5% for the GP1111/GP1111, IFX-EU/IFX-EU, and IFX-EU/GP1111 groups, respectively. Overall, post-dose ADA rates in TP2 were comparable between groups (52.1%, 60.1%, and 58.0% respectively).



**Abstract FRI0137 – Figure 1.** ACR20 response rate and change in DAS28-CRP score at Wk 30 and 54 for the overall population during TP2

**Conclusions:** Results from TP2 (Wks 30–54) continued to show the absence of clinically meaningful differences in efficacy, safety and immunogenicity between patients with RA remaining on GP1111 or IFX-EU, or when blindly switched from IFX-EU to GP1111.

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**FRI0138 TREAT TO TARGET STRATEGY PLUS CERTOLIZUMAB IN COMPARISON TO CONTINUED, FIXED CSDMARD PLUS CORTICOSTEROIDS IN PATIENTS WITH RHEUMATOID ARTHRITIS AND INADEQUATE RESPONSE TO CSDMARDS (REMISSION BY INTRA-ARTICULAR INJECTION PLUS CERTOLIZUMAB, THE RICE STUDY): A MULTI-CENTRE RANDOMISED CONTROLLED TRIAL**

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**Background:** Treatment of rheumatoid arthritis (RA) includes the use of conventional (cs) or targeted synthetic (ts) and biologic disease-modifying anti-rheumatic drugs (DMARDs) and oral or subcutaneous (SC) glucocorticoids (GC).

**Objectives:** We aimed to test the hypothesis that an improved outcome can be achieved by employing a treat to target (T2T) strategy optimising csDMARD, oral, and SC-GC treatment in parallel to a new onset certolizumab pegol (CZP) in RA patients with an incomplete response to csDMARD as compared to a conventional step up strategy with CZP.

**Methods:** We designed a randomised controlled trial in four specialised rheumatological units. 43 patients with active RA ( $\geq 6$  tender,  $\geq 6$  swollen joints, and ESR  $\geq 20$  mm/h or CRP  $\geq 7$  mg/L) despite csDMARD treatment for  $\geq 3$  months and

naïve to biologic DMARDs were randomly allocated either to CZP plus a treat to target strategy (T2T group, n=21) or add on of CZP to a fixed dose of the already established csDMARD with or without established GCs (fixed dose group, n=22). Patients of both groups received 400 mg CZP at week 0, 2, and 4 (loading dose), followed by 200 mg every 2 weeks. The T2T strategy consisted in a step up in, or to, SC-methotrexate (dose:  $15 \geq 20 \geq 25$  mg/week), followed by leflunomide (20 mg/d) and then by sulfasalazine ( $2 \times 1000$  mg/d). In parallel, oral GCs were initiated in the T2T group at 20 mg/d and tapered every 5 days (15–12.5–10–7.5–5–2.5–0 mg/d). The decision to take the next step in the DMARD modification and addition of oral GCs was taken depending on the achievement of LDA (low disease activity: DAS28  $< 3.2$ ) at the 4-weekly visits. Injections of up to five tender and/or swollen joints with triamcinolone (small joints 10 mg, intermediate 20 mg, and big joints 40 mg; max. 100 mg/visit) was allowed in the T2T group. The primary outcome measure was ACR 50 response after 24 weeks. The analysis was intention-to-treat.

**Results:** Three patients dropped out during the study (n=2 T2T, n=1 fixed dose). ACR 50 was achieved in 16 out of 21 T2T patients (76.2%) as compared to 8 out of 22 fixed dose patients (36.4%;  $\text{Chi}^2: 5.355, p=0.020$ ). ACR 20 and 70 responses were achieved in 90.5% and 71.4% of the T2T patients and 59.1% and 27.3% of the fixed dose patients, respectively ( $p=0.045$  and  $p=0.010$ , resp.). Mean reduction in DAS28 were significantly and HAQ-DI markedly greater in the T2T group than in the fixed dose group (DAS28:  $-3.9$  [SD 1.2] vs.  $-2.2$  [SD 1.5],  $p<0.0006$ ; HAQ-DI:  $-0.63$  [SD 0.58] vs.  $0.20$  [SD 0.67],  $p<0.14$ ). All but five of the T2T patients required only one modification of csDMARD and one additional course of oral GC. 10.2 joints (mean) were infiltrated with triamcinolone in the T2T group (av. dose 14.1 mg/injection). The adverse event rate was similar for both groups (T2T n=51; fixed dose n=55).

**Conclusions:** Treat to target management with optimisation of csDMARDs, oral and intra-articular glucocorticoids of RA patients in parallel to additional CZP treatment was safe and substantially improves disease activity and the patient related outcome HAQ-DI in comparison to additional CZP to a fixed dose of csDMARDs.

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**FRI0139 COMPARATIVE SAFETY OF ABATACEPT IN RHEUMATOID ARTHRITIS WITH COPD: A REAL-WORLD POPULATION-BASED OBSERVATIONAL STUDY**

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**Background:** In the ASSURE trial (NCT00048932) comparing abatacept with placebo for the treatment of RA, there was an increased incidence of respiratory serious adverse events (SAEs; COPD exacerbation/worsening, bronchitis and pneumonia) in those receiving abatacept among the subgroup of 54 patients with a history of chronic obstructive pulmonary disease (COPD).<sup>1</sup>

**Objectives:** To assess whether patients with RA and a history of co-morbid COPD treated with abatacept in a real-world, observational setting, have an increased risk of respiratory SAEs compared with similar patients treated with other biologic (b)DMARDs or the targeted synthetic DMARD tofacitinib (tofa).

**Methods:** The Truven MarketScan<sup>®</sup> Commercial and Supplemental Medicare databases were used to identify adult patients diagnosed with RA and COPD who were treated with abatacept, another bDMARD or tofa between January 2007 and December 2015. Other bDMARDs included adalimumab, anakinra, certolizumab, etanercept, golimumab, infliximab, rituximab and tocilizumab. A prevalent new-user study cohort design<sup>2</sup> was used in which each new user of abatacept was time- and propensity score-matched to two new users of other bDMARDs or tofa. Patients were required to have  $\geq 6$  months of continuous health plan enrolment before cohort entry and were followed up until the end of enrolment in the database or 31 December 2015. Propensity scores of abatacept treatment were estimated from the baseline covariates using a conditional logistic regression model separately in incident new users and prevalent new users. Patients with score ranges common to both abatacept and the comparator cohorts were included. An as-treated analysis based on the Cox proportional hazard regression model was used to estimate the hazard ratios (HRs) of respiratory SAEs associated with abatacept compared with other bDMARDs or tofa, further adjusted for confounders found to be unbalanced despite matching on propensity scores.

**Results:** A total of 9746 patients with RA and COPD initiated bDMARD or tofa therapy and included 1807 new users of abatacept matched to 3547 new users of another bDMARD or tofa. The matched cohort was followed for up to 9 years (mean 2.0 years); 53% were incident users. For users of abatacept relative to other bDMARDs or tofa, the adjusted HRs (95% CI) of respiratory SAEs were: hospitalisation for COPD exacerbation: 0.57 (0.30, 1.05); hospitalisation for pneumonia/influenza: 1.39 (0.91, 2.12); outpatient pneumonia/influenza: 1.04 (0.85,



1.28) and outpatient bronchitis: 0.80 (0.57, 1.14). Results remained unchanged with sensitivity analyses.

**Conclusions:** In this real-world study of patients with RA and COPD, the incidence of pre-specified respiratory SAEs was not significantly increased in patients using abatacept compared with those using other bDMARDs or tofa. The safety signal based on the subgroup of 54 patients from the ASSURE trial could not be confirmed in this large and long-term cohort study of over 5000 patients.

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### FRI0140 INDIVIDUALISED INFLIXIMAB TREATMENT: A TREATMENT STRATEGY BASED ON THERAPEUTIC DRUG MONITORING

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**Background:** Infliximab (INX) and other targeted therapies have greatly improved the treatment of patients with RA, SpA and PsA, but a significant proportion of patients either do not respond sufficiently to therapy or loose efficacy over time. Recent advances in assay development have revealed an extensive individual variation in serum drug concentrations suggesting both under- and overtreatment of a substantial proportion of patients. Many patients develop anti-drug antibodies (ADAb) during therapy, contributing to reduced drug levels, inefficacy and adverse events. Therapeutic drug monitoring (TDM), i.e. individual dose adjustments according to serum drug levels, can probably increase effectiveness of treatment with INX and other biological drugs.

**Objectives:** To develop an individualised treatment strategy based on TDM in order to optimise efficacy of INX treatment.

**Methods:** The treatment strategy has been developed by the steering committee of the Norwegian DRUG Monitoring study (NOR-DRUM), based on a systematic literature review (SLR), unpublished data and expert opinion. A SLR was performed in May 2016 to identify the therapeutic range. In Norway neutralising ADAb are measured with an "in house" assay. For this assay, ADAb levels >50 µg/L are defined as "high" leading to a recommendation to switch therapy. This cut-off is based on own s-INX and ADAb data (Diakonhjemmet Hospital during 2015–2016) and clinical experience. The proposed strategy has been developed through a series of meetings in the project group consisting of national leading experts in this field (both clinicians experienced with TDM and laboratory physicians) and with additional input from international key experts in the scientific advisory board of the NOR-DRUM study.

Serum INX level (µg/ml)	(3.0) and high ADAb (>50 µg/L)	<3.0	3.0–3.5	3.6–8.0	8.1–38.0	>60.0
Action	Switch therapy, possibly to another TNFi	Increase dose by 2-2.5 mg/kg or by decreasing the dose interval by 2 weeks to a min of 4 weeks	Consider increasing dose	No action	Consider decreasing dose	Decrease dose
Guideline for action		Increase the dose by increasing the dose by 2-2.5 mg/kg to a max dose of 10 mg/kg or by decreasing the dose interval by 2 weeks to a min of 4 weeks	Consider increasing the dose based on clinical judgement and the patients factors given below*	Within target range. Continue with the same dose and dosing interval	Consider to decrease the dose based on clinical judgement and the patients factors given below*	Decrease the dose by increasing the dose interval by 2 weeks to a max of 30 weeks or by decreasing the given dose by 2-2.5 mg/kg

\*Patient factors to be considered when making the treatment decisions in the yellow zones: Disease activity and trend in disease activity, the trend of the trough level over time, previous drug interval changes, availability of alternative drug, diagnosis (RA patients are expected to have lower trough levels due to lower recommended dosing)

**Results:** The treatment strategy from infusion number 4 onwards is depicted in the figure 1. The therapeutic range for serum INX (through levels) is defined as 3–8 µg/ml (figure 1, green zone). During the induction phase (infusion 1–3) the recommendation is to keep the level >20 µg/ml at infusion 2 and >15 µg/ml at infusion 3. A guideline for action according to levels outside the therapeutic range is given in the figure 1. Dose modifications may be performed either as changes in doses or intervals as stated in the figure 1. If the patients develop high levels of ADAb the recommendation is to switch therapy.

**Conclusions:** An individualised treatment strategy based on TDM has the potential to optimise therapy with infliximab and other biological drugs by; 1) prevention of treatment failure by identification of patients with drug levels below the therapeutic range, 2) reduction of overtreatment, which predispose to side effects and increase costs, and 3) early identification of ADAb development, with the possibility to detect treatment failures prior to a clinical flare and to prevent hypersensitivity reactions. This approach has high face validity, and the effectiveness compared to regular care is being investigated in an ongoing randomised clinical trial, NOR-DRUM (NCT03074656).

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### FRI0141 VACCINATION DECISIONS AND INCIDENCE OF NEONATAL INFECTIONS IN MOTHERS EXPOSED TO BIOLOGICALS DURING PREGNANCY

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**Background:** Rheumatologic diseases commonly affect women of childbearing age.<sup>1,2</sup> There is currently limited data available regarding the safety of vaccinations in infants after in utero exposure to biologics.

**Objectives:** To determine the vaccination decisions of mothers with rheumatologic diseases exposed to biologics during pregnancy and the incidence of serious neonatal infections after third trimester exposure.

**Methods:** All Australian women with inflammatory arthritis, exposed to biologics during the preconception, antenatal and/or postpartum periods, were invited to participate in the Pregnancy Exposed to Biological (PEB) study from May 2009 – Jan 2018. Recruitment was via direct invitation from patients treating rheumatologists, community groups, and via social media. Following self-referral to the study, retrospective data was collected, including biological exposure, vaccination history and the incidence of serious neonatal infections, defined as infection requiring hospitalisation.

**Results:** Preliminary data is available regarding 35 offspring from 28 mothers. 34 of 35 offspring were vaccinated. 29 received vaccinations in accordance with the Australian National Immunisation Program Schedule. 1 mother declined to immunise her infant due to personal preference.

13 infants were exposed to a tumour necrosis factor inhibitor (TNFi) during the third trimester. Of these, 4 had Rotavirus vaccine delayed from 2 to 4 months and 1 infant until 6 months. 1 infant did not receive the Rotavirus vaccine at 2 months due to exposure to a TNFi while breastfeeding. There were no incidences of serious neonatal infections.

**Conclusions:** Current guidelines recommend deferring live vaccines, such as rotavirus, until after 6 months if exposed to a biologic in the third trimester.<sup>3-5</sup> Compliance with these recommendations was only observed in one infant in our study. One infant received delayed Rotavirus vaccination due to concern about TNFi exposure during breastfeeding; this is not in keeping with current guidelines. Of the 12 infants exposed to a biologic during the third trimester who did not delay live vaccination until after 6 months, there were no incidents of serious neonatal infections, in keeping with the findings of current published case series.

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**FRI0142 THE COMPARISON OF THE ULTRASONOGRAPHIC SYNOVIAL FINDINGS BETWEEN INTRAVENOUS ADMINISTRATION AND SUBCUTANEOUS INJECTION OF TOCILIZUMAB**

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**Background:** Biologic disease-modifying anti-rheumatic drugs (bDMARDs) that target cytokines and cytokine receptors such as tumour necrosis factor (TNF) alpha and interleukin (IL) 6 have been established as a standard therapy in patients with rheumatoid arthritis (RA). Tocilizumab (TCZ) that targets IL-6 receptors has two administration routes such as intravenous administration (IV) or subcutaneous injection (SC). The effect of TCZ-SC therapy demonstrated comparable efficacy and safety to TCZ-IV therapy in clinical study.<sup>1, 2</sup> However, there have been no reports that evaluate the effect of TCZ-IV and SC for synovitis by imaging modality.

**Objectives:** The aim of this study was to compare the ultrasound findings between patients with rheumatoid arthritis (RA) treated by TCZ-IV and SC.

**Methods:** All patients with RA who treated with TCZ in Osaka City University RA registry (1140 patients with RA and 390 patients using bDMARDs) were included in this cross-sectional study. US examination was performed in MCP, PIP, wrist and MTP joints and finger flexor tendon and wrist extensor tendon, by using HI VISION Ascendus (Hitachi Medical Corporation, Japan) with a multifrequency linear transducer (18–6 MHz). The grey scale (GS) and power Doppler (PD) findings were assessed by the semi-quantitative method (0–3). GS score and PD score (both 0–156 points) were defined as the sum total of each score.

**Results:** We analysed total 76 patients who treated TCZ, 27 patients in IV group and 49 patients in SC group (mean age: 62.9±14.0 vs 66.0±13.2 years, p=0.343, mean duration of RA: 17.1±11.1 vs 13.7±12.3 years, p=0.218). The duration of TCZ use was significantly longer in IV (4.6±2.2 vs 3.0±2.4 years, p=0.004). Clinically, DAS28-ESR improved from 5.3±1.5 at baseline to 2.4±1.1 at US examination in IV group, and it improved from 5.2±1.4 to 2.8±1.5 in SC group. US findings were not significantly differenced in both groups, GS score: 11.7±12.5 vs 10.9±9.6 (p=0.751), PD score: 5.3±8.1 vs 5.7±6.8 (p=0.832), max PD grade: 1.3±0.9 vs 1.4±0.9 (p=0.571) in IV and SC respectively.

**Abstract FRI0142 – Table 1.** The comparison of demographic and ultrasonographic findings between TCZ-IV and SC patients with rheumatoid arthritis.

	TCZ-IV group (n=27)	TCZ-SC group (n=49)	P value
Age (years old)	62.9±14.0	66.0±13.2	0.343
Disease duration (years)	17.1±11.1	13.7±12.3	0.218
Duration of TCZ use (years)	4.6±2.2	3.0±2.4	0.004
DAS28-ESR at baseline	5.3±1.5	5.2±1.4	0.780
DAS28-ESR at ultrasound examination	2.4±1.1	2.8±1.5	0.175
CDAI at baseline	21.8±14.5	22.8±14.4	0.787
CDAI at ultrasound examination	7.3±5.9	10.6±10.4	0.082
Total GSUS score	11.7±12.5	10.9±9.6	0.751
Total PDUS score	5.3±8.1	5.7±6.8	0.832
Maximum PDUS grade	1.3±0.9	1.4±0.9	0.571

**Conclusions:** We compared the ultrasound findings between patients with RA treated by TCZ-IV and SC. Ultrasound findings between IV and SC were not significantly differenced. Both administration routes of TCZ are effective for the treatment in patients with RA.

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**FRI0143 INFLUENCE OF LOW-DOSE GLUCOCORTICOID TREATMENT ON PERSISTENCE ON BIOLOGIC DMARDS THERAPY: REAL-LIFE DATA FROM THE ITALIAN GISEA REGISTRY**

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**Background:** The use of glucocorticoid (GC) in Rheumatoid arthritis (RA) is recognised by the current treatment approach as a valid adjunct to DMARDs therapy. Despite its efficacy, safety of GC is still an issue and the best strategy of use is still debated, including patients under bDMARDs therapy

**Objectives:** To analyse in RA the differences of GC users versus non-users of baseline features, response to therapy and persistence in bDMARDs from the Italian biologics registry GISEA (Italian Group for the Study of Early Arthritis)

**Methods:** Consenting patients satisfying 1987 or 2010 ACR criteria for RA included in the Italian GISEA registry were enrolled. Data recorded comprehend demographic and clinimetric variables. Data are collected at baseline and 6 monthly during follow-up. To be included in the study patients needed a minimum follow-up time of 12 months and if data were not updated after 2012 patients were considered lost to follow-up. EULAR and HAQ responses were calculated. Statistical analysis included descriptive measures, parametric and nonparametric comparisons between groups and univariate analysis of survival on therapy

**Results:** A total of 8545 patients were enrolled, of them 4193 (49%) using a variable dose of GC. In 3035 (72%) the dose was ≤5 mg. Baseline demographic and disease-specific features at the start of bDMARD therapy were not different between GC users and non-users, both in 1st and 2nd line bDMARDs RA patients. EULAR response rates were generally better in GC users at 6 and 12 months, but without statistical significance: good/moderate EULAR responses at 6 months were attained in 76.5% of GC users versus 67% in non users, while at 12 months in 81.5% vs 73% respectively (both Ps not significant). Similarly, HAQ responses (<0.5) were slightly better in users vs non users at 6 (42.5% vs 37.4%) and 12 months (46.5% vs 42%) but again without statistical significance. Finally, mean survival on bDMARDs therapy after 2 years was significantly influenced by GC with better survival curves in steroid-treated patients (55.8% vs 47%, p<0.001). This difference was also maintained subanalysing patients in 1st or 2nd bDMARD lines of therapy (56.2% in users vs 48% in non users in 1st line and 55.3% vs 45.9% in 2nd line, both Ps <0.001).

**Conclusions:** Our data show that GC are used in a high percentage of RA patients on bDMARD therapy. GC significantly improve the persistence on bDMARDs therapy in 1st and 2nd line. No obvious other differences are evident in baseline, EULAR and HAQ response rates. This fact should be kept in mind when evaluating the persistence on bDMARD treatment reported in different registries. Safety evaluations in individual patients should be further analysed to guide the use of GC in this setting

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**FRI0144 PATIENT-REPORTED OUTCOMES WITH SARILUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS ARE SIMILAR REGARDLESS OF PRIMARY OR SECONDARY FAILURE WITH TUMOUR NECROSIS FACTOR INHIBITORS**

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**Background:** Sarilumab is a human monoclonal antibody that binds membrane and soluble IL-6 and was recently approved for the treatment of moderate-to-severe rheumatoid arthritis. Among inadequate responders to a TNF inhibitor (TNFi), patients may respond differently to sarilumab depending on whether they had a primary (1<sup>o</sup>) failure or initially responded but then subsequently lost response (secondary [2<sup>o</sup>] failure).

**Objectives:** To understand if changes in patient reported outcomes (PROs) differ among patients with 1° or 2° TNFi failure.

**Methods:** In TARGET (NCT10709758), patients with intolerance or an inadequate response to TNFi were randomised to placebo or sarilumab 150 mg or 200 mg plus csDMARD. For patients with an inadequate response to TNFi (92% of the sample), 1° or 2° failure was investigator-determined at enrollment. The following PROs were assessed at Week 0 (treatment initiation) and Week 24: HAQ-DI, patient global assessment of disease visual analogue scale (VAS), pain VAS, SF-36, morning stiffness VAS, EQ-5D, and Rheumatoid Arthritis Impact of Disease (RAID) scale. All scales produce global (total) scores, except the SF-36 which has eight domains and two summary scores (physical and mental component scores [PCS and MCS]) and the EQ-5D which has a single index utility score and a global health VAS. The PRO change from baseline was analysed through mixed model repeated measures with treatment, region, number of prior TNFis, baseline of the PRO analysed, visit, treatment-by-visit interaction, 1° and 2° subgroup, treatment-by-subgroup interaction, and treatment-by-visit-by-subgroup interaction. *Post-hoc* analysis of the sarilumab 200 mg data are reported here as this is the recommended dose of sarilumab.

**Results:** In this *post-hoc* analysis, 174 of 181 patients in the placebo group and 167 of 184 in the sarilumab 200 mg group were classified as TNFi 1° or 2° failures (the remaining patients were classed as intolerant or other and not included in this analysis); 75 and 64 were 1° and 99 and 103 were 2° treatment failures in the placebo and the sarilumab 200 mg groups, respectively. At Week 24, changes in all PROs were numerically similar in the 1° or 2° TNFi failures for both the sarilumab 200 mg and placebo groups (table 1). Furthermore, treatment-by-subgroup interaction testing did not show a statistically significant interaction of TNFi failure status and PRO outcome (all interaction *P*-values>0.05). Treatment emergent adverse events occurred in 65.6% of sarilumab 200 mg patients in the 1° failure group and 63.1% in the 2° failure group and were consistent with safety data reported previously.

**Abstract FRI0144 – Table 1.** Least square mean (SE) change from baseline to Week 24 in patient-reported outcomes with sarilumab 200 mg and placebo following primary and secondary TNFi failure

PRO	1° failure		2° failure		Interaction <i>P</i> -value
	Placebo (n=71)	Sarilumab 200 mg (n=64)	Placebo (n=99)	Sarilumab 200 mg (n=103)	
Physical global assessment	-2.58 (3.30)	-2.08 (3.41)	-1.91 (3.30)	-2.07 (3.41)	0.2945
Pain VAS	-21.25 (3.98)	-21.81 (3.87)	-21.86 (3.81)	-23.04 (3.78)	0.6389
HAQ-DI	-0.38 (0.08)	-0.20 (0.08)	-0.20 (0.07)	-0.20 (0.08)	0.1892
SF-36 PCS	4.25 (1.01)	4.18 (1.01)	4.81 (0.99)	7.88 (0.90)	0.7237
SF-36 MCS	4.78 (1.41)	5.28 (1.42)	6.94 (1.21)	6.81 (1.32)	0.8220
Physical functioning	5.18 (2.86)	16.28 (3.48)	10.40 (2.78)	14.71 (2.53)	0.2969
Role-physical	19.18 (3.02)	17.91 (3.00)	11.79 (2.78)	20.01 (2.49)	0.0878
Bodily pain	14.51 (3.98)	23.30 (2.51)	18.32 (2.63)	24 (2.2 24)	0.0047
General health	15.10 (2.26)	18.22 (2.88)	7.02 (1.15)	12.78 (1.98)	0.0169
Vitality	9.18 (2.81)	14.26 (2.88)	8.09 (2.38)	15.47 (2.12)	0.0288
Social functioning	12.80 (2.25)	17.88 (2.22)	12.78 (2.64)	18.88 (2.84)	0.0471
Role emotional	18.48 (3.34)	12.88 (3.28)	19.18 (3.04)	18.88 (2.72)	0.6884
Mental health	8.18 (2.88)	12.12 (2.88)	6.02 (1.15)	11.48 (1.84)	0.0177
FACT fatigue	7.18 (1.38)	7.32 (1.37)	8.02 (1.14)	10.82 (1.04)	0.1880
Morning stiffness VAS	-21.81 (3.98)	-22.21 (3.93)	-22.27 (3.28)	-22.27 (3.59)	0.8177
EQ-5D VAS	12.72 (3.32)	18.81 (3.28)	18.81 (2.63)	18.74 (2.48)	0.0118
EQ-5D single index utility	5.18 (0.24)	5.31 (0.24)	5.22 (0.23)	5.39 (0.23)	0.1002
RAID	-4.74 (0.51)	-4.46 (0.52)	-4.84 (0.49)	-5.21 (0.50)	0.1620

**Conclusions:** In TNFi inadequate response patients, following treatment with sarilumab 200 mg +csDMARD, changes in PRO outcomes were similar, regardless of whether they had experienced 1° or 2° TNFi failure, suggesting that sarilumab is suitable for both 1° and 2° TNFi failure patients.

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**FRI0145 A BAYESIAN NETWORK META-ANALYSIS ON EFFICACY OF BIOLOGICS AND SMALL MOLECULES IN EARLY RHEUMATOID ARTHRITIS**

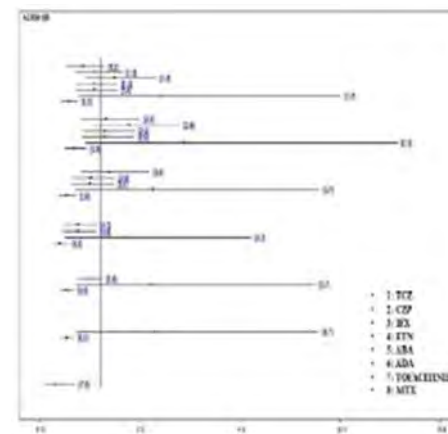
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**Background:** The use of several biologic drugs as well as small molecules, in combination or not with methotrexate (MTX), is licensed for the treatment of Rheumatoid Arthritis (RA). Treating patients within the 'therapeutic window of opportunity' may reset the disease's long-term trajectory. Which agent would fit better the need of promptly achieving remission of patients affected with early RA is

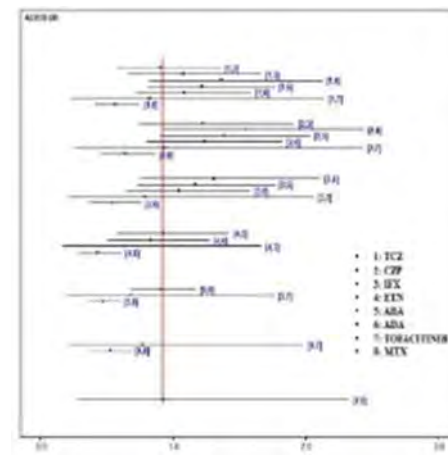
currently a matter of debate. Ideally head to head comparison are required to estimate which treatment is the most effective. Alternatively, indirect comparisons based on a common comparator may be useful. Previous indirect comparisons did not take into account all the biologics and small molecules approved for the treatment of RA, being also biased, identifying early RA in patients with high variance of disease duration, ranging from to 6 months to 2 years.

**Objectives:** To provide an estimate through a Bayesian Network Meta-Analysis of which biologic or small molecule in association with MTX is more likely to determine a good clinical response in patients affected with early RA (i.e. mean disease duration <1 year).

**Methods:** A literature search was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement to identify results of Randomised Controlled Trials (RCTs) of biologic agents and small molecules at licensed doses to treat patients affected by early RA. MEDLINE, EMBASE, Cochrane Library, and Clinicaltrials.gov were searched for all published RCTs ranging from 1990 to September 2017. Patients had to fulfil the ACR 1988 revised criteria and/or the 2010 ACR/EULAR criteria for classified RA. We included all completed RCTs of biologics or small molecules in combination with MTX, compared with MTX plus placebo or in combination with other biologics or small molecules, in patients whose RA had mean duration of less than 1 year. American College of Rheumatology (ACR) 50% response and ACR 70% response had to be evaluated after one year of continuous treatment both in examined drug branch and in placebo branch. WinBUGS 1.4 software (MRC Biostatistics Unit, Cambridge, UK) was used to perform the analyses, using a fixed-effect model.



**Results:** Thirteen studies were included in the analysis. All the biologics as well as Tofacitinib proved to be more effective than MTX plus placebo in inducing an ACR50 response. In this regard, Tofacitinib was the most effective overall (probability of being the best treatment: 75.04%) followed by Etanercept (21.52%). The agent with the highest probability of inducing ACR70 response was Etanercept (52.00%) followed by Abatacept (20.22%). All compared biologics in combination with MTX were superior to MTX alone in inducing ACR70 response.



**Conclusions:** After one year of continuous treatment, Tofacitinib and Etanercept are the agents with the highest probability of inducing ACR50 response in patients

affected by early RA, while Etanercept and Abatacept are the biologics with the highest probability of inducing ACR70.

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**Disclosure of Interest:** None declared

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FRI0146

#### CORRELATION BETWEEN THE RHEUMATOID FACTOR POSITIVITY AND THE HIGHER DISCONTINUATION RATE OF BIOLOGICAL THERAPY IN RHEUMATOID ARTHRITIS: A FINE-GREY PROPORTIONAL HAZARD REGRESSION ANALYSIS

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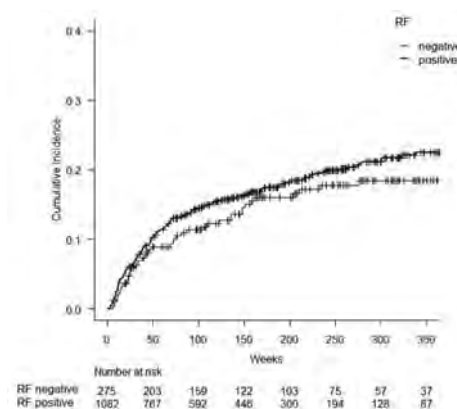
**Background:** As quantifying the occurrence of outcome over time holds vital importance in clinical medicine, the presence of competing risks must be considered when assessing the impact of prognostic factors on the incidence of an outcome over time. A competing risk is defined as an event that precludes the occurrence of an event of interest. For example, event arising from adverse effect causes is a competing risk when evaluating the effect of risk factors on the incidence of discontinuation of biological therapy because of inadequate response. The presence of biased estimates of the effect of covariates on the incidence in the presence of competing risks is attributed to the naïve use of the conventional Cox proportional hazards model that censors the competing event. Fine and Grey developed the subdistribution hazard model that facilitates modelling the effects of covariates on the cumulative incidence function in the presence of competing risks.

**Objectives:** The discontinuation of biological therapy in rheumatoid arthritis (RA) is attributed to several reasons, including inadequate response, adverse effect, remission, and changing hospital. In particular, inadequate response constitutes a principal and compelling reason. This study aims to investigate the correlation between covariates, including the rheumatoid factor (RF) positivity and the discontinuation of biological therapy due to inadequate response in bio-naïve patients with RA using the Fine–Grey proportional hazard regression for competing events.

**Methods:** In this study, we enrolled patients in the Tsurumi Biologic Communication Registry that comprises Nagoya University and 15 affiliated institutions in Japan. We assessed the correlation between individual characteristic components and patient outcomes using the Fine–Grey proportional hazard regression for competing events. Apparently, time-based models estimate the effects of various characteristics (e.g., RF positivity, sex, and age) on time to develop events of interest, including the discontinuation owing to inadequate response. The Fine–Grey proportional hazard regression considered competing events, implying that this model generated separate hazard ratios for each competing event. All analyses were conducted in EZR version 1.36.

**Results:** A higher crude discontinuation rate was observed due to inadequate response in RF-positive patients than that in RF-negative patients using the cumulative incidence function of competing events and Grey test (figure 1). After adjusting for the baseline characteristics, including age, sex, stage, disease at the baseline, methotrexate use, prednisolone use, and tumour necrosis factor inhibitor (TNFi) or non-TNFi (HR, 1.57; 95% CI: 1.01–2.43;  $p < 0.05$ ; table 1), the difference was significant in the Fine–Grey proportional hazard regression analysis.

	Hazard ratio	Lower 95% CI	Upper 95% CI	p.value
RF positivity	1.57	1.01	2.43	<0.05
Sex	0.91	0.61	1.36	0.67
Age	0.99	0.98	1.01	0.12
Das28esr at baseline	1.31	1.15	1.48	<0.05
non-TNFi	0.53	0.31	0.91	<0.05
MTX use	1.64	1.01	2.67	<0.05
PSL use	1.16	0.82	1.64	0.38
Stage	0.99	0.98	1.01	0.57



**Conclusions:** Using the Fine–Grey proportional hazard regression for competing events, this study demonstrated a correlation between the RF positivity and inadequate response to biological therapy on bio-naïve patients with RA.

**Disclosure of Interest:** None declared

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FRI0147

#### ANALYSIS OF RADIOGRAPHIC JOINT DESTRUCTION IN THE PATIENTS WITH RHEUMATOID ARTHRITIS WHO HAVE WITHDRAWN, SPACED AND CONTINUED BIOLOGICS AFTER ACHIEVING SUSTAINED REMISSION FROM LOCAL BIOLOGICS REGISTRY

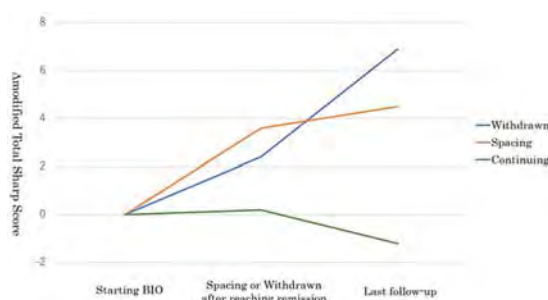
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**Background:** Increasing of remission reached by biologics agents in early and established RA patients<sup>1, 2</sup>. Data on withdrawn, spacing or reducing of biologics (BIO) medication after sustained remission are limited<sup>3, 4</sup>. After withdrawn, spacing or reducing, it is less known to be influenced the radiographic destruction of the joints.

**Objectives:** To retrospectively analyse the joint destruction using modified Total Sharp Score (mTSS) in RA patients in sustained remission, either withdrawing, spacing and continuing BIO.

**Methods:** Local prefectural (ZAO) registry which is open-labelled BIO cohort study has registered 356 RA patients. RA Patients were enrolled into this study if they maintained in DAS remission (DAS28-ESR<2.6) more than one year after starting BIO.  $\Delta$ mTSS1 was estimated between starting BIO and withdrawn or spacing or reaching remission in each group,  $\Delta$ mTSS2 between the beginning of withdrawn or spacing, or reaching remission in continuing group and latest follow-up or flare-up.

**Results:** 40 RA patients (32 female) using BIO was fulfilled in the criteria of this study in ZAO registry. Of 40 RA Patients, 10 has withdrawn BIO, 15 has spaced and 15 has continued it after maintain DAS remission more than one year. Mean age was 43, 55, 54 year-old, mean RA affiliation 4.6, 15.3, 9.1 years before BIO and mean duration of remission 6.2, 7.6, 7 years, mean dosage of MTX and PSL was 7.7, 6, 5 mg/week and 1.1, 3, 4 mg/day, respectively.  $\Delta$ mTSS1 and  $\Delta$ mTSS2 was +2.4 and +4.5 in withdrawn group, +3.6 and +0.9 in spacing group, +0.2 and -1.4 in continuing group, respectively (figure 1,  $p < 0.05$ ). Five cases in withdrawing group had resumed BIO because of flare-up of their disease activity.



**Abstract FRI0147 – Figure 1.** Radiographic destruction of joint in each withdrawn, spacing, continuing groups





lumbar spine specimens from mCIA mice. (G) A schematic diagram illustrating the theory in the current study.

**Disclosure of Interest:** None declared

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**FRI0150** **MTOR BLOCKADE BY RAPAMYCIN DECREASES ARTHRITIS AND SPONDYLITIS DEVELOPMENT AND SEVERITY IN HLA-B27 TRANSGENIC RATS**

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**Background:** HLA-B27 misfolding is thought to play an important role in the pathogenesis of spondyloarthritis (SpA), possibly through triggering of ER stress and the unfolded protein response. One of the mechanisms that regulates the unfolded protein response is autophagy. Autophagy is a process that degrades proteins, cytoplasmic particles and organelles in lysosomes and is regulated by protein kinases, mechanistic target of rapamycin (mTOR) and AMP activated protein kinase.

**Objectives:** To study whether blockade of mTOR will affect spondyloarthritis development and/or severity in the *Mycobacterium tuberculosis* (*M. tub*) induced disease HLA-B27 tg rat model.

**Methods:** 6 weeks old, female or orchietomized male HLA-B27/Huβ2m transgenic rats were immunised with 60–90 µg heat-inactivated *M. tub* in IFA. Rats were prophylactically or therapeutically treated three times a week intra-peritoneally with 1.5 mg/kg rapamycin or vehicle. Clinical measurements included weight, clinical scores for spondylitis and arthritis, and hind paw swelling measured by plethysmometry. After 5 weeks of treatment rats were sacrificed; axial and peripheral joints were isolated for histology and metacarpophalangeal joints, spleen and lymph nodes were isolated for RNA isolation.

**Results:** In the prophylactic experiment 72.7% (8/11) and 18.2% (2/11) rapamycin treated rats developed arthritis and spondylitis compared to respectively 100% (13/13; p=0.0225) and 92.3% (12/13; p<0.0001) control animals. Also severity of arthritis and spondylitis was significantly decreased in rapamycin treated animals compared to control treated animals; mean arthritis severity of diseased rats was respectively 0.45 versus 7.15 on a scale from 0–12 (p<0.0001) and mean spondylitis severity was respectively 0.18 versus 2.07 on a scale from 0–3 (p<0.0001). Clinical findings were confirmed by histology with a significant decrease of inflammation (p<0.0001), bone- and cartilage destruction (p=0.0021) and new bone formation (p=0.0010) in peripheral joints of rapamycin treated rats compared to vehicle treated rats and a similar trend was observed in spinal joints. Also in a therapeutic setting rapamycin treatment decreased arthritis severity (mean score of 6 compared to 8.8 in controls; p=0.0317) and spondylitis severity (mean score of 1.23 compared to 2.8 in controls; p=0.0159). Histology for the therapeutic experiment is currently being performed as well as RNA analyses for autophagy genes and pro-inflammatory cytokines, like IL-17A and TNF.

**Conclusions:** mTOR blockade significantly suppressed arthritis and spondylitis in the *M. tub* induced disease HLA-B27 transgenic rat model of SpA.

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**FRI0151** **PROTEIN INHIBITOR OF ACTIVATED STAT3 PREVENTS PERIPHERAL ARTHRITIS AND GUT INFLAMMATION BY REGULATING TH17/TREG CELL IMBALANCE VIA STAT3 SIGNALLING IN MICE MODEL OF SPONDYLOARTHRITIS**

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**Background:** Spondyloarthritis (SpA) is inflammatory arthritis, and interleukin (IL) –17 is crucial on pathogenesis of SpA. Type 17 helper T cell (Th17) is one of major IL-17 secreting cells. Signal transducer and activator of transcription (STAT)–3 signalling induces Th17 cell differentiation. Present study investigated the effect of protein inhibitor of activated STAT3 (PIAS3) on SpA pathogenesis.

**Methods:** Curdlan was injected to SKG ZAP-70<sup>W163C</sup> mice for SpA induction. Then PIAS3 or Mock vector was inserted to mice for 10 weeks. Clinical score and histologic scores of paw, spine, and gut were evaluated. Expressions of IL-17, tumour necrosis factor-α (TNF-α), STAT3, bone morphogenic protein (BMP) were

measured. Confocal stain and flow cytometry were used to assess helper T cell differentiation.

**Results:** PIAS3 significantly diminished the histological scores of paw and gut. PIAS3 group displayed lesser expression of IL-17, TNF-α, and STAT3 in the paw, spine, and gut. BMP-2/4 expressions were lower in spine of PIAS3 group. Helper T cell differentiation was polarised toward upregulation of regulatory T cell (Treg) and downregulation of Th17 in the PIAS3 mice.

**Conclusions:** PIAS3 showed preventive effects in mice with SpA by suppressing peripheral arthritis and gut inflammation. Proinflammatory cytokines and Th17/Treg differentiation were controlled by PIAS3. Additionally BMPs were decreased in spine of PIAS3 mice. These findings suggest that PIAS3 could be a potential therapeutic choice of SpA treatment.

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**Disclosure of Interest:** None declared

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**FRI0152** **INFLAMMASOMES ACTIVATION OCCURS IN THE INFLAMED TISSUES OF AS PATIENTS AND DRIVES IL-23 EXPRESSION**

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**Background:** A growing body of evidences indicate that the aberrant activation of innate immune systems, occurring in genetically predisposed patients, drives inflammatory processes in Ankylosing Spondylitis (AS).<sup>1</sup>

**Objectives:** Aim of this study was to evaluate the activation and the functional relevance of inflammasome pathways in patients with AS.

**Methods:** Intestinal, synovial and bone marrow expression of inflammasome pathways, pyroptosis and IL-1b and IL-18 was evaluated in AS patients. Organic acid extraction was performed on ileal samples as previously described on. The expression of the metabolite-sensing receptors GPR43 and GPR109A involved in the regulation of the intestinal inflammasome was also assessed. The role of intestinal dysbiosis in modulating inflammasome activation was also studied in AS patients and HLA-B27 transgenic rats. Inflammasome activation was evaluated in isolated peripheral AS monocytes. The role of LPS, PGE2 and nicotine in inducing monocyte inflammasome activation and the role of inflammasome in modulating IL-23 production was also evaluated.

**Results:** Activation of inflammasomes was observed in the inflamed gut, synovial and bone marrow samples of AS patients and associated with an increased expression of caspase-1, IL-1b and IL-18. In AS, AIM2 expression was observed in the context of tuft cells and of adherent ileal bacteria. Inflammasome activation in AS gut, was associated with the occurrence of dysbiosis and increased pyroptosis as demonstrated by the membrane localization of Gasdermin D. Isolated intestinal bacteria from AS ileal samples, significantly modulated inflammasome activation in isolated monocytes. Reduced Short-chain fatty acids concentrations and increased expression of GPR43 and GPR109 were demonstrated in the AS ileal samples. Inflammasome activation was also observed in the inflamed gut of HLA-B27 TG rats and suppressed by antibiotics treatment. Increased expression of NLRP3, NLRC4 and AIM2 was confirmed in AS isolated peripheral monocytes. Serum levels of IL-1b and IL-18 were increased in AS patients, especially in smoker patients, and directly correlated with the ASDAS-CRP. In *in vitro* studies, LPS and nicotine strongly activated NLRP3, NLRC4 and AIM2 pathways in AS monocytes. The CC genotype of PTGER4 SNP rs6896969 was associated with a significantly increased activation of inflammasome in AS. Finally, inflammasome activation in AS monocytes was required for the induction of IL-23p19 expression in an IL-1b-dependent way.

**Conclusions:** Inflammasome activation occurs in AS patients being modulated by a plethora of different stimuli. Inflammasome drives IL-23 production in an IL-

1b-dependent mechanism in AS patients supporting the auto-inflammatory nature of the disease and possibly representing a future therapeutic target in AS.

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**Disclosure of Interest:** None declared

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#### FRI0153 ROLE OF ROR GAMMA T INHIBITION IN THE IL-23 MINICIRCLE MODEL AND SPA PATIENT TISSUE CULTURES

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**Background:** Retinoic acid receptor related Orphan Receptor gamma t (ROR $\gamma$ t) is a nuclear hormone receptor expressed in a subset of pathogenic T cells and innate lymphoid cells. ROR $\gamma$ t regulates the transcription of key pro inflammatory cytokines such as IL-17 and IL-22 in response to multiple activation signals including cytokines and T cell receptor engagement. Antagonism of ROR $\gamma$ t is hypothesised to block transcription of these pathogenic cytokines resulting in reduced tissue inflammation and aberrant joint remodelling.

Spondyloarthropathy (SpA) is characterised by a peripheral oligoarthritis and enthesitis. A key feature of SpA is the imbalance between bone resorption and formation leading to aberrant bone formation and ankylosis. The contribution of the IL-23/IL-17 axis to the pathogenesis of SpA is supported by several lines of evidence. However, the specific role of ROR $\gamma$ t in regulating the cellular and molecular pathways contributing to enthesal and synovial inflammation remains incompletely understood.

**Objectives:** The goal of this study was to determine the role of ROR $\gamma$ t antagonism in both an IL-23 minicircle *in vivo* model and *ex vivo* tissue culture model.

**Methods:** Model 1: Mice were administered an IL-23 minicircle via hydrodynamic injection to induce systemic IL-23 expression on day 1. Starting on day 2, mice were dosed p.o. for 28 days. Mice were monitored daily for signs of arthritis. Upon sacrifice tissue was collected for mRNA biomarker analysis and histologic assessment.

Model 2: Patients undergoing total hip replacement were recruited into 2 groups: SpA (either psoriatic arthritis or ankylosing spondylitis) or OA (osteoarthritis). Enthesal and synovial tissues were collected and cultured  $\pm$ ROR $\gamma$ t inhibitor and cytokine stimulation (hTNF $\alpha$ /hIL23) for 24 and 48 hours and then analysed for gene expression.

**Results:** Model 1: Overexpression of IL-23 induced SpA like phenotype including enthesitis, synovitis and aberrant bone formation. ROR $\gamma$ t inhibition resulted in significant reduction of inflammation and arthritic score, histologic parameters of bone remodelling, and tissue biomarkers associated with the IL-23 axis (IL17A, IL17F, IL22).

Model 2: Both enthesal and synovial cultures from SpA patients expressed increased Th17 axis genes relative to OA after cultures. ROR $\gamma$ t inhibition reduced the expression of these Th17 axis genes (IL17A, IL17F, IL22) as well as reducing tissue remodelling related genes (FN1, MMP1/3, BMP5), in alignment with the results seen in model 1.

**Conclusions:** IL-23 induced Th17 axis gene expression induced a SpA-like phenotype in mice, including arthritis and aberrant bone formation, that was reversed upon ROR $\gamma$ t inhibition. Similarly, SpA patient explants showed increased expression of Th17 axis cytokines and tissue remodelling related genes that were decreased with ROR $\gamma$ t inhibition. Together, these complementary approaches support the hypothesis that ROR $\gamma$ t treatment could block inflammation as well the underlying pathologies associated with SpA.

**Disclosure of Interest:** K. Hoyt Employee of: Boehringer Ingelheim, J. Galdamez: None declared, M. Panzenbeck Employee of: Boehringer Ingelheim, D. Souza Employee of: Boehringer Ingelheim, E. Glynn Employee of: Boehringer Ingelheim, J. Pelletier Employee of: Boehringer Ingelheim, M. Lewis Employee of: Boehringer Ingelheim, G. Nabozny Employee of: Boehringer Ingelheim, E. Purdue: None declared, L. Mandl Consultant for: Boehringer Ingelheim, J. Wahle Employee of: Boehringer Ingelheim

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#### FRI0154 ADDED VALUE OF BIOMARKERS COMPARED TO ROUTINE CLINICAL PARAMETERS FOR THE PREDICTION OF RADIOGRAPHIC SPINAL PROGRESSION IN AXIAL SPONDYLOARTHRITIS

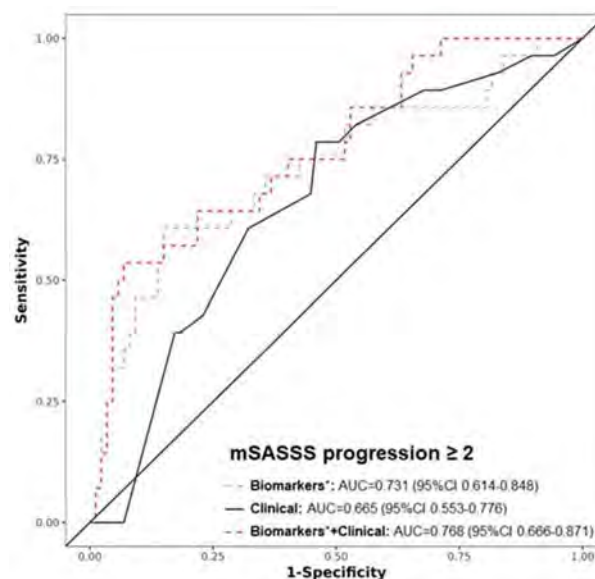
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**Background:** Structural damage in the spine determines the functional status and spinal mobility in axial spondyloarthritis (axSpA). Already present syndesmophytes, elevated C-reactive protein, cigarette smoking, and to a lesser extent male sex are routine clinical parameters predicting radiographic spinal progression. In the last years, several biomarkers with a predictive value for radiographic spinal progression were identified. It is, however, not known, if biomarkers have a meaningful added value over clinical parameters in prediction of radiographic spinal progression in axSpA.

**Objectives:** The objective of the study was to examine whether adding biomarkers to the routine clinical parameters would improve prediction of radiographic spinal progression in axSpA.

**Methods:** Altogether 117 patients with ankylosing spondylitis who completed a 2 year clinical and radiographic follow-up in the ENRADAS trial were included. Radiographic spinal progression was defined as a worsening of the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) by  $\geq 2$  points after 2 years. A clinical prediction model for radiographic spinal progression was constructed out of already present syndesmophytes, elevated CRP, cigarette smoking, and male sex. Serum biomarkers measured at baseline included: matrix metalloproteinase-3, vascular endothelial growth factor (VEGF), calprotectin, leptin, high molecular weight adiponectin (HWM-APN), osteoprotegerin, sclerostin, N-terminal telopeptide, procollagen type II N-terminal propeptide, and serum amyloid A.

**Results:** Repeated cross-validation analyses revealed the following biomarker combination with added predictive value for radiographic progression compared to the clinical model (syndesmophytes, smoking, elevated CRP, and sex): Leptin +HWM-APN+VEGF. A combination of these biomarkers resulted in an Area Under the Curve (AUC) of  $AUC_{\text{Biomarkers}}=0.731$  (95%CI 0.614–0.848), thus numerically superior to the clinical model ( $AUC_{\text{Clinical}}=0.665$  (95%CI 0.553–0.776)). A combination of both models resulted in improvement of the predictive value reflected by the  $AUC_{\text{Clinical+Biomarkers}}=0.768$  (95%CI 0.666–0.871); though this improvement was not statistically significant compared to the clinical model in the permutation test ( $p=0.051$ ). However, when only considering the part of receiver operating characteristic (ROC) curves with a specificity of  $\geq 75\%$ , the improvement becomes statistically significant (partial  $AUC_{\text{Clinical+Biomarkers}}=0.119$  versus partial  $AUC_{\text{Clinical}}=0.053$ ;  $p=0.010$ ).



**Abstract FRI0154 – Figure 1.** ROC curve analyses of biomarker and clinical model alone versus the combined model for the prediction of radiographic spinal progression (mSASSS worsening  $\geq 2$  after 2 years) in ankylosing spondylitis. Area under the curves (AUC) and respective 95% confidence intervals (CI) shown. \*Leptin + HWM-APN + VEGF.



**Conclusions:** Biomarkers are able to improve prediction of radiographic spinal progression in axSpA, especially if used in addition to the clinical parameters, but the added value seems to be rather small.

**Disclosure of Interest:** None declared

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FRI0155

#### GENES REGULATING BONE HOMEOSTASIS ARE DIFFERENTIALLY EXPRESSED AT PERIPHERAL VERSUS AXIAL ENTHELIAL SITES IN AN ANIMAL MODEL OF SPONDYLOARTHRITIS

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**Background:** In spondyloarthritis (SpA), mechanisms of enthesial bone formation are not well understood. Currently, no treatment can reverse this process, although TNF inhibitors may modify bone formation if initiated early. SKG mice exhibit features of SpA with both peripheral joint and axial inflammation after induction by curdlan via the Dectin-1 pathway residing upstream of TNF $\alpha$ , IL-23 and IL-17.

**Objectives:** The goal of this study was to identify genes and pathways that regulate enthesial bone formation. SKG mice were previously reported to develop axial bone formation within 12 weeks of curdlan injection, as well as enthesial bone formation around peripheral joints<sup>1</sup>.

**Methods:** 9 week-old SKG or control BALB/c mice were injected IP with curdlan. Histology and microCT scanning were performed at serial time points. Laser capture microscopy was performed on formalin-fixed paraffin-embedded (FFPE) tissue sections from enthesial sites around the ankle and tail vertebrae 3 weeks after curdlan injection. RNA was extracted using the Qiagen RNeasy FFPE kit and whole transcriptome analysis was performed using Affymetrix gene array MTA 1.0.

**Results:** Inflammation at axial entheses developed earliest at the tail base. Contrary to previous reports, we did not observe axial bone formation, but rather saw significant erosion of vertebral bodies, throughout the spine. The absence of axial bone formation was noted as late as 24 weeks post curdlan. In contrast, exuberant enthesial bone formation occurred around ankles at predictable sites of tendon/ligament insertions into bone. We identified distinct expression of genes involved in bone resorption and formation at ankle when compared to spine enthesial sites. IPA upstream regulator analysis identified significant gene expression of upstream regulators of TGF- $\beta$ , known to recruit early osteoblast precursors to bone (z-value 2.83), and WNT3A, a WNT signalling pathway agonist that promotes osteoblast differentiation and function (z-value 2.54), in the ankle, but not the spine. These findings support the histologic observation of bone formation at ankle, but not spine, enthesial sites. In addition, significant increased gene expression of upstream regulators of the aryl hydrocarbon receptor (AhR) (z-value 2.14) was found at spine, but not ankle, enthesial sites (z-value -1.78). AhR is a ligand-activated transcription factor that is a positive regulator of osteoclastogenesis via c-fos-mediated RANKL signalling.

**Conclusions:** Whole transcriptome analysis revealed increased expression of upstream regulators of genes in anabolic pathways, including WNT3A and TGF- $\beta$ , at ankle enthesial sites where bone formation occurs, but not at spine enthesial sites where bone erosions persist without bone formation. These pathways may thus contribute to peripheral enthesial bone formation. Significantly increased gene expression of upstream regulators of AhR, a positive regulator of osteoclastogenesis, was found at spine enthesial sites. AhR is thus a candidate regulator of continued bone resorption at spine enthesial sites in this murine model of SpA.

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FRI0156

#### AN ANTIMICROBIAL MECHANISM, NETOSIS, IS POTENTIALLY INVOLVED IN ANKYLOSING SPONDYLITIS PATHOGENESIS

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**Background:** Ankylosing spondylitis (AS) is a chronic inflammatory disease, of unknown etiology, that mainly affects the axial skeleton and the sacroiliac joints in the pelvis. Neutrophils are critical actors in innate immunity and their activation has been involved in the progression of AS symptoms. Recently, NETosis has been suggested to play a central role in several pathologic states, including rheumatology diseases. Nevertheless, this process has not been described yet in AS patients

**Objectives:** 1) To evaluate and characterise the presence of NETosis in AS patients. 2) To explore the relationship among NETosis markers and clinical characteristics of this disease

**Methods:** Thirty patients with AS and 32 healthy donors (HD) were included in the study. Disease activity was determined by BASDAI index and CRP and ESR levels; in parallel, inflammatory markers were determined in plasma by ELISA kits. Spinal mobility of AS patients was measured by the BASMI index, and structural damage was calculated by the mSASSS index. *Ex vivo*, spontaneous NETosis generation in purified neutrophils from AS patients and HDs were measured by fluorescence (n=6) and scanning electron (n=3) microscopy after 6 hour of incubation. PMA, known to promote NETosis, was used as positive control. DNA extrusion was analysed by fluorescence microscopy and fluorimetry after SYTOX staining, whereas elastase percentage (NE) was analysed by fluorescence microscopy after staining of neutrophils with NE antibody. *In vivo*, mieloperoxidase (MPO) and NE protein expression were measured by flow cytometry (FACSCalibur), whereas extracellular DNA was examined in plasma using fluorimetry after SYTOX staining

**Results:** Compared to HDs, AS neutrophils showed spontaneous extracellular release of a meshwork of DNA nuclear and granule proteins (NETs), as demonstrated by fluorescence microscopy, fluorimetry, and scanning electron microscopy. Indeed, analysis of DNA fibres staining by SYTOX revealed that NETosis rate was above baseline levels after 6 hour of *ex vivo* AS neutrophil incubation as compared to those from HDs (p<0.05). Furthermore, higher cell free-DNA levels were observed between AS patients and HDs at 6 hour (p<0.05). Increased spontaneous NETs production in this pathology was additionally corroborated by the observation of an enhanced percentage of NE-staining cells after 6 hour of incubation (p<0.05). *In vivo*, higher intracellular NE levels (p=0.036), and plasma DNA concentrations (p=0.021) were also found in AS patients as compared to HDs. Correlation studies showed that plasma DNA levels positively correlated with inflammatory markers (i.e. CRP, ESR and TNF $\alpha$ ), and with the spinal mobility index BASMI. In addition, a positive correlation was found between intracellular NE levels and plasma IL-1 $\beta$  concentration

**Conclusions:** 1) NETosis is increased in AS patients. 2) Raised NETosis in AS is associated with several markers of inflammation and mobility. Thus, NETosis might act as a key mediator in the etiopathogenesis of AS. Funded by JA PI-0314-2012, SER, ISCIII (RIER RD16/0012/0015)

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FRI0157

#### ALTERED EXPRESSION OF THE SPLICEOSOME COMPONENTS IN LEUKOCYTES SUBSETS FROM PATIENTS WITH ANKYLOSING SPONDYLITIS: ASSOCIATION TO DISEASE PATHOGENESIS AND THERAPEUTIC RESPONSE

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**Background:** Ankylosing spondylitis (AS) is a chronic inflammatory disease for which the etiopathogenesis has not yet been fully clarified. Splicing is a post-

transcriptional process involved in the RNA maturation. Recent studies have revealed that a pathological deregulation of the spliceosome is associated to several human diseases. Yet, the spliceosome alterations and their modulation in therapeutic response have not been described in AS

**Objectives:** 1) To evaluate the potential deregulation of the spliceosome in AS leukocytes and their involvement in the disease pathophysiology. 2) To analyse the *in vivo* effects of anti-TNF drugs on the spliceosome components of AS leukocytes

**Methods:** Thirty two AS patients and 29 healthy donors (HDs) were included in a cross-sectional study. Eight AS patients were selected for a three-month longitudinal study of response to anti-TNF $\alpha$  therapy. Disease activity was determined by BASDAI index and, CRP and ESR levels. Physical function was measured by the BASFI index, spinal mobility by the BASMI index, and structural damage by the mSASSS. The expression of selected components of the major-(n=12) and minor-spliceosome (n=4), and splicing factors (n=28) was evaluated in purified leukocyte by Fluidigm methodology; in parallel, inflammatory marker expression was determined by RT-PCR

**Results:** Compared to HDs, a significant deregulation in the expression of splicing factors and spliceosome components was found in lymphocytes, monocytes and neutrophils from AS patients, being neutrophils which displayed the highest number of altered molecules. Interestingly, a specific altered profile of spliceosome members was observed when compared lymphocytes (U1, U4, U5, SRSF6), monocytes (CELF4, ESRP2, RBM3, SRSF3, TIA1) and neutrophils (FBP11, SF3BTV1, U6, U12, PTB, RBM17, MAGOH, SRSF5, SRSF10). Correlation studies revealed that inflammatory profile, disease activity (CRP, ESR, BASDAI) and structural damage (BASMI, mSASSS) were associated to the alteration of a vast number of spliceosome components in all the leukocyte subsets evaluated. In addition, the BASFI index correlated with the expression of SKIP and U6atac in neutrophils.

Anti-TNF $\alpha$  treatment of selected AS patients reversed the altered expression of several spliceosome components and splicing factors in PBMCs (UA2F2, nSR100) and neutrophils (ESRP1, NOVA1, SND1, SRM160, SRSF1, CUGBP). Association studies demonstrated that disease remission was associated with reversing the altered expression of a high number of the spliceosome molecules

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- [2] Anti-TNF $\alpha$  therapy may reverse, at least partially, the altered expression of several spliceosome components and splicing factors. Alteration of the spliceosome may provide new biomarkers for disease and therapeutic response in AS. Funded:JA PI-0139–2017, ISCIII (RIER RD16/0012/0015)

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#### FRI0158 PROSTAGLANDIN E2 AND ITS RECEPTOR SUBTYPE EP4 ARE INVOLVED IN ANKYLOSING SPONDYLITIS DISEASE PROGRESSION

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**Background:** Single Nucleotide Polymorphisms (SNPs) in PTGER4 were found to be associated with Ankylosing spondylitis (AS) in GWAS. PTGER4 codes for the prostaglandin-E2 receptor EP4. PGE2/EP4 interaction can affect bone formation and inflammation.

**Objectives:** We studied serum PGE2 levels and SNPs in PTGER4 in relation to spinal fusion in AS patients. We also evaluated the interaction of smoking, PGE2 and EP4 in driving IL23 production and ILC3 functions.

**Methods:** Patients diagnosed with AS using the modified New York criteria and followed prospectively using a standardised protocol, were included in this study. Biological samples including serum, gut, synovial and bone marrow (BM) samples, DNA and RNA were stored and radiographs of the spine obtained every two years to assess progression. ELISA for Serum PGE2 and immunohistochemistry tissue expression of PTGS1, EP4 and pCREB were performed. Radiographs were scored by mSASSS. Patients with an increase of  $\geq 1$  mSASSS unit/year on follow up were deemed progressors. Five PTGER4 SNPs, associated with AS or related diseases, call rate above 90%, MAF >0.1 and not in LD above 0.8, were studied. Immune cell subsets from PBMCs were analysed for surface expression of the EP4 receptor. Additionally, PBMCs were incubated with nicotine, PGE2, or EP4 agonist to evaluate changes in ILC3 percentages and to determine cytokine expression by flow cytometry and RT-PCR.

**Results:** Serum PGE2 levels were significantly higher in AS progressors (n=88) than in non-progressors (n=101) (p<0.001). In multivariable regression analysis, there was significantly more progression in patients with higher baseline mSASSS

(B=0.02; p=0.01) and serum PGE2 (B=0.001; p=0.002), but lower progression with longer TNF inhibitor use (B=-0.01; p=0.03). There was a trend towards higher progression with higher baseline ESR (B=0.012; p=0.08). 3). A total of 172 AS patients had DNA and X-ray data for analysis. Patients with CC genotype of PTGER4 SNP rs6896969 were significantly more likely to progress compared to AA/AC (OR: 2.45, 95% CI: 1.3 to 4.6; p=0.006). Progressors tended to more likely be homozygous for the major allele G of the rs4957341 SNP (OR 2.1; 25% CI: 0.98–4.35; p=0.058). Increased expression of EP4, PTGS1 and pCREB were observed in the gut, BM and synovial samples of AS patients. EP4 expression was upregulated in circulating AS monocytes and ILC3, especially smokers, and the percentage of EP4<sup>+</sup> monocytes and ILC3 correlated with the BASDAI. Sorted EP4<sup>+</sup>CD14<sup>+</sup> cells showed a higher expression of CREB and IL-23 and *in vitro* stimulation of monocytes with PGE2 increased IL-23 expression, demonstrating the functional relevance of EP4 expression on monocytes. The expression of EP4 is dependent on the transcription factor AP-2a (TFAP-2a). *In vitro* stimulation of monocytes with nicotine induced a significant monocyte over-expression of EP4 and TFAP-2a. Finally, PGE2 stimulation of isolated PBMC from AS patients significantly expanded IL-23-producing ILC3.

**Conclusions:** PGE2 and its receptor EP4 are significant players in AS driving both inflammation and spinal fusion. The complex interaction of smoking, prostaglandin pathway upregulation and IL-23 dependent innate immune activation can contribute to the pathogenesis of AS

**Disclosure of Interest:** None declared

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#### FRI0159 ANTIBODIES TO POST-TRANSLATIONALLY MODIFIED COLLAGEN II IN SPONDYLOARTHRITIS

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**Background:** Spondyloarthritis (SpA) are a group of rheumatic diseases with either predominantly axial inflammatory symptoms of the spine and sacroiliac joints, or predominantly peripheral arthritis. The most common axial SpA (axSpA) are non-radiographic axSpA and in particular ankylosing spondylitis. The current gold standard diagnostic criteria for axSpA are clinical symptoms, radiology, MRI or ultrasound according to Assessment of SpondyloArthritis international Society (ASAS) criteria.<sup>1</sup> We have previously showed that antibodies to oxidative post-translationally modified collagen type II (oxPTM-CII) are present and specific in RA patients whether ACPA positive or negative.<sup>2</sup>

**Objectives:** The aim of the current study was to test the presence of antibody to oxidised collagen type II (CII) in axSpA, based on the hypothesis that spinal inflammation in axial SpA results in oxidative posttranslational modification (oxPTM) of axial joints cartilage matrix proteins such as CII with the consequently formation of neoepitopes and a secondary humoral autoimmune response.

**Methods:** CII was oxidised by exposing CII to ribose and hypochlorous acid. Levels of antibodies specific to native CII and CII post-translationally modified by oxidants (oxPTM-CII) was assessed by enzyme-linked immunosorbent assays (ELISA) in serum samples obtained from patients with axSpA (n=67) in remission and axSpA patients (n=14) non in remission. Reactivity in axSpA was compared to reactivity in samples from patients with predominantly peripheral arthritis such as psoriatic arthritis (PsA, n=54), undifferentiated arthritis (UA, n=49) and early rheumatoid arthritis (ERA, n=60). As a control we used fibromyalgia (FM, n=19) and healthy subjects (HC, n=70). The specificity of the binding was further assessed by competitive ELISA and western blot.

**Results:** Stronger binding to oxPTM-CII was observed in serum samples from axSpA patients, the positivity was 72% for patients in remission and 86% for patients not in remission (86%) compare to positivity in PsA group (33%), UA group (35%) and FM group (16%), (p<0.0001). Interestingly, binding of axSpA samples was similar to binding of serum samples from ERA (95%). Binding to ROS-CII was directed to a range of ROS-CII fragments between 25 and 150 kDa.

**Conclusions:** Formation of oxPTM-CII neoantigens in the inflamed axial joints results in an immune response that elicits antibodies specific to oxPTM-CII. Once established in future studies, antibodies to oxPTM-CII may be developed as potential biomarker for axSpA.

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### FRI0160 INTERLEUKIN-17A INDUCES INFLAMMATORY RESPONSE VIA NLRP3 INFLAMMASOME IN ANKYLOSING SPONDYLITIS

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**Background:** Inflammasomes are cytoplasmic multiprotein complexes that recognise various exogenous and endogenous danger signals in myeloid cells, particularly macrophages. Inflammasome activation eventually induces inflammatory responses in macrophages by activating gasdermin-d-mediated pyroptosis and the secretion of pro-inflammatory cytokines including interleukin (IL)-1 $\beta$  and IL-18 in a caspase-1-dependent manner. The production of IL-1 has been found to be highly induced in AS<sup>1</sup> and caspase-1 level was significantly elevated in spondyloarthritis patients than in those with other arthritic diseases,<sup>2</sup> suggesting the possibility that inflammasomes might be involved in pathogenesis of ankylosing spondylitis (AS). However, few studies have addressed the roles of inflammasomes in AS.

**Objectives:** This study was performed to investigate the role of NOD-like receptor family, pyrin domain containing 3 (NLRP3) inflammasome in the peripheral blood mononuclear cells (PBMCs) from AS patients.

**Methods:** PBMCs from 11 patients and 9 healthy controls were isolated and mRNA expression levels of NLRP3 inflammasome, pro-IL-1 $\beta$ , IL-1 $\beta$ , pro-caspase-1, and caspase-1 were determined using quantitative real-time PCR. IL-17A (100 ng/mL) was added to the cell cultures, then, cytokine expression, signalling pathways, and inflammasome machinery are determined using real-time RT-PCR and Western blot. After transfection of siNLRP3 to AS PBMCs, mRNA and proteins levels of IL-1 $\beta$  and caspase-1 were determined using real time PCR and western blot.

**Results:** Expressions of NLRP3, IL-1 $\beta$ , and caspase-1 mRNAs, but not IL-18, were increased in PBMCs from AS patients compared to controls. Incubation of AS PBMCs with IL-17A significantly increased NLRP3, IL-1 $\beta$ , IL-18, and caspase-1 expressions in AS PBMCs. Western blot showed IL-17A treatment induced the phosphorylation of Akt, p38 MAPK, and NF- $\kappa$ B p65 in AS PBMCs. Down-regulation of NLRP3 by transfection of siRNA decreased mRNA expressions and productions of IL-1 $\beta$  and caspase-1 in AS PBMCs.

**Conclusions:** Activity of NLRP3 inflammasome was increased in AS patients and IL-17A potentiated the activation of NLRP3 inflammasome. Our data suggest the possible role of NLRP3 inflammasome in inflammatory response in AS.

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### FRI0161 ROLE OF GITR/GITRL IN MODULATING TH9 RESPONSE IN PSORIATIC ARTHRITIS

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**Background:** GITR/GITRL interaction is pivotal in regulating the activity of Treg and Th9 effector cells.<sup>1</sup> Psoriatic arthritis (PsA) is a chronic inflammatory disease characterised by a strong expression of IL-9 and Th9 polarisation in the inflamed gut, synovial tissues and peripheral blood.<sup>2</sup> Factors involved in the regulation of Th9 responses in PsA have been not yet investigated.

**Objectives:** Aim of the study: to investigate the role of GITR/GITRL in PsA.

**Methods:** GITR, GITRL expression were assessed by rt-PCR and immunohistochemistry in synovial biopsies, gut specimens and bone marrow of PsA patients and healthy controls (HC). The co-localization of CD4 and GITR was analysed by immunofluorescence. The expression of GITR was also assessed by flow cytometry analysis in isolated PBMC of patients and controls (Tregs, CD4 and CD8).

Peripheral and intestinal IL-9 producing cell (Th9) percentages and cytotoxic activity of T lymphocytes were also studied by flow cytometry analysis *ex vivo* and after *in vitro* stimulation with GITRL. A mouse model of induced arthritis (collagen induced arthritis, CIA) was used to study GITR/GITRL axis and the effect of anti-GITRL blocking agent.

**Results:** Increased GITR and GITRL expression was observed in the inflamed gut and synovial samples of PsA patients. Analysis of GITR expression among PBMC and LPMC from PsA patients demonstrated its down-regulation among Tregs and upregulation on effector CD4<sup>+</sup> and CD8<sup>+</sup>T cells. In *in vitro* studies, GITR co-stimulation potently induced Th9 activation and IL-9 production. In particular, GITR ligation subverted the induction of Foxp3(+) Tregs, directing the activated CD4(+) T cells to a Th9 phenotype and enhancing the function of DCs and cytotoxic T lymphocytes. Moreover, in a murine model of CIA massive expression of IL-9 and GITR was observed in the synovial tissues and anti-GITR therapy significantly ameliorated arthritis score.

**Conclusions:** We demonstrated that GITR/GITRL axis modulates IL-9/Th9 responses in PsA, representing GITR activation a relevant upstream pathway involved in Th9 polarisation. A novel mechanism by which GITR agonist exert an inflammatory response was also demonstrated in PsA indicating GITR blocking agents as possible therapy in PsA.

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### FRI0162 THE LINK BETWEEN ANGIOGENESIS AND OSTEOGENESIS IN SPONDYLOARTHRITIS

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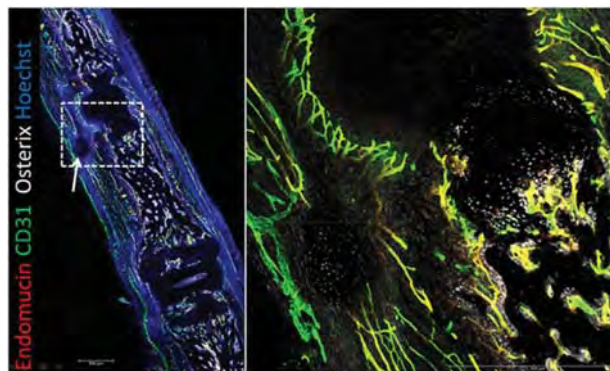
**Background:** Spondyloarthritis is characterised by inflammation, extensive angiogenesis and pathological osteogenesis. Transmembrane (tm)TNF transgenic (tg) mice<sup>1</sup> that overexpress tmTNF exhibit features of SpA, including chronic inflammation and pathological osteogenesis. tmTNF ligation to TNF receptor 2 in endothelial cells (ECs) can induce signal transduction pathways, that may promote these processes. Of note, angiogenesis and osteogenesis are coupled by EC differentiation towards a type H (CD31<sup>hi</sup>endomucin<sup>hi</sup>) phenotype.<sup>2</sup>

**Objectives:** To investigate the link between pathological angiogenesis and osteogenesis in tmTNF tg mice.

**Methods:** Vertebrae and ankles from 6 and 12 weeks and 8 months old tmTNF tg mice or sex-matched non-tg littermates (n=18) were prepared by cutting 60  $\mu$ m thick cryosections for confocal imaging.

**Results:** tmTNF tg mice exhibited ectopic osteogenesis which was not observed in non-tg littermates. The provided image demonstrates an ectopic lesion at the white arrow. Immunostainings showed that type H vessels are in the vicinity of the ectopic osteogenesis and osterix<sup>+</sup> osteoprogenitors. At six weeks of age, osterix<sup>+</sup> cells are located throughout the ectopic lesion, while at eight months, osterix<sup>+</sup> cells are only present at the border of the lesion. Furthermore, there is increased osteogenesis and a different vessel architecture within the vertebrae of tmTNF tg mice compared to non-tg littermates that progresses with age. Non-tg littermate vertebrae only have physiological osteogenesis, which is in the metaphysis and periosteum. In addition, tmTNF tg mice also exhibit altered bone marrow (BM) architecture containing extensive lymphoid aggregates, which predominantly consisted of B220<sup>+</sup> B cells.





**Abstract FRI0162 – Figure 1.** Type H vessel association with ectopic bone formation in 6-week-old murine vertebra. Left panel: Confocal tile scan of tmTNF tg vertebrae showing endomucin\* (red), which labels all vessels except arteries, and CD31\* (green) endothelial cells. Osterix (white) labels osteoprogenitors and nuclei are labelled by Hoechst (blue). Right panel: Higher magnification of osterix\* osteoprogenitors at ectopic location. Osterix\* cells are found around type H (CD31<sup>hi</sup>endomucin<sup>hi</sup>) vessels.

**Conclusions:** tmTNF overexpression in mice leads to development of type H vessels associated with ectopic osteogenesis. In addition, extensive lymphoid aggregates develop in the BM. Current studies are aimed at identification of signalling pathways in ECs that contribute to these processes.

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#### FRI0163 DEVELOPMENT OF A PRECLINICAL TESTING PIPELINE FOR A NOVEL TRANSMEMBRANE TNF-DRIVEN SPONDYLOARTHRITIS MODEL

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**Background:** Spondyloarthritis (SpA) is a complex disease characterised by chronic inflammation, bone erosion and pathological new bone formation. The TgA86 transmembrane TNF (tmTNF) transgenic mouse is a unique model of SpA, developing spontaneously and with 100% incidence early progressive SpA characterised by peripheral inflammatory arthritis and axial ankylosing spondylitis with cardiovascular involvement. This closely recapitulates the pathological findings and comorbid conditions described in human patients.

**Objectives:** To characterise in greater detail the development and progression of the TgA86 pathology and its similarities to human disease and to standardise reliable preclinical protocols and specific readouts for the assessment of the efficacy of human therapeutics.

**Methods:** TgA86 peripheral and axial pathology was assessed at different time points from 2.5 to 28 weeks of age. Disease severity was evaluated using clinical parameters and histopathological analysis of ankle and sacroiliac joints, lumbar and caudal vertebrae, as well as whole mount skeletal staining. Clinical and histopathological readouts were used to assess the therapeutic effect of Etanercept that was administered thrice weekly at 30 mg/Kg starting either from 2.5–5 weeks of age (prophylactic protocol) or from 9 weeks of age (therapeutic protocol).

**Results:** Clinical pathology in TgA86 mice appears already from 2.5 weeks of age, with signs of paw swelling, digit deformation and tail crinkling, while by 9 weeks of age pathology is fully established, with severe peripheral arthritis and tail and spine ankylosis. Pathology progression was also evident histopathologically, characterised by the originally described features of progressive inflammation, cartilage destruction and bone erosion observed in sacroiliac and ankle joints as well as in lumbar and caudal vertebra. Additionally, new pathology features were detected by identifying signs of enthesitis, new bone formation appearing as

cartilaginous structures at the edges of vertebrae endplates, presence of red bone marrow during all stages of disease progression as well as signs of intervertebral disc (IVD) degeneration. Prophylactic treatment with Etanercept ameliorated effectively all clinical and histopathological features of the peripheral and axial pathology. Therapeutic treatment while affecting only minimally the clinical signs of both peripheral and axial pathology, it was found to reduce the peripheral arthritis histopathological score by at least 50%. Finally, treatment with Etanercept was also efficient in ameliorating the comorbid heart valve pathology observed in these animals.

**Conclusions:** We have shown that TgA86 pathology includes features of sacroiliitis, enthesitis, new bone formation, persisting red bone marrow and intervertebral disk degeneration, further strengthening the similarities of this model to human pathology. Based on the assessment of all pathology features during prophylactic anti-TNF treatment we suggest that early on in disease there may be a therapeutic window during which optimal treatment of the pathology can be achieved.

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**Disclosure of Interest:** None declared

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#### FRI0164 ANTI-PFDN5 ANTIBODY AS A BIOMARKER FOR UVEITIS IN ANKYLOSING SPONDYLITIS

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**Background:** Noninfectious uveitis is the most common extra-articular manifestation of ankylosing spondylitis (AS). However, molecules related to the disease pathogenesis have yet to be identified, and no biomarkers are available for uveitis in AS.

**Objectives:** We aimed to identify the biomarkers for uveitis in AS, and elucidate the possible pathogenesis of uveitis in AS associated with the identified biomarkers.

**Methods:** Protein microarray using ProtoArray was performed to profile autoantibodies present in sera from patients with various autoimmune diseases, including eight AS patients with uveitis. The autoantibodies with higher reactivity in AS patients with uveitis compared with other patients were selected, and the levels of autoantibodies were measured using ELISA in the sera from AS patients with (n=32) or without uveitis history (n=32), patients with rheumatoid arthritis (n=20) and from healthy individuals (n=12). To evaluate the involvement of target antigen in pathogenesis of spondyloarthritis-related uveitis, we conducted an *in vivo* study using curdlan-induced SKG mice, which spontaneously develops arthritis as well as uveitis, and an *in vitro* study using retinal pigment epithelium cell-line (RPE19).

**Results:** 4 antibodies (Abs) were selected as a candidate for biomarker (anti-PFDN5, area under curve [AUC]=1.00; anti-serine threonine protein kinase 24 Ab, AUC=0.906; anti-odontogenic ameloblast associated protein Ab, AUC=0.859; anti-protocadherin alpha C2 Ab, AUC=0.859). In ELISA, anti-PFDN5 Abs was significantly elevated in AS patients with uveitis compared to AS patients without uveitis. Ocular histology showed that compared to PBS-treated SKG mice, SKG mice with uveitis had strong expression of PFDN5 in iris, ciliary body, and retina. PERK and pelf2 $\alpha$ , which are ER stress related proteins, were downregulated in PFDN5 siRNA-treated RPE19 cells in tunicamycin-induced condition, suggesting that PFDN5 enhances ER stress via PERK and pelf2 $\alpha$  pathway.

**Conclusions:** We identified anti-PFDN5 antibody as a putative biomarker for uveitis in AS. PFDN5 was increased in ocular lesion, which may be associated with disease pathogenesis.

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FRI0165

### MICRORNAS DYSREGULATION IN MONOCYTES AND CD4 LYMPHOCYTES FROM PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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**Background:** MicroRNAs have been shown to play a crucial role during innate or adaptive immune response. Dysregulation of miRNAs has been described in several autoimmune or rheumatic diseases including rheumatoid arthritis, inflammatory bowel disease or psoriasis. In spondyloarthritis (SpA), only few studies on miR expression have been reported with highly diverse methodologies and involving small samples of patients.

**Objectives:** Because T CD4 lymphocytes and monocytes are important cells in SpA pathophysiology, we wanted to assess the miR expression profile in these two cell types sorted from axial SpA (AxSpA) patients.

**Methods:** Eighty one AxSpA patients were included in this study. Among these patients, 74 fulfilled the ASAS classification criteria (imaging arm) with sacro-iliitis on X-rays (n=56) or objective signs of inflammation on MRI (n=18). Two independent cohorts of 22 and 59 SpA patients were compared to 17 and 38 age and sex-matched controls. Both SpA patients and controls were recruited from October 2014 to July 2017 in the department of rheumatology at Cochin Hospital in Paris, France. All SpA patients had an active disease despite NSAIDs intake (mean BASDAI score of 49±19 and mean ASDAS score of 3±0.9), were free of any biological treatment and were eligible for a TNF-blocker treatment. Seventy-seven percent were HLA-B27 positive. T lymphocytes and monocytes were isolated from PBMC by direct isolation with magnetic microbeads (CD4 +and CD14+). Three-hundred seventy two miRs were screened by q-RT-PCR on the exploratory cohort and only MiRs showing a significant differential expression in the first cohort were analysed in the validation cohort. An unpaired T-test was used for comparison of miR expression level.

**Results:** In the exploratory cohort, 51 (CD14+) and 70 miRs (CD4+) were found to be differentially expressed between patients and controls. Among these, 15 miRs (in CD14+), and 12 miRs (in CD4+) were also found dysregulated in the validation cohort. These validated miRNAs were found to play a key role in physiological pathways such as NFkB or TGFb, Wnt signalling and monocyte differentiation that have been involved in the pathophysiology of the disease. Neither clinical subphenotypes nor biological parameters were associated with different profiles of miR expression after adjusting for multiple tests. We found a negative correlation between miR-146a-5p level and BASDAI (r=-0.28, p=0.011) and ASDAS (r=-0.38, p=5.9 10<sup>-4</sup>) in monocytes.

**Conclusions:** We found a dysregulation of miR expression in monocytes and T CD4 lymphocytes from patients with axial spondyloarthritis, whose consequences could contribute to the pathophysiology of the disease and be of interest for therapeutic perspective. Moreover, identifying biomarkers with the potential of diagnostic signature should help the clinician in daily practice.

**Disclosure of Interest:** None declared

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FRI0168

### PHENOTYPIC, FUNCTIONAL AND MOLECULAR CHARACTERISATION OF IL-17+CD8+ T CELLS IN HUMAN HEALTH AND PSORIATIC ARTHRITIS

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**Background:** Psoriatic arthritis (PsA) is a spondyloarthritis affecting the joint and skin. The genetic association with HLA Class I and the clinical efficacy of IL-17A inhibitors in the treatment of PsA suggest a potential role for IL-17 +CD8+T cells in PsA pathogenesis. This concept is supported by our previous data showing that IL-17 +CD8+T cell frequencies are increased in the synovial fluid (SF) vs the peripheral blood (PB) of patients with PsA<sup>1</sup>. We hypothesise that IL-17 +CD8+T cells are pro-inflammatory contributors to PsA pathogenesis.

**Objectives:** To perform molecular, phenotypic and functional characterisation of IL-17 +CD8+T cells.

**Methods:** Healthy donor PB CD8 +T cells were cultured for 3 days with anti-CD3/CD28 mAb, IL-1β and IL-23 to induce IL-17 +CD8+T cells *in vitro*, whilst PB and SF mononuclear cells were isolated from patients with PsA and stimulated *ex vivo* with PMA/ionomycin. Cytokine secretion assays were used to sort IL-17 +CD8+T cells, from which RNA was extracted for RNA-sequencing of PsA PB and SF cytokine-secreting T cells. 24 hour supernatants were generated from cultured sorted cells for cytokine analysis (Luminex) or culture with fibroblasts (IL-6 and IL-8 secretion measured by ELISA).

**Results :** *In vitro*-generated IL-17 +CD8+T cells produced significant levels of IL-17A, IL-17F, IFN-γ, TNF-α, IL-22 and GM-CSF (10–9000 pg/ml range), but little IL-10. Flow cytometry showed that *in vitro*-generated IL-17 +CD8+T cells co-expressed IFN-γ (median 80%), TNF-α (40%) and GM-CSF (35%) at comparable frequencies to *ex vivo* PsA synovial IL-17 +CD8+T cells (70%, 50%, 55% respectively). Whilst only 5% of PsA SF IL-17 +CD8+T cells co-expressed the MAIT cell marker Vα7.2, 50% of *in vitro*-generated IL-17 +CD8+T cells co-expressed Vα7.2. The cytokine profile of *in vitro*-generated Vα7.2+and Vα7.2- IL-17 +CD8+T cell supernatants was however comparable, sharing the cytokine profile of total IL-17 +CD8+T cells. Functionally, *in vitro*-generated sorted IL-17 +CD8+T cell culture supernatants enhanced IL-6 and IL-8 production by synovial tissue fibroblasts from patients with PsA compared to IL-17- counterparts, thus exhibiting pro-inflammatory capacity; we will also determine if this response is IL-17 and/or TNF-mediated. Additionally, the majority of synovial IL-17 +CD8+T cells co-expressed cytotoxic molecule Granzyme B, which may contribute to PsA pathogenesis. Finally, RNA-sequencing revealed that IL-17 +CD8+T cells from PsA synovial fluid displayed a distinct transcriptomic signature compared to PB IL-17 +CD8+T cells as well as to synovial Th17 or Tc1 cells.

**Conclusions :** *In vitro*-generated and *ex vivo*-derived synovial IL-17 +CD8+T cells display a type 17 profile, as evidenced by flow cytometry and Luminex. In contrast to *ex vivo* PsA synovial IL-17 +CD8+T cells, 50% of *in vitro* IL-17 +CD8 +T cells co-express Vα7.2; however, both Vα7.2+and Vα7.2- subsets share a similar cytokine profile. Functionally, IL-17 +CD8+T cells exhibit pro-inflammatory potential, upregulating IL-6 and IL-8 production via fibroblasts. Analysis of our RNA-sequencing data will further reveal the molecular profile of human IL-17 +CD8+T cells, and how they may contribute to joint inflammation in PsA.

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### Spondyloarthritis – clinical aspects (other than treatment)

FRI0169

### FIRST VALIDATION OF CONSENSUS DEFINITIONS FOR MRI LESIONS IN THE SACROILIAC JOINT BY THE ASSESSMENTS IN SPONDYLOARTHRITIS INTERNATIONAL SOCIETY (ASAS) MRI GROUP

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**Background:** The diversity of MRI lesions in the sacroiliac joints of patients with axial spondyloarthritis (axSpA) has only recently been appreciated and consistent terminology, descriptions, and definitions have not yet been internationally accepted. The ASAS MRI group has generated updated consensus lesion definitions (ASAS\_MRI\_def<sup>®</sup>) and these now require validation in multi-reader exercises to support widespread adoption for clinical practice and research.

**Objectives:** To assess the reliability of detection of active and structural lesions as defined by (ASAS\_MRI\_def<sup>®</sup>) on MRI images from the ASAS Classification Cohort (ASAS-CC) in a multireader ASAS exercise.

**Methods:** ASAS\_MRI\_def<sup>®</sup> were recorded in an eCRF that comprises global assessment (lesion present/absent) and detailed scoring (SPARCC SIJ inflammation, SPARCC SIJ structural). MRI images were available in a variety of formats (DICOM (n=175), JPEG(n=71), DICOM film(n=32)) and sequences, axial and semicoronal orientations, from 278 of the 495 cases who had MRI performed in the ASAS-CC. Image quality was considered sufficient to record global data by 6 central readers in all cases. An additional reader assessed only images in DICOM format (n=175). Detailed SPARCC scoring data was based only on assessment of images in DICOM format. Detection of lesions assessed as



present/absent by global assessment was analysed using kappa. Reliability of detailed scoring was analysed by intraclass correlation coefficient (ICC).

**Results:** Reliability of detection of active and structural lesions was comparable and somewhat better when DICOM images were evaluated (table 1). The most frequently detected active lesion, subchondral inflammation, was detected to a comparable degree of reliability as the most frequently detected structural lesion, erosion. Fat metaplasia in the joint space (backfill) and ankylosis were also reliably detected despite low frequency of occurrence in this cohort. Mean ICC for detailed scores were BME-0.84, Erosion-0.55, Fatty lesion (any)-0.61, Fatty lesion (>1 cm depth)-0.55, Sclerosis-0.73, Fat metaplasia in joint space-0.36, Ankylosis-0.97, Bone bud-0.07.

**Abstract FRI0169 – Table 1.** Kappa values for detection of MRI lesions in the SIJ of patients in the ASAS-CC

	*Based on all images (n=278).	**Based on DICOM images (n=175).
	Mean of all reader pairs (95% CI)*	Mean of all reader pairs (95% CI)**
Active lesions typical of axSpA	0.73 (0.64-0.81)	0.70 (0.58-0.82)
Active lesions typical of axSpA (confidence ≥3) (1-4 scale)	0.77 (0.69-0.86)	0.80 (0.69-0.92)
ASAS positive MRI	0.74 (0.65-0.82)	0.73 (0.61-0.84)
ASAS positive MRI (confidence ≥3) (1-4 scale)	0.76 (0.67-0.85)	0.79 (0.67-0.90)
Structural lesions typical of axSpA	0.64 (0.53-0.74)	0.71 (0.59-0.83)
Structural lesions typical of axSpA (confidence ≥3) (1-4 scale)	0.61 (0.49-0.74)	0.75 (0.62-0.88)
Subchondral inflammation	0.66 (0.57-0.75)	0.60 (0.49-0.72)
Inflammation in Erosion cavity	0.29 (0.11-0.47)	0.37 (0.15-0.58)
Capsulitis	0.37 (0.12-0.62)	0.55 (0.18-0.90)
Joint fluid	0.35 (0.21-0.50)	0.41 (0.23-0.59)
Enthesitis	0.21 (0.04-0.39)	0.23 (0.03-0.45)
Sclerosis	0.42 (0.30-0.55)	0.48 (0.33-0.63)
Erosion	0.59 (0.47-0.70)	0.61 (0.47-0.75)
Fatty lesion (any)	0.61 (0.50-0.73)	0.61 (0.46-0.76)
Fatty lesion >1cm	0.57 (0.41-0.73)	0.66 (0.47-0.84)
Fat metaplasia in joint space	0.47 (0.27-0.67)	0.50 (0.26-0.74)
Bone bud	0.14 (-0.03-0.31)	0.11 (-0.06-0.29)
Ankylosis	0.54 (0.22-0.86)	0.58 (0.25-0.89)

\*Based on all images (n=278); \*\*Based on DICOM images (n=175)

**Conclusions:** The reliability of the ASAS\_MRI\_def<sup>1</sup> was substantial for the most frequently detected lesions.

**Disclosure of Interest:** None declared

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## FRI0170 CONSENSUS DEFINITIONS FOR MRI LESIONS IN THE SACROILIAC JOINTS OF PATIENTS WITH AXIAL SPONDYLOARTHRITIS: FIRST ANALYSIS FROM THE ASSESSMENTS IN SPONDYLOARTHRITIS INTERNATIONAL SOCIETY (ASAS) CLASSIFICATION COHORT

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**Background:** A broad spectrum of MRI lesions has been described in the sacroiliac joint (SIJ) of patients with axial spondyloarthritis and a recent consensus from the ASAS MRI group has culminated in updated lesion definitions (ASAS\_MRI\_def<sup>1</sup>). There has been no central reader evaluation of MRI scans from the ASAS Classification Cohort (ASAS-CC)<sup>1</sup> to determine the spectrum of MRI lesions in the SIJ in this cohort, to compare the frequencies of different lesion types, and to compare detection of lesions between central and ASAS-CC local site readers

**Objectives:** To determine the spectrum and compare the frequencies of active and structural lesions on MRI images from the ASAS-CC according to the consensus ASAS\_MRI\_def<sup>1</sup> update.

**Methods:** ASAS\_MRI\_def<sup>1</sup> were recorded in an eCRF that comprises global assessment (lesion present/absent) and detailed scoring (SPARCC SIJ inflammation, SPARCC SIJ structural). For global assessment, wording of lesions defining active and structural lesions typical of axSpA was the same as in the original ASAS-CC eCRF permitting comparisons between central and local site readers. MRI images were available in a variety of formats (DICOM (n=175), JPEG(n=71), DICOM film(n=32)) and sequences, axial and semicoronal orientations, from 278 of the 495 cases who had MRI performed in the ASAS-CC. Image quality was considered sufficient to record global data by 6 central readers in all cases. An additional reader assessed only images in DICOM format (n=175). Detailed SPARCC scoring data was based only on assessment of images in DICOM format. Comparison of active and structural lesion frequencies was assessed descriptively according to individual and majority of central readers data. Detection of active

lesions typical of axSpA in all available images from the ASAS-CC was compared between central and local readers.

**Results:** The percentage of cases with active lesions typical of axSpA recorded by central readers (28.4% by majority read) was lower than the 40% reported by local site readers in the ASAS-CC (table 1). This was similar to the frequency of structural lesions typical of axSpA (28.6% by majority read) (table 2). 11.2% had subchondral inflammation but not active lesions typical of axSpA but only 0.3% had active lesions typical of axSpA without subchondral inflammation. Erosion was the most frequently observed structural lesion (25.2%) followed by fatty lesion (19.8%). Results were very similar when only data from the 175 DICOM cases was analysed.

**Abstract FRI0170 – Table 1.** Frequencies of active MRI lesions in the SIJ in the ASAS-CC

Variable	Mean% (Range) of cases*	Number (%) of cases*
Active lesions typical of axSpA	31.5 (24.5-38.5)	79 (28.4%)
Active lesions typical of axSpA and level of confidence ≥3 (scale of 1-4)	22.4 (18.0-27.3)	58 (20.9%)
Active lesions typical of axSpA and meets ASAS definition for positive MRI	30.0 (22.6-37.4)	71 (25.5%)
Meets ASAS definition for positive MRI and level of confidence ≥3 (scale of 1-4)	23.1 (18.3-30.2)	58 (20.9%)
Subchondral inflammation	43.5 (38.5-51.1)	110 (39.6%)
Site of erosion cavity inflammation	8.9 (5.8-12.6)	10 (3.6%)
Capsulitis	4.0 (1.8-7.2)	6 (2.2%)
Joint Fluid	14.1 (6.8-20.5)	11 (4.0%)
Enthesitis	7.5 (1.8-12.2)	6 (2.2%)

(\*Individual data from 6 readers; majority reader (≥4) data).

**Abstract FRI0170 – Table 2.** Frequencies of structural MRI lesions in the SIJ in the ASAS-CC

Variable	Mean% (Range) of cases*	Number (%) of cases*
Structural lesions typical of axSpA	31.4 (23.5-39.9)	68 (28.6%)
Structural lesions typical of axSpA and level of confidence ≥3 (scale of 1-4)	20.8 (14.0-29.4)	46 (19.3%)
Subchondral sclerosis	24.2 (10.1-39.1)	36 (15.1%)
Erosion	27.9 (23.1-32.8)	60 (25.2%)
Fatty lesion (any)	23.5 (18.1-29.8)	47 (19.8%)
Fatty lesion (>1cm)	11.7 (8.0-15.6)	22 (9.2%)
Bone bud (yes)	2.1 (0.4-3.8)	1 (0.4%)
Fat metaplasia in joint space (yes)	8.1 (4.2-10.5)	11 (4.6%)
Ankylosis	1.1 (0.8-3.8)	5 (2.1%)

(\*6 readers; majority reader (≥4) data).

**Conclusions:** In this first central reader analysis of MRI images from the ASAS-CC we demonstrate similar frequencies of active and structural lesions typical of axSpA, erosion as a common lesion, some degree of false positive subchondral inflammation, and a lower frequency of active lesions typical of axSpA than noted by local site readers.

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**Disclosure of Interest:** None declared

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## FRI0171 WHICH IMAGING OUTCOMES FOR AXSPA ARE MOST SENSITIVE TO CHANGE? A 5-YEAR ANALYSIS OF THE DESIR COHORT

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**Background:** Several imaging outcomes have become available to assess inflammation and structural damage over time in patients with axial spondyloarthritis (axSpA). However, no formal comparison of their sensitivity to change has been made in the early phases of the disease.

**Objectives:** We aimed to compare the sensitivity to change of different MRI and radiographic scoring methods in patients with early axSpA.

**Methods:** Patients from the DESIR cohort fulfilling the ASAS axSpA criteria were included. Radiographs and MRI of the sacroiliac joints and spine were obtained at baseline, 1 year, 2 years and 5 years. Each film was scored by 2 or 3 readers in 3 'reading-waves' (wave 1: baseline; wave 2: baseline, 1 year, 2 years; wave 3: baseline, 2 years, 5 years). Outcomes measuring inflammation and structural damage both on MRI and radiographs in the spine and SIJ were assessed (table 1). The analysis of change captured over time was performed using generalised estimating equations (GEE) longitudinal models separately for each outcome, taking into account data from all readers and waves ('integrated analysis'). To allow



comparisons across outcomes, these were standardised (difference between the individual score and the mean of all scores divided by the standard deviation, per reader, wave and time-point) before running the models. The higher the standardised coefficient the more change in inflammation/damage is captured.

**Results:** In total, 345 patients were included (mean (SD) symptom duration: 1.6 (0.9) years; 53% males; 89% HLA-B27 positive). Inflammation on MRI-SIJ (according to both the ASAS definition of sacroiliitis and the continuous SPARCC score) was more sensitive to change as compared to inflammation on the spine that remained essentially unchanged regardless of the outcome (table 1). Structural damage on the SIJ was found to increase over time, but with a higher standardised yearly rate of change on MRI-SIJ (range: 0.015–0.274) as compared to X-SIJ (range: 0.043–0.126). Notably,  $\geq 3$  Fatty lesions on MRI-SIJ was the structural outcome in the SIJ with highest sensitive to change (0.274), while  $\geq 3$  erosions was the least sensitive (0.015). Spine structural damage slowly progressed over time but, in contrast to SIJ, radiographic outcomes (i.e.  $\geq 1$  syndesmophytes and mSASSS) were more sensitive to change than MRI structural outcomes.

**Conclusions:** Our data adds to the body of evidence showing that structural damage assessed in pelvic radiographs only has low sensitivity to change. MRI-SIJ is a promising alternative (especially fatty lesions) capturing more structural changes. In contrast, in detecting structural change in early axSpA radiographic outcomes outperform MRI outcomes.

**Disclosure of Interest:** None declared

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#### FRI0166 CHARACTERISATION OF PHOSPHODIESTERASE 4 (PDE4) BLOCKADE IN THE SYNOVIUM OF PSORIATIC ARTHRITIS PATIENTS: A FOCUS ON SYNOVIAL INVASIVENESS AND T-CELL POLYFUNCTIONALITY

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**Background:** Owing to the multi-faceted nature of the pathogenesis of psoriatic arthritis (PsA), the development of multi-targeted agents has been an area of intensive research. Such agents include the phosphodiesterase 4 (PDE4) inhibitors, Rolipram and Apremilast, which elevate intracellular cAMP levels to modulate a number of anti-inflammatory mechanisms. However, the effect of PDE4 blockade within the complex inflammatory environment of the inflamed synovium remains to be elucidated.

**Objectives:** To characterise the effect of PDE4 blockade in PsA using *ex vivo* synovial whole tissue explants and synovial single cell suspensions reflective of the complex synovial micro-environment.

**Methods:** *Ex-vivo* PsA whole tissue synovial explants were cultured in the presence of PDE4 inhibitor, Rolipram, for 24 hour. The expression of pro-inflammatory mediators were quantified by ELISA and MSD multiplex. A 21 day synovial explant matrigel model was utilised to examine synovial fibroblast (SFC) invasiveness to allow for a long-term assessment. For the characterisation of synovial T-cells, synovial explants were digested and cultured in the presence of Rolipram for 8 hours, stimulated and stained for surface and intracellular T-cell markers. Cell surface expression of CD161 was used to identify Th17 lineage (CD161+Th17 and exTh17 cells) or non-Th17 lineage (CD161-) Th1 cells. SPICE analysis was utilised to determine the proportions of mono- and polyfunctional T-cells, which were correlated with disease activity scores.

**Results:** Rolipram treatment inhibited the spontaneous secretion of inflammatory mediators IL-6, IL-8, MCP-1 and MMP-1 (all  $p < 0.05$ ), with a parallel increase in IL-10 expression. Under DMSO control conditions, a significant increase in SFC outgrowths from PsA explants (indicative of SFC invasiveness) was observed from day 8–21 (all  $p < 0.05$ ), effects of which were significantly decreased in the presence of Rolipram (all  $p < 0.05$ ). A comparative analysis of T cells in PsA PBMC and synovial tissue revealed an enrichment of Th1 ( $p < 0.05$ ), Th17 ( $p = 0.06$ ) and exTh17 ( $p < 0.05$ ) cells in PsA synovial tissue, which displayed distinct polyfunctional cytokine profiles, in particular Th17 cells, as compared to matched PBMC. The frequency of polyfunctional triple positive GM-CSF/TNF/IL-17 and/or IFN $\gamma$  producing Th1 ( $r = 0.8$ ,  $p < 0.05$ ), Th17 ( $r = 0.6$ ,  $p < 0.16$ ) and exTh17 ( $r = 0.9$ ,  $p < 0.05$ ) cells positively correlated with PsA disease activity, suggesting an important role of T-cell polyfunctionality in PsA synovial pathogenesis. Analysis of synovial tissue cell suspensions and matched PBMC cultured in the presence of Rolipram showed a significant decrease in the proportion of these triple positivesynovial T cells compared to DMSO ( $p < 0.05$ ), suggesting that PDE4 blockade can effectively targets the polyfunctional hyper-pathogenic synovial T cells in PsA, particularly polyfunctional CD8 +T cells and Th17 lineage, Th17 and exTh17 cells.

**Abstract FRI0171 – Table 1.** Standardised rate of change of imaging outcomes over 5 years of follow-up in early axSpA patients from the DESIR-cohort who fulfil the ASAS axSpA classification criteria.

Imaging outcomes	Baseline score* (N=313-344)	Standardized rate of change/year†
<b>SACROILIAC JOINTS</b>		
<b>Inflammatory lesions (MRI-SIJ)</b>		
Sacroiliitis (ASAS criteria)	134 (39.2%)	-0.278
SPARCC SIJ score (0-72)	4.7 (7.9)	-0.441
<b>Structural lesions (MRI-SIJ)</b>		
$\geq 5$ fatty lesion and / or erosions	66 (19.5%)	0.238††
$\geq 3$ erosions	60 (17.7%)	0.015
$\geq 3$ fatty lesions	56 (16.5%)	0.274
Number of fatty lesions and/or erosions (0-80)	2.9 (4.9)	0.111
Number of erosions (0-40)	1.3 (2.2)	0.030
Number of fatty lesions (0-40)	1.5 (3.5)	0.140
Total structural lesions‡ (0-144)	3.4 (5.9)	0.115
Total structural lesions without sclerosis (0-104)	3.2 (5.8)	0.124
<b>Structural lesions (X-SIJ)</b>		
mNY dichotomous	73 (21.2%)	0.044
mNY 1-grade change	NA	0.126
mNY 1-grade change and value $\geq 2$	NA	0.119
mNY continuous grade (0-8)	1.7 (1.8)	0.043
<b>SPINE</b>		
<b>Inflammatory lesions (MRI-Spine)</b>		
BME: $\geq 3$ lesions	32 (9.4%)	-0.032
BME: $\geq 5$ lesions	19 (5.6%)	-0.030
SPARCC Spine score (0-114)	2.6 (7.7)	-0.050
Berlin Spine score (0-69)	0.9 (2.7)	-0.055
<b>Structural lesions (MRI-Spine)</b>		
$\geq 5$ fatty lesions	5 (1.6%)	-0.013
Total structural lesions† (0-322)	0.4 (1.0)	0.016
Number of fatty lesions (0-92)	0.3 (0.8)	0.008
Number of corner erosions (0-92)	0.1 (0.2)	0.012
Number of corner bone spurs (0-92)	0.1 (0.3)	0.027
<b>Structural lesions (X-Spine)</b>		
$\geq 1$ syndesmophyte	19 (5.5%)	0.037
mSASSS score (0-72)	0.3 (1.3)	0.043

\* Agreement of  $\geq 2$  out of 3 readers for binary variables and mean (SD) of 3 readers for continuous variables from wave 3; † fatty lesions, erosions, sclerosis, partial ankylosis, total ankylosis; †† fatty lesions, erosions, bone spurs, ankylosis; NA, not applicable.

**Conclusions:** PDE4 blockade mediates broad anti-inflammatory mechanisms in PsA synovial tissue through the reduced expression of pro-inflammatory mediators, decreased invasiveness and reduced T cell polyfunctionality. We also demonstrate the feasibility of using *ex vivo* models to determine “*in situ* like” assessments of therapeutic agents and further our understanding of disease pathogenesis.

**Disclosure of Interest:** None declared

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#### FRI0167 EXPRESSION LEVELS OF IL-17, IL-22 AND IL-23 RECEPTORS IN FOUR OSTEOBLAST MODELS AND THE EFFECTS OF IL-17, IL-22 AND IL-23 ON OSTEOBLASTS

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**Background:** Ankylosing spondylitis (AS) is a chronic inflammatory joint disease that chiefly affects the sacroiliac joints and the spine. Radiographs reveal erosive changes at the corners of the vertebral bodies in the early stages of disease, and outgrowth of bony spurs known as syndesmophytes in the later stages. Some data imply a pivotal role of IL-23/IL-17 axis in the regulation of bone homeostasis. However, it remains unknown whether IL-17, IL-22 or IL-23 has any direct effects on osteoblasts or new bone formation in AS.

**Objectives:** To examine the expressions of IL-17, IL-22, and IL-23 receptors in four osteoblast models and the effects of IL-17, IL-22, and IL-23 on osteoblasts.

**Methods:** Gene expression levels of receptors, alkaline phosphatase (ALP), osteocalcin (OCN), and Runt-related transcription factor 2 (Runx-2), were

evaluated by RT-PCR and real-time RT-PCR. Proliferative responses and cell cycle analysis were detected by a CCK-8 assay and flow cytometry, respectively. ALP activity and ALP mass were detected by an ALP activity assay and ALP staining, respectively.

**Results:** In primary osteoblasts, only the IL-17 receptor was expressed. In C2C12, MC3T3-E1, and Saos-2 cells, the genes of IL-17, IL-22, and IL-23 receptors were not detectable. None of IL-17, IL-22, and IL-23 had an obvious effect on the proliferation of primary osteoblasts, but IL-17 exhibited an inhibitory effect on the gene expression of ALP, OCN, and Runx-2. The ALP activity and ALP mass of primary osteoblasts were downregulated by IL-17 treatment in a dose-dependent manner.

**Conclusions:** Primary osteoblasts constitutively express IL-17 receptors, but none of C2C12 cells, MC3T3-E1 cells, and Saos-2 cells express any receptors for IL-17, IL-22, and IL-23. IL-17 inhibits BMP-2-induced osteoblast differentiation.

**Disclosure of Interest:** None declared

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FRI0172

### INFLAMMATION ON MRI OF THE SACROILIAC JOINTS IS HIGHLY PREDICTIVE OF STRUCTURAL DAMAGE IN AXIAL SPONDYLOARTHRITIS PATIENTS IN CLINICAL PRACTICE: DATA FROM THE ASAS AND DESIR COHORTS

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**Background:** The effect of MRI-detected inflammation on the development of radiographic damage at the sacroiliac joints (SIJ) level in patients (pts) with axial spondyloarthritis (axSpA) has been previously shown when images were scored by trained central readers<sup>1</sup>. Central reading decreases measurement error, but does not translate easily to what is usually done in clinical practice.

**Objectives:** To test the possible effect of MRI-SIJ inflammation on structural damage in X-SIJ, when both are assessed by local readers as in daily clinical practice.

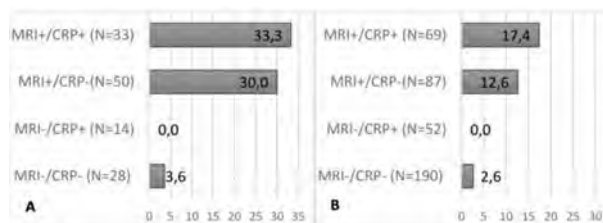
**Methods:** Pts with axSpA (according to the treating rheumatologist) from both the ASAS and DESIR cohorts were included. MRI-SIJ and X-SIJ were obtained at baseline (BL), and at follow-up (ASAS: mean 4.4 years; DESIR: 5 years) and scored by local readers (rheumatologists/radiologists). Images were taken unblinded to other imaging information and clinical characteristics. Readers had the option to view the baseline image when scoring the follow-up image. Bone Marrow Oedema (BME) at MRI-SIJ was assessed either without a formal definition (ASAS-cohort) or according to the ASAS definition (DESIR-cohort) as present/absent. Structural damage in the X-SIJ was defined according to the mNY criteria. The% of structural net progression (number of 'progressors' minus the number of 'regressors' divided by the total number of pts) was assessed in subgroups according to CRP and BME status at BL. The effect of BME on MRI-SIJ on X-SIJ damage was evaluated in logistic regression models adjusted for potential confounders selected *a priori* on clinical grounds (gender, HLA-B27, CRP, symptom duration, variables available in both cohorts).

**Results:** In total, 150 (ASAS-cohort) and 421 (DESIR-cohort) pts had complete 5 year X-SIJ data available. Remarkably, but not unexpectedly, the% of improvements in X-SIJ' was impressive both in the ASAS- and DESIR-cohorts (10% and 5.7% respectively), yielding a total% of net progression that was higher in the former than in the latter (14.7% and 5.9%). Net progression in X-SIJ ranged from 0.0% to 33% and from 0% to 17.4% according to the presence of objective signs of inflammation at BL in the ASAS- and DESIR-cohorts, respectively (figure 1). In the multivariable analysis, the presence of baseline BME at MRI-SIJ both in the ASAS (OR=3.2 [95% CI: 1.3–7.9]), and DESIR cohorts (OR=7.4 [95% CI: 4.3–12.7]) was highly predictive of X-SIJ structural progression at follow-up (table 1).

**Abstract FRI0172 – Table 1.** Effect of inflammation on MRI-SIJ at baseline on X-SIJ structural damage at follow-up

Predictor Outcome	mNY
	OR (95% CI)
Sacroiliitis on MRI-SIJ (ASAS-cohort)	3.2 (1.3; 7.9) *
Sacroiliitis on MRI-SIJ (DESIR-cohort)	7.4 (4.3; 12.7) *

\* Adjusted for gender, HLA-B27, CRP, symptom duration.



**Abstract FRI0172 – Figure 1.** Net progression from mNY-negative to mNY-positive according to baseline objective inflammatory markers in the ASAS (A) and DESIR (B) cohorts (ASAS: N=125; 25 patients miss baseline MRI-SIJ; DESIR: N=398; 6 patients miss baseline MRI-SIJ and 17 patients miss baseline CRP).

**Conclusions:** Our results, obtained in two independent cohorts, show that despite the expected increased 'noise' (measurement error) invoked by local reading, inflammation on MRI-SIJ still clearly predicts the later development of radiographic damage in axSpA.

#### REFERENCE:

[1] Dougados, et al. Ann Rheum Dis. 2017;76(11):1823–1828.

**Disclosure of Interest:** None declared

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FRI0173

### IDENTIFICATION OF A TYPICAL PATTERN OF MRI LESIONS OF SACROILIAC JOINTS IN PATIENTS WITH OSTEITIS CONDENSANS ILII AS COMPARED TO AXIAL SPONDYLOARTHRITIS

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**Background:** Osteitis condensans ilii (OCI) is regarded as a non-inflammatory disorder that is believed to be induced, for example, by mechanical stress and mechanical instability of the sacroiliac joints (SIJ) related to pregnancy/delivery. OCI is being increasingly recognised as an important differential diagnosis for axial spondyloarthritis (axSpA), due to onset at young age, possible inflammatory character of back pain and recently described presence of subchondral bone marrow oedema on magnetic resonance imaging (MRI) of the SIJ. So far, no systematic comparison of MRI changes in the sacroiliac joints in patients with OCI and axSpA has been performed.

**Objectives:** To compare active and chronic inflammatory lesions of the SIJ as detected by MRI in patients with OCI and axSpA.

**Methods:** Using medical database search we identified n=103 patients aged ≥18 years who were diagnosed with OCI upon presentation with chronic back pain in the Early Spondyloarthritis Clinic of the rheumatology department in the Charité University Hospital between January 2010 and May 2015. These patients were contacted in order to obtain an informed consent and to complete a survey on the disease-related history. A total of 27 patients had evaluable MRIs of the SIJ in STIR and T1-weighted sequences, which were used for the current study. These patients were matched to 27 patients with definite axSpA according to the back pain duration. MRIs were scored according to the Berlin scoring system for osteitis, fatty degeneration, erosions, sclerosis and ankylosis independently by 3 trained and calibrated readers who were blinded for all clinical data including diagnosis. In addition, the preferential localization of lesions (ventral, mid, or dorsal part of the SIJ) was recorded.

**Results:** There were no differences either in the osteitis score or in the proportion of patients with presence of osteitis on MRI of the SIJ between OCI and axSpA patients (table 1). The fatty degeneration score was significantly lower in OCI as compared to axSpA, although the difference in the prevalence of the fatty lesions did not reach the level of statistical significance. There was a non-significant trend towards a higher sclerosis score in OCI patients. Importantly, there was a highly significant difference in the erosion score and in the prevalence of erosions: only 2 (7.4%) OCI vs. 18 (66.7%) axSpA patients had at least one erosion (table 1). Importantly, none of the OCI patients had high-grade (>5 erosions) erosive changes.



There were substantial differences concerning localization of the lesions: in OCI, ventral localization was recorded in 96% of the cases for osteitis, in 100% for fatty degeneration, and in 96% for sclerosis, while in axSpA, osteitis was preferentially localised in the ventral part only in 29% of the cases, fatty degeneration in 25%, sclerosis in 29%. Ankylosis and erosions were localised in the mid part in almost all cases.

**Abstract FRI0173 – Table 1.** Active and chronic lesions of the sacroiliac joints as detected by MRI in patients with osteitis condensans ilii (OCI) and with axial spondyloarthritis (axSpA).

MRI changes	OCI N=27**	axSpA N=27	p-value***
Osteitis score (0-24), mean±SD	3.6 ± 2.3	4.4 ± 4.1	0.89
Osteitis present, n (%)	25 (96.2)	23 (85.2)	0.351
Fatty degeneration score (0-24), mean±SD	2.0 ± 2.3	4.5 ± 6.7	<b>0.001</b>
Fatty degeneration present*, n (%)	14 (51.9)	20 (74.1)	0.158
Erosions score (0-6), mean±SD	0.2 ± 0.4	3.0 ± 2.3	<b>&lt;0.001</b>
Erosions present*, n (%)	2 (7.4%)	18 (66.7%)	<b>&lt;0.001</b>
Ankylosis score (0-2), mean±SD	0	0.3 ± 0.7	<b>0.040</b>
Ankylosis present*, n (%)	0 (0)	4 (14.8%)	0.111
Sclerosis score (0-2), mean±SD	1.4 ± 0.6	1.0 ± 0.8	0.055
Sclerosis present*, n (%)	24 (88.9)	19 (70.4)	0.175

The absolute lesion scores represent mean values of 3 readers. Lesions were considered to be present if the corresponding score was ≥1 in the opinion of at least two readers.

\* N=26 for osteitis. \*\* Derived from the Mann-Whitney U-test for the scale variable or from the Fisher's exact test for the categorical variables.

**Conclusions:** MRI of sacroiliac joints in OCI is characterised by preferential ventral localization of lesions (osteitis, fatty degeneration, sclerosis), absence of ankylosis and absence of extended erosive changes. Such a findings constellation should be taken into account as suggestive of OCI for the differential diagnosis of axSpA in clinical practice.

**Disclosure of Interest:** None declared

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#### FRI0174 SPINAL RADIOGRAPHIC PROGRESSION IN EARLY AXIAL SPA: 5-YEAR DATA FROM THE DESIR COHORT

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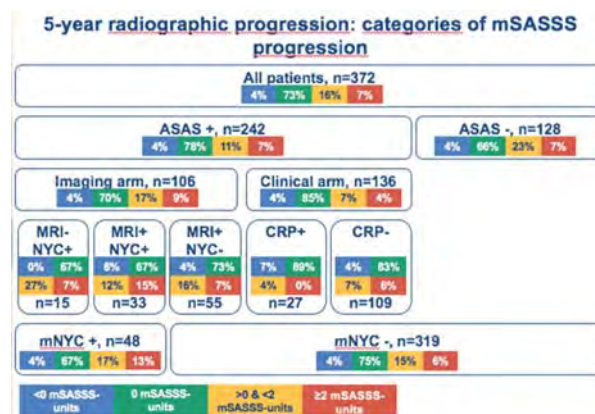
**Background:** Spinal radiographic progression has been investigated in patients (pts) with r-axSpA, but not yet as thoroughly in early axSpA.

**Objectives:** To analyse the progression of spinal radiographic damage in pts with early axSpA.

**Methods:** Five-year follow-up data (baseline, 2 and 5 years) from the DESIR cohort, including pts with early axSpA, were used. Cervical and lumbar radiographs were centrally and independently scored by 3 readers (averaged scores), blind for chronological order and clinical characteristics, according to the mSASSS (0–72). Change scores for all available intervals were calculated. Pts were included if they had ≥1 mSASSS interval available (0–2 y, 2–5 y or 0–5 y). The development of new syndesmophytes (2 out of 3 readers) was calculated as a net change, i.e. subtracting the number of pts in whom an existing syndesmophyte ('noise') is no longer reported from those with a new syndesmophyte ('true progression'), divided by all pts. Two- and 5 year mSASSS progression and development of new syndesmophytes were assessed in each subgroup of pts according to the ASAS axSpA criteria and its arms at baseline (see figure 1). In addition, pts were grouped according to the fulfilment of mNYC and also to the presence of baseline syndesmophytes.

**Results:** In total, 549 pts (mean age 34 (SD 9) years, 46% males, 63% fulfilling ASAS axSpA criteria, baseline mSASSS 0.46 (1.54)) were included. Thirty-eight pts (7%) showed syndesmophytes at baseline, 42% of which were ASAS axSpA criteria negative. Mean mSASSS progression was 0.15 (0.94) at 2 years and 0.42 (1.77) at 5 years. 18% of the pts fulfilling the ASAS axSpA criteria showed a 5 year positive mSASSS change (>0), compared to 30% in those not fulfilling the criteria (figure 1). 26% of the pts fulfilling the imaging arm had a positive change: highest positive change in MRI-mNYC+ (34%), followed by MRI+mNYC+(29%) and lastly MRI+mNYC- (23%). Mean mSASSS progression was highest in the mNYC +MRI + group (1.34 (3.98)). Eleven percent of the pts fulfilling only the clinical arm of the ASAS criteria had a positive change in mSASSS at 5 years, mean change of 0.13 (0.65). Pts with baseline syndesmophytes (across all subgroups) had the highest progression: 2.69 (5.02) mSASSS-units. At 5 years, 7% of all pts had a net change of any new syndesmophyte; this was 6% for ASAS+pts, 9% for ASAS-, 10% for pts

fulfilling the imaging arm (18% for mNYC +MRI+) and 3% for pts fulfilling the clinical arm only. Seventeen percent of the mNYC +pts had a net change in new syndesmophytes as well as 42% of the pts with baseline syndesmophytes.



**Abstract FRI0174 – Figure 1.** Five-year mSASSS radiographic progression categories according to the subgroups of the ASAS criteria, arms of the ASAS criteria and fulfilment of mNYC at baseline.

The totals of some groups are higher than the sum of the subgroups due to missing data not allowing to classify patients into the subgroups.

**Conclusions:** Spinal radiographic progression, though limited in early axSpA, can be captured already at 2 years of follow-up. Progression is higher in pts fulfilling the mNYC and also in pts with baseline syndesmophytes. Almost half of the pts with early axSpA with a syndesmophyte at baseline develop further syndesmophytes over 5 years.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.2928

#### FRI0175 RATES AND PREDICTORS OF RADIOGRAPHIC SACROILIITIS PROGRESSION AFTER CENTRAL READING IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS FROM THE ASAS COHORT: A 5-YEAR FOLLOW-UP STUDY

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**Background:** In patients with axial spondyloarthritis (axSpA), radiographic progression of sacroiliitis is relatively slow, with only few predictors identified. Recently, an analysis of data from Ankylosing Spondylitis Assessment Society (ASAS) Cohort, based on local assessment of X-Rays, revealed a surprisingly high rate of regression from radiographic axSpA (r-axSpA) to non-radiographic axSpA (nr-axSpA).

**Objectives:** To analyse the rates and predictors for radiographic progression of sacroiliitis in patients with axSpA from the ASAS Cohort, based on the central reading of radiographs.

**Methods:** Altogether 205 patients, who were included in the ASAS Cohort and diagnosed with axSpA by local rheumatologists, with baseline pelvic radiographs available for central reading, were included in the current study. Among them, 106 patients also had a pelvic radiograph at follow up (mean time to follow up 4.4±0.8 years). Images were independently assessed by 2 central readers (MP, FP), blinded for the chronology of the radiographs, according to the scoring system of the modified New York criteria (grade 0–4). In case of disagreement in classification (nr-axSpA or r-axSpA), the image was scored by an adjudicator (DP) that defined the final classification. In addition, we calculated a sacroiliitis sum score (0–8) based on scoring results of 2 (3) readers. The primary outcome was the proportion of patients with progression from nr-axSpA to r-axSpA at follow-up. Predictors of progression were investigated in univariable and multivariable logistic regression analyses.

**Results:** Among 205 patients, 82 (40%) were classified as nr-axSpA, and 123 (60%) as r-axSpA at baseline. Among 106 patients with available baseline and follow-up radiographs, 49 (46.2%) were classified as nr-axSpA, and 57 (53.7%) as r-axSpA at baseline. The agreement between two primary readers in classification (either nr-axSpA or r-axSpA) was moderate to substantial (κ=0.54 at baseline and



$\kappa=0.63$  at follow up); between local and central readers – poor to moderate ( $\kappa=0.18$  at baseline and  $\kappa=0.58$  at follow up). At follow up, 8 (7.5%) patients progressed from nr-axSpA to AS, while 6 (5.7%) were reclassified from AS to nr-axSpA, resulting in net progression of 1.9%. The sacroiliitis sum score increased in 43 (40.6%) patients, decreased in 21 (19.8%) and did not change in 42 (39.6%). Logistic regression analysis showed an association of active and chronic changes on MRI at baseline, already existing structural damage in the sacroiliac joints (sacroiliitis sum score) at baseline and younger age with higher odds for progression from nr-axSpA to r-axSpA.

**Conclusions:** There was a low but still detectable progression from nr-axSpA to r-axSpA after up to 5 years of follow-up in the ASAS cohort. Presence of active and chronic changes on MRI, initial structural damage on radiographs, and younger age at baseline were associated with a higher odds for progression from nr-axSpA to r-axSpA.

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#### FRI0176 PERFORMANCE OF SPINAL AND SACROILIAC JOINT MRI FINDINGS IN PATIENTS WITH AXSPA

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**Background:** Early diagnosis of axial spondyloarthritis (AxSpA) is challenging, particularly in patients with normal sacroiliac joints (SIJs) on radiographs. Currently, magnetic resonance imaging (MRI) is considered as the most sensitive imaging modality for detecting early SpA even before radiographic structural lesions develop. However, there are controversial reports, particularly for the spine, regarding the diagnostic utility of MRI.

**Objectives:** To determine the diagnostic utility of spine and sacroiliac joint lesions assessed by MRI in patients with ankylosing spondylitis (AS) or non-radiographic AxSpA (nr-AxSpA) compared to chronic mechanical back pain (MBP).

**Methods:** We included 151 AS, 110 nr-AxSpA, and 37 MBP patients. Spine and SIJ MRIs were performed in all patients. Two independent readers blinded to clinical details of the patients, scored the MRI images. A third reader participated in disputed cases. On T1 weighted sequences, the following structural changes in SIJs were scored: sclerosis ( $\geq 5$  mm) and extensive sclerosis ( $\geq 10$  mm), erosions, <sup>1-2</sup> extensive erosions ( $\geq 3$ ), partial or complete fusion, and fat deposition. Presence in at least two consecutive slices was required for erosions and fusion. On STIR sequences, the following inflammatory changes in the SIJs were determined: ASAS-defined bone marrow oedema (BME) and SPARCC SIJ scores. For the spine, the following were defined: fat infiltration at the vertebral corner on T1 and the number of corner inflammatory lesions (CILs) on STIR. We calculated sensitivity, specificity, and likelihood ratios (LR) of the above-mentioned structural and inflammatory lesions for both AS and nr-AxSpA groups.

**Results:** There were 298 patients in the study: 151 AS (mean age: 39 (16–77) years; 62.3% male), 110 nr-AxSpA (mean age 36 (17–64) years; 45.5% male), and 37 MBP (mean age 38 (19–59) years; 40.5% male). Presence of erosion was the most sensitive SIJ-MRI finding for structural lesions in AxSpA (AS 97%, nr-AxSpA 89%). However specificity of this variable was low (19%). Evidence of fusion and extensive sclerosis were the most specific SIJ-MRI findings for structural abnormalities with poor sensitivity levels in both groups. On the other hand, presence of extensive erosions showed acceptable sensitivity (78% and 58%) and specificity (62%) values in both AS and nr-AxSpA. For inflammatory lesions of SIJ, both ASAS BME and SPARCC  $\geq 2$  had similar sensitivity and specificity values in AxSpA. The presence of SIJ fat and evident erosions was associated with a slight increase in Likelihood of AxSpA. Among spinal lesions, spinal fat was the most sensitive finding in AxSpA (67% and 58%) with limited specificity (40%). CILs had moderate to high specificity but low sensitivity. All spinal parameters had low positive LRs.

**Abstract FRI0176 – Table 1.** Performance of different MRI derived SIJ and spine lesions in AxSpA

	Sensitivity (95% CI)		Specificity (95% CI)		+LR (95% CI)		-LR (95% CI)	
	AS	Nr	AS	Nr	AS	Nr	AS	Nr
<b>Sacroiliac joint</b>								
Sclerosis	51 (41-61)	22 (15-31)	65 (48-80)	65 (48-80)	1.5 (0.9-2.3)	0.6 (0.4-1.1)	0.8 (0.6-1.1)	1.2 (0.9-1.6)
Evident sclerosis	5 (2-11)	1 (0-5)	100 (91-100)	100 (91-100)			0.95 (0.9-0.99)	0.99 (0.97-1)
Fat	69 (61-77)	36 (27-46)	73 (56-86)	73 (56-86)	2.6 (1.5-4.4)	1.3 (0.7-2.4)	0.4 (0.3-0.6)	0.9 (0.7-1.1)
Erosion	97 (92-99)	89 (82-94)	19 (8-35)	19 (8-35)	1.2 (1-1.4)	1.1 (0.9-1.3)	0.2 (0.1-0.6)	0.6 (0.3-1.4)
Evident erosion	78 (66-85)	58 (48-67)	62 (45-78)	62 (45-78)	2.1 (1.3-3.1)	1.5 (1-2.4)	0.4 (0.2-0.6)	0.7 (0.5-0.9)
Fusion	29 (22-37)	0 (0-3)	100 (91-100)	100 (91-100)			0.7 (0.6-0.8)	25.3 (25.3-25.3)
ASAS BME	51 (43-59)	41 (31-51)	60 (42-75)	60 (42-75)	1.3 (0.8-1.9)	1 (0.6-1.6)	0.8 (0.6-1.1)	0.9 (0.7-1.4)
SPARCC SIJ $\geq 2$	51 (43-59)	41 (31-51)	60 (42-75)	60 (42-75)	1.3 (0.8-1.9)	1 (0.6-1.6)	0.8 (0.6-1.1)	0.9 (0.7-1.4)
<b>Spine</b>								
Spinal fat	67 (59-75)	58 (48-68)	40 (24-58)	40 (24-58)	1.1 (0.8-1.5)	0.9 (0.7-1.3)	0.8 (0.5-1.3)	1.1 (0.7-1.7)
CIL presence	45 (37-54)	31 (22-41)	46 (29-63)	46 (29-63)	0.8 (0.6-1.2)	0.6 (0.4-0.9)	1.2 (0.8-1.8)	1.5 (1-2.2)
CIL $\geq 5$ vs. $< 3$	27 (20-36)	10 (5-18)	74 (57-88)	74 (57-88)	1.1 (0.6-2)	0.4 (0.2-0.9)	0.9 (0.8-1.2)	1.2 (0.9-1.5)
CIL $\geq 5$ vs. $< 5$	19 (13-26)	8 (4-15)	80 (63-92)	80 (63-92)	0.9 (0.4-2)	0.4 (0.2-1)	1 (0.6-1.2)	1.1 (0.9-1.4)

**Conclusions:** Extensive erosions of SIJ showed the most balanced performance in whole spinal MRI assessment. Spinal lesions performed poorly when compared with SIJ findings in discriminating AxSpA from MBP.

**Disclosure of Interest:** None declared

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#### FRI0177 ASSESSING THE VALUE OF WHOLE BODY MAGNETIC RESONANCE IMAGING AS TO CLINICAL EXAMINATION TO PREDICT REMISSION AND RELAPSE IN EARLY PERIPHERAL SPONDYLOARTHRITIS

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**Background:** Evaluation of disease activity and treatment response in peripheral spondyloarthritis (pSpA) is currently based upon clinical findings, laboratory tests and ultrasound examination. Whole-body magnetic resonance imaging (WB MRI) is a relatively new imaging technique that could offer additional information regarding the inflammatory status of joints, entheses and soft tissues.

**Objectives:** To determine A) the value of WB MRI, performed at baseline, in relation to clinical remission in pSpA and B) the value of subclinical inflammation, detected by WB MRI, at time of clinical remission in predicting flare after treatment withdrawal in pSpA.

**Methods:** Clinical REmission in peripheral SPondyloArthritis (CRESPA) is a placebo-controlled trial of golimumab treatment in 60 early (symptom duration  $< 12$  weeks) pSpA patients (pts). All pts underwent a modified WB MRI at baseline and at the time of clinical remission when treatment was withdrawn. The WB MRI was performed by scanning multiple locations individually (using different coils) in order to investigate SpA-specific locations in detail. Several anatomical sites of pelvis and lower limbs were evaluated for bone marrow oedema (BME), synovitis and soft tissue inflammation (STI) by 3 readers, giving a score of 0 (no abnormalities), 1 (mild), 2 (moderate) or 3 (severe). For each site a mean of the scores of the 3 readers was calculated. For each patient at each time point, we calculated a sum score for synovitis, STI and BME separately adjacent to a total sum score. Changes scores are baseline minus remission sum scores.

**Results:** Pts reaching clinical remission had significant lower baseline BME sum scores than the non-remission group (mean 1.86 vs. 2.89,  $p=0.024$ ). At the time of clinical remission 10/45 (22%) and 11/45 (24%) pts had residual talocrural and subtalar synovitis respectively. However, there was no statistically significant difference between patients who relapsed after treatment withdrawal and those who remained in remission concerning synovitis sum scores ( $p=0.497$ ) as well as BME sum scores ( $p=0.741$ ) and STI sum scores ( $p=0.131$ ) at time of clinical remission (table 1).

**Abstract FRI0177 – Table 1.** BME, synovitis and STI presence in early pSpA pts who relapsed and did not relapse after stopping golimumab therapy

	Patients relapsed (n=20)	Patients not relapsed (n=25)
BME at baseline	1.82 ( $\pm 2.29$ )	1.69 ( $\pm 1.62$ )
BME at follow-up	1.32 ( $\pm 1.12$ )	1.09 ( $\pm 1.18$ )
Change score BME	0.50 ( $\pm 1.36$ )	0.52 ( $\pm 1.42$ )
Synovitis at baseline	2.53 ( $\pm 3.11$ )	3.53 ( $\pm 3.04$ )
Synovitis at follow-up	1.13 ( $\pm 1.41$ )	1.44 ( $\pm 1.49$ )
Change score synovitis	1.50 ( $\pm 2.71$ )	2.16 ( $\pm 2.81$ )
STI at baseline	1.67 ( $\pm 1.81$ )	2.07 ( $\pm 2.38$ )
STI at follow-up	0.93 ( $\pm 0.75$ )	1.01 ( $\pm 1.12$ )
Change score STI	0.70 ( $\pm 1.34$ )	1.00 ( $\pm 2.06$ )

**Conclusions:** Early pSpA pts who reach clinical remission have less BME on baseline WB MRI compared to those with ongoing disease activity. At time of clinical remission, a substantial part of the participants showed residual ankle synovitis on MRI. However, residual inflammatory lesions detected by WB MRI did not differ significantly between pts who relapsed after treatment withdrawal and those in ongoing clinical remission.

**Disclosure of Interest:** None declared

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#### FRI0179 INTEGRATED LONGITUDINAL ANALYSIS INCREASES PRECISION AND REDUCES BIAS: A COMPARATIVE 5-YEAR ANALYSIS IN THE DESIR COHORT

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**Background:** Evaluation of imaging is important in spondyloarthritis (SpA) research, but loss to follow up often jeopardises interpretation of the evaluation. The Interpretation may further be challenged by the fact that often different readers have contributed to scores, in multiple read 'waves'. A common approach is to evaluate patients (pts) with complete follow up (completers analysis), and aggregate scores of individual readers (eg. agreement  $\geq 2$  out of 3 readers). These approaches are not assumption-free, may cause non-random data loss, and may as such provide spurious estimates and loss of external validity.

**Objectives:** We aimed to investigate if the use of all data in an assumption-free manner (a so called 'integrated analysis') affects the precision of estimates for imaging outcomes in pts with axial SpA (axSpA), with completers analysis as reference standard.

**Methods:** Pts from the DESIR cohort fulfilling the ASAS axSpA criteria were included. Radiographs and MRIs of the SIJ and spine were obtained at baseline (BL), 1, 2 and 5 years. Each film was scored by 2 or 3 readers in 3 'reading-waves' (wave 1: BL only; wave 2: BL, 1, 2 years; wave 3: BL, 2, 5 years). Each outcome was analysed in two ways: i. according to a 'combination algorithm' ('2 out of 3' for binary and mean of 3 readers for continuous variables); and ii. per individual reader. The change of each outcome was analysed by generalised estimating equations (GEE) with 'time' as explanatory variable. Three analytical approaches were pursued: i) 'integrated-analysis' (including all pts with  $\geq 1$  score from  $\geq 1$  reader from all waves); ii) completers-only analysis (including only pts with complete 5 year follow-up, using scores from individual readers from wave 3); iii) aggregated completers analysis using a combination algorithm (the same as ii but using combined scores).

**Results:** In total, 413 pts were included (mean (SD) symptom duration: 1.6 (0.9) years) and 366 completed the 5 year follow up. An analysis with all data from different readers and 'waves' ('integrated analysis') was more inclusive, but did not result in a meaningful loss of precision (width of 95%CI) of the change-estimates as compared to both completers analyses (table 1). In fact, for low-incident outcomes (e.g.% of mNY-positive over 5 years), a similar incidence was 'captured', with more precision, by the 'integrated analysis' compared to the completers

analysis with combined scores (% change/year (95% CI): 1.1 (0.7; 1.5) vs 1.2 (0.5; 1.8), respectively). The same results were seen using continuous outcomes.

**Abstract FRI0179 – Table 1.** Change per year in the percentage of positive cases for binary imaging outcomes over 5-years of follow-up, according to 3 different analytical methods, in early axSpA patients fulfilling the ASAS axSpA criteria from the DESIR-cohort

	Integrated analysis	Completers analysis with individual readers scores	Completers analysis with combined scores for readers
Imaging outcomes	% change per year (95% CI) (N=399-411)	% change per year (95% CI) (N=342-364)	% change per year (95% CI) (N=338-364)
<b>SACROILIAC JOINTS</b>			
Sacroiliitis on MRI-SIJ (ASAS criteria)	-7.4 (-11.7; -3.1)	-5.4 (-8.9; -1.9)	-3.1 (-5.1; -1.2)
$\geq 3$ fatty lesions on MRI-SIJ	4.7 (2.7; 6.7)	3.3 (1.7; 4.9)	2.1 (1.1; 3.0)
mNY on X-SIJ (positive/negative)	1.1 (0.7; 1.5)	0.9 (0.5; 1.3)	1.2 (0.5; 1.8)
<b>SPINE</b>			
BME: $\geq 3$ lesions on MRI-Spine (ASAS criteria)	-0.8 (-2.3; 0.7)	-0.4 (-1.4; 0.5)	-0.1 (-1.2; 1.0)
$\geq 5$ fatty lesions on MRI-Spine	-0.2 (-0.9; 0.4)	-0.1 (-0.5; 0.2)	-
$\geq 1$ syndesmophyte on X-Spine	0.8 (0.5; 1.2)	0.5 (0.2; 0.8)	0.5 (0.3; 0.9)

**Conclusions:** An efficient and entirely assumption-free usage of all data from different readers and 'read-waves' does not compromise precision of the estimates of change in imaging parameters, and may yield increased statistical power for detecting changes with low incidence. In addition, integrated analysis may protect against attrition bias and avoid bias by 'convenient choices'.

**Disclosure of Interest:** None declared

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#### FRI0180 DIAGNOSIS JOURNEY OF PATIENTS WITH ANKYLOSING SPONDYLITIS IN THE UNITED STATES

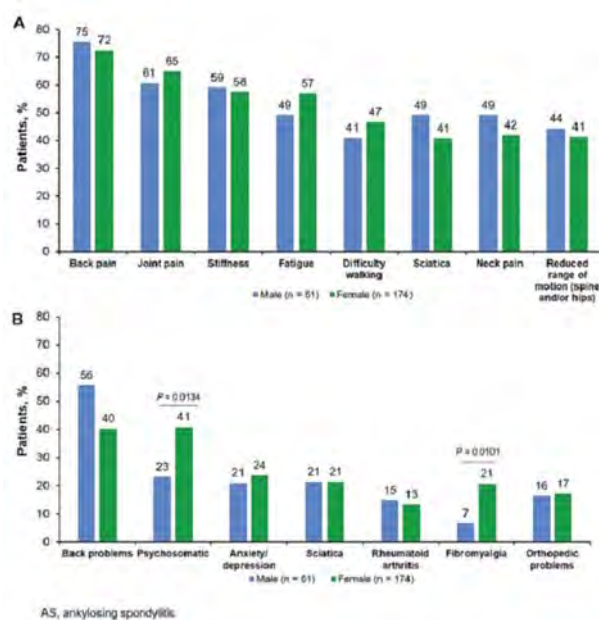
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**Background:** A US-based study demonstrated that patients with ankylosing spondylitis (AS) experience a significant delay (on average 14 years) from symptom onset to diagnosis of AS.<sup>1</sup> Understanding the diagnosis journey of patients with AS and identifying opportunities to reduce misdiagnosis and incorrect referral are crucial to reducing time to diagnosis, preventing irreversible joint damage, and preserving mobility.

**Objectives:** To describe the patient journey to AS diagnosis from the patient perspective and differences observed between females and males.

**Methods:** US adults aged  $\geq 18$  years with a self-reported diagnosis of AS were recruited through CreakyJoints, an online patient support community comprising patients with arthritis and arthritis-related diseases and their caregivers. Respondents completed a web-based survey on socio-demographics, clinical symptoms, disease burden, and diagnosis history, which included symptoms that led to seeking care, time from symptom onset to seeking care and from seeking care to AS diagnosis, types of healthcare providers seen, and misdiagnoses. Survey questions were developed following analysis of qualitative interviews of patients with AS and clinical experts, as well as a targeted literature review. Survey results were compared between females and males using 2-sample *t* tests for continuous variables and chi squared tests for categorical variables.

**Results:** Among 235 respondents, 174 (74%) were female. Mean (SD) age of female and male respondents were 48.6 (10.6) and 53.1 (10.3) years, respectively. Although the majority (58% female and 54% male) sought medical care within the first year of symptom onset, female respondents reported a mean of 17.2 years since first symptom onset and 7.5 years since AS diagnosis; while male respondents reported a mean of 20.0 years since first symptom onset and 11.4 years since AS diagnosis. The most common symptoms that led to seeking medical care were back pain, joint pain, stiffness, and fatigue (figure 1A). During the diagnosis process, patients reported seeking medical care from a general practitioner (87%), rheumatologist (65%), orthopedist (27%), chiropractor (26%), and urgent care/emergency room doctor (21%) with no differences between females and males. The most commonly reported misdiagnoses were back problems (56%), psychosomatic (23%), and sciatica (21%) in males, while psychosomatic (41%), back problems (40%), and anxiety/depression (24%) were most common in females. Significantly higher proportions of females reported misdiagnoses of fibromyalgia (21% vs 7%) and psychosomatic (41% vs 23%) (figure 1B).



**Abstract FRI0180 – Figure 1.** Most common first symptom to prompt seeking care (A) and most common misdiagnoses (B) in patients with AS

**Conclusions:** The diagnostic process differs among males and females with AS. Our study findings highlight gender differences in initial symptom presentation, misdiagnoses, and time to diagnosis of AS.

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#### FRI0181 TWELVE YEARS FOLLOW-UP OF PATIENTS WITH SPONDYLOARTHRITIS IN AN ENDEMIC CITY DEMONSTRATES HIGH RISK OF ACTIVE TUBERCULOSIS INFECTION

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**Background:** Anti-tumour necrosis factor (anti-TNF) agents can induce progression from latent tuberculosis infection (LTBI) to active tuberculosis (TB) in patient with rheumatic diseases<sup>1,2</sup>. In a high tuberculosis incidence setting, TB cases developed despite the screening and treatment for LTBI.

**Objectives:** To identify, in a high TB incidence setting, the TB incidence rate in patients with spondyloarthritis (SpA) during twelve years of follow-up.

**Methods:** Electronic medical records from patients attending the SpA Clinic between 2004 and 2016 in a public university hospital were reviewed. Patients were grouped in those exposed to anti-TNF therapy and those non-exposed. The tuberculosis incidence rate (IR) was calculated for both groups and expressed as number of events per 1 00 000 patients/year; the incidence rate ratio (IRR) associated to the anti-TNF therapy was calculated.

**Results:** A total of 274 patients were evaluated, 102 exposed to anti-TNF drugs and 172 non-exposed. All the 102 patients underwent screening for LTBI before anti-TNF therapy: 38.2% (n=39) were diagnosed with LTBI and underwent 6 months of isoniazid preventive therapy (IPT). The total follow up time (in patients/year) was 729 in the group exposed to anti-TNF and 1243 in the group non-exposed. Ten patients were diagnosed with TB: 4 exposed to anti-TNF therapy and 6 non-exposed. Among the 4 patients exposed to anti-TNF therapy who developed TB, three had negative screening for LTBI. The TB IR (per 1 00 000 patients/year) among those exposed to anti-TNF was 548, compared to 321 in non-exposed; the IRR associated with the use of anti-TNF drugs was 1.7.

**Conclusions:** In a region with high TB prevalence, patients with SpA exposed to anti-TNF drugs had a higher incidence of TB compared to those who have never been exposed to these drugs. Our data reinforces the American College of Rheumatology's recommendation that patients who live in endemic TB settings should be tested annually for LTBI.

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		CBP n=98	SpA n=100	p	Se	Spe	LR+
<b>MRI SIJ</b>							
	<b>N(%) patients with at least one structural lesion</b>	16/95 (16.8%)	24 (24%)	NS	0.2 (0.2–0.3)	0.8 (0.7,0.0)	1.4 (0.8–2.5)
<b>N(%) patients with ≥3 subchondral bone erosions</b>	10/95 (10.5%)	32 (32%)	<0.001	0.32 (0.2–0.4)	0.9 (0.8–1.0)	3.0 (1.6–5.8)	
<b>N(%) patients with ≥3 subchondral bone fatty lesions</b>	11/95 (11.6%)	29 (29%)	0.004	0.29 (0.2–0.4)	0.88 (0.8–0.9)	2.5 (1.3–4.7)	
<b>N(%) patients with ≥5 subchondral bone erosions or fatty lesions</b>	13/95 (13.7%)	33 (33%)	0.002	0.33 (0.2–0.4)	0.9 (0.8–0.9)	2.4 (1.4–4.3)	
<b>MRI spine</b>							
	<b>N(%) patients with at least one structural lesion</b>	49 (50.0%)	42/99 (42.4%)	NS	0.4 (0.3–0.5)	0.5 (0.4–0.6)	0.8 (0.6–1.2)
	<b>N(%) patients with ≥3 subchondral bone erosions</b>	6 (6.1%)	7/99 (7.1%)	NS	0.1 (0.0–0.1)	0.9 (0.9–1.0)	1.2 (0.4–3.3)
	<b>N(%) patients with ≥3 subchondral bone fatty lesions</b>	21 (21.4%)	15/99 (15.2%)	NS	0.2 (0.1–0.2)	0.8 (0.7–0.9)	0.7 (0.4–1.23)
	<b>N(%) patients with ≥5 subchondral bone fatty lesions</b>	8 (8.2%)	21/99 (21.2%)	0.02	0.2 (0.1,0.3)	0.9 (0.8–0.9)	2.5 (1.2–5.4)
	<b>N(%) patients with ≥5 subchondral bone erosions OR fatty lesions</b>	19 (19.4%)	11/99 (11.1%)	NS	0.1 (0.1–0.2)	0.8 (0.7–0.9)	0.6 (0.3–1.1)



**FRI0182** EROSIONS AT THE SACROILIAC JOINTS AND FATTY LESIONS AT THE SPINE ARE THE MOST DISCRIMINANT LESIONS FOR RECENT ONSET AXSPA RECOGNITION

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**Objectives:** To evaluate the performances of MRI (SIJ and Spine) structural lesions suggestive of axSpA for its recognition.

**Methods:** Observational cross-sectional national multicentre study. **Patients:** a) Recent onset axSpA patients: first, a sample of 100 patients representative in terms of imaging abnormalities of the global DESIR recent onset axSpA cohort based on the results of the previously published central reading of baseline films of DESIR were selected. b) Recent onset CBP patients: consecutive in- and out-patients consulting for recent mechanical CBP, initiating before the age of 45 y and with a maximum age of 50 y, in four tertiary care Hospitals were included in the study. **Imaging:** MRI scans (T2-STIR and T1 sequences) of the SIJ and cervico-thoracic and thoraco-lumbar spine were performed in both groups with identical protocol. **Central reading:** an experienced reader (AM) centrally read all MRI scans, blinded for clinical diagnosis. **Statistical analysis:** prevalence of lesions suggestive of axSpA was compared in both groups. Sensitivity, specificity and positive likelihood ratio (LR+) of each lesion were calculated.

**Results:** A total of 98 patients with recent onset CBP were included, and compared to 100 recent onset axSpA patients. Age and gender were comparable (mean (SD) 36.2 (9.9) vs. 32.2 (8.7)y, and 41.8% and 45% males, in the CBP vs. axSpA groups, respectively).

Prevalence of chronic lesions of the SIJ was significantly greater in the axSpA group. Presence of at least 3 subchondral bone erosions at the SIJ performed the best for axSpA discrimination. Prevalence of chronic lesions of the spine was comparable in the two groups. The presence of at least 5 fatty lesions was the most discriminant, with high specificity.

**Conclusions:** Presence of at least 3 erosions at the MRI-SIJ and at least 5 fatty lesions at the MRI-spine seemed to performed well for axSpA recognition.

**Disclosure of Interest:** None declared

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**FRI0183** CLINICAL PERIPHERAL ENTHESITIS IN THE DESIR PROSPECTIVE LONGITUDINAL AXIAL SPONDYLOARTHRITIS COHORT

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**Objectives:** 1) To describe the prevalence and characteristics of peripheral enthesitis in recent onset axial spondyloarthritis; 2) to estimate the incidence of peripheral enthesitis over time; 3) to determine the factors associated with the presence of peripheral enthesitis.

**Methods:** **Patients:** 708 patients with recent onset axial spondyloarthritis enrolled in the DESIR cohort (prospective multi-centre, longitudinal). **Data collected:** patients and spondyloarthritis characteristics at baseline with a specific focus on enthesitis and occurrence of peripheral enthesitis, during the five of years follow-up

**Results:** At inclusion, 395 patients (55.8%) reported peripheral enthesitis. The locations were mainly the plantar fascia (53.7%) and the Achilles tendon (38.5%). During the 5 year follow-up period, 109 additional patients developed peripheral enthesitis resulting in an estimated (Kaplan Meier technic) percentage of 71% (95% CI: 68–75). Variables associated with peripheral enthesitis in the univariate analysis were: older age, male gender, absence of HLA B27, MRI sacroiliitis and fulfilled Modified NY criteria, presence of anterior chest wall pain, peripheral arthritis, dactylitis, psoriasis, high BASDAI, BASFI, mean score ASAS and the use of NSAID. Only the history of anterior chest wall pain and of peripheral arthritis were retained in the multivariate analysis (Odds Ratio (OR)=1.6 [95% Confidence interval 1.6 [1.1–2.3], and OR=2.1 [1.4–3.0], respectively).

**Conclusions:** This study highlights the high prevalence of peripheral enthesitis in recent onset axial spondyloarthritis, and suggests that in combination with peripheral arthritis, enthesitis might have an impact on the burden of the disease.

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**Disclosure of Interest:** None declared

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**FRI0184** HIGH PREVALENCE OF HIDRADENITIS SUPPURATIVA, ESPECIALLY IN FEMALE AXIAL SPONDYLOARTHRITIS PATIENTS WITH HIGH DISEASE ACTIVITY AND POOR QUALITY OF LIFE

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**Background:** Hidradenitis suppurativa (HS) is a chronic debilitating inflammatory skin disease. Although HS and axial spondyloarthritis (SpA) share common denominators in the pathogenesis and treatment, little is known about HS associated patient characteristics in axial SpA.

**Objectives:** To identify patient characteristics associated with HS in a large cohort of axial SpA patients.

**Methods:** In this cross-sectional study, a self-screening questionnaire based on validated diagnostic HS questions was sent to all axial SpA patients from the Groningen Leeuwarden Axial Spondyloarthritis (GLAS) cohort. Verification of HS diagnosis was done by reviewing medical records for dermatologists diagnosis of HS and by telephone using another validated diagnostic HS question. These HS questions showed previously high sensitivity and specificity (92%–97%<sup>1</sup> and 97%<sup>2</sup>, resp.). Comparative analysis for axial SpA patients with versus without HS was performed. Multivariable logistic regression analysis of patient characteristics was performed to investigate independent predictors for HS in axial SpA.

**Results:** In total, 75.6% (449/592) questionnaires were eligible for analyses. Included patients had a mean age of 50±13 years, 63% were male, mean symptom duration was 23±13 years, and 78% were HLA-B27 positive. HS diagnosis could be confirmed in 41 of the 449 respondents, resulting in an estimated prevalence of 9.1%. Assuming that all non-responders never had HS, the minimal HS prevalence rate would be 6.9% (41/592).

In comparison to patients without a positive history of HS, these patients were more frequently female (54% vs. 35%, p=0.02), showed higher axial SpA disease activity (mean BASDAI 4.5 vs. 3.6, p=0.01 and ASDAS<sub>CRP</sub> 2.6 vs. 2.2 p=0.003), and worse quality of life (QoL) (median ASQoL 9.0 vs. 4.0, p<0.001). Also, a history of heel enthesitis and dactylitis was more prevalent (34% vs. 19%, p=0.03% and 15% vs. 6%, p=0.05, respectively). Multivariable analysis showed that a higher score on ASDAS was independently associated with HS (OR: 1.639, 95% CI 1.176–2.284).

**Conclusions:** In our cohort of axial SpA patients, HS is more prevalent than in the general population (6.9%–9.1% and ~1% resp.).<sup>3</sup> HS is associated with high ASDAS, especially in female patients experiencing poor QoL. Additionally, heel enthesitis and dactylitis seems also to be more prevalent in axial SpA patients with HS.

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**FRI0185** FACTORS DETERMINING WORK INSTABILITY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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**Background:** Work instability is defined as mismatch between the employee's ability to work and the employer's expectations<sup>1</sup>. 50% of Ankylosing spondylitis patient lose their job due to disease activity and 50% of those in job face work instability and job retention problem<sup>2</sup>. Work disability is preceded by a period of work instability, which can be measured by the Ankylosing spondylitis work instability scale (ASWIS)<sup>1</sup>.

**Objectives:** To determine the factors responsible for work instability in patients with Axial spondyloarthritis (axSpA).

**Methods:** Patients attending the Spondyloarthritis clinic at a UK centre from 2013 to 2017, were included, if in employment, and diagnosed with axSpA according to ASAS criteria. Number of patients having low (WIS  $\leq 10$ ) and moderate to high (WIS 11–20) and corresponding parameters were noted. Numerical values were analysed using Spearman rank test and categorical values using Pearson's test. Multiple regression analysis was done. P value  $\leq 0.05$  was considered significant.

**Results:** Of total 255 patients, 139 were in employment (54.5%), 97 were male and 42 were female. Mean age was 43.5 years (20–78 years). 59 patients in manual and 80 patients in non-manual job type, 52 had non-radiographic axSpA (nrSpA) and 87 had radiographic axSpA (rSpA). Mean diagnostic delay was 8 years (0–37 years). Mean ASWIS score was 10.43 (0–20). 75 patients (53.9%) were in Low WIS category and 64 (46%) in moderate to high WIS category. BASDAI and BASFI are found to be significantly correlating with WIS for the whole cohort.

Parameter	Spearman Rank Coefficient	p value
BASDAI	0.7633	0.00011*
BASFI	0.4250	0.00092*

Diagnostic delay, job type, comorbidities, extra articular features, HLAB27, CRP, Pain visual analogue scale (VAS), BASMI, smoking, alcohol and use of biologics were not found to be significant for the whole cohort.

In separate analysis for rSpA and nrSpA groups, the BASDAI and BASFI were of equal significance, but the Pain VAS strongly correlated with WIS in the nrSpA group only ( $r=0.62$ ) and the CRP correlated in the rSpA group only ( $r=0.64$ ).

**Conclusions:** Work instability is prevalent in axSpA, in all job types. Main factors contributing to work instability are disease activity (BASDAI) and function (BASFI). Drivers for work instability may be different in radiographic and non-radiographic patients. A prospective study will evaluate the impact of use of biologic on work instability.

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FRI0186

#### CONCOMITANT CSDMARDS INFLUENCE CLINICAL RESPONSE TO TNF INHIBITORS ONLY IN OVERWEIGHT PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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**Background:** In patients with axial spondyloarthritis (axSpA), the use of conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs), such as methotrexate (MTX) and sulfasalazine (SSZ), as well as the body mass index (BMI) have been associated with circulating TNFi levels. Recently, BMI has also been associated with TNFi clinical response but csDMARDs have not shown any significant clinical improvement for axial manifestations<sup>1</sup>. However, no study has assessed in the same population the influence of both factors -csDMARDs and BMI- on drug serum levels and clinical response

**Objectives:** To investigate the influence of csDMARD and BMI on circulating drug levels and clinical response to TNFi therapy in axSpA patients

**Methods:** A 1 year follow-up prospective observational study with two cohorts (Madrid and Amsterdam) including 180 axSpA patients treated with standard doses of infliximab (41%) or adalimumab (59%). Laboratory and clinical parameters were collected every 6 months. Patients were stratified by BMI: normal-weight (18.5–24.9 kg/m<sup>2</sup>) and overweight-obesity (>25.0 kg/m<sup>2</sup>). TNFi trough levels were measured by capture ELISA<sup>2</sup>. Clinical response to TNFi was defined as  $\Delta$ BASDAI  $\geq 2$ . The association between concomitant csDMARDs and BMI with drug levels and clinical response to TNFi at 1 year was analysed through multivariate log-regression models (odds ratio and 95% CI). The presence of significant interactions between covariates was tested and all models were adjusted for

age, gender, HLA-B27, disease duration, TNFi-type (for drug levels) and baseline BASDAI and CRP (for clinical response)

**Results:** Seventy-nine out of 180 patients (44%) received concomitant csDMARDs (MTX 14%, SSZ 20% and MTX +SSZ 10%), 78 (43%) patients were normal-weight and 102 (57%) overweight-obese. Mean (SD) age and disease duration was 47(13) and 11(9) years respectively, 59% were males, 73% HLA-B27 + and 78% had r-axSpA. Concomitant csDMARDs (OR: 3.82; IC 95%: 1.06–13.84) and being overweight-obese (OR: 18.38; IC 95%: 2.24–150.63) were independently associated with serum TNFi drug presence. Furthermore, a significant interaction between csDMARDs and BMI with clinical response was found. While the use of concomitant csDMARD contributed positively to achieve clinical response in overweight-obese patients (OR: 7.86; IC 95%: 2.39–25.78), no association was found for normal-weight patients (OR: 1.10; 0.33–3.58). Additionally, sensitivity analysis using remission status and ASDAS were performed and showed results along the same line

**Conclusions:** In patients with axSpA, TNFi drug persistence is positively influenced by the use of concomitant csDMARDs and especially by being normal-weight. However, TNFi clinical response is associated with the use of concomitant csDMARDs only in overweight-obese, but not in normal-weight patients. Based on this, the use of concomitant csDMARDs in patients with axSpA could be beneficial in overweight patients

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FRI0187

#### LIPOPROTEIN (A) AND POSSIBLE RELATED FACTORS IN PATIENTS WITH SPONDYLOARTHRITIS. RESULTS OF THE CARMA STUDY

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**Background:** Cardiovascular disease (CVD) is the main cause of mortality and morbidity in patients with spondyloarthritis (SpA), partially explained by traditional CV risk factors (CVRF). Other non-conventional CVRF, probably related to chronic systemic inflammation, may be involved. In this sense, lipoprotein (a) [Lp (a)], a non-conventional risk factor with proatherogenic and thrombogenic properties, could be involved, since it seems to act as an acute-phase reactant, there are few data on this aspect in these patients.

**Objectives:** To evaluate the prevalence of hyperlipoproteinemia (a) in patients with SpA and analyse the possible related factors.

**Methods:** Analysis of the baseline visit of patients with ankylosing spondylitis (AS) and psoriatic arthritis (PsA) of the CARMA project (CARDiovascular in REumatology), a prospective cohort study of 10 years of follow-up, to evaluate the cardiovascular risk in chronic rheumatic inflammatory diseases, including rheumatoid arthritis, AS and PsA, followed in 67 Spanish rheumatology centres. A multivariate logistic regression model was performed, in which the dependent variable was hyperlipoproteinemia (a), defined as the plasma concentration of lipoprotein (a) [Lp (a)]  $\geq 50$  mg/dl. Sociodemographic factors and those related to the disease itself have been included as independent variables.

**Results:** 1459 patients were analysed, 738 with AS and 721 with PsA. Plasma concentrations of Lp(a) were available in 57.7% of the patients with AS and in 57.1% of the patients with PsA. A 19.2% (95% CI: 16.80–22.05) of the patients with SpA, 20.7% (95% CI: 16.91–24.82) of AS and 17.7% (95% CI: 14.15–21.75) of PsA, respectively, had hyperlipoproteinemia (a), without statistically significant differences with respect to the control group: 16.7% (95% CI: 13.23–20.86;  $p=0.326$ ). After adjusted for age and sex, only patients with AS were more likely to have hyperlipoproteinemia (a) than the control group (OR: 1.806, 95% CI: 1.177–2.771,  $p=0.007$ ). In the model adjusted for possible confounding factors, high values of apolipoprotein B in all patients, non-steroidal anti-inflammatories in AS, and sex (men) and kidney disease as comorbidity in PsA, were associated with a higher probability of presenting hyperlipoproteinemia (a).

**Conclusions:** Patients with AS have a higher percentage of hyperlipoproteinemia (a) compared to the control group. No specific factors of the disease have

been identified that are associated with hyperlipoproteinemia (a) in each of the analysed groups.

**Disclosure of Interest:** None declared

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**FRI0188** **FACTORS ASSOCIATED WITH PATIENT-PHYSICIAN DISCORDANCE IN GLOBAL ASSESSMENT IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: AN ASIAN PERSPECTIVE**

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**Background:** Shared decision making between patients and physicians is important in the management of patients with axial spondyloarthritis. However patient's perspective on disease activity is not always similar to physician's perspective.<sup>1</sup> There are limited studies on patient-physician discordance, none of which is based on Asian population.

**Objectives:** To identify the factors associated with patient-physician discordance in patients with axial spondyloarthritis (axSpA) in an Asian population.

**Methods:** A cross-sectional study was conducted in 2 tertiary referral centres in Singapore. Patients who fulfilled ASAS 2009 criteria for axial spondyloarthritis (axSpA) were recruited. Sociodemographic, clinical, laboratory and patient reported outcomes (PROs) data were collected during study visits from 2014 to 2015. We performed univariate and multivariate logistics regression analysis to evaluate the factors associated with patient-physician discordance, which we defined as the absolute difference  $\geq 20$  mm between Patient Global Assessment (PGA) and Physician Global Assessment (PhGA).

**Abstract FRI0188 – Table 1.** Multivariate logistic regression analysis of patient-physician (PGA-PhGA) discordance with different variables.

Characteristics	PGA-PhGA	
	OR (95% CI)	p value
Current age	1.00 (0.98–1.02)	0.69
Education <sup>a</sup>	0.35 (0.12–0.98)	0.04
If post-secondary (6 years)		
Pain score	1.03 (1.01–1.05)	<0.01
BASFI	1.08 (0.94–1.25)	0.23
ASDAS CRP	0.82 (0.59–1.13)	0.23
Current Biologics use	2.63 (1.34–5.17)	<0.01

Abbreviations: ASDAS CRP: Ankylosing Spondylitis Disease Activity Score C-reactive protein; BASFI: Bath Ankylosing Spondylitis Functional Index

**Results:** 298 axSpA patients were included: 82% male, 81% Chinese, median age of 40 (range:20–78) years, median disease duration of 9 (range:0.1–48) years. 80% were on non-steroidal anti-inflammatory drugs and 23% were on biologics. In univariate logistic regression analysis, current age (OR:1.01, p=0.09), post-secondary education level (OR:0.34, p=0.02), pain score (OR:1.03, p<0.01), Bath Ankylosing Spondylitis Functional Index (BASFI) (OR:1.26, p<0.01), Ankylosing Spondylitis Disease Activity Score C-reactive protein (ASDAS-CRP) (OR:1.39, p<0.01) and current use of biologics (OR:1.80, p=0.05) were associated with patient-physician discordance. In multivariate logistic regression analysis, pain score (OR:1.03, p<0.01), post-secondary education level (OR:0.35, p=0.04) and current biologics use (OR:2.63, p<0.01) were associated with patient-physician discordance.

**REFERENCE:**

a with reference to pre-secondary

**Conclusions:** Higher pain score, lower education level and current biologics use were associated with greater patient-physician discordance. These factors should be taken into account during shared decision making.

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**FRI0189** **PERIPHERAL MANIFESTATIONS IN SPONDYLOARTHRITIS: IMPACT ON PATIENT-REPORTED OUTCOMES (PROS) AND TREATMENT. DATA FROM ASAS-COMOSPA**

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**Background:** Peripheral manifestations (arthritis, enthesitis and dactylitis) are frequent in patients with Spondyloarthritis (SpA)<sup>1</sup>. However, little is known regarding the impact of these manifestations on patients' disease perception and treatments.

**Objectives:** To evaluate the impact of the presence of peripheral manifestations on patient-reported outcomes (PROs) and treatment.

**Methods:** Data from the ASAS-COMOSPA study were analysed. Patients who reported peripheral arthritis were divided into three groups: current, past history and no history. The impact of the presence of peripheral arthritis on VAS-G (Global Visual Analogue Scale), BASDAI (Bath Ankylosing Spondylitis Activity Index), BASFI (Bath Ankylosing Spondylitis Functional Index), work and activity impairment was evaluated through the use of the ANOVA one factor test. Finally, NSAIDs, corticosteroids and DMARDs intake were compared among patients with and without peripheral articular involvement.

A similar statistical analysis was performed for enthesitis and dactylitis.

**Results:** Among the 3984 patients included in the ASAS-COMOSPA study, 1333 (33.5%), 718 (18%) and 1933 (48.5%) patients had current, past history and no history of peripheral arthritis, respectively. Patients with current peripheral arthritis showed higher levels in VAS-G, BASDAI, BASFI, as well as in work and activity impairment, in comparison to the other two groups, being these differences statistically significant (p<0.01). Patients with peripheral articular involvement at the time of the visit showed higher mean scores in all questions of the BASDAI questionnaire, in contrast to those with past history and/or no history (p<0.001). Impact on treatment is shown in table 1.

Regarding enthesitis, 642 (16.1%), 864 (21.7%) and 2478 (62.2%) patients had current, past history and no history of enthesitis, respectively. Patients with current enthesitis showed significant higher levels in all PROs against the other two groups of patients (p<0.05), as well as higher scores in all the BASDAI questions (p<0.001). Finally, 171 (4.3%), 447 (11.2%) and 3366 (84.5%) patients had current, past history and no history of dactylitis, respectively. The same results as the other two peripheral manifestations were obtained regarding impact on PROs and BASDAI questions.

**Conclusions:** The presence of any of the three peripheral manifestations at the time of the visit was associated to higher scores in all PROs. Patients with peripheral involvement showed greater use of NSAIDs, corticosteroids and DMARDs than those without peripheral manifestations.

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**Abstract FRI0189 – Table 1**

Patients using:	Current or past history of arthritis			Current or past history of enthesitis			Current or past history of dactylitis		
	Yes=2051 n (%)	No=328 n (%)	p-value	Yes=1506 n (%)	No=2478 n (%)	p-value	Yes=618 n (%)	No=3366 n (%)	p-value
NSAIDs	1858 (90.6)	1690 (87.4)	0.001	1402 (93.1)	2146 (86.6)	<0.001	568 (91.9)	2980 (88.5)	0.013
csDMARDs	1581 (77.1)	790 (40.9)	<0.001	1062 (70.5)	1309 (52.8)	<0.001	492 (79.6)	1879 (55.8)	<0.001
bDMARDs	987 (48.1)	755 (39.1)	<0.001	750 (49.8)	992 (40.0)	<0.001	330 (53.4)	1412 (41.9)	<0.001
Corticosteroids	1048 (51.1)	475 (24.6)	<0.001	738 (49.0)	785 (31.7)	<0.001	330 (53.4)	1193 (35.4)	<0.001



FRI0190

### RELATIONSHIP BETWEEN FAECAL CALPROTECTIN, HLAB-27 AND ACUTE PHASE REACTANTS IN PATIENTS WITH SPONDYLOARTHRITIS WITHOUT PRIOR DIAGNOSIS OF INFLAMMATORY BOWEL DISEASE

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**Background:** Faecal calprotectin (FC) is a biomarker of inflammatory bowel activity widely used in the diagnosis and follow-up of inflammatory bowel disease (IBD). Microscopic intestinal inflammation is described in approximately 50% of patients with spondyloarthritis (SpA), and it is associated with more severe disease.

**Objectives:** The purpose of this study was to describe the possible relationship between FC, HLAB27 and acute phase reactants in patients diagnosed of SpA without clinical suspicion or prior diagnosis of IBD.

**Methods:** Unicentric, cross-sectional observational study with prospective clinical data collection. We included consecutively selected patients in the Rheumatology Clinic diagnosed of SpA who fulfilled ASAS criteria and did not have digestive symptoms suggestive of IBD (chronic diarrhoea, rectal bleeding, perianal disease or chronic abdominal pain persistent/recurrent). Demographic, clinical and analytical data from SpA (Uveitis, HLAB27, acute phase reactants), treatments and FC were collected and a FC cut-off point >50 MG/kg was determined. For patients on NSAIDs suspension was recommended two weeks prior to collection of stool samples. The study was approved by the centre's Ethics Committee for Clinical Trials.

**Results:** Ninety-nine patients were included. 50% male, average age 46±11 years old. 3.7±2.5 BASDAI. 79% HLA-B27 positive, 31% had elevated levels of ESR, 9% elevated CRP (>10 mg/L). 49 patients (49.5%) had high levels of FC, with mean levels of 276 mg/kg (range 52–3,038). HLAB27 positive patients had significantly higher FC levels than HLAB27 negative patients (160 mg/kg vs 98 mg/kg; p<0.05). There were no differences in relation to the history of uveitis. Patients with high FC had significantly higher CRP levels than patients with normal FC (6.7 mg/L vs. 3.2 mg/L; p<0.05), in accordance with these results from the group of patients with CRP levels>10 mg/L, the percentage of FC elevation was 78% vs. 47% of patients with CRP <10 mg/L. There were no significant differences in relation to ESR.

**Conclusions:** Patients with spondyloarthritis (ASAS criteria), HLAB27 positive and elevated CRP have higher levels of faecal calprotectin, a biomarker of inflammatory bowel activity, which may indicate that inflammatory activity in SpA might be associated with subclinical intestinal inflammation.

**Disclosure of Interest:** None declared

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FRI0191

### SIMILARITIES AND DIFFERENCES BETWEEN OSTEITIS CONDENSANS ILII AND AXIAL SPONDYLOARTHRITIS PATIENTS PRESENTING WITH CHRONIC BACK PAIN IN A RHEUMATOLOGY SETTING

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**Background:** Osteitis condensans ilii (OCI) is regarded as a non-inflammatory disorder, which is considered to be induced by mechanical stress (e.g., by pregnancy and delivery). The diagnosis is normally based on wide spread sclerosis of the sacroiliac joint without erosions or ankyloses on imaging. More recently, par-articular bone marrow oedema has been described on MRI, which can occur early but also intermittently later in the course of the disease. The clinical characteristics of OCI patientst have not been well described. To date, there are no published systematic data on the characteristics of OCI as compared to axial spondyloarthritis (axSpA).

**Objectives:** The objective of this matched case-control study was to investigate demographic, clinical, and lab characteristics of OCI as compared to axSpA.

**Methods:** Using medical database search we have identified n=103 patients aged ≥18 years who were diagnosed with OCI upon presentation with chronic back pain in the Early Spondyloarthritis Clinic of the rheumatology department in the Charité University Hospital between January 2010 and May 2015. These patients were contacted in order to obtain an informed consent and to complete a survey on the disease-related history. n=60 OCI patients who provided an informed consent and completed the survey were included in the final analysis. These patients were matched with a 1:2 ratio according to the back pain duration to patients with definite axSpA diagnosed in the same setting in order to compare demographic, clinical and lab characteristics.

**Abstract FRI0191 – Table 1.** Demographic, clinical and lab characteristic of OCI as compared to axSpA in the rheumatology setting.

Characteristics	OCI N=60	axSpA N=120	p-value
Age, years	40.3±10.0	39.4±11.3	0.51
Female sex, %	96.7%	41.7%	<0.001
Age at back pain onset, years	29.7±9.0	30.5±9.0	0.59
Back pain duration, years	9.0±7.9	8.9±8.0	n.a.*
HLA-B27 positive, %	35.2%	84.2%	<0.001
CRP, mg/l	2.1±2.1	11.3±27.6	<0.001
Elevated CRP (>5mg/l), %	7.1%	41.3%	<0.001
Inflammatory back pain, %	39.5%	92.3%	<0.001
Good response to NSAIDs, %	73.8%	76.9%	0.67
Peripheral arthritis, %	4.5%	12.5%	0.25
Enthesitis of the heel, %	4.8%	15.8%	0.11
Dactylitis, %	0%	5.0%	0.60
Uveitis, %	0%	11.7%	0.011
Psoriasis, %	5.6%	3.3%	0.68
Inflammatory bowel disease, %	1.8%	2.5%	1.00
Family history of SpA, %	32.7%	20.8%	0.12
BASDAI, NRS points (0-10)	4.6±2.0	4.0±2.0	0.17
BASFI, NRS points (0-10)	3.4±2.2	3.1±2.3	0.49
Menell's test positive, %	37.5%	62.5%	0.09
Patrick's test positive, %	45.8%	69.6%	0.07
Tenderness in the SIJ area, %	75.6%	66.7%	0.48
Schober's test, cm	4.2±0.9	4.6±2.1	0.63
Lateral spinal flexion, cm	15.6±5.0	15.3±4.5	0.83

\*Matching variable

**Results:** The main characteristics of the two groups are presented in the table. Most importantly, all but 2 patients with OCI were females and had a significantly lower prevalence of inflammatory back pain, lower level of CRP stressing a rather non-inflammatory nature of this condition. All patients were referred because of possible axial SpA, therefore SpA features, although being lower than in axSpA patients (table 1), were higher than can normally be expected in OCI patients. This is probably the reason why a statistical significance in comparison to axSpA was observed for uveitis only. There was no difference in age of back pain onset (but age <45 years was a referral parameter). Signs of sacroiliitis at physical examination were only slightly more frequent in axSpA; there were no differences in spinal mobility. The level of symptoms (BASDAI) and the perceived level of functional disability (BASFI) were comparable between groups. 83% of female patients with OCI reported a history of at least one pregnancy with a mean number of pregnancies of 3 (median=3, range 1–8).

**Conclusions:** OCI manifesting with chronic back pain starting prior to 45 years of age represents an important differential diagnosis for axSpA. A constellation of a female sex (with a history of pregnancies), negative HLA-B27 and negative CRP seems to be of differential diagnostic value as compared to axSpA.

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FRI0192

### PREDICTORS OF SEVERE HIP INVOLVEMENT IN ANKYLOSING SPONDYLITIS: DATA FROM NATIONAL INPATIENT SAMPLE

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**Background:** Hip involvement in ankylosing spondylitis (AS) is common (24%–36%), leading to worse functional outcomes. While some cases achieve long-term remission, few develop progressive joint destruction with 5%–8% requiring hip replacement. Although studies in the past have looked at factors associated with severe hip involvement, these remain debated.

**Objectives:** To investigate the factors associated with severe hip disease in patients with AS using a large inpatient US database.

**Methods:** Using the Nationwide Inpatient Sample (NIS) data from 2009–2011, we identified patients with AS based on International Classification of Diseases, Ninth Revision (ICD-9) code 720.0 (first 5 positions) and identified patients with hip surgery with ICD-9 procedural codes 800.5, 801.5, 802.5, 803.5, 804.5, 807.5, 808.5, 809.5, 812.1, 815.1, 815.2, 815.3 (any position). NIS is the largest publicly available all-payer inpatient care database in the United States, sponsored by

Agency for Healthcare Research and Quality as a part of Healthcare Cost and Utilisation Project. Univariate and multivariate binomial logistic regressions were used to derive odds ratio for predictors of hip surgery. Statistical analysis was done using STATA version 13.0 (College Station, TX).

**Results:** NIS database from 2009–2011 contained 3538 (weighted counts in the whole US population n=17,480) patients with AS. Out of those, 190 (weighted n=934) had hip surgery (5.36%). Multivariate binomial regression analysis after controlling for confounders (table 1) showed male sex (OR 2.52, CI 1.65–3.83, p<0.001) and peripheral enthesopathy (OR 8.64, CI 2.48–30.12, p<0.001) to be significantly associated with hip surgery in AS patients, and an inverse relationship with inflammatory bowel disease (IBD) (OR 0.35, CI 0.16–0.76, p=0.01) was seen.

AS with Hip Surgery	Odds Ratio	Standard error	p-value	95% CI	
				Lower limit	Upper limit
Age	1	0	0.46	0.99	1.01
Male sex	<b>2.52</b>	<b>0.54</b>	<b>&lt;0.001</b>	<b>1.65</b>	<b>3.83</b>
Non-white	1.11	0.25	0.65	0.71	1.74
Income quartile	1.33	0.21	0.07	0.97	1.83
CAD	0.6	0.16	0.06	0.35	1.02
CKD	0.65	0.31	0.36	0.25	1.66
DM	0.64	0.17	0.09	0.38	1.07
CHF	0.14	0.14	0.05	0.02	1.04
Current smoking	0.75	0.18	0.23	0.46	1.20
Obesity	1.24	0.35	0.46	0.71	2.16
Uveitis	1.04	0.77	0.96	0.25	4.43
IBD	<b>0.35</b>	<b>0.14</b>	<b>0.01</b>	<b>0.16</b>	<b>0.76</b>
Psoriasis	0.85	0.64	0.84	0.2	3.74
Peripheral enthesopathy	<b>8.64</b>	<b>5.5</b>	<b>&lt;0.001</b>	<b>2.48</b>	<b>30.12</b>
Constant	0.04	0.01	<0.001	0.02	0.06

**Conclusions:** Our study found male sex and patients with peripheral enthesopathy to have higher odds of severe hip disease requiring surgery among hospitalised AS patients and significantly lower odds with IBD. Previous studies showed an association with age at onset, delay in diagnosis, bilateral involvement, axial/enthesial disease and severe sacroiliitis. Some of these associations could not be analysed in our study due to lack of individual level patient data. Interestingly, epidemiological factors like smoking and obesity which have been linked to severe disease in PsA, were not found to have any significant association. Routine clinical hip exam and radiological imaging might help to identify high-risk patients. Early therapeutic strategies might be indicated for this specific population to prevent severe hip disease and need for hip replacement surgery.

**Disclosure of Interest:** None declared

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**FRI0193** **PROGNOSTIC MARKERS IN AXIAL SPONDYLOARTHRITIS (PROMISE) – CROSS SECTIONAL EVALUATION OF SERUM BIOMARKERS IN AXSPA, MECHANICAL BACK PAIN AND HEALTHY CONTROLS**

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**Background:** In recent years there has been increasing interest in biomarkers in axial spondyloarthritis, for diagnosis, disease prognostication, and to monitor treatment effect.<sup>1,2</sup> Many biomarkers have been evaluated, but the role each of these plays and how they may interact is unclear.

**Objectives:** Our aim was to evaluate a broad panel of serum biomarkers in a large mixed cohort of patients, with Ankylosing Spondylitis (AS), non radiographic axial Spondyloarthritis (nr-axSpA), mechanical back pain (MBP) and healthy controls (HC), in order to identify any potential biomarkers for diagnosis by assessing the differences between the groups.

**Methods:** Cross sectional evaluation of 46 serum biomarkers was undertaken by Myriad RBM using multiplexed immunoassays of Multi-Analyte Panels, in a cohort of patients from a tertiary referral centre, consented as part of the Bath Spondyloarthritis BioBank. Validated patient reported outcomes (including BASDAI, BASFI) and BASMI were completed. 50 HC blood samples were also collected at University College London for biomarker analysis.

**Results:** 331 patients were included in the study, of which 59.5% AS, 8.2% nr-axSpA, 15.7% mechanical back pain, 15.1% HC. 64.7% were male, mean age 44.2 years (SD 16.6), mean disease duration in the AS group of 22.4 years (SD 13.6) with 84% HLA B27 positive.

IL1 alpha and beta, IL1 receptor antagonist, IL2, 3, 4, 5, 7, 10, 15, 17, IL12 subunit p70, factor VII, GM-CSF, IFN gamma, MMP9, TNF beta were the only biomarkers not to show statistical differences across the diagnostic groups (table 1.). 12 biomarkers showed a statistical difference between genders (table 1, column 1, p value significance indicated with \*<0.05, \*\*<0.01 using Mann Whitney U, in addition to Factor VII\*).

**Abstract FRI0193 – Table 1.** Statistically significant serum biomarker results by diagnosis

Mean (SD)	AS	nr-axSpA	Mechanical back pain	Healthy controls	P value using Kruskal Wallis
n	197	27	52	50	
Alpha 1 anti-trypsin, mg/ml	1.3 (1.2)	2.9 (0.8)	2.3 (0.8)	1.4 (0.4)	<0.001
Alpha 2 macroglobulin, mg/ml	4.0 (1.4)	3.7 (1.2)	3.6 (1.5)	3.1 (1.9)	<0.001
** Beta 2 macroglobulin, µg/ml	3.4 (2.7)	2.2 (0.8)	2.0 (0.9)	1.6 (0.3)	<0.001
Brain derived neurotrophic factor, ng/ml	28.4 (8.3)	30.3 (8.2)	28.9 (7.2)	31.0 (4.5)	<0.001
* C-reactive Protein, µg/ml	29.6 (69.1)	4.6 (9.2)	4.7 (3.0)	3.0 (4.4)	<0.001
Complement C3, mg/ml	2.8 (1.3)	1.9 (0.9)	1.8 (1.0)	0.8 (0.2)	<0.001
** Eotaxin 1, pg/ml	174.1 (193.5)	241.4 (174.8)	241.4 (161.2)	176.1 (129.5)	<0.001
** Ferritin, ng/ml	248.5 (211.2)	177.7 (127.3)	205.4 (122.0)	89.9 (74.3)	<0.001
** Fibrinogen, mg/ml	0.5 (0.0)	0.0 (0.0)	0.0	0.0 (0.0)	<0.001
Macrophage, mg/ml	4.0 (4.2)	2.5 (1.4)	1.5 (1.1)	1.5 (0.8)	<0.001
Intercellular Adhesion Molecule 1, ng/ml	175.2 (81.5)	149.4 (61.4)	154.5 (84.2)	98.8 (22.2)	<0.001
IL6, pg/ml	2.4 (6.2)	0.3 (1.4)	0.7 (1.6)	9.0	<0.001
IL8, pg/ml	13.4 (65.6)	328.7 (1484.3)	52.7 (127.0)	4.4 (7.1)	<0.001
IL12 subunit p40, ng/ml	0.4 (0.2)	0.4 (0.2)	0.3 (0.3)	0.3 (0.2)	0.501
IL18, pg/ml	321.8 (157.6)	295.1 (171.5)	281.8 (204.3)	146.2 (60.8)	<0.001
* IL23, ng/ml	0.8 (1.0)	0.3 (0.7)	0.3 (0.7)	0.1 (0.4)	<0.001
Microfibrage Inflammatory Protein 3 alpha, pg/ml	23.1 (62.1)	20.2 (41.2)	14.1 (27.6)	0.0	0.008
Microfibrage Inflammatory Protein 3 beta, pg/ml	678.5 (595.4)	604.0 (382.2)	618.3 (447.8)	290.8 (192.3)	<0.001
** Matrix Metalloproteinase 3, ng/ml	14.2 (15.9)	11.9 (4.8)	14.1 (8.3)	13.5 (6.7)	<0.001
** Stem Cell Factor, pg/ml	180.1 (221.4)	262.6 (259.0)	289.1 (235.5)	173.2 (144.3)	<0.001
T cell Specific Protein RANTES, ng/ml	26.5 (15.1)	25.0 (16.8)	21.3 (10.5)	20.4 (7.6)	0.03
** Tissue Inhibitor of Metalloproteinase 1, ng/ml	262.1 (94.4)	197.5 (55.8)	186.7 (44.9)	141.7 (82.0)	<0.001
Th17 alpha, pg/ml	13.3 (30.2)	8.9 (30.3)	0.6 (4.3)	0.0	<0.001
** Th17 receptor 2, ng/ml	296.2 (740.4)	32.9 (433.1)	9.7 (5.2)	5.8 (1.8)	<0.001
* Vascular Cell Adhesion Molecule 1, ng/ml	1093.0 (445.3)	931.6 (307.9)	965.9 (392.9)	651.0 (141.1)	<0.001
Vascular Endothelial Growth Factor, pg/ml	492.3 (359.1)	439.6 (316.8)	394.2 (215.4)	281.7 (168.6)	<0.001
Vitamin D Binding Protein, µg/ml	538.1 (233.7)	414.2 (188.5)	433.3 (227.4)	354.4 (135.1)	<0.001
Von Willebrand Factor, µg/ml	161.2 (89.9)	110.8 (51.9)	109.2 (77.8)	55.5 (31.1)	<0.001
Monocyte Chemoattractant Protein 1, pg/ml	484.7 (229.0)	524.9 (369.2)	394.5 (174.3)	314.7 (139.6)	<0.001

**Conclusions:** Serum biomarkers have been shown to vary with gender and diagnosis. Further work is planned to evaluate their relationship to disease activity using outcome measures such as the BASDAI, and radiographic scoring, to better understand the role of each factor and combination of factors, and any causal link.

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**FRI0194** **ANKYLOSING SPONDYLITIS DISEASE ACTIVITY SCORE (ASDAS) BASED ON A QUICK QUANTITATIVE CRP ASSAY PERFORMS SIMILARLY WELL TO ASDAS BASED ON CONVENTIONAL CRP IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS**

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**Background:** The Ankylosing Spondylitis Disease Activity Score (ASDAS) is a composite index to assess disease activity in patients with axial spondyloarthritis (axSpA). According to the treat-to-target (T2T) recommendations for SpA, and the



ASAS/EULAR management recommendations for axSpA, the C-reactive protein (CRP)-based ASDAS is the preferred instrument for the assessment of disease activity in the process of making decision on modification of axSpA treatment in clinical routine. Currently, measurement of CRP by routine lab methods takes hours to days what seriously challenges the feasibility of T2T approaches in clinical routine and clinical studies.

**Objectives:** To compare the performance of the ASDAS based on a quickCRP assay (ASDAS-quick-CRP) with the ASDAS-routine-CRP and with the erythrocyte sedimentation rate (ESR)-based ASDAS in the assessment of disease activity in patients with axSpA.

**Methods:** This cross-sectional study was performed in patients referred with a suspicion of axSpA as part of the Identification of the Optimal Referral Strategy for Early Diagnosis of Axial Spondyloarthritis (OptiRef) study. Briefly, referred patients underwent a structured assessment of SpA features by a rheumatologist. CRP was measured in the central lab (routine turbidimetric assay, lowest detection level: 0.3 mg/L) and locally by ESR and a quantitative quick-CRP test (QuickRead go, Orion Diagnostica Oy, lowest detection level: 5 mg/L, test duration approx. 2 min.). If the quick-CRP was below the limit of detection, the value of 2 mg/L was used. In patients with the final diagnosis of axSpA, ASDAS-routine-CRP, ASDAS-quick-CRP and ASDAS-ESR were calculated.

**A**

		ASDAS-quick-CRP (n=46)			
		Inactive disease (<1.3)	Moderate disease activity (1.3-2.1)	High disease activity (2.2-3.5)	Very high disease activity (>3.5)
ASDAS-routine-CRP	Inactive disease (<1.3)	3 (6.5%)	0	0	0
	Moderate disease activity (1.3-2.1)	1 (2.2%)	9 (19.6%)	0	0
	High disease activity (2.2-3.5)	0	0	22 (47.8%)	2 (4.3%)
	Very high disease activity (>3.5)	0	0	0	9 (19.6%)

**B**

		ASDAS-ESR (n=44)			
		Inactive disease (<1.3)	Moderate disease activity (1.3-2.1)	High disease activity (2.2-3.5)	Very high disease activity (>3.5)
ASDAS-routine-CRP	Inactive disease (<1.3)	2 (4.5%)	1 (2.3%)	0	0
	Moderate disease activity (1.3-2.1)	0	7 (15.9%)	3 (6.8%)	0
	High disease activity (2.2-3.5)	0	1 (2.3%)	16 (36.4%)	5 (11.4%)
	Very high disease activity (>3.5)	0	0	2 (4.5%)	7 (15.9%)

**Abstract FRI0194 – Figure 1.** Comparison of the disease activity state ascertainment by ASDAS-routine-CRP vs. ASDAS-quick-CRP (A) and ASDAS-routine-CRP vs. ASDAS-ESR (B).

**Results:** A total of 132 patients referred with suspicion of axSpA had available routine and quick CRP levels; 46 patients of them were diagnosed with axSpA. Mean  $\pm$ SD routine/quick CRP serum levels were  $3.20 \pm 6.86$  mg/L and  $4.52 \pm 6.78$  mg/L, respectively, in the entire group, and  $7.09 \pm 10.18$  mg/L and  $8.22 \pm 10.11$  mg/L, respectively, in patients with axSpA. There was no significant difference ( $p=0.11$ ) in the mean values of ASDAS-CRP ( $2.76 \pm 0.97$ ) and ASDAS-quick-CRP ( $2.80 \pm 1.00$ ), while the ASDAS-ESR ( $2.90 \pm 1.02$ ) was significantly higher than ASDAS-routine-CRP ( $p=0.034$ ). In 43 of the 46 cases of axSpA (94%) the status scores for disease activity showed no difference between ASDAS-routine-CRP and ASDAS-quick-CRP – figure 1. Two patients were assigned to a higher and one to a lower disease activity category (DAC) according to ASDAS-quick-CRP as compared to ASDAS-routine-CRP. For ASDAS-ESR compared to ASDAS-routine-CRP, only 32/44 patients (73%) were assigned to the same DAC.

**Conclusions:** ASDAS-quick-CRP performed similarly well to ASDAS-routine-CRP with an agreement on the status score for disease activity of 94%, that was clearly better than the agreement of 73% between ASDAS-ESR and ASDAS-routine-CRP. With a duration of approximately 2 min the quick-CRP test is, therefore, feasible for immediate decision making as a part of clinical routine or clinical trials.

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FRI0195

### CLINICAL CHARACTERISTICS OF 897 CHINESE ANKYLOSING SPONDYLITIS/SPONDYLOARTHRITIS REAL WORLD COHORT: DATA FROM A CHINESE COHORT WITH SMART MANAGEMENT SYSTEM FOR SPONDYLOARTHRITIS (SMSP)

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**Background:** With increasing global popularity of smartphone technology, there is a great opportunity for using mobile phone applications for disease management. Smart Management System for Spondyloarthritis (SpA) (SMSP) created a smart management system for SpA using eHealth technologies in China.

**Objectives:** The aim of this study was to report major characteristics of Chinese ankylosing spondylitis patients derived from a large, longitudinal and prospective database with SMSP.

**Methods:** SMSP was designated for multicenter, consecutive, and prospective cohorts, including patients' mobile terminal, the physician workstation system, and communication system. Patients' portal was used for self-assessment prior visiting clinics, short message consultation, monitoring symptoms between clinic visits as well as uploading/downloading medical records, while physician' portal was used for professional assessment at clinic, scheduled visits reminder, sending self-management strategies at intervals and making recommendations and delivering patient-specific guidance to the individual. In this preliminary analysis, all patients fulfilled the modified New York criteria. All data were collected online using SMSP.

**Results:** From April 2016 to June 2017, data were extracted online from the physician workstation system in 4 rheumatology centres across China. There was a total of 2790 times self-assessment of BASDAI, BASFI performed by patients (median times=3.1, from 1 to 14) and a total of 1960 evaluation performed by the physician at the clinic (median times=2.1, from 1 to 10).

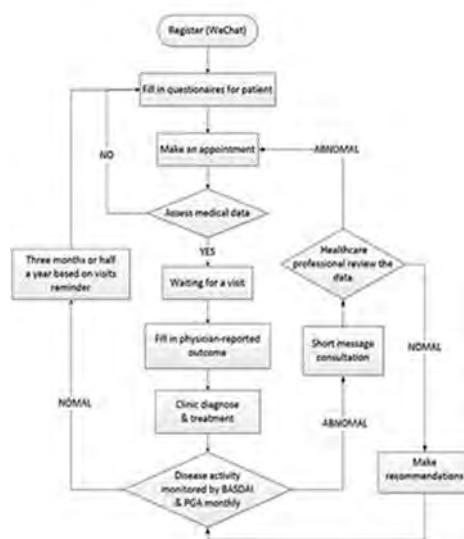
A total of 897 AS patients (mean age:  $30.8 \pm 8.8$  years, male 82.7%, HLA-B27 positive rate 88.0%) were recruited in this baseline analysis. The median disease duration was 7.1 (0.01 to 39.63) years. A history or current symptoms suggestive of acute anterior uveitis, psoriasis, and inflammatory bowel disease were observed in 17.2%, 2.6%, 7.1% of the patients, respectively. Differences in symptom duration ( $\leq 5$  years, 5 years to 10 years and  $>10$  years) were analysed. Acute anterior uveitis and inflammatory bowel disease were detected significantly more frequently in patients with symptom duration of  $>10$  years (27.0%, 11.0%, respectively), shown in table 1.

According to the ASDAS, at the baseline visit, 20.1% of patients achieved inactive disease, 30.8% with moderate disease activity, 37.3% with high disease activity and 10.6% with very high disease activity. The most commonly used medication was NSAIDs (98.9%). The patients using biological DMARDs possessed a percentage of 15.5%. 12.8% of the patients used etanercept which was the most commonly used biological DMARDs. 64.7% of the patients used conventional synthetic DMARDs.

**Abstract FRI0195 – Table 1.** Demographics and baseline clinical characteristics of the total cohort

Characteristic	Durations $\leq 5$ years (n=292)	5 years $<$ Durations $\leq 10$ years (n=322)	Duration $> 10$ years (n=283)	P value
Age, mean $\pm$ SD months	27.4 $\pm$ 8.2	29.0 $\pm$ 7.2	36.2 $\pm$ 8.5	$<0.001$
Age at disease onset, mean $\pm$ SD months	24.8 $\pm$ 8.3	21.7 $\pm$ 7.1	20.9 $\pm$ 7.2	$<0.001$
Duration, mean $\pm$ SD years	2.7 $\pm$ 1.4	7.3 $\pm$ 1.4	15.3 $\pm$ 5.4	$<0.001$
Male sex (%)	235 (80.5%)	274 (85.1%)	233 (82.3%)	0.313
HLA-B27 positive (%)	241 (88.9%)	254 (89.1%)	210 (85.7%)	0.411
Family history positive (%)	67 (22.9%)	84 (26.3%)	75 (26.7%)	0.523
Peripheral arthritis (current, %)	32 (11.5%)	37 (11.9%)	29 (10.7%)	0.907
Enthesitis (current, %)	52 (18.7%)	50 (16.1%)	35 (13.0%)	0.185
BASDAI, median (Q1-Q3)	1.9 (1.0-3.3)	2.0 (1.0-3.4)	2.2 (1.3-3.8)	0.023
BASFI, median (Q1-Q3)	0.8 (0.1-2.1)	1.1 (0.2-2.2)	1.5 (0.5-3.0)	$<0.001$
ESR, median (Q1-Q3)	9.0 (3.0-19.0)	10.0 (3.0-24.5)	13.0 (6.0-26.0)	0.050
CRP, median (Q1-Q3)	5.4 (2.6-15.0)	6.0 (3.0-16.8)	8.2 (3.2-18.1)	0.713
ASDAS-CRP, median (Q1-Q3)	1.8 (1.3-2.7)	2.0 (1.5-2.8)	2.2 (1.5-2.9)	0.095
BASMI, median (Q1-Q3)	0.0 (0.0-1.0)	0.0 (0.0-2.0)	2.0 (0.0-4.0)	$<0.001$
Acute anterior uveitis (%)	32 (11.0%)	46 (14.4%)	76 (27.0%)	$<0.001$
Inflammatory bowel disease (%)	11 (3.8%)	22 (6.9%)	31 (11.0%)	0.003
Psoriasis (%)	5 (1.7%)	9 (2.8%)	10 (3.6%)	0.387
NSAIDs (current, %)	216 (98.6%)	250 (99.6%)	222 (98.2%)	0.349
DMARD (current, %)	135 (61.6%)	168 (66.9%)	147 (65.0%)	0.483
TNF- $\alpha$ inhibitors (current, %)	35 (16.0%)	40 (15.9%)	33 (14.6%)	0.898





**Conclusions:** SMSM is an effective mobile interface to serve AS patients performing self-management as well as to supply physicians with valuable and reliable data with a minimal bias for online data collection and automatic quality controls. This large cohort may improve our knowledge of the characteristics, pathogenesis and natural course in Chinese patients with AS.

**Disclosure of Interest:** None declared

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#### FRI0196 TRADITIONAL DXA UNDERESTIMATES BONE MINERAL DENSITY OF THE SPINE IN AXIAL SPONDYLOARTHROPATHY

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**Background:** Axial spondyloarthritis (axSpA) is an inflammatory arthritis which can lead to new bone formation (syndesmophytes) and ankylosis of the spine. Osteoporosis is a recognised feature of axSpA, but can be challenging to diagnose. Traditional dual-energy x-ray absorptiometry (DXA) in the antero-posterior (AP) projection of the spine can overestimate bone mineral density (BMD) due to the presence of syndesmophytes, potentially under-diagnosing osteoporosis. There is a real need to find an accurate method to assess BMD in axSpA patients. Lateral DXA of the lumbar spine is unaffected by syndesmophyte formation and may be a promising tool.

**Objectives:** The aim of this study is to:

1. investigate different projections of DXA of the lumbar spine in axSpA patients
2. assess the effect of syndesmophytes on spine BMD.

**Methods:** AxSpA patients were assessed with clinical exam, questionnaires and laboratory investigations. The burden of syndesmophytes on lateral x-rays of the lumbar and cervical spine was assessed with the validated modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) score, which ranges from 0–72 (higher scores indicate more severe disease). DXA was performed of the spine in both the AP and lateral projections. SPSS was used for statistical analysis.

**Results:** One hundred patients with axSpA were recruited: 78% (n=78) male, mean (SD) age 52<sup>12</sup> years, disease duration 26<sup>13</sup> years, 85% (n=85) fulfil modified New York criteria. The median (IQR) mSASSS score was 10.<sup>33</sup>

Lumbar spine BMD was lower when measured by lateral DXA rather than AP (0.76 v 1.11 g/cm<sup>2</sup>, p<0.01). Lateral DXA detected more cases of spinal osteopenia or osteoporosis than AP (21% v 44%, p<0.01). Lateral spine BMD reduced with longer duration of disease (r=-0.3, p=0.02), whereas AP spine BMD increased with age (r=0.3, p=0.01). Women had significantly more cases of osteoporosis at the lumbar spine than men when measured by lateral DXA (32% v 12%, p=0.02), but not by AP DXA.

A higher mSASSS, reflecting more syndesmophytes/new bone formation, was associated with a rising AP spine BMD (r=0.5, p<0.01), but had no effect on lateral spine BMD. The gap between AP and lateral spine BMD, i.e. when AP BMD was higher than lateral BMD, increased significantly (p<0.05) with increasing age (r=0.38), disease duration (r=0.37) and mSASSS (r=0.52). mSASSS was the strongest independent predictor of a difference between AP and lateral BMD measurements, suggesting that syndesmophyte formation interferes with AP DXA assessment of the spine.

**Conclusions:** AP DXA of the spine is affected by a higher burden of syndesmophytes (new bone formation), raising concerns that traditional DXA assessment

may miss cases of osteoporosis. We suggest that lateral DXA of the spine may be a more accurate tool to detect osteoporosis in axSpA patients.

**Disclosure of Interest:** None declared

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#### FRI0197 ASSOCIATION OF THE ELECTROCARDIOGRAPHIC DISTURBANCES WITH AORTIC ROOT DILATION IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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**Background:** Ankylosing spondylitis (AS) is a disease with very characteristic extraarticular organ involvements. Cardiac conduction disturbances and aortic root diseases are some of the most particular manifestations of this disease<sup>1</sup>. The most frequent conduction disturbances are atrioventricular blocks (AVB), bundle branch blocks (BBB) and intraventricular conduction disturbances (IVCD)<sup>2</sup>. The prevalence of AVB is 3% and 8% for IVCD in the general population<sup>3</sup>. In some cross-sectional studies of the AS population<sup>4,5</sup> the prevalence was reported to be around 4.6%–9% for AVB and 4%–29% for IVCD. Some studies propose that there may be a relation between the conduction disturbances and the inflammation of the aortic root due to disease activity<sup>6,7,8</sup>.

**Objectives:** This study aims to evaluate association between the electrocardiographic alterations (AVB, BBB, IVCD) and aortic root dilation in patients with AS.

**Methods:** Out of a registry of 118 patients from a spondyloarthritis consultation, we selected patients with AS according to New York criteria. We included those patients who had undergone an electrocardiography (EKG) and an echocardiography, in order to rule out heart disease or to check up because of long term AS. Demographical and clinical data (cardiovascular risk factors, past heart disease, presence of arthritis, enthesitis, dactylitis, uveitis and HLAB27) were collected. The EKG were reevaluated looking for IVCD, AVB or BBB by a blinded arrhythmologist. Echocardiographical data about aortic root dilation were collected using aortic root diameter adjusted by body surface area. We carried out chi squared analysis as well as a comparison of proportions. We summarised descriptive data of our sample in table 1.

**Results:** Out of 118 patients, 38 patients met inclusion criteria. Fourteen of them (36.8%) were women. The average age was 60.3 years old and mean disease duration was 19.62 years.

Conduction disturbances were present in 12 (31.5%) patients of whom 4 were AVB (10.5%), 5 BBB (13.2%) and 3 IVCD (7.8%). Aortic root dilation was found in 6 (15.8%) of the 38 patients.

The conduction disturbances showed a statistically significant association with aortic root dilation (chi square p=0.02). In comparison of two proportions, the prevalence of aortic root dilation in abnormal EKG group (0.67 IC95% 0.36%–0.97%) was significantly higher than normal EKG group (0.6 IC95% 0.36%–0.97) p=0.02.

Abstract FRI0197 – Table 1

Variable	Number (patients)/Proportion (%)
Women	14 / 36.84%
B27	29 / 80.56%
Arthritis	14 / 36.84%
Enthesitis	13 / 34.21%
Uveitis	5 / 13.16%
Aortic root dilation	12 / 31.5%
Aortic insufficiency	12 / 31.5%
Exsmoker	23.68%
Smoker	34.21%
Hypertension	21 / 56.76%
Dyslipemia	22 / 59.49%
Diabetes	10 / 27.02%
Valve disease	2 / 5.55%
Ischaemic disease	7 / 29.44%
AVB	4 / 10.52%
Left BB	1 / 2.63%
Right BB	3 / 7.89%
Anterior BB	1 / 2.63%
Intraventricular conduction disturbances	3 / 7.89%

**Conclusions:** The prevalence of aortic root dilation and conduction disturbances was higher in our sample than in the general population. In our

sample the presence of aortic root dilation and conduction disturbances (AVB, BBB, IVCD) had a statistically significant association. The principal limitations of this study are the small sample size and the retrospective nature in patient selection.

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FRI0198

### WHICH FACTORS INFLUENCE PSYCHOLOGICAL WELL-BEING OF PATIENTS WITH AXIAL SPONDYLOARTHRITIS? – DATA FROM A CROSS-SECTIONAL SURVEY LINKED TO INSURANCE CLAIMS

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**Background:** Psychological well-being is considered an important determinant of quality of life. Importantly, well-being is related not only to medical factors, but also to social and economic factors.

**Objectives:** The aim of this study was to examine the psychological well-being of patients with axial spondyloarthritis (axSpA) and its determinants.

**Methods:** A stratified random sample of subjects with a diagnosis of axSpA (International Classification of Diseases, Tenth Revision, [ICD-10] code M45) was drawn from German health insurance data to whom a postal questionnaire was sent asking about disease-related, psychological, and lifestyle factors as well as socioeconomic status. Additional information to verify the axSpA diagnosis was collected. The psychological well-being was assessed by the World Health Organisation Well-Being Index (WHO-5), which is considered a sensitive and specific screening tool for depression. The following established cut-offs on the WHO-5 were applied: >50: good well-being, no depressive symptoms, 29–50: mild depressive symptoms, ≤28: moderate-to-severe depressive symptoms. Information on comorbidities, drug prescriptions and non-pharmacological treatment was retrieved from claims data and linked to the questionnaire data.

**Results:** A total of 1736 persons with a confirmed axSpA diagnosis were included; mean age was 55.8 years and 46.3% were female. We found a mean WHO-5 score of 44.70 in axSpA subjects, which is considerably below the WHO-5 score of 69.95 reported among the population in Germany aged 41 to 60 years.<sup>1</sup> Using the cut-offs on the WHO-5, 533 persons (31%) were found to have moderate-to-severe depressive symptoms, 479 (28%) had mild depressive symptoms, and 724 (42%) had a good well-being. Persons with moderate-to-severe depressive symptoms had higher disease burden of axSpA, lower household income and reported more often a lack of exercise and a perception of suffering from stress (table 1). Multivariable logistic regression revealed that higher disease activity of axSpA, higher level of functional impairment, lower income, self-reported stress and lack of exercise, and younger age were associated with moderate-to-severe depressive symptoms.

**Abstract FRI0198 – Table 1.** Main demographic, disease-related, lifestyle and socioeconomic characteristics of patients and axSpA.

	Total N=1736	Depressive symptoms			P-value
		no N=724 (42%)	mild N=479 (28%)	moderate/severe N=533 (31%)	
Sex, female	45.5	42.0	50.8	49.7	0.0000
Age, years	55.820.1	57.420.4	54.120.5	55.120.4	<.0001
Symptom duration, years	25.220.1	26.820.5	23.020.8	24.320.8	0.0015
Duration since diagnosis, years	19.420.1	11.320.5	17.920.8	1820.6	<.0001
In rheumatologic care, %	48.1	39.5	47.2	54.0	<.0001
HLA-B27 positive, %	86.0	87.4	83.3	86.6	0.2816
BASDAI, 0-10	4.520	3.320.1	4.820.1	5.820.1	<.0001
BASFI, 0-10	4.120.1	2.820.1	4.220.1	5.620.1	<.0001
Inflammatory bowel disease (ever, self-reported), %	8.8	8.9	8.2	13.9	<.0001
Uveitis (ever, self-reported), %	27.3	28.7	28	24.9	0.3182
Psoriasis (ever, self-reported), %	13.1	12.1	16.8	17.7	0.0152
Body Mass Index, kg/m <sup>2</sup>	2720.1	26.820.1	2720.2	27.420.2	0.0972
Lack of exercise, %	24.4	19.0	23.3	30.8	<.0001
Suffering from stress, %	38.8	25.5	47.8	52.6	<.0001
Full-time employment, %	31.7	32.2	35.6	27.4	0.0187
Household income, €					
<1500	25.9	20.1	26.7	33.1	<.0001
1500-3200	36.0	35.0	38.3	35.2	
>3200	18.1	24.9	15.0	11.7	
Smoking, current, %	18.8	14.8	20.0	23.4	0.0006
Pharmacological treatment, %					
NSAIDs	56.7	50.8	60.4	68.6	<.0001
Non-opioid analgesics	22.6	16.2	20.8	20.3	<.0001
Opioids	1.9	0.4	1.5	2.4	<.0001
DMARDs*	17.1	15.5	19.1	17.3	0.2520
csDMARDs**	11.7	10.8	10.5	14.4	0.0818
Glucocorticoids	18.5	15.8	17.5	22.8	0.0046
No pharmacological treatment, %	22.1	30.3	21.2	11.8	<.0001

Values are presented as mean ± standard error of the mean for continuous characteristics and as percentages otherwise. P-values were assessed using analysis of variance for continuous characteristics and chi-square/di-square tests otherwise.

WHO-5, 5-item World Health Organization Well-Being Index; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; NSAIDs, Nonsteroidal Anti-inflammatory Drugs; csDMARDs, conventional synthetic Disease-Modifying Anti-Rheumatic Drugs; bDMARDs, biological Disease-Modifying Anti-Rheumatic Drugs.

\* DMARDs: 17.0% TNF blocker, 0.07% sacralinimab, 0.08% tocilizumab, 0.08% ustekinumab, 0.05% abatacept.

\*\* csDMARDs: 5.7% sulfasalazine, 0.6% methotrexate, 0.9% leflunomide, 0.6% azathioprine, 0.2% cyclosporin.

**Conclusions:** Moderate-to-severe depressive symptoms are frequent in patients with axSpA. They are associated with a high disease burden as well as sociodemographic factors. These findings highlight the need for the careful evaluation of depressive symptoms as a part of the management strategy for axSpA, helping to improve axSpA outcomes.

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FRI0199

### FUNCTIONING CATEGORIES BY ASAS HEALTH INDEX IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS AND CONCOMITANT FIBROMYALGIA

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**Background:** Ankylosing spondylitis (AS) is a chronic rheumatic disease that characterised by prevalent inflammatory spinal involvement. Concomitant fibromyalgia (FM) can significantly modify this condition. In 2014, ASAS Health Index and Environmental Factors (ASAS HI/EF) appeared as new tool to assess the health status of patients with spondyloarthritis, able to describe the total impairments, restrictions and functional limitation due to AS.<sup>1</sup>

**Objectives:** The aim of this study was to evaluate the functional status of patients with active AS with concomitant FM by the functioning categories of ASAS HI.

**Methods:** The study included 72 patients with AS according to the modified. New York criteria (1984) Fifty-nine were male (81.94%), average age 39.5±11.72 (M ±SD) years. FM was diagnosed by modified criteria of the American College of Rheumatology (2010) The disease activity we assessed by Ankylosing Spondylitis Disease Activity Score (ASDAS-ESR). We used Ukrainian version of ASAS HI/EF.<sup>2</sup> Functional categories were established as recommended.<sup>3</sup> We categorised patients into 3 functioning categories: normal functioning (ASAS HI ≤4), moderate impairment of functioning (>4 and ≤8) and severe impairment of functioning (ASAS HI >8).

**Results:** Twenty patients met the criteria for FM (27.78%). Disease activity according to the ASDAS-ESR in patients with AS and AS with concomitant FM was almost the same: 3.58±0.84 and 3.98±0.91. However, ASAS HI in patients with AS and FM was significantly higher than in patients with AS (7.3±1.22 vs. 5.8±1.84).

According to ASAS HI we divided all patients into functioning categories. 10 of 52 patients with AS (19.23%) had normal functioning, 39 (75%) were classified as patients with moderate impairment of functioning and 3 (5.77%) had severe impairment of functioning. In the group AS +FM patients with normal function were not found, while others were distributed in a ratio of 2:1–13 (65%) patients with moderate and 7 (35%) with severe impairment of functioning. It was revealed relationship between ASAS HI and disease activity ( $r=0.549$ ).

**Conclusions:** Concomitant FM impairs the functional status in patients with AS. High and very high disease activity in patients with AS is associated with functional disability according to ASAS HI functioning categories. ASAS HI is reliable and sensitive clinical tool for determining impairment of functioning in patients with AS.

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#### FRI0200 INSIGHT INTO THE QUALITY OF LIFE OF PATIENTS WITH ANKYLOSING SPONDYLITIS: REAL-WORLD DATA FROM A US-BASED LIFE IMPACT SURVEY

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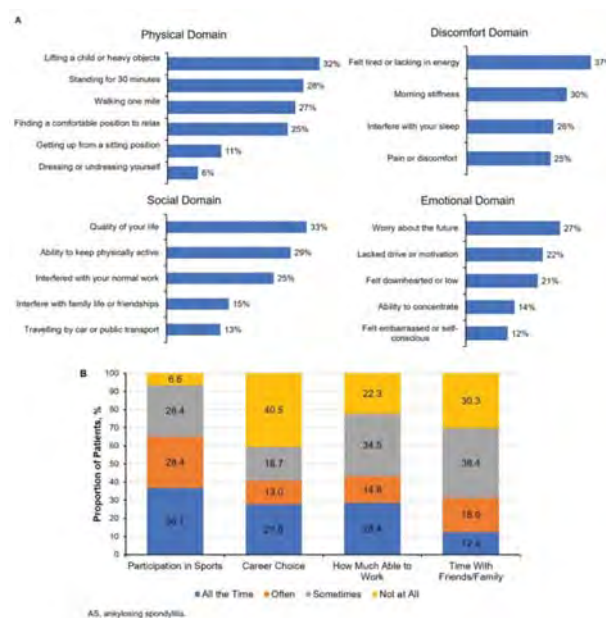
**Background:** While severe pain and stiffness are common hallmarks of ankylosing spondylitis (AS), disease progression is slow and not always visible; however, the quality of life (QoL) of patients with AS is still significantly impacted.

**Objectives:** To assess patient-reported impact of AS on QoL in the physical, discomfort, social, and emotional domains among US patients with AS in a real-world setting.

**Methods:** Descriptive data on demographics and QoL were collected from a random sample of patients associated with the Spondylitis Association of America (SAA). QoL measures were based on the Evaluation of Ankylosing Spondylitis Quality of Life (EASi-QoL) questionnaire (scale, 0–80, with higher score indicating more severe impact).<sup>1</sup> Between July 7 and December 31, 2017, 820 interviews were conducted with SAA contacts, including 720 completed via web survey (from 7750 emails) and 100 via follow-up over the phone (from 10 784 phone calls made to 5000 unique numbers). Of 820 participants who completed the survey, 716 self-reported receiving a diagnosis of AS from their doctor and were included in this study. Participants were queried on the impact of AS on their QoL within the day of survey participation with regard to the physical domain, and within the past week prior to participation with regard to the discomfort, social, and emotional domains. A 3:1 (male to female) weighting was performed to reflect the known

clinical prevalence that men are three times more likely to have AS compared to women.

**Results:** The mean age of the 716 respondents was 55.5 years; 46.9% were male. The most common locations of pain reported were the lumbar spine (86.8%), neck (84.1%), and hip joint (80.2%). The mean total EASi-QoL score was 28.9; overall, 34.7%, 31.7%, and 34.7% of respondents, respectively, reported low (EASi-QoL score 0–17), medium,<sup>18–35</sup> and high (≥36) impact of AS on QoL. Physical aspects of the disease contributed the most impact, with 41.9% of respondents reporting high impact of AS on the physical domain (EASi-QoL score ≥10). The proportion of respondents reporting high impact of AS (ie, the top 2 levels of impairment for each question) in the 4 QoL domains is shown in figure 1A. In several QoL aspects, AS impacts were reported more frequently by female vs male respondents, respectively, including lifting a child or heavy objects (43.2% vs 27.8%), worrying about the future (37.3% vs 23.5%), feeling tired or lacking in energy (46.4% vs 33.4%), sleep interference (32.7% vs 23.2%), trouble keeping physically active (35.9% vs 26.7%), standing for 30 min (34.9% vs 26.1%), and travelling by car or public transport (19.2% vs 10.5%). AS also impacted their lifestyle, as shown in figure 1B.



**Abstract FRI0200 – Figure 1.** (A) Proportion of respondents with AS reporting top two levels of impairment by their disease across 4 domains of disease, and (B) Patient-reported impact of AS on lifestyle. AS, ankylosing spondylitis.

**Conclusions:** Negative impacts in all QoL domains were reported, with a mean overall EASi-QoL score of 28.7. Gender differences were also pronounced in several aspects, including lifting a child or heavy objects, and worrying about the future. Incorporating subjective measures of disease via patient-reported outcomes should be considered with evaluation of disease progression.

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**FRI0201 HEALTHY INDIVIDUALS AT INCREASED RISK FOR AXIAL SPONDYLOARTHRITIS WOULD CONSIDER USING MEDICATION IN A PREVENTIVE SETTING**

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**Background:** Axial spondyloarthritis (axSpA) is a chronic inflammatory disease with a diagnostic delay of 5–10 years. Treating the disease in the pre-clinical phase before the disease becomes clinically manifest is not yet clinical practice, although initiatives to diagnose axSpA in an early phase such as the SPondyloArthritis Caught Early (SPACE) cohort and the pre-SpA cohort might enable early or even pre-clinical detection and thus treatment of SpA. Possibly, very early treatment might be able to stop the disease process hereby preventing the development of irreversible structural damage or, ideally, even disease onset.

**Objectives:** To study the willingness of individuals with an increased risk for SpA to use medication in a preventive setting.

**Methods:** Healthy first degree relatives of HLA-B27 positive axSpA patients from the Pre-SpA cohort completed a questionnaire consisting of different hypothetical scenarios varying in 1) the risk of developing axSpA, 2) the occurrence and nature of possible side effects, and 3) the effectiveness of the medication. Moreover, the survey included multiple choice questions about participants' perception towards SpA and preventive medication.

**Results:** The response rate was 81.5% (106 out of 130). Figure 1 shows the comparison of the different scenarios. The percentage of individuals willing to use preventive medication causing no side effects varied between 63.2% (with 30% SpA risk) and 91.5% (with 70% SpA risk). The percentage of individuals willing to use this medication varied between 27.4% (with 30% SpA risk) and 51.9% (with 70% SpA risk) if the preventive medication would possibly cause infections. This percentage was 32.1% (with 30% SpA risk) if the medication would possibly cause mild side effects. The percentage of individuals willing to use preventive medication that would cause a delay in onset of SpA of 10 years (with 70% SpA risk) was 72%. The willingness of individuals to use preventive medication was negatively influenced by their own risk assessment of developing SpA ( $B=0.16$ ,  $p=0.001$ ) and was not primarily influenced by costs (0.9%) or the route of administration (0%).

**Conclusions:** 1. Individuals at increased risk for SpA would consider using preventive medication.

2. Their willingness to use preventive medication is largely influenced by the formal likelihood to develop SpA, by their own perception of the disease and by the likelihood of side effects.

3. Their willingness to use preventive medication is not primarily influenced by costs and the route of administration.

**Disclosure of Interest:** None declared

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**FRI0202 INERTIAL MOTION SENSORS USING THE VIMOVE® SYSTEM IS A VALID METHOD TO ASSESS SPINAL MOBILITY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS**

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**Background:** Spinal mobility measures are recommended for the assessment axial spondyloarthritis (axSpA). Simple, low-tech tools as goniometers and metric tapes are commonly used, resulting in high variability and low accuracy of the measurements. More recently, advanced technological systems have facilitated the measurement of human mobility with high precision, such as motion capture systems like the UCOTrack and its index, the UCOASMI, validated for use in axSpA patients. The development of inertial measurement units (IMUs) has produce wearable, cheap and self-contained devices that can measure motion usually using triads of gyroscopes, accelerometers and magnetometers. Some of the mobility angles measured using motion capture systems can also be measured using IMUs placed in pre-defined anatomical locations.

**Objectives:** To evaluate the validity of IMUs using the ViMove® system for measuring spinal mobility in patients with axSpA.

**Methods:** We recruited 20 patients with axSpA from the HU Reina Sofia of Cordoba. The UCOTrack was used as the gold-standard system to obtain mobility measurements. UCOTrack measurements were compared with ViMove® measurements, a system that includes two IMU sensors located in the lumbar spine (pelvis and L1- figure 1) or in the neck (occiput and T3). Conventional metrology measures and patient-reported outcomes were also collected.

**Results:** The table presents the measurements obtained at the L1 and occiput levels. UCOTrack and ViMove® measurements were very similar, with Root

Mean Square Errors (RMSE) less than 10° and Variation Coefficients (VC) less than 10%. We found high intraclass correlation coefficients (ICC) between the two systems (0.84–0.99). Measurements with both systems correlated strongly and significantly with BASMI (0.60–0.92) and BASFI (0.51–0.84), but not with BASDAI.

Type of measurement	UCOTrack®	ViMove®	VC	RMSE	ICC
<i>Lumbar (L1)</i>					
Anterio flexion	103.6 (17.3)	99.0 (17.4)	4.4%	6.57	0.93
Extension	24.6 (9.3)	22.3 (9.6)	9.4%	4.22	0.90
Left rotation	27.7 (10.4)	27.4 (11.0)	1.1%	1.83	0.99
Right rotation	26.8 (10.4)	25.3 (10.1)	5.6%	3.14	0.95
Left lateral flexion	70.7 (13.9)	72.6 (16.6)	2.7%	8.71	0.84
Right lateral flexion	68.4 (15.4)	67.6 (16.7)	1.2%	7.87	0.88
<i>Cervical (occiput)</i>					
Flexion	50.9 (12.5)	52.3 (12.8)	2.8%	2.73	0.98
Extension	43.1 (16.0)	39.3 (14.4)	8.8%	5.44	0.94
Left rotation	66.1 (20.2)	63.8 (20.5)	3.5%	9.13	0.90
Right rotation	62.1 (19.2)	64.7 (21.7)	4.2%	9.72	0.89
Left lateral flexion	34.3 (15.8)	32.9 (15.5)	4.1%	7.77	0.88
Right lateral flexion	34.7 (15.9)	34.0 (16.3)	2.0%	7.10	0.90

All measures are expressed in degrees.



**Conclusions:** The ViMove®, an IMU based system, is a valid method to assess spinal mobility in patients with axSpA. There was excellent agreement between ViMove® and UCOTrack and a strong correlations with conventional metrology (BASMI) and patient-reported physical function (BASFI). IMU systems are more feasible than motion capture systems because they do not require a motion laboratory and results can be obtained more quickly in an objective and quantitative way. The ViMove® system has potential for use both in the clinical and research setting and further evaluation of its reproducibility and sensitivity to change should be undertaken.

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**FRI0203 THE LINK BETWEEN COPD AND ANKYLOSING SPONDYLITIS: A POPULATION BASED STUDY**

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**Background:** Ankylosing spondylitis (AS) is one of the most common and severe subtypes of the spondyloarthropathies. Extra-articular involvement among AS patients, including lung disease, has been described widely. Chronic obstructive pulmonary disease (COPD) has been linked to several autoimmune diseases, however, very few studies have investigated the association between AS and COPD.

**Objectives:** To assess whether an association exists between AS and COPD.

**Methods:** A population-based cross-sectional study was conducted using data retrieved from the largest electronic medical records database in Israel, the Clalit Health Services (CHS). Patients were defined as having AS or COPD when there was at least one such documented diagnosis in their medical records. The proportion of COPD was compared between AS patients and controls. A logistic regression model was used to estimate the association between AS and COPD in a multivariate analysis adjusted for age, gender and smoking status

**Results:** The study included 4076 patients with AS and 20 290 age- and sex-frequency matched controls. The proportion of COPD in AS patients was higher than in controls (46% vs. 18%, respectively,  $p < 0.001$ ). Multivariate logistic regression demonstrated a robust independent association between AS and COPD (OR 1.225,  $p = 0.031$ ).

**Abstract FRI0203 – Table 1.** Interactions between COPD, covariates by strata and AS

	ALL n=24 366	Controls n=20 290	AS n=4076	OR	P
COPD	628 (2.58%)	431 (2.12%)	197 (4.83%)	2.34 [1.97;2.78]	<0.001
Gender:	172 (1.95%)	117 (1.60%)	55 (3.74%)	2.40 [1.72;3.30]	<0.001
Female					
Gender: Male	456 (2.93%)	314 (2.42%)	142 (5.45%)	2.32 [1.89;2.84]	<0.001
Age: 18–44	14 (0.19%)	8 (0.13%)	6 (0.50%)	3.94 [1.27;11.6]	0.020
Age: 45–69	306 (2.42%)	189 (1.78%)	117 (5.70%)	3.34 [2.63;4.22]	<0.001
Age: 70+	308 (7.25%)	234 (6.83%)	74 (9.01%)	1.35 [1.02;1.77]	0.034
SES: Low	268 (5.35%)	193 (5.47%)	75 (5.04%)	0.92 [0.69;1.20]	0.542
SES: Medium	247 (4.72%)	154 (4.36%)	93 (5.47%)	1.27 [0.97;1.65]	0.077
SES: High	97 (3.46%)	68 (3.54%)	29 (3.27%)	0.93 [0.59;1.43]	0.729
BMI≤25	172 (4.11%)	111 (3.86%)	61 (4.64%)	1.21 [0.88;1.66]	0.242
BMI>25	338 (4.49%)	204 (4.20%)	134 (5.04%)	1.21 [0.97;1.51]	0.094
Smoking	454 (8.23%)	304 (8.34%)	150 (8.01%)	0.96 [0.78;1.17]	0.674

N: number of cases; AS: ankylosing spondylitis; BMI: body mass index ( $\text{kg}/\text{m}^2$ ); SES: socioeconomic class; COPD: chronic obstructive pulmonary disease.

Note: The table presents stratified analysis of COPD patients. Reference category for each stratum is patients without COPD.

**Abstract FRI0203 – Table 2.** Logistic regression – Covariates associated with COPD

Variable	OR	CI	P
Age (years)	1.078	1.071 1.085	<0.001
Gender:	1.042	0.863 1.263	.671
Male			
Smoking	9.862	8.174 11.949	<0.001
AS	1.225	1.017 1.472	.031

OR: odds ratio; CI: confidence interval; AS: ankylosing spondylitis; COPD: chronic obstructive pulmonary disease.

**Conclusions:** Our study supports an association between AS and COPD, further extending the link between COPD and autoimmune diseases. This finding highlights the importance of smoking cessation in AS patients and raises the question of whether COPD screening may be warranted.

**Disclosure of Interest:** None declared

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FRI0204

**RADIOGRAPHIC PROGRESSION OF SPONDYLOARTHRITIS PATIENTS AFTER 13 YEARS OF FOLLOW UP: DATA FROM THE REGISPONSER DATABASE**

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**Objectives:** To describe the radiographic evolution after 13 years of follow-up in a monographic consultation of patients with Axial Spondyloarthritis (EspAax) included in REGISPONSER at the Reina Sofia University Hospital in Córdoba.

**Methods:** Seventy eight SpA patients from the REGISPONSER registry were analysed in an observational study, which were evaluated for the first time in the year 2004–2005. The last x-rays analysis of the cervical and lumbar spine, pelvis and hips were recorded. Two independent observers evaluated the radiographs and calculated the BASRI index. The interobserver concordance was studied using Cohen's Kappa statistic. Finally, radiographic progression was assessed using the McNemar test.

**Results:** Sixty one SpA patients were radiographically evaluated at baseline and after 11 (1.7) years of follow-up. A complete radiographic study was recorded in 38 of them. The baseline characteristics, including BASRI values, as well as the treatment received are listed in table 1. The strength of the interobserver concordance in the radiographic analysis was considerable in hips ( $k = 0.77$ ,  $p < 0.001$ ) and almost perfect at the levels of the cervical spine ( $k = 0.88$ ,  $p < 0.001$ ), lumbar spine ( $k = 0.87$ ,  $p < 0.001$ ) and sacroiliac joints ( $k = 0.84$ ,  $p < 0.001$ ). The BASRIs and BASRII scores were 7.5 (2.9) and 8.8 (4.1) respectively. Moreover, during the follow-up, the BASRII was increased in 1.23 ( $p = 0.014$ ). Individual analysis of the different components of BASRI, showed that 42.1% of SpA patients got worse regarding the score corresponding to the cervical spine ( $p < 0.001$ ), 28.9% to the lumbar spine ( $p = 0.057$ ), 15.8% to the hip ( $p = 0.754$ ) and no worsening was found in sacroiliac ( $p = 0.500$ ).

**Abstract FRI0204 – Table 1.** Baseline characteristics and current treatment of the cohort N=38 for the radiographic study.

Type of SpA N(%)	AS 38 (100%)	BASRIs baseline Mean (DS)	6.44 (2.91) 7.60 (3.96)	Current treatment NSAIDs N(%)
				Daily treatment: 22 (57.9%)
		BASRII baseline Mean (DS)		Casual treatment: 13 (34.2%)
				Response: 35 (92.1%)
				Type: - 18 COX-2 selective (51.4%)
				- 7 Diclofenac (18.4%)
				- 5 Indomethacin (13.2%)
				- 5 Others(13.2%)
Time of evolution Diagnosis-inclusion in the registry Mean (DS) years	11 (7.1)	Degree of sacroiliitis Me (RI)	4 ( <sup>2-4</sup> )	Current treatment N (%) cDMARDs - Sulfasalazine 1 (2.7%)
Sex	34 (89.5)	Degree of cervical spine Me (RI)	1 (0-2)	- Methotrexate 1 (2.7%)
Male				Current treatment N(%) bDMARDs
Female	4 (10.5)			10 (26.3%) - 4
N(%)				Golimumab (10.5%)
				- 3 Etanercept (7.9%)
				- 1 Adalimumab (2.6%)
				- 1 Infliximab (2.6%)
				- 1 Secukinumab (2.6%)
Age Mean (DS) years	58.2 (7.9)	Degree of hips Me (RI)	1 (0-2)	

**Conclusions:** This study provides information related to the structural progression of patients followed in a monographic consultation of SpA after 13 years of follow-up. Radiographic evolution was significantly noticed in relation to the total score of the BASRI. However, analysing the individual scores it seems that the cervical spine was the segment where there was greater radiographic progression. We did not find worsening of BASRI in sacroiliac due to the fact that the most of patients already had an advanced degree of sacroiliitis in the first visit of the registry.

**Disclosure of Interest:** None declared

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FRI0205

### COMPARISON OF WORK DISABILITY, DEPRESSION AND QUALITY OF LIFE IN PATIENTS WITH ANKYLOSING SPONDYLITIS VS. PSORIATIC ARTHRITIS: INTERIM RESULTS FROM THE COMPLETE STUDY

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**Background:** Ankylosing Spondylitis (AS) and Psoriatic arthritis (PsA) are chronic progressive inflammatory diseases associated with severe pain and joint damage which may negatively impact patient reported outcomes (PRO), such as ability to work, depression and quality of life (QoL).

**Objectives:** To assess differences in PROs between patients with active AS and PsA requiring change in their treating regimen.

**Methods:** Patients eligible for the COMPLETE studies are anti-TNF $\alpha$  naïve adults, with active AS or PsA who require change in their regimen per the treating physician. Here, baseline data from patients enrolled between Jul/2011-Jun/2017 were included. PROs included the WLQ, BDI, and SF-12. Disease activity was classified as active/severe vs low/moderate based on BASDAI ( $\geq 4$  vs  $< 4$ ) for AS and based on DAS28 ( $\geq 5.1$  vs  $< 5.1$ ) for PsA. PsA patients were further stratified as per BSA  $\geq 3\%$  vs  $< 3\%$ . Differences between AS and PsA in WLQ, SF-12, and BDI were assessed with multivariate generalised linear models.

**Results:** 528 AS and 317 PsA (41% with BSA  $\geq 3\%$ ) patients were included. Upon multivariate adjustment, AS patients showed a trend towards higher scores in the SF-12 Physical Functioning subdomain compared to PsA patients with BSA  $< 3\%$  ( $p=0.069$ ) at baseline (table 1). Furthermore, PsA patients with BSA  $\geq 3\%$  had significantly higher scores in the SF-12 Role Functioning (Physical) subdomain ( $p=0.031$ ) and showed a trend towards higher scores in the SF-12 Mental Health subdomain ( $p=0.085$ ) compared to those with BSA  $< 3\%$ . No differences were observed between groups in any of the remaining SF-12 subdomains, WLQ, or BDI.

In terms of other determinants of PROs, high/very high disease state was associated with significantly higher BDI and worse scores in all WLQ and SF-12 dimensions and female gender was found to be a significant predictor of higher BDI scores and lower scores in the SF-12 physical functioning, vitality, social functioning and mental health subdomains.

Abstract FRI0205 – Table 1. PROs by disease type

Assessment	Parameter	AS (n=528)*	PsA w/BSA $\geq 3\%$ (n=130)*	PsA w/BSA $< 3\%$ (n=187)*
BDI	Total Score	12.6	13.8	13.7
WLQ	Mental Interpersonal Demands	24.9	27.2	26.7
	Output Demands	29.8	32.8	34.7
	Physical Demands	36.3	39.9	38.9
	Time Demands	37.8	41.1	42.0
SF-12	Productivity Loss Score	8.0	8.5	9.1
	General Health	50.2	49.8	45.3
	Physical Functioning	46.1	43.1	38.2
	Role Functioning (Physical)	43.0	47.9	39.2
	Bodily Pain	40.3	43.4	43.9
	Vitality	36.2	38.4	33.6
	Social Functioning	59.5	58.9	57.5
	Role Functioning (Emotional)	64.4	63.0	57.9
	Mental Health	56.7	58.6	52.2
	Physical Component Summary Scale	24.6	24.7	24.6
	Mental Component Summary Scale	18.9	18.9	18.8

\*Least square means adjusted for age, gender, disease duration, and disease activity.

**Conclusions:** AS and PsA affect multiple aspects of patients' lives without significant differences between the two diseases. Higher disease severity is associated with depressive symptoms and greater impairment in daily activities and work productivity. The impact of disease activity and treatment response over time on PRO will be evaluated in future analyses.

#### REFERENCE:

[1] JSS Medical Research, Montreal, Canada.

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FRI0206

### GENDER DIFFERENCES IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: RESULTS FROM THE ATLAS-2017

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**Background:** Recent data suggest gender differences on clinical manifestations, treatment access, and impact of the disease in patients with Axial Spondyloarthritis (axSpA). However, more data to confirm this hypothesis are needed.

**Objectives:** To assess gender differences on the physical, social, and psychological impact of the disease in patients with axSpA.

**Methods:** A sample of 680 axSpA patients was interviewed as part of the Spanish Atlas-2017 project. This aimed to promote early referral, improve healthcare, and the use of effective treatments in patients with axSpA. Among the recorded data, the following variables were collected: sociodemographic, smoking habits, degree of functional limitation in 18 daily activities (0–3 none, little, some, moderate), spinal stiffness level at cervical, thoracic, and lumbar spine (0–3 none, little, some, moderate), disease activity through BASDAI (0–10), risk of severe psychiatric illness using General Health Questionnaire – GHQ-12 (0–12), treatment received (NSAIDs and biological therapy), and disability. Differences for all of these variables between patients who are part of support group associations (associated-patients) and those who are not (non-associated patients) were tested using Mann-Whitney or Chi-square tests.

**Results:** In total, 323 (47.5%) men and 357 (52.5%) women participated in the survey. Compared with men, women reported a longer delay in diagnosis. Additionally, despite having a shorter disease duration, women reported significantly higher disease activity, worse functionality, and a higher risk of severe psychiatric illness than men. On the other hand, male patients had been treated more frequently with biological therapies and were significantly more likely to have had their disability legally recognised.

Abstract FRI0206 – Table 1. Sociodemographic and clinical outcomes of the disease characteristics stratified for the patient gender

	Men (mean $\pm$ SD or %)	Women (mean $\pm$ SD or %)	P
Age	48.1 $\pm$ 10.89	43.40 $\pm$ 10.29	<0.001
Marital Status (Married)	76.5%	66.9%	<0.05
Study Level (University)	31.9%	41.5%	<0.01
Smoker	56%	51.5%	0.2
Patient Association Membership	53.9%	35.6%	<0.001
Diagnostic Delay	7.85 $\pm$ 7.02	9.18 $\pm$ 8.19	0.07
Disease Duration	23.98 $\pm$ 12.48	17.91 $\pm$ 11.09	<0.001
HLA-B27 (Positive) (n=507)	83.4%	71.4%	0.001
Treatment			
- NSAIDs (without biology)	26.9%	32.5%	0.1
- Biology (with or without NSAIDs)	39.9%	33.1%	<0.06
BASDAI (n=442)	5.10 $\pm$ 2.14	5.88 $\pm$ 2.14	<0.001
Stiffness (High) (n=540)	44.4%	29.2%	<0.001
Functional Limitation (0–54) (n=605)	24.63 $\pm$ 13.10	30.55 $\pm$ 12.65	<0.001
GHQ-12 (n=474)	5.30 $\pm$ 4.52	6.19 $\pm$ 4.41	0.02
Inability to Work (n=344)	55.4%	33.3%	<0.001

**Conclusions:** Gender differences are observed regarding the impact of the disease in patients with axSpA. While women report a higher physical and psychological impact of the disease, men are more frequently legally recognised as disabled.

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**Disclosure of Interest:** None declared

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FRI0207

### THE INCORPORATION OF THE ANTERO-POSTERIOR LUMBAR SPINE VIEW IN THE MODIFIED STOKES ANKYLOSING SPONDYLITIS SPINE SCORE ONLY MARGINALLY IMPROVES DETECTION OF RADIOGRAPHIC SPINAL PROGRESSION IN AXIAL SPONDYLOARTHRITIS

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**Background:** The modified Stokes Ankylosing Spondylitis Spine Score (mSASSS) is considered currently as a gold standard of assessment of structural damage in the spine in patients with axial spondyloarthritis (axSpA). However, mSASSS takes into account only structural damage visible on lateral radiographs of the cervical and lumbar spine. Antero-posterior (AP) views might be able to detect structural damage not visible on lateral ones.

**Objectives:** To evaluate the performance of the extended mSASSS score including AP lumbar radiographs compared to the conventional mSASSS in detection of radiographic spinal progression in patients with axSpA.

**Methods:** A total of 210 patients with axSpA, 115 with ankylosing spondylitis and 95 with non-radiographic axSpA, from the German SPondyloarthritis Inception Cohort (GESPIC) were included in the analysis based on the availability of spinal radiographs (cervical spine lateral view, lumbar spine lateral and AP views), at baseline and year 2. Two trained readers independently scored lateral cervical and lumbar spine images according to the mSASSS system (0–72). In addition, left and right, upper and lower vertebral corners of vertebral bodies visible on lumbar AP radiographs (lower Th12 to upper S1) were assessed according to the same scoring system ranging from 0 (no abnormality) to 3 (bridging syndesmophyte). Thus, the extended mSASSS had a total range from 0 to 144. The reliability and the sensitivity to detect radiographic spinal progression of the extended mSASSS as compared to the conventional mSASSS were evaluated. Following definitions for progression were used: change of the absolute scores, change of  $\geq 2$  points, development of new syndesmophytes, and development of new syndesmophytes or growth of the existing syndesmophytes after 2 years.

**Results:** The reliability of both scores was excellent with intraclass correlation coefficients (ICCs) of 0.927 and 0.926 at baseline and 0.933 and 0.920 at year 2 for the extended and conventional mSASSS, respectively. The mean  $\pm$  SD score at baseline was 4.25 $\pm$ 8.32 and 8.59 $\pm$ 17.96 for mSASSS and extended mSASSS, respectively. The change score between baseline and year 2 was 0.73 $\pm$ 2.34 and 1.19 $\pm$ 3.73 for mSASSS and extended mSASSS, respectively (table 1). With the extended mSASSS score as compared to the conventional one, new syndesmophytes after 2 years were detected in 4 additional patients (1.9%), new syndesmophytes or progression of existing syndesmophytes – in 5 additional patients (2.4%), and progression by  $\geq 2$  points in the total score – in 14 additional patients (6.7%) – table 1.

**Abstract FRI0207 – Table 1.** Comparison of the conventional and extended mSASSS for the detection of radiographic spinal progression in patients with axSpA (n=210)

	Conventional mSASSS (range 0-72)	Extended mSASSS (range 0-144)
Mean score at baseline, mean $\pm$ SD	4.2 $\pm$ 8.3	8.5 $\pm$ 17.9
Mean score at year 2, mean $\pm$ SD	4.9 $\pm$ 9.5	9.7 $\pm$ 20
Mean change score, mean $\pm$ SD	0.7 $\pm$ 2.3	1.1 $\pm$ 3.7
Smallest detectable change	2.9	4.5
Standardized response mean	0.3	0.3
Change of $\geq 2$ units, n (%)	30 (14.3)	44 (21)
Total number of syndesmophytes at baseline, mean $\pm$ SD	0.9 $\pm$ 2.6	1.9 $\pm$ 5.2
Total number of syndesmophytes at year 2, mean $\pm$ SD	1.1 $\pm$ 3.0	2.2 $\pm$ 5.9
Development of new syndesmophytes, n (%)	16 (7.6)	20 (9.5)
Development or progression of syndesmophytes, n (%)	18 (8.6)	23 (11)

mSASSS, modified Stokes Ankylosing Spondylitis Spinal Score

**Conclusions:** The incorporation of the AP radiographs of the lumbar spine in the assessment of structural spinal damage provided only a relatively small improvement of detection of radiographic spinal progression in axSpA.

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FRI0208

### ANKYLOSING SPONDYLITIS QUALITY OF LIFE: DEFINING MINIMAL CLINICALLY IMPORTANT CHANGE

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**Background:** The Ankylosing Spondylitis Quality of Life (ASQoL) is a readable and simple to complete questionnaire relating to health-related quality of life (HRQoL) in ankylosing spondylitis (AS) and it has been shown to be a reliable and valid outcome measure<sup>1</sup>. Despite that this tool was used in various research settings over the last decade, the Minimal Clinically Important Difference (MCID) remains to be defined.

**Objectives:** Our objective is to define the MCID of ASQoL in subjects with axial spondyloarthritis(axSpA).

**Methods:** All subjects seen at the Spondylitis Clinic of the Toronto Western Hospital between July 2003 and January 2018 with a diagnosis of axSpA [AS or non-radiographic axSpA (nr-axSpA)] were included in this study. The ASQoL comprises 18 questions, and answers are dichotomized into yes/no. The weighted score for each item is 1 and poor HRQoL is associated with higher scores. The Medical Outcomes Study Short Form-36 (SF-36) is an instrument to assess for health status. Subjects completed ASQoL and SF-36 at the same time during yearly visits in the clinic. To determine MCID for ASQoL the SF-36 question 2 (SF-36 Q2: “compared to one year ago, how would you rate your health in general now?”) was used as an anchor measure. The answer to this question was incorporated in a 5 point Likert scale: “much worse”(–2 points), “somewhat worse”(–1 point), “about the same”(0 point), “somewhat better”(+1 point), “much better”(+2 points). An important change on the anchor was determined as +2 for improvement and –2 for worsening on the Likert scale. MCID was determined based on the optimal threshold that discriminated between change and no change (improvement or worsening) using receiver operating characteristic (ROC) curve analyses.

**Results:** A total of 1328 subjects were seen during the follow-up period. Of these, 66.2% were male, 75.3% were Caucasian, 61.8% had college or more education and the proportion AS/nr-axSpA was 84%/16%. At baseline, the mean age was 38.7 years and the mean disease duration was 14.9 years. On follow-up visit, patients who reported “much worse”, “somewhat worse”, “about the same”, “somewhat better” and “much better” had a mean change in ASQoL of respectively 3.85, 1.30, –0.24, –0.94 and –3.45 (table 1). Differences between mean change in ASQoL were statistically significant(p<0.02). The area under the ROC curve was 0.72 (95% CI 0.66–0.79) for subjects who worsened and 0.69 (95% CI 0.66–0.72) for those who improved. The ROC curve analyses showed that for thresholds of –2.5 and –3.5 points in deterioration there was a sensitivity/specificity of 0.536/0.841 and 0.474/0.890, respectively. Similarly, cut-offs of +2.5 and +3.5 points in improvement showed a sensitivity/specificity of 0.464/0.825 and 0.389/0.883, respectively.

SF-36 Q2	Mean ASQoL change	Standard deviation
Much improved (+2)	–3.45	4.98
Somewhat better (+1)	–0.94	3.87
About the same (0)	–0.24	3.23
Somewhat worse (–1)	1.30	4.20
Much worse (–2)	3.85	4.94

\* p-value<0.02 between all groups

**Conclusions:** We identified the MCID for ASQoL; a 3 points change for both improvement and worsening. Defining MCID will enhance the clinical utility of ASQoL in the management of patients with axSpA.

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**Disclosure of Interest:** None declared

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**FRI0209** **RECOMMENDATIONS FOR ACQUISITION AND CONSIDERATIONS FOR INTERPRETATION OF MRI OF THE SPINE AND SACROILIAC JOINTS IN THE INVESTIGATION OF AXIAL SPONDYLOARTHRITIS IN THE UK**

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**Background:** The use of magnetic resonance imaging (MRI) has been instrumental in the early recognition and characterisation of axial spondyloarthritis (axSpA). However, a recent survey in the UK showed that there is diverse practice in the use of MRI and limited knowledge of MRI features suggestive of axSpA among radiologists.<sup>1</sup>

**Objectives:** To develop clinical practice recommendations for the acquisition and interpretation of MRI of the spine and sacroiliac joints (SIJs) in the investigation of axSpA through a collaboration between rheumatologists and radiologists.

**Methods:** A working group comprising 9 rheumatologists and 9 musculoskeletal radiologists with an interest in axSpA was established. The EULAR standardised operating procedures were followed.<sup>2</sup> Two working group meetings were held, the first to define the scope of the exercise and the second to review the results of the Systematic Literature Review that informed the recommendations. An anonymised Delphi process was used to formulate the final set of recommendations. The level of evidence and strength of recommendation was added to the recommendations. The level of agreement by working group members was assessed using a numerical rating scale.

**Results:** A total of 2 overarching principles and 7 recommendations were formulated (figure 1). The first 3 recommendations address the MRI acquisition protocol, namely anatomical areas to be scanned and sequences to be used. The remaining 4 recommendations address the interpretation of active and structural lesions of the spine and SIJs.

OP1	The diagnosis of axSpA is based on clinical, laboratory and imaging features.
OP2	Some patients with axSpA have isolated inflammation of the SIJs or spine.
Rec1	When requesting an MRI for suspected axSpA, imaging of both the SIJs and the spine is recommended.
Rec2	T1-weighted and fat-suppressed, fluid sensitive sequences (including STIR, fat-saturated T2 or Dixon methods) are recommended when requesting an MRI for suspected axSpA.
Rec3	The minimum protocol when requesting an MRI for suspected axSpA should include sagittal images of the spine with extended lateral coverage and images of the SIJs which are coronal to the joint.
Rec4	In the SIJs, the presence of bone marrow oedema, fatty infiltration or erosion is suggestive of the diagnosis of axSpA. The presence of more than one of these features increases the diagnostic confidence of axSpA.
Rec5	In the spine, the presence of multiple corner inflammatory lesions and/or multiple corner fatty lesions increases the diagnostic confidence of axSpA.
Rec6	In the SIJs and/or spine the presence of characteristic new bone formation increases the diagnostic confidence of axSpA.
Rec7	The full range and combination of active and structural lesions of the SIJs and spine should be taken into account when deciding if the MRI scan is suggestive of axSpA or not.

**Abstract FRI0209 – Figure 1.** Overarching principles (OP) and recommendations (Rec)

**Conclusions:** A UK joint rheumatology and radiology consensus on the most appropriate MRI acquisition protocol and interpretation of images in the investigation of axSpA was achieved. This consensus will help standardise practices and ensure prompt and effective patient management in the diagnosis and treatment of axSpA.

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**FRI0210** **EXTRA-ARTICULAR MANIFESTATIONS ARE ASSOCIATED WITH WORSE QUALITY OF LIFE AND CLINICAL OUTCOME IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS**

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**Background:** In the 1960s, the association between axial spondyloarthritis (SpA) and extra-articular manifestations (EAMs), acute anterior uveitis (AAU),

inflammatory bowel disease (IBD) and psoriasis, was first reported. Still, knowledge of axial SpA disease outcome associated with the development of EAMs is scarce.

**Objectives:** To investigate the prevalence and 4 year incidence of EAMs and to explore associations of newly developed EAMs with disease outcome after 4 years of follow-up in a large cohort of axial SpA patients.

**Methods:** All consecutive patients fulfilling the modified New York criteria for AS or the ASAS criteria for axial SpA from the prospective observational Groningen Leeuwarden Axial Spondyloarthritis (GLAS) cohort with a baseline visit between November 2004 and December 2011 were included in the analyses. Baseline and follow-up data of EAMs from the GLAS database were verified in the medical records. EAMs were only recorded and used for analyses when a description of the diagnosis by an ophthalmologist, gastroenterologist or dermatologist was present. Prevalence and 4 year incidence of EAMs was calculated and comparative analyses regarding disease outcome was performed.

**Results:** 421 axial SpA patients were included with a mean age of 43.4±12.5 years, 65% were male, mean symptom duration was 17.4±11.7 years, 78% were HLA-B27 positive, mean ASDAS was 3.3±1.1 and 66% started TNF- $\alpha$  inhibitors at baseline. Of the 421 patients, 132 (31.4%) had a positive history of one or more EAMs: 104 (24.8%) AAU, 40 (9.5%) IBD, and 18 (4.3%) psoriasis. Of the 362 patients with 4 year follow-up data, 57 (15.7%) patients developed an EAM: 48 (13.3%) patients AAU, of which 13 (3.6%) had a first episode, 7 (1.9%) patients developed IBD, and 3 (0.8%) patients developed psoriasis.

Patients who developed a new EAM without a history of EAMs at baseline had higher ASQoL (mean 10.0 vs. 5.9, p=0.001), larger occiput to wall distance (median 6.3 vs. 2.0, p=0.021) and also the modified Schober test was more limited (mean 12.6 vs. 13.6, p=0.014) after 4 years of follow-up. The difference found for BASFI was not statistically significant (mean 4.4 vs. 3.4, p=0.12).

**Conclusions:** The prevalence rates of EAMs in our cohort are similar as found in other axial SpA studies. The 4 year incidence of EAMs was relatively low, possibly due to the relatively large proportion of patients starting TNF- $\alpha$  inhibitors at baseline. However, these axial SpA patients showed worse quality of life and clinical outcome than patients without a newly developed EAM.

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**FRI0211** **ASSOCIATION OF NEUROPATHIC-LIKE PAIN CHARACTERISTICS WITH CLINICAL AND RADIOGRAPHIC FEATURES IN PATIENTS WITH ANKYLOSING SPONDYLITIS**

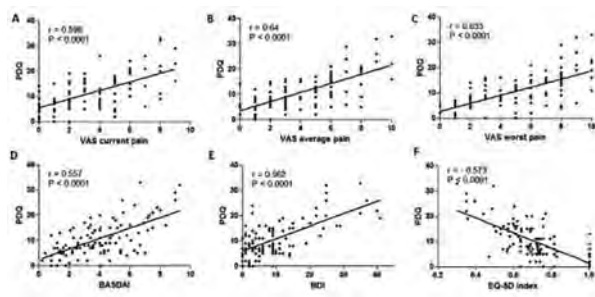
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**Background:** Ankylosing spondylitis (AS) is a chronic progressive inflammatory disorder that mainly involves the axial skeleton and causes chronic back pain. It is not unusual for patients with AS to have symptoms similar to neuropathic pain. There were several studies showing that various rheumatic diseases, including rheumatoid arthritis, primary Sjogren syndrome, and fibromyalgia, had neuropathic pain components. However, the existence of neuropathic pain in patients with AS has not been well investigated. The painDETECT questionnaire (PD-Q) is a relatively simple and self-administered screening tool for determining neuropathic pain and has high sensitivity, specificity, and positive predictive accuracy values.

**Objectives:** The aim of this study was to investigate the neuropathic pain component in patients with AS using PD-Q, and to assess the relation between neuropathic pain and disease characteristics of AS.

**Methods:** A single-centre prospective study was performed on 105 patients. The patients with AS completed three questionnaires: PD-Q, Beck depression inventory (BDI), and Euro Quality of life (EQ-5D) questionnaires. Patients were classified into three groups according to the PD-Q scores: nociceptive pain (NoP) (score <13), mixed pain (MP) (score 13–18), and neuropathic (NeP) (score >18) pain. Fifteen patients (14.3%) were classified in the NeP group, 22 patients (21.0%) in the MP group, and 68 patients (64.7%) in the NoP group. The questionnaires and clinical and radiographic findings were analysed.

**Results:** Patients with NeP and MP scored worse on Bath ankylosing spondylitis disease activity index (BASDAI), BDI, modified Stoke Ankylosing Spondylitis Spine Score, pain-visual analogue scale (VAS), EQ-5L index, and showed an increased prevalence of enthesitis and peripheral arthritis (table 1). There were no differences in objective inflammatory markers. PD-Q scores positively correlated with pain-VAS, BASDAI, BDI, and inversely correlated with EQ-5D index (figure 1). Presence of enthesitis, BDI, age, and pain VAS score independently associated with PD-Q scores.



**Conclusions:** The findings showed a neuropathic pain component in AS. Neuropathic pain in AS was associated with age, high disease activity, radiographic progression, enthesitis, peripheral arthritis, depression, and low quality of life.

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#### FRI0212 THE RELATIONSHIP BETWEEN ANTI-TNF THERAPY USE AND METABOLIC SYNDROME IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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**Background:** Ankylosing spondylitis (AS) is an inflammatory disease associated with accelerated atherosclerosis and the presence of metabolic syndrome (MetS) features. TNF- $\alpha$  is considered as one of the factors responsible for favouring insulin resistance and dyslipidemia, which are important features of the metabolic syndrome.

**Objectives:** In this study, we aimed to investigate the relationship between anti-TNF therapy and metabolic syndrome rate in patients with ankylosing spondylitis (AS).

**Methods:** AS patients who visited the outpatient rheumatology clinic between 2016 February and May were included in to the study. Systolic and diastolic blood pressures, body mass index (BMI), waist-hip circumference were measured. Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), fasting blood sugar, cholesterol panel were evaluated. MetS was defined by abdominal obesity, elevated blood pressure, elevated glucose, high triglycerides and reduced high-density lipoprotein cholesterol according to National Cholesterol Education Program's Adult Treatment Panel III report (NCEP ATP III) criteria. Duration of disease and use of anti-TNF was recorded. Bath Ankylosing Spondylitis Functional Index (BASFI) – Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) measurements were performed to assess the disease activity and functional capacities. Patients were divided into two groups as anti-TNF treated and anti-TNF naive. For comparisons between groups statistical analyses included descriptive statistics, *t*-tests and one-way ANOVA.

**Results:** A total of 223 patients were analysed. Of the total 223 patients, 78 (35%) were receiving anti-TNF therapy. Age distribution was similar in between groups. In the group receiving anti-TNF therapy, the number of male patients was higher (75.6% vs. 58.6%) and the duration of disease was longer (145.2 $\pm$ 90.8 vs 103.3 $\pm$ 97.1). Serum lipid levels, glucose, ESR, CRP, BASFI, BASDAI measurements, BMI and blood pressures were not significantly different in between the groups. MetS was present in 26 (33.3%) of 78 patients receiving anti-TNF and 29 (20%) of 145 patients in anti-TNF naive group. The effect of TNF- $\alpha$  inhibitor use on MetS was independent from the gender.

**Conclusions:** Patients with AS who received anti-TNF therapy were found to have a higher incidence of MetS than those who did not. Suppression of the catabolic effect of inflammation with treatment may have been effective in this result.

**Disclosure of Interest:** None declared

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#### FRI0213 THE PERFORMANCE OF 12 FLARE DEFINITIONS INCLUDING THE ASSESSMENT OF SPONDYLOARTHRITIS INTERNATIONAL SOCIETY (ASAS)-ENDORSED DEFINITION OF CLINICALLY IMPORTANT WORSENING IN ASDAS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS TREATED WITH ADALIMUMAB FOR 5 YEARS

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**Background:** In 2016 the Assessment of Spondyloarthritis International Society (ASAS) published proposals for 12 definitions of ‘flare’ (ref. 1) for patients with axial spondyloarthritis (axSpA). The definitions are based on pain, BASDAI and ASDAS (see table 1). In January 2018, ASAS published the ASAS-endorsed definition of clinically important worsening based on ASDAS ( $\Delta$ ASDAS $\geq$ 0.9) (ref. 2).

**Objectives:** The aim of this study was to describe the frequency of ‘flares’ as detected by the 12 flare definitions including the ASAS-endorsed definition.

**Methods:** Data from an investigator-initiated double-blinded randomised placebo-controlled trial of adalimumab versus placebo of 12 weeks with a 5 year open-label extension (NCT00477893, ref. 3) were used for this study. The number of patients experiencing a flare at each visit according to the 12 ASAS ‘flare’ definitions was recorded for 20 study visits performed from two weeks after initiation of treatment and to year 5.

**Results:** 52 patients started treatment and 41 (79%) patients completed the 5 year follow-up visit. The total number (percentage) of study visits where pain, BASDAI and ASDAS flares could be calculated was 879 (84.5%), 875 (84.1%) and 842 (81.0%), respectively. The mean (SD) number of patients with a flare per visit ranged from 0.7 (1.2) to 3.8 (2.2) and the median (inter-quartile-range (IQR)) from 0 (0–1) to 5 (3–7) (table 1). The mean number of patients per visit with a flare was significantly higher when the definition “change in ASDAS $\geq$ 0.6” ( $p<0.0001$  to  $p=0.001$ , *t*-test) and “change ASDAS $\geq$ 0.6 AND observed ASDAS $\geq$ 1.3” ( $p<0.0001$  to  $p=0.04$ ) were applied, and the mean number of patients was significantly lower when the BASDAI flare definitions were applied ( $p<0.0001$  to  $p=0.02$ ).

**Abstract FRI0213 – Table 2.** Patients per study visit fulfilling a ‘flare’ definition

Flare definition	Mean (SD)	Median (IQR)	Min-max	Number	Percent
$\Delta$ pain $\geq$ 2 AND final value $\geq$ 4	2.7 (1.7)	2 (1–4)	0–6	53	6.0
$\Delta$ pain $\geq$ 3	1.6 (1.0)	1 (1–2.75)	0–3	31	3.5
If observed value is $\geq$ 4: $\Delta$ pain $\geq$ 2 points. Otherwise: $\Delta$ pain $\geq$ 3 points	2.9 (1.7)	2.5 (1.25–4)	0–6	57	6.5
$\Delta$ BASDAI $\geq$ 2 points	1.9 (2.0)	1 (0–3)	0–7	37	4.2
$\Delta$ BASDAI $\geq$ 2 points AND final value $\geq$ 4	1.2 (1.9)	0 (0–1.75)	0–6	23	2.6
$\Delta$ BASDAI $\geq$ 3 points	0.8 (1.2)	0 (0–1)	0–4	15	1.7
$\Delta$ BASDAI $\geq$ 3 points AND final value $\geq$ 4	0.7 (1.2)	0 (0–1)	0–4	14	1.6
If observed value is $\geq$ 4: $\Delta$ BASDAI $\geq$ 2 points. Otherwise: $\Delta$ BASDAI $\geq$ 3 points	1.2 (1.9)	0.5 (0–1.75)	0–6	24	2.8
$\Delta$ ASDAS $\geq$ 0.6	5.0 (2.5)	5 (3–7)	0–9	100	11.9
$\Delta$ ASDAS $\geq$ 0.9 (endorsed by ASAS)	2.9 (2.2)	2.5 (1–4.75)	0–8	58	6.9
$\Delta$ ASDAS $\geq$ 1.1	2.1 (1.6)	1.5 (1–4)	0–5	42	5.0
$\Delta$ ASDAS $\geq$ 0.6 AND observed ASDAS $\geq$ 1.3	3.8 (2.2)	4 (2–5)	0–8	75	8.9

**Conclusions:** The frequency of flares as detected by the 12 ASAS flare definitions for patients with axial spondyloarthritis differed substantially. The ASAS-endorsed definition performed well.



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**FRI0214** **CLINICAL EVALUATION CORRELATES POORLY WITH ULTRASOUND AND MAGNETIC RESONANCE IMAGING OF JOINTS AND ENTHESES IN EARLY PERIPHERAL SPONDYLOARTHRITIS**

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**Background:** Enthesitis is a hallmark of spondyloarthritis (SpA), which occurs in 30% to 50% of psoriatic arthritis patients (pts).<sup>1</sup> Evaluation of tenderness at the site of an enthesitis with a standard palpation approach remains the gold standard for detection of enthesitis. However, inter- and intra-observer variability is rather high. All existing clinical enthesitis scoring systems lack validity. Imaging could avoid these drawbacks.

**Objectives:** To compare the performance of ultrasound (US) and magnetic resonance imaging (MRI) with clinical examination (CE) of joints and entheses in peripheral (p)SpA.

**Methods:** Clinical Remission in peripheral SPondyloArthritis (CRESPA) is a placebo-controlled trial of golimumab treatment in 60 early (symptom duration <12 weeks) pSpA pts. CE included tender and swollen joint count, dactylitis and enthesitis (evaluation of palpation tenderness) count. All pts underwent Power Doppler (PD)US of entheses and knee, talocrural (TC) and subtalar (ST) joints. Synovitis was scored according to the OMERACT-EULAR-US composite PDUS scale, giving a score of 0–3 for each joint. Enteseal sites were evaluated for hypoechoogenicity and intraenthesitis Doppler signal and were scored on a scale of 0–3. Modified whole-body MRI was performed at baseline. Bone marrow oedema (BME), synovitis and soft tissue inflammation (STI) were scored (scale 0–3) by 3 readers at several anatomical sites of pelvis and lower limbs. For each site a mean of the scores of the 3 readers was calculated.

**Results:** Abstract FRI0214 – Table 1. Prevalence of synovitis and enthesitis on CE, US and MRI

Joints/entheses	CE	US	MRI
Hip joint	3/60 (0)	-	4/60 <sup>1</sup>
Knee joint	21/60 <sup>6</sup>	25/60 <sup>6</sup>	24/60 <sup>7</sup>
Talocrural joint	14/60 <sup>1</sup>	9/60 <sup>1</sup>	24/60 <sup>13</sup>
Subtalar joint	7/60 <sup>2</sup>	10/60 <sup>12</sup>	15/60 (0)
Quadriceps tendon	10/60 <sup>2</sup>	9/60 <sup>1</sup>	4/60 (0)
Superior patellar ligament	8/60 <sup>2</sup>	8/60 <sup>1</sup>	7/60 <sup>1</sup>
Inferior patellar ligament			6/60 <sup>1</sup>
Achilles tendon	14/60 <sup>2</sup>	11/60 <sup>2</sup>	17/60 <sup>4</sup>
Plantar fascia	15/60 <sup>1</sup>	7/60 <sup>1</sup>	17/60 <sup>3</sup>

Prevalence of bilateral involvement is indicated between brackets.

Synovitis detected by US and MRI was most prevalent at knee joints (table 1). A discrepancy was noted between TC synovitis detected by CE, US and MRI. Enthesitis was most prevalent at Achilles tendon and plantar fascia. Regarding enthesitis, agreement between CE and US ranged from no (kappa –0.082) to moderate agreement (kappa 0.562). The highest agreement was observed at the enteseal sites of Achilles tendon (left 0.511, right 0.350) and plantar fascia (left 0.321, right 0.507). MRI did not correlate better with CE than US (kappa from –0.077 to 0.446). The correlation between MRI and US was overall poor and only in the Achilles tendon moderate (range –0.106 to 0.656).

**Conclusions:** There was a weak agreement between CE and imaging in detecting enthesitis. In general, US detects less enthesitis compared to CE, while MRI detects more.

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**FRI0215** **ASAS CONSENSUS ON SPANISH NOMENCLATURE FOR SPONDYLOARTHRITIS**

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**Background:** In the last three decades, major advances in the spondyloarthritis (SpA) field have been achieved leading to new terminology. Whilst this terminology is well established in English, there is concern about the disparity of translated words and acronyms in Spanish, which is used by more than 437 million people in 21 countries.

**Objectives:** To develop a consensus to standardise the use of the Spanish terms, abbreviations and acronyms employed in the field of SpA.

**Methods:** An international task force was created comprising of all ASAS Spanish-speaking native members representing 5 countries, the executive committee members of GRESSER, two methodologists, two linguists from Real Academia Nacional de la Medicina Española (RANM) and two patients from CEADE. First, a literature review spanning the last 15 years was performed to identify the conflicting terms/abbreviations/acronyms. This review examined available written sources in Spanish including manuscripts, ICF and ICD, guidelines, recommendations and consensus. A three-round Delphi method including a face-to-face meeting, then followed. The recommendations from the RANM based on the Panhispanic dictionary in medical terms were consistently followed throughout the process.

**Results:** Consensus was reached for 44 terms, abbreviations or acronyms related to the field of SpA. A Spanish translation was accepted for 6 terms and 6 abbreviations to name the disease or its subgroups (SpA, axSpA, nr-axSpA, pSpA, AS, r-SpA, PsA) and for 6 terms and 4 abbreviations related with the disease (enthesitis, sacroiliitis, IBP, MRI-SIJ, BME, mNY). Additionally, it was agreed not to translate into Spanish 15 acronyms because they are very well established (ASDAS, BASDAI, BASFI, BASMI, mSASSS, RASS, BASRI, BAS-G, ASQoL, PsAQoL, MASES, MASEI, PASI, PARS, ASAS). However, when mentioning these acronyms, it is recommended that the following structure is used: type of variable in Spanish and acronym and expanded form in English. With regards to the terms or abbreviations attached to 7 acronyms (ASDAS-CI, ASDAS-MI, ASAS-HI, ASASpr, ASAS 5/6, ASAS20, ASAS40 improvement criteria), it was agreed to translate only the expanded form and a translation was also selected for all of them.

**Conclusions:** A consensus in Spanish nomenclature for SpA has been developed by ASAS group. The implementation of this consensus across the Spanish-speaking community will be of substantial benefit, avoiding misunderstandings and time-consuming processes.

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**FRI0216** **DETECTION OF STRUCTURAL LESIONS ON T1 WEIGHTED MRI VERSUS RADIOGRAPHY OF THE SI JOINTS IN EARLY AXIAL SPONDYLOARTHRITIS: 2-YEAR DATA**

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**Background:** Sacroiliac joint (SIJ) structural damage may be evaluated using MRI, CT scan or radiographs.

**Objectives:** A post-hoc analysis of SIJ images from EMBARK (NCT01258738) and DESIR (NCT01648907) evaluated: <sup>1</sup> association between presence/absence of erosion on MRI and presence/absence of erosion or sacroiliitis on radiographs

at BL and Wk 104;<sup>2</sup> association between decrease/increase in erosion score on MRI and decrease/increase in erosion or sacroiliitis grade on radiographs, BL to Wk 104.

**Methods:** All patients had early axSpA. EMBARK: 12 wks double-blind placebo-control, then 92 wks open-label etanercept. DESIR: patients had no history of biologics and received no biologics for 104 wks. MRI images from both studies: combined, anonymized, and read per patient; radiographs combined, anonymized, read separately from MRI. Readers unaware of: image chronology, original cohort. Three experienced readers individually reviewed T1 weighted MRI using SpondyloArthritis Research Consortium of Canada SIJ Structural Score; 3 different readers assessed radiographic sacroiliitis using mNY grade; all were at level of each joint surface. Lesion presence/absence or decrease/increase recorded per patient if  $\geq 2$  of 3 readers agreed. Statistical analyses:  $\kappa$  coefficient of agreement, McNemar's test for discordance asymmetry.

**Results:** 224 patients had MRI and radiographs. At BL, concordance for presence or absence of erosion in 162/224 (72.3%) ( $\kappa=0.42$ ), table 1. Discordance: erosion more frequent on MRI (21.4%) than radiographs (6.3%;  $p<0.0001$ ). Wk 104 data similar to BL. Decrease in erosion more frequent than increase only on MRI; significantly more frequent on MRI than radiographs. Decrease in erosion on MRI significantly more frequent than decrease in sacroiliitis grade.

**Abstract FRI0216 – Table 1.** Concordance between MRI and Radiographs, BL and Wk 104; and Change BL to Wk 104

	N	Present/ Present n (%)	Absent/ Absent n (%)	Absent/ Present n (%)	Present/ Absent n (%)	$\kappa$ (95% CI)	P-value*
BL Erosion: MRI/ radiographs	224	50 (22.3)	112 (50.0)	14 (6.3)	48 (21.4)	0.42 (0.30– 0.53)	<0.0001
Wk 104 Erosion: MRI/ radiographs	222	44 (19.8)	119 (53.6)	15 (6.8)	44 (19.8)	0.41 (0.29– 0.53)	0.0002
BL: Erosion on MRI/ sacroiliitis on radiographs	224	60 (26.8)	97 (43.3)	29 (12.9)	38 (17.0)	0.39 (0.26– 0.51)	0.27
Wk 104: Erosion on MRI/sacroiliitis on radiographs	222	56 (25.2)	99 (44.6)	35 (15.8)	32 (14.4)	0.37 (0.25– 0.50)	0.71
Erosion decrease: MRI/radiographs	221	4 (1.8)	162 (73.3)	6 (2.7)	49 (22.2)	0.06 (–0.05, 0.16)	<0.0001
Erosion increase: MRI/radiographs	221	2 (0.9)	187 (84.6)	17 (7.7)	15 (6.8)	0.03 (–0.12, 0.18)	0.72
Erosion decrease on MRI/sacroiliitis grade decrease on radiographs	221	8 (3.6)	154 (69.7)	14 (6.3)	45 (20.4)	0.08 (–0.05, 0.21)	<0.0001
Erosion increase on MRI/sacroiliitis grade increase on radiographs	221	4 (1.8)	180 (81.4)	24 (10.9)	13 (5.9)	0.09 (–0.07, 0.25)	0.07

\*McNemar's test for discordance asymmetry.

BL, baseline; Wk, Week.

**Conclusions:** Findings of SIJ structural damage are observed differently on radiography and MRI in patients with early axSpA, and may appear to evolve differently.

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Employee of: InVentiv Health, B. Vlahos Shareholder of: Pfizer, Employee of: Pfizer, M. Dougados Grant/research support from: Pfizer, AbbVie, UCB, Merck and Lilly, Consultant for: Pfizer, AbbVie, UCB, Merck and Lilly

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## FRI0217 DIAGNOSTIC ASCERTAINMENT OF AXIAL SPONDYLOARTHRITIS IN PATIENTS PRESENTING WITH UNDIAGNOSED BACK PAIN: WHAT IS THE IMPACT OF MRI IN RHEUMATOLOGICAL PRACTICE?

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**Background:** In current rheumatology practice, the circumstances that prompt clinicians to order MRI in patients with suspected axSpA are unclear. In addition, the manner and degree to which MRI changes diagnostic ascertainment of axSpA in patients presenting with undiagnosed back pain has not been formally studied.

**Objectives:** 1. To determine whether any particular patient demographic and/or disease characteristics are associated with rheumatologist ordering of MRI. 2. To assess the impact of MRI evaluation on diagnostic ascertainment of axial SpA in patients presenting with undiagnosed back pain.

**Methods:** The multicenter Screening for AxSpA in Psoriasis, Iritis, and Colitis (SASPIC) Study is aimed at early detection of axial SpA in consecutive patients presenting with undiagnosed back pain to the rheumatologist. Consecutive patients with any one of psoriasis, iritis, or colitis diagnosed by the relevant specialist undergo routine evaluation by a rheumatologist. The rheumatologist determines the presence/absence of axial SpA and the degree of confidence in the diagnosis (–10 (definitely not SpA) to +10 (definite SpA) on a NRS) at 3 consecutive stages: 1. After the clinical evaluation; 2. After the results of labs (B27, CRP) and radiography; 3. After the results of MRI. Differences in patient demographics and/or disease characteristics between those who did or did not have MRI were assessed by chi-square and t-tests. We assessed the degree of diagnostic reclassification after each step at the categorical level (axial SpA yes/no) and also according to the degree of confidence.

**Results:** 244 patients (51.6% male, mean age 34.6 years, mean age at symptom onset 27.4 years, mean back pain duration 7.1 years, B27 +37.2%) were referred with AAU (29.9%), psoriasis (21.7%), Crohn's colitis (32.8%), ulcerative colitis (19.3%). A diagnosis of axSpA was made in 67.5% after stage 1 clinical evaluation and in 56.4% at stage 2 after review of the labs and radiography. MRI evaluation varied across sites (mean(range): 73% (16.7%>100%) of patients), ordered in 141 patients, and significantly more frequently in those with probable inflammatory type back pain (probability >5 (0–10 scale) ( $p=0.04$ ), when radiography was mNY- ( $p=0.005$ ) and in those without Crohn's colitis ( $p=0.001$ ). No differences in ordering of MRI were noted according to age, gender, disease duration, back pain severity, NSAID response, B27 status, or CRP level. In patients with completed MRI scans, a diagnosis of axSpA was made in 70.5% after stage 1 clinical evaluation, in 56.4% after review of the labs and radiography, and in 47.3% after MRI review. 24 (18.6%) were recategorized from SpA to non-SpA and 4 (3.1%) from non-SpA to SpA. Confidence in diagnostic categorization was increased after MRI.

Stage of Assessment	axSpA present n (%)	Mean (SD) confidence	axSpA absent n (%)	Mean (SD) confidence
1. Clinical only	n=91 (70.5)	5.5 (2.4)	n=38 (29.5)	3.4 (3.2)
2. Clinical plus labs and radiography	n=81 (62.8)	5.9 (2.9)	n=48 (37.2)	5.1 (3.6)
3. Clinical, labs, radiography, plus MRI	n=61 (47.3)	7.5 (2.9)	n=68 (52.7)	7.5 (2.5)

**Conclusions:** In a setting of undiagnosed back pain and higher risk for axial SpA, use of MRI is primarily driven by negative radiography. MRI was primarily helpful in ruling out SpA and reducing false positives.

**Disclosure of Interest:** None declared

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**FRI0218** VALIDATION OF ASSESSMENTS IN SPONDYLOARTHRITIS INTERNATIONAL SOCIETY (ASAS) MRI LESION DEFINITIONS IN AXIAL SPONDYLOARTHRITIS: DATA FROM THE ECHOGRAPHY IN SPONDYLOARTHRITIS COHORT (ECHOSPA)

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**Background:** The diversity of MRI lesions in the sacroiliac joints of patients with axial spondyloarthritis (axSpA) has only recently been appreciated and consistent terminology, descriptions, and definitions have not yet been internationally accepted. The ASAS MRI group has generated updated consensus lesion definitions and these now require validation to support widespread adoption for clinical practice and research.

**Objectives:** To assess the distribution by diagnosis, reliability of detection, and construct validity of active and structural lesions as defined by the ASAS-MRI group on MRI scans from the ECHOSPA cohort.

**Methods:** Consecutive outpatients with age <50 years and symptoms >3 months suggestive of SpA (inflammatory back pain, peripheral arthritis or inflammatory arthralgia, enthesitis or dactylitis, uveitis with B27 positivity, a family history of SpA) were enrolled in the prospective French ECHOSPA cohort. MRI scans from 412 of the 470 recruited cases were available for evaluation by 2 readers and an adjudicator. ASAS\_MRI\_def<sup>n</sup> were recorded in an ASAS consensus-derived eCRF that comprises global assessment (active and/or structural lesion typical of axSpA present/absent) and detailed scoring of individual lesions (SPARCC SIJ inflammation, SPARCC SIJ structural). Definite lesions were defined according to confidence  $\geq 3$  (0–4 scale). Reliability of detection of lesions assessed as present/absent by global assessment was analysed using kappa and detailed scoring of SIJ quadrants by intra-class correlation coefficient (ICC). For construct validity we calculated optimal cut-offs for bone marrow oedema (BME) and erosion that defined active and structural lesion typical of axSpA, respectively.

**Results:** At baseline, mean age of the 412 cases with MRI scans was 39.3 years, mean duration of symptoms was 2.5 years, 41.3% were HLA-B27 positive, and 63.2% were female. Active and structural lesions typical of axSpA were present in 9.7% and 10.8%, respectively, and ASAS positive MRI in 9.3%. Subchondral BME (13.6%) and erosion (9.4%) were the most frequent active and structural lesions, respectively. Active but not structural lesions were present in 3.0% while the converse was evident in 4.0%. AxSpA was diagnosed at baseline in 88.1% and all categories of active and structural lesions were higher in those with axSpA. Substantial  $\kappa$  values (95% CI) were evident for detection of these lesions with comparable reliability for active and structural lesions: active lesion (0.76 (0.65–0.88)), ASAS positive MRI (0.78 (0.66–0.89)), structural lesion (0.76 (0.65–0.87)). Detailed scoring per SIJ quadrant that reflect expert opinion as to what constitutes an active or structural lesion typical of axSpA are provided in the table 1.

Abstract FRI0218 – Table 1

Number of SIJ Quadrants	Active Lesion Typical of AxSpA	
	Sensitivity	Specificity
BME Score $\geq 2$	100%	90.27%
BME Score $\geq 3$	100%	95.14%
BME Score $\geq 4$	97.5%	96.76%
	Structural Lesion Typical of AxSpA	
	Sensitivity	Specificity
Erosion Score $\geq 2$	84.09	99.15
Fat metaplasia $\geq 2$	27.27	98.02
Backfill $\geq 2$	11.36	100
Ankylosis $\geq 2$	4.55	99.72

**Conclusions:** SPARCC BME score of  $\geq 3$  and Erosion Score  $\geq 2$  may optimally reflect active and structural lesions typical of axSpA, respectively. MRI lesions defined by the ASAS-MRI group can be reliably detected.

**Disclosure of Interest:** None declared

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**FRI0219** ANALYSIS OF THE DIFFERENT VALUE OF MAGNETIC RESONANCE IMAGING CHANGES IN THE SACROILIAC JOINTS FOR A DIAGNOSIS OF AXIAL SPONDYLOARTHRITIS AS JUDGED BY RHEUMATOLOGISTS AND RADIOLOGISTS

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**Background:** A classification of axial spondyloarthritis (axSpA) by the imaging arm of the ASAS criteria relies partly on the detection of a bone marrow oedema (BME) in the magnetic resonance imaging (MRI) of the sacroiliac joints (SIJ) suspicious of SpA.<sup>1</sup>

**Objectives:** To evaluate different types of MRI changes possibly relevant for a diagnosis of axSpA as judged by radiologists taking the rheumatologist's diagnosis as gold-standard.

**Methods:** Consecutive patients <45 years were included if they presented in a specialised rheumatologic centre with chronic low back pain (duration >3 months). Patients underwent a complete diagnostic workup including MRI of the SIJ. All clinical and laboratory information including images but no radiological reports was available for experienced rheumatologists to make a diagnosis of axSpA or non-axSpA. In parallel, two experienced musculoskeletal radiologists, blinded to patients' demographics and symptoms (except for back pain) evaluated all MR images without knowledge of the rheumatologist's diagnosis, by quantification of BME, fat metaplasia, erosions, sclerosis and ankylosis based on the Berlin SIJ score. The radiologists also stated whether the patient is likely to have axSpA or not, solely based on MRI findings.

**Results:** A total of 100 patients were recruited. The rheumatologist diagnosed axSpA in 54 patients (mean age 31.5 $\pm$ 8.0 years, 77.8% HLA-B27+, mean symptom duration 36.4 $\pm$ 42.0 months), while 46 patients were diagnosed as non-specific back pain (age 33.6 $\pm$ 7.1 years, 17.4% HLA-B27+, mean symptom duration 25.5 $\pm$ 31.6 months). According to the radiologists, 38 patients were identified as axSpA, 34 of which were also diagnosed as axSpA by the rheumatologist (overall agreement with the clinical diagnosis: 63%), and 4 patients were thought to have axSpA by the radiologist but not by the rheumatologist (disagreement with the clinical diagnosis: 8.7%). Similarly, the quantification of MRIs showed higher scores in patients diagnosed as axSpA by the rheumatologist (Tab.1). Only few patients had sclerosis or ankylosis.

From the radiologist's perspective, the calculated odds ratio (OR) for identification of axSpA by MRI only was 3.1 (95% CI:1.4–7.1) for the presence of BME, 3.5 (95% CI:1.4–9.0) for fat metaplasia, 2.8 (95% CI:1.1–7.0) for erosions, 2.0 (95% CI:0.7–5.5). For the combination of BME and any structural change, the OR was 3.7 (95% CI:1.6–8.5).

Tab. 1: Mean/median scores $\pm$ standard deviation for inflammatory and chronic lesions based on the Berlin SIJ score

	Lesion type	axSpA	non-SpA	p-value
Mean $\pm$ SD	Total score	12.3 $\pm$ 11.8	4.4 $\pm$ 4.8	p<0.001
	BME	3.3 $\pm$ 3.8	1.1 $\pm$ 1.5	p=0.001
	Fat metaplasia	3.4 $\pm$ 5.4	1.0 $\pm$ 3.0	p=0.004
	Erosions	3.2 $\pm$ 5.8	0.7 $\pm$ 2.1	p=0.011
Median	Sclerosis or Ankylosis	0	0	

**Conclusions:** This study reveals a discrepancy between the rheumatologist's and the radiologist's identification of axSpA, confirming that a diagnosis of axSpA in daily practice should not rely on imaging findings only. Nevertheless, the overall specificity of the radiologists was acceptable, although the sensitivity was relatively low. These data suggest also that not only BME but also fat metaplasia and erosions are of value to diagnose axSpA, beyond classification. The combination of MRI changes seems to enhance the discriminative diagnostic performance.

**REFERENCE:**

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**Disclosure of Interest:** None declared

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FRIDAY, 15 JUNE 2018

## Crystal diseases, metabolic bone diseases and bone diseases other than osteoporosis

FRI0220

### ULTRASOUND IN ASSESSMENT OF DISEASE COURSE IN GOUT: THE 24 MONTH SINGLE-CENTRE PROSPECTIVE OBSERVATIONAL STUDY

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**Background:** Today, despite the great potential of ultrasound (US) in gout, there is lack of longer duration US follow-up studies in this disease.

**Objectives:** The aim was to evaluate the 24 month's treatment effect of urate-lowering therapy on gout-specific US lesions and to determine the most representative target for US follow-up in gout.

**Methods:** A 24 month prospective observational single-centre study was carried out. Patients with gout diagnosis, confirmed by identification of monosodium urate crystals, with at least one tophus in the joint or tendon or one double contour sign (DC) on US, were selected for the study. The serum uric acid (SUA) level was assessed every three months. US evaluations of 36 joints and four tendons (m. triceps and patellar) were performed every six months starting from the baseline, by one rheumatologist, blinded to the SUA levels and clinical data. Outcomes were: change in US features (tophus, DC count and tophus size) in joints and tendons according median of SUA level during the follow up period from M3 to M24. Two stages of SUA levels were defined: high,  $\geq 360 \mu\text{mol/l}$ ; and low,  $< 360 \mu\text{mol/l}$  (considered as within the treatment target). Correlations between US findings modifications in different locations, and between US findings modifications and SUA levels, were estimated by the Pearson correlation coefficient.

**Results:** We included 40 gouty patients (mean  $\pm$ SD age 54.1 $\pm$ 9.7 years, 90.0% males, disease duration 8.5 $\pm$ 8.8 years). Mean  $\pm$ SD baseline SUA level was 504.8  $\pm$ 32.9  $\mu\text{mol/l}$ .

Among the 31 completers at M24, 21 (71%) achieved median SUA  $< 360 \mu\text{mol/l}$ . On month 24 the global number of patients with DC and tophus was reduced from 91% to 32% and from 100% to 64%, respectively. A total of sixty-four percent of patients in the study had not reached the US cure (DC or T being still found in at least one joint or tendon) after two years of treatment in the group with the median of SUA less than 360  $\mu\text{mol/l}$ . The comparison of crystal clearing process in joints and tendons showed an excellent correlation of mean percentage change in total tophus number ( $r=0.900$ ) and size ( $r=1.0$ ) in joints and tendons, investigating 21 gout patients who participated in all five US study visits during the 24 months of follow-up. A strong positive correlation was observed between the changes of tophus size in left and right first MTP joints ( $r=0.718$  [95% confidence interval: 0.370; 0.875],  $p<0.001$ ) also between the changes of tophus size in toe and total intra-articular tophus size, measured by US ( $r=0.726$  [95% confidence interval: 0.347; 0.925],  $p<0.001$ ) on month 24 (compared to month 0). It was found a negative correlation between the mean SUA during 24 months follow up and the reduction in tophus size on month 24 ( $r=0.602$ )

**Conclusions:** Only one third of patients with median SUA  $< 360 \mu\text{mol/l}$  were free of US gout signs after 2 years of treatment. Due to positive link between the change in tophus size in the first MTP joint and changes in the whole intraarticular urate pool, also tendons, the tophaceous deposition in the first MTP joint could be the most representative target for follow-up morphological analysis in gout clinical trials or monitoring the disease's activity in clinical practice with US.

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FRI0221

### GOUT IS ASSOCIATED WITH AN INCREASED RISK OF CANCER – A NATIONWIDE COHORT STUDY INCLUDING OVER 70,000 GOUT PATIENTS

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**Background:** In addition to the possible carcinogenic effect of chronic inflammation, gout patients may experience increased risk of cancer due to additional risk factors such as obesity, diabetes, sedentary lifestyle, smoking and increased alcohol consumption. There is limited data on the association between gout and different cancer types. We investigated the incidence of cancer among Danish gout patients compared to national cancer rates.

**Methods:** All patients diagnosed with gout in the period 1978–2015 according to the Danish National Patient Registry (including in- and outpatient hospital contacts) were linked with The Danish Cancer Registry to identify incident cancers. Follow-up for cancer started at date of first gout diagnosis and ended at date of cancer, death, emigration or end of 2015, whichever came first. Standardised incidence ratios (SIR) were calculated using sex and 5 year age and calendar-specific incidence rates for first primary cancers in the general population in Denmark.

**Results:** We observed 6205 first primary cancers among 70 591 gout patients. Compared to an expected number of 5308 in the general population, this corresponded to a SIR for any-cancer of 1.17 (95% confidence interval (CI): 1.14–1.20). SIRs were highest for cancer sites associated with smoking, obesity and excess alcohol consumption: mouth/tongue, pharynx, oesophagus, liver, pancreas, lung, pleura and kidney (table 1). Excess risks were also observed for colorectal cancer, breast cancer, endometrial cancer, multiple myeloma and other types of leukaemia but not for Hodgkin and Non-Hodgkin lymphomas.

**Conclusions:** Gout patients are at risk of cancer, especially cancer types associated with smoking, obesity and excess alcohol consumption, but also multiple myeloma and leukaemia. It is unknown if uric-acid lowering therapy and/or lifestyle changes reduce this risk.

Observed number (Obs) of incident cancers and standardised incidence ratios (SIRs) among 70 591 patients with gout.

Cancer site	Obs	SIR (95% CI)	Cancer site	Obs	SIR (95% CI)	Cancer site	Obs	SIR (95% CI)
<i>Buccal cavity and pharynx</i>			<i>Respiratory system</i>			<i>Male genital organs</i>		
Lip	14	0.74 (0.40–1.24)	Nasal, ear, sinus	11	0.89 (0.44–1.59)	Prostate	973	1.01 (0.95–1.08)
Tongue/mouth	88	<b>1.57 (1.27–1.93)</b>	Larynx	66	1.18 (0.91–1.50)	Testis	28	1.40 (0.93–2.02)
Pharynx	99	<b>1.93 (1.57–2.35)</b>	Lung	863	<b>1.12 (1.05–1.20)</b>	<i>Urinary tract</i>		
<i>Digestive organs</i>			Pleura	11	<b>5.53 (2.76–9.89)</b>	Kidney	214	<b>1.80 (1.57–2.06)</b>
Oesophagus	116	<b>1.32 (1.09–1.59)</b>	Melanoma	184	0.99 (0.85–1.15)	Renal pelvis and ureter	34	1.16 (0.80–1.62)
Stomach	149	1.04 (0.88–1.22)	Breast	385	<b>1.17 (1.06–1.29)</b>	Urinary bladder	462	1.07 (0.98–1.18)
Small intestine	20	1.28 (0.78–1.98)	<i>Female genital organs</i>			<i>Lymphatic and hematopoietic tissues</i>		
Colon	636	<b>1.18 (1.09–1.28)</b>	External	15	1.07 (0.60–1.76)	Hodgkin	10	0.84 (0.40–1.55)
Rectum	326	<b>1.11 (1.00–1.24)</b>	Cervix	29	1.21 (0.81–1.74)	Non-Hodgkin	124	<b>0.77 (0.64–0.92)</b>
Liver	158	<b>2.24 (1.90–2.62)</b>	Endometrial	114	<b>1.75 (1.44–2.10)</b>	Multiple myeloma	98	<b>1.37 (1.11–1.67)</b>
Gallbladder	50	1.26 (0.93–1.66)	Ovary	39	0.79 (0.56–1.08)	Lymphatic leukaemia	97	1.09 (0.88–1.33)
Pancreas	238	<b>1.41 (1.23–1.60)</b>				Other leukaemia	101	<b>1.59 (1.31–1.94)</b>

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**FRI0222 ASSOCIATION BETWEEN BLOOD LEAD LEVELS AND GOUT: THE UNITED STATES NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY 2007–2014**

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**Background:** Lead is a heavy metal with no physiological role in humans. It is well known that excessive exposure to lead is associated with cardiovascular, gastrointestinal and neurological complications. However, recent studies have demonstrated that lead can increase the tubular reabsorption of urate, resulting in hyperuricaemia and the development of gout.

Although blood lead levels are dropping in the US general population, the association between low blood lead levels and gout remains inconclusive.

**Objectives:** To evaluate the relationship between serum blood lead levels and the development of gout in the US general population.

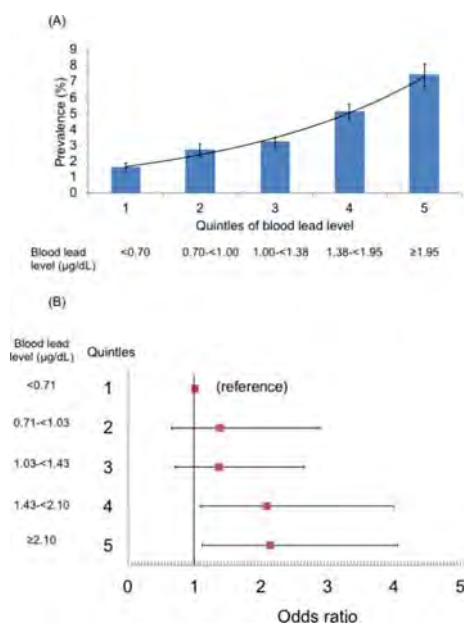
**Methods:** Adult participants with blood lead measurements and self reported gout in NHANES 2007–2014 were included in the analysis.

Results were analysed using SPSS complex sample module version 22. Logistic regression with sample weight adjustment was used to study the association between blood lead levels and gout. Odds ratio (OR) and 95% confidence interval (95% CI) were estimated. Sub-group analysis was conducted in participants with blood lead level <5 µg/dL.

**Results:** 18837 adult participants were included in the analysis. 18 270 participants had blood lead levels below 5 µg/dL (The current reference range for acceptable blood lead levels in healthy persons without excessive exposure to environment source of lead).

The prevalence of gout increased with blood lead levels. In the total population, the odd ratio of gout was 4.96 in subjects with blood lead levels above 2.21 µg/dL. After adjusting for body mass index, hypertension, renal function and use of diuretics, the odd ratio of gout was 2.65 which remained significant.

The subgroup analysis of subjects with blood lead levels below 5 µg/ml showed similar findings. The risk of gout is increased when blood lead levels are higher than 1.43 µg/dL.



**Abstract FRI0222 – Figure 1.** (A) Prevalence of gout according to quintiles of blood level. (B) Association between quintiles of blood lead level and gout at blood lead level <5µg/dL

**Conclusions:** Low blood lead levels are associated with gout. The risk of gout is increased when the blood lead level is higher than 1.43 µg/dL. Therefore, measures should be taken to minimise the environmental exposure to lead.

**Disclosure of Interest:** None declared

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**FRI0223 IS PERFORMANCE OF THE 2015 ACR/EULAR GOUT CLASSIFICATION CRITERIA AFFECTED BY DISEASE DURATION AND GENDER? RESULTS FROM AN ITALIAN MULTICENTRE STUDY FOCUSED ON THE MANAGEMENT OF CRYSTAL-INDUCED ARTHRITIDES (ATTACK STUDY)**

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**Background:** Gout is a common form of arthritis, but early disease and phenotypes related to gender<sup>1</sup> may favour diagnosis misclassification, unless monosodium urate (MSU) crystals are searched for in synovial fluid (SF). The 2015 ACR/EULAR gout classification criteria<sup>2</sup> were validated in Rheumatology and primary settings,<sup>3</sup> and the impact of disease features on performance were observed,<sup>4</sup> yet little studied.

**Objectives:** To assess the performance of the 2015 ACR/EULAR gout criteria in a cohort of crystal-induced arthritides stratified by disease duration and gender in a real-life setting in Italy.

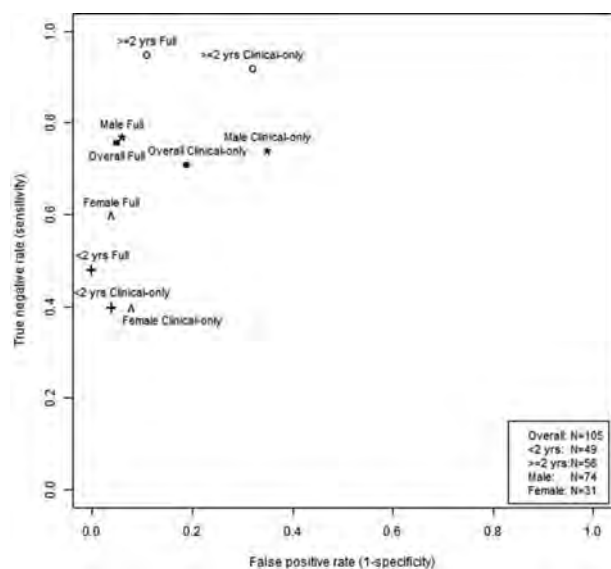
**Methods:** In/outpatients referring to Rheumatology Units for acute arthritis were enrolled into an ongoing multicentre cohort study designed for achieving improvement in the management of crystal-induced arthritis (ATTACK) by the Italian Society for Rheumatology. Gout was defined as MSU +SF (gold standard), irrespective of the clinical diagnosis, and the ACR/EULAR criteria were applied as full (all domains) and clinical-only set excluding imaging and SF analysis. To classify a patient as having clinical gout, the sufficient criterion (MSU +SF) was ignored and cutoff score ≥8 was used. Overall sensitivity and specificity were calculated. Disease duration (early if <2 years) was considered and gender effect explored.

**Results:** Of 199 adult patients (65±12 years, 75% male, 96% Caucasian) recruited in 11 hospitals, complete SF analysis and ACR/EULAR score were obtained in 105 (53%). MSU+ were 62/105 (59%), 47/62 (76%) were non-tophaceous and 25 (40%) early diseases. Calcium pyrophosphate (CPP) was the most prevalent crystal in non-MSU+. Details on performance (95% confidence intervals) are shown in table and on a receiver operating characteristic plot (figure 1).

**Abstract FRI0223 – Table 1**

	Sensitivity%		Specificity%	
	Full	Clinical-only	Full	Clinical-only
Overall n=105	76 (63–86)	71 (58–82)	95 (86–99)	81 (67–92)
<2 years n=49	48 (28–69)	40 (21–61)	100 (86–100)	92 (73–99)
≥2 years n=56	95 (82–99)	92 (78–98)	89 (67–99)	68 (44–87)
Male n=74	77 (64–87)	74 (60–85)	94 (71–100)	65 (38–86)
Female n=31	60 (15–95)	40 (5–85)	96 (80–100)	92 (75–99)

Overall good performance and high specificity of full and clinical-only sets were observed. In early disease criteria had high specificity, but low sensitivity, while performance was stable in longstanding gout. Specificity (clinical-only) and sensitivity were low when criteria were applied to males and females, respectively.



**Conclusions:** The overall performance of the 2015 ACR/EULAR gout criteria was good, particularly for the purpose of enrolling into trials. The impact of disease duration was confirmed and should be considered for misclassification issues as well as in clinical practice. Exploratory findings on gender effect seem relevant and deserve further studies.

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**Disclosure of Interest:** N. Ughi: None declared, A. Zanetti: None declared, P. Frallonardo: None declared, A. Hoxha: None declared, M. Lorenzin: None declared, A. Ariani: None declared, F. Ceccarelli: None declared, M. A. Cimmino Grant/research support from: Menarini, Speakers bureau: Menarini, C. Scirocco: None declared, B. Raffeiner: None declared, A. Bortoluzzi: None declared, A. Di Matteo: None declared, F. Furini: None declared, M. Manara: None declared, F. Salaffi: None declared, G. Carrara: None declared, C. A. Scirè: None declared, R. Ramonda: None declared

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**FRI0224 MANAGEMENT TO REDUCING LIVER FUNCTION IMPAIRMENT WHEN INITIATING FEBUXOSTAT FOR GOUT BASED ON THE PREDICTION NOMOGRAM**

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**Background:** Febuxostat is now used widely as urate-lowering therapy in gout, The most common adverse effects of which is liver function impairment (LFI). However, it is still not known in what conditions will the LFI happen.

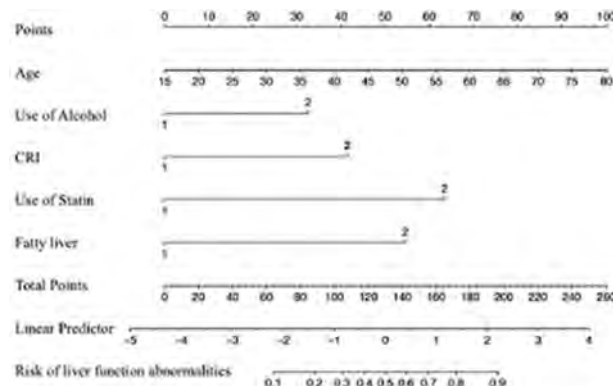
**Objectives:** To identify the potential factors associated with LFI and establish an effective prediction nomogram, and also to determine whether febuxostat with stepwise dose increase useful in reducing LFI in patients with high risk calculated basing the nomogram.

**Methods:** Part A: A retrospective study was performed among patients with gout. Nomogram was established based on logistic regression. The internal validation was performed via the area under the receiver operating characteristic (ROC) curve (AUC). Part B: In the follow-up prospective study, patients were divided into high-risk (>30%) group (stepwise dose increase of febuxostat from 10 to 40 mg/day) and low-risk (≤30%) group (fixed-dose febuxostat 40 mg/day) calculated basing the nomogram. Incidence rate of LFI were analysed.

**Results:** Part A: 306 subjects were recruited. LFI happened in 38 subjects after initiating fixed-dose febuxostat 40 mg/day. The logistic regression multivariate analysis indicated that age, use of alcohol, chronic renal insufficiency (CRI), medication use of statin and fatty liver were significantly associated with LFI. The AUC was 0.8424 (95% CI: 0.765–0.920). Part B: 108 subjects were recruited. LFI happened in 3/46 in high-risk group and 4/62 in low-risk group. The incidence rate of LFI after management basing prediction nomogram (7/108, 6.48%) was lower than previous study (38/306, 12.42%), with statistically difference (P<0.05).

**Abstract FRI0224 – Table 1.** Multivariate logistic regression analysis of variables (P<0.05) predicting LFI.

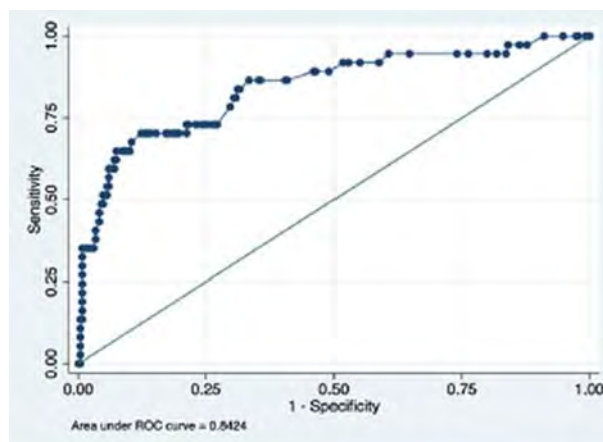
Variable	P value	Adjusted OR (95% CI)
Age	0.004	1.062 (1.020–1.106)
Gender	0.507	0.569 (0.109–2.996)
Chronic renal insufficiency (%)	0.038	5.905 (1.100–31.701)
Hypertension (%)	0.359	0.573 (0.174–1.884)
Coronary artery disease (%)	0.906	0.907 (0.181–4.552)
Hyperlipidemia (%)	0.638	1.395 (0.349–5.573)
Statin use (%)	0.021	6.608 (1.324–32.970)
Fatty liver (%)	0.024	6.005 (1.268–28.438)
Alcohol use (%)	0.028	2.882 (1.119–7.420)



The nomogram allows the user to obtain the probability of liver function impairment risk when initiating febuxostat. As an example, locate the patient's age and draw a line straight upward to the "Points" axis to determine the score associated with that age. Repeat the process for each variable, and sum the scores achieved for each covariate, and locate this sum on the "Total Points" axis. Draw a line straight down to determine the likelihood of liver function impairment. CRI – chronic renal insufficiency.

**Abstract FRI0224 – Figure 1.** Prediction nomogram for liver function impairment in gout treated with febuxostat.

The nomogram allows the user to obtain the probability of liver function impairment risk when initiating febuxostat. As an example, locate the patient's age and draw a line straight upward to the "Points" axis to determine the score associated with that age. Repeat the process for each variable, and sum the scores achieved for each covariate, and locate this sum on the "Total Points" axis. Draw a line straight down to determine the likelihood of liver function impairment. CRI – chronic renal insufficiency.



Internal validation using the receiver operating characteristic (ROC) curve. The area under the ROC curve was 0.8424, 95% confidence interval (95% CI: 0.765-0.920).

**Abstract FRI0224 – Figure 2.** Validation of the nomogram.

Internal validation using the receiver operating characteristic (ROC) curve. The area under the ROC curve was 0.8424, 95% confidence interval (95% CI: 0.765–0.920).



**Conclusions:** Predictors including age, use of alcohol, CRI, medication use of statin, and fatty liver, were combined to construct a nomogram. And the current nomogram might help to distinguish gouty patients with high-risk LFI when initiating febuxostat and avoid unnecessary adverse events. Stepwise dose increase of febuxostat in patients with high-risk calculated basing the nomogram effectively reduced incidence rate of LFI.

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#### FRI0225 ELECTRONIC CONSULTATION UTILITY IN THE MANAGEMENT OF GOUT

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**Background:** Gout is the most prevalent inflammatory arthritis in adults worldwide. Although it can be managed by primary care physicians (PCPs), complex cases often require rheumatology consultation. The average wait time for an initial rheumatology clinic visit varies from 38 days to 47 weeks after diagnosis. Utilising electronic consults (E-consults) allows for a swift two-way communication between referring and rheumatology physicians (pre-consult exchange). Rheumatologists can then triage patients to electronic management versus face-to-face rheumatological evaluation to provide timely insight to improve patient care.

**Objectives:** To analyse the effectiveness of gout management via E-consult compared to PCP or rheumatology management at the Veteran's Affairs Medical Centre in Long Beach (VALB), CA, USA.

**Methods:** A retrospective study of 171 VALB gout patients from 2009 to 2014 was constructed. Patients were placed into groups based on modes of management: PCP (n=48), direct rheumatology (n=67), or E-consult management (n=56). Electronic medical records were reviewed for a 24 month period from the first gout flare or E-consult date. The read-out for management effectiveness included change in frequency of gout flares, related emergency department (ED) and PCP visits, renal function (creatinine clearance, CrCl), and serum uric acid levels (sUA).

**Results:** Of the 56 E-consults, 43 cases were resolved electronically and 13 were converted to face-to-face rheumatology visits. The wait time for recommendations from E-consults was 2.1±4.6 days, and face-to-face rheumatology visits was 22.9±20.1 days after pre-consult exchange, vs 43.1±56.9 days for direct rheumatology consults. Both E-consult and rheumatology clinic patients had more gout attacks and related ED visits at baseline (p=0.08). They were also more likely to be treated with allopurinol, colchicine, febuxostat and corticosteroids than with NSAIDs alone (p<0.05). The number of gout attacks, and hence related PCP and ED visits, were significantly reduced when patients were managed by either a rheumatologist clinically or E-consult compared to PCP alone (p<0.05), with significant decrease in sUA and improved CrCl (p<0.001). Efficacy of E-consult management was comparable to rheumatology visits in the first 12 months, but at 18 months, direct rheumatology management superseded E-consults.

**Conclusions:** Gout management can be optimised when patients with uncontrolled disease are referred to rheumatology or E-consults within the first 12 months of active disease, and be transitioned to PCP management thereafter if disease is stable. E-consult serves as a reasonable alternative in managing gout with a shorter wait time for recommendations and rheumatology appointments. E-consults are an efficient means to address straight-forward clinical questions from PCPs, to expedite referrals to the rheumatology clinic.

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**Disclosure of Interest:** None declared

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#### FRI0226 ASSESSMENT OF THERAPY ADHERENCE AND TREATMENT RESULTS IN GOUT PATIENTS WHO ATTENDED SCHOOLS FOR PATIENTS AND IN THOSE WHO DID NOT

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**Background:** Gout is a poorly controlled disease despite the availability of effective treatment methods. One of the main reasons for its poor control is patients' low adherence to treatment, including due to insufficient knowledge of treatment principles.

**Objectives:** To assess adherence to therapy and results of treatment in gout patients who attended schools for patients and in those who did not.

**Methods:** All patients with crystal-verified gout were interviewed and invited to attend School for gout pts. Totally 301 pts with gout were observed, 36 (10%) females and 264 (90%) males, mean age 54.5±12.7 y., mean disease duration 9.02±1.12 y., with the gout diagnosis verified at average 48.71<sup>±12.60</sup> months after the onset, the target UA level <360 µmol/l initially was in 72 pts (24%).

All patients were divided into 3 groups: Group 1 included 111 (36%) patients who refused to attend the school, Group 2 included 90 (30%) patients who consented but failed to come, Group 3 consisted of 100 (34%) patients who attended the School (- 100 (34%).

The data from the questionnaires were used for baseline and on-treatment assessments of the following: patient's attitude to the disease, patient's compliance to treatment, satisfaction with quality of life, the fact of taking urate-lowering therapy, UA level control, achievement of the UA level of <360 µmol/l.

**Results:** In all 3 groups, after the visit to the doctor, the number of the patients taking urate-lowering therapy who reached the target level of uric acid, significantly increased, the maximum values were noted in the group who attended the School for gout pts. The UA target level achievement results in Group 2, of those who agreed to attend the School but never did for various reasons, were better than in Group 1 and comparable to that in Group 3. Table 1 presents the results of questionnaire survey at baseline and after one year.

Better adherence to treatment was noted in patients with poorer quality of life and a rational attitude toward their disease. The patients who report satisfaction with quality of life often decided to refuse to take their medications, visited the doctor less often and more seldom achieved the UA target level.

**Abstract FRI0226 – Table 1.** Parameters at baseline and after one year

parameters	Group 1 (patients who refused to attend the school), n=111		Group 2 (patients who consented but failed to come), n=90		Group 3 (patients who attended the school), n=100	
	baseline	after 1 year	baseline	after 1 year	baseline	after 1 year
Did not take urate lowering therapy, n (%)	86 (79%)	38 * (35%)	55 (62%)	12 (12%)	56 (56%)	8 (8%)
Monitored the level of UA, n (%)	62 (56%)	76 * (69%)	68 (75%)	72 (80%)	62 (62%)	90 (92%)
Achieved the target UA level<360 µmol/l, n (%)	8 (33%)	56* (51%)	14 (15%)	62 (69%)	13 (13%)	87 (87%)
Satisfied with the quality of life, n (%)	84 (67%)	85 (77%)	42 (47%)	75 (83%)	62 (62%)	95 (95%)
Not satisfied with the quality of life, n (%)	26 (33%)	5 (5%)	48 (53%)	3 (4%)	38 (38%)	3 (3%)

\*p<0,05 between the baseline and one-year

**Conclusions:** Patients' attendance of the School for gout pts increases their adherence to urate-lowering treatment and promote better quality of life. However, treatment adherence in gout patients largely depends on mental approach. Patients who are more actively involved in their health care achieve better results regardless of the source of information.

**Disclosure of Interest:** None declared

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FRI0227

**RISK FACTORS FOR SKIN REACTIONS TO ALLOPURINOL IN THE KINH POPULATION OF VIETNAM**

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**Background:** Allopurinol (ALLO) exposes to mild (M) and severe (S) cutaneous adverse reactions (CARs). SCARs have been associated with HLA\*B58 01 with various strength of across ethnicities. Little is known about ALLO tolerance in Vietnam (VN).

**Objectives:** The aim of this ongoing prospective study was to investigate risk factors, including HLA\*B-58 01, for MCARs and SCARs in the predominant Kinh ethnicity of VN

**Methods:** All included patients were Kinh Vietnamese. SCARs were recruited at Ho Chi Minh City hospitals, MCARs from the same departments and from the Vien Gut clinic at HCMC (specialised in gout care), and tolerant gouty patients (no skin reaction after at least 3 months from the last increment in ALLO dose) at the Vien Gut clinic. Clinical data were prospectively collected and HLA\*B-58 01 typing used the PG5801 DNA detection kit (Pharmigene-Taiwan). Fisher exact test for categorical variables and Kruskal/Wilkinson test for quantitative variables were used for statistics.

**Results:** 10 patients experienced a non-fatal SCAR. Toxic necrotic epidermolysis, Stevens-Johnson syndrome and mixed syndrome were diagnosed in 1, 8 and 1 patients respectively. 54 patients stopped ALLO because of MCAR. 112 ALLO tolerant patients were recruited. Table 1 shows the main features of interest in the 3 groups. The Odds ratio of HLA\*B-58 01 positive patients to develop SCARs was calculated at 171.2 (95% CI: 20; 7889)

**Abstract FRI0227 – Table 1.** Features associated with MCARs and SCARs

	SCARs (n=10)	MCARs (n=54)	Tolerant (n=112)	P value Global test	P value SCARs vs tolerant	P value MCARs vs tolerant
No Gout n (%)	5 (50%)	53 (98%)	112 (100%)	p<0,0001	p<0,0001	p=0,33
Females n (%)	2 (20%)	0	0	p=0003	p=0006	p=1
Age Mean (CI)	55 (CI :12)	47 (CI :12)	46 (CI :12)	p=0012	p=0,04	p=0,73
History of MCAR to ALLO	1/7 (14%)	1/52 (2%)	0	p<0,0001	p=0006	p=0,32
Diuretic intake n/known (%)	2/9 (22%)	1/52 (2%)	0	p=0002	p=0.005	p=0,32
ALLO dose/d Mean (CI)	345 mg/j (CI :142)	259 mg/j (CI :119)	356 mg/j (CI :114)	p<0,0001	p<0,0001	p=0.51
ALLO titration n (%)	0	49 (91%)	112 (100%)	p<0,0001	p<0,0001	p<0,0001
GFR<60 ml/ min n/known (%)	2/6 (33%)	1/51 (0.2%)	1/88 (0.01%)	p=0008	p=0,01	p=1
HLA-B*5801	10 (100%)	3 (5,6%)	6 (5,3%)	p<0,0001	p<0,0001	p=1

**Conclusions:** HLA\*B-58 01 was significantly associated with SCARs to ALLO in the VN Kinh population. Other known factors but not high ALLO dose were also associated. The only association with MCARs was lack of ALLO titration.

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FRI0228

**URATE CORRELATES TO CORONARY ARTERY CALCIFICATION BUT NOT TO INTIMA MEDIA THICKNESS**

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**Background:** Hyperuricemia is closely associated to cardiovascular disease (CVD) although it has not been definitively established whether it is a marker or a causative agent. Serum urate (SU) is strongly linked to the metabolic syndrome, hypertension, hyperlipidemia, kidney failure and higher BMI and higher levels are seen in men compared to women. Coronary artery calcification (CAC) is associated with future risk of atherosclerotic CV events in addition to the traditional cardiovascular risk factors (CVRF). CACs are present in atherosclerotic arteries and can be quantified and scored non-invasively by computed tomography. Carotid intima media thickness (CIMT) is a method of estimating atherosclerosis by assessing the level of arterial thickening present. CIMT can be used as a noninvasive marker of atherosclerotic disease with increasing CIMT linked to an increased risk of subsequent CV events. In the present study we have examined the relation between CACs, CIMT and SU in 1040 male and female with no history of myocardial infarction or stroke.

**Objectives:** To examine the association between SU and CAC and CIMT respectively in men and women separately.

**Methods:** We identified 1106 (552 males) individuals who were screened for traditional CVRFs, such as hypertension (HT), dyslipidemia (DL), diabetes mellitus (DM), smoking, physical activity (PA), educational level (EDU), socioeconomic status (SES), BMI, high sensitive CRP (hsCRP), kidney function by eGFR (eGFR). CACs, reflecting calcification of coronary arteries, was determined according to Agatston<sup>1</sup>. CIMT was calculated as the mean of CIMT of the left and right coronary artery. We measured SU and related quartiles of it to CACs and CIMT with multiple logistic regression analyses adjusting for traditional CVRFs. CAC was defined positive if  $\geq 1$ . CIMT was defined positive for  $\geq 75$  percentile. All study participants with a history of CVD (n=68, 44 male) were excluded.

**Results:** Of the 1106 participants, 68 were excluded due to history of CVD rendering a study population of 1040 individuals (508 males) with a mean age of 57.7 and 57.5 for male and female respectively. Age, BMI, EDU, SES, smoking status, PA, hsCRP, HT and DL showed no differences between sex while presence of CAC and diabetes was twice as common in men (table 1) and 65% of men displayed an eGFR below 90 mL/min compared to 12% of women (table 1a b). The three upper quartiles of SU (>306  $\mu\text{mol/L}$ ) all significantly ( $p<0.05$ ) predicted presence of CACs in male when adjusting for HT, DL, DM, smoking, PA, EDU, SES, BMI, hsCRP, eGFR and age in multivariate logistic regression, but not in women (table 2). CIMT showed no correlation to SU in men nor women.

**Abstract FRI0228 – Table 1.** Prevalence of gout I WSHCR by 2012–12–31, age above 20 years in total and by age and sex

Variables	Male, n=508	Female, n=532
Age, years, mean, (SD)	57.7(4.4)	57.5(4.3)
BMI, mean, (SD)	27.7(4.1)	26.8(4.9)
hsCRP (mean, SD)	2.2(3.4)	2.4(3.8)
CAC positive (%)	293(58%)	137(26%)
eGFR >90 ml/min	180(35%)	467(88%)
eGFR 60-90 ml/min	316(62%)	60(11%)
eGFR <60 ml/min	12(2%)	5(1%)
Smoking status, never	215(42%)	237(45%)
Smoking status, previous	206(41%)	191(36%)
Smoking status, active	86(17%)	102(19%)
Hypertension (%)	160(32%)	178(33%)
Diabetes mellitus (%)	39(8%)	21(4%)
Dyslipidemia (%)	144(28%)	121(23%)







**Conclusions:** CDS should be considered and craniocervical junction exposed in the context of acute cervical or occipital pain with stiffness and elevated inflammation markers not only in patients previously diagnosed with CPPD, but rather in diverse clinical settings. Particularly, CDS should be recognised as a possible alternative diagnosis in older patients referred with suspicion to giant cell arteritis because of new headache and elevated ESR/CRP. While generally believed to be a rare phenomenon, CDS was seen in 24 patients in 400-bed general hospital within 2 years and is probably widely underdiagnosed.

**Disclosure of Interest:** None declared

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#### FRI0231 STUDY OF URATE TRANSPORTERS IN PRIMARY HYPERURICEMIA AND GOUT

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**Background:** The urate transporters are one of the main genetic determinants of serum uric acid concentrations.

**Objectives:** In this study we investigated the effects of non-synonymous allelic variants of urate transporters in a cohort of patients with primary gout and/or asymptomatic hyperuricemia.

**Methods:** The cohort consisted of 165 gout patients (151 men, 14 women); 58 hyperuricemic individuals (39 men/19 women); 115 normouricemic controls were used for comparison. Gouty arthritis was diagnosed according to the 1977 preliminary criteria of the American College of Rheumatology. Coding regions of *ABCG2*, *SLC2A9*, *SLC22A11*, *SLC22A8*, *SLC17A3*, and *SLC17A1* genes were amplified and sequenced directly. To estimate the functions of the identified non-synonymous allelic variants, we used the protein prediction algorithms.

**Results:** In *ABCG2* gene, we detected nine non-synonymous variants (two common, seven rare including one novel): p.V12M, p.Q141K, p.R147W, p.T153M, p.K360del, p.F373C, p.T434M, p.S476P and p.D620N. The p.Q141K (rs2231142) variant had a significantly higher minor allele frequency (0.23) in the gout patients compared to the European-origin population (0.09) and was significantly more common among gout patients than among normouricemic controls (OR=3.15, p<0.0001). In addition, patients with non-synonymous *ABCG2* allelic variants had an earlier onset of gout (41.5 vs. 48 years, p=0.0478) and a greater likelihood of a familial history of gout (42% vs. 26%, OR=2.02, p=0.043)<sup>1</sup>. We identified novel intron variant c.689+1G>A which is associated with two abnormal splicing variants, leading to premature introduction of the stop codon, mislocalized *ABCG2* signal on plasma membrane and no urate uptake activity<sup>2</sup>.

In *SLC2A9* gene, seven missense variants were identified (six common, one rare): p.A17T, p.G25R, p.T275M, p.D281H, p.V282I, p.R294H, and p.P350L. In

*SLC17A3*, the analysis revealed common allelic variants p.A100T and p.G279R. Rare non-synonymous variants p.V202M and p.R343L were found in *SLC22A11*. Only one common missense variant p.T269I was identified in *SLC17A1*. In *SLC22A8* sequencing revealed three rare variants: p.R149C, p.V448I and p.R513G. The precise impact of *SLC22A11*, *SLC22A8*, *SLC17A3*, and *SLC17A1* in the context of hyperuricemia and gout in our cohort is unclear and will be further studied include functional characterisation of selected dysfunctional variants.

**Conclusions:** Genetic variants of *ABCG2*, common and rare, increased the risk of gout and had a significant effect on earlier onset of gout and the presence of a familial gout history. Genotyping the rare variants of *ABCG2* along with its common variants is essential for evaluating the individual risk for gout.

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#### FRI0232 ULTRASONOGRAPHIC FEATURES OF GOUTY DACTYLITIS OF THE HANDS

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**Background:** Dactylitis is a manifestation of gout that can occur on debut or throughout the course of the disease, although it is usually considered a sign of chronicity or a hallmark of long-term disease. Classically, the synovitis or tenosynovitis mediated by the deposit of microcrystals has been interpreted as an inflammatory effect due to proximity. The etiological prevalence based on imaging studies is unknown.

**Objectives:** To determine the prevalence of different ultrasonographic features of dactylitis of the hands in patients with gout.

**Methods:** A cross-sectional study was conducted based on a registry of ultrasound images of patients with gout and clinical dactylitis either in debut or throughout evolution. The selection of patients followed strictly clinical criteria based on the corresponding medical reports. All images were obtained in a medium-high gamma GE equipment and were obtained by the same operator over three years. Given that no comparisons were planned, no masking of the clinical situation of the patients was made in the eyes of the interpreter. The interpretation of findings was dichotomous in the determination of synovitis, tenosynovitis and enthesopathy according to EULAR definition criteria. The identification of tophi was made according to the definition of Avila Fernandes et al. (doi: 10.1007/s00256-010-1008-z) The overlapping of findings was counted independently at the moment of establishing the prevalence.

**Results:** We included images of 66 patients diagnosed with gout and with dactylitis of at least one finger at the time of the ultrasound evaluation. The mean age of the patients was 59.2 SD 4.3 years. Sixty-two patients were male. Of the total number of patients, 60 had tenosynovitis of the flexor tendinous apparatus (90.9%). Four of these patients also presented tenosynovitis of the tendinous extensor apparatus. No patient presented only extensor tenosynovitis. Enthesopathy was identified in 6 patients (9.1%), in no case did enthesopathy occur with power Doppler signal. Synovitis was identified in 43 patients (65.1%). Of these, in 13 patients a grade I was registered and in 26 a power Doppler signal was demonstrated. Tophi were identified in 16 patients (24%).

**Conclusions:** CONCLUSIONS: This is, as far as we know, the first iconographic study of gouty dactylitis based on ultrasound. According to our results, tenosynovitis of the flexors is the most frequent finding in gouty dactylitis while enthesopathy is rather rare. The presence of significant synovitis is the second most frequent finding while tophi as conditioning agents of synovitis were the least frequent finding. We understand that the knowledge of the echographic characteristics of gouty dactylitis can serve as a clinical guide when making therapeutic decisions in cases where this clinical sign lasts despite the control of other manifestations.

**Disclosure of Interest:** None declared

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**FRI0233 DOES GOUT PROTECT FROM PARKINSON'S DISEASE: A CASE-CONTROL STUDY FROM AN URBAN POPULATION**

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**Background:** It has been demonstrated that hyperuricemia protects from Parkinson's disease (PD), but this relation is controversial in patients with gout. Inflammatory properties of urate monosodium(UMS) crystals deposition that appears when uric acid(UA) levels exceed its solubility faces antioxidant and neuroprotective features of soluble UA. Both, UMS crystals deposition and hyperuricemia coexist in gouty patients.

There is several data that demonstrates that hyperuricemia protects from Parkinson's disease (PD). Results from different studies about the relation between them are controversial. Inflammatory properties of the urate crystals faces antioxidant and neuroprotective features of soluble UA. Both, UMS crystals and hyperuricemia coexist in gouty patients.

**Objectives:** To study if gout protects from Parkinson disease in a mediterranean urban population.

**Methods:** Primary care based matched case-control study. It has been carried out using the electronic clinical record database from the public health (Institut Català de la Salut) of the city of Barcelona. The database contains anonymous data from almost 1 million and a half people. Just people that were 40 years or older were studied. Were considered cases patients with a PD diagnose, or taking high specific anti-Parkinson's drugs (like l-dope, rasagiline, selegiline...), between 2006 and 2016. For every case we randomly selected four controls matched by gender and age. Data on risk factors was also collected for each individual (diabetes mellitus, hypertension, hypercholesterolemia and tobacco consumption before the PD diagnose), as well as age and gender. A multivariate logistic regression model was used to study the association of gout and PD adjusted by the presence of other risk factors. Adjusted Odds Ratios (aOR) and their 95% CI are provided.

**Results:** 21 789 persons with a PD diagnose and 87 156 controls were included. Mean age was 75.5 (SD 10.9) years. 55.6% were females. 2.5% of PD patients had a previous gout diagnose, compared to 4.8% of controls (p<0.001). Multivariate Logistic regression model showed for gout: aOR=0.55 (0.50–0.61). Diabetes mellitus: aOR=1.18 (1.14–1.23); hypertension: aOR=0.7 (0.72–0.77); tobacco: aOR=0.55 (0.52–0.58); high cholesterol levels: aOR=0.60 (0.58–0.61).

**Conclusions:** Gout shows a protective effect on the development of Parkinson's disease, pointing that the antioxidant and neuro protective effect of UA seems to overcome its inflammatory properties in gouty patients.

Gout shows a protective effect on the development of Parkinson's disease, pointing that the antioxidant and neuro protective effect of UA seems to overcome its inflammatory properties in gouty patients.

**Disclosure of Interest:** None declared

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**FRI0234 SEL-212: SELECTIVE MITIGATION OF ANTI-DRUG ANTIBODIES AGAINST PEGSITICASE TO CONTROL SERUM URIC ACID IN HYPERURICEMIC SUBJECTS**

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**Background:** We previously reported initial Phase 2 study results for 60 gout patients treated with SEL-212, a novel combination treatment comprised of pegsiticase (pegylated uricase) co-administered with a synthetic vaccine particle encapsulating rapamycin (SVP-R).<sup>1</sup> SEL-212 was well-tolerated, mitigated the formation of anti-drug antibodies, and enabled sustained control of serum uric acid (sUA) levels in most subjects.<sup>1</sup> In this ongoing study, new treatment cohorts involving higher SVP-R dose levels and extended combination regimens were introduced.

**Objectives:** To assess the tolerability and impact on sUA levels and ADA formation of escalated and expanded doses of SEL-212, designed to be the first non-immunogenic uricase therapy for refractory gout.

**Methods:** Patients with symptomatic gout ( $\geq 1$  tophus, gout flare within 6 months or gouty arthropathy) and elevated sUA ( $\geq 6$  mg/dL) were enrolled to SEL-212 treatment (n=6–12 pts/cohort) of fixed doses of pegsiticase (0.2 mg/kg or 0.4 mg/kg) alone or co-administered with SVP-R (0.05, 0.08, 0.1, 0.125, and 0.15 mg/kg). SEL-212 was infused in 28 day cycles x3 doses followed by challenge with pegsiticase alone on 28 day cycles x2 doses. In addition, 2 cohorts were added that

extended the combination treatment with SVP-R to all five q28 doses of pegsiticase. ADAs and sUA were assessed at baseline and 7, 14, 21, and 30 days after each dose to Day 140. Safety was monitored continuously.

**Results:** As previously reported, 5 of 6 patients dosed with pegsiticase alone developed ADAs after a single dose, correlating with loss of sUA control by 30 days. The addition of SVP-R to pegsiticase showed a dose-dependent inhibition of ADAs, enabling prolonged control of sUA levels. At a mid-dose of 0.1 mg/kg SVP-R, combined with either 0.2 or 0.4 mg/kg pegsiticase, the majority of patients showed sustained control of sUA through 18 weeks. However, control of ADAs and sUA tapered off in some patients by week 20, after two injections of pegsiticase alone. Preliminary results of treatment at increased SVP-R doses (0.125–0.15 mg/kg) are consistent with Phase 1b data indicating that higher doses of the SVP-R will increase the percentage of patients that remain ADA free. These results also suggest that extending treatment to 5 doses of SVP-R and pegsiticase may enable more subjects to complete the 5 month treatment with sustained reductions in sUA. In addition to mitigating immunogenicity, patients treated with SVP-R experienced a low rate of gout flares, with less than 25% of patients experiencing flares during the first month after treatment, despite profound drop in sUA level, and continued reduction was observed during months 2–5. SEL-212 has been generally well tolerated at clinically active dose levels and infusion reactions observed with repeat dosing were reduced with increasing doses of SVP-R.

**Conclusions:** SEL-212 has been well tolerated, mitigated immunogenicity, and sustained control of sUA levels. Escalation of the SVP-R component of SEL-212 may enhance the duration of sUA and ADA suppression without increased risk.

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**FRI0235 EFFECT OF SERUM URIC ACID (SUA) ON GOUT FLARES (GF) AND TOPHI RESOLUTION IN GOUT PATIENTS. POOLED POST HOC ANALYSIS OF CLEAR 1 & CLEAR 2 TRIALS**

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**Background:** Gout is caused by crystal deposition due to persistent hyperuricemia. EULAR<sup>1</sup> and other guidelines recommend a target sUA of <5–6 mg/dL (0.30 to 0.36 mmol/L) depending on severity. Despite physiological plausibility and abundant literature evidence there is an absence of consensus among physicians on the targets and necessity of long term urate lowering therapy (ULT)<sup>2</sup>.

**Objectives:** To investigate the effects of sUA and target sUA <5–6 mg/dl with respect to the occurrence of GF, flares requiring treatment (GFRT) and the percent change in the area of tophi (TR) from baseline irrespective of treatment arms.

**Methods:** Data of 1213 patients (PT) was pooled from CLEAR trials<sup>3&4</sup>, two randomized, double-blind, placebo-controlled Phase 3 studies that evaluated Lesinurad 200/400 mg daily in combination with allopurinol vs allopurinol. Prophylaxis for flares was given from baseline to month (M) 5. PT who met the sUA target of <5–6 mg/dl at M 6 and 12 were compared against those not on target with respect to the TR from baseline using a Wilcoxon test. In addition, the mean sUA measurements for PT with or without GFs and GFRT was compared at M 6 and 12 using a t-test.

**Results:** PT with sUA on target <5–6 mg/dl showed a larger decrease (increase in percent reduction) in area of tophi with a difference of 27.9%, and 17.3% at M 12 only compared to the PT not on target (table 1). The mean sUA levels were 0.227 mg/dL lower for PT with GF and 0.389 mg/dL lower for PT with GFRT compared to PT without GF and GFRT at M 6 (table 2), but not at M 12.

**Abstract FRI0235 – Table 1.** Percent Change from baseline Area of tophi vs. SUA on target <5–6 mg/dL at M 6 and 12

sUA (mg/dL) n=M6/M12	M6		p-value#	M12		p-value#
	Median	(Q1, Q3)		Median	(Q1, Q3)	
<5 (n=31/36)	-22.1	(-46.4, 5.63)	0.78	-59.6	(-98.3,-27.5)	0.01
$\geq 5$ (n=93/87)	-22.2	(-56.7, 6.91)		-31.7	(-77.4, 13.06)	
<6 (n=63/66)	-23.8	(-56.7, 1.59)	0.64	-49.0	(-93.3,-12.9)	0.06
$\geq 6$ (n=61/57)	-19.2	(-42.5, 10.30)		-31.7	(-60.1, 13.06)	

§ Number of PT with a target tophus at baseline was small. # Wilcoxon test with H0: Mean ranks in categories are equal

**Abstract FRI0235 – Table 2.** Mean sUA at M 6 and 12 by occurrence of GF and GFRT

Mean sUA mg/dL (95% CI) M6	p-value#	Mean sUA (95% CI) M12	p-value#
GF Yes	5.94 (5.80–6.07)	5.92 (5.79–6.06)	
GF No	5.71 (5.51–5.92)	5.91 (5.64–6.17)	
Difference	0.22 (–0.01–0.47)	0.01 (–0.28–0.31)	0.91
GFRT No	5.91 (5.79–6.03)	5.93 (5.80–6.05)	
GFRT Yes	5.530 (5.23–5.83)	5.83 (5.41–6.25)	
Difference	0.38 (0.06–0.71)	0.09 (–0.34–0.53)	0.65

# T-test with H0: No difference in means

**Conclusions:** These results confirm that sUA on target <5–6 mg/dl is essential for TR, and longer the control better the TR. The lower mean sUA levels for PT with GF and GFRT was observed at M6 and not at M 12, maybe owing to the fact that flares are common during the first months of ULT initiation and then taper off and urate deposits were more fragile and not completely dissolved. Also M 6 and 12 may not be optimal to observe statistically significant differences between treatments with respect to TR, GF and GFRT.

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FRI0236

#### ASSOCIATIONS BETWEEN COMORBIDITY AND URATE DEPOSITION IN SUBJECTS WITH ASYMPTOMATIC HYPERURICEMIA: A PILOT STUDY

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**Background:** Hyperuricemia is common and along with comorbidities, is increasing in prevalence. Though often asymptomatic and hence, under diagnosed, it may be associated with subclinical urate deposition. Ultrasound (US) imaging can detect urate deposition in individuals with asymptomatic hyperuricemia (ASU).

**Objectives:** To evaluate the association of comorbidities with urate deposition via US in ASU.

**Methods:** ASU was defined as serum urate (sUA) >6 mg/dl; sUA <6 mg/dl served as controls. Demographic (age, gender, BMI), comorbidity (CM – [hypertension (HTN), hyperlipidemia (HLD), diabetes mellitus (DM), cardiovascular (CVD) and renal disease (CKD)], diuretic/aspirin use, dietary data (alcohol, red meat, seafood) were collected. Ultrasonography (US) of joints (knee/MTP), tendons (triceps, quadriceps/patella, Achilles) was performed via standard procedure, OMERACT parameters of urate deposition documented, and images read by an Expert ultrasonographer blinded to sUA category. Correlations between sUA levels and MSK urate deposition with comorbidities, medication and dietary risk factors were analysed by 2-stage multivariable logistic regression model with propensity score weighting.

**Results:** Of 95 predominantly non-Hispanic Blacks (mean age 59.7 years, BMI ~32 kg/m<sup>2</sup>), ASU subjects (n=71, median sUA=8.0) were older men, with more frequent HTN, CVD, CKD, alcohol ingestion versus controls. In multivariate analyses adjusting for demographic characteristics, BMI, CKD, and alcohol use were positively associated with sUA >6 mg/dl; while HTN, CVD, and CKD were positively associated with sUA >8 mg/dl. Adjusting for comorbidities, sUA >8 mg/dl was significantly associated with urate deposition at knee (OR=3.20; p=0.03), quadriceps and Achilles tendons (OR=4.14; p<0.01), OR=9.51; p<0.01, respectively) but not at 1 st MTP (OR=2.14; p=0.06). A sUA >6 mg/dl alone, however, did not predict urate deposition.

**Conclusions:** Presence of HTN, CVD and CKD are associated with higher levels of sUA and increases the risk of urate deposition in ASU patients. Identifying a subset of ASU patients that may benefit from urate lowering therapy requires

further stratification and long term follow up for incident gouty arthritis in order to alter current urate lowering treatment guidelines.

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FRI0237

#### PEGLOTICASE TREATMENT SIGNIFICANTLY DECREASES MEAN ARTERIAL BLOOD PRESSURE IN PATIENTS WITH CHRONIC GOUT

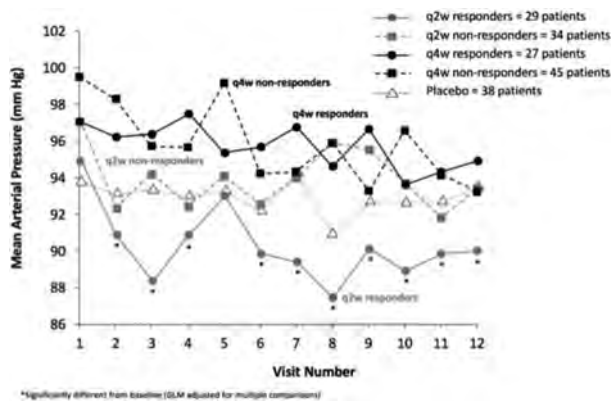
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**Background:** There are significant correlations between serum uric acid (sUA) and blood pressure (BP) in individuals with and without gout.<sup>1</sup> Limited data suggest that lowering sUA may decrease BP<sup>2</sup>, but no consistent effect has been noted.<sup>3</sup> Recent guidelines suggest the need for more aggressive management of increased BP.<sup>4</sup>

**Objectives:** To determine the impact of persistent, very low sUA levels on BP in subjects with chronic refractory gout treated with pegloticase, a recombinant uricase conjugated to polyethylene glycol approved for chronic refractory gout that decreases sUA to <1 mg/dL.

**Methods:** This analysis used results from two, 6 month randomised clinical trials (RCTs) in which subjects were treated with 8 mg pegloticase every 2 or 4 weeks (q2w or q4w) or placebo.<sup>5</sup> sUA responders maintained sUA <6 mg/dL.<sup>5</sup> Sitting BP was measured at each visit and estimated glomerular filtration rate (eGFR) was determined at baseline and after 3 and 6 months.

**Results:** Serial BP measures were obtained in 173 subjects during the course of the RCTs. Significant reductions in mean arterial pressure (MAP) from baseline to 6 months were noted in q2w responders (p=0.0029) (figure 1), whereas reductions in MAP in other groups were not significant. Notably, 18/29 (62.1%) of q2w sUA responders experienced persistent reductions in MAP (p=0.01 compared to other groups). Changes in both systolic and diastolic BP paralleled the change in MAP. Of the q2w sUA responders exhibiting persistent decreases in MAP, there were no significant differences in baseline age, gender, race, body mass index, history of hypertension, gout duration, MAP, sUA, cholesterol, eGFR, or urinary UA/creatinine ratio compared with those who did not lower MAP. There were no significant changes in eGFR in sUA responders to pegloticase treatment over the course of the study and there was no significant correlation between change from baseline MAP and eGFR in these subjects (p=0.43).



**Abstract FRI0237 – Figure 1.** \*Significantly different from baseline (GLM adjusted for multiple comparisons)

**Conclusions:** Responders to biweekly pegloticase experienced significant reductions in MAP that were independent of changes in renal function.

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### FRI0238 THE LEVEL OF LEPTIN IN PATIENTS WITH GOUT AND ITS ASSOCIATION WITH THE GOUT ACTIVITY SCORE

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**Background:** Leptin is a cytokine-like hormone mainly produced by adipose tissue. Its role in inflammation, obesity, diabetes mellitus, and cardiovascular pathology is well known.<sup>2</sup> Most of these pathological conditions usually accompany gout, but role of leptin in gout remains on the discussion.

**Objectives:** To determine the level of leptin in patients with gout and evaluate its association with the disease activity.

**Methods:** Study involved 151 patients with gout (100% men), aged (mean  $\pm$  SD) 52.4 $\pm$ 9.2 years, with a disease duration 8.9 $\pm$ 6.6 years. In 51 (33.7%) was diagnosed tophaceous gout. Control group was represented by 31 healthy subjects. Diagnosis of gout was based on the ACR/EULAR 2015 criteria. The disease activity was determined by the Gout Activity Score (GAS),<sup>2</sup> the intensity of the pain – by the visual analogue scale (VAS<sub>pain</sub>). Leptin in serum was determined by ELISA.

**Results:** The level of leptin in patients with gout was 2 times higher compare to those in the control group (6.6 $\pm$ 4.3 vs 3.0 $\pm$ 1.4 ng/ml). The number of attacks in the last year was 3.9 $\pm$ 2.7, number of affected joints was 8,1 $\pm$ 5.4, and uric acid in serum (sUA) was 8.1 $\pm$ 2.0 mg/dl. Mean value of VAS<sub>pain</sub> in gout patients was 5.4  $\pm$ 2.4 cm, and disease activity by GAS – 5.9 $\pm$ 2.1. Regarding GAS we divided our patients in three groups: low activity (GAS <25 th percentile), moderate activity (between 25th and 75th percentile) and high activity (>75 th percentile). In 36 patients with high disease activity (GAS >7.4) the level of leptin was the highest (11.7 $\pm$ 4.7 ng/ml), whereas in patients with moderate activity (GAS 4.5–7.4; n=77) and in patients with low disease activity (GAS <4.5; n=38) it was 5.3 $\pm$ 2.6 ng/ml and 3.9 $\pm$ 1.4 ng/ml, respectively. The difference in leptin levels between all groups was significant (p<0.01). The level of leptin correlated with the number of gout attacks (r=0.41), number of affected joints (r=0.55), sUA (r=0.39), VAS<sub>pain</sub> (r=0.35), and GAS (r=0.69).

**Conclusions:** Association of increased leptin level with high gout activity may indicate possible pathogenic role of leptin in gout. GAS is reliable and sensitive clinical tool for determining disease activity in patients with gout.

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### FRI0239 ABSOLUTE NUMBERS OF PERIPHERAL TH17 AND TH2 CELLS INCREASED IN PATIENTS WITH GOUT

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**Background:** Gout is generally considered as an acute or chronic inflammatory disease of the joints due to deposition of crystals of monosodium urate (MSU). However, crystals of MSU do not always elicit inflammation in joints, suggesting that the immunological basis is required for the development of gouty arthritis. Although T helper 17 (Th17) and regulatory T cell subsets in CD4 +T cells have been reported to play a key role in autoimmune diseases, their status in peripheral blood of gout patients are rare studied.

**Objectives:** Our present study is to explore whether the absolute numbers of peripheral CD4 +T subsets, especially Th17 cells and CD4 +CD25+FOXP3T regulatory (Treg) cells, is abnormal in gout.

**Methods:** A total of 72 patients with gout (70 male/2 female) and 41 age-sexual-matched controls were recruited from the Second Hospital of Shanxi Medical University (from March 1 st in 2016 to July 30th in 2017). Of these, 72 patients were categorised as acute gout who had redness, swelling, warmth and pain at the same time (Group1; n=18) or as acute gout without redness and warmth (Group2; n=52). All patients fulfilled 2015 Gout classification criteria developed by the American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR). Patients with a history of other autoimmune diseases, nephropathy, cancer, infectious processes, or hematopathy were excluded. The detail medical histories were collected, comprehensive laboratory examinations were performed, and then the differences between the patients and controls were investigated. The concentrations of CD4 +T cell subsets (the absolute numbers of Th1, Th2, Th17 and Treg cells) in peripheral blood were measured by flow cytometry combined with internal standard beads and then the ratios of Th1/Th2 and Th17/Treg were calculated.

**Results:** The duration of their disease was 46.73 $\pm$ 54.92 (Group1), or 61.54  $\pm$ 70.51 (Group2) months. The white blood cells (WBCs) and neutrophils in gout blood were significantly higher than those in controls (P<0.01) and ESR in Group1 was obviously increased (p=0.033). Levels of Total T lymphocyte counts (CD3 +CD19-), Total B lymphocyte counts (CD3-CD19+) and Helper T cells (CD3 +CD4+) were increased in Group2 (all p<0.05). Nevertheless, there was no difference between Group1 and healthy controls. The absolute number of peripheral Th2 in gout (both Group1 and Group2) was higher than that in healthy controls (p=0.001). Most importantly, the absolute number of peripheral Th17 cells was significantly increased in gout patients in Group2 (p=0.006) while, in Group1, the absolute number of Treg cells decreased despite no statistical significance (P>0.05).

**Abstract FRI0239 – Table 1.** Lymphocyte subsets of Gout Patients & Normal Persons

	Group1	Group2	Normal	F	P-values
N	18	52	41		
Total T cells,CD3+CD19- (cell/ $\mu$ L)	1475.50(1234.50)	1538.43(894.50)	1366.59(488.84) <sup>a</sup>	4.954	0.084
Total B cells,CD3-CD19+ (cell/ $\mu$ L)	206.51(195.92) <sup>a</sup>	306.50(224.27)	191.04(103.48)	13.610	0.001
Th cells, CD3+CD4+ (cell/ $\mu$ L)	783.34(527.75)	866.50(520.75)	625.84(187.63)	13.134	0.001
T <sub>H</sub> cells, CD8+ T (cell/ $\mu$ L)	608.00(472.25)	608.85(336.00)	536.13(220.43)	1.220	0.543
Th17, CD3+CD4+CD8+ T	1.15(0.31)	1.50(0.91)	1.11(0.63) <sup>a</sup>	11.625	0.003
NK cells, CD3-CD16-CD56+ (cell/ $\mu$ L)	278.00(208.75)	311.70(187.58)	340.59(280.05)	2.780	0.249
T <sub>H</sub> 17/NK cells,CD3+CD19-CD3-CD19+CD3-CD16-CD56+ (cell/ $\mu$ L)	2148.00(1501.23)	2253.00(1006.00)	1918.47(739.66) <sup>a</sup>	6.093	0.048

a. Total B lymphocyte counts (CD3-CD19+) were increased in Group1 compared with Group2 (p=0.037).

c. Total T and B lymphocyte counts (CD3-CD19+) were increased in Group2 compared with healthy controls. (all p < 0.05)

**Abstract FRI0239 – Table 2.** CD4+ T cell subsets of Gout Patients & Normal Persons

	Group1	Group2	Normal	F	P-values
N	18	52	41		
Th1 cells,IFN- $\gamma$ (cell/ $\mu$ L)	63.24(126.68)	115.03(183.53)	125.72(99.01)	1.610	0.447
Th2 cells,IL-4 (cell/ $\mu$ L)	12.92(16.62)	11.38(11.16) <sup>a</sup>	7.44(5.88) <sup>a</sup>	12.379	0.002
Th17 cells,IL-17 (cell/ $\mu$ L)	6.79(12.77)	13.07(9.37)	7.48(5.87) <sup>a</sup>	7.131	0.028
Treg cells, CD4+CD25+FoxP3+ (cell/ $\mu$ L)	23.62(28.06)	30.25(20.53)	30.22(16.72)	2.032	0.362
Th1/Th2, IFN- $\gamma$ /IL-4	3.14(7.66)	3.95(14.49) <sup>a</sup>	16.17(20.13) <sup>a</sup>	16.288	0.000
Th17/Treg, IL-17/CD25+FoxP3	0.29(0.83)	0.40(0.43)	0.24(0.20) <sup>a</sup>	6.986	0.030

b. the absolute number of peripheral Th2 cells was significantly increased in gout patients in Group1 compared with healthy controls (p=0.012)

c. the absolute number of peripheral Th2 and Th17 cells was significantly increased in gout patients in Group2 compared with healthy controls (all p < 0.05)

**Conclusions:** The increase of peripheral Th2 and Th17 cells led to an imbalance of CD4 +T cell subsets may correlate with gouty inflammation in an undefined way. The elevation of Th2 and Th17 cells may serve as important reference indices for gout attack and a target of gout treatment. Moreover, Th17 may contribute to the persistence of the disease.

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FRI0240

### CLINICAL TRIAL TO DETERMINE WHETHER ALTERING THE REGIMEN OF PEGLOTICASE ADMINISTRATION CAN INCREASE THE FREQUENCY OF SUBJECTS HAVING SUSTAINED LOWERING OF SERUM URATE

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**Background:** Pegloticase is a pegylated recombinant mammalian uricase approved for treatment of persons with chronic gout refractory to standard urate-lowering therapy.<sup>1</sup> Despite initial profound reduction of serum urate (sUA), patients may lose the urate lowering effect of pegloticase owing to the development of anti-drug antibodies.<sup>2</sup> As a result, only 42% of treated patients had sustained urate lowering in the registration trials, and infusion reactions (IRs) occurred in 26% receiving the biweekly dosing regimen compared to 5% of placebo-treated patients.<sup>1</sup> Examination of pegloticase pharmacokinetics<sup>2</sup> indicated that the biweekly regimen may not maintain sufficiently high levels of drug during the first 2 weeks of therapy, possibly contributing to immunogenicity.

**Objectives:** To determine whether an additional dose of 8 mg of pegloticase 1 week after the initial dose and 1 week before the subsequent dose might be sufficient to maintain high serum pegloticase levels and contribute to the development of high zone tolerance and a more persistent urate lowering effect. (NCT02598596)

**Methods:** This is a multi-centre, open-label trial enrolling patients with chronic gout whose sUA was not maintained  $\leq 6$  mg/dL. Background urate lowering therapy was discontinued and patients were treated with 3 weekly doses of 8 mg pegloticase followed by biweekly administration of 8 mg of pegloticase for a total of 10 doses over 17 weeks. After the first administration, dosing was only permitted if the sUA was  $\leq 6$  mg/dL. Standard infusion and gout flare prophylaxis were required. The primary outcome was the maintenance of sUA at  $\leq 6$  mg/dL throughout the treatment period.

**Results:** 50 patients have been enrolled with a mean age of  $59.8 \pm 16.3$  years. Of the 50 patients, 31 (62%) completed all study activities, 7 were non-compliant, 8 withdrew consent, 2 were discontinued by the PI and 2 were discontinued for an adverse event (AE). Patients have received a total of 315 infusions to date. Only 1 patient had a mild IR (0.3% of infusions) that did not meet the criteria for anaphylaxis. 38 patients reported at least 1 AE, the most common being a gout flare (52%). 8 patients (16%) reported severe AEs, including 5 with gout flares. Of the 50 evaluable patients, there were 22 responders (44%), 21 nonresponders (42%) and 7 patients were not evaluable (14%). It is notable that responders had significantly higher trough levels of pegloticase than nonresponders 1 week after the initial infusion (1.45 ug/ml, n=22 vs 1.02 ug/ml, n=21, p=0.02) that persisted throughout the trial, supporting the contention that higher levels of drug are required to promote tolerance and response.

**Conclusions:** The tolerization regimen of pegloticase treatment is well tolerated. Only one IR was noted as administration of pegloticase was avoided in those with a sUA  $> 6$  mg/dL. The tolerization regimen may be associated with a somewhat higher frequency of patients achieving a persistent urate lowering effect. Trough levels of pegloticase separated responders from nonresponders throughout the trial and may be useful to develop an optimal treatment regimen.

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FRI0241

### THE EFFECT OF FEBUXOSTAT ON INFLAMMATORY AND CARDIOVASCULAR BIOMARKERS IN HYPERURICEMIC HYPERTENSIVE PATIENTS

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**Background:** Hyperuricemia (HU) is associated with hypertension (HTN) and adverse cardiovascular (CV) events. Potential mechanisms include endothelial xanthine oxidoreductase (XO) activity, direct effects of circulating soluble urate, and inflammation from crystal deposits. A phase 2 double-blind placebo (PBO)-

controlled randomised trial tested the ability of 6 weeks treatment with the selective XO inhibitor febuxostat (FBX) to reduce blood pressure in hyperuricemic HTN patients who had no history of gout. A planned subgroup analysis showed reduction of systolic blood pressure (SBP) by 6.7 mmHg (95% CI 0–13.3) as assessed by 24 hour ambulatory BP measurement (ABPM) in HTN subjects with normal renal function (eGFR  $\geq 90$ ).<sup>1</sup>

**Objectives:** To explore mechanistic links between HU and CV disease we examined the effect of treatment with FBX on inflammatory and vascular biomarkers.

**Methods:** Entry criteria included ABPM SBP of  $\geq 130$  and  $\leq 165$  mmHg; taking  $\leq 2$  BP drugs at baseline; and baseline serum urate (sUA) of  $\geq 420$   $\mu$ M. 121 subjects were randomised 1:1 to FBX 80 mg OD or PBO for 6 weeks. Serum and whole blood mRNA samples were taken at screening (d-21), d1 pre-treatment, after 3 w and after 6 w of FBX/PBO.

Soluble markers were measured using a 50-analyte multiplex array (from Myriad RBM HuMAP panel v1.6) and included mediators previously implicated in gout and in CV associations with HU, including CCL2 (MCP-1), CXCL8 (IL-8), E- and P-selectins, cystatin C, ICAM-1, IL-6, leptin, MMPs, MPO, SerpinE1 (PAI-1), TNF $\alpha$ , VCAM-1 and vWF. Additional candidates (angiotensin (AT)-II, hsCRP, insulin) were measured by ELISA. RNAseq was done on the Illumina HiSeq2000 platform with 20–30 million 50 bp paired-end reads and analysed for fold change vs baseline.

**Results:** Serum urate was reduced by a mean of 190  $\mu$ M at week 6 in FBX-treated subjects and 0  $\mu$ M with PBO. Nominally significant differences in change from baseline between PBO and FBX were noted in ICAM-1 (PBO –9.5, FBX +7.0 ng/ml at w6; uncorrected p=0.006) and SerpinE1 (–4.1, +30.9; 0.004). There was no baseline association between sUA and key markers on univariate, multiple linear regression analyses, or principle component regression.

Nonparametric analysis showed marginally significant differences between FBX and PBO in the changes in CRP (unadjusted p=0.26 at w3, 0.018 w6), ICAM-1 (0.023, 0.063) and LOX-1 (0.356, 0.044). The effect of FBX was not significant for other soluble mediators including AT-II, CCL2, CRP, CXCL8, insulin, or MMPs.

Many mRNA transcripts of interest (including CXCL8, SERPINE1) showed low levels in blood and no association between fold-change and reduction in sUA. Changes in CST3, MIF, S100A8 and S100A9 expression were associated with change in sUA.

**Conclusions:** In these HU HTN subjects without gout no significant relationship was found between sUA and inflammatory or CV markers at baseline. FBX effects on these biomarkers are sporadic, expected when evaluating many markers in a relatively small sample. These findings do not support a direct role for soluble urate in HU-associated HTN or CV disease. Limitations include the non-gout population studied, the relatively narrow range of baseline BP, and short treatment duration.

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FRI0242

### IMPAIRMENT IN THE RATES OF INCIDENCE, MORTALITY, STAYS AND ANNUAL COSTS OF HOSPITALIZATIONS FOR GOUT IN THE SPANISH NATIONAL HEALTH SYSTEM

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**Background:** Gout is the most common inflammatory articular disease in adults concerning a 1%–2% of the general population, and even a 4%–5% in older than 70 years. Recently, it has been reported an increase of the prevalence of gout, especially in developed countries.

**Objectives:** The principal purpose of our study is to describe the clinical and epidemiological characteristics of hospitalised patients with diagnosis of gout in Spain including mortality, comorbidities and healthcare costs in the last decade

**Methods:** Retrospective observational study based on data from the Database of Hospital from the Spanish National Health Service. The study was conducted in patients over eighteen years old with any gout diagnosis as principal or other diagnosis, who were admitted in the hospital between the years 2005–2015. The clinical characteristics analysed were sex, age, costs and length of hospital stay. Comorbidities as diabetes, congestive heart failure, acute myocardial infarction and cerebrovascular disease were identified with *International Classification of Diseases, ninth revision, common modification* (ICD-9-CM).

**Results:** The study cohort included 192.037 patients with gout, 82.6% of those were males. There was a progressive increase in the number of hospitalised patients with gout from 12 851 patients in 2005 to 23 318 in 2015; this was associated with an increase in mortality, reaching its highest value in 2015 with a 4.9% of gout hospitalised patients. The average age at death in 2015 was 79.2 years and 85.16 years in male and female respectively, an age slightly lower than in the general population. The average cost in these hospitalised patients was 4931 €, reaching a peak of 5384 € in the last year. The hospital stay reached its lowest numbers in 2015 with an average of 8.9 days per patient. These comorbidities had statistical association with an added mortality risk in cerebrovascular disease (odds ratio [OR] 1.57, 95% confidence interval [CI] 1.46–1.49), liver disease (OR 2.61 95% CI 2.34–2.9), kidney disease (OR 1.34 95% CI 1.28–1.41), dementia (OR 2.13 95% CI 1.88–2.42). On the contrary, in type 2 diabetes (OR 0.92 95% CI 0.87–0.96), we found a statistically significant lower mortality risk. Furthermore, it was found a statistically reduced mortality risk in females (OR 0.85 95% CI 0.8–0.9)

**Abstract FRI0242 – Table 1.** Incidence, mortality, stays and annual costs of hospitalisation for gout of the Health National System

Year	Number of patients	Mortality Number (%)	Average hospital stay (SD)/cost (SD)	Cost/year In millions €
2005	12 850	532 (4.1%)	11.00/4219	54.2
2006	13 163	479 (3.6%)	10.63/4269	56.2
2007	13 896	544 (3.9%)	10.46/4459	61.6
2008	15 292	601 (3.9%)	10.58 4838	74
2009	16 172	630 (3.9%)	10.33/4997	80.8
2010	16 803	658 (3.9%)	9.96/5205	87.5
2011	18 482	781 (4.2%)	9.62/5385	99.5
2012	19 179	897 (4.7%)	9.21/5247	100.6
2013	20.777	926 (4.5%)	9.09/5166	107.3
2014	22.105	991 (4.5%)	8,94/5080	112.3
2015	23.318	1139 (4.9%)	8,90/5384	125.5
<b>Total</b>	<b>192.037</b>	<b>8178 (4.3%)</b>	<b>9,74/4999</b>	<b>959.5</b>

**Conclusions:** In Spain we have a progressive increase in the hospital admissions for gout, higher mortality rates and higher healthcare costs. This shows the need for changes in prevention and management of gout disease.

**Disclosure of Interest:** None declared

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## FRI0243 ANAKINRA FOR CALCIUM PYROPHOSPHATE CRYSTAL ARTHRITIS: AN EFFICIENT, SAFE ALTERNATIVE TREATMENT

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**Background:** Calcium pyrophosphate (CPP) deposition is a frequent joint disease with increased prevalence in older people in whom treatment of acute CPP arthritis with conventional therapies such as colchicine, corticosteroids or non-steroidal anti-inflammatory drugs (NSAIDs) could be contraindicated or not used at an optimal dose. As recommended in gout, anakinra might represent an alternative treatment for acute arthritis. In contrast, the relevance of anakinra in acute CPP arthritis has not given much attention.

**Objectives:** We further aimed to analyse the efficacy and safety of anakinra in acute CPP arthritis in a large cohort.

**Methods:** We retrospectively included all patients receiving anakinra for acute CPP arthritis between January 2011 and 2017. Medical history data were collected including hypertension, diabetes mellitus, cardiovascular disease, history of gastroduodenal ulcer, renal impairment and concomitant treatments including anticoagulants or antiplatelet drugs. The following data were collected before and 4 days after the first anakinra injection: swollen joint count (SJC), tender joint count (TJC), pain score on a visual analogue scale (VAS, 0–100 mm) and C-reactive protein (CRP) level. A good response was defined according the evaluation of the physician or documentation in the chart of the phrase “good response” after anakinra treatment.

**Results:** We included 33 patients (24 women; mean age 79.2±12.8 years). Mean duration of acute arthritis 13.2±12.9 days. CPP arthritis was confirmed by the presence of CCP crystals in synovial fluid in 28/33 (84.8%) patients. For the remaining 5 patients, the diagnosis was confirmed by CPP deposition features seen on imaging. Corticosteroids, NSAIDs and colchicine were previous treatments, without significant improvement in 12 (36.4%), 7 (21.2%) and 18 (54.5%) patients, respectively. The mean dose of corticosteroids was 20.8±8.2 mg/day. Among the 33 patients, 32 had a documented visit at day 4. The number of good responders was 27 (81.8%). At day 4, patients showed decreased mean VAS

pain score (from 64.8±26.5 to 21.2±19.7 mm, p<0.0001), TJC (5.8±5.0 to 1.0±1.0, p<0.0001), SJC (3.9±2.7 to 0.9±1.0, p<0.0001) and CRP level (116.1±71.6 to 26.0±23.1 mg/L, p<0.0001). Anakinra was well tolerated. Only one patient had pneumonitis that was resolved with oral antibacterial agents.

**Conclusions:** Our results suggest that anakinra could be a relevant alternative for managing acute CPP arthritis, leading to rapid relief of inflammatory symptoms, with a good tolerance.

**Disclosure of Interest:** None declared

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## FRI0244 LIFE STYLE FACTORS AND COMORBIDITIES IN GOUT PATIENTS COMPARED TO THE GENERAL POPULATION

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**Background:** Gout is the most common inflammatory arthritis and relatively much is known regarding its pathogenesis. It is clear that life style factors play a significant role in developing and maintaining disease.

**Objectives:** This study aimed to analyse lifestyle factors in prevalent gout patients by sex compared to age matched controls from the general population.

**Methods:** All patients above 18 years of age with an ICD 10-diagnosis of gout from Jan 2015 through Feb 2017 listed at any of twelve randomly selected primary health care centres or the rheumatology department at Sahlgrenska University hospital in the Western Sweden Health Care Region (WSHCR) were identified. They were sent a questionnaire, regarding demographics, life style factors such as smoking status, alcohol consumption, physical activity, body mass index (BMI); categorised into 4 levels in the analyses) and comorbidities such as diabetes and hypertension. All responders aged 18–84 years were matched to five control individuals, without gout, by sex and age. Control individuals were selected from a random sample of 52 348 individuals aged 16–84 years who participated in the National Public Health survey in Sweden year 2015 This survey is a national study on health, lifestyle and living conditions. Alcohol consumption was categorised as none and any with/without binge drinking behaviour. Binge drinking was (liberally) defined as consuming more than four (women) or five glasses (men) on any occasion.

Conditional logistic regression models were used to compare cases and controls with regard to lifestyle factors and comorbidities. Multivariate analyses were also performed, including BMI, smoking status, alcohol consumption, and physical activity.

**Results:** Of the 1589 invited gout patients, 868 responded and 79.7% were male. Non-responders were more often young men. Mean age was 69.3 (std:10.5) years for men and 71.8 (std: 9.9) years for women with gout.

Male gout patients were in multivariate analyses more likely to be overweight (OR 1.67 (95% CI: 1.31–2.14)), obese (OR 2.20 (95% CI: 1.64–2.94)), have binge drink behaviour (OR 3.32 (95% CI: 2.39–4.62)), and had lower levels of physical activity compared to controls (table 1). Current smoking habits did not differ between male gout patients and controls.

Female gout patients were in multivariate analyses more likely to be overweight (OR 1.87 (95% CI: 1.05–3.33)), obese (OR 3.62 (95% CI: 1.96–6.72)), and have binge drink behaviour (OR 4.28 (95% CI: 1.92–9.53)), but not did differ with regard to current smoking habits or physical activity compared to controls.

In bivariate analyses, comorbidities such as diabetes and hypertension, were significantly more common in gout patients among both sexes.

**Abstract FRI0244 – Table 1.** Prevalence of lifestyle factors and comorbidities between gout patients and sex-age matched healthy controls.

	Male (n=835)					Female (n=754)				
	Controls	OR	95% CI	AJG OR	95% CI	Controls	OR	95% CI	AJG OR	95% CI
Age (Mean (SD))	68.3(10.1)	68.3(10.1)	-	-	-	71.8(10.5)	71.8(10.5)	-	-	-
Male (SD)	38.1(15.7)	38.1(15.7)	-	-	-	28.4(15.4)	28.4(15.4)	-	-	-
Overweight, %	0	0.6	-	-	-	0.6	2.3	-	-	-
Hypertension, %	23.0	13.5	Ref	3	20.7	42.4	Ref	3	Ref	3
Diabetes, %	23.1	41.8	1.76	(1.58 to 2.12)	1.67	(1.39 to 2.14)	39.1	95.7	3.09	(1.21 to 8.32)
Obese, %	20.0	39.2	2.08	(1.81 to 2.39)	2.00	(1.64 to 2.46)	43.4	19.1	4.11	(1.47 to 11.04)
Comorbidities, %										
Hypertension, %	68.4	42.1	4.60	(3.65 to 5.72)	4.76	39.2	44.2	7.36	(4.49 to 12.08)	10.0
Diabetes, %	23.1	33.4	1.43	(1.26 to 1.61)	1.43	27.4	32.1	6.22	(3.99 to 9.88)	10.0
Obese, %	44.2	56.2	Ref	3	Ref	3	53.7	63.4	Ref	3
Pain, %	51.4	53.3	1.04	(1.01 to 1.07)	1.79	(1.48 to 2.15)	41.9	26.7	1.68	(1.11 to 2.67)
Current, %	1.5	0.6	0.42	(0.25 to 0.71)	0.49	(0.49 to 1.05)	1.0	0.7	0.70	(0.29 to 1.68)
Alcohol, %										
None	12.4	13.0	Ref	3	Ref	1	22.8	Ref	3	Ref
Any, without binge	68.7	76.0	1.30	(1.07 to 1.57)	0.98	(0.84 to 1.12)	76.9	74.2	0.98	(0.81 to 1.17)
Any, with binge	18.9	11.0	0.53	(0.39 to 0.72)	0.94	(0.31 to 2.80)	13.3	3.6	4.29	(1.83 to 9.93)
Physical activity, %										
0-5 hours	22.4	31.0	Ref	3	Ref	1	20.0	23.0	Ref	3
1-5 hours	22.0	27.6	1.23	(1.07 to 1.47)	1.34	(0.98 to 1.82)	20.8	29.4	1.42	(1.01 to 2.00)
1-5 hours	20.9	30.1	1.44	(1.24 to 1.66)	1.48	(1.13 to 1.94)	27.2	34.0	1.53	(1.11 to 2.11)
More than 5 hours	24.7	18.5	0.76	(0.66 to 0.87)	0.87	(0.66 to 1.14)	31.7	30.9	1.02	(0.79 to 1.31)

\* Multivariate analyses including BMI, alcohol consumption, smoking status and physical activity per week.

**Conclusions:** Compared to the general population, patients with gout were more often obese (in particular women) and had higher occurrence of binge drinking behaviour (in particular men). The lower level of physical activity (men) and normal frequency of smoking among gout patients may be a consequence of the high comorbidity rates.



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**FRI0245** **PREDICTORS FOR CLINICALLY DIAGNOSED GOUT – 30 YEARS FOLLOW-UP IN THE MALMÖ PREVENTIVE PROJECT COHORT, SWEDEN**

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**Background:** Gout is the most common form of inflammatory arthritis worldwide. Hyperuricemia is a crucial risk factor. The relative importance of other risk factors is slightly more controversial.

**Objectives:** Our aim was to identify predictors for clinical gout cohort from a population survey, the Malmö Preventive Project (MPP) – a large-scale screening and case finding program in Malmö, Sweden.

**Methods:** A total of 33 346 individuals (67% men, mean age 46 years, mean follow-up 28 years) were screened 1974–1992. The survey included: A Questionnaire (alcohol consumption, smoking); A Physical Examination and Laboratory tests. The Malmö modification of Michigan alcoholism screenings test (Mm-MAST) was used to identify alcohol risk consumption (Mm-MAST score  $\geq 2$ ). Subjects were followed to date of first gout diagnosis, death, migration from area, or December 2014. All gout diagnoses given at visits to physicians in primary or specialised care were identified by linking MPP cohort to regional Skåne Healthcare Register and to National Patient Register. Possible risk factors/markers at baseline associated with incident gout were analysed using Cox-regression models.

**Results:** In total, 1275 individuals (3.8%); 1014 men (4.5%) and 261 women (2.4%) were diagnosed with gout. In both sexes, baseline s-UA  $>405$  (age-adjusted) was the strongest factor associated with incident gout. Higher age, higher BMI, higher s-triglycerides, hypertension and smoking were also associated with gout in both sexes. Mm-MAST score  $\geq 2$  was associated with gout only in men while higher ESR was associated with gout only in women (table 1).

**Conclusions:** In this large cohort of middle-age individuals, hyperuricemia, higher age, hypertriglyceridemia and higher BMI were associated with incident gout in both sexes. Alcohol risk consumption predicted gout only in men. Higher ESR, as a possible marker of chronic inflammation, was a significant predictor only in women.

**Disclosure of Interest:** None declared

**FRI0246** **INVESTIGATING THE EFFECT OF SERUM URATE LEVELS ON GOUT FLARE RATES IN A LARGE-SCALE U.S. ADMINISTRATIVE CLAIMS DATABASE**

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**Background:** Reducing patients' serum urate (sUA) levels has long been the focus of gout treatments. Current evidence suggests that sUA levels  $\geq 6.0$  mg/dL significantly increase a subject's risk of an acute gout attack or "flare."

**Objectives:** To investigate the effects of sUA levels on gout flare rates (GFLR) over a 5 year period in a large-scale US commercial claims database.

**Methods:** Truven MarketScan administrative claims data from 2010 to 2015 were used for this analysis. The study population was patients with gout whose index gout diagnosis was defined as first gout diagnosis. Index sUA date (IsD) was defined as the sUA result closest to, but not preceding, a subject's index gout diagnosis. Patients were included if they had continuous health plan enrollment during the year prior to and after their IsD. Patients without an sUA result after their index gout diagnosis were excluded. Three sUA comparison groups were created based on mean sUA values calculated from sUA measurements at IsD through follow-up. Person-time was defined as time between IsD to the end of continuous enrollment or to the end of the study period, whichever came first. Gout flares were determined via a published algorithm Halpern 2009 combining health care visits and prescriptions by using ICD9/10, HCPCS, and NDC codes. Subjects' annual GFLR were calculated as their number of flares per person-time. Mean GFLR were calculated for each sUA comparison group. A generalised linear model was developed to investigate the effect of sUA levels on GFLR after adjusting for demographics and regions.

**Results:** 15 140 subjects were included in the analysis. Most subjects were male (78%) and from the south (47%) with a mean age of 52 years. Mean sUA was 6.9 mg/dL (min=1.4, max=17.5) where 58% of patients had sUA between 6.0 and 9.0 mg/dL. Subjects were followed for 2.1 years on average. sUA  $\geq 6.0$  and  $<9.0$  mg/dL (Group 2), and sUA  $\geq 9.0$  mg/dL (Group 3) were both associated with increased gout flare rates compared to sUA  $<6.0$  mg/dL (Group 1). Group 3 had 1.540 times of the annual flare rate of Group 1. Male sex and increasing age were associated with increased GFLR. North central, south, and west US regions were all positively associated with GFLR in relation to the northeast (table 1).

**Abstract FRI0245 – Table 1**

<b>MEN (n=22433) where 1014 had incident gout</b>	<b>Baseline variables</b>	<b>s-UA<math>&gt;405</math> <math>\mu</math>mol/L (yes,%)</b>	<b>Mean (SD)</b>	<b>Frequency (yes,%)</b>	<b>HR (95% CI)* (age adjusted) 5.4 (4.8–6.2)</b>	<b>HR (95% CI) (multivariate analysis**) 4.1 (3.4–4.9)</b>
	Age (years)		43.7 (6.6)		<b>1.4 (1.3–1.5)</b>	<b>1.4 (1.2–1.5)</b>
	Body mass index (kg/m <sup>2</sup> )		24.7 (3.3)		<b>1.4 (1.4–1.5)</b>	<b>1.3 (1.2–1.4)</b>
	e-GFR (ml/min)		79.1 (10.5)		<b>0.9 (0.8–0.9)</b>	0.9 (0.8–1.0)
	s-triglycerides (mmol/L)		1.5 (1.1)		<b>1.1 (1.1–1.2)</b>	1.1 (1.0–1.1)
	ESR mm/hour		5.9 (5.7)		1.0 (0.9–1.1)	1.0 (0.9–1.1)
	Hypertension (yes,%)			16.4%	<b>1.7 (1.5–2.0)</b>	<b>1.3 (1.1–1.5)</b>
	CVD at baseline (yes/no)			2.1%	<b>1.7 (1.1–2.8)</b>	1.4 (0.9–2.3)
	Smoking (yes/no)			49.2%	<b>1.1 (1.0–1.3)</b>	<b>1.3 (1.1–1.6)</b>
Mm-MAST $\geq 2$ (yes,%)			30.8%	<b>1.5 (1.3–1.7)</b>	<b>1.3 (1.1–1.5)</b>	
<b>WOMEN (n=10902) in where 261 had incident gout</b>		<b>s-UA<math>&gt;405</math> <math>\mu</math>mol/L (yes,%)</b>		1.5%	<b>12.5 (8.6–18.1)</b>	<b>5.9 (2.2–15.9)</b>
	Age (years)		49.7 (7.4)		<b>1.7 (1.5–2.1)</b>	<b>1.3 (1.1–1.6)</b>
	BMI (kg/m <sup>2</sup> )		24.4 (4.2)		<b>1.6 (1.5–1.8)</b>	<b>1.6 (1.6–2.0)</b>
	eGFR (ml/min)		75.6 (10.9)		0.8 (0.7–0.9)	0.8 (0.6–1.0)
	s-triglycerides (mmol/L)		1.1 (0.6)		<b>1.3 (1.2–1.4)</b>	<b>1.2 (1.0–1.5)</b>
	ESR (mm/hour)		9.6 (7.7)		<b>1.3 (1.2–1.4)</b>	<b>1.2 (1.0–1.5)</b>
	Hypertension (yes,%)			22%	<b>2.0 (1.6–2.0)</b>	1.1 (0.6–1.9)
	CVD at baseline (yes,%)			3.4%	<b>2.1 (1.3–3.6)</b>	3.0 (0.7–12.3)
	Smoking (yes,%)			34.9%	1.2 (0.9–1.5)	<b>1.7 (1.0–2.8)</b>
	Mm-MAST $\geq 2$ (yes,%)			2.8%	1.3 (0.6–2.6)	1.2 (0.6–2.4)

\*HR is calculated per 1 SD or for dichotomous covariates (yes vs. no)

**Abstract FRI0246 – Table 1.** Generalised linear model for association between sUA level and gout flare rates (n=15,140)

Variable	Rate Ratio	95% CI	p-value
Group 2: sUA $\geq 6.0$ and $<9.0$ mg/dl <sup>1</sup>	1.179	(1.143, 1.216)	<0.001
Group 3: sUA $\geq 9.0$ mg/dl <sup>1</sup>	1.540	(1.475, 1.608)	<0.001
Sex: Male	1.374	(1.326, 1.424)	<0.001
Age	1.012	(1.010, 1.014)	<0.001
North central <sup>2</sup>	2.198	(2.114, 2.285)	<0.001
South <sup>2</sup>	1.382	(1.339, 1.425)	<0.001
West <sup>2</sup>	2.038	(1.935, 2.145)	<0.001

<sup>1</sup> versus  $<6.0$  mg/dl (Group 1)<sup>2</sup> versus northeast

**Conclusions:** These results suggest that higher sUA levels are associated with higher flare rates and that sUA level may be an indicator of GFLR. This finding may encourage health providers to prioritise reducing sUA levels in gout patients to reduce the frequency of gout flares and improve gout management.

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FRI0247

### GOUT CHARACTERISTICS AND ITS ASSOCIATION WITH THE PRESENCE OF CARDIOVASCULAR DISEASE: A CASE-CONTROL STUDY

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**Background:** Gout is an independent risk factor for any type of cardiovascular disease (CVD). The exact mechanism behind remains to be elucidated, but persistent crystal-related inflammation is presumed as a key factor.

**Objectives:** The aim of this study was to assess whether gout characteristics that may indicate a more severe disease and higher inflammatory load are associated with the presence of CVD.

**Methods:** Case-control study, performed at baseline of an inception cohort including consecutive crystal-proven gout patients seen at a rheumatology unit. Gout features (time since first attack, number of attacks, number of joints affected, pattern of presentation, tophi) were registered after interview and physical exam. Presence and duration of CVD (which included coronary heart disease, heart failure, stroke or peripheral artery disease) was registered after interview and records review. Those patients who have suffered from CVD prior to the onset of gout were excluded. Other cardiovascular risk factors, as well as clinical and laboratory variables, were also registered. Odds ratios with 95% confidence intervals (95% CI) for each gout feature were calculated between patients with and without CVD, using a multiple logistic regression model to adjust for confounders.

**Results:** The inception cohort includes 308 patients; 54 were excluded for this study because gout onset occurred after CVD, so finally 254 cases were analysed. Mean age was 61.4 years (SD 13.9), being 225 (88.6%) men. Regarding gout, median duration was 5 years (IQR 1–12), median number of reported attacks was 5 (IQR 2–14) that had involved a median of 3 joints (IQR 2–5); presenting attack was monoarticular in 77.4% cases, oligoarticular in 16.7%, and polyarticular in 6%, and 58 patients (22.8%) showed tophi at enrolment. A total of 32 patients (12.6%) had suffered from CVD at enrolment. Table 1 shows the results of logistic regression analysis: time since first attack and polyarticular presentation of gout both significantly associated with the presence of CVD, while other variables showed no association. After multivariate analysis, time since first attack persisted associated with CVD, while polyarticular involvement showed a trend towards signification.

### Association between gout features and cardiovascular disease

	Simple regression		Multiple regression	
	OR (95% CI)	p	aOR (95% CI)*	p
<b>Gout duration</b>	1.07 (1.03–1.10)	<0.001	1.06 (1.02–1.11)	0.005
<b>Number of attacks suffered</b>	1.00 (0.99–1.00)	0.561	-	-
<b>Number of involved joints</b>	1.09 (0.96–1.22)	0.177	-	-
<b>Joint pattern at presentation</b>				
<b>i. Monoarticular</b>	1. (ref)	-	1.0 (ref)	-
<b>ii. Oligoarticular</b>	2.30 (0.93–5.72)	0.073	1.71 (0.44–6.65)	0.440
<b>iii. Polyarticular</b>	3.56 (1.02–12.32)	0.045	5.33 (0.92–30.78)	0.061
<b>Tophi</b>	1.64 (0.73–3.69)	0.234	-	-

\*aOR: adjusted OR for age, gender, hypertension, diabetes, dyslipidemia, smoking background, obesity, and renal failure.

**Conclusions:** Time since first attack and likely a polyarticular presentation, two variables that may estimate crystal and inflammatory load in gout patients, are independently associated with the presence of CVD, adding evidence to the role of persistent inflammation on its development.

**Disclosure of Interest:** None declared

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FRI0248

### VALIDITY OF RANDOM URINARY URIC ACID-TO-CREATININE RATIO FOR ESTIMATING 24-HOUR URINE URIC ACID EXCRETION IN PATIENTS WITH GOUT

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**Background:** Gout is one of a heterogeneous group of diseases related to hyperuricemia. The measurement of 24 hour urinary uric acid excretion is frequently used to evaluate disease status and select drugs that lower uric acid level. However, 24 hour urine collection is inconvenient and frequently unreliable, due to errors in collection. Therefore, a simpler alternative to the 24 hour urine collection is needed.

**Objectives:** We investigated the utility of the random urine uric acid-to-creatinine (UA/CR) ratio in predicting 24 hour urine uric acid excretion in patients with gout.

**Methods:** Ninety patients with gout without any use of uric acid lowering agents were enrolled in this study. The mean age was 50.0±16.7 years old and the male patient was 90.0% (81/90) of all participants. For the evaluation of uric acid excretion and renal function, patients were collected 24 hour urine. Random urine uric acid and creatinine specimens were gained on the same day of 24 hour urine collection. Chronic kidney disease was defined as a creatinine clearance (Cr) level of less than 60 ml/min/1.73m<sup>2</sup> measured in 24 hour urine collection sample. Excretion of more than 600 mg of uric acid in the 24 hour urine sample was defined as uric acid over-excretion.

**Results:** Mean serum uric acid level was 7.73±1.89 mg/dl, and the mean 24 hour uric acid excretion was 666.5±236.2 mg. The random urinary UA/CR ratio showed positive correlation with 24 hour urine uric acid excretion ( $\gamma=0.398$ ,  $p<0.001$ ). Correlation between these two variables was also found in the patients with chronic kidney disease ( $\gamma=0.762$ ,  $p=0.028$ ). In the linear regression analysis, absolute 24 hour urine uric acid excretion was estimated to be 581 × (random urinary UA/Cr)+432 ( $p<0.001$ , adjusted  $R^2=0.398$ ). The best cut-off value for the random urinary UA/Cr ratio to distinguish between uric acid over-excretion and normal uric acid excretion was 0.342, with a sensitivity of 74.1%, specificity of 66.7%. The areas under the curves (AUCs) of the random urine UA/CR ratio was 0.763 [95% confidence interval (CI), 0.665–0.861,  $p<0.001$ ].

**Conclusions:** The random urine UA/CR ratio correlated with 24 hour urine uric acid excretions in patients with gout. The best cut-off random urine UA/CR ratio value to discriminate uric acid over-excretion was 0.342, with a sensitivity of 74.1% and a specificity of 66.7%. The random urine UA/CR ratio would be a useful

predictor to detect patients with urinary uric acid underexcretion, who could then be treated with uricosuric drugs.

**Disclosure of Interest:** None declared

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### FRI0249 AUDIT OF THE MANAGEMENT OF GOUT -ARE WE DOING IT RIGHT?

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**Background:** Gout is the most prevalent inflammatory arthritis, affecting 2.5% of adults in the UK. However, management is often inadequate in both primary and secondary care, with only 45% of patients achieving target serum urate (SUA) level <360µmol/L over 12 months in UK rheumatology clinics. A better understanding of how well gout is managed in different areas of our service (discharge to GP, general rheumatology follow-up clinics, and specialist gout clinic) will inform service redesign.

**Objectives:** To compare the management of gout in the rheumatology service against the 2007 British Society for Rheumatology (BSR) and 2006 European League Against Rheumatism (EULAR) gout guidelines, and the NICE febuxostat technology appraisal (TA164).

**Methods:** We retrospectively audited all new out-patient referrals with gout seen in our department over a 12 month period (January-December 2015). Data were collected by electronic review of case notes and completion of a structured proforma. Three mutually exclusive groups were compared: those seen once in rheumatology and discharged to GP (group1), followed-up in general rheumatology clinics (group2), or followed-up in a specialist gout clinic (group3). Follow-up SUA levels were specifically compared to EULAR (<360µmol/L) and BSR (<300µmol/L) treatment targets.

**Results:** 150 new consecutive gout referrals (50 per group) were included in the audit: 83% were male and mean age was 62 years. Gout was diagnosed by monosodium urate crystal identification in 16 (11%) and 25% had tophi. 43 (29%) patients were already on ULT, and 107 (71%) patients were newly commenced on ULT. Prophylactic medications were co-prescribed in 86% (130) cases. 44 patients were taking diuretics; diuretics were advised to be stopped or reduced in 12% cases. Nearly all patients starting allopurinol commenced a daily dose of ≤100 mg (99% cases). Of the patients started on a uricosuric/febuxostat, 92% had taken allopurinol previously. Of the 15 patients commenced on febuxostat, 3 (15%) had ischaemic heart disease (IHD) or cardiac failure. Chronic kidney disease (CKD) stage 3 (group1 28%, group2 22%, group3 34%), CKD stage 4/5 (2%, 2%, 10%), IHD/cardiac failure (30%, 30%, 40%), clinically evident tophi (16%, 18%, 42%) and previous allopurinol intolerance (10%, 14%, 24%) were more common in group 3 than groups 1 and 2. After 12 months, only 90 (60%) patients achieved target <360µmol/L (group1 42%, group2 64%, group3 62%) and 47 (31%) patients achieved target SUA <300µmol/L (group1 20%, group2 34%, group3 36%).

**Conclusions:** Allopurinol starting dose, use of prophylaxis, and use of allopurinol first-line concurred well with national and international guidelines. We achieved target SUA levels more commonly than the UK national average in a recent national rheumatology audit. Patients discharged to the GP with a management plan prior to achieving a target SUA level achieved target less frequently suggesting that rheumatologists should follow patients in order to ensure treatment is escalated until the target SUA level is achieved.

**Disclosure of Interest:** None declared

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### FRI0250 BELIEFS ABOUT MEDICINES AMONG GOUT PATIENTS - DATA FROM THE NOR-GOUT STUDY

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**Background:** Low adherence to medication is a concern in gout where urate lowering therapy (ULT) is indicated to prevent disease severity and comorbidities. The beliefs patients have about medication may impact on the success of achieving these treatment goals.

**Objectives:** To study which factors were associated to beliefs about medicines in patients with a recent gout attack and a need for ULT.

**Methods:** Baseline data from a prospective observational study were used in patients with crystal-proven gout who presented after a recent gout flare with insufficiently treated serum urate (sUA) level (>360 µmol/L/>6 mg/dl). In these patients a treat-to-target approach was planned to meet the treatment target (sUA <360 µmol/L, or <300 µmol/L if clinical tophi). Assessment included demographic and clinical data, baseline serum urate levels, medication, self-administered

comorbidity questionnaire (SCQ), physical function (HAQ), and SF-36 mental (MCS) and physical component summaries.

The Beliefs in Medicines Questionnaire (BMQ)<sup>1</sup> assesses patient beliefs about medicines on four subscales: necessity and concerns specific for the patient, and generally on overuse and harm. Respondents indicated their degree of agreement with each individual statement about medicines on a 5-point Likert scale, (1=strongly disagree to 5=strongly agree). Scores within the four subscales (necessity, concerns, overuse, harm) were summed (ranges 5–25 and 4–20). Calculation of the necessity-concerns differential gave the relative importance for the patient for taking medicines.

**Results:** 163 patients were included at baseline, 93.3% men, 90.5% caucasian, mean (SD) age 57.0 (14.1) years, disease duration 8.0 (7.7) years). Mean sUA level was 487 (SD 82) µmol/L at baseline, body mass index 28.9 (4.7) kg/m<sup>2</sup>, comorbidity score (SCQ) 3.6 (3.2), and physical function (HAQ) 0.35 (0.55). 18.8% (n=28) had tophi, and 30.1% (n=43) were using allopurinol.

Scores for the BMQ subscales (SD) were for necessity 16.8 (4.3), concerns 13.7 (5.0), overuse 10.6 (2.7), and harm 9.5 (2.4). The specific necessity-concerns differential was 3.1 (5.7), with median 2.5. Patients expressing higher versus lower beliefs in importance of medication (necessity-concern higher than median) demonstrated in bivariate comparisons statistically significant differences (table 1). The level of serum urate was not associated with any BMQ subscale.

In logistic regression analyses, also adjusting for age and gender in the final model, high beliefs in the relative importance of medication were independently associated with not using allopurinol medication (OR 0.41, 95% CI 0.18–0.94), with higher BMI (OR=1.11 per unit, 95% CI 1.02–1.20), and better mental health (SF36 MCS) (OR 1.04 per unit, 95% CI 1.01–1.08).

	High belief (>median)	Low belief	p-value
BMI	29.6	28.2	0.048
Comorbidity score (SCQ)	2.3	4.4	0.02
Taking allopurinol	25.8%	37.9%	0.09
SF36 MCS	50.8	47.1	0.03
BMQ overuse	9.9	11.4	0.001
BMQ harm	8.9	10.2	0.001

**Conclusions:** Unexpectedly, using allopurinol medication was inversely associated with high beliefs, whereas higher BMI and better mental health were positively associated with high beliefs in the importance of medication in gout patients. These findings do not allow conclusions on causality, and beliefs in medicines in gout patients should also be studied longitudinally and in relationship to therapy response.

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### FRI0251 PREVALENCE OF GOUT AND THE USE OF URATE LOWERING AGENTS IN US GENERAL POPULATION NHANES 2007–2016

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**Background:** The prevalence of gout has been increasing worldwide. Previous study using National Health and Nutritional Examination Survey (NHANES) showed an increase of 1.2% in the prevalence of gout in the US general population from 1988 to 2007. However, it is unknown if this trend continued over the past decades. Therefore, we would like to determine the prevalence of gout in the US general population using NHANES 2007 to 2016. In addition, the use of urate lowering agents among patients with gout was analysed.

**Objectives:** To estimate the prevalence of gout and the use of urate lowering agents using the National Health and Nutritional Examination Survey from 2007 to 2016

**Methods:** Adult participants in NHANES 2007–2016 were included in the analysis. NHANES is a continuous national survey conducted by the US Centres for Disease Control and Prevention and is designed to evaluate the health and nutritional status of adults and children in the US. They are based on a representative sample of the non-institutionalised US civilian population. Each participant represents approximately 50000 Americans.

The primary outcome was self-reported gout. Factors associated with gout, such as body weight, drinking habit, history of chronic kidney disease, use of aspirin and thiazide diuretics were evaluated. Prescriptions of allopurinol, febuxostat or probenecid were retrieved from the NHANES dataset to evaluate the use of urate lowering agents among patients with gout.



Results were analysed using SPSS complex sample module version 22. Multiple regression was used to analyse the difference in prevalence of gout and utilisation of urate lowering agents.

**Results:** 23482 adults participants were included in the analysis. There was no further increase in the prevalence of gout in the general US population. The prevalence was 3.82% and 3.84% in NHANES 2007–2010 and 2011–2016, respectively (p=0.966).

Although there is a decreasing trend in the serum urate levels among patients with gout, the utilisation of urate lowering agents remained low. Only 28.2% and 29.4% of patients with gout were prescribed urate lowering agents in 2007–2010 and 2011–2014, respectively.

Among patients with gout, history of chronic kidney disease and use of thiazide diuretics are the most significant negative predictors for achieving the therapeutic target of SUV <6 mg/dL (Odds ratio of 0.23 and 0.41, respectively). Use of aspirin was not a significant predictor for treatment failure.

NHANES survey cycle	2007-2010	2009-2010	2011-2012	2013-2014	2015-2016	P-value
% of population included	52%	62%	56%	57%	57%	
Prevalence of gout (CN)	3.9 (3.4-4.3)	3.7 (3.4-4.1)	3.8 (3.5-4.0)	4.2 (3.8-4.6)	3.9 (3.5-4.3)	0.396
% of patients on urate lowering agents	28.2 (24.4)	29.4 (24.4)	28.2 (23.8)	29.4 (24.4)	28.2 (23.8)	

	2007-2010	2009-2010	2011-2012	2013-2014	P-value
% of patients with gout	259	277	239	334	
Prevalence of gout (%)	2.7 (1.9-3.4)	2.8 (2.0-3.6)	2.6 (1.7-3.7)	3.5 (2.4-4.6)	0.060
% of patients on urate lowering therapy	28.2 (24.4-32.1)	29.4 (25.3-33.5)	28.2 (23.7-32.7)	29.4 (24.7-34.1)	0.086
Median serum urate (mg/dL)	5.8 (5.3-6.3)	5.8 (5.3-6.3)	5.7 (5.2-6.2)	5.6 (5.1-6.1)	0.009
% of patients with chronic kidney disease	8.0 (6.8-9.2)	8.8 (7.6-10.0)	9.7 (8.5-10.9)	11.0 (9.8-12.2)	0.179
% of patients on thiazide diuretics	6.0 (4.8-7.2)	6.2 (5.0-7.4)	5.9 (4.7-7.1)	6.4 (5.2-7.6)	0.040
% of patients on aspirin	5.7 (4.5-6.9)	5.7 (4.5-6.9)	6.4 (5.2-7.6)	6.8 (5.6-8.0)	0.111
% of patients on NSAIDs	7.0 (5.8-8.2)	6.6 (5.4-7.8)	7.8 (6.6-9.0)	7.3 (6.1-8.5)	0.276
% of patients on colchicine	0.5 (0.3-0.7)	0.6 (0.4-0.8)	0.6 (0.4-0.8)	0.7 (0.5-0.9)	0.097

	10 years analysis	5 years analysis
OR		
95% CI		
10-15	0.72 (0.27-1.79)	0.71 (0.45-1.10)
15-20	0.48 (0.20-0.93)	0.48 (0.24-0.93)
20-25	0.44 (0.22-0.91)	0.44 (0.22-0.91)
25-30	0.56 (0.26-0.99)	0.56 (0.26-0.99)
30-35	1.20 (0.24-6.04)	1.20 (0.24-6.04)
35-40	0.58 (0.22-0.94)	0.41 (0.24-0.71)
40-45	0.72 (0.30-1.47)	0.59 (0.27-1.47)
45-50		0.73 (0.40-1.35)

**Conclusions:** The prevalence of gout in the US general population has not increased over the past 10 years. Although the use of urate lowering agents among patients with gout remained low, the percentage of patients with gout achieving the therapeutic target has increased over the past 10 years.

History of chronic kidney disease and use of thiazide diuretics are the most significant negative predictors for treatment success.

**Disclosure of Interest:** None declared

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**FRI0252 TESTING FOR A CAUSAL ROLE OF MITOCHONDRIAL VARIATION IN THE DEVELOPMENT OF GOUT**

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**Background:** Mitochondria execute critical roles in diverse cellular pathways. As a danger signal mitochondria induce inflammation in response to stress through NLRP3 inflammasome activation, central to gout development. We recently reported association of reduced mtDNA copy number (CN) with prevalent gout in New Zealand Māori and Pacific (Polynesian) populations<sup>1</sup>. However the cause-effect relationship is unknown. This could be evaluated by testing for association with gout using nuclear genetic variants that associate with mtDNA CN.

**Objectives:** 1) Genome wide association study (GWAS) for mtDNA CN to identify nuclear and mitochondrial loci controlling mtDNA copy number 2) test any such loci for association with gout.

**Methods:** The mtDNA CN GWAS comprised 1340 Eastern Polynesian (EP), 816 Western Polynesian (WP) and 4579 European samples (New Zealand, Germany, The Netherlands, Scotland) genotyped on the Illumina CoreExome v24 array. 343 mitochondrial single nucleotide polymorphisms (SNPs) were evaluated. As

previously described<sup>2</sup> the median of the absolute difference in X and Y probe intensities was used as a measure of mtDNA CN, and additional 10 000 randomly selected autosomal SNPs were used to calculate the principal components (PCs). A mtDNA CN GWAS was run on chromosomes 1–22 and the mitochondrial genome using Plink 1.9 .v2, adjusting for the first 10 PCs, age and sex followed by association analysis with gout adjusting by age, sex and the first 10 PCs generated from a separate set of 3000 autosomal SNPs.

**Results:** The association of reduced mtDNA CN with gout in the EP and WP groups was reproduced but there was no evidence of association of mtDNA CN with gout in Europeans. Two genome-wide significant (p<1x10<sup>-7</sup>) variants *MUC17 rs78010183* (T-allele) and *SLC16A8 rs75640043* (T-allele) were associated with increased mitochondrial CN in EP and WP, respectively, and mitochondrial variant *rs3928306* was associated with mtDNA CN (p=4.49x10<sup>-12</sup>) in Europeans. *MUC17 rs78010183* also associated with increased mtDNA CN in Europeans, with the T allele also increasing CN (β=0.06, p=1.07x10<sup>-4</sup>). The T-allele of *rs78010183* was associated with gout in Europeans (OR=9.32, p=5.53x10<sup>-3</sup>) and the *SLC16A8 rs75640043* T-allele was associated with gout in the WP group (OR=6.85, p=5.50x10<sup>-3</sup>). The mitochondrial variant *rs3928306* A-allele (very rare in Polynesian) was not associated with gout in Europeans (OR=1.09, p=0.36).

**Conclusions:** That genetic variants associated with mitochondrial copy number also associate with gout provides evidence for a potential causal role of mitochondrial copy number in gout. However, the nuclear genetic variants support a causal relation of increased mtDNA CN with gout, conflicting with our previous observational report of association of reduced mtDNA CN with gout<sup>1</sup>.

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**FRI0253 TRENDS FOR GOUT IN ADULTS IN AN URBAN AREA FOR A 5-YEAR PERIOD: INCIDENCE, PREVALENCE AND HOSPITALISATION RATES**

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**Background:** Gout is one of the most common arthritis nowadays which has a great influence on patient's quality of life, course and outcomes of cardiovascular and renal pathology.<sup>1</sup> Some recent papers demonstrate that the prevalence of gout has risen over the last decades and underline the scarcity or lack of epidemiologic data in different countries as well as the notable variations among them.<sup>2,3</sup>

**Objectives:** We estimated incidence, prevalence and hospitalisation rates for gout in Minsk (the Republic of Belarus) for the 5 year period (2011–2015).

**Methods:** Minsk is a typical urban area which is considered to be representative for the urban population of the whole country. The data on the new onset gout and the first visit for gout in a corresponding year were collected from all rheumatologic services of Minsk for the 5 year period from January, 1 of 2011 to December, 31 of 2015. Only patients older than 18 years old with the diagnosis of gout according to the ICD-10 (M10) were included. The data on age and sex structure of the population of the Republic of Belarus were obtained from the annual Statistical bulletins of the National Statistical Committee of the Republic of Belarus. Hospitalisation rates were calculated on the base of statistical reports on discharges for the corresponding year.

**Results:** There were no significant differences in age and sex structure of the population in Belarus and Minsk for the study period. The size of the adult population, incidence and prevalence of gout, hospitalisation rates and duration of hospitalizations for gout for the corresponding years in Minsk are presented in the table 1. According to these data the gout incidence for the 5 year period changed from 25.0 (CI 95% 24.7–25.2) to 35.5 (CI 95% 35.3–35.8) per 100 000 adults, the gout prevalence for the period 2011–2015 also increased from 178.9 (CI 95% 178.3–179.5) to 290.3 (CI 95% 289.6–291.0) per 100 000 adults (p<0.001 for both trends). There were 2688 hospitalizations in Minsk for gout for the study period. The mean age of hospitalised patients was 57.3±10.3 years (median 58.0; range 25–87), 91.4% were men (92%; 87.8%–94.9%). It is worth noting that 45.6% of hospitalised patients were at the age 55–65% and 90.2% were under 70 years old with sharp decrease of hospitalizations after 65 years of age. Hospitalisation rates

also increased from 28.7 to 38.2 per 100 000 adults ( $p < 0.001$ ). The mean duration of hospitalisation was  $12.5 \pm 2.7$  days (13 days; 2–26 days) and increased from 11.6 to 12.7 ( $p = 0.03$ ).

**Abstract FRI0253 – Table 1**

	2011	2012	2013	2014	2015
Population size in Minsk, adults	1537880	1555210	1568320	1585480	1598120
Incidence per 100 000	25.0	26.2	35.3	38.0	35.5
Prevalence per 100 000	179	228	248	255	290
Hospitalisation rate per 100 000	28.7	36.8	33.5	33.9	38.2
Hospitalisation duration, days	11.6	12.5	13.1	12.7	12.7

**Conclusions:** We revealed significant increase in incidence, prevalence as well as hospitalisation rates for gout in adults in Minsk (the Republic of Belarus) for the 5 year period (2011–2015) in 1.4, 1.6 and 1.3 times, correspondingly.

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FRI0254

#### CLINICAL FEATURES AND RISK FACTORS FOR DEVELOPING GOUT ATTACKS DURING ANTI-TUBERCULOSIS MEDICATION: A CASE-CONTROL STUDY IN SOUTH KOREA

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**Background:** Gout is a form of inflammatory arthritis that develops in some people with hyperuricemia. Several drugs may induce hyperuricemia and gout attack. Some anti-tuberculosis (TB) medications are also known to increase uric acid level and trigger acute gout attack. However, there have been no well-described studies for gout during anti-TB therapy.

**Objectives:** To investigate the clinical features and risk factors of gout attacks following anti-TB treatment in South Korea.

**Methods:** We conducted the case-control study including 49 patients who developed gout attack following anti-TB medications and 147 age- and sex- matched TB controls without gout attack. Demographic, clinical features and laboratory findings of patients with gout attacks following anti-TB medication were analysed and compared to those of controls in order to establish risk factors associated with gout attack during anti-TB treatment.

**Results:** The mean age was  $67.7 \pm 13.2$  years and 39 patients (79.6%) were male. Twenty-four patients (49.0%) had a previous history of gout. The mean time interval to develop gout attack from the initiation of anti-TB therapy was  $4.13 \pm 4.49$  months. The attacks tended to involve lower extremity joints (43/49, 87.8%), especially the ankle and the first metatarsophalangeal joint. Factors associated with experiencing gout attack during anti-TB medication were higher body mass index (BMI,  $23.7 \pm 3.6$  vs  $21.8 \pm 3.6$ ,  $p = 0.003$ ), higher pre-treatment uric acid level ( $7.2 \pm 2.5$  vs  $6.2 \pm 1.7$  mg/dL,  $p < 0.001$ ), previous history of gout (49.0% vs 1.4%,  $p < 0.001$ ), absence of dyslipidemia (4.1% vs 16.3%,  $p = 0.008$ ), and decreased renal function (eGFR  $63.6 \pm 27.5$  vs  $82.6 \pm 29.9$ ,  $p = 0.003$ ). In multivariate model, higher BMI, chronic kidney disease (CKD, eGFR  $< 60$  ml/min/1.73m<sup>2</sup>), previous history of gout, and pre-treatment hyperuricemia (uric acid  $\geq 6.8$  mg/dL) were

found to be independent risk factors for gout attack following anti-TB medication (table 1).

**Abstract FRI0254 – Table 1.** Multivariate analysis of risk factors for post-TB medication gout

	Odds ratio	95% CI	p-value
Body mass index (BMI)	1.202	1.029–1.403	0.020
Previous history of gout	71.39	12.790–398.467	<0.001
Chronic kidney disease (eGFR $< 60$ ml/min/1.73m <sup>2</sup> )	2.794	1.012–7.719	0.047
Pre-treatment hyperuricemia (Serum uric acid $\geq 6.8$ mg/dL)	4.866	1.770–13.378	0.002

**Conclusions:** TB patients with obesity, history of gout, pre-treatment hyperuricemia, and CKD have higher risk for having gout attack following anti-TB medication. When starting anti-TB therapy in TB patients with these risk factors, physicians should pay attention to the development of gout attack and educate the patients.

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#### SLE, Sjögren's and APS – etiology.3, pathogenesis and animal models

FRI0255

#### INJECTION OF CD40 DNA VACCINE AMELIORATES THE AUTOIMMUNE PATHOLOGY OF NON-OBESE DIABETIC MICE WITH SJOGREN'S SYNDROME

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**Background:** In the patients with primary Sjögren's syndrome (pSS), overexpression of CD40 was reported. The increased CD40 expression contributes to enhance CD40-CD40L interaction and promotes the inflammatory response in various ways.

**Objectives:** To investigate whether CD40 DNA vaccine could inhibit the immune response and slow the disease progression of SS in non-obese diabetic (NOD) mice.

**Methods:** Female 8-week-old NOD mice were randomly divided into 3 groups. CD40 DNA vaccine group received pTaget CD40 DNA vaccine at a weekly dose of 50 ug for 4 weeks. Vector and NS group were administered an equivalent amount of empty vector or NS. Serum anti-CD40 antibody was measured by ELISA. Lymphocytes infiltration in the salivary glands was monitored by focus score (FS) calculation. Salivary CD40 was stained by immunohistochemistry. Splenic lymphocyte phenotypes were analysed by flow cytometry. CD40, TNF- $\alpha$  and IL-6 levels in the salivary glands were detected by PCR. Serum ANA was monitored by immunofluorescence.

**Results:** 1) CD40 DNA vaccination induced anti-CD40 antibody response We found the positive rate on anti-CD40 antibody in vaccine group was 80% at week 6% and 100% at week 10, which was significantly increased compared with that in nonvaccinated ones ( $p < 0.05$  and  $p < 0.01$ , respectively)

2) Expression of CD40 decreased in salivary glands in vaccine group

At week 10, CD40 expression on ductal epithelial and endothelial cells in NOD mice of vaccine group was significantly decreased positive staining. CD40 mRNA expression level showed a significant reduction compared to vector group ( $0.51 \pm 0.31$  vs.  $1.56 \pm 0.53$ ,  $p < 0.05$ ).

3) Down-regulation of lymphocytes infiltration in the salivary glands of mice in vaccine group

At week 10, infiltration of lymphocytes was inhibited in treated group while increased in control group ( $F=5.275$ ,  $P < 0.05$ ). FS was significantly decreased in vaccine group as compared to NS group ( $2.00 \pm 1.73$  vs.  $11.33 \pm 5.51$ ,  $P < 0.05$ ).

Average weight of wet salivary gland and the ratio of average salivary gland weight to body weight of NOD mice in vaccine group were significantly lower than that in control groups ( $p < 0.05$  and  $p < 0.05$ , respectively).

4) CD40 DNA vaccine reduced the expression of TNF- $\alpha$  and IL-6 in the salivary glands

In vaccine group, the expression level of TNF- $\alpha$  mRNA in salivary glands were declined significantly as compared to baseline ( $0.41 \pm 0.25$  vs.  $0.98 \pm 0.16$ ,  $p < 0.05$ ) and IL-6 mRNA expression was down-regulated compared with control groups at week 10 ( $p < 0.05$ ;  $p < 0.01$ , respectively).

5) Disturbances in spleen DC and plasma cell subpopulations

At week 6, the total numbers of CD11c<sup>+</sup>DC decreased as compared with two control groups ( $p < 0.05$  and  $p < 0.05$ , respectively). CD11c<sup>+</sup>DC and CD19<sup>+</sup>CD138<sup>+</sup>plasma cells were significantly reduced compared to basal level ( $p < 0.01$  and  $p < 0.05$ , respectively).

6) Level of ANA reduced in the vaccine group

At week 10, the expression of ANA in HEp-2 cells is strong positive (++++) in both control groups, but only positive (+) in vaccine group.

**Conclusions:** These findings indicate that CD40 DNA vaccine can downregulate the expression of proinflammatory cytokines of TNF- $\alpha$  and IL-6, decrease the percentage of DCs and plasma cells, ameliorate the pathologic change in NOD mice with SS, and thus inhibit the autoimmune inflammation.

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FRI0256

#### EFFECTS OF ANIFROLUMAB ON OXIDATIVE STRESS AND MACROPHAGE ACTIVATION: NOVEL BIOMARKERS AND IMPACT OF TYPE I INTERFERON BLOCKADE IN SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Type I interferons (IFNs) drive several aspects of systemic lupus erythematosus (SLE) etiology and pathophysiology. Anifrolumab, a fully human anti-IFN- $\alpha$  receptor monoclonal antibody, substantially reduced disease activity compared with placebo in a Phase IIb study of SLE patients.<sup>1</sup> Previous results indicated beneficial effects of anifrolumab on dysregulated lymphocyte, neutrophil, and complement systems in SLE.<sup>2</sup> However, the impact of type I IFN blockade remains to be fully elucidated.

**Objectives:** We characterised biomarkers for oxidative stress and macrophage activation in SLE and assessed downstream effects of anifrolumab on those two key disease pathways.

**Methods:** In the MUSE study,<sup>1</sup> 305 patients with moderate to severe SLE were randomised in a 1:1:1 ratio to receive placebo or anifrolumab (300 or 1,000 mg) every 4 weeks for 48 weeks. A four-gene expression assay was used to define type I IFN gene signature (IFNGS) test status. In our study, four protein biomarkers were measured in sera of healthy controls (HCs) and SLE patients with samples available at baseline, and 85, 169, and 365 days after administration, using a multiplex luminex immunoassay. Wilcoxon rank-sum test was used to evaluate baseline protein concentrations and posttreatment changes between different groups.

**Results:** Two oxidative stress biomarkers, peroxiredoxin 4 (PRDX4) and aldose reductase (AKR1B1), were found in greater serum concentrations in 195 SLE patients than in 20 HCs ( $p < 0.01$ ). Their increased concentrations were associated with greater SLEDAI scores and abnormal anti-dsDNA concentrations ( $p < 0.05$ ). PRDX4 concentrations were greater for IFNGS test-high ( $n=144$ ) vs IFNGS test-low ( $n=51$ ) patients ( $p < 0.01$ ), whereas AKR1B1 was not associated with type I IFNGS-test status. Anifrolumab suppressed PRDX4 in IFNGS test-high patients compared with placebo ( $p < 0.05$ ). In contrast, no significant changes were observed for AKR1B1 after anifrolumab treatment. Folate receptor 3 (FOLR3) and CD163 are markers of activated macrophages, the former of which has not been characterised in SLE. Our results demonstrated greater concentrations of both FOLR3 and CD163 in IFNGS test-high than in IFNGS test-low patients and HCs, along with significant associations with SLEDAI score and anti-dsDNA concentrations. Anifrolumab reduced serum concentrations of both FOLR3 and CD163 in IFNGS test-high but not IFNGS test-low patients vs. placebo ( $p < 0.05$ ). Moreover, cellular enumeration data demonstrated anifrolumab-induced upregulation of

monocyte count in IFNGS test-high patients, which may result from reduced activation, apoptosis, and/or tissue infiltration of monocytes/macrophages.

**Conclusions:** Our results identified PRDX4 as an oxidative stress marker and FOLR3 as a macrophage activation marker associated with disease activities and type I IFNGS test status in SLE. Anifrolumab administration elicits reduced oxidative stress and decreased monocyte/macrophage activation, which may contribute to the clinical efficacy of anifrolumab in SLE patients.

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FRI0257

#### THE STAT4 SLE RISK ALLELE RS7574865[T] IS ASSOCIATED WITH INCREASED IL-12-INDUCED IFN-GAMMA PRODUCTION IN T CELLS FROM SLE PATIENTS

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**Background:** Genetic variants in the transcription factor *STAT4* are associated with increased susceptibility to systemic lupus erythematosus (SLE) and a more severe disease phenotype.

**Objectives:** This study aimed to clarify how the SLE-associated intronic *STAT4* risk variant rs7574865[T] affects the function of immune cells in SLE.

**Methods:** Peripheral blood mononuclear cells (PBMCs) were isolated from 52 SLE patients in remission (SLEDAI-2K $\leq$ 4). *STAT4* and *STAT1* protein levels and phosphorylation status in response to interferon (IFN)- $\alpha$ , IFN- $\gamma$ , or interleukin (IL)-12 were determined, before and after pre-activation of cells with phytohaemagglutinin (PHA) and IL-2, in CD56<sup>dim</sup> NK cells, CD56<sup>bright</sup> NK cells, B cells, CD4<sup>+</sup> T cells, CD8<sup>+</sup> T cells and monocytes by flow cytometry. The frequency of IFN- $\gamma$ <sup>+</sup> cells upon IL-12 or PMA (phorbol 12-myristate-13-acetate) stimulation and the frequency of T-bet<sup>+</sup> cells was determined in PHA/IL-2 pre-activated cells. Cellular responses and phenotypes were correlated with *STAT4* risk allele carrier status (rs7574865[T], 21 homozygous protective, 22 heterozygous and 9 homozygous risk) using an additive linear regression model. Janus kinase inhibitors (JAKi) selective for TYK2 (TYK2i, Compound 35) or JAK2 (JAK2i, BMS-911543) were evaluated for inhibition of IL-12 or IFN- $\gamma$ -induced activation of SLE PBMCs.

**Results:** In resting PBMCs, the *STAT4* risk allele was neither associated with protein levels of *STAT4* or *STAT1*, nor cytokine-induced phosphorylation of *STAT4* (pSTAT4) or *STAT1* (pSTAT1). However, following PHA/IL-2-activation, CD8<sup>+</sup> T cells from *STAT4* risk allele carriers displayed increased levels of *STAT4* ( $p=0.04$ ), resulting in increased pSTAT4 in response to IL-12 ( $p=0.003$ ) and IFN- $\alpha$  ( $p=0.04$ ). Analysis of T cell subsets revealed that the effect was seen in CD45RA<sup>+</sup>CD57<sup>-</sup> naïve and CD45RA<sup>+</sup>CD57<sup>+</sup> memory CD8<sup>+</sup> T cells, but not in CD45RA<sup>+</sup>CD57<sup>+</sup> memory or CD45RA<sup>+</sup>CD57<sup>+</sup> effector CD8<sup>+</sup> T cells. A slight increase in *STAT4* protein levels and IL-12-induced pSTAT4 was also observed in CD4<sup>+</sup> T cells from *STAT4* risk allele carriers ( $p=0.08$  and  $p=0.09$ , respectively). *STAT4* risk allele carriers displayed an augmented IL-12-induced IFN- $\gamma$  production in CD8<sup>+</sup> and CD4<sup>+</sup> T cells ( $p=0.03$  for both), whereas PMA-induced IL-12 production was normal ( $p=0.31$  and  $p=0.10$ , respectively). T-bet expression was not correlated to the *STAT4* genotype. The TYK2i and the JAK2i efficiently blocked IL-12 and IFN- $\gamma$ -induced activation of PBMCs from *STAT4* risk patients, respectively.

**Conclusions:** T cells from SLE patients carrying the *STAT4* risk allele rs7574865 [T] display an augmented response to IL-12 and IFN- $\alpha$ . This subset of patients may benefit from JAKi treatment.

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### FRI0258 COMPARISON OF ELISA AND MULTIPLEX TECHNIQUES FOR QUANTIFYING A URINE BIOMARKERS PANEL FOR LUPUS NEPHRITIS IN CHILDREN

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**Background:** A urine 'biomarker panel' comprising alpha-1-acid-glycoprotein (AGP), ceruloplasmin (CP), transferrin (TF) and lipocalin-like-prostaglandin-D synthase (LPGDS) has been shown to cross-sectionally perform to an 'excellent' level for Lupus Nephritis (LN) identification in children.<sup>1</sup> Quantification of all four biomarkers by enzyme linked immunoabsorbant assay (ELISA) techniques is time consuming and costly. Therefore, novel methods of biomarker panel quantification are required to facilitate future urine biomarker led monitoring studies.

**Objectives:** The main objective was to compare the ability of ELISA and multiplex biomarker quantification techniques to differentiate active versus inactive LN when the biomarkers are considered individually and in combination.

**Methods:** The urinary biomarkers were quantified by both ELISA and a newly developed, custom multiplex platform in participants of the UK Juvenile Systemic Lupus Erythematosus (JSLE) Cohort Study. Multiplex assay development involved identification of appropriate antibody pairs, assessment of JSLE urine sample matrix effects and range finding in JSLE patient samples. Patients were categorised as having active LN (renal domain BILAG score of A, B and previous histological confirmation of LN) or inactive LN (renal BILAG score D or E). Firth's penalised binary regression with AUC ROC analysis was used to compare the ability of multiplex and ELISA assays to detect active LN disease state univariately and in combination.

**Results:** Biomarker analysis was undertaken on 54 JSLE patients (13 active, 41 in-active). Assessment of each biomarker univariately demonstrated similar AUC values regardless of the biomarker quantification technique; LPGDS (ELISA AUC 0.826, multiplex AUC 0.829), TF (ELISA AUC 0.829, multiplex AUC 0.996), CP (ELISA AUC 0.901, multiplex AUC 0.983), AGP (ELISA AUC 0.934, multiplex AUC 0.979) (see table 1). Combining the multiplex biomarker data in the same order as the original ELISA based study<sup>1</sup> led to a similar progressive increase in AUC as biomarkers were added to the model (optimal model including AGP +CP + LPGDS+TF ELISA AUC=0.951, multiplex=0.995). For all biomarker combinations, the multiplex-derived AUC was higher than the ELISA AUC.

Abstract FRI0258 – Table 1. AUC values generated looking at each biomarker univariately

Individual biomarkers	ELISA AUC	Multiplex AUC
LPGDS	0.826	0.829
TF	0.829	0.996
CP	0.901	0.983
AGP	0.934	0.979

Abstract FRI0258 – Table 2. Comparison of biomarker combination AUC ROC values

Biomarker combinations	ELISA AUC	Multiplex AUC
AGP	0.880	0.979
AGP+CP	0.937	0.986
AGP+CP+LPGDS	0.942	0.985
AGP+CP+ LPGDS+TF	0.951	0.995

**Conclusions:** This new LN urine biomarker panel multiplex assay has been shown to display a comparable ability for active LN disease state identification as compared to existing ELISA techniques. The major advantage to this approach is that it reduces cost, processing time and the volume of sample required, as compared to ELISA techniques, representing a key enabler for future clinical studies.

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### FRI0259 IN VITRO INDUCED REGULATORY T-CELLS CAN AMELIORATE SEVERITY OF PRISTANE INDUCED LUPUS (PIL)

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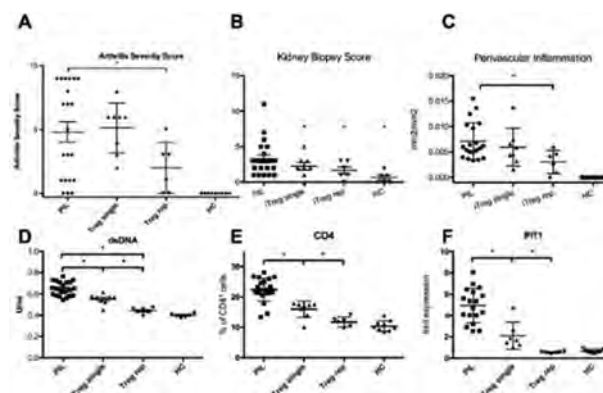
**Background:** Pristane induced lupus (PIL) is an established murine model of induced systemic lupus erythematosus (SLE). Mice develop specific autoantibodies and show symptoms of SLE including arthritis, glomerulonephritis and haemorrhagic pulmonary capillaritis.

**Objectives:** To investigate the therapeutic effects of *in vitro*-induced regulatory T cells (iTreg) in the murine model of PIL.

**Methods:** BALB/c mice were injected i.p. with 0.5 ml of pristane (PIL) or PBS (control). Naive CD4<sup>+</sup> thymocytes were sorted and cultured and cell suspensions with >80% CD4<sup>+</sup>FoxP3<sup>+</sup> cells (iTreg) were injected i.v. (i) once when PIL was induced (5 × 10<sup>6</sup> iTreg (iTreg-single)) or (ii) every 4 weeks (1 × 10<sup>6</sup> iTreg, iTreg-rep). Mice were monitored for paw swelling and grip strength. After 8 months, histological analysis quantified cartilage degradation, number of osteoclasts, extent of inflammation and bone erosion. Glomerulonephritis and pneumonitis were quantified using the kidney biopsy score and a histomorphometric image analysis system; inflammatory tissue was analysed by tissue cytometry. Serum levels of auto-antibodies were measured by ELISA. Frequencies of B cells, activated and regulatory CD4<sup>+</sup> T cells and Th1, Th2, Th17 cells were measured by flow cytometry. FlowCytomix Pro was used to measure serum cytokines. RT-qPCR was used to measure expression levels of interferon (IFN)-signature and T-cell subset related as well as inflammation-associated genes.

**Results:** Monthly injections of 1 × 10<sup>6</sup> iTreg reduced the clinical and histological severity of PIL-arthritis. This was seen by a higher mean grip strength, less mean paw swelling, retardation of symptom onset and a lower summative arthritis severity score (figure A). There was significant reduction of arthritis severity in all histological parameters and in the percentage of affected mice with erosive arthritis (33% of iTreg-rep mice vs 62% of PIL-mice). A single boost of 5 × 10<sup>6</sup> iTreg could not prevent joint manifestation, however a slight retardation in 'loss of grip strength' and significantly less erosive area was seen. In regards to cellular composition of the inflammatory tissue in paws, a significantly increased relative amount of CD4<sup>+</sup>Foxp3<sup>+</sup> cells was seen in the iTreg-rep group compared to PIL group.

Repeatedly injected mice (iTreg-rep) had significantly less renal disease (glomerular activity score) (figure B) and pulmonary involvement (perivascular inflammatory area) (figure C) compared to PIL. iTreg-rep mice had significantly lower serum levels of disease-associated auto-antibodies (figure D). Upon restimulation, splenic CD4<sup>+</sup> cells in iTreg-rep showed a less pronounced Th1, Th2 and Th17 response as well as lower percentages in B- and activated T-cells, whereas the percentage of Treg was higher than in all other groups (figure E). FlowCytomix analysis showed reduced cytokine production after repeated iTreg administration. Correspondingly, iTreg-rep showed decreased expressions of IFN-signature-, T-cell subset- and inflammatory cytokine related genes (figure F).



**Conclusions:** Repeated injections of iTreg ameliorate the clinical, histological, serological as well as the genetic severity of PIL-manifestations. A single boost of iTreg at time of disease induction does not prevent manifestations, but retards the

onset of symptoms. Thus iTreg have significant positive effects on PIL, which may have consequences for future approaches in treating SLE.

**Disclosure of Interest:** None declared

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FRI0260

### POLYMORPHISMS OF STAT4 AND MIR146A PREDICT THE ACHIEVEMENT OF 5 YEARS REMISSION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Systemic lupus erythematosus (SLE) is a chronic autoimmune disease with a complex pathogenesis in which genes and environmental factors interact leading to a protean clinical picture. Treat-to-target recommendations have identified 'remission' as a target in SLE, since achievement of remission improves the outcome and is associated with decreased damage progression. Nonetheless, predicting factors for the achievement of remission are lacking. It is likely that genes associated with SLE pathogenesis may influence the disease course.

**Objectives:** Thus, our aim was to analyse previously identified loci associated with SLE in a cohort of SLE patients to evaluate their influence on remission achievement.

**Methods:** We recruited 117 Italian SLE patients. A panel of 34 SNPs in 19 genes involved in immune response, autophagy and inflammation, was selected. SNPs genotyping was performed by allelic discrimination assay by TaqMan assays (Applied Biosystems, Foster City, CA, USA) and ABI PRISM 7000. The main clinical/laboratory features (including injury index and disease activity) were collected on an electronic platform. Remission was defined according to Zen et al.<sup>1</sup> and evaluated over 5 years. A genotype/phenotype correlation analysis was performed.

**Results:** The variant alleles of rs7574965 (STAT4) ( $p < 0.001$ ) and rs2910164 (MIR146a) ( $p = 0.031$ ) were significantly associated with lack of achievement of 5 years remission in SLE. Specifically, patients carrying the C allele of MIR146a were less likely to achieve 5 years remission ( $p = 0.01$ , OR 0.235, 95% CI 0.074–0.752) as well as to achieve remission after 1, 2 and 3 years of evaluation ( $p = 0.002$ ,  $p = 0.001$ ,  $p = 0.002$ , respectively). Among the clinical and laboratory features, 5 years remission was less likely to be achieved by patients who had arthritis in their clinical history ( $p = 0.007$ ), and who tested positive for anti-dsDNA ( $p = 0.005$ ). In a multinomial logistic regression analysis, arthritis ( $p = 0.022$ , Exp(B) = 0.255, 95% CI 0.079–0.820), anti-dsDNA ( $p = 0.003$ , Exp(B) = 0.166, 95% CI 0.051–0.537) and MIR146a rs2910164 gene variant ( $p = 0.046$ , Exp(B) = 0.250, 95% CI 0.064–0.974) were confirmed to be independent risk factors for unachieved 5 years remission (table 1).

Abstract FRI0260 – Table 1

REMISSION	Exp (B)	Exp (B) 95% CI	
		Lower	Upper
Arthritis	0255	0079	0,82
anti-dsDNA	0166	0051	0537
STAT4	0354	0,11	1139
mir146A	0,25	0064	0974

**Conclusions:** We describe for the first time the contribution of STAT4 and MIR146a SNPs as predicting factors for the achievement of 5 years remission in SLE. No genetic study has been performed so far in SLE, while a genetic profile of patients may be useful to predict the disease outcome.

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[1] Zen, et al. Ann Rheum Dis. 2017 Mar;76(3):562–565.

**Disclosure of Interest:** None declared

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FRI0261

### ASSESSMENT OF AUTOPHAGE FUNCTION IN SYSTEMIC LUPUS ERYTHEMATOSUS IN RESPECT OF HYPERLIPIDEMIA AND IMMUNOSUPPRESSIVE DRUGS

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**Background:** Autophagy is an orchestrated homeostatic process to eliminate unwanted proteins and damaged organelles. Lipid turnover, as well, is controlled by autophagy through a process described as lipophagy. Defective lipophagy has been already linked to important metabolic disorders such as fatty liver, obesity and atherosclerosis.

**Objectives:** Assessment of autophagy focusing on lipids regulation in untreated newly diagnosed systemic lupus Erythematosus (SLE) patients and after three months of treatment with immunosuppressive drugs.

**Methods:** Subjects in this study have been divided into three groups. Group 1 included 60 newly diagnosed SLE patients before receiving any treatment, group2 included the same subjects of group 1 after three months of treatment with immunosuppressive drugs and group 3 included 30 healthy donors of matched age and sex as a control group. For each subject, disease activity was assessed by (SLE-DAI) score, lipid profile was measured in addition to evaluation of lipids uptake, enhanced phagocytosis and intracellular killing ability of monocytes and neutrophils using Sudan Black B stain and Nitroblue tetrazolium stain mixed with latex particles coated with antibodies. Microscopic pictures were captured and quantified by ImageJ.

**Results:** 95% of patients were females(57/60) with mean of age(39.7±8.6). Mean of SLEDAI score in group 1 was (18.6±3.4) decreased in group 2 (3 months after treatment) to (10.4±4.2). There was a positive correlation between total cholesterol, LDL and triglycerides and disease activity(SLEDAI score) ( $r = 0.677$ ,  $r = 0.603$  and  $r = 0.718$ ; respectively). On the contrary, There was a negative correlation between HDL and disease activity( $r = -0.396$ ). Furthermore, there was a negative correlation between lipid content of cells and intracellular killing and disease activity( $r = -0.258$  and  $r = -0.324$ ; respectively). After 3 months, 100% of patients were taking Corticosteroids and Hydroxychloroquine(60/60).18.3% of patients received Azathioprine(11/60), 40.0% received Cyclophosphamide(24/60) and 15% received Mycophenolate(9/60) besides Corticosteroids and Hydroxychloroquine. Comparing group 2 to group 1, there was significant increase in cholesterol, LDL and triglycerides ( $p = 0.027$ ,  $p = 0.021$  and  $p = 0.017$ ; respectively) while HDL showed insignificant difference( $p = 0.0740$ ). Lipid content in cells and intracellular killing significantly decreased( $p = 0.0322$  and  $p = 0.0271$ ; respectively).

**Conclusions:** Autophagy is deficient in patients with SLE aggravated by immunosuppressive drugs so they are more susceptible to infections and dyslipidemia. Consequently, lipid lowering drugs are definitely required to decrease comorbidity.

**Disclosure of Interest:** None declared

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FRI0262

### MONITORING DISEASE ACTIVITY IN SYSTEMIC LUPUS ERYTHEMATOSUS WITH DIGITAL ELISA QUANTIFICATION OF SERUM INTERFERON- $\alpha$

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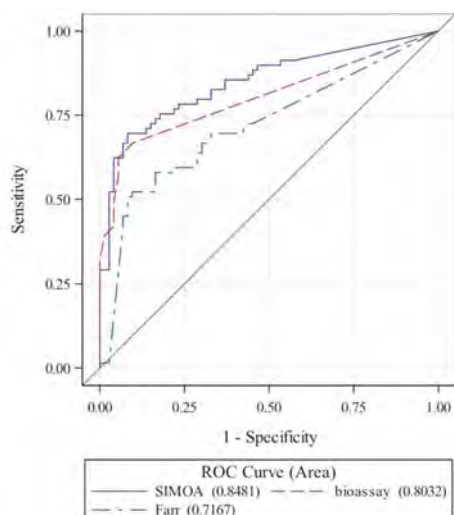
**Background:** To date, anti-dsDNA–Ab titration, better achieved with the Farr test, has been used to monitor global disease activity in systemic lupus erythematosus (SLE). Indeed, anti-DNA–Ab-positivity is associated with overall SLE activity. However, the sensitivity and specificity of that association are relatively low. The close association between Interferon alpha (IFN $\alpha$ ) expression and SLE activity suggests that monitoring this cytokine might help physicians better evaluate

disease activity. Unfortunately, no reliable simple or standardised assays to quantify IFN $\alpha$  are available in routine clinical practice. The new single-molecule array (Simoa) assay, also called digital ELISA, enables direct IFN $\alpha$  quantification at attomolar (i.e. fg/mL or 10<sup>-15</sup> moles/mL) concentrations corresponding to 5,000-fold-increased sensitivity over commercial ELISAs.

**Objectives:** We hypothesised that serum-IFN $\alpha$  levels determined with this new standardised assay would be a better biomarker of SLE activity than the Farr test, still considered the "gold standard" for this purpose. The primary objective of this study was to characterise the relationship between digital ELISA-determined serum-IFN $\alpha$  concentrations and clinically assessed SLE activity. We also compared that assay to a functional, sensitive biological assay (bioassay), based on IFN $\alpha$  antiviral properties, used routinely in our institution for 30 years.

**Methods:** IFN $\alpha$  concentrations in serum samples from 150 consecutive SLE patients and 68 healthy donors in a cross-sectional study were determined with the digital ELISA and the bioassay. For SLE patients, clinical characteristics, Systemic Lupus Erythematosus Disease Activity Index (SLEDAI), therapeutic regimen, Farr assay, C3 levels and other usual biological parameters were recorded on the day of the blood draw.

**Results:** Based on healthy blood donors, the abnormal serum-IFN $\alpha$  level threshold value was 136 fg/mL. Next, using receiver operating characteristics curves for an SLE-patient series, widely heterogeneous for disease activity and organ involvement, the threshold IFN $\alpha$  value associated with active disease was 266 fg/mL. The digital ELISA-assessed serum-IFN $\alpha$  level was a better biomarker of disease activity than the Farr test: its specificity, positive likelihood ratio and positive-predictive value better discerned active SLE and a flare. The digital ELISA was more sensitive than the bioassay to detect low-abnormal serum-IFN $\alpha$  concentrations and patients with low disease activity. In multivariate analyses, abnormal digital ELISA-determined IFN $\alpha$  concentrations were significantly associated with SLE-specific fever, active mucocutaneous lupus, active lupus nephritis and anti-Sm Abs but no other anti-ribonucleoprotein Abs (i.e., anti-Ro/SSA 52, anti-Ro/SSA 60, anti-La/SSB and anti-RNP).



**Conclusions:** Direct serum-IFN $\alpha$  determination with a highly sensitive assay might improve monitoring of clinical SLE activity and selection of the best candidates for anti-IFN $\alpha$  treatment.

**Disclosure of Interest:** None declared

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FRI0263

#### CHARACTERISATION OF EPITHELIUM-ASSOCIATED FCRL4+ B CELLS FROM PAROTID GLANDS OF PATIENTS WITH SJÖGREN'S SYNDROME USING SINGLE CELL RNA SEQUENCING

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**Background:** A subset of B cells expressing the inhibitory Fc receptor-like protein 4 (FcRL4) is found in salivary gland lesions of patients with primary Sjögren's

syndrome (pSS). FcRL4 +B cells are associated with ductal epithelial cells forming lymphoepithelial lesions (LEL), in particular within parotid glands<sup>1</sup>. Furthermore, FcRL4 is expressed by mucosa-associated lymphoid tissue (MALT) lymphoma B cells.

**Objectives:** We aimed to investigate, by single cell and bulk RNA sequencing, how the gene expression profile of FcRL4 +B cells differs from FcRL4-negative naive and memory B cells in salivary gland tissue from pSS patients. We hypothesised that FcRL4 +B cells contribute to LEL formation and are prone to lymphomagenesis.

**Methods:** Parotid gland biopsies of 5 pSS patients without MALT lymphoma were obtained. Single cell suspensions were prepared by mechanical disruption and enzymatic digestion. The cells were incubated with anti-CD19, anti-CD27 and anti-FcRL4 antibodies, and sorted as single cells or 5 cells per well based on the following definitions: CD19 +CD27-FcRL4- ('naive'), CD19 +CD27+FcRL4- (memory) and CD19 +FcRL4+ (FcRL4+). Library preparation was done using an in-house SMARTseq2 protocol and sequencing was done on an Illumina HiSeq2500.

**Results:** Samples from 4 pSS patients passed quality control and were included. A total of 160 single cells and 360 cells in bulk were included in the analysis. Genes identified by differential expression were subjected to gene pathway analysis. Both in single cell and bulk samples, multiple genes coding for integrins, such as *ITGAX* (CD11c), were significantly upregulated in FcRL4 +B cells. Gene Ontology pathways that showed the highest upregulation in FcRL4 +B cells (both single cell and bulk) were receptor binding, GTPase and protein kinase pathways. Analysis of bulk samples further revealed that expression levels of genes encoding for Src tyrosine kinases, genes involved in the NF- $\kappa$ B pathway, *CXCR3*, and *TNFRSF13B* (TACI), among others, were significantly upregulated in FcRL4 +B cells, compared with either naive or memory B cells. Expression levels of *CD40* were significantly decreased in FcRL4 +B cells.

**Conclusions:** FcRL4 +B cells in salivary glands of pSS patients show upregulation of genes involved in homing and cell adhesion, consistent with their tissue location close to the epithelium. FcRL4 +B cells also show increased levels of transcripts that induce inflammation and B cell survival. These cells exhibit all characteristics of chronically stimulated CD11c+memory B cells, and we speculate that FcRL4 +B cells contribute significantly to the epithelial damage seen in the glandular tissue of pSS patients.

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**Acknowledgements:** We thank Kim de Lange and Gerben van der Vries from the Genome Analysis Facility of the University Medical Centre Groningen for excellent technical and bioinformatics assistance.

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FRI0264

#### ROLE OF P-GP IN PATHOGENIC CONVERSION OF TH17 CELLS IN LUPUS NEPHRITIS LEADING TO GLUCOCORTICOID RESISTANCE

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**Background:** Th17 cells and cytokine IL-17 are mainly involved in autoimmunity. Recently IL-17/IFN- $\gamma$  double-positive Th17 cell were found to be allied with inflammatory diseases. P-glycoprotein (P-gp) +ve Th17 cells are refractory to steroid. P-gp on lymphocyte effluxes out steroid and prevents its action. We conducted this study with hypothesis that P-gp positive IL-17/IFN- $\gamma$  double +ve Th17 are one of key pharmacokinetic and pharmacodynamic modulator liable for steroid resistance in lupus nephritis (LN).

**Objectives:** We planned to study the frequency of P-gp expressing pathogenic Th17 cells in steroid responsive and non-responsive steroid patients.

**Methods:** We analysed the frequency of pathogenic IL-17/IFN- $\gamma$  double-positive Th17 lymphocytes and P-gp expression on their surface by flowcytometry in responsive (n=52; mean age 34.06 $\pm$ 10.84) and non-responsive (n=25; mean age 37.29 $\pm$ 13.73) patients. We also included 10 age and sex matched healthy controls. All patients were biopsy proven LN.

**Results:** We found a significant increase in the frequency of Th17 (p=0.001); Th17 (p=0.006) and IL-17/IFN- $\gamma$  double positive Th17 (p=0.006) and IL-17/IFN- $\gamma$  double-positive Th17 (<0.001) cells in non-responsive as compared to responsive patients and healthy controls (p<0.001). Of the total Th17; Th17 and pathogenic Th17; 78.45%; 72.37% and 95.8% cells expressed P-gp on their surface in non-responsive; 45.0%; 30.27% and 30.1% cells expressed P-gp in responsive group; and 30.91%; 15.51% and 15.62% in healthy control respectively.



**Conclusions:** Higher frequency of IL-17/IFN- $\gamma$  doublepositive Th17 cell with P-gp expression may be associated immunological and pharmacological factor for steroid resistance in LN.

**Disclosure of Interest:** None declared

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#### FRI0265 ANGIOGENIC T CELLS IN PRIMARY SJÖGREN'S SYNDROME: A DOUBLE-EDGED SWORD

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**Background:** Angiogenic T cells (Tang) have been recently identified within colonies of endothelial progenitor cells (EPCs) as mediators of endothelial repair. Both Tang and EPCs are reduced in rheumatoid arthritis and this contributes to persistent endothelial damage and eventually increased cardiovascular risk. In primary Sjögren's syndrome (pSS), EPCs are expanded but no data are currently available about Tang.

**Objectives:** Aim of this study was to assess Tang (CD3 +CD31+CXCR4+) in peripheral blood (PB) and target organs of pSS as well as the association with EPCs (CD34 +CD133+VEGFR-2+) and clinical and serological features of the disease.

**Methods:** Thirty-six pSS patients and 20 sex- and age-matched healthy donors (HD) were enrolled. Phenotypic analysis of peripheral blood mononuclear cells was performed by flow cytometry using FITC, Pe, Pe-Cy7 or AlexaFluor647 labelled anti-human CD3, CD31, CXCR4, CD4, CD8, CD28, CD34, CD133, VEGFR-2, and IL-17 antibodies. Minor salivary gland (MSG) biopsies from 8 pSS patients were studied and compared to samples from 12 patients with sicca symptoms and either non-specific chronic sialadenitis (NSCS) or normal parenchyma (n=6 each). MSG sections were subjected to immunofluorescence staining to assess the presence of CD3 +CD31+CXCR4+Tang cells and the expression of the CXCR4-ligand CXCL12/SDF-1 chemokine.

**Results:** Circulating Tang were expanded in pSS compared to HD and were directly correlated to EPCs. Both Tang and EPCs directly correlated with disease activity as calculated with the EULAR Sjögren's syndrome disease activity index (ESSDAI). Over 60% of Tang lacked CD28 revealing a senescent phenotype. Only a small proportion of Tang displayed either CD4 or CD8, the majority of Tang being therefore CD4-CD8- double negative (DN). A subset of Tang produced IL-17 and the highest proportion of IL-17-producing cells was observed among DN cells. Immunofluorescence analyses revealed the exclusive presence of infiltrating Tang cells along with increased expression of CXCL12/SDF-1 in pSS MSGs compared to either NSCS or normal MSGs.

**Conclusions:** Circulating Tang cells are expanded in pSS, display a senescent phenotype, are mainly CD4-CD8- DN and produce IL-17. Moreover, Tang cells home to and infiltrate MSGs in pSS, presumably through the SDF-1/CXCR4 chemotactic axis. Our data suggest that besides their positive effect together with EPCs in endothelial repair, Tang cells may contribute to disease pathogenesis.

**Disclosure of Interest:** None declared

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#### FRI0266 CD16+ MONOCYTE SUBSETS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS, PRIMARY ANTIPHOSPHOLIPID SYNDROME, AND ANTIPHOSPHOLIPID SYNDROME WITH LUPUS ARE ASSOCIATED WITH SPECIFIC CLINICAL/SEROLOGICAL FEATURES OF THESE DISEASES

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**Objectives:** This study, developed within the IMI-JU project PRECISESADS framework, aimed to determine the enrichment on CD14 +and CD16+ monocyte subpopulations in SLE, APS and APS +SLE patients, and to investigate their role in the pathogenesis of these diseases.

**Methods:** The frequencies of monocyte subpopulations in the peripheral blood of 54 healthy donors and 46 SLE patients included in the PRECISESADS study (preliminary data) were determined by flow cytometry. A second cohort of 21 APS +SLE patients and a third cohort of 19 APS patients were included. Clinical profile,

proinflammatory circulating mediators, and peroxide levels were analysed. Carotid intima media thickness (CIMT) was evaluated as atherosclerosis marker

**Results:** The CD14 +CD16+ (non-classical) monocyte subset was reduced in SLE patients. Their frequencies were negatively associated with the positivity for anti-dsDNA, anti-SSB, anti-SSA and anti-U1RNP autoantibodies, as well as with renal involvement, which might reflect a recruitment process of this subset in renal tissues. Correlation studies further indicated a link between the reduced frequency of non-classical monocytes and increased levels of circulating inflammatory mediators. Conversely, SLE patients with a previous history of thrombosis displayed a significant increase in circulating CD14 +CD16+ monocytes in relation to those without previous thrombotic manifestations. These results prompted us to evaluate the proportion and profile of this inflammatory subtype in parallel cohorts of SLE +APS and APS patients, on which thrombosis constitute the main clinical disorder.

SLE +APS patients showed enrichment in intermediate (CD14 ++CD16+) and non-classical monocytes, associated with the positivity for anti-dsDNA antibodies and the presence of atheroma plaques. Correlations among the frequency of those monocyte subsets and inflammatory mediators, and circulating cytokines, were also demonstrated. Yet, SLE +APS patients with renal involvement displayed reduced proportion of circulating intermediate and non-classical monocytes, suggesting that, as in the case of SLE patients, circulating CD16 +cells might have migrated to the kidney.

In APS patients we also saw enrichment of the CD16 +inflammatory subsets, associated to recurrent thrombotic events and a pathologic CIMT, pointing out that such subsets are associated with CVD. The scores of various markers related to autoimmunity, oxidative stress and prothrombotic molecules further correlated with the proportions of intermediate and non-classical monocytes.

**Conclusions:** Circulating CD16 +monocytes might constitute an important subpopulation of proinflammatory cells, whose frequency might identify APS, APS +SLE and SLE patients suffering thrombosis, atherosclerosis and organ involvement.

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**Disclosure of Interest:** None declared

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#### FRI0267 CHARACTERISATION OF THE MOLECULAR PROFILE OF ALTERED GENES AND PATHWAYS IN MONOCYTES OF ANTIPHOSPHOLIPID SYNDROME PATIENTS RELATED TO THEIR ATHEROTHROMBOTIC STATUS. EFFECTS OF IN VIVO UBIQUINOL SUPPLEMENTATION

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**Objectives:** This study was undertaken to: 1. Characterise monocytes molecular profile of altered genes and pathways involved in the pathology of APS. 2. To evaluate the role of antiphospholipid antibodies in the regulation of these processes. 3. To investigate the short-term effects of *in vivo* ubiquinol (reduced coenzyme Q10 [Qred]) supplementation on the modulation of genes related to inflammation and thrombosis in this autoimmune disorder.

**Methods:** Monocytes from peripheral blood of 60 subjects, including 30 APS patients and 30 healthy donors (HDs) were purified by negative immunomagnetic selection (Miltenyi). Total RNA was extracted from 6 subjects –as exploratory cohort- and microarray studies were performed in an Agilent G4112F platform (Whole Human Genome Microarray 44 k). Functional categorization of the altered gene signature and molecular pathways and networks was carried out using the Ingenuity Pathway Analysis Software (IPA). The most differentially expressed genes were validated by RT-PCR in monocytes purified from all the subjects recruited to the study. Correlation and association studies were performed with clinical and analytical variables. The effects of antiphospholipid antibodies (aPL) were also evaluated by *in vitro* studies. The short-term effects of *in vivo* Qred supplementation on the monocyte gene profile were further analysed.

**Results:** Gene expression array identified 518 altered genes in monocytes from APS patients in relation to the control group ( $p < 0,05$  and fold change  $> 2$ ). IPA analysis showed that the main canonical pathways integrated by these genes were leukocyte adhesion, diapedesis and extravasation signalling, interleukin and cytokine signalling, as well as oxidative stress production and antioxidant response. This analysis further identified that the most relevant diseases in which these altered genes are involved were inflammatory and cardiovascular diseases (44%), as well as reproductive (42%), neurological (11%), renal (1%) and ophthalmic diseases (2%). The alteration of several of these genes was validated by RT-PCR and protein analysis, and associated to clinical parameters of APS patients, including thrombotic recurrences and early atherosclerosis. *In vitro* studies

demonstrated the specific modulation of several genes by direct effect of aPLs. *In vivo* Qred supplementation of APS patients for one month significantly improved the monocytes' atherothrombotic gene profile, reversing the altered expression of a number of genes related to thrombosis, atherosclerosis, inflammation, oxidative stress, and intracellular signalling.

**Conclusions:** 1. Gene expression profile allowed the identification of relevant genes and pathways altered in monocytes of APS patients, which are associated with the pathogenesis of the disease and modulated, at least partially, by aPLs. 2. We have branded novel and specific mRNAs related to CVD in APS monocytes, further modified by effect of *in vivo* Qred supplementation.

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**Disclosure of Interest:** None declared

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### FRI0268 GLUCOCORTICOID-INDUCED LEUCINE ZIPPER (GILZ) REPRESENTS A CHECKPOINT LIMITING TYPE I INTERFERON (IFN) PRODUCTION IN SLE

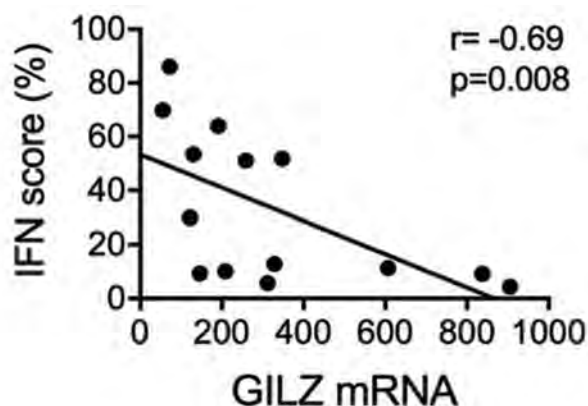
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**Background:** Glucocorticoids (GC) remain the mainstay of treatment in Systemic Lupus Erythematosus (SLE). Type I interferons (IFN), produced by plasmacytoid dendritic cells (pDC) in response to Toll-Like receptors (TLR) ligands, are critical to SLE pathogenesis, but are not suppressed by GC. Glucocorticoid-Induced Leucine Zipper (GILZ) is an endogenous anti-inflammatory protein induced by GC. Beaulieu et al., 2010 However, whether GILZ regulates IFN production in SLE is not known.

**Objectives:** To test the hypothesis that GILZ inhibits the production of Type I IFN in SLE.

**Methods:** We performed *in vitro* analysis on pDC and bone marrow-derived DC (BMDC), and *in vivo* studies, of WT and GILZ<sup>-/-</sup> mice using stimuli of TLR7 (Imiquimod), TLR7/8 (Resiquimod) and TLR9 (CpG). IFN was measured using a IFN luciferase assay, and other cytokines with ELISA. IFN-stimulated gene signatures (ISG) were measured using qPCR. To determine whether GILZ regulates IFN in human SLE, we mined a public gene expression dataset GSE10325. Becker et al., 2013

**Results:** Deletion of GILZ resulted in excess pDC secretion of IFN in response to TLR7 ( $p=0.0012$ ) and TLR9 ( $p=0.01$ ) stimulation, and BMDC secretion of IFN, IL-6 and TNF $\alpha$  in response to TLR7 ( $p=0.0039$ , 0.017, 0.033), TLR7/8 ( $p=0.001$ ,  $<0.0001$ ,  $<0.0001$ ) and TLR9 ( $p=0.005$ ,  $<0.0001$ , 0.0034) stimulation respectively. Dexamethasone (DEX) induced GILZ in WT pDC and BMDC, and TLR stimulation suppressed GILZ expression in BMDC, but TLR-stimulated GILZ<sup>-/-</sup> cell failed to suppress IFN in response to DEX. Moreover, GILZ deficiency was associated with increased ISG in naïve spleen cells, naïve BMDCs and TLR7/9 stimulated pDC of GILZ<sup>-/-</sup> mice compared to WT mice. Correspondingly, increased IFN was seen in GILZ<sup>-/-</sup> mice in response to TLR7/8 stimulation *in vivo*. In GSE10325, we show that lower expression of GILZ was associated with high ISG (*IFI44*, *IFI44L*, *RSAD2*, *IFI27*) ( $p=0.0021$ ) in SLE patient peripheral blood B cells, and GILZ mRNA was negatively correlated with IFN signature ( $r=-0.63$ ,  $p=0.017$ ) which in turn positively correlated with disease activity (SLEDAI2k) ( $r=0.77$ ,  $p=0.002$ ).



**Conclusions:** GILZ is an endogenous regulator of increased IFN production in response to TLR stimulation *in vitro* and in mice, and is negatively correlated with ISG in human SLE. This suggests that GILZ negatively regulates type I IFN production and GILZ based therapy may be a potential therapeutic strategy that could reduce steroid dependence in SLE.

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### FRI0269 DEFICIENCY OF GLUCOCORTICOID-INDUCED LEUCINE ZIPPER (GILZ) DISINHIBITS IFN PATHWAYS AND EXACERBATES NEPHRITIS IN THE LYN-DEFICIENT MURINE MODEL OF LUPUS

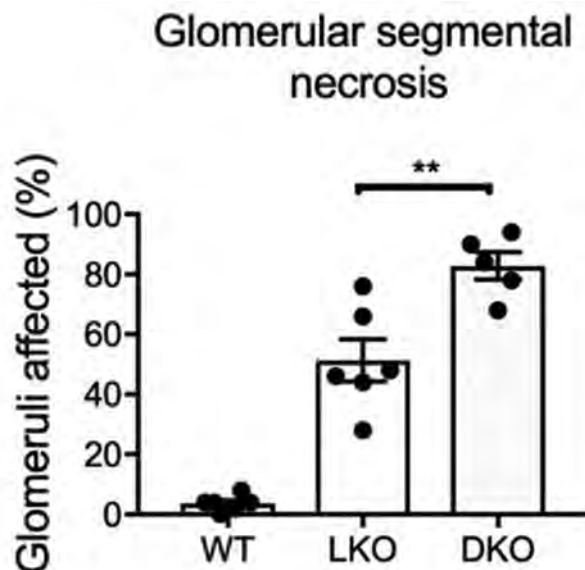
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**Background:** Systemic lupus erythematosus (SLE) is a multi-system autoimmune disease of unknown etiology. Lyn-deficient mice develop lupus-like autoimmunity due to hyperactive B cells resulting in excess IL-6 production, and cyclical exacerbation of inflammation by further activation of B and T cells. Tsantikos et al., 2010 C57BL/6 mice deficient in glucocorticoid-induced leucine zipper (GILZ), an intracellular protein involved in glucocorticoid effects on immunity, develop lupus-like autoimmunity and excess B cell activation. Jones et al., 2016. However, the effect of GILZ in lupus-prone mice is unknown.

**Objectives:** We aim to test the hypothesis that GILZ modulates autoimmunity in the lyn deficient murine model of lupus.

**Methods:** We generated GILZ-deficient mice on a lyn-deficient background (GILZ-lyn double knock out (DKO)) and compared them to WT and lynKO mice. The effects of GILZ deficiency on spleen weight, nephritis, Type I interferon-induced genes (ISG) and autoantibodies were examined.

**Results:** We observed heightened lupus-like autoimmunity in GILZ-lyn DKO mice, compared to LynKO, that include increased spleen weights ( $p=0.041$ ) and more severe glomerulonephritis, especially segmental necrosis. A panel of ISG (*ifi44*, *usp18*, *oas3*, *cxcl10*, *isg15*, *mx1*, *irf7*, *stat1* and *ifit3*) and an overall ISG score was significantly increased ( $p=0.0023$ ) in GILZ-lyn DKO mice compared to LynKO. In contrast, serum autoantibodies (dsDNA, Sm, histone, Jo-1, Scl-70, SSA, SSB, U1RNP, Ro52,) were not increased in GILZ-lyn DKO mice compared to LynKO mice.



**Conclusions:** In LynKO lupus-prone mice, spleen weight, glomerulonephritis, and ISG profiles were significantly exacerbated by GILZ deficiency, while autoantibody titres were unaffected. This suggests that endogenous GILZ exerts an inhibitory effect on IFN pathways, in this lupus model. Therefore, GILZ potentially regulates the cycle of inflammation in SLE by inhibiting IFN responses

downstream of autoantibodies. A GILZ-based treatment could be a potential therapeutic strategy in SLE.

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#### FRI0270 IDENTIFICATION OF NOVEL DYSREGULATED INTERFERON-INDUCIBLE NON-CODING RNAs IN SJÖGREN'S SYNDROME

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**Background:** Sjögren's syndrome (SS) is a chronic, heterogeneous disease with hallmark features of auto-inflammation and autoantibody production. Upregulation of type I and II interferon-stimulated genes (ISGs), known as the "Interferon (IFN) Signature" is correlated with anti-Ro titers and has been observed both in the salivary glands and peripheral blood of SS patients. Within the 2 p25.2 genomic interval, the long non-coding RNA (lncRNA) negative regulator of the interferon response (*NRIR*) has been identified as inducible by type I IFN and is responsible for the downregulation of the ISGs *CMPK2* and *RSAD2*.<sup>1</sup>

**Objectives:** We sought to identify additional unannotated ISGs lncRNAs that are differentially expressed (DE) in SS patients utilising correlated expression of *RSAD2*.

**Methods:** We evaluated and compared the transcriptome of anti-Ro(+) patients (n=27) and healthy controls (n=27) using RNA-seq with DE defined as q<0.05 and a fold change (FC) ≥2 or ≤0.5. qRT-PCR was used to validate DE with primers specific for each RNA of interest. To understand the biological relevance of these transcripts, we performed *in vitro* time-course experiments to compare the transcriptional changes of unstimulated cells and cells stimulated with either PMA/ionomycin (PMA/I) or universal type I IFN for 36 hours measuring 7 time points.

**Results:** One of the most overexpressed type I ISGs in the SS Ro(+) is *RSAD2* (FC=8.05, p=3.29x10E-07). Because of its role in the type I IFN pathway, pairwise correlation coefficients between all DE transcripts and *RSAD2* for SS Ro(+) patients were calculated. In total, we found 223 transcripts exhibiting correlation with *RSAD2* expression (Pearson's r>+0.70 or <-0.60), including *NRIR* (FC=2.72, p=5.87x10E-03) and *CMPK2* (FC=2.53, p=3.58x10E-03). Of the 223 transcripts, 14 DE expressed lncRNAs correlated with *RSAD2* expression. Several antisense ncRNAs situated nearby to other type I ISGs correlated with *RSAD2*, including: *AC099063.1* (FC=2.51), *AC004551.1* (FC=3.35), and *AP001610.1* (FC=4.12). We confirmed upregulation of these lncRNAs by qRT-PCR from the independent replication (14 Ro(+) and 36 controls) cohort (p=2.49x10E-02, 8.63 × 10E-06, 1.17 × 10E-04, respectively). Based on the locations of the lncRNAs to type I ISGs, HSB-2 cells were stimulated with PMA/I or universal type I IFN. Using qRT-PCR to measure the protein coding genes *MX1*, *OAS1*, and *GBP5* along with the lncRNAs, *AC099063.1* (*GBP5-AS1*), *AP001610.1* (*MX1-AS1*), and *AC004551.1* (*OAS123-AS1*) showed coordinated regulation with their protein coding counterparts with both stimuli.

**Conclusions:** Given the importance of the IFN signature to disease pathogenesis in the autoantibody positive patients, it is critical that we better understand how this complex pathway is coordinately regulated. Since one critical function of lncRNAs is to regulate the genome, characterising the mechanisms by which these 14 identified by this study regulate the ISG coordinately could result in new diagnostic and/or therapeutic options.

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**Disclosure of Interest:** None declared

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#### FRI0271 DIMETHYL FUMARATE INHIBITS UBE2L3 MEDIATED TLR7 SIGNALING AND AUTOREACTIVE B CELL DEVELOPMENT IN SLE

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**Background:** Genetic studies have identified a single *UBE2L3* risk haplotype which is associated with SLE and multiple autoimmune diseases, and leads to increased expression of *UBE2L3* in eQTL studies. The E2 ubiquitin-conjugating enzyme *UBE2L3* regulates NF-κB activation through regulation of the Linear Ubiquitination Chain Assembly Complex (LUBAC). Thus *UBE2L3* regulates CD40-driven B cell activation. The *UBE2L3* risk allele correlates with circulating plasmablast and plasma cell expansion in SLE individuals.

**Objectives:** To determine the effect of *UBE2L3* and linear ubiquitination on TLR7 signalling, and test the effect of Dimethyl Fumarate (DMF), which has recently been shown to inhibit *UBE2L3*, on B cell and plasmablast differentiation in SLE.

**Methods:** Confocal microscopy, immunoprecipitation and western blot were used to assess linear ubiquitin chain accumulation in TLR7-HEK293 cells after TLR stimulation by Resiquimod. The effect of *UBE2L3* and LUBAC on TLR7 signalling was dissected by the use of *UBE2L3*/LUBAC overexpression, dominant negative mutants and shRNA silencing, measuring NF-κB reporter activity, IkappaBalpha phosphorylation, gene expression by qPCR and IL-8 secretion. DMF was administered *in vitro* to human B cells isolated from SLE patients (n=15) and controls and cultured with Resiquimod and/or IFNα for 5–7 days. B cell viability/proliferation, plasmablast differentiation were analysed by 10-colour flow cytometry. Supernatants were assayed for immunoglobulin secretion and autoantibody production.

**Results:** TLR7 stimulation led to intracellular accumulation of linear ubiquitin chain comparable to TNFα. *UBE2L3* and LUBAC co-overexpression enhanced TLR7 driven NF-κB activation and led to increased NF-κB target mRNA expression and increased secretion of IL-8. The effect was specific to *UBE2L3* compared to other E2 enzymes. Dominant negative mutant *UBE2L3*(C86S) or HOIP (C885S) or *UBE2L3*/HOIP shRNA suppressed the response to TLR7 stimulation. DMF showed a dose-dependent inhibition of TLR7-mediated NF-κB activation. In primary SLE and healthy B cells, DMF suppressed proliferation of switched and unswitched CD27+ memory B cells and blocked plasmablast differentiation. DMF profoundly inhibited immunoglobulin secretion and anti-nuclear autoantibodies production in response to TLR7 and IFNα stimulus.

**Conclusions:** Our data demonstrate that linear ubiquitination and *UBE2L3* regulate TLR7 activation of NF-κB. *UBE2L3* silencing or pharmacological antagonism of *UBE2L3* by DMF suppressed the response to TLR7 activation. Excessive TLR7 signalling has been linked to SLE development and enhanced B cell autoreactivity. Thus our data identify a novel mechanism by which the *UBE2L3* risk haplotype contributes to SLE susceptibility. DMF suppressed plasmablast differentiation and inhibited TLR7 and IFNα induced autoantibody production. These results support a role for repositioning DMF (currently used to treat multiple sclerosis) in the treatment of SLE.

**Disclosure of Interest:** None declared

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#### FRI0272 PHARMACODYNAMIC EFFECTS OF ATACEPT TREATMENT IN A CYNOMOLGUS MONKEY KLH ANTIGEN CHALLENGE MODEL

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**Background:** Atacept is an antagonist of the B cell regulatory factors BlyS (B lymphocyte stimulator) and APRIL (a proliferation inducing ligand). It is capable of binding to all known conformations of BlyS and APRIL and is thus expected to modulate the maturation, differentiation, and effector function of B cells. We aimed to define the relationship between atacept drug exposure and pharmacodynamic (PD) effects *in vivo*. Here, we report results of our study examining the effects of atacept on the immune response in a keyhole limpet hemocyanin (KLH) challenge model in cynomolgus monkeys.

**Methods:** Cynomolgus monkeys (*Macaca fascicularis*) were injected with KLH on Day -33, and on Day 1 received the first dose of either atacept (0.3, 3, or 30 mg/kg) or vehicle followed by a KLH challenge. Animals were dosed weekly (Day 1, 8, 15) and were subsequently monitored for 2 weeks before the study ended on Day 29. Clinical signs, total and free drug levels, peripheral blood B and



T cell subpopulations, and total and KLH-specific immunoglobulin (Ig) levels were monitored. Additionally, gene expression in blood was analysed using the NanoString nCounter platform.

**Results:** Atacept was well-tolerated at all dose levels tested. All animals in the treatment arms had quantifiable levels of atacept in serum throughout the study. Reduction of serum IgM and IgG was detected 7 days after treatment, with a continuous reduction in the mean serum IgM and IgG levels observed until Day 29 (table 1). In animals treated with 3 and 30 mg/kg atacept, a significant decrease in serum anti-KLH IgG levels was observed versus vehicle-treated controls, beginning at Day 11 (table 2). A minor reduction in absolute CD3-CD20+, IgD +B cell numbers was seen in response to treatment, but no changes in T cell subsets were detected. Changes in gene expression following atacept treatment were predominantly observed in B cell-related and Ig genes.

**Abstract FRI0272 – Table 1.** Mean% reduction of total IgM and IgG relative to baseline

Mean reduction	Day 8			Day 29		
	0.3 mg/kg	3 mg/kg	30 mg/kg	0.3 mg/kg	3 mg/kg	30 mg/kg
IgG	7.1	14.2	16.3	10.6	27.2	46.3
IgM	9.1	17.1	22.3	21.5	52.3	64.1

**Table 2** Mean% reduction of KLH-specific IgM and IgG relative to vehicle group

Mean reduction	Day 11			Day 29		
	0.3 mg/kg	3 mg/kg	30 mg/kg	0.3 mg/kg	3 mg/kg	30 mg/kg
KLH-specific IgG	17.3	55.2	49.7	39.4	78.8	71.5
KLH-specific IgM	15.1	33.4	40.1	40.4	67.8	66.6

**Conclusions:** This study showed that atacept modulates B cell responses, IgM and IgG levels, and Ig isotype switching in a KLH-antigen-challenged cynomolgus monkey model, thus supporting its use in the treatment of antibody-mediated diseases. Additionally, gene expression PD markers identified in this study will be used in subsequent clinical trials as exploratory PD readouts.

**Disclosure of Interest:** E. Samy Employee of: EMD Serono Research and Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), A. Bender Employee of: EMD Serono Research and Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), Y. Wu Employee of: EMD Serono Research and Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), V. Castagna Employee of: Istituto di Ricerche Biomediche Antoine Marxer RBM SpA, an affiliate of Merck KGaA, E. Bertotti Employee of: Istituto di Ricerche Biomediche Antoine Marxer RBM SpA, an affiliate of Merck KGaA, R. Boggio Employee of: Istituto di Ricerche Biomediche Antoine Marxer RBM SpA, an affiliate of Merck KGaA, A. Paoletti Employee of: Istituto di Ricerche Biomediche Antoine Marxer RBM SpA, an affiliate of Merck KGaA, S. Riva Employee of: Istituto di Ricerche Biomediche Antoine Marxer RBM SpA, an affiliate of Merck KGaA, P. Schneider Grant/research support from: EMD Serono Research and Development Institute, Inc. and Merck KGaA, P. Haselmayer Employee of: Merck KGaA, J. DeMartino Employee of: EMD Serono Research and Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany)

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FRI0273

#### RNA SEQUENCING DETECTION OF GENE DYSREGULATION IN EPITHELIAL SORTED CELLS FROM SALIVARY GLAND TISSUE REVEALS INTERESTING PATHWAYS INVOLVED IN SJÖGREN'S SYNDROME PATHOPHYSIOLOGY

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**Background:** Primary Sjögren's syndrome (pSS) is a chronic autoimmune disorder characterised by lymphocytic infiltrates and destruction of the salivary glands. Several lines of evidence support the hypothesis that salivary gland epithelial cells (SGECs) are not only the target of autoimmunity in pSS patients but may also play a role for its initiation and maintenance.

**Objectives:** To establish high-resolution molecular maps of SGEC from pSS patients compared to controls using RNASeq analysis.

**Methods:** Patients had pSS according to 2016 EULAR/ACR criteria and controls had sicca symptoms without any antibodies and with normal lip biopsy. SGEC, B, T CD4 and CD8 lymphocytes were sorted from salivary gland biopsies from 9 pSS patients and 4 controls, using a FACS ARIA cell sorter. Total RNASeq profiling was performed using MiSeq (Illumina). For SGEC subset, 4 samples were excluded due to a contamination by B lymphocytes, thus analysis was performed on 5 pSS and 4 controls using R software, to identify transcriptional differences

between pSS and control SGEC. Functional Enrichment analysis was performed using Ingenuity Pathway Analysis software.

**Results:** In SGEC, 495 genes were differentially expressed between pSS and controls. 280 genes were up-regulated, and 215 genes were down-regulated. Enrichment analysis (table 1) highlighted IL-7 signalling pathways (including IL-7, STAT5A, STAT1 genes) and interferon signalling (including OAS1, IFIT3, IFI6, TAP1 genes). Other genes potentially involved in immune responses and interactions between SGEC and lymphocytes were significantly up-regulated, including bone marrow stromal cell antigen 2, HLA-DRA, BAFF-R and IL-23 A (table 2). These results need to be confirmed by RT qPCR. However, consistent results have already been obtained in our laboratory, showing that IL-7 serum level is increased in pSS patients compared to controls and that SGECs produce IL-7 after interferon stimulation. The analysis of the non-coding RNA part and the other sorted cells subtypes is ongoing.

**Abstract FRI0273 – Table 1.** Pathways identified as statistically over-represented with Ingenuity Pathways Analysis in epithelial cells from pSS patients compared to controls

Pathway	-log p-value
Primary Immunodeficiency Signalling	4,08
Interferon Signalling	3,52
B Cell Development	2,89
Role of JAK2 in Hormone-like Cytokine Signalling	2,73
IL-7 Signalling Pathway	2,51

**Abstract FRI0273 – Table 2.** Selection of genes differentially expressed between pSS and controls in SGEC

Gene Symbol	log2 fold-change	p-value
IL-7	2.56	0.002
BST2	4.08	0.0002
HLA-DRA	1.84	0.0372
IL-23 A	3.59	0.0155
BAFF-R	4.94	0.0097

**Conclusions:** Immune interactions between SGEC and B or T lymphocytes could represent a key in the understanding of the initiation and/or maintenance of autoimmunity in pSS. Our study highlights the key role of epithelial cells in activation of immune cells. *In vitro* experiments are needed to confirm these results and elucidate the molecular mechanisms.

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FRI0274

#### ELEVATED REACTIVITY OF CD38<sup>HIGH</sup> B CELLS AGAINST BAFF CONTRIBUTES TO IGG OVERPRODUCTION IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME

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**Background:** Primary Sjögren's syndrome (pSS) is often accompanied by hypergammaglobulinemia and production of autoantibodies, such as anti-Ro/SSA and anti-La/SSB antibodies. These serological aberrations suggest that abnormally activated B cells play a key role in the pathogenesis of pSS. We have previously reported that the proportion of peripheral CD38<sup>high</sup>IgD<sup>+</sup> B cells among CD19<sup>+</sup> B cells is significantly elevated in pSS patients and positively correlated with serum anti-Ro/SSA, anti-La/SSB titer, total IgG, and the European League against Rheumatism (EULAR) Primary Sjögren's syndrome disease activity index (ESSDAI). B cell activating factor belonging to TNF family (BAFF) is a well known cytokine which promotes differentiation, proliferation and survival of B cells. It has been reported that serum BAFF level is increased in pSS patients compared to HC and that BAFF is also highly expressed in salivary glands. Based on these background, it is conceivable that BAFF plays a pivotal role in the pathogenesis of pSS.

**Objectives:** To elucidate the involvement of BAFF in IgG overproduction in pSS.

**Methods:** Peripheral CD19<sup>+</sup> B cells were prepared from pSS patients (n=16) and gender-matched HC (n=10) by using CD19-microbeads. The cells were stimulated *in vitro* with an anti-IgM antibody, recombinant human CD40 ligand and recombinant human IL-4 ('multiple stimulation') with or without recombinant human soluble BAFF (rhsBAFF) for 96 hours. The amount of IgG produced by the cells in the culture supernatants was measured by ELISA. The proportion of B cell subsets, characterised by anti-CD19, anti-IgD and anti-CD38 antibodies, and the expression level of a BAFF receptor (BR3) in the subsets were analysed by FACS. Disease activities of the pSS patients were quantified based on the ESSDAI scores. The serological data of the patients were collected by clinical records.

**Results:** IgG production by CD19<sup>+</sup> B cells *in vitro* upon multiple stimulation was significantly increased in pSS patients as compared to HC (p=0.015). Notably, the IgG production was further enhanced by the addition of rbsBAFF to the culture, and that enhancement was significantly higher in pSS patients than HC (p=0.011). Moreover, the proportion of CD38<sup>high</sup>IgD<sup>+</sup> B cells among CD19<sup>+</sup> B cells was significantly and positively correlated with not only serum IgG level (p<0.0001), but also the amount of IgG produced *in vitro* by the multiple stimulated CD19<sup>+</sup> B cells (p=0.042). The mean fluorescence intensity of BR3 expression in CD38<sup>high</sup>IgD<sup>+</sup> B cells was significantly higher in pSS patients than HC (p=0.029), whereas no significant difference was observed between pSS and HC for total CD19<sup>+</sup> B cells.

**Conclusions:** Our results suggest that CD38<sup>high</sup>IgD<sup>+</sup> B cells, which are known as activated B cells, highly react to BAFF in pSS patients as compared to HC. Our findings may shed light on the mechanism of B cell activation triggered by BAFF during the pathogenesis of pSS.

**Disclosure of Interest:** None declared

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### FRI0275 ALTERED PROTEIN TYROSINE PHOSPHATASES ACTIVITY AND DISEASE SPECIFIC EXPRESSION PATTERN OF CD45 AND CD148 ON VARIOUS LYMPHOCYTE SUBSETS IN AUTOIMMUNE DISEASES

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**Background:** Previous studies demonstrated impaired B cell receptor (BCR) response in patients with systemic lupus erythematosus (SLE). Besides diminished cytokine production upon TLR9 stimulation<sup>1</sup> it was found that phosphorylation of Syk<sup>2</sup> and downstream Ca<sup>2+</sup> flux was reduced upon BCR stimulation. This led to the hypothesis of a "post activation" state of peripheral B cells (BCs) in autoimmunity which might be related to altered protein tyrosine kinase (PTK) versus phosphatase (PTP) activities. Prior studies in SLE showed enhanced PTP but not ser/thr phosphatase (PSP) activities in BCs.<sup>3</sup> Receptor PTPs (RPTPs) CD45/CD148 are described as regulators of initial steps of BCR signalling by regulating Lyn which phosphorylates CD79 ITAMs and thus activates Syk.<sup>4</sup>

**Objectives:** This study aimed at testing the hypothesis that altered phosphatase activity (PA) is a hall mark of autoimmunity. So, expression of RPTPs CD45/CD148 were compared on lymphocyte subsets in patients with rheumatoid arthritis (RA), primary Sjögren's Syndrome (pSS), SLE and healthy donors (HD). To check whether increased global PA is restricted to BCs of patients with SLE, the study extended analysis to T cells (TCs) and studied patients by including cohorts of RA and pSS.

**Methods:** Peripheral blood samples were analysed for expression of CD45 and CD148 in patients and HDs using flow cytometry (n(HD/RA/pSS/SLE)=13/8/18/22). PTP and PSP activities were analysed in isolated BCs and TCs lysates from patients and HD using a protein activity assay (n(HD/RA/pSS/SLE)=21/6/13/10).

**Results:** Compared to HDs CD45 expression is significantly enhanced on peripheral monocytes and CD3<sup>+</sup>/CD4<sup>-</sup> as well as CD3<sup>+</sup>/CD4<sup>+</sup> TCs from patients with RA. Further, CD3<sup>+</sup>/CD4<sup>-</sup> TCs of patients with RA express more CD148 (Tb1 1). In patients with SLE, CD148 expression is decreased on CD148<sup>+</sup> memory B cells. In addition, this study confirmed that enhanced PTP activity is characteristic of SLE BCs since TCs of any of the cohorts and BCs of patients with RA and pSS showed PTP and PSP activities comparable to HD.

**Abstract FRI0275 – Table 1.** Significant differences found in RA and SLE compared to HD.

		CD45	CD148		PTP activity	PSP activity
RA	monocytes	↑ 0.0354	ns	TCs	ns	ns
	CD3 <sup>+</sup> /CD4 <sup>-</sup>	↑ 0.0325	↑ 0.0451		ns	ns
	CD3 <sup>+</sup> /CD4 <sup>+</sup>	↑ 0.0277	ns		ns	ns
	naïve BCs	ns	ns		ns	ns
	memory BCs	ns	ns		ns	ns
SLE	monocytes	ns	ns	TCs	ns	ns
	CD3 <sup>+</sup> /CD4 <sup>-</sup>	ns	ns		ns	ns
	CD3 <sup>+</sup> /CD4 <sup>+</sup>	ns	ns		ns	ns
	naïve BCs	ns	ns		ns	ns
	memory BCs	ns	↓ 0.0054		BCs	↑ PTP = 0.0122 ↑ PSP = 0.0055

↑: significantly increased; ↓: significantly decreased; ns: not significant; PTP/PSP, phosphotyrosine 1/2

**Conclusions:** This study identified characteristic differences of PTP activities in BCs from patients with SLE compared to HD which were not identifiable by an enhanced CD45 or CD148 expression on PBMCs and did not correlate with disease activity. This suggests intrinsic abnormality in SLE BCs. While there is evidence that abnormal PTP is present in SLE BCs, further studies are needed to identify underlying individual PTPs to further analyse their pathogenic and potential therapeutic relevance. Among the tested autoimmune conditions increased

CD45 expression on TCs and monocytes was specific to RA, which might indicate disease dependent patterns of PTP/PSP expression.

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### FRI0276 ABERRANT DISTRIBUTION OF CD3+CD56+ NKT-LIKE CELLS IN PATIENTS WITH SJÖGREN'S SYNDROME

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**Background:** CD3<sup>+</sup>CD56<sup>+</sup> NKT-like cells are a subset of T cells co-expressing NK cell markers, and bridge innate and adaptive immunity. However, the phenotype and the potential role of NKT-like cells in the pathogenesis of Sjögren's Syndrome (SS) remains elusive.

**Objectives:** To elucidate the distribution of CD3<sup>+</sup>CD56<sup>+</sup> NKT-like cells in peripheral blood and labial salivary gland (LSG) of SS patients, as well as the immune function of NKT-like cells in SS patients.

**Methods:** SS patients (n=110) and healthy controls (HC, n=94) were enrolled. Peripheral CD3<sup>+</sup>CD56<sup>+</sup> NKT-like population, proliferation and apoptosis potential, surface chemokine receptors and proinflammatory cytokines secretion were quantified by flow cytometry. The infiltration of NKT-like cells in LSG was examined by immunofluorescence. Serum and tissue levels of CX3CL1 were detected by ELISA and immunohistochemistry, respectively. *In vitro* transwell migration assay was used to examine the chemotaxis of NKT-like cells induced by chemokines. NKT-like cells were stimulated with CX3CL1 and were quantified the TNF-α and IFN-γ secretion by flow cytometry.

**Results:** Peripheral CD3<sup>+</sup>CD56<sup>+</sup> NKT-like cells from SS patients were significantly lower than those from HC (3.09%±2.35% vs 5.37±4.06%, p<0.001), which was negatively correlated with ESSDAI (r=-0.523, p=0.009) and serum RF level (r=-0.586, p=0.015). The proliferation rate (35.1%±10.69% vs 36.4±10.75%, p=0.812) or apoptosis rate (13.01%±12.15% vs 12.48±5.28%, p=0.338) of NKT-like cells from SS and HC were comparable. However, NKT-like cells infiltrations into LSG were observed in SS patients but were rarely presented in HC. Serum level of CX3CL1 (936.8±99.82 vs 887.8±82.77 pg/ml, p=0.015) and epithelial CX3CL1 of LSG were higher in SS patients than those in HC. CX3CR1 were expressed on NKT-like cells from both SS and HC (68.25%±22.38% vs 70.06±17.34%, p=0.777). Furthermore, migration assay showed that CX3CR1 promoted NKT-like cells chemotaxis with a dose-dependent manner. Functionally, NKT-like cells from SS patients expressed higher level of CD69 (10.97%±6.75% vs 2.69±1.82%, p<0.0001). Peripheral NKT-like cells from both SS patients and HC secreted high level of TNF-α (70.29%±22.74% vs 81.33±10.76%, p=0.137) and IFN-γ (62.42%±16.66% vs 64.34±14.50%, p=0.759), and low level of IL-4 (4.39%±3.42% vs 2.64±1.90%, p=0.131) and IL-17 (0.30±0.28 vs 0.31±0.30, p=0.967). Importantly, CX3CL1 promoted TNF-α and IFN-γ production by NKT-like cells *in vitro*.

**Conclusions:** NKT-like cells were aberrantly depleted in peripheral blood and accumulated in LSG in patients with SS, which was driven by CX3CL1- CX3CR1 axis. NKT-like cells from SS were activated and secreted high level of TNF-α and IFN-γ, which were further promoted by CX3CL1. Thus, NKT-like cells were implicated in the pathogenesis of SS, which might be a potential therapeutic target for SS.

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FRI0277

### METFORMIN REDUCES SALIVARY GLAND INFLAMMATION BY CONTROLLING B CELL DIFFERENTIATION AND REGULATING BALANCE OF TH17 AND TREG CELL IN NON-OBESSE DIABETIC MICE

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**Background:** Sjögren's syndrome (SS) is a systemic autoimmune disease that affects exocrine glands and lymphoid organs. B cell hyperactivity and imbalance between T helper 17 (Th17) cells and regulatory T (Treg) cells are involved in pathogenesis of SS. Metformin, a commonly used anti-diabetic drug, is found to have immunomodulatory effect via AMP-activated protein kinase enhanced inhibition of mTOR-STAT3 signalling.

**Objectives:** We examined the therapeutic effect of metformin on SS by using animal model of SS, non-obese diabetic (NOD) mice.

**Methods:** Metformin (50 mg/kg) or vehicle (saline) was given per oral every day from 11 weeks after birth until 20 weeks. Salivary flow rate (SFR) was addressed on every 2 or 3 weeks between 11 weeks and 20 weeks. Histologic analyses of salivary gland and spleen were performed on week 20. Expression of Inflammatory cytokine was determined by immunohistochemistry analysis and real-time PCR. Flow cytometry was performed with peripheral blood to examine Th17 and Treg cells and germinal centre (GC) B cell populations. Serum immunoglobulin level was measured by enzyme-linked immunosorbent assay. Splenic cells of NOD mice were treated with metformin or vehicle *in vitro* and cultured for 3 days.

**Results:** SFRs of metformin-treated mice recovered, whereas SFRs of those treated with vehicle declined. Histologic examination of salivary gland showed decreased infiltration of lymphocytes and reduced expression of IL-6 and TNF-alpha in metformin-treated mice. Relative expression of IL-6, TNF-alpha, and IL-17 mRNA in salivary gland and spleen also declined in metformin-treated mice. Flow cytometric analysis revealed decreased Th1 and Th17 cells and increased Treg cells in peripheral blood of mice treated with metformin. In addition, GC B cells and immunoglobulin levels were reduced in peripheral blood of mice treated with metformin. Decreased Tfh cells and increased Tfr cells were observed from *in vitro* cultures of splenic cells treated with metformin.

**Conclusions:** Metformin controls B cell differentiation and keeps balance between Th17 and Treg cells in NOD mice, in addition to reducing lymphocytic infiltration and inflammatory cytokine expression in salivary gland. Metformin has potential therapeutic effects on SS.

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FRI0278

### ALTERATIONS IN MEMORY AND VISIO-SPATIAL LEARNING IN A PRISTANE-INDUCED LUPUS BALB/C MICE

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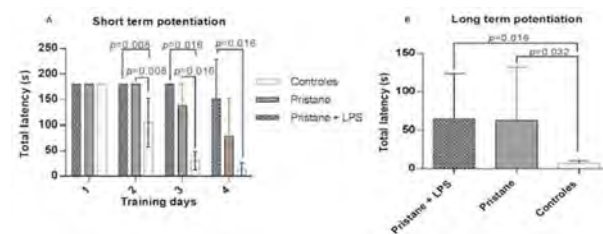
**Background:** Neuropsychiatric lupus is a condition that occurs in 30%–40% of systemic lupus erythematosus (SLE) patients and is associated with the presence of autoantibodies in central nervous system (CNS). The pristane-induced lupus in BALB/c mice is an experimental model that presents clinical and immunological similarities to SLE pathogenesis and it can be proposed as model to analyse affectations in visio-spatial learning and memory.

**Objectives:** To evaluate short and long term visio-spatial learning and memory in Balb/c pristane-induced lupus using Barnes maze test.

**Methods:** Fourteen female Balb/c mice were studied: 4 controls (single intraperitoneal injection of 0.5 mL NaCl 0.9%), 5 treated with pristane (single intraperitoneal injection of 0.5 mL pristane) and 5 treated with pristane plus lipopolysaccharide (LPS) 3 mg/kg 4 months post-administration of pristane. Short and long term visio-spatial learning and memory was evaluated in all groups at 7 weeks after the administration of LPS using Barnes maze test. The test consists of 3 phases: adaptation phase, acquisition phase and test phase. The short-term memory was evaluated during the acquisition phase (4 tests per day, D1-D4) and the long-term memory was evaluated 48 hour after the last test of the acquisition phase. Primary and total errors, primary and total latencies were analysed. The

results are shown as a mean ±SD. Kruskal-Wallis and Mann-Whitney U test was used for statistical analysis.

**Results:** All mice treated with pristane showed higher latencies to find the target hole in Barnes maze compared with controls during the short-term memory test (STP, D1-D4). In the long-term memory test (LTP) the highest latency in seconds (s) was observed in the pristane plus LPS group (64.6±59.1 s) followed by the pristane group (62.4±69.6 s) in comparison control group (7±3.6 s).



**Abstract FRI0278 – Figure 1.** Total. Latency in Barnes maze test. Total latency in seconds between mice groups (pristane, pristane + LPS and control) in STP (A) and LTP tests (B) in Barnes's maze

**Conclusions:** The increased latencies in the groups pristane plus LPS and pristane with respect to controls suggests that the autoantibodies produced in this model could be involved in alterations of the CNS, modifying the learning and memory processes. These results also suggest that pristane may have the potential to alter the permeability of the blood-brain barrier by itself. However, more experimental studies are needed to confirm the results obtained in this study.

**Disclosure of Interest:** None declared

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FRI0279

### DECREASED SPHINGOSIN-1-PHOSPHATE RECEPTOR 1 (S1P1) EXPRESSION IN ENDOTHELIAL PROGENITOR CELLS (EPCs) FROM SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) PATIENTS

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**Background:** SLE patients display an elevated cardiovascular risk when compared to the general population. <sup>1</sup> Interferon-alpha (IFN-α) appears to drive atherogenesis in SLE at least in part, by promoting abnormal phenotype and function of EPCs. <sup>1</sup> S1P1 is considered crucial for vasculogenesis and has been shown to attenuate IFN-α autoamplification by promoting IFN receptor 1 (IFNAR1) degradation. <sup>2,3</sup>

**Objectives:** To characterise S1P1 expression in EPCs from SLE patients and its putative association to type I IFNs effects on vasculogenesis.

**Methods:** SLE subjects that fulfilled SLE ACR classification criteria were recruited. Healthy controls were selected based on age and gender. Disease activity was assessed by SLEDAI-2K index. EPCs were quantified by flow cytometry in PBMC subsets as those cells that coexpress CD133<sup>+</sup>/CD34<sup>+</sup> in the CD3/CD56/CD79b<sup>-</sup> gate. <sup>1</sup> S1P1 expression was quantified in that subset. Control PBMCs were cultured in endothelial cell (EC)-enrichment medium for 2 weeks. Differentiated ECs were characterised by immunofluorescence (IF) as those cells that coexpress UEA-1 lectin and take up acetylated LDL. <sup>1</sup> These cells were stimulated with recombinant IFN-α in the presence or absence of the S1P1 agonist CYM-5442 and the S1P1 antagonist W-146 to assess the effect of this pathway on EC differentiation and type I IFN induced gene expression. <sup>3</sup>

**Results:** SLE and matched healthy controls (n=36/group) were compared. Demographic and clinical characteristics are depicted in table 1.

**Abstract FRI0279 – Table 1.** Demographic and Clinical features.

	Mean±SEM
Age (years)	32.2±1.35
Female (%)	34 (94.44)
Time since SLE diagnosis (months)	103.36±13.46
Time since remission (months)	16.6±3.07
SLEDAI-2K (points)	9.41±1.15

SLE patients displayed decreased absolute EPC numbers when compared to controls (2463.43±450.07 vs 39457.65±9063.34 EPCs/ml, p<0.001). Decreased EPC numbers negatively correlated with SLEDAI-2K (r=-0.405, p=0.026). S1P1 expression was decreased in lupus EPCs when compared to controls (48.27±1.55 vs 60.89±1.66%,



$p < 0.001$ ) and this was independent of disease activity. Recombinant IFN- $\alpha$  decreased EPC differentiation in healthy control cells ( $32.44 \pm 0.09$  vs  $79.69 \pm 0.27\%$ ,  $p = 0.001$ ), and this was attenuated in the presence of CYM-5442 and exacerbated in the presence of W-146. Moreover, type I IFN regulated genes were modulated by these compounds.

**Conclusions:** The S1P1 pathway is involved in the regulation of EPC differentiation by type I IFNs. Defects in S1P1 signalling pathway in lupus EPCs may contribute to the development of endothelial dysfunction in SLE.

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### FRI0280 A MOLECULAR NETWORK FOR FATIGUE IN PRIMARY SJÖGREN'S SYNDROME

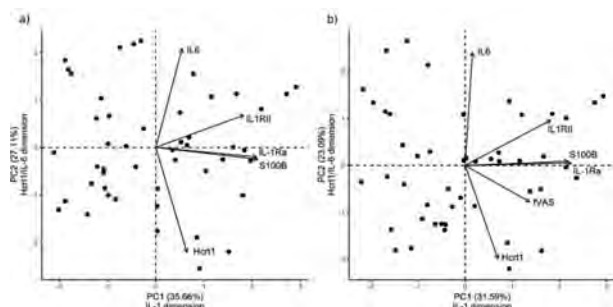
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**Background:** Fatigue is a common phenomenon in primary Sjögren's syndrome (pSS) and other chronic inflammatory diseases, cancer, and neurodegeneration. The underlying mechanisms for fatigue are not completely understood, but increasing evidence point to a biological basis for the phenomenon.

**Objectives:** Following the sickness behaviour hypothesis for fatigue, where pro-inflammatory cytokines and particularly interleukin 1 $\beta$  (IL-1 $\beta$ ) related signalling are essential, we wished to investigate how molecules that influence IL-1 $\beta$  activity may influence fatigue through complex networks (IL-1 $\beta$ , IL-1Ra, IL-1RII, IL-6 and S100B). We also hypothesised that the neuropeptide hypocretin-1 (Hcrt1), a regulator of sleep and wakefulness, could be an element in a network for fatigue.

**Methods:** In cerebrospinal fluid (CSF) from 49 patients with pSS, Hcrt1 was measured by RIA and the other proteins by ELISA. Fatigue was rated using the fatigue visual analogue scale (fVAS), and results analysed by univariate-, multiple regression, and principal component analysis (PCA).

**Results:** It was not possible to measure IL-1 $\beta$  due to very low concentrations in CSF. In simple univariate regression analysis with fatigue as a dependent variable a significant association was observed for depression ( $R^2 = 0.20$ ,  $p < 0.01$ ), and pain ( $R^2 = 0.23$ ,  $p < 0.01$ ) and the biochemical variable IL-1Ra ( $R^2 = 0.09$ ,  $p = 0.04$ ). In multiple regression with fVAS as dependent variable a model was obtained with depression, pain, and IL-1Ra as significant contributors ( $R^2 = 0.37$ ;  $p < 0.001$ ). In PCA two significant components were revealed (figure 1a). The first component (PC1) was dominated by variables related to IL-1 $\beta$  activity. The second component (PC2) showed a negative correlation between IL-6 and Hcrt1. fVAS was then introduced as an additional variable. In this new model fVAS correlated with the IL-1 $\beta$  related variables on PC1 and to a lesser degree with Hcrt1 on PC2 (figure 1b).



**Abstract FRI0280 – Figure 1.** a) PCA of biochemical variables only. b) PCA of biochemical variables including fatigue. Biplot illustrates scores of individuals and variables for PC1 and

PC2. Individual's scores are illustrated by dots. Arrows illustrate correlations of the variables to the components. Longer arrows mean higher correlation and arrows close to a component has higher contribution in generation of the component.

**Conclusions:** The main findings in this study indicate a functional network in which several IL-1 $\beta$  related molecules in CSF influence fatigue in addition to the clinical factors depression and pain. The neuropeptide Hcrt1 seem to participate in fatigue signalling, but probably not through the IL-1 pathway.

**Disclosure of Interest:** None declared

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### FRI0281 TRANSCRIPTOMIC PROFILING OF PDCs FROM PATIENTS WITH PSS IDENTIFIES CONSISTENTLY ALTERED GENE NETWORKS THAT INDICATE AN ACTIVATED PHENOTYPE AND ENHANCED ANTI-VIRAL STATE

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**Background:** Primary Sjögren's syndrome is an autoimmune disease characterised by lymphocytic infiltration of the exocrine glands and dryness of mouth and eyes. Type-I interferons (IFN) are thought to play an important role in pSS pathogenesis and plasmacytoid dendritic cells (pDCs) are capable of producing high levels of IFN. These cells infiltrate the salivary glands of pSS patients and their numbers correlate with local IFN-production.

**Objectives:** To understand the molecular mechanisms behind systemic dysregulation of pDCs, we performed RNA sequencing on pDCs isolated from peripheral blood of patients with pSS, non-Sjögren's sicca (nSS) and healthy controls.

**Methods:** We established two independent cohorts (each  $n = 31$ ), of patients and controls. pSS patients ( $n = 25$ ) were classified according to the 2002 AECG criteria. nSS patients ( $n = 20$ ) presented with dryness complaints without a known cause, did not have any generalised autoimmune disease, and did not fulfil the classification criteria for pSS. Healthy donors ( $n = 17$ ) were included as control group. Peripheral blood pDCs were isolated using MACS and RNA sequencing was performed for both cohorts.  $\pm 20$  million paired-end sequencing reads per sample were obtained using Illumina HiSeq 2500 platform.

**Results:** 8556 genes were differentially expressed ( $p$ -value  $< 0.05$ ) between all three groups in the discovery cohort. Of these, 3144 genes were also differential in the replication cohort. We generated gene modules from both cohorts and found 5 gene clusters comprising 1259 genes that were consistently dysregulated in both analyses. Pathway analysis showed that the 5 modules contain genes associated with cellular activation, including a group of genes involved in IFN-signalling and viral sensing, as well as regulation of intracellular transport. Generally, pDCs from patients with nSS displayed an intermediate phenotype.

**Conclusions:** We mapped transcriptomic differences in circulating pDCs from patients with nSS and pSS and identified gene clusters that are robustly replicated in two independent cohorts. We found 5 gene clusters that are dysregulated in patients with pSS and indicate enhanced cellular activation, including IFN-signalling and viral sensing which are key pathways in pSS pathogenesis. nSS patients showed similar transcriptomic dysregulation at an intermediate level. These data can help us better understand the role of pDCs in pSS.

**Disclosure of Interest:** None declared

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### FRI0282 MILK FAT GLOBULE EPIDERMAL GROWTH FACTOR 8 ON MONOCYTES IS A NOVEL BIOMARKER OF DISEASE ACTIVITY IN SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Milk fat globule epidermal growth factor 8 (MFG-E8) is an apoptosis-related secreted protein. It has been reported that MFG-E8 deficient or excess mice developed a systemic lupus erythematosus (SLE)-like autoimmune disease due to impaired clearance of apoptotic cells,<sup>1</sup> suggesting that abnormal expression of MFG-E8 is involved in the pathogenesis of SLE. Since elevated serum MFG-E8 level has been found in SLE patients,<sup>2</sup> it may possibly provide the

classification of the disease by pathological conditions.<sup>3</sup> However, the association with MFG-E8 expression and clinical features of SLE patients is not fully understood.

**Objectives:** To clarify the clinical significance of MFG-E8 in SLE, we analysed the correlation between the expression level of MFG-E8 in circulating phagocytic leukocytes and clinical parameters of the patients.

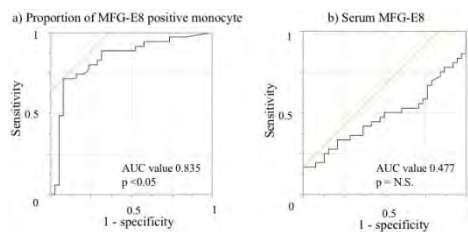
**Methods:** A multi-centre, exploratory and prospective SLE cohort was established. Among SLE patients who visited our division from May 2015 to March 2017 and satisfied the 1997 revised criteria, patients with one or both of BILAG A or B, or with SLEDAI-2K $\geq$ 4 and clinical symptoms were defined as active SLE. These patients were then matched with randomly selected patients by age, gender, history of nephritis, and daily glucocorticoid dose as an inactive SLE group. Age and sex matched healthy controls (HC) were also recruited. The expression level of MFG-E8 in monocytes and its concentration in serum of the patients were measured by FACS and ELISA, respectively. The clinical parameters of the patients were collected from their clinical records.

**Results:** A total of 108 cases were enrolled, consisting of 36 active (mean age: 44.2 $\pm$ 18.6, female: 80.6%, nephritis: 69.7%), 38 inactive SLE and 24 HC cases. The absolute number and the proportion of MFG-E8 positive-monocytes to total monocytes were significantly higher in the active SLE group ( $p<0.01$ ), whereas serum MFG-E8 level showed no significant difference among the group. Importantly, the proportion was also significantly correlated with SLEDAI-2K, serum levels of anti-ds-DNA antibody and complement and C1q (table 1). Notably, elevated proportion of MFG-E8-positive monocytes to total monocytes was observed in the patients with cutaneous or musculoskeletal involvement or leukocytopenia. In addition, the proportion of MFG-E8-positive monocytes to total monocytes significantly decreased from the baseline in active SLE patients after 6 months treatment and increased concordantly with disease activity in 6 refractory cases. Then we further analysed the accuracy to discriminate between active and inactive SLE patients and found that the proportion of MFG-E8 monocytes showed significant accuracy of disease activity, which is equivalent to serum levels of anti-ds-DNA antibody, complement and C1q, by receiver operating characteristic curve analysis (figure 1).

**Abstract FRI0282 – Table 1.** Correlation with SLEDAI and serological markers (Spearman's rho)

		#	Number of MFG-E8 positive monocyte	Proportion of MFG-E8 positive monocyte	Serum MFG-E8
a) Activity	SLEDAI-2K	74	0.570**	0.634**	-0.110
b) Serological markers	CH50	51	-0.503**	-0.591**	0.049
	Anti-ds-DNA antibody	74	0.425**	0.449**	-0.027
	C1q	69	0.526**	0.568**	0.001

\*  $p<0.05$ , \*\*  $p<0.01$  by Spearman's correlation coefficient



**Abstract FRI0282 – Figure 1.** Receiver operating characteristic curve analysis for discriminating active from inactive SLE

**Conclusions:** Our study indicate that the proportion of MFG-E8-positive monocytes to total monocyte in peripheral blood was positively associated with disease activity of SLE and may be a novel mechanistic biomarker to determine the disease activity.

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**Disclosure of Interest:** None declared

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**FRI0283 DYNAMIC CONTRAST ENHANCED MRI (DCE-MRI) DEMONSTRATES HIPPOCAMPUS PERMEABILITY IN SLE**

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**Background:** Cross-reactive, anti-dsDNA/N-methyl d-aspartate receptor antibodies (DNRAb) have been implicated in the pathogenesis of cognitive impairment in SLE. The mouse model demonstrates selective effects of DNRAb on hippocampal neurons following blood brain barrier (BBB) breach. <sup>1</sup> We previously identified abnormal hippocampal glucose hypermetabolism in SLE patients that correlated with serum DNRAb titers and poor performance on neuropsychological (NP) testing.<sup>2</sup> However, little is known about how antibodies access brain in humans.

**Objectives:** BBB permeability (BBBP) in SLE and healthy control (HC) subjects was evaluated with DCE-MRI. We hypothesised that brain areas with abnormal hypermetabolism<sup>2</sup> in SLE subjects would also demonstrate altered BBBP.

**Methods:** 6 SLE subjects with no history of NP symptoms and 6 HCs were recruited (all female). All subjects underwent NP testing and DCE-MRI on a 3.0 tesla magnet (Siemens Healthineers, GERMANY). MRI sequences were acquired according to standard protocols; permeability imaging used DCE technique with axial 3D-SPGR T1-WI sequences and 80 cine phases using TR=25 ms, TE=3.8 ms, FOV=24 mm, and matrix size of 128x256. Magnevist Gadolinium contrast (Bayer Healthcare, GERMANY) was dosed IV at 0.1 mmol/kg, at 5cc/sec following a 5 s delay. Post-processing of images into BBBP parameters of K-trans (mL/100 gm/min) and VE (mL/100 gm) was performed using Olea Sphere 2.2, 2.3 (Olea Medical, France) with the Tofts extended permeability model. This technique was standardised with the arterial input function centred in the cavernous ICA segment for all subjects.

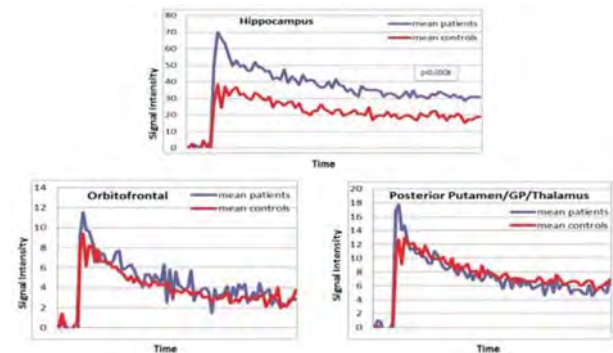
**Analyses:** Regions-of-interest (ROI) from previously identified hypermetabolic regions (hippocampus, orbitofrontal cortex, posterior putamen/globus pallidus/thalamus) were selected. Mirror ROIs were placed in bilateral MRI cerebral hemispheres for sampling at same brain levels. Regional DCE curves were generated to compare permeability phases. T-tests were used to evaluate demographic and NP testing differences.

**Results:** SLE subjects performed significantly worse than HCs on cognitive testing (table 1). Mean DCE curves (figure 1) show perfusion (initial spike) and permeability phases of contrast in the sampled tissues. Compared to HCs, SLE subjects demonstrate significantly increased signal in the permeability phase in the hippocampus, indicating leakage of contrast into the extravascular space.

**Abstract FRI0283 – Table 1.** Subject characteristics and neuropsychological testing scores

	Healthy Control (n=6)	SLE (n=6)	p
Age	35.04 $\pm$ 9.6	38.0 $\pm$ 13.2	.669
NP Testing*			
Matching Grids	40.9 $\pm$ 9.7	25.8 $\pm$ 9.2	.023
Match to Sample	35.4 $\pm$ 13.5	16.4 $\pm$ 5.9	.01
Continuous Processing	86.3 $\pm$ 13.9	65.6 $\pm$ 5.5	.013

\*Automated Neuropsychological Testing Metric: resulted as throughput scores that represent efficiency as a function of accuracy and time



**Abstract FRI0283 – Figure 1.** Dynamic Contrast Enhanced MRI Curves show increased hippocampus permeability in SLE

**Conclusions:** This is the first report of increased BBBP in SLE subjects that is specific to the hippocampus; a region that we have previously reported to have abnormal resting metabolism in SLE subjects. These data, including the abnormal NP testing, support the murine model of autoantibody-mediated cognitive impairment following disruption of the BBB. The results also suggest that DCE-MRI may be an effective, non-invasive tool to measure BBBP and its role in neuropsychiatric SLE pending confirmatory studies with increased sample size.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.7427

#### FRI0284 ALTERED PATTERNS OF HISTONE ACETYLATION POINT TO MECHANISMS OF TRANSCRIPTIONAL DYSREGULATION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

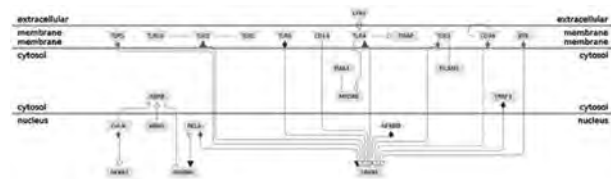
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**Background:** Systemic lupus erythematosus (SLE) is a chronic autoimmune disease designated by a heterogeneous course and systemic nature. It arises as a result of complex pathways, as well as the interaction of genetic and environmental factors, leading to the altered reactivity of the immune system that culminates in autoantibody formation. Epidemiological studies have shown an important role of the genetic component in the emergence of SLE and genome-wide association studies have identified more than 50 SLE-associated risk loci, pointing to a complex genetic background.

**Objectives:** The aim of the study was to further elucidate the genetic mechanisms influencing the development of SLE.

**Methods:** We performed chromatin immunoprecipitation experiments to ascertain the levels of histone acetylation in peripheral blood mononuclear cells collected from 5 recent onset and treatment naive SLE patients compared to 5 age and gender matched controls.

**Results:** The analysis revealed 16 379 significantly enriched genomic regions in control patients compared to 39 204 significantly enriched genomic regions in SLE patients. Among the SLE specific regions several pathways were significantly enriched including the adaptive immune system pathway, cytokine signaling in immune system, disease of immune system and inflammation mediated by chemokine and cytokine pathway.



**Conclusions:** The collective data point to a significant alteration of histone acetylation patterns in SLE patients possibly mediated by the DNA specific autoantibodies. The results of the study offer additional insight into the genetics of SLE pointing to putative mechanisms of transcriptional dysregulation.

**Disclosure of Interest:** None declared

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#### FRI0285 DETECTION OF OLIGOCLONAL B-CELL POPULATIONS BY SPECTRATYPING ANALYSIS IN THE RENAL TISSUE OF PATIENTS WITH ACTIVE LUPUS NEPHRITIS

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**Background:** Previous studies have shown, using polymerase chain reaction (PCR), cloning, sequencing and analysis of rearranged immunoglobulin heavy-chain (Ig-V<sub>H</sub>/D<sub>H</sub>/J<sub>H</sub>) genes, that clusters of clonally-related sequences are commonly found in the peripheral blood of patients with active lupus nephritis.

**Objectives:** Using an easy-to-perform method such as spectratyping analysis, to test the hypothesis that clonal B-cell populations are present in the renal tissue of lupus nephritis patients, induced perhaps as a result of local (auto)antigenic stimulation.

**Methods:** Genomic DNA extracted from renal biopsy samples from 18 patients with active lupus nephritis and 24 control patients with other (auto)immune-mediated glomerular diseases, as well as DNA from 25 paired peripheral blood samples, was subjected to multiplex PCR for the detection of Ig-V<sub>H</sub> clonal rearrangement. PCR products were analysed by capillary electrophoresis according to the Biomed-2 standard guidelines for the definition of clonal B cell populations. Immunohistochemistry using the B-cell-specific L-26 antibody was also performed in available renal samples.

**Results:** Electrophoregrams of PCR products derived from patients with biopsy proven active lupus nephritis revealed the presence of oligoclonal B-cell populations among polyclonal B-cells in renal tissue of 6/18 patients. No associations with clinical or histology class were evident. Oligoclonal B-cell populations were also found in renal samples derived from patients with untreated focal segmental glomerulosclerosis (6 of 7), minimal change disease (1 of 3), membranous nephropathy (1 of 3) and IgA nephropathy (3 of 4), and not in patients with pauci-immune vasculitis (n=4) or membranoproliferative glomerulonephritis (n=3). Oligoclonal B-cell populations were not found in any of the paired peripheral blood samples derived from 13 patients having renal B-cell oligoclonality, suggesting the existence of local (auto)antigens leading to clonal expansion rather than B-cell transfer through peripheral circulation. Finally, spectratyping analysis identified polyclonal or oligoclonal B-cells in all renal tissues in the absence of detectable B-cells by immunohistochemistry in the same samples.

**Conclusions:** These novel findings show that spectratyping analysis can detect oligoclonal B-cell expansions in renal tissue from patients with active lupus nephritis and other (auto)immune-mediated glomerular diseases. Whether this standardised method can identify individual patients who could benefit from therapeutic B cell depletion deserves further study.

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**Disclosure of Interest:** None declared

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#### FRI0286 RANK-L IS EXPRESSED BY SALIVARY GLAND EPITHELIAL CELLS IN PRIMARY SJOGREN'S SYNDROME: A NOVEL ACTOR IN ECTOPIC LYMPHOID STRUCTURE NEOGENESIS

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**Background:** Tertiary Lymphoid Organs (TLOs) are observed in target tissues of various immune-mediated inflammatory diseases (IMIDs) such as salivary glands in primary Sjögren's syndrome<sup>1</sup> (pSS). TLOs are mimicking secondary lymphoid organs (SLOs) architecture and strikingly share common features with lymph nodes.<sup>2</sup> SLOs organogenesis is coordinated by a complex stromal network that has not been fully characterised in TLOs yet. Although RANK-L (Receptor Activator of NF-κB Ligand) has been recently involved as a pivotal cytokine in precocious steps of lymph nodes development,<sup>3</sup> notably through a stromal cell expression, its contribution in TLOs neogenesis remains unclear.

**Objectives:** To characterise stromal cells subsets within TLOs arising in the salivary glands and to determine whether RANKL is expressed or not in the target tissue of pSS.

**Methods:** Stromal cells and RANK-L expression were analysed in TLOs from salivary glands by immuno-fluorescence on frozen sections in the NZB/NZW F1 mouse model and in minor salivary gland biopsies of patients fulfilling 2016 ACR-EULAR Sjögren's syndrome criteria and by flow-cytometry after enzymatic digestion of NZB/NZW F1 salivary glands. RANK-L expression has also been assessed by Real Time quantitative Polymerase Chain Reaction (RT-qPCR) and immunofluorescence on primary cultures of salivary gland epithelial cells (SGECs) with or without IL-1b or Interferon alpha (INF-α) stimulation.

**Results:** Most of SLOs stromal cells populations: Fibroblastic Reticular Cells (FRCs), Follicular Dendritic Cells (FDCs), Lymphatic Endothelial Cells (LECs), Blood Endothelial Cells (BECs) and High Endothelial Venules (HEVs) were identified in salivary TLOs of both NZB/NZW F1 mice and patients with pSS. FRCs were the dominant subset in salivary TLOs and their proportion correlated with the degree of lymphocytic infiltration (r=0,7 ; p=0,007). In SLOs, RANK-L was mainly expressed by MRCs, whereas, none of them could be detected in salivary TLOs. However, despite the absence of MRCs in TLOs, RANK-L was still expressed by



a few T-cells within the infiltrates and strikingly by epithelial cells. Furthermore, RANK-L expression by SGECS in primary cultures was increased after INF- $\alpha$  or IL-1 $\beta$  stimulation.

**Conclusions:** To our knowledge, this is the first report of a RANK-L contribution to primary Sjögren's syndrome. These results suggest that RANK-L could be an important actor of ectopic lymphoid neogenesis. RANK-L inhibition might represent, in the future, a relevant immuno-modulatory strategy in primary Sjögren's syndrome.

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**Disclosure of Interest:** None declared

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#### FRI0287 SEROLOGIC EVIDENCE OF VIRAL REACTIVATION AND INCREASED DISEASE ACTIVITY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Systemic lupus erythematosus (SLE) is a clinically heterogeneous disease oftentimes characterised by a waxing and waning disease course. However, mechanisms of disease flare remain elusive.

**Objectives:** This study examined relationships between SLE disease activity, immune pathways, and serologic evidence of viral exposures and reactivation within molecular subsets of SLE patients.

**Methods:** Serial or single samples of plasma, serum and RNA (n=290) were collected from 184 adult SLE patients who met ACR classification and cohort-matched controls (n=49). Disease activity was assessed by modified SELENA-SLEDAI. Immune pathways were evaluated by modular transcriptional analysis of Illumina Beadchip Microarray gene expression data, as well as by plasma soluble mediators (n=32) by multiplex, bead-based assay and ELISAs. This information was used to subset patients into seven molecular-defined categories by random forest modelling. Viral seropositivity and antibody concentrations were detected by ELISA for antibodies against EBV-Viral Capsid Antigen (VCA) (IgG and IgA), EBV-Early Antigen (EA) (IgG), Cytomegalovirus (CMV) (IgG), and Herpes Simplex Virus (HSV-1) (IgG).

**Results:** Serologic evidence of EBV reactivation was more common in SLE patients compared to controls, as measured by antibodies against EBV-EA [IgG] (40% vs 13%; OR=4.57, p=0.0006) or EBV-VCA [IgA] (36% vs 17%; OR=2.70, p=0.019). No differences were noted in CMV or HSV1 seropositivity rates between patients and controls. IgG responses against EBV-VCA were nearly universal among these adult patients and controls; however, concentrations of EBV-VCA IgG were higher in SLE patients compared to controls (ISR=4.44 vs 3.52; p=0.0021), as were EBV-VCA IgA and EBV-EA IgG antibody responses. In cross sectional analysis, SLE patients with higher disease activity (SLEDAI  $\geq 6$ ; n=126) had higher concentrations of EBV-EA IgG than patients with lower (n=166) disease activity (ISR=0.822 vs 0.540; p=0.033). SLE patients with serologic evidence of EBV reactivation by EA IgG responses had higher levels of interferon associated molecules, IP10 (p=3.4 $\times 10^{-14}$ ), BLYS (5.5 $\times 10^{-5}$ ), and IL-10 (p=0.00013). HSV1 IgG positive SLE patients also showed higher levels of IP10 (2.2 $\times 10^{-7}$ ). Antibody responses toward EBV-EA were enriched in molecularly defined patient clusters with higher expression levels of interferon and inflammatory modules, as well as with interferon and inflammatory soluble mediators. Patients within these clusters were also more likely to have major organ involvement, such as renal or neurologic disease.

**Conclusions:** Serologic evidence of EBV reactivation is more common in SLE patients compared to healthy controls. EBV-EA IgG responses are elevated in SLE patients with active disease and correspond with increases in interferon-associated mediators. This study provides serologic evidence suggesting a possible role for viral reactivation in SLE disease activity.

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**Disclosure of Interest:** None declared

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#### FRI0288 THYMIC STROMAL LYMPHOPOIETIN (TSLP) BIOLOGICAL EFFECTS ON HUMAN PERIPHERAL BLOOD B LYMPHOCYTES IN PRIMARY SJÖGREN'S SYNDROME

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**Background:** Thymic stromal lymphopoietin (TSLP) is an epithelial lymphopoietic cytokine belonging to interleukin (IL)–7 family, acting as a B-cell growth factor. A pathogenetic role of TSLP in primary Sjögren's syndrome (pSS) and pSS-related B-cell lymphoproliferation has been recently indicated.<sup>1</sup>

**Objectives:** to investigate the biological effects of TSLP on human peripheral blood B lymphocytes in pSS.

**Methods:** Peripheral blood B lymphocytes from 15 pSS patients, stratified according to their lymphoproliferative status (fully benign, fbSS: n=5; myoepithelial sialadenitis, MESA: n=5; B-cell non-Hodgkin lymphoma, NHL: n=5) and from 5 healthy blood donors (HBDs) were isolated by immunomagnetic negative selection and cultured with three different stimuli: i) TSLP; ii) combination of TSLP and IL-4; iii) combination of CD40 functional grade monoclonal antibody and IL-4. B-cell activation status was evaluated by flow cytometry, by analysing the expression of surface IgM after stimulation. An ELISA assay was also performed to assess the immunoglobulins (Ig) production in the B-cell culture supernatants after the exposure to the three different stimuli.

**Results:** peripheral blood B lymphocytes isolated from fbSS patients were significantly activated by the combination of TSLP and IL4 (p=0.0218), as well as by the classic co-stimulation of antiCD40 plus IL4 (p=0.044), but not when TSLP was used alone. This pattern of responsiveness was observed also in HBDs. By contrast, the peripheral B-cells of NHL pSS patients were significantly activated by the TSLP alone (p=0.0157), without the necessity of other additional stimuli. A similar response to TSLP alone was observed also in MESA B-cell cultures but with no significance. As concerns Ig production in culture supernatants of peripheral B-cells, in fbSS patients we observed a significant increase of Ig production both after the exposure to TSLP plus IL4 (p=0.0417) and after the stimulation with antiCD40 plus IL4 (p=0.0293), but not with TSLP alone. By contrast, TSLP alone induced Ig production both in MESA (p=0.0368) and in NHL peripheral B-cells (p=0.0268). Unexpectedly, the combined stimulus of TSLP plus IL4 did not produce any significant effect in both these subgroups, and was less effective than TSLP alone also in stimulating B-cell surface IgM expression.

**Conclusions:** human peripheral blood B-cells from pSS patients showed an increased responsiveness to TSLP, however with significant differences. In HBDs and in fbSS, TSLP induced a significantly higher B-cell activation and immunoglobulin production only with the addition of IL4, whereas in NHL TSLP alone was sufficient. In addition, IL-4 co-stimulus induced a lower activation than TSLP alone in NHL. Overall, also functional tests support a role of TSLP as an important driver of B-cell stimulation and lymphoma progression in pSS. Interactions of TSLP with other B-cell stimulating factors also deserve particular attention.

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**Disclosure of Interest:** None declared

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#### FRI0289 ROLE OF CXCL13 AND CXCL12 IN SJÖGREN'S SYNDROME: ASSOCIATION WITH HISTOLOGICAL, CLINICAL AND LABORATORY FEATURES

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**Background:** Ectopic production of the lymphoid chemokines CXCL13 and CXCL12 has been described in tertiary lymphoid structures (TLS) that harbour in the salivary glands of patients with Sjögren's Syndrome (pSS). Whilst CXCL13 expression correlates with clinical features, its potential role as a biomarker to





chemokine in the serum (pg/mL) of SLE patients compared to HC, respectively, included: sCX3CL1 (478.6±46.19; 235.4±140.8) and MCP-1 (2657±466.2; 648.5 ±69.6) (p<0.00001), MIP1β (141.0±10.71; 79.31±10.69) (p<0.0003), and TNFα (59.07±6.64; 29.31±3.15) (p<0.0041). Additionally, the disease severity and endothelial dysfunction associated biomarker VEGF increased in SLE patients (445.6.3±48.1 pg/mL) compared to HC (231.8±47.03 pg/mL) (p<0.0069). Lastly, HC monocyte subsets were stimulated with TLR7 and 8 ligands and supernatants evaluated for the analytes described above, see table 2.

Abstract FRI0291 – Table 1

Monocyte Subset	Marker	Healthy Control (Mean ± SEM)		SLE Patients (Mean ± SEM)		P-Value	
		Percentage	MFI	Percentage	MFI	Percentage	MFI
CD14 <sup>+</sup>	CCR1	71.18 ± 5.31	820.7 ± 55.8	71.81 ± 6.425	880.9 ± 110.4	0.799	0.775
CD16 <sup>+</sup>	CCR1	19.41 ± 5.14	1768.2 ± 548.7	33.90 ± 7.86	1716.6 ± 473.9	0.108	0.329
CD14 <sup>+</sup> /CD16 <sup>+</sup>	CCR1	34.87 ± 6.01	3533.2 ± 451.4	49.50 ± 7.13	1935.1 ± 396.4	0.124	0.430
CD14 <sup>+</sup>	CD11b	97.58 ± 0.9	5298.5 ± 410.9	98.44 ± 0.29	6886.2 ± 626.6	0.965	0.007
CD16 <sup>+</sup>	CD11b	95.22 ± 4.45	1289.6 ± 146.6	93.13 ± 4.34	2075.15 ± 324.4	0.619	0.021
CD14 <sup>+</sup> /CD16 <sup>+</sup>	CD11b	93.87 ± 1.60	4580.8 ± 327.5	93.72 ± 2.32	5640.9 ± 579.0	0.861	0.102
CD14 <sup>+</sup>	CD40	7.61 ± 2.72	612.2 ± 200.7	11.06 ± 3.08	806.7 ± 266.4	0.861	0.333
CD16 <sup>+</sup>	CD40	7.37 ± 3.05	1644.6 ± 575.6	15.65 ± 6.09	1468.1 ± 473.6	0.200	0.511
CD14 <sup>+</sup> /CD16 <sup>+</sup>	CD40	3.77 ± 2.92	1116.7 ± 325.2	12.33 ± 4.17	1389.1 ± 348.7	0.643	0.389
CD14 <sup>+</sup>	CD163	65.77 ± 5.42	1499.4 ± 110.4	85.24 ± 3.06	2198.3 ± 171.0	0.006	0.001
CD16 <sup>+</sup>	CD163	15.21 ± 3.06	563.88 ± 94.74	24.08 ± 3.34	757.6 ± 106.6	0.022	0.022
CD14 <sup>+</sup> /CD16 <sup>+</sup>	CD163	61.00 ± 4.96	1356.0 ± 108.6	76.72 ± 5.36	2028.3 ± 198.0	0.014	0.014
CD14 <sup>+</sup>	CX3CR1	42.82 ± 2.93	796.2 ± 70.58	63.0 ± 5.91	1062 ± 100.1	0.005	0.047
CD16 <sup>+</sup>	CX3CR1	36.47 ± 2.53	2471.8 ± 213.5	85.50 ± 4.08	2947.3 ± 336.3	0.742	0.378
CD14 <sup>+</sup> /CD16 <sup>+</sup>	CX3CR1	65.38 ± 4.66	2061.0 ± 164.6	81.73 ± 3.41	2579.1 ± 249.1	0.007	0.141

Abstract FRI0291 – Table 2

Cytokine / Chemokine	Stimulus	CD14 <sup>+</sup> Monocytes				CD14 <sup>+</sup> /CD16 <sup>+</sup> Monocytes				CD16 <sup>+</sup> Monocytes			
		pg/mL		Fold Change		pg/mL		Fold Change		pg/mL		Fold Change	
		Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM
CX3CL1	Control	29.2	3.8	1.0	0.0	60.1	8.8	1.0	0.0	22.9	9.6	1.0	0.0
	AP8B (TL7/8)	44.7	9.4	1.5	0.6	42.7	9.0	0.7	0.0	41.4	14.1	1.0	0.0
	AP8F (TL7)	46.2	15.1	1.6	0.0	89.1	2.2	1.5	0.2	51.7	24.7	2.3	0.3
	AP8N (AD) (TL8)	65.5	1.8	2.3	0.9	74.3	0.2	1.2	0.5	46.8	13.9	2.1	0.4
MIP-1β	Control	80.9	26.9	1.0	0.0	936.3	189.8	1.0	0.0	161.3	87.8	1.0	0.0
	AP8B (TL7/8)	354.5	396.6	4.4	1.1	739.8	201.5	0.8	0.2	743.9	217.4	4.1	0.7
	AP8F (TL7)	317.4	215.8	3.1	3.3	1477.0	404.5	1.6	0.7	334.8	341.2	2.0	0.6
	AP8N (AD) (TL8)	1362.0	374.6	16.7	4.2	2528.0	1038.0	2.7	1.4	396.1	367.0	6.0	2.9
MIP-2	Control	96.7	51.6	1.0	0.0	2488.0	809.8	1.0	0.0	213.8	80.0	1.0	0.0
	AP8B (TL7/8)	3484.0	3488.0	36.0	36.4	3411.0	184.1	1.4	0.7	2136.0	894.9	9.9	1.7
	AP8F (TL7)	1404.0	1230.0	14.7	5.2	3884.0	1118.0	4.0	0.8	689.8	429.8	3.7	0.9
	AP8N (AD) (TL8)	3951.0	1398.0	40.4	18.4	3889.0	437.2	1.6	0.5	2150.0	387.0	9.6	4.2
TNF	Control	1276.0	841.7	1.0	0.0	3182.0	3482.0	1.0	0.0	487.8	268.9	1.0	0.0
	AP8B (TL7/8)	4148.0	3038.0	3.3	2.3	1012.0	761.5	0.4	0.1	1389.0	614.7	3.1	0.8
	AP8F (TL7)	2879.0	3252.0	2.3	0.7	3415.0	2026.0	1.1	1.2	4894.0	4818.0	6.1	4.4
	AP8N (AD) (TL8)	1294.0	4036.0	10.0	2.8	1814.0	2287.0	0.6	0.3	1125.0	1033.0	2.8	1.0

**Conclusions:** Cell surface markers of activation and adhesion increased in SLE monocyte subsets compared to HC. In parallel, increased inflammatory cytokines and chemokines that attract monocytes to tissues were increased in the serum of these patients. Linking a possible source of this increase in serum analytes, HC monocyte subsets were stimulated with disease-relevant ligands and evaluated in culture. Along with increased monocyte expression of CX3CR1, preliminary data demonstrates an increase in CX3CL1 expression on endothelial progenitor cells (EPCs) and immature and mature circulating endothelial cells (iCECs and mCEC respectively) in active disease.

**Disclosure of Interest:** None declared

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**FRI0292 DYSFUNCTION OF TFH, TREG AND TR1 CELLS IN APOE-/- FASLG/D C57BL/6 MICE WITH LUPUS SYMPTOMS AND ATHEROSCLEROSIS**

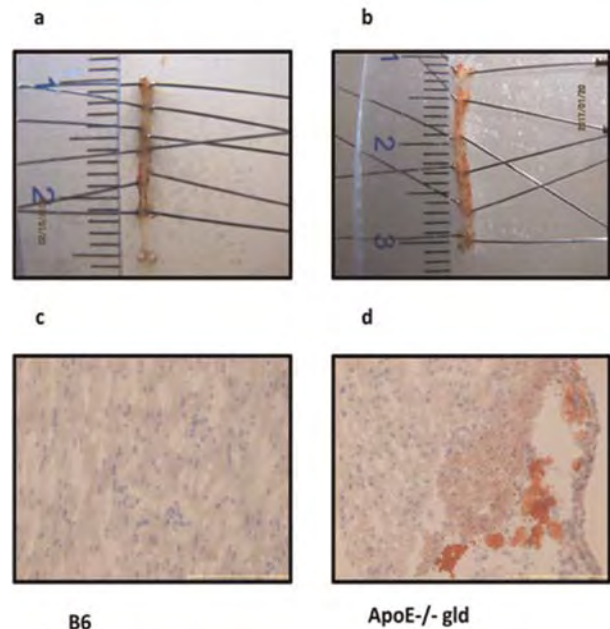
S. Wang, G. Yao, L. Sun. Department of Rheumatology and Immunology, The Affiliated Drum Tower Hospital of Nanjing University Medical School, Nanjing, China

**Background:** Cardiovascular disease due to atherosclerosis is currently recognised as one of the leading causes of death among patients with systemic lupus erythematosus (SLE). It is well established that dysfunction of lymphocytes contribute to the pathogenesis of SLE. Recent studies also showed infiltration of several subsets of lymphocytes in atherosclerotic lesions and their various contributions to atherosclerosis were uncovered in experimental models and patients. However, the predominant and specific subsets of lymphocytes that play critical role in the pathogenesis of SLE patients with cardiovascular complications remained to be elucidated.

**Objectives:** This study aims to define the dominant population of lymphocytes in mice with combination of lupus and atherosclerosis.

**Methods:** The mouse model of accelerated atherosclerosis in lupus (ApoE<sup>-/-</sup> FasI<sup>gld</sup> B6 mice) was generated from apolipoprotein E-deficient (apoE<sup>-/-</sup>) and FasI<sup>gld</sup> C57BL/6 mice. The lupus-like autoimmunity and atherosclerotic lesions was evaluated. The lymphocytes of spleen and peripheral blood were analysed by flow cytometry.

**Results:** The results of PCR and sequencing showed that the double-mutant ApoE<sup>-/-</sup> FasI<sup>gld</sup> B6 mice were generated. Splens from 5 month-old ApoE<sup>-/-</sup> FasI<sup>gld</sup> B6 mice were significantly enlarged compared with wild type mice (WT mice). ApoE<sup>-/-</sup> FasI<sup>gld</sup> B6 mice displayed a pattern of glomerulonephritis typically found in SLE and showed marked C3, IgG and IgM deposits in the glomeruli. Anti-dsDNA antibody and high levels of creatinine were detected in the serum of ApoE<sup>-/-</sup> FasI<sup>gld</sup> B6 mice. These results indicated that the ApoE<sup>-/-</sup> FasI<sup>gld</sup> B6 mice have typical characteristics of SLE. Oil red O staining revealed that there was significantly increased atherosclerotic lesion area at the proximal aorta in ApoE<sup>-/-</sup> FasI<sup>gld</sup> B6 mice compared with WT mice (figure 1 a,b). The frozen section of myocardium stained by oil red O revealed that lipid deposited in myocardial cells of ApoE<sup>-/-</sup> FasI<sup>gld</sup> B6 mice (figure 1 c,d). As expected, total cholesterol, LDL cholesterol and triglyceride were significantly increased, while HDL cholesterol decreased in the double-mutant mice. These results indicated that ApoE<sup>-/-</sup> FasI<sup>gld</sup> B6 mice had accelerated atherosclerosis.



**Conclusions:** The ApoE<sup>-/-</sup> FasI<sup>gld</sup> B6 mice simultaneously exhibit SLE and atherosclerosis characteristics. Our findings suggested that proinflammatory M1 macrophages and Th cells were increased, while the anti-inflammatory Treg and Tr1 cells were decreased and the imbalance of these cells and their releasing cytokines contributed to progression in atherosclerosis with SLE. Further studies may validate these cells as potential targets for treating SLE patients with atherosclerosis.

**Disclosure of Interest:** None declared

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**FRI0293 IMBALANCE IN CIRCULATING SUBSETS OF INNATE LYMPHOID CELLS IS LINKED TO DISEASE ACTIVITY AND TYPE I INTERFERON SIGNATURE IN PRIMARY SJÖGREN'S SYNDROME**

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**Background:** Recent studies indicate an important role for innate lymphoid cells (ILCs) in the pathophysiology of rheumatic diseases. In rheumatoid arthritis and spondyloarthropathies elevated numbers of subsets of ILCs have been found at the site of inflammation producing cytokines including IFN-γ and IL-22 and in addition, group 3 ILC have been suggested to be involved in formation of ectopic lymphoid structures in rheumatic diseases, Shikhaigie Nat Rev Rheumatol 2017 Wenink A and R 2017). ILC3-like cells producing IL-22 have been found in the salivary glands of pSS patients. Ciccia ARD 2012 However, circulating ILC have not yet been studied in primary Sjögren's syndrome (pSS) and systemic lupus erythematosus (SLE). Furthermore, SLE and pSS are characterised by presence of a type I interferon (IFN) signature in a large proportion of the patients. Animal studies in HIV and asthma implicate type I IFN, produced by plasmacytoid dendritic cells (pDCs), to regulate the survival of group 2 and group 3 ILCs (ILC2 and



ILC3) via increase of Fas (CD95) expression, rendering the ILC more susceptible to apoptosis, Maazi JACI 2017, Zhang JCI 2015. Duerr Nat Immunol 2016

**Objectives:** In this study, we explored for the first time the frequency and phenotype of circulating ILCs in pSS and SLE and their relation to the IFN signature.

**Methods:** Frequencies and phenotypes of ILC subsets and pDCs were assessed by flow cytometry in peripheral blood of patients with pSS (n=20), SLE (n=20) and healthy controls (n=17). Patients were stratified by the presence or absence of an IFN signature as assessed by RT-qPCR on peripheral blood mononuclear cells as previously described. Brkic ARD 2013

**Results:** ILC1 numbers were increased in peripheral blood of patients with SLE as compared to healthy controls and in pSS patients ILC1 numbers correlated with disease activity (ESSDAI score), serum IgG levels and anti-SSB auto-antibodies (all p<0.05). Numbers of ILC1, ILC2 or ILC3 did not significantly differ between patients with SLE and pSS. However, patients with a high expression of the type I IFN signature had significantly decreased numbers of ILC2 and ILC3 (p=0.04 and p=0.02, respectively). The decrease of ILC2s and ILC3s was related to increased expression of Fas (CD95) on these cells in patients with a high type I IFN signature (both p=0.01).

**Conclusions:** Both in SLE and pSS, a type I IFN signature is related to reduced numbers of circulating ILC2s and ILC3s in association with increased Fas expression on these cells possibly rendering them more susceptible to Fas/FasL-dependent apoptosis at peripheral sites.

**Disclosure of Interest:** None declared

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#### FRI0294 INJURED PODOCYTES EXPRESS COMPLEMENT FACTOR H AND PROCESS IMMUNE COMPLEX DEPOSITION IN GLOMERULAR SUBENDOTHELIAL AREA

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**Background:** Glomerular Immune complex (IC) deposition causes glomerulonephritis in lupus nephritis. The reaction of intrinsic glomerular cells differs according to the area of IC deposition. Subepithelial IC deposits cause functional and structural changes on podocytes (glomerular visceral epithelial cells) through complement pathway activation as is well known in membranous glomerulonephritis. In this setting, podocytes can induce some complement factors including complement factor H (CFH) which serves not only to regulate the alternative pathway but also to process subepithelial IC deposition.<sup>1</sup> However, whether podocyte processing of IC deposition is limited to only the subendothelial area is obscure.

**Objectives:** To clarify the role of podocytes in IC deposition in the glomerular sub-endothelial area.

**Methods:** NEP25 mice genetically expressing human CD25 in podocytes were used. Intravenous immunotoxin for human CD25 (LMB2) provokes podocyte-specific injury (NEP25/LMB2). By shortening the period of LMB2 exposure to NEP25 mice, we mitigated the podocyte injury. We administered intraperitoneally IgG3-producing hybridoma clones, 2B11.3, which were previously established from an unmanipulated MRL/lpr mouse, to NEP25 mice (NEP25/hybridoma). Furthermore, we also injected short-term LMB2 to NEP25/hybridoma mice (NEP25/hybridoma/LMB2). We investigated IC deposits by immunofluorescence and electronic microscopic study. We measured complement regulatory factor mRNA expression including CFH, complement factor I (CFI), decay-accelerating factor (DAF), complement receptor 1-related gene/protein y (Cry), C3a receptor (C3aR) and C5a receptor (C5aR) of isolated glomeruli of each mouse by quantitative real time-PCR. In an *in vitro* study, we assessed CFH mRNA expression of immortalised mouse podocytes injured by puromycin.

**Results:** First, NEP25/LMB2 mice showed glomerular tuft collapse with epithelial cell hyperplasia, suggesting podocyte loss by light microscopy study as reported previously. mRNA expression of all complement regulatory factors but C5aR was decreased in NEP25/LMB2 mice as compared with NEP25 mice. This result suggests that podocytes produce these complement regulatory factors. On the other hand, when the podocyte injury was mitigated, CFH and C3aR mRNA expression increased, and CFI, DAF and Cry mRNA expression decreased as compared with NEP25 mice. Second, we detected IC deposition only in the glomerular sub-endothelial area without endocapillary proliferative lesion in NEP25/hybridoma mice. They showed increase of C3aR mRNA expression, and decrease of CFI and DAF mRNA expression as compared with controls. Notably, subendothelial IC deposition did not alter CFH mRNA expression. Third, NEP25/hybridoma/LMB2 (milder podocyte injury) showed decrease of IC deposits in glomeruli and increase of only CFH mRNA expression (1.7-fold) as compared to NEP25/hybridoma mice, while there was no significant change in mRNA expression of other

complement regulatory factors. Finally, puromycin-induced mild podocyte injury promoted CFH mRNA expression in cultured podocytes as compared to controls.

**Conclusions:** Mildly injured podocytes induce CFH expression, and serve to process IC deposition in the glomerular subendothelial area.

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**Disclosure of Interest:** None declared

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#### FRI0295 INHIBITION OF CATHEPSIN S LEADS TO SUPPRESSION OF ANTIGEN SPECIFIC T CELLS FROM PATIENTS WITH PRIMARY SJÖGREN SYNDROME

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**Background:** Primary Sjögren syndrome (pSS) is an autoimmune disease characterised by an infiltration of T and B cells into exocrine gland tissue and its subsequent destruction<sup>1</sup>. Antigen presenting cells, including B cells, foster T cell activation and anti-SS-A/SS-B producing plasma cells, eventually leading to disease progression and systemic complications<sup>2</sup>.

**Objectives:** Cathepsin S (CatS) is crucially involved in MHCII processing in pSS mouse models<sup>3</sup> and patients<sup>4</sup>. In this translational study we investigated the *ex vivo* effects of the CatS inhibitor RO5459072 in different bio-compartments, including specific T cells, of pSS patients and healthy controls.

**Methods:** *Ex vivo* CatS activity was assessed in different bio-compartments of 15 pSS patients and 13 healthy controls and in presence or absence of RO5459072 using commercial activity and quantification assays. In addition, antigen (5 µg/mL SS-A, 5 µg/mL SS-B, 5 µg/mL Influenza H<sub>3</sub>N<sub>2</sub>; 2 µg/mL Tetanus Toxoid and 100 ng/mL SEB) specific T cell responses were examined using 2 × 10<sup>5</sup> PBMC/well IFN-γ/IL-17 Dual ELISPOT (48 hour incubation) and 5 × 10<sup>4</sup> PBMC/well BrdU proliferation assays after (72 hour incubation) in presence or absence of RO5459072.

**Results:** pSS patients showed significantly higher CatS activity in tear fluid than healthy controls (two-tailed t-test p<0.01). RO5459072 significantly suppressed CatS activity in tears of pSS patients (two-tailed t-test p<0.01). CatS inhibition also exerted a strong and dose-dependent suppression of T cell responses towards SS-A and SS-B antigen in *ex vivo* derived pSS patient cells in Elispot and BrdU assays (table 1).

Table 1 Suppression of antigen specific T cell responses (Elispot) and suppression of cell proliferation (BrdU) in the absence or presence of RO5459072 (0–100 µM). One-tailed t-test: \*p<0.05, \*\* p<0.01, \*\*\*p<0.001, \*\*\*\* p<0.0001

**Conclusions:** CatS activity in tear fluid seems to be a relevant biomarker for pSS disease activity. RO5459072 is a potent inhibitor of CatS and the pSS associated relevant antigen specific T cell responses.

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FRI0296

### KZR-616, A SELECTIVE INHIBITOR OF THE IMMUNOPROTEASOME, BLOCKS THE DISEASE PROGRESSION IN MULTIPLE MODELS OF SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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**Background:** The proteasome inhibitor bortezomib has been used successfully to treat patients with SLE. The immunoproteasome is a distinct class of proteasome found predominantly in immune effector cells. KZR-616 is an analogue of ONX 0914, Nature Medicine 2009) that selectively targets the LMP7 and LMP2 subunits of the immunoproteasome.

**Objectives:** To examine the therapeutic potential of KZR-616 in preclinical models of SLE and lupus nephritis (LN).

**Methods:** Cytokines were measured in human PBMCs stimulated with endotoxin and in CD4 + T cells stimulated with antibodies to CD3 and CD28. Human B-cells were stimulated with IL-21 and antibodies to CD40 and IgM to induce plasmablast differentiation. Immunoproteasome inhibition was measured in KZR-616 treated human PBMCs and in mice by measuring proteasome active site occupancy. The therapeutic effect of KZR-616 alone or in combination with mycophenylate mofetil (MMF) was evaluated in the NZB/W F1 model of SLE. T-dependent antibody responses (TDAR) were measured in mice and monkeys following 1, 4, or 13 weekly administrations.

**Results:** At a concentration resulting in inhibition of LMP7 and LMP2 by 89% and 59%, respectively, KZR-616 induced a decrease in pro-inflammatory cytokine production in human PBMCs, including TNF- $\alpha$ , GM-CSF, IL-6, and IL12/IL-23 p40. In lymphocytes, KZR-616 blocked T-cell production of IFN- $\gamma$ , TNF- $\alpha$  and GM-CSF, and the differentiation of B-cells to plasmablasts. KZR-616 administration to mice resulted in selective inhibition of LMP7 and LMP2 similar to levels *in vitro*. KZR-616 treatment in diseased mice resulted in a complete resolution of proteinuria and significant reductions in autoantibody production and renal IgG deposition. The halt in disease progression was durable as proteinuria levels did not significantly increase 8 weeks after treatment discontinuation. Histologic analysis following 12 weeks of treatment revealed a complete prevention in glomerular nephritis and sclerosis. Administration of KZR-616 in combination with MMF resulted in significantly greater disease inhibition and prolonged survival compared to either treatment alone. Levels of activated T- and B-cells and short- and long-lived plasma cells were effectively depleted in diseased animals following KZR-616 treatment. KZR-616 had no significant effect on TDAR in mice or monkeys and did not affect the number of circulating lymphocytes in monkeys.

**Conclusions:** KZR-616 is a novel and selective covalent inhibitor of the immunoproteasome that potentially blocks inflammatory cytokine production *in vitro* and disease progression in mouse models of SLE. Durable disease remission in animals was achieved at well tolerated doses without affecting normal T-cell dependent immune responses. KZR-616 is currently being developed for the treatment of LN and Phase 1 safety and pharmacokinetics results are presented elsewhere at this meeting.

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FRI0297

### MACROPHAGE-DERIVED LCN2 CONTRIBUTES TO DEVELOPMENT OF LUPUS NEPHRITIS

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**Background:** Renal involvement is a major concern in systemic lupus erythematosus (SLE). Many findings have indicated that plasma and urinary LCN2 is a potential marker of the presence and severity of renal involvement in SLE. However, whether LCN2 has a pathogenic or protective role in lupus nephritis (LN) is still unknown.

**Objectives:** In this study we analysed the expression of LCN2 in lupus patients and determined whether neutralisation of LCN2 with a monoclonal antibody or injection of recombinant LCN2 affects LN in mice.

**Methods:** Plasma and urine LCN2 was quantified by ELISA in SLE patients and healthy controls (HCs). The correlations between the levels of LCN2 and clinical features were analysed by Spearman's correlation test. CD14<sup>+</sup> monocytes were isolated from peripheral blood of HCs and SLE patients. We cultured human monocytes for 7 days with macrophage colony-stimulating factor (M-CSF) to generate macrophages. To investigate the production of LCN2 in lupus mice during progression of LN, plasma and urine LCN2 levels were measured by ELISA, mRNA and protein levels of LCN2 in different tissues were measured by qPCR and western blot respectively at different stages of disease. To investigate whether increased LCN2 levels contribute to the development of LN, the 16-week-old mice received weekly intraperitoneal of anti-LCN2 antibody or recombinant LCN2 for 4 weeks and analysed 1 week after the last injection. The renal pathology, proteinuria, spleen index were evaluated. The frequency of T lymphocyte subpopulation, B cells and plasma cells in spleen and lymph node was analysed by flow cytometry. Bone marrow derived macrophages (BMDMs) were isolated from tibia and femurs in mice. The expression of LCN2 in human macrophages and BMDMs were detected by qPCR.

**Results:** Plasma and urine LCN2 levels were markedly increased in SLE patients, and plasma LCN2 was positively correlated with urine LCN2. The levels of LCN2 in both plasma and urine were positively correlated with serum creatinine and 24 hour urine protein. The levels of LCN2 in the patients with LN were significantly higher than those without LN. At 10 weeks, when mice do not show any signs of systemic lupus, plasma LCN2 levels were low but increased significantly in 15- and 20-week-old mice. The increased plasma LCN2 was correlated with proteinuria and deposition of IgG in glomeruli. The mRNA level of LCN2 was increased in different tissues including liver, kidney and spleen. The same results were found in protein levels. Administration of LCN2 aggravated the disease with significantly higher renal activity scores and more IgG deposition. Neutralisation of LCN2 significantly improved renal pathology and reduced the glomerular deposition of IgG. Furthermore, anti-dsDNA antibody and proteinuria were significantly lower in the anti-LCN2 group. Flow cytometry revealed a significant decrease of T cells, B cells and Th1 cells in the anti-LCN2 group. While LCN2 significantly increased T cells, plasma cells and Th1 cells. LCN2 mRNA level in macrophages was significantly increased in SLE patients. And its expression was also increased in BMDMs with the progression of disease in lupus mice.

**Conclusions:** These findings suggested that LCN2 over-production by macrophages plays an important role in the pathogenesis of SLE and the progression of lupus nephritis. Thus, blockade of LCN2 may represent a new strategy for treatment of LN.

**Disclosure of Interest:** None declared

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FRI0298

### ALTERED FREQUENCIES OF CIRCULATING INNATE LYMPHOID CELLS AND ITS SUBSETS ARE CORRELATED WITH DISEASE ACTIVITY IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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**Background:** Systemic lupus erythematosus (SLE) is a chronic, multisystem autoimmune disorder with a heterogeneous clinical manifestations that results from abundant immunological abnormalities. Innate lymphoid cells (ILCs), one subset of the innate immune cells, are divided into cytotoxic ILCs (namely natural killer cells) and non-cytotoxic ILCs (namely helper-ILCs). Non-cytotoxic ILCs are composed of three groups, group 1 ILCs, group 2 ILCs and group 3 ILCs, based on depended transcription factors and producing cytokines. So far, alterations of ILCs and their subsets have been reported in some autoimmune diseases except SLE.

**Objectives:** To visualise differences in frequencies of ILCs and their subsets in the peripheral blood of patients with SLE and healthy controls in Chinese Han population.

**Methods:** Peripheral blood mononuclear cells (PBMCs) was obtained from twenty-five SLE patients and twelve healthy controls and were stained with antibodies to CD45, lineage (CD3, CD19, CD123, CD11c, CD14, CD16, CD34, CD94, and Fc $\epsilon$ R1 $\alpha$ ), CD4, CD8, CD127, CD117, CRTH2 and NKp44. Circulating total ILCs and its subsets were identified by flow cytometry. The associations between disease activity and all the detected cells were evaluated using the Pearson or Spearman correlation coefficient.

**Results:** Increased frequencies of ILC2 and ILC3 were observed in patients compared to controls, while decreased frequency of ILC1 was found in patients compared with controls ( $p=0.008$ ,  $p=0.004$ , and  $p=0.006$ , respectively). We also found the expression of T cell surface markers, CD4 or CD8, on ILCs and their subsets. The results showed that decreased frequencies of CD4<sup>+</sup>CD8<sup>+</sup> ILCs, CD4<sup>+</sup>CD8<sup>+</sup>ILC1, CD4<sup>+</sup>CD8<sup>+</sup> ILC2, CD4<sup>+</sup>CD8<sup>-</sup> ILC2, and CD4<sup>+</sup>CD8<sup>-</sup>CD336<sup>-</sup> ILC3 were found in patients compared with healthy controls ( $p=0.001$ ,  $p=0.017$ ,  $p=0.001$ ,  $p=0.004$ , and  $p=0.002$ , respectively). Furthermore, frequencies of CD4<sup>+</sup>CD8<sup>+</sup> ILCs and CD4<sup>+</sup>CD8<sup>+</sup> ILC2 were positively correlated with the SLEDAI-2000 score ( $r=-0.548$ ,  $p=0.005$  and  $r=-0.613$ ,  $p=0.001$ , respectively). Frequencies of CD4<sup>+</sup>CD8<sup>+</sup> ILCs and CD4<sup>+</sup>CD8<sup>+</sup> ILC1 were positively related with serum C3 level ( $r=0.519$ ,  $p=0.008$  and  $r=0.528$ ,  $p=0.007$ , respectively), and were positively related with serum C4 level ( $r=0.623$ ,  $p=0.001$  and  $r=0.643$ ,  $p=0.001$ , respectively).

**Conclusions:** In the present study, we demonstrated that frequencies of circulating ILCs and its subsets were altered in SLE patients and some subpopulations were negatively correlated with SLE disease activity.

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#### FRI0299 MUCOSAL-ASSOCIATED INVARIANT T CELL DEFICIENCY IN SYSTEMIC LUPUS ERYTHEMATOSUS IS RELATED TO AN INTRINSIC DEFECT IN THE CA2+/CALCINEURIN/NFAT1 SIGNALLINGPATHWAY

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**Background:** Mucosal-associated invariant T (MAIT) cells contribute to protection against certain microorganism infections and play an important role in mucosal immunity. However, the role of MAIT cells remains enigmatic in autoimmune diseases.

**Objectives:** Here, we examined the level and function of MAIT cells in patients with rheumatic diseases.

**Methods:** Patients with systemic lupus erythematosus (SLE;  $n=54$ ), rheumatoid arthritis (RA;  $n=66$ ), Behçet's disease ( $n=9$ ), ankylosing spondylitis ( $n=21$ ), and healthy controls ( $n=136$ ) were enrolled in the study. MAIT cell, cytokine and programmed death-1 (PD-1) levels were measured by flow cytometry.

**Results:** Circulating MAIT cell levels were significantly reduced in systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) patients. In particular, this MAIT cell deficiency was more prominent in CD8<sup>+</sup> and double-negative T cell subsets, and significantly correlated with disease activity, such as SLE disease activity index (SLEDAI) and 28-joint disease activity score (DAS28). Interestingly, MAIT cell frequency was significantly correlated with natural killer T (NKT) cell frequency in SLE patients. IFN- $\gamma$  in MAIT cells was impaired in SLE patients, which was due to an intrinsic defect in the Ca<sup>2+</sup>/calcineurin/NFAT1 signalling pathway. In SLE patients, MAIT cells were poorly activated by  $\alpha$ -galactosylceramide-stimulated NKT cells, thereby showing the dysfunction between MAIT cells and NKT cells. Notably, an elevated expression of PD-1 in MAIT cells and NKT cells was associated with SLE. In RA patients, MAIT cell levels were significantly higher in synovial fluid than in peripheral blood.

**Conclusions:** Our study primarily demonstrates that MAIT cells are numerically and functionally deficient in SLE. In addition, we report a novel finding that this MAIT cell deficiency is associated with NKT cell deficiency and elevated PD-1 expression. These abnormalities possibly contribute to dysregulated mucosal immunity in SLE.

**Disclosure of Interest:** None declared

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#### FRI0300 POLYMORPHISM OF 5,10-METHYLENETETRAHYDROFOLATE REDUCTASE (C677T) IN PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME, ITS ASSOCIATION WITH CARDIOVASCULAR LESIONS

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**Background:** Many studies have been conducted to determine the role of genetic polymorphism in the occurrence of cardiovascular diseases. The pathogenetic significance of MTHFR polymorphism is the subject of intensive research, especially its connexion with lesions of the cardiovascular system. The frequency of C677T polymorphism in the 5,10-MTHF gene is poorly known in patients with antiphospholipid syndrome (APS), and its relationship with vascular lesions has not been studied yet.

**Objectives:** The present study aimed to analyse the C677T mutation of the MTHFR gene and its association with endothelial dysfunction and clinical manifestations of cardiovascular lesions in APS.

**Methods:** We studied 82 patients with APS, including 34 (41.6%) with primary antiphospholipid syndrome (PAPS) and 48 (58.4%) with secondary antiphospholipid syndrome (SAPS). The analysis of the MTHFR C677T mutation was performed by PCR followed by digestion according to Frosst et al. All patients were assessed for the endothelium-dependent vasodilatation of brachial artery (EDVD), the thickness of the intima-media of the common carotid artery (IMT), the presence of atherosclerotic plaque (AP) and clinical manifestations of cardiovascular lesions

**Results:** There were 10.8% of homozygotes (677-TT), 37.8% of heterozygotes (677-CT) and 51.4% of homozygotes (677-CC) in the control group, and the frequency of T-alleles amounted to 29.7%. The incidence of T-alleles was higher among the patients with APS than in the control group and was 35.4%. The prevalence of homozygotes (677-TT), heterozygotes (677-CT) and homozygotes (677-CC) was not significantly different between the PAPS and SAPS groups (44.1%, 38.2%, 17.7% and 45.8%, 39.6%, 14.6% respectively  $p<0.05$ ). The frequency of T-alleles was higher in PAPS group than in SAPS group (36.8% against 34.4%, respectively  $p<0.05$ ). The analysis of structural and functional vascular lesions in homozygotes (677-CC), homozygotes (677-TT) and heterozygotes (677-CT) did not reveal significant differences in both mean values and the proportion of individuals with IMT thickness ( $0.86\pm 0.03$  mm,  $0.88\pm 0.05$  mm,  $0.90\pm 0.03$  and 35.3%, 38.5%, 51.7% respectively  $p<0.05$ ) with decrease of EDVD ( $7.09\pm 0.49$ ,  $6.32\pm 1.0$ ,  $6.92\pm 0.58$  and 47.0%, 53.8%, 48.3% respectively  $p<0.05$ ) and the presence of AP (26.5%, 23.1%, 48.3% respectively  $p<0.05$ ). Although there was a tendency of IMT thickness increase and EDVD decrease for T-carriers. The proportion of persons with IMT thickness ( $>0.90$  mm) and the decrease of EDVD BA ( $\leq 8.0\%$ ) among the homozygote 677-TT was 3%–6.5% higher than that of the 677-CC homozygote. The frequency of clinical manifestations of cardiovascular lesions (myocardial infarction, stroke, TIA) was in 1.2–1.8 times more often among the homozygotes 677-TT than 677-CC homozygote.

**Conclusions:** The mutation of the C677T of the MTHFR gene is not a risk factor for the development of atherosclerotic vascular damage in patients with APS, due to the lack of associative interrelationships between the decrease of EDVD, increase of IMT, clinical manifestations on the one hand, and the MTHFR polymorphism on the other

**Disclosure of Interest:** None declared

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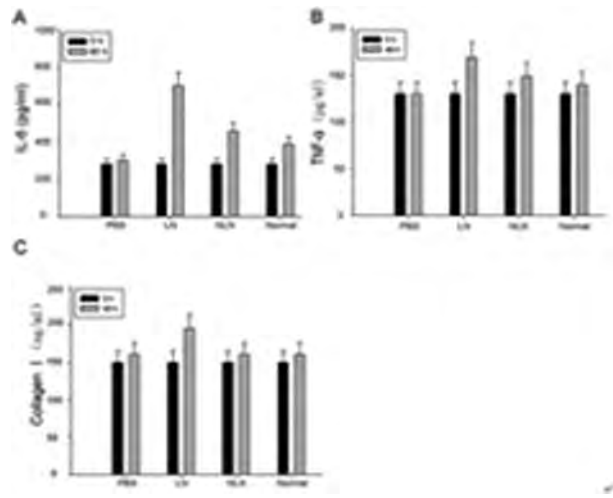
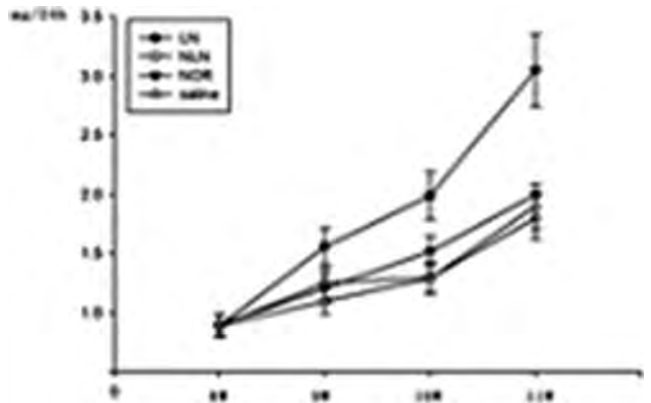
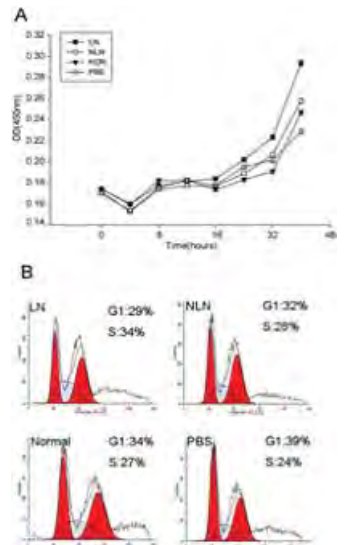
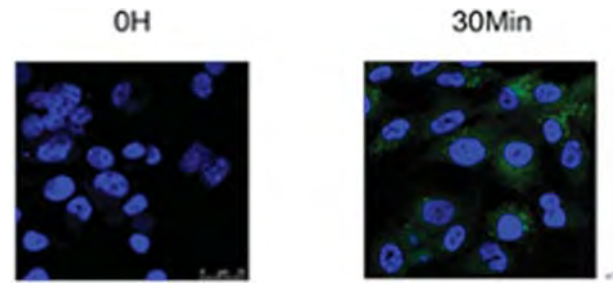
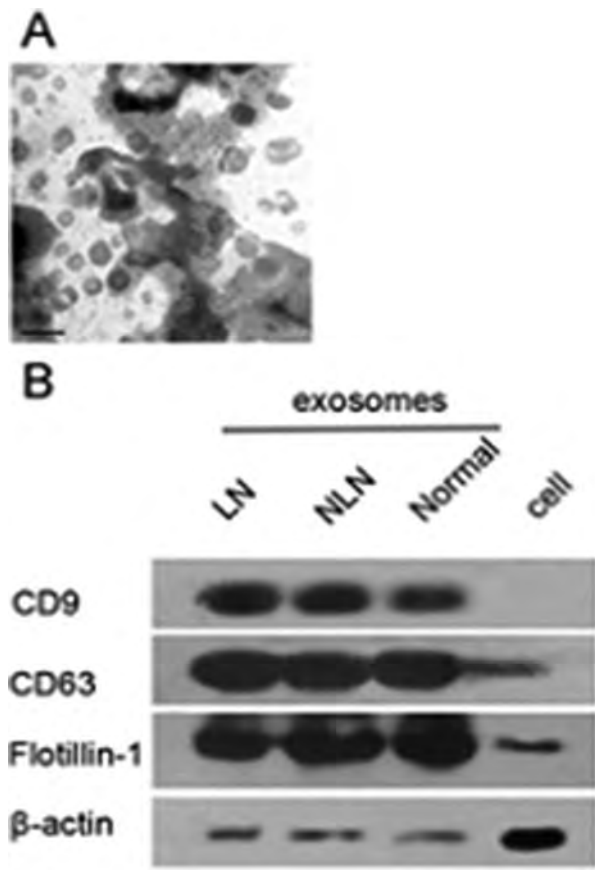
#### FRI0301 SERUM EXOSOMES INVOLVED IN THE PROGRESSION OF LUPUS NEPHRITIS

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**Background:** Systemic lupus erythematosus (SLE is a chronic autoimmune disease that systemically affects several important organs).<sup>1</sup> Lupus nephritis (LN is one of the most severe complications of SLE).<sup>2</sup> Exosomes are important mediators of biological information and play a part in the occurrence and development of various diseases including LN.<sup>3</sup>

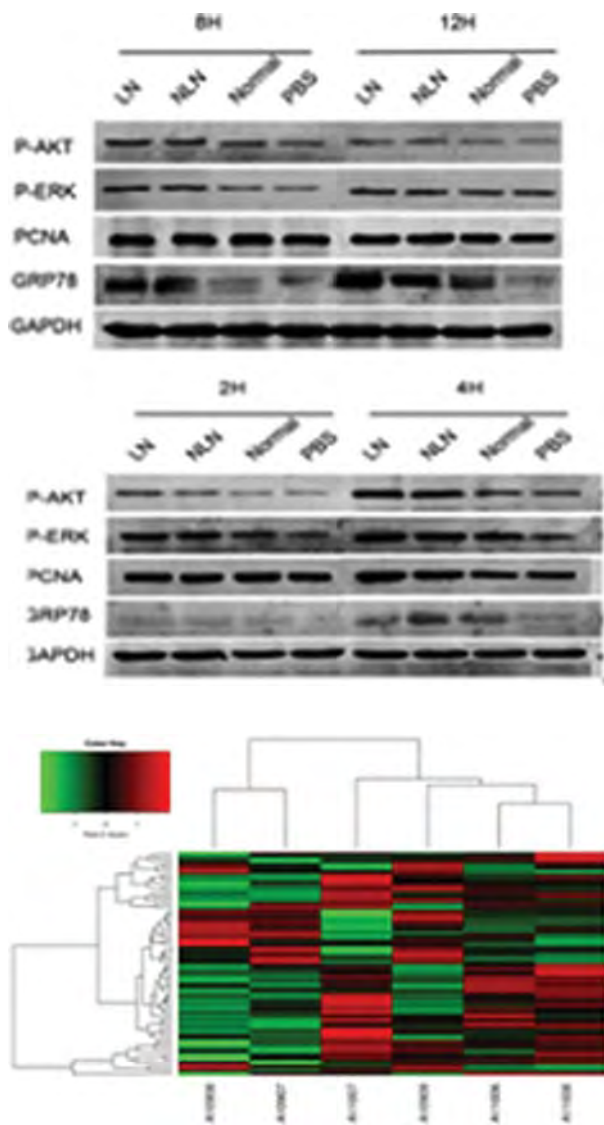
**Objectives:** The aim of study was to find whether exosomes participate in the pathogenesis of lupus nephritis.





**Methods:** We studied 10 patients with SLE but no LN, 10 patients with LN and 10 healthy people which are in line with the SLE classification criteria of American College of Rheumatology diagnostic (ACR) in 1997 and the LN pathological classification of ISN and RPS in 2003. Exosomes were isolated from the serum by ultracentrifugation and confirmed by transmission electron microscope and western blot. The internalisation of exosomes was detected by immunofluorescence. Then exosomes were injected into MRL/lpr mouse via the tail vein and co-cultured with mesangial cells. Flow cytometry was used to detect the alteration of cell cycle. The cell proliferation was determined by CCK-8 assay. The inflammatory cytokines (TNF- $\alpha$ , IL-6) and collagen I level in medium supernatant by ELISA, signal pathway by immunoblotting. Additionally, High-throughput sequencing was used to detect the expression of miRNAs in exosomes.

**Results:** The proteinuria and the percent of kidney crescent formation index of LN group was significantly high than other three groups. Exosomes can be absorbed by mesangial cells quickly. The secretion of inflammatory cytokines and collagen I of LN group were higher than NLN and control group ( $p < 0.05$ ). PI3K/AKT pathway are involved, but there was no significant difference between NLN group and control group. High-throughput sequencing revealed 11 up-regulated miRNA in SLE relative LN, 3 up-regulated miRNA in LN relative healthy people.



**Conclusions:** LN exosomes can enhance the proliferation and secretion of mesangial cells in which PI3K/AKT pathway is activated. This tip us exosomes may involve in the pathogenesis of LN.

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FRIDAY, 15 JUNE 2018

**SLE, Sjögren’s and APS – clinical aspects (other than treatment)**

**FR10302 SYSTEMIC LUPUS ERYTHEMATOSUS-ASSOCIATED THROMBOTIC MICROANGIOPATHIES IN 60 PATIENTS: CLINICAL FEATURES, PROGNOSIS AND TREATMENT IN A FRENCH MULTICENTRIC COHORT**

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**Background:** The occurrence of a TMA during SLE is a rare event that complicates 1% to 4% of lupus. The full spectrum of TMA can be encountered in the course of SLE: acquired thrombotic thrombocytopenic purpura (TTP), TMA associated with glomerulonephritis (TMA GN), atypical hemolytic uremic syndrome (aHUS), microangiopathic antiphospholipid syndrome (MAPS; defined or probable catastrophic antiphospholipid syndrome) or HELLP syndrome during pregnancy.

**Objectives:** To describe the clinical phenotype of TMA in lupus, to specify the prognosis and to identify factors allowing early classification and management of the different subtypes.

**Methods:** We performed a French multicentric retrospective study from January 1987 to December 2017 in units of internal medicine, nephrology and ICU. Inclusion criteria associated SLE defined by the ACR and/or SLICC criteria and a TMA defined either by the presence of microangiopathic anaemia and peripheral thrombocytopenia, either by histological signs of TMA.

**Results:** 68 events of TMA occurred in 60 SLE patients; median age was 24 years; 56 women (F/M ratio: 14). Diagnosis of SLE was assessed at a paediatric age in 24 (35.8%) patients. Clinical manifestations of SLE were: acute cutaneous lupus (n=48, 71%), arthritis (n=36, 53%), pleuritis (n=13, 19%), pericarditis (n=25, 37%), renal involvement (n=39, 57% including 20 class IV glomerulonephritis) and auto-immune cytopenia (n=22, 32%). Triggering factors of TMA were: lupus flare (n=38), infections (n=12), pregnancy and peripartum (n=3), or therapeutic rupture (n=4). Clinical and biological features at diagnosis of each subtypes of TMA are presented in table 1. A platelet count lower than 28 000/mm<sup>3</sup> was predictive of TTP diagnosis (Se=90,5%, Sp=88,5%), likewise a creatinine plasma level greater than 100 µmol/L was predictive of TMA GN (Se=88,5%, Sp=85%). The treatment of TMA included (alone or in combination): corticosteroids in all cases, plasma exchange (n=52), cyclophosphamide (n=28), Rituximab (n=15), Eculizumab (n=2), antiplatelet agent (n=36), and/or effective anticoagulation (n=26). The median duration of follow-up was 150 months. Among TMA GN patients, the final median GFR was 58 mL/min (range: 0–120) with 5 individuals on chronic dialysis and 1 kidney transplant. Among TTP patients, one died from TMA, whereas the final median GFR of survivors (n=59) was 97 mL/min (range: 64–150), without any patient requiring dialysis.

Table 1 Comparisons of clinical and laboratory data in different subtypes of TMA in SLE

	TTP	TMA GN	MAPS	HELLP syndrome	Anti-factor II antibodies
Number of events	20	24	12	4	8
Female (n/total)	18/20	23/24	10/12	3/4	6/8
Age at diagnosis of SLE (median [IQR], years)	24.3 [21-46]	25.5 [18-41]	27 [24-46]	24 [24-36]	30
Age at diagnosis of TMA (median [IQR], years)	29 [9-51]	25.3 [14-56]	41 [29-56]	29 [24-36]	35
Number with antiphospholipid disorder (%)	12 (60)	23 (96)	11 (92)	2 (50)	8 (100)
Number with acute renal failure (%)	12 (60)	24 (100)	12 (100)	2 (50)	8 (100)
APACHE II score (median [IQR], 0-40)	12 [7-17]	13 [7-18]	16 [9-23]	13 [7-23]	14
Platelets (median [IQR], 10 <sup>9</sup> /L)	62 [20-100]*	82 [20-400]*	142 [100-200]	107 [50-150]	65
Creatinine level (median [IQR], µmol/L)	101 [51-206]*	300 [11-206]*	128 [51-200]	147 [51-242]	90
LDH (median [IQR], U/L)	630 [40-810]*	624 [41-810]*	675 [41-810]	1,13 [41-810]	1,140
Anti-ADAMTS13 activity (median [IQR], %)	200 [1-283]	202 [1-228]	200 [1-280]	200 [1-140]	24
ADAMTS13 activity (median [IQR], %)	9 [1-24]	40 [1-24]	42 [1-30]	not available	60
Survival (median [IQR], 0-220)	63 [9-137]	4 [1-24]	4 [1-24]	4 [1-17]	63
Median survival of patients, %	9 (45)	0 (0)	0 (0)	0 (0)	0
ADAMTS13 activity (median [IQR], %)	17 [14-21]	12 [14-21]	12 [14-21]	12 [14-21]	12
ADAMTS13 activity (number of patients, %)	1 (5)	1 (4)	1 (8)	1 (25)	0

Abbreviations: SLE = systemic lupus erythematosus, TMA = thrombotic microangiopathy, IIR = renal/urinary, SLE = antiphospholipid, TMA GN = thrombotic microangiopathy associated with glomerulonephritis, MAPS = microangiopathic antiphospholipid syndrome, HELLP = hemolysis, elevated liver enzymes, low platelets.

\* p < 0.05 in comparison between patient suffering from TTP or TMA GN with the rest of the cohort.

**Conclusions:** SLE-associated TMA is a heterogeneous syndrome. TTP with a decreased ADAMTS13 activity and a low platelets level (<28000/mm<sup>3</sup>) have a good renal prognosis, whereas TMA GN with a high creatinine level (>100 µmol/L)

have a poor renal prognosis. Early subtypes classification is mandatory for the clinician to provide prompt and appropriate management of this life-threatening complication.

**Disclosure of Interest:** None declared

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FRIDAY, 15 JUNE 2018

## SLE, Sjögren's and APS – treatment

### FRI0303 EFFICACY AND SAFETY OF USTEKINUMAB IN PATIENTS WITH ACTIVE SYSTEMIC LUPUS ERYTHEMATOSUS: RESULTS OF A PHASE 2, RANDOMISED PLACEBO-CONTROLLED STUDY

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**Background:** IL12 and IL23 have been linked to SLE pathogenesis.

**Objectives:** The anti-IL12/23 monoclonal antibody ustekinumab (UST) was evaluated in pts with active SLE.

**Methods:** We conducted a Ph2, PBO-controlled study in 102 pts with active SLE. Pts were randomised(3:2) to UST IV~6 mg/kg or PBO at wk0, followed by UST SC 90 mg or PBO injections q8w, both added to standard care. Primary endpoint was proportion of pts achieving SLE responder index(SRI)-4 response at wk24. Secondary endpoints were change from baseline(BL) in SLEDAI-2K, PGA and BICLA response. Additional pre-specified endpoint analyses included no BILAG worsening(defined as no new BILAG A and  $\leq 1$  new BILAG B) and BILAG flare ( $\geq 1$  new BILAG A or  $\geq 2$  new BILAG B).

**Results:** SRI-4 response occurred in 60% UST vs 31% PBO pts( $p=0.005$ ) at wk24 (table 1). UST pts had greater median change from BL in SLEDAI-2K and PGA vs PBO. No difference was observed in BICLA response at wk24; however, in the UST group vs PBO, more pts had no BILAG worsening, and the risk of a new BILAG flare was significantly lower(HR 0.11 [95% CI 0.01–0.94]; $p=0.0078$ ). UST demonstrated improvement in musculoskeletal and mucocutaneous disease features vs PBO (table 1). Through wk24, 78% UST vs 67% PBO pts had  $\geq 1$  AE; 8.3%–9.5%, respectively, had  $\geq 1$  SAE; there were no deaths. The overall safety profile was comparable between UST and PBO.

**Abstract FRI0303 – Table 1.** Efficacy Results at Wk 24.

	PBO	UST
Pts randomised, n	42	60
SRI-4 response, n (%)	13 (31.0)	36 (60.0)
P value		0.005 <sup>a</sup>
Change from baseline SLEDAI-2K, median (range)	-2.0 (-20; 10)	-6.0 (-10; 3)
P value		0.026 <sup>a,b</sup>
Change from baseline PGA, median (range)	-1.6 (-5.6; 2.7)	-2.5 (-6.6; 2.8)
P value		0.211 <sup>a,b</sup>
BICLA response, n (%)	14 (33.3)	21 (35.0)
P value		0.994 <sup>a</sup>
Pts with no BILAG worsening, n/N (%)	11 (26.2)	29 (48.3)
P value		0.028
Pts with $\geq 50\%$ improvement from baseline in joint activity <sup>c</sup> , % (95% CI)	63.2 (61.7–64.6)	87.7 (86.8–88.6)
P value		0.021 <sup>d</sup>
Pts with $\geq 50\%$ improvement from baseline in CLASI activity score <sup>e</sup> , % (95% CI)	25.2 (23.1–27.4)	58.7 (57.4–60.1)
P value		0.043 <sup>e</sup>

<sup>a</sup>Prespecified analyses; all other analyses were post-hoc.

<sup>b</sup>One-sided test for no difference between treatment groups using a Wilcoxon non-parametric median test for difference of location

<sup>c</sup>Pt subpopulation (67% of total) with  $\geq 4$  active joints at baseline

<sup>d</sup>Pt subpopulation (58% of total) with baseline CLASI activity score  $\geq 4$

<sup>e</sup>Proportion of responders and p values based on mITT analysis using a multiple imputation model for missing data from wks 16 to 24

BICLA, BILAG-based Combined Lupus Assessment; BILAG, British Isles Lupus Assessment Group; CLASI, Cutaneous Lupus Erythematosus Disease Area and Severity Index; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000 PGA, physician's global assessment

**Conclusions:** UST treatment showed efficacy in pts with active SLE and was well-tolerated. UST may work via a novel mechanism of action in SLE.

**Disclosure of Interest:** R. van Vollenhoven Grant/research support from: Janssen Research and Development, LLC, B. Hahn Grant/research support from:

Janssen Research and Development, LLC, G. Tsokos Grant/research support from: Janssen Research and Development, LLC, C. Wagner Employee of: Janssen Research and Development, LLC, P. Lipsky Grant/research support from: Janssen Research and Development, LLC, B. Hsu Employee of: Janssen Research and Development, LLC, M. Chevrier Employee of: Janssen Research and Development, LLC, R. Gordon Employee of: Janssen Research and Development, LLC, M. Triebel Employee of: Janssen Biologics, S. Rose Employee of: Janssen Research and Development, LLC

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### FRI0304 LONG-TERM AND LOW-DOSE IL-2 THERAPY MAINTAINS THE TH17/TREG BALANCE IN PERIPHERAL BLOOD OF PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME

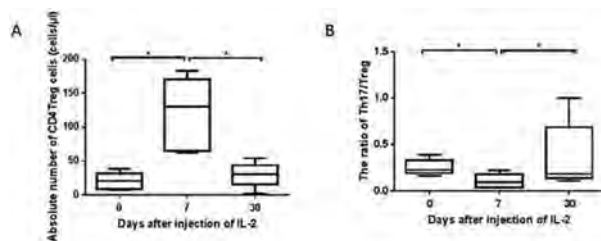
M. Miao<sup>1</sup>, Z. Hao<sup>1</sup>, Y. Guo<sup>1</sup>, X. Zhang<sup>1</sup>, S. Zhang<sup>1</sup>, J. Luo<sup>1</sup>, C. Zhang<sup>1</sup>, X. Zhao<sup>1</sup>, X. Liu<sup>1</sup>, X. Wu<sup>1</sup>, D. Xu<sup>1</sup>, J. Zhao<sup>2</sup>, C. Gao<sup>3</sup>, X. Li<sup>4</sup>. <sup>1</sup>The Second Hospital of Shanxi Medical University; <sup>2</sup>medical statistics department, Shanxi Medical University, Taiyuan, China; <sup>3</sup>Department of Pathology, Harvard Medical School, Boston, USA; <sup>4</sup>Department of Rheumatology, The Second Hospital of Shanxi Medical University, Taiyuan, China

**Background:** Primary Sjögren's syndrome (pSS) is a chronic autoimmune disease mainly affecting exocrine glands. To date, evidence-based guidelines for the management of pSS are lacking. Regulatory T cells (Tregs) are crucial in maintaining immune tolerance and immune homeostasis, but their role in pSS is unclear. Furthermore, low-dose Interleukin-2 (IL-2) has been shown considerable curative effect on expansion of (Tregs) in patients with GVHD. However, the effects of low-dose IL-2 on Tregs and Th17 cells in pSS are not fully elucidated.

**Objectives:** To explore the long-term effects of low dose IL-2 on Treg cells, Th17 cells and the ratio of them in peripheral blood of Chinese Han patients with primary Sjögren's syndrome.

**Methods:** A total of 190 pSS patients consented at enrollment to donate PB samples for comprehensive immune-phenotyping. In the study, BD Trucount tubes with the lyophilized pellet of a known number of internal counting beads were used for determining absolute counts of total CD4<sup>+</sup> T cells in PB and then calculating the absolute number of Th17 cells and CD4<sup>+</sup>Tregs. Eighty eight in 190 were given low-dose recombination human IL-2 (rhIL-2, 50 WIU/day for 5 days and then 50WIU/w for several months) by hypodermic injection combined with standard therapy, which includes glucocorticoid, immune-suppressants, biological agents or combination of them, while others (12 in 69) were given standard therapy only.

**Results:** (<sup>1</sup>The absolute number of Treg cells decreased significantly in peripheral blood of pSS patients compared with that of healthy control.<sup>2</sup>After short period therapy of low dose rhIL-2, Treg cells increased rapidly in one week but decreased to a lower level after one month[20.91 (9, 31.75) vs. 130.31 (65.18, 170.12) vs. 30.37(, <sup>16, 44</sup> $p<0.01$ ]. At the same time the ratio of Th17/Treg cells decreased rapidly in one week but increased to a higher level after one month[0.23 (0.19, 0.33) vs. 0.09 (0.04, 0.18) vs. 0.18 (0.14, 0.69),  $p<0.1$ ].<sup>3</sup>Long-term IL-2 could maintain the higher level of CD4<sup>+</sup>Treg cells and the balance of Th17/Treg.<sup>4</sup>Patients with balanced Th17/Treg have more obvious improvement of symptoms and more significantly decreased dose of glucocorticoid and HCQ compared with standard therapy group.



**Abstract FRI0304 – Figure 1.** The change of absolute numbers of Treg cells (A) and the ratio of Th17/Treg (B) after short-term and low-dose IL-2 therapy. (A) Absolute number (cells/ $\mu$ l) of Treg cells increased rapidly 7 days after IL-2 therapy but decreased to a lower level after 30 days. (B) Ratio of Treg cells decreased rapidly 7 days after IL-2 therapy but increased to a higher level after 30 days. Data are presented as median (Q1, Q3). Statistical analysis was performed using the Related Samples Friedman's Two-Way Analysis of Variance by Ranks. \*  $P<0.05$ , \*\*  $P<0.01$ , \*\*\*  $P<0.001$  vs. Healthy controls. Asymptotic significances (2-sided tests) are displayed. The significance level is  $p<0.05$ .

**Conclusions:** Therapy of low dose rhIL-2 could promote the proliferation of Treg cells and rebuild the balance of Th17/Treg for both short and long term. To rebuild



the balance of Th17/Treg for long-term, we should use IL-2 for a long time. Balance of Th17/Treg cells in pSS patients predicts a good prognosis.

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**Disclosure of Interest:** None declared

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#### FRI0305 PHASE 2 TRIAL OF INDUCTION THERAPY WITH ANTI-CD20 (RITUXIMAB) FOLLOWED BY MAINTENANCE THERAPY WITH ANTI-BAFF (BELIMUMAB) IN PATIENTS WITH ACTIVE LUPUS NEPHRITIS

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**Background:** Despite case series suggesting efficacy, controlled trials of anti-CD20 in lupus nephritis (LN) did not confirm benefit. *Arthritis Rheum* 2012;64:1215 and 2013;65:2368).

**Objectives:** One possible explanation for this failure stems from the fact that B cell depletion stimulates production of B cell activating factor (BAFF) which, in turn, facilitates maturation of autoreactive B cells in lymphoid organs or during B cell repopulation. The CALIBRATE study (NCT 02260934) was designed to test this hypothesis, to determine whether addition of anti-BAFF could enhance the clinical effects of anti-CD20, and to assess safety of the combination.

**Methods:** Forty-three patients with active LN despite conventional treatment enrolled in a prospective randomised open-label trial that compared two treatment strategies. All subjects received iv rituximab (1000 mg), CTX (750 mg), and methylprednisolone (100 mg) at wks 0 and 2, followed by 40 mg/d prednisone tapered to 10 mg/d by wk 12. At wk 4, subjects received either belimumab (10 mg/kg iv at wks 4, 6, 8 and then every 4 wks) plus prednisone (n=21) or prednisone alone (n=22). Complete response (CR) was defined as: (i) urine protein:creatinine ratio (UPCR) <0.5; (ii) eGFR ≥120 or, if <120, eGFR >80% of screening; and (iii) prednisone tapered to 10 mg/d. The definition of partial response (PR) differed only in the UPCR criterion (>50% reduction).

**Results:** The clinical outcome at wk 24 was similar in both groups (table 1). The CR rate was 24% in the belimumab group (RCB) and 23% in the control group (RC). Three subjects in each group withdrew (WD) prior to wk 24 (two withdrawals in each group due either to progressive nephritis or an infusion reaction, and one in each group for reasons unrelated to SLE or its treatment). B cell depletion from blood was virtually absolute in both groups at wk 12, but the pace of recovery differed. Six subjects experienced serious adverse events between wks 0 and 24; three subjects in the RC group (pneumonia followed by LN flare; deep vein thrombosis; SLE flare); and three subjects in the RCB group (anti-CD20 infusion reaction; soft-tissue abscesses prior to anti-BAFF treatment; quadriceps tendon rupture).

Median B Cell Count Median IgG Level

CR PR NR WD Wk 0 Wk 12 Wk 24 Wk 0 Wk 24

RC Group 23%–23% 41%–14% 105 1 31 1050 1100

**RCB Group 24% 24% 38% 14% 143 1 3 984 837:**

**Conclusions:** An interim analysis of data from CALIBRATE shows: (i) anti-BAFF following anti-CD20 for LN did not improve clinical outcome at week 24; (ii) anti-BAFF delayed blood B cell reconstitution following B cell depletion; and (iii) anti-BAFF following anti-CD20 was not associated with hypogammaglobulinemia or an increase in serious infections. Further analyses at 48 weeks and beyond will address how anti-BAFF therapy affects quantitative and qualitative recovery of B cells as well as long-term clinical outcome.

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#### FRI0306 DEVELOPMENT OF BAFF AND ICOSL BISPECIFIC INHIBITOR AMG 570 FOR SLE TREATMENT

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**Background:** Systemic lupus erythematosus (SLE) is a heterogeneous disease lacking highly effective treatment options. Among many cell types and pathways involved in SLE pathogenesis, aberrant B cells and T cells are critical drivers in autoantibody production and tissue damage. Autoreactive T cells drive autoreactive B cell expansion and autoantibody production. Amongst key pathways that modulate the function of these cells, inducible costimulator ligand (ICOSL) is critical for T follicular helper cell (T<sub>FH</sub>) development and T memory cell homeostasis, while B cell activating factor (BAFF) is a critical B cell survival factor. We hypothesised that targeting both BAFF and ICOSL would be more efficacious than single BAFF or ICOSL inhibition in SLE and other autoimmune diseases.

**Objectives:** We tested if targeting both BAFF and ICOSL has superior efficacy than single target inhibition in the mouse arthritis and lupus models. We aimed at generating BAFF and ICOSL bispecific molecule for potential treatment of autoimmune diseases such as SLE.

**Methods:** Murine BAFF/ICOSL bispecific, combination of BAFF and ICOSL inhibitors or single inhibitor was evaluated in the sheep red blood cell (SRBC) challenge model, mouse collagen induced arthritis (CIA) model, or NZB/NZW lupus models. AMG 570 was tested for human and cyno BAFF and ICOSL binding affinities by Kinexa A. AMG 570 dual target blocking activities was evaluated in human and cyno BAFF and ICOSL mediated B cell and T cell assay, respectively. Pharmacodynamics effect of AMG 570 was evaluated in cynomolgus monkey

**Results:** Compared to treatment with single inhibitor, combination of BAFF and ICOSL inhibitors was more effective in ameliorating arthritis incidence and severity in the mouse CIA model and NZB/NZW lupus model. The murine BAFF/ICOSL bispecific molecule inhibited murine BAFF and ICOSL mediated B and T cell bioassays, and dual target inhibition in mice. In addition, treatment with murine BAFF/ICOSL bispecific was more efficacious than single BAFF and ICOSL inhibitor in reducing anti-dsDNA IgG, delaying the onset of proteinuria and improving survival in the NZB/NZW lupus model. AMG 570 was selected as the clinical candidate with high binding affinity for human BAFF and ICOSL and strong potency in the human B cell and T cell bioassays. B cell reduction was observed after AMG 570 treatment in cynomolgus monkey, consistent with the pharmacological effect of BAFF inhibition.

**Conclusions:** Inhibition of both BAFF and ICOSL is more efficacious than single target inhibition in the mouse lupus and arthritis models. By targeting both BAFF and ICOSL, AMG 570 has the potential to achieve a large treatment effect size in autoimmune diseases such as SLE and rheumatoid arthritis.

**Disclosure of Interest:** H. Hsu Shareholder of: Amgen, M. Zhang Shareholder of: Amgen, K. Miner Shareholder of: Amgen, G. Kevin Shareholder of: Amgen, J. Whoriskey Shareholder of: Amgen, R. Jacobsen Shareholder of: Amgen, C. Chen Shareholder of: Amgen, K. Ishida Shareholder of: Amgen

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#### FRI0307 TBK1 INHIBITION DOWNREGULATES EXPRESSION OF INTERFERON TYPE I AND THE UPREGULATED EXPRESSION OF RIG-LIKE RECEPTORS AND DNA-SENSING RECEPTORS IN INTERFERON POSITIVE PRIMARY SJÖGREN'S SYNDROME PATIENTS

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**Background:** Type I interferon (IFN-I) upregulation is a hallmark of systemic autoimmune diseases like primary Sjögren's syndrome (pSS). Expression of IFN-I is induced by three different receptor families: Toll-like receptors (TLRs), RIG-like receptors (RLRs) and DNA-sensing receptors (DSRs). Previously we have shown increased mRNA levels of TLRs and RLRs in plasmacytoid dendritic cells (pDC) and CD14 +monocytes of IFN-I positive (IFNpos) pSS patients.<sup>1</sup> TANK-binding kinase (TBK1), is an important signalling hub downstream of RLRs and DSRs and leads to production of IFN-I and subsequent induction of interferon-stimulated genes (ISGs).

**Objectives:** Study RLRs and DSRs in pSS and explore the potential of a TBK1 inhibitor to downregulate IFN-I activation.

**Methods:** Expression of RLRs and DSRs was assessed by RQ-PCR and flowcytometry in CD14 +monocytes, BDCA4 +CD123+pDC and CD19 +B cells from IFNpos pSS patients. pDCs from IFNpos pSS patients were analysed by flowcytometry for phosphorylated-TBK1 (pTBK1). PBMCs of pSS patients were cultured with a TBK1 inhibitor, BX795, followed by analysis of IFN-I production and expression of ISGs.

**Results:** In addition to upregulated mRNA levels of RLRs IFIH1 (encoding for MDA5) and DDX58 (encoding for RIG-I), which we previously observed in pDC and monocytes of IFNpos pSS patients, gene expression of IFIH1 and DDX58 was also upregulated in B cells. Upregulation of mRNA levels of the DSRs IFI16 and ZBP1 was observed in monocytes and B cells from IFNpos patients. In pDC protein expression of MDA5, ZBP-1, IFI16 was increased in IFNpos pSS, while there were no differences in RIG-I. In monocytes protein expression of MDA5 was increased and a trend was visible for RIG-I and IFI16. B cells showed increased protein expression of MDA5 and a trend was observed for RIG-I, ZBP-1 and IFI16. These data indicate upregulation of RLRs and DSRs particularly in pDC of IFNpos pSS patients. To further look into the signalling of RLRs and DSRs, phosphorylation of TBK was studied in pDC, the main IFN-I producers, of pSS patients. Increased expression of pTBK1 was observed in pDCs from IFNpos pSS. Upon treatment with BX795, PBMCs from IFNpos pSS downregulated the production of IFN-I and mRNA expression of the ISGs MxA, IFI44, IFI44L, IFIT1 and IFIT3.

**Conclusions:** RLRs and DSRs are upregulated in IFNpos pSS. Signalling of these receptors could be blocked using a TBK1 inhibitor, which reduced IFN-I protein production and expression of ISGs in PBMCs of IFNpos pSS patients. As patented pharmacological inhibitors, amongst others a small molecule inhibitor, are available TBK1 inhibition is indicated as a potential future treatment target for IFNpos pSS.

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FRI0308

#### CORTICOSTEROIDS COMBINED WITH DOUBLET OR SINGLE-AGENT IMMUNOSUPPRESSIVE THERAPY FOR ACTIVE PROLIFERATIVE LUPUS NEPHRITIS

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**Background:** Current evidence exploring whether corticosteroids (C) plus doublet immunosuppressive therapy (IT) is superior to the classical combination of C with single-agent IT for active proliferative lupus nephritis (LN) is controversial.

**Objectives:** We aimed to clarify the efficacy and safety of C+doublet versus single-agent IT for active proliferative LN by a meta-analysis.

**Methods:** We searched for randomised clinical trials that evaluated the benefits and risks of C+doublet versus single-agent IT for active proliferative LN. The primary outcome was overall response rate (ORR). The second outcomes were the change from baseline in Systemic Lupus Erythematosus Disease Activity Index (SLE-DAI) score, negative conversion ratio of anti-double-stranded DNA (anti-dsDNA), and adverse events. The quality of the evidence was evaluated with the GRADE framework. The PROSPERO registry number is CRD42017068491.

**Results:** The analysis included 10 trials with 1587 unique patients. Compared with C+single agent IT, C+doublet IT was statistically significant with higher ORR (relative risk [RR], 1.22; 95% confidence interval [CI], 1.09 to 1.35;  $p < 0.0001$ ; moderate certainty). In subgroup analysis, C+doublet IT without biologics resulted into significant higher ORR than C+single agent IT (RR, 1.30; 95% CI, 1.13 to 1.50;  $p < 0.0001$ ; moderate certainty), while C+doublet IT including biologics improved ORR only for refractory severe LN (RR, 1.46; 95% CI, 1.09 to 1.96;  $p = 0.012$ ; very-low certainty). A larger change from baseline in SLE-DAI score (standardised mean difference,  $-0.49$ ; 95% CI,  $-0.68$  to  $-0.30$ ;  $p < 0.0001$ ; moderate certainty) and a higher negative conversion ratio of anti-dsDNA (RR, 1.34; 95% CI, 1.06 to 1.69;  $p = 0.014$ ; high certainty) were observed with C+doublet IT than with C+single agent IT. The rates of adverse events were similar between the two regimens (high to moderate certainty).

**Conclusions:** Compared with single-agent IT, the combination of corticosteroids with doublet IT improved clinical outcomes for active proliferative LN. C+doublet

IT including biologics may be a better regimen for refractory severe LN. There is imperative that prospective biomarker-driven trials to identify patients for whom C+doublet IT is most efficacious.

**Disclosure of Interest:** None declared

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FRI0309

#### THE IMPACT OF BELIMUMAB AND RITUXIMAB ON HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

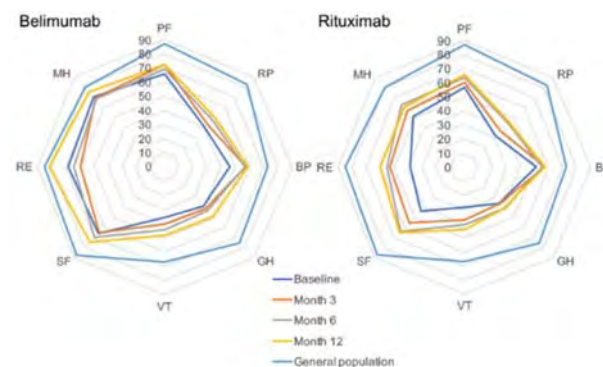
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**Background:** Accumulating evidence supports an impaired health-related quality of life (HRQoL) in patients with systemic lupus erythematosus (SLE). The impact of modern therapeutic interventions on patients' perception of HRQoL has not been explored in depth.

**Objectives:** The aim of this study was to investigate the effects of two biologic treatments – belimumab and rituximab – on SLE patients' HRQoL, fatigue and functional ability.

**Methods:** Patients with SLE from the Karolinska University Hospital treated with either belimumab (n=34) or rituximab (n=35) were included. Data were collected prospectively at treatment initiation and at months 3, 6, 12 and 24; these included the Medical Outcome Study short form-36 (SF-36) version 2, functional assessment of chronic illness therapy (FACIT)-Fatigue scale version 4, EuroQol research foundation 5-dimension (EQ-5D) health questionnaire, and Stanford health assessment questionnaire disability index (HAQ-DI).

**Results:** Substantial reductions compared to Swedish norms were observed across all SF-36 subscales at baseline (figure 1). SF-36 mental component summary scores were higher in patients who were on antimalarial agents (mean: 42.7; SD  $\pm 11.8$ ; n=29) compared to patients who were not (mean: 34.0; SD  $\pm 14.7$ ; n=32;  $p = 0.019$ ). Accordingly, patients who were on antimalarial agents performed better in SF-36 social functioning (mean: 63.7 versus 46.5;  $p = 0.022$ ) and mental health (mean: 68.7 versus 53.4;  $p = 0.023$ ) compared to patients who were not. Belimumab-treated patients reported gradual improvements in the SF-36 physical summary component (significant from month 12;  $p = 0.023$ ) and FACIT-Fatigue (significant by month 24;  $p = 0.001$ ), no changes in EQ-5D scores, and improvements in HAQ-DI by month 6 ( $p = 0.014$ ). Rituximab-treated patients reported rapid improvements in the SF-36 mental summary component and FACIT-Fatigue by month 3 ( $p = 0.031$  and  $p = 0.007$ , respectively), which declined at month 12, as well as improvements in EQ-5D at month 6 ( $p = 0.016$ ) and HAQ-DI at month 3 ( $p = 0.033$ ), which were not maintained at later time points.



**Conclusions:** HRQoL was considerably impaired in SLE patients compared to population-based norms at baseline, and was not fully compensated during follow-up. Patients' perceptions of HRQoL showed treatment-specific patterns over time, and could prove useful when evaluating the effects of biologics in SLE. Early evaluation of belimumab might underestimate improvements in HRQoL and fatigue. In severe SLE, antimalarial agents may have favourable effects on mental HRQoL aspects.

**Disclosure of Interest:** None declared

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FRI0310

### ACHIEVEMENT OF LOW DISEASE ACTIVITY IN LUPUS PATIENTS TREATED WITH BELIMUMAB IS INDEPENDENT OF SEROLOGIC STATUS AT BASELINE: A REAL-LIFE OBSERVATIONAL STUDY

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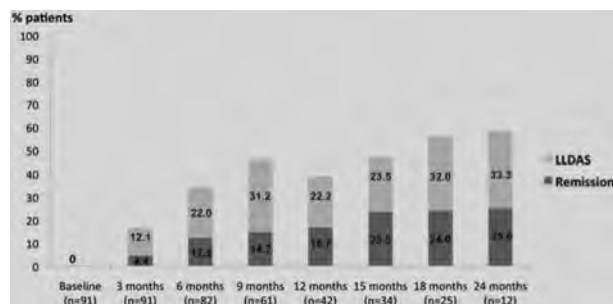
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**Background:** Low disease activity is a validated target of systemic lupus erythematosus (SLE) therapy.

**Objectives:** to assess the ability of belimumab to induce low disease activity states in real-life setting.

**Methods:** Multicentre prospective observational study of SLE patients receiving belimumab due to active disease, refractory to at least one conventional immunosuppressant. Disease activity, including attainment of lupus low disease activity state (LLDAS) and remission-on-glucocorticoids (GC) (clinical SLEDAI-2K=0 with prednisone ≤5 mg/day), accrual of organ damage, flares and side effects were documented.

**Results:** Ninety-one patients were included [94.5% women, mean (SD) age 45.9 (12.5) years]. Most frequent manifestations were arthritis (76.7%), rash (72.5%), serologic activity (low C3/C4 and/or high anti-dsDNA; 54.9%), hair loss (47.2%) and mucosal ulcers (27.5%). Median (range) duration of treatment was 10.5 (3.0–42.1) months. Belimumab decreased average SLEDAI-2K, physician global assessment and daily prednisone dose over time, as early as 3 months after initiation. Complete withdrawal of GC was achieved in 17.8%, 22.5%, 31.7% and 23.3% at 3, 6, 9 and 12 months, respectively. The number of flares and severe flares was reduced by 62% and 50%, respectively, during the first year of treatment. Although reduction in clinical SLEDAI-2K was more pronounced in patients who were serologically active (from 8 to 1.5 at 12 months) compared to serologically inactive (from 6 to 4) at baseline, attainment of low disease activity states (LLDAS or remission) did not differ between groups and was reached by more than 40% of completers after 9–12 months (figure 1). Twenty patients (22.0%) discontinued treatment due to inadequate response and two due to side effects potentially related to the drug.



**Conclusions:** Belimumab is efficacious in achieving low disease activity in over 40% of active SLE patients, accompanied by complete GC discontinuation in more than 20%. Serologically active and inactive patients respond equally to the drug.

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FRI0311

### THE EFFECT OF B CELL TARGETED THERAPIES ON AUTOANTIBODIES AND EXCESSIVE NEUTROPHIL EXTRACELLULAR TRAP FORMATION IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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**Background:** Systemic lupus erythematosus (SLE) is a severe systemic autoimmune disease characterised by immune-complexes which cause systemic inflammation and damage. Neutrophil extracellular traps (NETs) are an important source of autoantigens in SLE patients leading to the production of autoantibodies. Functionally, SLE-specific autoantibodies as immune-complexes are important triggers of excessive NET formation. As such, effective targeting of pathogenic autoantibodies in SLE is subject to several promising experimental treatment strategies. Recently, the combination of Rituximab (RTX) and Belimumab (BLM) in patients with severe SLE led to a strong decrease of autoantibodies and diminished excessive NET formation as well as improvement of clinical disease. A consortium was formed to study different experimental treatment strategies that target the humoral autoimmune system, including RTX, Bortezomib (BTZ) or combination treatment with RTX and BLM.

**Objectives:** The present study aimed to investigate the effects of B cell targeted therapies on relevant autoantibody levels and excessive NET formation in severe SLE.

**Methods:** This study involved three cohorts of anti-dsDNA positive, severe SLE patients that were eligible to experimental treatment with RTX (n=16), BTZ (n=6) or RTX +BLM (n=16). A cross-sectional cohort of 35 anti-dsDNA positive SLE patients served as a control cohort. A panel of SLE relevant autoantibodies against dsDNA, histones, nucleosomes and C1q were measured by ELISA. As a functional result of autoantibody levels, NET formation was quantified by our novel highly-sensitive NET quantification assay using 3D confocal microscopy<sup>1</sup>.

**Results:** Comparing three regimens, RTX +BLM resulted in the strongest reduction of anti-dsDNA (median ratio of baseline; 0.32 vs 0.78 vs 0.65; p=0.08), anti-histone (0.36 vs 0.51 vs 0.53; p=0.45), anti-nucleosome (0.38 vs 0.61 vs 0.58; p=0.15), and significantly the strongest reduction of anti-C1q antibodies (0.55 vs 0.91 vs 1.00; p=0.016) compared to RTX and BTZ. Excessive NET formation diminished significantly with a ratio of 0.66 [0.49–0.93] after RTX (p=0.005) and 0.25 [0.15–0.47] after RTX +BLM (p=0.0002), however it was not reduced after BTZ with 1.37 [0.90–1.61]. As such, excessive NET formation correlated with disease activity (p=0.004), except for the BTZ cohort. Importantly, regression of excessive NET formation was associated with reduction of anti-C1q antibodies. In an independent cohort of SLE patients, we confirmed that the presence of anti-C1q antibodies correlated with excessive NET formation (p=0.03). We further observed that the presence of three or more autoantibody specificities associated with excessive NET formation (p=0.02).

**Conclusions:** This study demonstrates a synergetic effect of RTX +BLM compared to RTX or BTZ on the reduction of relevant autoantibodies in SLE patients which associated with significant regression of NET formation. The reducing effects of RTX +BLM, RTX and BTZ on anti-C1q antibodies underpinned the observed, immunological effects on humoral autoimmunity.

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### FRI0312 ARTHRITIS IN PRIMARY SJÖGREN'S SYNDROME: CHARACTERISTICS, OUTCOME AND TREATMENT FROM FRENCH MULTICENTER RETROSPECTIVE STUDY

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**Background:** Primary Sjogren's syndrome (pSS) is a chronic inflammatory disorder characterised by diminished lacrimal and salivary gland functions. Joint involvement is reported in 20% to 60% of pSS patients, and among them one third of patients present synovitis. There is a lack of data concerning therapeutic management during pSS-associated synovitis.

**Objectives:** To describe the characteristics and the outcome of pSS associated arthritis and to compare the efficacy of different therapeutic regimen.

**Methods:** We conducted a retrospective study using Club Rhumatisme and Inflammation (CRI) and French Internal Medicine Society (SNFMI) networks. All patients with a diagnosis of primary Sjogren's Syndrome (pSS) and at least one clinical and/or echographic synovitis were included. Patients with synovitis (cases) were compared to pSS patients without synovitis (controls).

**Results:** 57 patients (93% women) were included with a median age of 54 years.<sup>45-63</sup> Patients with synovitis had more frequently lymph node enlargement (12.3% vs. 1.8%, p=0.007) and a higher ESSDAI score (8<sup>6-12</sup> vs. 2,<sup>1-4</sup> p<0.0001). There was no difference concerning CRP levels, rheumatoid factor and CCP-antibodies positivity. Among 57 patients with synovitis, 101 lines of various treatments have been used during the follow-up of 40 [22.5-77] months. First line treatment consisted in steroids alone (3.5%), steroids in association (79%) with hydroxychloroquine (HCQ) (49%), methotrexate (MTX) (35%), rituximab (RTX) (5.3%) or other immunosuppressive drugs (7%). The number of complete/partial joint responses significantly increased considering the number of overall lines of treatment for MTX, HCQ and RTX: 52% for the first line, 76% for the second line and 83% for the third line (p<0.05), and data were similar considering each drug separately. There was no difference of efficacy between HCQ, MTX, and RTX concerning tender and swollen joint count, CRP level, ESSDAI score and steroids sparing effect at the end of each drug regimen. We performed a propensity score based analysis to determine whether HCQ, MTX, or RTX treatment was associated with better joint outcome. No difference could be shown for the joint response between three treatment regimen (MTX vs. HCQ, OR 1.55 [0.18-13.55], p=0.69; MTX vs. RTX, OR 5.08 [0.49-52.17], p=0.17; HCQ vs. RTX OR 3.28 [0.28-38.02], p=0.34). All 3 treatments (HCQ, MTX, and RTX) were associated with a significant reduction of ESSDAI score and a significant steroids-sparing effect.

**Conclusions:** pSS articular manifestations may include synovitis which could mimic rheumatoid arthritis but differ by the absence of structural damage. Even if the use of HCQ, MTX, and RTX seem to be effective for joint involvement, the best regimen remains to be determined.

**Disclosure of Interest:** None declared

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### FRI0313 A RITUXIMAB AND BELIMUMAB COMBINATION THERAPY IN SLE PATIENTS

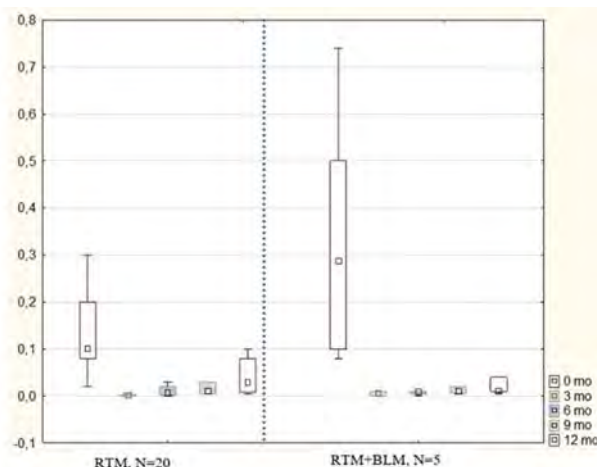
A.A. Mesnyankina, S.K. Soloviev, E.N. Aleksandrova, A.P. Aleksankin, A. Novikov, E.A. Aseeva, E.L. Nasonov. V.A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation

**Objectives:** To assess the efficacy of a rituximab and belimumab combination therapy in pts with active SLE and dynamics of CD19+ B-lymphocytes count in treated pts.

**Methods:** The study included 7 SLE pts (1M/6F) with high (SLEDAI2K<sub>≥</sub>10 - 4pts.) and moderate (SLEDAI2K<10- 2pts.) disease activity; out of them 1 patient had lupus nephritis, 1- vasculitis, and remaining 5 had predominantly mucocutaneous and articular manifestations of SLE. The dose of oral GCs at baseline did not exceed 20 mg/day, two pts were treated with prednisone 5 mg/day. The damage index at baseline was 0 in 3 pts, ≤1 in 3pts, and ≥1 - in 1 patient. Rituximab (RTM) was administered at 500-1000 mg, with subsequent adding of Belimumab (BLM) 3 months later at a standard dosing regimen 10 mg/kg once a month during 9mo. CD19+ B- lymphocytes counts were obtained before initiation RTM (0), and subsequently after 3, 6, 9, and 12mo. Depletion of CD19+ B- lymphocytes after RTM was assessed as the decrease of B-cell counts after 3mo<0,01 10<sup>9</sup>/l, where 0 10<sup>9</sup>/l was categorised as complete depletion, from 0001 to 0,01 10<sup>9</sup>/l - partial

depletion, and >0,011 10<sup>9</sup>/l - absence of depletion. The comparison group included 20 pts receiving a single 500-2000 mg dose of RTM.

**Results:** 6 pts demonstrated the decrease in clinical and laboratory SLE activity, starting from 3mo of follow-up (SLEDAI-2K 0 mo-Me 10, 9;16 3mo-Me 8, 4;86mo-Me 4, 2;6 9mo-Me 5,4;10 12mo-Me 2 2;6) with RTM+BLM combination therapy. The oral GCs dose was reduced to 7,5 5;10mg/day by 12mo, none of the patient required prednisone dose escalation during follow-up. There were no cases of severe infection. The damage index did not increase by 12mo. The combination therapy reduced the absolute counts of CD19+ B-cells. RTM therapy resulted in complete depletion in 2 pts, in partial depletion - in 3; in 1 patient the depletion was not documented. Addition of BLM resulted in slowing down of CD19 + B-cell repopulation (figure 1) among pts with complete and partial depletion (0mo-Me 0,11 × 10<sup>9</sup>/l[0,1;0,28], 12mo -Me 0,01 × 10<sup>9</sup>/l[0,0085; 0025]) vs pts receiving RTM monotherapy (0mo-Me 0,1 × 10<sup>9</sup>/l[0,06;0,2], 12mo -Me 0,03 × 10<sup>9</sup>/l[0,008; 0,08]). The decrease in CD19+ B-cell counts after RTM was also documented in the patient who didn't develop depletion initially (0mo-0,5 10<sup>9</sup>/l, 12mo-0,04 10<sup>9</sup>/l). RTM and BLM combination failure, as well as failure of standard GCs and cytostatic based therapy, was documented in one patient with cutaneous, articular and haematological SLE.



**Abstract FRI0313 - Figure 1.** Dynamics in CD19+ B-lymphocytes in pts treated RTM and RTM+BLM combination therapy

**Conclusions:** Combination therapy allows to gain control over disease activity in short time, due to the effect of RTM, while added BLM provides further prolongation of the effect achieved, minimising the risk of exacerbation. This combination may be used as a method of choice in pts with severe SLE involving vital organs, and in persistent cutaneous-articular disease and high immunological activity. Of notice is the fact, that use of RTM and BLM combination allowed to manage all pts on low and medium doses of GCs starting from RTM and BLM initiation and during the entire follow-up, thereby reducing the risk of irreversible organ damage. In these patients there were no signs of infection.

**Disclosure of Interest:** None declared

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### FRI0314 RISK OF OPHTHALMOLOGIC COMPLICATIONS AS A RESULT OF HYDROXYCHLOROQUINE THERAPY

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**Background:** Hydroxychloroquine is a drug therapy licensed for patients with cutaneous and systemic lupus. A major side effect is maculopathy that can result in permanent visual loss. Often, symptoms are preceded by signs, and screening for preclinical retinopathy can decrease incidence and development of 'bullseye retinopathy'<sup>1,2</sup>. More recent high quality studies suggest cases of confirmed toxicity in 1% of patients at 5-7 years and therefore documentation of monitoring is imperative<sup>3,4</sup>.

**Objectives:** In accordance with the British Rheumatology Society guidelines 2008 an audit was carried out in March 2017 to assess whether patients on hydroxychloroquine were being monitored for maculopathy while on therapy.

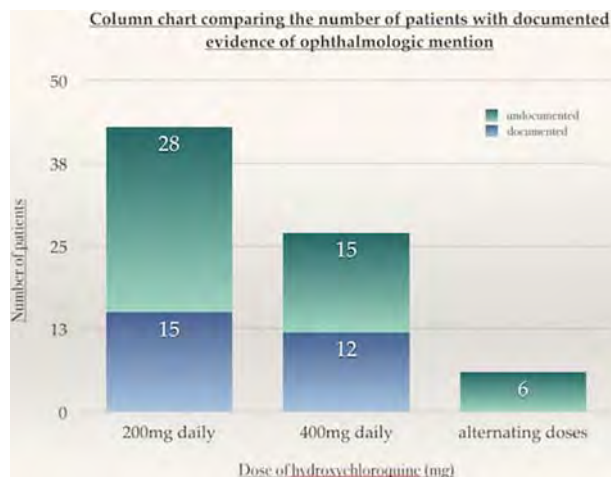
**Methods:** The sample group comprised of 76 patients who were on active hydroxychloroquine treatment for SLE, chosen through randomised computer generated numbers. Electronic notes for individual patients over the last 12 months was reviewed for mention of ophthalmologic monitoring, indicating the clinician is aware and surveilling possible signs of toxicity.

**Results:** Of all patients on hydroxychloroquine (regardless of dose), 64% of patients had no mention of ophthalmologic monitoring on their documented clinic letter. Documentation of monitoring did not vary by dose, despite the increased risk of toxicity for those on 400 mg daily.

**Table to show percentage of electronic documentation of patients screened on hydroxychloroquine**

Hydroxychloroquine	documented(%)	undocumented(%)
200 mg daily	35	65
400 mg daily	44	54
200 mg/400 mg alternate days	0	100

This audit suggests that Queens Medical Centre patients are not meeting the set standard of ophthalmological review.



**Conclusions:** The BSR guidelines have highlighted that there are organisational barriers to monitoring, but acknowledges that ophthalmological risks are present with the use of continued hydroxychloroquine therapy. High risk patients with existing or early signs of visual involvement, should be selected for early assessment and more vigilant follow up. SD-OCT was found to be significantly more cost effective than standard ophthalmological examination<sup>5</sup>. It should be acknowledged that the results of the audit reflect documentation as opposed to practice. Mention of ophthalmological monitoring does not ensure that doctors are actually asking about visual problems. Guidelines have since been updated in April 2017 that recommend annual screening only after 5 years of therapy is sufficient but with a full ophthalmological screening by an ophthalmologist.

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FRI0315

#### SAFETY, TOLERABILITY, PHARMACOKINETIC AND PHARMACODYNAMIC EFFECTS OF BIIB059, A MONOCLONAL ANTIBODY TARGETING BDCA2 FOLLOWING INTRAVENOUS (IV) AND SUBCUTANEOUS (SC) SINGLE OR MULTIPLE DOSES ADMINISTRATION IN HEALTHY VOLUNTEERS (HV) AND SUBJECTS WITH ACTIVE SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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**Background:** BDCA2 is a plasmacytoid dendritic cell (pDC)-specific receptor that, upon activation, inhibits the inflammatory factors production by human pDCs, including IFN- $\alpha$  a major player in the pathogenesis of SLE. This 3-Part Phase 1 study evaluated the safety, tolerability, pharmacokinetics (PK), pharmacodynamics (PD) and clinical efficacy of single and multiple ascending doses (SAD-MAD) of BIIB059 in HV and SLE subjects (NCT02106897).

**Objectives:** To compare PK and PD parameters between HV and SLE following single and multiple dose administration of BIIB059

**Methods:** In the SAD Part 2, 12 subjects with active SLE were randomised 2:1 to receive a single 20 mg/kg IV dose of BIIB059 or placebo. In the MAD Part 3, HV received either 2 or 3 SC administrations of Placebo or BIIB059 20, 50 or 150 mg) Q4W or 3 SC 300 mg Q2W. Subjects with active SLE, received either 2 or 3 SC placebo or BIIB059 50 mg or 300 mg. The dose levels were selected based on emerging data from the Part 1 in HV and was not to exceed the maximum tolerated dose. Blood samples were obtained before and after each dose administration to characterise PK and PD (BDCA2 on pDC) relationship for BIIB059.

**Results:** Part 1 PK and PD results (SAD) in HV and Part 2 PD results have been previously presented<sup>1-2</sup>. In Part 2 of the study, following IV administration, mean  $t_{1/2}$  in SLE subjects was 18.1 days, with a mean CL of 0.251 L/day and a mean volume of distribution  $V_{ss}$  of 5.41 L. Following SC administration, in Part 3a, mean  $t_{1/2}$  in HV subjects ranged from 13.3 to 19.5 days, mean  $CL_{ss}/F$  ranged from 0.267 to 0.367 L/day and  $V_z/F$  ranged from 7.23 to 9.36 L. In Part 3b, mean  $t_{1/2}$  in SLE subjects ranged from 12.6 to 20.5 days with a mean  $CL_{ss}/F$  of 0.455 to 0.485 L/day and a mean  $V_z/F$  of 5.93 and 12.8 L. Exposure (AUC and  $C_{max}$ ) for BIIB059 increased with dose in both HV and SLE subjects. However exposure in SLE subjects was approximately 40% lower compared to HV which could not be attributed to body weight differences. The observed mean accumulation ratio for AUC was slightly lower in SLE subjects (2.58) compared to HV (2.66) after BIIB059 SC administration. Complete BDCA2 internalisation was achieved at all dose levels, the duration of which was dose dependent, and similar for HV and SLE subjects. Reappearance of BDCA2 on circulating pDCs occurred when serum concentrations of BIIB059 dropped to  $\sim 1$   $\mu$ g/mL. Single and multiple IV and SC doses of BIIB059 appeared to be well-tolerated in HV and SLE subjects.

**Conclusions:** BIIB059 was generally well tolerated. Exposure in SLE subjects was lower compared to HV while BDCA2 internalisation was similar. Based on the Phase 1 data, BIIB059 is currently evaluated in a Phase 2 trial (NCT02847598).

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**Disclosure of Interest:** C. Barbey Shareholder of: Biogen, Employee of: Biogen, H. Naik Shareholder of: Biogen, Employee of: Biogen, C. Musselli Shareholder of: Biogen, Employee of: Biogen, R. Christmann Shareholder of: Biogen, Employee of: Biogen, L. Stevenson Shareholder of: Biogen, Employee of: Biogen, D. Rabah Shareholder of: Biogen, Employee of: Biogen, P. Gulati Shareholder of: Biogen, Employee of: Biogen, N. Franchimont Shareholder of: Biogen, Employee of: Biogen

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FRI0316

### THE PRESENCE OF ANTI-RITUXIMAB ANTIBODIES PREDICTS INFUSION-RELATED REACTIONS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Rituximab is a genetically engineered chimeric anti-CD20 monoclonal antibody commonly used in the treatment of a variety of autoimmune rheumatic conditions. Although generally well tolerated, serious infusion related reactions can occur and are difficult to predict. It has previously been suggested that patients with systemic lupus erythematosus (SLE) who are treated with Rituximab demonstrate a higher incidence of infusion reactions and a less predictable response to the therapy when compared with other diseases.

A major limitation of biologic therapies is the development of anti-drug antibodies (ADA). To date the presence of ADAs to Rituximab have not previously been explored in detail.

**Objectives:** To assess the prevalence of ADAs to Rituximab in patients receiving treatment for SLE and how the presence of these antibodies relates to:

1. the incidence of infusion-related reactions
2. the therapeutic efficacy of the drug

**Methods:** We assessed the presence of Rituximab ADAs using a Meso Scale Discovery platform in 58 SLE patients treated with Rituximab at University College London Hospital, UK. A subgroup of 42 patients were followed up longitudinally for up to 8 years after their first dose of Rituximab. Clinical parameters including BILAG, complement C3 levels, anti-double-stranded DNA (dsDNA) antibody titres, lymphocyte count and frequency of CD19<sup>+</sup> B cells were recorded. A retrospective review of patient notes was undertaken to assess for a history of infusion related reactions. Mann-Whitney U test was used to compare variables between the ADA positive group and ADA negative group.

**Results:** A total of 58 patients were recruited of which 88% were female (51/58). Median age was 38.9 years old with a median disease duration of 84 months. ADAs to Rituximab were detected in 60% (35/58) of patients. In those with a positive ADA (n=35), 22 were later retreated with Rituximab. Infusion reactions were noted in 68% (15/22) of those undergoing retreatment in the context of a previously positive ADA. In the remaining patients who were retreated but in which no infusion reaction was seen (7/22), the average level of ADA was significantly lower than in those who did have a reaction (median in those who suffered a reaction=200 unit; median in those who were ADA positive but did not develop a reaction on retreatment=10 units; p=0.008). There were no reactions observed in patients that did not display ADAs who were subsequently retreated.

In the first six months post-Rituximab there was no statistically significant difference in BILAG, C3 levels, dsDNA titres, lymphocyte count or CD19 between the groups in which ADAs were present when compared with those in which ADAs were absent.

**Conclusions:** For the first time, ADAs to Rituximab have been described in a cohort of SLE patients who have undergone B-cell depletion therapy. High levels of circulating ADAs to Rituximab were found in patients who later developed infusion reactions on retreatment. However, there was no obvious difference in clinical outcomes between those who were ADA positive compared with those in which it was negative. Together, this suggests the presence of ADAs can predict future infusion reactions but do not adversely impact upon the efficacy of treatment.

In future, the routine screening of ADAs to Rituximab will help to reduce the risk of serious infusion reactions in patients being treated.

**Disclosure of Interest:** None declared

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FRI0317

### REASONS FOR HOSPITALISATION AND IMMUNOSUPPRESSANT USE IN ADULT PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS ADMITTED TO A TERTIARY ACADEMIC MEDICAL CENTRE

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**Background:** An estimated 22% to 28% of US SLE patients are hospitalised each year.<sup>1</sup> SLE and other connective tissue diseases have been ranked the sixth most likely conditions to result in 30 day readmission to the hospital.<sup>2</sup>

**Objectives:** To determine if the number of SLE patient hospital admissions, primary reasons for hospitalisation, and mortality have changed over time. We also sought to evaluate changes in immunosuppressant use in these patients.

**Methods:** A retrospective chart review was conducted on all adult patients with SLE admitted to the University of California San Diego Medical Centre in 2005 and 2013. Patients were identified by SLE billing code 710.0 of the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM).

**Results:** The number of yearly SLE patient hospitalizations decreased from 178 to 86 between the two times of observation. Infection was the most common reason for

hospitalisation accounting for 39.9% of hospitalizations in 2005 versus 31.4% of hospitalizations in 2013 (p=0.29). Lupus flare accounted for 9.6% of admissions in 2005 versus 8.1% of admissions in 2013 (p=0.722). SLE patient mean length of hospital stay decreased from 7.6 days to 6.4 days compared to all patient length of stay which decreased from 6 days to 5.75 days. Seven patients (3.9%) died during their hospitalisation in 2005 as opposed no inpatient deaths in 2013. Of the 261 admissions between 2010 and 2013, six admissions resulted in death (2.3%). Corticosteroid use decreased (79.8% to 61.6%, p=0.109), while hydroxychloroquine (27.0% to 59.3%, p<0.001), mycophenolate mofetil (5.6% to 13%, p=0.060), and leflunomide (0.6% to 9.3%, p=0.008) use increased over time.

**Conclusions:** Hydroxychloroquine and leflunomide use in hospitalised patients more than doubled from 2005 to 2013 with statistical significance. Rise in mycophenolate mofetil use and drop in corticosteroid use trended toward statistical significance. Number of hospitalizations, length of stay, and mortality decreased. Infection was the primary reason for inpatient hospitalisation and there was a decrease in admission for both infections and SLE flares between the time points although this did not reach statistical significance. We hypothesise that changing medication prescribing patterns may have altered the rate of damage accrual and mortality in SLE patients, and plan to perform a national study to further evaluate SLE hospitalisation data on a larger scale.

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FRI0318

### HEALTH CARE RESOURCE UTILISATION (HCRU) AND COST ANALYSES OF SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) AS A FUNCTION OF DISEASE SEVERITY: ANALYSIS OF REAL-WORLD CLAIMS DATA FROM A GERMAN SICKNESS FUND

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**Background:** SLE is a severe, chronic autoimmune disease of the connective tissue involving multiple organ systems. Understanding the economic burden of SLE in the context of disease severity is important when considering new therapeutic options.

**Objectives:** HCRU and costs associated with SLE were examined retrospectively using anonymized data from a German Sickness Fund database.

**Methods:** Real-world claims for adult (≥18 years old) patients (pts) with SLE from a German Sickness Fund database of company health insurance schemes were analysed. HCRU and costs were assessed annually for 2009–2014 for pts diagnosed with SLE in 2009 and validated using repeated SLE-related claims, co-diagnosis codes, laboratory tests, prescription treatment, and the diagnosing physician's specialty. Pts had to have data available for 2009 and ≥3 years before the index quarter in 2009. HCRU and costs for SLE cases were compared with those of controls matched (4:1) by age, sex, and baseline Charlson Comorbidity Index (CCI). Continuous outcomes were compared with a nonparametric test (e.g., Wilcoxon–Mann-Whitney) because most outcome distributions were positively skewed.

**Results:** Of the 3,290,701 persons with data available for 2009 and ≥3 years prior, 1228 had an SLE diagnosis in 2009. SLE prevalence steadily increased from 37.32/100,000 (incidence: 5.96/100,000 per year) in 2009 to 47.36/100,000 in 2014. The final sample comprised 1,160 SLE-confirmed pts (mean age: 52 years; females: 84%; baseline CCI range: 1–13). Most (85%) pts were diagnosed with SLE before 2009 SLE disease severity at baseline was classified as mild for 148, moderate for 484, and severe for 528 pts using a combination of International Classification of Diseases-10 GM and medication/procedures codes. Compared with matched controls, SLE pts, overall and those with moderate and severe disease, had significantly greater mean annual medical costs in 2009 (all SLE: € 6895 vs. € 3,692; moderate SLE: € 4867 vs. € 3,380; severe SLE: € 10,001 vs. € 4,239; p<0.0001 for each comparison) and each year thereafter. Mean costs, total number of hospital days, numbers of outpatient visits, hospital stays, and outpatient prescriptions, and other benefits were significantly greater for all



pts with SLE and for those with moderate and severe disease vs. matched controls. For example, for pts with severe SLE vs. controls, mean costs for hospital stays, outpatient prescriptions, and other benefits were € 4335 vs. € 1,414, € 2582 vs. € 1,087, and € 1068 vs. € 691, respectively, in 2009.

**Conclusions:** In Germany, the economic burden of moderate and severe SLE was greater than that of sociodemographic- and morbidity-adjusted controls between 2009 and 2014. Pts with SLE incurred greater HCRU and total annual medical costs vs. matched controls. HCRU increased with increasing SLE disease severity, with the greatest burden among pts with severe disease. New treatments could reduce HCRU and future costs.

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### FRI0319 A PRACTICAL SIMPLE DOSE ESCALATION REGIMEN FOR MILD HYDROXYCHLOROQUINE-INDUCED HYPERSENSITIVITY REACTION

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**Background:** In a recent Japanese clinical trial of hydroxychloroquine (HCQ), HCQ-induced hypersensitivity reaction occurred in 4.9% (5/103) including a case of Stevens-Johnson syndrome.<sup>1</sup> Several desensitisation methods were proposed, however the protocols were very complicated for routine practice.<sup>2</sup> Recently, a simple dose-escalation regimen of sulfamethoxazole-trimethoprim (SMX-TMP) showed better tolerability than standard dosing.<sup>3</sup>

**Objectives:** To investigate the incidence and risk factors of HCQ-induced hypersensitivity and propose a simple dose-escalation regimen for HCQ-induced hypersensitivity.

**Methods:** This is a single-centre, retrospective study. The subjects were Japanese SLE patients who started HCQ between Apr 1, 2009 and June 30, 2017 at Tokyo Metropolitan Tama Medical Centre. HCQ was prescribed with a dosage of 6.5 mg/ideal body weight (IBW) kg or less. We identified the cases of HCQ-induced hypersensitivity by reviewing electronic medical charts and pictures taken by patients or physicians. We diagnosed with HCQ-induced hypersensitivity if generalised eruption occurred within a month of starting HCQ and resolved completely after withdrawal of HCQ. We used the simple dose escalation regimen, starting from 40 mg/day with weekly increments by 40 mg, for patients with HCQ-induced hypersensitivity who did not require hospitalisation or systemic administration of glucocorticoids. We compared the clinical parameters (age, sex, dosage/actual or ideal body weight, starting dose, use of immunosuppressives, use of SMX-TMP, profile of autoantibodies) between patients with HCQ-induced hypersensitivity and those without HCQ-induced hypersensitivity. We also evaluated the success rate of our dose escalation regimen.

**Results:** Total 234 SLE patients were analysed. HCQ-induced hypersensitivity reaction were identified in 20 cases (8.5%). All cases developed mild generalised maculopapular rashes 17 (IQR 7.8–28.8) days after initiation of HCQ. No patient required hospitalisation or systemic glucocorticoid therapy. Among the clinical parameters compared, only anti-Sm antibody was associated with HCQ-induced hypersensitivity (table 1). HCQ was restarted in 10 patients using the simple dose escalation regimen. Among them 9 patients successfully continued HCQ and only one discontinued due to reappearance of mild hypersensitivity reaction.

	Patients with HCQ-induced hypersensitivity (n=20)	Patients without HCQ-induced hypersensitivity (n=214)	P value
Age, years (SD)	39 (28-46)	40 (30-52)	0.460
Female, %	85.0	93.5	0.344
Body weight (kg) (SD)	59 (45-55)	52 (47-60)	0.178
Starting dose /IBW, mg/kg (SD)	9.1 (4.0-9.6)	3.2 (4.5-5.9)	0.039
IBW (kg)	26.3 (19.2-21.8)	29.9 (18.9-23.5)	0.091
HCQ starting dose			
- 100mg, %	5.0	0.0	
- 150mg, %	0	0.0	
- 200mg, %	45.0	43.0	
- 300mg, %	65.0	31.8	
- 400mg, %	5.0	4.7	
Usage of steroids, %	95.0	89.3	0.563
Dose of steroids, mg (SD)	6.8 (5.0-12.3)	6.8 (4.0-9.0)	0.984
Usage of immunosuppressants, %	50.0	50.0	0.994
Usage of SMX-TMP, %	25.0	21.5	0.325
Lower glabellum, %	0 (0/20)	0.5 (1/21)	0.759
Kidney glabellum, %	50.0 (5/20)	5.6 (12/21)	0.432
Positive anti-dsDNA antibody, %	45.0 (9/20)	59.8 (128/214)	0.465
Positive anti-Sm antibody, %	60.0 (12/20)	34.2 (73/214)	0.022
Positive anti-RNP antibody, %	50.0 (10/20)	49.9 (107/214)	0.588
Positive anti-SSA antibody, %	40.0 (8/20)	33.5 (71/214)	0.385

**Conclusions:** HCQ-induced hypersensitivity reaction typically presents with mild generalised eruption 1–4 weeks after starting HCQ. Restarting HCQ with the simple dose escalation regimen may be a practical option for patients with mild HCQ-induced hypersensitivity reaction.

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**Disclosure of Interest:** None declared  
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### FRI0320 ANTIMALARIALS PROTECTIVE EFFECTS IN SYSTEMIC LUPUS ERYTHEMATOSUS IN CHINA

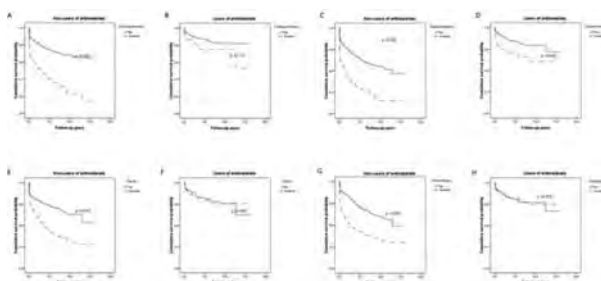
F. Wang, W. Zhang, X. Feng, L. Sun. *Department of Rheumatology and Immunology, the Affiliated Drum Tower Hospital of Nanjing University Medical School, Nanjing, China*

**Background:** Hydroxychloroquine (HCQ) and chloroquine (CQ), both known as antimalarial drugs, have become fundamental therapeutic elements in systemic lupus erythematosus (SLE) in these decades. However, their specific benefits on organs or in a large cohort of Chinese SLE patients haven't been elucidated.

**Objectives:** This retrospective multicenter study sought to examine the potential protective roles of antimalarials in a large retrospect multicenter study of SLE patients in China.

**Methods:** Data were collected from 1372 patients' first and following hospitalizations during 1999 to 2009. Laboratory variables, medications, disease activity, organ involvements, and survival statuses were analysed according to antimalarial usage.

**Results:** Antimalarials improved the survival of SLE patients as an independent predictor (HR 0.503, p=0.000). Using antimalarials protected patients with longer disease duration (>2 years), SLEDAI (>15) on admission, high SLEDAI (>10) on discharge, organ involvements (cardiopulmonary, gastrointestinal, renal, hematologic), anti-dsDNA positive, and no application of cyclophosphamide. In second hospitalisation, compared to non-users, SLE patients who had been treating with antimalarial drugs had lower levels of total cholesterol (TC) (4.47 (0.13) mmol/L vs 5.03 (0.21) mmol/L, p=0.027) and less chance of anaemia (46.5% vs 58.2%, p=0.033).



**Conclusions:** Using antimalarials benefits outcomes of SLE patients through multiple facets in Chinese patients.

**Disclosure of Interest:** None declared  
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### FRI0321 SURVIVAL RATE AND CAUSES OF WITHDRAWAL OF BELIMUMAB TREATMENT IN SLE IN A REAL LIFE SETTING

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**Background:** Systemic Lupus Erythematosus (SLE) is a chronic disease requiring long-term treatment. Even though immunosuppressive therapies improved the survival rate, a great percentage of SLE patients exhibit a persistently active disease, or disease flares. Belimumab (BLM), is currently the only biological drug

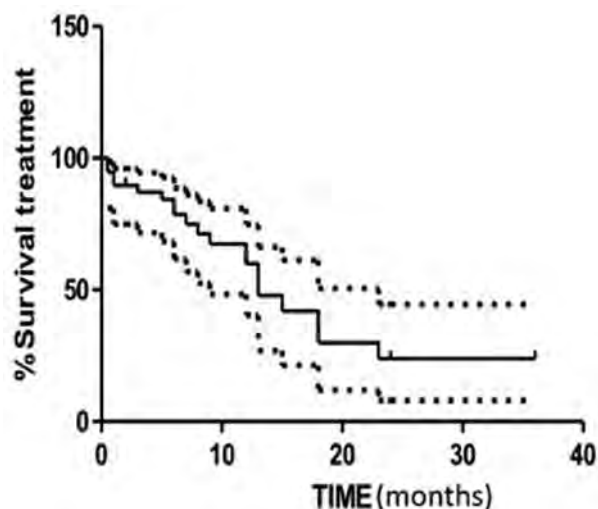
approved for the treatment of active SLE patients not responding to standard of care, without active kidney or neuropsychiatric (NP) involvement.

**Objectives:** Aim of the study was to analyse 36 months survival of BLM treatment, causes of withdrawal in a monocentric cohort of SLE patients followed-up in a daily practice setting.

**Methods:** The study was proposed to all the patients starting BLM. After the informed consent was obtained, demographic, clinical and serological data, indication to BLM and concomitant therapies were registered. At baseline and at 6,12,24,36 months of follow-up, disease activity (SLEDAI 2K), DAS28, C3 and C4 levels, anti-dsDNA status and weekly dose of glucocorticoids were recorded. Data were expressed as median-interquartile range; after 6,12,24,36 months, differences in all parameters compared to baseline were evaluated (Student t test) The treatment survival was evaluated by Kaplan-Meier analysis. P value<0.05 were considered significant.

**Results:** We enrolled 39 Caucasian individual, 38 females, 1 male, with median age of 43 (IQR 7.5) years and median disease duration 14.5 (5.5) years. Indications for starting BLM were: mucocutaneous involvement (n=11,28%), arthritis (n=25,64%), systemic symptoms (n=3,7%) and lung involvement (1 pt,2%). At baseline, all the patients were taking PDN;97% hydroxychloroquine,23% mycophenolate mofetil,23% azathioprine, 5% cyclosporine, 7% methotrexate and 2% thalidomide. Table 1 summarises trend of SLEDAI 2K, C3 and C4, DAS28 (for articular involvement), prednisone dose and percentage of patients positive for anti-dsDNA during the follow-up. Fourteen out of the 39 patients (35.8%) reached 12 months of observation and only 4 the 24 months, 3 the 36 months. Figure 1 shows the survival curve of Belimumab. In 8 patients (20%) adverse events were the cause of BLM withdrawal (severe infection in one patient, severe bradycardia in one and acute infusion reaction in another one). In 4 patients (10%) BLM was discontinued for lack of efficacy(articular and skin manifestations)after 4, 8, 12 and 23 months respectively; in 6 patients (15%) for loss of efficacy; one patient developed a severe NP flare after 2nd BLM infusion and was admitted in our hospital for depression. One patient was lost during the follow-up. Two patients withdrew BLM therapy to plan a pregnancy. We found significant reduction of PDN week levels, and improvement of C4 and aDNA levels at T6; as for disease activity, we found significant reduction of DAS28 at T6, and of SLEDAI-2k at T6 and T12.

	T0	T6	T12
N° of patients	39	25	14
PDN mg/sett	52.5 (39.5)	35 (17.5)	35 (0)
SLEDAI 2K	6 (3.5)	2 (2)	2 (0.75)
C3	79 (19.75)	84.5 (17.5)	73.5 (9.75)
C4	13.5 (12.75)	7 (10) <sup>s</sup>	10 (10.25)
aDNA(%)	100	20	5
DAS28	4.32 (0.7)	3.3 (1.33)	3 (0.65)



**Abstract FRI0321 – Figure 1.** the figure shows patients mantaining treatment with Belimumab

**Conclusions:** In our monocentric cohort of SLE patients, BLM demonstrated to be effective on disease activity and serology and led to a significant decrease of glucocorticoids dose; the main causes of BLM withdrawal were adverse events or disease flares.

**Disclosure of Interest:** None declared

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### FRI0322 RATIONALE FOR THE ATACEPT DOSE FOR A PHASE III STUDY IN PATIENTS WITH HIGHLY ACTIVE AND AUTO-ANTIBODY POSITIVE SLE

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**Background:** Atacept targets the B-cell stimulating factors BlyS and APRIL, and is currently in clinical development for the treatment of patients (pts) with active, auto-antibody positive SLE.

**Objectives:** Here, we evaluated integrated nonclinical, clinical and exposure-response (E-R) data from atacept studies to determine an appropriate atacept dose for a Phase (P) III study in SLE pts with high disease activity (HDA).

**Methods:** Nonclinical efficacy and pharmacokinetic (PK)/pharmacodynamic data for atacept were obtained from two murine models: An F1 hybrid NZBWF1/J spontaneous SLE model (given mouse Fc-protein control or mouse TACI-Fc 5 mg/kg intraperitoneal [IP] three times per week) and a 4-Hydroxy-3-nitrophenyl-acetyl-Keyhole Limpet Haemocyanin (NP-KLH) vaccinated C57BL/6 model to assess immunomodulation (given control protein 10 mg/kg or atacept 1, 3 or 10 mg/kg IP every third day). Clinical PK, efficacy, safety and E-R data were obtained from a PI PK study in healthy participants (Study 022; single dose atacept: 25, 75 or 150 mg) and two PII studies in pts with autoantibody-positive SLE (APRIL-SLE [EudraCT 2007-003698-13] and ADDRESS II [EudraCT 2013-002773-21]; randomization [1:1:1] to once weekly [QW] subcutaneous [SC] injections of atacept [75 or 150 mg] or placebo [PBO]). In APRIL-SLE, the primary endpoint was the proportion of pts with BILAG A/B flare over 52 weeks. In ADDRESS II, the primary endpoint was SRI-4 response at Week 24. SRI-6 response was analysed post-hoc in pts with HDA (SLEDAI-2K $\geq$ 10) at Screening. A population PK model was established using data from the PI and PII studies. Population PK model-derived exposure vs probability of clinical response (BILAG A/B flare, SRI-4, SRI-6) was assessed, and an exploratory analysis of exposure vs safety performed.

**Results:** TACI-Fc 5 mg/kg prevented proteinuria development and glomerular damage in the F1 hybrid NZBWF1/J spontaneous SLE model. Anti-KLH IgG decreased markedly in atacept-treated NP-KLH vaccinated mice (>50% reduction vs control protein at all doses), with mean atacept serum trough concentrations ( $C_{min}$ ) of ~2.3  $\mu$ g/mL (1 mg/kg), ~5  $\mu$ g/mL (3 mg/kg) and ~8.5  $\mu$ g/mL (10 mg/kg). In post-hoc analyses of the proportion of pts with BILAG A/B flare and time to flare in APRIL-SLE, and SRI-4 and SRI-6 response in SLE pts with HDA in ADDRESS II, treatment with atacept 150 mg QW demonstrated greater clinical response vs PBO. In both studies, atacept E-R relationships based on population PK-derived exposure were observed. For maximal flare reduction, an atacept exposure of  $AUC \geq 1$  mg\*hr/mL was identified. This exposure was more achievable with 150 than 75 mg (60% vs 15% probability) and corresponded to an atacept  $C_{min}$  of 5  $\mu$ g/mL, which was similar to the  $C_{min}$  values observed in the NP-KLH vaccinated mouse model. Both atacept 150 and 75 mg had acceptable safety profiles in SLE pts, with no apparent E-R relationship observed for serious infections.

**Conclusions:** Integrated nonclinical, clinical and E-R data demonstrate an acceptable benefit-risk profile for atacept in SLE pts with HDA and support the selection of the 150 mg QW dose for a PIII study.

**Disclosure of Interest:** J. Shen Employee of: EMD Serono Research and Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), O. Papisoulitis Employee of: Merck Institute for Pharmacometrics, Lausanne, Switzerland (an affiliate of Merck KGaA, Darmstadt, Germany), E. Samy Employee of: EMD Serono Research and Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), P. Haselmayer Employee of: Merck KGaA, Darmstadt, Germany), P. Chang Employee of: EMD Serono Research and Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), V. Ona Employee of: EMD Serono Research and Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), A. Kao Employee of: EMD Serono Research and Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany)

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**FRI0323 APREMILAST THERAPY IN REFRACTORY SKIN LUPUS LESIONS**

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**Background:** Skin lesions of lupus may be refractory to standard therapy. Apremilast is an orally small molecule which inhibits phosphodiesterase-4 (PDE-4) that modulates some inflammatory pathways.

**Objectives:** Our aim was to assess the efficacy of apremilast in lupus rashes refractory to conventional treatment.

**Methods:** Retrospective study on 5 lupus patients treated with apremilast at standard dose of 30 mg twice daily. The outcome was improvement of lupus rashes.

**Results:** We described 5 patients (4 women and 1 male) with a mean age of 44.2 ±8.5 years with extensive skin lesions due to lupus. Three patients had a discoid lupus and 2 patients had systemic lupus erythematosus (SLE) (one with panniculitis and the other with polycyclic ring lupus). The cutaneous lupus was confirmed in all patients by skin biopsy. Prior to apremilast all patients had received conventional treatment: topical corticosteroids (n=5), antimalarials (n=5), topical tacrolimus (n=2), oral corticosteroids (n=2), thalidomide (n=1), belimumab (n=1) and rituximab (n=1). After a mean follow-up of 6.2±2.9 months, all the patients experienced improvement of the skin lesions (in two patients was complete). In one patient it was necessary to reduce the dose of apremilast to 30 mg/day because of digestive symptoms.

**Conclusions:** Apremilast can be useful in the treatment of refractory skin lesions of lupus.

**Disclosure of Interest:** None declared

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**FRI0324 IMMUNOSUPPRESSION FOR PRIMARY SJOGREN'S SYNDROME: A SYSTEMATIC REVIEW AND META-ANALYSIS**

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**Background:** The current focus of treatment in primary Sjogren's Syndrome (pSS) is mainly symptom management. Since pSS is an autoimmune disease with multi-system involvement, there may be a role for systemic immunosuppression and/or biologic therapy. A wide variety of immune response targets have been examined in existing randomised controlled trials including inhibiting purine synthesis, blocking TNF-alpha, and depleting B lymphocytes. There is conflicting evidence as to whether immunomodulation alters disease progression.

**Objectives:** To assess the efficacy and safety of immunosuppressive therapy on pSS from clinical trials.

**Methods:** Five electronic databases (MEDLINE, EMBASE, CENTRAL, CLINICALTRIALS.GOV, WHO ICTRP) were searched to include randomised controlled trials of systemic immunosuppressive therapies in adults with pSS published in English prior to Oct 1, 2017. Efficacy measures included ocular dryness, oral dryness, fatigue, tear production, unstimulated and stimulated salivary flow, quality of life (QOL), ESSPRI, ESSDAI, ESR/CRP; Safety measures included serious adverse events (AEs) and withdrawals due to AEs.

**Results:** The searched yielded 32 trials evaluating 19 different medications. Studies enrolled anywhere between 7 to 133 patients, with the exception of 1 study with 497 patients. Mean age was in the fifth decade, with an average duration of diagnosis up to 9.2 years.

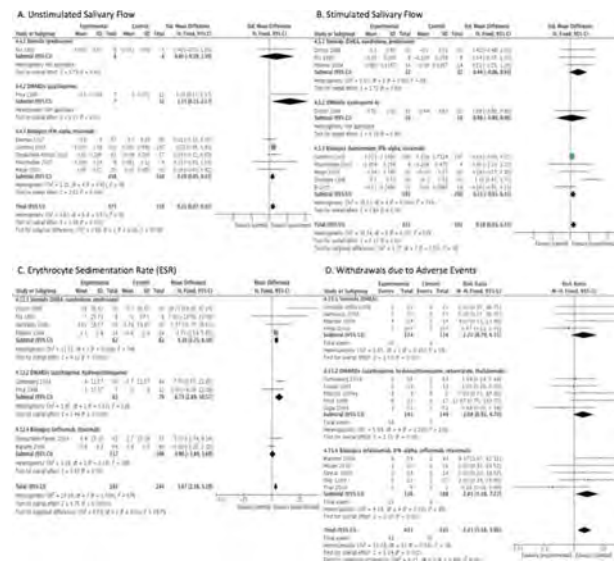
Twenty-two trials examined ocular and oral dryness, of which 2 and 3 revealed statistically significant improvements respectively (table 1). Only 1/14 trials found benefit for fatigue, none for tear production; 3/16 trials and 2/14 trials found increases in unstimulated and stimulated salivary flow respectively. Reductions in ESR were seen in 3/14 trials. Few studies examined QOL, ESSPRI, ESSDAI, and CRP. Trials often noted non-statistically significant trends toward improvement, but no particular drug or drug class consistently showed discrete benefit in subjective or objective efficacy measures possibly due to low statistical power.

**Abstract FRI0324 – Table 1. Efficacy Outcome Measures**

Outcome	# Trials Total	# Trials showing statistical improvement
Ocular dryness	22	1 of 1 Prednisone 1 of 2 Rituximab
Oral dryness	22	1 of 3 Prednisone 1 of 3 Rituximab 1 of 3 DHEA
Fatigue	14	1 of 4 Rituximab
Tear production	19	0
Unstimulated saliva production	16	2 of 3 Rituximab 1 of 3 Interferon alpha

Stimulated saliva production	14	2 of 4 Interferon alpha
Quality of life (mental component)	8	0
Quality of life (physical component)	8	0
ESSPRI	7	1 of 1 Igaruratimod
ESSDAI	6	1 of 1 Bamiercept 1 of 1 Igaruratimod
ESR	14	1 of 1 Nandrolone 1 of 1 Prednisone
		1 of 3 Hydroxychloroquine
CRP	3	1 of 1 Hydroxychloroquine

Meta-analyses of the above outcomes were performed at 6 months (figure 1). With pooled estimates, significant improvements were seen in unstimulated salivary flow (p=0.003), stimulated salivary flow (p=0.02), and ESR (p<0.001). There was a trend towards increased serious AEs in the intervention groups, and a significant increase in withdrawals from AEs (RR 2.33, 95% CI 1.38 to 3.96).



**Abstract FRI0324 – Figure 1. Meta-analyses at 6 months**

**Conclusions:** Reducing immune activity and inflammation potentially improves salivary gland function. Subjective measures may be less helpful as sicca symptoms likely have subtle progression if trials span less than 1 year. Given that most trials were small, beneficial treatment effects could be missed. Standardisation of objective, reliable, clinically meaningful outcome measures that are sensitive to change may allow for positive treatments in the future.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.3008

**FRI0325 RITUXIMAB IN PRIMARY SJÖGREN'S SYNDROME: A SYSTEMATIC REVIEW ON ITS EFFICACY**

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**Background:** Primary Sjögren's syndrome (pSS) is a systemic autoimmune disease that produces a limpho-plasmocitary infiltrate of the exocrine glands. Considering the primary role attributed to B-lymphocytes in pSS pathophysiology, it has been suggested that Rituximab (RTX) may have certain role in controlling the disease.

**Objectives:** To evaluate RTX efficacy in the treatment of xerostomia, xerophthalmia and systemic manifestations (including fatigue) in patients with pSS.

**Methods:** In the framework of the preparation of a recommendations document of the Spanish Society of Rheumatology on the use of biologics in pSS, a systematic search of the literature was carried out (until May 2017). Were included adults older than 18 years who met the 2002 American European Consensus Criteria, treated with RTX, with desired comparison to groups treated with other drugs or

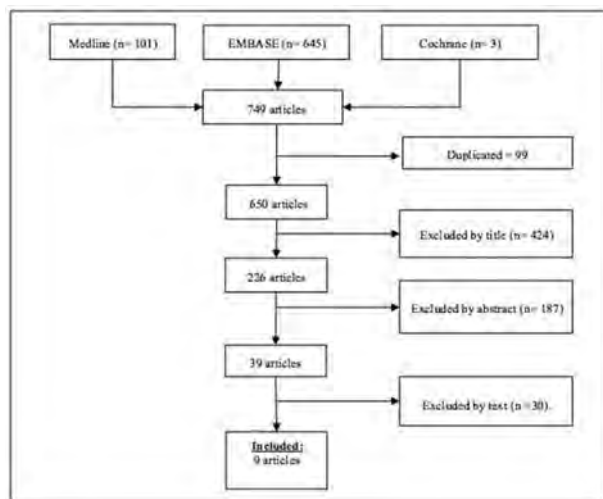


**Abstract FRI0325. Table 1..** \* Analysed in MA of Souza 2016

Author/year	Souza 2016	Devauchelle 2014*	Meijer 2010*	Dass 2008*	Carubbi 2013	Pipje 2005	Gottenberg 2013	Mekinian 2012	Seror 2007
Study type (LOE)	SR and MA (1+)	RCT (1+)	RCT (1+)	RCT (1-)	Not randomised (1-)	Not controlled <sup>3</sup>	Retrospective <sup>3</sup>	Retrospective <sup>3</sup>	Retrospective <sup>3</sup>
Groups and N	RTX 145/Pbo 131	RTX 63/Pbo 59	RTX 20/Pbo 10	RTX 8/Pbo 9	RTX 19/ <b>DMARDs22</b>	RTX 7	RTX 86	RTX 17	RTX 16
Dryness:									
VAS (oral, ocular, global).	-	-	-	-	+				
Salivary flow	+	-	-	-	+	+			
Schirmer	-	-	-	-	+	-			
Lissamine green			+						
Rose Bengal						+			
TBUT			-			+			
General and systemic manifestations:									
ESSDAI	-	-	-	-	+		+	+	
SF-36	-	-	-	-		+			
Fatigue VAS.	-	-	-	-	+	+			
Global VAS: patient/physician.		-/+			+/+				
Lab (IgG/A/M, beta2-microglobulin, RF, B cells).		+	+	+		+			+
Systemic:			+		+		+	+	

with placebo and a follow-up time of 6 months. The quality of the studies was assessed through the levels of evidence (LOE) of SIGN scale.

**Results:** The search resulted in a total of 749 articles and only 9 of them were selected (**figure 1**). The best available evidence for each variable studied is summarised in **chart 1** ("+" significant improvement; "-" no significant improvement). The most relevant results obtained in the studies with **LOE 1+**, showed significant differences comparing RTX with labebo ( $p < 0.05$ ) in: 1) Souza 2016: Salivary flow rate at 24 w (weeks) (0.09; 95% CI 0.02 to 0.16). 2) Meijer 2010: Ocular dryness VAS score at 24 (-27.00, 95% CI -46.28 to -7.72), 36 and 48 w. Lissamine green test at 24 w (-2.00, 95% CI -3.52 to -0.48). Absolute number of B cells from 5 to 48 w (-0.23; IC 95% -0.31 to -0.15). Rheumatoid Factor at 12, 24 and 36 w. Tendomyalgia at 12 and 36 w. Vasculitis at 24 w. 3) Devauchelle-Pensec 2014: 'immunoglobulin's G (1.2 g/L; 95% CI 0.4 to 2 g/L), A, M and beta2-microglobulin (1.6 g/L; 95% CI 0.5 to 2 g/L) at 24 w. The studies with **LOE 3** also report improvement in a percentage of patients in other systemic manifestations, but without demonstrating statistical significance.

**Abstract FRI0325 – Figure 1.** Flow chart.

**Conclusions:** The studies of high methodological quality that evaluate the efficacy of RTX in pSS do not find significant improvement in the primary outcome variables, such as ESSDAI, glandular involvement and other objective parameters of dryness. However, open and retrospective studies find significant improvement in activity parameters, systemic manifestations, glandular involvement and improvement of certain objective tests of dryness.

**Disclosure of Interest:** None declared

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### FRI0326 IMMUNE CELLULAR PROFILE ASSOCIATED WITH DIFFERENT TREATMENT OUTCOME IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS ON CYCLOPHOSPHAMIDE

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**Background:** Cyclophosphamide (CFA) is an effective immunosuppressive drug used for treatment of severe manifestations of systemic lupus erythematosus (SLE). The knowledge about modulatory effect of CFA on circulating immune cells and its changes associated with treatment response is limited.

**Objectives:** To determine the effect of a cumulative dose of CFA on circulating immune cells in SLE patients and to assess its association with treatment outcome.

**Methods:** Using 6-colour flow cytometry (BD FACSCanto II) we analysed T and B lymphocytes, NK cells, neutrophils, and monocytes in peripheral blood from 11 SLE female patients. SLE patients were investigated before and after cumulative 1000 mg and 3000 mg of CFA dose. Patients subgroups were assessed according to the treatment response (n=5, good responders; n=6, poor responders); SLEDAI (Systemic Lupus Erythematosus Disease Activity Index) was used to assess the disease activity. Healthy age-matched females (n=12) were included in the study. Statistics was done by GraphPad Prism and R statistical software package.

**Results:** Cumulative dose of 1000 mg of CFA resulted in decreased percentage of B lymphocytes ( $p=0.0004$ ) and CD4 +T lymphocytes ( $p=0.02$ ) and increased the percentage of total and CD8 +T lymphocytes ( $p=0.03$ ;  $p=0.0003$  respectively). After 3000 mg CFA, the percentage of B lymphocytes ( $p=0.002$ ), naïve B lymphocytes ( $p=0.005$ ), memory B lymphocytes ( $p=0.02$ ) and CD4+/CD8 +ratio ( $p=0.01$ ) decreased while the percentage of CD8 +T lymphocytes ( $p=0.0003$ ), Tregs ( $p=0.01$ ) and CD69 +NK cells ( $p=0.02$ ) increased. CFA treatment in our patients resulted in reduction of B lymphocyte percentage reaching the values of healthy controls. In good responders, decreased percentage of B lymphocytes ( $p=0.04$ ), CD4 +T lymphocytes ( $p=0.04$ ), CD4+/CD8 +ratio ( $p=0.007$ ) and increased percentage of CD8 +T lymphocytes ( $p=0.004$ ), CD69 +NK cells ( $p=0.04$ ) and non-classical monocytes ( $p=0.04$ ). In poorly responding patients percentage of CD8 +T lymphocytes ( $p=0.01$ ), activation marker HLA-DR on both CD4 +and CD8+T lymphocytes ( $p=0.01$ ;  $p=0.02$  respectively), Tregs ( $p=0.02$ ), memory B lymphocytes ( $p=0.03$ ) were increased and percentage of total B lymphocytes was decreased ( $p=0.02$ ). The analysis using advanced data mining methods for identification of treatment outcome related profiles are ongoing

**Conclusions:** Administration of CFA modulates several cell populations in SLE patients, whereas changes in B and T lymphocytes were associated with different treatment outcome. Whether the immune profile may predict the treatment response deserves further investigation.

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**Disclosure of Interest:** None declared

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FRI0327

**RELIABILITY OF LA AND DIAGNOSTIC PERFORMANCE OF APS/PT IN DIFFERENT CLINICAL SETTINGS OF APS: A MULTICENTER STUDY**

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**Background:** Correct interpretation of lupus anticoagulant (LA) tests is crucial for diagnosis of antiphospholipid syndrome (APS). However, testing patients during vitamin K antagonist (VKA) or other anticoagulant remains a contentious issue and has been discouraged by official guidelines<sup>1</sup> because of interpretational problems affecting the mixing test. Similarly, the clinical significance of weak LA, especially in the context of VKA, remains uncertain and certainly needs a more thorough evaluation. Autoantibodies that recognise a phosphatidylserine/prothrombin (PS/PT) complex have been reported to be associated with APS and may have diagnostic relevance in these settings.

**Objectives:** To evaluate the reproducibility of LA testing when performed in different centres and to assess the diagnostic performance of anti-PS/PT in different clinical settings of APS.

**Methods:** aPL testing was performed in a blind fashion in 4 centres. LA was tested as per the current criteria from the ISTH Subcommittee on LA-Phospholipid-dependent antibodies.<sup>1</sup> Thirty-two patients were enrolled in this study, as follows: 13 patients with thrombotic APS treated with vitamin K antagonist; 5 patients thrombotic APS treated with DOAC; 14 patients with transitory/low aPL titer. Anti-PS/PT IgG/IgM (aPS/PT, Inova Diagnostics) were tested by ELISA. We analysed the categorical agreement and degree of linear association, for LA and aPS/PT, respectively.

**Results:** Demographic, clinical and laboratory characteristics are summarised in table 1. Categorical agreement for LA among the centres, as expressed by Cohen's kappa coefficients, ranged between 0.61 and 0.80 (as substantial agreement). The correlation among quantitative results in the aPS/PT IgG was strong (when dichotomizing for positive Vs. negative results, Cohen's kappa coefficients=0.81–1. Spearman rho 0.84). We observed 12 (37.5% of the total) cases (7/12, 58% patients on VKA) in which LA results were discordant (as defined by lack of agreement in  $\geq 2$  laboratories) or inconclusive. Conversely, in those cases, we observed a good correlation for aPS/PT IgG testing (Cohen's kappa coefficients=0.81–1, Spearman rho 0.86).

	Patients	% (32 Patients)
<b>Anagraphic</b>		
mean age (S.D.) at data collection	49,4 (14,1)	
gender (females)	20	62.5
<b>Clinical manifestations of APS</b>		
Thrombosis	25	81.3
Arterial Thrombosis	10	31.3
Venous Thrombosis	15	46.9
Obstetric APS	0	0.0
<b>aPL profile at diagnosis</b>		
LA (positive, n)	26	81.3
ACA (IgG/M)	26	81.3
anti-β2GPI (IgG/M)	21	65.6
<b>Anticoagulant Therapy</b>		
VKA (warfarin)	13	40.6
LMWH	3	9.4
DOAC	5	15.6
None	11	34.4

**Conclusions:** Despite the progress in the standardisation of aPL testing, we observed up to 37.5% of discrepant results for LA, especially in patients on VKA. Our findings showed that some discordances in the reliability of LA testing still exist. The introduction of aPS/PT antibodies in the diagnostic process of APS might represent a further diagnostic tool, especially when LA is not available or nor reliable.

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FRI0328

**TARGETED THERAPY USING INTRADERMAL INJECTION OF ETANERCEPT FOR REMISSION INDUCTION IN DISCOID LUPUS ERYTHEMATOSUS (TARGET-DLE): FIRST RESULTS FROM A PROOF-OF-CONCEPT PHASE 2 TRIAL**

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**Background:** A significant proportion of patients with discoid lupus erythematosus (DLE) are resistant to conventional therapies. Tumour necrosis factor (TNF) is pathogenic in DLE. A concern with systemic TNF-i administration is induction of pathogenic autoantibodies and flare of disease. This could be overcome using a low-dose intra-dermal injection, which may be sufficient to neutralise the TNF in lesions, **without systemic TNF effects.**

**Objectives:** To assess the efficacy and safety of a novel route of administration of a TNF-i using a low dose intra-dermal injection of etanercept (ETN) for remission induction in DLE.

**Methods:** A prospective single arm, Simon's 2-stage minimax design with Hybrid adaptation, phase II open label trial was conducted in Leeds [NCT02656082]. Key inclusion criteria were i) adults aged 18–80 y; ii)  $\geq 1$  active DLE lesion and iii) refractory to anti-malarials. One index lesion with the highest activity was treated with weekly intra-dermal injection of up to 10 mg ETN. The primary endpoint was  $\geq 6$  patients achieving the modified limited Score of Activity and Damage in DLE (ML-SADDLE) 20 response (defined as reduction  $\geq 20\%$  in total activity comprises erythema, induration and scaling from baseline) at Week 12 for a Phase 3 trial to be recommended. Secondary endpoints included change in objective outcome measures; lesional thermography and laser Doppler imaging.

**Results:** All 25 DLE patients were recruited over 18 months (18 female, mean age 47 $\pm$ 12 y, 6 had SLE, 9 had positive ANA and median (range) no. of previous systemic therapies was 5(1–16) 17 patients completed the primary efficacy assessment [Did not attend Week 12 visit=1, early withdrawals=7 (personal choice=2, AE=2, worsening of DLE=1, non-compliance=1, pregnant=1)]. The primary endpoint was met with 13/25 (52%, 95% CI 31–73) meeting the ML-SADDLE 20 in full-set analysis. The rates for ML-SADDLE 50 and 70 were 48% and 20% respectively. Key secondary endpoints were met (table 1). Fifty-one AEs (treatment-emergent=28, Grade 3/4=4) were recorded. There was no worsening of BILAG or SLEDAI in patients with SLE. Trough serum ETN levels were detected in 6/23 (26%).

**Abstract FRI0328 – Table 1.** Secondary endpoints (per protocol; n=17)

Endpoint	Pre-Treatment	Post-Treatment	p-value
Physician VAS, mean (SD) mm	53.1 (16)	23.2 (20)	<0.001
Patient VAS, mean (SD) mm	56.9 (28)	29.7 (28)	0.001
DLQI, mean (SD)	11.4 (7)	6.5 (6)	<0.001
Laser Doppler Imaging, mean (SD) perfusion unit	495.1 (224)	376.2 (223)	0.018
Infrared thermography, mean (SD), °Celsius	1.92 (1.17)	1.08 (1.05)	0.005

**Conclusions:** Intradermal injection of ETN substantially reduced clinical activity, met its primary, secondary endpoints and was tolerable in DLE patients who were refractory to anti-malarials and other systemic therapies. This drug warrants further development in multi-centre trials. Analyses of other imaging and histological biomarkers are ongoing and can help stratifying patients for response.

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**Disclosure of Interest:** M. Y. Md Yusof: None declared, M. Wittmann: None declared, C. Fernandez: None declared, D. Wilson: None declared, S. Edward: None declared, G. Abignano: None declared, A. Alase: None declared, L. Sharples: None declared, P. Laws: None declared, M. J. Goodfield: None declared, E. M. Vital: None declared, P. Emery Grant/research support from: Abbott, BMS, Pfizer, MSD and Roche, Consultant for: BMS, Abbott, Pfizer, MSD, Novartis, Roche and UCB

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**FRI0329 THE NET-EFFECT OF COMBINING RITUXIMAB WITH BELIMUMAB IN SEVERE SYSTEMIC LUPUS ERYTHEMATOSUS**

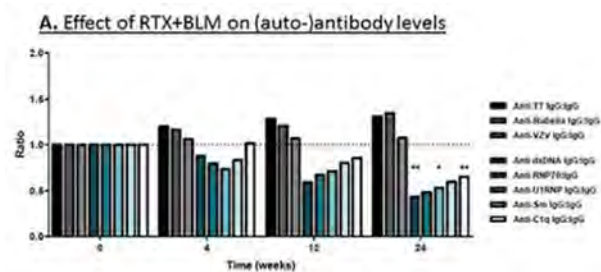
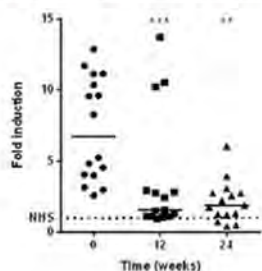
O. Teng<sup>1</sup>, T. Kraaij<sup>1</sup>, S. Kamerling<sup>1</sup>, E. de Rooy<sup>1</sup>, P. van Daele<sup>2</sup>, O. Bredewold<sup>1</sup>, J. Bakker<sup>3</sup>, I. Bajema<sup>4</sup>, H. Scherer<sup>5</sup>, R. Toes<sup>5</sup>, T. Huizinga<sup>5</sup>, T. Rabelink<sup>1</sup>, C. van Kooten<sup>1</sup>. <sup>1</sup>Nephrology, Leiden University Medical Center, Leiden; <sup>2</sup>Clinical Immunology, Erasmus Medical Center, Rotterdam; <sup>3</sup>Clinical Chemistry; <sup>4</sup>Pathology; <sup>5</sup>Rheumatology, Leiden University Medical Center, Leiden, Netherlands

**Background:** In systemic lupus erythematosus (SLE) patients, excessive formation of neutrophil extracellular traps (NETs) is observed while their degradation is impaired. *In vitro*, immune complexes (ICx) trigger NET formation while NET-derived DNA is a postulated autoantigen for anti-nuclear autoantibodies (ANAs), found in SLE. Based on these self-perpetuating mechanisms in SLE, we hypothesised that interfering with ICx formation should regress NET formation and potentially ameliorate disease.

**Objectives:** Investigate the effect of Rituximab+Belimumab therapy on pathogenic autoantibodies in relation to NET formation in severe refractory SLE

**Methods:** A phase 2A, open-label, single arm proof-of-concept study was performed wherein 16 SLE patients with severe, refractory disease were treated with a combination of CD20-mediated B-cell depletion with rituximab and sustained inhibition of B-cell activating factor with belimumab. Besides safety, the study's endpoints were chosen to address the concept of autoantibodies in relation to excessive NET formation.

**Results:** We demonstrated that SLE-derived immobilised IgG, but not soluble IgG, induced excessive NET formation, confirming *ex vivo* that ICx mediate excessive NET formation in SLE. We showed that therapeutic intervention with RTX+BLM led to specific reductions in ANAs and regression of excessive NET formation. RTX+BLM appeared to be safe and achieved clinically significant responses: low lupus disease activity state was achieved in 10 patients, renal responses in 11 patients and concomitant immunosuppressive medication was tapered in 14 out of the 16 patients.


**B. Effect of RTX+BLM on excessive NET formation**


**Conclusions:** This study provides novel insights into clinical beneficence of reducing excessive NET formation in SLE by therapeutic targeting ANA production with RTX+BLM. Altogether putting forward a new treatment concept that specifically ameliorates underlying SLE pathophysiology.

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**FRI0330 RITUXIMAB THERAPY IN SLE: EARLY RETREATMENT IS ASSOCIATED WITH LOWER DISEASE ACTIVITY AND A REDUCTION IN CORTICOSTEROID USE**

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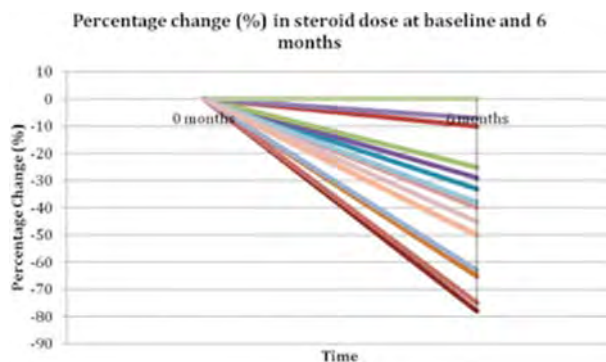
**Background:** The recently published UK guidelines for the management of SLE recommend biologic therapy for severe or refractory disease. The British Isles Lupus Assessment Group Biologics Register (BILAG-BR) has shown rituximab (RTX) to be safe, effective and corticosteroid [CS] sparing when used to treat refractory SLE. In 2013 NHS England published an interim clinical commissioning policy statement with criteria determining when RTX can be used to treat SLE.

**Objectives:** We evaluated our centre's RTX retreatment strategy in patients with SLE and the consequent outcomes (disease activity and CS dose).

**Methods:** Records for the first 50 patients receiving RTX for refractory SLE who consented to join BILAG-BR from our centre between December 2013 and January 2016 were analysed (data cut off July 2016). Demographics, disease activity<sup>BILAG</sup> 2004/SLEDAI-2K, change in CS dose, retreatment schedules and adverse events were analysed.

**Results:** Median(IQR) age and disease duration were 42.8 (33–53) years and 9.5 (4–15.8) years respectively. Male: female ratio was 1:25. 80% were Caucasian, 6% Asian, 4% Caribbean and 10% other. All patients met SLICC/ACR classification criteria for SLE. The median(IQR) SLEDAI-2K scores and BILAG 2004 scores reduced from 6 (4–8) to 4 (0–4) ( $p < 0.00001$ ) and 20 (10–24.5) to 9 (2–15.5) ( $p < 0.001$ ) respectively at 6 months. Complete response was achieved in 62.8% patients (defined as loss of all BILAG A and B scores to  $\leq 1$ B score with no new A/B scores in other organ domains). 66% patients lost all A scores at 6 months. Median(IQR) daily CS dose reduced from 10 mg(0–20) to 5 mg(0.5–9.5) at 6 months ( $P = < 0.001$ ) and was 5 mg (0–6.63) at last reported visit (median (IQR) 13 (12–19.5) months). 16 patients did not fully respond to baseline treatment but 11 responded to retreatment. Serious infections (requiring hospital admission) occurred in 6 patients (12%).

30/50 patients received their 1<sup>st</sup> course of RTX at BILAG-BR baseline visit. 23 met criteria for active disease (at least 1A or 2Bs), 6 were taking an unacceptably high maintenance CS dose, and 1 was planning pregnancy. Median(IQR) CS dose in this group at baseline was 10 mg(1.5–20), and 5 mg(3–9) at 6 months. 70.8% demonstrated complete response at 6 months. 17 (57%) went on to have retreatment due to active disease, of which 11 (64.7%) had responded at 6 months post retreatment. Median(IQR) time to retreatment was 8 (6–12) months. 20/50 patients had received retreatment at predetermined intervals prior to their baseline BILAG-BR visit. Median(IQR) numbers of previous RTX courses were 3 (2–6). Median(IQR) CS dose was 8.75 mg(0–11.3) at baseline BILAG-BR visit and 5.5 mg(0–10) at 6 months. Median(IQR) time from baseline to retreatment was 6 (6–9.5) months. Median(IQR) sustained response was 18 (13.5–18) months.



**Conclusions:** Historically, our centre used time from 1<sup>st</sup> treatment to flare as a guide to a patient's future RTX retreatment schedule; patients were, on average, treated 2 months earlier than those treated under the current commissioning policy. Findings suggest that earlier retreatment led to sustained disease control and reduction of CS dose with no increase in adverse events. 11/16 incomplete responders responded following retreatment. Early retreatment may be associated with better outcomes for the patient and further research is needed in this area.

**Disclosure of Interest:** None declared

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### FRI0331 TROUGH CONCENTRATION OF MYCOPHENOLIC ACID CORRELATES WITH RENAL FUNCTION AND SERUM ALBUMIN LEVEL IN JAPANESE PATIENTS WITH SLE

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**Background:** Mycophenolate mofetil (MMF) is an immunosuppressant used for treatment of lupus nephritis. MMF is converted to mycophenolic acid (MPA) by esterases, which is the active metabolite with pharmacological activities. A fixed dose of 2–3 g/day is administered as remission induction therapy.<sup>1</sup> The usefulness of therapeutic drug monitoring (TDM) of MMF has not been elucidated. Moreover, little is known about the factor that affects the concentration of MPA in Asian patients.

**Objectives:** The aim of this study is to investigate the factor that affects the trough concentration of MPA in Japanese patients with SLE.

**Methods:** We recruited the SLE cases whose trough concentrations of MPA were measured from 2014 to 2017 at Kyoto University Hospital. When trough concentrations were measured multiple times in each patient with the same dose of MMF, median concentration was used for the analyses. Linear regression analysis was performed to identify the factor that affects the trough concentration of MPA. The association of trough concentration of MPA and adverse effects of MMF was investigated as well.

**Results:** Total of 20 cases were recruited and 43 trough concentrations were included for the analyses. The median daily dose of MMF (g) was 1.5 (range; 0.25–3.0) and the median trough concentration of MPA ( $\mu\text{g/ml}$ ) was 2.0 (range; 0.4–15.0). Linear regression analysis (table 1) revealed that trough concentration of MPA was correlated with daily dose of MMF ( $p=0.0081$ ,  $r=0.40$ , figure 1A), serum albumin level ( $p=3.3 \times 10^{-4}$ ,  $r=0.52$ , figure 1B) and creatinine clearance ( $p=1.8 \times 10^{-5}$ ,  $r=-0.60$ , figure 1C). Daily dose of prednisolone and serum C4 level were correlated with trough concentration of MPA as well, though multicollinearity was found in these two variables and serum albumin or creatinine clearance. Multivariate analysis (table 2) revealed that serum albumin and creatinine clearance were independently associated with trough concentration of MPA ( $p=6.2 \times 10^{-4}$  and  $1.6 \times 10^{-5}$ , respectively). Adverse effects of MMF, such as diarrhoea and cytopenia, were not associated with trough concentration of MPA.

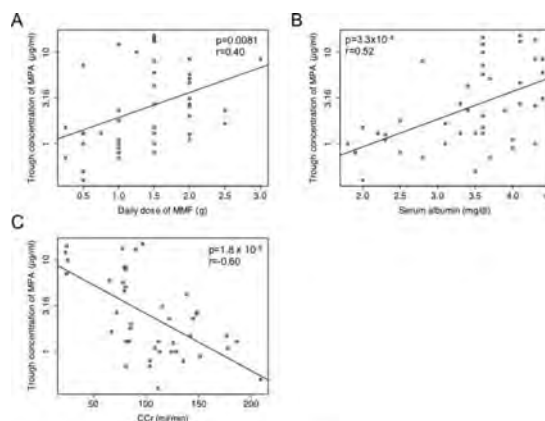
**Abstract FRI0331 – Table 1.** Linear regression analysis (Univariate analysis) of parameters influencing trough concentration of MPA

Variables*	Standardised beta coefficient	P-value	Odds ratio (95% CI)
Daily dose of MMF (g)	0.27	0.0081	1.31 (1.08–1.59)
Serum albumin (mg/dl)	0.30	$3.3 \times 10^{-4}$	1.35 (1.16–1.57)
CCr (ml/min)	-0.062	$1.8 \times 10^{-5}$	0.94 (0.91–0.96)
Age (years)	0.0039	0.52	1.00 (0.99–1.02)
BW (kg)	-0.0025	0.79	1.00 (0.98–1.02)
PSL (mg/day)	-0.015	0.0035	0.99 (0.98–0.99)
Serum C3	0.0073	0.055	1.01 (1.00–1.01)
Serum C4	0.019	0.023	1.02 (1.00–1.03)

**Abstract FRI0331 – Table 2.** Linear regression analysis (Multivariate analysis) of parameters influencing trough concentration of MPA

Variables*	Beta	P-value	Odds ratio (95% CI)
Daily dose of MMF (g)	0.14	0.068	1.15 (0.99–1.32)
Serum albumin (mg/dl)	0.23	$6.2 \times 10^{-4}$	1.26 (1.11–1.42)
CCr (ml/min)	-0.053	$1.6 \times 10^{-5}$	0.95 (0.93–0.97)

BW=body wt, PSL=prednisolone, \*Standardised beta coefficient and odds ratio of CCr was calculated with 10 as one unit.



**Conclusions:** Trough concentration of MPA was correlated with daily dose of MMF, serum albumin level and creatinine clearance.

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[1] Ann Rheum Dis 2012;71:1771–82.

**Disclosure of Interest:** None declared

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### FRI0332 THE EXTENT OF TUBULOINTERSTITIAL INFLAMMATION PREDICTS THE PROGNOSIS OF TREATED PATIENTS WITH LUPUS NEPHRITIS

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**Background:** Lupus nephritis is common clinical manifestation and contributes significantly to mortality of systemic lupus erythematosus (SLE)

**Objectives:** Recently it has been reported that severity of tubulointerstitial inflammation (TII) predicts subsequent renal failure. However, it has not yet been reported what histologic features affect the survival rate in patients with lupus nephritis who had conventional treatment.

**Methods:** Seventy-six patients with lupus nephritis, who had conventional treatment and renal biopsy, were enrolled in this study. The extent of tubulointerstitial lymphocytic infiltrates was semi-quantitated (grade 1–4) using standard histochemical staining. This was then compared to other established lupus nephritis classification (ISN/RPN classification) which focuses on histologic changes of the glomerulus as well as clinical and laboratory characteristics. Follow-up data were obtained and survival analysis was carried out to determine the predictive values for subsequent mortality.

**Results:** TII was a common pathologic finding, 64% percent of biopsy samples were graded as 1, 11% as 2, 14% as 3, and 11% as 4. In 29% of biopsies (22/76), there were well circumscribed lymphocytic aggregates in tubulointerstitium and 5% of biopsies (4/76), structures like germinal centre (GC) were observed. When TII was divided into mild (grade 1–2) and severe (grade 3–4), lymphocyte aggregates and GC formation were more common in patients with severe TII (15/19, 4/19) than those with mild TII (7/57, 0/57) ( $p<0.001$  and  $p=0.004$ , respectively). Patients with severe TII or lymphocyte aggregates were significantly higher in serum creatinine, but not with double-stranded DNA (ds DNA) antibodies, serum complement 3, SLE disease activity (SLEDAI) and degree of proteinuria at the time of biopsies compared to those without. The mean follow-up time was  $62.9 \pm 47.0$  months and overall, 9 patients died as a result of disease progression ( $n=6$ ) and infection ( $n=3$ ). Patients with severe TII, lymphocyte aggregates or GC formation were at greater risk for mortality compared to those without. However, both glomerular proliferation and laboratory markers including baseline ds DNA, complement, SLEDAI and degree of proteinuria did not affect on long term mortality. After multivariate logistic analysis including SLEDAI and histologic features, only GC formation provided poor prognostic information for mortality (hazard ratio 24.5, 95% confidence interval 2.2–274.6;  $p=0.009$ ).

**Conclusions:** TII severity, especially GC formation, was independent predictor for a worse outcome in lupus nephritis patients with conventional treatment. A larger study is needed to confirm whether the presence of GC formation influences disease outcome.

**Disclosure of Interest:** None declared

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**FRI0333 B-CELLS DEPLETION AS RESCUE THERAPY FOR EXTRA-CRITERIA MANIFESTATIONS OF PRIMARY ANTIPHOSPHOLIPID SYNDROME**

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**Background:** While immunosuppressive drugs may be helpful in patients with active systemic autoimmune diseases, their use in antiphospholipid syndrome (APS) is still controversial, and mainly limited to very selected cases of catastrophic APS or in severe cases refractory to standard therapy.<sup>1</sup> B-cells are likely to play a central role in the generation of the aPL-induced clinical manifestations of the disease, so they might constitute a logical therapeutic target in APS.

**Objectives:** To investigate PAPS patients with extra-criteria manifestations of APS treated with Rituximab (RTX) as a rescue therapy.

**Methods:** We retrospectively retrieved data from patients who attended the S. Giovanni Bosco Hospital, Turin, Italy, who met the following inclusion criteria: a) persistent aPL positivity and fulfilled the Sydney criteria for PAPS<sup>2</sup> b) presented with at least 1 extra-criteria manifestation; c) were treated with RTX as a rescue therapy (e.g. because they were refractory/intolerant/contraindicated to standard therapy) for the management of extra-criteria manifestations of APS.

**Results:** This retrospective study included 7 consecutive PAPS patients [median age 53 (range 38–66), female 6:1]. Table 1 resumes the characteristics of the PAPS patients included in the study. Six patients presented with severe thrombocytopenia (plts <50.000/mm<sup>3</sup>) and 1 patient presented with recurrent superficial venous thrombosis (3 events in 6 months despite ongoing anticoagulation therapy with VKA). Previous therapies included intravenous immunoglobulins (5 patients) and high doses of steroids (3 patients). One patient received RTX as rescue therapy as a steroid-sparing agent because of the high cardiovascular risk (high body mass index, uncontrolled arterial hypertension, and diabetes). We observed a full response after treatment with RTX in 6 out of 7 patients (86%, 5 with thrombocytopenia and 1 with recurrent superficial thrombosis). One patient who did not respond to the B-cell depletion therapy, and was treated with a splenectomy 1 month after RTX therapy and platelets levels normalised 3 months after the procedure. Overall, median time free from relapse was 27.5 months (range 4–97), no adverse events were reported, no patients developed infections.

**Abstract FRI0333 – Table 1.** Patients with PAPS with extra-criteria manifestations that followed a B-cells depleting protocol from the experience of our centre

	Age	aPL profile	Clinical manifestations of APS	Extra-criteria manifestations	RTX Protocol	Adverse events	Previous Immunosuppressive Therapy	Autoimmunity	Time free from relapse (months)
Patient 1 (male)	45	Triple positivity	1 episode of TVP and PE, 1 episode of retinal thrombosis	Recurrent superficial venous thrombosis	CYC 750mg/weekly for 2 weeks and RTX 375 mg/m <sup>2</sup> weekly for 4 weeks + 2 monthly infusions	None	IVIG	Warfarin, target INR 2.5-3.5	10 ongoing
Patient 2 (female)	38	Triple positivity	1 episode of stroke	Severe thrombocytopenia	RTX 375 mg/m <sup>2</sup> weekly for 4 weeks + 2 monthly infusions	None	IVIG	Warfarin, target INR 2-3	34 ongoing
Patient 3 (female)	66	Triple positivity	1 retinal haemorrhage, 1 thrombosis of distal venous sinus, 1 thrombosis of the jugular vein	Severe thrombocytopenia	RTX 1g/15 days, 2 infusions in total	None	IVIG, high doses of steroids	Warfarin 2.5-3.5, then Fondaparinux	12
Patient 4 (female)	53	LA positive	Recurrent miscarriages, Thrombosis of the Abdominal aorta	Severe thrombocytopenia	RTX 1g/15 days, 2 infusions in total	None	IVIG, high doses of steroids	Warfarin, target INR 2-3	8 ongoing
Patient 5 (female)	58	Triple positivity	1 episode of TVP and PE, 1 recurrence of TVP	Severe thrombocytopenia	RTX 375 mg/m <sup>2</sup> weekly for 4 weeks + 2 monthly infusions	None	None	Warfarin, target INR 2-3	43 ongoing
Patient 6 (female)	60	Triple positivity	1 episode of stroke	Severe thrombocytopenia	RTX 375 mg/m <sup>2</sup> weekly for 4 weeks + 2 monthly infusions	None	IVIG	Warfarin, target INR 2-3	97 ongoing
Patient 7 (female)	66	Triple positivity	1 episode of TVP	Severe thrombocytopenia	RTX 375 mg/m <sup>2</sup> weekly for 4 weeks	None	High doses of steroids	Warfarin, target INR 2-3	0

APS Antiphospholipid Syndrome, UC undifferentiated connective tissue disease, CYC cyclophosphamide, RTX rituximab, AZA azathioprine, MTX methotrexate, DVT deep vein thrombosis, PE pulmonary embolism

**Conclusions:** In selected case of patients with PAPS, RTX can represent a safe and efficacious therapeutic tool to manage the extra-criteria manifestations of the syndrome, especially when standard approaches have failed or cannot be pursued.

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**Disclosure of Interest:** None declared  
**DOI:** 10.1136/annrheumdis-2018-eular.2157

**FRI0334 COMPARISON OF DIFFERENT DEFINITIONS OF REMISSION IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) – A STUDY BASED ON THE BLISS-76 CLINICAL TRIAL**

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**Background:** Standardisation of a definition of disease remission in SLE is one of the most important unmet needs in rheumatology and up to today there is no gold standard for the definition of remission.<sup>1</sup>

**Objectives:** An international task force consisting of 60 rheumatologists, nephrologists, dermatologists, clinical immunologists and patient representatives agreed on various definitions of remission in SLE (DORIS).<sup>2</sup> Our aim was to apply these definitions on a clinical trial.

**Methods:** This is a post-hoc analysis of a prospective randomised controlled trial (RCT) in SLE, the BLISS-76 clinical trial.<sup>3</sup> We have applied two DORIS definitions (table 1) at three time points, week (wk) 24, 52 and 76. The patient could be in remission on or off treatment. Remission on treatment allowed maintenance anti-malarials, low dose glucocorticoids (GCs) (prednisone ≤5 mg/day or equivalent), maintenance immunosuppressives and maintenance biologics. Remission off treatment allowed maintenance anti-malarials only. Additionally, we applied each definition where the remission on treatment allowed a GC dose ≤10 mg/day (not a part of the original DORIS-definitions).

**Abstract FRI0334 – Table 1.** DORIS definitions of remission in SLE

Definition	1a	1b	3a	3b
cSLEDAI=0	√	√	-	-
PhGA<0.5	√	√	√	√
Serology	Regardless	Normal	Regardless	Normal
BILAG D/E only	-	-	√	√

cSLEDAI: clinical Systemic Lupus Erythematosus Disease Activity Index; PhGA: Physician Global Assessment; BILAG: British Isles Lupus Assessment Group  
**Note:** Anti-double stranded DNA and complement (C3 and C4) is included in serology. These definitions were first tested (a) regardless of serology and then (b) normal serology (negative anti-dsDNA antibodies AND normal complement).

**Abstract FRI0334 – Table 2.** Percent of Patients who started the BLISS-76 trial (n=819) who were in remission at week 24, week 52, and week 76 using different definitions

	Definition 1a, On treatment (GCs ≤5 mg allowed)	Definition 1a, On treatment (GCs ≤10 mg allowed)	Definition 1b, Off treatment	Definition 1b, On treatment (GCs ≤5 mg allowed)	Definition 1b, On treatment (GCs ≤10 mg allowed)	Definition 1b, Off treatment
% (n) in remission W24	4.2 (34)	7.3 (60)	0.4 (3)	1.0 (8)	1.7 (14)	0.1 (1)
% (n) in remission W52	7.4 (61)	11.8 (97)	0.7 (6)	2.6 (21)	3.2 (26)	0.5 (4)
% (n) in remission W76	9.5 (78)	13.8 (113)	1.0 (8)	3.2 (26)	4.4 (36)	0.4 (3)
	Definition 3a, On treatment (GCs ≤5 mg allowed)	Definition 3a, On treatment (GCs ≤10 mg allowed)	Definition 3b, Off treatment	Definition 3b, On treatment (GCs ≤5 mg allowed)	Definition 3b, On treatment (GCs ≤10 mg allowed)	Definition 3b, Off treatment
% (n) in remission W24	0.9 (7)	2.2 (18)	0	0.5 (4)	0.6 (5)	0
% (n) in remission W52	1.3 (11)	2.8 (23)	0.1 (1)	0.7 (6)	1.1 (9)	0.1 (1)
% (n) in remission W76	2.9 (24)	4.5 (37)	0.1 (1)	1.6 (13)	2.3 (19)	0.1 (1)

Def1a: cSLEDAI=0, PhGA<0.5 and normal serology

Def 1b: cSLEDAI=0, PhGA<0.5 and regardless of serology

Def3a: BILAG D/E only, PhGA<0.5 and normal serology

Def 3b: BILAG D/E only, PhGA<0.5 and regardless of serology

GCs: Glucocorticoids

On treatment: maintenance anti-malarials, low dose glucocorticoids (prednisone ≤ 5 mg/day or equivalent), maintenance immunosuppressives, and maintenance biologics are allowed.  
 Off treatment: maintenance anti-malarials only is allowed.

**Results:** There were 819 patients enrolled in BLISS-76. The proportions of patients that fulfilled remission according to the above definitions are shown in table 2. The highest point prevalence (9.5%) was when definition 1a on treatment was applied at wk 76. As expected, even more patients fulfilled definition 1a when a GC dose ≤10 mg/day was allowed at wk 76 (13.8%). More patients fulfilled the

remission criteria when clinical SLEDAI was used compared to when BILAG was used. When serology (anti-DNA antibodies and complement) was taken into consideration (definitions 1b and 3b), less patients fulfilled remission. Very low numbers of patients ( $\leq 1\%$ ) fulfilled remission off treatment.

**Conclusions:** Overall, few patients fulfilled remission according to these definitions. More patients fulfilled the definitions when serology was excluded and when a higher dose of GCs was allowed.

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#### FRI0335 HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR AUTOIMMUNE DISEASES – A 20 YEARS SINGLE CENTRE EXPERIENCE

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**Background:** Over the past 20 years, hematopoietic stem cell transplantation (HSCT) has been emerging as a promising treatment option for severe cases of autoimmune diseases (ADs). Meanwhile, positive results have been obtained in 3 randomised clinical trials for systemic sclerosis. The goal of this therapy is to induce medication-free remissions by ablating the pathologic autoreactive memory and restoring of self-tolerance.

**Objectives:** Here, we summarise the clinical outcomes of AD patients receiving HSCT at the Charité – University Medicine.

**Methods:** In this prospective study, the outcome of 22 patients been analysed after receiving a CD34<sup>+</sup>-selected autologous HSCT after immunoablation with ATG and cyclophosphamide for different ADs (10 SLE, 4 SSc, 3 vasculitis, 2 multiple sclerosis, 1 polycondritis, 1 inflammatory polyneuropathy, 1 autoimmune haemolytic anaemia) between 1998 and 2015. Multiparametric flow cytometry was applied to characterise peripheral blood lymphocytes subsets including analysis of the TCR-Vbeta repertoire on CD4<sup>+</sup> T cells, CD31 expression as marker for thymic output of CD4<sup>+</sup> T cells, including Foxp3<sup>+</sup> Tregs. In SLE, Siglec-1 on monocytes as surrogate for interferon activity and RNA expression profiling by microarray of FACS-sorted CD14<sup>+</sup> monocytes was performed (Affymetrix). Autoantibodies were investigated with ELISA.

**Results:** With a median follow-up of 135 months, the overall survival was 76.5% and progression-free survival 67.9%, respectively. 3 deaths were regarded treatment related, 1 patient had persisting disease (haemolytic anaemia) and 4 relapses occurred in SLE at 1, 18, 36 and 80 months, respectively. Remaining patients are in stable clinical remissions despite discontinuation of immunosuppressive therapy. HSCT was associated with significant reduction or normalisation of auto-antibody levels and a profound reconfiguration of the adaptive immune system, the latter characterised by a re-emergence of naïve T cells with markers of recent thymic emigrants and renewed TCR repertoire, including Foxp3<sup>+</sup> Tregs and regeneration of naïve B cells. In SLE patients, Siglec-1 expression on monocytes completely normalised and transcriptome analysis revealed an abrogation of type I interferon signalling in responding patients.

**Conclusions:** Our data provide the "...proof-of-concept" that a chronic autoimmune system can be reset into a naïve and self-tolerant state by HSCT, potentially providing cure in AD. Although applied as salvage therapy in severely affected patients with poor outcomes, TRM gradually improved due to accumulating centre experience and better patient selection and supportive care. Based on positive results from RCT in the major indications, HSCT should be placed earlier in the

treatment algorithm, especially in systemic sclerosis with rapid progress and lung involvement.

**Disclosure of Interest:** None declared

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#### FRI0336 BELIEF ABOUT MEDICINE QUESTIONNAIRE PREDICTS THERAPEUTIC ADHERENCE TO HYDROXYCHLOROQUINE DURING SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Therapeutic adherence is a key element of chronic disease management and one of the most difficult to assess. The Belief about Medicines Questionnaire (BMQ) evaluates patients' own beliefs related to medication. It is available in two sections: the BMQ-General and the BMQ-Specific. The BMQ-specific focuses on the representations of medication prescribed for personal use. It was set up as a screening test for poor therapeutic adherence during certain chronic diseases. Early detection of lupus patients at risk of poor therapeutic adherence could lead to preventive actions.

**Objectives:** To assess the BMQ-Specific as a predictive test of adherence to hydroxychloroquine in SLE.

**Methods:** Case-control, retrospective and monocentric study. Cases were enrolled according to the following criteria: systemic lupus erythematosus (SLE) according to the ACR classification criteria and HCQ dosage <100 ng/ml after a minimum of 2 months of treatment. The matched control was a lupus patient, enlisted within the centre the same week, with a HCQ dosage  $\geq 800$  ng/ml. Each patient answered the BMQ-Specific through a telephone interview. The BMQ-Specific comprises two 5-item factors assessing beliefs about the necessity of prescribed medication (*Specific-Necessity*) and concerns about the danger of dependence and long-term toxicity of medication (*Specific-Concerns*). Responses to each statement were scored on a five-point Likert scale (1=strongly disagree and 5=strongly agree). Scores obtained for the individual items within both scales were summed to give total scores for the Specific-Necessity and Concerns scales range from 5 to 25. A Necessity–Concerns (N-C) differential was calculated (range from –20 to +20). It expresses the cost–benefit perceived by the patient for taking the medication. Case and control characteristics were compared using usual tests. Diagnosis performance of each BMQ score and necessity-concern differential were studied by the mean of ROC curves.

**Results:** The BMQ-Specific questionnaire was submitted to 118 patients: 59 cases and 59 matched controls. The concern score was significantly higher in cases (mean 16.8 vs. 12.7,  $p < 0.0001$ ). The necessity score was significantly higher in control (mean 18.4 vs 15, respectively,  $p < 0.0004$ ). ROC curves show a better area under the curve (AUC) with the N-C differential compared to the AUC of separate scores (respectively 0,8 vs 0,7). The sensitivity and specificity are optimal for a N-C differential of 3.

**Conclusions:** During SLE, nonadherent patients are primarily concerned about the risks inherent to treatment, rather than its effectiveness. To date, we are the only study to show that specific BMQ is an efficient tool for detecting patients at risk of poor therapeutic adherence to HCQ during SLE. The necessity-concerns differential score must be preferred to the scores taken separately. Thus, targeted educational actions can be provided as soon as the patients are taken in charge, in order to improve their adherence to treatment.

**Disclosure of Interest:** None declared

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#### FRI0337 FACTORS ASSOCIATED WITH POOR THERAPEUTIC ADHERENCE TO HYDROXYCHLOROQUINE DURING SYSTEMIC LUPUS

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**Background:** Poor adherence to medication regimens is a major cause of relapse during systemic lupus erythematosus (SLE). Hydroxychloroquine (HCQ),



the main therapy of SLE, has a long half-life. Thus, undetectable blood HCQ concentrations can be used to identify patients who do not take their treatment

**Objectives:** To identify the determinants of poor therapeutic adherence in patients with SLE.

**Methods:** Case-control, retrospective, monocentric study. The cases were enrolled in our centre from 02/11/2011 to 13/01/2015 according to the following criteria: SLE defined according to ACR classification criteria and blood concentration of HCQ <100 ng/ml after a minimum of 2 months on therapy. For each case, the matched control was a lupus patient, enlisted from our centre the same week, with an HCQ dose greater than or equal to 800 ng/ml. Case and control characteristics were compared using standard tests and a uni-multivariate logistic regression.

**Results:** One hundred and fifty patients were included, 75 cases (68 women) and 75 controls (72 women), with an average age of 35.7 years ( $\pm 11.3$  years) vs 35.6 years ( $\pm 10.6$  years). Most patients had inactive lupus (3 patients had SLEDAI  $\geq 4$ ), 27% of them had benefited from therapeutic education sessions. The average dosage of HCQ was 1110 ng/ml within the control group. In our univariate analysis, nonadherent patients lived significantly further away from the centre than adherent patients (median distance [interquartile range]: 22<sup>11-52</sup> vs 14 km [5.9-35], respectively,  $p=0.03$ ) and were more likely to be unemployed, (23 vs 8%, respectively,  $p=0.006$ ). Nonadherent patients had less often benefited from the patient's therapeutic education program (18 vs 35%, respectively,  $p=0.018$ ), were taking less treatment (3 vs 4, respectively,  $p=0.008$ ), had a significantly lower level of education (61% compared to 89% of patients with at least a bachelor's degree,  $p<0.001$ ). In our multivariate analysis, a level of education below the A levels was the strongest factor explaining poor therapeutic adherence, OR (IC 95): 4.09 (1.5-10.8).

**Conclusions:** The main drivers of therapeutic adherence during SLE are socio-economic factors. The least educated and most disadvantaged patients are most likely to display poor therapeutic adherence. Targeted preventive actions and enhanced therapeutic education should be provided to them.

**Disclosure of Interest:** None declared

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### FRI0338 HYDROXYCHLOROQUINE MAY HELP TO IMPROVE THE IN VITRO FERTILIZATION-EMBRYO TRANSFER OUTCOMES IN ANA AND DS-DNA POSITIVE PATIENTS

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**Background:** Assisted reproductive technology has helped a large quantity of couples having trouble in natural pregnancy. Failure of *in vitro* fertilization-embryo transfer (IVF-ET) may be attributed to ANA and ds-DNA. ANA+/anti-dsDNA was related to low-quality embryos, low clinical pregnancy, and early miscarriage rate.<sup>1</sup> Hydroxychloroquine (HCQ) is recommended preconceptionally and throughout pregnancy for patients with SLE, and was proved to benefit the patients with Antiphospholipid syndrome. For those women with positive ANA and ds-DNA, but haven't any symptoms related to lupus or any other autoimmune diseases, the treatment for improving reproductive outcomes was controversial. In the present study, we retrospectively reviewed 156 patients with positive ANA and ds-DNA who underwent IVF-ET, compared the efficacy among different therapeutic strategies and observed side effects of the medication.

**Objectives:** To assess the efficacy, safety and tolerability of HCQ as preconceptionally and throughout pregnancy therapy in the treatment of IVF-ET patients with positive ANA and ds-DNA.

**Methods:** We retrospectively reviewed 156 patients in the treatment of IVF-ET with positive ANA and ds-DNA but without any symptoms in south China from January 2010 to December 2016 who received prednisone or prednisone +HCQ as preconceptionally and throughout pregnancy therapy. Prednisone was administered at a dose of 7.5 mg/day. HCQ was administered at a dose of 0.2 twice a day. Details of the IVF-ET outcomes and side effects were collected.

**Results:** Of the 156 patients, no significance of demographic variables and reproductive related parameters such as duration of infertility, basal sex hormone, total Gn dose, E2 level on the day of HCG initiation, and number of retrieved oocytes was found among prednisone group (65 cases) and prednisone +HCQ group (91 cases). Fertilisation rate, implantation rate and clinical pregnancy rate were significantly higher in prednisone +HCQ group than in prednisone group, 75.8% vs 60.0%,  $p=0.017$ , 29.7% vs 15.4%,  $p=0.032$ , and 62.6% vs 47.7%,  $p=0.028$ , respectively. Abortion rate was lower in prednisone +HCQ group, 7.0% vs 12.9%, but not significantly. Clinical pregnancy rate was not associated the titers of ANA or ds-DNA. Low C3 was correlated with failure of implantation. None of the cases on prednisone or prednisone plus HCQ had side effects affecting the treatment course.

**Conclusions:** Combination of prednisone and HCQ may be more effective than solo treatment of prednisone for patients underwent IVF-ET with positive ANA and ds-DNA who had no clinical symptoms of autoimmune diseases.

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### FRI0339 SLEDAI-2K RESPONDER INDEX-50 IS EFFECTIVE IN DEMONSTRATING PARTIAL RESPONSE IN A PHASE 2, RANDOMISED PLACEBO-CONTROLLED STUDY OF USTEKINUMAB IN PATIENTS WITH ACTIVE SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Ustekinumab (UST), a monoclonal antibody that targets shared p40 subunit of cytokines IL-12 and IL-23, is being investigated in pts w/active systemic lupus erythematosus(SLE). While traditional SLE Disease Activity Index 2000(SLEDAI-2K)scoring assesses complete SLE response for individual disease manifestations, SLEDAI-2K Responder Index-50(S2K RI-50)can be used to evaluate SLE responses using partial improvement( $\geq 50\%$ )in each domain.

**Objectives:** To evaluate SLEDAI-2K vs S2K RI-50 response in a randomised, PBO-controlled trial of UST in pts w/active SLE.

**Methods:** We conducted a Ph2, PBO-controlled study in adults w/active disease (SLEDAI score  $\geq 6$  w/ $\geq 1$  BILAG A and /or  $\geq 2$  BILAG B scores)despite standard-of-care therapy. Pts(n=102)were randomised(3:2) to UST IV~6 mg/kg or PBO at wk0, followed by SC inj of UST 90 mg q8w or PBO beginning at wk8, both added to standard-of-care. We calculated S2K RI-50 response at wk24 using various thresholds to define response including decrease of at least 1,2,3,4,5, or6 points from baseline(BL) in S2K RI-50 score. We also compared proportion of pts w/SLEDAI-2K response vs S2K RI-50 response in pts receiving UST(n=62)vs PBO (n=40)at wk24.

**Results:** Change from BL SLEDAI-2K and S2K RI-50 scores were strongly correlated( $R=0.89$ , $p<0.0001$ )at wk24. A greater proportion of UST vs PBO pts achieved S2K RI-50 response at wk24, regardless of threshold used to define response (table 1). The greatest differences in S2K RI-50 response rates between UST vs PBO were observed for a 4-point decrease(23.1%, $p=0.010$ ), a 5-point decrease(26.8%, $p=0.010$ ), and 6-point decrease (25.5%, $p=0.016$ ) from BL. S2K RI-50 captured more responders than SLEDAI-2K at wk24, however, the difference in SLEDAI-2K 4-point response in UST vs PBO was  $\Delta 27\%$ ( $p=0.005$ ) while S2K RI-50 was  $\Delta 23\%$ ( $p=0.010$ ).

**Abstract FRI0339 – Table 1.** S2K RI-50 response rates at Wk 24 for various thresholds to define response

Decrease from Baseline	UST (%) <sup>a,b</sup>	PBO (%) <sup>a,b</sup>	Difference between UST and PBO	p-value <sup>c</sup>
1 Point Decrease	96.0	94.2	1.8	0.3664
2 Point Decrease	90.0	84.2	5.8	0.2261
3 Point Decrease	86.9	74.1	12.8	0.0772
4 Point Decrease	86.2	63.1	23.1	0.0101
5 Point Decrease	74.5	47.7	26.8	0.0102
6 Point Decrease	66.3	40.8	25.5	0.0158

Note: S2K RI-50 response is defined differently in each row using different cutoffs. S2K RI-50 uses partial response definition of  $\geq 50\%$  improvement for each individual SLEDAI-2K descriptor.

<sup>a</sup> Values for pts meeting treatment failure criteria are set to missing from point of treatment failure forward.

<sup>b</sup> Response based upon multiple imputations for missing data from Wk16 to Wk24, where Markov chain Monte Carlo method is used to make missing pattern monotone and serial logistic regression is used to impute monotone missing. The imputation model includes treatment group and baseline SLEDAI-2K covariate.

<sup>c</sup> Test for greater treatment effect in UST over PBO (alternative hypothesis) is based upon logistic regression w/treatment group, baseline SLEDAI-2K, baseline medication use for SLE and race as covariates.

**Conclusions:** S2K RI-50 is an instrument that can capture partial clinically important improvement of  $\geq 50\%$  in SLE disease manifestations. The data suggests

cutpoints for defining S2K RI-50 response in clinical trials of pts w/moderate-severe SLE disease activity.

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#### FRI0340 DOSAGE OF HYDROXYCHLOROQUINE (PLAQUENIL) ONLINE SURVEY BY PATIENT ORGANISATION NVLE

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**Background:** Hydroxychloroquine (HCQ) has been proven effective in several immune mediated diseases. Long-term use of HCQ is very common in patients with systemic autoimmune disease. The greatest advantage of HCQ is that it may reduce the risk of flares and thereby allow glucocorticoid dose reduction. The risk/benefit ratio of HCQ is excellent but HCQ is also known for its potentially severe and fortunately rare side effect: retinal toxicity. In The Netherlands, there are no standard guidelines regarding the dosing of HCQ and ophthalmologic screening of HCQ-induced complications. The American Academy of Ophthalmology (AAO) has recently published their revised recommendations on screening and dosing of HCQ. Risk of retinal toxicity is mainly determined by the two most significant risk factors: daily dose of HCQ (mg/kg/day) and duration of HCQ therapy (years). The AAO recommends a maximum daily HCQ dosage of <5.0 mg/kg real weight, to reduce the risk of toxicity.<sup>Marmor, 2016</sup>

**Objectives:** To raise more attention for the revised recommendation of the AAO, our patient organisation started an online survey asking patients with (systemic) autoimmune diseases which dose of HCQ (mg) they take on a daily basis.

**Methods:** Patients in the Netherlands were given the opportunity to complete the online survey at the website of the NVLE (Dutch patient association for people with Lupus Erythematosus, Anti-Phospholipid Syndrome, Systemic Sclerosis and Mixed Connective Tissue Disease) from July 26th – November 18th, 2017. The promotion of the survey took place solely through Social Media with a link to the survey. A total of 24 questions had to be filled in to complete the survey. Each individual was asked to write down their real weight (kg) for calculating the daily HCQ dosage (mg/kg/day).

**Results:** A total of 705 individuals completed the online survey. The daily dosage (mg/kg/day) was available from 645 patients. The majority were females (n=645) and diagnosed with (systemic) lupus erythematosus (n=518). The average dosage of HCQ was 4.50±1.68 mg/kg/day. The daily dosage of 5 mg/kg was exceeded by 258 of the patients (40%). Eighty-one individuals (12.6%) used a daily dosage of ≥5 mg/kg for more than 10 years. The most reported HCQ-induced complications were gastrointestinal complaints (n=55), problems with vision (n=43), and nausea (n=32).

**Conclusions:** Patients (and prescribing physicians) should be informed about risk of toxicity, proper dose levels, and the importance of regular annual screening. Physicians prescribing HCQ must aim for a daily HCQ dosage of less than 5.0 mg/kg/day, especially for patients using HCQ for already more than 10 years. (Inter)national guidelines regarding the screening and dosing of HCQ should be provided by the authorities to secure patient safety and reduce the frequency of (severe) retinal complications.

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FRIDAY, 15 JUNE 2018

#### SLE, Sjögren's and APS – clinical aspects (other than treatment)

#### FRI0341 LUPUS LOW DISEASE ACTIVITY STATE (LLDAS) VERSUS CLINICAL REMISSION AS TREATMENT TARGETS IN THE FIRST 18 MONTHS OF SYSTEMIC LUPUS ERYTHEMATOSUS MANAGEMENT

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**Background:** In the view of applying a treat to target (T2T) strategy in the management of systemic lupus erythematosus (SLE), a novel definition of minimal acceptable disease activity – the lupus low disease activity state (LLDAS)<sup>[1]</sup> – and clinical remission (CR)<sup>[2]</sup> were recently proposed.

**Objectives:** To compare attainability and outcomes of LLDAS and CR as treatment targets in the early stages of SLE management.

**Methods:** LLDAS and CR prevalence were analysed at 6 (T1) and 18 (T2) months after treatment initiation (T0) in a monocentric cohort of 107 (median disease duration 9.7 months) prospectively followed Caucasian SLE patients. LLDAS was defined as SLE disease activity index 2000 (SLEDAI-2K)≤4 without major organ activity and no new disease activity, physician global assessment (0–3)≤1, prednisone ≤7.5 mg/day and well-tolerated immunosuppressant dosages. CR was defined as clinical SLEDAI-2K=0 (increased anti-dsDNA and low complement were excluded) and prednisone ≤5 mg/day in patients treated with/without stable immunosuppressants and/or antimalarials. Multivariate models were built to identify factors associated with failure to achieve LLDAS and CR, as well as to investigate relationship between the latter and early damage accrual (defined as SLICC/Damage Index≥1 at T2).

**Results:** LLDAS was achieved significantly more frequently than CR both at T1 [47 (43.9%) vs. 25 (23.4%); p<0.001] and T2 [48 (44.9%) vs. 35 (32.7%); p<0.001]. Out patients achieving LLDAS, 25 (53.2%) and 35 (66.7%) concomitantly fulfilled the criteria for CR at T1 and T2, respectively. A prednisolone (PDN) dose exceeding the minimal acceptable range set in the respective definitions was the most frequent reason for failure to achieve both LLDAS and CR (in 83.0% of no-LLDAS patients at T1% and 95.1% of no-CR at T1). The disease manifestations with the highest persistence rate during follow-up were: increased anti-dsDNA (persistently present in 85.7% and 67.5% of cases at T1 and T2, respectively), low complement (73.2% and 66.3%) and renal abnormalities (46.4% and 28.6%). Renal involvement at baseline significantly associated with failure to achieve LLDAS both at T1 (OR: 7.8, 95% CI: 1.41–43.40; p=0.019) and T2 (OR: 3.87, 95% CI 1.41–10.6; p=0.008) and CR at T2 (OR 9.46, 95% CI 1.13–78.8). High PDN dosage was significantly associated with no-CR achievement both at T1 (OR 6.23, 95% CI 2.2–18.3; p=0.01) and T2 (OR 1.11, 95% CI 1.02–1.20; p=0.02). Early damage was recorded in 23 (21.5%) patients and was significantly associated, on multivariate analysis, with older age at diagnosis (OR 1.05 95% CI 1.01–1.09; p=0.016) and failure to achieve LLDAS (OR 4.82, 95% CI 1.44–16.09; p=0.11) at T1. No significant association was found between early damage and failure to achieve CR, possibly due to its low prevalence among this cohort of early SLE patients.

**Conclusions:** During the early stages of SLE, LLDAS and CR overlap definitely less frequently than reported in long-standing disease (53.2%–66.7% vs 83.9%–96.5%<sup>[2]</sup>). Although remission is recommended as the primary treatment target in SLE, LLDAS may represent a valid alternative in the first stages of disease management, being more attainable compared to CR and negatively associated to early damage.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.2774

**FRI0342 DOES UNDERSTANDING SLE MATTER TO DISEASE ACTIVITY IN SLE PATIENTS?**

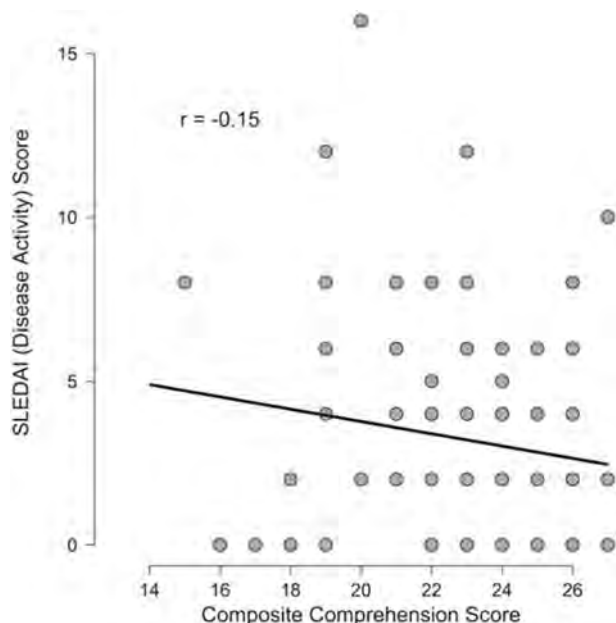
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**Background:** Systemic lupus erythematosus (SLE) is a heterogeneous disease with high morbidity and mortality with complex long-term treatments. These dynamic treatments can be daunting especially to the 25%–60% of SLE patients who have cognitive and neuropsychiatric deficits. Patients lacking understanding of their own baseline health status and treatment options cannot effectively collaborate in making informed choices with their physicians.

**Objectives:** This project aimed to identify SLE patients' comprehension of their medication regimens and disease outcomes in relation to standard markers of disease activity (SLEDAI) and damage (SLICC DI).

**Methods:** Patients >18 years were recruited from The Ohio State University (OSU) Lupus Vasculitis Glomerulonephritis (LVG) clinic. An IRB-approved 25-item true/false disease questionnaire was administered to 75 SLE patients who provided informed consent. Individual question and composite scores for each patient were correlated with their SLEDAI and SLICC DI scores. To our knowledge, a disease comprehension questionnaire has never been used in lupus patients.

**Results:** 75 SLE patients completed the comprehension questionnaire. Lower comprehension was associated with greater disease activity ( $r = -0.14$ ), while no correlation was found between composite score and disease damage (SLICC DI) ( $r = -0.03$ ). Figures 1 plot the comprehension composite scores against the SLEDAI. P values were not significant, but trending to correlate with the r. Evaluation of individual questionnaire items demonstrated: approximately 80% of patients did not associate heart disease with lupus, over 25% of patients did not recognise the side effects of prednisone, and over 15% of patients did not know lupus affects bone health.



**Conclusions:** These preliminary results suggest that patients with more understanding of their SLE diagnosis, comorbidities, and treatments had less measured disease activity. The comprehension questionnaire and SLEDAI characterize patients in their present disease state, so this correlation likely reflects the evolution of patient understanding and the fluctuating nature of their disease. Alternatively, higher disease activity scores represent more severe disease, which could be associated with greater neurocognitive deficits leading to poorer scores on the comprehension questionnaire. The lack of correlation between composite score and SLICC DI is likely attributed to the discrepancy between a metric evaluating current knowledge and a long-term indicator that may derive from decisions made when patients' comprehension was different than current. These initial results are promising and may represent a cost-effective opportunity for physicians to evaluate and address their patients' comprehension gaps in an effort to improve shared decision making. However, more data are needed to test the robustness of these trends.

**Disclosure of Interest:** None declared

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**FRI0343 BLOOD CONCENTRATIONS OF COMPLEMENT SPLIT PRODUCT IC3B AND SERUM C3 ASSOCIATE WITH SLE DISEASE ACTIVITY**

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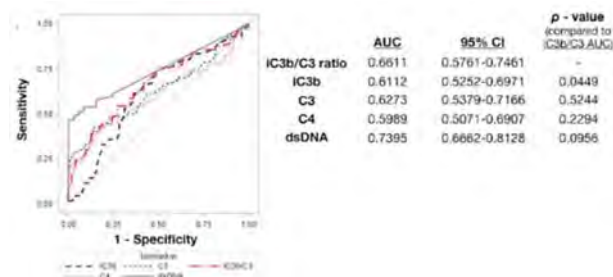
**Background:** The complement system plays a central role in systemic lupus erythematosus (SLE). Since complement activation occurs during SLE flares, complement proteins are predicted to be consumed with concomitant generation of activation-derived products at a rate proportional to the degree of disease activity. However, interpretation of values may be confounded due to the unknown impact of increased acute phase production of C3 and C4, as well as in individuals with low C4 gene copy number who have persistently low serum C4.

Improved detection of complement activation would enhance clinicians' ability to more readily assess SLE disease activity and promptly identify and treat flares. We hypothesize that complement split products are more sensitive measures of complement activation and better correlate with SLE disease activity.

**Objectives:** To examine correlations between blood levels of complement split product iC3b and serum component C3 with clinically meaningful changes in disease activity in patients with SLE.

**Methods:** 159 consecutive subjects with American College of Rheumatology or Systemic Lupus International Collaborating Clinics classified SLE were enrolled into CASTLE (Complement Activation Signatures in Systemic Lupus Erythematosus), a prospective observational study. Patients with 1–7 study visits were included in this longitudinal analysis. 48 healthy volunteers were enrolled to establish the normal reference range of iC3b/C3. Serum C3 and C4 were measured by nephelometry. Blood levels of iC3b were assessed by a lateral flow assay. SLE disease activity was monitored utilizing the Systemic Lupus Erythematosus Disease Activity Index 2K Responder Index-50 instrument.

**Results:** iC3b/C3 ratio, double-stranded (ds)DNA antibodies (Abs), and supra-physiologic prednisone dose (>7.5 mg/day) each independently correlated with SLE disease activity employing multilevel multiple logistic regression analysis. Only iC3b/C3 was significantly associated with clinically meaningful improvements in disease activity among subjects receiving supraphysiologic doses of prednisone (high disease activity). iC3b/C3 outperformed C3 and C4 levels in discriminating both active versus inactive SLE disease and major flares versus no disease activity (figure 1). Finally, iC3b/C3, dsDNA Abs, ESR, and supra-physiologic prednisone dose were independently associated with lupus nephritis, while none were associated with SLE rash.



**Abstract FRI0343 – Figure 1.** ROC curves of iC3b/C3, iC3b, C3, C4, and dsDNA levels distinguishing new major flares from subjects with no SLE activity

**Conclusions:** Blood iC3b/C3 ratio correlates with SLE disease activity and clinically meaningful improvement in disease activity. Furthermore, it discriminates between active versus inactive SLE, and major flares compared to those patients without disease activity.

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Inc., C. Stiening Employee of: Kypha, Inc., J. Atkinson Consultant for: Kypha, Inc., Compliment Corporation, Gemini Therapeutics, Inc., Celldex Therapeutics, Clinical Pharmacy Services, CDMI, Omeros Corporation, Achillion Pharmaceuticals, Inc., True North Therapeutics, BioMarin Pharmaceutical, Inc., Annexon Biosciences, Inc., and AdMiRx, Inc.

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#### FRI0344 SERUM FREE LIGHT CHAINS AS A FLARE BIOMARKER IN SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Complement levels are already known as biomarkers of flare in systemic lupus erythematosus (SLE); currently the usefulness of free light chains (FLC) in different autoimmune diseases in which the B cell has a relevant pathogenic role, as in the case of SLE, is being investigated.

**Objectives:** To explore the usefulness of FLC determination as a flare biomarker in patients with SLE and to analyse possible discriminative differences between FLC and complement C3 and C4 levels.

**Methods:** We performed an uncentric prospective longitudinal study with the following inclusion criteria: age greater than 18 years old and fulfilment of ACR or SLICC criteria for the diagnosis of SLE. Exclusion criteria were non-SLE related haematological disease, severe infection and severe kidney disease (Crea>2 mg/dl) to avoid interferences with FLC clearance. SLE flare definition was based on the SFI index. Receiver operator curves (ROC) and calculation of the area under the curve (AUC) were used to compare the discriminative ability between FLC and C3-C4 levels.

**Results:** 46 patients were enrolled. For the present communication, only baseline data were analysed. 41 (91%) patients were women. Most frequent clinical manifestations were haematological (83%) and cutaneous (72%). Laboratory findings were 98% positive ANA, 67% positive antiDNAc, 54% decreased C3% and 39% decreased C4. 6 (13%) patients presented a SLE flare and their characteristics compared to non-flare patients were lower C3 levels (70 vs 95; p=0,017) and C4 levels (10 vs 17; p=0,008) with higher concentrations of lambda light chains ( $\lambda$  LC) (27 vs 19; p=0,028). In addition, flare patients had higher IgA levels (402 vs 250; p=0,029), higher score in the global assessment of the doctor (4.3 vs 1.6; p=0,0003), longer time disease evolution (17.8 vs 14.3 years; p=0,844), higher values of SLEDAI (2.7±2 vs 1.4±1.3; p=0,083) and higher lymphopenia (982 vs 1474; p=0,068). We found no association between FLC levels and the presence of antiDNAc. The correlation of FLC with the rest of activity biomarkers (C3, C4, SLEDAI, VAS) occurred in the expected way although the magnitude of the association was moderate, with a higher correlation between C3 and  $\lambda$  LC.  $\lambda$  LC were the only FLC that showed ability to discriminate flares (AUC 0.781), with sensitivity 100%, specificity 65% and 69.6% of patients correctly classified for a cut-off point  $\geq 19.5$ . On the other hand, C3 and C4 also had a high discrimination capacity for flare (AUC 0.804 and 0.837 respectively). Comparing the three parameters, C4 achieved the highest AUC (0.837, 95% CI: 0.663–1000).

**Conclusions:** Lambda free light chains have a good discrimination capacity for SLE flares and could be useful as a SLE flare biomarker. Longitudinal studies with a larger number of patients are necessary to evaluate its usefulness as a flare predictor.

**Disclosure of Interest:** None declared

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#### FRI0345 ASSOCIATION BETWEEN CIGARETTE SMOKING AND SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) – AN UPDATED META-ANALYSIS OF CASE-CONTROL AND COHORT STUDIES

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**Background:** While the association between cigarette smoking and the occurrence of SLE has been studied over the past two decades, conflicting results have rendered such association controversial. With the global increase in woman smokers and more prospective data addressing the risk of the development of SLE and cigarette smoking being available, it is timely to provide an update on the evidence of the relationship between cigarette smoking and the occurrence of SLE.

**Objectives:** To study the association between cigarette smoking and the odds, as well as the risk of SLE occurrence by meta-analyses of case-control and cohort studies.

**Methods:** We performed an extensive literature search using the relevant keywords including “systemic lupus erythematosus”; “lupus”; “smoking”; “cigarette smoking”; “environmental”; “autoimmune disease” and “connective tissue disease” in various combinations to identify case-control and cohort studies addressing the relationship between cigarette smoking and SLE published in English in computerised databases including PubMed (from 1966 to , Jan 2018 Embase (1980 to Jan 2018 and Cochrane Central Register of Control Trials (last quarter of 2017). Effect sizes were pooled as odds ratio (OR) and relative risk (RR) and the corresponding 95% CI for case-control and cohort studies, respectively. Heterogeneity was studied by  $I^2$ . If the effect sizes were associated with low heterogeneity ( $I^2 < 40$ ), the fixed effects model was used. Otherwise ( $I^2 \geq 40$ ), the random effects model was used, based on the model suggested by DerSimonian and Laird.

**Results:** Thirteen relevant studies (10 retrospective case-control and 3 cohort) were selected for these meta-analyses. Data were aggregated based on smoking statuses comprising current, past, ever and never smoking. Analyses of case-control studies revealed significant relationships between the occurrence of SLE and current smoking (OR 1.639 [1.171–2.295], p=0.004,  $I^2=85.8$ ), and ever smoking (OR 1.438 [1.037–1.995], p=0.029,  $I^2=86.3$ ). However, no significant relationship was found between the occurrence of SLE and past smoking (OR 1.208 [0.853–1.711], p=0.286  $I^2=74.7$ ). While no relationship was found between the development of SLE and current smoking (RR 1.002 [0.680–1.475], p=0.994,  $I^2=51.6$ ), and ever smoking (RR 1.163 [0.944–1.433], p=0.157,  $I^2=0$ ) when the effect sizes of cohort studies were amalgamated, a significant risk in the development of SLE was found amongst ex-smokers compared with never smokers when the prospective data were combined (RR 1.351 [1.085–1.681], p=0.007,  $I^2=28.0$ ).

**Conclusions:** Smoking is associated with the occurrence of SLE based on the aggregation of effect sizes from case-control and cohort studies. The higher risk of development of SLE in ex-smokers but not among current and ever smokers compared to never smokers based on prospective data warrants further mechanistic studies to unravel the actual immunologic impact of cigarette smoke on SLE development in different subsets of SLE patients.

**Disclosure of Interest:** None declared

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#### FRI0346 NEUTROPENIA IN SYSTEMIC LUPUS: PREVALENCE, SPECIFIC FEATURES AND CLINICAL CONSEQUENCES. RESULTS FROM THE LARGE UPPER RHINE DATABASE LBBR

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**Background:** The prevalence, pathophysiology and underlying causes or consequences of neutropenia in systemic lupus erythematosus (SLE) are still not well defined even if neutropenia seems to be rather common in this disease.<sup>1</sup>

**Objectives:** To evaluate the prevalence of neutropenia in a large cohort of SLE patients and to identify correlation between neutropenia and other socio-demographical, clinical, serological or therapeutic factors.

To precise the influence of chronicity or severity of neutropenia in the course of SLE.

**Methods:** We used the LBBR database, a cross-sectional collection of detailed socio-demographic, clinical, serological and therapeutic data from 1,078 SLE patients (14 french or german Upper Rhine Hospitals).

Neutropenia was defined by the presence of less than 1800 circulating neutrophils  $\times 10^9/L$ . Patients with and without neutropenia were compared considering 47 variables.

The second part of the study focused on a subgroup of SLE LBBR patients for which full data were available about the duration and depth of neutropenia. Chronic neutropenia was defined by neutrophils count less than 1,500  $\times 10^9/L$  during at least 6 months and moderate and severe neutropenias were defined by neutrophils count less than 1,000  $\times 10^9/L$ .

**Results:** Among 1078 SLE patients, 223 (20.7%) were registered with neutropenia during their history. Mean age and sex ratio were comparable to the whole SLE cohort and to patients without neutropenia (mean age: 43.9 years old, sex ratio: 194 F/28 M). In multivariate analysis, neutropenia was associated with lymphopenia (OR=3.44 (2.48–4.80), p=0.0002) and thrombopenia (OR=3.59 (2.55–5.06), p=0.0002). There was no association with susceptibility to infections (OR 0.97 (0.52–1.80), p=0.6640), neither with SLEDAI score, SLE treatments or other ACR criteria.

Sixty-five patients out of 223, for which deepness and duration of neutropenia were available, were compared with patients without neutropenia. Moderate and severe neutropenias were again statistically associated with lymphopenia (OR 11.25 (2.60–48.61),  $p=0.0468$ ) and thrombopenia (OR 8.1 (3.28–19.99),  $p=0.0014$ ). There was again no association with susceptibility to infections or with treatment at sampling. In this group, using multivariate analysis, chronic neutropenia was statistically associated with lymphopenia (OR 9.48 (2.83–31.71),  $p=0.0177$ ), low C3 (OR 3.81 (1.59–9.14),  $p=0.0053$ ), anti-SSA antibodies (OR 2.40 (1.07–5.39),  $p=0.0042$ ) and Sjögren syndrome (2.56 (0.93–7.03),  $p=0.0435$ ).

**Conclusions:** The large LBBR cohort allows an approach of neutropenia prevalence and characteristics in SLE. Neutropenia concerns about 20% of SLE patients. Considering multivariate analysis, it is not directly linked to treatment and appears separated from infections occurrence, even when severe. Neutropenia in SLE is significantly associated with thrombopenia and lymphopenia, defining a subtype of SLE patients with haematological features and suggesting possible common pathophysiology.

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**Disclosure of Interest:** None declared

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#### FRI0347 PERFORMANCE OF POTENTIAL DEFINITIONS OF REMISSION IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) VERSUS QUALITY OF LIFE OVER 5 YEARS IN SWEDISH PATIENTS WITH RECENT-ONSET SLE

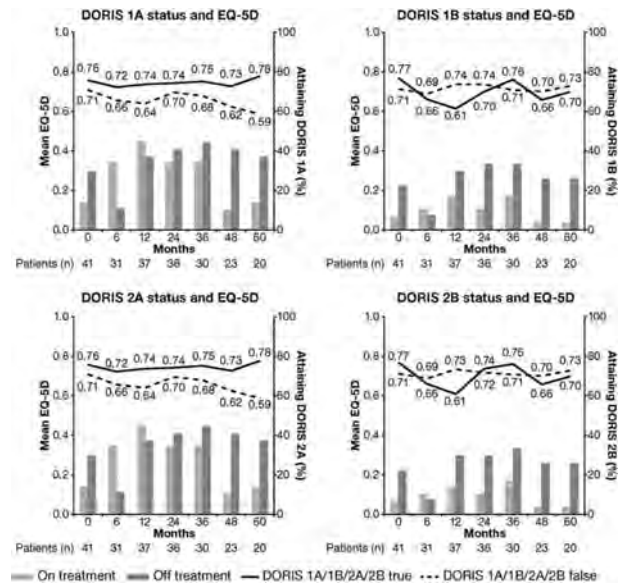
M. Björk<sup>1</sup>, R. Heijke<sup>1</sup>, M. Frodlund<sup>1</sup>, S. Ramagopalan<sup>2</sup>, E. Alemao<sup>3</sup>, C. Sjöwall<sup>1</sup>.  
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**Background:** Remission constitutes a desirable goal in the management and treatment of patients with systemic lupus erythematosus (SLE), but no universally accepted definition exists. Based on established disease activity measures (e.g. clinical SLE Disease Activity Index [cSLEDAI], physician's global assessment [PhGA] and British Isles Lupus Assessment Group [BILAG] index), serology (anti-double-stranded DNA antibodies and low complement) and ongoing therapy, an international task force recently suggested four preliminary definitions of remission in SLE (DORIS).<sup>1</sup> However, the definitions did not include any patient-reported outcome measures (PROMs).

**Objectives:** Using data from well-characterised Swedish patients with recent-onset SLE included in the KLURING (*Clinical Lupus Register In Northeastern Gothia*) cohort, we aimed to describe the performance of the four definitions over 5 years in relation to PROMs and quality of life (QoL) as defined by EuroQoL-5 Dimensions (EQ-5D).

**Methods:** Patients with SLE who met the 1982 ACR and/or the 2012 Systemic Lupus International Collaborating Clinics (SLICC) classification criteria were included and followed prospectively from the time point of SLE diagnosis. Patients were (at least) seen by a rheumatologist at Months 0 (inclusion), 6, 12, 24, 36, 48 and 60, with collection of disease activity measures, damage accrual, serology, therapy and PROMs such as fatigue, pain intensity, well-being (all visual analogue scale) and QoL (EQ-5D). Definitions of remission were: **DORIS 1A:** cSLEDAI 0, PhGA <0.5; **DORIS 1B:** cSLEDAI 0, PhGA <0.5, serology normal; **DORIS 2A:** PhGA <0.5, BILAG D/E only; **DORIS 2B:** PhGA <0.5, serology normal, BILAG D/E only. Each definition could be reached either on or off treatment (maintenance with antimalarials only was allowed).<sup>1</sup> The effect on QoL of achieving versus not achieving remission was assessed using multilevel regression modelling.

**Results:** A total of 41 patients were included in the study: median (interquartile range) age at baseline 39 years, (18–77) 33/41 (81%) female, 35/41 (85%) white and 18/41 (44%) former/current tobacco smokers. The median number of fulfilled 1982 ACR criteria was 4 (range 3–9) and 15/41 (37%) had lupus nephritis. Using DORIS 1A or 2A, patients with SLE achieving versus not achieving remission had higher QoL ( $p=0.01$ ), whether on or off treatment (figure 1). This association remained significant after adjusting for sex, tobacco smoking and treatment in multivariable analysis. Achieving remission according to DORIS 1B ( $p=0.93$ ) or 2B ( $p=0.86$ ) was not significantly decisive for QoL (figure 1).



**Abstract FRI0347 – Figure 1.** Months Since SLE Diagnosis

Bars represent % pts attaining remission (on vs off treatment) and lines represent mean EQ-5D (QoL) for pts (meeting vs not the definition of remission) at each time point since SLE onset

**Conclusions:** This pilot study demonstrates the first real-life performance of the suggested preliminary definitions of remission in SLE. Higher QoL was associated with achieving remission as defined by DORIS 1A or 2A. However, further evaluation of the accuracy of DORIS in larger longitudinal studies of recent-onset SLE is required before introduction in routine clinical practice.

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#### FRI0348 MBL2 GENE POLYMORPHISMS AND ITS ASSOCIATION WITH INFECTION IN BRAZILIAN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: A 10-YEAR STUDY

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**Background:** Systemic lupus erythematosus (SLE) is a multifactorial disease and *MBL2* genetics variants potentially affect its etiology and increase infection risk in this population. Systemic lupus erythematosus (SLE) is a multifactorial disease and *MBL2* genetics variants potentially affect its etiology and increase infection risk in this population.

**Objectives:** To evaluate the relation of *MBL2* gene polymorphisms of the coding and promoter region and their respective haplotypes on hospitalisation, number of admissions and days of admission for major infection causes in Brazilian SLE patients.

**Methods:** Three hundred and twenty-five SLE patients from a southern Brazilian outpatient SLE clinic were genotyped in 2006 for *MBL2* gene polymorphisms from coding and promoter region (rs1800450, rs1800451, rs5030737, rs11003125, and rs7096206) and followed until 2016. Clinical and laboratory data from each patient was obtained and information regarding the need for hospitalisation, the number of admissions and amount of days admitted for infection treatment were compiled and compared with *MBL2* gene polymorphisms and haplotypes. A linear regression analysis was constructed considering the variables of bivariate which demonstrated an association ( $p<0.05$ ) and variables which had a theoretical basement.

**Results:** No difference was found in polymorphism prevalence when comparing the group that was admitted for infection treatment and the group who did not. Allele C, and haplotypes LY and HY correlated with more infection hospitalizations (normal homozygosity for C: 2 (IQR 1–3), heterozygosity for C: 3 (IQR 2–6)  $p=0.038$ ; LY 2 (IQR 1–3)  $p=0.049$ ; HY 2 (IQR 1–3)  $p=0.005$ ) and haplotype HY staid fewer days in hospital for infection treatment: 18 (IQR 10–38)  $p=0.041$ . The table 1 shows the results after regression model was applied.

**Abstract FRI0348 – Table 1.** Linear regression model for days admitted for infection and total admissions for infection treatment.

Variables *	Days admitted for infection <sup>a</sup>		Total admissions for infection <sup>a</sup>	
	Coef B (IC 95%) <sup>†</sup>	p-value <sup>‡</sup>	Coef B (IC 95%) <sup>†</sup>	p-value <sup>‡</sup>
Haplotype HY of MBL2 gene	-18.11 (-33.48– -2.75)	0.021	-1.52 (-2.42– -0.62)	0.001
Haplotype LY of MBL2 gene			0.04 (-0.26– 1.55)	0.164
Allele C of MBL2 gene			1.22 (-0.15– 2.60)	0.082
<b>Serostitis</b>				
Haplotype HY regression model	14.00 (-0.008–26.02)	0.050	0.44 (-0.37–1.26)	0.280
Haplotype LY regression model			0.53 (-0.32–1.36)	0.221
Allele C regression model			0.55 (-0.28–1.30)	0.195
<b>Nephritis</b>				
Haplotype HY regression model	11.11 (-3.84–25.88)	0.138	-0.21 (-1.07–0.65)	0.629
Haplotype LY regression model			-0.01 (-0.91–0.89)	0.972
Allele C regression model			0.03 (-0.83–0.90)	0.937
<b>Myoephenolite</b>				
Haplotype HY regression model	11.44 (-14.33–37.21)	0.380	0.44 (-1.05–1.95)	0.557
Haplotype LY regression model			0.34 (-1.23–1.93)	0.064
Allele C regression model			-0.02 (-1.62–1.56)	0.979
<b>Corticoid need until 3 months before admission</b>				
Haplotype HY regression model	13.07 (-4.22–30.36)	0.136	0.67 (0.33–1.66)	0.197
Haplotype LY regression model			0.62 (-0.44–1.66)	0.249
Allele C regression model			0.53 (-0.51–1.58)	0.312
<b>Age at diagnose</b>				
Haplotype HY regression model	-0.40 (-0.98–0.17)	0.166	-0.64 (-0.98– -0.01)	0.006
Haplotype LY regression model			-0.04 (-0.98– -0.61)	0.010
Allele C regression model			-0.04 (-0.07– -0.095)	0.013
<b>SLECC</b>				
Haplotype HY regression model	1.70 (-2.5–5.9)	0.422	-0.04 (-0.29–0.19)	0.692
Haplotype LY regression model			-0.02 (-0.27–0.23)	0.889
Allele C regression model			-0.02 (-0.28–0.22)	0.831

<sup>a</sup>Were listed variables with p-value <0.05 in bivariate analyses besides age that were used to construct the multivariate model; <sup>b</sup> Variables with a p-value <0.05; <sup>c</sup> coef B (IC 95%) coefficient B and confidence interval of 95%; <sup>d</sup> Statistical significance was considered with a p-value <0.05.

**Conclusions:** The presence of the HY promoter haplotype leads to fewer in hospital care for infection treatment probably due to higher MBL plasma levels. Also, HY haplotype and older age at SLE diagnosis is related to less admissions for infection. It is important to consider that infection is a very import cause of mortality in SLE patients and not only related to aggressive immunosuppressive treatment.

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## FRI0349 LOW TITER ANTI-PHOSPHOLIPID ANTIBODIES CONVEY AN INCREASED OBSTETRIC RISK

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**Background:** Persistent positivity for anti-phospholipid antibodies (aPL) at medium-high titres is required to diagnose anti-phospholipid syndrome (APS), an

autoimmune condition characterised by thrombosis and/or pregnancy morbidity (PM). However, increasing evidence points towards the clinical relevance of low titre aPL in obstetric APS.

**Objectives:** This study investigated the association of low titre aPL with PM assessing the efficacy of low-dose aspirin (LDASA) and low-molecular weight heparin (LMWH).

**Methods:** Data on pregnancies in women with persistent aPL positivity at any titre were retrospectively collected at a single centre. An association model for repeated measures was applied to quantify the obstetric risk conveyed by low titre and criteria aPL, allowing to: i) evaluate pregnancy outcomes over time using available longitudinal data; ii) account that pregnancies of the same woman are not independent events; iii) consider that women had a different number of pregnancies; iv) estimate the role of several confounders and predictors. The association model envisaged as dependent variable pregnancy outcome as a binary outcome, defined for each pregnancy as “obstetric complication yes versus no” (pregnancy loss before 10 weeks, pregnancy loss after 10 weeks, premature birth before 34 weeks, according to updated APS classification criteria [Miyakis et al]).

**Results:** One hundred eleven women were recruited in this study: 160 pregnancies in women with low titer aPL and 178 pregnancies in women with criteria aPL. According to the association model, women with low titre aPL had a probability of PM of 63% (odds 1.72, 95% CI 1.05–2.80) in case of single positivity and of 79% (odds 3.78, 95% CI 1.96–7.30) in case of double positivity. Criteria aPL conveyed a 2.2-fold higher risk: the probability of PM was 79% in case of single positivity (odds 3.82, 95% CI 2.15–6.80), raising to 89% (8.41, 95% CI 3.99–17.73) for multiple aPL.

LDASA-treated women with single low titer aPL positivity had a 16% probability of experiencing an adverse outcome (odds 0.19, 95% CI 0.08–0.44) while LDASA did not significantly affect the probability of in patients with low titre double aPL positivity (odds 0.42, 95% CI 0.17–1.02). Similarly, LDASA significantly reduced PM among women with single, but not multiple, criteria aPL positivity (odds 0.42, 95% CI 0.19–0.94; odds 0.93, 95% CI 0.39–2.21). Among women treated with LDASA +LMWH, the probability of PM was 14% in case of single low titre aPL positivity (odds 0.17, 95% CI 0.08–0.37) and 28% in case of two low titre aPL (odds 0.38, 95% CI 0.18–0.80). Among women with aPL criteria, treatment with LDASA +LMWH reduced the probability of PM to 28% (odds 0.38, 95% CI 0.21–0.70) in case of a single positive test and, not significantly, to 45% (odds 0.84, 95% CI 0.45–1.55) in case of multiple positivities.

Parameter	Estimate	SE	z-value	OR [95%CI]	P
<b><math>\beta_0</math> Intercept</b>	0.54	0.25	2.17	1.72 [1.05–2.80]	0.030
<b>Covariates</b>					
$\beta_1$ =Criteria aPL vs low aPL	0.80	0.31	2.55	2.23 [1.20–4.13]	0.011
$\beta_2$ =Multiple vs single aPL	0.79	0.29	2.74	2.20 [1.25–3.86]	0.006
$\beta_3$ =LDASA vs no LDASA	-2.20	0.40	-5.54	0.11 [0.05–0.24]	<<0.001
$\beta_4$ =LMWH vs no LMWH	-1.85	0.77	-2.41	0.16 [0.03–0.71]	0.016
<b>Confounders</b>					
$\beta_5$ =LDASA*LMWH	1.74	0.86	2.01		0.044
$\beta_6$ =Age≥35 vs age<35	0.19	0.26	0.73		0.466
$\beta_7$ =HCQ vs no HCQ	-0.22	0.43	-0.52		0.600
$\tau$	1.07	0.04	25.88		

**Conclusions:** Low titre aPL are associated with PM; the association treatment with LDASA and LMWH is effective even among women with low titre aPL. The risk of PM and the response to treatment depend upon aPL profile, suggesting the importance of a tailored treatment.

**Disclosure of Interest:** None declared

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FRI0350

### LUPUS LOW DISEASE ACTIVITY STATE (LLDAS-50) IS A SIGNIFICANT PREDICTOR FOR DAMAGE ACCRUAL AND MORTALITY: A NORWEGIAN COHORT ANALYSIS

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**Background:** Disease activity in patients with Systemic Lupus Erythematosus (SLE) is an important contributor to organ damage and premature mortality. Current indices to capture disease activity are not well suited to reflect their contribution to long term outcome. Lupus Low Disease Activity State (LLDAS) has been developed as an alternative measure of long term disease activity.

**Objectives:** To determine whether 50% of time spent in Lupus Low Disease Activity State (LLDAS-50) impacts on mortality and damage accrual in SLE

**Methods:** A retrospective analysis of prospectively collected data was conducted on 3650 clinic visits by 207 patients in the Tromsø Lupus Cohort. Lupus Low Disease Activity State –50 (LLDAS50) score was defined as at least 50% of follow-up time with SLE Disease Activity Index (SLEDAI)  $\leq$ 4, no new disease activity, prednisone  $\leq$ 7.5 mg/day and no escalation of maintenance immunosuppressant therapy. Cox regression analysis was used to evaluate the impact of LLDAS50 in terms of mortality and damage development (either new or severe) by Systemic Lupus Erythematosus Clinical Criteria (SLICC)/American College of Rheumatology (ACR) Damage Index (SDI). New damage was defined as a rise in SDI by 1 from baseline whereas severe damage was defined as a rise of 3 points or more from baseline.

**Results:** The median age at diagnosis of the cohort was 34 years with the majority (84%) being female. The median follow-up time was 125 months. A total of 69 patients (33.5%) spent at least half of their follow up time in LDAS, thus achieving LLDAS50. After correction for age and gender, LLDAS-50 was associated with a significant reduction in risk of having any new damage (OR 0.65; 95% CI 0.44–0.96,  $p < 0.01$ ), severe damage (OR 0.46; 95% CI 0.25–0.83,  $p < 0.01$ ), and also a reduction in mortality risk (OR 0.42; 95% CI 0.21–0.82,  $p < 0.01$ ). These values were also tested for those patients who spent 30% or more time in LDAS, and were also found to be significant for death (OR 0.46, 95% CI 0.26–0.83,  $p < 0.05$ ) but not for new damage (OR 0.92, 95% CI 0.62–1.35,  $p = 0.67$ ) or severe damage (OR 0.71, 95% CI 0.42–1.19,  $p = 0.19$ ).

**Conclusions:** The significant reduction in the risk of long term damage and mortality supports the use of LLDAS50 as a therapeutic goal.

**Disclosure of Interest:** None declared

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FRI0351

### CLINICAL CHARACTERISTICS AND OUTCOMES OF EARLY-ONSET AND LATE-ONSET LUPUS NEPHRITIS AND ITS RISK FACTORS

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**Background:** The kidney is one of the most commonly involved major organ in systemic lupus erythematosus (SLE). It may occur as an initial presentation at the onset of SLE and it can also present later in the course of the disease.

**Objectives:** To compare clinical characteristics, management, and outcomes after 12 months in patients with early-onset lupus nephritis (LN) and late-onset LN and to assess the risk factors for late-onset LN.

**Methods:** Patients with lupus nephritis enrolled in the Hanyang BAE Lupus Cohort were retrospectively assessed. Patients who developed LN within one year of the diagnosis of SLE (early-onset) were compared with those who developed LN more than a year later from the diagnosis of SLE (late-onset). Clinical characteristics including the features of SLE, management, and outcomes including renal responses and SLE disease activity were assessed.

**Results:** From 1,294 SLE patients in the Hanyang BAE Lupus Cohort, 641 (49.5%) patients had LN. Early-onset LN was observed in 469 (73.2%) and late-onset LN in 172 (26.8%). Hypertension was more frequent in early-onset LN while malar rash, discoid rash, photosensitivity, oral ulcer, arthritis, leukopenia, anti-Sm Ab, and anti-RNP Ab were more frequent in late-onset LN. Late-onset LN patients also showed lower C3 and higher activity index in renal biopsy. There was no significant difference in ISN/RPS classification and in induction therapy. SLEDAI score at onset of LN and after 12 months was similar in the two groups. Complete and partial response rates at six months and twelve months were also similar and there were no differences in progression to end-stage renal disease or death between the two groups. Multivariate analysis identified younger age at onset, malar rash, arthritis, serositis, anti-dsDNA Ab, and anti-Sm Ab as independent risk factors for late-onset LN.

**Abstract FRI0351 – Table 1.** Clinical characteristics

	Early-onset LN (n=469)	Late-onset LN (n=172)	No LN (n=653)
Age at onset, mean $\pm$ SD, years	23.84 $\pm$ 10.38	22.66 $\pm$ 8.55	26.73 $\pm$ 10.51
Female, n (%)	417 (88.91)	161 (93.60)	615 (94.18)
Time to LN, mean $\pm$ SD, years	0.06 $\pm$ 0.19	5.48 $\pm$ 4.42	
Malar rash	200 (42.64)	105 (61.05)	262 (40.12)
Discoid rash	20 (4.26)	17 (9.88)	56 (8.58)
Photosensitivity	123 (26.23)	74 (43.02)	248 (37.98)
Oral ulcer	136 (29.00)	67 (38.95)	246 (37.67)
Arthritis	243 (51.81)	131 (76.16)	449 (68.76)
Serositis	152 (32.41)	46 (26.74)	120 (18.38)
Neurologic disorder	35 (7.46)	10 (5.81)	28 (4.29)
Hematologic disorder	383 (81.66)	147 (85.47)	539 (82.54)
Immunologic disorder	421 (89.77)	164 (95.35)	550 (84.23)
ANA positivity, %	469 (100.00)	172 (100.00)	653 (100.00)
Anti-SSa, %	150 (33.56)	69 (42.59)	265 (41.41)
Anti-SSb, %	33 (7.38)	10 (6.17)	40 (6.25)
Anti-RNP, %	130 (29.08)	62 (38.27)	219 (34.27)
Antiphospholipid Ab, %	124 (26.44)	57 (33.14)	219 (33.54)
Proteinuria, g	2.55 $\pm$ 2.43	2.45 $\pm$ 2.48	
SLEDAI	6.71 $\pm$ 4.75	7.20 $\pm$ 4.80	3.98 $\pm$ 2.86

**Conclusions:** Late-onset LN patients showed more mucocutaneous symptoms, autoantibodies, and higher activity index in renal biopsy compared to early-onset. However, there were no differences in outcomes after 12 months. Younger age at onset, malar rash, arthritis, serositis, anti-dsDNA Ab, and anti-Sm Ab were risk factors for late-onset LN.

**Disclosure of Interest:** None declared

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FRI0352

### DAMAGE ACCRUAL IN A LARGE MONOCENTRIC COHORT OF PRIMARY SJÖGREN'S SYNDROME PATIENTS: DETERMINANTS AND IMPACT ON PATIENT REPORTED OUTCOMES

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**Background:** Primary Sjögren's Syndrome (pSS) is a chronic progressive disease potentially leading to irreversible organ damage. To date only a limited number of studies have analysed prevalence and factors associated with damage accrual in pSS.

**Objectives:** a) to characterise cumulative damage in pSS patients, b) to identify determinants associated with its presence and c) to evaluate the impact of damage on patient reported outcomes (PROs).

**Methods:** Data from a monocentric cohort of 466 pSS patients were analysed. Glandular and extra-glandular damage manifestations were assessed by the Sjögren's Syndrome Disease Index (SSDDI). Additional items of damage defined 'a priori' as being potentially related to treatment (i.e osteoporosis, diabetes, infections) were analysed separately. The EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) was used to measure disease activity at baseline and prospectively during the follow-up. The EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI), Oral Health Impact Profile (OHIP) and Ocular Surface Disease Index (OSDI) were utilised to record PROs. Patients' comorbidities were assessed by the Charlson Comorbidity Index (CCI).

**Results:** A total of 466 pSS patients (446 F:20 M, median age (IQR): 59 years (48–69) were included in the study. The frequency of anti-Ro-SSA in the cohort was 69.5% (324/466). The median ESSDAI was 4 (IQR 1–8) at baseline and 2 (IQR 0–5) at the last evaluation, respectively. In addition to symptomatic agents, patients had been treated during the disease course with low-medium doses of glucocorticoids (GCs) (56%), hydroxychloroquine (HCQ) (62%) and DMARDs (16.6%). After a median follow-up of 5 years (IQR, 2–10), 208 patients (44.6%) had accrued some damage in either the oral damage items (33%), ocular damage items (20%) and/or systemic damage items (12%). In addition, 24/466 patients had developed a non-Hodgkin lymphoma and 2 patients a multiple myeloma. The SSDDI score ranged from 0 to 14. In the regression analysis: patients more likely to develop damage were those that were older, with a longer disease duration, higher baseline ESSDAI and who had been treated with DMARDs, whereas patients who had been ever treated with HCQ were less likely to develop disease-related damage. Similarly, treatment-related damage was independently associated with: disease duration, age of the patients, baseline ESSDAI, anti-Ro/SSA

positivity and use of GCs. Oral and ocular damage items significantly correlated with ESSPRI, OHIP and OSDI, whereas systemic damage items positively correlated with patients CCI.

**Conclusions:** This large pSS cohort confirmed that demographic and clinical characteristics as well as medication are independently associated with disease-related and treatment-related damage. In particular, this study shows a highly significant impact of baseline disease activity on the development of future damage and poor PROs in pSS patients.

**Disclosure of Interest:** None declared

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**FRI0353 DEVELOPMENT AND VALIDATION OF QUESTIONNAIRES TO ASSESS HEALTHCARE UTILISATION AND ACCESS IN COHORTS OF PATIENTS WITH PRIMARY SJOÖGREN'S SYNDROME AT THE DIAGNOSIS AND DURING THE DISEASE COURSE**

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**Background:** The geographic variation in healthcare spending, utilisation and quality, across and within countries is well documented. Part of this geographic variation is linked to differences in population health and needs. However, some of the variation may be unwarranted and driven by factors including provider discretion, availability and distribution of resources, financing and reimbursement models.

**Objectives:** To develop and validate an instrument a) to assess the pSS patients' experience and satisfaction along their clinical pathway including both primary care services and specialists, b) to collect comparable information in Europe to establish practice profiles in the diagnosis, management and treatment of patients with primary Sjögren's Syndrome (pSS).

**Methods:** The questionnaire consists of 32 items and collects patient-reported data on: type and intensity of treatments and services received (e.g. diagnostic testing, hospitalizations, specialist visits), costs, patients' satisfaction with the care received and general information covering patients' overall health, education, ethnicity and marital status. A narrative-based medicine section is also included in the questionnaire administered to newly diagnosed patients to explore their journey to pSS diagnosis. Additionally, a short questionnaire is administered to the specialists treating the pSS patients to collect data on the organisation of their clinical centres.

**Results:** The pilot version of the questionnaire was administered to 164 pSS patients (mean (SD) age: 60 (12.2) yrs) from 6 clinical centres. The majority of the respondents had a primary or secondary school (59%). Disease activity was significantly associated with frequency of rheumatologic visits and diagnostic tests ( $p < 0.001$ ). Both the total number of specialists involved in the care other than the rheumatologist and the number of treatments received in the last 12 months before the interview varies significantly among patients and across centres ( $p < 0.001$ ). Patients with lower education have attended on average less specialists than those with a high school or university degree ( $p < 0.001$ ). Construct validity was supported by the questionnaire's ability to discriminate between groups with different levels of activity of the disease and socio-demographic characteristics.

**Conclusions:** Preliminary results confirm that the questionnaire is a valid instrument to assess and compare patterns of care for pSS patients in terms of access and utilisation of treatments and services across and within providers. Patient-reported data linked with available information from clinical records will allow to measure quality of care more comprehensively and to identify best practices and opportunities for improvement, enhance care outcomes, and increase value for patients. Further analysis will be conducted in other clinical centres within the European Horizon2020 project "HarmonicSS" to verify the generalizability and additional psychometric properties of the instrument before collecting data across and within countries

**Disclosure of Interest:** None declared

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**FRI0354 URINE METABOLOMIC FINGERPRINT AS DIAGNOSTIC BIOMARKER FOR LUPUS NEPHRITIS**

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**Background:** Lupus nephritis (LN) represents the main prognostic factor for worsening in systemic lupus erythematosus (LES).<sup>1</sup> The relevant classes of LN –due to the need of treatment- are the proliferative (III, IV, III/IV+V) and membranous (V).

**Objectives:** The aim of the study was to find a urinary metabolomic fingerprint to diagnose proliferative and/or membranous LN.

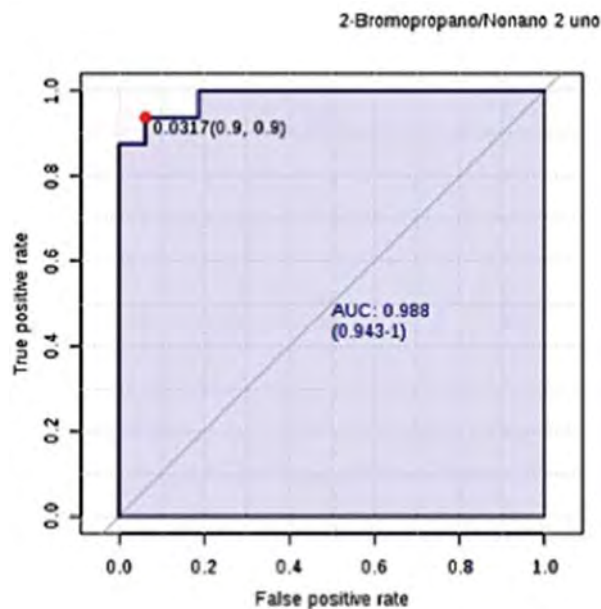
**Methods:** Cross-sectional study. Inclusion criteria: lupus patients with and without clinical significant lupus nephritis (classes III, IV, V and mixed classes). Urine samples were screened for metabolites using gas chromatography mass spectrometry (coupled with electronic nose). Statistical analysis: principal component analysis (PCA), and for the selection of the metabolites we used Random Forest.

**Results:** We included 29 lupus patients, 11 with LN. The median SLEDAI score in LN patients was of 13 vs. 3 in those without NL ( $p < 0.0001$ ). Class IV nephritis was present in 45%, mixed class in 36%, and class V in 18%. The median proteinuria of patients with NL was 1 g/L, (IQR 2.7).

The variance explained using the first two principal components was 80%.

With random forest we selected, 2 nonanone, as the metabolite with the best diagnostic accuracy, (sensitivity of 0.87 and specificity of 0.93) of proliferative LN. Obtaining the ratio of 2-bromopropane/2-nonanone, the diagnostic accuracy improved, with a positive likelihood ratio (LR) of 14 and a negative LR of 0.1 (AUC 90%).

Metabolic pathways involved in LN were: methane, glycolysis, pyruvate and glycerophospholipid pathways.



**Conclusions:** We identified a urinary metabolomic fingerprint that involved several metabolic pathways; 2-nonanone and the ratio of 2-bromopropane/2-nonanone had the best diagnostic accuracy in our study.

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**Disclosure of Interest:** None declared

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FRI0355

### PREDICTIVE ABILITY OF AVAILABLE 10 YEARS CARDIO-VASCULAR RISK ALGORITHMS IN SYSTEMIC LUPUS ERYTHEMATOSUS: A RETROSPECTIVE STUDY ON 2 ITALIAN LUPUS COHORT

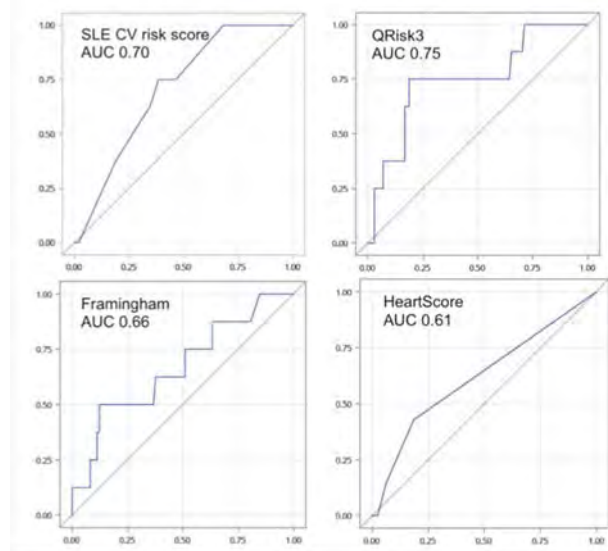
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**Background:** Patients with Systemic Lupus Erythematosus (SLE) present an increased incidence of Cardio-Vascular Events (CVE) compared to general population, and the difference with healthy subjects is particularly evident in young SLE women.

**Objectives:** The aim of this study is to assess the predictive ability of established 10 years CV risk models in SLE

**Methods:** A retrospective analysis of two Italian SLE prospective cohorts was performed. SLE patients without previous CVE, with age  $\geq 25$  years, a minimum continuative follow-up of 10 years and sufficient data to calculate the 10 years risk scores were enrolled. The 10 years CVE risk scores were calculated at the first observation and all CVE were prospectively recorded in the following 10 years. We calculated the following scores: the QRisk3, the Framingham CV disease 10 years score, the HeartScore (Europe Low Risk) and the SLE CV Risk Score proposed by Petri et al. Discriminatory ability for CV risk prediction was estimated by the area under the receiver operating characteristic curve. Hosmer-Lemeshov (HL) tests was used to evaluate calibration comparing the observed versus expected number of events

**Results:** Analysis was performed on 131 SLE patients (mean baseline age of 37  $\pm 11$  years). We observed 10 CVE during the 10 years follow-up from baseline (3 acute coronary syndrome, 4 stroke, 1 transitory ischaemic attack and 2 peripheral artery disease). The AUC values were 0.75 (95% CI 0.55–0.94) for QRisk3, 0.66 (0.45–0.88) for Framingham score, 0.62 (0.41–0.82) for the HeartScore and 0.7 (95% CI 0.55–0.85) for the SLE CV risk score. The p values of HL test were 0.8 for QRisk3 and SLE CV score and 0.4 for Framingham score and HeartScore, suggesting a good model fit for all the CV risk scores. Considering scores with better discriminative ability and calibration, 20% of CVE were observed with QRisk3 score lower than 3.6% and with SLE CV risk score between 6% and 8%. Discriminative ability and calibration were not improved by multiplying by 2 the Framingham score and the HeartScore.



**Conclusions:** The available CV risk scores demonstrate a moderate predictive ability of 10 years CVE in SLE. We observed a better model fit for QRisk3 and SLE CV risk score. Nevertheless, a considerable proportion of patients, with very low predicted CV risk, developed CVE during follow-up.

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FRI0356

### ORGAN DAMAGE IN SYSTEMIC LUPUS ERYTHEMATOSUS IS CONSISTENTLY ASSOCIATED WITH INCREASED MORTALITY: A META-ANALYSIS

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**Background:** More than half of all patients with systemic lupus erythematosus (SLE) develop organ damage over time, including damage to the kidney, skin, cardiovascular, musculoskeletal and central nervous systems. Several mechanisms have been associated with organ damage, including long-term steroid use. SLE organ damage, like comorbid disease, may contribute to increased mortality.

**Objectives:** We conducted a systematic literature review and meta-analysis of the association between organ damage in SLE and mortality.

**Methods:** A literature search (January 2000–February 2017) of PubMed, EMBASE, Cochrane Library, and Latin American and Caribbean Health Sciences Literature from four continents evaluating organ damage by the Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SDI) and mortality was conducted. Exclusion criteria included non-English language articles and study designs that did not report original, population-level measures of association. We used a random-effects meta-analysis to evaluate studies that modelled SDI as a continuous predictor of mortality and reported hazard ratios (HR) associated with a 1-unit SDI increase.

**Results:** The search yielded 10 420 articles, of which, 21 prospective cohort studies were selected. Ten studies evaluating SDI as a continuous variable and reporting HR as measure of association were pooled and meta-analysed. The pooled HR of mortality for a 1-unit increase in SDI was 1.34 (95% confidence interval [CI]: 1.21–1.44;  $p < 0.001$ ). A study of 213 patients followed for 13 years in China yielded the greatest risk of mortality for a 1-unit SDI increase (HR 3.65, [95% CI: 1.52–8.76]). When excluded from the meta-analysis, the pooled HR of mortality for a 1-unit increase in SDI was 1.32 (95% CI: 1.25–1.42;  $p < 0.001$ ). Four studies that evaluated SDI as binary variable reported HR for various SDI reference groups: SDI=0: HR 5.10 (95% CI: 1.99–13.03); SDI<1: HR 3.8 (95% CI: 1.30–16.40); SDI<3: HR 4.74 (95% CI: 1.55–14.51); and SDI<5: HR 55.12 (95% CI: 19.15–158.63). Two studies reported odds ratios (OR) as the measure of association; for a 1-unit SDI increase, the OR was 19.7 (95% CI: 5.30–72.50), and for SDI=0 as reference group, the OR was 12 (95% CI: 1.60–92.00).

**Conclusions:** Organ damage in SLE is consistently associated with increased mortality across studies from various countries, regardless of how it is modelled. Novel therapies that are potentially disease modifying and steroid sparing could reduce organ damage, improve overall outcomes, and decrease mortality in patients with SLE.

**Disclosure of Interest:** E. Hammond Employee of: AstraZeneca, I. Murimi: None declared, D. Lin: None declared, H. Nab Employee of: AstraZeneca, H. Kan Shareholder of: GlaxoSmithKline, O. Onasanya: None declared, J. Tierce: None declared, X. Wang Employee of: AstraZeneca, B. Desta Employee of: AstraZeneca, G. C. Alexander Consultant for: Chair of the FDA's Peripheral and Central Nervous System Advisory Committee, serves as a paid consultant to IQVIA, serves on the Advisory Board of MesaRx Innovations, and serves as a paid member of OptumRx's National P and T Committee. This arrangement has been reviewed and approved by Johns Hopkins University in accordance with its conflict of interest policies.

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FRI0357

### VALIDATION OF A DISEASE-SPECIFIC HEALTH – RELATED QUALITY OF LIFE MEASURE FOR RUSSIAN ADULT PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: LUPUSQOL-RUSSIAN

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**Background:** Improvements in the survival of patients with systemic lupus erythematosus (SLE) in Russia have to some extent paralleled that seen worldwide over the last 20 years, but have at times come at the cost of increased morbidity and reduction in health-related quality of Life (HRQoL). Recently, a specific questionnaire to evaluate HRQoL in adult SLE patients (LupusQoL) has been developed and validated in United Kingdom and in several European countries.

**Objectives:** To assess the validity of a LupusQoL-Russian in adult SLE patients **Methods:** The LupusQoL-Russian was administered to a cohort of Russian patients affected with SLE. To perform a control, QoL was evaluated also with SF-36. The Russian version of LupusQoL questionnaire was developed by the University of Central Lancashire and the East Lancashire Hospitals NHS Trust ([www.lupusqol.com](http://www.lupusqol.com)), after a linguistic validation process. Disease activity was evaluated by the SLEDAI-2K, and chronic damage by the Systemic Lupus International



Collaborating Clinics Damage Index score (SDI). Internal consistency and test-retest reliability, convergent and discriminant validity were examined.

**Results:** 328 Russian SLE patients were enrolled in the study (M/F 30/298, mean age 34.4±11.5 years, mean disease duration 106.3±97.9 months; mean SLEDAI 2K 9.6±8.0; mean SDI 0.2±0.6). The LupusQoL-Russian demonstrated substantial evidence of construct validity. Each domain showed good correlation when compared with equivalent domains of the SF-36 ( $p<0.001$  for all comparisons). LupusQoL-Russian discriminated between patients with different degrees of disease activity according to SLEDAI 2K: Lupus-QoL domains showed a trend to lower values in patients with higher disease activity (SLEDAI-2K $\geq$ 4) compared with those with lower disease activity (SLEDAI 2K<4), reaching statistically significant difference when considering the domains "Pain", "Planning", "Intimate relationship" and "Body image" ( $p=0.007$ ,  $p=0.0004$ ,  $p=0.003$  and  $p=0.007$ , respectively).

LupusQoL-Russian was significantly lower for "Physical health", "Planning" and "Fatigue" in patients with SDI $\geq$ 1 ( $p=0.002$ ,  $p=0.03$ , and  $p=0.03$ ) respectively (table 1). Test-retest reliability was good to excellent between baseline and day 3 (intra-class correlation coefficient (ICC) 0.7–0.9)

Abstract FRI0357 – Table 1. External divergent validity (N=328)

Domain	SLEDAI-2K $\leq$ 4 (n=113)	SLEDAI-2K $\geq$ 4 (n=215)	p-value	SDI $\leq$ 1 (n=142)	SDI $\geq$ 1 (n=186)	p-value
Physical health, mean $\pm$ SD	70,1 $\pm$ 22,0	64,9 $\pm$ 23,6	0,07	71,01 $\pm$ 22,5	63,3 $\pm$ 23,1	0002
Pain, mean $\pm$ SD	74,7 $\pm$ 23,6	67,5 $\pm$ 24,8	0007	72,3 $\pm$ 24,2	68,2 $\pm$ 24,8	0,1
Planning, mean $\pm$ SD	71,1 $\pm$ 27,9	60,1 $\pm$ 28,0	0,0004	67,7 $\pm$ 27,3	60,9 $\pm$ 29,0	0,03
Intimate relationship, mean $\pm$ SD	78,3 $\pm$ 28,7	69,9 $\pm$ 31,7	0003	76,06 $\pm$ 28,4	70,6 $\pm$ 32,5	0,22
Burden to others, mean $\pm$ SD	61,2 $\pm$ 26,8	54,2 $\pm$ 28,0	0,03	55,7 $\pm$ 28,4	57,4 $\pm$ 27,3	0,68
Emotional health, mean $\pm$ SD	67,3 $\pm$ 24,8	63,2 $\pm$ 24,6	0,13	66,2 $\pm$ 25,2	63,3 $\pm$ 24,3	0,24
Body image, mean $\pm$ SD	71,1 $\pm$ 24,7	62,02 $\pm$ 28,5	0007	66,6 $\pm$ 27,9	64,03 $\pm$ 27,3	0,33
Fatigue, mean $\pm$ SD	65,0 $\pm$ 24,5	65,09 $\pm$ 24,8	0,22	65,7 $\pm$ 25,3	60,35 $\pm$ 24,0	0,03

**Conclusions:** The LupusQoL-Russian is valid to assess quality of life in SLE patients

**Disclosure of Interest:** None declared

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#### FRI0358 FACTORS ASSOCIATED WITH PULMONARY MANIFESTATIONS IN SJÖGREN SYNDROME

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**Background:** Primary Sjögren's Syndrome (pSS) is a systemic autoimmune disorder characterised by lymphocytic infiltration of the exocrine glands resulting in dry syndrome. Approximately one-third of patients have extraglandular systemic findings, such as respiratory symptoms (43%–75%), that are also considered to be a cause of morbidity and conditioning quality of life. The aim of the study is to estimate the prevalence of pulmonary manifestations in pSS, and to identify factors associated with its development.

**Methods:** SJOGREN-SER (Spanish Rheumatology Society Registry of pSS) is a multicenter cross-sectional study of pSS patients under active follow-up at 33 rheumatology departments through Spain. Patients fulfilled the European-American consensus criteria of 2002. Airway disease (dry cough, xerotrachea, bronchial, hyperresponsiveness and airway obstruction) and pulmonary involvement (ILD, pulmonary amyloidosis, pulmonary arterial hypertension, vasculitis and pleural involvement) were considered according to the definition contained in EULAR Sjögren's Disease Activity Index (ESSDAI), as well as Sjögren's

Syndrome Disease Damage Index. Bivariate logistic regression models and multivariate analysis were used to establish the independent effect of patient characteristics associated with pulmonary manifestations. The results were considered significant when the P value was less than 0.05.

**Results:** The SJOGREN-SER registry included 437 patients (95% women, median age at inclusion 59 years [50–68 years] and mean of ESSDAI 2 (IQR 0–4)). One hundred and seventeen patients (26.8%) had pulmonary manifestations (19.2% airway disease and 9.8% pulmonary involvement). Ten patients presented both. Sociodemographic characteristics were: mean age 59.5 years (SD: 11.46), 94.9% women and 19.6% smokers or former smokers. Patients with pulmonary manifestations had higher ESSDAI score (6 (SD 6) vs 4 (SD 5)), prolonged disease duration (10.05 years (SD: 7.15) vs 7.7 (SD 6.3)) and were ANA positive more frequently (94.9% vs 62.2%). Airway involvement preceded or occurred at the time of diagnosis in 46.4% of patients. Pulmonary involvement occurred 5 years after the diagnosis of pSS in 37.2% of them. [RS1] Twenty-nine patients (6.6%) were diagnosed with ILD. The most frequent radiological patterns were: Non-Specific Interstitial Pneumonia n=14, Usual Interstitial Pneumonia n=5, Lymphocytic Interstitial Pneumonia n=5 and Cryptogenic Organised Pneumonia n=2. Stepwise multivariate analysis was performed including the following variables: sex, age, laboratory findings, disease duration, smoking and ESSDAI. Disease duration (OR of 1.05 (95% CI, 1.006–1.083)), ESSDAI score (OR of 1.044 (95% CI, 1.006–1.083)) and positivity for ANA (OR of 3.725 (95% CI, 1.141–12.159)) were found to be associated factors with pulmonary involvement in pSS.

**Conclusions:** Prevalence of pulmonary manifestations in this cohort of pSS patients is substantial due to both airway disease and pulmonary involvement. Disease duration, activity of pSS according to ESSDAI score and ANA positivity were factors associated with the development of pulmonary manifestation.

**Disclosure of Interest:** None declared

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#### FRI0359 ROUTINE CLINICAL PATHOLOGY MEASUREMENTS ARE ASSOCIATED WITH RISK OF ORGAN DAMAGE ACCRUAL IN SLE

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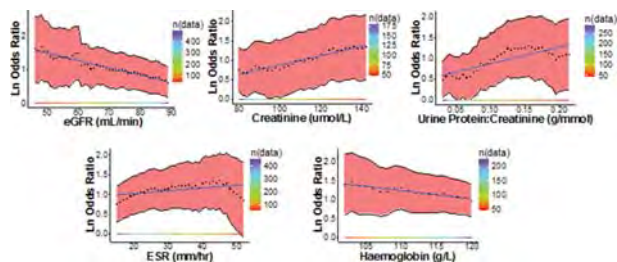
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**Background:** Prevention of permanent organ damage, a major predictor of morbidity and mortality, is a key goal in the treatment of SLE. Physician-measured disease activity scores, which entail some subjectivity, are associated with damage accrual risk, but there have been few studies of objective measures as indicators of organ damage risk. Routine pathology laboratory measurements provide objective biological data, but their association with damage accrual in SLE has not been studied.

**Objectives:** To evaluate the association of objective pathology laboratory measurements with risk of organ damage accrual in SLE.

**Methods:** A dataset of SLE patients between 2007–2017 from the Australian Lupus Registry and Biobank was studied. Variables recorded prospectively included disease activity (SLEDAI-2k), drug treatment and 16 routine pathology measurements at each visit, and organ damage (SLICC-SDI) annually. Longitudinal patient data was split into annual periods, and each visit classified as being either in a "transition" or "non-transition" period based on whether SDI increased during that period. Time adjusted means (TAMs) of the variables were calculated for each period, and multivariable logistic regression analysis of the association with being in a "transition" period (adjusting for age, gender, race, previous organ damage and prednisolone dose) was performed, with Holm-Bonferroni correction. An "odds ratio plot" was generated to depict the effect on risk of organ damage accrual at each threshold of the continuous variables.

**Results:** 893 periods, comprising 5082 visits from 245 patients (85.6% female, 50.2% Caucasian), were analysed. Five out of 16 laboratory variables: estimated glomerular filtration rate (eGFR), creatinine ( $p<0.01$ ), urine protein:creatinine ratio ( $p<0.01$ ), ESR ( $p<0.001$ ), and haemoglobin ( $p<0.001$ ) were significantly associated with risk of damage increase. Moreover, the odds of damage increase were approximately proportional to the deviation of each of these variables from its respective normal range. SLEDAI-2k was also significantly associated with damage increase ( $p<0.001$ ), but the association of SLEDAI-2k with damage did not exhibit this proportionality.



**Abstract FRI0359 – Figure 1.** Ln (natural log) odds ratio for damage transition vs time-adjusted mean of laboratory variables. Red region (95% CI) lying above the  $y=0$  line indicates the risk is statically significant ( $p<0.05$ ). Regression lines (blue) suggest the risk of damage increase is approximately proportional with the distance from normal pathology measure range.

**Conclusions:** Routine pathology measures were found to be proportionally associated with organ damage risk in SLE. The potential for the use of these measures as biomarkers, for example to generate an organ damage risk calculator for SLE, warrants further research.

**Disclosure of Interest:** None declared

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### FRI0360 DISEASE SEVERITY OF PROLIFERATIVE LUPUS NEPHRITIS IN MAGHREBIANS

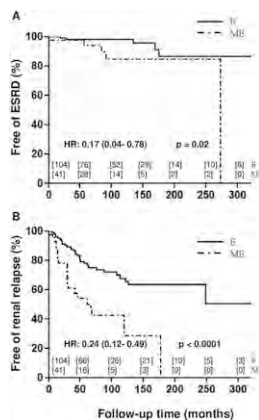
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**Background:** The negative influence of African-American ethnicity on the prognosis of lupus nephritis (LN) is well known but – to the best of our knowledge – the impact of Maghrebian ethnicity has never been evaluated, although the disease is purported to be quite prevalent and severe in North Africa.

**Objectives:** To study the influence of Maghrebian ethnicity on the clinical and pathological presentation of LN, the renal relapse rate, the renal and overall survival and the predictive value of an early proteinuria decrease for good long-term renal outcome in this population compared to native Europeans.

**Methods:** We retrospectively reviewed the files of an inception cohort of 194 patients with proliferative LN followed in 7 lupus centres belonging to three groups: Europeans living in Belgium/France (E;  $n=111$ ), Maghrebians living in Europe, *in casu* Belgium/France (ME;  $n=43$ ) and Maghrebians living in Morocco (MM;  $n=40$ ). Baseline presentation was compared between these 3 groups but complete long-term outcome data were available only for E and ME patients.

**Results:** At presentation, clinical (gender, age, nephrotic syndrome, serum creatinine, eGFR, uP/C ratio) and pathological (ISN/RPS class) characteristics of LN did not differ between E, ME and MM patients. At one year, renal remission was met in 73%, 63% and 68% in E, ME and MM patients, respectively. Achievement of a target proteinuria below 0.7 g/day one year after treatment initiation was 76%, 63% and 68%, respectively. Nevertheless, while proteinuria measured at month 12 accurately predicted a serum creatinine value  $<1$  mg/dl at 7 years in E patients, this was not the case in the ME group, in whom serum creatinine at month 12 performed better. Renal relapses were more common in ME patients (54% than in E patients (29%) ( $p<0.01$ ). Time to renal flare and to ESRD was shorter in ME patients compared to E patients ( $p<0.0001$  and  $p<0.05$ , respectively) as shown in figure 1. At last follow-up, mean proteinuria, serum creatinine and eGFR did not differ between E and ME patients, nor did the percentage of patients who died or suffered from ESRD or permanent renal impairment.



**Conclusions:** Despite a similar disease profile at onset, the prognosis of LN is more severe in Maghrebians living in Europe compared to native Europeans, with a higher relapse rate and a shorter time to ESRD.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.3070

### FRI0361 PREGNANCY OUTCOMES AND THERAPY IN SYSTEMIC LUPUS ERYTHEMATOSUS: RESULTS FROM OUR 30 YEARS' EXPERIENCE PREGNANCY CLINIC

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**Background:** The outcome of Systemic Lupus Erythematosus (SLE) pregnancies has dramatically improved thanks to pregnancy planning, multidisciplinary management and close monitoring during pregnancy. In our experience, programmed pregnancies in SLE patients had similar rates of pregnancy losses as compared to general obstetric population, but there are still open issues on some pregnancy complications that more frequently affect SLE patients.

**Objectives:** To analyse the obstetric outcome of SLE patients, according to specific therapy received during pregnancy.

**Methods:** A monocentric, retrospective study of 98 SLE patients with a total of 134 pregnancies followed prospectively by multidisciplinary team (1987–2015). Adverse Pregnancy Outcomes (APOs) were defined as one of the followings: premature miscarriage ( $<10$  th week), intrauterine fetal death ( $>10$  th week), perinatal death ( $<30$  th day of life), severe preterm birth ( $<34$  th week) and preterm birth (between 34th–36th weeks). We also evaluated the frequency of other pregnancy complications such as preterm premature rupture of membranes (pPROM) and pre-eclampsia (PE).

**Results:** Among the 134 pregnancies (including 3 twin pregnancies), flares occurred in 10 (7.5%) and APOs in 39 (29.1%) cases (table 1). pPROM complicated 9 pregnancies, all resulted in preterm deliveries, including 3 severe preterm birth; PE complicated 6 pregnancies resulting in 2 preterm birth, 1 intrauterine fetal death, 1 perinatal death and 2 term birth. The rates of APOs, pPROM and PE were compared according to receiving or not a specific therapy: hydroxychloroquine (HCQ), low dose aspirin (LDA), immunosuppressant (IS) during the overall pregnancy and corticosteroids  $>35$  mg/week (CS) during the 1st, the 2nd and the 3rd trimester. No statistical significant association was found between a specific therapy and the rate of PE. HCQ and LDA did not significantly affected the rate of APOs or pPROM while pregnancies exposed to IS showed a higher frequency of APOs (47% vs 20%,  $p.0.003$ ), in particular premature miscarriages (16% vs 2%,  $p.0.007$ ). Pregnancies exposed to CS had higher frequency of APOs (1st trimester 44% vs 28%,  $p.0.015$ ; 2nd trimester 36% vs 13%  $p.0.004$ ; 3rd trimester 34% vs 14%,  $p.0.019$ ). Considering only the 120 pregnancies resulted in live birth, those exposed to CS had higher frequency of preterm birth (1st trimester  $p.0.006$ ; 2nd trimester  $p.0.023$ ; 3rd trimester  $p.0.011$ ) (table 2). In particular, pregnancies exposed to CS in the 1st trimester had higher frequency of preterm birth on 34th–36th w ( $p.0.017$ ), while pregnancies exposed in the 3rd trimester had a higher frequency of preterm birth before 34th w ( $p.0.038$ ). Furthermore, a higher frequency of pPROM was observed in those exposed to CS (1st trimester  $p.0.001$ ; 2nd trimester  $p.0.003$ ; 3rd trimester  $p.0.001$ ).

**Abstract FRI0361 – Table 1.** frequency of APOs, pPROM and PE in the 134 analysed pregnancies

	N (%)
<b>N of live birth</b>	<b>120 (90%)</b>
<b>N of APOs</b>	<b>39 (29%)</b>
<b>Premature miscarriage (&lt;10<sup>th</sup> w)</b>	<b>9 (7%)</b>
<b>Intrauterine fetal death (&gt;10<sup>th</sup> w)</b>	<b>5 (4%)</b>
<i>with PE</i>	<i>1 (20%)</i>
<b>Perinatal death (&lt;30<sup>th</sup> day of life)</b>	<b>1 (1%)</b>
<i>with PE</i>	<i>1 (100%)</i>
<b>All preterm birth (&lt;37<sup>th</sup> w)</b>	<b>24 (18%)</b>
<b>Preterm birth (&lt;34<sup>th</sup> w)</b>	<b>3 (2%)</b>
<i>with pPROM</i>	<i>2 (67%)</i>
<b>Preterm birth (34<sup>th</sup>-36<sup>th</sup> w)</b>	<b>21 (16%)</b>
<i>with pPROM</i>	<i>7 (33%)</i>
<i>with PE</i>	<i>2 (10%)</i>

**Abstract FRI0361 – Table 2.** frequency of preterm birth and pPROM among the 120 live birth, according to exposure (or not) to corticosteroids >35 mg/week during the three trimesters

	CS >35w*	CS 0 or ≤35mg/w*	p*	CS >35w**	CS 0 or ≤35mg/w**	p**	CS >35w***	CS 0 or ≤35mg/w***	p***
<b>N of pregnancies</b>	39	81	-	48	72	-	41	79	-
All preterm birth (<37 <sup>th</sup> w)	14 (36%)	10 (12%)	0.006	15 (31%)	9 (13%)	0.023	14 (34%)	10 (13%)	0.011
Preterm birth (<34 <sup>th</sup> w)	2 (5%)	1 (1%)	0.246	3 (6%)	0 (0%)	0.616	3 (7%)	0 (0%)	0.038
Preterm birth (34 <sup>th</sup> -36 <sup>th</sup> w)	12 (31%)	9 (11%)	0.017	12 (25%)	9 (14)	0.128	11 (27%)	10 (13%)	0.092
pPROM	8 (21%)	1 (1%)	0.004	8 (17%)	1 (1%)	0.003	8 (20%)	1 (1%)	0.001

\* 1<sup>st</sup> trimester; \*\* 2<sup>nd</sup> trimester; \*\*\* 3<sup>rd</sup> trimester

**Conclusions:** Use of IS seems to be associated with premature miscarriages; this could reflect their use in patients with a more severe disease phenotype. The exposure to CS in doses greater than 35 mg/w in the 1<sup>st</sup> trimester seems to be associated with preterm birth at 34<sup>th</sup>-36<sup>th</sup> w, while in the 3<sup>rd</sup> trimester with severe preterm birth (<34<sup>th</sup> w), that could be related to the strong association observed between CS use and pPROM.

**Disclosure of Interest:** None declared

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### FRI0362 PREVALENCE, RISK FACTORS, AND IMPACT ON MORTALITY OF NEUROPSYCHIATRIC LUPUS: A LARGE PROSPECTIVE SINGLE-CENTRE STUDY

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**Background:** Neuropsychiatric involvement is one of the most serious involvement of SLE and generally associated with a worse prognosis. However, previous reports about the prevalence and risk factors of neuropsychiatric systemic lupus erythematosus (NPSLE) have yielded inconsistent findings. Also, there are only few studies of the prognosis of NPSLE, especially in a large prospective cohort.

**Objectives:** To identify the prevalence, risk profiles, and impact on mortality of NPSLE.

**Methods:** Patients from the Hanyang BAE lupus cohort were registered and followed from 1998 to 2015. Demographics, autoantibodies, SLEDAI-2K and SLICC/ACR damage index were collected at baseline and then annually. Patients registered within 12 months of SLE development were grouped as the inception cohort and analysed separately to elucidate the clinical features at disease onset. NP manifestations were defined using the ACR 19 case definitions and Ainiola NPSLE that did not include minor NP events<sup>1</sup>. Mortality data were derived by linking data from the Korean National Statistics Office.

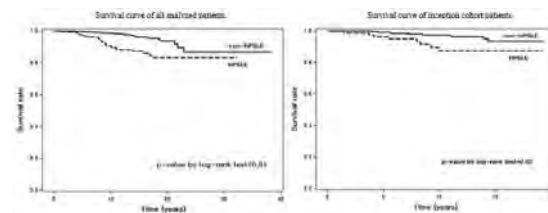
**Results:** The prevalence of NPSLE by ACR 19 case definition was 38.3%, and 19.3% by Ainiola criteria. Higher SLEDAI, APLA positivity, absence of anti-dsDNA antibody at SLE diagnosis and fewer years of education increased NPSLE risk.

Patients with any NPSLE manifestation had a three-fold increased risk of mortality (HR 3.09, p=0.04), and patients with focal CNS NPSLE showed nearly an eight-fold increased risk of mortality in SLE patients (HR=7.83, p<0.01). Among the 216 patients with Ainiola NPSLE, sixty-four (29.6%) had multiple events. The two most common symptom combinations were seizure with CVA (18 patients) and seizure with psychosis (8 patients).

**Abstract FRI0362 – Table 1.** Risk factors for the development of NPSLE in the inception cohort (N=388).

	NPSLE (n=88)	Non-NPSLE (n=300)	P	Adjusted OR (95% CI)	P
<b>Demographics</b>					
Age at SLE diagnosis	28.2 ±11.6	29.3±11.3	0.42	0.99 (0.97–1.01)	0.45
Female sex	81 (92.1)	270 (90.0)	0.71	1.88 (0.71–4.96)	0.20
SLEDAI at diagnosis, NP manifestations excluded <sup>a</sup>	4.7 ±4.5	3.8±3.3	0.10	1.08 (1.01–1.16)	0.02*
SDI at diagnosis, NP manifestations excluded <sup>b</sup>	0.2 ±0.4	0.1±0.4	0.43	1.23 (0.72–2.11)	0.45
HTN	5 (5.8)	16 (5.4)	1.00	1.14 (0.38–3.37)	0.82
Education (years)	12.2 ±3.1	13.0±3.3	0.05*	0.92 (0.85–1.00)	0.04*
Anti-dsDNA antibody positivity	61 (69.3)	238 (79.3)	0.07	0.43 (0.24–0.78)	<0.01*
APLA positivity	40 (45.5)	96 (32.0)	0.03*	1.72 (1.03–2.87)	0.04*

\*Values are number (percentage) or mean ±standard deviation. a. SLEDAI was calculated using the remaining items except CVA, seizure, organic brain syndrome, psychosis, visual disturbance, cranial nerve disorder. b.SDI was calculated using the remaining items except CVA, myelopathy, seizure, psychosis, cognitive impairment, carinal neuropathy, and peripheral neuropathy.



**Abstract FRI0362 – Figure 1.** Kaplan-Meier survival curves for NPSLE and non-NPSLE patients; Inception cohort and all analysed patients.

**Conclusions:** Higher SLEDAI, APLA positivity, absence of anti-dsDNA antibody at SLE diagnosis and fewer years of education are risk factors for development of NPSLE. Presence of NPSLE, especially focal CNS NPSLE, increased the risk of mortality in SLE patients.

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### FRI0363 POSITIVE REMODELLING INDEX AND LOW ATTENUATION NON-CALCIFIED CORONARY PLAQUES: MARKERS OF VULNERABLE CORONARY PLAQUES IN SYSTEMIC LUPUS?

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**Background:** Accelerated atherosclerosis leading to premature coronary artery disease remains the major cause of late death in SLE. Coronary plaques with a large necrotic/lipid core and/or a thin fibrous cap are prone to rupture, leading to acute coronary events. In coronary CT angiography, plaque lipid content correlates with lower CT attenuation values when compared with fibrotic tissue.



Positive (or outward) vessel remodelling has been postulated to explain the finding of atherosclerosis that does not encroach on the arterial lumen. Positive remodelling index and presence of low attenuation noncalcified plaque (<30 Hounsfield units) are characteristic vessel changes in unstable coronary plaques.

**Objectives:** We sought to characterise noncalcified plaque lesions in patients with systemic lupus erythematosus and to identify high risk lesions.

**Methods:** A total of 66 patients who meet the American College of Rheumatology classification criteria for SLE were included in the study. Of these, 30 patients had two studies. All patients underwent coronary CT angiography. Coronary plaque area was measured by manual tracing for the difference between the area within the external elastic membrane and the area of the vessel lumen at the site of maximal luminal narrowing as observed on a cross-sectional coronary CT angiography image. Each noncalcified plaque detected within the vessel wall was evaluated with the minimum CT density and vascular remodelling index (RI). Total low density plaque volume per patient and low density/high density noncalcified plaque ratio were then compared by patient characteristics which included age, sex, ethnicity, BMI, smoking, SLEDAI, PGA, anti-dsDNA, low complement, current prednisone, current hydroxychloroquine, current NSAID use, history of cardiovascular event, hypertension, lupus anticoagulant, antidiarrhoeal, hypercholesterolemia, and methotrexate use.

**Results:** All patients had at least one plaque with a positive remodelling index (>10%), and 83.1%(n=271) of total identified plaques had a positive remodelling index. Low density noncalcified plaque volume was associated with age ( $p<0.01$ ) and body mass index ( $p<0.01$ ). African Americans had significantly more ( $p<0.05$ ) low density noncalcified plaque compared to patients of other ethnicities. The low density/high density noncalcified plaque ratio did not correlate with any patient characteristics and was on average 46% (SD=10). There were only cardiovascular events in the studied group and there were no differences in remodelling index or low density noncalcified plaque observed in this group, but the number of events was small.

**Conclusions:** Positive remodelling index and low attenuation noncalcified plaques are characteristic vessel changes seen in unstable coronary plaques. They are common in patients with lupus and are significantly more likely to be seen among African American patients, patients with a BMI>30, and the elderly (age over 60).

**Disclosure of Interest:** None declared

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#### FRI0364 CLINICAL AND DIAGNOSTIC SIGNIFICANCE OF IMMUNOGLOBULIN A RHEUMATOID FACTOR IN PRIMARY SJOGREN'S SYNDROME

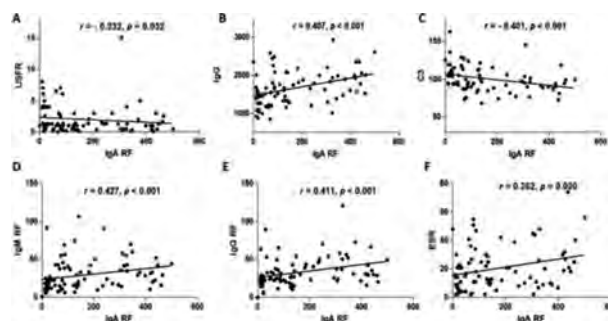
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**Background:** Rheumatoid factors (RFs) are among the autoantibodies associated with Primary Sjogren's syndrome (pSS). Although measurement of non-IgM RFs is not performed routinely in clinical practice due to technical difficulties, RFs can belong to any isotype. A few studies have suggested the prognostic value of non-IgM RFs in pSS. However, few studies evaluated the clinical and diagnostic value of non-IgM RF in pSS.

**Objectives:** This present study aimed to answer the question on whether the RF isotype has a potential diagnostic value for the detection of pSS, particularly for distinguishing pSS from idiopathic sicca syndrome. In addition, we assessed whether IgA RF may serve as a prognostic factor by evaluating their association with clinical and serological characteristics.

**Methods:** RF levels were measured in 85 and 38 patients with pSS and idiopathic sicca syndrome, respectively, using the ELISA and analysed with respect to clinical and laboratory disease characteristics. ROC curves were used to determine and compare the diagnostic accuracy of IgA RF with other diagnostic tests.

**Results:** Serum levels of IgA RF were significantly higher in patients with pSS than in those with idiopathic sicca syndrome. IgA RF showed a sensitivity, specificity, positive, and negative predictive value of 90.7%, 78.9%, 89.5%, and 81.1%, respectively, for pSS diagnosis. IgA RF was associated with xerostomia; abnormal Schirmer's test; severe sialoscintigraphic grade; low unstimulated salivary flow rate (USFR); antinuclear antibody and anti Ro/SSA positivity; high IgG and IgM/G RF levels; and low C3 levels in patients with pSS. IgA RF titres had positive correlations with sialoscintigraphic grade and IgG and IgG/M RF levels and had negative correlations with USFR, Schirmer's test value, and C3 levels (figure 1).



**Conclusions:** Our findings confirmed the potential of IgA RF to distinguish pSS from idiopathic sicca syndrome. The presence of IgA RF in patients with pSS was associated with significantly worse exocrine function and active serologic profile. No association between IgA RF and extra-glandular manifestations was noted.

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**Disclosure of Interest:** None declared

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#### FRI0365 FACTORS ASSOCIATED WITH LEFT VENTRICULAR DIASTOLIC DYSFUNCTION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Objectives:** Myocardial damage is common and often silent in patients with systemic lupus erythematosus (SLE). In this study, we investigated the clinical parameters associated with left ventricular diastolic dysfunction in SLE patients using algorithms of 2016 American Society of Echocardiography/European Association of Cardiovascular Imaging (ASE/EACVI) recommendations.

**Methods:** Sixty consecutive SLE patients and 38 controls matched for age and sex who were free of clinical cardiovascular disease were enrolled. Left ventricular diastolic dysfunction was assessed by echocardiography using 2016 ASE/EACVI guidelines. The demographic, clinical and laboratory data were obtained from medical records.

**Results:** Diastolic dysfunction was more common in SLE patients compared with controls (38.3% versus 13.2%,  $p=0.011$ ), while LV ejection fraction was not different between groups. When patients were divided into 2 groups according to the presence of diastolic dysfunction, patients with diastolic dysfunction had higher prevalence of hypertension ( $p<0.001$ ), dyslipidemia ( $p=0.031$ ) and chronic kidney disease ( $p=0.045$ ), but there was no difference between groups with regard to other organ involvement or autoantibody profile. Importantly, patients with diastolic dysfunction showed significantly higher SLICC/ACR damage index ( $p=0.001$ ) and C-reactive protein levels ( $p=0.005$ ). In multivariate regression analysis, hypertension (OR=16.6, 95% CI=3.466-79.479,  $p<0.001$ ), higher SLICC/ACR damage index (OR=1.68, 95% CI=1.039-2.720,  $p=0.034$ ), and CRP level (OR=1.12, 95% CI=1.004-1.254,  $p=0.042$ ) was independently associated with diastolic dysfunction in SLE patients.

**Conclusions:** Diastolic dysfunction is more common in SLE patients, and overall inflammatory burden reflected by SLICC/ACR damage index as well as conventional cardiovascular risk factors are associated with development of diastolic dysfunction in SLE patients.

**Disclosure of Interest:** None declared

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FRI0366

### PRIMARY RESPIRATORY DISEASE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: DATA FROM THE SPANISH RHEUMATOLOGY SOCIETY LUPUS REGISTRY (RELESSER) COHORT

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**Objectives:** To investigate the primary respiratory manifestations (PRM) in SLE. **Methods:** All patients in the RELESSER cohort were retrospectively investigated for the presence of PRM. **Results:** At least one PRM was present in 11.3% (365/3215) of cases. The most common was pleurisy, occurring in 21.1% of patients, followed by ALP in 3.6%, PE in 2.9%, PPH 4%, DILD in 2%, DAH in 0.8%, and SLS in 0.8%. The variables associated with the presence of PPM are shown in the following table 1:

	Odds Ratio	95% Confidence Interval	P
Age	1,03	1,02–1,04	0,000
SLEDAI score	1,03	1,00–1,07	0,02
Raynaud phenomenon	1,41	1,09–1,84	0,01
Severe nephritis	1,56	1,18–2,06	0,002
Secondary APS	2,2	1,63–2,97	0,000
Anti-RNP positivity	1,32	1,00–1,75	0,054
Cardiac disease	2,81	1,90–4,16	0,000
Vasculitis	1,81	1,25–2,62	0,002
Hematologic abnormalities	1,31	1,00–1,71	0,048
Neuropsychiatric manifestations	1,49	1,11–2,02	0,009
Gastrointestinal involvement	2,05	1,14–3,67	0,016

After adjusting for known confounders in the multivariable model, PPM remained a risk factor for diminished survival (HR: 3.13).

**Conclusions:** PPM independently contributed to a decreased survival in SLE

**Disclosure of Interest:** None declared

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FRI0367

### ASSOCIATION OF VITALITY AND SUBSEQUENT PHYSICAL FUNCTIONING IN SYSTEMIC LUPUS ERYTHEMATOSUS: ANALYSIS OF DATA FROM THE GERMAN LULA COHORT 2002 – 2013

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**Background:** Fatigue, defined as loss of vitality, is a major burden in patients with systemic lupus erythematosus (SLE). It is well-known from cross-sectional studies that fatigue is associated with physical functioning (PF) whereas the effect of fatigue on subsequent PF has not yet been further looked on.

**Methods:** Data from the German *Lupus-Langzeitstudie* (LuLa) cohort was used to explore the effect of self-reported vitality on PF. The ongoing LuLa study comprises patients from the German SLE self-help group. The current analysis uses data from 2002 to 2013. We looked for associations between the PF score (outcome) and the vitality score of the SF-12 questionnaire in one to four years preceding the outcome. Statistical analysis was accomplished by a linear mixed regression model (LMM) adjusting for the potential confounders age, sex, disease duration and disease activity as surveyed by the Systemic Lupus Activity Questionnaire score (SLAQ).

**Results:** 1511 patients (93.3% women) provided data with a total of 7841 person-years of observation. Median age at study entry was 46 (interquartile range: 37 to 57). The table 1 shows the regression coefficients of the vitality score (and 95% confidence intervals, CI) estimated by the LMM without and with adjusting for age, sex, disease duration and SLAQ.

Exposure: Vitality scale score	Crude estimates		Adjusted estimates	
	Estimate with 95% CI	p-value	Estimate with 95% CI	p-value
1 year ahead	0.08 (0.05–0.10)	<0.001	0.07 (0.05–0.09)	<0.001
2 years ahead	0.09 (0.07–0.11)	<0.001	0.07 (0.05–0.09)	<0.001
3 years ahead	0.05 (0.03–0.08)	<0.001	0.05 (0.03–0.07)	<0.001
4 years ahead	0.03 (0.001–0.06)	0.038	0.04 (0.01–0.07)	0.002

**Conclusions:** We found evidence that self-reported vitality in patients with SLE is associated with PF in the subsequent years. The data indicate a "window of opportunity" for treating fatigue symptoms of up to four years for maintenance of PF.

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FRI0368

### COMPARISON OF CLINICAL AND LABORATORY PROFILES IN 3575 SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS WITH AND WITHOUT SJÖGREN'S SYNDROME: DATA FROM A NATIONWIDE PATIENT REGISTRY (RELESSER)

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**Background:** The clinical coexistence of Systemic Lupus Erythematosus (SLE) and Sjögren's Syndrome (SS) was recognised in 1959. The prevalence of SS among patients with SLE varies considerably among the published studies (10%–30%). There is still controversy as to whether or not SLE patients with overlapping SS have a distinct and significantly milder lupus.

**Objectives:** To address the clinical and serologic features of SLE and differences from SLE that occurs in overlap with SS.

**Methods:** A retrospective cohort of 3575 unselected SLE patients from 45 Rheumatology Units across Spain was evaluated for the presence of overlapping SS

using the American-European consensus criteria. Cumulative clinical data were collected at the moment of the last assessment. Clinical and laboratory parameters in SLE patients with SS (SLEwSS) were compared with those in SLE patients without SS (SLEwoSS).

**Results:** SS was identified in 516 SLE patients (14.4%). Compared with the SLEwoSS group, patients with SLEwSS were significantly older, had a higher frequency of mucocutaneous manifestations, Raynaud's phenomenon, peripheral neuropathy, anti-Ro/SSA, anti-La/SSB, neoplasia, and older age at death, but had a significantly lower frequency of renal involvement, thrombocytopenia, anti-DNA, anti- $\beta$ 2-GPI IgM and complement consumption. Both groups displayed a clinically similar presentation of lymphadenopathy, systemic vasculitis, serositis, damage accrual, mortality, musculoskeletal and CNS manifestations.

FEATURES	SLEwSS N=516	SLEwoSS N=3059	P
Age, years $\pm$ SD	54.2 $\pm$ 14.9	45.6 $\pm$ 14.5	<0.001
Age at SLE onset, years $\pm$ SD	38.6 $\pm$ 15	32.1 $\pm$ 14	<0.001
Female	97.5	89.1	<0.001
Lymphadenopathy	11.8	10.0	0.233
Photosensitivity	65.0	57.2	0.002
Oral ulcers	55.8	42.7	<0.001
Alopecia	36.3	32.0	0.069
Raynaud's Phenomenon	39.9	32.7	0.001
Systemic vasculitis	9.6	8.4	0.352
Arthritis	75.0	76.5	0.467
Myositis	4.0	3.4	0.515
Fibromyalgia	13.9	5.1	<0.001
Pleurisy	22.7	22.4	0.893
Pulmonary fibrosis	2.3	1.9	0.563
Renal manifestations	18.3	32.7	<0.001
Seizures	6.3	6.6	0.805
Peripheral neuropathy	5.4	2.9	0.004
Hemolytic anemia	7.1	8.6	0.272
Leucopenia	55.6	53.5	0.428
Thrombocytopenia	15.5	20.8	0.007
Anti-Ro/SSA	69.2	34.4	<0.001
Anti-La/SSB	48.1	14.4	<0.001
Anti-Sm	19.8	21.2	0.495
Anti-RNP	23.2	25.2	0.317
Anti-DNA	55.9	65.1	<0.001
Anti- $\beta$ 2-GPI IgM	8.6	14.5	0.006
Antiphospholipid syndrome	13.0	14.0	0.520
Hypocomplementemia	62.3	69.0	0.012
SLICC-ACR DI	1.19 $\pm$ 1.8	1.03 $\pm$ 1.7	0.062
Neoplasia	7.8	5.5	0.042
Exitus	7.2	6.0	0.324
Age at death, years $\pm$ SD	67.3 $\pm$ 14.4	54.2 $\pm$ 18.0	<0.001

SLEwSS: Systemic lupus erythematosus with Sjögren's syndrome. SLEwoSS: Systemic lupus erythematosus without Sjögren's syndrome. SLICC-ACR DI: Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index. Except where indicated otherwise, values are the percentage.

**Conclusions:** SLEwSS appears to constitute a subgroup of SLE patients with distinct clinical and serologic features, in whom SS is expressed as an overlapping entity. A particular cluster of clinical variables, namely, mucocutaneous manifestations, Raynaud's phenomenon, peripheral neuropathy, renal involvement and thrombocytopenia, was found to be important overall for discriminating SLE patients with or without SS. SLEwSS patients constitute a subgroup of patients with SLE characterised by milder lupus: older age at death, similar rates of mortality and SLICC-ACR damage index, less renal and immunological manifestations.

**Disclosure of Interest:** None declared

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### FRI0369 PREGNANCY OUTCOMES IN WOMEN WITH ANTIPHOSPHOLIPID ANTIBODIES: INTERIM RESULTS FROM A SINGLE CENTRE COHORT STUDY

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**Background:** Persisting antiphospholipid antibodies (aPL) are associated with adverse obstetric events including recurrent miscarriage, late fetal loss or early

delivery due to pre-eclampsia or placental insufficiency (obstetric APS) and also thrombosis. We are a tertiary referral centre for those with aPL, and have a management protocol for women with aPL during pregnancy and the puerperium with the aim of preventing obstetric complications and maternal thrombosis.

**Objectives:** To report the fetal and maternal outcomes from a single centre cohort of 511 pregnancies in 372 women over a period of eight years.

**Methods:** This is an ongoing retrospective observational study registered as an audit. Data was collected from clinic lists attending the pregnancy clinic at the Thrombosis centre of St. Thomas' Hospital in London, UK between Jan 2010 to December 2017. Women persistently positive for aPL were included if pregnancy outcome data was available.

**Results:** 511 pregnancies in 372 women were included in the study (table 1). The overall live birth rate was 78.9%. Pregnancy outcomes are outlined in table 2.

#### Abstract FRI0369 – Table 1. Demographics

Age in years, median (range)	35 (18–50)
Ethnicity (white:black:asian:other:not specified)	(186 (50%):17(5%):35(9%):94(25%):40 (11%))

#### Antiphospholipid antibody profile at diagnosis

Lupus anticoagulant, n (%) (dAPTT:DRVVT:TSVT)	261 (70%) (183:144:27)
Anticardiolipin IgG and IgM, n (%)	119 (40%) and 144 (39%)
$\beta$ 2-glycoprotein-I IgG and IgM, n (%)	16 (4%) and 27 (7%)

#### APS history

Obstetric APS (any), n (%)	125 (34%)
Obstetric APS (1 st trimester loss), n (%)	74 (20%)
Obstetric APS (2nd trimester loss), n (%)	35 (9%)
Fetal death (>24 weeks), n (%)	19 (5%)
Intrauterine growth restriction, n (%)	30 (8%)
Pre-eclampsia, n (%)	19 (5%)
Thrombotic APS (any), n (%)	106 (29%)

#### Autoimmune profile

ANA:ENA:dsDNA, n (%)	141 (39%):94 (26%):19 (5%):56 (15%)
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Key: ANA, antinuclear antibodies, APS, antiphospholipid syndrome; aPL, antiphospholipid antibodies; aAPPT, dilute Activated Partial Thromboplastin Time; dRVVT, dilute Russel Viper Venom Time; dsDNA, doublestranded DNA, ENA, Extractable nuclear antigens, TSVT, Taipan Snake Venom Time

#### Abstract FRI0369 – Table 2. Pregnancy outcomes

Pregnancy outcomes	Total pregnancies, n=511
<b>Treatment during pregnancy</b>	
Aspirin, 75 mg daily, n (%)	502 (98%)
Low molecular weight heparin, n (%)	381 (75%)
Aspirin + Heparin	267 (52%)
Aspirin + Heparin + HCG	86 (17%)
Hydroxychloroquine, n (%)	158 (31%)
Azathioprine, n (%)	52 (10%)
Antithrombotics, n (%)	17 (3%)
Steroids, n (%)	113 (22%)
Steroids dose in mg, mean (SD, range)	105 (-/5.4, 1-40)
B12 supplements, n (%)	13 (3%)
VCA prior to pregnancy, n (%)	37 (7%)
IV treatment, n (%)	69 (13%)
<b>Pregnancy outcomes (n=511)</b>	
Live births, n (%)	404 (79%)
Twin pregnancies	13 (3%)
Gestational age at delivery/weeks, mean (SD, range)	39 (-/3, 25-44)
Birthweight <2500g	55 (10%)
Birthweight <1500g	7 (1%)
Birthweight in grams, mean (SD, range)	3320 (-/315, 575-6300)
Pregnancy loss, <10 weeks, n (%)	70 (14%)
Pregnancy loss, >10 weeks, n (%)	27 (5%)
Preterm delivery < 34 weeks gestation	13 (2.5%)
Preterm delivery < 37 weeks gestation	52 (10%)
Intrauterine death (>24 weeks), n (%)	7 (1%)
Pre-eclampsia	23 (4%)
Thrombosis during pregnancy, n (%)	9 (1%)
Cesarean section, n (%)	188 (37%)

Key: HCG, hydroxychloroquine

**Conclusions:** These results from the largest single centre cohort reported show that using our management protocol, nearly 80% of women with aPL had a successful pregnancy outcome.

**Disclosure of Interest:** None declared

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**FRI0370** **CLINICAL FEATURES AND OUTCOMES OF LUPUS NEPHRITIS WITH PODOCYTE INJURY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS**

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**Background:** Lupus podocytopathy is a recently recognised, new class of lupus nephritis (LN) characterised by diffuse foot process effacement (FPE) without capillary wall immune deposits and glomerular proliferation. However, the frequency, clinical features and treatment response to glucocorticoid and additional immunosuppressive agents of podocyte injury has not been well investigated.

**Objectives:** To clarify clinical characteristics of podocyte injury and its association with therapeutic response in patients with LN.

**Methods:** Consecutive patients with LN with available electronic microscopic findings in our institute were included. Patients were divided into 2 groups according to the presence or absence of FPE (FPE positive group and FPE negative group), and patient characteristics and laboratory data and pathological classification were compared.

**Results:** Twenty-seven patients with LN with electronic microscopic findings were enrolled. The mean age was 43.7 years old, and 22 (81.5%) were female. The ISN/RPS classification of lupus nephritis were 2 of unclassified, 1 class II, 3 class III, 3 class IV, 9 class V, 6 class III+V, and 3 class IV+V. Two cases were identified as lupus podocytopathy and their renal tissues showed focal segmental glomerulosclerosis pattern. Eighteen patients (67%) were identified to have FPE (FPE positive group) and the remaining 9 patients (33%) did not show FPE in their renal tissues (FPE negative group). The mean age was comparable (42.1 vs 41.2 y/o,  $p=0.84$ ). The mean estimated glomerular filtration rate (eGFR) at LN diagnosis was 77.5 and 70.9 ml/min/1.73 m<sup>2</sup> ( $p=0.39$ ), and the mean urine protein was 1.35 and 2.41 g/day ( $p=0.11$ ). During the mean observation period of 50.1 months, 19 patients (70%) achieved complete response (CR, urinary protein/urine creatinine ratio <0.5 mg/gcr or proteinuria by dipstick test  $\leq \pm$ ). While the dose of prednisolone at treatment initiation and subsequent immunosuppressive therapy was similar in both groups (prednisolone dose, 34.8 vs 39.2 mg/day,  $p=0.57$ ), the rate of CR achievement was significantly higher in the FPE positive group (15 cases, 83%) than the FPE negative group (four cases, 44%,  $p=0.04$ ). The duration to CR achievement was also significantly shorter in the FPE positive group (median, 8 vs 2 months,  $p=0.05$ ).

**Conclusions:** This study showed that podocyte damage was common in LN and pathological types and FPE was associated with renal prognosis in LN. We should be more aware of findings of electronic microscopic in patients with LN.

**Disclosure of Interest:** None declared

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**FRI0371** **CLINICAL CHARACTERISTICS AND OUTCOME OF ISOLATED LUPUS NEPHRITIS**

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**Background:** Lupus nephritis (LN) is a serious manifestation of systemic lupus erythematosus (SLE) associated with significant mortality and morbidity. At least 50% of patients will develop renal involvement at some point in their disease course. Rarely, patients may present with LN alone and have no extra-renal clinical manifestations of lupus. The clinical course, response to treatment and subsequent development of extra-renal manifestations of lupus is not well known in this subset.

**Objectives:** To study the treatment response and development of extra-renal manifestations of lupus in patients who present with isolated lupus nephritis.

**Methods:** Subjects were identified by searching a pathologic renal biopsy database for patients with immune complex glomerulonephritis and lupus nephritis (n=1015). Clinical records were reviewed for exclusion of infectious and secondary causes (e.g. IgA nephropathy, C1q nephropathy, C3 glomerulonephropathy, post-infectious glomerulonephritis etc.). Cases with isolated LN were defined per 2012 SLICC criteria as having biopsy proven LN with positive antinuclear antibody (ANA) and/or anti-dsDNA antibodies and who did not have any extra-renal clinical manifestations at onset. Demographics, biopsy information, clinical and laboratory features at onset, and during follow-up and treatment was recorded on a standardised data collection form. Complete and partial renal response were defined per the Dutch Working Party criteria.<sup>1</sup>

**Results:** Thirty four patients with isolated LN were identified. The median age at presentation was 41 years and majority were female (71%) Caucasians (77%). Median follow up was 5.4 years. At presentation, mean serum creatinine was 1.7 mg/dl (range 0.7–5.4), and mean proteinuria was 6.8 g/24 hours (range 0.1–62.9). Antinuclear antibodies were positive in 71%, positive dsDNA in 36%. Mean C3 and C4 levels were 78.2 mg/dl (range 26.5–133.0) and 11.0 mg/dl (range 3.0–40.0), respectively. Antibodies to extractable nuclear antigens were checked in 12

patients and positive for anti-SSA,<sup>5</sup> anti-SSB,<sup>2</sup> anti-Sm,<sup>2</sup> anti-RNP;<sup>3</sup> Anticardiolipin were positive in 7/13 and lupus anticoagulant in 4/4. Renal biopsies showed changes of Class III nephritis in 10 patients (29%), Class IV in 13 (38%) and class V in 7 (21%). Induction treatment included Corticosteroids (94%), mycophenolate mofetil (76%), cyclophosphamide (18%) and tacrolimus (3%). Maintenance treatment included corticosteroids (73%), MMF (79%), azathioprine (8%), rituximab (5%), cyclophosphamide (5%), calcineurin inhibitor (2%), chlorambucil (2%). At the last follow up CR was seen in 14 (42%) and partial response in 5 (15%). End-stage renal disease developed in 6 (18%) and 3 patients received renal transplant. Extra-renal manifestations of lupus developed in 8 patients (24%) and included acute cutaneous,<sup>2</sup> chronic cutaneous,<sup>3</sup> arthritis<sup>1</sup> and serositis.<sup>4</sup>

**Conclusions:** Majority of patients with isolated lupus nephritis respond well to treatment. The development of extra-renal manifestations of lupus after treatment is a rare occurrence.

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**Disclosure of Interest:** None declared

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**FRI0372** **COMPARISON OF CLINICAL FEATURES BETWEEN YOUNG AND ELDERLY ONSET IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME**

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**Background:** Primary Sjogren's syndrome (pSS) generally develops in middle-aged women. Currently, elderly-onset pSS has been increasing, however, differences in clinical and serological features between young-onset and elderly-onset pSS is unclear.

**Objectives:** The aim of this study was to compare clinical and serological features between young-onset and elderly-onset patients with pSS.

**Methods:** All patients with pSS diagnosed with 2016 ACR/EULAR classification criteria in our department from 1995 to 2017 were included. Patients were divided into 2 groups according to the age of diagnosis at 65 years old; young-onset and elderly-onset. The symptoms and laboratory findings were compared.

**Results:** Six hundred twelve pSS patients were reviewed. Five hundred seventy (93%) were female. Four hundred twenty six (70%) were young-onset and the remaining 186 (30%) were elderly-onset. The mean age at pSS diagnosis was 47.8 and 72.4 years old, the ratio of women:men is around 12:1 and 20:1. The observation period from the diagnosis to the last visit was 3.46 and 5.50 years, respectively. At diagnosis, the positivity of anti-SS-A antibody (86.8 vs 73.7%,  $p<0.001$ ), anti-SS-B antibody (48.3 vs 30.7%,  $p<0.001$ ), and rheumatoid factor (49.6 vs 35.2%,  $p<0.01$ ) were significantly higher in the young-onset patients than the elderly-onset patients. Also, the level of platelet cell count (23.0 vs 20.8\*10<sup>4</sup>/μl,  $p<0.001$ ), IgG (1996 vs 1745 mg/dl,  $p<0.001$ ) and IgM (154 vs 131 mg/dl,  $p<0.001$ ) were significantly higher in the young-onset patients. On the other hand, that of white blood cell count (4814 vs 5301/μl,  $p<0.001$ ), neutrophil count (2822 vs 3201/μl,  $p<0.001$ ), lymphocyte count (1512 vs 1632/μl,  $p<0.01$ ), C3 (87.2 vs 93.2 mg/dl,  $p<0.001$ ), C4 (22.1 vs 24.7 mg/dl,  $p<0.001$ ), and CH50 (48.2 vs 51.1/ml,  $p<0.001$ ) were significantly lower in the young-onset patients. While the young-onset patients had higher rate of liver dysfunction (3.99 vs 0.54%,  $p<0.05$ ), and arthritis (6.81 vs 2.69%,  $p<0.05$ ), the elderly-onset patients were more frequently complicated with pulmonary disease (4.2 vs 11.8%,  $p<0.001$ ). The C3 levels in the elderly-onset patients with pulmonary disease were conversely lower than the young-onset patients with pulmonary disease. The incidence of lymphoma was not different between two groups.

**Conclusions:** Although elderly onset pSS patients have milder symptoms and immune-disturbances than young-onset ones, pulmonary disease was more frequently affected in the elderly-onset patients with a decrease in complement levels, suggesting there may be difference in the pathogenesis in pSS according to onset ages and organ involvement.

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FRI0373

### LONG-TERM FOLLOW-UP OF 320 CHILDREN BORN TO MOTHERS WITH SYSTEMIC AUTOIMMUNE DISEASES: A MULTICENTRE ITALIAN SURVEY FROM 24 RHEUMATOLOGY CENTRES

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**Background:** Rheumatic Diseases (RD) frequently affect women during reproductive age, therefore counselling on family planning is crucial for their quality of life. Children's outcome is a major topic, but no large studies are available.

**Objectives:** To assess the long-term health conditions of children born to women with RD in a large multicentre cohort.

**Methods:** 24 Rheumatology Centres distributed the questionnaire (65 multiple-choice and 12 open-answer questions) to consecutive patients (18–55 years) in September 2015. Data were analysed dividing children upon maternal diagnosis: Chronic Arthritis (CA) and Connective Tissue Diseases (CTD).

**Results:** Data were collected for 320 children (166 males, 52%) born to 184 mothers (63 CA and 121 CTD). At the time of interview, children had a mean age of 17.1±9.6 years. Preterm delivery (<37 w) was observed in 72 cases (22.5%), including 13 (4%)<34 w. Data on autoimmune/inflammatory disease (AIID) and/or neurodevelopmental disorders (ND)/learning disabilities (LD) is reported in table 1. 12 children (3.7%) had a diagnosis of AIID, mostly coeliac disease (8/12, 67%) and 11 children (3.4%) of a ND and/or LD by a Paediatric Neuropsychiatrist. To rule out the possible effects of *in utero* exposure to maternal autoantibodies and/or anti-rheumatic drugs in the pathogenesis of ND, these data were retrieved for 280 children (88%) and a comparison was performed between 11 affected and 269 non-affected children (table 2).

**Abstract FRI0373 – Table 1.** DM: diabetes mellitus; LD: learning disorder; ADHD: attention deficit hyperactivity disorder

NEURODEVELOPMENTAL/ LEARNING DISORDERS	Present (n=11)	Absent (n=269)	p-value
Male	7 (64%)	140 (55%)	0.55
Preterm birth <37 weeks <34 weeks	3 (27%) 1 (9%)	56 (22%) 10 (3.7%)	0.44 0.36
Maternal diagnosis Chronic Arthritis Connective Tissue Diseases	2 (18%) 9 (82%)	95 (37%) 174 (63%)	0.34
Birth weight (mean Kg)	2.958	3.218	0.09
<b>In utero exposure to anti-rheumatic drugs</b>	5 (45%)	63 (24%)	0.14
Prednisone	5 (45%)	46 (17%)	0.22
Hydroxychloroquine	0 (0%)	23 (9%)	0.61
Azathioprine	1 (9%)	1 (0.4%)	0.08
<b>In utero exposure to maternal auto-antibodies</b>	4 (36%)	54 (20%)	0.99
Anti-nuclear	4 (36%)	46 (17%)	0.64
Anti-dsDNA	3 (27%)	14 (5%)	0.06
Anti-Ro/SSA	2 (18%)	24 (9%)	0.99
Anti-cardiolipin	2 (18%)	15 (6%)	0.28
Anti-beta2gpl	0 (0%)	12 (4%)	0.99
Lupus Anticoagulant	0 (0%)	8 (3%)	0.99

Abstract FRI0373 – Table 2

NEURODEVELOPMENTAL/ LEARNING DISORDERS	Present (n=11)	Absent (n=269)	p-value
Male	7 (64%)	140 (55%)	0.55
Preterm birth <37 weeks <34 weeks	3 (27%) 1 (9%)	56 (22%) 10 (3.7%)	0.44 0.36
Maternal diagnosis Chronic Arthritis Connective Tissue Diseases	2 (18%) 9 (82%)	95 (37%) 174 (63%)	0.34
Birth weight (mean Kg)	2.958	3.218	0.09
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Anti-cardiolipin	2 (18%)	15 (6%)	0.28
Anti-beta2gpl	0 (0%)	12 (4%)	0.99
Lupus Anticoagulant	0 (0%)	8 (3%)	0.99

**Conclusions:** In this long-term follow-up of children born to mothers with RD in this large, multicenter study of randomly interviewed women each AIID did not display a significantly increased frequency as compared to the literature; only coeliac showed a mild increased frequency. Children with LD had a tendency to cluster in the group of mothers with CTD, especially after maternal diagnosis (4/63, 6.3%), with a higher frequency as compared to general paediatric population. No significant relationships between ND/LD and prematurity, intrauterine drug exposure or maternal autoantibodies were identified.

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FRI0374

### MILDER CLINICAL PRESENTATION OF LUPUS NEPHRITIS AND IMPROVED RENAL SURVIVAL DURING THE LAST 50 YEARS: A MULTICENTRIC STUDY

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**Background:** Lupus nephritis (LN) presentation changed over time following earlier diagnosis and treatment.

**Objectives:** To evaluate changes in LN clinical and histological presentation in the last 5 decades.

**Methods:** This is a retrospective multicentric study on prospectively collected data in four Italian hospital centres. Patients diagnosed between 1970 and 2016 were recruited provided they had a biopsy-proven LN that was retrospectively reclassified according to the ISN/RPS classification criteria. Follow-up was subdivided into three periods (P) based on the year of LN diagnosis: P1:1970–1895; P2:1986–2000; P3:2001–2016. Predictors of patient and renal survival were investigated by univariate and multivariate analysis; survival curves were compared by log-rank test. Clinical pictures at presentation included isolated urinary abnormalities, nephrotic syndrome, nephritic syndrome, rapidly progressive renal failure. Outcome at last observation was defined as complete renal remission or



partial renal remission, or poor renal outcome, including chronic kidney disease (CKD) or end stage renal disease (ESRD).

**Results:** 499 patients were included (85.6% females) with a median follow-up of 10.6 years (IQR 4–18). We observed an increase in both age at diagnosis of LN (P1 28.4±10.4; P2 29±11.5; P3 34.4±13.3 years) and disease duration before LN diagnosis (P1 1.3±1.3; P2 2.6±4.5; P3 4.6±6.3 years) from 1970 to 2016 ( $p<0.001$  for both). At clinical presentation, renal insufficiency and acute nephritic syndrome became less common (P1 14.2%; P2 3.9%; P3 3.4% and P1 29%, P2 20.3%; P3 12.4%, respectively,  $p<0.0001$ ) while isolated urinary abnormalities became significantly more prevalent from P1 to P3 (P1 26.4%; P2 38%; P3 48.9%;  $p<0.0001$ ). Outcome was available in 95.8% of patients. Frequency of partial and complete renal remission progressively increased (P1 6.9%; P2 28%; P3 32% and P1 49.6%; P2 48%; P3 58.5%;  $p<0.001$  and  $p=0.01$ , respectively) while CKD, ESRD and death decreased (P1 7.9%; P2 8.5%; P3 4.5%; P1 24.8% P2 9%; P3 1.3%; P1 19.8%; P2 5.9%; P3 3.6%, respectively.  $p<0.001$  for all). Survival without ESRD at 10 and at 20 years was 87% and 80% in P1, 94% and 90% in P2 and 99% in P3 ( $p=0.0019$ ). Induction therapy with immunosuppressants was more frequently performed over time (P1 71%; P2 82%; P3 94.6%,  $p<0.0001$ ) and use of MMF significantly increased both as induction and maintenance treatment (P1 0, P2 2.7%; P3 33.8% and P1 1%; P2 15%; P3 54.8%, respectively,  $p<0.0001$ ). At multivariate analysis, logarithm of serum creatinine (RR:2.72), male gender (RR:3.34), activity index (RR:1.1), chronicity index (RR:1.29), arterial hypertension (RR:5.95), and lack of maintenance immunosuppressive therapy (RR:3.04) predicted ESRD. No significant changes in histological classes or active lesions at the time of renal biopsy were observed, while chronicity index significantly decreased from P1 to P3 ( $p=0.023$ ).

**Conclusions:** The clinical presentation of LN apparently became less severe in the last decades, likely due to earlier diagnosis and proper treatment, leading to an improved renal survival.

**Disclosure of Interest:** None declared

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FRI0375

#### DELAYED LUPUS NEPHRITIS IN THE COURSE OF SYSTEMIC LUPUS ERYTHEMATOSUS PREDICTS A POORER RENAL RESPONSE TO INDUCTION THERAPY, RENAL FLARES, AND WORSE LONG-TERM RENAL OUTCOMES: A MULTICENTER, RETROSPECTIVE COHORT STUDY

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**Background:** Some prognostic factors for lupus nephritis (LN) have been mentioned such as nephrotic syndrome, class 4 and chronicity on histology. In a previous single-centre study, we reported a potentially poorer renal response to induction therapy in LN that developed later after SLE onset (delayed, D-LN) compared with LN manifesting at SLE onset (early, E-LN) <sup>1</sup>. However, our study was limited by a small sample size and lack of long-term observation.

**Objectives:** This multicenter study aimed to validate whether D-LN was a useful predictor of a poor response to induction therapy with more detailed clinical and pathological parameters. Furthermore, we investigated whether D-LN was also a predictor of flares and long-term renal outcomes in addition to the established prognostic factors.

**Methods:** We retrospectively examined 215 biopsy-proven LN patients (136 E-LN, 79 D-LN) who attended 3 hospitals above between 1997 and 2014 and who were observed for 3–20 (median: 10.8) years from LN onset. We compared baseline clinical, pathological features and treatment options at LN onset between E-LN and D-LN. Then we compared the cumulative complete response (CR) rates, renal/extra-renal relapse rates, and the rates of renal insufficiency between the two groups. Renal insufficiency was defined as follows: <sup>1</sup> serum creatinine (SCr) doubling or ESRD for severe insufficiency, and <sup>2</sup> SCr increasing by 1.5 times and also >1.0 (female) or >1.2 mg/dl (male) for mild insufficiency. Moreover, we evaluated predictors of the response, flares and long-term renal outcomes with multivariate analysis.

**Results:** Anti-Sm/RNP antibodies and mixed proliferative and membranous nephritis (class 3+5 or 4+5) were significantly more prevalent in D-LN than E-LN (48.1 vs. 32.4%, 68.8 vs. 40.4%, 40.5 vs. 18.4%, respectively). Log-rank test showed that significantly lower cumulative CR rates over 3 years (65.8 vs. 83.1% at 12 months, 83.5 vs. 92.6% at 36 months,  $p<0.01$ ) and significantly higher relapse rates (both renal and extra-renal) over 20 years in D-LN than E-LN. Mild renal insufficiency was significantly more likely to occur in D-LN over 20 years (21.5 vs. 12.5%,  $p=0.04$ ). We performed multivariate Cox regression analysis for the response, flare, and renal outcomes including significant variables on univariate analysis. As independent predictors of CR, D-LN, nephrotic syndrome and chronicity index were identified. As those of renal flares, D-LN was detected.

Although D-LN was not associated with severe renal insufficiency, D-LN was identified as an independent predictor of mild renal insufficiency as well as some other factors (table 1).

Univariate analysis	Hazard ratio	P-value	Multivariate analysis	Hazard ratio	P-value
<b>Predictors of CR</b>					
D-LN	0.66(0.49-0.89)	0.006	D-LN	0.50(0.36-0.69)	<0.001
Serum creatinine	0.61(0.46-0.81)	0.001			
Nephrotic syndrome	0.54(0.40-0.73)	<0.001	Nephrotic syndrome	0.51(0.37-0.70)	<0.001
Class IV	0.86(0.49-0.87)	0.004			
Activity Index	0.94(0.90-0.97)	0.001			
Chronicity index	0.75(0.68-0.84)	<0.001	Chronicity index	0.81(0.70-0.92)	0.002
<b>Predictors of renal flare</b>					
D-LN	2.50(1.55-4.03)	<0.001	D-LN	2.17(1.30-3.65)	0.003
Anti-RNP antibodies	1.71(1.05-2.78)	0.030			
Non-CR at 12months after induction therapy	2.05(1.25-3.37)	0.005			
<b>Predictors of extra-renal flare</b>					
D-LN	1.92(1.05-3.52)	0.035	D-LN	1.64(0.89-3.05)	0.122
Anti-Sm antibodies	2.49(1.34-4.65)	0.004	Anti-Sm antibodies	2.31(1.23-4.34)	0.009
<b>Predictors of severe renal insufficiency</b>					
D-LN	2.31(0.89-5.99)	0.085			
Anti-RNP antibodies	9.41(2.14-41.3)	0.003	Anti-RNP antibodies	10.1(2.27-44.6)	0.002
Chronicity index	1.42(1.03-1.97)	0.032			
Non-CR at 6months after induction therapy	4.38(1.54-12.4)	<0.001	Non-CR at 6months after induction therapy	3.21(1.06-9.75)	0.039
<b>Predictors of mild renal insufficiency</b>					
D-LN	2.00(1.02-3.92)	0.044	D-LN	2.12(1.03-4.34)	0.041
Male	2.14(1.02-4.48)	0.044	Male	2.87(1.31-6.27)	0.008
Serum creatinine	1.97(1.45-2.67)	<0.001	Serum creatinine	1.97(1.30-2.99)	0.002
Nephrotic syndrome	2.48(1.26-4.88)	0.009			
Activity index	1.14(1.04-1.24)	0.003			
Chronicity index	1.77(1.42-2.19)	<0.001	Chronicity index	1.61(1.25-2.09)	<0.001
Non-CR at 6months after induction therapy	5.24(2.50-11.0)	<0.001	Non-CR at 6months after induction therapy	3.29(1.46-7.41)	0.004

**Conclusions:** D-LN might be a novel predictor of a poorer treatment response, renal flares and long-term renal outcomes independent of the established prognostic factors. The distinct differences in the autoantibody profiles between E-LN and D-LN groups suggest that D-LN patients might reflect a refractory SLE subset with a specific immunological profile.

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**Acknowledgements:** None

**Disclosure of Interest:** None declared

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FRI0376

#### DYSLIPIDEMIA AS A NEWLY RECOGNISED FACTOR ASSOCIATED WITH DAMAGE ACCRUAL IN EARLY DIAGNOSED SLE: RESULTS FROM THE MULTICENTER EARLY LUPUS PROJECT INCEPTION COHORT

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**Background:** Preventing organ damage is a major challenge in Systemic Lupus Erythematosus (SLE).

**Objectives:** To evaluate factors associated with development of damage in a prospectively followed cohort of early diagnosed SLE patients.

**Methods:** The Early Lupus Project<sup>1</sup> encompasses 9 Italian centres recruiting, from the 1st January 2012, an inception cohort of consecutive patients diagnosed with SLE within 12 months from appearance of four or more 1997 ACR classification criteria. At study entry and then every 6 months a large panel of data was recorded.

Here, we report on factors associated with the development of damage assessed by the SLICC/ACR Damage Index (SDI). Using univariate analysis, we assessed the contribution of covariates collected at baseline (demographic, comorbidities, serological, clinical by BILAG2004 domains, disease activity by ECLAM, HRQoL by visual analogic scale) in the development of damage (SDI from 0 to  $\geq 1$ ). Forward-Backward Cox-regression models were fitted with covariates with  $p<0.05$  to identify factors independently associated with increased risk of damage development.

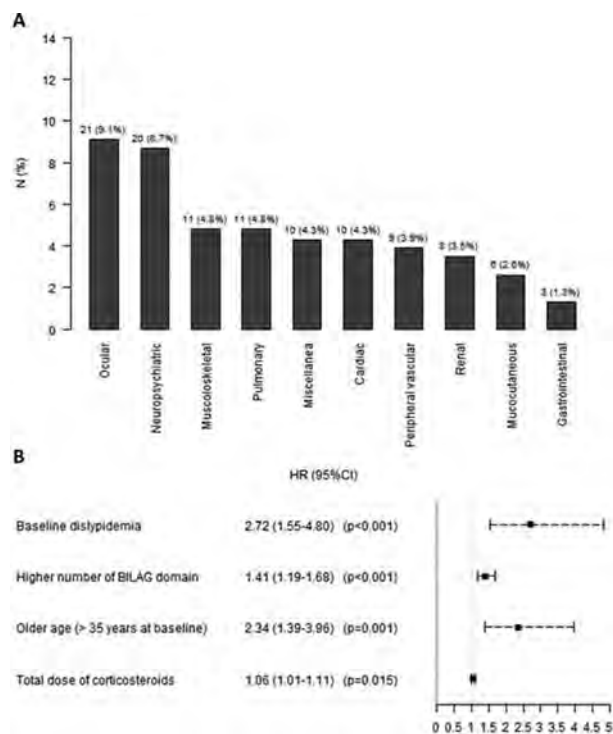
**Results:** Overall, 279 patients were enrolled in the Early Lupus Project inception cohort up to the 31st of December 2017; 230 patients (89.6% Caucasians, 13.4% males) were eligible for this study having SDI=0 at enrolment and at least 6



months of follow-up. Mean ( $\pm$ SD) age at recognition of 4 ACR criteria was 36.5 ( $\pm$ 14.4) years, median disease duration at recruitment was 1.1 months (interquartile range 0.0–4.8) and median follow-up duration was 27.4 months (interquartile range 7.2–48.0).

At last follow-up visit 84 patients (36.5%) had an SDI score  $\geq 1$  (median=0; interquartile range 0–1); see figure 1A for overall SDI domains involved.

Baseline dyslipidemia ( $p < 0.001$ ; HR 2.7 95% CI 1.5–4.8), higher number of BILAG domain involved ( $p < 0.001$ ; HR 1.4 95% CI 1.2–1.7) and older age ( $> 35$  year) at baseline ( $p = 0.001$ ; HR 2.3 95% CI 1.4–4.0) together with total dose of corticosteroids ( $p = 0.015$ ; HR 1.06 per gram of prednisone equivalent; 95% CI 1.01–1.11) during follow-up were the factors independently associated with increased risk of developing damage in this cohort (figure 1B). Their effect was confirmed after stratification for antimalarials (yes/no) and immunosuppressants (yes/no) use.



**Conclusions:** The early development of organ damage in this SLE patients cohort was associated with modifiable risk factors as baseline dyslipidemia and higher corticosteroid dose. Addressing them since the very early stages of the disease, and treating disease activity to target remission or minimal disease activity, may reduce damage and improve patients outcome.

**REFERENCE:**

[1] Sebastiani GD, et al. Early Lupus Project – A multicentre Italian study on systemic lupus erythematosus of recent onset. *Lupus* 2015 Oct;24 (12):1276–82.

**Disclosure of Interest:** None declared

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**FRI0377 THE RELATIONSHIP BETWEEN REMISSION AND HEALTH RELATED QUALITY OF LIFE IN A COHORT OF SLE PATIENTS**

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**Background:** a treat-to-target approach for SLE was suggested by an international board of experts to further improve outcome in SLE. Remission was specifically identified as a suitable target. The Definition of Remission in SLE (DORIS) task force recently achieved international consensus on criteria for remission.

**Objectives:** to investigate the relationship between remission and health-related quality of life (HRQoL) in patients with systemic lupus erythematosus (SLE) in a longitudinal observational cohort.

**Methods:** retrospective analysis of prospectively obtained data. HRQoL was assessed using the physical and mental component score (PCS and MCS, respectively) of the Short Form 36 (SF-36) questionnaire. DORIS remission categories (no remission/remission on therapy/remission off therapy) were applied. Determinants of PCS and MCS were identified with simple linear regression analyses. Association between remission and HRQoL was assessed using Generalised Estimating Equation (GEE) models.

**Results:** Data from 154 patients with 2 years of follow-up were analysed. At baseline 70/154 (45.5%) of patients were in either form of remission. Patients in remission had higher SF-36 scores in all subdomains compared to patients not in remission (figure 1). PCS was positively associated with remission and having employment and negatively associated with erythrocyte sedimentation rate, patient global assessment, SLICC damage index, prednisone use, immunosuppressant use, and body mass index. MCS was positively associated with Caucasian ethnicity and negatively associated with patient global assessment. In GEE analysis, a gradual and significant increase of PCS was observed from patients not in remission (mean PCS 36.0) to remission on therapy (41.8) to remission off therapy (44.8) (table 1). No significant difference in MCS was found between remission states.

**Abstract FRI0377 – Table 1.** GEE analysis of the association between PCS or MCS and remission in patients with SLE

**A. PCS:**

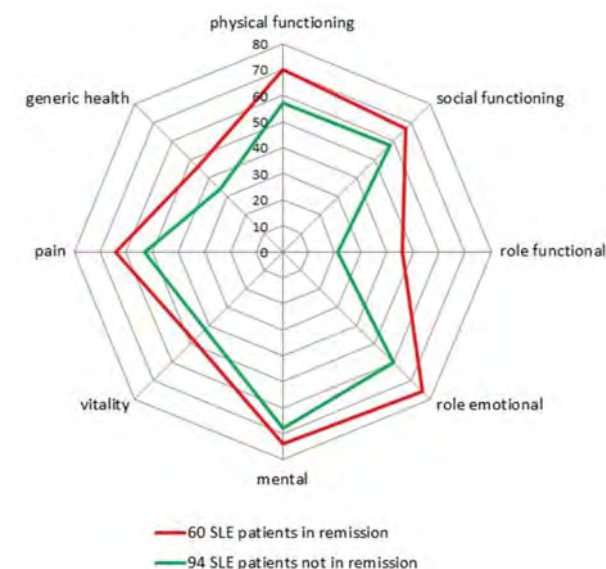
	Mean PCS ( $\pm$ SD)	Unadjusted		Adjusted*	
		B (95% CI)	p-value	B (95% CI)	p-value
No remission	36.0 (10.9)	Ref.		Ref.	
Remission on therapy	41.8 (10.0)	6.3 (3.2–9.3)	$< 0.001$	6.2 (3.3–9.0)	$< 0.001$
Remission off therapy	44.8 (10.4)	8.2 (5.3–11.2)	$< 0.001$	8.3 (5.4–11.1)	$< 0.001$

\*Adjusted for age and SDI

**B. MCS:**

	Mean MCS ( $\pm$ SD)	Unadjusted		Adjusted**	
		B (95% CI)	p-value	B (95% CI)	p-value
No remission	46.1 (10.6)	Ref.		Ref.	
Remission on therapy	49.3 (10.5)	2.9 (0.1–5.7)	0.041	2.3 (–0.5–5.1)	0.112
Remission off therapy	46.8 (10.1)	0.8 (–1.7–3.4)	0.52	0.4 (–2.1–3.0)	0.739

\*\*Adjusted ethnicity



**Abstract FRI0377 – Figure 1.** Mean SF-36 subdomain scores in 154 patients at baseline, categorised between SLE patients in remission (n=60) or not in remission (n=94). Patients in remission at baseline have higher mean scores in all SF-36 subdomains compared to patients not in remission.

**Conclusions:** we show a strong and persistent association between remission and PCS, but not MCS. These results support the relevance (construct validity) of

the DORIS remission definitions and the further development of a treat-to-target approach in SLE.

**Disclosure of Interest:** None declared

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### FRI0378 ANTIPHOSPHOLIPID SYNDROME IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

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**Background:** Antiphospholipid syndrome (APS) is a known cause of thrombotic disorders, including Acute Myocardial Infarction (AMI). Although the incidence of APS in AMI patients it's not known, it can be an important cause of myocardial infarction especially in young patients.

**Objectives:** The aim of this study is to evaluate the relationship between antiphospholipid syndrome and acute myocardial infarction in patients presented at cardiac emergency and cardiac reanimation at UHC Mother Teresa, Tirana, Albania

**Methods:** This is an observational study which included all patients from 23 to 45 years old presented as Acute Myocardial Infarction at our hospital from 10 december 2016–10 december 2017. In this period, there were diagnosed with AMI 61 patients fulfilling the inclusion criteria of the study: 37 males and 24 females. Besides the usual laboratory tests, all patients included in the study were completed with the titration of APS autoantibodies (Anti-cardiolipin, Lupus anticoagulant,  $\beta$ 2 glycoprotein 1 antibodies). If positive, according to diagnosis guidelines, the tests were repeated after 12 weeks.

**Results:** Of 61 patients with AMI, 17 patients were positive for Antiphospholipid Syndrome at the first test and after 12 weeks, APS was confirmed in 15 patients (24.6%): 10 females (67%) and 5 males (33%). Three of the patients diagnosed with APS underwent to a second Percutaneous transluminal coronary angioplasty due to rapid occlusion of stents placed in concomitant stenotic coronary arteries.

**Conclusions:** From this study it was found that Antiphospholipid syndrome in relatively young patients hospitalised for Acute myocardial infarction is a concomitant-causing disorder in a quarter of the patients included in our study. This implies that in young patients it should be kept in mind that APS could be the reason of the problem.

**Disclosure of Interest:** None declared

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### FRI0379 INFLAMMATORY JOINT INVOLVEMENT IS ASSOCIATED WITH SEVERE DRY EYE IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME

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**Background:** Primary Sjögren's syndrome (pSS) is characterised by lymphocytic infiltration of exocrine glands and other organs, resulting in dry eye, dry mouth and extraglandular systemic involvement such as pain, myalgia or polyarthralgia, among others.

**Objectives:** The aim of the present study is to explore the association of severe or very severe dry eye with extraocular involvement in patients with pSS.

**Methods:** SJOGRE-SER registry is a multicenter cross-sectional study of pSS patients fulfilling European/American consensus criteria 2002 from 33 Spanish rheumatology departments. Data were collected by reviewing clinical records and interviewing patients. For the construction of our main variable, "severe/very severe dry eye" (S/VSDE), we used those variables present in our cohort that represented a degree 3–4 of severity (S/VSDE) according to the dry eye TFOS DEWS I classification 2007 (Tear Film and Ocular Surface Society Dry Eye Work-Shop): Schirmer score ( $\leq 5$  mm/5 min) and/or corneal ulcers and/or use of autologous sera and/or contact lenses and/or Stenon conduit bypass and/or palpebral cleft reduction. First, bivariate logistic regression models were used to identify the effect of each independent variable on S/VSDE. Secondly, multivariate analysis using regression model was used to establish the independent effect of patient characteristics associated with the dependent variable.

**Results:** Four hundred and thirty-seven patients were included in SJOGRE-SER registry (female gender 95%; median age 58 (50.02–67.98) years). Mean time of evolution of the disease in the cohort was 8.3 years. ESSDAI mean score was 2 (0–4, P25-P75) in the full registry. Ninety-four per cent of the patients in SJOGRE-SER cohort complained of daily, persistent, troublesome dry eyes, 92% had sensation of sand in the eyes and 16% developed corneal ulcer. In the

full cohort Schirmer's test was performed in 402 patients and was pathological ( $\leq 5$  mm/5 min) in 371 patients (92%). The use of autologous sera was 14%, contact lenses 2%, Stenon conduit bypass 0.23% and palpebral cleft reduction 0.23%. Three hundred and seventy-eight patients (86.5%) presented S/VSDE; 95% were women, and the median age was years. Mean time of evolution of the disease was 8.51 and ESSDAI mean score was 5. Inflammatory articular involvement was significantly more frequent in patients with S/VSDE (82.5%) than in those without S/VSDE (69.5%) ( $p=0.028$ ). Inflammatory joint affection was associated with S/VSDE in the multivariate analysis, OR 2.079 (95% CI, 1.096–3.941). These results were adjusted by sex, age, time of evolution of the disease and ESSDAI score.

**Conclusions:** Severe or very severe ocular involvement is associated with the presence of inflammatory joint involvement in patients with pSS. These results suggest that a directed anamnesis including systemic comorbidities, such as the presence of inflammatory joint affection and dry mouth, in patients with severe dry eye, would be useful to suspect an pSS.

### REFERENCE:

[1] Report of the International Dry Eye Workshop (DEWS). *Ocul Surf* 2007;5:65.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.1961

### FRI0380 ASSESSMENT OF SUBMANDIBULAR GLAND QUALITATIVE CHANGES USING SHEAR WAVE ELASTOGRAPHY IN PATIENTS WITH SJÖGREN'S SYNDROME

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**Background:** We have reported that the submandibular gland ultrasonography (SGUS) is a useful noninvasive and inexpensive procedure for the evaluation of the structural changes of salivary gland (SG) in Sjögren's syndrome (SS), International Symposium on SS 2002, EULAR 2009, EULAR 2012, EULAR 2015. However, our previously study demonstrated that although SGUS findings were useful for the diagnosis of SS with low salivary flow they were not for early-stage SS with normal salivary flow. EULAR 2016. Recently, ultrasound elastography has been reported to be a new tool to evaluate tissue stiffness and diagnose tumour.

**Objectives:** The aim of this study was to examine the usefulness of SGUS using US staging and PD grading score in combination with shear wave elastography (SWE) in patients with SS.

**Methods:** Fifty-eight patients who fulfilled the American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) classification criteria for SS were studied. SS patients were divided into three groups according to salivary flow using gum test (VL/SS: $<5$  mL/10 min. (n=21), L/SS: 5–10 mL/10 min. (n=27) and N/SS: $\geq 10$  mL/10 min. (n=10)). All patients were examined SGUS by a single investigator who was blinded to device (TUS-A300; Canon Medical Systems, Tokyo, Japan) with a linear transducer (7.5–10MHz). The examination consisted of conventional B-mode US (US staging score), pulsed wave Doppler US (PD grading score) and SWE with quantitative assessment. US staging scores were assessed by glandular size, inhomogeneity and contrast of diaphragm muscle (stage 0 to 3). PD grading scores were graded by pulsed wave pattern in pulsed wave Doppler US at the internal SG facial arteries (grade 0 to 2). With the region-of-interest (ROI) placed over the stiffest areas of the lesion on SWE, the quantitative mean of the elasticity values were measured by shear wave velocity (Vs: m/s) and elasticity (E: kPa) for each lesion.

**Results:** The US staging scores of SS patients were 0.0% in stage 0; 17.2% in stage 1; 8.6% in stage 2; 74.1% in stage 3. The PD grading scores of SS patients were 20.7% in grade 0, 17.2% in grade 1, 62.1% in grade 2. The US staging and grading scores were significantly lower in N/SS patients (1.40 $\pm$ 0.70, 0.10 $\pm$ 0.32) than in L/SS (2.74 $\pm$ 0.66,  $p<0.001$ , 1.59 $\pm$ 0.69,  $p<0.001$ ) and in VL/SS (2.91 $\pm$ 0.30,  $p<0.001$ , 1.81 $\pm$ 0.40,  $p<0.001$ ) patients. The elasticity value measure by Vs and E were significantly higher in N/SS patients than in VL/SS patients (Vs: 1.90 vs 1.56 m/s,  $p<0.05$ , E: 11.2 vs 7.57 kPa,  $p<0.05$ ). The Vs and E were significantly decreased as US staging score (stage 1 vs 3: 1.91 vs 1.62 m/s,  $p<0.05$ , 11.3 vs 8.21 kPa,  $p<0.05$ ) and PD grading score (grade 0 vs 2: 1.90 vs 1.61 m/s,  $p<0.05$ , 11.1 vs 8.13 kPa,  $p<0.05$ ) increased.

**Conclusions:** The present study demonstrated that the tissue elasticity was increased due to inflammation and high viscosity in the SG at the early stage, but was decreased due to structural changes in the SG at the advanced stage of the

disease. The SWE may be a useful tool for elucidation of early stage pathological changes of the SG when salivary gland functions are not impaired in SS.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.2589

### FRI0381 ARE THE ANTIPHOSPHOLIPID ANTIBODIES A "NEW" INDEPENDENT RISK FACTOR FOR ACCELERATED ATHEROSCLEROSIS

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**Background:** The physiological function of phospholipids and their protein co-factors, which are aPL target, are well known. Beta 2 glycoprotein 1 is an important transport molecule that binds negatively charged particles to free circulation, including various lipoproteins, such as LDL. In this context,  $\beta$ 2GPI plays the role of protein co-factor of low density lipoprotein and is a key factor affecting serum levels of free LDL and total cholesterol, respectively. Its physiological function is suppressed by antibodies against it.

**Objectives:** We investigated the incidence of atherosclerosis in patients with antiphospholipid syndrome compared with systemic lupus erythematosus without aPL and healthy controls at pre-treatment sites.

**Methods:** We examined 219 people divided in three groups – APS (136), SLE, <sup>42</sup> healthy controls.<sup>41</sup>

We performed an ultrasound examination of the carotid arteries, measuring intima-media thickness as well and evaluate the vessel wall for atherosclerotic plaques.

We performed calcium score on the coronary arteries, aorta and aortic valve as well.

**Results:** Between our groups we do not find statistically significant difference for BMI.

Comparative analysis for LDL-cholesterol showed higher APS median values (3.13 mmol/L) compared to other groups. Using the Kruskal-Wallis test, we have a statistically significant result for a direct correlation with the antiphospholipid syndrome ( $p=0.001$ ). Patients with APS shows higher levels for LDL.

With the Kruskal-Wallis analysis, we found a statistically significant difference in IMT between the study groups for left ( $p=0.005$ ) and right ( $p=0.014$ ) carotid arteries.

With Mann-Whitney analysis, we do not detect statistically significant differences in IMT values between patients with primary antiphospholipid syndrome and those with secondary.

We investigated the frequency distribution of atherosclerotic plaques in individuals in the groups. In the right carotid artery, plaque was found in 18 (31.6%) patients with APS, 3 (7.3%) cases were recorded in healthy controls, and in the SLE group there were no reported cases. We establish a statistically significant correlation of carotid plaques in APS patients ( $p\leq 0.001$ ).

In our study group of patients with APS is characterised by the highest incidence of positive CaScore, and its maximum values are significantly higher than the other two groups. The maximum Agatston score for patients with antiphospholipid syndrome is 908 HU, with SLE being 2.1 HU, with healthy controls – 233HU.

We investigate the levels of anti-ox LDL antibodies and we found that there is a correlation between the levels of aPL and anti-oxLDL.

**Conclusions:** The conclusion from our study is that the aPL could be considered for independent risk factor for accelerated atherosclerosis. The aPL are responsible for dyslipidemia in some cases blocking the transport molecules like  $\beta$ 2GPI.

**Disclosure of Interest:** None declared

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### FRI0382 A STUDY OF MCP1 AND LIPOCALIN AS URINARY BIOMARKERS IN LUPUS NEPHRITIS

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**Background:** Currently, major efforts have been undertaken to identify biomarkers that can predict impending lupus renal flare, development of chronic kidney disease or reflect renal histology at the time of the flare.

**Objectives:** This study aims to assess the correlation of urinary biomarkers MCP1 and NGAL with the disease activity in lupus nephritis.

**Methods:** This was a prospective study conducted in a tertiary care centre. 60 patients with SLE were recruited. They were divided into 3 groups, one with Active Lupus Nephritis ( $n=22$ ), another with Inactive Lupus Nephritis ( $n=20$ ) and a third formed of SLE patients with no renal involvement ( $n=18$ ). For comparison another group of age and sex matched controls was taken ( $n=20$ ). Disease activity was correlated with disease activity indices, baseline characteristics and biopsy. Urinary MCP1 and NGAL were measured. Statistical analysis using SPSS11.5 was

done to find the correlation between levels of urinary biomarkers and disease activity.

**Results:** In patients with active LN, both UMCP1/Cr and UNGAL/Cr were significantly elevated (92.78, 76.11 pg/ml,  $p<0.001$ ). In both control group and SLE without renal involvement the values of UMCP1/Cr and UNGAL/Cr were normal (24.44, 22.22 pg/ml in control and 24.3, 22.80 pg/ml in SLE without renal involvement). In patients with inactive LN the values of UMCP1/Cr and UNGAL/Cr were observed to be significantly higher than control (44.18, 38.45 pg/ml,  $p<0.005$ ) and lower than those of active LN. Values of UMCP1/Cr and UNGAL/Cr were found to be in close correlation with mean rSLEDAI scores of active LN<sup>10</sup> and inactive LN (3.6).

**Conclusions:** Levels of urinary biomarkers UMCP1 and UNGAL were significantly elevated in active lupus nephritis and found to have excellent correlation with disease activity index and rSLEDAI scores.

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**Disclosure of Interest:** None declared

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### FRI0383 CHANGES IN WHITE MATTER MICROSTRUCTURE CORRELATE WITH SF-36 MENTAL COMPONENT SUBSCORE IN INFLAMMATORY NPSLE

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**Background:** The diagnosis and treatment of neuropsychiatric systemic lupus erythematosus (NPSLE) is challenging due to the lack of a diagnostic gold standard and controlled trials. Immunosuppressive therapy is prescribed for immune-mediated NPSLE manifestations, despite little evidence supporting its effectiveness. There is increasing evidence for the value of magnetization transfer imaging (MTI) in NPSLE. Recent research has demonstrated that white matter (WM) magnetic transfer ratio histogram peak height (MTR-HPH), a derived-MTI index, is a valuable radiological biomarker for the diagnosis and follow-up in inflammatory NPSLE.<sup>1</sup> It remains unknown whether the changes in WM MTR-HPH also correlate with the change in health-related quality of life (QoL) in these patients.

**Objectives:** To analyse the correlation between change in WM MTR-HPH and change in QoL in different subsets of NPSLE (inflammatory, ischaemic, non-NPSLE).

**Methods:** Patients that visited the Leiden University Medical Centre (LUMC) NPSLE clinic between 2007 and 2015 were included in this study. The attribution process of NP events to SLE and one of its underlying pathogenic mechanisms (ischaemic or inflammatory) was established by multidisciplinary consensus. All patients underwent MRI examination at two different time points and filled in the Short-Form 36 (SF-36). Summary scores were deducted from the SF-36, leading to a Physical Component subscore (PCS) and a Mental Component subscore (MCS) for QoL. Spearman rank correlation coefficient (SR) was used to correlate WM MTR-HPH and the overall difference in change between visits in MCS and PCS. Data was analysed per patient and per event.

**Results:** A total of 15 patients (mean age 39.5 $\pm$ 14.1 years, 93% female) were included. Thirty-one NPSLE events were present, of which 68% were inflammatory, 13% ischaemic and 19% non-NPSLE events. Average time between visits was 2.9 $\pm$ 1.5 years. The per patient analysis showed statistical significant correlation between WM MTR-HPH and MCS change (SR=0.62;  $p=0.01$ ) and no effect on PCS change (SR=0.09;  $p=0.76$ ). The per event analysis showed a significant correlation between change in WM MTR-HPH and MCS in inflammatory events (SR=0.56;  $p=0.01$ ), but not in ischaemic ( $p=0.20$ ) or non-NPSLE events ( $p=0.65$ ). No correlation was observed between change in WM MTR-HPH and PCS in any of the subsets ( $p=0.21$ ,  $p=0.40$  and  $p=0.91$  respectively).

**Conclusions:** We are the first to demonstrate a correlation between a radiological biomarker and change in the mental component of QoL in inflammatory NPSLE patients. Our study supplies evidence for the use of immunosuppressive therapy in inflammatory NPSLE and supports the use of this radiological biomarker as an outcome measure for future trials in NPSLE.



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**FRI0384** PRIMARY SJÖGREN'S SYNDROME STRATIFIED BASED ON THE SEVERITY OF PATIENT-REPORTED FATIGUE

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**Background:** fatigue is one of the most common symptoms reported by patients affected by primary Sjögren's syndrome (pSS), and a major contributor to impaired quality of life.

**Objectives:** to analyse the clinical, serological and histological features of pSS patients stratified according to the severity of their self-reported fatigue.

**Methods:** among pSS patients undergoing clinical evaluation in our Sjögren's Clinic in a six-months period (January-June 2017), 86 consecutive unselected patients, fulfilling the latest ACR/EULAR pSS classification criteria, accepted to report their degree of fatigue on a 10 cm VAS (range 0–100) and to complete the ESSPRI questionnaire. Four subgroups of fatigue severity were defined, as previously published<sup>1</sup>: no fatigue (VAS=0); low fatigue (VAS=1–24); moderate fatigue (VAS=25–74); high fatigue (VAS=75–100). For each subgroup demographic, serological, histological features and ESSDAI score were collected, as well as the prevalence of pSS-related lymphoma, fibromyalgia (FM), autoimmune thyroiditis, and anaemia.

**Results:** fatigue was reported by the 87.2% (n=75) of pSS patients, distributed in subgroups as following: 25.3% (n=19) with low fatigue, 58.7% (n=44) with moderate fatigue and 16% (n=12) with high fatigue. Lymphoma was significantly (p=0.0133) more frequent in the pSS subgroup with high fatigue (33.4%, by considering active lymphoma cases; 50%, by considering also the cases with lymphoma in remission). FM patients were a minority (4.7% ; n=4), and never complained of high fatigue, all of them reporting moderate fatigue. A significant correlation was finally found between fatigue severity and ESSPRI (p<0.0001), but not with ESSDAI (p=0.31). No significant age or sex difference was observed between subgroups. Also autoimmune thyroiditis, anaemia, anti-SSA and/or anti-SSB positivity, rheumatoid factor positivity, and cryoglobulinemia showed no significant difference between subgroups.

**Conclusions:** when fatigue is better stratified in pSS, it appears that it is usually moderate or severe, rather than mild. Furthermore, it is unrelated to FM. Overall, fatigue appears as a consequence of pSS itself. Of note, severe fatigue was related in this study with the most important complication influencing patient survival in pSS, i.e., lymphoma. Further studies are needed to disclose the pathogenetic events leading to fatigue in pSS, and investigation of lymphoma in pSS might be also helpful to this end.

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**Disclosure of Interest:** None declared

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**FRI0385** CLINICAL CHARACTERISTIC FEATURES OF BRAINSTEM ENCEPHALITIS IN NEUROPSYCHIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS

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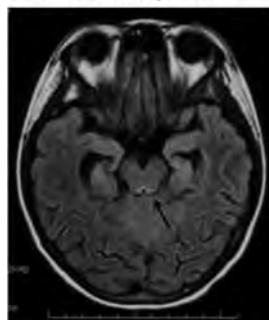
**Background:** Neuropsychiatric manifestation in systemic lupus erythematosus (NPSLE) is one of the most serious complications of the disease. The American College of Rheumatology (ACR) developed standardised nomenclature and case definitions for neuropsychiatric involvement in SLE (NPSLE) in 1999. Although myelopathy is included in the ACR nomenclature, no space is provided for the brainstem encephalitis. Moreover, it is still unclear whether the brainstem encephalitis is an independent clinical entity in NPSLE.

**Objectives:** The present study was designed in order to disclose the clinical characteristic features of the brainstem encephalitis in NPSLE.

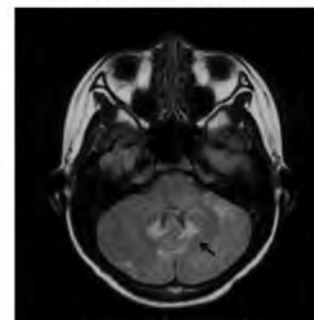
**Methods:** We prospectively collected the patients who presented brainstem lesions from 2005 to 2015. The diagnosis of the brainstem encephalitis was made by the elevation of cerebrospinal fluid (CSF) IL-6, Magnetic Resonance Imaging and response to steroid. Serum autoantibodies, including anti-ribosomal P protein antibodies (anti-P), anti-NMDA receptor NR2 antibodies (anti-NR2), anti-Sm antibodies and anti-aquaporin 4 antibodies (anti-AQP4) and anti-cardiolipin antibodies (anti-CL), were measured by ELISA.

**Results:** Seven patients presented the brainstem encephalitis during the period of 10 years. All the patients showed the elevation of CSF IL-6 (8.3–2716 pg/ml, median 377 pg/ml), whereas CSF cell count was elevated in 6 patients. The most common clinical symptoms were headache (4 patients), vertigo (3patients) and consciousness disturbance (3 patients). All the patients showed high intensity lesions in FLAIR images on MRI. Notably, 5 of the 7 patients also showed the high intensities periventricular regions, including cerebral aqueduct and the 4th ventricle (figure 1). Anti-NR2 and anti-P were positive in 7 patients and 6 patients, respectively. By contrast, anti-CL, anti-Sm and anti-AQP4 were positive in 4 patients, 3 patients and 1 patient, respectively. Six patients recovered after steroid therapy, while 1 patient died due to severe brainstem damages at the onset.

**Cerebral aqueduct**



**The 4th ventricle**



**Conclusions:** These results indicate that the brainstem encephalitis is an independent clinical entity in NPSLE, characterised by reversible high intensity lesions, especially in periventricular areas. Moreover, the data demonstrate that anti-AQP4-related neuromyelitis optica disorder is a minor population within the brainstem encephalitis. By contrast, it is suggested that anti-NR2 and anti-P might play an important role in the pathogenesis of the brainstem encephalitis.

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**Disclosure of Interest:** None declared

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**FRI0386** WORK DISABILITY AND QUALITY OF LIFE AMONG MULTI-ETHNIC MALAYSIAN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) PATIENTS

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**Background:** Patients with Systemic Lupus Erythematosus (SLE) are at risk of work disability due to the substantial impact of the disease towards their physical and mental health.

**Objectives:** To study the prevalence of work disability (WD) and unemployment rate among SLE patients, and their associations with the quality of life (QOL) in National University of Malaysia Medical Centre (UKMMC)

**Methods:** This was a cross-sectional study which recruited consecutive SLE patients who attended the Nephrology and Rheumatology clinic at Universiti Kebangsaan Malaysia Medical Centre (UKMMC) from March 2017 to July 2017. Information on their current and past employment history were obtained from a customised questionnaire and WD was defined as unemployment or an inability to do paid work due to illness at the time of study or at any time after the diagnosis of SLE being made. The disease characteristics, disease activity and damage were determined from the medical records. The quality of life was measured using SF-36 questionnaires. Statistical analyses were subsequently performed to determine the factors associated with WD. This study was approved by the UKMMC ethics research committee (FF FF-2017–109).

**Results:** A total of 197 patients were recruited, and their median age was 37 (32 to 47) years with median disease duration of 12 (8 to 17) years. Majority of them were Malays (n=116, 58.9%), followed by Chinese (n=69, 35%), Indians (n=8,

4.1%) and others (n=4, 2.0%). The prevalence of work disability was 35%(n=69) and the onset of WD was 4 (IQR:1 to 9) years after SLE diagnosis. WD was associated with older age, lower education level, more frequent disease flare, longer disease duration, higher SLICC ACR Damage Index, active disease (SLEDAI 2K and BILAG 2004 and had major organ involvement (lupus nephritis, haematological and neuropsychiatric), all p<0.05. Patients who received plasmapheresis, intravenous methylprednisolone, intravenous immunoglobulin, Mycophenolate Mofetil and calcineurin inhibitors were also associated with WD. Patients with work disability also had significantly impaired QOL with lower SF 36 scores. On multivariate logistic regression analysis, the independent predictors of WD were lower education level, being married and involvement of lupus nephritis, haematological and neuropsychiatric lupus (NPSLE).

**Conclusions:** More than one third of SLE patients had experienced work disability. Lower education level, being married and major organ involvement were the independent predictors for work disability. A larger prospective study is warranted to further delineate the risk factors.

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#### FRI0387 FACTORS ASSOCIATED WITH OSTEOPOROSIS AND FRACTURE IN PATIENTS WITH SJÖGREN PRIMARY SYNDROME

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**Background:** Primary Sjögren's syndrome (SSp) is a systemic autoimmune disease characterised by exocrine gland affectation and multisystem involvement. In addition to the systemic inflammatory affectation, patients with pSS have additional risk factors to develop osteoporosis (OP) and its major complication, osteoporotic fracture.

**Objectives:** The aim of the study is to determine the sociodemographic and clinical factors of pSS associated with the presence of OP and osteoporotic fracture in patients with pSS from the SJOGRENSER registry.

**Methods:** SJOGRENSER is a descriptive, cross-sectional and multicenter study of patients with pSS classified according to European-American consensus criteria. Patients attended in consultations of 33 Spanish rheumatology services were randomly included. Both the medical history and the medical interview were used to obtain the data. Epidemiological, clinical, serological and complications were collected. The continuous and categorical variables were analysed by means, medians and frequencies, with their respective deviations and interquartile ranges (p25-p75). Bivariate and multivariate analyses were carried out using a binomial logistic regression to study the factors associated with osteoporosis and osteoporotic fracture in pSS.

**Results:** In the SJOGRENSER registry, 437 patients were included (95% women, with a median age of 58.63 (50.02–67.98) years). The prevalence of OP in the cohort was 18.54% (81 patients). The prevalence of OP in men (n=21) was 19%, 2 men in the age group of 51–64 years and 2 in the group of >64 years. Three hundred of the women in the registry were menopausal (76.4%); a total of 67/300 women with menopause had OP (15%). A total of 37 osteoporotic fractures (8.5%) were recorded in the cohort. Factors associated with OP in women with SSp in the bivariate analysis were: age (60.5% in the group of >64 years, 28% in the group of 51–64 years and 2.6% in the group ≤50 years, p<0.001), the time course of the disease (11.35 (SD 7.95) vs 7.8 (SD 6.14), p<0.001), the age of menopause (47(SD 7.29) vs 48.11 (SD 5.67), p=0.020), the ESSDAI (6 (DS 7) vs 4 (DS 5), p=0.020), and presence of anti-La (77.6% vs 64.7, p=0.030). In the multivariate analysis, there was an association between OP and age in the 51–64 age group, OR 9.993 (95% CI, 2.301–43.399, p=0.002), age >64 years, OR 20.610 (CI 95% 4.679–90.774, p<0.001) and time course of the disease, OR 1.046 (95% CI 1.008–1.085, p=0.017). Similarly, an association was found between the fracture and age in the 51–64 age group, OR 5.068 (95% CI, 1.117–22.995, p=0.035), age >64 years, OR 7.674 (95% CI 1.675–35.151, p<0.009), the time course of the

disease, OR 1.049 (95% CI 1.003–1.097, p<0.036) and the ESSDAI score, OR 1.080 (95% CI, 1.029–1.134, p=0.002).

**Conclusions:** Patients with pSS have a considerable prevalence of osteoporosis and osteoporotic fracture. Age and time of evolution were factors associated with the development of OP, and similarly, age, time of evolution of the disease and ESSDAI were factors associated with the development of fracture in patients with pSS.

**Disclosure of Interest:** None declared

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#### FRI0388 RISK OF PREVENTABLE ADMISSIONS AMONG PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS PRIOR AND SUBSEQUENT DIAGNOSIS

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**Background:** Preventable hospitalizations for specific conditions are considered preventable because appropriate outpatient care should potentially avoid hospitalisation for these conditions. Although not all of the hospitalizations can be prevented, to identify the rate of preventable hospitalizations among patients with systemic lupus erythematosus (SLE) can help us to understand the excess potential preventable hospitalizations and to provide an action to the SLE patients.

**Objectives:** To investigate the risk of preventable hospitalisation in patients with SLE before and after initial diagnosis of the disease.

**Methods:** We identified 4483 adult patients with incident SLE between 2005 and 2009 using the Taiwan National Health Insurance Database. Each SLE patients were matched to five controls without SLE during the same study period, by age and sex. The index date was the first date of SLE diagnosis and their matched controls. We estimated the incidence and incidence rate ratios (IRRs) of preventable hospitalisation by conditional Poisson regression, adjusted for age, sex, Elixhauser Comorbidity Index, number of outpatient visits and hospitalizations 1-y prior to index date, residence urbanisation, income levels, occupation and the number of physicians at the patients' residence.

**Results:** The overall incidence of preventable hospitalisation was 1.88 (95% CI, 1.74 to 2.03) per 1000 person-months among SLE patients and 0.53 (95% CI, 0.49 to 0.56) per 1000 person-months among controls, giving an adjusted IRR of 3.57 (95% CI, 3.25 to 3.93). The IRRs especially higher in heart failure, bacterial pneumonia and urinary tract infection and the respective estimates were 2.85 (95% CI, 2.14 to 3.80), 4.67 (95% CI, 4.03 to 5.42) and 3.84 (95% CI, 3.35 to 4.41).

**Conclusions:** Risk of preventable hospitalisation is higher in patients with SLE.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.6959

#### FRI0389 BIOMARKERS AS DISEASE ACTIVITY INDICANTS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** In recent years, the search has been going on for the biomarkers potentially useful in the follow-up of patients with systemic lupus erythematosus (SLE).

**Objectives:** The aim of our study was to establish the importance of various immunological and biological parameters as disease activity indicants in SLE.

**Methods:** The study involved 85 SLE patients in whom disease activity assessment was performed using the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI). In addition to standard anti-dsDNA antibodies and C3 complement component, anti-nucleosome and anti-C1q antibodies and monocyte chemoattractant protein-1 (MCP-1) were determined in the serum and urine. The antibodies were determined using the ELISA test, while serum and urine MCP1 was determined using the sandwich enzyme immunoassay in accordance with the instructions by the manufacturer, R and D Systems, Inc. Minneapolis (USA).

**Results:** The studied group consisted of 78 women and 7 men, with the mean age of 45.27±9.71 years and average disease duration of 10.37±7.99 years. Univariate linear regression analysis showed that all of the examined parameters with the exception of C3 complement demonstrated a statistically significant impact on the SLEDAI values (for anti-dsDNA p=0.033, anti-nucleosome p=0.002, anti-C1q antibodies p=0.005, serum MCP1 p=0.006, urinary MCP1

$p < 0.001$ ). The SLEDAI value rose with increasing values of all the parameters except C3 complement. Using the standard multiple regression analysis, the impact of anti-dsDNA, anti-nukleosome, anti-C1q antibodies, complement C3, and serum and urinary MCP1 on SLEDAI was evaluated. The studied model was able to explain 26.60% of disease activity index variance (corrected  $r^2 = 0.246$ ,  $F = 4.755$ ,  $p < 0.001$ ). As the statistically significant risk factors, serum MCP1 (Beta=0.257,  $p = 0.040$ ) and urinary MCP1 (Beta=0.326,  $p = 0.008$ ) could be singled out. Serum MCP1 increased SLEDAI values and explains their variance with 4.80%. The impact of urinary MCP1 was stronger. SLEDAI values increased with elevated urinary MCP1. This parameter was able to explain 8.10% of SLEDAI variance.

**Conclusions:** The study showed that anti-dsDNA, anti-nukleosome and anti-C1q antibodies were associated with SLE disease activity, but the association was strongest with serum and urinary MCP1.

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**Disclosure of Interest:** None declared

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#### FRI0390 IMPAIRED OVARIAN RESERVE IN PATIENTS AFFECTED BY SYSTEMIC LUPUS ERYTHEMATOSUS: A CASE-CONTROL STUDY

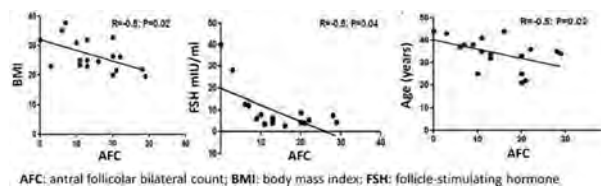
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**Background:** Systemic lupus erythematosus (SLE) is an autoimmune disease showing a strong predilection for reproductive age women (female/male ratio 9:1). This is in part due to the effects exerted by sexual hormones on immune system. The term ovarian reserve has been used traditionally to describe the number and quality of oocytes in women. This is assessed by detection of FSH, AMH and Estradiol (E2) and by ultrasonographic (US) evaluation of antral follicular bilateral count (AFC), as recommended by the Society of Reproductive Medicine. The evaluation of AFC should be conducted in the early follicular phase of the menstrual cycle. An AFC lower than 3–4 follicles is highly specific (73%–97%) of poor ovarian function. Data from the literature about ovarian reserve in SLE showed contrasting results.

**Objectives:** We aimed at assessing ovarian reserve in a SLE cohort, by US determination of AFC and by analysing serum levels of AMH, FSH, E2.

**Methods:** In this case control study, we enrolled consecutive SLE patients in reproductive age (<45 years), fulfilled the 1997 ACR revised criteria, not treated by gonadotoxic chemotherapy agents. Moreover, we enrolled age-matched healthy women (HS). Clinical and laboratory data were collected in a standardised, computerised and electronically filled form, including demographics, past medical history with date of diagnosis, autoantibody profile, comorbidities, previous and concomitant treatments. We assessed the disease activity and chronic damage by using SLEDAI-2K and SDI, respectively. In order to assess AFC, patients and HS underwent to transvaginal US evaluation by a single operator (Samsung Elite USS-WS8EL4U/WR) between the 2nd and 7th day of the menstrual cycle. At the same day of the US assessment, we obtained sample of peripheral venous blood from patients and HS to evaluate FSH, AMH and E2 dosages (ELISA kit CLOUD-CLONE Corp., My Biosource, USA).

**Results:** Nineteen SLE patients (median age 35 years, IQR 6.0; mean disease duration  $\pm$ SD 12.2 $\pm$ 7.7 months) and 8 HS were evaluated. A mean  $\pm$ SD SLEDAI-2K of 2.5 $\pm$ 1.5 was registered; 3 patients had a chronic damage (SDI=1). FSH values were significantly higher in SLE patients compared with HS [SLE: median (IQR) 35;<sup>6</sup> HS: median (IQR) 3 (1.5);  $p = 0.01$ ]. Concerning the AFC, we found significantly lower values in SLE patients than in HS [SLE: median (IQR) 13;<sup>11</sup> HS: median (IQR) 22.5 (10.5);  $p = 0.03$ ]. The Spearman analysis demonstrated a negative correlation between AFC and BMI ( $r = -0.5$ ,  $p = 0.02$ ), FSH ( $r = -0.5$ ,  $p = 0.04$ ) and age ( $r = -0.5$ ,  $p = 0.02$ ) (figure 1).



**Abstract FRI0390 – Figure 1**

**AFC:** antral follicular bilateral count; **BMI:** body mass index; **FSH:** follicle-stimulating hormone

**Conclusions:** The preservation of fertility is a crucial point in SLE patients and the evaluation of ovarian reserve should be included in the patients' management in order to assess ovarian function. Moving from these premises, in the present study we demonstrated an impaired ovarian reserve in SLE patients in terms of AFC values and a negative correlation with hormonal and some demographic features.

**Disclosure of Interest:** None declared

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#### FRI0391 THE RELATIONSHIP BETWEEN OESTROGEN RECEPTORS AND HYPERURICEMIA IN YOUNG FEMALE SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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**Background:** We have found that the incidence of hyperuricemia of young female systemic lupus erythematosus (SLE) patients was higher than that of healthy young women<sup>[1]</sup>. Why the high level of oestrogen didn't show protection in uric acid (UA) level of fertile female SLE patients? There few reports yet.

**Objectives:** To investigate the relationship between UA level and the levels of oestrogen, oestrogen receptors, antibodies to oestrogen receptors.

**Methods:** This was a cross-sectional study of 62 fertile female SLE patients that were divided into two groups including a high UA group (n=27) and a normal UA group (n=35). Serum UA levels, kidney index, SLE disease indicators and levels of oestrogen, oestrogen receptors, antibodies to oestrogen receptors were determined. Multiple linear regression analysis was applied to analyse the associations of UA levels with clinical features and levels of oestrogen, oestrogen receptors and antibodies to oestrogen receptors.

**Results:** 1. The mean ages of the two groups were (28.62 $\pm$ 7.89) years and (28.82 $\pm$ 8.28) years respectively, with no significantly different ( $t = 0.096$ ,  $p = 0.924$ ). There was no SLE patients manifested renal failure (CRE level higher than 120  $\mu$ mol/l). All the SLE patients were at the onset of disease.

2. The mean UA levels of the high UA group and the normal UA group were (531.74 $\pm$ 134.05)  $\mu$ mol/L and (238.86 $\pm$ 61.32)  $\mu$ mol/L respectively, with significant difference ( $t = -11.48$ ,  $p < 0.001$ ).

3. In the high UA group, the levels of CRE, LDL, cystatin, urine protein and were dramatically higher than those were found in the normal UA group ( $t = -3.617$ ,  $-3.319$ ,  $-2.782$ ,  $-2.979$ , and  $p = 0.001$ ,  $0.002$ ,  $0.007$ ,  $0.004$ , respectively), and oestrogen receptor  $\beta$  level were significantly lower than that of the normal group ( $t = 2.138$ ,  $p = 0.037$ ). The positive rate of urine blood of the high UA group were significantly higher than that of the normal UA subgroup ( $\chi^2 = 6.213$ ,  $p = 0.012$ ).

4. Multiple linear regression analysis revealed there were significant relationships between UA level and CRE, oestrogen receptor  $\beta$ , and urine protein, urine blood.



**Abstract FRI0391 – Table 1.** Independently-Associated Clinical Biomarkers with Serological UA levels in fertile SLE female patients

Variable	Unstandardized Coefficients	Standardised Coefficients	t	P	95% CI
	B	SEM			
CRE	1.145	0.462 0.263	2.478	0.016	0.223–2.068
oestrogen receptor $\beta$ urine protein	-2.758	0.933 0.239	2.299	0.033	3.132–44.38
UBLD	2.906	1.042 0.286	2.788	0.019	0.825–4.986
Constant	56.426	28.058 0.216	2.011	0.048	0.422–112.43
	177.283	42.179	4.203	0.001	93.09–216.47

**Conclusions:** Hyperuricemia in young female SLE patients indicated the renal damage, and low level of oestrogen receptor  $\beta$  may contribute to hyperuricemia.

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**Disclosure of Interest:** None declared

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### FRI0392 THE RELATIONSHIP BETWEEN SALIVARY FLOW RATES, ORAL HEALTH ASSESSMENT AND ULTRASONOGRAPHIC SCORING OF THE MAJOR SALIVARY GLANDS IN SJOGREN SYNDROME

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**Background:** Salivary flow rates (SFR) and oral health were known to be frequently impaired in Sjogren's syndrome (SjS) due to chronic inflammation and destruction of the salivary glands. Ultrasonography (USG) of major salivary glands (SG-USG) is a non-invasive widely used tool to evaluate salivary glands in SjS.

**Objectives:** The aim of the study was to assess the relationships between SFRs, oral health and USG changes of major salivary glands in patients with primary SjS.

**Methods:** Fifty-nine SjS patients (F/M:57/2) with the mean age of 52.2±11.5 years. The duration of follow-up period of 9.±7.1 years fulfilling ACR-EULAR classification criteria (2002) were included. Major salivary glands (bilateral parotis and submandibular glands) were scored according to two different scoring systems which are Hocevar A.(0–48) and Milic VD. (0–12). Oral health was assessed by indices. Measurements of whole unstimulated and stimulated SFRs were carried out in patients between 9 a.m. and 10 a.m in the morning. Oral health related quality of life (OHRQoL) as a patient reported outcome measure was evaluated by using Oral health impact profile (OHIP-14). High scores indicated poor OHRQoL status. Pathologic findings in oral health (GM) and USG images (NI) were evaluated by two authors as double-blind.

**Results:** Unstimulated SFR (0.2±0.2 ml/min) was correlated with stimulated SFR (1.1±0.7 ml/min) in the whole group ( $r=0.8$   $p=0.000$ ). Moderate correlations were seen between unstimulated and stimulated whole SFRs and scores of hypoechoic areas in bilateral parotid and submandibular glands ( $p<0.05$ ). Scores of Hocevar, Milic and OHIP-14 were found to be poor in patients with unstimulated SFR  $\leq 0.1$  ml/minute compared to those of others ( $p<0.05$ ) (table 1). In addition, the number of extracted teeth (8,6±7,5) was correlated with the number of carious teeth ( $r=-0.3$ ,  $p=0.036$ ).

**Abstract FRI0392 – Table 1.** Salivary Flow Rates, OHIP-14 and SG-USG Scores of SjS Patients

	Salivary Flow Rates (SFR)		P
	$\leq 0.1$ ml/minute (n=17)	$>0.1$ ml/minute (n=39)	
Hocevar-total score	24,8±8,9	16,4±5,8	P=0,003
Milic-total score	7,4±2,2	4,9±2,3	P=0,001
OHIP-14 score	36,4±15,2	15,1±8,3	P=0,001

**Conclusions:** Unstimulated and stimulated SFRs were found correlated with the structural changes of major salivary glands. Tooth loss and poor OHRQoL were shown in patients due to reduced salivary outputs. USG images of salivary glands

could give insight to physicians about oral health and OHRQoL as outcome measure in patients with SjS.

**Disclosure of Interest:** None declared

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### FRI0393 MATERNAL AND FETAL OUTCOMES IN SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Systemic Lupus Erythematosus (SLE) is associated with an increased risk of adverse pregnancy outcomes.

**Objectives:** We aim to evaluate the maternal and fetal outcomes in SLE pregnancies in a single tertiary referral centre.

**Methods:** We retrospectively analysed 75 pregnancies in 45 patients with SLE over a 16 year period from 2000 to 2016. All patients fulfilled the 1997 American College of Rheumatology (ACR) criteria or the Systemic Lupus International Collaborating Clinics (SLICC) criteria for diagnosis of SLE.

**Results:** In our multi-ethnic cohort, there were 65% Chinese, 23% Malays and 7% Indians. The mean age was 32 years old and majority (55%) were nulliparous. The mean SLE disease duration was 5.9 years. Baseline SLE manifestations were predominantly haematological (73%), arthritis (71%) and renal (57%). There were 33 pregnancies (44%) with anti-Ro (SS-A) antibody positivity. There were 9 pregnancies (12%) with SLE and antiphospholipid syndrome. In our cohort, the majority of the patients were on prednisolone (76%). Half of the patients (48%) were on hydroxychloroquine or chloroquine and 27% were on azathioprine. In the subgroup of patients with SLE and antiphospholipid syndrome, 67% (6/9 pregnancies) were treated with therapeutic clexane and 33% (3 pregnancies) with the combination of prophylactic clexane and aspirin. The mean SELENA-SLEDAI score at the booking visit was 4.0.

In our cohort, the live birth rate was 75%. More than half of the deliveries were via Caesarean section (57%). There were maternal and fetal complications in 61% of the pregnancies. Pregnancy losses occurred in 16 pregnancies with the majority (87%) being early pregnancy losses that occurred prior to 13 weeks gestation. There were 13 pregnancies (17%) with intrauterine growth restriction and 18 pregnancies (24%) with preterm delivery. In the subgroup of the preterm births, 2 were extremely preterm birth (<28 weeks gestation) and 2 were very preterm birth (28 weeks to <32 weeks gestation). There were no cases of congenital heart block or neonatal lupus. There was one neonatal death.

SLE flares occurred in 25 pregnancies (33%). The most common organ involvement were haematological (44%), renal (40%), mucocutaneous (28%) and arthritis (16%) Pre-eclampsia occurred in 2 pregnancies (2%). There were 3 cases of a first presentation of lupus nephritis in pregnancy. In the subgroup of SLE pregnancies with antiphospholipid syndrome, there were higher SLE flare rates (44%) and more adverse pregnancy outcomes with 3 pregnancies (33%) that resulted in miscarriages, 2 pregnancies (22%) with preterm delivery and one pregnancy (11%) complicated by pre-eclampsia (table 1). There were 7% of pregnancies with a post-partum SLE flare.

**Abstract FRI0393 – Table 1.** Comparison of maternal and fetal outcomes between SLE pregnancies and SLE with antiphospholipid (APS) pregnancies

Adverse pregnancy outcomes	SLE pregnancies (n=75)	SLE with APS pregnancies (n=9)
SLE flares, n(%)	25 (33.33%)	4 (44.44%)
Pre-eclampsia, n(%)	2 (2.67%)	1 (11.1%)
Miscarriages, n(%)	15 (20%)	3 (33.33%)
Early pregnancy loss (<13/40), n(%)	14 (18.67%)	3 (33.33%)
Late pregnancy loss ( $\geq 13/40$ ), n(%)	1 (1.33%)	0
Preterm delivery, n(%)	18 (24%)	2 (22.22%)
Neonatal death, n(%)	1 (1.33%)	1 (11.1%)

**Conclusions:** In our multi-ethnic cohort, more than half of the patients experienced an adverse pregnancy outcome. SLE flares in pregnancy occurred in a third of the cohort with the most common organ manifestation being haematological and renal flares. SLE pregnancies with antiphospholipid syndrome appeared to be associated with a higher risk of SLE flares and adverse pregnancy outcomes.

**Disclosure of Interest:** None declared

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**FRI0394 THE ROLE OF D-DIMER TEST AS A SCREENING TOOL FOR VENOUS THROMBOEMBOLISM IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AS COMPARED TO MATCHED CONTROL SUBJECTS**

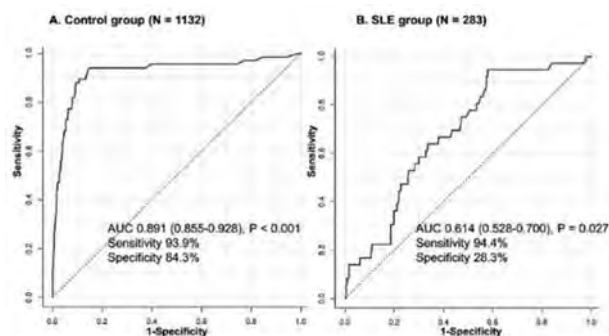
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**Background:** d-dimer test is widely used as a screening tool for venous thromboembolisms (VTE). Meanwhile, d-dimer can increase in various conditions including severe infection, and inflammation. However, it has been rarely reported whether d-dimer test is useful for screening of VTE in systemic lupus erythematosus (SLE) patients.

**Objectives:** We evaluated the role of d-dimer test as a screening tool for VTE in patients with SLE, compared to age-, and sex-matched non-autoimmune disease subjects.

**Methods:** In this retrospective cohort study, a total of 283 SLE patients and 1132 age-, and sex-matched control subjects (those who had no rheumatic diseases) who underwent d-dimer test as a screening test for VTE were enrolled at Seoul National University Hospital between January 2000 and July 2017. VTE was defined to be present when a thromboembolism was proven in imaging studies which included computed tomography, lung perfusion scan or duplex ultrasonography. Predictive value of d-dimer test for VTE was compared between SLE patients and control subjects by calculating area under the curves (AUC) in receiver operating characteristics (ROC) curves of d-dimer test. Finally, the usefulness of d-dimer test was evaluated in different subsets of SLE patients by analysing ROC curves.

**Results:** The mean (SD) age of the 283 SLE patients was 36.8 (13.5) years and that of 1132 control subjects was 38.2 (12.8) years. The mean (SD) plasma level of d-dimer was 2262.1 (3794.5) ng/ml in SLE patients, while it was 1087.5 (5063.1) ng/ml in the control group ( $p < 0.001$ ). The incidence of VTE was significantly higher in SLE patients than the controls (12.7% vs. 5.8%,  $p < 0.001$ ). When the cut-off value of d-dimer test was set to 500 ng/ml, the AUC for VTE was only 0.614 in SLE patients, while it was 0.891 in the control group, suggesting that d-dimer test may not be useful as a screening tool for VTE in SLE patients. When the SLE patients were divided according to the presence of antiphospholipid antibodies (APS Abs), the AUC value for VTE was 0.788 in patients who didn't have APS Abs but it was only 0.556 in patients who had APS Abs.



**Abstract FRI0394 – Figure 1.** ROC curves in control and SLE group (cut-off value of d-dimer = 500 ng/ml)

**Conclusions:** d-dimer test cannot predict VTE in SLE patients as accurately as in general population. In SLE patients, d-dimer's diagnostic capability for VTE is even lower in the presence of APS Abs.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.2250

**FRI0395 SLE DISEASE ACTIVITY INDEX GLUCOCORTICOID INDEX (SLEDAI-2KG) IDENTIFIES MORE RESPONDERS THAN SLEDAI-2K**

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**Background:** Systemic Lupus Erythematosus Disease Activity Index-2000 (SLEDAI-2K) is one of the most commonly used disease activity indices in clinical practice and research but this index doesn't account for severity within each descriptor. Moreover, in clinical trials, the use of standard of care (SoC), which includes glucocorticoid (GC) often confounds trial results.

We developed and validated a novel lupus disease activity index, SLEDAI-2K GC (SLEDAI-2KG), that describes disease activity while accounting for GC dose. SLEDAI-2KG has the same descriptors as SLEDAI-2K in addition to a new descriptor "GC" with different weight scores based on the dose of GC. Furthermore, SLEDAI-2KG has a low administration burden and a simple scoring system similar to SLEDAI-2K.

**Objectives:** We aimed to compare the performance of SLEDAI-2K and SGI in identifying responders in response to SoC.

**Methods:** Patients have been followed prospectively according to a standard protocol between January 2011 and January 2014, at a single lupus centre, with active disease (SLEDAI-2K ≥ 6), on prednisone ≥ 10 mg/day, and with follow up visits within 5–24 months were studied. Treatment was determined based on the judgment of the treating rheumatologist.

Response to SoC therapy, at first follow up visit, was assessed by SLEDAI-2K and SLEDAI-2KG. Responders were defined based on the decrease in SLEDAI-2K and SGI score by ≥ 4. The performance of SLEDAI-2K and SGI was also compared using different cut-off points; 5, 6 and 7. Descriptive analysis was used.

**Results:** 111 patients met the inclusion criteria of the study and were further analysed. Patients' characteristics are represented in table 1.

SLEDAI-2KG identified more responders at 6 months (94% vs. 84%) and at 12 months (92% vs. 76%) compared to SLEDAI-2K by cut off of 4. SLEDAI-2KG also identified more responders with cut off points 5, 6 and 7 (table 2).

**Abstract FRI0395 – Table 1.** Patient Characteristics

Variables	Total (n=111)
Sex (female)	98 (88.3%)
Age at baseline (mean±SD)	35.75±11.51
SLE duration at baseline (mean±SD)	9.02±7.74
Ethnicity	13 (11.7%)
Asian	23 (20.7%)
Black	51 (45.9%)
Caucasian	24 (21.6%)
Others	
Months from baseline to 1 st follow-up (mean±SD)	7.68±2.95
SLEDAI-2K at baseline (mean±SD)	12.39±6.03
Prednisone dose at baseline (mg/day) (mean±SD)	22.94±14.19
SLEDAI-2KG at baseline (mean±SD)	17.48±6.78
SLEDAI-2K at 1 st follow-up	8.08±6.04
Prednisone dose at 1 st follow-up (mg/day) (mean±SD)	15.23±10.94
SLEDAI-2KG at 1 st follow-up	12.67±6.98

**Abstract FRI0395 – Table 2.** Responders by SLEDAI-2K and SLEDAI2KG in 111 patients

Indices	Percentage of responders at 6 months			Percentage of responders at 12 months		
	≥4	≥5	≥6	≥4	≥5	≥6
SLEDAI-2K	84%	68%	68%	59%	76%	57%
SLEDAI-2KG	94%	88%	83%	79%	92%	80%
Additional Responders	10%	20%	15%	20%	16%	23%

**Conclusions:** The novel index, SLEDAI-2KG, is superior to SLEDAI-2K in identifying responders at 6 and 12 months accounting for steroid dose and thus adjusting for severity within each descriptor of SLEDAI-2K. SLEDAI-2KG has the ability to enhance analyses in clinical trials to differentiate between responders on minimal and moderate/large doses of GC.

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FRIDAY, 15 JUNE 2018

## Systemic sclerosis, myositis and related syndromes – etiology, pathogenesis and animal models

### FRI0396 THE ATM KINASE AND PTEN, DRIVE MYOFIBROBLASTS DIFFERENTIATION BY ACTIVATING THE TGFB AUTOCRINE LOOP

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**Background:** Pulmonary fibrosis is a major cause of mortality in scleroderma (SSc) and Idiopathic Pulmonary Fibrosis (IPF). Fibrosis is driven by inappropriate myofibroblast differentiation and persistence. Understanding this process, is vital for developing an effective treatment. Angiotensin II, is implicated in fibroblast activation in the heart and kidney, through interactions with growth factors (e.g. EGF and TGFβ).

**Objectives:** We examined the role of Angiotensin II in myofibroblast activation in the lung.

**Methods:** Lung fibroblasts were isolated from SSc, IPF, or control patient lungs (6 each). Fibroblasts were also cultured from PTEN null and wild-type mice. Protein expression after angiotensin II treatment (AngII) was investigated by western blotting. Myofibroblast differentiation and function was assayed through the contraction of 3D collagen gels and scratch migration assays. The signalling pathways involved were dissected using specific inhibitors: PI3-kinase/AKT (wortmannin, LY294002), TGFβ (1d11 neutralising antibody, SB431542 ALK5 inhibitor) Ataxia-Telangiectasia Mutated (ATM – Ku55933), AngII (Losartan).

**Results:** SSc and IPF lung fibroblasts showed increased AKT phosphorylation and suppressed PTEN expression (p<0.05). Their phenotype was more myofibroblast-like, with higher αSMA expression (p<0.05), increased collagen gel contraction (control; 207±14 vs SSc; 93±15 vs IPF 91±21, p<0.05), and enhanced migratory capacity (p<0.05). PTEN-null fibroblasts showed a similar phenotype. AngII treatment activated AKT, suppressed PTEN and induced myofibroblast differentiation in normal lung fibroblasts. In both AngII-treated and PTEN lung fibroblasts AKT activation required the ATM kinase. Inhibition of AKT either with PI3K or ATM inhibitor abrogated these effects. The increased expression of Myofibroblast-related genes after AngII treatment, was also blocked by inhibition of TGFβ with a neutralising antibody or an ALK5 inhibitor. AKT phosphorylation on the other hand was only partially blocked by TGFβ inhibition.

**Conclusions:** Our data demonstrate for the first time that AngII signals via the ATM kinase, which together with PTEN suppression are essential for the activation of AKT by AngII. AngII promotes myofibroblast differentiation, by stimulating the fibroblast TGFβ autocrine loop through AKT. Our data shows that activation of AKT through ATM and PTEN, may serve as the molecular link between pulmonary hypertension and lung fibrosis in fibrotic diseases.

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**Disclosure of Interest:** None declared

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### FRI0397 PECULIAR EXPRESSION OF AUTOPHAGY BIOMARKERS IN NECROTIZING AUTOIMMUNE MYOPATHY MUSCLE

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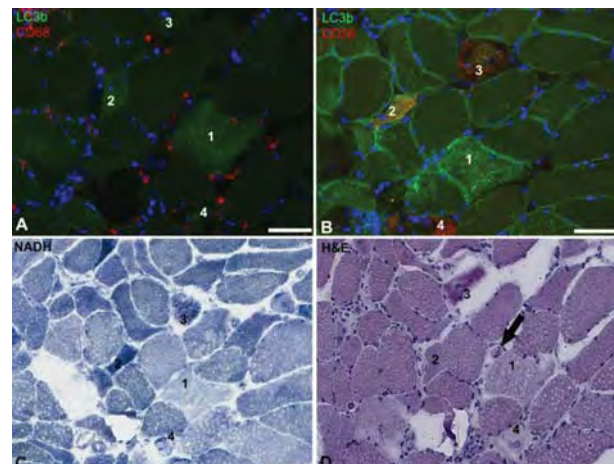
**Background:** Immune mediated necrotizing myopathy (IMNM) is a recently recognised pathology within the spectrum of idiopathic inflammatory myopathies (IIMs). Specific autoantibodies and the response to immunosuppressants aid to make the diagnosis and suggest immune-mediated pathogenesis, although histopathological features are not specific for IMNM. Autophagy and ubiquitin-proteasome system are two interacting systems by which dysfunctional cellular components are degraded in the cell. Their dysregulation, in sporadic Inclusion

Body Myositis (sIBM), seems to be responsible for the protein aggregates. The autophagy dysfunction in IMNM was not widely investigated.

**Objectives:** To investigate autophagy marker expression, macrophages localization and accumulation of misfolded proteins in non-necrotic fibres of IMNM muscle in comparison with Dermatomyositis (DM), Polymyositis (PM) and sIBM.

**Methods:** Among 52 IIMs diagnosed from January 2015 to June 2017, we reviewed muscle biopsies and stored sera. Six subjects were included in the IMNM group, characterised by many necrotic muscle fibres, regenerating muscle fibres and no significant inflammation despite of numerous but scattered macrophages removing necrotic muscle fibres. Two patients had anti-signal recognition particle (SRP) autoantibodies, two patients anti-3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMGCR), the others tested negative for specific autoantibodies. All IMNM patients had a positive response to immunosuppressants. Muscle sections were immunolabelled with the following antigens: ubiquitin, autophagy markers LC3b, p62 (a receptor of autophagy), TDP-43 (a marker of ubiquitinated proteic inclusions), SMI31 and SMI310 (Phosphorylated Neurofilaments), CD31 (endothelial cell marker), C5b-9 (membrane attack complex), CD4 (T-helper lymphocytes), CD8 (T-suppressor lymphocytes), CD68 (macrophages), CD20 (B-lymphocytes), CD56 (NK lymphocytes and regenerating muscle fibres), MHC I, MHC II. Quantitative results were compared among IMNM (n=6), DM (n=4), sIBM (n=4), PM (n=5) and healthy controls (n=4).

**Results:** In IMNM, inflammation was mild compared with DM, PM, sIBM, and consisted in sporadic endomysial and/or perivascular cells CD68+. Skeletal muscle fibres (SMFs) containing LC3b+puncta were significantly higher in IMNM and IBMs than in DM or PM. In all IMNM, the greater proportion of LC3b+puncta was localised in CD56+fibres (figure 1), instead, sIBM showed a high number of LC3b+puncta in vacuolated SMFs with low expression of CD56+SMFs. As expected, P62 and SMI31 aggregates were significantly higher in sIBM than in the other IIMs, even if, also in IMNM, there were moderate p62 accumulations and a little proportion of SMFs stained by SMI31. Finally, in IMNM there was the highest number of ubiquitin+SMFs.



**Conclusions:** These findings suggest an involvement of cellular clearance systems in the pathophysiology of IMNM similarly to sIBM. Nevertheless, LC3b+puncta in regenerating fibres can be considered a peculiar biomarker in IMNM. Further studies of larger cohort of patients are needed to better define IMNM.

**Disclosure of Interest:** None declared

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### FRI0398 SL-401, A NOVEL TARGETED THERAPY DIRECTED TO THE INTERLEUKIN-3 RECEPTOR (CD123), KILLS PLASMACYTOID DENDRITIC CELLS FROM SYSTEMIC SCLEROSIS PATIENTS

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**Background:** SL-401 is a novel biologic targeted therapy directed to the interleukin-3 receptor (CD123). SL-401 is comprised of human IL-3 recombinantly fused to a truncated diphtheria toxin (DT) payload engineered such that IL-3 replaces the native DT receptor-binding domain. In this way, the IL-3 domain of SL-401 directs the cytotoxic DT payload to cells expressing CD123. Upon internalisation, SL-401 irreversibly inhibits protein synthesis and induces apoptosis of the target cell.

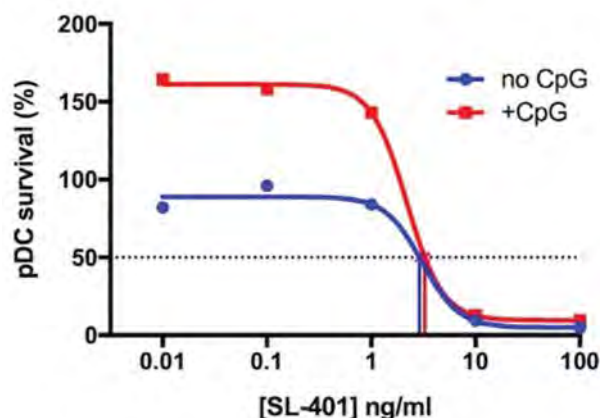


Plasmacytoid dendritic cells (pDCs) are immune cells that express CD123, secrete IFN- $\alpha$ , and play a role in inflammation and disease pathogenesis observed in systemic sclerosis (SSc) patients<sup>1,2</sup>. Therefore, depletion of pDCs or attenuation of pDC function may represent a novel approach to treating SSc patients.

**Objectives:** To assess the ability of SL-401 to deplete pDCs from healthy volunteers (HV) and SSc patients *ex vivo*.

**Methods:** Patients fulfilled the 2013 ACR/EULAR classification criteria for SSc<sup>3</sup>. PBMCs from either SSc patients or healthy volunteers (HV) were prepared using Ficoll-Paque density gradient from fresh blood. pDCs were isolated from PBMCs as previously described<sup>4</sup> and used to further enrich additional PBMCs. pDC-enriched PBMCs (3%–6% pDCs) were cultured at  $2 \times 10^5$  cells per well in the presence or absence of CpG-274 (0.5 mM) to activate pDCs and then incubated with SL-401 (0.01–100 ng/ml, 0.17 pM–1.7 nM) at 37°C, 5% CO<sub>2</sub>, and 95% humidity. After 24 hours of culture, pDC survival was assessed by flow cytometry (CD14<sup>+</sup>, CD3<sup>+</sup> B220<sup>+</sup> CD123<sup>+</sup>), and supernatants were collected for cytokine quantification by a multiplexed Luminex assay.

**Results:** CD123 expression levels on pDCs from HV and SSc donors were comparable, suggesting that targeting of pDCs in SSc can be modelled in HV. SL-401 was cytotoxic towards pDCs from both HV (n=5) and SSc donors (n=3) to a similar extent. The ED<sub>50</sub> of SL-401 against pDCs from HV and SSc was 4.3 and 3.3 ng/ml (74.5 and 57.2 pM), respectively (figure 1). No effect was observed on B or T cells across the SL-401 dose range tested. SL-401-mediated pDC depletion was further accompanied by a significant reduction in CpG-induced IFN- $\alpha$  secretion.



**Conclusions:** SL-401 is a novel CD123-targeted therapy capable of killing pDCs from both HVs and SSc patients. These data present a potentially novel approach of targeting pDCs in the treatment of SSc and warrant further investigation. A clinical trial is planned.

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FRI0399

#### RNAI-BASED IDENTIFICATION OF NOVEL DRUG TARGETS TO REDUCE ENDOTHELIAL TO MESENCHYMAL TRANSITION (ENDOMT) IN HUMAN DERMAL MICROVASCULAR ENDOTHELIAL CELLS: A TARGET DISCOVERY APPROACH FOR SCLERODERMA

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**Background:** Systemic sclerosis (SSc) is an autoimmune connective tissue disease characterised by early vascular abnormalities and subsequent fibroblast activation and differentiation into myofibroblasts, leading to fibrosis.<sup>1,2</sup> Recently, endothelial to mesenchymal transition (EndoMT), a complex biological process in which endothelial cells lose their specific markers and acquire a mesenchymal or myofibroblastic phenotype, was reported in SSc.<sup>3</sup>

**Objectives:** We developed a high-content screening assay with the aim to identify novel proteins which, upon inhibition, will reduce EndoMT in SSc.

**Methods:** Human dermal microvascular endothelial cells (HMVECs) were seeded in 384 well plates and transfected with a RNAi-based library targeting 866 genes. Cells were then triggered with either disease-related cytokines, such as transforming growth factor beta (TGF- $\beta$ ), or with serum from very early diagnosed, limited cutaneous and diffuse cutaneous SSc patients. Serum derived from healthy donors was used as a control. After 72 hours of triggering, changes in expression level of endothelial and mesenchymal markers were quantified by immunocytochemistry and high content imaging.

**Results:** We developed a high-throughput EndoMT assay that allows for monitoring of changes in endothelial and mesenchymal markers upon triggering with disease-related cytokines and serum derived from SSc patients. We used this assay to screen an RNAi-based library in HMVECs and identify more than 100 targets able to reduce EndoMT triggered by either TGF- $\beta$  or SSc patient serum. Identified hits subsequently will be extensively validated in secondary biological assays, and the validated targets will represent excellent candidate drug targets.

**Conclusions:** This program constitutes a critical path of experiments that will enable the selection of only those targets which meet pre-determined target acceptance criteria. We have chosen to identify targets in a human primary cell system and employ patient's serum as trigger of EndoMT to be able to closely investigate the cellular processes promoting EndoMT in SSc pathogenesis. By using this high-throughput screening platform, we aim to find disease-modifying targets that will be used as an entry point for small molecule drug discovery.

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**Disclosure of Interest:** None declared

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FRI0400

#### THE AP1 TRANSCRIPTION FACTOR CJUN AMPLIFIES HEDGEHOG-INDUCED FIBROBLAST ACTIVATION AND TISSUE FIBROSIS

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**Background:** The pathologic activation of fibroblasts is a key feature of fibrotic disorders such as Systemic Sclerosis (SSc). Deregulation of TGF $\beta$ - and Hedgehog signalling has been shown to be critical for the persistent, uncontrolled activation of fibroblasts in SSc.<sup>1–3</sup> However, the consequences of the concomitant upregulation of multiple profibrotic pathways are unknown and cross-talk between individual pathways in fibrotic diseases is currently poorly characterised. Mutual activation and amplification of profibrotic signals might be central for the persistent activation of fibroblasts.

**Objectives:** The aim of this study is to characterise the crosstalk between AP1- and hedgehog signalling in fibrotic tissue disease in SSc.

**Methods:** Co-localization of cJUN and GLI2 in fibrotic skin was analysed by confocal microscopy and interaction was shown by Co-IP. cJUN/AP1 signalling and GLI2 signalling were inhibited *in vitro* and *in vivo* using the pharmacological inhibitors T5224 and GANT61. Hedgehog signalling was activated in mice by fibroblast-specific overexpression of constitutively active Smoothened (Smo<sup>ACT</sup> mice).

**Results:** Expression profiling of all AP1 family members revealed most pronounced differences for cJUN in Smo<sup>ACT</sup> mice. The expression of cJUN colocalized with the hedgehog transcription factor GLI2. Overexpression and colocalization of cJUN and GLI2 were also observed in fibroblasts in the skin of SSc patients. The number of GLI2- and cJUN double-positive fibroblasts was strongly increased in involved SSc skin compared to healthy controls and was particularly high in samples of SSc patients with diffuse and progressive disease. Based on the upregulation of both cJUN and GLI2 and their colocalization, we hypothesised that cJUN and GLI2 might interact with each other to amplify fibroblast activation and tissue fibrosis. Stimulation of resting fibroblasts with TGFβ induces both cJUN and GLI2 mRNA and protein in a time-dependent manner. cJUN and GLI2 are also induced upon stimulation with Sonic hedgehog (SHH), demonstrating that TGFβ and SHH are both capable to activate cJUN and GLI2-dependent transcription. This crosstalk occurs by direct interaction of cJUN and GLI2, which amplifies the transactivation potential of both transcription factors. Co-immunoprecipitation demonstrated that stimulation of fibroblasts with TGFβ or SHH induces direct interaction of cJUN and GLI2. Overexpression of cJUN and Gli2 resulted in activation in both AP1 and Hedgehog target genes. The central role of the crosstalk between cJUN and GLI2 for tissue fibrosis was further highlighted by the finding that hedgehog-induced fibrosis was strongly reduced by AP1 inhibition. Smo<sup>ACT</sup> mice developed extensive skin fibrosis. Treatment with a cJUN/AP1 inhibitor T5224, however, strongly ameliorated hedgehog-induced fibrosis in Smo<sup>ACT</sup> mice.

**Conclusions:** We demonstrate in the present study that the concomitant activation of AP1- and hedgehog signalling amplifies signalling through both cascades to promote excessive fibroblast activation and tissue fibrosis. This finding may open venues for combined inhibition of AP1- and hedgehog signalling for the treatment of fibrosis.

**Disclosure of Interest:** None declared

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siRNA-mediated knockdown of *SHP2* and upon pharmacological inhibition of SHP2. We show that SHP2 can dephosphorylate JAK2 at the inhibitory Y570 site to promote TGFβ-dependent activation of JAK2 and its downstream mediator STAT3. In contrast, pharmacologic inhibition of SHP2, overexpression of a catalytically inactive SHP2 mutant or knockout of *SHP2* inhibits dephosphorylation of pJAK2<sup>Y570</sup> preventing phosphorylation of JAK2 at the activation site Y1007/Y1008 and subsequent activation of STAT3 in TGFβ-stimulated fibroblasts and in experimental fibrosis. Fibroblasts overexpressing SHP2 are more susceptible to the profibrotic effects of TGFβ, whereas the stimulatory effects of TGFβ on myofibroblast differentiation and collagen release are reduced in *Shp2* knockout fibroblasts. In addition, fibroblast-specific inactivation of *Shp2* *in vivo* protected from experimental fibrosis induced by overexpression of a constitutively active TGFβ receptor type I, by bleomycin injection and ameliorated fibrosis in TSK1 mice.

**Conclusions:** The present study describes for the first time a role of SHP2 in the pathogenesis of SSc. SHP2 is required for the activation of JAK2 and STAT3 by TGFβ. Inactivation of SHP2 prevents fibroblast activation and tissue fibrosis, providing evidence that SHP2 may be a potential target for the treatment of fibrosis.

**Disclosure of Interest:** A. Zehender: None declared, J. Huang: None declared, A.-H. Györfi: None declared, A.-E. Matei: None declared, C. Dees: None declared, C. Beyer: None declared, K. Gelse: None declared, A. Ramming: None declared, C. Bergmann: None declared, W. Birchmeier: None declared, O. Distler Grant/research support from: Actelion, Pfizer, Ergonex, BMS, Sanofi-Aventis, United BioSource Corporation, Roche/Genentech, Medac, Biovitrium, Boehringer Ingelheim, Novartis, 4D Science, Active Biotech, Bayer, Sinoxa, Serodapharm, EpiPharm, GSK, Pharmacyclics and Biogen, Consultant for: Actelion, Pfizer, Ergonex, BMS, Sanofi-Aventis, United BioSource Corporation, Roche/Genentech, Medac, Biovitrium, Boehringer Ingelheim, Novartis, 4D Science, Active Biotech, Bayer, Sinoxa, Serodapharm, EpiPharm, GSK, Pharmacyclics and Biogen, G. Schett: None declared, J. Distler Shareholder of: 4D Science GmbH, Grant/research support from: Anamar, Active Biotech, Array Biopharma, BMS, Bayer Pharma, Boehringer Ingelheim, Celgene, GSK, Novartis, Sanofi-Aventis and UCB, Consultant for: Actelion, Active Biotech, Anamar, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, Inventiva, JB Therapeutics, Medac, Pfizer, RuiYi and UCB

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#### FRI0402 MICRORNA-125B REGULATES APOPTOSIS IN SYSTEMIC SCLEROSIS

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**Background:** The role of apoptosis in systemic sclerosis (SSc) is an emerging topic. MicroRNAs (miRs) are a class of small noncoding RNAs that regulate many important biological processes including apoptosis.

**Objectives:** To analyse the differential expression, regulation and pathophysiological role of miR-125b in systemic sclerosis.

**Methods:** MiR-125b expression was assessed by qPCR on RNA derived from cultured fibroblasts, whole skin biopsies and paraffin embedded dermis and epidermis from healthy controls (HC) and SSc patients. Fibroblasts were stimulated with pro-inflammatory and/or pro-fibrotic cytokines and with different epigenetic stimuli. Knockdown with anti-miR-125b (or scrambled controls) in HC fibroblasts was performed to identify downstream effects. RNA from healthy fibroblasts (n=4) after knockdown was proceeded to RNAseq using Illumina HiSeq2000. Bioinformatics analysis included differential gene expression and pathway analysis. Sequencing data were validated using qPCR (on HC and SSc fibroblasts). Apoptosis was assessed by Caspase-Glo 3/7 assay, Western Blot of cleaved caspase 3 and Annexin V live assay on cultured fibroblasts.

**Results:** MiR-125b was downregulated in SSc skin biopsies (n=10, median 47%, Q<sub>1</sub>,35%, 69%; p<0.01) in comparison with HC skin (n=10). To localise its expression in the skin, we separately analysed miR-125b expression in dermis and epidermis of paraffin embedded skin where it was downregulated in both compartments (n=3 each). The expression of miR-125b in primary dermal fibroblasts was also downregulated (median 53%, Q<sub>1</sub>,36%, 58%; n=10, p<0.01) compared to HC fibroblasts (n=10).

MiR-125b expression was not affected by major cytokines operative in SSc such as TGFβ or PDGF. However, TSA (histone deacetylase pan-inhibitor) downregulated miR-125b expression in a time- and dose-dependent manner (n=5, median 23%, Q<sub>1</sub>,319%, 48%; p<0.01).

RNAseq identified >3500 differentially expressed genes with p<0.05. More than half of the differentially expressed genes with at least 15% change were predicted targets of miR-125b by TargetScan and MiRWalk, indicating successful functional

#### FRI0401 THE TYROSINE PHOSPHATASE SHP2 CONTROLS TGFβ-INDUCED STAT3 SIGNALLING TO REGULATE FIBROBLAST ACTIVATION AND FIBROSIS

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**Background:** SHP2, encoded by the PTPN11 gene, is a ubiquitously expressed non-receptor tyrosine phosphatase (PTP). Altered expression and activity levels of SHP2 have also been implicated into the pathogenesis of autoimmune diseases.

**Objectives:** In our study, we aim to characterise the role of SHP2 as a possible novel molecular checkpoint of transforming growth factor-β (TGFβ)-induced JAK2/STAT3 signalling in fibrotic diseases.

**Methods:** Mice carrying *Shp2*<sup>fl/fl</sup>*xCol1a2-CreER* were generated to specifically knockout *Shp2* in fibroblasts. SHP2 was inhibited using NSC-87877 inhibitor. The role of *Shp2* was investigated in three different mouse models: Bleomycin- and TBRI<sup>CA</sup> induced dermal fibrosis as well as TSK1 genetic model of skin fibrosis. The construct pCMV3-Flag-JAK2 was used for overexpression and for *in vitro* mutagenesis of human JAK2. Co-immunoprecipitation was performed to confirm the interaction between SHP2 and JAK2. STAT3 activation was analysed by reporter assay. Protein and mRNA expression levels were analysed by Western Blot and qPCR.

**Results:** Our data characterise SHP2 as an important regulator of TGFβ signalling in fibroblasts. Although SHP2 expression is decreased in systemic sclerosis (SSc), the moderate downregulation of SHP2 expression is not sufficient to counterbalance the hyper-activation of TGFβ signalling in SSc. However, *Shp2*-deficient murine fibroblasts are less responsive to TGFβ. An impaired response to the profibrotic effects of TGFβ was also observed in human SSc fibroblasts with

inhibition of miR-125b. Gene ontology revealed apoptosis regulation as the main activated pathway. Apoptotic genes included BAK1, BMF and BBC3, which are part of the BCL2 apoptosis pathway and predicted targets of miR-125b. Consistent with the sequencing results, qPCR confirmed that miR-125b knockdown upregulated these genes 24, 48 and 72 hours after transfection (n=12, p<0.01 for each). BAK1 showed the strongest induction, that was also confirmed on the protein level by Western blot. Accordingly, miR-125b knockdown resulted in an increased apoptosis (at least 1.5-fold, n=10, p<0.01) compared to scrambled controls, measured by Caspase-Glo 3/7 assay 24, 48 or 72 hours post-transfection. Consistently, miR-125b overexpression decreased apoptosis (by at least 50%, n=10, p<0.01) at these time points. Cleaved caspase 3 was upregulated in anti-miR-125b transfected cells (median 2.3 fold, Q<sub>1,3</sub> 1.6, 4; n=10, p<0.01) confirmed by Western Blot. Annexin V live assay showed prevailing of apoptosis after miR-125b downregulation.

**Conclusions:** MiR-125b is downregulated in SSc skin and primary SSc dermal fibroblasts. MiR-125b downregulation increases apoptosis in dermal fibroblasts that might be a compensatory strategy against excessive fibrosis that could be used for therapeutic purposes.

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#### FRI0403 MITOCHONDRIAL DYSFUNCTION AND OXIDATIVE STRESS IN MYOSITIS: A CENTRAL PATHOGENIC PATHWAY FROM MOUSE TO MAN

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**Background:** Myositides are severe diseases leading to a bedridden state and possibly death. The lack of animal model with spontaneously-occurring autoimmune myositis has hampered pathophysiological and therapeutic research. Auto-immune-prone NOD mice represent an invaluable model of type 1 diabetes (T1D). Inducible T cell co-stimulator (ICOS) is involved in germinal centre reaction and induction of helper T cell responses. We developed a unique model of myositis by invalidating the ICOS pathway in NOD mice<sup>1</sup>. Muscle holoproteome analysis in diseased mice together with observations of mitochondrial dysfunction in patients with dermatomyositis<sup>2</sup> suggest a main role of oxidative stress in disease pathogenesis.

**Objectives:** To determine the pathogenic role of oxidative stress and evaluate the effect of antioxidant therapy on *Icos*<sup>-/-</sup> NOD myositis.

**Methods:** Disease course was studied in *Icos*<sup>-/-</sup> NOD mice by grip strength, locomotor analysis and MRI. Muscle pathology was evaluated after conventional stainings, or by immuno-enzymology or immuno-histochemistry. Muscle-infiltrating cells were characterised by flow cytometry. New autoantibodies were identified in mice by serum proteomic analysis and sought for in myositis patients by ALBIA. Mouse muscle proteomic and transcriptomic analyses were performed by LC-MS/MS (Orbitrap) and RT-PCR, respectively. Muscle free radical production was assessed by EPR. Mice were treated by prednisolone (10 mg/kg/day) or N-acetylcysteine (2 g/L) in drinking water.

**Results:** *Icos*<sup>-/-</sup> NOD mice did not develop diabetes. Instead, myositis spontaneously occurred with decreased grip strength, impaired cadence, reduced print area and death around 40 wks. Pathological muscle analysis revealed necrotic myofibers and important inflammatory infiltrates (CD4<sup>+</sup> T cells, macrophages). Muscle lesions yielded MRI T2 hypersignals that regressed under steroids. CD4<sup>+</sup> T cells transferred disease to NOD.*scid* recipients. Serum proteomic analysis revealed a new autoantibody directed against a mitochondrial antigen. It was found present in ~1% individuals from a ~700 myositis patient cohort. Oxidative stress was manifest in *Icos*<sup>-/-</sup> NOD muscle by augmented free radical production, H<sub>2</sub>O<sub>2</sub> production-related atrophy, altered O<sub>2</sub> consumption and dysregulation of several mitochondrial genes and proteins. N-acetylcysteine partially prevented myositis or ameliorated established disease.

**Conclusions:** This work establishes *Icos*<sup>-/-</sup> NOD mice as a unique paradigm of myositis. A new autoantibody was discovered. Oxidative stress is present in diseased muscle. Antioxidant therapy is effective in a preventive or curative fashion. Together with our previous data in dermatomyositis patients<sup>2</sup>, this work indicates the central role of mitochondrial dysfunction and oxidative stress in myositis pathogenesis and opens new perspectives for therapy.

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#### FRI0404 CHARACTERISATION OF A MONOCYTES/MACROPHAGES CELL SUBSET CO-EXPRESSING BOTH M1 AND M2 PHENOTYPE MARKERS IN SYSTEMIC SCLEROSIS PATIENTS

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**Background:** In the pathogenesis of systemic sclerosis (SSc), the immune cell activation is an important event that includes alteration in the macrophage polarisation.<sup>1</sup>

Macrophages may polarise into classically activated (M1), which are characterised by the expression of specific markers such as Toll-like receptors (TLR2 and 4) and costimulatory molecules (CD80 and CD86), or alternatively activated (M2), which are characterised by the expression of specific phenotype markers such as mannose receptor-1 (CD206) and macrophage scavenger receptors (CD204 and CD163). M2 are present in the circulation and in the skin infiltrate of SSc patients (pts), where they seem to contribute to fibrosis.<sup>2-4</sup>

**Objectives:** To characterise circulating M2 monocytes/macrophages from SSc pts and healthy subjects (HSs) by their co-expression of CD204, CD163 and CD206, as well as cells expressing both M1 and M2 phenotype markers.

**Methods:** Fifty-eight SSc pts (54 females/4 males, mean age 63±13 years), fulfilling the new EULAR/ACR criteria for SSc, and 27 age-matched HSs were consecutively enrolled after Informed Consent was obtained. Peripheral blood was collected and the antibodies CD14-APC-Vio770 and CD45-VioGreen were used to identify the monocyte/macrophage lineage; CD204-VioBright-FITC, CD163-PE-Vio770 and CD206-PeerCP-Vio700 were used to characterise the M2 phenotype, whereas CD80-APC, CD86-VioBlue, TLR4-PE and TLR2-PE-Vio615 were used to characterise the M1 phenotype (Miltenij Biotech). Flow Cytometry analysis was performed using Navios Flow Cytometer and the related Navios analysis software (Beckman Coulter).

**Results:** In the CD14<sup>+</sup>cell subset (monocytes), the CD14<sup>+</sup>CD163<sup>+</sup>CD206<sup>+</sup>CD204<sup>+</sup>cell percentage was significantly increased in SSc pts compared to HSs (p=0.02). Inside the CD14<sup>+</sup>CD163<sup>+</sup>CD206<sup>+</sup>CD204<sup>+</sup> monocytes/macrophages a subset of cells co-expressing also TLR4, CD80 and CD86 was detected. This mixed population (M2/M1) of cells was significantly increased in SSc pts compared to HSs (p=0.003).

At the same time, circulating monocytes/macrophages showing a full M2 phenotype and characterised as CD204<sup>+</sup>CD163<sup>+</sup>CD206<sup>+</sup>cells were investigated independently of the expression of CD14, and they also resulted significantly increased in SSc pts compared to HSs (p<0.0001).

In the CD204<sup>+</sup>CD163<sup>+</sup>CD206<sup>+</sup>cell subset (M2), the percentage of cells expressing also TLR4, CD80 and CD86 (M1) was significantly increased in SSc pts compared to HSs (p<0.0001).

**Conclusions:** These results describe for the first time a subset of circulating cells belonging to the monocyte/macrophage lineage with a mixed phenotype, which are characterised by the expression of both M1 and M2 surface markers. These



cells were observed to be increased in the peripheral blood of SSc pts compared to HSs, suggesting their possible role in the pathogenesis of the disease.

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### FRI0405 A NOVEL ANIMAL MODEL FOR SYSTEMIC SCLEROSIS INDUCED BY IMMUNISATION OF ANGIOTENSIN II RECEPTOR 1

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**Background:** Systemic sclerosis (SSc) is a complex connective tissue disease which is characterised by autoimmunity, vasculopathy and fibrosis<sup>1</sup>. Our recent study showed that the progression of SSc was strongly associated with the autoantibodies against angiotensin II receptor I (AT1R), suggesting a role of autoimmunity to AT1R in the pathogenesis of the disease<sup>2</sup>

**Objectives:** In this study, we aimed to investigate the role of AT1R in the pathogenesis of SSc in mice.

**Methods:** C57BL/6J mice were immunised with membrane extract (ME) of CHO cell overexpressing human AT1R or with ME of CHO cells as control. Serum, lung and skin samples were collected and assessed 63 days after immunisation for autoantibody production, inflammation and fibrosis, which are hallmarks for SSc.

**Results:** Immunisation with hAT1R induced the production of autoantibodies against the receptor in mice, and autoantibody deposition was found in the lung. Histologically, mice immunised with hAT1R showed a SSc-like disease, including perivascular infiltrates and fibrosis in the skin as well as pulmonary inflammation. The inflammation in the skin and the lung were characterised by infiltration of T- and B-cells. Furthermore, transfer of immune cells from hAT1R-immunised mice into C57BL/6J mice induced inflammation in the lung.

**Conclusions:** This study demonstrates that immunisation with hAT1R can induce a SSc-like disease, thus showing a pathogenic role of autoimmunity to AT1R and providing a novel mouse model for the diseases. Furthermore, this study also introduces a new immunisation strategy to generate functional autoantibodies against receptors on the cell membrane.

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### FRI0406 INCREASED FREQUENCY OF CIRCULATING CD163+ NON-CLASSICAL MONOCYTES IN SCLERODERMA AND ENHANCED DUAL POLARISATION TOWARDS M1 AND M2-LIKE PHENOTYPES IN MONOCYTE-DERIVED MACROPHAGES

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**Background:** Scleroderma (SSc) is an autoimmune connective tissue disease involving complex interactions between various cell types leading to organ-based tissue fibrosis. Emergence of the monocytes (Mo)/macrophages (M $\phi$ ) lineage(s) as key contributors to inflammation, vascular dysfunction and scarring in scleroderma<sup>1,2</sup> have led to increased scrutiny of their phenotype and function.

**Objectives:** To determine the circulating Mo subpopulations and phenotypes of M $\phi$  in SSc.

**Methods:** PBMC were collected from healthy (HC) and SSc donors, and analysed by flow cytometry using Mo phenotypic antibodies or purified and cultured *in vitro*. For flow cytometry immunophenotyping, Mo were gated on

CD3<sup>+</sup>CD19<sup>-</sup>CD56<sup>+</sup>HLA-DR<sup>+</sup> populations, and subsets defined by CD14, CD16, CD163 and CD206 expression. For M $\phi$  cultures, Mo were negatively selected from PBMCs, cultured for 7 days, and treated with IFN- $\gamma$  (5 ng/ml) or IL-4 (20 ng/ml) for 24 hours. Cytokine levels in the conditioned media were evaluated by MSD analyses and normalised to total protein levels.

**Results:** The frequency of circulating CD163<sup>+</sup> non-classical Mo (CD14<sup>lo</sup>CD16<sup>hi</sup>) was 2-fold higher in SSc patients than in HC (unpaired t-test, p=0.026). No difference was found in the frequency of CD206<sup>+</sup> monocyte subsets between HC and SSc. *In vitro*, unstimulated SSc M $\phi$  (M0) secreted higher levels of classically-activated pro-inflammatory (M1) and alternatively-activated pro-regenerative (M2) cytokines. Compared to HC cells, SSc M $\phi$  were more readily polarised towards an M1 phenotype or an M2 phenotype, when cultured in the presence of IFN- $\gamma$  or IL-4, respectively. Th17 markers and MMPs were significantly increased in SSc M $\phi$  (table 2).

**Abstract FRI0406 – Table 1.** Demographics.

n	Mo (flow cytometry)		M $\phi$ supernatant (cytokine assay)	
	HC n=9	SSc n=10	HC n=13	SSc n=27
Age (years)	56.7±14.3	50.7±5.7	60.6±16.7	52.1±13.0
Female : Male	7:2	8:2	6:7	26:5
SSc subtype	-	dcSSc <sup>(10)</sup>	-	dcSSc <sup>(27)</sup>
Disease duration	-	≤5 years <sup>(10)</sup>	-	≤5 years <sup>(15)</sup> >5 year <sup>(12)</sup>

**Abstract FRI0406 – Table 2.** Cytokines significantly increased in SSc vs control. Unpaired t-tests, \*p<0.05, \*\*P<0.01.

Cell Population	M1 Markers	M2 Markers	Th17 Cytokines and MMP's
M0	CCL-3, CCL-4, IL-6, IL-18, IL-12, IL-15, TNF- $\alpha$	CCL-1, CCL-17, CCL-20, CCL-24, IL-1R $\alpha$ , YKL-40	IL-21, IL-22, IL-31, MMP1, MMP3
M0 + IFN- $\gamma$	CCL-3, CCL-4, CCL-11, CXCL8, IL-1 $\beta$ , IL-6, IL-18, TNF- $\alpha$	CCL-1, CCL-22, CCL-24, CCL-26, IL-1R $\alpha$ , YKL-40	IL-21
M0 + IL-4	CCL-3, CCL-4, IL-12, IL-18, TNF- $\alpha$	CCL-17, CCL-22, CCL-24, IL-1R $\alpha$ , YKL-40	IL-21, MMP3

**Conclusions:** Studies exploring Mo have revealed distinct populations with selective biological functions. Our observation of an increased number of CD163<sup>+</sup> non-classical Mo in SSc suggests that this subpopulation may play a key role in inflammatory-driven fibrosis and act as an important source of pro-fibrotic cytokines. This data is consistent with previous reports of elevated serum levels of CD163 and increased CD163 secretion by SSc PBMCs<sup>3</sup>. SSc M $\phi$  showed a pronounced and enhanced dual M1 and M2 polarisation basally compared to HC, indicating cells were 'primed' to undergo phenotypic polarisation. Our studies support the notion that M $\phi$  cytokine secretion generates a pro-fibrotic milieu in scleroderma tissues, playing a prominent role in dysregulated tissue repair in fibrosis.

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### FRI0407 DIPEPTIDYL-PEPTIDASE-4 (DPP4) IS A POTENTIAL NEW MOLECULAR TARGET FOR TREATMENT OF FIBROSIS

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**Background:** Dipeptidyl-peptidase-4 (DPP4) plays a role in tissue scarring and its inhibition leads to reduced scar formation. Its function in tissue fibrosis, however, is unknown.

**Objectives:** The aim of the study was to investigate the expression of DPP4 in fibrotic tissue of systemic sclerosis (SSc) patients, to characterise DPP4 positive cells, to study the mechanism of action of DPP4 in fibroblasts and to evaluate the antifibrotic effect of pharmacological and genetically inhibition of DPP4 in different preclinical models of SSc.

**Methods:** Expression of DPP4 in human and murine skin was analysed. Mouse fibroblasts were isolated and DPP4 positive cells properties were assessed.

Pulmonary fibrosis was induced by bleomycin in DPP4 knockout (KO) mice and wildtype littermates. Fibrosis of the lungs was additionally evaluated by computer tomography scans (CT). Two oral DPP4 inhibitors were tested in two concentrations in bleomycin-induced skin fibrosis and in scleroderma-like chronic graft-versus-host disease (scl-cGVHD) model. Antiinflammatory effects of DPP4 inhibition were assessed by CD45 staining of fibrotic and non-fibrotic mouse tissue upon DPP4 inhibition. Moreover, chimeric mice were generated by transplanting bone marrow from DPP4-KO mice in WT-littermates (DPP4→WT) and vice versa (WT→DPP4) and fibrosis was by intratracheal injections of bleomycin.

**Results:** DPP4 positive fibroblasts were increased in fibrotic skin of SSc patients and also in murine models of fibrosis. DPP4 expression is induced by TGF- $\beta$  in an Erk-dependent manner. DPP4-positive fibroblasts strongly express stress fibres after TGF- $\beta$  stimulation and released increased amounts of collagen. Mechanistically, inhibition of DPP4 selectively interferes with the TGF- $\beta$  induced activation of ERK signalling, but does not inhibit TGF- $\beta$  induced SMAD signalling, or other non-canonical TGF- $\beta$  pathways involving Fra2, c-Jun, p38, Akt or STAT3. Furthermore, pharmacological inhibition of DPP4 reduced the release of collagen and the expression of myofibroblast markers. DPP4-KO mice are less sensitive to bleomycin-induced pulmonary fibrosis as shown by milder changes on CT, reduced Ashcroft scores and reduced hydroxyproline content. DPP4-KO mice also show reduced skin fibrosis upon bleomycin challenge. Moreover, treatment with DPP4 inhibitors demonstrated potent antifibrotic effects in bleomycin-induced skin fibrosis and experimental scl-cGVHD mouse model. Treatment with DPP4 inhibitors also reduced leukocyte infiltrations into the skin. The extent of pulmonary fibrosis of DPP4→WT was comparable to that of WT→WT control mice. Fibrosis was strongly ameliorated in WT→DPP4 mice and results were comparable to that of DPP4→DPP4 mice, characterising resident cells such as fibroblasts as major target cells for the antifibrotic effects of DPP4 inhibitors.

**Conclusions:** DPP4 characterises an activated subpopulation of fibroblasts in SSc. Moreover, inhibitors of DPP4 show a significant anti-fibrotic effect in several mouse models of SSc in well tolerated doses. These results may have direct translational implications as DPP4 inhibitors are already in clinical use for diabetes.

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**Disclosure of Interest:** None declared

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#### FRI0408 INVARIANT NATURAL KILLER T CELLS IN SYSTEMIC SCLEROSIS

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**Background:** Systemic sclerosis (SSc) is a rare and heterogeneous immune-mediated disease. Its complex pathogenesis remains incompletely understood. Invariant natural killer T (iNKT) cells have been discussed in several autoimmune diseases<sup>1</sup>. They recognise selected endogenous as well as synthetic glycolipids like  $\alpha$ -galactosylceramide by their TCR with high affinity and when activated, they typically release high amounts of pro- and/or anti-inflammatory cytokines<sup>2</sup>.

**Objectives:** To evaluate numbers and function of invariant natural killer T cells in patients with systemic sclerosis and analyse their correlation with disease parameters.

**Methods:** Human iNKT cells from 91 patients with SSc and 23 healthy controls were analysed by flow cytometric analysis. Their proliferative capacity and cytokine production was investigated following activation with CD1d ligand  $\alpha$ -GalCer.

**Results:** We observed an absolute and relative decrease of iNKT cells in patients with SSc (0.036 iNKT cells/ $10^6$  lymphocytes) compared with healthy controls (0.159 iNKT cells/ $10^6$  lymphocytes,  $p < 0.001$ ). We could also demonstrate that iNKT cells from patients with SSc showed a significantly decreased expansion capacity upon stimulation with  $\alpha$ -GalCer. Interestingly, there was no difference concerning the subtype of SSc, disease severity or whether patients received immunosuppressive drugs.

**Conclusions:** iNKT cells are deficient and functionally impaired in patients with SSc. Therefore, adoptive transfer strategies using culture-expanded iNKT cells or administration of glycosphingolipids such as  $\alpha$ -GalCer could be a novel approach to treat SSc patients.

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#### FRI0409 MYOSITIS SPECIFIC ANTI-HISTIDYL TRNA SYNTHETASE (HISRS) AUTOANTIBODIES DISPLAY HIGH REACTIVITY AGAINST HISRS CONFORMATIONAL EPITOPES AND ASSOCIATE WITH LUNG AND JOINT INVOLVEMENT

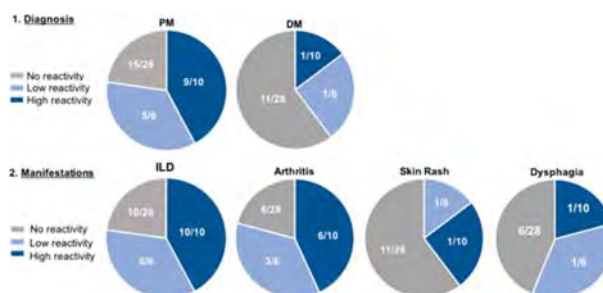
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**Background:** Autoimmune myositis (rheumatic muscle inflammation) associated with interstitial lung disease (ILD) and arthritis is strongly correlated with the presence of anti-histidyl tRNA synthetase (HisRS) autoantibodies.<sup>1</sup>

**Objectives:** The aims of this study were to investigate: 1) myositis IgG reactivity against HisRS conformational epitopes; and 2) association between clinical manifestations and anti-HisRS reactivity profiles.

**Methods:** Serum IgG was isolated using a protein G affinity column (from 25 anti-HisRS negative (-) and 19 anti-HisRS positive (+) myositis sera and 24 age/gender matched healthy controls, HC). Autoantibody reactivity was tested by in house ELISA developed against HisRS full-length protein and three HisRS conformational epitopes (WHEP domain – localised in the N-terminal; HisRS without WHEP (HisRS\_WHEP); and ABD – anticodon-binding domain located in the C-terminal). Correlations between diagnosis, clinical manifestations and anti-HisRS IgG reactivity were evaluated.

**Results:** HisRS(+) myositis IgG displayed stronger reactivity against full-length HisRS and HisRS\_WHEP (median 372 ng/mL and 334 ng/mL, respectively), compared to WHEP and ABD (6.38 and 6.48 ng/mL). The strongest anti-full-length HisRS reactivity (>371 ng/mL) was detected in patients presenting ILD (10/10 of patients), arthritis (6/10) and polymyositis diagnosis (PM 9/10), in comparison to patients with low anti-HisRS reactivity (<23 ng/mL, ILD – 5/6; arthritis – 3/6; PM – 5/6) or no anti-HisRS reactivity (ILD – 10/28; Arthritis – 8/28; PM – 15/28). On the contrary, myositis patients displaying no anti-HisRS reactivity were largely diagnosed with DM (11/28), skin rash (11/28) and dysphagia (6/28) when compared to patients with the highest anti-full-length HisRS reactivity (1 out of 10 patients was diagnosed with DM, skin rash or dysphagia). Similar associations were observed between the degree of anti-HisRS\_WHEP, anti-WHEP or anti-ABD reactivities and manifestations of ILD, arthritis, skin rash or dysphagia, and DM or PM diagnosis. No anti-HisRS reactivity was detected in the HC group.



**Abstract FRI0409 – Figure 1.** Anti-full-length HisRS IgG reactivity in myositis patients diagnosed with either polymyositis (PM) or dermatomyositis (DM), and presenting manifestations of interstitial lung disease (ILD), arthritis, skin rash and dysphagia. Numbers represent the patients included in the analysis.

**Conclusions:** This study provides evidences for a possible underlying role of anti-HisRS autoantibodies in the pathogenesis of myositis with interstitial lung disease and joint involvement.

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**Disclosure of Interest:** None declared

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**FRI0410 TGF $\beta$  PROMOTES FIBROSIS BY MYST1-DEPENDENT EPIGENETIC REGULATION OF AUTOPHAGY**

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**Background:** Autophagy is catabolic process allowing cells to degrade unnecessary or dysfunctional cellular organelles. Aberrant activation of autophagy has been also implicated into the pathogenesis of fibrotic diseases. Several stimuli present in fibrosis such as pro-fibrotic cytokines are known to activate autophagy. **Objectives:** The objective of this work is characterise the regulation of autophagy by TGF $\beta$  and analyse whether targeting of autophagy in fibroblasts may prevent their aberrant activation in fibrotic diseases.

**Methods:** To selectively disable autophagy in fibroblasts we generate *Atg7<sup>fl/fl</sup> × Col1a2;CreER* mice. The role of the autophagy was investigated in the model of bleomycin- and T $\beta$ R1act-induced dermal and pulmonary fibrosis. Overexpression of *Myst1* was achieved by adenovirus encoding for *Myst1*. Collagen release and protein expression were measure by Western blot. Target genes were analysed by RT-PCR. Co-immunoprecipitation and reporter assay were performed to study physical and functional interactions between MYST1 and SMAD3. To monitor the autophagic flux *in vitro* and *in vivo* we generate an adenovirus encoding for tandem fluorescent-tagged LC3 (mRFP-EGFP-LC3), defined as reliable autophagy maker.

**Results:** We provide evidence that transforming growth factor- $\beta$  (TGF $\beta$ ) activates autophagy by an epigenetic mechanism to amplify its profibrotic effects. TGF $\beta$  induces autophagy in fibrotic diseases by SMAD3-dependent downregulation of the H4K16-histoneacetyltransferase MYST1, which controls the expression of core components of the autophagy machinery such as ATG7 and BECLIN1. Activation of autophagy in fibroblasts promotes collagen release and is both, sufficient and required, to induce tissue fibrosis. Forced expression of MYST1 abrogates the stimulatory effects of TGF $\beta$  on autophagy and re-establishes the epigenetic control of autophagy in fibrotic conditions. Interference with the aberrant activation of autophagy inhibits TGF $\beta$ -induced fibroblast activation and ameliorates experimental dermal and pulmonary fibrosis. These findings link uncontrolled TGF $\beta$  signalling to aberrant autophagy and altered epigenetics in fibrotic diseases and may open new avenues for therapeutic intervention in fibrotic diseases.

**Conclusions:** We demonstrate that the epigenetic control of autophagy is disturbed by a TGF $\beta$ -dependent downregulation of MYST1. The increased activation of autophagy induces fibroblast-to-myofibroblast transition and promotes fibrotic tissue remodelling. Re-expression of MYST1 prevents aberrant autophagy, limits the profibrotic effects of TGF $\beta$  and ameliorates experimental fibrosis. Restoration of the epigenetic control of autophagy might thus be a novel approach to ameliorate fibrotic tissue remodelling.

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**FRI0411 DUAL PRO-INFLAMMATORY AND ANTI-FIBROTIC ROLE OF IL-17A IN SYSTEMIC SCLEROSIS SKIN**

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**Background:** Increased levels of IL-17A have been reported in systemic sclerosis (SSc) which role in fibrogenesis is still debated.<sup>1</sup> Furthermore, epithelial cells

are preferential targets of IL-17A and recent findings suggest that keratinocytes may participate in dysregulated extracellular matrix homeostasis.<sup>2</sup>

**Objectives:** Our aim was to investigate the interactions between epidermis and dermis in the presence of IL-17A, taking into perspective the fibrotic process.

**Methods:** Primary human keratinocytes were primed with IL-17A and/or TGF- $\beta$  and conditioned-media were used to stimulate healthy donors (HD) and SSc fibroblasts. Alternatively, organotypic cultures of HD full human skin were challenged with these cytokines. Responses were assessed by quantifying inflammatory mediators and type I collagen (Col-I) levels. The factors produced by keratinocytes were identified by a proteomic approach and their contribution was evaluated by neutralisation assays. Changes in gene expression in full human skin after treatment with IL-17A and/or TGF- $\beta$  were analysed by RNA sequencing (RNA-seq).

**Results:** Unstimulated HD- and SSc-derived keratinocyte-conditioned media (KCM) promoted collagen production by fibroblasts to a similar extent and in a dose-dependent manner. Cytokine array analysis and neutralising assays showed that TGF- $\beta$  was, at least in part, responsible for the pro-fibrotic effect of KCM. Priming of keratinocytes with IL-17A directly decreased Col-I production and significantly reduced Col-I induced by TGF- $\beta$  both in SSc and HD fibroblasts. In full human skin, IL-17A promoted pro-inflammatory responses by inducing 2- to 4-fold increase of IL-8, IL-6, MCP-1 and MMP-1 levels, while showing direct anti-fibrotic effects, as well as decreasing by 2-fold collagen production triggered by TGF- $\beta$  (p=0.02). RNA-seq revealed that TGF- $\beta$  induced the expression of many collagen genes, while this was not the case for IL-17A. However, IL-17A promoted a pro-inflammatory signature in the skin and strongly downregulated expression of serpin family members, known to be involved in fibrogenesis.

**Conclusions:** Keratinocytes profoundly influence dermal fibroblast responses, which are further modulated in the presence of IL-17A. These data support a role for keratinocytes in the pathogenesis of SSc. IL-17A acts as a potent anti-fibrotic factor in the model of keratinocyte – fibroblast interactions, as well as in the full human skin, promoting pro-inflammatory and anti-fibrotic responses.

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**FRI0412 B CELL DEPLETION AMELIORATES TISSUE FIBROSIS THROUGH REGULATING MACROPHAGE DIFFERENTIATION IN A BLEOMYCIN-INDUCED SYSTEMIC SCLEROSIS MODEL MOUSE**

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**Background:** B cells play a critical role in pathogenesis of autoimmune diseases through various functions such as cytokine production and induction of other immune cell activation. Recent studies have shown the efficacy of B cell depletion therapy with rituximab, a human CD20 chimeric monoclonal antibody, in systemic sclerosis (SSc) patients. However, it still remains unclear why B cell depletion can be effective for SSc.

**Objectives:** The purpose of this study is to assess the role of B cell depletion in SSc. We evaluated the skin and lung fibrosis of bleomycin (BLM)-induced SSc model mice treated with B cell depletion. Furthermore, we investigated effects of B cell depletion on T cells and macrophages.

**Methods:** To generate BLM-induced SSc model mice, 200  $\mu$ g of BLM was injected subcutaneously to C57BL/6 mice every other day for 4 weeks. Anti-mouse CD20 monoclonal antibodies, which can deplete mouse B cells, were also injected every 2 weeks from either one week before (the pre-depletion group) or 2 weeks after (the post-depletion group) BLM treatment. After 4 weeks of BLM treatment, skin and lung fibrosis was assessed histopathologically. To examine the effect of B cell depletion on T cells and macrophages, purified B cells were cultured with T cells or macrophages and then T cell cytokine production and macrophage phenotype were analysed.

**Results:** Skin and lung fibrosis increased in BLM-induced SSc mice. In the coculture experiments, B cells from BLM-induced SSc mice promoted differentiation of T cells producing fibrogenic cytokines such as interleukin-4 compared with control B cells, while they inhibited regulatory T cell (Treg) differentiation. Skin and lung fibrosis was inhibited in both pre- and post-depletion groups with the inhibition greater in the pre-depletion group than in the post-depletion group. Despite the finding that greater fibrosis remained in the post-depletion group than in the pre-depletion group, the post-depletion group showed significantly higher frequencies



of Treg compared with the pre-depletion group. Furthermore, the post-depletion group also exhibited lower fibrogenic cytokine-producing T cell frequencies, suggesting that the change in T cell cytokine production could not account for the more strongly reduced fibrosis observed in the pre-depletion group. Therefore, we examined other immune cell response to B cell depletion. Recent studies have revealed that macrophages are divided into two subtypes: M1 and M2 and that M2 macrophages show fibrogenic effects in SSc. This study showed that macrophages cultured with B cells from BLM-induced SSc mice exhibited enhanced M2 differentiation compared with control B cells. Remarkably, frequencies of M2 macrophage with fibrogenic capacity significantly decreased in the pre-depletion group compared with the post-depletion group, which could account for the more strongly inhibited tissue fibrosis in the pre-depletion group.

**Conclusions:** Our results indicate that therapeutic effects of B cell depletion on tissue fibrosis exert through regulating macrophage differentiation rather than T cell cytokine production in SSc, first demonstrating that interaction between B cells and macrophages in development of fibrosis in SSc.

**Disclosure of Interest:** None declared

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### FRI0413 ARYL HYDROCARBON RECEPTOR EXPRESSION IS ASSOCIATED WITH LUNG INVOLVEMENT IN SYSTEMIC SCLEROSIS

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**Background:** Systemic sclerosis (SSc) is characterised by autoantibody production, microvascular injury and systemic excessive fibrosis<sup>1</sup>. Genetic and environmental factors are thought to be important for the trigger of development of the disease, however, direct connexion between these factors and pathogenesis of SSc is not yet elucidated<sup>2,3</sup>. Recent reports showed that environmental toxic pollutants, such as dioxins, play a significant role in the disturbance of immune system and the trigger of autoimmunity through binding aryl hydrocarbon receptor (AhR)<sup>4,5</sup>. However, little is known about the association between AhR and pathogenesis of SSc yet.

**Objectives:** To elucidate the association between AhR and the clinical characteristics of SSc.

**Methods:** Twenty-one patients with SSc who fulfilled 2013 ACR/EULAR classification criteria and 10 healthy controls (HC) were analysed. Peripheral blood mononuclear cells (PBMCs) were isolated from heparinized whole blood by using gradient centrifugation and total RNA was prepared from PBMCs. Expression of AhR mRNA was detected by quantitative polymerase chain reaction and standardised by mRNA level of 18S ribosomal RNA in each sample. Level of AhR mRNA in the cells was compared between SSc and HC and also between SSc patients with and without various clinical features.

**Results:** The proportion of diffuse cutaneous subset (dcSSc) was 33%. Mean disease duration was 9±9 years. The positive proportion of anticentromere antibodies, anti-topoisomerase I antibodies, anti-U1 ribonucleoprotein antibody, anti-RNA polymerase III antibody and antinuclear antibody positive without SSc-specific antibodies among 21 patients were 33.3%, 33.3%, 4.8%, 9.5% and 9.5%, respectively. Antinuclear antibody was negative in 2 (9.5%) patients. AhR mRNA expression level was tended to be higher in SSc compared to HC (1.7±1.1 versus 1.2±0.6, p=0.1). Notably, the expression level of AhR mRNA in dc SSc was tended to be higher than that of limited cutaneous SSc (p=0.15), whereas no significant difference was detected between with or without SSc related autoantibodies, vasculopathy such as pulmonary arterial hypertension or digital tip ulcer. Importantly, the expression level of AhR mRNA was significantly higher in patients with interstitial lung disease (ILD) (n=14) than those without (n=7) (2.0±1.1 versus 1.0±0.4, p<0.05). Furthermore, AhR mRNA expression level was significantly and negatively correlated with DLCO% predicted (r=-0.57, p<0.05).

**Conclusions:** Expression level of AhR mRNA was higher in patients with SSc, especially in SSc patients with ILD. In addition, AhR expression level was correlated with a parameter of pulmonary function test, DLCO% predicted. These results collectively suggest that AhR possibly plays an important role in the disease process of ILD in SSc.

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### FRI0414 EVALUATION OF A NOVEL MULTI-ANALYTE ASSAY FOR THE DETECTION OF AUTOANTIBODIES IN THE DIAGNOSIS OF SYSTEMIC SCLEROSIS

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**Background:** Systemic sclerosis (SSc) is a chronic autoimmune disease characterised by vascular changes and progressive fibrosis of skin and various internal organs. In SSc a variety of autoantibodies have been detected which are useful for the diagnosis and management of the disease. Some of these autoantibodies are well-established tools strongly associated with SSc (e.g. anti-centromere, anti-topoisomerase I, anti-RNA polymerase III). Other autoantibodies are less frequent and/or less-specific for SSc even if potentially useful to better assess disease subsets and prognosis.

**Objectives:** Our goal was to assess the frequency of SSc-related autoantibodies detected using a novel technology as well as to study the associations between these antibodies and clinical features in an Italian SSc cross sectional cohort.

**Methods:** Serum samples from 218 consecutive patients with SSc collected at three Italian sites were tested for a variety of autoantibodies (see table 1) using a novel fully automated system utilising bead-based immunoassays (research use only, Inova Diagnostics, San Diego, CA). The Italian cohort included: women 200 (92%), limited cutaneous SSc (lc-SSc) 166 (76%), patients with history of digital ulcers 91 (42%), calcinosis 46 (21%), lung fibrosis 84 (39%), heart involvement 38 (17.4%), pulmonary arterial hypertension 20 (9%), and esophageal involvement 138 (63.3%).

**Results:** The prevalence of antibodies is summarised in the table 1 below. Of note, anti-BICD2, anti-CENP-B, and anti-nucleosome antibodies were significantly associated with lc-SSc subtype (p=0.0237, p<0.0001, p=0.0096, respectively), while anti-Ro60, anti-SSB, anti-ScI-70, and anti-DFS70 antibodies were significantly associated with the diffuse cutaneous SSc (dc-SSc) subtype (p=0.0102, p<0.0001, p<0.0001, and p=0.0032, respectively). When analysing all antibodies with multivariate analysis, SSc patients showed significant clustering based on antibody profile and clinical phenotype.

Antibody	Total SSc No. (NPos, 95% CI)	dc-SSc No. (NPos, 95% CI)	lc-SSc No. (NPos, 95% CI)	p-value (dc-SSc vs. lc-SSc)
dsDNA	10 (4.6%, 95% CI 2.5-8.2)	2 (3.8%, 1.1-10.9%)	8 (4.8%, 2.9-9.2%)	N.S.
ENP	11 (5.0%, 95% CI 2.8-8.0)	3 (5.8%, 2.0-15.6%)	8 (4.8%, 2.9-9.2%)	N.S.
Ro52	32 (14.7%, 95% CI 10.0-20.0)	10 (19.2%, 10.0-31.9%)	22 (13.3%, 8.9-19.3%)	N.S.
Ro60	15 (6.9%, 95% CI 4.2-11.0)	8 (15.4%, 6.0-27.5%)	7 (4.2%, 2.1-8.4%)	0.0102
SS-B	7 (3.2%, 95% CI 1.6-6.5)	2 (3.9%, 0.7-25.3%)	0 (0.0%, 0.0-2.3%)	<0.0001
SS-A	39 (17.3%, 95% CI 12.4-23.8)	19 (37.0%, 21.8-54.8%)	20 (12.0%, 7.9-17.9%)	<0.0001
DFS70	8 (3.6%, 95% CI 1.9-6.9)	5 (9.6%, 4.2-20.6%)	3 (1.8%, 0.1-5.3%)	0.0032
ScI-70	2 (0.9%, 95% CI 0.3-3.3)	1 (1.9%, 0.3-13.1%)	1 (0.6%, 0.1-3.3%)	N.S.
CENP-B	111 (50.9%, 95% CI 44.3-57.5)	5 (9.6%, 4.2-20.6%)	106 (63.9%, 56.3-70.8%)	<0.0001
Nucleosome	38 (17.4%, 95% CI 13.0-23.0)	15 (28.8%, 16.3-42.3%)	23 (13.9%, 9.4-19.9%)	0.0096
Ribo-P	1 (0.5%, 95% CI 0.1-2.6)	1 (1.9%, 0.3-13.1%)	0 (0.0%, 0.0-2.3%)	N.S.
Sm	0 (0.0%, 95% CI 0.0-1.7)	0 (0.0%, 0.0-6.9%)	0 (0.0%, 0.0-2.3%)	N.S.
Ku	8 (3.6%, 95% CI 1.9-6.9)	2 (3.9%, 2.2-13.0%)	6 (3.6%, 2.2-5.9%)	N.S.
PCNA	1 (0.5%, 95% CI 0.1-2.6)	0 (0.0%, 0.0-6.9%)	1 (0.6%, 0.1-3.3%)	N.S.
RNA Pol III	4 (1.8%, 95% CI 0.7-4.6)	2 (3.9%, 2.2-13.0%)	2 (1.2%, 0.3-4.3%)	N.S.
Rpp25	2 (0.9%, 95% CI 0.3-3.3)	0 (0.0%, 0.0-6.9%)	2 (1.2%, 0.3-4.3%)	N.S.
Rpp36	3 (1.4%, 95% CI 0.5-4.0)	0 (0.0%, 0.0-6.9%)	3 (1.8%, 0.9-5.2%)	N.S.
PmScl	10 (4.6%, 95% CI 2.5-8.2)	1 (1.9%, 0.3-13.1%)	9 (5.4%, 2.9-10.0%)	N.S.
BICD2	31 (14.2%, 95% CI 10.3-19.4)	8 (15.4%, 6.0-27.5%)	45 (27.1%, 20.9-34.3%)	0.0237
MIT3	18 (8.3%, 95% CI 5.3-12.7)	2 (3.9%, 1.1-10.9%)	16 (9.6%, 6.0-15.1%)	N.S.
UMMP-1	0 (0.0%, 95% CI 0.0-1.7)	0 (0.0%, 0.0-6.9%)	0 (0.0%, 0.0-2.3%)	N.S.
SLA	1 (0.5%, 95% CI 0.1-2.6)	0 (0.0%, 0.0-6.9%)	1 (0.6%, 0.1-3.3%)	N.S.
tp100	2 (0.9%, 95% CI 0.3-3.3)	1 (1.9%, 0.3-13.1%)	1 (0.6%, 0.1-3.3%)	N.S.
tp230	2 (0.9%, 95% CI 0.3-3.3)	1 (1.9%, 0.3-13.1%)	1 (0.6%, 0.1-3.3%)	N.S.
PCP	0 (0.0%, 95% CI 0.0-1.7)	0 (0.0%, 0.0-6.9%)	0 (0.0%, 0.0-2.3%)	N.S.
LC-1	1 (0.5%, 95% CI 0.1-2.6)	0 (0.0%, 0.0-6.9%)	1 (0.6%, 0.1-3.3%)	N.S.
LC-2	5 (2.3%, 95% CI 1.0-5.3)	2 (3.9%, 2.2-13.0%)	3 (1.8%, 0.9-5.2%)	N.S.
Kat5L	2 (0.9%, 95% CI 0.3-3.3)	0 (0.0%, 0.0-6.9%)	2 (1.2%, 0.3-4.3%)	N.S.

N.S. = not significant

**Conclusions:** Autoantibodies identified via the novel system in this SSc cohort were found in the expected frequencies and also correlated to clinical features of the patients. The multiparameter approach combined with cluster analysis holds promise for a molecular and more precise stratification of SSc subsets.

**Disclosure of Interest:** None declared

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**FRI0415 HUMAN SKELETAL MUSCLE XENOGRAFTS TO MODEL SPORADIC INCLUSION BODY MYOSITIS**

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**Background:** Sporadic inclusion body myositis (IBM) is the most common acquired muscle disease in adults over the age of 50, yet the underlying cause of the disease is unknown, and there are no disease-modifying therapies<sup>1</sup>. The robust endomysial inflammation in addition to an increased association of IBM with specific HLA haplotypes and other autoimmune diseases suggests that IBM is primarily an autoimmune disease<sup>2</sup>. However, an association with ageing, a lack of response to immunotherapy, and presence of pathological features such as ubiquitinated protein aggregates seen in neurodegenerative diseases suggest the immune response may be secondary to myodegeneration. Thus, the relationship between inflammation, inclusions, and myodegeneration in IBM is poorly understood.

**Objectives:** Fundamental obstacles to therapeutic development for IBM include the limited understanding of disease pathogenesis as well as a lack of animal models. It is our objective to address these deficiencies by developing a novel mouse xenograft model of IBM.

**Methods:** In this xenograft model, human muscle biopsy specimens are transplanted into immunodeficient mice. The human myofibers cut during the biopsy procedure degenerate, but new muscle fibres regenerate from the patient's satellite cells. This newly regenerated muscle is revascularized and innervated by the mouse host<sup>2</sup>. Xenografts are collected at various post-operative timepoints ranging from three to eleven months and cryosectioned to carry out histochemical and immunohistochemical analysis.

**Results:** Our preliminary data show that IBM xenografts develop pathologic features of the human disease.

At 4 months, collections of xenografts from a patient with healthy muscle, a dermatomyositis patient, and an IBM patient display successful regeneration. Regeneration appears less robust in IBM xenografts and is inversely associated with number of human CD3+ cells and sarcoplasmic MHC-I upregulation. A proportion of the CD8+ T cells within the IBM xenografts are proliferative at 4 months, and this is significantly reduced at 6 months (Fisher exact test,  $p < 0.0001$ ). In addition, at 8.5 months, the IBM xenograft shows rare fibres containing p62 positive puncta.

**Conclusions:** This xenograft model will allow us to investigate the interactions between human muscle and immune system in a mouse host. We are using this model for mechanistic studies and preclinical therapeutic testing in IBM.

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**FRI0416 XIAP AS NOVEL INTEGRATOR OF TGF BETA SIGNALLING AND CANONICAL WNT SIGNALLING IN TISSUE FIBROSIS**

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**Background:** Aberrant activation of profibrotic pathways is a key feature of systemic sclerosis (SSc). Extensive evidence characterises TGF $\beta$ - and canonical WNT-signalling as key drivers of fibroblast activation. The crosstalk between those pathways, however, remains largely unknown. A better understanding of the interplay of different profibrotic pathways may be the key to the development of effective targeted therapies. XIAP (X-linked inhibitor of apoptosis protein) is an ubiquitously expressed member of the IAP protein family with important functions in tissue turnover. XIAP was recently described to be implicated in canonical Wnt signalling and TGF $\beta$  signalling.

**Objectives:** The aim of this study is to characterise the role of XIAP in fibrotic disease.

**Methods:** XIAP-expression was analysed by qPCR, IF and Western blot. XIAP was targeted pharmacologically with Embelin. The activation of the canonical Wnt pathway was assessed by analyses of Wnt target genes and by TOPflash/FOP-flash luciferase reporter assay. *In vivo*, XIAP inhibition was analysed in two different models of fibrosis.

**Results:** The expression of XIAP is increased in the skin of SSc patients compared to matched healthy individuals with a particularly prominent expression in fibroblasts. The overexpression of XIAP is more pronounced in SSc patients with diffuse and active skin fibrosis compared to SSc patients with limited and inactive disease. The overexpression of XIAP is also reflected in several experimental fibrosis models: the model of sclerodermatous graft versus host disease, the model of bleomycin induced skin fibrosis and in Wnt10b transgenic mice. Stimulation with either recombinant Wnt1 or TGF $\beta$  cytokine induces the expression of XIAP in cultured fibroblasts. Inhibition of XIAP reduced the Wnt1- and TGF $\beta$  induced activation of fibroblasts with reduced collagen release and expression of myofibroblast markers. In addition, XIAP inhibition reverted the activated fibroblast phenotype in SSc fibroblasts with reduced expression of stress fibres and  $\alpha$ SMA. The antifibrotic effects of XIAP inhibition occurred in non-toxic doses. Mechanistically, XIAP inhibition reduced the activation of canonical Wnt signalling as demonstrated by TOPflash reporter assays and by the analysis of canonical Wnt target genes. XIAP inhibition also reduced the expression of canonical Wnt target genes in Wnt10b transgenic mice. To analyse the effects of XIAP inhibition *in vivo*, two mouse models were used: the model of bleomycin-induced dermal fibrosis and Wnt10b-transgenic mice. In both models, the pharmacological inhibition of XIAP exerted anti-fibrotic effects with reduced dermal thickening, reduced myofibroblast counts and reduced hydroxyproline contents.

**Conclusions:** XIAP is upregulated in SSc fibroblasts in a TGF $\beta$ -dependent manner and promotes fibroblast activation by fostering canonical WNT signalling. Our data suggest that XIAP mediates an amplification loop between TGF $\beta$  and canonical Wnt signalling. Inhibition of XIAP may thus be a novel approach to target aberrant canonical WNT signalling in fibrotic diseases.

**Disclosure of Interest:** None declared

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**FRI0417 CD86 EXPRESSION ON CULTURED SKIN FIBROBLASTS FROM SYSTEMIC SCLEROSIS PATIENTS: IN VITRO EFFECTS OF CTLA4-IG**

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**Background:** Skin fibroblasts (SFs) are involved in the excessive production of extracellular matrix (ECM) proteins which characterises fibrosis in systemic sclerosis (SSc).<sup>1</sup> Myofibroblasts which are characterised by a higher expression of pro-fibrotic molecules (a-SMA: alpha-smooth muscle actin; S100A4: fibroblast-specific protein-1) as well as by the over-production of ECM proteins (FN: fibronectin; collagens type I and III), may originate from the activation and differentiation of resident fibroblasts after multiple profibrotic stimuli.<sup>2</sup>

CTLA4-Ig interacts with the cell surface costimulatory molecule CD86 and can downregulate the target cell activation.<sup>3</sup>

**Objectives:** To evaluate CD86 expression and the *in vitro* effects of CTLA4-Ig on skin fibroblasts (SFs).

**Methods:** Skin biopsies were obtained from 8 "limited" cutaneous SSc patients (treated only with vasodilators, mainly cyclic prostanoids) and 4 healthy subjects (HSs), after EC and patient informed consent. After 8 days (T8) of culture, SFs obtained from biopsies were treated for 24 and 48 hours, in the absence or in the presence of CTLA4-Ig (10, 50, 100 and 500 micrograms/ml). Evaluation of CD86 expression was performed by quantitative real-time polymerase chain reaction (qRT-PCR). In addition, also human macrophages obtained from PBMCs of SSc patients, were cultured. The statistical analysis was carried out by the non-parametric Mann-Whitney U test.

**Results:** Cultured SSc fibroblasts showed a very low gene expression level of CD86, compared to cultured macrophages of SSc patients, taken as positive control for CD86 expression (99% less). Therefore, cultured SSc fibroblasts treated for 24 hours and for 48 hours with CTLA4-Ig (10, 50, 100 and 500 micrograms/ml) did not show any significant modulation in the gene expression levels of CD86, compared to untreated fibroblasts (CNT). Interestingly, cultured HSs fibroblasts treated with CTLA4-Ig for 24 hours and for 48 hours showed a significant decrease in the gene expression of CD86, limited to the highest dose (500 micrograms/ml), compared to CNT (0.16% and 0.64% less, respectively) ( $p < 0.05$ ).



**Conclusions:** In the present short-term study (24 and 48 hours), no significant effects at qRT-PCR resulted after CTLA4-Ig treatment of cultured SSc SFs. The result might arise from a limited expression of CD86, as consequence of a retained advanced differentiation of the the SSc fibroblasts. On the contrary, a significant reduction of CD86 expression on HSs fibroblasts treated with CTLA4-Ig was observed.

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### FRI0418 IN VITRO EFFECTS OF CTLA4-IG TREATMENT ON CULTURED FIBROCYTES FROM SYSTEMIC SCLEROSIS PATIENTS

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**Background:** Circulating fibrocytes (CFs) are progenitor cells derived from bone marrow, expressing markers of both hematopoietic cells (CD45, MHC class II) and stromal cells (collagen I and III), together with the chemokine receptors, which regulate their migration into inflammatory lesions (CXCR4, CCR2, CCR7).<sup>1</sup> CFs can migrate into SSc-affected tissues and can differentiate into fibroblasts/myofibroblasts.<sup>2</sup> CFs express the CD86 (B7.2) costimulatory molecule and the adhesion molecules CD11a, CD54, ICAM-1, and CD58. The fusion molecule CTLA4-Ig interacts with CD86 and can downregulate the target cell.<sup>3</sup>

**Objectives:** To study the *in vitro* effects of CTLA4-Ig on cultured CFs.

**Methods:** CFs were obtained from the peripheral blood samples of 8 “limited” cutaneous SSc patients (treated only with vasodilators, mainly cyclic prostanoids) and from 4 healthy subjects (HSs). CFs were characterised by fluorescence-activated cell sorter analysis (FACS), at basal time (T0) and after 8 culture days (T8), for CD45, collagen type I (COL I), CXCR4, CD14, CD86, and HLA-DRII expression. T8-cultured CFs were treated for 3 hours in the absence or in the presence of CTLA4-Ig (10, 50, 100 and 500 micrograms/ml). Quantitative real-time polymerase chain reaction (qRT-PCR) for CD86, COL I, IL1b, TGFb, αSMA, S100A4, CXCR2, CXCR4, CD11a were performed. The statistical analysis was carried out by the nonparametric Mann-Whitney U test. Skin samples for fibroblast (SFs) cultures were obtained from the same patients after EC and patient informed consent.

**Results:** At qRT-PCR, T8-SSc fibrocytes, in the absence of CTLA4-Ig treatments, showed higher CD86 expression levels compared to HSs fibrocytes. Similarly also αSMA, S100A4, TGFb and COL I gene expression resulted higher in SSc fibrocytes compared to HSs. After CTLA4-Ig treatments, only in SSc fibrocytes, the αSMA and COL I gene expression resulted significantly decreased (p<0.01, p<0.05), whereas the gene expression for S100A4 resulted significantly increased (p<0.01), compared to untreated fibrocytes. Interestingly, in skin fibroblasts from the same SSc patients, the CD86 gene expression was found to be very low, compared to CFs.

**Conclusions:** Circulating fibrocytes from patients affected by limited cutaneous SSc seem to be responsive and downregulated after *in vitro* CTLA4-Ig treatments, suggesting a possible antifibrotic effect on progenitor cells before their final homing and differentiation in active myofibroblasts. Fibroblasts from the same patient do not show the same expression of target molecules and reactivity to CTLA4-Ig.

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### FRI0419 INTRAVENOUS IMMUNOGLOBULINS PREVENTS EXPERIMENTAL FIBROSIS IN A MURINE MODEL OF SYSTEMIC SCLEROSIS

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**Background:** Systemic sclerosis (SSc) is an autoimmune disease characterised by an extensive multi-organs fibrosis. Immunosuppressants are effective in some extent but their incomplete efficacy is hampered by a higher infection risk. Intravenous immunoglobulins (IVIg) have a good safety profile, exhibit immunomodulatory and antifibrotic properties and hence could be a relevant treatment for SSc.

**Objectives:** The purpose of this study was to investigate the effects of IVIg in an experimental model of SSc.

**Methods:** SSc was induced in 6 weeks old Balb/c mice by subcutaneous injections of HOCl five days a week during six weeks (n=20), whereas control mice received subcutaneous injections of PBS (n=20). Human IVIg was administered intravenously by single retro-orbital injection at a dose of 2 g/kg the first day of HOCl administration (n=20). A control group received an injection of 2% Maltose (n=20). Skin thickness was assessed during the protocol until the sacrifice (day 42). Skin tissues were collected in 4% PFA and processed for histological analysis. Dermal thickness was measured by performing a May-Grünwald-Giemsa staining of 4 μm skin sections; collagen deposition was assessed by performing a Picrosirius red-staining and quantified by using a colour deconvolution method. In addition, immunostaining of skin sections was performed in order to evaluate the α-smooth muscle actin (α-SMA) expression. Frozen skin tissues were analysed to also assess the mRNA expression of main inflammatory and pro-fibrotic genes (by quantitative reverse transcription polymerase chain reaction). Collagen deposition was also evaluated by measuring the content of hydroxyproline in 10 mg of frozen tissue.

**Results:** Mice exposed to HOCl developed a diffuse cutaneous SSc with higher dermal thickness compared to the PBS group. IVIg significantly reduced dermal thickness and collagen deposition in HOCl-receiving mice. The amount of α-SMA positive cells evaluated by immunofluorescence was reduced in the HOCl treated mice receiving IVIg. mRNA expression profile of various markers of fibrosis (fibronectin, TGFβ) or inflammation (TNFα, IL-1β, IL-6) were also significantly decreased in the skin of HOCl mice treated with IVIg compared to HOCl-treated mice receiving 2% maltose.

**Conclusions:** These results demonstrate the efficacy of IVIg in preventing experimental fibrosis in a HOCl murine model of SSc.

**Disclosure of Interest:** None declared

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### FRI0420 ALTERED TRANSCRIPTOME OF CIRCULATING CD14+ MONOCYTES IN SYSTEMIC SCLEROSIS

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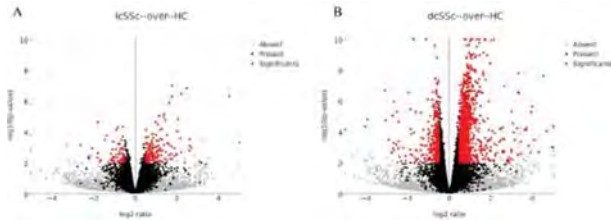
**Background:** Previous studies indicated monocyte-derived cells as important players in the development of multiple organ fibrosis. Although changes in monocyte's phenotypes as well as an increased infiltration into fibrotic organs were reported in systemic sclerosis (SSc), the detailed role of these cells in multi-organ fibrogenesis remains unclear.

**Objectives:** We aimed to characterise a contribution of circulating CD14<sup>+</sup> monocytes in the disease course in limited cutaneous (lc) and diffuse cutaneous (dc) SSc.

**Methods:** CD14<sup>+</sup> monocytes were isolated from peripheral blood of lcSSc (n=5, age=54.4±6.7), dcSSc patients (n=5, age=51.8±7.2) and age- and sex-matched healthy controls (HC) (n=5, age=50.8±9.7). Total RNA was isolated and polyA libraries were prepared using TruSeq Stranded mRNA kit. Next Generation Sequencing was performed using Illumina HiSeq 4000 platform. Differentially expressed genes were computed using DESeq2 algorithm. Principal Component Analysis (PCA) was accomplished as well as pathway analysis using Metacore software. mRNA levels of top targets were confirmed by qPCR.



**Results:** We detected 1440 differentially expressed genes between dcSSc vs HC and 225 between lcSSc and HC respectively ( $p < 0.01$ ;  $\log_2$  ratio  $\geq 0.5$ , figure 1). Among those, in dcSSc 1076 were upregulated (e.g. MMP9, IL1R2, FLT3, MIF, TLR9) and 364 were downregulated (e.g. TGFBR1, CD44, CD244, HLA-DRA, HLA-G). In lcSSc 160 transcripts were upregulated (e.g. CCL2, WNT5B, MMP17) and 65 were downregulated (e.g. KLF11, IRAK2). We identified 123 commonly deregulated genes between SSc subgroups (e.g. CCL3, CD14, IL27, MMP17). Principal component analysis showed close clustering within SSc subgroups and clear separation from healthy controls. Pathway analysis revealed alterations in several biological processes important in fibrogenesis including antigen presentation, MIF-induced immune responses, TGF- $\beta$ , NOTCH and WNT signalling pathways. qPCR analysis further confirmed differences in gene expression on mRNA level (n HC=8, n SSc=25,  $p < 0.05$ ).



**Abstract FRI0420 – Figure 1.** Volcano plots representing differentially expressed genes in lcSSc vs HC (A) and dcSSc vs HC (B). Red dots stand for significantly deregulated transcripts ( $p < 0.01$ ;  $\log_2$  ratio  $\geq 0.5$ ).

**Conclusions:** To our knowledge, this is the first global transcriptome analysis of peripheral blood CD14<sup>+</sup> monocytes in SSc. Our results suggest an initial activation of monocytes in peripheral blood, which might be further translated into novel cellular biomarker of the disease and potentially used for distinguishing between responders and non-responders to a novel treatment in future clinical trials.

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#### FRI0421 TOLL LIKE RECEPTOR-7/8 ACTIVATION EXACERBATES MURINE EXPERIMENTAL AUTOIMMUNE MYOSITIS

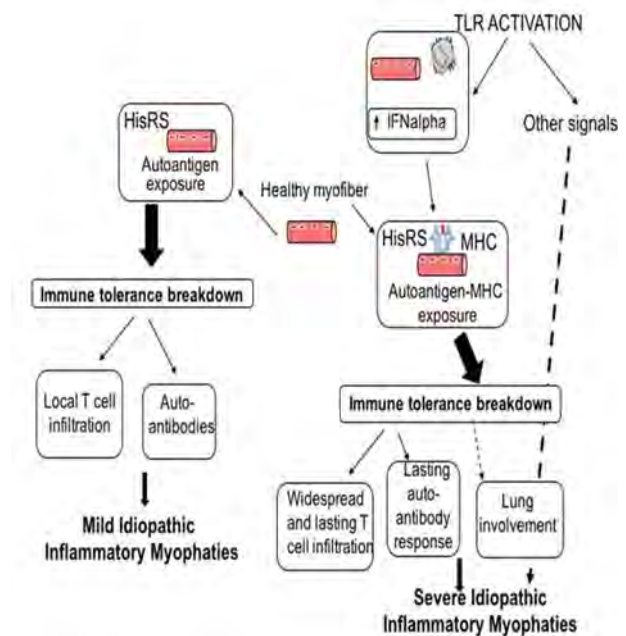
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**Background:** Type I interferon (IFN)-regulated proteins are upregulated in muscle and skin tissues of patients with idiopathic inflammatory myopathies (IIM).<sup>1</sup> Type I IFN induction might rely upon the activation of toll-like receptors (TLRs).<sup>2</sup> Specifically, TLR-7/8 is indeed upregulated in infiltrating leukocytes and muscle tissue of IIM patients.<sup>3</sup>

**Objectives:** To investigate whether the activation of TLR-7/8 and type I IFN influences the natural history of the IIM.

**Methods:** Experimental autoimmune myositis (EAM) was induced by injection of the amino-terminal portion of the murine Histidyl t-RNA synthetase (HisRS). Disease activity was compared in the presence or absence of the TLR-7/8 agonist R848 in wild-type mice and in mice that failed to express the IFN $\alpha$ R receptor (IFN $\alpha$ R null).

**Results:** EAM induced by a single intramuscular immunisation with HisRS spontaneously abated after 7–8 weeks. In contrast, the levels of anti-HisRS autoantibodies, endomysial/perimysial leukocyte infiltration and myofiber regeneration persisted until the end of the follow-up period (22 weeks after immunisation) in mice immunised with HisRS in the presence of R848. Myofiber MHC class I molecules were detectable in HisRS +R848 immunised mice only. Muscle MHC expression occurred in parallel with leukocyte infiltration. Type I IFN was necessary for the prolonged autoantibody response to occur and for the spreading of the autoimmune response, as demonstrated using IFN $\alpha$ R null mice.



**Abstract FRI0421 – Figure 1.** Role of TLR7/8 activation in HisRS-induced myositis

**Conclusions:** TLR7/8 activation is needed to induce and maintain a systemic autoimmune response against the skeletal muscle. This EAM model reproduces many characteristics of human IIM and may represent a tool for pre-clinical studies.

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#### FRI0422 ROLE OF THE PROLYL 3-HYDROXYLASE LEPREL1 IN FIBROSIS

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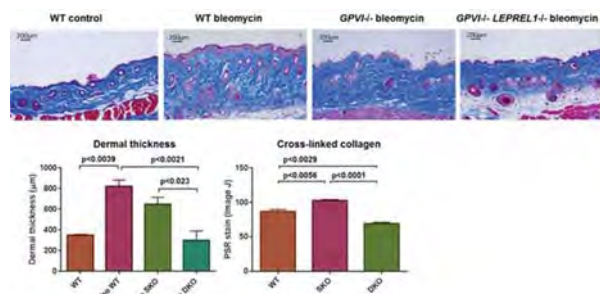
**Background:** Three prolyl 3-hydroxylase enzymes, *LEPRE1*, *LEPREL1* and *LEPREL2*, are known to modify prolines in certain sequences in the C-terminal helical region of the polypeptide chains of procollagens converting them to 3-hydroxyproline residues. This modification appears to facilitate correct alignment of the chains in forming the triple helical domains of the procollagen molecules prior to secretion. Increased deposition of triple helical collagen and other extracellular matrix (ECM) proteins by activated fibroblasts underlies pathological fibrosis in systemic sclerosis (SSc), and may be dependent on prolyl 3-hydroxylase activity as a rate-limiting step.

**Objectives:** The objectives of this study were: 1) to screen candidate genes with large first introns containing regulatory elements for association with systemic sclerosis (SSc) through copy number variation (CNV), 2) to study the lead candidate gene *LEPREL1* further, as a fibrosis-related factor in genetically modified mice subject to bleomycin induced skin fibrosis, 3) to determine the levels of

LEPREL1 protein in SSc and control fibroblasts and measure possible induction by profibrotic factors, and 4) measure the effect of *LEPREL1* gene editing on triple helical collagen secretion by SSc disease fibroblasts.

**Methods:** DNA samples from SSc patients and controls were assayed by qPCR for CNVs within regulatory regions of 40 candidate genes. The lead candidate, *LEPREL1* was studied further through tagging SNP analysis, of rs7612998, rs1447936, s1018343, s696065, in 564 SSc and 627 controls. In wild type (WT), GPVI  $-/-$  single knockout (SKO) or *LEPREL1* $-/-$  GPVI  $-/-$  double knockout (DKO) mice skin fibrosis was initiated by daily subcutaneous bleomycin for 14 days (*LEPREL1* $-/-$  embryonically lethal due to placental thrombosis). Skin fibrotic lesions sampled on day 21 were analysed by histology and picrosirius red stain. SSc and control skin fibroblasts grown from forearm skin biopsies, were cultured at passage 3–5, with or without the pro-fibrotic TGF $\beta$ , or with or without estradiol in cells grown in oestrogen depleted conditions (no phenol red). *LEPREL1* was assayed by Western blot. CRISPR/Cas9 was used to edit the *LEPREL1* gene in SSc skin fibroblasts.

**Results:** Initial screening of candidate genes revealed a weak statistical association between a first intron CNV nsv514192 and SSc susceptibility in males ( $p < 0.028$ ). However SNP analysis demonstrated that a haplotype, identified as CTA across the 4 SNPs, was associated with increased risk of SSc development (OR 3.45,  $p < 0.0023$ ). This allele opens a FOXA1 site in the first intron and was seen predominantly in females. In cultured dermal fibroblasts *LEPREL1* protein levels were raised in SSc samples and induced to SSc levels in control fibroblasts by culture with TGF $\beta$ . Estradiol also induced *LEPREL1* and collagen I protein. In genetically modified *LEPREL1* knockout mice, resistance to bleomycin skin fibrosis was seen (figure 1). Silencing of *LEPREL1* in SSc fibroblasts by CRISPR/Cas9 preferentially reduced triple helical collagen I secretion.



**Conclusions:** The prolyl 3-hydroxylase *LEPREL1* is confirmed as a fibrosis-related gene associated with SSc susceptibility. Small molecule inhibitors of this endoplasmic reticulum enzyme may limit the overproduction of collagen as a therapy for fibrosis.

**Disclosure of Interest:** None declared

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#### FRI0423 EFFECTS OF SELEXIPAG IN CULTURED SCLERODERMA SKIN FIBROBLASTS

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**Background:** In systemic sclerosis (SSc), the transition of fibroblasts into profibrotic myofibroblasts contributes to fibrosis through their over-production of extracellular matrix (ECM) proteins, primarily type I collagen (COL-1) and fibronectin (FN), a process which is mediated by the activation of fibrogenic intracellular signalling transduction molecules, including Erk1/2 and Akt kinases.<sup>1,2</sup> Selexipag and its active metabolite (ACT-333679) are prostacyclin receptor agonists which leads to vasodilation in the pulmonary circulation and mainly used in the treatment of pulmonary arterial hypertension.

**Objectives:** To investigate the possible effects of selexipag and ACT-333679 in downregulating the profibrotic activity of cultured SSc fibroblasts/myofibroblasts and the fibrogenic signalling molecules involved in the process.

**Methods:** After obtaining Ethics Committee (EC) approval and informed consent, fibroblasts isolated from skin biopsies of 6 SSc patients (mean age 63±13 years) were cultured until the 3rd culture passage and then either maintained in normal growth medium (untreated cells) or independently treated with different

concentrations of selexipag (from 30 µM to 0.3 µM) or ACT-333679 (from 10 µM to 0.1 µM) for 48 hours. Protein and gene expressions of  $\alpha$ -smooth muscle actin ( $\alpha$ -SMA), fibroblast specific protein-1 (S100A4), COL-1, and FN were investigated by Western blotting and qRT-PCR.

Erk1/2 and Akt phosphorylation was investigated in untreated and ACT-333679 treated cells at 15 and 30 min as well as at 48 hours by Western blotting.

**Results:** Selexipag and ACT-333679 significantly reduced the protein synthesis and the gene expression of  $\alpha$ -SMA, S100A4, and COL-1 in cultured SSc fibroblasts/myofibroblasts compared to untreated cells, primarily at the concentrations of 3 µM and 0.3 µM for selexipag and 1 µM and 0.1 µM for ACT-333679 ( $p < 0.05$ ). Differently, FN was significantly downregulated at protein level ( $p < 0.05$  vs. untreated cells).

Of note, ACT-333679 significantly reduced the phosphorylation of Erk1/2 and Akt kinases already after 30 min of treatment in cultured SSc fibroblasts/myofibroblasts, and this effect was further maintained at 48 hours from treatment ( $p < 0.05$  vs. untreated cells, for all tested concentrations).

**Conclusions:** For the first time selexipag and mainly its active metabolite ACT-333679 were found to interfere with the profibrotic activity of cultured SSc fibroblasts/myofibroblasts, possibly through the downregulation of fibrogenic Erk1/2 and Akt intracellular signalling molecules.

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#### FRI0424 COMPARATIVE ANALYSIS OF CLINICALLY AFFECTED AND UNAFFECTED SKIN BIOPSIES FROM SCLERODERMA PATIENTS BASED ON RNA-SEQUENCING

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**Background:** Systemic sclerosis (SSc) is a complex chronic autoimmune disease characterised by vasculopathy, inflammation and fibrosis across different organ systems. The origin and pathogenesis of the disease are not well understood and symptoms may vary among affected individuals, complicating the diagnosis and therapy.

**Objectives:** We aimed at characterising gene expression profiles in biopsies from affected and unaffected skin of SSc patients.

**Methods:** RNA isolated from affected and unaffected skin biopsies of 23 SSc patients was analysed using polyA-selected RNA sequencing. Paired differential expression analysis was performed with DESeq2, and Molecular Signatures Database gene set collections were used for functional annotation.

**Results:** Paired analysis of SSc gene expression profiles identified over 900 genes differentially regulated between the affected and unaffected skin biopsy samples (adjusted p value < 0.05). Macroscopically unaffected skin samples showed clear gene expression differences from the affected skin samples, even though the histological examination showed that pathological changes were already present in most of the samples classified as unaffected. Clustering of differentially expressed genes and subsequent functional characterisation of the resulting gene modules revealed sets of co-expressed genes involved in inflammatory response, extracellular matrix interaction, metabolic function and epithelial differentiation, and highlighted the importance of a number of transcription drivers, such as serum response factor (SRF) or interferon regulatory factor 7 (IRF7). Several genes from the HOX family of transcription factors were found to be among the most significantly differentially expressed genes, pointing to an important role of wound healing and regeneration processes in SSc skin lesions. Additionally, we found significant association between expression of several proteasome subunits and the inflammation score obtained by histological assessment of the skin biopsies.

**Conclusions:** RNA sequencing analysis in paired skin biopsy samples revealed coordinated changes in the gene expression between SSc lesions and macroscopically unaffected skin, providing insights into the SSc skin pathogenesis at the molecular level.

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FRIDAY, 15 JUNE 2018

## Scleroderma, myositis and related syndromes

### FRI0425 ASSOCIATION BETWEEN TISSUE OXYGEN DELIVERY AND DIGITAL ULCERS IN SYSTEMIC SCLEROSIS

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**Background:** Digital ulcers (DUs) are common manifestations of vascular disease in systemic sclerosis (SSc) patients.

**Objectives:** To investigate the association between the amount of oxygen delivered to peripheral tissues and the development of DUs in SSc patients.

**Methods:** One hundred and eleven SSc patients (103 female) were recruited consecutively to the study. Thirty age and sex matched controls were also enrolled. Transthoracic echocardiography (TTE) was performed for each patient to estimate cardiac output (CO). Arterial oxygen saturation (SaO<sub>2</sub>) with pulse oximeter in room temperature and serum haemoglobin concentration (Hb) were measured at the time of TTE. The amount of oxygen delivered to tissues (D0<sub>2</sub>) in 1 min was estimated using the equation  $D0_2 = CO \cdot (SaO_2 \cdot 1.39 \cdot Hb)$  and adjusted for body weight. Demographic, clinical and laboratory data were retrieved from hospital records. DUs were described as ulcerations on the skin distal to proximal interphalangeal joints (PIF) of the digits. Patients were divided into 2 groups according to presence of DUs within 1 year of study enrollment (Group1=with DU, Group2=without DU). Chi-square and Mann-Whitney U tests were used for comparing categorical and continuous variables between the groups, respectively.

**Results:** Mean age was 52.6 (11.8) years in SSc patients and 51.3 (13.0) in controls. Median disease duration was 138.0 (1.8–415.2) months. Diffuse disease was present in 30.6% of patients. There were no differences in terms of Hb level, left ventricular ejection fraction (LVEF) and calculated D0<sub>2</sub> between SSc patients and controls. Mean CO was higher in healthy controls (6.1 vs. 5.1,  $p=0.004$ ). Interestingly, mean S0<sub>2</sub> measurements was lower in control group (96.8 vs. 98.0,  $p=0.005$ ). Comparison of demographics, disease characteristics, tissue oxygen delivery and relevant variables were summarised in table 1. When patients with active DUs were compared with patients without active DUs; no difference was found in Hb, S0<sub>2</sub>, CO and D0<sub>2</sub> between groups.

**Abstract FRI0425 – Table 1.** Comparison of demographics, disease characteristics and D0<sub>2</sub> parameters between patients with and without DUs

	Group 1 (n=64)	Group 2 (n=47)	p
Age, years (SD)	52.3(12.0)	49.9(14.4)	0.34
Disease duration, months (SD)	141.0(96.8)	177.3(97.4)	0.06
Female, n (%)	58(90.6)	44(93.6)	0.56
Diffuse disease, n (%)	11(17.2)	23(48.9)	<0.01
ILD, n (%)	32(50.0)	35(74.5)	0.01
PAH, n (%)	3(4.7)	1(2.1)	0.63
Ever smoked, n (%)	16(25.0)	13(27.6)	0.82
HT, n (%)	15(23.4)	6(12.7)	0.22
DM, n (%)	12(18.7)	3(6.3)	0.09
Cardiac involvement, n (%)	1(1.5)	1(2.1)	1.0
Hb, g/dL	12.8(1.4)	12.2(1.4)	0.04
S0 <sub>2</sub> , % (SD)	97.8(2.5)	98.3(1.1)	0.13
CO, ml/min (SD)	5.1(1.5)	5.1(1.6)	0.91
D0 <sub>2</sub> , ml/min/kg (SD)	13.6(4.5)	14.3(4.6)	0.89

**Conclusions:** Although the haemoglobin concentration was higher in the non ulcer group, there was no difference in the amount of delivered oxygen between patients with and without DUs. These findings imply that vasculopathy and/or peripheral artery disease plays a major role in the development of ulcers.

**Disclosure of Interest:** None declared

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FRI0426

### RESPONSE OF THE REACTIVE SPECIES INTERACTOME TO HYPOTHERMIA INDUCED RAYNAUD'S ATTACK IN PRIMARY RAYNAUD AND SYSTEMIC SCLEROSIS

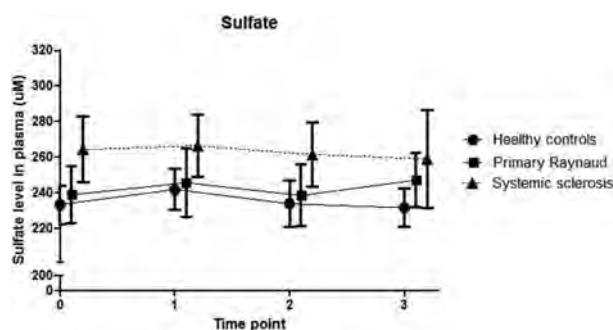
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**Background:** Although the exact etiology of systemic sclerosis (SSc) remains unknown, a current hypothesis is that reactive species (including reactive oxygen species (ROS), reactive nitrogen species (RNS and reactive sulfur species (RSS)) play an important role in the pathogenesis. In addition, the chemical interactions between these molecules, also known as the reactive species interactome, may lead to the formation of more harmful free radicals, thus leading to more damage. We have previously shown a rapid free thiol increase in SSc patients during a cooling and recovery experiment, however the implications of RNS and RSS in this process remain uncharacterized.

**Objectives:** The aim of the current study was to explore nitric oxide and sulfate response, as a measure of the unified reactive species interactome, during hypothermia induced Raynaud's attack in systemic sclerosis (SSc), primary Raynaud's phenomenon (PRP) and healthy controls (HC).

**Methods:** Healthy controls (n=10), PRP patients (n=10) and SSc patients (n=10), all aged ≥ 18 years, were included. All SSc patients fulfilled the ACR/EULAR 2013 criteria. Fingertip photoelectric plethysmography was performed during a standardised cooling and recovery experiment. Patient characteristics were obtained and blood was drawn at four predetermined time points (T<sub>0</sub>, T<sub>1</sub>, T<sub>2</sub> and T<sub>3</sub>). In addition to the previously mentioned free thiols, the following markers were also measured: nitros(yl)ated species, nitrite, nitrate, sulfate and the vascular leakage related molecules angiotensin-1 and angiotensin-2).

**Results:** Our results revealed a significantly longer median duration of hypoperfusion and longer recovery time in SSc patients compared to PRP patients and HC. This coincided with stable levels of angiotensin-1/angiotensin-2 throughout the experiment. In regards to the thiol modification related molecules, (nitrate, nitrite and RXNO) an increased median level of nitrate (T<sub>2</sub>: median 29.6 μmol, range 21.99–41.70 μmol,  $p=0.041$ ) was found in SSc patients. Correspondingly, the same trend was observed for the median plasma concentrations of sulfate ( $p>0.05$  at all time points).



**Conclusions:** We have previously shown an increase of free thiols in all patients during the reperfusion phase. This finding sheds new light on the possibility that processes related to oxidative thiol modification, are rapidly reversible. The current findings revealed also a trend in increased levels of nitrate and sulfate in SSc patients. Therefore, it is plausible that these markers of the redox system interact with one another through the same pathway, underlining the complexity of the redox interactome and suggesting potential novel approaches for therapeutic intervention.

**Disclosure of Interest:** None declared

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**Abstract FRI0428 – Table 2.** Associations between mean number of capillaries at baseline and disease activity (ESSG score 2003) at FU (linear regression)

Predictors	B (95% CI)	p
m_nr/pat rater 2	-0.45 (-0.834,-0.07)	0.02
m_nr/3rd dom rater 2	-0.33(-0.62,-0.03)	0.03
m_nr/4th non-dom rater 2	-0.27 (-0.57,0.02)	0.07

**Conclusions:** The mean number of capillaries had a good association with the history of DUs and predicted disease activity at 6 months follow-up. The m\_nr/pat performed better in our analysis than the m\_nr/3rd dom and m\_nr/4th non-dom, however these could be used alternatively in clinical practice as they are less time consuming.

**Acknowledgements :** This work is part of the QUANTICAP project

**Disclosure of Interest:** None declared

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#### FRI0429 DISTINCT CLINICAL AND IMMUNOLOGICAL PICTURE OF MCTD PATIENTS WITH SKIN INVOLVEMENT

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**Background:** Mixed connective tissue disease (MCTD) is characterised by the co-existence of systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), systemic sclerosis (SSc) and polymyositis/dermatomyositis (PM/DM) symptoms. The majority of patients have skin symptoms typical of at least one of the diseases making up the clinical picture MCTD. MCTD is characterised by an auto-reactive antibody response to RNP antigen and resultant formation of anti-U1RNP antibodies. Current knowledge on cytokine biology and their documented role in the pathogenesis of SLE, SSc and PM/DM suggests that also in MCTD some of them may affect clinical course, activity and/or degree of organ damage.

**Objectives:** To compare clinical and immunological characteristics of MCTD patients with/without skin involvement.

To identify clinical and immunological parameters increasing the risk for a specific (SLE- or SS-like) type of skin lesions and protecting against them.

**Methods:** 79 MCTD patients based Kasukawa' MCTD diagnostic criteria were included. The patients were divided into groups based on the presence of skin lesions typical for a given MCTD component: SLE- SSc- and DM-specific.

**Results:** Skin lesions were found in the majority of the MCTD patients (81%). The SLE-, SSc- and DM-specific skin symptoms were found in 54%, 61% and 5% of the patients, respectively. The group of patients with skin symptoms typical of DM was too small to distinguish it separately (4/79). The measures of disease activity (mean AI=10.6 vs 5.5; p=0.006) and MCTD-related damage (DI=4.1 vs 2.1; p=0.009) in patients with skin involvement were twice as high as in individuals with the intact skin. Furthermore, patients with skin involvement had higher mean serum concentrations of TNF- $\alpha$  (46.4 vs 2.3 pg/ml; p=0.013), and lower levels of IFN- $\gamma$  (43.2 vs 120.8 pg/ml; p<0.001) than patients without any skin symptoms.

The following clinical and immunological parameters were shown to be independently associated with specific types of skin involvement in MCTD patients on multivariate logistic regression analysis:

Independent risk factors for:

- SLE-like skin changes: increased ESR (OR=8.9, 4.47 and 2.6, respectively), higher AI scores and swelling of the hands,
- SSc-like skin changes: higher DI scores (OR=1.522), and presence of anti-Ro60 antibodies (OR=15.903)

Independent protective factors for:

- SLE-like MCTD: chronic progressive course of the disease (OR=0.248) and higher serum concentration of IFN- $\gamma$  (OR=0.988)
- SSc-like MCTD: acute onset of the disease (OR=0.155).

**Conclusions:** The course of MCTD in patients with skin involvement is more severe with specific panel of cytokine levels (increased TNF- $\alpha$  and decreased IFN- $\gamma$  serum concentrations) is characteristic, as compared to patients with the intact skin.

In patients with SLE-like skin lesions MCTD is more often multiphasic, its clinical activity and levels of inflammatory markers are higher while serum concentration of IFN- $\gamma$  is diminished. Patients with SSc-like skin lesions more often have chronic MCTD, associated with more severe organ damage and elevated serum levels of TNF- $\alpha$ .

**Disclosure of Interest:** None declared

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#### FRI0430 EFFECT OF ORAL NUTRITIONAL INTERVENTION ON NUTRITIONAL STATUS IN PATIENTS WITH SYSTEMIC SCLEROSIS

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**Background:** Patients with systemic sclerosis (SSc) are at risk of malnutrition, which ranges from 18% to 56% of cases.<sup>1,2</sup> The high impact of nutritional status on clinical outcome has been shown for many diseases. The optimal nutritional treatment can lead to improvement or preservation of the current nutritional status and increases probability of long-term survival.<sup>3</sup>

**Objectives:** The aim of the study was to determine whether nutritional support has an impact on improvement of nutritional status in SSc patients.

**Methods:** The study included 61 patients with SSc and 49 healthy adults. Nutritional status was determined with subjective global assessment (SGA), body mass index (BMI), bioelectrical impedance analysis (BIA) and anthropometric measurements. Nutrition-related laboratory tests were measured. Appetite was assessed by simplified nutritional appetite questionnaire (SNAQ).

**Results:** Impaired nutritional status was confirmed in 16 patients with SSc (26,2%). Those patients had significantly lower SGA, BMI (p=0,0019), hand grip strength (p=0,0019), appetite (p=0,019) and BIA parameters such as lean tissue mass (p=0,013), intracellular water (p=0,0006), adipose tissue mass (p=0,04). In laboratory tests levels of haemoglobin, albumin and HDL cholesterol were significantly lower, while erythrocyte sedimentation rate (ESR) was higher (p=0,0025). Thirteen patients had dietary intervention (high-energy, high-protein, oral, liquid nutritional supplements) for 12 weeks. SGA (p=0,017) and hand grip strength (p=0,006) improved after nutritional treatment. BMI, appetite, BIA parameters, lipid profile and ESR after 12 weeks remained stable.

**Conclusions:** Assessment of nutritional status in SSc patients should be performed regularly, because inclusion of oral nutritional intervention may improve SGA and hand grip strength.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.6703

#### FRI0431 DYSREGULATION OF LYMPHANGIOGENETIC FACTORS IN SYSTEMIC SCLEROSIS PATIENTS WITH PULMONARY ARTERIAL HYPERTENSION

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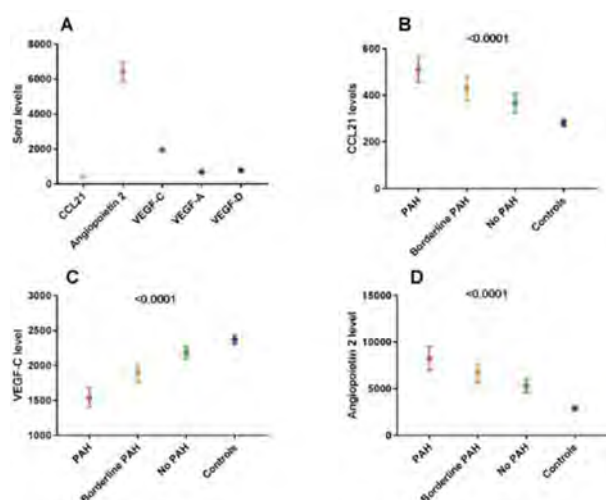
**Background:** Pulmonary arterial hypertension (PAH) continues to be a major complication in systemic sclerosis (SSc); indicating an unmet need for rational therapeutic targets. Recently, we found that chemokine CCL21 was upregulated in SSc and associated with PAH. CCL21 appears to be a key regulator of the expression and secretion of vascular endothelial growth factor-C (VEGF-C); a critical growth factor for lymphatic vessels. This is interesting as SSc is marked by lymphatic vessel abnormalities; and high blood levels of Angiotensin-2, which is a known regulator of VEGF-C. Moreover, it was recently shown that VEGFR3, the cognate receptor for VEGF-C, is down-regulated in pulmonary arterial endothelial cells from human idiopathic PAH subjects with BMPR2 gene defects. Based on these observations, we reasoned that the observed upregulation of CCL21 in SSc-PAH could be linked to VEGF-C and Ang-2 dysregulation.

**Objectives:** Assess serum concentrations of CCL21, the VEGF family and Ang-2 in right heart catheterization (RHC) verified SSc-PAH patients and compare these to patients with borderline PAH, no PH and to healthy controls.

**Methods:** Sera from the prospective Oslo University Hospital SSc cohort (n=372) and healthy controls (n=100) were analysed for VEGF-A,C,D, CCL21 and Ang2 using Luminex kits from Millipore. Patients with an incident RHC (n=167) were included in the present study. PAH was defined as precapillary PH (mean

pulmonary arterial pressure, mPAP  $\geq 25$  mmHg) in the absence of significant interstitial lung disease (ILD), based on high resolution computed tomography and lung function tests. Borderline PAH was defined as mPAP of 20–24 mmHg in the absence of significant ILD. Patients with pulmonary hypertension (PH) due to other causes were excluded. Descriptive statistics and logistic regression analyses were performed and tested by the goodness-of-fit test with area under the curve (AUC).

**Results:** Mean age at onset was  $54 \pm 14.1$ , at RHC  $61 \pm 10.9$  years. The time from sera to RHC was  $0.9 \pm 3.1$  years. In total, 73.7% (123) patients had limited cutaneous SSc, 46.7%<sup>48</sup> were positive for anti-centromere antibody and 80.2% (134) were females. Of these, 123 (73.7%) patients were included in the study, 28 patients with PAH, 45 borderline PAH and 50 patients with no PH. Mean VEGF-A, C, D, CCL21 and Ang2 levels are shown in figure 1A. VEGF-A was significantly higher in SSc patients compared to healthy controls ( $p=0.001$ ), no significant differences between PAH and no PH patients were found. VEGF-D was decreased in SSc-PAH but not significantly. CCL21 and Ang2 levels were increased in patients with PAH, whereas in VEGF-C was significantly decreased in patients with PAH (figure 1 B-D). In univariable logistic regression analyses, VEGF-C (OR 0.99, 95% CI 0.997–0.998,  $p=0.001$ , AUC=0.79), CCL21 (OR 1, 95% CI 1–1.003,  $p=0.050$ , AUC=0.69) and Ang2 (OR 1, 95% CI 1–1.0001,  $p=0.49$ , AUC=0.67) were associated with PAH compared to no PH patients. Due to few event numbers, no multivariable analyses were performed.



Abstract FRI0431 – Figure 1. Serum levels of A) all; B) CCL21; C) VEGF-C and D) Ang2

**Conclusions:** The present study is the first to demonstrate dysregulation of lymphangiogenic factor expression of multiple targets in sera of SSc-PAH patients.

**Disclosure of Interest:** None declared

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**FRI0432 SINGLE-PORT THORACOSCOPIC SYMPATHICOTOMY FOR TREATMENT RESISTANT RAYNAUD'S PHENOMENON. FIRST REPORT OF A NOVEL MINIMALLY-INVASIVE ENDOSCOPIC TECHNIQUE**

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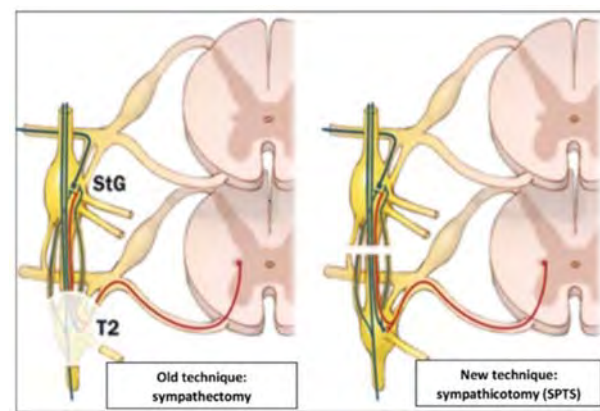
**Background:** Raynaud's phenomenon of the hands is a great burden in daily life and reduces quality of life in patients with or without an underlying connective tissue disease. Although vasodilatory treatment may be effective in some patients, complaints may be resistant to treatment, for which additional treatment options are very limited. In earlier years, thoracic sympathectomy by anterior or axillary thoracotomy has been shown effective, but with a great surgical burden and limited durability. In the 90 s, endoscopic procedures were introduced. However, these techniques needed multiple endoscopic ports and still performed a relatively

mutilating sympathectomy of the sympathetic ganglia. In our centre, the single-port thoracoscopic sympathectomy (SPTS) was developed, which is a new minimally-invasive endoscopic technique with a limited surgical burden.

**Objectives:** The aim of the current pilot study was to evaluate feasibility and efficacy of SPTS in patients with treatment resistant Raynaud's.

**Methods:** This new technique entails only a single-port endoscopic procedure, during which a sympathectomy (figure 1) of the nerve is performed, thus sparing the ganglia. Hospital stay is limited to one day. The procedure has been developed for treatment of hyperhidrosis and performed in our hospital in over 550 patients without major adverse events with a success rate of 98%. In the current study, we aim to include 10 patients with treatment resistant Raynaud's, defined as unsatisfactory effect or contraindications of oral vasodilatory agents and iv prostaglandin analogues. Sympathectomy was performed on the left hand first and the effects were compared with the contralateral hand after 3 and 12 months. Major exclusion criteria were severe lung involvement or proximal vascular stenosis. The primary end point was Raynaud's Condition Score (RCS) and Quality of life (SF-36). Among others, cooling fingertip plethysmography (PPG) and laser doppler imaging (LDI) were used as secondary end points for objective assessment of hand perfusion.

**Results:** This is an interim report, and 4 patients have been included so far (age 20,29,32,56 years), male/female 3/1, 3 primary, 1 secondary), without a history of digital ulcers. No adverse events have been observed, apart from some hyperaemia in the first post-operative week. RCS significantly in each patient. Additionally, a clear improvement in hand perfusion following cooling was observed with PPG and LDI, as compared to the contralateral site. All 4 patients were satisfied and agreed to have their contralateral site operated on also. Patients will be followed in the outpatient clinic to assess long term efficacy.



**Conclusions:** Single-port thoracoscopic sympathectomy is a novel minimally-invasive technique which appears to be safe and feasible in patients with treatment resistant Raynaud's phenomenon. However, this study is ongoing and long-term efficacy needs to be established.

**Disclosure of Interest:** None declared

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**FRI0433 ASSESSING MORTALITY MODELS IN SYSTEMIC SCLEROSIS RELATED INTERSTITIAL LUNG DISEASE**

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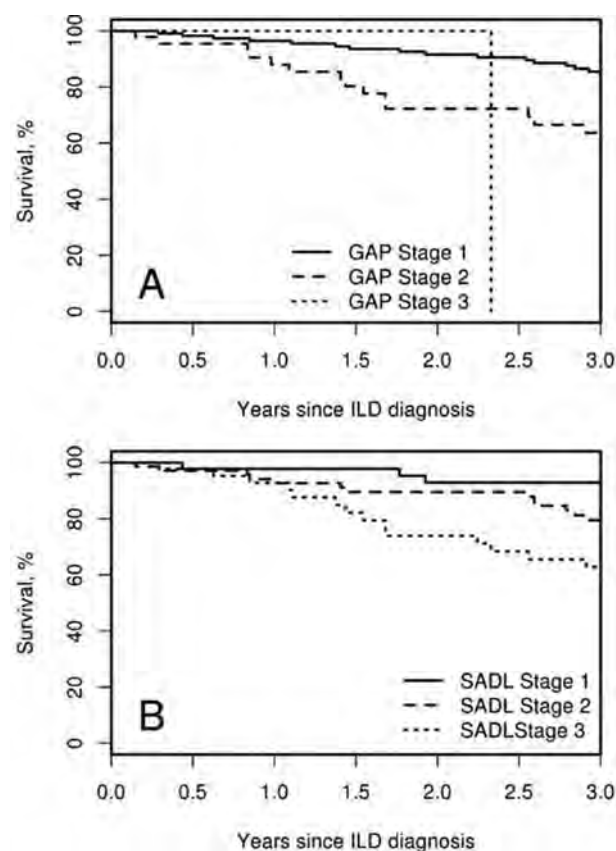
**Background:** Interstitial lung disease (ILD) is a major cause of morbidity and mortality in systemic sclerosis (SSc). However, the severity of lung involvement can vary widely, and current evidence-based treatment options have modest benefit. Prognosis assessment is particularly important for initial management decisions at the time SSc-ILD is diagnosed. There are now multiple mortality models available for use in SSc-ILD which utilise patient's baseline parameters

**Objectives:** The Gender, Age, and Lung Physiology (GAP) model,<sup>1</sup> interstitial lung diseases –GAP (ILD-GAP) model,<sup>2</sup> and the Smoking history, Age, and Diffusion capacity of the Lung (SADL) model<sup>3</sup> were compared using a systemic sclerosis-ILD (SSc-ILD) cohort to evaluate which best determined prognosis.

**Methods:** The models were applied to a cohort of patients with SSc (meeting the 2013 ACR/EULAR classification criteria) seen at a tertiary care centre within 1 year of ILD diagnosis from 2000–2013. Demographics, clinical characteristics,



and mortality were recorded. The performance of the models was assessed using standardised mortality ratios (SMR) of observed vs. predicted outcomes for calibration, and concordance (c)-statistics for discrimination.



**Results:** The cohort included 179 patients with SSc-ILD. Mean age at ILD diagnosis was 57.8 years. There was a female predominance (73%). The mean length of follow up after ILD diagnosis was 4.3 years (SD 4.0). Based on high resolution chest CT (or biopsy when available), 147 (83%) were characterised as nonspecific interstitial pneumonia (NSIP), 31 (17%) as usual interstitial pneumonia (UIP), 1 as unclassifiable ILD. A history of smoking was noted in 49%, and this was not associated with ILD pattern (former/current 46% in NSIP vs. 61% in UIP,  $p=0.11$ ). Pulmonary hypertension (PHTN) was noted in 66 (49%) at baseline, and this did not differ between ILD subtypes. 84% had limited cutaneous SSc, 9% had diffuse cutaneous, and 7% SSc sine scleroderma. SSc specific serologies (i.e., SCL-70, centromere, and/or RNA Pol III) were positive in 73 (43%) patients, somewhat more common in NSIP than UIP (47% vs 26%;  $p=0.034$ ). During a median of 3.2 years of follow-up, 65 patients died. SSc-ILD patients with UIP had a higher mortality than those with NSIP (hazard ratio: 2.27; 95% CI: 1.03–4.97). Other risk factors for progression included baseline DLCO ( $p<0.001$ ), FVC ( $p<0.001$ ) and PHTN ( $p=0.012$ ). All 3 models had comparable discrimination ( $c=0.72$ ,  $0.72$ , and  $0.70$ , respectively). Figure 1 shows the differential mortality based on the GAP and SADL staging systems. (Note the staging in the GAP and ILD-GAP models are identical.) Regarding calibration, the ILD-GAP model underestimated mortality (SMR: 1.5; 95% CI: 1.05–2.14). Calibration was acceptable for SADL (SMR: 0.77; 95% CI: 0.54–1.10) and GAP (SMR: 0.90; 95% CI: 0.63–1.29). The SADL model overestimated mortality in Stage III ILD.

**Conclusions:** The ILD-GAP model underestimated mortality, and the SADL model overestimated mortality in certain subgroups. However, the GAP model performed well in this cohort, providing the best prognostic information for SSc-ILD.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrhumdis-2018-eular.3331

## FRI0434 PATIENTS WITH INFLAMMATORY MYOPATHIES ADMITTED IN ICU ARE CHARACTERISED BY RECENT ONSET AND UNTREATED ACTIVE DISEASE AS WELL AS OLDER AGE AND HIGH COMORBIDITIES

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**Background:** Inflammatory myopathies (IM) are life-threatening but treatable diseases. The risk factors for admission in Intensive care unit (ICU), the management and the outcome of patients with IM admitted to ICU has not yet been assessed.

**Objectives:** To assess the clinical features, risk factors and outcome of patients with IM admitted in ICU.

**Methods:** A single centre cohort of 509 patients with IM was screened for admission in ICU from 1992 to 2017. Patients admitted for trauma or for complications from elective surgery were excluded. Control patients with IM who had not been hospitalised in ICU were randomly selected from the cohort.

**Results:** Thirty-two ICU admissions were recorded in 27 IM patients during the study period ( $<0.05\%$  of admissions over this 25 year period). Three IM patients were admitted more than once.

Characteristics and prognosis of patients in ICU

Patients hospitalised in ICU had a mean age of  $63\text{ y.} \pm 15$  with SAPS II score of  $58 \pm 24$  and LODS score of  $9 \pm 5$  corresponding to an intermediate severity at admission in ICU. The delay between IM diagnosis and first ICU admission was  $27 \pm 43$  months. It is noteworthy that 12 patients (44%) were admitted in the ICU within the first month of IM diagnosis, among whom 4 (15%) were diagnosed with IM during ICU stay. Sixteen patients (60%) were not treated at the time of their first ICU admission. In 56% of the ICU stays, patients had active disease at admission. Patients were most frequently admitted for respiratory failure (88%) but cardiac (47%), renal (47%), neurologic (47%), haematological (22%) and hepatic (15%) failures were also recorded. Infections were present in 72% of the ICU stays, with septic shock in 44%. Nine patients (33%) died in ICU and 3 others (11%) within 90 days of the last ICU discharge (vs. 15% during a  $7.5 \pm 5$  years period of follow-up in the control group,  $p<0.0001$ ).

**Risk factors of ICU admission:** The case control analysis identified 6 risk factors significantly associated with hospitalisation in the ICU, 3 of which were independently associated with hospitalisation in multivariate analysis. ICU patients had a higher age at first clinical signs of illness ( $62 \pm 13$  years old vs.  $53 \pm 13$  years old,  $p<0.05$ ), they had a higher rate of chronic kidney failure (26% vs. 0%,  $p<0.05$ ) and higher incidence of arterial or venous thrombosis history (37% vs. 0%,  $p<0.05$ ). Other risk factors that were only identified in univariate analysis included lower BMI ( $22.6 \pm 4.5$  vs.  $25.4 \pm 6.3$ ), a history of interstitial lung disease (48% vs. 30%) and a higher Charlson comorbidity index ( $4.6 \pm 2.6$  vs.  $3.3 \pm 2$ ).

The type of myositis was not significantly associated with admission in ICU, although no patient admitted in ICU had sIBM. It is noteworthy that cumulative number of immunomodulatory treatments in patients at the time of hospitalisation in ICU was lower than in the control group ( $0.5 \pm 0.7$  vs.  $1.9 \pm 0.8$   $p<0.001$ ).

**Conclusions:** IM patients admitted in ICU frequently have recent onset and untreated active IM with respiratory failure. Admission to ICU is associated with older age and a higher number of comorbidities. Mortality of IM patients in ICU is high.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrhumdis-2018-eular.6148

FRI0435

### CLINICOPATHOLOGICAL CORRELATION IN INFLAMMATORY MYOSITIS: ANALYSIS OF THE REMICAM COHORT (REGISTRY OF INFLAMMATORY MYOSITIS FROM MADRID, SPAIN)

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**Background:** Associations between muscle pathology and clinical features in inflammatory myositis (IM) are not well defined

**Objectives:** to describe the pathological findings in REMICAM<sup>1</sup> muscle biopsies, and analyse their associations with clinical features

**Methods:** All patients with available biopsy were included. According to the score proposed by ENMC workshop<sup>2</sup>, from muscle biopsy reports was extracted: inflammatory cells and location (endomysial, perimysial, perivascular), rimmed vacuola, fibre atrophy, necrosis, regeneration, and HLA expression. Descriptive analysis and association studies between histology and clinical features were performed (t and chi square tests, univariate logistic regression with OR)

**Results:** From 479 patients, 244 (51%) had available biopsy. Most frequent findings were: inflammatory infiltrates (75%): endomysial (44%), perimysial (49%) perivascular (26%); fibre atrophy (54%), perifascicular (27%); necrosis (55%) and regeneration (47%). HLA expression was + in 60/75 cases (80%). Endomysial infiltrate was associated with PM (OR 0.4; p<0.0001), cardiac involvement (OR 2.2; p=0.014), less arthritis (OR 0.5; p=0.01) and older age (51 vs 42 y; p<0.01); perimysial infiltrate and perifascicular atrophy with DM (OR 3.8; p<0.0001) and younger age (40 vs 48 y; p<0.05); necrosis with cardiac involvement (OR 2.1; p=0.035), neoplasia (OR 2.5; p=0.02) and no connective tissue disease (OR 0.4; p=0.01); and HLA with PM (OR 0.1; p=0.003)

**Conclusions:** most frequent histologic findings in IM muscle are inflammatory infiltrates, necrosis, HLA expression and perifascicular atrophy. Endomysial infiltration and HLA are characteristic of PM, and perimysial infiltration/perifascicular atrophy of DM. Endomysial infiltrates are associated with cardiac involvement. Necrosis is more frequent in neoplasia and less in connective tissue diseases, and is associated with cardiac involvement and older age. Our data suggest that muscle biopsy might help to identify those IM patients at higher risk of severe complications, as neoplasia or cardiac involvement

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FRI0436

### COMPARISON OF THE 2017 EULAR/ACR CRITERIA WITH BOHAN AND PETER CRITERIA FOR THE CLASSIFICATION OF ADULT AND JUVENILE IDIOPATHIC INFLAMMATORY MYOPATHIES

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**Background:** The 2017 EULAR/ACR classification criteria provide a validated scoring system for the classification of both adult and juvenile idiopathic inflammatory myopathies (IIM) with reasonable sensitivity and specificity.

**Objectives:** To assess the performance of the 2017 EULAR/ACR criteria<sup>1</sup> in retrospective cohort of IIM and compare with Bohan and Peter criteria.<sup>2,3</sup>

**Methods:** We conducted a retrospective study of all patients clinically diagnosed to have IIM in a tertiary care centre in the last ten years. Performance of both the criteria in the cohort was assessed and compared with clinical diagnosis.

**Results:** One hundred and seven patients were included in the study. Nine patients had juvenile onset. Clinical features are summarised in table 1. 80.4% of the patients were classified as probable/definite myositis using the Bohan and Peter criteria. 81.3% of the patients were classified as having probable/definite inflammatory myositis using the new criteria (score  $\geq 5.5$  without biopsy or  $\geq 6.7$  with biopsy). However the agreement between the two classification criteria was weak in our cohort (kappa=0.43). Complete details of muscle biopsy were available in 44 patients. In this subgroup 95.5% were classified by and Bohan and Peter and 84.1% by EULAR/ACR criteria. Both criterias performed poorly in patients without biopsy data and in polymyositis subset (table 2).

**Abstract FRI0436 – Table 1.** Clinical features of patients with idiopathic inflammatory myositis

Age (at diagnosis)	38.73 years	Proximal Muscle weakness	104 (97.2%)
Sex (Female:male)	3.12:1	Dysphagia	33 (30.8%)
Raynauds	22 (20.6%)	ILD	10 (9.3%)
Arthralgia/arthritis	71 (66.4%)	Anti Jo1 positivity (n=91)	3 (2.8%)
ANA positivity	59 (55.1%)	Elevated muscle enzymes	94 (87.9%)
Clinical Diagnosis	52 (48.9%)	Cutaneous involvement (s/o DM)	65 (60.7%)
Dermatomyositis	2 (1.9%)	Heliotrope	35 (32.7%)
Amyopathic DM	20 (18.7%)	Gottron's papules	21 (19.6%)
Polymyositis	22 (20.6%)	Gottron's Sign	8 (7.5%)
Myositis Overlap Syndrome	8 (7.5%)	Other rashes	18 (16.8%)
Juvenile Dermatomyositis	1 (0.9%)		
Juvenile onset myositis	2 (1.9%)		
overlap			
Cancer associated myositis			

**Abstract FRI0436 – Table 2.** Classification using Bohan and Peter and 2017 EULAR/ACR criteria

	Bohan and Peter	EULAR/ACR
Total IIM (n=107)	86 (80.4%)	87 (81.3%)
With Biopsies (n=44)	42 (95.5%)	37 (84.1%)
Without Biopsies (n=63)	44 (69.8%)	50 (79.4%)
DM (n=67)	62 (92.5%)	61 (91.0%)
PM (n=40)	24 (60%)	26 (65%)

**Conclusions:** The new EULAR/ACR criteria did not perform better than Bohan and Peter criteria in our cohort. The new criteria are more time consuming and seem to be of limited utility in daily clinical practice.

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FRI0437

### IS EXTENDED AUTO ANTIBODY PROFILING ASSOCIATED WITH THE PREVALENCE OF DISEASE COMPLICATIONS?

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**Background:** Auto antibodies play a prominent role in both classification and disease prognosis of systemic sclerosis (SSc). In several cohorts the association between auto antibodies and prognostic factors has been described. In recent years, new methods of antibody profiling have become available, and have shown an important prognostic role for anti-RNAPolymerase 3 antibodies (anti-RNAP3). However, it is uncertain whether other auto antibodies have associations with complications as well.

**Objectives:** The aim of this study is to determine prevalence of auto antibodies in a well characterised cohort of SSc and to evaluate the associations with complications.

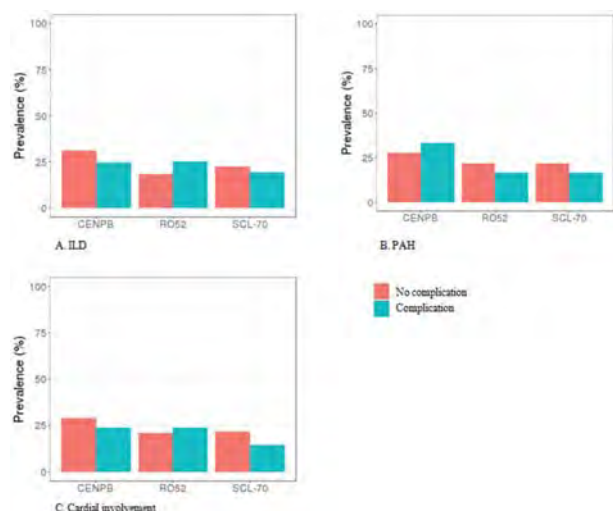
**Methods:** A total of 319 patients from the Nijmegen SSc Cohort were consecutively included in this study. All patients fulfilled the ACR/EULAR 2013 classification criteria for SSc. Patients were subclassified as limited cutaneous SSc (LcSSc), diffuse cutaneous SSc (DcSSc) or SSc overlap syndrome according to Leroy and Medsger. Blood samples were collected at regular outpatient clinic visits and analysed using LIA. (SSc and ENA immunoblot, Euroimmun, Lubeck, Germany). Clinical data was collected prospectively.

**Results:** The Nijmegen cohort comprises mainly of Caucasians. The percentage of male patients and diffuse patients is higher compared to other cohorts<sup>1</sup> (table 1). There is a relative anticentromere antibody (ACA) dominance in our cohort and ACA antibodies are more common in patients with pulmonary arterial hypertension (PAH), which is consistent with previous studies.<sup>1</sup> However, in our cohort we

found a relatively high prevalence of anti-RO52 antibodies in patients with complications (figure 1).

Clinical/laboratory feature/ total	No.	%
Male gender	100	31%
LcSSc	182	57%
DcSSc	102	32%
Overlap	35	11%
PAH	36	11%
ILD	134	42%
Cardiac involvement	21	7%
Renal crisis	3	0.9%
ACA	90	28%
ATA	63	21%
Anti-RNAP3	14	4.4%
Anti-SSA/Ro52	30	9.4%
RP-11	22	6.9%
RNP-SM	22	6.9%
RP-155	21	6.5%
M2-3E	21	6.5%
M2	21	6.5%
PM-75	19	5.9%
PM-100	19	5.9%

**Abstract FRI0437 – Table 1.** Demographic and clinical characteristics



**Abstract FRI0437 – Figure 1.** Prevalence of auto antibodies in SSc with and without complications. Antibodies < 10% prevalent not shown. ILD interstitial lung disease; PAH pulmonary arterial hypertension.

**Conclusions:** The distribution of the main auto-antibodies is comparable to other Caucasian cohorts.<sup>1</sup> Because the prevalence of anti-RNAP3 is relatively low, it is of limited value in our population. In contrast, the prevalence of anti-Ro52 was high in patients with the three major disease complications, but this antibody was also present in a number of patients who did not (yet) have these complications. Previous studies have shown ambiguous results concerning the relevance of this autoantibody.<sup>2</sup> Furthermore, RNP/SM and RNP-70 may be associated with cardiac involvement. To evaluate the prognostic value of anti-Ro52, RNP/SM and RNP-70 in SSc, a large prospective cohort study is necessary.

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FRI0438

#### HOSPITALISATION MORTALITY AND ASSOCIATED RISK FACTORS IN PATIENTS WITH POLYMYOSITIS AND DERMATOMYOSITIS: A RETROSPECTIVE CASE-CONTROL STUDY

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**Background:** Polymyositis and dermatomyositis (PM/DM) are systemic autoimmune diseases with multiple organ involvements that manifest as muscular and cutaneous disorders, interstitial lung disease (ILD) and malignancies. However, information concerning the outcomes and associated factors for PM/DM patients who are hospitalised is limited.

**Objectives:** We retrospectively reviewed the medical records of 982 PM/DM patients admitted to our centre from 2008 to 2014 and performed a case-control analysis to identify possible related risk factors for death among PM/DM patients in China.

**Methods:** We retrospectively reviewed the medical charts of PM/DM patients admitted to a Chinese tertiary referral hospital (Peking Union Medical College Hospital, PUMCH) from 2008 to 2014. The deceased group included 63 patients who had “deceased discharge” status or were confirmed to have died within two weeks of hospital discharge. The demographic data, clinical manifestations, and direct causes of death were analysed retrospectively. Medical records for 126 age- and sex-matched PM/DM patients were selected as controls from 982 inpatients successively admitted to the same centre during the same period. In addition to the comparison of clinical manifestations between the two groups, binary logistic regression was conducted to explore the risk factors related to PM/DM mortality.

**Results:** Over the past 6 years at PUMCH, the in-hospital mortality rate of PM/DM patients was 4.58%. The male gender and the elder patients had a high risk of death ( $p=0.031$  and  $p=0.001$  respectively). The three most frequent causes of death for PM/DM patients were pulmonary infection (35%), ILD exacerbation (21%) or both conditions (25%). Pulmonary infection ( $p<0.001$ , OR=5.63, 95% CI, 2.37–13.36), pneumomediastinum ( $p=0.041$ , OR=11.02, 95% CI, 1.10–110.54), Gottron’s papules ( $p=0.010$ , OR=3.24, 95% CI, 1.32–7.97), and elevated erythrocyte sedimentation rate (ESR) ( $p=0.005$ , OR=9.9, 95% CI 2.0–49.0) were independent risk factors for in-hospital mortality of PM/DM patients.

**Conclusions:** PM/DM patients continue to display high in-hospital mortality. Pulmonary infection is the strongest predictor of poor prognosis in PM/DM patients, followed by pneumomediastinum, Gottron’s papules, and elevated ESR.

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FRI0439

#### THE PROMISING ROLE OF LUNG MRI IN DETECTING SYSTEMIC SCLEROSIS (SSC)-RELATED INTERSTITIAL LUNG DISEASE (ILD)

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**Background:** Interstitial lung disease (ILD) is very frequent and highly disabling in patients with systemic sclerosis (SSc). Magnetic resonance imaging (MRI) is not routinely used for the evaluation of the lung, since MRI generally provides a less detailed view of the pulmonary parenchyma, as well as poorer spatial resolution, compared to the non-invasive gold-standard of high resolution computed tomography (HRCT). Thus, its usefulness in the evaluation of interstitial lung disease (ILD) is limited at present.

**Objectives:** To evaluate MRI signals in different pathological and non-pathological lung areas, and to establish their clinical and instrumental correlations.



**Methods:** Thirty-two SSc patients underwent a cardiac MRI with dedicated lung scanning and chest HRCT on the same day. One-hundred-thirty-five regions of interest (ROIs) were identified, and STIR and T1 sequences were acquired [before (T0) and after 5 (T5), 10 (T10) and 15 (T15) minutes from gadolinium injection]. The ROIs were classified according to HRCT as normal, dependent areas (probably related to blood pooling in supine position) and pathological areas (ground glass ±reticulation on HRCT). Mean STIR and T1 times were also calculated for each patient, and correlated with FVC, DLco, B-lines on lung ultrasound and HRCT semi-quantitative scoring (Scleroderma Lung Study score). Patients were followed-up and lung worsening was defined on the basis of clinical judgement and at least >15% DLco decline.

**Results:** Mean STIR and mean T1 times were significantly different between normal, dependent and pathologic areas ( $p < 0.001$  between groups). Patients' mean STIR showed a significant correlation with DLco ( $R = -0.56$ ,  $p < 0.01$ ), HRCT Scleroderma Lung Study score ( $R = 0.52$ ,  $p < 0.01$ ) and B-lines on lung ultrasound ( $R = 0.63$ ,  $p < 0.01$ ). The mean STIR of the 10 patients who developed a worsening pulmonary involvement had significantly different MRI signal intensity in comparison to the 25 patients without worsening pulmonary involvement ( $125 \pm 46$  vs  $66 \pm 37$  msec,  $p < 0.01$ ).

**Conclusions:** Our data highlight the usefulness of lung MRI in SSc patients to differentiate normal, dependent and pathologic areas, without need for contrast medium administration, and with good correspondence to other functional and imaging parameters. STIR values may have prognostic implications to predict lung worsening. Lung MRI, although still very preliminary, is a promising imaging tool that in the future may integrate HRCT in SSc-related ILD.

**Disclosure of Interest:** None declared

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#### FRI0440 RENAL INVOLVEMENT IN MIXED CONNECTIVE TISSUE DISEASE: A SINGLE CENTRE EXPERIENCE

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**Background:** Kidney injury in mixed connective tissue disease (MCTD) is an uncommon manifestation. Prevalence has been reported to be <4% in some cohorts. The frequency of renal involvement in Hispanic patients with MCTD is not known.

**Objectives:** We aimed to describe the prevalence, clinical characteristics and outcomes of renal involvement in Mexican patients with MCTD.

**Methods:** We conducted a retrospective single-centre study. We included patients with a diagnosis of MCTD according to the Alarcón-Segovia criteria who regularly attended to a referral centre in Mexico City (2003–2017) and we identified those with renal involvement defined as proteinuria >500 mg/d with or without active sediment, creatinine elevation 50% above baseline or development of glomerular filtration rate (GFR) <60 ml/min, with no other known cause. We collected demographics, clinical manifestations, follow-up time, treatment, outcomes and damage (SLICC/ACR-DI), renal function, serological and histological variables.

**Results:** One hundred and thirty one patients with MCTD were followed at our centre. We identified 14 patients with renal involvement with a prevalence of 10.7%. Among those patients, 13 were women (92.8%); mean age at onset of renal involvement was  $44 \pm 8$  years. Most frequent manifestations were Raynaud's phenomenon in 13 (92.8%) patients, arthritis in 12 (85.7%), puffy hands in 12 (85.7%), sclerodactyly in 8 (77.1%), sicca syndrome in 8 (77.1%) and myositis in 7 (50%). Median time elapsed from MCTD diagnosis to renal involvement was 83 (2–365) months. In 3 patients, renal involvement was present at MCTD onset. Seven (50%) patients had other signs of MCTD activity at the time of renal involvement onset. Four (28.5%) patients presented with sub-nephrotic proteinuria, 3 (21.4%) with nephrotic range proteinuria and kidney injury, 2 (14.3%) with sub-nephrotic proteinuria and kidney injury, 2 (14.3%) with nephrotic range proteinuria, 1 only with nephrotic range proteinuria and 1 (7.1%) with end-stage renal disease. Microscopic hematuria was present in 9 (64.3%) patients and leukocyturia in 6 (42.8%). Renal biopsy was performed in 8 (57%) patients; pathological diagnoses were: crescentic and necrotizing glomerulonephritis (GN) (2 patients; one of these patients developed positive ANCA antibodies), GN ISN/RPS 2003 class III+V, 1 GN ISN/RPS 2003 class III+V with thrombotic microangiopathy, 1 GN ISN/RPS 2003 class IV+V and vasculopathy, 1 membranous GN, 1 minimal mesangial GN<sup>1</sup> and chronic tubulointerstitial nephritis with vasculopathy. 1 Ten (71.4%) patients achieved either total or partial remission at a median follow up of 82 (1–367) months. Only one patient required dialysis. At last follow up the median SLICC/ACR-DI was 1.5 (0–4) points. Two patients died.

**Conclusions:** In our cohort of MCTD patients, prevalence of renal involvement was low, although higher than the one reported in other populations. Clinical presentation and pathological diagnoses were diverse. Renal biopsy was helpful, since glomerulonephritis, vasculopathy and overlap with ANCA associated

vasculitis were found in several patients; these options should be considered in the differential diagnoses of MCTD patients with renal involvement.

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**Disclosure of Interest:** None declared

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#### FRI0441 IDIOPATHIC INFLAMMATORY MYOPATHIES: CLINICAL CHARACTERISTICS, SURVIVAL AND POOR PROGNOSTIC FACTORS OF 110 PATIENTS FROM TURKEY

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**Objectives:** In this study, we aimed to assess clinical features, poor prognostic factors and survival analysis of patients with Idiopathic inflammatory myopathy (IIM).

**Methods:** Records of 110 patients with IIM that had at least 6 months of follow-up, fulfilling Bohan and Peter's criteria were analysed for this study. Survival analysis was done by using Kaplan Meier method and multiple "Cox" regression analysis was applied to calculate the effect of multiple factors.

**Results:** Sixty-eight percent of 110 patients was female, the mean age of the patients was 46 years, and the average follow up time was 77.5 months. Diagnosis of these patients was dermatomyositis (DM) in 68%, polymyositis (PM) in 26%, autoimmune necrotizing autoimmune myopathy (NOM), inclusion body myositis (IBM) 6%. The percentage of periungual erythema, arthritis, dysphagia, respiratory muscle involvement and interstitial lung disease (ILD) 56, 22, 24, 32, 11 and 30. Malignancy was identified in 26% of patients. The percentages of malignancies diagnosed at the time of diagnosis, before the diagnosis and during the follow-up were 3.6, 11.8 and 8.2. The most frequent malignancy was breast cancer. Others are carcinoma of gastrointestinal tract, lung, and genitourinary tract. ANA was present in 36% and 12% of patients was positive for anti-Jo-1 antibody. The average daily dose of prednisolone was 7.5 mg, the average usage time was 35.5 months. Causes of death were aspiration pneumonia-sepsis (50%) and malignancy (25%). Significant associations with mortality was found between systemic symptoms, periungual erythema, respiratory muscle involvement, dysphagia, presence of malignancy. Mortality was higher in ANA negative patients ( $p < 0.001$ ), Five and 10 year survival in these patients were 83% and 75%. Five year survival rate in patients with respiratory muscle involvement was 38% and 68% in those with dysphagia. The presence of systemic symptoms, and malignancies were identified as risk factors for mortality in multivariable analysis.

**Conclusions:** ILD and malignancies are frequent in our IIM cohort. Malignancies are mostly detected at diagnosis. The mortality rate was high and the most common cause was infection. 10 year survival rate was 79%. Malignancy, respiratory muscle involvement, dysphagia, negative ANA have a detrimental effect survival in IIM patients.

**Disclosure of Interest:** None declared

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#### FRI0442 LONG-TERM TREATMENT WITH RITUXIMAB IN INTERSTITIAL LUNG DISEASE RELATED TO SYSTEMIC SCLEROSIS: OUR CLINICAL EXPERIENCE

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**Background:** Systemic sclerosis (SSc) is an immune-mediated disorder characterised by abnormal fibrosis and diffuse microangiopathy with skin and internal organ involvement. Interstitial lung disease (ILD) represents one of the most challenging complication of SSc, difficult to manage and correlate with a poor prognosis. Chest Computed Tomography (CT) is the gold standard for detection and evaluation of SSc-ILD by means of semi-quantitative scoring of extent of lung involvement. Some preliminary data suggest that rituximab (RTX) may be usefully employed in the treatment of SSc patients.

**Objectives:** To investigate the role and effect of RTX on ILD in our SSc patients' series.

**Methods:** We retrospectively evaluated a series of 18 SSc patients (M/F 6/12, mean age  $54.6 \pm 17.6$  SD years, mean disease duration  $11.4 \pm 6.5$  SD years, L/D cutaneous subsets 6/12) who received one or more cycles of RTX (4 weekly infusions of 375 mg/m<sup>2</sup>) every 6 months for a total of 1–6 cycles. Lung involvement was studied by means of pulmonary function tests (PFTs) (18/18) and inspiratory

chest CT (10/18) before and after treatment. In particular, we considered PFTs performed 6 months before RTX, at time 0, one year after the first RTX cycle, and at the end of follow-up (13.7±7.3 years). ILD extent score was assessed by the semi-quantitative method proposed by Goh et al (2008).<sup>1</sup>

**Results:** Forced vital capacity (FVC%) significantly reduced during the year before RTX treatment [from 95.2±17.4 to 84.8±16.4; p=0.0017], as well as the diffusing capacity for carbon monoxide (DLCO%) [from 58.1±14.3 to 47.6±12.9; p=0.0002]. Conversely, FVC% and DLCO% stabilised one year after the first RTX cycle (80.8±23 and 47.8±15.7, respectively), and at the end of the follow-up (84.3±24.6 and 54.8±12.3, respectively; p=0.0001). In our cohort, only 7/10 patients had ILD detectable on CT before treatment. At the end of the follow-up we observed that ILD extended in 6/7 cases one patient remained stable, the three subjects without ILD did not developed pulmonary fibrosis.

**Conclusions:** According to PFTs results, our study showed that RTX could stabilise the progression of lung function tests in SSc patients. However, the semi-quantitative visual score identified radiological pulmonary worsening in many patient with stabilised PFTs. Therefore, the correlations between functional and radiological outcomes are so weak that many Authors suggested they should be considered together in SSc-ILD assessment.

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#### FRI0443 DIGITAL ARTERY VOLUME INDEX: THE FIRST OBJECTIVE, AUTOMATED, NON-INVASIVE IMAGING DIAGNOSTIC OF MACROVASCULAR INVOLVEMENT IN SSC

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**Background:** Macrovascular involvement in Systemic Sclerosis (SSc) is caused by proliferation of vascular smooth muscle cells within the intima of arteries (neointimal proliferation). The resulting decrease in arterial volume is responsible for the severity of Raynaud's and for the onset of severe clinical manifestations such as Renal Crisis and Pulmonary Artery Hypertension.

Several RCTs have demonstrated the efficacy of Endothelin Receptor Antagonists (ERAs) in targeting neointimal proliferation, which makes them to date, the only disease modifying agent available in SSc. Nevertheless, the lack of validated early diagnostics means the intention to treat with ERAs remains limited to the diagnosis of end stage clinical manifestations of neointimal proliferation, such as presence of Digital Ulcer (DU) and PAH.

**Objectives:** Here we aimed to determine the proof of concept validity of automated Digital Artery Volume Index (DAVIX) measured by non-contrast Time of Flight (TOF) MRI as an objective diagnostic tool to be used as surrogate outcome measure of neointimal proliferation in SSc.

**Methods:** 10 Healthy Volunteers (HV) and 8 SSc patients were enrolled. Six patients underwent longitudinal assessments at least 12 months apart. MRI scans were performed on a 3T Magnetom Verio (Siemens) and consisted of a VIBE 3D T1 scan and a 2D TOF sequence of 8 min. DAVIX was calculated as the percentage of the ratio of digital artery and the respective finger volumes. The vessels and fingers were manually outlined by an expert radiologist and used as a 'gold standard' (DAVIX-1) and compared to a 2nd independent radiologist assessment (DAVIX-2). An automated segmentation algorithm was developed using threshold based segmentation and region growing (DAVIX-A) and validated against gold standard. Intraclass correlation coefficient (ICC) and absolute agreement were calculated to estimate reliability. Bland-Altman bias and 95% limits of agreement (LoA) were calculated as well.

**Results:** SSc patients and HV had comparable age (44±8 vs 45±8) and gender (F:M=5:2 vs 4:2). 4 fingers were affected by DUs at baseline and two fingers were affected by new DU at follow up. Mean(±SD) DAVIX in HV was 1.21 (±0.39) with no significant difference among individual fingers. Mean DAVIX in SSc patients was 0.37 (±0.18) and 0.32 (±0.39) at baseline and follow-up, respectively (p<0.0001 vs HV for both). The fingers with DU had an average DAVIX of 0.24 (±0.08) vs 0.40 (±0.18) of the fingers without DU (p=0.02). DAVIX changed over time in both directions. In the fingers affected by new DU, DAVIX dropped by 56% (0.161 vs 0.072) and 86% (1.149 vs 0.132), respectively. ICC among two independent readings was 0.90 (95% LoA -0.139, 0.118) with overall r<sup>2</sup>=0.74 (p<0.0001). Automated segmentation showed superior correlation to gold standard with r<sup>2</sup>=0.80 (p<0.0001).

**Conclusions:** This proof of concept study demonstrated validity and sensitivity to change of DAVIX for the automated volumetric assessment of digital arteries, which reflected clinical worsening in patients with new DU. Larger, longitudinal studies are planned to assess DAVIX' predictive value for the onset of DU and its potential use as early diagnostic of neointimal proliferation in SSc.

**Disclosure of Interest:** None declared

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#### FRI0444 PERIOSTIN IN SYSTEMIC SCLEROSIS: SERUM LEVELS AND SKIN EXPRESSION OF A NOVEL POSSIBLE BIOMARKER

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**Background:** Periostin(PN), a matricellular protein, serves as a regulator of wound healing and fibrosis. PN<sup>-/-</sup> mice develop lower degrees of fibrosis when exposed to bleomycin(BLM), suggesting a possible role in the pathogenesis of Systemic Sclerosis(SSc)<sup>1</sup>. PN serum levels are increased in SSc and seem to be associated with skin disease severity<sup>2</sup>.

**Objectives:** To evaluate the role of serum PN as a biomarker of SSc severity, and to determine PN tissue expression in SSc patients.

**Methods:** PN serum levels were assessed by ELISA in 48 patients: 3 primary Raynaud's, 12 early SSc, 11 SSc without organ involvement, 22 SSc with organ involvement. All SSc patients met 2013 ACR/EULAR criteria. PN serum levels were evaluated in 28 sex-/age-matched healthy-controls(HCs). Data regarding disease subtypes and organ involvement were correlated. PN skin expression was determined by immunohistochemistry on paired involved and uninvolved skin biopsy samples in 10 patients(4 lcSSc and 6 dcSSc) in combination with a-SMA, CD68, CD3, CD4, CD8, CD163, CD20 and CD131.

**Results:** PN serum levels were higher in SSc patients compared to HCs(32.7±8.0 vs 27.7±7.3 ng/ml, p<0.001). Its levels were comparable among different groups. No differences in PN serum levels were detected when comparing disease subtypes, disease duration, presence and extent of organ involvement, autoantibodies profile and current or previous treatment. Higher PN levels were found in SSc patients with active pattern at nailfold videocapillaroscopy and a history of digital ulcers(p<0.02). PN serum levels did not correlate with skin or lung disease extent. Skin samples from involved SSc skin showed high PN expression in the upper dermis and in the fibrotic area of the lower dermis(more evident in dcSSc), suggesting a role in skin fibrosis. In all SSc involved skin, PN was expressed in areas where ongoing fibroproliferation and macrophage/T lymphocytic infiltration occurred, indirectly suggesting a pathogenic role in inflammation driven-fibrosis. Interestingly, an identical PN immunohistochemical expression was evident in uninvolved dcSSc skin, but not in lcSSc skin.

**Conclusions:** In our cohort PN serum levels are elevated in SSc patients but they do not correlate with disease features. Its postulated role as a severity biomarker needs to be further elucidated. The different immunohistochemical expression of PN in uninvolved skin from dcSSc and lcSSc patients suggests a possible pathogenic role in the progressive inflammation-driven fibrosis that characterise diffuse cutaneous involvement.

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#### FRI0445 A RANDOMISED CONTROLLED TRIAL TO COMPARE THE EFFICACY OF ORAL MYCOPHENOLATE MOFETIL WITH PLACEBO IN PATIENTS WITH SYSTEMIC SCLEROSIS RELATED EARLY INTERSTITIAL LUNG DISEASE

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**Background:** Previous studies showed benefit of immunosuppressants in moderate to severe ILD in systemic sclerosis (SSc).<sup>1,2</sup> Initiation of immunosuppression early in the course of SSc-ILD might help in halting disease process and improve long term morbidity and mortality.

**Objectives:** Aim of the study was to determine efficacy and safety of mycophenolate mofetil (MMF) in treating early and mild SSc-ILD (ILD on HRCT, FVC ≥70%

predicted). Primary outcome was to compare the change in FVC after 6 months of therapy with MMF or placebo. Secondary outcomes were change in SF-36v2, Mahler dyspnoea index (MDI) and adverse events profile of MMF and placebo.

**Methods:** This was a double-blind, randomised, placebo-controlled trial conducted at a tertiary care centre in north India. SSc-ILD patients with FVC  $\geq 70\%$  and aged  $>18$  years were randomised to receive either MMF (up to 2 g/day) or placebo for 6 months. FVC, DLCO, MRSS, SF36v2, MDI and 6 min walk distance (6MWD) were noted at baseline and 6 months. Outcome was categorised into improved/stabilised (any increase in FVC or fall in FVC  $<10\%$  from baseline) and worsened (fall in FVC  $\geq 10\%$  from baseline). Trial was approved by the institute ethics committee and was registered at ClinicalTrials.gov (NCT02896205).

**Results:** Forty-one subjects were included in the study (20 MMF and 21 placebo). Mean age was  $40.3 \pm 10.1$  years and 95.1% were females. Median duration of illness was 5 years (IQR: 3–9). Mean baseline FVC was  $81.71\% \pm 9.35\%$ , DLCO was  $50.36\% \pm 14.24\%$ , MDI was  $7.68 \pm 2.72$ , 6MWD was  $423.61 \pm 61.64$  m, MRSS was  $17.07 \pm 8.36$ . Fifteen subjects in MMF arm and 19 in placebo arm completed 6 months study duration. Mean change in FVC was  $-1.79 \pm 7.32\%$  in MMF arm and  $1.34\% \pm 4.47\%$  in placebo arm. Mean absolute difference in FVC change from baseline to 6 months between the two arms was 3.13% (95% CI,  $-1.02$  to  $7.28$ ;  $p=0.131$ ). In mITT analysis, 15 subjects improved/stabilised and 5 subjects worsened in MMF arm compared to 19 and 2 subjects respectively in placebo arm. SF36v2 scores showed significant improvement in both the groups. No significant difference was noted between the two groups in mean change in focal score of MDI (3.33 vs 2.79;  $p=0.638$ ), DLCO (2.46% vs 2.31%;  $p=0.412$ ), 6MWD (2.8 m vs 12.11 m;  $p=0.522$ ) and FVC among subjects with Scl-70 positivity ( $-2.19\%$  vs  $1.51\%$ ;  $p=0.184$ ). The MRSS decreased by a mean of 4.73 points in MMF arm compared to 1.53 points in placebo arm ( $p=0.042$ ). MMF was well tolerated and rates of diarrhoea and infections were similar to that with placebo. Three subjects on MMF and 1 on placebo discontinued drugs.

**Conclusions:** In this small study, MMF for 6 months was not effective in stabilising the lung disease in early and mild SSc-ILD but was effective in controlling skin disease and was well tolerated.

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**Disclosure of Interest:** None declared

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#### FRI0446 INITIAL PREDICTORS FOR MORTALITY IN PATIENTS WITH CANCER-ASSOCIATED MYOSITIS: A MULTICENTER RETROSPECTIVE COHORT IN JAPAN

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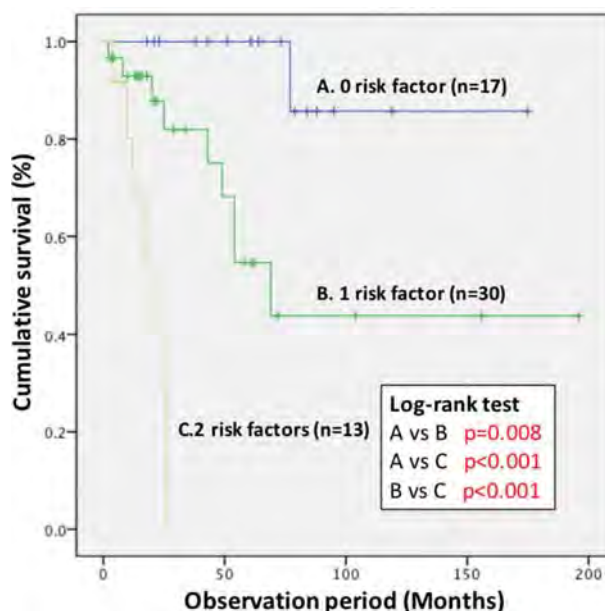
**Background:** Concomitant malignancy is one of the prognostic factors in patients with myositis,<sup>1</sup> but clinical parameters for mortality still remain unknown in patients with cancer-associated myositis (CAM).

**Objectives:** Initial predictors for mortality were examined using a multicenter cohort of CAM patients.

**Methods:** This retrospective study enrolled 67 consecutive patients diagnosed as having CAM in 3 referral hospitals between 1995 and 2017. Clinical data at diagnosis of myositis as well as treatment regimens and outcomes of myositis and malignancy were collected by review of medical charts. Myositis-specific autoantibodies (MSAs) were comprehensively detected using RNA immunoprecipitation (IP), enzyme-linked immunosorbent assay, and IP-immunoblotting. We initially conducted a univariate analysis to select variables that were different between survivors and dead cases. In multivariate analysis, the Cox proportional hazard model with backward selection method ( $p > 0.20$ ) was employed to identify factors independently associated with mortality. Explanatory variables were chosen

based on the following three models. The Model 1 included age at diagnosis of myositis, gender and candidate variables ( $p < 0.1$ ) selected by the univariate analysis. The Model 2 included age, gender, prognostic factors previously reported in myositis, such as dermatomyositis, dysphasia, interstitial lung disease (ILD), anti-ARS, and anti-MDA5, and malignancy type and staging, as explanatory variables. In the Model 3, age, gender, disease duration before diagnosis of myositis, period between diagnosis of myositis and tumour, myositis classification, MSAs, dysphasia, ILD, myositis disease activity after treatment, and malignancy type and staging were used as explanatory variables. Cumulative survivals calculated using the Kaplan-Meier method were compared between the patients with and without risk factors.

**Results:** The median age at diagnosis of myositis was 63 years, and 62% were female. MSAs were detected in 47 patients: anti-TIF1- $\gamma$  in 27, anti-ARS in 6, anti-MDA5 in 5, anti-Mi-2 in 3, anti-NXP2 in 3, anti-SAE in 2, and anti-SRP in 1. During the median observation period of 2 years, 19 (28%) of 67 CAM patients were dead due to tumour in 16, ILD in 1, and an unknown cause in 2. The univariate analysis identified significant poor prognostic factors ( $p < 0.1$ ) as follows: male ( $p=0.04$ ), elder age at diagnosis of myositis ( $p=0.08$ ), longer period between diagnosis of myositis and tumour ( $p=0.07$ ), absence of breast cancer ( $p=0.001$ ), malignancy stage III/IV ( $p=0.006$ ). In multivariate analysis, male (HR 8.1, 95% CI 2.6–25.2;  $p < 0.001$ ) and malignancy stage III/IV (HR 12.1, 95% CI 3.3–44.9;  $p < 0.001$ ) were identified as independent risk factors for mortality in the Model 1, and identical variables were identified in the Models 2 and 3. Cumulative survival rates of patients with 0, 1, or 2 risk factors were 100%, 93%, and 69% at 1 year, and 100%, 82%, and 0% at 3 years, respectively. Cumulative survival rates were statistically different between the groups stratified by the number of risk factors (figure 1).



**Abstract FRI0446 – Figure 1.** Cumulative survival rates of patients with CAM with 0, 1, or 2 or risk factors.

**Conclusions:** Male and progression of malignancy at diagnosis of myositis were identified as predictors of survivals in CAM patients.

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- [1] Callen JP. Dermatomyositis. *Lancet* 2000;355:53–7.

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FRI0447

### WORLDWIDE EXPERT AGREEMENT ON UPDATED EULAR/EUSTAR RECOMMENDATIONS FOR THE TREATMENT OF SYSTEMIC SCLEROSIS

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**Background:** In 2017, updated EULAR/EUSTAR recommendations for treatment of Systemic sclerosis (SSc) were published.<sup>1</sup> Implementation in clinical practice of these recommendations might be dependent on agreement and local drug availability.

**Objectives:** To evaluate worldwide agreement of the updated recommendations for treatment of SSc among SSc experts. To determine factors that might influence agreement.

**Methods:** An online survey was set out (June – September 2017), containing the 17 EULAR/EUSTAR updated recommendations. Levels of agreement were determined for each item on a 10-point scale (0=not at all; 10=completely agree). Local drug availability was assessed (yes/no). An e-mail containing a web link to the survey was sent out to international SSc-networks (EUSTAR, Scleroderma Clinical Trials Consortium, Australian Scleroderma Interest Groups, International Systemic Sclerosis Inception Cohort) and to 54 additional SSc-experts representing South-America and Asia. Levels of agreement were compared between subgroups stratified for EUSTAR membership, geographical area, drug availability, and years of experience.

**Results:** In total 269 responders participated, of whom n=209 completed each single item. The majority are rheumatologists (n=200, 83%), currently working in Europe (n=185; 71%); 65% (n=156) are EUSTAR member, and have >10 years of experience in the SSc field (n=150; 63%). Other geographical areas are also represented (Africa n=2, 1%; Asia n=18,7%; Australia n=13,5%; North-America n=27,10%; South-America n=17,6%). Mean level of agreement was high (8.0; standard deviation [SD, 2.5], with top-3 highest mean agreement for ACE-inhibitors for scleroderma renal crisis (9.2 [2.1]), blood pressure control in case of corticosteroids (9.0 [2.2]) and treatment with protonpump inhibitors to prevent reflux complications (9.0 [2.2]). Top 3 of lowest mean agreement included fluoxetine for Raynauds phenomenon (RP) (4.6 [2.8]), hematopoietic stem cell transplantation (HSCT) for severe SSc (7.1 [2.9]) and methotrexate for skin involvement in early diffuse SSc (7.4 [2.8]). When comparing Europe to other regions agreement differed significantly (p<0.05) for the following recommendations: iloprost for RP, iloprost and bosentan for digital ulcers, methotrexate for early diffuse SSc, cyclophosphamide for SSc-related lung disease, and HSCT for severe SSc. Comparison of agreement between responders stratified for EUSTAR membership (yes/no), years of clinical experience (<or>10 years) and local availability of the drug/treatment option (yes/no) showed that in case of iloprost, bosentan and HSCT availability of drug/treatment option contributed to differences in agreement. Neither EUSTAR membership nor years of experience could explain these differences.

**Conclusions:** In general, worldwide agreement on recently updated recommendations for treatment of SSc is high. Differences in agreement are partially explained by geographical area and local drug availability. Future evaluations should focus on implementation of published recommendations and take drug availability into account to further improve guideline-development.

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[1] Ann Rheum Dis. 2017 Aug;76(8):1327.

**Disclosure of Interest:** None declared

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FRI0448

### MDA5 ANTIBODY POSITIVE CLINICAL AMYOPATHIC DERMATOMYOSITIS (CADM): A SINGLE TERTIARY CENTRE CASE SERIES OF 13 PATIENTS

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**Background:** Positive anti-melanoma differentiation-associated gene 5 (MDA5) antibody has been reported in 50%–73% of patients with clinical amyopathic dermatomyositis (CADM)<sup>1</sup>. About half of MDA5 +CADM patients die of rapid

progressive interstitial lung disease (RP-ILD), defined as worsening dyspnea within 1 month that required high-flow oxygen therapy or ventilator support in previously stable patients.

**Objectives:** This descriptive study aims to systematically characterise the clinical features, treatment and outcome of 13 cases of MDA5 +CADM patients at a single referral centre.

**Methods:** Myositis antibody testing became available at Vancouver Coastal Health, Canada since 2014. We retrospectively reviewed clinical presentations, laboratories, imaging studies, treatment and outcome of patients with MDA5 antibody. The data is presented descriptively.

**Results:** Total 13 cases (4 male and 9 female) of MDA5 +CADM were identified (2014–2017). Mean age was 49.9±11.5. Ten were Asian descent (8 Chinese, 1 Philippine, and 1 Indo-Mauritian) and 3 Caucasians. All 13 patients had typical DM rash (heliotope, Gottron's, mechanic's hands, periungual erythema). Cutaneous ulcers over the extensor surfaces of joints were seen in 7/13 and palmar papules in 4/13, both of which were characteristic for MDA5 +CADM. Only 3/13 patients had CK elevation with little muscle weakness; all others had normal CK and no detectable weakness.

ILD was present in all 13 patients. 7/13 (53.8%) patients had RP-ILD and 4/13 (30.7%) died within 3 months of onset of worsening dyspnea, despite steroid, cyclophosphamide, Rituximab, cyclosporine and IVIG; 3 survived after receiving lung transplant. 6/13 (46.2%) patients had stable ILD and are still alive. 5/7 patients with RP-ILD (71.4%) had coexisting Ro52 antibody whereas only 1/6 patients with stable ILD (16.7%) had Ro52. Of the 6 patients with stable ILD, one had worsening cutaneous ulceration and ILD that required IV cyclophosphamide; one had refractory dermatitis and recurrent pneumomediastinum eventually stabilised on rituximab; one responded to tacrolimus with improving respiratory symptoms; one had panniculitis refractory to IVIg, hydroxychloroquine, azathioprine and tofacitinib, and ultimately responded to IV cyclophosphamide; one had mild ILD but severe cutaneous disease who eventually agreed to rituximab, and the last patient went with traditional Chinese medicine and lost follow up. None had underlying malignancy.

**Conclusions:** In this case series of 13 patients with MDA5 +CADM, 54% were Chinese, a finding similar to previous reported higher incidence in Asians. It is important to recognise the characteristic cutaneous and pulmonary features of this entity early on as mortality is high. Refractory panniculitis can be found in MDA5 +CADM. All patients had ILD with 54% RP-ILD and 31% mortality within 3 months. Coexisting Ro52 may be predictive of worse prognosis. Early intensive immunosuppression is instrumental for refractory cutaneous manifestation and/or progressive ILD. As lung transplantation became more available, three patients with RP-ILD in this series received lung transplant successfully and they were maintained on mycophenolate and tacrolimus after transplant.

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**Disclosure of Interest:** None declared

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FRI0449

### OVERLAP MYOSITIS AND PRIMARY MYOSITIS: CLINICAL OUTCOMES AND PROGNOSIS

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**Background:** Among the subtypes of idiopathic inflammatory myopathy (IIM), it has been recognised that primary polymyositis (PM) and primary dermatomyositis

(DM) have a worse prognosis than overlap syndrome (OM). However, the benign course of OM has not been confirmed in other studies. The identification of specific characteristics that could allow a correct classification may be important for its prognosis.

**Objectives:** To analyse clinical characteristics and survival of patients diagnosed with OM, and to compare if there are differences with other IIM subgroups in a multicentric cohort.

**Methods:** Retrospective, multicentric longitudinal observational study of a cohort of patients followed between January 1980 and December 2014, with a diagnosis of IIM. The patients were divided into 2 groups: OM and primary idiopathic inflammatory myositis (PIIM), which included PM and DM. Patients classified as OM had to meet IIM criteria and criteria for rheumatoid arthritis (RA), systemic sclerosis (SSc), systemic lupus erythematosus (SLE), mixed connective tissue disease (MCTD) or primary Sjögren's syndrome (SS).

**Results:** The present study included a total of 348 patients (98 OM, 250 PIIM). The connective tissue diseases associated with OM were: MCTD in 32 (32.7%), SSc in 29 (29.6%), SLE in 21 (21.4%), RA in 8 (8.2%) and SS in 8 (8.2%). Patients with OM showed remarkable differences compared to PIIM. In general, OM exhibited more extramuscular involvement and more complications, with more serious infections (41% vs. 24%,  $p < 0.001$ ) and higher mortality (31% vs. 20%,  $p = 0.043$ ). In the multivariate study of mortality prognostic factors, the overlap syndrome contributed significantly to a higher mortality (OR 5.56 (95%CI 2.32–13.23);  $p < 0.0001$ ).

**Conclusions:** In the REMICAM registry of 348 inflammatory myopathies, 98 cases of myositis with overlap syndrome have been included, presenting with more extramuscular complications, more severe infections and higher mortality than other myopathies. It would be important to identify these patients at the onset of the disease, in order to closely monitor for development of possible complications.

**Disclosure of Interest:** None declared

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FRI0450

#### ASSOCIATIONS OF ALTERATIONS OF PERIPHERAL REGULATORY T AND TH17 ABSOLUTE CELL NUMBERS WITH CLINICAL FEATURES IN PATIENTS WITH SYSTEMIC SCLEROSIS

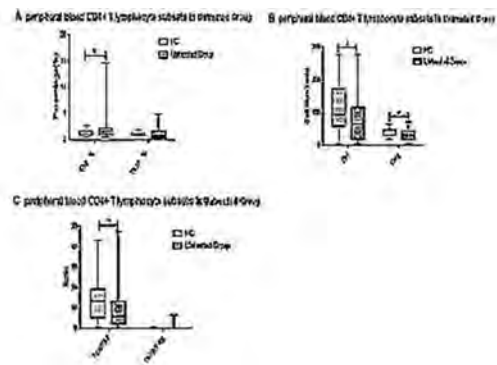
L. Shang<sup>1</sup>, J. Luo<sup>1</sup>, J. Yuan<sup>1</sup>, Q. Li<sup>1</sup>, X. Liu<sup>1</sup>, C. Gao<sup>2</sup>, X. Li<sup>1</sup>, H. Gao<sup>1</sup>.

<sup>1</sup>Rheumatology, The Second Hospital of Shanxi Medical University, Taiyuan, China; <sup>2</sup>Pathology, Brigham and Women's Hospital, Boston, USA

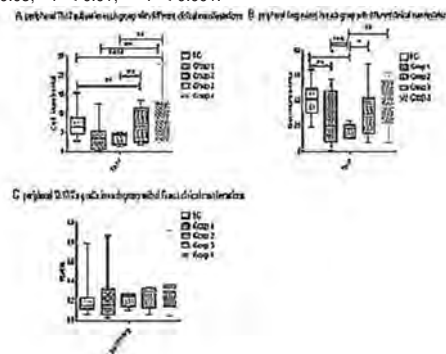
**Background:** Systemic sclerosis (SSc) is a chronic inflammatory disease with complex pathogenesis. The role of regulatory T cells (Tregs) in the development of SSc has started being studied during the last decade with new aspects being disclosed continuously. Although there is a general agreement in the medical literature regarding the decreased functional capacity of circulating Tregs in SSc, the alteration of absolute number of Treg and Th17 cells as well as their associations with clinical characteristics of SSc are still unclear.

**Objectives:** The aim of the present study was to explore the relationship between absolute reduction of peripheral CD4 + regulatory T and Th17 cell subset and clinical characteristics in SSc patients.

**Methods:** The peripheral CD4 + T subsets from 54 patients with SSc and 30 healthy control subjects were analysed. The patients were divided into the untreated group (n=29) and treated group (n=25). The patients were also divided into group 1 (n=9) for the prominent pulmonary lesions, group 2 (n=5) for prominent esophageal involvement, group 3 (n=8) for both lung lesions and esophageal involvement, and group 4 (n=10) who had fingers swelling, sclerosis, ulceration prominent. Directly using the results from flow cytometry combined with internal standard beads, absolute number of peripheral Th17 and Treg cells from the subjects in each group were calculated.



**Abstract FRI0450 – Figure 1.** Comparison of the levels of CD4+T lymphocyte subgroups among different groups. (A) The percentage of Th2 cells were significantly increased in untreated group compared with healthy controls. (B) The number of CD4+CD25+FOXP3+Treg cells decreased in patients with prominent pulmonary lesions. (C) The ratio of Th1/Th2 cells was not found to be significantly decreased in each group. \* $P < 0.05$ ; \*\* $P < 0.01$ ; \*\*\* $P < 0.001$ .



**Abstract FRI0450 – Figure 2.** Comparison of absolute number of Treg and Th17 cells in each group with different clinical manifestations. (A) The number of Th17 cells were significantly increased in group 4 compared with group 1 and group 2. (B) The number of CD4+CD25+FOXP3+Treg cells decreased in patients with SSc. (C) The ratio of Th17/Treg cells was no statistically significant different in each group. \* $P < 0.1$ ; \*\* $P < 0.01$ ; \*\*\* $P < 0.01$ .

**Results:** Although there were some changes among CD4 + T cell subsets in peripheral blood from these SSc patients, the major alteration was the reductions of Treg cell absolute number. Compared with the normal controls, the number of CD4+CD25+FOXP3+Treg cells were significantly decreased in untreated group ( $p = 0.029$ ), in group 1 ( $p = 0.014$ ) and in group 2 ( $p = 0.073$ ) as compared with healthy controls. Interestingly, Tregs in group 2 were significantly lower than those in group 1 ( $p = 0.006$ ), in group 3 ( $p = 0.098$ ) and in group 4 ( $p = 0.034$ ). In addition, the number of Th17 cells were significantly higher in group 3 ( $p = 0.003$ ) and 4 ( $p < 0.001$ ) when compared with the normal controls, as well as in group 4 was significantly higher than that in group 1 ( $p = 0.044$ ), in group 2 ( $p = 0.016$ ), moreover, the number of Th17 cells in group 3 was significantly higher than that in group 2 ( $p = 0.017$ ).

**Conclusions:** The absolute number of peripheral CD4 + CD25+FOXP3+Treg cells decreased in untreated patients, indicating that this reduction arising from the disease itself. Our findings suggest that the severity of clinical manifestations in patients with SSc is related to the absolute decrease of peripheral Treg cells. Although there was no statistically significant different, absolute number of the Treg cells trended to decrease in patients who had more severe clinical manifestations. With the involvement of vital organs, the absolute number of Treg cells decreased more significantly. Moreover, in patients with relatively mild clinical manifestations, the increase in the absolute number of Th17 cells is even more obvious, suggesting that Th17 also plays an important role in early and intermediate stages.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.5394

FRI0451

### CONTINUOUS PRESENCE OF IGM ANTI-TOPOISOMERASE I ANTIBODIES INDICATES AN ONGOING IMMUNE RESPONSE IN SYSTEMIC SCLEROSIS

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**Background:** Small case-series of anti-topoisomerase I antibodies (ATA) in Systemic Sclerosis (SSc) show a highly varying immune response over time. IgA and IgG levels were shown to correlate with skin scores. One small study showed that increasing IgG levels can precede increasing skin scores. Thus far, detailed analysis of ATA characteristics with disease features in larger cohorts have not been performed.

**Objectives:** By taking advantage of our well described SSc cohort with annual follow-up data, we aimed to evaluate whether clinical heterogeneity within ATA +patients can be explained by ATA characteristics.

**Methods:** ATA IgG, IgM and IgA levels were assessed in consecutive serum samples of baseline ATA-IgG +patients from the Leiden SSc cohort. Disease progression during the first year of follow-up was defined as increase of modified Rodnan Skin Score (mRSS) with  $\geq 5$  points, progression of pulmonary involvement ( $<10\%$  of predicted forced vital capacity [FVC] or diffusion capacity of the lung [DLCO]), development of digital ulcers, renal crisis, pulmonary arterial hypertension and/or mortality. Here, we present data on the association between the presence of ATA-IgM and disease progression.

**Results:** In total 344 samples of 102 ATA +patients were measured. Baseline and follow-up samples were available from 70 patients. Median follow-up was 3.7 years (range 0.9–7.4 years). At baseline 42/70 patients were positive for ATA IgM and 69/70 patients for ATA IgA (table 1). Strikingly, while clinical characteristics did not differ, mean ATA-IgM at baseline was higher in disease progressors (table 2). The possible relevance of an ATA-IgM response for disease progression was confirmed by the observation that of those patients positive for ATA-IgM both at baseline and at FU, 59% of cases showed disease progression, as compared to 15% of patients negative for ATA IgM at both time points ( $p=0.02$ ).

**Abstract FRI0451 – Table 1.** Changes in presence and levels of ATA isotypes in paired serum samples

	ATA isotype status at baseline/ follow-up				median ATA level (aU/mL[IQR])		p
	+/+	±	-/-	-/+	baseline	follow-up	
IgG	66	4	-	-	454 (193–876)	283 (79–647)	<0.01
IgM	29	13	25	3	627 (271–2081)	348 (167–1315)	0.06
IgA	65	4	1	0	2832 (812–8069)	2210 (645–7593)	0.01

**Abstract FRI0451 – Table 2.** Baseline characteristics of SSc patients with and without disease progression during the first year of follow-up

	progressors (n=25)	non-progressors (n=36)	p
female, n(%)	18 (72)	28 (78)	0.61
age, mean[yr.]±SD	55±16	50±15	0.15
time since onset first non-Raynaud symptom, median [yr.] (IQR)	4 (1–8)	3 (1–12)	0.75
mRSS, median (IQR)	4 (3–8)	5 (2–13)	0.94
DLCO, mean [% of predicted]±SD	69 (56–81)	63 (49–75)	0.17
ATA IgG level, median [aU/mL](IQR)	636 (301–1127)	312 (111–900)	0.09
ATA IgM level, median [aU/mL](IQR)	933 (533–3122)	447 (215–1293)	0.03
ATA IgA level, median [aU/mL](IQR)	5217 (2003–14187)	2202 (513–6240)	0.07

**Conclusions:** The presence of ATA-IgM at baseline and at follow-up and its association with disease course suggests that the ATA response in SSc patients is an ongoing process that possibly explains the heterogenic disease course of ATA +patients over time.

**Disclosure of Interest:** None declared

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FRI0452

### NAILFOLD CAPILLAROSCOPY IN ANTISYNTHEASE SYNDROME (NASCAR): RESULTS OF A MULTICENTER, INTERNATIONAL STUDY OF THE AMERICAN AND EUROPEAN NETWORK OF ANTISYNTHEASE SYNDROME (AENEAS)

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**Background:** Antisynthetase syndrome (ASSD) is an autoimmune disease characterised by the clinical triad arthritis, myositis, and interstitial lung disease (ILD). Despite Raynaud's phenomenon (RP) is another typical feature of ASSD, nailfold videocapillaroscopy (NVC) assessment of these patients has been only sporadically described, without the elucidating data for clinicians.

**Objectives:** To describe NVC features of ASSD patients and to investigate possible correlations with clinical and serological features of the disease.

**Methods:** We retrospectively analysed NVC images of 190 ASSD patients (females/males 3.76, mean age 49.7±12.8 years, mean disease duration 51.2±71.4 months, 133 anti-Jo-1 and 57 non-anti-Jo-1 positive patients). For each patient, we examined number of capillaries, giant capillaries, micro-haemorrhages, avascular areas, ramified capillaries, and the presence of scleroderma (SSc) patterns. Finally, we correlated NVC features with clinical and serological findings of ASSD patients.

**Results:** NVC abnormalities were observed in 62.1% of ASSD patients compared with 29.3% of a group of 75 patients with primary Raynaud's phenomenon ( $p<0.001$ ). A SSc-like pattern was detected in 67 (35.3%) patients and it was associated with anti-Jo-1 antibodies ( $p=0.002$ ) and also with a longer disease duration ( $p=0.004$ ). Interestingly, there was no significant correlation between the presence of SSc-like pattern and RP, and only 47% of patients with SSc-like pattern had RP.

**Conclusions:** NVC abnormalities are commonly observed in ASSD, independently to the occurrence of RP. The presence of a SSc-like pattern should let to identify a more defined ASSD subtype and prospective studies could confirm the association with clinical and serological features of ASSD.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.2859



FRI0453

### HOSPITALISATION AND SURVIVAL ANALYSIS IN SYSTEMIC SCLEROSIS PATIENTS WITH CONCOMITANT OR ISOLATED PULMONARY HYPERTENSION AND INTERSTITIAL LUNG DISEASE IN THE MULTIETHNIC SCLERODERMA COHORT SINGAPORE

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**Background:** Concomitant pulmonary hypertension and interstitial lung disease in systemic sclerosis (SSc-PH-ILD) represents a distinct subpopulation of SSc with poorer prognosis in Western studies. In Asian patients, characterisation of SSc-PH-ILD is still lacking.

**Objectives:** To analyse hospital admissions, survival and prognostic markers among SSc patients with PH, ILD or concomitant PH-ILD in the Scleroderma Cohort Singapore.

**Methods:** In this study involving 3 tertiary Rheumatology institutions Jan 2008 to , Oct 2016 SSc patients with significant pulmonary involvement were included. ILD was based on high resolution computed tomography and predicted FVC <70%. PH was based on either echocardiographic systolic pulmonary arterial pressure (sPAP)  $\geq$ 50 mmHg, or right heart catheterization (RHC) findings of mean PAP  $\geq$ 25 mmHg. Hospitalisation rates and survival of SSc patients with PH, ILD or PH-ILD were compared. Risk factors of poor outcomes were identified by multivariate stepwise Cox regression analysis.

**Results:** Among 490 patients, 92 had ILD, 50 PH and 43 PH-ILD (table 1). Of 93 patients with PH or PH-ILD, 56 were based on echocardiography and 37 on RHC. The 5 year survival was 79%, 87% and 90% in PH, PH-ILD and ILD subgroup, respectively (figure 1). In multivariable analysis, PH was significantly associated with 2.8-fold increased risk of death. Male gender, malabsorption, digital ulcerations and renal crisis were also significantly associated with mortality (table 2). No significant difference in hospital admissions/year among different subgroups. Increased hospital admissions were associated with renal crisis, right heart failure and use of PH medications.

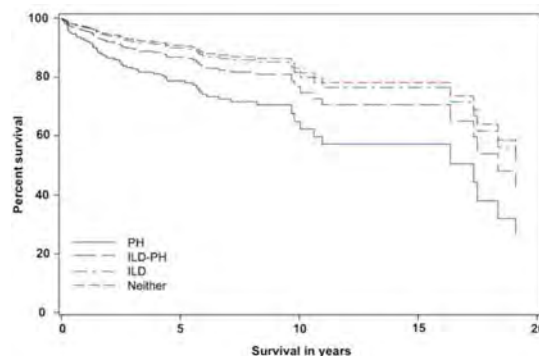
**Abstract FRI0453 – Table 1.** Clinical characteristics

	PH (n=50)	ILD (n=92)	PH-ILD (n=43)	No PH/ILD (n=305)
Female, n	44	76	38	270
Follow up duration (months)	53.46	101.5	88.71 $\pm$ 65.53	64.66 $\pm$ 36.27
$\pm$ SD	$\pm$ 55.76	$\pm$ 80.04		
Age at SSc diagnosis (years)	51.08	46.87	53.84 $\pm$ 15.17	46.44 $\pm$ 14.59
$\pm$ SD	$\pm$ 16.44	$\pm$ 12.4		
Duration of SSc at entry (years)	5.85 $\pm$ 6.95	6.93 $\pm$ 7.45	6.14 $\pm$ 7.98	5.20 $\pm$ 8.24
$\pm$ SD				
Dc-SSc, n	13	45	11	100
PH specific treatments*, n	28	N/A	26	N/A
Immunosuppressants**, n	25	64	27	176

\*Prostacyclin, phosphodiesterase type 5 inhibitors, endothelin receptor antagonist; \*\*Methotrexate, cyclophosphamide, mycophenolate mofetil.

**Abstract FRI0453 – Table 2.** Survival analysis

	Hazard Ratio (95% CI)	P Value
Male gender	2.85 (1.53–5.33)	0.0010
Malabsorption	2.89 (1.67–5.01)	0.0002
Renal crisis	2.00 (1.00–3.99)	0.0490
Digital ulcerations	2.06 (1.21–3.50)	0.0076



**Abstract FRI0453 – Figure 1.** Adjusted survival curve comparing survival of SSc patients with PH, ILD, and concomitant PH-ILD. X-axis shows years of survival from diagnosis of PH or ILD.

**Conclusions:** Compared to those with ILD or PH-ILD, SSc-PH patients had increased mortality, but not hospitalisation rates. This could be due to small sample size or short follow up duration. We identified risk factors associated with worse outcomes in SSc patients with significant pulmonary involvement.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrhumdis-2018-eular.3185

FRI0454

### ARTERIAL STIFFNESS OF THE FOREARM IS ASSOCIATED WITH NAIL-FOLD CAPILLARY COUNT IN SSC: A NOVEL MARKER OF EARLY VASCULOPATHY?

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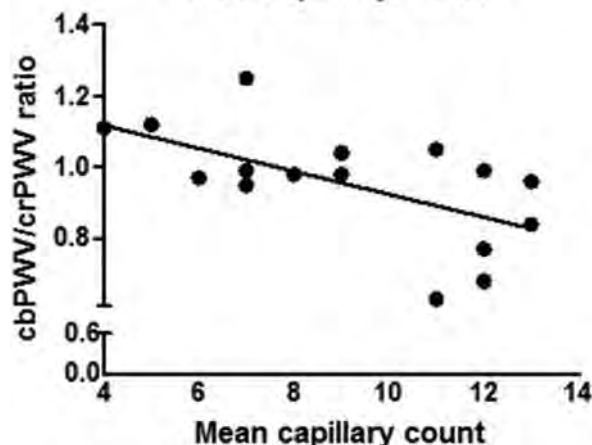
**Background:** Microvascular disease, characterised by rarefaction of capillaries, is the hallmark of systemic sclerosis. Remarkably, obliteration of the ulnar and radial artery is regularly observed, implicating involvement of the larger forearm arteries. Pulse wave velocity (PWV) is a widely accepted non-invasive measure for arterial stiffness and may serve as an early biomarker of forearm artery involvement, before the occurrence of irreversible arterial obliteration.

**Objectives:** The aim of the current study was to investigate arterial stiffness of the aorta and of the upper extremities in SSc patients compared to healthy controls and to correlate these findings with nail-fold capillary count, skin involvement, and extent of disease.

**Methods:** In total, 19 SSc patients (median age 51 years, 68% female) and 19 age and gender matched healthy controls (median age 53 years, 68% female) were included. Patients characteristics were obtained and blood was drawn. Measurements of arterial stiffness were carried out by using the SphygmoCor System (AtCor Medical, Sydney, Australia) and pressure waveforms were measured at four sites, i.e. carotid, femoral, brachial, and radial. Aortic PWV was defined as carotid-femoral (cf) PWV. Upper extremity PWV was measured as carotid-brachial (cb) and carotid-radial (cr) PWV, and the ratio between cbPWV/crPWV was used as an indication of the relative change in PWV in the forearm. Capillary count was defined as the mean capillary count per 3 mm of 8 fingers. Skin involvement was assessed by the modified rodnan skin score. The number of ACR/EULAR 2013 criteria points was used as a surrogate for extent of disease.

**Results:** Upper extremity PWV measures were significantly higher compared to aortic PWV in patients and in controls (SSc:  $p < 0.001$ ; HC:  $p = 0.03$ ), but did not significantly differ between both groups (table 1). CbPWV/crPWV ratio correlated strongly with capillary count ( $r = -0.55$ ,  $p = 0.022$ , figure 1) in SSc patients with a borderline significant trend in regards to its relation with the extent of disease ( $r = 0.48$ ,  $p = 0.053$ ) and skin involvement ( $r = 0.41$ ,  $p = 0.10$ ).

### Correlation between cbPWW/crPWW and Capillary count



**Conclusions:** Our findings demonstrate that arterial stiffness of the forearm has a relationship with nailfold capillary count and tends to be associated with the extent of disease in patients with SSc. These preliminary data may suggest that vascular damage may concomitantly occur in both capillaries as well as larger arteries of the forearm, which may potentially serve as a novel tool for assessing of early vascular involvement in SSc.

**Disclosure of Interest:** None declared

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#### FRI0455 INCREASING INCIDENCE OF ADULT IDIOPATHIC INFLAMMATORY MYOPATHIES: A TEN-YEAR UK EPIDEMIOLOGICAL STUDY

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**Background:** Studying the epidemiology of rare conditions such as the idiopathic inflammatory myopathies (IIM) can assist in the identification of risk factors, disease associations and temporal trends. Interrogation of differing geographically and genetically diverse populations can help to construct a more complete picture of underlying disease patterns. A number of UK centres have contributed to national and international IIM research collaborations, but to date there has been no published report detailing the incidence or prevalence of adult IIM in the UK, or to establish the relative proportion of the varying clinical subtypes. Moreover, previous international studies have focussed on specific IIM subtypes, such as inclusion body myositis (IBM) or immune-mediated necrotising myopathy (IMNM), are historic, were undertaken before recent developments in our understanding of the range of IIM subtypes, and utilised widely varying methodologies and case acquisition strategies.

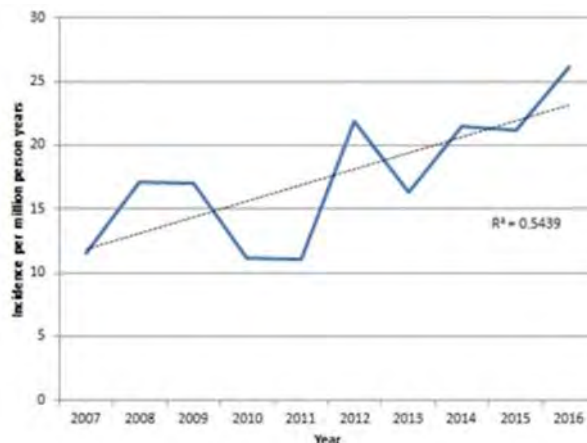
The recently published combined European League Against Rheumatism and American College of Rheumatology (EULAR/ACR) classification criteria for adult and juvenile IIM represent potential progress in identifying IIM, as well as various disease subtypes<sup>1</sup>. We present here the first epidemiological study to utilise these new criteria as part of disease verification.

**Objectives:** Identify and characterise all incident adult cases of IIM between Jan 1 st 2007 and Dec 31 st 2016 in the City of Salford, UK.

**Methods:** Adults first diagnosed with IIM within the study period were identified by: i) a Salford Royal NHS Foundation Trust (SRFT) inpatient episode IIM-specific ICD-10 coding search; ii) all new patient appointments to SRFT neuromuscular outpatient clinics; iii) all Salford residents enrolled within the UKMYONET study. All patients with 'definite' IIM by the 2017 EULAR/ACR classification criteria were included, as were 'probable' cases if expert opinion agreed. Cases were excluded if <18 years at disease onset, if they did not meet 'probable' criteria, or when 'probable' but expert opinion concluded a non-IIM diagnosis.

**Results:** The case ascertainment procedures identified 1156 cases which, after review and application of exclusion criteria, resulted in 32 incident cases during

the study period. 23/32 were female with a mean age of 58.1 years. The mean incidence of adult IIM was 17.6/1,000,000 person years (py), higher for females than for males (25.2 versus 10.0/1,000,000py respectively). A significant incidence increase over time was apparent (13.6 versus 21.4/1,000,000py;  $p=0.032$ ). Using EULAR/ACR classification criteria, the largest IIM subtype (21/32) was polymyositis, followed by dermatomyositis (8/32), inclusion body myositis (2/32) and amyopathic dermatomyositis (1/32). Expert opinion subtype differed from EULAR/ACR Classification criteria in 19/32 cases.



**Conclusions:** The incidence of adult IIM in Salford is 17.6/1,000,000py, higher in females and is increasing over time. Disagreement exists between EULAR/ACR-derived and expert opinion-derived IIM subtype assignments.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.6079

#### FRI0456 PREDICTORS FOR DISEASE WORSENING DEFINED BY ORGAN FAILURE IN DIFFUSE SYSTEMIC SCLEROSIS: A EUROPEAN SCLERODERMA TRIALS AND RESEARCH (EUSTAR) ANALYSIS

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**Background:** Mortality and worsening of organ function are desirable endpoints for clinical trials in systemic sclerosis (SSc). However, these events are relatively rare, making clinical trial design challenging.

**Objectives:** To identify factors in a population of patients with diffuse SSc from the European Scleroderma Trials and Research (EUSTAR) group database that predict these endpoints and hence allow enrichment of those patients.

**Methods:** Inclusion criteria were a diagnosis of diffuse SSc and follow-up after 9–15 (12±3) months. This timeframe was chosen to reflect typical clinical trial design. Disease worsening/organ progression was fulfilled if any of the following events occurred: new renal crisis, decrease in forced vital capacity (FVC) ≥10%, new left ventricular ejection fraction (LVEF) <45% or decrease in LVEF by >10% for patients with baseline LVEF <45%, new pulmonary (arterial) hypertension, or

death. These parameters had been defined by expert nominal group technique. Methodologically, two main limitations had to be addressed:<sup>1</sup> the problem of missing data and<sup>2</sup> the low number of events, which prohibits the simultaneous exploration of a large set of predictors in a regression model. We addressed these issues by (a) imputing multiple predictors based on different algorithms (multiple imputation), and (b) using least absolute shrinkage and selection operator (LASSO) regression for 42 clinical parameters.

**Results:** Of 1451 patients who met the inclusion criteria, 706 had complete data available on all parameters for disease worsening. Of 706 patients originally evaluated, 228 (32.3%) had disease progression, most of which was either a decrease in FVC (103 patients, 14.6%) or death (92 patients, 13.0%) within the observation period (12±3 months). Of the 42 clinical parameters introduced into the model as outcome predictors, 8 remained in the final regression model, which was chosen by the Bayesian information criterion (table 1). Bootstrap with 10 000 repetitions successfully validated the model.

**Abstract FRI0456 – Table 1.** Predictive factors in the final LASSO regression model

Factor	p-value	Odds ratio	95% confidence interval
(Intercept)	<0.0001	0.06	0.03–0.14
Age (per 1 year)	0.001	1.02	1.01–1.04
Active digital ulcers	0.026	1.64	1.06–2.54
C-reactive protein elevation	0.002	1.80	1.23–2.63
Significant dyspnoea	0.491	1.20	0.72–2.00
Lung fibrosis	0.0004	2.21	1.43–3.41
Muscle weakness	0.015	1.64	1.10–2.45
Pericardial effusion	0.098	1.65	0.91–2.97
Proteinuria	0.064	1.75	0.97–3.16

**Conclusions:** The use of the predictive factors presented here could enable cohort enrichment with patients at risk for overall disease worsening in clinical trials.

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FRI0457

#### RELATIONSHIP BETWEEN DIGITAL ULCERS AND SEVERITY OF LUNG FUNCTION TEST IN SYSTEMIC SCLEROSIS OVER A FIVE-YEAR PERIOD

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**Background:** Systemic sclerosis-related interstitial lung disease (SSc-ILD) is the leading cause of death in SSc. Predictors of the outcomes of ILD in SSc are under investigation.

**Objectives:** to assess association of the digital ulcers with dynamics of forced vital capacity (FVC) and diffusing capacity for carbon monoxide (DLco) in patients with SSc-ILD.

**Methods:** It was a longitudinal study involving 83 pts with SSc-ILD (mean age was 46,2±13,4; 69% have limited subset of the disease; 95% were female). The mean duration of follow up was 58,9±12,0 months. At the end of the study a number of pts with digital ulcers (DUs) was 29 (35%). Additionally 77 pts. with SSc-ILD were investigated with HRCT and were divided into 3 groups; The 1 st group (16 pts) with improvement; 2nd group (39 pts) without any changes and 3rd group (22 pts) with worsening of fibrosis.

**Results:** After 5 years of follow up FVC increased significantly in all pts without DUs (n=54) from 88,5%±19 to 96%±23 (p<0,05); in group 1 – from 92%±20.5 to 106%±19 (p<0,05); in group 2 from 87%±18 to 94%±23.5 (p<0,05) and only in group 3 FVC was stable (88±22 and 87±24.5) (p>0,05). The mean value of FVC in all pts with DUs didn't change (88%±14 and 86%±16, p>0,05) with tendency to decreasing in group 3 (from 83%±12,5 to 74%±13 (p>0,05).

After 5 years of follow up DLco declined significantly in all pts with or without DUs, however in the 1 st group decline of DLco wasn't significant. The decreasing of DLCO was more prominent in group 3 than in group 2. Therefore, in group 2 in patient without DU (n=24) – from 65%±16 to 60%±11 (p<0,05) and in patients with DU (n=14) DLCO changed from 61%±15 to 57%±14 (p<0,05). In 3rd group in patients without DU (n=13) DLCO decreased from 55%±15 to 48%±15 (p<0,05) and in patients with DU (n=9)- from 50%±20 to 44,5%±15 (p<0,05).

**Conclusions:** In patients without DUs significant increasing of FVC during 5 years long follow up was observed. The worsening of fibrosis on HRCT in pts with DUs was associated with the lowest value of FVC and DLco at the entry and at the end of the study.

**Disclosure of Interest:** None declared

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FRI0458

#### THE ONSET, CLINICAL COURSE AND OUTCOMES OF SSC- OVERLAP WITH PM/DM OR RA (SSC-PM/DM AND SSC-RA)

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**Background:** Systemic sclerosis (SSc) concurrent with other connective tissue diseases (poly/dermatomyositis, rheumatoid arthritis and oths) seem to be still underexplored clinical forms of SSc.

**Objectives:** To study specific features of the onset, clinical course and outcomes of systemic scleroderma- poly/dermatomyositis (SSc-PM/DM) and SSc-RA overlap syndromes.

**Methods:** Totally 115 patients were examined, 75 – with SSc-PM/DM and 40 with SSc-RA, among them 98 women and 17 men aged 17–74 years (mean age 44 ±14,5) and disease duration from 6 months to 35 years (median 8[2–8]).

**Results:** In 18% of overlapping SSc pts the disease manifested with isolated Raynaud's syndrome (RS) at the onset, in 61% – RS came in combination with cutaneous and/or joint and muscle pathology, and in remaining 7% and 2% overlapping SSc manifested with the isolated articular syndrome or muscular involvement (proximal weakness), respectively. During the first 3 years SSc generalisation with emerging signs of PM/DM occurred in 61% of patients, erosive arthritis manifested in 51%; and in 20% of pts arthritis was detected later. Limited skin involvement predominated, while diffuse skin lesions were present in 23% of SSc-PM/DM cases, 1/3 of them showed signs of DM. All pts with overlapping SSc syndrome received a glucocorticoids (GCs)-based combination therapy (SSc-PM/DM 30–60 mg/day, SSc-RA –10–20 mg/day), with NSAIDs and vascular drugs, 74% were administered cytotoxic agents, more often methotrexate (48%) and 7% – antifibrotic drugs. Two types of overlapping SSc evolution patterns were identified: type I is favourable (stabilisation and slow progression without significant disease activity, and preserved work capacity); type II is unfavourable (continuing activity, rapid progression, disability and deaths). Favourable overlapping



SSc pattern prevailed (79%) in this study group, while unfavourable (21%) mainly consisted of SSc-PM/DM cases. Favourable overlapping SSc evolution was observed in patients with the onset before the age of 40 y, while unfavourable course was documented in pts with the late SSc onset at >40 y, with prevailing SSc-PM/DM. Fatal outcomes in 10% of cases mostly belong to SSc-PM/DM pts (8%). The specific features of overlapping SSc evolution included augmentation of SSc-characteristic symptoms – both, peripheral – teleangiectasias, calcification, osteolysis and digital trophic lesions, mainly in SSc-PM/DM pts, and visceral – involving heart, lungs, and oesophagus, which determined the unfavourable prognosis. RA manifestations (articular syndrome) in overlapping SSc pts tended to decrease, while signs of PM tended to resolve.

**Conclusions:** Timely detection of overlapping SSc pathological symptoms with administration of adequate therapy and dynamic monitoring of patients will improve the prognosis and outcomes of the disease.

**Disclosure of Interest:** None declared

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FRI0459

#### MICROVASCULATURE CHANGES AND ANGIOGENIC FACTORS IN SYSTEMIC SCLEROSIS – A SINGLE CENTRE STUDY

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**Background:** In systemic sclerosis (SSc) low capillary density in acral parts leads to a reduced blood flow, to tissue ischemia. Tissue hypoxia usually initiates the formation of new blood vessels from the pre-existing microvasculature. Despite the reduced blood flow and partial oxygen pressure levels, there is no evidence for a sufficient angiogenesis in the skin of patients with SSc. Nailfold capillaroscopy is a safe, noninvasive routine way for the microvascular investigation. At the same time different cytokines and angiogenic factors are produced.

**Objectives:** The aim of this study was to assess whether blood levels of angiogenic biomarkers are associated with microvasculature changes in SSc patients.

**Methods:** Microvasculature changes were assessed using nailfold videocapillaroscopy (NVC) which was performed by two independent examiners. The obtained images were analysed anonymously by two investigators blinded for the clinical and serum status of SSc patients and classified as early, active and late pattern.<sup>1</sup> Serum or plasma levels of soluble vascular adhesion molecule-1 (sVCAM-1) and soluble intercellular adhesion molecule-1 (sICAM-1) were measured by ELISA, big endothelin-1 (BET-1) concentrations using competitive enzyme-immunoassay and von Willebrand factor antigen (vWFAg) concentrations using ELISA kit were measured. As potential disease activity markers soluble receptor of interleukin-2 (sIL-2r) and interleukin-6 (IL-6) serum levels using commercial kits were assayed. For statistical evaluation Pearson's correlation coefficient and univariate analysis were used.

**Results:** Total 40 patients (38 females) were investigated: 30 individuals with limited form, 5 with diffuse, 3 patients with scleroderma sine scleroderma, 1 with overlap syndrome and 1 with undifferentiated connective tissue disease. The mean age ±standard deviation (SD) of the whole cohort was 51±22 years and the mean disease duration ±SD was 10±7 years. 3 patients (7.5%) had early NVC pattern, 12 patients (30%) had active, 10 (58%) late pattern, and 15 (37.5%) had nonspecific changes or normal picture.

The patients with late NVC pattern exhibited higher vWFAg levels than patients with active pattern (p<0.01). BET-1 and sICAM-1 serum levels were higher in the active pattern compared with late patterns (p<0.01 and p<0.05, respectively). When correlating these potential biomarkers with SSc-related clinical characteristics we found only these associations: vWFAg levels with heart arrhythmias and modified Rodnan skin score (p<0.01, p<0.05, respectively).

**Conclusions:** vWFAg and ET-1 increase in the late NVC pattern can be considered as an attempt to support deficient vasculogenesis. Further studies are needed to determine the role of other potential biomarkers of endothelial injury and repair in SSc.

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FRI0460

#### THE COMPARISON BETWEEN PATIENTS WITH SYSTEMIC SCLEROSIS, POSITIVE FOR FOR ANTIBODIES TO RIBONUCLEOPROTEIN AND CLASSICAL SUBTYPES OF SYSTEMIC SCLEROSIS

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**Background:** Different clinical subtypes of systemic sclerosis (SSc) vary in frequency and severity of symptoms, progression of internal organ involvement and outcomes. The frequency of antibodies to ribonucleoprotein (RNP) in SSc varies from 5% to 30% according to reports of different studies and can be connected with separate clinical subtype of SSc.

**Purpose:** to characterise the main clinical features of patients with SSc positive for antibodies to RNP and to compare them with ACA and Scl-70 positive subtypes of SSc.

**Objectives:** to characterise the main clinical features of patients with SSc positive for antibodies to RNP and to compare them with ACA and Scl-70 positive subtypes of SSc.

**Methods:** The study included 330 patients (289 women and 41 men, mean age 50±13 years) meeting the criteria of the SSc (ACR/<sup>EULAR</sup> 2013) observed between 2011 and 2017. The level of anti-nuclear antibodies was determined by ELISA. The normal level of antibodies to RNP (U1-RNP-70) was 0–25 U/ml. The level greater than 3 times the upper limit of normal considered as highly positive.

**Results:** In study group of 330 patients 49 (15%) had antibodies to ACA, 154 (46%) – to Scl-70, 67 (20%) – to RNP antibodies. Also 4 patients simultaneously had antibodies to Scl-70 and RNP, 4 patients – to ACA and RNP, 1 patient to ACA, Scl-70 and RNP. Among RNP +group 85% of patients were highly positive and 15% – low-positive.

The vast majority of patients were female (91%), mean age 44,2±15 years. RNP +group was similar to ACA +group by predominance of a limited form of the disease which was 67,3% and 97% correspondingly. At the same time RNP +group was similar to Scl-70 +group by frequent involvement of internal organs – intestinal lung disease 67,3 and 69% correspondingly, involvement of cardiovascular system – 21% and 34%, esophagitis 61% and 44,5%.

RNP +group had scleredema frequently – 40%, in comparison with ACA+ (10%, p<0,005) and Scl-70+ (6,5%, p<0,005), involvement of joints (arthralgia/arthritis) – 65% in comparison with ACA+ (24%, p<0,005) and Scl-70+ (24%, p<0,005), muscle weakness/pain – 43%, in comparison with ACA+ (0,2%, p<0,005) and Scl-70+ (10,4%, p<0,005). All 3 groups did not differ significantly by the presence of Raynauds syndrome, telangiectasia and vascular manifestations (fingertip pitting scars or digital tip ulcers).

Furthermore patients with SSc highly positive for antibodies to RNP, met the criteria of mixed connective tissue diseases<sup>Kasukawa et al., 1987</sup> in 71%.

**Conclusions:** Our cohort of patients with SSc have high frequency of highly positive level of antibodies to RNP – 17%. Combination of specific SSc anti-nuclear antibodies (ACA, Scl-70) and antibodies to RNP was uncommon (2,7%) and predominantly in low-positive for antibodies to RNP patients.

The distinctive features of RNP +group in contrast to the "classical" subtypes of SSc were more mild skin involvement (puffy fingers) and more severe muscle and joints involvement.

Despite the limited form of the disease and mild skin involvement, RNP +group is more similar to Scl-70 +group by frequent involvement of internal organs.

We propose that well known relation between skin involvement in diffuse form of SSc with Scl-70 +and organ damage is not so evident in RNP +group of SSc.

**Disclosure of Interest:** None declared

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FRI0461

#### EFFICACY AND SAFETY OF ANTIFIBROTIC AGENTS IN IDIOPATHIC PULMONARY FIBROSIS

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**Background:** Antifibrotic (AF) agents are a family of drugs that improve the survival and quality of life of patients with idiopathic pulmonary fibrosis (IPF). Given that pulmonary fibrosis is also a common manifestation of many autoimmune diseases, we think of interest to know the efficacy and safety data of these agents in real life, which will likely soon reach the therapeutic arsenal of the rheumatologist.

**Objectives:** To analyse the efficacy and safety of treatment with AF pirfenidone (Pi) and nintedanib (Ni) at one year in patients with mild-moderate IPF treated in our hospital according to clinical practice.

**Methods:** Retrospective observational study in which all patients diagnosed with mild-moderate IPF who started treatment with Pi and/or Ni between January 2012 and May 2017 in our Hospital were included. The response was evaluated according to the results obtained in the Respiratory Function Tests: forced vital capacity (FVC) and carbon monoxide diffusion test (DLCO), which were carried out every 3

months during the first year of treatment. Some of the patients received both drugs in different evolutionary periods of their disease. The study was approved by the Clinical Research Ethics Committee (CREC) of our hospital.

**Results:** Of the 42 patients included, 29 received Pi, 69% men and 31% women, with a mean age of 71 years (78% ex-smokers). Baseline FVC was 2140 ml (74.4% of the predicted value) and DLCO was 40.8% with respect to the expected value. The absolute loss in FVC after 52 weeks of follow-up was 200 ml. 48.3% required treatment with glucocorticoids (GC) at some point, either due to exacerbations of the disease or as concomitant treatment. 65.5% presented some adverse reaction to Pi, being gastrointestinal discomfort (GI) the most frequently observed, although mainly of self-limiting course, with the definitive suspension of the drug being necessary in 6 cases. As for the patients treated with Ni, 70.6% were men and 29.4% women, 82% ex-smokers, with an average age of 72 years. Baseline CVF value was 2480 ml (83.8% of the predicted value) and DLCO value was 54.7%. The decrease in FVC in absolute terms was 70 ml. Similarly, 4 patients required the use of GC at some point in the study. With regard to adverse reactions, 76.5% presented some type of adverse event, GI discomfort being the most frequent, followed by increased transaminases and mild diarrhoea. The great majority were of limited duration, requiring the definitive suspension of the drug in 5 patients. Five patients treated with Pi died due to exacerbations of their disease.

**Conclusions:** This project supports, with data from usual clinical practice, the beneficial effect of the AF drugs available for the treatment of mild-moderate IPF. Both drugs have been shown to slow down the natural evolution of the disease, reducing the loss of FVC, a variable directly related to mortality. This therapy has acceptable safety margins. However, there are still no references regarding its administration in incipient and advanced stages of the disease nor on their combined use with each other or with immunomodulators for the control of immune mediated diseases.

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#### FRI0462 SERUM KL-6 IS A STRONG PREDICTOR FOR RELAPSE OF MYOSITIS-ASSOCIATED INTERSTITIAL LUNG DISEASE

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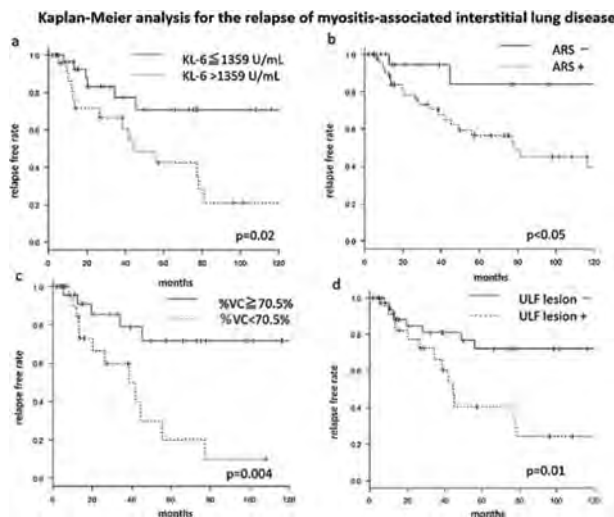
**Background:** Polymyositis (PM), dermatomyositis (DM) and clinically amyopathic DM (CADM) are autoimmune myositis which can be associated with interstitial lung disease (ILD).<sup>1,2</sup> The relapse rate of ILD is high, reported as approximately 20%–55%.<sup>3,4</sup> Since relapses result in decreased pulmonary function, it is important to identify the predictive factors for the relapse.

**Objectives:** The aim of this study was to elucidate the predictive factors for the relapse of ILD associated with myositis (PM/DM/CADM).

**Methods:** We conducted an observational retrospective study. Patients with myositis-associated ILD who have ever visited our institution between 2002–2017 and achieved remission once were enrolled. Patients who died before remission were excluded. We collected their clinical information from medical records. We compared patient characteristics between relapse group and non-relapse group by Fisher's exact test or Mann-Whitney U test at first. Relapse was defined as exacerbation of radiological findings of which doctor-in-charge decided to intensify therapy for ILD. We performed Kaplan-Meier analysis to compare the relapse-free survival for the characteristics that had significant differences between two groups. To perform Kaplan-Meier analysis, continuous variables were converted to dichotomous variables for analysis by setting cut-off values determined by receiver-operating characteristics (ROC). Then, using each characteristic which showed significant difference in Kaplan-Meier analysis, we conducted Cox's proportional hazard analysis for multivariate analysis. For relapse group, we examined the changes of serum KL-6 levels from the initial treatment of myositis-associated ILD to the relapse of ILD. We calculated the average of serum KL-6 levels of 3 months and 6 months before relapse, respectively, then compared them with KL-6 levels at the time of relapse.

**Results:** Seventy-two patients with myositis-associated ILD at our institution were enrolled. Among 72 patients, 24 experienced relapse (relapse group) and 48 did not experience relapse (non-relapse group). Median observational period was 31.5 months and 39.0 months, respectively. Median levels of serum KL-6, the rate of patients who had upper lung field (ULF) lesion by CT, and anti-ARS antibody prevalence were significantly higher in relapse group than in non-relapse group (1870 vs 935 U/mL,  $p=0.003$ ; 62 vs 27%,  $p=0.01$ ; 88 vs 60%,  $p=0.03$ , respectively). Median levels of %VC was significantly lower in relapse group than in non-relapse group (65.7 vs 81.2%,  $p=0.02$ ). By ROC analysis, the cut-off levels of serum KL-6 and %VC were determined as 1359 U/mL and 70.5%, respectively. Kaplan-Meier analysis showed serum KL-6 >1359 U/mL ( $p=0.02$ ), anti-ARS

antibody ( $p<0.05$ ), %VC <70.5 ( $p=0.004$ ), and ULF lesions ( $p=0.01$ ) were significantly related to the relapse (figure 1). Multivariate analysis revealed only serum KL-6 >1359 U/mL was an independent risk factor for relapse (hazard ratio: 4.9 (95%CI 1.0–24.0),  $p<0.05$ ) among the 4 characteristics. At the time of the relapse, serum KL-6 levels were increased 37% from the 3 months average and 51% from the 6 months average.



**Conclusions:** Serum KL-6 was a strong predictor for relapse of myositis-associated ILD.

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**Disclosure of Interest:** None declared

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#### FRI0463 A NEW COMPUTED TOMOGRAPHY INDEX FOR QUANTIFICATION OF INTERSTITIAL LUNG DISEASE IN SYSTEMIC SCLEROSIS IS ASSOCIATED WITH LUNG FUNCTION PARAMETERS IN THE SHORT TERM FOLLOW-UP

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**Background:** New computer-assisted methods for the objective quantification of interstitial lung disease (ILD) at computed tomography (CT), based on the evaluation of mean lung attenuation (MLA), skewness and kurtosis have been recently investigated in Systemic Sclerosis (SSc). We developed a computerised integrated index (CII) based on a weighted evaluation of MLA, skewness and kurtosis and investigated its reliability for the quantitative assessment of SSc-ILD and its associations with lung function parameters in a cross-sectional study.

**Objectives:** To identify the CII cut off value with the highest sensitivity and specificity for CT-detected ILD and to investigate its impact on lung function parameters over-time of baseline assessed CII.

**Methods:** SSc patients meeting the new ACR/EULAR classification criteria, who had undergone a volumetric lung CT study from July 1 st 2014 to June 30th 2015, had been evaluated at baseline for ILD quantification by Goh et al. method and the previously referred dedicated software and had their CII calculated, were enrolled in a prospective study including complete clinical, serological, and functional assessment at baseline and at 1 year follow-up (FU).

**Results:** Thirty-nine out of 83 (47%) SSc patients (79 females, 4 males; mean age 56.4±11.3 years; median disease duration 12 years;<sup>2-54</sup> 18 diffuse cutaneous and 65 limited cutaneous SSc) had evidence of ILD as assessed by volumetric CT of the lungs at baseline. CII in patients with ILD was significantly lower than in those without ILD (-0.4929±0.9933 versus 0.4145±0.8059 HU;  $p<0.0001$ ). ROC analysis revealed that the best discriminating CII value for ILD was 0.1966:

sensitivity 0.81 (95% C.I. 0.68 to 0.92); specificity 0.66 (95% C.I. 0.52 to 0.80). Out of the 44 ILD negative patients, 22 (50%) presented a CII value lower than the cut-off, and 13 of them (59%) were found to have a diffusing lung capacity for CO (DLCO)<80% of predicted. At 1 year FU, the CII was significantly correlated with total lung capacity -TLC ( $r=0.45$ ,  $p=0.004$ ) and DLCO ( $r=0.29$ ,  $p=0.045$ ). Out of the 22 patients with a CII <0.1966 but no ILD at visual evaluation, 11 (50%) developed a FVC decline at 1 year, and 8 (36.7%) a DLCO decline.

**Conclusions:** Here we confirm that quantitative computer-assisted CT of the lungs could be a reliable method for SSc-ILD evaluation and found that it could also be useful in predicting the evolution of lung function in the short-term FU.

**Disclosure of Interest:** None declared

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FRI0464

#### CLINICAL MANIFESTATIONS OF PERSISTENT ANTIPHOSPHOLIPID ANTIBODIES IN SYSTEMIC SCLEROSIS PATIENTS

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**Background:** Antiphospholipid antibodies (aPL) can be detected in systemic sclerosis (SSc) patients. While their clinical signification is well known in the primary antiphospholipid syndrome (APS), their frequency and clinical association remain debated matter of issue. In a previous study, we reported the prevalence and their clinical association of a single aPL testing a French cohort of SSc patients. Yet, the persistence of aPL during follow-up of patients has never been assessed.

**Objectives:** This study aimed to assess i. the persistence of aPL at least 12 weeks after the first dosage and ii. the clinical associations.

**Methods:** At least 12 weeks apart after the first test, 213 SSc patients were consecutively tested for lupus anticoagulant (LA), anticardiolipin (aCL) and anti-β2glycoproteine 1 (anti-β2Gp1) antibodies. aCL and anti-β2Gp1 were measured using commercial ELISA assays (Orgentec, Trappes, France), positivity was defined as  $\geq 10$  UGPL/mL (aCL) or  $\geq 10$  UA/mL (anti-β2Gp1). Clinical associations were studied using binomial logistic regressions.

**Results:** The mean time between two tests was  $13.2 \pm 6.3$  months. One or more type of aPL was persistent in 7 patients (3%). Patients with persistent aPL developed more frequently venous thrombosis (VT) [4/7 (57%) versus 23/205 (11%),  $p=0.006$ ]. Arterial or/and venous thrombosis were more common in patients with persistent aPL than other patients [4/7 (57%) versus 33/205 (16%),  $p<0.001$ ]. Persistent aPL was also associated with miscarriages [4/6 (67%) versus 33/155 (21%),  $p=0.023$ ].

Association between aPL positivity persistence and clinical manifestations

	aPL positivity	aPL negativity	p
Arterial or venous thrombosis	4 (57.1%)	33 (16.1%)	<0.001
Venous thrombosis	4 (57.1%)	23 (11.2%)	0.006
Arterial thrombosis	1 (14.3%)	14 (6.8%)	0.406
Miscarriage	4 (66.7%)	32 (20.6%)	0.023
Digital ulceration	0 (0%)	40 (19.8%)	0.351
PAH	1 (14.3%)	13 (6.7%)	0.402

**Conclusions:** The prevalence of persistent aPL in our cohort was 3%. VT and miscarriages were associated with persistent aPL.

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FRI0465

#### QUANTITATIVE ASSESSMENT OF INTERSTITIAL LUNG DISEASE IN IDIOPATHIC INFLAMMATORY MYOPATHIES: VISUAL SCORE AND COMPUTERISED PROCESSING ANALYSIS OF HIGH RESOLUTION COMPUTERISED TOMOGRAPHY

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**Background:** High resolution computed tomography (HRCT) is an essential technique for the characterisation of interstitial lung disease (ILD) in patients with idiopathic inflammatory myopathies (IIM). Although several visual scores are available for a semiquantitative evaluation of ILD, an automatic quantitative analysis of lung involvement may represent a valuable improvement to reproducibly determine the extent of the disease.

**Objectives:** To compare the semiquantitative visual score to a volumetric texture and local volumetric histogram feature-based analysis software (CALLIPER) to quantify the lung involvement in IIM patients.

**Methods:** 21 consecutive IIM patients (Bohan and Peter criteria) who underwent a HRCT between November 2016 and November 2017 were prospectively enrolled. Twelve were affected by polymyositis and 9 by dermatomyositis. We collected smoking habits data and myositis specific autoantibodies positivity, respiratory symptoms according to MRC dyspnea scale and two patients reported outcome questionnaires: Leicester cough questionnaire (LCQ) and St. George's Respiratory questionnaire (SGRQ). Patients underwent a non-contrast, supine, volumetric CT ( $\leq 2$  mm slice thickness) that was evaluated by an expert radiologist according to Warrick's score (WS) and also quantified by CALLIPER (Mayo Biomedical Imaging Resource – USA). CALLIPER analysis of the extent of interstitial lung abnormalities (ground glass, lung reticulation, honeycombing) was performed and a total score, expressed as percentage of lung involved (ILD%), was obtained. Analysis of the vascular involvement were performed as percent of pulmonary vessel volume (VESS%).

**Results:** Between the 21 patients, five (23.8%) were smokers. Four patients were positive for anti-synthetase autoantibodies -ASS (3 Jo-1, 1 PL-7), 1 SRP, 1 Mi2. Dyspnea was present in 19 patients (90%): 9 grade 1, 7 grade 2, 3 grade 3 according to MRC scale. There were strict correlations between WS and ILD ( $r=0.802$   $p<0.001$ ) and VESS% ( $r=0.746$   $p<0.001$ ). LCQ score was negative correlated to WS ( $r=-0.728$   $p=0.007$ ) but the correlations were stricter with ILD score ( $r=-0.868$   $p<0.001$ ) and VESS% ( $r=-0.801$   $p<0.002$ ). SGRQ did not correlate both to WS and CALLIPER parameters. Patients with ASS have higher ILD and VESS% compared to seronegative patients (respectively  $p=0.003$  and  $p=0.006$ ).

**Conclusions:** CALLIPER represents an innovative technique to quantify the lung involvement in IIM patients: the main advantage of CALLIPER is the reproducibility that avoids the inter and intra-reader bias. Although more data are needed in larger cohorts, the use of CALLIPER may open new routes for the evaluation of ILD in IIM patients, both in medical practice and in randomised controlled trials.

**Disclosure of Interest:** None declared

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FRI0466

#### ARTICULAR AFFECTATION IN SYSTEMIC SCLEROSIS: CORRELATION OF ULTRASOUND FINDINGS WITH CLINICAL, BIOLOGICAL AND RADIOGRAPHICAL FINDINGS

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**Objectives:** To evaluate the prevalence of subclinical synovitis in systemic sclerosis (SS), as well as the correlation of sonographic findings in hands with radiographs and with clinical-analytical parameters. In addition, the correlation with scales of functionality will be determined.

**Methods:** Cross-sectional observational-analytical study that included 40 patients with ES and 23 patients with rheumatoid arthritis (RA) as a control group during the period 10/2015–03/2016. Clinical, analytical, immunological, ultrasound and the radiological characteristics of both groups and their respective statistical correlations were compiled.

**Results:** The mean age of the group with SS was  $53.3 \pm 14.1$  years; 87.5% were women and 75% of the cases were cutaneously limited. The average time of evolution of the disease was 6.8 years from the diagnosis. Regarding the clinical joint involvement in the carpus and hands, frank arthritis was present in 16 cases (40%), with an average of DAN: 3.77 and TAN: 1.57; with an average of EVA global pain: 30/100 and elevated CRP in 42.5% of cases. The prevalence of subclinical synovitis with ultrasound expression of synovial effusion  $\pm$ synovial hypertrophy in the SS group was at carpal level (77%), FCM (60%), PFI 32.5% and DFI (15%). The statistical linear correlation between findings of carpal erosions at the ultrasound level versus the radiological data was positive only in the involvement at the joint level FCM and FID. In the group with SS, the HAQ questionnaire



had an average of 0.95 (mild disability) versus 0.77 in the RA group, and the average hand function score or Cochin index: 20.6 (moderate disability) against 17.5 of the RA group. There was no statistically significant correlation ( $\chi^2$ ) between the elevated CRP values and these 2 questionnaires in the SS group. The radiological findings of calcinosis and acroosteolysis in the group with SS were double the cases of the group with RA (7 versus 3, and 14 versus 7 respectively).

**Conclusions:** Subclinical joint involvement in systemic sclerosis had a high prevalence, similar in rheumatoid arthritis, with ultrasound being a fundamental test when evaluating subclinical inflammatory activity. It also presents an important correlation with the findings found in radiographs in the same locations.

**Disclosure of Interest:** None declared

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FRI0467

#### THE RELATIONSHIP BETWEEN <sup>99m</sup>Tc-PERTECHNETATE HAND PERFUSION SCINTIGRAPHY AND NAIFOLID CAPILLOSOPY IN SYSTEMIC SCLEROSIS PATIENTS: A PILOT STUDY

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**Background:** The aim of this study was to assess possible relationship between the altered blood perfusion at hands analysed by <sup>99m</sup>Tc-pertechnetate hand perfusion scintigraphy (<sup>99m</sup>TcPHPS) and, morphological microvascular abnormalities detected by nailfold capillaroscopy (NC) in SSc patients.

**Methods:** The study group consisted of 25 patients with SSc (14 with diffuse SSc, and 11 with limited SSc) and 28 control subjects (18 patients with primary RP, and 10 healthy individuals). NC and <sup>99m</sup>TcPHPS was performed in all the groups examined. The capillaroscopic pattern was classified as normal or scleroderma ("early", "active", or "late") pattern. Gamma-camera dynamic first-pass study during the first 60 s and a static scintigraphy after 5 min were recorded following a bolus injection of <sup>99m</sup>Tc-pertechnetate via a cubital vein. Regions of interest were drawn on the summed images around the fingers and the palmar region. The fingers-to-palm ratios were then calculated.

**Results:** SSc patients showed a significantly lower blood flow (BF) and blood pool (BP), ( $0.43 \pm 0.21$  vs  $0.36 \pm 0.07$ , respectively), than PRP patients ( $0.45 \pm 0.18$  vs  $0.42 \pm 0.06$ , respectively) and healthy subjects ( $0.58 \pm 0.19$  vs  $0.44 \pm 0.06$ , respectively), (p-value 0.039 vs 0.004, respectively). A gradual decrease of BF and BP was found in SSc patients with progressive severity of NVC patterns of microangiopathy ["early" ( $0.49 \pm 0.03$  vs  $0.39 \pm 0.04$ , respectively), "active" ( $0.43 \pm 0.11$  vs  $0.38 \pm 0.06$ , respectively) or "late" ( $0.40 \pm 0.28$  vs  $0.36 \pm 0.08$ , respectively), (p-value 0.462 vs 0.728 respectively), but these differences were not statistically significant. Patients with diffuse SSc showed lower BF, and higher BP ( $0.42 \pm 0.26$  vs  $0.37 \pm 0.07$ , respectively) than those with limited SSc, ( $0.44 \pm 0.14$  vs  $0.35 \pm 0.064$ , respectively), but this differences is not statistical significantly (p=0.76 vs p=0.53, respectively). There was no significant correlation between BF and BP values and type of SSc (limited or diffuse) ( $r = -0.06$ , p=0.77;  $r = 0.13$ , p=0.54, respectively) as well as three microangiopathy patterns ( $r = -0.253$ , p=0.22;  $r = -0.13$ , p=0.54, respectively).

**Conclusions:** NC represents the best method to analyse microvascular damage in rheumatic diseases, especially SSc. <sup>99m</sup>TcPHPS improves the evaluation of vascular damage in SSc patients. There is no direct relationship between these two methods, but one method complements another in the study of vascular damage in SSc patients.

**Disclosure of Interest:** None declared

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FRI0468

#### ABNORMAL OESOPHAGEAL MOTILITY DURING A SOLID TEST MEAL IN SYSTEMIC SCLEROSIS – DETECTION IN VERY EARLY DISEASE AND ASSOCIATION WITH DISEASE PROGRESSION

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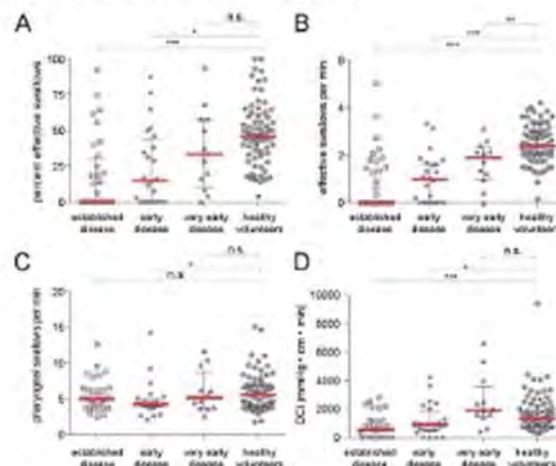
**Background:** Ineffective oesophageal motility (IEM) is frequent in patients with systemic sclerosis (SSc). High-resolution oesophageal manometry (HRM) is the reference standard test for oesophageal motility and addition of a test meal increases diagnostic sensitivity and specificity.

**Objectives:** This study assessed whether using a test meal instead of standard water swallow in HRM increases sensitivity and can detect clinically relevant, abnormal motility in already very early SSc and whether this finding is associated with subsequent disease progression.

**Methods:** This prospective, longitudinal cohort study recruited 68 consecutive SSc patients (group #1: 32 established disease (ACR/EULAR 2013 and ACR 1980 criteria fulfilled); group #2: 24 early disease (only ACR/EULAR 2013 fulfilled); group #3: 12 very early disease (clinical expert diagnosis of SSc, no classification criteria fulfilled) and 72 healthy controls. HRM evaluated oesophageal motility for water swallows and a solid test meal using validated methods.

**Results:** SSc patients had less frequent effective oesophageal contractions during the test meal compared to healthy controls. Notably, this was detected even in very early disease (0.15, 1.0, 2.1/min for group #1, #2 and #3, vs. 2.5/min in health, p<0.001; p<0.001 and p<0.009, respectively). No other significant abnormality on HRM was found in patients with very early disease (group 1). Ineffective motility at HRM was associated with a higher modified Rodnan skin score at baseline. Moreover, at mean 18<sup>10-31</sup> months follow-up, the presence of ineffective motility at baseline was associated with progression of skin disease for the overall SSc cohort (p<0.010). In a secondary analysis, below-average lower oesophageal sphincter pressure was associated with progression of skin disease and organ disease, in particular interstitial lung disease (p<0.009).

Key HRM findings in SSc patients and healthy volunteers.



**A** Percentage of effective swallows in the test meal **B** Number effective swallows per min in the test meal. **C** Number pharyngeal swallows per min in the test meal. **D** Vigour of peristalsis (DCI) in standard HRM. Median (red bar) and IQR (error bars) are indicated. Please, note the significant decrease in effective swallows per minute which in patients with very-early disease, which is only observed for the test meal. Statistical analysis: Mann-Whitney U test. \* p<0.05. \*\* p<0.01. \*\*\* p<0.001.

**Conclusions:** Ineffective motility during a test meal is present already in patients with very early SSc. In cross-sectional analysis, findings on HRM studies at baseline are associated with disease severity and prospectively with progression of

skin disease during follow-up. Thus, performance of HRM already in very early disease stages can support individual risk-stratification of SSc patients.

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FRI0469

#### ACUTE AND CHRONIC EFFECTS OF TWO DIFFERENT INTRAVENOUS ILOPROST REGIMENS IN SYSTEMIC SCLEROSIS: A SINGLE CENTRE PRAGMATIC NON-RANDOMISED TRIAL

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**Background:** In systemic sclerosis (SSc) vascular involvement plays a pivotal role in the pathogenesis and clinical manifestations.<sup>1</sup> Intravenous (IV) iloprost (ILO), a prostacyclin analogue, is administered in SSc, according to EULAR recommendations, to improve Raynaud's phenomenon (RP) and to achieve digital ulcers (DU) healing and prevention,<sup>2</sup> even though no further indications about the regimen are specified.

**Objectives:** The aim of this study was to evaluate acute and chronic effects of IV ILO administered with two different regimens as assessed by power Doppler ultrasound (PDUS) and nailfold videocapillaroscopy (NVC) and in a group of patients not treated with ILO.

**Methods:** This was a single centre pragmatic non-randomised trial on 96 patients with SSc divided in 3 groups: no ILO (group A), ILO once monthly (group B) and ILO for 5 consecutive days every 3 month (group C). At each evaluation patients underwent PDUS and NVC. Group A patients were examined at baseline and after 3 months. Group B every month before and after IV ILO monthly therapy for 3 months. Group C before and after the 1 and 5 days of therapy at baseline and after 3 months. PDUS parameters included resistivity index (RI), finger pulp blood flow (FPBF) and periungual vascularisation. The sum of capillaries apex width in one millimetre was assessed through NVC. Results were analysed considering the average outdoor temperature at the place of residence.

**Results:** An acute IV ILO effect was observed for FPBF in group B and C ( $p < 0.001$  and  $0.005$  respectively). An acute effect was observed for RI and periungual vascularisation only in group B. A progressive increase was observed for the other parameters without being statistically different. On the contrary IV ILO effects were not observed any longer before the following infusion. Moreover, some parameters (FPBF in group B and RI in group C) showed a statistically higher increase as low as the outdoor temperature was.

**Conclusions:** IV ILO therapy was able to cause an acute effect with respect to PDUS parameters, especially in group B. The acute effect was not any longer maintained until the following infusion. Future studies are needed to assess time for re-treating.

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FRI0470

#### A PHASE 2 STUDY OF SAFETY AND EFFICACY OF LENABASUM (JBT-101), A CANNABINOID RECEPTOR TYPE 2 AGONIST, IN REFRACTORY SKIN-PREDOMINANT DERMATOMYOSITIS

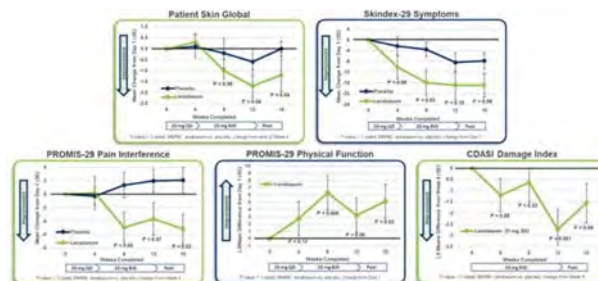
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<sup>1</sup>Philadelphia Veteran Affairs Medical Center; <sup>2</sup>University of Pennsylvania, Philadelphia; <sup>3</sup>Corbus Pharmaceuticals, Inc., Norwood, USA

**Background:** Effective treatment options are limited for refractory skin disease in dermatomyositis (DM). Lenabasum is a non-immunosuppressive, synthetic, oral preferential CB2 agonist that triggers resolution of innate immune responses and reduces cytokine production by PBMC from DM patients.

**Objectives:** The purpose of this study was to test safety and efficacy of lenabasum (aka JBT-101, anabasum) in DM subjects with refractory, moderate-to-severely active skin disease.

**Methods:** A double-blind, randomised placebo-controlled 16 week Phase 2 trial (JBT101-DM-001; NCT02466243) enrolled adults with documented DM and a Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI) activity score  $\geq 14$ , minimal active muscle involvement and failure or intolerance to hydroxychloroquine and stable DM medications including immunosuppressants. Subjects received 2 escalating dose levels of lenabasum (20 mg QD X 4 weeks, then 20 mg BID X 8 weeks) or PBO X 12 weeks. Subjects were followed off study drug X 4 weeks. Safety and efficacy outcomes were assessed from Day 1 through end of study at Week 16. The primary efficacy objective was to assess efficacy of lenabasum using CDASI activity score.

**Results:** 11 adults each received lenabasum and PBO (n=22). Demographic and disease characteristics were similar in both cohorts. Both cohorts had mean CDASI activity scores in the severe range<sup>33–35</sup> despite immunosuppressants (19/22 subjects). Lenabasum subjects had clinically meaningful improvement in CDASI activity scores with mean reduction  $\geq 5$  points at all visits after 4 weeks. Improvement had statistical significance at end of study (figure 1,  $p=0.02$ , 2-sided MMRM) that first became apparent after 4 weeks. Lenabasum provided greater improvement than placebo in CDASI damage index, patient-reported global skin disease and overall disease assessments, skin symptoms including photosensitivity and itch, fatigue, sleep, pain interference with activities, pain, and physical function (examples in figure 1). Improvements in secondary efficacy outcomes reached statistical significance ( $p \leq 0.1$ , 1-sided MMRM) at multiple visits after week 4 (figure 1). There were no serious, severe or unexpected adverse events (AEs) related to lenabasum. Tolerability of lenabasum was excellent with no study drop-outs. Subjects in the lenabasum cohort had numerically more mild AEs than placebo subjects (29 vs. 19) and fewer moderate AEs (4 vs. 7). AEs in  $\geq 3$  subjects in any cohort were diarrhoea, dizziness (lightheadedness), fatigue and dry mouth.



**Abstract FRI0470 – Figure 1.** Effects of Lenabasum on Efficacy Outcomes in Refractory, Skin-Predominant DM

**Conclusions:** Lenabasum demonstrated consistent evidence of clinical benefit across multiple efficacy outcomes and had acceptable safety and tolerability in this Phase 2 trial in refractory skin disease in DM. Further evaluation of lenabasum in the treatment of DM is warranted.

**Disclosure of Interest:** V. Werth Consultant for: Corbus Pharmaceuticals, Inc., E. Hejazi: None declared, S. Pena: None declared, J. Haber: None declared, J. Okawa: None declared, R. Feng: None declared, K. Gabre: None declared, J. Concha: None declared, C. Cornwall Employee of: Corbus Pharmaceuticals, Inc., N. Dgetluck Employee of: Corbus Pharmaceuticals, Inc., S. Constantine Employee of: Corbus Pharmaceuticals, Inc., B. White Employee of: Corbus Pharmaceuticals, Inc.

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**FRI0471** PREDICTION OF PROGRESSION OF INTERSTITIAL LUNG DISEASE IN PATIENTS WITH SYSTEMIC SCLEROSIS: THE SPAR MODEL

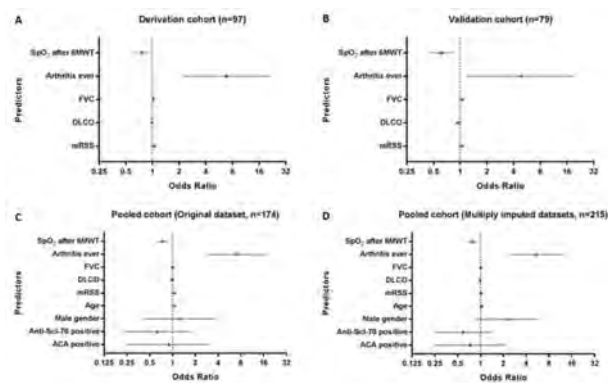
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**Background:** The natural disease course of interstitial lung disease associated with systemic sclerosis (SSc-ILD) is highly heterogeneous. Currently, no data are available to distinguish a progressive disease course from a stable course when mild interstitial lung disease (ILD) is diagnosed in patients with systemic sclerosis (SSc).

**Objectives:** This study aimed to identify predictive clinical characteristics and establish a prediction model for the progression of mild ILD at 1 year follow-up in SSc patients.

**Methods:** Patients with SSc from two independent prospective cohorts were included in this observational study. All patients fulfilled the ACR<sup>EULAR</sup> 2013 criteria, had mild ILD at baseline diagnosed by HRCT (ILD extent <20% lung involvement on HRCT), available baseline and follow-up pulmonary function tests, at least one annual follow-up visit, and no concomitant pulmonary hypertension or airflow obstruction. ILD progression was defined as a relative decrease in FVC % $\geq$ 15%, or FVC% $\geq$ 10% combined with DLCO% $\geq$ 15% at 1 year follow-up. Candidate predictors for multivariate logistic regression were selected by expert opinion based on previous studies and clinical significance. Multiple imputation was used to address missing data. A prediction model for ILD progression was established in the derivation cohort and validated in the multinational validation cohort.

**Results:** A total of 25/98 and 25/117 SSc patients showed ILD progression in the derivation cohort and the validation cohort, respectively. Lower SpO<sub>2</sub> after six-minute walk test (6MWT) and arthritis ever were identified as independent predictors for ILD progression in the derivation, validation and pooled cohorts (figure 1). The optimal cut-off value for SpO<sub>2</sub> after 6MWT for ILD progression was determined as 94% by ROC curve analysis. In a simplified model, the presence of both SpO<sub>2</sub> after 6MWT $\leq$ 94% and Arthritis ever were set to 1, giving a SPAR score ranging from 0 to 2. The derived SPAR model increased the prediction rate for ILD progression from 7.4% (scoring 0) to 91.7% (scoring 2) with an AUC [95% CI] of 0.83 [0.73 to 0.93] in the derivation cohort, and a similar AUC [95% CI] of 0.82 [0.70 to 0.94] in the validation cohort.



**Abstract FRI0471 – Figure 1.** Multivariate logistic regression models in the derivation cohort, the validation cohort and the pooled cohort (both original and multiply imputed datasets, adjusted for age, gender, Anti-Sci-70 positive, ACA positive in the pooled cohort)

**Conclusions:** The evidence-based SPAR prediction model developed in our study might be helpful for the risk stratification of patients with mild SSc-ILD in clinical practice and cohort enrichment for future clinical trial design.

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**FRI0472** TOWARDS A MULTIDIMENSIONAL PATIENT REPORTED OUTCOME MEASURES ASSESSMENT: DEVELOPMENT AND VALIDATION OF A QUESTIONNAIRE FOR PATIENTS WITH SYSTEMIC SCLEROSIS/ SCLERODERMA

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**Background:** Systemic sclerosis is a chronic multisystem autoimmune disorder associated with high morbidity and mortality rates. A multidisciplinary approach is necessary due to the complexity of the disease and its associated multi-organ affection. It is important to understand and monitor the impact of systemic sclerosis on the patients, provide them with high quality of care and to endorse the ownership of their disease process as early as possible to prepare them for the management this life-long illness.

**Objectives:** To assess the validity, reliability of a specific multidimensional patient self-reported questionnaire that can assess construct outcome measures of patients with systemic sclerosis/scleroderma.

**Methods:** The questionnaire was developed by integrating information obtained from patients suffering from systemic sclerosis as well as scleroderma based on the Rasch model. The questionnaire includes assessment of functional disability, quality of life, 0–10 numeric visual analogue scale (VAS) to rate the severity of the musculoskeletal pain, difficulty in breathing, gastrointestinal symptoms (e.g. swallowing difficulty/reflux/bloating/Faecal soilage/diarrhoea/constipation), Raynaud's phenomenon, fingers ulcers as well as the global assessment of the disease impact on the patient's life. In addition, the questionnaire includes 2 mannequins, one for self-reported body pains and the other one for self-reported skin tightness. Also there is a review of the possible comorbidities for the patient to tick in front of whatever he/she developed in the past month; as well as patient motivation. The questionnaire was completed by 52 consecutive patients with systemic sclerosis<sup>31</sup> and scleroderma.<sup>21</sup>

**Results:** The multidimensional PROMs questionnaire was reliable as demonstrated by a high-standardised alpha (0.894–0.993). The questionnaire items correlated significantly ( $p<0.01$ ) with clinical parameters of disease activity. Patient reported tender spots and skin tightness correlated significantly with the physician's as well as Rodnan skin scores (correlation coefficient 0.848 and 0.821 respectively). Changes in functional disability, quality of life and motivation scores showed significant variation ( $p<0.01$ ) with diseases activity status. The PROMs questionnaire showed also a high degree of comprehensibility (9.3).

**Conclusions:** The developed PROMs questionnaire is a reliable and valid instrument for assessment of patients suffering from systemic sclerosis/scleroderma. Being short, rapid and comprehensive, this adds more to its applicability. The data support the value of completion of the simple 2 pages patient questionnaire, which provides a quantitative written documented record by the patient, at each visit to the rheumatologist.

**Disclosure of Interest:** None declared

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**FRI0473** MPO-ANCA POSITIVITY IS RELATED TO INTERSTITIAL LUNG DISEASE IN SYSTEMIC SCLEROSIS

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**Background:** Recently, there were several reports that patients with systemic sclerosis (SSc) showed acute renal failure with anti-neutrophil cytoplasmic



Case	1	2	3	4	5	6	7	8
Sex	Female	Female	Female	Female	Female	Female	Female	Female
Age (years old)	73	62	34	64	64	59	58	75
Disease Duration (years)	6	30	9	3	17	26	6	25
Disease Type	Diffuse	Diffuse	Diffuse	Diffuse	Diffuse	Limited	Limited	Diffuse
Autoantibody	ARA	ACA	ATA	ATA	ATA	ATA	ND	ND
Digital Ulcer	-	+	-	-	-	-	-	+
Interstitial Lung Disease	+	+	+	+	+	+	+	+
CKD (eGFR<60 mL/min/1.73 m2)	+	-	-	-	-	-	-	-
MPO-ANCA titer (IU/mL)	14.2	10.0	63.8	38.7	9.1	11.5	20.1	13.9
PSL administration	+	+	-	+	+	+	+	-
PSL Dosage (mg/day)	1	5	-	10	10	2	6	-
Previous History of IVCY	+	-	-	+	+	-	+	-
Follow-up Period (months)	39	39	5	39	38	38	39	23
Newly Onset of AAV	-	-	+	-	-	-	-	-
Newly Onset of Acute Renal Dysfunction	+	-	+	-	-	-	-	-

ARA: anti RNA polymerase 3 antibody, ATA: anti topoisomerase 1 antibody, ACA: anti centromere antibody, ND: not detected, CKD: chronic kidney disease, PSL: prednisolone, IVCY: intravenous cyclophosphamide pulse therapy, ACEi: angiotensin converting enzyme inhibitor, ARB: angiotensin receptor blocker

antibody (ANCA) positivity. On the other hand, it is also reported that 7%–13% of patients with SSc revealed myeloperoxidase-ANCA (MPO-ANCA) positivity without vasculitis manifestation in 1990s, but their clinical characteristics were unclear. It is also unknown whether ANCA positivity leads to AAV or not in patients with SSc. It is important for physicians to clarify the characteristics of SSc patients with ANCA positivity, and answer the question whether they will shift ANCA-associated vasculitis (AAV).

**Objectives:** To assess the prevalence of ANCA positive patients with SSc, and clarify the characteristics of these patients.

**Methods:** We enrolled the 333 consecutive patients with SSc who visited our clinic during October 2014 to September 2015, all of who were checked MPO-ANCA using fluorescent-enzyme immune-assay. Clinical manifestation and laboratorial data were obtained from medical chart. The data were assessed by chi-square analysis and Welch's t test.

**Results:** Two patients were diagnosed AAV before October 2014. Eight patients (2.4%) revealed MPO-ANCA positivity without vasculitis manifestation. All of MPO-ANCA positive patients were female, and mean age and disease duration were 61.1 years old and 17.2 years, respectively, and there's no statistically significant differences comparing MPO-ANCA negative patients. As a result of evaluating clinical manifestations, we found that patients with MPO-ANCA positivity more frequently had interstitial lung disease than patients without MPO-ANCA positivity (87.5% vs. 36.7%,  $p < 0.01$ ). The clinical characteristics of 8 patients were shown in table 1. Only one patient out of 8 patients with MPO-ANCA positivity newly diagnosed AAV during mean of 33 months follow-up period.

**Conclusions:** The prevalence of MPO-ANCA positivity in SSc patients were lower than previous reports. MPO-ANCA positivity may be related to interstitial lung disease in SSc. MPO-ANCA positive patient may occasionally reveal AAV in the future, and careful observation are needed.

**Disclosure of Interest:** None declared

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## Vasculitis

FRI0474

### CLASSIFICATION OF SKIN INVOLVEMENT IN LEVAMISOLE-ADULTERATED COCAINE INDUCED VASCULOPATHY

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**Background:** Up to 88% of cocaine is tainted with levamisole, an anthelmintic withdrawn from the market due to toxicity. Since 2010 levamisole-adulterated cocaine induced vasculopathy (LACIV) patients, characterised by retiform purpura, ear necrosis, multisystemic compromise and positivity for multiple autoantibodies, have been reported. Knowing the pattern and the severity of skin involvement is essential in the approach of these patients.

**Objectives:** To describe the cutaneous manifestations of patients with LACIV and to propose a classification of skin involvement.

**Methods:** We describe the skin compromise of 30 patients with LACIV evaluated between December 2010 and May 2017. Based on this series and the review of the literature, we propose a classification according to the distribution and severity of the lesions.

**Results:** All patients were mestizo, median age of 31 (IQR 27–38), male:female ratio 5:1, time from symptoms to diagnosis 12 months (IQR 6–24). The most frequent clinical manifestations were skin lesions: ear necrosis (73%) and retiform purpura (83%) affecting the extensor part of the limbs, buttocks, face, and abdomen; sparing the scalp, palms and soles. Retiform purpura was classified in four grades according to distribution and severity (image). Skin biopsies revealed leukocytoclastic vasculitis (24%), pseudo-vasculitis (19%), thrombotic vasculopathy with leukocytoclastic vasculitis (19%), thrombotic vasculopathy with pseudo-vasculitis (19%), and pyoderma gangrenosum with vasculopathy (5%).

**Image: LACIV retiform purpura classification. A. Grade 1:** livedo reticularis or racemosa with incipient purpura (individual lesions  $\leq 1$  cm). **B. Grade 2:** More extended purpuric lesions which sometimes coalesce (individual lesions  $> 1$  cm). **C. Grade 3:** Purpuric lesions with haemorrhagic blisters. **D. Grade 4:** Deep purpuric lesions with associated ulceration.



**Conclusions:** Given the higher consumption of cocaine and its contamination with levamisole, the report of LACIV patients is increasing. A classification of the skin involvement in LACIV is proposed, according to the frequency of affection and the stratification of purpuric lesions in four degrees of severity. Cutaneous involvement is one of the pillars for the diagnosis and properly treatment, therefore a detailed description of distribution and characteristics of the lesions are fundamental for these patients care.

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**FRI0475 LUNG DAMAGE IN PATIENTS WITH MICROSCOPIC POLYANGIITIS**

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**Objectives:** We evaluated the frequency of clinical and CT features of lung damage in patients with microscopic polyangiitis (MPA).

**Methods:** We enrolled 97 patients with MPA, that was diagnosed according to CHCC2012. The median age at disease onset was 50.7±16.6 (M±SEM) years, the median duration of follow-up was 47.6±47.5 (M±SEM) months. 64 (66.0%) patients were ANCA-MPO-positive, 24 patients (24.7%) were ANCA-PR-3-positive, and 9 (9.3%) patients had undifferentiated ANCA. Diffuse alveolar haemorrhage (DAH) was diagnosed by the presence of dyspnea, hemoptysis, anaemia and pulmonary infiltrates on chest CT.

**Results:** Lung damage was diagnosed in 77 (79.4%) patients. 43 (55.8%) patients had pulmonary damage at the disease onset, while 34 (44.2%) patients developed signs of lung involvement within 8.0±4.1 (M±SEM) months. At baseline, the median pulmonary BVAS was 4.<sup>2, 6</sup> The interstitial changes occurred in more than half of cases at the onset of the disease. The most frequent CT-patterns included pulmonary infiltrates (n=49) and ground-glass opacity (n=39) (table 1). DAH developed in 30 (30.9%) patients, among them 15 (15.5%) had DAH at the onset of the disease.

The pulmonary fibrosis was the most common CT-pattern at the end of follow-up (52 patients). Notably, interstitial damages at the onset of disease were associated with the development of fibrotic changes (OR=4.7, 95% CI 1.7–12.9) and bronchiectasis (OR=9.8, 95% CI 1.2–78.3) at the end of follow-up. The median of pulmonary VDI was 1 (0;4) at the end of the follow up.

PR-3-positive group had higher occurrence of consolidations at the end of the follow-up as compared to patients with anti-MPO-antibodies (53.8% versus 16.0%, p=0.023).

Abnormality	N (%) of cases	
	At baseline (n=77)	At the end of follow-up (n=47)
Interstitial damage	68 (70.1%)	18 (18.6%)
Infiltrates	49 (50.5%)	0 (0%)
Ground-glass opacity	39 (40.2%)	16 (16.5%)
Consolidation	5 (5.2%)	8 (8.2%)
Bronchial wall thickening	10 (10.3%)	18 (18.6%)
Bronchiectasis	4 (4.1%)	18 (18.6%)
Bronchiolitis	3 (3.1%)	5 (5.2%)
Pleural lesions	11 (11.3%)	5 (5.2%)
Pleural effusion	12 (12.4%)	0 (0%)
Pleural thickening	3 (3.1%)	5 (5.2%)
Pulmonary fibrosis	14 (14.1%)	52 (53.6%)
Honeycombing	0 (0.0%)	4 (4.1%)
Atelectasis	3 (3.1%)	8 (8.2%)
Emphysema	0 (0.0%)	13 (13.4%)
Pulmonary hypertension	0 (0.0%)	7 (7.2%)

The pulmonary fibrosis was the most common CT-pattern at the end of follow-up (52 patients). Notably, interstitial damages at the onset of disease were associated with the development of fibrotic changes (OR=4.7, 95% CI 1.7–12.9) and bronchiectasis (OR=9.8, 95% CI 1.2–78.3) at the end of follow-up. The median of pulmonary VDI was 1 (0;4) at the end of the follow up.

PR-3-positive group had higher occurrence of consolidations at the end of the follow-up as compared to patients with anti-MPO-antibodies (53.8% versus 16.0%, p=0.023).

**Conclusions:** In patients with MPA, the CT signs of interstitial damage were usually reversible. However, they predicted a higher incidence of lung fibrosis and bronchiectasis at the end of follow-up. DAH occurred in one third of patients with MPA.

**Disclosure of Interest:** None declared

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**FRI0476 THE MYRIAD OF NEPHRITIS IN LEVAMISOLE-ADULTERATED COCAINE VASCULOPATHY**

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**Background:** Up to 88% of cocaine is tainted with levamisole, an anthelmintic withdrawn from the market due to toxicity. Since 2010 levamisole-adulterated

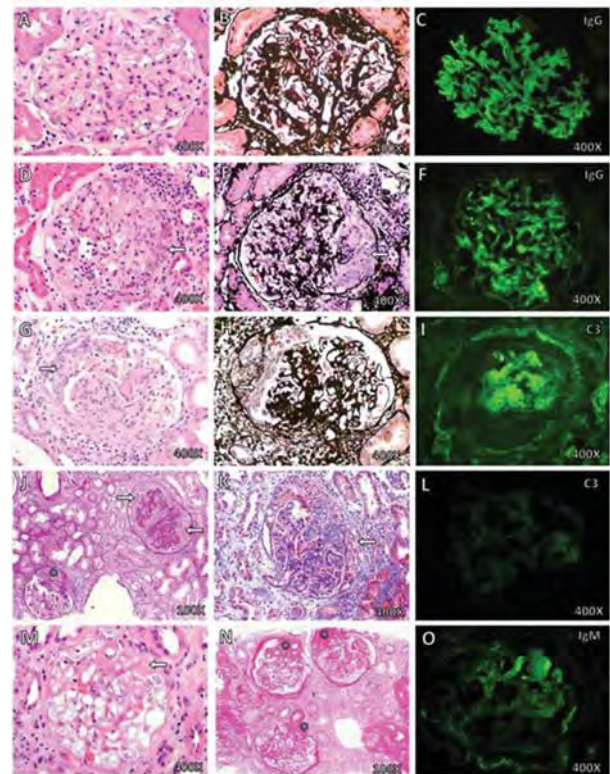
cocaine vasculopathy (LACIV) patients, characterised by retiform purpura, ear necrosis, multisystemic compromise and positivity for multiple autoantibodies, have been reported. Renal involvement is the most serious and heterogeneous manifestation.

**Objectives:** To describe the renal involvement of patients with LACIV.

**Methods:** We describe the renal manifestations of 30 patients with LACIV evaluated from December 2010 to May 2017.

**Results:** All patients were mestizo, median age of 31 (IQR 27–38), male:female ratio 5:1, time from symptoms to diagnosis 12 months (IQR 6–24). Nephritis found in 57%, creatinine elevation in 40%, median 1.85 mg/dl (IQR 1.2–4.0), 70% had proteinuria, median 3184 mg/day (IQR 552–5100), 58% in nephrotic-range; 88% had hematuria and 41% pyuria and cilindruria. Biopsy was performed in 7 patients (41%), showing immune complex mediated extracapillary glomerulonephritis (29%), membranous glomerulonephritis (29%), pauci-immune proliferative glomerulonephritis (14%), focal and segmental glomerulosclerosis (14%) and C3 mediated extracapillary glomerulonephritis (14%) (image). Three patients (10%) developed end-stage kidney disease.

**Image:** **A. Membranous glomerulonephritis:** HE: glomerular thickened capillary walls, mild mesangial cellularity increase. **B. GMS:** capillary wall thickening and spikes (arrow). **C. DIF:** strong and diffuse IgG deposits on capillary walls. **D. Immune complex mediated Extracapillary Focal Necrotizing Glomerulonephritis:** HE: endocapillary proliferation, epithelial crescent (arrow). **E. GMS:** capillary wall rupture next to the crescent (arrow). **F. DIF:** Mesangial strong and diffuse IgG deposits. **G. C3 mediated extracapillary glomerulonephritis:** HE: glomerular capillary narrowing, epithelial crescent (arrow). **H. GMS:** normal capillary networks, epithelial crescent (arrow). **I. DIF:** C3 strong and diffuse positivity. **J. Pauci-immune proliferative glomerulonephritis:** PAS: epithelial crescents (arrows and asterisk). **K. Trichrome:** epithelial crescent (arrow). **L. DIF for C3:** weak deposits on capillary tuft. Non-immune complexes. **M. Focal and segmental glomerulosclerosis:** HE: segmental sclerosing lesions (arrow). **N. PAS:** segmental sclerosing lesions (asterisks). **O. DIF for IgM:** nonspecific positivity on a sclerotic segment.



**Conclusions:** Although skin manifestations are the most characteristic and prevalent features in LIVEN, renal involvement is frequent, clinically and histologically heterogeneous, and potentially serious. The great heterogeneity on the histopathological findings suggests the participation of different physio-pathological mechanisms, establishing renal biopsy as necessary to identify the type of nephropathy and thus, optimal guidance of therapy.

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**FRI0477 IMMUNOGENICITY OF INFLIXIMAB AMONG PATIENTS WITH BEHÇET'S SYNDROME: A CONTROLLED STUDY**

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**Background:** Immunogenicity of anti-TNFs has been recognised as an important problem that may cause loss of efficacy and adverse events such as infusion reactions. Anti-TNFs are being increasingly used among patients with Behçet's syndrome (BS).

**Objectives:** We aimed to investigate the prevalence of anti-drug antibodies against infliximab (IFX) in patients with BS together with controls.

**Methods:** We collected serum samples from 66 consecutive BS patients (51 M, 15 F and mean age 37±9 years) who were treated with IFX. IFX was used for eye involvement in 43, vascular involvement in 12, nervous system involvement in 8 and arthritis in 2 patients. Additionally, 53 ankylosing spondylitis (AS), 25 Crohn's disease (CD) and 27 rheumatoid arthritis (RA) patients, and 31 healthy subjects were included as controls. We included patients who had received at least 4 cycles of IFX. Samples were collected just before an infusion, stored at -80°C until analysis, and serum IFX trough levels and anti-IFX antibodies were measured by ELISA at the same time. We used a cut-off value of 1 µg/mL for serum IFX trough level, extrapolating from RA studies. After serum sampling, we continued to follow up patients.

**Results:** Anti-IFX antibodies were detected in 4 (6%) BS, 5 (18.5%) RA, 3 (12%) CD, and 1 (2%) AS patient, and in none of the healthy subjects. The mean number of IFX cycles was 19±14 in BS, 21±13 in RA, 19±21 in CD, and 33±18 in AS patients. Allergic reactions had occurred in 9 (14%) BS, 6 (22%) RA, 5 (20%) CD, and 4 (7.5%) AS patients. 3/6 RA patients and 3/5 CD patients who had experienced an allergic reaction had anti-IFX antibodies whereas none of BS and AS patients did.

The median serum IFX trough level was significantly lower in patients with anti-IFX antibodies compared to those without antibodies (2.32 (IQR: 0.6–3.6) vs 3.35 (IQR: 1.63–5.6; p=0.019). The serum IFX trough level was lower than the cut off value in 6/13 patients with anti-IFX antibodies and in 25/158 without anti-IFX antibodies (46% vs 16%; p=0.015).

We were able to get samples before at least 2 consecutive infusions in 27 BS patients and the presence of anti-IFX antibodies was consistent across the samples in all of these patients. We were able to get samples before the infusion and at week 2 in 5 BS patients. Serum IFX level was below 1 µg/mL before IFX and above 1 µg/mL at week 2 in all of these 5 patients.

During a median follow up of 1.5 years, 2/4 BS patients with anti-IFX antibodies had flares. Among the 62 patients without anti-IFX antibodies, 49 are still on IFX and IFX was stopped due to remission in 12 and due to infusion reaction in one patient. Overall, 5 infusion reactions occurred during the follow up (4 without anti-IFX antibodies and 1 with anti-IFX antibodies; 6.5% vs 25%).

**Conclusions:** Immunogenicity does not seem to be an important problem in BS patients treated with IFX. The frequency of anti-IFX antibodies was lower than RA and CD patients. This might be related to concomitant immunosuppressive and corticosteroid use among BS patients. The presence of anti-IFX antibodies may not be associated with efficacy loss in BS. However, longer follow-up is needed to make that statement as BS has a relapsing-remitting course.

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**FRI0478 OCCURRENCE OF GENUINE VASCULITIS IN PATIENTS WITH EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS**

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**Background:** Many patients with eosinophilic granulomatosis with polyangiitis (EGPA) lack a "vasculitic" phenotype and/or are ANCA negative. Recently, the Groupe d'Etudes et de Recherche sur les Maladies Orphelines Pulmonaires developed a revised nomenclature for EGPA and proposed to differentiate it from hypereosinophilic asthma with systemic (nonvasculitic) manifestations (HASM).

**Objectives:** To evaluate the occurrence of genuine polyangiitis and HASM in a cohort of patients with EGPA.

**Methods:** We retrospectively studied the medical records of patients with EGPA that fulfilled the classification criteria of the American College of Rheumatology. Patients with genuine vasculitis were identified by at least one of the following criteria: <sup>1</sup> definite vasculitis feature as defined: biopsy-proven necrotizing vasculitis of any organ, biopsy-proven necrotizing glomerulonephritis or crescentic glomerulonephritis, alveolar haemorrhage, palpable purpura, myocardial infarction due to proven coronary arteritis; <sup>2</sup> strong surrogate of vasculitis as defined: haematuria associated with red casts or ≥10% dysmorphic erythrocytes, or haematuria and 2 +proteinuria on urinalysis related to the systemic disease; and any organ manifestation other than ENT or bronchopulmonary manifestation associated with leukocytoclastic capillaritis and/or eosinophilic infiltration of the arterial wall; <sup>3</sup> mononeuritis multiplex; <sup>4</sup> ANCA with at least one extra-thoracic non-ENT manifestation of disease.

**Results:** We followed 68 patients with EGPA for a mean ±SD of 6.3±6.5 years (587.7 patient-years). There were 19 males and 49 females. Their mean ±SD age was 49.5±13.8 years. In 18 patients (26.5%) with EGPA diagnosis was revised in favour of HASM using the new criteria (table 1). Notably, 19 of 50 patients (38%) with genuine polyangiitis were ANCA-negative but have histological evidence or clinical signs (rapidly progressive glomerulonephritis in 1, mononeuritis multiplex 7, palpable purpura in 5) of definite vasculitis. The majority of patients in both groups were females of similar age at disease onset. The occurrence of constitutional symptoms, except myalgia, nasal involvement, cardiovascular and pulmonary manifestations did not differ between patients with genuine polyangiitis and HASM. However, patients with EGPA usually required more intensive immunosuppressive treatment, including cyclophosphamide, while monotherapy with moderate to high dose corticosteroids was adequate for the majority of patients with HASM.

Table 1 Clinical and demographic characteristics of patients with genuine EGPA and HASM

	All, n=68	HASM, n=18	EGPA, n=50	p
Age at diagnosis, years	49.5 (36; 56)	50 (35; 55)	49.0 (37; 57)	0.91
Females, n (%)	49 (72.1)	17 (94.4)	32 (64.0)	0.014
Follow up, months	52.5 (22; 89)	57 (33; 92)	49.0 (19; 83)	0.44
Asthma, n (%)	64 (94.1)	16 (88.9)	48 (96.0)	0.28
Chronic rhinosinusitis, n (%)	56 (82.4)	14 (77.8)	42 (84.0)	0.72
Nasal polypsis, n (%)	28 (41.2)	6 (33.3)	22 (44.0)	0.58
<b>General manifestation</b>				
Fever >38°, n (%)	49 (72.0)	11 (61.1)	38 (76.0)	0.24
Weight loss, n (%)	19 (27.9)	5 (27.8)	14 (28.0)	1.00
Myalgia, n (%)	32 (47.1)	4 (22.2)	28 (56.0)	0.026
Arthralgia, n (%)	40 (58.8)	13 (72.2)	27 (54.0)	0.26
Arthritis, n (%)	17 (25.0)	4 (22.2)	13 (26.0)	1.00
<b>Definite vasculitis features</b>				
Alveolar hemorrhage, n (%)	1 (1.5)	0	1 (2.0)	1.00
Purpura, n (%)	13 (19.1)	0	13 (26.0)	0.015
<b>Strong vasculitis surrogates</b>				
Haematuria, n (%)	11 (16.2)	1 (5.6)	10 (20.0)	0.26
<b>Other features of polyangiitis</b>				
Mononeuritis multiplex, n (%)	19 (27.9)	0	16 (32.0)	0.001
ANCA, n (%)	31 (45.6)	0	31 (62.0)	<0.0001
<b>Cardiac and vascular manifestations</b>				
Pericarditis (echocardiography and/or CT), n (%)	11 (16.2)	2 (11.1)	9 (18.0)	0.71
Myocarditis, n (%)	9 (13.2)	1 (5.6)	8 (16.0)	0.43
Venous thrombo-embolism, n (%)	7 (10.3)	0	7 (14.0)	0.18
<b>Renal manifestation</b>				
Renal disease, n (%)	6 (10.3)	0	6 (12.0)	0.18
Proteinuria, n (%)	4 (5.9)	0	4 (8.5)	0.30
Urinary syndrome, n (%)	14 (20.6)	0	14 (28.0)	0.014
The increase in creatinine, n (%)	5 (7.4)	0	5 (10)	0.31
Other glomerulonephritis, n (%)	3 (4.4)	0	3 (6.0)	0.56
<b>Neurologic manifestations</b>				
Peripheral neuropathy, n (%)	50 (73.5)	8 (44.4)	42 (84.0)	0.004
<b>Cutaneous manifestations</b>				
Livedo, n (%)	3 (4.4)	1 (5.6)	2 (4.0)	1.00
Urticaria, n (%)	7 (10.3)	3 (16.7)	4 (8.0)	0.37
Erythema, n (%)	12 (17.7)	3 (16.7)	9 (18.0)	1.00
Papules, n (%)	6 (8.8)	2 (11.1)	4 (8.0)	0.65
<b>Gastro-intestinal manifestations</b>				
Eosinophilic gastroenteritis, n (%)	5 (7.4)	1 (5.6)	4 (8.0)	1.00
Abdominal pain, n (%)	6 (8.8)	0	6 (12.0)	0.18
<b>Other manifestations</b>				
Lung infiltrates, n (%)	35 (51.5)	12 (66.7)	23 (46.0)	0.17
Pleural effusion, n (%)	6 (8.8)	1 (5.6)	5 (10.0)	1.00
Perforation of the nasal septum, n (%)	5 (7.4)	0	5 (10.0)	0.31

**Conclusions:** At least a quarter of patients with EGPA classified according to the ACR criteria do not have genuine polyangiitis. The revised criteria of EGPA and HASM may have a significant value for choosing treatment options.

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### FRI0479 PRIMARY CENTRAL NERVOUS SYSTEM VASCULITIS WITH TUMOR-LIKE PRESENTATION

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**Background:** Primary central nervous system vasculitis (PCNSV) rarely presents as a tumor-like mass lesion (ML).

**Objectives:** The aim of this study was to determine the frequency of ML in a large cohort of patients with PCNSV and compare the presenting clinical, laboratory, and imaging features in those with ML to those without.

**Methods:** We retrospectively studied a cohort of 191 consecutive patients with PCNSV who were seen at the Mayo Clinic, Rochester, MN over a 35 year period. The diagnosis of PCNSV was based on brain/spinal cord biopsy or cerebral angiography. We compared PCNSV patients with tumor-like presentation to those without.

**Results:** 13/191 (6.8%) patients had tumor-like presentation. In all 13 patients PCNSV diagnosis was established by cerebral biopsy (stereotactic in 10, open-wedge in 3). 4 patients had cerebral angiography, and vasculitis was suggested in one patient. A granulomatous inflammatory histologic pattern was found in 11 biopsies, accompanied by vascular deposits of  $\beta$ -amyloid peptide in 7. In the other 2 biopsies a lymphocytic vasculitis was observed. The 13 patients with tumor-like presentation were compared with the 178 patients without. The patients with ML were more frequently males (77% vs 44%,  $p=0.04$ ), were less likely to present with transient ischaemic attacks (TIA) (0 vs 27.5%,  $p=0.023$ ) and more likely to present with seizures (46% vs 17%,  $p=0.022$ ) at presentation. No significant differences in the CSF findings and ESR levels (normal in 100% and 82% of the patients, respectively) at diagnosis were observed in the two groups. Intracerebral gadolinium-enhancing lesions were more frequently observed in patients with ML (46% vs 21%,  $p=0.07$ ), while meningeal gadolinium-enhancing lesions were equally observed (31% vs 20%,  $p=0.48$ ). The frequencies of PCNSV recurrence (38% vs 29%), patients not requiring therapy at last follow-up (15% vs 25%), response to therapy (100% vs 74%), and poor outcomes (modified Rankin disability score  $\geq 4$ ) at last followup (8% vs 26%) were not significantly different in the two groups. No differences in survival were observed between the 2 groups ( $p=0.57$ ). Considering all 191 patients, univariate Cox proportional hazards modelling showed an increased mortality rate in those with increasing age (hazard ratio, HR, 1.4), cerebral infarction on initial MRI (HR 2.95), and angiographic large vessel involvement (HR 3.2), while mortality rate was lower in those with gadolinium-enhancing lesions on MRI (HR=0.3).

**Conclusions:** Tumor-like presentation represents a subset of PCNSV characterised by vascular deposits of  $\beta$ -amyloid at biopsy, seizures at presentation, and gadolinium-enhancing cerebral lesions on MRI. As in PCNSV without ML, treatment response and prognosis was favourable in most patients.

**Disclosure of Interest:** None declared

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### FRI0480 TOCILIZUMAB MONO-THERAPY FOR POLYMYALGIA RHEUMATICA ~ RESULTS OF 104-WEEK TREATMENT OF A PROSPECTIVE, SINGLE-CENTRE, OPEN TRIAL

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**Background:** Polymyalgia rheumatic (PMR) is a chronic inflammatory rheumatic disease in the elderly people. Glucocorticoid (GC) is still definitely a mainstay for the treatment of PMR, but long-term GC therapy is a major risk factor of osteoporotic fractures, diabetes, hyperlipidemia, cardio-cerebral vascular events, glaucoma, etc. So GC-free treatment strategies for PMR are awaited for some PMR patients with these comorbidities. IL-6 is involved in the pathogenesis of PMR and several case reports have already shown the efficacy of tocilizumab (TCZ), anti-IL-6 receptor antibody, in PMR patients<sup>1,2</sup> and there is a report of TCZ mono-therapy as the first-line therapy in PMR<sup>3</sup>.

**Objectives:** To assess the efficacy and safety of TCZ mono-therapy for PMR

**Methods:** Thirteen PMR patients (male 3, female 10) who had been diagnosed by 2012 ACR/EULAR classification criteria from Jan 2013 to Feb 2015 were enrolled in our single-centre, prospective study (IRB application No. 638, UMIN No. 000008812) after obtaining the written informed consent. TCZ (8 mg/kg) was administered biweekly for the first 8 weeks (5 infusions) and every 4 weeks thereafter for 40 weeks (total 15 infusions). ESR, CRP, patient's global health assessed by visual analogue scale (VAS), PMR activity score<sup>4</sup> were evaluated every 4 week prospectively. Primary endpoint was remission rate at week 52. Remission was defined as PMR activity score less than 1.5<sup>4</sup>. Patients were followed up for another one year without any treatment and flare rate was assessed at week 104.

**Results:** Baseline patients' characteristics revealed various kinds of comorbidities in 11 patients; hypertension in 7, hyperlipidemia in 5, diabetes mellitus in 3,

osteoporotic vertebral fractures in 2, history of angina pectoris in 1, history of brain infarction in 1, history of hematemesis due to NSAID ulcer in 1 and glaucoma in one patient. Nine patients could complete this 104 week trial and all 9 patients could achieve remission at week 52 and 8 of 9 patients fulfilled remission criteria at week 104. Two patients discontinued TCZ because of no response at week 6 (No.1) and week 16 (No. 8) respectively. One patient (No.2), who were in clinical remission of PMR, dropped out from this study due to pemphigoid at week 50 and received GC therapy. Patient No. 12 abandoned TCZ at week 12 because of lung infiltrates although she was treated successfully with TCZ mono-therapy, and she had been in remission without any treatment until week 104. The other 3 patients could obtain remission with GC therapy at week 52. There were no serious adverse events during 104 week treatment period.

**Conclusions:** TCZ mono-therapy was effective in most (9 out of 13) PMR patients although response was not so rapid as compared to GC. TCZ mono-therapy may be a good alternative therapy instead of GC for elderly patients with various comorbidities.

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### FRI0481 GIANT CELL ARTERITIS AND INFLAMMATORY BOWEL DISEASE – IS THERE A CONNEXION? RESULTS FROM A POPULATION-BASED STUDY

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**Background:** Giant cell arteritis (GCA) is an autoimmune disorder which primarily affects large vessels, whilst inflammatory bowel disease (IBD), which includes Crohn's disease (CD) and ulcerative colitis (UC), mainly targets the gut. Co-existence of the two maladies has been reported sporadically in the literature<sup>1–3</sup>.

**Objectives:** The purpose of this study was to assess the authenticity of such an association in a large, cross-sectional study.

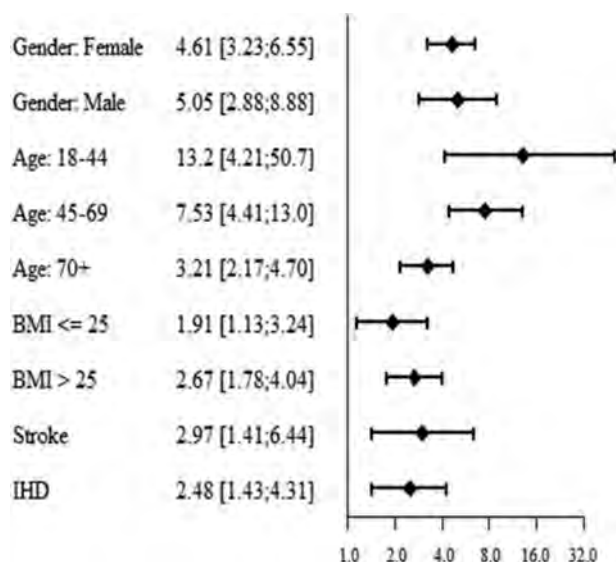
**Methods:** Utilising data derived from the Clalit Health Services' registry, the largest health maintenance organisation in Israel, we compared the proportion of CD and UC in GCA patients with age- and gender-matched controls. Univariate analysis was performed using Chi-square and student *t*-test and a multivariate analysis was performed using a logistic regression model.

**Results:** The study included 5,657 GCA patients and 28 298 age- and gender-matched controls. GCA patients had a significantly increased proportion of both CD and UC in comparison with controls (0.81% vs. 0.12% and 0.69% vs. 0.2%,  $p$ -value<0.001, respectively). The strength of the association between GCA and IBD was negatively correlated with the patients' age; thus the association was most robust amongst younger patients aged 18–44 (OR=13.2, figure 1). The association between GCA and IBD remained significant when evaluated independently of confounding factors (OR=2.367,  $p$ -value<0.001, table 1).

**Abstract FRI0481 – Table 1.** Multivariate logistic regression of covariates associated with IBD

Characteristic	OR	CI	P
Age	0.99	0.98–1	0.49
Gender	1.25	0.87–	0.22
(Female)		1.84	
BMI	0.95	0.92–	0.007
		0.98	
SES:			
Medium vs. Low	1.42	0.94–2.1	0.1
High vs. Low	1.74	1.13–2.69	0.012
GCA	2.36	1.71–3.27	<0.001

IBD: Inflammatory bowel disease; BMI: Body Mass Index, kg/m<sup>2</sup>; SES: Socioeconomic status; GCA: Giant Cell Arteritis



Abstract FRI0481 – Figure 1. Interactions between GCA, IBD and covariates

**Conclusions:** The probability that GCA patients may also suffer from IBD is increased in comparison with age- and gender-matched controls. Our findings indicate that this association is most prominent in younger patients (<70). Screening for IBD amongst GCA patients in this age group may be warranted.

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#### FRI0482 CAUSES OF DEATH IN CONNECTIVE TISSUE DISEASE (CTD'S) AND VASCULITIDES; DATA FROM THE NORWEGIAN CONNECTIVE TISSUE DISEASES AND VASCULITIS REGISTRY (NOSVAR)

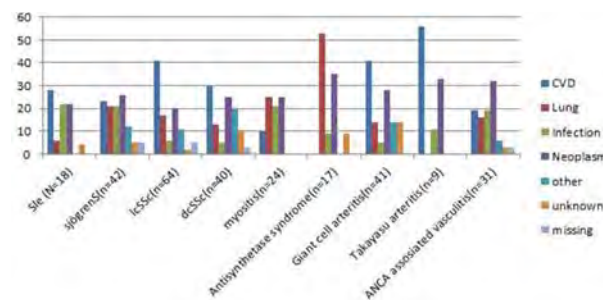
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**Background:** Mortality as an outcome of disease's severity and causes of death can give extended insight into the nature of each specific diagnose and highlight distinct needs for monitoring. In connective tissue diseases (CTD) and systemic vasculitides, mortality and causes of death have been studied within most single diseases, but with heterogeneity of the studies and widely varying results. Studies applying similar methods across the diagnoses are lacking. Consequently, it is difficult to compare causes of death between the different diagnoses.<sup>1</sup>

**Objectives:** To identify the causes of death within different CTDs and systemic vasculitides.

**Methods:** We performed a prospective, observational, controlled study between 1999 and 2017 of adult patients (at least 18 years of age) with diagnosis of CTD or vasculitides. All patients were included in the Norwegian connective tissue disease and vasculitis Registry (NOSVAR). In total, 2140 patients were diagnosed and followed up until death or study end by April 31th 2017. To avoid bias by selection, we included only incident cases, excluding patients with diagnoses set prior to 1999. Moreover, cases with a disease course not consistent with the initial diagnoses were excluded. Causes of death were identified by linking NOSVAR to the Norwegian Causes of Death Registry and by reviewing hospital charts. We divided the causes of death into the main groups of cardiovascular diseases (CVD), neoplasms, chronic respiratory disease (CRD), infections and other (gastrointestinal, renal insufficiency and trauma). To compare causes of death to the general population we used data from WHO Mortality Database, Causes of death.<sup>2</sup>

**Results:** During a mean (SD) follow-up time of 9.2 years (4.7), 279 patients (13%) deceased. The major causes of death were, in descending order of frequency; CVD (27%), neoplasms (25%), CRD (16%), infections (11%), gastrointestinal manifestations (4%), renal insufficiency (2%). Data from the general population, adjusted for age and gender, showed that deaths by CVD, CRD and infections were more prevalent among the patients.<sup>2</sup> The leading causes of death are shown in figure 1. In Takayasu arteritis and ISSc, CVD was the most frequent cause of death; (56%) and (41%), respectively. More than half of the patients (53%) with antisynthetase syndrome died of CRD. Those with dermatomyositis died most frequently of neoplasms (50%).



**Conclusions:** Compared to general population, patients with CTD and vasculitis died more often of CVD, CRD and infections. CVD as a cause of death was most prevalent in patients with Takayasu arteritis, giant cell arteritis and systemic sclerosis, while neoplasm was the major cause of death in dermatomyositis. In antisynthetase syndrome, both CRD was the major causes of death. The study gives the clinician valuable information on how to monitoring the different CTDs and vasculitidis regarding serious outcome.

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#### FRI0483 SULFASALAZINE AS A POTENTIAL TREATMENT FOR IGA-VASCULITIS (HENOCH-SCHÖNLEIN PURPURA) IN ADULTS

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**Background:** Primary IgA-vasculitis and inflammatory bowel diseases (IBD) share many clinical, endoscopic, and radiological signs. It may suggest a common pathogenetic background for both pathological conditions. While sulfasalazine (SASP) is one of the well-known potential agents able to improve symptoms in IBD, the usefulness of SASP in treatment of the primary IgA-vasculitis remains unclear.

**Objectives:** Retrospective study to assess a therapeutic value of the SASP in primary IgA-vasculitis.

**Methods:** Totally 78 adult patients with primary IgA-vasculitis were enrolled in this study. Diagnosis was made on the basis of EULAR/PRES criteria<sup>1</sup> after thorough screening to exclude a secondary nature of the disease, including colonoscopy. Purpura/petechia was present in all patients being mandatory diagnostic criterion. Arthritis/arthralgia was seen in 48 patients (61,5%). There were no patients with abdominal syndrome just before enrollment, although 46 (59%) patients had transient abdominal pains in the history. Mild to moderate signs of renal involvement (hematuria and/or proteinuria) was seen in 35 (45%) patients without renal impairment. There were 20 (25%) drug-naïve patients, 40 (51%) patients after unsuccessful immunosuppressive treatment and 18 (23%) patients failed to respond to anticoagulants or antiplatelet agents. Initially SASP was prescribed in a daily dose 1 g followed with gradual titrating up to the 2 g/day depending on tolerability and clinical response. Most patients (96%) have been taking SASP longer than 6 month and about a half of the patients (56%) – longer than year. The longest treatment was 5 years.

**Results:** Complete clinical remission of the skin rash was achieved in 48 patients (58,9%). In 27 patients (35%), there was partial improvement of the skin eruptions, characterised with less quantity of the skin purpura or longer periods free of

symptoms (see table 1). Four patients failed to improve at all. Persistent remission of the arthritis/arthralgia was found in 41 patients (85%). One patient did not improve. Complete resolution of the urinary abnormalities were registered in 14 patients (40%), improvement – in 17 cases (48.5%), further deterioration in 4 patients (11.5%).

There were side effects in 13 patients (16%). In 4 (5.1%) cases there were headache and nausea, respectively. In 2 (2.5%) cases treatment was accompanied with skin itching and urticarial rash. Most severe complication presented with reversible cytolysis, characterised with increase of AST and ALT up to the 2–5 normal limits in 3 cases (2.5%).

**Abstract FRI0483 – Table 1.** Clinical response to SASP treatment in primary IgA-vasculitis (n=78)

Clinical features	Complete remission		Partial remission		No response		Worsening	
	n	%	n	%	n	%	n	%
Skin purpura (n=78)	46	58.9	27	35	4	5.1	-	-
arthritis or arthralgia (n=48)	41	85	6	13	1	1.2	-	-
hematuria and/or proteinuria (n=35)	14	40	17	48.5	-	-	4	11.5

**Conclusions:** To our knowledge, this is the first experience of SASP in treatment of primary IgA-vasculitis not reported before. Preliminary results look promising and worthy of further evaluation.

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#### FRI0484 OVERALL SURVIVAL AND MORTALITY RISK FACTORS IN TAKAYASU'S ARTERITIS: A MULTICENTER STUDY OF 318 PATIENTS

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**Background:** Takayasu arteritis (TA) is a rare large vessel vasculitis of unknown origin. Main epidemiological data come from Asia. TA significantly increases morbidity and mortality and there is an unmet need to identify patients with higher complications and mortality risks.

**Objectives:** To report the long term mortality in Takayasu arteritis (TA) and to identify risk factors associated with mortality.

**Methods:** We analysed epidemiological data according to gender and ethnic origins, the causes of death, and the factors associated with mortality in a cohort of 318 patients [median age at diagnosis was 36<sup>25–47</sup> years and 276 (86%) patients were women] fulfilling American College of Rheumatology and Ishikawa criteria of TA. Overall survival and factors associated with death and vascular complications were identified. A prognostic score for death and vascular complications was elaborated based on a multivariate model.

**Results:** In a cohort of 318 patients, men tended to be more frequently smokers (42% vs. 26%, p=0.07), had more frequently cardiac insufficiency (14% vs. 9%, p=0.034), but less frequently aneurysmal lesion (51% vs. 76%, p=0.005). Ethnic origins were Caucasian/White (n=87, 37%), North-Africa (n=73, 31%), Black (n=56, 18%), and other (n=17, 5%). White patients were more frequently smokers and diagnosis was more frequently made after 35 years. Black patients had less frequently a supra-aortic vessels involvement and more frequently a vessel wall thickening at diagnosis (78% vs. 62%, p=0.033).

Among 318 TA patients, 16 (5%) died after a median follow-up of 6.1 years. The mean (±SD) age at death was 38<sup>25–47</sup> years with 88% of women. Main causes of death included mesenteric ischemia (n=4, 25%), aortic aneurysm rupture (n=4, 25%), sudden death (n=3, 19%), septic shock (n=3, 19%), pulmonary embolism (n=1, 6%), and cardiogenic shock (n=1, 6%). One, five, and ten years' overall survival were 98.9% [97.8–100], 98.1% [96.4–99.8], and 96.1% [93.4–98.9%], respectively. Factors associated with mortality were ethnic origin (White 9.5% vs. North Africa 7.1% vs. Black 0%, p=0.049), and tobacco smokers (10.8% vs. 4.2%, p=0.002).

We define high risk patients for death and vascular complications according to the presence of two of the following factors (i.e a progressive clinical course, thoracic aorta involvement and/or retinopathy) elaborated based on the multivariate model. The probability of death and complication free survival at five years was 78.4% (69.4–88.6) and 51.5% (38.3–69.2) (p=0.001) in the low risk and high risk group, respectively.

**Conclusions:** The overall mortality in our Takayasu cohort was 5% after a median follow-up of 6.1 years. Caucasian and tobacco smokers were associated with mortality in TA. We developed a simple and useful prognosis score to identify patients at risk for vascular complication and death.

**Disclosure of Interest:** None declared

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#### FRI0485 PHENOTYPE OF ANCA ASSOCIATED VASCULITIS ASSOCIATES WITH MAJOR CARDIOVASCULAR EVENTS: A RETROSPECTIVE OBSERVATIONAL STUDY FROM THE LEEDS VASCULITIS COHORT

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**Background:** Patients with ANCA-associated vasculitides (AAV) are at increased risk of cardiovascular (CV) disease than the general population. The factors associated with CV involvement in AAV are poorly understood.

**Objectives:** To explore whether patient and disease-related characteristics associated with CV disease from a single-centre AAV cohort.

**Methods:** Medical records from 145 patients with AAV were reviewed and patients' diagnoses reclassified according to a validated algorithm.<sup>1</sup> CV events (CVE) were defined as myocardial infarction, cerebrovascular accident, thromboembolic event, heart failure, or death/hospitalisation due to CV cause. Time to first CVE was calculated; patients without CVE were censored at most recent clinical follow-up. Data on CV risk factors (hypertension, hyperlipidaemia, diabetes mellitus, chronic kidney disease stage III or higher) were collected. Putative predictors included age, sex, diagnosis (GPA, MPA, EGPA, unclassifiable AAV – UAAV), ANCA (absent, PR3, MPO), number of BVAS items, prior CV disease and number of CV risk factors. Cox proportional hazards regression was used to assess the relationship between CVE and predictors. In this exploratory analysis we used p<0.10 to indicate potential associations.

**Results:** 122 patients who had been followed up for between 6 months and 23 years were included in the analysis. 11/122 patients (10%) had prior history of CV disease. 17 patients (14%) experienced a CVE within median (IQR) 5.8 (1.4, 7.6) years of diagnosis. Univariable analyses indicated older age at diagnosis, MPA and prior CVD were associated with increased risk of CVE, and that those with UAAV were at decreased risk compared to GPA. With the exception of previous CVD an adjusted model confirmed the same associations (table 1).

Variable	No CVE n=105	CVE n=17	Unadjusted HR (90% CI)	Adjusted HR (90% CI)	P value
Age: mean (SD)	49 (17)	57 (13)	1.04 (1.01–1.07)	1.03 (1.00–1.06)	0.049
Female:% (n)	55% (58)	41% <sup>7</sup>	0.76 (0.34–1.67)	0.69 (0.28–1.64)	0.488
Diagnosis:% (n)					
GPA	54% (57)	65% <sup>7</sup>	Ref.	Ref.	0.370
MPA	13% <sup>14</sup>	6% <sup>1</sup>	0.71 (0.12–2.44)	0.38 (0.05–2.21)	0.031
EGPA	10% <sup>10</sup>	29% <sup>5</sup>	3.37 (1.34–7.76)	4.81 (1.46–15.36)	0.071
UAAV	23% <sup>24</sup>	- (0)	0.15 (0.00–0.91)	0.09 (0.00–0.83)	
ANCA:% (n)					
Absent	25% <sup>26</sup>	12% <sup>2</sup>	Ref.	Ref.	0.259
PR3	45% <sup>47</sup>	65% <sup>11</sup>	1.65 (0.58–6.25)	0.33 (0.08–1.79)	0.207
MPO	30% <sup>32</sup>	24% <sup>4</sup>	1.62 (0.46–6.77)	0.27 (0.05–1.52)	
BVAS items: median (IQR)	4 (3–5)	4 (4–5)	1.26 (0.96–1.65)	1.35 (0.95–1.92)	0.156
Prior CVD:% (n)	10% <sup>11</sup>	18% <sup>3</sup>	1.28 (1.17–9.23)	2.58 (0.72–8.03)	0.211
CV risk factors: median (IQR)	1 (0–2)	1 (0–2)	0.92 (0.59–1.39)	0.64 (0.36–1.04)	0.135

**Conclusions:** This exploratory analysis suggests that, among AAV, MPA may have a higher CV risk, whereas UAAV may be associated with a decreased risk. Along with ANCA status, AAV phenotype may inform future CV risk reduction interventions in AAV.



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**Disclosure of Interest:** None declared

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### FRI0486 POTENTIAL PREDICTORS OF VISCERAL INVOLVEMENT IN ADULT IGA VASCULITIS

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**Background:** Predictors of severity of visceral involvement in acute adult IgA vasculitis (IgAV) are poorly recognised.

**Objectives:** The aim of our study was to evaluate the role of smoking and extension of skin lesions on the visceral manifestations of acute adult IgA vasculitis.

**Methods:** We analysed medical records of adult, histologically proven IgAV cases, diagnosed at our secondary/tertiary rheumatology centre between 1 January 2010 and 31 December 2017. Purpura was defined as generalised when skin lesions extended above the waistline. Gastrointestinal (GI) disease was considered severe in case of bloody diarrhoea, ileus or bowel perforation. Renal disease was defined as severe when nephritic syndrome with acute renal failure or nephrotic syndrome developed.

**Results:** During the study period we identified 230 incident IgAV cases (57.8% males, median (IQR) age 64.8 (45.6–77.3) years). Ninety-eight (42.6%) patients were smokers (56 past and 42 current). Skin, joint, GI, renal and involvement were present in 230 (generalised purpura in 114 (49.6%), necrotizing in 108 (47.0%), 93 (40.4%), 70 (30.4%; severe in 17) and 102 (44.3%; severe in 27) patients, respectively. Smoking was associated with renal disease (RR 1.3 (95% CI 1.0–1.8)) and its severity (RR 3.2 (95%CI 1.5–7.0)), but not with GI involvement or its severity. Generalised purpura was associated with GI involvement (RR 2.9 (95%CI 1.8–4.7) and its severity (RR 3.3 (95%CI 1.1–9.8)), as well as with renal involvement (RR 1.4 (95%CI 1.0–1.9)). Data of combined influence of smoking and purpura extension on visceral involvement are presented in table 1. The risk of severe renal involvement in IgAV was the highest in ever-smoker with generalised purpura (RR 8.1 (95%CI 1.9–34.7) in comparison to IgAV non-smoker with localised purpura).

Table 1 The influence of smoking and purpura extension on visceral involvement in IgAV

Visceral involvement	Nonsmokers with localized purpura	Ever-smokers with localized purpura	Nonsmokers with generalized purpura	Ever-smokers with generalized purpura
Number of cases	69	47	63	51
GI (%)	13.0	19.1	47.6	43.1
Severe GI (%)	2.9	4.3	11.1	11.8
Renal (%)	30.4	46.8	47.6	56.9
Severe renal (%)	2.9	14.9	9.5	23.5

Legend: GI gastrointestinal; severe GI involvement: bloody diarrhea or ileus or bowel perforation; severe renal involvement: nephritic syndrome with acute renal failure or nephrotic syndrome;

**Conclusions:** Smoking and generalised purpura were associated with visceral involvement in adult IgAV.

**Disclosure of Interest:** None declared

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### FRI0487 SERUM INTERLEUKIN-6 LEVELS IN ANTINEUTROPHIL CYTOPLASMIC ANTIBODY-ASSOCIATED VASCULITIS

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**Background:** The deregulated overproduction of interleukin (IL)–6 has been implicated in several inflammatory and antibody-mediated autoimmune diseases.

**Objectives:** To investigate serum IL-6 levels (sIL-6) during active disease, remission, and relapse in antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV), and to explore the association of changes in sIL-6 with repopulation of blood B cells and disease relapse.

**Methods:** sIL-6 levels (explanatory variable) were measured longitudinally over 18 months in 78 patients with AAV enrolled in a prospective, double-blinded, randomised, control trial comparing treatment with rituximab (RTX) (n=45) or cyclophosphamide (CYC)/azathioprine (AZA) (n=33). Outcome variables included baseline clinical features, ANCA type and titers, disease activity (status of active disease versus complete remission (CR)), time to B cell repopulation, relapse and severe relapse.

**Results:** Baseline sIL6 levels were detectable (>0.49 pg/ml) in 81% of patients. At baseline, sIL-6 positively correlated with proteinase (PR3)-ANCA levels ( $r_s=0.36$ ,  $p<0.01$ ), but not with myeloperoxidase (MPO)-ANCA levels ( $r_s=-0.17$ ,  $p=0.47$ ). Higher baseline sIL-6 levels were associated with the presence of fever, pulmonary nodules/cavities, PR3-ANCA, and absence of renal involvement ( $p<0.05$  for all comparisons).

The median sIL-6 level was higher at baseline and promptly declined with induction therapy at following time-points (baseline, median [25%>75% IQR], 2.66 [0.76–20.98]; month 6th, 0.49 [0.49–1.16];  $p<0.01$ ) in a similar fashion in both treatment arms.

An increase in sIL-6 during clinical remission was a predictor for subsequent severe relapse in RTX-treated patients (Hazard Ratio (HR) 7.24,  $p=0.01$ ), but not in CYC/AZA-treated patients (HR 0.62,  $p=0.50$ ).

In RTX-treated B cell depleted patients (CD19 +B cell/microliter<10), the rise of sIL-6 levels did not precede B cell reappearance, regardless of whether a cut-off of  $\geq 10$  CD19+B cell/microliter (HR=0.97;  $p=0.97$ ) or of  $\geq 69$  CD19+B cell/microliter (HR=1.50;  $p=0.41$ ) was considered. Eighty percent of the patients who subsequently had a severe relapse in the RTX arm had B cell redetection before or at the time of the IL-6 increase, with a mean time between the redetection of B cells and sIL-6 increase of 55 days (25%>75%IQR: 0–184.25; range 0–210 days).

**Conclusions:** At baseline, sIL-6 correlates with PR3-ANCA titers and associates with the presence of fever and pulmonary nodules/cavities. A rise in sIL-6 levels after complete remission is associated with subsequent severe relapse only in RTX-treated patients. The observed discrepancies between treatments deserve confirmation and further study.

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### FRI0488 INSUFFICIENT IMMUNOSUPPRESSIVE USE IS THE LEADING CAUSE OF VASCULAR RELAPSES IN BEHCET'S DISEASE

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**Background:** Vascular involvement is observed in up to 40% in Behcet Disease (BD) patients, as an important cause of mortality and morbidity, especially for males (Kural-Syahi E et al,1984).

**Objectives:** Purpose of this study is to describe clinical-demographic properties, treatments and prognosis of vascular BD patients in a tertiary rheumatology clinic.  
**Methods:** BD patients fulfilling ISG 1990 criteria are recruited from the multi-disciplinary Behcet's Clinic in Marmara University, Istanbul for this retrospective study. All data is collected from patient files (ISG for BD, 1990).

**Results:** Mean age of BD patients (M/F:102/22) was 29.3±7.3 years at diagnosis and 32.4±9.5 years old during first vascular event. Median follow up was 47<sup>17-71</sup> months. Mean age of female patients was significantly older during first vascular event (table 1). 73.2% of vascular involvement was venous, mostly deep vein thrombosis (table 2). 32% (n=40) of patients presented first with a vascular event and diagnosed as BD. Twenty (16%) patients were diagnosed with a median of 12<sup>1-120</sup> months after the first vascular event. 15 (6.5%) patients were using immunosuppressive (IS- mainly azatiopirin) drugs either for resistant mucocutaneous symptoms or major other organ involvement during the first vascular event.

Vascular relaps rate was 40.7% and it was similar between sexes (F: 33.3% vs M: 42.2%,  $p=0.6$ ). After the first vascular event, 96 (85.7%) patients had been treated with ISs and 58.9% used anticoagulants. Median IS and anticoagulant usage duration was 25.5 (5–48) and 2 (0–12) months respectively. Relaps rate was higher in patients who had stopped ISs (87.5% vs 32.3%). IS treatment duration

was shorter at relapsing patients (44 vs 64 months,  $p=0.001$ ). Smoking rate was higher at male patients but no association was observed with vascular relapses.

**Abstract FRI0488 – Table 1.** Clinic and demographic features of Behçet's Disease patients

		Female (n=22)	Male (n=102)	p
Mean age at first vascular event		37±12.6	31.5±8.5	0.019
Mean age at BD diagnosis		30.5±9.5	29.1±7.5	0.467
Smoking	Yes	4 (%33.3)	32 (%68.1)	0.018
	No	8 (%66.7)	15 (%31.9)	
Pteryg	Positive	12 (%66.7)	54 (%62.8)	0.99
	Negative	6 (%33.3)	32 (%37.2)	
Number of vascular events	1	14 (%63.6)	55 (%54.5)	
	2	6 (%27.3)	39 (%38.5)	
	3 or more	2 (%9.1)	7 (%7)	

**Abstract FRI0488 – Table 2.** Type and characteristics of vascular involvement

Venous n=134 (%73.2)	Ekxtremities	106 (% 79.1)	Arteries n=44 (%23.5)	Pulmoner Trombus	36 (% 81.8)
	Cerebral	16 (% 12)		Aneurysme (2 coronary, 2 pulmoner, 2 aorta)	6 (% 13.6)
	Others (SVC, IVC, renal, retinal)	12 (8.9)		PAT+PAA	2 (% 4.6)

IVC: inferior vena cava, PAA: pulmoner arter aneurysmei, PAT: pulmoner arter trombus, SVC: superior vena cava

**Conclusions:** Our results show that female BD patients have a vascular event at a later age compared to males, but the course of vascular disease is not influenced with gender. Early termination of immunosuppressive treatments seems to be the most important cause of vascular relapses

**Disclosure of Interest:** None declared

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### FRI0489 UTILITY OF APREMLAST IN REFRACTORY ORAL AND/OR GENITAL ULCERS IN BEHÇET'S DISEASE

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**Background:** Behçet's disease (BD) is characterised by recurrent oral and/or genital ulcers accompanied by ocular, cutaneous, articular, gastrointestinal, and/or neurologic manifestations. Oral and/or genital aphthous ulcers are often refractory to conventional treatment. Apremilast is an orally-active small molecule which inhibits phosphodiesterase-4 (PDE-4) that modulates some inflammatory pathways.

**Objectives:** Our aim was to assess the efficacy of apremilast in BD patients with oral and/or genital ulcers refractory to conventional treatment.

**Methods:** Retrospective national multicenter open-label study on 19 BD patients treated with apremilast at standard dose of 30 mg twice daily. The main outcome was achievement of oral ulcers remission.

**Results:** We included 19 patients (14 women and 5 men) with a mean age of 43.6 ±14.8 years. Before apremilast, all patients had also received several systemic conventional drugs: oral corticosteroids (n=18), colchicine (n=19), NSAIDs (n=10), methotrexate (n=10), azathioprine (n=10), cyclosporine (n=6), infliximab (n=3), adalimumab (n=5), dapsone (n=3), etanercept (n=1), mycophenolate mofetil (n=1), tocilizumab (n=1). The main clinical symptoms for starting apremilast were oral aphthous ulcers (n=19) and genital ulcers (n=14). Other manifestations present at apremilast onset were arthralgia/arthritis (n=6), folliculitis/pseudofolliculitis (n=6), asthenia (n=5), furunculosis (n=1), erythema nodosum (n=1), erythematous and scaly skin lesions (n=1), psoriasis (n=1), deep venous thrombosis (n=2) and ileitis (n=1). Table 1 shows the evolution of the patients. After a median follow-up of 6 [interquartile range, 5–10] months, most of the patients experienced clinical improvement. In this period of time, 11 patients developed any side-effect: dyspepsia (n=5), nausea (n=4), diarrhoea (n=4), abdominal pain (n=4), headache (n=3), loss of appetite (n=3), weight loss (n=1) and halitosis (n=1). Three patients had to reduce the dose to 30 mg/day. Apremilast was discontinued in 4 patients: because of not obtaining the expected improvement (n=2), due to desire of pregnancy (n=1) and due to development of neurological involvement (n=1).

**Abstract FRI0489 – Table 1**

	Basal n=19	Week 1-2 n=19	Week 4 n=19	Month 3 n=18	Month 6 n=11
Resolution of main symptom, oral and/or genital ulcers (n, %)					
Complete	7/19 (36.8)	12/19 (63.1)	13/19 (68.4)	13/18 (72.2)	7/11 (63.6)
Partial	8/19 (42.1)	4/19 (21.1)	4/19 (21.1)	3/18 (16.7)	3/11 (27.3)
Resolution of other symptoms (n, %)					
Complete	3/19 (15.8)	6/19 (31.6)	8/19 (42.1)	8/17 (47.1)	5/11 (45.5)
Partial	3/19 (15.8)	2/19 (10.5)	4/19 (21.1)	4/17 (23.5)	3/11 (27.3)
Dose of prednisone (mg/day), median [IQR]	7.5 [3-13.0]	3.5 [0-7]	2.2 [0-5]	3 [0-5]	2.5 [0-4.9]

**Conclusions:** Apremilast leads to a rapid and maintained improvement in many patients with refractory mucocutaneous ulcers of BD. Even in patients refractory to several systemic drugs including biologic therapy. However, the development of adverse digestive effects is frequent.

**Disclosure of Interest:** None declared

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### FRI0490 MORTALITY AND EARLY SEVERE INFECTION IN PATIENTS WITH ANCA-ASSOCIATED VASCULITIS

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**Background:** The introduction of treatment regimens comprising of cyclophosphamide or rituximab combined with corticosteroids has brought about dramatic improvements in the prognosis of ANCA-associated vasculitis.<sup>1</sup> Severe infectious events, especially in the early phase of treatment, associated with risk of death have been reported in the past several studies.<sup>2,3</sup>

**Objectives:** We retrospectively investigated the association between mortality and early severe infection in patients with antineutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis (AAV), and we also attempted to identify the potential predictors for early severe infection.

**Methods:** We recruited 182 consecutive hospitalised patients newly diagnosed with AAV at our hospital, from January 2000 to June 2017, in this retrospective cohort study. All cause mortality, relapse, and severe infections within six months after starting treatment (early severe infection) were analysed.

**Results:** The mean age was 70 years at diagnosis, and the classification according to the Chapel Hill Conference definition were microscopic polyangiitis (MPA) in 82 patients (45.1%), granulomatosis with polyangiitis (GPA) in 36 patients (19.8%), eosinophilic granulomatosis with polyangiitis (EGPA) in 24 patients (13.2%), and renal-limited vasculitis in 32 patients (17.6%).<sup>4</sup> Median follow up was 158 weeks (range 0–182 w). Using Cox regression analysis, elderly onset (age ≥75 years) AAV ( $p=0.027$ ) and early severe infection ( $p<0.001$ ) were independent predictors of all cause mortality (table 1).

Early severe infection tended to increase among patients who received immunosuppressive therapy of a corticosteroid combined with cyclophosphamide or rituximab (conventional treatment), and this trend was significant in non-severe (BVAS <20) AAV patients ( $p=0.030$ ) (table 2). Treatment response rate ( $p=0.058$ )

and relapse rate ( $p=0.137$ ) were not significant between the different treatment groups.

**Abstract FRI0490 – Table 1.** Risk factors affecting survival according to Cox regression analysis

Risk factor	Hazard ratio	95% CI	P value
Age $\geq 75$ years old	2.35	(1.1–5.03)	0.027
BVAS $\geq 20$	2.08	(0.99–4.32)	0.05
Creatinine $\geq 1.5$ mg/dl	1.18	(0.58–2.38)	0.654
Early severe infection	3.23	(1.63–6.48)	<0.001

\*Birmingham Vasculitis Activity Score (BVAS) Version.3

**Abstract FRI0490 – Table 2.** Risk factors affecting early severe infection in non-severe AAV patients

Risk factor	Hazard ratio	95% CI	P value
Age $\geq 75$ years old	2.1	(0.85–5.32)	0.105
Conventional treatment	3.0	(1.11–7.89)	0.030
Lung involvement	1.0	(0.43–2.48)	0.936
Creatinine $\geq 1.5$ mg/dl	1.0	(0.41–2.33)	0.963

**Conclusions:** Early severe infection is an independent predictor of death in patients with AAV, and conventional treatment has a potential risk of death due to severe infection. This study supports the current EULAR recommendation that several treatment strategies are recommended according to the disease severity of vasculitis.<sup>5</sup> AAV patients who receive conventional treatment should be carefully monitored to reduce the occurrence of severe infection, especially in early phase of treatment.

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FRI0491

#### SMOKING AS A RISK FACTOR FOR GIANT CELL ARTERITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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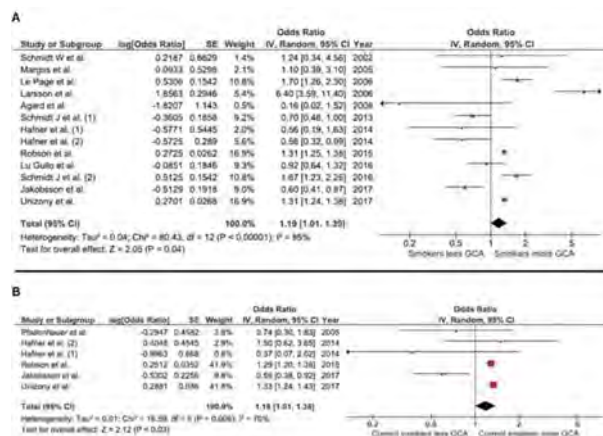
**Background:** Tobacco smoking is a well-established risk factor for the development of several autoimmune diseases such as rheumatoid arthritis and systemic lupus erythematosus. A similar association between smoking and giant cell arteritis (GCA) has been suspected but remains unclear due to limited study size and conflicting epidemiologic data.

**Objectives:** To conduct a systematic review and meta-analysis to further investigate the association between smoking and the development of GCA.

**Methods:** Two investigators (D.B. and M.K.) independently searched published studies indexed in MEDLINE and EMBASE from inception to February 2017 using the terms “giant cell arteritis,” “temporal arteritis,” “cranial arteritis,” and “Horton disease.” Recent conference abstracts available online were also reviewed. The following inclusion criteria were used: 1) original observational study comparing patients with GCA to healthy controls; 2) inclusion of smoking history; 3) provision of absolute numbers and/or statistical comparisons with 95% confidence intervals. Study eligibility was independently determined by the two investigators, with disagreements reviewed by a third investigator (P.U.) and resolved by consensus. RevMan 5.3 software was used for the data analysis. Point estimates and standard errors were extracted from individual studies and were combined by the generic inverse variance method of DerSimonian and Laird. Given the high likelihood of between-study variance, we used a random-effect model rather than a fixed-effect model. Statistical heterogeneity was assessed using the Cochran’s Q test.

**Results:** The initial search yielded 3312 articles. Of these, thirteen studies (8 prospective and, 5 retrospective case-control studies) with unique cohorts were identified and included in the primary analysis (ever vs. never smoking history). Patients in the GCA cohort were more likely to have a history of smoking with an odds ratio of 1.19 (95% CI, 1.01–1.39) [figure 1A]. Considerable heterogeneity

was present ( $I^2=85\%$ ). Five of these studies included information on current smoking status. One additional study, which only reported current smoking status, was also included. The GCA cohort showed an association with current tobacco use with an odds ratio of 1.18 (95% CI, 1.01–1.38) [figure 1B].



**Conclusions:** Our study demonstrated a statistically significant increased risk of GCA among smokers compared to non-smokers.

**Disclosure of Interest:** None declared

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FRI0492

#### CLINICAL CHARACTERISTICS OF PARENCHYMAL NEURO-BEHCHET'S DISEASE: A RETROSPECTIVE ANALYSIS

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**Background:** Neurological involvement is one of the most serious complications in Behcet's disease (BD).

**Objectives:** To investigate the clinical characteristics of parenchymal neuro-Behcet's Disease (pNBD).

**Methods:** We retrospectively reviewed all the medical records of BD patients who were admitted to our institute between 2000 and 2016. The diagnosis of NBD was based on the 2014 International Consensus criteria for NBD.<sup>1</sup> Eighty-four BD patients without neurological involvement were randomly matched by sex and age as control.

**Results:** 42 patients (25 male and 17 female) with pNBD accounted for 4.2% of the 1009 hospitalised BD patients during that period. The mean age at BD onset and at neurological onset was (30.1±11.1 years old and (35.3±12.1 years old, respectively). The majority of patients developed neurological symptoms after other initial systemic symptoms of BD in a median period of 2 months (range from 0–49). Neurological onset was concomitant with the onset of BD in 6 cases (14.3%). The most frequent location was brainstem (23/42, 54.8%). Spinal cord involvement was presented in five cases, in which four with cervical cord involved. 13 cases suffered from multiple lesions. Pyramidal (21/42, 50.0%) and headache (14/42, 33.3%) were the most common manifestations of pNBD. Lumbar puncture was performed in 40 patients, in which 80% (32/40) of patients had normal pressure and 55% (22/40) had elevated protein levels ((0.51±0.24) g/L). Compared with the controls, the prevalence of ocular involvement (uveitis, retinal vasculitis, scleritis) was significantly higher in pNBD (35.7%) (p=0.041, OR=2.36, 95% CI=1.03–5.44) (table 1). Cranial MRI in 32 patients showed the lesions were mainly in the midline structures, including brainstem (22/42, 52.4%), periventricular (13/42, 31.0%), centrum semiovale (8/42, 19.0%). Typically, the lesions were in hypersignal in T2. All pNBD patients received corticosteroids ( $\geq 1$  mg/kg/d) and 23 patients (54.8%) received the pulse dose (1 g/d). Cyclophosphamide was the most commonly used immunosuppressant (39/42) and 10 cases took more than one immunosuppressants (including methotrexate and azathioprine). Biological agents were administered in six refractory pNBD patients, including Infliximab in 4 cases, Tocilizumab in 1 case, and Interferon- $\alpha 2a$  in 1 case. Intrathecally injection of dexamethasone 10 mg and methotrexate 10 mg was given to 28 patients. With a median follow-up of 28 months (4 to 156 months), 22 patients (52.4%) achieved clinical improvements, while 10 patients (23.8%) relapsed and 4 patients died (the mortality was 9.5%). Six patients lost to follow up.



**Table 1.** Clinical Comparison of pNBD and BD without neurological involvement<sup>a</sup>

Parameters	pNBD (n=42)	Controls <sup>b</sup> (n=84)	P Value	OR(95%CI)
Age (years, mean±SD)	36.3±11.6	35.2±10.9	0.601	1.01 (0.98-1.04)
Gender (F/M)	25/17	30/34	1.000	—
<b>Clinical Features of BD</b>				
Oral Ulceration	42 (100%)	84 (100%)	1.000	—
Genital Ulceration	27 (64.3%)	61 (72.6%)	0.337	0.68 (0.31-1.50)
Skin Lesions	19 (45.2%)	40 (47.6%)	0.801	0.91 (0.43-1.91)
Gastrointestinal lesions	3 (7.1%)	17 (20.2%)	0.058	0.30 (0.09-1.10)
Ocular involvement <sup>c</sup>	15 (35.7%)	16 (19.0%)	0.041*	2.36 (1.03-5.44)
Vascular involvement	6 (14.3%)	10 (11.9%)	0.705	1.23 (0.42-3.66)
<b>Laboratory tests</b>				
ESR(mm/h, median and range)	15(0-85)	11(1-80)	0.072	1.01(0.99-1.03)
CRP (mg/L, median and range)	3.0(0.14-124)	5.3(0.13-104)	0.995	1.00 (0.98-1.02)

OR= Odds Ratio, CI=Confidential Interval.

<sup>a</sup>Values are the number (percentage) unless otherwise indicated.<sup>b</sup>Eighty-four age- and gender-matched BD patients without neurological involvement were served as control.<sup>c</sup>Ocular involvement includes uveitis, retinal vasculitis, scleritis.

\*P&lt;0.05.

**Conclusions:** The parenchymal neurological involvement is a rare complication of BD with a high mortality. Its most frequent location is brainstem. Ocular involvement is a risk factor for pNBD. Early identification and active treatment are vital for a good prognosis.

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FRI0493

### PET/CT IN PATIENTS WITH GIANT CELL ARTERITIS AFTER 1 YEAR OF TREATMENT WITH TOCILIZUMAB PLUS PREDNISONE TAPER OR ONLY PREDNISONE TAPER

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**Background:** The arterial uptake of <sup>18</sup>fluorine-2-deoxy-d-glucose (FDG) by positron emission tomography-computed tomography (PET/CT) has been used for the diagnosis of giant cell arteritis (GCA). The role for PET/CT in following disease activity and monitoring treatment effects, however, remains unclear

**Objectives:** To examine the degree of FDG uptake within the large arteries of GCA patients after 1 year of treatment

**Methods:** We studied a subgroup of patients enrolled in the GiACTA trial.<sup>1</sup> Patients received either tocilizumab (TCZ) given weekly or every other week plus a 26 week prednisone taper, or placebo (PBO) plus either a 26- or 52 week prednisone taper. PET/CTs were done according to site feasibility and not as part of the GiACTA protocol. For this analysis, the 2 TCZ and PBO groups, respectively, were combined. Patients had whole-body PET/CT imaging within 16 weeks of week 52 visit. The ascending aorta, carotid artery and subclavian artery territories were assessed by maximum standardised FDG uptake values (mSUV) measurement. For each territory, we calculated average, most diseased segment (MDS) and most diseased slide mSUVs and target background ratios (TBR). PET/CTs were read centrally by investigators blinded to the clinical and treatment data

**Results:** From 251 patients enrolled in GiACTA, 24 patients underwent PET/CT within 16 weeks of week 52 visit. Seventeen patients (71%) received TCZ plus a prednisone taper (TCZ group) and 7 patients received a prednisone taper alone (PBO group). There were no significant differences between groups in baseline characteristics (table 1). Mean (SD) cumulative prednisone dose at week 52 was 2.5 g (1.7 g) in the TCZ group and 3.2 g (1.2 g) in the PBO group (p=0.11). FDG

uptake was consistently numerically lower in all vascular territories in TCZ-treated patients compared to PBO-treated patients except in the ascending aorta. However, the between-group differences were statistically significant only in the left subclavian artery (table 2). Adjustment for selected confounders (new onset disease, baseline prednisone dose, prednisone dose at the time of PET/CT, cumulative prednisone dose, flare prior to PET/CT and clinical activity at the time of PET/CT) did not alter the conclusions derived from the univariate analyses

**Table 1 Baseline characteristics:** All results represent means (SD) except otherwise indicated. PBO=placebo, TCZ=tocilizumab

	PBO group (n=7)	TCZ group (n=17)	p-value
New onset disease, n (%)	6 (86)	9 (53)	0.19
Baseline prednisone dose (mg)	30 (30-50)	30 (20-40)	0.30
Cumulative prednisone dose (g) at week 52	3.2 (1.2)	2.5 (1.7)	0.11
Prednisone dose (mg) at PET time, median (IQR)	0 (0; 3)	0 (0; 7.5)	0.44
PET time point (weeks from baseline)	54.47 (5.75)	57.38 (8.33)	0.11
Primary outcome met, n (%)	4 (57)	11 (65)	1.00
Clinically active disease at the time of PET, n (%)	1 (14)	3 (18)	1.00
Disease relapse before PET, n (%)	3 (43)	8 (47)	0.61
TCZ treatment at the time of PET, n (%)	0 (100)	7 (41)	0.07

All results represent means (SD) except otherwise indicated. PBO = placebo, TCZ = tocilizumab

**Table 2 Results:** All results represent means (SD). mSUV=maximum standardised uptake value, MDS=most diseased segment, TBR=target to background ratio

	PBO group (n=7)	TCZ group (n=17)	p-value
<b>Left subclavian artery</b>			
Average mSUV	2.74 (0.77)	2.33 (0.42)	0.11
Average MDS mSUV	3.05 (0.90)	2.47 (0.46)	0.04
Hottest spot mSUV	3.23 (1.02)	2.56 (0.48)	0.04
TBR	2.94 (0.86)	2.47 (0.45)	0.09
<b>Right subclavian artery</b>			
Average mSUV	2.59 (0.86)	2.28 (0.43)	0.25
Average MDS mSUV	2.72 (0.88)	2.35 (0.42)	0.17
Hottest spot mSUV	2.82 (0.91)	2.49 (0.49)	0.26
TBR	2.76 (0.88)	2.41 (0.40)	0.19
<b>Left carotid artery</b>			
Average mSUV	2.51 (0.49)	2.36 (0.41)	0.50
Average MDS mSUV	2.64 (0.54)	2.52 (0.49)	0.66
Hottest spot mSUV	2.70 (0.54)	2.64 (0.54)	0.82
TBR	2.67 (0.52)	2.51 (0.43)	0.78
<b>Right carotid artery</b>			
Average mSUV	2.86 (0.77)	2.38 (0.44)	0.14
Average MDS mSUV	3.12 (0.95)	2.63 (0.65)	0.14
Hottest spot mSUV	3.23 (0.94)	2.76 (0.69)	0.16
TBR	2.98 (0.67)	2.54 (0.46)	0.31
<b>Ascending aorta</b>			
Average mSUV	2.85 (0.63)	2.86 (0.51)	0.93
Average MDS mSUV	2.99 (0.68)	2.98 (0.56)	0.97
Hottest spot mSUV	3.01 (0.71)	3.12 (0.61)	0.97
TBR	3.05 (0.65)	3.05 (0.61)	0.99
<b>Hottest spot total score</b>	<b>13.40 (4.08)</b>	<b>12.62 (3.30)</b>	<b>0.62</b>
<b>Average MDS total score</b>	<b>12.84 (4.01)</b>	<b>12.04 (3.06)</b>	<b>0.60</b>

All results represent means (SD). mSUV = maximum standardized uptake value, MDS = most diseased segment, TBR = target to background ratio

**Conclusions:** In this exploratory study, subclavian FDG-uptake was significantly reduced in GCA patients treated with TCZ plus prednisone versus prednisone monotherapy despite lower cumulative prednisone doses. A larger, carefully designed prospective study is required to fully understand the utility of PET/CT in the longitudinal evaluation of large-vessel vasculitis associated with GCA

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FRI0494

### SPECTRUM OF VISUAL INVOLVEMENT IN GIANT CELL ARTERITIS

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**Background:** The dreaded complication of giant cell arteritis (GCA), irreversible sight loss (SL), is present in 15%–25% of patients at diagnosis. This is likely due to delayed presentation, recognition and treatment. Fast track pathways for urgent assessment of suspected GCA reduce SL with associated cost savings. Information regarding the burden of SL in GCA is required to guide health strategy and has been explored in this UK wide study.

**Methods:** This is a prospective observational multi-centre study of visual involvement attributable to GCA. Demographic, disease features and treatment information was collected on all patients with new or relapsing GCA with or without visual symptoms (VS) or SL. SL was defined as symptomatic loss of acuity, field of vision or diplopia ascribable to ischaemic complications of GCA. Patients with transient VS were not considered to have SL. Analyses were performed using chi-squared and rank sum tests.

**Results:** Patients were predominantly female (274/388) and Caucasian; 3 non-Caucasian (Asian British, Black/Afro-Caribbean and Turkish). VS were present in 135/388 patients (35%) from 19 UK sites. Of patients with VS, these were transient or intermittent SL (n=9,7%), diplopia (n=33,24%), blurred vision (n=17,13%), flashing lights (n=4,3%) and eye pain (n=7,5%). Transient or permanent loss of acuity occurred in 92 patients (48 anterior ischaemic optic neuropathy [AION], 6 central retinal artery occlusion [CRAO], 1 posterior ischaemic optic neuropathy, all attributed to GCA); 1 hemispheric retinal vein occlusion, 1 branch retinal artery occlusion, 1 peri-papillary haemorrhage, 1 vitelliform dystrophy macula. 8 had oculomotor nerve palsies (NP) (1 bilateral 3rd, 1 bilateral 6th and 6 unilateral 3rd or 6th NP). Patients with VS were older than those without (mean  $\pm$ SD age 75.9 $\pm$ 9.3 and 73.5 $\pm$ 8.5 respectively,  $p < 0.001$ ). Patients with VS had less headaches ( $p = 0.012$ ) and scalp tenderness ( $p = 0.05$ ) but more frequently tongue claudication ( $p = 0.014$ ), shorter symptom duration (3.9 $\pm$ 5.5 days,  $p = 0.001$ ), lower CRP although not statistically significant ( $p = 0.059$ ), were less likely to meet ACR criteria and to improve than those without VS ( $p < 0.001$ ). No association was found with comorbidities or deprivation index. SL in 54 (40%) patients was due to AION or CRAO. Transient CRAO or AION was described in 17 and 30/47 (64%) had permanent SL (data missing from 7 patients). Patients with AION/CRAO were older (80.9 $\pm$ 6.7 years) than those without AION/CRAO (73.3 $\pm$ 8.7 years,  $p < 0.001$ ). They had shorter symptom duration (4.2 $\pm$ 7.0 days,  $p = 0.024$ ), less likely to improve than those without AION/CRAO ( $p < 0.001$ ), less likely to have headaches ( $p < 0.001$ ) or polymyalgic symptoms ( $p = 0.002$ ), and more likely to have jaw claudication ( $p = 0.043$ ) and hypertension ( $p = 0.002$ ). Only 7 had diplopia on presentation. 5 patients experienced AION as manifestation of recrudescing disease.

**Conclusions:** VS often leading to SL in GCA requires urgent management. Patients with VS were older, without 'typical symptoms' such as headache and polymyalgia but more likely to have ischaemic symptoms such as jaw and tongue pain and hypertension. Recognition of VS associated features should be embodied in public and professional awareness programs to prevent permanent SL in GCA.

**Disclosure of Interest:** None declared

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#### FRI0495 BEHÇET'S SYNDROME IN NEW YORK AND AMSTERDAM: EVOLUTION FROM PROBABLE BEHÇET'S TO ISG CRITERIA POSITIVE BEHÇET'S

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**Background:** Behçet's syndrome (BS) is an auto-inflammatory vasculitis, most common in countries along the ancient Silk Road. Classification of BS most often is done with the International Study Group criteria (ISG criteria)<sup>1</sup>. ISG criteria positivity for BS is reached when a patient has recurrent oral ulceration and any two of the following symptoms: recurrent genital ulceration, uveitis, skin lesions and pathergy positivity. However, many other manifestations are reported<sup>1</sup>. Differences in clinical presentation can complicate classification of the diagnosis, especially in areas where the disease is low in prevalence. Thus, some patients are classified as "probable BS". In some of these cases patients developed additional symptoms over time and met the ISG criteria in a later stage.

**Objectives:** To describe characteristics of patients presenting with a probable diagnosis of BS in Amsterdam and New York and to study if patients who eventually met the ISG criteria differ from those who did not.

**Methods:** We included consecutive patients classified as possible BS to our out-patient clinics in New York and Amsterdam. Patients fulfilling ISG criteria at enrollment were excluded, as well as patients in whom an alternative diagnosis was made at enrollment. Baseline data were evaluated retrospectively and patients were divided into two groups: those developing ISG positive (ISG + or "true") BS during follow up and those who did not meet ISG criteria after follow-up (ISG-). Turkey, Asia, Middle and Far Eastern countries, Arabic countries and Northern Africa were considered endemic areas; Italian, Greek, Hispanic, Portuguese, African-American and Caucasian patients were considered not from endemic areas. Statistical analysis was performed using SPSS, with Chi-square tests or Fisher's exact tests for categorical data and independent sample t-tests for numerical data.

**Results:** 189 patients were included, of whom 20 were from Amsterdam. During follow up, 71 patients (37.6%) could be classified as "true" Behçet's syndrome after a mean period of 9.4 years ( $\pm$ 8.3 years) after onset of symptoms. Age,

gender, ethnicity, duration of symptoms at enrollment, duration of follow up as well as RAPID3 and almost all clinical manifestations at baseline were comparable for both groups. Labial ulcers and skin manifestations at enrollment were more frequently reported. Genital ulcers as a group was not significantly associated with developing "true" Behçet's, nor were specific skin manifestations such as erythema nodosum. We also considered HLA-B\*51, pathergy, erythrocyte sedimentation rate and C-reactive protein, but due to a large amount of missing data, we were unable to draw any significant conclusions for these variables.

Characteristics	All patients (n=189)	ISG + (n=71)	ISG - (n=118)	P-value
Age years (SD)	34.3 (13.7)	34.1 (13.4)	34.5 (14.0)	ns
Male n (%)	46 (24.3)	13 (18.3)	33 (28.0)	ns
Duration of follow up years (SD)	3.2 (2.4)	3.3 (2.5)	3.1 (2.4)	ns
Ethnicity: endemic area n (%)	43 (22.8)	14 (19.7)	29 (24.6)	ns
RAPID3 mean score (SD)	9.8 (6.8)	9.6 (6.9)	9.9 (6.7)	ns
Duration of symptoms years (SD)	7.3 (7.8)	7.7 (7.9)	7.0 (7.8)	ns
Oral ulcers n (%)	174 (92.1)	66 (93.0)	108 (91.5)	ns
Genital ulcers n (%)	108 (57.1)	47 (66.2)	61 (51.7)	ns
- Labia	63 (33.3)	31 (43.7)	32 (27.1)	0.019
Skin disease n (%)	58 (30.7)	31 (43.7)	27 (22.9)	0.003
Eye disease n (%)	33 (17.5)	17 (23.9)	15 (12.7)	ns
Deep venous thrombosis n (%)	4 (2.1)	2 (2.8)	2 (1.7)	ns
Thrombophlebitis n (%)	5 (2.6)	2 (2.8)	3 (2.5)	ns
Central nervous system n (%)	22 (11.6)	6 (8.5)	16 (13.6)	ns
Vascular disease n (%)	7 (3.7)	1 (1.4)	6 (5.1)	ns
Pulmonary disease n (%)	3 (1.6)	0 (0)	3 (2.5)	ns
Arthritis n (%)	35 (18.6)	16 (22.5)	19 (16.1)	ns
Gastrointestinal disease n (%)	40 (21.2)	14 (19.7)	26 (22.0)	ns
Headache n (%)	12 (6.3)	5 (7.0)	7 (5.9)	ns
Epididymitis n (% of males)	3 (6.5)	0 (0)	3 (9.1)	ns

ISG +: patients who did fulfill ISG criteria after follow-up; ISG -: patients who did not fulfill ISG criteria after follow-up; SD: standard deviation; ns: not significant

Figure 1 Baseline data from all patients who were classified as probable Behçet's syndrome at enrollment

**Conclusions:** About a third of patients classified as probable Behçet's syndrome at enrollment develop new manifestations over time. Thus, they can be reclassified as ISG positive ("true") BS. Based on our data, presence of skin manifestations and labial ulcers at enrollment was significantly higher in the group eventually developing a ISG criteria positive BS.

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#### FRI0496 POLYARTERITIS NODOSA: OVER 20 YEARS' CLINICAL EXPERIENCE

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**Background:** Polyarteritis nodosa (PAN) is a necrotizing vasculitis of predominantly medium size vessels.

**Objectives:** The present study aimed to summarise the characteristics of PAN patients, and also analyse the trend of decreasing PAN frequency in the last 25 years, in Turkey

**Methods:** Paediatric and adult PAN patients followed up in Hacettepe University and Istanbul University Cerrahpaşa Faculty of Medicine between 1990 and 2015, were included. The demographics, clinical findings and outcomes were evaluated retrospectively.

**Results:** One hundred thirty-three patients, including 66 children, were enrolled in the study. The mean follow-up duration was 13<sup>2-27</sup> years. Among 133 patients, 86 (64.7%) had fever, 108 (81.2%) had skin involvement, 54 (40.6%) had renal involvement, 43 (32.3%) had neurological involvement, 32 (24.1%) had gastrointestinal involvement, 10 (7.5%) had cardiac involvement, 6 (4.5%) had pulmonary involvement. The median (minimum-maximum) leukocyte count, erythrocyte sedimentation rate and C-reactive protein levels at the time of diagnosis were 10400 (6100-32000)/mm<sup>3</sup>, 58(2-132) mm/h and 5.22 (0-46) mg/dL, respectively. All patients were ANCA negative. Hepatitis serology was analysed in 121 patients and found positive in 13 of them. *MEFV* mutations were screened among 65 patients, 24 of them had mutations in at least one allele. Myalgia and skin involvement were significantly more frequent in children whereas neurologic involvement

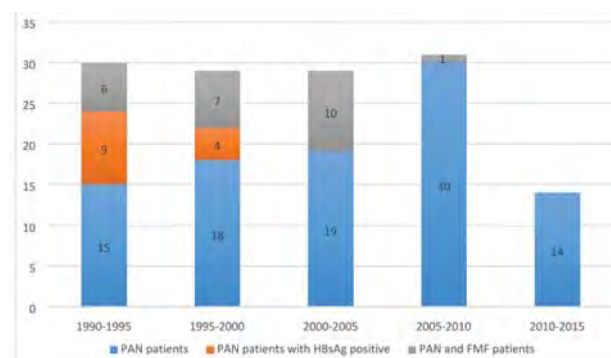


was much more common among adults (table 1). The number of PAN patients declined significantly after 2010 (figure 1). 9 patients were re-categorised as DADA2 after 2014 and no patient were diagnosed with FMF+. PAN after 2008

**Abstract FRI0496 – Table 1.** Characteristics of paediatric and adult PAN patients

Features, n (%)	Patients (n=133)	Paediatric patients (n=66)	Adult patients (n=67)	P value
Gender, female	55 (41.4)	35 (53)	20 (29.8)	0.07
Fever	86 (64.7)	50 (75.7)	36 (52.9)	0.06
Myalgia	79 (59.4)	48 (72.7)	31 (46.2)	<b>0.01</b>
Abdominal pain	65 (48.9)	40 (60.6)	25 (37.3)	0.05
Weight loss	56 (42.1)	20 (30.3)	36 (53.7)	0.06
Arthralgia	87 (65.4)	48 (72.7)	39 (58.2)	0.06
Arthritis	23 (17.3)	11 (16.6)	12 (17.9)	0.58
Skin involvement	108 (81.2)	63 (95.5)	45 (67.2)	<b>&lt;0.001</b>
GI <sup>a</sup> involvement	32 (24.1)	17 (25.7)	15 (22.3)	0.64
Renal involvement	54 (40.6)	22 (33.3)	32 (47.7)	0.09
Cardiac involvement	10 (7.5)	8 (12)	2 (2.9)	0.04
Neurologic involvement	43 (32.3)	14 (21.2)	29 (43.2)	<b>0.007</b>
WBC <sup>a</sup> , x10 <sup>3</sup> /mm <sup>3</sup>	10400 (4200–32000)	11800 (4300–32000)	9850 (4200–21800)	0.02
PLT <sup>a</sup> , x10 <sup>3</sup> /mm <sup>3</sup>	365000 (259000–7 26 000)	456000 (259000–696000)	300000 (268000–726000)	<b>&lt;0.001</b>
CRP <sup>a</sup> , mg/dl	5.22 (0–46)	4.6 (0.1–46)	5.8 (2–29.8)	0.88
Exitus	6 (4.5)	0 (0)	6 (8.9)	0.007

<sup>a</sup>CRP, C reactive protein; GI, gastrointestinal; PLT, platelet; WBC, white blood cell



**Abstract FRI0496 – Figure 1.** Distribution of the PAN patients by years

**Conclusions:** Our results suggest a decrease in PAN in our country which may be due to improved healthcare and dissecting mimicking diseases. Further prospective studies with prolonged follow-up could help us to better understand the disease characteristics.

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#### FRI0497 CLINICAL CHARACTERISTICS AND TREATMENT OUTCOMES OF PATIENTS WITH BEHÇET'S DISEASE AND VASCULAR INVOLVEMENT

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**Background:** The international Chapel Hill Consensus Conference (CHCC) categorised Behçet's disease (BD) as variable vessel vasculitis, which was defined as vasculitis that can affect vessels of any size and type. Vascular manifestations

have been reported in up to 50% of patients with BD, most commonly as venous thrombosis.

**Objectives:** The aim of this study is to investigate characteristics and treatment outcomes of patients with vascular BD, particularly with large vessel involvement.

**Methods:** A retrospective review was performed on 2496 patients with ICD-10 code of Behçet's disease and/or aortic disease who visited Samsung Medical Centre between 2004 and 2014. Patients who were suspected to have BD and vascular involvement were enrolled.

**Results:** Eighty-three patients with clinical features of BD and vascular involvement were identified. Although less than half satisfied the classic International Study Group (ISG) criteria, greater proportion fulfilled the International Criteria for BD (ICBD), and all of the patients satisfied at least "suspected BD" according to the Japanese criteria. Fifty patients had arterial lesions including 34 with aorta involvement. Another 33 patients had venous thrombosis without arterial lesions. Patients showed a male predominance (87%) and a predilection of young age with the median of 42 years old. The most prominent type of arterial lesions was aneurysm (80%) with a high frequency of pseudoaneurysms. Among the aorta, the thoracic aorta was most commonly involved and 18 patients had aortic valve regurgitation. Seventy-five (90%) patients received glucocorticoids with a median initial dose of prednisolone of 30 mg per day and 68 (82%) received immunosuppressive treatment. Half of the patients had more than one relapse after stabilisation of the first vascular event. During the course, 44 patients underwent surgery and/or endovascular treatment and 60% of these patients had repeated treatment for the relapse. These included 31 aortic valve replacements on 13 patients.

**Conclusions:** Patients with vascular BD showed a predilection of young male and 60% of patients had arterial involvement. The aorta was affected in more than half of the patients who had arterial involvement. Aneurysmal change was frequent finding and relapse rate was high during disease course. Further studies into a practical and specialised diagnostic tool for vascular BD and optimal treatment strategies are required.

**Disclosure of Interest:** None declared

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#### FRI0498 COMPARATIVE STUDY OF THE TREATMENT OF REFRACTORY CYSTOID MACULAR OEDEMA TO CONVENTIONAL IMMUNOSUPPRESSIVE THERAPY: TOCILIZUMAB VS ANTI-TNF. MULTICENTER STUDY OF 59 PATIENTS

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**Background:** Cystoid macular oedema (CME) is the most serious complication of uveitis. This potentially severe complication may lead to irreversible visual loss.<sup>1-2</sup>

**Objectives:** To compare efficacy and safety of Tocilizumab (TCZ) vs. Anti-TNF- $\alpha$  drugs in patients with refractory CME to conventional immunosuppressant (IS).

**Methods:** Multicenter study of patients with refractory CME to treatment with glucocorticoids and at least 1 conventional IS. The main objective was the improvement of macular thickness. Secondary objectives were the enhancement in best corrected visual acuity (BCVA) and the degree of ocular inflammatory activity.

**Results:** 59 patients/112 affected eyes. Causes of uveitis were: Behçet's disease (n=41), Birdshot's retinochoroidopathy (n=4), Juvenile Idiopathic Arthritis (n=9), Sarcoidosis (n=1) and idiopathic (n=4). No significant differences were observed at baseline in both groups (TCZ vs Anti-TNF- $\alpha$ ) in sex ( $\chi^2$ ; 8/17 vs. 15/19), mean age (35.6 $\pm$ 18.9 vs 40.0 $\pm$ 9.1), BCVA (0.40 $\pm$ 0.31 vs. 0.48 $\pm$ 0.31), Tyndall (1 [0-1] vs. 1 [0-2]), vitritis (1 [0-2] vs. 1 [0-3]) and macular thickness (431.8 $\pm$ 165.9 vs. 397.1 $\pm$ 138.1) (table 1).

25 patients were treated with TCZ as follows: 8 mg/kg/4 weeks (n=24) and 162 mg sc/2 weeks (n=1). Anti-TNF- $\alpha$  therapy was used in the remaining 34 as



follows: IFX (n=12) (5 mg/kg 0, 2 y 6 weeks and every 4–8 weeks) and ADA (n=22) (40 mg/sc/2 weeks).

We observed a rapid and sustained improvement in macular thickness after 1 year follow-up in both groups, without objectifying significant differences between them. In the same way, secondary ocular parameters also improved (table 1).

Abstract FRI0498 – Table 1

	TCZ	Anti-TNF- $\alpha$	P
<b>Baseline</b>			
BCVA	0.40 $\pm$ 0.31	0.48 $\pm$ 0.31	0.98
Tyndall	1 [0-1]	1 [0-2]	0.13
Vitritis	1 [0-2]	1 [0-3]	0.07
OCT	431.82 $\pm$ 165.99	397.18 $\pm$ 138.12	0.21
<b>1st month</b>			
BCVA	0.50 $\pm$ 0.30	0.61 $\pm$ 0.28	0.58
Tyndall	0 [0-0]	0 [0-0]	0.47
Vitritis	0 [0-0.5]	0.5 [0-1]	<0.01
OCT	330.86 $\pm$ 104.21	328.41 $\pm$ 86.53	0.25
<b>6th month</b>			
BCVA	0.56 $\pm$ 0.33	0.71 $\pm$ 0.31	0.73
Tyndall	0 [0-0]	0 [0-0]	0.04
Vitritis	0 [0-0.5]	0 [0-0]	<0.01
OCT	275.07 $\pm$ 73.80	264.90 $\pm$ 45.92	0.006
<b>1st year</b>			
BCVA	0.59 $\pm$ 0.33	0.72 $\pm$ 0.32	0.76
Tyndall	0 [0-0]	0 [0-0]	<0.01
Vitritis	0 [0-0.5]	0 [0-0]	0.36
OCT	259.10 $\pm$ 49.51	261.42 $\pm$ 37.71	0.14

**Conclusions:** TCZ and Anti-TNF- $\alpha$  are effective in the treatment of CME refractory to conventional therapy.

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FRI0499

#### A MULTINATIONAL QUALITATIVE STUDY IN GIANT CELL ARTERITIS: PATIENT PERCEPTIONS OF DIAGNOSIS, TREATMENT, IMPACT ON HEALTH-RELATED QUALITY OF LIFE AND CONTEXTUAL FACTORS

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**Background:** Giant cell arteritis (GCA) is the commonest form of systemic vasculitis caused by inflammation of the blood vessels around the head and neck, with the highest incidence in women aged 70–79 years (7.4 per 10 000 person-years). Patients present with headache, jaw claudication and polymyalgia rheumatica with visual loss in 20%. Treatment is with high dose glucocorticoids.

**Objectives:** Identify and define the range of patient experiences in relation to GCA, and effects on health related quality of life in patients from the United Kingdom and Australia.

**Methods:** Semi-structured qualitative interviews with patients from the UK and Australia explored health-related quality of life and patient perspectives on the experience of GCA. Interviews were recorded, transcribed and analysed. Patients were purposively sampled to include both genders, a range of disease durations and organ involvement (visual loss and large vessel involvement). Data were analysed with inductive thematic analysis and managed using NVivo 10. The sample size was determined by the point at which no new substantive themes emerged.

**Results:** Thirty-one interviews were conducted. Demographics and disease features shown in table 1. Individual sub-codes were identified then grouped into overarching themes: "Anxieties around getting a diagnosis of GCA", "Description of symptoms related to GCA and its treatment", "Lack of bodily strength, stability and stamina; difficulties with completing daily tasks", "Difficulties with participating in social activities, work and caring roles", "Not feeling normal and impact on general perception of health", "Anxiety and fear of the future". Contextual factors impacted on how patients experienced GCA including "Response to treatment and adverse effects", "Receiving support from family, friends and health care workers", "Adopting successful self-management techniques, e.g. keeping fit and active" and "Presence of pre-existing co-morbidities and development of secondary conditions e.g. cardiovascular disease, osteoporosis or diabetes".

Demographics		United Kingdom (n=25)	Australia (n=6)	Total (n=31)
<b>Sex, n (%)</b>	Male	9 (36.0)	1 (7.7)	10 (32.3)
	Female	16 (64.0)	5 (92.3)	21 (67.7)
<b>Age, n (%)</b>	<70 years	5 (20.0)	3 (50.0)	8 (25.8)
	≥70 years	20 (80.0)	3 (50.0)	23 (74.2)
	Mean	75	69	74
<b>Diagnostic test, n (%) *</b>	Biopsy	21 (84.0)	5 (83.3)	26 (83.9)
	Ultra/S	5 (20.0)	0 (0)	5 (16.1)
	CTA	2 (8.0)	0 (0)	2 (6.45)
	PET	2 (8.0)	1 (16.7)	3 (9.68)
<b>Visual Loss (%)</b>	Yes	10 (40.0)	2 (33.3)	12 (38.7)
<b>ESR≥50 or CRP≥10</b>	Yes	24 (96.0)	5 (83.3)	29 (93.6)
<b>Time from diagnosis, n (%)</b>	<1 year	13 (52.0)	4 (66.7)	17 (54.8)
	≥1 year	12 (48.0)	2 (33.3)	14 (45.2)
<b>Disease Active, n (%)</b>	Yes	11 (44.0)	4 (66.7)	15 (48.4)
	No	14 (56.0)	2 (33.3)	16 (51.6)
<b>Flare&lt;1 year, n (%)</b>	Yes	13 (52.0)	3 (50.0)	16 (51.6)
	No	10 (40.0)	3 (50.0)	13 (41.9)
	Never	2 (8.0)	0 (0)	2 (6.5)

**Conclusions:** Patients with GCA have described a range of themes of interest in relation to their disease. These data could be used as the basis of developing a patient reported measure of outcome in GCA.

**Disclosure of Interest:** None declared

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FRI0500

#### EXTRACRANIAL VASCULAR AFFECTION IN GIANT CELL ARTERITIS

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**Background:** Giant cell arteritis (GCA) is a large vessel vasculitis with a predisposition for the cranial branches of the external carotid artery. However, aorta and/or its main branches may also be involved (1–3).

**Objectives:** To assess the vascular territories most frequently affected in a series of patients with GCA who presented extracranial vessel involvement.

**Methods:** Retrospective study of patients with GCA who presented compromise of extracranial vessels confirmed by PET/CT. Visual analysis of vascular uptake was performed on supra-aortic trunks (SAT), aortic arch (AA), thoracic aorta (TA), abdominal aorta (AA), iliac arteries (IA), lower limb arteries (LLA), and upper limb arteries (ULA). We carried out a comparative study between both sexes to see if there was any difference in the pattern of affection.

**Results:** We evaluated 68 patients with GCA (51W/17M) with a mean age of 68.06±8.33 years. The vascular territories affected were: TA (n=58, 85.29%), SAT (n=38, 55.88%), AA (n=28, 41.18%), LLA (n=17, 25%), IA (n=13, 19.12%) and ULA (n=6, 8.82%). We also made a study of the number of vascular territories affected: 1 vascular territory (n=13, 19.12%), 2 territories (n=22, 32.35%), 3 territories (n=18, 26.47%), 4 territories (n=12, 17.65%) and more than 4 territories (n=3, 4.41%). Likewise, a comparative study between both sexes was conducted, in which only statistical significance was achieved in the involvement of ULA, which was more frequent in men (table 1).

Abstract FRI0500 – Table 1

	Men (n=17)	Women (n=51)	p
Age, mean ± SD	69.3 ± 8.6	67.6 ± 8.6	0.48
<b>Vascular territories affected, n (%)</b>			
Supra-aortic trunks	8 (47.1)	30 (58.8)	0.57
Aortic arch	4 (23.5)	14 (27.4)	0.99
Thoracic aorta	12 (70.6)	46 (90.2)	0.11
Abdominal aorta	5 (35.3)	22 (43.1)	0.78
Iliac arteries	1 (5.9)	12 (23.5)	0.21
Upper limb arteries	4 (23.5)	2 (3.9)	0.04
Lower limb arteries	6 (35.3)	7 (13.7)	0.11
<b>Number of vascular territories affected, n (%)</b>			
1	5 (29.4)	8 (15.7)	0.37
2	5 (29.4)	20 (39.2)	0.66
3	5 (29.4)	13 (25.5)	0.99
4	1 (5.9)	11 (21.6)	0.27
>4	1 (5.9)	2 (3.9)	0.73

**Conclusions:** In patients with GCA the involvement of TA is very frequent, followed by the SAT and the AA. To a lesser extent, the AA and the LLA vessels are affected. The involvement of the IA and the ULA vessels is less frequent; the latter more frequently in men. On the other hand, the involvement of 2–3 vascular territories are the most frequent patterns.

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FRI0501

#### NEGATIVE TEMPORAL ARTERY BIOPSIES: COMPARISON BETWEEN BIOPSY-NEGATIVE GCA AND NON-GCA PATIENTS

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**Background:** Temporal artery biopsy (TAB) plays a key role in diagnosis of giant cell arteritis (GCA). However, approximately 15%–20% of patients ultimately diagnosed with GCA have negative biopsies. Among patients with negative TAB, it is often challenging to identify patients with GCA from those with an alternate (non-GCA) diagnosis.

**Objectives:** To compare TAB-negative GCA with patients receiving a non-GCA alternate diagnosis.

**Methods:** Two cohorts were retrospectively identified through direct medical record review. The first cohort consisted of patients with TAB-negative GCA diagnosed between 1/1/1998 and 12/31/2013. The second cohort included all patients with a negative TAB performed between 1/1/2009 and 12/31/2010 in which a non-GCA alternate diagnosis was provided after a minimum of 6 months of follow up. Final diagnoses were confirmed by consensus among two rheumatologists and a

physician abstractor. Baseline characteristics were compared between the two cohorts using chi-square and rank sum tests.

**Results:** 110 patients with TAB-negative GCA and 195 non-GCA patients with a negative TAB were identified. Alternate diagnoses for non-GCA patients are listed in table 1. Age, sex, number of days on glucocorticoids prior to biopsy, and biopsy length were similar in both groups. Time from first symptom to diagnosis was longer in non-GCA patients [mean (SD); 2.6 (2.5) vs 1.5 (2.1) months; p<0.001] and fewer non-GCA patients fulfilled ≥3 ACR criteria for GCA (27% vs 64%; p<0.001). Although headache was the primary symptom in both cohorts (66% TAB-negative GCA; 68% non-GCA), patients with biopsy-negative GCA had more frequent anorexia, fatigue, fever, polymyalgia rheumatica, temporal artery tenderness and claudication (jaw, arm, or leg). Baseline transient (5% TAB-negative GCA; 6% non-GCA; p=0.58) and permanent (3% TAB-negative GCA; 3% non-GCA; p=0.86) vision loss were infrequently observed. ESR was higher in TAB-negative GCA patients [64.0 (35.1) vs 55.2 (67.4); p=0.002] compared to non-GCA patients but CRP did not differ [44.3 (53.6) vs 43.8 (61.9); p=0.39].

Abstract FRI0501 – Table 1

Alternate diagnosis, n (%)	Negative biopsy with alternate diagnosis (N=195)
Neurologic condition	75 (38%)
Isolated PMR	38 (19%)
Rheumatic disease other than PMR or GCA	26 (13%)
Non-arteritic AION	10 (5%)
Fever of unknown origin	9 (5%)
Infectious disease	7 (4%)
Non-malignant hematologic condition	7 (4%)
Malignant disease	6 (3%)
Other vasculitis	6 (3%)
Cervical arthritis	5 (3%)
Systemic disease of unknown etiology	5 (3%)
Other	1 (1%)

AION: anterior ischemic optic neuropathy; GCA: giant cell arteritis; PMR: polymyalgia rheumatica

**Conclusions:** In this cohort, neither headache nor vision loss at presentation were associated with an ability to discriminate between diagnosis of TAB-negative GCA compared to patients without GCA. ACR criteria may be helpful in identifying patients with TAB-negative GCA. Among patients with negative TAB, constitutional symptoms and claudication (jaw/limb) were more frequently associated with an ultimate diagnosis of TAB-negative GCA.

**Disclosure of Interest:** None declared

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FRI0502

#### RISK OF CANCER IN PATIENTS DIAGNOSED WITH GIANT CELL ARTERITIS IN WESTERN NORWAY 1972–2012

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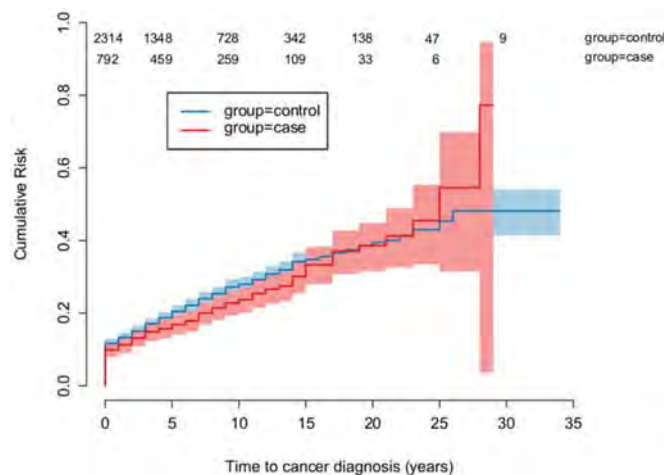
**Background:** A meta-analysis from 2014 reported a low but statistically significant increased malignancy risk among patients with giant cell arteritis (GCA), but individual epidemiological studies have shown conflicting results.<sup>1</sup>

**Objectives:** To determine the risk of cancer in GCA patients during a 41 year period.

**Methods:** Hospital-based retrospective cohort study including patients diagnosed with GCA in Bergen Health Area during 1972–2012. Patients were identified through computerised hospital records using the International Classification of Diseases (ICD)-coding system. Clinical information was extracted from patients' medical journals. We excluded patients if data were unavailable, if the reviewing rheumatologist found GCA to be an implausible diagnosis or if the American College of Rheumatology (ACR) 1990 classification criteria for GCA were not fulfilled. Each patient was matched for age, sex, and county of residence to 3 control subjects randomly selected from the Central Population Registry of Norway. Information on the occurrence of cancer was obtained from the Cancer Registry of Norway. The cumulative incidence of malignancy in cases and controls were estimated using Kaplan-Meier plots.

**Results:** The patient inclusion process and patient characteristics have been published previously.<sup>2</sup> A total of 792 patients were included, 566 (71.5%) women (mean age 73.5 years, SD 8) and 226 (28.5%) men (mean age 72.1, SD 9). There were 2314 matched controls (excluding duplicate controls and control subjects

which were also among the cases). The mean duration of follow-up for the GCA-patients was 7.2 years (SD 6.7). The mean duration of follow-up for the controls was 6.6 years (SD 6.1). The relative risk of malignancy during follow-up was higher for controls compared to cases during the majority of the observation period, but the overall difference was not statistically significant ( $p=0.060$ , figure 1). However, the subset of 528 patients (66.7%) with a positive temporal artery biopsy (TAB) had a statistically significant lower risk of malignancy compared to their matched controls ( $p=0.006$ ).



**Conclusions:** We did not find a significant difference in the risk of malignancy in the overall GCA cohort compared to their matched controls. However, we found a statistically significant reduced risk of malignancy during follow-up for the subset of GCA-patients with a positive TAB. This is in contrast to the results of a meta-analysis which found an increased risk of malignancy in the subgroup with positive TAB. Further studies are required to determine whether this is a true difference, and what the potential causes may be.

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**Acknowledgements:** The study has used data from the Cancer Registry of Norway (CRN). The interpretation and reporting of these data are the sole responsibility of the authors, and no endorsement by CRN is intended nor should be inferred.

**Disclosure of Interest:** L. Brekke Grant/research support from: MSD, A. Diamantopoulos: None declared, B.-T. Fevang Consultant for: Lilly, Novartis, AbbVie, J. Assmus: None declared, C. Gjesdal: None declared

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#### FRI0503 RISK FACTORS OF CARDIAC VALVULAR INVOLVEMENT IN PATIENTS WITH TAKAYASU'S ARTERITIS

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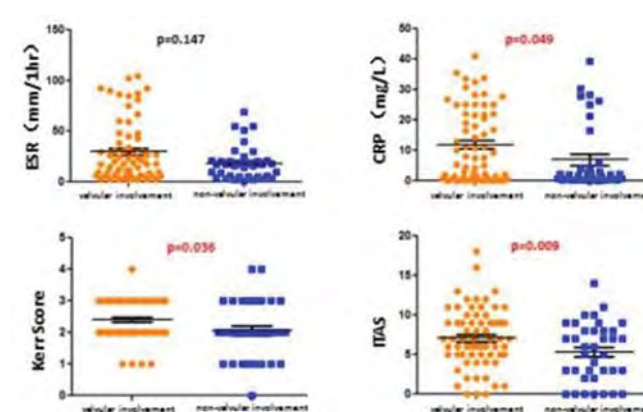
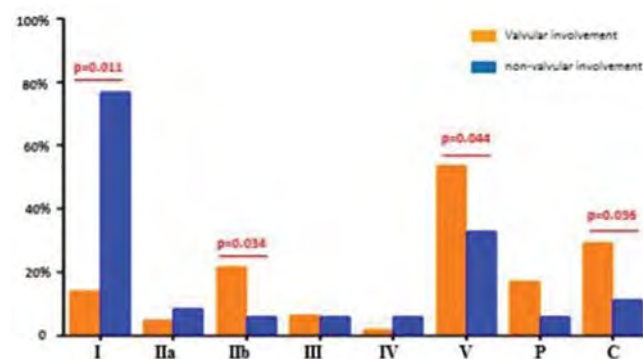
**Background:** Takayasu's arteritis (TA) patients with higher disease activity have more cardiovascular morbidity compared to the TA patients with low disease activity, and active group showed a higher incidence of significant aortic valve regurgitation<sup>[1]</sup> which may linked heart failure and poor prognosis.<sup>2</sup>

**Objectives:** The aim of this study is to investigate the imaging and serological features and evaluated disease activity in TA patients with valvular involvement, to find the risk factors of valvular involvement in those patients.

**Methods:** 103 patients of TA were divided into 2 groups according to with or without valvular involvement. We compared the difference of serological and imaging features in 2 groups. Logistic model was used to determine the risk factors of valvular involvement in TA patients.

**Results:** Aortic insufficiency (62.12%) was most common in valvular involvement group, followed by mitral insufficiency (59.09%), tricuspid involvement (54.55%) and pulmonary involvement (6.06%). In which of them, single valvular involvement was 36.36%, multiple valvular involvement was 63.64%. There were 12

(22.22%) patients developed to heart failure. In valvular involvement patients, most common angiographic type was Numano type V (53.30% vs. 32.43%,  $p=0.044$ ). The second was Numano type IIb ( $p=0.034$ ), which were significantly higher than that of non-valvular involvement group. Numano type I was most common type in non-valvular involvement patients, and the proportion was higher than that in the patients with valvular involvement ( $p=0.034$ ). At the same time, we analysed the involvement of pulmonary and coronary in the 2 groups. TA patients with valvular involvement showed a higher incidence of the coronary lesion than the patients without valvular involvement ( $p=0.036$ ) (figure 1). Serum level of IgA ( $p=0.032$ ) and IgG ( $p=0.015$ ) were significantly higher in the patients with valvular involvement than that the patients without valvular involvement. We also evaluated the parameters of TA disease activity between 2 groups, in patients with valvular involvement, level of CRP was higher than that of non-valvular involvement group ( $p=0.049$ ). Kerr score ( $p=0.036$ ) and ITAS ( $p=0.009$ ) were all higher than those in non-valvular involvement group (figure 2). Logistic regression showed that the risk of valve involvement in TA patients with elevated level of IgG is 23 times higher than the patients with normal level of IgG. ( $p=0.001$ , OR=22.068, 95% CI:3.676–132.488), the risk of valvular involvement in TA patients with Numano type IIb ( $p=0.002$ , OR=20.352, 95% CI:3.146–131.655) and V ( $p=0.001$ , OR=9.437, 95% CI:2.661–33.465) was 20.35 times and 9.44 times higher than other types.



**Abstract FRI0503 – Figure 1.** Angiographic type in TA patients with or without valvular involvement. The prevalence of Numano type IIb (21.21% vs. 5.41%,  $p=0.034$ ) and type V (53.30% vs 32.43%,  $p=0.044$ ) were higher in TA patients with valvular involvement, TA patients with valvular involvement showed a higher incidence of the coronary lesion than that of non-valvular involvement group (28.79% vs 10.81%,  $p=0.036$ ).

Note P: pulmonary; C: coronary

**Conclusions:** Our study showed that the level of IgA, IgG and CRP were significantly higher in TA patients with valvular involvement and the disease activity was higher in those patients. Elevated IgG, Numano type IIb and type V were the risk factors of valvular involvement in patients with TA.

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**Disclosure of Interest:** None declared

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**FRI0504** **DIFFUSE ALVEOLAR HAEMORRHAGE IN ANCA-ASSOCIATED VASCULITIS: CAN WE PREDICT OUTCOME? AN ITALIAN MULTICENTRE RETROSPECTIVE LONG-TERM STUDY OF 102 PATIENTS**

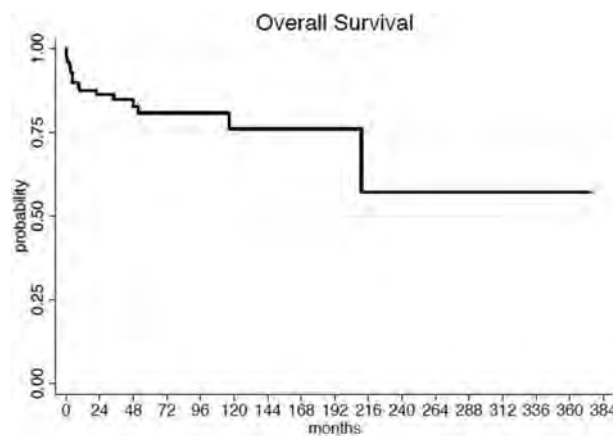
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**Background:** Diffuse alveolar haemorrhage (DAH) is a rare and severe manifestation of ANCA-associated vasculitides (AAV).

**Objectives:** To identify predictors of survival in patients with AAV-DAH.

**Methods:** A retrospective study of 102 consecutive patients (50% females; mean age 59±17 years) from 27 Italian Centres diagnosed with AAV-DAH was planned. Cox regression unadjusted analyses were performed.

**Results:** Among AAV patients, 47% had Granulomatosis with Polyangiitis (GPA), 47% Microscopic Polyangiitis (MPA) and 6% Eosinophilic Granulomatosis with Polyangiitis (EGPA). At DAH onset, mean BVAS was 20±8 and most patients had renal involvement (RI). Admission to Intensive Care Unit was needed in 27% of patients, while ventilatory support (VS) was required in 46%. At least one cardiovascular risk factor (CVRF) was recorded in 48%. Over a median follow-up of 39 months (25%–75% IQR 66 months), 19/102 patients (18.6%) died (figure 1). All patients received high-dose glucocorticoids in association with Cyclophosphamide (CYC 78%, mean cumulative dose 8±7 g) or Rituximab (37%). Plasma exchange was performed in 46%. Infections occurred in 38%. Age>65 years (HR 3.05 [95% CI 1.18–7.9], p=0.04), CVRF ≥2 (HR 8.85 [95% CI [AG7] 2.34–33.50], p=0.01), BVAS (v.3) (HR 1.07 [95% CI 1.01–1.13], p=0.01) were associated with mortality, whereas FFS was not. The need for VS (HR 4.54 [95% CI 1.48–13.85], p=0.008) and infections (HR 3.98 [95% CI 1.48–10.69] were also associated with mortality.



**Conclusions:** Older age, VS, CVRF and infections affect the survival in AAV. There is a need for specific outcome measures.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrhumdis-2018-eular.4196

**FRI0505** **VALIDATION OF THE PROGNOSTIC VALUE OF THE HISTOPATHOLOGICAL CLASSIFICATION OF ANCA-ASSOCIATED GLOMERULONEPHRITIS: A META-ANALYSIS**

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**Background:** In 2010, a histopathological classification of antineutrophil cytoplasmic autoantibody (ANCA)-associated glomerulonephritis (AAGN) was proposed by an international consortium of renal pathologists and nephrologists. It comprises four biopsy classes: focal, crescentic, mixed and sclerotic, the order of which was shown, in the initial publication, to correspond to increasing severity of renal impairment during follow-up.

**Objectives:** The aim of this meta-analysis was to evaluate the prognostic value of the phenotypical classes by means of validation studies that have been published since.

**Methods:** A literature search was performed using Web of Science, Google Scholar, PubMed and Embase in March 2017, selecting studies that associated histopathological class to renal outcome in adult patients with AAGN. The risk of developing end-stage renal disease (ESRD) during follow-up was compared between classes using a meta-analysis with random effects model. Weighted relative risks (RR) with 95% confidence intervals (95% CI) were reported.

**Results:** Nineteen studies were included with a total of 2408 patients. Using sclerotic class as a reference category, ESRD risk was lower in the crescentic class (RR 0.53, 95% CI 0.43–0.64); RR in focal was lower than in crescentic class (RR 0.27 95% CI 0.20–0.37). RR in crescentic compared to mixed class was 1.18 (95% CI 0.95–1.45); RR in focal compared to mixed class was 0.34 (95% CI 0.25–0.47).

**Conclusions:** Our meta-analysis shows that the risk for developing ESRD increased with more severe histopathological lesions. We found no difference between the crescentic and mixed classes, pointing towards a comparable risk profile with regard to ESRD. We are currently performing an individual patient data meta-analysis, as this technique is better equipped to deal with study heterogeneity. For the moment, this meta-analysis confirms the use of the histopathological classification system as a predictor of renal outcome in the prognostication of patients with AAGN.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrhumdis-2018-eular.7111

FRI0506

### CLINICAL ANALYSIS OF BEHÇET'S DISEASE MANIFESTATIONS IN 453 EGYPTIAN PATIENTS: GENDER COMPARISON

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**Background:** Behçet's disease (BD) is characterised by the presence of vasculitis of veins and arteries of all sizes.<sup>1</sup> Persistent oral and genital ulcers are hallmarks of the disease. BD may be associated with inflammation of eyes, joints, vessels, GIT, nervous system, and other systems.<sup>2</sup> 70% of BD patients suffer from ocular complications mainly recurrent uveitis that may lead to loss of vision.<sup>3</sup> **Objectives:** To describe the demographic and clinical features including ocular manifestations of BD in Egyptian patients and to compare the incidence of disease complications between males and females.

**Methods:** 453 subjects fulfilling 1990 Classification criteria for BD were included. Detailed history, physical examination and complete ocular examination were done. Both, a rheumatologist and an ophthalmologist did clinical examination and follow-up. Further comparison of disease manifestations between both genders was done. Patients were followed up every 2 weeks for 4 years for monitoring of disease complications.

**Results:** Median (range) age of patients was 45<sup>32-63</sup> years old. Our sample included 297 (65.6%) males and 156 (34.3%) females. Patients' disease duration ranged between one to 16 years. At baseline, acute phase reactants (ESR and CRP) were significantly higher in females compared to males ( $p < 0.01$ ) indicating a higher disease activity.

Oral ulcers were present in 100% of patients. Prevalence of genital ulcers, erythema nodosum and joint involvement was similar between both sexes. Subcutaneous thrombophlebitis and follicular papules were more common in males compared to females ( $p = 0.009$  and  $p = 0.041$  respectively).

Recurrent iridocyclitis was found in 100% of patients. All ocular findings were significantly more common in females compared to males except retinal haemorrhages that were more common in males (49.8% vs 37.2%). Incidence of secondary cataract and glaucoma in addition to vitreous opacities were similar between both sexes.

14.8% of patients had GIT manifestations including Budd-Chiari syndrome in 10 males and 5 females; bloody diarrhoea was found in 10 males. Disturbed bowel habits were present in 27 males and 10 females.

Deep venous thrombosis (DVT) was found in 11.8% of males and 3.2% of females. Mediastinal vein syndrome was found in 3.7% of males only, pulmonary artery aneurysm in 1.3% of males and 3.2% of females. Aseptic meningitis and hemiplegia were found 3.4% and 3% of males respectively. 1.7% males and 3.2% females suffered from brain stem involvement. Superior sagittal sinus thrombosis was present in 3.4% females.

**Conclusions:** BD has wide range of complications most commonly oral ulcers and recurrent iridocyclitis. Surprisingly, disease activity was higher in females at baseline and ocular complications were more common in females compared to males.

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**Disclosure of Interest:** None declared

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FRI0507

### THE PREVALENCE OF LATENT TUBERCULOSIS INFECTION IN INDIAN PATIENTS OF TAKAYASU ARTERITIS

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**Background:** Studies have shown a correlation between Tuberculosis (TB) and Takayasu arteritis (TA). Some even postulate that infection with TB is required for the initiation of aortoarteritis. Hence, this project was undertaken to find an association of TB and TA by studying the prevalence of Latent Tuberculosis Infection (LTBI) in Indian TA patients.

**Objectives:** To study the prevalence of LTBI in Indian TA patients and see whether LTBI is more in these patients as compared to the historical cohort (40% in Indian population).

**Methods:** This was a cross sectional observational study. All consecutive patients with TA (satisfying the ACR 1990 criteria) were included prospectively from a period of May 2016 to December 2017. Their clinical, laboratory and radiological data were collected after obtaining informed consent. Patients were divided into groups based on the angiographic classification. LTBI was assessed by the Mantoux test and Quantiferon TB Gold test. Mantoux test (MT) was done with 5TU and results were read after 48-72 hours. An induration more than 10 mm was considered positive. Quantiferon TB Gold assay (QTB) was done by ELISA technique and (patient minus control) value  $> 0.35$  IU/ml was considered positive. A positive result of MT and /or QTB was considered positive for LTBI. Chest X-ray was included to access evidence of past or active TB lesions. Active infection was defined as clinical and microbiological and /or radiological evidence of TB. The study was approved by the Ethics committee of Medanta hospital.

**Results:** Out of 66 consecutive TA patients, 46 patients had tests available for LTBI and these were included in the analysis. The mean age of the cohort was 34.9 years with a median disease duration of 24 months. Males consisted of 11 patients whereas females formed the majority i.e. 35 patients (M: F = 1: 3.1). Angiographic Type V (54.3%) was the commonest in the cohort followed by Type IIB (17.3%), Type IV, I, IIA and III (15.2%, 8.6%, 2.1% and 2.1% respectively). LTBI positivity was present in 32.6% of the cohort; with 5 patients (10.8%) having both tests positive. 6 patients were MT positive without being QTB positive and 4 patients were only QTB positive. Eight patients had history of Tuberculosis out of which 1 was diagnosed with TB and TA simultaneously. Four patients were diagnosed as TA during the course of Anti tubercular treatment (ATT) between 4 to 6 months, whereas the rest were diagnosed after ATT completion. The mean duration of Anti tubercular treatment was 8 months. Koch's contact was seen in 7 patients.

**Abstract FRI0507 – Table 1.** Patient characteristics and LTBI

	Characteristic	Value	Percentage (%)
n=46	MT positive only	6	13
	QTB positive only	4	8.6
	Both MT and QTB positive	5	10.8
	LTBI positive	15	32.6
n=8	H/O TB	8/46	17.3
	TB LN	4	50
	Pulmonary TB	1	12.5
	(progression)		
	Intestinal TB	2	25
	TBM	1	12.5
	Empirical ATT for PUO	1	12.5
	MT	2	25
	QTB	0	0
	Both	1	12.5
	n=7	TB contact	7/46
MT		1	14.2
QTB		0	0
Both		0	0

**Conclusions:** The prevalence of LTBI in Indian Takayasu patients was 32.6%, which was not higher than the population prevalence (40% in the historical cohort). However, a larger cohort and further association studies are needed for the relationship between TA and Tuberculosis.

**Disclosure of Interest:** None declared

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FRI0508

### ANALYSIS OF RISK FACTORS OF ADVERSE OBSTETRICAL OUTCOME IN PATIENTS WITH TAKAYASU ARTERITIS

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**Background:** Takayasu arteritis (TA) is a large-vessel vasculitis that affects young women of childbearing age. Several small case-series described the pregnancy outcome in TA patients with lack of study determining risk factors associated with adverse pregnancy outcome.

**Objectives:** We performed a French retrospective study, to determine the risk factors associated with obstetrical adverse outcome; and the relation between pregnancy outcome and TA disease activity.

**Methods:** French nationwide retrospective study of pregnancies that lasted at least 12 weeks of gestation (WG) in TA patients.

**Results:** Forty-three pregnancies occurred in 33 patients. The diagnosis of TA was preexisting in 29 patients, and done during pregnancy in 4.

For the 39 pregnancies in the 29 patients with a preexisting diagnosis of TA: steroids were maintained throughout pregnancy in 23/39 (59%) with a median dose of 5 mg/day<sup>2-40</sup> immunosuppressive treatment during pregnancy included azathioprine (n=9, 21%) or infliximab (TNF- $\alpha$  antagonist) (n=1, 2%). For the 4 pregnancies with TA diagnosis during, only one was treated by steroids. Aspirin (100 mg/day) was used in 27/43 pregnancies (63%) and antihypertensive drugs were used in 10 pregnancies (23%).

Before pregnancy, immunosuppressive treatment had been used in 16 patients: azathioprine (n=10, 30%), methotrexate (n=7, 21%), TNF- $\alpha$  antagonist (infliximab in 3 and adalimumab in 1; n=4, 12%) and cyclophosphamide (n=2, 6%).

Maternal adverse events were noted in 20 pregnancies (47%). The most frequent adverse event was arterial hypertension (n=12; 28%): 10 worsening of previous arterial hypertension and 2 *de novo* arterial hypertension. Other adverse events included pre-eclampsia (n=3; 7%), HELLP syndrome (n=1; 2%) and post-partum haemorrhage (n=2; 5%). No maternal death was observed.

There were 42 live births (98%) delivered at a median term of 38<sup>27-42</sup> WG with 9 (21%) before 37 WG and one medical termination of pregnancy for major IUGR at 21WG. IUGR was observed in 6 pregnancies (14%) associated with hypertension and pre-eclampsia or HELLP syndrome in 2 cases.

The median birth weight was 2940 [610-4310] grams. Five children (12%) required intensive care units hospitalisation. One premature boy (27 WG) died after 2 days. Treatment during pregnancy included steroids (n=25/43, 58%), azathioprine (n=9/43; 21%) and infliximab (n=1/43; 2%). Pre-eclampsia were less frequent in patients treated with steroids during pregnancy (p=0.02).

The risk of developing arterial hypertension was associated with previous chronic arterial hypertension, and an infra-diaphragmatic vasculitis injury (p=0.01 and p=0.04). Activity of TA was observed in the course of 12/43 pregnancies (28%).

**Conclusions:** We observed both a high rate of obstetrical complications and of live birth. A preexisting chronic arterial hypertension, the infra-diaphragmatic location of vasculitis and/or an active disease in the 6 months preceding the pregnancy were associated with an impaired pregnancy outcome. TA disease activity did not seem to be influenced by pregnancy.

**Disclosure of Interest:** None declared

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#### FRI0509 THE FACTORS ASSOCIATED WITH ANXIETY/DEPRESSIVE DISORDERS IN BEHÇET'S DISEASE PATIENTS

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**Background:** The anxiety/depressive disorders (ADD) is a special psychopathological problem for Behçet's Disease (BD) patients. ADD has high rates in BD, but their causes aren't enough investigated.

**Objectives:** To determine the main factors associated with anxiety/depressive disorders in BD patients.

**Methods:** The investigation has been realised in accordance with the interdisciplinary program "Stress factors and mental disorders in immune-mediated inflammatory rheumatic diseases".

116 BD patients were enrolled in the study. The majority of patients were men (69,8%), natives of the North Caucasus (51,9%), with mean age (M $\pm$ m) 33,3 $\pm$ 0,98 years. All the patients met the criteria of the International Study Group for BD (1990) classification. The disease activity was assessed by scoring system BDCAF.

ADD were diagnosed by psychiatrist in accordance with the ICD-10 in semi-structured interview. The severity of depression was evaluated by Montgomery-Asberg Depression Rating Scale (MADRS) and anxiety – by Hamilton Anxiety Rating Scale (HAM-A). The severity of stress was evaluated by PSS-10 scale.

**Results:** ADD were diagnosed in 87 BD patients (75%). The dysthymia (29,3%) and recurrent depressive disorder (21,5%) prevailed in these patients, generalised anxiety disorder (6,03%) and single depressive episode (7,76%) were rare. Cognitive disorders of different severity were diagnosed in 87 (75%) patients. The presence of ADD didn't depend on gender and duration of the disease. The factors associated with ADD were found during Pearson correlations. Then linear regression analysis was done and obtaining prognostic model showed that ADD was associated with: sleep disorders ( $\beta=0,401$ ), asthenia ( $\beta=0,176$ ), cognitive disorders ( $\beta=0,145$ ), chronic stress ( $\beta=0,036$ ) and stress severity (PSS-10 score) ( $\beta=0,115$ ), age of eye damage ( $\beta=0,135$ ), onset of ADD before BD onset ( $\beta=0,147$ ), pure quality of life (QoL) estimated by visual analogue scale (VAS)

( $\beta=0,163$ ), gastrointestinal BD symptoms ( $\beta=0,101$ ), higher CRP level ( $\beta=0,174$ ), younger age of patients ( $\beta=-0,053$ ) and early childhood trauma (before 7 years old) ( $\beta=0,15$ ) (area under the ROC curve=0,957) (figure 1).

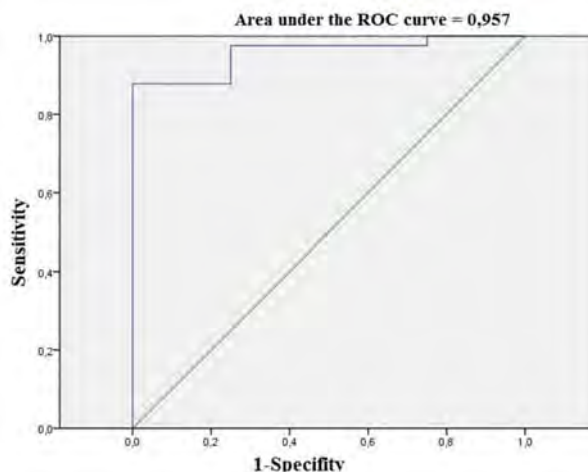


Figure 1 Area under the ROC curve=0957

**Conclusions:** The results demonstrated high prevalence of ADD in surveyed BD patients. ADD in BD is much more associated with early childhood trauma, chronic severe stress, onset before BD, younger age of patients, older age of eye damage, gastrointestinal involvement, higher CRP level, accompanied by sleep disturbances, asthenia, cognitive disorders and had a negative impact on QoL.

**Disclosure of Interest:** None declared

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#### FRI0510 INCREASED EXPRESSION OF V-DOMAIN I $\kappa$ B SUPPRESSOR OF T-CELL ACTIVATION (VISTA) ON LEUKOCYTES OF GRANULOMATOSIS WITH POLYANGIITIS (GPA) PATIENTS

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**Background:** Vascular inflammation in GPA is the result from an inflammatory event combined with a highly specific immune response. Antineutrophil cytoplasmic antibodies (ANCA) specific for GPA are directed against neutrophil granule proteins. Neutrophils are known to play an important role in the pathogenesis of GPA. Under normal conditions, activation of immune cells is positively and negatively regulated by stimulatory and inhibitory checkpoint molecules. The right balance between the expression of both molecules is crucial in fine-tuning the immune response and preventing autoimmunity. Recently, VISTA (V-domain Ig suppressor of T cell activation) has been identified as a potent negative regulator of T cell activation.

**Objectives:** This study aimed to investigate the expression of VISTA on circulating leukocytes of GPA-patients and compare it with vasculitis control (VC) patients with Giant Cell Arteritis (GCA) and healthy controls (HC).

**Methods:** In a cross-sectional study, fresh blood samples were obtained from 43 GPA-patients in remission on immunosuppressive treatment, 24 VC and 34 sex and age-matched HC. The frequency of VISTA expression was determined on Th-cells (CD45RO<sup>-</sup> and CD45RO<sup>+</sup>), NK cells, monocyte subsets (classical/non classical/intermediate) and on neutrophils (suppressive/non suppressive subsets) by flow cytometry.

**Results:** The proportion of VISTA expressing Th-cells was significantly increased in GPA-patients compared with HCs, this increase could be seen in both, the CD45RO<sup>-</sup> compartment as well as in the CD45RO<sup>+</sup> compartment. NK cells from GPA-patients showed an increase in the proportion of VISTA expressing cells when compared to the VCs and HCs. Among monocyte subsets, a slight decrease in the proportion of VISTA on the Intermediate subset could be seen. Interestingly, on neutrophils a significant increase in the proportion of VISTA<sup>+</sup> cells was seen in GPA-patients in comparison to HCs and VCs. This increase was most pronounced in the suppressive neutrophil subset.

**Conclusions:** VISTA expression is increased in both naïve and memory Th cells of GPA patients in remission. Interestingly, neutrophils of GPA patients showed higher levels of VISTA and this was most pronounced in the suppressive neutrophil subset. Whether the increased expression of VISTA has functional consequences needs further investigation.



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**FRI0511** **THYROID ARTERY INVOLVEMENT DETECTED BY COLOUR-DOPPLER ULTRASONOGRAPHY IN AN INCIPIENT, SINGLE CENTRE GIANT CELL ARTERITIS COHORT**

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**Background:** The inflammation of thyroid arteries (ThA) is not commonly considered and investigated in giant cell arteritis (GCA).

**Objectives:** To estimate the frequency of the superior and/or inferior ThA involvement as detected by Colour Doppler Sonography (CDS).

**Methods:** We conducted a prospective single centre study between 1 October 2013 and 30 September 2017. The CDS of superior and inferior ThA was performed in all newly diagnosed, treatment naive GCA patients in addition to the routinely evaluated temporal, facial, occipital and large supraaortic arteries. The superior and inferior ThA were identified at their respective anatomical locations in close proximity to the thyroid gland and examined using the standard Doppler settings for temporal arteries. Arteries were evaluated in two planes for the highly specific halo sign. Laboratory thyroid function tests consisted of TSH, T3 and T4 measurements at the time of GCA diagnosis (prior to any steroid therapy). Characteristics of GCA cases with inflamed ThA were explored and compared to the GCA group without ThA involvement.

**Results:** During the 48 months we performed the CDS of the multiple arteries in 124 consecutive GCA patients (median age 74.7 (IQR 66.5–79.1) years, 65% female). We observed the halo sign on either superior or inferior ThA in 11 (8.9%) cases. All the patients with ThA involvement also had CDS signs of temporal artery involvement, which was confirmed by temporal artery biopsy in all 11 cases. There was a positive trend for correlation between fever ( $\geq 38^\circ\text{C}$ ) and/or dry cough in the patients with ThA involvement (fever: RR 2.99, CI 0.98–9.06,  $p=0.07$ ; dry cough: RR 2.73, CI 0.89–8.3,  $p=0.10$ ). Four patients reported symptoms consistent with thyroid gland pathology. None of the patients with ThA involvement had symptoms of polymyalgia rheumatica. No correlation was found with other clinical and demographic characteristics, including weight loss, headache, jaw claudication and visual disturbances.

Sixteen out of 124 GCA patients (12.9%) had a history of thyroid dysfunction (11 hypothyroidism, 1 hyperthyroidism, 1 euthyroid goitre; 3 patients had thyroid surgery because of either goitre or suspected malignancy). In 2/16 patients we also found CDS signs of ThA involvement, yet the thyroid function tests were normal at the time of GCA diagnosis in these patients. Laboratory signs of thyroid dysfunction were found in 3/11 (27.2%) patients with ThA involvement (2 latent hyperthyroidism, 1 latent hypothyroidism), none of these patients had previous history of thyroid disease.

**Conclusions:** In our incipient GCA cohort, a tenth of all patients had ultrasonographic signs of ThA involvement. To the best of our knowledge, this is the first study that systematically assessed the ThA involvement.

**Disclosure of Interest:** None declared

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**FRI0512** **RISK OF OPPORTUNISTIC INFECTIONS IN PATIENTS WITH ANTINEUTROPHIL CYTOPLASMIC ANTIBODY-ASSOCIATED VASCULITIS USING JAPANESE HEALTH INSURANCE DATABASE**

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**Background:** It has been reported that patients with antineutrophil cytoplasmic antibody associated vasculitis (AAV) had a high risk of infections<sup>1–3</sup>. Among infections, opportunistic infections (OIs) influence patients' vital prognosis and complicate treatments. It is essential to investigate risk of OIs for appropriate management of patients with AAV. However, data about incidence of OIs and risk factors in patients with AAV is limited to date.

**Objectives:** To identify incidence and risk factors of OIs under the remission-induction therapy in patients with AAV using Japanese health insurance database.

**Methods:** This retrospective longitudinal population-based study was conducted using claims data provided by Medical Data Vision Co., Ltd. We defined individuals as AAV cases receiving remission-induction therapy if they met all of the following: 1) had at least one ICD10 code (M300 or M301 or M313 or M318); 2) had at least one prescription of oral corticosteroids (CS) with prednisolone (PSL)-equivalent dosage  $\geq 30$  mg/day, methylprednisolone (mPSL) pulse therapy, immunosuppressive drugs (IS) (cyclophosphamide, methotrexate, mycophenolate mofetil), or rituximab during hospitalisation between April 2008 and April

2017 and 3) had at least 7 days of hospitalisation. If patients had multiple hospitalizations for AAV remission-induction therapy defined as above, the first hospitalisation between April 2008 and April 2017 was analysed in this study. OIs were defined as follows: at least one ICD10 code and one prescription of predefined drugs for each OI during hospitalisation. We calculated incidence proportion and adjusted odds ratio (OR) of risk factors for OIs using a logistic regression model.

**Results:** Two thousands and two hundreds ninety nine patients were included in this study. The median age was 73 years and 55.2% were female. The number of patients with ICD10 code M300 for microscopic polyangiitis, M301 for eosinophilic granulomatosis with polyangiitis, M313 for granulomatosis with polyangiitis, M318 for AAV, and two or more of these ICD10 codes was 1015 (44.1%), 385 (16.7%), 234 (10.2%), and 665 (28.9%), respectively. mPSL pulse therapy, oral PSL  $\geq 30$  mg/d, at least one IS, and rituximab was used in 37.5%, 83.3%, 26.2%, and 5.4%. OI occurred in 203 patients (8.8%) and the most frequent OI was cytomegalovirus infection ( $n=79$ , 3.4%). The numbers (%) of candida infection, aspergillus infection, and pneumocystis jirovecii pneumonia were 28 (1.2), 24 (1.0), and 22 (1.0). No case with tuberculosis was observed. After adjusting for comorbidities, age by decade (OR: 1.34 [95% CI, 1.16–1.57]), IS or rituximab use (OR 1.60 [1.17–2.18]), mPSL pulse therapy (OR 2.62 [1.93–3.56]), PSL dosage per 1 mg (OR 1.02 [1.01–1.03]) were associated with occurrence of OIs significantly.

**Conclusions:** Older age, immunosuppressive treatments were identified as significant risk factors of OIs under the remission-induction therapy in patients with AAV using health insurance database.

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**FRI0513** **THE IMPACT OF DEPRESSION, ANXIETY AND FATIGUE IN PATIENTS WITH BEHÇET'S DISEASE**

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**Background:** Behçet's disease (BD) is a type of systemic vasculitis and inflammatory disease with unknown etiology which is associated with fatigue and lower quality of life (QoL).<sup>1</sup>

**Objectives:** In this study we aimed to assess the relationship between BDCAF and BDQoL, depression, anxiety and fatigue in Behçet's disease.

**Methods:** This is a cross-sectional study of 155 Behçet's syndrome (BS) patients and 107 healthy controls in Turkey. All subjects completed the Multidimensional Assessment of Fatigue (MAF) questionnaire, Hospital Anxiety and Depression (HADS) scale. Disease activity among BS patients was assessed using the Behçet's Disease Current Activity Form (BDCAF), and the physician's global assessment (PGA). And BD patients completed the Behçet's Disease Quality of Life (BDQoL) questionnaire.

**Results:** There was no significant difference with age and gender between the groups. BS patients had significantly higher HADS-anxiety (HADS-A), HADS-depression (HADS-D) and MAF scores than the healthy controls ( $p<0.05$ ) (table 1). BS patients with active disease had significantly higher MAF and HADS-A scores compared to inactive BS patients ( $p<0.05$ ). MAF scores showed positive correlations with HADS-A, HADS-D, BDCAF and BDQoL (table 2).

**Abstract FRI0513 – Table 1.** Comparison of BS patients and healthy controls

	Patients	Healthy controls	p
BDCAF	2.7±1.6	-	
BDQoL	9.4±9.2	-	
HADS-Anxiety	67 (%43.2)	11 (%10.3)	<b>0.001</b>
HADS-AnxietyScore	8 (0–21)	6 (0–13)	<b>0.004</b>
HADS-Depression	63 (%40.6)	23 (%21.5)	<b>0.001</b>
HADS-Depression Score	5 (0–20)	4 (0–10)	0.340
MAF	25.0 (6.5–48)	19.2 (7.3–44.2)	<b>0.000</b>

**Abstract FRI0513 – Table 2.** Correlations between MAF score and BDCAF, BDQoL, HADS-A, HADS-D in BS patients

Parametre	MAF score	
	R	p
HADSD	0459	<0001
HADSA	0548	<0001
BDQoL	0572	<0001
BDCAF	0359	<0001
DrVAS	0285	<0001
Patient VAS	0434	<0001
Age	0119	0141
Disease duration	0070	0384

**Conclusions:** Fatigue and anxiety is common in clinically active BS patients compared with healthy controls and inactive BD patients.

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**Disclosure of Interest:** None declared

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**FRI0514 ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODIES POSITIVITY IN INTERSTITIAL LUNG DISEASE PATIENTS**

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**Background:** Interstitial lung disease (ILD) is a possible manifestation of several rheumatic diseases. Although lung involvement is common in Anti-neutrophil cytoplasmic antibodies (ANCA) vasculitides (AAV), the presence of ILD is relatively rare. Moreover, a very small subgroup of patients may present ILD along ANCA positivity without other systemic signs of AAV.

**Objectives:** To describe the phenotypic characteristics of ILD patients with ANCA positivity without a definite diagnosis of AAV.

**Methods:** ANCA-ILD patients from 7 tertiary care hospitals (6 from Italy, 1 from Spain – 2 rheumatology centres, 4 pneumology centres, 1 internal medicine) were included. The mean follow-up was of 62.6±49.8 months. We collected epidemiologic, demographic, clinical, serological, pulmonary function test (PFT) data and high resolution computed tomography (HRCT) pattern.

**Results:** 19 patients with ANCA-ILD (M:F=9:10, mean age at diagnosis 66.2±8 years) were enrolled. The mean latency between the first respiratory symptom onset and the diagnosis was 26.4±37.0 months. Sixteen patients (84%) had ANCA-MPO positivity while 3 ANCA-PR3. Antinuclear autoantibodies were positive in 12 patients (63%).

Usual interstitial pneumonia was the main HRCT pattern (10, 52.6%), followed by non specific interstitial pneumonia (8, 42%, 1 associated with organising pneumonia), 1 combined pulmonary fibrosis and emphysema. Six patients with ILD-ANCA presented also a non-erosive oligoarticular inflammation (n=6).

During the follow-up, the majority of the patients (16/19) did not require oxygen therapy at last evaluation. However, 1 patient required continuous O<sub>2</sub>, 1

intermittent O<sub>2</sub>, 1 patient underwent lung transplant due to respiratory failure. Five patients required hospitalisation due to respiratory insufficiency. Two patients died, both for respiratory insufficiency.

All patients were treated with glucocorticoids as induction therapy (4 intravenous pulses), combined with an immunosuppressant in 11 cases: cyclophosphamide (3, 15%), azathioprine (6, 31%), mycophenolate (2, 10.5%), methotrexate (1, 5.5%) or rituximab (2, 10.5%).

**Conclusions:** the observation of ANCA positivity in patients with ILD may open new prospective in the assessment of interstitial lung diseases. Although most of patients had a good prognosis, up to 25% presented unfavourable respiratory outcome. Further prospective studies in larger cohorts and longer follow-up may clarify the prognosis of this particular lung disease and if ILD-ANCA should be classified as a distinct subset or an incomplete form of AAV.

**Disclosure of Interest:** None declared

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**FRI0515 EFFECTIVENESS OF DIRECT-ACTING ANTIVIRAL THERAPY ON CRYOGLOBULINEMIA ASSOCIATED WITH HEPATITIS C VIRUS**

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**Background:** Hepatitis C virus (HCV) is the most frequent cause of mixed cryoglobulinemia, reaching up to 30%–50% of patients with chronic infection. Cryoglobulinemia can manifest as arthritis, vasculitis, hypocomplementemia, peripheral neuropathy or renal involvement. A new direct-acting antiviral therapy against HCV is available for 4 years, and it achieves a sustained virologic response, close to the definition of cure for this viral infection.

**Objectives:** To evaluate the effectiveness of treatment with direct-acting antivirals in HCV-associated cryoglobulinemia and its clinical manifestations.

**Methods:** In a retrospective cross-sectional observational study, we enrolled all consecutive patients with positive serum cryoglobulins and HCV infection with high viral load. Patients with or without associated rheumatological or systemic manifestations were included. All of them were treated with a combination of the new antivirals: sofosbuvir +ledipasvir, or ombitasvir +paritaprevir +ritonavir +dasabuvir; during 8 to 24 weeks, between January 2014 and December 2016. Post treatment blood studies were made in all patients during the first year. Seronegativization of cryoglobulins and improvement of associated clinical manifestations after treatment were analysed.

**Results:** Thirty patients were included, 24 (80%) women. The median age of was 61.4 years. The HCV genotype: 1B in 76.6%, 1A in 16.6% and type 4 in the rest. Eighteen (60%) patients had systemic manifestations: 11 had joint involvement, 11 hypocomplementemia, 8 had leukocytoclastic vasculitis or skin ulcers, 5 Raynaud's phenomenon, 5 sensory-motor peripheral neuropathy, 3 renal involvement with glomerulonephritis, 2 Sjögren's syndrome and 1 patient with autoimmune hemolytic anaemia.

The sustained viral response was achieved in 29 patients (96.6%), maintaining an undetectable viremia after finishing the treatment. Cryoglobulins were negativized in 22 (73%) of patients, and complement was normalised in 36% of those who had hypocomplementemia before treatment. There was a clinical improvement in 54.2% of patients with previous associated rheumatologic or systemic manifestations. The arthritis and cutaneous vasculitis had better response than the other manifestations. No significant correlations were found between the serological and clinical responses.

**Conclusions:** Direct-acting antiviral therapy is very effective against HCV infection. It is also useful for the treatment of mixed cryoglobulinemia, negativizing cryoglobulins in almost 3/4 of the cases, and with clinical response in more than half of the patients, being more favourable in the cases of joint involvement and cutaneous vasculitis.

**Disclosure of Interest:** None declared

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**FRI0516 INSIGHT INTO INFLAMMATORY CELL AND CYTOKINE PROFILES IN ADULT IGA VASCULITIS**

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**Background:** Immunoglobulin A vasculitis (IgAV) is a small vessel, immune complex vasculitis, involving skin, joints, gastrointestinal tract (GIT) and kidney. While different diagnostic/prognostic and inflammatory markers have already been studied in paediatric IgAV, data on adult cases are scarce<sup>1</sup>.

**Objectives:** To examine the inflammatory cell profile in peripheral blood and cytokine profile in sera of newly diagnosed, biopsy-proven and treatment-naïve adult

IgAV compared to healthy blood donors (HBD), and determine associations with IgAV clinical signs.

**Methods:** Flow cytometry of stained, lysed and fixed whole blood was performed in IgAV (n=30), and HBD (n=17) (Miltenyi). Cytokines were quantitated by multiplex bead assay (Luminex), ELISA (IL-6) and immunonephelometry (acute phase serum amyloid A (SAA)) in 57 IgAV vs. 53 HBD.

**Results:** Percentage of CD16<sup>+</sup> neutrophils was significantly higher, while percentages of CD3<sup>+</sup> T-cells (including CD4<sup>+</sup> and CD8<sup>+</sup> cells), as well as CD19<sup>+</sup> B-cells were significantly lower in peripheral blood of IgAV patients vs. HBD. The expression of I-selectin (CD62L) on CD16<sup>+</sup> neutrophils was significantly increased in IgAV vs. HBD, as were the sera levels of TNF- $\alpha$  (2-fold), IL-6 (3-fold), IL-8 (2.2-fold) and SAA (11.7-fold changed levels) (table 1). Association was found between GIT involvement and lower neutrophil expression of integrin  $\alpha$ M (CD11b) (median; IQR: 7.2; 4.2–16.0), compared to skin limited (17.8; 9.9–40.5) IgAV cases (p=0.047). There was no association found between different cytokines and IgAV clinical phenotype.

**Abstract FRI0516 – Table 1.** Cell profiles, neutrophil surface proteins and cytokines in IgAV patients compared to HBD

Cells (% of WBC)	MEDIAN (Q <sub>25</sub> - Q <sub>75</sub> )		P value	Cytokines (pg/ml)	MEDIAN (Q <sub>25</sub> - Q <sub>75</sub> )		P value
	HBD (n=15)	IgAV (n=15)			HBD (n=53)	IgAV (n=57)	
<b>Neutrophils</b>	51.0 (47.1– 56.9)	67.5 (63.6– 73.3)	<b>&lt;0.001</b>	IL-1 $\beta$	0.4 (0.4– 0.4)	0.4 (0.4– 1.5)	ns
<b>T-cells</b>	26.4 (23.0– 31.8)	16.6 (10.2– 21.4)	<b>&lt;0.001</b>	<b>IL-6</b>	2.0 (1.0– 6.0)	6.0 (2.8– 14.3)	<b>0.015</b>
<b>CD4<sup>+</sup>T cells</b>	13.6 (11.7– 18.4)	10.4 (7.7– 14.4)	<b>0.003</b>	<b>IL-8</b>	53.3 (10.9– 195.0)	117.1 (29.3– 443.9)	<b>0.018</b>
<b>CD8<sup>+</sup>T cells</b>	10.3 (6.0– 12.6)	5.0 (1.9– 7.9)	<b>0.002</b>	IL-9	19.0 (19.0– 19.0)	19.0 (19.0– 19.0)	ns
<b>B-cells</b>	3.8 (2.9– 4.7)	2.4 (1.6– 2.9)	<b>0.006</b>	IL-10	1.0 (0.8– 2.8)	0.04 (0.04– 1.3)	ns
NK cells	4.6 (3.8– 6.3)	3.6 (2.3– 6.1)	ns	IL-13	665.2 (354.1– 1668.0)	23.0 (23.0– 102.2)	ns
<b>Neutrophil surface proteins (MFI)</b>	<b>HBD (n=17)</b>	<b>IgAV (n=30)</b>		IL-23	1.4 (1.4– 82.9)	1.4 (1.4– 118.6)	ns
<b>CD62L</b>	56.4 (44.9– 73.7)	86.5 (45.4– 107.5)	<b>0.036</b>	<b>TNF-<math>\alpha</math></b>	3.9 (0.8– 15.5)	8.1 (3.0– 20.2)	<b>0.003</b>
CD11b	8.7 (5.5– 27.4)	15.7 (6.4– 31.3)	ns	<b>SAA (<math>\mu</math>g/ ml)</b>	2.8 (1.9– 4.7)	32.8 (7.2– 168.0)	<b>&lt;0.001</b>

**Conclusions:** We found significant up-regulation of neutrophils and their CD62L expression, as well as sera levels of IL-6, IL-8, TNF- $\alpha$  and SAA in IgAV, implying a pathogenic role of neutrophils in IgAV. CD11b might represent a promising surface marker of GIT involvement in adult IgAV.

#### REFERENCE:

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**Disclosure of Interest:** None declared

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FRI0517

#### VESSEL WALL MORPHOLOGY IN GIANT CELL ARTERITIS– A LONGTERM SONOGRAPHIC FOLLOW-UP STUDY

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**Background:** Ultrasound (US) is a cornerstone in the diagnosis of GCA. Only limited data on how US documented large vessel wall thickening changes during treatment is available.

**Objectives:** To assess arterial vessel wall findings by US during long term follow-up in GCA patients with large vessel vasculitis (LVV) and to correlate findings with the disease course

**Methods:** Patients with GCA and US defined LV vasculitis were scheduled semi-annually for clinical and laboratory assessment as well as US of the temporal (TA), vertebral (VA), carotid (common, internal, external), subclavian (SA), axillary (AXA), deep (DFA), superficial (SFA) and common (CFA) femoral, and popliteal arteries (PA). US findings were classified as normal, moderate or marked vessel wall thickening.

**Results:** From 42 patients (16 male) with a median age of 75 years at diagnosis 28 had typical vessel wall thickening in the temporal artery and in at least one LV segment and 14 in the LV only. The following vessels (marked/moderate) were most often involved: PA in 11/21, SFA in 13/20, AxA in 14/5, SA in 8/13 patients respectively.

A reduction of the vessel wall thickening in the temporal artery during follow-up was found in 79% of patients after in median 7 months, with bilateral normalisation in 10 patients after in median 13 months.

In contrast 55% had no, 43% a partial and only one patient a complete reduction of thickening of all LV walls during follow-up. From initially marked supra-aortic LV segments 35% were moderate and 16% normal and from initially moderate LV 13% were normal at 1 year FU. From initially marked infra-aortic LV segments 36% were moderate and 3% normal and from initially moderate 10% were normal at 1 year FU.

Progression of vessel wall thickening in the LV during FU was seen in a total of 3 patients, in 2 of those, a clinical relapse of GCA was diagnosed one respectively 2 months before US.

There was no difference between patients with reduction of the vessel wall thickening and without during follow-up in respect to clinical parameters (relapse rate over the observation time, cumulative steroid dose after one year).

**Conclusions:** Regression of US morphological documented thickening of LV in patients with GCA is rare despite clinical remission. US remains sensitive for the diagnosis of LVV long after treatment initiation. Most plasticity is seen in the TA and more rarely in the supra-aortic segments.

**Disclosure of Interest:** None declared

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FRI0518

#### INCIDENCE, CHARACTERISTICS AND MANAGEMENT OF GIANT CELL ARTERITIS IN FRANCE: A STUDY BASED ON NATIONAL HEALTH INSURANCE CLAIMS DATA

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**Background:** Giant cell arteritis (GCA) is an immune-mediated, primary systemic vasculitis that affects large and medium-sized arteries. GCA may cause vision loss in up to 20% and requires long term glucocorticoids (GCs). There are currently few data available in France on the epidemiology, patients' (pts) characteristics, diagnosis and management of GCA in a real-world setting.

**Objectives:** The objectives of this study were to address these questions using Health insurance claims data.



**Methods:** This retrospective cohort study used the EGB (*Echantillon Généraliste des Bénéficiaires*) database which is a 1% random and representative sample of the French national Health insurance system. EGB contains anonymous demographic and comprehensive medical data on conditions with long-term disease (LTD) status, hospitalizations and reimbursement claims for medications dispensed in the community. The study used the data collected between January 1, 2007 and December 31, 2015. Inclusion criteria were: 1) age  $\geq 50$  years; 2) hospitalisation for GCA or LTD status for GCA (ICD-10 codes: M31.5/6); and 3) at least 4 drug dispensing of oral GCs within 6 months around the index date. The index date was defined as the date of 1<sup>st</sup> occurrence of GCA code and cases were considered as incident if the GCA code first occurred after  $\geq 2$  years of follow-up. Demographics, co-morbidities, diagnostic tests and therapies were analysed. A treatment sequence was defined as the start of a new drug or the resumption of the same drug after a stop  $\geq 3$  months. Annual incidence was calculated by using the people recorded in the EGB as denominator.

**Results:** Among the 7 52 717 pts recorded in the EGB, 241 pts fulfilled our criteria. Around 24 pts were newly diagnosed/year with an annual incidence of 7 to 10/100,000 people  $\geq 50$  years-old. 72% of the 241 pts were females, mean age was 77.5 ( $\pm 8.9$ ) years, mean follow-up 3.7 ( $\pm 2.6$ ) years. In the 12 months before index date, 74.3% of the pts had at least 1 proxy for hypertension, 39.4% for depression/insomnia and 33.6% for osteoporosis. After index date, temporal artery biopsy (TAB) was performed in 43.2%, high-resolution Doppler ultrasound in 35.3% and positron emission tomography (PET) in 11.6%. Among the 235 pts (97.5%) who had at least 1 drug dispensing of oral GCs, 198 pts (84.3%) used only GCs while 37 (16.7%) also received 1 to 3 adjunctive agents. Mean 1<sup>st</sup> GCs sequence duration was 17.2 months ( $\pm 16.5$ ) in 96.6%. 95 pts (40.4%) had a 2<sup>nd</sup> sequence, i.e. resume GCs and/or start a new drug for a duration of 6.7 months ( $\pm 8.1$ ) for GCS alone or 12.2 months ( $\pm 8.8$ ) for GCs+adjunctive drug. The most prescribed GCs-sparing agent was methotrexate (12.0%). Others were marginal: hydroxychloroquine 7 pts, azathioprine 4, cyclophosphamide 1, infliximab 1, adalimumab 2 and etanercept 1 pt.

**Conclusions:** These real-world data indicate an incidence of GCA in France of 7 to 10 cases/100,000 people  $\geq 50$  years-old and underline that most patients with GCA are treated with GCs alone whereas adjunctive agents, mainly methotrexate, are given to 17% of patients. The utilisation of TAB in only half of the patients might reflect a shift towards increasing use of imaging techniques to diagnosed GCA.

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#### FRI0519 WORK PRODUCTIVITY IS IMPAIRED IN PATIENTS WITH BEHÇET'S SYNDROME

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**Background:** Behçet's syndrome (BS) is most active during young adulthood and working years, thus affecting productivity. Work disability was previously reported especially among BS patients with eye, vascular and joint involvement.

**Objectives:** In this study, we aimed to evaluate the work productivity and instability of patients with BS compared to ankylosing spondylitis (AS) patients and healthy controls (HC).

**Methods:** 100 (80 M/20 F) consecutive BS patients who were routinely followed in our dedicated BS centre were studied. Patients with AS;<sup>26</sup> 22 M/4 F) who were followed in the rheumatology outpatient clinic of our unit and HC;<sup>30</sup> 18 M/12 F) were included as controls. Work Productivity and Activity Impairment Questionnaire (WPAI), Work Productivity Survey (WPS), Work Instability Scale (WIS) were used. Quality of life was assessed with the Behçet Disease Quality of Life (BDQoL) scale and disease activity with the Behçet's Disease Current Activity Index.

**Results:** Table 1 shows the characteristics of the included subjects. 28 of BS patients with only mucocutaneous, 28 with eye, 23 with vascular and 21 with neurologic involvement were included. Among BS patients 41% reported missing work days (mean 1.4 days/mo), and 49% reported that their productivity was reduced at least by half (mean 4.1 days/mo). The mean WIS score was 11.7 (5.8) in BS patients. 52 BS patients had moderate and 14 BS patients had high work instability. Patients with BS had significantly higher absenteeism (8.4% vs. 1.7%), presenteeism (37.6% vs. 9.3%), and daily activity impairment (27.5% vs. 8.6%) than HCs ( $p < 0.001$ ) assessed by WPAI. Scores were similar between BS and AS patients. WIS and WPS scores were also similar between BS and AS patients and worse than healthy controls. Work impairment was more pronounced in patients with eye involvement compared to mucocutaneous involvement ( $p = 0.006$ ) and there were no differences between other BS groups. The WPAI presenteeism score was moderately correlated with Behçet Disease Quality of Life scale score

( $r = -0.57$ ). Multivariate analysis showed that QoL (OR=0.77, 95% CI=0.66–0.88) and disease activity (OR=1.66, 95% CI=1.01–2.50) were related with WPAI-presenteeism.

**Abstract FRI0519 – Table 1.** Characteristics of the included subjects

	Behçet's syndrome (n=100)	Ankylosing spondylitis (n=26)	Healthy controls (n=30)
Male, n (%)	80 (80)	22 (85)	18 (60)
Mean (SD) current age,	36 $\pm$ 7.8	36 $\pm$ 6.4	31 $\pm$ 8.1
Mean (SD) disease duration	8 $\pm$ 5.5	7.46 $\pm$ 4.6	N/A
WIS (mean $\pm$ SD)	12 $\pm$ 6	11 $\pm$ 5.5	6 $\pm$ 4
WPAI-Absenteeism (mean $\pm$ SD)	8 $\pm$ 15	8 $\pm$ 19	2 $\pm$ 7
WPAI-Presenteeism (mean $\pm$ SD)	38 $\pm$ 29	32 $\pm$ 26	9 $\pm$ 21
WPS-Absenteeism (mean $\pm$ SD)	1.4 $\pm$ 3	1.2 $\pm$ 3	0.1 $\pm$ 0.3
WPS -Presenteeism (mean $\pm$ SD)	4 $\pm$ 7	4 $\pm$ 6	1 $\pm$ 3
BDCAF (mean $\pm$ SD)	4.47 $\pm$ 2.79	N/A	N/A
BSAS (mean $\pm$ SD)	21.47 $\pm$ 17.5	N/A	N/A
BDQoL (mean $\pm$ SD)	19.53 $\pm$ 8.3	N/A	N/A
BASDAI (mean $\pm$ SD)	N/A	3.3 $\pm$ 1.8	N/A
BASFI (mean $\pm$ SD)	N/A	2.8 $\pm$ 2.9	N/A

N/A: Not applicable; Behçet Disease Quality of Life: BDQoL; Behçet's Disease Current Activity Index (BDCAI); Behçet's Syndrome Activity Score (BSAS)

**Conclusions:** Work productivity is impaired in BS patients, especially among those with eye involvement. Work instability is frequent and correlated with disease activity and quality of life.

**Disclosure of Interest:** None declared

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**FRIDAY, 15 JUNE 2018: Osteoarthritis**

#### FRI0520 DISCOVERY OF POTENTIAL BIOMARKERS FOR THE DIAGNOSIS OF EROSIIVE AND NODAL HAND OSTEOARTHRITIS

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**Background:** Two different phenotypes of hand osteoarthritis (HOA) have been defined: nodal hand osteoarthritis (NHOA) and erosive hand osteoarthritis (EHOA). NHOA involve bone enlargement of the underlying interphalangeal joints, which may typically give rise to Heberden's nodes, synovitis and swelling. EHOA is a particularly aggressive form characterised by an abrupt onset, as well as signs of inflammation and subchondral erosions. In the absence of efficient diagnostic methods, searching for specific biomarkers for each subtype may help to characterise them.

**Objectives:** To define a panel of specific protein markers for the characterisation of EHOA and NHOA and its potential use in clinic.

**Methods:** A proteomic approach based on peptide labelling with Isobaric tags for relative and absolute quantitation (iTRAQ) was performed using two different sets of sera (n=55). Samples were classified in 4 groups of study (EHOA, n=10; non-EHOA, n=10; NHOA n=10; non-NHOA, n=5) and 2 control groups (rheumatoid arthritis (RA), n=10 and psoriatic arthritis (PSA), n=10). Serum proteins were digested and peptides from each condition to be compared were differentially labelled with iTRAQ reagents (Sciex). Then, samples were combined and analysed by two-dimensional liquid chromatography coupled to mass spectrometry in a TripleTOF 5600 Mass Spectrometer System (Sciex). Protein identification and quantitation was carried out using ProteinPilot software v.5.0.1.

**Results:** A total of 257 different proteins were identify with more than two peptides and a total score  $\geq 2$  at 95% confidence. In order to identify specific biomarkers for the characterisation of NHOA and EHOA phenotypes, each group was compared with the non-NHOA or non-EHOA respectively, and also with the control groups. After all the comparisons were made, 26 unique different proteins were found specific of the nodular phenotype. Vasorin (VAS) showed elevated levels in patients diagnosed with NHOA when compared to non-NHOA, RA and PSA groups. On the other hand, 36 unique proteins were identified in those patients with EHOA. Extracellular matrix protein 1 (ECM1) was found with higher concentrations in EHOA than in non-EHOA, RA and PSA patients. In addition, both HOA phenotypes were compared to the control groups and a panel of 30 different proteins

were defined. Among these proteins, vascular cell adhesion molecule-1 (VCAM1) was found increased in HOA compared to RA and PSA groups.

**Conclusions:** A specific protein profile for the characterisation of EHOA and NHOA disorders has been established. VAS showed elevated levels in patients with NHOA, whereas ECOM1 was increased in patients diagnosed with the erosive form of the disease. As none of them were identified in the other phenotype, they might be phenotype-specific biomarkers. In addition, VCAM1 was found with higher levels in both phenotypes of HOA when compared with RA and PSA and might be used to differentiate hand osteoarthritis from other rheumatic diseases.

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**FRI0521** **COMBINING FRACTAL- AND ENTROPY-BASED BONE TEXTURE ANALYSIS FOR THE PREDICTION OF OSTEOARTHRITIS: DATA FROM THE MULTICENTER OSTEOARTHRITIS STUDY (MOST)**

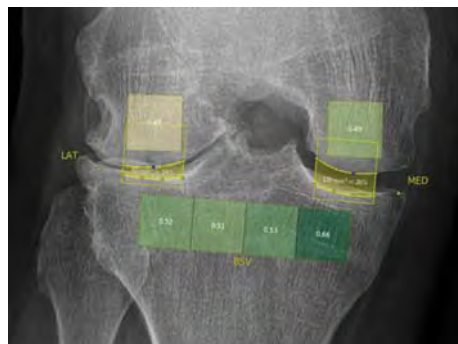
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**Background:** Osteoarthritis (OA) is one of the leading causes of long-term pain and disabilities associated with musculoskeletal disorders. Effective treatment and disease-progression slowdown depend on early detection and quantification of risk. However, current disease parameters, like joint space width (JSW), have proven to be insufficient for the prediction of OA.

**Objectives:** The purpose of the present study was to investigate if combining fractal- and entropy-based bone texture analyses with joint space width (JSW) and joint space area (JSA) may improve prediction of OA. Conventional posterior-anterior (PA) knee radiographs of men and women were obtained from the Multicenter Osteoarthritis Study (MOST) database, which provides valuable information to identify and define modifiable biomechanical, bone and structural, nutritional, and other risk factors for new disease and progression of existing disease.<sup>1</sup>

**Methods:** Oriented fractal- and entropy based texture algorithms were developed, using state-of-the-art computer hardware and software as well as specific machine-learning algorithms. The selected subchondral area used for textural analyses included 4 regions of interest (ROI) in the proximal tibia and one on each condyle of the distal femur (figure 1). Furthermore, JSW and JSA were assessed using newly developed and fully automated software.

**Results:** 1092 conventional knee radiographs obtained from one study centre were screened for eligibility. Of these, a total of 574 radiographs (230 women, 344 men) met the inclusion criteria, i.e. a Kellgren & Lawrence (KL) score of 0 at baseline. At month 84, 41 female and 79 male patients had developed KL<sub>≥1</sub>, and 189 female and 265 male patients remained at KL0. Area-Under-the-Curve (AUC) for incident OA using JSW/JSA and clinical features was 0.67±0.08 for women, and 0.61±0.1 for men. In contrast, combining fractal/entropy-based texture, JSW/A and clinical features resulted in significantly improved AUC for women and men (0.80±0.07 for women and 0.69±0.1 for men, respectively). To test whether these differences in predicting incident-OA were significant, we performed classifier comparison: t=3.84; p<10<sup>-3</sup> for women, and t=3.38; p<10<sup>-3</sup> for men.



**Conclusions:** This study provides strong evidence, that a combination of fractal- and entropy-based textural analyses of plain subchondral bone radiographs together with JSW/A and clinical features is superior to JSW/A and clinical features alone in predicting incident OA in men and women.

**REFERENCE:**

[1] <http://most.ucsf.edu/studyoverview.asp>

**Disclosure of Interest:** R. Ljuhar Shareholder of: ImageBiopsy Lab, Z. Bertalan : None declared, S. Nehrer: None declared, B. Norman : None declared, H.-P. Dimai : None declared, A. Fahrleitner-Pammer: None declared, D. Ljuhar: None declared

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**FRI0522** **VITAMIN D SUPPLEMENTATION IMPROVES DEPRESSION IN KNEE OSTEOARTHRITIS PATIENTS OVER 24 MONTHS**

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**Background:** Although depression is prevalent in osteoarthritis (OA) patients and the positive association between vitamin D deficiency and depression has been demonstrated, no study has examined the effect of vitamin D supplementation on depression in OA patients.

**Objectives:** To determine the effect of vitamin D supplementation and maintaining sufficient serum vitamin D on depression in patients with knee OA and vitamin D deficiency.

**Methods:** Participants with symptomatic knee OA and vitamin D deficiency were enrolled in a randomised, placebo-controlled trial and received 50,000IU vitamin D<sub>3</sub> (n=209) or placebo (n=204) monthly for 24 months. Serum 25-hydroxyvitamin D [25(OH)D] was measured at baseline, month 3 and 24. Depression was measured using the patient health questionnaire (PHQ-9), and knee symptoms were assessed using Western Ontario and McMaster Universities Arthritis Index (WOMAC) at baseline, month 3, 6, 12 and 24. Multilevel mixed-effect models were used to estimate the association between exposures and outcomes adjusting for potential confounders.

**Results:** Over 24 months, 340 participants (82.3% retention rate) completed the study. The prevalence and incidence of depression were 25.4% and 11.2%, respectively. Depression improved more in the vitamin D supplementation group (β: -0.45, 95% CI: -0.84 to -0.07) compared to the placebo group (β: 0.21, 95% CI: -0.19 to 0.61) (p=0.02) and in those participants who maintained vitamin D sufficiency (β: -0.44, 95% CI: -0.88 to -0.00) compared to those who did not maintain sufficiency (β: 0.40, 95% CI: -0.18 to 0.97) (p=0.02) over 24 months.

**Abstract FRI0522 – Table 1.** Effects of vitamin D supplementation over 24 months on change in PHQ-9

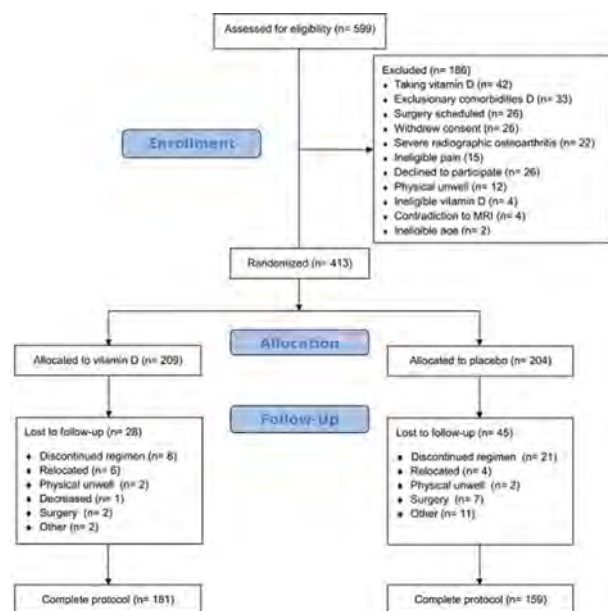
	Mean change, (95% CI)	Between-group difference change, mean (95% CI)	P value
Placebo Group (n=204)	0.21 (-0.19 to 0.61)	-0.66 (-1.22 to -0.11)	0.02
Vitamin D Group (n=209)	-0.45 (-0.84 to -0.07)		

Changes in outcomes are generated from mixed-effect models adjusted for age, sex and body mass index.

**Abstract FRI0522 – Table 2.** Effects of vitamin D status over 24 months on change in PHQ-9

	Mean change, (95% CI)	Between-group difference change, mean (95% CI)	P value
Not maintaining sufficient vitamin D (n=114)	0.40 (-0.18 to 0.97)	-0.83 (-1.56 to -0.11)	0.02
Maintaining sufficient vitamin D (n=226)	-0.44 (-0.88 to -0.00)		

Changes in outcomes are generated from mixed-effect models adjusted for age, sex and body mass index.



Abstract FRI0522 – Figure 1. Flowchart of the study

**Conclusions:** These findings suggest that vitamin D supplementation and maintaining sufficient vitamin D levels over 24 months may have beneficial effects on depression in patients with knee OA.

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**Disclosure of Interest:** None declared

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FRI0523

#### ZOLEDRONIC ACID PLUS PREDNISOLONE VERSUS ZOLEDRONIC ACID ALONE OR PLACEBO IN THE TREATMENT OF KNEE OSTEOARTHRITIS: A RANDOMISED TRIAL

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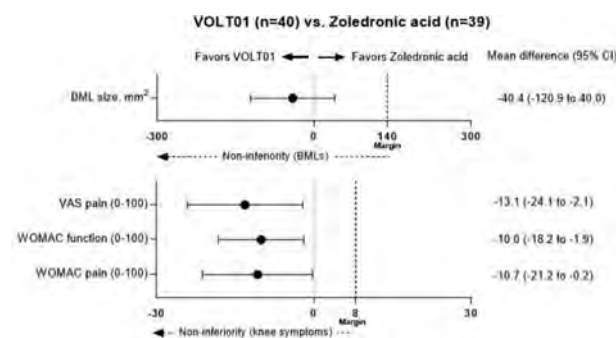
**Background:** Disease-modifying therapeutic options are needed for patients with osteoarthritis (OA). Zoledronic acid (ZA) is a potential option as it reduced both knee pain and knee bone marrow lesion (BML) size over 6 months in patients with knee OA. However, ZA infusions are often accompanied by a suite of side effects within 3 days of infusion (acute phase reactions (APRs)), which include flu-like symptoms. These may be caused by upregulation of pro-inflammatory cytokines. A preliminary study (n=20) suggested that a combination of ZA and prednisolone (VOLT01) was superior to ZA alone in reducing APR and knee pain in knee OA patients. A larger study was needed to confirm these findings and examine the new combination's effect on OA outcomes.

**Objectives:** To compare the effect of once-off infusion of ZA, VOLT01 and placebo on APRs, knee BML size and knee pain symptoms over 6 months in knee OA patients with significant knee pain and BMLs.

**Methods:** Knee OA patients  $\geq 50$  years with significant knee pain (defined as a 100 mm Visual Analogue Scale (VAS)  $\geq 40$  mm) and knee BMLs visualised on proton density weighted MRI were randomised to receive one infusion of ZA (5 mg in 100 ml saline), VOLT01 (5 mg ZA in 100 ml saline plus a 10 mg prednisolone bolus) or placebo (100 ml saline). Co-primary hypotheses were that VOLT01 would significantly reduce APRs compared to ZA, and that VOLT01 would be non-inferior to ZA in reducing BML size over 6 months. Secondary hypothesis was that VOLT01 would be non-inferior to ZA in improving knee pain and dysfunction (assessed using the Western Ontario and McMasters

Universities Osteoarthritis Index (WOMAC) and VAS) over 6 months. Mixed effect models were performed for data analyses. Analyses for change in knee pain and function scores were adjusted for baseline imbalanced values (baseline pain and utility scores, and pain medications). Non-inferiority margins were defined as 140 mm<sup>2</sup> for change in knee BML size and 8 mm for change in knee pain and function scores (WOMAC pain and function scores were averaged to a 100 mm VAS).

**Results:** 117 knee OA patients (63 females, mean  $\pm$  standard deviation (SD) age 62.2 $\pm$ 8.1 years) were enrolled. At baseline, mean  $\pm$ SD knee pain VAS score was 50.1 $\pm$ 18.9 mm and median BML size 370 mm<sup>2</sup>. APRs were more frequent in the two active treatment groups (ZA: 87%; VOLT01: 90%) than the placebo group (55%) (both p<0.01). Compared to placebo, neither ZA nor VOLT01 significantly reduced BML size (ZA mean difference [95% CI] -21.6 [-103.0 to +59.9], VOLT01 -62.0 [-142.5 to +18.4]) or knee pain scores (WOMAC pain: ZA 2.6 [-8.5 to +13.8], VOLT01 -8.1 [-18.8 to +2.6]; VAS pain: ZA 5.4 [-6.4 to +17.1], VOLT01 -7.7 [-19.0 to +3.6]) over 6 months, but WOMAC knee function improved significantly (-9.9 [-18.2 to -1.6], p=0.02) in VOLT01-treated group. VOLT01 was non-inferior to ZA in reducing knee BML size and superior to ZA in reducing knee pain and function scores (figure 1).



**Abstract FRI0523 – Figure 1.** Non-inferiority tests between VOLT01 and zoledronic acid for change in BML size, knee pain and function scores. Values represent the mean difference between VOLT01 and zoledronic acid. An upper bound of 95% CI for BML size less than 140 mm<sup>2</sup> or knee symptoms less than 8 indicates that a non-inferiority of VOLT01 to zoledronic acid is demonstrated.

**Conclusions:** Combining prednisolone with ZA does not appear useful for reducing APRs, though there may be a small benefit over ZA alone for knee symptoms. Neither showed evidence of disease modification by changing BML size.

**Disclosure of Interest:** None declared

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FRI0524

#### CENTRAL SENSITISATION IN HAND OSTEOARTHRITIS AND ASSOCIATIONS WITH RADIOGRAPHIC SEVERITY, SYNOVITIS ON ULTRASOUND AND SYMPTOM DURATION

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**Background:** Patients with painful hand osteoarthritis (HOA) have enhanced central pain sensitisation (CS). Structural and inflammatory joint tissue damage over time might lead to CS. However, increased pain sensitisation can also represent an 'a priori trait' of a subgroup of patients.

**Objectives:** This study explored whether structural pathology, inflammation and symptom duration of HOA are associated with enhanced CS.

**Methods:** Through a cross-sectional study we included 300 subjects (89% women, median age 61 years (IQR 57, 67), mean body mass index (BMI) 26.5 (SD 4.9) kg/m<sup>2</sup>) with clinical and/or ultrasound verified HOA. All were examined with ultrasound (grey scale (GS) synovitis and power Doppler activity (PD)) and conventional radiographs of both hands. GS-synovitis was scored on a semi-quantitative 0–3 scale and PD to be present or not. The bilateral interphalangeal, metacarpophalangeal, first carpometacarpal and scaphotrapezotrapezoidal joints were scored for global HOA (using Kellgren and Lawrence scale (KL), 0–4). Erosive HOA in the interphalangeal joints was defined with the Verbruggen-Veys anatomical phase score (VV). In addition, participants answered a question about the year of onset of their hand symptoms.

CS was measured with temporal summation (TS), the increase in perceived pain to repetitive noxious stimuli, using a mechanical probe. First, probes with increasing weight (32, 64, 128, 256 or 512mN) were applied at the wrist until the patients reported pain of at least 4/10. The selected probe was applied to the wrist times at



1 Hz. Subjects reported pain on first, fifth and tenth touch. Enhanced TS is a marker of central sensitisation and we defined the magnitude of TS as TS- $\Delta$ : highest pain value of fifth or tenth touch minus the first pain value.

We analysed whether sum scores of KL (0–128), GS (0–90), PD (0–30), number of erosive interphalangeal joints (0–20) and symptom duration were associated with TS- $\Delta$  using separate models of linear regression with adjustments for age, sex and BMI.

**Results:** Median radiographic KL sum score was 28 (IQR 15, 44) and ultrasound sum scores (GS, PD) were 3 (IQR 1, 7) and 0 (IQR 0, 1), respectively. Median number of erosive joints was 0 (IQR 0, 1) and symptom duration was 6 (IQR 3, 13) years. Median TS- $\Delta$  among the participants was 1 (IQR 0, 2).

Neither KL sum score ( $p=0.18$ ), GS-synovitis sum score ( $p=0.18$ ), PD sum score ( $p=0.86$ ), number of joints with erosive HOA ( $p=0.078$ ) nor symptom duration ( $p=0.21$ ) were associated with TS- $\Delta$  (table 1).

Table 1 Associations between OA features and temporal summation \*

Associations between OA features and temporal summation *		
	Unstandardized beta (95% CI)	P-value
Symptom duration in years	0.015 (-0.01, 0.04)	0.21
Kellgren-Lawrence sum score	0.007 (-0.00, 0.02)	0.18
Grey scale synovitis sum score	-0.001 (-0.03, 0.03)	0.96
Power Doppler sum score	0.001 (-0.05, 0.06)	0.86
Number of erosive joints	0.070 (-0.01, 0.15)	0.08

\*Adjusted for sex, age and BMI.

**Conclusions:** We found no relationship between the severity of HOA pathology and CS. This is in line with the hypothesis that factors other than OA disease severity itself contribute to CS associated pain, and that CS may be a trait in some individuals. However, it does not exclude other aspects of HOA as an initiator of CS in a subgroup of patients.

**Disclosure of Interest:** None declared

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FRI0525

#### ASSOCIATION BETWEEN DIETARY VITAMIN K INTAKE WITH KNEE SYMPTOMS AND BACK PAIN IN PATIENTS WITH KNEE OSTEOARTHRITIS

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**Background:** Vitamin K could be implicated in structural change of osteoarthritis (OA), but current evidence is limited or conflicting so the association between vitamin K and OA symptoms remains unclear.

**Objectives:** This study aims to investigate the association of vitamin K intake with knee symptoms and structural features in people with knee OA.

**Methods:** The parent study, Vitamin D Effect on Osteoarthritis (VIDEO) study, was conducted between June 2010 and December 2013 in Tasmania and Victoria, Australia. Knee symptoms were assessed using the Western Ontario and McMaster University Index of osteoarthritis (WOMAC) and a Visual Analogue Scale (VAS) for pain. A validated Food Frequency Questionnaire (FFQ) (developed by the Cancer Council Victoria in Australia) was completed at baseline and used to determine dietary vitamin K intake. Knee Magnetic Resonance Imaging (MRI) scans were obtained according to a standardised protocol using a 1.5 T whole-body MRI unit. Cartilage volume, cartilage defects, bone marrow lesions and effusion volume were measured. The associations between vitamin K intake quartile and changes in clinical or MRI features were analysed using linear regressions.

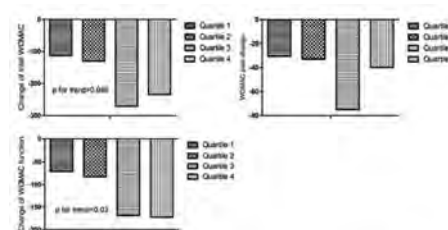
**Results:** 261 participants were included at baseline and 213 completed 2 years of follow-up. There were no significant differences between two equal divisions with high or low level of vitamin K intake in term of baseline characteristics. As table 1 and figure 1 show, higher vitamin K intake quartiles were significantly associated with greater decrease in total WOMAC score and WOMAC function score over 24 months. Similar trends were seen in WOMAC pain score and stiffness score, though not statistically significant. There were no significant associations

between baseline vitamin K intake and changes in total cartilage volume, cartilage defects, bone marrow lesions and effusion volume over 24 months.

**Abstract FRI0525 – Table 1.** Associations between vitamin K intake quartile and changes in clinical symptoms over 24 months

		Value of change, Mean (SD)	Multivariable*, $\beta$ (95% CI)	P value	P for trend
Total WOMAC Score	Vitamin K intake quartile 1	-112.9 (327.7)	Reference:		<b>0.046</b>
	Vitamin K intake quartile 2	-130.0 (482.6)	-3.6 (-165.3,158.1)	0.97	
	Vitamin K intake quartile 3	-270.6 (403.3)	-149.8 (-313.8,14.2)	0.07	
	Vitamin K intake quartile 4	-234.4 (415.5)	-122.4 (-281.3,36.5)	0.13	
WOMAC Pain Score	Vitamin K intake quartile 1	-30.4 (81.8)	Reference:		0.33
	Vitamin K intake quartile 2	-32.9 (115.5)	3.3 (-37.3,43.8)	0.87	
	Vitamin K intake quartile 3	-74.8 (103.1)	<b>-41.1 (-82.1,-0.22)</b>	<b>0.05</b>	
	Vitamin K intake quartile 4	-39.7 (107.5)	-7.5 (-47.2,32.1)	0.71	
WOMAC Function Score	Vitamin K intake quartile 1	-71.4 (241.2)	Reference:		<b>0.03</b>
	Vitamin K intake quartile 2	-82.8 (339.4)	-5.7 (-120.3,108.8)	0.92	
	Vitamin K intake quartile 3	-168.7 (275.2)	-94.7 (-210.9,21.5)	0.11	
	Vitamin K intake quartile 4	-172.5 (301.8)	-104.1 (-216.6,8.5)	0.07	

\*Adjusted for age, sex, BMI and vitamin D intervention group



P values were from analyses after adjustment for age, sex, BMI and vitamin D intervention group  
\*,  $p<0.05$  compare with the first quartile. \*\*,  $p<0.01$  compare with the first quartile.

Figure 1 Change in WOMAC score over 24 months among those with different vitamin K intake quartiles

**Conclusions:** Higher baseline vitamin K intake was associated with decreased knee symptoms over 24 months in patients with knee OA. These suggest that vitamin K intake may be beneficial for knee OA.

**Disclosure of Interest:** None declared

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FRI0526

#### THE IMPACT OF DISEASE CHARACTERISTICS IN KNEE AND HIP OSTEOARTHRITIS ON RECOMMENDATIONS FOR JOINT REPLACEMENT

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**Background:** Joint replacement in osteoarthritis (OA) is a major reason for hospitalisation in Germany.<sup>1</sup>

**Objectives:** Which factors are associated with recommendations for joint replacement in patients with symptomatic hip and/or knee OA?

**Methods:** A total of 9734 persons, insured in a large statutory health insurance in Germany (Barmer), who had a diagnosis of OA (ICD-10 codes M15 [polyarthrosis], M16 [coxarthrosis] or M17 [gonarthrosis]) in at least two quarters in 2014 were randomly selected, stratified by age, sex and diagnosis (M15/M16/M17). They were contacted by mail and asked to complete a questionnaire regarding sociodemographics, health behaviour, the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC, 0: no impairment- 100: extreme pain/stiffness/difficulty) and whether they had ever discussed total joint replacement (TJR) surgery with a physician. Patient-reported outcomes of the responders ( $n=3,564$ ) were linked to claims data on prescriptions of pain medication and physical therapy. Persons with a diagnosis of M15 ( $n=1,212$ ) were excluded from the present analysis. Patients who reported pain in the corresponding joints were analysed in three groups: OA of the knee, of the hip or of both. Logistic regression models

were used to assess which parameters (age, sex, BMI >30, prescription of opioids or physical therapy, WOMAC, whether the OA was mainly treated by an orthopaedist) were associated with having discussed a TJR.

**Results:** Of 2352 persons with knee or hip OA, 932 had symptomatic OA of the knee, 478 of the hip, 94 of both, and 848 did not report pain in the relevant joint(s). Mean age was 64 to 67 years, 63% to 68% were female and mean BMI was high, especially in patients with knee OA (29 kg/m<sup>2</sup>). 54%–74% had considerable impairment (WOMAC>39). 72%–83% had any pain medication, 12%–25% opioids and 33%–46% physical therapy. 63%–72% were treated by orthopaedists and 45%–50% had discussed TJR. In knee as well as hip and knee OA male sex and an orthopaedist as main treating physician was associated with having discussed a TJR (table 1). Age, WOMAC and opioid prescription was only associated with a higher OR of discussing a TJR in knee OA.

**Abstract FRI0526 – Table 1.** Results from multivariable logistic regression models showing parameters associated with having discussed TJR.

	OR for knee and hip OA (n=94), 95% CI	OR for hip OA (n=478), 95% CI	OR for knee OA (n=932), 95% CI
Orthopaedist is treating	7.2 (1.9,26.8)	1.6 (0.9,2.8)	1.7 (1.1,2.6)
Age, per 10 years	1.0 (0.56,1.8)	1.0 (0.8,1.3)	1.2 (1.1,1.5)
BMI≤30 vs>30	0.9 (0.2,3.6)	1.0 (0.6,1.8)	1.3 (0.9,2.0)
Male vs female	5.3 (1.3,21.8)	1.1 (0.6,1.8)	1.5 (1.1,2.2)
WOMAC, per 10%	1.3 (0.8,1.9)	1.1 (0.9,1.3)	1.3 (1.2,1.5)
Opioids	0.8 (0.1,6.1)	0.5 (0.2,1.2)	1.9 (1.0,3.3)
Physical therapy	1.1 (0.3,3.3)	1.1 (0.6,2.0)	1.2 (0.8,1.7)

**Conclusions:** Disease burden is highest in persons with concomitant knee and hip OA. Men are more likely to discuss TJR with their physician, but not in hip OA. Disease burden and treatment recommendations were only weakly associated. Therefore, other factors may be more important when considering surgery in knee and hip OA.

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#### FRI0527 EFFICACY OF BIO-OPTIMISED CURCUMA EXTRACT (FLEXOFYTOL®) FOR PAINFUL KNEE OSTEOARTHRITIS: DATA FROM COPRA, A MULTICENTER RANDOMISED CONTROLLED STUDY

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**Background:** Flexofytol is a Curcuma Longa extract with an increased bioavailability (bio-optimised) by mixing curcuma extract with polysorbate.

**Objectives:** To demonstrate the effects of Flexofytol on OA symptoms and soluble biomarkers.

**Methods:** 141 patients with symptomatic knee OA (mean age 61.8 years [min.45-max.86]; 80.1% female; mean K and L grade of the knee 2.4; mean BMI 29.7 kg/m<sup>2</sup>) were randomised in a prospective double blinded, 3 parallel groups, comparative and multicenter, study (NCT02909621). At inclusion, all patients took pain killers or anti-inflammatory drugs which were authorised during the study. Patients received 6 months continuous treatment with either high dose Flexofytol (n=49, 140.01 mg Curcuma longa L. extract/treatment), low dose Flexofytol (n=47, 93.34 mg Curcuma longa L. extract/treatment) or placebo (n=45, Sunflower seed oil fill ingredient). Each treatment corresponded to 3 oral capsules two

times a day to respect the blinding. All patients had clinical assessment (knee pain, knee function and patient global assessment of disease activity [PGADA]) and blood sampling for biomarkers measurements (usCRP and sColl2-1) at baseline (T0), 1 month (T1), 3 months (T3) and 6 months (T6). Additionally, patient compliance, satisfaction and tolerance were assessed at each timepoint following baseline. Primary outcome was the change at 3 months versus baseline in type II collagen degradation-specific biomarker sColl2-1 and VAS PGADA.

**Results:** Comparison of time evolution curves showed that sColl2-1 levels were lower in the treated groups but differences were not significant. The decrease in PGADA overtime was significantly more important in low dose group than in placebo group only at the 1 month evaluation timepoint (low dose ΔT1-T0, -12.5 mm vs placebo ΔT1-T0, -2 mm, p=0.035). Further, the knee pain relief was significantly higher in low dose group at T1 and T3 than in placebo (low dose ΔT1-T0, -16.5 mm vs placebo ΔT1-T0, -4 mm p=0.046; low dose ΔT3-T0, -36.5 mm vs placebo ΔT3-T0, -8 mm p=0.043). No difference was observed at T6. No differences were seen for any parameter when the high dose group was compared with the placebo group at any time point. The global KOOS score and its subscales significantly decreased overtime but changes were comparable in each group. Additionally, patient compliance was good and patient satisfaction remained stable overtime in each group. The ratio of patients with adverse events (AE) related to the product were similar in placebo and treated groups but the number of AE linked to the product was higher in the high dose group than in placebo (p=0.012).

**Conclusions:** Flexofytol, at a low dose, induced a rapid symptomatic relief on knee pain and a beneficial effect on the patient assessment of disease. This study also provides information on the dose to use and the design of a larger phase III clinical trial.

**Disclosure of Interest:** Y. Henrotin Consultant for: Tilman SA, M. Malaise: None declared, R. Wittoek: None declared, K. Devlam: None declared, J.-P. Brasseur: None declared, F. Luyten: None declared, Q. Jiangang: None declared, M. Van den Bergh: None declared, R. Uhoda: None declared, J. Bentina: None declared, T. De Vroey: None declared, L. Ercicum: None declared, Y. Dierckxsens Employee of: Tilman SA

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#### FRI0528 LONG-TERM EFFECTS OF VITAMIN D SUPPLEMENTATION AND MAINTAINING VITAMIN D SUFFICIENCY ON KNEE OSTEOARTHRITIS OVER 5 YEARS

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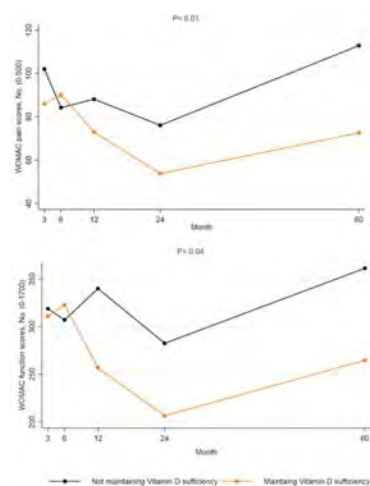
**Background:** Epidemiological studies suggest that vitamin D deficiency is associated with knee symptoms and structural progression of knee osteoarthritis (OA). However, randomised controlled trials (RCTs) failed to demonstrate a significant effect of vitamin D supplementation on OA, probably due to selecting OA participants with and without vitamin D deficiency, short duration of follow-up and a large proportion of participants in the placebo group reaching vitamin D sufficiency (61.3% of patients in the placebo group achieved a serum 25(OH)D level of >60 nmol/L at 3 months of a clinical trial).

**Objectives:** To examine whether those maintaining sufficient serum vitamin D levels over 5 years had reduced knee symptoms compared with those who did not maintain adequate vitamin D levels in patients with knee OA. We also explored the effect of 2 year vitamin D supplementation on knee symptoms compared to placebo after 3 years of cessation of treatment.

**Methods:** Participants with symptomatic knee OA and low 25-hydroxyvitamin D [25(OH)D] (12.5–60 nmol/L) were randomly assigned to receive monthly treatment with oral vitamin D3 (50 000 IU; n=209) or an identical placebo (n=204) for 2 years. 172 participants who enrolled in the study from Hobart were followed up after 3 years (5 years from baseline) of the cessation of the treatment to assess knee symptoms and vitamin D levels. Participants were classified as maintaining sufficient vitamin D group if they maintained serum 25(OH)D>50 nmol/L at month 3, 24 and 60 (n=79), and not maintaining sufficient vitamin D group (25(OH)D≤50 nmol/L at month 3, 26 and 60, n=62) groups. Knee symptoms were assessed at baseline, 3, 6, 12, 24 and 60 month using Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC).

**Results:** The level of 25(OH)D dropped in the vitamin D group (87.0 nmol/L to 53.3 nmol/L) and slightly increased (53.3 nmol/L to 61.7 nmol/L) in the placebo group 3 years after the cessation of the treatment. Knee pain increased from the end of the study to 5 years of follow-up in the treatment (81.8 to 91.7) and placebo (75.8 to 101.1) groups. 16.7% of the participants in vitamin D and 18.5% of the participants in placebo group underwent total knee replacement (TKR) surgery. There were no significant differences in WOMAC symptoms, TKR rates or change in symptoms between Vitamin D and placebo groups after 3 years of cessation of the supplementation.

Participants who maintained adequate vitamin D levels over 5 years had significantly less WOMAC knee pain ( $\beta$ : -38.4, 95% CI: -69.2, -7.7) and physical dysfunction ( $\beta$ : -98.5, 95% CI: -193.8, -3.1) than participants with vitamin D deficiency over 5 years in multivariable analyses.



**Conclusions:** Vitamin D supplementation over 2 years did not result in significant differences in change in knee symptom score over 5 years compared to placebo. However, knee OA patients maintaining sufficient serum vitamin D levels over long-term had more improvement in knee pain and physical function than those who did not maintain adequate vitamin D levels, suggesting a beneficial effect of maintaining sufficient serum vitamin D for knee OA.

**Disclosure of Interest:** None declared

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#### FRI0529 PREOPERATIVE PAIN SEEMS TO MODIFY THE EFFECT OF RADIOGRAPHIC OSTEOARTHRITIS SEVERITY ON POSTOPERATIVE PAIN AND FUNCTION 1 YEAR AFTER TOTAL KNEE ARTHROPLASTY

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**Background:** Radiographic osteoarthritis (OA) severity and pain play an important role in the indication for total knee arthroplasty (TKA). It is however unknown whether preoperative self-reported clinical pain modifies the effect of radiographic OA severity on postoperative pain and function in OA patients after TKA.

**Objectives:** To investigate whether preoperative self-reported clinical pain modified the effect of radiographic OA severity on postoperative pain and function in OA patients 1 year after TKA.

**Methods:** Data from the Longitudinal Leiden Orthopaedics Outcomes of Osteoarthritis Study (LOAS), a multicentre cohort study on outcomes after TKA were used. Radiographic OA severity was assessed with the Kellgren and Lawrence (KL) score (0–4). Pain and function were evaluated with the Knee Injury and Osteoarthritis Outcome Score (KOOS). After adjustment for confounders (BMI, age, gender and Mental Health Component Scores from the Short Form-12), multivariate linear regression analyses with an interaction term between KL-score and preoperative pain were performed.

**Results:** 560 patients were included. Both KL-score and preoperative pain were associated with postoperative pain ( $\beta$ : 6.1, 95% CI: 1.7–10.5 and  $\beta$ : 0.4, 95% CI 0.1–0.7) and function ( $\beta$ : 8.0, 95% CI: 3.7–12.3 and  $\beta$  0.5, 95% CI 0.2–0.8). A trend towards effect modification of preoperative pain on the association between KL-score and postoperative pain ( $\beta$  -0.1, 95% CI -0.2–0.0) and function ( $\beta$  -0.1, 95% CI -0.2–0.0) was found indicating that effect of preoperative pain on postoperative pain and function seems to become less important when more severe radiographic severity is present.

**Conclusions:** Patients with less preoperative pain and higher KL grades have better function and pain outcomes 12 months after TKA. However preoperative pain seems less important in patients with more severe radiographic OA.

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**Disclosure of Interest:** None declared

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#### FRI0530 TOTAL JOINT REPLACEMENT (TJR) AS CLINICAL ENDPOINT IN OA; PREVALENCE AND INCIDENCE RATES OF TJRS FROM THE PROSPECTIVE EPIDEMIOLOGIC RISK FACTOR (PERF I) STUDY

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**Background:** Osteoarthritis (OA) is a heterogeneous disease described by a combination of joint pain, physical disability and radiographic alterations leading to joint failure and total joint replacement (TJR). Commonly used endpoints in OA trials are worsening of pain and joint space narrowing. TJR is normally not considered an endpoint. Age and female gender are considered as major risk factors for developing OA.

**Objectives:** We hypothesise that TJR can be used as an endpoint in OA outcome studies within reasonable time frame. To investigate the basis for this hypothesis, we explored the prevalence and incidence of TJR as a reflection of joint failure in the Prospective Epidemiologic Risk Factor (PERF I) study.

**Methods:** A total of 5,855 Danish postmenopausal women aged 49–88 enrolled in the Prospective Epidemiologic Risk Factor (PERF I) study during 1999–2001 (baseline). Three, six and twelve year follow-up data from the Danish National registry was collected in end of 2014, including occurrence of TJR, OA and other relevant diagnosis. Also, women where at baseline and in 2014 asked whether they had a TJR or OA. The biomarker C1M was measured in baseline serum samples. The PERF I study was carried out in accordance with ICH-GCP and the study protocol was approved by the local ethics committees.

**Results:** There were 798 women that had their first TJR between baseline and 12 year follow-up; giving an incidence proportion of 13.6%. The TJR women were on average 1 year older ( $p=0.010$ ) and heavier (1.7 kg/cm<sup>2</sup>,  $p<0.0001$ ), compared to women with no TJR in the follow-up period. The incidence after three and six years, of first ever TJRs, were 171 and 362 corresponding to an incidence proportions of 2.9% and 6.2%. Next we investigated the TJR incidence rates at 3, 6 and 12 years in different subgroup of women: 1) All, PERF I women that experience their first ever TJR (5855); 2) Prior TJR, had a TJR before baseline (266); 3) OA diagnose at baseline but no prior TJR (1757) and 4) OA diagnose at baseline and high C1M (>40 ng/mL, median) that after baseline underwent their first ever TJR (841). Group 1 is as described above. The 3, 6 and 12 incidence rates were 9.0, 17.3% and 29.7% for the prior TJR group, 6.2, 12.1% and 23.3% for the OA group, and 7.6, 13.6% and 25.1% for the OA +C1M group. The age-dependent prevalence and incidence for the first TJR. The prevalence was insignificant for the age group younger than 60 years old (<0.1%). The prevalence increased steadily from the age group 60 to age group 85; from 0.1% to 13.2%.

**Conclusions:** Within a timeframe of 3, 6 or 12 years TJR incidence for women with an OA diagnosis reached 6, 12% and 23%, which was a doubling compared to the All population. The incidence increased by adding a single diagnostic measure. This reflects that TJRs are frequent amongst elderly women and that if designed minutiously, such as including specific diagnostic criteria (e.g. biomarker, OA diagnose), it may be feasible to conduct clinical studies with TJR as an endpoint. However, special attention must be directed to the objectiveness of the criteria for TJR. This may build a case for design of outcome studies (joint failure) for developing drugs in OA.

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FRI0531

**DETERMINANTS OF CLINICAL AND RADIOLOGICAL PROGRESSION OF HAND OSTEOARTHRITIS OVER 2 YEARS**

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**Objectives:** The objectives of this prospective observational study were to assess the clinical and radiological changes in hand osteoarthritis (HOA) and to identify the determinants of these changes, over a two year period.

**Methods:** 203 patients were included in Liège Hand Osteoarthritis Cohort (LIHOC) and followed during 2 years. They met the American College of Rheumatology x-ray/clinical criteria for HOA. At baseline, demographic and clinical characteristics of the population were recorded. Various radiological and clinical parameters were selected to investigate progression.

**Results:** The general health measures remained stable over time. The number of nodes increased significantly over 2 years while the other clinical parameters did not vary significantly over time (number of painful joints at rest or at pressure and swollen joints). The pinch force decreased over time and the grip strength remained stable. The two tools assessing function (FIHOA and AUSCAN), showed a progressive deterioration over time (statistically significant for FIHOA ( $p < 0.05$ ) and borderline ( $p = 0.17$ ) significant for the AUSCAN). Almost all patients showed radiologic change during follow-up. Thus, the radiological scores deteriorated significantly over 2 years. An increase in Verbruggen and KL scores was present in 162 (92.04%) and 174 (98.86%) patients, respectively. 39 patients (22.16%) had new erosive joints.

From a clinical perspective, using backward logistic regression, diabetes (OR 2.67%–95% CI 1.13–6.33,  $p = 0.03$ ), high degree of radiologic severity (OR 1.23%–95% CI 1.09–1.39,  $p < 0.01$ ) and age between 40 and 60 (OR 2.67%–95% CI 1.21–5.90,  $p = 0.02$ ) at baseline are predictors of FIHOA worsening over-time. The predictors of AUSCAN progression included the pain intensity (OR 0.98%–95% CI 0.97–0.99,  $p < 0.01$ ) and the degree of radiologic severity (OR 1.06%–95% CI 1.01–1.12,  $p = 0.03$ ) at baseline.

The following factors are associated with radiological deterioration: symptomatic HOA (OR 2.17%–95% CI 1.04–4.51,  $p = 0.04$ ) and the number of severely affected joints at baseline (OR 1.11%–95% CI 1.04–1.18,  $p < 0.01$ ). In contrast, a high number of erosive or remodelled joints (OR 0.89%–95% CI 0.81–0.98,  $p = 0.02$ ) reduce the risk of radiological disease progression.

**Conclusions:** These results help to better understand the clinical and radiologic progression of HOA, as well as the determinants that have resulted in them.

**Disclosure of Interest:** None declared

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FRI0532

**RELATIONSHIP BETWEEN PATIENT-REPORTED OUTCOMES AND PROPRIOCEPTIVE ACUITY IN PATIENTS WITH TOTAL KNEE ARTHROPLASTY**

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**Background:** Total knee arthroplasty (TKA) is offered to patients who have end-stage knee osteoarthritis (OA) to reduce pain and improve functional performance. Pain and functional level in patients with TKA can be measured using self-report questionnaires such as the Numeric Pain Rating Scale (NPRS), Hospital for Special Surgery (HSS), Iowa Level of Assistance Scale (ILAS), and Iowa Ambulation Velocity Scale (IAVS). Proprioception plays an integral role in neuro-motor control of the knee joint and deficits in knee joint proprioception are well documented in individuals with knee osteoarthritis. However, the patient-reported functional level relevance of these deficits is not clear in both individuals with knee OA and with TKA.

**Objectives:** The aim of this study was to assess relationship between pre-/post-surgery patient-reported outcomes and proprioceptive acuity in patient with TKA due to knee OA.

**Methods:** The study group consisted of 68 patients (12 males, 56 females), who underwent primary TKR because of knee arthrosis were included in the study with mean age  $64.9 \pm 9.1$  years. Patients were evaluated regarding the knee proprioception (in knee joint angle  $15^\circ$ ,  $30^\circ$ ), pain (NPRS), HSS knee function score. Functional activities were evaluated using the ILAS and walking speed was evaluated using the IAVS. Patients were evaluated preoperatively and at discharge. All patients underwent the same rehabilitation program.

**Results:** While there were correlations in different rates in individuals with knee OA between patient-reported outcomes and proprioceptive acuity, there were no

correlations in individuals with TKA between patient-reported outcomes and proprioceptive acuity. Preoperatively, low-to-moderate significant correlations was found between pain and proprioceptive acuity deficit scores in knee joint angle  $15^\circ$ ,  $30^\circ$  ( $r = -0.196$ ,  $p = 0.046$  and  $r = -0.378$ ,  $p < 0.001$ , respectively). There were low significant correlations preoperatively between HSS knee score and proprioceptive acuity deficit scores in knee joint angle  $15^\circ$ ,  $30^\circ$  ( $r = 0.217$ ,  $p = 0.027$ , and  $r = 0.275$ ,  $p = 0.005$ , respectively). There were not significant correlations between proprioceptive acuity deficit scores and all other evaluation tests ( $p > 0.05$ ).

**Conclusions:** There were correlations in different rates in patients with knee OA between patient-reported outcomes and proprioceptive acuity, however there were no correlations in patients with TKA between patient-reported outcomes and proprioceptive acuity. These results suggest that patients who have knee OA and with poor proprioception show more limitation in functional ability and have more pain level. On the other hand, deficits in joint position sense in patients with TKA may be due to factors other than pain and functional disability. Poor proprioception in patients with TKA may be due to surgery related resection of articular cartilage, meniscuses, articular ligaments.

**Disclosure of Interest:** None declared

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FRI0533

**ASIAN MITOCHONDRIAL DNA HAPLOGROUP B IS ASSOCIATED WITH THE DEVELOPMENT OF KNEE OSTEOARTHRITIS IN KOREAN**

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**Background:** In our previous study, we have conducted a case-control study to demonstrate the mitochondrial DNA (mtDNA) haplogroups in the development of knee osteoarthritis (OA). However, there were no mtDNA haplogroups associated with the development of knee OA.

**Objectives:** The objective of this study was to elucidate the role of mtDNA haplogroups in the development of knee OA in prospective on-going community-based cohort.

**Methods:** This cohort was established in 2001 to investigate the epidemiologic characteristics of major chronic diseases in Korea by the Korean Genome and Epidemiology Study, Centre for Disease Control (KCDC). The epidemiologic data and knee radiographs were obtained from the second follow-up (2005–2006) and the sixth follow-up (2013–2014), and DNA was distributed from the fourth follow-up (2009–2010). The Kellgren-Lawrence (K/L) score was measured using a knee X-ray taken at each visit. The mtDNA was analysed by multiplex mutagenetically separated polymerase chain reaction to determine the mtDNA haplogroups (M, G, D, D4, D5, M7, M8, M9, M10, N, A, N9, R, F, B). The frequency of the mtDNA haplogroup was compared between the group with knee OA ( $K/L \geq 2$  or underwent total knee replacement arthroplasty) and the group without knee OA ( $K/L < 2$ ) at the 6th follow-up in the cohort of  $K/L = 0$  at the second follow-up. Multiple logistic regression was used to determine relative risk (RR) of mtDNA haplogroups for OA by adjusting sex, age, and body mass index (BMI).

**Results:** A total of 1115 epidemiological data, knee radiographs, and DNA samples were distributed. Of these, 572 were cohorts with  $K/L = 0$  in the second follow-up, and 438 underwent knee X-ray examination at the sixth follow-up visit. Among them, 160 were classified as Knee OA by K/L grading and 278 were classified as control group. The mean age ( $59.4 \pm 8.5$  and  $64.3 \pm 6.8$ ), the number of male patients (61 [21.9%] and 11 [6.9%]), and the mean BMI ( $24.0 \pm 3.1$  and  $25.0 \pm 3.0$ ) were significantly different between normal and OA group ( $p < 0.001$ ). In comparison of frequency of mtDNA haplogroup between two groups, haplogroup B was significantly higher in OA group (unadjusted  $RR = 1.794$ ,  $p = 0.030$  and adjusted  $RR = 2.346$ ,  $p = 0.005$ ).

**Conclusions:** Our data suggested that mtDNA haplogroup B contributed to the development of knee OA in Korean. Further study is ongoing to confirm the relationship between the progression of knee OA and mtDNA haplogroups.

**Acknowledgements:** Our previous study was presented at 4th International Congress on Controversies in Rheumatology and Autoimmunity, Bologna, Italy, 9–11 March 2017.

**Disclosure of Interest:** None declared

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FRI0534

### RADIOGRAPHIC OUTCOMES WERE ASSOCIATED WITH PAIN AND FUNCTION RESPONSES: POST-HOC ANALYSIS FROM A PHASE 2 STUDY OF A WNT PATHWAY INHIBITOR, SM04690, FOR KNEE OSTEOARTHRITIS TREATMENT

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**Background:** SM04690, a small molecule intra-articular (IA) Wnt pathway inhibitor is in development as a potential disease modifying knee osteoarthritis drug. A phase 2, 52 week, randomised controlled trial evaluated changes in Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Pain and Function and medial joint space width (mJSW). It was hypothesised that observed mJSW increases led to WOMAC subscore responder improvements. To address this question, a concordance analysis was performed.

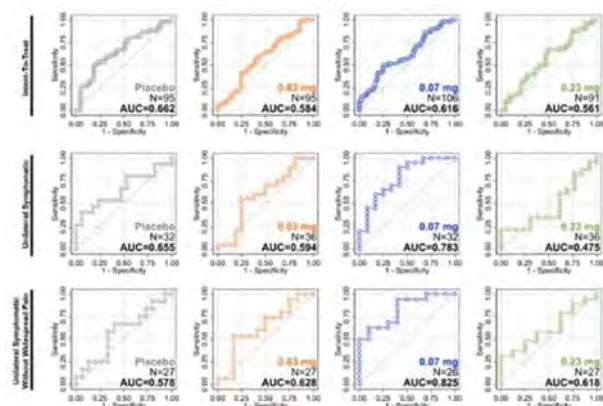
**Objectives:** To evaluate concordance, or level of agreement, between mJSW and WOMAC Pain and Function 'responders.'

**Methods:** Subjects with ACR-defined knee OA, Kellgren-Lawrence (KL) grades 2–3, received 2 mL IA SM04690 (0.03, 0.07, or 0.23 mg) or placebo (PBO) in the target (most painful) knee. WOMAC Pain [0–50] and Function [0–170] were assessed at Weeks 0, 4, 13, 26, 39 and 52 and knee radiographs at Weeks 0, 26 and 52. Baseline-adjusted logistic regression group analyses estimated concordance between mJSW change and pain and function changes for responders who achieved both WOMAC Pain and Function improvements of >50% and >20 [scaled to 100] points. Receiver-operator characteristic (ROC) curves were generated with area under curve (AUC) to estimate concordance (AUC >0.7='acceptable' and >0.8='excellent' concordance<sup>1</sup>). ITT and two subgroups were analysed: 1) unilateral symptomatic knee OA (pre-specified: UNI) and 2) unilateral symptomatic knee OA without widespread pain or comorbid symptoms (Widespread Pain Index≤4 and Symptom Severity≤2, post-hoc: UNI-WP).

**Results:** 455 subjects were enrolled (mean age 60.3 [±8.7] years, BMI 29.9 [±4.6] kg/m<sup>2</sup>, 268 [58.9%] female, 292 [64.2%] KL Grade 3, 164 [36.0%] UNI knee OA).

In the ITT, approximately 53% were responders across all groups. In UNI, 20 (56%) 0.03 mg; 20 (63%) 0.07 mg; 23 (64%) 0.23 mg and 15 (47%) PBO, and in UNI-WP, 15 (56%) 0.03 mg; 16 (62%) 0.07 mg; 19 (70%) 0.23 mg and 12 (44%) PBO were responders. The 0.03 mg (UNI, NS; UNI-WP, p=0.047) and 0.07 mg (UNI, p=0.009; UNI-WP, p=0.013) doses also demonstrated increased mJSW compared to PBO at Week 52.

In ITT, no treatment group achieved AUC >0.7 (figure 1). In UNI, the 0.07 mg dose demonstrated 'acceptable' concordance between response and mJSW (AUC=0.783). In UNI-WP, the 0.07 mg dose showed 'excellent' concordance (AUC=0.825).



**Abstract FRI0534 – Figure 1.** ROC Curves Illustrating Concordance between WOMAC Pain and Function Response and mJSW Change by Treatment Group and Analysis Group

**Conclusions:** In this post-hoc analysis, treatment with SM04690 maintained or increased mJSW in the 0.03 and 0.07 mg doses compared to PBO over 52 weeks. In UNI and UNI-WP 0.07 mg cohorts, changes in mJSW were concordant with WOMAC Pain and Function response.

#### REFERENCE:

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FRI0535

### THE CLINICAL AND RADIOGRAPHIC EARLY COURSE OF KNEE AND HIP OSTEOARTHRITIS OVER 10 YEARS IN CHECK (COHORT HIP AND COHORT KNEE)

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**Background:** Osteoarthritis (OA) is the most prevalent joint disease and one of the leading causes of chronic pain and disability worldwide. Yet, relatively little is known about the early course of OA.

**Objectives:** To describe the clinical and radiological early course of hip and/or knee OA.

**Methods:** CHECK (Cohort Hip and Cohort Knee) is a multicenter, prospective observational cohort study of 1002 participants. Inclusion criteria were: 1) age 45–65 years at the time of inclusion, 2) pain in knee(s) and/or hip(s), 3) never or not longer than 6 months ago for the first time consulted a physician for these symptoms. Participants were included through general practitioners and advertisements. Visits took place at baseline, and at 2, 5, 8, and 10 year follow-up (T0, T2, T5, T8 and T10). At each visit, questionnaires, including joint pain presence (Numeric rating score, NRS), morning stiffness, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), were inquired, and physical examination, and x-ray imaging were performed. Clinical OA was defined by the clinical American College of Rheumatism (ACR) criteria. Radiographic OA (ROA) was defined as Kellgren and Lawrence score (K and L) of ≥2.

**Results:** 1002 participants (age 56±5 years (mean ±sd); 79% female; BMI 26±4 kg/m<sup>2</sup>) were included. 83% reported knee pain at baseline, 59% reported hip pain, and 42% reported both. 10 year follow-up data were complete for 85% of the participants. The total WOMAC score showed a median of 21 (range 0–80) at baseline and remained rather constant over time (T2=20 (0–83); T5=20 (0–86); T8=19 (0–88); T10=19 (0–81)). The same was observed for pain (NRS). At baseline, 520 participants fulfilled the clinical ACR criteria for knee and/or hip OA. Of these, only 91 (17.5%) participants subsequently fulfilled the ACR criteria at every follow-up visit. 138 participants did never fulfil the clinical ACR criteria for hip or knee OA. At baseline, 157 participants showed ROA in on or both knees and 161 participants showed ROA in on or both hips. After 10 years follow-up, 601 (60%) participants had ROA in one or both knees and 513 (51%) participants had hip ROA in one or both hips. Of those with hip OA in at least one hip, 256 (50%) had bilateral knee ROA at T10. Of the participants with knee OA in at least one knee, 256 (43%) had bilateral hip ROA at T10. Most joint replacements took place between 2 and 8 years follow-up (11 knees, 29 hips), predominantly in participants with multiple affected joints. Only 115 (13.5%) participants did not develop ROA of knee or hip.

**Conclusions:** Although mean pain scores remain fairly stable over time, individual scores tend to fluctuate over time. Therefore, only few participants constantly fulfil the clinical criteria for OA. More than half of the participants had ROA after 10 year follow-up and a large overlap of knee and hip ROA was observed. Numbers of joint replacements were highest in participants developing both hip and knee OA.

**Disclosure of Interest:** None declared

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FRI0536

### PREGABALIN EFFICACY IN TREATMENT OF CHRONIC PAIN IN PATIENTS WITH KNEE OSTEOARTHRITIS

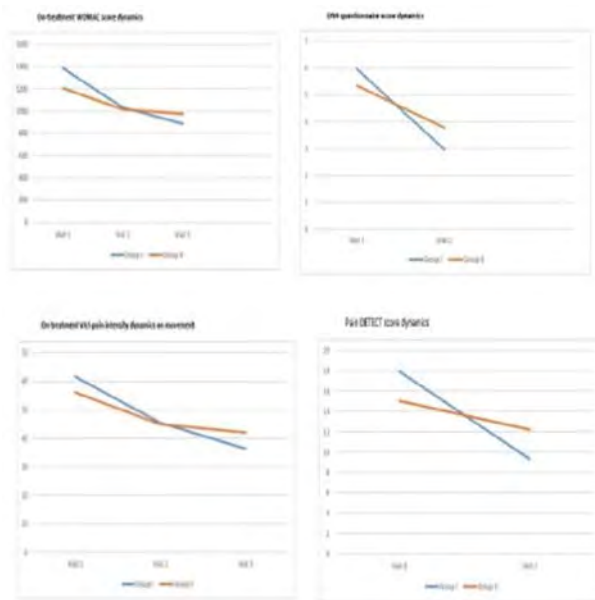
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**Background:** Modern methods of treatment of osteoarthritis have mainly anti-inflammatory action. A few studies show the effectiveness of centrally acting drugs for chronic pain in osteoarthritis (OA) of the knee.

**Objectives:** To study the efficacy of Pregabalin in treatment of chronic pain in patients with knee OA.

**Methods:** The study involved 60 female patients with knee OA having neuropathic pain component (NPC; DN4 >4). Mean age 59.82±4.46 y (min 49, max 65 years). All patients were randomly divided into two groups to be treated with 2 therapeutic regimens: aceclofenac +pregabalin (Group I) or aceclofenac (Group II) for 5 weeks (3 visits). All patients were subjected to clinical and neurological examination, total WOMAC score assessment, verification of neuropathic pain (NP) (questionnaire DN4 and Pain DETECT), and VAS pain intensity assessment at rest.

**Results:** The therapy was successful in both groups with respect to WOMAC score [figure 1] (Group I – 1385,30±365,83 vs 1034,70±402,37 vs 886,64 ±456,31; Group II – 1206,04±358,72 vs 1016,45±428,52 vs 976,55 ±408,02 respectively, p=0.01). Significant reduction of pain intensity at rest was documented in both groups [figure 2]. Group I 61,60±14.91 vs 45,34±16,14 vs 36,24±18,09; Group II 56,07±22,58 vs 44,86±18,68 and vs of 41,96±of 24.04, p=0.01, respectively). Therapeutic regimens in both groups had positive impact on NPC based on DN4 questionnaire and Pain DETECT scores. However, a combination of a NSAID with anticonvulsants agent (pregabalin) resulted in a more pronounced effect. Changes in DN4 values in Group I (visit1/visit3) were: 5.97 ±1,24/2,97±1,83 p=0.001; and in Pain DETECT values – 17,93±3,87/9,34±6,18, p=0.001; while in Group II DN4 scores were 5,35±0,93/3,79±2,29, p=0.001; and Pain DETECT – 15,03±5,26/12,24±6,29 p=0.02. [figures 3–4]



**Conclusions:** Complex therapy with the use of Pregabalin in patients with OA of the knee, with signs of NPC, allows not only effectively reduce pain intensity and improve functional activity of patients and, consequently, the quality of life.

**Disclosure of Interest:** None declared

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#### FRI0537 NEUROPHYSIOLOGICAL DATA IN PATIENTS WITH CHRONIC PAIN IN KNEE OSTEOARTHRITIS

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**Background:** Traditionally, chronic pain in OA is considered to be a classical model of nociceptive pain. Nociceptive mechanism can't explain the presence: referred pain, secondary hyperalgesia and other sensitive phenomena.<sup>1</sup> Recent studies has shown that besides nociceptive pain there is another mechanism that takes place in chronic pain OA –central sensitisation.<sup>2</sup> Explore of chronic pain OA can be reached only by a complex approach in examining patients with chronic knee OA that includes not only a rheumatological examination, but examination of the neurological sphere and algometria. At the moment there are only few studies dedicated to neurophysiological changes in pain OA<sup>3</sup>

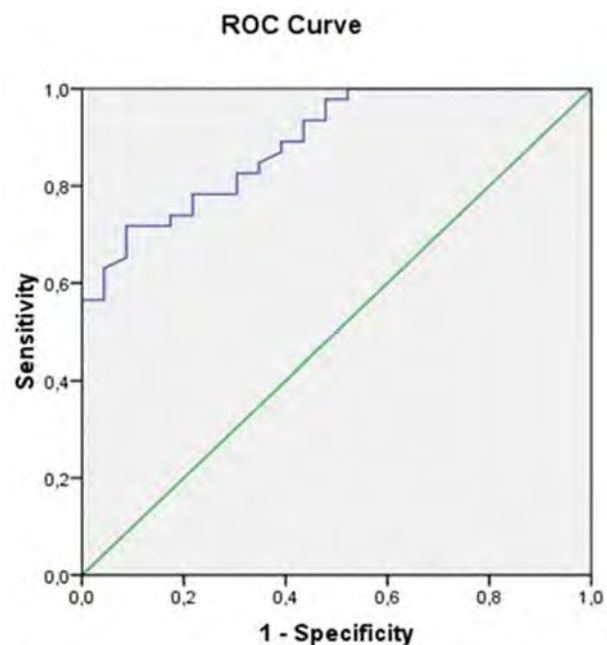
**Objectives:** to assess pain system with neurophysiological examination in chronic pain OA

**Methods:** 46 chronic knee pain OA and 23 healthy group control women, 45–65 years old, were included. The study included clinical rheumatologic, neurological examinations, neuropathic pain scales (DN4 and Pain DETECT). Knee X-ray and

ultrasound studies. Neurophysiological examination included algometria with algometer and wind-up phenomena observed by Neuropen. Five test sites in the peripatellar region and one control site on tibialis anterior (5 cm distal to the tibial tuberosity) were located and marked for examination

**Results:** Neuropathic pain scales demonstrated neuropathic descriptors present in OA patients. Neurological examination revealed no somatosensory deficit. But examination of the sensitive sphere indicated hyperalgesia: primary hyperalgesia (increased sensitivity to pain in the damaged joint) and secondary hyperalgesia. Algometria revealed low pressure pain threshold (PPT) above injured knee and intact region compared with healthy group. (tab.1) PPT in intact region was compared between OA patients and control group by ROC-analysis. Max of PPT in intact region in patient with OA was –14,70, min – 1,80, mean value – 7,34. Mean value of PPT in control group was 15,18. Area under curve was- 0888. Sensitivity – 70%. Specificity – 83%. ROC-analysis demonstrated that low PPT in OA patients is a specific feature of central sensitisation (figure 1) Wind-up phenomena examination in intact region revealed significant difference of data in OA patients with referred pain and control group (4,3±2,1 vs 2,44±1,3 p=0,003)and OA patients without referred pain and control group (3,67±1,43 vs 2,44±1,3 p=0,011).

PPT data	OA patients n=46	Control group n=23	P
V1	7,04±2,92	15,13±5,08	0000
V2	8,41±4,39	14,86±4,5	0001
V3	7,75±3,45	16,08±4,97	0000
V4	4,57±2,2	11,27±4,98	0000
V5	4,41±2,1	10,7±4,8	0000
V6	7,34±3,66	15,18±5,07	0000



Diagonal segments are produced by ties.

Figure 1 Diagonal segments are produced by ties.

**Conclusions:** Chronic OA is a complex of mechanisms and includes nociceptive and central sensitisation. Neurophysiological changes: low ppt in demaged area and even intact region and wind-up phenomena were revealed in all OA patients and charecterises central sensitisation. Mechanism-oriented treatment should also target CNS, including anticonvulsant, and antidepressant agents.

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FRI0538

**STRUCTURAL EFFECTS OF INTRA-ARTICULAR SPRIFERMIN IN SYMPTOMATIC RADIOGRAPHIC KNEE OSTEOARTHRITIS: A POST-HOC ANALYSIS OF CARTILAGE AND NON-CARTILAGINOUS TISSUE ALTERATIONS OF THE 2-YEAR DATA FROM A 5-YEAR RANDOMISED, PLACEBO-CONTROLLED, PHASE II STUDY**

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**Background:** Sprifermin, a recombinant human fibroblast growth factor 18, is currently being investigated as a potential disease-modifying osteoarthritis (OA) drug. Recently, a dose-dependent increase in femorotibial cartilage thickness, as well as medial and lateral compartment cartilage, over two years was reported<sup>1</sup>.

**Objectives:** The aim of this post-hoc analysis is to evaluate potential effects of sprifermin on additional structure endpoints, based on semi-quantitative MRI assessment over 24 months.

**Methods:** Patients aged 40–85 years with symptomatic radiographic knee OA, KLG 2 or 3, and medial mJSW  $\geq 2.5$  mm in the target knee were randomised (1:1:1:1) to receive double-blinded placebo or sprifermin (30  $\mu$ g or 100  $\mu$ g), administered as 3 weekly intra-articular injections in cycles every 6 or 12 months. 1.5T or 3T MRIs were acquired at baseline, 6, 12, 18 and 24 month follow-up visits using a standard protocol (ClinicalTrials.gov identifier: NCT01033994).

MRIs were read using the Whole-Organ Magnetic Resonance Imaging Score (WORMS) system (time points of baseline, 12 and 24 months) by three trained musculoskeletal radiologists. Analyses of all sprifermin and placebo arms included multiple MRI-defined osteoarthritis features and multi-dimensional assessments: (a) delta-subregional approach (the difference in the *number of subregions* with worsening as compared to improvement) and (b) delta-sum approach (absolute *scores of all subregions*). Analyses were performed on a whole knee level and separately for medial, lateral, and patellofemoral compartments. To test for potential dose-response effects, Jonckheere-Terpstra (asymptotic) test was used. P-values were not adjusted for multiple testing.

**Results:** 549 patients were included. Dose-dependent treatment effect on cartilage morphology (i.e., less cartilage damage) was observed for the entire knee from baseline to 24 months using both delta sum and delta subregion approaches (table 1). For bone marrow lesions (BMLs), a dose-dependent treatment effect (improvement of BMLs) was observed from baseline to 24 months for the patellofemoral joint using both delta sum and delta subregion approaches but not the other compartments (table 2). No significant effects were seen for baseline to 24 month changes in Hoffa-synovitis, effusion-synovitis, menisci, or osteophytes.

**Abstract FRI0538 – Table 1.** Cartilage morphology change from baseline to 24 months, ITT analysis set

Compartment	Analysis approach	Placebo (N=108) Mean (95% CI)	Sprifermin - 30 mcg q 2 (N=112) Mean (95% CI)	Sprifermin - 50 mcg q 4 (N=111) Mean (95% CI)	Sprifermin - 100 mcg q 2 (N=112) Mean (95% CI)	Sprifermin - 100 mcg q 4 (N=112) Mean (95% CI)	P-value
Entire knee	Delta Sum	1.61 (0.49, 2.34)	1.78 (1.29, 2.27)	1.20 (0.66, 1.74)	1.31 (0.62, 1.78)	0.98 (0.37, 1.59)	0.028*
	Delta Subregion	0.79 (0.49, 1.09)	0.90 (0.65, 1.15)	0.60 (0.37, 0.83)	0.50 (0.30, 0.70)	0.55 (0.35, 0.75)	0.008*
LFTJ	Delta Sum	0.20 (0.08, 0.30)	0.37 (0.25, 0.49)	0.45 (0.30, 0.61)	0.38 (0.22, 0.54)	0.23 (0.09, 0.36)	0.102
	Delta Subregion	0.18 (0.08, 0.29)	0.29 (0.19, 0.40)	0.24 (0.16, 0.32)	0.12 (0.01, 0.23)	0.13 (0.04, 0.22)	0.077
MFTJ	Delta Sum	0.86 (0.32, 1.41)	0.77 (0.36, 1.16)	0.52 (0.26, 0.79)	0.83 (0.41, 1.21)	0.48 (0.23, 0.72)	0.2274
	Delta Subregion	0.40 (0.20, 0.59)	0.68 (0.24, 0.95)	0.25 (0.13, 0.38)	0.39 (0.23, 0.56)	0.22 (0.11, 0.34)	0.2207
PFJ	Delta Sum	0.46 (0.21, 0.70)	0.43 (0.20, 0.67)	0.22 (0.06, 0.44)	0.15 (0.02, 0.28)	0.27 (0.04, 0.51)	0.0073
	Delta Subregion	0.21 (0.09, 0.33)	0.23 (0.10, 0.36)	0.10 (0.01, 0.20)	0.08 (0.01, 0.16)	0.20 (0.06, 0.32)	0.1796

**Abstract FRI0538 – Table 2.** Bone marrow lesion change from baseline to 24 months, ITT analysis set

Compartment	Analysis approach	Placebo (N=108) Mean (95% CI)	Sprifermin - 30 mcg q 2 (N=112) Mean (95% CI)	Sprifermin - 50 mcg q 4 (N=111) Mean (95% CI)	Sprifermin - 100 mcg q 2 (N=112) Mean (95% CI)	Sprifermin - 100 mcg q 4 (N=112) Mean (95% CI)	P-value
Entire knee	Delta Sum	0.09 (-0.26, 0.51)	0.39 (0.01, 0.78)	0.00 (-0.39, 0.39)	0.10 (-0.34, 0.54)	-0.03 (-0.40, 0.33)	0.1007
	Delta Subregion	0.06 (-0.23, 0.37)	0.21 (-0.07, 0.48)	-0.05 (-0.24, 0.13)	0.07 (-0.26, 0.39)	-0.13 (-0.41, 0.15)	0.1680
LFTJ	Delta Sum	0.13 (0.00, 0.27)	0.28 (0.06, 0.49)	0.01 (-0.23, 0.21)	0.20 (0.04, 0.37)	0.17 (-0.04, 0.38)	0.2784
	Delta Subregion	0.13 (0.02, 0.25)	0.16 (0.04, 0.28)	-0.03 (-0.17, 0.11)	0.13 (0.03, 0.23)	-0.07 (-0.05, 0.19)	0.2545
MFTJ	Delta Sum	0.05 (-0.20, 0.30)	0.14 (-0.10, 0.36)	0.12 (-0.10, 0.30)	0.13 (-0.17, 0.43)	0.05 (-0.12, 0.24)	0.1617
	Delta Subregion	-0.03 (-0.23, 0.18)	0.13 (-0.06, 0.31)	0.08 (-0.12, 0.28)	0.15 (-0.05, 0.30)	0.08 (-0.07, 0.23)	0.1341
PFJ	Delta Sum	-0.10 (-0.30, 0.10)	-0.06 (-0.26, 0.13)	0.13 (-0.34, 0.08)	-0.24 (-0.40, -0.08)	-0.26 (-0.50, 0.02)	0.0171*
	Delta Subregion	-0.05 (-0.22, 0.12)	-0.11 (-0.28, 0.07)	-0.11 (-0.30, 0.07)	-0.22 (-0.40, -0.04)	-0.24 (-0.40, -0.09)	0.0195*

\* p-values using Jonckheere-Terpstra (asymptotic) test

**Conclusions:** This post-hoc analysis indicates that sprifermin has a positive effect on cartilage morphology, in addition to the previously reported effect on cartilage thickness. Sprifermin was also associated with BML improvement in the patello-femoral joint. There were no significant effects associated with sprifermin on other joint tissues assessed, and no safety concerns raised.

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FRI0539

**A SAFETY, TOLERABILITY, PHARMACOKINETICS (PK) AND PHARMACODYNAMICS (PD) STUDY WITH INCREASING ORAL DOSES OF GLPG1972 ADMINISTERED DAILY FOR 29 DAYS SHOWS A STRONG BIOMARKER EFFECT IN PATIENTS WITH KNEE AND/OR HIP OA**

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**Background:** Osteoarthritis (OA) is characterised by structural changes of the joint, of which degradation of articular cartilage is one of the major signs<sup>1</sup>. The main proteoglycan component of the extracellular matrix of articular cartilage is aggrecan. GLPG1972 as a potent and selective inhibitor of ADAMTS-5, a key aggrecan-cleaving enzyme involved in cartilage degradation, is being developed as a potential disease-modifying OA drug (DMOAD). Aggrecan cleavage by ADAMTS-5 results in release of N-terminal ARGS neo-epitope fragments of which serum levels significantly decreased in healthy subjects treated with GLPG1972 during 14 days in a previous study<sup>2</sup>.

**Objectives:** To assess safety, tolerability, PK and PD (serum ARGS-aggrecan levels) during and following administration of GLPG1972 in patients with knee and/or hip OA.

**Methods:** This was a single centre, randomised, double-blind, placebo-controlled, age and gender stratified, ascending dose Phase Ib study, with three semi-sequential cohorts of 10 patients each, randomised to active drug or placebo in a 4:1 ratio. Doses tested were once daily 100, 200 and 300 mg. Treatment duration was 29 days. Patients had follow-up visits 14 and 21 days after last dosing for additional PD assessments. Methods for PD have been described previously<sup>3</sup>.

**Results:** Thirty patients were included. Of these, 24 patients (M/F rate 8/16, 14 aged 50–64 and 10 aged 65–75) received active medication.

All adverse events (AE) were mild and transient. No serious AEs were reported during the study; one female patient in the 300 mg group was discontinued after 15 days of treatment due to drug-related elevated transaminase values which returned to normal 9 days later while her bilirubin levels remained normal. There were no overall trends in lab abnormalities over time or significant changes in vital signs, ECG and Holter parameters.

Steady state in plasma exposure was reached after 3 days of dosing. Exposure increased dose-proportionally. Mean serum ARGS levels (SEM) decreased steadily over time in all patients receiving GLPG1972: -40% (2.9), -46% (4.5) and -53% (2.8) at day 15 compared to baseline in the 100, 200 and 300 mg group respectively. These levels remained stable until last dose on day 29, then consistently returned to pre-dose levels for all groups 14 and 21 days after last dose. Placebo group levels remained unchanged.

**Conclusions:** When administered daily for 29 days in patients with knee and/or hip OA, GLPG1972 at oral doses of 100, 200 and 300 mg q.d. was generally well tolerated and safe. Serum ARGS levels, as a marker for target engagement and potential proxy of cartilage degradation, showed a dose-dependent decrease over time up to 53% below baseline in the 300 mg group. These PK-PD findings are consistent with what we observed in a previous study in healthy subjects<sup>2</sup> and reinforce the rationale for developing GLPG1972 as a DMOAD.

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#### FRI0540 IDENTIFICATION OF BIOMARKERS OF OA ASSOCIATED TO DEFECTIVE AUTOPHAGY

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**Background:** In osteoarthritis (OA), defects in cellular homeostasis, and in particular in autophagy, are evident and precede joint damage. In this sense, we have shown that there is a defect in autophagy in OA human chondrocytes and cartilage, and pharmacological activation of autophagy protects against joint damage. These data suggest that joint damage could be due, at least in part, to a failure of autophagy, by inducing an abnormal accumulation of cellular products related to disease.

**Objectives:** These observations represent a unique opportunity to identify and validate potential biomarkers associated with autophagy defects that could facilitate the development of therapeutic strategies to prevent OA progression.

**Methods:** A comparative analysis of 86 autophagy genes was performed in blood from non-OA and knee OA patients. Non-OA patients (Age: 61,17±1,370 years; BMI: 25,76±0,69; Sex: Females; n=12) and Knee OA patients (Age: 65,75±1,528 years; BMI: 30,25±0,88; Sex: Females; n=12, OA grade III-IV) were profiled using a human autophagy PCR array (PrimePCR autophagy human panel, BioRad) and analysed using the PrimePCR analysis software, Biorad. In addition, we performed a quantitative proteomic analysis of defective autophagy by genetic deletion of Atg5 in human OA chondrocytes by using iTRAQ (isobaric tags for relative and absolute quantitation) labelling coupled with on-line 2D LC/MS/MS. Protein identification and quantification were performed using Protein Pilot Software 4.0. Each MS/MS spectrum was searched in the Uniprot/Swissprot database for *Homo sapiens*.

**Results:** 16 autophagy-related genes were significantly down-regulated in blood from knee OA patients compared to non-OA patients. No significant up-regulation was observed in blood from Knee OA patients, however a trend-toward up-regulation was detected in several genes involved in the mTOR signalling pathway. Importantly, 5 key autophagy-related genes, such as, ATG16L2, ATG12, ATG7, ATG4B and MAP1LC3B involved in initiating autophagy, phagophore extension and autophagosome formation were significant downregulated in knee OA patients compared to non-OA patients (p<0.05). Interestingly, HSP90AA1 and HSPA8, a chaperone-mediated autophagy genes involved in stress response and protein folding, were significant downregulated (p<0.001) in blood from knee OA patients. In addition, several regulators of autophagy and apoptosis, such as BNIP3, BCL-2 and BCL2L1 were a significantly downregulated in OA patients (p<0.01). Total proteome screening in human OA chondrocytes with defective autophagy, showed a significant reduction of Heat shock protein HSP90-alpha (HSP90A1) (p<0.05), suggesting that reduced autophagy is associated to OA pathology and could be a potential biomarker for OA progression and development.

**Conclusions:** This approach represents a unique opportunity to identify and validate early-stage biomarkers associated with defective autophagy that could facilitate the development of therapeutic strategies to prevent joint damage.

**Disclosure of Interest:** None declared

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#### FRI0541 INCREASING A PERSON'S OWN PHYSICAL ACTIVITY AND STRENGTH CAN MINIMISE CARTILAGE VOLUME LOSS IN OLDER-ADULTS: A BETWEEN- AND WITHIN-PERSON ANALYSIS ON A POPULATION-BASED PROSPECTIVE COHORT

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**Background:** The relationship between physical activity (PA) and osteoarthritis (OA) has been controversial, with some studies showing a detrimental effect and others showing either no effect or a beneficial effect. Traditionally, analysis has

focused on examining the effect PA and/or strength have on OA between individuals (between-person comparison). Yet, how the variability in PA and strength over time within the same individual (within-person comparison) is associated with OA is not well recognised. Statistical methods, such as multilevel models that properly capture the within-person processes can be used to tell us whether changes within an individual over time relate to changes in OA outcomes in that same individual.

**Objectives:** This study aimed to investigate the associations of between-person and within-person variability in PA and leg strength with knee cartilage volume loss over 10.7 years in older adults.

**Methods:** 479 community-dwelling older-adults (50% female, mean age 61±6 years, range 50–80 years) were studied at baseline, 2.7, 5.1, and 10.7 years. PA (measured objectively as steps/day) and leg strength (measured objectively in kg) were assessed at all four time-points. Knee cartilage volume was measured using MRI at baseline and 10.7 years. Linear mixed-effect regression models were used to estimate the association of between-person and within-person variability in PA and leg strength with cartilage volume loss over 10.7 years. Models were adjusted for age, sex, body mass index and history of knee injury or surgery.

**Results:** Mean cartilage volume loss over 10.7 years was 465±231 mm<sup>3</sup>. No between-person associations existed between PA and cartilage volume loss (Beta: 18.8 per 1000 steps/day, 95% CI –6.1, 43.7). However, within-person variability in PA was protectively associated with changes in cartilage volume, such that having higher PA compared to an individual's average level of PA minimised their cartilage volume loss over time (Beta: 32.8 per 1000 steps/day, 95% CI 20.8, 44.6). Between-person effects showed that participants with greater leg strength lost less cartilage volume over time (Beta: 5.4 per 1 kg, 95% CI 3.1, 7.8). Within-person variability in leg strength was also protectively associated with changes in cartilage volume, such that having higher leg strength compared to an individual's average strength minimised their cartilage volume loss over time (Beta: 3.3 per 1 kg, 95% CI 2.1, 4.5).

**Conclusions:** Our unique analysis method adds a new perspective to the PA and OA debate. The implication of these findings demonstrate that individuals can minimise cartilage volume loss by increasing their own PA and strength, which supports the clinical recommendations of promoting PA and strength to prevent and treat OA.

**Disclosure of Interest:** None declared

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#### FRI0542 POTENTIAL NOCICEPTIVE PAIN RELIEF OF INTRA-ARTICULAR SALINE CONTROL IN CLINICAL TRIALS OF KNEE OSTEOARTHRITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMISED TRIALS

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**Background:** Hyaluronic acid, corticosteroids and platelet-rich plasma (PRP) are widely used intra-articular (IA) therapies for the management of mild to moderate knee osteoarthritis (OA). Many trials evaluating the efficacy of IA-administered therapies commonly use IA saline injections as a placebo comparator arm. A previously published systematic review Altman et al, 2016 showed significant reductions in pain relief with IA saline in both the short- (3 months) and long-term (6–12 months).

**Objectives:** The aim of this updated systematic review and meta-analysis was to assess the clinical benefit and harm associated with use of IA saline in trials of IA therapies for patients with painful knee OA.

**Methods:** We searched MEDLINE and Embase databases for randomised controlled trials (RCTs) published up to and including October 12th, 2017. Two reviewers independently assessed the eligibility of potential reports and the risk of bias of included trials. We analysed short (≤3 months) and long-term (6–12 months) pain reduction from baseline of the saline arm of included trials using standardised mean differences (SMDs; estimated assuming a null-effect in a comparator group) that were weighted and pooled using a random-effects model. Pain scores were transformed to a 100-point scale when necessary. We summarised and presented treatment-related adverse events (AEs) descriptively.

**Results:** We included 46 RCTs, of which 44 provided sufficient data to be included in the meta-analysis for benefit. IA saline significantly improved short-term knee pain from baseline vs. a null effect for a comparator group across 36 studies involving 1908 patients (SMD –0.85, 95% CI –1.05 to –0.66; I<sup>2</sup>=87%). There was also significant reduction in long-term knee pain following IA injection with saline across 25 studies involving 1758 patients (SMD –0.78, 95% CI –1.02 to –0.55) with a substantial degree of heterogeneity (I<sup>2</sup>=90%). Thirty-three of the included trials reported on adverse events, none of which found any serious treatment-related AEs following IA injection with saline.

**Conclusions:** The pain relief observed with IA saline should prompt one to consider the added effectiveness of current IA treatments that use saline comparators in clinical studies, and challenges of classifying IA saline injection a "placebo."

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**FRI0543 HEALTH RESOURCE USE AND COST-OF-ILLNESS OF SYMPTOMATIC KNEE AND/OR HIP OSTEOARTHRITIS : DATA FROM KHOALA COHORT**

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**Background:** Hip and knee Osteoarthritis are a major public health problem. Data on the economic impact are scarce.

**Objectives:** The purpose of our study was to estimate the annual direct costs of patients followed for hip and/or knee osteoarthritis from the KHOALA cohort.

**Methods:** The KHOALA cohort is a French population-based multicenter cohort of 878 patients with symptomatic knee and/or hip OA, aged between 40 and 75 years old recruited between 2007 and 2009. Direct costs were collected annually for 5 years. Costs were annualised and expressed in euros per patient.

**Results:** Over the 5 years, the average total direct costs were € 2575 (sd 8085) per patient per year and median € 1015 (IQR 430–2500) (figure 1).

Drugs represented the main health expenditure item (>50% of total costs). However, the proportion attributable to osteoarthritis drugs accounted for less than 5% of total costs. The second item of expenditure was hospitalizations (hip and/or knee arthroplasty represents 7% of total average costs). Medical consultations were the third item of health expenditure (2.5% to 4% of total average costs). Physiotherapy represented 1% to 2% of total average costs.

Costs increased with older age, female sex, retirement, a high BMI, a high Charlson index and poor health status.



Abstract FRI0543 – Figure 1. Average annual total direct costs over 5 years per patient

**Conclusions:** These data are important results to describe the cost of care consumption of a sample of patients with symptomatic osteoarthritis of the hip and/or knee recruited to the general population in France. However, the specific cost attributable to osteoarthritis needs to be studied.

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FRI0544

**URINARY 6-SULFATOXYMELATONIN EXCRETION AND GALECTIN-3 PLASMA LEVEL IN PATIENTS WITH OSTEOARTHRITIS**

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**Background:** Melatonin and galectin-3 are considered as factors in the development of immune-inflammatory and destructive changes in joints.<sup>1–5</sup> Melatonin has chondrogenic and antinociceptive properties,<sup>2, 4</sup> while galectin-3 plays an important role in cell-cell adhesion, macrophage activation, angiogenesis, and apoptosis.<sup>1, 3</sup> The clinical and pathogenetic significance of melatonin and galectin-3 in osteoarthritis remains on the discussion.

**Objectives:** To study the excretion of 6-sulfatexymelatonin (metabolite of melatonin) and galectin-3 level in the blood and evaluate their association with the clinical manifestation and life quality in patients with OA.

**Methods:** Study involved 141 patients with OA of knee joints (76.6% women), aged 58.4±7.91 years, duration of the disease 10.5±6.50 years (M±SD). 47 (33.3%) patients had knee and hip OA, 38 (27%) patients had reactive synovitis. The control group was presented by 36 practically healthy subjects (72.2% female) aged 57.1±9.95 years (M±SD). 6-sulfatexymelatonin (6-SMT) in urine and galectin-3 in blood were determined by ELISA. The severity of pain, stiffness, and physical functioning of the joints were evaluated by the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). Quality of life was evaluated by Short Form-36 (SF 36).

**Results:** It was established in patients with OA a decrease in 6-SMT excretion, (mean 25.3 vs 38.8 ng/mg creatinine in control, p<0.001). 6-SMT excretion correlated with age (r=–0.40; p<0.001) and was more significant in patients with knee +hip OA (mean 26.5 vs 23.0 ng/mg creatinine in patients with OA of the knee only, p<0.001). Lower levels of 6-SMT excretion associated with higher pain and with lower quality of life. Patients with OA had increased galectin-3 levels in the blood (mean 16.4 vs 10.1 ng/ml in the control, p<0.001). In patients with OA of knee and hip joints were estimated higher levels of galectin-3. Levels of galectin-3 were significantly higher in patients with synovitis (mean 21.5 vs. 13.8 ng/ml without synovitis, p<0.001). The increase of galectin-3 in the blood was associated with a marked increase of the total WOMAC index and with decrease of life quality. The level of galectin-3 directly correlated with age, disease duration (r=0.28, 0.23, p<0.01) and inversely correlated with 6-SMT excretion (r=–0.28; p<0.01).

**Conclusions:** Lower levels of melatonin and higher of galectin-3 were associated with higher WOMAC index and poorer quality of life in patients with OA. This association may reflect possible pathogenic role of melatonin and galectin-3 in OA.

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FRI0545

**RISK FACTORS PREDICTING RADIOLOGICAL PROGRESSION OF KNEE OSTEOARTHRITIS**

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**Background:** Currently a number of risk factors (RF) are considered to be responsible for radiological progression of knee osteoarthritis (OA), nevertheless key predictors of OA progression have not yet been established.

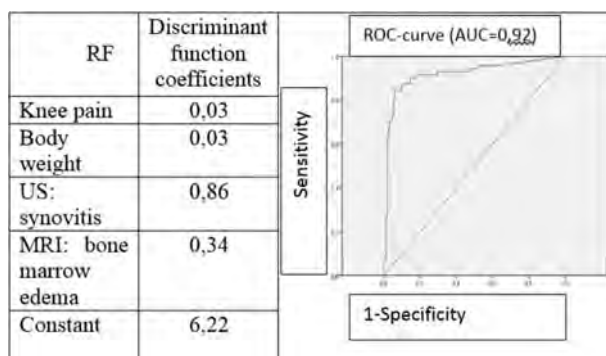
**Objectives:** To identify RF predicting radiological progression of knee joint osteoarthritis (OA) in a 5 year multicenter prospective study.

**Methods:** This study of RF predicting knee OA progression was the first with multicenter prospective design ever conducted in Russia. The study included 344 female patients 40–75 y.o with primary stage I-III knee OA (ACR criteria) from 6 centres. Radiological stage was identified by Kellgren J.- Lawrence J. grading



scale. The follow up (FUP) was 5 years. Individual patients' files described 90 parameters. Instrumental diagnostic methods included plain radiography of knee joints, dual energy X-ray absorptiometry (DEXA) of lumbar spine L1–4, femoral neck and subchondral tibia, ultrasound (US) and MRI examination of knee joints. OA progression was verified based on evolution of radiological stage. At baseline 24 pts (7%) had stage I OA, 227 (66%) – stage II, and 93 (27%) – stage III. Discriminant analysis was applied to verify most reliable RF predicting radiological progression.

**Results:** Radiological progression was documented in 45% participants during 5 year FUP. The groups with and without progression were comparable in terms of age and disease duration ( $>0.05$ ). Pts who progressed suffered more intensive knee pain – 68(52–72) vs 41(30–63) mm,  $>0.01$ , had higher body weight – 82(77–93) vs 72(65–81) kg,  $>0.01$ , had higher rates of knee synovitis (US) 44% vs 26%,  $>0.03$ , (RR=1.67, 95% CI 1.07–2.59) and mid-tibia bone marrow oedema – 60% vs 28%,  $>0.01$  (RR=2.12, 95% CI 1.34–3.35). The discriminant analysis showed that knee pain, excessive body weight, synovitis and mid-tibia bone marrow oedema (MRI) can be considered as predictors of OA radiological progression. A model capable of predicting OA course in an individual patient with high 88% accuracy, 87.7% sensitivity and 70% specificity has been developed based on identified RF and their coefficients. Area under the ROC-curve 0, 921 (95% CI 0,875–0,966).



**Conclusions:** Knee pain, excessive body weight, synovitis and bone marrow oedema should be considered as key RF predicting knee OA radiological progression.

**Disclosure of Interest:** None declared

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#### FRI0546 RELATIVE EFFICACY OF DIFFERENT EXERCISES IN KNEE AND HIP OSTEOARTHRITIS

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**Background:** All osteoarthritis (OA) guidelines recommend exercise as one of the core treatments for OA.<sup>1</sup> However, it is unclear whether one exercise is better than another and for which outcome. Due to the limited evidence that compare different types of exercise, we undertook this network meta-analysis (NMA).

**Objectives:** To determine the relative efficacy of different exercises for pain and self-reported function at (or nearest to) eight weeks.

**Methods:** Nine electronic databases were searched for eligible randomised controlled trials (RCTs) that compared any types of exercise. The search was first performed in December 2015 and was updated in December 2017. Studies comparing exercise with usual care or with another exercise were included for this NMA. Common comparators such as usual care were used to network different types of exercise. Frequentist NMA was used to estimate the relative effect size (ES), i.e. standard mean difference and its 95% confidence interval (CI).<sup>2</sup>

**Results:** 217 RCTs (n=20419) met the inclusion criteria. Of these, 89 trials (n=7070; 97 comparisons) were analysed for pain outcome (figure 1), whilst 87 trials (n=7039; 97 comparisons) were analysed for function. Mind-body exercise was the most effective for pain relief, closely followed by aerobic exercise (See the last column, table 1). While mind-body remained the best for improving function, strength and flexibility/skills exercise were better than aerobic exercise (See the last row, table 1). Single exercises were consistently better than mixed exercise.

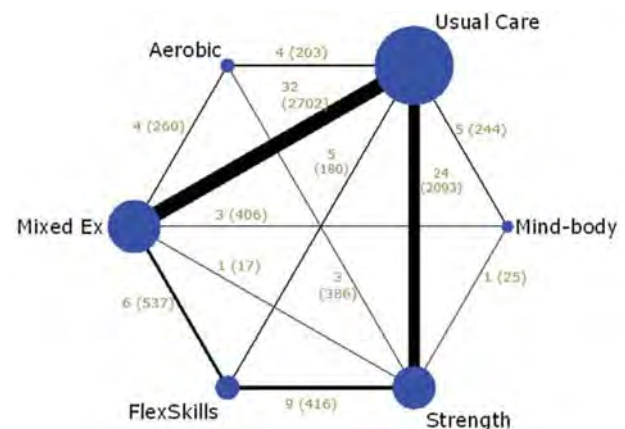
Table 1 Effect size (95% confidence interval) between different exercises

#### Pain outcomes:

Mind-body	0.05 (-0.49, 0.60)	0.42 (-0.04, 0.87)	0.51 (0.01, 1.02)	0.66 (0.23, 1.09)	1.07 (0.65, 1.49)
0.23 (-0.37, 0.84)	<b>Aerobic</b>	0.36 (-0.02, 0.75)	0.46 (0.0–0.91)	0.61 (0.23–0.98)	1.02 (0.65–1.39)
0.1 (-0.40, 0.60)	-0.13 (-0.57, 0.31)	<b>Strength</b>	0.09 (-0.22, 0.4)	0.24 (-0.02, 0.50)	0.65 (0.44–0.86)
0.16 (-0.40, 0.72)	-0.07 (-0.58, 0.43)	0.06 (-0.28, 0.40)	<b>Flex/Skills</b>	0.15 (-0.17, 0.47)	0.56 (0.25–0.87)
0.4 (-0.08, 0.87)	0.17 (-0.25, 0.58)	0.3 (0.01–0.59)	0.24 (-0.10, 0.58)	<b>Mixed exercise</b>	0.41 (0.23–0.59)
0.78 (0.32–1.25)	0.55 (0.14–0.96)	0.68 (0.45–0.92)	0.62 (0.28–0.96)	0.38 (0.17–0.60)	<b>Usual Care</b>

#### Functional outcomes:

**Note:** Exercises are in order from the top left to the bottom right. Pain outcomes are at the top and functional outcomes are at the bottom. Numbers in each cell represent effect size (95% confidence interval) between higher comparator versus lower comparator.



**Abstract FRI0546 – Figure 1.** Network diagram for pain

Aerobic: walking, cycling; FlexSkills: flexibility exercise, neuromotor training, proprioceptive training; Strength: resistance training; Mind-body: Tai-chi, Yoga; Mixed Ex: multi-component exercises

**Conclusions:** This exercise hierarchy and their relative efficacy provide a useful basis for patients and clinicians to select the most appropriate exercise whilst taking treatment goals (pain relief or functional improvement) and patient preference into consideration. The reason for the relative poor efficacy of mixed exercise warrants investigation as it contradicts current guidelines.

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#### FRI0547 IN HAND OSTEOARTHRITIS, DECREASE IN SYNOVITIS RESULTS IN LESS JOINT PAIN; A LONGITUDINAL MAGNETIC RESONANCEIMAGING STUDY

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**Background:** Current treatment options to alleviate pain in hand osteoarthritis (OA) are limited in number, efficacy, and safety. Local inflammation and subchondral bone activity are interesting as potential treatment targets, since synovitis and bone marrow lesions (BMLs) have the ability to change over time and were shown to have positive cross-sectional associations with joint tenderness.

**Objectives:** To investigate the longitudinal associations between features on magnetic resonance (MR) imaging and joint tenderness in patients with primary hand OA over two years.

**Methods:** Eighty-five consecutively included patients (81.2% women, mean age 59.2 years) with primary hand OA (89.4% fulfilling ACR classification criteria) from a rheumatology outpatient clinic received contrast-enhanced MR imaging (1.5T) and physical examination of the right hand interphalangeal joints of digits 2–5 at baseline and at follow-up two years later. MR images were scored paired in unknown time order, following the Hand OA MRI scoring system: synovitis, BMLs, and osteophytes on a 0–3 scale (higher score reflects worse condition), with half-point increments allowed for synovitis and BMLs delta-scores. Joint tenderness upon palpation was assessed by trained research nurses on a 0–3 ordinal scale. We tested the associations between decreased MR features and decreased tenderness by calculating odds ratios on joint level (n=680), using generalised estimating equations to account for the within patient effects. Additional adjustments were made for change in MR-defined osteophytes, synovitis, and BMLs, when appropriate. Similarly, we tested the associations between increased MR features and increased tenderness, and we explored interactions between the different MR features by stratifying for one another.

**Results:** Decrease in synovitis was seen in 90 joints and decrease in BMLs in 56, however when restricted to the 116 joints with baseline tenderness, at follow-up: 76 had reduced tenderness, 21 decreased synovitis, and 13 decreased BMLs. A decrease in synovitis, but not in BMLs, was associated with attenuated tenderness (table 1). Of 678 joints without maximum baseline tenderness, at follow-up: 115 had increased tenderness, 132 increased synovitis, 96 increased BMLs, and 44 increased osteophytes. An increase in synovitis, osteophytes, and, to a lesser extent, BMLs, was associated with increased tenderness (table 2). Through stratification it became apparent that BMLs were merely an effect modifier of the synovitis-tenderness association.

**Table 1** The associations between decreased MRI features and decreased joint tenderness (in joints with tenderness and MRI feature present at baseline)

	N/total (%) joints with decreased tenderness	Adjusted analyses* OR (95% CI)	Adjusted analyses* OR (95% CI)
<b>Synovitis</b>			
Stable/increase	30/58 (51.7)	1.0 (reference)	1.0 (reference)
Decrease	17/21 (81.0)	3.99 (0.95 – 16.76)	5.88 (1.12 – 30.95)
<b>Bone marrow lesions</b>			
Stable/increase	23/39 (59.0)	1.0 (reference)	n.a.
Decrease (≥0.5)	6/13 (46.2)	0.39 (0.10 – 1.50)	n.a.
Decrease (≥1)	5/11 (45.5)	0.53 (0.14 – 1.95)	n.a.

OR=Odds ratio; CI=confidence interval; \*Adjusted for patient effect; †Adjusted for patient effect, increase of MRI-defined osteophytes, and decrease of BML/synovitis.

**Table 2** The associations between increased MRI features and increased joint tenderness (in joints without maximum tenderness at baseline)

	N/total (%) joints with increased tenderness	Adjusted analyses* OR (95% CI)	Adjusted analyses* OR (95% CI)
<b>Synovitis</b>			
Stable/decrease	78/536 (14.6)	1.0 (reference)	1.0 (reference)
Increase	36/132 (27.3)	1.80 (1.11 – 2.91)	1.81 (1.11 – 2.94)
<b>Bone marrow lesions</b>			
Stable/decrease	94/569 (16.5)	1.0 (reference)	1.0 (reference)
Increase (≥0.5)	17/96 (17.7)	1.40 (0.99 – 1.97)	1.14 (0.81 – 1.60)
Increase (≥1)	11/51 (21.6)	1.66 (0.99 – 2.78)	1.33 (0.82 – 2.17)
<b>Osteophytes</b>			
Stable	102/632 (16.1)	1.0 (reference)	1.0 (reference)
Increase	13/44 (29.5)	2.58 (1.53 – 4.38)	2.75 (1.59 – 4.77)

OR=Odds ratio; CI=confidence interval; \*Adjusted for patient effect; †Adjusted for patient effect and increase of MRI-defined synovitis/BML/osteophytes.

**Conclusions:** In hand OA, a decrease in MR-defined synovitis is associated with a decrease in joint tenderness. Furthermore, an increase in synovitis or osteophytes is associated with increased tenderness, which is further augmented by co-occurrence of BMLs. These findings support targeting synovitis in hand OA.

**Disclosure of Interest:** None declared

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**FRI0548 ASSOCIATION OF OMERACT CORE DOMAINS OF PAIN AND FUNCTION WITH PATIENT SATISFACTION AFTER TOTAL JOINT REPLACEMENT**

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**Background:** Up to 20% of Total Joint Replacement (TJR) patients are dissatisfied, but this is difficult to study as it is challenging to pool data due to the lack of unified core outcome measures. The OMERACT TJR Special Interest Group has

recently endorsed a core domain set that include pain and function, and now seeks validation prior to development of a TJR trial core measurement set.

**Objectives:** To assess the association of pain relief and improved function with patient satisfaction 2 years after TJR.

**Methods:** We identified all patients undergoing total hip (THR) and knee (TKR) replacement in a hospital-based registry from 2007–2011, and evaluated those with 2 year satisfaction scores. Pain and function were measured using the Knee and Hip injury and Osteoarthritis Outcome Score (KOOS, HOOS) and satisfaction was measured using 5 primary questions, each rated on a Likert scale. Each question was weighted equally and a satisfaction summary score was calculated (range 0–100, higher scores corresponding to greater satisfaction). Expectations were measured using the validated HSS Expectations survey. Correlation was analysed with Spearman coefficients, and scores were compared by quartiles using the Kruskal-Wallis test.

**Results:** We included 4796 primary unilateral TKR and 4801 THR. 78% of TKR and 90.7% of THR were very satisfied with pain relief, and 6.5% of TKR and 2.5% of THR were somewhat or very dissatisfied (table 1). Satisfaction correlated moderately with pain (TKR  $\rho=0.61$ , THR  $\rho=0.47$ ) and function (TKR  $\rho=0.65$ , THR  $\rho=0.51$ ) at 2 years; there was no correlation with baseline expectations. When comparing satisfaction by pain, function and expectation quartiles, there were statistically significant differences (table 2); those with the best scores and greatest change in pain and function were the most satisfied.

**Abstract FRI0548 – Table 1.** Satisfaction Questions and Distribution

Satisfaction Questions and Distribution	n (%) n=4,796 TKR	n (%) n=4,801 THR
<b>Pain relief</b>		
Very satisfied	3754 (78.3)	4451 (92.7)
Somewhat satisfied	823 (17.0)	399 (8.3)
Neither satisfied nor dissatisfied	108 (2.3)	61 (1.2)
Somewhat dissatisfied	188 (3.9)	42 (0.9)
Very dissatisfied	143 (3.0)	87 (1.8)
<b>Improving ability to do household errand work</b>		
Very satisfied	3214 (67.0)	4161 (86.7)
Somewhat satisfied	918 (19.2)	285 (5.9)
Neither satisfied nor dissatisfied	301 (6.3)	169 (3.5)
Somewhat dissatisfied	217 (4.5)	102 (2.1)
Very dissatisfied	148 (3.0)	77 (1.6)
<b>Improving ability to do recreational activities</b>		
Very satisfied	2714 (57.8)	3981 (82.9)
Somewhat satisfied	1177 (24.5)	819 (17.3)
Neither satisfied nor dissatisfied	358 (7.4)	234 (4.8)
Somewhat dissatisfied	273 (5.7)	133 (2.8)
Very dissatisfied	218 (4.5)	114 (2.4)
<b>Overall satisfaction with surgery results</b>		
Very satisfied	3561 (74.7)	4793 (99.8)
Somewhat satisfied	721 (15.0)	482 (10.0)
Neither satisfied nor dissatisfied	169 (3.5)	56 (1.2)
Somewhat dissatisfied	205 (4.3)	34 (0.7)
Very dissatisfied	158 (3.3)	85 (1.8)
<b>Improved quality of life</b>		
More than ever dreamed possible	258 (5.4)	118 (2.5)
Great improvement	2202 (45.8)	3128 (65.1)
Moderate improvement	194 (4.1)	400 (8.3)
A little improvement	204 (4.3)	91 (1.9)
No improvement at all	164 (3.4)	39 (0.8)
Quality of life worse	106 (2.2)	39 (0.8)

**Abstract FRI0548 – Table 2.** Association between outcomes and Satisfaction

Association between outcomes and Satisfaction	TKR Satisfaction score median [IQR]	p-value	THR Satisfaction score median [IQR]	p-value
<b>2-year pain*</b>				
Q1	72 [41, 88]	<0.001	NA	<0.001
Q2	91 [61, 98]		84.3 [67, 98]	
Q3	98 [91, 98]		98 [91, 98]	
Q4	98 [98, 100]		98 [98, 100]	
<b>3 pain</b>				
Q1	77 [47, 90]	<0.001	98 [81, 98]	<0.001
Q2	91 [71, 98]		98 [91, 98]	
Q3	98 [98, 98]		98 [98, 100]	
Q4	98 [98, 100]		98 [98, 100]	
<b>2-year function</b>				
Q1	71 [47, 88]	<0.001	98 [81, 98]	<0.001
Q2	91 [61, 98]		98 [91, 98]	
Q3	98 [94, 98]		98 [98, 100]	
Q4	98 [98, 100]		98 [98, 100]	
<b>3 function</b>				
Q1	81 [49, 95]	<0.001	98 [81, 98]	<0.001
Q2	92 [61, 98]		98 [91, 98]	
Q3	98 [98, 98]		98 [98, 100]	
Q4	98 [98, 100]		98 [98, 100]	
<b>Baseline expectations</b>				
Q1	91 [76, 98]	<0.001	98 [88, 98]	<0.001
Q2	98 [81, 98]		98 [91, 98]	
Q3	98 [91, 98]		98 [91, 100]	
Q4	98 [98, 98]		98 [98, 100]	

Scores are summarised as median [interquartile range] and compared using the Kruskal-Wallis test. \*The median 2-year pain score for THR was 100, so the third and fourth quartiles are the same; Quartiles differ for THR and TKR.

Scores are summarised as median [interquartile range] and compared using the Kruskal-Wallis test. \*The median 2 year pain score for THR was 100, so the third and fourth quartiles are the same; Quartiles differ from THR and TKR

**Conclusions:** These findings confirm that with increasing relief of pain and functional improvement, the strength of the association of 2 core domains with satisfaction increases, further validating these core domains for use in TJR clinical trials. A core outcome measurement set needs to be defined for use in TJR clinical trials that includes validated measures of these domains.

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FRI0549

### OSTEOARTHRITIS (OA) AND RHEUMATOID ARTHRITIS (RA) PATIENTS HAVE SIMILAR DISEASE BURDENS AT FIRST VISIT TO AN ACADEMIC RHEUMATOLOGY SETTING, BUT OA PATIENTS HAVE A HIGHER BURDEN AT A 6-MONTH FOLLOW-UP VISIT

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**Background:** Osteoarthritis (OA) commonly is regarded as less severe than rheumatoid arthritis (RA). However, limited data are available for direct comparisons, largely because different measures traditionally are used in RA – primarily a HAQ (Health Assessment Questionnaire) vs OA – a WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index). RAPID3 (Routine Assessment of Patient Index Data) on an MDHAQ (Multi-Dimensional HAQ) is a self-report index that is informative in RA and most rheumatic diseases, including OA.<sup>1</sup> A recent analysis of unselected patients from 4 rheumatology settings indicated that RAPID3 and other MDHAQ scores were similar or higher in OA versus RA patients,<sup>2</sup> but those findings were from a cross-sectional convenience sample of unselected patients likely affected by treatment, rather than from an initial visit prior to rheumatologic therapy.

**Objectives:** To analyse MDHAQ/RAPID3 scores in patients with a primary diagnosis of either OA or RA at their initial visit and at 6 month follow-up at an academic rheumatology centre.

**Methods:** At one site, all patients complete an MDHAQ/RAPID3 prior to seeing the rheumatologist. The 2-page MDHAQ/RAPID3 includes 0–10 scores for physical function (FN) (converted from 0–3) and visual analogue scale (VAS) scores for pain (PN) and patient global assessment (PATGL), compiled into a 0–30 RAPID3. New patients seen between 2013 and 2017 with physician-diagnosed primary OA or RA and complete RAPID3 data were studied. Mean FN, PN, PATGL and RAPID3 scores in RA and OA at baseline and 6 month follow-up (range 3–9 months) were compared for differences between first and second visits using t-tests, and between OA and RA using MANOVA.

**Results:** At first visit, mean RAPID3 was 15.9 in OA vs 15.3 in RA (table 1). At a mean of a 5 month (actual) follow-up visit, RAPID3 fell from 15.9 to 14.9 (-1.0, p=0.06) in OA vs 15.3 to 11.1 (-4.2, p<0.001) in RA, resulting in significantly higher scores in OA vs RA (table 1). These differences remained significant adjusted for age, sex, body mass index, and education level.

Mean and standard deviation (SD) at first visit and 5 month follow up visit MDHAQ/RAPID3 of patients with OA and RA seen in routine care

Measures	OA (n=109)	RA (n=102)	OA vs RA p value	OA vs RA p adjusted*
Initial visit				
Function (0–10)	3.15 (1.9)	2.89 (2.2)	0.34	0.60
Pain (0–10)	7.01 (2.3)	6.36 (2.9)	0.07	0.49
PATGL (0–10)	5.69 (2.8)	5.85 (3.0)	0.69	0.30
RAPID3 (0–30)	15.9 (5.9)	15.3 (7.0)	0.52	0.47
5 months follow-up visit				
Function(0–10)	2.93 (1.9)	2.24 (2.2)	<b>0.02</b>	<b>0.006</b>
Pain (0–10)	6.36 (2.5)	4.60 (3.0)	<b>&lt;0.001</b>	<b>0.03</b>
PATGL (0–10)	5.62 (2.7)	4.10 (3.2)	<b>&lt;0.001</b>	<b>0.001</b>
RAPID3 (0–30)	14.9 (6)	11.1 (7.6)	<b>&lt;0.001</b>	<b>0.001</b>

\*adjusted for age, sex, BMI and education

**Conclusions:** Patients with OA or RA have similar disease burdens at first visit to a rheumatology site, but OA patients have a considerably higher burden 5 months later, reflecting more effective treatments for RA than for OA. Nonetheless, OA is a severe disease at first visit, suggesting a need for further research in OA toward improved treatment and outcomes. MDHAQ/RAPID3 is feasible and useful to assess and monitor clinical status in routine care of patients with different rheumatic diseases.

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**Disclosure of Interest:** J. Chua: None declared, I. Castrejon: None declared, J. Block: None declared, A.-M. Malfait: None declared, T. Pincus Shareholder of: Dr. Pincus holds a copyright and trademark on MDHAQ and RAPID3 for which he receives royalties and license fees. All revenue is used to support further development of quantitative questionnaire measures for patients and doctors in clinical rheumatology care.

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FRI0550

### DIFFERENTIAL IMPACT OF OBESITY, STRUCTURAL SEVERITY AND THEIR COMBINATION ON THE EFFICACY OF VISCOSUPPLEMENTATION IN PATIENTS WITH KNEE OSTEOARTHRITIS. POST-HOC ANALYSIS OF A DOUBLE-BLIND, CONTROLLED, MULTICENTER, RANDOMISED TRIAL

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**Background:** It has been demonstrated that radiological severity and obesity were independent factors of VS failure and that the percentage of patients fulfilling the OMERACT-OARSI response criteria was only 41.7% in patients with both marked joint space narrowing and obesity while it was 87.1% in those who did not have any of these two risk factors.<sup>1</sup>

**Objectives:** The aim of the study was to assess the impact of obesity, radiographic severity and their combination on pain and function scores, 6 months after viscosupplementation in patients with knee osteoarthritis.

**Methods:** Post-hoc analysis of a prospective, double-blind, randomised, multi-centre, parallel-group trial, aimed to compare 2 viscosupplements (x 3 weekly intra articular injections of HANOX-M or Bio-HA) in patients with symptomatic knee OA. Patients were classified according to body mass index (BMI<or>=30 kg.<sup>2</sup>) and to OARSI radiological grade (1–2 versus 3). Responses in terms of WOMAC pain and function scores (differences between baseline and 6 months, as well as their variation over time) were compared according to BMI, radiological grade and to the combination of the 2 parameters.

**Results:** One-hundred and sixty-six patients from the intent-to-treat population, were analysed: Forty-seven patients (28.3%) were classified as obese (BMI ≥30 kg.<sup>2</sup>). At baseline WOMAC pain score was similar in obese and non-obese patients, whereas WOMAC function score was statistically higher in obese versus non-obese subjects. At month 6, WOMAC pain and function scores decreased significantly by 43.4% and 41.9% (p<0.0001). At month 6, WOMAC pain was significantly lower in non-obese than in obese patients (4.9±4.1 versus 7.1±4.9; p=0.008) and in patients OARSI grade 1–2 versus 3 (4.8±4.3 versus 6.4±4.5; p=0.009). WOMAC pain score, was 85.7% greater in obese/grade 3 patients than in non-obese/grade 1–2 subjects (7.8±5.1 versus 4.2±4.1, p=0.001). Lastly, the decrease of pain was twice greater in non-obese patients with OARSI 1–2 than that of obese patients with OARSI grade 3 (-5.7±4.3 versus -2.8±4.3, p=0.007). Similarly, WOMAC function score at month 6 was significantly higher in obese versus non-obese patients, in OARSI 3 versus OARSI 1–2 and in obese/grade 3 than in non-obese/grade 1–2.

**Conclusions:** This trial confirms that obesity and advanced stage are independent predictors of a lower response to viscosupplementation in knee OA. We identified a population sub-group (patients with both obesity and severe joint space narrowing) for who HA should not be recommended, regarding the weak benefit it provides.

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- [1] Eymard F, Chevalier X, Conrozier T. Obesity and radiological severity are associated with viscosupplementation failure in patients with knee osteoarthritis. J Orthop Res 2017. doi:10.1002/jor.23529

**Acknowledgements:** The authors acknowledge LABRHA SAS for having allowed them to use the study database

**Disclosure of Interest:** T. Conrozier Consultant for: LABRHA SAS, Speakers bureau: LABRHA SAS, F. EYMARD: None declared, X. CHEVALIER: None declared, J.-C. BALBLANC: None declared

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FRI0551

### COMPARISON OF PHYSICAL ACTIVITY (PA) BETWEEN PATIENTS WITH DIFFERENT STAGES OF OSTEOARTHRITIS(OA) AND THE GENERAL POPULATION: A CROSS-SECTIONAL STUDY

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**Background:** The benefit of Physical Activity (PA) in different stages of osteoarthritis (OA) is unambiguous considering the positive effects on pain and physical functioning. However, insight in the characteristics of PA (i.e. duration and



intensity) between patients in different stages of OA is scarce. Also, comparisons with the general population are understudied.

**Objectives:** To compare the amount (i.e. duration and intensity) of PA in patients in different stages of OA (i.e. patients in primary and secondary care, and post Total Joint Arthroplasty (TJA)) and the general population.

**Methods:** This study is based on secondary analyses of baseline data from four studies:<sup>1</sup> an effectiveness study of an educational program for OA patients in primary care,<sup>2</sup> a study on effectiveness of a multidisciplinary self-management program for generalised OA in secondary care,<sup>3</sup> a study among patients whom underwent TJA for end-stage OA in preceding 7–22 months, and<sup>4</sup> a nationwide study among the general population in the Netherlands (n=14,000) on general health.<sup>1</sup> In the current study only patients aged  $\geq 40$  years were included. The SQUASH questionnaire was used to assess PA in all 4 studies and to calculate adherence to PA recommendations, duration (hrs/wk) and intensity (MET.hrs/wk). To compare the amount (hrs/wk) and intensity (MET.hrs/wk) between different stages of OA and the general population, we applied multiple linear regression analysis, adjusted for age, gender and Body Mass Index (BMI).

**Results:** Demographic characteristics and adherence to PA recommendations are illustrated in table 1. Mean duration and intensity of PA in the general population were 41.3 hrs/week and 145.7 MET.hrs/week, respectively. Patients after TJA showed higher PA levels (both in terms of duration and intensity) than patients in secondary care and the general population (table 2).

**Abstract FRI0551 – Table 1.** Demographic characteristics of three OA stages and the general population in the Netherlands

	Primary care n=117	Secondary care n=144	Post-TJA n=519	General population n=4448
Age (years (SD))	68.3 (10.5)	59.9 (7.6)	70.1 (9.0)	59.2 (11.5)
Gender,% Female	59.8	85.4	65.3	51.8
Adherence to Dutch PA recommendations(% yes)	72.6	72.9	76.7	68.8

**Abstract FRI0551 – Table 2.** Relative difference (%) in mean duration (hours/week) and intensity (MET.hours/week) of PA between groups adjusted for age, gender and BMI.

MET.hrs/week	hrs/week	General population	Primary care	Secondary care	Post TJA
General population			0.3	5.4	-5.0*
Primary care	1.2			5.1	-5.2
Secondary care	-2.5		-3.6		-9.9*
Post TJA	5.3*		4.1		8.0*

\*Indicates p-value $\leq 0.05$ .

**Conclusions:** The results of this study show small non-significant differences in PA levels between primary care patients and the general population. Patients after TJA are more physically active than secondary care patients and the general population. However, low adherence rates to PA recommendations indicate the necessity to promote PA in a substantial group of OA patients.

#### REFERENCE:

[1] Centraal Bureau voor de Statistiek (CBS). Gezondheidsenquête 2012. DANS. 2014. <https://doi.org/10.17026/dans-zcc-5tsc>

**Disclosure of Interest:** None declared

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#### FRI0552 SM04690, A WNT PATHWAY INHIBITOR: ANTI-INFLAMMATORY AND CARTILAGE PROTECTIVE EFFECTS IN PRECLINICAL OA MODELS

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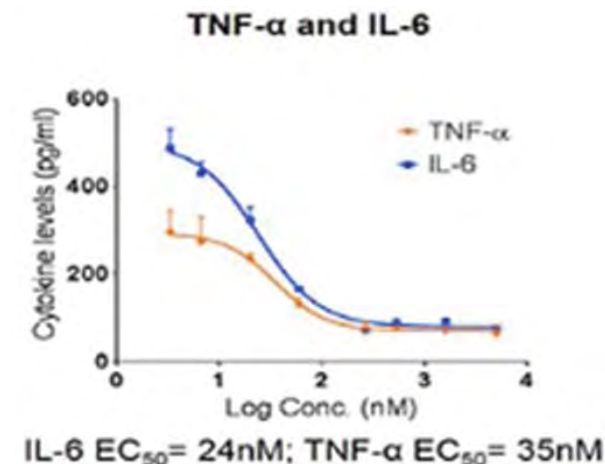
**Background:** Osteoarthritis (OA) is characterised by pain, swelling, and reduced function in the knee joint. Upregulated Wnt signalling drives OA through synovial inflammation, increased subchondral bone, and thinning cartilage.

**Objectives:** SM04690, a small molecule Wnt pathway inhibitor that demonstrated chondrogenic and anti-inflammatory properties preclinically<sup>1</sup>, was further evaluated to determine its potential to reduce inflammation, protect cartilage, improve joint health and modify pain in OA.

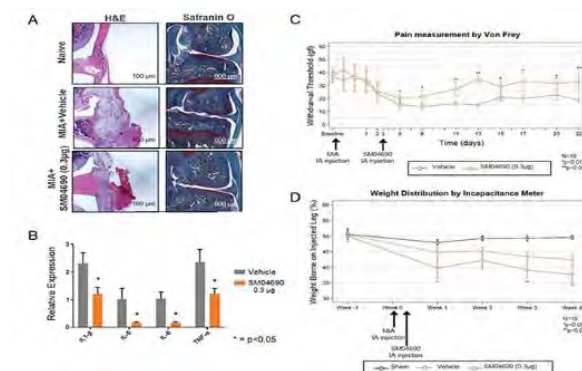
**Methods:** Cytokine secretion (IL-6 and TNF- $\alpha$ ) from IL-1 $\beta$ -stimulated and SM04690-treated synovial fibroblasts was measured by ELISA. A single intra-

articular injection of SM04690 or vehicle was evaluated in an *in vivo* rat knee monosodium iodoacetate (MIA) OA model. Joint inflammation was evaluated by H and E staining, inflammatory cytokines (IL-1 $\alpha$ , IL-1 $\beta$ , IL-6, TNF- $\alpha$  and IFN- $\gamma$ ) by qPCR, and cartilage protection by qPCR for matrix metalloproteinases (MMPs). Histological evaluation of cartilage health was performed using OARSI score and thickness by Safranin-O staining. Pain was measured as paw withdrawal threshold using Von Frey apparatus and weight distribution using incapitance metre and analysed using generalised estimating equation regression.

**Results:** SM04690 dose-dependently inhibited IL-1 $\beta$ -induced cytokine secretion in synovial fibroblasts (EC<sub>50</sub> ~30 nM; figure 1). In the rat MIA OA model, compared to vehicle, SM04690 injection reduced visible knee swelling, inflammatory cells, and proinflammatory cytokine and MMP production (p<0.05). SM04690 increased (p<0.01) paw withdrawal threshold from day 6 and improved weight distribution to the affected limb in treated rats, at multiple timepoints, compared to vehicle (figure 2). SM04690 increased Safranin-O stained cartilage thickness and decreased OARSI score (p<0.05) compared to vehicle.



**Abstract FRI0552 – Figure 1.** SM04690 inhibited inflammatory cytokine production in synovial fibroblasts *in vitro*



**Abstract FRI0552 – Figure 2.** SM04690 inhibited inflammatory cytokine production and decreased inflammation and pain in the MIA model of OA

**Conclusions:** In a rat MIA OA model, SM04690 injection reduced inflammation, protease production, and pain, with improved cartilage and joint health, compared to vehicle. Previously demonstrated regenerative effects in nonclinical studies<sup>1</sup>, along with anti-inflammatory properties, show SM04690 may improve symptoms and potentially provide disease modification in OA. Clinical studies are ongoing.

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[1] Deshmukh V, et al. Osteoarthritis Cartilage 2018;26:18–27.

**Disclosure of Interest:** V. Deshmukh Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, T. Seo Shareholder of: Samumed, LLC, Employee

of: Samumed, LLC, C. Swearingen Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Y. Yazici Shareholder of: Samumed, LLC, Employee of: Samumed, LLC

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### FRI0553 THE ROLE OF AGE-RELATED SARCOPENIA IN OSTEOARTHRITIS OF LOWER EXTREMITY

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**Background:** Sarcopenia, defined as the age-related loss of muscle mass and low muscle function.<sup>1</sup> The prevalence of sarcopenia worldwide by meta-analysis of 35 articles was 10% (95% CI: 8%–12%) in men and 10% (95% CI: 8%–13%) in women, respectively.<sup>2</sup> A review of the literature on osteoarthritis (OA) and sarcopenia has shown that the age factor that contributes to the development of OA includes a decrease in muscle strength. In people with OD of the lower extremity, the frequency of falls was increased by a factor of 2–5.<sup>3</sup> OA contributed to the development of sarcopenia in elderly women.<sup>4</sup>

**Objectives:** Perform body composition and muscle analysis in patients with osteoarthritis and identify risk factors for sarcopenia that affect patients with osteoarthritis.

**Methods:** Prospective study of 159 women, mean age 74±13.3. The walking speed, handgrip strength were evaluated to apply the European Working Group on Sarcopenia. Assessment of appendicular skeletal muscle mass (ALM/h<sup>2</sup>) and total body fat were assessed using DXA, on Hologic Explorer machines. Covariates were determined by questionnaires and interviews.

**Results:** 31.45% of people with OA older than 65 years had sarcopenia. Patients with OA had a decrease in muscle strength and function, regardless of sarcopenia. Statistically significantly more frequent in patients with OA were lower indexes of lean mass index (ALM/h<sup>2</sup>) and body mass index (BMI) (p<0.01). The incidence of sarcopenia increased with age (p<0.01). 61.5% of patients with sarcopenia significantly more often had high values of c-reactive protein – CRP (x<sup>2</sup>=31.18, p<0.0001). Patients with sarcopenia were statistically significantly more likely to have vitamin D deficiency than patients without sarcopenia (x<sup>2</sup>=8.11, p<0.01). Cases of falls were observed in 90% of patients with sarcopenia (x<sup>2</sup>=79.29, p<0.001). Low physical activity 86% of patients with sarcopenia are statistically significantly higher than in patients without sarcopenia (95% CI: 73.3–94.2, p<0.01).

**Conclusions:** With age, patients with sarcopenia and OA had a significant decrease in muscle mass and physical activity, an increase in the incidence of falls. Patients with sarcopenia had high CRP levels and vitamin D deficiency than patients without sarcopenia.

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**Disclosure of Interest:** None declared

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FRIDAY, 15 JUNE 2018

## Diagnostics and imaging procedures

### FRI0554 WHICH AXIAL MAGNETIC RESONANCE IMAGING COMBINATION IS OPTIMAL FOR ASSESSING ACTIVITY IN SPONDYLOARTHRITIS?

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**Background:** None

**Objectives:** To determine the optimal axial Magnetic Resonance Imaging (MRI) combination for assessing disease activity in spondyloarthritis

**Methods:** In this single centre cross-sectional study, patients with a known diagnosis of axial spondyloarthritis were selected. Clinical activity was defined by an Ankylosing Spondylitis Disease Activity Score-CRP (ASDAS-CRP) ≥1.3. Bone marrow oedema was quantified by the Berlin spine score and the global score for sacroiliac joints (SIJ). The ASDAS-CRP and MRI activity evaluation of the full spine and SIJ were available in the entire cohort. Receiver operating characteristic curves were done to test the performance of different MRI combinations in identifying patients with ASDAS-CRP ≥1.3. Performance was interpreted as follows: 0.61–0.70=fair, 0.71–0.80=moderate. A pairwise comparison of the area under the curves (AUC) was made to rank these MRI scores according to their diagnostic performance.

**Results:** 44 patients were assessed (30 were men; mean age was 37 years; mean disease duration was 5.0 years; median serum CRP level was 4.0 mg/L; mean ASDAS-CRP was 2.6; n=36 with ASDAS≥1.3, and n=8 for ASDAS<1.3). MRI activity score (MRIAS) performance was moderate for thoracic spine alone and SIJ in combination with thoracic spine or thoraco-lumbar spine or cervico-thoracic spine or total spine. Performance was fair for SIJ alone and total spine alone. MRIAS yielded the highest specificity for SIJ alone (Se=44%, Sp=100%), and the highest sensitivity for thoracic spine alone (Se=89%, Sp=50%). MRIAS for SIJ in combination with the thoracic spine yielded the highest AUC (0.78, p=0,0002). However, no significant difference was observed between MRIAS with a moderate performance (p>0.05, whatever AUCs comparisons).

**Conclusions:** For assessing disease activity in axial spondyloarthritis MRI of the SIJ in combination with the thoracic spine performed as good as MRI based on a more extended imaging of the spine.

**Disclosure of Interest:** None declared

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### FRI0555 MUSCLE ELASTOGRAPHY AS A POTENTIAL NOVEL IMAGING BIOMARKER IN MYOSITIS

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**Background:** Idiopathic inflammatory myopathies are a group of autoimmune muscle disorders characterised by muscle pain, stiffness and weakness. Diagnosis can be challenging; it relies on subjective clinical assessments, expensive MRI scans and invasive muscle biopsies. Novel quantitative ultrasound technologies like shear wave elastography could provide a new valuable non-invasive bedside imaging biomarker for diagnosis and management.

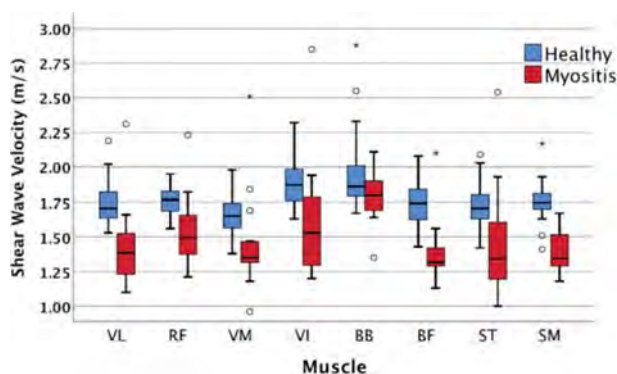
**Objectives:** 1-to determine if there are muscle elasticity differences between myositis patients and healthy controls. 2-to test the correlation between elasticity and measures of strength, function and muscle enzymes (disease activity).

**Methods:** Muscle elasticity, evaluated using shear wave velocity (SWV), was measured in 16 active myositis patients (5 males/11 females; 5 dermatomyositis, 5 polymyositis, 2 inclusion body, 4 undifferentiated) with a mean age of 51.3 years and 26 healthy controls (8 males/20 females) with a mean age of 42.0 years. Active myositis was defined as a decreased muscle strength and an elevated muscle enzyme. The investigated muscles included the four quadriceps [vastus lateralis (VL), rectus femoris (RF), vastus medialis (VM) and vastus intermedialis (VI)], the three hamstrings [biceps femoris (BF), semitendinosus (ST) and semi-membranosus (SM)] and the biceps brachii (BB). The myositis patients performed the expanded timed-get-up-and-go (ETGUG) test to assess walking function in addition to the handgrip strength and isokinetic knee extension/flexion tests to assess muscle strength. Mann-Whitney test and Spearman's correlation coefficients were utilised to test for difference and correlation respectively.

**Results:** Myositis patients had a significantly lower SWV (p<0.001) in all muscles except the BB (table 1 and figure 1). The mean elasticity difference ranged from 12% for VM to 21.1% for SM (table 1). Muscle enzyme (creatinine kinase) correlated with SWV for the VM (r=0.50; p=0.04) and BB (r=0.55; p=0.03). A strong correlation was detected between ETGUG walking time and VL (r=-0.73) as well as VI (r=-0.64). Handgrip strength correlated with VL, RF and BF (r=0.64, 0.56 and 0.62 respectively). There was, however, no significant correlation between SWV and isokinetic knee strength.

**Abstract FRI0555 – Table 1.** Mean SWV and differences in the examined muscles between myositis patients and controls

Muscle	Shear wave velocity (m/s)		Mean difference (95% CI)	Difference percentage	Significance (p value)
	Healthy	Myositis			
Vastus lateralis	1.74	1.42	-0.32 (0.19, 0.46)	18.4%	<0.001*
Rectus femoris	1.77	1.53	-0.24 (0.12, 0.34)	13.6%	<0.001*
Vastus medialis	1.66	1.45	-0.21 (0.06, 0.35)	12.7%	<0.001*
Vastus intermedius	1.89	1.60	-0.29 (0.11, 0.47)	15.3%	<0.001*
Biceps brachii	1.94	1.79	-0.15 (-0.01, 0.30)	7.7%	0.088
Biceps femoris	1.73	1.38	-0.35 (0.24, 0.46)	20.2%	<0.001*
Semitendinosus	1.72	1.45	-0.27 (0.09, 0.43)	15.7%	<0.001*
Semimembranosus	1.75	1.38	-0.37 (0.28, 0.45)	21.1%	<0.001*



**Conclusions:** Muscle elasticity in myositis patients has been shown to be 21% lower in comparison to healthy participants and seems to moderately correlate with disease activity, muscle strength and function. To our knowledge, this is the first study to show that shear wave elastography can detect changes in muscle elasticity in myositis patients. Further validation is required to evaluate the value of this novel ultrasound technology as an imaging biomarker for myositis.

**Disclosure of Interest:** None declared

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### FRI0556 AUTOMATED SCORING OF KNEE OSTEOARTHRITIS (OA) ON ROUTINE RADIOGRAPHS IDENTIFIES DISEASE SEVERITY IN OA

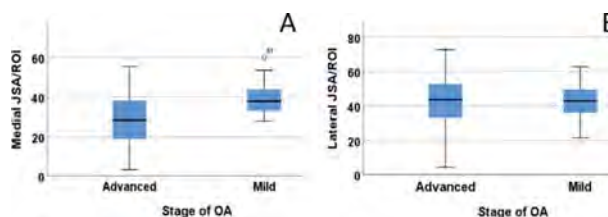
A. Law<sup>1</sup>, L. Assi<sup>1</sup>, A. Harrison<sup>1</sup>, F.A. Howe<sup>2</sup>, N. Sofat<sup>1</sup>. <sup>1</sup>Institute of Infection and Immunity; <sup>2</sup>Molecular and Clinical Sciences Research Institute, St George's, University of London, London, UK

**Background:** Knee osteoarthritis (OA) causes pain and limited function of the knee, linked to cartilage loss, bone remodelling and inflammation<sup>1</sup>.

**Objectives:** We aimed to find out whether joint space measures can stratify patients into mild and advanced OA using an automated scoring tool<sup>2</sup>.

**Methods:** 86 weight-bearing radiographs (target joint: 41 left, 45 right knee) were analysed by using ImageBiopsy Lab software (JSx). Automated joint space (JS) measures were joint space width (JSW), minimum height (minH) and joint space area/region of interest (JSA/ROI, in mm<sup>2</sup>). JS measures were compared against Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) of pain, stiffness and function, with each subscale score normalised to a total score of 100. Body-mass index (BMI) and age data were available as potential covariates. Image analysis was initiated with landmarks automatically placed on the end of tibial plateau for each compartment, with fine manual adjustment of landmarks and contour spline if necessary. Clinical scores were compared between mild OA (n=24) and advanced OA (n=62); patient groups were defined according to their clinical pathway of standard care: medical management for early OA and knee replacement for advanced OA. SPSS Statistics 25 was used for analysis. An independent-samples t-test was used to compare the automated radiological and clinical scores between the groups of different OA severity. Subsequently the General Linear Model (GLM) was used to evaluate group differences with appropriate covariates and fixed factors.

**Results:** Joint space measures were strongly linked to the two clinical groups of OA severity (mild and advanced OA). Differences were significant in the medial JSA/ROI (p<0.001), medial JSW (p=0.001), medial MinH (p<0.001), WOMAC pain (p=0.001), stiffness and function (both p=0.003). Age (p=0.014) and BMI (p=0.019) were also different between the two groups of OA severity in the t-test, and were then used as co-variables in the GLM analysis along with gender and ethnicity as fixed factors. Medial JSA/ROI (p=0.027) and medial MinH (p=0.041) were still significantly different between mild and advanced OA in the multivariate test. Receiving Operating Characteristic (ROC) curves showed that medial JSA/ROI was the better discriminator for severity of OA (AUC=0.738) when compared to WOMAC scores (AUC=0.719 for WOMAC pain).



**Abstract FRI0556 – Figure 1.** Boxplots showing the relationship between stage of OA (mild and advanced) and (A) medial JSA/ROI, (B) lateral JSA/ROI

**Conclusions:** Medial joint space measures are possible markers for identifying the stage of disease if only radiographs were used. In particular, medial JSA/ROI may be utilised as an automated tool for characterising patient severity.

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### FRI0557 THERMOGRAPHIC ANALYSIS OF HANDS AND WRISTS OF RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Thermography has been utilised in a number of studies in rheumatoid arthritis (RA),<sup>1</sup> however there is a paucity of evidence as regards to the possibility of applying this non-invasive technology to the detection of synovitis of the hands and wrists. With normative data having been already published,<sup>2</sup> it is now possible to compare the thermographic characteristics of RA patients without active synovitis to those with a normal thermal distribution in order to determine the baseline characteristics of RA hands and wrists. This would consequently provide a foundation against which further studies investigating RA patients with synovitis can be compared.

**Objectives:** To determine whether rheumatoid arthritis (RA) patients without active synovitis in their hands exhibit different baseline thermographic patterns of the fingers and palms when compared to healthy individuals

**Methods:** Data from 31 RA patients were compared to 51 healthy controls. Inclusion criteria were confirmed absence of synovitis by clinical examination and musculoskeletal ultrasound in rheumatoid patients. Thermographic imaging of the regions of interest (ROIs) were obtained as per established protocols<sup>2</sup>

**Results:** Significant differences were found between the mean temperatures of the palm regions and fingers of the healthy participants when compared to the palm regions and fingers of their RA counterparts (p=0.001), with the latter group exhibiting higher temperatures in all ROIs. No significant differences were found between ROIs of the palms and fingers of both hands in either group. Logistic regression models confirm that both palm and finger temperature increase significantly in RA



**Conclusions:** RA patients without active inflammation of the hands demonstrate a significantly higher mean temperature compared to healthy individuals. These findings provide evidence that baseline thermal data in RA differs significantly from healthy individuals. Thermal imaging may have the potential to become an adjunct assessment method of disease activity in patients with RA.

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#### FRI0558 FURTHER VALIDATION OF THE US7 SCORE IN A LARGE COHORT OF PATIENTS WITH RHEUMATOID ARTHRITIS WITH DIFFERENT DISEASE STAGES

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**Background:** Musculoskeletal ultrasound (US) is increasingly used in rheumatology clinical practice and research. Standardisation of US scanning techniques and definitions of pathologies is driven forward by the EULAR and OMERACT (Outcome measures in rheumatology) definitions and guidelines. However, no international consensus on a globally accepted US score system on patient level has been achieved so far. The US7 score, first published in 2009, assesses soft tissue lesions (synovitis, tenosynovitis/paratenonitis) as well as bone erosions of 7 preselected joints in one score.<sup>1</sup>

**Objectives:** The aim of this retrospective analysis was to further validate the US7 score by a detailed analysis of affected joint regions in patients with different RA disease stages.

**Methods:** The US7 score<sup>1</sup> examines the most commonly affected joints in RA, including the wrist, MCP2,3, PIP2,3 and MTP2,5 joints, for synovitis and tenosynovitis/paratenonitis and bone erosions from dorsal, palmar, ulnar (wrist), radial (only MCP2) and lateral (only MTP5) by greyscale (GS) and power Doppler (PD) US. In this retrospective analysis, our population of 524 patients with RA was divided into 3 subgroups – 69 patients (13.2%) with very early RA (max. 6 months disease duration), 98 patients with early RA (>6 month, ≤2 years of disease duration), and 343 patients (65.5%) with established RA (>2 years disease duration). Patients were examined at baseline, 3, 6 and 12 months after starting or changing therapy (csDMARD/bDMARD).

**Results:** MCP2 and the wrist (especially from dorsal) were most frequently affected by GS/PDUS synovitis in all groups. PDUS showed a slight tendency towards the dorsal versus the palmar joint side being more often affected in all groups. The group of established RA was more often affected by synovitis, while tenosynovitis/paratenonitis appeared more frequently in very early RA. Significant sensitivity to change within 12 months was detected by GSUS in the group of very early RA in all hand joint regions (for synovitis:  $p < 0.001$  MCP2,3 and wrist;  $p = 0.046$  PIP2;  $p = 0.001$  PIP3) and MTP2 ( $p = 0.024$ ), but not in MTP5 ( $p = 0.313$ ). PDUS demonstrated that the palmar sides of MCP2, PIP2 ( $p < 0.001$  for all) as well as the dorsal sides of MCP2 ( $p = 0.019$ ), MCP3 ( $p = 0.008$ ), PIP2 and 3 ( $p = 0.029$  both), MTP5 ( $p = 0.025$ ) and all wrist sides ( $p < 0.001$ ,  $p = 0.013$ ,  $p = 0.001$ , respectively) responded significantly to therapy, while MCP3, PIP3 palmar and MTP 2 dorsal did not show significant response ( $p = 0.054$ ,  $p = 0.494$ ,  $p = 0.172$ , respectively). In established RA, all joint regions included significantly responded to therapy (PIP2 GS:  $p = 0.004$ , all others  $p \leq 0.001$ ) in GS as well as PDUS.

**Conclusions:** Based on these results, we recommend to include wrist and MCP2 joints in a global US score on the patient level to monitor RA, independent of the disease stage, since they are<sup>1</sup> most commonly affected by synovitis and<sup>2</sup> most responsive to therapy. Tenosynovitis/paratenonitis is frequent in very early RA and should therefore be implemented in an US score monitoring early disease stages.

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#### FRI0559 BIOMECHANICAL PROPERTIES OF RADIAL BONE ARE DIFFERENT BETWEEN AUTO-ANTIBODY POSITIVE AND NEGATIVE RHEUMATOID ARTHRITIS

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**Background:** Functional properties of bone in rheumatoid arthritis (RA) are still not well characterised.

**Objectives:** This study aimed to define the impact of anti-citrullinated antibodies (ACPA) on biomechanical properties in RA.

**Methods:** Based on high-resolution peripheral quantitative computed tomography (HR-pQCT) data from the distal radius of ACPA-positive RA (RA+), ACPA-negative RA (RA-) and healthy controls (HC) micro-finite element analysis (μFEA) was carried out to measure failure load and stiffness of bone. (1) Comparisons of μFEA parameters between groups was calculated and multivariate models were used to determine the role of demographic, disease-specific and structural data of bone strength.

**Results:** A total of 276 subjects (96 RA+, 84 RA- and 96 HC) were analysed. Age and sex distributions were not significantly different between the three groups. In RA +but not in RA- failure load and stiffness were significantly decreased compared to HC (both  $p < 0.001$ ). Lower bone strength affected both female and male RA +patients and was related to longer disease duration. Impaired bone strength was correlated with altered bone density and microstructural parameters, which were all decreased in RA+. Multivariate models showed that ACPA status ( $p = 0.007$ ) and sex ( $p < 0.001$ ) were independently associated with reduced biomechanical properties of bone in RA.

**Conclusions:** In summary, μFEA showed that bone strength is significantly decreased in RA +but not in RA- disease.

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**Disclosure of Interest:** None declared

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#### FRI0560 QUANTITATIVE CT INDEXES IN THE EVALUATION OF INTERSTITIAL LUNG DISEASE RELATED TO RHEUMATOID ARTHRITIS

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**Background:** In rheumatoid arthritis (RA), interstitial lung disease (ILD) is the most common pulmonary complication and it is associated with poor prognosis.

The gold standard to detect ILD is the chest Computed Tomography (CT). CT semiquantitative scoring and quantitative methods are used to estimate the extension of ILD; however the first ones are time consuming and they have a considerable inter/intra-observer variability. Quantitative scores are based on the detection of the parameters of distribution of lung attenuation (also called quantitative CT indexes – QCTi).

Previously a good correlation between QCTi calculated through an open-source program (OsiriX) and semi-quantitative score performed by experienced radiologists was demonstrated in a cohort of systemic sclerosis (SSc) patients. Furthermore, the QCTi were demonstrated to be able to discriminate between SSc subjects with different mortality risk based on ILD extent (<20% vs >20%) or lung functional values.

**Objectives:** Main aim is to investigate if in RA-ILD there is a correlation between QCTi and semiquantitative scores. Secondary aims are: a) to verify if there is a difference of QCTi distribution in RA-ILD patients with severe vs mild ILD extent; b) to evaluate the discriminative ability of QCTi in identifying patients with severe ILD.

**Methods:** Two experienced radiologists assessed the ILD on chest CT of 45 patients with RA according to the semiquantitative score proposed by Goh et al. ILD extent <and >20% were considered mild and severe, respectively.

All CTs were blindly processed by a rheumatologist using OsiriX to obtain the QCTi (kurtosis, skewness, mean lung attenuation).

The semiquantitative scores and the QCTi were correlated through the Spearman rank test. QCTi distribution and discriminative ability were, respectively, verified using Mann-Whitney test and ROC curves.

**Results:** The majority of QCTi showed a statistically significant correlation of moderate degree ( $0.40 < r < 0.59$ ) with the semiquantitative assessment ( $p$ -value  $< 0.01$ ).

Patients with severe and mild ILD had dissimilar QCTi values ( $p < 0.001$ ). Among QCTi, kurtosis (tKurt) had the best discriminative ability (AUC=0.80, 95% CI 0.65 to 0.91,  $p < 0.0001$ ). The best tKurt cut-off value that identifies patients with severe pulmonary involvement was 3.67.

**Conclusions:** In RA-ILD, QCTi correlate with the CT semiquantitative scores. Our preliminary findings suggest that RA-ILD severity is related to QCTi. Moreover a QCTi (tKurt) has a cut-off that can discriminate patients with severe ILD. So, QCTi may become simple tools to help the rheumatologist to quickly evaluate the severity of ILD in RA patients and estimate the prognosis.

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#### FRI0561 MACROPHAGE PET IMAGING FOR PREDICTING TREATMENT OUTCOME OF DE NOVO RHEUMATOID ARTHRITIS

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**Background:** Treatment of rheumatoid arthritis (RA) should be initiated as early as possible to prevent further damage and functional disability.<sup>1</sup> However, clinical assessment of treatment response usually takes 12 weeks or longer. Tools that detect earlier response can improve timely treatment decision. Previously, positron emission tomography (PET) using the macrophage tracer [11C]-(R)-PK11195 has shown promise for both early diagnosis and monitoring response to therapy in RA patients.<sup>2,3</sup>

**Objectives:** To determine the value of [11C]-(R)-PK11195 PET to identify RA responders and non-responders to COBRA-light therapy after 2 weeks of treatment.

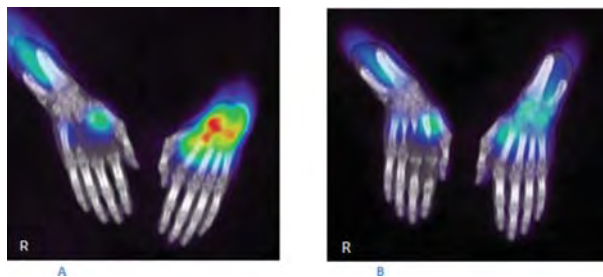
**Methods:** Twenty RA patients (female 10/20, age 54±10 years) with clinically active *de novo* RA based on ACR/EULAR criteria<sup>4</sup> and at least two clinically active joints were included. All patients were given COBRA-light therapy (methotrexate and prednisolone). They received standard clinical care and (clinical) evaluations were performed at 0, 2, 4 and 12 weeks of treatment. Whole body [11C]-(R)-PK11195 PET-CT scans were acquired at baseline and after 2 weeks of treatment. An experienced reader blinded to clinical data scored the 44 joints of the Disease Activity Score (DAS44) visually from 0 to 3. PET response was predefined as either positive if there was a decrease in whole body PET score of  $\geq 10\%$  after two weeks, or as negative if the score increased or remained unchanged. PET outcome was compared with EULAR clinical response at 12 weeks.<sup>5</sup>

**Results:** After 12 weeks of COBRA-light treatment, 16 out of the 20 patients were classified as EULAR responders (13 'good' and 3 'moderate') and 4 patients as non-responders. At baseline, a total of 134 PET positive lesions were observed in the joints of 20 patients, ranging from 1 to 21 lesions per patient. Most frequently, lesions were located in hands and feet: 19% in the wrists (e.g. figure 1A), 37% in the small hand joints and 39% in the small feet joints. After 2 weeks of COBRA light treatment, the number of PET positive lesions decreased to 122 (e.g. figure 1B).

A positive whole body PET response was observed in 13 patients. Table 1 shows a side by side comparison between PET response after 2 weeks and EULAR response after 12 weeks. In 15 of the cases (75%), there was an agreement between the PET response and EULAR response.

		EULAR response at 12 weeks	
		Positive	Negative
PET response at 2 weeks	Positive	12	1
	Negative	4	3

**Abstract FRI0561 – Table 1.** Correspondence between early PET response and clinical EULAR response.



**Abstract FRI0561 – Figure 1**

**Conclusions:** This is the first study to explore the potential of macrophage PET for monitoring therapy in early RA. Preliminary visual assessment demonstrates its ability to monitor arthritis activity changes within 2 weeks of treatment. This offers a window of opportunity for development of precision medicine in the early phase of treatment. Future analyses are in progress to assess whether performance can be further improved by quantification of tracer uptake.

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#### FRI0562 ASSOCIATION BETWEEN JOINT REGIONS WITH ULTRASOUND-DETERMINED SYNOVITIS AND SYSTEMIC INFLAMMATORY MARKERS

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**Background:** It is unknown which joint arthritis the inflammatory markers such as CRP or MMP-3 reflect.

**Objectives:** We analysed the association between joint regions with ultrasound-determined synovitis and systemic inflammatory markers.

**Methods:** We enrolled 152 patients with untreated arthritis and performed musculoskeletal ultrasound on 40 joints and determined a semiquantitative grade for power Doppler (PD) signals. We analysed the associations between PD scores in 8 joint regions and CRP/MMP-3 levels using multiple linear regression models with forced entry method.

**Results:** Mean age was 55 years and 112 patients were female. Median CRP and MMP-3 were 0.36 mg/dl and 65.7 ng/ml. Median total PD score was 2. Standard regression coefficients for 8 joint regions were  $-0.009$  for MCPs,  $0.05$  for PIPs,  $0.372$  for wrists,  $0.183$  for elbows,  $0.628$  for shoulders,  $0.377$  for knees,  $0.261$  for ankles, and  $-0.0131$  for MTPs in a regression model to explain CRP using PD scores as dependent variables. Standard regression coefficients for the same joint regions were  $-5.134$ ,  $-4.449$ ,  $24.061$ ,  $27.839$ ,  $22.508$ ,  $64.108$ ,  $36.501$ , and  $2.539$  to explain MMP-3.

**Conclusions:** Systemic inflammatory markers such as CRP and MMP-3 do not accurately reflect the inflammation in small joints. Conversely, it is necessary to weight the large joints for the global ultrasound synovitis score to represent the severity of systemic inflammation.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.5340

**FRI0563 MUSCULOSKELETAL ULTRASOUND (MSUS) IS SUPERIOR TO CLINICAL EXAMINATION REGARDING DETECTION OF ARTHRITIS IN PATIENTS WITH SYSTEMIC SCLEROSIS**

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**Background:** Arthralgia is a frequent complaint in patients with systemic sclerosis (SSc). However, correct assessment of arthritis remains challenging especially in patients with severe scleroderma and/or soft tissue oedema.

**Objectives:** This study investigates the frequency of arthritis in SSc using musculoskeletal ultrasound (MSUS) compared to clinical investigation and in SSc.

**Methods:** Effusion, as well as synovitis in B- and PD-mode using MSUS was assessed in 31 consecutive patients with SSc; hand, finger, upper and lower ankle joints as well as metatarsophalangeal (MTP) joints were scanned totaling 1364 joints. In all patients carotid intima media thickness (CIMT) was assessed by Doppler ultrasound. Arthritis disease activity was assessed by the HAQ, and the DAS66/68, respectively; joint pain and patient global health (PGH) were quantified on a visual analogue scale (VAS). Skin involvement was measured using the modified Rodnan Skin Score (mRSS). CRF such as smoking, hypertension or positive family history were registered

**Results:** All patients were negative for ACPA and rheumatoid factors. 58.06% (n=18) of patients had joint pain, 22.58% (n=7) clinical joint swelling. In MSUS, 82 joints with effusion were detected in 23 patients (I°: n=50 joints, II°: n=32 joints). 25 joints in 11 patients were detected by B-mode synovitis (I°: 9 joints, II°: 16 joints). 7 joints in 3 patients showed PD-synovitis (I°: 2 joints, II°: 5 joints). In 10 patients MSUS could detect effusion where clinical examination could not; none of the clinically suspicious joints had effusion in MSUS. B-mode synovitis was detected in 3 clinically normal patients, in 6 patients with joint pain, and in 3 patients with joint pain and swelling. 1 patient with PD-synovitis each had TJC-/SJC-, TJC+/SJC+, or TJC+/SJC- at clinical examination. The overall correlation of MSUS with clinical examination was poor (p>0.05). B-mode synovitis and PD-mode synovitis prevailed the MTPs (60%, n=15% and 85.71%, n=6, respectively). For median nerves, a cutoff area of >13 mm<sup>2</sup> was deemed pathologic, >11 mm<sup>2</sup> and <13 mm<sup>2</sup> was intermediate. 11/31 patients had either pathologic or intermediate median nerves. Doppler ultrasound found 10 pathological CIMT in 8 individual patients; carotid plaques were detected in 25 carotid arteries in 20 patients. Patients with CIMT and/or carotid plaques were elderly (60.52 years±10.84), long term sick (156.48±123.19 months), and had at least one cardiovascular risk factor.

**Conclusions:** In patients with arthralgia MSUS could detect clinically not obvious arthritis. Especially in joints with soft tissue oedema and sclerotic skin MSUS was superior to clinical examination. Interestingly, arthritis was most frequently found in the MTP and wrist joints supporting recent data.<sup>1</sup> In this small cohort there was no significant correlation between CRP positivity and arthritis. Not surprisingly, carotid plaques were more frequent in elderly and/or long-term patients with one or more CRF. We plan to pursue this investigation in a larger cohort.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.7499

**FRI0564 ULTRASONOGRAPHIC EVALUATION OF SHOULDER TENDONS IN PATIENTS WITH HASHIMOTO'S DISEASE**

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**Background:** Hashimoto's disease is an autoimmune disease characterised by autoantibody positivity in the blood and diffuse lymphocyte infiltration in the thyroid. Thyroxine is an important hormone in collagen and matrix metabolism. Low levels

of thyroid hormones or antibodies positivity may lead to tendon pathologies and subsequent shoulder pain in patients with Hashimoto's disease.

**Objectives:** 1) To investigate tendon thickness and pathologies in patients with Hashimoto's disease. 2) To investigate if shoulder pain in Hashimoto's disease is associated with ultrasonographic tendon pathologies.

**Methods:** Assuming a 0.5 mm mean difference and 0.7 mm SD of thickness at rotator cuff tendons with 80% power and 5% significance 119 female subjects (40 patients euthyroid Hashimoto's disease, 28 subclinical hypothyroid Hashimoto's disease and 51 healthy subjects) were recruited.<sup>1</sup> Participants were divided into three groups: Group 1: patients with subclinical hypothyroid Hashimoto's disease, Group 2: patients with euthyroid Hashimoto's disease, Group 3: healthy controls. A rheumatologist experienced in musculoskeletal ultrasonography and blind to clinical data of the patients evaluated the thickness of biceps, subscapularis, supraspinatus, infraspinatus tendons at both shoulders according to standard protocol.<sup>2</sup> The presence of subacromial bursitis, effusion, tendon rupture or tendinosis were recorded. The participants of TSH (thyroid stimulated hormone), free T3 (triiodothyronine), free T4 (thyroxine), anti TPO (thyroid peroxidase) and anti TG (thyroglobulin) antibodies levels were measured. In addition the presence and duration of shoulder pain of the participants were recorded.

**Results:** Height, weight, BMI (body mass index), free T3 and free T4 levels were similar between three groups (p=0.830, p=0.205, p=0.374, p=0.430 and p=0.497, respectively). Tendon thicknesses in patient groups are presented in table 1. Biceps brachii, subscapularis, supraspinatus and infraspinatus tendon thicknesses were increased significantly in both euthyroid Hashimoto's disease and subclinical hypothyroid Hashimoto's disease groups at dominant and non-dominant arms compared to healthy controls. However there was no such difference between euthyroid Hashimoto's disease and subclinical hypothyroid Hashimoto's disease groups. There was no correlation between levels of TSH, anti TPO, anti TG and tendon thickness. Two participants in three groups had shoulder pain for 1–3 months. These participants had no ultrasonographic shoulder tendon pathology.

**Abstract FRI0564 – Table 1.** Differences between euthyroid Hashimoto's disease, subclinical hypothyroid Hashimoto's disease and healthy controls in dominant and non-dominant arms.

	Group 1 (n=28)	Group 2 (n=40)	Group 3 (n=51)	P value	p value*	p value**	p value***
<b>Dominant arm</b>							
Biceps brachii	2.39±0.63	2.64±0.65	2.24±0.43	0.007	0.798	0.004	0.819
Subscapularis	4.09±0.89	3.96±0.64	3.66±0.52	0.017	0.397	0.021	0.818
Supraspinatus	4.90±0.80	4.96±0.99	4.50±0.72	0.034	0.410	0.032	0.828
Infraspinatus	1.96±0.81	2.16±0.84	1.52±0.28	0.000	0.847	0.000	0.020
Acromioclavicular distance	10.57±1.09	10.25±1.40	10.41±1.28	0.419	0.176	0.592	0.436
<b>Non-dominant arm</b>							
Biceps brachii	2.59±0.61	2.48±0.50	2.24±0.43	0.030	0.798	0.020	0.040
Subscapularis	4.21±0.92	4.06±0.68	3.74±0.50	0.018	0.516	0.023	0.016
Supraspinatus	4.80±0.73	4.84±0.92	4.44±0.75	0.022	0.793	0.025	0.017
Infraspinatus	2.07±0.95	2.05±0.81	1.55±0.31	0.001	0.476	0.000	0.043
Acromioclavicular distance	10.53±1.03	10.21±1.29	10.25±1.33	0.363	0.162	0.990	0.224

Data are presented as the mean ± standard deviation. All data are presented in millimeters. P<0.05. Group 1: subclinical hypothyroid Hashimoto's disease; Group 2: euthyroid Hashimoto's disease; Group 3: Healthy controls

p value\* difference between patients with euthyroid Hashimoto's disease and subclinical hypothyroid Hashimoto's disease

p value\*\* difference between patients with euthyroid Hashimoto's disease and healthy controls

p value\*\*\* difference between patients with subclinical hypothyroid Hashimoto's disease and healthy controls

**Conclusions:** Presence of autoimmune thyroid disease may lead to increased shoulder tendon thickness. However increase in tendon thickness is not seemed to be associated with shoulder pain.

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**FRI0565** **ERAMRS: A NEW MR SCORING SYSTEM FOR EARLY RHEUMATOID ARTHRITIS**

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**Background:** Early rheumatoid arthritis (ERA) is defined as having symptoms for less than 24 months and MRI allows quantification of several inflammatory features of ERA. Due to inclusion of some less relevant MR features and non-inclusion of other more relevant features, three MRI scoring systems currently employed are not ideally suited for use in ERA. We therefore devised a new more inclusive system suited for ERA, known as the ERA MR score ('ERAMRS'). The clinical relevance of this new ERAMRS system over the other MR scoring systems can be gauged by seeing how well these MR scoring systems correlate with clinical scoring systems.

**Objectives:** To (a) introduce a new scoring system (ERAMRS) for measuring the degree of inflammation on MR in early rheumatoid arthritis (RA) and (b) to see how well this ERAMRS system correlates with clinical scoring systems and serological parameters compared to currently used MR scoring systems.

**Methods:** 106 patients (81 females, 25 males, age, 53±12 years) with early (i.e. symptoms<24 months) untreated RA underwent clinical/serological testing as well as 3T MRI of the most symptomatic wrist. Clinical assessment included Patient Global Assessment (PtGA), Physician Global Assessment (PGA) and Simple Disease Activity Index (SDAI). Erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) were also measured. ERAMRS (Early Rheumatoid Arthritis Magnetic Resonance Score) was semi-quantitatively assesses wrist joints synovitis (no=0, mild=1, moderate=2, severe=3) and enhancement (no=0, mild=1, moderate=2, severe=3), tenosynovitis (no=0, mild=1, moderate=2, severe=3) and enhancement (no=0, mild=1, moderate=2, severe=3) as well as bone marrow oedema (no=0,<50% of the whole bone=1,>50% of the whole bone=2). Seven wrist joints, nine wrist tendons as well as 15 wrist bones were assessed. This ERAMRS method was compared to currently used methods of scoring inflammation on wrist MRI ('RAMRIS' [1], 'McQueen' [2] and 'MRI detected inflammation score' [3]).

**Results:** Synovitis was present in 104 (98%), bone marrow oedema in 77 (73%), and tenosynovitis in 82 (77%) of the 106 wrists at presentation. RAMRIS system had the lowest correlation (PtGA, PGA, SDAI, CRP) or no correlation (ESR) while the ERAMRS system had the highest correlation with clinical disease activity level scoring systems ( $r=0.44$ ,  $p<0.001$ ) and serological parameters ( $r=0.41$ ,  $p<0.001$ ) among these four scoring systems.

**Conclusions:** The ERAMRS system, designed to grade inflammation on wrist MRI in early RA, provided the best correlation with clinical scoring systems and serological parameters indicating its improved clinical relevance over other MR scoring systems.

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**Disclosure of Interest:** None declared

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**FRI0566** **OEDEMA-FIBROSIS IN SYSTEMIC SCLEROSIS: COMPARISON OF A PARAMETRIC CARDIOVASCULAR MAGNETIC RESONANCE MODEL TO THE LAKE LOUISE CRITERIA**

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**Background:** Myocardial disease is a major cause of death in systemic sclerosis (SSc). We hypothesised that the in SSc patients with suspected myocarditis, the Lake Louise criteria underdiagnose myocarditis compared to diagnostic models that incorporate parametric cardiovascular magnetic resonance (CMR) indices (extracellular volume fraction [ECV], native T1- and T2-mapping).

**Methods:** 32 patients with diffuse SSc (dSSc) and a clinical suspicion of myocarditis were prospectively evaluated with a 1.5 T scanner using the Lake Louise criteria, and the aforementioned parametric indices were determined. The Lake Louise criteria were compared with parametric indices individually and in two models (with and without taking late gadolinium enhancement [LGE] into account), with regard to diagnostic agreement.

**Results:** Native T1-mapping and ECV individually had the greatest discordance with the Lake Louise criteria. The presence or absence of LGE in the proposed parametric models did not lead to changes in identified patient proportions. Native T1-mapping led to the same proportion of diagnosis of myocarditis as either parametric model, with the exception of 2 patients. Most importantly, patients identified only by parametric models, had a significantly subtler presentation than those identified by the Lake Louise criteria, as exemplified by significantly lower T2 ratio, early gadolinium enhancement and T2-mapping values.

**Conclusions:** In dcSSc patients with a clinical suspicion of myocarditis, novel parametric models including native T1-mapping, T2-mapping and ECV, identified a significantly greater proportion of patients with myocarditis compared to those identified by the Lake Louise criteria, and native T1 mapping had the greatest utility in this cohort.

**Disclosure of Interest:** None declared

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**FRI0567** **THE DIAGNOSTIC VALUE OF AUTOANTIBODY ISOTYPES IN RHEUMATOID ARTHRITIS**

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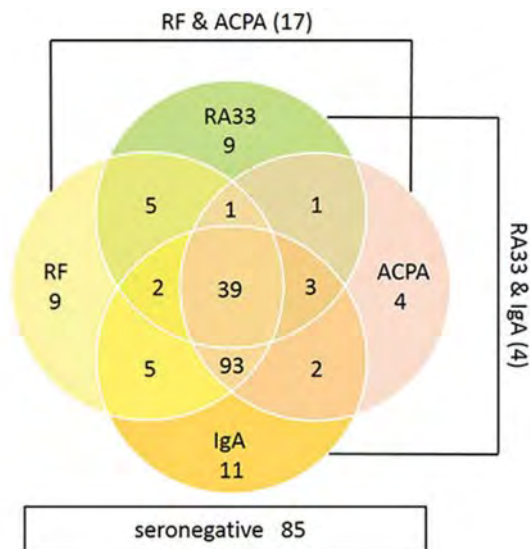
**Background:** Anti-citrullinated protein antibodies (ACPA) and rheumatoid factor (RF) are the most specific diagnostic markers of rheumatoid arthritis (RA). These antibodies are predominantly of the IgG (ACPA) or IgM (RF) isotype. Other subtypes of both antibodies – such as IgA – and other autoantibodies like RA33 have been repeatedly reported but their diagnostic value has still not been fully elucidated.

**Objectives:** To investigate the diagnostic value of IgA, IgG and IgM subtypes of RF, ACPA and RA33 antibodies in patients with RA and their potential predictive value regarding therapeutic response to methotrexate (MTX).

**Methods:** To determine the diagnostic specificity and sensitivity, sera from 290 RA patients (including 165 MTX starter), 261 disease controls and 100 healthy subjects were tested for the presence of IgA, IgG and IgM isotypes of RF, ACPA and RA33 by EliA<sup>TM</sup> (Thermo Fisher Scientific). Cut-offs for prototype anti-RA33 (IgA, IgG and IgM) and the IgM-ACPA EliA<sup>TM</sup> were calculated by Receiver Operating Characteristic (ROC) curve analysis against disease controls and healthy subjects. In addition, RF and ACPA had been routinely measured by nephelometry and the anti-CCP EliA<sup>TM</sup>, respectively.

**Results:** The most specific antibodies were IgG and IgA-ACPA as well as IgG-RF, closely followed by IgG- and IgA-RA33 while IgM isotypes were found to be less specific. However, IgM-RF was the most sensitive isotype (65%) followed by IgG-ACPA (59.5%) and IgA-RF (50.7%). Other subtypes were less prevalent ranging from 35% (IgA-ACPA) to 6% (IgA-RA33). Concerning RA33 antibodies, 14 patients were positive for IgA- and 18 for IgG-RA33. Interestingly, the major RA33 subtype was IgM which was detected in 43 patients. However, in contrast to RF and ACPA the overlap between the RA33 isotypes was marginal. RA33 antibodies as well as IgA-RF and IgA-ACPA were found to increase the diagnostic sensitivity of serological testing since they were found also in 22% of seronegative patients. Moreover, analysing IgM-RF by EliA<sup>TM</sup> proved more sensitive than RF measured by nephelometry which further reduced the number of seronegative patients. Thus, additional antibodies were detected in 30% of the seronegative population and, importantly, most patients had several antibodies, in contrast to disease controls which generally showed only one antibody species. The majority of antibody positive RA patients was found to be triple positive for RF, ACPA and either IgA-RF or IgA-ACPA. Among the 64 RA33 positive patients 48 were also positive for IgA-RF and/or IgA-ACPA (figure 1).

Interestingly, we found high levels of IgM-RF (>124 IU/ml) to be associated with achieving a SDAI50 response to MTX (17 of 24 cases). Furthermore, also the presence of RA33 antibodies was associated with a MTX response as 50% of RA33 positive patients (n=32) achieved a SDAI50 response compared to 34% in the RA33 negative population (p=0.034).



**Abstract FRI0567 – Figure 1.** Added diagnostic value of IgA-RF/ACPA and RA33 antibodies. Venn chart visualising the diagnostic overlap of RA33 and IgA antibodies with routine diagnostics (RF nephelometry, IgG-ACPA). The numbers of seronegative patients (n=85), RF and IgG-ACPA positive but RA33 and IgA-RF/ACPA negative patients (n=17) as well as patients positive for both RA33 and IgA-RF/ACPA but negative for RF and ACPA (n=4) are also indicated.

**Conclusions:** Thus, increasing the number of antibodies in serological routine testing would provide valuable additional information allowing to better distinguish between RA and other rheumatic disorders also in patients negative in current routine diagnostics and may provide valuable additional information regarding the prediction of treatment responses.

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## FRI0568 MR – ENTEROGRAPHY FINDINGS OF INTESTINAL INFLAMMATION IN SPONDYLOARTHRITIS WITH HIGH FAECAL CALPROTECTIN LEVELS

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**Background:** Intestinal inflammation is seen in half of patients with spondyloarthritis (SpA), and can be detected by faecal calprotectin (Fcal)<sup>1</sup>. Small bowel inflammation is detected by MR Enterography (MRE), accurately<sup>2</sup>.

**Objectives:** Definition of MRE changes in SpA patients with high Fcal levels.

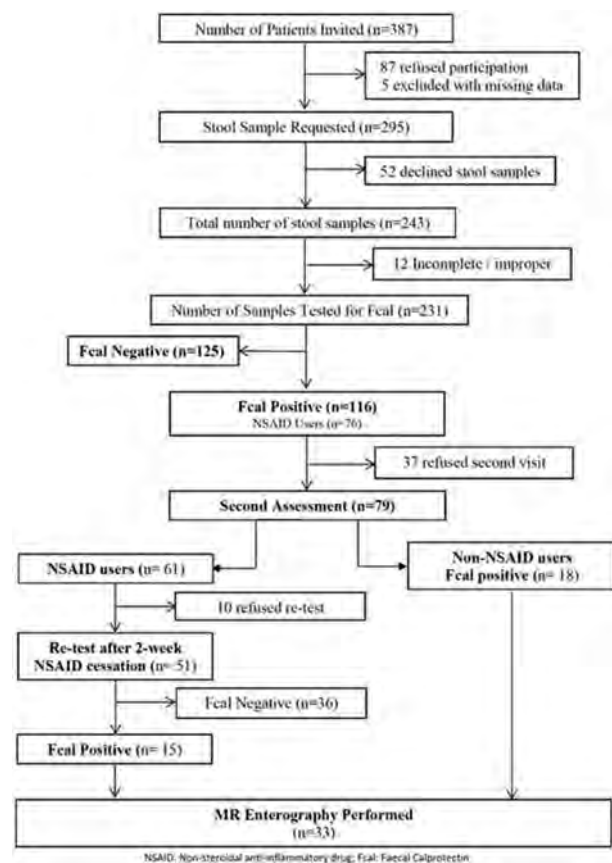
**Methods:** A total of 231 SpA patients, 50 healthy subjects and 50 inflammatory bowel disease (IBD) patients were included. Stool specimens were obtained and data on BASDAI scores, abdominal pain, diarrhoea, NSAID and TNF inhibitor usage were noted. Fcal was measured by IDK ELISA 2 weeks after the cessation of NSAID. MREs were obtained in Fcal >50 µg/g SpA patients. Contrast enhanced MRE was performed using 3 Tesla MRI device after 6 hours of fasting.

**Results:** Demographic and clinical characteristics are summarised in table 1 and flow diagram (figure 1). Median Fcal of SpA patients was higher than healthy controls and lower than IBD patients. Fcal levels were high in 15 (33.3%) of 45 healthy cases and all but two of them were NSAID users. The Fcal test was high in 45.9% (n=106) of SpA patients. There was no correlation between BASDAI index and Fcal results (r=0,08 p=0,42). Mean Fcal levels of active and in remission patients were 78.2±20 and 77.8±7.02 µg/g respectively (p=0.97). Fifty-two of the Fcal-high SpA patients were retested after cessation of NSAIDs for 14 days. In 15 patients Fcal levels remained elevated. MRE was performed 33 SpA patients with high Fcal levels. MRE findings were observed in 29 of 33 (87%) patients. Four out of 33 (%12,1) MRE imaging was totally normal. Patients with MRE findings had higher median Fcal levels than those with normal MRE imaging (98 vs. 52 µg/g p=0.002). All patients had increased mesenteric fat density and presence of mesenteric lymph nodes. Increased mesenteric vascularity (28/29), increased bowel wall enhancement (23/29) and thickness (18/29) were frequently detected.

Approximately one-third of the patients had a luminal stricture (13/29) and loss of haustration (12/13).

**Abstract FRI0568 – Table 1.** Demographic and clinical characteristics

	SpA (n=231)	Healthy Controls (n=45)	IBD (n=50)	P Value (SpA vs Healthy Controls)
Age (Mean±SD)	45.2±9.8	43.4±14.9	39.9 ±13.1	p=0.33
Gender (Female/Male)	117/114	27/18	18/32	p=0.25
NSAID Users (%)	%54.8	%53.3	%0	p=0.85
NSAID dose/2 wks	8.8±8.3	10,6±8.3	0	p=0.37
Anti-TNF users (%)	%53.0	%0	%36.0	
BASDAI (Mean±SD)	2,58 ±2,16			
BASDAI≥4 (n/%)	60/194 (%26)			
Fcal (Median, Min-Max)	45.4 (0– 830)	34.7 (2–324)	69.5 (0– 840)	p=0.004
Fcal high (>50 µg/g) (%)	%45.9 (n=106)	%33.3 (n=15)	%58.0 (n=29)	p=0.12
Fcal of NSAID Users (Median, Min-Max)	63 (0– 830)	54 (2–324)		p=0.30
Fcal of non-NSAID Users (Median, Min-Max)	27 (0– 507)	16 (2–72)		p=0.06



**Conclusions:** In SpA patients with high Fcal levels MRE detected inflammation of mucosal as well as serosal surfaces, as in early CD.

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FRI0569

### TO WHAT EXTENT IS INTEROBSERVER RELIABILITY FOR DETECTING ULTRASOUND URATE CRYSTAL DEPOSITS DEPENDENT ON THE EXPERIENCE OF THE ULTRASONOGRAPHER?

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**Background:** Musculoskeletal (MS) ultrasound (US) is used for diagnosing and managing gout in clinical practice and has the potential to become an outcome measure for clinical trials. Cartilage double contour sign (DC) and tophi(T) are elementary US lesions of urate crystal deposits. OMERACT MSUS Working Group developed the first consensus-based definitions for DC and T and showed that the reliability of the definitions ranged from moderate to excellent in static images and somewhat lower in patients when tested in highly experienced MS ultrasonographers.<sup>1</sup>

**Objectives:** To compare the agreement between a group of rheumatologist-ultrasonographers (RU) with a variable experience in MSUS with the agreement between rheumatologist-ultrasonographers highly experienced in MSUS and teachers (ExRU) for detecting DC and T in in patients.

**Methods:** 16 RU with a variable experience in MSUS were trained in the OMERACT U definitions for DC and T. Next, as a preliminary reliability exercise, they read 30 different US joint static images from gout patients and healthy subjects for the presence or absence of DC or T. Afterwards the RU group and a group of 5 ExRU consecutively, independently and blindly carried out each a reliability exercise in 5 subjects (3 crystal proven gout patients and 2 healthy controls) for the presence or absence of DC or T. Both groups performed a standardised 8 min bilateral grey-scale UU examination of the following: the suprapatellar knee recess for T, femoral knee cartilage for DC, medial and lateral knee compartments for T and dorsal first metatarsal phalangeal for T and metatarsal head for DC. Fleiss kappa was used to assess interobserver reliability. K values 0–0.20 were considered poor; 0.20–0.40 fair; 0.40–0.60 moderate; 0.60–0.80 good and 0.80–1 excellent.

**Results:** Kappa values were moderate for the RU group inter-reader agreement in static US images (K 0.514 for DC and 0.465 for T). However, there were significant differences between the interobserver agreement from both groups in patients, being kappa values fair (K 0.344 for DC and 0.305 for T) for the RU group while good for the ExRU group (K 0.674 for DC and 0.673 for T) ( $p < 0.001$  for DC and T). Worst agreement among RU and ExRU was for detecting DC in MTF joint.

	RU <sup>16</sup>			ExRU <sup>5</sup>			p
	kappa	Lower 95% CI	Upper 95% CI	kappa	Lower 95% CI	Upper 95% CI	
Tophi (T)	0.305	0.275	0.336	0.673	0.575	0.771	<0.001
Double contour (DC)	0.344	0.301	0.387	0.674	0.535	0.812	<0.001

CI, confidence interval

**Conclusions:** This study showed that although inter-reader agreement for gout lesions can be acceptable in static US images, interobserver agreement in patients is highly dependent on the experience of the ultrasonographers.

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FRI0570

### SERUM KL-6 LEVEL REFLECTS SEVERITY OF INTERSTITIAL LUNG DISEASE ASSOCIATED WITH CONNECTIVE TISSUE DISEASE

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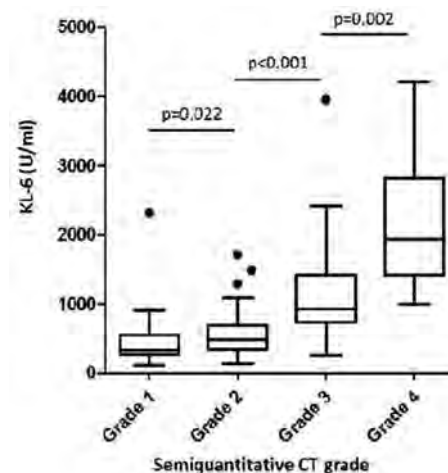
**Background:** Measuring severity of interstitial lung disease (ILD) usually depends on the extent or pattern of imaging findings on computed tomography

(CT) and the parameters of pulmonary function test. Krebs von den Lungen 6 (KL-6) is a sialylated glycoprotein mainly expressed on the surface membrane of type II pneumocytes and bronchiolar epithelial cells. Serum level of KL-6 had been reported to be associated with presence or outcome of ILD associated with connective tissue diseases (CTD-ILD).

**Objectives:** We aimed to evaluate KL-6 as a potential biomarker reflecting severity of CTD-ILD.

**Methods:** Study population was a retrospective cohort of 549 Korean patients with rheumatoid arthritis (RA), systemic sclerosis (SSc), inflammatory myositis (IM), Sjogren's syndrome (SS), and systemic lupus erythematosus (SLE) who had concurrent ILD or not. Serum concentration of KL-6 (U/mL) was measured by Nanopia KL-6 assay (SEKISUI MEDICAL, Tokyo), using latex enhanced immunoturbidimetric assay method. Semi-quantitative grade of ILD extent (grade 1: 0%–25%, grade 2: 26%–50%, grade 3: 51%–75%, grade 4: 76%–100%) was evaluated by CT scan. To suggest cutoff value of KL-6 level to differentiate each semi-quantitative grade, receiver operating characteristic curves were drawn. Student t-test and Pearson's coefficient (PC) were applied to evaluate the correlation of KL-6 level and severity of ILD.

**Results:** The patients with CTD-ILD (n=165) had elevated serum level of KL-6 compared to CTD without ILD (n=384) (mean  $\pm$ SD, 741.0 $\pm$ 724.3 vs 236.1 $\pm$ 157.0 U/mL,  $p < 0.001$ ). In subgroup analysis, RA (563.9 $\pm$ 627.0 vs 231.3 $\pm$ 188.5,  $p < 0.001$ ), SSc (766.4 $\pm$ 754.6 vs 224.0 $\pm$ 120.3,  $p = 0.002$ ), IM (808.1 $\pm$ 746.9 vs 291.4 $\pm$ 238.6,  $p < 0.001$ ), and SS or SLE (884.9 $\pm$ 762.3 vs 225.7 $\pm$ 107.0,  $p < 0.001$ ) also had significant difference according to the presence of ILD. Semi-quantitative grade of ILD in CT scan was significantly proportional to KL-6 level among consecutive grade (figure 1). The optimal cutoff values to differentiate each semi-quantitative grade were 684.3 U/ml (grade  $\geq 2$ ; sensitivity 58.3%, specificity 91.8%), 689.7 U/ml (grade  $\geq 3$ ; 86.7%, 86.0%, respectively), and 958.3 U/ml (grade 4; 100%, 84.0%, respectively). Percent diffusion capacity for carbon monoxide (DLCO%) and forced vital capacity (FVC%) had negative correlation with KL-6 level (PC = -0.587,  $p < 0.001$ ; PC = -0.399,  $p < 0.001$ , respectively).



**Abstract FRI0570 – Figure 1.** Serum level of KL-6 of the ILD patients stratified by semiquantitative CT grade.

**Conclusions:** Serum levels of KL-6 were increased in CTD-ILD and had good correlation with CT grade, FVC, and DLCO. Higher serum level of KL-6 may reflect severity of CTD-ILD.

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FRI0571

### ADDITIONAL SCREENING FOR LOW THORACIC BONE MINERAL DENSITY IN PATIENTS REFERRED FOR CARDIAC CT – A DANISH, MULTI-CENTRE, AND CROSS-SECTIONAL STUDY

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**Background:** Quantitative computed tomography (QCT) can precisely and with high reproducibility measure spine bone mineral density (BMD) using cardiac computed tomography (CT) scans.<sup>1</sup> Standard for diagnosing osteoporosis is a dual-energy X-ray absorptiometry (DXA) scan.<sup>2</sup> Despite DXA being fast and with low radiation, many patients with osteoporosis goes undiagnosed.<sup>3</sup>

**Objectives:** The aim was to characterise the bone mineral density (BMD) status in a group of patients with low to intermediate risk of coronary artery disease (CAD).

**Methods:** This study is a retrospective, cross-sectional study analysing prospectively acquired data from the Dan-NiCAD study. Participants were patients with symptoms suggestive of CAD referred for a cardiac CT between 2014–09 and 2016–03. Patient data were collected from interviews. BMD was measured in 3 vertebrae starting from the left main coronary artery using QCT. We used the American college of radiology cut-off values for lumbar spine QCT to categorise patients into very low (<80 mg/cm<sup>3</sup>), low (80–120 mg/cm<sup>3</sup>), or normal BMD (>120 mg/cm<sup>3</sup>).

**Results:** Analyses included 1487 patients. Mean age was 57 years (range 40–80), 52% were women. The total number of patients with very low BMD was 179 (12%) (105 women, 74 men). The majority of patients with very low BMD was not previously diagnosed with osteoporosis (87%) and received no anti-osteoporotic treatment (90%). Compared to patients with normal BMD, individuals with very low BMD had more risk factors for osteoporosis such as higher age (p<0.001), predisposition to osteoporosis (p<0.001), and were more often former smokers (p<0.01).

**Conclusions:** Very low BMD seems present in a significant proportion of men and women, a majority of which were not diagnosed with osteoporosis or receiving anti-osteoporotic medication. Patients with very low BMD had more osteoporotic risk factors compared to patients with normal BMD. Additional screening for osteoporosis can potentially prevent osteoporotic fractures. However, thoracic spine QCT is a new method without diagnostic cut-off values and prospective studies regarding fracture risk prevention are missing.

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FRI0572

### PREVALENCE OF ECHOCARDIOGRAPHIC FINDINGS IN CONNECTIVE TISSUE DISEASES – A RETROSPECTIVE COHORT STUDY

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**Background:** Echocardiography is routinely performed in patients with connective tissue diseases (CTD), mostly to evaluate cardiac involvement or development of pulmonary arterial hypertension (paH). Despite its frequent application there is incomplete data for the range and frequency of findings.

**Objectives:** 1) To study the frequency of echocardiographic findings in routinely examined patients with different CTD. 2) To report which findings were associated

with a history of inflammatory cardiac involvement. 3) To analyse whether findings changed over time in patients with several examinations.

**Methods:** Retrospective chart review of all consecutive patients from a tertiary rheumatological referral centre with CTD diagnosis and echocardiographic examination between 01/01/2006 and 31/12/2015. For each echocardiographic finding, the proportion of patients per diagnosis with a pathological result in at least one examination was calculated. Each finding's frequency was compared between patients with and without previously documented inflammatory cardiac involvement; p<0.05 in Fisher's exact test was considered significant. For patients with more than one visit, we recorded how often findings developed or resolved between two consecutive examinations.

**Results:** 1004 patients with different CTD and a total of 1660 performed echocardiographies were analysed. Table 1 displays the frequency of findings in the whole cohort and for each CTD. The following findings were significantly more common in patients with known inflammatory cardiac involvement (n=109) than in those without (n=896): regurgitation of tricuspid valve (45.0% (n=49) of patients with cardiac involvement vs. 23.2% (n=206) of patients without, p<0.001) and of pulmonary valve (15.6% (n=17) vs. 6.1% (n=54), p=0.001); global hypokinesia (3.7% (n=4) vs. 0.4% (n=4), p=0.007); dilatation of left atrium (33.9% (n=37) vs. 17.5% (n=156), p<0.001), of left ventricle (LV) (11.0% (n=12) vs. 5.1% (n=45), p=0.025), of right atrium (15.6% (n=17) vs. 1.7% (n=15), p<0.001) and of right ventricle (15.6% (n=17) vs. 1.9% (n=17), p<0.001); signs of paH (28.4% (n=31) vs. 5.3% (n=47), p<0.001), and pericardial effusion (43.1% (n=47) vs. 6.5% (n=58), p<0.001). 314 patients had consecutive examinations; median interval between first and last examination was 40 months (SD: 28, range: 0.9–115). New development or resolution of findings between consecutive examinations was common. The findings which most commonly developed were mitral valve regurgitation in 24% (n=76) of patients, tricuspid regurgitation in 21% (n=67), aortic valve sclerosis in 18% (n=55) and LV dysfunction in 20% (n=62). The findings which most commonly resolved were mitral regurgitation in 15% (n=47) of patients, tricuspid regurgitation in 16% (n=49), aortic valve sclerosis in 10% (n=31) and LV dysfunction in 13% (n=42).

**Abstract FRI0572 – Table 1.** Frequency of echocardiographic findings in patients with CTD

Number of patients	Systemic Scleroderma										Limited Scleroderma				Myositis									
	All patients	SLE	Primary	Secondary	Diffuse	Systemic	Myositis	PM	DM	Anti-Jo1	UCTD	MCTD	All patients	SLE	Primary	Secondary	Diffuse	Systemic	Myositis	PM	DM	Anti-Jo1	UCTD	MCTD
<b>Valvular regurgitation</b>	1004	190	209	115	84	145	17	21	29	17	93	45												
Mitral	868 (37)	87 (46)	78 (38)	44 (38)	44 (41)	46 (32)	3 (18)	6 (29)	10 (34)	4 (24)	20 (22)	29 (34)												
Aortic	176 (16)	26 (14)	44 (21)	29 (25)	15 (13)	29 (20)	1 (6)	3 (14)	3 (10)	3 (18)	4 (4)	17 (20)												
Tricuspid	755 (25)	45 (24)	58 (28)	25 (22)	31 (27)	52 (36)	5 (29)	3 (14)	2 (7)	5 (29)	20 (22)	17 (20)												
Pulmonary	71 (7)	6 (3)	20 (10)	5 (4)	10 (9)	11 (8)	2 (12)	1 (5)	0	1 (6)	4 (4)	7 (8)												
<b>Valvular stenosis</b>																								
Mitral	96 (10)	20 (11)	18 (9)	15 (13)	13 (11)	15 (10)	1 (6)	0	2 (7)	2 (12)	6 (6)	3 (4)												
Aortic	202 (20)	25 (13)	38 (18)	43 (37)	26 (23)	33 (23)	5 (29)	2 (10)	4 (14)	5 (29)	11 (12)	10 (12)												
Tricuspid	3 (0)	0	0	1 (1)	0	1 (1)	0	0	0	0	0	1 (1)												
Pulmonary	1 (0)	0	0	1 (1)	0	0	0	0	0	0	0	0												
<b>Valvular stenosis</b>																								
Mitral	10 (1)	2 (1)	1 (0)	0	1 (1)	1 (0)	0	0	1 (4)	1 (6)	0	1 (1)												
Aortic	45 (4)	4 (2)	6 (3)	13 (11)	9 (8)	6 (4)	0	0	2 (7)	1 (6)	2 (2)	2 (2)												
Tricuspid	1 (0)	0	0	0	0	1 (1)	0	0	0	0	0	0												
Pulmonary	1 (0)	0	0	1 (1)	0 (0)	0	0	0	0	0	0	0												
<b>Contraction and ejection</b>																								
LV dysfunction	214 (22)	29 (15)	38 (18)	33 (29)	24 (20)	42 (29)	4 (24)	5 (17)	1 (4)	1 (6)	20 (22)	15 (18)												
EF reduced (all)	93 (9)	19 (10)	11 (5)	11 (10)	14 (12)	18 (13)	2 (12)	1 (5)	1 (3)	3 (18)	10 (11)	5 (6)												
EF 45–54%	30 (3)	10 (5)	3 (1)	4 (3)	10 (8)	9 (6)	1 (6)	1 (3)	1 (3)	1 (6)	4 (4)	4 (5)												
EF 30–44%	20 (2)	7 (4)	5 (2)	4 (3)	3 (2)	5 (3)	0	0	0	0	0	1 (1)												
EF < 30%	13 (1)	2 (1)	2 (1)	3 (3)	1 (1)	2 (1)	1 (6)	0	0	0	0	2 (2)												
Local akinesis	66 (7)	16 (9)	19 (9)	17 (15)	11 (9)	17 (12)	0	2 (7)	0	4 (24)	5 (5)	5 (6)												
Global hypokinesia	8 (1)	1 (1)	0	0	3 (3)	2 (1)	0	0	0	1 (6)	0	1 (1)												
<b>Muscular hypertrophy and cavity dilatation</b>																								
LV hypertrophy	86 (3)	9 (5)	7 (3)	9 (8)	8 (7)	4 (3)	0	1 (3)	0	2 (12)	5 (5)	1 (1)												
Concentric hypertrophy	6 (1)	1 (1)	1 (0)	0	0	0	0	0	0	1 (6)	1 (1)	0												
Septal hypertrophy	50 (5)	7 (4)	7 (3)	10 (9)	8 (7)	8 (6)	0	1 (3)	2 (7)	2 (12)	1 (1)	4 (5)												
LA dilatation	193 (19)	23 (12)	35 (17)	38 (33)	28 (23)	29 (20)	3 (18)	4 (13)	3 (10)	8 (47)	13 (14)	10 (12)												
LV dilatation	57 (6)	12 (6)	10 (5)	9 (8)	5 (4)	2 (1)	0	3 (14)	0	4 (24)	8 (9)	4 (5)												
RA dilatation	12 (1)	1 (1)	1 (0)	5 (4)	1 (1)	5 (3)	1 (6)	1 (5)	0	1 (6)	1 (1)	3 (4)												
RV dilatation	34 (3)	5 (3)	9 (4)	1 (1)	5 (4)	5 (3)	2 (12)	1 (3)	0	1 (6)	2 (2)	3 (4)												
<b>Other findings</b>																								
Signs of paf	78 (8)	11 (6)	13 (6)	5 (4)	20 (18)	16 (11)	1 (6)	1 (3)	0	4 (24)	3 (3)	5 (6)												
Pericardial effusions	101 (10)	12 (6)	14 (7)	9 (8)	15 (13)	10 (7)	2 (12)	1 (3)	3 (10)	5 (29)	4 (4)	8 (9)												
Aneurysms	11 (1)	6 (3)	1 (0)	1 (1)	0	1 (1)	0	0	0	1 (6)	0	0												

Abbreviations: SLE: Systemic Lupus Erythematosus; Myositis: Myositis; PM: Polymyositis; DM: Dermatomyositis; UCTD: Undifferentiated Connective Tissue Disease; MCTD: Mixed Connective Tissue Disease; LV: left ventricle; EF: ejection fraction; LA: left atrium; RA: right atrium; RV: right ventricle; paf: pulmonary artery hypertension.

**Conclusions:** Echocardiographic examinations frequently revealed structural and/or functional abnormalities in patients with CTD. Some findings were associated with previous cardiac involvement and might be disease-related. When reevaluating a patient, findings had often newly developed or resolved since the last examination. Overall, repeated echocardiographic examinations may be a valuable part of follow-up in CTD patients.

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FRI0573

### ULTRASONOGRAPHY AND HISTOLOGICAL DIAGNOSIS CONCORDANCE IN PATIENTS WITH SUSPECTED PRIMARY SJÖGREN SYNDROME

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**Background:** Minor salivary gland biopsy (MSGB) is the most used diagnostic tool for primary Sjögren Syndrome (SS). The potential relevance of an alternative

non-invasive, fast, low cost and choice by the patient technique, like mayor salivary gland ultrasonography (MSGUS), has to be investigated.

**Objectives:** To evaluate the utility of MSGUS as a diagnostic tool for primary SS and to study the concordance with MSGB.

**Methods:** 36 patients were consecutively recruited with clinical and/or analytical suspicion of SS, from outpatient Rheumatology consultations from 2015–2017. All patients received a MSGB and a MSGUS. Two echographers performed two images readings with an interval of at least one week. They worked blinded for clinical and histological results. Demographics, clinical, serological, ESSPRI and ESDAI were recorded. The histological results were classified according to *Chisholm* and *Mason* score and the US results according to the system by *Cornec et al.* The final SS diagnosis was made using the 2002 classification criteria. Subsequently the data was analysed using the statistical software STATA/MP. Adjusted concordance intra and interobserver (kappa coefficient) was calculated for the diagnoses performed by US (normal/pathological). The validity of US and biopsy to diagnose SS according to the 2002 criteria was evaluated by calculating the percent agreement between the tests, along with the specificity, sensitivity, PPV, NPV and area below the curve (AUC). Further, the percent association of the diagnoses between serology and US were determined, and the statistical significance of it was evaluated with chi-square test.

**Results:** 94% were female, with an average age of 58 years. 69% were non-smokers. 89% showed pathological Schirmer test, 78% extraglandular features, 19% hypocomplementemia and 44% hypergammaglobulinemia. As for the serological data, 81% had positive ANAS, 44% antiRo52, 39% antiRo60% and 28% antiLa. 39% of the patients were RF positive. 69% fulfilled the 2002 classification criteria with an average ESSPRI of 5.3 and ESSDAI of 1.5. Using these criteria as a gold-standard, the total percentage agreement was 83.3% for US and 80.6% for biopsy (S 92, Sp 64.3%). A good concordance was found between both observers (kappa=0.8) along with intraobserver (kappa=0.64 and 0.78 for first and second observer respectively). The percentage of patients with positive antibodies (48% antiRo52, 41% antiRo60, 30% antiLa) had pathological US. Significant statistical differences were not found in patients with normal US ( $p>0.44$  in all associations explored).

**Conclusions:** MSGUS is a non-invasive imaging method useful for the diagnosis of primary SS in common clinical practice with a diagnostic value similar to the MSGB. MSGUS has good correlation intra and interobserver. There was no statistical significant association found between the positive autoimmune antibodies and US.

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FRI0574

#### RADIOFREQUENCY ECHOGRAPHIC MULTI SPECTROMETRY (REMS) FOR THE NON-IONISING DIAGNOSIS OF OSTEOPOROSIS AT FEMORAL NECK: RESULTS OF A MULTICENTER CLINICAL STUDY COMPARING REMS AND DXA

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**Background:** Radiofrequency Echographic Multi Spectrometry (REMS) is an innovative densitometric technique able to automatically provide BMD values, which it has been shown to highly correlate with BMD obtained by DXA.<sup>1</sup>

**Objectives:** To evaluate the accuracy of REMS measurements in postmenopausal women's femoral neck health assessment versus DXA results in a multicenter clinical study.

**Methods:** In seven Italian referral centres for osteoporosis management, 1659 postmenopausal women (51–70 years old) were enrolled. Both DXA and REMS examinations were performed on each patient at femoral neck, in the strictest adherence to the corresponding guidelines. After excluding the scans affecting by errors, the REMS diagnostic accuracy was evaluated by assessing sensibility and specificity in the discrimination between "osteoporotic" and "healthy" patients; the degree of correlation between DXA-BMD and REMS-BMD was quantified through Pearson's correlation coefficient (r) evaluation. In addition, the agreement between DXA-BMD and REMS-BMD was measured calculating the root mean square error (RMSE).

**Results:** A strong correlation ( $r=0.94$ ,  $p<0.001$ ) was detected between BMD obtained by DXA and REMS – estimated BMD at femoral neck, with a low residual error ( $RMSE=0.034$  g/cm<sup>2</sup>). In addition to this, REMS resulted to have a high capability to discriminate osteoporotic from healthy patients (sensitivity=94.4%, specificity=95.6%).

**Conclusions:** Thanks to its high capability to identify osteoporotic patients, and the strong correlation with DXA parameters, REMS has been shown to be an accurate non-ionising approach to detect osteoporosis at femoral neck.

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FRI0575

#### EVALUATION OF SCREENING QUESTIONNAIRES FOR PSORIASIS ARTHRITIS IN A SAMPLE OF PATIENTS WITH PSORIASIS IN A THIRD LEVEL HOSPITAL

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**Background:** Psoriatic arthritis (PsA) is an erosive joint inflammatory disease associated with psoriasis. Between 5% and 35% of patients with psoriasis may develop PsA. Screening questionnaires have been developed for dermatologists in order to make them suspect which patients should be referred to the rheumatologist for evaluation.

**Objectives:** To know the percentage of patients with PsA detected by the questionnaires in a group of psoriasis patients coming from an outpatient dermatology clinics.

**Methods:** The study was carried out in the rheumatology unit in collaboration with dermatology. Patients with cutaneous psoriasis who had not previously been diagnosed of any type of arthritis, from a dermatology clinic, were recruited consecutively. Patients were invited to participate in the study and referred to the rheumatology research unit where they signed the informed consent. Then, the questionnaires were administered.

**Results:** From November 2014 to December 2015, 53 patients were recruited: 30 women and 23 men. The mean age was 44 ( $\pm 13$ ) years. The average duration of psoriasis was 11 ( $\pm 9$ ) years. 61% had affected nails and skin. 11% of patients received no treatment for psoriasis and 13% received treatment with MTX or PUVA. The mean PASI was 3 ( $\pm 4$ ). The quality of life, measured by DLQI, was 1 ( $\pm 2$ ). 50% of patients had all the screening questionnaires positive. EARP was the questionnaire that tested positive in a higher percentage of patients, 70%. 68% of the patients had some painful joint and only 8% had some inflammation. Only 9 patients met CASPAR classification criteria and were diagnosed as PsA, of which 56% were in topical treatment by dermatology. These 9 patients had higher PASI than those undiagnosed and were the only ones who had swollen joints. The screening questionnaire that detected all these 9 patients was the EARP, but it was positive in 65% of patients who did not meet CASPAR criteria.

	S	E	VPP	VPN
ToPAS	0,55	0,61	0,22	0,87
PASE	0,33	0,81	0,27	0,85
PEST	0,44	0,70	0,23	0,86
EARP	1	0,36	0,24	1

**Conclusions:** The percentage of patients with PsA who was identified by EARP questionnaire was 100%, but with a high proportion of FP. PASE detected 33%, TOPAS 55% and PEST 44%. Therefore, questionnaires available are useless in daily clinical practice, due to lack of specificity or sensitivity. The development of a small questionnaire for dermatologist based on CASPAR criteria could be more effective

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**FRI0576 PULMONARY ULTRASOUND IN THE ASSESSMENT OF INTERSTITIAL LUNG DISEASE IN RHEUMATOID ARTHRITIS**

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**Background:** Interstitial lung disease (ILD) is an extra-articular complication in rheumatoid arthritis (RA) that may lead to severe impairment of respiratory function. High-resolution computer tomography (HRCT) is the most common imaging technique used in the assessment of ILD. However, the costs and the ionising radiation may limit its use in routine practice. Recently, US is generating interesting data that may support its use and validity in the assessment of ILD in rheumatic diseases<sup>1,2</sup>.

**Objectives:** To investigate the correlation between lung US and HRCT findings in the assessment of ILD in patients with RA.

**Methods:** Patients with diagnosis of RA according to ACR 2010 classification criteria with respiratory symptoms and previous diagnosis of ILD by HRCT were included. Clinical examination, pulmonary function test (PFT) and lung US were performed in all patients. Lung US was performed by a rheumatologist expert in US who was blinded to clinical and HRCT data. Serologic tests (anti-CCP, ESR, RF, ANA) were taken. Lung US was performed in 14 intercostal spaces (IS) and quantified according to the following semiquantitative scoring: grade 0=normal ( $\leq 5$  B-lines); grade 1=mild ( $\geq 6$  to  $\leq 15$  B-lines); grade 2=moderate ( $\geq 16$  to  $\leq 30$  B-lines); and grade 3=marked ( $\geq 30$  B-lines). The Warrick score (extension) was used to interpret the HRCT findings.

**Results:** A total of 32 patients with RA (25 women and 7 men) were included. Mean age was 59.37 ( $\pm$ SD 13.66) years, and the mean disease duration was 58.75 ( $\pm$ SD 52.52) months. Sixteen patients were smokers and 75% were positive to anti-CCP. Moreover, the mean of DAS-28 was 3.71 ( $\pm$ SD 1.01). A total 448 IS were assessed by US. Lung US was positive for ILD in 28 patients (87.5%). From those, 7 patients (21.8%) with severe ILD, 12 patients (37.5%) with moderate, 9 patients (28.1%) with mild. Four patients (12.5%) showed normal lung US assessment. A significant linear correlation was found between the US score and the HRCT score ( $p < 0.000$ ; correlation coefficient = 0.75). A negative correlation was found between US B-line assessments and DLCO ( $p \leq 0.000$ ). No association was founded with DAS28, anti-CCP, PFT. Sensitivity and specificity of ultrasound for ILD was 87.5% and 98% respectively.

**Conclusions:** Our study demonstrates that lung US may be a potential tool for the assessment of ILD also in patients with RA. It can be adopted in future as a screening tool to use at moment of the first diagnosis of RA.

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**Disclosure of Interest:** None declared

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FRI0577

**MRI-BONE MARROW OEDEMA COMBINED WITH LOW-DOSE CT SCANNING PERFORM OPTIMALLY IN THE DIAGNOSIS OF AXIAL SPONDYLOARTHRITIS**

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**Background:** The evidence of sacroiliitis on radiography and MRI have been regarded as crucial for diagnosis of ankylosing spondylitis (AS) and axial spondyloarthritis (axSpA). Low-dose CT (ldCT) has advantages on sacroiliitis has not been taken into consideration until now.

**Objectives:** To compare the performance of plain radiography, ldCT, and MRI for facilitating the diagnosis of sacroiliitis in radiographic negative axial spondyloarthritis (nr-axSpA) or AS from suspected axSpA.

**Methods:** Patients presenting with chronic back pain (>3 months duration) were recruited and assessed by axSpA-experienced rheumatologists. Patients not meeting the ASAS clinical criteria for axSpA were recruited as controls, and divided into non-inflammatory and inflammatory groups on the basis of presence of inflammatory back pain and/or CRP/ESR elevation. The ASAS clinical axSpA or modified New York AS criteria were used to define nr-axSpA or AS cases respectively. Clinical variables, pelvic radiography, sacroiliac joint (SIJ) ldCT (voltage 120 kV, electricity 70mAs) and SIJ MRI (SPAIR, T1-weighted, T2-weighted sequences) were obtained in one week period. All images were read by two expert musculoskeletal radiologists independently and differences in initial reads resolved by consensus. Plain radiographic and ldCT SIJ images were graded 0–4 according to the modified New York criteria. MRI-BMO was defined by the presence of periarthral or subchondral BMO lesions. Fat deposition, sclerosis, erosions or bony ankylosis were regarded as signs MRI-structural lesions. Subjects were considered MRI positive if they had either BMO or structural lesions.

**Results:** 130 patients were included in the study and had SIJ radiography and ldCT, of whom 71 additionally had SIJ MRI. 28 (39.3% female, 36% B27 prevalence) non-inflammatory controls, 24 (33.3% female, 50% B27 prevalence) inflammatory controls, 34 (26.5% female, 86.3% B27 prevalence) nr-axSpA and 44 (36.4% female, 95.3% B27 prevalence) AS cases were recruited in total. Positive imaging results according to clinical diagnoses are given in the table. These findings show that ldCT had much higher sensitivity than radiography for nr-axSpA and similar specificity. Whilst no non-inflammatory control was positive for ldCT and only one for radiography, three inflammatory controls were positive for ldCT but negative for radiography, with two being negative by MRI, and all being HLA-B27 negative, suggesting that they may be false positives. MRI-BMO had the highest sensitivity for nr-axSpA, but had lower specificity, with 31% of non-inflammatory controls being positive for this modality, and lower sensitivity for AS. MRI-structural had intermediate performance with slightly lower sensitivity to ldCT for both AS and nr-axSpA, but lower specificity than ldCT, and lower sensitivity for nr-axSpA than MRI-BMO.

Abstract FRI0577 – Table 1

Diagnosis	Plain Radiography	ldCT	MRI-BMO	MRI-structural
AS	44/44 (100%)	44/44 (100%)	19/21 (90%)	20/21 (95%)
nr-axSpA	0/34 (0%)	15/34 (44.1%)	19/24 (79%)	10/24 (42%)
Non-inflammatory control	1/28 (3.6%)	0/28 (0%)	5/16 (31%)	6/16 (38%)
Inflammatory control	0/24 (0%)	3/24 (12.5%)	3/10 (30%)	1/10 (10%)

**Conclusions:** ldCT and MRI-BMO examination are more sensitive than either plain radiography or MRI-structural assessment, but MRI overall is less specific than plain radiography or ldCT. The relative position of these imaging modalities in screening patients for axSpA needs to be reconsidered in the light of these findings, also taking into account the costs involved.

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**FRI0578 INCREASED VEIN WALL THICKNESS IN BEHÇET'S SYNDROME**

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**Background:** Lower extremity vein thrombosis (LEVT) is the key feature of vascular involvement in Behçet's syndrome (BS). Vein wall thickness (VWT) is proposed to be a surrogate marker of venous disease. A pilot MR study done in 7 BS patients and controls, had demonstrated increased VWT and signal enhancement in the lower extremity veins of BS patients without vascular disease.<sup>1</sup> Another study, using USG, found that VWT was increased among BS patients without vascular disease compared to patients with ankylosing spondylitis and healthy controls.<sup>2</sup>

**Objectives:** We reassessed VWT in proximal lower extremity veins in BS patients with LEVT and suitable controls in a formal, masked protocol.

**Methods:** We studied 47 (40 M/ 7 F) BS patients with LEVT, 50 (43 M/ 7 F) BS patients without any vascular involvement and 38 (31 M/ 7 F) age and gender matched apparently healthy controls. Two independent radiologists, blinded to the diagnosis of BS, used USG to measure VWT of common femoral vein (CFV), superficial femoral vein (SFV) and vena saphena magna (VSM) in both legs.

**Results:** As shown in table 1, mean age at disease onset and the disease duration were similar between BS study groups. The mean age at thrombosis onset of the patients with LEVT was 26.4±5.8 years. There was good concordance between the 2 observers (kappa: 0.9) The mean VWT was significantly increased among both BS patients with LEVT and those without any vascular involvement when compared to the healthy controls while those with LEVT had the thickest veins.

**Abstract FRI0578 – Table 1.** Disease duration and VWT

	BS with vascular involvement (n=47; 40 M/ 7 F)	BS without vascular involvement (n=50; 43 M/ 7 F)	Healthy controls (n=38; 31 M/ 7 F)	P value
Age, years	37.06±5.26	36.98±4.47	34.87±7.22	0.296
Disease duration	10.96±6.45	9.68±5.89	-	0.310
Vein wall thickness, mean±SD, mm				
Right CFV 1 st observer	0.91±0.67	0.69±0.15	0.57±0.11	0.001
Right CFV 2nd observer	0.93±0.76	0.70±0.18	0.58±0.09	<0.001
Left CFV 1 st observer	1.04±0.85	0.66±0.11	0.56±0.07	<0.001
Left CFV 2nd observer	1.09±0.83	0.69±0.16	0.57±0.07	<0.001
Right SFV 1 st observer	0.79±0.38	0.60±0.11	0.51±0.9	<0.001
Right SFV 2nd observer	0.80±0.42	0.62±0.13	0.52±0.07	<0.001
Left SFV 1 st observer	0.88±0.38	0.62±0.12	0.49±0.09	<0.001
Left SFV 2nd observer	0.90±0.40	0.63±0.13	0.51±0.07	<0.001
Right VSM 1 st observer	0.60±0.22	0.52±0.11	0.43±0.07	<0.001
Right VSM 2nd observer	0.64±0.25	0.53±0.13	0.46±0.08	<0.001
Left VSM 1 st observer	0.67±0.23	0.53±0.11	0.42±0.09	<0.001
Left VSM 2nd observer	0.65±0.27	0.53±0.11	0.43±0.07	<0.001

CFV: common femoral vein, SFV: superficial femoral vein, VSM: vena saphena magna

**Conclusions:** VWT of proximal deep and superficial lower extremity veins was found to be increased among BS patients without any clinical and radiological vascular involvement.

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**FRI0579 DIAGNOSTIC UTILITY OF METATARSOPHALANGEAL SYNOVITIS IDENTIFIED BY ULTRASONOGRAPHY FOR EARLY RHEUMATOID ARTHRITIS**

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**Background:** In patients with rheumatoid arthritis (RA), synovitis can occur at not only hand and finger joints but also the metatarsophalangeal (MTP) joints. However, power Doppler ultrasonography (PDUS) findings of the MTP joints and its diagnostic utility remain unclear in patients with early RA.

**Objectives:** The present study investigated whether the detection of MTP synovitis by PDUS is useful for the diagnosis of early RA.

**Methods:** The study enrolled 174 patients with suspected RA within 6 months of onset. We assessed the articular synovium using grey scale (GS) and power Doppler (PD) signals with a semi-quantitative method (grades 0–3) in both hand and finger joints (22 joints) and MTP joints (10 joints) by PDUS. In addition, we evaluated bone erosion and intermetatarsal bursitis. We defined GS grade  $\geq 1$  and PD grade  $\geq 1$  as PDUS synovitis. We evaluated the diagnostic accuracy of PDUS synovitis for RA.

**Results:** Of the 174 patients, 59 were diagnosed with RA and 115 did not have RA. Among the patients with RA, 47 (80%) had PDUS synovitis in the hand and finger joints and 32 (54%) had PDUS synovitis in the MTP joints. The frequencies of PDUS synovitis in each MTP joint, bone erosion of the fifth MTP joint, and intermetatarsal bursitis were significantly higher in patients with RA than in those without RA. The diagnostic accuracy of PDUS synovitis in the hand and finger joints was good, with a sensitivity of 80%, specificity of 77%, and accuracy of 78%. On considering the MTP joints in addition to the hand and finger joints, the diagnostic accuracy improved, with a sensitivity of 92%, specificity of 74%, and accuracy of 80%. In this study, 7 patients (12%) with RA had synovitis in the MTP joints and not in the hand and finger joints.

**Conclusions:** When synovitis cannot be detected in the hand and finger joints by PDUS, scanning of the MTP joints could be useful for the diagnosis of early RA.

	RA n = 59	non-RA n = 115	p-value
PDUS synovitis	32/59 (54%)	5/115 (4%)	<0.001
1 <sup>st</sup> MTP	24/118 (20%)	7/230 (3%)	<0.001
2 <sup>nd</sup> MTP	16/118 (14%)	5/230 (2%)	<0.001
3 <sup>rd</sup> MTP	13/118 (11%)	3/230 (1%)	<0.001
4 <sup>th</sup> MTP	10/118 (8%)	0/230 (0%)	<0.001
5 <sup>th</sup> MTP	17/118 (14%)	0/230 (0%)	<0.001
Bone erosion	8/59 (14%)	0/115 (0%)	<0.001
1 <sup>st</sup> MTP	2/118 (2%)	0/230 (0%)	0.114
2 <sup>nd</sup> MTP	1/118 (1%)	0/230 (0%)	0.339
3 <sup>rd</sup> MTP	0/118 (0%)	0/230 (0%)	1.000
4 <sup>th</sup> MTP	0/118 (0%)	0/230 (0%)	1.000
5 <sup>th</sup> MTP	5/118 (4%)	0/230 (0%)	0.004
Intermetatarsal bursitis	3/118 (3%)	0/230 (0%)	0.038

RA, rheumatoid arthritis

Fisher's exact probability test

**Abstract FRI0579 – Figure 1.** Power Doppler ultrasonography (PDUS) findings in the metatarsophalangeal (MTP) joints

RA, rheumatoid arthritis

Fisher's exact probability test

**Disclosure of Interest:** None declared

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**FRI0580** **QUANTITATIVE MRI OF SINGLE VS. MULTIPLE JOINTS IN JUVENILE IDIOPATHIC ARTHRITIS AS PREDICTIVE MEASURE OF CLINICAL OUTCOMES**

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**Background:** Clinical examination of juvenile idiopathic arthritis (JIA) patients does not always adequately reflect disease activity, whereas quantitative Dynamic Contrast Enhanced (DCE)-MRI based biomarkers extracted from images of multiple joints have been shown to reliably predict the course of the disease<sup>1</sup>.

**Objectives:** To investigate the association between DCE-MRI measures of inflammation in a single and in multiple joints and the treatment related clinical changes.

**Methods:** 18 patients (12 girls, med. age 12.6 years, med. disease 1.2 years) with polyarticular JIA with more than 3 affected joints or intolerance to more than 3 months of MTX were given Etanercept. Their most clinically affected hand was imaged with DCE-MRI (0.2T Esaote C-Scan) at baseline, 3 and 6 months following the treatment. DCE-MRI was analysed using dedicated software package (DYNAMIKA, IAG). Dynamic Enhanced MRI Quantification (DEMRIQ-V) was calculated as the volume of enhancing voxels within Region of Interest placed around a single or multiple MCPJs. DEMRIQ-V was also weighted by the mean of Maximum Enhancement (ME) and Initial Rate of Enhancement (IRE), the parameters corresponding to the height and slope of the signal intensity vs time curves extracted from the enhancing voxels.<sup>2</sup> Clinical scores included active joint (AJ) count. Involvement of less than 3 AJ was considered a clinical response. The differences in DEMRIQ-V between the visits were analysed using t-test, assuming  $p < 0.05^*$  to be statistically significant and  $p < 0.025^{**}$  to be clinically meaningful.

**Results:** In all patients, in clinically unaffected joints, MRI was able to detect sub-clinical disease, and in all but 3 patients, significant and/or clinically meaningful changes were documented for DEMRIQ-ME. In 4 patients, DEMRIQ-V scores showed corresponding clinical changes whereas all other patients these markers were non-concordant. DEMRIQ-V score was predictive of clinical outcome:

- · in 5 patients, improvement of DEMRIQ-V at month 3 predicted response to treatment at month 6;
- · in 4 patients, increase or persistence of a high DEMRIQ-V at month 3 predicted non-response to treatment at month 6;
- · DEMRIQ-V measured in a single most affected joint was as predictive as when it was measured in all MCPJs.

**Conclusions:** We conclude that DCE-MRI's ability to detect early disease can reliably support clinical examination. Use of DEMRIQ-V and DEMRIQ-ME scores, which either followed clinical response (DEMRIQ-ME) or predicted clinical outcomes at 6 months (DEMRIQ-V) in most patients can support early clinical and research decisions.

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**FRI0581** **ULTRASONOGRAPHY IN THE DETECTION OF JOINT DESTRUCTION IN RA PATIENTS: A COMPARISON WITH CONVENTIONAL RADIOGRAPHY**

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**Background:** RA evolves erosive polyarthritis resulting in destructive changes in the joints. Ultrasonography (US) is used in current practice as early diagnostic modality for identification of structural damage to the articular surfaces.

**Objectives:** To compare US and radiographic assessment of hands and feet joint destruction in RA patients, and to evaluate the contribution of early US detection of damage into long-term RA outcomes.

**Methods:** 75 patients with RA, mean age 54.0,<sup>44.0;</sup> <sup>62.0</sup> disease duration <sup>7.4;</sup> <sup>20</sup> months, were treated with MTX and biologics according to Treat-To-Target concept. Hands and feet US were analysed before initiation of treatment and in 3, 6, 9 and 12 months after. Deepening of the bony contour  $>2$  mm in width and  $>1$  mm

in depth, visualised in 2 orthogonal planes, was considered as the key US sign of destructive changes (erosions) according to OMERACT criteria. A binary scoring system (presence/absence of erosions) of the joints examined was used. Radiographs were obtained at baseline, at 12 month and 4 years, radiographic changes were assessed using Sharp/van der Heijde modified scoring method. Radiographic progression was documented based on Sharp/Van der Heijde modified score changes during the follow up.

**Results:** There was a significant correlation between the counts of joints with erosions obtained with two diagnostic methods – US and radiography. This correlation was moderate before initiation of therapy ( $r=0.37$ ;  $p=0.0008$ ), and weak – after 12 month follow up ( $r=0.28$   $p=0.016$ ). During one year US showed increase in the count of joints with erosions (from 1 [0; 2] to 2<sup>1; 3</sup>) while radiography did not show any significant change (from 0 [0; 1] to 0 [0; 1]).

Bland-Altman analysis showed statistical agreement between the results obtained by two methods. Mean difference between the two modalities before initiation of treatment was  $-0.42$  (95% CI  $-0.68$ ;  $-0.16$ ), and at 12 month follow up  $-1.16$  (95% CI  $-1.52$ ;  $-0.80$ ), which is comparable with actual values. We identified the relationship between the difference in variables and the count of affected joints before and 12 month after initiation of treatment ( $r=-0.35$ ,  $r=-0.53$  respectively). 8% of variables were outside 2 standard deviations at baseline, and 4% – at 12 month. Logistic regression analysis showed no relationship between annual radiological progression and US diagnosed increasing count of joints with erosions at 3, 6 and 9 months follow up. However, dynamic radiographs assessment at 4 years revealed a correlation with US diagnosed count of joints with erosions at 6 month and 9 month follow up ( $r=0.24$ ,  $p=0.03$ ;  $r=0.24$ ,  $p=0.04$ , respectively). Quality indicator of US diagnosed count of erosions at 6 month follow up: OR=2.8 95% CI 1.05–7.5,  $p=0.037$ , with 71% sensitivity and 54% specificity; Quality indicator of US diagnosed count of erosions at 9 month follow up: OR=2.73 95% CI 1.02–7.27,  $p=0.041$ , with 64% sensitivity and 61% specificity. Quantitative assessment of the dynamics at these time periods did not show any relationship.

**Conclusions:** Therefore, our study confirms the relevance of US in assessment of bone erosions in spite of week agreement with radiography data. We found a prognostic value of US-diagnosed erosions during the first year of follow up for long-term (4 years) clinical outcomes, and the relevance of control assessment at 6 month after initiation of treatment.

**Disclosure of Interest:** None declared

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**FRI0582** **CHANGE IN MUSCLE VOLUME AND MUSCLE FAT FRACTION AS POTENTIAL NON-INVASIVE BIOMARKERS OF DISEASE PROGRESSION: MACHINE LEARNING FRAMEWORK FOR QUANTITATIVE ANALYSIS OF MRI DATA**

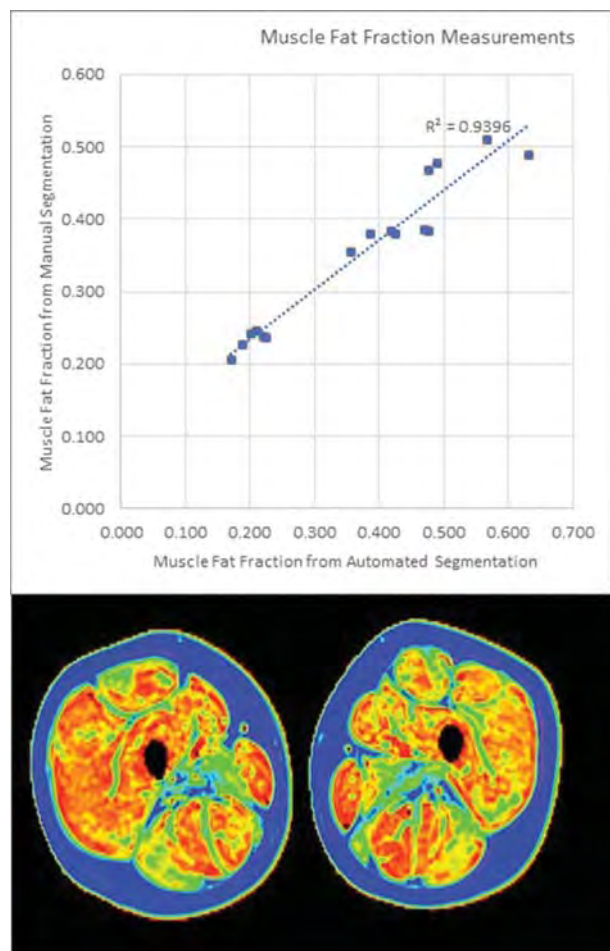
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**Background:** Change in muscle volume and muscle fat fraction are potential non-invasive biomarkers of disease progression in a number of diseases, including sporadic inclusion body myositis<sup>1</sup> and osteoarthritis<sup>2</sup>. Their measurement from magnetic resonance images (MRI) usually involves time consuming manual segmentations of the images by trained readers, which limits the use of these biomarkers in clinical research and practise.

**Objectives:** In this study, we present a novel unsupervised k-means-classifier based image processing framework, developed for machine learning approach to segmentation of thigh muscles from MRI and the subsequent calculation of fat fraction from Dixon images. Further, we present validation of the new approach against manual segmentation using longitudinal retrospectively acquired data.

**Methods:** Axial MR images from the upper thighs including in-phase and out of phase sequences were recorded in a group of 8 subjects at baseline and at a follow up. The 16 imaging time points were manually segmented by an expert reader, who delineated the muscle. For these regions the mean fat fraction was calculated from the in-phase and out of phase Dixon images. The fully automated segmentation was then run on the same images and the resulting fat fractions compared with the manual results. The proposed k-means approach classifies each image pixel according to signal intensity and creates image masks for bone, muscle and fat in three dimensions. The pixel counts from bone, muscle and fat are automatically measured to produce the volume and mean fat fraction.

**Results:** We compared the mean fat fraction for the two approaches and found linear correlation was good ( $R^2=0.9396$ ). Manual segmentations typically took 40 min or more to execute, compared to the automated segmentations, which required less than 5 min on a standard desktop computer



Example Fat Fraction Map

Abstract FRI0582 – Figure 1. Example Fat Fraction Map

**Conclusions:** In the present study, we reported a segmentation framework based on unsupervised k-means to measure muscle volume and fat fraction. It offers time savings versus manual segmentations and correlates well with fat fraction measurements. This could be useful for muscle quantification in the fields of osteoarthritis, sports medicine and rehabilitation. Further studies are planned to compare sensitivity of automatically acquired measures to clinical progression.

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FRI0583

### CLINICAL UTILITY OF ANA-ELIA VS ANA-IMMUNOFLUORESCENCE IN CONNECTIVE TISSUE DISEASE

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**Background:** Antinuclear antibody (ANA) detection by indirect immunofluorescence technique (ANA-IIF) is the standard test for connective tissue disease (CTD) screening for last 5 decades, which has low specificity and it is labour intensive. ANA detection by fluoroenzyme immunoassay (ANA-Elia) has been developed recently as an alternative method to include 17 ANA-targeted recombinant antigens.

**Objectives:** Compare the sensitivity and specificity of the new ANA-Elia with conventional ANA-IIF.

**Methods:** Randomly selected 1458 patient's sera from primary and secondary health care were tested for both the standard ANA-IIF (Diasorin S.P.A, saluggia, Italy) and the new ANA-Elia (Phadia GmbH, Ferieiburg, Germany). ANA-Elia is fluoroenzyme immunoassay performed on the Phadia-250 automated platform. It contains 17 ANA-targeted recombinant antigens; dsDNA, Sm-D, Rib-P, PCNA, U1-RNP (70, A, C), SS-A/Ro (52 and 60), SS-B/La, Centromere B, Scl-70, Fibril-larin, RNA Polymerase III, Jo-1, Mi-2, and PMScl. Result with ratio >1.0 considered positive for the new technique. For ANA-IIF our lab cut off for positive test is  $\geq 1:80$ . Patients were evaluated in our rheumatology clinic for fulfilling the corresponding international clinical criteria for various connective tissue diseases.

**Results:** 75.7% were females with mean age of  $43 \pm 13$  years. 201 (11.5%) patients confirmed to have clinical CTD as follow: 142 SLE, 24 Sjogren's syndrome, 15 scleroderma, 7 MCT, 10 Myositis and 10 undifferentiated CTD. The specificity of ANA-Elia at cut off ratio of >1 and ANA-IIF at titer of  $\geq 1:80$  was almost equal, 88.5% and 87.6% respectively. However, ANA-Elia has higher sensitivity (74.5%) as compared to ANA-IIF (61.6%). At a higher cut off ratio of >2 and titer of  $\geq 1:160$ , the specificity improved to 93.6%–92.6% respectively.

	ANA-Elia		ANA-IIF	
	>1	>2	$\geq 1:80$	$\geq 1:160$
<b>Sensitivity</b>	74.5%	67.6%	61.6%	50.7%
<b>Specificity</b>	88.5%	93.6%	87.6%	92.6%

**Conclusions:** The ANA testing with the newly developed, use friendly, fully automated and less labour intense method of ANA-Elia can replace the standard conventional ANA-IIF with better specificity.

**Disclosure of Interest:** None declared

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FRI0584

### FLUORESCENCE OPTICAL IMAGING ENHANCEMENT IS ASSOCIATED WITH JOINT PAIN IN HAND OSTEOARTHRITIS

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**Background:** Joint inflammation plays a role in the pathogenesis of hand osteoarthritis (OA), and previous studies have presented an association between pain and synovitis detected by MRI and ultrasound. No previous hand OA studies have explored the validity of fluorescence optical imaging (FOI), a novel imaging technique demonstrating altered microcirculation in wrist and finger joints, as a sign of inflammation.

**Objectives:** The aims of the current study were to quantify the distribution of FOI findings in different joint groups in hand OA patients and explore the association between FOI findings and self-reported pain and tender joints on clinical examination.

**Methods:** The NOR-HAND study is an observational hand OA study, in which 251 patients (88% female, median age 61 (interquartile range 56–66) years) underwent FOI of both hands, bilateral clinical examination for tender joints on palpation and movement, and self-reported their pain in individual joints during the last 24 hours and the last 6 weeks on the homunculus. The FOI-scan was performed after the administration of an intravenous fluorescence dye (indocyanine green, ICG) and 360 images (1/second) were produced in 6 min. Based on the inflow and washing out of the dye the pictures were divided into 3 phases. Ultimately, the prima vista mode (PVM) represented a composite picture of the first 240 images of the examination. For each phase, fluorescence enhancement in the joints was graded from 0–3 based on signal intensity (grade 1=diffuse red, grade 2=intense red and diffuse white <50% of the joint, grade 3=intense white >50% of the joint). To study the association between FOI findings and pain in the same joint we applied logistic regression analyses with generalised estimating equations adjusting for age and sex. Separate models were applied for each of the FOI phases and pain outcomes.

**Results:** The median (interquartile range) number of DIP/PIP joints with FOI enhancement within each patient ranged from 0 (0–0) in phase 1,  $14^{11-16}$  in phase 2, 3 (0–8) in phase 3 and  $9^{7-11}$  in PVM. CMC-1 and MCP-joints showed no and uncommon enhancement on the examination, respectively, regardless of the phase, and the associations between FOI and pain were therefore analysed in the DIP and PIP joints only. FOI enhancement in the DIP and PIP joints was associated with pain in the same joint, consistent for all three pain outcomes. A dose-



response relationship was found for phase 2, phase 3 and PVM, but not in phase 1 (table 1). Few joints showed enhancement in phase 1 and a clear dose-response relationship was found for pain during the last 24 hours only (data not shown).

Associations between FOI Enhancement and Pain in the same DIP and PIP Joints.			
	Self-reported pain last 24 hours	Self-reported pain last 6 weeks	Tender joint on clinical exam
	OR (95 % CI)	OR (95 % CI)	OR (95 % CI)
<b>FOI phase 1</b>			
Grade 0	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)
Grade 1-3	1.50 (0.94, 2.40)	1.92 (1.20, 3.09)	2.42 (1.37, 4.25)
<b>FOI phase 2</b>			
Grade 0	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)
Grade 1	1.26 (1.02, 1.55)	1.15 (0.93, 1.44)	2.15 (1.81, 2.55)
Grade 2	1.94 (1.58, 2.38)	1.92 (1.52, 2.41)	2.69 (2.21, 3.26)
Grade 3	2.25 (1.61, 3.15)	2.53 (1.73, 3.69)	4.00 (2.85, 5.59)
<b>FOI phase 3</b>			
Grade 0	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)
Grade 1	1.76 (1.42, 2.17)	1.73 (1.40, 2.14)	2.15 (1.77, 2.61)
Grade 2+3*	2.29 (1.30, 4.06)	2.51 (1.33, 4.73)	3.21 (1.91, 5.39)
<b>FOI Prima Vista Mode</b>			
Grade 0	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)
Grade 1	1.36 (1.14, 1.61)	1.38 (1.14, 1.68)	2.20 (1.88, 2.56)
Grade 2**	2.37 (1.88, 2.98)	2.33 (1.81, 3.00)	3.22 (2.57, 4.04)

\* Grades 2 and 3 combined due to few joints with grade 3 in phase 3. \*\* No joints with grade 3 in prima vista mode (PVM).

**Conclusions:** In this first hand OA study, FOI enhancement was frequently found in the DIP and PIP joints, whereas the method seems insensitive to detect inflammation in the CMC-1 joints. FOI enhancement was related to self-reported pain and to tender joints on clinical examination, supporting the validity of the FOI examination in patients with hand OA.

**Disclosure of Interest:** None declared

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**FRI0585** **PREVALENCE OF ANTI-ACETYLATED PROTEIN ANTIBODIES IN INFLAMMATORY ARTHRITIS, OSTEOARTHRITIS, CONNECTIVE TISSUE DISEASES AND ITS DISCRIMINATIVE CAPACITY AS DIAGNOSTIC MARKER FOR EARLY RHEUMATOID ARTHRITIS**

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**Background:** Numerous post-translationally modified proteins have been described as auto-antigens in rheumatoid arthritis (RA) patients. Antibodies (abs) against acetylated (ac) peptides (AAPA) have recently been reported in RA patients, but not yet been evaluated in other inflammatory and non-inflammatory

rheumatologic conditions; therefore their specificity (spec) and sensitivity (sens) remains unclear.

**Objectives:** To determine the prevalence of AAPA in RA, healthy subjects and other rheumatic diseases in order to evaluate their diagnostic potential for discriminating RA, healthy and other rheumatic diseases.

**Methods:** We obtained serum samples of patients with early untreated RA, established RA (>3 years), osteoarthritis (OA), systemic lupus erythematosus, granulomatosis with polyangiitis (GPA), polymyositis, axial spondyloarthritis, primary Sjögren's syndrome and healthy subjects. AAPA were measured by ELISA using peptides derived from mutated vimentin (acetylation of lysine or ornithine in position 7 or 2 (inverse peptide), as antigen. Receiver operating characteristics and logistic regression analyses were used to assess the discriminative capacity of AAPA.

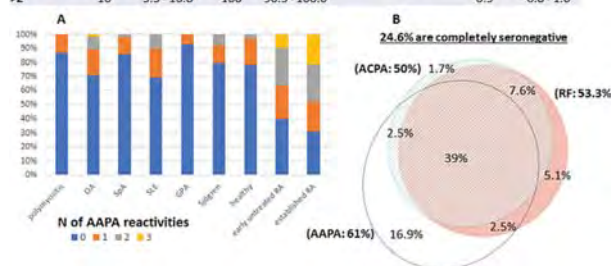
**Results:** Areas under the curves (AUC) were significant in early RA (eRA; n=120; 75% female, mean disease duration: -0.07±0.51 years, mean symptom duration 1.49±2.01 years) versus healthy subjects for IgG-abs against ac lysine, inverse lysine and ornithine (AUC of 0.666, 0.687, 0.800, respectively). We chose a cutoff of 20 U/ml putting an emphasise on high spec, with balanced sens (ac-lysine: spec: 97.0%; sens: 32.5%;+likelihood ratio (LR) 10.7, CI: 3.4–33.7; ac-inverse-lysine: spec: 80.7%; sens: 42%;+LR 2.2, CI: 1.3–3.6; ac-ornithine: spec: 93.9%; sens: 39.2%;+LR 6.5; CI: 2.9–14.5). Analyses of positivity for multiple ab-reactivity revealed increasing +LR by number of abs, with 100% specificity when all 3 AAPAs are detected (table 1). Testing this cutoff against OA patients showed similar specificities, but with lower +LR (2 AAPA:+LR 3.48, CI: 1.9–6.6). Sens is increased when testing established RA versus healthy controls, with ac-ornithine performing best (ac-lysine: 49.2%, CI: 42.0–56.5; ac-inv-lysine: 35.2%, CI: 28.5–42.4; ac-ornithin: 53.9%, CI: 46.6–61.0)

We found that practically only RA patients showed three different AAPA reactivities (in eRA: 39% positive for ac-ornithine abs, 33% for ac-lysine abs, 48% for inverse ac-lysine abs). Polymyositis and GPA patients showed the lowest prevalence of AAPA (**Graph 1A**).

Among eRA patients 17% were found to be exclusively positive for AAPA, while 39% were also positive for rheumatoid factor (RF) and anti-citrullinated antibodies (ACPA) (distribution in **Graph 1B**). Also in RF- and ACPA- patients the presence of one AAPA identified RA patients vs. healthy subjects with a spec of 77.7% and those with 2 AAPA reactivities with even 97% respectively.

**Abstract FRI0585 – Table 1.** Sensitivity, specificity, positive and negative likelihood ratio (LR) for identifying early RA patients against healthy controls by the number of AAPA reactivities

N of AAPA	Sensitivity	95% CI	Specificity	95% CI	+LR	95% CI	-LR	95% CI
>0	60	50.7- 68.8	77.78	68.3- 85.5	2.7	1.8- 4.0	0.51	0.4- 0.7
>1	36.67	28.1- 45.9	96.97	91.4- 99.4	12.1	3.9- 37.8	0.65	0.6- 0.8
>2	10	5.3- 16.8	100	96.3- 100.0			0.9	0.8- 1.0



**Graph 1A:** Prevalence (in%) of IgG antibodies against the 3 different acetylated peptides using 20 U/ml as cutoff

**Graph 1B:** Venn diagram, outlining the distribution and overlap of AAPA (blue circle), ACPA (striped circle) and RF (rose circle) in early rheumatoid arthritis patients (n=120)

**Conclusions:** AAPA are highly prevalent autoantibodies in early RA, closing a further gap of seronegativity, with only 24.6% of early RA patients remaining negative for RF, ACPA or AAPA. In particular, multiple reactivity to AAPA increased the specificity for eRA, also adding diagnostic value beyond RF and ACPA.

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FRI0586

### LONGITUDINAL ASSESSMENT OF CORTICAL INTERRUPTIONS AND VBMD IN RA AND HEALTHY SUBJECTS USING HR-pQCT

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**Background:** Preservation, repair and progression of cortical interruptions in finger joints has been observed in RA using conventional radiography, MRI, ultrasound and high-resolution peripheral quantitative computed tomography (HR-pQCT). Accurate and quantitative information about such changes over time, however, is still lacking.

**Objectives:** To evaluate changes over one year in cortical interruptions (number, surface area and volume), bone density (vBMD) and micro-structural parameters from HR-pQCT scans of finger joints in RA and healthy subjects (HS) using a recently developed semi-automatic algorithm for cortical interruptions detection.<sup>1</sup>

**Methods:** Baseline and 1 year follow up HR-pQCT scans of finger joints of 32 patients with RA (221 joints, 53% on biologic DMARDs (bDMARDs)) and 32 HS (117 joints) were analysed for changes in cortical interruption, density and morphological parameters. Mean changes (at the group level) and proportions of joints (at the joint level) with changes beyond least significant changes were calculated after correction for baseline damage.

**Results:** At baseline, 530 interruptions (3.25/joint) were identified in RA, and 136 (1.45/joint) in HS. The mean of the interruption parameters did not change in either group, except for a significant increase in number of interruptions in PIP joints in RA. However, the proportion of joints showing repair in interruption volume was higher in RA than in HS (6.6% versus 1.7%,  $p=0.041$ ). Changes in cortical interruption parameters were negatively correlated with changes in cortical BMD and thickness ( $p<0.01$ ). Mean vBMD decreased more and more joints showed loss of vBMD in RA than in HS ( $-4.4$  versus  $-1.1$  mgHA/cm<sup>3</sup> and 26.7% versus 12.9%, respectively, both  $p<0.01$ ). Proportionally more joints showed interruptions and loss of vBMD in patients with synthetic DMARDs (sDMARDs) compared to bDMARDs (6.1% versus 1.8% and 31.3% versus 17.2%, respectively, both  $p<0.05$ ).

**Conclusions:** Using HR-pQCT based semi-automatic cortical interruption analysis a large number of interruptions was identified in RA and HS. Cortical interruptions, vBMD and micro-structural parameters were more impaired in RA, of which vBMD and micro-structural parameters further deteriorated. Patients on sDMARDs had more joints with progression in number of interruptions and more loss of vBMD compared to bDMARDs.

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FRI0587

### LOW BACK PAIN DUE TO ENTHESOPATHY OF ERECTOR SPINE MUSCLE: A COMPARATIVE US AND MRI STUDY IN PATIENTS WITH ILIAC CREST PAIN SYNDROME

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**Background:** Iliac crest pain syndrome (ICPS) is a regional pain syndrome, that is particularly common in patients with low back pain (LBP). It is characterised clinically by pain perceived maximally at the most medial part of the posterior iliac crest, and patients' recognition of the pain provoked by a systematic digital palpation in this area, as "their" typical one. Though ICPS is very frequently encountered in LBP, the exact etiology of this syndrome was not established. Based on anatomical data, it was suggested that ICPS could be caused by a tendopathy/ enthesopathy of erector spine (ES) muscle attachments to the medial iliac crest (MIC).<sup>(1)</sup> In a previous anatomical and ultrasound (US) study we showed that this in fact might be the case.

**Objectives:** The purpose of this study was, regarding the existing clinical diagnostic criteria for the ICPS as a "gold standard", to establish the sensitivity,

specificity, positive and negative predictive values (PPV and NPV) and the overall accuracy of the US and the Magnetic Resonance Imaging (MRI) assessment of the entheses of the ES muscle at the MIC in patients with LBP and features indicative of ICPS.

**Methods:** 25 patients (9 men, 16 women, mean age 43.12±11.83, mean BMI 25.07±2.36) with anamnesis of chronic "nonspecific" (after lateral X-ray and standard clinical examination) LBP perceived maximally in the region of the MIC uni- or bilaterally were included. First a systematic palpation of the posterior MIC bilaterally was performed to diagnose ICPS clinically. Then in two successive days each patient underwent MRI examination of the lower back (lumbar and sacroiliac regions), with an enlarged field of view in the sagittal plane, and a standardised US examination of the ES terminal tendons and entheses bilaterally. The MRI were assessed by a radiologist with 10 years of experience in MRI. The sonographies were performed by a rheumatologist with 7 years of experience in US and analysed in regards with the OMERACT definition of enthesopathy. As a single US lesion at any enthesis is a common finding, the presence of at least two pathological features were required to classify given entheses as abnormal.

**Results:** ICPS was identified clinically in 20 of the patients (15 unilateral and 5 bilateral), thus 25 of the total 50 entheses were clinically pathological. Comparing to the clinical findings, the calculated sensitivity, specificity, PPV, NPV and overall accuracy of the US and the MRI assessments of the ES entheses at the MIC are placed in table 1:

	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	Accuracy (95% CI)
US	88% (69%–97%)	80% (60%–93%)	82% (67%–91%)	87% (69%–93%)	84% (71%–93%)
MRI	64% (43%–82%)	80% (59%–93%)	76% (58%–88%)	70% (56%–80%)	71% (59%–85%)

**Conclusions:** This study shows that enthesopathy of the ES muscles could be the unrecognised cause for most of the cases of ICPS –a regional syndrome particularly common in LBP. US performed better than the MRI in diagnosing this pathological condition, that may reflect the fact that radiologists are not used to assess these structures. The good diagnostic properties of US in ICPS could be of value when assessing patients with otherwise "nonspecific" LBP.

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FRI0588

### ULTRASOUND COULD HAVE PREVENTED DMARD ESCALATION IN RHEUMATOID ARTHRITIS WITH FIBROMYALGIA

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**Background:** Despite the growing body of evidence, the proper use of ultrasound (US) in monitoring disease activity still needs better understanding.<sup>1,2</sup> As an objective measure, US could prevent overtreatment in situations of overestimation of clinical disease activity, such as fibromyalgia, present in up to 20% of patients with rheumatoid arthritis (RA).<sup>3–5</sup>

**Objectives:** To verify how ultrasound (US) could impact rheumatoid arthritis (RA) treatment decision in real life when fibromyalgia (FM) was also present.

**Methods:** A retrospective cohort study was performed from 2011 through 2016, including RA patients with FM. Patients were grouped according to US examination (Group DAS28: never performed US examination; Group US: at least one US exam). RA was considered active if DAS28  $\geq 3.2$  in Group DAS28 or PD  $\geq 2$  in any single joint in Group US.

**Results:** Out of 230 RA patients, 22 women with concomitant FM (Group DAS28=10 and Group US=12) were seen in 280 visits from 2011 through 2016. DAS28 was 4.4 (2.5–6.3) vs. 4.0 (2.0–5.0) ( $p=0.592$ ) in Groups DAS28 and US, respectively.

DMARD treatment was escalated in 12.9% of visits in Group DAS28 versus 8.2% in Group US ( $p=0.791$ ) (table 2). The relative risk (RR) for DMARD escalation in Group US compared to Group DAS28 was 1.08 (95%CI 0.60–1.95). However, in 74% of visits in Group US, DMARD was escalated despite a negative US result. In a theoretical scenario where US result oriented treatment decision, DMARD was escalated in 3.6% of visits in Groups DAS28 and US, respectively (table 1). Also, in this US-based scenario, the RR for DMARD escalation in Group US compared to Group DAS28 was 0.39 (0.19–0.83).

The proportion of visits with US evaluation increased over time, nonetheless the level of agreement between US synovitis (PD  $\geq 2$ ) and DMARD escalation

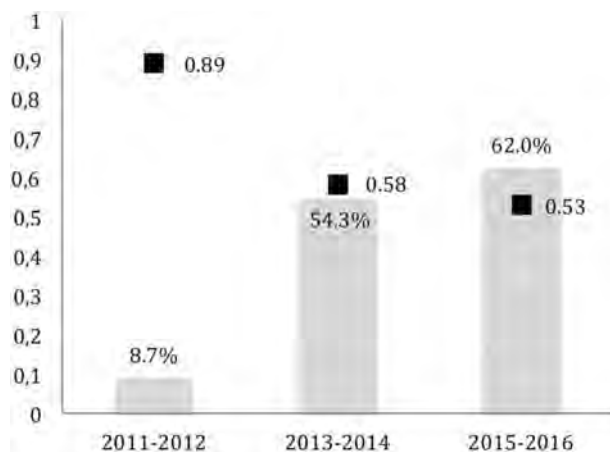


decreased (figure 1). Despite indicating US examination more frequently, rheumatologists did not base their DMARD escalation decision on PD synovitis.

**Abstract FRI0588 – Table 1.** Visits distribution according to DMARD escalation and groups

	Group DAS28 (n=175)	Group US (n=105)	
	DAS28	Observed	Theoretical
DMARD escalated*	36 (12.9)	23 (8.2)	10 (3.6)
DMARD not escalated*	139 (49.6)	82 (29.3)	95 (33.9)

\*Numbers (%) of visits;  $p=0.791$  (chi-square test) between Group DAS28 and Observed Group US;  $p=0.012$  (chi-square test) between DAS28 and Theoretical Group US



**Abstract FRI0588 – Figure 1.** Proportion of visits with US evaluation (bars) and level of agreement between US synovitis ( $PD \geq 2$ ) and DMARD escalation (kappa coefficients;  $P < 0.001$  for all).

**Conclusions:** In this real-life study of RA patients with FM, the growing use of US for evaluating RA activity over time was associated with an increasing discordance between US result and clinical judgement. When clinical judgement and US findings were discordant, RA treatment decision was mostly based on clinical judgement. If US result oriented treatment decision, DMARD escalation risk would be 61% smaller.

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FRI0589

#### A JOINT PROCEDURAL RECOMMENDATION ON FDG-PET/CT(A) IMAGING IN LARGE VESSEL VASCULITIS AND POLYMYALGIA RHEUMATICA FROM THE CARDIOVASCULAR AND INFLAMMATION & INFECTION COMMITTEES OF THE EANM, THE CARDIOVASCULAR COUNCIL OF THE SNMMI, THE PET INTEREST GROUP (PIG), AND ENDORSED BY THE ASNC

R. Slart on behalf of Members of EANM Cardiovascular, EANM Infection & Inflammation Committees, SNMMI Cardiovascular Council, PET Interest Group, and ASNC. *Medical Imaging Center, departments of Nuclear Medicine and Radiology, University Medical Center Groningen, Groningen, Netherlands*

**Background:** [18F]-fluorodeoxyglucose positron emission tomography combined with anatomical computed tomography angiography, (FDG-PET/CTA) is increasingly used in Large Vessel Vasculitis (LVV, consisting of Giant Cell Arteritis (GCA) and Takayasu Arteritis (TA)) and Polymyalgia Rheumatica (PMR), and may be of value for optimal diagnosis, disease activity monitoring, and evaluation

of damage development. There are currently no general accepted procedural guidelines regarding PET imaging acquisition for LVV and PMR.

**Objectives:** The aim of our study is to provide recommendations and statements, based on the available evidence in the literature combined with consensus of experts in the field, for patient preparation, FDG-PET/CT(A) acquisition and interpretation.

**Methods:** A systematic literature review was conducted to retrieve data on FDG-PET/CT(A) imaging in LVV and PMR. Expert consensus was used to propose recommendations in the absence of sufficiently robust data. Levels of evidence and grades of recommendations were attributed to the statements of different indications according to published criteria.

**Results:** Based on the literature review combined with expert consensus recommendations and statements that could be formulated: see table 1.

Recommendations and statements	Level of evidence	Grade
Fasting the patient for at least 6 hours prior to FDG administration	II	B
Normal blood glucose levels are desirable, but glucose levels below 10 mmol/L (180 mg/dL) are acceptable	II	B
FDG/PET within three days after start of GC is optional as a possible alternative	III	B
A minimum interval of 60 minutes is recommended between FDG administration and acquisition for adequate biodistribution	III	B
Use of a standardized grading system	II	B
Typical FDG joint uptake patterns should be evaluated and reported if present	II	B
Normalization of the arterial wall uptake to the background activity of venous blood pool provides a good reference to assess vascular inflammation	II	B
Normalization of the arterial wall uptake to the background activity of venous blood pool provides a good reference to assess vascular inflammation	II	B
Based on the available evidence, FDG-PET imaging has high diagnostic performance for the detection of LVV and PMR	II	B
CTA and FDG-PET have complementary roles in the diagnosis of LVV	III	B
CTA has incremental value in detecting structural vascular changes and potential complications of vasculitis	II	A
FDG-PET/CT(A) may be of value to evaluate response to treatment by monitoring functional metabolic information and detecting structural vascular changes	III	C

**Conclusions:** This joint recommendation highlights that standardisation and general consensus regarding the optimal procedural performance of FDG-PET/CT(A) imaging in LVV and PMR are highly needed. Some recommendations and statements could be formulated however, there are also a lot of open issues which need to be studied for optimal performance of FDG-PET/CT(A) in the diagnosis, (treatment)monitoring and future theranostics in LVV/PMR to increase the levels of evidence and improve the grades of the recommendations.

**Disclosure of Interest:** None declared

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FRI0590

#### ULTRASOUND EXAMINATION OF THE WRIST JOINTS: FREQUENCY OF CRISTAL DEPOSITS (CHONDROCALCINOSIS) IN PATIENTS WITH DIFFERENT ARTHROPATHIES

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**Background:** Hand involvement in the rheumatic diseases is often precocious and predominant as compared to other skeletomuscular regions. The Ultrasound (US) has an important role in early calcium pyrophosphate deposition disease (CPPD) diagnosis. Recent studies suggest a positive association of CPPD and other rheumatic disease.<sup>1,2</sup>

**Objectives:** To investigate the frequency of the US features of chondrocalcinosis (CC) at the triangular fibrocartilage complex (TFC) of the wrist in patients (pts) with different arthropathies.

**Methods:** A total of forty persons were included in the study and were divided into 4 groups (on ten in each group): basic group – CPPD pts (crystal-proven at synovial fluid analysis; median age 58.5 (range 45–63) years; 6M/4F) and the control groups – rheumatoid arthritis pts (RA, ACR/EULAR 2010 age 50.5 (44–56) years; 3M/7F), psoriatic arthritis pts (PsA, CASPAR criteria; age 50(37–59) years; 3M/7F), healthy volunteers (age 37.5 (33–55) years; 3M/7F). All subjects were carefully age and gender matched with the CPPD pts. US examinations (“Voluson-i” (GE, USA), 4–13 MHz probe) were performed by one examiner. TFC of the wrist was assessed to detect US findings of crystal deposits.<sup>3</sup> The Mann-Whitney U-test was applied for intergroup comparison.

**Results:** In all CPPD pts (100%) CC of TFC was detected in at least one joint. In the control groups intra-cartilaginous hyperechoic spots were found in 6 of 10



cases with RA (60% vs. 100%,  $p=0.029$ ), in 2 with PsA (20% vs. 100%,  $p<0.01$ ), 3 cases in healthy volunteers (30% vs. 100%,  $p<0.01$ ).

**Conclusions:** The results of the present study indicate that US is a very sensitive and specific technique for detecting calcifications in patients with crystal-related arthropathy. The US findings were detected a trend of association between CC and RA. However, more studies, involving a larger number of pts, are required.

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**Disclosure of Interest:** None declared

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FRI0591

#### WHOLE-BODY MRI DEMONSTRATES REDUCTION OF INFLAMMATION IN PERIPHERAL JOINTS AND ENTHESES DURING TNF-INHIBITOR TREATMENT IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS, BUT ALSO AGE-DEPENDENT PERSISTENT INFLAMMATION IN JOINTS PRONE TO OSTEOARTHRITIS

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**Background:** Patients with predominantly axial spondyloarthritis (axSpA) may also have inflammation of peripheral joints and entheses. Using a whole-body MRI (WBMRI) approach, peripheral joints and entheses can be assessed objectively and followed during treatment.

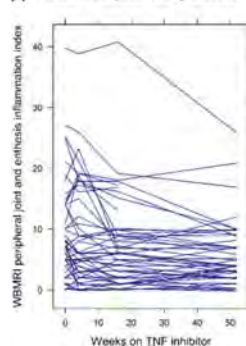
**Objectives:** To describe the localization and extent of inflammation of peripheral joints and entheses by WBMRI in patients with axSpA initiating TNF-inhibitor therapy, and to assess treatment-induced changes.

**Methods:** Fifty-three patients that fulfilled the ASAS criteria for axSpA were included. MRI of SIJs and spine and WBMRI of peripheral joints and entheses were performed at baseline and 4/16/52 weeks after starting TNF inhibitor treatment. 75 peripheral joints and 30 peripheral entheses were scored in chronological order by an experienced musculoskeletal radiologist (IE). Osteitis, synovitis and enthesal soft tissue inflammation were scored separately [0(none)/1(mild)/2 (moderate/severe)]. A WBMRI peripheral joint and entheses index (WBMRI index) was derived by summing scores of all peripheral lesions.

**Results:** Median age (IQR/range) was 35 years. (28–44/22–73); median symptom duration was 5 years. (3–13/0–31); 53% were male. Baseline median WBMRI index (n=53) was 7.4–14; 0–40 after 52 weeks (n=46) 4 (2–9; 0–26). WBMRI index decreased mean 0.6 at week 4 ( $p=0.17$ , paired t-test), 2.3 at week 16 ( $p<0.001$ ) and 3.2 at week 52 ( $p<0.001$ ). Thirty-seven patients (70%) had a relatively low baseline WBMRI index ( $\leq 10$ ) with minor change over time, while patients with higher baseline scores tended to change more (figure 1A). The most frequently involved sites ( $\geq 15\%$  of patients) were typical for SpA (sternoclavicular joint/planter fascia) or osteoarthritis (carpometacarpal-1/metatarsophalangeal-1 synovitis). In univariate analysis, WBMRI index at week 52 was associated with age (2.5 higher per 10 years increase in age,  $p<0.001$ ) and male sex (3.6 lower in men,  $p=0.021$ ), but not with body-mass index, HLA-B27, C-reactive protein or ASDAS at week 52. In multivariate regression with age and sex as covariates, only age was significantly associated with WBMRI index (2.3 per 10 years increase in age,  $p<0.001$ ) whereas sex was not ( $p=0.24$ ).

In univariate analysis, higher age was not significantly associated with change in WBMRI index, but when adjusted for baseline WBMRI index, higher age was associated with a less prominent reduction in WBMRI index (+0.9 per 10 years increase in age).

#### A Individual patient trajectories



#### B Most frequently involved sites ( $\geq 15\%$ of patients) for 46 patients with available data at baseline and 52 weeks of follow-up

	Baseline	52 weeks
<b>JOINTS:</b>		
Wrist synovitis	23	20
CMC1 synovitis	17	7
Ankle synovitis	11	7
MTP1 synovitis	15	10
MTP2-5 synovitis	9	5
Sternoclavicular synovitis	13	10
Sternoclavicular osteitis	16	11
Manubriosternal osteitis	7	5
Acromioclavicular synovitis	14	13
Shoulder synovitis	8	5
Knee synovitis	7	3
<b>ENTHESES:</b>		
Plantar fascia osteitis	7	4
Plantar fascia soft tissue infl.	6	2
Tuberculum humeri osteitis	8	8
Pubic symphysis osteitis	8	2
Greater trochanter soft tissue infl.	17	12

**Conclusions:** Inflammation of peripheral joints and entheses decreased over time in a cohort of patients with predominantly axSpA. Most patients had WBMRI index above zero during follow-up, and this was related to age and involved sites prone to osteoarthritis. Thus, the WBMRI Index may capture both disease activity related to axSpA and age-related degenerative changes.

**Disclosure of Interest:** None declared

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FRI0592

#### SCORING MRI INFLAMMATION AND STRUCTURAL LESIONS IN SACROILIAC JOINTS OF PATIENTS WITH AXIAL SPONDYLOARTHRITIS: IS INTER-READER RELIABILITY DEPENDENT ON THE NUMBER OF MRI SLICES?

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**Background:** The SPARCC sacroiliac joint (SIJ) scoring system assesses 6 semicoronal MRI slices for inflammation and 5 slices for structural lesions in patients with axial spondyloarthritis (axSpA).<sup>1,2</sup> However, the cartilaginous SIJ compartment may show 1–2 additional slices anteriorly or posteriorly, depending on body size and scan orientation/tilt.

**Objectives:** To investigate inter-reader reliability of an “all slices” approach versus the standard SPARCC scoring of 6/5 slices.

**Methods:** Fifty-three patients with axSpA were treated with TNF inhibitor and had MRIs obtained at weeks 0/4/16/52. An experienced (UW) and two newly trained (GK, SK) blinded readers independently scored 199 SIJ MRI scans in chronological order. The cartilaginous SIJ compartment was scored slice by slice by the SPARCC 6/5 slices approach and by all available cartilaginous slices. Initially, the most anterior and posterior slices covering the cartilaginous compartment and the transitional slice were identified. The transitional slice was defined as the most anterior cartilaginous slice with the first portion of the ligamentous compartment, clearly visible on the left and/or right side. We scored SIJ inflammation, fat metaplasia, erosion and backfill, and a combined erosion and backfill score was created. Inter-reader reliability for reader pairs SK-UW/GK-UW/SK-GK was assessed using percent agreement (for individual scores) and intra-class correlation coefficients for sum scores.

**Results:** Pairwise percent agreement was 67%/63%/79% for identification of anterior slice, 47%/56%/44% for posterior slice and 69%/68%/72% for transitional slice. Using the “all slices” approach, readers UW/SK/GK scored mean 7.2/7.7/7.0 slices per MRI scan.

“6/5 slices” and “all slices” correlated closely with each other for status scores at baseline/status scores at week 52, and change scores at week 52; BME 0.983/0.985/0.983; fat metaplasia 0.994/0.982/0.953; erosion 0.981/0.974/0.957; backfill 0.993/0.983/0.978; combined erosion and backfill 0.983/0.971/0.919.

Inflammation (standard 6 slices)		Inflammation ("all slices")		Inflammation (extra slices in "all slices" not part of 6 slices)		
Scores	ICC(3,1)	Scores	ICC(3,1)	Scores	ICC(3,1)	
Status score at baseline	13 (6-21, 0-49)	0.81/0.77/0.84	14 (6-23, 0-49)	0.84/0.77/0.86	1 (0-3, 0-15)	0.65/0.52/0.73
Status score at week 52	2 (0-4, 0-12)	0.67/0.70/0.50	2 (0-5, 0-13)	0.67/0.69/0.46	0 (0-1, 0-2)	0.19/0.65/0.20
Change score (baseline to week 52)	-12 (-2 to -3)	0.84/0.81/0.87	-13 (-26 to -4)	0.86/0.79/0.90	-1 (-1 to 0)	0.61/0.54/0.74
Fat metaplasia (standard 5 slices)		Fat metaplasia ("all slices")		Fat metaplasia (extra slices in "all slices" not part of 5 slices)		
Scores	ICC(3,1)	Scores	ICC(3,1)	Scores	ICC(3,1)	
Status score at baseline	3 (0-10, 0-38)	0.89/0.64/0.81	4 (1-12, 0-48)	0.92/0.63/0.77	0 (0-2, 0-30)	0.80/0.40/0.49
Status score at week 52	7 (1-14, 0-25)	0.81/0.53/0.77	8 (2-19, 0-51)	0.87/0.57/0.79	1 (0-4, 0-16)	0.70/0.53/0.55
Change score (baseline to week 52)	1 (0 to 4)	0.75/0.39/0.47	2 (0 to 7)	0.84/0.34/0.46	0 (0 to 1)	0.60/0.64/0.48
Erosion (standard 5 slices)		Erosion ("all slices")		Erosion (extra slices in "all slices" not part of 5 slices)		
Scores	ICC(3,1)	Scores	ICC(3,1)	Scores	ICC(3,1)	
Status score at baseline	7 (1-11, 0-18)	0.70/0.66/0.73	8 (1-14, 0-23)	0.74/0.67/0.70	1 (0-2, 0-4)	0.45/0.18/0.62
Status score at week 52	8 (1-6, 0-16)	0.43/0.39/0.75	4 (1-8, 0-18)	0.42/0.38/0.69	1 (0-2, 0-4)	0.39/0.09/0.40
Change score (baseline to week 52)	-2 (-5 to 0)	0.23/0.23/0.60	-1 (-4 to 0)	0.23/0.29/0.37	0 (-1 to 0)	0.04/0.05/0.29
Backfill (standard 5 slices)		Backfill ("all slices")		Backfill (extra slices in "all slices" not part of 5 slices)		
Scores	ICC(3,1)	Scores	ICC(3,1)	Scores	ICC(3,1)	
Status score at baseline	0 (0-3, 0-11)	0.53/0.42/0.60	0 (0-3, 0-13)	0.48/0.39/0.63	0 (0-0, 0-2)	0.08/0.40/0.50
Status score at week 52	1 (1-5, 0-9)	0.26/0.44/0.75	4 (1-6, 0-18)	0.23/0.43/0.71	0 (0-1, 0-4)	-0.01/0.28/0.4
Change score (baseline to week 52)	1 (0 to 3)	0.33/0.41/0.66	2 (0 to 4)	0.35/0.41/0.74	0 (0-1)	0.01/0.22/0.58
Combined erosion and backfill (standard 5 slices)		Combined erosion and backfill ("all slices")		Combined erosion and backfill (extra slices in "all slices" not part of 5 slices)		
Scores	ICC(3,1)	Scores	ICC(3,1)	Scores	ICC(3,1)	
Status score at baseline	10 (2-14, 0-18)	0.68/0.47/0.73	12 (2-16, 0-24)	0.70/0.68/0.73	1 (0-3, 0-7)	0.52/0.31/0.66
Status score at week 52	8 (1-11, 0-20)	0.57/0.49/0.78	10 (4-14, 0-24)	0.41/0.71/0.79	1 (0-3, 0-8)	0.46/0.36/0.71
Change score (baseline to week 52)	-1 (-3 to 0)	0.22/0.18/0.45	-1 (-2 to 0)	0.18/0.25/0.30	0 (-1 to 0)	0.09/0.08/0.40

Scores reported as median (IQR), range. ICCs are ICC(3,1), single rater. Agreements, in pairwise comparisons (SK-UW/UK-UW/SK-GK). N = 53 for status score at baseline; N = 46 for status score at week 52 and change score (baseline to week 52).

**Conclusions:** The standardised 6/5 slices SPARCC methods had equal reliability as compared to evaluation of all cartilaginous slices. There was limited reliability to identify the posterior slice in the "all slices" approach, as opposed to good reproducibility to determine the transitional slice in the "6/5 slices" approach. Combining erosion and backfill scores tended to result in superior reliability compared to the 2 lesions separately, indicating a challenge to identify the transition from erosion to backfill.

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**Disclosure of Interest:** None declared

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FRI0593

#### MANTOUX TEST IS INADEQUATE TO DEFINE ALL SUBJECTS WITH LATENT TUBERCULAR INFECTION

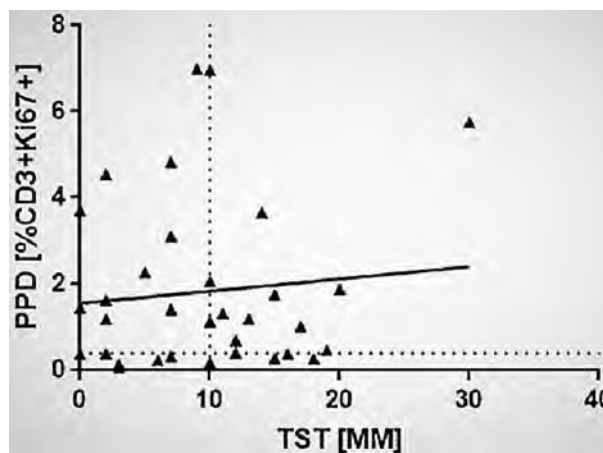
S. Arya<sup>1</sup>, S. Kumar<sup>1</sup>, A. Nath<sup>2</sup>, P. Kapoor<sup>3</sup>, A. Aggarwal<sup>1</sup>, R. Misra<sup>1</sup>, S. Sinha<sup>1</sup>.  
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**Background:** Latent TB infection (LTBI), defined as 'a state of persistent immune response to *Mycobacterium tuberculosis* without clinically-manifested disease', inflicts a third of the world's population and nearly 10% of LTBI positive persons develop TB within 2-5 years. The tuberculin skin test (TST) and, more recently, interferon gamma release assays (IGRAs) are most commonly used for detection of LTBI. However, in a high TB burden setting such as India, both the assays have been found to grossly underestimate the true prevalence of LTBI, since almost equal number of new TB cases emerged from the test-positive and test-negative groups during the follow-up<sup>1</sup>.

**Objectives:** This study was aimed at exploring whether an *in vitro* CD3 + T cell response to PPD can complement the *in vivo* TST response for the determination of true prevalence of LTBI in healthy Indians.

**Methods:** In this ongoing study, 80 apparently healthy workers (age 19-61 years) at SGPGIMS have been recruited. Their demographic data, including BCG vaccination status and duration of contact with TB patients, was recorded. TST was performed with 5 TU of PPD. Blood T cell (CD3+) responses to PHA (a mitogen, used as positive control) and PPD were determined by flow cytometry in terms of expression of the proliferation-induced nuclear protein Ki67.

**Results:** 48% of the study subjects showed positivity for TST (skin induration  $\geq 10$  mm) and the size of reaction could be correlated with age. There was no association between BCG vaccination status and TST positivity. 72% of the TST positive and 62% of TST negative persons showed positivity for CD3 + T cell response to PPD. Positivity for either assay was found to be 82%.



**Conclusions:** By combining TST with CD3 + T cell responses, the positivity for PPD was enhanced from 48% (TST alone) to 82%. Therefore, both the assays could be considered as complementary. It remains to be seen whether these assays, either singly or jointly, show a correlation with the emergence of TB in our study population during the follow-up.

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**Disclosure of Interest:** None declared

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FRI0594

#### RETROCALCANEAL BURSTITIS PRECEDES OR ACCOMPANIES ACHILLES TENDON ENTHESITIS IN THE EARLY PHASE OF RHEUMATOID ARTHRITIS

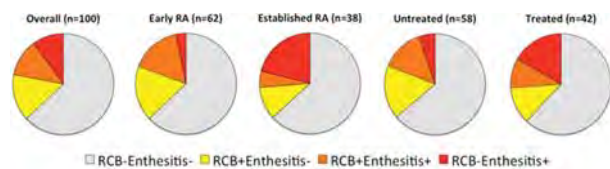
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**Background:** We had reported the frequencies of various pathologies detected by ultrasound (US) in symptomatic ankles and heels in rheumatoid arthritis (RA) patients<sup>1</sup>. Through that study, we recognised that Achilles tendon (AT) involvement is not rare in RA, because retrocalcaneal bursitis (RCB), AT enthesitis, AT tendonitis and AT paratendonitis was detected in 27%, 22%, 13%, and 6% of the symptomatic ankles examined, respectively. Recently, it has been reported that RA and SpA patients did not differ in enthesial abnormalities seen on US<sup>2</sup>. However, we think that there is fundamental difference between the inflammation of synovio-enthesial complexes in RA and that in SpA.

**Objectives:** This study aims to investigate characteristics of enthesial abnormalities in RA by evaluating the association between US-detected RCB or AT enthesitis and clinical data.

**Methods:** We reviewed consecutive records of 100 ankles in 74 RA patients (fulfilling the 2010 criteria) who underwent US examination of symptomatic ankles because of clinical need. The patients consist of 52 women and 22 men (median age 63.3 years, range 26-83 years) with median disease duration of 4.2 months (range 0.23 months to 19.4 years), as described previously. 55/74 (74%) of them were positive for RF and/or ACPA. The association between presence of RCB or AT enthesitis in a narrow definition (i.e., insertional tendinitis) and clinical data were analysed using Fisher's exact test or Mann-Whitney U test.

**Results:** Among the overall 100 ankles, the frequency of RCB-positive/AT enthesitis-negative ankles, that of RCB-positive/AT enthesitis-positive ankles and that of RCB-negative/AT enthesitis-positive ankles were all more than 10%. Interestingly, the frequency of RCB-negative/AT enthesitis-positive ankles among the 62 ankles with early RA (disease duration <6 months) was significantly lower as compared to that among the 38 ankles with established RA (p=0.00595). Similarly, the frequency of RCB-negative/AT enthesitis-positive ankles among the 58 ankles of untreated patients was lower as compared to that among the 42 ankles of already-treated patients. The disease duration was significantly longer in the RCB-negative/AT enthesitis-positive ankles than in the rest of the ankles (43.8±74.6 months vs. 16.7±35.3 months, p=0.0179).



**Conclusions:** McGonagle et al. advocated the concept of synovio-enthesal complex and suggested that the inflammation occurs primarily at the enthesis and spreads to adjacent synovial tissues such as bursae in SpA patients. Our cross-sectional data indirectly indicated that RCB precedes or accompanies AT enthesitis in a narrow definition in the early phase of the RA, suggesting that the inflammation around the enthesis of RA patients occurs primarily at the synovial tissues and spreads to the enthesis in an opposite way. In addition, the isolated AT enthesitis without RCB in the established and/or treated RA patients may suggest several possibilities as follow: 1. Enthesitis is more refractory to RA treatment than bursitis; 2. Enthesitis is partially due to the degenerative changes related to damages and deformities caused by RA synovitis; 3. US-detected enthesitis in RA basically represents repair process rather than ongoing inflammation.

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**Disclosure of Interest:** None declared

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#### FRI0595 THE BEACH TOOL: A QUANTITATIVE MRI-BASED METHOD FOR MEASURING OEDEMA AND FAT METAPLASIA IN SPONDYLOARTHRITIS

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**Background:** Magnetic resonance imaging (MRI) is an important part of diagnostic pathways in spondyloarthritis (SpA), and can be used to stratify patients and assess severity. However, measurements of the burden of inflammation currently rely on qualitative assessment, which is subjective and time-consuming thus impractical for clinical practice. There is a need for a more objective, faster method for measuring inflammation and damage with potential for automation, and quantitative MRI is a candidate tool.

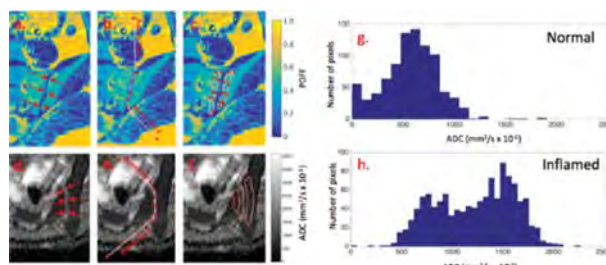
**Objectives:** We aimed to provide proof-of-principle for the BEACH (Bone Oedema and Adiposity quantification with Apparent diffusion coefficient and Chemical shift imaging with histograms) tool, which quantifies bone marrow oedema and fat metaplasia – features of active and chronic inflammation – in the SIJs.

**Methods:** Fifty-three patients aged 12–24 years with either SpA or mechanical back pain were recruited prospectively, and underwent quantitative MRI consisting of diffusion weighted imaging (DWI) and fat fraction (FF) mapping,<sup>2,3</sup> and conventional MRI scans. Apparent diffusion coefficient (ADC) and FF maps were assessed using the BEACH tool, which automatically propagates ROIs on sub-chondral bone after the observer defines the SIJ. Pixel values were analysed to derive the histographic parameters for ADC and FF: median, 10th, 25th, 75th and 90th percentiles (denoted ADC<sub>10</sub>, ADC<sub>25</sub>, FF<sub>10</sub>, FF<sub>25</sub>, etc), and P<sub>high</sub> and plough (the proportion of high and low value pixels respectively).

Conventional MRI scans were assessed using visual scoring.<sup>4</sup> Patients were deemed to have active inflammation if their inflammation score was  $\geq 2$ , and to have fat metaplasia if this score was  $\geq 3$ . Quantitative measurements were compared between inflamed and non-inflamed SIJs.

**Results:** Use of the BEACH tool is demonstrated in figure 1(a)-(f). Example ADC histograms are shown in (g),(h).

**ADC<sub>75</sub>, ADC<sub>90</sub>, and P<sub>high(ADC)</sub> were significantly increased in inflamed SIJs ( $P=0.041$ ,  $0.006$  and  $0.003$  respectively), although median ADC values did not differ significantly between inflamed and uninfamed joints ( $P=0.31$ ). Diagnostic performance was superior for histographic parameters (AUC=0.59, 0.67 and 0.69) than for the median (AUC=0.54): Median FF, FF<sub>75</sub>, FF<sub>90</sub> and P<sub>high(FF)</sub> were all significantly increased in SIJs with fat metaplasia compared to those without (all  $p<0.0001$ ). Diagnostic performance was superior for histographic parameters FF<sub>75</sub>, FF<sub>90</sub> and P<sub>high(FF)</sub> (AUC=0.89, 0.92 and 0.92) than for the median (AUC=0.87).**



**Conclusions:** ADC and FF measurements can differentiate between inflamed and non-inflamed SIJs, and between joints with and without fat metaplasia. Compared to simple averages such as the median, histographic parameters can increase diagnostic performance for detecting inflammation and fat metaplasia. There is minimal subjectivity associated with ROI placement using the BEACH tool, which can potentially make inflammation scores more reproducible.

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**Disclosure of Interest:** None declared

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#### FRI0596 FEASIBILITY OF JOINT STRUCTURAL ANALYSIS IN HEMOCHROMATOSIS HAND ARTHROPATHY USING HIGH-RESOLUTION PERIPHERAL QUANTITATIVE COMPUTED TOMOGRAPHY – FIRST RESULTS AND CLINICAL CORRELATIONS

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**Background:** Hereditary Hemochromatosis (HH) is a common inherited disorder and characterised by an excess iron accumulation in several organs with consecutive organ dysfunction.<sup>1</sup> Apart from the liver, the joints are a major site of excess iron deposition. Joint pain counts among the most frequent (>50%), earliest, and most debilitating symptoms of HH.<sup>2</sup> To date, joint health status in HH patients is routinely assessed on hand radiographs.<sup>3</sup> However, plain radiography is a low-resolution, 2D-technique with limited sensitivity to detect early joint changes or to monitor subtle progression of joint damage.<sup>4</sup> With the advent of high-resolution peripheral quantitative computed tomography (HR-pQCT), a promising imaging tool has emerged allowing for *in vivo* 3D characterisation of human joint microstructure at a spatial resolution of 130  $\mu\text{m}$ .<sup>5</sup> Due to its high sensitivity to detect and monitor subtle, short-term joint changes, HR-pQCT has been successfully applied to patients with RA.<sup>6</sup> However, to date, HR-pQCT has not been used to characterise joint and bone changes seen in HH arthropathy.

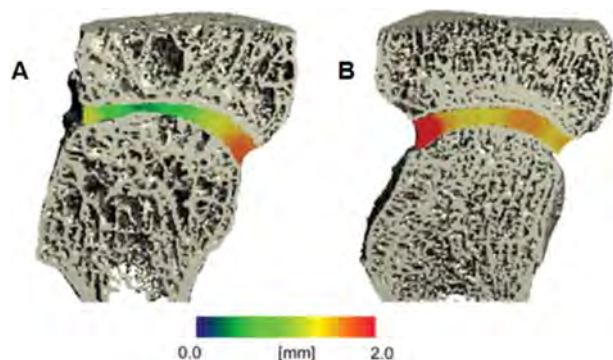
**Objectives:** Here, we aimed to investigate in a cohort of HH patients 1) if the usage of HR-pQCT is feasible on HH patients; 2) to quantify joint microstructure of metacarpophalangeal joints (MCP2–4) in this specific patient group; and 3) investigate the relationship between HR-pQCT-derived joint microstructural parameters and clinical outcomes.

**Methods:** 25 HH patients were enrolled and their HH history and treatment were recorded. MCP joints of all patients were imaged at a clinical HR-pQCT system (XtremeCT, Scanco Medical AG). 330 images were acquired covering MCP 2, 3 and 4. The joint space (JS) morphology of each MCP was quantified from the HR-pQCT images semi-automatically<sup>4</sup> and volume (JSV), joint space width mean (JSW), JSW variance (JSW.SD), and JSW asymmetry (JSW.AS) were calculated.

**Results:** Out of the 75 MCP joints available for analysis, 79% were successfully segmentable, and 19% required semi-manual intervention to separate the individual bones. 3 joints were excluded due to motion artefacts, and 1 joint was unsegmentable. HH patients were 32–72 years old, in 64% male, and had been diagnosed with HH 2 months to 40 years ago. 15% were pain free at the study



date. HH patients with pain showed significantly lower JSV at MCP 2 and 4 ( $p=0.009$ ) and exhibited a significantly higher joint asymmetry in MCP 3 ( $p=0.012$ ) compared to their pain free colleagues. When looking at clinical correlations we found that time since HH diagnosis was positively correlated with the MCP4 JSV asymmetry ( $R^2=0.451$ ,  $p=0.040$ ) and MCP 4 JSV.SD ( $R^2=0.475$ ,  $p=0.030$ ). The number of phlebotomies since diagnosis was strongly correlated with the JSV.SD (MCP2-4:  $0.4552 < 0.581$ ,  $p < 0.050$ ) at all MCP sites.



**Abstract FRI0596 – Figure 1.** 3D surface reconstructions of the MCP3 with the local joint space width mapped into the joint space in pseudo-colour. Blue and green colours reflect narrow joint space width, while red colours code for a broader joint space width. A) 55 year old male with a BMI of 21.9 kg/m<sup>2</sup> who has been diagnosed with hemochromatosis 8 years ago, but received only occasionally phlebotomies. B) 48 year old male (BMI 22.9 kg/m<sup>2</sup>) with a diagnosis of hemochromatosis of 8 years who received regular phlebotomies every 2 months. Both patients presented at the study date with hand pain. Note the larger and more symmetrical joint space width in patient B.

**Conclusions:** Our study provides the first evidence that joint space assessment of MCPs via HR-pQCT in patients with hereditary hemochromatosis is feasible and can provide a thorough structural joint characterisation and thus support the physician in his initial HH arthropathy assessment. Our findings suggest, that regular phlebotomies since diagnosis may preserve joint space morphology leading to a more evenly maintained joint space. However, larger studies are needed to validate our results.

**Disclosure of Interest:** None declared

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### FRI0597 VALIDATION OF WEB-BASED CALIBRATION MODULES FOR IMAGING SCORING SYSTEMS BASED ON PRINCIPLES OF ARTIFICIAL INTELLIGENCE: THE SPARCC MRI SACROILIAC JOINT INFLAMMATION SCORE

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**Background:** The application and appropriate use of imaging-based scoring instruments is usually based on passive learning from published manuscripts while real-time interaction with instrument developers is often non-feasible. Moreover, most instruments lack knowledge transfer tools that would facilitate attainment of pre-specified performance targets for reader reliability.

**Objectives:** 1. To develop a web-based calibration module for the SPARCC MRI SIJ Inflammation Score based on consensus scores from these instrument developers, experiential game psychology, and real-time iterative feedback. 2. To test

the feasibility and attainment of pre-specified performance targets for reader reliability.

**Methods:** The scoring of inflammatory lesions of the SIJ on MRI using the SPARCC method is based on SIJ quadrants and the calibration module is comprised of 50 DICOM cases, each with scans from baseline and 12 weeks after the start of TNF inhibitor therapy. Scans are scored blinded-to-time-point. Continuous visual real-time feedback regarding concordance/discordance of scoring per SIJ quadrant with expert readers is provided by a color-coding scheme. Reliability is additionally assessed by real-time intra-class correlation coefficient with the first ICC data being provided after 20 cases. Accreditation for SPARCC BME score is achieved with status and change score ICC of  $>0.8$  and  $>0.7$  and is based on the final 20 cases. 26 readers scored the SPARCC BME module (7 rheumatology fellows, 2 chiropractors, 1 undergraduate, 8 rheumatologists, 8 radiologists) with 21 having no prior experience. Feasibility was assessed by 8-item survey.

**Results:** The majority of readers achieved accreditation for SPARCC BME score on the basis of sufficient reliability with instrument developers for both status and change scores, irrespective of prior experience (table 1). All readers who completed the module a second time, 6 months after the first exposure, achieved accreditation for SPARCC BME score. All readers rated the modules as easy and intuitive with average time for reading each case for SPARCC BME being 8 min.

**Abstract FRI0597 – Table 1**

	Status Score			Change Score		
	Mean ICC (95%CI)	Median ICC	N (%) Achieving ICC $>0.80^*$	Mean ICC (95% CI)	Median ICC	N (%) Achieving ICC $>0.70^*$
All readers (N=26)	0.84(0.81-0.87)	0.84	18(69.2%)	0.74(0.69-0.79)	0.76	17(65.4%)
Second read (N=8)	0.89(0.87-0.91)	0.89	8(100%)	0.84(0.79-0.90)	0.86	8(100%)
Naive readers** (N=10)	0.83(0.79-0.87)	0.84	8(80%)	0.74(0.66-0.83)	0.79	7(70%)
Rheumatologists (N=8)	0.86(0.79-0.92)	0.85	6(75%)	0.78(0.69-0.87)	0.79	6(75%)
Radiologists (N=8)	0.84(0.77-0.91)	0.82	4(50%)	0.70(0.59-0.81)	0.72	4(50%)

\*Proficiency targets for reader reliability

\*\*7 rheumatology fellows, 2 chiropractors, 1 undergraduate

**Conclusions:** Experiential web-based learning is an effective and feasible calibration tool to achieve proficiency targets in the scoring of MRI scans for SIJ inflammatory lesions.

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### FRI0598 THE AGREEMENTS BETWEEN CLINICAL SIGNS AND ULTRASOUND-DETERMINED JOINT INFLAMMATION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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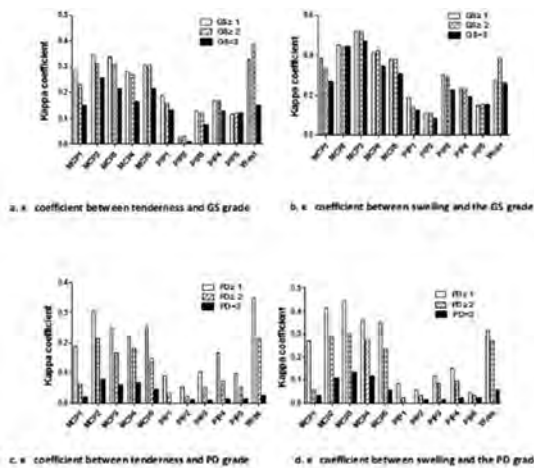
**Background:** The identification of synovial inflammation in rheumatoid arthritis (RA) patients mainly depends on the presence of tenderness and/or swelling joints by physical examination, however not entirely reliable. Ultrasound, especially the synovial hyperplasia evaluated by grey scale (GS) and synovitis by power Doppler (PD), is more sensitive in reflecting joint inflammation, but their clinical significance has not been fully understood<sup>[1]</sup>.

**Objectives:** To investigate the agreement between clinical-detected signs and US features of joint inflammation in wrists and hands, and further determine the grades of GS synovial hyperplasia and PD synovitis which correspond to presence of tenderness or swelling in an individual joint in RA patients.

**Methods:** Twenty-two joints, including bilateral wrists, proximal interphalangeal (PIP) and metacarpophalangeal (MCP) joints, were respectively evaluated by clinical and ultrasound examination by different rheumatologists in 258 RA patients. Ultrasound-determined joint inflammation, including synovitis, tenosynovitis/peritendinitis, were detected, by using semi-quantitative scoring systems (0–3) for GS

synovial hyperplasia and PD synovitis, and qualitative scoring systems (0/1) for tenosynovitis/peritendinitis.

**Results:** The median age of 258 enrolled patients were 51.4 years with 82.9% females. Their median disease duration was 55 months, and median disease activity score based on 28 joint count were 4.6. In a total of 5676 joints assessed, 968 joints (17.1%) were swollen and 1296 joints (22.8%) were tender, while on ultrasonography GS synovial hyperplasia was present in 801 (14.1%) joints, PD synovitis in 476 (8.4%) joints and tenosynovitis/peritendinitis in 108 (1.9%) joints. The general agreement between clinical signs and ultrasound-determined joint inflammation in all joints was fair ( $\kappa=0.365$ ,  $p<0.01$ ). In wrists, joint tenderness showed higher  $\kappa$  coefficient ( $\kappa=0.329$ ,  $p<0.01$ ) with ultrasound-determined joint inflammation than swelling ( $\kappa=0.263$ ,  $p<0.01$ ), while on the contrary, swelling showed higher  $\kappa$  coefficient ( $\kappa=0.156-0.536$ ,  $p<0.01$ ) with ultrasound-determined joint inflammation than tenderness ( $\kappa=0.061-0.355$ ,  $p<0.05$ ) in MCP and PIP joints. Both synovial hyperplasia and synovitis detected by ultrasound had consistently higher agreement with tenderness/swelling than tenosynovitis/peritendinitis. Joint tenderness and swelling had the highest  $\kappa$  coefficient with GS  $\geq 1$  synovial hyperplasia in most MCP and PIP joints, while with GS  $\geq 2$  synovial hyperplasia in wrists. For all 22 joints, PD  $\geq 1$  synovitis had the highest  $\kappa$  coefficient with clinical tenderness and swelling.



**Conclusions:** Synovitis had better agreement with clinical signs than tenosynovitis/peritendinitis. Joint swelling showed better agreement with these ultrasonographic changes than tenderness for MCP and PIP joints, while the opposite for wrists. The minimal requirements of synovial hyperplasia/synovitis which correspond to clinical signs are GS  $\geq 1$  for MCP and PIP joints, GS  $\geq 2$  for wrists, but PD  $\geq 1$  for any joint.

**REFERENCE:**

[1] Yamada Y, Ogasawara M, Gorai M, et al. The synovial grade corresponding to clinically involved joints and a feasible ultrasound-adjusted simple disease activity index for monitoring rheumatoid arthritis. *Mod Rheumatol* 2016;26:844–849.

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**Disclosure of Interest:** None declared

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**FRI0599 THE RELEVANCE OF THERMOGRAPHY AND NAILFOLD CAPILLAROSCOPY IN OLDER PATIENTS WITH PRIMARY AND SECONDARY RAYNAUD'S PHENOMENON**

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**Background:** Raynaud's phenomenon (RP) is defined as episodic attacks of artery and arteriole vasoconstriction. To differentiate between the benign RP (pRP) and the form associated with connective tissue diseases (sRP) the capillary morphology can be studied using nailfold capillaroscopy (nCS). However, abnormal morphology can also be caused due to age-related changes and has been described in patients with diabetes and cardiovascular disease. In addition, this technique cannot provide functional information. Thermal imaging (thermography; TG) is a non-invasive technique which enables quantification of cutaneous blood vessel function. In veterinary medicine, thermal

imaging is applied for various clinical settings. A combined approach using both nCS and TG could improve the differentiation between pRP and sRP.

**Objectives:** The aim of this pilot study was to determine which technique (TG versus nCS) allows the best discrimination amongst older patients with pRP and sRP.

**Methods:** Thirty patients with RP (pRP, n=21; sRP, n=9) underwent nCS (Olympus SZ51) and TG (Flir B 620). Nailfold morphologic features were measured and scored on capillary density, giant capillaries, ramification and hemorrhages. The patients were divided into three categories: normal, slightly abnormal (slightly enlarged capillaries) and severely abnormal (destruction of capillary structure and hemorrhages).

TG of the hand was performed before, directly after and 10 min after a cold challenge test with cold manchetts of 3°C. Rewarming and reperfusion were monitored and baseline images and rewarming curves were analysed.

**Results:** Capillary abnormalities with nCS were found in all patients with sRP (9/9) and in 52% (11/21) of patients with pRP. Out of 11 pRP patients with altered capillary morphology, 7 (63%) had a cardiovascular disease.

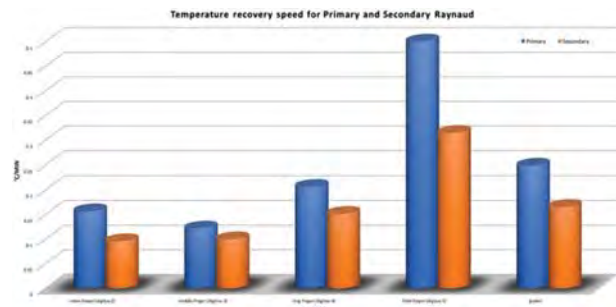
TG demonstrated a lower average temperature at baseline in the pRP group compared to the sRP group (d 1.68°C,  $p<0,01$ ). In patients with pRP temperature decreased after cold induction (-2.34°C,  $p=0,01$ ), whereas in sRP patient temperature stayed consistent (+0.07°C,  $p=0,46$ ) (table 1). In both groups temperature increased ten minutes after cold induction (pRP +2.62°C,  $p<0,01$ ; sRP +1.57°C,  $p<0,01$ ).

The gradient of the rewarming curve was significantly lower in patients with sRP compared to the pRP group (median 0.16 vs. 0.26 °C/min;  $p=0.015$ ).

**Abstract FRI0599 – Table 1**

Average temperature of the fingers before the immersion in cold water (in °C)	Average temperature of the fingers just after the immersion test (in °C)	Average temperature of the fingers 10 min after removing the hand from cold water (in °C)	Average temperature recovery speed (in °C/min)
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Primary Raynaud Phenomenon 29.49 27.15 29.77 0.26 Secondary Raynaud Phenomenon 31.17 31.24 32.81 0.16 Capillaroscopy abnormalities 25.80 25.60 27.92 0.23 Secondary Raynaud phenomenon and Capillaroscopy abnormalities 27.99 28.15 31.52 0.34



**Conclusions:** Nailfold capillaroscopy and thermography can reliably be used to measure microvascular damage and dysfunction. TG is better suitable to differentiate between older patients with pRP and sRP.

Furthermore, in presence of cardiovascular disease, TG appears to be a more reliable technique than nCS for differentiating between patients with pRP and sRP.

**Disclosure of Interest:** None declared

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FRIDAY, 15 JUNE 2018

**Public health, health services research and health economics**

**FRI0600 METHODS FOR THE ANALYSIS OF ADHERENCE DATA FROM A MEDICATION EVENT MONITORING SYSTEM (MEMS): A SYSTEMATIC REVIEW**

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**Background:** Medication adherence can be measured with several methods: medication bottles with an electronic cap are regarded as the gold standard. The cap contains an electronic device which records the date and time of each

opening and closing of the bottle. This is termed Medication Event Monitoring System (MEMS). To our knowledge, there is no standard method to summarise and analyse the adherence data from MEMS.

**Methods:** A literature search was conducted in July 2017 in the databases PubMed, Embase and Cochrane. Search terms were related to the following MESH search terms: medication (non)adherence/compliance, medication persistence, chronic disease/illness, chronically ill, medical electronics, treatment, (drug) therapy, data analysis, statistical study.

**Results:** We identified 1493 articles, and immediately excluded 1127 off-topic articles and 48 double entries after screening of title and abstract. In the end, 207 articles were included.

The mean age of the patients in the studies was 52 (SD 46) years. A total of 62 different health conditions were studied. Most patients had HIV (29%) or heart failure (10%). The MEMS cap was used for a median of 3 months (IQR: 4; range: 1 week-24 months).

**Outcome measures:** Most studies computed an adherence score, expressed as the percentage of days on which the correct dose of medication was taken. The threshold to mark people as adherent was most frequently (38 studies) set at 80% (range 67%–95%). Timing compliance (i.e. the percentage of doses taken at the appropriate time) and dose compliance (i.e. the percentage of correct doses taken on each day) were also calculated in several studies (in 14% and 23%, respectively). In addition, a few studies (4%) calculated 'drug holidays', i.e. periods of a certain number of days on which the medication bottle was not opened, followed by a bottle opening.

**Statistical analyses:** Multilevel modelling and slopes in combination with one-sample t-tests were used to examine adherence patterns over time.

Ten studies assessed an intervention to improve adherence. Generalised Estimating Equation (GEE) model (n=4), ANOVA, McNemar's exact test, multilevel modelling, a summary analysis (details not reported), T-test or Wilcoxon test were used to compare the differences in adherence before and after an intervention.

**Conclusions:** Apart from the adherence score threshold, often set at 80% of days with correct medication dosing, we found that many different outcome measures and methods were used for the analysis of MEMS data, pointing to a lack of standardisation. Apparently, there is no consensus on the best outcome measures and a lack of validation studies that compare different methods to analyse MEMS data.

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**Disclosure of Interest:** None declared

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## FRI0601 THE NATURE AND EXTENT OF DATA ITEMS COLLECTED ACROSS EUROPEAN PREGNANCY REGISTERS – FIRST RESULTS OF THE EUROPEAN NETWORK OF PREGNANCY REGISTERS IN RHEUMATOLOGY (EUNEP)

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**Background:** There is a high unmet need of robust data on the outcomes of pregnancies and drug safety in various inflammatory rheumatic diseases (IRD). The aims of the European Network of Pregnancy Registers in Rheumatology (EuNeP) are to bring together experts who run pregnancy registers, to define a core data set and to perform concerted data analyses.

**Objectives:** To describe data items collected in existing multicentre European pregnancy registers in rheumatology.

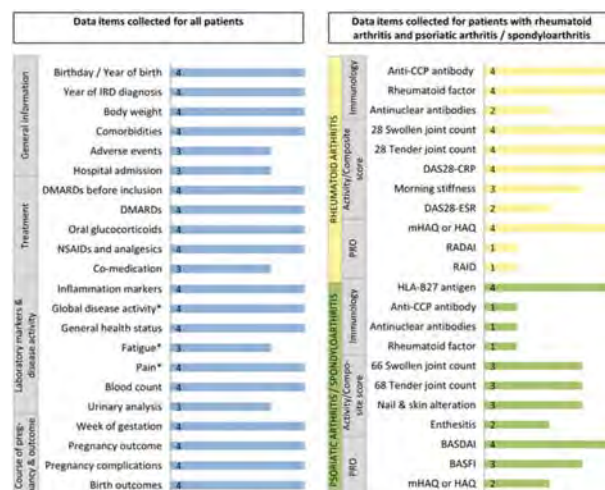
**Methods:** A comprehensive survey on details of the registers was performed encompassing patient enrolment, inclusion criteria, demographics, disease specific and general outcomes, medical treatment, course and outcome of pregnancy and outcomes of the child. Free text answers were possible for all questions. Questionnaires were sent to the principle investigator(s) of the participating studies. The completed questionnaires were reviewed, and responses were evaluated descriptively. Only data items collected during pregnancy are shown.

**Results:** The following registers are involved in the collaboration: EGR2 (France), RePreg (Switzerland), REVNATUS (Norway) and Rhekiss (Germany). All registers collect data prospectively and nationwide. Patients can be included before pregnancy (child wish) or during pregnancy in all registers, and in RePreg also up

to week 8 postpartal. Enrolment during pregnancy is possible up to gestation week 12 or thereafter in some specific cases (EGR2), week 20 (Rhekiss) or during complete pregnancy (RePreg and REVNATUS). All registers capture data via IT-based systems, REVNATUS documented on paper until 2016. During pregnancy, data is reported once every trimester by physicians and patients. Current figures, baseline characteristics and included IRD are presented in the table. Most of the data items that are independent of the underlying IRD are collected by all registers (figure 1). However, there are differences in the way data is collected and in the level of details.

	EGR2	RePreg	REVNATUS	Rhekiss
<b>No. of enrolled patients</b>	879	64	513*	777
<b>No. of observed pregnancies</b>	780	32	287	595
<b>No. of completed pregnancies</b>	446	6	266	344
<b>No. of participating units</b>	66	16	13	91
<b>Year of register start</b>	2014	2017	2006 <sup>IT</sup> 2016	2015
<b>Patient age (yrs), mean (SD)</b>	32.1 (4.8)	33.6 (4.0)	30.8 (4.8)	32.4 (4.2)
<b>Patient disease duration (yrs), mean (SD)</b>	7.3 (6.1)	11.0 (7.4)	6.5 (6.8)	11.2 (81.7)
<b>Diagnoses, N (%)</b>				
<b>RA</b>	60 (6.9)	23 (35.9)	139 (27.1)	225 (29.0)
<b>PsA</b>	0**	11 (17.2)	44 (8.6)	66 (8.5)
<b>SpA</b>	55 (6.3)	24 (37.5)	107 (20.9)	101 (13.0)
<b>JIA</b>	-	-	78 (15.2)	43 (5.5)
<b>Systemic lupus erythematosus</b>	238 (27.4)	-	67 (13.1)	162 (20.8)
<b>Other connective tissue diseases</b>	371 (42.6)	-	36 (7.0)	129 (16.6)
<b>Other IRDs</b>	146 (16.8)	6 (9.4)	42 (8.2)	51 (6.6)

\*Only patients enrolled in the IT-System are considered. \*\* PsA patients are included as peripheral SpA.



Figures in the bars represent the numbers of reporting registers. \*Only for selected diseases in one register. Abbreviations: (m)HAQ, (modified) Health Assessment Questionnaire; IRD, Inflammatory Rheumatic Disease; PFO, Patient Reported Outcome.

**Abstract FRI0601 – Figure 1.** Figures in the bars represent the numbers of reporting registers.

**Conclusions:** Although the registers in this collaboration have similar designs, we found considerable differences in data items collected. In particular, the level of details of documented data and the information on disease-specific characteristics varied. Harmonisation of data collected in pregnancy registers would facilitate collaborative analysis.

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FRI0602

### EULAR 'POINTS TO CONSIDER' FOR THE CONDUCTION OF WORKFORCE REQUIREMENT STUDIES IN RHEUMATOLOGY

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**Background:** EULAR has developed several recommendations and strategies for early referral, diagnosis and treatment of rheumatic diseases. These strategies, however, can only be implemented if sufficient manpower is available. An estimation of how many rheumatologists are needed to meet current and future population needs must be provided in order to counsel health care planners and decision makers. Current methods used for forecasting manpower are disparate, as are the variables incorporated into workforce projection models. Consequently, projections for the need of rheumatologists may vary by a factor of five between studies.<sup>(1)</sup>

**Table.** EULAR points to consider for the conduction of workforce requirement studies in rheumatology

No	Recommendation	LoA	LoE*
1	Workforce models should integrate supply, demand and needs of the respective geopolitical entity (e.g. municipality, region, state, country), and should express results as full time equivalents and as number of rheumatologists	9.5 (0.9) 95%≥8	5
2	Workforce models should provide projections over a period of 5-15 years	9.1 (1.1) 90%≥8	5
3	Workforce models should not assume a current balance between supply and need	9.0 (0.7) 100%≥8	5
4	Workforce models should, where possible, rely on several data sources and include uncertainty analyses	9.8 (0.4) 100%≥8	5
5	Workforce models should be regularly updated; updates should include an analysis of the actual performance (i.e. prediction validity) of the previous model	9.5 (0.6) 100%≥8	5
6	Workforce needs for patient care should be based on the prevalence and referral rates of diseases managed by rheumatologists as well as on an estimation of time needed per patient	9.7 (0.7) 100%≥8	5
7	Workforce needs for patient care should consider current and future demographics, sociocultural characteristics of the population and disease patterns	9.5 (0.9) 95%≥8	5
8	Workforce needs and supply should consider work outside rheumatology patient care (e.g. administrative tasks, research, teaching, non-rheumatologic disease management), as well as patient care performed by other health professionals in rheumatology	9.4 (0.9) 95%≥8	5
9	Workforce supply should account for demographic composition of rheumatologists, the number of rheumatologists entering and leaving the workforce, and generational attitudes of rheumatologists towards scope of practice and work-life balance	9.1 (2.3) 85%≥8	5
10	Workforce models should consider the effects of medical developments, including new technologies, medications, artificial intelligence and e-health, on demand and supply	9.4 (1.1) 85%≥8	5

Numbers in column 'LoA' indicate the mean and SD (in parentheses) of the LoA, as well as the percentage of task force members with an agreement ≥8.  
LoA, Level of agreement; LoE, level of evidence according to Oxford Centre for Evidence-Based Medicine 2011 levels of evidence  
\*study design does not correspond to any of the levels of the OCEBM.

**Objectives:** The aim of this project was to develop EULAR points to consider on the methodology of future workforce calculation models for rheumatologists in order to produce reliable, standardised and realistic estimates.

**Methods:** The EULAR Standardised Operating Procedures were followed. A systematic literature review (SLR) was conducted to retrieve workforce models in rheumatology and other specialities. The task force consisted of 20 experts (rheumatologists, health professionals and representatives of PARE) from 11 EULAR countries and the USA. Points to consider were based on expert opinion informed by the SLR, followed by group discussions with consensus obtained through informal voting. The level of agreement with the recommendations was voted anonymously.

**Results:** A total of 10 points to consider were formulated (table 1). The task force recommends models integrating supply (=workforce available to rheumatology), demand (=health services requested by the population) and needs (=health services that are considered appropriate to serve the population). Projections of workforce requirements should consider all factors relevant for current and future workload in and outside rheumatology patient care. Forecasts of workforce supply should consider demography and attrition of rheumatologists, as well as the effects of new developments in health care.

**Conclusions:** These are the first EULAR points to consider providing guidance on the methodology and the parameters to be applied in future national and international workforce requirement studies in rheumatology.

### REFERENCE:

[1] Dejaco C, et al. Arthritis Care Res 2016.

**Disclosure of Interest:** None declared

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FRI0603

### THE POTENTIAL USES OF AN INFODEMOLOGY APPROACH FOR HEALTH-CARE SERVICES IN RHEUMATOLOGY

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**Background:** Infodemiology can help achieve the patient-centred care model. It is the science of determinants and distribution of information on electronic media. It can provide data to develop, collect, and evaluate metrics and indicators for information and communication patterns that are related to epidemiologic data or are useful for public health, policy making or even clinical practice. Google Trends (GTr) and Google AdWords (GAd) are two useful tools to assess demand-based infodemiology indicators. Its use is scanty in rheumatology.

**Objectives:** To illustrate the potential use of GTr and GAd, we present three case-studies: A) What search terms related to rheumatology are typed by people in Mexico (MX), the United States of America (USA), and Canada (CAN)? B) What is the search volume for specific DMARDs typed by people in MX, USA, and CAN?, and C) What is the positioning of the search term "arthritis" compared with two non-rheumatic diseases ("hepatitis C", "breast cancer") among MX, USA, and CAN?

**Methods:** GTr output is a relative search volume (the biggest volume is transformed to 100 and the rest are given as a proportion of it) and GAd output is the average number of searches per unit of time. We ran 3 different queries (MX, USA, CAN) for each case-study using GTr and GAd for years 2015–2017. Results were exported to a database for further analysis. Search volumes were adjusted per country's population and expressed as crude rates (searches per million; spm) when appropriate.

**Results:** To look for information on "rheumatology" people used 298 (MX), 654 (USA), and 637 (CAN) associated terms. "Arthritis" had 656, 550, and 548 associated terms in MX, USA, and CAN, respectively. For "arthritis treatment" there were 635, 569, and 569 associated terms in MX, USA, and CAN, respectively. Regarding DMARDs, there were 1,053 million searches during this period: methotrexate (28.5%), adalimumab (15.6%), rituximab (10.4%), and infliximab and etanercept (8.6% each). However, for every b- or tsDMARD search, there were fourteen (USA, CAN) to fifty-eight (MX) "turmeric" searches for the "treatment of arthritis". In 2015, search volume for "arthritis" was 120, 638, and 668 spm in MX, USA, and CAN, respectively. For 2016 and 2017 figures remained similar for MX and CAN, but showed a 12% increase for the USA. In MX, "hepatitis C" had 114 spm in 2015, with a 32% increase by 2017. The USA and CAN had 1131 and 648 spm in 2015, with a 5% increase and an 8% decrease by 2017, respectively. For "breast cancer", search rates were 4 times higher than for "arthritis" for the three years in MX, with an average increase of 250% each October, concurrent with public awareness campaigns. In the USA and CAN, search volume was 36% and 56% less than that for "arthritis", with a 57% and 33% increase each October, respectively.

**Conclusions:** Infodemiology can have an added value to traditional research designs. It can serve for diverse purposes, such as assessing the penetration and impact of public awareness campaigns, patients' perceived needs, the appearance of new remedies, the positioning of diseases, disease-related cultural differences in ethnic groups, people perceptions on specific health-care systems, etc.

**Disclosure of Interest:** None declared

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FRI0604

### TRENDS OF INFORMED CONSENT FORMS FOR INDUSTRY-SPONSORED CLINICAL TRIALS IN RHEUMATOLOGY OVER A 17-YEAR PERIOD: READABILITY, AND ASSESSMENT OF PATIENTS' HEALTH LITERACY AND PERCEPTIONS

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**Background:** The therapeutic arsenal in rheumatology has improved drastically during the last 20 years with the availability of biological and synthetic disease-modifying antirheumatic drugs. All these drugs required randomised controlled trials (RCTs) with thousands of rheumatic patients. All these patients went through the informed consent process and signed corresponding informed consent forms (ICFs).

**Objectives:** To assess trends in the length and readability of ICFs for industry-sponsored RCTs over a 17 year period. Additionally, to assess the health literacy (HL) and perceptions on ICFs among participants of current RCTs.

**Methods:** The grammatical readability (GR) of six pre-defined ICF sections (global, introduction, methods, risks/benefits, rights/responsibilities, and voluntary participation statement) of pivotal ICFs from industry-sponsored RCTs conducted at an outpatient rheumatology clinic during a 17 year period was assessed by using the INFLESZ instrument. Differences in GR were assessed by company, by disease and by study phase (95% CI of the mean and proportions; statistical significance assumed if no overlap), and by the years ICFs were written (1999—2005, 2006—2010, and 2011—2016; Kruskal-Wallis test). HL of patients was assessed with the SALHSA (inadequate, adequate) and S-TOFHSA (inadequate, marginal, adequate) instruments. Differences by age and schooling were determined by one-way ANOVA. Patient's perceptions and opinions on the ICF were assessed using a structured, self-reported, in-office questionnaire on an independent patient sample that had signed a pivotal ICF in the past 6 months.

**Results:** Thirty-nine ICFs about 22 drugs (18 biological or targeted synthetic DMARDs; 13 currently available on the market) from 13 pharmaceutical companies were analysed. The global mean readability was 57±3 (95% CI 56–58), and all ICFs were categorised as either "somewhat difficult to read" or "average". Readability remained at these levels without significant changes from 1999 to 2016. The "somewhat difficult" reading score was significantly more frequent in the "rights and responsibilities" and in the "informed consent statement" sections (p<0.001). The mean length of the ICFs written between 1999 and 2005 was 13±5 pages, with a significant increase thereafter (22±8 pages, p<0.01). Depending on the instrument, of 95 patients participating in the HL assessment, between 18% and 44% had limited HL. Of 90 patients participating in the perceptions questionnaire, 84% reported understanding the ICF well. However, 2%–57% misunderstood basic concepts, including the study drug name, randomization and placebo.

**Conclusions:** It seems that the considerable progress that has been made in medical research methods over time has not produced improvements in the process of informed consent in the industry-sponsored RCTs. The disparity between the readability of ICFs with patients' HL and their comprehension of ICFs continues, even after decades of attempts of regulatory agencies and numerous published suggestions.

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FRI0605

### THE DEVELOPMENT PROCESS OF MOBILE HEALTH APPLICATIONS FOR SELF-MANAGEMENT IN PATIENTS WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES IS HETEROGENEOUS AND OFTEN INCOMPLETE: RESULTS OF A SYSTEMATIC LITERATURE REVIEW

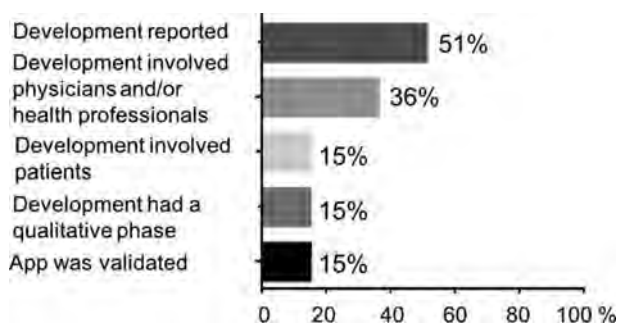
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**Background:** Mobile health (mHealth) is exponentially growing in the current era, providing new potential and transforming the face of healthcare delivery. While the increasing availability of applications (apps) may enable people with rheumatic and musculoskeletal diseases (RMDs) to better self-manage their health, there is a general lack of evidence on ways to ensure appropriate development and evaluation of apps.

**Objectives:** To obtain an overview of existing mHealth apps for self-management in patients with RMDs, regarding content and development methods in particular, through a systematic literature review.

**Methods:** A search was performed up to December 2017 using EMBASE, Pubmed, Cochrane library, Web of Science and Psychinfo databases, with relevant key words and MeSH terms addressing three key domains: RMDs, self-management and mHealth. Double screening was performed on 15% of all abstracts against agreed inclusion criteria. For each publication relevant to an app for RMDs, the content, the aims, the target population of the apps and their development strategies were noted. The analysis was descriptive.

**Results:** Of 562 abstracts, 57 full text were screened. 39 articles were included in the analysis. 13 articles referred to an app linked to a connected device. Most of the apps targeted rheumatoid arthritis patients (n=11), juvenile idiopathic arthritis (n=7) and osteoarthritis (n=8). The development process of the app was poorly described in 19/39 (48.7%) of the studies (figure 1). Only 6/39 (15.4%) included patients, and 14/39 (35.9%) included health professionals or physicians in the development of such apps. Moreover, a qualitative phase occurred in only 6/39 (15.4%) of the cases. The app was tested and evaluated by physicians in 6/39 (15.4%). Patients were more frequently involved in app evaluation (29/39, 74.4%) but mostly indirectly through their adherence to the app. Only few of the apps published on were commercially available (5/39, 12.8%), 4/5 are free. One app is currently under development.



Abstract FRI0605 – Figure 1. Description of the development process of the apps in the 39 articles.

**Conclusions:** The development process of most apps was poorly described and potentially not satisfying in many studies. Despite patient willingness to use mHealth apps for self-management of their RMDs, a strong effort needs to be made to provide a standard and ensure quality and safety of newly-developed apps. This work will further inform EULAR points to consider for development, evaluation and implementation of mobile health applications for self-management of RMDs by patients.

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FRI0606

### THE LIFT STUDY'S DIRECT-TO-PATIENT DESIGN PROVIDES RELIABLE SELF-REPORTED DATA FROM LUPUS PATIENTS

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**Background:** Direct-to Patient (D2P) clinical studies that rely upon social media, mobile connectivity, wearables, self-collected patient samples, and patient reported outcome data have the potential to revolutionise health research by enabling population-scale studies without the cost and complexity of traditional multi-site trials. D2P studies are particularly interesting for longitudinal studies where the burden of participants travelling to a central site is high; however, the quality and reliability of patient reported outcome data is unclear<sup>1</sup>.

**Objectives:** The study evaluated the accuracy of self-reported data from a subset of patients in a 1000+participant D2P lupus study (www.thelifstudy.com) by comparing patient-reported data to medical records as well as genomic testing of individuals using participant-collected fingerstick blood samples.

**Methods:** The study was reviewed and approved by a central IRB (WIRB; Puyallup, WA). Subjects were recruited online across the U.S using social media. Electronically consented participants with self-reported lupus were asked to complete online surveys about their disease and drug history as well as provide medical record review (MRR) consent. A third party firm was employed for MRR and an independent physician summarised the following information: 1) participant age 2) confirmation of lupus 3) current lupus medications and 4) current steroid medications.

**Results:** Of the 1043 participants enrolled over the first 6 weeks of the study, 327 had completed all aspects of the study. Thirty-seven participants (11%) were selected at random for MRR. Average age was 44±12 years with 35 females and 2 males. Self-reported (SR) age at time of enrollment was 100% confirmed by MRR. Lupus diagnosis was confirmed in 100% of the participants by the MRR directly or by conclusion of the independent physician based upon review of the medical record. SR and MRR drug information showed variable concordance upon review, with several patients reporting medications at the time of the survey that were not confirmed in their medical records (table 1). Percent agreement was determined by comparing the SR vs. the MRR for each participant (data not shown). Overall, there was an 88% agreement between SR and MRR for each of the medications where at least 1 participant reported prescription.

**Abstract FRI0606 – Table 1.** Common Lupus Medications and Steroids (n=36 unless otherwise noted)

Medications	SR		MR		% Agreement
	Yes	No	Yes	No	
cyclophosphamide	0	36	0	36	100%
methotrexate	4	32	2	34	94.4%
azathioprine	2	34	2	34	100%
cyclosporine	0	36	0	36	100%
belimumab	6	30	5	31	97.2%
chloroquine	0	36	0	36	100%
hydroxychloroquine (n=35)	26	10	21	14	77.1%
mycophenolate	6	30	4	32	94.4%
leflunomide	0	36	0	36	100%
steroids (n=37)	12	25	13	24	64.9%

**Conclusions:** Using a D2P study design, the resulting SR data corresponded well with the MRR for subject age, lupus diagnosis, and lupus medications. While there were some discrepancies in use of medications, many of these could be explained by the time-dependency of our questionnaire, where the date of prescription in the MRR was just outside of the 30 day window. The LIFT Study shows that a D2P study design is an effective method to rapidly enrol lupus patients and decrease study costs while collecting reliable self-reported data.

#### REFERENCE:

[1] Wallitt, et al. *J Rheumatol.* 2008 May;35(5):811–818.

**Disclosure of Interest:** A. Cheeks Employee of: DxTerity, L. Borisov Employee of: DxTerity, K. Warren Employee of: DxTerity, R. Terbruggen Shareholder of: DxTerity, Employee of: DxTerity

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#### FRI0607 HOW TO DESIGN CLINICAL TRIALS TO BE MORE PATIENT ORIENTED: AN EXAMPLE FROM PREVENTATIVE TREATMENTS FOR RHEUMATOID ARTHRITIS

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**Background:** It is widely acknowledged that many clinical trials do not always provide results that are meaningful to patients. We sought to utilise market research techniques, widely used in non-health consumer product development, to understand patient preferences that could improve the design of clinical trials. We use an example from preventative treatments in patients with preclinical asymptomatic RA where many trials are being designed or ongoing.

**Objectives:** To consider how to inform trial design for: i) which outcome/s should be primary? ii) what difference in the primary outcome between arms is important? iii) will patients want to use the intervention if it meets its primary endpoint/s?, and iv) does an alternative strategy exist that patients would prefer?

**Methods:** We developed a discrete choice experiment and surveyed first-degree relatives of patients. Focus groups of RA patients, first-degree relatives of RA patients and rheumatologists identified 5 key attributes of treatment (reduction in risk of RA, how treatment is taken, chance of side effects, certainty in estimates, health care providers opinion). DCE data was analysed using a conditional logit regression models to estimate the significance and relative importance of attributes in influencing preferences. We predicted uptake using estimates from the opt-out data analysed using a logit model.

**Results:** 288 first-degree relatives of people with RA started and completed all tasks in the survey. The majority of the sample were aged between 18 and 39 years (60%), and 60% female. All attributes levels significantly influenced preferences for treatments, but how treatment is taken (oral vs. infusion  $\beta$ 0.983,  $p < 0.001$ ) was the most influential, followed in similar magnitude by increasing risk

reduction (60 to 24 in 100) ( $\beta$ 0.922,  $p < 0.001$ ), matching of patient and health care professional preferences ( $\beta$ 0.900,  $p < 0.001$ ), and reducing risk of side effects ( $\beta$ 0.839,  $p < 0.001$ ). If a risk reduction of RA from 60 in 100 over 5 years to 44 in 100 is realised with only minor, reversible side-effects likely, then the uptake of hydroxychloroquine was predicted to be 86%. If all treatments currently under study in the pre-clinical phase of RA were assumed to be options for the asymptomatic phase and met hypothesised outcomes, the uptake of oral methotrexate was predicted to be 46% and hydroxychloroquine 20%. Predicted uptake of biologic drugs was 6% for abatacept and 4% for rituximab.

**Conclusions:** The study illustrates how market research can be used to design clinical trials that address patient centred priorities and outcomes. The results illustrate that a trial of preventative treatments for RA should: i) be powered to detect both a difference in preventing the development of RA, and the increase in minor side-effects, ii) require a significant reduction in risk of developing RA if any side-effects are possible. We calculate iii) that hydroxychloroquine would be likely to be used by pre-clinical asymptomatic patients, but biologics would likely not, iv) and that methotrexate should also be explored as an earlier option.

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#### FRI0608 A SYSTEMATIC REVIEW AND CRITICAL APPRAISAL OF ECONOMIC EVALUATIONS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** New strategies to manage systemic lupus erythematosus (SLE), including the use of biomarkers to target novel or existing therapies, will require evidence of relative cost-effectiveness before being recommended in routine clinical practice. Decision-analytic model-based economic evaluations can synthesise all available evidence to estimate the cost-effectiveness of health technologies. Complexities in the diagnosis, management, and progression of disease pose challenges when estimating the cost-effectiveness of care for SLE. No systematic appraisal of economic evaluations in SLE has been published to date.

**Objectives:** To identify and critically appraise all economic evaluations of treatments for SLE.

**Methods:** A systematic review of published economic evaluations in SLE was performed. Studies were included if they had reported a full economic evaluation of any pharmacological therapy for SLE. Medline and Embase were searched electronically from inception until November 2016. The search strategy comprised disease-specific terms for SLE and published filters to identify economic evaluations. Abstracts were screened independently by two reviewers and read in full by one reviewer. Key features (study characteristics, data sources, methods of analysis, and results) were extracted from each economic evaluation. The Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement was used to appraise whether each economic evaluation had reported eighteen items with respect to its methods and results in full, partially, or not at all.

**Results:** The search strategy identified 2,001 abstracts and six published economic evaluations of treatments for SLE were included in the systematic review. These studies considered azathioprine (n=4), mycophenolate mofetil (n=3), cyclophosphamide (n=2), and belimumab (n=1) as relevant comparator therapies. The types of decision-analytic model included individual patient-level simulations (n=3), decision trees (n=2), and a cohort Markov model (n=1). Six elements of the CHEERS statement were reported incompletely across the sample: (1) target population, (2) choice of comparators, (3) measurement and valuation of preference-based outcomes, (4) estimation of resource use and costs, (5) choice and structure of the decision-analytic model, and (6) characterisation of heterogeneity.

**Conclusions:** The choice of treatments that are available currently for SLE are limited and this is reflected in the quantity of economic evaluations published to date. The incomplete reporting of methods within these economic evaluations highlighted notable gaps within the literature. Deficiencies in the evidence base manifest as parameter and structural uncertainties within decision-analytic model-based economic evaluations which, ultimately, affect the estimated expected cost-effectiveness of care. Greater use of existing datasets for SLE, including those from randomised controlled trials and observational cohort studies, can reduce these uncertainties in subsequent economic evaluations of strategies to manage SLE.

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FRI0609

### EUROPEAN MEDICINES AGENCY'S GUIDELINE ON THE CLINICAL INVESTIGATION OF MEDICINAL PRODUCTS FOR THE TREATMENT OF RHEUMATOID ARTHRITIS

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**Background:** The European Medicines Agency (EMA) in consultation with regulatory authorities in the EU Member States prepares scientific guidelines, to help drug developers prepare marketing authorisation applications. The scope of the rheumatoid arthritis (RA) guideline is to provide a European common position on the clinical evaluation of new medicinal products.

**Objectives:** The EMA guideline is an update of the Points to Consider adopted in 2003. A revision of the guideline was required as the pharmacological therapy of RA has advanced. Treat-to-target strategies are now employed, and the optimum treatment goal is remission, or at least low disease activity (LDA). New classification criteria for RA have been developed and validated by the ACR-EULAR, which allows for earlier DMARD use. Increasing knowledge of the risk associated with DMARDs has been gained from trials and registries.

**Methods:** The guideline has been prepared by the Rheumatology-Immunology Working Party of the EMA. The guideline was revised based on literature, and recent trial and safety data from regulatory dossiers of RA products. External experts, investigators, industry and patient representatives were consulted ("Public consultation"), and in person during a Targeted consultation meeting in 2016.

**Results:** New primary endpoints (PE) were defined, reflecting treatment targets LDA or remission, in place of the previous PE of ACR20. Different validated scales may be used (either DAS28-ESR, DAS28-CRP, SDAI, or CDAI). The PE of choice should be corroborated by other outcomes as secondary endpoints. E.g if DAS28-CRP is chosen, more stringent outcomes like SDAI and DAS-ESR, or CDAI, which is independent of biomarkers CRP or ESR, should point at the same direction.

A distinction is made between study populations of DMARD naïve patients, where remission at 3 months is considered as a realistic target and methotrexate a suitable comparator; and patients irresponsive (or insufficiently responsive) to prior DMARDs, where LDA at 3–6 months is considered as an acceptable endpoint. For patients with long-standing disease irresponsive to multiple DMARDs, including two biologic DMARDs of different classes, ACR20 is still acceptable.

Long-term safety data of 12 months should be available before marketing authorisation.

The ultimate goal of RA treatment is the prevention of structural joint damage. However, showing an effect on structural damage has become increasingly challenging, since the placebo control should be kept short, and milder or more controlled patients may be eligible for studies of new DMARDs. Therefore, maintenance of remission and LDA could serve indirectly as an indicator for the prevention of structural damage, provided that these clinical outcomes are compelling, and routine monitoring by X-ray does not indicate a deviating trend as compared to an established comparator.

**Conclusions:** The EMA guideline on the development of products in the treatment of RA has undergone major revisions regarding the choice of endpoints and study design. The revision comes into force in July 2018.

#### REFERENCE:

- Guideline on clinical investigation of medicinal products for the treatment of rheumatoid arthritis 14 December 2017. [CPMP/EWP/556/95 Rev. 2] [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/Scientific\\_guideline/2018/01/WC500241042.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2018/01/WC500241042.pdf)

**Disclosure of Interest:** None declared

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FRI0610

### PATIENT NON-ATTENDANCE CHARACTERISTICS AT RHEUMATOLOGY OUTPATIENT CLINICS WITHIN A LARGE MULTI-ETHNIC REGION

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**Background:** Patient non-attendance for outpatient appointments is increasingly becoming more important in an era where resources have to be used in the most cost effective way. The Leicestershire region of the United Kingdom has a very diverse multi-ethnic population of just over 1 million people. Across 3 large hospital sites the University Hospitals of Leicester, United Kingdom caters for the rheumatology needs of this diverse population.

**Objectives:** The aim of our observational study was to identify the patient characteristics of the non-attenders and investigate if ethnicity and socioeconomic class contribute to the non-attendance rate.

**Methods:** The study was based on patient appointments scheduled at a busy rheumatology outpatient clinic across three large hospital sites from January 2017 to June 2017. Extensive data on various outcomes such as cancellation on the part of the patients and non-attendance from the patients without giving formal notice were collected from the main electronic administrative systems of three hospitals in the region. The data for the appointment characteristics were also collected. Logistic regression was used for statistical analysis.

**Results:** Of the 22,011 appointments scheduled over the study period. The non-attendance rate of 3.5% was recorded for this study period without the patients giving notice. The age range of the study population was 16 to 95 years. The median age was 50 years. Majority (24%) of non-attenders were in the 45–54 year age bracket. The 85–95 year age group had the lowest non-attendance rate at 2%. When the data was analysed for ethnicity, the percentage of patients who did not attend in the black Asian and minority ethnic group (BAME) was 44%. Only 33% of the study population were recorded on the hospital database as employed. The remainder included retirees (29%), students (4%) whilst the remaining 34% were either unemployed or we had no formal recording of their employment status.

**Conclusions:** The cost implications of missed appointments is so significant that even small percentage reductions in non-attendance rates could lead to significant savings. Various studies have identified many contributory factors such as age and ease of access to hospital facilities.

Few studies have looked at the role of ethnicity and socioeconomic class. From our data there was a significant (P value <0.05) difference between the employed and unemployed group. The working class group also had a significant non-attendance rate which suggests that more can be done at looking at the appointment scheduling by the health service provider.

Patient factors are likely to play a role in the BAME group not attending hospital appointments. The existing letter and text reminder service might need to explore several language options as this may play a contributory role in non-attendance rates. Addressing these issues may go a long way in ensuring that existing resources are not wasted due to non-attendance.

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FRI0611

### ENGLISH LANGUAGE PROFICIENCY AND TOTAL KNEE/ HIP REPLACEMENT OUTCOMES: IS THERE A RELATIONSHIP?

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**Background:** Health care disparities are recognized for medical and surgical outcomes in patients with Limited English Proficiency (LEP) (1).

**Objectives:** The purpose of this study is to assess the association of LEP on Total Knee Replacement (TKR) and Total Hip Replacement (THR) outcomes.

**Methods:** Individual patient-level variables were obtained from a single institution TKR and THR registry between 5/1/07 and 2/1/11. Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain and function scores at baseline and 2 years after elective TKR and THR were collected and retrospectively analyzed. We used census tract LEP-“Less than very well” as recommended for screening individuals, since individual LEP data is not collected in most cohorts. We obtained census level data using patients’ geocodable addresses (2). Only patients from closest states (NY, NJ and CT) were included. Data was analyzed using univariate and multivariable linear mixed effects models, with census tracts variables treated as random effects.

**Results:** Table 1 describes the characteristics of the patients with THR (n=4009) and TKR (n=3898). In univariable analyses, for every percent increase in LEP, the WOMAC scores at baseline and 2 year were universally decreased and are statistically significant (p value <0.001). However in the multivariable model when adjusted for neighborhood poverty age, BMI, sex, comorbidities, and the Gini

coefficient these changes were not statistically significant, suggesting potential confounders (table 2). While women had worse baseline and 2-year WOMAC pain and function scores (all  $p \leq 0.04$ ), this difference was not significantly influenced by neighborhood LEP (all interaction NS).

**Methodology:** Categorical variables are summarized as frequency (percent). Continuous variables are summarized as mean <?> standard deviation

**Methodology:** Univariate and multivariable linear mixed-effects models were analyzed, with census tracts treated as random effects. In addition to neighborhood Limited English Proficiency; variables included in the model were; age, BMI, sex,  $\geq 1$  comorbidity; neighborhood percent poverty (<10%, 10% – < 20%, 20% – < 30%, 30% – < 40%,  $\geq 40%$  [reference group]), neighborhood Gini coefficient was also included.

Table 1. Total Joint Replacement Patient characteristics

Characteristic	Total Hip Replacement (n=4009)	Total Knee Replacement (n=3593)
<b>Patient demographics</b>		
Age at surgery (year), mean $\pm$ SD	65.6 $\pm$ 10.6	67.8 $\pm$ 9.5
Sex: female, n (%)	2169 (53.9%)	2346 (65.3%)
BMI (kg/m <sup>2</sup> )	27.9 $\pm$ 5.8	30.0 $\pm$ 5.8
Race, n (%)		
White	3794 (94.8%)	3568 (99.5%)
Black	131 (3.3%)	174 (4.9%)
Asian	23 (0.6%)	24 (0.7%)
Other	47 (1.2%)	38 (1.1%)
Unknown	16 (0.4%)	28 (0.8%)
Ethnicity, n (%)	102 (2.5%)	129 (3.6%)
<b>Patient status</b>		
ASA class		
I-II	3307 (82.5%)	3124 (87.0%)
III-IV	699 (17.5%)	469 (13.0%)
One or more comorbidity	695 (17.3%)	1057 (29.4%)
<b>Census tract characteristics</b>		
Poverty, n (%)		
<10%	2325 (58.0%)	2787 (77.6%)
10% – <20%	307 (7.7%)	311 (8.7%)
20% – <30%	115 (2.9%)	129 (3.6%)
30% – <40%	49 (1.2%)	28 (0.8%)
$\geq 40%$	13 (0.3%)	27 (0.8%)
Percent poverty, mean $\pm$ SD	6.2 $\pm$ 8.5	8.8 $\pm$ 1.2
Limited English Proficiency (LEP), n (%)		
<10%	2981 (74.4%)	2787 (77.6%)
10% – <20%	614 (15.3%)	650 (18.4%)
20% – <30%	209 (5.2%)	251 (7.0%)
30% – <40%	120 (3.0%)	113 (3.1%)
$\geq 40%$	85 (2.1%)	97 (2.7%)
Percent LEP, mean $\pm$ SD	3.6 $\pm$ 9.6	9.2 $\pm$ 10.0
Gini coefficient, mean $\pm$ SD	0.45 $\pm$ 0.07	0.45 $\pm$ 0.07
<b>Patient-reported outcomes</b>		
Baseline survey results, mean $\pm$ SD		
WOMAC pain	53.3 $\pm$ 17.8	54.8 $\pm$ 17.5
WOMAC function	49.5 $\pm$ 18.0	50.7 $\pm$ 17.6
2-year survey results		
WOMAC pain, mean $\pm$ SD	35.7 $\pm$ 11.3	37.9 $\pm$ 13.8
WOMAC function, mean $\pm$ SD	51.1 $\pm$ 13.1	52.8 $\pm$ 13.1

Table 2. Impact of every 10% change in neighborhood limited English proficiency on WOMAC pain and function

Time-point	WOMAC pain Estimate $\pm$ SE	p-value	WOMAC function Estimate $\pm$ SE	p-value
<b>Total Hip Replacement</b>				
Baseline (Univariable)	-1.4 $\pm$ 0.3	<0.001	-1.7 $\pm$ 0.5	<0.001
2-year (Univariable)	-0.8 $\pm$ 0.2	<0.001	-1.2 $\pm$ 0.2	<0.001
Baseline (Multivariable)	-0.6 $\pm$ 0.3	0.10	-0.8 $\pm$ 0.3	0.07
2-year (Multivariable)	-0.4 $\pm$ 0.2	0.054	-0.6 $\pm$ 0.2	0.01
<b>Total Knee Replacement</b>				
Baseline (Univariable)	-1.1 $\pm$ 0.3	<0.001	-1.3 $\pm$ 0.3	<0.001
2-year (Univariable)	-1.0 $\pm$ 0.3	<0.001	-1.4 $\pm$ 0.3	<0.001
Baseline (Multivariable)	-0.8 $\pm$ 0.3	0.02	-0.7 $\pm$ 0.3	0.13
2-year (Multivariable)	-0.2 $\pm$ 0.3	0.43	-0.2 $\pm$ 0.3	0.54

**Conclusions:** Patients coming from neighborhoods with lower english proficiency have worse pain and function scores in unadjusted models. However when adjusted for potential confounders, the difference is not significant. Community factors which contribute to healthcare disparities are multidimensional, prospective studies collecting individual LEP data would be warranted to study this aspect in detail.

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**FRI0612 HOW EFFECTIVE ARE INTERVENTIONS TARGETING PATIENT ACTIVATION IN PEOPLE WITH LONG TERM PHYSICAL CONDITIONS? A SYSTEMATIC REVIEW**

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**Background:** Patient activation is an increasingly referenced concept in the self management of long term physical conditions. It refers to someone’s ability to take an active role in self-managing their health. There has been a substantial increase in the number of studies trailing interventions targeting patient activation in a variety of formats. The findings from this review will contribute to maximising the impact of current rheumatology interventions, and to increase the understanding of patient activation to develop a framework to describe its core components within a rheumatology context.

**Objectives:** This study aimed to identify the effectiveness of interventions targeting patient activation in people with long-term conditions, including rheumatoid arthritis.

**Methods:** Studies that were randomised control trials of interventions targeting patient activation in adults with long term physical conditions were included in the review. PsycINFO, Medline, AMED, CINAHL, and ProQuest were searched during January 2017, as well as a variety of grey literature locations, snowballing and hand-searching to identify potential studies for inclusion. The Cochrane Collaboration’s Risk of Bias Tool was used to determine the methodological quality of included studies, and any differences were resolved by the two reviewers. Authors were contacted if any additional information was required to extract data or to clarify risk of bias.

**Results:** 17 papers were included in the review. There was a great deal of heterogeneity in the types of interventions available targeting patient activation in a variety of populations, and a meta-analysis was not possible as a result. Interventions were delivered via face to face, telephone, internet and resource-based approaches. The studies also included a mix of group and individually delivered interventions. Outcome measures used also varied, including both direct and proxy measures for patient activation.

The findings suggest that in studies with interventions that are more structured, there appear to be a trend towards differences in patient activation scores between groups in favour of the intervention. It is possible that these increases in patient activation may occur with an increase in health literacy, as the literature suggests an association between the two constructs. This is discussed in terms of a proposed model for patient activation for rheumatology.

**Conclusions:** There is some initial evidence for the benefit of increasing structure in interventions targeting patient activation. There is no evidence for a medium of delivery that is most effective in people with long term conditions. Studies would benefit from reporting information about engagement and adherence to interventions to understand the mechanisms behind engaged participants becoming more active in managing their health. There is a need for increased research into patient activation within Rheumatology.

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**FRI0613 USEFULNESS OF SMARTPHONES APPLICATIONS IN THE FOLLOW-UP OF PATIENTS WITH INFLAMMATORY RHEUMATOLOGICAL DISEASES: ARE THEY REALLY BENEFICIAL IN OBJECTIVE TERMS?**

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**Background:** The use of computer programs developed for their use through smartphones has been incorporated into the health field. In recent years there have been countless new applications aimed at easing the work of the clinician through access to commonly used tools, image atlases, real-time information or to facilitate the monitoring of patients. In this last group, there are different applications oriented to multiple purposes.

**Objectives:** The aim of this study is to assess the performance of two personally developed applications for the follow-up of patients with gout and rheumatoid arthritis (ReumApp-Gota and ReumApp-AR).

**Methods:** We surveyed 65 patients who were users of ReumaApp-Gota and 35 patients who were users of ReumaApp-AR. All were direct users with at least 6 months of experience with the application. Both applications were developed by the author of the work on a free distribution platform and whose extension and

contents have been discussed in a previous abstract. The survey was completed upon request and in the presence of the reference clinician throughout the last quarter of 2017. The survey assessed three areas: therapeutic and hygienic-dietetic adherence, the perception of personalized follow-up and overall practical utility. In parallel, the number of annual attacks of patients using ReumaApp-Gota and the relative annual reduction of the uric acid level in peripheral blood were determined. In the case of patients using ReumaApp-AR, the demand for unscheduled visits due to flares of RA and the relative reduction of DAS28 were evaluated. In both cases, their results were compared with cohorts of patients who had not used any of the applications (35 of the drop group and 29 of the AR group).

**Results:** Users of ReumAPP-Gota: Improvement in adherence 25/65, personalized follow-up is perceived 56/65, has utility in day-to-day 52/65. Users of ReumAPP-AR: Improve adherence 31/35, personalized follow-up is perceived 30/35, has utility in day to day 29/35. The number of annual gout attacks in patients users of the APP was 1.32 OF 0.45 and that of non-users was 1.27 OF 0.52 ( $P=0.848$ ), the relative annual reduction of patients with gout users of the APP was 36.6 OF 6.6 % and that of non-users 33.7 of 11.2% ( $P=0.106$ ). The number of urgent visits in a year of patients with RA users of the APP was 0.55 of 0.12 and that of the non-users group 0.83 of 0.29 ( $P<0.001$ ). The relative reduction of the DAS28 of patients using the APP was 34.9 of 5.9% and of the non-users was 31 of 7.7% ( $P<0.025$ ).

**Conclusions:** Although the use of applications for smartphones seems to generate a greater sense of medical vigilance on the part of patients and is globally considered useful, its impact on the therapeutic adherence in patients with gout is low and is reflected in the objective results of reduction of plasma uric acid figures and the number of annual attacks. In the case of patients with RA the use of the application significantly reduces the need for urgent visits, most likely because it allows the clinician to contact the patient priorly when certain parameters entered exceed certain margins. But on the other hand the relative reduction of DAS28 may be due to the fact that patients not users of the application are usually older than those who accept its use.

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#### FRI0614 PHYSICIAN-PATIENT INTERACTIONS IN AFRICAN AMERICAN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** African American (AA) patients with systemic lupus erythematosus (SLE) are at high risk for poor outcomes. Patient characteristics and disease severity influence physician-patient interactions, which in turn can impact outcomes.

**Objectives:** Examine the relationships between physician-patient interactions and demographics, disease activity, and depression in AA SLE patients.

**Methods:** The Georgians Organized Against Lupus (GOAL) is a population-based cohort of patients with a documented diagnosis of SLE. We conducted a cross-sectional analysis of patient-reported data among 698 AA participants (out of 863 GOAL participants). We assessed patients reports of physician-patient interactions (communication, patient-centered decision making, and physician interpersonal style) through the Interpersonal Processes of Care survey (IPC-29), disease activity through the Systemic Lupus Activity Questionnaire, and depression through the Patient Health Questionnaire-9. We used non-parametric tests to assess IPC-29 by demographics, linear trend test to assess demographic-adjusted scores of IPC-29 by disease activity and depression, and multivariate logistic regression to assess the association of disease activity and depression with suboptimal IPC scores.

**Results:** Lowest IPC-29 scores were for patient-centered decision making, specifically for the "asked patient" subdomain (how often doctors assessed patients' problems to follow recommendations and treatment) in women compared with men (mean score 3.1±1.4 and 3.6±1.4, respectively;  $p=0.02$ ). Scores for the "assumed socioeconomic level" subdomain (how often doctors make assumptions about a patient's socioeconomic level) in the interpersonal style domain were higher (worse) in patients aged 18–34 (mean score 1.6±0.9), compared to those aged 35–55 (mean score 1.5±0.9;  $p=0.03$ ). Patients with higher educational attainment ( $\geq$ college) reported poorer mean scores for most communication and interpersonal style scales than those with  $\leq$ high-school. We found significant linear trends of poorer scores for all communication scales across more severe

disease activity and depression, and poorer scores for all interpersonal style scales across more severe disease activity. Neither disease activity nor depression was associated with worse patient-centered decision-making. In multivariate models depression was associated with suboptimal quality of communication (OR 1.2; 95% CI 1.04–1.4) and interpersonal style (OR 1.1; 95% CI 1.0–1.3); and disease activity increased the odds of suboptimal communication (OR 1.1; 95% CI 1.0–1.3).

**Conclusions:** In AA patients with SLE, perceptions of physicians' communication, shared decision-making, and physicians' interpersonal style vary by sex and education. While disease activity and depression were associated with worse reports of physician-patient communication and interpersonal style, neither disease activity nor depression influenced shared-decision making. Our data suggest that in addition to standard of care treatment, AA SLE patients with active disease and depression might need provider-based interventions focused on communication and interpersonal style.

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#### FRI0615 NORMALISED TOXICITY TO PREGABALIN DID NOT INCREASE WITH CHANGES IN APPROVAL MECHANISM AND USE IN AUSTRALIA

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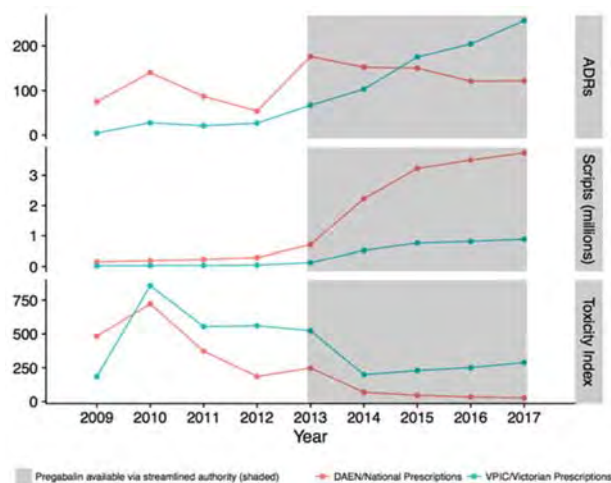
**Background:** Pregabalin is a potent antagonist of neuronal voltage-gated calcium channels used to treat neuropathic pain. Although first registered with the Therapeutic Goods Administration (TGA) in April 2005, rapid uptake of pregabalin in the Australian market only came after its listing on the Pharmaceutical Benefits Scheme (PBS) with a streamlined code on 1st March 2013 for the indication of neuropathic pain. Recently, there has been concern raised about the growing off-label use of pregabalin for chronic pain syndromes and the subsequent potential for undue adverse drug reactions (ADRs).<sup>1</sup>

**Objectives:** The aim of this study was to measure how broadening access to pregabalin in Australia affected the rate of pregabalin-associated ADRs, and whether such an effect was disproportionate to the change in pregabalin prescription rates.

**Methods:** We extracted ADRs reported in the TGA Database of Adverse Event Notifications (DAEN) between 1st January 2009 and 18th October 2017, in which pregabalin was thought to have been causative. We also extracted calls to the Victorian Poisons Information Centre (VPIC) between 1st January 2009 and 31st December 2017 in which pregabalin was a reported exposure. For both databases, ADR rates were annualised, with the missing DAEN ADR reports between 19th October 2017 and 31st December 2017 imputed using a linear model based on year-to-date ADR rates. The annual ADR rates were normalised by dividing by the estimated number of pregabalin prescriptions filled (in millions), to obtain a normalised Toxicity Index (number of ADRs per million scripts). Because the data was annualised, the 1st January 2013 was used as the approximate starting date of PBS streamlined listing.

**Results:** The estimated number of pregabalin prescriptions filled in Australia increased over the study period from 155,336 in 2009 to 3,739,421 in 2017. A total of 886 ADRs were reported to VPIC over the study period, and 1056 reported to DAEN (1076 after extrapolation). The mean Toxicity Index (TI) for the VPIC database was 539 ADRs/million scripts before PBS streamlined listing, and 298 ADRs/million scripts after; there was no evidence that the TI had increased ( $p=0.9$ , one-tail t-test). Similarly, the TI for the DAEN database was 441 ADRs/million scripts prior to PBS streamlined listing, versus 85 ADRs/million after; there was no evidence that TI increased ( $p=0.98$ , one-tail t-test).





**Conclusions:** After adjusting for the total volume of scripts dispensed, the rate of ADRs involving pregabalin in both the VPIC and DAEN databases did not increase after a streamlined approval mechanism was adopted, leading to significantly increased use. These data do not support the emergence of undue adverse drug reactions from increased off-label use of pregabalin.

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FRI0616

#### COST-EFFECTIVENESS OF SWAPPING STRATEGY FOR ESTABLISHED PSORIATIC ARTHRITIS AND IMMEDIATE VERSUS STANDARD SWAPPING STRATEGY FOR EARLY PSORIATIC ARTHRITIS

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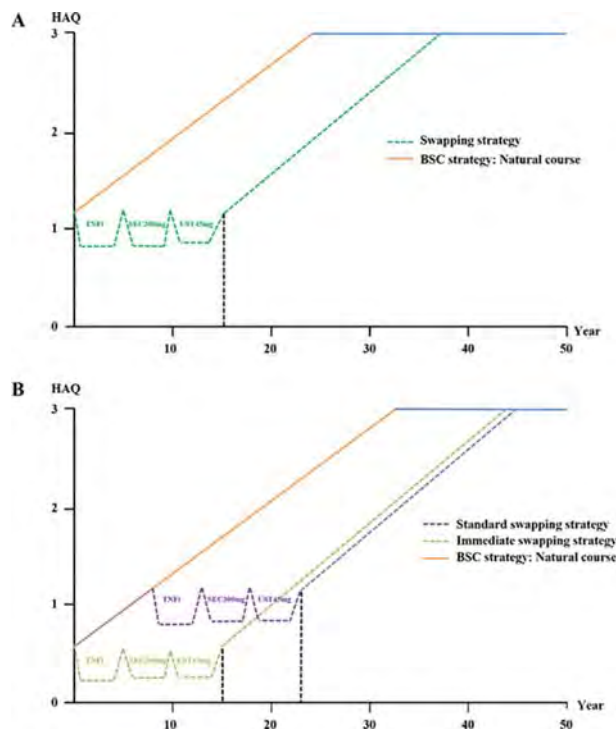
**Background:** For patients with psoriatic arthritis (PsA) failing the first TNF-inhibitor, switching to biologic DMARDs [bDMARDs] with different mechanism of actions (swapping strategy) may be superior than switching to another anti-TNF (cycling strategy) [1,2].

**Objectives:** To evaluate the cost-effectiveness of 1) swapping strategy for established PsA and 2) immediate versus standard swapping strategy for early PsA from the Hong Kong (HK) societal perspective

**Methods:** Based on comparative effectiveness from network meta-analysis of randomized controlled trials and treatment-specific withdrawal and serious adverse event rate, a swapping York model with life time horizon was developed to evaluate swapping strategy relative to best supportive care (BSC) for PsA failing the first anti-TNF. Initial response to bDMARDs was determined using the Psoriatic Arthritis Response Criteria. The impact of biologics on the arthritis component of the disease is modelled via a change in the HAQ and the impact of the skin component measured using the Psoriasis Area and Severity Index. The model was specified for two hypothetical subpopulations including patients with 1) established PsA (age=47, HAQ=1.22, figure 1A) received five swapping strategies and 2) early PsA [3] (age=40, HAQ=0.71, figure 1B) received immediate (start bDMARDs after diagnosis) or standard (initially given BSC and then start bDMARDs when HAQ increase to 1.22) use of the most cost-effective swapping strategy. Both subpopulations were further classified according to the level of concomitant psoriasis [mild to moderate psoriasis (MMP, PASI=0.73) or moderate to severe psoriasis (MSP, PASI=12.5)]. All five swapping strategies started with an anti-TNF (infliximab, adalimumab, etanercept, certolizumab or golimumab), followed by secukinumab 300 mg and then ustekinumab 45 mg. The cost-effectiveness of each strategy was determined using a willingness-to-pay (WTP) threshold of £32,356/ quality-adjusted life-year (QALY) (HK Gross Domestic Product per capita).

**Results:** For the base-case scenario, all five swapping strategies are cost-effective versus BSC strategy for established PsA, which are associated with greater QALY gain and lower treatment related direct costs, psoriasis cost and

productivity loss. In established PsA with MMP and MSP, etanercept swapping strategy is likely to be the most cost-effective strategy with an incremental cost £9,518.93 and £9,084.58 per QALY gained over BSC strategy respectively. For early PsA with MMP and MSP, the base-case results indicated that standard etanercept swapping strategy was cost-saving (£-50,635.74 and £-67,843.32) and more effective (1.20 and 1.32 QALYs); while immediate etanercept swapping strategy was costlier (£13294.95 and £8986.16), more effective (3.82 and 3.27 QALY), and had relative low ICER (£3482.36 and £2745.35 per QALY gained) relative to BSC strategy.



**Conclusions:** Swapping strategy showed favorable cost-effectiveness for established PsA as well as early PsA. The increased costs of biologic agents are offset by the gain in benefits from long-term HAQ reduction.

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FRI0617

#### UPTAKE ON FLU AND PNEUMONIA VACCINATION AT THE RHEUMATOLOGY CLINIC AT A UK DISTRICT GENERAL HOSPITAL- ARE WE BETTER THAN 10 YEARS AGO?

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**Background:** Patients with rheumatic diseases are at increased risk of contracting infection due to the disease itself or because of the use of immunomodulatory medication. EULAR has developed recommendations and supports vaccination against influenza and pneumococcal infections in immunocompromised patients<sup>1</sup>. Despite convincing data regarding the efficacy of vaccination with the use of disease-modifying anti rheumatic drugs (DMARDs), previously published data from our trust in 2007 showed that uptake of vaccination was suboptimal especially in those aged <65 years<sup>2</sup>.

**Objectives:** To establish the influenza or pneumococcal (pneumovax) vaccination uptake and explore reasons for reduced uptake in patients attending a rheumatology clinic.

**Methods:** Prospective audit of 100 patients attending the Rheumatology clinic in a UK district hospital using an anonymised survey during November to December 2017 and comparison with the data of 10 years ago.

**Results:** A total of 100 questionnaires were given out, with return rate of 98%. Female:male ratio was 3.8:1, mean age 55±17. Most patients were treated for RA (24%), Psoriatic arthritis (20%), Ankylosing spondylitis (14%) and others, see figure 1. Regarding immunosuppression 16% were on biologics and 78% on DMARDs. Most were on methotrexate (26%), Prednisolone (16%), hydroxychloroquine (12%), sulfasalazine (12%) whereas biologics were <10% each (see figure 1).

With regards to vaccination for influenza, overall 47% had received the vaccine (see table 1). Of those who did not take the vaccine 35% had an allergy or did not believe it was effective, but 65% were not offered the vaccine. A total of 52% commented that a health professional had discussed influenza vaccination with them, 42% mentioned that this was never discussed and 6% were unsure. In RA population uptake was 48% compared to 44% 10 years ago ( $p=0.81$ ).

Regarding pneumovax 29% commented that a health professional had discussed pneumococcal vaccination and only 28% had received the vaccine. Of those who did not take the vaccine 12% had an allergy or did not believe it was effective, and 83% were not aware that the vaccine existed or were not offered the vaccine. In RA population uptake was 61% compared to 62% 10 years ago ( $p=0.62$ ). RA patients had better vaccination than psoriatic patients for influenza ( $p=0.03$ ), but not pneumovax ( $p=0.52$ ).

UPTAKE OF VACCINE	Influenza vaccination	Pneumonia vaccination
All patients -2017	47%	28%
RA patients- 2007	62%	44%
RA patients- 2017	16/23 (61%)	11/23 (48%)
Psoriatic Arthritis	6/18 (33%)	6/18 (33%)
Prednisolone	10/14 (71%)	9/14 (64%)
Methotrexate	14/22 (63%)	11/19 (58%)



**Conclusions:** Although this is a small audit conducted in a routine rheumatology clinic in the UK, it is of concern that with increased patient education seen in the last 10 years, vaccination for influenza and pneumococcus has not improved. Perhaps healthcare professionals are not discussing this with the patients sufficiently. Further patient and healthcare involvement is required to reverse the declining trend and protect our patients.

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#### FRI0618 CONCORDANCE WITH LATEST GUIDELINES FOR DMARD SCREENING AND MONITORING IN SECONDARY CARE

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**Background:** DMARDs need to be prescribed safely. Screening and monitoring for toxicity is essential when using these medications. The British Society of

Rheumatology (BSR) has recently published guidance on screening and monitoring of non-biologic DMARDs.

**Objectives:** The aim of this audit was to assess current practice on synthetic DMARD screening and monitoring within our rheumatology department, in a secondary care setting, using the BSR 2017 guidelines as the standard of care.

**Methods:** 81 consecutive adult patients who were started on synthetic DMARDs in 2016 were recruited. The data required was collected from case notes and isoform clinical manager after obtaining data protection clearance. DMARDs included Hydroxychloroquine (HCQ), Methotrexate (MTX), Sulfasalazine (SSA), Azathioprine (AZA) and Leflunomide (Lef). Baseline screening was assessed by checking for documentation of height, weight, baseline blood tests including virology and documentation of known lung disease and smoking with the relevant investigations when necessary. Specialist nurse referral and content of consultation was assessed for discussion regarding fertility/pregnancy when relevant, intercurrent illnesses and vaccinations. Drug-specific screening and monitoring included folic acid prescription (FA) for MTX, TPMT testing for AZA, ophthalmic review for HCQ as well as weight and blood pressure (BP) monitoring for Lef. Finally all patients were checked for regular blood monitoring at weeks 2,4,6 and every 3 months thereafter with the exception of SSA & HCQ monotherapy. Calibri (Body)

**Results:** Weight and height were not documented in 50.6% and 66.7% of patients respectively. Baseline blood tests were present in all but 1 patient with the exception of virology. The latter was present in 6.2% of cases only. Smoking status was assessed in 92.6% of cases. CXR and pulmonary function tests were warranted for 9 patients but were only done in 4 cases. 98.8% of patients were referred to the specialist nurse for DMARD education. Discussion on fertility and pregnancy, where applicable, was discussed in 95% of cases, vaccinations in 97.5% of cases and advice regarding management of intercurrent illnesses in 2.5% of cases. Drug monitoring at 2, 4 and 6 weeks was done in 33.3%, 90.1% and 80.2% of cases respectively. BP and weight were checked for all patients on Lef whilst blood monitoring for SSA monotherapy persisted after 1 year in 80% of cases. Drug specific recommendations including FA prescription, TPMT testing and ophthalmic reviews were done in all patients.

**Conclusions:** This audit showed a high level of concordance with the BSR monitoring guidelines for synthetic DMARDs. Aspects that require improvement have been highlighted. By ensuring that there is proper documentation of all aspects pertaining to the work-up prior to starting a patient on a DMARD, one can then introduce screening and monitoring schedules targeted at the prevention and early detection of adverse treatment outcomes.

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#### FRI0619 PREDICTORS AND TEMPORAL TREND OF SEASONAL INFLUENZA VACCINATION IN AUTO-IMMUNE RHEUMATIC DISEASES IN THE UK: A NATIONWIDE PROSPECTIVE COHORT STUDY

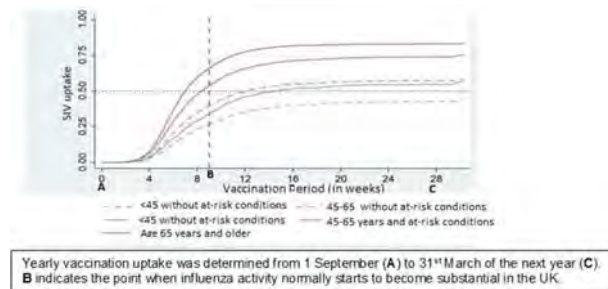
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**Background:** Autoimmune rheumatic diseases (AIRDs) are associated with an increased risk of influenza and its complications which may be compounded by the use of potent disease modifying anti-rheumatic drugs (DMARDs). In the United Kingdom, seasonal influenza vaccination (SIV) is recommended for people older than 65 years, and for those at a higher risk of influenza due to underlying diseases or immunosuppressive treatment. Understanding SIV uptake in AIRD patients on DMARDs could identify subsets who need targeted effort to optimise SIV uptake in this group.

**Objectives:** To [1] examine temporal trends in uptake of SIV; [2] explore disease and demographic factors associated with receiving the SIV; and [3] calculate the proportion of people with AIRDs who are vaccinated in time before the seasonal flu virus circulates.

**Methods:** 32,751 people with AIRDs prescribed DMARDs between 2006 and 2016 were identified from the Clinical Practice Research Datalink (CPRD). CPRD is one of the world's largest prospective databases of primary care records, and includes primary-care medical, prescription and immunisation data on 8% of the UK population at any one time. The proportion of eligible cases vaccinated between 01/September of one year and 31/March of the next year (flu-season) was calculated and stratified by age, presence of additional indications for vaccination, AIRD type, and number of DMARDs prescribed. We used Joinpoint regression analysis to determine the temporal trend in SIV uptake while Poisson regression with robust error variance was used to examine the univariate and multivariate association between age, sex, AIRD type, additional indication for being vaccinated, total number of different DMARDs prescribed in the 12-month period with receiving SIV. The analysis was conducted in the open source Joinpoint regression software and Stata-MP.

**Results:** SIV uptake was high in those  $\geq 65$  years old (82.3% and 80.7% in 2006–07 and 2015–16 respectively). However, it was significantly lower in other age groups, but improved over time with 51.9% and 61.9% in the 45–64 year age group, and 32.3% and 50.1% in the <45 year age group being vaccinated in 2006–07 and 2015–16 respectively. While 64.9% of the vaccinations in those  $\geq 65$  years old occurred by the 3rd November (week 9 in Graph 1), in time to mount a protective immune response before the influenza activity becomes substantial in the UK, only 38.9% in the 45–64 year and 26.2% in the <45-year age group without any other reason for vaccination received SIV before this date (Graph 1). Men, those without additional indications for vaccination, and those on single DMARDs were significantly less likely to be vaccinated.



**Conclusions:** The uptake of SIV is low in the under 65s, and many do not get vaccinated in time to confer immunity. Additional effort is required to promote the timely uptake of SIV in this population. To our knowledge, this is the first study to assess temporal trends in uptake of SIV among AIRDs and to compare uptake across different AIRDs.

**Disclosure of Interest:** None declared

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#### FRI0620 LOW EDUCATIONAL ATTAINMENT IS ASSOCIATED WITH POOR PATIENT STATUS AT THE INITIAL VISIT OF PATIENTS WITH RHEUMATOID ARTHRITIS (RA) OR OSTEOARTHRITIS (OA) AT THE INITIAL VISIT TO A RHEUMATOLOGY SETTING, WITH SIMILAR PATTERNS IN PATIENTS WITH EITHER DIAGNOSIS

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**Background:** Low educational attainment is associated with a higher prevalence, morbidity, and mortality of many diseases, including rheumatoid arthritis (RA) (J Chronic Dis 1985; 38:973–84) and osteoarthritis (OA) (J Clin Epidemiol 1992;45:139–47). These associations often are attributed to limited access of disadvantaged people to medical services (Ann Intern Med 1998;129:412–6), although some have suggested that these differences are explained primarily by differences in patient self-management (Ann Intern Med 1998;129:406–11).

**Objectives:** To study clinical status of patients with RA or OA, all of whom had access to rheumatology care, at their initial visit.

**Methods:** All patients with all diagnoses seen at an academic rheumatology site complete a self-report multidimensional health assessment questionnaire (MDHAQ) at each visit. MDHAQ includes 30–10 scales for physical function (FN), pain (PN) and global assessment (PATGL), compiled into a 0–30 routine assessment of patient index data (RAPID3). Patient-reported FN, PN, PATGL and RAPID3 were compared in new patients with a primary diagnosis of either RA (n=66) or OA (n=66) at a first visit in 3 groups according to years of formal education, <12, 12, and >12 years, using analysis of variance (ANOVA).

**Results:** Mean MDHAQ scores were quite similar in OA vs RA, and varied similarly according to education level (table 1). In all patients, mean RAPID3 was 15.4 in OA vs 15.3 in RA; in those with <12 years, 18.2 in OA vs 19.8 in RA; in those with 12 years, 15.9 in OA vs 16.0 in RA; in those with >12 years, 14.0 in OA vs 13.7 in RA (p=0.11 for OA, p=0.04 for RA) (table 1). FN scores were 3.9 in both groups with <12, 3.3 in both groups with 12, and 2.3 in OA vs 2.4 in RA patients with >12 years of education (p=0.02 for OA, p=0.08 for RA). PN scores were 7.3 and 8.5 for OA vs RA with <12 years, 7.1 and 6.2 for OA vs RA with 12 years, and 6.7 vs 5.9 for OA vs RA patients with >12 years of education (p=0.69 for OA, p=0.02 for RA). PATGL was 7.0 vs 7.4 for OA vs RA with <12 years, 5.5 and 6.5 for OA vs RA with 12 years, and 5.1 and 5.4 in OA vs RA patients with >12 years of education (p=0.14 for OA, p=0.12 for RA).

Table 1 Mean & standard deviation (SD) for 0–10 physical function, pain, patient global assessment and 0–30 RAPID3 of patients with RA or OA at first visit, by formal education level

OA – measures	Total N=66	Groups by level of education (years)			p
		<12 (n=12)	12 (n=21)	>12 (n=33)	
Function (0–10)	2.9 (2.0)	3.9 (1.5)	3.3 (2.3)	2.3 (1.7)	0.02
Pain (0–10)	6.9 (2.3)	7.3 (1.7)	7.1 (2.4)	6.7 (2.5)	0.69
PATGL (0–10)	5.6 (2.9)	7.0 (2.1)	5.5 (3.1)	5.1 (2.9)	0.14
RAPID3 (0–30)	15.4 (6.0)	18.2 (3.9)	15.9 (6.8)	14.0 (5.9)	0.11
RA – measures	Total N=66	Groups by level of education (years)			p*
		<12 (n=12)	12 (n=21)	>12 (n=33)	
Function (0–10)	2.9 (2.2)	3.9 (3.0)	3.3 (2.1)	2.4 (1.8)	0.08
Pain (0–10)	6.4 (2.9)	8.5 (1.5)	6.2 (3.4)	5.9 (2.7)	0.02
PATGL (0–10)	6.0 (3.0)	7.4 (3.1)	6.5 (3.3)	5.4 (2.8)	0.12
RAPID3 0–30)	15.3 (7.2)	19.8 (6.3)	16.0 (8.1)	13.7 (6.5)	0.04

**Conclusions:** Low education was associated with RAPID3 and all component scores similarly in RA and OA. Differences according to formal education level were greater than by diagnosis, which were negligible. These variations do not appear attributable to differences in access to medical services.

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#### FRI0621 HOSPITAL ADMISSIONS AND READMISSIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS. ASSOCIATED FACTORS AND DIRECT HEALTH-CARE COSTS IN A THIRD LEVEL UNIVERSITY HOSPITAL

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**Background:** In last years, the direct health-care costs derived from admissions and readmissions to Rheumatology departments of patients with Rheumatoid Arthritis (RA) have diminished. Presumably, the higher survival rate and the amount of comorbidities of these patients have derived in an increased of admissions and direct costs to other medical and surgical departments.

**Objectives:** To describe the admission and readmission causes of all patients with RA admitted during 2015 and 2016 and to identify factors associated to readmission. Finally to estimate the costs derived from these events in the same period.

**Methods:** All electronic medical reports were revised; demographic, medical and therapeutic data, as well as diagnosis at discharge were collected. A descriptive analysis followed by a logistic regression analysis were done to identify readmission-associated variables. Financial analysis was done by calculating the price of the stay according to established in 2015-scale.

**Results:** 240 admissions of 158 patients were found. Mean age 63.8 years, 69% women and mean evolution of RA of 13.1 years. At admission, 53% were on oral steroids and 45% with synthetic DMARD. Admissions were mainly distributed in Internal Medicine department (26%). Infections were the most frequent admission cause (33%), followed by cardiovascular events (20%) and oncological processes (13%). Forty-nine patients (31%) were readmitted, 47% due to infections. Age (OR/year 1.02 CI 95% 1.00–1.04), diabetes (OR 2.1 CI 95% 1.1–4.4) and chronic kidney disease (OR 3.3 CI 95% 1.0–10.2) were the associated risk factors. There were a total of 2172 days of stay with an estimated cost of 530420 euros and 783 days of stay due to readmissions with a total cost of 203218 euros. Departments which generated more costs either for admissions or readmissions were Oncology (65064 euros/19585 euros respectively) and Intensive Care (68011 euros/42651



respectively). Costs for admission and readmission in Rheumatology department were 5230 and 3175 euros respectively.

**Conclusions:** Admission and readmission of patients with RA are mostly due to infections and cardiovascular causes. Estimated direct costs are higher for patients admitted to Intensive Care Unit or Oncology

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FRI0622

### TRENDS IN ENCOUNTERS WITH RHEUMATOLOGISTS IN A PUBLICLY-FUNDED SINGLE PAYER HEALTHCARE SYSTEM

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**Background:** Rheumatology workforces are challenged by too few physicians, increasing incidence and prevalence of MSK diseases (and complexity of co-morbid conditions) in aging populations, and expanding therapeutic options that increase demand for service. Understanding trends in rates of rheumatology encounters with new and existing patients will help to identify why patients have delays to rheumatology care and mobilize efforts to help meet patients' needs.

**Objectives:** To describe trends in patient encounters with rheumatologists over time in Ontario, Canada.

**Methods:** We analyzed administrative health data from 2000 to 2013 in Ontario, Canada, where all 13 million residents are covered by a publicly-funded healthcare system and access to rheumatologists is dependent upon referrals. During this time, Ontario had a stable rheumatology supply of 1 rheumatologist per 75,000 population (0.7 FTEs/75,000). We determined annual incident, follow-up and total patient encounters seen by rheumatologists. Rates were calculated using the total population of Ontario residents 18 and older, each year. Diagnosis codes assigned at each encounter were used to assess changes in the case-mix of patients under rheumatology care over time.

**Results:** From 2000 to 2013, the proportion of all Ontario residents seen by rheumatologists was constant over time (2.7%). The total number of rheumatology encounters increased from 561,452 to 742,952 but the total encounter rate remained relatively stable over time (table 1). The annual new consultation rate significantly declined over time from 1.6 to 0.8 new patients per 100 population. Both the annual proportion of incident patients and the ratios of incident to established patients and incident to total patient encounters declined significantly over time. We observed a shift in the diagnostic case-mix over time: encounter rates for systemic inflammatory conditions significantly increased over time and encounter rates for non-systemic conditions (OA, regional MSK conditions) decreased. The volume of rheumatoid arthritis (RA) encounters increased the most, with 17% of all rheumatology encounters related to RA in 2000 versus 32% in 2013.

Table 1 Trends in rheumatology encounters over time, rates expressed per 100

Year	Total Number of Unique Patients (%) <sup>1</sup>	Total Patient Encounters	Total Encounter Rate <sup>2</sup>	New Consultation Rate <sup>3</sup>	Proportion of New Patients out of all Unique Patients	Proportion of New Patients out of Total Encounters	Ratio of New / Established Patients
2000	245486 (2.7%)	561452	6.2	1.6	59%	26%	1.5
2001	255289 (2.8%)	586581	6.4	1.4	52%	23%	1.1
2002	263139 (2.8%)	599278	6.4	1.4	48%	21%	0.9
2003	250176 (2.6%)	571368	6.0	1.2	44%	19%	0.8
2004	258751 (2.7%)	599821	6.2	1.1	41%	18%	0.7
2005	273462 (2.8%)	634730	6.5	1.1	40%	17%	0.7
2006	286309 (2.9%)	663302	6.7	1.1	39%	17%	0.6
2007	280072 (2.8%)	652933	6.5	1.0	35%	15%	0.5
2008	282959 (2.8%)	667337	6.5	0.9	34%	14%	0.5
2009	284158 (2.7%)	685195	6.6	0.9	33%	14%	0.5
2010	285103 (2.7%)	693667	6.6	0.9	32%	13%	0.5
2011	288422 (2.7%)	725807	6.9	0.8	31%	12%	0.5
2012	281754 (2.6%)	698384	6.5	0.8	31%	12%	0.4
2013	293704 (2.7%)	742952	6.8	0.8	30%	12%	0.4

<sup>1</sup> Percentage represents the proportion of Ontario Residents seen by a rheumatologist  
<sup>2</sup> Numerator: Total rheumatology encounters; Denominator: Total population  
<sup>3</sup> Numerator: Number of new patients; Denominator: Total population

**Conclusions:** The significant decline in new patient consultation rates over time helps illustrate the growing supply-demand mismatch in rheumatology care. An increasing fraction of rheumatology encounters in Ontario are with established

patients, which may be limiting access for new consultations and increasing wait times. We also observed a shift in the patient case-mix over time with rheumatologists seeing/prioritizing more systemic inflammatory conditions. Our findings provide new inputs for rheumatology workforce planning models.

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FRI0623

### COST-EFFECTIVENESS ANALYSIS FOR THE TREATMENT OF EARLY RHEUMATOID ARTHRITIS WITH BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS (DMARDS) COMPARED TO STANDARD OF CARE IN SINGAPORE

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**Background:** Biologic disease modifying anti-rheumatic drugs (bDMARDs) are known to be effective in controlling disease activity and reducing radiographic progression in patients with rheumatoid arthritis (RA) who have failed methotrexate (MTX). The cost-effectiveness of bDMARDs in comparison to combination conventional synthetic DMARD (csDMARD) therapy in Asian countries has not been well studied, and their place in the DMARD escalation algorithm is unclear.

**Objectives:** To assess the cost-effectiveness of step-up combination csDMARD versus bDMARD therapy for patients who have failed initial MTX monotherapy over one year.

**Methods:** We prospectively recruited all adult patients with inflammatory polyarthritis (IP) affecting  $\geq 2$  peripheral joints and symptom onset after September 1, 2012 from the only two hospitals serving Western Singapore to the Singapore Early Arthritis Cohort (SEAC). Baseline data on demographics, time of symptom onset and DMARD prescription, utility values (EQ-5D) and costs were collected by face to face interview, chart review, hospital financial records and assessment by a trained nurse. A cost-effectiveness analysis (CEA) was then performed using a decision tree comparing four sequences of DMARD therapy: MTX and infliximab, MTX and etanercept, triple therapy (TT) [MTX, sulphasalazine (SSZ) and hydroxychloroquine (HCQ)] and combination MTX and HCQ. An effective treatment was defined as achieving Disease Activity Score 28 (DAS28 (ESR)) < 2.6; "remission". A treatment switch to a rescue therapy (MTX and adalimumab) was factored in case of not achieving remission or if serious adverse event was experienced. Cost and utility (using Singapore preference weights<sup>1</sup>) information were derived from patients diagnosed with rheumatoid arthritis in the SEAC database as of June 16, 2017. Efficacy, rates of adverse events, disutility from adverse events, indirect costs and cost of serious adverse events were assumed from literature. One-way and probabilistic sensitivity analysis with 10,000 runs was performed.

**Results:** For the base case, the treatment with MTX and etanercept was dominated by conventional TT. The incremental cost of switching from TT to MTX and infliximab was SGD\$16,118. The net gain in quality-adjusted life years (QALY) was 0.02. The incremental cost-effectiveness ratio (ICER), representing the additional cost of one unit of QALY gained by MTX and infliximab compared with TT, was \$1,024,785/QALY. The probabilistic sensitivity analysis predicted that triple therapy would be the preferred treatment (89.6%) at a willingness-to-pay threshold of SGD\$70,000.

Table 1

Arm	Incremental Cost	QALY	Incremental QALY	ICER
Triple Therapy	-	0.90	-	-
MTX + HCQ	2,587	0.88	-0.02	Dominated
MTX + etanercept	16,024	0.89	-0.01	Dominated
MTX + infliximab	16,117	0.91	0.02	1,024,785

**Conclusions:** Our model suggests that the ICER of bDMARD therapies explored do not compare favorably to csDMARD therapies. In the Singapore context, societal funding for bDMARDs can only currently be recommended after failure of combination csDMARD.

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FRI0624

### MUSCULOSKELETAL PROBLEMS AMONGST TRAIN OPERATORS: A COLLABORATIVE APPROACH TO IDENTIFY SOLUTIONS

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**Background:** Transport for London (TfL) Occupational Health Dept identified musculoskeletal (MSK) problems as matters of concern in train operating staff on 3 of the underground lines (JNP). These issues were contentious and the subject of continued discussion between the management of TfL, train operators, Unions and other stakeholders. The Bone and Joint Research Group (BJRG) were invited to undertake work to provide insight into the MSK health issues of train operators from a neutral perspective.

**Objectives:** To assess the problems and issues relating to the musculoskeletal health of train operators.

**Methods:** A steering committee was created with representatives from the train operators, the Unions, TfL managers and other stakeholders. Participants were recruited to 6 focus groups. Separate focus groups were held for operators, managers and for other stakeholders. The groups were asked to discuss the status of their own MSK health, the impact of work on their MSK health, the support they receive from their employer and others, barriers and facilitators to maintaining MSK health, the role of managers in improving MSK health in the workplace and what interventions would improve MSK health.

The focus groups were recorded transcribed and analysed using Thematic Analysis.

The findings informed a survey of JNP train operators. The survey was co-produced and endorsed by the BJRG, TfL and the Unions and circulated to train operators. The survey included questions on demographics, lifestyle, work role, posture training, MSK problems, actions taken and ideas on how MSK risks could be managed and MSK health protected and improved.

**Results:** 20% of train operators (338) completed the survey. Respondents reflected the demographic profile of the total JNP train operators. 72% reported not receiving adequate posture training. 74% experienced MSK pain, either currently or in the past. Of these 52% were currently in pain. The average number of months in pain was 59. Lower back, neck and shoulders were the most frequently reported sites of pain. 74% said the pain was caused by or worsened by work. An average of 7 days of work was lost per year due to MSK problems. 44% had not told their manager. Most respondents said their MSK health could be improved by improvements to their seating and cab ergonomics.

Participants acknowledged that it is an individual's responsibility to look after their own MSK health and suggested ways to do this. These included changing position when driving, stretching, improved posture, employing good manual handling techniques, exercising outside of work and eating healthily.

**Conclusions:** MSK problems are a significant issue among JNP train operators and structural problems are perceived to be the main cause. Operators are aware of their own role in maintaining their MSK health both at work and at home. The study illustrates that it is possible to work effectively and collaboratively with a range of workplace stakeholders to achieve a common goal of improved MSK health. The active involvement of all stakeholders throughout the process and the engagement of a neutral research organisation increased "buy-in" and gave credibility to the project. The findings are currently being considered by the steering committee to produce a series of recommendations at the policy, operational and individual level to protect the MSK health of train operators.

**Disclosure of Interest:** None declared

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FRI0625

### DIFFERENT STRATEGIES TO IMPLEMENT THE EULAR GUIDELINE FOR CARDIOVASCULAR RISK MANAGEMENT IN DAILY PRACTICE

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**Background:** The updated EULAR cardiovascular risk management (CVRM) guideline recommends cardiovascular disease risk assessment at least once every five years in all patients with rheumatoid arthritis (RA).<sup>1</sup> A literature search indicates that this guideline is marginally applied in clinical practice.<sup>2</sup> An important factor explaining dissimilarities in the quality of CVRM could be the different strategies being used to implement this guideline in daily care.

**Objectives:** This study describes the differences in cardiovascular risk identification and management for patients with RA between outpatient clinics of the members of the Trans-Atlantic Cardiovascular Consortium for Rheumatoid Arthritis (ATACC-RA).

**Methods:** A questionnaire was sent to all members of ATACC-RA, which included 16 questions about 'the organisation and responsibility of CVRM in their hospital', 'the screening of cardiovascular risk factors', 'communication about CVRM between medical professionals' and 'availability of data regarding CVRM'.

**Results:** Six out of eight outpatient clinics reported that they work according the EULAR CVRM recommendations. Three strategies to organise CVRM in daily practice could be distinguished: 1) The treating rheumatologist performs CVRM during the outpatient visits; 2) Cardiologists, rheumatologists and/or a general practitioners co-operate in a cardio-rheuma-clinic/team with different tasks and responsibilities and 3) the general practitioner screens and treats cardiovascular risk factors. Six outpatient clinics reported that they have (digital) data about the current CVRM status of their RA patients and are willing to share them to compare the quality of the CVRM care between the different strategies.

**Conclusions:** Each cardiovascular risk management strategy was based on agreements between medical professionals about who is responsible to perform CVRM. However, each strategy is also (partly) dependent of the national health-care system and financial resources. Independent of how CVRM is organised, communication and feedback between medical professionals about the current CVRM status of each RA patient, are important factors to perform CVRM adequately. Further analyses on the effectiveness of the various systems are warranted.

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**FRI0626** **SCREENING FOR TUBERCULOSIS BEFORE TNF INHIBITOR THERAPY REMAINS SUBOPTIMAL: A MULTI-SPECIALTY, REAL WORLD, NATIONWIDE EXPERIENCE IN THE UNITED STATES**

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**Background:** Tumor necrosis factor- $\alpha$  inhibitors (TNFi's) effectively treat various autoimmune conditions, but drastically increase the risk of tuberculosis (TB) reactivation. Multiple international guidelines recommend screening for TB prior to initiating TNFi therapy. In the United States, this has also been incorporated into the Medicare Merit-Based Incentive Payment Systems (MIPS) quality measures, which affect physician remuneration.

**Objectives:** To determine the proportion of patients screened for TB prior to initiating TNFi therapy.

Table 1 Baseline Characteristics of Patients Who Initiated New TNFa Inhibitor Therapy

	Total (n = 78,088)
Age, mean $\pm$ SD years	44.8 $\pm$ 12.4
Sex	
Male	30,467 (39.0)
Female	47,621 (61.0)
Geography <sup>†</sup>	
Urban	64,937 (83.2)
Rural	11,191 (14.3)
Underlying Autoimmune Disease <sup>†‡</sup>	
Rheumatologic	39,675 (50.8)
Gastrointestinal	17,487 (22.4)
Dermatologic	13,773 (17.6)
Ophthalmologic	651 (0.8)
TNFi Inhibitor	
Adalimumab	37,576 (48.1)
Etanercept	23,210 (29.7)
Infliximab	12,810 (16.4)
Certolizumab	2,445 (3.1)
Golimumab	2,047 (2.6)
Steroids Use	
No	42,134 (54.0)
Yes	35,954 (46.0)
Prescribed non-biologic DMARD	
No	37,652 (48.2)
Yes	40,436 (51.8)
HIV	39 (0.0)
Travel <sup>#</sup>	30 (0.0)
Institutionalization	2 (0.0)

\* The ages of the patients are those at the index event.  
<sup>†</sup> Some data missing, percentages calculated from number of patients with available information.  
<sup>‡</sup> 5.5% of patients contributed to multiple categories  
<sup>#</sup> Surrogates for travel include malaria diagnosis, prophylaxis, yellow fever vaccine.

**Methods:** We retrospectively analyzed patients in the Truven MarketScan Database from 2011–2015. This is the largest dataset of its kind and contains deidentified inpatient and outpatient health information on over 100 million patients. We included patients  $\geq$ 18 years old in our cohort who were initiating TNFi therapy, based on at least 1 filled prescription. To ensure these were new TNFi starts, we excluded patients without a 6-month washout period (i.e. during which time they could not be receiving biologic DMARDs). Continuous enrollment in the database was required during the washout period and 3 months after TNFi initiation. Our primary outcome was whether patients were screened for TB during the 6-month washout period, either by interferon gamma release assays (IGRA) or tuberculin skin testing (TST). Sensitivity analysis was performed to extend the eligible screening period to 12 months pre-drug. Descriptive statistics were represented as means and medians for continuous variables and as frequencies and percentages for categorical variables.

**Results:** We identified 78,088 patients starting a TNFi. The mean age was 44.8 years and the cohort was 61% female. Adalimumab and Etanercept were the most common TNFi's. Regarding indication for TNFi, 50.8% of patients had a rheumatologic diagnosis, 22.4% gastrointestinal, 17.6% dermatologic, and 0.8% ophthalmic. Most patients received care from a rheumatologist, while 16.4% were managed by primary care alone. 36,918 (47.3%) were not screened for TB in the 6-month washout. By extending the pre-drug washout to 12 months, the proportion of unscreened patients improved mildly to 40.7%. 48.5% were screened by IGRA, 27% by TST, and 24.5% unknown. Steroid use, DMARD use and urban residence were associated with increased TB screening rates.

**Conclusions:** Screening for latent TB prior to initiating TNFi therapy was poor, such that only 52.7% received appropriate pre-drug screening. Our study population of over 78,000 patients starting a new TNFi represents nationwide, real world data across various specialties in the United States. As clinicians, these results suggest we need to improve compliance with guidelines and quality measures.

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**FRI0627** **INADVERTENT YELLOW FEVER VACCINATION OF PATIENTS WITH IMMUNE MEDIATED INFLAMMATORY DISEASE IN PRIVATE PRACTICE.**

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**Background:** Yellow Fever (YF) is an endemic disease, in specific areas of Brazil. Since 1942, no new urban cycle cases have been observed. Yet, in early 2017, outbreaks of YF were reported in many states, outside the endemic areas, where YF was not considered a risk. Hence, new and some fatal cases have been reported including in highly populated areas close to the city of São Paulo. As it has been widely broadcasted, population searching for vaccination significantly increased and cases of inadvertent vaccination have been registered.

**Objectives:** To analyze the consequences of inadvertent YF primo-vaccination in patients with immune mediated inflammatory diseases (IMID).

**Methods:** Observational study (12/2017–01/2018), 54 rheumatologists from private practice at different areas of São Paulo included specific YF information in their patients' orientations and actively searched for IMID patients that have received YF vaccination (YFV) inputting the data in a web-based questionnaire.

**Results:** 56 patients received YFV; female 42 (75%), mean ( $\pm$ SD) age= 56 $\pm$ 14 yr, median disease duration= 7 yr (6 months-45 yr), Diagnosis: RA (n=39; 72%), PsA (n=5), AS (n=4), 2 SLE, 3 vasculitis, 2 SS, one ReA and 2 UA. Treatment: 30 (54%) were considered under current strong immunosuppression (CE $\geq$ 20 mg, MTX>20 mg, leflunomide, tofacitinib and biologic agents (BA); 18 (32%) were on biologic agents (9 anti-TNF, 2 abatacept, 3 tocilizumab, 1 rituximab, 1 patient each secukinumab and tofacitinib). Remaining patients were receiving csDMARDs isolated or in combination, with or without low CE ( $\leq$ 10 mg).

Vaccination: 54 (96%) cases were primo YFV and 43 (80%) related inadvertent YFV. Adverse events (AE): 7 patients (13%) had AE after a median of 4 days (hours-60 days); 3 of them were on BA, corresponding to 17% of the total subjects on various BA. Severity of AE: 4 patients had mild AE (local pain, vertigo, fever, headache, myalgia), in 2 of them, symptoms promptly resolved while 2 needed medical assistance (one was on tocilizumab). Of the 3 remaining cases, one had severe reaction one hour after YFV (probably anaphylaxis); Finally, 2 patients had severe AE requiring hospitalization: one had meningitis (RTX+MTX) and other (ADA+MTX), abdominal pain, myalgia, fever, headache, vertigo and increased liver enzymes. No fatal events were observed. Concerning the vaccine effect on disease activity, only 5 (9%) patients related worsening of the disease after YFV, but 2 of them also presented AE.

**Conclusions:** The small number of reports precludes any conclusion about rate/severity of AE and YFV in immunosuppressed rheumatic patients. Nevertheless, it emphasized the necessary awareness and careful analysis of the risk-benefice of YFV in this population. The interference of YFV on IMID disease activity seems to be marginal. On the other hand, this descriptive analysis clearly demonstrated persistence of patient's unfamiliarity with concepts of immunosuppression and its consequences, disclosing another unmet need in the management of patients with RD.

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**FRI0628 DIGITAL TECHNOLOGIES TO PROMOTE SELF-MANAGEMENT IN MUSCULOSKELETAL HEALTH: A SYSTEMATIC REVIEW**

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**Background:** With the emergence of musculoskeletal conditions as a major threat to health status and one of the largest causes of health care expenditures, the role of self-management strategies has emerged. Digital media as a platform for self management interventions in musculoskeletal health is a new and evolving landscape in health care.

**Objectives:** To review the published evidence to support the self-management of rheumatic and musculoskeletal conditions through digital technologies.

**Methods:** MEDLINE, EMBASE, PsycINFO, Global Health, The Cochrane Library (Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials (CENTRAL), Cochrane Methodology Register), and Web of Science (science and social science citation index) were searched and the papers selected were screened by two independent reviewers. Methodological validity prior to inclusion was assessed using the appropriate critical appraisal tools developed by the Critical Appraisal Skills Programme (CASP).

**Results:** Database searches identified 5179 studies. Five randomised controlled trials assessing digital media in the self management of musculoskeletal diseases were selected. The participants in the studies were predominately females with a mean age of 50. The mean number of participants in the studies was 140.8 (range 92–228). Two studies targeted self management strategies for patients diagnosed with rheumatoid arthritis [1, 2]. One study included fibromyalgia patients [3] and the two other studies included patients that reported arthritis pain [4] or general non cancer related pain [5]. A robust and meaningful comparison between the studies was infeasible because of heterogeneity between studies and small sample size in the studies. Positive effects of self-management were demonstrated in arthritis self-efficacy, pain, physical functioning, opioid misuse and overall quality of life.

**Conclusions:** All studies showed an improvement in a number of different self-management outcomes. Digital media may be effective in the delivery of self-management programmes of patients with rheumatic and musculoskeletal conditions. Further research is necessary to increase the scope of these findings using rigorous study designs so we can harness the full potential of digital technologies as a medium for delivering self-management interventions.

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**FRI0629 PATIENT-TARGETED SMARTPHONE APPS FOR SYSTEMIC LUPUS ERYTHEMATOSUS: A SYSTEMATIC REVIEW AND ASSESSMENT OF FEATURES AND QUALITY**

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**Background:** Smartphone apps are readily accessible eHealth tools that may support the self-management of patients with systemic lupus erythematosus (SLE). However, knowledge on the availability and quality of apps targeted to this population is limited.

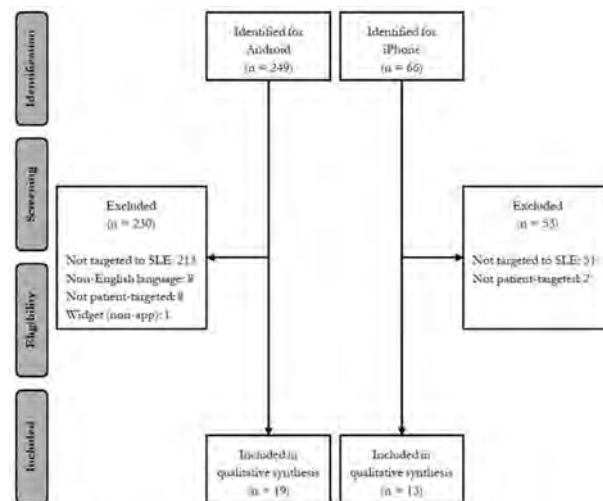
**Objectives:** To identify smartphone apps targeted to patients with SLE and to classify their functions and assess their quality using a reliable and objective scale.

**Methods:** We applied a systematic review framework to the search, screening, and assessment of apps. Android and iPhone apps were searched on the Google Play Store and the App Store, respectively in January 2018. Search terms included "lupus" or "SLE". Apps were included if they were: (1) smartphone-based; (2) compatible with the Android or the iOS operating systems; (3) in the English language; (4) targeted to people with SLE; and (5) available for download in either of the two app stores. Apps were excluded if they were: (1) targeting a condition other than SLE; (2) including only treatment algorithms; or (3) explicitly only for health care providers. App name, platform (Android, iPhone), developer, current version, cost, and user star ratings and comments were extracted. The Mobile App Rating Scale was used to classify the apps.

**Results:** We identified 315 apps, including 249 from the Google Play Store and 66 from the App Store (figure 1). Of these, 32 met inclusion criteria (19 Android, 13 iPhone).

Of the 19 Android apps, 16 were free to download and the remaining cost 2.93 – 5.65 CAD. The focus across apps were mainly to increase patient well-being. The theoretical background or strategies behind the apps varied, the most common ones included: providing information/education regarding SLE for the user (14 apps), providing advice/tips/strategies/skills training for SLE management (9 apps), and providing capabilities for monitoring/tracking of symptoms (6 apps). The user star ratings of the apps ranged from 1.5 – 5.0 stars (out of 5.0) and the number of user ratings ranged from 1 – 288. Common user critiques indicated the need for increased functionality in entering and tracking symptoms in apps that provided this feature.

Of the 13 iPhone apps, 10 were free to download and the remaining cost 2.79 – 6.99 CAD. The focus across apps were mainly to increase patient well-being. The theoretical background or strategies behind the apps varied, the most common ones included: providing information/education regarding SLE for the user (9 apps), providing capabilities for monitoring/tracking of symptoms (6 apps), and providing advice/tips/strategies/skills training for SLE management (5 apps). No user ratings or comments were available.



**Conclusions:** Applying a systematic review framework, we identified and classified 32 apps mainly focusing on increasing patient well-being in SLE. These findings have practical implications for helping patients identify potential eHealth tools to support self-management of SLE.

**Disclosure of Interest:** None declared

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**FRI0630 CAN COMMUNITY PHARMACY SERVICES BE THE MISSING LINK IN ACHIEVING EARLY DIAGNOSIS OF PSORIATIC ARTHRITIS?**

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**Background:** There is an urgent need to look at New Models of Care to improve quality of care for patients whilst providing the best value for money. Community Pharmacy has been an untapped resource which can assist in achieving the goals of managing long term conditions. Psoriasis is one such example affecting 1% to 3% of the population with upto 40% of these patients at risk of developing psoriatic

arthritis (PsA). There is plenty of evidence that early diagnosis of PsA remains suboptimal leading to poorer outcomes.

**Objectives:** The objective of this proof-of-concept study was to utilise community pharmacists in collaboration with the local Rheumatology service to screen patients with psoriasis aiming to achieve earlier diagnosis of PsA.

**Methods:** A pilot site was identified including a community pharmacy with a neighbouring GP surgery. An educational session was organised with the team to help them understand the need for the project. Logistics were finalised and a dedicated teaching was delivered covering PsA and Psoriasis Epidemiology Screening Tool (PEST) tool. PEST was chosen for its high sensitivity and specificity and positive NICE recommendation.

The dispensing personnel highlighted all patients requesting prescribed standard psoriasis-treating topical applications to the pharmacists. They confirmed the history of psoriasis with the patients, ensured the absence of a formal diagnosis of arthritis and offered the PEST questionnaire. Those who scored positive were signposted to their GPs for further consultation. The data was gathered anonymously and analysed to assess the utility of the service.

**Results:** 37 patients were identified during the 12-week proof of concept phase. 24 (65%) participants were women. Median age of the group was 48 years (range 19–73). 23/37 (62%) were white Caucasians with eight Asian and three each of Afro-Caribbean or Mixed race background. 18/37 (48%) answered yes to three or more of five-question PEST tool thereby scoring positive. Ten (27%) replies were negative and another nine (24%) declined to participate. No reasons were offered for not filling in the questionnaire. Two of the positive patients have since been reviewed by GP and referred to Rheumatology for further evaluation.

**Conclusions:** To our knowledge, this is the first study ever conducted utilising community pharmacists to employ a screening questionnaire to help early identification of possible PsA patients. This novel approach of involving community pharmacy helps explore new and proactive ways of early detection of psoriasis patients at risk of PsA and challenges the traditional model of confining the screening process to GPs in primary care. Early findings have already identified nearly half of this cohort with hitherto potentially undiagnosed PsA. This pioneering development highlights a new model of care streamlining the diagnostic pathway thereby providing better quality of care. Considering over 90% of psoriasis is managed in primary care, it would also encourage quicker assessment by a rheumatologist without burdening the already busy GP practices. Focused strategy and better utilisation of community pharmacists can be pivotal to providing better care for PsA patients in the long term.

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FRI0631

#### WORKFORCE REQUIREMENTS IN RHEUMATOLOGY: A SYSTEMATIC LITERATURE REVIEW INFORMING THE DEVELOPMENT OF A WORKFORCE PREDICTION QUALITY APPRAISAL TOOL

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**Background:** Workforce requirement studies should be conducted in order to ensure the right number of people with the right skills, in the right place at the right time to deliver organizational objectives.

**Objectives:** As part of the EULAR project to develop points to consider for the conduction of workforce studies in rheumatology, we reviewed the literature on workforce prediction with the aim to develop a workforce prediction quality appraisal tool and apply it to existing studies in rheumatology.

**Methods:** Two literature searches were performed in Ovid MEDLINE, EMBASE, CINAHL, Cochrane Library and the grey literature comprising: (1) an update of a previous systematic literature review (SLR) of workforce prediction studies in rheumatology[1] and (2) a hierarchical SLR of workforce prediction studies in other medical fields. We extracted data on type of model used, details on need, demand and supply factors considered in the model, and other relevant aspects such as regional heterogeneity or uncertainty analyses. Based on the results, key

general as well as specific need/demand, and supply factors for workforce calculation in rheumatology were identified and each factor was assigned a quality level (low, moderate, high). The quality appraisal tool was applied to the existing workforce modeling studies in rheumatology.

**Results:** Data was extracted from 14 original workforce prediction studies in rheumatology and 10 SLRs in other fields. Studies used a variety of prediction models based on a heterogeneous set of need and/or demand and/or supply factors. While only a few studies attempted to empirically validate the prediction quality of the model (n=3), the consensus was that an integrated model including all these factors is expected to have the highest validity. Based on the different factors considered in existing studies, our quality appraisal tool included the three groups of factors: general factors (e.g. type of the model, stakeholder involvement), need/demand factors (e.g. scope of diseases covered by rheumatologists, morbidity, demography) and supply factors (e.g. time dedicated to clinical work, entry to profession, demographic composition of workforce) (table 1). The majority of studies scored low or moderate on most of the factors.

Table 1 Workforce prediction quality appraisal tool

Factor*	Evidence grading	N of studies
<b>General factors</b>		
Type of model	<b>Low:</b> model that was only based on demand or need or supply factors	N=4
	<b>Moderate:</b> integrated model that considered demand, need and supply [supply (s)=demand (d) at baseline]	N=0
	<b>High:</b> integrated model that considered demand, need and supply (s<=>d at baseline)	N=4
Regional heterogeneity	<b>Low:</b> regional heterogeneity was not considered	N=8
	<b>Moderate:</b> calculations were performed on national level but anticipated regional discrepancies are discussed	N=4
	<b>High:</b> calculations took into account relevant regional profile of the country	N=2
<b>Need/demand factors</b>		
Scope of diseases covered by rheumatology specialty	<b>Low:</b> either not listed or not deemed representative (e.g. insufficient number of disease groups, unjustified author's estimate etc.)	N=3
	<b>Moderate:</b> stated but the probability that they are representative is limited	N=0
	<b>High:</b> stated and the probability that they are representative is high	N=6
Projection of population development	<b>Low:</b> not considered or only size of population is included	N=6
	<b>Moderate:</b> age or/and sex structure and/or other factors were included but using single data source and not relying on published statistics	N=5
	<b>High:</b> age or/and sex structure and/or other factors were included using more than one source and relying on published statistics or national population projections	N=0
<b>Supply factors</b>		
Time spent on clinical (rheumatologic) care	<b>Low:</b> not considered	N=4
	<b>Moderate:</b> % of time dedicated to clinical duties was defined without detailed estimation of number, duration, and type of visit OR % of time dedicated to clinical duties was calculated through estimating the number, duration and type of visits, but using single data source	N=10
	<b>High:</b> % of time dedicated to clinical duties was calculated through estimating the number, duration and type of visits, using more than one published data source	N=0
Demographic trends in workforce	<b>Low:</b> not considered	N=6
	<b>Moderate:</b> one demographic trend (e.g. ageing, feminization, millennial trend) was considered	N=3
	<b>High:</b> more than one demographic trends were considered	N=5

\* 6 out of the 21 factors of the tool are depicted in this excerpt

**Conclusions:** The existing evidence on workforce prediction in rheumatology and other fields is scarce, heterogeneous and of low or moderate quality. The workforce prediction quality appraisal tool will enable future evaluation of workforce prediction studies. This review informs the EULAR points to consider for the conduction of workforce requirement studies in rheumatology.

#### REFERENCE:

- Dejaco C, et al. Arthritis Care Res (Hoboken) 2016.

**Disclosure of Interest:** None declared

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FRI0632

#### IMPACT OF A TIGHT CONTROL MULTIDISCIPLINARY RHEUMATOLOGY PROGRAM ON THE QUALITY OF LIFE OF PATIENTS WITH AUTOIMMUNE DISEASES IN COLOMBIA

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**Background:** Autoimmune diseases are chronic inflammatory pathologies of complex etiology and variable clinical expression that usually affect young individuals, generating chronic pain and altering their functionality. Therefore, one of the mainstays of the treatment is to improve the quality of life (QoL) of these patients

**Objectives:** To determine the impact of a tight control multidisciplinary rheumatology program in the QoL of patients with rheumatoid arthritis (RA), systemic lupus erythematosus (SLE) and seronegative spondyloarthropathies (SpA).

**Methods:** A analytical quasi-experimental study was conducted were 3812 patients with RA, 590 patients with SLE and 605 patients with SpA were included and followed between February 2015 and December 2016. Two separated measurements of QoL were developed through the EuroQol Five Dimensions Questionnaire (EQ-5D) by time trade-off (TTO) valuation technique and the visual analogue scale valuation technique (EQ-VAS). Sociodemographic characteristics

were analyzed with univariate statistic. The impact on QoL was determined by McNemar test and repeated measures analysis of variance (rANOVA)

**Results:** The most affected dimensions of the EQ-5D were pain/discomfort and anxiety/depression, while the least affected was self-care. When comparing each dimension before and after the entry to the tight control program, a significant increase in the proportion of patients that perceive level 1 for each aspect evaluated was found. In addition, significant improvement was found in the global EQ-VAS (table 1)

Table 1 Percentage of the levels of EuroQol by dimension according to the diagnosis

		RA N=3812		SLE N=590		SpA N=605		Total N=5007		P- Value
		Initial (%)	Final (%)	Initial (%)	Final (%)	Initial (%)	Final (%)	Initial (%)	Final (%)	
<b>Mobility</b>	1	43	55,7	59,8	45,4	56,5	65,9	46,1	52,6	0,003
	2	54,9	42,1	38,8	52,8	41,5	32,4	53,4	46,4	
	3	2	2,2	1,4	1,8	2	1,7	0,5	1	
<b>Self-care</b>	1	61	69,1	76,9	62,7	70,1	79,2	59	67,4	0,001
	2	37,8	29,4	21,9	36,2	28,5	19,5	40,3	32,2	
	3	1,1	1,5	1,2	1,1	1,4	1,4	0,7	0,3	
<b>Usual activities</b>	1	48	55,8	61,4	49,7	56,8	68	48,6	52,2	0,001
	2	47,9	41,3	35,8	46,5	40,8	30	47,9	45,5	
	3	4,1	2,9	2,9	3,9	2,7	2	3,5	2,3	
<b>Pain/discomfort</b>	1	23,3	31,7	33,2	24	32	40,3	19,7	25,8	0,002
	2	53,3	54,4	50,7	53,4	54,1	48,6	56,9	57,2	
	3	23,4	13,9	16,1	22,5	14	11	23,5	17	
<b>Anxiety/depression</b>	1	56,5	65,6	53,9	56,1	65	66,1	56,5	60,7	0,001
	2	33,4	27,5	35,9	33,8	27,8	26,3	34,2	31,7	
	3	10,2	7	10,2	10,1	7,1	7,6	9,3	7,6	
<b>Global VAS mean (SD)</b>		68,8 (19,8)	70,4 (22,6)	72 (19,8)	68,8 (19,9)	70,5 (22,2)	75 (18,6)	65,7 (20,5)	65,9 (21)	0,001

Significant statistical differences were found for all the dimensions in each pathology (initial vs final) except:

<sup>1</sup> Self-care in SLE (p=0,719)

<sup>2</sup> Usual activities in SpA (p=0,337)

<sup>3</sup> Anxiety/depression in SpA (p=0,27)

<sup>4</sup> Global VAS in SpA (p=0,889)

**Conclusions:** The tight control multidisciplinary rheumatology program is an efficient strategy to improve the QoL and the health perception of patients with chronic autoimmune diseases which impacts on the functionality, performance of everyday activities and productivity

#### REFERENCE:

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FRI0633

#### HOW DO WE IMPLEMENT THE EULAR RECOMMENDATION THAT RHEUMATOLOGISTS CAN SEE EARLY ARTHRITIS PATIENTS WITHIN SIX WEEKS AFTER SYMPTOM ONSET? A FIVE-YEAR COMPARATIVE STUDY OF AN EARLY ARTHRITIS RECOGNITION CLINIC.

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**Background:** Early treatment of inflammatory arthritis (IA) associates with improved outcomes. Therefore, the first recommendation in the 2016 update of the EULAR guidelines for management of early IA states that patients presenting with IA should be seen by a rheumatologist ≤6 weeks. Data on how to implement this recommendation are lacking. A screening clinic situated in between primary and secondary care, the Early Arthritis Recognition Clinic (EARC), has previously shown to increase early identification of rheumatoid arthritis patients. However, it is unknown if this effect is sustained when applied for several years and if this approach is of added value to identify patients within the 6-week limit set by EULAR.

**Objectives:** To study if an EARC approach can lead to sustained early identification of patients with IA (as compared to regular referral to our Early Arthritis Clinic (EAC)) and to determine the efficacy to identify patients ≤6 weeks after symptom onset.

**Methods:** To promote early recognition of IA, the EARC was initiated in September 2010 in the Netherlands. General practitioners (GPs) were instructed to refer to this screening clinic without a scheduled appointment if they were unsure about the presence of IA (instead of a 'wait-and-see' approach or performing additional tests). At the EARC, patients were seen for a 5-minute visit by an experienced rheumatologist who performed a full 66-joint examination for clinical synovitis. GPs can also refer directly to the EAC, where patients are seen <2 weeks' time. Thus, GPs in our region can refer directly for a full visit in secondary care, or to a short visit to a screening clinic that is situated in between primary and secondary care. Patients identified with IA at the EARC or after (direct) referral to the EAC between September 2010 and December 2014 were compared for symptom duration at IA identification.

**Results:** Of the 1,151 patients visiting the EARC, 475 (41%) were diagnosed with IA. Firstly, proportions of patients with IA at the EARC were studied per year. These remained stable over time: 45% in 2010, 39% in 2011, 45% in 2012, 42% in 2013 and 36% in 2014. Clinical characteristics of these patients were similar over time. In the same period 675 referred patients were diagnosed with IA at the EAC; these were compared to the 475 IA patients that were identified via the EARC. Demographic characteristics were similar. However, median symptom duration of the IA patients in the EARC-group versus the EAC-group at identification of IA were 10.7 vs 17.0 weeks in 2010 (p<0.0001), 7.3 vs 13.7 weeks in 2011 (p=0.0001), 6.3 vs 9.8 weeks in 2012 (p=0.056), 5.6 vs 10.7 weeks in 2013 (p=0.012) and 5.7 vs 8.3 weeks in 2014 (p=0.060). Proportions of patients with IA seen by a rheumatologist ≤6 weeks in the EARC-group versus the EAC-group were: 34% vs 19% in 2010, 43% vs 20% in 2011, 43% vs 33% in 2012, 48% vs 30% in 2013 and 44% vs 33% in 2014.

**Conclusions:** A screening clinic in between primary and secondary care has sustainable benefit with regards to early identification of inflammatory arthritis and allows >40% of patients to be identified within the timelines as recommended by EULAR.

**Disclosure of Interest:** None declared

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FRI0634

#### COST SAVINGS OF USING HLA-B\*27 TAG SNP GENOTYPING TO DETERMINE HLA-B\*27 STATUS IN A CANADIAN POPULATION

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**Background:** HLA-B\*27 is a useful genetic marker for screening axSpA [1,2] to determine who can benefit from rheumatologic evaluation in a primary care setting [3]. Currently, entire HLA-B locus tests are the gold standard for determining HLA-B\*27 status but they are expensive. With a sensitivity of 97.6%, the cheaper HLA-B\*27 tag-SNP assay could offer a less expensive yet rigorous testing option. Specifically, the HLA-B\*27 tag-SNP assay could be ordered as first-line screening test for patients with inflammatory axial pain by primary care doctors, with the HLA-B locus assay only requested by rheumatologists for patients with a negative tag-SNP test result but a strong clinical suspicion of HLA-B\*27 positivity. Economic impact of this hybrid testing strategy is not yet established.

**Objectives:** To determine the cost savings of using the hybrid testing strategy instead of giving HLA-B locus assay to all patients with inflammatory axial pain.

**Methods:** We estimated the total cost of using the HLA-B\*27 tagSNP assay for a sample of 510 patients who underwent the test between August 1, 2016 and July 31, 2017 in Newfoundland and Labrador, Canada. We compared this cost with the cost that would have been incurred if these same patients were instead tested with the HLA-B locus test.

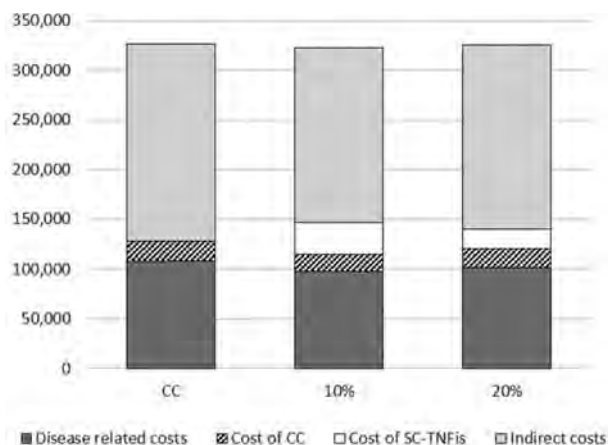
**Results:** Total cost of testing 510 patients with HLA-B locus test was \$30,557 at an average cost of \$60 per test. Cost of testing these patients with HLA-B\*27 tagSNP assay was \$1,673 (with average cost per test of \$3.28). Among those who tested negative on the HLA-B\*27 tagSNP assay, 2.3% (~10 patients) would be falsely diagnosed negative. The HLA-B locus test would be ordered in half of these patients after medical history is reviewed by a rheumatologist. Hence, total costs of testing 510 patients with the HLA-B\*27 tagSNP assay were \$1,963. Consequently, cost savings from using HLA-B\*27 tagSNP assay instead of HLA-B locus tests were \$28,594 for this sample of 510 patients. This amounted to a 94% reduction in costs relative to the scenario where all patients are tested with HLA-B locus tests.

**Conclusions:** Screening for HLA-B\*27 status among axSpA patients of Caucasian descent with HLA-B\*27 tag-SNP testing with the gold standard HLA-B locus test only requested for those in whom such need is determined by rheumatologists can result in significant cost savings relative to giving HLA-B locus tests to all patients with inflammatory axial pain.

**Acknowledgements:** 1. Robinson PC, Brown MA. *Mol Immunol.* 2014;57:2–11.







**Conclusions:** Persistence appears to be a driver of cost-effectiveness of SC-TNFi treatment in patients with AS, especially when a societal perspective is taken. Therefore, prescribing the SC-TNFi with the best persistence may be a cost-effective strategy.

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FRI0637

#### BARRIERS TO REMAIN IN WORK: RESULTS FROM THE NATIONAL RHEUMATOID ARTHRITIS SOCIETY SURVEY (NRAS)

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**Background:** Problems at work and work loss are still major socio-economic consequences for patients with Rheumatoid Arthritis (RA), employers and the society. Currently, there is a lack of understanding what the main barriers and facilitators are to remain in paid work. For patients and employers identifying these barriers and facilitators will enable them to make the right adjustments at a personal level. For policy makers these factors can determine future policies, aiming to reduce the overall socio-economic burden of RA.

**Objectives:** i) To understand reasons for work loss in people with RA; and ii) to compare problems at work in employed RA patients and those who had to stop working due to RA.

**Methods:** An online survey about employment was sent to UK NRAS members and distributed to non-members via social media including questions about problems at work in those employed or problems related to work in those who had to stop working or retire early due to RA. Rates of problems related to work were compared using Chi2 tests.

**Results:** 891 patients who completed the survey were in paid employment and 189 had stopped working due to RA or retired early due to their RA. Median [IQR] symptom duration was 12.5 [7.5–23.2] years and the majority were women (91%). Main reasons for leaving work included (patients could tick all that applied): unable to carry out duties (73%); time off sick (46%); fatigue (74%); problems with colleagues (12%); need for specific adaptations (11%); unable to travel to work (13%); lack of family support (3%); lack of support from employer (33%); and side effects of medication (24%). The majority of patients left their job >5 years earlier

than they had expected (72%) and 62/172 (36%) mentioned that their employer had not been helpful in assisting them to stay in work. For those in employment, the main challenges to remain in work were: demanding role; RA symptoms; no reasonable adjustments; commuting to work; and lack of understanding. Compared to patients in employment at time of survey, those who had to stop work due to their arthritis, reported having significantly serious problems regarding commuting to work, lack of understanding employers/colleagues, time off due to flare or medical appointments, health and safety and reluctance to make adjustments in their last job (table 1). Lack of family support was not significantly significant.

	not at all serious/ not very serious		neither serious nor non-serious		serious / very serious		P
	Employed	Stopped working due to arthritis	Employed	Stopped working due to arthritis	Employed	Stopped working due to arthritis	
Getting to and from work	326/609 (53%)	58/166 (35%)	136/609 (22%)	36/166 (22%)	142/609 (24%)	72/166 (43%)	<0.001
Lack of understanding from colleagues	300/603 (50%)	38/159 (24%)	129/603 (21%)	42/159 (26%)	174/603 (29%)	79/129 (50%)	<0.001
Health and Safety issues	303/594 (51%)	56/161 (35%)	170/594 (29%)	41/161 (25%)	123/594 (21%)	64/161 (40%)	<0.001
Time of medical appointments	162/624 (26%)	62/167 (37%)	108/624 (17%)	39/167 (23%)	154/624 (25%)	66/167 (40%)	<0.001
Lack of family support	378/617 (61%)	93/147 (63%)	113/617 (18%)	29/147 (20%)	128/617 (21%)	25/147 (17%)	0.577
Time off when having a flare or unwell	245/603 (41%)	29/165 (18%)	107/603 (18%)	17/165 (10%)	257/603 (43%)	119/165 (72%)	<0.001
Employer reluctant to make adjustments	282/538 (52%)	38/151 (25%)	114/538 (21%)	35/151 (23%)	122/538 (23%)	78/151 (52%)	<0.001
Lack of understanding employer	283/573 (49%)	36/156 (23%)	118/573 (21%)	37/156 (24%)	178/573 (31%)	93/156 (60%)	<0.001

**Conclusions:** Barriers to remain in work with RA are multi-factorial and related to the disease, nature of the work and understanding from employers and colleagues. Increasing understanding about RA amongst employers and colleagues in addition to often simple work adjustments, such as adaptations in the workplace and the opportunity to work more flexible, can prevent problems at work and work loss in the long-term and reduce the socio-economic burden.

**Disclosure of Interest:** None declared

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FRI0638

#### A NOVEL GROUP CLINIC MODEL FOR NEW PATIENTS ENHANCES PATIENT ACTIVATION

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**Background:** Group clinics are a widely used, key alternative care model in USA (as shared medical appointments and other labels), especially in centres of excellence like the Cleveland Clinic. They are increasingly seen as 'a transformative innovation'<sup>1</sup> and recognised as an effective solution to the universal health-care challenges: increasing demand and limited resource<sup>2</sup>. We have extensive experience of follow up group clinics for inflammatory arthritis patients since 2008 with a co-designed model integrating patient and team views<sup>3</sup>. Qualitative research showed robust themes associated with successful delivery: Efficiency, Empathy, Education, Engagement and Empowerment. 'Patient activation' describes the knowledge, skills and confidence a person has in managing their own healthcare, but there is no published data in group clinics. A group model has also never been used for seeing new patients in secondary care, so this is an original application of an established care model.

**Objectives:** To show feasibility for new patients seen in a group setting and assess patient experience, including activation.

**Methods:** A mixed methods pilot study. New patients awaiting Rheumatology appointments were invited to pilots at one of two hospitals: 1) with experience of group clinics 2) without. Patients agreeing to attend knew this was a new application of an established innovation with an option to stay for a focus group or be interviewed by telephone afterwards. Sessions were videoed for educational purposes and qualitative interviews were conducted under existing research approvals with relevant consents for both. Numerical data included Patient Activation Measure before/after the two-hour clinic, EQ-5D and a standard feedback tool. Qualitative data was analysed using nVivo and compared to previously identified themes.

**Results:** 19 patients were seen in two two-hour clinics (mean 13 mins/patient vs. 30 mins/patient usual care), including complex patients with multiple diagnoses. 69 patients were phoned, of whom 16 did not answer, 20 declined, 6 failed to attend, 3 declined to see a Rheumatologist at all, 2 were deemed not suitable and 3 already had an appointment. Feedback was very positive: median 10 (IQR 8–10) across all domains, so was consistent with usual clinics and follow up group clinics. Free text positive comments far outweighing the negative. EQ-5D showed a highly impacted group (mean global health index 54 vs. UK age norm 77). Patient Activation Measure showed significant improvement over each two-hour

session: (54–63 & 67–74;  $p < 0.03$ ). Qualitative analysis mapped to previous themes will be summarised at the meeting.

**Conclusions:** It is feasible and effective to see new patients in a group setting with an experienced team. New patients group clinics have a powerful effect in empowering patients and may become an important option for hard to manage patients especially where resources are limited.

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**Disclosure of Interest:** None declared

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#### FRI0639 THE IMPACT OF DISEASE ACTIVITY AND PAIN LEVEL ON PRODUCTIVITY IN RHEUMATOID ARTHRITIS (RA) PATIENTS

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**Background:** Rheumatoid arthritis (RA) is a disabling and progressive chronic autoimmune disease with associated burden in terms of work disability.

**Objectives:** To investigate the impact that RA associated pain and disease activity have on the level of work impairment patients experience, using data from the Burden of Rheumatoid Arthritis across Europe: a Socioeconomic Survey (BRASS).

**Methods:** Data were extracted from BRASS, a societal perspective observational RA dataset across 10 European countries (EU5, Denmark, Sweden, Hungary, Poland and Romania). 476 RA specialising clinicians provided information on 4,079 adult patients; of these, 2,087 patients completed corresponding questionnaires about the burden of RA. 646 patients were included in the analysis, having completed a patient questionnaire and with the physician having provided a DAS28-CRP score.

Descriptive analysis was used to explore the association between pain level, disease activity and productivity impairment due to RA. Summary measures were derived from BRASS data in which the Work Productivity and Activity Impairment Questionnaire was used to quantify impairment caused by the patient's RA, taking into account not only the proportion of time the patient is absent, but also the impact on their ability to perform their job. The relationship between disease severity (as measured by DAS28-CRP score), pain level (measured across 4 categories from 'no pain', 'mild', 'moderate' to 'severe pain') and overall work impairment was further explored using a generalised linear model where pain level and severity were modelled as explanatory variables against the overall work impairment outcome, while adjusting for covariates including age, gender and BMI.

**Results:** Of the 646 included in the analysis, average age was 54.6(14.1) years; mean (standard deviation), average DAS28-CRP score was 3.1(1.2), and average disease duration was 7(10) years; median (interquartile range). Descriptive analysis indicated that with greater levels of pain and/or disease activity, patients suffered increased levels of both work and activity impairment. The average marginal effect of covariates was calculated from regression outputs. Both pain level and DAS28-CRP score independently had a statistically significant association with work impairment; a unit increase in DAS28 score meant an increase in work impairment of 4.7% ( $p=0.011$ ), whereas existence of 'mild', 'moderate' or 'severe pain' versus 'no pain' increased impairment by 33.3%, 43.4% and 45.0% respectively ( $p < 0.05$ ), with confounders age, gender, BMI and either DAS28-CRP or pain level held constant.

**Conclusions:** Results from this large, multinational survey in Europe show that subjective domains of the disease, such as pain, could be as important as objective measures of RA activity in affecting a patient's ability to work; analysis suggested both pain and severity independently have a significant impact on work and activity impairment due to RA.

**Disclosure of Interest:** J. Galloway Consultant for: Receiving honorarium for speaking from Pfizer, UCB, Celgene and BMS, J.-P. Capron Employee of: Eli Lilly & Company, F. De Leonardis Shareholder of: Eli Lilly & Company, Employee of: Eli Lilly & Company, W. Fakhouri Employee of: Eli Lilly & Company, T. Burke: None declared

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FRIDAY, 15 JUNE 2018

## Validation of outcome measures and biomarkers

#### FRI0640 AUTOANTIBODIES TO TWO NOVEL PEPTIDES IN SERONEGATIVE AND EARLY RHEUMATOID ARTHRITIS IN THREE LARGE INDEPENDENT COHORTS

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**Background:** Despite recent progress in biomarker discovery for RA diagnostics, still over one third of RA patients are seronegative for RF and ACPA, a number which is even higher in early disease. In both the University of Hasselt (UH) cohort ( $n=292$ ) and Leiden Early Arthritis Clinic (EAC) cohort ( $n=600$ ), 38% of RA patients were seronegative for RF and ACPA. Testing for novel autoantibodies to UH peptides UH-RA.1 and UH-RA.21, reduced the serological gap from 38% to 29% in the UH cohort ( $P=0.03$ ) and from 38% to 32% in the EAC cohort ( $P=0.01$ ), with associated specificities in rheumatic controls ranging from 88–96%<sup>1</sup>.

**Objectives:** Our aim is to validate the reactivities of autoantibodies against UH-RA.1 and UH-RA.21 peptides in early and seronegative RA patients from the CareRA cohort.

**Methods:** Peptide enzyme-linked immunosorbent assays have been developed to screen for the presence of antibodies to UH-RA peptides. Cut-off for seropositivity was defined by 2 x SD above the mean antibody level of the healthy control group<sup>1</sup>. Antibody reactivity to UH-RA.1 and UH-RA.21 was evaluated in baseline samples, collected before the start of treatment, of 223 early RA patients from the CareRA cohort.

**Results:** Antibodies to UH-RA.1 and UH-RA.21 were found in respectively 5% and 21% of the baseline samples from the CareRA cohort. These antibodies were found in similar levels in both RF/ACPA seropositive and seronegative patients. In the CareRA cohort, 24% of patients were seronegative for RF and ACPA and combining the presence of autoantibodies to UH-RA.1 and UH-RA.21 with RF/ACPA serology, reduced the seronegative population from 24% to 18% ( $P=0.13$ ).

**Conclusions:** Screening for antibodies against novel UH peptides UH-RA.1 and UH-RA.21 has now been performed in three large independent cohorts. This study validates the presence of antibody reactivity to these UH-RA peptides in seronegative and early RA. This might reinforce current diagnostics and improve early diagnosis and intervention in RA.

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1. De Winter, et al. *Rheumatology (Oxford)* 2016;55(8):1431–6.

**Disclosure of Interest:** None declared

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#### FRI0641 DETECTION OF CHANGES IN SLE DISEASE ACTIVITY IS HIGHLY IMPROVED WITH SLE-DAS AS COMPARED TO SLEDAI: DERIVATION AND PRELIMINARY VALIDATION OF THE SLE DISEASE ACTIVITY SCORE (SLE-DAS)

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**Background:** SLEDAI is a widely used instrument to measure disease activity of systemic lupus erythematosus (SLE). However, it lacks sensitivity to discriminate improvement/worsening as it only scores items categorically and does not include several relevant lupus features, such as hemolytic anemia.

**Objectives:** To derive and validate a SLE Disease Activity Score (SLE-DAS) with improved sensitivity to change, while maintaining the high specificity and simplicity of use of the SLEDAI.

**Methods:** 324 patients fulfilling ACR'97 and/or SLICC'12 classification criteria for SLE and regularly followed at a tertiary care lupus clinic from January 2014 to December 2017 were included. At each outpatient visit, clinical and laboratory data were collected and disease activity (last 30 days) was scored with Physician Global Assessment (PGA) (0–3 scale) and SLEDAI-2K. To derive the SLE-DAS



we analyzed data from the study visit with higher disease activity from each patient, applying multivariate linear regression analysis, with PGA as dependent variable/gold-standard. Independent variables tested in the models included items from SLEDAI-2K and continuous variables for swollen joint count, proteinuria, platelet and white blood cells counts. Some features absent from SLEDAI, such as hemolytic anemia, gastrointestinal and cardiopulmonary involvement were added to the model.

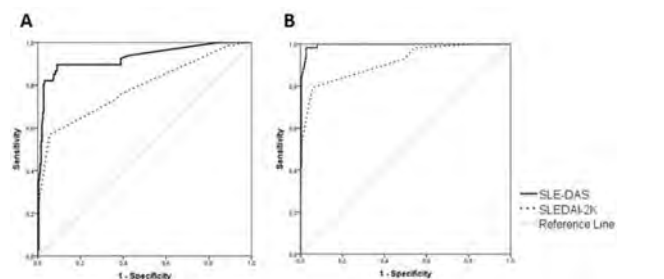
To assess correlation validity we performed a Spearman's correlation between the SLE-DAS, PGA and SLEDAI-2K at last follow-up visit. We tested performance of SLEDAI-2K (change  $\geq 4$ ) and SLE-DAS to discriminate a clinically meaningful worsening and improvement in SLE disease activity (change in PGA  $\geq 0.3$ ) using Receiver Operating Characteristic (ROC) curve analysis. We determined the best cut-offs values of SLE-DAS to detect changes in PGA  $\geq 0.3$  and calculated the sensitivity, specificity, positive and negative predictive values (PPV, NPV). Statistical significance was set at 0.05.

**Results:** The final SLE-DAS model included 17 items. The SLE-DAS score at last follow-up visit presented high correlation with PGA ( $\rho=0.975$ ,  $p<0.0005$ ) and SLEDAI-2K ( $\rho=0.94$ ,  $p<0.0005$ ). For improvement in PGA  $\geq 0.3$ , in ROC analysis a change in SLE-DAS presented a much higher performance [area under curve (AUC)=0.927 (95% CI=0.885–0.969,  $p<0.0005$ )] than SLEDAI-2K [AUC=0.787 (95% CI=0.718–0.857),  $p<0.0005$ ] (figure 1). For worsening of PGA  $\geq 0.3$ , change in SLE-DAS and SLEDAI-2K presented an AUC of 0.994 (95% CI=0.988–1.000,  $p<0.0005$ ) and 0.914 (95% CI=0.870–0.959,  $p<0.0005$ ), respectively (figure 1). The optimal discriminative cut-off for either a PGA increase or reduction was change in SLE-DAS  $\geq 1.72$  (table 1).

**Table 1** Performance of SLE-DAS and SLEDAI-2K to detect change in SLE disease activity

	$\Delta$ SLE-DAS $\geq 1.72$				$\Delta$ SLEDAI-2K $\geq 4$			
	Sens	Spec	PPV	NPV	Sens	Spec	PPV	NPV
<b>Improvement</b> <b>PGA <math>\geq 0.3</math></b>	82.1	96.9	87.3	95.4	44.8	96.5	76.9	87.0
<b>Worsening</b> <b>PGA <math>\geq +0.3</math></b>	93.1	97.7	90.0	98.5	46.6	99.6	96.4	89.5

Sens: Sensitivity(%); Spec: Specificity(%); PPV: Positive predictive value(%); NPV: Non predictive value(%).



**Figure 1** Receiver operating curve (ROC) comparing the performance of SLE-DAS and SLEDAI-2K to detect a clinical meaningful improvement (A) and worsening (B) in SLE disease activity.

**Conclusions:** The SLE-DAS presents good construct validity and much higher discriminative power to detect changes in SLE disease activity as compared to SLEDAI-2K. External validation in another SLE cohort is underway.

**Disclosure of Interest:** None declared

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#### FRI0642 SEPTIC ARTHRITIS SCREENING WITH A FAST DIAGNOSTIC TOOL USING MID INFRARED SPECTROSCOPY: A MULTI-CENTRIC STUDY

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**Background:** Septic arthritis diagnostic is an emergency which implies a treatment with antibiotics and hospitalization. The diagnosis is based on the cyto-bacteriological examination of the synovial fluid (SF), but direct bacteriological examination is insensitive and the result of the culture is obtained only after several days. Therefore, there is still a need for a rapid, simple and reliable method for

the positive diagnosis of septic arthritis. Such method must allow avoiding both unrecognized septic arthritis leading to major functional consequences, and over-diagnosis that will induce unnecessary expensive hospitalization and unjustified treatment with consequences in term of health and social costs.

Mid-infrared (MIR) spectroscopy, that gives a metabolic profiling of biological samples, has been proposed for early and fast diagnosis.

**Objectives:** The objective of this study was to confirm <sup>(1)</sup> the interest of mid-infrared (MIR) spectroscopy to discriminate synovial fluid samples from patients with septic arthritis from other causes of joint effusion.

**Methods:** Synovial fluids from patients referred for suspected arthropathies were prospectively collected in six hospitals in western France and stored at -80°C. The infrared absorption spectrum was acquired for each of the frozen samples using a chalcogenide fibre sensor. The most informative spectral variables (allowing to discriminate between septic arthritis and non-septic arthritis with reference to cytobiological examination) were selected and then used to develop an algorithm. Non-frozen synovial fluids were also analysed at Rennes University Hospital, the pilot centre, to validate the algorithm.

**Results:** The cohort consists of synovial fluid samples from patients exhibiting various etiologies. These samples (n=402), by using SF bacteriological analysis and culture and 16S PCR analysis were classified as septic arthritis (n=30) or non septic arthritis (n=372).

On the frozen samples the performances of the algorithm show a sensitivity of 97%, a specificity of 71%, a **VPN of 99%** and a VPP of 21%, the area under the ROC curve (AUROC) was 0.91.

**Conclusions:** This study confirms the interest of optical fibre infrared spectroscopy for the discrimination between septic and non septic synovial fluids. The high negative predictive value and the very short time (about ten minutes) required to obtain the result makes it possible to quickly rule out an infection diagnosis, which could make it possible to avoid unnecessary hospitalization and antibiotic therapy.

#### REFERENCE:

- Albert J-D, et al. Joint Bone Spine 2016;83:318–323.

**Disclosure of Interest:** J.-D. ALBERT: None declared, M. Le Corvec Employee of: DIAFIR, A. MARTIN: None declared, X. GUENNOG: None declared, C. DAVID: None declared, S. HOANG: None declared, C. GUEDES: None declared, M. FERREYRA: None declared, E. HOPPE: None declared, B. LEGOFF: None declared, S. JOUSSE-JOULIN: None declared, H. TARIEL Shareholder of: DIAFIR, O. SIRE Consultant for: DIAFIR, A. JOLIVET-GOUGEON: None declared, P. GUGGENBUHL: None declared, O. LOREAL Shareholder of: DIAFIR  
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#### FRI0643 AUTOANTIBODY STATUS IS NOT ASSOCIATED WITH EARLY TREATMENT RESPONSE TO FIRST-LINE METHOTREXATE IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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**Background:** In rheumatoid arthritis (RA), the relationship between autoantibody status and treatment response to methotrexate remains unclear. As methotrexate is the most widely used anti-rheumatic drug in clinical practice, it would be important to know whether the presence of autoantibodies is associated with better treatment response, since patients may benefit from treatment tailored to "autoantibody status".

**Objectives:** We investigated the relationship between autoantibody status and remission in newly diagnosed RA-patients treated with first-line methotrexate.

**Methods:** RA-patients initially treated with methotrexate were selected from an international observational database (METEOR). Patients were stratified into autoantibody-positive (rheumatoid factor (RF)- and/or anti-citrullinated-protein antibodies (ACPA)-positive) or -negative (RF- and ACPA- negative). The effect of autoantibody status on the chance of achieving remission within 3 to 6 months was analysed using Cox-proportional hazards regression.

**Results:** Data from 1826 RA-patients were available for analysis. DAS remission was achieved in 17% (318/1,826). This was similar in autoantibody-positive (17% (282/1629)) and -negative patients (18% (36/197)). Hence, autoantibody positivity was not associated with remission (HR0.89, 95%CI 0.57;1.38). Similar findings were found when stratified for methotrexate monotherapy (HR0.75, 95%CI 0.41;1.37) or combination treatment (HR0.76, 95%CI 0.37;1.54). Good physical

function (HAQ<0.5) was achieved in 33% (530/1590) of all patients. Autoantibody-positivity was also not associated with HAQ<0.5 (HR1.05, 95%CI 0.71;1.57).

Table 1 Patient characteristics at baseline

Characteristic	All RA patients n=1,626		Autoantibody-positive n=1,629		Autoantibody-negative n=1,197	
	Values available	Summary statistics	Values available	Summary statistics	Values available	Summary statistics
ACPA (positivity) n (%)	1,222	848 (70)	924	849 (92)	297	9 (3)
RF (positivity) n (%)	1,810	1,504 (83)	1,613	1,554 (96)	197	0 (0)
Gender (female) n (%)	1,854	1,429 (77)	1,620	1,288 (80)	194	143 (73)
Age at diagnosis (years), mean ±SD	1,835	48±11	1,629	47±11	197	54±16
Symptom duration (months), median (IQR)	1,826	15 (6-30)	1,629	18 (7-36)	197	7 (1-17)
Visit count, mean ±SD	4,765	3.14±1.05	3,782	3.13±1.02	463	3.27±1.24
Follow-up duration (months), mean ±SD	1,829	4.2±1.2	1,629	4.2±1.2	197	4.2±1.1
Cigarette smoking n (%)	1,602	1,461	1,461	1,411	141	103 (73)
Never		1,353 (85)		1,250 (86)		103 (73)
Current		208 (13)		191 (13)		38 (27)
Pass		91 (6)		71 (5)		20 (14)
ESR (mm/hr), median (IQR)	1,588	51 (29-85)	1,413	55 (31-95)	176	30 (15-60)
CRP (mg/L), median (IQR)	1,498	23 (9-49)	1,329	24 (11-52)	154	10 (5-24)
VAS, median (IQR)	1,367	50 (30-70)	1,217	50 (31-70)	145	50 (30-70)
ESR in 44 joints, median (IQR)	1,664	5 (2-13)	1,492	5 (2-16)	172	6 (3-13)
RAI, median (IQR)	1,663	9 (5-16)	1,489	10 (5-18)	172	6 (4-12)
DAS, median ±SD	1,678	3.8±1.1	979	3.8±1.0	117	3.4±1.1
HQI, median (IQR)	1,500	1.0 (0.6-1.4)	1,384	1.0 (0.6-1.4)	121	1.1 (0.5-1.8)
First-line treatment strategy						
MCP (monotherapy) n (%)	1,826	653 (36)	1,629	549 (34)	197	104 (52)
MTP & peripheral n (%)	1,826	800 (44)	1,629	738 (45)	197	79 (40)
MTP & systemic DMARD n (%)	1,826	353 (19)	1,629	339 (21)	197	13 (7)
MTP & biological DMARD n (%)	1,826	36 (2)	1,629	34 (2)	197	7 (4)

RA, Rheumatoid Arthritis; ACPA, anti-cyclic citrullinated peptide antibody; RF, rheumatoid factor; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; VAS, visual analogue scale for health perception; DAS, disease activity score; HQI, Health Assessment Questionnaire; IQR, Interquartile Range; MCP, methotrexate; MTP, methotrexate plus peripheral; DMARD, disease-modifying anti-rheumatic drug.

**Conclusions:** In conclusion, we found that autoantibody status was not associated with early remission in newly diagnosed RA-patients receiving methotrexate in real-world clinical practice. These results do not support the hypothesis that treatment should be tailored to “autoantibody status” when it comes to initiating methotrexate therapy as first-line anti-rheumatic treatment. Rather, our results indicate that that methotrexate is effective as primary anchor drug regardless of autoantibody status.

**Disclosure of Interest:** None declared

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FRI0644

**THE USE OF MRI-DETECTED SYNOVITIS TO DETERMINE THE NUMBER OF INVOLVED JOINTS FOR THE 2010 ACR/EULAR CLASSIFICATION CRITERIA FOR RHEUMATOID ARTHRITIS – IS IT OF ADDITIONAL BENEFIT?**

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**Background:** The 2010 ACR/EULAR classification criteria have been developed, as early classification of Rheumatoid Arthritis (RA) is important. The 2010-criteria states that imaging can be used to determine the number of joints with synovitis. This seems reasonable as previous studies on Magnetic Resonance Imaging (MRI) in early arthritis patients have shown that synovitis is present in a substantial number of joints that were neither swollen nor tender at clinical examination. Although the development of the 2010-criteria was primarily data-driven, the suggestion to also use advanced imaging modalities to detect synovitis was based on expert opinion. Scientific data supporting the use of MRI is lacking.

**Objectives:** To assess the value of MRI-detected synovitis to determine the number of involved joints on the performance of the 2010-ACR/EULAR classification criteria for RA.

**Methods:** 277 consecutive patients with a clinical diagnosis of RA or undifferentiated arthritis (UA) were studied. They underwent contrast enhanced 1.5T MRI of MCP-, wrist- and MTP-joints at baseline. Two outcomes were studied after 1 year follow-up: disease modifying anti-rheumatic drugs (DMARD)-initiation and fulfilling the 1987-criteria. Test characteristics were calculated when the number of involved joints was determined with and without MRI-detected synovitis.

**Results:** At baseline, 143 of 277 patients did not fulfil the 2010-criteria when the number of involved joints was determined by clinical evaluation of swelling and tenderness. When MRI-detected synovitis was also considered 69 patients had increased joint counts. Of these, 36 patients received more points for the item ‘number of involved joints’ and 14 reached ≥6 points and now fulfilled the 2010-criteria for RA. Thus, 10% of patients that were formally classified as UA were additionally classified as having RA.

Without considering MRI-detected synovitis, the sensitivity of the 2010-criteria was 62% and the specificity 90%, for DMARD initiation as outcome. With the addition of MRI-detected synovitis, the sensitivity increased to 67% and the specificity decreased to 84%. The AUC changed from 0.76 to 0.75. The net proportion of correctly reclassified patients was -2.4%. Of the additionally classified patients, 64% (9/14) were started on DMARDs and were considered true positives, whereas 36% (5/14) were not treated with DMARDs and developed alternative clinical diagnoses during the first year.

Results for the outcome 1987-criteria fulfilment after 1-year were similar. The sensitivity changed from 79% to 81% and the specificity from 78% to 71% the proportion of correctly reclassified patients was -5.1%.

**Conclusions:** To our knowledge, this study is the first providing evidence on the value of MRI-detected synovitis in addition to tender and swollen joints for the classification of RA. We did not find an increased accuracy of the 2010 criteria when incorporating MRI-detected synovitis. Further research on this subject in other longitudinal cohorts is needed, but at present there is no scientific proof that MRI-detected synovitis is of additional benefit for classifying RA.

**Disclosure of Interest:** None declared

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FRI0645

**ANTI-DRUG ANTIBODIES TO CERTOLIZUMAB PEGOL ARE ASSOCIATED WITH LOW DRUG LEVELS AND REDUCED CLINICAL RESPONSE AT 3 MONTHS IN PATIENTS WITH INFLAMMATORY JOINT DISEASES. DATA FROM THE NOR-DMARD STUDY.**

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**Background:** Anti-drug antibodies (ADAb) to biological drugs predispose patients to low drug levels and lack of treatment response. For certolizumab pegol (CP) knowledge about the frequency and clinical relevance of ADAb is limited in patients with inflammatory joint diseases (IJD).

**Objectives:** To assess the frequency and clinical relevance of early ADAb development in patients with inflammatory joint diseases treated with CP.

**Methods:** Patients from the NOR-DMARD study (n=310) with a clinical diagnosis of rheumatoid arthritis (RA, n=91), psoriatic arthritis (PsA, n=61), axial spondyloarthritis (axSpA, n=116) and other IJD (42) starting treatment with CP, who had available biobank sample at 3 months follow-up, were included. Serum samples are non-trough samples collected at 3 months. Drug concentrations were analysed using an in-house immunofluorometric assay automated on the AutoDEL-FIA immunoassay platform. ADAb was detected by a principal assay measuring neutralising ADAb and two confirmational tests (antigen-bridging test and a 3-step immunofluorometric assay). Patients with RA, PsA and axSpA were included in response analyses. Treatment response was defined by EULAR good/moderate response in RA, DAS28 improvement ≥0.6 in PsA, and ASDAS clinically important improvement (CII) in axSpA.

**Results:** After 3 months of treatment, 19 of 310 (6.1%) patients were ADAb positive (5 RA, 4 PsA, 6 axSpA and 4 other IJD). ADAb positive patients had significantly lower CP levels than ADAb negative patients, median 1.0 (IQR 0.2–6.8) vs 34.4 (IQR 21.2–44.7) mg/L (P<0.001). Response data were available for 245 patients. Of these, only 1/11 (9%) ADAb-positive patients was classified as a responder, while 10/11 (91%) were non-responders. Among ADAb-negative patients with response data, 129/234 (55%) were responders, while 105/234 (45%) were non-responders.

**Conclusions:** ADAb against CP were detected in 6.1% of patients after 3 months of treatment and were associated with low drug levels and reduced treatment response. These results suggest that drug levels and ADAb may be important for monitoring efficacy of treatment with TNF inhibitors, but the clinical significance needs to be examined in randomised clinical strategy trials.

**Disclosure of Interest:** J. E. Gehin Consultant for: Roche, G. Goll Consultant for: Abbvie, Biogen, Boehringer Ingelheim, Orion Pharma, Eli Lilly, Novartis, Pfizer, MSD, Roche, UCB, D. Warren: None declared, S. Syversen Consultant for: Roche, J. Sexton: None declared, E. Strand Consultant for: Pfizer, T. Kvien Consultant for: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celgene, Celltrion, Eli Lilly, Epirus, Hospira, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz, UCB, N. Bolstad Consultant for: Pfizer, Orion Pharma, Napp pharmaceuticals, Takeda, Roche, E. Lie: None declared

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FRI0646

**SYNOVIAL TISSUE HISTOPATHOLOGY FINDINGS IN EARLY RA. IS IT USEFUL? ANALYSIS OF THE BELGIAN CAP48 COHORT.**

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**Background:** The development of ultrasound-guided synovial biopsy will enable synovial tissue collection from small joints and will facilitate histopathological studies, thus improving the understanding of early rheumatoid arthritis (ERA). The CAP48 cohort is an original multicentre prospective observational study of early

Rheumatoid Arthritis (RA) patients up to 50 years old supported by a charity program of the Belgian French speaking radio-television (RTBF).

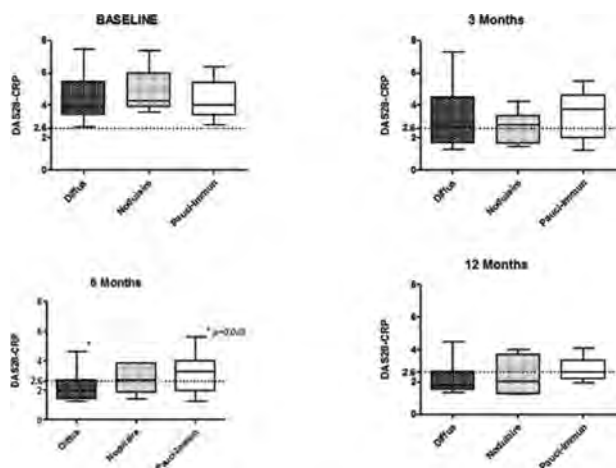
**Objectives:** The objectives of this cohort are to observe if a tight control favour remission at 6 months and to define synovial markers for severity and response to therapy.

**Methods:** RA patients fulfilling the ACR/EULAR 2010 criteria and naïve to DMARDs therapy were recruited. Synovial biopsies before treatment were obtained using an ultrasound guided needle biopsy (US-NB) of the small joints or miniarthroscopy of the knee. RA disease activity measures including DAS28CRP domains were evaluated every 3 months and treatment was adapted by the treating physician. Tissues were assessed for quality. Retrieved tissue was fixed, stained and paraffin embedded for blinded tissue pathology description.

**Results:** A synovial biopsy was performed in 37 patients using US-NB in n patients. Patients were classified according 4 types of synovial histopathology findings. Baseline characteristics of the cohort is summarized in table 1. All patients in the diffuse lymphoid group were ACPA negative and the majority of the ACPA positive patients were classified in the pauci immune and fibrous group. As shown in figure 1, the pauci immune ERA group showed lower DAS28-CRP response than the other groups.

Table 1

	All patients n=37	Group 'Diffuse' n=17	Group 'Nodules' n=7	Group 'Pauci- Immun' 'Fibrous' n=13
Age mean (SD)	34.4 (± 1.9)	31.3 (± 2.9)	36.1 (± 4.4)	33.0 (± 5.8)
Gender	30F/7M	14F/3M	5F/2M	11F/2M
ACPA % (n=)	37.8% (n= 14)	0% (n=0)	57.1% (n=4)	76.9% (n=10)
RF % (n=)	48.6% (n=18)	11.8% (n=2)	85.7% (n=6)	76.9% (n=10)
Erosion % (n=)	35.1% (n=13)	17.6% (n=3)	57.1% (n=4)	38.4% (n=5)
Baseline DAS28-CRP	4.60 (± 0.23)	4.52 (± 1.50)	5.00 (± 1.37)	4.76 (± 1.44)



**Conclusions:** Synovial tissue analysis could provide a step change towards personalized medicine in daily clinical practice for disease stratification and treatment selection of ERA. In the CAP48 cohort, a high number of these young and ERA patients achieved remission at 6 months but a lower response was observed in the pauci immune group. Further analyses are ongoing to define individual synovial markers of severity and response.

**Disclosure of Interest:** None declared

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FRI0647

#### ESTIMATION OF MINIMUM CLINICALLY IMPORTANT DIFFERENCE IN FIBROMYALGIA FOR FIQR USING BPI AS THE ANCHOR MEASURE

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**Background:** The FIQ (Fibromyalgia Impact Questionnaire) was first published in 1991 and had 19 items which were recalled over a week. The scoring system is highly reliable and is recognised as an outcome measure that covers the multiple domains of Fibromyalgia<sup>1</sup>. A prior study by Bennett et al<sup>2</sup> have shown that 14% change in the FIQ total score represents the Minimum Clinically Important Difference(MCID) in the Fibromyalgia. The FIQ was revised in 2009 to the 20 item

Fibromyalgia Impact Questionnaire Revised or FIQR. However, there has been no study done for assessing the MCID of the FIQR in Fibromyalgia.

**Objectives:** The aim of our study is to estimate the MCID for Fibromyalgia Impact Questionnaire Revised using anchor-based methodology with average pain score on Brief Pain Inventory as the anchor.

**Methods:** We have used data from our prospectively followed cohort of fibromyalgia patients. They were treated as per protocol with duloxetine in escalating doses. Data from this cohort was used to estimate the MCID for the FIQR using anchor-based methodology The anchor used was the average pain score on Brief Pain Inventory(BPI). The MCID for BPI average pain score was calculated by Mease et al to be 30%<sup>3</sup>. Thus, all patients in our cohort having an improvement of greater than 30 % were classified as responders. All other patients were non-responders. Within these two groups, the means and standard deviations of the FIQR scores at baseline and at the end of treatment were obtained. The MCID was calculated as the difference in the unadjusted mean change in the FIQR scores between the "non-responder" group and the group with "responder group". It was also expressed as a percentage reduction from the mean baseline FIQR.

**Results:** Table 1 shows the mean and standard deviation of FIQR scores at baseline, endpoint and the mean change along with the calculated MCID. Table 1

Anchor status	No. of patients	Baseline Mean ± SD	Endpoint mean ± SD	Mean change ± SEM	MCID
Responder	58	58.50 ± 19.03	26.62 ± 14.76	31.88 ± 2.53	27.04
Non-responders	18	62.17 ± 16.97	57.33 ± 13.00	4.83 ± 3.75	

**Conclusions:** Based on our data, we suggest that a "27.04 point" or "45.5 %" improvement on the FIQR score represents the minimum clinically important difference for FIQR in fibromyalgia patients presenting with moderate to severe pain. Strengths of this work include the usage of prospectively followed patient population for analysis, protocol-based treatment with duloxetine and representation of a local population which more is applicable to our clinical practice. That MCID obtained for the FIQR score is much higher than the 14 % which was the MCID obtained for the older FIQ score may suggest a population-based variation in improvement of outcome measures.

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FRI0648

#### DIRECTLY COMPARING LATENT FUNCTIONAL ABILITY IN ADOLESCENTS WITH JIA USING THE CHAQ AND HAQ: AN ITEM RESPONSE THEORY ANALYSIS

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**Background:** Measuring and comparing functional ability in adolescents with JIA is challenging due to the use of multiple questionnaires, including the proxy-completed Childhood Health Assessment Questionnaire (P-CHAQ), the adolescent version (A-CHAQ) and the Health Assessment Questionnaire (HAQ).

Item response theory (IRT) allows items on multiple questionnaires to be linked to an underlying continuous variable. This allows scores to be corrected for characteristics of the administered items, thus making them comparable between different questionnaires. Recently, a common reporting metric for functional ability was developed in a combined dataset of 16386 patients with various inflammatory rheumatic diseases, including 1029 paediatric patients with JIA.

**Objectives:** i) To cross-validate the item response models using three functional ability questionnaires in adolescents with JIA. ii) To assess agreement between overall function scores obtained from the different questionnaires.

**Methods:** Adolescents aged 11 to 17 with JIA were enrolled to a UK, multicentre inception cohort, the Childhood Arthritis Prospective Study (CAPS). In a sub-



study, adolescents were asked to complete the A-CHAQ and HAQ and their guardians the P-CHAQ. Adolescents were selected if at least two of the questionnaires had been completed simultaneously within the first year following diagnosis.

Fit of the item response models was assessed by comparing model expected item scores with those observed in CAPS for each item (i.e. residuals). An item response model was considered to adequately describe item response behaviour of CAPS patients when the mean of the residuals was  $<\pm 5\%$ . Agreement of overall questionnaire IRT scores were then compared using limits of agreement (2SD) and intra-class correlations.

**Results:** Of 303 adolescents, 61% were female and median age at JIA diagnosis was 13 years (range 11 to 17). Raw HAQ scores consistently fell below both CHAQ scores.

IRT model fit in the CAPS population was good, with 1% of item residuals  $>\pm 5\%$ . When modelled using IRT, the mean differences in overall scores approximated zero, with narrow limits of agreement, at 15 (PCHAQ vs ACHAQ), 12 (PCHAQ vs HAQ) and 10 (ACHAQ vs HAQ), on a 0–100 scale. High intra-class correlations between overall scores were evident (range 0.83 to 0.90). There was therefore high agreement between IRT-modelled scores obtained for different questionnaires. A scale characteristic curve (figure 1) illustrates the relationship between the expected scores for CHAQ and HAQ questionnaires with the latent functional ability variable.

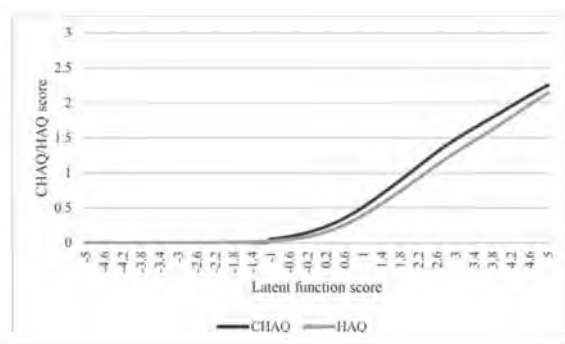


Figure 1 Comparing CHAQ and HAQ scores with latent function.

**Conclusions:** IRT models for functional ability previously developed in a mixed population of adult and paediatric patients with inflammatory arthritides are applicable to adolescents with JIA in CAPS. IRT scores across CHAQ and HAQ measures had high agreement. IRT scores for functional ability can therefore be used in clinical practice and research to directly compare scores on the CHAQ and HAQ. This will be important as adolescents transfer from paediatric to adult rheumatology.

**Disclosure of Interest:** None declared

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#### FRI0649 SYSTEMIC LEVELS OF TYPE VI COLLAGEN METABOLITES ARE ELEVATED IN RA PATIENTS AND MODULATED BY TREATMENT WITH ANTI-IL6R THERAPY

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**Background:** Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by progressive inflammation systemically and local joint deterioration. Chronic inflammation leads to elevated levels of tissue remodeling and release of extracellular matrix (ECM) metabolites into circulation. Type VI collagen (Col-VI) is found at the interface between the interstitial- and the basement membrane where it binds other matrix proteins and support cell-cell interactions. Blood levels of Col-VI metabolites (C6M) have been associated with increased tissue turnover and disease activity in animal models and clinical studies of lung<sup>1</sup> and liver<sup>2</sup> fibrosis and ankylosing spondylitis<sup>3</sup>. These studies indicate that systemic levels of C6M are released ubiquitously from many organs and may be modulated by anti-inflammatory treatments. Treatment with the  $\alpha$ IL-6 receptor agent Tocilizumab (TCZ) results in decreased ECM remodeling

**Objectives:** Investigate the modulation of Col-VI metabolites in circulation by TCZ treatment and its association with treatment response.

**Methods:** Systemic Col-VI metabolism was measured in the LITHE study (n=740), a one year double blind, placebo controlled phase III parallel group study

in patients receiving placebo, 4 mg/kg or 8 mg/kg TCZ in combination with MTX. Col-VI degradation was measured using the C6M assay, measuring a specific MMP generated metabolite at bl, w4 and w16. The odds ratio (OR) of treatment response (ACR20, 50 or 70) at  $>$ median decrease was calculated using logistic regression, adjusting for age, sex, BMI, dis. duration (model 1) and treatment (model 2).

**Results:** TCZ treatment dose dependently reduced of Col-VI metabolites in serum at w4 in both 4 and 8 mg/kg (9% ns and 46%  $p<0.0001$ ) doses compared to placebo and the reduction persisted throughout the study. Patients with a high suppression of Col-VI turnover were more likely to respond to treatment compared to patients with low suppression. In patients with high suppression after 4 weeks the OR and ACR20 response at w16 was 1.6 (95% CI, 1.16–2.20), although this was not significant when adjusting for treatment. The OR of ACR50 was 2.2 (95% CI, 1.507–3.296) and for ACR70 2.6 (95% CI, 1.407–4.631).

Table 1 Association of high/low C6M median % change with ACR response after 16 weeks using logistic regression

Determinant	Model	Outcome		ACR20		ACR50		ACR70	
		OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value		
$\Delta$ C6M % week 4	Model 1	1.596 (1.160–2.198)	0.004	2.228 (1.507–3.296)	<0.001	2.553 (1.407–4.631)	0.002		
	Model 2	1.319 (0.929–1.873)	0.122	1.820 (1.189–2.785)	0.005	2.390 (1.265–4.517)	0.007		

**Conclusions:** Suppression of Col-VI turnover was significantly associated with a higher level of response to TCZ treatment in RA patients after already 4 weeks. We hypothesize that there is an increased systemic connective tissue turnover in RA and connective tissue metabolites may be used as indicators of treatment response.

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#### FRI0650 THE DIAGNOSTIC VALUE OF THE AESKULISA PR3 SENSITIVE & AESKULISA MPO IN THE EUVAS-COHORT

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**Background:** Anti-neutrophil-cytoplasmic-antibodies directed against proteinase-3 (PR3-ANCA) and myeloperoxidase (MPO-ANCA) are serological hallmarks of small vessel vasculitis, particularly granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA). In a recent multicentre European-Vasculitis-Study-Group (EUVAS) evaluation, the performance of IIF was compared to that of various antigen-specific immunoassays.

**Objectives:** The aim was to evaluate the diagnostic accuracy of the third-generation antigen-specific immunoassays PR3-ANCA (AESKULISA-PR3-sensitive) and MPO-ANCA (AESKULISA-MPO) and to compare these data with the results from the other assay (Orgentec).

**Methods:** 257 samples from the EUVAS cohort were tested for the presence of ANCA by PR3-ANCA ELISA (AESKULISA-PR3-sensitive) and MPO-ANCA ELISA (AESKULISA-MPO). Newly diagnosed GPA/MPA (n=66) patients and diseased controls (n=191): systemic lupus erythematosus (n=60), systemic sclerosis (n=10), rheumatoid arthritis (n=90), Scleroderma (n=11) and Sjögren's syndrome (n=30) were analyzed.

**Results:** In AAV patients, ANCAs were detected with both methods in 56 cases; divergent results were obtained in only 1 patient sample. 191 patients with other rheumatic diseases were analyzed and only 13 vs 11 (AESKU/Orgentec) were

positive for ANCA (SLE, sclerosis, RA, RA/RV). This study shows that the PR3- and MPO-ANCA ELISA are highly specific (93.2%/94.2%) and sensitive (85.9%/85.9%) in the detection of ANCA to identify AAV or conditions known to be associated ANCA.

**Conclusions:** Our comparison of PR3- and MPO-ANCA ELISAs showed (i) a high diagnostic performance of these PR3- and MPO-ANCA ELISAs to discriminate AAV from disease controls. (ii) very good correlation between the other methods tested. In conclusion, these novel assays can be used as screening method for detection of ANCA-associated diseases.

**Disclosure of Interest:** None declared

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#### FRI0651 QUANTITATIVE CHEST CT PREDICTS 8-YEARS-MORTALITY AND COMORBIDITY IN SYSTEMIC SCLEROSIS

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**Background:** Interstitial Lung Disease (ILD) is the main cause of death in Systemic Sclerosis (SSc). Serious lung involvement increase the hospitalization rate and sometimes oxygen therapy is required.

An prompt treatment in ILD-SSc patients is essential, but nowadays there is not a feasible method to identify patients with poor prognosis.

Although chest Computed Tomography (CT) is the gold standard to detect ILD, there is no standardized assessment of its severity. Quantitative CT (QCT) is an innovative and operator independent method to assess ILD-SSc extent and severity. An increasing number of evidences confirm that QCT is extremely useful for detecting SSc-ILD with the worst prognosis. However is not well established if QCT can predict death or comorbidity associated to ILD.

**Objectives:** The main aim of this study is to verify if QCT predict 8-years mortality or clinical worsening (i.e. hospitalization for respiratory complications or chronic oxygen therapy) in SSc.

**Methods:** Consecutive SSc patients (according to ACR/EULAR classification criteria) from ten different centers underwent a chest CT. Their clinical history was carefully recorded in the following 96 months. A rheumatologist post-analyzed every CT with an open source DICOM viewer in order to obtain QCT indexes. Patients were clustered in two subgroups: according to QCT indexes' cutoff previously found (see Ariani et al., 2017). The survival time of each patient was considered the time interval between the CT date and death, hospitalization related to lung worsening, beginning of chronic oxygen therapy or last medical examination

**Results:** We enrolled 342 patients; during the 8-years follow-up 15.5% (53/342) died and 4.4% (15/342) had a clinical worsening. The Kaplan-Meier survival analysis demonstrates a worse survival in patients with QCT indexes above or below the previously observed cutoffs. (p<0.01). In particular the QCT index cutoff which the best performance was total lung kurtosis (tKurt) equal to 4.89 (p<0.0001).

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The QCT indexes' cutoffs previously found (see Ariani, et al., 2017) identify the SSc-ILD subjects with an high risk of 8-years mortality and comorbidity. These findings suggest that QCT could become a pivotal assessment in SSc management because its role in identifying patients with poor prognosis and who deserve an early aggressive treatment.

**Disclosure of Interest:** None declared

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#### FRI0652 THE DEVELOPMENT AND VALIDATION OF FAMILIAL MEDITERRANEAN FEVER QUALITY OF LIFE SCALE (FMF-QOL)

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**Background:** Quality of life (QoL) was negatively affected in FMF patients. A QoL scale specific to FMF is not existing in the literature.

**Objectives:** To develop valid and reliable quality of life scale in familial Mediterranean fever (FMF).

**Methods:** The psychometric method was used to develop the FMF-QoL. In the first step, the question pool was formed by using existing QoL scales in the literature. Outpatients with FMF according to Livneh criteria were recruited. After patients' interviews, some identical and irrelevant questions eliminated and new ones were added by an expert committee. Cognitive debriefing interviews concerning QoL were done with another 20 FMF patients. Minor changes (few words) after these interviews were made. In the second step, the preFMF-QoL with 101 questions was formed and it was filled out by FMF patients. Confirmatory factor analysis (CFA) by varimax rotation, assessment of data' skewness and kurtosis, evaluation of invalid questions and participants were performed. After this, the internal consistency with Cronbach alpha was calculated. The face, content and construct validities were assessed. Convergent validity which was the relation of the FMF-QoL with functional parameters (Euro Health Impact Scale (EURO-HIS), Short Form 36 (SF36), Beck Depression Inventory for Primary Care (BDI-PC), Jenkins Sleep Scale (JSS), Health Assessment Questionnaire (HAQ) and the discriminant validity which was the relation of the FMF-QoL with nonfunctional parameters such as demographic and clinical characteristics were analyzed. The Mann Whitney U test, Kruskal-Wallis test and Spearman correlation coefficient (rho) were used to compare quantitative variables.

**Results:** In our study, the FMF-QoL was applied to 125 FMF patients however 123 (84 women) patients were designed to statistical analysis. It has been determined by the expert committee that the face and content validity of the FMF-QoL was good. According to the factor analysis the FMF-QoL were represented by 4 factor groups (eigenvalues >1) which were physical impact, social and recreational impact, psychological impact, and sleep impact factors. All question's factor loadings after Varimax rotation were bigger than 0.5 and the cumulative variance of the scale was 68.11%. The strongest correlation of the FMF-QoL was found with other QoL scales like EUROHIS (rho: -0.64, p<0.01) and SF36-physical functioning subscale (rho: -0.63, p<0.01). The correlations between the FMF-QoL and other functional parameters were found to be moderate [BDI-PC (rho: 0.46, p<0.01), JSS (rho: 0.44, p<0.01), HAQ (rho: 0.44, p<0.01)]. This shows that the FMF-QoL has good convergent validity. In the discriminative validity, most of the parameters had not significant correlation with the FMF-QoL. Only the number of attacks in the previous year, age and education level were correlated moderately with the FMF-QoL. This shows the FMF-QoL has discriminative validity.

**Conclusions:** The FMF-QoL scale was developed with psychometric method. It is a valid and reliable disease specific scale which has 20 questions with 4 factors. It is already a practical, not time consuming that can be used in the clinical follow-up and the treatment evaluation.

**Disclosure of Interest:** None declared

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#### FRI0653 VALIDITY OF POLYMYALGIA RHEUMATICA DIAGNOSES, AND CLASSIFICATION CRITERIA, IN PRIMARY HEALTH CARE

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**Background:** Polymyalgia rheumatica (PMR) is an inflammatory disorder that mainly affects elderly women, and usually is diagnosed in primary health care (PHC). A number of classification criteria have been proposed, most recently the American College of Rheumatology (ACR)/ European League Against Rheumatism (EULAR) criteria from 2012 (1). The ACR/EULAR criteria were developed in a cohort of patients recruited from rheumatology clinics.

**Objectives:** To examine the validity of PMR diagnoses in primary care, and to validate the use of classification criteria for PMR in a retrospective survey of a PHC cohort.

**Methods:** Patients were recruited from two PHC centers. All patients with a registered diagnosis of PMR between 2000 and 2013 in the patient administrative system were identified. The electronic case records, including hospital records,

for all patients were reviewed through June 2015. Patients with a diagnosis of PMR prior to 2000, or at another care facility, and those with an incorrectly registered PMR diagnosis code, were excluded. In a structured review of the case records, information required for classification according to the ACR/EULAR criteria, the Bird criteria, the Healey criteria, the Chuang&Hunder criteria and the Jones&Hazelman criteria was extracted. For the ACR/EULAR criteria, a modified version, in which patients who had never been tested for rheumatoid factor (RF) and anti-citrullinated peptide antibodies (ACPA) only required 2 points to be classified as having PMR, was used. Furthermore, as duration of morning stiffness (MS) was usually not recorded, criteria components for MS were considered to be fulfilled whenever MS was mentioned in the records. The reference method was an independent review, with assessment of the long term disease course and differential diagnoses, by an experienced rheumatologist with access to all electronic records.

**Results:** A total of 305 patients with a registered diagnosis of PMR were reviewed. Of these, 117 were excluded. Among 188 with an incident PMR diagnosis at the study sites during the study period, 49 (26 %) fulfilled the modified ACR/EULAR criteria, whereas 145 (77 %) fulfilled the Bird criteria and 93 (49 %) fulfilled the Healey criteria. Patients could not be classified according to the Chuang&Hunder or the Jones&Hazelman criteria due to missing data in most patients for several components. RF and ACPA were tested in only 42 cases (4 positive) and 29 cases (none positive), respectively. The PMR diagnosis was verified using the reference method in 113 cases (60 % of total; 68 % female, mean age at diagnosis 75 years). Among those fulfilling the modified ACR/EULAR criteria, the diagnosis was verified in 84 % of the patients. The corresponding proportion for the Bird criteria was 66 %, and for the Healey criteria 74 %.

**Conclusions:** In this study of patients with PMR diagnosed in PHC, the diagnosis could be verified in 60 % of the patients. This underlines the heterogeneity of PMR patients and related diagnostic procedures in PHC. A modified version of the ACR/EULAR criteria can be used to identify patients with a valid PMR diagnosis in retrospective surveys, but does not capture all PMR patients. The modified ACR/EULAR criteria appear to be more stringent than some of the older criteria sets.

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**Disclosure of Interest:** None declared

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FRI0654

#### IS THE PATIENT-ACCEPTABLE STATUS SIMILAR ACROSS 7 DOMAINS OF HEALTH IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA)? POST-HOC ANALYSES FROM THE VALIDATION IN 549 PATIENTS OF THE RHEUMATOID ARTHRITIS IMPACT OF DISEASE (RAID) SCORE

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**Background:** Patient Acceptable Symptom State (PASS) is the highest acceptable level of symptoms which patients consider satisfactory. In the Rheumatoid Arthritis Impact Disease (RAID) questionnaire, seven domains of health of importance for RA patients are collected.<sup>1</sup>. It is possible that levels judged acceptable by patients vary according to the domain of health.

**Objectives:** To explore the relationship between seven RA domains of health (collected in the RAID) and PASS, and to define their PASS cut-off values.

**Methods:** This is a *post-hoc* analysis of the cross-sectional study for RAID validation. Each of 7 domains (table 1) was evaluated through a Numeric Rating Scale from 0 (best) to 10 (worst). PASS was calculated using the anchored method based on patients' perspective. Disease activity was assessed based on the DAS28–3 values (joint counts and ESR). Comparison of patients in PASS or not was assessed through Mann-Whitney or Chi-square test, as adequate. Variables with  $p < 0.05$  were included in multivariate logistic regression (Forward Conditional) analysis. The thresholds of PASS for each domain was calculated using the receiver-operating characteristic (ROC) curve and the optimal cut-off was determined through Youden Index. 75th percentile analyses were also performed (not shown).

**Results:** 549 patients [78% female, mean age 56.7 years, mean disease duration 12.3 years, mean (SD) DAS 28–3 2.7(1.2)] were analysed. The majority of patients (60.7%) considered themselves to be in PASS. Disease activity (DAS 28–3 mean 2.3 vs 3.4,  $p < 0.01$ ) and all seven domains of health were significantly lower in patients in PASS versus not in PASS ( $p < 0.001$ ). In multivariate analyses, lower disease activity (OR 0.72; 95%IC 0.56–0.92), lower pain (OR 0.75; 95%

IC:0.65–0.86) and better physical well-being (OR 0.74 95%; IC:0.65–0.85) were associated with being in PASS.

The cut-off for PASS was  $\leq 4.2$  for the total RAID score but varied across the seven domains (table 1), with Pain ( $\leq 5$ ) and Fatigue ( $\leq 5$ ) having the highest acceptability cut-offs. Sleep Disturbance and Coping were the domains with lowest thresholds compatible with PASS ( $\leq 3$ ).

**Table 1** Thresholds for Acceptable Status for each RAID domain, AUC: Area Under the Curve, and sensitivity and specificity versus PASS

Domain	Cut-off	AUC	Sensitivity (%)	Specificity (%)
Pain	$\leq 5$	0.84	80.5	72.9
Function	$\leq 4$	0.82	69.7	80.8
Fatigue	$\leq 5$	0.75	74.9	62.2
Sleep	$\leq 3$	0.70	64.2	67.4
Emotional Well-Being	$\leq 4$	0.76	75.0	64.5
Physical Well Being	$\leq 4$	0.81	69.3	77.1
Coping	$\leq 3$	0.79	65.5	77.1

**Conclusions:** Pain and physical well-being appeared as major drivers of PASS. The cut-offs defining PASS were not the same for all RAID domains, indicating that being in PASS doesn't mean the same acceptable severity for all domains of health. This observation suggests that individualised management, for each domain, should be considered.

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FRI0655

#### TITLE: THE CONSISTENCY OF OUTCOMES REPORTED IN TRIALS OF SYSTEMIC SCLEROSIS. IMPROVING OVER TIME?

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**Background:** Standardisation of outcome domains and measures in trials in rheumatology has generally improved the consistency and relevance of outcomes reported in rheumatic conditions over the last two decades. The Outcome Measures in Rheumatology (OMERACT) 'core response set' for trials in Systemic Sclerosis (SSc) was developed in 2008 and comprises 11 domains and 31 measures<sup>1</sup>.

**Objectives:** We aimed to assess the scope, and consistency of outcomes reported in trials of SSc, and the uptake of this core response set.

**Methods:** MEDLINE, Cochrane CENTRAL, Embase and clinicaltrials.gov were searched to identify randomised clinical trials published between 2000 and June 2016 in adults with SSc. Outcomes and measures were recorded for each trial and classified into domains. The scope and consistency of domains were compared between those trials published from 2000 to 2010 and 2011 to mid-2016 to determine whether has been uptake of the core domain and measurement set reported. A two-year lag between publication of the core set in 2008 and start of the second-time period was set to allow to allow for core response set uptake.

**Results:** Overall 114 trials (4860 patients, median sample size of 33) were identified. The majority of trials were interventions for immunotherapeutic agents or vasodilators and included a total of 2736 measures (of 78 domains), with a mean of 24 measures per trial. The proportion of trials reporting any outcome from the each domain is listed: (% of 2000–2010 trials, % of 2011–2016 trials, change in %): health-related quality of life and function (42.6, 56.5, +13.9); skin (39.7, 47.8, +8.1); pulmonary (33.8, 43.5, +9.7); global health (14.7, 21.7, +7.0); gastrointestinal (4.4, 10.9, +6.5); ; cardiac (13.2, 15.2, +2); biomarkers of ESR/CRP (7.4, 8.7, +1.3%) musculoskeletal (5.9, 6.5, +0.6); Raynaud's phenomenon (20.6, 19.6, -1.0) renal (14.7, 10.9, -3.8); digital ulcers (23.5, 19.6, -3.9%). Six measures had a greater than 5% increase in reporting frequency across trial periods: HAQ-DI (from 38.2% to 47.8%), SF-36 (from 17.6% to 28.3%), Modified Rodnan Skin



Score (from 38.2 % to 47.8%), pulmonary function tests (from 30.9% to 43.5%), measures of dyspnoea (4.4% to 10.9%) and patient global disease (from 10.3% to 21.7%).

**Conclusions:** There was a wide range of domains reported in trials in systemic sclerosis. The uptake of domains and measure as per the core response set is low in SSc trials compared to other rheumatic diseases with only modest improvement in reporting of 6 out of 31 measures. Improvements in reporting of specific measures align with the recent development of a composite response index in systemic sclerosis (CRISS)2.

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#### FRI0656 PREDICTIVE VALIDITY OF PRESENTEEISM MEASURES WITH DUAL ANSWER KEYS IN INFLAMMATORY ARTHRITIS

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**Background:** Employment studies in arthritis have emphasized the importance of decreased productivity at work, or presenteeism. However, consensus is still lacking on how to best measure this construct. Instruments used include the Work Limitations Questionnaire (WLQ), which measures the amount of time people are limited, and the Workplace Activity Limitations Scale (WALS), which measures the degree of difficulty. We modified the response keys of the WLQ and WALS, creating a dual answer key assessing both degree of difficulty and amount of time with difficulty. Previous work by our group has shown that scores obtained from combining responses to the dual answer keys exhibit good internal consistency, criterion and construct validity.

**Objectives:** The objective of this study was to evaluate the ability of the combined scores to predict future work cessation and number of work days missed due to arthritis.

**Methods:** A longitudinal study used baseline and 6-month data from the RCT of an employment intervention, the "Making It Work" Program. Inclusion criteria were: inflammatory arthritis, age 19–59, working at baseline, and concerns about arthritis affecting work. 327 participants were included (RA:173, PsA:48, SLE:42, AS:64). Combined scores were obtained by i) multiplying, and ii) adding, the scores of difficulty and time answer keys at the item level. We assessed the predictive ability of the combined scores, and the original scores, of the WALS and WLQ to predict work cessation due to arthritis within 6 months using binary logistic regression models, or number of work days missed due to arthritis using zero-inflated Poisson models.

**Results:** WLQ and WALS original and combined scores were significant predictors of future work cessation and number of work days missed. The WLQ combined scores predicted work cessation better than the original score (AIC:117.6 & 118.2 for multiplicative and additive combinations, respectively vs. 125.4 for time) and work days missed (AIC:2179.8 & 2177.8 vs. 2188.7). WALS original score (ie. degree of difficulty) predicted work cessation better than combined scores (AIC:95.8 vs. 109.3 & 109.4). However, WALS combined scores predicted number of work days missed better (AIC:1696.9 & 1673.4 vs. 1795.2).

**Conclusions:** Combined scores from dual answer keys applied to the WLQ and WALS significantly predicted future work cessation and number of work days missed. Using combined scores, rather than original answer keys, improved the ability of the WLQ to predict both work cessation and work days missed, but only improved the ability of the WALS to predict work days missed.

**Disclosure of Interest:** None declared

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#### FRI0657 CONSTRUCT VALIDITY AND RESPONSIVENESS OF THREE STIFFNESS ITEMS IN RHEUMATOID ARTHRITIS: AN APPLICATION OF THE OMERACT FILTER 2.1

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**Background:** Stiffness is frequent and important to people with rheumatoid arthritis (RA), but measuring it is an unmet need. Qualitative research with people with RA has shown that stiffness duration, severity and interference have face and content validity. These items are being evaluated to develop a patient reported outcome measure (PROM) for stiffness.

**Objectives:** To evaluate individual stiffness item measurement properties using the OMERACT Filter 2.1.

**Methods:** Consecutive patients in a longitudinal RA cohort were enrolled. Participants completed 3 items assessing stiffness severity, interference, and duration. PROMs collected included patient global assessment (PGA), pain VAS, self-reported flare (Y/N), PROMIS measures, and patient global impression of change (PGIC). Physician assessments included 28 tender/swollen joint counts, and global (EGA). Disease activity indices were CDAI and DAS28-CRP. Stiffness construct validity was assessed using Spearman correlation coefficients. To assess discrimination in groups expected to change vs stable groups, we calculated standardized response means (SRMs) using multiple anchors.

**Results:** 196 patients with RA were included. **Construct validity:** all stiffness items correlated highly with pain; moderately with DAS-28 CRP and CDAI; and low with joint counts and EGA. Stiffness severity and interference correlated highly with PGA, pain interference and fatigue. Stiffness interference correlated highly with physical function. **Discrimination:** all stiffness items had moderate effect size for resolution of flare, and for 'much improved' by PGIC. Interference had moderate effect for improved CDAI category and for 'little improved' by PGIC. Stiffness duration had large effect for new RA flare, and 'much worse' by PGIC; severity and interference had moderate effect for RA flare; severity had moderate effect for worsened CDAI and for 'little worse' and 'much worse' by PGIC (Tb).

Table 1 Discrimination of stiffness items by anchor in RA longitudinal sample (n=181). SRM=mean change/pooled SD of change. SRM >0.8 large, 0.5–0.79 moderate, 0.2–0.5 small effect.

Stiffness Anchors	Duration SRM	Severity SRM	Interference SRM
<b>Flare status (n=181)</b>			
Flare to No flare (improved) (n=26)	0.67	0.68	0.54
No flare to No flare (unchanged) (n=111)	0.01	0.01	0.14
Flare to Flare (unchanged) (n=14)	0	0.19	0.27
No flare to Flare (worse) (n=30)	0.81	0.60	0.54
<b>PGIC vs baseline (n=181)</b>			
Much improved (n=26)	0.52	0.61	0.79
Little improved (n=25)	0.43	0.46	0.60
No change (n=68)	0.08	0.08	0.11
Little worse (n=49)	0.41	0.67	0.42
Much worse (n=13)	1.05	0.59	0.39
<b>CDAI vs baseline (n=181)</b>			
Better CDAI category (n=45)	0.25	0.21	0.61
Unchanged CDAI category (n=87)	0.07	0.12	0.04
Worse CDAI category (n=49)	0.48	0.52	0.29

**Conclusions:** In this cohort of RA patients there is emerging evidence for good construct validity for stiffness duration, severity and interference; moderate discrimination for improvement in RA disease state, and moderate to high discrimination for worsening RA. Additional items are being tested to assemble an instrument for measuring stiffness in RA.

**Disclosure of Interest:** None declared

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#### FRI0658 PROGNOSTIC MARKERS FOR RESPONSE ACCORDING TO THE NEW ACR/EULAR 2016 RESPONSE CRITERIA FOR IDIOPATHIC INFLAMMATORY MYOSITIS

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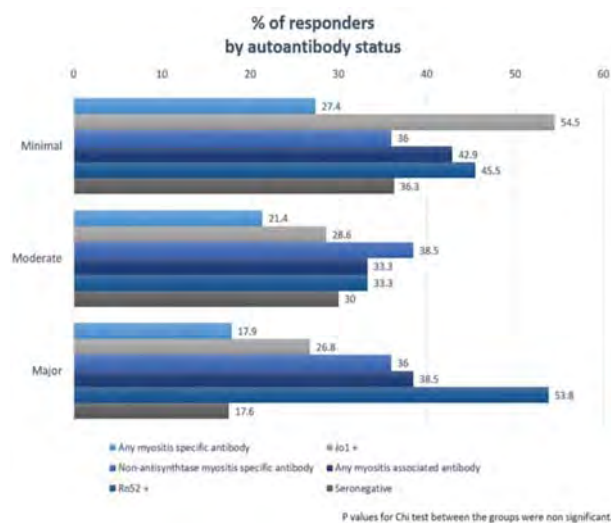
**Background:** Idiopathic inflammatory myopathies (IIM) is a heterogeneous group of chronic, inflammatory diseases with varying response to treatment. To

date there is no biomarker to predict such response. Autoantibodies are found in up to 80% of patients with IIM; myositis associated (MAA) and myositis specific antibodies (MSA) are associated with certain clinical features. Whether MSAs can be used as biomarkers to predict response to treatment is unknown.

**Objectives:** To investigate predictors of response according to the New ACR/EULAR 2016 response criteria for idiopathic inflammatory myositis using a national rheumatology register.

**Methods:** Patients with IIM who were included in the Swedish Rheumatology Quality Register (SRQ) between January 1st, 2003 and December 31st, 2015 within 12 months of diagnosis were included in this study. Response was assessed at the visit registered closest to one year after inclusion. IIM subgroup (dermatomyositis (DM), polymyositis (PM) and overlap myositis), autoantibody profile, time to diagnosis and treatment were categorized into dichotomous variables. Time to diagnosis (from first symptoms) less than 3 months was considered as early; initial dose of glucocorticoids was considered high when >45 mg. The ACR/EULAR 2016 criteria for Clinical Response were applied to measure response, and it was categorized in minimal (20–39/100), moderate (40–59/100) and major (>60/100) response. The association between response and clinical characteristics was assessed by multinomial logistic regression.

**Results:** 179 patients were included. Median age at inclusion was 58.9 years (Interquartile range (IQR) 46.7–68.6), 65% were female and 49% had ever smoked. Thirty-three percent had DM, 45% PM and 22% overlap myositis. Lung disease was present in 37% and cancer within  $\pm 3$  years from IIM diagnosis was present in 13%. Ninety-one percent were given glucocorticoid treatment, 72% immunosuppressive drugs, 22% cyclophosphamide and 13% a biological drug. **Response rates.** Two thirds (62%) were responders, 23% had minimal, 20% moderate and 18% major response. Minimal response was associated with high initial glucocorticoid dose (OR 3.4, CI95% 1.4–8.1); moderate response to high initial glucocorticoid dose (4.8 CI95% 1.9–11.8) and major response to early diagnosis (OR 3.9 CI95% 1.3–11.9), and high initial glucocorticoids dose (OR 9.5 CI95% 3.0–29.8). No associations between IIM subgroup, autoantibody profile and response rates were observed.



**Conclusions:** Early and intensive treatment with high doses of glucocorticoids was associated with high rates of clinical response. These data suggest that early intensive immunosuppressive treatment is important in IIM.

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FRI0659

#### INVESTIGATION OF SELF-REPORTED PAINFUL JOINT COUNT AS OUTCOME MEASURE IN HAND OSTEOARTHRITIS

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**Background:** Hand osteoarthritis (OA) research is in need of disease-specific validated instruments to measure patient-reported outcomes. Self-reported painful joint count (PJC) could be useful to assess pain, including information about the distribution of painful joints, while being less time-consuming than assessor-reported tender joint count (TJC).

**Objectives:** To investigate the metric properties of self-reported PJC compared to assessor-reported TJC to measure pain.

**Methods:** Symptomatic hand OA patients from the Hand Osteoarthritis in Secondary care (HOSTAS) study marked which joints were painful on standardized hand diagrams. Pain upon palpation was scored on similar diagrams by trained nurses, who were unaware of patients' scores. Self- and assessor-reported joint counts were calculated as the sum of painful/tender joints of both hands (range 0–30). Patients also rated pain on visual analogue scale and completed Australian/Canadian Hand Osteoarthritis index pain subscale, Short Form-36 Mental/Physical Component Summary scales, and Hospital Anxiety and Depression Scale. Radiographs were scored according to Kellgren-Lawrence. MRIs of the right distal and proximal interphalangeal joints (DIPs/PIPs) were evaluated for bone marrow lesions and synovitis. Validity was investigated by assessing correlations between self-reported PJC and assessor-reported TJC, and of both joint counts with other outcome measures. Absolute agreement on joint level, and patient level intra-class correlation coefficients (ICCs) were calculated.

**Results:** Of 524 hand OA patients (86% women, mean age 61, 90% fulfilling ACR criteria), 506 (96.9%) reported  $\geq 1$  painful joint (median PJC 8 [interquartile range (IQR) 4–13]), while nurses reported  $\geq 1$  tender joint in 426 (81.3%) patients (TJC 3 [1–7]). Patients and assessors both most frequently reported pain/tenderness in DIP 2–3, PIP 2–3 and the thumb base, and least often in metacarpophalangeal joints (MCPs) 2–5. Correlation between the joint counts was 0.38. Correlations of both joint counts with other measures were comparable, ranging from 0.11 to 0.37 (table 1). Absolute agreement was highest in MCPs 2–5 and lowest for thumb base, DIP 2–3 and PIP 2–3 (range 61%–89%). ICC between joint counts was 0.28 (95% confidence interval 0.08–0.14).

**Table 1** Correlation coefficients for painful joint count (PJC), tender joint count (TJC), and selected clinical and imaging outcomes.

	Self-reported PJC	Assessor-reported TJC
Self-reported PJC	-	
Assessor-reported TJC	0.38**	-
VAS pain	0.37**	0.37**
AUSCAN pain	0.36**	0.36**
SF-36 PCS	-0.30**	-0.27**
SF-36 MCS	-0.12**	-0.11**
HADS depression scale	0.14**	0.15**
Kellgren-Lawrence score	0.08	0.04
MRI synovitis†	0.22*	0.21*
MRI BML†	0.14	0.22*

AUSCAN, Australian/Canadian osteoarthritis hand index; BML, bone marrow lesion; HADS, Hospital Anxiety and Depression Scale; MCS, mental component summary; MRI, magnetic resonance imaging; PCS, physical component summary; SF-36, Short Form 36; VAS, visual analogue scale. \* $p < 0.05$ ; \*\* $p < 0.01$ ; †Joint count of DIP and PIP joints of right hand (n=92) was used (range 0–8).

**Conclusions:** Hand OA patients reported more painful joints than assessors reported tender joints. Self-reported PJC correlated weakly with assessor-reported TJC, and other instruments measuring pain and physical health. Divergent correlations with mental health and imaging scores were even lower. Agreement between patients and assessors was highest in joints with low prevalence of pain/tenderness, but overall agreement was low. Despite apparent advantages, these results suggest that self-reported PJC and assessor-reported TJC cannot be used interchangeably, and further study of PJC as an outcome measure in hand OA is warranted.

**Disclosure of Interest:** None declared

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FRI0660

**USEFULNESS OF MICHIGAN HAND OUTCOMES QUESTIONNAIRE (MHQ) IN HAND OSTEOARTHRITIS**

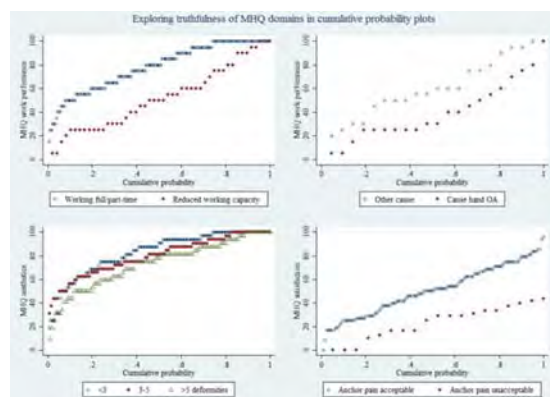
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**Background:** Several tools are available to measure hand pain and function in hand osteoarthritis (OA), though all have their disadvantages, e.g. being not freely available (Australian/Canadian Hand OA Index, AUSCAN), outdated (Functional assessment In Hand OA, FIHOA) or a single-item tool (Visual Analogue Scale, VAS). The MHQ is free to use, validated in other diseases, and has 6 scales assessing pain, function (overall function and activities of daily living [ADL]), and 3 unique domains: work performance, aesthetics, satisfaction (all range 0–100, and higher is better except for pain).

**Objectives:** To investigate truth and discrimination of MHQ in hand OA.

**Methods:** At baseline (n=383) and two-year follow-up (n=293) symptomatic hand OA patients from the Hand Osteoarthritis in Secondary care (HOSTAS) cohort completed questionnaires (MHQ, AUSCAN, FIHOA, VAS pain). Work status was categorized into (fulltime/part-time) employed, reduced working capacity (sick leave or partial/complete disability to work), or not in the workforce (unemployed or retired). Reduced working capacity could be due to hand OA or other causes. Anchor questions assessed whether level of pain/function was acceptable or unacceptable, and different (worse, unchanged or improved) compared to baseline. Number of joints with deformities was assessed, and split into tertiles (<3, 3–5, >5). To appraise validity of MHQ pain and function domains correlation with existing instruments (Spearman correlation coefficients,  $r_s$ ) was evaluated. Using external anchors to categorize patients, validity of the unique domains and discrimination of all domains was visualized in cumulative probability plots (figure 1), and mean between-group difference (MD) was calculated with linear regression.

**Results:** At baseline patients (84% women, median age 60.3, 90% fulfilling ACR criteria) reported moderate pain (median, interquartile range MHQ pain 45, 31.3–60) and functional impairment (MHQ overall function 57.5, 50–67.5; ADL 80.5, 68.2–89.6). MHQ pain and function scales correlated well with existing instruments (table 1). Patients with reduced working capacity had worse MHQ work performance scores than employed patients (MD -25.7, 95% confidence interval [CI] -32.8; -18.6), and scores were worse if it was due to hand OA than when there was another cause (MD -21.4, -37.1; -5.8). MHQ aesthetics scores were worse in patients with more deformities (MD -1.03, -1.60; -0.45 per additional deformity). Patients with 'unacceptable' pain/function had worse MHQ satisfaction scores (eg. pain: MD -27.2, -37.1; -17.3). All instruments measuring pain/function could discriminate between patients with acceptable vs. unacceptable pain/function (not shown). MHQ ADL scale and AUSCAN function outperformed MHQ overall function and FIHOA in discriminating between patients whose function improved vs. worsened over time (not shown). For discrimination of change in pain over time, MHQ and AUSCAN pain both outperformed VAS pain.



**Conclusions:** MHQ performs at least as good and may replace existing instruments in measuring pain and function in hand OA. In addition, MHQ provides information on work performance, aesthetics and satisfaction, which is not measured by other questionnaires. Sensitivity-to-change has to be assessed in future trials.

**Disclosure of Interest:** None declared

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FRI0661

**ULTRASOUND OF SUBTALAR JOINT SYNOVITIS IN PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS OF AN OMERACT RELIABILITY EXERCISE USING CONSENSUAL DEFINITIONS**

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**Background:** The incidence of subtalar joint (STJ) disease in patients with rheumatoid arthritis (RA) is greatly increased between five and ten years of disease duration and regularly precedes changes in the tibiotalar joint [1]. The joint is notoriously difficult to assess clinically and frequently overlooked in favour of the more accessible tibiotalar joint.

We hypothesized that US might be used as a reliable outcome measure to evaluate synovitis of the STJ in patients with RA. The objectives of this study were first, to develop an expert consensus derived definition of synovitis and scanning protocol for the STJ and second, to test the reliability of the definitions and protocol.

**Objectives:** To evaluate the intra- and interobserver reliability of the US assessment of STJ synovitis in patients with RA.

**Methods:** Following a Delphi process, twelve sonographers conducted an US reliability exercise on 10 RA patients with hindfoot pain. The anteromedial, posteromedial, and posterolateral STJ was assessed using B-mode and power Doppler (PD) techniques according to an agreed US protocol and using a 4-grade semi-quantitative grading score for synovitis (synovial hypertrophy (SH) and power Doppler (PD) signal) and a dichotomous score for the presence of joint effusion (JE). Intraobserver and interobserver reliability were computed by Cohen and Light kappa ( $\kappa$ ). Weighted  $\kappa$  coefficients with absolute weighting were computed for B-mode and PD signal.

**Results:** Mean weighted Cohen's kappa for SH, PD, and JE, was 0.80 (0.62–0.98), 0.61 (0.48–0.73), and 0.52 (0.36–0.67), respectively. Weighted Cohen's kappa for SH, PD, and JE in the anteromedial, posteromedial and posterolateral STJ was -0.04–0.79, 0.42–0.95, and 0.28–0.77; 0.31–1, -0.05–0.65, and -0.2–0.69; 0.66–1, 0.52–1, and 0.42–0.88, respectively. Weighted Light kappa for SH was 0.67 (95%CI 0.58–0.74), 0.46 (0.35–0.59) for PD, and 0.16 (0.08–0.27) for JE. Weighted Light kappa for SH, PD, and JE was 0.63 (0.45–0.82), 0.33 (0.19–0.42) and 0.09 (-0.01–0.19), for the anteromedial; 0.49 (0.27–0.64), 0.35 (0.27–0.4), and 0.04 (-0.06–0.1) for posteromedial, and 0.82 (0.75–0.89), 0.66 (0.56–0.8), and 0.18 (0.04–0.34) for posterolateral STJ, respectively.

**Conclusions:** Ultrasound is a feasible and reliable tool for assessing synovitis of the posterolateral STJ in RA, but not for the anteromedial and posteromedial STJ. SH can be reliably detected in B-mode and PD mode, but this is not true for JE.

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**Disclosure of Interest:** None declared

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FRI0662

**CALPROTECTIN S100 A8/A9 IN A SOUTH AFRICAN RHEUMATOID ARTHRITIS (RA) COHORT**

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**Background:** Calprotectins (CLP) S100 A8/A9 are small calcium binding proteins [1] belonging to the group of damage-associated molecular patterns (DAMPs) or alarmins. They play a key role in the inflammatory response in RA. [2, 3] The measurement of CLP S100 A8/A9 in serum may be a useful strategy to optimize management of patients with RA. [4]



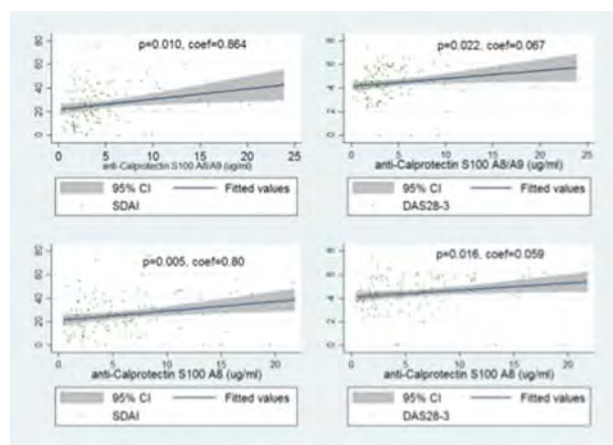
**Objectives:** To evaluate serum calprotectin S100 protein (A8 and A8/A9) levels in a South African RA Cohort in relation to disease severity at presentation in comparison with traditional RA-associated autoantibodies.

**Methods:** This was an observational, single-centre study, involving patients attending the Rheumatology Clinic of the Department of Internal Medicine, Chris Hani Baragwanath Academic Hospital (CHBAH) and University of the Witwatersrand, South Africa. The cohort consisted of 128 ethnic black RA DMARD-naïve patients. The study was approved by the local ethics committee and patients gave informed consent to participate.

**Results:** The baseline demographics and clinical data of the cohort are summarized in table 1. Calprotectin S100 A8 demonstrated a statistically significant association with disease severity [(both SDAI ( $p=0.005$ ) and DAS 28 ( $p=0.016$ )] by linear regression analysis. Calprotectin S100A8/A9 also showed significant associations with SDAI ( $p=0.010$ ) and DAS28 ( $p=0.022$ ) figure 1.

**Table 1** Clinical and demographic data of patients with RA

Sex	Freq	Percent	Cum
Male	23	17.97	17.97
Female	105	82.03	100.00
DAS 28	25	19.53	19.53
Inactive			
DAS 28	57	44.53	64.06
Moderate			
DAS 28	46	35.94	100.00
Very Active			
SDAI	9	7.03	7.03
Remission			
SDAI	16	12.50	19.53
Low DA			
SDAI	45	35.16	54.69
Mod DA			
SDAI	58	45.31	100.00
High DA			
CCP	10	7.81	7.81
Negative			
CCP	118	92.19	100.00
Positive			
RF	8	6.25	6.25
Negative			
RF Positive	120	93.75	100.00
MCV	7	5.47	5.47
Negative			
MCV	121	94.53	100.00
Positive			



**Conclusions:** Unlike those of traditional autoantibodies, serum levels of calprotectin correlate strongly with disease severity of RA patients. These findings suggest that calprotectin S100 is a promising biomarker for assessment and monitoring of disease activity in RA.

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#### FR10663 THE FINE SPECIFICITY OF ANTI-DRUG ANTIBODY RESPONSES TO ORIGINATOR AND BIOSIMILAR INFLIXIMAB: ANALYSES ACROSS FIVE DISEASES FROM THE 52-WEEK RANDOMIZED NOR-SWITCH STUDY

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**Background:** Norway's government funded the NOR-SWITCH study to investigate switching from originator infliximab (INX) to biosimilar CT-P13 in Crohn's disease (CD), ulcerative colitis (UC), spondyloarthritis (SpA), rheumatoid arthritis (RA), psoriatic arthritis (PsA) and chronic plaque psoriasis (Ps). Previously, the main analyses have been published<sup>1</sup>. Immunogenicity is associated with treatment failure and is of particular concern in switching<sup>2</sup>.

**Objectives:** To evaluate the consistency and fine specificity of anti-drug antibody (ADAb) responses to INX and CT-P13, in arthritis and IBD patients, after switching from INX to CT-P13.

**Methods:** The study included adult patients with CD, UC, SpA, RA, PsA or Ps<sup>1</sup>. Assays for drug serum levels and ADAb have been described<sup>1</sup>. ADAb positive sera were tested for cross-reactivity to 5 batches of INX and CT-P13. We quantified IgG4 ADAb, testing for functional inhibition. Infliximab peptides were used to compare epitope recognition of positive sera. Immunogenic infliximab-epitopes were identified by ELISA and sera compared across diseases.

**Results:** We tested 15 controls, 15 arthritis, 21 IBD patients. No Ps patients had ADABs in our study. All 23 anti-CT-P13 and 13 anti-INX sera cross-reacted with INX and CT-P13, respectively. ADAb concentrations to INX or CT-P13 correlated strongly (r values between 0.92 and 0.99,  $p<0.001$  for all experiments, Spearman's correlation test). Sera negative for CT-P13 ADAb (10 healthy controls, 5 RA patients) were also anti-INX negative. IgG4 ADAb in all sera recognized 5 different batches of CT-P13 and INX. All positive sera had similar functional inhibition of CT-P13 or INX TNF-binding capacity, showing reduced binding to CT-P13 in the presence of 5 different batches of CT-P13 and INX. 60%-79% of patients recognized 7 synthetic peptides corresponding to major anti-infliximab epitopes, with no significant differences between CT-P13 and INX ADAb. Three minor epitopes in framework regions of infliximab showed reduced antibody reactivity in 30%-50% of patients. Stratifying by diagnosis, we found two epitopes in the variable and constant heavy-chains of infliximab specifically recognized in IBD patients but not rheumatic patients.

**Conclusions:** ADABs to INX also recognize CT-P13, with similar epitopes. We found no consistent difference in ADAb epitope specificity between diagnoses. However, two specific minor epitopes are only recognized by IBD patients which might reflect the importance of HLA background for ADAb.

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#### FRI0664 BIOMARKERS FOR RELAPSE IN PATIENTS WITH ADULT ONSET STILL'S DISEASE TREATED WITH IL-6 INHIBITOR.

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**Background:** Symptoms and laboratory data in patients with adult onset Still's disease patients (AOSD) at relapse are often non-specific. Especially in AOSD patients treated with tocilizumab, IL-6 receptor inhibitor, inflammatory markers such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are almost normal despite flared disease activity.

**Objectives:** To identify useful biomarkers for assessing disease activity and relapse in AOSD patients treated with tocilizumab.

**Methods:** Consecutive AOSD patients diagnosed by Yamaguchi's criteria in our institution from January 2007 until January 2018 were reviewed. Clinical information was collected from their medical charts. Relapse was defined as a case who required immunosuppressive treatment intensification for AOSD according to their attending physicians. Biomarkers were compared between before relapse and at relapse.

**Results:** Forty eight patients with AOSD were enrolled. Thirty relapses during the observation period of 3.5 years were identified. At relapse, white blood cell count (WBC), CRP, ESR, serum ferritin levels, and serum lactate dehydrogenase (LDH) levels significantly increased compared to before relapse (WBC,  $12123 \pm 1238$  / $\mu$ L vs  $7184 \pm 607$  / $\mu$ L,  $P=0.002$ ; CRP,  $4.37 \pm 1.08$  mg/dL vs  $0.32 \pm 0.18$  mg/dL,  $P=0.003$ ; ESR  $39.1 \pm 7.78$  mm/hr vs  $6.67 \pm 1.46$  mm/hr,  $P=0.001$ ; ferritin,  $78.9 \pm 30.9$  ng/mL vs  $24.9 \pm 3.8$  ng/mL,  $P=0.036$ ; LDH,  $374.8 \pm 48.1$  IU/mL vs  $214.7 \pm 16.8$  IU/mL,  $P=0.005$ ). Six patients were identified to experience relapse with fever, active synovitis, rash or lymphadenopathy while treated with tocilizumab. In patients treated with tocilizumab, while neither CRP nor ESR increased in all patients at relapse (CRP < 0.30 mg/dL in all; ESR,  $4.50 \pm 1.04$  mm/hr vs  $3.75 \pm 1.18$  mm/hr,  $P=0.893$ ), LDH was significantly elevated at relapse compared to before relapse ( $451.2 \pm 92.1$  IU/mL vs  $211.2 \pm 24.6$  IU/mL,  $P=0.04$ ). WBC and serum ferritin levels tended to increase but with no significant difference (WBC:  $14620 \pm 1547$  / $\mu$ L vs  $9500 \pm 2285$  / $\mu$ L,  $P=0.21$ ; ferritin,  $236.4 \pm 91.2$  ng/mL vs  $49.2 \pm 24.2$  ng/mL,  $P=0.091$ ).

**Conclusions:** Instead of CRP and ESR, LDH level was a useful clinical biomarker for relapse of AOSD, especially in those treated with tocilizumab.

**Disclosure of Interest:** None declared

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#### FRI0665 IMPACT OF THE MULTI-BIOMARKER DISEASE ACTIVITY SCORE RESULTS ON WHETHER RHEUMATOLOGISTS CHANGED BIOLOGIC THERAPY FOR RA PATIENTS

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**Background:** The multi-biomarker disease activity (MBDA) score is a validated test used to assess disease activity for patients with rheumatoid arthritis (RA). How it is used in clinical practice in the U.S. is unclear.

**Objectives:** We evaluated the likelihood that rheumatologists would add or switch biologic therapies based on the MBDA test result.

**Methods:** Using previously published methods, we linked results of MBDA tests obtained as part of routine clinical care to 2012–2014 Medicare fee for service claims data for RA patients. We characterized patients as being on a biologic or targeted synthetic DMARD in the 90 days prior to the MBDA test and evaluated biologic/tofacitinib treatment changes in the 90 days following the MBDA test. MBDA test scores were classified as low (<30), moderate (30–44), and high (>44). The unit of analysis was the 90-day interval before and after each MBDA test score. Alternating logistic regression was used to compute odds ratios (OR) to quantify the likelihood that patients made any change (add or switch), accounting for the clustered nature of the data (intervals nested within patients, and patients nested within doctor practices) and physician-level variability, controlling

for patient age and sex. Sensitivity analyses used a 6-month interval for outcome ascertainment after the MBDA test.

**Results:** Using previously validated methods, a total of 27,621 unique RA patients were linked to 44,438 MBDA test scores. For the 27,256 intervals where RA patients were not on biologic therapy when the MBDA score was obtained, a total of 13.2% of patients added a biologic. Patients with high MBDA scores were significantly more likely to add a biologic (table 1). For the 17,182 intervals where RA patients were already on a biologic, a total of 19.1% of patients switched or stopped the biologic that they were taking. Patients with lower MBDA scores were significantly more likely to stay on their therapy, whereas those with higher scores were more likely to stop and/or switch biologics. After adjustment, results from the regression analyses showed that patients with moderate MBDA scores were 1.47 (95% 1.29–1.67)-fold more likely to add or switch biologics, and those with high MBDA scores were 2.54 (95% CI 2.19–2.94)-fold more likely to add or switch biologics. Men (OR=0.90, 95% 0.82–0.98) and older patients (OR=0.92 per 5 year increment, 95% CI 0.91–0.93) were less likely to add or switch therapy, even after controlling for variability between physicians (OR=1.10, 95% CI 1.02–1.19). These results were robust and ORs were numerically larger when extending the interval to 6 months.

Table 1 Proportion of patients who added or switching biologics after the MBDA test

MBDA Score	Non-biologic users who added a biologic after the MBDA test N=27,256	Biologic Users Who Switched or Stopped their Current Biologic after the MBDA test N=17,182
Low (<30)	8.4%	14.0%
Moderate (30–44)	10.8%	16.2%
High (>44)	16.3%	23.1%
Chi-square p value	<0.0001	<0.0001

**Conclusions:** Results from the MBDA score were significantly associated with the likelihood that a physician added or switched biologic therapies, with either type of change being more frequent when the MBDA score was high. Further evaluation of outcomes after switching, conditional on the MBDA score, is warranted.

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#### FRI0666 CIRCULATING MIR-99B-5P AS A PREDICTOR OF EROSION PROGRESSION IN EARLY RHEUMATOID ARTHRITIS: A 1-YEAR FOLLOW-UP STUDY BY HR-pQCT

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**Background:** Bone erosion is a key feature of RA reflecting both disease severity and progression. HR-pQCT is an in-vivo clinical imaging system allowing detailed analysis of bone structure, including bone erosion. Several circulating microRNAs have already been suggested as potential biomarkers in RA.

**Objectives:** To determine whether plasma cell-free circulating miRNAs are 1) associated with bone erosion at presentation and 2) predictive of erosion progression at 12 months as determined by HR-pQCT in patients with early rheumatoid arthritis (ERA).

**Methods:** In this prospective study, 124 ERA patients were treated with a tight control protocol aiming at remission by using conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs). The second metacarpophalangeal joint (MCP2) was assessed for erosions by HR-pQCT at baseline and after 12 months. Plasma cell-free circulating miRNAs at baseline were identified by microRNA array in 10 treatment-naïve ERA patients with maximal erosion volume at MCP2; in 10 treatment-naïve ERA patients without erosion; and in 6 age- and sex-matched healthy controls. The 4 most dysregulated miRNAs were identified by TaqMan<sup>®</sup> qRT-PCR in these same 20 ERA patients. Thereafter, the expression of these 4 selected miRNAs was validated in all 124 ERA patients at baseline.

**Results:** Of the 377 screened miRNAs, 155 miRNAs were detectable. 94 (60.6%) of these detectable miRNAs were upregulated in ERA patient with erosions, with 13 (8.4%) upregulated more than twofold. 61 (39.4%) miRNAs were

downregulated in ERA patients with erosions, with 6 (3.9%) downregulated more than twofold. A total of 16 miRNAs were differentially expressed ( $P < 0.05$ ) and 4 were possibly differentially expressed ( $P \leq 0.1$ ) between ERA patients with and without erosions. At baseline, expressions of miR-143-3p, miR-145-5p and miR-99b-5p were significantly higher in ERA patients with erosions than those without erosions ( $P < 0.05$  for all). After 12 months of csDMARDs treatment, 31.7%, 47.7%, and 20.6% of the ERA patients had erosion progression, stable erosion and partial erosion repair respectively. Logistic regression analysis revealed baseline expression of miR-99b-5p to be an independent predictor of erosion progression at 12 months (Exp [B]= 4.203, 95% CI 1.166–15.147,  $P=0.028$ ) (table 1).

	Univariate			Multivariate		
	P value	Exp (B)	95% CI	P value	Exp (B)	95% CI
Depth	0.068	0.479	0.217–1.056	0.085	0.177	0.025–1.269
Width	0.108	0.746	0.522–1.067	0.871	1.069	0.481–2.373
RF+	0.102	3.833	0.764–19.224	0.087	5.407	0.784–37.317
ACPA>250U	0.062	3.281	0.941–11.439	0.084	4.238	0.822–21.843
miR99b-5p	0.075	2.512	0.913–6.905	0.028	4.203	1.166–15.147

**Conclusions:** Increased level of cell-free circulating miR-99b-5p was associated with erosions at presentation in ERA patients and could predict erosion progression as assessed by HR-pQCT over a period of 12 months, indicating that it may well serve as a biomarker of poor response to csDMARDs. Whether early biologic DMARDs use in these miR-99b-5p positive patients could reduce or prevent progression of erosion will need to be addressed in future studies.

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#### FRI0667 DEVELOPMENT AND VALIDATION OF A RHEUMATOLOGIST SATISFACTION WITH PRACTICE SCALE- "THE RHEUMATOLOGIST SATISFACTION SCALE" (RSS)

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**Background:** Rheumatology practice improvement research routinely measures patient satisfaction and disease-specific outcomes but seldom considers the satisfaction of physicians who deliver the care. Studies suggest that physician dissatisfaction may pose a barrier to implementing quality improvement efforts. There is a paucity of succinct measures of physician satisfaction.

**Objectives:** As part of a Performance Improvement Project, in an academic rheumatology practice and an affiliated practice, we developed and piloted a simple questionnaire to study physician satisfaction in Rheumatology.

**Methods:** Thirty-five rheumatologists in the academic or private setting were sent opened-ended questions to determine the factors that made them satisfied or dissatisfied with respect to their rheumatology practice. From the responses we formed 14 questions on a 0 to 10 scale centering on satisfaction and dissatisfaction. We then administered the questionnaires to a small pilot of 30 rheumatologists in academic and/or private setting.

**Results:** Our sample included 30 rheumatologists, from whom 60% were faculty members, 27 % were fellows. 53% (N=16) were males and the majority (77%) were salaried. Racial distribution was 57% white, 40% Asian, with 7% Hispanic/Latino ethnicity. The most common practice setting was academic medicine (80%, N=24), followed by multi-specialty group (10%, N=3), private practice (7%, N=2), and rheumatology group (3%, N=1). 40% (N=12) and 37% (N=11) had been in practice <5 and >30 years, respectively. Coefficient Alpha for each factor was 0.54 (raw), 0.66 (standardized) for satisfaction and 0.60 (raw), 0.60 (standardized) for dissatisfaction. Based on the results of this survey, mean satisfaction factor in rheumatologists was high (8.6±0.99). 91.3% of rheumatologists (N=21) had mean satisfaction factor >8 (range 5.5–9.9). The ability to make a difference in patient's life and having the opportunity to work with great colleagues were the strongest contributors to physicians' satisfaction (mean 9.2±1.1 and 9.4±0.8, respectively). Time spent on documentation and getting inappropriate referrals that are not in the scope of practice were among the strongest contributors to physicians' dissatisfaction (mean 3±1.9 and 3.9±1.3, respectively). None of the items were highly correlated with each other. This work has now been expanded to more than 150 rheumatologists including in the United States(US) and Latin American countries. Analysis is in progress.

**Conclusions:** A simple and practical questionnaire to measure physician satisfaction was developed and successfully piloted on a predominately academic sample of rheumatologists. The strongest correlates of physician satisfaction

were the "ability to make a difference in a patient's life" and to "work with great colleagues" whereas the greatest correlates of dissatisfaction were "time spent on documentation" and "inappropriate referrals." With further testing on a larger sample from the US and Latin American countries, we aim to gain a deeper understanding of how the cultural differences and practice of medicine may affect physician satisfaction. It is hoped that, this scale will serve as a means of determining aids and barriers to improving rheumatology practice for both patients and physicians and become a useful tool in rheumatology performance practice implementations and studies.

**Disclosure of Interest:** None declared

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#### FRI0668 ITEM RESPONSE THEORY TO STANDARDIZE PATIENT REPORTED PHYSICAL FUNCTION OUTCOMES; LINKING 10 COMMONLY USED QUESTIONNAIRES TO A COMMON METRIC

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**Background:** Physical function is a core outcome domain in clinical trials in various inflammatory rheumatic diseases. It is also included in the recently developed International Consortium for Health Outcomes Measurement (ICHOM) standard set for patients with inflammatory arthritis. Physical function patient reported outcome measures (PROMs) are commonly collected in patient registries and are used by decision makers in ways that require outcomes to be aggregated across different data sources. A major barrier to such initiatives is that many different physical function PROMs are in widespread use, and results cannot be meaningfully compared across them, if the traditional scoring procedures based on summing of the individual item scores are used. This is because summed scores depend on both patient- and item characteristics. To facilitate standardization of physical function outcome measurement, we developed a common metric for ten commonly used physical function PROMs using item response theory (IRT), that can be used to adjust PROM scores for item characteristics.

**Methods:** Data of 16.386 patients with inflammatory arthritis from the United States National Databank of Rheumatic Disease, the Swiss Clinical Quality Management Registry, the National Database of the German Collaborative Arthritis Centres, the Dutch Rheumatoid Arthritis Monitoring Study, and several smaller observational studies were used to map the items of 10 commonly used physical function PROMs on a continuous latent physical function variable. The resulting common metric was cross-validated in an independent dataset of 243 patients with gout, osteoarthritis or polymyalgia rheumatica, in which four of the linked PROMs were administered

**Results:** Our analyses supported that all 97 items of the 10 included PROMs relate to a single underlying physical function variable and that responses to each item could be described by the generalized partial credit IRT model. In the cross-validation analyses we found congruent mean scores for four different PROMs when the IRT based scoring procedures were used.

**Conclusions:** We showed that scores obtained using the IRT based common metric developed in this study can be used to make physical function outcomes obtained using different physical function PROMs comparable.

**Disclosure of Interest:** None declared

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#### FRI0669 PHYSICIAN GLOBAL ASSESSMENTS FOR DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS ARE ALL OVER THE MAP!

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**Background:** Assessments of disease activity in rheumatoid arthritis (RA) determine the course of treatment. Physician global assessments of disease activity (MD globals) are important outcomes in trials as they are part of the CDAI and

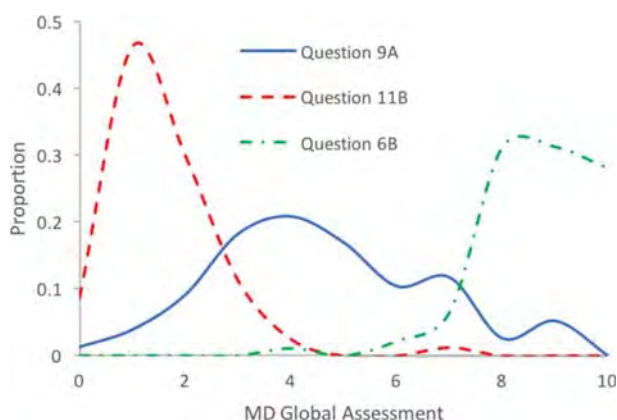


SDAI composite scores. MD globals may vary between physicians based on their age, sex, practice setting, experience, and years in practice.

**Objectives:** Our research goal was to determine which factors contribute to the variability of MD globals. We expected assessments to be lower as physician experience increased.

**Methods:** After obtaining ethics approval, we surveyed rheumatologists who were members of the Canadian Rheumatology Association with RA patient scenarios where each was rated as a MD global for disease activity from 0 – 10. The cases covered a range of disease activity; to determine extreme cases and cases in between. There were some scenarios where a change in status was given (i.e. a rating with one disease state and then the patient returned and another rating was given by each participant when the patient was obviously better or worse). Kappa, Intra-class correlation (ICC) coefficients, and linear mixed models were used to analyze the data

**Results:** We received 145 responses from eligible physicians spanning the above categories (approximately 40% response rate). Contrary to our original hypothesis, MD global assessments were not significantly different between physicians in any category (number of RA patients seen per year, years of experience, age, sex, type of practice [community vs. university], and self-reported expertise in RA). Moreover, the range of answers for the same scenario was as high as 7.6 out of a possible 10, indicating vast discrepancies between physicians. We checked to ensure the questions were not answered backwards by individuals using the scenarios where a patient changed disease activity over time. The agreement was highest in the extreme scenarios (very low and very high disease activity, but in the spectrum in between agreement was extremely poor). Some scenarios outlined changes in individual patients, however physicians surveyed were often in disagreement as to how well the patient recovered or worsened. The change in MD globals between one time and the next in the cases had better agreement than the actual scores.

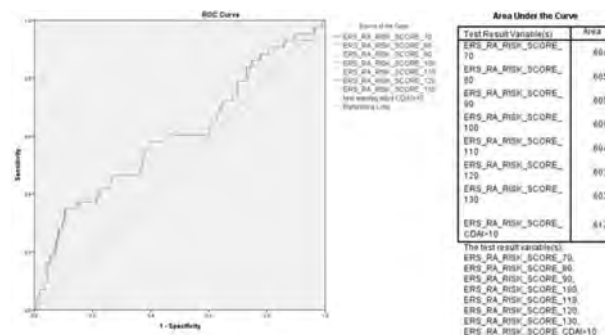


normal population do not predict the CV risk in RA patients adequately due to the additional systemic inflammatory burden which is pathogenic for CV disease. Recently, Solomon et al developed the ERS-RA Risk Score, a newly and expanded CV risk score predicting the 10 year CV event risk in RA patients<sup>2</sup>. This is based on a cohort from the Consortium of Rheumatology Researchers of North America registry. In this abstract we present the results of a validation test performed with the ERS-RA Risk Score in the Dutch CARRÉ study<sup>3</sup>.

**Objectives:** To perform a validation test of the ERS-RA Risk Score in the Dutch CARRÉ study.

**Methods:** We validated the ERS-RA Risk Score in the CARRÉ cohort by performing a ROC curve analysis. The CARRÉ study is a Dutch cohort study investigating CVD and its risk factors in RA-patients who have been followed prospectively for at least five years. RA patients registered at Reade (location Jan van Breemen institute in Amsterdam, the Netherlands) participated if they fulfilled the 1987 ACR classification criteria, were diagnosed between 1989 and 2001, and were aged between 50 and 75 years. In contrast to the cohort used in study of Solomon et al, the CARRÉ study used the HAQ instead of the m-HAQ and the CARRÉ lacks the Predictor's Global Assessment to calculate the CDAl. However, to approximate the true outcome of the m-HAQ and the CDAl we conducted the following modifications of the CARRÉ cohort data. To calculate the CDAl we estimated the Predictor's Global Assessment as 70%, 80%, 100%, 110%, 120% and 130% of the Patient's Global Assessment. Furthermore, we approximated the m-HAQ score 50% lower than the HAQ score as described in a recent published article<sup>4</sup>.

**Results:** The CARRÉ study included 352 RA patients with 60 CV events over a 10 year follow up period. The mean age was 63.3 years of which 121 (34%) male participants. The ROC curve analysis shows an area under the curve of 0.603–0.612 depending on the predicted Predictor's Global Assessment (see figure 1).



**Figure 1.** ROC curve analysis of the ERS-RA Risk score in the CARRÉ cohort with different approximated CDAl scores

**Conclusions:** This research emphasizes the need to establish stringent evaluation criteria of disease activity as rated by the physician in RA; particularly if remission and low disease activity is used clinically by CDAl or SDAI. Perhaps a catalogue examples of patient scenarios of MD globals that range from 0 to 10 should be developed, standardized and agreed upon; to decrease the wide variability of ranking by rheumatologists.

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**Disclosure of Interest:** None declared

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#### FRI0670 VALIDATION OF THE ERS-RA RISK SCORE IN THE DUTCH CARRÉ STUDY.

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**Background:** The most frequent cause of death in patients with chronic rheumatoid arthritis (RA) is of cardiovascular (CV) origin<sup>1</sup>. CV risk prediction scores in the

**Conclusions:** In conclusion, the ERS-RA Risk Score has a limited validity in the CARRÉ study, a Dutch RA cohort and can therefore not be used for risk prediction in Dutch RA patients

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**Disclosure of Interest:** None declared

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FRI0671

### ADAPTATION AND VALIDATION OF THE ANKYLOSING SPONDYLITIS QUALITY OF LIFE (ASQOL) QUESTIONNAIRE FOR USE IN SERBIA

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**Objectives:** To translate and adapt a Serbian version of the Ankylosing Spondylitis Quality of Life (ASQoL) questionnaire and to validate it in Serbian speaking AS patients.

**Methods:** The ASQoL development was conducted in three stages. The first stage comprised of a dual-panel translation: a bilingual panel (to provide the initial translation into the target language) and a lay panel (where items are assessed by people of average and below average education levels for comprehension and "naturalness" of language). The second stage involved cognitive debriefing interviews to assess the applicability, relevance and comprehensiveness of the new questionnaire. The third stage was a psychometric evaluation of the new questionnaire to assess construct validity, convergent validity and known-group validity. Convergent validity determined associations between ASQoL and NHP section scores by using Spearman's rank correlation coefficients. Known-group validity was evaluated by testing of the ASQoL ability to distinguish between groups of patients who differed according to perceived general health, incidence of flare-ups and perceived disease severity. Nonparametric tests for independent samples (Mann-Whitney U test for two groups or Kruskal-Wallis one-way analysis of variance for three or more groups) were used. Internal consistency was assessed using Cronbach's alpha coefficient. Reproducibility was measured by test-retest reliability.

**Results:** Cognitive debriefing interviews were conducted with 10 AS individuals (50% male), aged 38,4 (8,8) years. A few items (i.e. chronically and 'I get frustrated...') were not fully understood by all participants and were amended to be more natural sounding in Serbian. The Serbian ASQoL was deemed relevant, clear and easy to complete. Psychometric evaluation was conducted in 60 patients (70% male), aged 37,9 (11,1) years. No significant differences in ASQoL scores were found between males and females or between older and younger patients ( $p=0.41$ ,  $p=0.16$ ). Considering convergent validity, the ASQoL correlated the most strongly with the Pain ( $r=0.79$ ) and Emotional reactions ( $r=0.78$ ) sections of the NHP. The ASQoL highly correlated with the Physical mobility ( $r=0.77$ ) and Energy scales ( $r=0.75$ ), indicating the importance of these factors on QoL in AS. The ability of the Serbian ASQoL to detect meaningful differences was demonstrated by ASQoL scores according to patients perceived general health ( $p<0.05$ ) and disease severity ( $p<0.05$ ). Cronbach's alpha coefficient for the ASQoL was 0.95 at Time 1 and 0.91 at Time 2, indicating good internal consistency. Test-retest reliability was good, with a correlation coefficient of 0.84.

**Conclusions:** The Serbian version of the ASQoL demonstrated good psychometric properties proving it to be a valid and reliable tool for use in routine clinical practice and in clinical trials.

**Disclosure of Interest:** None declared

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FRI0672

### ANTI-SACCHAROMYCES CEREVISIAE ANTIBODIES IN SPONDYLARTHROPATHIES: PREVALENCE AND ASSOCIATIONS WITH DISEASE PHENOTYPE

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**Background:** It has been speculated that increased gut inflammation is of aetiopathogenic importance in the development of Spondylarthropathies (Spa). Serological markers, as anti-Saccharomyces cerevisiae antibodies (ASCA), which are rarely positive in healthy controls (<5%), possess clinical significance in inflammatory bowel disease (IBD) management.<sup>1</sup> Because Spa and IBD share similarities and even subclinical intestinal inflammation may be present in a high number of Spa patients, evaluation of this antibodies has gained increasing relevance.

**Objectives:** To investigate the status and frequency of ASCA in Spa patients and the association of these serological markers with the clinical profile.

**Methods:** We performed a retrospective study including SpA individuals treated with biologic therapy, followed at our Rheumatology department. Classification of SpA was based on the ASAS criteria. Medical records were obtained by consulting the national database (Reuma.pt). ASCA IgA and IgG levels were measured in the period time between 2016 and 2017 and determined by ELISA. The quantitative ASCA results were expressed in RU/ml and 20 was established as the cut-off point. X<sup>2</sup> or Fisher tests were used for analysis of categorical variables and t-test or Mann-Whitney for continuous variables (SPSS 23.0). The adopted significance was of 0.05.

**Results:** We included 231 Spa patients, 117 of which were men (51%), with a mean age of 48.6±12.5 years. The median disease duration was 17 years [min:2; max: 53]. In total, 39% of the patients had isolated axial form (n=90), 10% isolated peripheral form (n=23) and 51% presented axial and peripheral involvement (n=118). Nine patients had associated IBD [7 cases with Crohn Disease (CD) and 2 with Ulcerative Colitis (UC)] and 66 patients presented concurrent psoriasis (28.6%). Ninety-three patients (40%) were HLA-B27+ and 59 (26%) presented history of uveitis (current or previous). ASCA IgA were positive in 14% of the whole sample (n=33; 14 patients with isolated axial form, 4 with isolated peripheral form and 15 with axial and peripheral form). ASCA IgG positivity was found in 5% of the Spa (n=12; 7 patients with isolated axial form, 1 with isolated peripheral form and 4 with both forms). The median ASCA IgA and IgG titers were 72 RU/ml [min:22;max:200] and 45.5 RU/ml [min:28;max:200], respectively. We found no statistically significant difference in the number of ASCA IgA or IgG-positive patients in CD vs UC ( $p=0.722$ ;  $p=0.583$ ). Current age and at diagnosis, disease duration, gender, active or past smoking habits were similar between ASCA IgA or IgG-positive and negative groups. Also, disease phenotype including peripheral arthritis, axial involvement, psoriasis, HLA-B27 positivity and uveitis were unrelated to ASCA IgA and IgG status.

**Conclusions:** Our results showed that Spa patients presented an increase of ASCA IgA positivity, in agreement to previous data. No relationship of ASCA status was found with the demographic aspects or clinical presentation. In the future, our purpose is to investigate the relationship between antibody reactivity and endoscopic findings.

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**Disclosure of Interest:** None declared

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FRI0673

### DO PATIENT REPORTED OUTCOME MEASUREMENT INFORMATION SYSTEM (PROMIS) COMPUTER ADAPTIVE TESTS CORRELATE WITH DISEASE ACTIVITY IN JUVENILE IDIOPATHIC ARTHRITIS?

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**Background:** The importance of patient-reported outcomes is increasingly recognized both in clinical care and in research. PROMIS is an NIH-supported collection of patient-reported outcome measures, covering a variety of domains that are designed without disease specificity. While 'short forms' have been studied in juvenile idiopathic arthritis (JIA), PROMIS computer adaptive tests (CATs) have not.

**Objectives:** This study evaluates whether PROMIS CATs correlate with disease activity in patients with JIA.

**Methods:** A convenience sample of patients with JIA (N=21) were recruited from a single center. Patients aged 10-17 years completed all available pediatric PROMIS CATs, and parents of patients aged 2-9 years completed all available parent proxy PROMIS CATs (fatigue, pain interference, peer relations, anxiety, depressive symptoms, and mobility). Correlation of the CATs t-scores with disease activity, as measured by the Juvenile Disease Activity Score-71 (JADAS-71), (0-101, higher being worse) was evaluated using Spearman correlation coefficients.

**Results:** All families approached completed the PROMIS CATs: 13 patients and 8 parents (table 1). Median age was 12.7 years (range 1.3 - 18.6 years), and mean JADAS-71 score was 9.58 (SD 2.07). 69% of patients completed PROMIS CATs remotely via smartphone. Anxiety ( $r=0.74$ ,  $p=0.006$ ), depressive symptoms ( $r=0.84$ ,  $p<0.001$ ), and pain interference ( $r=0.64$ ,  $p=0.018$ ) CATs correlated

strongly with JIA disease activity (table 2). Among parent proxy CATs, only anxiety correlated with disease activity ( $r=0.71$ ); however the association was not statistically significant.

Table 1 Patient characteristics

Characteristic	N=26 patients
Age, years, median [IQ range]	12.7 [6.0, 14.5]
Male	8 (30.8%)
White or Caucasian	20 (76.9%)
Insurance	
Medicaid	6 (23.1%)
Device	
Smartphone	18 (69.2%)
iPad	3 (11.5%)
Location	
In hospital	8 (30.8%)
Remotely	18 (69.2%)

Table 2 Spearman correlation coefficients for PROMIS domains and JADAS71 score

PROMIS domain	JADAS71 score Spearman correlation coefficient
<b>PATIENT SCORES</b>	
Fatigue T-score	0.488
<b>Pain Interference T-score</b>	<b>0.640</b>
Peer Relations T-score	-0.345
<b>Anxiety T-score</b>	<b>0.738</b>
<b>Depressive Symptoms T-score</b>	<b>0.840</b>
Mobility T-score	-0.671

**Conclusions:** Our results demonstrate that the PROMIS CATs are feasible to administer in an outpatient pediatric rheumatology setting. Anxiety, depressive symptoms, and pain interference were significantly correlated with disease activity, even though mean disease activity was relatively low. This underscores the negative effect on quality of life of even mild disease. Parent proxy CATs showed poor correlations with disease activity, suggesting parents are inaccurate in assessing important aspects of their child's health. Larger prospective studies are needed to evaluate the sensitivity of PROMIS CATs to change in disease activity over time.

**Disclosure of Interest:** None declared

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#### FRI0674 APPLICABILITY OF THE PSAID12 QUESTIONNAIRE AS A CORE OUTCOME MEASUREMENT IN PSA CLINICAL TRIALS: AN EVALUATION USING OMERACT FILTER 2.1 INSTRUMENT SELECTION CRITERIA

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**Background:** The Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA)–Outcome Measures in Rheumatology (OMERACT) Psoriatic Arthritis (PsA) Core Set working group is in the process of selecting core outcome measurements for PsA randomised trials, following OMERACT Filter 2.1 for instrument selection<sup>1</sup>. The Psoriatic Arthritis Impact of Disease questionnaire (PsAID12) passed the first two steps (domain match and feasibility) at the GRAPPA 2017 annual meeting and is a candidate instrument to measure PsA specific health related quality of life (HRQOL)/Life impact.

**Objectives:** To conduct a systematic review (SR) of the PsAID literature to review the measurement properties in the OMERACT Filter 2.1, assess specifically construct validity (truth) and discrimination of the PsAID12 questionnaire based on available evidence, and to identify gaps in knowledge that need to be covered in order for PsAID12 to pass Filter 2.1.

**Methods:** A SR of PsA patient reported outcomes (PROs) was performed January 1 2017 and updated by hand search (22/11/2017). All articles assessing the measurement properties of the PsAID12 were reviewed. Strength of evidence was rated using COSMIN-OMERACT Good Methods checklist, and performance of measurement properties using the OMERACT standards<sup>1</sup>. We extracted data on domain match (face and content validity), construct validity, test-retest reliability, longitudinal construct validity, clinical trials discrimination, and thresholds of meaning.

**Results:** We identified six studies (129–474 patients in each study) assessing the measurement properties of the PsAID12 in adults with PsA. Domain match: PsAID12 was developed with 12 patient research partners, 139 patients who ranked domain importance and cognitive interviews with 65 patients. Construct validity: Three studies assessed correlation of the PsAID12 with PROs and clinical outcomes, and one study with two PROs. There was strong correlation with measures of function (n=3 studies,  $r>0.66$ ), participation (1,  $r>0.69$ ), disease

activity (2,  $r=0.64–0.87$ ), and measures of pain, fatigue and stiffness (1 each,  $r>0.83$ ); moderate-strong with patient and physician global (3,  $r=0.49–0.84$ ); and moderate with 66/68 joint counts (1,  $r=0.4–0.57$ ) and dactylitis (1,  $r=0.49$ ). Test-retest reliability was high (0.91 (95%CI 0.87–0.94) and 0.95 (0.92–0.96)). Longitudinal construct validity was good with moderate to large standardized response mean (SRM) 0.74 (n=53, changed therapy) and 0.91 (n=71, changed therapy and rated themselves improved). The patient acceptable symptom state (PASS) was 4 in a single study. The minimal clinically important improvement (MCII) varied between 3 (original PsAID development study) and 1.25 (subsequent UK study).

**Conclusions:** This review suggests there is evidence for excellent content validity and reliability and good construct validity and responsiveness of the PsAID12 questionnaire as a measure of HRQOL in PsA. MCII and discrimination in clinical trials need to be defined.

#### REFERENCE:

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**Disclosure of Interest:** None declared

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#### FRI0675 RABIOPRED, AN INNOVATIVE THERANOSTIC TOOL TO ASSIST CLINICIANS SELECT AN OPTIMAL ANTI-TNF ALPHA BIOLOGICAL THERAPY FOR RHEUMATOID ARTHRITIS PATIENTS

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**Background:** TNF alpha blockers form 2nd line treatment choice for Rheumatoid Arthritis (RA) patients. Up to 30% of RA patients do not respond to TNF alpha blockers for unknown reasons, causing a significant impact on patients' outcome and healthcare industry. Therefore, there is an unmet need for a tool to predict treatment response that could help clinicians to choose an optimal treatment for RA patients.

**Objectives:** By using Immuno-Detect, an innovative targeted gene sequencing panel of 2155 mRNA targets associated with immune-inflammatory pathways, we aimed to develop an algorithm, RABIOPRED, that predicts non-response to TNF alpha blockers.

**Methods:** Paxgene samples obtained at baseline from 68 patients naïve to TNF alpha blockers were directly profiled without extraction with Immuno-Detect panel on HTG EdgeSeq platform, a combination of a nuclease protection assay & next generation sequencing (NGS). Patients were treated with Infliximab, Etanercept or Adalimumab and disease activity score was measured based on DAS28 score at 3 months. Response to treatment was assessed by categorizing the patients according to EULAR response criteria. Gene combinations were selected using variable importance score (VIS). Predictive modeling performance was evaluated using the area under the curve (AUC) and confusion matrix.

**Results:** Analytical validation of Immuno-Detect panel shows a very high reproducibility on Paxgene and extracted RNA samples with correlation factor of 0.975 and 0.96 respectively. In paxgene samples, among 2155 genes, 1172 mRNAs are significantly expressed with a mean CV of 9.77% (976 mRNAs and mean CV of 11.98% for RNA). Most expressed target represent only 5% of the total reads and only 20 targets are reaching 1% of total reads showing a very well balanced panel. Performance of our predictive model shows an AUC of 0.905 with 0.88 accuracy. Our algorithm predicts non-responders to TNF alpha blockers with the sensitivity of 0.78 and positive predictive value of 0.91. This algorithm will be further validated within the ongoing RABIOPRED Proof-of-Performance study (ClinicalTrials.gov Identifier: NCT03016260) based on 720 patients treated by anti-TNF alpha drugs (5 originators & 3 biosimilars) launched in December 2016.

**Conclusions:** We are showing that Immuno-Detect panel accurately measures mRNA expression using HTG-EdgeSeq NGS platform. This panel can be further used to build signatures to predict TNF alpha blocker's non-response. The algorithm obtained in the current study will be later on validated in a multi-centric proof-of-performance clinical study.

**Disclosure of Interest:** None declared

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FRI0676

### RESPONSIVENESS OF PATIENT REPORTED OUTCOMES MEASUREMENT INFORMATION SYSTEM (PROMIS®) COMPUTERIZED ADAPTIVE TESTS (CATS) IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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**Background:** The accurate measurement of patient reported outcomes is a priority for patient-centered care in SLE, a chronic systemic disease with significant impact on quality of life. PROMIS CATs are precise measures of physical, mental, and social health with construct validity in SLE. The longitudinal responsiveness (sensitivity to change) of PROMIS CATs in SLE patients is unknown.

**Objectives:** To evaluate the responsiveness of PROMIS CATs in SLE outpatients using patient and physician-derived anchors.

**Methods:** Adult SLE patients were recruited from an SLE Center of Excellence. Subjects completed 14 selected PROMIS CATs at two visits a minimum of one month apart. SLE disease activity was measured with a patient global assessment of change, a physician global assessment and the physician-derived SELENA-SLEDAI. Responsiveness of PROMIS scores was evaluated using known-groups validity. Effect sizes were compared across groups of patients who differed in their patient global assessment of change, physician global assessment, and SELENA-SLEDAI using Wilcoxon rank-sum tests.

**Results:** A diverse cohort of 228 SLE patients, including 45 (19.8%) patients flaring by SELENA-SLEDAI, completed baseline surveys. Follow up surveys were completed by 190 (83%). There was poor agreement between patient and physician global assessments (weighted kappa statistic [95% CI]=0.16 [0.04–0.28]). Using the patient-based anchor, Anger, Pain Interference, and Physical Function CATs showed low to moderate responsiveness (table 1). Using the physician global assessment, only Anxiety CAT showed low to moderate responsiveness (effect size -0.27, -0.17, and 0.06 [p=0.03] with ≥0.5 point decrease, <0.5 point change, and ≥0.5 point increase respectively), while with the SELENA-SLEDAI as anchor, only Applied Cognition-Abilities CAT showed responsiveness (0.34, -0.01, 0.0 [p<0.01] with ≥3 point decrease, <3 point change, and ≥3 point increase respectively).

PROMIS CAT	Patient Global Assessment of Change			p-value
	Better (n=74)	Same (n=79)	Worse (n=33)	
Ability to Participate in Social Roles	0.14	0.00	0.00	0.19
<b>Anger</b>	<b>-0.37</b>	<b>-0.08</b>	<b>0.00</b>	<b>0.03</b>
Anxiety	-0.38	-0.04	-0.02	0.13
Applied Cognition-Abilities	0.15	0.00	-0.03	0.30
Applied Cognition-General Concerns	-0.08	0.00	-0.06	0.47
Depression	-0.15	0.00	0.36	0.15
Fatigue	-0.16	0.00	-0.15	0.51
Mobility	0.14	0.00	0.00	0.26
Pain Behavior	-0.14	0.00	0.10	0.07
<b>Pain Interference</b>	<b>0.00</b>	<b>0.00</b>	<b>0.25</b>	<b>0.02</b>
<b>Physical Function</b>	<b>0.15</b>	<b>0.01</b>	<b>-0.14</b>	<b>0.02</b>
Satisfaction with Social Roles & Activities	0.18	0.00	0.00	0.21
Sleep Disturbance	0.00	-0.14	-0.04	0.50
Sleep-Related Impairment	-0.07	0.00	-0.02	0.95

**Conclusions:** PROMIS CATs showed modest responsiveness to patient-reported, but generally not physician-derived changes in lupus health status in domains of anger, pain interference, and physical function. These data suggest that certain PROMIS CATs are precise and sensitive tools which may be used to measure and monitor important aspects of the patient experience of lupus not captured by physician-derived metrics. Further studies are needed to evaluate the responsiveness of PROMIS CATs in populations with greater SLE disease activity and more regular follow up.

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**Disclosure of Interest:** None declared

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FRI0677

### PREVALENCE AND SEROLOGICAL PROFILE OF ANTI-DFS70 POSITIVE SUBJECTS: DATA FROM A ROUTINE ANA COHORT

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**Background:** Anti-Dense Fine Speckled 70 (DFS70) antibodies are a common finding in clinical laboratory referrals. High prevalence of DFS70 autoantibodies in

healthy population and usual negative association with Antinuclear Antibody (ANA)-associated autoimmune rheumatic diseases were reported.

**Objectives:** The aim of this study was to evaluate the prevalence of anti-DFS70 antibodies in a routine diagnostic laboratory setting and their association with other circulating serum autoantibodies.

**Methods:** Consecutive sera submitted for ANA screening were analyzed for anti-DFS70 antibodies by indirect immunofluorescence (IIF) (n=3175, 1030 men and 2145 women) then confirmed by Immunoblotting. IIF DFS70 positive adult patients were recruited previous written consent and tested for the following autoantibodies: anti-ENA, anti-dsDNA, -anti-TPO, anti-TG, anti-tTG, aCL, anti-PCA, AMA, ASMA, anti-LKM, anti-MPO, anti-PR3 and ASCAs.

**Results:** The prevalence of anti-DFS70 antibodies was 1.7% (n= 55) in the whole population and 4.6% in the ANA-positive samples. Comparison between DFS70 IIF and Immunoblotting showed an excellent correlation between the two methods (R=0.99). Analysis of anti-DFS70 antibodies titers distribution revealed that 63% of the total cohort showed high titers (≥1:640). Gender difference (female: male, 4:1) was observed in anti-DFS70 positive group and in anti-DFS70 negative/ANA positive group. The prevalence of anti-DFS70 positive female (2.1%, 45/2145) was statistically significant higher than males (1.0%, 10/1030) (p<0.05). The comparison among referring sources evidenced a prevalence of anti-DFS70 positive subjects from Endocrinology Department (9.1% versus 2.6% from Haematology, 2.1% from outpatients, 1.6% from Neurology, 1.2% from Internal Medicine, 1% from Cardiology, 0.6% from Rheumatology). Of note, our data evidenced isolated reactivity of anti-DFS70 autoantibodies in males group, while 51% of females showed concomitant disease-marker autoantibodies.

**Conclusions:** We found a prevalence of anti-DFS70 antibodies in adult sera from routine ANA cohort of 1.7%. The serological profile of DFS70-positive females required further investigations in order to define the presence of serum autoantibodies. Anti-DFS70 reactivity in male population may represent an exclusive biomarker predicting the absence of other autoantibodies.

**Acknowledgements:** The authors would like to express their especial appreciation and thanks to Prof. Ignazio Olivieri who died on July 28th, 2017. He was an example of strength and tenacity with a contagious enthusiasm for a rigorous scientific research.

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FRI0678

### VALIDITY OF THREE 0–10 VISUAL ANALOG SCALES (VAS) FOR QUANTITATIVE PHYSICIAN ASSESSMENT OF INFLAMMATION, DAMAGE, AND DISTRESS TO SUPPLEMENT A PHYSICIAN GLOBAL ASSESSMENT 0–10 VAS

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**Background:** Rheumatologists generally view their primary goal as control of inflammation in order to prevent long-term damage, and quantitative assessment involves measures of inflammatory activity (lab tests, joint counts, and indices). Although structural damage and patient distress (fibromyalgia, depression, etc.) are widely recognized, these problems generally are described narratively, and not assessed quantitatively. Recent advances in control of inflammation, as well as increased degenerative diseases in an aging population and recognition of a high prevalence of fibromyalgia, may have shifted rheumatologists' patient mix more prominently toward damage and distress vs inflammation.

**Objectives:** To analyze physician global assessment (DOCGL) on a 0–10 visual analog scales (VAS), and 3 additional 0–10 VAS for inflammation, damage, and distress, as well as estimates of the proportion of each to explain DOCGL.

**Methods:** Rheumatologists at one academic site complete a 0–10 DOCGL VAS, 3 further 0–10 VAS to assess inflammation (reversible disease) (DOCINF), joint and other organ damage (irreversible disease) (DOC DAM), and patient distress (fibromyalgia, depression), etc. (DOCSTR), in routine care. The proportion of DOCGL attributed to inflammation, damage, and distress (total=100%) also is estimated. Mean values were analyzed in a cross-sectional study of 570 patients, and compared in subgroups with rheumatoid arthritis (RA), osteoarthritis (OA), or fibromyalgia (FM), using t tests and analysis of variance (ANOVA).

**Results:** Mean DOCGL VAS was 4.4/10 in all patients, 4.4 in 131 with OA, 4.6 in 98 with RA, and 5.2 in 89 with FM (table 1). Highest mean scores were seen for DOCINF in RA, DOC DAM in OA, and DOCSTR in FM (p<0.001), indicating face validity. Nonetheless, mean DOC DAM was higher than DOCINF in all groups, including RA, and mean estimates of the proportion of DOCGL attributed to damage was greater than to inflammation in all groups (table 1). Scores for DOCSTR were higher than for DOCINF in all groups other than RA.

**Table 1** Mean VAS Scores and % of clinical management decision attributed to inflammation, damage, and distress in patients with rheumatic diseases

Mean VAS Scores	ALL	RA	OA	FM	P*
	N=570	N=98	N=1311	N=89	
VAS DOCGL	4.4 (1.6)	4.6 (1.8)	4.4 (1.5)	5.2 (1.6)	0.04
VAS DOCINF	1.8 (2.0)	2.8 (2.4)	0.7 (1.1)	0.8 (1.3)	<0.001
VAS DOCDAM	3.1 (2.2)	3.8 (2.3)	4.4 (1.8)	1.7 (1.9)	<0.001
VAS DOCSTR	2.1 (2.9)	1.2 (2.2)	1.5 (2.5)	6.0 (2.5)	<0.001
p (DOCINF vs DOCDAM)	0.001	0.01	<0.001	<0.001	
p (DOCINF vs DOCSTR)	0.11	<0.001†	<0.001	<0.001	
<b>Mean % of clinical management decision attributed to...</b>					
% inflammation	29 (31)	39 (29)	12 (19)	6 (11)	<0.001
% damage	48 (35)	52 (30)	73 (31)	18 (23)	<0.001
% distress	22 (34)	9 (20)	15 (27)	76 (27)	<0.001

\*ANOVA – RA vs OA vs FM † -only comparison in which DOCINF higher than DOCSTR

**Conclusions:** VAS scores and estimates of the proportions of DOCGL attributed to damage were higher than for inflammation in all groups, including RA patients as a group. Control of inflammation remains a primary concern for rheumatologists, but has improved considerably in recent years, and damage and distress may have become more prominent in routine care. Systematic quantitation of inflammation, damage, and distress, in addition to DOCGL, appears feasible and of value in routine clinical care.

**Disclosure of Interest:** T. Pincus Shareholder of: Dr. Pincus holds a copyright and trademark for MDHAQ and RAPID3 for which he receives royalties and license fees. All revenue is used to support further development of quantitative questionnaire measures for patients and doctors in clinical rheumatology care., I. Castrejon: None declared, J. Block: None declared

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#### FRI0679 HIGH SENSITIVITY CARDIAC TROPONIN T IN PSORIATIC ARTHRITIS PATIENTS: A CROSS-SECTIONAL CONTROLLED STUDY

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**Background:** High sensitivity cardiac troponin (hs-cTnT) is a biomarker for cardiovascular disease (CVD) in the general population. (1) Psoriatic arthritis (PsA) confers an increased risk for CVD (2) but there are no biological markers to stratify CVD risk in PsA patients.

**Objectives:** To determine the level of serum hs-cTnT in a PsA cohort and controls without inflammatory disease, and further characterize the PsA cohort with detectable hs-cTnT.

**Methods:** Serum hs-cTnT level was measured with a sandwich immunoassay method in a consecutive PsA cohort (n=96). The control cohort was based on apparently healthy individuals recruited during routine annual health examination, Tel-Aviv Medical Center Inflammatory Survey (TAMCIS) (n=6,052). hs-cTnT was measured in carefully matched controls (n=88), manually selected from the TAMCIS, based on gender, age, BMI, hypertension, and hyperlipidemia prevalence. Hs-cTnT  $\geq 5$  ng/L was used as a cutoff for the detectable level. Multiple regression analysis was used to determine the factors associated with hs-cTnT.

**Results:** The characteristics of the PsA cohort are presented in table 1. Remarkably, in the majority of patients, both skin and joint disease were well controlled. PsA and TAMCIS cohorts had a similar range of age (51.5 vs 48 yr) but different gender representation: 47% vs 72.5% of males (p<0.001). PsA exhibited a higher prevalence of traditional CVD risk factors compared to the TAMCIS cohort: BMI 28 vs 26.5 (p=0.002), current smokers 20.8% vs 10.1% (p=0.002), hypertension 25% vs 15% (p=0.007), dyslipidemia prevalence 34% vs 27% (p= 0.101), diabetes 19.8% vs 4.6% (p<0.0001). Due to these differences, a matched control group was used for comparison of troponin. Detectable hs-cTnT was present in 29.5% of the PsA patients compared to 19.3% in the controls. (p=0.114) Factors associated with detectable hs-cTnT in PsA were consistent with traditional factors and included male gender (p=0.007), age (p=0.005), hypertension (p<0.001), and DM (p<0.001). No correlation between detectable hs-cTnT level and psoriasis/PsA duration, disease severity, treatment with DMARDs or biologics was found.

**Table 1** Characteristics of the PsA cohort (n=96)

Gender, % males	47%
Age, years	51.5±13
Psoriasis duration	17±13
Psoriasis activity: remission/mild/moderate to severe	34%/56%/10%
PsA duration	9.4±8.1
PsA activity: remission/low/moderate/severe	37%/33%/22%/8%
Concomitant sDMARDs treatment (%)	49%
Concomitant biologic treatment (%)	65%
Biologic treatment exposure (past or present) (%)	71.8%

**Conclusions:** This is the first study to report a detectable hs-cTnT level in up to 30% in patients with well controlled PsA, asymptomatic for CVD, warranting a special attention to monitoring CVD risk factors and manifestations in this group. Traditional CVD risk factors but not measures of disease activity were associated with detectable hs-cTnT. The latter may be explained by a potential positive impact of anti-rheumatic therapies on the cardiovascular profile. Further prospective studies addressing the predictive role of hs-cTnT for CVD events in PsA are needed.

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#### FRI0680 TETHERIN, A NOVEL TYPE I INTERFERON BIOMARKER ON BLOOD LEUCOCYTES CAN CAPTURE INTERFERON STATUS AND CORRELATES WITH USTEKINUMAB (STELARA) THERAPY RESPONSE IN PSORIATIC DISEASE.

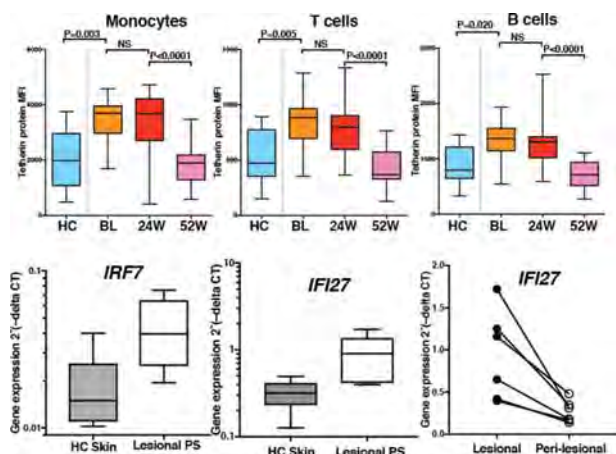
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**Background:** Recently Ustekinumab, an IL12/23 p40 monoclonal antibody that is licensed for Psoriatic Arthritis and Psoriasis, showed promising results in phase II trials in SLE- a prototype IFN mediated disease. We previously confirmed a novel IFN gene scoring system associated with the different SLE symptoms (manuscript in review). Additionally, we also recently validated in two independent cohorts the value of BST2/ tetherin as IFN-I biomarker assay correlates with clinical activity and predicts clinical flare in SLE. Given that psoriasis has several SNPs in the IFN pathway; Thus mechanistic studies of the effect of Ustekinumab on the IFN pathway can be explored in this disease setting.

**Objectives:** This work tested the hypothesis that a novel interferon type I (IFN-I) status markers in the blood and skin of Ustekinumab treated psoriasis patients might correlate with therapy responses and provide insights into how p40 blockers may affect IFN pathways in a relevant human disease model.

**Methods:** Skin biopsies and peripheral blood at baseline (before therapy, 24weeks, 54 weeks) from 23 Ustekinumab patients with psoriasis who had ultrasound imaging confirmed subclinical enthesopathy) were recruited. Cellular immunophenotyping was performed using multi-parameter flow cytometry to detect tetherin on (Monocyte, B cells, T cells and neutrophils). All data was compared to age-matched samples from healthy controls (HC). Skin biopsies were digested and RNA extracted, qPCR of common ISGs genes were analysed in lesional and peri-lesional at corresponding time points.

**Results:** Tetherin showed a higher level of expression on blood subsets of psoriasis compared to HC at baseline on Monocytes, T cells, NK cells and B cells (p=0.003, =0.005, =0.035, =0.002) compared to the baseline. No significant changes observed between baseline and 2nd visit 24 weeks. Interestingly, a substantial reduction in tetherin expression at (52 weeks) in psoriasis was observed in all subsets in Monocytes, T cells, NK cells and B cells (all p<0.0001) correlating with patient response to therapy. IFN signature by TaqMan revealed higher expression in skin biopsies distinctive ISGs compared to HC, e.g. IFI27, STAT1, IFI16 and IRF7 all corrected post-Ustekinumab therapy to normal levels. Paired analysis revealed a stronger IFN signature in lesional biopsies vs non-lesional biopsies, e.g. IFI27 (p=0.0312, Wilcoxon matched pair-rank test).



**Conclusions:** Psoriasis which is genetically and mechanistically linked to IFN-I signatures shows responses to Ustekinumab therapy that correlate with improvement in IFN-I signatures in blood and tissues. Given that whole blood ISG signatures were complex and weakly correlating with disease activity. We provide a convenient, validated method to analyse IFN pathway in routine clinical practice using tetherin which could be a future research tool for the cell-specific IFN-I response. These studies support the idea that p40 efficacy in psoriasis is associated with IFN-I pathway modulation and relevant for exploring how p40 blockers may exert potential benefit in SLE.

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**Disclosure of Interest:** None declared

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#### FRI0681 FOUR COMORBIDITY INDEXES AMONG PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Previous studies have reported an increased risk of multiple comorbidities in people with RA therefore it is necessary to systematically quantify the comorbidity burden of these patients.[1] The comorbidity index is a tool developed under this concept and has multiple clinical and research uses.

**Objectives:** We compared four comorbidity indexes in patients with rheumatoid arthritis in Taiwan (Charlson Comorbidity Index (CCI), Elixhauser Comorbidity Index (ECI), Mutimorbidity index (MMI), Rheumatic Disease Comorbidity Index (RDCI))

**Methods:** All patients with rheumatoid arthritis diagnosed during 1998–2008 in Taiwan were identified using the Taiwan National Health Insurance Database and followed up to 31 Dec 2013. Score accumulation between periods during diagnosis (4 months before and after initial diagnosis) and before/after the diagnostic period was compared. Poisson regression was used to calculate incidence rate ratio.

**Results:** Among 24767 patients with rheumatoid arthritis, median age at diagnosis is 51 years old and female is 79.2%. The mean score at diagnosis is 0.8 in CCI, 2.8 in ECI, 0.7 in MMI and 1.3 in RDCI. The annual percentage changes are 11.0%, 11.3%, 9.7% and 6.8%, respectively. The score of four comorbidity indexes increased with time after rheumatoid arthritis was diagnosed. The incidence rate ratios (IRR) for any increase in comorbidity score during versus before diagnostic period are higher than after versus before diagnostic period. (IRR 1.8 [CI 1.68 to 1.92] vs. 1.57 [CI 1.47 to 1.69] in CCI, IRR 2.77 [CI 2.67 to 2.87] vs. 2.44 [CI 2.36 to 2.53] in ECI, IRR 1.33 [CI 1.26 to 1.40] vs. 1.26 [CI 1.19 to 1.33] in MMI, IRR 1.47 [CI 1.41 to 1.54] vs. 1.31 [CI 1.26 to 1.37] in RDCI)

Table 1 Incidence rates (IR) per 1000 patient months and incidence rate ratios (IRR) for occurrence of any disease in comorbidity index before, during, and after diagnosis\* in patients with incident rheumatoid arthritis, 2001–2008, Taiwan.

Comorbidity indexes	Before diagnosis		During diagnosis		After diagnosis		IRR (95% CI)
	No of events	Crude IR	No of events	Crude IR	No of events	Crude IR	
CCI	1,311	0.007	2,353	0.013	2,062	0.012	1.80 (1.68 to 1.92)
ECI	4,099	0.023	11,933	0.064	10,011	0.057	2.77 (2.67 to 2.87)
MMI	2,249	0.013	2,985	0.017	2,828	0.016	1.33 (1.26 to 1.40)
RDCI	8,601	0.020	5,309	0.030	8,778	0.027	1.47 (1.41 to 1.54)

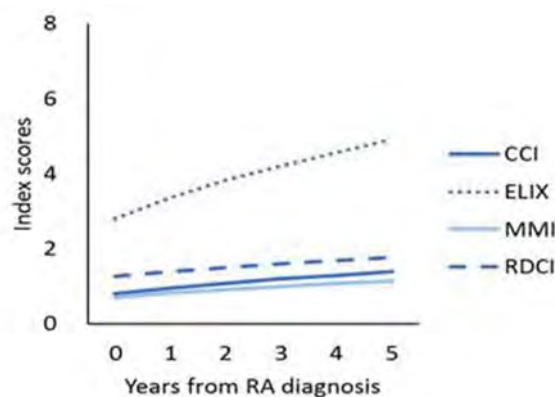


Figure 1 Mean scores of comorbidity indexes from diagnosis year by Rheumatoid arthritis

**Conclusions:** Our study showed that comorbidities continue to accumulate after the initial diagnosis. The comorbidity tends to occur during diagnostic period in patients with rheumatoid arthritis. Different comorbidity indexes are all good at assessing comorbidity burden. Clinicians should screen different comorbidities, determine primary prevention and control disease activity to improve the functional status, quality of life and mortality of rheumatoid arthritis.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.2940

FRIDAY, 15 JUNE 2018

#### Rehabilitation

#### FRI0682 EXERCISE MAY DECREASE SYNCOPE SECONDARY TO POSTURAL CHANGE IN FEMALES WITH RHEUMATOID ARTHRITIS: PILOT STUDY

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**Background:** The autonomic nervous system (ANS) regulates the heart rate via sympathetic and parasympathetic influences. Literature has shown that rheumatoid arthritis (RA) patients suffer from autonomic dysfunction. This may consequently lead to syncope with possible falls after posture change i.e. rising from supine to the standing position. Previous research has shown general improvement of the ANS after exercise, but not in specific relation with posture change.

**Objectives:** To determine the effect of exercise on posture change (supine to standing position) in females with RA as measured by short-term heart rate variability (ANS function).

**Methods:** Patients with confirmed RA were randomly selected to a control group (RAC) or an exercise group (RAE). The RAE group (n=19) trained two to three times per week under supervision. The RAC group (n=18) continued with their current sedentary lifestyle. The medium intensity exercise programme lasted for



12 weeks. No change in medication was allowed during this time. ANS function and balance were determined by quantification of the variability of the inter-beat interval detected with the Polar 810i heart rate monitor system. Frequency domain analyses were used for quantification, including LF (ms<sup>2</sup>) – indicating mainly sympathetic influence, HF (ms<sup>2</sup>) – indicating parasympathetic influence, and LF/HF – indicator of autonomic balance.

**Results:** The two groups matched regarding baseline demographic data (age, sex, disease activity, disease duration). Due to small sample sizes and variables not following a normal distribution, non-parametric Mann Whitney U analyses were performed on the heart rate variability parameters. Comparing posture change (i.e. standing value minus supine value) from pre- to post intervention, all frequency domain parameters changed as anticipated (i.e. vagal withdrawal and increased sympathetic influence) for the RAE group. For the RAC group the measurements deteriorated.

**LF (ms<sup>2</sup>):** RAE -1.03 to 22.03 (stronger sympathetic influence); RAC 43.45 to -31.21 (weaker sympathetic influence)

**HF (ms<sup>2</sup>):** RAE -24.03 to -33.34 (better vagal withdrawal); RAC -191.7 to -114.1 (less vagal withdrawal)

**LF/HF:** RAE 10.57 to 15.04; RAC 2.9 to 7.6

**Conclusions:** From these preliminary results it appear that exercise may indeed improve autonomic function in RA patients, in such a way that posture change will not be an added burden for falls in an already otherwise compromised population.

**Disclosure of Interest:** None declared

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### FRI0683 INVESTIGATION OF THE RELATIONSHIP BETWEEN PLANTAR PRESSURE DISTRIBUTION AND LUMBAR MULTIFIDUS MUSCLE THICKNESS

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**Background:** Lumbar multifidus is a muscle which is responsible for lumbopelvic stability primarily. Foot-ankle posture and function disorders affecting the lumbopelvic region muscles and biomechanics, cause increased stress in the lumbopelvic region and may cause low back pain in many studies (1,2,3). However, it is not known whether the lumbar multifidus muscle is affected by this condition (4,5).

**Objectives:** Plantar pressure distribution can change due to foot-ankle postural disorders. Our aim is to examine whether the plantar pressure distribution affects the lumbar multifidus muscle thickness.

**Methods:** 40 healthy young adults aged 18 to 25 years were included in the study. Static and dynamic pedobarographic assessments were performed to determine the plantar pressure distribution, on a 3x1 meter sensed walking platform with the DIASU Digital Analysis System<sup>®</sup>. Peak pressures (N/cm<sup>2</sup>) of 9 zones of the foot (medial of heel, lateral of foot, 5 metatarsal, thumb and 2,3,4 and 5. digits) were recorded. Ultrasonographic imaging was used to assess lumbar multifidus muscle thickness.

**Results:** There was statistically significant correlation between lumbar multifidus muscle thickness and peak pressure medial of heel and 1. metatarsal bone in static pedobarographic analysis (p<0.05). As the peak pressure on the medial part of foot increased, m. lumbar multifidus muscle thickness was reduced. There was statistically significant correlation between lumbar multifidus muscle thickness and pressure medial of heel and 2,3,4. and 5. digits in dynamic pedobarographic analysis (p<0.05). As the peak pressure on the medial part of foot increased, m. lumbar multifidus muscle thickness was reduced.

**Conclusions:** Our results show that plantar pressure distribution affected lumbar multifidus muscle thickness. Based on these results, the lumbopelvic region and foot posture should be considered together in therapeutic interventions.

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**Disclosure of Interest:** None declared

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### FRI0684 EFFICIENCY OF COMPLEX REHABILITATION PROGRAM IN PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING ABATACEPT

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**Background:** Rehabilitation techniques (physical exercises, physiotherapy, occupational therapy, patient education) help to manage rheumatoid arthritis (RA) in addition to drug treatment [1–4].

**Objectives:** To evaluate the efficiency of 12-month complex rehabilitation program in patients with RA receiving abatacept.

**Methods:** 50 patients with RA (94% females, 72% with moderate disease activity by DAS28, age of 18 to 57 years, disease duration of 10 months to 12 years) were included and randomized into 2 groups. All patients received abatacept (intravenously 10 mg/kg (mean 750 mg) once every 4 weeks or subcutaneously 125 mg once a week) with methotrexate 20–25 mg per week. 28 study group patients underwent 12-months complex rehabilitation program: laser therapy of 12 to 16 min (infrared low intensity laser radiation, wavelength of 0,89 micrometers, pulse frequency of 1000 to 1500 Hz) for hand, knee, ankle, shoulder and elbow joints, 3 courses for 14 sessions with a mean interval of 3,2 months; 45-min dynamic exercises using gym apparatus Enraf-Nonius under the supervision of a trainer 3 times a week; 45-min exercises for hands 3 times a week; 45-min occupational therapy (joint protection strategies, use of assistive devices and adaptive equipment), 10 sessions; wrist, ankle and knee orthoses, orthopedic insoles; education program (4 daily 90-min studies). 22 patients received only drug therapy (control). Tender and swollen joint count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), joint pain on 100-mm VAS, DAS28, HAQ, RAPID3, hand grip strength, the average powers of knee extension and ankle flexion by EN-TreeM movement analysis were evaluated at baseline and at 12 months.

**Results:** After 12 month in the study group tender joint count decreased by 69,3% (p<0,01), swollen joint count – by 66,2% (p<0,01), ESR – by 63,7% (p<0,01), CRP – by 58,5% (p<0,01), pain on VAS – by 82,3% (p<0,01), DAS28 – by 39,6% (ΔDAS28=2,89±0,99, p<0,05), HAQ – by 72,2% (ΔHAQ=1,73±0,44, p<0,01), RAPID3 – by 78,3% (ΔRAPID3=8,45±0,85, p<0,01). The grip strength of a more affected hand enhanced by 57,1% (p<0,01), of a less affected – by 46,2% (p<0,05). The average extension power of a weaker knee increased by 72,1% (p<0,01), of a stronger – by 65,8% (p<0,01). The average flexion power of a more affected ankle joint elevated by 48,9% (p<0,05), of a less affected – by 69,4% (p<0,01). In the study group there were statistically significant differences from the control group in the most parameters (p<0,05), excluding CRP, ESR, DAS28 and the average flexion power of a more affected ankle joint (p>0,05). After 12-months in the study group there was significantly more frequently a good response to treatment according to the EULAR criteria (DAS28) (85,7% vs 63,6% in the control group, p<0,05).

**Conclusions:** 12-month complex rehabilitation program relieves pain, improves quality of life, functional status, motion activity and helps to control disease activity in patients with RA receiving abatacept.

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### FRI0685 HAND FUNCTIONS ARE AFFECTED DEPENDING ON THE CURVE PATTERN IN IDIOPATHIC SCOLIOSIS

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**Background:** Idiopathic scoliosis (IS) is a three-dimensional deformity and causes postural distortions in head, trunk, scapular region and upper extremities. Hand functions have not been evaluated in relation to lateral curvature of the spine in IS previously. There is a need to evaluate possible changes in hand functions with scoliotic curve in idiopathic scoliosis.

**Objectives:** The aim of this study was to investigate hand functions in individuals with idiopathic scoliosis.

**Methods:** Ninety-four individuals with mild or moderate idiopathic scoliosis (Cobb angle range: 10° – 45°) were included. Curves were classified as single thoracic (n= 18), single thoracolumbar (n= 33), single lumbar (n= 22) and double curves (n= 21). Assessments included hand dexterity with Minnesota test, hand reaction time with Nelson test, hand-eye coordination with finger-to-nose test, throwing accuracy with Functional Throwing Performance Test, and upper extremity stability with the Closed Kinetic Chain Upper Extremity Stability Test. One-way ANOVA was used to compare continuous variables between different curve pattern groups and a Tukey's hsd means comparison was used to examine the nature of the significant difference found by ANOVA. In addition, Student's t test was used to compare the parameters between the convex and concave side of the curve for each group.

**Results:** Hand-eye coordination and throwing accuracy was significantly worse in thoracic curve pattern group than lumbar ones for both convex and concave sides of the curve. There was no difference between curve patterns in terms of hand dexterity, hand reaction time and upper extremity stability. When compared with concave side, hand dexterity was greater in the convex side for thoracic curves (p<.05). For double curves, convex side had better hand dexterity and reaction time than concave side (p<.05). But there was no difference between convex and concave side for thoracolumbar and lumbar curve patterns (p >.05).

**Conclusions:** This study showed that hand function is affected, depending on the curve pattern in idiopathic scoliosis. There is no knowledge about how hand function is affected in patients with scoliosis in the literature. Further research following these findings may lead to an understanding of the change in hand functions and its relation with scoliosis-related characteristics, such as age, curve magnitude and trunk deformity.

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FRI0686

#### THE EFFECT OF FOOT ORTHOSES ON BALANCE IN RHEUMATOID ARTHRITIS PATIENTS: A RANDOMIZED CLINICAL TRIAL

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**Background:** Rheumatoid patients(RA)have increased rate of falls and an impaired balance. Foot orthoses are commonly used in RA. Despite the evidence of pain relief with foot orthoses, it is not clear if their use can improve or even impair balance in RA.

**Objectives:** The aim of this study was to evaluate the effect of foot orthoses on balance of RA patients.

**Methods:** 94 RA patients in the outpatient clinic of the Rheumatology Division of Unicamp were randomly assigned to intervention group/IG(n=48)with foot orthoses or control group/CG(n=46)without orthoses. At initial visit, subjects were assessed regarding:sociodemographic and clinical data(number of falls in last year, fear of falling, disease duration, rheumatoid factor, Imedication, visual impairment, vertigo, physical activity, body mass index, comorbidity index, foot tactile sensitivity, number of lower limbs swollen and tender joints count, disease activity-CDAI and disability-HAQ). Subjects answered The Foot Function Index-FFI and were submitted to Berg Balance Scale-BBS, the Timed Up and Go-TUG and the 5-Time Sit Down-to-Stand up-SST5 tests.IG subjects received custom made insoles according to each foot needs. After four weeks, subjects were reassessed for FFI, BBS and TUG. To compare baseline values of groups, the chi-squared test, Fisher's exact test and Mann-Whitney test were applied.ANOVA for repeated measures was used to compare differences between groups and times for BBSTUG and FFI. Effect size was analyzed using the Cohen's d test. All data were analyzed with a 5%level of significance.

**Results:** 81 subjects completed the research protocol,40 in the IG and 41 in the CG. Groups were similar at baseline for most variables with exception of

comorbidity index(worst index in IG) and race(p<0.05). After four weeks, FFI-total, FFI-Pain, FFI-activity limitation disclosed a significant improvement only in IG. Significant differences between times were noted for TUG and BBS only in IG. Interaction group versus time was significant for FFI and BBS. Subjects from IG reported a mean wearing time of 7.32hs/day. Adverse effects were noted in ten subjects(foot pain, hot foot).

Comparison between IG and CG at baseline (t1) and after 4 weeks (t2)

Variables	IG vs CG, p <sup>*</sup>	t1 vs t2, p <sup>*</sup>	Interaction groups vs time, p-value	Effect Size <sup>**</sup>
FFI-pain	0.0001	<0.0001	0.001 <sup>a</sup>	-0.60
FFI- disability	0.050	0.001	0.036 <sup>b</sup>	-0.28
FFI-activity limitation	0.007	0.004	0.011 <sup>a</sup>	-0.61
FFI-Total	0.002	<0.0001	0.001 <sup>a</sup>	-0.57
TUG	0.454	<0.0001	0.079 <sup>c</sup>	No interaction
BBS	0.358	0.0001	0.011 <sup>b</sup>	0.35
NCS	0.422	0.102	0.022	0.44

\*ANOVA for repeated measures (variables converted into ranks) \*\* d de Cohen

**Conclusions:** Foot orthoses were well accepted and worn during long periods with FFI and balance tests (BBS, TUG)improvement. Prospective placebo controlled studies are recommended to assure the possibility to use insoles as adjuvant interventions to improve balance in RA.

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FRI0687

#### EFFECT OF PERINEURAL INJECTION THERAPY IN MODERATE AND SEVERE KNEE OSTEOARTHRITIS; A COMPARATIVE STUDY

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**Background:** Osteoarthritis (OA) is the most common rheumatologic disease. Knee OA is the most common form of symptomatic OA. It is the fourth most important global cause of disability in women and the eighth most important cause in men<sup>1</sup>.

Studies found that subcutaneous prolotherapy is an effective treatment for several painful conditions. Some author hypothesizes that subcutaneous prolotherapy injections induce apoptosis of proliferating peptidergic nociceptors and neovessels by reducing vascular endothelial growth factor levels and restoring effective repair processes, with reduction of pain<sup>2</sup>.

**Objectives:** To assess the effectiveness of perineural injection therapy as a new modality in management of pain, physical function, ambulation activity, disability and psychological status in moderate and severe knee osteoarthritis.

**Methods:** In this study; we selected 100 patients with moderate and severe knee osteoarthritis diagnosed clinically and radiologically by plain x-ray. Patients were classified into four equal groups (25 patients in each group). Group I received 6 weekly subcutaneous injections of 0.5–1 ml of buffered dextrose 5% in each chronic constriction injury points and tender points around knee. Group II received therapeutic continuous US three times weekly for 6 weeks using 1-MHz US head, set to an intensity of 1 W/cm<sup>2</sup> for 10 min. Group III received combined perineural and US therapy. Group IV received sham US. All patients received 15 min of quadriceps isometric exercise of both knees.

Assessments were performed at baseline, at the end of the treatment and after three and six months. using the following measurements: Primary outcome was pain on movement assessed by visual analog scale (VAS). Secondary outcomes consisted of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores, 50 meters walking time, Lequesne index, Hospital Anxiety and Depression Scale (HADS).

**Results:** No baseline differences existed between all groups. The improvement in group IV was non-significant (p>0.05), while there was significant improvement in all other groups (p<0.05) in all primary and secondary outcomes after treatment, 3 and 6 months later. In comparing groups I, II, III the best improvement was in

group III then group I then group II after treatment and 3 months later but there was no significant difference between the three groups after 6 months follow up.

Table 1 Pre- and post-treatment clinical measurement of the patient groups

	Baseline				After treatment				After 3 months				After 6 months			
	G I	G II	G III	G IV	G I	G II	G III	G IV	G I	G II	G III	G IV	G I	G II	G III	G IV
VAS	8.54	8.75	8.27	7.94	5.24	5.58	4.65	7.27	5.61	6.3	5.02	7.03	5.94	6.18	5.75	7.79
	±1.42	±1.07	±1.92	±3.93	±2.41	±5.8	±2.06	±1.42	±2.74	±1.90	±1.76	±2.06	±2.30	±2.03	±1.82	
WOMAC (Total)	88.35	87.95	89.58	86.7	43.75	49.14	40.2	46.14	43.35	48.84	46.09	44.3	45.7	50.27	43.0	49.42
	±14.87	±15.02	±13.4	±18.1	±17.4	±18.5	±15.38	±21.3	±14.9	±16.8	±16.21	±16.81	±15.28	±16.46	±15.51	
50 meters walking time(s)	77.95	80.9	79.26	80.32	64.75	66.57	60.5	63.95	64.2	64.17	61.25	76.00	64.4	65.52	62.1	60.84
	±10.4	±11.33	±10.7	±10.56	±5.4	±5.14	±3.47	±2.93	±3.54	±2.2	±2.4	±2.53	±3.4	±3.01	±3.1	
Lequesne index	14.2	13.88	14.81	13.1	10.2	10.2	10.0	13.1	10.18	10.31	10.07	13.6	10.3	10.29	10.13	14.1
	±3.34	±2.5	±4.2	±3.21	±4.5	±3.51	±3.52	±3.53	±3.45	±3.81	±3.31	±3.6	±4.53	±3.51	±3.5	±2.95
-HAD anxiety subscore	9.05	8.30	8.8	8.0	7.4	6.5	6.5	8.8	7.8	8.4	6.9	9.2	7.6	8.8	6.5	8.9
	±4.05	±1.81	±4.8	±4.63	±4.0	±2.83	±3.7	±3.7	±3.6	±2.3	±3.2	±4.0	±3.5	±3.6	±4.0	
-HAD depression subscore	7.60	7.20	7.4	7.3	6.6	6.25	5.8	7.0	6.7	6.3	5.5	7.0	6.8	6.5	6.0	7.3
	±1.93	±4.82	±5.67	±4.6	±4.5	±4.25	±4.0	±4.5	±4.7	±4.9	±3.6	±4.0	±4.3	±2.6	±3.7	±3.2

**Conclusions:** Perineural Injection Therapy is an effective new modality in management of pain, physical function, ambulation activity, disability and psychological status in moderate and severe knee osteoarthritis.

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FRI0688

#### FAST ACCESS TO ASSESSMENT SUPPORT AND TREATMENT (FAAST): INNOVATION TO IMPROVE SERVICE

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**Background:** Physiotherapy is integral to rheumatology MDT. Early physiotherapy interventions optimise education, self-management and enhance outcomes. Delay in first physiotherapy assessment leads to non engagement, altered clinical features and adverse outcomes<sup>1</sup>. Our physiotherapy service provided appointment based assessments. Each new patient appointment was for 60 minutes. We had an average of 43 day wait to see routine patients. Non attendance rate was high, patients did not value the benefits of physiotherapy and therapist was not able to provide input in patient management.

To improve service, a new system of Fast Access to Assessment, Support and Treatment (FAAST) was introduced in April 2017, allowing patients same day access to physiotherapy on the day of referral.

**Objectives:** 1. To assess the impact of FAAST on non-attendance rate and subsequent visits.

2. To analyse the type of interventions, time spent on assessment and benefits on resource utilisation.

**Methods:** Patients completed a body chart to document their symptoms and a baseline Burton-Patient Reported Outcome Measure (B-PROM)<sup>2,3</sup>. These informations allowed the therapist to assess patients' priorities. Physiotherapist and patient then decided upon the appropriate and possible intervention on the day and subsequent visits. Follow up appointments were made based on clinical need and patient's convenience. We collected data prospectively on type of intervention, time spent on assessment, attendance to subsequent sessions and compared to the data from conventional physiotherapy clinics.

**Results:** FAAST project started in April 2017. This ran parallel to the conventional clinic. Now it is the main portal of referral to physiotherapy. We present data from April 2017 to November 2017. 495 out of 952 patients referred in this period were assessed in the FAAST clinic.

1. Average wait time in conventional clinic was 43 days for routine and 19 days for urgent. In FAAST clinic, every patient was assessed by the physiotherapist on the day of referral eliminating waiting time. Average time to second review after FAAST clinic was 23 days.

2. Type of assessment was decided on the first visit to FAAST clinic. About 70% patients were booked for one to one sessions and about 15% were booked into group sessions designed for specific disease conditions. FAAST assessment

helped to identify patients needed to be referred to other specialist therapy areas also.

3. Non-attendance rate for the first appointment in conventional clinic for preceding three year period was 13%. Every patient referred to FAAST clinic attended the first appointment and non-attendance at second appointment improved to 9.5%.

4. Average time spent by the therapist at first FAAST clinic was 29 minutes which equated to saving of 242 hours compared to conventional clinic. Pre FAAST era, 100 new patients were seen a month on an average. Since FAAST clinic started, this increased to 136 a month.

**Conclusions:** 1. FAAST clinic achieves its objective of reducing waiting times and non-attendance rate.

2. Average assessment time was flexible, saved time and helped to improve efficiency of the clinic.

3. Assessment and intervention on the day of assessment helped to target the therapy more effectively.

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FRI0689

#### A CONSERVATIVE TREATMENT OPTION FOR CARPAL TUNNEL SYNDROME: EXTRACORPOREAL SHOCK WAVE THERAPY. PROSPECTIVE, RANDOMIZED, DOUBLE BLIND PLACEBO CONTROLLED STUDY

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**Background:** Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy that occurs as a result of median nerve compression at the wrist. Extracorporeal shock wave therapy (ESWT) is specified as a treatment with high amplitude acoustic waves that focus on a region of the body. While ESWT is frequently used to treat musculoskeletal disorders such as plantar fasciitis and tendinitis, in recent years ESWT has become a new treatment option in CTS. Positive results have been reported from limited number of studies which were assessed efficacy of ESWT in CTS treatment. On the other hand it is noteworthy that the number of patients in these studies is not high and there is no clear consensus on the concept of shock wave energy density and frequency due to lack of experience (1,2,3).

**Objectives:** To evaluate the efficacy of ESWT in CTS and compared to wrist splint treatment in this prospective, randomized double-blind, placebo-controlled trial.

**Methods:** One hundred eighty-nine patients with mild/moderate CTS were included. Patients were assigned to 4 different treatment groups (1-Splint, 2-Splint + ESWT, 3-ESWT, 4-Splint+ placebo ESWT) by using stratified randomization to ensure balance of the treatment groups respect to the various combinations of the prognostic variables in terms of in terms of age, gender, and severity of CTS. 168 patients completed the study at third month. ESWT was performed on the area included 2 cm proximal to the pisiform bone. It was applied with 1000 shots, 0.05 mJ/mm<sup>2</sup> intensity of energy and frequency of 5 Hz. (3 weeks, once a week). Wrist splint with suitable size and neutral position was suggested. Patients were evaluated at baseline, first and third month. Pain, finger pinch strength, Boston Carpal Tunnel Questionnaire (BCTQ), Leeds Neuropathic Symptom and Finding Assessment (LANSS) and electrophysiological examination were assessed.

**Results:** Demographics, clinical characteristics of the patients are shown in table 1. Significant pain and functionality improvement was found in all groups (p<0.05) at first and third months. The improvements in clinical and electrophysiological variables were compared between four groups In group 2, baseline- first month finger pinch increase was higher than groups 1 and 4, and the baseline- third month finger pinch increase was higher than group 4. In group 2, the increase in mMNVCV was higher than group 1.



Table 1 Baseline demographic and clinic characteristics of patients

	Group 1 n=47	Group 2 n=47	Group 3 n=45	Group 4 n=50	p
Age (year)	48.1 ± 10.13	48.38 ± 10.12	50 ± 8.56	48.48 ± 9.79	0.325 <sup>‡</sup>
Gender					
Female n, %	40, 85.1%	39, 83%	41, 91.1%	47, 94%	0.298 <sup>†</sup>
Education duration (year)	5.68 ± 3.49	7.48 ± 4.21	5.51 ± 3.25	6.84 ± 3.25	0.002*
Co-morbid disease					
DM: %	15%	15%	8.8%	22%	
Hypothyroidism: %	19.2%	25.6%	13.3%	18%	
HT: %	21.4%	23.5%	20%	26%	0.940 <sup>†</sup>
Symptom duration (month)	22.21 ± 26.93	33.68 ± 38.10	23.48 ± 27.27	24.8 ± 31.47	0.152
VAS night	6.23 ± 3	6.11 ± 2.69	5.89 ± 2.86	6.01 ± 2.56	0.899
VAS	4.17 ± 3.04	4.22 ± 2.3	4.13 ± 2.55	4.54 ± 2.39	0.876
BCSS	2.63 ± 0.86	2.54 ± 0.67	2.53 ± 0.89	2.54 ± 0.74	0.914 <sup>‡</sup>
BCFS	2.23 ± 0.95	2.3 ± 0.73	2.24 ± 0.76	2.47 ± 0.69	0.480
Finger pinch (kg)	5.02 ± 1.66	5.74 ± 1.83	5.1 ± 1.32	4.9 ± 1.4	0.017* <sup>‡</sup>
LANSS	9.85 ± 6.81	9.13 ± 5.93	9.56 ± 6.15	9.45 ± 5.95	0.900
Neuropathic pain + ** (n, %)	30 (41.7%)	27 (38.6%)	26 (40.6%)	24 (29.3%)	0.361 <sup>†</sup>

Group 1: Only wrist splint treatment, Group 2: ESWT + wrist splint treatment, Group 3: Only ESWT, Group 4: Placebo ESWT + wrist splint treatment, n: number of patients, DM: Diabetes mellitus, HT: Hypertension; VAS: Visual Analog Scale, (0-10 cm), BCTQs: Boston Carpal Tunnel Symptom Severity Score, BCTQf: Boston Carpal Tunnel Functional Capacity Score, LANSS: Leeds Assessment of Neuropathic Symptoms and Signs; kg: Kilogram, <sup>†</sup> Chi square test<sup>‡</sup> one way analysis of variance (kruskal wallis analysis was used for parameters without normal distribution)

\* difference between Group 1 and Group 2 p=0.021

‡ difference between Group 2 and Group 3 p=0.006

† difference between Group 2 vs Group 4, p=0.018

\*\* LANSS score ≥ 12

**Conclusions:** In the group with ESWT and using wrist splint together, it was found that the improvement of hand function and electrophysiological measures was higher than other groups. ESWT, a valuable and practical treatment modality without serious side effects, reduces pain, neuropathic symptoms, disability and improves electrophysiological findings for patients with mild to moderate CTS.

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FRI0690

#### COMPARISON OF EFFECTIVENESS OF DIFFERENT STRETCHING EXERCISES COMBINED WITH PRESSURE RELEASE TECHNIQUE ON LATENT TRIGGER POINTS IN THE PECTORALIS MINOR MUSCLE

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**Background:** A myofascial trigger point (MTrP) is a hyperirritable spot located in a palpable taut band of skeletal muscle which are painful upon compression, stretching, or overload of the muscle. It is well known that latent triggerpoint (LTrPs), highly prevalent in healthy subjects, are usually silent even though they can easily develop into ATrPs under the influence of perpetuating factors; therefore LTrPs need to be treated.

**Objectives:** To investigate which type of stretching exercise using after a single-session ischemic compression is more effective for muscle length, pressure pain threshold (PPT), pulmonary function, and respiratory muscle strength in subjects with latent trigger point in the pectoralis minor (PM) muscle.

**Methods:** Two-hundred-six individuals were screened for possible inclusion criteria. Fourty subjects were randomized to the Group-1 (ischemic compression with modified contract-relax PNF stretching), Group-2 (ischemic compression with static stretching), Group-3 (ischemic compression with myofascial release) or Group-4 (no intervention). The assessments were performed at baseline, immediately after the intervention, and at 24-hours later. The pectoralis minor length (PML) was measured using a standard tape measure. Then, pectoralis minor index (PMI) was calculated. Rounded shoulder posture (RSP) was assessed by the measuring the distance between the posterior border of the acromion and the table 1. Digital algometer was used to evaluate the PPT; spirometer and respiratory pressure meter were used to assess pulmonary function and maximal respiratory pressure, respectively.

**Results:** Improvements were found for PML and PMI between baseline and immediately after intervention in Group-1 and Group-3 (p<0.05). RSP showed a significant improvement only in Group-3 (p=0.03), whereas there was a statistically significant improvement for PPT value in Group-1 immediately after intervention (p=0.005). Significant difference were found in the PEmax at baseline to 24-hours later in Group-1 (p<0.05). There was a statistically significant difference in the PIMax and PEmax in Group-3 (p<0.05).

**Conclusions:** For effective trigger point therapy, ischemic compression should be followed by myofascial release or contract-relax PNF stretching exercises.

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FRIDAY, 15 JUNE 2018

#### Education

FRI0691

#### EFFECT OF AN EDUCATIONAL INTERVENTION BASED ON CLINICAL SIMULATION IN THE DIAGNOSIS OF PSORIATIC ARTHRITIS IN LATIN AMERICAN DERMATOLOGISTS

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**Background:** Previously our group has shown the use of clinical simulation in rheumatology, an area in which it had not been used. We demonstrated the effectiveness of an educational intervention based on clinical simulation to improve the diagnostic approach to RA<sup>1</sup>, so we wanted to apply this same principle in the learning of Psoriatic Arthritis (PsA) and SpA (Spondyloarthritis).

**Objectives:** This paper wants to quantify the rate of improvement in the diagnosis of Psoriatic Arthritis (PsA) among a group of Latin American dermatologists who received an educational intervention based on clinical simulation.

**Methods:** Observational study before and after

**Results:** 192 Latin American dermatologists received an educational intervention based on clinical simulation. The topic of this educational intervention was based on PsA. A workshop that includes clinical simulation models of feet, fingers and a mannequin with prominent entheses was created for this purpose. It was used an strategy of problem-based learning. The workshop lasted 5 hours and it was divided into two parts: the first was about the clinical approach of joint pain and lumbar pain diagnosis and relevant aspects of PsA. The second part focused on clinical cases applied to clinical simulation models, applying the knowledge acquired during the theoretical phase. Participants made a several stations where they could appreciate for periods of 15 minutes each simulator of 3 feet, 6 simulated fingers and a mannequin where they can identify entheses, dactylitis, arthritis, psoriasis lesions and improve visual and tactile sensitivity in each semiologic findings for the diagnosis of PsA. The participants filled out a pre and post test, which included 6 (six) clinical cases with simulators and photographs of hands and feet of patients with suspected PsA. 192 participants (82 %

women) from 5 Latin American countries (Argentina, Brazil, Colombia, Mexico and Peru), average age 42.43 years (SD 6.2 years). Dermatologists obtained an improvement in the correct diagnosis of PsA of 56,1 % (the correct diagnosis increased from 33,1 % to 89,2 %). the total number of exams requested in the cases presented decreased significantly, from an average of 9 to 3 exams requested by each clinical case presented. 95 % of participants would recommend to other colleagues to make this workshop. 98,8 % believe that this educational intervention will improve the diagnostic approach to patients with suspected PsA.



**Conclusions:** The present research is a pioneer and innovator in the rheumatology education. We have shown the usefulness of clinical simulation given by an improvement in the diagnostic sensitivity towards the diagnosis of PsA, highlighting the semiology as a key element at the time of making the diagnosis. A significant decrease in the total number of exams requested for each of the clinical cases analyzed was documented, which can have a positive effect on costs for the national health systems in each country of the participating dermatologists.

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FRI0692

#### ANTI-TNF TREATMENTS FOR WOMEN WITH CHRONIC INFLAMMATORY DISEASES: COMPARING ATTITUDES AND PERCEPTIONS OF PHYSICIANS IN EUROPE AND THE US

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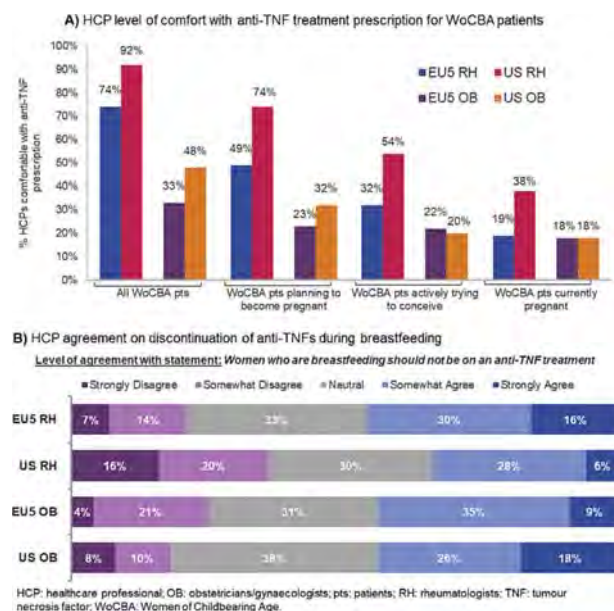
**Background:** For Women of Childbearing Age (WoCBA) with chronic inflammatory diseases (CID), onset, diagnosis and treatment initiation often overlap with peak reproductive years. High disease activity is associated with increased risk of pregnancy complications and adverse outcomes, and achieving disease control in these patients (pts) is therefore an important goal. Tumour necrosis factor antagonists (anti-TNFs) are effective treatments, but few data are available on how physicians utilise them in clinical practice for this specific pt group.

**Objectives:** To help better understand physicians' perceptions and attitudes towards treating WoCBA pts with anti-TNFs during pregnancy and lactation, and gain insights into differences between Europe- and US-based physicians.

**Methods:** The survey was conducted online in the US in July 2017, and in EU5 (France, Italy, Spain, UK and Germany) in Nov/Dec 2017, through SERMO Real-Time. WoCBA were defined as female pts aged 18–45. Participants included

rheumatologists (RH), gastroenterologists (GI), dermatologists (DM) and obstetricians/gynaecologists (OB). Here, we present data for RH and OB.

**Results:** 203 healthcare professionals (HCPs) from the US participated, of whom 50 were RH and 50 OB; 401 HCPs from EU5 participated, of whom 152 were RH and 114 OB; over half of the female pt population with CID among the prescribing specialists were WoCBA. Overall, EU5 HCPs were less inclined to prescribe anti-TNF treatments for WoCBA pts; compared to the other specialists, US RH (43%) had the highest proportion of WoCBA pts prescribed anti-TNFs (EU5 RH: 33%; EU DM: 24%; US DM: 27%; US GI: 31%). However, HCPs' comfort with prescribing anti-TNF treatments consistently declined in both US and EU5 with onset of family planning (figure 1A). EU5 RH (61%) and OB (67%) were more likely to recommend discontinuation of anti-TNFs before conception than US HCPs (RH: 46%; OB: 62%); similarly, >50% EU5 RH and OB agreed that women should stop anti-TNFs post-conception (US RH: 34%; OB: 54%). These findings may be explained by the fact that more US HCPs strongly agreed on making disease control during pregnancy their priority (US RH: 42% vs EU5 RH: 25%) and that controlled disease reduces risk of pregnancy complications (US RH: 42% vs EU5 RH: 28%), as well as the observation that more EU5 RH (34%) than US (12%) were very concerned about adverse events, including infection or poor birth outcomes, in pregnant pts taking anti-TNFs. More EU5 than US RH strongly believed breastfeeding pts should not take anti-TNFs, although a high degree of uncertainty was indicated (figure 1B).



**Figure 1A** HCP level of comfort with anti-TNF treatment prescription for WoCBA patients.

**1B** HCP agreement on discontinuation of anti-TNFs during breastfeeding. HCP: healthcare professional; OB: obstetricians/gynaecologists; pts: patients; RH: rheumatologists; TNF: tumour necrosis factor; WoCBA: Women of Childbearing Age.

**Conclusions:** Our survey demonstrates the variability in confidence in clinical management of women with CID and highlights differences in physicians' attitudes between RH vs OB and EU vs US. Uncertainty and concerns about risks of anti-TNF use during pregnancy and breastfeeding are common, emphasising the need for better information and education of HCPs, especially in Europe, regarding the appropriate use of anti-TNFs during pregnancy and breastfeeding.

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FRI0693

### FEARS AND MISCONCEPTIONS OF WOMEN WITH CHRONIC RHEUMATIC DISEASES ON THEIR JOURNEY TO MOTHERHOOD

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**Background:** Recent EULAR 'Points to Consider' provide guidance on management and treatment of Women of Childbearing Age (WoCBA) with chronic rheumatic diseases (CRD: RA, axSpA, PsA). However, it is still unclear if these patients (pts) feel adequately supported to make informed treatment decisions around pregnancy and breastfeeding.

**Objectives:** To gain insight into perspectives of women with CRD regarding disease management and pregnancy, and assess whether current clinical practice provides adequate support.

**Methods:** WoCBA (aged 18–45 years) from Germany, France, UK, Italy, Spain (EU5), the US and Japan participated in a 20-min online survey (Jul–Oct 2017; InSites Consulting). We report data from pts with moderate-severe CRD who were pregnant or had been pregnant in the past 2–5 years.

**Results:** 622/1052 participants had CRD (RA, n=298; axSpA, n=182; PsA, n=142) and resided in the EU5 (n=306), US (n=293) and Japan (n=23). 87% pts reported having moderate CRD; 49% WoCBA stated that they had actively planned their most recent pregnancy. Fewer than half (46%) of WoCBA visited a healthcare professional (HCP) before pregnancy, of whom 53% consulted a rheumatologist among other HCPs (figure 1A). Although guidelines recommend addressing family planning/pregnancy in women with CRD before conception, 69% pts who visited an HCP before pregnancy had to initiate these discussions with their HCPs. 54% WoCBA admitted delaying their decision to become a mother; their main fear was passing on health issues to their child (figure 1B). 32% pts reported having inadequately controlled disease activity during pregnancy; 51% experienced disease improvement, 22% disease worsening. 82% pts visited an obstetrician/gynaecologist (OB/GYN) across trimesters, 68% a rheumatologist among other HCPs (figure 1A); 65% had a treatment plan aligned between different HCPs. Stopping treatment during pregnancy was largely driven by fear of harming the foetus (78%). Among the 113 pts on anti-TNFs, 22% decided to stop treatment themselves at the start of/during pregnancy, and 47% were advised to stop by their HCP. Although 89% pts reported discussing breastfeeding with an HCP (OB/GYNs were most influential), 66% mothers felt they had to decide between treatment and breastfeeding. While information provided by their HCP was generally satisfactory, pts still felt they lacked information on the impact of treatment decisions on pregnancy (38%) and breastfeeding (24%).

**Conclusions:** Despite current treatment recommendations, WoCBA with CRD continue to have many fears and misconceptions about their journey to motherhood, due to lack of guidance and consistent information regarding family planning, pregnancy and breastfeeding. Survey findings suggest that women's decisions to delay pregnancy and interrupt their treatment may be linked to a need for greater awareness of disease management options to optimise pregnancy outcomes. Access to this information, consultation with specialists and OB/GYNs earlier in the pregnancy planning process, and an aligned treatment plan could help prevent unnecessary decisions.



**Figure 1A)** Obstetricians/gynaecologists are the main healthcare professionals consulted during pregnancy. **1B)** WoCBA with chronic rheumatic diseases are concerned about pregnancy [a] n=622; [b] Multiple answers were possible; n=334. WoCBA: Women of Childbearing Age.

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FRI0694

### TWITTER: A NEW PLATFORM FOR PUBLIC HEALTH CAMPAIGNS: SYSTEMIC LUPUS ERYTHEMATOSUS AND RHEUMATOID ARTHRITIS AS EXAMPLES

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**Background:** Social media is widely used these days and has the capacity to distribute information widely and rapidly to a large audience. Twitter is a popular social network site with hundreds of millions of users and over 500 million Tweets being sent each day. Patients commonly receive information about their condition from social media sites including Twitter. Patient education plays an important role in the management of systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA). The role of Twitter and its present application in SLE and RA patients' education was analyzed.

**Methods:** Twitter advanced search function was used to retrieve all tweets (English language only) containing the words systemic lupus erythematosus, lupus and/or SLE, as well as rheumatoid arthritis over one week (October 23, 2017 to October 29, 2017). Contents of collected tweets were analyzed, and tweets were categorized into 2 groups: general public (editorial/blogging, social/conversational, and advertisement tweets) and professional sources (tweets from physicians, rheumatologists, including hyperlinks to academic publications and websites of professional organizations, and educational tweets by awareness groups).

**Results:** Over the one-week timeframe, a total of 618 tweets mentioned lupus, systemic lupus erythematosus and/or SLE, and a total of 178 tweets mentioned rheumatoid arthritis. In the respective disease groups, tweets assigned to the professional sources category were 32% of the total tweets for SLE (200/618) and 51% for RA (92/178). Tweets sent by physicians constituted 2.6% (21/796) and by rheumatologists 1% (8/796) of the total tweets. Tweets with links to reliable sources (defined as hyperlinks to academic publications, professional organizations and awareness groups) were 23% of the total tweets. Finally, educational tweets by patient advocate groups were 10% of the total tweets.

**Conclusions:** Twitter has the capability of engaging a wide audience in a topic-specific conversation. Thus, it can be used as cost-effective platform for public health campaigns and to distribute evidence-based knowledge to educate patients. At this time, disease-specific search revealed a smaller percentage of content is employed for public health education and awareness. Links to reliable sources were 23% of the total tweets, indicating shortage of contribution from healthcare organizations and professionals. Majority of tweets were in the general public category (including tweets by patients) indicating an audience waiting for professional input. Health advocates should use Twitter to construct public health campaigns. Further research should be conducted to examine approaches to target specific Twitter users that engage in SLE and RA conversations.

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FRI0695

### DMARD MONITORING GUIDELINES AND SHARED PRESCRIBING IN PRIMARY CARE – IS MORE EDUCATION REQUIRED?

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**Background:** DMARDs remain the mainstay of inflammatory arthritis therapy. Though an effective treatment, these drugs have the potential to cause serious harm. Vigilant drug monitoring, reflected in recently updated BSR guidelines, is necessary to prevent potentially life threatening complications. National Patient Safety Agency has also issued several alerts regarding DMARDs and methotrexate overdose remains a 'never event'. Prescribing medications, including DMARDs for rheumatology patients, is one of the chief responsibilities of primary care doctors.



**Objectives:** We undertook a pilot survey of regional GPs to understand their level of prescribing confidence with an aim to develop a targeted teaching program.

**Methods:** Based on BSR DMARD monitoring audit tool and regionally approved shared care guidelines, a focus group discussion with GP educators and CCG Medicine Optimisation Team was organised. Ten items were unanimously identified as core knowledge required for safe prescribing. A questionnaire was created based on these elements. GPs were surveyed at their educational meeting in our academic institution. Replies were compiled to ascertain their understanding of safe prescribing and troubleshooting DMARD related issues.

**Results:** There are 95 actively practicing GPs in the region. 41 (43%) GPs contributed to the survey. 22 (56%) were men. 27 (65%) had been practicing for 5–15 years (range <5 to >20 years). 34 (83%) regularly prescribed DMARDs. Only 15/41 (36%) felt confident in prescribing whereas 7/41 (17%) were neutral and remaining 46% did not feel confident. 49% participants were able to rightly answer questions pertaining to safe prescribing. Again most (70%) felt unable to confidently manage blood-monitoring issues such as neutropenia or abnormal liver function tests. Only four (9%) were able to correctly address the concerns related to administration of live vaccines whilst taking DMARDs. Nine GPs were unaware of avoiding trimethoprim co-prescription with methotrexate.

**Conclusions:** To our knowledge, this is the first survey to demonstrate that there are serious shortcomings in GPs' understanding of safe DMARD prescribing. Lack of confidence amongst front line medical staff remains the main cause of this issue. Despite frequent education bulletins and alerts from national bodies including NICE, BSR and NPSA and active measures taken in recent past to identify better ways to address the concerns, this study highlights major knowledge gaps among everyday prescribers in primary care. Dedicated strategy and better collaboration with GPs, with focus on drug monitoring education, are pivotal to providing better care for patients prescribed DMARDs in the community.

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#### FRI0696 PATIENT ACTIVATION AND ADHERENCE TO BIOLOGICAL THERAPY: PRELIMINARY RESULTS

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**Background:** Medication non-adherence is associated with treatment failure. Some authors show a positive relationship between patient activation and both, adherence to treatment for chronic conditions and improved outcomes.

**Objectives:** To present preliminary results of a study measuring adherence to biological therapy and its relationship with the Patient Activation Measure (PAM) in the outpatient setting.

**Methods:** Ambispective longitudinal observational descriptive study in a general tertiary university hospital.

Patients on treatment with the same biological drug for  $\geq 6$  months were included in order of arrival. Patients with some degree of mental disability, which prevented understanding of the purpose and parameters of the study, were excluded.

Demographic variables (sex, age, environment, educational level), diagnosis and treatment were collected. To measure adherence, the Simplified Medication Adherence Questionnaire (SMAQ), validated in Spain, and the medication possession ratio (MPR) were used. Patients were considered as non-adherent if MPR<80% and/ or non-adherent SMAQ. To measure patient's ability to play an active role in their health care, PAM questionnaire, consisting on 13 items and validated in Spain, was used. It sorts patients into 4 activation levels, which were grouped together into not activated (PAM 1–2) or activated (PAM 3–4). Relationship between adherence to treatment, as a combined variable, and PAM was analyzed using chi-square, considering significance level  $p < 0.05$ . Statistical analysis were performed with spss v17.0.

**Results:** Fifty patients (58% women) were included. Mean age: 48 years (95% CI: 33 to 63); 92% lived in urban areas, 28% completed elementary education, 44% high-school and 28% university studies.

Diagnosis: rheumatoid arthritis (38%), Crohn's disease (20%), psoriasis (20%), ankylosing spondylitis (16%) and psoriatic arthritis (6%). Treatment: adalimumab (44%), etanercept (16%), tocilizumab (16%), secukinumab (12%), ustekinumab (6%), golimumab (4%) and ixekizumab (2%). Median time on the biological drug treatment: 26 months (IQR 53). PAM level: 2, 16, 54 and 28% for levels 1,2,3 and 4, respectively.

Table 1 Global distribution and relationship between adherence and PAM

n(%)	Adherent patients			Total
	SMAQ	MPR	Combined	
	38 (76%)	29 (59%)*	23 (47%)*	
<b>Activated patients</b>				
Yes	32 (78%)	25 (63%)*	20 (50%)*	41 (82%)
No	6 (67%)	4 (44%)*	3 (33%)*	9 (18%)
$\chi^2$ ; p	0,524; 0,668	0,991; 0,456	0,819; 0,472	

\*1 lost patient.

The proportion of adherent patients was 47% (23/49), being higher (50%) among the activated patients compared to the non-activated patients (33%), even though the differences were not statistically significant.

**Conclusions:** Among biologic treated patients, 82% show a high degree of activation on their disease and treatment self-management. However, only 47% were adherent to treatment, when combining the SMAQ questionnaire and the medication possession ratio quantification.

The greater proportion of adherence found among patients with a higher degree of activation could indicate a positive relationship between activation and adherence, so analyzing and promoting patient activation seems important in order to improve adherence to biologic drugs.

**Disclosure of Interest:** None declared

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#### FRI0697 EXPECTATIONS, MOTIVATING FACTORS AND BARRIERS TO BASIC RESEARCH AMONG YOUNG RHEUMATOLOGISTS IN GERMANY– RESULTS OF A NATIONAL ONLINE SURVEY

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**Background:** In Germany, the number of clinical fellows, who decide for a scientific career in basic research, is decreasing, leading to a growing lack of junior physician scientists (PS) highly needed to advance basic research.<sup>1</sup> Structured mentoring and funding programs as well as other incentives might be necessary to attract young physicians and support starting a scientific career in basic science.

**Objectives:** To identify expectations, motivating factors and barriers of final year medical students interested in rheumatology, of fellows and of physicians in rheumatology to start a scientific career in basic research.

**Methods:** An online survey was distributed by email and via facebook and twitter to members of the German Network of Young Rheumatologists (rheumadocs), medical students in their final year participating in a student program of the German Society for Rheumatology (DGRh), and by direct contact to PS. The questions focused on demographics, scientific background (including experience in basic research), expectations such as scientific self-realization, acquirement of a postdoctoral degree, enhanced career options, as well as motivating factors (e.g. "fun", financial benefits, travel bursaries, mentoring programs and others) and barriers (e.g. positions in basic science, exemption from clinical duties, lack of experience and/or assistance in fund-raising and scientific methods) with regard to a career in basic research.

**Results:** Of the 91 responders, 75% was aged below 35 years (11% <25 yrs, 32% 25–29 yrs, 57% >29 yrs) and 58% were female. 19% were currently working in basic research. 23% were students. 35% were fellows currently in the clinic. 23% were primary attendants. Basic research experience was reported by 49% of all clinicians. Only 10% indicated not to be interested in performing basic research. Among the students, 48% were currently performing a laboratory-based medical thesis. Of interest, no substantial differences in expectations or barriers were found between students, PS and clinicians. As to motivational factors, PS named time spent in research accounted for rheumatology training (74%), support by excellence programs (71%) and enhanced career options with a postdoctoral degree (65%) more often than clinicians and students (57%, 50% and 42% respectively). Other common motivational factors were "fun" (76%) and travel bursaries for international meetings (62%). Financial benefits in terms of standard or even senior physician salaries were no major motivators (41% and 24%, respectively). Regarding expectations, 71% indicated scientific self-realization, 58% named enhanced career options. 78% indicated lacking exemption from clinical

duties and lack of experience in fund-raising and scientific methods (58% and 48%) as a barrier for basic research.

**Conclusions:** This study shows a high interest among young rheumatologists and students to work in basic research, and indicates a need for programs, which facilitate the start of a career as physician scientist by providing a general framework with no drawbacks regarding rheumatology specialty training, (at least partial) exemption from clinical duties and support in development of research projects.

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#### FRI0698 SURVEY OF 1,318 PATIENTS ON THEIR KNOWLEDGE OF THE PULMONARY MANIFESTATIONS OF RHEUMATOID ARTHRITIS AND THEIR NEEDS IN TERMS OF INFORMATION AND FOLLOW-UP

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**Background:** Pulmonary involvement is one of the main extraarticular manifestations of rheumatoid arthritis (RA) and can be influenced by the different therapies used to treat RA. In order to detect any pulmonary changes and rapidly institute appropriate care when necessary, the participation of the patient is essential. Patients must report any respiratory symptoms to their doctor who can then adapt the clinical examination and determine the need for additional investigations.

**Objectives:** Evaluate patients' knowledge about the pulmonary manifestations of RA, their follow-up and their needs in terms of information.

**Methods:** A 20 item questionnaire was developed by a group of patients and posted online using Survey Monkey software with a link sent to 6,702 members of the Association Française des Polyarthritiques. Anonymous responses were collected between November 8–23, 2017.

**Results:** 1,318 patients answered the questionnaire (19.7% response rate). Among the 1,297 patients with rheumatoid arthritis (RA): 1,110 were women (86.1%), the mean age was 60.3 years [16–86], 54% (701/1,284) were diagnosed with RA more than 10 years earlier, 76.4% (927/1,213) were on pharmaceutical maintenance treatment and 44.11% (535/1,213) on biologic therapy, and 56% (679/1,213) had received pneumococcal vaccination.

45.5% (552/1212) of respondents did not know that RA could affect the lungs. Among the others, two-thirds (417/659) had been informed of this by their rheumatologist.

39.8% (481/1,209) reported possible respiratory symptoms or dry cough. Among them, 69.1% (188/272) of those who knew that RA could affect the lungs had discussed their symptoms with their rheumatologist, 62.9% (171/272) were referred to a pulmonologist and 83.2% (188/272) were prescribed specific tests (x-ray, CT scan, etc.). Among respondents who did not know that RA could affect the lungs, only 32.8% (67/204) discussed their symptoms with their rheumatologist, 32.4% (66/204) were referred to a pulmonologist and 52.7% (107/207) underwent further tests.

In 44.6% (149/334) of cases, the specific tests revealed lung changes.

86.5% (1016/1,174) of respondents expressed the need to be better informed about the lung manifestations of RA and 60.4% (709/1,174) felt that they did not receive a thorough evaluation of their pulmonary status. Those who were referred to a pulmonologist gave an average score of 5.38/10 for the coordination between rheumatologist and pulmonologist.

Among the solutions proposed, the respondents would find it very appropriate (8 to 10/10): 76.2% (895/1,174) to be informed if they are among those at risk; 74% (869/1,174) to be alerted to symptoms that should prompt them to react; 60% (707/1,174) to benefit from regular monitoring of their respiratory status by the rheumatologist. On the other hand, regular consultation with the pulmonologist was considered very appropriate by only 48% (563/1,174).

**Conclusions:** The rate of participation in this survey illustrates patients' interest and need for information on this subject. The high percentage of patients (45.5%) who had not been informed about the risks of RA-related pulmonary involvement proves that there is room for improvement in patient education so that patients can be able and aware of how to detect any symptoms that need to be brought to the attention of their rheumatologist.

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#### FRI0699 RHEUMATOLOGY TALKS TO THE COMMUNITY: RESULTS OF AN EDUCATIONAL INTERVENTION

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**Background:** Rheumatology is a relatively new medical specialty, and mostly unknown to the general population. Thanks to close collaboration between rheumatologists and primary care physicians (PCP), and the availability of revolutionary drugs in the last decades, it has become a fundamental part of the management of patients with musculoskeletal disorders.

Besides information to PCP, it is equally important that the population is aware of what rheumatology is, and the diseases it treats. We decided to inform the population about the most prevalent disorders: osteoarthritis (OA), osteoporosis and gout, through talks in both urban and rural settings.

**Objectives:** To evaluate the short-term acquired knowledge after rheumatology talks in people from the general population.

**Methods:** Through a consulting firm, informative talks were offered in different city councils. They were finally conducted in 5 urban and rural towns between March 2016 and January 2017. The activity dissemination was in charge of each council and offered to the whole community.

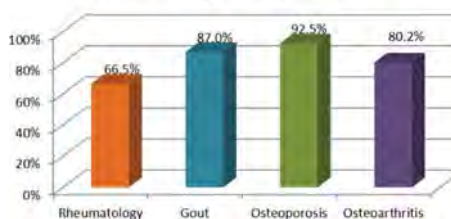
Each talk lasted about 1.5 hours: a theoretical part in both co-official languages during 60 minutes, with some questions from the audience afterwards, as well as the completion of a 6-multiple choice-question survey evaluating some concepts from the talk. Topics included were: an explanation of what is rheumatology, and general aspects of OA, osteoporosis and gout. The answers to the survey were classified as correct and incorrect.

**Results:** 94.3% of the audience answered the survey. A total of 174 surveys from 5 towns were recovered. There was a higher participation from urban locations (40.2% of the total attendance). Despite being an educational activity for the whole community, the audience was mostly female (90.3%), with a median age of 69 years (IQR 63 to 74 years). Regarding language, 13.2% of attendees answered the survey in the other language.

Concerning the topics, 66.5% answered correctly about the definition of rheumatology and 87% about foods to avoid in gout. OA and osteoporosis had two questions each, with 92.5% of correct answers in the former and 80.2% in the latter. Osteoporosis recorded the highest percentage of correct answers within the survey (96.9%), in a question related to calcium-rich foods.

When comparing rural and urban locations, there were only statistically significant differences in the question related to gout, with a greater percentage of correct answers amongst attendees of rural towns (94.7 vs 75.8% respectively).

#### Percentage of correct answers in community survey after talk



**Conclusions:** According to our results, Rheumatology talks seem to be more attractive to elderly female population.

Knowledge acquired after talks has been good for OA and osteoporosis, both being prevalent conditions in this group of patients. We believe it is important to encourage rheumatology-related educational activities for the general population, and that these activities should be adjusted to the demographic characteristics of the focus group.

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FRI0700

### PATIENTS AND RELATIVES COPING WITH INFLAMMATORY ARTHRITIS: A TEAM WORK

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**Background:** Adjustment to inflammatory arthritis (IA) is complex for the patient but also for the relative and there is room for improvement in the support provided to the dyad

**Objectives:** to explore patients and relatives experience of IA, their difficulties, mutual expectations, communication, coping strategies and needs

**Methods:** Participants were recruited by 7 rheumatologists during their consultations. Eligibility criteria were: having a rheumatoid arthritis (RA) or a spondyloarthritis (SpA). Relatives were invited to participate by the patients. Face to face interviews with the dyad were conducted by 3 psychologists with an interview guide built by the project working group. A thematic analysis was conducted by 2 psychologists, following a general inductive approach

**Results:** 20 patients and their relative (18 partners, 1 mother, 1 friend) were included: 13 RA and 7 SpA, median disease and couple duration 10 (range 1–36) and 28 years (range 1.5–57). The analysis revealed 4 main themes: disease leaved together, impact of the disease on the relationship, social impact of the disease on the dyad, difficulties and needs of the relative. Disease leaved together: dyads explained the new roles of the relative: providing material help, understanding and emotional support, acting as a driving force, take part of medical care (medical decisions, support in adhesion, searching for information). Communication around the disease is an important theme; reasons to avoid talking about the disease were: not focusing on the disease, respecting the need to be alone, words are not always needed. For other dyads, talking about the disease allows for improving knowledge about the disease or for security reasons. Impact of the disease on the relationship: if they do not feel the IA has changed their relationship, they acknowledged some tensions because of the disease: disease get too much attention in their relationship, lack of communication create tensions. Social impact of the disease on the dyad: social isolation was highlighted: patients need sometimes to be alone, invisibility of the disease creates misunderstandings, people around don't realize what it means to live with IA. Unpredictability of the symptoms makes it difficult to organize everyday life and to have projects. Difficulties and needs of the caregiver were rarely raised when the dyads were interviewed together: sometimes disease is not well accepted by the caregiver, not being able to help is frustrating, finding the right way to help is difficult. Knowledge of the disease and the patient symptoms are important needs expressed by the caregiver

**Conclusions:** The current qualitative study offers new insights into the perception of patient and relative of their shared life with the disease and is a first step to develop interventions to support them. This study has highlighted the importance of the recognition of the role of the relative in the disease management. Joint approach to treatment is a basis for coping with the disease. This supposes: 1) a good understanding of one another, which can be improved by providing information on the disease, its symptoms and coping strategies to both the patient and the relative 2) shared determination of relative roles 3) good communication skills

**Disclosure of Interest:** None declared

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FRI0701

### FRENCH SPECIALISTS AND IMMUNE-RELATED ADVERSE EVENTS OF CANCER IMMUNOTHERAPY: A STATE OF THE ART FROM SEVERAL NATIONAL EXPERT NETWORKS.

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**Background:** Immunotherapeutic strategies with immune checkpoint inhibitors (ICI) are now commonly used in treating patients with advanced-stage cancer. An important proportion of patients experiences inflammatory or autoimmune side

effects, also known as immune-related adverse events (irAEs), as a consequence of dysregulated immunity which can affect any organ system (1). A recent survey conducted by our colleagues from United States highlighted that rheumatologists had limited experience and lacked confidence in the management of rheumatic irAEs (2).

**Objectives:** To evaluate the knowledge of French specialists regarding ICI and irAEs through an online survey.

**Methods:** The online survey has been sent in January 2018 to several French national expert networks: Société Française de Rhumatologie (SFR), Club Rhumatismes et Inflammations (CRI), Société Nationale de Médecine Interne (SNFMI), Groupe d'Etude Thérapeutique des Affections Inflammatoires du Tube Digestif (GETAID) and Société Française d'Endocrinologie (SFE).

**Results:** 349 French specialists participated to this study: rheumatologists (n=159), internists (n=112), endocrinologists (n=55), gastroenterologists (n=22) and one respiratory physician. As detailed in table 1, participants were mainly working in academic or hospital with various levels of experience in clinical practice. Overall, half of the specialists reported some basic knowledge of ICI and irAEs. Around 25% either have never heard about these therapies and their side effects or were not knowledgeable. The majority of the participants has never or rarely managed irAEs (31% and 40% respectively), and only 11% declared being very confident in treating such patients. The type of content requested for education was mainly about treatment algorithms (80%) followed by clinical description of irAEs (59%) then general information on ICI (mechanism of action, administration, efficacy).

Table 1 Demographics and knowledge of ICI and irAEs among french specialists, n (%)

	Rheumatologists (n=159)	Internists (n=112)	Endocrinologists (n=55)	Gastroenterologists (n=22)	Pulmonologist (n=1)	Total (n=349)
<b>Gender</b>						
Male	81 (51)	72 (64)	13 (23)	11 (50)	0 (0)	184 (53)
Female	78 (49)	40 (36)	37 (67)	9 (41)	1 (100)	165 (47)
<b>Practice setting</b>						
Academic hospital	54 (34)	57 (51)	21 (38)	13 (60)	0 (0)	147 (42)
Non-academic hospital	29 (18)	38 (34)	14 (26)	5 (23)	0 (0)	86 (25)
Private practice	41 (26)	9 (8)	9 (16)	1 (4.5)	0 (0)	60 (17)
Mixed (private & hospital)	32 (20)	5 (4)	10 (18)	1 (4.5)	1 (100)	49 (14)
Residents / in training	3 (2)	3 (3)	1 (2)	0 (0)	0 (0)	7 (2)
<b>Years of medical practice</b>						
< 10	41 (26)	39 (35)	13 (24)	8 (36)	0 (0)	101 (29)
10-20	45 (28)	37 (33)	14 (26)	10 (45.5)	1 (100)	107 (31)
20-30	38 (24)	21 (19)	15 (26)	3 (14)	0 (0)	77 (22)
> 30	35 (22)	15 (13)	13 (24)	1 (4.5)	0 (0)	64 (18)
<b>Knowledge of ICI</b>						
None	5 (3)	3 (3)	1 (2)	2 (9)	0 (0)	11 (3)
I have heard of ICI	49 (31)	25 (22)	9 (16)	2 (9)	0 (0)	85 (24)
Some basic knowledge	72 (44)	62 (55)	28 (51)	12 (55)	1 (100)	172 (49)
Familiar	27 (17)	15 (13)	12 (22)	7 (32)	0 (0)	61 (18)
Very familiar	7 (5)	8 (7)	5 (9)	0 (0)	0 (0)	20 (6)
<b>Knowledge of irAEs</b>						
None	14 (9)	9 (7)	3 (5)	2 (9)	0 (0)	27 (8)
I have heard of irAEs	30 (19)	21 (19)	6 (11)	1 (4.5)	0 (0)	58 (17)
Some basic knowledge	72 (45)	56 (50)	23 (42)	9 (41)	1 (100)	161 (46)
Familiar	31 (19)	17 (15)	17 (31)	7 (32)	0 (0)	72 (20)
Very familiar	12 (8)	10 (9)	6 (11)	3 (13.5)	0 (0)	31 (9)
<b>Management of patients with irAEs</b>						
Never	58 (36)	40 (36)	5 (9)	6 (27)	0 (0)	109 (31)
Maybe, but I didn't link symptoms with ICI	15 (10)	7 (6)	4 (7)	0 (0)	0 (0)	26 (8)
Rarely	64 (40)	44 (40)	22 (40)	9 (41)	1 (100)	140 (40)
Several times (> 5 patients)	17 (11)	16 (14)	12 (22)	5 (23)	0 (0)	50 (14)
Frequently (>10 patients)	5 (3)	5 (4)	13 (22)	2 (9)	0 (0)	24 (7)
<b>Level of confidence</b>						
I don't know the topic	21 (13)	6 (6)	5 (9)	2 (9)	0 (0)	34 (10)
Not confident	28 (18)	29 (26)	7 (13)	3 (14)	1 (100)	68 (19)
Somewhat confident	32 (20)	35 (31)	13 (24)	3 (14)	0 (0)	83 (24)
Moderately confident	68 (42)	34 (30)	17 (31)	10 (45)	0 (0)	128 (36)
Very confident	13 (8)	8 (7)	13 (24)	4 (18)	0 (0)	38 (11)

**Conclusions:** Since there has been an increasing emphasis on irAEs within the last three years, we confirmed the need of a dedicated medical education regarding this new clinical entity.

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SATURDAY, 16 JUNE 2018

**Innate immunity in rheumatic diseases**

SAT0001

**MECHANISM AND SIGNIFICANCE OF COMPLEMENT C3 RECEPTOR IN COLLAGEN-INDUCED RHEUMATOID ARTHRITIS MICE MODEL**

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**Background:** Rheumatoid arthritis (RA) is a kind of chronic autoimmune disease, mainly manifested as small joint synovitis. Disease progression appears joint swelling, bone and cartilage damage, deformity and activity limited. The etiology of RA is still unclear and is generally considered to be an immune-mediated inflammatory disease. The activation pathway and regulation function of the complement system have become the hotspot of the research of RA pathogenesis. Previous studies have found that C3<sup>-/-</sup> mice had lower levels of antibodies to collagen in the Type II collagen-induced rheumatoid arthritis (CIA model), and the molecular mechanism is unclear. The small fragment C3a and large segment iC3b produced by C3 activation are the main effect products, and their biological effects are performed by combining with the specific receptor, C3aR and CD11b respectively.

**Objectives:** To investigate the mechanism of C3a and C3b, the cleavage products of complement C3 in rheumatoid arthritis, binding to their corresponding receptors, the signalling pathway of complement activation and the effect on arthritic conditions.

**Methods:** This study was intended to establish a CIA model on C3aR knockout and CR3 knockout mice (C3aR<sup>-/-</sup> or CD11b<sup>-/-</sup>) to investigate the effect of complement C3a-C3aR signalling and iC3b-CR3 signalling on rheumatoid arthritis. Methods using C57BL/6 background transgenic mice (Gifted by King's College London), Mice were divided into 3 groups according to the experimental mouse strains: C3aR<sup>-/-</sup> group, CD11b<sup>-/-</sup> group and WT control group. The clinical score of the joints in each group was measured after the establishment of the CIA model through collagen induction. Moreover, joint specimens were collected for pathologic grading. Besides, the level of CD4<sup>+</sup>T cell, CD8<sup>+</sup>T cell, Th17/Treg ratio and the level of IFN-gamma of NK cell in mouse spleen were detected by flow cytometry.

**Results:** 1. The clinical score of C3aR<sup>-/-</sup> group was slightly lower than that of WT group, and the clinical score of CD11b<sup>-/-</sup> group was significantly higher than that of WT group; 2. Pathological score (12 points): The CIA scores of CD11b<sup>-/-</sup> group, C3aR<sup>-/-</sup> group and WT group were 9.35±0.75, 4.81±0.63 and 5.85±0.55 respectively. The CIA scores of CD11b<sup>-/-</sup> group was significantly higher than that of WT group, which were consistent with clinical score; 3. Through the flow cytometry detection, compared with the WT group, CD4<sup>+</sup>T cell, CD8<sup>+</sup>T cell and Th17 percentage increased significantly, and Treg cell decreased. In addition, the secretion of IFN-gamma of Splenic NK cell was significantly reduced.

**Conclusions:** iC3b as well as C3a could bind to their respective complement receptor, and express different influence in the immune mechanism of RA, The iC3b-CD11b signalling has a protective effect in RA, while the C3a-C3aR signalling has an inflammatory aggravation effect. Through this study, it helps us to invent the drug related to complement components and their receptors, and further be used in the clinical treatment of RA.

**Disclosure of Interest:** None declared

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SAT0002

**THE INTRACELLULAR ITAM TYROSINES OF FC RECEPTOR GAMMA-CHAIN ARE CRITICAL FOR EXPERIMENTAL AUTOIMMUNE ARTHRITIS**

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**Background:** Activating Fc $\gamma$ -receptors on neutrophils associate with the Fc-receptor  $\gamma$ -chain (FcR $\gamma$ ), an immunoreceptor tyrosine-based activation motif (ITAM) containing transmembrane adapter molecule. Previously, we carried out *in vitro* experiments that showed not only a chaperon-like function of FcR $\gamma$ , but also a signalling role through its intracellular ITAM-tyrosines.

**Objectives:** Here, we investigated the participation of these tyrosines in an auto-antibody-induced arthritis model (in the KBxN serum transfer arthritis, for the

development of which neutrophils and Fc-receptors are essential) using wild type and ITAM tyrosine mutant (Y65F/Y76F) transgenic mice.

**Methods:** The experimental animals expressed wild type or ITAM tyrosine mutant (Y65F/Y76F) Fc-receptor  $\gamma$ -chain on the FcR $\gamma$ <sup>-/-</sup> genetic background. The arthritis was initiated by a single intraperitoneal injection of control or arthritic serum. The severity of joint inflammation was followed by clinical scoring, measuring ankle thickness changes and detecting joint dysfunction. Homozygous transgenic mice were identified by quantitative PCR.

**Results:** Compared to wild type mice, FcR $\gamma$  knockout animals failed to exhibit a measurable joint inflammation. Surprisingly, the arthritis could not develop in wild type FcR $\gamma$  transgene heterozygous mice. To enhance the expression level of the wild type transgene (which was approximately one third of the expression of the mutant transgene), we crossed our wild type transgene heterozygous mice with each other. As a consequence, wild type FcR $\gamma$  transgene homozygous mice on the  $\gamma$ -chain knockout background were able to undergo arthritic development. In contrast, FcR $\gamma$  knockout mice carrying the ITAM-mutant FcR $\gamma$  transgene (both at heterozygous and homozygous forms) were fully protected from the development of arthritis despite of comparable neutrophil cell surface Fc $\gamma$  receptor expressions.

**Conclusions:** Our *in vivo* experiments show that the intracellular Fc receptor  $\gamma$ -chain ITAM tyrosines play a critical role in the initiation and progression of an auto-antibody-induced experimental arthritis model, confirming a signalling, rather than just a chaperon-like function of the molecule.

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**Disclosure of Interest:** None declared

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SAT0003

**SYNOVIAL TISSUE CD1c+ DENDRITIC CELLS IN RHEUMATOID ARTHRITIS EXPRESS HIGH LEVELS OF THE EPIGENETIC REGULATOR OF INFLAMMATION, MICRORNA-155 AND INFLAMMATORY CYTOKINES**

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**Background:** Dendritic cells (DCs) direct the immune response against pathogens while maintaining self-tolerance by instructing T/B cells in lymphoid organs and peripheral tissues. However, their aberrant activation can lead to chronic inflammation and autoimmunity. Based on the distinct transcriptomics, function and distribution, DCs can be broadly categorised as plasmacytoid and myeloid (conventional) DCs. Based on recent single cells sequencing and secretome data, can be divided into CD141<sup>+</sup> DCs (DC1), DC2\_A (DC2) defined as "CD1c<sup>high</sup>CD32B<sup>high</sup>CD36<sup>neg</sup>CD163<sup>neg</sup>" and DC2\_B (DC3) defined as "CD1c<sup>low</sup>CD32B<sup>neg</sup>CD163<sup>high</sup>CD36<sup>high</sup>." In addition, populations of CD1c<sup>+</sup>CD141<sup>+</sup>CD16<sup>+</sup> DC (named DC4), that shares some gene expression with CD16<sup>+</sup> monocyte and inflammatory DC (infDC). Most to date studies on Rheumatoid Arthritis patients investigated DCs in circulation or in synovial fluid (SF). This provided important insight into epigenetic changes in DC-precursors before they enter synovial tissue, e.g. RA blood CD1c<sup>+</sup> have deregulated microRNA-34a driven epigenetic control of anti-inflammatory Axl pathway<sup>2</sup> or into the influence of inflammatory milieu on DCs, respectively. However, neither (peripheral blood) PB or SF are major sites for DC regulated T/B cell activation; instead, DCs control immune responses in the appropriate structures of lymphoid organs and tissues.

**Objectives:** In this study, we sought to investigate myeloid DCs in synovial tissue with the prospect of better understanding their role in driving autoimmunity in RA.

**Methods:** We developed a flow cytometry sorting strategy to characterise the phenotype of distinct myeloid DC subsets in multiple biological compartments (PB, SF and synovial tissue). Synovial tissue (ST) biopsies (RA n=9; Psoriatic arthritis n=3) were digested with liberase prior the analysis. Peripheral blood DCs (RA n=19, Psoriatic arthritis n=16, healthy donors n=12), and SF DC (n=3) were used as comparators. Synovial tissue, SF and PB DCs were sorted and micro-RNAs, pro-inflammatory and regulatory cytokine expression analysed by amplified qPCR. In addition, DCs were mapped in synovial tissue in RA (n=8), PsA (n=7) and control non-inflammatory OA (n=5) by immunohistochemistry.

**Results:** Myeloid DCs are scarce in control non-inflammatory OA synovial tissues and their number increased substantially in PsA and RA tissues. Phenotyping data revealed that all myeloid DC subsets can be present in inflamed RA and PsA synovium. However, CD1c<sup>+</sup> DC populations (DC2/DC3) were the most abundant in RA synovial tissues and the gene expression analysis of CD1c<sup>+</sup> sorted from RA synovial biopsies showed an increase in the expression of epigenetic regulator of inflammatory response miR-155 and IL-6, TNF and IL-23 as compared to circulating cells.

**Conclusions:** CD1c<sup>+</sup>DCs from RA synovial tissues had epigenetically regulated activated phenotype (miR-155 and miR-34a<sup>2</sup>) that through the production of cytokines could maintain tissue activation of autoreactive Th1 and Th17 cells and contribute to inflammation.

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**Disclosure of Interest:** None declared

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#### SAT0004 INTRA-ARTICULAR INJECTION OF ADIPOSE-DERIVED MESENCHYMAL STROMAL CELLS REDUCE EXPERIMENTAL OA PATHOLOGY VIA IL-1B-MEDIATED REALLOCATION AND ENHANCED PHAGOCYTOSIS OF POLYMORPHONUCLEAR LEUCOCYTES

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**Background:** Injection of adipose-derived mesenchymal stromal cells (ASCs) into knee joints after induction of experimental inflammatory osteoarthritis (CiOA) reduces development of joint pathology.<sup>1</sup> This protection is only achieved when ASCs are applied in early CiOA, which is characterised by synovitis and high levels of S100A8/A9 and IL-1 $\beta$ , suggesting that inflammation boosts the protective effect of ASCs.<sup>2</sup>

**Objectives:** To examine the role of synovitis in ASC-mediated amelioration of CiOA pathology.

**Methods:** CiOA was induced by intra-articular collagenase injection. Knee joint sections were stained with haematoxylin/eosin and immunolocalization of polymorphonuclear leucocytes (PMNs) and ASCs was performed using antibodies for NIMP-R14 and CD271, respectively. Chemokine expression induced by IL-1 $\beta$  or S100A8/A9 was assessed with qPCR and Luminex. Migration of PMNs through transwell membranes towards ASC-conditioned medium (CM) was examined using flow cytometry. ASC-PMN co-cultures were analysed microscopically and with Luminex. Phagocytic capacity of PMNs was measured with labelled zymosan particles.

**Results:** Intra-articular injection of saline in knee joints of day 7 CiOA induced a flare already after 6 hours, characterised by particularly PMNs scattered throughout the synovium. Although ASC injection resulted in comparable numbers of PMNs, these cells however, were clustered around ASCs. IL-1 $\beta$ -stimulation of ASCs *in vitro* strongly increased expression of PMN-attracting chemokines KC, CXCL5, and CXCL7, whereas S100A8/A9 did not. Migration of PMNs towards CM of IL-1 $\beta$ -stimulated ASCs (IL-1 $\beta$ -CM) was significantly enhanced (2.9-fold increase) when compared to CM of non-stimulated ASCs (NS-CM). After 6 hours co-culturing PMNs with IL-1 $\beta$ -stimulated ASCs, the number of clustered PMNs per ASC was significantly increased. Interestingly, association of PMNs with ASCs significantly diminished the release of KC protein by ASCs (69% lower after 24 hour), and also strongly reduced the release of S100A8/A9 protein by the PMNs. Moreover, phagocytic capacity of PMNs was strongly enhanced after priming with CM of IL-1 $\beta$ -stimulated ASCs.

**Conclusions:** Local application of ASCs in inflamed CiOA knee joints results in attraction and clustering of PMNs with ASCs in the synovium, which is likely mediated by IL-1 $\beta$ -induced up-regulation of chemokine release by ASCs. This results in lowered S100A8/A9 levels and enhanced phagocytic capacity of PMNs, enabling the clearance of debris to attenuate synovitis and promote tissue repair.

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reflected by S100A8/A9 serum levels. *Osteoarthritis Cartilage* 2014 Aug;22(8):1158–66.

**Disclosure of Interest:** None declared

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#### SAT0005 INTERLEUKIN-33 AMELIORATES MURINE LUPUS VIA INDUCTION OF REGULATORY T CELLS AND M2 MACROPHAGE POLARISATION

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**Background:** The levels of IL-33, a Th2 promoting cytokine, and the soluble form of its receptor ST2 were reported to be elevated in serum of patients with active systemic lupus erythematosus (SLE), suggesting a role of the IL-33/ST2 axis in the pathogenesis of SLE.

**Objectives:** This study aims to examine the effect of IL-33 in disease severity of murine lupus.

**Methods:** IL-33 was injected intraperitoneally 3 times per week to pre-diseased MRL/lpr mice aged 12 weeks for 6 weeks. Control group was given 1% BSA injection. Urine protein was monitored weekly by albustix and protein assay. Immunophenotyping of splenocytes was examined by flow cytometry. Splenic CD11b<sup>+</sup> monocytic cells were isolated by microbeads for mRNA examination.

**Results:** IL-33-treated mice (n=9) developed significantly less proteinuria compared to BSA-treated group (n=9). Kidney histology of the IL-33-treated group showed remarkably less mesangial deposit, diffuse proliferative glomerular changes and crescents, and had significantly lower renal composite score compared to controls (median 2.0 vs 9.9, p<0.001). Kidneys of these mice expressed lower mRNA levels of TNF- $\alpha$  (32.1 $\pm$ 14.7 vs 77.0 $\pm$ 27.8, p<0.001), IL-6 (median 0.6 vs 4.7, p=0.003), IL-1 $\beta$  (31.1 $\pm$ 10.1 vs 77.8 $\pm$ 24.6, p<0.001) and iNOS (p=0.006). Immunophenotyping of splenocytes showed significantly increased CD4<sup>+</sup>CD25<sup>+</sup>regulatory T (Treg) cells (4.0% $\pm$ 1.2% vs 2.2 $\pm$ 0.2%, p<0.001) that expressed remarkably higher Foxp3 (76.0% $\pm$ 5.0% vs 59.3 $\pm$ 12.6%, p=0.002). Splenic extracts showed predominant Gata3 (0.37 $\pm$ 0.20 vs 0.12 $\pm$ 0.09, p=0.01) and Foxp3 (0.42 $\pm$ 0.16 vs 0.17 $\pm$ 0.11, p=0.002) mRNA in IL-33-treated mice. These Treg cells expressed high cell surface ST2 (8.9% $\pm$ 2.7% vs 4.5 $\pm$ 2.0%, p=0.008). There was significant expansion of splenic CD11b<sup>+</sup> population in IL-33-treated mice (17.8 $\pm$ 10.5 vs 8.8 $\pm$ 3.0, p=0.01) that expressed significantly higher CD206 (5.2% $\pm$ 0.9% vs 2.9 $\pm$ 0.9%, p=0.002). Isolated splenic CD11b<sup>+</sup> cells expressed significantly higher mRNA of Arg1, FIZZ1 and Ym-1 and IL-10 (all p=0.01) with reduced expression of iNOS (p=0.02). Kidney extracts of IL-33 treated mice also had elevated mRNA levels of M2 markers including Arg1 (median 199.8 vs 36.1, p=0.004) and FIZZ1 (median 25.0 vs 2.7, p<0.001) and reduced MCP-1 (12.7 $\pm$ 6.5 vs 35.1 $\pm$ 12.0, p<0.001). There was also significantly higher levels of mRNA of Foxp3 (median 43.0 vs 20.8, p=0.006) and Gata 3 (1.7 $\pm$ 0.5 vs 0.9 $\pm$ 0.5, p=0.008) but lower Rorc (2.6 $\pm$ 1.0 vs 3.8 $\pm$ 0.8, p=0.008) and Tbx21 (12.6 $\pm$ 6.0 vs 29.6 $\pm$ 13.7, p=0.003) in the kidneys.

**Conclusions:** Exogenous IL-33 led to significantly less proteinuria and renal inflammation. These mice had significantly higher splenic Treg cells with prominent Foxp3 expression. Isolated CD11b<sup>+</sup> cells from spleen and kidney extracts demonstrated mRNA levels of M2 macrophage polarisation.

**Disclosure of Interest:** None declared

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#### SAT0006 P2X7 RECEPTOR IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE). EXPLORING A NOVEL PATHOGENETIC PATHWAY IN LUPUS RELATED SEROSITIS

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**Background:** Recent studies have focused attention on the involvement of innate immunity and in particular on the activation of NLRP3 inflammasome by purinergic signalling mediated by P2  $\times$  7 receptor (P2  $\times$  7R), in SLE pathogenesis.<sup>1</sup> Serositis are typical SLE manifestations often associated with increased inflammatory indices and promptly responding to colchicine whose action could be mediated by its effect on microtubules during P2  $\times$  7R assembly.

**Objectives:** To explore the role of innate immune system in SLE evaluating expression and activity of P2  $\times$  7R and NLRP3, comparing patients with positive and negative history of serositis with healthy control subjects (HC).

**Methods:** We studied SLE patients with (LS) or without (LN) history of serosites and HC matched for sex and age. Demographic, clinical, therapeutic and clinimetric data were retrospectively collected. After isolation of peripheral blood mononuclear cells (PBMCs) from whole blood by centrifugation on Ficoll gradient, P2 x 7R and NLRP3 expression were evaluated by RT-PCR analysis while activity was analysed after stimulation with BzATP (P2 x 7R agonist), by measuring intracellular calcium changes using Fura2-AM fluorescent probe. Finally *in vitro* IL-1 $\beta$  and IL6 production by short term cultured PBMCs (in RPMI and after stimulation with either LPS or BzATP or BzATP +LPS), and IL-1 $\beta$  and IL6 plasma levels were evaluated by ELISA.

**Results:** 30 HC and 31 patients were enrolled: 13 (40,6%) LS vs 18 (59,4%) LN. 30 were female. No significant differences about demographic, disease activity and serological features were found between LS and LN and almost all patients were taking low dose steroids and immunomodulatory therapy (table 1). No significant difference in plasmatic levels of IL-1 $\beta$  and IL-6 were found between SLE and HC also considering separately the LS group. RT-PCR analysis of PBMC from SLE subjects showed reduced P2 x 7 and slightly augmented NLRP3 expression. *In vitro* IL-1 $\beta$  release was diminished in SLE patient (both LS and LN) respect to HC (especially comparing LN vs HC) while IL-6 levels appeared to be higher in SLE patients (especially LN) (table 2).

Abstract SAT0006 – Table 1. Clinical features of SLE patients (LS vs LN)

	LS (13)	LN (18)	P
Age (95% CI)	43 (35,8-50)	40 (35,0-44,2)	0,68
Disease duration (months) (95% CI)	143,5 (82,9-200,2)	107,1 (62,7-151,5)	0,31
SLEDAI 2K (95% CI)	5,2 (2,0-8,3)	3,9 (1,4-6,8)	0,34
ECLAM (95% CI)	1,3 (0,2-2,6)	1,6 (0,4-2,8)	0,68
SIJCC (95% CI)	0,8 (0,3-1,4)	0,5 (0,05-0,8)	0,19
ANTI DNA positivity (n%)	13 (100%)	15 (83,3%)	0,49
Low levels of Complement C3 and C4 (n%)	10 (76,9%)	6 (33,3%)	0,03
VES mm/h (95% CI)	15 (12-18)	18 (11-24)	0,37
RCP mg/dl (95% CI)	0,77 (0,13-1,14)	0,47 (0,08-0,56)	0,24
Ongoing immunosuppressive drugs n(%)			
Hydroxychloroquine	10 (76,9%)	14 (77,8%)	1
Azathioprine	2 (11,1%)	2 (15,4%)	1
Mycophenolate mofetil	1 (7,7%)	3 (16,7%)	0,62
Cyclosporine	0	1 (5,6%)	1
Rituximab	0	1 (5,6%)	1
Belimumab	1 (7,7%)	0	0,42
Methotrexate	2 (20%)	1 (6,3%)	0,54
Steroids ongoing (n%, dosage)	12 (92,3%)	13 (72,2%)	0,35
Cumulative steroid gr (95% CI)	25,4 (12,6-38,2)	14,1 (6,2-22)	0,09

Abstract SAT0006 – Table 2. activity of P2X7 in HC vs SLE

	HC	LS	LN	p (HC vs LS)	p (LS vs LN)	p (HC vs LN)
IL-1 $\beta$ plasma levels pg/ml, mean (SD)	7,1(10,0)	7,0(10,7)	1,7(6,1)	0,96	0,08	0,19
IL-6 plasma levels pg/ml, mean (SD)	0,52 (1,0)	0,50 (0,4)	0,76(0,5)	0,90	0,47	0,63
Basal Ca2+ (Fura2) nM mean (SD)	308(11,1)	305,1(11,4)	303,6(10,7)	0,86	0,35	0,74
BzATP (Fura2) nM mean (SD)	279,2(10,7)	287,4(10,3)	281,0(10,7)	0,002	0,01	0,01
Stimulant's dosage of IL-1 $\beta$ produced by PBMC (300 000 cells) pg/ml, mean (SD)						
IFN $\gamma$	0,1(0,3)	0,1(0,1)	0,1(0,1)	1,00	1,00	0,01
LPS	0,1(0,1)	0,1(0,1)	0,1(0,1)	0,01	0,001	0,001
LPS+BzATP	0,1(0,1)	0,1(0,1)	0,1(0,1)	0,001	0,001	0,001
BzATP	0,1(0,1)	0,1(0,1)	0,1(0,1)	0,001	0,001	0,001
Stimulant's dosage of IL-6 produced by PBMC (300 000 cells) pg/ml, mean (SD)						
IFN $\gamma$	1,1(4,3)	1,1(3,0)	1,1(3,0)	0,01	0,01	0,01
LPS	0,1(0,1)	0,1(0,1)	0,1(0,1)	0,01	0,01	0,01
LPS+BzATP	0,1(0,1)	0,1(0,1)	0,1(0,1)	0,01	0,01	0,01
BzATP	0,1(0,1)	0,1(0,1)	0,1(0,1)	0,01	0,01	0,01
RT-PCR P27R mean (SD)	1,2(1,3)	1,0(1,0)	0,9(0,9)	0,12	0,40	0,30
RT-PCR NLRP3 mean (SD)	2,1(1,1)	1,0(1,0)	0,9(0,9)	0,01	0,01	0,01

**Conclusions:** P2 x 7R expression and activity appeared to be reduced in SLE compared to HC as demonstrated by evaluation of intracellular calcium changes and IL-1 $\beta$  levels produced by PBMC. Conversely, IL-6 was released at higher levels from PBMC of patients compared to HC, thus suggesting that production of this cytokine could be mediated by another pathway (possibly TLR pathway<sup>2</sup>). Other P2 x 7 dependent responses, such as pyroptosis or T and B lymphocyte functions, need to be investigated. Overall, these preliminary results suggest that P2 x 7R and inflammasome activation do not seem to be the main pathogenetic pathway in SLE patients with history of serositis.

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**Disclosure of Interest:** None declared

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**SAT0007 DISTINCT MACROPHAGE PHENOTYPE AND BIOENERGETIC PROFILES IN RHEUMATOID ARTHRITIS**

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**Background:** Diversity of macrophage subsets within the joint remains unknown. The concept of macrophage polarisation into M1 inflammatory macrophages and M2 tissue-resolving macrophages, paralleled by changes in the bioenergetic cell profile, has received much attention. Hence, we aimed to examine the phenotype of macrophages within the inflamed RA joint, along with the metabolic and inflammatory capacity of RA monocyte-derived macrophages compared to healthy individuals.

**Objectives:** To examine the phenotype, metabolic and inflammatory profile of pro-inflammatory and anti-inflammatory macrophages within the inflamed RA joint.

**Methods:** Blood obtained from healthy and RA donors, CD14 +cells sorted and differentiated into macrophages for 8 days. Macrophages were polarised to either M1 (LPS and IFN $\gamma$ ) or M2 (IL-4). Markers of polarisation, metabolism and inflammation were quantified by Real Time-PCR. Seahorse technology measured the major energy-using pathway, oxidative phosphorylation (OCR). Finally, synovial tissue (ST) was digested to yield a single cell suspension, this was then stained using a panel of fluorochrome antibodies (CD45, CD40, CD68, CD64, CD163, CD206, CD253), and subsequently analysed using FlowJo software.

**Results:** M1 macrophages were confirmed by increased expression of KLF6 while M2 macrophages expressed high TGM2, PPARG and STAB1. M1 cells had significantly higher expression of pro-glycolytic genes (HIF1 $\alpha$ , HK2, LDHA, PFKFB3 and PKM2), which were deficient in M2 macrophages and higher compared to healthy control. This was paralleled by higher pro-inflammatory cytokines levels (IL-8, OSM, MCP-1, RANTES IRAK-1, CCR5 and SOCS3) in M1 vs M2 macrophages, with RA derived macrophages showing higher expressions of pro-inflammatory mediators compared to healthy control. G6PD, PHD3 and PDK1/2 were significantly decreased in M1 yet increased in M2 macrophages, and along with this seahorse technology demonstrated that M2 macrophages have higher baseline OCR. Finally, ST analysis determined approximately 40% of CD45 +cells are positive for the pan-macrophage marker CD68. Interestingly, the classical paradigm of M1 and M2 macrophages is not found. Instead, a spectrum of macrophages were identified with approximately 57% of ST macrophages expressing M2 markers (CD206, CD163) with the M1 activation marker CD40.

**Conclusions:** This study demonstrated distinct metabolic profiles in M1/M2 RA macrophages; their opposing roles in perpetuating and resolving inflammation, respectively. We have identified, for the first time, a transitional subtype of tissue-specific macrophages, suggesting that these cells remain plastic and function according to their microenvironment.

This study demonstrated distinct metabolic profiles in M1/M2 RA macrophages; their opposing roles in perpetuating and resolving inflammation, respectively. We have identified, for the first time, a dominant transitional subtype of tissue specific macrophages with at least six other phenotypically distinct subtypes also present, suggesting that these cells remain plastic and function according to their microenvironment.

**Disclosure of Interest:** None declared

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**SAT0008 DYSREGULATION OF THE CIRCULATING AND RENAL CLUSTERIN IN LUPUS NEPHRITIS**

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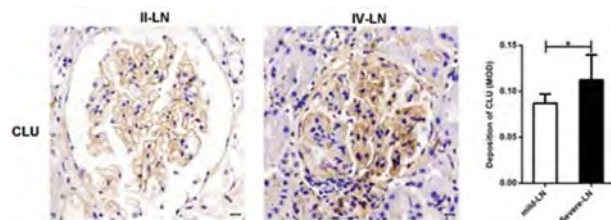
**Background:** Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease with lupus nephritis (LN) as one of the main causes of poor prognosis. Although the complement system participates in the development of LN, the exact mechanism is not clear. The present study was to investigate the pathogenesis of LN by detecting the levels of Clusterin (CLU, one of complement regulatory proteins) in the plasma and renal specimens of patients with LN.

**Objectives:** To determine the circulating and renal Clusterin levels and its clinical associations in patients with LN.

**Methods:** Plasma Clusterin levels were examined by enzyme-linked immunosorbent assay in 66 SLE including 50 LN patients and 40 healthy controls. Immunohistochemical method was used to detect the expression of Clusterin in renal biopsy tissues of 16 LN patients. Severity of LN was assessed according to the abbreviated version of the International Society of Nephrology/Renal Pathology Society classification.



**Results:** Plasma levels of Clusterin were significantly decreased in active LN patients when compared to healthy controls ( $p < 0.05$ ). Plasma Clusterin levels were negatively correlated with CRP, SLEDAI, and 24 hours proteinuria ( $p < 0.01$ ,  $p < 0.05$ , and  $p < 0.05$ ). In sixteen patients with lupus nephritis, we found that the expression of Clusterin in glomeruli was significantly enhanced in severe LN when compared to mild LN (figure 1,  $p < 0.05$ ).



**Abstract SAT0008** – Figure 1. Deposition of Clusterin in LN. \* $P < 0.05$ .

**Conclusions:** Decreased Clusterin could involve in the pathogenesis of LN, and the role of renal Clusterin need to be further explored. These findings suggested that Clusterin would be a therapeutic target for lupus nephritis in the future.

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**Disclosure of Interest:** None declared

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#### SAT0009 TYROSINE KINASE PATHWAYS IN MONOSODIUM-URATE CRYSTAL-INDUCED INFLAMMATORY RESPONSES

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**Background:** Deposition of monosodium urate (MSU) crystals in the joints or other tissues is a hallmark in the pathogenesis of gout. The urate crystal-induced inflammation is known to be mediated mainly by neutrophils besides monocytes and macrophages. Although MSU crystal-mediated signal transduction is in the focus of recent investigations, the molecular mechanism is only partially characterised.

**Objectives:** In this study, we investigated the role of Src family kinases in MSU crystal-induced *in vitro* activation of primary murine and human neutrophils and their *in vivo* significance in experimental model of gout.

**Methods:** Bone marrow isolated neutrophils from wild type and triple Src family kinases-deficient (Hck<sup>-/-</sup>Fgr<sup>-/-</sup>Lyn<sup>-/-</sup>) mice or vehicle and Src-inhibitor treated human neutrophils were stimulated with different concentration of MSU crystals. The superoxide production of the cells was measured by a luminometric assay, while the supernatants of MSU crystal activated cells were analysed by using various enzyme-linked immunosorbent assay (ELISA) kits. The phagocytosis of the urate crystals by neutrophils was followed by videomicroscopy and flow cytometry. Gouty arthritis was induced by injection of MSU crystals into the hind paws of the experimental mice and was assessed by ankle thickness measurements and detection of the synovial cytokine levels by ELISA.

**Results:** The MSU crystal-induced superoxide release, cytokine production and the crystal-phagocytosis were abrogated in Src family kinases-deficient murine or in Src-inhibitor treated human neutrophils. In contrast to wild type animals, Src family kinases-deficient mice showed significantly decreased paw swelling and neutrophil accumulation at the site of inflammation. In line with this, the synovial levels of interleukin-1 $\beta$  and CXCL2 were also strongly reduced in Src family kinases-deficient mice compared to wild type animals.

**Conclusions:** Src family kinases play an indispensable role in MSU crystal-induced superoxide and cytokine production as well as crystal-phagocytosis of neutrophils. The fact, that Src family kinases-deficient mice are partially protected from crystal-induced inflammatory reactions indicate the important role of these kinases in *in vivo* gouty arthritis. These kinases are also play important role in the

development of *in vivo* gouty arthritis as the. Identification of these key players in urate crystal-induced intracellular signalling pathways in neutrophils leads to a better understanding of the pathogenesis of gout and may help to develop novel therapeutic strategies in MSU crystal-associated inflammatory diseases.

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#### SAT0010 EXCESSIVE FORMATION OF NEUTROPHIL EXTRACELLULAR TRAPS HAVE A DIFFERENT ROLE IN THE PATHOGENESIS OF ANCA-ASSOCIATED VASCULITIS AND SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Renal involvement in ANCA-associated vasculitis (AAV) and systemic lupus erythematosus (SLE) manifests as autoimmune-mediated glomerulonephritis (AIGN). In AAV, crescentic lesions and a pauci-immune immunofluorescence is typically seen while in SLE endo- and extracapillary proliferative lesions and a full-house immunofluorescence is seen. Although these are clinically divergent autoimmune diseases, neutrophil extracellular traps (NETs) are postulated to be involved in their pathogenesis. NETs are immunogenic, extracellular DNA structures harbouring relevant ANCA- and nuclear auto-antigens. However, it is still unclear how and if NETs can act as a common pathway for both AAV and SLE.

**Objectives:** To increase our understanding of the potential pathogenic role of NETs in AAV and SLE, the aim of this study was to compare the characteristics of *ex vivo* AAV- and SLE-induced NET formation.

**Methods:** *Ex vivo* NET formation was quantified by our highly-sensitive NET quantification assay using 3D-confocal microscopy<sup>1</sup> for 82 AAV, 56 SLE patients and 10 healthy controls (HC). Live cell imaging was used to study the morphology and kinetics. Qualitative characteristics of NETs were investigated by immunofluorescence microscopy that detected co-localisation of NET-markers, including citrullinated histon-3 (CitH3) and high mobility group box-1 (HMGB1). Also, the presence of IgG, IgM or IgA autoantibodies on AAV- and SLE-induced NETs was studied. Autoantibodies as trigger of NET formation were investigated by depleting serum from IgG and NET inhibition assays were performed using peptidylarginine deiminase-4 (PAD4) and NADPH inhibitors.

**Results:** Quantifying *ex vivo* NET formation demonstrated excessive NET formation for both AAV and SLE as compared to HC. AAV-induced NET formation (median [Q1 – Q3]: 20.7 [9.6–74.1]) was significantly higher compared to SLE-induced NET formation (5.6 [2.3–14.3];  $p < 0.0001$ ). Secondly, live cell imaging revealed lytic NET formation in AAV peaking after 2–4 hours while in SLE non-lytic NET formation with neutrophil clustering occurred within minutes. Thirdly, the presence of CitH3 was significantly higher on AAV-induced NETs, whereas SLE-induced NETs contained significantly more HMGB1. AAV-NETs were triggered independent of IgG, in contrast to IgG dependence of SLE-NETs. Intriguingly, immunofluorescence staining of immunoglobulins revealed a pauci-immune expression on AAV-NETs compared to a full-house expression of IgG, IgM and IgA on SLE-NETs. Both PAD4 and NADPH were involved in AAV- but not in SLE-induced NET formation. To further corroborate on these differences, we found that SLE-NETs were enriched for oxidised mitochondrial DNA as demonstrated by TOMM20 and MitoSOX.

**Conclusions:** This study demonstrates that excessive NET formation in AAV is intrinsically different to NET formation in SLE. AAV-NETs are characterised by a suicidal lytic PAD4- and NADPH-dependent expulsion of citrullinated NETs, whereas SLE-NETs are characterised by rapidly-induced clusters with HMGB1, enriched for mitochondrial DNA and enhanced immune complex formation altogether supporting a pro-inflammatory role of NETs in the pathophysiology of SLE, including immune-complex mediated, full-house lupus nephritis.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.2429

SAT0011

### MERTK+ MONOCYTES ARE EXPANDED IN THE PERIPHERAL BLOOD OF PATIENTS WITH ACTIVE IGG4-RELATED DISEASE AND INFILTRATE AFFECTED ORGANS

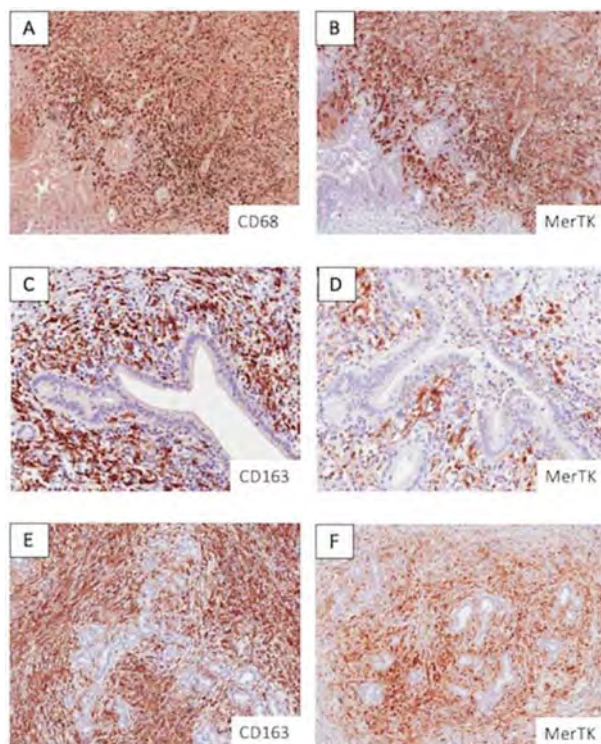
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**Background:** IgG4-Related Disease (IgG4-RD) is a multi-organ fibro-inflammatory disorder characterised by tumefactive lesions with well-defined histological features including lymphoplasmatic infiltrate rich in IgG4<sup>+</sup> plasma cells, storiform fibrosis and obliterative phlebitis<sup>1</sup>. Alternatively-activated macrophages (M2) have also been reported to abundantly infiltrate IgG4-RD lesions, but their role in IgG4-RD pathogenesis remains elusive. M2 macrophages have been recently shown to modulate innate and adaptive immune responses as well as tissue fibrosis by direct interaction with stromal cells<sup>2-4</sup>. Both these roles can be mediated by Mer tyrosine kinase (MerTK), a member of the TAM – Tyro3, Axl and MerTK-receptor family, which is highly expressed on M2 macrophages<sup>5</sup>. The relevance of MerTK and of its ligands Protein S (ProS) and Growth arrest-specific protein 6 (Gas6) in IgG4-RD has never been assessed before.

**Objectives:** To assess a pathogenetic relevance of the MerTK-ProS/Gas6 axis in IgG4-RD.

**Methods:** Immunohistochemical studies for CD68, CD163 and MerTK were performed on 8 cases of IgG4-RD involving different organs. MerTK expression within the different circulating monocyte subsets was quantified by flow cytometry both in 11 active untreated IgG4-RD patients and in 10 healthy controls (HC). Plasma levels of ProS, Gas6 and of their decoy receptor – soluble Mer (sMer) – were measured by ELISA in 34 IgG4-RD patients and 20 HC.

**Results:** MerTK was abundantly expressed in IgG4-RD lesions both within the inflammatory infiltrate and in the newly formed fibrous tissue. The pattern of MerTK expression was similar to that of the M2 macrophage marker CD163 (figure 1). Total circulating monocytes and their subsets were not expanded in active untreated IgG4-RD compared to HC. However, MerTK<sup>+</sup> monocytes were significantly increased in the peripheral blood of patients with IgG4-RD compared to HC ( $p < 0.001$ ). Plasma levels of Gas6 and ProS were significantly higher in IgG4-RD patients compared to HC ( $p = 0.003$  and  $p = 0.01$ , respectively), while the plasma level of sMer was comparable to that of HC. The number of MerTK<sup>+</sup> monocytes correlated positively with the number of circulating plasmablasts ( $r = 0.6$ ;  $p < 0.05$ ) and negatively with Gas6 plasmatic concentration ( $r = -0.7$ ;  $p < 0.05$ ).



**Abstract SAT0011 – Figure 1.** Distribution of macrophages and MerTK-expressing cells in the lung (A-B), pancreas (C-D) and biliary tree (E-F) of IgG4-RD patients. Each set of sections was stained with MerTK, CD68 as a marker of both M1 and M2 macrophages and CD163 as a marker of M2 macrophages.

**Conclusions:** A subset of MerTK<sup>+</sup> M2 macrophages abundantly infiltrates IgG4-RD fibrotic lesions and their MerTK<sup>+</sup> monocyte precursors are expanded in the peripheral blood of patients with active IgG4-RD. MerTK ligands are also increased in IgG4-RD, suggesting an augmented activation of MerTK signalling pathways. Further studies are needed to better characterise this monocyte/macrophage subpopulation, to understand its role in IgG4-RD and to identify possible biomarkers and therapeutic targets.

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SAT0012

### C-REACTIVE PROTEIN: NOT ONLY A MARKER, BUT ALSO A CAUSE OF INFLAMMATION THROUGH METABOLIC REPROGRAMMING OF HUMAN MACROPHAGES

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**Background:** C-reactive protein (CRP) is an acute-phase protein produced in high quantities by the liver in response to infection and during chronic inflammatory disorders such as rheumatoid arthritis (RA). As a consequence, CRP is in widespread clinical use as a general marker of inflammation. Although CRP is known to facilitate clearance of cell debris by phagocytic cells by binding to its ligand phosphocholine on dead cells, additional functions of CRP are still not completely understood.

**Objectives:** Here, we set out to investigate whether CRP, which is present in high concentrations in synovial fluid of active RA patients, also plays a role in the orchestration of inflammation in the inflamed joint.

**Methods:** Human macrophages were differentiated from blood monocytes of healthy volunteers. Cells were stimulated with complexed CRP (c-CRP) and/or ligands for Toll-like receptors (TLRs), mimicking the stimuli in the inflamed joint. Responsible signalling pathways were identified using small molecule inhibitors and RNA interference. Metabolic pathways were identified using specific inhibitors and the Seahorse metabolic analyzer.

**Results:** Strikingly, we here provide evidence that CRP is not only a marker, but also a cause of inflammation by strongly amplifying the production of RA-associated pro-inflammatory cytokines. We show that complex formation of CRP as a result of binding to its ligand phosphocholine selectively enhanced TNF $\alpha$ , IL-1 $\beta$ , and IL-23 production by human macrophages. While c-CRP did not induce cytokine production individually, c-CRP synergized with TLRs to amplify cytokine gene translation. We identified Fc gamma receptor I and IIa (Fc $\gamma$ RI and Fc $\gamma$ RIIa) as the main receptors responsible. Moreover, we unravelled the responsible molecular mechanism of c-CRP-induced inflammation, which crucially depends on signalling through kinases Syk and PI3K, resulting in enhanced gene translation of pro-inflammatory cytokines through metabolic reprogramming, particularly through amplified glycolysis and fatty acid synthesis.

**Conclusions:** These data indicate that CRP is not only a marker, but might also be a cause of inflammation in RA patients by selectively promoting RA-associated pro-inflammatory cytokine production by human macrophages, thereby exacerbating pathology. From a therapeutic point of view, inhibition of c-CRP-induced immune activation, e.g. by targeting the identified molecular mechanisms, may be a valuable tool to suppress inflammation.

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SAT0013

### IL-1A AND ADAMTS5 MEDIATED TISSUE DAMAGE IN HUMAN CARTILAGE EXPLANTS LEADS TO GENERATION OF TLR2 ACTIVATING DAMPS

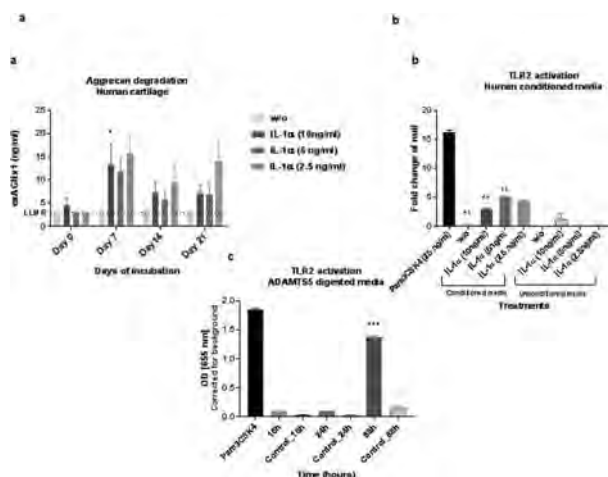
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**Background:** The innate immune system is important for the initiation and development of joint diseases such as rheumatoid arthritis (RA) and Osteoarthritis (OA). Exogenous TLR (Toll like receptor) ligands are abundant in the synovial joints of RA and OA patients and induce the first immune response. Stimulation of TLRs results in an increased immune response and is characterised by induction of cytokines expression which in turn causes tissue damage and results in generation of more DAMPs. Hence, resulting in a self-perpetuating loop of TLR activation and TLR mediated tissue damage.

**Objectives:** The aim of this study was to investigate the effect of degradation fragments of human cartilage generated *ex vivo* or *in vitro*, on TLR-2 activation in a TLR-2 reporter cell system.

**Methods:** Human cartilage biopsies retrieved from OA patients undergoing total knee replacement at Gentofte hospital were used to generate human explants (HEX). HEX were cultured for 21 days either without (w/o) treatment or in the presence of IL-1 $\alpha$  (10 ng/ml, 5 ng/ml and 2.5 ng/ml). Unconditioned media incubated without cartilage tissue was used as control. Tissue degradation was verified by measuring the release of aggrecan neo-epitope biomarkers AGNx1 and FFGV into the conditioned media (CM). Correspondingly, human cartilage was digested with ADAMTS5 for different time intervals (16 hour, 24 hour and 88 hour) at 37°C. The digested cartilage was removed by centrifugation and the supernatant was stored. Crushed cartilage in buffer alone was used as a control set up for each time point and buffer alone was subtracted as background. The CM and digested media (DM) was tested in the SEAP (secreted embryonic alkaline phosphatase) reporter gene based HEK hTLR2 cell line. The HEK null 1 parent cell line was used as a control. Pam3CSK4 was used as a positive control for the hTLR2 cell line.

**Results:** IL-1 $\alpha$  induced aggrecan degradation was confirmed by increased exAGNx1 and exFFGV release in the conditioned media compared to w/o (p<0.01) (figure 1a). CM from IL-1 $\alpha$  treated explants induced a significant signal in the hTLR2 cells compared to w/o CM or to UCM with IL-1 $\alpha$  (p<0.0001). (figure 1b). Similarly, DM showed a significant induction in the hTLR2 cells after 88 hours compared to undigested human cartilage. (p<0.0001) (figure 1c).



**Conclusions:** IL-1 $\alpha$  induced cartilage degradation leads to the release of aggrecan fragments into the CM, and this CM as well as *in vitro* cleavage products from ADAMTS-5 digestion of human cartilage was able to activate the TLR2 receptor *in vitro* in a specialised reporter cell system. These data indicate that DAMPs may be released from human cartilage in the presence of pro-inflammatory cytokines and proteolytic enzymes. The released fragments can lead to TLR2 activation and cause further inflammation. These data suggest that DAMPs may play a role in the onset and maintenance of inflammation in diseases such as OA and RA.

**Disclosure of Interest:** None declared

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SAT0014

### DRUG REPURPOSING TO BLOCK TLR4-ASSOCIATED INFLAMMATION IN OA CHONDROCYTES

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**Background:** The rising prevalence of rheumatic diseases in our society has caused a dramatic impact on the welfare of the population as well as becoming an economic burden to the health system. Osteoarthritis (OA), the most common rheumatic disease, is defined by joint-space narrowing due to progressive cartilage degradation. Despite the growing knowledge in OA pathophysiology, no treatment has yet proved to be efficient enough. The activation of innate immune receptors, such Toll-like receptor 4 (TLR4), by damage-associated molecular patterns (DAMPs) has been involved in chondrocyte-mediated inflammatory responses. There are currently no available drugs aimed to block TLR4-mediated inflammatory responses. Nonetheless, there are already known drugs being employed in other indications that could have this activity; namely amitriptyline, naloxone, and thalidomide.

**Objectives:** Determine the ability of amitriptyline, naloxone and thalidomide to block TLR4-mediated innate immune responses in chondrocytes.

**Methods:** The effect of amitriptyline, naloxone and thalidomide on TLR4-mediated inflammatory responses was determined in mouse chondrogenic cell line (ATDC5) and in human primary OA chondrocytes. The mRNA expression of key inflammatory factors lipocalin-2 (LCN2), interleukin-6 (IL-6), and monocyte chemoattractant protein-1 (MCP-1) was studied by RT-PCR. Cell viability was tested using the methyl-thiazolyl-tetrazolium (MTT) reagent and nitrite accumulation (nitric oxide production) in cell culture media was assessed by Griess reaction and validated by determining nitric oxide synthase 2 (NOS-2) mRNA expression.

**Results:** The co-stimulation of human OA chondrocytes with the TLR4 agonist LPS [100 ng/ml] and amitriptyline [1  $\mu$ M], reduced the mRNA expression of LCN2 (90%), IL-6 (95%) and MCP-1 (87%). The pre-stimulation of naloxone [100  $\mu$ M] with LPS also reduced the mRNA expression of LCN2 (53%), IL-6 (78%) and MCP-1 (79%). Similar results LCN2 (63%), IL-6 (74%), and MCP-1 (78%) were obtained upon the pre-stimulation of these cells with thalidomide [500  $\mu$ M]. The anti-inflammatory effect of these drugs on these pro-inflammatory factors was also observed but lowered in ATDC5 cells. Consistent with these results in ATDC5 cells these drugs also reduced the expression of mRNA NOS-2 gene expression as well as nitrite accumulation in the cell culture medium. At the studied concentrations, amitriptyline, naloxone and thalidomide did not affect to chondrocytes viability.

**Conclusions:** The data presented here have shown that amitriptyline, naloxone and thalidomide block TLR4 innate immune responses in human OA chondrocytes. These drugs have passed many toxicology and safety tests for their clinical use and could be ready for its repurposing in the management of TLR4-mediated OA cartilage inflammation.

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**Disclosure of Interest:** None declared

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SAT0015

### IDENTIFICATION AND CHARACTERISATION OF HIGH MOLECULAR WEIGHT HMGB1 PROTEIN COMPLEXES: IMPLICATIONS FOR STRESS RESPONSE, INNATE IMMUNITY AND AUTOIMMUNE DISEASE

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**Background:** High mobility group box one protein (HMGB1) is a chromatin associated protein, which in response to stress or injury translocates from the nucleus to the extracellular milieu to serve as an alarmin. HMGB1 has a remarkable ability to form complexes with proinflammatory molecules. This is underscored by the emerging role of HMGB1 in rheumatic diseases such as systemic erythematous (SLE), where the presence of HMGB1 in complex with endogenous nuclear



components such as dsDNA or nucleosomes was shown to play an important role in breaking immune tolerance against nuclear antigens.<sup>1</sup> Although the function of HMGB1 is in-part determined by the complexes it forms with other molecules, structural modifications in the HMGB1 polypeptide that may regulate complex formation have not been described.

**Objectives:** In this study we investigated the presence of HMGB1 in large protein complexes (HMGB1c) in human plasma. The objectives of this study were to isolate and characterise HMGB1c as well as to determine the mechanism of its formation.

**Methods:** We examined the presence of HMGB1c in plasma from SLE patients and healthy controls using semi-denaturing detergent agarose gel electrophoresis (SDD-AGE) followed by Western blot analysis. Immunoblotting, coimmunoprecipitation, confocal microscopy, and mass spectrometry were used to detect and characterise novel high molecular weight HMGB1 variants *in vitro* as well as in cell lines and primary cells. Mechanisms of HMGB1c formation were delineated via mass spectrometry, RNA interference, and *in vitro* enzyme reactions.

**Results:** In this study we note the presence of high molecular weight, denaturing resistant HMGB1 protein complexes (HMGB1c) that were present in the plasma of SLE patients and to a much lesser extent, healthy subjects. Similarly, HMGB1c were induced when cells were incubated with endotoxin or alum. Here we report that HMGB1c formation is catalysed by the calcium-activated protein crosslinking enzyme transglutaminase-2 (TG2). HMGB1-TG2 interaction was demonstrated via coimmunoprecipitation as well as by confocal microscopy after co-transfection of cells with plasmids encoding fluorescent-tagged HMGB1 and TG2 constructs. Moreover, HMGB1c formation was suppressed in cells by TG2 siRNA. Crosslink site mapping and analysis by mass spectrometry revealed that HMGB1 can be crosslinked to TG2 as well as a number of additional proteins, including human autoantigens.

**Conclusions:** TG2 catalyses the formation of high molecular weight HMGB1 protein complexes. Given the immunoadjuvant properties of HMGB1 and the implication of TG2-mediated protein complex formation as a possible mechanism by which immune tolerance can be broken to self-molecules,<sup>2</sup> these findings have significant physiological implications for the role of HMGB1 in cellular stress responses and innate immunity in lupus.

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SATURDAY, 16 JUNE 2018

## Cytokines and inflammatory mediators

### SAT0016 IL-12 SUPPRESS TR1 CELLS IN THE SJÖGREN'S SYNDROME

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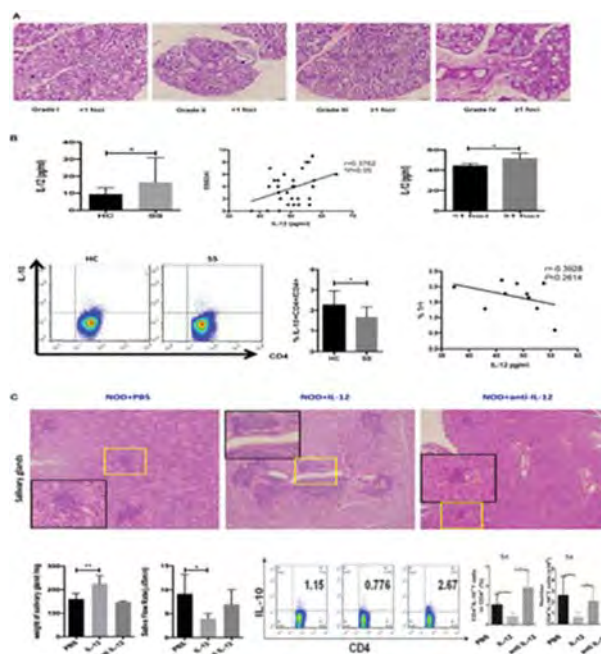
**Background:** Sjögren's syndrome (SS) is a systemic autoimmune disorder characterised by lymphocytic infiltration of salivary and lacrimal gland leading to dry mouth and eye dryness progressively. It is known that pro-inflammatory cytokines and dysfunction of immune cells play an important role in the pathogenesis of SS. The regulatory T cell type 1 (Tr1) cells have strong immunosuppressive properties and alleviate inflammatory diseases. However, the role of Tr1 cells in SS and the underlying mechanism is still not fully understood.

**Objectives:** This study aims to determine the association of Tr1 cells with the disease pathogenesis using a murine model of SS and patients with SS.

**Methods:** The frequencies of Tr1 cells in blood, cervical lymph nodes and their association with disease severity were determined in SS mice. Since proinflammatory interleukine 12 (IL-12) have the ability to regulate the generation of Tr1 cells, the serum IL-12 and its association with disease severity and Tr1 cells were also examined. The involvement of IL-12 and a Tr1 response was examined by recombinant IL-12 treatment or anti-IL-12 antibody neutralisation in SS mice and

monitored for SS development. The mouse naive CD4<sup>+</sup> cells were treated with IL-12 under Tr1 polarising condition. The frequency of Tr1 cells and their association with IL-12 and disease activity were verified in SS patients.

**Results:** Tr1 cells significantly decreased in SS mice and patients with SS, which correlated negatively with disease activity and proinflammatory IL-12 (figure 1A, B). IL-12 suppressed Tr1 cell polarisation *ex vivo*. SS mice treated with the recombinant IL-12 displayed significantly lower saliva flow rates and pronounced inflammation and tissue damage in salivary glands, accompanying with reduction of Tr1 cells. However, anti-IL-12 antibody treatment profoundly increased the numbers of Tr1 cells and ameliorated the reduction in salivary secretion and inflammation and tissue damage in salivary glands in SS mice (figure 1C).



**Conclusions:** Our findings indicate that proinflammatory IL-12 with its capacity to inhibit Tr1 cell generation may be a critical pathogenic factor in Sjögren's syndrome. Targeting IL-12 and Tr1 cells may be a novel therapeutic strategy for the treatment of Sjögren's syndrome.

**Disclosure of Interest:** None declared

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### SAT0017 THE RHEUMATOID FACTOR RESPONSE IS COMPOSED OF MULTIPLE REACTIVITIES AGAINST DIFFERENT EPITOPES

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**Background:** Rheumatoid arthritis (RA) is a complex autoimmune disorder in which autoantibodies likely play an important role. Rheumatoid factors (RFs) are autoantibodies that bind to the constant domain (Fc) of immunoglobulin G (IgG). It is known that they can bind in various ways; most RA patients probably have multiple types of RFs that all bind different parts of antibodies. It is presently unknown how this differs between patients. Furthermore, it is possible that RF responses in RA have a different reactivity pattern compared to those present in other diseases and in RF +healthy donors. Currently, these RA-specific RFs have not yet been identified.

**Objectives:** To develop a method to identify and dissect different RF responses, to classify the RF response in different stages of RA, and to characterise differences in reactivity between RF responses in the context of RA and RF responses in other diseases or healthy donors.

**Methods:** Variants of human IgG antibodies to which only a few different types of RFs can bind at a time were generated and used as target antibodies in newly

developed ELISA-based RF assays. RF responses were analysed in healthy donors, arthralgia patients at risk for RA and RA patients at different disease stages.

**Results:** RF responses in all cohorts were shown to be primarily directed against epitopes at the interface of the second and third IgG heavy chain domains (CH2-CH3) and the tip of the CH3 domain. The generated target antibodies were able to separate these RF responses and discriminate them from RF responses targeting epitopes outside these reactivity hotspots. Furthermore, certain RF responses against the CH2-CH3 interface were shown to depend on the presence of a single specific amino acid residue.

Pilot experiments using the target antibodies in clinical cohorts revealed that, in arthralgia patients and RA patients at various disease stages, the pattern of RF reactivity differs between individual patients as well as between cohorts. The degree to which an RF response against the CH2-CH3 interface depends on the single specific amino acid residue varied substantially between patients. One particular RF response pattern, RFs binding only the CH3 domain, was found exclusively in non-RA patients and healthy donors.

**Conclusions:** Using newly developed target IgGs, RF responses against different epitopes can be characterised. RF response patterns differ between RA and non-RA cohorts and between RA patients. These new tools may lead to identification of RA-specific RF responses and provide more insight into the pathogenic role of these autoantibodies.

**Disclosure of Interest:** None declared

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SAT0018

### BLOOD CHEMOKINE SYSTEM PROFILE ASSOCIATED WITH DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS

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**Background:** Chemokine receptors and their chemokine ligands (chemokine system), key mediators of inflammatory and immune cell trafficking, are involved in the pathogenesis of rheumatoid arthritis (RA). There is still limited information of blood chemokine system signature associated with disease activity.

**Objectives:** To identify RA-associated chemokine system signature using highly sensitive multiplex Proximity Extension ImmunoAssay (PEA) in serum together with analysis of CCR5, CCR6 and CXCR3 expression in blood cell subsets and assess its relationship with disease activity as evaluated by activity score (DAS28).

**Methods:** We investigated the serum levels of 92 inflammation-related proteins in 78 Czech patients with RA by PEA (Proseek Multiplex, Olink Bioscience, Sweden). Disease activity was assessed by means of DAS28 and subgroups were formed based on the disease activity, where DAS28 of  $\geq 3.2$  was taken as active RA (inactive RA, n=40; active RA, n=38). The expression of CCR5, CCR6 and CXCR3 receptors were analysed using 6-colour flow cytometry (BD FACSCanto II) on T and B lymphocytes, NK, dendritic cells, and monocytes in peripheral blood from 11 patients with active RA and 9 age-matched healthy control subjects. Statistical tests (Mann-Whitney U test, Spearman correlation) were performed using GenEx (Sweden) and GraphPad Prism 5.01 (CA, USA). *P*-values  $\leq 0.05$  was considered as significant.

**Results:** In patients with active RA, 16 serum proteins were upregulated ( $P_{corr} \leq 0.05$ ). Top-ranked proteins distinguishing active and inactive RA were CCL20, CXCL9, CCL7, CXCL10, IL-6, sCD137, and CXCL1 ( $P_{corr} < 0.03$ ). Levels of all these proteins positively correlated with disease activity ( $r > 0.30$ ,  $p < 0.006$ ) and the best correlation was observed for chemokines CCL20 ( $r = 0.495$ ,  $p = 0.000004$ ) and CCL7 ( $r = 0.442$ ,  $p = 0.00005$ ). Based on these results we analysed the expression of corresponding chemokine receptors: CCR5, CCR6, and CXCR3 in blood cells. Expression of CCR6 was increased on CD4 +T and CD8 +T lymphocytes ( $p = 0.008$ ,  $p = 0.01$  respectively) and on total and activated NK cells ( $p = 0.01$ ,  $p = 0.004$  respectively) in active RA compared with healthy controls. Regarding CCR5, decreased percentage of CCR5 positive CD4 +T lymphocytes were registered in RA patients compared with healthy controls ( $p = 0.008$ ). No differences were observed in the expression of CXCR3 on investigated immune cell populations.

**Conclusions:** We identified the blood chemokine system signature associated with disease activity in RA further supporting a critical role of CCL20/CCR6 axis in the ongoing inflammation related to the disease activity in RA.

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**Disclosure of Interest:** None declared

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SAT0019

### TNF- $\alpha$ REGULATES PLASMACYTOID DENDRITIC CELLS BY SUPPRESSING IFN- $\alpha$ PRODUCTION AND ENHANCING TH1 AND TH17 CELL DIFFERENTIATION

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**Background:** Human plasmacytoid dendritic cells (pDCs) play a vital role in modulating immune responses. pDCs can produce massive amounts of type I IFNs in response to nucleic acids via toll-like receptors (TLRs) and they are known to possess weak antigen-presenting properties inducing CD4<sup>+</sup> T cell activation. Previous data showed a cross-regulation between TNF- $\alpha$  and IFN- $\alpha$  but the effect of TNF- $\alpha$  on pDCs remains unclear.

**Objectives:** To investigate how TNF- $\alpha$  regulates the immune function of human pDCs.

**Methods:** Fresh PBMCs were treated with TNF- $\alpha$ , TLR7 and TLR9 synthetic agonists. pDCs were immunophenotyped using flow cytometry. RNA from sorted pDCs was extracted and sequenced using Smart-seq2 for sensitive full-length transcriptome profiling. For pDC/T cell co-culture, fresh or TNF- $\alpha$ -treated pDCs were cultured with naïve CD4<sup>+</sup> T cells for 5 days. The production of cytokines was measured by intracellular staining and ELISA.

**Results:** Upon stimulation with TLR7 and TLR9 agonists, there were three main pDC populations: non-producers, TNF- $\alpha$ -producers, TNF- $\alpha$ /IFN- $\alpha$ -producers. Exogenous TNF- $\alpha$  significantly reduced the production of both IFN- $\alpha$  and TNF- $\alpha$  in TLR9-stimulated pDCs but only IFN- $\alpha$  in TLR7-stimulated pDCs. Neutralisation of autologous TNF- $\alpha$  with anti-TNF antibody partially sustained IFN- $\alpha$  secretion by TLR9-stimulated pDCs after 24 hours. Exogenous TNF- $\alpha$  significantly promoted pDC maturation by upregulation of costimulatory molecules and chemokine receptors such as CD80, CD86, HLA-DR, and CCR7. RNAseq data analysis suggested that TNF- $\alpha$  inhibits IFN- $\alpha$ /TNF- $\alpha$  production by interfering with the NF- $\kappa$ B pathway, promotes antigen processing and presentation pathways as well as T cell activation and differentiation. Indeed, TNF- $\alpha$ -treated pDCs induced *in vitro* higher CD4<sup>+</sup> T cell proliferation and favoured Th1/Th17 polarisation.

**Conclusions:** Although pDCs possess weak antigen-presenting properties, TNF- $\alpha$  can enhance pDC maturation by switching their main role as IFN- $\alpha$ -producing cells to a more conventional DC phenotype. The functional status of pDCs might be strongly influenced by overall inflammatory environment and TNF- $\alpha$  might regulate IFN- $\alpha$ -mediated aspects of a range of autoimmune and inflammatory diseases.

**Disclosure of Interest:** None declared

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SAT0020

### IMPACT OF IL12B SINGLE NUCLEOTIDE POLYMORPHISMS ON CIRCULATING PRO-INFLAMMATORY CYTOKINES IL-12P40 AND IL-23 IN ANKYLOSING SPONDYLITIS

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**Background:** Ankylosing spondylitis (AS) is an immune-mediated rheumatic disease belonging to the spectrum of axial spondyloarthritis, characterised mainly by chronic inflammatory back pain and radiographic sacroiliitis. Since genetic factors have been shown to be major determinants of susceptibility to the disease and contribute to amplification of immune responses, polymorphic variability in immune response genes are of interest. The interleukin-12p40 gene (IL12B) encodes the p40 polypeptide chain, which, together with p19, composes IL-23, a member of the IL-12 superfamily.

**Objectives:** In this study, we examined functional association between two IL12B polymorphisms – IL12B<sub>pro</sub> (rs17860508) and IL12B 3' UTR A/C (rs3212227), and cytokine production of both pro-inflammatory cytokines IL-12p40 and IL-23 in AS patients.

**Methods:** A total of 69 AS patients with a mean age 43±16 years and 257 healthy individuals from Bulgarian population were genotyped. Genotyping for the rs3212227 was performed by restriction fragment length polymorphisms-PCR assay and for the rs17860508 by allele specific-PCR. Serum IL-12p40 and IL-23 concentrations measurement was done using ELISA test.

**Results:** We found significant differences in the genotype ( $p = 0.029$ ) and allele ( $p = 0.006$ ) frequencies of rs17860508 polymorphism between AS patients and controls. An association between AS and the rs17860508 polymorphism was established under the allelic model (allele 2 vs. allele 1; OR=1.698), the dominant model (1.2+2.2 vs. 1.1; OR=2.427), and the co-dominant model (2.2 vs. 1.1;

OR=2.812; 1.2 vs. 1.1; OR=2.252). Genotype and allele frequencies of rs3212227 polymorphism of the IL12B were similar in cases and controls. The mean ( $\pm$ SEM) levels of IL-12p40 and IL-23 in AS patients (176.5 $\pm$ 20.7 pg/ml; 26.98 $\pm$ 3.4 pg/ml, respectively) was significantly higher than in controls (88.8 $\pm$ 9.6 pg/ml; 12.1 $\pm$ 1.5; respectively) ( $p$ <0.001). Stratification based on *IL12B* *pro* 1.1 and 1.2 genotypes than controls. Highest IL-23 serum levels were associated with *IL12B* *pro* 2.2 genotype. With regard of polymorphic variability of *IL12B* 3' UTR, AC genotype in AS has been linked to a higher IL-12p40 production and lower one of IL-23.

**Conclusions:** Allelic variants in the *IL12B* genes have the potential to alter the expression of both IL-12p40 and IL-23 cytokines in specific manner for AS patients. Carriage of the *IL12B* *pro* variant 1-allele and of the 3'-UTR A-allele in the genotype regardless of homo- or heterozygosity could enhance systemic IL-12p40 and IL-23 levels.

**Disclosure of Interest:** None declared

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#### SAT0021 INNATE LYMPHOID CELLS ARE NOT A MAIN SOURCE OF IL-17A IN THE INFLAMED SPONDYLOARTHRITIS JOINT

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**Background:** Clinical trials of the anti-IL-17A antibody secukinumab demonstrated the crucial role of IL-17A cytokine in the pathogenesis of spondyloarthritis (SpA), however, its cellular source in this condition remains controversial. Group 3 innate lymphoid cells (ILC3s) have been recently identified in a number of different tissues as potent producers of proinflammatory cytokines, including IL-17A and IL-22.

**Objectives:** In this study we set out to characterise the presence and composition of ILCs and investigate whether these cells are the important source of IL-17A in the synovial tissue of patients with SpA.

**Methods:** Matched synovial tissue (ST), synovial fluid (SF) and peripheral blood (PB) were obtained from SpA and rheumatoid arthritis (RA) patients with actively inflamed knee joints. ILCs subsets were characterised by flow cytometry. Gene expression analysis at the single-cell level was performed directly *ex vivo* and after stimulation with PMA ionomycin. IL-17A ELISPOT assay was used to detect IL-17A-secreting cells.

**Results:** Analysis revealed that ILCs, and particularly NKp44-positive ILC3s, are expanded in the inflamed arthritic joint. Single cell expression analysis revealed that ST ILCs are clearly distinguishable from ST T cells and from their PB counterparts. We detected expression of Th17 signature transcripts *RORC*, *AHR* and *IL-23R* in the notable fraction of ST ILC3s. Furthermore these cells were capable to induce *IL-22*, but not *IL-17A* expression in response to *in vitro* re-stimulation

**Conclusions:** We demonstrate in this study that ILC3s are absolutely and relatively enriched in the synovial joint of patients with SpA, however these cells are not a significant source of IL-17A cytokine in this pathology.

**Disclosure of Interest:** None declared

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#### SAT0022 MIR-15A/16 SUPPRESS INFLAMMATORY RESPONSE AND CELL INVASION AND MIGRATION IN FIBROBLAST-LIKE SYNOVIOCYTES IN RHEUMATOID ARTHRITIS VIA TARGETING SOX5

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**Background:** Aberrant expressions of miRNAs play a critical role in the inflammatory and immune response in rheumatoid arthritis (RA). The microRNA cluster which encodes for miR-15a and miR-16, located at 13q14.3. Both these microRNAs have been implicated in the pathogenesis of many diseases, but little is known of their role in RA.

**Objectives:** In this study, we aim to investigate the underlying molecular mechanisms of MiR-15a/16 in RA, which will provide new insight into understanding the pathogenesis of RA and identifying novel therapeutic targets for this disease.

**Methods:** The expression of MiR-15a/16 in the peripheral blood mononuclear cell (PBMC) and synovium from RA, osteoarthritis (OA) and healthy controls (HC) was determined by RT-qPCR and Western blotting. Mimics of MiR-15a/16 were

transfected into the human rheumatoid fibroblast-like synoviocytes (FLS) MH7A cell line. The effect of MiR-15a/16 on proinflammatory cytokines expression, migration and invasion of FLS was detected by RT-qPCR, transwell and F-actin staining. The potentially target gene of miR-15a/16 was predicted by bioinformatics analysis. The 3'UTR of Sox5 containing wild-type or mutated miR-15a/16 binding sites was cloned to the downstream of a luciferase vector and transfected into MH7A, respectively.

**Results:** There is no significant difference of MiR-15a/16 expression in PBMC in RA and HC at baseline. However, the MiR-15a/16 expression is lower in PBMC from non-responders (defined DAS28 changes<1.2 after 3 months DMARDs therapy) than those in responders after 3 months DMARDs therapy. The levels of MiR-15a/16 expression were significant decreased in the synovium from RA patients, as compared with OA patients. Transfection of MH7A with MiR-15a and 16 mimic suppressed IL-1b, TNFa, IL-17 expression, decreased cell migration and invasion and affected the cytoskeletal reorganisation in RA-FLS. We co-transfected MH7A with luciferase-reporter constructs with either wild-type or mutated miR-132 or miR-15a/16 mimics. Luciferase assay showed that either miR-15a or 16 reduced the luciferase intensity of Sox5 3'UTR. However, mutated miR-15a/16 alleviated the inhibitory effect of miR-15a/16 on the intensity of Sox5 3'UTR. To determine whether Sox5 mediates the roles of miR-15a/16 in cell migration and invasion, we constructed recombinant Adenovirus SOX5 recombinant Adenovirus SOX5 overexpressing vector. We then found that overexpression of Sox5 restored the cell invasion, and migration in MH7A that were inhibited by and miR-15a/16.

**Conclusions:** In conclusion, our data indicate that MiR-15a/16 play an important role in inflammatory response and cell invasion and migration in RA-FLS by directly targeting Sox5, and imply that these miRNAs have potential as therapeutic targets for RA.

**Disclosure of Interest:** None declared

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#### SAT0023 CONTROL OF CYTOKINE MRNA DEGRADATION BY THE HISTONE DEACETYLASE INHIBITOR ITF2357 IN RHEUMATOID ARTHRITIS FIBROBLAST-LIKE SYNOVIOCYTES

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**Background:** Control of cytokine mRNA degradation acts as an essential checkpoint to limit the overproduction of inflammatory proteins.<sup>1</sup> In rheumatoid arthritis (RA), altered expression of the mRNA-degrading protein TTP (tristetraprolin, *ZFP36*) has been recently reported in synovial tissue, possibly contributing to the perpetuating inflammatory loop in the synovium.<sup>2</sup> Histone deacetylase inhibitors (HDACi) are small molecule drugs suppressing cytokine production *in vitro* and *in vivo* and displaying initial safety and efficacy in the treatment of systemic onset juvenile idiopathic arthritis.<sup>3,4</sup> However, their transcriptional and post-transcriptional mechanisms of action are not yet completely characterised.

**Objectives:** We aimed to investigate the mRNA degrading properties of the HDACi ITF2357 on a panel of inflammatory mediators in RA fibroblast-like synoviocytes (FLS).

**Methods:** The effects of ITF2357 on the expression and mRNA stability of IL-1 $\beta$ -inducible genes in FLS were analysed using array-based qPCRs and Luminex. The expression of primary and mature cytokines transcripts, the mRNA levels of TTP and other AU-rich element binding proteins (ARE-BP) and the cytokine profile of fibroblasts derived from *ZFP36*<sup>+/+</sup> and *ZFP36*<sup>-/-</sup> mice was measured by qPCR. ARE-BP silencing was performed by siRNA-mediated knockdown, and TTP post-translational modifications analysed by immunoblotting.

**Results:** ITF2357 reduced the expression of 85% of the analysed IL-1 $\beta$ -inducible transcripts, including cytokines (*IL6*, *IL8*), chemokines (*CXCL2*, *CXCL5*, *CXCL6*, *CXCL10*), matrix-degrading enzymes (*MMP1*, *ADAMTS1*) and other inflammatory mediators. Analyses of mRNA stability demonstrated that ITF2357 accelerates *IL6*, *IL8*, *PTGS2*, and *CXCL2* mRNA degradation, a phenomenon associated with the enhanced transcription of TTP, but not other ARE-BP, and the altered post-translational status of TTP protein. TTP knockdown potentiated cytokine production in RA FLS and murine fibroblasts.

**Conclusions:** Our study identifies that regulation of cytokine mRNA stability is a predominant mechanism underlying ITF2357 anti-inflammatory properties, occurring via regulation of TTP. These results highlight the therapeutic potential of ITF2357 in the treatment of RA.



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**Disclosure of Interest:** None declared

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SAT0026

### DIFFERENTIAL LEVELS OF IL-7 EXPRESSION IN ADVENTITIA OF NON-RA AND RA PATIENTS WITH CORONARY ARTERY DISEASE

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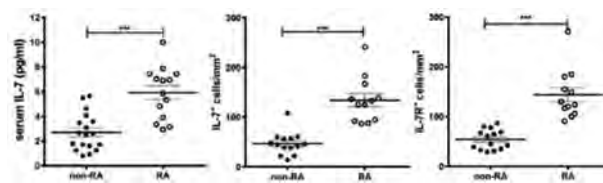
**Background:** Rheumatoid Arthritis (RA) patients have increased cardiovascular risk due to accelerated atherosclerosis (ATS), which significantly contributes to excess mortality in RA<sup>1</sup>. The increased cardiovascular risk cannot be fully explained by traditional risk factors and systemic chronic inflammation appears to play a crucial role. Interestingly, IL-7, a proinflammatory cytokine involved in RA pathogenesis, appears to play a role also in atherosclerosis<sup>2</sup> but its effect on cardiovascular disease (CVD) in RA has not been studied yet.

**Objectives:** To examine serum IL-7 levels and expression of IL-7, IL-7R, CD3 and CD20 in aortic adventitia of RA and non-RA patients with coronary artery disease (CAD) and to search for relationships between systemic IL-7 levels and expression of vascular markers, cardiovascular risk factors including metabolic and inflammatory markers.

**Methods:** We examined 19 RA patients and 20 non-RA patients undergoing coronary artery bypass graft surgery included in the Feiring Heart Biopsy Study. Serum IL-7 levels were measured by chemiluminescence (MSD). Biopsies from the adventitia of thoracic aorta from a subset of patients (12 RA and 14 non-RA) were stained for IL-7, IL-7R, CD3 and CD20 by immunohistochemistry and scored per mm<sup>2</sup> of tissue.

**Results:** Non-RA patients had lower IL-7 serum levels than RA (3.4±3.3 vs. 6.7±3.5, p<0.05). Independently of RA diagnosis, IL-7 significantly correlated with CRP (rho=0.450, p=0.008), triglycerides (TG, rho=0.566, p=0.005), glucose (rho=0.642, p=0.001) and hypertension (p=0.036). Levels of IL-7 were associated with New York Heart Association class (rho=0.429, p=0.014) and this was stronger in non-RA patients (rho=0.577, p=0.010). No associations were found with smoking or markers of CVD severity (i.e. numbers of arteries with significant stenosis or number of previous myocardial infarcts (MI)).

The number of IL-7+ and IL-7R+cells/mm<sup>2</sup> in adventitia were significantly higher in RA (134.2±45.5 and 144±49.9 respectively) than non-RA patients (46.9±22.8 and 54.4±20.2, p<0.005) and were associated with serum IL-7 levels (rho=0.551 and rho=0.588, p<0.01). Both IL-7+ and IL-7R+cells were associated with a positive history of MI (p=0.047 and p=0.005) and IL-7R+cells with the number of previous MIs (rho=0.408, p=0.038). Only in RA patients, IL-7R+cells showed a trend for correlation with TG (rho=0.771, p=0.072). IL-7+ and IL-7R+cells correlated with CD3 (rho=0.688, p=0.013 and rho=0.630 p=0.028), but no correlation was found with CD20. Cholesterol and HDL levels were associated with IL-7+ cells only in non-RA patients (rho=0.729 p=0.04 and rho=0.733, p=0.038).



**Conclusions:** Among patients with CAD, those with RA had higher serum IL-7 and a greater expression of both IL-7/IL-7R in aortic adventitia. Systemic levels of IL-7 were related to its vascular expression. Thus, the IL-7/IL-7R axis may play a role in the accelerated atherogenesis observed in RA; further studies are needed to elucidate the precise role of IL-7 and impact of potential IL-7R blockade in CV risk in RA.

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**Disclosure of Interest:** None declared

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SAT0027

### CO-EXPRESSION OF RECEPTORS TO TNFA AMONG NAIVE T-CELLS AND MEMORY T-CELLS IS ALTERED IN RHEUMATOID ARTHRITIS AND THE CHANGES CORRELATE WITH DISEASE ACTIVITY

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**Background:** Changing the ratio of TNF $\alpha$  receptors of different types can lead to shift in the balance between pro-apoptotic and proliferative signalling pathways which is crucial for rheumatoid arthritis (RA) inflammatory processes.

**Objectives:** To study the level of expression of type 1 and 2 receptors for TNF $\alpha$  (TNFR1/TNFR2) on individual subpopulations of peripheral blood actively involved in immunopathological processes in RA

**Methods:** The study included 20 healthy donors aged 18–60 years (11 men (55%)) and 36 RA patients with high (n=14), medium (n=15) and low (n=7) disease activity at the age of 22–77 years (31 women (86, 1%)). Co-expression and number of type 1 and 2 receptors for TNF $\alpha$  were calculated for monocytes, B-cells, T-cells, as well as among: cytotoxic T-cells (CD8+), T-helper cells (CD4+), activated CD8+ cells, activated CD4+ cells, memory T-cells (CD45RO+) and naive T-cells (CD45RA+) from cytotoxic and T-helper cells, and T-regulatory cells (CD4+CD25highCD127low) by flow cytometry analysis (BD FACSVerse, USA).

**Results:** Seven indicators of receptor expression were revealed, which differed in patients with RA with high disease activity in comparison with HD, and didn't differ between HD and patients with low disease activity. These were 4 indicators on the number of receptors on cells and 3 cell percentages with specific combinations of expressed. The association between disease severity and activity indexes (DAS-28 index, disease duration, X-ray stage, activity stage, RF level, ASCP and C-RB, systemic manifestations and erosive arthritis) and parameters of TNF $\alpha$  receptor expression on immunocompetent cell subpopulations were studied. The following associations were revealed: RF level positively correlated with the percentage of double-positive TNFR1+TNFR2+ cells among naive and memory T-cells for both T-helpers and cytotoxic T-cells (r levels from 0.62 to 0.68 with p<0.05); the level of C-reactive protein positively correlated with the percentage of cells carrying only receptor type 1 among all the T-lymphocyte subpopulations studied (r levels from 0.73 to 0.9 with p<0.05); the presence of systemic manifestations is negatively correlated with the number of receptors of both types 1 and 2 on naive T-helper and cytotoxic cells (r levels from -0.63 to -0.74 with p<0.05).

**Conclusions:** The active inflammatory process in rheumatoid arthritis with DAS28 >5.1 is accompanied by a change in the ratio of cells with different variants of co-expression of receptors to TNF $\alpha$  among populations actively involved in the pathological process (naive T-cells and memory T-cells among T-helpers and cytotoxic T-cells). The selected parameters will be used to construct and verify the predictive models of response to therapy of different subclasses

**Disclosure of Interest:** None declared

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**SAT0028 THE IMPORTANCE OF PROPER HANDLING OF HUMAN SYNOVIAL FLUID FOR ARTHRITIS RESEARCH**

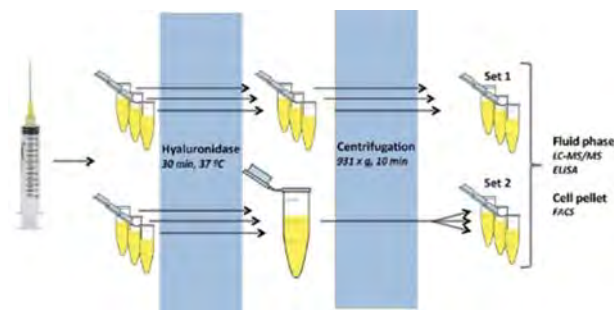
H. Brouwers<sup>1</sup>, J.H. von Hegedus<sup>1</sup>, R.E.M. Toes<sup>1</sup>, T.W.J. Huizinga<sup>1</sup>, M.A. Giera<sup>2</sup>, M. Kloppenburg<sup>1</sup>, A. Ioan-Facsinay<sup>1</sup>. <sup>1</sup>Rheumatology; <sup>2</sup>Center for Proteomics and Metabolomics, Leiden University medical Center, Leiden, Netherlands

**Background:** Synovial fluid (SF) is commonly used for diagnostic and research purposes since it is easily obtained and is thought to represent the local inflammatory environment. Common practice to obtain insight in the disease pathogenesis of arthritic diseases is the characterisation and quantification of synovial fluid cells and the measurement of inflammatory mediators. SF has a complex composition, containing hyaluronic acid which makes the fluid viscous and non-homogeneous, hampering subsequent analyses. Hyaluronic acid can be broken down by the addition of hyaluronidase, however, this is not commonly used in arthritic research.

**Objectives:** To determine the effect of hyaluronidase treatment on quantification and identification of SF cells and soluble mediators.

**Methods:** SF was obtained from twelve arthritis patients after knee aspirations as part of standard clinical care. Nine patients were diagnosed with rheumatoid arthritis, two with osteoarthritis and one with juvenile idiopathic arthritis. For cell analysis, synovial fluid was first centrifuged and the pellet was separated from the fluid. The fluid was subsequently treated with hyaluronidase and centrifuged again to isolate remaining cells. Cell numbers and phenotype were determined using flow cytometry. For soluble mediator measurements, 6–10 aliquots were taken and treated as represented in figure 1 resulting in set 1 and set 2. Set 1 contains replicates taken from SF before hyaluronidase treatment while set 2 mimics replicates which are taken after hyaluronidase treatment. Interleukin (IL)-8 was measured by ELISA and a total of seven fatty acid and oxidised fatty acid levels were determined using LC-MS/MS in all aliquots.

**Results:** Between 0.8%–70% of immune cells (median 5%) are lost when the SF is not treated with hyaluronidase. This percentage is higher for T and B cells: 7%–85% (median 22%) and 7%–88% (median 23%), respectively. To assess the variation between the soluble mediator concentrations in set 1 and set 2, the coefficients of variation (CV) of the replicate measurements were compared. Aliquots in set 2 showed a lower CV for the oxidised lipids 17-HDHA, leukotriene B<sub>4</sub> and prostaglandin E<sub>2</sub> for all patients tested. For IL-8, the oxidised lipid 15-HETE, and fatty acids arachidonic acid (AA), eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), it did not matter whether the aliquots were taken before or after hyaluronidase treatment. While in general the average levels of the soluble mediators tested were comparable between set 1 and set 2, we did observe large differences in IL-8 and AA levels in two independent patients.



**Conclusions:** Up to 70% of the synovial fluid cells are missed in analysis when the SF is not treated with hyaluronidase before cell isolation, leading to erroneous conclusion especially when investigating rare cells populations like antigen specific B or T cells, when searching for novel cell populations, or when correlations are made between clinical parameters and cell numbers. In addition, some cytokine as well as lipid levels determined in SF without hyaluronidase treatment might not accurately reflect their actual concentrations in SF.

**Disclosure of Interest:** None declared

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**SAT0029 IMPACT OF GLUCOCORTICOIDS ON SIRTIUIN 1 EXPRESSION AND PROINFLAMMATORY CYTOKINE PRODUCTION IN RATS WITH ADJUVANT-INDUCED ARTHRITIS**

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**Background:** Sirtuin 1 (SIRT1) is a class III histone deacetylase which could play a critical role in several biological functions including lifespan, stress, and inflammation.

**Objectives:** Our main objective was to evaluate SIRT1 expression in peripheral blood mononuclear cells (PBMCs) isolated from rats with adjuvant induced arthritis (AIA) treated or not with low and high doses of glucocorticoids (GCs). Our second aim was to determine the production of proinflammatory cytokines such as tumour necrosis factor alpha (TNF), interleukin-1 beta (IL-1) and interleukin-6 (IL-6) in tissues (liver and spleen) of these rats, and to assess a potential correlation between SIRT1 expression and the production of cytokines in tissues of rats with AIA treated or not with low and high doses of glucocorticoids.

**Methods:** We performed a study on rats with AIA treated with low and high doses of prednisolone or left untreated. The SIRT1 expression was quantified in PBMCs using western blotting. Levels of proinflammatory cytokines TNF, IL-1 and IL-6 were assessed in liver and spleen from rats with AIA treated with GCs or left untreated using an ELISA assay.

**Results:** SIRT1 expression was increased in PBMCs isolated from rats with AIA treated with LD-GCs and HD-GCs compared to untreated animals. In culture, resveratrol enhanced the SIRT1 expression in PBMCs isolated from rats with AIA in a dose-dependent manner. We observed increased levels of TNF alpha in liver (correlated with SIRT1 expression) and decreased IL-6 levels in spleens (negatively correlated with SIRT1 expression) from rats with AIA treated with LD-GCs and HD-GCs compared to controls.

**Conclusions:** SIRT1 expression is increased in PBMCs isolated from rats with AIA and treated with GCs parallel to decreased levels of IL-6 in spleen and increased levels of TNF in liver. This study shows that the SIRT 1 expression is measurable in circulating PBMCs of rats with AIA and is increased under GC treatment. The potential epigenetic effect of GCs on production of proinflammatory cytokines in tissues, namely liver and spleen, is also studied.

**Disclosure of Interest:** None declared

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**SAT0030 VISFATIN DOWN-REGULATES GROWTH PROMOTING LINC RNA H19 IN OSTEOGENIC DIFFERENTIATION OF MESENCHYMAL STROMAL CELLS**

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**Background:** Destructive bone diseases like osteoarthritis and osteoporosis are causes of chronic pain and disability. Mesenchymal stromal cells (MSC) are key regulators for bone homeostasis due to their potential for osteogenic differentiation, preventing bone loss and promoting tissue repair. Pro-inflammatory factors including adipokines such as visfatin alter the osteogenic potential of MSCs and may contribute to the shift towards adipogenic differentiation observed in osteoporosis. Long non-coding RNA H19 is one of the first lncRNAs discovered and best understood e.g. in embryonic growth and tumour formation. lncRNAs interact directly with DNA, RNA as well as proteins and fill a regulatory gap between the ribonucleic and protein world. H19 upregulation was shown in osteogenic differentiation of MSCs<sup>1</sup>. H19 increases the osteogenic potential by acting as a sponge for miRNA 675, 141 and 22, influencing TGFβ1 and Wnt/β-catenin pathways<sup>2,3</sup>. H19 may hence be involved in MSC mediated bone homeostasis.

**Objectives:** To analyse the link between adipokines and bone remodelling in destructive bone disease. To investigate the influence of adipokines on MSCs and on the expression of lncRNA H19 during osteogenesis.

**Methods:** Commercial human MSCs (hMSC) and primary human MSCs (phMSC) from osteoarthritis patients after knee replacement surgery were treated with differentiation medium to induce osteogenic differentiation (OD). Matrix mineralization was quantified after 21 days of OD by Alizarin Red. Expression of H19

and IL-6 protein production were measured using realtime PCR and ELISA at day 2/7/14 of OD.

**Results:** H19 up-regulation in MSCs during OD could be confirmed in a time dependent manner. Visfatin-stimulation of MSC during OD increased matrix mineralization over time as well as IL-6 production (day 7, 14, 21: 46-, 93-, 78-fold). Visfatin stimulation down-regulated H19 expression up to 10-fold over the course of OD compared to non-stimulated control. The effect was significant in pHMSCs in 2/3 measured time points (day 7,  $p=0.03$ ; day 14,  $p=0.002$ ,  $n=3$ ) and in hMSCs on day 14 ( $p=0.0003$ ,  $n=4$ ).

**Conclusions:** During osteogenic differentiation of MSCs, visfatin showed pro-inflammatory and mineralization promoting effects. However, H19 was significantly down-regulated by visfatin during osteogenic differentiation. This may contribute to the loss of osteogenic potency of MSCs in inflamed tissues with increased visfatin concentration as observed in affected areas of destructive bone disease. Further research to understand the H19 effector mechanisms on osteogenic differentiation and osteogenic potency of MSCs are in progress.

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#### SAT0031 INTERLEUKIN 29 INHIBITS OSTEOCLAST DIFFERENTIATION AND FUNCTION IN RANKL-INDUCED OSTEOCLASTOGENESIS

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**Background:** Interleukin-29 (IL-29) is a new member of the recently discovered interferon (IFN)  $\lambda$  family and known to modulate immune functions of monocyte or macrophage. We have demonstrated that IL-29 is dysregulated in patients with rheumatoid arthritis (RA) and contributes to RA pathogenesis via inducing pro-inflammatory cytokines, chemokines or matrix metalloproteinases production in synovial fibroblasts,<sup>1,2</sup> as well as stimulating inflammation and cartilage degradation in osteoarthritis disease.<sup>3</sup> However, the role of IL-29 in bone resorption is unclear.

**Objectives:** Bone erosion in RA is associated with increased production of pro-inflammatory cytokines and accelerated osteoclastogenesis in affected joints.<sup>4</sup> IL-29 is an important proinflammatory cytokine in RA. We investigated the effect of IL-29 on receptor activator of nuclear factor  $\kappa$ B ligand (RANKL)-induced osteoclastogenesis *in vitro* to determine whether IL-29 can stimulate or attenuate osteoclast-mediated bone resorption that is a hallmark of RA.

**Methods:** The viability and apoptosis of RAW264.7 cells after IL-29 different treatment were assessed by Cell Counting Kit-8 and flow cytometry, respectively. Osteoclasts were generated from RAW264.7 cells, bone-marrow-derived monocyte/macrophage precursor cells (BMMs) and blood-derived human PBMC cells. The effects of IL-29 on osteoclast formation were evaluated by tartrate-resistant acid phosphatase (TRAP) staining and counting the number of TRAP + multinucleated cells. Bone resorption experiment was assessed by pit formation. The expression of key molecules implicated in osteoclastogenesis (TRAP, CTSK, MMP-9, NFATC1 and c-Fos) was measured by real time RT-PCR.

**Results:** Although IL-29 did not show significant effect on the viability and apoptosis of RAW264.7 cells, it inhibited multinucleated cells in the differentiation of murine and human osteoclastogenesis, the bone-resorbing activity of mature osteoclasts. In addition, IL-29 downregulated osteoclast specific genes expression of TRAP, CTSK, MMP-9, NFATC1 and c-Fos.

**Conclusions:** IL-29 inhibits murine and human osteoclastogenesis by a direct mechanism suppressing responses of osteoclast precursors to RANKL. Our findings suggest that IL-29 may play a previously unrecognised role in the osteoclast formation.

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#### SAT0032 MESENCHYMAL STEM CELLS ALLEVIATE EXPERIMENTAL AUTOIMMUNE CHOLANGITIS THROUGH IMMUNOSUPPRESSION MEDIATED BY GALECTIN-9

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**Background:** Mesenchymal stem cells (MSCs) play anti-inflammatory role by secreting some kinds of bioactive molecules. However, the effect of MSCs on chronic autoimmune liver disease, such as primary biliary cholangitis (PBC) and its underlying mechanism remains elusive.

**Objectives:** The aim of this study was to assess the efficacy of UC-MSCs treatment (UC-MSCT) in 2OA-BSA-induced murine autoimmune cholangitis and explore its underlying mechanisms.

**Methods:** UC-MSCs were transplanted into experimental autoimmune cholangitis mice. Biochemical and histological analysis were performed based on the blood and liver tissues. The immunomodulatory effects of UC-MSCs and its cytoprotective function were also investigated.

**Results:** We found that UC-MSCT significantly ameliorated liver inflammation in 2OA-BSA induced autoimmune cholangitis mice, primarily by diminishing Th1 and Th17 responses, and modifying liver chemokine activity. We also found that UC-MSCs significantly repressed the proliferation of CD4 +T cells and suppressed the differentiation of Th1 and Th17 cells, both of which were dependent on galectin-9 (Gal-9). Furthermore, we determined the signal transducer and activator of transcription (STAT) and c-Jun N-terminal kinase (JNK) signalling pathways were involved in the production of Gal-9 in MSCs.

**Conclusions:** The present study shows that UC-MSCs exert profound inhibitory effects on inflammatory responses and that they ultimately alleviate the liver injury in experimental autoimmune cholangitis mice. Further, we demonstrate that UC-MSCs inhibit Th1 and Th17 cell responses as well as aberrant chemokine activity through Gal-9 mediated immunosuppression. Additionally, our research reveals that the induction of Gal-9 in MSCs is mediated by the involvement of the STAT and JNK signalling pathways. These findings may help in the development of stem cell therapies for the treatment of PBC.

**Disclosure of Interest:** None declared

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#### SAT0033 TIME-DEPENDENT RELATIONSHIPS BETWEEN BIOLOGICAL PARAMETERS AND DISEASE ACTIVITY IN SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease characterised by high inter-patient variability of clinical features, pathology, and disease time-course. Relationships between biomarkers and disease remission/relapse cycles are especially complex and poorly understood.

**Objectives:** To investigate the relationship between disease activity and biomarker expression in a longitudinally-followed SLE cohort.

**Methods:** We measured 4 candidate protein biomarkers implicated in SLE (MIF, CCL2, CCL19 and CXCL10) and 13 routinely collected serum and urine biological parameters, and assessed disease activity (SLEDAI-2k) on each clinic visit. We analysed these data by first focusing on the magnitude of expression levels of the 17 biological markers and then on the temporal dimension, to untangle their relationship to disease activity.

**Results:** Data from 843 visits in 110 SLE patients (median age 47, 83% female, 49% Asian ethnicity) were analysed. We demonstrated highly heterogeneous time-dependent relationships between disease activity and the measured



biological markers. Using unbiased magnitude-based hierarchical clustering of biomarker expression levels, we isolated a patient subset (n=9) with distinctively heterogeneous patterns of expression of the 17 biological parameters, compared to the other (n=101) patients who were more homogeneous. The smaller subgroup had significantly higher levels of MIF, CCL2, CCL19 and CXCL10, but the larger subgroup had stronger associations between biological parameters and SLEDAI-2k, based on leave-one-out cross-validated regression analysis. In this subgroup, when we constructed a time-dependent regression model, compared to the equivalent time-agnostic regression model, the biological parameters had significantly stronger predictive power for disease activity, suggesting a time-dependent relationship. To disentangle the effect of magnitude versus temporal correlation, we used dynamic time-warping analysis to align longitudinal clinical and laboratory profiles. This revealed a further subset (n=69) in whom a time-dependent regression model showed significantly stronger associations between biological parameters and disease activity, despite no significant difference in simple magnitude. This subgroup was characterised by lower rates of flare, lower disease activity and lower damage scores, suggesting that this patient cluster is highly clinically meaningful.

**Conclusions:** Using aggregated longitudinal clinical data and samples, we demonstrated significant subgroups of time-dependent relationships between disease activity and biological markers among patients with SLE. These results imply the association between biological parameters and disease activity may exist in a multi-dimensional time-dependent pattern. Longitudinal SLE data presents potential opportunities to identify patient-stratifying biomarker patterns that are concealed when time is not considered. This finding has significant implications for the design of SLE biomarker studies.

**Disclosure of Interest:** None declared

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SAT0034

#### POSSIBLE INVOLVEMENT OF BAFF AND MATRIXMETALLOPROTEINASE-9 IN THE ACTIVATION OF MONOCYTES OF PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME

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**Background:** B cell activating factor belonging to TNF family (BAFF) is well known as a factor which regulates proliferation, differentiation and survival of B cells, and plays a pivotal role in the pathogenesis of primary Sjögren's syndrome (pSS). In our previous study, we found that BAFF significantly enhanced IL-6 production by pSS monocytes and the amount of IL-6 produced by BAFF-stimulated monocytes was positively and significantly correlated with the expression level of a BAFF receptor (BR3). These data collectively suggest that the BAFF signalling through BR3 is involved in activation of monocytes to promote production of inflammatory cytokines, such as IL-6. Matrix metalloproteinase-9 (MMP-9) is well known as one of the enzymes involved in degradation of extracellular matrix (ECM) and mainly produced by activated T cells and monocytes. It has been reported that the concentration of MMP-9 in saliva was significantly higher in pSS patients as compared to healthy controls (HC). Therefore, it is conceivable that MMP-9 is involved in the pathogenesis of pSS through degradation of ECM of salivary glands, which consequently results in decrease in saliva, one of the clinical manifestations of pSS.

**Objectives:** To explore the relationship between BAFF and MMP-9 in the pathogenesis of pSS.

**Methods:** Peripheral monocytes from pSS patients (n=37) and HC (n=19) were prepared by using CD14 +microbeads and cultured *in vitro* in the presence or absence of recombinant human soluble BAFF (rhsBAFF) for 96 hours. The amounts of IL-6 and MMP-9 in the culture supernatants were measured by ELISA. Signal transduction pathways were investigated by exposing rhsBAFF-stimulated pSS monocytes to several inhibitors against NF- $\kappa$ B (BAY11-7082 and BAY11-7085) and PI3 kinase (LY294002). FACS analysis of whole blood samples was performed to investigate the expression levels of BR3 and MMP-9 in monocytes. The expression level of MMP-9 was also analysed by quantitative RT-PCR (qPCR). Serum levels of BAFF and MMP-9 were measured by an electrochemiluminescence assay.

**Results:** Serum levels of BAFF and MMP-9 in pSS patients were significantly higher than those of HC, and the levels showed positive and significant correlation. FACS analysis of whole blood samples demonstrated that MMP-9 was mainly expressed in monocytes and that the expression level was significantly higher in pSS than in HC. ELISA and qPCR revealed that stimulation of pSS monocytes with rhsBAFF drastically enhanced the expression of MMP-9 as compared to normal monocytes. Remarkably, the amount of MMP-9 produced by the cells was positively and significantly correlated with the expression level of BR3 in pSS monocytes, suggesting that BAFF-signalling is involved in the production of MMP-9 by the cells. Moreover, the elevated production of MMP-9 was significantly

suppressed by specific inhibitors against NF- $\kappa$ B and PI3 kinase in a dose dependent manner.

**Conclusions:** The present study suggests that BAFF stimulates monocytes through BR3 to promote MMP9 production and may contribute to ECM degradation. Our study also suggests that NF- $\kappa$ B and PI3 kinase are involved in the pathway.

**Disclosure of Interest:** None declared

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SAT0035

#### THE EFFECTS OF VISFATIN, RESISTIN AND IL-17 ON SYNOVIAL FIBROBLASTS FROM DIFFERENT RHEUMATIC DISEASE BACKGROUNDS

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**Background:** Although rheumatoid arthritis (RA) and psoriatic arthritis (PsA) have several features in common, they also possess distinct differences. We hypothesised that RA and PsA synovial fibroblasts (SF), known key effector cells in the pathophysiology of inflammatory arthritis, differentially respond to various stimuli including adipokines and cytokines and that this may contribute to those differences. For example, IL-17 (also found in synovial tissue) is of particular therapeutic significance in PsA but not as effective in RA. Thus far, IL-17 in its isoform IL-17A has been the major therapeutic target in PsA but IL-17F also plays a role in the IL-23/IL-17 axis of inflammatory diseases.

**Objectives:** Therefore, we analysed the responses of SF from patients with PsA, RA or no rheumatic disease to IL-17A/F $\pm$ TNF- $\alpha$  and the adipokines visfatin and resistin, which show strong expression in the synovium of inflammatory arthritis.

**Methods:** SF were isolated from patients with PsA, RA or non-rheumatic disease controls (N), each undergoing joint surgery. PsASF, RASF and NSF were stimulated with human recombinant IL-17A/F, TNF- $\alpha$ , visfatin, and resistin. A neutralising anti-IL-17A antibody was used to verify specificity of the IL-17A effects. Secretion of the proinflammatory cytokine IL-6 was used as the initial readout parameter and was quantified using a commercial immunoassay.

**Results:** Stimulation with visfatin caused a strong increase in IL-6 secretion in all SF types (n=3 each), while resistin had no effect. Differences in responses were not statistically significant between the SF types studied. IL-17A at concentrations found in serum or synovial fluid did not induce IL-6 secretion in any of the SF. Dose-response curve analysis showed that considerably higher concentrations of IL-17A, which may occur locally in tissue, are required for the induction of IL-6 secretion. An anti-IL-17A antibody abolished the effect, thus showing that the effect is specific for IL-17A. The effects of IL-17A and IL-17F on IL-6 secretion by PsASF could be strongly amplified by a co-stimulation with TNF- $\alpha$  (IL-17A: 5-fold vs 113-fold; IL-17F: 1.7-fold vs 39-fold; TNF- $\alpha$  alone: 12-fold). The effects were stronger for IL-17A than for IL-17F with or without TNF co-stimulation. No effect of IL-17F alone was observed on NSF (n=1).

**Conclusions:** SF from RA and PsA patients were not differentially affected by the adipokines visfatin and resistin or IL-17A when used at serum or synovial fluid concentrations suggesting inflammatory cells to be the primary target of anti-IL-17 therapy. In its use as a therapeutic target, the attribute of IL-17F affecting PsASF would potentially increase the beneficial effects.

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SAT0036

#### NICOTINE PROMOTES MMP-3 AND RANKL SECRETION THROUGH OVEREXPRESSED NICOTINIC ACETYLCHOLINE RECEPTOR A7 IN RHEUMATOID ARTHRITIS FIBROBLAST-LIKE SYNOVIOCYTES

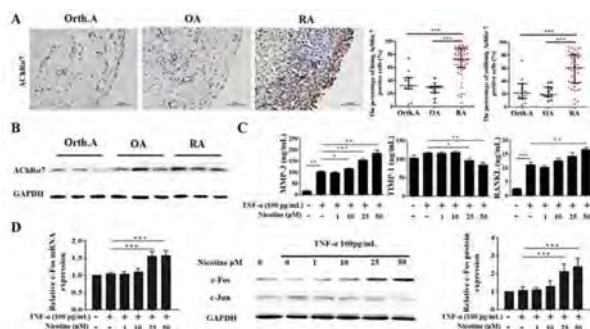
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**Background:** Smoking has been reported not only an established environmental risk factor for developing rheumatoid arthritis (RA), but also a predictor of radiographic progression. Nicotine, the major constituent of cigarette smoke, has been demonstrated inhibitory effect on proinflammatory cytokines through its receptor nicotinic acetylcholine receptor  $\alpha 7$  (AChR $\alpha 7$ ) in RA fibroblast-like synoviocytes (FLS). However, its effects on other function of RA-FLS remain elusive.

**Objectives:** To explore the effect of nicotine on matrix metalloproteinases (MMPs) and RANKL expression from RA-FLS and its possible intracellular signalling mechanism.

**Methods:** Synovial tissues were obtained from 45 patients with active RA as well as 11 osteoarthritis (OA) and 11 noninflammatory orthopaedic arthropathies (Orth.A) patients for control. The expression of AChR $\alpha$ 7 in synovial membrane and cultured FLS were detected by immunohistochemistry staining and Western blot. RA-FLS were treated *in vitro* with different concentration of nicotine and its effect on RA-FLS viability was evaluated by cell counting kit-8. After nicotine pretreatment on TNF- $\alpha$  stimulated RA-FLS, the expression of MMP-2, MMP-3, MMP-9, TIMP-1, TIMP-2, RANKL, and OPG in culture supernatant were measured by ELISA, while the change of AP-1 pathway including c-Fos and c-Jun were detected by quantitative real-time PCR and Western blot.

**Results:** Immunohistochemical analyses showed intense endochylema staining for AChR $\alpha$ 7 mainly in lining layer. The percentage of both lining and sublining AChR $\alpha$ 7 positive cells were significantly higher in RA than that in OA or Orth.A (figure 1A). Further western blot showed significantly higher expression of AChR $\alpha$ 7 in RA-FLS than that in Orth.A-FLS ( $p=0.003$ , figure 1B). Nicotine (0.1  $\mu$ M~50  $\mu$ M) showed no cytotoxicity on RA-FLS proliferation. Pretreatment with 50  $\mu$ M nicotine for 24 hours significantly promoted the secretion of MMP-3 and RANKL but inhibited TIMP-1 secretion in TNF- $\alpha$  stimulated RA-FLS (all  $p<0.05$ , figure 1C). Further, 25  $\mu$ M and 50  $\mu$ M nicotine treatment for 24 hours upregulated both mRNA and protein expression of c-Fos but not c-Jun which indicated that nicotine might activate AP-1 signalling pathway by c-Fos (all  $p<0.05$ , figure 1D).



**Abstract SAT0036 – Figure 1.** Effects of nicotine on the secretion of MMPs, RANKL and OPG as well as AP-1 signalling pathway activation in RA-FLS. A Immunohistochemistry staining for AChR $\alpha$ 7 in RA synovium. The data were representative as median and interquartile range from 45 RA, 11 OA and 11 Orth. A patients. B The expression of AChR $\alpha$ 7 in RA-FLS was measured by Western blot. C After nicotine treatment for 24 hours, the levels of MMP-3, TIMP-1 and RANKL in culture supernatant of TNF- $\alpha$  stimulated RA-FLS were measured by ELISA. D After nicotine treatment for 24 hours, the expression of c-Fos and c-Jun in RA-FLS was measured by quantitative real-time PCR and Western blot. The data were representative as means $\pm$ SD from six different RA patients, \* $P<0.05$ , \*\* $P<0.01$ , \*\*\* $P<0.001$ .

**Conclusions:** Nicotine can promote MMP-3 and RANKL expression through overexpressed AChR $\alpha$ 7 in RA-FLS which might be involved in the pathogenesis of osteogenesis and bone destruction in RA.

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SAT0037

#### IGURATIMOD AMELIORATES BLEOMYCIN-INDUCED ALVEOLAR INFLAMMATION AND PULMONARY FIBROSIS IN MICE BY SUPPRESSING EXPRESSION OF MMP-9

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**Background:** Interstitial lung disease (ILD) occurs in 15% of patients with connective tissue diseases (CTD) It contributes significantly to morbidity and mortality, and is difficult to manage<sup>(1)</sup>. Despite advances in management strategies, CTD-ILD have a significant adverse effect on quality of life and is still a leading cause of mortality, highlighting an urgent need for optimal treatment regimens. It is known that inflammatory cytokines played an important role in alveolitis and the development of pulmonary fibrosis<sup>(2)</sup>. Iguratimod (IGU) has a reported effect on

preventing the inflammatory processes by inhibiting the production of various inflammatory cytokines<sup>(3)</sup>.

**Objectives:** To investigate the potential therapeutic efficacy of IGU on mouse model of bleomycin (BLM) induced pulmonary fibrosis.

**Methods:** A total of 75 C57BL/6 mice were randomly and evenly divided into control group, BLM (5 mg/kg) group, BLM +IGU (90 mg/kg) group, BLM +methylprednisolone (MP, 10 mg/kg) group and BLM +pirfenidone (PF, 100 mg/kg) group. The mice were sacrificed on day7, day 14, day 28 respectively. The lung tissue was examined by Hematoxylin and eosin staining and Masson staining to evaluate the degree of alveolitis and fibrosis, and plasma cytokines were measured.

**Results:** Histopathological results showed that IGU attenuated BLM-induced alveolar inflammation and decreased collagen deposition in lung tissue from day 7 till day 28. Both the pathological alveolitis scores and fibrosis scores in drug treated group (IGU group, MP group and PF group) were decreased dramatically compared with BLM group on day7, day 14 and day 28 respectively ( $p<0.05$ ). There were no statistical significances among those three groups. Cytokine profile showed that IGU decreased the level of tumour necrosis factor- $\alpha$  (TNF- $\alpha$ ), interleukin (IL)-1, IL-6 and matrix metalloproteinase (MMP)-9 which were up-regulated by BLM on day 7, day 14 and day 28 respectively ( $p<0.05$ ). Furthermore, there is a strong correlation between the severity of the pulmonary fibrosis and the plasma MMP-9 levels ( $r=0.836$ ,  $p<0.001$ ).

**Conclusions:** IGU was effective in suppressing BLM-induced alveolar inflammation and pulmonary fibrosis, and it has the equal anti-inflammatory and anti-fibrotic effects as MP or PF. The therapeutic effects by IGU may be attributed to the inhibition of MMP-9 either directly or indirectly. Therefore, IGU presents as a promising agent for pulmonary fibrosis treatment.

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**Disclosure of Interest:** None declared

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SAT0038

#### MEMBRANE-ASSOCIATED AMPD2, A NOVEL REGULATOR IN SHIFTING THE BALANCE BETWEEN EXTRACELLULAR ATP AND ADENOSINE?

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**Background:** Extracellular ATP and adenosine are potent immunomodulatory molecules that accumulate in states of inflammation. ATP/ADP are released from damaged or stressed cells and sequentially catabolized to AMP which is then catabolized to adenosine by the action of the ectonucleotidases CD39 and CD73, which drives a shift from an ATP-driven proinflammatory environment to an anti-inflammatory milieu induced by adenosine. Intracellularly, AMPD2 which encodes one of three known AMP deaminase homologs executes AMP deamination to IMP thereby reducing the formation of adenosine. Here, we postulate that this mode of action is also present on the cell surface of immune cells, which may lead to an increased state of inflammation such as found in chronic inflammatory diseases.

**Objectives:** Therefore, we analysed surface AMPD2 expression and its modulation on distinct human cell lines and primary human immune cells.

**Methods:** To this end, surface AMPD2 expression was evaluated on cell lines (THP1, Jurkat, HMEC1, and HEK293), human PBMCs and isolated monocytes by flow cytometry. Moreover, co-expression of surface AMPD2, CD73 and CD39 has been analysed on PBMCs and isolated monocytes. Association of surface AMPD2 and cell death was visualised using annexin V and 7-AAD staining and examined by flow cytometry. In addition, expression of AMPD2 was analysed by immunoblot of precipitated AMPD2 from membrane fractions and by mass spectrometry after precipitation from membrane fractions and from biotinylated surface-molecules using the surface AMPD2 positive cell line HEK293.

**Results:** Here, we demonstrate that (i) surface AMPD2 is present on T cells and monocytes in PBMCs from healthy donors, (ii) that LPS enhances surface expression of AMPD2 in PBMCs on both cell populations after 24 hour, (iii) that LPS also enhances surface expression of AMPD2 in isolated monocytes, (iv) that surface AMPD2 does not correlate to the expression of the ectonucleotidases CD39 and CD73 and (v) that all cell lines analysed are capable of expressing surface

AMPD2. Using HEK293, surface AMPD2 expression was reduced after Golgi transport inhibition. AMPD2 surface expression was not accompanied by enhanced cell death. Expression of AMPD2 could be confirmed in membrane fractions of HEK293 using immunoblot of precipitated AMPD2 and mass spectrometry, respectively.

**Conclusions:** Here, we demonstrate for the first-time surface expression of AMPD2 on immune cells enabling these cells to extracellularly convert AMP into IMP constituting a shunt-like mechanism to control the levels of adenosine and extracellular ATP formed from adenine nucleotides thereby controlling immunomodulation.

**Disclosure of Interest:** None declared

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SAT0039

### LL37 UP-REGULATION AND ANTI-LL37 REACTIVITY ARE SHARED BY PSORIASIS AND PSORIATIC ARTHRITIS PATIENTS

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**Background:** The antimicrobial peptide LL37 plays a pathogenic role in psoriasis (Pso) due to its adjuvant and auto-antigenic properties. At least a third of Pso patients develop psoriatic arthritis (PsA) but mechanisms that lead PsA development in Pso patients remain elusive.

**Objectives:** To understand the role of LL37 in PsA pathogenesis and its relationship with inflammatory molecules IFN $\alpha$ , GMCSF, C5a.

**Methods:** Blood samples were collected from 32 biologic-naïve PsA, 12 active Pso (without PsA) patients and 8 healthy donors (HD). Synovial fluids (SF) were collected from 17 PsA and 12 osteoarthritis (OA) patients. Synovial biopsies from 3 biologic-naïve PsA patients were studied by confocal microscopy. Native-LL37 was synthesised and carbamylated LL37 (LL37carb) produced by incubating LL37 with 1 M potassium cyanate and verified by dot-blot assay. Antibodies to native-LL37/LL37carb and levels of LL37, GMCSF, IFN $\alpha$  and complement C5a were measured by in-house and commercial ELISA tests, respectively, in SF and plasma.

**Results:** High LL37 levels were detectable in SF of PsA compared to OA. Anti-LL37 [24% in SF (4/17)] and anti-LL37carb antibodies [47% in SF (8/17), 46% in plasma (15/32)] were present in PsA but not in OA and HD. Anti-LL37carb antibodies [41% (5/12)] were also detectable in Pso plasma. IFN $\alpha$  was present in 37% of SF PsA (7/16; not detectable in OA) and correlated with C-reactive Protein (CRP); GMCSF and C5a levels were significantly higher in SF PsA than in SF OA. Notably, GMCSF was also detectable in 40% and 30% of PsA and Pso plasma, respectively, but not in HD; Plasma C5a levels were comparable between PsA and Pso and significantly higher than in HD. SF GMCSF correlated with anti-LL37carb autoantibodies. Anti-LL37carb antibodies correlated with levels of C5a in Pso and PsA plasma. In synovial tissues of PsA the expression of the IFN-related gene MX1 was highly up-regulated in close proximity of neutrophil markers myeloperoxidase and LL37.

**Conclusions:** LL37 and, in particular, LL37carb is the target of autoantibodies that correlate with pro-inflammatory GMCSF and C5a in both Pso and PsA, suggesting immunological pathways in common between psoriasis and psoriatic arthritis.

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**Disclosure of Interest:** None declared

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SAT0040

### SAFETY, TOLERABILITY, PHARMACOKINETICS AND PHARMACODYNAMICS OF BCD-089, NOVEL MONOCLONAL ANTI-IL-6 RECEPTOR ANTIBODY: RESULTS FROM THE FIRST-IN-HUMAN SINGLE DOSE ESCALATION STUDY IN HEALTHY VOLUNTEERS

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**Background:** BCD-089 is a fully human monoclonal antibody targeting membrane-bound and soluble forms of IL-6R $\alpha$ , thereby blocking of IL-6 classic and trans- signalling. IL-6, a proinflammatory cytokine, plays a central role in the pathogenesis of many chronic inflammatory and autoimmune diseases. Thereby inhibition of IL-6 signalling is a promising approach in the treatment of immune-mediated pathology.

**Objectives:** To assess safety, immunogenicity, pharmacokinetics and pharmacodynamics of a single administration of BCD-089.

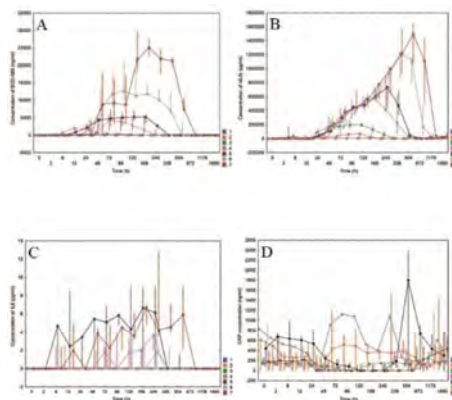
**Methods:** This was a phase I, open label, single ascending dose clinical study in healthy male volunteers, aged 22–37 years (n=19). In 1 st cohort, one «sentinel» volunteer received 0.006 mg/kg of BCD-089. Volunteers in cohorts 2–7 received single doses of BCD-089 0.3, 0.625, 1.0, 1.6, 2.2 and 2.9 mg/kg, respectively. Every next cohort was included after completed safety evaluation for the previous one. Safety, PK/PD and immunogenicity were assessed during 71 days follow up.

**Results:** All enrolled subjects have completed follow up period of 71 days. No withdrawals occurred. Single SC administration of BCD-089 was well tolerated and showed good safety profile at all tested doses: no grade 3/4 AEs, SAEs, DLTs or allergic reactions were reported in any cohort. None of the volunteers developed ADA to BCD-089. The only AEs reported were grade 1 or 2 laboratory abnormalities.

**Abstract SAT0040 – Table 1.** Subjects with abnormal test results, n (%). Table shows only cohorts where at least one abnormal test result was reported.

Adverse events	0.3 mg/kg (n=3)	0.625 mg/kg (n=3)	1.0 mg/kg (n=3)	2.2 mg/kg (n=3)	2.9 mg/kg (n=3)
Grade 1 WBC decrease	-	-	1 (33.3%)	2 (66.6%)	1 (33.3%)
Grade 1 neutropenia	-	-	1 (33.3%)	1 (33.3%)	-
Grade 2 neutropenia	-	-	-	1 (33.3%)	1 (33.3%)
Grade 2 t.bilirubin increase	-	1 (33.3%)	-	-	-
Grade 1 AST decrease	1 (33.3%)	-	-	-	-
Grade 1 Creatinine decrease	-	1 (33.3%)	-	-	-

Single SC administration of BCD-089 had a dose-dependent PK: the drug became detectable in the serum within the first 12 hour after injection for all tested doses (2–8 hour for doses>1.0 mg/kg). Serum concentration dose-proportionally increased and reached maximum at day 3 after administration, then gradually decreased. Elimination half-life showed significant inter-personal variability and dose-dependency, reflecting non-linear PK typical for drugs with target-mediated disposition.



**Abstract SAT0040 – Figure 1.** BCD-089(A), sIL6R(B), IL6(C) and CRP(D) serum concentration (Median and IQR).



The concentration of soluble IL-6 receptor increased after BCD-089 administration in a dose-dependent manner. A raise in the concentration of IL-6 was seen at doses >1.0 mg/kg. Membrane IL-6R saturation of 90%>100% was seen at doses  $\geq$ 0.6 mg/kg. Regardless to the dose, serum CRP decreased below the limit of detection in most volunteers within the first week after injection. All tested PD markers returned to baseline at the end of the follow-up.

**Conclusions:** Single SC administration of BCD-089 was well tolerated, showed favourable safety profile and low immunogenicity at all tested doses in healthy volunteers. PK/PD assessment revealed non-linear PK and significant capacity to inhibit the IL-6 signalling pathway. These findings support further clinical development of BCD-089.

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SAT0024

### IL-36 AXIS IS AN EMERGING THERAPEUTIC TARGET IN PSORIATIC ARTHRITIS SYNOVIAL TISSUE

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**Background:** The IL-36 family of cytokines includes three agonists, IL-36 $\alpha$ , IL-36 $\beta$  and IL-36 $\gamma$ , and two established or hypothetical antagonists, respectively IL-36Ra and IL-38. IL-36 agonists are pro-inflammatory cytokines highly expressed in skin and involved in the pathogenesis of psoriasis. A recent study demonstrated that only a subset of patients with rheumatoid arthritis (RA) had an elevated IL-36 agonists/antagonists ratio within the synovium and could potentially respond to IL-36 inhibition strategies but little is known about the expression and biologic functions of the IL-36 axis in synovial tissue of psoriatic arthritis (PsA) so far hardly been studied.

**Objectives:** In this study, we aimed to comparatively investigate the expression and role of IL-36 cytokines in synovial tissue of early RA and PsA patients.

**Methods:** Synovial tissue samples were collected from patients with early RA and PsA (disease duration <12 months) DMARDs (Disease Modifying Anti-Rheumatic Drugs) and steroids-naïve. All patients underwent an ultrasound-guided synovial biopsy before starting the treatment; the procedure was repeated following six months of treatment with conventional DMARDs. The expression of IL-36 family members was investigated in synovial tissue at gene level by RNA-Sequencing (87 RA, 15 PsA), at protein level by immunohistochemistry (IHC) and immunofluorescence (IF) (20 RA, 26 PsA) and in plasma by ELISA (22 RA, 38 PsA). RA and PsA-fibroblasts-like-synoviocytes (FLS) and peripheral blood mononuclear cells (PBMCs) were treated *in vitro* to assess their response to IL-36 stimulation.

**Results:** Gene and protein expression of IL-36 agonists was comparable between RA and PsA synovial tissue; conversely, the antagonists IL-36Ra and IL-38 were significantly lower in PsA compared to RA. Accordingly, the agonists/antagonists ratio was considerably higher in PsA synovium, suggesting an activation of the IL36 pro-inflammatory pathway. Among the immune cells infiltrating the PsA synovium, macrophages (CD68+), T lymphocytes (CD3+) and plasma cells (CD138+) were the primary IL36 $\alpha$ -expressing cells. At baseline, the synovial expression of IL-36 $\alpha$  was significantly higher in PsA patients who did not respond to DMARDs treatment at 12 months; this differential synovial expression of IL-36 $\alpha$  between responders and non-responders was also maintained at six months. In keeping with this observation, we showed that treatment with methotrexate or sulfasalazine did not reduce the expression of IL-36 in PsA cells *in vitro*. Finally, we observed that PsA-FLS and PsA-PBMCs produced significantly higher levels of IL-8 upon stimulation with IL-36 $\alpha$  in comparison with cells isolated from RA patients.

**Conclusions:** The expression of the anti-inflammatory IL-36 cytokines antagonists are differently regulated in early RA and PsA, being significantly lower in the latter. Moreover, the pro-inflammatory IL-36 $\alpha$  is up-regulated in synovial tissue of PsA non-responders to conventional DMARDs. The impaired balance between agonists and antagonists might contribute to the persistent inflammation characterising the diseased tissue. The exogenous replacement of the IL-36 antagonists may be a novel promising therapeutic target for PsA patients.

**Disclosure of Interest:** None declared

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SAT0025

### CXCL4 ALTERS TRANSCRIPTOMIC AND EPIGENETIC IMPRINTING OF DENDRITIC CELLS THEREBY DRIVING FIBROSIS THROUGH EXTRACELLULAR MATRIX FORMATION

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**Background:** Aberrant accumulation of extracellular matrix (ECM) in multiple organs or fibrosis is one of the three hallmarks that characterises the pathogenesis of systemic sclerosis (SSc), together with immune dysregulation and small vessel vasculopathy. Recent studies have shown that CXCL4 (Chemokine CXC motif ligand 4) levels are increased in patients with SSc and correlated with skin and lung fibrosis.<sup>1</sup> CXCL4 plays key role in physiological processes, although it has been also implicated in several pathological conditions such as autoimmune diseases and cancer. We and others have shown that CXCL4 modulates the phenotype and function of immune cells<sup>2</sup>, suggesting a critical role of this chemokine in innate and adaptive immune responses. However, how CXCL4 exactly modulates immune cell responses remains unclear.

**Objectives:** Here we investigated the impact of CXCL4 exposure on the transcriptome and DNA methylation of monocyte-derived dendritic cells (moDCs), and the consequence on their function.

**Methods:** We differentiated human moDCs in the presence of CXCL4. After 6 days differentiation, cells were stimulated with a TLR3 ligand (polyI:C) as described in our previous study.<sup>2</sup> RNA sequencing and DNA methylation profiling was performed at various time points during differentiation and stimulation.

**Results:** Integration of high-throughput analyses of RNA sequencing and DNA methylation reveals that CXCL4 drives to dramatic changes on the transcriptome and epigenome levels. This is reflected in the dysregulation of critical innate and adaptive immune pathways, like antigen presentation, and cytokine signalling. For the first time, we show that CXCL4 potentiates a novel function to dendritic cells, namely, the production of ECM molecules, such as fibronectin (FN1) and osteopontin (OPN). Furthermore, we also found that CXCL4 exposure results in epigenetic imprinting during moDC differentiation. Using novel bioinformatic methods, we have found that CXCL4 mediates the altered cell function via key transcriptional regulators.

**Conclusions:** This study provides better understanding how CXCL4 affects moDCs through several immune and non-immune pathways and shows for the first time the direct implication of CXCL4 on the production of ECM by inflammatory cells, thereby underscoring the pivotal role of CXCL4 in inflammatory and fibrotic conditions such as SSc.

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SAT0041

### COMPARISON OF DIFFERENT TYPE 1 IFN SIGNATURES DEMONSTRATES CONCORDANCE IN A REAL WORLD, HOME MONITORED SYSTEMIC LUPUS ERYTHEMATOSUS COHORT

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**Background:** Type 1 Interferon (IFN) expression has been shown to correlate with disease severity in systemic lupus erythematosus (SLE) patients<sup>1</sup> and anti-IFN biologics are being evaluated in a clinical setting.<sup>2</sup> The 4-gene IFN response signature of IFI27, IFI44, IFI44L and RSAD2<sup>2</sup> is frequently used to determine IFN expression. However, numerous studies have reported on the use of different gene signatures.<sup>3, 4, 5</sup> The impact of using different IFN gene signatures to stratify SLE patients is unclear.

**Objectives:** The present study compares the relative performance of 4 IFN gene signatures in a cohort of 687 participants with self-reported SLE.

**Methods:** A centralised site, IRB-approved, SLE cohort was recruited using social media. Qualified participants with self-reported SLE were consented electronically and asked to provide medical record review consent, complete an online questionnaire regarding their disease as well as provide 3 fingerstick blood samples over approximately a 6 week period. Blood samples from 687 participants were tested using a multi-modular gene expression assay containing 11 IFN response genes (primarily from the IFN- $\alpha$  response pathway). Normalised gene expression values were calculated, and the resulting data analysed to determine concordance between IFN gene signatures.

**Results:** 10 of the 11 IFN response genes were highly correlated with one another ( $\rho \geq 0.80$ ). The 4-gene signature of IFI27, IFI44, IFI44L, and RSAD2<sup>2</sup> identified 36.5% of the participants as IFN high. Three other literature reported IFN signatures<sup>3, 4, 5</sup> provided similar classification results with participants being assigned to the same IFN sub-group over 90% of the time, and nearly identical patient distributions.

Abstract SAT0041 – Table 1

Signature	Genes	IFN High (%)	IFN Low (%)	% Agreement (95% CI) to Furie et al.
Furie et al. <sup>2</sup>	IFI27, IFI44, IFI44L, RSAD2	36.5	63.5	N/A
Niewold et al. <sup>3</sup>	EIF2AK2, IFIT1, MX1	36.3	63.7	94.8% (93.4–95.9)
Kirou et al. <sup>4</sup>	EIK2AK2, IFIT1, IFI44	36.0	64.0	95.1% (93.7–96.2)
Westra et al. <sup>5</sup>	IFI6, HERC5, IFIT1, MX1	36.0	64.0	94.8% (93.4–95.9)

**Conclusions:** The study demonstrated that commonly used IFN gene signatures provide similar IFN subtyping to the 90th percentile. The use of social media to engage patients directly along with self-collection of blood samples provides new opportunity for testing clinical study participants and potentially patients without requiring an office visit.

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**Disclosure of Interest:** M. Abedi Shareholder of: DxTerity, Employee of: DxTerity, F. Flores Employee of: DxTerity, P. Naranatt Employee of: DxTerity, J. Spangler Employee of: DxTerity, L. Pan Employee of: DxTerity, R. Terbrueggen Shareholder of: DxTerity, Employee of: DxTerity

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#### SAT0042 EVIDENCE OF NETOSIS IN CIRCULATING NEUTROPHILS AND SKIN LESIONS WITH VASCULITIS AND PANNICULITIS IN BEHÇET'S DISEASE

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**Background:** Behcet's disease (BD) pathophysiology is poorly understood. It is characterised by recurrent episodes of acute inflammation consisting of neutrophil infiltration in affected organs and around blood vessels. Recently, NETosis, trapping and killing pathogens by activated neutrophils, has been described. These Neutrophil Extracellular Traps (NETs) were shown to promote inflammation in a number of autoimmune diseases such as Systemic Lupus Erythematosus, ANCA-Associated Vasculitis and Rheumatoid Arthritis. We hypothesise that in BD, neutrophils trigger inflammation and vasculitis via NETosis.

**Objectives:** The aim of this study is to demonstrate the implication of NETosis in the pathophysiology of this disease.

**Methods:** Blood specimens from BD patients and matched healthy volunteers were collected at the American University of Beirut Medical Centre. Circulating neutrophils were isolated and cultured in Roswell Park Memorial Institute (RPMI) 1640 medium. Cultured cells were treated with colchicine, dexamethasone or corresponding vehicle, and stimulated with serum from BD patients, controls or left unstimulated. The kinetic and amount of NET formation was assessed by cell counting using Hoechst 33 342 and Sytox green staining and fluorescent microscopy. Moreover, previously described NET-bound proteins (elastase, myeloperoxidase, citrullinated histone-3 and PR-3) were identified by immunolabeling and mRNA expression levels of PAD4, a key enzyme that promotes citrullination of arginine residues on chromatin, was evaluated in neutrophils from BD compared to controls. Finally, evidence of NETosis *in vivo* was assessed on paraffin embedded specimens from damaged organs of BD patients using immunolabeling and confocal microscopy.

**Results:** The percentage of unstimulated neutrophils undergoing NETosis *in vitro* was significantly higher in BD patients compared to controls. Treatment of unstimulated BD neutrophils with colchicine and dexamethasone resulted in significant decrease in NETs formation compared to controls. Interestingly, the percentage of NETs increased upon exposure of neutrophils to serum from BD patients. Moreover, PAD4 mRNA expression was 3 times higher in BD patients compared to controls. Immunolabeling assay demonstrated that NET-bound proteins were present in NETs scaffold of unstimulated neutrophils from BD patients *in vitro*. Additionally, NETs were detected in skin tissues of BD patients focally distributed in proximity to small vessels in vasculitis patients and to inflamed adipose tissue in panniculitis patients. These were associated with elastase and citrullinated histone-3 proteins.

**Conclusions:** We show here for the first time that circulating neutrophils from BD patients are prone to NETosis *in vitro*. NET formation was inhibited by the addition of colchicine and dexamethasone reflecting their therapeutic benefits in BD. The increase of NETosis upon serum stimulation suggests the presence of soluble factors and cytokines triggering NETs in BD. Combined, these results suggest a major role of NETs in the pathophysiology of BD.

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**Disclosure of Interest:** None declared

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#### SAT0043 IL-33/ST2-MEDIATED INFLAMMATION IN ENDOTHELIAL CELL IS DIRECTLY AGGRAVATED BY IL-6 DURING LUPUS NEPHRITIS

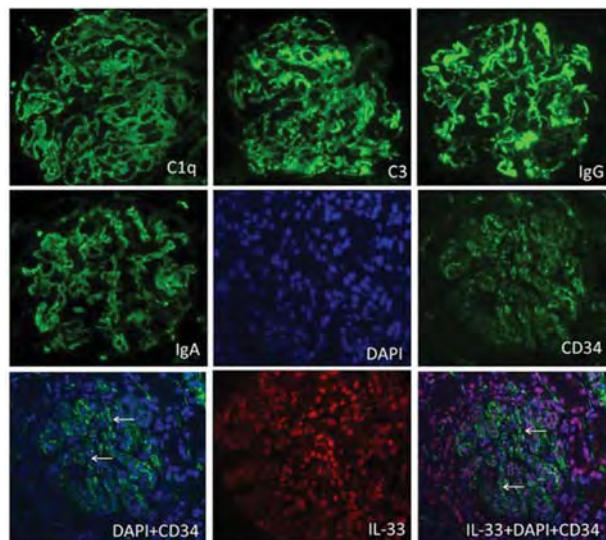
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**Background:** "Alarmins" are prototypic endogenous pro-inflammatory factors as they are released from necrotic cells and provoke local damage or systemic inflammation. Evidences are accumulating to support the inclusion of "Alarmins" as targets of autoreactivity as well as inducers in the pathogenesis of Systemic Lupus Erythematosus (SLE). Interleukin (IL)-33 is a novel member of the family of "Alarmins" because of its characteristics and functions in mediating host immune responses. On this background, we sought to determine the role of IL-33/ST2 axis in lupus pathogenesis. The role of IL-33/ST2 axis has not previously been described in lupus nephritis.

**Objectives:** This project will study the followings:<sup>1</sup> To determine whether IL-33 was present in renal glomerular endothelial cells;<sup>2</sup> To assess the functional and intracellular signal transduction mechanisms regulating the link between IL-33/ST2-mediated innate immunity and inflammation in human umbilical vein endothelial cells (HUVECs).

**Results:** This study, for the first time, showed that IL-33 was pathologically expressed in the kidney tissue of patients with lupus nephritis and not in that of subjects with relative normal renal tissues from atrophy. However, no significant difference was observed between patients with lupus nephritis and kidney cancer. Immunofluorescence (IF) for IL-33 in kidney was performed in lupus patients. IL-33 was clearly seen in glomeruli and also in peritubular areas. To determine whether the IL-33 staining in glomeruli area was in endothelium, multiple staining for IL-33, CD34 (a marker for endothelial cells) and 4',6-diamidino-2-phenylindole

(DAPI) stained for cell nuclei was performed. Co-localization of IL-33 and DAPI in CD34 positive cells demonstrates IL-33 staining in the nucleus of glomerular endothelial cell of lupus kidney. Expression of intracellular but not surface ST2 was increased in plasmacytoid dendritic cells/pDC (CD16-CD14-CD85k+CD123+) of lupus patients when compared with healthy controls. Incubation of HUVECs with IL-33 and/or IL-12 increased the production of IL-6, but IL-4, IL-5, IL-6, IL-13 and TNF- $\alpha$  was not produced.



**Conclusions:** As a result of external stimuli or infection, renal glomerular endothelial cells undergo cellular death and release the "Alarmin", IL-33, to alert the lupus immune system. Released IL-33 interact with their target cells, pDC via their specific receptor ST2 to subsequently induce innate and adaptive responses, activate inflammatory pathways in the pathogenesis of lupus nephritis.

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**Disclosure of Interest:** None declared

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SAT0044

#### LIN28A IS OVEREXPRESSED IN OSTEOARTHRITIS AND IS ESSENTIAL FOR THE STABILITY AND HIGH LEVEL EXPRESSION OF IL-6 AND COX-2 IN HUMAN CHONDROCYTES

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**Background:** Osteoarthritis (OA), the most common type of joint disease, is characterised by progressive and irreversible degradation of articular cartilage. Dysregulated gene expression has also been linked to disease pathogenesis. Lin28A is an evolutionarily conserved RNA binding protein and known to play a critical role in development, metabolism and tumorigenesis. However, the role of Lin28A in osteoarthritis is not yet explored.

**Objectives:** To study the role of Lin28A in the regulation of genes associated with OA pathogenesis in human chondrocytes.

**Methods:** Primary human chondrocytes were isolated from the undamaged portion of the knee OA cartilage by enzymatic digestion and were cultured in DMEM/F12% and 10% FCS. Total RNA from cartilage explants or chondrocytes was prepared using Trizol and was made DNA-free by on-column digestion method. mRNA expression levels of Lin28A, Lin28B, MMP-13, IL-6, COX2 and iNOS were quantified by TaqMan assays. Protein expression was analysed by immunoblotting using validated antibodies. Nucleofection was used for the siRNA mediated depletion or plasmid mediated overexpression of Lin28A gene was used to study its role in chondrocyte function under pathological conditions. RNA immunoprecipitation (RIP) with anti-Lin28A antibody was performed to identify the interacting mRNA partners. Stability of the mRNAs was determined by Actinomycin-D chase experiments.

**Results:** Human OA cartilage samples (n=6) analysed were found to express Lin28A but not Lin28B transcripts. Lin28A mRNA expression was significantly high in the damaged OA cartilage compared to the smooth cartilage from the same patient (n=3, p<0.05). Stimulation with IL-1 $\beta$  induced the high levels of Lin28A mRNA and protein expression in OA chondrocytes in a time dependent as

well as dose dependent manner. siRNA mediated depletion of Lin28A expression in OA chondrocytes inhibited the IL-1 $\beta$ -induced expression of MMP-13, IL-6, COX2 and iNOS mRNAs. Importantly, the overexpression of Lin28A induced the expression of MMP-13, IL-6, COX-2 and iNOS mRNA and protein in OA chondrocytes. Immunoblotting analysis showed that the Lin28A depleted OA chondrocytes treated with IL-1 $\beta$  also produced significantly low levels of IL-6, MMP-13 and COX-2 protein compared to chondrocytes transfected with scrambled siRNAs (n=3, p<0.05). RIP analyses in IL-1 $\beta$  treated OA chondrocytes with anti-Lin28A antibody revealed that the MMP-13, IL-6 and COX2 mRNAs were pulled down with anti-Lin28A and were highly enriched when compared with the mRNA population pulled down by isotype control antibody. siRNA mediated depletion of Lin28A expression resulted in decreased half-life of IL-6 and COX-2 mRNAs, while the overexpression of Lin28A had the opposite effect in IL-1 $\beta$  stimulated OA chondrocytes. This indicated that Lin28A contributes towards the stability of IL-6 and COX-2 mRNAs.

**Conclusions:** Our data for the first time demonstrate that Lin28A plays a key role in OA pathogenesis by stabilising the expression of catabolic gene transcripts in human chondrocytes under pathological conditions. These data revealed a previously unidentified role of Lin28A in chondrocytes and identify it as a potential therapeutic target for the treatment of OA.

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SAT0045

#### DNA METHYLATION OF SOCS3 AS A POSSIBLE MECHANISM FOR PERSISTENT URATE INDUCED INFLAMMATION

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**Background:** Hyperuricemia is a metabolic condition associated with cardiovascular diseases.<sup>1</sup> However, mechanisms for a causal relation have not been fully elucidated yet. Previously, we showed that monocytes primed with urate show a shift in the balance of cytokine production: increased proinflammatory cytokines and decreased levels of IL-1 receptor antagonist.<sup>2</sup>

**Objectives:** In this study we investigate if these changes to urate exposure are persistent and whether changes in DNA methylation serve as a molecular substrate for these effects of hyperuricemia.

**Methods:** DNA methylation was assessed in whole blood of 80 individuals of Maori ancestry with varying serumurate levels. Human PBMCs and monocytes from Dutch healthy volunteers were isolated and pretreated for 24 hour with urate. Cells were either directly stimulated with LPS or LPS/MSU or subjected to increasing resting days before restimulation. Cytokine levels were determined in supernatants by ELISA. SOCS3 mRNA levels were determined by qPCR after 24 hour urate priming. Phosphorylation of STAT3 was assessed after stimulation by flow cytometry with intracellular staining for pSTAT3.

**Results:** Human PBMCs primed with urate demonstrated increased IL-1 $\beta$  and IL-6 responses and decreased IL-1Ra production compared to controls. Although IL-1 $\beta$  production was diminished after increasing resting days, persistent effects were observed for the reduction of IL-1Ra and induction of IL-6. To investigate whether these persistent changes were mediated by epigenetic changes, differences in DNA methylation between normouricemic and hyperuricemic individuals were assessed. SOCS3 gene was higher methylated at 3 neighbouring SOCS3 intragenic positions in hyperuricemic individuals. *In vitro*, SOCS3 mRNA levels were significantly increased in monocytes after 24 hour urate treatment. Moreover, urate dose-dependently suppressed the phosphorylation of STAT3 after stimulation.

**Conclusions:** In this study we demonstrated that urate has persistent proinflammatory effects on human monocytes. Higher SOCS3 DNA methylation is observed in hyperuricemic individuals. *In vitro*, urate priming leads to increased levels of SOCS3 mRNA and consequently suppression of STAT3 phosphorylation. Interestingly, STAT3 inhibition has been reported to mediate IL-1Ra downregulation.<sup>3</sup> Therefore, we hypothesize urate induced inflammation is at least partly mediated by changes in methylation of the SOCS3 gene. However, further validation of this pathway is needed to elucidate possible targets for therapy.



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SAT0046

### TRANSCRIPT-PROTEIN ASSOCIATIONS IN EARLY RA PATIENTS ACHIEVING SUSTAINED DRUG-FREE REMISSION AFTER TREATMENT WITH TOCILIZUMAB

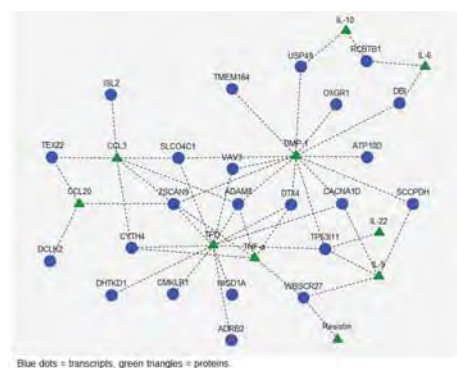
X.M. Teitsma<sup>1</sup>, J.W. Jacobs<sup>1</sup>, A.N. Concepcion<sup>1</sup>, A. Pethö-Schramm<sup>2</sup>, M.E. Borm<sup>3</sup>, J.M. van Laar<sup>1</sup>, J.W. Bijlsma<sup>1</sup>, F.P. Lafeber<sup>1</sup>. <sup>1</sup>Rheumatology and Clinical Immunology, UMC Utrecht, Utrecht, Netherlands; <sup>2</sup>F Hoffmann-La Roche, Basel, Switzerland; <sup>3</sup>Roche Nederland BV, Woerden, Netherlands

**Background:** In disease modifying anti-rheumatic drug (DMARD)-naïve early rheumatoid arthritis (RA) patients, we previously identified networks of differentially co-expressed genes associated with achieving sustained drug-free remission (sDFR).<sup>1</sup> A better understanding of processes involved with translation of mRNA into proteins might be used to develop personalised treatment for early RA patients.

**Objectives:** To identify inflammatory proteins associated with achieving sDFR by performing multi-analyte profiling in pre-treatment serum and subsequently to study significantly enriched biological pathways and compare these with the pathways previously found in the transcriptomic analyses.

**Methods:** In this exploratory study, baseline serum was analysed of 24 patients (n=13 achieved sDFR, n=11 controls) treated-to-target with tocilizumab (TCZ) therapy in the U-Act-Early trial. TCZ (intravenously, 8 mg/kg) was given every 4 weeks; if no remission, hydroxychloroquine (HCQ) was added and if subsequently remission was still not achieved, HCQ was replaced by (oral) methotrexate. Thereafter, if the target, remission, still was not achieved, patients switched to standard of care (e.g. tumour necrosis factor inhibitor). Provided remission persisted, therapy was tapered and subsequently discontinued. sDFR was reached when patients remained  $\geq 3$  months in remission while being drug-free until the end of the study period; those not able to discontinue therapy were selected as controls. Luminex<sup>®</sup> multi-analyte profiling (xMAP<sup>®</sup>) was used to measure 85 inflammatory proteins; partial least square discriminant analyses (PLS-DA) was applied to identify relevant proteins associated with achieving sDFR.

**Results:** No significant differences in clinical baseline characteristics were found between those achieving sDFR vs controls ( $p > 0.05$ ). PLS-DA identified 14 proteins of which 6/14 (n/N) were associated with a decreased chance of achieving sDFR. The protein considered most important (i.e. highest variable on importance (VIP) score) was chemokine (C-C motif) ligand 20 (CCL20, VIP 1.49). In total, 88 significantly enriched Gene Ontology (GO) terms were identified analysing the proteins; 5 terms, of which "positive regulation of leukocyte migration" ( $p < 3.41 \times 10^{-2}$ ) and "leukocyte chemotaxis" ( $p < 3.49 \times 10^{-3}$ ) were found in both proteomic and transcriptomic analyses. Significant transcript-protein correlations are shown in figure 1; the TIMP metalloproteinase inhibitor 1 (TIMP-1) protein showed the highest number (n=12) of correlations.



**Abstract SAT0046 – Figure 1.** Network visualisation of significant transcript-protein correlations.

Blue dots=transcripts, green triangles=proteins.

**Conclusions:** Several relevant proteins were found associated with achieving sDFR after treatment with TCZ. When performing pathway analyses, several enriched pathways within the protein biomarkers were also previously identified in the transcriptomic analyses, providing further insight into gene expression and translation of inflammatory proteins in early RA patients.

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SAT0047

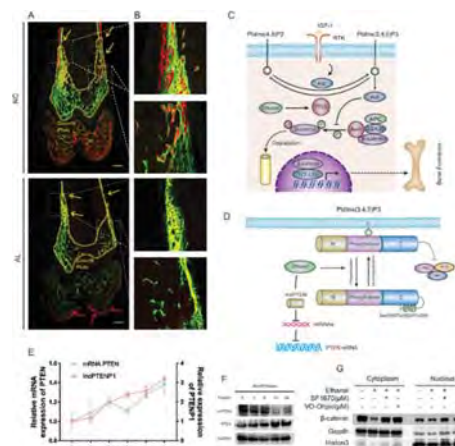
### PTEN REGULATION ALLEVIATES THE ALCOHOL-INDUCED OSTEOPENIA IN RAT VIA AKT/GSK-3B/B-CATENIN PATHWAY IN BMSCS

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**Background:** Alcohol is regarded as a leading risk factor of osteopenia. Our previous works indicated Akt/GSK-3 $\beta$ / $\beta$ -catenin pathway plays crucial role in the ethanol-induced anti-osteogenic effect in bone mesenchymal stem cells (BMSCs). It was acknowledged that PI3K/Akt is negatively regulated by the phosphatase and tensin homologue (PTEN) phosphatase. PTEN expression was reported to be upregulated in ethanol-administrated animals.

**Objectives:** In this study, we explored the molecular mechanisms underlying alcohol-induced osteopenia and investigated the role of PTEN and Akt/GSK-3 $\beta$ / $\beta$ -catenin axis in this pathological process.

**Methods:** *In vitro*, Western blotting, separation of nucleus and cytosolic extracts, confocal scanning, RT-PCR were used to investigate the inhibition of ethanol on Akt/GSK3 $\beta$ / $\beta$ -catenin signalling pathway via upregulation of PTEN in hBMSCs. *In vivo*, micro-computerised tomography, hematoxylin and eosin (H and E) staining, Van Gieson staining, Masson's trichrome and fluorochrome labelling were employed to reveal that PTEN inhibition provided protective effects against ethanol on bone tissue.



**Results:** We found that ethanol increased PTEN expression both in BMSCs and in bone tissue of ethanol-administrated rats. PTEN upregulation impaired the recruitment of Akt to the plasma membrane, and suppressed Akt phosphorylation at Ser473, there by inhibiting the Akt/GSK3 $\beta$ / $\beta$ -catenin signalling pathway in BMSCs and inhibited the expression of osteogenic genes *COL1* and *OCN* both *in vitro* and *in vivo*. To counteract the inhibitory effect of ethanol, two selective PTEN inhibitors were introduced. The result of micro-computerised tomography,

hematoxylin and eosin (H and E) staining, Van Gieson staining, Masson's trichrome and fluorochrome labelling indicated PTEN inhibition provided protective effects against ethanol on bone tissue. Interestingly, our data revealed that the mRNA of PETN, paralleled with PTENP1, was increased in a time-dependent manner upon ethanol stimulation, which resulted in increasing PTEN protein level. In addition, ethanol increased PTEN expression while decreased p-PTEN expression in a time-dependent manner, which indicated the generation of more functional PTEN.

**Conclusions:** Taken together, dual regulations of PTEN by ethanol via transcriptional and post-transcriptional process impaired the downstream signalling of Akt/GSK3 $\beta$ / $\beta$ -catenin and osteogenic differentiation of hBMSC. Therefore, we propose that PTEN inhibition treatment for Akt/GSK3 $\beta$ / $\beta$ -catenin activation could be tested in the clinic as a potential therapeutic approach to preventing the development of alcohol-induced osteopenia.

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**Disclosure of Interest:** None declared

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SATURDAY, 16 JUNE 2018

## Cartilage, synovium and bone

### SAT0048 ANALYSIS OF DIFFERENT THERAPEUTIC REGIMES IN PATIENTS WITH HEMOPHILIC ARTHROPATHY

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**Background:** The greater morbidity of the patient with haemophilia is due to hemarthrosis. The treatment is based on the administration of deficient coagulation factor (FC). The treatment is divided into prophylactic (TP) and on demand (AD). Prophylaxis consists in the administration of FC in order to maintain adequate levels of factor to prevent or reduce spontaneous bleeding and AD is the application of the factor when there is clinical evidence of bleeding. The TP is the recommended treatment in severe haemophilia, plasma and recombinant concentrates are used, safe and effective, but with a short half-life, which requires frequent intravenous infusions, being a barrier to compliance. Another drawback of the current treatment in haemophilia A (HA) is that up to 30% develop inhibitor (antibodies that neutralise the activity of a CF).

New subcutaneous drugs (NSD) have begun to be used in clinical trials, such as:

- Emicizumab: Bispecific anti-IXa/X monoclonal antibody.
- Concizumab: Anti-TFPI antibody.

This new therapeutic strategy can have implications both from a clinical and economic point of view.

**Objectives:** To analyse the different treatment regimens and their economic implications in a cohort of patients with hemophilic arthropathy (HA).

Evolution of hemarthroses in patients with AH after starting treatment with NSD in the clinical trial phase.

**Methods:** Retrospective descriptive study, in the Haemophilia Unit of our hospital (regional reference), in patients with AH (Haemophilia A and moderate-severe B), followed in consultation with episodes of joint bleeding, from January 2007 to October 2017. Gravity of the haemophilia determined by the percentage of FC activity (VIII and IX), moderate from 1% to 5%, severe <1%. The number of joint bleeds was analysed 6 months before and after the start of treatment with the NFS in patients who have participated in a multicenter phase III study and continue with the treatment

**Results:** We included 89 patients (88 men and 1 carrier woman), mean age 31 ±17 years, HA (severe 56%, moderate 26%), HB (severe 15%, moderate 1%). 17% develop inhibitor (10 severe HA, 3 moderate HA, 3 severe HB). Treatment on demand 44% and prophylaxis 38%. Replacement therapy: FC VIII (44% severe HA, 22% moderate HA), FC IX (11% severe HB, 1% moderate HB), recombinant active factor VII (rFVIIa) (2 patients with severe HB with inhibitor).

In treatment with monoclonal antibody (patients currently in Clinical Trial): 15% Emicizumab, of these 4 are with inhibitor (2 severe HA, 1 moderate HA, 1 severe HB and 1% Concizumab (severe 1HB with inhibitor).

The number of hemarthroses was analysed 1 year before the administration of NFS until now, achieving a statistically significant reduction in the rate of joint bleeding of 86% (p<0.005) compared to conventional pre-treatment.

**Conclusions:** The majority of patients with severe and moderate haemophilia are on demand treatment, despite existing recommendations.

It can also be said that there are drugs in the research phase that may involve a paradigm shift in the therapeutic approach of patients with haemophilia, which will allow more personalised treatment, to achieve better joint protection and a better quality of life.

**Disclosure of Interest:** None declared

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### SAT0049 11BETA-HYDROXYSTEROID DEHYDROGENASE TYPE 1 REGULATES CHRONIC SYNOVITIS WITH LOCAL AND SYSTEMIC COMPLICATIONS

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**Background:** Inflammation, local joint destruction and systemic bone loss are common complications in patients with rheumatoid arthritis (RA). We have identified that localised pre-receptor activation of glucocorticoids (GC) by the enzyme 11beta-hydroxysteroid dehydrogenase type 1 (11 $\beta$ -HSD1) is increased within sites of inflammation and surrounding tissues, such as synovium and bone. Whilst this greatly increases local bioavailability of cortisol, which supports resolution of inflammation, in chronic disease, GCs drive may drive catabolic pathways that contribute to joint destruction and systemic bone loss.

**Objectives:** To determine the contribution of 11 $\beta$ -HSD1 activated glucocorticoids to joint destruction and inflammatory bone loss, we crossed an 11 $\beta$ -HSD1 null mouse onto a transgenic murine model of chronic polyarthritis (TNF-Tg) to generate TNF-tg<sup>11 $\beta$ KO</sup> mice.

**Methods:** Clinical measures of joint inflammation, mobility and behaviour were collected between 4 and 9 weeks of age. Paw swelling was determined using calliper measurements. Histology was assessed in formalin fixed sections following staining with haematoxylin and eosin, safranin O or TRAP staining. Juxta articular and systemic bone losses were measured by micro-Ct. synovitis was determined by Image J analysis of histology sections.

**Results:** 11 $\beta$ -HSD1 was completely knocked out within sites of inflammation in the TNF-tg<sup>11 $\beta$ KO</sup> mouse. At 9 weeks, both clinical and inflammation scores were markedly exacerbated in TNF-tg<sup>11 $\beta$ KO</sup> animals relative to TNF-tg counterparts (inflammation score; TNF-tg, 4.3±2.26 versus TNF-tg<sup>11 $\beta$ KO</sup>, 11.08±0.86; p<0.001). This was supported by marked increases in joint swelling and juxta articular bone loss from these animals (erosion scores, TNFtg, 5.2±0.61 versus TNF-tg<sup>11 $\beta$ KO</sup>, 9.0±0.66; p<0.005). Closer examination of joint destruction revealed that the pannus was larger and more extensive within subchondral bone, whilst evidence of cartilage degradation was significantly worse in the TNF-tg<sup>11 $\beta$ KO</sup> mouse (synovitis size, TNFtg, 26 763 (AU) ±3200 versus TNF-tg<sup>11 $\beta$ KO</sup>, 530276 ±3225; p<0.005). Systemic bone loss determined by bone volume to tissue volume (BV/TV), trabecular thickness (TT) and trabecular number (TN) was also greatly exacerbated within the TNF-tg<sup>11 $\beta$ KO</sup> mouse (TNF-tg, BV/TV 5.7±0.75, TT 73.5±6.4, TN 0.00077±0.00004 versus TNF-tg<sup>11 $\beta$ KO</sup> BV/TV 1.8±0.36, TT 7359.77 ±3.7, TN 0.0003±0.00005; p<0.001, p<0.005, p<0.001 respectively).

**Conclusions:** This study demonstrates that rather than contributing to catabolic pathways of tissue destruction, local GC activation by 11 $\beta$ -HSD1 is critical in mediating the suppression inflammation, joint destruction, synovitis and inflammatory bone loss in this murine model of chronic polyarthritis.

**Acknowledgements:** We would like to thank Professor George Kollias (Hellenic Pasteur Institute, Athens, Greece) for providing the hTNFtg mice. This research was supported by the Arthritis Research UK grants (Reference: 19859 and 20843).

**Disclosure of Interest:** None declared

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**SAT0050 STANDARDISATION OF SYNOVIAL BIOPSIES ANALYSIS: A EULAR SYNOVITIS STUDY GROUP INITIATIVE USING A DELPHI SURVEY.**

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**Background:** Synovial biopsies are increasingly performed in both clinical setting and translational research.<sup>1</sup> An unmet need in the field is the standardisation of synovial biopsies handling and analysis procedures.

**Objectives:** The aim of this collaborative work was to create a consensual set of points to consider for handling and analysis of synovial biopsies in clinical practice and translational research through EULAR Synovitis Study Group (ESSG).

**Methods:** The items were identified and formulated based on a comprehensive literature review.<sup>1</sup> A task force (TF) of EULAR Synovitis Study Group (ESSG) members were constituted and TF members were consulted through a 2-stage eDelphi process. The 2 sequential rounds occurred in 9 months. The first written round occurred in June 2016. Members were sent a written questionnaire containing items divided in 2 parts. The items were identified and formulated based on a comprehensive literature review. The first part of the questionnaire referred to clinical practice containing 5 subsections: biopsy sampling, biopsy handling, histological analysis, staining and immunohistochemistry (IHC), biopsy analysis and pathologist's report. The second part referred to translational research and contained 6 subsections (same 5 plus RNA analysis). Every participant was asked to score each item with a 5 points Likert (0: strongly disagree, 5: strongly agree), comments were allowed for each item. Items with a median score above 3.5 on 5 and a percentage of agreement above 70% were for the next round. Items with lower score were either suppressed or modified according to participants' comments. Anonymized detailed results were circulating through participants between each round. The face to face meeting occurred at ESSG meeting in June 2017.

**Results:** 27 ESSG members from 19 centres were contacted by email. 20 participants from 17 centres answered (response rate of 74%). Response rates for next rounds were 100%. First questionnaire contained 44 items for Part 1 Clinical practice. 52.3% (23items/44) were selected for the second round based on their score and agreement percentage. 83% (19items/23) were selected for the third round. First questionnaire contained 43 items for the second part about translational research. 44% (19 items/43) were selected for second round based on their score and agreement percentage. 95% (18 items/19) were selected for third round (figure 1). Third oral round allowed to obtain a final set of items unanimously (table 1).

Item	Consensus Points	Median score	% Agreement	Median score	% Agreement
<b>1. Biopsy sampling</b>					
A minimum of 3 synovial biopsies needs to be collected in each patient	100.00	5	100.00	5	100.00
A minimum of 3 synovial biopsies needs to be collected in each joint	92.31	5	92.31	5	92.31
Biopsies shall be removed in different areas of the joint, if possible	94.50	5	94.50	5	94.50
If it is clinically relevant, bacteriological, fungal and mycobacteriological assessment should be performed	75.00	5	75.00	5	75.00
Microscopic chain reaction analysis for ANA, ANCA, IgG4 should be performed if clinically relevant. Specialized laboratory facilities have been started	71.43	5	71.43	5	71.43
If it is clinically relevant, immunogenetic analysis for Lyme and HLA-B*27:05 should be performed	71.43	5	71.43	5	71.43
<b>2. Biopsy processing</b>					
The biopsies should be stored at -80°C in formalin-free	100.00	5	100.00	5	100.00
At least 2 biopsies should be formalin-fixed and paraffin-embedded	76.92	5	76.92	5	76.92
<b>3. Histological criteria</b>					
Synovial histology should be assessed on 3 biopsies	100.00	5	100.00	5	100.00
A scoring system should be used	94.50	5	94.50	5	94.50
Morphology of the synovial tissue should be preserved	94.50	5	94.50	5	94.50
<b>4. Staining and immunohistochemistry (IHC)</b>					
IHC staining should always be performed	100.00	5	100.00	5	100.00
CD68 staining should be performed	75.00	5	75.00	5	75.00
CD3, CD59 or CD38 staining should be performed	66.67	5	66.67	5	66.67
Additional CD 31 or P401, CD34, CD38 staining might be performed depending on the question	66.67	5	66.67	5	66.67
In particular clinically relevant cases, additional staining should be performed (CD3, CD38, CD31, CD34 or P401)	66.67	5	66.67	5	66.67
If performed, IHC results can be given using a semi-quantitative score	100.00	5	100.00	5	100.00
In formalin, IHC results can be given using a semi-quantitative score	66.67	5	66.67	5	66.67
In formalin, IHC results can be given using a semi-quantitative score	66.67	5	66.67	5	66.67
<b>5. Biopsy interpretation and pathologist report</b>					
A systematic report should be performed, including: lining layer hyperplasia, inflammatory infiltrate and resident cell activation (if relevant)	100.00	5	100.00	5	100.00
Microscopy should be included	100.00	5	100.00	5	100.00
The distribution of resident cells per field or per high-power field should be assessed	100.00	5	100.00	5	100.00
Lining layer hyperplasia should be assessed	100.00	5	100.00	5	100.00
Resident cell activation should be assessed	100.00	5	100.00	5	100.00
Presence or absence of lymphoid follicles within the membrane should be described	83.33	5	83.33	5	83.33
Analysis can be semi-quantitative or quantitative depending on the question	100.00	5	100.00	5	100.00
If semi-quantitative or quantitative analysis is performed for multiple biopsies, an average score should be calculated and given for the analysis of inflammation and activation	75.00	5	75.00	5	75.00
The pathologist should mention the presence of all granulomas	66.67	5	66.67	5	66.67
In granulomas and giant cells, the presence of all granulomas	66.67	5	66.67	5	66.67
<b>6. RNA Analysis</b>					
Biopsies can be stored for RNA extraction if needed	100.00	5	100.00	5	100.00

**Conclusions:** We hereby propose a set of consensual points to consider on analysis of synovial biopsies in clinical practice and translational research. This standardisation initiative was conducted through ESSG members using a validated consensus method.

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**Disclosure of Interest:** None declared

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**SAT0051 EXAMINING THE ROLE OF TRPC5 IN OSTEOARTHRITIS PAIN**

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**Background:** Transient receptor potential canonical 5 (TRPC5) is a cation channel that putatively acts as a sensor of one or more chemical factors but the exact biology is not fully known. It was recently found to be expressed in fibroblast-like synoviocytes where TRPC5 activation by endogenous thioredoxin – which has been shown to be elevated in synovial fluid of patients with rheumatoid arthritis – results in the suppression of matrix metalloproteinases secretion.<sup>1</sup> Genetic deletion or pharmacological blockade of TRPC5 receptor in arthritic mice resulted in marked exacerbation of hyperalgesia and critically increased localised inflammation in the synovium, characterised by increased cellular infiltration, secretion of early response cytokines and enhanced synovial vascularisation.<sup>2</sup> Interestingly, in this study, mRNA expression of TRPC5 was reduced in inflamed human arthritis samples particularly in the synovium from patients with osteoarthritis (OA), highlighting a potential role for TRPC5 in OA.

**Objectives:** With the aim to investigate putative mechanisms mediated by TRPC5 signalling in OA pain, we have examined the development of monoiodoacetate (MIA)-referred mechanical hypersensitivity and joint pathology in wild type and mice carrying a TRPC5 deletion.

**Methods:** Wild type and TRPC5 knock-out (TRPC5) mice were intra-articularly injected with 0.75 mg of MIA, and hind-paw mechanical thresholds and weight bearing changes were assessed at regular intervals up to 28 days. Knee joint histochemical analysis of cartilage degradation using toluidine blue staining and synovial inflammation using haematoxylin and eosin staining was also performed.

**Results:** Both TRPC5 KO and WT mice developed referred mechanical hypersensitivity following MIA injection, however the onset was faster (day 3 vs day 10) in TRPC5 KO mice. By the end of the study, at 28 days after MIA injection, mechanical hypersensitivity had reached similar levels in TRPC5 KO and WT mice. Moreover, at a 0.7 mg MIA dose administered, TRPC5 KO, but not WT mice developed weight bearing asymmetries over the course of the study and most significantly from 14 to 28 days after MIA injection. In paraformaldehyde-fixed joints obtained 28 days post MIA injection from TRPC5 KO and WT mice no significant differences in cartilage degradation or inflammatory content were observed.

**Conclusions:** This study suggests that deletion of the TRPC5 receptor signalling is associated with a faster onset of referred allodynia and increased guarding/on-going pain like behaviour in a model of OA.

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**SAT0052 THE COLL2-1 PEPTIDE OF COLLAGEN TYPE II: A NEW ACTOR OF SYNOVITIS IN OSTEOARTHRITIS**

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**Background:** Osteoarthritis (OA) is characterised by degradation of the extracellular matrix associated with inadequate repair responses including pro-inflammatory pathways of nonspecific natural immune response.

**Objectives:** We evaluated the inflammatory effect of Coll2-1 peptide in osteoarthritic synoviocytes and rats by comparing peptide-induced inflammatory reaction with the one induced by bovine type II collagen or streptococcal cell wall.

**Methods:** Human synoviocytes from knee OA patients (n=10) were pre-treated with AS0619 or CLI-095 (500 nM, 1 and 2.5 µM) before a 24 hours treatment with Coll2-1 peptide (<sup>108</sup>HRGYPGLDG<sup>116</sup>; 0.45 or 4.5 nmol). Expression of Interleukin (IL)-8, Vascular Endothelium Growth Factor (VEGF) and phosphorylation of the IκB-α and p65 were evaluated. Either Coll2-1 peptide, bovine type II collagen (CIA), streptococcal cell wall (SCW) or saline solution (100 µl SC or 50 µl IA) were injected into Lewis rats (n=108). The Coll2-1 peptide was subcutaneously injected (SC; 20 and 200 µg/100 µl/animal) or intra-articular (IA; 0.5 and 5 µg/50 µl/animal). The bovine type II collagen was SC injected (200 µg/100 µl/



animal), streptococcal cell wall in IA (5 µg/50 µl/animal). The animals were injected on day 10 and monitored for 21 or 28 days. Visual evaluation of the severity of arthritis and histological lesions were performed.

**Results:** Coll2-1 at 0.45 nmol (\*\* $p<0.01$ ) and 4.5 nmol (\*\* $p<0.05$ ) significantly increased IL-8 gene expression and tended to increase VEGF expression by synovocytes. With AS0619, a specific antiserum for Coll2-1 peptide, IL-8 expression significantly decreased (\*\* $p<0.05$ ). Coll2-1 also induced both translocation of p65 and IκB-α degradation. The latter being reduced with oxidative stress inhibitors. With CLI-095, we observed a decrease of IL-8 expression. *In vivo*, bovine type II collagen injection and Coll2-1 peptide injection resulted in an increase in visual arthritis score from D7. The global histological score was also increased by bovine type II collagen on D21 ( $p=0.0005$ ) and on D28 ( $p<0.0001$ ) and by the peptide Coll2-1 on D21 at the concentration of 200 µg ( $p=0.0252$ ) and on D28 at the concentration of 20 µg ( $p=0.0025$ ). Compared to control, all the components of the histological score were similarly modified by bovine type II collagen and the peptide Coll2-1 at both on D21 and on D28: increase in the inflammatory parameter (D21 200 µg  $p=0.0217$  and D28 20 µg  $p=0.0021$ ), reduction of proteoglycan contents (D28 200 µg  $p=0.0072$  and 20 µg  $p=0.0024$ ), increased cartilage degradation (J28 200 µg  $p=0.0070$  and 20 µg  $p=0.0024$ ) and modification of the subchondral bone (D21 200 µg  $p=0.0025$  and D28 20 µg  $p=0.0065$ ). Similarly, both the injection of SCW and that of Coll2-1 peptide induced an increase in the visual score from D10. The effect of Coll2-1 peptide on this score was identical to that of the SCW. Compared to control, SCW and Coll2-1 peptide increased the global histological score (D21  $p=0.0119$  and D28  $p=0.0045$ ). Like SCW, the injection of Coll2-1 peptide caused both inflammatory reaction, loss of proteoglycan, appearance of cartilage structural lesions (D28 0.5 µg  $p=0.0201$ ) and subchondral bone modification.

**Conclusions:** Coll2-1 peptide is able to induce an inflammatory reaction and structural changes in articular cartilage and subchondral bone comparable to those induced by SCW and bovine type II collagen. In conclusion, Coll2-1 may initiate nonspecific natural immunity and therefore be a therapeutic target for biotherapy.

**Disclosure of Interest:** None declared

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#### SAT0053 IDENTIFICATION OF NOVEL DRUGS WITH SENOLYTIC ACTIVITY AS OSTEOARTHRITIS THERAPEUTICS

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**Background:** Disease-modifying treatments for Osteoarthritis (OA) are not available. Aging-related features such as failure of cellular homeostasis mechanisms, including autophagy, cause extracellular matrix damage, chondrocyte senescence and death, which leads to articular cartilage degeneration as well as loss of joint function.

**Objectives:** The objective of this study was to identify senolytics and activators of autophagy by cell-based imaging of approved drugs in human chondrocytes.

**Methods:** To induce cellular senescence and reduced autophagy, High Content Screening system. Validation assays with readouts for senescence, autophagic flux, inflammation and apoptosis in primary human chondrocytes were performed. The anabolic effect on human cartilage and chondrocytes was evaluated by Safranin O staining and Nitric oxide production. To define the effects on senescence (senomorphic or senolytic), TC28a2 chondrocytes and human lung fibroblasts (IMR90) were employed. Senescence was induced in TC28a2 and IMR90 by treatment with IL-6 (20 ng/ml) for 72 hours and Etoposide (20 µM) for 48 hours, respectively, and treated with serial dilutions of identified compounds. The number of senescence cells and the number of total cells were determined with Cell Analyzer 6000 Confocal Imaging System. Navitoclax (2,5 µM) and Rapamycin (10 µM) were employed as reference controls for senolytic and senomorphic effects, respectively.

**Results:** Our primary screen yielded 279 senotherapeutic compounds. The effects of hits at inducing the autophagic flux were evaluated. 37 compounds with both senotherapeutic and pro-autophagy effects were selected. An approved drug with a defined molecular mechanism of action was selected for further validation. The compound reduced senescence ( $p<0.001$ ) and increased autophagic flux ( $p<0.0001$ ). Furthermore, we found that it protects against defective autophagy and inflammation in response to IL-6 and IL-1b. This protective effect was

confirmed in human cartilage explants by a reduction of proteoglycans loss ( $p<0.05$ ) and in primary human chondrocytes by a reduction of NO production and chondrocyte death by apoptosis ( $p<0.0001$ ). Moreover, a significant senolytic effect of the selected compound was observed in both chondrocytes and fibroblasts ( $p<0.05$ ). This effect was also observed for structurally different compounds sharing the same mechanism of action, suggesting that pharmacological modulation of this mechanism may provide therapeutic benefits in OA.

**Conclusions:** Our imaging screening methodology provides a unique opportunity to identify drugs and mechanisms to prevent cartilage pathology. Autophagy activation and disruption of senescence may provide benefits for delaying cartilage degeneration.

**Acknowledgements:**

**Disclosure of Interest:** None declared

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#### SAT0054 SIGNIFICANT DECREASE OF T-CELLS BUT NOT MACROPHAGES IN THE SYNOVIUM OF PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS AFTER TREATMENT WITH TOCILIZUMAB

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**Background:** Tocilizumab (TCZ) is an anti-IL6R monoclonal antibody approved for the treatment of Rheumatoid Arthritis (RA). There is limited data on synovial tissue histology changes.

**Objectives:** The aim of this study was to evaluate the effect of TCZ on synovial cell populations and on citrullination.

**Methods:** 15 patients with RA, according to ACR 1987 criteria, independent of disease duration, were included. Synovial biopsies were obtained before and after 8 weeks of treatment. We evaluated by immunohistochemistry (IHC) expression of citrullinated proteins (CP) and protein arginine deiminase (PAD) enzymes in synovial tissue before and after treatment (1325:C03, 1325:B09, PAD2, PAD4). Negative controls were used for each antibody. Expression of CD68, CD3, CD20 and CD55 was also evaluated. Evaluation of all IHC variables was performed by two blinded independent observers using a semiquantitative score on a 0–3 scale (0, no staining; 1, low amounts of staining; 2, moderate amounts of staining; 3, high amounts of staining). Paired-wised Wilcoxon Signed Ranks Test was used to compare the median values.

**Results:** The median (IQR) age, disease duration, N. prior biologic DMARDs and DAS28 at baseline was 66, 58–79, 4 (1–13), 1 (0–2), 6 (5–7), respectively. 93% were female, 53% were RF + and 60% ACPA+, 53% had concomitant glucocorticoids and only 27% had concomitant conventional synthetic DMARDs. Significant reductions in DAS28, swollen and tender joint count (SJC and TJC, respectively), and acute phase reactants (ESR and CRP) were observed between baseline and 8 weeks (table 1). By IHC, TCZ induced significant decrease in the number of CD3, C03 and CD55, but not in the number of the other CP, PAD2, PAD4 and CD68 (table 1).

#### Abstract Sat0054 – Table 1

##### Baseline 8 weeks p-value (Wilcoxon Signed Ranks Test)

DAS28 BL	5.9 (4.7–6.8)	2.98 (2.0–3.8)	0.028
SJC BL	9 (3–14)	1 (0–4.25)	0.009
TJC BL	10 <sup>4–15</sup>	1 (0–2.25)	0.017
ESR BL	34 <sup>15–69</sup>	6 (5–16)	0.001
CRP BL	11 <sup>5–27</sup>	1 (1–2)	0.005
CD68 2	(1–3)	2 (0.75–3)	0.41
CD3 2	(1–3)	1 (0–2)	0.046
CD55 2	(2–3)	1.5 (1–2)	0.05
C03 (cit)	1 (0–1)	0 (0–1)	0.025
B09 (cit)	2 (1–2)	2 (1–2)	0.20
PAD2 3	(2–3)	2 (1.5–3)	0.16
PAD4 2	(2–3)	2 (2–3)	0.37

**Conclusions:** Treatment with tocilizumab reduced the number of synovial tissue T cells. This was observed in the responders but not in non-responders. Significant reduction in citrullination as assessed by expression of 1325:C03 but not 1325:B09. No significant reduction in macrophages was observed.

**Acknowledgements:** This study was funded by Roche.

**Disclosure of Interest:** None declared

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**SAT0055 SIMULATING THE PATHOGENESIS OF ARTHRITIS IN VITRO BY DEVELOPING A HUMAN-BASED MULTICOMPONENT 3D JOINT MODEL**

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**Background:** Our ultimate goal is to develop a valid human *in vitro* 3D joint model to simulate the pathogenesis of arthritis. The *in vitro* 3D joint model consists of different components including an<sup>1</sup> osteogenic and<sup>2</sup> chondrogenic part,<sup>3</sup> the synovial fluid and<sup>4</sup> the synovial membrane and contains all involved cell types and thus, to allow interactions between cells by cell contacts and signalling molecules. As an alternative experimental setup for animal models, our *in vitro* 3D joint model will enable us to study the influence and efficacy of drug treatment. Currently, there is no valid 3D model which is able to mimic an arthritic joint.

**Objectives:** Here, we aim to mimic the<sup>1</sup> osteogenic and<sup>2</sup> chondrogenic part,<sup>3</sup> the joint space with synovial fluid and<sup>4</sup> the synovial membrane.

**Methods:** For the osteogenic component of the 3D joint model, we populated  $\beta$ -tricalcium phosphate (TCP) – mimicking the mineral bony part – with osteogenic pre-differentiated human bone marrow-derived mesenchymal stromal cells (hMSC) and coated the particles with an hMSC monolayer cell-sheet to get a compact bony component. Survival, adhesion and structural integrity of the cells were evaluated by Scanning Electron Microscopy (SEM), LIVE/DEAD staining and cellular release of LDH. Osteogenic differentiation was analysed by  $\mu$ CT for mineralization and on gene expression level using qRT-PCR. To mimic the chondrogenic part, a scaffold-free 3D cartilage construct was generated by chondrogenic differentiation of hMSC under hypoxia with intermittent mechanical stimulation. Constructs were analysed by histology and qRT-PCR. Simulating the synovial fluid, hyaluronic acid was applied to the osteochondral model. To model the synovial membrane, a confluent monolayer of hMSC was formed on a polycarbonate membrane and visualised by hemacolor staining.

**Results:** We developed an *in vitro* 3D bone model by successfully seeding pre-differentiated hMSC on a  $\beta$ -TCP scaffold. Cells consistently adhere onto the scaffold for up to 3 weeks as observed by SEM. The analysis of cell viability via LDH detection and LIVE/DEAD staining showed no toxic effects on the cells even after 3 weeks of incubation as compared to the corresponding control. mRNA expression of bone-related genes such as *RUNX2*, *SPP1* and *COL1A1* as well as  $\mu$ CT analysis confirmed the osteogenic phenotypic of hMSC grown in 3D. Mimicking the articular cartilage component, we verified its chondrogenic phenotype by HE and Alcian Blue staining as well as by the reduced mRNA expression of *COL1A1* and an abundant expression of *COL2A1*. Interestingly, co-cultivation of the osteogenic and chondrogenic part for up to 3 weeks demonstrated successful colonisation, connectivity and initial calcification implying a functional transitional bridging area. Modelling the synovial membrane, we successfully and reproducibly created a confluent monolayer of hMSC, which is easily transferable to the model.

**Conclusions:** First steps towards the *in vitro* simulation of an arthritic joint based on a multi-component model confirm good cell vitality and phenotypic stability which indicates successful progression. To finalise the development of healthy joint model, we will combine the established parts to provide a suitable 3D multi-component joint model which enables us to study the efficacy of drug treatment *in vitro*.

**Disclosure of Interest:** None declared

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**SAT0056 OSTEOARTHRITIS SEVERITY IS REDUCED BY INTRA-ARTICULAR ADMINISTRATION OF HYDROGEN SULFIDE**

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**Background:** Osteoarthritis (OA) is a chronic inflammatory disease leading to cartilage loss and eventual joint destruction. Exogenous supplementation of hydrogen sulphide ( $H_2S$ ) with synthetic salts in *in vitro* models of OA has been shown to exert anti-inflammatory effects and to result in reduced cartilage degradation<sup>1</sup>

**Objectives:** To evaluate the effects of administering an  $H_2S$ -producing compound intra-articularly in an experimental model of OA.

**Methods:** Experimental OA was induced in Wistar rats by transecting the medial collateral ligament and removing the medial meniscus of the left knee. Right knees were used as control. Animals were randomised into 3 groups (3 rats per group). Group 1 (intra-articular sulphide, IS): A single intra-articular injection of GYY4137

(200 mM in saline, 50 ml) at day 7. Group 2 (intra-articular control, IC): A single intra-articularly injection of vehicle (saline, 50 ml) at day 7. Group 3 (Surgical control, C): No treatment.

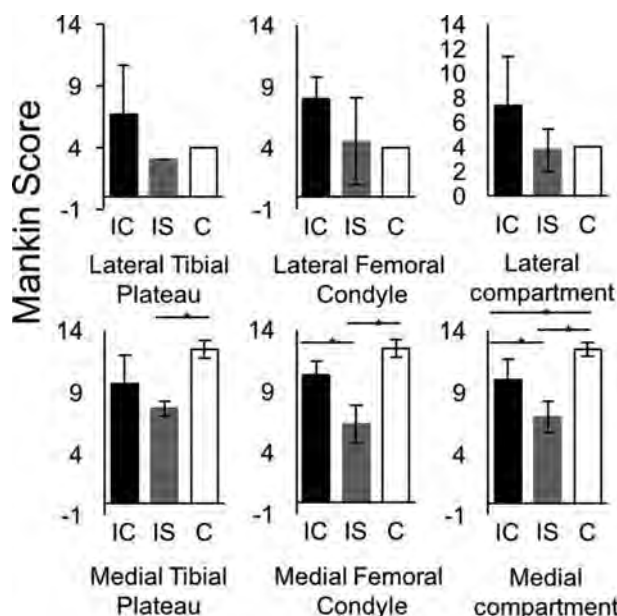
Gross evaluation of the animals at days 0 (before surgery), 7, 15 and 40 (euthanasia) included indirect evaluation of pain in a Rotarod performance test. Histopathological changes in articular cartilage and synovium were evaluated with the Mankin Score (MS) and the Krenn Score (KS), respectively.

**Results:** All 3 groups showed worse performance in the Rotarod test at day 7 after surgery. Number of falls was significantly increased (except in IC) and time to 1 st fall was reduced (table 1). At day 40, there was no significant improvement in either of these parameters in group C, while in IC the n# of falls had returned to pre-surgical levels. In IS there were significant improvements with respect to day 0 and both C and IC groups (table 1). Times to 1 st fall were also significantly better in the IS group vs. C and IC both at days 15 and 40.

Histology showed no significant differences among groups in the lateral tibial plateau (TP) or femoral condyle (FC) separately or in the compartment as a whole. Conversely, MS in the medial compartment were significantly better in the IS group vs the C group, both when considering TP or FC separately, and for the whole compartment (figure 1). No significant differences were found among groups on the Krenn Scores.

**Abstract SAT0056 – Table 1.** Number of falls (n±sd) and time to first fall (s) in a Rotarod. C: control group; IC: intra-articular control; IS: intra-articular sulphide (n=3/group). #p<0.05 vs. T0; \*p<0.05 vs. C. §p<0.05 vs. IC.

	Falls (n±sd)				Time to 1 st fall (s)			
	T0	T7	T15	T40	T0	T7	T15	T40
C	0.8 ±0.7	4.0 ±0.9#	4.0 ±0.9#	3.7±1.7#	233.7 ±77.8	57.2 ±35.2#	90.3±67.5#	77.8 ±40.2#
IC	1.7 ±1.0	3.3 ±1.7	2.2±1.0	2.0±0.9	209.2 ±78.2	31.7 ±11.7#	90.8±20.9#	143.3 ±50.3
IS	1.3 ±0.8	4.0 ±1.5#	2.5 ±1.1	0.0 ±0.0#§	265.3 ±58.8	78.5 ±65.9#	196.3 ±81.3*§	300.0 ±0.0*§



**Conclusions:** Exogenous  $H_2S$  administered intra-articularly (200 mM GYY4137 in 50 ml saline) can reduce the severity of cartilage destruction in an *in vivo* model of OA as compared to no treatment or a vehicle control.  $H_2S$  also led to a reduction in pain levels as demonstrated by a performance test. Therefore, hydrogen sulphide is a viable pharmacological candidate for OA treatment and should be further tested, including human clinical trials.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.3635

**SAT0057 THE EFFECT OF EXOSOMES FROM BONE MARROW MESENCHYMAL STEM CELLS ON OSTEOARTHRITIS**

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**Background:** Mesenchymal stem cells (MSCs) exert chondroprotective effects in clinical models of osteoarthritis (OA), but the exact mechanisms were still unclear. Exosomes that serve as carriers of genetic information have been implicated in many diseases and are known to participate in many physiological processes.

**Objectives:** Here, we investigate the therapeutic potential of exosomes from human bone marrow MSCs in alleviating OA and explore the mechanism.

**Methods:** Exosomes were harvested from conditioned culture media of BM-MSCs by a sequential centrifugation process. The anterior cruciate ligament transection and destabilisation of the medial meniscus (DMM) surgery were performed on the knee joints of SD female rat as an OA model. After four weeks, the animals were followed by intra-articular injection of either BM-MSCs or their exosomes every week for four weeks. Cartilage destruction, matrix degradation and subchondral bone changes were evaluated with histological staining and micro-CT at the post-surgery 8 weeks. Primary human chondrocytes treated with IL-1 $\beta$  were used as an *in vitro* model to evaluate the effects of exosomes for 24 hours.

**Results:** We found that intra-articular injection of BM-MSCs and BM-MSCs derived exosomes improve cartilage destruction and subchondral bone remodelling in ACLT+DMM model. BM-MSCs and exosomes equally protected rat from joint damage. These exosomes maintained the chondrocyte matrix by increasing collagen type II synthesis and decreasing ADAMTS5, MMP13 and Col II expression in the presence of IL-1 $\beta$  *in vitro*. In addition, BM-MSCs derived exosomes were also shown to protect chondrocytes from apoptosis and senescence.

**Conclusions:** The exosomes from BM-MSCs exert a beneficial therapeutic effect on OA by not only repairing the degenerative cartilage, but also improving subchondral bone remodelling, which in turn provides a new target for OA drug and drug-delivery system development.

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**Acknowledgements:** No.

**Disclosure of Interest:** None declared

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**SAT0058 ADALIMUMAB:TNF COMPLEXES ARE CLEARED MORE EFFICIENTLY BY HUMAN OSTEOCLASTS THAN THOSE WITH ETANERCEPT THROUGH FCG-RECEPTOR BINDING AND INTERNALISATION**

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**Background:** TNF-alpha (TNF $\alpha$ ) has been shown to contribute to osteoclastogenesis (OCgenesis) independently and in conjunction with M-CSF or RANKL, two key cytokines involved in osteoclast (OC) development. We have previously demonstrated that TNF enhances the kinetics of RANKL-induced human OCgenesis and that its effects are mitigated more effectively by the anti-TNF biologic adalimumab (ADA) as compared to etanercept (ETN).

**Objectives:** To determine whether Fc-gamma receptor (Fc $\gamma$ R)-mediated internalisation of the biologic:TNF complexes is a contributing mechanism responsible for the difference in effectiveness between ADA and ETN in preventing TNF-enhanced OCgenesis.

**Methods:** TNF biologics [ADA and ETN] alone or in preformed complexes with TNF $\alpha$  at 50:1 molar ratio were tested for Fc $\gamma$ R binding by flow cytometry using CHO stably transfected with human Fc $\gamma$ Rs (Fc $\gamma$ RI, Fc $\gamma$ RIIA, -RIIB, -RIIC, Fc $\gamma$ RIIIA and -RIIIB). Fc $\gamma$ R expression and binding of preformed biologic:TNF complexes at 10:1 ratio  $\pm$ Fc $\gamma$ R blocking antibodies to primary human OC precursors (OCP) was evaluated by flow cytometry. Fc $\gamma$ R-mediated internalisation was

assessed by monitoring a reduction in OC survival in response to preformed biologic:TNF complexes (25:1 ratio) bound with saporin (ZAP), a ribosome-inactivating toxin, as anti-human Fc IgG Fab conjugate  $\pm$ Fc $\gamma$ R blocking antibodies.

**Results:** The binding study to CHO (human Fc $\gamma$ Rs) cell lines showed that monomeric ADA and ETN bind similarly to Fc $\gamma$ R (highly on high affinity Fc $\gamma$ R and loosely on low affinity Fc $\gamma$ Rs) while preformed biologics: TNF complexes bind differently. ADA:TNF complexes bind to low affinity Fc $\gamma$ R, whereas ETN:TNF keep a monomeric binding profile with no gain of binding to low affinity Fc $\gamma$ R. OCP were found to express mostly Fc $\gamma$ RII early in development with predominant binding of only ADA:TNF, not ETN:TNF, to this Fc $\gamma$ R with additional binding to undefined receptor(s). Despite subsequent increases in Fc $\gamma$ RI and RIII later on, ADA:TNF still preferentially bound to Fc $\gamma$ RII on the matured OCP with minimal binding to RIII, whereas ETN:TNF binding was observed only to Fc $\gamma$ RI. Exposure of OCP to ADA:TNF:ZAP(toxin) complexes led to a significant reduction (4-fold) in mature OC due to complex internalisation as compared to human IgG:ZAP +TNF conditions that was partially rescued only with the addition of Fc $\gamma$ RII blocking antibody. Interestingly, a 1.5-fold reduction in mature OC was observed with ETN:TNF:ZAP.

**Conclusions:** Our *in vitro* findings demonstrate that human OCP can bind and internalise ADA:TNF complexes more efficiently than ETN:TNF complexes. In addition, this process is partially mediated through Fc $\gamma$ RII. Clearance of the ADA:TNF complexes may help reduce exposure of the OCP to localised TNF by removing TNF more effectively in the joint environment. Additional *in vivo* analysis need to be done to verify these *in vitro* findings.

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**SAT0059 IMPAIRMENT IN HYDROGEN SULFIDE SYNTHESIS IN OSTEOARTHRITIC CHONDROCYTES FROM DIABETIC PATIENT AND UNDER A HIGH GLUCOSE STRESS**

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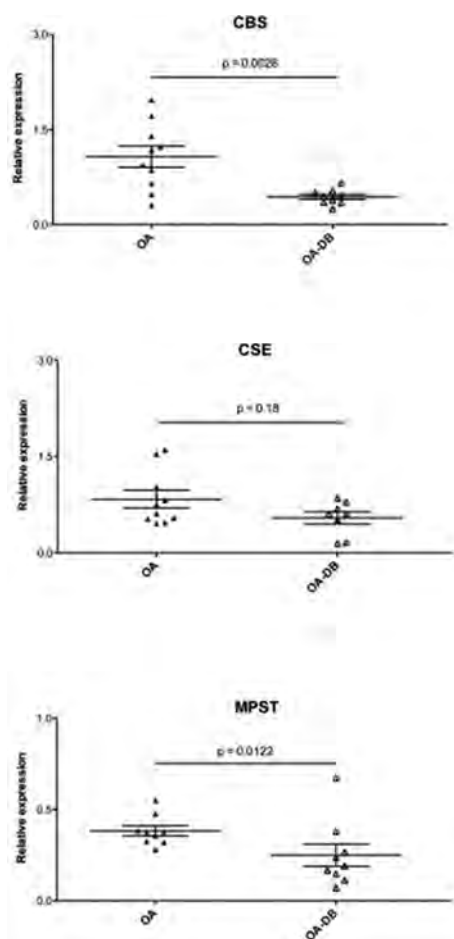
**Background:** A growing number of findings support the hypothesis that type 2 diabetes is an independent risk factor of osteoarthritis (OA). However, the mechanisms underlying the connexion between both diseases remain unclear. Hydrogen sulfide (H<sub>2</sub>S) plays an important role in the pathogenesis of diabetes and its complications. In relation, we and other authors have observed a protective impact of H<sub>2</sub>S induction on activation of pathological pathways in the chondrocyte.<sup>1</sup>

**Objectives:** In this study we examined the modulation of H<sub>2</sub>S levels in osteoarthritic chondrocytes from diabetic (DB) or non-diabetic (non-DB) patients subjected or under glucose stress, in order to elucidate whether impairment in H<sub>2</sub>S-mediated signalling could participate in the establishment of diabetes-related OA.

**Methods:** Chondrocytes were isolated from OA cartilage of diabetic (DB) or non diabetic (non-DB) patients. T/C28a2 and primary human chondrocytes were stimulated w/o IL-1 $\beta$  (5 ng/mL) under a normal (5.5 mM; NG) or a high (25 mM; HG) glucose environment. Gene and protein expression of enzymes involved in H<sub>2</sub>S synthesis (cystathionine  $\gamma$ -lyase [CSE], cystathionine  $\beta$ -synthase [CBS], and 3-mercaptopyruvate sulfurtransferase [3-MT]) and HO-1 were assessed by RT-qPCR and WB, respectively. To determine the involvement of H<sub>2</sub>S in catabolic pathways activated by HG in chondrocytes, NaSH and GYY 4137 (500  $\mu$ M), a fast and slow-releasing H<sub>2</sub>S donor respectively, were employed.

**Results:** Fresh isolated chondrocytes from OA cartilage of diabetic patients showed lower levels of H<sub>2</sub>S synthesising enzymes (CSE, CBS and 3-MT) than those of non-DB patients (figure 1). In relation, chondrocytes T/C28a2 exposed to HG stress expressed lower mRNA and protein levels of these 3 enzymes after 3 days of incubation compared to those incubated in NG conditions (0.41-fold and 0.83-fold [CSE], 0.42-fold and 0.66-fold [CBS], and 0.52-fold and 0.79-fold [3-MT] for mRNA and protein expression, respectively; n=6, p<0.05). IL-1 $\beta$  also attenuated the gene and protein expression of CBS elicited by chondrocytes incubated in NG (0.47-fold and 0.86-fold, respectively; n=6, p<0.05). Additionally, the expression of pro-inflammatory chemokine IL-8 induced by IL-1 $\beta$  was significantly higher in chondrocytes under HG than NG condition (6-fold; n=5, p<0.05); whereas protein levels of heme oxygenase 1, an anti-inflammatory enzyme, were reduced in HG exposed chondrocytes (0.77-fold; n=6, p<0.05). GYY 4137 and NaSH co-treatment recovered HO-1 expression and reduced IL-8 levels in chondrocytes under IL-1 $\beta$ +HG conditions. Furthermore, similar results were registered in primary human chondrocytes from OA cartilage.





**Conclusions:** The results indicate a reduction of H<sub>2</sub>S synthesis as a critical feature involved in hyperglucidic-mediated dysregulation of articular chondrocytes. The impairment of H<sub>2</sub>S signalling could participate in the mechanisms underlying the predisposition to OA development in diabetic individuals and may open new opportunities for treating patients with a diabetes-related OA phenotype.

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**Disclosure of Interest:** None declared

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#### SAT0060 PROTEOMIC ANALYSIS OF OSTEOBLASTS SECRETOME PROVIDES NEW INSIGHTS IN MECHANISMS UNDERLYING OSTEOARTHRITIS SUBCHONDRAL BONE SCLEROSIS

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**Background:** Osteoarthritis (OA) is characterised by cartilage degradation but also by other joint tissues modification like subchondral bone sclerosis

**Objectives:** In this study, we used a proteomic approach to compare secretome of osteoblasts isolated from sclerotic (SC) or non sclerotic (NSC) area of OA subchondral bone

**Methods:** Secretome was analysed using differential quantitative and relative label free analysis on nanoUPLC G2 HDMS system. mRNA of the more differentially secreted proteins were then quantified by RT-PCR and the most relevant proteins identified using western-blotting and immunoassays

**Results:** 175 proteins were identified in NSC osteoblasts secretome. Compared to NSC osteoblasts secretome, 13 proteins were significantly less secreted (Osteomodulin, CSF-1, IGFBP5, VCAM-1, IGF2, 78 kDa glucose-regulated

protein, versican, calumenin, IGFBP2, thrombospondin-4, periostin, reticulocalbin 1 and osteonectin), and 12 proteins significantly more secreted by SC osteoblasts (CHI3L1, fibulin-3, SERPINE2, IGFBP6, SH3BGRL3, SERPINE1, reticulocalbin3, alpha-2-HS-glycoprotein, TIMP-2, IGFBP3, TIMP-1, SERPINF1). Similar changes in periostin, osteomodulin, SERPINE1, IGFBP6, fibulin-3 and CHI3L1 mRNA levels were observed. Finally, osteomodulin and fibulin-3 specific sequences were quantified by western blot and immunoassays in serum and osteoblasts conditioned culture supernatants.

**Conclusions:** We highlighted some proteins differentially secreted by NSC and SC osteoblasts of OA subchondral bone sclerosis. These changes contribute to explain some features observed in OA subchondral bone, like the increase of bone remodelling or abnormalities in bone matrix mineralization. Among identified proteins, osteomodulin was found decreased and fibulin-3 increased in serum of OA patients. These findings suggest that osteomodulin and fibulin-3 fragments could be biomarkers to monitor early changes in subchondral bone metabolism in OA.

**Acknowledgements:** The D-Board project has received funding from the European Union's Seventh Framework Programme for research, technological development and demonstration under grant agreement No. 3 05 815.

**Disclosure of Interest:** None declared

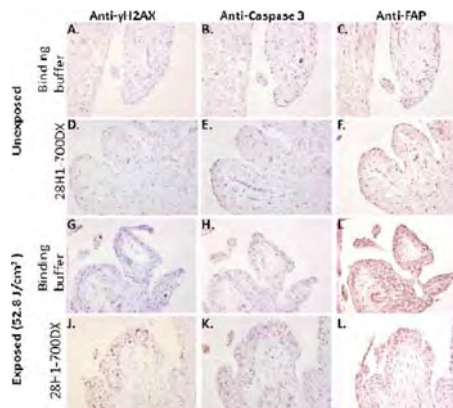
**DOI:** 10.1136/annrheumdis-2018-eular.1028

#### SAT0061 TARGETING ACTIVATED SYNOVIAL FIBROBLASTS USING PHOTODYNAMIC THERAPY IN RHEUMATOID ARTHRITIS

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**Background:** Activated synovial fibroblasts (SF) play an important role in the pathogenesis of rheumatoid arthritis (RA). They contribute to the pro-inflammatory environment in the joint as well as to the degradation of cartilage. Depleting SF could ameliorate both the symptoms of joint inflammation and degradation in RA. SF are characterised by the expression of Fibroblast Activation Protein (FAP). Here, we investigated the potential of photodynamic therapy (PDT) targeting FAP to selectively induce cell death in these cells as well as in synovial tissue from RA patients. In PDT, a light-sensitive molecule is delivered to a target cell and activated with light of a specific wavelength. This causes cell death through the production of reactive oxygen species.

**Methods:** The anti-FAP antibody 28 H1 was conjugated with the photosensitizer IRDye700DX (28 H1–700DX). *In vitro* PDT assays were performed with 3 T3 fibroblasts stably transfected with FAP. 3T3-FAP cells were incubated with 28 H1–700DX or a control conjugate for 4 hours, and exposed to varying 690 nm light exposures. Subsequently, cell viability was measured using the CellTiter-Glo assay. For *ex vivo* evaluation of PDT efficiency, human RA synovial tissue obtained after joint replacement surgery was processed into standardised 6 mm biopsies and used for FAP-based PDT. The biopsies were incubated with 28 H1–700DX for 4 hours, subjected to 52 J/cm<sup>2</sup> light exposure and fixed in formalin after 1 hour. Tissue was then embedded in paraffin and stained for the presence of gH2AX and caspase 3 as indicators of DNA double-strand breaks and early apoptosis on sequential slides. The presence of FAP was also determined on subsequent slides.



**Results:** The effect of PDT was optimal at 13.7 J/cm<sup>2</sup> light exposure to 3T3-FAP cells incubated with 6.67 pM 28 H1–700DX, which dramatically reduced cell viability with 89.27%±2.48 compared to control (p<0.001). No cell death was observed with the control 700DX-conjugate (p=0.16).

In the PDT experiment on human RA synovial biopsies, the groups incubated with 28 H1-700DX and exposed to light showed apparent cell death in the synovial tissue as evidenced by the positive staining of both the gH2AX and caspase 3 markers (figure J and K). Staining of these markers co-localised with areas of high FAP staining (figure L). This was not the case in the control samples that were not exposed to either 28 H1-700DX and/or light (figure A – I). All biopsies did show FAP staining indicating that the cell death was only achieved when the biopsies were exposed to both the antibody and the light.

**Conclusions:** We have demonstrated fibroblast-specific cell death by targeted PDT using 700DX-conjugated 28 H1. Furthermore, we demonstrated that PDT also induces cell death of FAP-positive cells in synovial tissue from RA patients, suggesting FAP-targeted PDT as a promising new tool in treating RA.

**Disclosure of Interest:** None declared

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SAT0062

### METABOLOMICS AND METABOLIC FUNCTION ANALYSIS OF THE SECRETOME OF ARTICULAR CARTILAGE AND CHONDROCYTES IN RESPONSE TO PRO-INFLAMMATORY CYTOKINES

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**Background:** Chondrocytes rely primarily on glycolysis to meet their energy requirements, but can support cell survival and matrix synthesis during periods of nutrient stress by enhancing glycolysis with mitochondrial respiration. Accessing this 'spare respiratory capacity' requires optimal mitochondrial function. Impaired mitochondrial function is implicated in osteoarthritis (OA). Metabolic adaptation is evident in early-stage OA, however cartilage from late-stage disease does not seem to have this flexibility. A deeper understanding of these complex metabolic pathways may identify new markers of disease stage, and support therapeutic strategies for treating OA.

**Objectives:** Metabolomics has the potential to reveal pathological pathways and identify novel biomarkers. The aim was to identify metabolic processes involved in early stage disease by analysis of metabolites and metabolic function in pro-inflammatory models of cartilage degradation.

**Methods:** Macroscopically normal articular cartilage was obtained from equine and bovine metacarpophalangeal joints. Equine cartilage explants (n=6), and primary chondrocytes seeded at 105,000/cm<sup>2</sup> (n=4), were cultured for 7 days in serum-free DMEM (Gibco) with or without 10 ng/ml equine interleukin-1 $\beta$  (IL-1 $\beta$ ) and 10 ng/ml tumour necrosis factor- $\alpha$  (TNF- $\alpha$ ). Secretome metabolite levels were measured using AbsoluteIDQ p180 targeted metabolomics kit (Biocrates), with Waters Xevo TQ-S mass spectrometer coupled to an Acquity UPLC system. PCA and OPLS-DA were performed using SIMCA-P v12.0 software. Metabolic function of primary equine (n=9) and bovine chondrocytes (n=3) was determined using Seahorse XFp and XF24 analyzers. Cells were treated with species-specific 10 ng/ml IL-1 $\beta$  and/or 10 ng/ml TNF- $\alpha$  for 18 hour, and metabolically challenged with the Mito Stress Test. Metabolite levels, and oxygen consumption rates, were normalised to total cell protein, and values analysed by ANOVA with Tukey's multiple comparison post-tests.

**Results:** Cytokine treatment decreased proline, ornithine and alpha-aminoadipic acid (p<0.0001) in explant secretome. Citrulline increased with cytokine treatment (p<0.0001) and glutamate, present in DMEM, was also elevated (p<0.0001). Metabolomic analysis of chondrocyte secretome showed that glutamine decreased (p<0.02) with cytokine treatment whereas citrulline was elevated (p<0.003). Metabolic analysis showed that cytokine treatment reduced basal respiration and negated spare respiratory capacity in chondrocytes (p<0.01), and the effect was due to IL-1 $\beta$  alone.

**Conclusions:** Explant metabolites which decreased with cytokine treatment are all downstream of glutamate. With elevated glutamate, this suggests that cytokines inhibit glutamate uptake and metabolism. Elevated citrulline in cell and explant models may be attributed to disruption of the urea cycle via induction of nitric oxide synthase. IL-1 $\beta$  alone negated spare respiratory capacity, and chondrocytes remained glycolytic. In conclusion, cytokines disrupt glutamate and citrulline metabolism, normally tightly regulated mitochondrial pathways, and IL-1 $\beta$  alone is responsible for the metabolic switch. These metabolic pathways could provide markers of early-stage inflammatory disease.

**Disclosure of Interest:** None declared

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SAT0063

### EFFECTS OF INTRA-ARTICULAR INJECTED DIACEREIN-LOADED NANOPARTICLES ON JOINT IN RAT MODEL OF OSTEOARTHRITIS

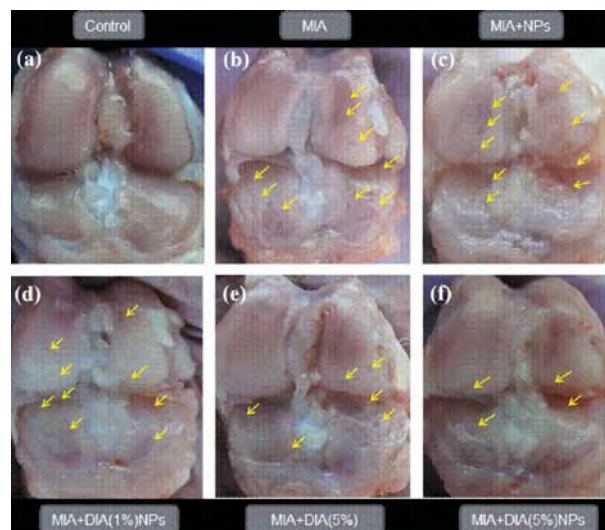
J.H. Jung, G.G. Song, S.J. Choi, J.D. Ji, Y.H. Lee, J.-H. Kim. *Internal Medicine, Korea University Medical Center, Seoul, Korea, Republic Of*

**Background:** Osteoarthritis (OA) is a major health problem in recent years, but the current medical treatment is mainly symptom control and joint disability improvement. Diacerein (DIA) reduces the level of interleukin (IL)-1 receptor on the surface of chondrocytes, alleviates the pain, and prevents the structural degradation of the joint tissue. However, DIA has the side effects such as diarrhoea and urine discoloration when taken orally. To increase bioavailability and reduce systemic side effects, it is preferable to inject DIA directly into the joints. Nanoparticulate drug carriers have been attempted with the advances in drug delivery systems.

**Objectives:** We investigated that DIA-loaded nanoparticles (DIA/NPs) can efficiently inhibit the inflammatory reaction in synoviocytes stimulated by lipopolysaccharide *in vitro* and alleviate both inflammation and cartilage degeneration in monosodium iodoacetate (MIA)-induced OA rat model *in vivo*.

**Methods:** DIA/NPs were fabricated by water/oil/water emulsion method. *In vitro*, the mRNA levels of pro-inflammatory cytokines (IL-1, IL-6, MMP-3, MMP-13, COX-2, ADAMTS-5, and TNF- $\alpha$ ) were measured at 1 st and 3rd day after the administration of NPs only and DIA/NPs to synoviocytes using real-time PCR. MIA was intra-articular injected through the infrapatellar ligament of the rats' knee to induce OA. The rats were randomly divided into the six treatment groups: <sup>1</sup> control, <sup>2</sup> MIA, <sup>3</sup> MIA and NPs, <sup>4</sup> MIA and DIA(1%)/NPs, <sup>5</sup> MIA and DIA(5%)/NPs, and <sup>6</sup> MIA and DIA(5%) solution injection. After NPs, DIA(1%)/NPs, DIA(5%)/NPs, and DIA(5%) solution were injected, at 8th week, the rats were sacrificed to evaluate the plain radiographic and micro-computed tomography (micro-CT), histological study, and pro-inflammatory cytokines expression.

**Results:** The mRNA expression levels for pro-inflammatory cytokines in cells seeded with DIA(5%)/NPs and DIA(5%) solution were significantly lower than those in cells seeded with NPs at 1 st and 3rd day. Moreover, the mRNA levels of pro-inflammatory cytokines in cells injected with DIA(5%) solution decreased much greater than in cells injected with DIA(5%)/NPs. The rats injected DIA(5%)/NPs showed the least amount of cartilage and bone damage on plain radiography and micro-CT and had the less cartilage loss and the bony erosions on microscopic observation. The pro-inflammatory cytokines expression was lowest in the rats injected DIA(5%)/NPs, followed by NPs, DIA(1%)/NPs, and DIA(5%) solution.



**Abstract SAT0063 – Figure 1.** The macroscopic observations for 9 weeks after the MIA injection and for 8 weeks after treated with NPs, DIA (1%)/NPs, DIA (5%)/NPs, or DIA (5%) solution injections (arrows indicate erosions).

**Conclusions:** DIA(5%)/NPs are a promising therapeutic material to control the symptoms and prevent the progression of OA.

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**Disclosure of Interest:** None declared

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**SAT0064** **CD14+CD16+ MONOCYTE SUBPOPULATION IS DOMINANT IN THE INFLAMMATION OF OSTEOARTHRITIS SYNOVIAL FLUID**

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**Background:** In osteoarthritis (OA), the activation of inflammation response involving the interaction of cartilage and synovial hyperplasia may contribute to disease progression. However, inflammatory cells in OA synovial fluid (OASF) have been rarely studied.

**Objectives:** To investigate the phenotype of CD14 +cells and the secretion of proinflammatory cytokines by these cells

**Methods:** Immunohistochemistry staining in OA synovium was performed using anti-CD14, anti-CD16 and anti-CD56 antibody. The OASF was obtained through arthrocentesis. Mononuclear cells from OASFs were stained with anti-CD3, anti-CD4, anti-CD14, anti-CD16, anti-CD16 and anti-CD16 or anti-CD16 and analysed using flow cytometry. CD14 +CD16+ and CD14+CD16 mononuclear cells in OASF were selected with magnetic microbeads. In the supernatant of these cells culture, the concentration of IL-1 $\beta$ , IL-6, IL-8, TNF $\alpha$ , MMP-1, -3 were measured by Luminex.

**Results:** In OA synovium, CD14 or CD16 was stained, but CD56 was not expressed. In OASF, there was a substantial number of CD14 +cells (36.6%  $\pm$  25.2%), CD3 +cells (37.4%  $\pm$  12.9%), with a rarity of CD90 +cells (1.7%  $\pm$  1.3%). The proportion of CD14 +cells was increased significantly in recurrent synovial fluid, compared with the proportion in initial synovial fluid. Among CD14 +cells in OASF, CD14 +CD16+ monocyte subpopulation (21.2%  $\pm$  21.8%) was more abundant than CD14 +CD16- monocyte subpopulation (10.9%  $\pm$  10.0%). TLR4 and TLR2 expressions were higher in CD14 +CD16+ cells than in CD14 +CD16- cells. The concentration of IL-8 and MMP-3 was more increased in the supernatant of CD14 +CD16+ cells than in that of CD14 +CD16- cells.

**Conclusions:** In OASF, the proportion of CD14 +cells was increased in recurrent synovial effusion. Compared to CD14 +CD16- monocyte subpopulation, CD14 +CD16+ monocyte subpopulation released more cytokine such as IL-8 and MMP-3, and had higher expressions of TLR4 and TLR2.

**Disclosure of Interest:** None declared

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**SAT0065** **CHONDROCYTES UNDER PATHOLOGICAL CONDITIONS PREFERENTIALLY DEGRADES SELECTED tRNAs TO INHIBIT PROTEIN SYNTHESIS**

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**Background:** Oxidative and ER stress play an important role in the pathogenesis of osteoarthritis (OA). These stress conditions can induce the cleavage of transfer RNA (tRNA) via angiogenin. This cleavage at the anticodon loop of the tRNA produces 5'-tRNA and 3'-tRNA halves known as tiRNAs.

**Objectives:** We aim to identify specific tRNA to tiRNA isotype fragments that occur during oxidative or ER stress in human OA chondrocytes.

**Methods:** Primary human articular chondrocytes were enzymatically isolated from OA cartilage. Cells were cultured *in vitro* for 72 hour and then treated with tert-butyl hydroperoxide (TBHP) over a 12 hour time course or with Interleukin-1b (IL1b) over a 24 hour time course. RNA was collected for mRNA expression analysis (qRT-PCR). Protein was harvested for western blot analysis. A tRF and tiRNA PCR Array that profiles 55 known tiRNAs was used to perform an unbiased dissection of the formation of tiRNAs in OA chondrocytes. Total RNA was adapted using a First-Strand cDNA Synthesis Kit designed to create cDNA libraries from small RNAs for qPCR detection to identify ten novel tiRNAs associated with cell stress in OA chondrocytes.

**Results:** Using qRT-PCR RNase gene expression was measured. Of these RNases 250  $\mu$ M TBHP treatment at 12 hour induced KIAA0430 ( $p < 0.05$ ), RNase7 ( $p < 0.0001$ ) and ZC3H12A ( $p < 0.0001$ ) but not angiogenin or SND1. 10 ng/ml IL1 $\beta$  treatment at 6 hour induced SND1 ( $p < 0.0001$ ), RNase 7 ( $p < 0.01$ ), ZC3H12A ( $p < 0.01$ ) but not angiogenin or KIAA0430. Chondrocytes undergoing oxidative or ER stress produced tiRNA halves in a time dependent manner, tiRNA formation was highest at 6 hour of IL1 $\beta$  treatment and after 12 hour of TBHP treatment. tiRNA fragments of tRNAs specific for arginine, glutamic acid, glycine, histidine, lysine and valine were increased after TBHP or IL1 $\beta$  treatment. Ten tiRNAs that were induced by IL1 $\beta$  and TBHP were selected for further study. Primer sets for these tiRNA and the parent tRNAs were designed and screened across a wider time course, and with higher patient numbers.

**Conclusions:** The expression of several RNases was increased in a time dependent manner in stressed OA chondrocytes and may be involved in the cleavage of tiRNA fragments. tiRNA halves were grouped together based on their parent tRNA amino acid target. We hypothesised that an increase in fold change in these grouped tiRNAs may result in less production of proteins that contain a high percentage of that specific amino acid. These changes in amino acid distribution may account for decreases seen in amino acid rich proteins such as Type II collagen (a glycine rich protein) in stressed chondrocytes. By designing tiRNA and parent tRNA primers we will discover if tiRNA formation effects total levels of parent tRNAs. The outcomes from this research will provide us with an increased understanding of tRNA to tiRNA formation in human chondrocytes and may allow us to identify therapeutic targets for the treatment of OA and provide insights into novel stress signalling pathways.

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**Disclosure of Interest:** None declared

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**SAT0066** **THE LONG NONCODING RNA (LNCRNA) HOTTIP IS A MASTER REGULATOR OF CELL CYCLE IN HAND SYNOVIAL FIBROBLASTS IN ARTHRITIS**

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**Background:** Rheumatoid arthritis (RA) and other types of inflammatory arthritis follow a characteristic anatomical pattern of joint involvement. We have recently shown that local synovial stromal cells, specifically synovial fibroblasts, exhibit joint-specific transcriptomes and functions. In particular, hand SF exhibited prominent proliferative and chemotactic activities. Density of stroma and leukocyte infiltration were increased in hand synovium.

**Objectives:** To explore the role of hand/feet-specific lncRNA HOTTIP in shaping the function of hand synovial fibroblasts in arthritis.

**Methods:** We studied transcriptomes and epigenomes of hand, shoulder and knee SF from patients with RA or osteoarthritis and from knees of non-arthritic subjects using RNA-seq (Illumina HiSeq 2000 n=21), histone ChIP-seq (Illumina HiSeq 2500, n=7) and Infinium HumanMethylation450 BeadChip (n=12). qPCR was used to confirm RNA-seq data in a larger cohort of SF from different joints. We silenced the lncRNA HOTTIP in hand SF using LNA GapmeRs, followed by RNA-seq, qPCR, protein-protein interaction analysis of RNA-seq data (STRING), and *in vitro* assays for proliferation (BrdU assay) and apoptosis (Annexin V/PI staining).

**Results:** Genome-wide DNA methylation patterns and histone marks at actively transcribed DNA regions (H3K27ac) and enhancers (H3K4me1) defined joint-specific origin of SF. SF from hands and feet specifically expressed the lncRNA HOTTIP. This distal-specific HOTTIP expression coincided with the enrichment of H3K4me3 and H3K27ac and a decrease in repressive marks (H3K27me3, DNA methylation) at the HOTTIP promoter in hand SF. In contrast, the HOTTIP promoter displayed scarce activating, but abundant repressive epigenetic marks in shoulder and knee SF. Silencing of HOTTIP in hand SF altered the expression of 447 protein-coding genes (log ratio  $> 2$ , FDR  $< 0.05$ ). These genes were strongly enriched in the mitotic cell cycle protein interaction network (n=48 genes,  $p = 3.3 \times 10^{-7}$ ). Several of the enriched mitotic cell cycle genes, including NCAPG, CENPO, ZWILCH and BUB1 were confirmed as downregulated by HOTTIP silencing in a larger cohort of hand SF (n=6). The basal expression of 36 out of the 48 enriched cell cycle genes correlated with the basal HOTTIP expression in hand SF (n=6, RNA-seq,  $R > 0.06$ ). We further measured these correlations in a larger cohort of hand SF (n=21) for a subset of the 36 genes using qPCR. Among the measured genes, TADA 3 and CDC27 were confirmed to correlate with HOTTIP expression in hand SF ( $R = 0.5$ ,  $p < 0.05$ ). Silencing of HOTTIP for 24 hour, 48 hour and 72 hour decreased the incorporation of BrdU into DNA of



hand SF as measured by BrdU proliferation assay ( $p < 0.05$ ,  $n = 3$ ). Apoptosis of hand SF increased at 48 hour of HOTTIP silencing ( $p < 0.05$ ,  $n = 3$ ).

**Conclusions:** The lncRNA HOTTIP, which is specifically expressed in hand joints via epigenetic mechanisms, is a master regulator of mitotic cell cycle genes and proliferation in hand SF. Distal-specific expression of HOTTIP might imprint hand SF with enhanced proliferative potential, thereby shaping the location-specific joint pathology, e.g. prominent synovial hyperplasia and increased severity of hand arthritis in RA.

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#### SAT0067 ROLE OF NOX2-DERIVED REACTIVE OXYGEN SPECIES IN S100A8/A9-DRIVEN INFLAMMATORY OSTEOARTHRITIS

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**Background:** Synovitis in inflammatory osteoarthritis (OA) is driven by locally released DAMPs like S100A8/A9 proteins that have been shown to enhance joint destruction. S100A8/A9 induce ROS (reactive oxygen species) release by phagocytes in OA synovium via the NADPH-oxidase 2 (NOX2)-complex. Assembly of this complex is dependent on the neutrophils cytosolic factor (Ncf1). In this complex, the NOX2 protein is responsible for ROS production.

**Objectives:** In the present study we investigated whether NOX2-derived ROS are involved in joint pathology during collagenase-induced OA (CiOA).

**Methods:** CiOA was induced in knee joints of wild type (WT) and Ncf1-deficient (Ncf1<sup>-/-</sup>) mice. Synovial gene expression of NOX2-subunits was measured with qRT-PCR. Joint pathology was assessed using histology and antibodies against aggrecan neo-epitope VDIPEN. Levels of inflammatory proteins were measured with Luminex or ELISA. Phagocytes present in synovium, blood, bone marrow and spleen were analysed with flow cytometry. Extracellular ROS production by bone marrow-derived phagocytes was measured using an Amplex Red ROS detection assay.

**Results:** CiOA induction in knee joints of WT mice caused significantly increased synovial gene expression of NOX2 subunits. On day 7 of CiOA, synovial thickening, synovial S100A8/A9 levels and synovial percentages of inflammatory macrophages, PMNs, and monocytes were comparable between WT and Ncf1<sup>-/-</sup> mice. Cartilage damage and MMP activity, as measured by VDIPEN staining, were comparable, as well as levels of inflammatory mediators in serum and phagocyte percentages in blood, bone marrow and spleen. On day 42 of CiOA, synovitis, cartilage damage, and osteophyte formation in Ncf1<sup>-/-</sup> mice were unaltered when compared to WT mice. ROS production by Ncf1<sup>-/-</sup> PMNs was completely absent but Ncf1<sup>-/-</sup> macrophages, the more predominant phagocyte involved in development of pathology during CiOA, produced ROS in similar amounts as WT macrophages. Ncf1 deficiency thus seems to exclusively affect PMNs, this surprising finding might explain the lack of differences observed between CiOA development in WT and Ncf1<sup>-/-</sup> mice. ROS production by WT and Ncf1<sup>-/-</sup> macrophages was strongly upregulated by S100A8 and almost completely inhibited by the pan-NOX inhibitor diphenyleneiodonium chloride (DPI). In order to determine whether NOX1 complexes caused the compensation responsible for Ncf1 independent ROS production, we co-stimulated Ncf1<sup>-/-</sup> macrophages with NOX1-specific inhibitor ML171. However, no ML171-induced inhibition of ROS production was observed.

**Conclusions:** Absence of PMN-derived ROS does not alter synovitis and joint pathology in S100A8/A9-driven experimental inflammatory OA. The mechanism that enables Ncf1-independent ROS production by macrophages should be further investigated.

**Disclosure of Interest:** None declared

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#### SAT0068 BILIRUBIN PROMOTES DOWN-REGULATION OF RUNX2 AND UP-REGULATION OF RANKL GENE EXPRESSION IN BONE EXPLANTS AND IN OSTEOBLASTIC AND OSTEOCYTIC CELL LINES

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**Background:** *In vitro* studies have shown that the retained substances of cholestasis have deleterious effects in human osteoblasts and osteocytic cells. Bilirubin (BIL) and lithocholic acid (LCA) induce alterations in the proliferation, differentiation and apoptosis of osteoblastic and osteocytic cells. However, their effects in human bone tissue and in bone cell lines have not been deeply analysed.

**Objectives:** To investigate the effects of BIL, LCA and ursodeoxycholic acid (UDCA) in gene expression of human trabecular bone explants as well as in osteoblastic (SAOS2) and osteocytic cells (MLO-Y4/MLO-A5).

**Methods:** Bone tissue harvested from trabecular bone fragments, SAOS2 and MLO-Y4/MLO-A5 cells were cultured and treated with BIL (50  $\mu$ M), LCA (10  $\mu$ M) and UDCA (10/100  $\mu$ M) for 24 hour. Gene expression of osteocalcin (*BGLAP*), *Cbfa1* (*RUNX2*)/*Osterix* (*OSX*) and *RANKL* (*TNFRSF11B*) were quantified by real time PCR.

**Results:** BIL diminishes *RUNX2* gene expression in bone tissue (-37%), SAOS2 (-75%), MLO-Y4 (-56%) and MLO-A5 (-77%), and increases *RANKL* expression in 60%, 27%, 72% and 60%, respectively ( $p \leq 0.02$ ). In bone tissue and in osteoblastic and osteocytic cells, LCA increases gene expression of *BGLAP* (NS) and *RANKL* ( $p \leq 0.03$ ). UDCA 100  $\mu$ M increases *RUNX2* and *OSX* expression in bone tissue (78% and 82%), MLO-Y4 (72% and 80%) and SAOS2 (75% and 70%) ( $p \leq 0.03$ ). In addition, UDCA 100  $\mu$ M significantly increases expression of *BGLAP*, *OPG* and *RANKL* in bone tissue and in osteocytic lines. UDCA 10/100  $\mu$ M counteracts the decrease in *RUNX2* induced by BIL in bone tissue, SAOS2, MLO-A5 and MLO-Y4 cells.

**Conclusions:** The retained substances of cholestasis, particularly bilirubin, cause noxious effects on transcription factors of osteoblast differentiation and on osteoclastic activators in bone tissue and in osteoblastic and osteocytic cells. Ursodeoxycholic acid reverses the harmful effects of bilirubin. These results provide new insights into the low bone formation and at some stages, high resorption, associated with chronic cholestasis.

**Disclosure of Interest:** None declared

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#### SAT0069 ABNORMAL BONE AND CARTILAGE METABOLISM COULD BE ANTAGONISED BY SLEED ELECTROMAGNETIC FIELDS (PEMFs) AND TNF-A AND IL-6 GENE KNOCKOUTS IN A SIMILAR MECHANISM

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**Background:** Pulsed electromagnetic fields (PEMFs), as a safe and non-invasive method, could positively affect bone and cartilage metabolism. However, the effect and underlying mechanisms of PEMFs on osteoporosis and osteoarthritis remain poorly understood.

**Objectives:** The present study is designed to investigate the effect of PEMFs on osteoporotic bone and degenerative cartilage together with its potential molecular mechanisms in mice with different gene background.

**Methods:** Twenty 12 week male and Female wild-type (WT), *TNF $\alpha$*  knockout (*TNF $\alpha$ <sup>-/-</sup>*) or *IL6* knockout (*IL6<sup>-/-</sup>*) mice, respectively, were sham-operated (SHAM) or subjected to destabilisation of the medial meniscus (DMM) and ovariectomy (OVX) surgeries. After surgeries, WT mice were equally assigned to the non-treatment and PEMFs groups. Mice in PEMFs group were subjected to daily 1 hour PEMFs exposure with 8 Hz, 3.8 mT (peak value). Then all mice were euthanized after 4 weeks. Bone mass and subchondral microarchitecture were determined using micro-CT. Bone and cartilage metabolism was assessed by histological analysis, serum analyses, qRT-PCR and Western-Blot.

**Results:** The surgical models of osteoporosis and osteoarthritis were proved successful evidenced by the analysis of micro-CT data and histological analysis. The bone loss and damaged cartilage were largely repaired by *TNF $\alpha$*  and *IL6* gene knockout and partially inhibited by PEMFs exposure. Interestingly, no difference

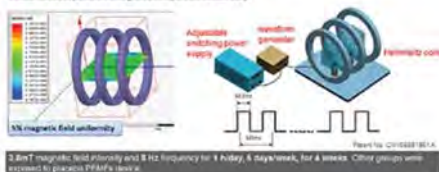
in Micro-CT data analysis was found between PEMFs group and gene knockouts, although a slight increase could be observed in  $TNF\alpha^{-/-}$  mice when compared to the PEMFs group. Negative effects on bone and cartilage was proved by testing key cytokines in anabolism and catabolism. PEMFs treatment and gene knockouts corrected the negative effects by targeting mediators in molecular pathways like Wnt and RANK. The differences in mRNA and protein level changes between PEMFs and gene knockouts were minor.



### PEMFs exposure system (Version 1.0)



### PEMFs exposure system (Version 2.0)



**Conclusions:** PEMFs alleviated surgeries induced bone loss and cartilage degeneration by promoting anabolism and inhibiting catabolism possibly in a similar mechanism to  $TNF-\alpha$  and  $IL-6$  gene knockouts, which imply that  $TNF-\alpha$  and  $IL-6$  may become new potential targets for PEMFs in treating degenerative bone diseases.

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SAT0070

### ROLE OF C/EBPβ IN 1,25D-INDUCED ACTIVATION OF RANKL EXPRESSION

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**Background:** 1 alpha 25-dihydroxyvitamin D3 (1,25D) is the active form of vitamin D3, which is responsible for osteoblast activation, subsequently bone formation. Although recent studies have shown that 1,25D stimulates RANKL expression in osteoblast differentiation<sup>1</sup>, its molecular mechanism of action is not fully understood.

**Objectives:** The aims of this study were to evaluate cellular response of human bone-derived cells to 1,25D treatment by observing expression during osteoblast differentiation

**Methods:** In this study, MG63, SaOS2, and primary bone-derived cells (BdCs) were cultured and isolated to further elucidate the effect of 1,25D on osteoblasts. Those were incubated in osteogenic medium (ascorbic acid, beta-glycerol phosphate, and dexamethasone) for 1, 3, and 7 days with or without 20 μM 1,25D. The

osteoblast activity and differentiation status were evaluated by intercellular Alkaline Phosphatase (ALP) activity, ALP staining, Alizarin Red S (ARS) staining, and hydroxyapatite staining. In this situation, C/EBPβ gene manipulation with siRNA or overexpression system were subjected to report assay of human RANKL promoter, quantitative PCR(qPCR), immunoblotting and immunostaining of osteoblastic gene expression (alkaline phosphatase, osteocalcin, vitamin D3 receptor, RANKL, and C/EBPβ etc.)

**Results:** 1,25D promotes osteoblast differentiation and expression of osteogenic markers in three different cells. Intriguingly, treatment of 1,25D to those cells are accompanied by stabilising C/EBPβ proteins and stimulating RANKL expression. Moreover, Overexpression of C/EBPβ significantly increases RANKL mRNA and protein. In contrast, suppression of C/EBPβ decreases RANKL expression. Thus, C/EBPβ is a key mediator involved in 1,25D induced RANKL expression.

**Conclusions:** our preliminary data indicated that human bone-derived cells response to vitamin D3 promoted RANKL expression via activation of C/EBPβ, and enhanced osteoblast activity and differentiation. This study provides insight into the molecular mechanism of RANKL expression and osteoblast activation in human bone-derived cells response to 1,25D.

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**Disclosure of Interest:** None declared

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SAT0071

### SUBCHONDRAL OSTEOGENESIS BUT NOT CARTILAGE DAMAGE IS PREVALENT IN KNEE JOINTS OF PREMATURELY AGEING MITOCHONDRIAL DNA MUTATOR MICE

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**Background:** Mitochondrial dysfunction has been demonstrated in ageing and osteoarthritic tissues. However it remains unclear whether dysfunctional mitochondria are directly implied in the pathogenesis of osteoarthritis.

**Objectives:** We investigated knee joints of prematurely ageing mitochondrial DNA mutator mice (*Polg<sup>D275A</sup>*) to evaluate a causal relationship between mitochondrial dysfunction and different features of osteoarthritis.

**Methods:** Bone structural parameters and chondrocyte were evaluated in knee joints of mice displaying increased mtDNA mutations rates and accelerated ageing, due to expression of a proofreading-deficient mtDNA polymerase, using micro-computed tomography and histopathological analysis.

**Results:** Homozygous mutants displayed osteopenia of the epiphyseal trabecular bone and subchondral cortical plate in comparison to wild type controls and heterozygous mutants. Osteopenia was associated with a strong increase of osteoclast numbers (0.88±0.30/mm bone perimeter) compared to heterozygous (0.25±0.03/mm) and wild type mice (0.12±0.04/mm). New bone formation was not observed. Wild type mice displayed only low grade cartilage degeneration (OARSI grade ≤1) due to loss of cartilage proteoglycans. Increased tibio-femoral chondrocyte was not apparent in hetero- and homozygous mitochondrial DNA mutator mice.

**Conclusions:** Mitochondrial dysfunction and premature ageing in mice with somatically acquired mtDNA mutations predisposes to enhanced subchondral bone resorption as potential early step of osteoarthritis, but not to cartilage damage or new bone formation. This phenotype potentially corresponds to an osteoporotic osteoarthritis phenotype in humans.

**Disclosure of Interest:** None declared

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SAT0072

### MIRNA-146A IS A KEY PLAYER IN BONE METABOLISM AND OSTEOPOROSIS

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**Background:** Micro RNAs (miRNAs) play a crucial role in the regulation of bone metabolism. MiR-146a, an important anti-inflammatory miRNA, was found to negatively impact osteogenesis and bone regeneration *in vitro*, by controlling the differentiation of mesenchymal stem cells. But to date the role of miR-146a in bone

remodelling, its influence on bone stability and development of osteoporosis is not known.

**Objectives:** The objective of this project is the analysis of the role of miR-146a in bone metabolism.

**Methods:** Systemic bone, tibiae and femur, of wt and miR-146a deficient animals was assessed histologically and via  $\mu$ CT analysis, over a period of 3 to 18 months of age. Serum cytokine levels were analysed by Elisa. mRNA expression levels in bone were analysed by qPCR. To induce osteoporosis, ovariectomy (OVX) induced bone loss was performed.

**Results:** When we analysed bone volume of long bones histologically as well as with  $\mu$ CT analysis we detected significantly increased trabecular bone mass in miR-146a deficient compared to wt animals, starting at an age of 6 months. However, cortical thickness of systemic bones from miR-146a knock out animals was significantly reduced compared to control mice. Analysis of serum in aged miR-146a deficient animals displayed elevated activity of bone resorbing osteoclasts as amounts of CTX I in miR-146a<sup>-/-</sup> mice were significantly increased compared to wt animals. Q-PCR analysis of important osteoclast as well as osteoblast marker genes in bones *ex vivo* displayed elevated expression of signature molecules of both cell types in aged miR-146a deficient mice, suggesting a regulatory role of miR-146a in both osteoclasts as well as osteoblasts. When we induced osteoporosis using the OVX disease model, histological analysis of long bones showed significant trabecular bone loss in ovariectomized wt mice. In contrast, we detected no trabecular bone loss in ovariectomized miR-146a knock out animals, suggesting that loss of miR-146a deficiency protects bone loss induced by oestrogen deficiency.

**Conclusions:** MiR-146a seems to control bone turnover and miR-146a deficient mice accrue bone over time. Moreover this miRNA has a negative influence on bone loss occurring during oestrogen loss induced osteoporosis. Therefore miR-146a could be possibly used as a therapeutic target in the treatment of osteoporosis.

**Disclosure of Interest:** None declared

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SATURDAY, 16 JUNE 2018

## Rheumatoid arthritis – prognosis, predictors and outcome

SAT0073

### ACPA AND RF AS PREDICTORS OF SUSTAINED CLINICAL REMISSION IN RHEUMATOID ARTHRITIS PATIENTS: RESULTS FROM THE ONTARIO BEST PRACTICES RESEARCH INITIATIVE (OBRI)

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**Background:** Positive anti-citrullinated protein antibody (ACPA) and rheumatoid factor (RF) are included among the 2010 ACR/EULAR classification criteria for rheumatoid arthritis (RA). Previous studies have shown that autoantibodies are positive predictors of response in RA patients treated with some biologics whereas other studies suggest worse prognosis if positive for ACPA and RF.

**Objectives:** The purpose of this study was to evaluate the interaction of RF and ACPA in predicting sustained clinical response in a large observational registry of RA patients followed in routine practice.

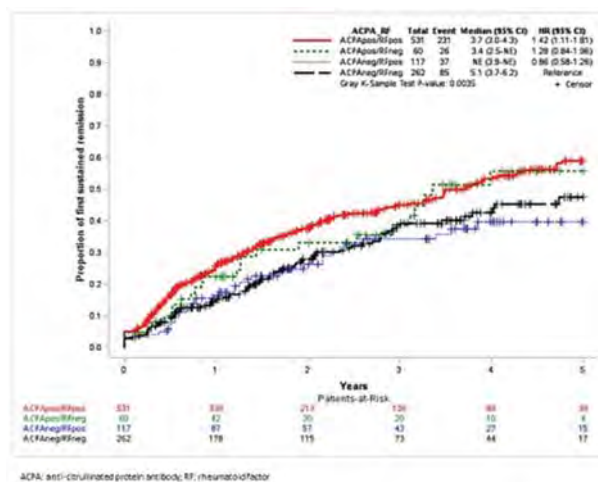
**Methods:** RA patients enrolled in the Ontario Best Practices Research Initiative (OBRI) registry, with active disease ( $\geq 1$  swollen joint), available autoantibody information, and at least 1 follow-up assessment were included in the analysis. Sustained clinical remission was defined as CDAI  $\leq 2.8$  in at least 2 sequential visits separated by at least 3 and maximum of 12 months. Time to sustained remission was assessed by plotting cumulative incidence curves and multivariate cox regression.

**Results:** A total of 970 (30%) out of 3251 patients in the registry were included, of whom 262 (27%) were anti-CCP<sup>neg</sup>/RF<sup>neg</sup>, 60 (6.2%) anti-CCP<sup>pos</sup>/RF<sup>neg</sup>, 117 (12.1%) anti-CCP<sup>neg</sup>/RF<sup>pos</sup>, and 531 (54.7%) anti-CCP<sup>pos</sup>/RF<sup>pos</sup>. At baseline, significant differences were observed between groups in age ( $p=0.02$ ), CDAI ( $p=0.03$ ), tender joint count ( $p=0.02$ ), and HAQ-DI ( $p=0.002$ ), with anti-CCP<sup>pos</sup>/RF<sup>pos</sup> and anti-CCP<sup>pos</sup>/RF<sup>neg</sup> patients being youngest and having the lowest disease activity and disability. No differences were observed in terms of biologic use (20.2% of patients).

Sustained remission was 10% more likely if anti-CCP<sup>pos</sup>, and was achieved by 43.5% of anti-CCP<sup>pos</sup>/RF<sup>pos</sup> patients, 43.3% of anti-CCP<sup>pos</sup>/RF<sup>neg</sup> patients, 31.6%

of anti-CCP<sup>neg</sup>/RF<sup>pos</sup> patients and 32.4% of anti-CCP<sup>neg</sup>/RF<sup>neg</sup> patients ( $p=0.01$ ). Significant differences were observed in the time to achieving sustained clinical response from enrolment in the OBRI based on anti-CCP status ( $p<0.001$ ), RF status ( $p=0.06$ ), and both ( $p=0.004$ ) (figure 1). ACPA<sup>pos</sup>/RF<sup>pos</sup> (median: 3.7 years; 95% CI: 3.0–4.3) and ACPA<sup>pos</sup>/RF<sup>neg</sup> (median: 3.4 years; 95% CI: 2.4–NE) patients achieved sustained remission earlier than ACPA<sup>neg</sup>/RF<sup>neg</sup> patients (median: 5.1 years; 95% CI: 3.7–6.2), respectively (figure 1).

Multivariate cox regression adjusting for baseline CDAI score, age and sex also showed differences between groups; statistically significance in anti-CCP<sup>pos</sup>/RF<sup>pos</sup> vs. anti-CCP<sup>neg</sup>/RF<sup>neg</sup> patients (HR [95% CI]: 1.30 [1.01–1.67];  $p=0.04$ ).



**Abstract SAT0073 – Figure 1.** Cumulative incidence of first sustained remission by ACPA/RF status

**Conclusions:** These results suggest that anti-CCP but not RF positivity may be associated with a higher chance of remission, possibly due to an improved treatment response.

**Disclosure of Interest:** J. Pope Grant/research support from: OBRI was funded by peer reviewed grants from CIHR (Canadian Institute for Health Research), Ontario Ministry of Health and Long-Term Care (MOHLTC), Canadian Arthritis Network (CAN) and unrestricted grants from: Abbvie, Amgen, Celgene, Hospira, Janssen, Lilly, Merck, Novartis, Roche, Sanofi, and UCB, M. Movahedi Employee of: OBRI, E. Rampakakis Employee of: JSS Medical Research, A. Cesta Employee of: OBRI, J. Sampalis: None declared, C. Bombardier Grant/research support from: OBRI was funded by peer reviewed grants from CIHR (Canadian Institute for Health Research), Ontario Ministry of Health and Long-Term Care (MOHLTC), Canadian Arthritis Network (CAN) and unrestricted grants from: Abbvie, Amgen, Celgene, Hospira, Janssen, Lilly, Merck, Novartis, Pfizer, Roche, Sanofi, and UCB, Consultant for: Dr. Bombardier holds a Canada Research Chair in Knowledge Transfer for Musculoskeletal Care and a Pfizer Research Chair in Rheumatology

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SAT0074

### IDENTIFICATION OF A PROTEIN PANEL USEFUL FOR THE PREDICTION OF RESPONSE TO METHOTREXATE IN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** The treatment of rheumatoid arthritis (RA) aims to control a patient's signs and symptoms, prevent joint damage, and maintain his/her quality of life. Among the best known disease-modifying antirheumatic drugs, Methotrexate (MTX) is one of the most effective and widely used medications. It is used as a general first-choice drug, although some patients will not respond to this treatment and it is not free from side effects.

**Objectives:** To identify circulating proteins that could be useful as predictors of the patient's response to MTX.



**Methods:** Serum samples from patients enrolled in the Pathobiology of Early Arthritis Cohort (PEAC) were collected before treatment with MTX. Response to therapy was determined after 6 months by calculating the initial and final DAS28 of the patients. Their classification was performed following the EULAR response criteria. Sixty samples at baseline from this cohort (30 good responders and 30 non-responders) were depleted from the 14 most abundant proteins by affinity chromatography to remove background. Then, they were analysed by reversed-phase nanoliquid chromatography coupled to mass spectrometry using a SWATH strategy in a tripleTOF MS (Sciex). The quantitative data obtained in this proteomic analysis were processed using the ProteinPilot 5.0.1 and PeakView 2.1 software (Sciex). Machine learning analyses were performed on a train set of 30 samples (15 responders and 15 non-responders) via support vector machine (SVM) using the Classyfire, e1071 and caret R packages. Results were verified in an independent set of 24 samples by a two-stage support vector machine (TSSVM) with RBF kernel and 10 cross-fold validation for each meta-model.

**Results:** The proteomic analysis led to the identification and quantification of 229 proteins that were common between the screening and validation sets. Independent screening and validation data sets were preprocessed by PCA for dimension reduction and analysed by machine learning tools, leading to the definition of a panel of 8 proteins (one of them involved in MTX metabolism) differentiating the groups of responders and non-responders to MTX with strong agreement (Kappa >0.80), very high accuracy and good relevant metrics (table 1).

**Abstract SAT0074 – Table 1.** Metrics of the classification performance of the 8-protein panel identified in this work to predict response of the patient to MTX. Cut-off for significance was p-value <0.05.

Train set							
Accuracy	95% CI	p-value	Kappa	Sensitivity	Specificity	Pos pred value	Neg pred value
0.9333	(0.7793 - 0.9918)	1.108e-05	0.8667	0.8824	1.0000	1.0000	0.8667
Validation set							
Accuracy	95% CI	p-value	Kappa	Sensitivity	Specificity	Pos pred value	Neg pred value
0.9583	(0.7888 - 0.9989)	0.0007722	0.9091	1.0000	0.9375	0.8889	1.0000

**Conclusions:** We have defined a panel of circulating proteins useful to predict the response to MTX therapy in rheumatoid arthritis patients.

**Disclosure of Interest:** None declared

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### SAT0075 ADDITIONAL TARGET OF NORMAL SERUM MATRIX METALLOPROTEINASE-3 IS A POTENTIAL BIOMARKER FOR LESS ONE-YEAR RADIOGRAPHIC PROGRESSION IN RHEUMATOID ARTHRITIS

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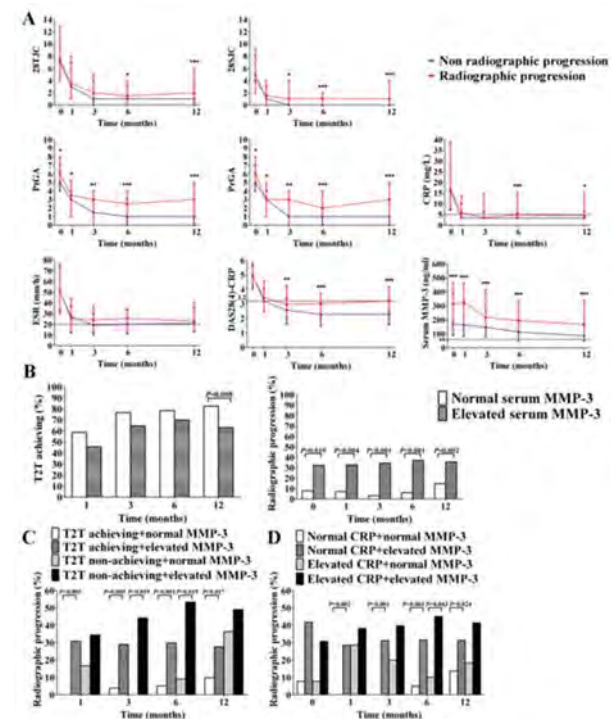
**Background:** Matrix metalloproteinase (MMP)-3 plays important roles in bone and cartilage destruction in rheumatoid arthritis (RA). Our previous study showed continuously elevated serum MMP-3 for 3–6 months predict one-year radiographic progression in RA (Arthritis Res Ther. 2015 17:289). However, whether serum MMP-3 normalisation is a biomarker for better outcome remains elusive.

**Objectives:** To explore the association of serum MMP-3 normalisation with clinical and radiographic outcome in RA.

**Methods:** RA patients with moderate to high disease activity (DAS28-CRP>3.2) were treated according to treat to target (T2T) strategy and followed up at regular intervals (0, 1 st, 3rd, 6th and 12th months). Demographic and clinical data were collected according to the 2017 EULAR recommendation and serum MMP-3 was detected by ELISA at each visit. X-ray assessment of hand/wrist was repeated at baseline and month 12 and radiographic progression was defined as a change of the Sharp/van der Heijde modified sharp score  $\geq 0.5$  units.

**Results:** (1) Among 200 RA patients recruited, there were 163 (81.5%) female, with median disease duration 24 (11–84) months, median DAS28-CRP 4.9 (4.2–5.7). There were 29% patients showed one-year radiographic progression. (2) The median MMP-3 was 209.7 (108.6–430.0) ng/ml. RA patients without radiographic progression had significant lower level of serum MMP-3 than those with radiographic progression at baseline and each visit (figure 1A, all p<0.001). (3) There were 13.0%, 14.5%, 17.0%, 25.5% and 31.0% patients having normal MMP-3 at baseline and 1 st, 3rd, 6th and 12th months, respectively. There were significantly

lower percentage of RA patients with normal MMP-3 at baseline and each visit showed radiographic progression than those with elevated MMP-3 (figure 1B, all p<0.05). (4) There were 8.5%, 13.0%, 20.0% and 25.5% patients who achieved therapeutic target and showed normal MMP-3 at 1 st, 3rd, 6th and 12th months, respectively. Among patients achieved therapeutic target, there were significantly lower percentage of normal MMP-3 patients showed radiographic progression than those with elevated MMP-3 (figure 1C, all p<0.05). (5) There were 6.5%, 11.0%, 14.5%, 20.5% and 25.5% patients who had normal CRP and normal MMP-3 at baseline and 1 st, 3rd, 6th and 12th months, respectively. Among patients with normal CRP, there were significantly lower percentage of normal MMP-3 patients at 1 st, 3rd, 6th and 12th months showed radiographic progression than those with elevated MMP-3 (figure 1D, all p<0.05).



**Abstract SAT0075 – Figure 1.** Dynamic change of serum MMP-3 and indicators of disease activity and radiographic progression in RA. **A** Comparison of disease activity and radiographic progression indicators between RA patients with and without radiographic progression. **B** Comparison of T2T achieving and the percentage of RA patients showing radiographic progression between normal and elevated serum MMP-3 groups at each visit. **C** Comparison of the percentage of RA patients showing radiographic progression among groups with or without T2T achieving and normal serum MMP-3. **D** Comparison of the percentage of RA patients showing radiographic progression among groups with or without normal CRP and normal serum MMP-3.

**Conclusions:** Additional target of normal serum MMP-3 may be a potential biomarker for less one-year radiographic progression.

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### SAT0076 SYNOVIAL MAST CELLS AND RESPONSES TO SYNTHETIC AND BIOLOGIC DMARDS IN EARLY AND ESTABLISHED RHEUMATOID ARTHRITIS

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**Background:** Mast cells (MCs) are immune cells implicated in the pathogenesis of Rheumatoid Arthritis (RA), but their presence in synovia has not been assessed systematically and their association with disease progression and treatment response is unknown.

**Objectives:** To analyse MCs in the synovia of patients with early vs established RA in correlation with histological and clinical phenotype.

**Methods:** DMARDs-naïve patients with early (<12 months) RA (n=97) and patients with established RA failing synthetic DMARDs and candidate to biologic treatment (n=27) underwent ultrasound-guided synovial biopsy. Sections of paraffin embedded synovial tissue were stained with H and E to measure the degree of synovitis (Krenn Score). Sequentially cut sections were stained by immunohistochemistry to evaluate the presence of immune cells, including CD117 (c-kit) positive mast cells. Upon SQ scoring (0–4), patients were stratified into synovial pathotypes (Lymphoid, Fibroid, and Myeloid), as previously described

**Results:** In the cohort of DMARDs-naïve early RA (mean disease duration 6 months), MC+ve patients (67.7%) had significantly higher synovial inflammation (Krenn score), higher prevalence of the lymphoid pathotype, higher inflammatory markers and disease activity; however, they did not differ in terms of response to sDMARDs at 6 months (table 1, left). In established RA (mean disease duration 5 years), MC+ve patients (48.1%) had significantly higher synovial inflammatory scores and higher prevalence of the lymphoid pathotype, while systemic inflammatory markers or disease activity scores were not different. At 6 months follow-up, MC+ve patients had significantly higher rates of response to anti-TNF $\alpha$  (table 2, right).

Abstract SAT0076 – Table 1

	Early RA				Established RA			
	All (n=99)	MC- (n=32)	MC+ (n=67)	P value*	All (n=27)	MC- (n=14)	MC+ (n=13)	P value*
Disease duration, months (SD)	6 (3)	5 (3)	6 (3)	0.664	62.6 (56.2)	68.5 (62.1)	56.3 (50.77)	0.616
ESR, mean (SD)	38 (30)	28 (24)	44 (31)	0.008	33 (26)	31 (31)	36 (22)	0.231
CRP, mean (SD)	17 (25)	8 (14)	21 (29)	0.007	11 (23)	13 (32)	10 (5)	0.025
ACPA+, %	75.8%	75%	76.1%	0.839	63%	64.3%	61.5%	0.883
DAS28, mean (SD)	5.65 (1.41)	5.55 (1.41)	5.95 (1.00)	0.405	6.53 (0.88)	6.54 (0.94)	6.52 (0.86)	0.905
Lymphoid pathotype, %	45.9%	9.4%	63.6%	<0.001	53.8%	30.8%	76.9%	0.018
High synovitis, %	48.4%	12%	62.1%	<0.001	46.2%	23.1%	69.2%	0.018
6 months DAS28, mean (SD)	3.48 (1.95)	3.13 (1.79)	3.67 (2.02)	0.248	3.87 (1.3)	4.44 (1.23)	2.89 (0.71)	0.004
6 months DAS28<3.2, %	52.4%	62.1%	47.2%	0.196	36.8%	8.3%	85.7%	0.001

\*Mann-Whitney or Chi square as appropriate

**Conclusions:** We here show that early RA patients with MC+ve synovitis and high levels of local and systemic inflammation do not respond differently to synthetic DMARDs. In the context of established RA after sDMARDs failure, patients with MC+ve synovitis, despite having similar levels of systemic inflammatory markers and disease activity, had higher chances of responding to anti-TNF- $\alpha$ . Although the latter observation will need validation on larger cohorts, our data suggests that the analysis of synovial MCs might help defining synovial histopathology and possibly contribute to the prediction of treatment response.

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**DOI:** 10.1136/annrheumdis-2018-eular.6839

SAT0077

#### CHANGE IN FREQUENCY OF ARTHROPLASTY SURGERY IN RHEUMATOID ARTHRITIS: A 13 YEAR POPULATION HEALTH STUDY

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**Background:** Improvement in the medical management of rheumatoid arthritis (RA) over the past two decades may have reduced the need for arthroplasty surgery but the literature to date has reported inconsistent findings.

**Objectives:** To compare the annual frequency of hip, knee and other arthroplasty surgery in a prevalent cohort of RA cases and matched controls over 13 years.

**Methods:** A retrospective cohort study was performed utilising administrative healthcare data from approximately 1 million people with access to universal

healthcare between 1997 and 2010. RA cases were identified using a previously validated RA case definition in the same dataset.<sup>1</sup> Each case was matched by age and sex to 4 randomly selected controls. The annual frequency of arthroplasties in cases and controls was compared. In addition the frequency of coronary artery interventions (bypass grafting, angioplasty and stenting) was compared. Data included physician billings, hospital discharges and patient registry information using ICD-9 and ICD-10. Statistical analysis used least squares regression t-tests and 2-proportion z-tests.

**Results:** The number (prevalence) of RA cases increased from 3913 (0.42%) to 4911 (0.52%) over the study. The mean (SD) age changed from 56.7 (15.9) to 60.1 (14.9) years and the proportion of females from 70.8% to 73.9%. In both the first and last years of the study the frequency of all arthroplasty procedures was higher in cases than controls (p<0.001) (Table). Over time there was a gradual and significant reduction in arthroplasty surgery in RA cases by 51.9% (p<0.001). This was in contrast to controls in whom the frequency of procedures increased by 31.9% (p=0.002) with the exception of hip arthroplasty. For the latter procedure, the frequency decreased by 63% in RA cases (p<0.001) and 35% in controls (p=0.617). In contrast to arthroplasty procedures the frequency of cardiac procedures, which were higher in RA cases in both the first (p=0.013) and final (p=0.003) years of observation, increased in both cases and controls over time although did not reach statistical significance in either.

Abstract SAT0077 – Table 1. Demographics and surgical procedures in RA patients and controls

Demographics	1997		2010	
	RA cases	Controls	RA cases	Controls
Age (SD) in years	56.7 (15.9)	56.7 (15.9)	60.1 (14.9)	60.1 (14.9)
Female (%)	70.8	70.8	73.9	73.9
	% population undergoing procedure in 1997		% population undergoing procedure in 2010	
Surgical procedures	RA cases	Controls	RA cases	Controls
Total arthroplasties	4.78	0.47	2.30	0.62
Hip arthroplasty	1.43	0.20	0.53	0.13
Knee arthroplasty	1.74	0.13	0.81	0.27
Other arthroplasty	1.76	0.13	0.98	0.22
Cardiac procedures	0.36	0.16	0.57	0.29

**Conclusions:** There was a striking reduction in arthroplasty surgery in RA cases over 13 years of observation. Lack of similar changes in controls and sustained rates of cardiac procedures over the same time suggests that this was not due to limited surgical access for RA patients. Improvement in medical treatment of RA is likely responsible.

#### REFERENCE:

- [1] Hanly JG, Thompson K, Skedgel C. The use of administrative healthcare databases to identify patients with Rheumatoid Arthritis. *Access Rheumatology: Research and Reviews* 2015;7:69–75.

**Disclosure of Interest:** None declared

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SAT0078

#### WHICH CDMAID STRATEGY IS MOST EFFECTIVE IN NEWLY DIAGNOSED SERONEGATIVE RHEUMATOID ARTHRITIS PATIENTS; POST-HOC ANALYSIS OF THE TREATCH STUDY

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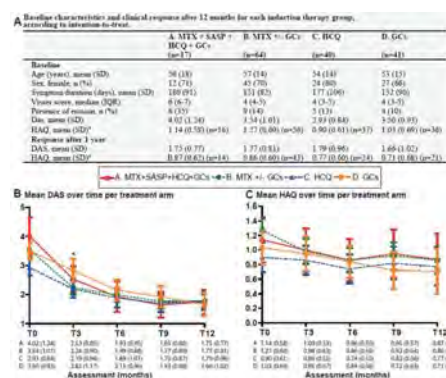
**Background:** The disease spectrum of rheumatoid arthritis (RA) is heterogeneous. Literature suggests that these different disease subsets could be treated differently, with less aggressive treatment for rheumatoid factor and anti-citrullinated protein antibody negative RA patients ("seronegative RA"). Current treatment guidelines, however, do not take this into account since evidence is lacking. Especially, data about standardised treatment strategies in seronegative patients are needed.

**Objectives:** To compare 1 year clinical efficacy of 4 different initial treatment strategies in newly diagnosed, seronegative RA patients, according to the 2010 criteria.

**Methods:** For this post-hoc analysis data of the tREACH trial (stratified, single-blinded, randomised clinical trial) were used. Eligible patients, for the tREACH, were stratified into 3 probability tertiles (low, intermediate and high) according to their likelihood of progressing to persistent arthritis based upon the prediction model of Visser. For this analysis we selected all seronegative RA patients, of whom respectively 81% and 19% were in the intermediate and high stratum. Patients received 1 of the following 4 initial treatment strategies, which were

based upon the tREACH randomization within each stratum (figure 1): [A] triple DMARD combination therapy (MTX 25 mg/wk.+SASP 2 gr/day+HCQ 400 mg/day+GCs (intramuscular or an oral tapering scheme, starting with 15 mg/day), [B] MTX 25 mg/wk.±GCs orally starting with 15 mg/day, [C] HCQ 400 mg/day and [D] GCs orally starting with 15 mg/day. Treatment strategies were 'tightly controlled', with patients being examined every 3 months. Treatment decisions were based upon the original Disease Activity Score (DAS) threshold for low disease activity (DAS <2.4). Primary outcomes were DAS and functional ability, measured with the Health Assessment Questionnaire (HAQ), over time, using a linear mixed model (LMM). In our final model we corrected for baseline DAS and HAQ and visser score, which is a confounder by indication on forehead.

**Results:** 162 patients were grouped into treatment arms A (n=17), B (n=64), C (n=40) or D (n=41). Patients were mostly female (67%) with an average symptom duration of 161 days (95% CI: 146–175). At baseline the average visser score was 4 out of 13 (IQR 4–5). The difference in visser score was mainly due to the difference in erosions (figure 1A). Figure 1B and C show the DAS and HAQ over time per treatment arm. Our corrected LMM showed that there was no significant difference between treatment arms for DAS over time. After 3 months 56%, 38%, 35% and 69% respectively treated with A, B, C and D had an active disease (DAS ≥ 2.4), and thus needed a treatment intensification (P<0.003 for C versus D). However, after 1 year there was no difference between DAS over all treatment arms. HAQ over time did differ between treatment arms. Patients who received HCQ showed a better functional ability over time compared to patients receiving 1 of the other treatments (C versus respectively B ( $\beta = -0.18$ , p<0.000), D ( $\beta = -0.14$ , p<0.004) and A ( $\beta = -0.17$ , p<0.016)).



**Abstract SAT0078 – Figure 1.** (A) Baseline characteristics and clinical response after 12 months for each induction therapy group, according to intention-to-treat. (B) Mean DAS over time per treatment arm. (C) Mean HAQ over time per treatment arm. <sup>a</sup> Not everyone filled out a (complete) questionnaire and therefore n is different for HAQ. MTX 25 mg/wk, SASP 2 gr/day, HCQ 400 mg/day, GCs intramuscular or an oral tapering scheme starting with 15 mg/day for treatment A and only oral for treatment B+D. \* P<0.011 for C versus D. Abbreviations: DAS, Disease Activity Score; GCs, glucocorticoids; HAQ, Health Assessment Questionnaire; HCQ, hydroxychloroquine; MTX, methotrexate; RA, rheumatoid arthritis; SASP, sulfasalazine

**Conclusions:** This research supports current hypothesis that seronegative RA patients can be treated with less aggressive treatment with similar efficacy.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.3214

### SAT0079 TREATMENT EXPECTATIONS INFLUENCE BOTH SUBJECTIVE AND OBJECTIVE OUTCOME PARAMETERS IN PATIENTS WITH RHEUMATOID ARTHRITIS - A PROSPECTIVE COHORT STUDY

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**Background:** The prediction of individual response to treatment in rheumatoid arthritis (RA) is challenging and often limited. Here we evaluate the influence of patients' expectations and attitudes towards newly initiated disease-modifying anti-rheumatic drugs (DMARDs) on clinical outcome in RA.

**Methods:** 100 patients (74 female) with RA according to 2010 ACR/EULAR classification criteria with upcoming change in DMARD treatment were included. Patients' treatment beliefs, health related quality of life, treatment expectations, and pain-related cognitions were measured using *the beliefs about medicines*

*questionnaire* (BMQ), the SF-36, the *questionnaire about patient expectation* (PE), and the *pain-related self-statement scale* (PRSS), respectively before treatment initiation (T0) and their DAS28-CRP was calculated at T0 and after 4 months (T4). Associations between patients' beliefs, expectations and their attitude according to the questionnaires and changes in DAS28-CRP between T0 and T4 were explored by regression analyses using the Aikake information criterion.

**Results:** Regression analyses revealed that 42.2% of all variability in treatment response measured as a decline in DAS28-CRP ( $\Delta$ DAS28) could be explained by expectations, psychological factors and laboratory parameters assessed with the applied questionnaires. Among these we identified the expected *improvement rate* with 23.4% as well as the patients' *fear of side effects* with 22.0% as the main predictors of  $\Delta$ DAS28. The CRP-value at T0 accounted with 15% to the variability in  $\Delta$ DAS28. Other highly influential factors were PRSS *catastrophizing* scale (10.7%), the BMQ *concern* scale (8.1%), other BMQ scales (7.9%) and medications' route of administration (8.0%).

**Conclusions:** The present study indicates a high impact of patients' expectations and their attitude towards new therapies on clinical response effecting both objective and subjective outcome parameters. Integration of individual patient's preferences and their expectations in treatment decisions and management can significantly increase treatment response.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.4847

### SAT0080 SECULAR TRENDS PRIOR TO-AND AFTER DISSEMINATION OF BEST PRACTICE RECOMMENDATIONS SHOWED EARLIER INTENSIFIED MEDICATION STRATEGIES AND IMPROVED OUTCOMES IN CANADIANS WITH EARLY INFLAMMATORY ARTHRITIS

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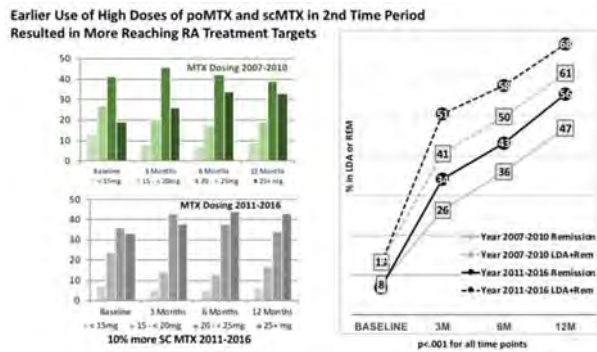
**Background:** International and local best-practice recommendations released in 2010–11 aimed to improve outcomes in early RA via earlier diagnosis and a treat-to-target approach. These should be associated with improved outcomes.

**Objectives:** To examine secular trends in patient characteristics and treatment strategies at RA diagnosis and disease activity outcomes in the 1st year of follow-up comparing earlier (2007–2010) and later (2011–2016) time periods, prior to and following dissemination of 2011 guidelines in a large Canadian early inflammatory arthritis (EIA) cohort of RA patients.

**Methods:** Data were from patients with early classifiable (87%) or probable (13%) RA (<1 year of symptoms) enrolled each year in an ongoing prospective multi-centre cohort study between 2007–2016 with  $\geq 12$  M follow-up undergoing 3-monthly visits including clinical assessments, questionnaires, and laboratory tests in the 1st year. Treatment was decided by their rheumatologist. These were cohort investigators who met annually to discuss means to improve outcomes. Descriptive statistics compared patient characteristics, early treatment strategies with conventional synthetic(cs) and biologic(b) DMARDs and disease activity (DAS28) outcomes. Differences in DAS28 targets achieved per time period were compared using Chi-Squares and medication doses by Cochrane Hermitage trend tests.

**Results:** Of 2227 patients enrolled in CATCH (Canadian Early Arthritis Cohort), symptom duration was 6 (3) months. There was a slight increase in number recruited, education and income and slight decrease in baseline symptom duration from early to later time periods. Baseline smoking, obesity rates, comorbidities, positive serology, inflammatory markers and joint counts did not differ significantly between time periods. Baseline erosions were less frequent (17% vs. 24%, p<0.0001) and mean symptom duration decreased slightly (5.6 vs. 5.9 months, p=0.018) in earlier vs later periods. Most (87%) entered in moderate or high disease activity (MDA or HDA);disease activity at 3, 6 and 12 M markedly improved over calendar time (figure 1). Respective DAS28 REM/LDA rates at 12 M from early to late periods significantly increased (p<0.01), 20% (p<0.001) used higher doses of MTX ( $\geq 20$  mg); and more used subcutaneous (sc) MTX, MTX combo therapies sooner and more rapidly escalation to bDMARDs all p's<0.05).





Abstract SAT0080 – Figure 1. Earlier Use of High Doses of poMTX and scMTX in 2nd Time Period Resulted in More Reaching RA Treatment Targets

**Conclusions:** This 10 year Canadian prospective study of classifiable/probable RA patients, who were assessed for 1 year suggests that earlier, more intensified treatment promoted in practice recommendations were implemented and resulted in lower disease activity with a greater proportion of patients reaching targets of LDA and/or REM, although 25%–30% of patients still did not achieve LDA or REM by 12 M.

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**Disclosure of Interest:** None declared

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**SAT0081 CHANGES IN INCIDENCE OF SHOULDER, ELBOW, WRIST AND FINGER REPLACEMENT SURGERY AMONG RHEUMATOID ARTHRITIS PATIENTS FOLLOWING THE INTRODUCTION OF BIOLOGICAL DMARDS: AN INTERRUPTED TIME SERIES ANALYSIS USING DANISH HEALTH CARE REGISTERS**

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**Background:** We have previously shown that the incidence rate of total knee replacements started to decrease among rheumatoid arthritis (RA) patients following the introduction of biological (b) DMARDs, but less is known on the impact of bDMARDs on the need for joint replacements (JR) of the upper limbs.

**Objectives:** To investigate the association between bDMARD introduction for the treatment of patients with RA on the trends of upper limb JR among newly diagnosed RA patients compared with a matched general population cohort (GPC) in Denmark.

**Methods:** Nationwide register-based interrupted time-series analysis using the Danish National Patient Register and Civil Registration System. **Study populations:** incident RA patients diagnosed at a rheumatology or general internal medicine clinic/department from 1996–2010. **Intervention:** introduction of bDMARDs

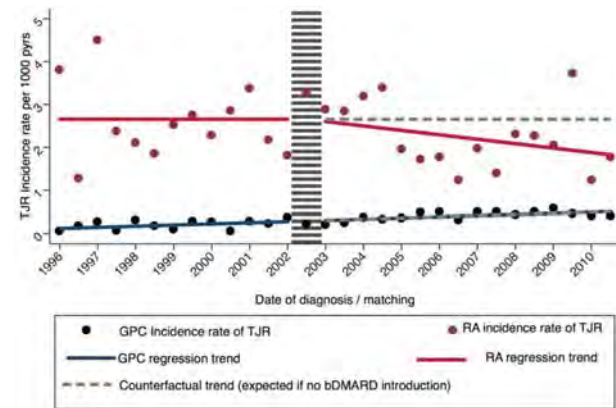
Abstract SAT0081 – Table 1. Changes in 5-year incidence rate of upper limb joint replacements (JR) in incident rheumatoid arthritis (RA) patients following introduction of biological DMARDs in 2002 compared with secular trends in a matched general population cohort (GPC).

Cohort	N	Mean age at start of follow-up	Females, n (%)	n JR	PYRS	Baseline incidence rate/1000 pyrs	Δ per year*	Δ in level 2003	Δ per year*	Absolute/relative Δ at midpoint in bDMARD era (mid-2006) compared with counterfactual value
RA	26 458	58.9 years	18 691 (71%)	295	1 23 814	2.65 (2.27–3.04)	-	-	-0.10 (-0.21+0.01)	-0.44 (-0.49 to -0.39)/-17%
GPC	2 57 505	58.4 years	1 82 192 (71%)	377	1,152,052	0.11 (0.04–0.17)	0.03 (0.02–0.03)	-	0.03 (0.02–0.03)	No change

in Denmark in 2002. **Comparison:** Each RA patient was matched on age, sex and municipality with up to 10 non-RA individuals (GPC). **Outcome:** Composite outcome of first shoulder, elbow, wrist, or finger replacement surgery (JR). **Statistical analyses:** 5 year age- and sex-standardised incidence rates of JR calculated for incident RA patients diagnosed biannually compared with GPCs. Outcome trends in the pre-bDMARD era (1996–2001) were compared with those in the bDMARD era (2003–2015) with a 1 year lag period in 2002.

**Results:** From 1996 to 2010, 26 458 incident RA patients were identified and compared with 257,505 GPCs (Table). The JR incidence rate was stable among RA patients in 1996–2001, but started to decrease from 2003 and onwards. Among GPCs, the incidence rate increased throughout the study period. Stepwise backward elimination to produce most parsimonious model: p-entry <0.05 and p-exit >0.2.

\* Δ per year based on biannual data. Abbreviations: pyrs, person years



**Conclusions:** Following the introduction of bDMARDs, the incidence rate of upper limb JR started to decrease among RA patients, whereas the incidence rate steadily increased from 1996–2015 among matched GPCs. The baseline incidence rate was 7-fold higher among RA patients than GPCs, but the absolute need for upper limb JR was low in both groups.

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**SAT0082 OSTEOPOINTINE AND OSTEOPTROTEGRINE AS MARKERS OF ALTERED PRECLINICAL BONE METABOLISM IN RHEUMATOID FIRST DEGREE RELATIVES**

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**Background:** First degree relatives (FDR) of RA are known to have increased risk of developing the disease. The detection of altered bone metabolism in FDR could be a predictor of the preclinical phase of the disease.

**Objectives:** To study osteopontine (OPN) and osteoprotegrine (OPG) in FDR of RA patients as markers of altered bone metabolism in relation to clinical manifestations, inflammatory and RA seromarkers.

**Methods:** 55 persons were included, divided into 20 RA patients, 25 FDR of RA patients (without evidence of arthritis) and 10 healthy matched controls. Clinical evaluation, with emphasis on joint symptoms and signs was done for all, in addition to measurement of ESR, CRP, RF, anti-CCP, serum OPN and serum OPG.

**Results:** Mean ESR was significantly higher in RA ( $64.15 \pm 34.29$ ) than in FDR ( $15.6 \pm 11.04$ ,  $p \leq 0.001$ ) and controls ( $6.0 \pm 2.05$ ,  $p \leq 0.001$ ) and significantly higher in FDR than controls ( $p = 0.001$ ). Mean CRP was significantly higher in RA ( $26.38 \pm 29.14$ ) than FDR ( $5.99 \pm 5.08$ ,  $p \leq 0.001$ ) and controls ( $2.02 \pm 0.53$ ,  $p \leq 0.001$ ) and significantly higher in FDRs than in controls ( $p = 0.011$ ). Mean RF and anti-CCP were statistically higher in RA than in FDR and controls. Mean anti-CCP was higher in FDR than in controls but without reaching statistical significance while there was no difference regarding mean RF between FDR and controls. OPN was higher in RA ( $3.66 \pm 4.20$ ) than in FDR ( $1.97 \pm 1.04$ ) and controls ( $2.81 \pm 1.31$ ) without statistical significance ( $p = 0.102$ ). While OPG was significantly higher in RA ( $143.89 \pm 365.47$ ) than in both FDR ( $22.23 \pm 65.73$ ,  $p = 0.009$ ) and controls ( $6.20 \pm 12.43$ ,  $p = 0.003$ ). Mean serum OPN in RA was higher in RF and CCP positive ( $3.77 \pm 4.43$  and  $4.13 \pm 3.48$  respectively) than RF and CCP negative ( $2.65 \pm 0.35$  and  $3.58 \pm 2.58$  respectively) but without reaching statistical difference. Mean serum OPG in RA was higher in RF and CCP positive ( $153.15 \pm 384.64$  and  $161.78 \pm 394.67$  respectively) than RF and CCP negative ( $60.50 \pm 85.56$  and  $42.47 \pm 68.09$  respectively) but without reaching statistical difference. 8/25 (32%) FDR had arthralgia while 17/25 (68%) FDR were asymptomatic. FDRs with arthralgia had significantly higher ESR ( $27.88 \pm 11.22$ ) and CRP ( $10.36 \pm 5.21$ ) than asymptomatic FDR ( $9.82 \pm 4.13$ ,  $p = 0.003$ ) and ( $3.93 \pm 3.58$ ,  $p = 0.003$ ) respectively. OPG was higher in FDR than in controls and higher in those with arthralgia ( $51.55 \pm 114.68$ ) than those without ( $8.44 \pm 9.67$ ) but without reaching statistical difference ( $p = 0.314$ ). Similarly, serum OPN was higher in FDR with arthralgia ( $2.09 \pm 1.19$ ) than asymptomatic ( $1.70 \pm 0.55$ ) but also without significant difference ( $p = 0.620$ ). Furthermore, mean RF and anti-CCP were higher in FDR with arthralgia but didn't reach significant difference.

**Conclusions:** OPN and OPG are markers of altered bone metabolism in RA. Their elevation in FDR than controls denotes a state of altered bone metabolism. Moreover, FDR with arthralgia experience higher levels of OPN, OPG, ESR, CRP, RF, and anti-CCP than asymptomatic FDR. These findings reflect an ongoing disturbed bone metabolism and inflammation in FDR which could precede the clinical disease phase. Thus, OPN and OPG could serve as markers of altered preclinical bone metabolism in rheumatoid FDR. Results need to be confirmed on larger numbers of FDR.

**Disclosure of Interest:** None declared

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SAT0083

### THE GENETIC AND CLINICAL PREDICTION MODELS FOR EFFICACY AND HEPATOTOXICITY OF METHOTREXATE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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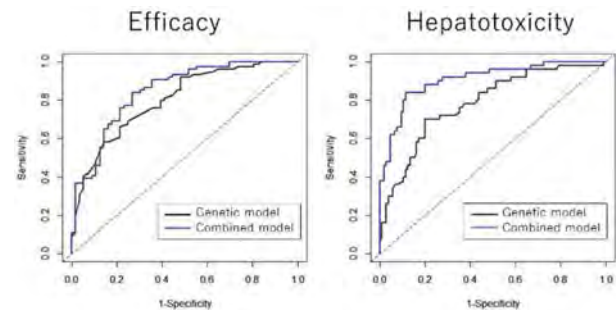
**Background:** The efficacy and toxicity of methotrexate (MTX) depend on individual patients with rheumatoid arthritis (RA) and are difficult to predict before treatment although MTX is the anchor drug and achieving the treatment target earlier is desirable to prevent progression of structural and functional damage. Our previous studies revealed high predictive accuracy of single nucleotide polymorphisms (SNPs) to predict the efficacy and toxicity of MTX, suggesting the influence of genetic variations in enzymes associated with MTX metabolism and folate metabolic pathway<sup>1,2</sup>. However, higher accuracy and replicability is demanded for clinical application.

**Objectives:** To develop combined genetic and clinical models to predict the efficacy and hepatotoxicity of MTX.

**Methods:** Patients with RA under the treatment of MTX according to Japanese guideline for the management of RA with MTX were enrolled. To predict the efficacy and hepatotoxicity, 1971 polymorphisms of 246 enzymes/transporters potentially relevant to pharmacokinetics and pharmacodynamics of MTX were measured by the DMET microarray (Affymetrix Inc.) and direct-sequencing method and clinical variables at baseline were collected. As for efficacy, the EULAR-CRP response criteria was chosen to classify patients with RA as responders (good response) and non-responders (moderate or no response). Hepatotoxicity was defined as either serum AST or ALT levels higher than 1.5 times the upper limit of the normal range. Among SNPs and clinical variables with significant association with outcomes using univariate analyses, stepwise model selection

was conducted by Akaike information criterion in logistic regression model and receiver operating characteristic (ROC) analyses were performed. Bootstrapping ( $n = 100,000$ ) was used to assess the robustness of the results.

**Results:** A total of 166 patients with RA was included. The median age was 61.5 years with 81.3% of women. For efficacy, genetic prediction model using 7 SNPs showed area under the curve of ROC (AUC) was 0.822 with sensitivity of 74.3% and specificity of 76.8%, while combined clinical and genetic model indicated AUC was 0.844 with sensitivity of 81.5% and specificity of 76.9%. By incorporating clinical variables into the genetic model, overall category-free net reclassification improvement (NRI) was 0.700 ( $p < 0.0001$ ) and overall integrated discrimination improvement (IDI) was 0.089 ( $p = 0.0005$ ). For hepatotoxicity, genetic prediction model using 7 SNPs showed AUC was 0.783 with sensitivity of 70.0% and specificity of 80.0%, while combined clinical and genetic model indicated AUC was 0.906 with sensitivity of 85.1% and specificity of 87.8%. Overall category-free NRI was 1.122 ( $p < 0.0001$ ) and overall IDI was 0.279 ( $p < 0.0001$ ).



**Conclusions:** Genetic and clinical models showed higher predictive accuracy for both efficacy and hepatotoxicity of MTX. These models should be validated with a larger scale of prospective study.

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SAT0084

### ANTI-CARBAMYLATED PROTEIN ANTIBODIES AS POTENTIAL BIOMARKERS OF DISEASE ACTIVITY IN EARLY ARTHRITIS PATIENTS

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**Background:** It has become increasingly clear that appropriate initial management of rheumatoid arthritis (RA) increases the chances of success and improves long-term prognosis. Therefore, rheumatologists need prognostic biomarkers to select patients requiring aggressive management. It is possible that anti-carbamylated protein antibodies (anti-CarPA) may serve as such biomarkers because they are associated with erosions and their progression, and with mortality in some studies. Recently, the possibility that they are also associated with disease activity in early arthritis (EA) has been examined by several studies with discordant results.

**Objectives:** We aimed to explore the relationship between variation in disease activity and anti-CarPA in EA patients.

**Methods:** EA patients from two prospective clinics, Hospital Universitario La Paz ( $n = 492$ ) and Hospital Universitario La Princesa ( $n = 501$ ), were included. DAS28 was available at baseline and at months 6 (M6), 12 (M12) and 24 (M24) of follow-up. Anti-CarPA were determined in baseline serum samples by ELISA using *in vitro* carbamylated fetal calf serum. Student t test and main effects general linear regression were used for analysis.

**Results:** The 27.4% of EA patients that were positive for anti-CarPA showed higher DAS28 at baseline than the negative patients ( $4.93$  vs  $4.31$ ,  $p = 1.6 \times 10^{-5}$ ). The difference persisted at all visits during follow-up ( $3.60$  vs  $3.19$  at M6;  $3.47$  vs  $3.09$  at M12; and  $3.31$  vs  $2.79$  at M24; all with  $p \leq 0.001$ ). These differences were independent of patient sex and age, smoking, time since symptoms onset, the specific EA clinic and the year of onset. In addition, they persisted after accounting for the presence of RF or ACPA at baseline ( $p = 1.3 \times 10^{-5}$ , and  $p = 5.7 \times 10^{-5}$ , respectively) and at later visits ( $p < 0.05$  for all analyses). Analysis of the relation

between anti-CarPA and  $\Delta$ DAS28 showed association only with  $\Delta$ DAS28 from baseline to M6 ( $p=0.005$ ). In this period, the positive patients showed less decrease of DAS28 than the negative patients. This was independent of all the variables mentioned above and of the initial DAS28. As a result of this association, 20.5% of the anti-CarPA positive patients reached remission at M6, in comparison with 34.6% of the negative patients. In contrast,  $\Delta$ DAS28 from M6 to M12 and from M12 to M24 were small and not associated with anti-CarPA.

**Conclusions:** Anti-CarPA were associated with high disease activity at presentation and with less improvement in the first 6 months of follow-up in EA patients. These results reinforce the possibility that anti-CarPA could be useful in the clinic as prognostic biomarkers.

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**Disclosure of Interest:** None declared

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**SAT0085 RELATIONSHIP BETWEEN SERUM CALPROTECTIN, DISEASE ACTIVITY PARAMETERS AND THE 7-JOINT ULTRASOUND SCORE IN RHEUMATOID ARTHRITIS**

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**Background:** Calprotectin may be a sensitive biomarker of rheumatoid arthritis (RA) disease activity.

**Objectives:** In this study we aimed to investigate whether calprotectin is a better biomarker than known inflammation markers for predicting clinical activity and ultrasound parameters in patients with RA.

**Methods:** A total of 80 RA patients were underwent to clinical (swollen joint count, tender jointcount, disease activity score-DAS28, simplified disease activity index-SDAI and clinical disease activity index-CDAI) and ultrasound (German US7) examination. Correlation of clinical, laboratory and ultrasound measures were analyzed using Spearman's correlation coefficient. The RA patients were divided into two subgroups according to their DAS28-ESR (erythrocyte sedimentation rate) score; group 1 (DAS-28  $\leq$ 3.2 remission and low activity), group 2 (DAS28  $>$ 3.2 moderate and high activity), respectively. Thirty healthy controls were simultaneously studied.

**Results:** The serum calprotectin levels of the RA patients were significantly higher than those of healthy controls (96.3 $\pm$ 45.9, 54.7 $\pm$ 50.0, respectively;  $p<0.001$ ). Distribution of age (years; 57.2 $\pm$ 9.6, 53.9 $\pm$ 10.5, respectively;  $p=0.115$ ) and sex (female; 78.8%, 70%, respectively,  $p=0.336$ ) between these groups were similar. The clinical, laboratory and ultrasound characteristics of the patients are shown in table 1. The calprotectin levels were 74.8 $\pm$ 45.5 in group 1 ( $n=37$ ) and 114.7 $\pm$ 37.9 in group 2 ( $n=43$ ) ( $p<0.001$ ). The association between calprotectin and scores of DAS28-ESR are shown in figure 1A. Serum calprotectin was significantly associated with DAS28-ESR, DAS28-CRP (C-reactive protein), SDAI, CDAI, ESR, CRP and US7 parameters. We also found a moderate to strong correlation of US7 score with DAS28-ESR, DAS28-CRP, SDAI, CDAI, CRP and ESR (table 2). The correlation between calprotectin and US7 is shown in figure 1B.

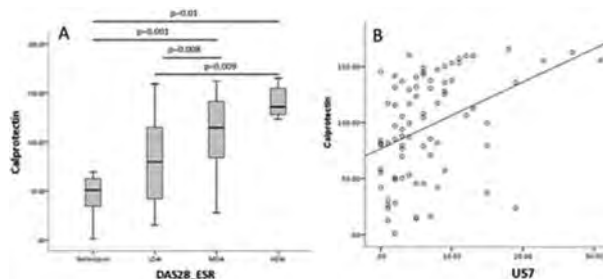
**Abstract SAT0085 – Table 1.** Baseline characteristics of patients with RA

	Group 1 (n=37)	Group 2 (n=43)	p
Female Sex, n (%)	30 (81.1)	33 (76.7)	0.64
Age, years	55.4 $\pm$ 9.4	58.8 $\pm$ 9.6	0.12
Disease duration, years	13.2 $\pm$ 9.1	12.2 $\pm$ 7.6	0.61
Seropositivity, n (%)	24 (64.9)	28 (65.1)	0.98
ESR, mm/hour	14.2 $\pm$ 7.2	42 $\pm$ 18.5	<b>&lt;0.001</b>
CRP, mg/dl	8.2 $\pm$ 11.8	23 $\pm$ 25.7	<b>0.002</b>
CDAI	4.3 $\pm$ 2.1	11.4 $\pm$ 6.9	<b>&lt;0.001</b>
SDAI	12.4 $\pm$ 11.9	34.4 $\pm$ 29.4	<b>&lt;0.001</b>
US7 total score	4.9 $\pm$ 4.8	8.1 $\pm$ 6.9	<b>0.021</b>
Calprotectin, ng/ml	74.8 $\pm$ 45.5	114.7 $\pm$ 37.9	<b>&lt;0.001</b>

**Table.2** Spearman's rank correlation coefficients between calprotectin, US7 scores and other variables:

	ESR	CRP	DAS28-ESR	DAS28-CRP	CDAI	SDAI	US7
Calprotectin	0.361***	0.306**	0.488***	0.495***	0.482***	0.429***	0.444***
ESR		0.494***	0.816***	0.561***	0.467***	0.554***	0.247*
CRP			0.512***	0.780***	0.408***	0.923***	0.309**
DAS28-ESR				0.828**	0.846***	0.695***	0.441***
DAS28-CRP					0.856***	0.924***	0.501**

CDAI 0.670\*\*\* 0.509\*\*\*  
SDAI 0.418\*\*\*  
\*\*\* $p<0.001$ , \*\* $p<0.01$ , \* $p<0.05$



**Abstract SAT0085 – Figure 1.** A Box plots between calprotectin and DAS28-ESR B. Correlation graph between calprotectin and US7 score

**Conclusions:** The results of our study support an additional role of calprotectin in assessing inflammatory activity in patients with RA. Therefore, the combination of serum calprotectin levels and the US7 score could be a simple and practical assessment approach for detection of RA disease activity.

**Disclosure of Interest:** None declared

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**SAT0086 EVALUATION OF DIAGNOSTIC PERFORMANCE OF MAGNETIC RESONANCE IMAGING (MRI) AND ULTRASOUND (US) TOWARD EARLY RHEUMATOID ARTHRITIS FROM NAGASAKI EARLY ARTHRITIS COHORT**

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**Background:** We previously reported that the presence of autoantibodies, magnetic resonance imaging (MRI) bone oedema, ultrasound (US) power Doppler (PD)  $\geq$  grade 2 articular synovitis are indispensable markers to predict the development of RA from undifferentiated arthritis whereas combination analysis used by the above variables, focusing on very early phase of arthritis, remains to be done in our cohort.

**Objectives:** To investigate and re-confirm the diagnostic performance of autoantibodies, MRI findings and US findings toward early RA from NAGASAKI EARLY ARTHRITIS COHORT.

**Methods:** One hundred and three patients, suffering arthralgia less than 6 months and examined by both MRI and US of wrist and finger joints, were selected from NAGASAKI EARLY ARTHRITIS COHORT dating from September 2009 to August 2017. US were evaluated by synovitis score of semi-quantitative manner by gray-scale (GS) and power Doppler (PD) proposed from EULAR. In MRI, synovitis, bone oedema and bone erosion were assessed by the Rheumatoid Arthritis Magnetic Resonance Imaging Scoring system (RAMRIS). After univariate analysis, multivariate analysis was employed to clarify the diagnostic predictors of early RA.

	odds ratio	95% confidence interval	p-value
ACPA titer	1.05	1.01-1.08	0.0069
PD $\geq$ grade 2	17.43	5.15-59.06	0.00025

**Results:** Median of age was 60 years and that of symptomatic duration was 2 months. Female was 68.9%, positive rate of RF was 64.7% and that of ACPA was 47.1%. Total GS score was 4.0, total PD score 2.0, MRI synovitis score 3.0, MRI bone oedema score 0, MRI bone erosion score 0. Seventy patients were diagnosed as early RA during follow-up periods. A univariate analysis showed ACPA, CRP, MMP-3, fulfilment of 2010 ACR/EULAR criteria, MRI synovitis score, MRI bone oedema score, total GS score, total PD score and PD  $\geq$  grade 2 articular synovitis were associated with early RA. Multivariate analysis revealed ACPA and PD  $\geq$  grade 2 articular synovitis at any joints were independent predictors toward diagnosis of early RA.



**Conclusions:** Our present study re-confirms the importance of ACPA, PD  $\geq$  grade 2 articular synovitis and MRI bone oedema, especially the former two, to predict the development of early RA from undifferentiated arthritis patients.

**Disclosure of Interest:** None declared

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SAT0089

### INITIATING TOFACITINIB IN A TREAT TO TARGET STRATEGY FOR RHEUMATOID ARTHRITIS LEADS TO BLUNTED MULTI-BIOMARKER DISEASE ACTIVITY SCORES AS COMPARED TO ANTI-TUMOUR NECROSIS FACTOR AGENTS

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**Background:** The use of a treat-to-target (T2T) strategy for the management of rheumatoid arthritis (RA) leads to better outcomes<sup>1</sup> but requires the regular use of disease activity measures (DAMs) to make clinical decisions. The optimal DAMs that should be used for this purpose have yet to be determined.

**Objectives:** To assess the utility of various DAMs for clinical decision making at a rheumatology clinic implementing a T2T strategy, following the initiation of Tofacitinib (tofc) and anti-tumour necrosis factor (anti-TNFs) agents.

**Methods:** Patients at a community based rheumatology clinic (authors) undergo DAM assessments on a routine basis as part of the implementation of a T2T strategy. These assessments include conventional clinical assessments, DAS28CRP, and the CDAI, as well as the ultrasound power Doppler joint count (UPDJC)<sup>2</sup> and multi-biomarker disease activity score (MBDA). Patients undergo regular assessments, and if found to be under inadequate control, changes are made in their clinical regimen, and then the patients are reassessed three to six months later. Clinical significance was determined by Paired-samples T tests.

**Results:**

	Before			After			
	N	DAS28CRP ±SD	Avg ±SD	DAS28CRP ±SD	Avg ±SD	% Change	Prob
Tofacitinib	39	4.90	±1.00	3.78	±1.20	23%	p<0.001
Anti-TNFs	40	5.07	±1.08	4.09	±1.01	19%	p<0.001
		CDAI		CDAI			
Tofacitinib	37	29.7	±11.1	17.6	±12.1	41%	p<0.001
Anti-TNFs	40	29.9	±11.8	21.4	±12.4	28%	p=0.001
		UPDJC		UPDJC			
Tofacitinib	37	8.9	±4.0	7.0	±3.9	21%	p=0.002
Anti-TNFs	38	9.3	±4.5	7.3	±3.1	22%	p=0.03
		MBDA		MBDA			
Tofacitinib	37	48.1	±12.2	44.3	±10.4	7%	NCS
Anti-TNFs	38	50.0	±11.0	39.3	±10.9	21%	p<0.001

Over the past four years, Thirty nine patients at this clinic were determined to be under inadequate control and were started on tofc. Also, the last forty patients started on anti-TNFs at the clinic were assessed for comparison. The two groups of patients had similar demographics with a combined average duration of clinical disease found to be >10 years. Sixty eight% of these patients were female, and 85% of patients were rheumatoid factor positive.

Table I shows that all of the DAMs listed resulted in significant clinical responses with the exception that following the institution of tofc, the MBDA did not result in clinically significant improvement. When individual biomarkers from the MBDA were analysed, anti-TNFs therapy lead to significant reduction in six of twelve biomarkers (IL-6, TNF-R1, TNF-R2, MMP-2, SSA and CRP) whereas treatment with tofc lead to significant reduction of two (VCAM and Resistin) and borderline reduction in two (IL-6 and TNF-R1) and a significant increase in one (Leptin).

**Conclusions:** Several DAMs performed well with the exception of the MBDA after tofc therapy. The MBDA showed a blunted response when compared to other DAMs in the tofc treated group, as well as when compared to patients treated with anti-TNFs. This finding is most likely due to tofc's unique mode of action, as reflected in the relatively small number of biomarkers that decreased following treatment, and the fact that leptin significantly increased.

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**Disclosure of Interest:** None declared

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SAT0090

### EVALUATION OF THE USE OF ULTRASOUND TO MANAGE PATIENTS WITH RHEUMATOID ARTHRITIS OVER TIME: RESULTS FROM THE CORRONA REGISTRY

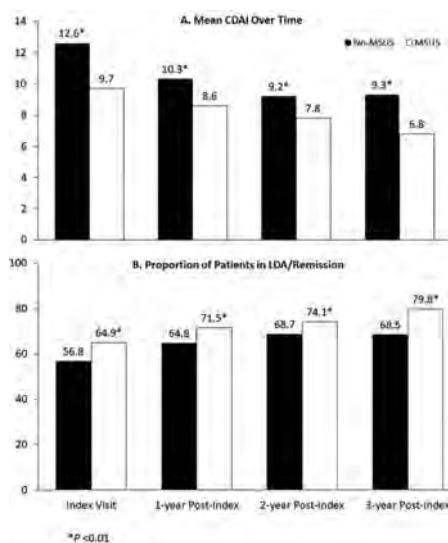
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**Background:** Musculoskeletal ultrasound (MSUS) imaging in patients with rheumatoid arthritis (RA) can detect synovial inflammation with higher sensitivity compared to physical examination alone.<sup>1</sup> Not all rheumatologists have adopted the use of MSUS in their daily practice.

**Objectives:** To compare clinical outcomes in patients whose physicians use MSUS to assess joint inflammation vs those who do not.

**Methods:** Data from patients  $\geq$ 18 years old with a confirmed diagnosis of RA who had an index visit in the Corrona RA Registry from 01/01/2012 to 12/31/2015 with  $\geq$ 12 months of follow-up were stratified into 2 groups: patients whose physicians use MSUS frequently—ie, in >50% of their patient encounters—(MSUS group) and patients whose physicians do not use MSUS at all (No-MSUS group). Frequency of MSUS can be recorded and updated by the rheumatologist in the registry questionnaires at every Corrona visit. The index visit was the first visit in which the physician reported the frequency of MSUS use. Outcomes included mean Clinical Disease Activity Index (CDAI) and the proportion of patients in low disease activity (LDA)/remission (CDAI  $\leq$ 10) at each time point and were evaluated at index and 1, 2, and 3 years post-index. Comparisons between groups were made using 2-sample *t*-tests for mean CDAI and Chi-square tests for achievement of LDA/remission.

**Results:** 21 physicians reported using MSUS frequently compared with 111 who did not use MSUS at all. 5446 of their patients met the criteria for analysis; 1018 (18.7%) were in the MSUS group and 4428 (81.3%) were in the No-MSUS group. At the index visit, the MSUS group was younger (mean age 57.7 years vs 59.8 years,  $p<0.01$ ) and had shorter disease duration (mean 8.7 years vs 11.0 years,  $p<0.01$ ) compared with the No-MSUS group. At the index visit, the MSUS group had lower mean CDAI (9.7 vs 12.6,  $p<0.01$ ) and a greater proportion of patients in LDA/remission (64.9% vs 56.8%,  $p<0.01$ ) compared with the No-MSUS group; these differences were also present at 1, 2, and 3 years post-index (figure 1).



**Conclusions:** A greater percentage of patients whose physicians use MSUS were in LDA/remission over time. Average disease activity of these patients was lower compared with patients whose physicians did not use MSUS. This pattern was observed at 4 different time points over a 3 year period.

#### REFERENCE:

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SAT0091

### CLINICAL REMISSION PREDICTION USING BASELINE GENE EXPRESSION IN THE PERIPHERAL BLOOD OF DMARD-NAÏVE RHEUMATOID ARTHRITIS PATIENTS TREATED WITH METHOTREXATE

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**Background:** Rheumatoid arthritis (RA) is an autoimmune disease of unknown etiology, which is characterised by erosive arthritis (synovitis) and systemic inflammation. Methotrexate (MTX) is a basic drug for RA treatment. However, presently it is not possible to predict MTX efficacy in every patient while some patients are non-responsive to MTX or the drug may induce adverse effects. Therefore, identification of patients sensitive to MTX before treatment could significantly improve therapy outcome.

**Objectives:** To investigate the importance of baseline expression of genes involved in the metabolic and energy generation pathways in RA patients, which could serve prognostic biomarkers of treatment response to methotrexate.

**Methods:** Peripheral blood of 40 DMARD-naïve RA patients aged 47.5±15.5 years old, disease duration 7.9±6.0 weeks treated with MTX (15 mg/week) during two years and 26 healthy age-matched control subjects were examined. Clinical response was assessed by disease activity score (DAS) 28, serum levels of ACPA antibodies, C-reactive protein (CRP), and rheumatoid factor (RF). Clinical remission was assessed according to ACR criteria and DAS28 (DAS28 <2.6). Bone erosion and joint space narrowing (JSN) scores were monitored by X-ray analysis. Protein concentrations were measured using ELISAs. Total RNA was isolated and used in gene expression studies performed with quantitative real-time RT-PCR.

**Results:** MTX treatment significantly decreased the disease activity according to DAS28. At the end of the study the majority of patients demonstrated moderate disease activity (DAS28 >3.2 <5.1), four patients retained high disease activity while 12, attained remission (DAS28 <2.6). Gene expression analysis has revealed that RA patients, which attained clinical remission after MTX treatment demonstrated significantly higher baseline expression of genes associated with glycolysis (Glut1, PKM), hypoxia (HIF1 $\alpha$ ), and cell cycle related cyclin D1 compared to other examined RA patients and healthy subjects. RA patients, which retained high disease activity after treatment had baseline expression of genes related to apoptosis (p21, caspase 3), tissue regeneration (TGF $\beta$ 1, RUNX2) and cyclin D1, significantly lower than that in the controls and other examined RA patients.

**Conclusions:** Clinical remission attainment in DMARD-naïve RA patients treated with methotrexate is associated with high baseline expression of genes associated with glycolysis, hypoxia and cyclin D1 compared to other examined patients. Non-responsiveness to MTX is accompanied by lower baseline expression of genes related to apoptosis, tissue regeneration, and cyclin D1 compared to controls. Increased baseline expression of cyclin D1 gene compared to healthy subjects could serve a positive prognostic marker of sensitivity to methotrexate therapy.

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SAT0092

### PALINDROMIC RHEUMATISM (PR): EXPERIENCE IN A REAL WORLD SETTING – THE NOTTINGHAM CASEMIX REGISTER (NCR)

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**Background:** PR is an unusual arthritis characterised by brief, self-limiting attacks of synovitis usually affecting one joint at a time with outcomes including transformation to persistent inflammatory rheumatic disease, usually rheumatoid arthritis (RA), continuation of PR and spontaneous remission. Seropositivity for rheumatoid factor (RF) or ACPA may predict transformation to RA. We examined the experience of PR in a large UK teaching hospital rheumatology department using data collected routinely at outpatient encounters. The NCR records a primary rheumatology diagnosis, demographic data, administrative details (type of consultation, grade of clinician and outcome) for every rheumatology consultation. Between March 2016 and February 2017 19 832 clinical encounters were logged forming the basis of this study.

**Objectives:** To identify the burden of PR in a large UK teaching hospital and its management in a real world setting.

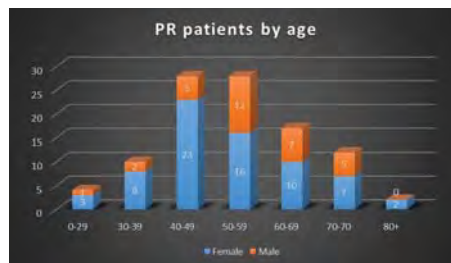
**Methods:** PR patients were extracted from the NCR and their electronic record (Bloods/Radiology/Clinic letters) analysed for any change in diagnosis (prior to or following PR diagnosis), treatments prescribed, serological status and radiological findings. In the subgroup whose diagnosis changed, a separate analysis to look at predictive factors was carried out.

**Results:** 101 patients (149 attendances) were analysed (24 new patient appointments, 125 follow ups). The female:male ratio was 2.16, mean age 53.5. Over half were between 40–59. 31 new diagnoses of PR were made in the study period. The NCR prevalence of PR was 1%. Duration of PR in previously diagnosed patients was a mean of 4 years. The diagnosis was changed in 13 PR patients (to RA in 9). Serological status is shown below:

Status	RhF	ACPA	Dual Rhf/ACPA
Positive	53	48	43
Borderline	7	3	NA
Negative	37	39	27
Not known	4	11	13

Plain radiographs were available for 88 patients (hands- 69, feet- 54). Erosions were noted once (RA was then diagnosed). Synovitis was detected in 10 of 25 patients who underwent ultrasound and in 2 of 18 patients who underwent small joint MRI. 63 patients were on DMARDs, most often HCQ.<sup>4,3</sup> 9 received dual DMARD therapy. DMARD therapy was more frequent in sero-positive patients. PR patients later diagnosed as RA were older (64.9 vs 53.5 years) and more commonly seropositive (6 being dual antibody positive) with similar gender ratio (2:1 F:M). The duration of PR diagnosis ranged from 6 months to 10 years (average 4.2).

Duration of PR prior to new Diagnosis	Change to RA	Change to other diagnosis
Less than 1 year	1	2
1–2 years	2	1
2–5 years	3	1
>5 years	3	0



Abstract SAT0092 – Figure 1. PR patients by age

**Conclusions:** PR accounted for 1% of all patients on the NCR with 10% of patient's having their diagnosis changed in the study period. RA patients on the NCR numbered 2292, making the RA:PR ratio 22.7:1. Approximately half of PR patients were RF/ACPA positive or both with over half the PR population on DMARD treatment, most often HCQ. PR patients developing RA were older and ACPA/RF positivity was more common. Although a third PR patients who later developed RA did so within 2 years, the majority took longer with some diagnosed as RA over 5 years later suggesting PR patients, especially if seropositive, should be followed long term. Two year follow up will be available from March 2018.

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SAT0093

### MALE SEX PREDICTS A FAVOURABLE OUTCOME IN SERONEGATIVE EARLY RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid factor (RF) and anti-citrullinated peptides antibodies (anti-CCP) are universally recognised negative prognostic factors in rheumatoid arthritis (RA). The majority of studies of early RA have focused on RF and anti-

CCP positive patients. Much less is known about prognostic markers in seronegative RA. Several studies report worse drug survival and worse patient reported outcomes in women with RA. This affects outcomes such as the 28-joint disease activity score (DAS28) and the health assessment questionnaire (HAQ). How these differences relate to autoantibody status is unknown.

**Objectives:** To investigate if the relation between sex and clinical outcomes varies by autoantibody status in patients with early RA.

**Methods:** An inception cohort of patients with early RA (n=233; symptoms duration ≤12 months), recruited in 1995–2005, was studied. All the patients fulfilled the 1987 American College of Rheumatology criteria for RA. The patients were managed according to usual care, with no pre-specified protocol for pharmacotherapy or rehabilitation. In a structured follow-up program, all patients were examined by the same rheumatologist. In the present study we divided the patient population in three groups according to autoantibodies status: RF and anti-CCP seropositive (double positive), RF or anti-CCP seropositive, RF and anti-CCP seronegative (double negative). We examined the relation between sex and different outcomes at 12 months (EULAR good response, clinical remission (DAS28 <2.6), HAQ≤0.5 and low pain score (VAS pain 0–100 of <20) by means of logistic regression.

**Results:** Complete data on autoantibody status at baseline was available for 201 patients (mean age at inclusion 61 years, 72% female, 60% RF positive and 58% anti-CCP positive). Twenty-eight% of the patients were double negative, 27% were single positive and 45% were double positive. Mean baseline DAS28 was 4.53. All patients were treated with a conventional synthetic DMARD (48% with methotrexate). Oral glucocorticoids were prescribed in 38% of patients. At the 1 year follow up, 19% had a EULAR good response, 21% were in remission, 40% had low pain and 53% low HAQ. Male patients in the double negative group were more likely to reach remission (odds ratio (OR) 6.40; 95% confidence interval (CI) 1.6–26.2) and EULAR good response (OR 4.67; 95% CI 1.2–18.3) compared to females. There were no such associations among the double positive patients (Table). Results were similar in analyses adjusted for DAS28 at baseline (Table). There was a similar pattern among double negative patients for low pain at 1 year (OR for male vs female patients 2.25; 95% CI 0.58–8.67 – adjusted for baseline pain), but no association between male sex and low HAQ at 1 year in double negative patients (OR 0.99; 95% CI 0.23–4.22 – adjusted for baseline HAQ) or the other subgroups.

#### Abstract SAT0093 – Table 1

Impact of sex on the chance of EULAR good response and clinical remission at the 1-year follow-up in patients with early RA. Logistic regression analysis.

	Sex	EULAR good response OR (95% CI)		Clinical remission* OR (95% CI)	
		Crude	Adjusted for baseline DAS28	Crude	Adjusted for baseline DAS28
All	Female (n=144)	(reference)	(reference)	(reference)	(reference)
	Male (n=57)	1.9 (0.9-3.7)	1.9 (0.9-3.7)	2.0 (1.0-3.9)	2.1 (1.0-4.1)
RF and anti-CCP negative	Female (n=42)	(reference)	(reference)	(reference)	(reference)
	Male (n=14)	4.7 (1.2-18.3)	6.0 (1.3-26.4)	6.4 (1.6-26.2)	6.3 (1.5-25.9)
RF or anti-CCP positive	Female (n=41)	(reference)	(reference)	(reference)	(reference)
	Male (n=13)	3.2 (0.6-17.2)	3.4 (0.6-20.6)	3.8 (0.8-17.7)	2.1 (0.3-12.3)
RF and anti-CCP positive	Female (n=61)	(reference)	(reference)	(reference)	(reference)
	Male (n=30)	1.3 (0.4-4.5)	1.2 (0.3-4.2)	0.9 (0.3-2.9)	1.1 (0.3-3.7)

\*DAS28 <2.6

**Conclusions:** In the subgroup of patients with seronegative early RA, male patients are more likely than female patients to reach DAS28 remission and EULAR Good Response after treatment with conventional synthetic DMARDs.

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#### SAT0087 ASSOCIATION OF BIOMETRICS WITH DISEASE CHARACTERISTICS AND SYNOVIAL PHENOTYPE IN INFLAMMATORY ARTHRITIS

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**Background:** The potential importance of altered body composition in the development of and disease course in inflammatory arthritis is increasingly being recognised. Body composition in different types of inflammatory arthritis and its influence on synovial pathology remains to be fully characterised.

**Objectives:** To evaluate body composition in seropositive and seronegative rheumatoid arthritis (RA) and psoriatic arthritis (PsA) patients and assess associations with disease characteristics and baseline synovial arthroscopic findings.

**Methods:** We performed a prospective observational study of consecutive inflammatory arthritis patients seen in outpatient clinics. Demographic and clinical characteristics were collected on all patients. Synovial biopsy was performed by needle arthroscopy, and macroscopic and histologic features recorded. The degree of synovitis and vascularity were recorded on a 0–100 mm visual analogue scale, and chondropathy on a semi-quantitative scale from 0–3. Mann-Whitney U test was used to compare groups. Spearman's Rank Correlation Coefficient was used to assess for associations between biometrics and demographic and clinical markers. GraphPad Prism Version 7 and IBM SPSS Statistics Version 24 were used for data analysis.

**Results:** We included 58 patients, 32 with seropositive RA, 10 with seronegative RA, and 16 with PsA. 37 (64%) were female. Mean (SD) age was 52.8 (13.9) years. Mean (SD) BMI was 29.7 (6.3) kg/m<sup>2</sup>, waist circumference was 94.4 (20.3) cm, and hip circumference 104.3 (21) cm. Full demographic and clinical details are shown in table 1. Seronegative RA patients had significantly increased BMI (p=0.033) and waist circumference (p=0.017), but not hip circumference (p=0.248) compared to seropositive RA patients. PsA patients had significantly increased BMI (p<0.001), waist circumference (p=0.001), and hip circumference (p<0.001) compared to seropositive but not seronegative RA patients. There was a significant correlation between waist circumference and both synovitis (r=0.31, p=0.018) and vascularity (r=0.34, p=0.010) at arthroscopy. BMI and hip circumference did not correlate with arthroscopic findings.

	Seropositive RA	Seronegative RA	PsA
Female, n (%)	18 (56.3)	7 (70)	12 (75)
Age, mean (SD), years	55.9 (14.6)	46.7 (15.8)	50.6 (9.6)
Rheumatoid Factor+, n (%)	31 (96.9)	0 (0)	3 (18.8)
ACPA+, n (%)	24 (75)	0 (0)	2 (12.5)
BMI, mean (SD), kg/m <sup>2</sup>	26.9 (4.8)	31.9 (7.1)	34.0 (5.8)
Waist circumference, mean (SD), cm	86.4 (20.4)	101.3 (16.3)	105.9 (15.4)
Hip circumference, mean (SD), cm	98.4 (23.9)	105.8 (16.4)	115.4 (11.1)
CRP, mean (SD), mg/L	12.8 (17.8)	18.6 (27.1)	7.5 (6.0)
ESR, mean (SD), mm/hr	28.2 (24.5)	18.9 (19.7)	17.5 (8.8)
Swollen Joint Count, mean (SD)	4.1 (5.0)	2.4 (3.1)	3.2 (6.1)
Tender Joint Count, mean (SD)	6.2 (6.8)	7.5 (7.5)	4.4 (7.1)
VAS general health, mean (SD), mm	49.1 (31.0)	51.3 (21.3)	49.1 (25.2)
DAS28-CRP, mean (SD)	3.91 (1.54)	3.98 (0.94)	3.6 (1.4)
Synovitis, mean (SD), mm	65.3 (20.3)	60.0 (14.1)	75.0 (12.6)
Vascularity, mean (SD), mm	62.5 (19.8)	58.0 (17.5)	75.0 (13.2)
Chondropathy, mean (SD)	1.6 (0.7)	1.4 (0.6)	1.5 (0.7)

**Conclusions:** Different types of inflammatory arthritis have distinct body composition profiles. Waist circumference, but not other biometrics, correlates with baseline synovial inflammation and vascularity.

**Disclosure of Interest:** None declared

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#### SAT0088 PREDICTIVE FACTORS FOR INTERSTITIAL LUNG DISEASE PROGRESSION IN PATIENTS WITH RHEUMATOID ARTHRITIS: A ROLE FOR BIOLOGICAL INFLAMMATION AND DISEASE MODIFIED ANTI RHEUMATIC DRUGS (DMARDs)

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**Background:** Interstitial Lung Disease (ILD) related to Rheumatoid Arthritis (RA) is frequent. ILD is associated with an increased mortality in RA patients. Predictive factors for ILD progression are not well studied.

**Objectives:** In RA patients with an ILD according to CT scan criteria, identify clinical and biological predictive factors for ILD progression.

**Methods:** It is a retrospective multicentric study. RA patients with ILD confirmed by a first thoracic CT scan (tCT at T0) were included if ILD progression could be studied with a second CT scan (Tx) done at least 6 months after T0. RA patients were classified in two groups after double tCT evaluation on a blind review of data: those with ILD progression (pILD) and those with a stable ILD (sILD). Predictive factors for tCT ILD progression were studied by comparing these two groups.



Studied data were ILD pattern, classified into typical UIP (Usual Interstitial Pneumonia) or not typical UIP, RA disease characteristics, biological parameters, and RA treatments, collected for each patient at T0 and Tx.

**Results:** Thirty-six RA patients with ILD confirmed by tCT were included. During an average follow-up of 3 years, 21 RA patients (58.1%) had ILD progression. Predictive factors for ILD progression at T0 are shown in table 1. In pILD group, we observed a significant higher value of the C Reactive Protein (CRP). A CRP rate superior to 20 mg/L was highly associated to ILD progression (Odds ratio=14.4; IC95%(1.36–15.2); p=0.02). Eight patients were treated at T0 by a DMARD different from Methotrexate (MTX). They all were in pILD group (p=0.01). Thirteen patients were treated with MTX at T0. Eight of them were in sILD group (61.5%) and only 5 patients in pILD group (38.5%). Eight patients continued MTX treatment after ILD diagnosis and for one patient, MTX was introduced between T0 and Tx. For these 9 patients exposed to MTX after ILD diagnosis, during 27 months on average, no significant ILD progression was observed.

**Abstract SAT0088 – Table 1.** Predictive factors for tCT ILD progression

Variable	pILD tCT (n=21)	sILD tCT (n=15)	P value
ACPA positivity – no. (%)	15 (70.4)	13 (86.7)	NS
DAS28CRP – pts	3.8±1.42	4.9±1.63	NS
<b>T0 CRP rate – mg/L</b>	<b>29.3±21.1</b>	<b>13.7±18.6</b>	<b>0.03</b>
<b>T0 CRP rate&gt;20 mg/L</b>	<b>OR=14.4; 95% CI (1.36–15.2)</b>		<b>0.02</b>
MTX at T0 – no. (%)	5 (23.8)	8 (53.3)	NS
<b>non-MTX DMARDs (LFN or SSZ) at T0 – no. (%)</b>	<b>8 (38.1)</b>	<b>0</b>	<b>0.01</b>
Biotherapy at T0 – no. (%)	10 (47.6)	6 (40.0)	NS
Corticosteroids at T0 – no. (%)	17 (81.0)	9 (60.0)	NS
MTX exposure between T0 and Tx – no. (%)	5 (55.6)	4 (44.4)	NS
Death – no. (%)	6 (28.6)	3 (20.0)	NS

CI: Confidence Interval; NS: Not Significant; ACPA: Anti-cyclic Citrullinated Peptide Antibody, +>10 U/mL; DAS: Disease Activity Score; LFN: Leflunomide; SSZ: Sulfasalazine; \*: p significant

**Conclusions:** Factors associated with ILD progression were biological inflammation and exposure to a DMARD different from MTX. Exposure to MTX before or after ILD diagnosis was not associated with ILD worsening during the follow up.

**Disclosure of Interest:** None declared

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**SAT0094** **PHYSICAL FUNCTION AND HEALTH RELATED QUALITY OF LIFE IN EARLY RHEUMATOID ARTHRITIS PATIENTS WHO ACHIEVED ONLY LOW DISEASE ACTIVITY COMPARED WITH REMISSION**

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**Background:** Current treatment target for rheumatoid arthritis (RA) aims at reaching sustained remission or Low Disease Activity (LDA). It is unclear whether achieving clinical remission is necessary or achieving stable LDA is already sufficient to maintain physical function and Health Related Quality of Life (HRQoL) in patients with early RA.

**Objectives:** To compare physical function and health related quality of life in early RA patients who achieved sustained remission and those who achieved only sustained LDA.

**Methods:** Early RA patients with symptom onset <2 years were recruited. Disease activity over time was determined by the cumulative average of Disease Activity Score 28 (caDAS28) and Simple Disease Activity Index (caSDAI) measured at month 3, 6, 9 and 12. Physical function was measured by the Health Assessment Questionnaire Disability Index (HAQ-DI). HRQoL was assessed by the Physical Component Scale (PCS) and Mental Component Scale (MCS) of the 36-Item Short Form Survey (SF-36) and the Euro Quality of Life Five Dimensions Questionnaire (EQ-5D).

**Results:** A total of 308 (53±13 years old, 80 [26.0%] male) patients completed one year follow up (table 1). 132 (42.9%) and 87 (28.2%) patients achieved caDAS28 remission and caDAS28 LDA while 48 (15.6%) and 156 (50.6%) patients achieved caSDAI remission and caSDAI LDA. Patients who achieved caDAS28 remission have better SF-36 PCS, HAQ-DI and EQ5D at year 1 than patients who achieved only caDAS28 LDA or remained active after adjusting for

other potential confounders at baseline with multivariable regression analysis (Image 1). However, SF-36 PCS, HAQ-DI were not different between caSDAI remission and caSDAI LDA after adjustment for confounders.

**Abstract SAT0094 – Table 1**

	n=308		p value
	Baseline	Month 12	
Symptom duration, months	9.76±8.29	–	–
VAS pain, 0–10	4.61±2.32	2.41±2.08	<0.001
VAS patient global, 0–10	51.95 ±23.32	25.22 ±21.47	<0.001
VAS physician global, 0–10	50.64 ±26.44	17.77 ±17.99	<0.001
Tender joint count, 0–28	7.36±5.95	1.99±2.98	<0.001
Swollen joint count, 0–28	4.35±3.87	0.86±1.72	<0.001
ESR, mins	57.08 ±34.19	33.94 ±24.35	<0.001
CRP, mg/L	21.84 ±31.65	6.29±11.07	<0.001
SDAI	24.14 ±13.22	7.78±7.25	<0.001
DAS28 CRP	4.46±1.25	2.52±0.98	<0.001
csDMARDs, n (%)	134 (43.8%)	282 (92.2%)	<0.001
bdDMARDs, n (%)	0 (0%)	11 (4.9%)	<0.001
Prednisolone, n (%)	104 (34.1%)	97 (31.8%)	0.649
NSAID, n (%)	207 (69.4%)	143 (48%)	<0.001
PCS, (0–100)	27.84 ±12.92	39.81 ±12.65	<0.001
MCS, (0–100)	43.46 ±10.60	48.12 ±11.87	<0.001
HAQ-DI, (0–3)	0.82±0.63	0.33±0.43	<0.001
EQ5D, (0–1)	0.67±0.15	0.79±0.16	<0.001

Image 1		Coefficient	p value
<b>PCS at Month 12 (Multivariable analysis)</b>			
caDAS28	LDA vs Remission	-3.64 (-6.67, -0.60)	0.019
	Active vs Remission	-10.54 (-13.63, -7.46)	<0.001
caSDAI	LDA vs Remission	-3.34 (-6.85, 0.18)	0.063
	Active vs Remission	-11.88 (-15.68, -8.08)	<0.001
Adjusted for Sex, age, baseline disease activity and baseline PCS			
<b>MCS at Month 12 (Multivariable analysis)</b>			
caDAS28	LDA vs Remission	0.15 (-2.81, 3.11)	0.920
	Active vs Remission	-3.12 (-6.16, -0.09)	0.044
caSDAI	LDA vs Remission	-2.21 (-5.75, 1.33)	0.220
	Active vs Remission	-5.42 (-9.26, -1.59)	0.006
Adjusted for Sex, age, baseline disease activity and baseline MCS			
<b>HAQ-DI at Month 12 (Multivariable analysis)</b>			
caDAS28	LDA vs Remission	0.12 (0.02, 0.22)	0.024
	Active vs Remission	0.36 (0.26, 0.47)	<0.001
caSDAI	LDA vs Remission	0.10 (-0.02, 0.22)	0.096
	Active vs Remission	0.41 (0.28, 0.54)	<0.001
Adjusted for Sex, age, baseline disease activity and baseline HAQ-DI			
<b>EQ5D at Month 12 (Multivariable analysis)</b>			
caDAS28	LDA vs Remission	-0.06 (-0.10, -0.01)	0.009
	Active vs Remission	-0.13 (-0.17, -0.09)	<0.001
caSDAI	LDA vs Remission	-0.05 (-0.10, -0.002)	0.041
	Active vs Remission	-0.14 (-0.19, -0.09)	<0.001
Adjusted for Sex, age, baseline disease activity and baseline EQ5D			

**Conclusions:** Patients who achieved sustained caDAS28 LDA had significantly worse physical function and HRQoL than patients who achieved caDAS28 remission.

**Disclosure of Interest:** None declared

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SAT0095

### A PERCEIVED BIOLOGICAL CAUSE OF RHEUMATOID ARTHRITIS ONSET IS ASSOCIATED WITH LOWER LEVELS OF DEPRESSED AND ANXIOUS MOOD OVER ONE YEAR COMPARED TO PATIENTS WHO ATTRIBUTED ONSET TO OTHER CAUSES

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**Background:** Patients with rheumatoid arthritis (RA) attribute onset of their condition to a range of causes including biological, psychological, work-related causes or stressful life events. Causal attributions are associated with a range of short- and long-term outcomes.

**Objectives:** To compare the 1 year outcomes of early RA patients who attribute a biological cause of onset of RA with patients who perceive non-biological causal attributions.

**Methods:** The Rheumatoid Arthritis Medication Study (RAMS) is a prospective cohort of patients with RA starting methotrexate for the first time in the United Kingdom. Demographic and clinical data (pain and fatigue visual analogue scales [VAS-pain/VAS-fatigue], disease activity [DAS28], the Hospital Anxiety and Depression Scale [HADS-A, HADS-D] and the Health Assessment Questionnaire [HAQ]) were collected at baseline and 1 year later. At baseline, patients completed the Brief Illness Perception Questionnaire (Brief IPQ), which assesses key beliefs about the impact, controllability, and chronicity of RA. The final item of the Brief IPQ asks patients to report the most important factor they believe caused their disease. These causal attributions were coded as either biological (e.g. age, genetics) or other causes (e.g. work related, stressful life event). Brief IPQ item response scores were compared between these groups using linear regression, adjusted for age and gender. HAQ, DAS28, VAS-pain, VAS-fatigue, HAD-A and HADS-D over follow-up were compared between the two groups using random effects models.

**Results:** Of 1171 patients, 483 (41.2%) reported a biological cause to be the most important factor in causing their arthritis and 688 (58.8%) reported a non-biological cause. Patients who believed in biological causes were younger (median 58 vs. 61 years;  $p=0.003$ ) and more likely to be women (72.1% vs. 59.2%;  $p<0.001$ ). Other baseline characteristics were similar (Table). Patients who perceived biological causes reported significantly lower concerns about their illness (median: 8 vs. 9;  $p=0.004$ ) and significantly lower emotional impact (median: 5 vs. 6;  $p<0.001$ ). Over follow-up, patients who attributed biological causes reported lower depression and anxiety HADS scores than those holding non-biological attributions (mean difference [95% CI]: HADS-D = -0.76 [-1.19, -0.33]; HADS-A = -0.94 [-1.41, -0.47]). Other outcomes over follow-up were similar.

**Abstract SAT0095 – Table 1.** Baseline and one year characteristics, stratified by perceived cause of patients' illness

Characteristic	Biological cause		Other cause		p <sup>†</sup>
	N	median(IQR)	N	median(IQR)	
Age, years	483	58 (48, 68)	688	61 (52, 69)	0.003
Female	348 (72.1)		407 (59.2)		<0.001
Disease duration at baseline, months	483	7 (4, 11)	688	6 (3, 11)	0.094
Swollen joint count					
Baseline	469	4 (2, 9)	650	4 (2, 9)	0.822
One year	301	1 (0, 3)	409	1 (0, 3)	0.527
Tender joint count					
Baseline	470	5 (2, 11)	651	5 (2, 11)	0.959
One year	301	2 (0, 5)	408	2 (0, 6)	0.7823
DAS28					
Baseline	457	4.2 (3.3, 5.1)	630	4.2 (3.3, 5.2)	0.690
One year	271	3.0 (2.3, 4.0)	386	2.8 (2.1, 4.0)	0.283
HAQ Score					
Baseline	481	1.00 (0.38, 1.50)	685	1.00 (0.50, 1.63)	0.602
One year	287	0.75 (0.13, 1.25)	376	0.63 (0.13, 1.25)	0.996
HADS-D					
Baseline	479	4 (2, 8)	682	6 (2, 9)	0.001
One year	285	3 (1, 7)	374	4 (1, 7)	0.071
HADS-A					
Baseline	479	5 (3, 5)	682	6 (3, 10)	0.010
One year	285	4 (2, 8)	372	5 (2, 8)	0.130

<sup>†</sup> (Univariable analysis (Mann-Whitney U test)

DAS28 = Disease Activity Score (28); HADS-A = Hospital Anxiety and Depression Scale (anxiety); HADS-D = Hospital Anxiety and Depression Scale (depression); HAQ = Health Assessment Questionnaire

**Conclusions:** Different causal attributions of RA are associated with different outcomes and may suggest that education about RA causality could improve patient-centred outcomes; however, that would require further evaluation.

**Disclosure of Interest:** None declared

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SAT0096

### WINDOW OR NO WINDOW: EARLIER IS BETTER WHEN TREATING RHEUMATOID ARTHRITIS

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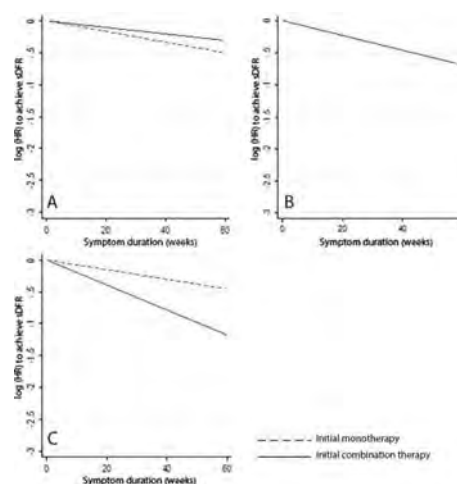
**Background:** Previous reports on a window of opportunity in rheumatoid arthritis (RA) may be related to the use of slow acting c(ontventional) s(ynthetic) DMARDs. We hypothesised that onset of action of therapy might influence whether there is a window of opportunity or whether 'earlier is just better'.

**Objectives:** To investigate the association between symptom duration at treatment onset and the achievement of sustained drug free remission (sDFR) in early RA patients initiating therapy including fast acting prednisone or infliximab, compared to patients initiating csDMARD monotherapy.

**Methods:** We analysed the shape (hyperbolic or linear) of the association between symptom duration and achievement of sDFR (DAS<1.6 and no DMARDs for  $\geq 1$  year) for patients initiating combination therapy in 3 cohorts: BeSt, IMPROVED study and METEOR. All patients had arthritis symptoms <2 years. In the BeSt study, early RA patients (1987 criteria) were randomised to 4 targeted treatment strategies: arm 1 and 2 started with csDMARD monotherapy, arm 3 with csDMARDs and tapered high dose prednisone and arm 4 with csDMARD and infliximab. Subsequent treatment adjustments aimed at DAS $\leq 2.4$ . In the IMPROVED study early RA patients (2010 criteria) were treated with csDMARD and tapered high dose prednisone. Subsequent treatment adjustments aimed at DFR. METEOR is an international observational cohort including daily practice data from patients with a diagnosis and treatment of RA according to the rheumatologist. We selected patients who started on csDMARD monotherapy or a combination of csDMARD with prednisone or anti-TNF and at least 1.5 year follow-up.

Missing DAS were imputed using last observation carried forward. We performed Cox regression analyses with as outcome sDFR and as predictor symptom duration and compared the likelihood ratio tests of a linear model and a model with inclusion of natural cubic spline functions (resulting in a hyperbola), to investigate which model was a better fit for the data.

**Results:** In BeSt (n=469), IMPROVED (n=421) and METEOR (n=1653) 54, 110 and 10 patients who started with csDMARD and prednisone or anti-TNF combination therapy, and 53 in BeSt and 15 in METEOR who started with csDMARD monotherapy (no monotherapy in IMPROVED) achieved sDFR. A hyperbolic model did not show a better fit for the data than a linear model (for combination therapy in BeSt  $p=0.743$ , IMPROVED  $p=0.337$ , METEOR  $p=0.608$ , for csDMARD monotherapy in BeSt  $p=0.609$ , in METEOR  $p=0.758$ ). Figure 1 shows the linear association between symptom duration and sDFR per study. These results indicate that the earlier treatment is started, the higher the likelihood of achieving sDFR. However, the data do not suggest that a hyperbolic relationship between treatment onset and outcome sDFR fit the data better.



**Conclusions:** Our data suggest that there is no evidence for a window of opportunity in early RA in 3 cohorts. This was not related to use of fast acting combination therapy including prednisone or anti-TNF instead of slow acting csDMARD monotherapy nor was it dependent on strict treatment to target in a clinical trial. It remains that earlier treatment initiation is better when aiming to achieve sDFR.

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SAT0097

### RISK OF PREVENTABLE HOSPITALISATION BEFORE AND AFTER DIAGNOSIS AMONG RHEUMATOID ARTHRITIS PATIENTS COMPARED TO CONTROLS

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**Background:** Rheumatoid arthritis (RA) generally requires intensive medical intervention, which along with the progression of the disease itself, may lead to the occurrence of comorbidities and hospitalisation that can be prevented with a quality primary care. We assessed the risk of preventable hospitalizations in RA patients, for whom preventable hospitalizations have not been well studied. We compare the incidence rate of preventable hospitalizations in newly-diagnosed RA patients and non-RA patients using data from the Taiwan National Health Insurance (NHI) Database.

**Objectives:** To investigate the risk of preventable hospitalisation before and after diagnosis between RA and non RA patients.

**Methods:** 11 852 incident RA patients and 59 260 age-, sex-, and index year-matched controls were identified from the Taiwan National Health Insurance Database. Index date was defined as the initial diagnosis date for RA patients and this date was assigned to their matched controls. The incidence and incidence rate ratios (IRRs) of preventable hospitalisation between RA patients and controls were estimated using conditional Poisson regression adjusted for age, sex, Elixhauser Comorbidity Index, number of outpatient visits and hospitalizations 1 year prior to index date, residence urbanisation, income levels, occupation and the number of physicians practicing near the patients' residence.

**Results:** The overall incidence of preventable hospitalisation in RA patients and controls was 1.71 vs 0.95 events per 1000 person-months, corresponding to adjusted incidence rate ratio (IRR) of 1.43 (95% CI, 1.35–1.51). The crude IRR for preventable hospitalisation was 1.84 (1.61–2.11) one year prior to RA diagnosis. Adjusted IRRs (95% CI) for preventable hospitalisation categories were 1.43 (1.22–1.67) for chronic obstructive pulmonary disease, 1.28 (1.02–1.62) for asthma, 1.76 (1.62–1.91) for bacterial pneumonia, 1.47 (1.35–1.61) for urinary tract infection.

**Conclusions:** This population-based study indicates that RA is independently associated with a higher risk of preventable hospitalisation, and the risk was already greater prior to formal diagnosis of RA. These results signal gaps in the care and management of RA patients in this population.

#### REFERENCE:

[1] Billings J, Anderson GM, Newman LS. Recent findings on preventable hospitalizations. *Health Aff (Millwood)* 1996;15(3):239–249.

**Disclosure of Interest:** None declared

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SAT0098

### PATIENT AND DISEASE CHARACTERISTICS THAT PREDICT SWITCHING FROM A TNF INHIBITOR TO ANOTHER BIOLOGIC OR TARGETED SYNTHETIC DMARD IN PATIENTS WITH RA IN CLINICAL PRACTICE

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**Background:** Specific patient demographics or disease characteristics may be associated with switching from one therapy to another for patients with RA. Identifying these predictive factors may help inform prospective treatment decisions.

**Objectives:** To examine factors predicting switching among patients with RA from a TNF inhibitor (TNFi) to a subsequent biologic (b)DMARD (TNFi or non-TNFi [abatacept, tocilizumab, rituximab]) or the targeted synthetic (ts)DMARD tofacitinib.

**Methods:** This analysis included patients aged  $\geq 18$  years, who were enrolled in a large sequential RA registry established in October 2001 and who initiated a TNFi on/after 1 January 2005 and had  $\geq 24$  months' follow-up. Switch was defined as discontinuation of a TNFi and initiation of another bDMARD or tofacitinib within 6 months. Of TNFi initiations, 67% were randomly selected as a prediction dataset and used to develop the final model; 33% were considered in the validation dataset. Logistic regression modelling was used to predict switching status; baseline demographics (age, sex, race), patient attributes (smoking status, BMI, work status) and clinical characteristics (RF and anti-cyclic citrullinated protein status, erosive disease, history of co-morbidities, prior and current treatment, disease activity, patient-reported pain, fatigue, morning stiffness) were considered. Goodness-of-fit statistics were used to assess model fit and receiver operating characteristic curves (area under the curve [AUC]) to validate the model.

**Results:** Among 6909 eligible TNFi initiations, there were 1343 switchers (prediction dataset: 4623 TNFi initiations, including 898 switchers). Compared with non-switchers, switchers were younger, had a shorter duration of RA and higher baseline mean CDAI score. Fewer switchers were positive for erosive disease or on combination therapy with MTX, but more were on monotherapy or combination therapy with a non-MTX DMARD. After investigation of several models, the best-fit model (Table) to predict switching from a TNFi yielded an AUC=0.705 (sensitivity=81%; false positive rate=49%).

Table 1. Predictive Model for TNFi Switching in Patients with RA

Covariate	Value	Odds ratio (95% CI)	p value
Age (10 year effect)		0.85 (0.79–0.92)	<0.0001
Duration of RA, years	0–2	Reference:	
	3–5	0.85 (0.67–1.07)	0.17
	6–10	0.65 (0.51–0.85)	0.001
	>10	0.52 (0.41–0.66)	<0.0001
History of diabetes		1.26 (0.94–1.68)	0.12
History of malignancy		0.66 (0.47–0.94)	0.02
History of serious infection		1.16 (0.82–1.64)	0.41
Prior number of conventional DMARDs		1.17 (1.08–1.27)	0.0002
Number of prior non-TNFi	0	Reference:	
	1	1.17 (0.88–1.55)	0.29
	$\geq 2$	1.36 (0.90–2.05)	0.15
CDAI score	Remission (0–2.8)	Reference:	
	Low (>2.8–10)	1.72 (1.11–2.66)	0.01
	Moderate (>10–22)	2.75 (1.82–4.16)	<0.0001
	High (>22)	2.75 (1.82–4.14)	<0.0001
Year of initiation		1.33 (1.28–1.37)	<0.0001

**Conclusions:** The model identified in this analysis revealed that factors including age, duration of RA, CDAI, history of co-morbid conditions, prior treatment and year of TNFi initiation predicted switching from a TNFi to another bDMARD or tsDMARD.

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SAT0099

### SARCOPENIA IS ASSOCIATED WITH JOINT DAMAGE IN RHEUMATOID ARTHRITIS: A CROSS-SECTIONAL STUDY

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**Background:** The association of metabolic status with disease characteristics of rheumatoid arthritis (RA) remain controversial. Body composition (BC) instead of body mass index (BMI) has been more and more recommended to assess metabolic status.

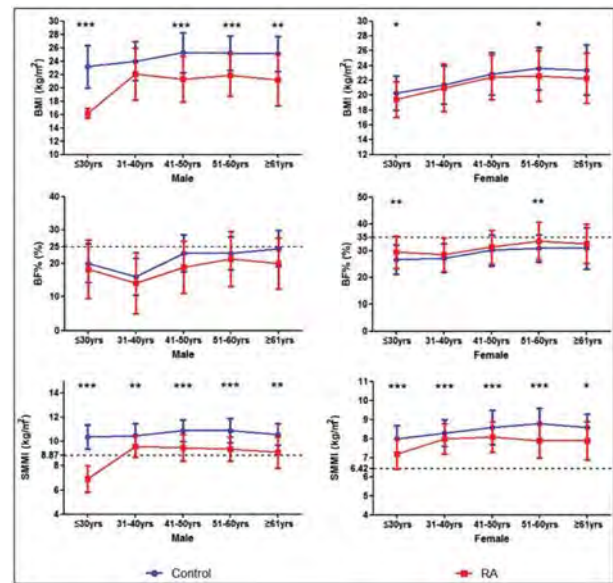
**Objectives:** To investigate the characteristics of BC in RA patients and their association with RA disease characteristics.

**Methods:** BC was assessed in RA patients and control subjects by bioelectric impedance analysis. Overfat was defined by body fat percentage (BF%) as  $\geq 25\%$  for men and  $\geq 35\%$  for women. Sarcopenia was defined by skeletal muscle mass



Characteristics	BF%		P	SMMI		P
	Normal fat (n=309)	Overfat (n=148)		Non-sarcopenia (n=405)	Sarcopenia (n=52)	
Female, n (%)	253 (81.9)	125 (84.5)	0.494	353 (87.2)	25 (48.1)	<0.001
Age, yrs, median (IQR)	49 (37-58)	54 (48-61)	<0.001	50 (41-58)	57 (27-63)	0.397
Disease duration, month, median (IQR)	48 (24-96)	64 (27-141)	0.005	52 (24-108)	66 (24-129)	0.382
Positive RF, n (%)	203 (65.7)	97 (65.5)	0.974	259 (64.0)	41 (78.8)	0.033
Positive ACPA, n (%)	212 (68.6)	105 (70.9)	0.612	283 (69.9)	34 (65.4)	0.508
Core disease activity indicators						
28TJC, median (IQR)	2 (0-5)	2 (0-8)	0.145	2 (0-5)	4 (0-9)	0.091
28SJC, median (IQR)	1 (0-4)	1 (0-4)	0.248	1 (0-4)	2 (0-8)	0.200
ESR, (mm/h), median (IQR)	26 (15-44)	32 (15-52)	0.133	26 (14-45)	42 (26-74)	<0.001
CRP, (mg/L), median (IQR)	3.8 (3.3-12.9)	5.4 (3.3-20.0)	0.008	3.8 (3.3-12.4)	15.5 (5.2-32.8)	<0.001
DAS28-CRP, median (IQR)	3.2 (2.0-4.1)	3.4 (2.3-4.8)	0.043	3.1 (2.0-4.2)	4.0 (2.6-5.5)	0.003
HAQ-DI, median (IQR)	0.13 (0-0.50)	0.38 (0-1.00)	<0.001	0.13 (0-0.63)	0.50 (0.03-1.25)	0.002
Functional limitation, n (%)	38 (12.3)	32 (21.6)	0.010	53 (13.1)	17 (32.7)	<0.001
Radiographic assessment						
mTSS, median (IQR)	11.0 (3.8-32.5)	16.5 (6.6-50.8)	0.005	12.0 (4.0-32.5)	24.0 (10.0-79.8)	0.001
JSN subscore, median (IQR)	3.0 (0-11.8)	3.0 (0-20.0)	0.158	2.5 (0-12.3)	9.0 (1.1-34.1)	0.001
Erosion subscore, median (IQR)	9.0 (2.5-21.0)	11.8 (6.0-29.8)	0.001	9.5 (3.0-21.0)	19.0 (6.1-47.6)	0.002
RJD, n (%)	168 (54.4)	95 (64.2)	0.047	225 (55.6)	38 (73.1)	0.016

Functional limitation, HAQ-DI score>1; RJD, radiographic joint damage (mTSS>10).



**Figure 1.** Comparison of BMI and BC between RA patients and control subjects in age and gender stratification. Underweight, BMI<18.5 kg/m<sup>2</sup>; Normal weight, 18.5 kg/m<sup>2</sup><BMI<24 kg/m<sup>2</sup>; Overweight, 24 kg/m<sup>2</sup>≤BMI<28 kg/m<sup>2</sup>; Obesity, BMI≥28 kg/m<sup>2</sup>; Overfat, BF%≥25% for men and ≥35% for women; Sarcopenia, SMMI≤8.87 kg/m<sup>2</sup> in men and ≤6.42 kg/m<sup>2</sup> in women; \* P<0.05, \*\* P<0.01, \*\*\* P<0.001.

**Conclusions:** This study showed lower SMMI and higher prevalence of sarcopenia in RA patients which were positively associated with joint damage.

**Disclosure of Interest:** None declared

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**SAT0100 THE DETERMINANTS OF REFRACTORY RHEUMATOID ARTHRITIS**

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**Background:** It is an ongoing matter of research, whether the course of rheumatoid arthritis (RA) can be altered by an early intervention, a concept historically referred to as the “window of opportunity”.<sup>1</sup> With the inherent challenge of underlying self-limiting disease in early patients, it remains unclear, whether the ultimate disease course of definite RA is really affected by the timing of initial treatment.

**Objectives:** To explore whether the long-term course of RA is different according to the delay of initial treatment.

**Methods:** Patients were identified from a longitudinal clinical database, and patients with refractory RA (“reRA”) were compared with patients with treatment amenable RA (“taRA”). reRA was defined as ≥3 treatment courses (≥1 biological) over ≥18 months since diagnosis without reaching low disease activity (LDA) or remission (REM) defined by a Clinical Disease Activity Index (CDAI, ≥10); taRA patients reached at least LDA within their first 2 treatment courses. We performed both matched and adjusted logistic regression analysis to compare differences in timing of first treatment between these two groups.

**Abstract SAT0100 – Table 1.** Patient characteristics at first clinical visit.

Features Characteristics	Populations		Differences (p-value*)					
	reRA (n=70)	Other (n=240)	taRA (n=102)	reRA matched** (n=50)	taRA matched** (n=50)	Across all three unmatched groups	reRA vs taRA (unmatched)	reRA vs taRA (matched**)
First Visit (month/year)	12/2005 (03/2002; 03/2009) <sup>#</sup>	06/2006 (08/2001; 08/2010)	12/2009 (10/2005; 11/2012)	06/2007 (12/2003; 07/2010)	07/2007 (09/2004; 08/2010)	<0.001	<0.001	0.786
Time to First Treatment (years from onset of symptoms)	3.17 (4.10)	1.38 (2.61)	1.45 (2.80)	2.61 (3.76)	0.88 (0.97)	<0.001	0.001	0.003
Female (%)	92.9	75.4	70.6	94	70	0.002	<0.001	0.002
Age at Symptom Onset (years)	44.37 (14.44) <sup>†</sup>	46.88 (14.53)	51.14 (14.08)	46.73 (14.02)	53.42 (12.11)	0.006	0.002	0.012
CDAI (0-76)	26.06 (12.22)	17.94 (12.49)	15.39 (9.81)	25.36 (11.98)	16.93 (9.42)	<0.001	<0.001	<0.001

\* ANOVA, t-test, or Chi<sup>2</sup>, as appropriate; \*\* matched for date of first clinical visit;

† mean (SD)/% as applicable; # date: median (quartiles)

**Results:** We enrolled 412 patients, of whom 70 were reRA and 102 taRA; 240 patients fulfilled neither definition. As can be seen in table 1, reRA patients were more frequently female (92.9 vs. 70.6%,  $p<0.001$ ), younger (44.37 vs. 51.14 years,  $p=0.002$ ), and had higher CDAI levels at first presentation (26.06 vs. 15.39,  $p<0.001$ ); time to first DMARD treatment was significantly longer for reRA than taRA (3.17 vs. 1.45 years,  $p=0.001$ ). In a multivariate analysis, treatment delay also showed statistical significance ( $p=0.007$ ). After matching reRA with taRA patients for the date of their initial presentation at our clinic, treatment delay was significantly longer univariately ( $p=0.013$ ) and adjusted for other significant predictors ( $p=0.027$ ). As our matching allowance for calendar year was  $\pm 1$  year, we could only use 50 (of 70) identified reRA patients from the cohort study approach. Based on the significant predictors, a discriminative matrix model could be constructed (figure 1).

Characteristics	reRA n=70, non-reRA n=342			
	Univariate		Multivariate	
	OR (95% CI)	Sig. (p)	OR (95% CI)	Sig. (p)
Time to First Treatment	1.15 (1.07; 1.24)	<0.001	1.12 (1.03; 1.21)	0.007
Female gender	4.57 (1.78; 11.72)	0.002	3.07 (1.14; 8.23)	0.026
Age at Symptom Onset	0.98 (0.97; 1.00)	0.048	0.99 (0.99; 1.01)	0.381
CDAI	1.06 (1.03; 1.08)	<0.001	1.06 (1.03; 1.08)	0.001

Gender		reRA vs. non-reRA			Time to First Treatment
		REM/LDA ( $\leq 10$ )	MDA ( $>10, \leq 22$ )	HDA ( $>22$ )	
Female	>2 years	10.6 (2.8; 44.3)	36.6 (18.4; 69.7)	51.8 (29.9; 72.9)	>2 years
	>1; $\leq 2$ years	3.4 (0.8; 24.3)	15.2 (6.1; 33.3)	25.1 (11.2; 47.0)	>1; $\leq 2$ years
Male	>2 years	2.1 (0.5; 20.1)	10.8 (4.6; 27.3)	18.6 (9.0; 34.6)	>2 years
	>1; $\leq 2$ years	3.1 (0.5; 19.0)	13.2 (5.5; 45.9)	22.1 (6.6; 69.6)	>1; $\leq 2$ years
	<1 year	0.9 (0.1; 25.3)	4.6 (1.0; 24.8)	8.3 (2.0; 36.0)	<1 year
	<1 year	0.6 (0.1; 18.0)	3.0 (0.7; 18.4)	5.8 (1.5; 26.8)	<1 year

**Abstract SAT0100 – Figure 1.** Comparing reRA vs non-reRA in a cohort study (logistic regression model) and predicting the probability of reRA including all selected baseline risk factors\* in a matrix risk model

\*Colour scheme: blue: 0%–5%; green: 5.1%–15%; orange: 15.1%–25%; red: >25% predicted probability of reRA; results are estimated for patient presenting in the year 2010

**Conclusions:** Our data suggest that delay to initial treatment affects the long-term course of RA. Earlier treatment initiation thus may change the severity of RA.

#### REFERENCE:

- [1] Van Nies JAB, et al. What is the evidence for the presence of a therapeutic window of opportunity in rheumatoid arthritis? A systematic literature review. *Ann Rheum Dis* 2014;73(5):861–70.

**Disclosure of Interest:** None declared

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#### SAT0101 ATLANTOEPITROPHIC MAGNETIC RESONANCE IMAGING INVOLVEMENT IN EARLY RHEUMATOID ARTHRITIS

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**Background:** The involvement of the cervical spine in rheumatoid arthritis (RA) can be essential regarding prognosis and mortality. The early detection of a cervical spine involvement in RA is essential to avoid possibly fatal complications.

**Objectives:** To assess the involvement of the atlantoaxial joint in patients with early rheumatoid arthritis (ERA) to evaluate the role of magnetic resonance imaging (MRI) in depicting this early joint involvement and to establish a risk-profile for the individual patient.

**Methods:** Fifty patients (13 men and 37 women), mean age of 58.2 years (range 36–79 years) with clinical and laboratory evidence of ERA (mean disease duration <12 months) were included in our study. MRI of the atlantoaxial joint was performed in all patients. The MRI features were correlated with clinical, radiological and biochemical variables. All patients underwent radiographic examination of the hands, wrists and feet. The assessment of the structural damage was carried out by two experienced readers, according to simple erosion narrowing scores (SENS).

**Results:** Twelve (24%) of the 50 patients with early ERA had positive MR findings. In all cases the MR showed pannus surrounded the dens, with additional erosions in 8 patients, bone marrow oedema at atlantoaxial in 9 patients and an abnormal cervico-medullary angle (<135°), in 2 patients. Compared with patients without cervical involvement, these 12 patients showed significantly higher anti-CCP antibodies (ACPA) titre [mean 200.25 UI (SD 262.44) vs. mean 22.05 (SD

40.21) ( $p<0.001$ ); higher swollen joint count (SJC) [mean 13.66 (SD 3.39) vs mean 8.65 (SD 3.38) ( $p<0.001$ ); higher Ritchie Articular Index (RAI) [mean 33.25 (SD 5.94) vs. mean 20.86 (SD 4.22) ( $p=0.047$ ); higher GH [mean 69.58 (SD 13.49) vs. mean 45.92 (SD 9.55) ( $p<0.001$ ); higher Disease Activity Score (DAS) in 44 joints level [mean 5.72 (SD 0.44) vs. mean 4.52 (SD 0.53) ( $p<0.001$ ); higher Health Assessment Questionnaire Disability Index (HAQ-DI) [mean 1.55 (SD 0.37) vs. mean 1.09 (SD 0.33) ( $p<0.001$ ), and higher simple erosion narrowing (SENS) scores [mean 15.83 (SD 4.52) vs mean 7.71 (SD 3.43) ( $p<0.001$ ). Multivariate analysis showed meaningful relationship between ACPAs, high level of DAS and the presence of hand and wrist erosive lesions (SENS) with cervical involvement.

**Conclusions:** Our results showed that ERA patients with higher disease activity and advanced peripheral erosiveness are indicators of higher risk of early involvement of the atlantoaxial inflammatory synovitis. In daily clinical practice the MRI of cervical spine it should be proposed in patients with prognostic factors of unfavourable disease evolution, even if asymptomatic.

#### REFERENCES:

- [1] Zoli A, Priolo F, Galossi A, Altomonte L, Di Gregorio F, Cerase A, et al. Craniocervical junction involvement in rheumatoid arthritis: a clinical and radiological study. *J Rheumatol* 2000;27:1178–1182.  
[2] Joaquim AF, Appenzeller S. Cervical spine involvement in rheumatoid arthritis—a systematic review. *Autoimmun Rev* 2014;13:1195–1202.

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#### SAT0102 PRISTANE-INDUCED ARTHRITIS IN DARK AGOUTI RAT: A NEW ANIMAL MODEL TO STUDY CARDIOVASCULAR DYSFUNCTION IN RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is characterised by an increased cardiovascular (CV) mortality. Animal models provide the opportunity to study CV features in RA, however, most used animal models develop a “monophasic” arthritis, making those models inappropriate for long-term studies on CV impairments.

**Objectives:** The aim of this study was to characterise vascular function and cardio-metabolic parameters in the “chronic” model of pristane-induced arthritis (PIA) in Dark Agouti (DA) rats.

**Methods:** 80 rats DA received an intradermal injection of 150  $\mu$ L of pristane (PIA) or of saline solution (controls) at day 0. Arthritis score was daily followed. Acetylcholine (Ach) and sodium nitroprusside (SNP)-induced vasorelaxation were studied in macrovascular (aortic rings pre-contracted with serotonin) and in microvascular levels (mesenteric artery segments pre-contracted with phenylephrine) at day 28 (acute phase) and day 120 (chronic phase). Radiographic score, circulating markers of inflammation, lipid and glucose levels were also measured.

**Results:** PIA rats developed an acute arthritis phase from day 13 to day 50 followed by a remission phase, then by a chronic arthritis phase from day 70 to day 120. Radiographic score was higher in chronic than in acute phase in PIA ( $p<0.001$ ). Levels of IL-6, total cholesterol and triglycerides were higher in PIA than in controls at both phases ( $p<0.001$ ) whereas plasma myeloperoxidase activity and glycaemia were unchanged. Adiponectin levels were lower in PIA compared to controls in acute ( $p<0.001$ ) but not in chronic phase. Ach-induced vasorelaxation in macrovascular bed was significantly reduced in PIA compared to controls in acute ( $p<0.05$ ) but not in chronic phase. Furthermore, an altered Ach-induced vasorelaxation was shown in microvascular bed in PIA in chronic ( $p<0.001$ ) but not in acute phase. No altered SNP-induced vasorelaxation was observed between groups at both phases in both vascular beds. Endothelial function (EF) negatively correlated with arthritis score ( $p<0.001$ ), IL-6 ( $p<0.05$ ) and total cholesterol ( $p<0.05$ ) levels in macrovascular but not in microvascular bed. No correlation was found between EF and myeloperoxidase activity, adiponectin and triglycerides levels in both vascular beds.

**Conclusions:** PIA model shares several features of the CV alterations in RA: an endothelial dysfunction at the micro- and macrovascular level with independency of course among these vascular beds, a link between inflammation and macrovascular endothelial dysfunction, associated with low lipid levels. These data suggest that this model would be very useful for long-term pharmacological studies as well for deciphering the complex pathophysiology of increased CV risk in RA.

**Disclosure of Interest:** None declared

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SAT0103

### THREE-MONTHLY ULTRASOUND MONITORING OF RHEUMATOID ARTHRITIS PATIENTS TAPERING THEIR MEDICATION HAS LIMITED VALUE IN PREDICTING DISEASE RELAPSE

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**Background:** Prognostic factors that may guide tapering decisions for DMARDs and TNFi on individual patient level are not available. To improve successful tapering subclinical synovitis may play a role in maintaining the remission state. Studies using ultrasound suggest that the presence of subclinical synovitis may elicit early disease relapse in remission.

**Objectives:** Our aim is to determine if ultrasound synovitis precedes disease relapse while tapering synthetic DMARD (sDMARD) or TNFi in patients with RA who achieved clinical remission on sDMARD and TNFi.

**Methods:** We included 125 RA patients (aged >17 years) treated with an sDMARD and a TNF-inhibitor who were in remission (DAS44 ≤ 2.4 & SJC ≤ 1). Demographic characteristics, swollen and tender joints, laboratory variables and ultrasound synovitis (MCP2-5; PIP2-5; wrists; MTP2-5) were recorded at each visit (every three months) during one year follow-up. Patients were randomised to two tapering strategies: i) tapering sDMARD; ii) tapering TNFi. Disease relapse was defined as DAS44 > 2.4 or SJC > 1. Ultrasound synovitis was defined as GS ≤ 1 and/or PD ≤ 0. To estimate whether ultrasound is able to identify patients who will have a disease relapse within three months follow-up a Cox proportional regression model for time to event data was used.

**Results:** Ultrasound synovitis was found in 58% of RA patients in clinical remission. After one year follow-up 36% of RA patients had a disease relapse of whom 60% had ultrasound synovitis at baseline. Table 1 shows the distribution of relapse on ultrasound synovitis for every three months. In the multivariate Cox model increasing number of joints with ultrasound synovitis was not significantly associated with disease relapse within three months follow-up (HR 1.21; 95%CI: 0.97-1.51) [table 2].

T0	T3	T6	T9	T12	
<b>US synovitis</b>	72/125 (58)	60/124 (48)	62/112 (55)	40/96 (42)	-
<b>Disease relapse</b>	0	6/124 (5)	8/112 (7)	23/96 (24)	8/67 (12)
<i>US synovitis at previous visit</i>	-	4/6 (67)	5/8 (63)	14/23 (61)	6/8 (75)
<b>No disease relapse</b>	0	118/124 (95)	104/112 (93)	73/93 (78)	59/67 (88)
<i>No US synovitis at previous visit</i>	-	46/118 (39)	47/104 (45)	23/73 (32)	29/59 (49)

	Model US synovitis HR (95% CI)	Model PD synovitis HR (95% CI)
<b>Age</b>	0.99 (0.97-1.02)	0.99 (0.97-1.02)
<b>Gender</b>	1.08 (0.53-2.17)	1.05 (0.53-2.11)
<b>Time since diagnosis</b>	1.02 (0.92-1.13)	1.03 (0.93-1.14)
<b>ACCP</b>	0.47 (0.24-0.91)	0.51 (0.27-0.97)
<b>DAS (at time of US)</b>	2.25 (1.21-4.19)	2.34 (1.25-4.41)
<b>US synovitis</b>	1.21 (0.97-1.51)	
<b>PD synovitis</b>		1.35 (1.02-1.80)

US = ultrasound; PD = power Doppler; HR = hazard ratio; ACCP=anti-cyclic citrullinated peptide antibody; DAS = disease activity score

**Conclusions:** Monitoring RA patients who started tapering their medication every three months showed limited value for ultrasound to identify patients who will have a disease relapse.

**Disclosure of Interest:** None declared

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SAT0104

### TREATMENT WITH METHOTREXATE IN RHEUMATOID ARTHRITIS PATIENTS ON STABLE BIOLOGICAL TREATMENT GIVES BETTER OUTCOMES OVER TIME

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**Background:** In patients with rheumatoid arthritis (RA) biological-Disease Modifying Anti-Rheumatic Drugs (bDMARDs) should be used preferentially in combination with methotrexate (MTX) as prescribed by EULAR<sup>[1]</sup>. The longitudinal treatment-effect of combination treatment compared to bDMARD monotherapy in daily clinical practice is not yet well known.

**Objectives:** To test in a registry of patients with RA the longitudinal effect of combination therapy (i.e. MTX and bDMARDs) compared to monotherapy (i.e. bDMARDs only) on the likelihood to be in clinical remission over time.

**Methods:** Adult RA patients on stable treatment with conventional synthetic disease modifying drugs (csDMARDs) and/or biologic DMARDs (bDMARDs) were followed in one centre. During clinical visits every 3 months up to 3 years rheumatologists/research nurses collected clinical- and medication data. The effect of a (time-varying) combination treatment strategy (i.e. MTX and bDMARDs) as compared to monotherapy with bDMARDs on the likelihood to be on DAS28 (≤ 2.6) and RAPID3 (0-30) (≤ 3) remission was tested in longitudinal binomial generalized estimating equations (GEE) models (one model per outcome). In addition, the effect of combination therapy compared to monotherapy on each individual component of DAS28 [tender joint count (TJC; 0-28); swollen joint count (SJC; 0-28); patient global assessment (PGA; 0-10) and ESR (mm/h)] was tested in separate longitudinal linear GEE models. All models were adjusted for possible confounders selected 'a priori' on clinical grounds: age, gender, drugs for comorbidities (yes/no), oral steroids (yes/no) and NSAID (yes/no).

**Results:** A total of 330 patients were included [mean (SD) age: 62 (12) years, 68% female, baseline mean (SD) DAS28: 3.3 (1.4) and RAPID3: 11.5 (6)]. The mean (SD) follow-up period and disease duration were 10.7 (9.7) months and 11.2 (9.6) years respectively. Combination treatment was significantly associated with a 55% higher likelihood to be in DAS28-remission (but not RAPID3-remission) over time compared with bDMARDs monotherapy (table 1). In addition, combination treatment resulted in a decrease on the SJC over time as compared to monotherapy [ $\beta = -0.91$  (95% CI: -1.77; -0.06)]. No significant differences between the two treatment strategies were seen for the other DAS28 components.

**Abstract SAT0104 Table 1.** Longitudinal effect of treatment with both MTX and bDMARDs compared to treatment with bDMARDs only (reference level)

aOR (95% CI) <sup>‡</sup>	
Outcome: DAS28 remission	
MTX + bDMARD vs bDMARD only	1.55 (1.04; 2.31)
Outcome: RAPID3 remission	
MTX+ bDMARD vs bDMARD only	1.16 (0.55; 2.42)

<sup>‡</sup> adjusted for treatment with NSAIDs, oral steroids, drugs for comorbidities, age and gender.

**Conclusions:** These results give support to the recommendation that continuing MTX in patients with RA under biological therapy increases the likelihood of clinical remission (especially when assessed with objective measures) and thus should be encouraged.

#### REFERENCE:

[1] Smolen JS, et al. Ann Rheum Dis 2014;73:492-509.

**Disclosure of Interest:** None declared

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SAT0105

### PRELIMINARY ANALYSIS OF GENETIC VARIANTS IN THE IMMUNE SYSTEM RELATED TO THE BODY MASS INDEX IN EARLY ARTHRITIS PATIENTS

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**Background:** We have observed in previous analyzes in our early arthritis (EA) cohort that patients with a higher body mass index (BMI) are, more frequently, ACPA negative and these patients carry, with a lower frequency, HLADRB1 alleles that encode for the shared epitope.

**Objectives:** To identify SNPs (Single Nucleotide Polymorphisms) of immune system genes related to BMI in EA patients.

**Methods:** The 257 patients of the PEARL (Princess Early Arthritis Register Longitudinal) cohort in which high density genotyping was available (using the Immunochip array of Illumina Inc) were included. As a previous step, those SNPs that did not meet the requirements of a genotyping call rate lower than 98%, being out of Hardy-Weinberg equilibrium ( $p < 10^{-4}$ ) and minor allele frequency lower than 1% were excluded. IMPUTE v.2 was used for the genotype imputation of the SNPs that failed in the immunochip, using as reference the data of phase III of the 1000 G project. The association analysis of the remaining SNPs was made by linear regression adjusted by sex, age and study level with PLINK v1.9. Of the 1384 SNPs associated with BMI with a value of  $p < 0.01$ , 250 SNPs were selected according to the lowest values of the division of  $p$  divided by the absolute value of its  $\beta$  coefficient. After analyzing and excluding the SNPs that were in linkage disequilibrium, the importance of the 186 resulting SNPs was quantified with the "Random Forest" and "Boosted Regression Tree" techniques using %IncMSE (Mean Decrease Accuracy).

**Results:** Table 1 shows the selection of the 15 SNPs that were more important in both "machine learning" techniques according to BMI. Although most of these SNPs are located in non-coding regions (intergenic or intronic), some of the genes where the SNPs belong or the neighboring genes have shown association in some GWAS (Genome-Wide Association) with a minor (BMP7) or a greater (RSPO3) BMI; and some of them have shown to have a regulatory role in the immune system in patients with RA (WDFY4, BMP7).

SNP	Gene	$\beta$ Coef. [CI 95%]	$p$
rs2746187	LOC728666/RSPO3	2.018 [0.949,3.087]	2.646x10 <sup>-4</sup>
rs8103026	SIGLEC6/ZNF175	-2.135 [-3.09,-1.18]	1.724x10 <sup>-5</sup>
rs2419678	LOC100132349	-2.001 [-2.826,-1.175]	6.623x10 <sup>-6</sup>
rs17842463	SULT2B1	-3.515 [-5.446,-1.585]	3.402x10 <sup>-3</sup>
rs1131878	UGT2B4	1.337 [0.542,2.131]	1.114x10 <sup>-3</sup>
rs12757445	CDC73/KCNT2	1.804 [0.737,2.871]	1.057x10 <sup>-3</sup>
rs1638020	PTPRN2	-1.329 [-2.1,-0.558]	8.409x10 <sup>-4</sup>
rs11019575	MULTIPLE GENES: 399942, 100131364	3.356 [1.309,4.307]	2.939x10 <sup>-4</sup>
rs72917213	MEX3C/LOC729051	2.319 [1.172,3.466]	9.677x10 <sup>-5</sup>
rs6014959	BMP7	-1.942 [-3.122,-0.762]	1.434x10 <sup>-3</sup>
rs2870662	DOK5/CBLN4	1.455 [0.615,2.295]	7.993x10 <sup>-4</sup>
rs10776644	WDFY4	-2.159 [-3.49,-0.828]	1.661x10 <sup>-3</sup>
rs7800039	STEAP4/ZNF804B	1.564 [0.76-2.368]	1.725x10 <sup>-4</sup>
rs12517451	ANKRD34B/DHFR	1.629 [0.695,2.562]	7.351x10 <sup>-4</sup>
rs12722531	IL2RA	-3.544 [-5.713,-1.376]	1.535x10 <sup>-3</sup>

**Conclusions:** Our preliminary approach allowed us to select 15 SNPs that may have more relevance related to BMI in patients with early arthritis. However, this is a preliminary study and it is necessary to validate these results in other populations to ensure their involvement in the relationship between the BMI and EA.

**Disclosure of Interest:** None declared

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SAT0106

### ADVANCES IN THERAPEUTIC MANAGEMENT WITH FIRST BIOLOGICAL THERAPY IN RHEUMATOID ARTHRITIS THROUGHOUT 15 YEARS

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**Background:** In the last two decades the treatment in patients with rheumatoid arthritis (RA) has undergone major advances, especially due to the appearance of

new therapies, the use of the "treat to target" strategy and a better understanding of the "window of opportunity" concept. However, data from clinical practise confirming the benefits of using these strategies are scarce.

**Objectives:** To investigate whether the proportion of patients (pts) with RA in maintained remission (R) or low disease activity (LDA) after starting a first biological agent has increased over time and which factors are associated with this change.

**Methods:** Analysis of a database from a prospective cohort including 365 pts with RA starting a 1st biological agent (BA) (TNF inhibitor, abatacept or tocilizumab) in a tertiary hospital between 2000-2014. Demographic, clinical and analytical data were collected at the beginning of treatment and clinical activity (DAS28) was measured every 6 months. For this study, 3 groups were established according to BA initiation date: interval 1 (i1) (between 2000-2004), (i2) 2005-2009 and (i3) 2010-2014, with a minimum follow-up of 2 years at all pts. For each interval, the percentage of pts achieving maintained (at least 3 consecutive visits) R (DAS28 <2.6) or LDA (DAS28 <3.2) was determined. In addition, all variables collected were compared between groups by ANOVA and chi square test.

**Results:** Out of the 365 pts initiating a 1st BA, 133 started in i1, 122 in i2 and 110 in i3. Of these, 38% (n=137) achieved maintained R/LDA. This percentage increased significantly in successive intervals (31% in i1 vs, 38% in i2 vs 45% in i3,  $p=0.02$ ). Baseline characteristics of pts achieving R/LDA are shown in table 1A. For patients in i2 and i3, compared to the previous interval (i1 and i2 respectively), a significant higher frequency of use of BA with different mechanisms of action (0% in i1 vs 2.2% in i2 vs 34% in i3,  $p < 0.001$ ), women (56% in i1 vs 76% in i2 vs 84% in i3,  $p=0.01$ ) and concomitant methotrexate (56% in i1 vs 74% in i2 vs 81% in i3,  $p=0.03$ ) was found. On the other hand, the percentage of optimized pts increased significantly over time (13% in i1 vs 32% in i2 vs 56% in i3,  $p < 0.001$ ; table 1B).

	2000-2004 (n=41)	2005-2009 (n=46)	2010-2014 (n=58)	p value
Table 1A: Characteristics at the beginning of biological therapy				
Non-TNF $\alpha$ BA (Tocilizumab)	0%	2.2%	34%	<0.001
Age (years)	52 $\pm$ 11.1	51 $\pm$ 15.7	54 $\pm$ 12.1	0.5
Sex (female)	58%	78%	84%	0.01
Non smokers	54%	61%	45%	0.6
BMI (Kg/m <sup>2</sup> )	26.5 $\pm$ 4.7	25.9 $\pm$ 4.4	26 $\pm$ 5.8	0.3
Disease duration (years)	9.2 $\pm$ 6.3	10.7 $\pm$ 7.8	7.9 $\pm$ 6.1	0.1
RF +	85%	80%	78%	0.7
Anti-CCP +	65%	84%	85%	0.8
DMARDs (MTX/SZP/LEFL)				
- Methotrexate	76%	89%	98%	0.02
- Leflunomide	56%	74%	81%	0.03
- Sulfapyridine	7%	4%	8%	0.8
- Salicylic acid	27%	35%	35%	0.7
CPR	7.3 $\pm$ 10.6	12.1 $\pm$ 12.7	8.7 $\pm$ 11.4	0.001
ESR	33 $\pm$ 20.5	34 $\pm$ 20.5	19 $\pm$ 10.2	<0.001
DAS28	5.2 $\pm$ 1.4	4.8 $\pm$ 1.1	4.7 $\pm$ 1.1	0.2
HAQ	8.1 $\pm$ 5.6	7.9 $\pm$ 5.8	7.9 $\pm$ 4.5	0.9
Table 1B: Follow-up characteristics				
Follow-up time (years)	4.0 $\pm$ 2.9	4.7 $\pm$ 2.4	4.8 $\pm$ 2.6	0.06
Time under biologic (years)	3.8 $\pm$ 2.1	4.4 $\pm$ 2.6	4.1 $\pm$ 2.7	0.2
DAS28 < 3.2 at end of interval (%)	23%	30%	75%	0.1
Optimized at the end of interval (%)	13%	32%	56%	<0.001

**Conclusions:** The percentage of pts with RA achieving maintained R/LDA after initiating a 1st BA has progressively increased over time. This is probably related to a greater use of BAs with different mechanisms of action and concomitant methotrexate. The sustained control of disease activity may allow using more frequently optimized doses of BA.

**Disclosure of Interest:** None declared

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SAT0107

### SEQUENTIAL ULTRASOUND SHOWS A LATE INCREASE IN INFLAMMATORY BURDEN IN ANTI-CCP POSITIVE PATIENTS WITH NON-SPECIFIC MUSCULOSKELETAL SYMPTOMS JUST BEFORE PROGRESSION TO INFLAMMATORY ARTHRITIS.

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**Background:** US abnormalities occur in patients with new rheumatoid arthritis (RA) and can also predict the development of clinical synovitis in anti-CCP positive patients with musculoskeletal symptoms (MSK) (CCP+) [1]. However, the timing of development of US synovitis in relation to clinical synovitis has not been longitudinally studied.

**Objectives:** To investigate whether US synovitis (grey scale (GS) and power doppler (PD)) changes in the period prior to the development of inflammatory arthritis (IA) in CCP+ individuals compared to those who do not develop IA.

**Methods:** CCP+ individuals were prospectively followed until the development of clinical synovitis in at least one joint (progressors). Progressors were compared to CCP+ individuals who did not develop clinical synovitis (non-progressors). For all subjects, US scans were performed at baseline, 6 and 12 months and then annually, and/or at the time of onset of clinical synovitis. A 22 paired joint US score was calculated for PD and GS >1 using the wrists, MCPJs (1-5) and PIPJs (1-5). Comparisons were made between baseline, the ultrasound prior to progression (or time equivalent in non-progressors)(scan 2) and progression scan (or time-equivalent) (scan 3).

**Results:** Patients with at least 3 serial US were included: 22 CCP+ progressors and 22 CCP+ non progressors. Age and gender was similar between groups.

The majority of patients in both groups showed no change in PD or GS >1 between baseline and scan 2 (table 1). All 22 non-progressors (100%) had a PD score of 0 at baseline, compared with 16/22 (72.7%) progressors. In contrast, between scan 2 and 3 (progression scan), the majority of patients in the progressor group increased total PD and GS scores, while non-progressors remained the same (table 1). Time between scan 2 and 3 was similar between groups.

**Table 1.** Direction of change in 22 paired joint PD and GS >1 scores between baseline and scan 1 and between interim scan and scan 3.

Between Baseline and Scan 1				
		DECREASED	REMAIN SAME	INCREASED
P	Progressor	13.6% (3/22)	68.2% (15/22)	18.5% (4/22)
D	Non-Progressor	All 0 at baseline	95.5% (21/22)	4.5% (1/22)
G	Progressor	27.3% (6/22)	54.5% (12/22)	18.5% (4/22)
S	Non-Progressor	18.2% (4/22)	77.3% (17/22)	4.5% (1/22)
Between Scan 2 and Scan 3/ Progression Scan				
		DECREASED	REMAIN SAME	INCREASED
P	Progressor	0	45.5% (10/22)	54.5% (12/22)
D	Non-Progressor	4.5% (1/22)	86.4% (19/22)	9.1% (2/22)
G	Progressor	0	31.8% (7/22)	68.2% (15/22)
S	Non-Progressor	4.5% (1/22)	63.6% (14/22)	31.8% (7/22)

**Conclusions:** After a period of stability the burden of US inflammation in CCP+ patients that progress to IA increases directly before the development of IA. This later increase in US inflammation may reflect a second hit in these at risk patients occurring prior to progression to IA. This may suggest that an intervention aiming to prevent the development of IA should target the subclinical phase prior to an escalation in US inflammation.

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**Disclosure of Interest:** None declared

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SAT0108

### EFFICACY OF ABATACEPT VERSUS ADALIMUMAB ON THE PROPORTION OF PATIENTS WITH SEROPOSITIVE, EROSION EARLY RA ACHIEVING DAS28 (CRP) <2.6 OR VALIDATED MEASURES OF REMISSION: A POST HOC ANALYSIS OF THE 2-YEAR AMPLE TRIAL

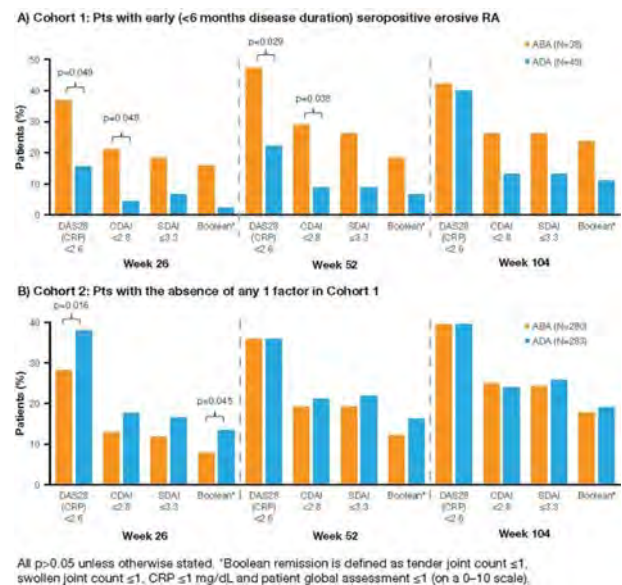
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**Background:** Binary cut-offs for disease activity are frequently used in clinical decision-making for patients with RA because they are accurate reflections of disease activity, discriminate well between disease activity states and are feasible to perform in routine clinical practice.<sup>1</sup> Results from a previous *post hoc* analysis of the randomized, controlled, head-to-head AMPLE trial (NCT00929864) indicated a trend for increased efficacy, as assessed using DAS28 (CRP), for abatacept (ABA) compared with the TNF inhibitor adalimumab (ADA) in patients with seropositive, erosive early RA.<sup>2,3</sup>

**Objectives:** To evaluate *post hoc* the impact of treatment with either SC ABA or ADA on sustained validated definitions of remission and DAS28 (CRP) <2.6 in patients with seropositive, early, rapidly progressing RA with inadequate response to MTX.

**Methods:** This *post hoc* analysis of the AMPLE trial builds on previous work<sup>3</sup> to compare clinical outcomes between treatment groups in two subsets: patients with disease duration ≤6 months, RF or anti-citrullinated protein antibody seropositivity and >1 radiographic erosion (Cohort 1), and patients in whom ≥1 of these inclusion criteria were absent (Cohort 2). Disease activity and patient-reported outcomes were evaluated at Weeks 26, 52 and 104. Endpoints were defined as percentages of patients with DAS28 (CRP) <2.6, SDAI ≤3.3, CDAI <2.8 or Boolean remission. Endpoints were compared between ABA and ADA treatment groups using chi-square tests.

**Results:** Of 646 randomized patients, 83 were included in Cohort 1 (ABA, n=38; ADA, n=45) and 563 in Cohort 2 (ABA, n=280; ADA, n=283). At Week 52, significantly more ABA- than ADA-treated patients achieved DAS28 (CRP) <2.6 in Cohort 1 (p=0.03), a trend that was not seen at Week 104 or in Cohort 2 at either time point. At Weeks 52 and 104, more ABA- than ADA-treated patients achieved CDAI, SDAI and Boolean remission in Cohort 1, a trend not seen in Cohort 2.



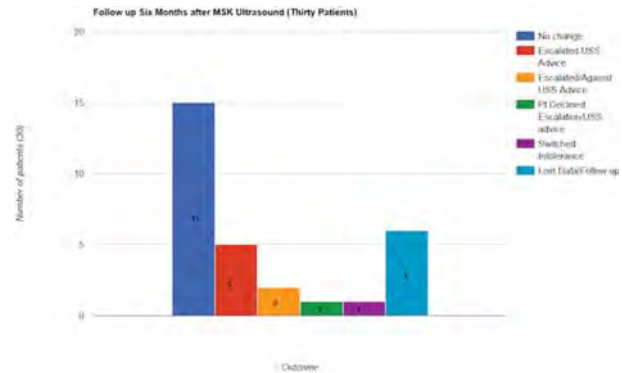
**Figure 1.** Comparison of Treatments by Sustained Remission Outcomes and DAS28 (CRP) <2.6) Cohort 1: Pts with early (<6 months disease duration) seropositive erosive RA. B) Cohort 2: Pts with the absence of any 1 factor in Cohort 1. All p > 0.05 unless otherwise stated. \*Boolean remission is defined as tender joint count ≤1, swollen joint count ≤1, CRP ≤1 mg/dL and patient global assessment ≤1 (on a 0-10 scale).

**Conclusions:** This *post hoc* analysis indicates a trend towards increased efficacy for abatacept compared with adalimumab on measures of sustained remission and DAS28 (CRP) <2.6 in patients with seropositive, erosive early RA. These results, along with results from other studies,<sup>4,5</sup> support the pursuit of a clinically definable subset of patients who may respond differentially to targeted therapies.

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**Conclusions:** US significantly reduced the need to switch treatment in this cohort of patients compared with DAS28. Longitudinal follow up supports the validity of US to determine those with active disease whilst on a biologic. The use of US may prevent over-treatment, and subsequently reduce morbidity and financial cost. Further work is needed to evaluate the clinical impact and cost effectiveness of routine US prior considering a change in biologic therapy.

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**Disclosure of Interest:** None declared  
**DOI:** 10.1136/annrheumdis-2018-eular.4264

**SAT0109** **ULTRASONIC EVALUATION OF JOINT INVOLVEMENT IN ESTABLISHED RA: ACTIVE SYNOVITIS PREDICTS SUSTAINED TREATMENT CHANGES IN SUSPECTED BIOLOGIC FAILURE**

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**Background:** EULAR guidelines recommend treatment of rheumatoid arthritis (RA) targeted to remission.<sup>1</sup> Biologic switching should be considered where there is at least moderate disease activity (DAS28 >3.2). The role of ultrasound (US) in guiding treatment is perhaps less clear. D'Agostino et al have proposed a novel algorithm based on current best evidence.<sup>2</sup>

**Objectives:** We present a case series of 30 RA patients with perceived biologic failure. By applying the algorithm to this group of patients we reviewed the impact of musculoskeletal ultrasound findings on treatment changes when compared to DAS28 assessment alone.

**Methods:** All patients had US of the Backhaus 7 joints on the most affected side, and any additional symptomatic joints. A global OMERACT-EULAR synovitis score (GLOESS) was calculated for each patient.<sup>3</sup> DAS28 was calculated at the time of US, and clinician opinion to continue or switch biologic was documented pre and post US. Patient notes were reviewed at 6 months to assess whether treatment changes were sustained.

**Results:** 26 patients had DAS28 >3.2. Of these, 10 were found to have GLOESS >6 and subsequently switched biologic therapy. 4 patients had DAS28 <3.2, despite clinical suspicion of persistent inflammatory disease. Of these patients, 2 were found to have GLOESS >6, and subsequently switched to an alternative biologic. At 6 months 20/24 patient's management remained consistent with previous US findings, 2 patients escalated treatment despite a previously negative US, 1 patient declined escalation (although US showed synovitis), 1 patient switched due to intolerance and 6 were lost to follow-up.

**Table 1.** Proposed treatment outcome (switch biologics) in symptomatic patients based on clinician opinion, DAS28 and US findings

	Clinician opinion pre-US	DAS28 at time of US	Clinician opinion post-US
Switch Biologics	23	26 (DAS28 >3.2)	12 (GLOESS>6) <sup>a</sup>
Don't Switch Biologics	7	4 (DAS28 <3.2)	18 (GLOESS<6)
Total	30	30	30
<b>P value</b>			<b>&lt;0.01<sup>b</sup>, &lt;0.01<sup>c</sup></b>

<sup>a</sup> 1 patient GLOESS <6 with severe tenosynovitis <sup>b</sup> Fisher's Exact test <sup>c</sup> Chi squared

**SAT0110** **TRAJECTORIES OF FUNCTIONAL DISABILITY IN PATIENTS WITH EARLY INFLAMMATORY POLYARTHRITIS AND MODERATE DISEASE ACTIVITY: RESULTS FROM THE EARLY RHEUMATOID ARTHRITIS NETWORK AND NORFOLK ARTHRITIS REGISTER**

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**Background:** A large group of patients with inflammatory polyarthritis (IP), and its subset rheumatoid arthritis (RA), have moderate disease activity, despite disease modifying therapy. Identifying patients with moderate disease who are likely to have subsequent high disability may prompt different treatment strategies for these patients.

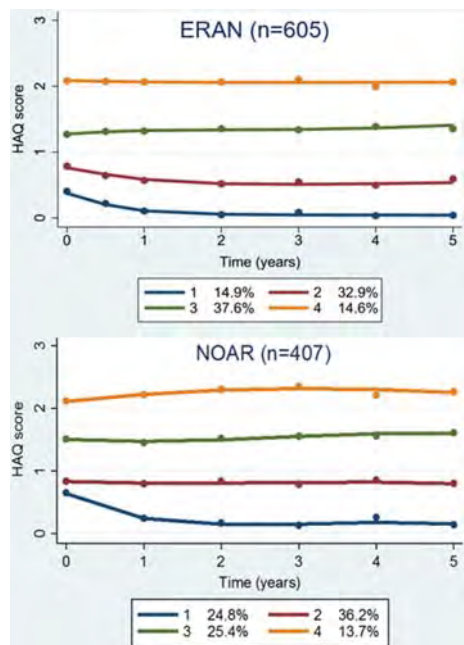
**Objectives:** To identify common trajectories of disability progression in patients with moderate disease in two large prospective observational studies.

**Methods:** The Early Rheumatoid Arthritis Network (ERAN) recruited 1236 patients with RA (<36 months symptoms) from 23 centres in England from 2002-11. The Norfolk Arthritis Register (NOAR) recruited 1054 IP patients (<24 months symptoms) from Norfolk, England, from 2000-8. At baseline and subsequent follow-ups, functional disability was assessed using the Health Assessment Questionnaire (HAQ). Included patients scored ≥3.2 and <5.1 on the Disease Activity Score (DAS28) at either baseline, year 1 or year 2, and had previously received csDMARDs (N<sub>ERAN</sub>=605; N<sub>NOAR</sub>=407). Latent class growth models (LCGMs) were used to identify HAQ trajectories independently in each cohort. Age, sex, fulfilment of ACR RA criteria, symptom duration, DMARDs at baseline, and baseline



DAS28 were included as predictors of trajectory group membership using multinomial logistic regression.

**Results:** Baseline characteristics of the cohorts were similar (ERAN vs NOAR: mean age = 57 vs 56 years; female = 70% vs 69%; met ACR criteria = 88% vs 77%; mean DAS28 = 4.7 vs 4.2). For both cohorts, LCGM analysis indicated 4 subgroups provided best fit (Bayesian Information Criterion), with similar shaped trajectories (figure 1). Multinomial logistic regression indicated that older age (ERAN & NOAR,  $p < 0.005$ ), female gender (ERAN & NOAR,  $p < 0.01$ ), meeting ACR criteria (NOAR only,  $p < 0.05$ ), use of DMARD (ERAN & NOAR,  $p < 0.01$ ), and baseline DAS28 (ERAN & NOAR,  $p < 0.005$ ) were related to an increased likelihood of being in a subgroup with higher disability (vs. lowest disability subgroup).



**Conclusions:** Four disability trajectories were observed in both the ERAN and NOAR cohort of patients with moderate disease activity. Patients on a worse trajectory who may benefit from more intensive treatment could potentially be identified earlier in the disease the group of patients with moderate disease activity.

**REFERENCE:**

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**Disclosure of Interest:** None declared

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**SAT0111 EFFICACY OF TOFACITINIB IN PATIENTS WITH MODERATE TO SEVERE RHEUMATOID ARTHRITIS BY BASELINE C-REACTIVE PROTEIN LEVELS AND ERYTHROCYTE SEDIMENTATION RATES**

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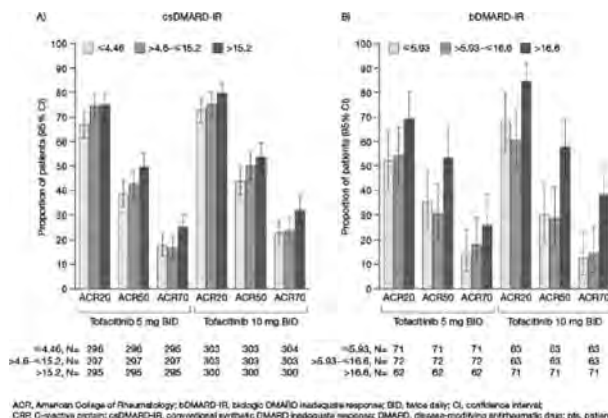
**Background:** C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) levels are serum markers of inflammation in rheumatoid arthritis (RA). Tofacitinib is an oral JAK inhibitor for the treatment of RA.

**Objectives:** To investigate the impact of baseline (BL) inflammation severity, measured by CRP and ESR levels, on tofacitinib efficacy and safety.

**Methods:** Data were analysed from tofacitinib studies in patients (pts) with RA and prior inadequate response (IR) to conventional synthetic (cs) or biologic (b) DMARDs, who initiated tofacitinib 5 or 10 mg BID as monotherapy or with csDMARDs, mainly methotrexate. Data were pooled from 4 Phase 2 trials (NCT00413660; NCT00550446; NCT00603512; NCT00687193) and 5 Phase 3

randomised, double-blind, placebo-controlled trials (ORAL Scan [NCT00847613]; ORAL Solo [NCT00814307]; ORAL Sync [NCT00856544]; ORAL Standard [NCT00853385]; ORAL Step [NCT00960440]). Analyses were stratified by BL CRP and ESR levels (tertiles) separately. Efficacy analyses at Month 6 (M6) included ACR20/50/70 response rates and changes from BL in CDAl, DAS28-4 (ESR) and SDAl. Summary/descriptive statistics were provided. Adverse events (AEs) to M6 were summarised. Results were not adjusted for multiplicity.

**Results:** A total of 2161 pts were included in the csDMARD-IR group (grp) and 512 pts in the bDMARD-IR grp. Pt BL characteristics were generally similar between grps and across CRP and ESR tertiles, except that a numerically higher proportion of csDMARD-IR pts were Asian and RA disease duration was numerically shorter for csDMARD-IR pts vs bDMARD-IR pts. In both dose grps, ACR20/50/70 response rates at M6 were generally numerically higher in the highest BL CRP grp for csDMARD-IR and bDMARD-IR pts (figure 1). Generally, a trend for greater improvement from BL in disease activity at M6 was observed with higher BL CRP. Trends across endpoints were less clear when stratified by BL ESR (data not shown). Proportions of pts with AEs, serious AEs, serious infections and discontinuations due to AEs to M6 were generally similar regardless of BL CRP or ESR.



**Figure 1.** ACR20/50/70 response rates at Month 6 for tofacitinib 5 and 10 mg BID by baseline CRP concentrations (mg/L) in A) csDMARD-IR and B) bDMARD-IR pts

**Conclusions:** While efficacy outcomes in csDMARD-IR and bDMARD-IR pts with RA were improved after 5 and 10 mg BID across all BL CRP/ESR tertiles, this post hoc analysis suggests that ACR response rates and disease activity improvements may be numerically greater in the highest BL CRP tertile, especially in bDMARD-IR RA pts. This trend was less clear with BL ESR. The tofacitinib safety profile was generally similar regardless of BL CRP or ESR, although changes in selected laboratory parameters have previously been associated with BL CRP following tofacitinib treatment.<sup>1</sup> These results suggest that subsets of pts with particularly good responses to therapy may be identified, but need further investigation.

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SAT0112

### GUIDELINE-BASED CARE IMPROVES OUTCOMES THAT MATTER TO PATIENTS: TIGHTER CONTROL, LESS SUFFERING, AND GREATER WELL-BEING OVER THE PAST DECADE IN CANADIAN RA PATIENTS

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**Background:** Best practice recommendations can increase the quality of care and improve clinical outcomes, however, the impact of guideline-based care on outcomes that matter most to early RA patients before and after implementation of treat to target (T2T) recommendations has not been evaluated.

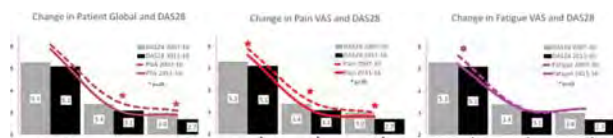
**Objectives:** We compared changes over the first year of treatment in outcomes valued most by RA patients: 1) in relation to disease activity; and 2) prior (2007-10) and subsequent (2011-16) to the release of T2T and Canadian RA Recommendations.

**Methods:** Data included early RA adults enrolled in CATCH (Canadian Early Arthritis Cohort) between 2007-16 who met 1987/2010 RA criteria with active disease at enrolment. Treatment was at the discretion of the rheumatologist and cohort investigators met annually to discuss ways to improve outcomes. We compared changes in DAS28, pain (0-10), fatigue (0-10), patient global (0-10), and HAQ-DI at 6 and 12 months prior to and after the release of guidelines using Cochran-Armitage trend tests and regression.

**Results:** The sample included 1942 adults who were mostly female (72%) with a mean (SD) age of 55 (15), 2 (2) comorbidities, and symptom duration of 6 (3) months. At enrollment, almost all (95%) were in DAS28 moderate disease activity [MDA; 42%] or high disease activity [HDA; 53%], and were initially treated with csDMARDs (92%) and MTX (75%). CDAI, DAS28 and PROs by DAS28 disease levels are shown in the Table.

Participant characteristics.

Mean (SD)	Total	LDA	MDA	HDA
<b>N (%)</b>	1942	93 (5%)	828 (42%)	1021 (53%)
<b>DAS28</b>	5.3 (1.3)	2.9 (0.2)	4.2 (0.5)	6.2 (0.8)
<b>CDAI</b>	28.1 (13.8)	10.8 (5.3)	19.4 (8.0)	36.9 (11.8)
<b>Patient Global (0-10)</b>	6.0 (2.8)	3.2 (2.2)	4.9 (2.7)	7.2 (2.4)
<b>Pain (0-10)</b>	5.7 (2.8)	3.3 (2.3)	4.6 (2.6)	6.8 (2.4)
<b>Fatigue (0-10)</b>	5.4 (3.0)	3.8 (2.8)	4.6 (2.9)	6.1 (2.9)
<b>HAQ-DI (0-3)</b>	1.1 (0.7)	0.6 (0.5)	0.8 (0.6)	1.4 (0.7)



As mean DAS28 decreased over the year, similar improvements in patient global, pain, HAQ, and fatigue were also evident (-3.0, -2.8, -2.3, -0.6; p's<0.001). When comparing change in PROs in the two time periods, there were more rapid improvements in patient global and pain at 6 and 12 months (p's<0.001; figure 1) and similar improvements in HAQ and fatigue.

**Conclusions:** Results from this large country-wide study suggest that T2T results in better disease control in the first year of RA with similar improvements in pain, fatigue, and disability—symptoms that patients identify as important—resulting in greater overall well-being. These data offer additional evidence supporting the importance of early identification and rapid control of RA to improve long-term outcomes and QOL.

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**Disclosure of Interest:** None declared

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SAT0113

### CLUSTERIN SERUM LEVELS ARE ELEVATED IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS AND PREDICT DISEASE ACTIVITY AND TREATMENT RESPONSE

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**Background:** Clusterin (also known as apolipoprotein J) is an extracellular chaperone that participates in a number of biological processes, including inflammation and apoptosis. Recent data suggest its possible protective role in the development of bone erosions and autoimmune disorders.

**Objectives:** The aim of our study was to analyze the serum levels of clusterin in patients with early rheumatoid arthritis (RA) and in healthy individuals, and to examine their potential association with disease activity and treatment response.

**Methods:** The serum levels of clusterin were determined by ELISA (BioVendor) in 56 patients with early RA before and three months after initiation of treatment, and in 56 age /sex-matched healthy subjects. Disease activity was evaluated by Clinical Disease Activity Index (CDAI), Simplified Disease Activity Index (SDAI) and 28-joint Disease Activity Score (DAS28). Response to therapy was assessed based on the SDAI/CDAI definition. Receiver operating characteristic (ROC) curve analysis of clusterin levels was performed to predict disease activity and treatment response after six months of treatment. The area under the curve (AUC) and the 95% confidence interval (CI) were calculated. Data are presented as mean±SD.

**Results:** Clusterin levels at baseline were significantly higher in patients with early RA than in healthy individuals (75.1±12.4 vs 56.7±9.7, p<0.001). After three months of therapy, the concentrations of clusterin decreased and reached levels comparable to those in healthy subjects (57.7±9.7 vs 56.7±9.7, p>0.05). Although there was no association between clusterin levels and disease activity at baseline, clusterin levels positively correlated with SDAI and CDAI at month 3 (r = 0.269, p=0.047 and r = 0.294, p=0.030, respectively) and at month 6 (r = 0.339, p=0.013 and r = 0.318, p=0.021, respectively) after treatment initiation. Using ROC analysis, clusterin baseline levels predicted remission and low disease activity according to SDAI (AUC = 0.709 (95% CI 0.548; 0.869), p=0.019) and CDAI (AUC = 0.829 (95% CI 0.721; 0.937), p<0.001), and major treatment response after 6 months of therapy (AUC = 0.696 (95% CI 0.549; 0.842), p=0.015 for both).

**Conclusions:** We demonstrate elevated serum concentrations of clusterin in patients with early rheumatoid arthritis and suggest clusterin as a biomarker for predicting disease activity and treatment response.

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**Disclosure of Interest:** None declared

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SAT0114

### TRENDS IN THE INCIDENCE OF SOLID TUMORS IN PATIENTS WITH RHEUMATOID ARTHRITIS IN SPAIN. A NATIONAL OBSERVATIONAL COHORT STUDY.

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**Background:** During the last 20 years, the rheumatoid arthritis (RA) treatment has changed. Considering the increasing use of biological immunomodulators to treat this disease and the concern that immunomodulation may alter cancer risk, it's important to know the tumors incidence in RA.

**Objectives:** To analyze the incidence and trend of hospital admissions for solid tumors in patients with RA in Spain during the period between 1999 and 2015.

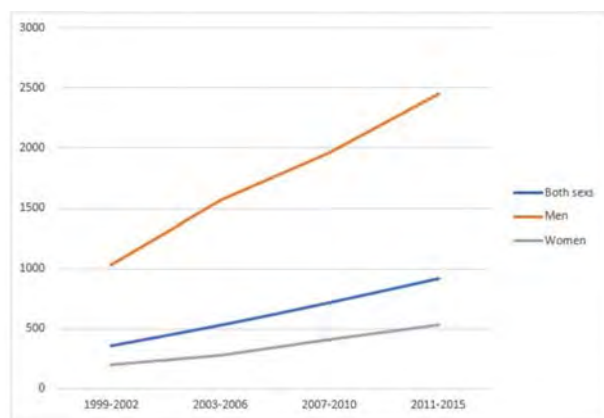
**Methods:** This is a retrospective population based study. We analyzed a national administrative database that includes a Minimum Basic Data Set (MBDS) of all hospital admissions of RA patients. Period: 1999 to 2015. We selected the MBDS for solid tumors. Cases were identified by the presence in primary and secondary diagnosis of ICD 9 codes. The population at risk was estimated through the

population census of the National Institute of Statistics, with an estimated prevalence of RA of 0,5% (women: 0,8%, men:0,2%). Crude and adjusted rates of the solid tumors were calculated. The trend was analyzed by Generalized Linear Model (GLM).

**Results:** 338.343 RA hospital admissions were detected in the study period, being 18.401 (5,4%) due to solid tumors. The main clinical-demographic characteristics are shown in the next table.

	Total	Women	Men	P value
N (%)	18.401 (5,4)	8689 (3,8)	9712 (8,6)	$P<0,001$
Age, mean (SD)	69,98 (11,21)	68,62 (12,3)	71,20 (9,99)	$P<0,001$
In-hospital exitus n (%)	2455 (13,34)	1035 (11,9)	1420 (14,62)	$P<0,001$
Charlson Index, mean (SD)	5,72 (2,95)	5,63 (2,95)	5,80 (2,95)	$P<0,001$
Stay, mean (SD)	10,94 (11,6)	10,76 (11,6)	11,1 (11,77)	$P=0,051$

The solid tumor adjusted rate during the study period was  $647,53/10^5$  inhabitants/yr ( $366,97/10^5$  in women and  $1792,99/10^5$  in men; relative risk men:women =4,8). This rate increased from  $305,65/10^5$  in 1999 to  $993,19/10^5$  inhabitants/yr in 2015 (from  $814,06/10^5$  in 1999 to  $2535,5/10^5$  in 2015 in men; from  $181,68/10^5$  in 1999 to  $607,71/10^5$  in 2015 in women). The annual age-adjusted rate increased significantly: 7,37% (6,52% in men and 8,02% in women;  $p<0,001$ ). figure 1



**Conclusions:** There was an increasing incidence of hospital admissions due to solid tumors in RA in Spain during the period 1999-2015. An annual rate increase of 7.37%, is estimated.

**Disclosure of Interest:** None declared

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SAT0115

#### TRENDS IN THE ACTIVITY OF RHEUMATOID ARTHRITIS AS THE CONSEQUENCE OF TREAT-TO-TARGET STRATEGY: EIGHT-YEAR DATA FROM 2009 TO 2016

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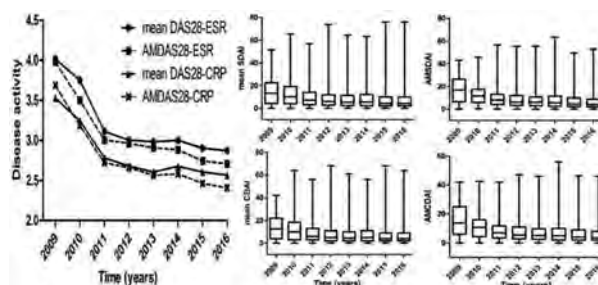
**Background:** In past decades, treatment of rheumatoid arthritis (RA) has advanced greatly, driven largely by the advent of new medications and treat-to-target (T2T) strategy, but the secular trends in the activity and remission of RA over past years and the efficacy of T2T strategy are not fully validated in large population in real life practice.

**Objectives:** To investigate the trends in the activity of RA over past 8 years and evaluate the value of T2T strategy in daily practice.

**Methods:** All the medical records of RA patients from 2009 to 2016 were retrospectively reviewed. Disease activity scores at obtained visits were measured by DAS28-CRP, DAS28-ESR, SDAI and CDAI. To display trends over years, both mean and time-adjusted methods were applied in calculation of annual disease activity and remission rate. Disease activity and remission rate were also compared before and after the year of 2011 when application of T2T strategy was initiated in our center. Furthermore, a sub-cohort study including T2T and non-T2T period groups was conducted with outcome of cumulative percentage of remission and time to achieve first remission during the first year follow-up.

**Results:** In total, 1,001 patients with 6,944 clinical visits were included. Over eight-year period, significant improvements were witnessed in disease activity and remission rate, measured by all four indices ( $p<0.0001$ ). More patients achieved lower disease activity and higher remission rates after T2T adherence in 2011 compared to those in the years of 2009 and 2010 ( $P<0.0001$ ). Moreover, sub-cohort study revealed that more patients (49.3%>73.2% vs. 19.1%>34.5%,

OR=2.4-3.0) achieved remission with a shorter median time compared with the non-T2T period group ( $p<0.0001$ ), particularly in DAS28-CRP (21 vs. >52 weeks), DAS28-ESR (37 vs. >52 weeks).



**Figure 1.** Trends in disease activity scores over 8 years by four indices in mean and adjusted mean (AM) methods. (A) Trends based on DAS28-CRP and DAS28-ESR in two methods (B) Trends based on SDAI and CDAI in two methods

**Conclusions:** Over past 8 years, the RA activity has substantially decreased and T2T strategy was directly attributable to the favorable changes in clinical practice.

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SAT0116

#### THE STUDY OF BASELINE SERUM sICAM-1 AND CXCL13 LEVELS IN PREDICTING RESPONSE TO TUMOR NECROSIS FACTOR-A INHIBITOR THERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** TNF- $\alpha$  inhibitors are not effective for each patient, leading to poor response as well as financial burden. There is an urgent need for biomarkers to assist us in individualized treatment. However, reliable biomarkers that predict therapeutic response to TNF- $\alpha$  inhibitors are still lacking.

**Objectives:** We aimed to investigate whether baseline serum soluble intercellular adhesion molecule-1 (sICAM-1) and C-X-C motif chemokine ligand 13 (CXCL13) could serve as biomarkers to predict therapeutic response to TNF- $\alpha$  inhibitor therapy in RA patients.

**Methods:** RA patients were enrolled from the 12-week TNF- $\alpha$  inhibitor clinical trial in our center between October 2014 and October 2017. 20 age- and gender-matched healthy controls were also recruited. Serum samples at baseline and week 12 were collected from RA patients, then serum levels of sICAM-1 and CXCL13 were measured by enzyme-linked immunosorbent assay. Clinical and laboratory data were recorded from baseline to week 12. RA patients were classified into responders and non-responders at week 12 according to EULAR response criteria.

**Results:** 51 RA patients were enrolled in this study. Serum levels of sICAM-1 and CXCL13 in RA patients were significantly higher than healthy controls ( $p<0.001$  and  $p<0.001$  respectively). Serum sICAM-1 and CXCL13 levels were higher in seropositive RA patients ( $p=0.012$  and  $p=0.005$  respectively). Baseline serum levels of sICAM-1 and CXCL13 were correlated with changes in ESR, DAS28-ESR, DAS28-CRP, SDAI and CDAI. Baseline serum sICAM-1 levels were higher in responders to TNF- $\alpha$  inhibitor therapy at week 12 by EULAR response criteria ( $p=0.010$ ). However, there was no significant difference in CXCL13 levels. In addition, serum sICAM-1 and CXCL13 levels were decreased after treatment in



responders ( $p < 0.001$  and  $p < 0.001$  respectively), nevertheless, non-responders showed a rising trend ( $p = 0.086$  and  $p = 0.051$  respectively). Binary logistic regression model revealed that baseline serum sICAM-1 levels had a positive effect on response to therapy. ROC curve analysis for predictive ability of baseline serum sICAM-1 showed an area under the curve (AUC) of 0.775 ( $p = 0.010$ ).

**Conclusions:** Serum sICAM-1 and CXCL13 levels were elevated in RA patients, and they were higher in seropositive patients than in seronegative patients. Elevated baseline serum sICAM-1 levels were associated with favorable response to TNF- $\alpha$  inhibitor therapy. The decrease of serum sICAM-1 levels after treatment in responders was consistent with their therapeutic response. Thus, baseline serum sICAM-1 could be a predictive biomarker for TNF- $\alpha$  inhibitor therapy in RA patients. There was a lack of reliable evidence that baseline serum CXCL13 had predictive ability, possibly due to different mechanisms of action or small sample size.

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SATURDAY, 16 JUNE 2018

## Rheumatoid arthritis - comorbidity and clinical aspects

### SAT0117 HIGH URIC ACID AS A RISK FACTOR FOR CARDIOVASCULAR DISEASES IN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Rheumatoid arthritis (RA) patients have an increased risk of cardiovascular diseases (CVD). It is unclear whether an elevated serum uric acid (UA) further increases that risk.

**Objectives:** We study CVD and their risk factors in association with UA in RA patients.

**Methods:** Adult patients who satisfied the ACR classification criteria for RA from The Kuwait Registry for Rheumatic Diseases (KRRD) from four major hospitals were evaluated from February 2013 through May 2017. Patients with recorded UA were identified and CVD and their risk factors were studied in those patients. To optimize classifier number and prediction accuracy, hierarchical cluster analyses for multiple factors were performed, which indicated nine possible independent CVD risk factors. A binary logistic regression was conducted to examine their significant association with CVD and the independence of UA as a risk factor.

**Results:** A total of 564 RA patients with available UA were identified, 353(62.6%) females. Mean age was 50.8 $\pm$ 11.5 years and disease duration 10.5 $\pm$ 2.9 years. Mean UA was 271 $\pm$ 78  $\mu$ mol/L. Of those patients, 31 (5.5%) were reported to have CVD. UA was significantly correlated to the presence of CVD ( $\chi^2 = 6.49$ ,  $p = 0.011$ ). Logistic regression model indicated a 10% increase of CVD with every 10  $\mu$ mol/L increase in UA. A correlation matrix between UA and other risk factors showed a significant association between high uric acid and a younger age at RA diagnosis ( $r = -0.262$ ), hyperlipidemia ( $r = 0.191$ ) and diabetes mellitus ( $r = 0.244$ ).

**Conclusions:** Our study suggests that UA may be an independent risk factor for CVD and is associated with the presence of other risk factors. UA should be measured and carefully approached in RA patients.

**Disclosure of Interest:** None declared

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### SAT0118 ASSOCIATION OF RENIN-ANGIOTENSIN SYSTEM IMBALANCE WITH SUBCLINICAL ATHEROSCLEROSIS AND DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is an independent risk factor for cardiovascular disease (CVD). The renin-angiotensin system (RAS) is a hormonal cascade with important role in hydroelectrolytic homeostasis, blood pressure and regulation of cardiovascular remodeling. Angiotensin II (Ang II) acts as a proinflammatory mediator (1).

**Objectives:** To investigate the association of serum levels of RAS components with the presence of subclinical atherosclerosis using carotid ultrasonography in women with RA.

**Methods:** Women with RA according to ACR/EULAR 2010 or ACR 1987 criteria and without clinical ischemic CVD were included. Disease activity was assessed using the DAS28. The presence of atherosclerotic plaques and the thickness of the medium-intimal complex (EMI) of the arterial wall in the common carotid artery were evaluated by ultrasonography. Serum levels of angiotensin (Ang) II, Ang-(1-7), angiotensin converting enzyme (ECA) and ECA II were determined by enzyme immunoassay.

**Results:** 50 women with RA, mean age 48.2 years ( $\pm 7.32$ ), mean duration of disease of 15.35 years ( $\pm 8.56$ ), DAS28 of 4.02 ( $\pm 1.41$ ) and CDAI of 14.23 ( $\pm 11.53$ ) were included. Seven patients presented altered EMI, eight had atherosclerotic plaque. The prevalence of risk factors for CVD was: 12% of smoking, 12% of family history of premature CVD, 46% of arterial hypertension, 10% of diabetes, 62% of dyslipidemia, 94% of abdominal obesity and 46% of metabolic syndrome. The control group consisted of 30 healthy women, mean age of 46.3 years ( $\pm 7.72$ ). RA patients had a higher serum concentration of Ang II ( $p < 0.01$ ), Ang-(1-7) ( $p < 0.01$ ), and ACE ( $p < 0.01$ ) than the control group (table 1). There was a negative correlation between ECA II and EMI ( $p = 0.041$ ,  $\rho = -0.290$ ). EMI correlated positively with age ( $p = 0.022$ ,  $\rho = 0.324$ ), disease duration ( $p = 0.012$ ,  $\rho = 0.315$ ) and overall Framingham risk ( $p = 0.008$ ,  $\rho = 0.368$ ) and Ang II correlated positively with DAS28 ( $p = 0.034$ ,  $\rho = 0.301$ ) and CDAI ( $p = 0.040$ ,  $\rho = 0.291$ ).

**Table 1.** Comparison between plasma concentrations of SRA biomarkers in patients with rheumatoid arthritis (RA) and the control group (CG).

RAS Biomarkers (pg/mL)	RA (n = 50) Mean $\pm$ SD	CG (n = 30) Mean $\pm$ SD	p value
Ang II	407.60 $\pm$ 278.68	198.77 $\pm$ 105.48	<0.01 <sup>a</sup>
Ang-(1-7)	162.06 $\pm$ 234.58	36.94 $\pm$ 61.36	<0.01 <sup>a</sup>
ACE	266.21 $\pm$ 103.64	222.69 $\pm$ 147.61	<0.01 <sup>a</sup>
ACE II	71.86 $\pm$ 27.32	153.57 $\pm$ 225.04	0.17 <sup>a</sup>

RA = rheumatoid arthritis; CG= control group; SD= standard deviation; Ang = angiotensin, ACE =angiotensin converting enzyme. <sup>a</sup>Mann-Whitney Test.

**Conclusions:** Imbalance of RAS components, especially Ang II and ECA II, may be associated to CVD in RA patients. Ultrasonography of the carotid arteries can identify patients that could benefit from ECA blockade.

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**Disclosure of Interest:** None declared

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### SAT0119 PHYSICAL ACTIVITY IN TUNISIAN ADULTS WITH RHEUMATOID ARTHRITIS

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**Background:** Physical activity (PA) is associated with multiple health-related benefits among the general population and adults with chronic diseases like

rheumatoid arthritis (RA) (1). As known, RA affects primarily synovial joints and can lead to loss of function and decreased mobility.

**Objectives:** The aim of this study was to explore the PA levels of adults with RA and to examine associations between PA and socio-demographic characteristics, immunological features, disease activity and treatment type.

**Methods:** This is a cross-sectional study including patients with RA (ACR/EULAR criteria). Disease activity was evaluated by Disease Activity Score erythrocyte sedimentation rate (DAS28 ESR). Physical activity was measured using IPAQ-SF (International Physical Activity Questionnaire-Short Form). Its items records the time spent on physical activity of three intensity levels (vigorous, moderate and walking) as well as the time spent on sitting in the past week. Both continuous [expressed as metabolic equivalent of task (MET-min/week)] and categorical (low, moderate and high level of PA) scores of IPAQ-SF were determined. Sedentary time (median) was reported in minutes/week. A p value <0.05 was considered significant.

**Results:** A total of 56 patients with RA were evaluated, 7 men and 47 women. The mean age was 54.9±9.8 years, the mean disease duration was 12.5±11.1 years and the mean DAS28 ESR was 4.3±1.3. The mean body mass index was 28.6 kg/m<sup>2</sup>. Eighty two point two percent of patients were on sDMARD, 17.9% were on Biologics and 64.3 were on prednisone. The mean sedentary time was 1777.5±729.6 minutes/week and the mean IPAQ-SF continuous score was 2962.2±3327.9 MET- min/week. Thirty point four percent of patients had low level PA, 46.4% had moderate level, and 23.2% of patients had high level PA. Patients with low level PA were significantly older (58.5 years for low level PA versus 55.3 years for moderate level PA versus 49.3 years for high level PA; p=0.035), and significantly more active (DAS28 ESR= 5.2 for low level PA versus 3.9 for moderate level PA versus 3.8 for high level PA; p=0.003). There were no significant differences in the other characteristics across the PA categories. Correlation analysis revealed a significant negative correlation between PA (Total MET-min/week) and both age (p=0.007; r = -0.354) and DAS28 ESR (p=0.023; r = -0.304). Moreover, there was a significant positive correlation between sedentary time and disease activity (p=0.021; r = 0.307).

**Conclusions:** Our study proved that PA in patients with RA decreased with age and activity disease with a concomitant increase in sedentary time. Given the risks of developing secondary chronic disease as a result of low levels of PA, physical exercise should be recommended as part of comprehensive RA care.

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SAT0120

#### MULTIFOCAL RECURRENT PANCREATITIS CAUSED BY SYSTEMIC SECONDARY AA AMYLOIDOSIS IN RHEUMATOID ARTHRITIS - A POSTMORTEM CLINICOPATHOLOGIC STUDY OF 161 PATIENTS

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**Objectives:** The aim of this study was to describe the prevalence and formal pathogenesis of multi (micro) focal liponecrotic pancreatitis (LnP) caused by systemic secondary AA amyloidosis (AAa) in rheumatoid arthritis (RA).

**Methods:** A randomized autopsy population of 161 in-patients with RA was studied. RA was confirmed clinically according to the criteria of the ACR. Tissue samples of pancreas were available for histologic evaluation in 111 of 161 patients. Pancreatitis and AAa were diagnosed histologically [1]. The possible role of AAa in the pathogenesis of LnP was analyzed by Pearson's chi-squared ( $\chi^2$ ) test.

**Results:** AAa complicated RA in 29 (26.12%) of 111 patients. Amyloid A deposition on different tissue structures of pancreas was detected in 25 (86.2 %) of 29 cases. Marked amyloid A deposition was found in the walls of arterioles, small and medium size arteries, and on different tissue structures of the pancreas.

Acute or chronic LnP with or without AAa was present in different stages of the pathological process (necrotic foci with or without inflammatory reaction, and/or consecutive focal accentuated fibrosis) in 15 (13.51%) of 111 patients. Seven (46.66 %) of these 15 were associated with massive AAa. The correlation between LnP and prevalence of AAa was significant ( $c^2=5.7939$ ,  $p<0.016$ ). Two (33.33%) of 15 LnP showed a special scattered multifocal appearance throughout the pancreas, characterized by necrotic foci of different size and stage of necrobiosis, without or with inflammation, and in association with severe AAa. The pancreatitis was basically not hemorrhagic, differing from hemorrhagic pancreatitis due to arterial erosions. Ductal changes were not present. The histological picture

was dominated by more or less pronounced atrophy of pancreatic glands. The link between this special type of LnP and AAa very strong and significant ( $c^2=16.2658$ ,  $p<0.0005$ ).

**Conclusions:** The close relationship between AAa and LnP suggests a relationship between amyloidosis and the prevalence of pancreatitis, that even may lead to a special multi (micro) focal pancreatitis. Amyloid A deposition in the walls of the pancreatic arterioles, small and medium size arteries (branches of splenic artery, upper and lower gastroduodenal arteries) can lead to local ischemia and to regressive changes in the pancreatic gland. This process is more or less widespread and multifocal, depending on the number of involved vessels. The size of necrobiotic areas is determined by the size of involved blood vessels. Multi (micro) focal necrosis of the pancreas caused by diminished blood supply is followed by reactive inflammation, and later fibrosis, depending on the stages of the pathological process.

AAa is a progressive cumulative process involving more and more blood vessels of different sizes, thus the regressive changes accumulate in the pancreas with time, and exist in different stages at death. Different size and stage of focal necrosis, and the co-existent marked AAa may identify this type of pancreatitis. The progressive and cumulative process of AAa with multi (micro) focal necrosis in the pancreas may cause recurrent abdominal symptoms. This form of pancreatitis may be regarded a special manifestation of AAa or a new vasculogenic entity caused by AAa in RA. Plausible similar changes of pancreas may be expected in other autoimmune diseases complicated with AAa.

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**Disclosure of Interest:** None declared

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SAT0121

#### PREVALENCE OF FIBROMYALGIA AMONG PATIENTS WITH RHEUMATOID ARTHRITIS IN DUBAI (WHAT IS THE CLINICAL RELEVANCE?)

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**Background:** Fibromyalgia (FM) is a multi-symptom syndrome characterized by chronic widespread pain, fatigue, and poor sleep quality. Some of these symptoms such as fatigue and disturb sleep seen in patients with rheumatoid arthritis (RA). Moreover, FM and RA can coexist creating a diagnostic challenge in rheumatology clinical practice and influence clinical decisions. Data on the prevalence of fibromyalgia in general population in Dubai 1.36%<sup>1</sup>. There is scarcity of data on the prevalence of FM in RA in the Middle East. We took the opportunity to study the prevalence of FM in our cohort of RA patients

**Objectives:** To assess the prevalence of fibromyalgia among RA patients in our practice.

**Methods:** We explored the prevalence of FM in 575 adult RA patients fulfilling the 2010 ACR/EULAR classification Criteria for RA<sup>2</sup>, attending the Rheumatology outpatient services in Dubai Hospital. Electronic Medical records (EMR) and medical files were reviewed for the occurrence of FM in the period from July 2017 to January 2018. We verified the documented diagnosis of FM using the 2016 revisions version of the 2010 ACR fibromyalgia classification criteria<sup>3</sup>. Grouping: Group 1 RA with FM, Group 2 RA without FM. A 2x2 contingency table (Fisher's exact test) was used to compare demographic, laboratory, drug use and biologics in both groups. Group 1 was further analyzed according to the drug used for FM.

**Results:** We identified fibromyalgia in 10.43% (60 out of 575) RA patient. FM in RA was predominately in females 58 (96.7%) versus male 2 (3.3%). Medications were used to control the symptoms of FM in 91.7% (55 of 60) and these were as follow Pregabalin (55%), Duloxetine (18.3%), Gabapentin (16.7%) and Amitriptyline (1.7%). Interesting, only 20% (12 out of 60) of patients had Vitamin D insufficiency. Five patients (8.3%) didn't use specific drug for Fibromyalgia.

On comparing the two groups there was no difference in regards to demographic data, and clinical parameters including treatment. However, RA patients with FM were twice likely to use more biologics than RA patients without FM Odds Ratio= 2, though it did not reach statistical significance (P-Value= 0.16).

**Conclusions:** The prevalence of fibromyalgia is 10.4% among RA patients in Dubai Hospital. Ten times higher than the general population (historical control). Females are the predominant gender affected. Pregabalin is the most commonly used medication in this group.

Odds ratio showed that RA patients with FM are twice likely to use biologic DMARDs than RA patients without FM, although this trend didn't reach statistical significance. Indeed, fibromyalgia can affect clinical decision in RA. Further prospective studies are recommended in different cohorts to clarify the true effect size.

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SAT0122

### EXPERIENCE OF MUSCULOSKELETAL ULTRASOUND SCANNING IMPROVES SKILL OF PHYSICAL EXAMINATION IN ASSESSMENT OF SYNOVITIS

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**Background:** Assessment of presence/absence of joint swelling is one of the most essential factors in the management of rheumatoid arthritis (RA) patients. Although physical examination by touch is the basic assessment, it often varies among physicians. In contrast, it has been reported that musculoskeletal ultrasound (US) assessment is more objective and sensitive than physical examination in detecting synovitis.

**Objectives:** We hypothesized accumulation of experience of physical examination by touch with checking results of simultaneous US assessment as right answers could improve the accuracy of physicians' physical examination by touch. This study aimed to compare the accuracy of physicians' physical examination by touch according to physicians' US experience when considering the results of US assessment as right answers.

**Methods:** Seventy RA patients who planned to take US in daily clinical practice were enrolled. Twenty three physicians affiliated with Department of Allergy and Clinical Immunology at Chiba University Hospital were also participated in this study. Written informed consent was obtained from all the patients and physicians. At first plural physicians touched wrists, metacarpophalangeal (MCP) joints and proximal interphalangeal (PIP) joints and assessed swelling/non-swelling ("Ph swelling/non-swelling") of the joints. Subsequently, US assessment was performed by another physician blinded to the results of physical examination. In this study, "US swelling" and "US non-swelling" were defined as gray-scale imaging score (GS) 2 and GS 1. The positive predictive value (PPV) of physical examination by touch was calculated (= "Ph swelling" joint count/"US swelling" joint count). Negative predictive value (NPV) was also calculated (= "Ph non-swelling" joint count/"US non-swelling" joint count). The associated factors for PPV and NPV were identified by the univariate and multivariate logistic regression analysis.

**Results:** The patients were median 65 years old with median 5 year history of RA. A majority of the patients was rheumatoid factor positive (59/70) and median DAS28-CRP was 2.63.

A total of 6116 joints per physician were evaluated by touch, and the numbers of "Ph swelling" and "Ph non-swelling" joints were 990 and 5126. A total of 1540 joints were examined by US, the numbers of "US swelling" and "US non-swelling" joints were 172 and 1368. Overall PPV and NPV were 51.7% and 88.3%.

Regarding PPV, multivariate analysis identified duration of physicians' attending to rheumatology clinic, wrists, tender joints, patients' gender, patients' age and Steinbrocker Stage as significant factors increasing the accuracy and patients' disease duration as a significant factor decreasing the accuracy. Regarding NPV, multivariate analysis identified duration of physicians' US experience and patients' disease duration as significant factors increasing the accuracy and wrists, tender joints, presence of osteophytes and DAS28-CRP as significant factors decreasing the accuracy.

**Conclusions:** Experience of US improved accuracy of physicians' physical examination by touch in non-swelling joints and prevented overestimation, while experience of attending to rheumatology clinic rather than US improved the accuracy in swelling joints.

**Disclosure of Interest:** None declared

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SAT0123

### THE EFFECTS OF TRIMETHOPRIM-SULFAMETHOXAZOLE ON DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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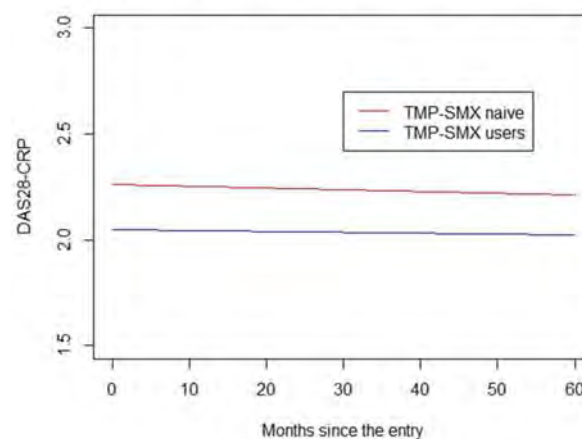
**Background:** Some experimental models suggested bacterial infection, such as periodontal disease and gut microbiota, might be an inciting and aggravating factor in rheumatoid arthritis (RA)<sup>1</sup>. Moreover, medications that have an antibacterial effect such as minocycline and sulfasalazine are used as DMARDs. However, the antibacterial effect itself on disease activity are unknown in patients with RA whereas trimethoprim-sulfamethoxazole (TMP-SMX) is often used for *Pneumocystis jirovecii* pneumonia (PCP) prophylaxis because PCP is a prevalent and potentially life-threatening opportunistic infection among patients with RA, especially in Japan<sup>2,3</sup>.

**Objectives:** To identify the effect of TMP-SMX on disease activity in patients with RA in a multi-center cohort study (ANSWER cohort study).

**Methods:** RA patients with a sampling interval of less than 1 year and at least two assessment of disease activity were enrolled. Disease activity was assessed using disease activity score 28-CRP (DAS28-CRP). Linear mixed effect models were used to evaluate the trajectories of disease activity in RA patients. Time from baseline, TMP-SMX administration, and their interaction were included as fixed effects while participant identification number and time from baseline were included as random factors. Age, sex, disease duration, RF, ACPA, HAQ, and DMARDs were included as covariates.

**Results:** A total of 49878 samples (mean sampling interval: 49 days) from 3255 patients was included. The median age at baseline was 64.0 years (interquartile range, 53.0 to 71.0 years) with 78.2 % of women (ACPA positivity, 79.2%; RF positivity, 70.8 %). The median DAS28-CRP was 2.83 with 33.8 % of patients taking TMP-SMX at baseline. Patients with taking TMP-SMX had a significantly but minimally better longitudinal trajectory on disease activity than patients without (-0.00012/month,  $P=0.009$ ). This result was similar even when patients taking sulfasalazine were excluded from analysis.

Evolution of disease activity over time based on ST use



**Conclusions:** TMP-SMX has minimal impact on disease activity, and therefore clinical utility of TMP-SMX for controlling disease besides PCP prophylaxis is limited. These results did not support a theoretical effect of bacterial infection on



disease activity in RA, although the effect of the other antibiotics on disease activity should be examined.

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#### SAT0124 AORTIC STIFFNESS AND TIME TO WAVE REFLECTION ARE ASSOCIATED WITH LEFT VENTRICULAR DIASTOLIC DYSFUNCTION MEASURES IN RHEUMATOID ARTHRITIS

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**Background:** Patients with rheumatoid arthritis (RA) experience an increased frequency of heart failure with a preserved ejection fraction (HFpEF) (1). The treatment of HFpEF is currently suboptimal. Elucidation of the underlying pathophysiological mechanisms of HFpEF may provide potential targets for its management. Diastolic dysfunction often precedes the progression to HFpEF (2). Abnormalities in aortic function contribute to diastolic dysfunction in non-RA populations (3,4).

**Objectives:** The aim of this study was to determine whether impaired aortic function is associated with left ventricular diastolic dysfunction in RA.

**Methods:** Arterial function was determined by applanation tonometry using SphygmoCor software and left ventricular diastolic function was assessed by echocardiography in 176 patients with RA. Markers of arterial function included carotid femoral pulse wave velocity (PWV), central systolic and pulse pressure, pulse pressure amplification and the magnitude and timing of the forward and reflected waves. Markers of diastolic function included the ratio of early-to-late transmitral blood flow velocity (E/A), the ratio of E to the mean of the lateral and septal wall myocardial tissue lengthening at the mitral annulus (e')/(E/e') and the septal and lateral e'. Relationships of comprehensively evaluated arterial function with markers of LV diastolic function were determined in confounder adjusted multivariate regression models.

**Results:** The timing of the forward (Ft) and reflected (Rt) waves were each associated with E/A (Ft: partial r=0.20, p=0.02; Rt: partial r=0.30, p=0.001) and Rt was further associated with lateral e' (partial r=0.36, p<0.0001) and septal e' (partial r=0.36, p<0.0001); PWV was associated with E/e' (partial r=0.18; p=0.03). Reflected wave timing was associated with two indices of impaired relaxation (E/A<0.8: OR (95% CI)=0.51 (0.29-0.91), p=0.01; lateral e'<10: OR (95% CI)=0.43 (0.26-0.71), p=0.001); PWV was associated with an increased left ventricular filling pressure (E/e'>12: OR (95% CI)=1.58 (1.04-2.38), p=0.03).

**Conclusions:** Aortic stiffness and time to wave reflection are associated with increased filling pressure and impaired relaxation of the left ventricle, respectively. The development of diastolic dysfunction in RA may be partly mediated by changes in large artery function.

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SAT0125

#### THE IMPACT OF SELECTED COMORBIDITIES ON TREATMENT OUTCOME IN PATIENTS WITH RHEUMATOID ARTHRITIS: AN EXPLORATORY COHORT STUDY.

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**Background:** Patients with Rheumatoid Arthritis (RA) may present with various comorbidities resulting in worse treatment response.[1-2]

**Objectives:** To investigate the impact of selected comorbid diseases on RA outcome with the aim of Disease Activity Score in 28 joints-C-Reactive Protein (DAS28-CRP).

**Methods:** All our RA patients were included in this study. Patients' demographics, serology results and DAS28-CRP at the time of diagnosis and after 4 months of treatment initiation were collected. Patients' electronic hospital records were evaluated for a positive history of thyroid diseases, Diabetes Mellitus (DM), primary hyperparathyroidism, vitamin B12 deficiency and presence of other diagnosed autoimmune diseases.

**Results:** 1035 RA patients were included. 63.4% were female, mean of age 67.1 years, mean of disease duration 9.6 years, 58.6% rheumatoid factor positive and 51.3% anti-cyclic citrullinated peptide positive. The observed prevalence of thyroid diseases was 11.8%, DM 10.4%, primary hyperparathyroidism 2.8%, vitamin B12 deficiency 5.8%, and other diagnosed autoimmune diseases 1.6%. There were significant associations between presence of thyroid diseases and female gender (p<0.001); DM and greater age (p<0.001); primary hyperparathyroidism and longer disease duration (p=0.002); other diagnosed autoimmune diseases and antinuclear antibody positivity (p<0.001). RA patients with thyroid diseases (p=0.001) and other comorbid autoimmune diseases (p<0.001) had significantly poorer initial response to the RA treatment compared to patients with isolated RA. Univariate analyses revealed that age, presence of thyroid diseases, presence of other diagnosed autoimmune diseases and DAS28-CRP at the time of diagnosis were significantly associated with ΔDAS28-CRP. Additionally, multivariate analysis demonstrated that ΔDAS28-CRP deterioration was significantly correlated to the presence of thyroid diseases (unstandardized regression coefficient (standard error); -0.188(0.088), p=0.030) and presence of other diagnosed autoimmune diseases (-0.537(0.208), p=0.010). (table 1)

**Table 1.** Univariate and multivariate analysis of risk factors for ΔDAS28-CRP.

	Variables	Univariate analysis	Multivariate analysis
	Backward analysis		
	Gender	0.028 (0.066)	0.058 (0.056)
Age	<b>0.007 (0.002)**</b>	0.003 (0.002)	
	Disease duration	0.000 (0.003)	- 0.003 (0.003)
IgM-rheumatoid factor	-0.055 (0.065)		0.014 (0.068)
Anti-cyclic citrullinated peptide antibody	-0.098 (0.065)		-0.041 (0.068)
Antinuclear antibody	0.003 (0.086)		-0.042 (0.067)
Presence of Thyroid diseases	<b>-0.315 (0.098)**</b>		<b>-0.188 (0.088)*</b>
<b>0.160 (0.081)*</b>	Presence of Primary		

Hyperparathyroidism-0.059 (0.193)0.008 (0.159)Presence of Diabetes Mellitus0.077 (0.104)-0.023 (0.086)Presence of vitamin B12 deficiency0.102 (0.136)0.047 (0.112)Presence of other diagnosed autoimmune diseases-**0.895 (0.249)\*\*-0.537 (0.208)\*-0.565 (0.204)\***Thyroid stimulating hormone level0.013 (0.008)0.011 (0.007)DAS28-CRP at time of diagnosis**0.724 (0.027)\*\*0.711 (0.029)\*\*0.715 (0.029)\*\***P value <0.05, \*\* P value <0.005

**Conclusions:** RA patients are at increased risk of specific comorbidities with possible impact on the treatment outcome. The authors, therefore, recommend to do periodical assessment of comorbidities to diagnose concurrent comorbid diseases as early as possible.

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**SAT0126 CHARACTERIZING HETEROGENEOUS CARE PATHWAYS OF INCIDENT RHEUMATOID ARTHRITIS PATIENTS**

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**Background:** Clinical pathway analysis is the process of characterizing clinical activities in patients' (pts) care. Little is known about the clinical pathways that pts with rheumatoid arthritis (RA) follow after their diagnosis, and how treatment patterns differ between such pathways.

**Objectives:** To identify and characterize distinct clinical pathways in the management of incident RA pts and evaluate differences in treatment patterns.

**Methods:** A retrospective cohort study was conducted in RA pts identified using electronic medical records of the Kaiser Permanente Southern California health plan. Between 01/01/2007 and 31/12/2015, we identified adult pts (aged ≥18 years) who had at least two RA diagnoses within a 12-month period, a disease-modifying antirheumatic drug (DMARD) prescription and laboratory test for anti-citrullinated peptide antibody. Latent class analysis (LCA) method was applied to identify ≥2 heterogeneous care pathways. RA-specific healthcare utilization during the first year following the RA diagnosis was used as a marker of underlying latent classes. We characterized the latent classes based on the distribution of markers, co-morbidities and RA treatment patterns including switch, augmentation and discontinuation of DMARDs. Chi-square and F-tests were used to evaluate differences between the classes.

**Results:** We identified 2843 incident RA pts. LCA indicated five latent classes representing mutually exclusive pathways of managing pts with RA. Pts in Class 1 (low disease activity-low progression) had lowest RA office visits and labs to detect inflammation with the highest DMARD discontinuation. Pts in Class 2 (low-disease activity-moderate progression) were characterized by higher lab, imaging and DMARD augmentation. Class 3 (moderate disease activity with pain) was characterized by highest use of NSAIDs across any class. Pts in Class 4 (high disease activity-moderate progression) were characterized by above-average RA office visits and the highest corticosteroid use. Class 5 (high disease activity-high progression) had pts with the highest number of RA office visits, biologic DMARD use, DMARD augmentation, DMARD switching and the lowest initial treatment discontinuation.

Classification factors	Class 1 n=367	Class 2 n=1105	Class 3 n=516	Class 4 n=616	Class 5 n=239	Total N=2843
Age, years (mean)*	54	56	56	60	50	56
Co-morbidities, n (mean)*	0.7	0.9	0.7	1.0	0.6	0.8
Female, %*	76	78	80	72	74	76
Medicare/Medicaid, %*	22	30	26	37	10	28
Switch to new DMARD, %*	2	5	9	8	13	6
Augment initial DMARD, %*	7	16	37	36	80	29
Discontinue initial DMARD, %*	73	49	31	30	6	41
<b>Mean predicted utilization of select markers</b>						
RA office visits, mean count	3	5	7	8	9	6
Traditional DMARD fills, mean count	3	4	6	6	5	5
Biologic DMARD fills, mean count	<0.01	0.01	0.02	0.04	6.5	0.56
NSAID fills, mean count	1	1	4	<0.5	2	1
Corticosteroid fills, mean count	1	1	2	4	3	2
CT scans, %	9	13	19	28	17	17
MRI, %	5	8	15	13	16	11
RF lab, %	2	22	17	19	15	17
ESR lab, %	29	98	88	93	97	85
CRP lab, %	7	74	66	65	75	61

\*Difference between classes are statistically significant; p<0.05

**Conclusions:** We identified five distinct classes/care pathways; these could be used to identify care gaps, implement standardized care plans and guide quality initiatives in the management of pts with RA.

**Disclosure of Interest:** A. Kawatkar/Grant/research support from: Bristol-Myers Squibb, J. An Grant/research support from: Bristol-Myers Squibb/Pfizer, A.

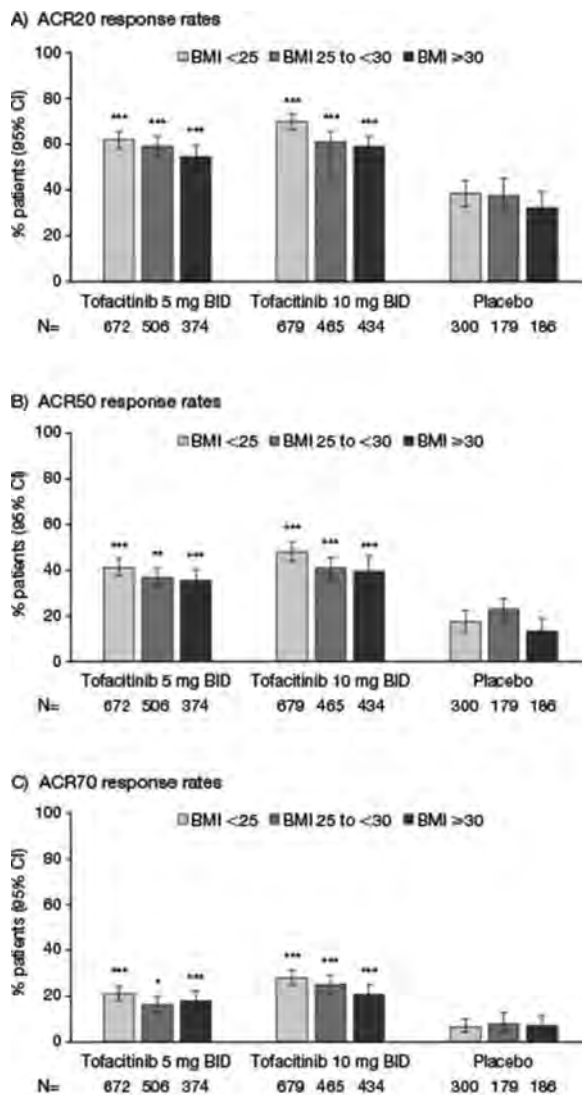
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**SAT0127 THE EFFICACY OF TOFACITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS STRATIFIED BY BASELINE BODY MASS INDEX**

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**Background:** Tofacitinib is anoral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA).

**Objectives:** This post hoc analysis aims to explore the efficacy of tofacitinib in patients (pts) with RA based on their baseline (BL) body mass index (BMI).



\*p<0.05; \*\*p<0.001; \*\*\*p<0.0001 vs placebo  
 ACR, American College of Rheumatology; BID, twice daily; BMI, body mass index; CI, confidence interval; FAS, full analysis set; NRI, non-responder imputation

**Figure 1.** ACR20/50/70 response rates at Month 6 for each treatment group stratified by BMI category (FAS, NRI). \*p<0.05; \*\*p<0.001; \*\*\*p<0.0001 vs placebo. ACR, American

College of Rheumatology; BID, twice daily; BMI, body mass index; CI, confidence interval; FAS, full analysis set; NRI, non-responder imputation

**Methods:** Data were analysed from six Phase 3 studies for pts who were methotrexate-naïve (NCT01039688) or had an inadequate response to DMARDs (NCT00960440, NCT00847613, NCT00814307, NCT00856544, NCT00853385) and received  $\geq 1$  dose of tofacitinib 5 or 10 mg twice daily (BID) or placebo (PBO). Pts were stratified by BL BMI (<25, 25 to <30,  $\geq 30$ ). Efficacy endpoints (American College of Rheumatology [ACR]20/50/70 response rates at Month [M]6; changes from baseline [ $\Delta$ ] in Health Assessment Questionnaire-Disability Index [HAQ-DI], Disease Activity Score in 28 joints based on Erythrocyte Sedimentation Rate [DAS28-4(ESR)], DAS28 based on C-reactive protein [DAS28-4(CRP)] and Clinical Disease Activity Index [CDAI] at M3 and M6) were assessed. Non-responder imputation was used for the binary endpoints. No imputation was used for continuous endpoints. No multiplicity adjustment was performed in this post hoc analysis.

**Results:** Overall, 1589, 1611 and 681 pts received tofacitinib 5 and 10 mg BID and PBO, respectively, with 1690, 1173 and 1017 pts in the BMI <25, 25 to <30 and  $\geq 30$  categories, respectively. BL demographics were generally similar between BMI categories with the exception of higher rates of diabetes (12.9-14.2% vs 3.5-9.8%), hypertension (53.2-58.9% vs 22.0-39.8%), and use of prior TNFi (23.7-46.8% vs 15.0-26.9%), and numerically higher tender (28.8-29.9 vs 23.5-26.9) and swollen joint counts (16.5-17.1 vs 14.5-16.3) and HAQ-DI scores (1.6 vs 1.4-1.5) in the BMI  $\geq 30$  group vs BMI <25 or 25 to <30. ACR response rates were significantly higher ( $p < 0.05$ ) in the tofacitinib vs PBO groups, regardless of BMI category (figure 1). In general, there appeared to be a trend towards lower ACR20/50/70 response rates with increasing BMI at M6 in tofacitinib- and PBO-treated pts; however, confidence intervals (CI) overlapped. At M6,  $\Delta$ HAQ-DI was numerically smaller for pts receiving tofacitinib 5 mg BID with BMI  $\geq 30$  vs lower BMI categories, with overlapping CI. The  $\Delta$ DAS28-4(ESR),  $\Delta$ DAS28-4(CRP) and  $\Delta$ CDAI scores were similar within each treatment group regardless of BL BMI. Generally similar trends were observed when stratified by weight.

**Conclusions:** Results of this post hoc analysis suggest that tofacitinib is associated with improvements in RA outcomes compared with PBO regardless of BL BMI category. In both tofacitinib and PBO groups, similar trends in improvements were seen in most endpoints regardless of BMI category, implying that the effect of BL BMI is not specific to tofacitinib. Further investigation is needed to assess the degree of impact of BMI on tofacitinib efficacy.

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### SAT0128 THE RISK FACTORS FOR SEVERE EXACERBATION OF INTERSTITIAL LUNG DISEASE IN RHEUMATOID ARTHRITIS DURING bDMARD THERAPY

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**Background:** Rheumatoid arthritis (RA) is a systemic inflammatory disease that affects joints and various organs. The lung is one of the most common site of extra-articular involvement. Interstitial lung disease (ILD) is one form of the lung involvement and influences prognosis of the patients. RA-ILD frequently developed acute exacerbation. Once acute exacerbation occurs, the prognosis of patients is poor. However, it is not fully elucidated what the risk factors for severe exacerbation of ILD are.

**Objectives:** The purpose of this study was to identify the risk factors for severe exacerbation of ILD in RA patients during bDMARDs therapy. The purpose of this study was to identify the risk factors for exacerbation of ILD in RA patients under the bDMARDs therapy.

**Methods:** A retrospective cohort study. Subjects were consecutive 208 RA patients who were treated with bDMARDs from 2004 to 2015 in our department and received HRCT scan before and during the therapy. Based on HR-CT imaging, pulmonary abnormalities were classified into 4 categories (ILD, nodular lesions, airway disease (AD) and others) and 20 lesions such as ground-glass opacity (GGO), reticular pattern, bronchiolitis and bronchiectasis. We recorded their existence and distribution before and during the therapy and examined their changes. Severe exacerbation of ILD was judged when patients revealed newly emerging/worsening of ILD lesions regardless of pre-existing pulmonary lesions and deceased or had to stop bDMARDs due to exacerbation of ILD. To identify risk factors, logistic regression analysis was conducted.

**Results:** Subjects were 208 RA patients, M/F; 64/144, mean age; 59.2 years old, disease duration; 7.9 years positive for RF in 84.1%. bDMARDs used for the longest period were TNFi in 79.8% of the subjects, abatacept in 15.4% and tocilizumab in 4.8%.

Pulmonary abnormalities were found in 146 (70.2%) of RA patients before bDMARDs (ILD 81, (38.9%); nodular lesions 45, (21.6%); and ADs, 115, (55.3%)). GGO, consolidation, reticular pattern and honeycombing was found in 14.8%, 19.8%, 51.9%, and 17.3% of ILD patients. Most of ILD lesions coexisted with ADs. During the observation period (3.26 $\pm$ 2.61 years), newly emerging/worsening pulmonary lesions were found in 42.3% of patients and the incidence of which was 13.7/100 person year. The incidence of newly development and worsening of ILD were 7.0/100 person years and 1.5/100 person years, respectively.

Severe exacerbation of ILD was developed in 13 patients (6.3%) and the incidence of which was 2.0/100 person year. Of 13 patients, 9 died of respiratory failure. All patients with severe exacerbation revealed GGO/consolidation. Interestingly, all these active ILD lesions were newly emerging lesions, however, most of the patients had pre-existing pulmonary lesions.

We identified risk factors for severe exacerbation of ILD (Table 1). The risk factors for severe exacerbation of ILD were older age and pre-existing pulmonary lesions of ILD and of ADs, particularly reticular pattern, honeycomb and bronchiectasis. Sero-positivity and choice of biologics were not identified as risk factors.

#### Risk factors for severe exacerbation of ILD

	Frequencies of an indicated factor in severe ILD exacerbation (-) vs (+)	Odds (95% CI) (ref: (-))	P
<b>Male</b>	55/195 (30.3%) vs 5/13 (38.0%)	1.44 (0.45-4.59)	0.54
Age of the entry	58.70 $\pm$ 13.20** vs 67.32 $\pm$ 10.36		0.022
Age of RA onset	50.71 $\pm$ 10.19 vs 60.80 $\pm$ 13.56		0.028
Disease duration (year)	8.00 $\pm$ 9.37 vs 7.01 $\pm$ 8.64		0.71
Smoking	65/144 (45.1%) vs 8/12 (66.7%)	2.43 (0.70-8.44)	0.16
RF positive	162/195 (83.1%) vs 12/13 (92.3%)	5.57 (0.32-95.9)	0.03
Anti-CCP antibody Positive	144/166 (86.7%) vs 8/10 (80.0%)	0.63 (0.13-3.20)	0.60
DAS28-ESR at the entry	4.36 $\pm$ 1.43 vs 3.66 $\pm$ 0.93		0.28
DAS28-ESR at following CT scan	3.26 $\pm$ 1.27 vs 3.73 $\pm$ 0.69		0.40
<b>TX</b>			
TNF vs non-TNF	156/209 (80.0%) vs 10/1 (76.9%)	0.83 (0.22-3.17)	0.79
Methotrexate	127/195 (65.1%) vs 9/13 (69.2%)	1.20 (0.36-4.00)	0.76
Glucocorticoid	147/195 (75.4%) vs 10/13 (76.9%)	1.09 (0.29-4.12)	0.90
<b>Pre-existing pulmonary abnormalities</b>			
Pulmonary abnormality	134/195 (68.7%) vs 12/13 (92.3%)	5.46 (0.69-42.96)	0.044
Interstitial lung disease	71/195 (36.4%) vs 10/13 (76.9%)	5.81 (1.55-21.80)	0.004
Reticular pattern	34/195 (17.4%) vs 8/13 (61.5%)	7.58 (2.34-24.58)	0.0007
Honeycomb	9/195 (4.6%) vs 5/13 (38.5%)	15.92 (3.51-71.50)	0.0004
Nodular lesions	43/195 (22.1%) vs 2/13 (15.4%)	0.64 (0.14-3.01)	0.56
Airway disease	104/195 (53.3%) vs 11/13 (84.6%)	4.81 (1.04-22.58)	0.050
Bronchiectasis	76/195 (38.9%) vs 11/13 (84.6%)	8.80 (1.00-80.80)	0.0009

\* Positive number/ number of live or dead cases. \*\* mean  $\pm$  SD

**Conclusions:** The incidence of severe exacerbation of ILD was 2.0/100 person years. The risk factors for severe exacerbation of ILD were older age and pre-existing reticular pattern, honeycomb and bronchiectasis.

**Disclosure of Interest:** None declared

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### SAT0129 TRENDS IN THE INCIDENCE OF CARDIOVASCULAR DISEASES IN PATIENTS WITH RHEUMATOID ARTHRITIS IN SPAIN: AN OBSERVATIONAL COHORT STUDY OF HOSPITAL DISCHARGES FROM 1999 TO 2015 (TREND-AR STUDY)

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**Background:** Several changes have appeared in the last years in the management of Rheumatoid Arthritis (RA), and also a greater awareness about cardiovascular risk has emerged. However, the trend of CVDs in RA in Spain is unknown.



**Objectives:** To analyze the incidence and trend of hospital admissions for CVDs in patients with RA in Spain during the period between 1999 and 2015.

**Methods:** We performed an observational retrospective population study analyzing the spanish administrative database that includes a Minimum Basic Data Set (MBDS) of hospital admissions of patients with RA 1999-2015. We selected the MBDSs for CVDs, myocardial infarction (MI), ischemic heart disease (IHD), congestive heart failure (CHF), cerebrovascular disease (CeVD) and aortic aneurysm (AA). Cases were identified by the presence in primary and secondary diagnosis of ICD9 codes. The population at risk was estimated through the population census with an estimated prevalence of RA of 0,5% (0,8% women, 0,2% men). Crude and adjusted rates were calculated, and the trend was analyzed using the Generalized Linear Model (GLM) with the year as the analysis variable. SPSS statistical package version 20 (SPSS Inc, Chicago, IL) was used.

**Results:** 338.343 RA hospital admissions were detected in the period, being 207.597 (61,3%) due to CVDs. table1 summarizes the data of the six subgroups of CVDs.

**Conclusions:** CVDs were the first cause of hospital admissions in Spain in RA patients during the period 1999-2015. Moreover, in that period there was an increasing incidence of hospital admissions due to CVDs in all the studied subgroups, being strikingly higher in men after age-adjusted rates. An annual rate increase is estimated in all the different studied subgroups oscillating between 5 and 9% annual increasing.

	Cardiovascular disease	Myocardial infarction	Ischemic heart disease	Congestive heart failure	Cerebrovascular disease	Aortic aneurysm
Total admissions	207597	12244	97881	31760	18689	2144
Men (%)	7124 (44.5)	4008 (33.4)	10845 (12.2)	9779 (31.4)	6509 (35.3)	1492 (69.5)
Women (%)	136357 (65.5)	8236 (66.6)	87036 (87.8)	21981 (68.6)	12180 (64.7)	1002 (46.5)
Mean age (SD)	72.42 (11.0)	72.26 (11.3)	67.82 (11.7)	72.33 (11.2)	72.83 (12.2)	74.12 (11.9)
Stroke (%)	14484 (7.0)	1149 (9.4)	2018 (2.1)	4224 (13.3)	2282 (12.2)	205 (9.6)
Stroke mortality (%)	39379 (19.1)	277 (2.3)	9404 (23)	6881 (21.5)	3748 (20.3)	259 (12)
Age-adjusted rate	1997.58	849.82	1104.92	1111.25	864.13	922.88
Men	14275.88	1266.08	1045.64	1873.88	1222.71	1428.31
Women	5698.70	237.46	1104.92	930.36	516.58	116.13
Age-adjusted rate increase 1999-2015	3793.83 → 9376.71	212.71 → 533.18	688.78 → 1776.24	582.62 → 2378.79	516.13 → 1984.1	561.7 → 1802.36
Men	8497.91 → 38285.19	548.71 → 1427.98	1798.63 → 9769.41	888.77 → 2989.88	619.88 → 1718.88	115.07 → 417.31
Women	1996.92 → 5547.52	118.82 → 343.01	478.15 → 1072.64	693.85 → 1433.47	276.21 → 781.72	16.68 → 54.99
Annual increase % adjustment (CI 95%)	2.58 (1.94-3.28)	3.02 (1.68-4.36)	4.38 (3.48-5.28)	5.81 (4.94-6.68)	6.11 (4.94-7.28)	8.1 (6.78-9.42)
Relative risk (95% CI)	2.49	3.84	8.5	1.97	2.88	12.87

**Disclosure of Interest:** None declared

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**SAT0130 IMPROVEMENT OF NUTRITIONAL CONDITIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS STARTING FIRST DISEASE MODIFYING ANTI-RHEUMATIC DRUGS**

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**Background:** Rheumatoid arthritis (RA) is a chronic inflammatory condition, and has been associated with adreased life expectancy. Although life expectancy has improved in many RA patients recently, the reason for this is not entirely clear.

**Objectives:** We hypothesized that better disease activity control of RA led to relief from chronic inflammation, which resulted in better nutritional conditions, and contributed to a longer life expectancy. The aim of this analysis was to examine the relationship between RA disease control and the improvement of nutritional conditions.

**Methods:** We analyzed data obtained from 111 patients with RA (male 44, female 67) who were referred to our hospital and received first disease modifying anti-rheumatic drugs (DMARD) in 2016 and 2017, retrospectively. The patient data were obtained retrospectively from medical records for a 6-month period starting at the date DMARDs were initiated. We chose serum albumin (Alb), total lymphocyte count (TLC), and hemoglobin (Hb) concentration, as the indicators of the nutritional condition. Furthermore, D-values and nutrition index 40 (N.I.40), indicators of anastomotic leakage after gastrointestinal surgery were also analyzed. Comparisons between the two groups were performed using Mann-Whitney U test. Comparisons between the parameters at different time points were performed using Wilcoxon signed-rank test. The association among the ordered European League Against Rheumatism (EULAR) response rate and the magnitude of improvement in the nutritional condition were analyzed by using the Jonckheere-Terpstrat test. Data on each patient's age and duration of RA were calculated as median (IQR<sub>1/4-3/4</sub>) values.

**Results:** The patient age was 64.0 (54.0-74.5) years, and the duration of RA was 3.0 (1.0-7.0) months. Oral prednisolone (PSL) was used in 51 patients. Other drugs administered to patients over the 6-month period included: methotrexate (63 patients), iguratimod (42 patients), bucillamine (29 patients), sulfasalazine (25 patients), tacrolimus (6 patients), and bDMARD (13 patients). The level of C-reactive protein (CRP) and the disease activity score for 28 joints based on theory-thrombocytosis rate (DAS28-ESR) before and 6 months after the initiation of DMARD treatment improved from 0.50 (0.12-1.7) mg/dL to 0.10 (0.010-0.20), p<0.001, and from 4.62 (3.51-5.52) to 2.52 (1.53-3.13), p<0.001, respectively. The EULAR good response was achieved in 59 patients, and moderate response was

achieved in 31 patients. Serum Alb level, Hb concentration, D-value, and N.I.40 showed significant improvement 6 months after the starting of DMARD [3.9 (3.6-4.3) vs 4.2 (4.0-4.5) mg/dL, p<0.001; 12.5 (11.7-13.4) vs 12.6 (11.8-13.6) g/dL, p=0.0164; 0.155 (-0.47- 0.91) vs -0.26 (-0.72-0.18), p<0.001; 47.2 (41.8-51.1) vs 49.8(46.1-52.2), p<0.001, respectively]. Furthermore, we found a significant trend towards improvement of serum Alb level, Hb concentration, D-value, and N.I. 40 in patients with a better EULAR response (p value for trend=0.0124, 0.033, 0.0057, and 0.0040, respectively).

**Conclusions:** There was a statistically significant trend towards better nutritional improvement in patients with a better EULAR response. Control of RA may contribute not only to joint deterioration prevention, but may also help to improve the nutritional condition of patients.

**Disclosure of Interest:** None declared

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**SAT0131 THE ROLE OF ULTRASOUND FOR THE ASSESSMENT OF PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS**

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**Background:** Rheumatoid arthritis (RA) a chronic systemic connective tissue disease, one of the main symptoms is inflammation that is mainly present in hands and feet. The evaluation and follow-up of disease activity relies on composite indexes with clinical outcomes. However, many studies have shown there are differences between disease activity measured by clinical examination and ultrasound findings (1).

**Objectives:** The aim of this study was to evaluate the utility of ultrasound in patients with RA stratified as moderate or severe disease activity based on DAS28.

**Methods:** We performed across-sectional study including patients with RA; patients were followed-up under T2T standards and a multidisciplinary approach. Clinical follow-up was designed by the authors according to DAS28 as follows: every 3-5 weeks (DAS28 >5.1), every 7-9 weeks (DAS28 ≥3.1 and ≤5.1), and every 11-13 weeks (DAS28 <3.1). Additionally the patient was evaluated by a rheumatologist expert in ultrasound; US studies were carried out with a Esaote MyLab Seven® US equipment (Biomedica, Genoa, Italy) equipped with a 10-18 MHz linear transducer; PD was adjusted according to the following parameters: frequency, 8.0, PRF, 0.500, wall filter 3, gain between 50 and 70. The rheumatologist reported erosions, synovitis, osteophytes and power Doppler; we defined as active disease when patients had synovitis or positive power Doppler. We calculated means, and standard deviations for continuous variables and categorical variables were presented as rates. We performed a bivariate analysis using Pearson's Chi<sup>2</sup>

**Results:** 272 patients meet the inclusion criteria; most of patients were woman 87%, mean age were 57 years ± 11, mean DAS was 4.45 ± 1.1, 70% of patients were in moderate disease activity (MDA), and 30% in severe disease activity (SDA), 81% of patients were receiving conventional DMARDs therapy and 19% biological therapy. Regarding the findings of the ultrasound, the most prevalent elementary lesions in hands and feet were erosions, 75% and 6% see table 1. Active disease was found in 66% (11% of patients had only synovitis and 55% had synovitis plus Doppler) see table 2. Thus, in patients where we assumed that had MDA or SDA, by ultrasound we found that 34% did not have disease activity. We did not find statistical association between ultrasound and age, sex or type of pharmacological therapy.

VARIABLE	PRESENT		ABSENT	
	n	%	n	%
<b>HANDS</b>				
SYNOVITIS	181	67	91	33
POWER DOPPLER	152	56	120	44
<b>FEET</b>				
SYNOVITIS	9	4	263	96
POWER DOPPLER	5	2	267	98
EROSIONS	16	6	256	94
OSTEOPHYTES	19	7	253	7

**Conclusions:** In RA patients with moderate or severe disease activity ultrasonography can complement the clinical evaluation, since there are a third of patients without disease activity according to ultrasound findings; where by there is a need

for further research in order to identify the reasons of non-active disease activity in patients classified clinically as in moderate or severe disease activity.

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**Disclosure of Interest:** None declared

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### SAT0132 COMORBIDITIES AFFECT THE RETENTION RATE BUT NOT THE CLINICAL RESPONSE IN A COHORT OF RHEUMATOID ARTHRITIS PATIENTS TREATED WITH TUMOR NECROSIS FACTOR INHIBITORS.

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**Background:** Rheumatoid arthritis (RA) is frequently complicated by other comorbid diseases that may drive therapeutic strategy or interfere with achieving clinical response.

**Objectives:** To retrospectively evaluate the impact of comorbidities on treatment choice, 12-month clinical response, and 24-month retention rate in a cohort of RA patients treated with a first-line subcutaneous tumor necrosis factor alpha inhibitor (TNFi).

**Methods:** Study population was extracted from a local registry which included all RA patients receiving adalimumab (ADA) or etanercept (ETN) as first-line biologic drug between January 2001 and December 2013. The prevalence of common RA comorbidities was computed and the study population was stratified according to Rheumatic Disease Comorbidity Index (RDCl) RDCl=0 vs RDCl≥1 for evaluating the role of comorbidities on the choice between ETN and ADA; the prescription of concomitant methotrexate (MTX); and the impact of comorbidities on 1-year Disease Activity Score 28 (DAS28-ESR) remission and EULAR good-moderate response rates. The 24-month retention rate was computed by the Kaplan-Meier method and a Cox proportional hazard model was developed to examine the role of RDCl and other baseline factors as predictors of TNFi persistence.

**Results:** 310 RA patients (153 ADA and 157 ETN) were included (female 82.1%, mean±standard deviation (SD) age 53.6±13.1 years, mean disease duration 11.6±9.2 years, mean baseline DAS 28.5±1.21, RF positivity 76.4%, mean HAQ 1.39±0.56). 41.2% of patients had at least one comorbidity (overall mean RDCl 0.73) and the prevalence of conditions is reported in table 1. The proportion of patients with RDCl≥1 was similar in the subgroup receiving or not concomitant MTX (55.1% versus 44.8%, respectively; p=0.57) and similar (p=0.22) in patients treated with ADA (44.8%) or ETN (37.8%). No individual comorbidity was associated with the prescription of MTX or the choice between the two TNFis. No difference was found in the rates of both EULAR good-moderate response (61.3% vs 53.7%, p=0.175) and DAS28-ESR remission (31.4% vs 27.2%, p=0.463) according to baseline RDCl score. On the other hand, elevated RDCl is a predictor of biologic drug discontinuation (Hazard Ratio [HR] 1.17, confidence interval [95% CI] 1.00-1.37; p=0.04), where as treatment with ETN (HR 0.50, 95% CI 0.35-0.71; p<0.001) and concomitant MTX (HR 0.57, 95% CI 0.40-0.81; p=0.002) were both associated with a lower risk of TNFi withdrawal.

COMORBIDITY	PREVALENCE (n=310)
Osteoporosis (no fractures)	24.5%
Hypertension	20.3%
Depression	11.8%
Cardiovascular disease	10.6%
Lung disease	7.9%
Fibromyalgia	7.6%
Autoimmune Thyroid disease	5.8%
Dyslipidemia	5.5%
Gastrointestinal disorders	5.1%
Diabetes	3.3%
Osteoporotic fractures	2.4%
Neurological disorders	1.8%
History of malignancy	0.3%

**Conclusions:** in our real-life experience, the baseline presence of comorbidity seemed to not influence the prescription of concomitant MTX and to not drive the choice between ADA and ETN. Comorbidities did not affect 1-year clinical response, but were associated with a higher risk of TNFi discontinuation over a 2-

year follow-up period. The use of ETN and concomitant treatment with MTX were both strong predictors of drug persistence.

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### SAT0133 PREVALENCE OF TYPE 2 DIABETES AND EVALUATION OF PATIENT CHARACTERISTICS AMONG PATIENTS WITH AND WITHOUT RA FROM COMMUNITY RHEUMATOLOGY CLINICS

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**Background:** RA and type 2 diabetes (T2D) have common core pathophysiologic pathways, such as insulin resistance and increased glycated end products related to endothelial dysfunction, which may portend cardiovascular disease.<sup>1</sup> Currently there is limited real-world evidence of T2D prevalence among patients (pts) with RA.

**Objectives:** To estimate the prevalence of T2D and insulin resistance among pts with RA vs control (osteoarthritis [OA] pts). To evaluate characteristics among RA pts with/without T2D.

**Methods:** A retrospective study was conducted on a subset of the JointMan database (an electronic medical record of >6000 pts from >10 providers. At each visit, diagnosis, medications, test results, co-morbidities and demographic data were collected. Pts aged ≥18 years with ≥2 diagnoses of RA or satisfying ACR criteria from 1 Jan 2009 to 30 Nov 2017 were included with a control group (pts with ≥2 OA diagnoses in the same period). Pts were considered to have T2D if they had a diagnosis code, diabetic medications prescription, HbA1c ≥6.5%, random glucose test ≥200 mg/dL or prior report of T2D. Between-group prevalence was compared using a chi-squared test and characteristics of pts with/without T2D were compared using Fisher's exact, chi-squared and Mann-Whitney tests.

**Results:** Data were analysed from 4181, 1157 and 1626 pts in RA-only, OA-only and dual (RA plus OA) cohorts, respectively. The RA-only cohort was younger and had a lower proportion of white pts compared with other cohorts (Table). T2D prevalence was significantly higher in the dual cohort (24.3%, n=395) vs RA-only (16.2%, n=676; p<0.001) and OA-only cohorts (10.5%, n=121; p<0.001). T2D prevalence was significantly higher in the RA-only vs OA-only cohorts (p<0.001). Sicca and Sjögren's syndromes were more prevalent co-morbidities in pts with RA only with vs without T2D (16.3 vs 13.0%; p=0.023) and a similar trend was observed for thyroid disorder (6.4 vs 3.7%; p=0.001).

**Table 1.** Pt Characteristics by Cohort

	RA only (n=4181)		OA only (n=1157)		Dual (RA plus OA) (n=1626)	
	With T2D (n=676)	No T2D (n=3505)	With T2D (n=121)	No T2D (n=1036)	With T2D (n=395)	No T2D (n=1231)
<b>Age (years), mean (SD)</b>	59.6 (13.5)	59.6 (14.8)	68.6 (9.8)	65.4 (11.4)	64.7 (10.5)	64.5 (11.1)
<b>Female, n (%)</b>	504 (74.6)	2643 (75.4)	83 (68.8)	761 (73.5)	294 (74.4)	943 (76.6)
<b>Race, n (%)</b>						
American Indian or Alaska Native	29 (4.3)	71 (2.0)	6 (5.0)	9 (0.9)	12 (3.0)	27 (2.2)
White	521 (77.1)	2579 (73.6)	105 (86.8)	921 (88.9)	363 (91.9)	1127 (91.6)
<b>Co-morbidities, n (%)</b>						
Sicca/Sjögren's syndromes	110 (16.3)	456 (13.0)	20 (16.5)	117 (11.3)	92 (23.3)	356 (28.9)
Thyroid disorders	43 (6.4)	128 (3.7)	3 (2.5)	65 (6.3)	27 (6.8)	68 (5.5)
<b>Charlson Comorbidity Index, mean (SD)</b>	1.02 (0.15)	1.01 (0.18)	1.05 (0.34)	1.01 (0.12)	1.01 (0.14)	1 (0.09)

**Conclusions:** A higher prevalence of T2D was observed in pts with RA compared with controls. In addition, co-morbidities of Sjögren's syndrome and thyroid disorder were higher in T2D pts with RA but not for dual RA plus OA.

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**SAT0134 MORTALITY AND MULTIPLE CAUSES OF DEATH IN RHEUMATOID ARTHRITIS PATIENTS. RESULTS FROM A LARGE POPULATION-BASED COHORT IN THE VENETO REGION, 2010-2015.**

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**Background:** Mortality rates in patients with rheumatoid arthritis (RA) are 1.5-1.6 fold higher than in the general population<sup>1,2</sup>. No recent data on mortality in large cohorts of RA patients in Italy are available.

**Objectives:** The aim of this study was to assess standardized mortality ratios (SMRs) and multiple causes of death in RA subjects living in the Veneto Region between 2010 and 2015.

**Methods:** We identified in the electronic archive of the Veneto Region a cohort of patients aged 20-89 years who were exempt from copayment for RA in January 2010, and linked them with the archive of causes of deaths of the period 2010-2015. The record-linkage was performed on previously anonymized records. In the Veneto Region a copy of all death certificates is transmitted to the Regional Epidemiology Service for coding of causes of death according to the International Classification of Diseases, 10th Edition. Each subject was followed from 1st January 2010 either until death, or 90 years of age, or 31st December 2015, whichever came first.

In the Veneto Region, the archive of causes of death include all diseases mentioned in the death certificate, and the selection of the underlying cause of death (UCOD) is performed by means of the Automated Classification of Medical Entities, a computer program developed by the US National Center for Health Statistics. SMRs with 95% confidence intervals, were computed as the ratios between deaths observed in the cohort, and those expected according to age- and gender-specific regional mortality rates.

Number of deaths and standardized mortality ratio (SMR) with 95% Confidence Interval (CI)	Deaths (n)	
	Deaths (n)	SMR (95% CI)
Certain infectious and parasitic diseases (A00-B99)	88	2.34 (1.89-2.89)
Septicemia (A40-A41)	66	3.07 (2.37-3.90)
Neoplasms (C00-D48)	519	0.98 (0.90-1.07)
Diseases of the blood and blood-forming organs (D50-D89)	23	3.22 (2.04-4.83)
Endocrine, nutritional and metabolic diseases (E00-E90)	57	0.86 (0.73-1.25)
Diabetes mellitus (E10-E14)	43	0.93 (0.67-1.26)
Mental and behavioural disorders (F00-F99)	50	0.90 (0.67-1.18)
Dementia (F00-F03)	44	0.86 (0.62-1.15)
Diseases of the nervous system (G00-G99)	61	0.89 (0.68-1.14)
Alzheimer's disease (G30)	27	0.90 (0.59-1.31)
Diseases of the circulatory system (I00-I99)	783	1.56 (1.45-1.67)
Hypertensive diseases (I10-I15)	101	1.51 (1.23-1.83)
Ischemic heart diseases (I20-I25)	247	1.51 (1.33-1.71)
Other heart diseases (I00-I09, I26-I51)	201	1.64 (1.42-1.88)
Cerebrovascular diseases (I60-I69)	182	1.43 (1.23-1.65)
Diseases of the respiratory system (J00-J99)	177	1.83 (1.57-2.12)
Pneumonia (J12-J18)	61	2.22 (1.70-2.86)
Chronic lower respiratory diseases (J40-J47)	54	1.47 (1.10-1.92)
Interstitial pulmonary diseases (J84)	20	3.47 (2.12-5.36)
Diseases of the digestive system (K00-K93)	117	1.93 (1.60-2.32)
Vascular disorders of intestine (K55)	21	2.40 (1.48-3.66)
Diseases of liver (K70-K76)	20	0.95 (0.58-1.47)
Diseases of the musculoskeletal system (M00-M99)	149	17.3 (14.7-20.4)
Rheumatoid arthritis (M05-M06)	130	63.3 (52.9-75.2)
Diseases of the genitourinary system (N00-N95)	27	1.29 (0.85-1.88)
External causes of mortality (V01-Y84)	70	1.65 (1.29-2.08)
Falls (W00-W19)	20	1.95 (1.19-3.01)
<b>All causes</b>	<b>2142</b>	<b>1.42 (1.36-1.48)</b>

**Results:** Overall 16,098 residents diagnosed with RA and aged 20-89 years were enrolled in the cohort. Follow-up was complete for above 99% of study subjects. The overall follow-up amounted to 88,599 person-years, with 2,142 registered decedents. The most common causes of death were circulatory diseases (36.6%), neoplasms (24.2%), and respiratory diseases (8.3%). SMR in RA

subjects was 1.42 (1.36-1.48). Mortality was significantly increased from circulatory, respiratory, digestive, infectious, hematological diseases and falls (figure 1). Mortality from neoplasms was similar to that expected based on rates from the general population. RA was selected as the underlying cause of death in 6.1% of all deaths in the cohort and was mentioned in 25.4% of death certificates.

**Conclusions:** Overall, a 42% excess risk of death could be observed among patients with RA in the Veneto Region. These data confirm results from previous studies in large cohorts of RA subjects [1,2].

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**SAT0135 CYTOKINE ACTIVATION AND FORMATION OF NEPHROPATHY IN EARLY RHEUMATOID ARTHRITIS: CLINICAL AND PATHOPHYSIOLOGICAL PARALLELS**

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**Background:** RA is characterized by not only joints destruction, but also of other organs and systems, particularly, lungs, heart, blood vessels, kidneys, etc. Nephropathy is currently the leading symptomatic complex of Rheumatoid Arthritis (RA), with upto 73% frequency, being identified as a prognostic criterion of disease severity and outcome. The development of renal insufficiency, as a rule, is the main cause of the fatal outcome of RA without possibility of regular hemodialysis to such patients.

**Objectives:** of the study are to determine pathophysiological relation between cell-mediated immunity (tumornecrosis factor-alpha (TNF-α) activation and renal dysfunction in the patients with early RA (eRA).

**Methods:** We analyzed the data from 35 early RA patients of average age of 50,71±2,25 years (ranged 18 - 76 years, 80% of women) with 9,21±0,43 months mean duration of the disease by the time of the study initiation. Urine and blood tests were performed to verify the main indicators of kidney function and inflammation cytokines significant interaction.

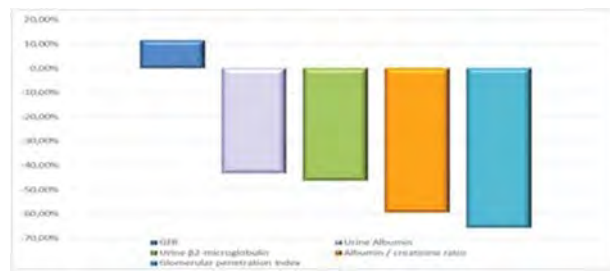
**Results:** All signs of renal dysfunction at the baseline in the patients with eRA were associated with glomerular filtration rate decrease and excretion of urine protein increase. Dynamics of albumin urine, according to the analysis of variance for one-factor scheme, were significantly determined by the state of disease activity, reflecting the severity of joint damage. High urine β-2-microglobulin level was significantly associated with the expression rate of main inflammatory cytokines as per binary regression analysis.

**Table 1.** Differences in the renal function features in the patients with early RA depending on the TNF-α expression (M±m (95%- confidence interval)).

Indicator, units of measure	Patients with RA (n=35)			The level of significance of differences between groups
	The TNF-α level less than the median 170 pg/ml (n = 18)	The TNF-α level higher than the median 170 pg/ml (n = 17)	In general, for the group (n = 35)	
GFR Cockcroft-Gault, ml/min	135,66±4,15	121,38±5,55	129,54±3,93	p<0,05
Albumin urine, mg/L	70,48±15,09 (40,3-100,67)	124,27±15,02 (94,22-154,32)	70,48±15,09 (40,3-100,67)	p<0,05
β <sub>2</sub> -microglobulin urine, μg/L	983,28±72,39 (758,5-1128,06)	1438,53±100,21 (1258,11-1639,95)	1283,28±72,39 (1138,5-1428,06)	p<0,05
The ratio of albumin: creatinine urine, mg/g creatinine	38,79±3,8 (31,2-56,39)	95,93±14,9 (71,13-110,73)	83,83±9,63 (64,38-103,09)	p<0,05
Glomerular permeation index, mg/l	0,42±0,04 (0,34-0,5)	1,23±0,24 (0,74-1,72)	0,81±0,14 (0,54-1,09)	p<0,05

**Conclusions:** The obtained dependence showed the dynamics of expression of tubular disorders in early RA with a progressive deterioration which did associate with the levels of TNF-α expression, and variety of the urine microglobulin rates in the interval 200-350 μg/L. Reliable correlation (r=0.51, p<0.05) between beta-2-microglobulinuria and TNF-α levels was clearly shown, revealing the relationship described by the formula MGU = - 481 + 937 × log<sub>10</sub> (TNF-α) as per regression analysis. The severity of tubular damage in early RA is associated with TNF-α expression, especially in the patients with TNF-α above 250 pg/mL, when microalbumin urine rates were significantly higher (p=0.00043). We identified robust data that in the early RA patients with high TNF-α, the number of reported cases of microalbumin urine was significantly higher than in those with low levels.





**Figure 1.** Differences in values of nephropathy markers in the patients with early RA, depending on TNF- $\alpha$  level.

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#### SAT0136 THE INFLUENCE OF HDL-CHOLESTEROL AND CRP ON INCREASED INSULIN RESISTANCE AND IMPAIRED BETA-CELL FUNCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Increased CRP in RA pts is associated with lower levels HDL cholesterol. HDL cholesterol may enhance insulin secretion and stimulate glucose uptake into skeletal muscle, adipose tissue, and liver.

**Objectives:** To investigate whether low HDL, alone or in combination with CRP, could explain increased insulin resistance (IR) and impaired  $\beta$ -cell function in RA pts in comparison to healthy controls.

**Methods:** The study population included 127 nondiabetic subjects (90 RA pts and 37 matched controls). We determined body mass index, waist circumference (WC), and presence of metabolic syndrome (MetS). All pts were on disease modifying antirheumatic drugs, 65.6% on steroids (none on steroids >10 mg/day), and 27.8% on biologic therapy. Laboratory analyses included hsCRP, glucose, insulin, and C-peptide (as a marker of insulin secretion). Insulin resistance (IR) was calculated using the updated Homeostasis Model Assessment (HOMA2-IR), based on fasting plasma glucose and specific insulin concentrations. The output of the HOMA2 model was calibrated to give IR of 1 as normal. HOMA2-B indicates the potential of  $\beta$ -cells to compensate increased IR. Lack of compensatory rise of HOMA2-B implied impaired  $\beta$ -cell function.

**Results:** IR was detected in 74.4% of RA pts and in 54.2% controls,  $p=0.025$ . RA pts had significantly higher concentration of specific insulin, C peptide, and HOMA2-IR than controls, while HOMA2-B was not statistically different. Both groups were comparable regarding all other factors known to affect glucose metabolism (age, WC, presence of MetS). We found significant differences in inflammation markers between RA pts and controls: ESR 29.5 (14-44) vs. 16.0 (10.0-20.0); hsCRP 5.5 (2.8-15) vs. 3.0 (1.8-3.9);  $p<0.000$  for both, as well as in lipids, especially HDL concentration  $1.5\pm 0.4$  vs  $1.60\pm 0.3$ ,  $p=0.027$  and a number of the pts with low HDL (37.8 vs 13.5%,  $p=0.007$ ). Univariate regression analysis revealed significant positive effect of HDL on logHOMA2-B ( $\beta$  0.099, 95%CI 0.029-0.169,  $p=0.006$ ) and negative, but not significant effect on HOMA2-IR. In the logistic regression, after adjustment for HDL concentration, significant differences for HOMA2-IR and insulin became less important but still persisted (Table), while significance for C peptide became more prominent. When we added the influence of inflammation, this favourable effect of HDL-cholesterol on C-peptide disappeared.

**Conclusions:** RA pts had higher IR and impaired  $\beta$ -cell function in comparison to healthy controls. The augmentation of statistical significance for C peptide, as a marker of insulin secretion, after adjustment for low HDL-cholesterol and significant effect of HDL on logHOMA2-B implicate its important role in disturbances of glucose metabolism in RA.

**Disclosure of Interest:** None declared

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#### SAT0136 THE INFLUENCE OF HDL-CHOLESTEROL AND CRP ON INCREASED INSULIN RESISTANCE AND IMPAIRED BETA-CELL FUNCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Increased CRP in RA pts is associated with lower levels HDL cholesterol. HDL cholesterol may enhance insulin secretion and stimulate glucose uptake into skeletal muscle, adipose tissue, and liver.

**Objectives:** To investigate whether low HDL, alone or in combination with CRP, could explain increased insulin resistance (IR) and impaired  $\beta$ -cell function in RA pts in comparison to healthy controls.

**Methods:** The study population included 127 nondiabetic subjects (90 RA pts and 37 matched controls). We determined body mass index, waist circumference (WC), and presence of metabolic syndrome (MetS). All pts were on disease modifying antirheumatic drugs, 65.6% on steroids (none on steroids >10 mg/day), and 27.8% on biologic therapy. Laboratory analyses included hsCRP, glucose, insulin, and C-peptide (as a marker of insulin secretion). Insulin resistance (IR) was calculated using the updated Homeostasis Model Assessment (HOMA2-IR), based on fasting plasma glucose and specific insulin concentrations. The output of the HOMA2 model was calibrated to give IR of 1 as normal. HOMA2-B indicates the potential of  $\beta$ -cells to compensate increased IR. Lack of compensatory rise of HOMA2-B implied impaired  $\beta$ -cell function.

**Results:** IR was detected in 74.4% of RA pts and in 54.2% controls,  $p=0.025$ . RA pts had significantly higher concentration of specific insulin, C peptide, and HOMA2-IR than controls, while HOMA2-B was not statistically different. Both groups were comparable regarding all other factors known to affect glucose metabolism (age, WC, presence of MetS). We found significant differences in inflammation markers between RA pts and controls: ESR 29.5 (14-44) vs. 16.0 (10.0-20.0); hsCRP 5.5 (2.8-15) vs. 3.0 (1.8-3.9);  $p<0.000$  for both, as well as in lipids, especially HDL concentration  $1.5\pm 0.4$  vs  $1.60\pm 0.3$ ,  $p=0.027$  and a number of the pts with low HDL (37.8 vs 13.5%,  $p=0.007$ ). Univariate regression analysis revealed significant positive effect of HDL on logHOMA2-B ( $\beta$  0.099, 95%CI 0.029-0.169,  $p=0.006$ ) and negative, but not significant effect on HOMA2-IR. In the logistic regression, after adjustment for HDL concentration, significant differences for HOMA2-IR and insulin became less important but still persisted (Table), while significance for C peptide became more prominent. When we added the influence of inflammation, this favourable effect of HDL-cholesterol on C-peptide disappeared.

Laboratory parameters	RA pts (N=90)	Controls (N=37)	P	Adjusted for HDL	Adjusted for CRP	Adjusted for HDL+CRP
Glucose (mmol/l)	4.8 $\pm$ 0.6	4.7 $\pm$ 0.8	ns	/		
Insulin (pmol/L)	68.5 (50.2-102.7)	55.3 (36.0-69.1)	0.008	0.018	0.048	0.054
C peptide (pmol/L)	785 (520-1010)	600 (450-880)	0.046	0.025	0.078	0.066
HOMA2-IR	1.4 (1.0-2.3)	1.2 (0.8-1.4)	0.008	0.019	0.046	0.053
HOMA2-B	148 (116-190)	141 (114-158)	0.186	0.136	0.258	0.165
HOMA2-IS	70 (46-100)	84 (71.0-132)	0.010	0.017	0.074	0.089

**Conclusions:** RA pts had higher IR and impaired  $\beta$ -cell function in comparison to healthy controls. The augmentation of statistical significance for C peptide, as a marker of insulin secretion, after adjustment for low HDL-cholesterol and significant effect of HDL on logHOMA2-B implicate its important role in disturbances of glucose metabolism in RA.

**Disclosure of Interest:** None declared

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SAT0137

### CAROTID INTIMA-MEDIA THICKNESS AND ATHEROSCLEROTIC PLAQUE IN PATIENTS WITH REACTIVE AND RHEUMATOID ARTHRITIS

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**Background:** It is well-known that the leading cause of premature mortality in patients with rheumatoid arthritis (RA) is cardiovascular disease, myocardial infarction, heart failure, stroke.<sup>1,2</sup> Another important group of rheumatic diseases that attract the attention in connection with possible proatherogenic effects are the seronegative spondyloarthropathies. Reactive arthritis (ReA) may involve the cardiovascular system, aortitis, myocarditis, pericarditis.<sup>3,4</sup>

**Objectives:** to estimate atherosclerotic changes of arteries in patients with RA and ReA, to confront the revealed changes with clinical features of joint pathology, activity of inflammatory process.

**Methods:** We included 75 patients with RA (age 38,7±7,4, disease duration 8,3±5,4), 41 patients with chronic ReA (age 35,8±7,2 disease duration 6,4±4,5) and 29 healthy subjects, matched for age and gender, without a history of CVD. An ultrasound investigation of the arterial vessel with measurement of the intima-media thickness (IMT) of carotids was performed.

**Results:** It has been determined, that in RA group IMT was 0,8 mm (0,7–0,9), compared with 0,6 mm (0,6–0,7) in ReA and 0,6 mm (0,6–0,7) in control group. In RA group IMT positively correlate with the age, duration of disease, Ritchie index, C-reactive protein level. In ReA group disease duration, C-reactive protein level, Ritchie index are not associated with IMT.

In 22 (29,3%) patients with RA we found atherosclerotic plaques lesion in carotids, aorta, and vessels of the lower extremities. Only in 1 (2,4%) patient with PeA we found atherosclerotic plaques. Presence of atherosclerotic plaques associated with RA ( $c^2=8,75$ ,  $p<0,05$ ). In RA detection of atherosclerotic plaques associated with disease durations (12 years (10–15) in group with plaques and 5 years (3–8) in group without plaques). The presence of atherosclerotic plaques is associated with rheumatoid factor ( $c^2=1,02$ ,  $p>0,05$ ), and systemic manifestations of RA ( $c^2=15,89$ ,  $p<0,001$ ).

**Conclusions:** Patients with RA had an increase thickness of IMT and atherosclerotic plaques, which appear in various vascular regions. Long-term duration of ReA is not associated with development atherosclerotic lesion.

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SAT0138

### A DELAY TO DIAGNOSIS, BUT NOT TO TREATMENT INITIATION, IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA) IS ASSOCIATED WITH ETHNIC GROUP AT ONE US ACADEMIC SITE

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**Background:** Disparities in the initiation of disease modifying antirheumatic drugs (DMARDs) therapy in ethnic minorities have been described in rheumatoid arthritis (RA)(1). These disparities are of particular concern in view of the emergence of early diagnosis and aggressive treatment as a cornerstone of management. Delays in diagnosis and treatment have been ascribed in part to lack of awareness, insidious onset, and atypical clinical presentation, but patient-dependent factors may be as important.

**Objectives:** To evaluate disparities in referral and initiation of treatment in RA patients at a USA academic rheumatology site.

**Methods:** We conducted a retrospective study and reviewed the medical records of patients with a primary diagnosis of RA seen at one USA academic setting (2011–2016). Among 642 RA patients, 50 received their initial evaluation by a rheumatologist during the observation period, and were naïve to any DMARD. Data extraction included time between first symptoms and initial visit to our rheumatology facility, demographics, family history, and laboratory tests. In addition, a Multidimensional-Health Assessment Questionnaire (MDHAQ) allowed us to calculate a RAPID3 score as the sum of 0–10 scores for a pain visual analogue scale

(VAS), patient global VAS, and physical function. The time to initiation and type of DMARD prescribed after the first visit was also collected. Statistical analyses were performed using Kruskal-Wallis for differences between medians and chi-squared tests for comparisons between proportions according to ethnicity groups.

**Results:** Fifty new patients with RA were seen in the rheumatology outpatient clinic; 43% were White, 34% Black, and 23% Hispanic. The median delay to be seen by a rheumatologist was 7.2 months for White patients, 12 months for Black, and 11.9 months for Hispanic patients. There were no significant differences in time to initiation of DMARD according to ethnicity. Methotrexate was the DMARD most frequently prescribed, ranging from 86% in White patients to 60% in Hispanic patients. Disease severity according to RAPID3 scores was higher in Black and Hispanic groups, although laboratory tests did not differ between the 3 groups (Table).

**Table 1.** Patient characteristics by ethnicity

	White N=23	Black N=17	Hispanic N=10
Age, mean (SD)	55.5 (13.1)	52.6 (12.3)	49.7 (10.2)
Female, %	74%	88%	80%
Family History of RA, %	15%	9%	20%
Median disease duration (IQR) at the time of first rheumatology evaluation, months	<b>7.2</b> <b>(4.7, 23.9)</b>	<b>12.0</b> <b>(7.7, 22.9)</b>	<b>11.9</b> <b>(5.0, 47.9)*</b>
Time to initiate DMARDs, months, median (IQR)	1.0 (0.5,1.8)	0.8 (0.6,1.6)	0.5 (0,0.7)
Methotrexate	86%	75%	60%
Rheumatoid Factor, %	50%	64%	75%
Anti-CCP, %	69%	64%	80%
ESR, mean (IQR)	15 (10, 25)	23.5 (17, 41)	38 (19, 46)
CRP, mean (IQR)	5 (5, 15)	5 (5, 5.8)	5 (5, 7)
RAPID3, mean (IQR)	<b>12.9</b> <b>(8.2, 16.9)</b>	<b>18.8</b> <b>(14.6, 19.4)</b>	<b>18.5</b> <b>(10.2, 21.5)*</b>

Statistical significance in **bold \*p<0.05**.

**Conclusions:** There is a considerable delay in initial referral to a rheumatologist, which appears to be more pronounced among Black and Hispanic patients. However, once seen in the clinic, initiation of DMARDs occurred within 1-month, regardless of ethnicity. These findings suggest that ethnic minorities are at risk of deleterious outcomes as a consequence of delayed presentation to a rheumatology setting.

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SAT0139

### SUBCLINICAL IMPAIRMENT OF MYOCARDIAL FUNCTIONALITY DURING THE VERY EARLY STAGE OF INFLAMMATORY JOINT DISEASES

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**Background:** cardiovascular (CV) disease morbidity is increased in inflammatory joint diseases (IJD), as rheumatoid (RA) and psoriatic arthritis (PsA). Whereas accelerated subclinical atherosclerosis and endothelial dysfunction have been widely studied, less attention has been paid to myocardial function. RA patients with established disease who develop heart failure often have impaired left ventricular (LV) diastolic functionality with preserved LV ejection fraction (EF) and present fewer signs than non-RA patients. Then, additional and more sensitive screening tools as myocardial strain imaging are needed. In this sense, speckle-tracking echocardiography (STE) has been demonstrated to be suitable for detecting impaired systolic function. Although CV risk is increased at disease onset, whether abnormal myocardial functionality could be found already in the early phase of IJD remains unknown.

**Objectives:** to evaluate the myocardial functionality by STE in recent onset RA and PsA patients and its associations with clinical features.

**Methods:** STE was used to assess the myocardial functionality in patients with very early RA (n=41) (2010 EULAR/ACR criteria) and PsA (n=35) (CASPAR criteria) without traditional CV risk factors, and 58 matched healthy controls (HC). Global longitudinal and circumferential strain (GLS and GCS) were estimated.

**Results:** RA patients exhibited impaired GLS ( $-18.13 \pm 1.36\%$ ) and GCS ( $-20.15 \pm 1.34\%$ ) compared to HC ( $-23.25 \pm 1.80\%$ ,  $p < 0.001$  and  $-24.50 \pm 0.70\%$ ,  $p < 0.001$ ; respectively), GLS being also altered in PsA ( $-21.57 \pm 2.59\%$ ,  $p = 0.020$  vs HC). No differences in LV mass index, posterior wall thickness, LV DD, E/A index or EF were found among groups (all  $p > 0.050$ ). DAS28 was correlated to GLS ( $r = 0.908$ ,  $p < 0.001$ ) and GCS ( $r = 0.868$ ,  $p < 0.001$ ) in RA. These findings were further confirmed by multivariate regression analyses adjusted for age, gender, BMI, CRP, ESR, SBP, DBP and duration of the symptoms, DAS28 being the only independent predictor of GLS ( $p < 0.001$ ) and GCS ( $p = 0.002$ ). Principal Component Analyses retrieved equivalent results. Although GCS was not significantly different in PsA compared to HC, a positive correlation with DAS28 ( $r = 0.438$ ,  $p = 0.008$ ) was observed. Consequently, GLS and GCS were impaired in PsA patients with high disease activity (DAS28 > 2.9) compared to HC (GLS:  $p = 0.066$  and GCS:  $p = 0.007$ ).

**Conclusions:** a subclinical myocardial dysfunction can be observed in IJD patients with preserved LV function and without traditional CV risk factors. The subclinical impairment of the myocardial function was found to be a very early event in IJD. Disease activity was the main predictor of myocardial strain impairment. Strain imaging by STE may detect early myocardial dysfunction in IJD.

**Disclosure of Interest:** None declared

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SAT0140

#### RISK OF VENOUS THROMBOEMBOLISM IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH BIOLOGIC AND NON-BIOLOGIC DMARDS

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**Background:** Individuals with rheumatoid arthritis (RA) have an increased risk of venous thromboembolism (VTE), including pulmonary embolism (PE) and deep vein thrombosis (DVT), compared with non-RA populations based on several recent studies<sup>1,2</sup>. However, information is sparse on the risk of VTE among patients receiving treatment with specific disease-modifying antirheumatic drugs (DMARDs) or categories of therapies.

**Objectives:** To estimate the incidence of VTE among patients receiving routine clinical care for RA, specifically during treatment with conventional (c) and biologic (b) DMARDs.

**Methods:** Incidence rates were estimated in a retrospective cohort study of patients with RA (defined as at least two International Classification of Disease, Ninth Revision, Clinical Modification [ICD-9-CM] Diagnostic codes) enrolled in US health insurance plans between October 1, 2010 to September 30, 2015 and participating in the Innovation in Medical Evidence Development and Surveillance (IMEDS) program. These data are formatted into the U.S. Food and Drug Administration's Sentinel Common Data Model and Sentinel's publicly available standardized analysis tools were used to estimate the incidence rates of VTE following initiation of cDMARDs or bDMARDs. Patients were required to be new users of the study drug class, with no evidence of use in the 365 days preceding initiation and were not allowed to re-enter the cohort. Patients were required to demonstrate continuous use of the study drug class to be considered at risk for VTE. VTE was defined based on ICD-9-CM codes, but patients diagnosed in outpatient settings were also required to have evidence of oral anticoagulant dispensing within 31 days of the event. PE and DVT ICD-9-CM codes were also disaggregated to produce separate incidence rates.

**Results:** During treatment with cDMARDs (i.e., methotrexate or leflunomide) or bDMARDs (i.e., abatacept, adalimumab, certolizumab pegol, etanercept, golimumab, infliximab, rituximab, and tocilizumab), patients experienced VTE at a crude incidence rate of 1.49 (95% CI 1.30, 1.71) per 100 person-years (PY) and 0.98 (95% CI 0.83, 1.14) per 100 PY, respectively. For each study drug class, age was an important risk factor for VTE, with increasing age associated with higher rates of VTE; for example, during treatment with bDMARDs incidence rate (IR)<sub>18-49 years</sub>=0.69, IR<sub>50-59 years</sub>=0.65, IR<sub>60-64 years</sub>=0.94, and IR<sub>65+ years</sub>=2.11 per 100 PY (figure 1). Men also had higher incidence rates of VTE than women. In the analyses of PE and DVT, DVT incidence rates were higher than PE incidence rates, and similar incidence rate trends overall and across age strata for cDMARD and bDMARD cohorts were noted.

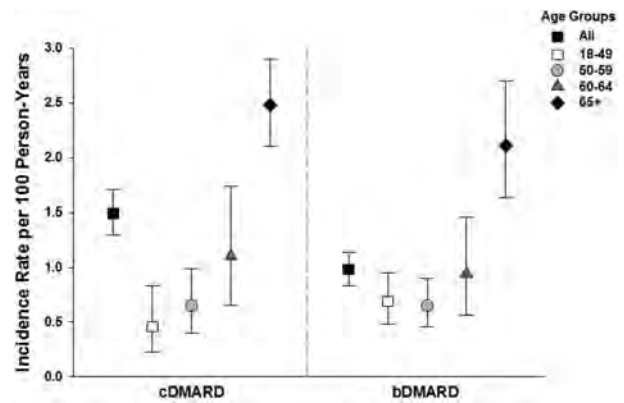


Figure 1 Incidence of VTE among patients with RA treated with cDMARDs and bDMARDs, overall and by age. (Data displayed as incidence rates with 95% confidence intervals.)

**Conclusions:** Venous thromboembolism is an important clinical concern among patients with RA and incidence rates vary by age and sex during routine clinical treatment with DMARDs.

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SAT0141

#### TRENDS IN THE INCIDENCE OF LYMPHOMAS AND LEUKEMIAS IN PATIENTS WITH RHEUMATOID ARTHRITIS IN SPAIN: AN OBSERVATIONAL COHORT STUDY OF HOSPITAL DISCHARGES FROM 1999 TO 2015 (TRENDR-AR STUDY)

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**Background:** Oncohematological diseases have an increased incidence in Rheumatoid Arthritis (RA) patients. However, their trend in RA in Spain is unknown

**Objectives:** To analyze the incidence and trend of hospital admissions for lymphomas and leukemias in RA patients in Spain from 1999–2015

**Methods:** We performed an observational retrospective population study analyzing the Spanish administrative database that includes a Minimum Basic Data Set (MBDS) of hospital admissions of RA patients from 1999–2015. We selected MBDSs for lymphomas and leukemias. Cases were identified by the presence in primary/secondary diagnosis of ICD9 codes. The population at risk was estimated with a prevalence of RA of 0.5% (0.8% women and 0.2% men). Crude and adjusted rates were calculated, and the trend was analyzed using the Generalized Linear Model with the year as the analysis variable. SPSS version 20 (Chicago, IL) was used

**Results:** 338.343 RA hospital admissions were detected, being 3561 (1.1%) lymphomas (61.5% women, 38.5% men) and 1664 (0.5%) leukemias (52.3% women,



47.7% men). Mean age 68.94(SD 11.38) in lymphomas and 71.46(SD 11.24) in leukemias. Age-adjusted rate during the period for lymphoma was 152,19/10<sup>5</sup> inhab/year (92,05 women and 240,14 men). Lymphoma age-adjusted rate increased from 52,46/10<sup>5</sup> inha/year in 1999 to 187,57 in 2015, both women (from 42,74 to 142,95) and men (from 280,77 to 326,63). An annual increase in lymphoma rate of 6,9% is estimated (RRI 1,069; CI 95% 1,054–1,085). Age-adjusted rate during the period for leukemia was 90,87/10<sup>5</sup> inhab/year (37,09 women and 144,65 men). Leukemia age-adjusted rate increased from 18,86/10<sup>5</sup> inhab/year in 1999 to 94,05 in 2015, both women (13,80 in 1999 to 65,93 in 2015) and men (38,70 in 1999 to 204,84 in 2015). An annual increase in leukemia rate of 8,2% is estimated (RRI 1,083; CI 95% 1,069–1,097).

**Conclusions:** In Spain from 1999–2015 lymphoma and leukemia hospital admissions in RA patients increased, with an estimation of 6,9% and 8,2% annual increase respectively.

**Disclosure of Interest:** None declared

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### SAT0142 PULMONARY HYPERTENSION AMONG HISPANIC PATIENTS WITH RHEUMATOID ARTHRITIS: A CASE-CONTROL STUDY

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**Background:** Rheumatoid arthritis (RA) is a chronic, systemic, inflammatory, multifactorial disease that mainly affects synovial joints. Pulmonary artery hypertension (PAH) can appear as a complication of connective tissue diseases. It is possible that pulmonary artery systolic pressure (PASP) in RA may be elevated due to interstitial lung disease, pulmonary vasculitis, pulmonary veno-occlusive disease, or cardiac disease (1). Although right heart catheterization is the gold standard, Doppler echocardiography has proved to be a reliable non-invasive method for detecting PAH (2).

**Objectives:** To determine the prevalence of PAH in RA patients and compare it to matched controls.

**Methods:** A case-control study with RA patients aged 40 to 75 years that fulfilled the 2010 ACR/EULAR criteria and matching controls were included. Exclusion criteria: poor acoustic window, absence of tricuspid regurgitation (TR), prior atherosclerotic cardiovascular (CV) disease and overlap syndromes. Patients were matched using age, sex and comorbidities. Transthoracic echocardiogram was performed by a board-certified cardiologist. PASP was calculated using the Bernoulli equation: TR velocity<sup>2</sup> × 4 + right atrial pressure according to ASE's guidelines. We used Denton's definition of PAH on Doppler echocardiography as an estimated PASP ≥ 30 mmHg (3).

**Results:** A total of 76 RA patients and 52 matched controls were included. Demographic and clinical characteristics of both groups are shown on table 1. As shown on table 2, the mean PASP was higher RA patients (27.14±6.34 mmHg) than controls (24.68±5.44 mmHg) (*P*=0.024). PASP ≥ 30 mmHg prevalence was significantly higher in RA patients (34.2% vs 11.5%; *P*=0.004).

**Table 1** Demographic characteristics

	RA (n = 76)	Control (n = 52)	<i>P</i>
Women, n (%)	74 (97.4)	46 (88.5)	0.041
Age, mean±SD	55.71 ±8.84	53.86 ±6.14	0.195
BMI, mean±SD	29.11 ±5.42	28.31 ±4.37	0.343
Hypertension, n (%)	26 (34.2)	12 (23.1)	0.176
Type 2 Diabetes mellitus, n (%)	8 (10.5)	7 (13.5)	0.612
Active smoking, n (%)	6 (7.9)	6 (11.5)	0.487

**Table 2** Echocardiographic findings

	RA (n = 76)	Control (n = 52)	<i>P</i>
TR Vmax (m/s), mean±SD	2.27±0.32	2.18±0.33	0.157
PASP (mmHg), mean±SD	27.14 ±6.34	24.68 ±5.44	<b>0.024</b>
PASP ≥ 30 mmHg, n (%)	26 (34.2%)	6 (11.5%)	<b>0.004</b>

TR Vmax – Tricuspid regurgitation maximum velocity. **Conclusions:** Elevated PASP, suggesting PAH, was more prevalent on RA patients than controls. A higher number of CV events that cannot be explained by traditional risk factors have been reported in RA patients; and it is possible that the elevation in the PASP could contribute to the problem. Prospective studies are needed to evaluate the role of elevated PASP in morbidity and mortality of RA patients.

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**Disclosure of Interest:** None declared

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### SAT0143 THE ARREST OF BONE MINERAL DENSITY LOSS AT THE LUMBAR SPINE AND HIP IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS DURING RITUXIMAB THERAPY

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**Background:** One of the well-known characteristics of rheumatoid arthritis (RA) is generalized bone loss.<sup>1–2</sup> Although rituximab is a frequently prescribed biologic disease-modifying anti-rheumatic drug (bDMARD) for the treatment of RA, data regarding changes in bone mineral density (BMD) in RA patients during rituximab therapy are limited.

**Objectives:** To study the extent of BMD loss at lumbar spine and hip in patients with active rheumatoid arthritis treated with rituximab.

**Methods:** Consecutive RA patients with an active disease status (DAS28 > 3.2) starting rituximab treatment were enrolled in a prospective cohort study. BMD of the lumbar spine and hip was measured before treatment and after one year using dual energy X-ray absorptiometry (DXA) to assess BMD changes. Clinical response was defined using the European League Against Rheumatism (EULAR) response criteria.

**Results:** A total of 43 subjects (18.6% men) with mean age of 53.6 (SD 10.7) years were included in the study. Median disease duration was 9.5 (IQR 0.7–40.2) years and baseline mean DAS28 was 5.6 (SD 1.3). In responders, the DAS28 decreased with 1.97 points (SD 0.78) 95% CI 1.67 – 2.28 *p* < 0.001; and in non-responders, the DAS28 decreased with 0.01 points (SD 0.67) 95% CI -0.35 – 0.37 *p* = 0.945. All changes in BMD were not statistically significant (table 1).

**Table 1** BMD change after one year categorized by EULAR response

	Mean (SD) baseline BMD	Mean (SD) follow-up BMD	Mean change	% change
LS total (n=43)	1.015 (0.182)	1.011 (0.186)	-0.004	-0.4
LS responders (n=27)	1.026 (0.169)	1.017 (0.182)	-0.009	-1.0
LS non-responders (n=16)	0.997 (0.206)	1.001 (0.198)	0.004	+0.7
Hip total (n=43)	0.845 (0.144)	0.849 (0.143)	0.003	+0.5
Hip Responders (n=27)	0.836 (0.126)	0.838 (0.129)	0.003	+0.3
Hip Non-responders (n=16)	0.862 (0.174)	0.867 (0.166)	0.005	+0.8

BMD is presented in g/cm<sup>2</sup>; BMD; bone mineral density; LS, lumbar spine.

**Conclusions:** The findings of this study indicate that patients with active RA treated with rituximab have arrest of bone loss at both the lumbar spine and hip. Moreover, these results suggest that rituximab has bone-saving abilities even in the absence of clinical response.

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**Disclosure of Interest:** None declared

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SAT0144

**EFFECT OF AGING ON BONE MASS AND SKELETAL MUSCLE MASS IN ELDERLY PATIENTS WITH RHEUMATOID ARTHRITIS: TOMORROW STUDY**

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**Background:** Both osteoporosis and sarcopenia are common in patients with chronic inflammatory conditions such as rheumatoid arthritis (RA). Fragility fractures occur on osteoporotic bone on falling. Unstable gait caused by sarcopenia increases the frequency of such falls.

**Objectives:** To evaluate the relationship between bone mineral density (BMD) and appendicular skeletal muscle index (ASMI) in patients with RA and healthy controls.

**Methods:** We used data collected over a 7-year period from 2010 to 2016 as part of a prospective cohort study (TOMORROW Study: UMIN00003876) that included RA patients and age- and sex-matched volunteers recruited through mass media as controls. BMD of the lower leg and ASMI were determined using whole-body dual-energy X-ray absorptiometry. These were collected for all participants together with baseline characteristics including anthropometric data and blood test data related to lipid and sugar metabolism. Each parameter for the RA patients was compared with that for the healthy controls. Multiple regression analysis was carried out in the RA population only. In RA patients, treatment regimen and disease activity score 28 were recorded.

**Results:** Among 413 participants of the TOMORROW Study (208 RA patients; 349 women; mean age 58 years), 137 participants age 65 years or older (77 RA; 117 women) were enrolled in the present study. BMD and ASMI decreased significantly over the 7-year study period in RA patients and healthy controls from baseline. BMD and ASMI were lower in RA patients than in healthy controls at every time point through the 7-year study period. There was no interaction between time and RA ( $p=0.194, 0.089$ ; repeated measure ANOVA). The change of BMD at year 7 from baseline ( $\Delta$ BMD) and change of ASMI at year 7 from baseline ( $\Delta$ ASMI) did not correlate in health controls, however, in RA patients,  $\Delta$ BMD correlated positively with  $\Delta$ ASMI ( $r=0.331, p=0.023$ ) (Fig). Multiple regression analysis with  $\Delta$ BMD as the outcome variable and anti-citrullinated peptide antibody, Rheumatoid factor, ASMI, body mass index, disease activity score 28, homeostatic model assessment (HOMA)-R, Matrix metalloproteinase (MMP)-3 and sex as independent variables revealed that male sex ( $p=0.0036$ ) and ASMI ( $p=0.0020$ ) were independently related with  $\Delta$ BMD.

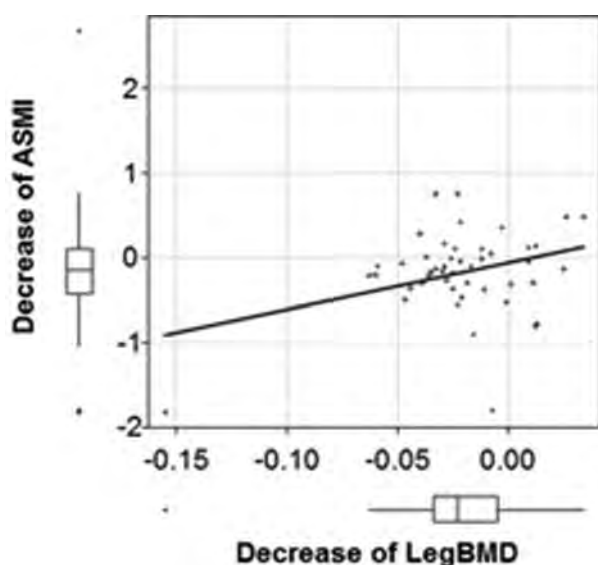


Figure 1 Correlation between change of ASMI and BMD for 7 years in elderly patients with RA. (pearson correlation coefficient;  $r=0.331, P=0.0229$ )

**Conclusions:** Decrease of BMD and ASMI were correlated with each other in elderly patients with RA.

**Disclosure of Interest:** None declared

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SAT0145

**FEATURES OF PATIENTS WITH RHEUMATOID ARTHRITIS WHOSE DEBUT JOINT IS A FOOT OR ANKLE JOINT: A 5,479 CASES STUDY FROM THE IORRA COHORT**

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**Background:** Foot and ankle joint disorders are serious issues for patients with rheumatoid arthritis (RA). Rheumatoid foot is reported as the first symptom of the disease in 20–53% of RA patients<sup>1–3</sup>. However, there are few studies investigating the features of patients with RA whose debut joint is a foot or ankle joint.

**Objectives:** The aim of this study is to compare the differences between RA patients whose first symptom was a foot or ankle joint (FOOT group) and was other joints (OTHER group) by using the Institute of Rheumatology, Rheumatoid Arthritis (IORRA) cohort in our institute.

**Methods:** In the IORRA survey conducted in April 2016, patients were asked about first symptom at RA onset. Disease activities, clinical laboratory variables, functional disability, quality of life, and the use and ratio of anti-inflammation and anti-rheumatic drugs were compared between the FOOT group and OTHER group.

**Results:** Among 5,637 Japanese patients with RA who participated in the IORRA survey on April 2016, 5,479 patients (97.2%) responded to the questionnaire regarding debut joint. Of these 5,479 patients, 2,402 (43.8%) reported their first symptom of RA were a foot or ankle. Comparing the two groups, the FOOT group had higher disease activity, higher disabilities, lower quality of life, low activities of daily living, and poorer mental health and used higher dose and rate of anti-inflammatory drugs significantly than the OTHER group (all  $P<0.01$ ). On the other hand, medications to suppress the disease activity of RA have no statistical differences between the two groups (table 1).

Table 1 Comparison of clinical features and outcomes between the FOOT group and the OTHER group

	FOOT group (n=2,164)	OTHER group (n=2,164)	P
DAS28	2.82±1.1 (0.0–7.0)	2.51±0.95 (0.0–6.1)	<0.01
CRP, mg/dl	0.44±0.92 (0.0–9.7)	0.32±0.80 (0.0–18.3)	<0.01
RF, IU/ml	118.5±260.7 (3–7150)	97.2±217.1 (3–5544)	<0.01
J-HAQ	0.69±0.76 (0–3)	0.47±0.66 (0–3)	<0.01
EQ5D	0.78±0.18 (-0.1–1.0)	0.85±0.2 (0.1–1.0)	<0.01
NSAID use, no. (%)	1,162 (53.7)	972 (44.9)	<0.01
PSL use, no. (%)	659 (30.5)	569 (26.3)	<0.01
PSL dose, mg/day	1.17±2.3 (0–18)	0.9±2.0 (0–15)	<0.01
DMARD use, no. (%)	1,926 (89.0)	1,921 (88.8)	0.85
MTX use, no. (%)	1,671 (77.2)	1,656 (76.5)	0.61
MTX dose, mg/week	6.18±4.8 (0–17.5)	5.88±4.7 (0–20)	0.059
Biologic DMARD use, no. (%)	495 (22.9)	458 (21.2)	0.19

**Conclusions:** Patients whose debut joint was a foot or ankle had higher disease activity, higher dysfunction, lower quality of life, and used higher dose and rate of anti-inflammatory drugs than patients whose debut joint was the other joints on RA onset. Clinicians should have more attentions to foot and ankle joints in daily practice so as not to underestimate the disease activity of RA.

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**Disclosure of Interest:** K. Yano Speakers bureau: Bristol-Meyers, Pfizer, Eisai, Tanabe-Mitsubishi, Chugai, AbbVie, Janssen Pharmaceutical, Asahi-Kasei and Takeda., K. Ikari Grant/research support from: Astellas, UCB, Bristol-Meyers, Pfizer, Eisai, Tanabe-Mitsubishi, Chugai, AbbVie, Janssen Pharmaceutical, Otsuka, Kaken, Asahi-Kasei, Hisamitsu and Takeda., Speakers bureau: Astellas, UCB, Bristol-Meyers, Pfizer, Eisai, Tanabe-Mitsubishi, Chugai, AbbVie, Janssen Pharmaceutical, Otsuka, Kaken, Asahi-Kasei, Hisamitsu and Takeda., K. Okazaki: None declared, A. Taniguchi Grant/research support from: AbbVie, Eisai, Takeda, Speakers bureau: AbbVie, Eisai, Takeda, Tanabe-Mitsubishi, Teijin Pharma and Pfizer., H. Yamanaka Grant/research support from: MSD, Ayumi, AbbVie, Eisai, Ono, Astellas, Daiichi-Sankyo, Taisyo-Toyama, Takeda, Tanabe-

Mitsubishi, Chugai, Teijin Pharma, Torii, Nippon Shinyaku, Pfizer. UCB. Nippon Kayaku, YL biologics, Bayer and Bristol-Meyers., Consultant for: MSD, Ayumi, AbbVie, Eisai, Ono, Astellas, Daiichi-Sankyo, Taisyo-Toyama, Takeda, Tanabe-Mitsubishi, Chugai, Teijin Pharma, Torii, Nippon Shinyaku, Pfizer. UCB. Nippon Kayaku, YL biologics, Bayer and Bristol-Meyers., Speakers bureau: MSD, Ayumi, AbbVie, Eisai, Ono, Astellas, Daiichi-Sankyo, Taisyo-Toyama, Takeda, Tanabe-Mitsubishi, Chugai, Teijin Pharma, Torii, Nippon Shinyaku, Pfizer. UCB. Nippon Kayaku, YL biologics, Bayer and Bristol-Meyers.

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**SAT0146 AT DIAGNOSIS OF RHEUMATOID ARTHRITIS, AT-RISK PATIENTS FOLLOWED IN CCP+ CLINIC SHOWED Milder DISEASE ACTIVITY THAN CONVENTIONALLY REFERRED PATIENTS.**

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**Background:** Early treatment of rheumatoid arthritis (RA) improves clinical and radiological outcomes<sup>1</sup>. Risk stratification models can identify patients at high risk of developing RA,<sup>2-5</sup> which may lead to an extension of the window of opportunity. Whether identifying and following at-risk individuals improves outcomes after the development of RA however is yet to be determined.

**Objectives:** The hypothesis is that patients followed in a specific at-risk clinic will have less severe disease at diagnosis than those referred via the conventional route if/when they develop RA.

**Methods:** In two single-centre prospective observational cohorts, patients fulfilling the 2010 EULAR classification criteria for RA were compared on a demographic and clinical approach. The first group was composed of 59 patients positive for anti-cyclic citrullinated protein antibodies (CCP) with non-specific musculoskeletal symptoms, considered to be "at-risk of RA", who were followed until RA diagnosis. The second group was composed of 92 CCP positive RA patients referred to a standard 'Early Arthritis' rheumatology clinic.

**Results:** Demographic data at RA development were consistent between both groups including smoking history and BMI. Immunological features were also similar. CCP titre: at risk median 193U/ml (IQR 41,300), standard care 300U/ml (IQR 81,300, p=0.176). Rheumatoid factor (RF) titre: at risk median 84iU/mL (IQR 15,223), standard care 87iU/mL (IQR18,161, p=0.850). RF positivity: at risk 75%, standard care 70% (p=0.544). High-titre CCP blood levels: at risk 95%, standard care 97% (p=0.566).

As shown in table 1, DAS28CRP score were significantly lower in the at risk group than in standard care, this was due to a difference in the general health Visual Analogue Scale score and the CRP levels. Patients in the at risk group also had fewer swollen large joints and reported significantly shorter time between onset of subjective joint swelling and diagnosis. There was no difference between the presence of erosions on ultrasound scans (at risk: 39%, standard care 38%, p=0.921).

	At Risk of RA*	Standard care*	P-value
Age mean (SD)	55.3 y (12.6)	56.4 y (19.1)	0.711
Women	73%	71%	0.815
BMI mean (SD)	28 (5.4)	27 (6.5)	0.299
Ever smoker	70%	55%	0.075
DAS28CRP	3.9 (3.2,4.6)	4.9 (3.4,5.6)	0.003
TJC28	5 (3,9)	7 (2,14)	0.447
SJC28	2 (1,5)	4 (2,9)	0.001
GH VAS	41 (18,64)	57 (37,75)	0.003
CRP	5.4 (0,11)	26 (18,49)	0.000
HAQ	10 (2,17)	12 (5,20)	0.197
Large joint swelling mean (SD)	0.14 (0.4)	0.39 (0.7)	0.014
Weeks before subjective swelling to RA diagnosis	6 (2,12)	29 (16,52)	0.00

\*Median (IQR) unless specified

**Conclusions:** Patients who were diagnosed with RA while being followed in an at-risk cohort had milder disease activity and less pain than those diagnosed through standard referral despite equivalent demographics and serology. This reflects an earlier diagnosis and hence shorter exposure to inflammation. Follow-up will be required to see if these differences convert to long-term benefits.

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**Disclosure of Interest:** None declared

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**SAT0147 PRESENCE OF HEPATITIS B VIRUS IN SYNOVIUM AND ITS CLINICAL SIGNIFICANCE IN RHEUMATOID ARTHRITIS**

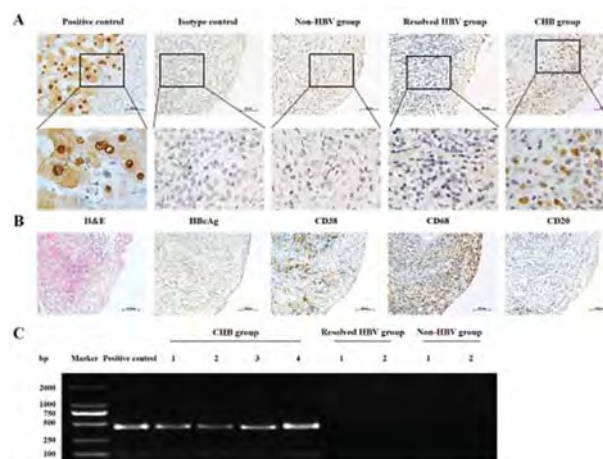
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**Background:** Previous studies have shown that hepatitis B virus (HBV) infection may be associated with rheumatoid arthritis (RA). However, no study regarding the presence of HBV in the synovial membrane from RA patients has been reported.

**Objectives:** To investigate the presence of HBV in RA synovium and determine its influence on histopathological characteristics of synovitis as well as clinical and radiographic outcomes in RA.

**Methods:** 57 consecutive patients with active RA (DAS28-CRP $\geq$ 2.6) and qualified synovium (at least 6 pieces of synovial tissues per patient, containing lining layer and sublining area) obtained by closed Parker-Pearson needle biopsy who had completed one year follow-up were retrospectively recruited from a prospective RA cohort (n=239). The patients were divided into chronic HBV infection (CHB, positive HBsAg and/or HBV DNA in serum persisting for over 6 months; n=11), resolved HBV (negative HBsAg and HBV DNA in serum, but positive anti-HBc; n=22), and non-HBV (negative HBsAg, HBeAg, anti-HBe, anti-HBc, and HBV DNA in serum, regardless of anti-HBs; n=24) groups according to baseline HBV infection status. Clinical data were collected at baseline and follow-up visits at months 1, 3, 6, and 12. Radiographic assessments of hand/wrist at baseline and month 12 were performed with the Sharp/van der Heijde-modified sharp score (mTSS). Serial tissue sections were stained immunohistochemically for HBsAg, HBeAg, CD3, CD15, CD20, CD34, CD38, and CD68. Nested PCR was used to detect HBV S gene DNA in synovium.

**Results:** Immunohistochemical staining and nested PCR revealed the presence of HBcAg and S gene DNA in the synovium from RA patients with CHB (figure 1). Compared with the non-CHB group (n=46), significantly more CD15-positive neutrophils, CD20-positive B cells, and CD68-positive macrophages infiltrated the CHB synovium (all p<0.05), together with smaller improvements from baseline in most disease activity indicators mainly at month 12. A significantly higher percentage of CHB patients experienced one-year radiographic progression ( $\Delta$ mTSS $\geq$ 0.5units/year, 64% vs. 26%, p=0.024). Multivariate logistic regression analysis showed that CHB status (OR: 14.230, 95%CI: 2.213–95.388; p=0.006) and the total count of CD68-positive macrophages (OR: 1.002, 95%CI: 1.001–1.003; p=0.003) were independently associated with one-year radiographic progression.



**Figure 1 Identification of HBV in RA synovium. (A) Representative immunohistochemical staining for HBcAg in RA synovium.** Representative images illustrated detection of HBcAg in a RA patient with CHB, but not in RA patients with resolved HBV or no infection. **(B) Representative staining of HBcAg in one RA patient with CHB compared to stains for CD38 and CD68.** Serial sections of synovium from one RA patient with CHB were stained with H&E and immunohistochemically. HBcAg immunoreactivity was



observed in the sublining inflammatory cells including plasma cells (CD38+) and macrophages (CD68+), mainly located in the cytoplasm. (C) **Detection of HBV S gene in RA synovium by nested PCR. Nested PCR showed HBV S gene only in all four CHB synovial tissues.** Liver tissue from a patient with HBV-related hepatocellular carcinoma was used as positive control.

**Conclusions:** Our results reveal definite presence of HBV in the synovium which may be involved in the pathogenesis of local lesion and exacerbate disease progression in RA patients with CHB.

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#### SAT0148 ORAL CARE AND HEALTH IN RHEUMATOID ARTHRITIS PATIENTS BASED ON A SELF-ASSESSMENT QUESTIONNAIRE INVESTIGATION

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**Background:** Some investigations indicate a higher prevalence of periodontal disease (PD) in rheumatoid arthritis (RA) patients compared to healthy individuals without RA. Significant improvements in clinical parameters and laboratory tests were demonstrated in RA patients following periodontal therapy. Periodontal diseases – gingivitis and periodontitis are inflammatory, multifactorial pathologies of periodontal tissues, which support the teeth. The factor responsible for the inflammation is a plaque with specific bacteria.

In gingivitis, which is the first stage of PD, only gingiva is involved. Then in susceptible patients, periodontitis is developing and the deeper laying structures surrounding the teeth are involved and destroyed. The patients' own observation of gingival bleeding strongly indicates gingival disease.

The effectiveness of oral hygiene, including self-care, in controlling periodontal health is crucial and supported by several studies. RA patients frequently experience reduced function of fingers and wrists that makes oral hygiene troublesome.

**Objectives:** The purpose of this study was to assess RA patient's oral care and health based on a self-assessment questionnaire.

**Methods:** Questionnaires were mailed to 300 patients treated for RA in a Danish rheumatology outpatient clinic.

**Results:** A total of 164 patients completed the questionnaires. The mean age of patients was 65 years, and the average value of DAS28 was 2.31. Twelve percent were active smokers. The "dry mouth" syndrome, as a problem when chewing or swallowing, pointed out 4% of patients. Difficulties in biting or chewing revealed 10% of patients. As much as 87% stated they regularly visit a dentist, min. one time a year.

Regarding self-oral care 15% of patients answered, they brush teeth only once a day. Most of the patients (51%) used manual toothbrush vs electrical – which can be more convenient for patients with problems of the hands/wrists. Only 21% used mouth-rinsing liquid. Difficulties in performing home oral hygiene procedures were reported by 9% when brushing teeth, and by 17% using dental floss or interdental brushes. 11% of responders rated the status of their gingiva as poor. Gingival bleeding spontaneous or related to brushing was experienced by respectively 15% and 49% of patients. No patients stated knowledge of an association between oral health and RA.

**Conclusions:** The oral care in RA patients, including self-care, seems to require improvement. Providing important information to the patients about the relationship between the oral/periodontal health and RA disease activity should raise the patient's awareness, which may improve the course of the RA disease.

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**Disclosure of Interest:** None declared

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#### SAT0149 IS ESTABLISHED SERONEGATIVE RHEUMATOID ARTHRITIS EVEN A MILD FORM OF THE DISEASE?

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**Background:** Established Seronegative Rheumatoid Arthritis (SNRA) was considered a mild form of the disease with a good response to therapy on the past<sup>1</sup>. Lately evidence indicates this form of arthritis in early stage is serious and should not be underestimated in terms of disease activity and radiographic damage<sup>2</sup>. By other hand early SNRA presents shorter symptoms duration and different response to therapy compare to seropositive (SP) patients<sup>3,4</sup>. At present, the influence of seronegative (SN) status of clinical course and treatment choice is still controversial. Data of this issue are scarce and often insufficiently powered.

**Objectives:** To determine demographical, clinical and treatment differences between established SN and SP Rheumatoid Arthritis (RA) in a Mexican cohort.

**Methods:** 511 patients with established RA (>2 years from time at onset of diagnosis) that fulfilled ACR/EULAR 2010 criteria ( $\geq 18$  years) from a Mexican cohort from 2012 to 2017 were examined. Patients without presence of rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA) were considered SN. Demographic factors, clinical features, disease activity measured using DAS28, functional status, comorbidities and pharmacologic treatments were examined for patients with established SN and SP RA. Charlson's clinical co-morbidity index was used to analyze comorbidities. Chi-square and Student-t test was performed by univariate analysis and logistic regression was used by multivariate analysis, both were adjusted for age and gender. Standard deviation and mean of modified Charlson's index was obtained by ANOVA analysis. Statistical test were conducted at 5% level of significance.

**Results:** Of 511 patients with established RA 89% were women. The mean age [standard deviation (SD)] was 55.6 (11.8) years. The mean of time at onset of RA (SD) was 12.1 (8.7) years. A total of 77 (15.1%) patients had established SNRA. In the univariable analyses established SNRA patients were more likely to have shorter time at onset of RA, minor disease activity and radiographic progression, lesser extra-articular and sicca manifestations, reduced demand of hip and knee arthroplasty, also present lower comorbidities including osteoporosis and fibromyalgia, besides to use fewer methotrexate and corticosteroids. As expected, the modified Charlson's comorbidity index score was lower in established SNRA patients. No differences were found for use of biologic agents in both groups. In multivariable analyses, minor disease activity (OR 0.33, 95% CI 0.17–0.60,  $p \leq 0.001$ ), less frequently use of methotrexate (OR 0.38, 95% CI 0.17–0.82,  $p = 0.014$ ) and minor radiographic progression (OR 0.13, 95% CI 0.40–0.39,  $p \leq 0.001$ ), remained significant in established SNRA patients.

**Conclusions:** This study suggests that established SNRA present less disease activity and radiographic damage as well as fewer use of MTX than established SPRA. However differences in activity disease and response to treatment can be found in early stages of RA not included in this study. Therefore early SNRA cannot be considered to be a generally mild form of the disease like as established SNRA. These observations must be confirmed in larger studies including early stages of RA.

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**Disclosure of Interest:** None declared

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#### SAT0150 INADEQUATE CARDIOVASCULAR RISK MANAGEMENT IS NOT RHEUMATOID ARTHRITIS SPECIFIC AMONG PATIENTS WITH PREVALENT RHEUMATIC AND MUSCULOSKELETAL DISEASES

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**Background:** Preventive pharmacotherapy for atherosclerotic cardiovascular disease (ACVD) is reportedly underused in patients with rheumatoid arthritis (RA). Whether this shortcoming is RA specific amongst patients with prevalent rheumatic and musculoskeletal diseases (RMD) is currently unknown.

**Objectives:** This study aimed to compare high ACVD risk profiles and statin use by indication between RA and non-RA patients with RMD.

**Methods:** We investigated 470 consecutive RMD patients of which 80 had RA, 92 undifferentiated inflammatory/early arthritis (UIA), 127 fibromyalgia and 171

osteoarthritis. High risk profiles comprised established ACVD (coronary artery disease, ischemic cerebrovascular disease or/and peripheral artery disease), diabetes (type 2 or type 1 aged >40 years), high LDL cholesterol concentration ( $\geq 190$  mg/dl), chronic kidney disease (CKD) (Chronic Kidney Disease Epidemiology Collaboration equation value  $< 60$  ml/min/1.73 m<sup>2</sup>), and a Systemic Coronary Risk Evaluation (SCORE) of  $\geq 5\%$  and Framingham score of  $\geq 20\%$  both before and after application of the recently reported European League Against Rheumatism (EULAR) multiplier (SCORE and Framingham score  $\times 1.5$  in the presence of RA) (1). The prevalence of high ACVD risk profiles and statin use by indication were compared between RA and non-RA patients in age, sex and race adjusted logistic regression models.

**Results:** RA patients were older (mean (SD) age=62.1 (15.8) versus 54.0 (15.4) years,  $p < 0.0001$ ) and less frequently women (66.3% versus 79.7%,  $p = 0.009$ ) than their non-RA counterparts; RA and fibromyalgia were the most frequent diseases in white and North-African patients, respectively. The prevalence of ACVD, diabetes, high LDL cholesterol, CKD, high SCORE and Framingham score did not differ between RA and non-RA patients. Only upon applying the EULAR multiplier (1) was RA associated with a high SCORE (OR (95% CI)=2.18 (1.01–4.72)) and Framingham score (OR (95% CI)=3.46 (1.63–7.36)). The prevalence of any high risk ACVD profile before (OR (95% CI)=1.02 (0.53–1.98)) and after application of the EULAR multiplier (OR (95% CI)=1.85 (0.93–3.69)) were similar in RA and non-RA patients. Statin use by indication was consistently similar in RA compared to non-RA patients. Overall, 38.3% of RA patients and 40.0% of non-RA patients that had any high risk ACVD profile used a statin (OR (95% CI)=0.79 (0.38–1.66)).

**Conclusions:** In this single center study, having one or more high ACVD risk profiles was equally prevalent in non-RA and RA patients. Circa 60% of patients with RMD and any high risk ACVD profile did not use statins and this finding did not differ in non-RA compared to RA patients. There is a vast and urgent need for improved ACVD risk management among patients with RMD irrespective of RA status.

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**Disclosure of Interest:** None declared

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### SAT0151 CARDIORESPIRATORY FITNESS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Mortality rates are higher in RA patients compared to the general population, mostly due to cardiovascular disease (CVD). Cardiorespiratory fitness (CRF) is inversely associated with CVD, but little is known about CRF levels in RA patients.

**Objectives:** To study the association between CRF in RA patients (measured as VO<sub>2</sub>peak), and CVD risk factors and RA-specific clinical variables.

**Methods:** 93 patients were recruited from a hospital rheumatology outpatient clinic. VO<sub>2</sub>peak was measured by ergospirometry during a treadmill test. Tender and swollen joint count, height, weight, waist circumference, resting heart rate, blood pressure and hsCRP were measured. RA characteristics and information on comorbidity were recorded from an interview and from medical records. Based on a previously published index weighting frequency, intensity and duration of self-reported physical activity (PA) (1), patients were categorized into four different PA categories (table 1). VO<sub>2</sub>peak was analyzed using multivariate linear regression, adjusting for age and gender. All participants signed an informed consent and the regional ethics committee approved the study.

**Results:** Table 1 Patient characteristics (n=93)

Gender, female, n(%)	68 (73)	Seropositivity (anti-CCP and/or RF pos.), n(%)	75 (81)
Age (yrs), median (IQR)	60 (52–66)	Disease duration (yrs), median (IQR)	10 (5–19)
BMI (kg/m <sup>2</sup> ), mean (SD)	26.7 (3.9)	VAS Global (0–100), median (IQR)	24 (10–37)
Smoking, present or previous, n(%)	58 (62)	DAS28CRP (%Remission/LowDA/IntermedDA/HighDA)	42/25/30/3
PA categories:		mHAQ, median (IQR)	0.13 (0–0.44)
Inactive, n(%)	25 (27)	Medications:	
Mod. active, n(%)	11 (12)	Biologics, n(%)	54 (58)
Active, n(%)	39 (42)	DMARDs, n(%)	74 (80)
Very active, n(%)	18 (19)	Corticosteroids, present or last year n(%)	39 (42)

In the multivariate regression model ( $R^2=0.79$ ), VO<sub>2</sub>peak was positively associated with the PA categories “Active” ( $p=0.018$ ) and “Very active” ( $p=0.008$ ), and negatively associated with BMI ( $p < 0.001$ ) and resting heart rate ( $p=0.017$ ). VO<sub>2</sub>peak was not associated with disease duration ( $p=0.47$ ), mHAQ ( $p=0.71$ ), DAS28 ( $p=0.43$ ), VAS Global ( $p=0.24$ ), hsCRP ( $p=0.14$ ), seropositivity ( $p=0.44$ ), use of biologics ( $p=0.91$ ), other DMARDs ( $p=0.66$ ) or corticosteroids ( $p=0.60$ ). There was a trend towards a negative association with smoking ( $p=0.096$ ).

**Conclusions:** We observed a strong association between common CVD risk factors (inactivity, high BMI, high resting heart rate) and lower CRF in RA patients, similar to published findings from the general population. Patients in the “Active” and “Very active” PA categories showed significantly higher VO<sub>2</sub>peak, whereas RA-specific variables such as seropositivity, disease activity, disease duration and medications had no impact on VO<sub>2</sub>peak. We cannot exclude a selection bias because more fit patients could be more likely to participate in the study.

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**Acknowledgements:** The VO<sub>2</sub>peak testing was performed at the core facility NeXt Move, NTNU – Norwegian University of Science and Technology.

**Disclosure of Interest:** None declared

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### SAT0152 SYSTEMIC AND RENAL AA AMYLOIDOSIS IN RHEUMATOID ARTHRITIS – A COMPARATIVE POSTMORTEM CLINICOPATHOLOGIC STUDY OF 161 PATIENTS

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**Objectives:** The aim of our study was to determine the prevalence and severity of systemic AA amyloidosis (sAAa), to specify amyloid A deposits in different tissue structures of the kidneys, to outline the development of renal AA amyloidosis (rAAa), and to estimate the role of sAAa and rAAa in mortality.

**Methods:** At the National Institute of Rheumatology 9475 patients died between 1969 and 1992; among them 161 with RA (females 116, average age: 64.95 years, range 87–16, onset of RA: 50.19, average disease duration: 14.79 years; males 45, average age: 66.29 years, range 88–19, onset of RA: 52.57, average disease duration: 13.46 years at death); who were autopsied.

RA was confirmed clinically according to the criteria of the ACF.

sAAa was specified histologically, based on evaluation of 5 organs (heart, lung, liver, kidney and pancreas) in each of 161 patients. Amyloid A deposition was diagnosed histologically according to Romhányi by a modified (more sensitive) Congo red staining. Amyloid A deposits were identified in serial sections by immunohistochemical and histochemical methods. The prevalence (existence) and severity (extent) of amyloid A deposition were evaluated microscopically with an Olympus BX51 polarizing microscope.

**Results:** sAAa complicated RA in 34 (21.12 %) of 161 patients; in 127 (78.88 %) of 161 patients amyloid A deposits were not found.

Amyloid A deposits were found in 29 (87.88 %) kidneys of 33 patients with sAAa; kidneys were negative for amyloid in 4 (12.12 %) of 33 cases (in 1 of 34 patients with sAAa tissue blocks of kidneys were not available).

sAAa was lethal in 17 (50.0 % of 34) patients due to massive amyloid A deposition in the kidneys, leading to renal insufficiency and uremia. Cardiac amyloid A deposition led to death in 3 (8.82 % of 34) patients with sAAa (and contributed to the lethal outcome in further 5). Fourteen (41.18 % of 34) patients with sAAa died of other causes such as peritonitis, lethal septic infection, etc.

sAAa was clinically diagnosed in 9 (26.47 %) and missed in 25 (73.52 %) of 34 patients, and only cases with massive renal amyloid A deposits were recognized. Cardiac AAa or its pathogenic role in mortality was not diagnosed.

**Conclusions:** sAAa is one of the main and the most insidious complications of RA affecting the kidneys with high prevalence and severity. sAAa is related to the cardiovascular system, and rAAa is associated with it. sAAa and rAAa may be developed in both sexes, and at any time in the course of the disease.

Systemic and renal amyloid A deposition is a progressive and cumulative process, involving in its early stage only a few structures in various organs, and increasingly more in the later stages of the disease.

In sAAa the renal amyloid A deposition starts after a latent stage. This latency may be caused by a not specified local protective mechanism, e.g. great excretion capacity of the kidneys.

Amyloid A deposition starts in the most frequently involved structures of the kidneys with more massive deposits. The chronology of amyloid A deposition allows

an indirect assessment of the stage of renal amyloidosis, which may have a prognostic value in everyday surgical pathology.

Half of the patients with **sAA** died of uremia caused by massive **rAA** and only 9 of these were clinically recognized. Renal amyloid A deposition should be considered a very serious, life-threatening complication of **RA**.

**Disclosure of Interest:** None declared

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SAT0153

### ANALYSIS OF CLINICAL-ANALYTICAL CHARACTERISTICS IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA) AND INTERSTITIAL LUNG DISEASE (ILD): CASE-CONTROL STUDY

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**Objectives:** To study the differences in severity marker and disease activity in patients with RA and ILD and patients with RA without DILD, and to identify factors associated with ILD in RA patients.

**Methods:** Design: Observational case-control study. Patients: consecutive RA-patients (ACR/EULAR 2010 criteria) with ILD (American Thoracic Society) selected from a prospective cohort from Regional Hospital and Virgen Victoria Hospital of Málaga were included. Controls: RA-patients without ILD. Sex-age matched controls were collected from a prospective cohort of Regional Hospital. Protocol: RA Patients are reviewed every six months in general clinic and patients with biological therapy every three months. All patients are reviewed according to a protocol with systematic data collection. The data of patients with RA and ILD are also collected in a database according to a specific protocol for these patients. The day that was reviewed the last time in consultation will be marked as inclusion date. Data will be collected on the date of inclusion and their clinical records. Outcomes: Difference in severity marker in both groups on the date of inclusion (RF, ACPA, erosive arthritis); in disease Activity Score (DAS28-ESR) and Health Assessment Questionnaire (HAQ); description of modifying antirheumatic drugs (DMARDs); Variables: Demographic, clinical-analytical variables: number of tender joints (TJ), number of swollen joints (SJ), CRP, ESR, general evaluation, DAS28-ESR, HAQ and adverse effects (description, severity and number). Statistical analysis: Descriptive and paired T-test or Chi-square test followed by binary logistic regression (RLB) (Vd:ILD in patients with RA).

VARIABLE	RA-ILD (n=29)	RA (n=24)	P- value
Age (years), mean (SD)	67.7 (8.0)	66.9 (7.2)	0.682
Sex (female), n (%)	18 (55.2)	13 (54.2)	0.942
Sex (male), n (%)	11 (44.8)	11 (45.8)	
Smoker			0.003
Non-smoker, n (%)	13 (44.8)	16 (66.7)	
Ex-smoker, n (%)	11 (37.9)	9 (40.0)	
Smoker, n (%)	5 (17.2)	8 (33.3)	
Disease duration RA, median (p75-p25)	130.9 (93.4-208.2)	99.9 (73.4-121.8)	0.002
Socio Economic Status			0.500
No income, n (%)	9 (31.0)	8 (33.3)	
<1500 €/month, n (%)	17 (58.6)	11 (45.8)	
>1500 €/month, n (%)	3 (10.3)	5 (20.8)	
Educational level			0.345
None, n (%)	12 (41.4)	9 (25.0)	
Primary and secondary school, n (%)	12 (41.4)	14 (58.3)	
University, n (%)	8 (11.3)	4 (16.7)	
Rheumatoid factor, n (%)	27 (93.1)	20 (83.3)	0.264
Anti-cyclic citrullinated peptide, n (%)	27 (93.1)	20 (83.3)	0.264
Anti-cyclic citrullinated peptide elevated (>340), n (%)	22 (75.9)	10 (43.5)	0.008
Erosions, n (%)	24 (82.8)	12 (50.0)	0.013

**Results:** Fifty-three patients were included, 29 RA with ILD and 24 RA controls. The differences between clinical and epidemiological characteristics to cases and controls are shown in table 1. RA patients with ILD showed more months with RA duration (p=0.002), more number of exsmokers (p=0.003), erosive arthritis (p=0.011) and ACPA positive (P=0.008). No significant differences in the mean of

DAS28 in cases and controls were observed (2.61 vs 2.68; p=0.789), but RA patients with ILD presented worse in physical function parameters by HAQ (1.12 VS 0.63; P=0.032). All patients were treated with disease modifying antirheumatic drugs (DMARDs). RA patients with ILD had: 5 (17.2%) monotherapy with bDMARDs, 17 (58.62) monotherapy with sDMARD and 7 (24.1) sDMARDs with a bDMARDs. In multivariate analysis, the independent variables that were associated with ILD in RA patients were: ACPA elevated (OR [IC95%] =5.0 [1.2-9.9]; p=0.023) and RA duration (months) (OR [IC95%]=1.1 [1.0-1.2]; p=0.037). This model would explain 28% of the variability of the ILD in RA (R<sup>2</sup>=0.28).

**Conclusions:** The evolution time of arthritis and the presence of ACPA to high titres (>340) were the predictors of ILD in patients with RA in our study. More prospective studies with a greater number of patients are necessary to identify the possible association.

**Disclosure of Interest:** None declared

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SAT0154

### ASSESSMENT OF BONE TURNOVER MARKERS IN PRE- AND POSTMENOPAUSAL WOMEN WITH RHEUMATOID ARTHRITIS

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**Background:** To compare bone metabolism in pre- and postmenopausal women with RA

**Objectives:** GCs and inflammation lead to BMD loss through increase the expression of RANK-ligand and decrease the expression of osteoprotegerin in stromal and osteoblastic cells. Determination of indicators relevant for clinical practice for identification a high-risk BMD loss group of RA patients is needed.

**Methods:** The bone turnover markers were analyzed in 58 women with RA: 36 premenopausal (PreM) and 22 postmenopausal (PM). The two groups were significantly different in age (35.9±8.7 PreM vs 57.1±4.1 PM) and BMI (23.8±4.3 PreM vs 28.6±5.0 PM). By disease duration (8.9±5.7 years vs 10.0±6.1 years), disease activity by DAS28, x-ray changes, GC, MTX and biologic therapy both group were comparable. BMD was measured in 3 part of the skeleton: hip, lumbar spine, distal part of forearm. Serum levels of 25 (OH) vitamin D (Vit D), parathormone (PTH), osteoprotegerin (OPG), RANKL were analyzed.

**Results:** Low level of Vit D (25(OH)D<30 ng/ml) was observed in 46.6% of patient and was preferable in PreM women. Vit D deficiency was associated with age (R=-0.31, p<0.05) and positive anti-CCP (R=-0.46, p<0.05). The mean level of PTH was normal in 74.1%. Serum OPG level was significantly higher in more than 50% of patients. It was associated with presence of erosion (R=0.97, p<0.05), decreased cortical index (R=-0.28, p<0.05) in PreM patient and DAS28 (R=-0.44, p<0.05) in all patients. High level of RANKL was preferable in PM women (47.6%), decreased level more often was observed in PreM patient (38.9%). In PM patients increased level of RANKL was correlated with BMI, duration of menopause and DAS28, in PreM – only with DAS28. In PreM women the changes in serum levels of PTH and vitamin D was negatively correlated with levels of RANKL and C-TP, low level of vitamin D had negative correlation with OPG (R -0.47). According to lineal regression analysis positive correlation between disease duration, Sharp van der Heijde erosion score and PTH (r=0.31; p=0.01, r<sup>2</sup>=0.11) was observed in all patients, more often in PreM women. Low spine BMD in PreM associated with high PTH (R=0.82, p<0.05), in PM – with high PTH, OPG/RANKL and low level of RANKL. Low hip neck BMD correlated with decreased level of vit D in PM patients. Low levels of vit D, C-TP and high levels of OPG and OPG/RANKL index was significantly associated with forearm low BMD in all patients. In PreM women strong association between low vit D (R=-0.60, p<0.05), high OPG (R=0.89, p<0.05) and BMD in medium part of forearm was observed.

**Conclusions:** In premenopausal women vitamin D deficiency had high predictive value for decrease BMD in the medium part of forearm, high level of PTH – for decrease BMD in the spine. In PreM RA patients low Vit D, low cortical index and high PTH can be considered as an indication for BMD assessment. PM women with high BMI, longstanding postmenopausal period and high disease activity may be candidate for bone markers assessment.

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SAT0155

### TRADITIONAL AND NONTRADITIONAL CARDIOVASCULAR RISK FACTORS IN PATIENTS WITH EARLY ONSET ARTHRITIS OF THE PANLAR-EOA

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**Background:** Inflammation plays a significant role in atherosclerosis and cardiovascular disease (CVD). Patients with chronic inflammatory diseases are at increased risk of CVD, but it is debated whether this association is causal or dependent on shared risk factors or inflammatory pathways.

**Objectives:** Identify the mScore value and the association between traditional and nontraditional cardiovascular risks factors (CVRF) in an early onset arthritis (PANLAR-EOA)

**Methods:** Prospective, longitudinal cohort study. Patients were protocolled according to the PANLAR-EOA project. For this analysis only patients with 12 and 24 months follow up were included. Patients were registered in REPANARC (www.panlareoa.org) database. The mScore evolution and the nontraditional CVRF linked to the disease (i.e. DAS28) association with the traditional CVRF (i.e. obesity) were studied. The Wilcoxon Test and the Spearman correlation test, depending on whether the variables were categorical or numerical, were utilized.

**Results:** Initially 136 patients with early onset arthritis were included, out of which 88 completed the 12 months follow up and 58 the 24 months one. There was a female predominance 86% (117/136) of patients, with a median age of 44.80 ±14.47 years. When comparing the change ratio of the values obtained with the mScore on the initial, the 12 months and 24 months visit, the results were not statistically significant (p=0.106 at 12 months and p=0.175 at 24 months). An association between the elevated erythrocyte sedimentation rate and obesity (p=5.807e-03) and diabetes (p=3.739e-02) was found in the initial visit. An association between elevated prednisone doses and high levels of total cholesterol (2.084e-02), high levels of diastolic blood pressure (p=1.967e-02) and low HDL values were observed (7.706e-03). At 12 months a significant association between obesity and high CRP (p=3.649e-02) and between high glycaemia levels with elevated prednisone doses and high CRP levels (p=2.549e-02). In the 24 months visit analysis, an association between elevated HDL-cholesterol with high prednisone doses (p=5.016e-03) and elevated CRP levels (3.492e-02).

**Conclusions:** An increment in Cardiovascular Risk (CVR) was not found at 12 and 24 months follow up according to the mScore. We have observed that there is an association between traditional and nontraditional CVRF. Therefore, the prevention strategies should be aimed not only towards the control of traditional CVRF, but also against the nontraditional CVRF associated with disease activity, which in a certain way could influence over the previous ones and modify the global CVR of patients with EOA

**Disclosure of Interest:** None declared

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SAT0156

### ASSOCIATION BETWEEN CUMULATIVE METHOTREXATE DOSE, NON-INVASIVE SCORING SYSTEM AND HEPATIC FIBROSIS DETECTED BY FIBROSCAN IN RHEUMATOID ARTHRITIS PATIENTS RECEIVING METHOTREXATE.

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**Background:** Methotrexate (MTX) is recommended by recent ACR and EULAR guideline as a first-line drug for RA. Liver fibrosis, which occurs as long-term side effect is one of the most concerns.

**Objectives:** To find the association between clinical parameters, cumulative MTX dosage, liver fibrosis scoring systems and the presence of liver fibrosis assessed by transient elastography (TE; Fibroscan<sup>®</sup>).

**Methods:** Rheumatoid arthritis, prescribed MTX, patients had been evaluated of liver fibrosis with TE. Two subgroups of patients were compared: non-fibrosis and fibrosis (TE >7 kPa). Univariate and multivariate logistic regression analysis were performed to identify factors associated with liver fibrosis.

**Results:** One hundred and eight patients were recruited. Twenty-nine patients (26.8%) were classified by transient elastography as liver fibrosis cases. The multivariate analysis demonstrated only the statistically significant of the association in BMI (OR=1.217; 95%CI 1.048–1.414; P=0.010); fatty liver (OR=2.318; 95%CI 0.584–9.189; P=0.232); ALT (OR=1.044; 95%CI=1.003–1.087; P=0.036) and cumulative MTX dosage (OR 1.001; 95%CI 1.000–1.001; P=0.001).

**Conclusions:** Liver fibrosis measured with Fibroscan was associated with cumulative MTX. RA patients with metabolic syndrome including high BMI, IFG, fatty liver had higher risk of MTX-induced hepatic fibrosis. RA patients with high cumulative MTX dose, especially patients with concurrent metabolic syndrome should be cautiously monitored for liver fibrosis.

**Disclosure of Interest:** None declared

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SAT0157

### THE PREVALENCE OF DYSLIPIDEMIA AND DAILY NUTRITIONAL INTAKE IN RHEUMATOID ARTHRITIS PATIENTS: A STUDY OF THE KOREAN NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY (KNHANES)

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**Background:** Lipid metabolism appear to be changed in rheumatoid arthritis (RA) patients because of disease activity and inflammation.

**Objectives:** It was not clear in the previous studies that lipid profiles status is associated with nutritional intake in RA patients.

**Methods:** We analyzed RA, dyslipidemia, serum lipid profiles (total cholesterol, TG, HDL, and LDL) and nutritional intake data related lipid from the data of

**Abstract Sat0156 – Table 1.** The univariate and multivariate logistic regression analysis of factors associated with significant liver fibrosis.

Parameter	Univariate	Logistic	Regression	Multivariate	Logistic	Regression
	Odds ratio	95% confident interval	P-value	Odds ratio	95% confident interval	P-value
Body weight(kg)	1.042	1.002–1.083	0.039	-	-	-
BMI (kg/m <sup>2</sup> )	1.266	1.107–1.449	0.001	1.217	1.048–1.414	0.010
IFG	3.400	1.240–9.320	0.017	-	-	-
Fatty liver	3.652	1.114–11.971	0.032	2.318	0.584–9.189	0.232
HLP	4.397	1.803–10.722	0.001	-	-	-
RA duration (y)	1.122	1.022–1.233	0.016	-	-	-
MTX duration (wk)	1.005	1.002–1.008	0.001	-	-	-
MTX cumulative dose (mg)	1.001	1.000–1.001	0.000	1.001	1.000–1.001	0.001
Prednisolone dose(mg/d)	2.235	0.939–5.319	0.069	-	-	-
Statin	3.391	1.374–8.370	0.000	-	-	-
TJC	1.305	1.012–1.682	0.040	-	-	-
AST (IU/L)	1.047	0.998–1.098	0.058	-	-	-
ALT (IU/L)	1.040	1.008–1.074	0.014	1.044	1.003–1.087	0.036
GGT (IU/L)	1.131	1.080–1.184	0.000	-	-	-
INR	48853.68	169.313–1.41e	0.000	-	-	-
Ultrasound	6.961	2.666–18.175	0.000	-	-	-
AST/ALT ratio	0.420	0.156–1.128	0.085	-	-	-

KNHANES (N=22,948, estimated population size=48,402,221). We analyzed the prevalence of RA and abnormal status of lipid profiles using general linear model and logistic regression with complex sample design method adjusted by age and sex and evaluated the association between RA and dyslipidemia including nutritional intake data.

**Results:** The prevalence of RA was 1.21% [95% CI: 1.07–1.38]. The prevalence of dyslipidemia with RA (3.31% [95% CI: 2.63–4.17]) was significantly increased compared with that of dyslipidemia without RA (1.37% [95% CI: 1.17–1.59],  $p < 0.001$ ).

LDL (RA vs. control:  $117.77 \pm 3.87$  mg/dL vs.  $114.47 \pm 0.51$  mg/dL,  $p < 0.001$ ) was significantly increased, whereas TG (RA vs. control:  $129.21 \pm 6.38$  mg/dL vs.  $136.72 \pm 1.20$  mg/dL,  $p < 0.001$ ) was significantly decreased in RA. Total cholesterol tended to be higher in RA (RA vs. control:  $198.12 \pm 3.09$  mg/dL vs.  $188.11 \pm 0.39$  mg/dL,  $p = 0.051$ ), but HDL (RA vs. control:  $54.16 \pm 1.42$  mg/dL vs.  $52.46 \pm 0.15$  mg/dL,  $p = 0.98$ ) was not different between two groups.

There were no differences in nutritional intake volume including total diet volume, energy intake, water, carbohydrate, protein, fat, other fatty acids and dietary fiber (Table).

Table 1 Nutritional intake difference between RA and control

	RA	control	p
Total diet (g/day)	1447.96 ± 55.81	1658.24 ± 11.50	0.40
Energy intake (kcal/day)	1826.19 ± 61.89	2121.24 ± 12.16	0.87
Water (g/day)	1027.92 ± 46.74	1182.23 ± 9.66	0.38
Protein (g/day)	61.06 ± 2.88	74.71 ± 0.58	0.85
Carbohydrate (g/day)	298.90 ± 8.76	318.72 ± 1.64	0.45
Fat (g/day)	36.66 ± 2.46	47.71 ± 0.49	0.72
Cholesterol (mg/day)	207.17 ± 33.49	278.72 ± 6.63	0.62
Saturated fatty acid (g/day)	10.05 ± 0.77	13.75 ± 0.15	0.95
Monounsaturated fatty acid (g/day)	10.97 ± 0.77	15.17 ± 0.18	0.86
Polysaturated fatty acid (g/day)	10.08 ± 0.76	11.94 ± 0.14	0.88
n-3 fatty acid (g/day)	1.59 ± 0.19	1.70 ± 0.03	0.46
n-6 fatty acid (g/day)	8.56 ± 0.67	10.31 ± 0.12	0.77
Crude fiber (g/day)	8.53 ± 0.71	7.71 ± 0.09	0.74
Dietary fiber (g/day)	23.85 ± 1.62	24.53 ± 0.30	0.25

Adjusted by age, sex and body mass index

**Conclusions:** We showed increased prevalence of dyslipidemia patients in the individuals with RA than those without RA. Serum LDL levels was increased and TG was decreased in RA patients of the Korean population survey.

**Disclosure of Interest:** None declared

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#### SAT0158 THE ASSESSMENT OF SAFETY AND EFFICACY OF USING SELF-MONITORING OF DISEASE ACTIVITY VIA WEB PORTAL IN THE MANAGEMENT OF PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** According to the Treat-to-Target guidelines for the RA, the main goal of treatment is remission or, alternatively, a lower activity of the disease. However, persistent remissions and preservation of working capacity are observed in no more than 5–6% of cases. As a result of the analysis of possible causes of the strategy's lack of efficacy, it seemed to us urgent to create and approve the method of managing RA patients via the "Web portal for self-monitoring of rheumatoid arthritis activity".

**Objectives:** Maximally quickly identify the exacerbation of the disease and timely strengthen the therapy, for more rapid achievement of remission or low disease activity.

**Methods:** The authors created an interactive web portal for self-monitoring of RA activity. The patient management model using this method is that a patient conducts a monthly self-evaluation of the disease activity and transmits this information to his treating doctor in a remote manner via the web portal. The doctor receives information about the patient's health as quickly as possible. In case of worsening and in the absence of any dynamics, according to the patient, he was invited to the center, where this information was verified by a doctor and, if necessary, correction of therapy was made. If, in the patient's opinion, there was an improvement, he did not come to clinic, but continued therapy. During the management of patients with RA using this method (1 year) initially and further regularly clinical, laboratory and radiological monitoring of efficacy and safety was conducted. Currently, 30 women with RA, age 57 (38; 71), who completed the 6-month treatment period, are included in the study. All patients underwent a clinical examination, hand and feet X-ray, laboratory tests and assessment of the RA activity by DAS28 index. Initially, all patients were trained by a rheumatologist to carry out a self-assessment of tender and swollen joints according to the original

author's technique "Structured curriculum for teaching RA patients self-monitoring of disease activity".

**Results:** During 6 months, there was a positive dynamics of the course of the disease, the activity of the RA by DAS 28 decreased. Initially, 5 patients (16.7%) had high DAS activity, 24 – moderate (80%), 1 – low (3.3%). After 6 months of treatment 8 patients (26.7%) had low activity, 22 (73.3%) achieved remission. The mean value of the DAS 28 index at the time of inclusion was 3.99 (2.46; 5.78) and after 6 months of management 2.175 (0.79; 4.31), a statistically significant decrease (Wilcoxon T-test = 5). Initially, all patients received methotrexate at an average dose of 12.9 mg (10 mg; 30 mg), at 6 months of follow-up, the average dose was 14.6 mg (10 mg; 25 mg). An increasing the dose of methotrexate was required in 11 (36.6%) patients. Analysis of clinical and laboratory parameters did not reveal statistically significant deviations.

**Conclusions:** The 6-month period of patient management via the "web portal for self-monitoring of rheumatoid arthritis activity" proved the possibility of achieving remission and low disease activity in all patients.

**Disclosure of Interest:** None declared

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#### SAT0159 THYROID FUNCTION IN EARLY VERSUS ESTABLISHED RHEUMATOID ARTHRITIS

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**Background:** Thyroid dysfunction is common in rheumatoid arthritis (RA). Sub-clinical hypothyroidism is the first most common, followed by clinical hypothyroidism. Thyroid dysfunction in RA had been found to increase the risk of cardiovascular disease. Subclinical hypothyroidism is defined as increased serum TSH concentration with normal serum free thyroxine (T4) level.

**Objectives:** The aim of this study was to compare the thyroid function in early RA patients (of less than one-year duration of RA symptoms) versus established RA patients (of more than or equal to one-year duration of RA symptoms)

**Methods:** We recruited 35 early RA patients (ERA) and 52 established RA patients attending specialized rheumatology clinic. All the patients had no clinical evidence of thyroid dysfunction. Patients with diabetes, pregnancy, renal and liver impairment were excluded. Fasting Free thyroxine (FT4), Free triiodothyronine (FT3), and thyroid stimulating hormone (TSH) were assessed in all the participants. t-test was used to compare the RA disease characteristics and the thyroid function between early and established RA. P value of <0.05 was considered significant.

**Results:** Rheumatoid arthritis patients had been recruited through a specialized rheumatology clinic, 35 were with new onset rheumatoid arthritis (early RA; ERA of less than a year of RA symptoms onset) and 52 were with established RA (of more than a year of RA symptoms onset). The mean RA duration was  $7.4 \pm 2.0$  months for ERA and  $96 \pm 92$  months for the established RA group. There were no significant differences in age ( $45.76 \pm 2.45$  years for ERA vs. established RA respectively,  $p = 0.49$ ), or in gender distribution (31 F and 4 M in ERA vs. 46 F and 6 M in established RA,  $p = 0.9$ ) between the two groups.

ERA compared to the established RA group had more active RA as manifested by more swollen 28- joints (5.7 vs 1.7, respectively,  $p = 0.001$ ), more tender 28-joints (17 vs 11, respectively,  $p = 0.01$ ), higher DAS-28-ESR score (5.8 vs 4.5, respectively,  $p = 0.0001$ ), higher DAS 28-CRP score (5.1 vs. 3.9, respectively,  $p = 0.001$ ), and longer morning stiffness duration ( $p = 0.04$ ). As well, ERA had lower HDL level (1.4 vs 1.2, respectively,  $p = 0.04$ ). On the other hand, established-RA patients had RA disease onset at an earlier age than the EAR group (36.5 vs 44 years, respectively,  $p = 0.02$ )

While the mean TSH, T3 and T4 were within normal range in both groups, there were significant differences in the mean values between ERA and established RA. TSH was  $2.12 \pm 1.52$  in ERA vs.  $5.8 \pm 8.3$  in established RA (NR:  $0.27 - 4.2$  mIU/L),  $p = 0.04$ . Mean FT3 was  $4.54 \pm 0.53$  in ERA vs.  $3.61 \pm 1.13$  in the established RA (NR:  $4 - 6.8$  pmol/L),  $p = 0.04$ . Average FT4 was  $17.7 \pm 4.77$  in ERA vs.  $15.3 \pm 2.51$  in the established RA (NR:  $12 - 22$  pmol/L),  $p = 0.01$ .

**Conclusions:** RA patients with more than a year of RA symptoms are at a higher risk of silent autoimmune thyroid disease than their age sex matched RA patients with new onset RA; of less than a year of RA symptoms onset. Regular assessment of thyroid function might be an important part in the routine biochemical and immunological profile screening of RA.

**Disclosure of Interest:** None declared

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### SAT0160 EFFECT OF PERIODONTAL TREATMENT ON E-SELECTIN LEVEL IN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Cardiovascular (CV) disease is the main cause of mortality in rheumatoid arthritis (RA).<sup>1</sup> Studies showed that periodontitis is associated with RA and CV diseases.<sup>2-4</sup> Endothelial dysfunction is the first step in the pathogenesis of atherosclerosis. E-selectin is a marker of endothelial dysfunction and was expressed specifically in endothelial cells. To date, there is no study on the effect of periodontal treatment on endothelial dysfunction in RA patients.

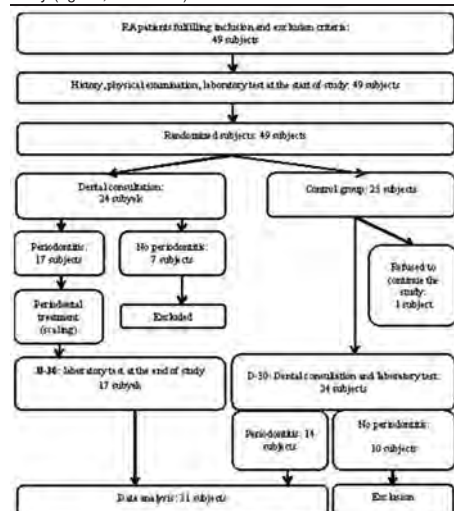
**Objectives:** To determine the effect of periodontal treatment on E-selectin level in RA patients.

**Methods:** This was a clinical trial in RA patients visiting Rheumatology Clinic in our hospital between March-May 2017. Inclusion criteria: adult RA patients, has periodontitis, low-high RA disease activity, RA duration of 10 years or less, has received DMARD. Exclusion criteria: subjects who smoke, have diabetes, underwent dental treatment for the past 3 months, have other autoimmune diseases, and patients who refused to join the study. Subjects was randomized into intervention group (periodontal scaling for 1 month) and control group. Study flow is visualized in figure 1. E-selectin level was measured at the start and at the end of the study. T-test was used to measure the difference of E-selectin level changes before-after study between groups.

**Results:** There were 31 subjects who completed the study. The prevalence of periodontitis was 64.5%. There was no statistically significant difference on delta E-selectin before-after treatment between both groups (table 1). We further divided the subjects based on disease activity and lipid profile at the end of the study. Subjects on the treatment group who was on remission and has normal lipid profile (normal LDL and decreased total cholesterol/HDL ratio) has decreased E-selectin level compared to other subjects.

Table 1 Study subjects and intervention

Characteristics	Total (n = 31)	Intervention group (n = 17)	Control group (n = 14)
Age (years, mean±SD)	55,4±8,8	52,6±9,6	58,9±6,4
RA duration (months, mean±SD)	68,8±36,5	57,8±36,5	83,5±32,3
Disease activity (n, %)	16	10 (58,3%)	6 (37,5%)
- Low	(53,3%)	6 (35,3%)	8 (53,8%)
- Moderate	14	1 (3,3%)	0 (0%)
- High	(43,3%)		
	1 (3,3%)		
Taking glucocorticoid (n, %)	20	12 (70,6%)	8 (57,1%)
	(64,5%)		
BMI (kg/m <sup>2</sup> , mean±SD)	24,9±3,17	24,89±3,47	24,92±2,86
Oral Hygiene Index (median, min-max)	0,85 (0,14 - 3,2)	0,8 (0,14 - 2)	0,82 (0,2 - 3,2)
Delta of E-selectin level start-end of study (ng/mL, mean±SD)	-	-6,3±9,3	-2,7±9,7 (p value 0,303)



**Conclusions:** Periodontal treatment for a month has no effect on E-selectin level in RA patients. Further studies on the effect of periodontal treatment on endothelial dysfunction in RA patient needs to be done on patients on remission, without dyslipidemia, and with longer treatment period.

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**Disclosure of Interest:** None declared

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### SAT0161 INFLUENCE OF DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS ON RADIOGRAPHIC PROGRESSION OF CONCOMITANT INTERPHALANGEAL JOINT OSTEOARTHRITIS

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**Background:** The role of inflammation in distal interphalangeal (DIP) osteoarthritis (OA) is not clear. Unlike the situation in psoriatic arthritis, DIP joints are considered not to be affected in rheumatoid arthritis (RA). Despite synovitis and bone marrow edema are also associated with radiographic progression of hand OA, the radiological course of DIP-OA and joints affected from RA differ substantially.

**Objectives:** To clarify the influence of RA disease activity and bone erosions on radiologic progression of DIP joint OA.

**Methods:** In sequential radiographs of 1988 RA patients available within the Swiss rheumatic disease registry (SCQM), we scored 15904 DIP joints for the presence of erosions as well as the severity of osteophytes, subchondral sclerosis and joint space narrowing according to the modified Kellgren Lawrence Grade (KLG). Progression was defined as an increase of KLG.

**Results:** The mean patient age was 56.1 years (SD 11.1). The median follow-up time was 4.5 years (IQR 3.1 – 7.0). DIP-OA was present in 60% of patients at baseline. Age, female sex and higher body mass index but not anti-citrullinated protein antibodies or rheumatoid factors were associated with the presence of DIP-OA. Preexisting DIP-OA (odds ratio [OR] 4.7, p<0.001) and female sex (OR 1.4, p=0.009) were predictors for radiologic progression, whilst metacarpophalangeal joint erosions or DAS28-ESR had no influence on the radiological course of DIP-OA.

**Conclusions:** Known risk factors for DIP-OA are replicated in patients with RA. RA disease activity, autoantibody status or metacarpophalangeal joint erosions were not associated with DIP-OA presence or progression, indicating distinct roles of inflammation in the pathogenesis of RA and OA.

**Disclosure of Interest:** None declared

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### SAT0162 WHERE SHOULD WE SEEK FOR SUBCLINICAL SYNOVITIS USING ULTRASOUND IN RHEUMATOID ARTHRITIS?

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**Background:** The role of ultrasound imaging (US) in rheumatoid arthritis (RA) management is fundamental by sharpen diagnosis, predicting prognosis, monitoring disease activity and identifying remission. The detection of subclinical synovitis and articular inflammatory changes represent the real advantages of this technology. However, joint US is time-consuming, thus identifying the area of sub-clinical synovitis should be useful to overcome this difficulty.

**Objectives:** We aimed to assess the most profitable joint locations in detecting subclinical synovitis in RA.

**Methods:** We performed a cross-sectional study of one hundred patients with inflammatory joint pain or synovitis for more than 6 weeks and less than 2 years. All patients were free of conventional or biological DMARD's at inclusion. An experienced radiologist performed the MSUS scan of 22 joints (2 wrists, 10 metacarpophalangeal joints MCP and 10 proximal interphalangeal joints PIP) unaware of clinical and biological findings. MSUS was performed using a Philips HD11. The used frequency ranged from 15 to 17 MHz and we used a Power Doppler (PD). After US assessment, patients were classified as having RA according to ACR/EULAR 2010 criteria.

**Results:** We enrolled 100 patients (77 women and 23 men) with a mean age of 51.8 years [16-77]. Fifty-five patients (55%) fulfilled the ACR/EULAR 2010 criteria for the diagnosis of RA. The mean disease duration was 10.96 months [2-24]. Rheumatoid factor and ACPA were positive in 53% and 25% cases respectively. The mean disease activity score at the time of study was 5.36 [1.36-8.61]. A clinical wrist synovitis was found in 92 cases (46%). In the 54 wrists with no clinical



synovitis, a total number of US wrist synovitis was detected at 30 (15%) radioulnar (of which half was Doppler +), 91 (45.5%) radiocarpal (of which 60% was Doppler +) and 105 (52.5%) intercarpal joints (of which 67% was Doppler +). Concerning the MCP and PIP joints, the most frequent location of subclinical synovitis were 1st MCP in 51 cases (25.5%), 4th MCP in 49 cases (24.5%), 5th MCP in 50 of cases (25%), 1st PIP in 24 cases (12%) and 5th PIP in 22 cases (11%).

**Conclusions:** Our study highlighted the low sensitivity of physical examination of synovitis in hand and wrist joints, especially in some locations. We showed the most frequent location for detecting subclinical synovitis were radiocarpal and intercarpal joint, 1st-4th -5th MCP and 1st-5th PIP. About half of those subclinical synovitis were Doppler +.

**Disclosure of Interest:** None declared

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**SAT0163 ABSOLUTE NUMBER OF PERIPHERAL CD4-CD25+FOXP3+ T CELLS DECREASES AND RESTORES AFTER LOW-DOSE INTERLEUKIN-2 TREATMENT IN RHEUMATOID ARTHRITIS**

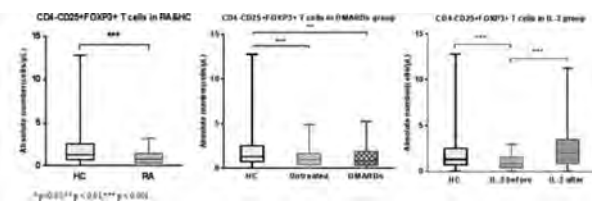
X. Jia<sup>1</sup>, H. An<sup>1</sup>, K. Fan<sup>1</sup>, F. Li<sup>1</sup>, C. Gao<sup>2</sup>, X. Li<sup>1</sup>. <sup>1</sup>Rheumatology, The Second Hospital Of Shanxi Medical University, Taiyuan, China, <sup>2</sup>Pathology, Brigham and Women's Hospital, Boston, United States

**Background:** Recently, several studies have suggested that abnormal quantity and function of regulatory T cells (Tregs) may play a vital role in the development of rheumatoid arthritis (RA). CD25<sup>+</sup>FOXP3<sup>+</sup> T cells include CD4<sup>+</sup> (CD4<sup>+</sup> Tregs) and CD8<sup>+</sup> cells (CD8<sup>+</sup> Tregs). Recently studies have shown that CD8<sup>+</sup> Tregs also have immunosuppressive function, similar to even stronger than CD4<sup>+</sup> Tregs, and are more sensitive to IL-2 in vivo. However, the status of CD8<sup>+</sup>Treg cells in RA is unknown.

**Objectives:** Our study was designed to clarify the level of CD4<sup>+</sup>CD25<sup>+</sup>FOXP3<sup>+</sup> T cells in RA patients, and to investigate the role of low-dose interleukin-2 (IL-2) therapy in the regulation of CD4<sup>+</sup>CD25<sup>+</sup>FOXP3<sup>+</sup> T cells in RA patients to provide another theoretical basis besides CD4<sup>+</sup> Tregs to IL-2 therapy.

**Methods:** Three hundred and four RA patients (diagnosis according to the 2010 ACR criteria) were enrolled; no treatment group (N = 75), DMARDs treatment group (N = 73), low dose IL-2 treatment group (50WU/day × 5 days, subcutaneous injection) (N = 156), and healthy control group (N = 90). The absolute numbers of CD4<sup>+</sup>CD25<sup>+</sup>FOXP3<sup>+</sup> T cells in peripheral blood were detected by flow cytometry. We assumed that CD4<sup>+</sup> T cells with CD25<sup>+</sup> and FOXP3<sup>+</sup> were mostly CD8<sup>+</sup>CD25<sup>+</sup>FOXP3<sup>+</sup> Treg cells, which was CD4<sup>+</sup>CD25<sup>+</sup>FOXP3<sup>+</sup> T cells in this study. The levels of CD4<sup>+</sup>CD25<sup>+</sup>FOXP3<sup>+</sup> T cells among these groups were compared with that of health group or each other respectively, and then the statistical software SPSS 20.0 was used for analysis; p<0.05 was considered significant.

**Results:** As compared with the healthy group, the absolute number of CD4<sup>+</sup>CD25<sup>+</sup>FOXP3<sup>+</sup> T cells decreased significantly in the untreated RA patients [0.94(0.41,1.61) vs 1.31(0.72,2.52), P<0.001] and more dramatically in DMARDs treatment patients [0.86(0.36,1.83) vs 1.31(0.72,2.52), P<0.01]. After treatment with IL-2, the absolute count of CD4<sup>+</sup>CD25<sup>+</sup>FOXP3<sup>+</sup> T cells increased significantly compared with that before treatment [0.91(0.48,1.54) vs 2.10(1.12,3.56), P<0.001].



**Conclusions:** The absolute number of CD4<sup>+</sup>CD25<sup>+</sup>FOXP3<sup>+</sup> T cells in untreated RA patients were lower than those health, implying that CD4<sup>+</sup>CD25<sup>+</sup>FOXP3<sup>+</sup> T cells deficiency was caused by disease itself but not immunosuppressive therapy, which may be an important factor in the pathogenesis of RA. The traditional DMARDs therapy did not improve this reduction. Low dose IL-2 can increase the absolute number of CD4<sup>+</sup>CD25<sup>+</sup>FOXP3<sup>+</sup> T cells in peripheral blood. We are about to detect the number of CD8<sup>+</sup>CD25<sup>+</sup>FOXP3<sup>+</sup> Treg cells accurately to verify this theory.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.4123

**SAT0164 ADVERSE DRUG REACTIONS DUE TO DISEASE MODIFYING DRUGS IN PATIENTS WITH INCIDENT RHEUMATOID ARTHRITIS**

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**Background:** There is a well-known risk of developing adverse drug reactions (ADR) in rheumatology due, mainly, to the Disease Modifying Antirheumatic Drugs (DMARD) used. There is no doubt about their efficacy in Rheumatoid Arthritis (RA), but it is necessary to increase our knowledge of their ADR, especially those that lead to discontinuation

**Objectives:** To describe the incidence and characteristics of ADR related with DMARD in patients with incident RA as well as the factors involved in their development

**Methods:** Observational retrospective longitudinal study between April 15th 2007 and December 31st 2016. **Inclusion criteria:** patients diagnosed with RA between April 15th 2007 and June 31st 2011 followed until December 31st 2016 whom started any DMARD. **Primary endpoint:** development of an ADR that required discontinuation of the DMARD (moderate: discontinuation; severe: discontinuation with hospitalization or death). **Co-variables:** sociodemographic; clinical and therapy. **Statistical analysis:** incidence rates of discontinuation (IR) per 100 patient-years were estimated using survival techniques with their respective 95% confidence interval [CI]. Comparisons between associated factors were run by Cox bivariate and multivariate regression models. Results were expressed by hazard ratio (HR) and [CI]

**Results:** We included 1054 courses of DMARD treatment in 405 patients (2277.9 patient-years). 78.3% were women with a mean age at diagnosis of 57 ±15 years. During follow-up, 16.3% of patients were taking biological DMARD, 73.3% were using monotherapy and 89% were taking corticoids. There were 369 ADR in 212 patients, 88.9% moderate. Gastrointestinal was the most frequent cause of ADR (26.3%), followed by infections (12.2%). IR are shown in table 1 and the multivariate analysis in table 2. Regarding type of DMARD, Abatacept had the highest risk of ADR development (HR:4.9[2.1–11.2]) compared to the other drugs followed by Gold (HR:1.6[1–2.6]) and Leflunomide (HR:1.4[1.1–1.9]). Methotrexate was the safest drug compared with the others (0.6[0.5–0.8])

Table 1

<b>Global</b>	2277.9	369	16.2	14.6–17.9
Women	1835.4	296	16.1	14.4–18.1
Men	442.5	73	16.5	13.1–20.7
<b>By therapy regimen</b>	1609.5	200	12.4	10.8–14.3
Monotherapy	568.9	132	23.2	19.6–27.5
Double therapy	99.4	37	37.2	26.9–51.4
Triple therapy				
<b>By type of DMARD</b>	2048.3	326	15.9	14.3–17.7
Synthetic	229.5	43	18.7	13.9–25.3
Biological				
<b>By drug</b>	8.3	5	60.6	25.2–
Abatacept	81.5	10	12.3	145.5
Adalimumab	749.7	157	20.9	6.6–22.8
Antimalarials	19	3	15.7	17.9–24.5
Azathioprine	16	4	24.8	5.1–48.8
Certolizumab	65.2	12	18.4	9.3–66.2
Etanercept	9.1	5	54.9	10.5–32.4
Golimumab	18.4	6	32.7	22.9–
Infliximab	340.4	85	25	131.9
Leflunomide	1463.5	206	14.1	14.7–72.7
Methotrexate	83.6	33	39.5	20.2–30.9
Gold	26.3	1	3.8	12.3–16.1
Rituximab	154	45	29.2	28–55.5
Sulfasalazine				0.5–27
				21.8–39.1

Table 2

Monotherapy	1	-	-
Double therapy	2	1.5–	0 0
Triple therapy	4.2	2.5	2.6–
		6.8	
Congestive heart failure	1.8	1.2–	0.002
		2.7	
Liver disease	2	1.2–	0.012
		3.3	

**Conclusions:** The IR of ADR was 16.2%, being similar in all age categories. Gastrointestinal was the main cause of ADR followed by infections. We have found differences in discontinuation rates among DMARD due to ADR, being Abatacept, Gold and Leflunomide the drugs with the highest risk. Methotrexate had a lower risk of ADR compared to other DMARD. Caution should be taken in patients receiving combined therapy and with certain comorbidities

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Rheumatoid arthritis - biological DMARDs

**SAT0165 REASONS FOR bDMARD CESSATION AND SUBSEQUENT PERSISTENCE OF SECOND LINE TREATMENT IN A LARGE REAL WORLD RHEUMATOID ARTHRITIS REGISTRY**

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**Background:** The current recommendations for treating Rheumatoid Arthritis (RA) patients (pts) who fail on conventional disease modifying anti-rheumatic drugs (DMARDs) is to use biologic (b) or targeted synthetic (ts) DMARDs. Pts who fail first (1st) line b/tsDMARDs are recommended to go on other b/tsDMARDs; however, reasons for stopping or switching between bDMARDs according to mode of action and the persistence on treatment are not well characterized in real world patient populations.

**Objectives:** The primary objective was to identify the reasons for stopping 1st line b/tsDMARDs in RA pts treated in the clinical practice setting. The secondary objectives were to identify second (2nd) line b/tsDMARDs choices in pts who stop TNF inhibitors (TNFis) within 6 months (mo) due to lack of efficacy and the persistence on these treatments.

**Methods:** Pts  $\geq 18$  years with confirmed RA who were treated with 1st line b/tsDMARDs, from 1 August 2010 to 30 June 2017, by physicians participating in the OPAL-QUMI database, were included in the analyses. Reasons for stopping b/tsDMARDs were recorded by the treating physician during routine visits. The following b/tsDMARDs were included abatacept (ABA), adalimumab, certolizumab pegol, etanercept, golimumab, infliximab and tocilizumab (TCZ), rituximab (RTX) and tofacitinib (TFB). Data were analysed using descriptive statistics for continuous variables and frequency counts for categorical variables. Persistence on treatment was summarised using Kaplan-Meier (K-M) methodology. Individual TNFis were combined for simplicity.

**Abstract Sat0165 – Table 1.** Patients receiving 1st line treatment by mechanism of action.

First-line Treatment	RTX	TCZ	TFB	ABA	TNFis
Started, n	230	555	518	609	5002
Stopped, n(%)	51(22)	238(43)	105(20)	233(38)	2029(41)
Stopped within 6 months: n(%) <sup>a</sup>	11(22) <sup>a</sup>	41(17) <sup>a*</sup>	57(54)	72(31) <sup>b</sup>	733(36) <sup>a*</sup>

percentage relative to subset stopped treatment  
<sup>a</sup>p<0.001: RTX vs TFB; TCZ vs ABA; TNFis vs TFB  
<sup>b</sup>p<0.0001: TCZ vs TFB; TNFis/ABA vs TFB

**Abstract Sat0165 – Table 2 K-M.** estimates of persistence on 2nd line b/tsDMARDs after discontinuation of 1st line TNFis due to lack of efficacy.

	RTX	TCZ	TFB	ABA	TNFis
N	13	49	25	92	130
6 months, %	75	78	71	61	60
12 months, %	75	57	ND	49	40

ND=not determined

**Results:** A total of 6914 pts received 1st line b/tsDMARDs. Median age was 61 years, median disease duration (RA onset to last visit) was 10 years. The majority

(75%) were females. Treatment was stopped in 2656 pts (38%); 914 (34%) of these stopped within 6 mo of treatment initiation. The highest and lowest percentage of pts stopping treatment within 6 mo was in pts receiving TFB (54%) and TCZ (17%), respectively (table 1). The most common reasons for stopping therapy within 6 mo were lack of efficacy (45%>ABA, 44%>TNFis, 33%>TFB and 27%>TCZ) and adverse reactions (21%>TFB, 20%>TCZ, 15%>TNFis, 13%>ABA). Stopping due to lack of efficacy-primary failure was highest for TFB (23%). The percentage of pts remaining on 2nd line b/tsDMARD treatment after stopping 1st line TNFis due to lack of efficacy was the highest for TCZ (78%) at 6 mo and RTX (75%) at 12 mo (table 2). Median time to stopping 2nd line treatment was 48 mo (95% CI:17–74) for RTX, 21 mo (95% CI:11–62) for TCZ, 21 mo (95% CI:6–21) for TFB; 11 mo (95% CI:8–22) for ABA and 9 mo (95% CI:7–12) TNFis.

**Conclusions:** The primary failure rate is lower than previously reported. In pts who failed 1st line TNFis within 6 mo of commencement due to lack of efficacy, 2nd line TNFis resulted in the lowest treatment persistence. These real world data will assist clinicians with treatment choices post primary TNFis failure.

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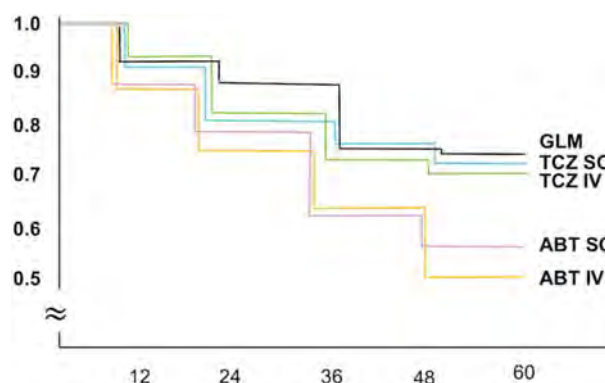
**SAT0166 WHICH BIOLOGIC AGENT IS MOST SUITABLE FOR AN EXTENDED-INTERVAL TREATMENT FOR RHEUMATOID ARTHRITIS ? RESULTS FROM A MULTICENTER STUDY**

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**Background:** Biological disease-modifying antirheumatic drugs (bDMARDs) have made apparent development of treating rheumatoid arthritis (RA). However, prescription of them appeared to be relatively difficult due to high cost. The newest EULAR recommendation advocates tapering of bDMARDs when RA activity is controlled.

**Objectives:** A multicenter clinical study on a longer interval treatment with three bDMARDs, Golimumab (GOL), which is one of TNF inhibitors, and two of non-TNF inhibitor, Tocilizumab (TCZ) and Abatacept (ABT) was investigated.

**Methods:** Patients, who were maintained at low disease activity by DAS28 score for more than 3 months treated with GLM, TCZ, ABT, were enrolled. These selected patients were treated with these drugs with 1.5 fold longer interval of standard schedule for 60 weeks, and the rate of patients, who preserved low disease activity were determined. The patients who were not tolerated these drugs because of the side effects or adverse events, were withdrawn from this study.



**Results:** One hundred thirty-one patients treated with GLM, 149 with ABT (S.C. 61, I.V. 88) and 299 with TCZ (S.C. 87, I.V. 212) were enrolled. Among these, 57 patients treated with GLM (43%), 40 with ABT (26%, S.C. 18, I.V. 22), 93 with TCZ (31%, S.C. 21, I.V. 72) were successfully maintained at low disease activity with

this 1.5 folds longer interval treatment, respectively. The age of patients in ABT group was 73.5±10.6, and significantly higher than those in TCZ (58.8±13.9) and GOL (58.1±14.7) groups. At 60 weeks, DAS28 in ABT group was 3.1±0.5, and significantly higher than those in TCZ (2.6±0.7) and GLM (2.6±0.7) groups. On the other hand, CDAI in GOL was 6.6±3.4, and was significantly higher than those in TCZ (4.4±2.6) or ABT (4.6±2.3) groups. Accordingly, successive rate at 60th week in ABT group was 52% and significantly lower than those in TCZ (69%) or in GOL (73%) groups as shown in figure. Finally, no significant difference in successive rate was observed between s.c. and i.v.

**Conclusions:** This study clarified that TCZ and GLM had higher successive rate than ABT for maintaining low disease activity for 60 weeks by longer interval treatment. This effectiveness might relate to the high therapeutic efficacy of TCZ and low antigenicity of GOL.

**Disclosure of Interest:** None declared

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SAT0167

### COMPARISON OF THE EFFICACY AND TOLERABILITY OF TOCILIZUMAB, SARILUMAB, AND SIRUKUMAB IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS: A BAYESIAN NETWORK META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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**Background:** A humanized, anti-human IL-6 receptor monoclonal antibody, tocilizumab, was developed to block IL-6 signaling and has been used as an effective therapeutic agent for patients that do not respond to methotrexate (MTX) or tumor necrosis factor (TNF) inhibitor. The successful use of tocilizumab in RA stimulated the development of other biologics targeted to the IL-6 pathway, such as anti-IL-6R (sarilumab) or anti-IL-6 (sirukumab) antibodies.

**Objectives:** The relative efficacy and tolerability of tocilizumab, sarilumab, and sirukumab were assessed in patients with rheumatoid arthritis (RA) and an inadequate response to MTX or TNF inhibitors.

**Methods:** We performed a Bayesian network meta-analysis to combine direct and indirect evidence from randomized controlled trials (RCTs) to examine the efficacy and safety of tocilizumab, sarilumab, and sirukumab in RA patients and an inadequate MTX or TNF inhibitor response.

**Results:** Fourteen RCTs, comprising 9,753 patients, met the inclusion criteria. Tocilizumab 8 mg combined with MTX or as monotherapy was the most effective treatment for active RA with an inadequate MTX or TNF antagonist response, followed by sarilumab and sirukumab, regardless of MTX combination. The ranking probability based on the surface under the cumulative ranking curve (SUCRA) indicated that tocilizumab 8 mg+MTX had the highest probability of being the best treatment to achieve the ACR50 response rate, followed by tocilizumab 8 mg, sarilumab 200 mg, sarilumab 200 mg+MTX, sirukumab 100 mg, tocilizumab 4 mg +MTX, sirukumab 100 mg+MTX, sirukumab 50 mg+MTX, sarilumab 150 mg +MTX, adalimumab 40 mg, and sirukumab 50 mg, and placebo+MTX. No significant differences were observed in withdrawals owing to adverse events after treatment with tocilizumab 8 mg+MTX, sirukumab 100 mg+MTX, or sarilumab 200 mg+MTX.

**Conclusions:** In RA patients with an inadequate MTX or anti-TNF therapy response, tocilizumab 8 mg as monotherapy and combined with MTX showed acceptable tolerability and the highest performance based on the ACR50 response rate, followed by sarilumab and sirukumab.

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SAT0168

### MRI RESULTS FOLLOWING DISCONTINUATION OF METHOTREXATE IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH SUBCUTANEOUS TOCILIZUMAB: RESULTS FROM A RANDOMIZED CONTROLLED TRIAL

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**Background:** Although previous studies have established the efficacy of tocilizumab (TCZ) initiated as monotherapy (MONO) for the treatment of rheumatoid arthritis (RA),<sup>1,2</sup> changes in active intra-articular inflammation after discontinuation of methotrexate (MTX) in patients achieving good clinical control with TCZ + MTX have not been evaluated. Magnetic resonance imaging (MRI) effectively images synovitis and osteitis and can detect changes in bone erosion with greater sensitivity than radiography.<sup>3</sup>

**Objectives:** This study used MRI to assess differences in joint damage between patients with RA who achieved low disease activity with TCZ + MTX and then continued or discontinued MTX in the COMP-ACT trial (NCT01855789).

**Methods:** US patients with RA who were inadequate responders to MTX were enrolled; initial combination therapy included MTX (≥15 mg/week orally) plus TCZ 162 mg subcutaneous (SC) either weekly or every 2 weeks. Patients who achieved DAS28-ESR ≤3.2 at week 24 were randomized 1:1 to receive TCZ-MONO or continue TCZ + MTX until week 52 (double blind). A subset of these patients was included in this MRI substudy; 1.5 Tesla MRI was used to obtain images of bilateral hands and wrists at Weeks 24 and 40. Two independent radiologists evaluated images at a central reading facility using RAMRIS (synovitis, osteitis, erosion) and CARLOS (cartilage loss). Outcomes included changes in MRI scores from Week 24 to 40 and the proportion of patients with progression of each score.

**Results:** Of the 296 patients who achieved DAS28 ≤3.2 at Week 24 and were randomized to TCZ + MTX or TCZ-MONO, 79 were enrolled in the MRI substudy (n = 41 and 38, respectively); 74.7% were women, and the mean (SD) age was 56.3 (12.8) years. Patient demographics in the MRI substudy were similar to overall study demographics. Mean changes from Week 24 to 40 in bone erosion, synovitis, osteitis and cartilage loss scores were not significantly different between the TCZ + MTX and TCZ-MONO groups for both bilateral hands and the dominant hand (table 1). There were no significant differences between the groups in the proportion of patients with no progression in each outcome measure (range, 89.7% to 97.4% with TCZ + MTX and 87.9% to 100.0% with TCZ-MONO).

**Table 1** MRI Changes in Patients Receiving TCZ in Combination With MTX or TCZ as Monotherapy

	Both Hands			Dominant Hand		
	TCZ + MTX (n = 41)	TCZ-MONO (n = 38)	Difference (95% CI) (TCZ-MONO minus TCZ + MTX)	TCZ + MTX (n = 41)	TCZ-MONO (n = 38)	Difference (95% CI) (TCZ-MONO minus TCZ + MTX)
Bone erosion score (0-250) mean (SE)	-0.06 (0.18)	0.18 (0.19)	0.24 (-0.21 to 0.60)	0.06 (0.24)	0.49 (0.25)	0.43 (-0.14 to 1.01)
Synovitis score (0-24) mean (SE)	-0.24 (0.15)	-0.10 (0.15)	0.06 (-0.30 to 0.41)	-0.22 (0.12)	-0.11 (0.12)	0.11 (-0.16 to 0.40)
Osteitis score (0-75) mean (SE)	-0.16 (0.34)	0.37 (0.36)	0.53 (-0.36 to 1.36)	-0.39 (0.52)	0.69 (0.54)	1.07 (-0.16 to 2.33)
Cartilage loss score (0-100) mean (SE)	0.20 (0.14)	-0.03 (0.15)	-0.23 (-0.58 to 0.11)	0.11 (0.10)	-0.05 (0.19)	-0.16 (-0.59 to 0.27)

MTX, methotrexate; TCZ, tocilizumab; TCZ-MONO, TCZ monotherapy

\* ANCOVA model for estimated means includes Week 24 bone erosion as a covariate, treatment group and the randomization stratification factors: DAS28 remission status at Week 24 (< 2.6, ≥ 2.6 to < 3.2), patient anti-TNF exposure (Yes or No) and baseline weight-by-dosing group (< 80 kg q2w, 80 to < 100 kg q2w, 80 to < 100 kg qw, ≥ 100 kg qw)

**Conclusions:** In patients who achieved low disease activity with TCZ + MTX, MRI changes were minimal and showed no difference in the response of active intra-articular inflammation in patients who discontinued MTX vs those who continued TCZ + MTX within the period of observation, consistent with the result of similar mean change in DAS28 between the groups in the primary analysis.

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**SAT0169 NO EVIDENCE THAT CONCOMITANT GLUCOCORTICOID THERAPY AFFECTS EFFICACY AND SAFETY OF TOCILIZUMAB MONOTHERAPY IN RHEUMATOID ARTHRITIS CLINICAL TRIALS**

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**Background:** For rheumatoid arthritis (RA) patients included in clinical trials, background treatment with glucocorticoids (GCs) is quite common (40–60%), but their potential contribution to efficacy and safety of the disease modifying anti-rheumatic drug (DMARD) tested in that trial has rarely been evaluated.

**Objectives:** To establish whether a stable GC dose at baseline and during the study contributed to the efficacy and safety of TCZ monotherapy initiated in RA patients in 4 TCZ RCTs. In addition, to investigate the same issue in the comparator arms of these trials, in which adalimumab (ADA) or methotrexate (MTX) was initiated.

**Methods:** Data from 4 randomized controlled double-blind trials (AMBITION, ACT-RAY, ADACTA and FUNCTION) with TCZ monotherapy arms was analysed in this post hoc analysis [1–4]. Study participants were MTX-naïve, intolerant or had an inadequate response to conventional synthetic DMARDs (csDMARD-IR). Because of differences between the studies in region, and baseline RA duration and disease severity, analyses were done separately for each study. Stable GC dose at baseline was allowed and was to be continued unchanged during the first 24 weeks. Analyses of covariance (ANCOVA) of change from baseline to Week 24 in CDAI and DAS28 and logistic regression analyses at Week 24 for CDAI remission and ACR50 were performed. Repeated measures analyses using all visits up to week 24 were also done. Incidence rates of serious adverse events (SAEs) were assessed by GC use.

Table 1 Disease Activities at week 24 of GC Users versus non-GC Users per Treatment per Study

**Results:** Baseline characteristics were mostly comparable between GC users and non-GC users in each treatment arm for each study. The adjusted differences (95% CIs) of CDAI change at week 24 between GC and non-GC users in TCZ arms of AMBITION, FUNCTION, ACT-RAY and ADACTA were -1.4 (-4.8, 2.1), 0.8 (-2.5, 4.1), 1.2 (-4.0, 6.3) and -4.2 (-9.7, 1.4), respectively (table 1). CDAI remission rates, ACR50 response rates and DAS28 score changes at 24 weeks neither were significantly different between GC users and non-GC users in the TCZ arms, nor in the MTX and ADA arms (table 1). Repeated measures analyses to week 24 showed no significant differences in DAS28 or CDAI. Statistically significant predictors for the various clinical outcomes included baseline CDAI, baseline DAS28, age, sex, RA duration and region. A numerically higher but not significantly different SAE rate was seen in the GC-arms of all four trials, compared to the non-GC-arms.

**Conclusions:** No evidence was found that GC treatment at baseline and continued at a stable dose affects either clinical efficacy or safety over 24 weeks of TCZ, MTX, or ADA monotherapy initiated at baseline in RA clinical trials.

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**SAT0170 ANTI-IL-6 THERAPY MODULATES LEPTIN IN PATIENTS WITH RHEUMATOID ARTHRITIS**

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**Background:** Leptin is an adipocytokine that plays an important role in the regulation of body weight and also participates both in immune homeostasis and inflammatory processes [1,2]. Chronic systemic inflammation is of major importance in the development of atherosclerosis in rheumatoid arthritis (RA) [3]. IL-6 blocker yields a rapid improvement of endothelial function [4].

**Objectives:** To determine whether the infusion of IL-6 blockade improves the endothelial function by altering circulating Leptin concentrations in patients with RA.

**Methods:** 50 Spanish patients on treatment with anti-IL-6 monoclonal antibody-Tocilizumab who fulfilled the 2010 classification criteria for RA [5] were recruited. Patients with diabetes mellitus or plasma glucose >110 mg/dl were excluded. Leptin serum levels were determined immediately prior to (time 0) and after (time 60 minutes) Tocilizumab infusion by Enzyme-Linked ImmunoSorbent Assay (ELISA).

**Results:** A significant reduction in Leptin concentration was observed following Tocilizumab infusion (mean±standard deviation (SD): 9.24±7.98 ng/ml versus 7.91±7.36 ng/ml, p<0.0011). In addition, a significant positive correlation between Leptin concentration and insulin resistance (HOMA at the time of the study) was found (r= 0.40; p=0.0046). Furthermore, a significant negative correlation between Leptin levels and insulin sensitivity (QUICKI) was disclosed (r= -0.46; p=0.0009).

**Conclusions:** Our study confirms that circulating Leptin concentrations are modulated by anti-IL-6 treatment. In addition, Leptin concentration correlates with insulin resistance and sensitivity. The beneficial effect of anti-IL-6 blockage on cardiovascular mortality in RA may be mediated by reduction in serum levels of leptin.

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SAT0171

### REVERSIBLE DECREASES IN ABSOLUTE NEUTROPHIL COUNT (ANC) IN RHEUMATOID ARTHRITIS (RA) PATIENTS (PTS) ON SARILUMAB: COMPARISON OF DOSE DELAY AND DOSE DECREASE VS CONTINUED TREATMENT

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**Background:** In randomized studies (RCTs: MOBILITY, TARGET and MONARCH), and open-label [OLE] EXTEND, for those patients who experienced decreases in ANC this typically occurred early after initiating sarilumab. For sarilumab patients with decreased ANC in the RCTs and the OLE, we assessed the outcomes associated with either continuing treatment, decreasing the sarilumab dose or delaying the dose.

**Objectives:** The effects of a dose decrease (200 to 150 mg), dose delay (>17 days), vs no change in treatment were evaluated in RA patients who experienced decreased ANC while on sarilumab 150 or 200 mg q2w. Outcomes data from patients in MONARCH, MOBILITY and TARGET, and MOBILITY and TARGET patients entering EXTEND were analyzed to compare the three strategies. In MONARCH, patients received sarilumab 200 mg q2w. In MOBILITY and TARGET, patients received sarilumab 150 or 200 mg q2w. In EXTEND, patients were switched to, or initiated on, 200 mg q2w.

Table 1 Outcomes following dose delay, dose decrease, or continued treatment with sarilumab among pts who experienced ANC <1000/mm<sup>3</sup> at any time

Table: Outcomes following dose delay, dose decrease, or continued treatment with sarilumab among pts who experienced ANC <1000/mm <sup>3</sup> at any time	RCTs		OLE		
	Continued without change (n=88)	Dose delay (n=43)	Continued without change (n=31)	Dose delay (n=82)	Dose decrease (n=62)
Total treated (n)	1346	1351	105 (8)	147 (11)	
ANC <1000/mm <sup>3</sup> at any time (n, %)	105 (8)	147 (11)	24 (23)	15 (19)	
Pts who did not continue* (n, %)	24 (23)	15 (19)	81 (77)	132 (90)	
Normalized on treatment after 21 episodes of ANC <1000/mm <sup>3</sup> (n, %)	31 (35)	27 (63)	29 (94)	66 (80)	51 (82)
Median time to normalization for patients with 1 episode (days)	9	15	27	17	28
Pts with >1 episode of ANC <1000/mm <sup>3</sup> who normalized on treatment** (n, %)	6 (7)	6 (14)	3 (10)	33 (40)	22 (35)
Renormalized after treatment discontinuation (n, %)	2 (3)	9 (21)	1 (3)	7 (9)	5 (8)
Did not normalize after 31 episode of ANC <1000/mm <sup>3</sup> (n, %)	11* (13)	7* (16)	1 (3)	9 (11)	8 (13)
Discontinued treatment due to abnormal ANC after last episode (n)	1	1	1	9	6
ANC at last episode: (<2000/<1500/<1000/mm <sup>3</sup> )	10/1/0	0/0/1	1/0/0	2/6/1	1/4/1

\*10 and % pts enrolled into EXTEND  
 \*\*ANC <500/mm<sup>3</sup> confirmed or had evidence of an infection or had ANC 500 to 1000/mm<sup>3</sup> and were discontinued at the investigator's discretion.  
 \*\*\*pts >1 episode of ANC <1000/mm<sup>3</sup> was defined as pts who, at least once, experienced ANC <1000/mm<sup>3</sup>, then displayed normalized ANC levels and were able to resume treatment, but later experienced ANC <1000/mm<sup>3</sup> again.

**Methods:** In RCTs, patients were required to have baseline neutrophil levels  $\geq 2000/\text{mm}^3$ . In RCTs and EXTEND, patients who experienced ANC <500/mm<sup>3</sup> (grade 4 [G4] neutropenia) or  $\geq 500$  to <1000/mm<sup>3</sup> (grade 3 [G3] neutropenia) and signs of infection were required to permanently discontinue treatment. Patients with G3 neutropenia (no signs of infection) temporarily discontinued treatment (or permanently discontinued at the investigators discretion); patients were retested  $\leq 48$  hrs after identifying decreased ANC and before the next scheduled dose, and could resume if ANC  $\geq 1000/\text{mm}^3$ . In RCTs, patients restarted sarilumab at their randomized dose. In OLE, patients restarted sarilumab at 150 mg q2w, as per the protocol, or otherwise were able to restart at 200 mg q2w at the investigators discretion. In OLE, patients who required a dose decrease to 150 mg q2w sarilumab

received the reduced dose for the remainder of the treatment period. ANC normalization was defined as a return to the patient's baseline or within normal ranges.

**Results:** Of the 8–11% of patients who experienced ANC <1000/mm<sup>3</sup> at any time, 81/105 (RCTs) and 132/147 (OLE) were able to continue or reinstate sarilumab; the majority of patients who experienced ANC <1000/mm<sup>3</sup> one or more times displayed normalized ANC levels and continued treatment when ANC  $\geq 1000/\text{mm}^3$  (25/38 in RCTs; 29/31 in OLE). The majority of patients who dose delayed (27/43 in RCTs; 66/82 in OLE) or dose decreased (51/62, OLE) before ANC normalized resumed treatment.

**Conclusions:** More than three-quarters of patients who discontinued treatment until ANC normalized were able to reinstate at their randomized dose (RCT), or at the open-label study dose (200 mg q2w; OLE) or were able to resume at the lower dose (150 mg q2w; OLE).

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SAT0172

### LONG-TERM EFFICACY WITH 5-YEAR-RADIOGRAPHIC RESULTS AND SAFETY OF SARILUMAB IN COMBINATION WITH csDMARDs IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Long-term data are being collected on sarilumab in combination with csDMARDs in patients with RA originally enrolled in six trials (TARGET, NCT01709578; MOBILITY, NCT01061736; NCT01764997; NCT01768572; NCT02057250; NCT01217814) including those who continued into extension trials.

**Objectives:** To assess efficacy and safety of long-term treatment with sarilumab plus csDMARDs in patients with RA.

**Methods:** Long-term efficacy and safety data were available in patients enrolled in placebo-controlled trials of sarilumab 150 or 200 mg sc q2w who continued into the open-label EXTEND trial of sarilumab 200 or 150 mg sc q2w (NCT01146652). Safety data were evaluated in 2887 patients who received  $\geq 1$  dose of sarilumab sc in combination with csDMARDs.

**Results:** Clinical and radiographic efficacy of sarilumab plus csDMARDs was maintained over 5 years' follow-up (table 1; figure 1). Initial treatment with either dose of sarilumab was associated with significantly better radiographic outcome than placebo. Initial treatment with sarilumab 200 mg portended better radiographic outcome than sarilumab 150 mg or placebo. Mean duration of sarilumab treatment in the safety population was 2.6 years (max 6.8), representing 7412 cumulative patient-years of exposure. Incidence rate of adverse events of special interest (AESIs; table 2) was generally stable over >5 years' treatment, with no signal for increased rate of any AESI (including serious AEs and serious infection) over time. Incidences of injection site reaction, ANC <1 Giga/L, & elevated ALT declined over time.

Table 1 Clinical response, % (number of patients assessed)

Initial treatment	DAS28-CRP<2.6 (remission)			CDAI ≤2.8 (remission)		
	MOBILITY (52 weeks)→EXTEND					
Week	148	196	244	148	196	244
Placebo	58.6 (249)	59.3 (231)	63.8 (207)	28.1 (249)	32.9 (231)	36.4 (209)
Sarilumab 150 mg	61.9 (239)	63.0 (219)	63.1 (195)	30.5 (239)	32.6 (221)	34.2 (199)
Sarilumab 200 mg	67.5 (237)	65.3 (225)	70.7 (208)	36.6 (238)	36.7 (226)	39.8 (211)
Week	48	96	144	48	96	144
Placebo	38.1 (139)	39.3 (122)	41.0 (117)	15.9 (138)	19.5 (123)	17.2 (116)
Sarilumab 150 mg	44.9 (136)	49.1 (116)	53.8 (104)	18.1 (138)	22.4 (116)	23.4 (107)
Sarilumab 200 mg	41.4 (140)	49.2 (126)	53.5 (114)	15.7 (140)	23.0 (126)	24.3 (115)

Table 2 Treatment emergent adverse event rates per 100 patient-years

	Any AE/SAE	147/9.6
AEs of special interest	AE leading to death/discontinuation	0.4/9.1
	Infections (all/serious/opportunistic/TB)	54.7/3.7/0.9/0.1
	Injection site reactions	24.9
	Hypersensitivity reaction	5.6
	Malignancy (all/excluding NMSC)	0.7/0.5
	MACE (primary/narrow)	0.4/0.5
	Medically adjudicated GI perforation	0.1
	Lupus-like syndrome	0.1

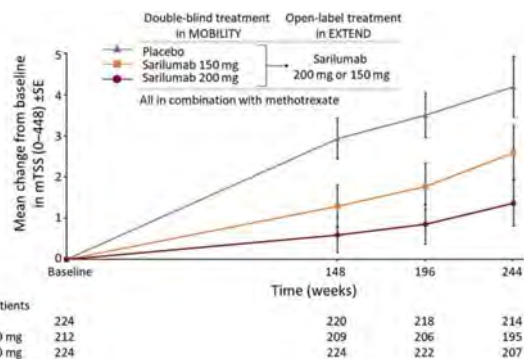


Figure 1 Change in mTSS in patients who completed 52-week double-blind MOBILITY study and subsequently entered open-label EXTEND study. **Conclusions:** Clinical efficacy and inhibition of progression of structural damage with sarilumab plus csDMARDs was sustained up to 5 years of follow-up in patients with diverse prior pharmacologic therapies. The safety profile of sarilumab plus csDMARDs remained stable over >5 years' treatment.

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**SAT0173 EFFECTS OF DENOSUMAB, A SUBCUTANEOUS RANKL INHIBITOR, ON THE PROGRESSION OF STRUCTURAL DAMAGE IN JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH csDMARDs: RESULT FROM THE LONG-TERM TREATMENT OF PHASE 3, DESIRABLE STUDY**

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**Background:** Denosumab is a fully human monoclonal antibody (IgG<sub>2</sub> subclass) that inhibits bone resorption by inhibiting RANKL, a key mediator of osteoclast formation, function, and survival. The effect of denosumab on the progression of joint damage in patients with RA on csDMARDs background treatment from the first 12 months (double-blind, placebo-controlled) of the Phase 3 DESIRABLE study has previously been reported.<sup>1</sup>

**Objectives:** To evaluate the safety and efficacy of long-term treatment with denosumab 60 mg every 6 months (Q6M) or every 3 months (Q3M) with RA patients in long term treatment phase of the DESIRABLE study.

**Methods:** Upon completion of the 12-month, double-blind phase, all patients were to receive denosumab 60 mg/Q6M or 60 mg/Q3M and calcium and vitamin D daily during the 36-month, open-label extension phase. Patients were randomized in a 1:1:2:2 ratio to receive one of four treatments (figure 1). In this analysis, the continuous administration group received 36 months of denosumab treatment, and the cross-over group received 24 months of denosumab treatment (12 month of placebo in DB phase and 24 months of denosumab treatment phase). The radiographic evaluation was the change from baseline to 12, 24 and 36 months in the van der Heijde modified total Sharp score (mTSS). Radiographs of hands and feet at baseline, 12, 24 and 36 months were scored with blinded time order by 2 readers independently. Average score of the 2 readers is used for the analysis. Missing scores were imputed using linear extrapolation/interpolation.

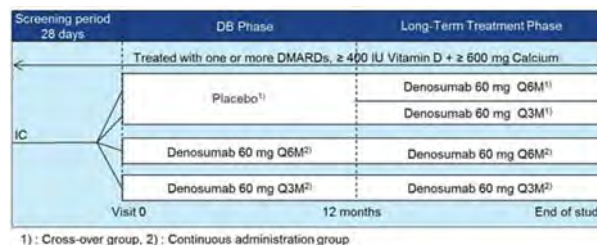


Figure 1 Study design

Characteristic	Visit	Cross-over group		Continuous administration group	
		Placebo/denosumab 60mg Q6M N = 105	Placebo/denosumab 60mg Q3M N = 101	Denosumab 60mg Q6M N = 191	Denosumab 60mg Q3M N = 195
mTSS	12 months	1.29 ± 2.86	1.60 ± 3.62	1.25 ± 4.16	0.98 ± 3.01
	24 months	2.33 ± 4.73	2.05 ± 4.35	2.12 ± 9.10	1.42 ± 4.02
	36 months	2.93 ± 6.56	2.49 ± 4.70	2.26 ± 6.66	1.71 ± 4.59
ES	12 months	0.79 ± 1.76	0.87 ± 2.48	0.70 ± 2.39	0.27 ± 0.98
	24 months	1.23 ± 2.36	1.01 ± 2.48	1.09 ± 3.55	0.36 ± 1.35
	36 months	1.54 ± 3.39	1.18 ± 2.96	0.96 ± 3.36	0.40 ± 1.51
JSN score	12 months	0.51 ± 1.44	0.63 ± 1.75	0.59 ± 2.13	0.71 ± 2.42
	24 months	1.10 ± 2.87	1.04 ± 2.27	1.03 ± 3.13	1.07 ± 3.20
	36 months	1.39 ± 3.83	1.31 ± 2.87	1.30 ± 4.04	1.31 ± 3.67

Table 1 Change from baseline in mTSS, ES and JSN score in DB and long-term treatment phase. Data presented are mean ± SD

**Results:** 667 (placebo/Q6M (P/Q6M), n=113; placebo/Q3M (P/Q3M), n=110; Q6M, n=222; Q3M, n=222) received at least one dose of study drug, and 607 (P/Q6M, n=105; P/Q3M, n=103; Q6M, n=199; Q3M, n=200) completed the DB period and entered the long-term extension. In both continuous administration and



cross-over group, sustained inhibition of mTSS and erosion score (ES) progression was observed during long-term treatment phase (table 1). No effect on joint space narrowing (JSN) was observed (table 1). Overall proportions of patients with no progression (ie, mTSS change  $\leq 0.5$ ) at 36 months were 56.8% in P/Q6M, 53.3% in P/Q3M, 66.3% in Q6M group, and 65.7% in Q3M group. Incidence of adverse events (AEs), serious AEs and AEs leading to discontinuation of study drug were similar across treatment groups. No events of atypical femoral fracture were observed.

**Conclusions:** Denosumab treatment was associated with sustained inhibition of progression of joint destruction for up to 36 months and was generally well tolerated in Japanese patients with RA on csDMARDs. Denosumab has the potential to be a new therapeutic option to inhibit the progression of structural damage for patients with RA.

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#### SAT0174 DOES ABATACEPT INCREASE PERIOPERATIVE ADVERSE EVENTS IN PATIENTS WITH RHEUMATOID ARTHRITIS COMPARED WITH CONVENTIONAL SYNTHETIC DISEASE MODIFYING DRUGS? - A RETROSPECTIVE MULTICENTER NESTED CASE-CONTROL STUDY

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**Background:** Abatacept (ABT) is clinically used as the only T-cell modifier available for rheumatoid arthritis treatment and has shown similar efficacy as tumour necrosis factor inhibitors and a safer profile, especially a lower infection ratio in registry data. Latourte et al. recently published the results of perioperative complications of orthopaedic and other types of surgery in patients using ABT. However, they did not compare the complication rates with those in patients who received

csDMARDs. It remains unknown whether ABT is associated with more postoperative complications than conventional synthetic DMARDs (csDMARDs).

**Objectives:** The aims of this study were to investigate whether ABT is associated with more adverse events after orthopaedic surgery compared with csDMARDs and, if so, to identify significant risk factors for those events.

**Methods:** A retrospective multicenter nested case-control study was performed in 18 institutions. Patients receiving ABT were matched individually with patients receiving csDMARDs and/or steroid. Serious adverse events were defined as surgical site infection, delayed wound healing, deep vein thrombosis or pulmonary embolism, flare-up, serious infection in other organs. The incidence rates of serious adverse events in both groups were compared with Mantel-Haenszel test. Risk factors for serious adverse events in the ABT group were analyzed by logistic regression model.

**Results:** A total of 3358 cases were collected. After inclusion and exclusion, 2651 patients were selected for matching, and 194 patients in 97 pairs were chosen for subsequent comparative analyses between the ABT and control groups. No between-group differences were detected in the incidence rates of each adverse event or in the combined incidence rate of adverse events. The odds ratio of the history of serious infection for serious adverse events was 12.6 (95%CI 1.12-141, P=0.04) in patients who received ABT and underwent orthopaedic surgery.

**Conclusions:** Compared with csDMARDs and/or steroid without ABT, adding ABT to the treatment does not appear to increase the incidence rates of postoperative adverse events in rheumatoid arthritis patients undergoing orthopaedic surgery. A history of serious infection is a significant risk factor for both infection and other serious adverse events, and such patients should be treated with particular caution.

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#### SAT0175 RESPONSE TO BIOLOGIC TREATMENT IMPROVES SEXUAL HEALTH ASSESSED BY THE QUALISEX SCORE IN RA

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**Background:** Sexual health of RA patients is an aspect of the care often neglected and about which little is known. Qualisex is a simple (10 questions) and valid tool investigating impact of RA on sexuality. This tool can be useful to assess this important aspect of quality of life. (Gossec and al, *Clin Exp Rheum*, 2012).

**Objectives:** Qualisex questionnaire was used in active RA patients of the ROC (Rotation or change) study (Gotteberg et al, *JAMA* 2016) in order to investigate the association between disease activity and response to a biologic treatment and sexual health.

**Methods:** Among 153 patients of the randomized controlled trial "ROC", which compared a second anti-TNF to a non-TNF biologic in RA patients with inadequate response to a first anti-TNF. Qualisex questionnaire was proposed to 83 RA patients, and 57 of them filled the questionnaire before and after 6 months of their allocated biologic. Changes in the qualisex score was analyzed according to the variation of the clinical and biological parameters.

**Results:** The mean age of the 57 RA patients studied was 50.2 (9.6) years. The mean duration of disease was 11.2 (9.5) years, and 43 (75.4%) were female. After 6 months of treatments, 19 were considered with a good response to the treatment according to EULAR response (DAS 28 VS  $< 3.2$  and a variation of 0.6 of the DAS from the base line).

The mean value of qualisex score was 4.05 (+/- 2.53) at V0 and 3.91 (+/- 2.45) after 6 months of treatment. The variation of the qualisex score was more important among the 19 responder patients than among the 43 patients with a persistently active disease. Changes in the qualisex score was significantly correlated to the changes in DAS28, in asthenia, and in SF36 mental score, but not with changes in pain, or in SF36 physical score.

Variables correlation with qualisex score P value

Variation of DAS 28 CRP 0.33 0.01

Variation of DAS 28 VS 0.27 0.04

Variations of asthenia 0.31 0.03

Variation of pain 0.13 NS

Variations of SF 36 physical score -0.21 NS

Variation of SF36 mental score -0.3 0.03

**Conclusions:** This first study of sexual health of RA patients in a randomized trial demonstrates an improvement in sexual health in patients responders to a biologic treatment. Improvement of sexual health was associated with a decrease in disease activity and asthenia.

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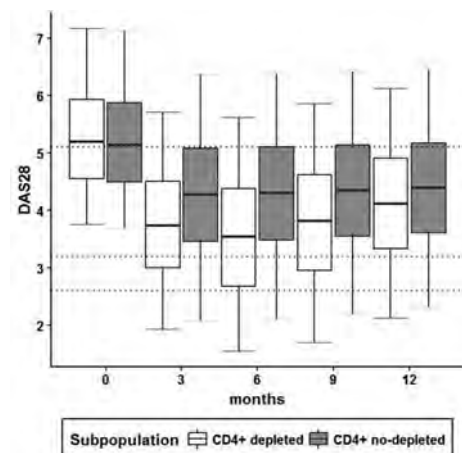
#### SAT0176 CONTRIBUTION OF CD4+ T CELLS DECREASE ON CLINICAL RESPONSE TO RITUXIMAB IN RHEUMATOID ARTHRITIS

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**Background:** Rituximab (RTX) is approved for the treatment of rheumatoid arthritis (RA), but there is a large inter-individual variability in clinical response. A better response was previously associated with a decrease in CD4+ T cell counts [1, 2].

**Objectives:** This study aimed at analyzing the contribution of CD4+ T cell decrease in the clinical response in RA patients treated with RTX.

**Methods:** In this retrospective monocentric observational study, 52 patients were assessed. All patients had received 2 infusions of 1000 mg of RTX 2 weeks apart. Disease activity score in 28 joints (DAS28) was used as clinical endpoint. RTX serum concentrations, peripheral blood CD4+ counts, and DAS28 were measured before and after each RTX infusion and at 3, 6 and 9 months after last infusion. A population PK-PD model, including a physiological turnover and direct response model, was developed to estimate the probability of CD4+ counts decrease. The turnover model was used to describe the effect of RTX on CD4+ T-cell counts, and the direct model was used to describe both RTX and CD4+ T cell count effect on DAS28.



**Results:** The probability of CD4+ counts decrease was estimated at 0.75. Patients with a CD4+ decrease had a higher  $\Delta$ DAS28 than the patients without CD4+ decrease, with a maximal  $\Delta$ DAS28 of -1.34 and -0.64 in patients with and without CD4+ cell decrease, respectively. Moreover, at M6, patients with CD4+

cell decrease had a median DAS28 of 3.5 (IQR: 2.7 – 4.4), among them 39.5 % with low disease activity (DAS28 $\leq$ 3.2) and 22.3 % in remission (DAS28<2.6). At the same time point, median DAS28 of patients without CD4+ cell decrease was 4.3 (IQR: 3.5 – 5.1), among them 17.7 % with low disease activity, and 8.6 % in remission (see Figure 1 Box plot of DAS28 in patients with and patients without CD4+ decrease.).

**Conclusions:** This is the first study to quantify the contribution of CD4+ T cell decrease to the clinical response in RA patients treated with RTX.

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- Lavielle M, et al. Repeated decrease of CD4+ T-cell counts in patients with rheumatoid arthritis over multiple cycles of rituximab treatment. *Arthritis Res Ther* 2016.

**Disclosure of Interest:** A. Bensalem: None declared, D. Mulleman Grant/research support from: Abbvie and Nordic Pharma, Consultant for: MSD, Novartis, UCB and Pfizer, G. Thibault: None declared, N. Azzopardi: None declared, G. Paintaud Grant/research support from: Novartis, Roche Pharma, Genzyme, MSD, Chugai and Pfizer, P. Goupille Consultant for: Abbvie, Biogaran, BMS, Hospira, Janssen-Cilag, MSD, Pfizer, Sanofi-Genzyme and UCB, D. Ternant Consultant for: Amgen and Sanofi

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#### SAT0177 REAL-WORLD INTERRUPTIONS IN JANUS KINASE INHIBITOR THERAPY OBSERVED AMONG BIOLOGIC-NAÏVE AND BIOLOGIC-EXPERIENCED RHEUMATOID ARTHRITIS PATIENTS

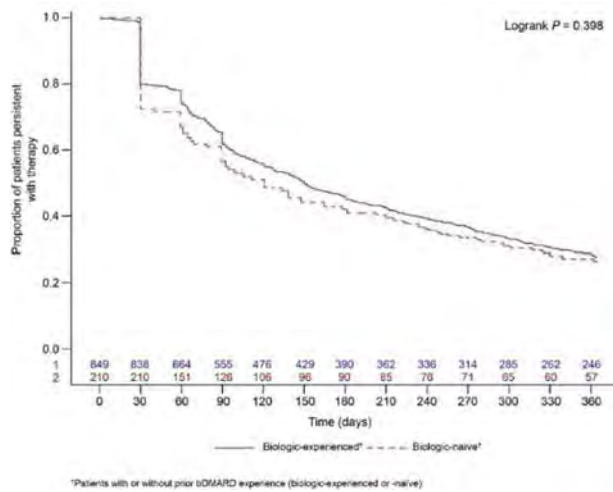
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**Background:** Orally administered janus kinase inhibitors (JAKi) can be used to treat moderate-to-severe rheumatoid arthritis (RA).

**Objectives:** Examine real-world patterns of use, including interruptions in therapy and switching, in biologic-naïve and biologic-experienced patients with RA newly prescribed a JAKi.

**Methods:** A retrospective analysis was performed using healthcare claims data from the Optum Research Database. Commercial and Medicare Advantage patients aged  $\geq$ 18 years were included with:  $\geq$ 1 pharmacy claim for a JAKi 01 January 2012–29 February 2016 (index date = date of first claim); continuous enrollment in health plan for  $\geq$ 12 months before and 13 months post-index; and  $\geq$ 1 claim with a RA diagnosis (ICD-9 = 714.0x; ICD-10 = M05\* or M06\*) during baseline or on the index date. A variable length pre-index period to 01 January 2006 was implemented to capture certain measures. Persistence was defined as the time from index prescription fill to earliest gap in fills  $\geq$ 30 days (interruption) or switching to a biologic disease-modifying antirheumatic drug (bDMARD). Patients were classified as being: persistent with the index therapy for the full year, switching before interruption, switching after interruption, interruption with restart, and interruption without restart (discontinuation). Patients were assigned to two groups: those with and without  $\geq$ 1 claim for bDMARD treatment during the variable length pre-index period (biologic-experienced and biologic-naïve). Data were expressed as % or mean (SD). Sensitivity analyses assessed prescription fill gaps  $\geq$ 90 days.

**Results:** Of 1059 patients who met the inclusion criteria, 80.2% were biologic-experienced, 81.8% female, mean age 56.2 (11.8) years. More biologic-naïve patients (48.6%) had Medicare Advantage coverage than biologic-experienced (22.3%). For the primary analysis, 72.4% of patients were not persistent for the 1-year following initiation of a JAKi, with 39.1% not persistent beyond 90 days (figure 1). Among non-persistent patients, 42.4% interrupted and restarted a JAKi (time from index to restart, 168.9 [83.8] days), 16.8% switched to a bDMARD before interruption, 13.3% switched after interruption and 27.5% discontinued bDMARD and JAKi therapy (time to discontinuation, 148.4 [117.6] days). More biologic-naïve than biologic-experienced patients neither initiated a bDMARD nor restarted a JAKi after interruption (44.2% vs 23.3%, respectively;  $P<0.001$ ). For the sensitivity analysis, 52.6% were non-persistent for the full year.



**Figure 1** Kaplan-Meier curve of persistence with JAKi therapy

**Conclusions:** Most patients (80.2%) newly initiating JAKi therapy had prior bDMARD experience. Over 70% were non-persistent with JAKi treatment for 1 year, with 39% non-persistent beyond 90 days. For non-persistent patients, the pattern of JAKi use was characterized most as interrupting with restart (42%), followed by switching (30%), and then discontinuation (28%). Reasons for the high non-persistence rate are unknown but may include suboptimal efficacy or intolerance. Further research is needed to elucidate these points.

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## SAT0178 PREDICTORS OF DRUG SURVIVAL OF ABATACEPT IN RHEUMATOID ARTHRITIS – RESULTS FROM A LARGE NATIONAL QUALITY REGISTER COHORT STUDY

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**Background:** Abatacept is a biologic disease modifying anti-rheumatic drug (bDMARD) used to treat rheumatoid arthritis (RA). There is growing experience with abatacept in many countries. National registers are useful resources for investigation of long term real world outcomes.

**Objectives:** To compare the effectiveness of abatacept in the treatment of RA between bionative patients and patients with previous bDMARD treatment, and to investigate predictors of remaining on treatment with abatacept.

**Methods:** This was an observational cohort study, based on a national quality register database. Patients with a diagnosis of RA who initiated treatment with abatacept between April 1, 2006 and November 20, 2017, were included. Patients were censored at abatacept discontinuation, death, migration, or the end of the study period. Analyses were stratified by previous exposure to bDMARDs. Survival on drug was estimated using the Kaplan-Meier method. Predictors of discontinuation of abatacept were investigated in Cox Proportional Hazards analyses, with significance-based backwards stepwise selection of variables for the final multivariate model.

**Results:** A total of 2716 patients with RA (80 % females, mean age 59 years, mean duration of RA 14 years) started abatacept during the study period. Of these, 17 % had no previous bDMARD treatment (bionative patients), 27 % had received 1 bDMARD previously, and 56 % had been treated with  $\geq 2$  bDMARDs.

Fifty percent each of the patients received intravenous and subcutaneous therapy. At the time of abatacept initiation, 57 % were on methotrexate (MTX), and 48 % were treated with glucocorticosteroids. There were significant differences in drug survival across categories of previous bDMARD exposure ( $p=0.002$ ). The median survival time on treatment was 2.23 years for bionative patients (95 % confidence interval (CI) 1.69–2.79), 1.68 years for those with 1 previous bDMARD (95 % CI 1.34–2.01) and 1.56 years for those with  $\geq 2$  previous bDMARDs (95 % CI 1.35–1.76). At 6 months, 88 % of bionative patients remained on abatacept, compared to 74 % at 12 months. The corresponding figures for those with 1 or  $\geq 2$  previous bDMARDs were 78 % and 61 %, and 76 % and 59 %, respectively. In bivariate analyses, bionative patients were less likely to discontinue treatment compared to those treated with  $\geq 2$  previous bDMARDs previously (Table). Bionative patients were more often male (28 % vs 18 %) and had lower pain scores (mean Visual analogue scale score 58 vs 62) compared to those previously exposed to  $\geq 2$  bDMARDs. Measures of disease severity were associated with reduced drug survival (Table), but age, RA duration and method of administration had no significant impact on discontinuation. In the final multivariate model, pain increased the risk of abatacept discontinuation, whereas male patients and those on concurrent MTX had a reduced risk of stopping abatacept (Table).

### Significant predictors for abatacept discontinuation. Cox regression analysis

		Unadjusted analysis HR (95 % CI)	Multivariate analysis = final model HR (95 % CI)
Sex	Male	0.85 (0.75-0.96)	0.86 (0.74-0.98)
No of previous bDMARDs	$\geq 2$ bDMARDs	reference (1.0)	*
	Bionative	0.78 (0.68-0.90)	*
	1 bDMARD	0.94 (0.84-1.05)	*
Baseline clinical characteristics	DAS28-CRP (per SD)	1.11 (1.04-1.17)	*
	VAS pain (per SD)	1.14 (1.08-1.21)	1.14 (1.07-1.20)
	Current Methotrexate	0.86 (0.78-0.96)	0.85 (0.76-0.95)
	HAQ-DI (per SD)	1.10 (1.04-1.17)	*

\*Not included in the final model

**Figure 1.** Significant predictors for abatacept discontinuation. Cox regression analysis\*Not included in the final model

**Conclusions:** Survival on abatacept was significantly longer in bionative RA patients compared to those previously exposed to bDMARDs. In the bionative subset, 50 % of the patients remained on treatment after 2.2 years. Concomitant MTX therapy, male sex and low pain scores were associated with longer drug survival for abatacept.

**Disclosure of Interest:** G. Cagnotto Paid instructor for: Novartis, M. Willim: None declared, J.-Å. Nilsson: None declared, S. Saevarsdottir: None declared, C. Turesson Grant/research support from: AbbVie, Bristol Myers-Squibb, Roche. The present study was supported by an unrestricted grant from Bristol Myers-Squibb, Consultant for: MSD, Bristol Myers-Squibb, Roche, Paid instructor for: AbbVie, Bristol-Myers Squibb, Janssen, MSD, Pfizer, Roche and UCB

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## SAT0179 THE BLOOD B-CELL SUBSETS AND EFFECT OF TOCILIZUMAB THERAPY ON THEM IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** The use of the IL-6 receptor antagonist, tocilizumab (TCZ), in rheumatoid arthritis (RA) produce pleiotropic effects that also involve circulating B-cells. Preliminary reports have suggested that B cell function and humoral immune responses might be modulated by TCZ treatments in RA pts.

**Objectives:** To assess the effect of 12 months (mo) TCZ therapy on B-cell phenotype and gene expression in RA and to analyze the association between B-cell subsets and RA activity.

**Methods:** 24 active RA pts (20 F/4 M); median age 55[49; 64] years; disease duration 72[24; 108]m; DAS28 score 5,8[5,3;6,3]; RF+100%, ACCP+ 87% were treated in an open-label study with tocilizumab (8 mg/kg every 4 weeks). Immunophenotyping was performed at baseline and 12 mo. Pts were assessed for B-cell subpopulations and laboratory data: ESR, RF, ACCP, CRP. CD19+B cells, memory B cells (CD19+CD27+), non-switched memory B cells (CD19+CD27+ IgD-), switched memory B cells (CD19+ CD27+IgD-), naive (CD19+CD27-IgD+), double-negative (CD19+CD27-IgD-), transitional (CD19+CD38++CD10+IgD+CD27-) B cells, and plasmablasts (CD19+CD38+++CD27+IgD-CD20-) were analyzed using multicolor flow cytometry.

**Results:** At baseline, the absolute counts of memory B cells (CD19+CD27+) and switched memory B cells (CD19+CD27+IgD-) were lower in RA pts compared to



healthy donors: 0,0015(0,001–0,003) vs 0,003(0,001–0,007) and 0,01(0,005–0,02) vs 0,02(0,01–0,04), respectively,  $p < 0,01$  for both cases. At baseline, a significant correlation was found in RA pts between absolute counts of memory B cells (CD19+CD27+) and CRP ( $r = 0,50$ ,  $p < 0,05$ ); the percentage and absolute counts of plasmablasts (CD19+CD38+++CD27+IgD-CD20-) and RF ( $r = 0,41$  and  $r = 0,52$ ,  $p < 0,05$ ). After 12 mo of TCZ therapy, 54% of pts were categorized as good responders, 46% of pts – as moderate responders according to the EULAR response criteria. Reductions in the percentages and absolute counts of plasmablasts (CD19+CD38+++CD27+IgD-CD20-) were documented after 12 mo of TCZ therapy: 0,15%(0,1–0,3) vs 0,1%(0,01–0,1) and 0,0003(0,00007–0,004) vs 0,0001(0–0,0003), respectively,  $p < 0,05$ . The median percentages/absolute counts of switched memory B cells (CD19+CD27+IgD-) were 6,8%(3,6–11,6)/0,01(0,005–0,02) at baseline; and 3,1%(1,1–4,2)/0,003(0,002–0,006) after 12 mo of TCZ therapy,  $p > 0,05$ . After 12 mo of TCZ therapy, the median percentages and absolute counts of memory B cells (CD19+CD27+) and switched memory B cells (CD19+CD27+IgD-) became lower in RA pts than in the controls: 1,0%(0,7–1,2) vs 2,2%(1,1–3,0); 0,001(0,006–0,003) vs 0,003(0,001–0,007); 3,1%(1,1–4,2) vs 12,8%(9,3–17,0); 0,003(0,002–0,006) vs 0,02(0,01–0,04), respectively,  $p < 0,05$ , respectively, for all cases. Other B-cell subpopulations did not changed after 12 mo of TCZ therapy as compared to baseline values.

**Conclusions:** Immunophenotyping in pts with active RA showed the decrease in the absolute counts of memory B cells (CD19+CD27+), switched memory B cells (CD19+CD27+IgD-) as compared to healthy subjects. Positive correlation between the counts of memory B cells and plasmablasts and values of laboratory indicators of RA (CRP, RF) suggests that B-lymphocytes may be involved in RA pathogenesis. The reduction in the levels of plasmablasts after 12 mo of TCZ therapy was observed.

**Disclosure of Interest:** None declared

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#### SAT0180 TWO-YEAR CONSOLIDATED SAFETY DATA FOR ABP 501 IN PATIENTS WITH MODERATE TO SEVERE RHEUMATOID ARTHRITIS

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**Background:** Biosimilars are expected to have similar long-term safety profiles as originator products.

**Objectives:** To describe the consolidated, 2-year safety data on ABP 501, an approved biosimilar to adalimumab.

**Methods:** We combined individual patient data from a 26-week randomized controlled head-to-head study (parent study) comparing ABP 501 with adalimumab (NCT01970475) and its 72-week open-label extension (OLE) study (NCT02114931) in which all patients received only ABP 501. Safety data were reported by exposure-adjusted incidence rate as the number of subjects with the specified adverse events \*(AEs) per 100 person-years. AEs from the parent and OLE studies were summarized; for each category, patients were included only once based on the 1st event in that AE category. All comparisons were performed descriptively.

**Results:** In the parent study, 264 patients received ABP 501 and 262 patients received adalimumab reference product (RP). Of these, 229 in the ABP 501 arm and 237 in the RP arm entered and were treated in the open-label extension study. The exposure-adjusted incidence rate for treatment-emergent AEs by treatment group are shown in the Table.

Adverse Event Category	ABP 501/ABP 501 (N = 264)	Adalimumab RP/ABP 501 (N = 262)
Exposure-adjusted incidence rate n/E (r)		
Any AE	187/187.6 (99.7)	197/192.2 (102.5)
Any grade $\geq 3$ AE	32/405.2 (7.9)	30/410.6 (7.3)
Any treatment-related AE	72/345.3 (20.9)	79/344.3 (22.9)
Any grade $\geq 3$ treatment-related AE	6/427.2 (1.4)	5/433.6 (1.2)
Any serious AE	34/407.6 (8.3)	32/410.1 (7.8)
Any treatment-related serious AE	6/427.9 (1.4)	2/434.3 (0.5)
Any events of interest	141/261.5 (53.9)	154/254.7 (60.5)
Infections and infestations	125/289.9 (43.1)	130/287.4 (45.2)
Liver enzyme elevations	25/401.4 (6.2)	20/415.6 (4.8)
Hypersensitivity	19/407.7 (4.7)	22/412.2 (5.3)
Injection site reactions	6/417.9 (1.4)	13/418.3 (3.1)
Hematological reactions	6/421.8 (1.4)	7/426.1 (1.6)
Malignancies	6/423.9 (1.4)	3/433.6 (0.7)
Heart failure	1/428.4 (0.2)	2/435.6 (0.5)

n = number of subjects with the specified AE; E = total subjects exposure-time (patient-years); r = exposure-adjusted incidence rate per 100 patient-years ( $100 * n/E$ ).

**Conclusions:** Over the 2-year observation period, there were no meaningful differences in AEs between adalimumab reference product and ABP 501.

**Disclosure of Interest:** E. Krishnan Shareholder of: Amgen Inc., Employee of: Amgen Inc., N. Zhang Shareholder of: Amgen Inc., Employee of: Amgen Inc., H. Wang Shareholder of: Amgen Inc., Employee of: Amgen Inc.

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#### SAT0181 EFFECT OF ANTI-IL-6 THERAPY ON SERUM LEVELS OF METABOLIC SYNDROME-RELATED BIOMARKERS IN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Metabolic syndrome (MeS) is a pathologic state that encompasses metabolic anomalies such as hyperglycemia, dyslipidemia, obesity and hypertension and that, apart from being a cardiovascular risk factor, it has been associated with chronic inflammatory diseases such as rheumatoid arthritis (RA)<sup>1,2</sup>. Ghrelin and retinol binding protein-4 (RBP-4) are two biomarkers associated with MeS, and are also linked to different cardiometabolic risk factors. In this regard, it is known that ghrelin exerts an anti-inflammatory role<sup>2</sup>.

**Objectives:** Since a beneficial effect on endothelial function has been reported for anti-IL-6 therapy<sup>3</sup>, we aimed to evaluate the effect of a single infusion of anti-IL-6 on the serum levels of ghrelin and RBP-4 in patients with RA.

**Methods:** Ghrelin and RBP-4 levels were measured in serum samples from 50 Spanish individuals with RA that fulfilled the 2010 classification criteria<sup>4</sup>, and that were under treatment with the anti-IL-6 monoclonal antibody Tocilizumab. Patients with diabetes mellitus or plasma glucose levels  $>110$  mg/dL were excluded. Blood samples were taken in the fasting state, immediately before (time 0) and after (time 60 minutes) Tocilizumab infusion.

**Results:** A significant increase in serum levels of ghrelin was observed after a single infusion of Tocilizumab (mean  $\pm$  standard deviation: 72.99  $\pm$  58.43 pg/mL versus 134.02  $\pm$  225.93 pg/mL, before and after Tocilizumab infusion,  $p = 0.04$ ). Serum levels of RBP-4 were not affected by the administration of Tocilizumab (mean  $\pm$  standard deviation: 23.48  $\pm$  13.99  $\mu$ g/mL versus 20.90  $\pm$  15.54  $\mu$ g/mL, before and after Tocilizumab infusion,  $p = 0.42$ ).

**Conclusions:** Our results show that ghrelin levels increase after a single infusion of Tocilizumab, supporting the hypothesis that IL-6 blockade has a rapid beneficial effect on factors associated with MeS and cardiovascular risk in RA patients. Hence, long-term treatment with anti-IL-6 may reduce the risk of developing cardiovascular disease in RA.

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**Disclosure of Interest:** None declared

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**SAT0182 TOCILIZUMAB S.C. – IMPROVEMENT OF THE DEPRESSIVENESS, FATIGUE AND PAIN IN RA THERAPY**

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**Background:** The non-interventional ARATA study (NCT02251860) observes the clinical effectiveness and safety of subcutaneous Tocilizumab [TCZ] s.c. treatment under routine conditions over a 2-year period.

**Objectives:** In this interim analysis, the treatment with TCZ s.c., in particular with respect to patient-reported outcomes regarding depression, fatigue and pain, was evaluated.

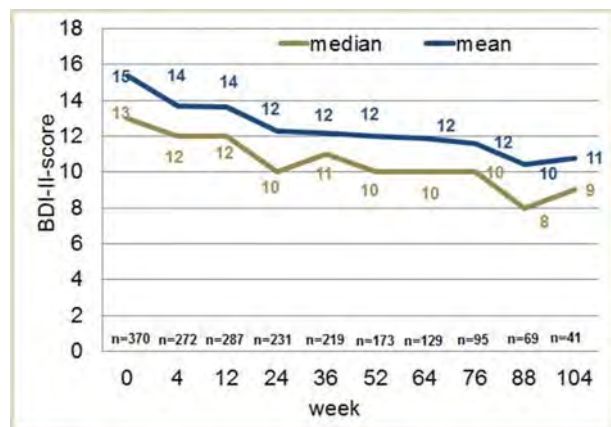
**Methods:** TCZ-naïve patients (Pts) (>18 years) with RA, who receive TCZ s.c. treatment, could be included in the study since 2014. Demographic and disease-specific characteristics, the progression of the disease under treatment, concomitant medications, adverse events (AE) and patient questionnaires were documented.

**Results:** This interim analysis (reporting date 01-FEB-2017) included 912 Pts. 75% of the Pts were female, the average age at baseline (BL) was 57 years, the median disease duration was 8 years. 319 Pts (35%) were pretreated exclusively with sDMARD and 585 Pts (64%) were also pretreated with bDMARD. For the readjustment, TCZ s.c. was applied for 69% without sDMARD, 31% in combination with MTX and for 66% with glucocorticoids.

In the course of the study, 65% of the Pts achieved a DAS28-BSG remission. Furthermore, the functional restrictions in day-to-day life (HAQ-DI D from BL: -0.3) improved. No new safety signals were observed.

By means of the Beck Depression Inventory (BDI-II) score (Englbrecht et al., Arthritis Care Res 2017; 69:58–66), validated for RA, the depressive symptoms could be documented. At baseline, 186 Pts (50%) showed no, 70 (19%) minor, 67 (18%) moderate and 47 (13%) severe depression. Under the treatment with TCZ, the depressive symptoms improved (compare figure 1).

The patients reported a significant improvement of the pain (VAS: average change from BL to week 52 by -21 points and to week 104 by -24 points) as well as the fatigue (VAS: average change from BL to week 52 by -11 points and 104 by -12 points).



**Conclusions:** In the ARATA study, TCZ s.c. demonstrated an effective and persistent reduction in the disease activity of the treated RA patients. The patients confirmed improved physical functionality as well as less fatigue and pain. Depression plays an important role in RA, as the results of BDI-II highlight, whereby the depressive symptoms also improved distinctively under treatment with TCZ s.c.

**Disclosure of Interest:** F. Behrens Grant/research support from: Abbvie, Pfizer, Roche, Chugai, Janssen, Novartis, Consultant for: Abbvie, Pfizer, Roche, Chugai, UCB, BMS, Celgene, MSD, Novartis, Biotest, Janssen, Genzyme, Lilly, Boehringer, Sandoz, M. Englbrecht: None declared, W. A. Biewer: None declared, G.-R. Burmester Consultant for: Lilly, Pfizer, Sanofi, Roche, M. Feuchtenberger Consultant for: MSD, Roche, Abbvie, Chugai, Pfizer, UCB, J.-P. Flacke Employee of: Roche Pharma AG, M. Hofmann Employee of: Chugai Pharma Europe Ltd., P. Kästner: None declared, H. Kellner Consultant for: Roche, T. Klopsch: None declared, C. Kühne Consultant for: Celgene, Roche, Pfizer, Novartis, BMS, H.-P. Tony Consultant for: Roche Pharma, Abbvie, BMS, Chugai, Janssen, Novartis, Sanofi, Lilly, Speakers bureau: Roche Pharma, Abbvie, BMS, Chugai, Janssen, Novartis, Sanofi, Lilly, C. Amberger Consultant for: Chugai, AbbVie, Celgene, MSD, Pfizer, BMS, Hexal

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**SAT0183 SWITCHING FROM ADALIMUMAB TO SARILUMAB IS ASSOCIATED WITH COMPARABLE EFFICACY BUT LOWER FUNCTIONAL IMPROVEMENT VERSUS CONTINUOUS SARILUMAB MONOTHERAPY THROUGH 48-WEEK OPEN-LABEL EXTENSION (OLE) OF THE PHASE 3 MONARCH TRIAL**

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**Background:** Sarilumab is a human mAb blocking IL-6R $\alpha$ . In Phase 3 MONARCH (NCT02332590), sarilumab (200 mg subcutaneously [SC] every 2 wks [q2w] for 24 wks) was superior to adalimumab monotherapy (40 mg SC q2w) in reducing disease activity and improving physical function in RA patients (pts) with an inadequate response or intolerance to methotrexate.

**Objectives:** To assess whether pts who achieved clinical response on sarilumab during MONARCH sustained this response in the OLE and to evaluate efficacy and safety of switching from adalimumab to sarilumab vs continuous sarilumab treatment.

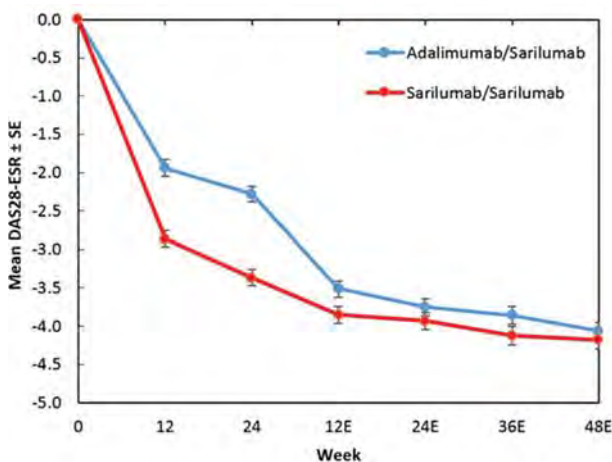
**Methods:** Pts completing the double-blind phase of MONARCH were eligible for the ongoing OLE, in which all pts receive sarilumab (200 mg SC q2w) for a maximum duration of 276 wks. Disease activity, physical function, and safety were assessed regularly.

**Results:** 320/369 Pts enrolled in MONARCH entered the OLE; pts either switched from adalimumab to sarilumab (n=155) or continued on sarilumab (n=165). At OLE entry (Wk 24 of the double-blind phase), the mean  $\Delta$  from baseline DAS28-ESR was -2.28 in the switch group vs -3.36 in the continuation group, and by Wk 48 was -4.06 vs -4.18, respectively. By Wk 48 of the OLE, the proportion of pts in the switch and continuation groups who achieved DAS28-ESR $\leq$ 3.2 was 61.3% vs 61.2%, DAS28-ESR $<$ 2.6 was 43.9% vs 49.7%, and DAS28-CRP $<$ 2.6 was 52.9% vs 52.1%, respectively. From OLE entry to Wk 48, mean HAQ-DI improved in the switch group from 1.21 to 0.91, but did not reach the level of improvements in the continuation group (1.01 to 0.84). See table 1 for ACR responses. After 166 vs 182 cumulative patient-years exposure in the switch vs continuation groups, treatment-emergent adverse events (TEAEs) were observed in 76.1% vs 70.9%, serious TEAEs in 11.0% vs 3.6%, and infections in 41.9% vs 35.8%, respectively, with 2 deaths in the switch group (malignancy; cerebrovascular accident) and 1 death (subarachnoid hemorrhage) in the continuation group. No GI related AEs (ulcerations, perforations or diverticulitis) were observed in either group.

**ACR responses & mean HAQ-DI in the OLE of MONARCH (OLE ITT Popn)**

	Wk 0 OLE		Wk 48 OLE	
	Switch group: Adalimumab 40 mg q2w $\rightarrow$ Sarilumab 200 mg q2w (N=155)	Continuation group: Sarilumab 200 mg q2w (N=165)	Switch group: Adalimumab 40 mg q2w $\rightarrow$ Sarilumab 200 mg q2w (N=155)	Continuation group: Sarilumab 200 mg q2w (N=165)
ACR20/50/ 70, % responders	68.4/35.5/14.2	79.4/50.9/26.1	77.4/59.4/38.1	81.2/63.0/41.8
HAQ-DI, mean	1.21	1.01	0.91	0.84





**Figure 1** Mean V from baseline in DAS28-ESR (OLE population; as observed). **Conclusions:** Switching from adalimumab (40 mg q2w) to sarilumab monotherapy (200 mg q2w) improved the signs and symptoms of RA to a similar level as continuous sarilumab treatment, and was associated with a lower HAQ-DI score, which may have resulted in numerical differences in ACR responses between the two groups.

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the analysis. Treatment response was evaluated as achievement of “BASDAI50” or “ASDAS Clinically important improvement (CII)” at the 3-months’ and 6 months’ visits. Clinical and demographic parameters were compared between current/never and current/previous smoker groups. Demographic and descriptive data are presented by medians/interquartile ranges (IQRs). Groups were compared by non-parametric tests ( $\chi^2$ , Kruskal Wallis and Mann Whitney tests). Kaplan Meier plots, Cox and logistic regression analyses were calculated for treatment adherence and treatment response.

**Results:** Among 561 AS patients included in the study, 506 (90%) had known smoking status (37% current, 35% never, 17% previous smokers). The median follow-up time was 1.9 years (IQR 0.85–3.5) and disease duration was 3.1 years (0.6–7.7). At baseline, current smokers were younger (34, IQR 29–41) compared with never (38, IQR 30–46  $p=0.007$ ) and previous smokers (42, IQR 34–49  $p<0.001$ ). Current smokers had male predominance ( $n=148$ , 43.9%;  $n=85$ , 25.2%); lower erythrocyte sedimentation rate (28 mm/h (13–42); 34 mm/h, (20–49) and higher change in BASMI (40, IQR 10–57.5; 10, IQR 4–30) compared with never smokers (all  $p<0.005$ ). HLA status, body mass index, CRP, baseline disease indexes (BASDAI, BASFI, BASMI, HAQ, ASDAS) and treatment response was not found to be different between current and never smoker patients in our population (table 1). In multivariate analysis, male (OR:1.98; 95% CI (1.39–2.82),  $p<0.01$ ), HLA positive (OR:1.54; 95%CI (1.08–2.18),  $p=0.016$ ) and active DMARD user (OR:1.84; (95%CI 1.12–3.01)  $p=0.015$ ) patients had better treatment response and treatment adherence (HR:1.93; 95% CI (1.36–2.73); HR:1.60; 95% CI (1.13–2.27); HR:1.80; 95% CI (1.10–2.95) all  $p<0.005$ ) but smoking status were not significant ( $p>0.05$ ).

	Smoking status		p	p <sup>1</sup>	p <sup>2</sup>	p <sup>3</sup>	p <sup>4</sup>	p <sup>5</sup>	p <sup>6</sup>	p <sup>7</sup>	p <sup>8</sup>	p <sup>9</sup>	p <sup>10</sup>	p <sup>11</sup>	p <sup>12</sup>	
	Current	Never														
Number, n (%)	208 (37)	298 (53)	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001
Age, median (IQR)	34 (29-41)	38 (30-46)	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001
Sex, %	43.9	25.2	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001
Disease duration, median (IQR), years	3.1 (0.6-7.7)	3.1 (0.6-7.7)	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001
Baseline, n (%)	148 (71)	158 (53)	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001
Male, %	43.9	25.2	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001
ESR, median (IQR)	28 (13-42)	34 (20-49)	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001
BASMI, median (IQR)	40 (10-57.5)	10 (4-30)	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001
HAQ, median (IQR)	1.9 (1.3-2.8)	1.9 (1.3-2.8)	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001
ASDAS, median (IQR)	3.1 (0.6-7.7)	3.1 (0.6-7.7)	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001
DMARD use, %	43.9	25.2	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001
Active DMARD user, %	43.9	25.2	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001
CRP, median (IQR)	3.1 (0.6-7.7)	3.1 (0.6-7.7)	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001
HLA status, %	43.9	25.2	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001
HLA positive, %	43.9	25.2	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001

**Conclusions:** In this study of TNFi-treated AS patients in clinical practice, smoking was not found to be associated with disease activity, treatment response and treatment adherence.

**Disclosure of Interest:** None declared  
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**SAT0184 THE EFFECT OF SMOKING ON RESPONSE TO TUMOR NECROSIS FACTOR-ALPHA INHIBITOR TREATMENT IN ANKYLOSING SPONDYLITIS PATIENTS: RESULTS FROM THE TURKBIO REGISTRY**

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**Background:** Although there is good evidence that smoking has a dose-dependent impact on structural damage progression in ankylosing spondylitis (AS) the evidence is poor for its impact on disease activity, physical mobility, life quality and treatment response.

**Objectives:** We aimed to investigate the impact of smoking on disease activity, treatment adherence and treatment response in Turkish patients with AS treated with their first tumour necrosis factor-alpha inhibitor (TNFi) therapy in a real-life cohort.

**Methods:** 561 patients fulfilling the modified New York criteria for AS and treated with their first TNFi therapy since 2011 from 8 centers in Turkey were included in

**SAT0185 CERTOLIZUMAB PEGOL SERUM LEVELS ≥20 MG/L ARE ASSOCIATED WITH IMPROVEMENT IN DAS28 IN RHEUMATOID ARTHRITIS PATIENTS. DATA FROM THE NOR-DMARD STUDY**

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**Background:** Measurement of serum drug levels can help clinicians tailor treatment with TNF-inhibitors. An association between certolizumab pegol (CP) serum levels and treatment response in rheumatoid arthritis (RA) patients (pts) has previously been demonstrated in a prospective observational study (1). These results need to be confirmed in other studies, with particular focus on finding an optimal therapeutic serum level for CP.

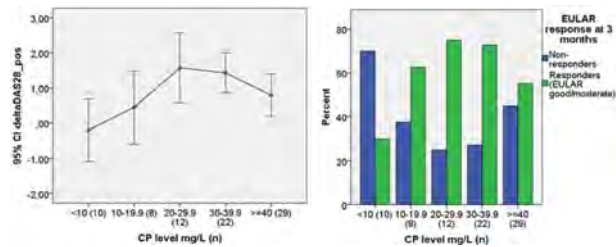
**Objectives:** To examine the association between serum CP drug levels and treatment response in RA pts and to identify a therapeutic target level.

**Methods:** Patients with a clinical diagnosis of RA starting standard treatment with CP included in the NOR-DMARD registry with biobank sample at 3 months follow-up, were included in the present analyses. Serum drug levels (non-trough) were analysed with an in-house immunofluorometric assay automated on the AutoDELFA immunoassay platform. We studied association between serum CP level and ΔDAS28 and EULAR good/moderate response at 3 months by multi-variable linear and logistic regression analyses, respectively, adjusting for age, sex and prior bDMARD (Y/N).

**Results:** In 91 included patients, median serum drug level at 3 months follow up was 34.7 mg/L (17.6–44.6). Response data were available in 81/91 patients. Serum CP level ≥20 mg/L was associated with greater improvement in DAS28 at



3 months ( $\beta=0.89$  (95% CI 0.03–1.74),  $P=0.04$ . 44.4 % of pts with CP level <20 mg/L achieved EULAR response after 3 months treatment, while 73.5 % of pts with CP level 20–40 mg/L and 55.2 % with  $\geq 40$  mg/L were responders. However, the difference in EULAR response between pts with CP level  $\geq 20$  vs. <20 mg/L did not reach statistical significance (OR 1.5 (95% CI 0.5–5.1),  $P=0.48$ ).



**Conclusions:** Certolizumab serum levels  $\geq 20$  mg/L were associated with DAS28 improvement, but not significantly with EULAR response after 3 months treatment in RA pts. We suggest 20 mg/L as a lower target limit for non-trough CP samples in RA-patients. No additional benefit of having a certolizumab level over 40 mg/L was observed.

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SAT0186

#### TREATMENT RESPONSE OF INTRAVENOUS TOCILIZUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS BASED ON THE LEVEL OF PRIOR EXPOSURE TO BIOLOGIC THERAPY: RESULTS FROM THE KOBIO

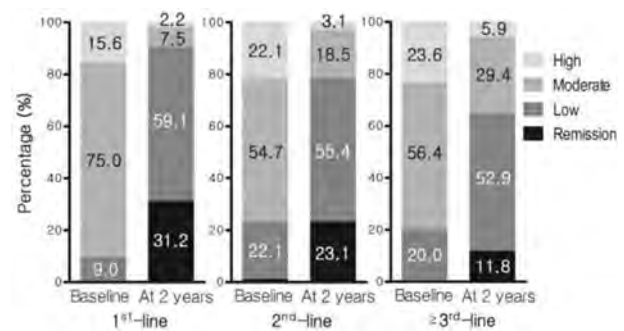
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**Background:** Previous studies have showed that response rate to biologic therapy in patients with rheumatoid arthritis (RA) are lower in those who had prior exposure to multiple biologic agents compared with first-time users. However, most of these studies targeted on patients undergoing anti-TNF therapy.

**Objectives:** To investigate the treatment response of RA patients using intravenous tocilizumab (TOC) as the first biologic agent, comparing with those who had prior exposure to other biologic agents

**Methods:** Data of RA patients treated with TOC were obtained from the Korean College of Rheumatology Biologics Registry (KOBIO). Patients were grouped as first (1st)-line, second (2nd)-line, and third or more ( $\geq 3$ rd)-line users. Clinical outcomes including SDAI changes at the first year and second year of TOC therapy were evaluated, and subsequent switching to another biologic agent and its associated factors were analyzed using the Cox proportional hazard model.

**Results:** A total of 408 patients were included in the study; 1st-line ( $n=258$ ), 2nd-line ( $n=95$ ),  $\geq 3$ rd-line ( $n=55$ ) users. The mean age was 54.0 years, and mean disease duration of 8.2 years. At baseline, mean SDAI was 30.0, and 7.1% of patients were treated without a concomitant conventional DMARD, which increased to 21.6% at the end of the second year. The clinical response of related parameters in 1st-line TOC users were more robust than the 2nd-line or  $\geq 3$ rd-line users, and greater proportion of 1st-line users achieved remission or low disease activity at the second year ( $p=0.00291$ ) (figure). In addition, switching to another agent was more frequent in the 2nd-line or  $\geq 3$ rd-line users within 2 years (1st, 2nd,  $\geq 3$ rd-line users, 4.7%, 15.1%, 11.1%, respectively). A multivariate analysis revealed that higher baseline SDAI (HR 1.1018,  $p=0.00680$ ) and multiple prior exposure to biologics (HR 2.5751,  $p=0.0139$ ) were predictors of subjects switching to other agents.



**Conclusions:** Amongst RA patients with high disease activity who receive TOC, patients naïve to biologics have better treatment response and lower switch rates after two years.

#### REFERENCE:

[1] Karlsson JA, et al. Treatment response to a second or third TNF-inhibitor in RA: results from the South Swedish Arthritis Treatment Group Register. *Rheumatology* 2008;47:507–13.

**Disclosure of Interest:** None declared

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SAT0187

#### GOLIMUMAB IMPROVES WORK PRODUCTIVITY AND ACTIVITY IMPAIRMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA), ANKYLOSING SPONDYLITIS (AS) AND PSORIATIC ARTHRITIS (PSA): 1-YEAR RESULTS FROM A NON-INTERVENTIONAL TRIAL IN GERMANY

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**Background:** Non-interventional studies (NIS) are essential instruments in pharmaceutical research not only for pharmaceutical companies but also for regulatory authorities or reimbursement bodies in Germany.

Aside from direct costs by a disease, German sick funds as well as health authorities have a keen interest in indirect costs, such as costs derived from loss of work productivity.

**Objectives:** It is the aim of this study to show the benefit of Golimumab (GLM) in work productivity and activity for RA, AS and PsA patients in Germany. The analysis was performed using the validated indication-specific Work Productivity Activity Impairment (WPAI) Questionnaire as primary endpoint. The WPAI is rated to be the most psychometrically validated and frequently used instrument for measuring of health-related work-productivity.

**Methods:** As primary endpoint, the change of work productivity impairment and ability for daily activities in month 3 (V1) versus baseline visit (V0) was evaluated.

All 4 subscores of the WPAI were analysed: disease related absence from work (absenteeism), working while sick (presenteeism), total work productivity impairment (TWPI) and activity impairment with TWPI as primary score.

In addition, an evaluation of the activity impairment in the mITT population (modified-Intention-To-Treat) was performed.

As exploratory endpoint, the change in work productivity/activity impairment after 6 months and 12 months versus baseline as measured by WPAI for PsA, RA and AS patients treated with Golimumab in German clinical practice was evaluated.

**Results:** Of 748 patients (100%) who started treatment with Golimumab at V0 (baseline), 666 (89.0%), 634 (84.8%) and 552 patients (73.8%) continued treatment until V1 (Month 3), V2 (Month 6), and V3 (Month 12/end of observation period), respectively.

Efficacy analyses were performed on the mITT population which included 700 patients (RA=237, PsA=235, AS=228) who had at least 2 documented visits.

The statistically significant improvements (all  $p$ -values  $<0.05$ ) in the mean WPAI domain scores were maintained over the 12-month observation period in all 3 indications with a higher treatment effect regarding “activity impairment” and “presenteeism” than with “absenteeism”. The magnitude of improvements in the 4 WPAI domains and the time course of improvements varied between the underlying disease (RA, PsA, AS).

In general, the improvements in the 4 WPAI domains were greater in patients with AS and PsA compared to RA patients. A continuous improvement over time was seen in AS patients regarding the domain “activity impairment”. A positive effect of pre-treatment with biologics (i.e. better improvement in WPAI) was seen in RA

patients for 3 domains (TWPI<sup>®</sup>, absenteeism, presenteeism), and in PsA patients for 2 domains (absenteeism, activity impairment).

**Conclusions:** Golimumab s.c. 1 x monthly is an effective treatment in patients with RA, AS and PsA.

All scores of the WPAI showed a significant ( $p < 0.05$ ) reduction in mean score values in each indication.

Golimumab leads to an improvement of work productivity and daily activities in all patients already within the first 3 months of treatment and provided sustained improvement in WPAI in patients with RA, PsA and AS.

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### SAT0188 TOCILIZUMAB IN EARLY RHEUMATOID ARTHRITIS DELIVERS CLINICAL AND ULTRASOUND-CONFIRMED RAPID AND DEEP REMISSION WITH ABOLITION OF PD – TREMERA STUDY

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**Background:** Tocilizumab (TCZ) has shown impressive outcomes in early RA (ERA) with clinical remission rates of up to 80%<sup>1</sup>. The speed and depth of remission of TCZ in treatment-naïve ERA have not been specifically evaluated.

**Objectives:** To evaluate the rate and depth of clinical and imaging response and remission, and timing of optimal response in ERA.

**Methods:** A prospective, open-label, RCT of active (DAS28  $\geq 3.2$ ), new-onset (symptom duration  $\leq 12$  months) treatment-naïve RA (2010 ACR/EULAR RA classification criteria), randomised 1:1, and treated with either TCZ 8 mg/kg (4-wkly) monotherapy or TCZ 8 mg/kg (4-wkly) and methotrexate (MTX) combination for 48 weeks.

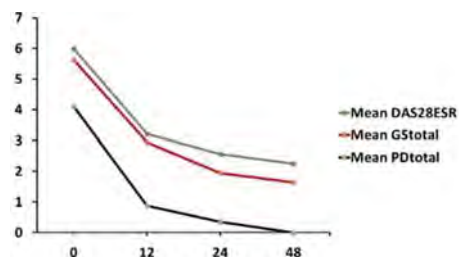
Clinical response/remission rates, and patient reported outcomes (PRO) were evaluated at early (wks 4 and 12) timepoints, and wks 24 and 48. High resolution US dominant hand (together baseline active joints) was performed at baseline, wks 12, 24 and 48. Odds ratios were calculated using Firth logistic regression.

**Results:** 20 pt [16 female; 13 RF+, 15 ACPA+; mean(SD) age 55.25(12) years] were recruited; baseline mean(SD) DAS28-ESR 5.98(1.21), HAQ 1.64(0.67). High-hurdle endpoints: at wk4, 30%, 95% and 35% achieved DAS28-ESR rem, EULAR and ACR50 response respectively; and continued to increase, peaking at wk48 with 67%, 93% and 63% respectively [OR wk4 1.0, 0.3, 0.7 and wk48 1.4, 3.0, 4.0 respectively]. Sustained DAS28-ESR remission (8 successive weeks) was observed in 40%;  $\text{chisq}=0.5$ ,  $p=0.462$ ; mean (90% CI) time to remission 38.3 (33.2, 43.3) wks.

PRO: Baseline median(IQR) VASGH 56.5(29,71.5) improved by wk4 to 24 (14,54), maintained wk48 24.5(3.5,46.5); VASDA from 62(54,77.5) to wk4 22 (12.5,49.5), further improved by wk48 14.5(3.5,44.5); VASPain from 63.5(42,77) to wk4 19.5(4,53), maintained wk48 17.5(2.5,49.5). Similarly, median(IQR) HAQ at baseline 1.63(1.25,2.13) decreased by wk4 1.13(0.19,2.0) and wk48 0.75 (0.19,1.38).

**Ultrasound:** Baseline mean grey scale (GS) and power Doppler (PD) (as well as DAS28-ESR) are shown in the figure below, illustrating rapid reduction by wk4 that continued through the study period to all achieving PD=0 by wk48. Baseline median (IQR) erosions 0 (0, 0) remained unchanged throughout study. Baseline GS and PD appeared to associate with achievement of DAS44ESR remission ( $p=0.038$  and  $p=0.043$  respectively).

No meaningful numerical differences between the two treatment arms was recorded.



**Conclusions:** Conclusion TCZ in ERA (both monotherapy and TCZ/MTX combination) was associated with rapid clinical and imaging improvements, strikingly abolishing PD; with sustained remission in almost half the patients. The peak imaging response was noted at 48 weeks. Impressively, rapid PRO improvement

was also observed. These data indicate convincing patient-relevant, imaging-determined depth of remission in a new-onset, treatment-naïve RA cohort.

### REFERENCE:

[1] Bijlsma JWJ, et al. Lancet 2016; 388:10042;343–355.

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**Disclosure of Interest:** L. Hunt: None declared, E. Hensor: None declared, K. Naraghi: None declared, R. Wakefield: None declared, P. Emery Grant/research support from: Abbvie, AstraZeneca, Pfizer Ltd, Roche, Consultant for: Abbvie, AstraZeneca, BMS, Eli Lilly, MSD, Pfizer, Roche, Sandoz, M. Buch Grant/research support from: Pfizer Ltd, Roche, Consultant for: Abbvie, BMS, Eli Lilly, Pfizer, Roche, Sandoz

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### SAT0189 DYNAMICS OF CIRCULATING TNF DURING ADALIMUMAB TREATMENT OF RHEUMATOID ARTHRITIS USING A NOVEL DRUG-TOLERANT TNF ASSAY

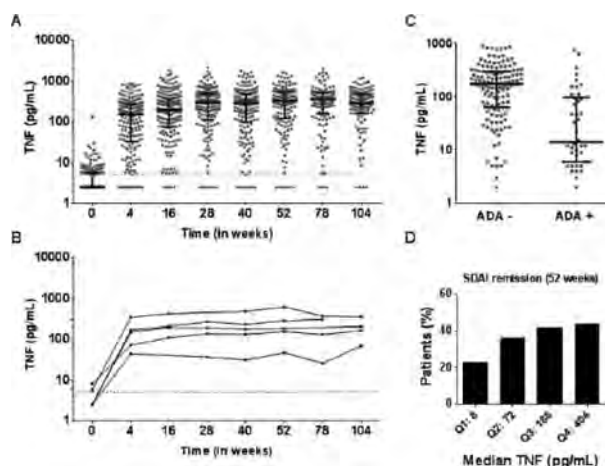
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**Background:** Tumor necrosis factor- (TNF) inhibitors are effective in the treatment of rheumatoid arthritis (RA); these include adalimumab, which binds TNF to form inactive complexes. Once in remission, a proportion of patients can successfully discontinue adalimumab treatment, indicating that blocking TNF is no longer necessary for disease control. We developed a novel assay that can quantify TNF in the presence of large amounts of TNF-inhibitor, i.e. a 'drug-tolerant' assay.

**Objectives:** To investigate, for the first time, the relationship between TNF levels and disease course during adalimumab treatment.

**Methods:** The new drug-tolerant competition enzyme-linked immunosorbent (ELISA) assay was used to quantify TNF levels on initiation and during 2 years of adalimumab treatment in 206 consecutive RA patients. The relationship between TNF levels and clinical response was evaluated.

**Results:** Circulating TNF levels were close to the detection limit at baseline, but TNF levels increased on average >50-fold upon adalimumab treatment (**figure 1A**; black lines show median (IQR)), and reached a stable level in time in the majority of patients (**figure 1B**; representatives of n=206), regardless of disease activity. During treatment, TNF was in complex with adalimumab, and recovered as inactive 3:1 adalimumab:TNF complexes. Low TNF levels at week four were associated with a higher frequency of anti-drug antibodies (ADAs) at subsequent time points (**figure 1C**) and significantly less methotrexate (MTX) use at baseline. Furthermore, week four TNF levels were significantly correlated with SDAI score, with significantly lower TNF levels in patients who did not reach remission (Spearman  $r = -0.18$ ;  $p=0.015$ ; **figure 1D**)



**Conclusions:** TNF levels, mostly in complexed form, do not appear to decline in patients that reach remission, and may therefore not be predictive for treatment

discontinuation. However, low complexed TNF levels in the early phase of treatment (wk 4) are strongly associated with ADA formation and can be used to identify non-responders in the early phase of treatment.

**Disclosure of Interest:** L. Berkhout: None declared, M. l'Ami: None declared, J. Ruwaard: None declared, M. Hart: None declared, P. Ooijevaar-de Heer: None declared, K. Bloem: None declared, M. Nurmohamed Consultant for: Abbott, Roche, Pfizer, MSD, UCB, SOBI, BMS, Speakers bureau: Abbott, Roche, Pfizer, R. van Vollenhoven Grant/research support from: AbbVie, BMS, GSK, Pfizer, UCB, Consultant for: AbbVie, AstraZeneca, Biotest, BMS, Celgene, GSK, Janssen, Lilly, Novartis, Pfizer, UCB, M. Boers: None declared, C. Smith: None declared, G. Wolbink Grant/research support from: Pfizer, Speakers bureau: Pfizer, UCB, AbbVie, Biogen, BMS, T. Rispens Grant/research support from: Genmab, Speakers bureau: Pfizer, AbbVie, Regeneron  
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### SAT0190 RISK FOR OPPORTUNISTIC INFECTIONS IN RHEUMATOID ARTHRITIS TREATED WITH bDMARDs IN CLINICAL PRACTICE, 10 YEARS OF FOLLOW UP

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**Background:** Biologic disease-modifying anti-rheumatic drugs (bDMARDs) may be associated with opportunistic infections (OI).

**Objectives:** Our purposes were to describe the incidence of OI in Rheumatoid Arthritis (RA) taking bDMARDs, and compare the risk of OI between TNF-targeted and non-TNF-targeted biologics.

**Methods:** Retrospective longitudinal observational study from 2007 to 2017. We included RA patients, diagnosed and followed in our outpatient clinic, whom started treatment with a TNF-targeted bDMARD [etanercept (ETN), golimumab (GOLI), certolizumab (CTZ), infliximab (IFX), adalimumab (ADA)], or non-TNF-targeted bDMARD [rituximab (RTX), abatacept (ABA), or tocilizumab (TCZ)]. According to microbiologist criteria, we consider OI when there was a positive culture (virus, fungus, bacterial, parasitary) or compatible symptoms that respond to specific treatment. The independent variable was the Type of targeted bDMARD: TNF-targeted vs non-TNF-targeted. Secondary variables: sociodemographic; clinical and other therapies. We used survival techniques to estimate the incidence of OI, expressed per 1000 patient-year [CI 95 %]. The exposure time was defined from the start date of each bDMARD to the development of an OI, loss of follow up or end of study (01/02/2017). We performed Cox multivariate regression models to compare the risk of OI between the types of bDMARD used. Results were expressed in Hazard ratio (HR).

**Results:** 441 RA patients were included, starting 761 different courses of bDMARD treatment. 81% were women with a mean age at first bDMARD of 57.3 ± 14 years. The median time from onset of bDMARD until onset of OI was 3.1 years [0.5–4.6]. More than 90% of patients were on steroids. 71.3% of the courses were TNF-targeted bDMARD (ADA 39%, ETN 33%, CTZ 15%, IFX 9%, GOLI 2%), and 28.7% non-TNF-targeted bDMARD (RTX 60%, ABA 21%, TCZ 18%). There were 38 OI [26 Virus (18 Herpes Zoster, 2 virus B reactivation, 3 virus C reactivation, 1 Epstein Barr, 1 Avian flu, 1 CMV), 6 Fungus (5 Candida, 1 Trichophyton), 5 Bacterian (1 Legionella, 1 Salmonella, 3 TB)] and 1 parasitary (Leishmania)]. 9 of them required hospitalization and one died (Candida). The global incidence of OI was 23.1 [16.8–31.8]. TNF-targeted bDMARD had 26 OI, with an incidence of 20.8 [14.1–30.6], and non-TNF-targeted bDMARD with 12 OI, incidence 30.4 [17.3–53.6]. We not find statistical differences in the rate of OI between TNF-targeted vs non-TNF-targeted in the multivariate model, adjusted by age, sex and calendar-time (HR 1.37, p=0.4). Male sex was found a predictor of OI in the multivariate analysis (HR 2.17, p=0.04). Age (HR 1.02, p=0.08), concomitant treatment with corticosteroids (HR 6.61, p=0.05) and leukopenia (HR 2.7, p=0.08) showed a tendency to increase the risk of OI.

**Conclusions:** Incidence of OI due to bDMARDs was near 23 cases per 1000 patients-year. Crude incidence was higher for non-TNF-targeted bDMARD compared to TNF-targeted bDMARD. Nevertheless this difference was not maintained in the multivariate model, reflecting that many of the variability in patients' risk of OI development were driven by factors other than biological agent exposure. Close monitoring should be taken in those RA patients taking bDMARD, corticosteroids, and with leukopenia.

**Disclosure of Interest:** None declared

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### SAT0191 THE PATIENT PERSPECTIVE ON bDMARD DOSE REDUCTION: A MIXED METHODS STUDY

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**Background:** Dose reduction of bDMARDs, after low disease activity is reached, is safe and effective.(1) To date, few studies have focused on bDMARD dose reduction from the patient perspective.

**Objectives:** The aim of this study was to identify the factors that play a role for patients with RA when considering bDMARD dose reduction, and to determine their relative importance.

**Methods:** A mixed methods design was used in which we 1) identified influencing factors with interviews and 2) ranked these factors using a Maximum Difference Scaling (MaxDiff) survey.

**Sub study 1:** We performed semi-structured interviews with 22 RA patients. Interviews were transcribed verbatim and two researchers analyzed the transcriptions by inductive thematic analysis.

**Sub study 2:** The influencing factors were derived from the interviews and used in a MaxDiff survey with RA patients from 3 different centers in the Netherlands (N=192; an academic hospital, a specialized hospital and a large general hospital). Besides questions about patient characteristics, the survey included 18 MaxDiff questions in which patients were asked to choose the most and least important factor from a subset of 5 factors. A relative importance score for each factor was calculated using hierarchical Bayes modeling.

**Results:** Thirty factors were identified from the interviews and used in the survey. Most respondents had a positive attitude towards bDMARD dose reduction (table 1). The top-10 of factors (table 2) shows that patients are concerned that dose reduction will lead to a disease flare that affects their daily life (pain, function). It is important for them to know that it is possible to increase the dose if (further) reduction is not possible and that the bDMARD will be effective again. Patients value the opinion of their rheumatologist, and being involved in the decision to start tapering is highly ranked as well.

Table 1 Patient characteristics (mean (sd) or n (%))

Characteristic	Sub study 1 (n=22)	Sub study 2 (n=192)
Female	15 (68%)	125 (65%)
Age (years)	62 (7.6)	59 (12.1)
Disease duration (years)	13 (9.4)	16 (10.0)
Experience with bDMARD dose reduction	Yes: 16 (73%) No: 6 (27%)	Yes: 117 (61%) No: 71 (37%) I don't know: 4 (2%)
Attitude towards bDMARD dose reduction	Not applicable	Very positive: 64 (33%) Positive: 78 (41%) Neutral: 27 (14%) Negative: 11 (6%) Very negative: 2 (1%) I don't know: 10 (5%)

Table 2 Top-10 factors

Rank	Factor
1	The possibility to increase the dose when disease symptoms worsen
2	The risk that my disease activity will increase
3	My current disease activity
4	The risk that my physical function will deteriorate (e.g. I won't be able to work)
5	The confidence I have in my rheumatologist
6	To what extent I'm involved in the decision on bDMARD dose reduction
7	Whether the bDMARD is (still) necessary for the RA
8	The advice of my rheumatologist regarding bDMARD dose reduction
9	The risk that I will experience more pain
10	The efficacy of the bDMARD after increasing the dose

**Conclusions:** The results from this study could facilitate implementation of bDMARD dose reduction by informing care providers on what is important for patients and providing a basis for shared decision making.

#### REFERENCE:

[1] Nam JL, et al. Ann Rheum Dis 2017 Jun;76(6):1113–1136.

**Disclosure of Interest:** None declared

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SAT0192

### COMPETITIVE ELISA AND BRIDGING ELISA WITH ACID DISSOCIATION DETECT ANTI-DRUG ANTIBODIES IN A GREATER PROPORTION OF PATIENTS TREATED WITH TNF-ALPHA INHIBITORS THAN CLASSICAL BRIDGING ELISA

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**Background:** Therapeutic drug monitoring is used to guide treatment in patients treated with TNF- $\alpha$  inhibitors. Current bridging ELISA (bELISA), mostly used in routine analysis, cannot detect anti-drug antibodies (ADA) in immune complexes and differentiate between neutralizing and non-neutralizing ADA. Reporter Gene Assay (RGA), which detects only neutralizing ADA, is both costly and labour-intensive. Therefore, alternative assays are warranted to obviate these limitations.

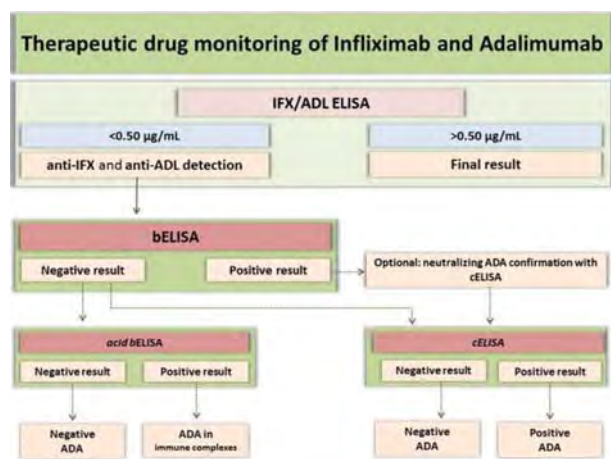
**Objectives:** To develop an *in-house* competitive ELISA (cELISA) for detection of neutralizing ADA, to compare results between four different assays for ADA detection and to propose an algorithm to assist clinicians in personalized therapeutic drug monitoring of Infliximab (IFX) and Adalimumab (ADL).

**Methods:** Samples from 105 patients on IFX or ADL therapy ( $n_{IFX}=61$ ,  $n_{ADL}=44$ ) from the Departments of Rheumatology and Gastroenterology, University Medical Centre Ljubljana, with undetectable drug levels, were tested with *in-house* cELISA, *in-house* bELISA, *in-house* bELISA with acetic acid dissociation (acid bELISA (1)) and RGA. cELISA was developed following the principles of RGA, briefly, diluted samples were pre-incubated with a fixed amount of IFX or ADL, linked to horseradish peroxidase. After incubation on a TNF- $\alpha$  plate, the reaction was detected using TMB substrate. Within and between-run imprecisions for cELISA were determined. Correlation coefficient and agreement between results from different assays were calculated.

**Results:** Within and between-run imprecisions in cELISA met the validation criteria (<20%). We found high correlation between cELISA and RGA (anti-IFX  $r=0.932$  ( $p<0.0001$ ) and anti-ADL  $r=0.948$  ( $p<0.0001$ )) and 100% agreement between results. cELISA also correlated with bELISA (anti-IFX  $r=0.663$  ( $p=0.0002$ ) and anti-ADL  $r=0.896$  ( $p<0.0001$ )). Agreement between bELISA and cELISA was 79% for anti-IFX and 82% for anti-ADL samples.

The more sensitive cELISA and functional RGA detect 13% (8/61) more positive samples in anti-IFX group and 18% (8/44) more samples in anti-ADL group. Acid bELISA found 3% (2/61) more positive samples in anti-IFX group and 14% (6/44) of samples in the anti-ADL group.

In total, 16% (10/61) more samples in anti-IFX and 30% (13/44) more samples in anti-ADL group were confirmed having ADA. Based on our results we propose a sequential algorithm, which enables reliable, affordable and increased detection of ADA (figure 1).



**Figure 1.** Algorithm for therapeutic drug monitoring of IFX and ADL. IFX – Infliximab, ADL – Adalimumab, ADA – anti-drug antibodies, bELISA – bridging ELISA, acid bELISA – bELISA with acid dissociation, cELISA – competitive ELISA;

**Conclusions:** cELISA and acid bELISA, together, can detect ADA in 16% more samples in anti-IFX and 30% in anti-ADL group than classical bELISA used in current practice. The proposed algorithm can assist in everyday practice and enables better evaluation of patients treated with TNF- $\alpha$  inhibitors.

### REFERENCE:

[1] Van Stappen, et al. Drug Test Anal 2017;9(2):243–7.

**Disclosure of Interest:** None declared

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SAT0193

### EARLY DISCONTINUATION OF FIRST LINE BIOLOGICAL TREATMENT WITH ETANERCEPT IN PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS FROM THE ITALIAN GISEA REGISTRY

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**Background:** Tumor necrosis factor- $\alpha$  inhibitors (TNFi) are usually the first biologic drugs employed in rheumatoid arthritis (RA) after failure of conventional disease-modifying antirheumatic drugs (DMARDs). Retention rate is a useful surrogate marker of effectiveness and safety in real life, but few studies investigated the causes of early discontinuation of these drugs.

**Objectives:** Aim of the study was to investigate the possible predictors of early discontinuation (within 1 year of treatment) of etanercept (ETA) in RA patients enrolled into the GISEA (Italian Group for the Study of Early Arthritis) registry.

**Methods:** RA patients who began etanercept as first biologic DMARD were included in the study. For all patients age, sex, disease duration, smoking status, the intake of glucocorticoids and DMARD, clinical and serological data, comorbidities and extra-articular manifestations were collected.

**Results:** We analyzed 477 RA patients (females/males 382/95, mean age 51.3  $\pm$  14.1 years; mean DAS28 5.4  $\pm$  1.5); rheumatoid factor (RF) and anti-citrullinated peptide antibodies (ACPA) were positive in 66% and 62.3%, respectively. Comorbidities were observed in 16.6% of patients, mainly cardiovascular diseases, while extra-articular RA manifestations were recorded in 6.3%. Concurrent DMARDs therapies were reported in 54.3% of patients, mainly methotrexate (40.5%), while 52.4% of subjects taken low doses of steroids.

Seventy patients (14.7%) discontinued ETA during the first year (for inefficacy in 43 patients, adverse events in 22, and other reasons in 5). The presence of comorbidities and a combination therapy with DMARDs different by MTX were independent predictors of early discontinuation of ETA at multivariate analysis (see table 1). The association with MTX didn't increase the 1-year retention rate of ETA. No significant associations were observed with steroids, presence of RF or ACPA or the disease activity at baseline.

**Table 1.** Multivariate analysis. Factors associated to early discontinuation of etanercept

Parameter	Standard Error	Odds ratio	95% Confidence Interval	p
Comorbidities	0,28	1,86	1.07–3.25	0,029
DMARDs different by MTX	0,35	2,01	1.014–3.982	0,045
ETA monotherapy	0,297	0,701	0.392–1.256	0,232

**Conclusions:** ETA demonstrated a high persistence in RA patients and after 12 months more than 85% of patients continued the treatment. The presence of comorbidities and a combination therapy with DMARDs different by MTX were associated to an early withdrawal of the drug.

**Disclosure of Interest:** None declared

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SAT0194

**SIGNIFICANT OVERTREATMENT WITH BIOLOGICAL DRUGS IS COMMON IN ROUTINE CARE FOR PATIENTS WHERE SERUM DRUG LEVELS ARE MONITORED**M. E. Perry<sup>1</sup>. <sup>1</sup>Rheumatology, Royal Alexandra Hospital, Paisley, United Kingdom

**Background:** Current challenges in treating rheumatic disease include using the right drug at right dose for the right length of time. Measuring serum drug levels can help prevent over-treatment, inform regarding secondary drug failure on account of immunogenicity and improve confidence to extend the interval of drug dosing.<sup>1</sup> This pilot work was a prelude to the implementation of the first national monitoring service worldwide within the relatively endogenous Scottish population.

**Objectives:** 1. To develop skill and familiarity with TDM at a Scottish laboratory prior to a business case for a national service  
2. To understand the reasons why a clinician would use the service as part of clinical practice  
3. To understand the current extent of over and undertreatment in an endogenous population

**Methods:** ELISA assays (Promonitor) were supplied by GRIFOLS (Barcelona) for the detection of serum levels of adalimumab (ADA), infliximab (IFX), Golimumab (GOL), Etanercept (ETA) and Rituximab (RIX). A single laboratory site was selected and laboratory training was provided. A bespoke clinical request form was developed. Adult & paediatric rheumatologists across Scotland were invited to send serum biological drug trough samples for analysis. The clinical indication for testing was also captured.

Reference ranges for free drug levels and anti-drug antibody levels: Analyte: Lower limit of measurement-Upper limit of measurement. Units ug/mL: Adalimumab 0.024–12, Infliximab 0.2–14.4, Etanercept 0.035–40, Golimumab 0.036–12.8, Rituximab 0.75–204.

**Results:** Internal calibration and quality control for the assays were established. A total of 39 IFX, 26 ADA, 14 ETA, 3 RIX, 14 GOL samples were received (total n=96). Only 4 (4%) of patients had serum levels below the reference range and of these just one had anti drug antibodies, suggesting that immunogenicity was not a significant clinical factor in this population. Overtreatment was common: 19 patients (20%) had drug levels greater than the maximum value in the reference range. 12 patients had anti-drug antibodies, but only one of these had poor disease control, suggesting a high proportion had non-neutralising antibodies. Based on this study, if all overtreated patients had dosing interval extended by 33%, this would produce a drug budget reduction of 6–7%, easily dwarfing the setup and running costs of a biological drug monitoring service.

Clinicians requested samples to help assess flaring patients to determine if immunogenicity had occurred or drug levels were too low (n=36) confidence around tapering drug (n=28), switching to biosimilar (n=6) and miscellaneous other reasons (n=15)

**Conclusions:** In this population, immunogenicity was not clinically relevant. Overtreatment with biological drugs was common, highlighting potential longer term safety risk and opportunity for cost reduction by dose interval prolongation. Clinicians primarily indicate the usefulness of serum biological drug testing in determining if secondary failure has occurred or to aid decisions about drug dose tapering.

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SAT0195

**OPTIMIZATION OF BIOLOGIC THERAPIES IN RHEUMATOID AND PSORIASIS ARTHRITIS: A SINGLE-CENTRE EXPERIENCE**

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**Background:** A timely diagnosis and a suitable therapy allow a better control of disease activity and limit joint damage in autoimmune arthritis. Biological therapies played a key role, modifying disease natural history. However, the use of these drugs implies several risks and increases health-care costs [1]. This has

raised a question: could be possible, in patients in a state of sustained remission or low disease activity (LDA), choose an optimized regimen of treatment? Recommendations provided by EULAR in 2013 includes this possibility, especially if biologic therapy is in association with DMARDs [2]. While optimized regimen has been attempted in different clinical trials with good results, strong evidences are currently lacking [3].

**Objectives:** The aim of our study was to analyse the effectiveness of optimization of biologic therapies in a cohort of patients with Rheumatoid and Psoriasis Arthritis (RA and PA).

**Methods:** We retrospectively included patients undergoing optimized therapy in a cohort of 328 outpatients (190 RA, 128 PA) treated with first-line biologic therapy from 2006 to 2017. Optimization was considered as predefined dose downtitration and/or expansion of dose interval in patients with a sustained remission or LDA (DAS 28 -ESR <2.6 or 2.6–3.2 respectively, for at least 24 months). Relapse was defined by an increase in DAS28-ESR >20% over baseline or by the onset of at least one tender and swollen joint. Our principal end-points were: (I) estimate the proportion of subjects able to optimize therapy (II) define the rate of relapse at 6–12 and 24 months follow-up (FU) in patients undergoing optimization (III) compare the effectiveness of optimized therapy in RA and PA patients and value the rate of optimization in relation to different biologic drugs. Survival analysis (Kaplan-Meier Curves) and Chi Square test were used and a p value <0.05 was considered as statistically significant.

**Results:** During FU, 15/190 (8%) RA patients and 16/138 (12%) PA patients reached a persistent LDA or remission and started the optimized biologic therapy. In survival analysis, rates of relapse at 6 months were 10% and 0% in RA ad PA respectively, increasing to 21% and 8% at 12 months and finally to 48% and 34% at 24 months. No significant differences emerged between the two groups. The use of Etanercept was associated with higher possibility to optimize biologic treatment (p=0.007).

**Conclusions:** Biologic therapy optimization is a workable option in RA ad PA patients who reached persistent remission or LDA. In our cohort Etanercept seems to be the most promising drug. Further studies are needed to better define the predictive factors of response in order to identify eligible patients.

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SAT0196

**TIME TO DISCONTINUATION OF BIOLOGIC THERAPY BY MECHANISM OF ACTION IN RHEUMATOID ARTHRITIS: RESULTS FROM THE ONTARIO BEST PRACTICE RESEARCH INITIATIVE (OBRI) COHORT**

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**Background:** Patients with rheumatoid arthritis (RA) may discontinue their biologic disease modifying antirheumatic drug (bDMARDs) due to non-response, loss of response or adverse events. However, time to discontinuation may be related to mechanism of action.

**Objectives:** We aimed to compare drug survival of tumor necrosis factor inhibitors (TNFi) versus non-TNFi in patients initiating bDMARD treatment in a Canadian (Ontario) observational cohort.

**Methods:** Patients enrolled in the Ontario Best Practice Research Initiative (OBRI) who started bDMARD therapy within 30 days before or any time after OBRI enrolment were included in the primary analysis. Patients were followed from bDMARD start until discontinuation/switching, death, lost to follow-up, or last visit, whichever came first. Time to discontinuation/switching of bDMARD due to (i) any reason, (ii) non-response or loss of response, and (iii) adverse events (AEs), were assessed using Kaplan-Meier survival analysis for TNFi versus non-TNFi users.

**Results:** Among the 943 patients included in the primary analysis, 187 (19.8%) received non-TNFi and 756 (80.2%) TNFi. Mean (SD) age and disease duration were 56.4 (12.7) years and 9.6 (9.8) years, respectively, and the majority were females (79.1%) and biologic naïve (84.4%). TNFi included Etanercept,

Adalimumab, Certolizumab, Golimumab, and Infliximab; and non-TNFi included Abatacept, Rituximab, Tocilizumab, and Tofacitinib.

Over a mean (SD) follow-up of 2.4 (2.0) years, bDMARD discontinuation/switching was reported for 37.6% of patients, with significant difference in time to discontinuation between TNFi and non-TNFi users (Logrank  $p=0.01$ ). However, there was no significant difference due to non-response or loss of response (Logrank  $p=0.67$ ) between the two groups. At 2 years, more patients remained on TNFi (71.0%) compared to non-TNFi (57.0%). At 5 years, 51.0% and 44.0% of patients still remained on TNFi and non-TNFi, respectively.

**Conclusions:** The overall retention rate for biologics was comparable to finding in European registries. We found that patients stay on TNFi longer compared to non-TNFi. However, no significant difference was found between the two groups, for discontinuation or switching of bDMARDs due to non-response or loss of response. Further analyses are required to adjust for the effect of potential confounders (e.g. age, sex, disease activity, and other treatment regimens) on biologic discontinuation.

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#### SAT0197 ADHERENCE TO BIOLOGIC THERAPY OF RHEUMATOID ARTHRITIS PATIENTS – IS THERE ANY RELATION WITH DISEASE ACTIVITY?

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**Background:** In the last years, there has been an increase interest in using Patient Reported Outcomes (PROs) in clinical trials and daily clinical practice in Rheumatology to provide patient-centered care. The most frequently reported PROs are patient's pain, patient's global assessment (PGA) of disease activity and reports of functional capacity, fatigue, anxiety and depression. To date, studies that explore patient adherence to rheumatic medications are scarce.

**Objectives:** To study the level of adherence to biologic therapy of Rheumatoid Arthritis (RA) patients, followed at a day care hospital of Rheumatology.

**Methods:** Observational and cross-sectional study which took place in two months of consultation of day care hospital (5 periods per week). Patients with a diagnosis of RA according to 1987 American College of Rheumatology (ACR) and/or 2010 ACR/European League Against Rheumatism criteria, on biologic therapy, able to complete a questionnaire autonomously and who agreed to participate were included. Demographic and clinical data (DAS28, CDAI and SDAI to assess RA disease activity, HADS-A for anxiety, HADS-D for depression, FACIT-F for fatigue) were collected. To assess adherence, a Portuguese version of the Morisky Medication Adherence Scale (MMAS-8) was used and the patients were asked to apply it only to biologic therapy. Three levels of adherence were considered based on the following scores: 0 to <6 (low); 6 to <8 (medium); 8 (high). Statistics: Kruskal-Wallis and Mann-Whitney tests,  $p<0.05$ , SPSS<sup>®</sup> v.23.

**Results:** In total, 61 patients were included, 91.8% female, 82.0% on anti-Tumor Necrosis Factor (anti-TNF), the others on Tocilizumab (16.4%) or Abatacept (1.6%). Table 1 reports the means and medians of demographic and clinical variables included. The mean MMAS-8 score was  $7.0\pm 1.2$ , the median 7.0 (6.8–8.0), with a minimum of 2.5 and a maximum of 8. The adherence was medium in 50.8%, high in 36.1% and low in 13.1% patients. The median of current age was significantly higher for patients with high and medium levels of adherence compared to those with low levels ( $p=0.030$ ). The time on treatment with the current biologic therapy was significantly different between the levels of adherence ( $p=0.028$ ); the median of time on treatment for patients with medium levels of

adherence was significantly higher comparatively to the other patients ( $p=0.009$ ). No other significant difference was found among the levels of adherence for the studied variables.

**Conclusions:** The adherence to biologic therapy was at least medium for 86.9% of patients. Differences between levels of adherence were found only for current age and time on treatment. Disease activity of RA does not seem to influence the levels of adherence.

Table 1 Means and medians of demographic and clinical variables.

	Mean ±SD	Median (IQR)
Current age – years	56.1 ±11.1	58.1 (48.1– 62.8)
Disease duration – years	15.0±7.5	13.1 (10.1– 18.2)
Time on treatment with the current biologic therapy – years	3.5±2.7	2.8 (1.0–5.6)
DAS28–4V	3.4±1.2	3.3 (2.6–4.2)
CDAI	9.7±7.8	7.0 (3.6–15.1)
SDAI	10.1±8.0	7.0 (4.0–15.7)
HAQ	0.9±0.6	0.9 (0.4–1.4)
HADS-A	6.5±3.9	6.0 (3.0–9.0)
HADS-D	5.4±3.7	5.0 (2.0–8.0)
FACIT-F	36.5±8.8	37.0 (29.1– 43.5)

**Disclosure of Interest:** None declared

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#### SAT0198 DRUG SURVIVAL AND EFFICACY OF ABATACEPT IN RHEUMATOID ARTHRITIS PATIENTS IN ROUTINE CARE – 7 YEAR EXPERIENCE FROM A SINGLE CENTRE IN THE UNITED KINGDOM

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**Background:** Even after the advent of multiple biologic drugs, optimum treatment of rheumatoid arthritis (RA) in a real-world situation continues to be challenging. The data on long-term drug survival of biologic drugs in routine clinical practice is lacking. We extended our earlier analysis of abatacept use in RA patients<sup>1,2</sup> from a single centre in the United Kingdom over 7 years.

**Objectives:** To assess the efficacy, tolerability and drug survival of abatacept use in RA patients in a routine clinical setting like ours.

**Methods:** From November 2010 to December 2017, all RA patients with at least 6 months of follow up after abatacept initiation were included in the analysis. Data on demographics, disease duration, previous biologics, mode of administration, reasons for discontinuation and length of abatacept therapy were retrospectively collected from biologics database and medical records. Effectiveness was assessed by change in Disease activity scores (DAS 28) and European League Against Rheumatism response criteria (EULAR) after 6 months of therapy.

**Results:** 220 patients had received abatacept with at least 6 months follow up until December 2017. 176 were females and 44 males with mean age of 67.83 years (SD = 10.32). Mean disease duration in these patients was 14.42 years (SD = 8.11). 152 (69%) patients were seropositive (Rheumatoid factor and/or anti-CCP antibody). 207 (94%) patients had received a prior biologic and only 13 (6%) patients were biologic naïve. 193 (87.7%) patients were initiated on intravenous (iv) abatacept and 27 (12.2%) patients on subcutaneous (s/c) abatacept. 90 (40.9%) patients were successfully switched from iv to s/c abatacept.

The mean number of prior biologic drugs use per patient was 1.70 (SD = 1.03). 83.6% patients were co-prescribed DMARDs at the initiation of abatacept therapy. Mean baseline DAS 28 score was 6.02 (SD = 3.11). Average DAS 28 change at 6 months was -1.5 (95% CI -1.27, -1.33). 75% patients had a positive EULAR response (38% good, 37% moderate) and 25% had no response at 6 months.

Overall 57 (25.9%) patients discontinued treatment. 43 (19.5%) patients discontinued abatacept early (<9 months) due to primary inefficacy (10.9%) and adverse reactions (8.6%). 24 (10.9%) patients discontinued abatacept later, after a mean 27.46 (SD = 12.9) months of use, due to secondary loss of efficacy (6.3%) and adverse reactions (4.5%).

82% (180/220) of RA patients continued taking abatacept beyond 6 months. 61.5% (91/148) patients were still adherent at 2 years, 51.3% (39/76) retained the drug beyond 48 months.



**Conclusions:** Abatacept continues to be a safe and effective treatment option for patients with RA who are biologic naïve or after discontinuation of prior biologic due to failure or intolerance. A significant number of patients continue on abatacept even after 4 years.

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SAT0199

#### SWITCH FROM INNOVATOR ETANERCEPT TO BIOSIMILAR ETANERCEPT IN INFLAMMATORY RHEUMATIC DISEASES: THE EXPERIENCE OF COCHIN UNIVERSITY HOSPITAL PARIS-FRANCE.

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**Background:** Etanercept biosimilar (bETN) is available for treatment of spondyloarthritis (SpA) and rheumatoid arthritis (RA) since 2016 in France. Data showing effectiveness and safety of bETN are still limited.

**Objectives:** 1/To evaluate the RA and SpA patients' and treating rheumatologists' characteristics associated with the switch 2/To evaluate the safety and efficiency of bETN.

**Methods:** Patients: All the patients receiving innovator etanercept for at least 3 months on October 2016 and monitored in the department of rheumatology B of Cochin hospital. Physicians: All the 9 physicians in charge of at least one patient. Study design: After information (one hour session) on the biosimilars, all the physicians were invited to propose a switch from innovator etanercept to bETN. Data collected: physicians' characteristics, patients' characteristics (demographics, diagnosis of the rheumatic disease, disease activity parameters).

**Results:** Of the 435 outpatients who had received etanercept; 304 were receiving etanercept in 2016 and 183 were eligible for a potential switch (the remaining 121 patients did not attend any out-patient-clinic between October 1st 2016 and April 1st 2017).

The percentage of patients who switched to bETN was 51.6% (94 patients).

This switch was more frequently performed in patients monitored by older physicians (mean age: 50.4±14.3 vs 44.8±11.3, p=0.005) and by physicians with a full-time academical position (56.4% vs 13.5%, p<0.001)

The patients' characteristics were similar: % RA (51.1% vs 44.9%), age (52.1±15 vs 50.5±15), female gender (57.4% vs 51.6%), disease duration (16.8±11.9 vs 14.8±11.3) except for the NSAID intake (28.3% vs 12.3%, p=0.014) and the global evaluation (25.2±19.4 vs 19.1±21.8, p=0.02) in the switchers vs non-switchers, respectively. However, no independent factors were associated with the switch in the multivariate analysis.

The bETN retention rate was 83% [0.76–0.92] after a 6 month follow-up period. The bETN was discontinued in 26 patients with the following reasons: inefficiency 13 patients, adverse event 13 patients (painful injection site n = 4, fatigue = 2, pruritus n = 2, "allergic reaction" n = 1, headache n = 1, pollakiuria n = 1, dizziness n = 1, supply problem n = 1).

The univariate analysis aimed at evaluating the baseline predisposing factors of bETN discontinuation overtime picked up the baseline objective sign of inflammation (defined by CRP≥6 mg/L or ESA ≥28 mm) (OR=4.18 [1.19 – 14.66] p=0.0256), p=0.002) and global disease activity score (OR = 1.57 [1.04 – 2.36], p=0.03). Nevertheless, no independent factors were associated with the switch in the multivariate analysis.

There was no difference in the changes in the disease activity parameters in both the completer and ITT population.

**Conclusions:** This study suggests that:

- 1/The probability to switch from etanercept innovator to bETN was mainly related to physicians' behavior
- 2/Using an open design, the percentage of patients complaining of a lower efficiency and/or a worse safety profile of the biosimilar was high
- 3/There was no objective parameter permitting to conclude at a lower efficiency and/or a worse safety profile of the bETN in comparison to the innovator etanercept.

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SAT0200

#### LONG TERM SAFETY OF FILGOTINIB IN THE TREATMENT OF RHEUMATOID ARTHRITIS: WEEK 108 DATA FROM A PHASE 2B OPEN-LABEL EXTENSION STUDY

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**Background:** Filgotinib (FIL) is an orally administered, selective inhibitor of Janus Kinase 1 (JAK1) in Phase 3 development for the treatment of rheumatoid arthritis (RA).

**Objectives:** Assess the long-term safety and efficacy of FIL in the DARWIN 3 open-label extension study.

**Methods:** Two 24-week Phase 2b studies were completed in patients (pts) with moderately to severely active RA (DARWIN 1, DARWIN 2; Ref 1, 2). Following study completion, pts were offered FIL in the ongoing DARWIN 3 extension study: 100 mg QD (US males), 200 mg QD, or 100 mg BID. This report summarizes safety data from the first dose of FIL in the DARWIN program to 11 Oct 2017 and efficacy data from the DARWIN 3 baseline visit to Week 108, which all ongoing pts have completed.

**Results:** Of 877 pts, 790 (90%) completed DARWIN 1/2, and 739 (84%) enrolled in DARWIN 3; 603 (82%) were female, mean age 53 years. At analysis, 491/739 (66%) were on study. Cumulative patient years of exposure (PYE) was 1931, median time on study drug was 1072 days. Key data are summarized in table 1. 87%, 68%, and 48% of pts achieved ACR20/50/70, respectively, and 72% achieved DAS28-CRP≤3.2 (by observed case analysis).

Table 1 Key Safety Events and Lab Abnormalities per 100 PYE\*

Events Per 100 PYE	Filgotinib + MTX		Filgotinib Monotherapy	Total* (N=739)
	100 mg BID (N=249)	200 mg QD (N=250)	200 mg QD (N=222)	
Treatment-emergent AEs (TEAEs)	146.7	141.7	150.3	146.2
Serious TEAEs	5.9	3.9	7.4	5.7
TEAEs for infections	44.5	39.3	37.2	40.9
Serious TEAEs for infections	1.2	0.6	2.2	1.3
Malignancy (excl. NMSC <sup>†</sup> )	0.8	0.4	0.7	0.6
Herpes Zoster	1.2	1.5	1.1	1.2
Deep Vein Thrombosis <sup>‡</sup>	0.2	0	0	0.1
Pulmonary Embolism <sup>‡</sup>	0.2	0	0	0.1
Active Tuberculosis	0	0	0	0
≥ Grade 3 Laboratory Abnormalities				
Hemoglobin ↓	0.5	0.1	0	0.2
Lymphocytes ↓	1.2	0.9	0.4	0.8
Neutrophils ↓	0.3	0.1	0.2	0.2
Platelets ↓	0	0.3	0	0.1
ALT ↑	0.2	0.1	0.2	0.2
Creatinine ↑	0.3	0	0	0.1
LDL ≥ 190 mg/dL	17.0	5.5	18.4	13.1
HDL < 40 mg/dL	5.4	7.3	6.9	7.1

\*Treatment groups with fewer than 10 subjects were omitted for clarity; <sup>†</sup>Non-melanoma skin cancer; <sup>‡</sup>Single patient DVT leading to PE

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**Conclusions:** Filgotinib long-term RA data demonstrates an acceptable safety and durable efficacy profile.

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**Disclosure of Interest:** R. Westhovens Grant/research support from: Galapagos and Celltrion, Roche and BMS, Consultant for: Galapagos and Celltrion, Roche and BMS, R. Alten Grant/research support from: Galapagos/Gilead, K. Winthrop Consultant for: Pfizer, Lilly, Galapagos, Gilead, AbbVie, M. Greenwald Grant/research support from: Gilead, L. Ponce: None declared, F. Enriquez-Sosa: None declared, M. Stanislavchuk: None declared, M. Mazur: None declared, A. Spindler: None declared, R. Cseuz: None declared, N. Nikulenkova: None

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SAT0201

### REAL WORLD EVIDENCE ON SWITCHING BETWEEN ETANERCEPT AND ITS BIOSIMILAR IN RHEUMATIC DISEASES

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**Background:** Etanercept (Etn) is a biologic agent (BA) that has been proved to be successful in the treatment of rheumatic diseases, by acting as tumour necrosis factor inhibitor, but it is costly. In February 2016, the first etanercept biosimilar (EtnBS) was launched in Germany as a relatively cheaper alternative.

**Objectives:** In a recent study using the German Longitudinal Prescriptions database IQVIA® (LRx) we showed that despite many patients (approximately 50%) were moved from EtnBA to EtnBS treatment over the year following its launch, some (10%) switched back to the original product after few months<sup>1</sup>. As new data are available from the database, the objective of this second analysis was to evaluate switching-back dynamics over longer follow-up durations.

**Methods:** The German LRx covers prescription data from January 2008, representing approximately 60% of the German statutory health insurance market. The study period was from February 2016, date of EtnBS launch in Germany, to August 2017 (last available data). Patients receiving first EtnBS prescription (index date) during the study period were retrospectively identified and separated into two groups based on treatment received in the 12 months prior to index date: treatment-naïve patients (no prior biologic treatment) and patients previously treated with EtnBA or other anti-TNF biologics. For the latter group, the cumulative proportion of patients switching back from EtnBS to EtnBA and the median time to the switch-back were evaluated over 3 time periods corresponding to dates of new data availability within the data source: February 2016-September 2016 (1), February 2016-March 2017 (2), and February 2016-August 2017 (3). The results were compared using the chi square test with significance set at p<0.05. Data on the market share for biologic agents and their biosimilars in rheumatic diseases are also shown on a monthly basis, between January 2015 and August 2017.

**Results:** A total of 707, 1,607 and 2,229 patients were identified who received prior EtnBA treatment before switching to EtnBS in time periods 1, 2 and 3 respectively. Of these patients, the proportion of those who switched back to EtnBA significantly (p<0.05) increased over time: 53 (7%) in time period 1, 153 (10%) in time period 2 and 320 (14%) in time period 3. Patients generally switched back to the biologic agent within 3–4 months of starting EtnBS treatment. The use of EtnBS by rheumatologists has constantly grown since February 2016, with a market share of 6% in Dec 2016 increased to 12% in August 2017.

**Conclusions:** This study confirmed previous findings on switching dynamics between EtnBA and its biosimilar. In addition, the study shows that despite a constant increase in the use of EtnBS since its launch, from September 2016 to August 2017, the proportion of patients who switch back to EtnBA after 3–4 months of initiating EtnBS has doubled.

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SAT0202

### COMPARISON OF THE BIOAVAILABILITY OF A SINGLE DOSE OF CERTOLIZUMAB PEGOL INJECTED BY PRE-FILLED SYRINGE OR BY ELECTRO-MECHANICAL AUTO-INJECTION E-DEVICE: A PHASE 1, OPEN-LABEL, RANDOMISED, PARALLEL GROUP, SINGLE-CENTRE BIOEQUIVALENCE STUDY

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**Background:** When administered subcutaneously (SC) using a pre-filled syringe (PFS), the anti-TNF certolizumab pegol (CZP) has a half-life of ~14 days and has shown good bioavailability (~80%) at all tested doses in healthy volunteers and patients with rheumatoid arthritis.<sup>1,2</sup> A reusable electro-mechanical auto-injection device (e-Device), ava<sup>®</sup>, was recently approved in the EU,<sup>1</sup> providing an alternative SC-delivered CZP option in addition to the PFS and autoinjector device (AutoClicks<sup>®</sup>).<sup>1,3</sup>

**Objectives:** To determine if a single 200 mg CZP dose is bioequivalent when delivered SC by PFS or e-Device, and to assess the safety and tolerability of both administration methods.

**Methods:** NCT02806219 was a phase 1, open-label, randomized, parallel group, single-center bioequivalence study. Healthy volunteers were randomized 1:1 to receive CZP via either the PFS or e-Device. Primary outcomes were assessed using the pharmacokinetic per-protocol set (PK-PPS): maximum CZP plasma concentration (C<sub>max</sub>), area under the plasma concentration vs time curve (AUC), and AUC from baseline (BL) to final data point (AUC<sub>(0-t)</sub>). At BL (Day 1), volunteers received a single 200 mg CZP dose. CZP plasma concentrations were measured on Day 1 prior to CZP administration, at 12 hours (h) post-dose, and on Days 2–7, 10, 14, 21, 28, 42, 56, and 70. Safety and tolerability were assessed using the safety set (all receiving a CZP dose) via reported treatment-emergent adverse events (TEAEs), serious AEs, and adverse device events (ADEs: AEs considered by the investigator to be related to/caused by the device). An injection site pain visual analog scale (VAS; 0–100 mm) was completed immediately post-injection (0 h) and 1 h post-injection.

**Results:** 100 healthy volunteers were randomized to receive CZP either via PFS (n=50) or e-Device (n=50). The mean plasma CZP concentration vs time profiles for the e-Device and PFS were comparable. Point estimates and 90% confidence intervals (CIs) for test/reference geometric mean ratios in C<sub>max</sub> and AUC were contained within bioequivalence limits of 80–125% (table 1). Both administration methods were equally well tolerated; all reported TEAEs were mild or moderate, with no ADEs or injection site reaction TEAEs. Mean VAS pain scores were low at 0 h (PFS: 10.7 [SD 14.3], e-Device: 18.0 [24.4]) and 1 h (1.4 [2.9] vs 2.7 [7.0]).

Table 1 Results of the bioequivalence analysis comparing the PFS and e-Device

	Reference		Test		Test/Reference		ANCOVA CV (%)
	CZP 200mg PFS	CZP 200mg e-Device	CZP 200mg PFS	CZP 200mg e-Device	Point estimate	90% CI	
C <sub>max</sub> (µg/mL)	48	50	28.8 (27.1, 30.5)	28.7 (27.1, 30.4)	1.00	0.93, 1.07	20.6
AUC <sub>0-t</sub> (µg·d/mL)	47	50	670.8 (623.7, 721.5)	668.7 (623.1, 717.7)	1.00	0.92, 1.09	25.6
AUC (µg·d/mL)	45	49	701.8 (653.3, 754.0)	688.6 (643.0, 737.6)	0.98	0.90, 1.07	24.8

PK-PPS: ANCOVA: analysis of covariance; AUC: area under the curve; AUC<sub>(0-t)</sub>: AUC from baseline to final data point; CI: confidence interval; C<sub>max</sub>: maximum plasma concentration; CV: coefficient of variation; d: day; CZP: certolizumab pegol; LS: least squares; PFS: pre-filled syringe; PK-PPS: pharmacokinetic per-protocol set.

**Conclusions:** CZP 200 mg doses were bioequivalent whether administered by PFS or e-Device. The SC-delivered CZP injections were well tolerated in healthy volunteers when using either method.

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**SAT0203 OPTIMIZATION OF BIOLOGIC TAPERING USING ULTRASOUND IN RA PATIENTS**

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**Background:** Optimal treatment using Treat 2 Target regimen has reduced morbidity and mortality rates in RA patients. However the use of biological therapies is expensive and a huge financial burden on Health budgets.

Current guidelines suggest to consider tapering biological therapies in patients with sustained low disease activity<sup>1</sup>.

There is a risk of overtreatment in this cohort, with potential risks from sustained immunosuppression of increased infection rates and the chance of malignancy.

**Objectives:** Studies have shown biologic tapering is possible. Some studies have performed progressive tapering using DAS28 scores, others with ultrasonography assessment<sup>2</sup>.

We used a progressive tapering strategy in tapering biological DMARDs in a selected RA cohort in a busy UK University Teaching Hospital, using ultrasound to guide the tapering process throughout and for detecting early recurrence during longer term followup.

**Methods: Inclusion Criteria:** Patients identified from routine clinic appointments as being either in clinical remission (DAS 28<2.6), or with low disease activity (DAS 28<3.2 and no swollen joints), and with no flares of their RA for at least 12 months.

**Assessment:** At each clinic visit the patients' joints were examined, a DAS 28 and HAQ completed. Ultrasound was performed on hand and wrist joints (MCPJ's, PIPJ's, Wrists) in both Grey scale and Power Doppler to assess for inflammation. Biologic medication was progressively tapered according to results. Adalimumab was tapered to '3 weekly – 4 weekly – stop' and Etanercept to '2 weekly – 3 weekly – stop'. Patients were given 3 monthly appointments. If patient flared or Ultrasound showed active synovitis, tapering was stopped and medication adjusted according to the findings. Patients were followed up for a year at 3 monthly intervals, a year at 6 monthly intervals and then referred back to routine outpatient clinic.

**Results:** 28 patients were identified on Adalimumab and 8 on Etanercept. Adalimumab: 17 patients (61%) stopped completely. At the time of writing, 16 (94%) remained off at 6 months. 12 (71%) at 12 months and 5 (29%) for >23 months. 6/17 flared and had to restart medication – 3 returned to a 4 weekly dose, 1 to 3 weekly and 2 to 2 weekly. 11/17 (65%) remain off medication.

At present 7 patients (25%) are on a 4 weekly dose, 1 (4%) patient is on a 3 weekly dose and 9 (32%) remain on 2 weekly.

Etanercept: 4 patients (50%) stopped completely. 1 of these has remained off for over 12 months and 1 over 24 months. 1 of these patients returned to weekly injections within 4 months

1 patient (12.5%) is on a 2 weekly dose and 4 (50%) remain on weekly

The management of 72% of patients was optimised using Ultrasonography. Ongoing cost savings as a result of tapering were in the region of £250,000.

**Conclusions:** Our study shows Ultrasound significantly aided in successful biologic tapering. It helped in selection of appropriate patients, as well as in monitoring during/after tapering. It also resulted in significant cost savings in the region of £250,000

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**SAT0204 NAÏVE AND RECENT THYMIC EMIGRANT CD4+ T CELLS INCREASE IN RHEUMATOID PATIENTS TREATED WITH ABATACEPT.**

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**Background:** CD4+ T cells in rheumatoid arthritis (RA) display a peculiar restriction of the T-cell receptor (TCR) repertoire which compromises their ability to react to novel antigens (1). We demonstrated that this process could be partially reverted by abatacept (ABA), which is a blocker of T lymphocyte co-stimulation, used in the treatment of RA (2). This effect could be at least in part due to a reduced generation of oligoclonal effector T cells, such as CD4+CD28-T cells (2). To better understand the mechanisms underlying this phenomenon, we speculated that ABA could influence the frequency of other peripheral T cell subpopulations, even at early stages of maturation. The homeostasis of the naïve T cell pool is maintained not only by thymus production, but also by mechanisms of peripheral replication involving TCR activation, which can be revealed by CD31 (PECAM-1) down-modulation (3). Indeed, CD4+CD45RA+CD31+ T cells have been described as recent thymic emigrants (RTE) newly produced by the thymus and CD4+CD45RA+CD31- T cells as central naïve, involved in a self-renewal peripheral process. This latter population may have a restriction of TCR repertoire and was shown to be involved in mechanisms of cardiovascular damage in patients with coronary syndrome (4).

**Objectives:** We aimed at profiling circulating naïve CD4+CD45RA+ T cells, by assessing their expression of CD31.

**Methods:** Thirty-one RA patients (median age [10<sup>th</sup>-90<sup>th</sup> percentile] 42 [25–64] years) were evaluated before and after 6 months of ABA therapy. The response to treatment was evaluated with the EULAR criteria. Phenotypic analysis of peripheral blood T lymphocytes was made by flow-cytometry.

**Results:** After ABA therapy, the absolute number of total T CD4+ increased from 780 [423–1351] to 1000 [658–1566] cells/mm<sup>3</sup> (p=0.01). Total naïve CD4+ increased in percentage (33 [18–56] vs 40 [20–61] % of CD4+; p=0.02) and in absolute number (257 [82–568] vs 344 [62–689] cells/mm<sup>3</sup>; p=0.03). In parallel, the number of RTE increased in percentage (10.6 [2–26] vs 11.6 [3–25] % of CD4+; p=0.04) and in absolute number (51 [15–194] vs 110 [23–271] cells/mm<sup>3</sup>; p=0.01). The central naïve counterpart did not show significant variations in percentage (29 [23–40] vs 27 [20–38] % of CD4+; p=0.20) nor in absolute number (191 [41–404] vs 242 [76–526] cells/mm<sup>3</sup>; p=0.20). The modifications of T cell number were not significantly different when good and moderate responder (n=22) and no responder (n=9) patients were compared, at baseline and after therapy. No correlation was found between age of patients, clinical features of the disease and RTE number at baseline and after 6 months.

**Conclusions:** The number of total naïve T cells increases after therapy with ABA together with the number of RTE, suggesting a thymic output boost. Besides the peripheral effect in reducing the number of effector T cells which was showed by previous studies (5), ABA could have a role in promoting the immune reconstitution at the early stage of T cell development. Furthermore, a consequent favorable effect on possible cardiovascular damage mechanisms mediated by CD31-T cells might be hypothesized.

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**SAT0205 COMPARISON OF DISEASE STATUS IN UK PATIENTS WITH RA RECEIVING TNFI VS CDMARD**

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**Background:** UK NICE guidance recommends initiation of tumour necrosis factor-alpha inhibitor (TNFi) for patients with severe RA unresponsive to intensive



therapy with conventional disease-modifying anti-rheumatic drugs (cDMARD). Data comparing cDMARD and TNFi in clinical trial settings are common, but there is limited published real-world evidence on their comparative effectiveness.

**Objectives:** Compare disease status and outcomes in UK patients with RA receiving cDMARD vs TNFi.

**Methods:** Data derive from Adelphi's RA Disease Specific Programme 2017, a cross-sectional survey of 49 UK rheumatologists providing information on demographics, disease history, disease status and treatment of patients with RA. All patients (n=640) were included in the RA treatment analysis; patients were included in the comparative analysis if at the time of survey they had been receiving current treatment for at least 3 months, with either cDMARD (and had never received biologic(b)DMARD), or a TNFi (and had never received prior bDMARD). A propensity score based on BMI, duration on current therapy, RA severity and disease duration at initiation of current therapy was used to match treatment groups. Using Abadie-Imbens standard errors, clinical characteristics and measures of disease activity were compared between the matched groups.

**Results:** Current therapy of 640 patients: 379 (59.2%) bDMARD, of which 253 (66.8%) were receiving TNFi; 212 (33%) cDMARD; 18 (2.8%) had never received any DMARD, 15 (2.3%) had discontinued bDMARD. Mean DAS28 at initiation of therapy was 4.94 in overall cDMARD and 5.77 in TNFi groups. Table 1 shows the comparative analysis of cDMARD vs TNFi matched treatment groups. The cDMARD group had a higher proportion of moderate/severe and active/very active disease at time of survey, a higher proportion of patients in this group had no improvement in disease severity or activity since initiation of current therapy, and they were less likely to have achieved a EULAR response. A higher proportion of cDMARD patients and physicians were not satisfied with their disease control. Mean DAS28 scores at time of survey had declined from time of initiation of therapy to time of survey in matched cDMARD vs TNFi groups, from 5.27 to 3.1 vs 5.77 to 2.7 respectively.

Table 1

	%	%	P=
<b>Physician reported current disease status</b>			
Moderate or severe	43.5	22.4	0.02
'Active' or 'very active' disease	58.8	44.1	0.10
<b>Change in disease status since initiation of current treatment</b>			
'No improvement' in severity	25.3	7.7	0.04
'No improvement' in disease activity <sup>1</sup>	22.0	7.7	0.08
Not achieved EULAR response (based on DAS28) <sup>2</sup>	16.0	6.9	0.08
<b>Satisfaction with current disease control</b>			
Physicians 'not satisfied'	39.4	8.2	<0.01
Patients 'not satisfied' <sup>3</sup>	31.7	16.7	0.35

Lower sample size due to missing values: <sup>1</sup> cDMARD 147, TNFi 168; <sup>2</sup> cDMARD 75, TNFi 131; <sup>3</sup> cDMARD 54, TNFi 60

**Conclusions:** UK patients with RA receiving cDMARD have poorer outcomes, in terms of measured disease status and control, than their matched counterparts receiving TNFi. Despite having a higher mean DAS score at initiation, patients in the TNFi group had a lower mean score at time of survey than patients receiving cDMARD. This real-world evidence highlights the continued utility of TNFi as effective treatments for patients with RA. Potential benefit of early TNFi initiation merits further research.

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SAT0206

#### RESULTS OF THE ALTERRA CLINICAL TRIAL – THE EFFICACY OF THE ALTERNATIVE DOSING REGIMEN FOR RITUXIMAB BIOSIMILAR IN bDMARDS NAIVE PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Rituximab (RTX) is successfully used in patients with active rheumatoid arthritis (RA) who previously received biological disease-modifying

antirheumatic drugs (bDMARDs) at a dose of 1000 mg. Previous preclinical and clinical studies showed that BCD-020 is highly similar to innovator RTX. ALTERRA study demonstrated that first-line use of 600 mg BCD-020 is very effective in bDMARDs naive patients with RA.

**Objectives:** The goal of ALTERRA study was to evaluate the efficacy and safety of the alternative dosing regimen (600 mg) of BCD-020 in bDMARDs naive patients with RA.

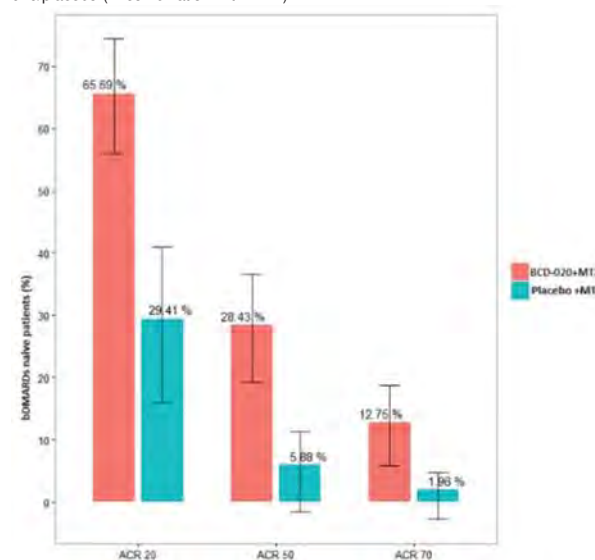
**Methods:** ALTERRA study was conducted as multicenter randomized double-blind placebo-controlled phase 3 study. After the screening patients were stratified by age, anti-CCP level and DAS28 score, randomized (2:1) into 2 arms and received BCD-020 (in combination with methotrexate (MTX)) in a dose 600 mg IV or placebo (in combination with MTX) on day 1 and day 15, then, if the activity of arthritis persisted after 24 wks of study, a second course was provided. Patients were observed up to 52 wks.

**Results:** A total of 159 patients were enrolled in ALTERRA study, 107 patients in BCD-020 arm and 52 patients in placebo arm.

**Efficacy:** ACR20 at wk 24 was reached by 65.69% of patients in BCD-020 arm and 29.41% in placebo arm (p=0.00005, the difference in proportion of registration ACR20 with 95%CI was 29.41 [19.27%; 53.28%], margin 10.5%) in per protocol population, so hypothesis of superiority was confirmed. The performed analysis showed a much more pronounced decrease in the DAS28-4 (ESR) index in BCD-020 arm compared with placebo arm (p=0.0006) at wk 24. A much more significant decrease in change of the HAQ-DI index was also shown in the BCD-020 arm (p=0.008). Analysis of efficacy at wk 52 showed the preservation of the response after 2 courses of therapy with BCD-020, 600 mg (in combination with MTX): ACR20 reached by 84.5%, ACR50 – by 54.6%, ACR70 – by 29.9 % of patients.

**Safety:** BCD-020 showed a favorable safety profile with no significant difference with placebo use (in combination with MTX). After 24 wks patients of both groups developed high similar level of related adverse events: 16.8% of patients in BCD-020 arm and 11.76% in placebo arm (p=0.555). There were only 3 cases of severe adverse events (2.8%) in BCD-020 arm and 2 cases (3.92%) in placebo group. From wk 24 to wk 52: 13.08% of patients (who received 2 courses of BCD-020) and 19.61% of patients (who received one course of BCD-020 after 24 wk) developed related adverse events.

Figure 1 ACR 20/50/70 in bDMARDs naive patients with RA after 24-wk treatment of BCD-020/placebo (in combination with MTX).



**Conclusions:** ALTERRA study showed high efficacy and favorable safety profile of RTX biosimilar BCD-020 at a dose of 600 mg in combination with MTX in bDMARDs naive patients with RA.

**Disclosure of Interest:** V. Mazurov: None declared, L. Denisov: None declared, I. Gordeev: None declared, O. Nesmeyanova: None declared, T. Plaksina: None declared, E. Ilivanova: None declared, D. Krechikova: None declared, E. Zonova: None declared, L. Knyazeva: None declared, A. Artemeva Employee of: JSC BIOCAD, E. Dokukina Employee of: JSC BIOCAD, E. Chernyaeva Employee of: JSC BIOCAD, R. Ivanov Employee of: JSC BIOCAD

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SAT0207

### DEPRESSIVE SYMPTOMS IN PATIENTS WITH RHEUMATOID ARTHRITIS IN SARILUMAB TARGET AND MOBILITY TRIALS AND IMPACT OF TREATMENT

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**Background:** In patients with clinical depression, elevated interleukin-6 (IL-6) levels have been associated with higher symptom severity and greater resistance to standard antidepressant treatments. Depression and IL-6 elevation are highly prevalent in patients with rheumatoid arthritis (RA), and their co-occurrence may have an impact on health-related quality of life (HRQoL). Sarilumab is a human immunoglobulin G1 anti IL-6 receptor  $\alpha$  (anti-IL-6R $\alpha$ ) monoclonal antibody for treatment of moderately-to-severely active RA.

**Objectives:** To explore the effect of sarilumab on HRQoL in patients with moderate-to-severely active RA with co-existing symptoms of depression.

**Methods:** *Post-hoc* statistical analyses were performed on the Medical Outcomes Study Short Form 36 (SF-36) in 2 randomized controlled trials, MOBILITY (NCT01061736) and TARGET (NCT01709578), of sarilumab subcutaneous 150 mg or 200 mg every 2 weeks vs placebo, each combined with conventional synthetic disease modifying anti-rheumatic drugs. Patients were classified at baseline for probable major depressive disorder<sup>1</sup> (PMDD; SF-36 mental health (MH) domain score  $\leq 56$ ) or probable depressed mood and anhedonia<sup>2</sup> (PDMA; score  $\leq 10$  on both items of the MH domain: "Have You Felt Downhearted and Depressed" and "Have You Felt So down in the Dumps that nothing could cheer you up"). Analyses of least squares mean differences in changes from baseline in SF-36 domain scores for sarilumab versus placebo in the PMDD and PDMA subgroups were performed at Weeks 4, 12 and 24 for TARGET and Weeks 24 and 52 for MOBILITY. Sensitivity analysis adjusted for baseline Disease Activity Score 28 C-reactive protein (DAS28-CRP).

**Results:** Of the 546 patients from TARGET and 1197 from MOBILITY, 59.5% and 60.2% were classified as PMDD respectively, and 50.4% and 51.6% as PDMA. In both RCTs disease duration and baseline DAS-28 CRP, tender and swollen joint count (table 1) and SF-36 domain scores (figure 1) were similar between sarilumab and placebo within the PMDD and PDMA subpopulations. TARGET: MH scores for PMDD and PDMA subgroups were nominally higher ( $p < 0.05$ ) for sarilumab 200 mg versus placebo at all assessments. Both subgroups also scored nominally higher ( $p < 0.05$ ) in the domains of physical functioning (PF), role-physical (RP), bodily pain (BP), general health (GH), vitality (VT) and social functioning (SF) but not role-emotional (RE) in the PMDD subgroup at Week 24 (figure 1). MOBILITY: all scores except PF and RE were nominally higher ( $p < 0.05$ ) for sarilumab 200 mg versus placebo for Weeks 24 (figure 1). Sensitivity analysis provided similar results. Exploratory results also suggested reduced prevalence of depressive symptoms over the course of the trial.

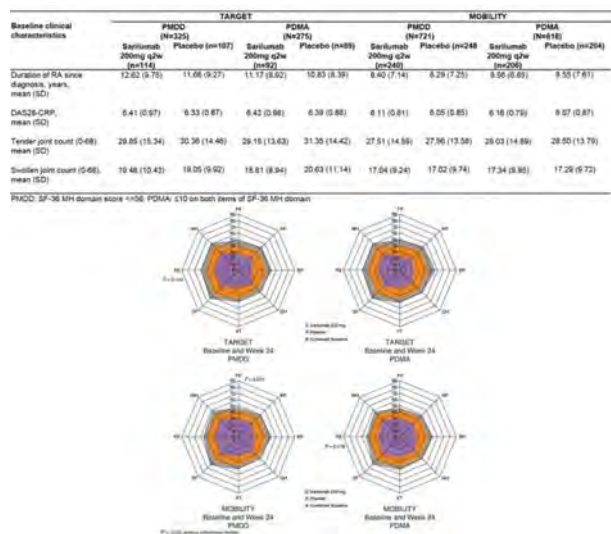


Figure 1. PMDD: SF-36 MH domain score  $\leq 56$ ; PDMA:  $\leq 10$  on both items of SF-36 MH domain

**Conclusions:** In patients with RA and depressive symptoms, sarilumab provided clinically meaningful improvements in most domains of health status/HRQoL compared with placebo, which may be a function of targeting the IL-6R $\alpha$  and subsequent reduction in disease activity.

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SAT0208

### HOW GOOD ELDERLY RHEUMATOID ARTHRITIS PATIENTS RESPOND AT FIRST YEAR OF TREATMENT WITH CERTOLIZUMAB PEGOL?

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**Background:** In rheumatoid arthritis (RA), the efficacy and safety of Certolizumab pegol (CZP) is well established, as reported in randomized clinical trials (RCT)<sup>1</sup> and some registries<sup>2</sup>. Only the 30% of RA patients are within the age range of 65 years or older. However, they are usually excluded from the RCT. Aging is associated with declining immune cell function and age-related comorbidities<sup>3,4</sup>.

**Objectives:** The aim of this study was to determine the effectiveness and safety of CZP in elderly patients in a real world setting at 12 months follow-up.

**Methods:** Observational longitudinal prospective study of RA patients from 40 sites in Spain. Variables (baseline, 3- and 12-month assessment): socio-demographics, smoking status, previous synthetic DMARD (sDMARD) and biological DMARD (bDMARD) use; TJC, SJC, ESR, CRP, DAS28. Response variables EULAR Moderate/Good Response and DAS28 remission and Safety were assessed. Low Disease Activity as DAS28 remission or mild DAS28. Descriptive, comparative and Logistic regression analyses were performed comparing  $< 65$  vs.  $> 65$  yr population. Kaplan-Meier survival curve was performed.

**Results:** A total of 501 RA patients were included, 23% were aged  $\geq 65$  yr (mean age 70.8 ( $\pm 4.5$  SD)yr). Sociodemographics and baseline features are shown in table 1.

Table 1.

	$< 65$	$> 65$	P
Women	77.7%	80.7%	NS
Disease evolution (yr)	6.7 ( $\pm 6.5$ SD)	10.4 ( $\pm 9.1$ SD)	$< 0.001$
- $\leq 2$ yr	-30.5%	-18.3%	-0.012
Smoking status:			0.024
Current	19.9%	9.1%	
Exsmoker never	13.6%	11.1%	
Bio-naïve	66.5%	79.8%	
	56%	53.1%	NS
		*previous Abatacept use was higher in $> 65$ yr ( $p = 0.017$ )	

Efficacy variables are shown in table 2.

Variable	$< 65$ years	$\geq 65$ years	p value
DAS28 Remission (yes)	43%	31.3%	0.026
DAS28 Low Disease Activity	57.5%	47.3%	NS
DAS28 $> 1.2$ score reduction	55.4%	60.7%	NS
EULAR Response	67.7%	75%	NS
CZP Retention rate	74.6%	67.5%	NS
Adverse Events	11.3%	19.3%	0.026

**Comorbidities (yes)** 34.8% 46.5% 0.024

The only associated factors to a better response in patients  $\geq 65$  yr were: higher DAS28 score, lower HAQ score and bio-naïve ( $p < 0.05$ ).

**Conclusions:** The effectiveness of CZP among  $\geq 65$  yr only differed from their younger counterparts from DAS28 remission rate, with a lower percentage, and side-effects (higher percentage, with higher comorbidities percentage too). However, after one year of real-life data CZP seemed as both safety and effective enough as younger RA patients in real-life scenario.

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#### SAT0209 A COMPARATIVE REAL-WORLD UTILIZATION PATTERNS OF INNOVATOR AND BIOSIMILAR INFlixIMAB IN A TREATMENT NAÏVE AND SWITCH POPULATION FROM GERMANY: A PRESCRIPTION CLAIMS ANALYSIS

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**Background:** Data on treatment utilization patterns for innovator infliximab (IFX) and biosimilar infliximab (CT-P13) in IBD are scarce. Given low uptake of biosimilars in Canada to date, evaluation of treatment initiation and discontinuation was undertaken in a proxy country, Germany, which has similar demographic factors and neither have a mandated biosimilar switch policy.

**Objectives:** Retrospective prescription claims analysis comparing utilization patterns of innovator (IFX) and biosimilar (CT-P13) infliximab in treatment naïve population at 12 months and in patients continuing IFX vs switching to CT-P13 at 6 months.

**Methods:** QuintilesIMS™ longitudinal health insurance prescription data from Germany identified patients with an index claim of IFX or CT-P13 in all indications between Feb 2015-Oct 2016. Twelve-month post-drug initiation and 6-month post innovator-to-biosimilar switch retention analyses were conducted. All patients had sufficient claims history post-index and  $\geq 2$  claims of IFX or CT-P13 within the analysis period. Six-month analyses included: 1) matched analysis where each CT-P13 switch patient was matched to 5 IFX patients for IFX exposure prior to switch; 2) unmatched analysis where CT-P13 switch patients were compared to the first 6 months of the IFX treatment naïve population. Log-binomial regression analyses were conducted to determine the relative risk (RR) of being retained on treatment at 6 or 12 months adjusted for age, sex, biologic treatment history and prescriber specialty.

**Results:** 6,491 patients had a claim of IFX or CT-P13. Of these, 1,160 and 1,324 patients had follow up time for inclusion in the 12-month naïve and 6-month post-switch analyses, respectively. Only IFX to CT-P13 switch utilization ( $n=101$ ) was investigated. The risk adjusted probability of being retained on treatment after 12 months was 23% greater in the IFX group than in the CT-P13 group (RR IFX=1.23, 95% Confidence Interval [CI]: 1.12–1.36,  $p < 0.0001$ ). The probability of being retained was also greater in men, those who were bio-naïve and those prescribed drug by a rheumatologist. In the matched 6 months post-switch analysis the risk adjusted probability of being retained on treatment was 26% greater in the IFX maintenance group than in the CT-P13 switch group (RR IFX=1.26, 95%CI: 1.10–1.45,  $p=0.0007$ ). The probability of being retained was also greater in those prescribed drug by a rheumatologist. Similar results were found in the unmatched analysis (RR IFX =1.32, 95%CI: 1.16–1.51,  $p < 0.0001$ ), where the probability of being retained was also greater in men and in those who were bio-naïve.

**Conclusions:** The findings from Germany demonstrate significant differences in the real-world utilization patterns of patients treated with IFX or CT-P13 in all labelled indications. Limitations of this study include a heterogeneous population, disease severity and reasons for staying on treatment or switching could not be determined. Future analyses should capture clinical outcomes to better understand observed utilization patterns.

**Disclosure of Interest:** E. Ewara Employee of: Janssen, L. Ellis Employee of: Janssen, K. Goyal Employee of: Janssen, V. Jairath Consultant for: Abbvie, Takeda, Shire, Janssen, Ferring, Sandoz, Speakers bureau: Ferring, Takeda, Shire, Janssen, A. M. Marrache Employee of: Janssen, X. Baraliakos: None declared

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#### SAT0210 TREATMENT RETENTION RATE OF BIOLOGICAL TREATMENT IN ELDERLY RHEUMATOID ARTHRITIS PATIENTS COMPARED WITH YOUNGER RHEUMATOID ARTHRITIS PATIENTS – A SINGLE CENTER COHORT STUDY -

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**Background:** Biological (BIO) therapy has become a standard therapy in the treatment of rheumatoid arthritis (RA) and long-term outcomes has increasingly evaluated. Elderly people has increased in Japan and 27.3% of whole people in Japan was 65 years of age or older in 2016. We reported treatment retention rate of BIO therapy in RA patients in EULAR2015 annual meeting as mixed data of elderly RA patients (ERA) and younger RA patients (YRA) <sup>1</sup>.

**Objectives:** This observational cohort study investigated the treatment retention rate in ERA compared with YRA.

**Methods:** Toyohashi RA Database (TRAD) was used. 330 RA patients who initiated any of BIO agents (infliximab, etanercept, adalimumab, tocilizumab, abatacept, golimumab, infliximab-BS) as first Bio in our institute from 2003 to 2016 were included in this study. Switching from one Bio agent to another was defined as continuation of Bio therapy in this study. Stopping of BIO therapy was defined as non-administration for longer than 3 months for any reasons other than remission and pregnancy related. We divided whole patients into two categories using age at initiation of BIO therapy such as YRA (64 years of age or younger) and ERA (65 years of age or older). ERA was further subdivided into two categories such as yERA (65–74 years of age) and oERA (75 years of age or older). We investigated patients' characteristics, treatment retention rate by Kaplan-Meier method and reasons of stopping BIO therapy and compared them between categories.

**Results:** Baseline characteristics at the initiation of BIO treatment: %female was 82.4%. Mean age was 58.1 years old (210 YRA, 98 yERA and 22 oERA). Mean RA duration was 10.9 years. % methotrexate (MTX) concomitant was 82.1% and mean used dose was 8.9 mg/weeks (MTX dose was restricted up to 8 mg/weeks until 2011 in Japan and 16 mg/w after 2011). % prednisolone (PSL) concomitant was 50.9%. % Bio monotherapy was 9.1%. Mean baseline DAS28-CRP and SDAI was 4.6 and 24.4, respectively. % high disease activity measured using DAS28 and SDAI at baseline was 44.4% and 42.2%, respectively (Fig1). Baseline disease activity were getting lower year by year. Continuation rate of BIO treatment in whole patients is 88.4% at 1 year, 82.0% at 3 years, 72.2% at 5 year and 57.1% at 10 years. There were significant differences in continuation rate of BIO treatment between YRA and ERA (Fig2), between yERA and oERA and between YRA and oERA, but not between yERA and oERA. Major reasons (over 10%) of stopping BIO therapy in YRA were infection other than respiratory system (15.7%), infection of respiratory systems (11.8%), ineffectiveness (11.8%) and malignancy (11.8%). Major reasons in ERA were infection of respiratory systems (21.3%) and infection other than respiratory systems (10.6%).

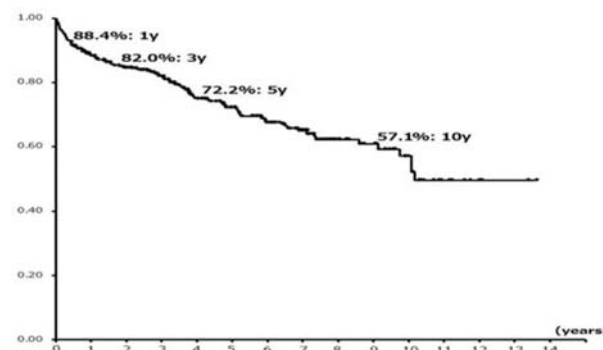


Figure 1 Continuation rate of biological therapy in whole patients



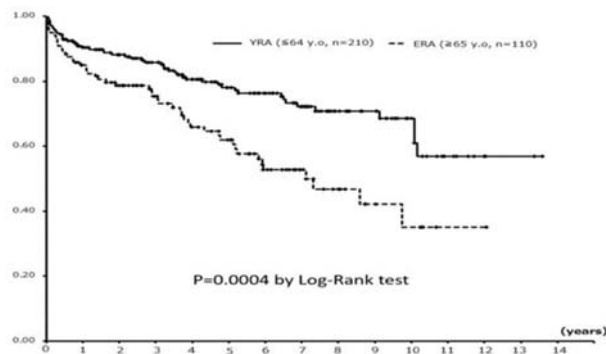


Figure 2 Continuation rate of biological therapy in YRA and ERA

YRA: younger RA patients, ERA: elderly RA patients

**Conclusions:** Although continuation rate of BIO treatment in ERA was inferior to that in YRA, that in yERA was not significantly different from that in oERA. Serious infection, especially in respiratory systems, was most frequent reason for stopping BIO therapy in ERA. These results suggested that BIO therapy in ERA demands close attention to infection and special strategies might need in the treatment of ERA people.

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[1] Hirano Y, et al. *Ann Rheum Dis* 2015;74:700.

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SAT0211

#### IS THERE A POTENTIAL FOR THERAPEUTIC DRUG MONITORING OF SUBCUTANEOUS TOCILIZUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS IN DAILY PRACTICE?

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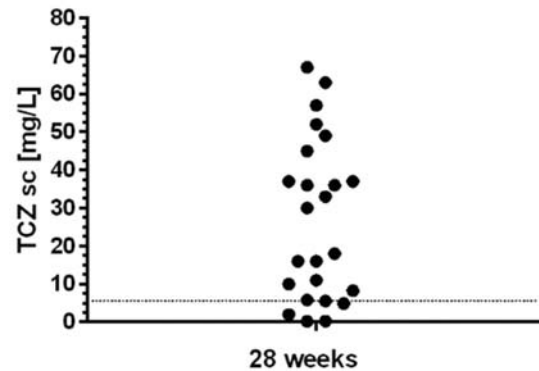
**Background:** Tocilizumab (TCZ), is a humanized antibody that competitively inhibits membrane-bound and soluble IL-6 receptors. Subcutaneous (sc) TCZ might be a potential candidate for therapeutic drug monitoring (TDM) since a high variability in serum concentrations has been reported. Considering that TCZ concentrations above 1 µg/mL have been claimed to be sufficient for normalizing CRP production (1), there might be an overexposure in a substantial proportion of patients. We expect that patients can at least reduce to a dose aiming for a trough concentration of 5 µg/mL. Insights in serum concentrations of sc TCZ with clinical efficacy are lacking, but are necessary to reduce overexposure, potential dose-dependent adverse effects and at the same time reduce costs.

**Objectives:** To describe TCZ trough serum concentrations in patients with rheumatoid arthritis (RA) treated with sc TCZ.

**Methods:** Prospective study with consecutive RA patients starting treatment with sc TCZ between June 2015 to October 2017 who had previously failed treatment with at least two DMARDs, including MTX. TCZ was administered at a dose of 162 mg every week and patients were followed for 28 weeks. The study was conducted at the Amsterdam Rheumatology and Immunology Center | Reade. Serum trough samples were collected at baseline and at 4, 16, 28 weeks thereafter. An enzyme-linked immunosorbent assay (ELISA) was used for TCZ measurement. To analyze the concentration variability among patients at 28 weeks, a last observation carried forward approach was used.

**Results:** In total, 26 patients were included in the study and 94 TCZ serum concentrations were measured. Median and interquartile range (IQR) of the follow-up period was 28 (16-28) weeks and 54% of the patients accomplished week 28. Drug concentrations ranged from 0.2 to 63 µg/mL, with an overall median (IQR) of 26.0 (10.5-42.0) µg/mL. In the majority of patients, TCZ concentrations stabilized after 4 weeks of treatment. Variability in drug concentrations at 28 weeks is shown in figure 1. Median (IQR) TCZ serum concentrations at 28 weeks was 24.0 (6.4-43.0) µg/mL, 92% of the patients achieved a concentration above 1 µg/mL and 88% had a concentration > 5 µg/mL.

#### [TCZ] at 28 weeks with LOCF



**Conclusions:** The Interindividual variability among patients on sc TCZ is remarkably high. The majority of the patients achieved serum concentrations far above 5 µg/mL, suggesting overexposure in those patients. Therefore, TDM might be useful to optimize treatment, reduce (potential) side effects and achieve cost-effectiveness.

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**Disclosure of Interest:** Z. Layegh: None declared, M. L. 'Ami: None declared, C. Bastida: None declared, A. Huitema: None declared, C. Kriekkaert Speakers bureau: Pfizer, M. Nurmohamed Grant/research support from: Pfizer, AbbVie, Roche, BMS, MSD, Mundipharma, UCB, Janssen, Menarini, Eli Lilly, Sanofi, and Celgene, Speakers bureau: Pfizer, AbbVie, Roche, BMS, MSD, Mundipharma, UCB, Janssen, Menarini, Eli Lilly, Sanofi, and Celgene, T. Rispens Grant/research support from: Pfizer, Speakers bureau: Pfizer, UCB, AbbVie, Biogen, BMS, G. Wolbink Grant/research support from: Pfizer, Speakers bureau: Abbvie, UCB, BMS, Pfizer, Biogen

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SATURDAY, 16 JUNE 2018

#### Rheumatoid arthritis - non biologic treatment and small molecules

SAT0212

#### THE SAFETY AND TOLERABILITY OF INTRA-ARTICULAR INJECTION OF TOLEROGENIC DENDRITIC CELLS IN PATIENTS WITH RHEUMATOID ARTHRITIS: THE PRELIMINARY RESULTS

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**Background:** Dendritic cells (DCs) are known to contribute to the pathogenesis of rheumatoid arthritis (RA) through the presentation of cartilage glycoprotein, production of proinflammatory cytokines and activation of Th1/Th17 responses. Along with stimulating activity, DCs may exhibit suppressive functions via capacity to induce T cell apoptosis/anergy and to generate regulatory T cells. Since these DCs have potential to control autoreactive T-lymphocytes, utilization of tolerogenic DCs seems to be a promising immunotherapeutic tool to treat RA.

**Objectives:** The aim of our study is to evaluate the safety and tolerability of a single intra-articular injection (into the knee joint) of autologous monocyte-derived dendritic cells generated in the presence of IFN-α/GM-CSF and tolerated with Dexamethasone in RA patients.

**Methods:** DCs were generated by culturing blood monocytes for 5 days with GM-CSF and IFN-α in the presence dexamethasone, applied on third day. Azoximer bromide as maturation stimuli was added on fourth day. Ten RA patients with moderate and high disease activity and ultrasound-defined knee synovitis were recruited in this study. All patients fulfilled ACR/EULAR criteria (2010) and received methotrexate, leflunomide, sulfasalazine or their combination. The patients received intra-articular injections of 1\*10<sup>6</sup>, 3\*10<sup>6</sup>, 5\*10<sup>6</sup>, 8\*10<sup>6</sup> DCs in knee joints. Safety was assessed by evaluation of adverse events (AE). Acceptability was assessed by questionnaire. DAS28 and HAQ were used for assessment of treatment efficiency. This trial registered on clinicaltrials.gov (ID: NCT03337165).

**Results:** DCs injections were safe and well tolerated. No one participants showed worsening of symptoms in targeting knee, fever, elevation of blood pressure or other AE within 7 days after injection. After one month the median pain VAS score decreased from 45 (40–65) mm to 40 (15–40) mm;  $p=0.03$ . Ultrasound and clinical examination did not detect synovitis. At 3 month no patients demonstrated recurrence of synovitis and median DAS28-ESR improved from baseline 5.1 to 4.4 ( $p=0.008$ ;  $n=10$ ). Five patients, evaluated at 6 months follow-up showed a good EULAR response (improvement of DAS28-ESR  $>1.2$ ). The median DAS28-ESR in this group decreased from 5.1 to 3.3 ( $p=0.04$ ). In addition, we detected median HAQ improvement (from 1.45 to 1.0;  $p=0.04$ ).

**Conclusions:** The data obtained suggest that single intra-articular injection of autologous tolerogenic dendritic cells is safe, well tolerated, and according to preliminary data have a potential efficiency. However, the final conclusion should be done after the completion of the trial.

**Disclosure of Interest:** None declared

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SAT0213

### TIGHT TREATMENT OF PATIENTS WITH RHEUMATOID ARTHRITIS IN THE EARLY STAGES OF DISEASE LEADS TO HIGH LEVELS OF REMISSION AND REDUCED USE OF BIOLOGICS

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**Background:** Early treatment with synthetic DMARDs has demonstrated favourable outcomes in patients with Rheumatoid Arthritis (RA). It leads to a reduction in inflammation, limits articular and extra-articular manifestations of RA, enables earlier functional improvement and causes less radiographic damage.<sup>1</sup> Treat to target (TTT) approaches have been used to adapt therapy according to disease activity in order to achieve clinical remission, providing a standardised treatment algorithm that allows for rapid treatment escalation when needed.

**Objectives:** To evaluate the remission rate of patients in a real life TTT clinic at a district general hospital in the United Kingdom and to compare our local data to the United Kingdom 2015–2016 Healthcare Quality Improvement Partnership (HQIP) audit. To evaluate the proportion of patients starting biological therapy post follow up in a TTT clinic.

**Methods:** The electronic records of patients referred to the TTT clinic between September 2012 and December 2015 were accessed retrospectively and data collected. All patients with a diagnosis of RA were included in data analysis. Patient demographics and clinical data were collected. Statistical analysis was performed using GraphPad Prism. Comparisons of outcomes for antibody status and smoking status were made using Fisher's exact test.

**Results:** 242 patients were seen at least once in the TTT clinic. Follow-up data was available for 216 patients. 65% were female with a median age of 62 years (range 19–90). 69% patients were either rheumatoid factor or anti-CCP positive and 80% were started on combination therapy (Methotrexate and Hydroxychloroquine) at their first clinic appointment. Overall 46% of patients entered remission (disease activity score (DAS) of  $<2.6$ ). 49% of seropositive patients achieved remission compared to 39% of seronegative patients although this was not statistically significant ( $P=0.249$ , Fisher's exact test). A statistically significant fewer number of people who were current smokers achieved remission ( $p=0.005$ , Fisher's exact test). Only 9 patients (4.2%) required the addition of biologic drugs within the first year of treatment.

**Conclusions:** Our TTT clinic was successful in starting a significant proportion (80%) of patients on combination DMARDs (compared to an estimated national average of 46% based on HQIP data).<sup>2</sup> This approach also resulted in a higher proportion of patients entering DAS remission (46%, national average 31%), though understandably this was lower than the remission rate achieved in clinical trials.<sup>3</sup> Only 4.2% of patients went onto biological DMARDs within the first year, which is far less than the proportion commencing biologics prior to TTT. This data demonstrates that TTT approaches in a real life clinical setting are important in achieving remission in patients with RA and reducing the need for expensive biologic treatment.

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SAT0214

### EFFECTIVENESS OF A RANDOMIZED STEP-DOWN TO METHOTREXATE OR LEFLUNOMIDE MAINTENANCE THERAPY IN PATIENTS WITH LOW DISEASE ACTIVITY, 40 WEEKS AFTER STARTING COMBINED METHOTREXATE-LEFLUNOMIDE REMISSION INDUCTION THERAPY IN EARLY RHEUMATOID ARTHRITIS: RESULTS FROM THE CARERA TRIAL

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**Background:** Combination of methotrexate, leflunomide and a short-term course of glucocorticoids is an effective initial treatment strategy for early rheumatoid arthritis (ERA) (1). However, evidence concerning further maintenance or step-down strategies after achieving remission or low disease activity is lacking.

**Objectives:** To evaluate efficacy and tolerability of a step-down to methotrexate versus leflunomide monotherapy in ERA patients achieving low disease activity (LDA) after induction therapy with a combination of both.

**Methods:** The care in ERA (CareRA) trial is a 2-year randomized pragmatic superiority trial comparing different remission induction strategies in ERA. For the purpose of the current sub-study, DMARD-naïve ERA patients initially randomized into the COBRA Avant-Garde arm (methotrexate 15 mg weekly + leflunomide 10 mg daily + prednisone step-down from 30 mg) were re-randomized, after a period of 40 to 52 weeks, to a methotrexate 15 mg weekly or leflunomide 20 mg daily maintenance therapy when achieving LDA (DAS28-CRP  $\leq 3.2$ ). Disease activity, functionality and X-ray damage were registered. Efficacy of both regimens was compared at week 65 after re-randomization as well as their safety profiles and drug retention rates (ITT analysis).

**Table 1** Clinical and radiological outcomes at week 65 per treatment arm Data are presented as mean  $\pm$  SD or number of patients and percentages; LDA, low disease activity; SvdH, Sharp van der Heijde score.

**Table 2** Effectiveness analysis after re-randomization AE, adverse event; SAE, serious adverse event; other AEs include all other AEs less likely to be related to methotrexate or leflunomide.

	Methotrexate N=32	Leflunomide N=26	p-value
Remission DAS28-CRP $<2.6$	30 (93.8%)	19 (73.1%)	0.031
LDA DAS28-CRP $\leq 3.2$	32 (100%)	23 (88.5%)	0.048
$\Delta$ DAS28-CRP from re-randomization	0.2 $\pm$ 0.7	-0.2 $\pm$ 1.0	0.214
Remission CDAI $\leq 2.8$	21 (65.6%)	14 (53.8%)	0.362
LDA CDAI $\leq 10$	32 (100%)	21 (80.8%)	0.009
$\Delta$ CDAI change from re-randomization	0.6 $\pm$ 2.7	-2.8 $\pm$ 8.1	0.462
Remission SDAI $\leq 3.3$	20 (62.5%)	14 (53.8%)	0.506
LDA SDAI $\leq 11$	32 (100%)	22 (84.6%)	0.021
$\Delta$ SDAI change from re-randomization	0.8 $\pm$ 3.1	-3.1 $\pm$ 8.2	0.244
HAQ (0-3)	0.3 $\pm$ 0.5	0.3 $\pm$ 0.4	0.968
Change in SvdH from baseline CareRA	0.7 $\pm$ 0.9	0.9 $\pm$ 1.8	0.702

Data are presented as mean  $\pm$  SD or number of patients and percentages; LDA, low disease activity; SvdH, Sharp van der Heijde score.

	Methotrexate	Leflunomide
Patients still on monotherapy on w65	23 (71.9%)	14 (53.4%)
Patients with AE related to study therapy	10 (31.2%)	9 (34.6%)
Total number of AEs	80	79
Infection	14	16
Gastrointestinal discomfort	7	13
Liver function disturbances	3	1
Other AEs	56	49
Total number of SAEs	7	4
Number of SAEs related to study therapy	0	0

AE, adverse event; SAE, serious adverse event; other AEs include all other AEs less likely to be related to methotrexate or leflunomide.

**Results:** We re-randomized 58 patients to either methotrexate ( $n=32$ ) or leflunomide ( $n=26$ ) monotherapy. At re-randomization 81.2% of patients in the methotrexate group (26/32) was in remission (DAS28-CRP  $<2.6$ ), versus 92.3% (24/26) in the leflunomide group ( $p=0.225$ ). At 65 weeks post re-randomization significantly more patients achieved DAS28-CRP remission in the methotrexate group (93.8%) than in the leflunomide group (73.1%) ( $p=0.031$ ). Patients re-randomized to methotrexate also achieved more frequently a state of LDA measured by DAS28-CRP, CDAI and SDAI in comparison to patients re-randomized to leflunomide (table 1). Safety analysis after re-randomization did not show differences between groups with regards to number or type of adverse events (AEs). Numbers of patients with AEs related to study medication were comparable (31.2% in the methotrexate and 34.6% in the leflunomide group). Throughout these 65 weeks 71.9% of patients in the methotrexate and 53.8% ( $p=0.098$ ) in the leflunomide arm remained on the assigned DMARD monotherapy. At the end of the study, in patients remaining on methotrexate monotherapy the mean dose was 15.3 mg weekly versus a mean dose of 17.1 mg daily in patients remaining on leflunomide monotherapy.

**Conclusions:** Step-down to methotrexate monotherapy instead of leflunomide monotherapy seems more efficacious, is well tolerated and has a good drug retention rate in ERA patients in LDA after combination therapy with methotrexate and leflunomide.

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SAT0215

### LIVER BLOOD TEST ABNORMALITIES ARE RARE IN PATIENTS ON METHOTREXATE: EVIDENCE FROM A LARGE COHORT OF INFLAMMATORY ARTHRITIS PATIENTS

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**Background:** National British Society of Rheumatology guidelines for monitoring non-biologic disease-modifying anti-rheumatic drugs (DMARDs) suggest reducing the frequency of blood monitoring for patients on stable doses of methotrexate to 12 week intervals.<sup>1</sup> Implementation of this recommendation would reduce pressure on services, reduce costs and enhance patient experience. However, it remains unclear whether patient safety would be compromised with 12 week interval blood monitoring in a real world setting.

**Objectives:** The primary objective was to establish whether reducing blood monitoring frequency from monthly to 12 week intervals would compromise the safety of patients on methotrexate by either late detection or missing signs of transaminitis on blood results.

**Methods:** Between June 2016 and July 2017, monthly liver function test results were monitored in 1,964 patients on methotrexate. Demographic data were collected and abnormal results were reviewed. Patients with raised alanine aminotransferase (ALT) (>34 U/l) were categorised as either: isolated (only one abnormal result), persistent (at least two consecutive abnormal results) or intermittent (more than one abnormal result separated by at least one normal result). For those with an ALT>100 U/l, medical records were reviewed to determine causality.

**Results:** ALT results for 1,964 patients were reviewed (F=1288, M=676). 775 were on one concomitant DMARD, 82 were on triple DMARD therapy (hydroxychloroquine and sulfasalazine) and 396 were on biologic therapy. Indications for methotrexate were rheumatoid arthritis (n=1262), psoriatic arthritis (n=611) and spondyloarthritis (n=91). Ten patients (0.51%) had an ALT>100 U/l over 13 months: 8 were persistent, 1 was intermittent and 1 was isolated. Further investigations revealed fatty liver in one patient (necessitating methotrexate discontinuation) and a weakly positive anti-smooth muscle antibody in another (both with persistent ALT>100), but were unremarkable in the other 8. A further 48 patients had at least one ALT rise of 35–100 U/l which did not alter therapy.

**Conclusions:** Over 13 months monitoring 1,964 patients on methotrexate, only 0.51% developed an ALT>100 U/l of whom only one patient discontinued methotrexate. In this patient the ALT rise was persistent for more than 12 weeks. Therefore 12 week interval blood monitoring would have reliably detected this abnormality. In those with intermittent and isolated ALT rises >100 U/l, there were no concerning features requiring cessation of methotrexate. This suggests that although a proportion of ALT rises would not be captured on 12 week blood monitoring intervals, isolated or intermittent rises are unlikely to pose harm to patients. Reducing the frequency of blood monitoring to 12 week intervals would be an efficient use of resources whilst being safe for patients. Furthermore this study provides evidence that less frequent blood monitoring may be feasible in patients on combination DMARDs, particularly relevant in an era where combination treatment is the standard of care in inflammatory arthritis.

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SAT0216

### THE ADDITION OF COLCHICINE TO METOTREXATE MIGHT HELP ACHIEVE LOW DISEASE ACTIVITY IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS BY DOWNREGULATING THE ACTIVITY OF CASPASE-1.

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**Background:** NLRP3 inflammasome is an intracellular protein complex involved in the production of pro-inflammatory cytokines as IL-1 $\beta$  and IL-18, which has been reported to have a role in the pathogenesis of RA<sup>1,2</sup>. Since colchicine (CCH) is a potent inhibitor of NLRP3<sup>3</sup>, we hypothesized that it may significantly modify the expression and function of this molecular complex, reducing the inflammatory phenomenon in early rheumatoid arthritis (eRA).

**Objectives:** To evaluate the possible effect of CCH administration on the expression and activity of NLRP3 in patients with eRA and evaluate if it has an effect on disease activity.

**Methods:** Inflammasome expression by monocytes was assessed by two-color flow cytometry (CD14<sup>+</sup>NLRP3<sup>+</sup> cells), and its function was estimated through the analysis of caspase-1 activity (colorimetric assay). Clinical activity was assessed by HAQ-DI, CDAI, SDAI and DAS28ESR at 0, 4 and 12 weeks.

**Results:** Twenty DMARD naive patients were recruited, 18 women, mean age 47.55 (30–72), mean time with symptoms 20 months and seropositive (RF/ACCP) in 60% of patients; all described in table 1. All patients had increased levels of caspase-1 activity and NLRP3 in week 0. At week 12, MTX+CCH patients showed decreased activity of caspase-1 and numerical difference in the expression of NLRP3. Patients with MTX+CCH at week 12 had significant clinical improvement, with low disease activity in 6/10 patients vs 2/10 patients with MTX (p<0.05). Mean change in HAQ was -0.64 in patients with MTX compared with -1.5 in patients with MTX+CCH (p<0.05).

Table 1 Demographic characteristics

	MTX	MTX +CCH
Male	1	
Female	9	
Age – years	48	47.1
	$\pm 12.85$	$\pm 7.69$
Smoking	5	4
Time with symptoms – weeks	20.8 $\pm$ 13	17.7
		$\pm 13.5$
Rheumatoid factor	6	5
ACCP	5	4

Table 2 Clinical and laboratory results at week 0 and 12 in patients with eRA

	Week 0		p	Week 12		p
	MTX	MTX +CCH		MTX	MTX +CCH	
HAQ-DI	1.39	1.7 $\pm$ 0.4	0.49	0.75 $\pm$ 0.62	0.19 $\pm$ 0.12	<b>0.02</b>
	$\pm 0.65$					
CDAI	39.72	43.08	0.4	21.72	10.6 $\pm$ 7.3	<b>0.04</b>
	$\pm 11.94$	$\pm 9.60$		$\pm 11.7$		
SDAI	42.83	47.25	0.4	23.51	10.85 $\pm$ 7.5	<b>0.03</b>
	$\pm 12.9$	$\pm 10.59$		$\pm 12.66$		
DAS28ESR	6.24	5.88	0.91	4.59 $\pm$ 1.14	3.09 $\pm$ 1.6	<b>0.03</b>
	$\pm 0.79$	$\pm 0.35$				
DAS28CRP	5.53	5.51	0.65	4.06 $\pm$ 1.34	2.93 $\pm$ 1.1	<b>0.01</b>
	$\pm 0.59$	$\pm 0.53$				
CD14+NLRP3+ Cells – %	30.63	27.06	0.47	26.12	17.48 +	0.1
	$\pm 11.5$	$\pm 7.85$		$\pm 14.7$	4.34	
Immunofluorescence CD14 +NLRP3+	576.8	514.9	0.62	402.6	319.8	0.3
	$\pm 267.35$	$\pm 252.44$		$\pm 236.99$	$\pm 201.7$	
Caspase-1 activity- nm	0.572	0.463	0.27	0.300	0.120 +	<b>0.005</b>
	$\pm 0.159$	$\pm 0.243$		$\pm 0.176$	0.07	

**Conclusions:** The data suggest that CCH administration is associated with decrease in the expression NLRP3 inflammasome and activity of caspase-1. This phenomenon contributes to decrease inflammation and may help to achieve low disease activity. The administration of CCH might block additional targets in patients with eRA.

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**SAT0217 IDENTIFICATION OF DISTINCT DISEASE ACTIVITY TRAJECTORIES IN PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING TOFACITINIB OVER 12 MONTHS**

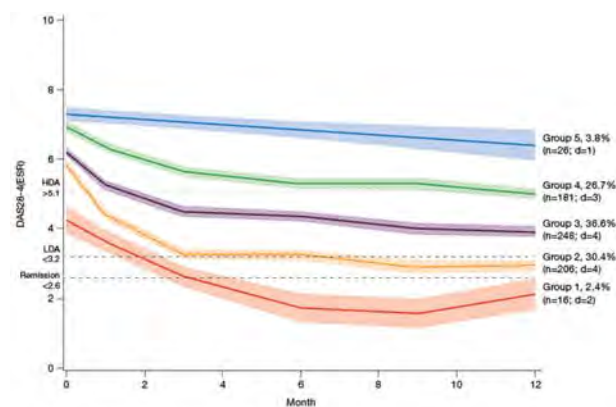
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**Background:** Persistence of active disease in patients (pts) with rheumatoid arthritis (RA) is highly variable following treatment initiation. One possible explanation is the existence of distinct disease activity/response trajectories influenced by baseline variables, such as sociodemographics, disease characteristics and health status.<sup>1</sup>

**Objectives:** To identify distinct disease activity trajectories over 12 months and distinguishing baseline factors using pooled data from 3 randomised, controlled Phase 3 (P3) studies of tofacitinib 5 mg twice daily (BID) in pts with active RA who were inadequate responders (IR) to conventional synthetic (cs)DMARDs, with or without prior biologic (b)DMARDs (NCT00847613, NCT00856544 and NCT00853385).

**Methods:** Disease Activity Score in 28 joints, erythrocyte sedimentation rate (DAS28-4[ESR]) data from 3 P3 studies were pooled. A group-based trajectory modelling strategy was applied to find unique longitudinal groups of pts with similar disease activity over time.<sup>2</sup> Trajectories were latent models, fit as polynomials. The number of groups and polynomial degree of each group were specified and fit for all combinations of up to 6 groups and up to a 4th degree polynomial; a best-fit model was chosen using Bayesian information criteria.

**Results:** csDMARD-IR/bDMARD-naïve pts (n=677) were separated into 5 unique disease activity trajectories (figure 1); csDMARD-IR pts who received prior bDMARDs (n=149) were separated into 4 trajectories (not shown). In the bDMARD-naïve pts, Group 5 (3.8%) had the highest predicted baseline DAS (7.3) with minimal improvement (6.4) at Month 12; Group 4 (26.7%) had baseline DAS 7.0, improving to DAS 5.0 at Month 12; Groups 2 (30.4%) and 3 (36.6%) had baseline DAS 5.9 and 6.2, respectively, leading to low DAS (2.9) and moderate DAS (3.9), respectively, at Month 12; Group 1 (2.4%) had the lowest baseline DAS of 4.3, improving to remission (DAS 2.1) at Month 12 (figure 1). The 4 trajectories in csDMARD-IR pts who received prior bDMARDs were similar to Groups 2–5 in bDMARD-naïve pts. While baseline demographics were generally similar between bDMARD-naïve groups, there were statistically significant differences in baseline disease activity measures and pt-relevant outcomes between groups.



n = sample size of trajectory; d = degree of polynomial of trajectory  
 Solid lines represent predicted values, with 95% CI indicated by shading. Percentages reflect the proportion of subjects in each group  
 csDMARD, Conventional synthetic DMARD; BID, twice daily; CI, confidence interval; csDMARD, conventional synthetic DMARD; DAS28-4(ESR), Disease Activity Score in 28 joints, erythrocyte sedimentation rate; DMARD, disease-modifying antirheumatic drug; HDA, high disease activity; IR, inadequate responder; LDA, low disease activity; RA, rheumatoid arthritis

**Figure 1.** Predicted group trajectories based on DAS28-4(ESR) with 95% CI identified using group-based trajectory modeling in patients with active RA who were csDMARD-IR and bDMARD-naïve and receiving tofacitinib 5 mg BID = sample size of trajectory; d = degree of polynomial of trajectory

**Conclusions:** It was possible to identify heterogeneous phenotypic subgroups as distinct disease activity trajectories in csDMARD-IR pts treated with tofacitinib.

The groups were characterised by differences in disease activity and pt-relevant outcomes, including baseline pain and physical function. Very high disease activity may limit pts' ability to achieve low disease activity. The identification of distinct trajectory groups could be used to develop personalised treatment optimisation algorithms incorporating clinical and molecular phenotypes.

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**SAT0218 EFFICACY AND SAFETY OF BARICITINIB IN MTX-IR PATIENTS WITH RHEUMATOID ARTHRITIS: 52 WEEK RESULTS FROM A PHASE 3 STUDY (RA-BALANCE)**

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**Background:** Baricitinib (BARI) is an oral selective inhibitor of Janus kinase 1 (JAK1) and JAK2. In the EU and some other countries, baricitinib has been approved for the treatment of moderately to severely active rheumatoid arthritis (RA) in adult patients. This abstract reports efficacy and safety results from a phase 3, double-blinded, 52-week study (RA-BALANCE) that enrolled patients (pts) in China, Argentina and Brazil (NCT02265705).

**Objectives:** To assess the efficacy and safety of BARI vs placebo (PBO) in the treatment of RA.

**Methods:** Patients with moderately to severely active RA (tender joint counts  $\geq 6$  & swollen joint counts  $\geq 6$  & hsCRP  $\geq 6$  mg/L) despite stable background methotrexate (MTX), were randomized 1:1 to PBO (n=145) or BARI 4-mg (n=145) once daily (QD), stratified by country and baseline joint erosion status. Background MTX was continued. Non-responders were rescued from Week 16. At Week 24, pts receiving PBO were switched to BARI 4-mg QD. ACR20 at Week 12 was the primary endpoint and there were multiple secondary endpoints e.g., assessing physical function, low disease activity and pain.

**Results:** The primary ACR20 response was significantly greater for BARI than PBO (58.6% vs 28.3%,  $p \leq 0.001$ , Table). At Weeks 12 and 24, significant improvements were seen in pts receiving BARI vs PBO for ACR20/50/70, DAS28-hsCRP, CDAL low disease activity and SDAL low disease activity, many as early as by Week 1. At Week 16, significantly less radiographic progression was seen in pts receiving BARI vs PBO and numerical improvement was observed at Week 24. At Week 12, significant improvement in HAQ-DI minimum clinically important difference  $\geq 0.3$  (physical function), duration of morning joint stiffness, severity of morning joint stiffness numeric rating scale (NRS), worst tiredness NRS and reduced pain (0–100 mm VAS) were seen in pts receiving BARI vs PBO.

During Weeks 0–24, treatment emergent adverse events and infections were reported in 74.5% and 42.1% of BARI pts and 62.1% and 28.3% of PBO pts, respectively. Serious adverse events were reported in 2.8% of pts in both groups. There was 1 nonserious esophageal candidiasis in the BARI group for Week 0–24. Four herpes zoster events (1 PBO, 3 BARI) were reported for Week 0–24. No major cardiovascular events, deaths, tuberculosis, venous thromboembolic

events or malignancies were reported in the study through Week 24 for PBO and through Week 52 for BARI group. No unexpected safety signals were observed.

**Table 1.** Study RA-BALANCE efficacy measures

	Week 12		Week 24		Week 52 <sup>†</sup>
	PBO (N=145)	BARI (N=145)	PBO (N=145)	BARI (N=145)	BARI (N=145)
ACR20, n (%)	41 (28.3)	85 (58.6)***	47 (32.4)	93 (64.1)***	91 (62.8)
ACR50, n (%)	12 (8.3)	44 (30.3)***	17 (11.7)	56 (38.6)***	68 (46.9)
ACR70, n (%)	2 (1.4)	14 (9.7)**	6 (4.1)	27 (18.6)***	36 (24.8)
DAS28-hsCRP <3.2, n (%)	13 (9.0)	36 (24.8)***	15 (10.3)	51 (35.2)***	67 (46.2)
DAS28-hsCRP <2.6, n (%)	4 (2.8)	17 (11.7)**	10 (6.9)	21 (14.5)**	40 (27.6)
CDAI <10, n (%)	13 (9.0)	26 (17.9)**	13 (9.0)	39 (26.9)***	67 (46.2)
SDAI <11, n (%)	12 (8.3)	30 (20.7)**	14 (9.7)	40 (27.6)***	67 (46.2)
HAQ-DI MCID ≥0.22, n (%)	89 (61.4)	102 (70.3)	51 (35.2)	94 (64.8)***	89 (61.4)
HAQ-DI MCID ≥0.3, n (%)	67 (46.2)	90 (62.1)**	45 (31.0)	85 (58.6)***	83 (57.2)
LS mean Δ Patient's Assessment of Pain (0-100 mm VAS) <sup>‡</sup>	-17.7	-31***	-20.1	-34.8***	-40.2
LS mean Δ Patient's Global Assessment of Disease Activity (0-100 mm VAS) <sup>‡</sup>	-20.0	-31.3***	-18.5	-33.4***	-37.8

PBO, placebo; BARI, baricitinib; MCID, minimum clinically important difference; VAS, visual analogue scale. Patients received stable background MTX throughout the study. Data are % patients (N/N), unless otherwise stated. <sup>†</sup>Data are least-squares (LS) mean change from baseline; <sup>‡</sup>Initially randomized to baricitinib. \*p<0.05, \*\*p<0.01, \*\*\*p<0.001 vs PBO.

**Conclusions:** Compared to PBO, BARI provided significant improvements in control of signs and symptoms, including pain and physical function with an acceptable safety profile.

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SAT0219

**UPADACITINIB IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS AND INADEQUATE RESPONSE OR INTOLERANCE TO BIOLOGICAL DMARDs: A PHASE 3 RANDOMIZED, PLACEBO-CONTROLLED, DOUBLE-BLIND STUDY OF A SELECTIVE JAK1 INHIBITOR**

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**Background:** Upadacitinib (UPA), an oral, selective JAK1 inhibitor was effective in ph 2 trials in rheumatoid arthritis (RA) pts with inadequate response (IR)/intolerance to csDMARDs and bDMARDs.

**Objectives:** To evaluate safety and efficacy of UPA in bDMARD-IR pts on stable background csDMARDs.

**Methods:** Pts with active RA (TJC≥6, SJC≥6; hsCRP≥3 mg/L) were randomized 2:2:1:1 to receive UPA 15 mg or 30 mg once daily (QD) or PBO for 12 wks followed by UPA 15 mg or 30 mg QD starting at Wk 12. The primary endpoints were the proportion of pts achieving ACR20 (for FDA) and the proportion achieving DAS28CRP≤3.2 (for EMA) at Wk 12 (NRI).

**Results:** Of 499 randomized pts, 498 received study drug; 451 (90.6%) and 419 (84.1%) completed Wks 12 and 24 respectively. BL disease characteristics

indicated long-standing severe, refractory disease: (means) duration since diagnosis 13 yrs; DAS28CRP, 5.8; TJC68, 27.9; SJC66, 16.8; 53% experienced ≥2 prior bDMARDs. At Wk 12, more pts (p<0.001) on UPA 15 and 30 vs PBO achieved the primary endpoints (ACR20: 64.6% and 56.4% vs 28.4%; DAS28CRP≤3.2: 43.3% and 42.4% vs 14.2%) and other secondary endpoints (Table). Among pts with IR to multiple bDMARDs/MOAs, and pts with lack of efficacy for α-IL-6, the proportions achieving ACR20 on UPA vs PBO were comparable to the overall treated population. By Wk 1, more pts achieved ACR20 on UPA 15 and 30 vs PBO (27.4% and 24.8% vs 10.7%, p<0.001). At Wk 12, significant improvements were observed on UPA 15 and 30 vs PBO for HAQ-DI (LSM change -0.39 and -0.42 vs -0.17, p<0.001). At Wk 24, responses were similar or greater for pts originally on UPA and comparable for pts who switched to UPA after 12 wks of PBO.

Up to wk 12, the frequency of AEs was comparable for PBO and UPA 15, but higher for UPA 30 (table 1). Overall AE rates (E/100 PY) through Wk 24 for UPA 30 were similar or slightly higher vs UPA 15; more AEs led to study drug discontinuation in UPA 30. Occurrence of infections was similar in all arms, but there were more serious infections and herpes zoster cases in UPA 30. Malignancies were reported in 3 pts over 12 wks with 1 additional case through Wk 24. Through Wk 12, pulmonary embolism (PE) was reported in 2 pts (1 each on UPA 15 and 30), none with DVT; through Wk 24, PE were reported in 4 more pts (UPA 15: 3, 1 of whom also had a DVT; UPA 30:1). All had risk factors for DVT/PE. 2 deaths were reported (UPA30: 1 before Wk 12; UPA 15:1 after Wk12).

Efficacy Measures <sup>†</sup> , Percentage of Patients with a Response	Week 12			Week 24			
	PBO N=169	UPA 15 N=164	UPA 30 N=165	PBO N=165	UPA 15 N=164	UPA 30 N=164	UPA 30 N=165
ACR20	28.4	64.6***	56.4***	61.2	60.1	61.6	59.4
DAS28-CRP≤3.2	14.2	43.3***	42.4***	38.8	38.0	52.4	51.5
ACR50	8.3	34.1***	35.8***	25.3	29.1	42.7	43.0
ACR70	1.4	9.7**	10.9**	22.4	21.4	22.0	24.2
CDAI <10	9.0	17.9**	18.9**	24.1	23.6	47.0	45.6
CDAI <8	4.7	7.9	11.5*	12.9	14.3	10.4	15.2
DAS28-CRP <2.6	2.8	11.7**	14.5**	28.2	24.5	32.3	34.5
ACR20 in pts who failed ≥2 bDMARDs and/or α-IL-6	18.1	70.8	50.0	-	-	-	-
ACR20 in pts with LoE for anti-IL-6	30.0	55.6	58.1	-	-	-	-
Summary of AEs, n (%)	Week 0-12			Week 12-24			
	PBO N=169	UPA 15 N=164	UPA 30 N=165	PBO N=165	UPA 15 N=164	UPA 30 N=156	UPA 30 N=168
All	95 (56.2)	93 (56.5)	111 (67.3)	101 (61.2)	100 (60.7)	82 (52.0)	83 (56.1)
All Leading To D/C	3 (1.8)	4 (2.4)	15 (9.1)	2 (1.2)	3 (1.8)	5 (3.2)	5 (3.4)
Serious AEs	0	3 (1.8)	12 (7.3)	5 (3.0)	5 (3.0)	5 (3.2)	5 (3.4)
Patients with Adverse Events of Special Interest, n (%)							
Infection	51 (30.2)	54 (32.9)	56 (33.9)	36 (21.8)	31 (19.0)	47 (29.5)	47 (31.8)
- Serious Infection	0	1 (0.6)	4 (2.4)	2 (1.2)	1 (0.6)	1 (0.6)	2 (1.4)
- Opportunistic Infection <sup>‡</sup>	0	1 (0.6)	2 (1.2)	0	0	0	1 (0.7)
- Herpes Zoster <sup>§</sup>	1 (0.6)	1 (0.6)	4 (2.4)	0	1 (0.6)	2 (1.2)	2 (1.4)
- Tuberculosis	0	0	0	0	0	0	0
Malignancy (exc. NMISCI) <sup>¶</sup>	0	1 (0.6)	2 (1.2)	0	0	1 (0.6)	0
NMISCI	0	0	0	0	0	0	0
Lymphoma	0	0	0	0	0	0	0
Herpes Zoster	2 (1.2)	2 (1.2)	8 (4.8)	0	2 (1.2)	4 (2.6)	4 (2.7)
GI Perforation	0	0	0	0	0	0	1 (0.7)
PE	0	1 (0.6)	1 (0.6)	2 (1.2)	1 (0.6)	1 (0.6)	0
CV Events adjudicated <sup>‡</sup>	0	1 (0.6)	0	0	1 (0.6)	2 (1.2)	0
Deaths <sup>¶</sup>	0	0	1 (0.6)	0	0	1 (0.6)	0

D/C, discontinuation; LoE, lack of efficacy; NMISCI, non-melanoma skin cancer; PE, pulmonary embolism; GI, gastrointestinal; CV, cardiovascular.

<sup>†</sup>Opportunistic infections: oral candidiasis, one case of mucocutaneous candidiasis.

<sup>‡</sup>Herpes Zoster: most were mild and all but one were single dermatome; 2 serious cases.

<sup>§</sup>Malignancies: through Wk 12-UPA 15: 1 malignant melanoma; UPA 30: 2 pts with prostate cancer; Wk 12-24, UPA 15: 1 pt with bladder cancer.

<sup>¶</sup>1 pt also had DVT; <sup>‡</sup>adjudicated CV events: through Wk 12-UPA 15 mg: 1 pt with ischemic stroke; Wk 12-24, UPA 15: 1 pt with CV procedure, 1 pt with cardiac arrest adjudicated to undetermined/unknown cause of death; UPA 30: 1 pt with myocardial infarction; <sup>‡</sup>Deaths: through Wk 12-UPA 30: 1 due to cardiac failure & PE; Wk12-24, UPA 15:1 unwhimpered death adjudicated as undetermined/unknown cause of death.

**Conclusions:** In this treatment-refractory, bDMARD-IR RA population, rapid, significant improvements were observed with UPA at both doses vs PBO during 12 wks of treatment, and maintained through 24 wks. Overall safety was consistent with ph2 and other ph3 studies with UPA. The rates of PE and DVT observed in this study have not been reported for the other ph3 studies that have been unblinded to date. Overall data from the ph3 program will allow a comprehensive evaluation of the benefit:risk profile of UPA in RA.

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SAT0220

### EVALUATION OF LIVE ZOSTER VACCINE IN A SUBSET OF PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH TOFACITINIB WITH OR WITHOUT METHOTREXATE, AND ADALIMUMAB WITH METHOTREXATE: RESULTS FROM A PHASE 3B/4 RANDOMISED TRIAL

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**Background:** Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA). Patients (pts) with RA are at increased risk for herpes zoster (HZ) and this risk is further increased with tofacitinib treatment.<sup>1</sup>

**Objectives:** To evaluate the effect of live zoster vaccination (LZV) on HZ rates in a subset of methotrexate inadequate responder (MTX-IR) pts with RA who received tofacitinib with or without MTX, or adalimumab (ADA) with MTX in the ORAL Strategy randomised controlled trial (RCT).<sup>2</sup>

**Methods:** ORAL Strategy (NCT02187055) was a Phase 3b/4, 1-year, triple-dummy active-comparator-controlled RCT. Pts were randomised 1:1:1 to receive tofacitinib 5 mg twice daily (BID; tofa mono), tofacitinib 5 mg BID+MTX (tofa +MTX), or subcutaneous ADA 40 mg every other week + MTX (ADA+MTX); target MTX dose was 15–25 mg/week. In countries where LZV was available, pts aged ≥50 years received LZV at the investigator's discretion, 28 days before the first dose of study drug. HZ incidence rates (IR; pts with events per 100 pt-years) and 95% confidence intervals (CI) were calculated for each treatment arm and for vaccinated vs non-vaccinated pts.

**Table 1.** IRs and 95% CIs of HZ (serious and non-serious), and demographic characteristics among patients vaccinated and not vaccinated against HZ in the ORAL Strategy RCT

	Tofacitinib 5 mg BID monotherapy		Tofacitinib 5 mg BID+MTX		ADA 40 mg EQW+MTX	
	N=336	N=336	N=336	N=336	N=336	N=336
Vaccinated at study screening, n (%)	89 (18.0%)	75 (19.9%)	75 (19.9%)	75 (19.9%)	75 (19.9%)	75 (19.9%)
Vaccinated prior to study, n (%)	11 (1.9%)	9 (2.4%)	9 (2.4%)	9 (2.4%)	9 (2.4%)	9 (2.4%)
HZ, n (%)	4/364 (1.0%)	5/376 (2.1%)	5/376 (2.1%)	5/376 (2.1%)	5/368 (1.6%)	5/368 (1.6%)
(95% CI)	(1.0 [0.31, 2.89])	2.33 (1.00, 4.18)	2.33 (1.00, 4.18)	2.33 (1.00, 4.18)	1.60 (0.62, 3.67)	1.60 (0.62, 3.67)
Vaccinated at screening	1/89 (1.1%)	2/75 (2.7%)	2/75 (2.7%)	2/75 (2.7%)	2/75 (2.7%)	2/75 (2.7%)
(95% CI)	0.59 (0.04, 8.35)	3.09 (0.56, 18.04)	3.09 (0.56, 18.04)	3.09 (0.56, 18.04)	0.60 (0.01, 5.79)	0.60 (0.01, 5.79)
Not vaccinated at screening	3/315 (1.0%)	6/301 (2.0%)	6/301 (2.0%)	6/301 (2.0%)	5/314 (1.6%)	5/314 (1.6%)
(95% CI)	0.64 (0.21, 3.04)	2.18 (0.79, 4.71)	2.18 (0.79, 4.71)	2.18 (0.79, 4.71)	2.04 (0.75, 4.48)	2.04 (0.75, 4.48)
Characteristics of patients who had HZ	Vaccinated		Vaccinated		Vaccinated	
	N=1	N=3	N=2	N=6	N=6	N=6
Mean age, years	75.0	48.7	58.0	84.8	59.0	52.3
Gender, M/F	0/1	0/3	1/1	0/6	0/6	2/4
Geographic region <sup>a</sup>						
North America <sup>b</sup>	0	1	1	3	0	0
Latin America <sup>b</sup>	0	1	0	2	0	0
Eastern Europe <sup>b</sup>	0	1	0	2	0	0
Western Europe <sup>b</sup>	0	0	1	0	0	0
Asia <sup>c</sup>	1	0	0	0	0	0
Serious HZ infection <sup>d</sup>	0	0	0	1	0	1
Adjusted OI <sup>e</sup>	1	0	0	0	0	2

<sup>a</sup>From LZV sites not available in Canada, Israel or Thailand at the beginning of ORAL Strategy. In some instances, the other countries did not allow the vaccine to be given. <sup>b</sup>USA, n=7; Mexico, n=2; Latin America, n=1; Poland, n=3; Russia, n=1; Bosnia and Herzegovina, n=1; UK, n=1; Taiwan, n=1. <sup>c</sup>HZ cases requiring hospitalization or parental HZ treatment. <sup>d</sup>Defined as disseminated or multifocal/monoclonal (monoclonal or >2 adjacent dermatomes) HZ. <sup>e</sup>One case of varicella adjudicated as an OI was included as an HZ case. ADA, adalimumab; BID, twice daily; CI, confidence interval; EQW, every other week; HZ, herpes zoster; IR, incidence rate; patients with events per 100 pt-years; LZV, live zoster vaccination; MTX, methotrexate; OI, opportunistic infection; RCT, randomised controlled trial.

**Results:** Of 1146 pts who received study drug (mean age: 50.1 years), 216 received LZV (proportion of pts who received LZV by treatment group: tofa mono: 18.0%; tofa+MTX: 19.9%; ADA+MTX: 18.7%) 28 days before randomisation in this RCT; 30 pts self-reported prior vaccination (Table). No pts had zoster-like lesions within 42 days of vaccination; 1 pt had vaccination site erythema. In the overall study population, HZ IR was similar between tofa mono and ADA+MTX and numerically higher (overlapping CI) with tofa+MTX. IRs were generally similar for pts who received LZV (18.8% of pts were vaccinated) vs those who did not (81.2%) (Table). Overall, 18/1146 pts had HZ. Among vaccinated pts, 3 (1.4%) had HZ: no events were serious and 1 (0.5%) event was multidermatomal (tofa mono). Among pts not vaccinated, 15 (1.6%) had HZ: there were 2 (0.2%) serious HZ events (tofa+MTX: n=1; ADA+MTX: n=1), 2 (0.2%) multidermatomal events (tofa mono: n=1; ADA+MTX: n=1) and 1 (0.1%) disseminated event (ADA+MTX).

**Conclusions:** In MTX-IR pts with RA, LZV was well-tolerated. HZ IR was numerically similar between tofa mono and ADA+MTX and higher with tofa+MTX. HZ rates were generally similar in pts who received LZV vs those not vaccinated. LZV has shown efficacy in prevention of HZ in 51% (pts ≥60 years old) and 70% (50–59 years old) of immunocompetent adults.<sup>3</sup> Efficacy of LZV could not be fully evaluated as a minority (<20%) of pts received LZV and not all geographic regions studied in other tofacitinib studies were represented.

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SAT0221

### EFFECT OF TOFACITINIB ON REDUCING PAIN IN PATIENTS WITH RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS AND ANKYLOSING SPONDYLITIS

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**Background:** Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA) and psoriatic arthritis (PsA), which has also been evaluated in other inflammatory rheumatic diseases (IRD) including ankylosing spondylitis (AS). Pain contributes substantial morbidity in patients (pts) with IRD and directly impacts treatment adherence, assessment of disease improvement and health-related quality of life.

**Objectives:** To evaluate the effectiveness of tofacitinib in reducing pain in randomised controlled clinical trials in pts with RA, PsA and AS.

**Methods:** Five pt populations treated with tofacitinib 5 mg twice daily (BID), 10 mg BID or placebo (PBO) were evaluated: [1] conventional synthetic disease-modifying antirheumatic drug (csDMARD)-inadequate response (IR) RA pts pooled from ORAL Scan (NCT00847613), ORAL Sync (NCT00856544) and ORAL Standard (NCT00853385), [2] tumour necrosis factor inhibitor (TNFi)-IR RA pts from ORAL Step (NCT00960440), [3] csDMARD-IR PsA pts from OPAL Broaden (NCT01877668), [4] TNFi-IR PsA pts from OPAL Beyond (NCT01882439) and [5] AS pts from a Phase 2 study (NCT01786668). Pain outcomes evaluated from baseline to Month (M)6 (Week [W]12 in the AS population) included Pt's Assessment of Arthritis Pain (PAAP) (RA and PsA populations only), Short-Form Health Survey (SF)-36v2 Q7 (bodily pain in the past week), SF-36v2 Bodily Pain Domain (BP), EuroQol Five Dimensions Questionnaire Pain/Discomfort Domain (EQ-5D PD; all populations) and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) Q2 (level of AS neck, back or hip pain) and Q3 (other pain) score (PsA and AS populations only; PsA pts had presence of spondylitis at screening and baseline BASDAI total score >0 in the full analysis set [FAS]). Data were analysed descriptively.

**Results:** The csDMARD-IR RA, TNFi-IR RA, csDMARD-IR PsA, TNFi-IR PsA and AS populations comprised a total of 2066, 399, 316, 394 and 155 pts in the FAS, respectively. In each RA or PsA csDMARD-IR and TNFi-IR population treated with tofacitinib, mean PAAP at baseline (5 mg BID, range 55.7–65.7 mm; 10 mg BID, 54.4–60.1 mm) decreased as early as W2 (1st post-baseline assessment; 45.8–49.8 mm; 38.9–44.8 mm) and continued to decrease through M6 (30.9–34.4 mm; 28.2–36.7 mm); decreases were numerically greater vs PBO and the magnitude of change in RA and PsA populations was similar (Table). Improvements in SF-36v2 Q7 (Table), SF-36v2 BP (Table) and EQ-5D PD were observed in all 4 RA and PsA csDMARD-IR and TNFi-IR populations, and in BASDAI Q2 and Q3 in the csDMARD-IR PsA and TNFi-IR PsA populations. In the AS population, improvements from baseline in mean SF-36v2 Q7 (Table), SF-36v2 BP (Table), EQ-5D PD and BASDAI Q2 were reported at W12 and were numerically greater vs PBO.



**Table 1.** Mean (SE) PAAP score,<sup>a</sup> SF-36v2Q7 score<sup>b</sup> and SF-36v2 BP<sup>c</sup> at baseline through M6(FAS) in RA and PsA csDMARD-IR or TNFi-IR population, and SF-36v2Q7 score,<sup>b</sup> and SF-36v2 BP<sup>c</sup> at baseline and W12 (FAS) in the AS population

Time point	Subpopulation 1: RA				Subpopulation 2: PsA				Subpopulation 3: AS			
	Mean	SE	95% CI	n	Mean	SE	95% CI	n	Mean	SE	95% CI	n
Baseline	4.2 (0.1)	0.1	3.9-4.5	100	4.1 (0.1)	0.1	3.8-4.4	100	4.3 (0.1)	0.1	4.0-4.6	100
W6	4.5 (0.1)	0.1	4.2-4.8	100	4.4 (0.1)	0.1	4.1-4.7	100	4.6 (0.1)	0.1	4.3-4.9	100
W12	4.8 (0.1)	0.1	4.5-5.1	100	4.7 (0.1)	0.1	4.4-5.0	100	4.9 (0.1)	0.1	4.6-5.2	100

**Conclusions:** Treatment with tofacitinib is associated with a rapid improvement and sustained reduction of pain in pts with RA and PsA who are csDMARD-IR or TNFi-IR, and in pts with AS.

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**SAT0222 CLINICAL RISK STRATIFICATION FOR HYDROXYCHLOROQUINE PRESCRIBING IN A LARGE URBAN DISTRICT GENERAL HOSPITAL**

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**Background:** New 2017 British Society of Rheumatology guidelines have recommended baseline formal ophthalmic examination, ideally including objective retinal assessment for example using optical coherence tomography, within 1 year of commencing an antimalarial drug. While the feasibility and costing of this recommendation is being assessed, we audited the current risk assessment for hydroxychloroquine prescriptions (HCQ) against the American College of Ophthalmology (ACO) guidelines for HCQ published in 2016. Table 1 shows the clinical criteria for assessment.

**Methods:** We identified all prescriptions of HCQ documented on the electronic patient records (EPR) from January to September 2017 by the Rheumatology department of Croydon University Hospital. This generated 237 records of which 114 were new prescriptions and 117 were continuation prescriptions. 8 records were excluded due to inadequate patient compliance. Cumulative doses were estimated from dates in the EPR going back to 2013

**Results:** New patient records were assessed for compliance with the ACO guidelines. Patients were assessed for kidney function, pre-existing renal disease, pre-existing eye disease. 74.6% patients were counselled regarding side effects and were advised to have optician retinal screening and 3.5% who had pre-existing eye disease were referred to ophthalmologists. 50.0% of patients had their weight documented prior to prescription. There was no documentation of dose calculated by weight. The commonest indication for HCQ were Systemic Lupus Erythematosis, Inflammatory Arthritis and Sjogren's Syndrome. 13.2% discontinued HCQ due to side effects. The commonest side effects were diarrhoea, dizziness, rashes, and mood swings.

Long-term patient records were assessed for cumulative dose of HCQ estimated from documentation. The average cumulative dose for these patients was with a maximum of 810,000 mg and a minimum of 49,600 mg. Overall, 3.0% percentage of patients did not have cumulative doses calculated due to documented compliance issues and 64.0% of patients had tightly monitored renal function.

Table 1 Clinical criteria for HCQ risk assessment based on American College of Ophthalmology guidelines (2016)

TABLE 1. Clinical criteria for HCQ risk assessment based on American College of Ophthalmology guidelines (2016)	
Factors Assessed	Explanation
Cumulative dose <5mg/kg daily dose for 5years	Guidelines recommend a daily dose of <5mg/kg. Any higher can incrementally increase the risk of retinopathy
Duration of Use	Decades of use can increase the risk, even in patients on the recommended daily dose.
Renal Disease Screening	HCQ is cleared by the kidneys, any drop in GFR can increase circulating drug doses therefore increase risk of toxicity.
Retinal Baseline Screening	Retinal screening is recommended for all patients to monitor the Retinal Pigment Epithelium damage therefore preserve central vision
Tamoxifen Use	Use of tamoxifen alongside HCQ can increase the risk of toxicity approximately 5-fold.
Pre-existing Retinal OR Macular disease	Eye sight can worsen on initiating HCQ.

**Conclusions:** 50% of patients had weight documented prior to prescription and this was not used to determine dosage. The majority of patients were well informed regarding side-effects of HCQ, had tightly monitored renal function and advised to have baseline retinal screening.

**Disclosure of Interest:** None declared

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**SAT0223 PREDICTIVE FACTORS OF EARLY FAILURE TO FIRST LINE TREATMENT WITH METHOTREXATE IN PATIENTS WITH RHEUMATOID ARTHRITIS. RESULTS FROM THE GISEA REGISTRY.**

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**Background:** Methotrexate (MTX) is generally recommended as first-line treatment of rheumatoid arthritis (RA). Despite its efficacy is well established, a percentage of patients fails the treatment. Few studies investigated the causes of early discontinuation of MTX; a two-year retention rate of about 66% is described for RA patients with lower age and longer disease duration as independent predictors for discontinuation.

**Objectives:** Aim of this study was to detect possible predictive factors for early discontinuation of MTX prescribed as first line treatment in RA patients enrolled in the GISEA (Italian Group for the Study of Early Arthritis) registry.

**Methods:** RA patients who began MTX as first line treatment were included in the study. For all patients age, sex, disease duration, smoking status, the intake of glucocorticoids, clinical and serological data, comorbidities and extra-articular manifestations were collected.

**Results:** We analyzed 612 RA patients (females/males 477/132, mean age 55.73±14.5 years; mean DAS28 5.35±1.5); rheumatoid factor (RF) was positive in 64.9%, anti-citrullinated peptide antibodies (ACPA) in 42.7%. Comorbidities were observed in 17.5% of patients, while extra-articular RA manifestations were recorded in 1.5%; 68.3% of subjects taken low doses of steroids. One hundred and forty-nine (24.3%) patients discontinued MTX during the first year (for inefficacy in 66/149 (44.3%) patients, adverse events in 51/149 (34.2%), and other reasons in 32/149 (21.5)). At univariate analysis early discontinuation of MTX was associated to a lower mean age (p=0.041) and a higher mean tender

and swollen joints count ( $p=0.001$  and  $p=0.024$ , respectively). Age and tender joints count were confirmed at multivariate analysis (OR 1.014, CI95% 1.001–1.027 and OR 0.951, CI95% 0.923–0.981, respectively) as independent predictors of early withdrawal of MTX.

**Conclusions:** More than 75% of RA patients treated with MTX as first-line therapy remained in treatment after 12 months. Age was directly correlated and tender joints count was inversely correlated with early withdrawal of MTX in RA patients.

**Disclosure of Interest:** None declared

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SAT0224

#### AMELIORATION OF INFLAMMATORY DISEASE ACTIVITY AND VASCULAR INFLAMMATION WITH HMG-CoA REDUCTASE INHIBITION AND ANGIOTENSIN RECEPTOR BLOCKADE IN RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid Arthritis (RA) has 50% increased risk of cardiovascular (CV) mortality<sup>1</sup>. Similarities between atherosclerosis and RA and proven benefit of Angiotensin receptor Blockers and HMG-CoA reductase inhibitors in atherosclerotic vascular disease provide strong rationale to investigate the impact of Rosuvastatin, HMG-CoA reductase inhibitor and Olmesartan, an angiotensin receptor blocker on inflammatory disease activity and vascular inflammation in RA.

**Objectives:** To investigate the impact of Rosuvastatin and Olmesartan on inflammatory disease activity and vascular inflammation in RA

**Methods:** 84 RA patients randomized to 3 groups to receive 24 weeks of treatment with Rosuvastatin (Rvs) (10 mg/day, n=28), Olmesartan (OLME) (10 mg/day, n=28) and placebo (PL) (n=28) as an adjunct to existing stable antirheumatic drugs. 2 patients from the OLME group were lost to follow up. FMD was assessed by AngioDefender. EPCs were estimated by flow cytometry. Measures of vascular inflammation: serum nitrite, TBARS, adhesion molecules (ICAM-1 and VCAM-1) and lipids were measured at baseline and after treatment. Inflammatory measures included DAS28, SDAI, CRP and ESR, pro-inflammatory cytokines (TNF- $\alpha$ , IL-6 and IL-1). SCORE system estimated the 10 year risk of a first fatal atherosclerotic event. Quality of life was assessed with HAQ-DI and SF-36.

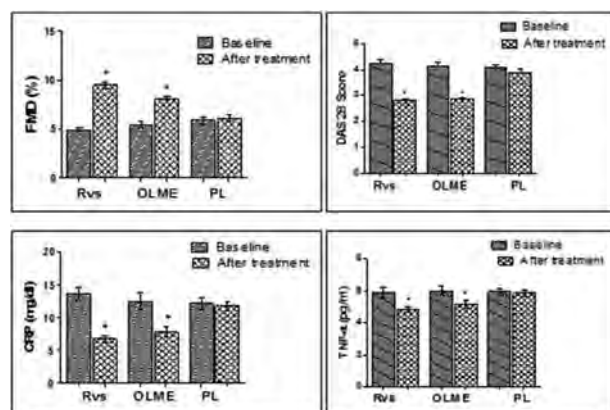


Figure 1A Effect on Flow Mediated Dilation (FMD).Rvs vs. OLME vs. PL (Rvs vs. PL ( $p<0.01$ ), OLME vs. PL ( $p\leq 0.01$ ), Rvs vs. OLME ( $p=0.03$ ) after 24 weeks. Figure 1B Effect on Disease Activity Score of 28 joints (DA S28). Rvs vs. OLME vs. PL (Rvs vs. PL ( $p<0.01$ ), OLME vs. PL. ( $p\leq 0.01$ ), Rvs vs. OLME ( $p=0.08$ ) after 24 weeks. Figure 1C Effect on C-Reactive Protein (CRP).Rvs vs. OLME vs. PL (Rvs vs. PL ( $p<0.01$ ), OLME vs. PL ( $p\leq 0.01$ ), Rvs vs. OLME ( $p=0.05$ ) after 24 weeks. Figure 1D Effect on Tumour Necrosis Factor- $\alpha$  (TNF- $\alpha$ ). Rvs vs. OLME vs. PL (Rvs vs. PL ( $p<0.01$ ), OLME vs. PL ( $p\leq 0.01$ ), Rvs vs. OLME ( $p=0.86$ ) after 24 weeks.

**Results:** At baseline, FMD correlated inversely with DAS28 ( $r = -0.42$ ,  $p<0.05$ ) and TNF- $\alpha$  ( $r = -0.50$ ,  $p<0.05$ ) and positively correlated with EPCs ( $r = 0.44$ ,  $p<0.05$ ) in all three groups indicating high inflammatory disease activity and decreased EPCs population associated with endothelial dysfunction. FMD also correlated inversely with CRP in both Rvs ( $r = -0.46$ ,  $p<0.05$ ) and OLME ( $r = -0.40$ ,  $p<0.05$ ) groups. After treatment, FMD improved significantly in the Rvs vs. OLME

vs. PL group from their baseline levels, respectively {Rvs vs. PL ( $p<0.01$ ), OLME vs. PL ( $p\leq 0.01$ ), Rvs vs. OLME ( $p=0.03$ )} (Fig.1A). The improvement in FMD after treatment with Rvs was significantly greater than OLME [Rvs vs. OLME ( $p=0.03$ )]. EPCs and nitrite levels were improved significantly in both Rvs and OLME groups. A significant reduction was found in ICAM-1 after Rvs treatment ( $p<0.01$ ) where as OLME significantly decreased VCAM-1 and TBARs ( $p=0.04$ ), ( $p=0.01$ ) respectively. Both Rvs and OLME resulted in significant reductions of DAS28 (figure 1B), SDAI, ESR, CRP (figure 1C), IL-6 and TNF- $\alpha$  (figure 1D) vs. PL. There was a significant reduction in the SCORE, HAQ-DI and SF-36 score after treatment with Rvs and OLME.

**Conclusions:** Rvs and OLME ameliorate inflammatory disease activity and vascular inflammation in RA. Both Rvs and OLME lowers the TNF- $\alpha$  & IL-6 which down regulates the production of CRP and NO and improved EPC population and FMD. However, Rvs also favourably impacted ICAM-1 and lipid abnormalities while OLME has beneficial effect on VCAM-1, TBARs and blood pressure. Thus, both Rvs and OLME ameliorate inflammatory disease activity, reduce cardiovascular risk in context of vascular inflammation, endothelial dysfunction and EPCs biology.

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SAT0225

#### COMPARATIVE EFFECTIVENESS IN PAIN AND HAQ-DI IMPROVEMENT FOR BARICITINIB VERSUS ADALIMUMAB, TOCILIZUMAB, AND TOFACITINIB MONOTHERAPIES IN csDMARD-NAÏVE RHEUMATOID ARTHRITIS PATIENTS: A MATCHING-ADJUSTED INDIRECT COMPARISON (MAIC)

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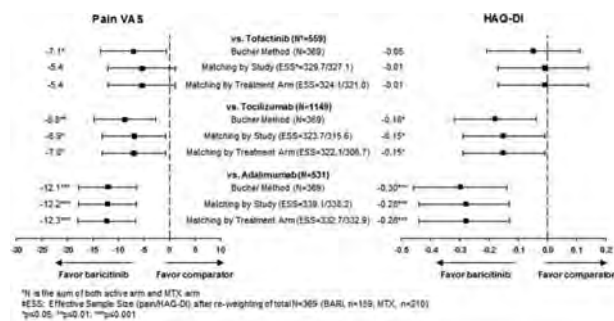
**Background:** In Phase 3 trial, RA-BEGIN, baricitinib (BARI) monotherapy demonstrated superiority to MTX in pain reduction and HAQ-DI improvement in treatment of csDMARD-naïve active RA patients.<sup>1</sup> No prospective head-to-head (H2H) trial data are available comparing BARI monotherapy vs. bDMARD monotherapy in csDMARD-naïve RA patients.

**Objectives:** To assess pain and HAQ-DI for BARI monotherapy from a randomized, MTX-controlled trial vs adalimumab (ADA), tocilizumab (TCZ), and tofacitinib (TOFA) monotherapy from similar randomized, MTX-controlled trials in csDMARD/bDMARD naïve RA patients using matching-adjusted indirect comparison (MAIC).

**Methods:** Individual patient data from the RA-BEGIN BARI 4 mg arm were weighted to match baseline characteristics of the ADA arm from PREMIER,<sup>2</sup> TOFA 5 mg arm from ORAL-START,<sup>3</sup> and TCZ 8 mg/kg arm from combination of AMBITION and FUNCTION,<sup>4,5</sup> respectively; MTX arms were also matched between trials. Method of moments was used to determine weights for age, gender, baseline disease scores, and baseline values of the outcome variable. Mean change on pain VAS and HAQ-DI at Week 24 for BARI were adjusted for the above baseline characteristics with the weighted linear model, and then indirectly compared vs. respective published results for Week 24 TCZ and TOFA and for Week 26 ADA data. Statistical significance of the weighted treatment effect was assessed with the bootstrap method. Sensitivity analyses included MAIC with study level matching<sup>6</sup>, Bucher's method without matching adjustment<sup>7</sup>, and inclusion of disease duration as an additional matching variable.

**Results:** Across trials, the mean baseline pain VAS ranged from 58.7 to 65.2 with a 6-month mean change in pain of -28.3 to -33.5 for the MTX arm, indicating comparability between trials. Similar HAQ-DI and changes in HAQ-DI for the MTX arm were observed. At Week 24, BARI showed numerically greater improvement over MTX in pain than that for TCZ, ADA, and TOFA; statistically significant pain improvement were observed for BARI vs ADA and TCZ with all 3 matching methods but only with the Bucher method for TOFA (figure 1). BARI-treated patients showed significantly greater improvement in HAQ-DI at Week 24 than TCZ and ADA but not TOFA (figure 1). Sensitivity analyses showed consistent results.





**Conclusions:** This indirect comparison of different studies in cs/bDMARD-naïve RA patients, after adjusting for differences in baseline characteristics, suggest a greater pain reduction and improved physical function for BARI monotherapy vs. TCZ and ADA monotherapy. There is suggestion of greater pain reduction for BARI monotherapy vs. TOFA monotherapy, but no differences in improved physical function between the JAK inhibitors. A H2H clinical trial would be needed to confirm these results.

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SAT0226

#### A PHASE 1, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, SINGLE- AND MULTIPLE-RISING DOSE STUDY OF THE BTK INHIBITOR TAK-020 IN HEALTHY VOLUNTEERS

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**Background:** TAK-020 is a highly selective covalent inhibitor of the Btk enzyme. Btk is involved both in B cell receptor and FcR signaling. TAK-020 showed anti-inflammatory and disease-modifying efficacy in a rat collagen-induced arthritis model and is in clinical development, with potential for immune disorders including RA and SLE.

**Objectives:** To assess the safety, tolerability, pharmacokinetic (PK) and pharmacodynamic (PD) properties of TAK-020.

**Methods:** The study population comprised healthy volunteers aged 18 to 55 years. The SRD had 9 cohorts and the MRD 6, each randomized 6 active- to 2 placebo-treated subjects. 72 subjects were enrolled in the SRD, with 6 each receiving 0.1 mg, 0.5 mg, 2.5 mg, 4.4 mg, 8.8 mg, 17.5 mg, 35 mg, 70 mg, or 105 mg of TAK-020; and 18 subjects received placebo. 48 subjects were in the MRD, six

each receiving 7 once-daily (OD) doses of 3.75 mg, 5.75 mg, 13 mg, 25 mg, 45 mg, or 60 mg. A total of 30 subjects received placebo.

The PD effects of TAK-020 were assessed by measuring Btk occupancy and the inhibition of FcεR1-mediated activation of basophils, a Btk-dependent process resulting in increased CD63 expression.

**Results:** In the SRD the same percentage of subjects (11.1%) in the pooled placebo group and the overall TAK-020 group experienced treatment-emergent adverse events (TEAE). All TEAEs were of mild intensity. Abdominal distension, upper abdominal pain, nausea, and headache were reported as drug-related TEAEs in 3 subjects in the TAK-020 group. In the MRD a lower percentage of subjects receiving TAK-020 had TEAEs than with placebo (30.6 vs 41.7%). In 4 subjects (11.1%) these were considered drug-related and included nausea, diarrhea, dizziness and headache.

There were no serious AEs or AEs leading to study drug discontinuation. No subject had clinically significant changes in laboratory tests, vital signs, or ECGs.

TAK-020 was rapidly absorbed (median Tmax 45- 60 min), and had a mean elimination half-life of approximately 3- 9 hr after single and multiple dosing. Plasma exposure was in general proportional to dose up to 70 mg administered as a single dose and up to 60 mg after 7d of OD dosing.

Single doses of TAK-020 were associated with rapid binding of Btk, with occupancy >80% and maintained for 72 hours. Sustained binding of Btk was associated with >80% reduction from baseline in the proportion of CD63-positive basophils. This PD effect was sustained throughout the entire 24 hr dosing interval after administration of the 2 highest repeat doses of TAK-020 (45 and 60 mg) but fully reversed 1 week after the last dose.

**Conclusions:** TAK-020 was well tolerated in healthy volunteers after single and multiple doses, and demonstrated target engagement and biological activity. The PD effects outlasted PK exposures, as expected for a covalent inhibitor.

**Disclosure of Interest:** E. Esfandiari Shareholder of: Takeda, Employee of: Takeda, H. Gevorkyan Employee of: Parexel, H. Faessel Shareholder of: Takeda, Employee of: Takeda, Z. Zhao Shareholder of: Takeda, Employee of: Takeda, K. Hanna Employee of: PRA, G. Smithson Shareholder of: Takeda, Employee of: Takeda, J. Wagner Shareholder of: Takeda, Employee of: Takeda, E. Fedyk Shareholder of: Takeda, Employee of: Takeda, L. Mclean Shareholder of: Takeda, Employee of: Takeda

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SAT0227

#### RHEUMATOID ARTHRITIS PATIENTS TREATED WITH A LOW-DOSE AND SHORT-TERM GLUCOCORTICOID WERE SATISFIED WITH EARLIER IMPROVEMENT AND REPORTED DECREASED ANXIETY REGARDING ADVERSE EVENTS.

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**Background:** At EULAR 2017, we reported that the treatment of early rheumatoid arthritis (RA) patients by a low-dose and short-term glucocorticoid therapy (low and short GC) enabled earlier improvement and didn't worsen the rate of new complications. Currently, in RA treatment, subjective assessment of patients as well as objective assessment of doctors is gaining more importance<sup>(1)</sup>. What do patients think about the risks of low and short GC? Does low and short GC improve patients' satisfaction?

**Objectives:** In this study, we investigated the change in each factor of the disease activity index (DAI) and patients' expectation of and anxiety regarding low and short GC through a questionnaire.

**Methods:** We include 96 Japanese patients with RA and <2-years disease duration. Patients were treated with a T2T strategy; if the disease activity was not improved within 3 months, their DMARDs were replaced with alternatives or additional DMARDs were added. We classified patients into two groups: those treated with DMARDs alone (N group; 35 females, 10 males) and those treated with ≤5 mg/day GC for a maximum of 1 year along with DMARDs (GC group; 40 females, 11 males). The mean ages of the N and GC groups were 56.3 and 60.9 years, respectively. In the GC group, the mean GC dose was 2.46 mg/day. No significant differences were observed between the groups regarding MTX or Biologics agent use rates. We evaluated changes in the number of swollen joints and tender joints, DAS28-CRP score, CRP and VAS of pain for 3 years and compared each factor of DAI between both groups. We then asked them by a questionnaire what was beneficial from the therapies and how much paid attention to the adverse events.

**Results:** There were no significant differences in all factors of DAI at baseline between the groups. At 1 month after treatment, there were significant differences in the improvement rate of VAS, CRP and DAS28-CRP score in the GC group compared with the N group. However, no significant difference was observed between the groups at ≥3 months after treatment (figure 1). In the questionnaire (figure 2), pain improvement was the most expected effect from the treatment (89%), and early therapeutic effect was the second (80%) in the GC group. The pain improvement and the early therapeutic effect were significantly higher in the



GC group than in the N group. The patients in both groups equally recognized the reduction in arthritis, morning stiffness, fatigue and the recovery of activities of daily living (ADL). Anxiety regarding adverse events was eliminated in the GC group as GC administration was restricted to a low dose for a short term. Almost identical results were obtained from the two groups.

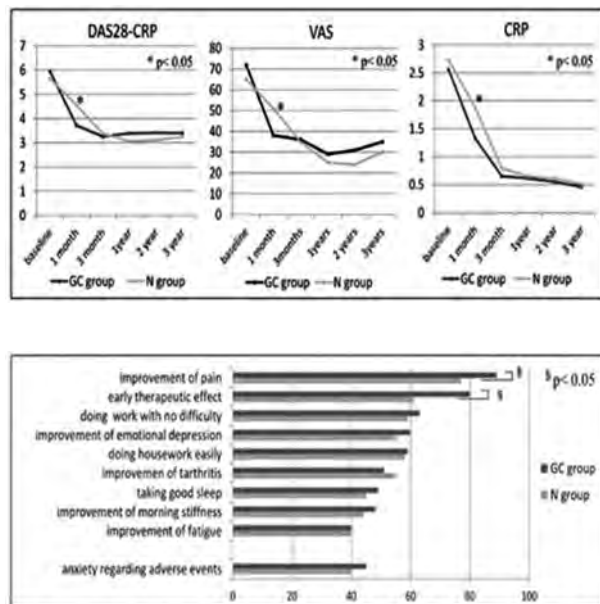


Figure 2. questionnaire results

**Conclusions:** The treatment of early RA patients with low and short GC enables earlier improvement of disease activity, particularly VAS and CRP. Patients also reported that low and short GC were an improvement effect from the early stage, particularly regarding pain and anxiety about adverse events. These data confirm that the treatment with low and short GC in RA patients leads to improved patient satisfaction.

#### REFERENCE:

1) Vibeke Strand, et al. J Rheumatol 2015.

**Disclosure of Interest:** None declared

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SAT0228

#### STEP-DOWN METHOTREXATE THERAPY IN RHEUMATOID ARTHRITIS (STEMETRA): A PILOT STUDY TO ASSESS THE SAFETY AND THE TOLERABILITY OF HIGH-DOSE METHOTREXATE.

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**Background:** Methotrexate (MTX) remains the cornerstone of the treatment of rheumatoid arthritis (RA). However, MTX is frequently underutilized in terms of suboptimal dosage, insufficient duration of treatment, and route of administration.

**Objectives:** To evaluate the tolerability and the safety of higher-dose, subcutaneous methotrexate (MTX) in patients with rheumatoid arthritis (RA).

**Methods:** The STEP-down METHotrexate Therapy in Rheumatoid Arthritis (STEMETRA) was an open-label, monocentric, pilot study of 12-week duration. The protocol treatment schedule consisted of subcutaneous (SC) MTX 50 mg/week for 4 consecutive weeks, followed by 25 mg/week for 4 weeks and then 15 mg/week for 4 weeks. All patients received oral supplementation of folic acid (leucovorin) 12 mg, administered twelve hours after the injection of SC-MTX.

**Results:** Ten patients (7 females and 3 males), with a mean age of 58.1 (±12.1), were enrolled in this study; one of them withdrew consent before taking study drug. Therefore, nine patients were treated. MTX was well tolerated: a total of 5 adverse events (AEs) occurred in 4 patients, none of which was severe. AEs consisted in: transient elevation of alanine aminotransferase (<2 ULN), which resolved spontaneously, and vertigo, in the same patient; moderate fatigue in one patient; one case of urinary tract infection; low back pain in one patient. At week 12, four patients (44.4%) achieved DAS28(ESR) remission, two (22.2%) reached

low disease activity, one (11.1%) patient showed moderate disease activity, and two (22.2%) had still had high disease activity. Overall, 8 out of 9 patients (88.8%) showed a reduction in DAS28>1.2 from baseline.

Table 1 Adverse events in patients who received study drug. MTX: methotrexate; ALT: alanine aminotransferase; ULN: upper limit of normal; UTI: urinary tract infection. \*: this adverse event resolved by the time of the next visit. +: at week 12, this patient decided to withdraw MTX. §: this patient was taking MTX 20 mg/week instead of 15 mg/week as an escape treatment for insufficient disease control (see main text).

	Baseline	Week 2	Week 4	Week 8	Week 12
MTX dose	-	50 mg/week	50 mg/week	25 mg/week	15 mg/week
Patient #1	none	none	none	none	none
Patient #2	none	none	none	none	none
Patient #3	none	none	none	none	none
Patient #4	none	none	none	none	none
Patient #5	none	none	none	none	none
Patient #6	none	none	Increased ALT (<2 ULN)*	Vertigo	Vertigo+
Patient #7	none	none	none	Fatigue*	none
Patient #8	none	none	none	none	UTI <sup>§</sup>
Patient #9	none	none	none	Low back pain*	none

**Conclusions:** In this study, short-term higher dose MTX was well tolerated. Based on the tolerability observed in this preliminary study, a randomized controlled study of higher dose induction therapy versus traditional dosing will be conducted.

**Disclosure of Interest:** None declared

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SAT0229

#### RHEUMATOID ARTHRITIS TREATMENT WITH COMBINATION OF THREE CONVENTIONAL SYNTHETIC DISEASE MODIFYING ANTI-RHEUMATIC DRUGS (csDMARDs) AND ITS EFFECTIVENESS ON DISEASE CONTROL IN A SHORT TERM COMPARED TO BIOLOGIC DMARDs TREATMENT AFTER PROPENSITY SCORE MATCHING PROCEDURE IMPLEMENTED

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**Background:** Rheumatoid arthritis (RA) treatment has now many variations with use of biologic or targeted synthetic disease modifying anti-rheumatic drugs (b/tsDMARDs) and conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs). In these, triple csDMARD combination therapy (tri-TX), that has comparable disease activity control effectiveness compared to anti-TNF therapy is one of alternative [1].

**Objectives:** Aim of this study is to evaluate the effectiveness of tri-TX compared to bDMARD with methotrexate treatment (bm-TX) for RA statistically, with the use of propensity score matching (PSM) technique.

**Methods:** Five hundred and fifty RA patient had been treated for more than one year in our clinic. In these, 74 patients had been treated with tri-TX and 135 had been treated with bm-TX, were recruited. Their sex distribution (Sex), anti-cyclic citrullinated peptide antibodies (ACPA), age, 28-joints disease activity score with C-reactive protein (DAS28-CRP), Health Assessment Questionnaire Disability Index (HAQ-DI), Sharp/van der Heijde Score (SvdHS), and pain score measured with visual analog scale (PS-VAS) at start of the treatment were measured for each patient, and their values were compared for each group. Thus, sample selection was performed with PSM technique in order to reduce bias on each of treatment groups. After selection, change of DAS28-CRP, HAQ-DI, PS-VAS for every three months until one year since start, and SvdHS at one year after were compared statistically with Mann-Whitney U test.

**Results:** After selection, twenty-three patients for each treatment group were harvested, and there demonstrated no significant difference in Sex, ACPA, DAS28-CRP, HAQ-DI, PS-VAS, and SvdHS at start of the treatment (table 1). Average DAS28-CRP demonstrated 2.76, 1.88, 1.91, 1.77, and 1.67 in bm-TX, while 2.71, 2.03, 2.41, 2.56, and 2.39 in tri-TX, at start, 3 month, 6 month, 9 month, and 1 year, respectively. There is no statistical significant difference between the two groups, but bm-TX demonstrated more significant improvement at every time after six month than tri-TX (<0.05), while no significant difference demonstrated in PS-VAS. Average HAQ-DI demonstrated 0.603, 0.579, 0.598, 0.609, and 0.625 in bm-TX, while 0.707, 0.654, 0.619, 0.594, and 0.567 in tri-TX, respectively. HAQ-DI showed tendency that improved more in tri-TX compared to bm-TX, whereas significant more improvement for tri-TX than for bm-TX had demonstrated at one-year (<0.05), however until then there demonstrated no statistical significance for both of absolute value and improvement. SvdHS demonstrated 62.4 to 61.6 from

start to one year in bm-TX, while 75.6 to 78.7 in tri-TX. Improvement of SvdHS demonstrated better result in bm-TX than in tri-TX significantly ( $p < 0.05$ ).

**Table 1.** Average values of each parameter and their  $p$ -values

	bm-TX	tri-TX	$p$ -value
Women	17 (73.9%)	16 (69.6%)	0.75
age	65.7	70.3	0.16
ACPA	171.1	452.6	0.14
GCs use	26.1%	21.7%	0.85
MTX use	100%	100%	1.00
DAS28-CRP	2.76	2.71	0.70
HAQ-DI	0.603	0.706	0.94
SvdHS	62.39	75.61	0.37
PS-VAS	41	39.7	0.79

bm-TX, a group of rheumatoid arthritis (RA) patient who is undertaken with biologic disease modifying anti-rheumatic drug (bDMARD) and methotrexate (MTX) therapy ; tri-TX, a group of RA patient who is undertaken with combination of three conventional synthetic DMARDs therapy ;  $p$ -value, statistical level of significance used with Mann-Whitney U test. Women express number and percentage in parenthesis. ACPA, anti-cyclic citrullinated peptide antibodies ; GCs, glucocorticoid steroid ; DAS28-CRP, 28-joints disease activity score with C-reactive protein ; HAQ-DI, Health Assessment Questionnaire Disability Index ; SvdHS, Sharp/van der Heijde Score ; PS-VAS, pain score measured with visual analog scale.

**Conclusions:** PSM is useful technique to diminish artificial bias. tri-TX is one choice for RA patient, but not superior for clinical results compared to bm-TX.

#### REFERENCE:

- [1] Matsuno H, et al. The usefulness of a new triple combination treatment utilizing methotrexate, salazosulfapyridine, and bucillamine in rheumatoid arthritis. *Modern rheumatology* 2016 Jan 2;26(1):51-6.

**Disclosure of Interest:** None declared

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SAT0230

#### COMPARISON OF EFFICACY OF TOFACITINIB VS. ETANERCEPT TREATMENT IN RHEUMATOID ARTHRITIS PATIENTS WITH HIGH ACTIVITY DISEASE BY ULTRASOUND EVALUATION WITH POWER DOPPLER (1 YEAR TREATMENT PERIOD).

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**Background:** Modern clinical recommendations rule us to timely and rational treatment of rheumatoid arthritis (RA) patients with biologics or tofacitinib when traditional DMARDs failed in achievement of remission or low disease activity (LDA). Ultrasound power Doppler (PD) was recently recommended by some investigators for accuracy of evaluation of local inflammation in small joints to predict the possible flares of RA.

**Objectives:** To compare the efficacy of tofacitinib vs. etanercept in real clinical practice by complex evaluation including PD during 1-year treatment of RA patients with high disease activity.

**Methods:** In this randomized open study, we assign 30 patients to receive either etanercept 50 mg subcutaneous weekly (10 pts) or tofacitinib 5 mg BID orally (20 pts). There are 21 females and 9 males with severe RA (average DAS 28 >5,8) with inadequate response to methotrexate in effective dose enrolled into the study. Average age was 48.2±5.6 (42,1 for etanercept group and 51,9 for tofacitinib group), average disease history was 5,3 (1,5-25) years. Patients evaluated at baseline, after 3, 6 and 12 months of treatment: number of painful and swollen joints, ESR, C-protein, RF, anti-MCV, DAS 28, SDAI, ultrasound examination of hands and feet (German US7 score) by grey scale (GS) and power Doppler (PD).

**Results:** Patients in both groups had statistically significant decrease of disease activity. In etanercept group median DAS 28 decreased from 6.05 to 2.5

( $p < 0.001$ ), 5 pts achieved remission, 3 - LDA. In tofacitinib group median DAS 28 decreased from 5.86 to 3.23 ( $p < 0.001$ ), 5 pts achieved remission, 3 - LDA. Number of painful and swollen joints decreased to 3-8 times, ESR and C-protein normalized in 8 patients in etanercept group and 12 pts in tofacitinib group. SDAI evaluation showed lowering down the score of activity from range 37,10 to range 6,50 in etanercept group and from 40,78 to 14,25 in tofacitinib group. US dynamics: median GS score decreased from 6.5 to 2,5 ( $p < 0.01$ ) in etanercept group and from 8 to 3 ( $p < 0.01$ ) in tofacitinib group. Number of bone erosions still unchanged. In PD mode number of joints with hypervascularized synovium decreased from 3 to 0 ( $p < 0.001$ ) in both groups.

Also it was noticed that by 3rd month of the treatment LDA was achieved for 2 patients (out of 10) in etanercept group and 5 (out of 15) in tofacitinib one, and relatively by 12 month - 8 in etanercept group and 8 in tofacitinib. The most significant decrease of SDAI (more than 2 times) was achieved by 3rd month and go further with the same dynamics in etanercept group and slightly less in tofacitinib group.

**Conclusions:** Integrated evaluation of efficacy of treatment of patients with severe RA showed that both etanercept and tofacitinib have good effect in achieving of remission or LDA (DAS28 and SDAI). Tofacitinib acts similar to etanercept in 3 months of therapy, but then its effect progressed more slowly. PD is additional method of monitoring of sinovial inflammation and shows us the significant regression of tissue hypervascularisation (activity of inflammation) by 6 months of treatment both etanercept and tofacitinib. Follow up of patients within the year and later on helps to adjust therapy.

**Disclosure of Interest:** None declared

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SAT0231

#### EFFECTS OF THE JAK1-SELECTIVE INHIBITOR FILGOTINIB ON GENE EXPRESSION PROFILE IN BLOOD OF PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS

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**Background:** Filgotinib (FIL), an oral selective JAK1 inhibitor, has shown good safety and efficacy in two phase 2b studies (background methotrexate (MTX, DARWIN 1) and as monotherapy (DARWIN 2)) in active rheumatoid arthritis (RA) patients with inadequate response to MTX<sup>1,2</sup>. We conducted a large-scale RNA sequencing study of genes expressed in blood samples from these studies.

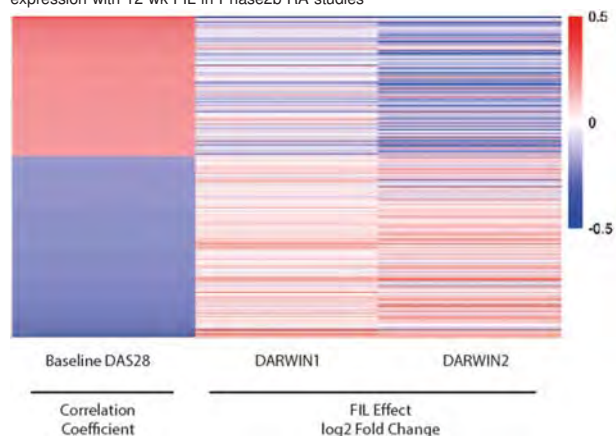
**Objectives:** Identify RA-associated gene transcripts that are altered in response to FIL treatment.

**Methods:** PAXgene blood samples from 242 RA patients receiving either a stable dose of MTX and placebo (PBO) or FIL 200 mg once daily (QD, DARWIN 1); or PBO, FIL 100 mg, or 200 mg monotherapy QD (DARWIN 2), were collected and analyzed at baseline, week 1 and/or week 12. RNA in whole blood was sequenced (Illumina HiSeq 2500) after globin depletion. Differential gene expression analysis was performed on all time-paired data after subtracting gene expression changes in the PBO group. Spearman's rank correlation of gene expression to time, dose, and disease activity score (DAS28) were calculated on samples without missing values. A false-discovery rate (FDR) of 10% was applied for all analyses

**Results:** Top-ranked gene sets positively associated with DAS28 disease activity at baseline over both studies included interferon alpha (IFN- $\alpha$ ) and IFN gamma (IFN- $\gamma$ ) response, IL6/JAK/STAT3 signaling, and toll-like receptor signaling pathways (FDR<10%). Of 197 genes that positively correlated with disease score (increased gene expression with increased DAS28, FDR<10%), 117 (59%) trended toward reduced expression at 12 weeks with FIL in both studies. These genes were enriched in pathways which included granulocyte and macrophage activation. Conversely, of 256 genes negatively correlated with disease score (FDR<10%), 169 (66%) trended toward increased expression post-FIL (figure 1). Of 14724 genes expressed at >1CPM in at least 5% of the samples, 607 were differentially expressed following FIL treatment in either DARWIN1 or DARWIN2 with 48 genes significant in both studies (FDR<10%). Genes reaching significance in at least one study showed consistent magnitude and direction of change in both studies and were enriched in JAK/STAT, innate and adaptive immunity, and autoimmune associated pathways. CISH, SOCS2, SOCS3, VWA5a,

APCCD1, DNASE1L3, and PIM3 correlated with both duration of treatment and FIL dose (FDR<10%). CISH and SOCS confirm JAK pathway modulation.

**Figure 1** Heatmap of 453 DAS28-correlated genes and the corresponding change in gene expression with 12 wk FIL in Phase2b RA studies



**Conclusions:** RA patients treated with FIL show reproducible changes in gene expression consistent with modulation of JAK/STAT signaling and innate and adaptive immunity. FIL was shown to partially reverse the dysregulated gene expression profile associated with baseline DAS28 score, consistent with the efficacy observed in RA patients.

#### REFERENCES:

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- [2] Westhovens R, et al. *Ann Rheum Dis* 2017;76:998–1008.

**Disclosure of Interest:** P. Taylor Consultant for: AbbVie, Biogen, BMS, Galapagos, GSK, Janssen, Lilly, MSD, Novartis, Sandoz, UCB;; J. Tarrant Employee of: GSI Employee, L. Zhao Employee of: GSI Employee, Y. Gindin Employee of: GSI Employee, A. Mirza Employee of: GSI Employee, P. Harrison Employee of: GLPG Employee, C. Tasset Employee of: GLPG Employee, R. Galien Employee of: GLPG Employee, A. Van der Aa Employee of: GLPG Employee, B. Downie Employee of: GSI Employee

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#### SAT0232 REACTIVATION OF IMMUNE CHECKPOINTS BY AN EPITOPE-SPECIFIC VACCINE REINSTATES TOLERANT PATHWAYS AND INDUCES CLINICAL AMELIORATION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Immune checkpoints like PD-1 that govern immune tolerance are attractive therapeutic targets in diseases driven by the dysregulation of tolerogenic pathways. We have previously reported that the induction of immune tolerance by epitope-specific immunotherapy with dnaJP1, a peptide sharing sequence homology to the HLA alleles implicated in the pathogenesis of rheumatoid arthritis (RA), results in clinical improvement in RA and represents a promising therapeutic intervention.

**Objectives:** In the present work, we adopt a holistic approach in deciphering the tolerogenic immune mechanisms underlying the efficacy of epitope-specific immunotherapy with dnaJP1 in a fully human context. We hypothesize that clinical amelioration of RA by dnaJP1 immunotherapy is attributed to the reactivation of immune checkpoints that triggers immune mechanisms modulating immune tolerance and clinical control.

**Methods:** Peripheral Blood Mononuclear Cells (PBMCs) were obtained at the end of the Phase II trial (Day168), from clinical responders treated with dnaJP1 (n=6) and clinical non-responders treated with placebo (n=10). Gene expression analysis was performed by quantitative PCR. The T cell compartment was studied by multi-coloured flow cytometry using specifically designed antibody panels. Flow cytometry results were then analysed by clustering with Multi-Dimensional Automated Reduction and Visualization (MARVis).

**Results:** Analysis of the T cell immunomes of dnaJP1 responders and placebo non-responders revealed a subset of CD4+FoxP3+ regulatory T (Treg) cells exclusively in dnaJP1 responders that displayed a higher expression of the

inhibitory immune checkpoint receptor, PD-1. The expression of PD-1 contributes to an enhancement of the tolerogenicity of this Treg cell subset by upregulating the production of signature anti-inflammatory cytokines such as TGFβ. In addition, we observed a corresponding reshaping of the effector T (Teff) cell compartment in which the expression of pro-inflammatory cytokines such as IL-17A and IFNγ was downregulated. Importantly, epitope-specific immunotherapy also induced a subset of active antigen-experienced memory T cells (CD4+CD45RO+CD69+) which sustains the tolerogenic immune response by secreting TGFβ. Lastly, our preliminary findings demonstrate that the concurrent use of Hydroxychloroquine (HCQ) exerts a synergistic effect in reinstating immune homeostasis by promoting the immunomodulatory capacity of antigen-presenting cells (APCs). The switch to a tolerogenic DC phenotype in the presence of HCQ in turn skews effector T cells towards a functionally protective phenotype by upregulating the expression of PD-1.

**Conclusions:** Our data exemplifies that the toggle between inflammation and tolerance is delicately controlled by a unique subset of Treg cells in which the immune checkpoint protein, PD-1 is switched on. We have also provided mechanistic knowledge on the synergistic relationship between HCQ and the clinical effectiveness of dnaJP1. Taken together, we demonstrate a vaccine-like therapeutic strategy that modifies the multitudinous perturbations in the auto-reactive immune system by reactivating immune checkpoints governing tolerogenic pathways.

**Disclosure of Interest:** None declared

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#### SAT0233 METHOTREXATE TREATMENT IN RHEUMATOID ARTHRITIS AND ELEVATED LIVER ENZYMES: A LONG-TERM FOLLOW-UP OF OCCURRENCE, PREDICTORS, SURVEILLANCE, AND OUTCOME IN CLINICAL PRACTICE

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**Background:** Hepatotoxicity is an important safety issue in long-term methotrexate (MTX) treatment. Guidelines, including the widely used American College of Rheumatology guidelines, therefore recommend testing of liver enzymes at intervals of 8–12 weeks in all MTX-treated patients with rheumatoid arthritis (RA), making this one of the most frequent screening tests in rheumatology care. Although a number of potential risk factors for liver toxicity have been identified, individual risk stratification is still not part of guidelines. Besides, it is unclear what proportion of all monitoring tests that captures liver enzyme elevations and what happens after an alanine aminotransferase (ALT) elevation in clinical practice.

**Objectives:** To assess predictors of ALT elevation in an unselected population of MTX-treated RA patients, describe monitoring of liver enzymes in clinical practice, including the handling and outcome of elevated ALT levels.

**Methods:** All RA patients starting MTX treatment January, 2005–April, 2013 at a rheumatology clinic, (Uppsala university hospital, Sweden) were identified. Clinical and laboratory data from onset of RA until MTX treatment stopped or the end of the study period September, 2013, were obtained from medical records and supplemented by a telephone interview. Predictors for ALT>1.5 the upper limit of normal (ULN) were identified by multiple regression analysis.

**Results:** The study comprised 213 RA patients starting MTX therapy. During a mean follow-up (MTX-treatment period) of 4.3 years, 6288 ALT tests were performed. ALT >ULN was observed in 84 (39%) of the patients and 7% of all tests. The strongest predictor for ALT >1.5 x ULN was a pre-treatment ALT elevation (mean observation period 1.5 years before MTX start) (adjusted OR=6.8, 95% CI 2.2–20.5). In the patients with pre-treatment ALT elevation, the mean time to first ALT elevation was shorter than in those without pre-treatment elevation (p<0.001), and all had recurrent elevations during MTX treatment. In all patients with ALT >ULN, re-elevations occurred in 70%, with similar proportions in those without active interventions and in those where e.g. MTX dose reduction was performed (73% vs. 67%, p=0.43). In patients who permanently stopped MTX due to ALT elevation (n=7), ALT >ULN recurred in 5 (71%) after stopping MTX. Two patients were eventually diagnosed with nonalcoholic fatty liver disease. No patient developed signs of hepatic failure.

**Conclusions:** Pre-treatment ALT elevation is a strong predictor for early and recurrent ALT elevations during therapy. Overall, re-elevations are common, but only a minority of performed ALT tests captures elevations. More individualized or alternative means to follow these patients could be considered to more effectively identify those with MTX-related liver toxicity, and those who despite recurrent ALT elevations could continue MTX treatment without risk for deleterious liver damage.

**Disclosure of Interest:** None declared

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SAT0234

### TOFACITINIB, AN ORAL JANUS KINASE INHIBITOR, IN THE TREATMENT OF RHEUMATOID ARTHRITIS: SAFETY AND EFFICACY IN OPEN-LABEL, LONG-TERM EXTENSION STUDIES OVER 9 YEARS

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**Background:** Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA).

**Objectives:** To report tofacitinib safety and tolerability up to 114 months and clinical efficacy up to 96 months in long-term extension (LTE) studies.

**Methods:** Data were pooled from 2 open-label studies (NCT00413699 [database locked as of March 2017]; and NCT00661661) of patients with RA who had participated in qualifying Phase 1/2/3 studies of tofacitinib. Patients received tofacitinib 5 or 10 mg twice daily (BID) as monotherapy or with background conventional synthetic (cs)DMARDs. As patients in the LTE studies were allowed to switch doses, they were assigned to the 5 mg BID group if the total daily dose (TDD) was <15 mg/day, and to the 10 mg BID group if TDD was ≥15 mg/day. Primary endpoints were adverse events (AEs) and confirmed laboratory safety data. Other endpoints included clinical efficacy measures (ACR20/50/70 response rates, mean DAS28-4[ESR] score, mean HAQ-DI score and mean change from baseline in Clinical Disease Activity Index score). Safety data were included up to Month 114 and completer-analyzed efficacy data up to Month 96 (n<100 post-Month 96).

Table 1 Safety data (Month 114) and clinical efficacy outcomes (up to Month 96; as observed) in LTE studies of tofacitinib in patients with RA

Table. Safety data (Month 114) and clinical efficacy outcomes (up to Month 96; as observed) in LTE studies of tofacitinib in patients with RA	Tofacitinib (5 and 10 mg BID) ± background csDMARDs, N=4967		
		IR per 100 py (95% CI)	
<b>AEs of interest</b>			
Serious adverse events		9.13 (8.67, 9.61)	
Serious infections		2.46 (2.23, 2.70)	
Malignancies (excluding NMSC)		0.83 (0.71, 0.98)	
<b>Confirmed laboratory abnormalities</b>	n (%)	IR per 100 py (95% CI)	
Decrease from baseline in hemoglobin ≥3 g/dL or hemoglobin ≤7 g/dL	104 (2.1)	0.59 (0.48, 0.71)	
Neutropenia, ANC <0.5 x 10 <sup>9</sup> /mm <sup>3</sup>	0 (0.0)	0 (0.0, 0.0)	
Lymphopenia, ALC <0.5 x 10 <sup>9</sup> /mm <sup>3</sup>	70 (1.4)	0.39 (0.30, 0.49)	
<b>Amniontransferases</b>			
ALT >3 x ULN	285 (5.7)	1.63 (1.44, 1.82)	
AST >3 x ULN	166 (3.3)	0.93 (0.79, 1.09)	
Serum creatinine increase >50% from baseline	138 (2.8)	0.77 (0.65, 0.91)	
<b>Clinical efficacy outcomes</b>	Baseline	Month 1	Month 96
<b>ACR response rates, %</b>	N=4907	N=163	N=163
ACR20	NA	73.7	77.9
ACR50	NA	49.9	59.5
ACR70	NA	29.2	41.7
<b>DAS28-4[ESR] score, mean (SE)</b>	N=4782	N=4776	N=161
	6.32 (0.01)	3.75 (0.02)	3.34 (0.09)
<b>HAQ-DI score, mean (SE)</b>	N=4924	N=4880	N=163
	1.42 (0.01)	0.82 (0.01)	0.77 (0.05)
<b>CDAI score, mean change from baseline (SE)</b>	NA	N=4802	N=161
		24.5 (0.21)	10.7 (1.05)

ACR20/50/70, American College of Rheumatology 20%/50%/70% improvement; AE, adverse event; ALC, absolute lymphocyte count; ALT, alanine aminotransferase; ANC, absolute neutrophil count; AST, aspartate aminotransferase; BID, twice daily; CDAI, Clinical Disease Activity Index; CI, confidence interval; csDMARD, conventional synthetic disease-modifying antirheumatic drug; DAS28-4[ESR], Disease Activity Score in 28 joints; erythrocyte sedimentation rate; HAQ-DI, Health Assessment Questionnaire-Disability Index; IR, incidence rate; LTE, long-term extension; N, number of evaluable patients; NA, not applicable; NMSC, non-melanoma skin cancer; py, patient-years; RA, rheumatoid arthritis; SE, standard error; ULN, upper limit of normal

**Results:** Overall, 4967 patients were treated (mean [max] duration: 3.5 [9.4] years). Total tofacitinib exposure was 17,738.5 patient-years (py); 76.4% of patients maintained their initial dose. In total, 2518 patients (50.7%) discontinued (AEs: 1189 [23.9%]; insufficient clinical response: 179 [3.6%]). The most common classes of AE were infections and infestations (69.6%; exposure adjusted event rate [EAER; events per 100 py], 19.71) and musculoskeletal/connective tissue disorders (40.3%; EAER, 11.40). The most common AEs were nasopharyngitis (19.1%; EAER, 5.41), upper respiratory tract infection (17.9%; EAER, 5.07), bronchitis (12.6%; EAER, 3.58) and urinary tract infection (12.5%; EAER, 3.55). Serious AEs occurred in 29.4% of patients and serious infections (SIEs) in 8.9% of patients. Malignancies, excluding non-melanoma skin cancer, were reported in 3.0% of patients. Incidence rates (IR; patients with events per 100 py) for AEs of interest, with 95% confidence intervals, are provided in the table 1. IRs for SAEs, SIEs and malignancies through Month 114 did not increase vs reported data through Month 105.<sup>1</sup> Confirmed laboratory data are provided in the table 1. No new safety risks were identified. Clinical responses were sustained from Month 1 to Month 96 (table 1).

**Conclusions:** In patients with RA who remained in the LTE studies, tofacitinib (5 or 10 mg BID), with or without background csDMARDs, was associated with consistent safety through Month 114 and sustained clinical efficacy through Month 96.

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SAT0235

### SUBCUTANEOUS METHOTREXATE IS SAFER AND MORE EFFECTIVE THAN ORAL METHOTREXATE ALONE AND IN COMBINATION

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**Background:** Methotrexate (MTX) is established as both first line therapy and combination therapy anchor drug for Rheumatoid Arthritis (RA) and other peripheral inflammatory arthritis such as Psoriatic Arthritis (PsA). There is evidence subcutaneous (sc) MTX is more effective than oral MTX, with fewer treatment failures<sup>1-3</sup>, but it is not known if this holds true in routine practice and in combination.

**Objectives:** To show the safety & efficacy of sc MTX therapy in routine practice, compared to oral MTX, alternate monotherapy and combination therapies.

**Methods:** The Therapy Audit Monitoring System (TAMS, www.therapyaudit.com/tamonitor) was installed Jan 2014. Since then all new patients starting disease modifying therapy and existing patients are entered. The database was queried for diagnosis, dose and response, together with adverse events (defined as ALT>80U/l or neutrophils<2.0x10<sup>9</sup>/l). Statistical comparisons used the two proportion Z test, T-test or exact rate ratio test, as appropriate: significance threshold p<0.05.

### Results:

Patient groups	Oral MTX only	sc MTX only	Biologics only	Conventional Combination	Biologic Combination
Total patients ever exposed – n	2093	949	570	1596	552
Patients affected by abnormal LFTs n (%)	198 (10%)	100 (10%)	47 (8%)	154 (10%)	72 (13%)
Patients affected by low neutrophils n (%)	140 (7%)	64 (7%)	66 (12%)	219 (14%)	115 (21%)
Current patients	920	425	345	921	384

8394 patients had received one or more therapies with 4109 current patients identified. Including combinations, 2650 started oral MTX (1463 current) and 1343 sc MTX (911 current). Mean (range) oral MTX dose was 17 (2.5–30) mg and sc MTX was 21 (5–40) mg (p<0.0001). 4356 adverse events were observed over follow-up in 2382 patients, with 1710 (39%) due to ALT>80U/l and 2646 (61%) to neutrophils<2.0x10<sup>9</sup>/l. Abnormal ALT events by drug: oral MTX 486, sc MTX 222 (p=0.92 sc vs. oral). Similarly, low neutrophil count (<2.0x10<sup>9</sup>/l): oral MTX 491, sc MTX 151 (p<0.00001 sc vs. oral). Rate ratios (RR) for low neutrophils for oral MTX-only vs. sc MTX-only showed highly significant differences (RR=1.40, 95% CI: 1.17–1.70; p=0.0002). 14% (1197/8294) of all patients had post-treatment DAS28 scores. Of these 59% (67/113) patients on sc MTX only, and 72% (273/377) on conventional combination achieved DAS<5.1 compared to 69% (69/98) biologic-only and 78% (102/131) biologic-combination. Sensitivity analyses examined response & toxicity by group (data not included).

**Conclusions:** sc MTX is safe and effective in routine practice at doses up to 40 mg. It has lower toxicity than oral MTX in monotherapy and combination, despite a higher mean dose with highly significant reduction in neutropenia rate and the same rate of liver problems compared to oral. This is the largest study of sc MTX yet reported and supports use of higher doses in selected patients and aggregation or replication of data like this may support license extension for sc MTX beyond 30 mg. If patients are usually switched to sc MTX when oral MTX is ineffective or not tolerated, many do not progress to biologic therapy: delivering good care at lower cost.

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Efficacy of baricitinib in patients with RA who failed 2 or more DMARDs

Efficacy measure, Week 24 <sup>†</sup>	RA-BEACON (N=527)			RA-BUILD (N=381) <sup>§</sup>			RA-BEAM (N=704) <sup>§</sup>		
	PBO N=176	Bari 2-mg N=174	Bari 4-mg N=177	PBO N=131	Bari 2-mg N=122	Bari 4-mg N=128	PBO N=283	Bari 4-mg N=244	ADA N=177
ACR20	27	45***	46***	45	58*	71***	33	73***	68***
ACR50	13	23*	29***	25	39*	49***	17	51***	49***
ACR70	3	13***	17***	10	25**	25**	6	30*** <sup>‡</sup>	19***
ΔCDAI	-10.96	-15.42**	-19.41***	-14.74	-19.94***	-23.55***	-12.50	-23.98***	-21.96***
CDAI ≤10	15	23	31***	30	44*	56***	17	48***	47***
CDAI ≤2.8	3	5	9*	5	11	17**	2	14***	11***
ΔSDAI	-10.67	-15.89**	-20.20***	-14.92	-20.72***	-24.29***	-12.70	-25.56***	-23.09***
SDAI ≤11	14	22*	31***	31	48**	57***	17	50***	49***
SDAI ≤3.3	2	5	9**	4	13*	14**	2	14***	12***
DAS28-CRP≤3.2	11	20*	33***	24	46***	55***	16	53***	48***
DAS28-CRP≤2.6	6	11	22***	9	30***	37***	5	35***	31***
ΔHAQ-DI	-0.15	-0.38***	-0.43***	-0.39	-0.60**	-0.59**	-0.30	-0.71*** <sup>‡</sup>	-0.61***
ΔmTSS <sup>¶</sup>	-	-	-	0.72	0.33	0.08**	0.77	0.35**	0.26**

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**SAT0236 LONG-TERM SAFETY AND EFFICACY OF UPADACITINIB (ABT-494), AN ORAL JAK-1 INHIBITOR IN PATIENTS WITH RHEUMATOID ARTHRITIS IN AN OPEN LABEL EXTENSION STUDY**

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**Background:** Upadacitinib (UPA, ABT-494) is a selective, oral JAK-1 inhibitor studied in two phase 2 randomized controlled trials (RCTs) in patients (pts) with rheumatoid arthritis (RA).

**Objectives:** We assessed UPA safety and efficacy in BALANCE-EXTEND, an ongoing, combined open-label extension (OLE) of the phase 2 RCTs.

**Methods:** Pts completing the two 12-week RCTs (in TNF-IR and (MTX-IR pts)<sup>1,2</sup> could enter the OLE. Pts switched to 6 mg UPA from their RCT dose of UPA 3, 6, 12, 18 mg twice daily (BID), 24 mg once daily (QD) or Placebo. A dose increase to 12 mg BID was required for pts with <20% improvement in both SJC and TJC on 6 mg BID (at wk 6 or 12), and permitted for pts not meeting CDAI LDA. Pts without 20% improvement in SJC and TJC 6 wks after escalation, or at any 2 consecutive visits, were discontinued. The dose was decreased to 6 mg BID only in pts with a safety concern or intolerability. Pts are grouped as: Never-titrated (on 6 mg BID throughout); Titrated-up (from 6 to 12 mg BID); Titrated-up and back down (to 6 mg BID). After Jan 2017, the 6 and 12 mg BID doses were replaced by 15 and 30 mg QD extended-release equivalents currently being studied in phase 3. Data up to Jan 13 2017 are reported. Adverse events (AE) per 100 yrs of pt exposure (PY) are summarized starting from day 1 of OLE. Efficacy is assessed by ACR20/50/70 and LDA (by DAS28-CRP and CDAI), and observed data are presented up to Wk 72 of OLE due to sample size consideration.

**Results:** Out of 516 pts who completed the 2 RCTs, 494 entered the OLE, 493 were dosed, 328 (66.5 %) were never-titrated, 150 (30.4%) were titrated-up, and 15 (3%) were titrated-up and back down; 150 pts (30.4%) were discontinued [42 (8.5%) withdrew consent, 37 (7.5%) due to AE and 24 (4.9%) due to lack of efficacy]. Mean exposure to UPA was 525.4±221.4 days (range 1-961 days), and cumulative exposure was 725.1 PY (Table). The E/100PY for any AE in the OLE (170.5) were lower than for the RCTs in the TNF-IR (697.9, 48 PY) and MTX-IR (408.4, 54.6 PY) study populations. The E/100PY were 2.3 for serious infection, 3.7 for herpes zoster, 0.8 for malignancies excluding non-melanoma skin cancer, and 0.7 for adjudicated cardiovascular events. There were 2 deaths: one sudden death (adjudicated as undetermined or unknown cause of death) and one death due to Hodgkin's lymphoma. Changes from baseline in laboratory parameters were consistent with observations from phase 2 RCTs. For those pts completing Wk 72, efficacy was maintained in pts on 6 mg BID UPA from day 1 of OLE (never-titrated); 55% pts met ACR70 and 83% were in LDA by DAS28-CRP and CDAI based on as observed data (Table).

Summary of Adverse Events in Patients who Entered the OLE	Efficacy Measures at Week 72 in Patients who Entered the OLE			
	Never-titrated	Titrated-up	Discontinued	Overall (n/N)
Any AE	1226 (170.5)	1062 (111.90)	769 (17.9)	2997 (217.1)
AE leading to discontinuation	42 (5.8)	37 (3.5)	22 (2.1)	101 (7.4)
AE leading to death	5 (0.7)	4 (0.4)	1 (0.1)	10 (0.7)
Infections	427 (58.9)	344 (35.8)	245 (5.6)	1016 (74.3)
Serious infections	11 (1.5)	9 (0.9)	3 (0.3)	23 (1.7)
Opportunistic infections	3 (0.4)	2 (0.2)	1 (0.1)	6 (0.4)
Herpes zoster	17 (2.3)	13 (1.4)	8 (0.8)	38 (2.8)
Aspergillus	1 (0.1)	1 (0.1)	0	2 (0.1)
Lymphomas	17 (2.3)	13 (1.4)	8 (0.8)	38 (2.8)
CD performance	0	0	0	0
MACE <sup>†</sup>	3 (0.4)	2 (0.2)	1 (0.1)	6 (0.4)
Malignancy other than MACE	9 (1.2)	7 (0.7)	4 (0.4)	20 (1.5)
CYP inhibition	26 (3.6)	22 (2.3)	14 (1.6)	62 (4.5)
Drug-drug interaction	33 (4.5)	28 (2.9)	17 (1.9)	78 (5.7)
VTE	5 (0.7)	4 (0.4)	2 (0.2)	11 (0.8)
Serious VTE	2 (0.3)	2 (0.2)	1 (0.1)	5 (0.4)
Adjudicated cardiovascular events	6 (0.8)	5 (0.5)	3 (0.3)	14 (1.0)
MACE	3 (0.4)	2 (0.2)	1 (0.1)	6 (0.4)
Other cardiovascular events	3 (0.4)	3 (0.3)	2 (0.2)	8 (0.6)

**Conclusions:** The safety profile of UPA remained consistent with that expected for an RA population treated with JAKi. Efficacy responses were maintained up to 72 wks in pts on 6 mg BID UPA in the OLE.

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**SAT0237 EFFICACY OF BARICITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS WHO FAILED 2 OR MORE DMARDS**

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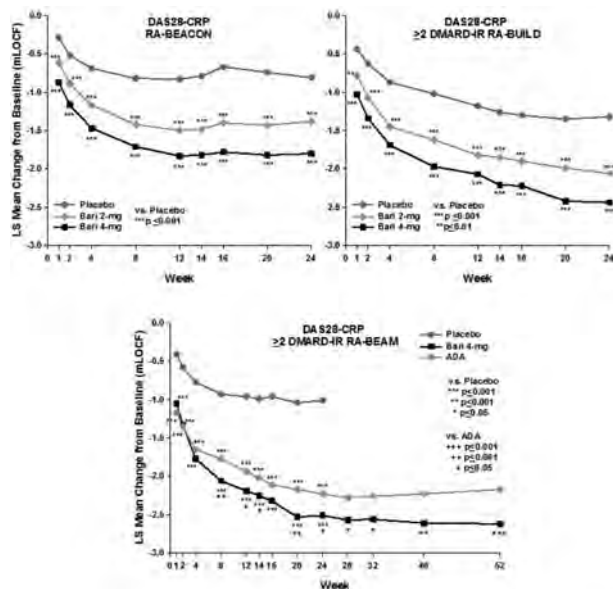
**Background:** Baricitinib (Bari) is an oral Janus Kinase (JAK)1/JAK2 inhibitor in development for patients with active rheumatoid arthritis (RA). In Phase 3 studies, Bari has demonstrated clinical efficacy and has a favorable safety profile.

**Objectives:** To evaluate Bari 2- and 4-mg in patients who have failed multiple DMARDs, across several studies.

**Methods:** Data from the subgroup of patients who had failed  $\geq 2$  DMARDs, including approx. one-half of patients in RA-BUILD (csDMARD-IR) and RA-BEAM (MTX-IR) and all patients from RA-BEACON (bDMARD-IR) were assessed, post hoc, for comparison of Bari 2-mg and 4-mg to placebo across time points using the following measures: ACR20, ACR50, ACR70, SDAI, CDAI, DAS28-CRP, HAQ-DI, and radiographic assessment of structural damage (mTSS), as well as safety. For patients who had failed  $\geq 2$  DMARDs from RA-BEAM, a comparison was also made between Bari 4-mg and adalimumab.

**Results:** In the  $\geq 2$  DMARD-IR populations from RA-BEACON, RA-BUILD, and RA-BEAM, >95% had failed MTX as one of the DMARDs. Compared to PBO in this population, Bari resulted in statistically significantly greater improvement in efficacy measures at Week 24, including physical function (Table). In the  $\geq 2$  DMARD-IR population from RA-BEAM (all patients received background MTX), Bari 4-mg was associated with greater improvements compared to adalimumab (table 1 and figure 1). Compared to PBO, Bari 4-mg statistically significantly inhibited structural progression at Week 24 in the  $\geq 2$  DMARD-IR subsets of RA-BEAM and RA-BUILD. The overall safety profile of Bari 4-mg in the  $\geq 2$  DMARD-IR population was consistent with findings from the overall baricitinib-treated population.

<sup>v</sup>Data are the proportion (%) of pts who achieved the response at Week 24 (non-responder imputation), unless otherwise indicated. <sup>s</sup>Approximately 56% of patients in RA-BUILD and 54% of patients in RA-BEAM failed  $\geq 2$  DMARDs. <sup>Δ</sup>least squares mean change from baseline (modified last observation carried forward). <sup>¶</sup>mTSS data are as randomized using last observation carried forward. \*p $\leq$ 0.05, \*\*p $\leq$ 0.01, \*\*\*p $\leq$ 0.001 for Bari 4-mg or Bari 2-mg vs. PBO; <sup>†</sup>p $\leq$ 0.05 Bari 4-mg vs. ADA



**Conclusions:** These data demonstrate that a dose response is present between Bari 2-mg and Bari 4-mg, with both doses providing benefit in the patients who failed multiple DMARDs in the phase 3 program by improving signs and symptoms, physical function, and structure.

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**SAT0238 RAPID ELEVATION OF ERYTHROCYTE METHOTREXATE-POLYGLUTAMATE3 (MTX-PG3) LEVELS RELATED TO THE EFFICACY OF MTX IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA).**

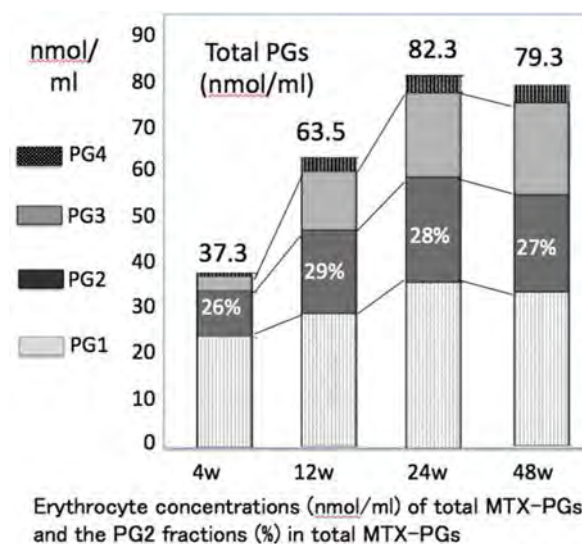
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**Background:** MTX is transported into cells and retained long after polyglutamation. Recently, it has been described that the response to MTX treatment is related to the intracellular MTX-polyglutamate (MTX-PG) levels, but little is known about its details and determinants<sup>1</sup>.

**Objectives:** To clarify the association of erythrocyte concentrations of MTX-PGs (PG1 to PG4) with the efficacy of MTX in 35 MTX naïve patients with RA.

**Methods:** We measured erythrocyte MTX-PGs at 4, 12, 24, and 48 weeks after administration of MTX using liquid chromatography (LC)-mass spectrometry (MS)/MS assay. The associations of MTX-PG concentrations with disease activity and the 9 SNPs including 5 SNPs reported for associations with MTX-efficacy were analyzed.

**Results:** As shown in the figure, MTX-PG1 and PG2 elevated at week 4, and total MTX-PGs as well as MTX-PG3 and MTX-PG4 increased until week 12. The MTX-PG2 fraction (as percentage of total) was 26% to 29% and almost constant throughout the course. MTX-PG3 and MTX-PG4 fractions were gradually elevated over time, although MTX-PG1 fraction was decreased. A negative association of Disease Activity Score in 28 joints (DAS28) at week 4, 12 and 24 was observed with levels of MTX-PG2 (p=0.008), MTX-PG3 (p=0.0045), MTX-PG4 (p=0.0142) and total MTX-PG (p=0.023). On the other hand,  $\Delta$ DAS28 (change in DAS28 scores from baseline) was positively correlated to fraction of MTX-PG3 (p=0.011) but negatively correlated to that of MTX-PG1 (p=0.0071). At week 12 and 24, MTX-PG2 fraction was higher (p=0.0783) in the patients who achieved the EULAR good response criteria than in those who did not. MTX-PG3 levels were associated with SLC19A1c.80G>A and FMO2\_c.585A>G, and the fraction of MTX-PG2 in total MTX-PGs was associated with GGH c.452C>T and with FMO2\_c.585A>G.



**Conclusions:** This study suggests that rapid elevation of erythrocyte MTX-PG3 levels from MTX-PG1 through MTX-PG2 and higher distribution of MTX-PG3 is



important to exert certain efficacy of MTX. We previously reported in retrospective study that MTX-PG concentration in RA patients keeping remission for long time was associated with several SNPs<sup>2</sup>, and some of the results were confirmed in this prospective study.

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**SAT0239 RAPID RESPONSE WITH UPADACITINIB TREATMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS AND AN INADEQUATE RESPONSE TO CSDMARDS OR bDMARDS**

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**Background:** Upadacitinib (UPA), an oral JAK inhibitor selective for JAK1, demonstrated efficacy in patients (pts) with moderate to severe rheumatoid arthritis (RA) with an inadequate response (IR) to csDMARDs or bDMARDs in the SELECT-NEXT<sup>1</sup> and SELECT-BEYOND<sup>2</sup> trials, respectively.

**Objectives:** To investigate the speed of response to UPA across disease measures in csDMARD- and bDMARD-IR pts.

**Methods:** 661 pts in NEXT and 498 in BEYOND received UPA 15 mg or UPA 30 mg once daily (QD) or placebo (PBO) for 12 weeks (wks)<sup>1,2</sup>. Time to first achievement of clinically meaningful outcomes, including ACR20/50, DAS28-CRP≤3.2 and Low Disease Activity (LDA) measures of CDAI (≤10) and SDAI (≤11) was evaluated. The cumulative incidences of ACR20/50, DAS28-CRP≤3.2 and LDA by CDAI and SDAI over 12 wks were estimated. Hazard ratios between UPA and PBO were obtained using Cox proportional hazards model with treatment group, corresponding baseline values and main stratification factors, without control for multiple comparisons. All analyses were based on observed data without imputation.

Table 1. Summary of Median Time (in Weeks) to Achieve First Response Over 12 Weeks

		csDMARD-IR			bDMARD-IR		
		N	Median (Q1, Q3)	HR	N	Median (Q1, Q3)	HR
ACR20	PBO	221	12.1 (9.9, NE)		169	11.9 (2.9, NE)	
	UPA 15	219	9.1 (2, 12.1)	2.1***	194	4.1 (2.9, 12.1)	2.0***
	UPA 30	216	2.4 (1.9, 8.1)	2.5***	184	2.7 (1.6, 12.1)	2.0***
ACR50	PBO	221	12.9 (12.4, NE)		169	NE (NE, NE)	
	UPA 15	219	12.8 (4.3, NE)	2.4***	194	12.7 (6, NE)	2.8***
	UPA 30	218	8.6 (4.1, 13.4)	3.4***	185	12.1 (4.1, NE)	3.6***
DAS28-CRP ≤3.2	PBO	221	NE (12.1, NE)		169	NE (12.2, NE)	
	UPA 15	214	12.1 (4.1, 13)	2.9***	183	12.2 (4.1, NE)	2.8***
	UPA 30	215	8.1 (2.6, 12.7)	3.9***	182	8.7 (4.1, 13)	3.3***
CDAI LDA	PBO	210	NE (12.1, NE)		158	NE (NE, NE)	
	UPA 15	208	12.3 (6, 13)	2.3***	156	12.1 (6.1, NE)	2.3***
	UPA 30	209	12.1 (4.5, 13.3)	2.6***	156	12.3 (4.3, NE)	2.9***
SDAI LDA	PBO	210	NE (12.1, NE)		160	NE (12.9, NE)	
	UPA 15	208	12.3 (4.1, 13)	2.6***	156	12.4 (7.7, NE)	2.2***
	UPA 30	209	12 (4.5, 13.4)	3.2***	156	12.1 (4.1, NE)	2.9***
FK68-50s Improvement	PBO	221	3.1 (2.5, NE)		169	3.1 (2.1, 12.4)	
	UPA 15	220	4.1 (2.0, 12.1)	1.6***	184	4.1 (1.9, 12.1)	1.6**
	UPA 30	216	4.1 (2.1, 8.6)	1.7***	185	4.3 (2.0, 9.4)	1.9**
SK66-50s Improvement	PBO	221	4.4 (2.1, 12.9)		169	4.1 (1.1, 12.9)	
	UPA 15	220	4.0 (1.8, 8.1)	1.5***	184	3.9 (1.8, 8.4)	1.4**
	UPA 30	216	2.2 (1.9, 8.1)	1.8***	185	3.9 (1.4, 8.1)	1.4**

HR, Hazard ratio; NE (not estimable) indicates that the response was not reached within the 12-week period. \*\*\*p<0.001

HR, hazard ratio, NE (not estimable) indicates that the response was not reached within the 12-week period. \*\*\*p<0.001

**Results:** Pts had a disease duration of 7 and 13 years in NEXT and BEYOND respectively.<sup>1,2</sup> In BEYOND, pts were treatment-refractory as evidenced by 53% having received ≥2 prior bDMARDs<sup>2</sup>. Median times to achieve ACR20 were similar, irrespective of pt population, being 4 wks for UPA 15 mg QD and 2–3 wks for

UPA 30 mg QD vs 12 wks on PBO (p<0.001). In general, the median times to achieve ACR50 and DAS28-CRP≤3.2 for UPA 15 mg and 30 mg QD were ~12 wks and ~8 wks for both csDMARD-IR and bDMARD-IR pts, whereas the median was not reached for pts on PBO during the first 12 wks (p<0.001, table 1). The median time to LDA by CDAI and SDAI was ~12 wks across UPA doses and populations, but was not reached for pts receiving PBO within that time. Pts receiving UPA were 2–4 times more likely to achieve clinical responses vs pts receiving PBO. In general, both UPA doses performed similarly across pt populations, with numerically quicker responses observed in pts receiving UPA 30 mg vs UPA 15 mg QD. Median times to achieve 20% and 50% improvements in tender and swollen joint counts were 1–2 wks and 2–4 wks respectively, for both UPA doses, irrespective of pt population. Median times to achieve 20% improvements in morning stiffness duration and severity were approximately 2 wks in each of the UPA arms vs 4 wks on PBO (p<0.001).

**Conclusions:** Pts receiving UPA at either 15 mg or 30 mg QD were more likely to achieve clinical responses at significantly earlier time points when compared with pts receiving PBO. Irrespective of being csDMARD-IR or bDMARD-IR, times to achieve various clinical responses were consistent between pt populations.

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**SAT0240 VAGUS NERVE STIMULATION IN PATIENTS WITH RHEUMATOID ARTHRITIS: TWO-YEAR SAFETY AND EFFICACY**

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**Background:** Rheumatoid arthritis (RA) is a debilitating chronic disease with an unmet need for additional therapeutic approaches. Activating neuro-immune reflex pathways by stimulation of the vagus nerve (VNS) could represent a novel means of treating RA [1] and other immune-mediated inflammatory diseases. Last year we reported a 12-week proof-of-concept study using a VNS device, approved for drug-resistant epilepsy, showing reduction in the DAS28-CRP clinical disease activity score, with concomitant reductions in TNF and IL-6 levels [2].

**Objectives:** To understand the long term safety and efficacy of this novel treatment approach, we followed the patients in a 24 months long-term extension study and report on the safety and clinical efficacy data.

**Methods:** VNS devices were implanted into 17 RA patients, mostly with insufficient response to multiple conventional and biologic disease-modifying antirheumatic drugs (DMARDs), on stable background of methotrexate (≤25 mg weekly) therapy. The devices electrically stimulated the vagus nerve, 1–4 min/day, over a 12 week open label period. On completion, subjects were offered to enroll into a follow-up study, where the study physicians were given flexibility to alter VNS dosing parameters and/or to add a biologic DMARD to the treatment regimen. DAS28-CRP and Health Assessment Questionnaire-Disability Index (HAQ-DI) were collected over 2 years.

**Results:** All subjects electively continued on VNS treatment through 24 months of the long term follow-up study. Biologic DMARDs were started in 1 and restarted in 8 of 17 subjects; of these, 4 were non-responders to VNS, and 5 had stable improvement but had not yet achieved disease remission on VNS alone (table 1). At the start of the follow-up study, the mean DAS28–28 and HAQ-DI were significantly reduced compared to the pre-implant baseline (mean difference±SE in DAS28-CRP=-1.60±0.37, p<0.0001; mean difference±SE in HAQ-DI = -0.44 ±0.21, p<0.037), and the depth of effect was retained through 24 months. At 24 months, there was no significant difference in DAS28-CRP between the subjects using VNS monotherapy or those using a combination of VNS and biologic

DMARDs (VNS monotherapy= 3.76±1.77 vs. VNS and biologic DMARD= 3.21±1.44,  $p<0.54$ ). No difference in the adverse events profile between the two groups was seen.

**Table 1** Two Year Efficacy of VNS Treatment. Mean DAS28-CRP at primary study baseline (month -3-5) and at visits over 2 years of long term follow up (months 0-24). **Conclusions:** The data presented here demonstrate that VNS in subjects with RA is associated with a substantial reduction in disease activity that is sustained for 24 months without untoward safety signals. In addition, the data suggest that biological DMARDs can be initiated safely in combination with VNS treatment, though this requires further study in larger cohorts. These results support further development of VNS devices as an alternative therapeutic approach for RA treatment, which potentially can safely be combined with biologic DMARDs.

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#### SAT0241 PATIENTS' PERSPECTIVE ON THE EFFICACY AND RISKS OF GLUCOCORTICOIDS IN RA – AN INITIATIVE UNDER THE GLORIA PROJECT

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**Background:** The Glucocorticoid Low-dose Outcome in Rheumatoid Arthritis Study (GLORIA) is an international investigator-initiated pragmatic randomised trial designed to study the effects of low dose glucocorticoids (GC) in elderly patients with Rheumatoid Arthritis (RA). The research team is also committed to promote a better understanding of the risks and benefits of these drugs among health professionals and patients. In order to achieve these goals, it is important to assess the current concepts and concerns of patients regarding GC.

**Objectives:** In this study, we evaluated the beliefs about GC in RA patients who are, or have been treated with GC.

**Methods:** Patients with RA from three different countries (United States (US), Portugal, and the Netherlands) completed an online survey which was presented in their native language.

Members of People with Arthritis and Rheumatism, and national associations were involved in the development of the questionnaire. In Europe, patients were invited to participate through national patients' organizations, and SurveyMonkey<sup>®</sup> was used to disseminate the online surveys. In the US, patients were invited to participate and surveyed through MediGuard.org.

Patients with RA from three different countries (United States (US), Portugal, and the Netherlands) completed an online survey which was presented in their native language.

Members of People with Arthritis and Rheumatism, and national associations were involved in the development of the questionnaire. Participants were asked to agree or disagree with statements on a 5-point scale. In Europe, patients were invited to participate through national patients' organizations, and SurveyMonkey<sup>®</sup> was used to disseminate the online surveys. In the US, patients were invited to participate and surveyed through MediGuard.org.

**Results:** Data was collected from 314 RA patients with exposure to GCs (table 1). Mean education level was around 15 years and duration of GC exposure was

skewed (median 48 months [inner quartiles 8, 120]). The majority of US patients had received prednisone and in Europe, prednisolone. The majority of participants in all three regions had already read articles or pamphlets on the benefits or harms related to GC therapy.

Regarding GC risk, about half of the European patients stated that they had already suffered a serious adverse event (SAE) due to GC. US patients were not asked if they suffered GC-related SAE due to regulatory reporting rules, but 82% showed concern about experiencing an SAE from GC use.

Regarding GC efficacy, high levels of endorsement were found for the three questions asked: more than 78% of patients considered that GC were very useful in their case, more than 61% considered that GC were effective even in low doses, and more than 60% agreed that GC improved RA symptoms within days.

**Table 1** Patient beliefs about GC from surveys in USA, Portugal and The Netherlands.

	USA	Portugal	Netherlands
Number of patients	139	131	44
Education, mean ± SD (years)	14 ± 3	15 ± 5	16 ± 4
GC prescribed (%)			
Prednisone	78	18	33
Prednisolone	11	73	62
Methylprednisolone	9	10	5
Other	1	0	0
Treatment duration, median (inner quartiles, months)	24 (5-84)	120 (36-180)	36 (4-108)
Have you read any articles or pamphlets on the benefit or harm of GC therapy? (%)	72	64	75
Level of agreement for statements (%)*			
If I take GC, I am concerned that I may suffer a serious adverse event	82 (55)	NA	NA
I have suffered serious adverse events due to GC	NA	48 (18)	51 (23)
GC are or have been very useful to me	79 (56)	86 (55)	85 (69)
At a dose of less than or equal to 7.5 mg of prednisolone/day, GC:			
- are very effective in the control of signs and symptoms of RA	61 (38)	78 (41)	69 (44)
- improve RA symptoms within days	60 (41)	74 (45)	69 (49)

\* Total of 'slightly agree' and 'agree' in parentheses the percentage of 'agree'; SD: Standard Deviation; GC: Glucocorticoid; RA: Rheumatoid Arthritis; NA: Not Asked.

**Conclusions:** Patients with RA exposed to long-term GC report a high prevalence of SAE or fear thereof. This is accompanied by a strong conviction that GC are very useful and effective for the treatment of their RA, even at low dosages.

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#### SAT0242 EFFECTIVENESS OF CONVENTIONAL DMARD THERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED UNDER A TREAT TO TARGET MODEL – LESSONS FROM A REAL-LIFE COHORT

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**Background:** Rheumatoid arthritis (RA) is a common chronic inflammatory disease. It is characterized by progressive, joint damage, impaired joint function and pain, the disease causes disability and reduces quality of life. Treat-to-target (T2T) is an acknowledged management strategy for RA; it proposes that the therapeutic target in RA should be a state of remission or low disease activity. There are two types of pharmacological therapy available: biological DMARDs that are considered highly expensive for our countries and conventional DMARDs which have demonstrated effectiveness and is a low-cost treatment (1,2).

**Objectives:** The aim of this study was to describe global change in Disease Activity Score 28 (DAS28) using a T2T strategy during three years in a cohort of patients receiving conventional DMARDs.

**Methods:** A descriptive cohort study was conducted. Medical records of patients from specialized in RA center were reviewed during 2015–2017; those patients were followed-up under T2T standards and a multidisciplinary approach. Clinical follow-up was according to DAS28: every 3–5 weeks (DAS28 >5.1), every 7–9 weeks (DAS28 ≥3.1 and ≤5.1), and every 11–13 weeks (DAS28 <3.1). Therapy had to be adjusted with DAS28 >3.2 unless patient's conditions don't permit it; We divided patients in four groups: remission (REM), low disease activity (LDA), moderate disease activity (MDA) and severe disease activity (SDA) patients and the aim of the study was to look at what percentage of patients reached LDA or REM. Descriptive epidemiology was done, we calculated means, and standard deviations for continuous variables and categorical variables were presented as rates.



We analyzed normality for DAS28, in order to compare disease activity at beginning and the end of follow-up.

**Results:** During 3 years we included 1953 patients were 39% were in low disease activity, 47% in moderate disease activity and 14% were in severe disease activity, 84% were female, mean age was 60 years±12. At baseline mean DAS28 was 4.45±0.90 with a median of 4.3 at three years the mean DAS28 was 3.83 ±1.08 with a median of 3.60. At the end of follow-up 46% of population achieved remission and 25% achieved low disease activity; at overall 71% improved disease activity, see table 1. In our study DAS28 was not normally distributed, thus we performed a Wilcoxon test in order to compare the mean DAS28 at baseline/36 months showing statistical significance (P<0.05).

ACTIVITY LEVEL	BASELINE		3 YEARS FOLLOW-UP	
	n	%	n	%
REM			898	46
LDA	759	39	488	25
MDA	912	47	528	27
SDA	282	14	39	2

**Conclusions:** Patients treated with conventional DMARD therapy and under a T2T model achieve favorable results in regards of disease activity. This is real life evidence that can support the advantages of treating RA patients with a multidisciplinary team under a T2T model with a low-cost treatment.

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**SAT0243** **INCIDENCE OF THROMBOEMBOLIC EVENTS IN THE TOFACITINIB RHEUMATOID ARTHRITIS, PSORIASIS, PSORIATIC ARTHRITIS AND ULCERATIVE COLITIS DEVELOPMENT PROGRAMMES**

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**Background:** Tofacitinib is an oral Janus kinase (JAK) inhibitor that preferentially inhibits signalling by JAK3 and JAK1, with functional selectivity over JAK2. Potential increased risk of venous thromboembolic events (VTE) in patients (pts) with rheumatoid arthritis (RA) has been reported for a JAK 1/2 inhibitor.<sup>1</sup>

**Objectives:** To assess VTE risk with tofacitinib in pts with RA, psoriasis (PsO), psoriatic arthritis (PsA) and ulcerative colitis (UC).

**Methods:** Data from Phase (P)2 (RA, PsO, UC) and P3 (RA, PsO, PsA, UC) randomised clinical studies of tofacitinib as monotherapy or in combination with conventional synthetic (cs)DMARDs were reviewed. Two cohorts were defined; 1) the placebo (PBO)-controlled cohort: pts randomised to tofacitinib 5 or 10 mg BID, or PBO up to Month (M)3 in RA, PsO and PsA studies, and pts randomised to tofacitinib 10 mg BID or PBO for the 9-week induction period in UC studies; 2) the dose-comparison cohort: pts randomised to tofacitinib 5 or 10 mg BID, adalimumab (ADA) 40 mg SC Q2W (RA and PsA only) or methotrexate (MTX) 20 mg QW (RA only) throughout the P2/3 studies for RA (up to M24), PsO (up to M12) and PsA (up to M12), and for the 12-month P3 UC maintenance study. First deep vein thrombosis (DVT) and pulmonary embolism (PE) events were identified using the MedDRA embolic and thrombotic SMQ preferred terms restricted to the respiratory, thoracic, mediastinal and vascular disorder System Organ Classes; incidence rates (IRs; pts with events/100 pt-years) were based on single events occurring during treatment or ≤28 days after the last dose or up to the cohort cut-off date. IRs for PE in RA pts were compared with Corrona Registry data (May 2017 cut-off).

**Results:** Up to M3 in the PBO-controlled cohort, DVT and PE each occurred in 2 pts receiving PBO (1 RA pt and 1 UC pt per event); no tofacitinib-treated pts had DVT or PE events (Table). In the dose-comparison cohort 2 DVT events occurred in tofacitinib-treated pts with RA (5 mg BID, n=1; 10 mg BID, n=1) and 1 DVT event in a pt with PsA (tofacitinib 10 mg BID) (Table). IRs (95% CI) were 0.1 (0.0, 0.3) for both tofacitinib doses in RA and 0.5 (0.0, 2.8) for tofacitinib 10 mg BID in PsA. Two DVT events occurred with MTX; none with ADA. Five PE events occurred in the dose comparison cohort, all in RA (5 mg BID, n=2; 10 mg BID, n=3). IRs were 0.1 (0.0, 0.4) for tofacitinib 5 mg BID and 0.2 (0.0, 0.4) for 10 mg BID. IRs for PE with tofacitinib in RA were similar to those reported by the Corrona Registry in RA pts treated with tofacitinib (0.1 [0.0, 0.4]), biologic DMARDs (0.2 [0.1, 0.3]) and csDMARDs (0.2 [0.0, 0.5]).

**Table 1** Incidence rates for deep vein thrombosis and pulmonary embolism from randomised controlled studies across the tofacitinib clinical development programme

Study	Placebo-controlled cohort <sup>a</sup>				Dose-comparison cohort <sup>b</sup>			
	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Adalimumab 40 mg SC Q2W	Methotrexate 20 mg QW	
<b>Randomised arthritis</b>								
DVT	0/149 0.0%	0/204 0.0%	1/197 0.5%	1/159 0.6%	1/204 0.5%	0/217 0.0%	2/213 0.9%	
PE	0/149 0.0%	0/204 0.0%	0/197 0.0%	0/159 0.0%	0/204 0.0%	0/217 0.0%	0/213 0.0%	
<b>Psoriasis<sup>c</sup></b>								
DVT	0/123 0.0%	0/123 0.0%	0/123 0.0%	0/123 0.0%	0/123 0.0%	0/123 0.0%	0/123 0.0%	
PE	0/123 0.0%	0/123 0.0%	0/123 0.0%	0/123 0.0%	0/123 0.0%	0/123 0.0%	0/123 0.0%	
<b>Psoriatic arthritis<sup>d</sup></b>								
DVT	0/123 0.0%	0/123 0.0%	0/123 0.0%	0/123 0.0%	0/123 0.0%	0/123 0.0%	0/123 0.0%	
PE	0/123 0.0%	0/123 0.0%	0/123 0.0%	0/123 0.0%	0/123 0.0%	0/123 0.0%	0/123 0.0%	
<b>Ulcerative colitis<sup>e</sup></b>								
DVT	0/54 0.0%	0/54 0.0%	0/54 0.0%	0/54 0.0%	0/54 0.0%	0/54 0.0%	0/54 0.0%	
PE	0/54 0.0%	0/54 0.0%	0/54 0.0%	0/54 0.0%	0/54 0.0%	0/54 0.0%	0/54 0.0%	

<sup>a</sup>Includes Month 0-3 of Phase 2/3 studies for RA, PsO and PsA, and the 12-month maintenance period of Phase 2/3 studies for RA, PsO and PsA, and the 12-month P3 UC maintenance study. <sup>b</sup>Dose-comparison cohort for tofacitinib 5 mg BID and 10 mg BID compared patients randomised to tofacitinib 5 mg BID + placebo (addition) randomised to tofacitinib or PBO + tofacitinib 5 mg BID, and patients randomised to tofacitinib or tofacitinib 10 mg BID + placebo (addition) randomised to tofacitinib or PBO + tofacitinib 10 mg BID, respectively. <sup>c</sup>Includes studies 1-3 of Phase 2/3 studies for RA, PsO and PsA, and the 12-month maintenance period of Phase 2/3 studies for RA, PsO and PsA, and the 12-month P3 UC maintenance study. <sup>d</sup>Includes studies 1-3 of Phase 2/3 studies for RA, PsO and PsA, and the 12-month maintenance period of Phase 2/3 studies for RA, PsO and PsA, and the 12-month P3 UC maintenance study. <sup>e</sup>Includes studies 1-3 of Phase 2/3 studies for RA, PsO and PsA, and the 12-month maintenance period of Phase 2/3 studies for RA, PsO and PsA, and the 12-month P3 UC maintenance study.

**Conclusions:** Analysis of DVT and PE across randomised clinical studies for RA, PsO, PsA and UC showed no evidence of an increased risk of these events with tofacitinib vs other therapies.

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SAT0244

### IMPACT OF 12 WEEKS OF UPADACITINIB TREATMENT ON INDIVIDUAL AND COMPOSITE DISEASE MEASURES IN PATIENTS WITH RHEUMATOID ARTHRITIS AND INADEQUATE RESPONSE TO CONVENTIONAL SYNTHETIC OR BIOLOGIC DMARDS

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**Background:** Upadacitinib (UPA), an oral, JAK1-selective inhibitor, demonstrated efficacy through 12 and 24 weeks (wks) in phase 3 trials of patients (pts) with active rheumatoid arthritis (RA) and inadequate response (IR) to csDMARDs and bDMARDs, respectively.<sup>1,2</sup> Efficacy evaluations at Wk 12 are an important assessment point according to T2T recommendations.<sup>3</sup>

**Objectives:** To assess the impact of UPA at 12 wks on individual and composite measures of RA disease activity.

**Methods:** Pts received UPA 15 mg or 30 mg once daily (QD) or PBO for 12 wks in two phase 3 trials. SELECT NEXT<sup>1</sup> and SELECT BEYOND<sup>2</sup> enrolled csDMARD- and bDMARD-IR pts, respectively. For this investigation, responses at Wk 12, were defined as  $\geq 50\%$  improvement in ACR components. Among ACR50 responders, the proportions of pts achieving  $\geq 50\%$  improvement in all 7 components of the ACR response criteria [Tender Joint Count (TJC68), Swollen Joint Count (SJC66), Pt Global Assessment (PtGA), Physician Global Assessment (PhGA), Pt Pain, Health Assessment Questionnaire-Disability Index (HAQ-DI), and high sensitive C-reactive protein (hsCRP)] were assessed. Differences in the cumulative distributions of CDAI, DAS28-CRP, and SDAI between baseline (BL) and Wk 12 were assessed. All analyses were based on observed data without imputation.

**Results:** Pts in both studies, on average, had established, moderate to severe RA at BL, with (mean) disease durations of 7.3 and 13.2 years, CDAI of 38.2 and 40.9, in csDMARD-IR and bDMARD-IR pts, respectively; 53% of bDMARD-IR pts had exposure to  $\geq 2$  bDMARDs.<sup>1,2</sup> In both populations, significantly more pts on UPA vs PBO achieved  $\geq 50\%$  improvement in each ACR component at Wk 12 (Table). Among pts who achieved ACR50 at Wk 12, approximately one-half of the csDMARD-IR and one-third of the bDMARD-IR pts achieved  $\geq 50\%$  improvement in all 7 ACR components. While there were no differences at BL, cumulative distributions of CDAI, DAS28-CRP, and SDAI separated by treatment at Wk 12 ( $p < 0.001$ ); for the lowest quartiles for UPA 15 mg and 30 mg vs PBO, CDAI levels dropped to 6.2 and 5.1 vs 12.5 in csDMARD-IR; and 7.2 and 8.2 vs 13.1 in bDMARD-IR.

Proportions of Patients Achieving 50% Improvements in Core Components of the ACR Score at Week 12							
		SELECT-NEXT			SELECT-BEYOND		
		(csDMARD-IR)			(bDMARD-IR)		
		N	n (%)	$\Delta$ from	N	n (%)	$\Delta$ from
TJC $\geq 50\%$ Improvement	PBO	207	35 (46.3)	-	147	68 (46.3)	-
	UPA 15	210	140 (66.7)***	20.0***	157	116 (79.9)***	27.6***
	UPA 30	201	143 (71.1)***	25.2***	149	105 (70.5)***	24.2***
SJC $\geq 50\%$ Improvement	PBO	207	114 (55.1)	-	147	81 (55.1)	-
	UPA 15	210	153 (72.9)***	17.6***	157	123 (78.3)***	23.2***
	UPA 30	201	158 (78.6)***	23.5***	149	109 (73.2)***	18.1***
Pain $\geq 50\%$ Improvement	PBO	206	42 (20.4)	-	145	34 (23.4)	-
	UPA 15	207	112 (54.1)***	33.7***	156	67 (42.9)***	19.5***
	UPA 30	200	111 (55.5)***	35.1***	146	70 (47.9)***	24.5***
PtGA $\geq 50\%$ Improvement	PBO	206	49 (23.8)	-	145	33 (22.8)	-
	UPA 15	207	108 (52.2)***	28.4***	156	73 (46.8)***	24.0***
	UPA 30	200	109 (54.5)***	30.7***	147	74 (50.3)***	27.5***
PhGA $\geq 50\%$ Improvement	PBO	192	74 (38.5)	-	137	56 (40.9)	-
	UPA 15	193	129 (66.8)***	28.3***	150	97 (64.7)***	23.8***
	UPA 30	187	140 (74.9)***	36.4***	137	94 (68.6)***	27.7***
HAQ-DI $\geq 50\%$ Improvement	PBO	206	48 (23.3)	-	145	22 (15.2)	-
	UPA 15	206	91 (44.2)***	20.9***	156	41 (26.3)**	11.1*
	UPA 30	200	83 (41.5)***	18.2***	146	41 (28.1)**	12.9**
hsCRP $\geq 50\%$ Improvement	PBO	207	38 (18.4)	-	146	35 (24.7)	-
	UPA 15	208	155 (76.1)***	57.7***	155	114 (73.5)***	46.8***
	UPA 30	201	145 (72.1)***	53.7***	146	100 (68.5)***	41.8***
$\geq 50\%$ Improvement in all 7 ACR	PBO	32	2 (6.3)	-	20	2 (10)	-
	UPA 15	84	58 (69.0)***	36.8***	56	39 (69.6)***	23.5*
	UPA 30	94	59 (62.8)***	35.2***	59	39 (65.9)***	22.6*

\* \*\* \*\*\* p < .05, .01 and .001 respectively for comparisons of UPA vs PBO; delta ( $\Delta$ ) = difference

**Conclusions:** In pts with an insufficient response to either csDMARDs or bDMARDs, treatment responses at 12 wks were observed in significantly higher proportions with UPA vs PBO. Favorable effects with UPA were seen in the composite scores and the individual parameters, including PROs and acute-phase reactants.

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SAT0245

### AZD9567: A NOVEL ORAL SELECTIVE GLUCOCORTICOID RECEPTOR MODULATOR, DEMONSTRATED TO HAVE AN IMPROVED THERAPEUTIC RATIO COMPARED TO PREDNISOLONE IN PRE-CLINICAL STUDIES, IS SAFE AND WELL TOLERATED IN FIRST CLINICAL STUDY.

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**Background:** Glucocorticoids (GC) are highly effective in the treatment of inflammatory diseases but chronic treatment is limited by severe adverse effects including hyperglycemia and bone re-modelling. AZD9567 is a novel, orally delivered, non-steroidal Selective Glucocorticoid Receptor Modulator (SGRM) with the potential to demonstrate an improved therapeutic ratio (TR) compared to steroidal GC such as prednisolone.

**Objectives:** To investigate the effects of AZD9567 and prednisolone on biomarkers of inflammation, glucose metabolism and bone re-modelling in pre-clinical models. To confirm the inhibition of inflammatory biomarker production and to evaluate safety and pharmacokinetics (PK) of AZD9567 in a first clinical study.

**Methods:** The effects on biomarkers of gluconeogenesis (tyrosine aminotransferase, TAT mRNA), bone re-modelling (osteoprotegerin, OPG mRNA) and anti-inflammatory activity (TNF $\alpha$ ) were evaluated *in vitro* using human hepatocytes, an osteoblast cell line and whole blood, respectively. *In vivo*, effects on plasma insulin and osteocalcin levels were compared with inhibition of whole blood TNF $\alpha$  release in rats. Efficacy was evaluated in an adjuvant-induced rat arthritis model. In a human single ascending dose study the effect of AZD9567 on TNF $\alpha$  inhibition was investigated, together with assessment of safety profile and PK.

**Results:** Potent *in vitro* anti-inflammatory activity (IC<sub>50</sub>, 6.2 nM, 7-fold more potent than prednisolone) was observed, whilst no effect on TAT mRNA expression in human hepatocytes was detected for AZD9567 (prednisolone EC<sub>50</sub> 92 nM). This resulted in a substantially better TR compared to prednisolone. Furthermore, AZD9567 showed a 7-fold superior TR compared to prednisolone based on OPG mRNA expression in human osteoblasts. An improved profile for AZD9567 was also demonstrated *in vivo* in the rat (TR of 7.5 for osteocalcin and 3.6 for insulin). Efficacy was demonstrated in the rat arthritis model where an inhibition of joint inflammation was observed (ED<sub>50</sub> 0.1 mg/kg). In human, AZD9567 was safe and well tolerated after single doses (2–155 mg). The PK properties showed a fast absorption with a median t<sub>max</sub> of 0.50 to 1.25 hour and a dose-dependent increase in exposure, with a mean terminal half-life of 3.9 to 6.4 hours, suitable for a once daily dosing regimen. TNF $\alpha$  release was inhibited in a concentration-dependent manner (IC<sub>50</sub>, 5.2 nM), consistent with pre-clinical findings.

**Conclusions:** In pre-clinical models, AZD9567 demonstrated anti-inflammatory activity with a reduced effect on gluconeogenesis and biomarkers of bone re-modelling compared to prednisolone. Single oral dosing of AZD9567 was well tolerated and showed good PK properties in healthy subjects. These results support that AZD9567 has the potential to improve the treatment of several inflammatory diseases with a better TR compared to prednisolone. AZD9567 is currently in clinical evaluation in rheumatoid arthritis.

**Disclosure of Interest:** R. Hendrickx Employee of: AstraZeneca, T. Hegelund-Myrbäck Employee of: AstraZeneca, M. Dearman Employee of: AstraZeneca, S. Prothon Employee of: AstraZeneca, G. Edenro Employee of: AstraZeneca (former employee), J. Leander Employee of: AstraZeneca, R. Fuhr Employee of: Parexel International GmbH, T. Körnicke Employee of: Parexel International GmbH, P. Svanberg Employee of: AstraZeneca, A. Berggren Employee of: AstraZeneca, T. Drmota Employee of: AstraZeneca (former employee), C. Keen Employee of: AstraZeneca, U. Eriksson Employee of: AstraZeneca

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SAT0246

### AT WHICH POINT AND FOR WHICH REASONS ARE ORAL MTX FORMULATIONS SWITCHED TO INJECTABLE ONES IN RA PATIENTS? COMBINED RESULTS FROM 3 INDEPENDENT OBSERVATIONAL AND CLINICAL TRIALS

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**Background:** MTX is considered as a cornerstone in RA treatment since the 1990s and its injectable forms have proven their enhanced clinical and pharmacological efficacy and safety in case of insufficient response or poor tolerance of oral formulations. Few data are available considering the timepoint at which the route of administration is changed in current practice.

**Objectives:** The objective of this work was to investigate across 3 independent trials if there was a consistency in patterns of MTX oral ->injectable switches in terms of RA characteristics, MTX dosages (before and after the switch) and reasons of passage.

**Methods:** Three trials were considered for this work: 1/STRATEGIE (observational study designed to investigate the therapeutic strategies used in current practice in RA patients insufficiently responding to initial MTX monotherapy), 2/APRIM (observational study aimed to investigate the treatment adherence of RA patients switching from oral to injectable MTX or between two different MTX prefilled syringes) and 3/SELFI (phase III randomized trial aiming to compare a new MTX autoinjector to the historical MTX prefilled syringe in terms of treatment adherence and functional capacity in RA patients at 6 months). In all three studies we selected baseline data concerning patients switching from oral to injectable MTX at the inclusion visit.

#### Results:

	STRATEGIE N = 151	APRIM N = 270	SELFI N = 98
RA duration, years (mean±SD) (median (min;max))	4.9±6.1 2.8 (0.0; 29.0)	6.6±8.1 3.0 (0.0; 40.0)	4.5±5.9 2.0 (0.2; 30.5)
MTX treatment duration, years (mean±SD) (median (min;max))	3.6±4.5 1.9 (0.0; 24.3)	3.3±4.2 1.4 (0.0; 23.6)	2.5±2.8 1.4 (0.1; 15.4)
DAS28 (mean±SD)	4.4±0.9	3.9±0.9	3.5±1.2
MTX oral dosage at V0, mg/wk (mean±SD)	15.3±3.7	15.0±4.1	14.8±3.8
MTX injectable dosage at the end of V0, mg/wk (mean±SD)	17.0±4.0	16.3±3.8	17.0±4.0
Distribution MTX dosage unchanged/raised/ reduced	50%/45%/ 5%	62%/34%/ 4%	51%/42%/ 7%

Consistent data were observed across the three considered trials concerning the oral/injectable MTX switch. It occurs after about 3 years of treatment, at a DAS28 of 4 and at an average dose of 15 mg/wk (which is consistent with bioavailability data shown before). In most situations, MTX dosage is unchanged or very slightly raised at the switch timepoint. The main switch reasons were "non-achievement of treatment target" and "RA worsening", the safety reasons were mentioned only in 5% of cases.

**Conclusions:** Our work showed a consistent pattern across 3 independent trials concerning the oral/injectable MTX switch. It generally occurs at 15 mg/wk, the new injectable dosage being either unchanged or very slightly raised as compared to the last oral one. Surprisingly, the MTX route of administration seems to be modified mostly for efficacy reasons, safety issues being anecdotal.

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SAT0247

### IMPACT OF GLUCOCORTICOIDS ON EFFICACY AND SAFETY OF TOFACITINIB WITH AND WITHOUT METHOTREXATE AND ADALIMUMAB WITH METHOTREXATE FOR RHEUMATOID ARTHRITIS: RESULTS FROM A PHASE 3B/4 RANDOMISED TRIAL

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**Background:** Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA). Glucocorticoids (GC) are an established therapy in RA that are often used to rapidly reduce pain and inflammation while awaiting the effects of disease-modifying antirheumatic drugs.

**Objectives:** A post hoc analysis to describe the impact of background GC on the efficacy and safety of tofacitinib with and without methotrexate (MTX) and adalimumab (ADA) with MTX in ORAL Strategy.

**Methods:** ORAL Strategy (NCT02187055) was a 1-year, double-blind, Phase 3b/4, head-to-head, non-inferiority randomised controlled trial in adult patients (pts) with active RA despite MTX therapy. Pts were randomised 1:1:1 to receive tofacitinib 5 mg twice daily (BID; tofa mono), tofacitinib 5 mg BID + MTX (tofa+MTX) or subcutaneous ADA 40 mg every other week + MTX (ADA+MTX). Pts receiving low-dose GC (≤10 mg/day prednisone or equivalent) before enrolment maintained a stable dose throughout the study period. The following efficacy endpoints were assessed through Month 12 for pts receiving tofa mono, tofa+MTX and ADA+MTX with/without GC: ACR20, ACR50 and ACR70 response rates, proportions of patients achieving low disease activity (LDA; DAS28-4[ESR]≤3.2) and remission (DAS28-4[ESR]<2.6) and change from baseline (BL) in HAQ-DI (ΔHAQ-DI). Safety endpoints were evaluated throughout the study and included adverse events (AEs), serious AEs (SAEs), discontinuations due to AEs and serious infection events (SIEs).

**Results:** 1146 patients were randomised and treated; low-dose BL GC were received by 228/384 (59.4%) pts receiving tofa mono (mean [SD] BL GC dose: 7.5 [13.7] mg/day), 215/376 (57.2%) pts receiving tofa+MTX (mean [SD] BL GC dose: 6.5 [2.5] mg/day) and 223/386 (57.8%) pts receiving ADA+MTX (mean [SD] BL GC dose: 6.4 [2.6] mg/day). BL demographics and disease characteristics were generally similar across treatment groups, regardless of BL GC use. Efficacy endpoints (ACR50 response rate, LDA and remission rates, ΔHAQ-DI) were generally similar for each treatment group when stratified by GC use (figure 1, table 1; similar results were seen for ACR20/70 response rates – data not shown). GC use did not appear to be associated with higher rates of AEs, discontinuations due to AEs, SIEs and SAEs; some AE rates were higher with MTX than without MTX (table 2). SIEs in pts using GC included herpes zoster (HZ; tofa mono, n=2) and tuberculous meningitis (tofa+MTX, n=1); in pts not using GC, there was 1 event each of cytomegalovirus chorioretinitis (tofa+MTX), pulmonary TB (tofa+MTX), HZ (ADA+MTX) and varicella (ADA+MTX).

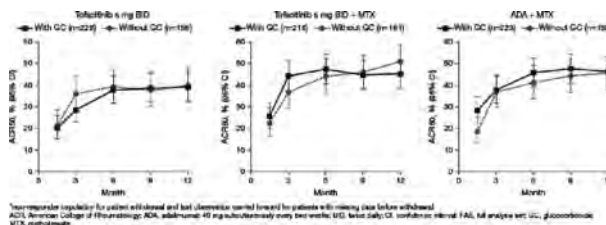


Figure 1. Proportion of patients achieving ACR50 response according to treatment group and GC use (FAS, with imputation\*)







naive T-, B-cells and CD16<sup>+</sup> NK-cells along with a relative increase in memory lymphocytes and CD16<sup>+</sup> NK-cells. These effects were also observed but less pronounced in controls.

**Conclusions:** Bowel cleanse and fasting in RA induces a reduction of inflammation related to monocyte activation and turnover immediately within few days. Changes in the monocyte compartment were specific for RA compared to controls and dominated the immunological changes, suggesting that innate triggering mechanisms from gut and its microbiota are etiologically relevant in RA.

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#### SAT0250 THE DOSING OF INTRA-ARTICULAR TRIAMCINOLONE HEXACETONIDE FOR KNEE SYNOVITIS IN CHRONIC POLYARTHRITIS – A RANDOMIZED CONTROLLED STUDY

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**Background:** Intra-articular glucocorticoid (IAGC) injection treatment is an easy and effective way to treat signs and symptoms of arthritis and it has been used for decades. Serious adverse reactions are rare, but IAGC therapy has impact on endocrine balances. There is limited knowledge of the adequate dosing for different joints and dosing traditions vary all over world.

**Objectives:** To compare the relapse rate during 6 months after IAGC for knee synovitis, between two common doses (20 mg vs 40 mg) of triamcinolone hexacetonide (THA).

**Methods:** A total of 159 adult patients with rheumatoid arthritis (RA) or psoriatic arthritis (Psoa) and active knee synovitis were randomized to IAGC injection with either 20 mg or 40 mg THA blinded to the participants. The primary endpoint was relapse of arthritis. When symptoms from the treated joint recurred and signs of arthritis could be confirmed on a following clinical examination a relapse was recorded and days from injection to relapse was calculated. At the end of the observation period those without relapse had a phone call to verify persistence of good treatment response.

**Results:** In this material there was no significant difference in patient characteristics at baseline and the proportion of relapse after 6 months were equal in the treatment arms (30% versus 32%, p=0.822). Additionally no significant differences were found in the subgroups with RA and Psoa patients.

**Conclusions:** To reduce the risk for endocrine side effects and as no difference in treatment outcome between the compared doses was found the lower 20 mg THA dose should be preferred in IAGC treatment for knee synovitis in chronic polyarthritis.

**Disclosure of Interest:** None declared

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#### SAT0251 SELECTIVE GLUCOCORTICOID RECEPTOR MODULATOR SHOWS POTENT ANTI-INFLAMMATORY EFFECT WITH IMPROVED METABOLIC PROFILE IN A PHASE I STUDY SUPPORTED BY IN VITRO DATA

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**Background:** AZD9567 is a novel oral selective glucocorticoid receptor modulator (SGRM) developed to have an improved safety profile versus prednisolone while maintaining efficacy.

**Objectives:** To show clinical evidence of safety differentiation for AZD9567 compared to prednisolone with respect to glucose homeostasis and to investigate the underlying effects on the glucose metabolism in human cell systems *in vitro*.

**Methods:** In a dose escalation study (NCT02760316), healthy volunteers were randomized to a 5-day once-daily treatment with AZD9567 (20, 40, 80, 125 mg) or prednisolone (5, 20, 40 mg). We monitored the anti-inflammatory effect by TNF $\alpha$  release from *ex vivo* LPS stimulated whole blood and modelled the relationship with pharmacokinetics (PKPD). Plasma glucose was measured (AUC<sub>0-4h</sub>) during an oral glucose tolerance test (OGTT) before and after four days of treatment.

We also studied the effects of AZD9567 and prednisolone on mRNA expression of key gluconeogenesis enzymes (tyrosine aminotransferase (TAT), phosphoenolpyruvate carboxykinase (PEPCK) and glucose 6-phosphatase (G6Pase)) in primary human hepatocytes as well as on insulin secretion in human islets microtissues.

**Results:** The inhibition of TNF $\alpha$  release increased with the plasma concentrations of AZD9567. PKPD modeling of TNF $\alpha$  inhibition data showed that 40 mg AZD9567 results in an anti-inflammatory activity similar to that predicted for 20 mg prednisolone.

A significantly smaller increase of the glucose AUC was observed following treatment with 20 to 125 mg AZD9567 compared to 20 mg prednisolone (p<0.05). Mean (95% CI) changes from baseline for 20, 40, 80 and 125 mg AZD9567 were 16% (6.5–26, n=7), 19% (9.3–30, n=7), 19% (9.8–30, n=7) and 34% (24–46, n=7), respectively. The corresponding values for 5, 20 and 40 mg prednisolone were 17% (10–24, n=13), 53% (43–62, n=13), and 68% (58–79, n=12), respectively.

We found significant induction of TAT, PEPCK, and G6Pase mRNA in hepatocytes after prednisolone treatment. In contrast, AZD9567 did not change the expression of these enzymes and inhibited the effect of prednisolone when co-administered. Furthermore, AZD9567 showed less suppression of insulin secretion in human islets microtissues compared to prednisolone at concentrations with comparable inhibition of TNF $\alpha$  release, resulting in a 12-fold better therapeutic ratio.

**Conclusions:** In healthy individuals, AZD9567 showed significantly reduced effect on glucose homeostasis versus prednisolone at doses with similar anti-inflammatory activity. Thus, AZD9567 shows potential as an anti-inflammatory treatment with an improved metabolic safety profile compared to prednisolone.

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#### SAT0252 CLINICAL AND FUNCTIONAL RESPONSE TO TOFACITINIB AND ADALIMUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS: PROBABILITY PLOT ANALYSIS OF RESULTS FROM THE ORAL STRATEGY TRIAL

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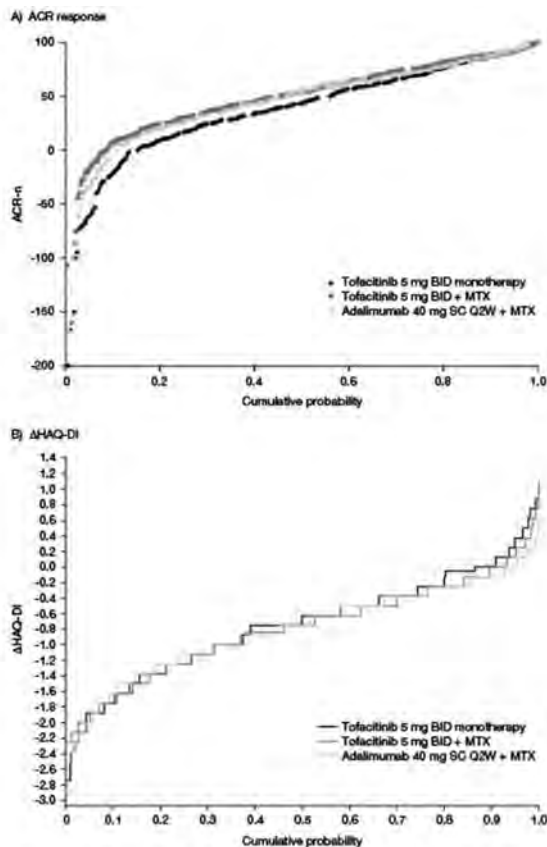
**Background:** Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA). ORAL Strategy (NCT02187055), a 12-month, global, Phase 3b/4 study, demonstrated that in patients with RA and an inadequate response to methotrexate (MTX), tofacitinib + MTX was non-inferior to adalimumab + MTX, while tofacitinib monotherapy was not non-inferior to either combination based on American College of Rheumatology (ACR)50 response rates at Month 6.<sup>1</sup>

**Objectives:** To assess clinical and functional efficacy across treatments in the ORAL Strategy trial using cumulative probability plots.

**Methods:** Efficacy was evaluated between patients who received tofacitinib 5 mg twice daily (BID) as monotherapy (N=384), tofacitinib 5 mg BID + MTX (N=376) and adalimumab 40 mg subcutaneously once every 2 weeks + MTX (N=386) based on ACR responses and changes from baseline in Health Assessment Questionnaire-Disability Index ( $\Delta$ HAQ-DI) score at Month 12. Cumulative probability plots for ACR-n (where ACR is the % improvement from baseline in ACR components, and n represents the minimum % achieved by each patient)

and  $\Delta$ HAQ-DI are presented. The area under the curve (AUC) was calculated for ACR-n up to Month 12 (in months), and an analysis of covariance model was used to assess treatment effects in terms of the AUC of ACR-n at Month 12; there was no adjustment for multiplicity for this post hoc analysis.

**Results:** The cumulative probability plots of ACR responses at Month 12 indicated that the proportion of patients who achieved responses of ACR20, ACR50 and ACR70 was similar for tofacitinib + MTX and adalimumab + MTX, but was numerically smaller for tofacitinib monotherapy (figure, A). Responses of approximately  $\geq$ ACR80 were achieved by a similar proportion of patients in each treatment group. Least squares mean (standard error) AUC of ACR-n up to Month 12 (in months) was similar for tofacitinib + MTX (437 [35]) and adalimumab + MTX (402 [35]), but was smaller for tofacitinib monotherapy (319 [35];  $p < 0.05$ ). The cumulative probability plots of  $\Delta$ HAQ-DI suggested that, in general, reductions from baseline in HAQ-DI were similar across treatment groups (figure, B), although a slightly higher proportion of patients who received tofacitinib monotherapy reported an increase in HAQ-DI vs other treatments.



ACR-n, American College of Rheumatology response, where n represents the minimum % response achieved by each patient; BID, twice daily;  $\Delta$ HAQ-DI, change from baseline in Health Assessment Questionnaire-Disability Index; MTX, methotrexate; Q2W, once every 2 weeks; SC, subcutaneous

Figure 1 Cumulative probability plot of A) ACR response and B)  $\Delta$ HAQ-DI at Month 12. Two outlets for ACR response are not shown: tofacitinib 5 mg BID monotherapy, ACR-n-1700, cumulative probability-0.0003; adalimumab 40 mg SC Q2W + MTX, ACR-n-463, cumulative probability-0.003

**Conclusions:** These data support the primary ORAL Strategy findings,<sup>1</sup> indicating that in patients with RA, clinical efficacy, based on ACR response, was generally similar for tofacitinib + MTX and adalimumab + MTX, while a smaller proportion of patients who received tofacitinib monotherapy achieved ACR response in general, and particularly for  $<$ ACR80. Functional efficacy, based on  $\Delta$ HAQ-DI, was generally similar across all treatment groups. Cumulative probability analyses for CDAI will be further evaluated.

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SAT0253

#### DOSE REDUCTION OF BARICITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS ACHIEVING SUSTAINED DISEASE CONTROL: RESULTS OF A PROSPECTIVE STUDY

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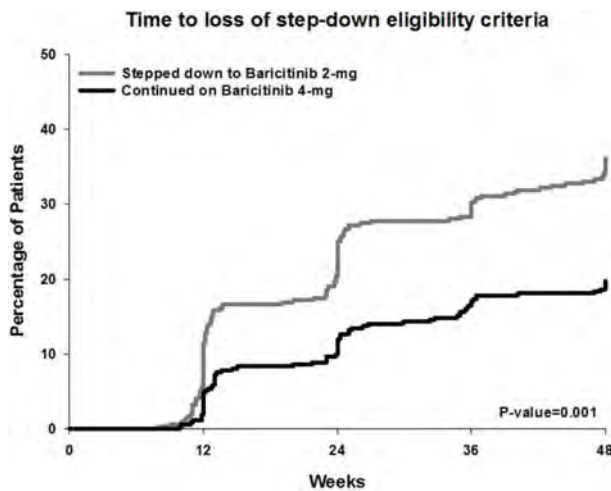
**Background:** In patients with rheumatoid arthritis (RA) and inadequate response (IR) to DMARDs, ph3 studies demonstrated efficacy of baricitinib (Bari) (2-mg and 4-mg).

**Objectives:** To investigate the effects of Bari dose step-down in patients who achieved sustained disease control with Bari 4-mg.

**Methods:** Patients with RA participating in the Bari ph3 long-term extension study who received Bari 4-mg for  $\geq 15$  months and who achieved sustained low disease activity (LDA) – CDAI score  $\leq 10$  or remission (REM) – CDAI  $\leq 2.8$   $\geq 3$  months apart were re-randomised in a blinded manner to continue Bari 4-mg or step down to 2-mg. Patients could rescue to Bari 4-mg. Efficacy and safety were assessed through 48 weeks (wks) following re-randomisation.

	Patients Originating from RA-BEAM, RA-BUILD, RA-BEACON Combined <sup>†</sup>					
	Wk 12		Wk 24		Wk 48	
	Continued Bari 4-mg N=374	Stepped Down to Bari 2-mg N=376	Continued Bari 4-mg N=374	Stepped Down to Bari 2-mg N=376	Continued Bari 4-mg N=374	Stepped Down to Bari 2-mg N=376
<b>Efficacy measure</b>	<b>NRI after rescue or for missing data</b>					
CDAI LDA $\leq 10$	338/374 (90.4)	310/376 (82.4)**	327/374 (87.4)	280/376 (74.5)***	300/374 (80.2)	254/376 (67.6)***
CDAI REM $\leq 2.8$	149/374 (39.8)	134/376 (35.6)	161/374 (43.0)	130/376 (34.6)*	145/374 (38.8)	121/376 (32.2)
	<b>NRI only for missing data (observed data used after rescue)</b>					
CDAI LDA $\leq 10$	338/374 (90.4)	310/376 (82.4)**	334/374 (89.3)	304/376 (80.9)**	321/374 (85.8)	295/376 (78.5)**
CDAI REM $\leq 2.8$	149/374 (39.8)	134/376 (35.6)	164/374 (43.9)	137/376 (36.4)*	149/374 (39.8)	134/376 (35.6)
<b>Safety measure</b>	<b>Wks 0–48</b>					
n [EAIR]	<b>Continued Bari 4-mg N=374</b>			<b>Stepped down to Bari 2-mg N=376</b>		
SDEAE	235 [69.30]			202 [63.46]		
Infection	108 [31.85]			78 [24.50]		
SAE	27 [7.96]			26 [8.17]		
Serious infection	10 [2.95]			4 [1.26]		
AE	9 [2.64]			12 [3.74]		
	—discontinuation					

Efficacy and safety data are n/N (%), and n [EAIR], respectively. <sup>†</sup>RA-BEAM=MTX-IR patients; RA-BUILD=csDMARD-IR patients; RA-BEACON=bDMARD-IR patients; EAIR=exposure-adjusted incidence rate; NRI=nonresponder imputation; SDEAE=step-down emergent adverse event; \*  $p \leq 0.05$ , \*\*  $p \leq 0.01$ , \*\*\*  $p \leq 0.001$  vs. continued Bari 4-mg



**Figure 1.** Data represent patients who have completed 48 weeks in the step-down period, or would have completed 48 weeks if not discontinued prior to the data cut-off date (April 1, 2017). Relapse defined as loss of step-down eligibility criteria, CDAI >10 for patients originating from RA-BUILD, RA-BEAM, or RA-BEACON. The p-value was computed using the Wilcoxon test.

**Results:** The majority of patients in both groups maintained the state of LDA or REM over the 48 wks. However, dose reduction to 2-mg resulted in significant increases in disease activity at 12, 24, and 48 wks (Table). Dose reduction also resulted in a shorter time to relapse (defined as loss of step-down eligibility criteria); significantly more patients relapsed over 48 wks compared to the 4-mg group (figure 1). Rescue rates were 8.3% for Bari 4-mg, 16.6% for Bari 2-mg. Most rescued patients could regain LDA or REM. Dose reduction was associated with a lower rate of infections; rates of SAEs and AEs leading to discontinuation were similar across groups.

**Conclusions:** These data indicate that disease control was better maintained with Bari 4-mg than 2-mg. However, most stepped-down patients could maintain LDA or REM, or recapture control with re-introduction of the 4-mg dose. Stepping down to a dose of 2-mg daily may be a viable option for many patients who have achieved sustained LDA or REM on the 4-mg dose.

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**SAT0254 UPADACITINIB IMPROVES PATIENT-REPORTED OUTCOMES IN PATIENTS WITH RHEUMATOID ARTHRITIS AND INADEQUATE RESPONSE TO CONVENTIONAL SYNTHETIC DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS: RESULTS FROM SELECT-NEXT**

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**Background:** Upadacitinib (UPA), a selective JAK-1 inhibitor, has demonstrated efficacy in active RA among patients with an inadequate response to conventional synthetic disease-modifying anti-rheumatic drugs (csDMARD-IR).<sup>1</sup> To understand treatment effectiveness from the patients' perspective we examined the impact of UPA on patient-reported outcomes (PROs).

**Objectives:** To evaluate the effect of UPA vs placebo (PBO) on PROs in SELECT-NEXT (NCT02675426), a randomized controlled trial assessing the efficacy and safety of UPA in csDMARD-IR RA patients.

**Methods:** Patients in SELECT-NEXT received UPA 15 mg or 30 mg daily or PBO for 12 weeks followed by a 5-year extension phase. PROs included physical function (Health Assessment Questionnaire Disability Index [HAQ-DI]), Patient's Global Assessment of Disease Activity (PtGA) by visual analog scale (VAS), pain by VAS, fatigue by FACIT-F, duration and severity of morning (AM) stiffness, quality of life (QoL) by Short Form 36 Health Survey [SF-36], and Work Instability Scale for RA (RA-WIS). Changes in least square means (LSMs) from baseline (BL) to week 12 were based on mixed effect repeated measures models. Percentages of patients reporting changes in PRO scores from BL to week 12 ≥ minimum clinically important differences (MCIDs) or scores ≥ normative values (age- and gender-matched for SF-36 only) were determined for UPA and PBO arms; comparisons between groups used chi-square tests. For each PRO, the incremental number needed to treat (NNT) to achieve clinically meaningful improvement from BL (≥MCID) was calculated.

**Results:** Data from 661 patients (221 in UPA 15 mg; 219 in UPA 30 mg; 221 in PBO) were analysed. Mean age was 56 years, 79% were female; 45% had RA for ≥5 years. Statistically significant LSM changes from BL to week 12 were reported with both UPA doses vs PBO for HAQ-DI, PtGA, pain, FACIT-F, duration and severity of AM stiffness, SF-36 (PCS; 6 or 7/8 domains), and RA-WIS (Table). Compared with PBO at week 12, significantly more UPA-treated (both doses) patients reported improvement ≥MCID in HAQ-DI, PtGA, pain, FACIT-F, duration and severity of AM stiffness, SF-36 (PCS; 4 or 7/8 domains), and RA-WIS as well as scores ≥ normative values in HAQ-DI, PtGA, FACIT-F, SF-36 (PCS; 4 or 5/8 domains). For most PROs, NNTs with UPA ranged from 4 to 8 patients.

Table 1 LSM changes from baseline and percentage of responders at week 12 after UPA initiation

PRO	Change from Baseline			% Responders					
	LSM			Reporting Scores ≥ MCID, n (%)			Reporting Scores ≥ Normative Values, n (%)		
	PBO N=221	UPA 15 mg N=221	UPA 30 mg N=219	PBO N=221	UPA 15 mg N=221	UPA 30 mg N=219	PBO N=221	UPA 15 mg N=221	UPA 30 mg N=219
HAQ-DI	-0.26	-0.21*	-0.55*	109 (49.3)	156 (70.2)*	148 (67.6)*	30 (13.6)	56 (25.3)*	54 (24.7)*
PtGA	-10.36	-29.67*	-30.53*	94 (42.5)	151 (70.5)*	158 (72.1)*	32 (14.5)	78 (35.3)*	84 (38.4)*
Pain VAS	-10.26	-29.92*	-31.71*	97 (43.9)	158 (72.4)*	160 (73.1)*	—	—	—
FACIT-F	-2.96	7.91*	7.74*	91 (41.2)	138 (62.9)*	129 (58.7)*	35 (15.8)	60 (27.8)*	66 (30.4)*
Duration AM stiffness <sup>a</sup>	-34.27	-85.28*	-85.13*	29 (13.4)	57 (26.3)*	57 (26.5)*	—	—	—
Severity AM stiffness <sup>a</sup>	-1.33	-2.88*	-3.26*	130 (60.3)	165 (76.0)*	172 (80.4)*	—	—	—
SF-36 PCS	3.03	7.58*	8.01*	106 (48.0)	152 (69.4)*	151 (69.5)*	18 (8.1)	39 (17.8)*	23 (10.5)*
SF-36 MCS	2.58	4.85*	3.47	91 (41.2)	120 (54.8)*	98 (45.2)	102 (46.2)	114 (52.1)	108 (49.8)
SF-36 PF	2.96	6.97*	6.81*	126 (57.0)	175 (79.2)*	143 (65.3)	26 (11.8)	52 (23.5)*	53 (24.2)*
SF-36 RP	2.88	6.50*	6.96*	115 (52.0)	156 (70.6)*	141 (64.4)*	18 (8.1)	39 (17.6)*	44 (20.1)*
SF-36 BP	4.66	9.44*	10.38*	123 (55.7)	162 (73.3)*	163 (74.4)*	39 (17.6)	75 (33.9)*	71 (32.4)*
SF-36 GH	1.92	5.61*	5.00*	112 (50.7)	143 (64.7)*	141 (64.4)*	35 (15.8)	51 (23.1)	54 (24.7)*
SF-36 VT	2.52	6.77*	7.05*	104 (47.1)	148 (67.0)*	141 (64.4)*	56 (25.3)	85 (38.5)*	88 (40.2)*
SF-36 SF	2.53	6.27*	6.81*	99 (44.8)	125 (56.6)*	112 (51.1)	67 (30.3)	81 (36.7)	85 (38.8)
SF-36 RE	2.62	5.58*	4.10	85 (38.5)	112 (50.7)*	104 (47.5)	75 (33.9)	88 (39.8)	89 (40.6)
SF-36 MH	3.39	4.78	4.77	121 (54.8)	135 (61.1)	115 (52.5)	75 (33.9)	85 (37.6)	87 (39.7)
RA-WIS	-1.25	-4.28*	-3.48*	17 (7.5)	44 (19.9)*	29 (13.9)*	43 (19.3)	56 (25.6)	41 (18.9)

\*P<0.05 for UPA vs PBO. <sup>a</sup>Duration in minutes. % responders reporting scores ≥ minimal important difference. <sup>b</sup>Assessed on a numeric scale of 1-10, 10 being the worst level.

**Conclusions:** Treatment with UPA 15 mg or 30 mg daily for 12 weeks resulted in significant and clinically meaningful improvements in physical function, pain, fatigue, AM stiffness, QoL, and less work instability among csDMARD-IR RA patients. The NNTs to achieve these improvements were favourable.



REFERENCE:

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**SAT0255 PATIENT REPORTED OUTCOMES OF UPADACITINIB: RESULTS FROM BIOLOGIC INADEQUATE RESPONDERS (SELECT BEYOND PHASE III TRIAL)**

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**Background:** Patient reported outcomes (PROs) were studied in patients with active rheumatoid arthritis (RA) who had an inadequate response to biologic disease modifying anti-rheumatic drugs (bDMARD-IR) in a trial of upadacitinib (UPA), a selective JAK-1 inhibitor. Improvements in PROs are important when evaluating comprehensive efficacy of treatments for RA.

**Objectives:** The objective of this post-hoc analysis was to compare PRO responses and numbers needed to treat (NNT) in order to assess clinically meaningful improvements in bDMARD-IR patients with RA receiving UPA.

**Methods:** Data from the SELECT BEYOND randomised controlled trial (RCT) (NCT02706847) were used to compare PRO responses between UPA (15 mg QD and 30 mg QD) and PBO. PROs included physical function by Health Assessment Questionnaire Disability Index (HAQ-DI), Patient's Global Assessment of Disease Activity (PtGA) by visual analogue scale (VAS), pain by VAS, duration and severity of morning (AM) stiffness, health-related quality of life by Short Form 36 Health Survey (SF-36), and severity of insomnia by Insomnia Severity Index (ISI). Changes in least squares means (LSM) from baseline to week 12 were based on mixed effect repeated measures models. Percentages of patients reporting changes in PRO scores from baseline to week 12 ≥ minimum clinically important difference (MCID) values or scores ≥ normative values (age- and gender-matched for SF-36 only) were determined; comparisons between groups used chi-square tests. For each PRO measure, the incremental NNT to achieve clinically meaningful improvements from baseline (≥ MCID) was calculated.

Abstract SAT0255 – Table 1. LSM Changes From Baseline and Percentage of Responders at Week 12

PRO	Change from Baseline						% Responders					
	LSM			Reporting Scores ≥ MCID, n (%)			Reporting Scores ≥ Normative Values, n (%)					
	PBO N=169	UPA 15mg N=164	UPA 30mg N=165	PBO N=169	UPA 15mg N=164	UPA 30mg N=165	PBO N=169	UPA 15mg N=164	UPA 30mg N=165	PBO N=169	UPA 15mg N=164	UPA 30mg N=165
HAQ-DI	-0.16	-0.41*	-0.44*	61 (36.6)	102 (62.6)*	89 (55.3)*	11 (6.6)	26 (16.0)*	21 (13.0)			
PtGA	-10.03	-26.04*	-29.77*	71 (42.8)	119 (73.0)*	101 (62.0)*	25 (15.5)	46 (28.2)*	58 (35.6)*			
Pain VAS	-10.38	-25.91*	-30.92*	76 (45.8)	120 (73.6)*	103 (64.0)*						
Duration AM stiffness	15.07	81.47*	79.13*	17 (10.1)	33 (20.1)*	40 (24.2)*						
Severity AM stiffness	-1.57	-3.86*	-3.22*	95 (56.2)	131 (79.9)*	119 (72.1)*						
SF-36 PCS	2.39	5.88*	7.02*	65 (39.2)	98 (60.1)*	104 (64.2)*	9 (5.4)	18 (11.0)	24 (14.8)*			
SF-36 MCS	3.01	4.54	3.77	72 (43.4)	89 (54.0)	77 (47.5)	73 (44.0)	88 (54.0)	78 (48.1)			
SF-36 PF	1.54	4.56*	4.15*	78 (46.2)	103 (62.8)*	107 (64.8)*	16 (9.5)	26 (15.9)	23 (13.9)			
SF-36 RP	2.15	5.00*	5.07*	73 (43.2)	101 (61.6)*	101 (61.2)*	12 (7.2)	24 (14.6)	24 (14.5)*			
SF-36 SF	-4.71	-8.23*	-9.05*	91 (53.8)	120 (73.2)*	111 (67.3)*	19 (11.2)	39 (23.8)*	40 (24.2)*			
SF-36 GH	2.17	4.31*	4.25*	71 (42.2)	104 (63.4)*	97 (59.8)*	24 (14.2)	29 (17.7)	27 (16.4)			
SF-36 VT	3.10	6.28*	6.36*	86 (50.9)	108 (65.9)*	109 (66.1)*	83 (49.5)	50 (30.5)	46 (27.9)			
SF-36 SF	3.45	5.87*	5.35*	81 (47.9)	103 (62.8)*	79 (47.9)	42 (24.9)	50 (30.5)	49 (29.7)			
SF-36 RE	2.66	4.72*	3.78	61 (36.1)	84 (51.2)*	66 (40.0)	55 (32.5)	67 (40.9)	61 (37.0)			
SF-36 MH	2.96	3.81	3.53	80 (47.3)	92 (56.1)	88 (52.1)	56 (33.1)	72 (43.9)	61 (37.0)			
ISI	-1.69	-3.51	-3.32*	12 (7.8)	22 (14.5)	24 (15.9)*	50 (32.7)	57 (37.5)	67 (44.4)*			

\*P<0.05 for UPA vs PBO.  
 \*Quotient in minutes. \*% Incidence reporting across 2 minimal important differences. \*Assessed on a numeric scale of 1-20 with 10 being the worst level.  
 RP, bodily pain; GH, general health; MCS, Mental Component Summary; MH, mental health; PCS, Physical Component Summary; PF, physical functioning; RE, role emotional; RP, role physical; SF, social functioning; VT, vitality.

**Results:** Data from 498 patients (169 in PBO, 164 in UPA 15 mg, 165 in 30 mg UPA) were analysed. Mean age was 57 years, 84% were females, and 55% had RA for ≥10 years. Both UPA doses resulted in statistically significant LSM

changes from baseline vs PBO in HAQ-DI, PtGA, pain, duration and severity of AM stiffness, SF-36 Physical Component Summary (PCS), 7/8 domains (15 mg), and 6/8 domains (30 mg) (Table). Compared with PBO at week 12, UPA-treated patients reported higher responses that were statistically significant and clinically meaningful for HAQ-DI, PtGA, pain, duration and severity of AM stiffness, SF-36 PCS, 7/8 domains (15 mg), 5/8 domains (30 mg), and ISI (30 mg). The Table presents the proportion of patients reporting scores that were ≥ normative values at week 12. Across most PROs, the NNTs with UPA ranged from 4 to 7 patients.

**Conclusions:** This RCT demonstrated that even in difficult-to-treat bDMARD-IR patients with active RA, treatment with UPA resulted in significantly more patients with clinically meaningful improvements in PROs or responses that approached normative values. The NNT to achieve a meaningful response was favourable.

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**SAT0256 TOFACITINIB WITH AND WITHOUT METHOTREXATE VERSUS ADALIMUMAB WITH METHOTREXATE FOR THE TREATMENT OF RHEUMATOID ARTHRITIS: PATIENT-REPORTED OUTCOMES FROM A PHASE 3B/4 RANDOMISED TRIAL**

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**Background:** Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA).

**Objectives:** To compare patient-reported outcomes (PROs) among patients receiving tofacitinib monotherapy, tofacitinib +methotrexate (MTX) and adalimumab (ADA) +MTX, in a head-to-head trial of patients with RA and inadequate responses to MTX (MTX-IR).

**Methods:** ORAL Strategy (NCT02187055) was a Phase 3b/4, 1 year, triple dummy, active randomised controlled trial (RCT). Patients were randomised 1:1:1 to receive tofacitinib 5 mg twice daily (BID; tofa mono), tofacitinib 5 mg BID+MTX (tofa +MTX) or subcutaneous ADA 40 mg every other week +MTX (ADA +MTX); MTX doses were 15–25 mg/wk. PROs (secondary endpoints in this RCT) assessed at Months (Mos) 6 and 12 included mean changes from baseline in: patient global assessment of disease activity (visual analogue scale [VAS]); arthritis pain (VAS); Health Assessment Questionnaire-Disability Index (HAQ-DI); Short Form-36 Health Survey; EuroQol 5-dimensions Questionnaire; Work Productivity and Activity Impairment Questionnaire; Functional Assessment of Chronic Illness Therapy-Fatigue; and the proportion of patients reporting improvements in HAQ-DI ≥ minimum clinically important difference (MCID; -0.22). Nominal p values were calculated with no adjustment for multiple comparisons.

**Results:** Among 1146 patients treated (tofa mono: n=384; tofa +MTX: n=376; ADA+MTX: n=386), baseline demographics and disease characteristics were comparable. At Mos 6 and 12, improvements in all PROs were similar for tofa +MTX and ADA+MTX (there were essentially no differences based on nominal p values) and numerically greater than with tofa mono (Table). Mean changes from baseline in HAQ-DI scores were similar in each treatment group at Mos 6 and 12; similar proportions reported improvements ≥ MCID.

**Abstract SAT0256 – Table 1.** LSM (SE) changes from baseline in patient-reported outcomes and proportion of patients reporting improvements in HAQ-DI ≥MCID at Month 6 and Month 12 in ORAL Strategy

	Tofacitinib 5 mg BID		Tofacitinib 5 mg BID + MTX		ADA-MTX 5 mg EOPR + MTX	
	N=181	N=176	N=176	N=176	N=176	N=176
PGA VAS (0-100)	-21.7 (1.0)	-21.7 (1.0)	-21.4 (1.0)	-21.4 (1.0)	-21.8 (1.0)	-21.8 (1.0)
Pain VAS (0-100)	-26.8 (1.3)	-26.8 (1.3)	-26.7 (1.3)	-26.7 (1.3)	-26.8 (1.3)	-26.8 (1.3)
HAQ-DI (0-1)	-0.5 (0.02)	-0.6 (0.02)	-0.6 (0.02)	-0.6 (0.02)	-0.5 (0.02)	-0.6 (0.02)
Patients reporting improvement in HAQ-DI (≥MCID) [4.32, %]	75.1	78.4	75.9	78.9	75.9	78.1
3P-28						
MCES	4.2 (0.4)	7.8 (0.3)	7.8 (0.4)	8.1 (0.3)	7.8 (0.4)	8.1 (0.3)
PCS	5.2 (0.5)	4.8 (0.3)	5.7 (0.5)	5.7 (0.5)	5.8 (0.5)	5.8 (0.5)
Depression (Clinician-rated score)						
Physical functioning	6.9 (0.3)	7.3 (0.3)	7.3 (0.3)	8.0 (0.3)	7.3 (0.3)	8.0 (0.3)
Role physical	8.7 (0.3)	8.8 (0.3)	7.9 (0.3)	8.4 (0.3)	8.2 (0.3)	7.8 (0.3)
Role mental	12.2 (0.3)	8.8 (0.3)	10.3 (0.3)	11.3 (0.3)	10.3 (0.3)	10.3 (0.3)
General health	3.4 (0.4)	5.2 (0.3)	5.3 (0.4)	5.4 (0.3)	5.4 (0.4)	5.8 (0.3)
Vitality	1.8 (0.3)	5.8 (0.3)	4.1 (0.3)	7.8 (0.3)	5.7 (0.3)	7.1 (0.3)
Social functioning	4.3 (0.3)	7.4 (0.3)	7.3 (0.3)	8.3 (0.3)	8.7 (0.3)	8.4 (0.3)
Role emotional	8.1 (0.4)	8.8 (0.4)	7.7 (0.4)	7.8 (0.4)	8.0 (0.4)	7.8 (0.4)
Mental health	1.8 (0.4)	5.7 (0.3)	5.8 (0.3)	6.7 (0.3)	6.0 (0.3)	6.8 (0.3)
EQ-5D VAS (0-100)	-30.8 (1.1)	-27.3 (1.1)	-31.0 (1.1)	-31.9 (1.1)	-30.8 (1.1)	-30.3 (1.1)
WPAI (0-100)						
Activities of daily living	8.1 (0.3)	5.0 (0.3)	5.4 (0.3)	5.4 (0.3)	5.9 (0.3)	5.0 (0.3)
ADL	19.4 (0.3)	-14.7 (0.3)	-14.4 (0.3)	-19.3 (0.3)	-19.3 (0.3)	-14.5 (0.3)
Overall work impairment	-38.2 (1.7)	-18.5 (1.8)	-22.3 (1.8)	-26.0 (1.8)	-21.8 (1.7)	-24.8 (1.8)
Activity limitation	-22.4 (1.4)	-22.8 (1.4)	-24.7 (1.4)	-26.5 (1.4)	-22.3 (1.4)	-24.8 (1.4)
FACT-G (0-100)	71.0 (3.2)	74.0 (3.2)	74.0 (3.2)	74.0 (3.2)	71.0 (3.2)	74.0 (3.2)

**Conclusions:** MTX-IR patients with RA reported PRO improvements with all 3 treatment regimens that were clinically meaningful, comparable for tofacitinib +MTX and adalimumab +MTX and numerically higher with combination therapy than with tofa mono. Nominal p values should be interpreted with caution as they were not controlled for Type 1 error.

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**SAT0257 A PHASE 2B/3 RANDOMISED, PLACEBO-CONTROLLED, DOUBLE-BLIND STUDY OF UPADACITINIB, A SELECTIVE JAK1 INHIBITOR, IN JAPANESE PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS AND INADEQUATE RESPONSE TO TRVENTIONAL SYNTHETIC DMARDS**

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**Background:** Upadacitinib (UPA) is an oral, JAK1-selective inhibitor found to be effective in Phase 2 and 3 studies in rheumatoid arthritis (RA) patients with inadequate response or intolerance to csDMARDs and bDMARDs.<sup>1-4</sup>  
**Objectives:** To evaluate the efficacy and safety of UPA in Japanese active RA patients with inadequate response to csDMARDs (csDMARD-IR).  
**Methods:** During the 12 week double-blind period, patients on stable csDMARDs were randomised to receive UPA 7.5, 15 or 30 mg once daily or PBO (1:1:1:1). The primary endpoint was proportion of patients achieving ACR20 at Wk 12 (NRI).  
**Results:** Of 197 patients treated, 187 completed the double-blind period. At Week 12, more patients receiving UPA 7.5, 15 and 30 mg vs PBO met ACR20 (75.5%, 83.7%, 80% vs 42.9%, p<0.001). A significant difference in ACR20 was observed as early as Week 1 (table 1). The more stringent responses, such as ACR50/70, DAS28-CRP≤3.2, were achieved by significantly higher proportions of patients on UPA vs PBO with more patients on UPA 15 mg and 30 mg achieving

these responses vs UPA 7.5 mg (Table). At Week 12, patients receiving UPA vs PBO had greater improvements from baseline (p<0.001) in DAS28-CRP (-2.08,-2.39, -2.41 vs -0.79) and HAQ-DI (-0.41,-0.45, -0.49 vs -0.10).

Overall adverse events (AE), serious AEs, infections (including serious infections, opportunistic infections and herpes zoster) were numerically higher in UPA 30 mg. There were no events of pulmonary embolism, deep vein thrombosis, tuberculosis or malignancy and there were no deaths. Mean haemoglobin levels improved with UPA 7.5 (+0.35 g/dL) and remained stable with UPA 15 (-0.03 g/dL) vs UPA 30 (-0.54 g/dL) and PBO (-0.17 g/dL). CPK elevations and lymphopenia occurred more frequently in UPA 30 mg.

Efficacy Endpoints at Week 12 <sup>1</sup>				
Endpoint	PBO, N=49	UPA 7.5 MG, N=49	UPA15 MG, N=49	UPA 30 MG, N=50
ACR20 (%)	42.9%	75.5%***	83.7%***	80.0%***
ACR50 (%)	16.3%**	40.8%**	65.3%***	68.0%***
ACR70 (%)	2.0%	20.4%**	34.7%***	28.0%***
DAS28 (CRP), mean change	-0.79	-2.08***	-2.39***	-2.41***
HAQ-DI, mean change	-0.10	-0.41***	-0.45***	-0.49***
SE-36 PCS, mean change	-2.09	7.21***	6.38***	8.81***
DAS28 (CRP) ≤ 3.2	16.4%	63.1%***	89.4%***	87.0%***
DAS28 (CRP) ≤ 3.2	8.1%	36.7%***	67.1%***	80.0%***
ACR20 at Week 1%	6.2%	30.6%**	24.5%**	34.0%**

Adverse Events (AE) Summary, n (%)				
AE	PBO, N=49	UPA 7.5 MG, N=49	UPA 15 MG, N=49	UPA 30 MG, N=50
Any AE	23 (46.9)	29 (59.2)	28 (57.1)	37 (74.0)
Serious AE	0	1 (2.0)	1 (2.0)	8 (16.0)
AE leading to Study Drug Dis.	0	0	1 (2.0)	7 (14.0)
Severe AE	0	2 (4.1)	2 (4.1)	4 (8.0)

AE of Special Interest, n (%)				
Infection	PBO, N=49	UPA 7.5 MG, N=49	UPA 15 MG, N=49	UPA 30 MG, N=50
Infection	11 (22.4)	18 (36.7)	16 (32.7)	22 (44.0)
Serious Infection <sup>2</sup>	0	0	1 (2.0)	3 (6.0)
Opportunistic Infection <sup>3</sup>	0	0	0	2 (4.0)
Herpes Zoster <sup>4</sup>	1 (2.0)	1 (2.0)	0	3 (6.0)
Tuberculosis	0	0	0	0
Malignancy	0	0	0	0
Haemoglobin	2 (4.1)	0	1 (2.0)	1 (2.0)
GI Perforation	0	0	0	0
PE/VT	0	0	0	0
Cardiovascular event ( adjudicated)	0	1 (2.0) <sup>5</sup>	0	0
Death	0	0	0	0

<sup>1</sup>Results for binary endpoints are based on NRI analysis. Results for continuous endpoints are based on MMRM (Mixed Effect Model Repeat Measures) analysis. \*\* p<0.01 and p<0.001, respectively.  
<sup>2</sup>Serious infections: UPA 15 mg, Cellulitis; UPA 30 mg, 1 case each of HZ, hand, foot and mouth disease and pneumocystis pneumonia.  
<sup>3</sup>Opportunistic infections: UPA 30 mg, 1 case each of oral candidiasis and pneumocystis pneumonia (counted also under serious infections).  
<sup>4</sup>Herpes zoster: all cases were non-serious, except one in UPA 30 which was single dermatome and considered by the investigator as possibly related to study drug.  
<sup>5</sup>Cardiovascular event ( adjudicated): Non-MACE (transient ischaemic attack).

**Conclusions:** In this Japanese RA csDMARD-IR population, the efficacy of UPA was demonstrated, with better responses for more stringent endpoints on UPA 15 mg and 30 mg vs 7.5 mg. The frequency of overall AEs was numerically higher in UPA 30 mg. Overall, safety and tolerability were consistent with Phase 2 and 3 studies to date.

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SAT0258

### WEEKLY SPLIT DOSE COMPARED WITH SINGLE DOSE ORAL METHOTREXATE REDUCED POLYGLUTAMYLATION IN RED BLOOD CELLS AND INCREASED THE RISK OF ADVERSE EVENTS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Methotrexate (MTX) is a well-known anchor drug for rheumatoid arthritis (RA); however, dose regimens vary. We previously reported in EULAR2015 that split dose weekly oral methotrexate induced elevation of AST and ALT in association with elevation of MTX with 2 glutamates (MTX-PG2) in a single-centre trial.

**Objectives:** We performed a multi-centre randomised controlled trial to compare the incidence of adverse events using single and split dose regimens.

**Methods:** Six hospitals and 2 rheumatology clinics participated in this study. Seventy-eight patients with insufficient control on MTX 8 mg/week were randomly assigned to 2 groups, i.e., a single weekly dose regimen with 39 patients and a 3 dose per week regimen with 39 patients. The MTX dose in all patients was gradually increased to 16 mg/week. The primary endpoint was the occurrence of liver dysfunction during the observation period (20 weeks). Other endpoints included the incidence of adverse events and the changes from baseline in the disease activity score (DAS28) based on ESR or CRP, the Simplified Disease Activity Index (SDAI), and MTX-PG at week 20.

**Results:** There were no differences between the groups in baseline data and MTX dose at 20 weeks (single dose: 10.2±0.8 vs. 3-dose: 10.2±0.9 mg/week). Liver dysfunction occurred in 3 patients (7.7%) receiving the single dose regimen and in 5 patients (13.2%) receiving the 3-dose regimen, but there was no significant difference in the incidence in both groups (p=0.455). There was a significant difference in the incidence of adverse events (gastrointestinal disorder was most common) between single dose (11 patients, 28.9%) and 3-dose (20 patients, 52.6%) regimens (p=0.036). There was no significant difference in the changes from baseline in DAS28-ESR (-1.55 vs. -1.36), DAS28-CRP (-1.31 vs. -1.26), or SDAI (-9.45 vs. -10.11). Compared to the single dose regimen, MTX-PG2 was significantly increased in the 3-dose regimen, and MTX-PG3, -PG4, and -PG5 were significantly increased in the single dose regimen (table 1).

**Abstract SAT0258 – Table 1.** MTX-PG changes from baseline in red blood cells at week 20.

	Single dose Mean (n=28) (nmol/L) (1)	3-dose Mean (n=27) (nmol/L) (2)	Difference (2) – (1) Mean (95% CI)	P (Wilcoxon)
MTX-PG1	22.95	57.9	34.95 (-56.99, 126.89)	0.448
MTX-PG2	-1.14	17.36	18.50 (12.73–24.27)	<0.001
MTX-PG3	39.24	27.83	-11.41 (-21.51, -1.32)	0.032
MTX-PG4	15.43	5.10	-10.33 (-15.03, -5.63)	<0.001
MTX-PG5	3.36	0.15	-3.22 (-4.73, 1.69)	<0.001

**Conclusions:** There were no differences in the incidence of liver dysfunction and efficacy according to the oral MTX dose regimen; however, split weekly dosing

compared with single weekly dosing reduced polyglutamylation and increased the risk of adverse events.

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SATURDAY, 16 JUNE 2018

### Spondyloarthritis - treatment

SAT0259

### LOW RATE OF SPINAL RADIOGRAPHIC PROGRESSION OVER 2 YEARS IN ANKYLOSING SPONDYLITIS PATIENTS TREATED WITH SECUKINUMAB: A HISTORICAL COHORT COMPARISON

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**Background:** Secukinumab, a fully human interleukin 17A (IL-17A) inhibitor, improved signs and symptoms of ankylosing spondylitis (AS) in patients (pts) in the MEASURE 1 core trial at 2 years and through 4 years in the extension study.<sup>1,2</sup> A low radiographic progression rate was reported for the modified Stoke Ankylosing Spondylitis Spinal Score ( $\Delta$  mSASSS at Yr 2=0.3).<sup>1</sup> Comparison of anti-TNF agents with historical NSAID-treated cohorts have not shown a significant benefit at 2 years in reducing radiographic progression.<sup>3,4</sup>

**Objectives:** This retrospective analysis compared spinal radiographic progression over 2 years in the MEASURE 1 cohort of secukinumab-treated AS patients (C1; NCT01358175) vs a historical cohort of biologic-naïve AS pts (ENRADAS [C2; NCT00715091]).<sup>5</sup>

**Methods:** Baseline (BL) and 2 year X-ray data from the 2 cohorts were compared. Only data from pts with X-rays at BL and Yr 2 (data capture window for Yr 2 X-rays: 31–744 days) were included (n=168 [C1], n=69 [C2]). X-rays were independently re-evaluated using the mSASSS by 2 reviewers and an adjudicator blinded to the timing and cohorts; averaged values were analysed. Cases with the highest difference in  $\Delta$  mSASSS between readers (top 10%) were adjudicated. The primary outcome was to compare the % pts with no radiographic progression ( $\Delta$  mSASSS at Year 2 $\leq$ 0) in C1 vs C2. The difference between C1 and C2 was analysed using a logistic regression with cohort as a factor and BL mSASSS as a covariate.

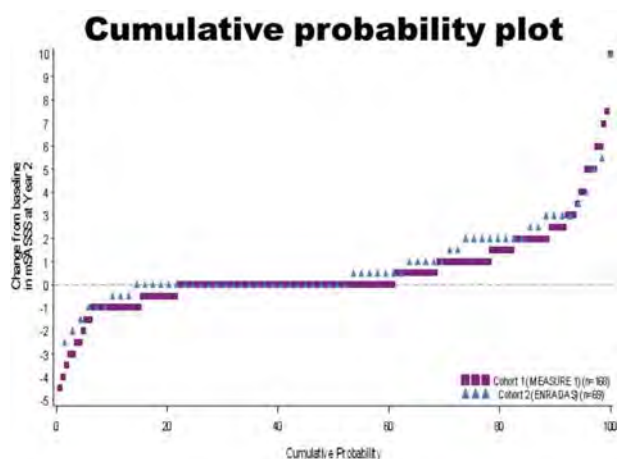
**Results:** BL demographics were comparable across cohorts, with mean age 40.9 vs 42.6 years, and gender 72.8% vs 66.7% male in C1 vs C2, respectively. Over 2 years, least squares (LS) mean  $\Delta$  mSASSS was 0.55 for C1 vs 0.89 for C2 (p=0.185) and % pts with no radiographic progression ( $\Delta$  mSASSS at Year 2 $\leq$ 0) was slightly higher in C1 vs C2 (table 1).

**Abstract SAT0259 – Table 1.** Radiographic status at Yr 2

	C1 (MEASURE 1) n=168	C2 (ENRADAS) n=69	Odds ratio/difference of LS mean (95% CI), p-value
BL mSASSS (SD)	9.55 (14.14)	9.95 (13.76)	
mSASSS at Yr 2 (SD)	10.10 (14.70)	10.85 (14.66)	
$\Delta$ mSASSS over 2 years, LS mean (SE)	0.55 (0.14)	0.89 (0.22)	p=0.185
No progression ( $\Delta$ mSASSS $\leq$ 0), %	61%	52%	1.43 (0.79, 2.60), p=0.243
No progression ( $\Delta$ mSASSS $<$ 2), %	82%	73%	1.84 (0.90; 3.77), p=0.093

CI, confidence interval; SD, standard deviation; SE, standard error





**Conclusions:** Over 2 years, a numerically lower rate of progression was seen in secukinumab-treated pts vs a control cohort of biologic-naïve AS pts. Further research is needed to understand the impact of IL-17A inhibition with secukinumab on spinal disease progression in AS pts; SURPASS (NCT03259074), an ongoing H2H study powered to compare differences in spinal radiographic progression with secukinumab vs biosimilar adalimumab, will help answer these questions.

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**SAT0260 ELIGIBILITY CRITERIA FOR TNFI THERAPY IN AXSPA: GOING BEYOND BASDAI**

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**Background:** A BASDAI  $\geq 4$  has been often used to start TNFi therapy in patients with axSpA. However, this cut-off of high disease activity (HDA) is largely arbitrary. Unlike BASDAI, ASDAS incorporates objective measures (e.g. CRP) and has a validated definition of HDA ( $\geq 2.1$ ). It has thus been suggested that ASDAS could also be used to guide treatment decisions, but evidence to support this is still scarce.

**Objectives:** To compare the impact of applying the ASDAS and BASDAI definitions of HDA in selecting patients for TNFi-treatment in daily clinical practice

**Methods:** Patients from Reuma.pt (Rheumatoid Diseases Portuguese Register), with diagnosis of axSpA according to their rheumatologists (both treated and not treated with their first TNFi), with complete baseline BASDAI and ASDAS data, and complete 6 month of follow-up (i.e. baseline, 3 and 6 months visits available) were included. Four subgroups [cross-tabulation between ASDAS ( $\geq 2.1$ ) and BASDAI ( $\geq 4$ ) definitions of HDA], were compared according to baseline demographic and clinical characteristics in the 'eligible population' (i.e. irrespective of TNFi-treatment). In addition, for patients starting TNFi and with complete follow-up BASDAI/ASDAS data ('efficacy population'), the subgroups were also compared according to different response criteria (see table 1), at 3 and 6 months.

**Results:** In total, 466 patients were included (59% males and 66% HLA-B27 positive). The large majority (n=382; 82%) fulfilled the definition of HDA according to both BASDAI and ASDAS at baseline (i.e. BASDAI  $\geq 4$  and ASDAS  $\geq 2.1$ ). The frequency of ASDAS  $\geq 2.1$ , if BASDAI  $< 4$ , was much higher than the opposite condition (i.e. ASDAS  $< 2.1$ , if BASDAI  $\geq 4$ ) (70% vs 0.5%). Compared to patients fulfilling both definitions, those who were ASDAS  $\geq 2.1$  only, were more likely to be male (82.5% vs 54%), HLA-B27 positive (79% vs 54%), to show higher levels of CRP ( $2.6 \pm 2.5$  vs  $2.2 \pm 2.8$  mg/dL) and lower BASFI ( $3.1 \pm 2.6$  vs  $5.6 \pm 2.3$ ). In the 'efficacy population' (n=296), better responses were observed among patients with ASDAS  $\geq 2.1$  only, especially for the most 'stringent' outcomes [e.g. ASDAS inactive disease (ASDAS ID): 59% and 50%, at 3 and 6 months respectively], compared to patients fulfilling both definitions (ASDAS ID: 26% and 25% at 3 and 6 months respectively) (table 1).

**Abstract SAT0260 – Table 1.** TNFi response criteria across subgroups according to BASDAI/ASDAS category ('efficacy population')

Variables	Overall (N=296) *	ASDAS $\geq 2.1$		ASDAS $< 2.1$		p-value **
		BASDAI $\geq 4$ (N=256)	BASDAI $< 4$ (N=34)	BASDAI $\geq 4$ (N=1)	BASDAI $< 4$ (N=5)	
<b>Outcomes - 3 months, n (%)</b>						
ASAS20	359 (59)	142 (60)	15 (56)	0 (0)	2 (40)	0.48
ASAS40	327 (47)	111 (46)	14 (52)	0 (0)	2 (40)	0.74
ASAS PR	73 (26)	56 (22)	14 (56)	0 (0)	3 (60)	<b>&lt;0.01</b>
BASDAI50	384 (62)	160 (63)	21 (62)	0 (0)	3 (60)	0.64
ASDAS CR	207 (70)	179 (70)	26 (77)	0 (0)	2 (40)	0.16
ASDAS MI	323 (42)	111 (43)	12 (35)	0 (0)	0 (0)	0.16
ASDAS ID	90 (30)	66 (26)	20 (59)	0 (0)	4 (80)	<b>&lt;0.01</b>
<b>Outcomes - 6 months, n (%)</b>						
ASAS20	360 (61)	139 (61)	18 (62)	0 (0)	3 (60)	0.67
ASAS40	324 (46)	104 (45)	12 (57)	0 (0)	3 (60)	0.43
ASAS PR	74 (27)	57 (24)	13 (48)	0 (0)	4 (80)	<b>&lt;0.01</b>
BASDAI50	388 (64)	167 (65)	18 (53)	0 (0)	5 (60)	0.29
ASDAS CR	216 (73)	190 (74)	25 (74)	0 (0)	1 (20)	<b>0.02</b>
ASDAS MI	128 (43)	117 (46)	11 (32)	0 (0)	0 (0)	0.08
ASDAS ID	84 (28)	63 (25)	17 (50)	0 (0)	4 (80)	<b>&lt;0.01</b>

\* ASDAS patients treated with TNFi with complete 3 months of follow-up and data for BASDAI/ASDAI at every timepoint \*\* comparison between subgroups according to BASDAI/ASDAI category of disease activity (ASDAI) for continuous variables and Chi for categorical variables. ASDAS CR, ASDAS clinically important improvement; ASDAS MI, ASDAS major improvement; ASDAS ID, ASDAS inactive disease.

**Conclusions:** Our results show that the ASDAS-HDA definition (ASDAS  $\geq 2.1$ ) is more inclusive than the BASDAI-HDA definition ( $\geq 4$ ) in selecting axSpA patients for TNFi treatment. Importantly, the additionally 'captured' patients respond better and have higher likelihood of predictors thereof. These results support the use of ASDAS  $\geq 2.1$  as a selection criterion for treatment decisions.

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SAT0261

### CERTOLIZUMAB PEGOL SERUM LEVELS $\geq 20$ MG/L ARE ASSOCIATED WITH TREATMENT RESPONSE IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS. DATA FROM THE NOR-DMARD STUDY

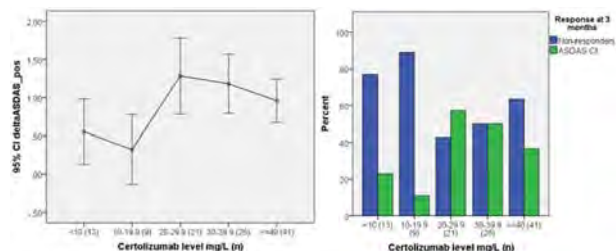
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**Background:** Measurement of serum drug levels can help clinicians tailor treatment with TNF-inhibitors. An association between certolizumab pegol (CP) serum levels and response has previously been found in patients (pts) with rheumatoid arthritis. <sup>1</sup>Data for pts with axial spondyloarthritis (axSpA) are lacking.

**Objectives:** To examine the association between serum CP levels and treatment response in pts with axSpA and to identify a therapeutic target level.

**Methods:** Patients with a clinical diagnosis of axSpA starting standard treatment with CP included in the NOR-DMARD study with biobank sample at 3 months follow-up, were included in the present analyses. Serum drug levels (non-trough) were analysed with an in-house immunofluorometric assay automated on the AutoDELFI immunassay platform. Associations between CP level and improvement in ASDAS-CRP and response (defined as ASDAS clinically important improvement (CII)) were assessed by multivariable linear and logistic regression (adjusting for age, sex and prior bDMARD (Y/N)), respectively.

**Results:** Median serum drug level at 3 month follow up was 35.0 mg/L (IQR 21.3–45.3) in 116 pts. Response data were available in 110/116 patients. Serum CP level  $\geq 20$  mg/L was associated with improvement in ASDAS at 3 months ( $\beta=0.55$ , (95% CI 0.12–1.98),  $p=0.01$ ). Serum CP level  $\geq 20$  mg/L was associated with ASDAS CII at 3 months (OR 3.4 (95% CI 1.0–11.1,  $p=0.045$ )). Only 18.2% of pts with CP level  $< 20$  mg/L achieved ASDAS CII at 3 months, while 53.2% of pts with CP level 20–40 mg/L and 36.6% with  $\geq 40$  mg/L were responders.



**Conclusions:** Serum CP level was associated with clinical response after 3 months of treatment in pts with axSpA. We suggest 20 mg/L as a lower target level for non-trough samples. No additional benefit of having a certolizumab level over 40 mg/L was observed. These results suggest that a therapeutic level of 20–40 mg/L can be implemented in clinical practice for non-trough serum samples in pts with axSpA.

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SAT0262

### 3-YEAR FOLLOW-UP OF A DOSE TAPERING PROTOCOL OF ANTI-TNF THERAPY IN A COHORT OF PATIENTS WITH SPONDYLOARTHRITIS (SPA) IN CLINICAL REMISSION UNDER CONDITIONS OF CLINICAL PRACTICE

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**Background:** The dose tapering of biological therapy in patients in clinical remission is a strategy used in recent years in Rheumatology, consists in the reduction of the dose administered or in the extension of the interval between two doses, some studies suggest the possibility that patients with sustained remission could obtain the same benefit with a lower dose.

**Objectives:** Evaluate the effectiveness of 3 year follow-up of a dose tapering in patients with SpA in maintained clinical remission and detect possible predictors of maintenance of the response.

**Methods:** Retrospective observational study, all patients with SpA were included, according to ASAS criteria, treated with antiTNF, with dose tapering, from October 2014-December 2017. Clinical remission defined by BASDAI  $\leq 2$  and/or CRP  $\leq 5$  mg/L for at least 6 months, establishing dose tapering as lower doses or longer intervals (according to the guidelines of the Spanish Society of Rheumatology and Pharmacy). Those patients who relapsed (BASDAI  $> 2$  and/or CRP  $> 5$  mg/L) at any time during the study returned to the standard dose. Clinical and analytical parameters were collected (baseline and at the time of optimisation), as well as the survival of the drug and the efficacy parameters until the time of relapse and who continued in dose tapering.

**Results:** 149 patients with SpA in treatment with antiTNF, 38/149 (25.5%) included in the dose tapering protocol, 84.4% men and the mean age  $47.2 \pm 10.6$  years. The antecedents 25% uveitis, 6.3% psoriasis and 6.3% inflammatory bowel disease. Regarding the type of optimisation strategy, 32 patients (84.37%) followed the protocol for increasing the interval between doses, compared to the rest (15.62%) who used reduced doses. We found 27/38 patients (71.05%, CI: 55.2–83) maintained clinical remission with tapering, 9 (33.3%) infliximab, 7 (25.9%) golimumab, 6 (22.2%) etanercept and 5 (18.5%) adalimumab, at a time of drug follow-up of  $57.9 \pm 29.7$  months. The demographic factors analysed sex, age, time of evolution and clinical remission, were not found as possible predictors of greater survival in the dose tapering.

	PATIENTS RELAPSE (n=11)			PATIENTS REMISSION (n=27)		
	Basal	Start tapering	Relapse	Basal	Start tapering	Last visit
BASDAI (0–10)	3.8 $\pm$ 2.4	2 $\pm$ 1.8	3.18 $\pm$ 2.27	4.4 $\pm$ 2.8	2.1 $\pm$ 2.5	1.5 $\pm$ 1.6
BASFI (0–10)	4.3 $\pm$ 2.8	2.8 $\pm$ 2.8	2.9 $\pm$ 2.37	3.7 $\pm$ 2.6	2.8 $\pm$ 3.1	2.0 $\pm$ 2.4
ESR (mm/1 <sup>h</sup> )	17.1 $\pm$ 22.5	9.3 $\pm$ 11.1	11.84 $\pm$ 11.29	20.4 $\pm$ 18.8	7.8 $\pm$ 6.1	8.4 $\pm$ 7.6
CPR	10.9 $\pm$ 12.2	9.7 $\pm$ 12.4	3.84 $\pm$ 4.54	14.6 $\pm$ 22.5	3.7 $\pm$ 6.1	2.69 $\pm$ 3.0

	n=38	
	Age (years, mean $\pm$ SD)	47.2 $\pm$ 10.6
Sex (%) Man/woman	84.4/15.6	
Time of evolution disease (years, mean $\pm$ SD)	12.2 $\pm$ 10.4	
Start biological therapy (months, mean $\pm$ SD)	22.84 $\pm$ 12.68	
	Start antiTNF	Start tapering
BASDAI(0-10)	4.2 $\pm$ 2.6	2.07 $\pm$ 1.96
BASFI(0-10)	4 $\pm$ 2.7	2.8 $\pm$ 2.9
CPR(mg/L)	13.1 $\pm$ 18.7	6.4 $\pm$ 9.7
ESR(mm/1 <sup>h</sup> )	19 $\pm$ 20.1	8.5 $\pm$ 8.5

**Conclusions:** The monitoring of dose tapering of biological therapy in patients with SpA is possible and allows more than 70% of patients to maintain the clinical remission of the disease. However, a greater number of patients and longer follow-up are necessary for a solid conclusion. Additionally, our results do not show possible predictors of a longer survival in tapering protocol.

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**Disclosure of Interest:** None declared

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**SAT0263 PREDICTORS OF REMISSION MAINTENANCE AND SUCCESSFUL THERAPY DISCONTINUATION IN PATIENTS WITH NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS (NR-AXSPA) WHO ACHIEVED SUSTAINED REMISSION ON OPEN-LABEL ADALIMUMAB (ADA) TREATMENT**

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**Background:** Sustained remission is an important treatment goal in patients (pts) with non-radiographic axial SpA (nr-axSpA). Factors predicting successful remission maintenance are unknown.

**Objectives:** We sought to identify predictors of remission maintenance in nr-axSpA pts who achieved remission after open-label (OL) adalimumab (ADA) treatment in the ABILITY-3 trial (NCT01808118) and were subsequently randomised to continuation or withdrawal of ADA therapy.

**Methods:** ABILITY-3 enrolled adult pts with nr-axSpA with objective evidence of active MRI inflammation in the SI joints or spine or elevated high-sensitivity CRP at screening, active disease at baseline (ASDAS<sub>2.1</sub>≥2.1, BASDAI<sub>4</sub>≥4, and Patient's Assessment of Total Back Pain score ≥4), and inadequate response to ≥2 NSAIDs (table 1). Pts received ADA 40 mg every other wk during a 28-wk OL lead-in period. Pts who achieved sustained remission, defined as ASDAS inactive disease [ID] score <1.3 at wks 16, 20, 24, and 28, were randomised to double-blind withdrawal (placebo; PBO) or continued ADA for 40 wks during period 2 (study wk 68). Stepwise logistic regression was used to identify predictors of sustained remission in those in the continued ADA and withdrawal (PBO) groups. Remission maintenance in period 2 was assessed with the following: ASAS partial remission (PR; score ≤2.0) and ASDAS ID at wk 68, ASAS PR and ASDAS ID at every visit, and ASDAS ID for ≥5 of 10 visits.

**Abstract SAT0263 – Table 1. Characteristics at Baseline and Wk 28**

Variable	ADA (40 mg EOW) n=152	PBO n=153	P Value	Wk 28, mean (SD)	ADA (40 mg EOW) n=152	PBO n=153	P Value
Age, y	54.7 (10.3)	55.3 (10.2)	0.611	ASDAS	0.7 (0.4)	0.6 (0.4)	0.355
Female, n (%)	56 (37)	60 (39)	0.724	BASDAI	0.8 (0.8)	0.7 (0.7)	0.145
SpA symptom duration, y	6.4 (6.9)	7.1 (6.8)	0.358	BASFI	0.7 (1.0)	0.7 (1.2)	0.994
HLA-B27 positive, n (%)	132 (87)	134 (88)	0.866	Hi-CRP, mg/L	1.5 (2.4)	1.4 (1.8)	0.617
ASDAS	3.5 (0.9)	3.5 (0.8)	0.851	Pt total back pain	1.1 (1.4)	1.0 (1.4)	0.565
BASDAI	6.8 (1.4)	6.8 (1.5)	0.851	PGA	0.8 (1.0)	0.9 (1.1)	0.386
BASFI	5.1 (2.3)	5.0 (2.3)	0.776	SPARCC SI joint score*	2.6 (6.1)	2.5 (4.0)	0.755
Hi-CRP, mg/L	9.9 (11.1)	9.1 (13.3)	0.576	SPARCC spine score*	1.2 (3.8)	1.2 (3.8)	0.809
Pt total back pain	7.0 (1.7)	7.0 (1.8)	0.946				
PGA	6.6 (1.5)	6.4 (1.4)	0.150				
SPARCC SI joint score*	8.5 (12.8)	10.3 (13.4)	0.226				
SPARCC spine score*	3.3 (7.5)	3.6 (7.2)	0.671				

**Results:** By wk 68, 100/145 (69%) ADA pts had not flared, 41% achieved ASAS PR and 56% ASDAS ID at wk 68; 23% achieved ASAS PR and 29% ASDAS ID at every visit, while 70% achieved ASDAS ID for ≥5 of 10 visits. By wk 68, 70/148 (47%) PBO pts had not flared, 28% achieved ASAS PR and 33% ASDAS ID at wk 68; 14% achieved ASAS PR and 15% ASDAS ID at every visit, while 52% achieved ASDAS ID for ≥5 of 10 visits. Shorter symptom duration, lower wk 28 BASDAI, and male sex were associated with absence of flare in the continued ADA group. Lower wk 28 ASDAS was associated with absence of flare with ADA withdrawal. Lower wk 28 ASDAS consistently predicted ASAS PR and ASDAS ID

at wk 68, ASAS PR and ASDAS ID at every visit, and ASDAS ID for ≥5 of 10 visits in pts who continued or withdrew ADA.

**Conclusions:** In nr-axSpA pts who achieved remission after 28-wk OL ADA therapy, lower wk 28 ASDAS is a consistent predictor of remission maintenance using all definitions in both the adalimumab continuation and withdrawal groups, except absence of flare in the adalimumab continuation group, suggesting early aggressive treatment may be beneficial in achieving sustained remission.

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**Disclosure of Interest:** J. Sieper Consultant for: AbbVie, Janssen, Lilly, Merck, Novartis, Pfizer, Sun Pharma, and UCB, Speakers bureau: AbbVie, Janssen, Lilly, Merck, Novartis, and Pfizer., R. Landewé Grant/research support from: Abbott, Amgen, Centocor, Novartis, Pfizer, Roche, Schering-Plough, UCB, and Wyeth, Consultant for: consulting or advisory board fees from Abbott/AbbVie, Ablynx, Amgen, Astra-Zeneca, Bristol Myers Squibb, Celgene, Janssen (formerly Centocor), Galapagos, GlaxoSmithKline, Novartis, Novo-Nordisk, Merck, Pfizer, Roche, Schering-Plough, TiGenix, UCB, and Wyeth, Employee of: he is director of Rheumatology Consultancy BV, a registered Dutch company., Speakers bureau: Abbott/AbbVie, Amgen, Bristol Myers Squibb, Janssen (formerly Centocor), Merck, Pfizer, Roche, Schering-Plough, UCB, Wyeth, M. Magrey Grant/research support from: Amgen, AbbVie, and UCB Pharma, Consultant for: UCB and Janssen, J. Anderson Shareholder of: AbbVie, Employee of: AbbVie, S. Zhong Shareholder of: AbbVie, Employee of: AbbVie, X. Wang Shareholder of: AbbVie, Employee of: AbbVie, A. Lertratanakul Shareholder of: AbbVie, Employee of: AbbVie

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**SAT0264 DOES BIOLOGICAL DISEASE-MODIFYING ANTI-RHEUMATIC DRUG NAÏVE VERSUS NON-NAÏVE PATIENTS WITH INFLAMMATORY JOINT DISEASES HAVE SIMILAR GOLIMUMAB DRUG SURVIVAL AND EFFICACY? DATA FROM THE PROSPECTIVE OBSERVATIONAL NOR-DMARD STUDY**

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**Background:** Knowledge is limited regarding the impact of previously used biological disease modifying anti-rheumatic drugs (bDMARD) on golimumab drug survival and efficacy in inflammatory joint diseases (IJD).

**Objectives:** To explore golimumab drug survival and efficacy in bDMARD naïve vs. non-naïve IJD patients, as well as predictors of golimumab discontinuation.

**Methods:** From the observational prospective multicenter Norwegian-DMARD (NOR-DMARD) study rheumatoid arthritis (RA), psoriatic arthritis (PsA) and axial spondyloarthritis (ax-SpA) patients starting golimumab were included. Drug survival was explored by Kaplan-Meier analyses with comparison of bDMARD naïve vs. non-naïve patients with log rank test, stratified by diagnosis. 3 month responses were compared with independent t-test, and with ANCOVA adjusted for age, gender, disease duration and baseline values of the respective composite scores. Univariable and multivariable Cox regression analyses including age, gender, disease duration, smoking, concomitant synthetic DMARDs (sDMARDs) and previous bDMARD use were performed to identify predictors of golimumab discontinuation.

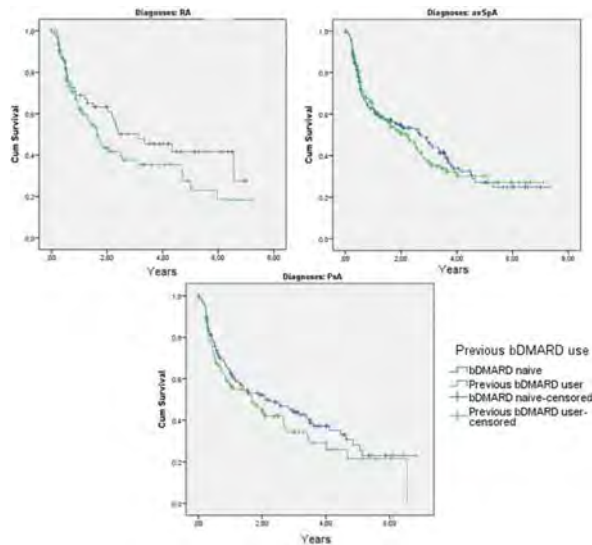
**Results:** Mean (SD) age of the 163 RA, 267 PsA and 382 ax-SpA patients was 51.2 (14.1)/48.1 (11.7)/41.8 (11.1) years, disease duration 11.3 (10.0)/8.7 (9.0)/10.6 (11.2) years, %females 76.1/55.1/44.1%, respectively. Golimumab drug

Diagnosis	Composite score	Changes (baseline minus 3 months)			
		Unadjusted analyses		Adjusted analyses	
		Mean (SD)	p-value	Estimated marginal means (95% CI)	p-value
	bDMARD naïve patients	Previous bDMARD users	bDMARD naïve patients	Previous bDMARD users	
RA	Δ DAS28	-1.1 (1.3)	0.39	-1.7 (-2.6,-0.7)	0.08
	Δ CDAI	-9.0 (10.8)	0.99	-11.7 (-14.5,-8.9)	0.10
PsA	Δ DAS28	-1.2 (1.1)	<0.001	-1.0 (-1.3,-0.8)	0.01
	Δ CDAI	-7.1 (7.8)	0.005	-6.2 (-7.6,-4.8)	0.18
	Δ BASDAI	-1.4 (2.1)	0.08	-1.2 (-1.6,-0.8)	0.38
Ax-SpA	Δ BASDAI	-1.9 (2.4)	<0.001	-1.9 (-2.3,-1.6)	<0.001
	Δ ASDAS	-1.2 (1.3)	<0.001	-1.1 (-1.3,-0.9)	<0.001

Identified predictors for golimumab discontinuation were [Hazard Ratio (95% CI)]: RA, None; PsA, female gender [1.63 (1.18–2.25), p=0.003] and no concomitant sDMARDs [1.39 (1.01–1.90), p=0.04]; ax-SpA, female gender [1.97 (1.50–2.60), p<0.001].



survival for bDMARD naïve vs. non-naïve patients was similar for all diagnoses (RA,  $p=0.15$ ; PsA,  $p=0.23$ ; ax-SpA  $p=0.71$ ), with trend towards better drug survival in bDMARD naïve RA and PsA patients (figure). 4 year drug survival in bDMARD naïve/non-naïve patients were: RA, 54/48%; PsA, 47/43%; ax-SpA, 48/46%, respectively. Subgroup analyses of patients with and without concomitant sDMARDs showed similar findings. A trend was seen towards better 3 month responses in bDMARD naïve vs. non-naïve patients, with statistically significant better responses for DAS28 in PsA and BASDAI and ASDAS in ax-SpA (table 1).



**Conclusions:** Golimumab drug survival was similar in bDMARD naïve vs. non-naïve RA, PsA and ax-SpA patients. A trend was seen towards better responses for bDMARD naïve patients. Identified predictors for golimumab drug discontinuation was female gender and no concomitant sDMARDs in PsA and female gender in ax-SpA.

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#### SAT0265 THE RESPONSE TO TNF-BLOCKERS TREATMENT OF SPA PATIENTS IS INFLUENCED BY THE INTERPLAY BETWEEN HLA-B27 AND GUT MICROBIOTA COMPOSITION AT BASELINE

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**Background:** The response to TNF-blockers in axial spondyloarthritis (AxSpA) is at least partially influenced by HLA-B27 through a still poorly understood mechanism.

**Objectives:** Given that HLA-B27 regulates the gut microbiota composition in rats<sup>1,2</sup>, we seek to evaluate the predictive value of the gut microbiota composition in AxSpA patients on their responsiveness to TNF-blockers.

**Methods:** A total of 58 patients was monocentrically recruited between October 2014 and May 2015. At baseline, these patients had an active disease despite NSAIDs intake and were eligible for treatment with a TNF-blocker, while having no history of inflammatory bowel disease (IBD). The mean BASDAI ( $\pm$ SD) was  $45.6 \pm 21.4$ ; ASDAS  $2.8 \pm 0.9$  and CRP  $9.7 \pm 11.4$  mg/L. Among these patients, 56 fulfilled the ASAS classification criteria (imaging arm) with sacro-iliitis on X-rays ( $n=37$ ) or objective signs of inflammation on MRI ( $n=48$ ). Two patients fulfilled the clinical arm. These patients were not subjected to antibiotics within 3 months before stool sample collection. Bacterial 16S rRNA gene sequencing of the V3-V4 region was performed on stools samples before and 3 months after TNF-blocker

treatment. Beta diversity metrics were calculated on the abundance of operational taxonomic units (OTU) after their taxonomic assignment on quality-filtered sequences.

**Results:** Principal component analysis (PCA) ordination of Bray-Curtis similarity revealed that current smoking (compared with never or ever smokers) and HLA-B27 genotype were significantly associated with the overall composition of the microbiota at baseline. Meanwhile, the abundance of eleven bacterial OTUs was influenced by HLA-B27 genotype at baseline but not after 3 month of treatment. In contrast, we identified a bacterial signature that was linked to the smoking behaviour independently of TNF-blocker treatment, whereas the BASDAI and ASDAS indices were significantly associated to the general composition of the gut microbiota after the 3 month treatment. In line with a previous report<sup>3</sup>, the abundance of *Ruminococcus gnavus* was not associated with disease activity in the absence of IBD. Interestingly, the abundance of 5 and 7 bacterial OTUs at baseline was associated with the response to TNF-blockers assessed by BASDAI and ASDAS, respectively. Among these candidates, the abundance of one bacterial OTUs belonging to the *Clostridiales* order was associated with a better response to the treatment and with the HLA-B27 genotype.

**Conclusions:** Anti-TNF treatment was found to modulate the HLA-B27-induced variations of the intestinal microbiota of AxSpA patients. Moreover, the abundance of a subset of OTUs at baseline was found to predict the responsiveness to TNF-blockers. Further functional studies will be conducted to assess how these taxa can be used as predictors of the treatment outcome.

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**Disclosure of Interest:** None declared

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#### SAT0266 USE OF CONVENTIONAL SYNTHETIC DMARDS AND BIOLOGICAL DMARDS IN PATIENTS WITH ENTEROPATHIC SPONDYLOARTHRITIS: A COMBINED GASTRO-RHEUMATOLOGICAL APPROACH

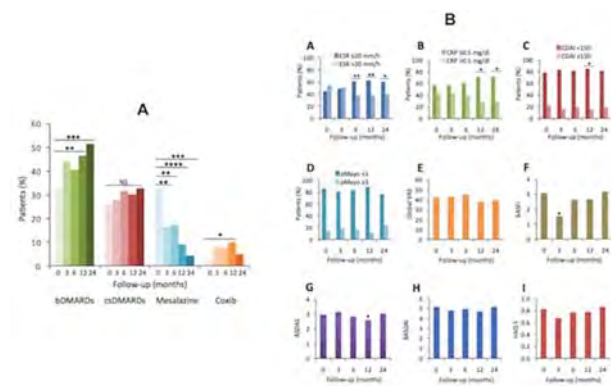
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**Background:** Enteropathic spondyloarthritis (eSpA) is a chronic autoimmune disease associated with inflammatory bowel disease (IBD) that is poorly diagnosed and managed.

**Objectives:** To assess the diagnostic and therapeutic effect of a combined gastro-rheumatological approach in eSpA patients.

**Methods:** IBD-patients with joint pain referred to a dedicated rheumatologist by gastroenterologist were enrolled. Clinical and biochemical variables, SpA and intestinal disease activity measures, and treatment (biologic; bDMARDs and conventional synthetic; csDMARDs) were recorded at baseline, 3, 6, 12 and 24 months. The association between treatment on demographic and clinical characteristics was evaluated by logistic regression.

**Results:** From a total of 229 IBD patients, 147 (64.2%) were diagnosed with eSpA; 96 (65.3%) showing peripheral involvement and 51 (34.7%) with axial involvement. The majority (67.3%) of eSpA patients were female ( $n=99$ ), median age and disease duration of 46 and 14.6 years. bDMARD treatment increased over the follow-up period (baseline-24 months: 32.6% $\rightarrow$ 60%; AOR:3.45, 95% CI: 1.93–6.2,  $p<0.001$ ), however, their use was less frequent in elderly patients (AOR: 0.73, 95% CI: 0.56–0.96,  $p=0.023$ ), in ulcerative colitis patients (AOR:0.43, 95% CI:0.2–0.94,  $p=0.034$ ) and in patients with peripheral involvement (AOR:0.53, 95% CI:0.3–1.04,  $p=0.067$ ). csDMARD use was increased in patients with peripheral involvement (AOR: 4.65, 95% CI:2.09–10.33,  $p<0.001$ ) and in patient with ulcerative colitis (AOR:2.30, 95% CI:1.13–4.67,  $p=0.021$ ) (figure 1). CRP, ESR, ASDAS-ESR levels and BASFI were significantly decreased over the follow-up period whereas pMayo score, BASDAI and HAQ-S were unchanged (figure 2).



**Conclusions:** A multidisciplinary approach can improve in the therapeutic management and outcome (e.g. disease activity measures) of eSpA patients. bDMARD use paralleled an improvement in disease measures and confirmed a good safety profile.

**Disclosure of Interest:** None declared

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**SAT0267 EFFICACY AND SAFETY OF BCD-055, PROPOSED INFLIXIMAB BIOSIMILAR, COMPARED TO INFLIXIMAB: 54-WEEK RESULTS FROM ASART-2 PHASE 3 CLINICAL STUDY**

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**Background:** Non-inferiority of BCD-055 in direct comparison to infliximab originator after 30 weeks of treatment in patients with ankylosing spondylitis (AS) was shown previously<sup>1</sup>. Here we present 54 week safety and efficacy data in ITT population from international double-blind randomised ASART-2 clinical trial.

**Objectives:** To compare BCD-055, proposed infliximab biosimilar and infliximab originator in terms of efficacy and safety in patients with AS.

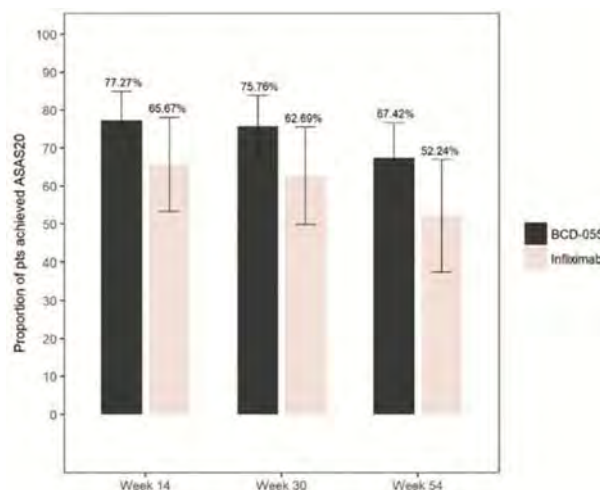
**Methods:** Adult patients (n=199) aged 18–65 years, with active AS (BASDAI>4) received 5 mg/kg of BCD-055 (n=132) or infliximab (n=67) IV on w0, w2 and w6 and then every 8 w until w54. The results of the primary endpoint assessment (ASAS20 at w30) were presented earlier<sup>1</sup>. Secondary endpoints were proportion of patients, achieved ASAS20/40, and mean change from baseline in BASDAI, BASMI, BASFI, MASES, SF36 scores, chest excursion and TJC<sup>44</sup> at w54. Rate of AEs and proportion of patient with ADA to infliximab in both groups were also evaluated.

**Results:** The proportions of patients achieved ASAS20/ASAS40 were similar in both study groups at w54 (Abstract SAT0267 – figure 1). Improvement in AS symptoms showed similar dynamics in both groups: significant decrease in AS activity (BASDAI) and improvement in other secondary endpoints has developed within the first 14 weeks of treatment in both study groups and remained at achieved level until w54. The magnitude of changes of all evaluated parameters did not differ between groups.

No statistically significant differences in rates of AEs were found between study groups (table 1). Most common reported AEs were infections, hematologic and vascular disorders, hypersensitivity reactions. Formation of ADA to infliximab was detected with similar frequency in both groups.

**Abstract SAT0267 – Table 1.** 54 w safety data

	BCD-055, n (%)	Infliximab, n (%)	p value
Any AE/SAE	82 (62.12)	43 (64.18)	0.898
Any SAE	7 (5.30)	5 (7.46)	0.376
Therapy-related AE/SAE	40 (30.30)	26 (38.81)	0.296
Therapy-related SAE	5 (3.79)	4 (5.97)	0.489
Any SAE/AE grade 3–5	18 (13.64)	11 (16.42)	0.754
Therapy-related AE grade 3–5	11 (8.33)	7 (10.45)	0.818
Treatment withdrawal due to SAE/AE	11 (8.33)	7 (10.45)	0.818
Deaths	1 (0.76)	0 (0)	1.000
ADA positive	27 (21.26)	13 (20.63)	0.920
ADA positive, confirmed by neutralisation assay	4 (3.15)	4 (6.35)	0.443



**Abstract SAT0267 – Figure 1.** Proportion of patients achieved ASAS20 at weeks 14, 30 and 54 (%; 95%CI).

**Conclusions:** The 54 week results supports previously confirmed similar efficacy and safety of BCD-055, proposed infliximab biosimilar, and infliximab originator in patients with active AS. At all evaluated time points the efficacy as well as rate of AEs/SAEs did not differ between BCD-055 and infliximab originator groups.

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**Disclosure of Interest:** L. Denisov: None declared, P. Shesternya: None declared, T. Plaksina: None declared, T. Kropotina: None declared, N. Soroka: None declared, E. Kunder: None declared, A. Lutskii Employee of: JSC BIOCAD, A. Ereemeva Employee of: JSC BIOCAD, E. Dokukina Employee of: JSC BIOCAD, E. Chernyaeva Employee of: JSC BIOCAD, R. Ivanov Employee of: JSC BIOCAD, V. Mazurov: None declared

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**SAT0268 SECUKINUMAB DEMONSTRATES LOW RADIOGRAPHIC PROGRESSION AND SUSTAINED EFFICACY THROUGH 4 YEARS IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS**

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**Background:** The MEASURE 1 core trial reported improved signs and symptoms of ankylosing spondylitis (AS) with secukinumab, a fully human anti-interleukin-17A monoclonal antibody.<sup>1</sup>

**Objectives:** To assess efficacy, including imaging outcomes, and safety from the MEASURE 1 extension trial (NCT01863732) up to 4 years.

**Methods:** Patients (pts) had completed 104 wks (2 years) in the core study with SC secukinumab 150 (IV→150 mg) or 75 mg (IV→75 mg) every 4 wks, following IV loading to Wk4, or placebo to Wk16/24. Efficacy data at Wk208 are reported for pts originally randomised to secukinumab 150 mg (approved dose). Lateral cervical and lumbar spine radiographs were assessed with the modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS), and MRIs with the Berlin SI joint total oedema score and Berlin spine score (derived from ASspi-MRI-a results). Images were evaluated by 2 central readers blinded to treatment/visit; mean scores were used. Descriptive statistics on observed/imputed data are provided.

**Results:** Of the 274 pts enrolled in this extension study, 89.7% (78/87) originally assigned to secukinumab 150 mg completed 208 wks. Δ mSASSS (mean ±SD) from baseline (BL) to Wk208 was numerically lower with secukinumab 150 mg (1.2±3.91) vs 75 mg (1.7±4.70). No definite radiographic progression (Δ mSASSS from BL <2) was seen in 79% of pts on secukinumab 150 mg over 208 wks (figure 1). Mean Δ mSASSS at Wk208 was numerically higher in males, and in pts with

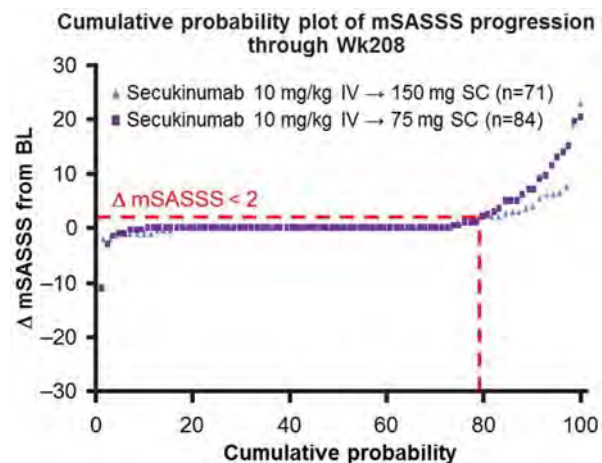
BL syndesmophytes or elevated BL hsCRP. Reductions from BL in the Berlin SI joint oedema and Berlin spine scores were seen with secukinumab 150 mg. Sustained efficacy in signs/symptoms was seen through 208 wks (Table). Exposure-adjusted incidence rates per 100 pt-yrs (total exposure [mean  $\pm$ SD]=3.4  $\pm$ 1.44 years) were: serious infections (1.0), IBD (0.7), uveitis (1.8) and malignant/unspecified tumours (0.5).

Abstract SAT0268 – Table 1. Efficacy at Wk208

	Secukinumab IV $\rightarrow$ 150 mg (n=87)
<b>mSASSS<sup>a,b</sup></b>	
BL (n=71 with X-rays at BL and Wk208)	8.8 $\pm$ 16.23
$\Delta$ BL to Wk208	1.2 $\pm$ 3.91
$\Delta$ BL to Wk104/ $\Delta$ Wk104 to 208 <sup>d</sup>	0.5 $\pm$ 1.69/0.8 $\pm$ 3.34
<b>MRI<sup>a,b</sup></b>	
Berlin SI joint total oedema score, $\Delta$ BL to Wk104/ $\Delta$ BL to Wk208	-2.3 $\pm$ 3.06 <sup>18</sup> / $-1.6\pm 3.03$ <sup>22</sup>
Berlin spine score, $\Delta$ BL to Wk104/ $\Delta$ BL to Wk208	-0.9 $\pm$ 2.17 <sup>18</sup> / $-0.6\pm 2.01$ <sup>22</sup>
<b>Clinical efficacy</b>	
ASAS20/40 <sup>e</sup>	76.4/58.0
BASDAI, <sup>f</sup> $\Delta$ from BL	-3.3 $\pm$ 0.23
ASDAS inactive disease <sup>g</sup>	27.6
BASFI/BASMI, <sup>h</sup> $\Delta$ from BL	-2.9 $\pm$ 2.39 (80)/-0.5 $\pm$ 1.12 (76)

n, no. of pts assessed; N, total no. of pts in extension trial

<sup>a</sup>Radiographs/MRIs taken at BL and Wk104 were re-read for pts completing Wk208 of treatment; <sup>b</sup>Mean $\pm$ SD (n) for observed data; <sup>c</sup>Based on n=67 pts with X-rays at BL, Wk104 and Wk208 and BL mSASSS of 8.01 $\pm$ 15.29 and 9.01 $\pm$ 16.77, calculated from matched vertebral edges at BL and Wk104, and BL and Wk208, respectively; <sup>d</sup>% pts estimated using multiple imputation; <sup>e</sup>Least-squares mean $\pm$ standard error for MMRM estimates



**Conclusions:** Secukinumab 150 mg showed numerically lower radiographic progression vs 75 mg at 4 years. Secukinumab also demonstrated sustained efficacy on signs and symptoms, and MRI outcomes and a consistent safety profile.<sup>1</sup>

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**Disclosure of Interest:** X. Baraliakos Grant/research support from: AbbVie, Merck, Pfizer, UCB, Novartis, and Chugai, Consultant for: AbbVie, Merck, Pfizer, UCB, Novartis, and Chugai, Speakers bureau: AbbVie, Merck, Pfizer, UCB, Novartis, and Chugai, J. Braun Grant/research support from: AbbVie (Abbott), Amgen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, EBEWE Pharma, Medac, MSD (Schering-Plough), Mundipharma, Novartis, Pfizer (Wyeth), Roche, Sanofi-Aventis and UCB, Consultant for: AbbVie (Abbott), Amgen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, EBEWE Pharma, Medac, MSD (Schering-Plough), Mundipharma, Novartis, Pfizer (Wyeth), Roche, Sanofi-Aventis and UCB, A. Deodhar Grant/research support from: AbbVie, Eli Lilly, GSK, Janssen, Novartis, Pfizer, UCB, Consultant for: AbbVie, Eli Lilly, Janssen, Novartis, Pfizer, UCB, D. Poddubny Grant/research support from: AbbVie, MSD, Novartis, Consultant for: AbbVie, BMS, MSD, Novartis, Pfizer, UCB, Speakers bureau: AbbVie, BMS, Janssen, MSD, Novartis, Pfizer, UCB, P. Emery Consultant for: AbbVie, BMS, Merck, Novartis, Pfizer, Roche, UCB, E. Delicha Employee of: Novartis Pharma AG, Z. Tallocozy Shareholder of: Novartis, Employee of: Novartis Pharmaceuticals Corporation, B. Porter Shareholder of: Novartis, Employee of: Novartis Pharmaceuticals Corporation

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SAT0269

### THE EFFECT OF BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS IN TARGETING DISEASE REMISSION IN AXIAL SPONDYLOARTHRITIS (AXSPA): A SYSTEMATIC LITERATURE REVIEW

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**Background:** The treat-to-target concept is currently recommended in axSpA management and remission is the main objective of treatment. Although consensual definitions of remission are lacking, most authors assume remission as a state of inactive disease or, alternatively, of low disease activity, as a near concept. In current practice, ASAS-Partial Remission (ASAS-PR) and ASDAS-Inactive Disease (ASDAS-ID) scores have gained wide acceptance as clinical remission-like definitions.

**Objectives:** In this review we assessed the efficacy of different biologic disease-modifying anti-rheumatic drugs (bDMARD) in achieving ASAS-PR or/and ASDAS-ID as remission-like primary outcomes. Data from randomised controlled trials (RCT) conducted in radiographic axSpA (r-axSpA) and non-radiographic axSpA (nr-axSpA) patients were included.

**Methods:** A systematic literature review was performed using the MEDLINE database (August 17 2017) with the filters “published in the last 10 years” and “humans”. The PICO (P, population; I, intervention; C, comparison; O, outcome) concept was used to perform the analysis according to: Patients – adults (>18 years old) with r-axSpA or nr-axSpA; Intervention – any bDMARD regardless of formulation or duration; Comparison – placebo and/or any different drug; Outcomes: ASAS-PR and ASDAS-ID.

**Results:** After screening 557 references (after de-duplication), 7 RCTs fulfilled the inclusion criteria, all concerning tumour necrosis factor inhibitors (TNFi) bDMARDs – table 1. ASAS-PR was the most commonly used remission-like definition in 6 of the 7 trials, 1 of those as a composed measure with a magnetic resonance score. Despite different baseline populations (including r-axSpA and nr-axSpA), all these trials provide evidence of TNFi efficacy in achieving remission. The proportion of patients achieving ASAS-PR and ASDAS-ID varied between 33%–61.9% and 27.3%–55%, respectively, with a minimum and maximum follow-up periods of 28 to 254 weeks for ASAS-PR and 24 weeks to 5 years for ASDAS-ID.

Abstract SAT0269 – Table 1. bDMARD trials addressing ASAS-PR or ASDAS-ID as primary outcomes

Reference	Phenotype	Study design and duration	Drug (number of patients enrolled)	Primary Outcome	Results
Braun, 2008	r-axSpA	Extension 254 weeks	IFX/IFX vs PBO/IFX (38)	ASAS-PR	34.2% of patients achieved ASAS-PR
Sieper, 2012	r-axSpA and nr-axSpA	RCT 28 weeks	NPX + PBO (51) vs NPX + IFX (105)	ASAS-PR	ASAS-PR in 61.9% NPX+IFX vs 35.3% NPX+PBO (p<0.05)
Sieper, 2013	r-axSpA and nr-axSpA	Extension 52 weeks	NPX (40) vs no treatment (40) after partial remission under IFX+NPX or NPX+PBO	ASAS-PR	No statistically significant differences between the groups
Davis, 2008	r-axSpA	Extension 192 weeks	ETN/ETN (128) vs PBO/ETN (129)	ASAS-PR	44% of patients achieved ASAS-PR
Song, 2012	nr-axSpA	RCT (first part) 48 weeks	ETN (40) vs SSZ (36)	ASAS-PR plus MRI remission	ASAS-PR+MRI remission in 33% ETN vs 11% SSZ (p<0.05)
Sieper, 2011	r-axSpA	RCT and Extension 5 years	ADA/ADA vs PBO/ADA (311)	ASAS-PR and ASDAS-ID	ASAS-PR in 45% ASDAS-ID in 55%
van Heijde, 2014	r-axSpA	RCT (first part) 24 weeks	GOL (278) vs PBO (78)	ASDAS-ID	ASDAS-ID in 27.3% GOL vs 2.8% PBO (p<0.001)

Legend : ADA: adalimumab; ASAS-PR: ASAS-Partial Remission; ASDAS-ID: ASDAS Inactive Disease; ETN: etanercept; GOL: golimumab; IFX: infliximab; MRI: magnetic resonance image; NPX: naproxen; nr-axSpA: non-radiographic axial spondyloarthritis; PBO: placebo; r-axSpA: radiographic spondyloarthritis; RCT: randomised controlled trial; SSZ: sulfasalazine, vs – versus

**Conclusions:** Clinical trials addressing remission-like concepts as primary outcomes are scarce. ASAS-PR score was the most commonly used remission outcome. Depending on the studies, between one third to one half of patients treated with TNFi achieved ASAS-PR or ASDAS-ID. Considering nowadays aimed treatment targets, these data raise the unmet need for improved treatment options and strategies, that favour optimised remissions rates in axSpA patients.

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SAT0270

**LOW INCIDENCE OF BOTH NEW-ONSET AND FLARES OF UVEITIS IN SECUKINUMAB-TREATED PATIENTS WITH ANKYLOSING SPONDYLITIS: CLINICAL TRIAL AND POST-MARKETING SAFETY ANALYSIS**

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**Background:** Uveitis, a common extra-articular manifestation of SpA, has an estimated prevalence in patients (pts) with ankylosing spondylitis (AS) of 33.2%, which increases with disease duration and positive HLA-B27 status.<sup>1</sup> Uveitis occurs in 10%–50% of SpA pts.<sup>1</sup> The exposure-adjusted incidence rate [EAIR] of uveitis (combined new-onset and flares) reported in AS pts treated with TNF inhibitors is 2.6–3.5 per 100 patient-years (pt-yrs).<sup>2–5</sup>

**Objectives:** To assess the incidence of uveitis in secukinumab-treated AS pts in long-term pooled clinical data from three phase 3 trials (MEASURE 1–3 [NCT01358175, NCT01649375, NCT02008916]) and from post-marketing analyses.

**Methods:** Analysis included pooled pt-level data from all pts in MEASURE 1 who received any dose ( $\geq 1$ ) of secukinumab up to the last pt attending Week 156 study visit, and up to visit Week 156 in MEASURE 2 and visit Week 104 in MEASURE 3 for each patient, respectively. Post-marketing data were from the most recent periodic safety surveillance report. Incidence of uveitis is reported as EAIR per 100 pt-yrs of secukinumab exposure.

**Results:** In the phase 3 AS clinical trials, 135 (17%) pts reported pre-existing (but not active or ongoing) uveitis at baseline and 589 (74.2%) pts were HLA-B27 positive. The EAIR for uveitis was 1.4 per 100 pt-yrs over the entire treatment period (n=794). Among all cases of uveitis (n=26), 14 (54%) were flares in pts with a history of uveitis at baseline (Table). The EAIR of uveitis in the post-marketing data (based on cumulative secukinumab exposure of 96 054 pt-yrs) was 0.03 per 100 pt-yrs.

**Abstract SAT0270 – Table 1.** Safety Analysis for Uveitis with Secukinumab in AS

**Data from Clinical Studies**

Number of clinical studies/pts included	3/794
Uveitis cases reported, n (%)	
Total	26 (3.3%)
New onset cases	14 (1.8%)
Treatment discontinuation	2 (0.3%)
Treatment interruption	1 (0.1%)
EAIR (95% confidence interval) per 100 pt-yrs <sup>a</sup>	1.4 (0.9–2.0)
<b>Post-Marketing Data<sup>b</sup></b>	
Cumulative estimated market experience (pt-treatment yrs) <sup>c</sup>	96 054
Cumulative number of cases reported	29
Crude incidence rate per 100 pt-yrs	0.03

<sup>a</sup>Rates are for uveitis MedDRA preferred term

<sup>b</sup>Data from the periodic safety update report (PSUR) dated 10th August 2017 – includes all indications

<sup>c</sup>Estimated based on cumulative worldwide sales volume and the average maintenance dose

**Conclusions:**

In secukinumab-treated pts with active AS, a low incidence of uveitis was observed, including new-onset cases and flares, in both clinical trials and post-marketing analyses.

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**Disclosure of Interest:** A. Deodhar Grant/research support from: AbbVie Inc., Eli Lilly, GSK, Janssen, Novartis, Pfizer Inc., UCB, Consultant for: AbbVie, Eli Lilly, Janssen, Novartis, Pfizer, UCB, C. Miceli-Richard Grant/research support from: Pfizer, Roche, UCB, Wyeth, Merck, Consultant for: Abbott/AbbVie, Bristol-Myers Squibb, Novartis, Merck, Pfizer, Wyeth, Speakers bureau: Abbott, Bristol-Myers Squibb, Merck, Pfizer, Roche, Schering-Plough, Wyeth., X. Baraliakos Grant/research support from: AbbVie, BMS, Celgene, Chugai, MSD, Novartis, Pfizer, UCB, Consultant for: AbbVie, BMS, Celgene, Chugai, MSD, Novartis, Pfizer, UCB, Speakers bureau: AbbVie, BMS, Celgene, Chugai, MSD, Novartis, Pfizer, UCB, H. Marzo-Ortega Grant/research support from: Janssen and Pfizer, Consultant for: AbbVie, Celgene, Janssen, Novartis and UCB, Speakers bureau: AbbVie, Celgene, Janssen and UCB, D. Gladman Grant/research support from: Amgen, AbbVie, BMS, Celgene, Eli Lilly, Janssen, Novartis, Pfizer and UCB., Consultant for: Amgen, AbbVie, BMS, Celgene, Eli Lilly, Janssen, Novartis, Pfizer and UCB., R. Martin Shareholder of: Novartis, Employee of: Novartis, J. Safi Jr Shareholder of: Novartis, Employee of: Novartis, B. Porter Shareholder of: Novartis, Employee of: Novartis, A. Shete Shareholder of: Novartis, Employee of: Novartis

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SAT0271

**SECUKINUMAB, A FULLY HUMAN ANTI-INTERLEUKIN-17A MONOCLONAL ANTIBODY, EXHIBITS LOW IMMUNOGENICITY IN PATIENTS WITH PSORIATIC ARTHRITIS AND ANKYLOSING SPONDYLITIS DURING A 52-WEEK TREATMENT PERIOD**

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**Background:** Secukinumab (SEC), a fully human monoclonal antibody (mAb) that selectively targets IL-17A, is highly efficacious for the treatment of psoriatic arthritis (PsA) and ankylosing spondylitis (AS). mAb therapies may be associated with immunogenicity (IG) and production of anti-drug antibodies (ADAs) that may cause adverse events (AEs), and affect drug pharmacokinetics (PK) and clinical response.

**Abstract SAT0271 – Table 1.** Overview of pts with TE-ADA<sup>1</sup>

PsA studies	Study	SEC dose	Prior biologics	ADA (titer)/ Neut-Ab	AE IG related	Impact on efficacy <sup>2</sup>	PK behaviour <sup>3</sup>
	F2306	PBO-75 mg	0	W24 (no titer)/Y	N	None	Normal
	F2312	PBO-150 mg	0	W52 (2.99)/N	N	None	Normal
	F2318	150 mg	Infliximab	W52 (2.14)/N	N	None	Normal
		150 mg	0	W24 (1.00)/N	N	None	Normal
		150 mg	0	W52 (2.59)/N	N	None	Normal
<b>AS studies</b>	F2305	10 mg/kg–150 mg	0	W52 (2.39)/N	N	None	Normal
		PBO-150 mg	0	W52 (10.61)/N	N	None	Normal
	F2310	PBO-75 mg	0	W52 (39.39)/N	N	None	Normal
	F2314	PBO-300 mg	0	W52 (1.02)/N	N	None	Normal
	F2320	150 mg	0	W16 (6.35)/N	N	None	Normal
		150 mg	0	W52/ (2.96)/N	N	None	Normal
		No Load	0	W16 (2.70)/N	N	None	Normal
		150 mg	0	W24/ (2.80)/N	N	None	Normal
		PBO–150 mg	0	W52/ (2.89)/N	N	None	Normal

Neut-Ab=neutralising antibodies; PBO, placebo; Y, yes; N, No. <sup>1</sup>Only positive ADA results at the respective study week are shown; <sup>2</sup>Impact on efficacy is defined as: PsA, failure to achieve >20% reduction, compared to baseline, in both tender and swollen joint counts; AS, failure to achieve ASAS20, after previously achieving such improvement for at least 2 consecutive visits prior to the first detection of ADA; <sup>3</sup>Normal PK: Concentrations in ADA-positive pts within observed range for all pts without ADA

**Objectives:** To assess the IG of SEC in PsA and AS patients (pts) treated with SEC for up to 52 weeks (W).

**Methods:** IG in pts with PsA (FUTURE 1–3 studies, n=1414) and AS (MEASURE 1–4 studies, n=1163) exposed to SEC was evaluated at baseline (BL) and at W 12, 16 (AS only), 24 and 52. Treatment emergent (TE)-ADA were defined as a positive ADA signal in  $\geq 1$  post-treatment sample in pts negative at BL. TE-ADA positive samples were analysed for drug-neutralising potential, SEC impact on PK, IG-related AEs and TE-ADA impact on efficacy through W52.

**Results:** Of 1414 treated PsA and 1163 treated AS pts with samples for IG evaluation, 5 (0.35%) and 8 (0.68%) developed TE-ADAs respectively, over 52 weeks (Table). All but 1 PsA pt were biologic naïve; 2/5 PsA and 1/8 AS pts received concomitant methotrexate, 2/8 AS pts received concomitant sulfasalazine. Associations between TE-ADAs and SEC dose, frequency or mode of administration were not observed. Other than 1 PsA pt, all TE-ADAs were non-neutralising and none were associated with any IG-related AE. All TE-ADAs were associated with normal PK and none were associated with loss of SEC efficacy over 52 weeks.

**Conclusions:** SEC treatment was associated with a low incidence of IG in PsA and AS pts, as shown by TE-ADA detection in only 0.35% PsA pts and 0.68% AS pts over 52 weeks in a database of >2500 pts, which is consistent with the low incidence of IG (0.4%) seen with SEC in pts with plaque psoriasis.<sup>1</sup>

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SAT0272

#### DO TNF INHIBITORS IMPACT THE COMORBIDITIES AND EXTRA-ARTICULAR MANIFESTATIONS, AND THEREBY ALTER THE NATURAL HISTORY OF ANKYLOSING SPONDYLITIS?

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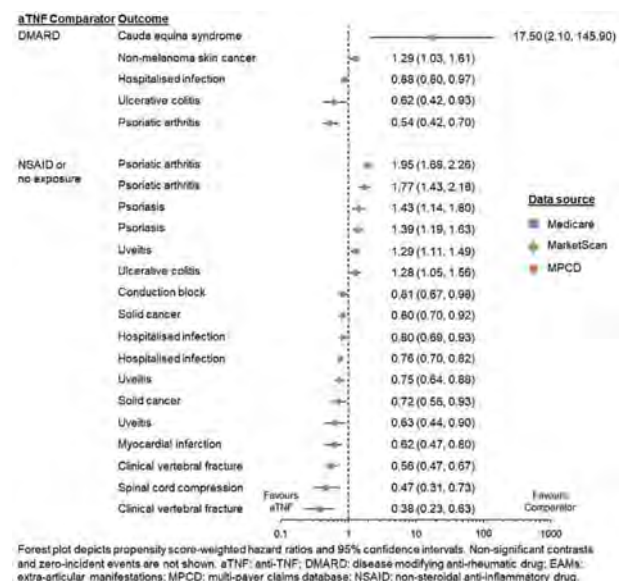
**Background:** Anti-tumour necrosis factor (anti-TNF) treatment has led to reduction in signs and symptoms, and improvements in physical function and quality of life in ankylosing spondylitis (AS) patients (pts). Whether anti-TNFs impact the incidence of AS-related comorbidities and extra-articular manifestations (EAMs) is not known.

**Objectives:** To evaluate the incidence and prevalence of AS-related comorbidities and EAMs in AS pts in the US.

**Methods:** This was a retrospective cohort study of 3 commercial insurance claims databases (Multi-Payer Claims Database [MPCD 2007–2010], Truven MarketScan [2010–2014], and US Medicare Fee-for-Service Claims [2006–2014]) to evaluate EAMs (uveitis, psoriasis, inflammatory bowel disease) and physician-diagnosed comorbidities (cardiac, renal, pulmonary, neurologic) in AS pts diagnosed by a rheumatologist (index date), having 6 months' baseline data prior to the index date, and drug-specific exposures after AS diagnosis (ICD-9 720.0). Three mutually exclusive hierarchical exposure groups were examined (low to high):<sup>1</sup> no therapy or prescription NSAIDs;<sup>2</sup> conventional DMARDs;<sup>3</sup> anti-

TNFs. Prevalence of comorbidities was ascertained in a 12 month period (6 months pre- and post-index date). Incidence of comorbidities and EAMs was assessed during the period between treatment initiation and the earliest of death, loss of medical coverage, end of study, first outcome occurrence, treatment discontinuation or initiation of therapy at a higher level in exposure hierarchy. Pts with a history of prior events (except infections) were excluded from the incidence assessment for that event. Hazard ratios comparing anti-TNFs vs DMARDs and NSAIDs/no therapy were estimated using inverse probability treatment weighted Cox proportional hazards models.

**Results:** A total of 37,566 AS pts were included. Prevalence of AS in the MPCD population was 0.26% and in the Medicare population was 1.21%. As expected, comorbidities were more common in Medicare AS pts vs those in MPCD or MarketScan databases in all exposure groups. The propensity score-weighted incidences of solid cancers, myocardial infarction, conduction block, cord compression and vertebral fractures were lower in anti-TNF treated pts vs those treated with NSAIDs or DMARDs alone, although anti-TNF treated Medicare pts had a higher incidence of EAMs such as psoriatic arthritis, uveitis and ulcerative colitis (figure 1).



Abstract SAT0272 – Figure 1. Propensity score-weighted hazard ratios of physician-diagnosed outcomes and EAMs by treatment exposures

**Conclusions:** This investigation of the prevalence and incidence of comorbidities and EAMs of AS in US pts suggests that anti-TNF use is associated with a lower incidence of some comorbidities, and a trend of higher incidence of EAMs, which may reflect channelling of more severe AS pts to anti-TNFs. Although results vary somewhat by data source and may be explained by different baseline characteristics (e.g. Medicare pts were older), our results suggest that anti-TNF use is associated with lower incidence of those comorbidities that confer substantial morbidity in AS.

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SAT0273

### GOLIMUMAB RETENTION RATE IN PATIENTS WITH SPONDYLOARTHRITIS. DIFFERENCES BETWEEN ANKYLOSING SPONDYLITIS AND NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS

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**Background:** The efficacy of Golimumab treatment in spondyloarthritis (SpA) has been widely documented.

**Objectives:** The aim of this study was to analyze the long-term retention rate of Golimumab and to identify independent predictors of retention in patients with SpA.

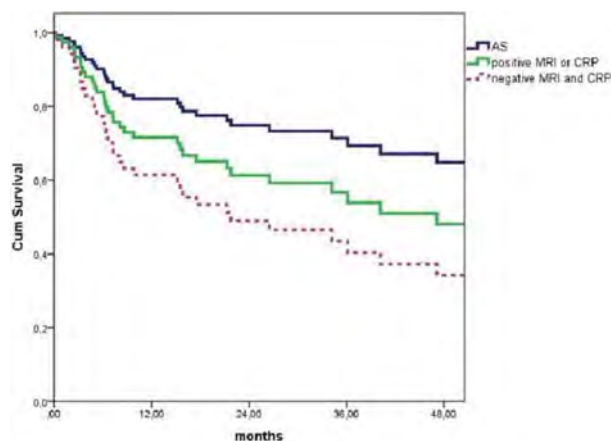
**Methods:** Prospective monocentric cohort of SpA patients treated with Golimumab according with clinical practice. Study was approved by local Ethics Committee. Demographic and clinical variables were analysed with Cox proportional hazard regression model.

**Results:** 105 patients were included, 49 (46.7%) Ankylosing Spondylitis (AS), 40 (38.1%) non-radiographic axial SpA (nr-AxSpA) and 16 (15.2%) peripheral SpA. The baseline characteristics of the patients are shown in table 1. Follow-up time was 206.6 patients-year. Mean survival time was 47.2 months (95% CI: 39.4–54.9). Age, gender, HLA-B27, radiographic or nr-AxSpA and previous biological use were significant in the univariate analysis. Concomitant DMARD had no influence on Golimumab retention rate (HR: 1.2; 95% CI: 0.6–2.4; p: 0.6).

**Abstract SAT0273 – Table 1.** Baseline demographic and clinical characteristics of the patients.

	All (axial and peripheral SpA)	AS	nr-AxSpA
Age -mean (SD)-years	45.1 (13.2)	51.1 (10.8)	39,8 (10.1)
Male gender (%)	52 (49.5%)	30 (61.2%)	19 (47.5%)
Mean evolution time (SD)- years	11.8 (12.3)	18.8 (10.1)	7.3 (10.3)
Positive HLA-B27 (%)	73 (69.6%)	44 (90.7%)	21 (52.6%)
Uveitis (%)	17 (16.2%)	12 (24.5%)	4 (10.0%)
Back pain -mean (SD)	7.5 (7.0)	6.5 (2.4)	9.1 (10.7)
BASDAI -mean (SD)	6.2 (1.6)	6.3 (2.1)	6.2 (1.2)
BASFI -mean (SD)	5.8 (2.3)	6.0 (2.4)	5.4 (2.1)
CRP mg/dl – mean (SD)	1.1 (1.7)	1.5 (2.1)	0.65 (1.4)
Concomitant DMARD (%)	31 (29.8%)	15 (31.3%)	3 (7.5%)
Biological Therapy naive (%)	48 (45.7%)	15 (30.6%)	24 (60%)

Golimumab retention rate of patients with nr-AxSpA and objective inflammation (positive MRI or CRP) was not different compared to AS patients (p=0.19). Patients with nr-AxSpA without objective inflammation (negative MRI and CRP) had worse retention rate compared to AS patients (HR: 2.47; 95% CI: 1.09–5.57; p<0.03), figure 1. There was a numerically better Golimumab retention rate in patients treated previously with less number of biologicals, but did not reach statistical significance. 39/105 patients (37%) withdrew Golimumab treatment. 26/39 (66.7%) due to lack of efficacy, 6/39 (15.4%) due to adverse events and 7/39 (17.5%) due to other reasons.



**Abstract SAT0273 – Figure 1.** retention rate

**Conclusions:** Real-world Golimumab retention rate in patients with Spondyloarthritis was good and did not depend on concomitant treatment with DMARD. Patients with Ankylosing Spondylitis and non-radiographic axial SpA with objective inflammation had a better Golimumab retention rate than patients with non-radiographic axial SpA without objective inflammation. A better retention rate was expected in patients who had previously used less biological, but was not found.

**Disclosure of Interest:** None declared

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SAT0274

### RETENTION RATES OF CERTOLIZUMAB PEGOL IN ANKYLOSING SPONDYLITIS AND NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS PATIENTS: HUR-BIO REAL LIFE RESULTS

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**Background:** Drug survival rate is generally accepted as a reliable indicator of both efficacy and safety profile of a biological DMARD.

**Objectives:** To evaluate survival rates of certolizumab-pegol (CZP) in ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nrAxSpA) patients registered in HUR-BIO (Hacettepe University Rheumatology Biologic Registry).

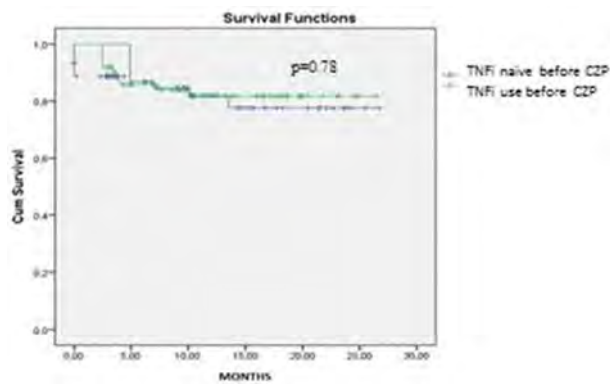
**Methods:** HUR-BIO is a monocentric database of biologics including 2058 SpA patients (226 were prescribed CZP) by June 2017. All AS (n=142) and nrAxSpA (n=54) patients in HUR-BIO prescribed CZP at least once were enrolled in the study. Twenty-three patients who was already on CZP before admitting Hacettepe University were excluded. Patients prescribed CZP within 6 months period before analysis defined as drug continuing. Demographic, clinical and laboratory data of AS and nrAxSpa patients were evaluated. Kaplan-Meier analysis was used to estimate CZP survival rates.

**Results:** In total, 124 AS and 49 nrAxSpA patients were analysed. Baseline characteristics of patients were shown in Table. Median duration of CZP usage was 7.54 (3–26.5) months in AS and 6.27 (3–26.7) months in nrAxSpA group (p=0.53). CZP survival was similar between AS and nrAxSpA patients (figure 1). Forty-nine (27.2%) patients had used at least one TNFi and 38 (21.9%) patients had used more than one TNFi before CZP. There was no difference in drug survival between those who used TNFi and those who did not use TNFi before CZP (figure 2). BASDAI 50 response was reached in 27.6% of AS and 36.0% of nrAxSpA patients and at the last control visit (p=0.44).

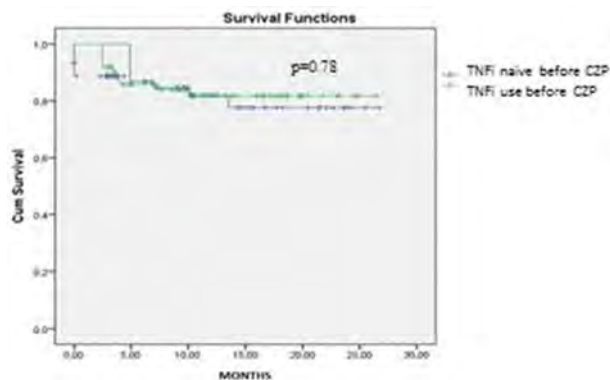
**Abstract SAT0274 – Table 1.** Baseline demographic and clinical characteristics of patients.

	AS	nrAxSpA	p
Age, years (min-max)	36.5 (18–60)	32 (18–54)	0.041
Male, n (%)	58 (46.8)	21 (42.9)	0.641
Female, n (%)	66 (53.2)	28 (57.1)	
Disease duration, months (min-max)	48 (3–312)	24 (3–144)	0.011
Disease duration ≥ 5 years, n (%)	59 (47.6)	16 (32.7)	0.07
History of smoking, n (%)	79 (63.7)	26 (53.1)	0.196
History of uveitis, n (%)	9 (7.3)	3 (6.1)	0.791
Previous biological use, n (%)	59 (47.6)	26 (53.1)	0.516
Baseline BASDAI	57 (4–100)	57 (0–94)	0.495
Baseline BASFI	41 (0–100)	42 (0–94)	0.422
Baseline back pain VAS	70 (0–100)	70 (10–100)	0.961
ESR, mm/h (min-max)	15 (2–105)	13 (2–97)	0.177
CRP, mg/dL (min-max)	0.83 (0.1–18.2)	0.91 (0.1–8.32)	0.810
ESR > UL, n (%)	48 (39.7)	14 (29.8)	0.286
CRP > UL, n (%)	64 (52.9)	25 (54.39)	0.866
Syndesmophytes on X-ray, n (%)	21 (16.9)	3 (6.1)	0.064





Abstract SAT0274 – Figure 1. CZP survival in AS and nrAxSpA patients



Abstract SAT0274 – Figure 2. CZP survival in patients with and without history of TNFi use before CZP

**Conclusions:** In this single centre biological SpA cohort, adherence to CZP therapy seems to be high with a first year survival rate of 83% and there was no difference between AS and nrAxSpA patients.

**Disclosure of Interest:** None declared

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#### SAT0275 VITAMIN D INSUFFICIENCY IS ASSOCIATED WITH VERTEBRAL FRACTURES IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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**Background:** Vitamin D insufficiency is common in general population, and it has been associated with the development and activity of several diseases, such as cardiovascular and autoimmune diseases. In patients with axial spondyloarthritis (axSpA) vitamin D (25(OH)D) insufficiency has been associated with disease activity, but studies in these patients that associate 25(OH)D insufficiency with vertebral fractures (VF) are scarce.

**Objectives:** To evaluate the associations between 25(OH)D levels and VF, as well as the 10 year-estimated risk (FRAX) and low bone mineral density (BMD), in patients with axSpA.

**Methods:** Cross-sectional study of patients with axSpA (ASAS criteria); 25(OH)D insufficiency when <30 ng/mL and BMD measured by Lumbar spine (LS) and femoral neck (FN) Dual X-ray absorptiometry (DXA). Evaluation of VF with semi-quantitative method (Genant) in thoracolumbar X-rays. Bivariate and multivariate analyses performed, and p values <0.05 considered significant.

**Results:** We included 206 axSpA patients (70% male; 86% AS714% nr-axSpA); age 52±14 and disease duration 12.9±10.3 years; ASDAS-CRP 2.2±0.9, ASDAS-ESR 2.5±0.9; total mSASSS 20.5±19.1 and 25(OH)D levels 19.8±9.3 ng/mL (all values are mean ±SD); with 85.7% of the patients having insufficiency; VF were observed in 34% of the patients. The prevalence of low BMD was higher in FN 45.2% (z-score) and 28.9% (t-score) than in LS 25.7% (z-score) and 29.9% (t-score).

These differences were even higher when 25(OH)D insufficiency was also present (table).

In multivariate analysis, 25(OH)D was associated with FN BMD (p=0.001); without association with LS BMD. Vitamin D insufficiency was directly associated with the presence of VF [OR 0.95 (95%CI 0.86–0.98); p=0.029] and a higher 10 year-estimated risk of fracture (major FRAX [OR 0.92 (95%CI 0.81–0.96); (p=0.036)].

Differences between axSpA patients with/without 25(OH)D insufficiency			
	Insufficiency	No insufficiency	p value
Patients (%)	85.7%	14.3%	
Vertebral fractures (%)	38.7%	32.48%	p=0.049
FRAX major	8.7±6.7	7.5±6.4	p=0.036
BASDAI	4.2±2.2	3.1±1.3	p=0.003
BASFI	3.8±2.5	3.0±2.4	p=0.000
ASDAS-CRP	2.21±0.15	1.89±0.16	p=0.003
ASDAS-ESR	2.72±0.21	2.19±0.25	p=0.002
Low FN BMD (%)	56.4%	44.6%	p=0.014
FN t-score	0.80±0.31	0.92±0.44	p=0.002
FN z-score	0.84±0.28	0.9±0.31	p=0.002

Values are mean ±standard deviation (SD) unless otherwise specified.

**Conclusions:** In patients with axSpA, vitamin D insufficiency is even more generalised than in general population. Low 25(OH)D is associated with lower FN BMD and more vertebral fractures, as well as increased disease activity and disability. Vertebral fractures are a serious complication of axSpA, so 25(OH)D insufficiency should be taken into account in the management of the comorbidities of the patients with axial spondyloarthritis.

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**Disclosure of Interest:** None declared

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#### SAT0276 UVEITIS DURING ANTI-TNF THERAPY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: A PARADOXICAL EVENT OR DISEASE MANIFESTATION?

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**Background:** Although widely recognised as extra-articular manifestations of axial spondyloarthritis (axSpA), uveitis developing throughout anti-TNFα treatment is difficult to be classified as disease related or paradoxical event.

**Objectives:** We aimed to evaluate the incidence of new onset or relapsing uveitis in patients with axSpA receiving TNF inhibitors.

**Methods:** We performed a cross-sectional retrospective study evaluating 126 consecutive active axSpA exposed to TNFα inhibitors according to the local recommendations, followed-up in a single rheumatology department. Patients identified with uveitis were systematically assessed based on a predefined protocol comprising (i) *data about uveitis* (de novo or flare; unique episode or recurrence; acute or chronic; anterior, posterior, intermediary or panuveitis; uni or bilateral; outcomes), (ii) *responsible medication* (drug exposure prior to uveitis, biologic-naïve or experimented axSpA, continuation or switching to another biologic) and (iii) *rheumatic condition* (activity, response to treatment, extra-articular manifestations, disease duration).

**Results:** 91 biologic naïve axSpA and 35 receiving more than one anti-TNFα were recruited; among them, 318 patient-years exposed to etanercept, 225.37 patient-years to adalimumab, 113.52 patient-years to infliximab, 30.49 patient-years on golimumab. A history of uveitis was found in 27.77% (35 cases).

We reported 12 patients developing at least one episode of uveitis during biologic treatment (7 de novo, 10 recurrent uveitis); etanercept was mostly associated with uveitis (8 episodes, 2.51 per 100 patient-years), but also monoclonal antibodies, 3 with golimumab (9.83 per 100 patient-years), 2 under infliximab (1.76 per 100 patient-years), surprisingly, 3 with adalimumab (1.33 per 100 patient-years). Only 3 axSpA had uveitis before starting anti-TNFs.

Uveitis was described irrespective of the prior exposure to biologics, mainly in biologic-naïve patients, aged between 26 and 72, with disease duration of 6 to 38 years, occurring any-time during biologics (2–116 months). Acute anterior uveitis was commonly reported, only one case of complicated panuveitis.

3 cases (one infliximab, two golimumab) had benefit with switching to another TNF blocker, but in most reported cases uveitis was solved without anti-TNFα

interruption. Further, continuation of the same anti-TNF $\alpha$  did not cause relapse in some cases.

The underlying SpA was well controlled (ASDAS-CRP) when uveitis, patients being classified as responders compared to previous visit, suggesting paradoxical uveitis.

**Conclusions:** Although rare, new onset or flare of uveitis may occur during anti-TNF therapy in axSpA. Surprisingly, not only TNF receptor but also monoclonal antibodies were responsible, etanercept being involved mainly in new onset uveitis.

**Disclosure of Interest:** None declared

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### SAT0277 IMMUNOGENICITY AND LOSS OF RESPONSE TO TNF INHIBITORS IN AXIAL SPONDYLOARTHRITIS: RESULTS FROM AN OBSERVATIONAL COHORT STUDY

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**Objectives:** We aimed to evaluate the immunogenicity of TNF- $\alpha$  inhibitors and to assess potential influence on serum drug levels and clinical efficacy in patients with axial spondyloarthritis (axSpA).

**Methods:** We performed a cross sectional observational cohort study in 87 consecutive axSpA receiving anti-TNFs (either for the first time or switched), followed-up in a single outpatient rheumatology department. Treatment with anti-TNF agents was recommended in accordance with the local regulations on the initiation and continuation of biologics, as well as ASAS/EULAR guidelines.

Disease activity scores were assessed at baseline (V1) and study visit (V2), while drug trough levels and anti-drug antibodies were measured in serum samples (ELISA, Progenika) and collected before the next administration as a single-point data. Serum drug levels were considered positive if >0.035  $\mu$ g/mL IFX, >0.024  $\mu$ g/mL ADL and >0.035  $\mu$ g/mL ETN, while the cut-offs for anti-IFX was 5AU/mL, anti-ADL 10AU/mL, anti-ETN 142 AU/mL. Statistical analysis was performed using SPSS version 19.0, p<0.05.

**Results:** Among 150 axSpA treated with TNF inhibitors in our centre, 28 (32.18%) receiving adalimumab (ADL), 19 (21.83%) infliximab (IFX) and 40 (45.97%) etanercept (ETN) were included in the immunogenicity analysis. Only 11 patients (12.64%) developed anti-drug antibodies, 8 under ADL (28.57%) and 3 under IFX (15.78%), with significant decrease in drug levels (3.97  $\mu$ g/mL vs. 0.07  $\mu$ g/mL ADL, p<0.05; 1.82  $\mu$ g/mL vs. 0.05  $\mu$ g/mL IFX, p<0.05) and impact on disease outcomes (p<0.05).

Higher disease activity scores (BASDAI, ASDAS-CRP) were reported in anti-drug positive axSpA irrespective of the background therapy (p<0.05), with more patients classified as being in a high or very high disease activity status at V2. Furthermore, a relation between clinical improvement (change in ASDAS) and immunogenicity was reported: positive anti-drug antibodies axSpA achieved worse clinical response than negative anti-drug antibodies cases, with a significant association between ADL respectively IFX levels and ASDAS (p<0.05).

No anti-drug antibodies were found in patients treated with ETN; significant higher persistence on ETA than under monoclonal antibodies was registered in our axSpA (p<0.05).

**Conclusions:** Immunogenicity may impact disease outcomes and drug survival, particularly in the adalimumab and infliximab treated axSpA. Measuring anti-drug antibodies and serum drug levels may help to optimise therapeutic strategies in selected patients.

**Disclosure of Interest:** None declared

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### SAT0278 NSAIDS REDUCES RADIOGRAPHIC PROGRESSION IN SACILOIAC JOINTS IN EARLY AXIAL SPONDYLOARTHRITIS

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**Background:** According to the ASAS-EULAR management recommendations for axial spondyloarthritis (axSpA) patients (pts) suffering from pain and stiffness should use an NSAIDs as first-line drug and for pts who respond well to NSAIDs continuous use is preferred if symptomatic otherwise. Two studies have suggested that the continuous use of NSAIDs in patients with an elevated CRP results in reduced progression of structural damage in the spine in comparison to on-demand use.<sup>1,2</sup> But up-to-date the question of the effect of NSAIDs on radiographic progression in early axSpA remains open.

**Objectives:** To compare continuous and on-demand treatment groups on radiographic progression sacroiliac joints (SIJ) in axSpA.

**Methods:** The research included 68 pts with early axSpA<sup>ASAS criteria, 2009</sup> from Moscow CORSAR cohort with disease duration <5 years, age onset <45 years and at least 2 years follow up (FUP). 33 (48,5%) males, pts mean age was 28,5 (5,8) y., average disease duration – 24,1 (15,4) mo, 63 (92,6%) pts were HLA-B27 positive. Pts were randomised into two treatment groups: group 1 – continuous uses of NSAIDs; group 2 – on-demand uses of NSAIDs. The dosages of NSAIDs accounted by the ASAS NSAID index. At baseline 6 pts received TNF inhibitors, after 2 y. FUP 14 pts receives TNF inhibitors.

**Results:** No significantly differences in axSpA disease activity between two groups at baseline (table 1) and after 2 y. FUP (table 2). At group №1 8,2% pts had radiographic progression in SIJ (from nr-axSpA to AS), at group №2%–13,3% pts (p=0,000).

**Abstract SAT0278 – Table 1.** Outcome parameters at baseline.

	Group №1 (n=31)	Group №2 (n=31)	p
Ankylosing spondylitis, n,%	22 (70,9%)	15 (50,0%)	0088
Non-radiographic axSpA, n,%	9 (29,1%)	17 (50,0%)	0257
ASDAS CRP, Me, [25%; 75%]	2,5 <sup>1,5</sup> ; 3,5	2,3 <sup>1,2</sup> ; 2,7	0300
BASDAI, Me, [25%; 75%]	4,0 <sup>2,4</sup> ; 5,1	2,8 <sup>1,5</sup> ; 4,4	0299
CRP, Me, [25%; 75%]	5,1 <sup>1,7</sup> ; 20,0	4,5 <sup>1,0</sup> ; 12,8	0648
BASFI, Me, [25%; 75%]	1,4 [0,5; 2,5]	0,5 [0,2; 1,7]	0152
Positive MRI of the SIJs, n,%	22 (70,9%)	15 (50,0%)	0088
LEEDS score, Me, [25%; 75%]	1,0 [0; 3,0]	0,5 [0; 2,0]	0217

**Abstract SAT0278 – Table 2.** Outcome parameters after 2 years of NSAIDs treatment.

	Group №1 (n=24)	Group №2 (n=30)	p
Ankylosing spondylitis, n,%	19 (79,1%)	19 (63,3%)	0201
Non-radiographic axSpA, n,%	5 (20,9%)	11 (36,7)	0229
ASDAS CRP, Me, [25%; 75%]	1,2 [0,9; 2,4]	1,3 [0,7; 2,1]	0754
BASDAI, Me, [25%; 75%]	2,1 <sup>1,0</sup> ; 3,0	1,8 [0,9; 2,4]	0553
CRP, Me, [25%; 75%]	1,9 [0,85; 11,3]	1,3 [0,6; 5,0]	0292
BASFI, Me, [25%; 75%]	0,4 [0,1; 2,1]	0,1 [0; 0,4]	<b>0,0097</b>
Positive MRI of the SIJs, n,%	8 (33,3%)	8 (26,6%)	0573
LEEDS score, Me, [25%; 75%]	0 [0; 1,0]	0 [0; 2,0]	0571
NSAID index, Me, [25%; 75%]	100 <sup>58,5</sup> ; 100	28,5 <sup>10,7</sup> ; 75,0	<b>0,0012</b>

**Conclusions:** The frequency of NSAIDs treatment does not affect on the activity of axSpA. Continuously uses of NSAIDs reduces radiographic progression in sacroiliac joints in pts with early axSpA.

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### SAT0279 COMPARISON OF RETENTION RATES BETWEEN TUMOUR NECROSIS FACTOR-A INHIBITORS IN ANKYLOSING SPONDYLITIS PATIENTS: DATA FROM THE KOREAN COLLEGE OF RHEUMATOLOGY BIOLOGICS REGISTRY

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**Background:** Drug persistence of tumour necrosis factor-a inhibitors (TNFi) tends to be higher in patients with ankylosing spondylitis (AS) than rheumatoid arthritis but there are few studies of Asian AS patients in the literature.

**Objectives:** To investigate drug retention rates of various TNFi used in Korean AS patients.

**Methods:** Subjects were AS patients enrolled in the Korean College of Rheumatology Biologics registry<sup>KOBIO, Dec 2012 -</sup>). All approved and commonly prescribed TNFi were included in the analysis. Discontinuation was defined as switching or stopping the biologic agent. Kaplan-Meier curve and Cox proportional hazard model were used for further analysis. Reason of TNFi discontinuation was also assessed. Univariate and multivariate analyses were used to identify possible predictors of discontinuation.

**Results:** Data of total of 1005 AS patients were analysed (median follow-up period: 14 months). The mean age of patients was 40.7, and 77.4% were males. The mean disease duration was 7.1 years, HLA-B27 were positive in 82.4%, and 33.2% of patients had lesion(s) of syndesmophytes. Seventy-six percent of patients were first-time biologic users. Discontinuation of TNFi occurred in 24.2% (switching in 9.6%) of patients during follow-up. The drug survival function estimate showed that the adjusted hazard ratio (HR) of golimumab (compared with etanercept) was 0.441 (95% CI 0.277–0.703,  $p < 0.001$ ). The reason of discontinuation was inefficacy (32.6%), adverse events (23.6%), clinical improvement (11.2%), and others (32.6%). A multivariate analysis indicated predictors of discontinuation to be shorter disease duration (HR 0.973,  $p = 0.044$ ), and negative HLA-B27 (HR 1.623,  $p = 0.0093$ ).

**Conclusions:** Our study demonstrates that few AS patients switched to other TNFi during their course of treatment. The drug retention rate of golimumab was higher compared with other agents prescribed in Korean AS patients.

**Disclosure of Interest:** None declared

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SAT0280

### RAPAMYCIN RESTORES THE BALANCE BETWEEN TH17 AND REGULATORY T CELLS IN USPA PATIENTS

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**Background:** The association of undifferentiated spondyloarthritis (uSpA) with the imbalance of Th17/Treg cells is still unclear. By inhibiting mTOR, rapamycin promotes the proliferation of Treg cells and inhibits the growth of Th17 cells.

**Objectives:** Therefore, we aimed to investigate the status of Treg and Th17 cells in uSpA patients and explore the therapeutic effect of Rapamycin on uSpA patients with imbalanced of Th17 and Treg cells.

**Methods:** Two hundred thirty-seven new onset uSpA patients and 93 healthy controls were enrolled. These patients fulfilled ESSG criteria for SpA but did not fulfill the criteria for any established disease of the group. Both absolute numbers and proportions of Treg (CD4 +CD25+Foxp3+T) and Th17 (CD4 +IL-17+T) cells in peripheral blood were analysed by flow cytometry. The 21 new onset Patients with imbalance of Th17/Treg cells were treated with rapamycin at a dose of 0.5 mg twice for a weeks or every 2 days for 6 weeks combined with conventional treatment (salazosulfapyridine 500 mg three times per day; etoricoxib 60 mg once per day or other NSAIDs drugs).

**Results:** Increase in absolute number and percentage of Th17 (Th17% 1.11 ±0.66 vs 2.43±1.21,  $p < 0.05$ ; Th17 cells/μl 7.54±4.07 vs 19.54±18.45,  $p < 0.05$ ) and decrease in those of Tregs (Treg% 4.8±1.60 vs 3.35±1.76,  $p < 0.05$ ; Treg cells/μl (33.77±13.67 vs 27.79±28.62,  $p < 0.05$ ) were found in 18.6% (44/237) of patients with uSpA as compared with that of healthy controls. The patients with imbalance of Th17/Treg cells displayed higher BASDAI scores and ESR as compared with other uSpA patients [BASDAI (3.27±1.06 vs 1.13±0.91  $P < 0.05$ ); ESR (29.27±19.32 vs 21.80±18.34  $P < 0.05$ )]. The absolute count of Th17 in 21 patients received rapamycin reduced after 6 weeks (12.35±11.00 vs 6.69±5.54,  $p < 0.05$ ) whereas that of Treg cells showed increase trend but the difference did not reach statistical significance.

**Conclusions:** Absolute number of Treg decreased and that of Th17 cells increased in the peripheral blood of uSpA patients, suggesting that imbalance of the two subsets contributes to the pathogenesis of uSpA. Rapamycin recovered the balance between Th17 and Treg cells in uSpA patients by reducing Th17 cells.

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SAT0281

### BIOLOGICS IN SAPHO SYNDROME. A SYSTEMATIC REVIEW

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**Background:** The SAPHO (Synovitis, Acne, Pustulosis, Hyperostosis, Osteitis) syndrome is a relatively rare clinical entity characterised by a wide range of dermatological and musculoskeletal manifestations. Treatment is largely empiric since guidelines do not exist. Biologics have been used in cases refractory to conventional treatment.

**Objectives:** To systematically review all cases of patients with SAPHO syndrome treated with biologics to date.

**Methods:** We performed a systematic electronic search (PubMed) using the key words SAPHO combined with any of the following: treatment, biologics, anti-TNF, infliximab, adalimumab, etanercept, certolizumab, golimumab, IL-1, anakinra, canakinumab, IL-17, secukinumab, IL-23, ustekinumab, IL-6, tocilizumab, abatacept, rituximab. The only limit set was English language. The computerised search was supplemented by a manual one on the reference lists of the retrieved articles.

The search identified 461 articles; the abstracts of these articles were assessed in order to identify studies related to the therapeutic use of biologics in patients with SAPHO syndrome. Only 36 articles fulfilled the search criteria and were included in the analysis.

**Results:** We identified 64 cases treated with biologics (44 with TNF blockers, 7 with IL-1 blockers, 12 with biologics targeting the IL-23/IL-17 axis and 1 with tocilizumab). Data support a positive effect of anti-TNF treatment in SAPHO with a response rate in bone and joint manifestations of 95.4%. Skin disease also improved in 21/29 cases (response rate 72.4%). Data related to IL-1 inhibition in SAPHO are encouraging with most patients (6/7) exhibiting a significant response in musculoskeletal manifestations (response rate 85.7%). However, IL-1 inhibition is not effective in skin manifestations. Ustekinumab seems to have some efficacy with 2/4 patients responding in skin and 3/5 in bone/joint manifestations. Data related to IL-17 blockade indicate efficacy in skin disease with 4/7 patients responding (response rate 57.1%). Joint/bone manifestations improved in 2/7 patients (response rate 28.6%).

**Conclusions:** In SAPHO patients not responding to conventional treatment, TNF blockers should be the first choice. In patients failing TNF blockers, IL-1 inhibitors and biologics targeting the IL-17/IL-23 axis could be used.

**Disclosure of Interest:** None declared

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SAT0282

### OCCURRENCE OF ANTERIOR UVEITIS IN PATIENTS WITH SPONDYLOARTHRITIS AND PSORIATIC ARTHRITIS TREATED WITH TUMOUR NECROSIS FACTOR INHIBITORS: A RESTROSPECTIVE MONOCENTRIC STUDY COMPARING THE SOLUBLE RECEPTOR TO THE MONOCLONAL ANTIBODIES

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**Background:** The efficacy of tumour necrosis factor inhibitors against anterior uveitis has been shown, but discrepancies remain as to the difference in efficacy between soluble receptor and monoclonal antibodies.

**Objectives:** The objective of this study was to compare the occurrence of anterior uveitis with soluble receptor and monoclonal antibodies in patients with spondyloarthritis (SPA) and psoriatic arthritis (PA).

**Methods:** This was an observational, retrospective, monocentric study. Patients attending the rheumatology department of the Montpellier University Hospital for a SPA or a PA and who were prescribed anti-TNF agents between 2000 and 2014 were included in our cohort. Data on the diagnosis of rheumatism, the history of the disease and the extra-articular symptoms were collected from medical records. The risk of uveitis has been interpreted qualitatively (number of subjects with at least one flare of uveitis) and quantitatively (number of uveitis flares for each patient). Logistic regression models were used for qualitative analyses and Poisson models for quantitative analyses.

**Results:** 429 patients were included (302 with SPA and 127 with PA, 203 were treated with a monoclonal antibody as first TNF alpha inhibitor and 226 with the soluble receptor). No difference between monoclonal antibodies and soluble receptor was found in the risk of uveitis occurring during the first year of treatment (OR=0.94 [0.35; 2.54],  $p = 0.90$  in qualitative analysis and RR=0.62 [0.26; 1.46];  $p = 0.27$  in quantitative analysis). The risk of uveitis was higher with the soluble receptor for the first-line TNF inhibitors, as well as for all therapeutic lines, but this difference was not statistically significant ( $p = 0.09$  and  $0.08$  respectively in quantitative analysis and  $0.68$  and  $0.53$  in quantitative analysis).

**Conclusions:** In view of our observations, the risk of uveitis does not appear to be significantly higher with the soluble receptor than with the monoclonal



antibodies in SPA and PA, to recommend systematically the eviction of etanercept in subjects with a moderate risk of developing anterior uveitis.

**Disclosure of Interest:** None declared

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SAT0283

**SECUKINUMAB 150 MG PROVIDES SUSTAINED IMPROVEMENTS IN THE SIGNS AND SYMPTOMS OF ACTIVE ANKYLOSING SPONDYLITIS WITH HIGH RETENTION RATE: 4-YEAR RESULTS FROM THE PHASE III TRIAL, MEASURE 2**

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**Background:** Secukinumab, a fully human monoclonal antibody that neutralises IL-17A, has shown significant and sustained improvement in the signs and symptoms of active ankylosing spondylitis (AS) through 3 years in the MEASURE 2 study (NCT01649375).<sup>1</sup>

**Objectives:** To report the longer-term (4 year) efficacy and safety of subcutaneous (s.c.) secukinumab 150 mg in the MEASURE 2 study.

**Methods:** AS patients (pts; n=219) were randomised to receive s.c. secukinumab 150 mg, 75 mg or placebo at baseline, Weeks (Wks) 1, 2 and 3 and every 4 weeks from Wk 4. At Wk 16, placebo-treated pts were re-randomised to receive secukinumab 150/75 mg. Efficacy results are reported for pts initially randomised to secukinumab 150 mg and those who switched from placebo to secukinumab 150 mg at Wk 16. Safety analyses included all pts who received  $\geq 1$  dose of secukinumab. Results are reported as observed.

**Results:** The retention rate from Wk 16 to 208 was 85% (85/100) for secukinumab 150 mg. Sustained improvements were observed with secukinumab 150 mg across all endpoints through 4 years (Table). These improvements were maintained regardless of prior exposure to anti-TNF therapy; greater responses were demonstrated in anti-TNF-naïve pts. Over the entire study period, the mean exposure ( $\pm$ SD) to secukinumab was 1189.3 $\pm$ 452.9 days. Exposure-adjusted incidence rates (per 100 pt-years) with any secukinumab dose for selected adverse events were: serious infections/infestations (1.5), *Candida* infections (1.2), Crohn's disease (0.6), major adverse cardiovascular events (0.6), uveitis (0.6), and malignant/unspecified tumours (0.4).

**Abstract SAT0283 – Table 1.** Clinical improvements with secukinumab 150 mg at Weeks 52 and 208

Variable	Week	Secukinumab 150 mg <sup>a</sup>		
		Total	Anti-TNF-naïve	Anti-TNF-IR
ASAS20,% responders (n)	52	74.2 (93)	80.0 (60)	63.6 (33)
	208	73.3 (86)	74.6 (59)	70.4 (27)
ASAS40,% responders (n)	52	57.0 (93)	63.3 (60)	45.5 (33)
	208	60.5 (86)	62.7 (59)	55.6 (27)
BASDAI, mean change $\pm$ SD (n)	52	-3.2 $\pm$ 2.3 (93)	-3.3 $\pm$ 2.3 (60)	-3.0 $\pm$ 2.1 (33)
	208	-3.2 $\pm$ 2.3 (86)	-3.5 $\pm$ 2.4 (59)	-2.7 $\pm$ 2.0 (27)
SF-36 PCS, mean change $\pm$ SD (n)	52	7.6 $\pm$ 7.7 (94)	8.0 $\pm$ 7.5 (61)	6.9 $\pm$ 8.1 (33)
	208	8.3 $\pm$ 8.3 (85)	9.4 $\pm$ 8.5 (58)	6.2 $\pm$ 7.8 (27)
ASAS partial remission,% responders (n)	52	24.7 (93)	28.3 (60)	18.2 (33)
	208	27.9 (86)	32.2 (59)	18.5 (27)

<sup>a</sup>Includes placebo switchers. Data are reported as observed.

ASAS; Assessment in SpondyloArthritis International Society; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; IR, inadequate response; SD, standard deviation; SF-36 PCS, Short Form<sup>36</sup> Health Survey Physical Component Summary; TNF, tumour necrosis factor

**Conclusions:** Secukinumab 150 mg provided sustained improvement in the signs, symptoms and physical function in pts with AS through 4 years of treatment with 85% retention rate. The safety profile of secukinumab remained favourable and was consistent with previous reports.<sup>1-3</sup>

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SAT0284

**AN ADD-ON TRAINING PROGRAM INVOLVING BREATHING EXERCISES, COLD EXPOSURE, AND MEDITATION ATTENUATES INFLAMMATION AND DISEASE ACTIVITY IN AXIAL SPONDYLOARTHRITIS**

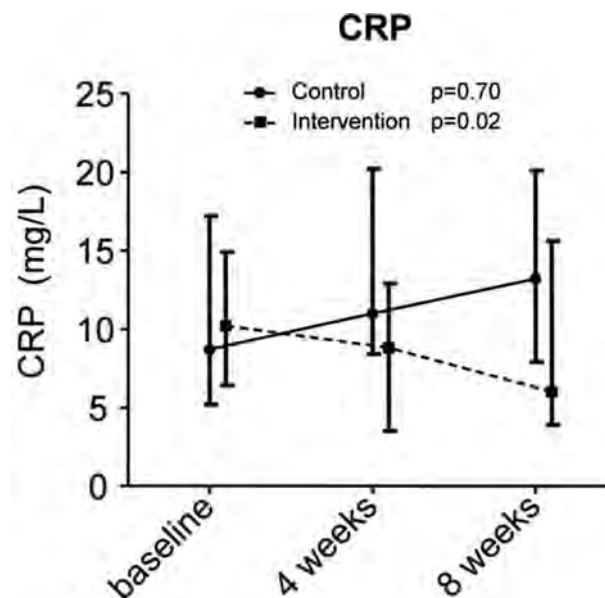
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**Background:** A training program involving breathing exercises, cold exposure, and meditation (further referred to as: 'add-on training program') was shown to exert immunomodulating properties in healthy individuals undergoing experimental endotoxemia.

**Objectives:** Assessment of safety and anti-inflammatory effects of the add-on training program in patients with axial spondyloarthritis (axSpA).

Primary objectives: safety (24 weeks) and change in serum CRP levels (week 8). Secondary objectives: changes in erythrocyte sedimentation rate (ESR), serum calprotectin levels, disease activity as measured by the ASDAS-CRP and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), quality of life measures (SF-36, EQ-5D), and hospital anxiety and depression scale (HADS).

**Methods:** 24 patients with moderately active axSpA (ASDAS >2.1 and CRP >5 mg/L) were included in this trial. The intervention consisted of an 8 weeks add-on training program comprising three elements: breathing exercises (cyclic hyperventilation followed by breath retention), gradual cold exposure (immersions in ice cold water), and meditation (third eye meditation). An open-label randomised one-way crossover design was used to rule out regression to the mean by comparing an intervention group with a control group.



**Results:** There was no significant difference in adverse events between groups, with one serious adverse event (hypertensive crisis) occurring 8 weeks after end of the intervention and judged 'unrelated'. The study met its primary efficacy endpoint, with a significant decline in serum CRP at week 8 in the intervention group

(median [interquartile range] from 10.2 [6.5–17.1] to 6.0 [3.9–15.6] mg/L;  $p=0.02$ ), but not in the control group (from 8.7 [5.2–17.2] to 13.2 [7.9–20.1] mg/L;  $p=0.70$ ). A similar trend was seen for serum calprotectin ( $p=0.065$  in intervention versus  $p=0.31$  in control), but not for ESR. In addition, ASDAS-CRP ( $p=0.02$ ), BASDAI ( $p=0.04$ ), SF-36 physical component score ( $p=0.01$ ), EQ-5D ( $p=0.049$ ), and EQ-5D VAS ( $p=0.02$ ) decreased significantly in the intervention group, but not the control group.

**Conclusions:** This proof-of-concept study in axSpA revealed a significant decrease in serum CRP levels upon add-on training program, in the absence of safety signals. Together with the significant improvement in disease activity and quality of life, these findings warrant full-scale randomised controlled trials of this novel therapeutic approach in patients with axSpA and other inflammatory conditions.

**Disclosure of Interest:** None declared

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SAT0285

#### EFFICACY OF EARLY VERSUS DELAYED INITIATION OF ANTI-TNF-ALPHA TREATMENT IN AXIAL SPONDYLOARTHRITIS. DATA FROM THE CZECH REGISTRY ATTRA

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**Background:** Anti-TNF- $\alpha$  agents are the mainstay of pharmacotherapy for patients with axial spondyloarthritis (AxSpA) who failed treatment with NSAIDs. A little is known about the influence of early versus delayed treatment initiation on their clinical efficacy.

**Objectives:** To compare change of disease activity in AxSpA patients on anti-TNF- $\alpha$  therapy based on symptom duration prior to treatment initiation.

**Methods:** Baseline demographic data and efficacy parameters of patients starting their first anti-TNF- $\alpha$  treatment  $\leq 10$  years (EARLY) or  $> 10$  years (DEALYED) after first symptoms of AxSpA from the Czech national registry ATTRA were compared. Mean  $\pm$ SD and absolute/relative frequencies were used to describe continuous and categorical variables, respectively. P-value of Fisher's exact test and Mann-Whitney test is given when assessing difference between groups in categorical and continuous variables. ATTRA is a centralised prospective computerised registry of patients receiving bDMARD therapy for rheumatic diseases collecting data on efficacy, safety and quality of life of all patients treated in the Czech Republic. Anti-TNF- $\alpha$  therapy was indicated for patients with AxSpA who have failed treatment with NSAIDs with CRP  $\geq 1$  mg/dl and BASDAI score  $\geq 4$ .

**Results:** Data from 1290 axSpA patients were available for analysis. 618 patients started treatment  $\leq 10$  years (EARLY) and 672  $> 10$  years (DEALYED) after the onset of AxSpA symptoms. There was no significant difference in gender distribution (71.4 vs 72.5% males;  $p=0.67$ ) or age at AxSpA diagnosis ( $33.3 \pm 10.4$  vs  $33.5 \pm 10.4$ ;  $p=0.68$ ) between the two groups. At the time of anti-TNF- $\alpha$  initiation EARLY patients were significantly younger ( $36.4 \pm 10.6$  vs  $44.0 \pm 11.2$  years;  $p < 0.001$ ) with shorter symptom duration ( $5.5 \pm 2.7$  vs  $18.9 \pm 8.1$ ;  $p < 0.001$ ), but disease activity assessed by BASDAI ( $6.3 \pm 1.8$  vs  $6.3 \pm 1.6$ ;  $p=0.81$ ) and serum CRP levels ( $2.6 \pm 2.5$  vs  $2.4 \pm 2.0$  mg/dL;  $p=0.34$ ) were comparable in both groups. Mean change of BASDAI scores from baseline during anti-TNF- $\alpha$  therapy was significantly greater in the EARLY group at all time-points ( $3.7 \pm 2.5$  vs  $3.4 \pm 2.2$  at month 3,  $4.2 \pm 2.5$  vs  $3.8 \pm 2.3$  at month 6,  $4.4 \pm 2.5$  vs  $4.0 \pm 2.3$  at month 12 and  $4.4 \pm 2.5$  vs  $4.0 \pm 2.4$  at month 24;  $p < 0.05$  for all) suggesting better treatment response. The difference in survival on therapy between the two groups was not statistically significant.

**Conclusions:** AxSpA patients starting anti-TNF- $\alpha$  therapy more than 10 years after onset of symptoms have significantly worse response to treatment compared to patients with earlier treatment initiation.

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SAT0286

#### RETENTION RATE AND SAFETY DATA OF BIOSIMILAR CT-P13 IN ANKYLOSING SPONDYLITIS PATIENTS: DATA FROM THE KOREAN COLLEGE OF RHEUMATOLOGY BIOLOGICS REGISTRY

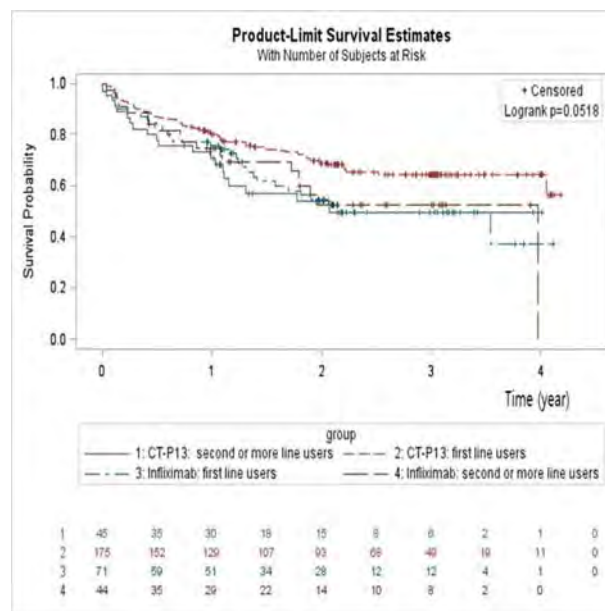
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**Background:** CT-P13 is a biosimilar prescribed in a number of countries for indications approved for the reference infliximab (RINF), including ankylosing spondylitis (AS), rheumatoid arthritis, and inflammatory bowel diseases. Clinical data of CT-P13 have been analysed in previous clinical trials, demonstrating equivalence of efficacy and pharmacokinetic profile to RINF. However, there are few studies showing long-term data of its drug survival or safety.

**Objectives:** To investigate the drug retention rate and safety data of biosimilar CT-P13 in Korean AS patients.

**Methods:** Subjects were AS patients enrolled in the Korean College of Rheumatology biologics registry (KOBIO). Data from patients who received RINF and CT-P13 were included in the analysis<sup>Dec 2012 ~ Dec 2017</sup>. Discontinuation was defined as switching or stopping the biologic agent. Kaplan-Meier curve and Cox proportional hazard model were used for further analysis. Reason for RINF or CT-P13 discontinuation was also assessed.

**Results:** Data from 399 AS patients (CT-P13; 256, RINF; 143) were analysed. The mean age of patients was 39.0 in the CT-P13 group, and 73% were males. The mean disease duration was 4.1 years. Eighty percent of patients were first-time biologic users. Discontinuation of CT-P13 occurred in 30.9% (switching in 17.6%) of patients during follow-up. The drug retention rate of first-line users of CT-P13 was marginally higher compared with second or more ( $\geq 2$ )-line users of CT-P13, first-line users of RINF, and  $\geq 2$  line users of CT-P13 in Korean AS patients ( $p=0.0518$ ). The reason of discontinuation was inefficacy (42.7%), adverse events (20.2%), clinical improvement (7.9%), and others (18.0%) in the CT-P13 group. The incidence of adverse events of CT-P13, including infusion reaction ( $n=10$ ), mycobacterial infection ( $n=2$ ), and skin eruption ( $n=1$ ) was comparable to that of RINF.



**Conclusions:** Our study demonstrates that the drug retention rate of CT-P13, especially in first-line users was relatively higher than that of RINF, [H1] and CT-P13 showed a reasonable long-term safety profile in Korean AS patients.

**Disclosure of Interest:** None declared

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SAT0287

### WHAT ARE THE ECONOMIC IMPLICATIONS OF ANTI-TNF THERAPY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS? – RESULTS OF A HEALTH INSURANCE CLAIMS DATA ANALYSIS

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**Background:** Tumour necrosis factor (TNF)- $\alpha$  inhibitors are an effective but rather expensive treatment option in axial spondyloarthritis (axSpA) patients who fail conventional treatment.

**Objectives:** The aim of this study was to analyse the changes in healthcare costs and resource utilisation after initiation of TNF- $\alpha$  inhibitors in patients with axSpA.

**Methods:** Data of patients with axSpA newly exposed to TNF- $\alpha$  inhibitors between January 1, 2011 and December 31, 2015 were studied by using health insurance claims data in Germany. Resource utilisation, direct healthcare costs and productivity costs were assessed. Direct healthcare costs comprised costs for outpatient care (i.e., visits to physicians, laboratory visits, non-physician visits [e.g., visits to physical therapists], emergency department visits, outpatient hospital services, and aids [e.g., walkers]), costs for inpatient care (i.e., inpatient admissions) and costs for pharmacotherapy. Productivity costs comprised costs due to absence from paid work and were calculated using the friction cost method (FCM) and the human capital approach (HCA). Costs and resource utilisation were analysed the year before (baseline period) and the year after (follow-up period) initiation of TNF- $\alpha$  inhibitors.

**Results:** Data from 1452 persons were included in the analyses; mean age was 44.6 years and 47.9% were female. AxSpA-related pharmacotherapy use (non-steroidal anti-inflammatory drugs [NSAIDs], non-opioid analgesics, opioid analgesics, systemic steroids, local steroids and conventional synthetic disease-modifying anti-rheumatic drugs [csDMARDs]) and admissions to hospital decreased significantly in the follow-up period compared to the baseline period. However, due to anti TNF- $\alpha$  therapy, mean direct healthcare costs increased from € 4494 per patient in the baseline period to € 26 473 per patient in the follow-up period. Mean total costs increased from € 8072 to € 29 959 using the HCA and from € 6377 to € 28 162 using the FCM (Table). Excluding costs for anti-TNF therapy, total costs decreased by 15% to € 6876 or by 20% to € 5080 based on whether the HCA or the FCA was used.

**Abstract SAT0287 – Table 1.** Mean costs per patient before and after initiation of TNF- $\alpha$  inhibitors in axial spondyloarthritis (n=1,452).

	Baseline period mean $\pm$ SD	Follow-up period mean $\pm$ SD	P-value
Outpatient care*, €	1,402 $\pm$ 1,008	1,381 $\pm$ 1,054	0.0285
Hospital admissions*, €	1,890 $\pm$ 3,681	1,134 $\pm$ 3,558	<0.0001
with diagnosis of axSpA*	612 $\pm$ 1582	136 $\pm$ 714	<0.0001
Pharmacotherapy, €	1,201 $\pm$ 2,939	23,957 $\pm$ 5,480	<0.0001
excluding anti-TNF therapy	1,201 $\pm$ 2,939	875 $\pm$ 1,721	<0.0001
NSAIDs	130 $\pm$ 159	83 $\pm$ 151	<0.0001
non-opioid analgesics	21 $\pm$ 77	12 $\pm$ 46	<0.0001
opioid analgesics	118 $\pm$ 517	123 $\pm$ 564	0.3352
systemic steroids	23 $\pm$ 52	17 $\pm$ 54	<0.0001
local steroids	1 $\pm$ 4	1 $\pm$ 4	0.0091
csDMARDs	159 $\pm$ 366	97 $\pm$ 278	<0.0001
Absence at work, HCA, €	3,578 $\pm$ 7,211	3,486 $\pm$ 7,896	0.0458
Absence at work, FCM, €	1,883 $\pm$ 2,943	1,690 $\pm$ 2,934	0.0021
Total costs, HCA, €	8,072 $\pm$ 9,734	29,959 $\pm$ 10,679	<0.0001
excluding anti-TNF therapy	8,072 $\pm$ 9,734	6,876 $\pm$ 9,626	<0.0001
Total costs, FCM, €	6,377 $\pm$ 6,401	28,162 $\pm$ 7,609	<0.0001
excluding anti-TNF therapy	6,377 $\pm$ 6,401	5,080 $\pm$ 5,813	<0.0001

Values are presented as mean  $\pm$  standard deviation. P-values were assessed using Wilcoxon signed-rank tests. Total costs per patient were calculated as the sum of the domains outpatient care, hospital admissions, pharmacotherapy and absence at work.

TNF, Tumour Necrosis Factor; NSAIDs, Nonsteroidal Anti-inflammatory Drugs; csDMARDs, conventional synthetic Disease-Modifying Anti-Rheumatic Drugs; HCA, Human Capital Approach; FCM, Friction Cost Method; SD, standard deviation.

\* excluding costs for pharmacotherapy.

**Conclusions:** Overall resource utilisation decreased after initiation of TNF- $\alpha$  inhibitors. The rise in pharmacotherapy costs driven by anti-TNF agents is accompanied by significantly lower costs for outpatient and inpatient care, as well as significantly lower productivity costs. However, the effect of TNF-blocker therapy on

the patient's disease activity, function or quality of life could not be assessed in this analysis.

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SAT0288

### SECUKINUMAB DEMONSTRATES RAPID AND SUSTAINED EFFICACY IN ANKYLOSING SPONDYLITIS PATIENTS WITH NORMAL OR ELEVATED BASELINE CRP LEVELS: POOLED ANALYSIS OF TWO PHASE 3 STUDIES

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**Background:** Elevated baseline (BL) CRP levels is one of the predictors of treatment response in patients (pts) with active AS.<sup>1</sup> The relationship between BL CRP levels and the treatment response to IL-17A inhibition has not been assessed in AS pts thus far.

**Objectives:** This *post-hoc* analysis assessed the response to secukinumab (SEC) treatment in AS pts with normal or elevated BL CRP from the phase 3 MEASURE 1 and MEASURE 2 studies over 3 years.

**Methods:** The study designs of MEASURE 1 and 2 have been reported.<sup>2</sup> This analysis pooled data from all pts with available BL CRP levels who received subcutaneous (s.c.) SEC 150 mg (approved dose; n=197) or placebo (PBO; n=195). Efficacy endpoints included ASAS20/40, BASDAI, BASDAI50, ASDAS inactive disease, and ASAS partial remission (PR) stratified by normal (<5 mg/L) and elevated ( $\geq$ 5 mg/L) BL CRP; elevated BL CRP group was further subdivided into a range of elevated CRP levels: >5–10, >10–15, >15 mg/L. Data are presented as non-responder imputation (NRI) at Week (Wk)16 and multiple imputation (MI) at Wk156 for binary variables and mixed-effect model repeated measure (MMRM) at Wks 16 and 156 for continuous variables.

**Results:** Overall, 36.5% (143/392) of pts with normal CRP and 63.5% (249/392) of pts with elevated BL CRP were included in the pooled analysis. BL characteristics were balanced across normal and elevated BL CRP groups.<sup>3</sup> At Wk16, efficacy endpoints were improved with SEC 150 mg vs PBO in pts with normal or elevated BL CRP.<sup>3</sup> Results were consistent across all levels of elevated BL CRP with a trend for greater improvement in pts with more elevated CRP (Table). Improvements were sustained or further improved at Wk156 in all groups (Table).

**Abstract SAT0288 – Table 1.** Summary of Clinical Efficacy

Clinical outcomes	Wk	Normal BL CRP (<5mg/L)		Elevated BL CRP					
		SEC (N=72)	PBO (N=71)	>5–10mg/L	>10–15mg/L	>15mg/L			
ASAS20, %	16	56.9 <sup>b</sup>	28.2	42.1	32.3	68.4 <sup>b</sup>	29.0	73.5 <sup>a</sup>	27.4
	156	61.3	–	85.0	–	82.8	–	85.0	–
ASAS40, %	16	34.7 <sup>f</sup>	7.0	31.6	16.1	42.1	22.8	48.5 <sup>e</sup>	11.3
	156	42.4	–	50.0	–	78.4	–	67.9	–
BASDAI, LS mean change from BL	16	-2.2 <sup>f</sup>	-1.0	-1.5	-0.7	-2.8 <sup>f</sup>	-0.6	-2.8 <sup>f</sup>	-0.6
	156	-2.7	–	-2.8	–	-3.6	–	-3.7	–
BASDAI50, %	16	27.8 <sup>b</sup>	7.0	34.2	19.4	42.1 <sup>b</sup>	6.5	41.2 <sup>a</sup>	8.1
	156	40.4	–	56.1	–	75.5	–	68.5	–
ASDAS inactive disease, %	16	19.4 <sup>c</sup>	4.2	21.1	6.5	26.3	0	8.8	1.8
	156	28.9	–	28.5	–	16.9	–	15.1	–
ASAS PR, %	16	12.5	2.8	23.7 <sup>a</sup>	3.2	15.8	3.2	11.8	4.8
	156	14.4	–	34.6	–	33.4	–	30.2	–

<sup>a</sup>P<0.0001, <sup>b</sup>P<0.001, <sup>c</sup>P<0.01, <sup>d</sup>P<0.05 vs PBO; NRI/MMRM data presented at Wk16. MI and MMRM presented at Wk156 included n=56 in normal and n=32, 18, and 53 in >5 to 10, >10 to 15, and >15mg/L elevated CRP groups, respectively. Data included pts (87/125) continuing in the extension trial for MEASURE 1 and all pts for MEASURE 2 at Wk156. LS, least squares; N, number of pts with available BL CRP at Wk16; n, number of pts at Wk156.

**Conclusions:** SEC 150 mg demonstrated sustained efficacy through 3 years in AS patients with both normal and elevated CRP levels, with an increased effect in elevated CRP patients.

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SAT0289

#### LONG-TERM EFFECTS OF TNF-ALPHA INHIBITORS ON BONE MINERAL DENSITY AND THE INCIDENCE OF VERTEBRAL FRACTURES IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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**Background:** Ankylosing Spondylitis (AS) is not only characterised by pathological bone formation leading to ankylosis, but also by bone loss which may lead to vertebral fractures (VFX). TNF-alpha inhibitors (TNFi) have proven to be effective in blocking the inflammatory process. A few studies also showed an increase of Bone Mineral Density (BMD) in AS patients treated with TNFi<sup>1-3</sup>; however, the incidence of VFX after two years of treatment was increased.<sup>3-4</sup>

**Objectives:** To evaluate the long-term effect of TNFi on BMD and the incidence of VFX in patients with AS.

**Methods:** Consecutive TNFi naive AS patients (who fulfilled the Modified New York criteria) were included. Patients were recruited from the VUmc and Reade and were treated with TNFi for 4 years. BMD at hip and lumbar spine (LS) were measured at baseline and after 4 years. T-scores were categorised as 'normal BMD', 'osteopenia' and 'osteoporosis', based on the WHO osteoporosis criteria.<sup>5</sup> The incidence of VFX was determined by two observers using the Genant method.<sup>6</sup>

**Results:** In total, 107 AS patients with complete datasets (68.2% male) were included. The mean age was 42.6 years and the disease duration (time since diagnosis) was 11.0 years. The use of steroids or osteoporosis prophylaxis varied respectively between 0.9% and 2.8%. At baseline 40.1% of the patients had a decreased BMD of the hip and 40.2% of the spine, of whom 27 patients (26%) had both a decreased hip BMD as well as a decreased lumbar BMD. The BMD of spine and hip improved after 4 years of TNFi treatment (table 1). In 13 patients (12.1%), 14 VFX were observed both at baseline and after 4 years of TNFi-treatment, 26 VFX were observed in 21 patients.

After 4 years, 4 out of 21 patients with  $\geq 1$  VFX had a decreased BMD at hip and lumbar spine whereas the other 17 patients had a normal BMD. The majority of VFX was localised in the mid or lower thoracic spine.

Table 1 BMD measurement in spine and hip of 107 AS patients treated with TNFi.

	Baseline*	After 4 years of TNFi**
Osteopenia LS	34 (31.8)	25 (23.4)
Osteoporosis LS	9 (8.4)	2 (1.9)
Abnormal BMD LS	43 (40.2)	27 (25.3)
Osteopenia total hip	39 (36.4)	31 (29.0)
Osteoporosis total hip	4 (3.7)	3 (2.8)
Abnormal BMD total hip	43 (40.1)	34 (31.8)
Patients with VFX	13 (12.1)	21 (19.5)
Total number of VFX	14	26

\* 1 patient with spondylolysis; 4 patients with a total hip replacement

\*\* 2 patients with spondylolysis; 5 patients with a total hip replacement

LS: lumbar spine, Abnormal BMD = osteopenia and/or osteoporosis according to WHO guideline<sup>6</sup>

Vertebral fractures (VFX) are presented in number of patients with a VFX and the actual prevalence of VFX. Outcomes are presented in n (%)

\* p < 0.05, \*\* p < 0.001

**Conclusions:** The percentage of relatively young AS patients with a decreased BMD at baseline of the hip and lumbar spine was high (40%). After 4 years of TNFi-treatment, the BMD of the lumbar spine improved in 14.9% of the patients and of the hip in 8.3% of the patients. At baseline, 12% of the patients had vertebral fractures which increased to 21% after 4 years of treatment. A normal population of 1984 individuals above 50 years showed a prevalence of 8.9% osteoporotic spinal fractures.<sup>7</sup> Probably, the start of treatment with TNFi at an earlier stage of the disease might prevent the onset of fractures in AS.

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SAT0290

#### CANADIAN ADALIMUMAB POST-MARKETING OBSERVATIONAL EPIDEMIOLOGICAL STUDY ASSESSING THE EFFECTIVENESS OF ADALIMUMAB VS. NON-BIOLOGIC DMARDS IN ANKYLOSING SPONDYLITIS (COMPLETE-AS): 12-MONTH EFFECTIVENESS DATA

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**Background:** COMPLETE-AS is an ongoing Canadian observational study of anti-TNF $\alpha$  naive adults with active AS per the judgment of the treating physician, who require change in current AS treatment to either<sup>1</sup> a subsequent NSAID or non-biologic disease modifying antirheumatic drug (nbDMARD group), or<sup>2</sup> to adalimumab (ADA group).

**Objectives:** The aim of this analysis was to describe and compare the baseline demographic and disease parameters of patients in the nbDMARD and ADA groups and to compare the 12 month effectiveness of the two treatment methods.

**Methods:** In the current analysis patients enrolled between July/2011 – Jun/2016 were included. Outcome measures analysed were extra articular manifestations (EAM 1: IBD, psoriasis, uveitis, enthesitis; EAM 2: IBD, uveitis, enthesitis), disease activity (BASDAI), functional status (BASFI), and quality of life (QoL; SF-12). Between-group differences in baseline parameters were assessed with the Chi-square test for categorical variables and the independent samples t-test for continuous variables. Baseline-adjusted changes in BASDAI and BASFI over time were compared between the two groups using linear mixed models.

**Results:** A total of 609 patients (nbDMARD n=177, ADA n=432) were included in the current analysis. No significant differences in baseline demographics were observed between the two groups. However, at baseline, patients initiating ADA were more likely to be unemployed (38% ADA vs. 27.1% nbDMARD, p=0.009), had higher mean BASDAI (6.4 vs. 5.0; p<0.001) and BASFI (5.5 vs. 3.7; p<0.001) scores, and worse QoL (SF-12 PCS: 24.4 vs. 24.7, p=0.002) at baseline. The baseline prevalence of EAMs was comparable between the two groups (EAM 1: 34.7% vs. 31.6%, p=0.454; EAM 2: 25.9% vs. 22.6%, p=0.381). However, IBD was more common among patients initiating ADA treatment (9% vs. 4.5%, p=0.062).

After 12 months of treatment the prevalence of EAMs decreased significantly in the ADA group (EAM 1: p=0.004; EAM 2: p=0.033) but not in the nbDMARD group. After adjusting for baseline values, patients treated with ADA had numerically lower BASDAI score (least square means – LSM: 3.7 vs. 4.3, p=0.171) significantly lower BASFI score (2.9 vs. 3.6, p=0.031) scores, and comparable SF12-

PCS (24.9 vs. 24.7, p=0.210) and SF12-MCS (19.1 vs. 18.9, p=0.532) scores at 12 months.

During follow-up, 7.4% of ADA patients initiated another biologic and 23.7% of patients in the nbdMARD group initiated biologic treatment (p<0.001).

**Conclusions:** AS patients initiating ADA in Canadian routine clinical care have significantly greater disease severity and impaired quality of life at baseline compared with those initiating non-biologic treatment. Treatment with ADA for 12 months resulted in greater reduction in the prevalence of EAMs and a greater reduction in disease severity scores compared to treatment with non-biologic agents.

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SAT0291

**CREATION OF A EUROPEAN DATABASE OF PATIENTS WITH AXIAL SPONDYLOARTHRITIS TREATED IN CLINICAL PRACTICE– INITIAL, PRELIMINARY FINDINGS FROM THE EUROSPA RESEARCH NETWORK COLLABORATION**

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**Background:** A research network collaboration of 15 European registries sharing data on patients with spondyloarthritis (SpA), “EuroSpA”, has recently been created to strengthen research capabilities in the real world setting<sup>1</sup>. Here we present the first results from the collaboration.

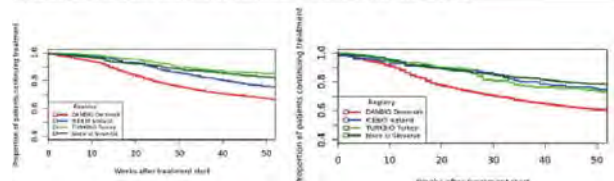
**Objectives:** To investigate the feasibility of creating a common database for axial SpA (axSpA), including non-radiographic SpA and ankylosing spondylitis, within the EuroSpA collaboration and to conduct proof-of-concept analyses by investigation of baseline characteristics, disease activity at baseline and after 6 months, and crude 12 months’ Tumour Necrosis Factor inhibitor (TNFi) retention rate in patients with axSpA initiating TNFi.

**Methods:** A common data model was agreed upon by the EuroSpA Scientific Committee. Virtual meetings between the EuroSpA and registry data managers clarified data availability and structure. This was followed by upload of anonymized data through the secure Virtual Private Network pipelines to the EuroSpA server. Baseline characteristics and disease activity at baseline and after 6 months were investigated with non-parametric descriptive statistics. Kaplan-Meier estimation was used to investigate TNFi retention rates.

**Results:** By January 8th 2018, four of the 15 registries participating in EuroSpA had completed data upload to the EuroSpA database resulting in 6756 patients with AxSpA in a pooled dataset. Baseline characteristics of the participating registry populations at initiation of first TNFi are shown in Table I. Crude 12 months’ TNFi retention rate varied from 66%–85% for 1 st TNFi and 61%–78% for 2nd TNFi (see figure 1). For the pooled dataset crude 12 months’ TNFi retention rates were 73% and 66% for the 1 st and 2nd TNFi, respectively.

**Abstract SAT0291 – Table 1.** Baseline demographic and disease characteristics of patients with social spondyloarthritis registered in four registries participating in the EuroSpA Research Network Collaboration.

	DANBIO (Denmark)	Biorx.si (Slovenia)	TURKBIO (Turkey)	ICEBIO (Israel)				
	N=3848	N=616	N=1877	N=315				
Age, years	41 (32-50)	45 (36-55)	37 (30-45)	43 (34-53)				
Male, n(%)	2353 (61)	396 (64)	1231 (62)	210 (67)				
HLA-B*27, n(%)	3665 (95)	404 (66)	728 (62)	78 (25)				
nbdMARD, n(%)	1071 (28)	93 (15)	372 (19)	69 (22)				
Disease duration, years	1 (0-6)	5 (2-13)	3 (1-8)	3 (0-13)				
Smoking status, current, n (%)	1157 (30)	135 (22)	633 (34)	50 (16)				
First TNFi drug, n(%)								
• INF	1371 (36)	96 (15)	337 (27)	258 (82)				
• ETA	542 (14)	139 (23)	379 (29)	28 (9)				
• ADA	1091 (28)	208 (34)	547 (27)	6 (2)				
• CER	372 (10)	7 (1)	99 (8)	0 (0)				
• GOL	372 (10)	106 (17)	225 (13)	23 (7)				
First TNFi start, n(%)								
• Before 2009	563 (15)	112 (18)	139 (8)	115 (37)				
• 2009-2011	868 (23)	179 (29)	211 (11)	46 (15)				
• 2012-2017	2025 (53)	425 (69)	1608 (84)	154 (48)				
	Baseline	6 months	Baseline	6 months	Baseline	6 months	Baseline	6 months
BASDAI, mm	66 (47-73)	22 (13-49)	70 (57-80)	23 (15-47)	56 (36-62)	16 (5-32)	60 (46-72)	29 (9-40)
BASFI, mm	49 (33-67)	23 (8-47)	58 (46-73)	23 (12-46)	31 (17-51)	10 (6-17)	43 (32-57)	18 (7-33)
VAS Patient global, mm	72 (33-85)	29 (12-60)	70 (60-80)	40 (26-50)	70 (31-78)	27 (16-39)	67 (56-81)	14 (6-40)
VAS Pain, mm	64 (49-70)	25 (10-50)	70 (50-80)	30 (16-50)	72 (50-80)	28 (16-50)	65 (46-77)	14 (6-33)



**Conclusions:** Preliminary analyses showed differences across European registries regarding baseline characteristics and crude retention rates in axSpA patients initiating TNFi. These initial, preliminary analyses demonstrate that the creation of a large European database of axSpA patients treated in routine care based on a common data model is feasible, offering important opportunities for future research.

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SAT0292

### EVALUATION OF RADIOGRAPHIC PROGRESSION AFTER 4 YEARS OF ETANERCEPT (ETN) IN ANKYLOSING SPONDYLITIS (AS): RESULTS FROM THE OPEN-LABEL EXTENSION (OLE) OF THE PHASE 3 CLINICAL TRIAL

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**Background:** ETN was well tolerated and showed clinical efficacy (ASAS 20: ETN 59%, placebo 28%,  $p < 0.0001$ ) through 24 wks in a phase 3 AS trial;<sup>1</sup> efficacy was sustained up to 2 years in pts who completed the study and continued ETN in an OLE.<sup>2</sup> No significant difference was found in change in modified Stoke AS Spine Score (mSASSS) from baseline (BL) to yr 2 of the OLE among ETN-treated pts vs a historic cohort not treated with tumour necrosis factor inhibitors (TNFi).<sup>3</sup>

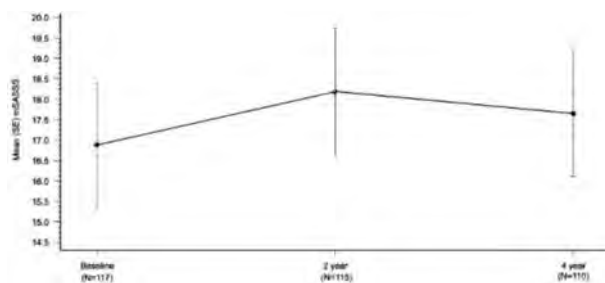
**Objectives:** Report radiographic progression through 4 years in ETN-treated pts with AS.

**Methods:** In the double-blind, placebo-controlled phase 3 study, pts with active AS were randomised to ETN 25 mg BIW or placebo for 24 wks. Pts who completed the study could enrol in a 168-wk OLE and were treated with ETN 25 mg BIW (amended after 17 months to 50 mg QW). The primary radiographic endpoint was change in mSASSS from BL to yr 2 vs change in mSASSS from yr 2 to yr 4.

**Results:** 257 pts were treated in the OLE, of whom 126 (49.0%) completed the study and 131 (51.0%) withdrew prior to 168 wks (most common reasons [ $>5\%$ ]: pt refusal [10.1%]; adverse event, infection, or injection-site reaction [8.2%]; lack of efficacy [7.8%]). ETN resulted in sustained improvement in signs and symptoms of active disease for up to 168 wks beyond the 24-wk double-blind study. Of 267 pts who received  $\geq 1$  dose of ETN in the phase 3 study or OLE, 124 were included in the 4 year primary radiographic endpoint analysis (8 received a prohibited TNFi and were excluded). BL characteristics were similar between these pts and all pts who received  $\geq 1$  dose of ETN in the phase 3 study. Mean change in mSASSS among completers was 1.96 from BL to yr 4 ( $n=110$ ) while change in mean mSASSS between yr 2 and yr 4 was 0.66 ( $n=109$ ). The nominal  $p$ -value for change in mSASSS from BL to yr 2 vs change from yr 2 to yr 4 was 0.0536. Radiographic data suggest disease progression continued in pts receiving ETN continuously over 4 years; however, mean mSASSS increased from BL to year 2 and not from yr 2 to yr 4 (figure 1) due to a few outlier patients with large mSASSS values at yr 2 but missing 4 year data.

Abstract SAT0292 – Table 1. Baseline Demographic and Disease Characteristics

	Pts Who Received $\geq 1$ Dose of ETN in the Phase 3 Study or Its Extension and Had Baseline, 2 year, and 4 year X-rays ( $n=127$ )
Mean (SD) age, yrs	42.43 (9.63)
Male, n (%)	89 (70.1)
HLA-B27 positive, n (%)	100 (78.7)
Used NSAIDs, n (%)	115 (90.6)
Used DMARDs, n (%)	43 (33.9)
Used corticosteroids, n (%)	16 (12.6)
Mean (SD) mSASSS	16.7 (16.3)
Mean (SD) disease duration, yrs	10.61 (8.67)



Abstract SAT0292 – Figure 1. Mean mSASSS

**Conclusions:** This is the first report of 4 year radiographic ETN data in AS, and these data suggest that disease progression continued in pts who received ETN continuously throughout, but that disease progression may be slower after longer-term treatment with ETN vs shorter term. This adds to the already-existing data that demonstrate TNFi seem to reduce radiographic progression in pts with AS.

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SAT0293

### SAFETY AND EFFICACY OF TOFACITINIB, AN ORAL JANUS KINASE INHIBITOR, UP TO 36 MONTHS IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS: DATA FROM THE THIRD INTERIM ANALYSIS OF OPAL BALANCE, AN OPEN-LABEL, LONG-TERM EXTENSION STUDY

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**Background:** Tofacitinib is an oral Janus kinase inhibitor for the treatment of psoriatic arthritis (PsA).

**Objectives:** To report the safety, tolerability and efficacy of tofacitinib in patients (pts) with active PsA from an ongoing, open-label, long-term extension (LTE) study (OPAL Balance, NCT01976364; November 2017 data-cut; database not locked).

**Methods:** Eligible pts from 2 Phase (P)3 tofacitinib PsA studies (OPAL Broaden, NCT01877668; OPAL Beyond, NCT01882439) entered a 3 year LTE  $\leq 3$  months after completing the P3 study or discontinuing for reasons unrelated to study drug. Pts received tofacitinib 5 mg BID to Month (M)1, after which dose adjustments between 5 and 10 mg BID were permitted to improve efficacy, or for safety reasons. Pts receiving a csDMARD at P3 study entry continued the same csDMARD in the LTE. Primary endpoints were incidence and severity of adverse events (AEs) and changes from baseline ( $\Delta$ ) in laboratory values. Safety data are reported up to M36. Efficacy was evaluated up to M30 (when  $n > 50$ ) as a secondary endpoint.

**Results:** 686 pts were treated in OPAL Balance; 468 (68.2%) remained in the study at data cut-off. Mean (range) LTE tofacitinib exposure was 614 (1–1032) days. On Day 1, 675 pts (98.4%) received a csDMARD, which was discontinued in 86 pts (12.7%). To M36, 2189 AEs were reported in 546 pts (79.6%), 95 pts (13.8%) had serious AEs and 59 pts (8.6%) discontinued due to AEs. Serious infections occurred in 12 pts (1.7%), herpes zoster (HZ) in 20 pts (2.9%; 1 serious event), major adverse cardiovascular events in 5 pts (0.7%), malignancies in 24 pts (3.5%; including 12 pts with NMSC) and uveitis in 2 pts (0.3%). No AEs of gastrointestinal perforation or inflammatory bowel disease were reported. There were 5 deaths (not attributed to treatment, as assessed by the investigator) due to metastatic pancreatic carcinoma, acute cardiac failure/hypertensive heart disease, chronic obstructive pulmonary disease, pulmonary embolism and cardiovascular insufficiency. Four AEs of latent tuberculosis were reported in pts whose previously negative QuantiFERON response became positive. ALT was elevated  $\geq 3 \times$  ULN in 27 pts (4.0%), and AST  $\geq 3 \times$  ULN in 15 pts (2.2%). Changes in laboratory values observed in P3 studies were generally stable in the LTE, except for a modest decrease in absolute lymphocyte count over time. Eight pts (1.2%) discontinued (protocol-mandated) due to laboratory value changes. ACR responses,  $\Delta$ HAQ-DI, PASI75 response,  $\Delta$ Leeds Enthesitis Index,  $\Delta$ Dactylitis Severity Score and  $\Delta$ Pain were maintained up to M30.

**Conclusions:** Over 36 months in the LTE, the safety profile of tofacitinib in active PsA pts was generally similar to that of the P3 studies. No new safety risks were identified. Efficacy across various PsA disease domains was maintained over time.

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SAT0294

### ASSOCIATION OF ENTHESITIS WITH ACHIEVEMENT OF NORMAL QUALITY OF LIFE AND CLINICAL RESPONSE IN PATIENTS WITH NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS TREATED WITH ADALIMUMAB

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**Background:** Enthesitis, a key pathology in axial spondyloarthritis (axSpA), has been difficult to treat with conventional therapies and may take longer to resolve than other disease manifestations. It is unknown if failure to attain resolution of enthesitis affects achievement of normal quality of life (QoL) and clinical response.

**Objectives:** To assess if enthesitis at baseline (BL) and after 12 wks of adalimumab (ADA) treatment in the ABILITY-3 study associates with achieving normal QoL and clinical response in patients (pts) with non-radiographic axSpA (nr-axSpA).

**Methods:** ABILITY-3 enrolled adult pts with nr-axSpA with objective evidence of inflammation (MRI positive or elevated hsCRP), active disease at BL (ASDAS  $\geq 2.1$ , BASDAI $\geq 4$ , and Patient's Assessment of Total Back Pain score  $\geq 4$ ), and an inadequate response to  $\geq 2$  NSAIDs. Pts received ADA 40 mg every other wk during a 28-wk open-label lead-in. Pearson's correlation coefficients were used to assess the relationship between total enthesitis count (sum of Maastricht Ankylosing Spondylitis Enthesitis Score [MASES] and plantar fascia enthesitis score) and QoL and disease activity at BL. Multivariable stepwise logistic regression was used to evaluate the relationship between total enthesitis count or enthesitis location and normal QoL (EQ-5D $\geq 0.898$  or SF36 MCS/PCS $\geq 50$ ) and clinical response (ASDAS-ID [ASDAS  $< 1.3$ ], ASAS40, or BASDAI50) at wk 12.

**Results:** At BL, 74% (501/673) of pts had enthesitis, and mean (95% CI) total enthesitis count was 3.7 (3.42, 3.98). Enthesitis resolved in 39% (196/501) of pts, and total enthesitis count was 1.9 (1.68, 2.12) at wk 12 of ADA treatment. At BL, total enthesitis count significantly correlated with all QoL and disease activity measures (Table). Each 1-unit increase in BL total enthesitis count was associated with 7% lower odds of ASDAS-ID (OR [95% CI]: 0.93 [0.88, 0.99],  $p=0.018$ ) and 6% lower odds of BASDAI50 (0.94 [0.89, 0.99],  $p=0.024$ ) at wk 12 and was not associated with normal QoL or ASAS40 at wk 12. Total enthesitis count at wk 12 was associated with lower odds of normal QoL and clinical response at wk 12 (Table). Achievement of normal QoL at wk 12 was less likely if pts had BL enthesitis at the posterior (EQ-5D $\geq 0.898$ ) or anterior superior iliac spine (SF36 PCS  $\geq 50$ ), and pts with BL enthesitis at the 7th costochondral joint were less likely to achieve clinical response at wk 12 (Table).

**Abstract SAT0294 – Table 1.** Association of Total Enthesitis Count With QoL and Disease Activity at BL and Clinical Response at Wk 12

Baseline			
Measure	n	Pearson Correlation Coefficient	
EQ-5D	672	-0.23*	
SF-36 PCS	672	-0.18*	
SF-36 MCS	672	-0.15*	
BASDAI50	673	0.27*	
ASDAS	673	0.18†	
Patient Global Assessment	673	0.14*	
Physician Global Assessment	671	0.17*	
Wk 12			
Measure	n	Odds Ratio (95% CI)	
EQ-5D $\geq 0.898$	658	0.62 (0.48, 0.78)*	
SF-36 PCS $\geq 50$	658	0.70 (0.61, 0.81)*	
SF-36 MCS $\geq 50$	658	0.85 (0.80, 0.91)*	
ASDAS-ID	628	0.82 (0.75, 0.91)*	
ASAS40	632	0.82 (0.76, 0.88)*	
BASDAI50	632	0.74 (0.69, 0.81)*	
Enthesitis Location at baseline			
Measure at wk 12	n	Location	Odds Ratio (95% CI)
EQ-5D $\geq 0.898$	660	Posterior superior iliac spine L/R	0.58 (0.34, 0.99) <sup>‡</sup>
SF-36 PCS $\geq 50$	660	Anterior superior iliac spine L/R	0.60 (0.37, 0.96) <sup>‡</sup>
SF-36 MCS $\geq 50$	663	—	—
ASDAS-ID	630	7th costochondral joint L/R	0.57 (0.36, 0.91) <sup>‡</sup>
ASAS40	637	7th costochondral joint L/R	0.62 (0.42, 0.91) <sup>‡</sup>
BASDAI50	634	7th costochondral joint L/R	0.60 (0.40, 0.91) <sup>‡</sup>

Locations evaluated included 1st costochondral joint L/R, 7th costochondral joint L/R, anterior superior iliac spine L/R, posterior superior iliac spine L/R, iliac crest L/R, 5th lumbar spinous process, proximal insertion of Achilles tendon L/R, and plantar fascia L/R. ASAS40, Assessment of SpondyloArthritis international Society 40% improvement; ASDAS-ID, Assessment of SpondyloArthritis international Society inactive disease; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; EQ-5D, EuroQol 5 dimension; MCS, mental component summary; PCS, physical component summary; QoL, quality of life; SF-36, short form health survey.

\* $P < 0.001$ ; † $P < 0.01$ ; ‡ $P < 0.05$ .

**Conclusions:** 39% of pts achieved complete resolution of enthesitis after 12 wks of ADA treatment. Total enthesitis count at BL was not associated with normal QoL and inversely associated with clinical response at wk 12. Total enthesitis count at wk 12 was negatively associated with normal QoL and clinical response. Our exploratory analysis suggested possible inverse associations of specific BL enthesitis sites with achievement of normal QoL and clinical response; however, additional research is needed to further define these relationships.

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SAT0295

### TOOL FOR THE PRESCRIPTION OF EXERCISE IN SPONDYLOARTHRITIS WITH MULTIMEDIA ANIMATIONS (EJES-3D): PILOT STUDY

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**Background:** Exercise is a basic pillar in the management of axial spondyloarthritis (SpA-axe), together with pharmacological treatment<sup>1,2</sup>. Since it has been shown to improve pain, inflammation, mobility, physical and respiratory function. The information provided to the patient on paper on exercises has limitations of understanding. To this must be added the barriers to exercise that patients perceive, such as the lack of adaptation of the exercises according to the SpA phases

and the contradictory messages among professionals. Therefore we decided to develop an electronic tool to facilitate and encourage the prescription of exercise.

**Objectives:** To evaluate the usefulness of a computer tool and a training workshop to improve the prescription of physical exercise in SpA by rheumatologists.

**Methods:** An online platform was developed for the individualised prescription of exercise to patients with SpA according to stage and with 3D animations (EJES-3D), which was presented in a training workshop. Tests were conducted before and after the workshop to assess the change in knowledge. Six months after the workshop, the degree of use and acceptance of the tool was evaluated through a survey aimed at rheumatologists and the fulfilment of the concepts learned through a survey of 100 consecutive patients attended in the centres of the attendees.

**Results:** The level of knowledge improved with the workshop (6.8/10 to 7.7). After 6 months 77.8% indicated that the contents of the workshop were useful and adapted to their expectations and all applied the knowledge. 22% stated that they prescribed exercise more regularly and 44% with greater confidence. 67% of rheumatologists considered the tool EJES-3D useful. The 82 patients who completed the survey agreed in their majority that they had been prescribed exercise, they had been informed and the messages received had been positive and coherent. 50% of the patients were prescribed specific exercises, which were qualified by them as simple, adaptable and attractive. And 64% were satisfied with the degree of exercise they performed. On the other hand, aspects to be improved at the tool and training level were identified.

**Conclusions:** The specialised training in the prescription of the exercise directed to the professionals who are in charge of the management of patients with SpA can be very beneficial to homogenise the type of exercise in each phase of the disease and help to gain confidence. In addition to having a specific tool (EJES-3D) to perform individualised prescription, it can be very useful.

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**Disclosure of Interest:** None declared

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SAT0296

#### PATIENTS WITH DIFFUSE IDIOPATHIC SKELETAL HYPEROSTOSIS AND LOW BACK PAIN – EVALUATION AND REHABILITATION

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**Background:** Diffuse Idiopathic Skeletal Hyperostosis (DISH) generally occurs in people between the ages of 50 and 60, more often in men than women. Physical therapy and kinetic program may help delay the loss of motion in affected joints and control the low back pain (LBP). In most cases of DISH with LBP, certain muscles of the back that stabilise the spine are reflexively inhibited and do not spontaneously recover even if patients are pain free with a return to normal activity levels.

**Objectives:** In our observational study we evaluated the role of rehabilitation program in quality of life and assessed the thickness of the erector spinae (ES) muscle in these patients and to evaluate the correlation between thickness difference in three different trunk postures and functional parameters.

**Methods:** 38 male patients (61.5 years mean age) with DISH and LBP were enrolled in this study. Frontal (AP) and lateral lumbosacral regions were radiologically evaluated. Clinical and functional parameters were collected by a physiotherapist, that applied rehabilitation program (12 sessions of TENS, interferential current, ultrasound, aerobic training) and an US examination was performed by a physiatrist within 72 hours of the clinical examination. We performed ultrasonography to measure the thickness of the ES muscle at L4 and L5 level in maximum flexion, neutral posture, and maximum extension. All collected clinical and imaging data were statistical analysed, pre-post rehabilitation.

**Results:** Multivariate analysis showed that thickness differences between flexed and neutral, and flexed and extended maximally positions were correlated statistically with functional parameters (VAS and The Roland-Morris Disability Questionnaire score). We obtained a significant improvement in VAS ( $p < 0.01$ ) and Disability Questionnaire score ( $p < 0.05$ ) after supervised rehabilitation program.

**Conclusions:** Although ossification in DISH generally affects the ligament of the spine, pain is more likely to arise in correlation with the erector vertebral muscle status. Visual observation of the image during contraction indicates that US may

be a valuable biofeedback tool. Kinetic program (regular exercises that strengthen spine, walking and global stretching), avoiding sitting position for long periods of time, sleep on a correct mattress and optimal daily activities are the most important recommendations for all patients with DISH.

**Disclosure of Interest:** None declared

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SAT0297

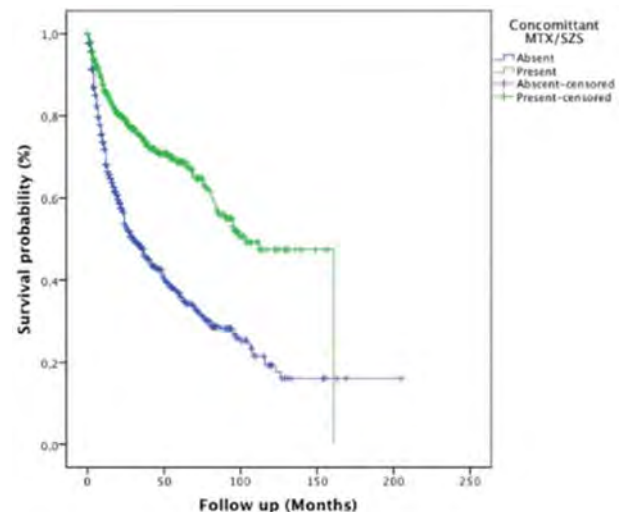
#### THE ROLE OF BASELINE CONCOMITANT USE OF CONVENTIONAL SYNTHETIC DISEASE MODIFYING ANTI-RHEUMATIC DRUGS WITH TNF INHIBITORS IN SPONDYLOARTHRITIS PATIENTS

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**Background:** Conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs) are drugs of choice in the treatment of rheumatoid arthritis and their concomitant use with TNFi is also of unequivocal importance. On the other hand there is limited evidence regarding the efficacy of csDMARD in axial spondyloarthritis (SpA) and concomitant use with TNFi are not recommended. However recently there is conflicting results about the comedication with csDMARD on the TNFi drug survival in patients with AS.

**Objectives:** To evaluate the effect of concomitant csDMARD use on first TNFi drug survival in patients with spondyloarthritis.

**Methods:** The data of patients that have been included in two Turkish registries (TURKBIO (n=356) and TReasure (n=1382)) with the diagnosis of ankylosing spondylitis (AS) or SpA obtained. Drug survival was calculated from the date of first TNFi prescription to the last visit or until the stop date of first biologic agent. For drug survival analysis Kaplan-Meier method with log-rank test. Cox proportional hazard method was used to evaluate the relative effects of each covariate on the drug survival.



**Results:** In total 1738 patients (1040 [59.1%] male, median [range] age 39<sup>16–81</sup> years) with SpA initiating first TNFi were included in the analysis. Median disease duration was 116 months. 690 (39.7%) patients received adalimumab and 135 (22.3%) etanercept, 324 (18.6%) infliximab, 202 (11.6%) golimumab and 135 (7.8%) certolizumab. At the time of first biologic prescription 794 (45.7%) were using sulfasalazine or methotrexate. Baseline median BASDAI score was 60 (0–100), BASFI score was 46 (0–100), patient global assessment of disease activity was 70 (0–100), ESR was 23<sup>1–140</sup> mm/h and median CRP value was 13 (0–659) mg/L. In our study group median drug survival time was 12 (0–205) months. In total 585 (33.7%) of our patients stop their first TNFi. 323 (55.2) patients discontinued the medication due to inefficacy, 133 (22.7) due to adverse effect. Drug survival was significantly better in patients using concomitant csDMARDs at baseline (with a median survival 104 vs 30 months;  $p < 0.001$ ; figure). In Cox regression model baseline age (HR 0.978,  $p = 0.028$ ), and concomitant csDMARD usage (HR 0.341,  $p < 0.001$ ) were found to be as the predictors for better drug survival, female sex (HR 1.546,  $p = 0.039$ ), presence of psoriasis (HR 3.803,  $p = 0.015$ ), enthesitis

(HR 1.619,  $p=0.018$ ) and uveitis (HR 1.732,  $p=0.025$ ) as predictors for worse drug survival. At the time of censoring only 202 (11.6%) patients were using csDMARDs with TNFi agent. When we repeat the analysis with patients continuing csDMARDs we showed that there is no significant differences regarding TNFi survival.

**Conclusions:** The results of present study showed that considerable amount of SpA patients were using csDMARDs at time of first TNFi initiating and drug survival was significantly better in those patients.

**Disclosure of Interest:** None declared

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### SAT0298 TRANSCUTANEOUS VAGUS NERVE STIMULATION IN PATIENTS WITH PSORIATIC ARTHRITIS OR ANKYLOSING SPONDYLITIS

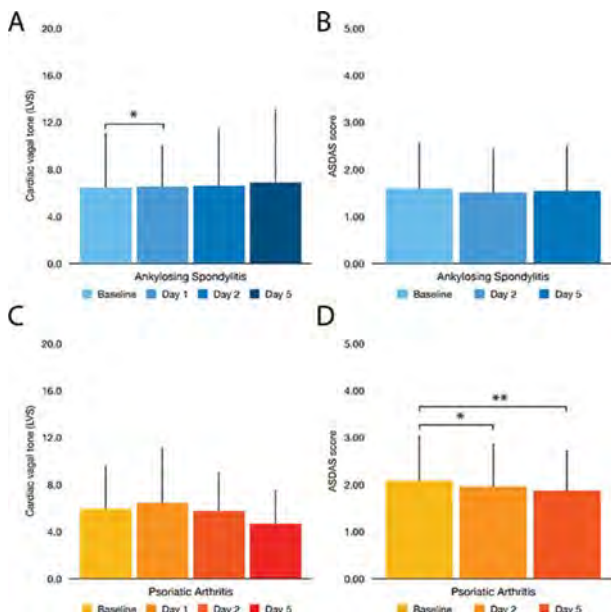
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**Background:** Psoriatic arthritis and ankylosing spondylitis are chronic autoimmune diseases characterised by inflammation of both peripheral and spinal joints. The chronic inflammation may lead to impaired functionality and absenteeism from work. It has become increasingly accepted that the vagus nerve plays a pivotal role as a communicator between the immune and nervous systems<sup>1</sup>. Recent studies in similar immune-mediated inflammatory diseases have demonstrated promising anti-inflammatory effect of vagus nerve stimulation<sup>2,3</sup>.

**Objectives:** We hypothesised that transcutaneous vagus nerve stimulation (t-VNS) would increase the activity of the vagus nerve, and that this enhanced parasympathetic tone would reduce inflammation and disease activity. The aims of this study were to investigate the effects of t-VNS on cardiac vagal tone and disease activity in patients with psoriatic arthritis or ankylosing spondylitis.

**Methods:** Twenty patients diagnosed with psoriatic arthritis (median disease duration 7.0 years) and 17 patients diagnosed with ankylosing spondylitis (median disease duration 4.5 years) were included in the study. Transcutaneous vagus nerve stimulation for 120 s was performed bilaterally, thrice daily for four days, using a non-invasive handheld device. Cardiac vagal tone, measured on a linear vagal scale (LVS), and disease activity scores were assessed on the 1st, 2nd and 5th day.

**Results:** In the ankylosing spondylitis group, cardiac vagal tone was significantly increased 30 min after t-VNS in comparison to baseline (6.46 vs. 6.57. LVS,  $p<0.05$ ) (figure 1A), accompanied by a significant reduction in heart rate (68.44 vs. 65.37,  $p<0.01$ ). Transcutaneous vagus nerve stimulation did not change cardiac vagal tone in the psoriatic arthritis group (figure 1C), however, a significant reduction in heart rate 30 min after t-VNS in comparison to baseline was observed (71.26 vs. 68.04,  $p<0.01$ ). A significant reduction in ASDAS score was demonstrated in the psoriatic arthritis group on both day 2 (2.09 vs. 1.96,  $p<0.05$ ) and day 5 (2.09 vs. 1.88,  $p<0.01$ ) (figure 1D).



**Abstract SAT0298 – Figure 1.** Cardiac vagal tone and ASDAS score. \* $p<0.05$ , \*\* $p<0.01$

**Conclusions:** Transcutaneous vagus nerve stimulation may have an acute effect on cardiac vagal tone and heart rate in patients with ankylosing spondylitis and psoriatic arthritis. The observed effect of t-VNS on ASDAS scores in patients with psoriatic arthritis was not associated with a modulation of cardiac vagal tone.

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**Disclosure of Interest:** None declared

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### SAT0299 REAL WORLD SECUKINUMAB STUDY IN AS AND PSA – COMORBIDITIES AND EXTRAARTICULAR MANIFESTATIONS: INCIDENCE AND STATUS THROUGHOUT NON-INTERVENTIONAL AQUILA STUDY IN GERMANY

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**Background:** Patients with psoriatic arthritis (PsA) or ankylosing spondylitis (AS) may suffer from extraarticular manifestations (EAM) (uveitis, psoriasis) and have higher rates of comorbidities like cardiovascular diseases (CVD) or depression than the normal population. Comorbidities should be kept in mind when managing pts with PsA and AS, as they can contribute to increased mortality and influence disease activity<sup>1</sup>.

**Objectives:** The aim of this interim analysis is to evaluate the incidence of selected EAM and comorbidities at baseline and the impact of secukinumab on the status of these attributes compared to baseline.

**Methods:** The presence and severity of uveitis and psoriasis (assessed by PASI) as well as diagnosis of coronary heart disease (CHD), stroke, heart insufficiency, and depression (assessed by Becks Depression Inventory (BDI-II)) were documented according to clinical routine at baseline and at week 4, 16, 24 and 52 after initiation of secukinumab. At baseline 486 patients were included and observed up to 52 weeks, at the time of analysis not all patients have already reached the end of the study, therefore the results are presented as observed.

**Results:** As expected, current plaque psoriasis was very frequent in PsA pts (63.3%), but also present in AS pts (11.5%) at baseline. For PsA pts, median PASI improved from 5.0 at baseline to 0.0 at wk 52. Half of pts with available PASI achieved clear skin at wk 52 (Tab 1).

Uveitis was more frequent in AS pts than in PsA pts (6.2% vs 0.9%). Only 1 AS pt and 2 PsA pts experienced new onset of uveitis.

CVD were more frequent in PsA than in AS patients at baseline: CHD (PsA 8.9%, AS 3.5%), heart failure (PsA 3.3%, AS 0.7%) and stroke (PsA 2.4%, AS 0.0%). During 52 wks study duration none comorbidity worsened with secukinumab treatment. Two patients with PsA were newly diagnosed with CHD and heart insufficiency throughout wk 52. No new stroke occurred.

Depression was common in both populations (PsA 15.4%, AS 12.2%) at baseline. Up to wk 52 median BDI-II improved from 12.0 to 6.0 (AS pts) and from 9.0 to 6.0 (PsA pts [Tab 1]).

**Abstract SAT0299 – Table 1.** PASI and BDI response under secukinumab

	Baseline	Wk 4	Wk 16	Wk 28	Wk 40	Wk 52
PASI 100 n(%)	0 (0.0)	7 (13.0)	23 (34.3)	28 (47.5)	18 (41.9)	15 (50.0)
PASI 75 n(%)	0 (0.0)	9 (16.7)	26 (38.8)	33 (55.9)	21 (48.8)	18 (60.0)
BDI-II (AS pts)	12.0	9.0	8.0	8.0	7.5	6.0
BDI-II (PsA pts)	9.0	8.0	7.5	8.0	7.0	6.0



**Conclusions:** Incidence of CVD and depression in PsA and AS pts is generally comparable to the published literature<sup>2,3</sup>. However, in contrast to other studies<sup>4</sup>, previous uveitis was less frequently reported in SpA pts selected for treatment with a IL-17 inhibitor, particularly in the AS group. Cardiovascular comorbidities remained overall stable under secukinumab up to wk 52. Plaque psoriasis and depressive mood improved with Secukinumab treatment.

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SAT0300

#### TREATMENT EXPERIENCE AND SATISFACTION IN ANKYLOSING SPONDYLITIS PATIENTS TREATED WITH SECUKINUMAB: RESULTS FROM A US WEB-BASED SURVEY

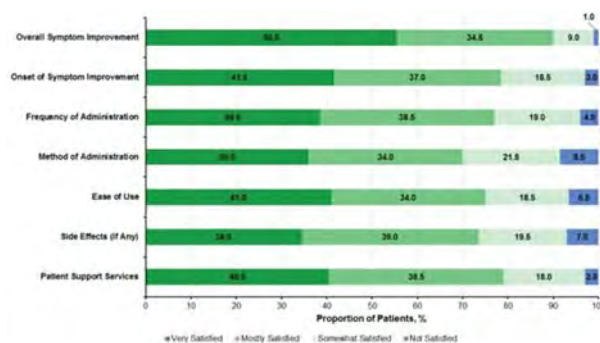
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**Background:** Secukinumab is the only interleukin-17A inhibitor approved for the treatment of ankylosing spondylitis (AS). There are limited real-world data about treatment experience and patient satisfaction with secukinumab among patients with AS.

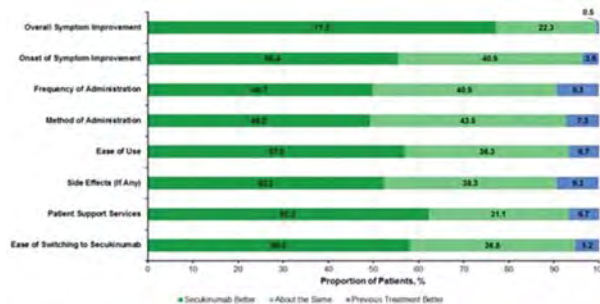
**Objectives:** To evaluate real-world treatment experience and satisfaction with secukinumab in US patients with AS.

**Methods:** Data on demographics, AS symptoms, treatment history, and treatment satisfaction were collected from a cross-sectional, web-based panel survey from July 10 to August 3, 2017. A random sample of US patients were invited to participate in the survey by Survey Sampling International via their patient panels. Eligibility criteria included patients aged  $\geq 18$  years with a self-reported diagnosis of AS who initiated secukinumab  $\geq 3$  months before participation and received secukinumab continuously since initiation. The outcomes evaluated were AS patient experience and satisfaction with effectiveness and symptom improvement with secukinumab, both overall and when compared to their previous treatment. Outcomes were summarised descriptively.

**Results:** Of 2755 patients screened, 200 patients with AS were eligible for the analysis. The mean (SD) age of survey participants was 34.4 (10.6) years; 60.0% were male and 66.0% were white. Equal proportions of patients (86.5%) had a history of biologic and nonbiologic use, and 98.5% of patients had previously received treatment for AS; the primary reason for discontinuation of their previous treatment was lack of efficacy (25.4%). Most patients (74.0%) reported overall improvement in AS symptoms compared with their previous treatment before secukinumab initiation (“a little better,” 34.5%; “moderately better,” 21.0%; “much better,” 18.5%). Overall, the majority of patients were satisfied with secukinumab treatment (Abstract SAT0300 – figure 1), and expressed better treatment experience with secukinumab compared with their previous treatment (Abstract SAT0300 – figure 2).



**Abstract SAT0300 – Figure 1.** Overall satisfaction with secukinumab treatment reported by patients with AS



**Abstract SAT0300 – Figure 2.** Treatment satisfaction with secukinumab for AS compared with previous treatment

**Conclusions:** Overall, >90% of patients with AS who were treated with secukinumab expressed overall satisfaction with their treatment experience, even when compared with their previous treatment. These data provide early insight into the secukinumab treatment experience and satisfaction of US patients with AS.

**Acknowledgements:** This study was sponsored by Novartis Pharmaceuticals Corporation, East Hanover, NJ.

**Disclosure of Interest:** M. Magrey Grant/research support from: AbbVie, Consultant for: Janssen, Novartis, UCB, M. Bozyczko: None declared, D. Wolin Employee of: RTI-Health Solutions, M. Mordin Employee of: RTI-Health Solutions, L. Mcleod Employee of: RTI-Health Solutions, E. Davenport Employee of: RTI-Health Solutions, Y. Park Employee of: Novartis Pharmaceuticals Corporation

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SAT0301

#### SIMILAR EFFICACY OF RHU-TNFR-FC TEPERING AND MAINTENANCE FOR HIP ARTHRITIS IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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**Background:** Hip involvement is common in patients with ankylosing spondylitis (AS) and eventually leads to functional impairment. Recent studies indicated tumour necrosis factor inhibitors (TNFi) might be an effective therapy for hip arthritis in AS patients. However, the conventional dose of TNFi associates with high cost and increasing risk for adverse effects, so dose reduction is necessary.

**Objectives:** We compared the efficacy between recombinant human soluble tumour necrosis factor receptor II: IgG Fc fusion protein (Rhu-TNFR-Fc) dose reduction and maintenance in terms of disease activity, function and change of imaging examination.

**Methods:** Fifty-one AS patients (102 hips) who admitted to our hospital from January 2015 to December 2017 were involved in this retrospective cohort study. Patients who had previously received disease modifying anti-rheumatic drugs or systemic glucocorticoid therapy were excluded. After being treated by Rhu-TNFR-Fc (YISAIPU) 50 mg/week for 12 weeks, subcutaneous injections were performed every other week for patients in the tapering group, while the control group maintained the same therapy till the 24th week. AS disease activity score-C reactive protein (ASDAS-CRP), Bath AS function index (BASFI) and Harris hip score were recorded at every follow-up. Pelvic X-ray and MRI examinations for hips were conducted before treatment and in the 24th week. Bath AS radiology index-hip (BASRI-h) was employed to assess the change in X-ray, and definition of hip MRI finding was described by Huang et al. Bone marrow oedema, enthesitis and synovitis was thought to be a marker for active inflammatory changes. Chronic inflammatory changes included bone erosion, fat accumulation and ankylosis.

**Results:** After markedly descending to the minimum at week 12 ( $p<0.05$ ), ASDAS-CRP, BASFI and Harris hip score kept stable till the end in both groups (table 1). BASRI-h of these groups unchanged during 24 weeks ( $p>0.05$ , figure 1). Nevertheless, active inflammatory changes improved dramatically in the second MRI examination ( $p<0.05$ , table 2). No statistical significant was existed between groups ( $p>0.05$ ).

**Abstract SAT0301 – Table 1.** Changes in the variables of patients with ankylosing spondylitis at follow-ups (Mean±SD)

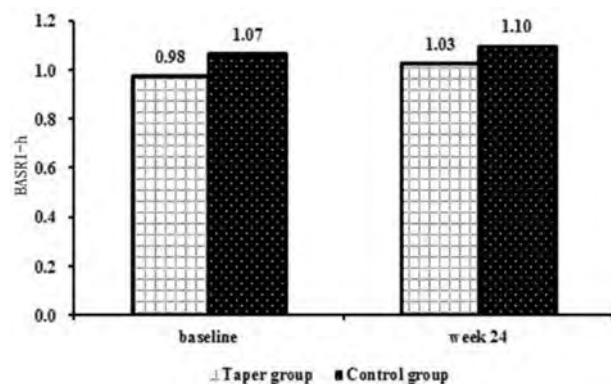
Variables	Tapering group (n=31)			Control group (n=20)		
	Week 0	Week 12	Week 24	Week 0	Week 12	Week 24
ASDAS-CRP	3.9±0.8	1.0±0.6*	1.1±0.7*	4.0±0.6	1.0±0.6*	1.1±0.7*
BASFI	3.5±1.4	1.2±0.9*	1.5±1.2*	3.7±1.2	1.2±0.8*	1.2±1.1*
Harris hip score	51.7±12.5	75.9±11.1*	72.0±10.4*	51.9±11.0	76.0±9.6*	75.9±8.8*

\* $P<0.05$  compared with week 0 in the same group. ASDAS-CRP, ankylosing spondylitis disease activity score-C reactive protein; BASFI, Bath ankylosing spondylitis function index

**Abstract SAT0301 – Table 2.** Changes in the MR features of hips in patients with ankylosing spondylitis at week 0 and week 24 (n,%)

Variables	Tapering group (n=62)		Control group (n=40)	
	Week 0	Week 24	Week 0	Week 24
Active inflammatory change	49 (79.0)	14 (22.6)*	32 (82.5)	5 (12.5)*
Chronic inflammatory change	17 (27.4)	17 (27.4)	10 (25.0)	10 (25.0)

\* $P<0.05$  compared with week 0 in the same group



**Abstract SAT0301 – Figure 1.** Changes of Bath AS radiology index-hip

**Conclusions:** Rhu-TNFR-Fc tapering might maintain remission of hip arthritis in patients with AS, and it shares similar therapeutic effect of full-dose Rhu-TNFR-Fc. Therefore, dose reduction of TNFi tends to be an acceptable therapy for AS-related hip arthritis.

## REFERENCE:

[1] Eur J Radiol. 2013;82(9):1487–93.

**Disclosure of Interest:** None declared

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SATURDAY, 16 JUNE 2018

## Psoriatic arthritis

### SAT0302 EVALUATION OF SUBCLINICAL GUT INFLAMMATION USING FAECAL CALPROTECTIN LEVEL AND COLONIC MUCOSAL BIOPSY IN PATIENTS WITH PSORIASIS AND PSORIATIC ARTHRITIS

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**Background:** The association between gut inflammation and ankylosing spondylitis is well established, while it is not so in psoriatic arthritis (PsA).

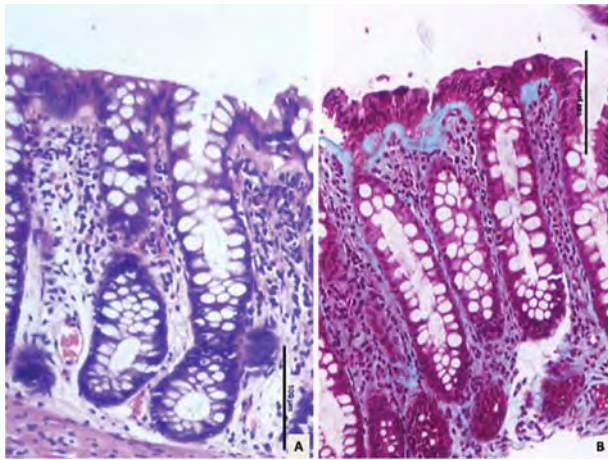
**Objectives:** To study the prevalence of subclinical gut inflammation in PsA and Psoriasis (PsO) patients using faecal calprotectin levels and colonic mucosal biopsies and its correlation with disease phenotypes and activity scores.

**Methods:** Fifty patients with active PsA and hundred with active PsO were recruited. Faecal calprotectin levels of more than 43.2 µg/gm by ELISA was considered positive. Sigmoidoscopy and multiple colonic mucosal biopsies were done in twenty PsA patients and eight PsO patients. Thirty consecutive patients with irritable bowel syndrome (IBS) according to ROME III criteria were disease control population. Mann Whitney u test and Kruskal Wallis H test were used.

**Results:** Baseline characteristics are given in table 1. Faecal calprotectin level was elevated in 29 (58%) PsA patients and 26 (26%) PsO patients ( $p=0.000$ ). The mean value of faecal calprotectin was higher in PsA patients than PsO (86.6±81.5 µg/gm vs 32.9±48.1 µg/gm,  $p=0.000$ ). The Odds for a positive faecal calprotectin level in PsA was 3.9 (95% CI 1.9–8.0) in comparison to PsO. Faecal calprotectin levels were significantly higher in PsA patients with high body surface area (BSA) and psoriasis area and severity index (PASI) scores. Those with axial phenotype had higher calprotectin levels and the levels correlated with BASDAI. Mean faecal calprotectin level was 22.0±18.5 µg/gm in IBS patients which was significantly lower than PsA patients (0.002) but was comparable with that of PsO patients ( $p=0.8$ ). Sigmoidoscopy was normal in all PsO patients while two PsA patients had mucosal erythema. Fifteen PsA and all PsO patients showed increased lymphoplasmocytic infiltration of lamina propria. Evidence of active colitis with cryptitis was seen in two and collagenous colitis was seen in seven PsA patients (figure 1). No PsO patient had active or collagenous colitis.

**Abstract SAT0302 – Table 1.** Baseline characteristics (TJC Tender Joint Count, SJC Swollen Joint Count, BASDAI Bath Ankylosing Spondylitis Disease Activity Index, LEI Leeds enthesitis index, BSA Body Surface Area, PASI Psoriasis Area And Severity Index, DLQI Dermatology Life Quality Index, CPDAI Composite Psoriatic Disease Activity Index)

Variable	Psoriatic Arthritis (n=50)	Psoriasis (n=100)
Mean age (years)	44.4±12.0	41.5±14.6
Male: Female	26:24	70:30
Duration of skin involvement (yrs)	9.3±9.0	8.6±8.4
Mean duration of joint involvement (yrs)	3.5±4.8 (0.25–30)	
Mean TJC	4.8±4.0 (0–20)	
Mean SJC	4.5±4.0 (0–19)	
BASDAI	1.8±2.3 (0–7.4)	
LEI	0.3±0.7 (0–3)	
BSA	5.7±13.2 (0–90)	13.6±19.3 (1–90)
PASI	3.5±7.0 (0–48)	8.1±9.1 (0.3–44)
DLQI	4.9±5.3 (0–25)	8.8±6.1 (1–29)
CPDAI	3.8±2.0 (1–10)	1.7±0.8 (1–3)
Nail involvement	21 (42%)	45 (45%)



**Figure 1.** Photomicrograph of A showing mild to moderate increased intra-epithelial lymphocytes with thickened basement membrane B. shows the thickened basement membrane highlighted better in Masson's trichrome staining

**Conclusions:** Subclinical gut inflammation was significantly higher in PsA patients in comparison to PsO patients and is more prevalent among those with axial phenotype.

**Acknowledgements:** IRA

**Disclosure of Interest:** None declared

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SAT0303

**PAIN MECHANISMS AND ULTRASONIC INFLAMMATORY ACTIVITY AS PROGNOSTIC FACTORS IN PATIENTS WITH PSORIATIC ARTHRITIS: RESULTS OF A DANISH PROSPECTIVE, EXPLORATORY COHORT STUDY**

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**Background:** Pain is a major concern for patients with psoriatic arthritis (PsA) in spite of treatment with biologic/conventional disease modifying drugs (b/cDMARDs). Studies on the prognostic role of pain mechanisms in PsA, are scarce.

**Objectives:** To investigate the presence of widespread non-arthritis pain (WP) in patients with PsA, and determine its relation to patient-reported, clinical- and ultrasound (US) disease measures, as well as to achievement of 4 months response to b/cDMARD therapy. Secondly, to study if US Colour Doppler activity (CD) at baseline is associated to treatment response.

**Methods:** A prospective cohort study was performed following a protocol.<sup>1</sup> Patients initiating b/cDMARDs for PsA were recruited from rheumatology clinics in Copenhagen. Clinical- and US examinations and patient-reported outcomes (PROs) were performed at baseline and after 4 months. WP was defined as a Widespread Pain Index  $\geq 4$ , and pain in  $\geq 4/5$  regions. CD activity in selected joints, entheses and tendons (73 projections) was summed. Response was assessed by American College of Rheumatology 20% (ACR20), Disease Activity in Psoriatic Arthritis 50% (DAPSA 50) and Minimal Disease Activity (MDA). Main response analyses were based on intention to treat with non-responder imputation, and consisted of logistic regressions adjusting for gender and age.

**Results:** Of 123 screened patients, 69 were included. Of these, 24 (35%) fulfilled the WP definition. At baseline (Table), WP was associated with worse PROs and composite scores, while CD activity and clinical measures were similar to those without WP. WP profile was significantly related to achievement of MDA at follow-up but not to other response criteria (table 1). Presence of CD activity at baseline was not significantly associated to 4 months response by any criteria, e.g. 19%/31% with CD=0/CD >0, reached ACR20, (p=0.262).

**Abstract SAT0303 – Table 1.** Baseline characteristics

Females, n (%)	15 (63)	24 (53)	0.634
PsA impact of Disease (PsAID)	6.2 (1.7)	4.2 (2.2)	<0.001
HAQ-DI (0–3)	1.2 [0.9 to 1.5]	0.6 [0.3 to 1.0]	<0.001
VAS Pain (0–100)	68.8 (19.2)	44.5 (27.6)	<0.001
DAPSA (0–164)	49.3 (18.1)	29.8 (18.5)	<0.001
SPARCC enthesitis (0–16)	7.5 (3.4)	4.2 (3.0)	<0.001
CD score (0–200)	1.0 [0.0 to 4.3]	1.0 [0.0 to 5.0]	0.686
Swollen Joints (0–66)	3.0 [1.0 to 6.3]	4.0 [2.0 to 8.0]	0.352
Tender Joints (0–68)	26.5 [24.5 to 37.0]	11.0 [6.0 to 20.0]	<0.001
<b>4 months responses</b>			
ACR20, n (%)	6 (25)	12 (28)	0.779
DAPSA 50, n (%)	7 (29)	15 (33)	0.724
MDA, n (%)	0 (0)	9 (20)	0.022

Data as mean(SD) or median[IQR] P-value from T test/Mann Whitney U-test/ $\chi^2$  test,

**Conclusions:** WP was present in 1/3 of patients, and associated with worse PROs, composite measures, and failure to achieve MDA at follow-up. Neither WP nor CD at baseline was related to other response measures.

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**Disclosure of Interest:** None declared

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SAT0304

**PRECLINICAL PHASES OF PSORIATIC ARTHRITIS: A CROSS-SECTIONAL ULTRASONOGRAPHIC STUDY ON PSORIASIS AND PSORIATIC ARTHRALGIA PATIENTS**

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**Background:** Identify the preclinical phase of arthritis could be clinically relevant. In this scenario, musculoskeletal ultrasonography (US) may play an important role, since it may detect subclinical disease. Psoriatic Arthritis (PsA) is a perfect disease to identify risk factors, since the risk pool group [i.e. patients with only cutaneous Psoriasis (Pso)] is known.

**Objectives:** To evaluate in Pso patients, with and without clinical arthralgia (CA), defined by the presence of joint pain without other clinical evidence of musculoskeletal inflammation: I) the prevalence of subclinical US inflammation in joints, entheses, tendons and bursae; II) the prevalence of US structural damage; III) the relationship between US lesions and clinical data.

**Methods:** Cross-sectional prevalence study of US abnormalities in Pso patients with or without CA and healthy controls (HCs). Inclusion and exclusion criteria (e.g. osteoarthritis and fibromyalgia) are pre-defined. Forty-four joints (MCP, PIP and DIP joints, wrists, knees, MTP joints) and 12 entheses (achilles, quadriceps, proximal and distal patellar, plantar aponeurosis and common extensor tendon entheses) were scanned in each patient. US scans were performed using a ESAOTE MyLabClassC equipped with a high frequency linear probe. Active synovitis was defined by the presence of a grade  $\geq 2$  for grey scale (GS) and  $\geq 1$  for PD, while active enthesitis if there was hypoechogenicity in GS and an enthesial PD signal ( $\leq 2$  mm from bone insertion).

**Results:** Sixty-four Pso patients and 21 HCs were included; globally 2816 joints and 768 entheses were scanned. Twenty-three out of 64 (35.9%) Pso patients displayed CA. Baseline characteristics are reported in table 1. Active synovitis was found, in at least one joint, in 20/64 (31.3%) Pso patients and 0/21 HCs (p=0.002), while active enthesitis in 14/64 (21.9%) Pso patients and 0/21 HCs (p=0.017). No significant differences were found for active synovitis or enthesitis between the two subgroups of Pso, with or without CA. In the Pso cohort, 5/23 (23.8%) patients with CA and 2/41 (5%) without CA displayed tenosynovitis or paratenonitis (p=0.042). Furthermore, active synovitis, as well as GS-synovitis  $\geq 2$ , was associated with higher NAPSI (9.7 $\pm$ 8.0 vs 4.6 $\pm$ 7.1, p=0.04 for GS  $\geq 2$ ),



whereas active enthesitis was associated with higher PASI (5.4±3.0 vs 3.7±2.9, p=0.02). No significant differences were found between Pso patients and HCs for the structural damage (i.e. osteoproliferation and erosions), both for joints and entheses.

**Abstract SAT0304 – Table 1.** \* p significant Pso with CA vs HCs; \*\* p significant Pso with CA vs Pso without CA

Baseline data	Pso without CA (n=41)	Pso with CA (n=23)	Healthy controls (n=21)
Age mean (±SD)	51.37 (±15.88)	49.91 (±14.23)	45.76 (±15.89)
Female n. (%)	23 (56.1%)	10 (43.5%)	12 (57.1%)
Smoking n. (%)	12 (29.3%)	2 (9.0%)	6 (28.6%)
BMI mean (±SD)	25 (4.0%)	27 (±4.3%)	24 (±4.2)
Clinimetric data	Pso without CA (n=41)	Pso with CA (n=23)	Healthy controls (n=21)
VAS pain (0-10) mean (±SD)	2 (±2.4)	4 (±2.4) * **	2 (±2.35)
HACQ mean (±SD)	0 (±0.31)	0 (±0.45) * **	0 (±0.21)
Joints tenderness mean	0.34 per patient	2.56 per patient * **	0.17 per patient
Comorbidities	Pso without CA (n=41)	Pso with CA (n=23)	Healthy controls (n=21)
Obesity n. (%)	4 (9.8%)	0 (0%)	1 (4.8%)
Diabetes Mellitus n. (%)	3 (7.3%)	0 (0%)	2 (9.5%)
Hypertension n. (%)	7 (17.0%)	7 (30.4%)	5 (23.8%)
Metabolic syndrome n. (%)	5 (12.2%)	3 (13.4%)	4 (19.0%)
Fatty liver disease n. (%)	5 (12.2%)	4 (17.4%)	1 (4.8%)
Uveitis n. (%)	2 (4.9%)	0 (0%)	0 (0%)
Depression n. (%)	2 (4.9%)	3 (13.0%)	0 (0%)
CV disease n. (%)	3 (7.3%)	0 (0%)	1 (4.8%)

**Conclusions:** In Psoriasis subclinical US active synovitis and/or enthesitis are present in 20%–30% of patients. In Pso the comparison between groups, with or without CA, show no significant difference in active subclinical synovitis or enthesitis, but Pso patients with CA present more frequently US tenosynovitis or paratenonitis. In Pso subclinical US synovitis or enthesitis are significantly associated with higher NAPSI and PASI. The relevance of these results, to possibly identify a subgroup of Pso more prone to develop PsA, deserve further investigation and prospective evaluation.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.4305

### SAT0305 ASSESSMENT OF SUB CLINICAL HAND JOINT SYNOVITIS IN PATIENTS WITH PSORIATIC ARTHRITIS AND PSORIASIS BY ULTRASOUND AND ITS RELATIONSHIP WITH CLINICAL DISEASE ACTIVITY

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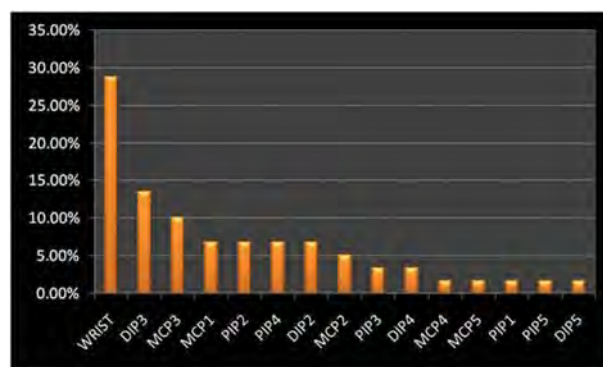
**Background:** Articular involvement in Psoriatic arthritis (PsA) can have diverse presentations; oligoarticular involvement is predominant in early disease. Ultrasound (US) detected subclinical synovitis can be present in early PsA and a substantial portion of oligoarthritic PsA patients are being reclassified as having polyarthritides.<sup>1</sup> Asymptomatic US synovitis and enthesopathy can be present in Psoriasis (Pso) patients which probably indicate subclinical musculoskeletal involvement.<sup>2</sup>

#### Objectives:

- To evaluate sub-clinical synovitis of hand joints in patients with PsA and Pso by B-mode and Power Doppler US.
- Correlation of PsA and Pso disease activity with US detected synovitis.

**Methods:** 27 patients of PsA (disease duration <2 years, no clinical evidence of hand joint involvement), 36 Pso patients and 30 controls were recruited. PASI and DAPSA score used for assessment of cutaneous and articular disease activity respectively. US [grey scale (GS) and power Doppler (PD)] used to assess synovitis of hand joints. A GS score ≥2 and/or a PD score ≥1 were used to identify US detected synovitis.

**Results:** Significantly more patients with PsA had sub-clinical hand joint synovitis than controls (62.96% versus 20%, p value=0.001, relative risk: 3.148, 95% C.I.: 1.455 to 6.814), and Pso patients [(27.78%), p value=0.0095, relative risk=2.267, 95% C.I.: 1.243 to 4.135]. Median number of joints involved in PsA group was 4 (inter quartile range: 2–5). Among 810 hand joints scanned in PsA group, 59 (7.28%) joints showed evidence of sub-clinical synovitis. Wrist joint was most commonly involved (28.81%), followed by DIP3 (13.56%) and MCP3 (10.17%). Less involvement noted in MCP4, MCP5, PIP1, PIP5 and DIP5 (1.69%). In Pso patients, evidence of sub-clinical synovitis was not significantly different from control. (p value=0.5689, relative risk=1.389, 95% C.I.: 0.5710 to 3.378). However, wrist and DIP involvement was significantly more in Pso than control. No correlation noted between numbers of joints with subclinical synovitis with DAPSA or PASI score.



#### Conclusions:

- Almost two third patients with early PsA had PDUS evidence of sub-clinical synovitis in hand joints, most commonly in wrist joint followed by DIP3 and MCP3.
- No significant increase of sub-clinical synovitis in Pso compared to control group. However, wrist and DIP joint involvement was significantly more in Psoriasis.
- There was no correlation between number of joints with sub-clinical synovitis and disease activity indices.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.1977

### SAT0306 FINGER FLEXOR TENDON PULLEY COMPLEX INVOLVEMENT IN PSA DACTYLITIS: AN ULTRASONOGRAPHY STUDY

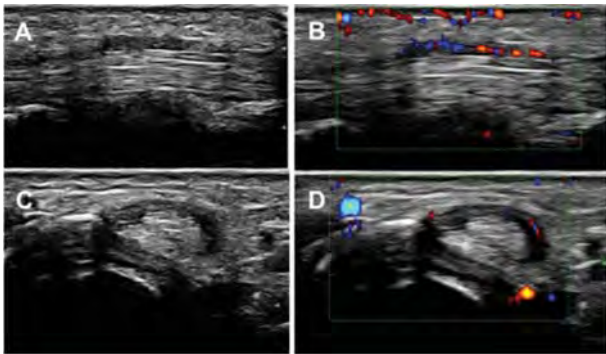
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**Background:** Dactylitis is a hallmark of psoriatic arthritis (PsA) occurring in around 40% of cases at some point in the disease course. At the micro anatomical level PsA is strongly linked to disease localisation to entheses and other sites of high mechanical stress. Recently high resolution MRI has shown prominent abnormalities at the mini-entheses of the flexor tendon pulleys may be common

**Objectives:** . In this study we aimed to understand the changes within the pulleys for patients with PsA, with or without dactylitis to explore the role of the pulley disease in the dactylitis.

**Methods:** Consecutive 20 cases of PsA with dactylitis were recruited and had an US scan of the A1, A2 and A4 pulleys of the digit with dactylitis and the contralateral side. A high resolution probe (22 MHz) was used to explore a) the thickness of the pulleys, b) the presence of Doppler signals. A comparison was made within digits with or without dactylitis

	Dactylitis (-)	Dactylitis (+)	p
A1- longitudinal	0.69 (0.10)	1.00 (0.34)	0.001
A2- longitudinal	0.77 (1.11)	0.75 (0.15)	<0.001
A4- longitudinal	0.50 (0.09)	0.65 (0.15)	<0.001
A1- transverse	0.68 (0.10)	1.01 (0.33)	<0.001
A2- transverse	0.51 (0.09)	0.73 (0.16)	<0.001
A4- transverse	0.50 (0.08)	0.71 (0.27)	<0.001



**Abstract SAT0306 – Figure 1.** The increased thickness and the presence of Doppler signals in the A1 pulley in a digit with dactylitis in longitudinal (A and B) and transverse (C and D)

**Results:** Half of the A1 pulleys with dactylitic digits had Doppler signals (10/20, 50%), which was less common in A2 (6/20 (30%)) and A4 pulleys (6/20 (30%)) (figure). The digits without dactylitis had Doppler signals less frequently (A1: 1/19 (5%); A2: 1/19 (5%); A4: 1/19 (5%))

A1, A2 and A4 pulleys were significantly thicker in dactylitis fingers compared to fingers without dactylitis, both in longitudinal and transverse planes (table 1).

**Conclusions:** This study demonstrates that pulleys contribute to the pathogenesis of dactylitis with increased vascularity and thickening, probably due to the micro-enthesitis at the level where the flexor tendons are exposed to high mechanical stress. This is important to understand the anatomical basis of a complex disease feature in PsA, dactylitis

**Disclosure of Interest:** None declared

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SAT0307

#### IMPACT OF THE MODIFIED RHEUMATIC DISEASE COMORBIDITY INDEX (mRDCI) ON DRUG SURVIVAL OF FIRST LINE ANTI-TNF $\alpha$ DRUGS IN PATIENTS AFFECTED WITH PSORIATIC ARTHRITIS IN REAL LIFE SETTING

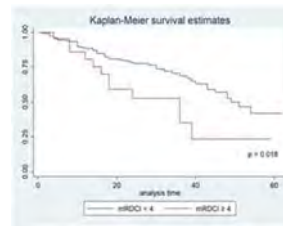
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**Background:** Psoriatic Arthritis (PsA) is a chronic condition resulting in significant physical disability and, in many cases, accelerated mortality. Studies have shown that patients with PsA suffer also from associated comorbidities, including cardiovascular diseases, obesity and metabolic syndrome, diabetes, osteoporosis, malignancy and depression; these could also play a role in determining discontinuation from therapy, especially if anti-TNF $\alpha$  drugs are prescribed.

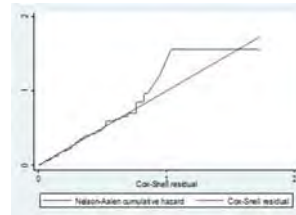
**Objectives:** Our study's goal is to demonstrate the impact of comorbidities on drug survival of first line anti-TNF $\alpha$  treatment in a cohort of patients affected with PsA.

**Methods:** We retrospectively assessed 208 patients, (136 female, 72 male) mean age ( $\pm$ SD) 51.35 $\pm$ 12.34 years, fulfilling the CASPAR criteria for PsA who underwent first line anti-TNF $\alpha$  therapy in two centres for a mean duration of 23.34  $\pm$ 15.50, from 2011 to 2016. Disease characteristics were registered at first entry. To evaluate the burden of comorbidities we used the modified Rheumatic Disease Comorbidity Index (mRDCI),<sup>1</sup> a validated score including lung illnesses, cardiovascular diseases, stroke, hypertension, gastrointestinal disorders, diabetes, fractures, depression, obesity, kidney diseases and cancer. The mRDCI was scored at baseline as well. Drug retention was analysed using Kaplan-Meier curves. Cox regression models were used to estimate the inference of mRDCI and several disease characteristics on drug discontinuation. Goodness of fit of the final model was assessed comparing Cox-Snell residuals to Nelson-Alen cumulative hazard function.

**Results:** Drug persistence in first line therapy was significantly higher in patients with mRDCI <4 (70.43%) than in those with mRDCI  $\geq$ 4 (45.45%). Compared to mRDCI  $\geq$ 4, those with mRDCI <4 showed significantly higher drug survival rate (p=0.018). Multivariate Cox model showed that mRDCI  $\geq$ 4 (HR 1.94) and female gender (HR 2.39) were strong predictors of drug discontinuation. Nelson-Alen hazard function followed very closely Cox-Snell residuals showed final model fitted well the data except for large values of time.



**Abstract SAT0307 – Figure 1.** Drug survival in first-line anti-TNF $\alpha$  treatment assessed by Kaplan-Meier and comparison among patients with mRDCI <4 and mRDCI  $\geq$ 4.



**Abstract SAT0307 – Figure 2.** Nelson-Alen Hazard function and Cox-Snell residual

**Conclusions:** This study shows that a high mRDCI at baseline negatively impacts the persistence on first line anti-TNF $\alpha$  treatment in patients affected with PsA in real life setting; hence Rheumatologists should take into account comorbidities in the management of PsA and in administering anti-TNF $\alpha$  therapy as these may condition the persistence on therapy.

#### REFERENCE:

- [1] Staetgens, et al. Content and construct validity of the Rheumatic Diseases Comorbidity Index in patients with gout. *Rheumatology* 2015 Sep;54 (9):1659–1663.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.2216

SAT0308

#### PROSPECTIVE OBSERVATIONAL STUDY ON OCULAR INVOLVEMENT IN PATIENTS AFFECTED BY MODERATE TO SEVERE PSORIATIC ARTHRITIS

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**Background:** Psoriatic Arthritis (PsA) is a chronic inflammatory arthritis typically often associated to several comorbidities. The presence of eye involvement in terms of uveitis is well known in PsA patients while retinal abnormalities and dry eye need to be characterised

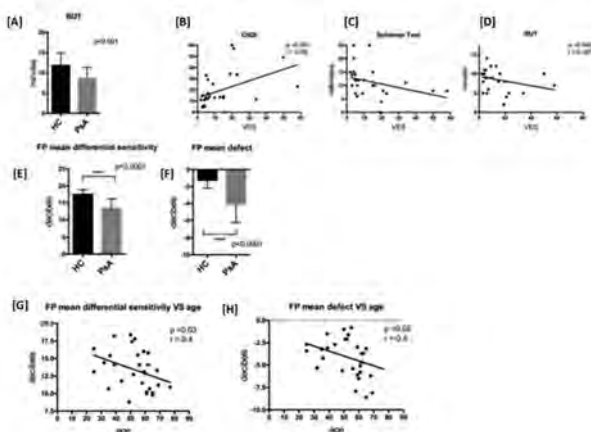
**Objectives:** The aim of the study was to analyse subclinical retinal abnormalities and dry eye in a cohort of PsA patients who were naïve to biologic treatments

**Methods:** In a prospective cross-sectional study, consecutive PsA patients without clinical eye involvement were enrolled (time frame January 2017-December 2017). Joint disease activity and ESR and CRP were measured. Functional and morphological eye assessment included: complete ophthalmological examination, ocular surface disease index (OSDI), Schirmer test, BUT, spectral-domain optical coherence tomography (SD-OCT), standard automated perimetry (SAP, measured as mean defect – MD – and pattern standard deviation – PSD), and fundus perimetry (FP). Data were compared to findings from the eyes of 24 age/sex matched healthy controls (HC).

**Results:** A total of 58 eyes from 29 PsA patients (21 women and 8 men; age 52.7  $\pm$ 13.3 years) and 48 eyes from HC (14 women and 10 men; age 47.6 $\pm$ 15 years) were evaluated.

Overall, most of the PsA patients showed a normal Schirmer test, with the exclusion of three patients (10.3%). PsA patients showed abnormal OSDI in 55.2% and lower BUT in compared to HC (p<0.001, Fig.1A). ESR resulted positively correlated with OSDI (p<0.001, r=0.6, Fig.1B), and negatively related with Schirmer test (p=0.005, r=-0.5, Fig.1C) and BUT (p=0.04, r=-0.4, Fig.1D). In the PsA group, SAP tests showed a lower MD (p<0.0001) and a higher PSD (p=0.0043) in

comparison with the HC. The latter PSD analysis resulted positively correlated with ESR ( $p=0.01$ ;  $r=0.5$ ) and CRP values ( $p=0.001$ ;  $r=0.4$ ). FP mean differential sensitivity and FP mean defect values were lower in PsA patients with respect to HC ( $p<0.0001$  for both the comparisons, figure 1E-F) and resulted negatively correlated with the age ( $p=0.03$   $r=-0.4$  for both the correlations, figure 1G-H). SD-OCT in the posterior pole (superior and inferior hemifields) did not reveal differences for the mean retinal thickness between PsA patients and HC.



**Conclusions:** Intriguingly, an impairment in quality of tear film in PsA patients was observed compared to HC. The correlation between ESR and dry eye tests may be explained with a potential relationship between systemic inflammation and sicca syndrome.

Interestingly, PsA patients showed a retinal functional impairment by reduced retinal sensitivity measured by MD, FP mean differential sensitivity and FP mean defect values.

To our knowledge this is the first study investigating eye function and morphology in PsA patients. Further studies are needed to confirm and explain these results.

**Disclosure of Interest:** None declared

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### SAT0309 UNDERESTIMATION OF CARDIOVASCULAR EVENTS BY CARDIOVASCULAR RISK SCORES IN PSORIATIC ARTHRITIS PATIENTS

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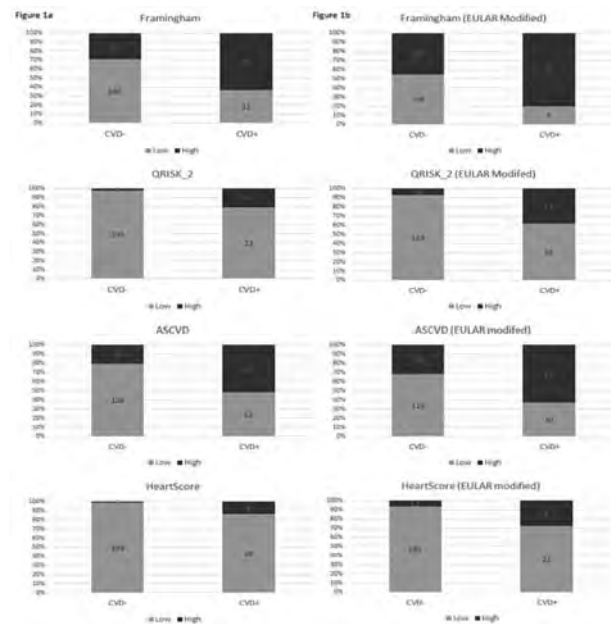
**Background:** Compared with the general population, patients with Psoriatic Arthritis (PsA) have elevated risks of developing cardiovascular diseases (CVD). The performances of established CVD risk scores in PsA patients have not been fully evaluated yet. European League Against Rheumatism (EULAR) recommends a 1.5 multiplication factor to these CVD risk scores when it is applied in rheumatoid arthritis patients. Whether the same multiplication factor could improve the performance of the risk scores in PsA patients is unknown.

**Objectives:** To investigate the performances of various CVD risk scores and their EULAR modified versions for predicting CVD events in PsA patients

**Methods:** Prospectively collected data from the two Hong Kong PsA cohort was used. Discriminatory ability for CV risk prediction was estimated by the area under the receiver operating characteristic curve (AUC). Four different CVD risk scores namely Framingham risk score (FRS), QRISK II, HeartScore and American College of Cardiology and American Heart Association (ACC/AHA) 10 year atherosclerotic cardiovascular disease (ASCVD) and their EULAR modified versions were calculated at baseline. The primary outcome was first CVD events, including stable and unstable angina, myocardial infarction, ischaemic and haemorrhagic stroke, transient ischaemic attack, heart failure, coronary insufficiency, pericardial disease, peripheral arterial disease, thrombosis, percutaneous coronary intervention (angioplasty), coronary artery bypass graft, implantation of pacemaker or defibrillator and CVD death.

**Results:** 228 patients [48.9±11.8 years, male: 124 (54.4%)] were recruited between 2006 to 2016. Baseline data were available from 227, 226, 226 and 188 patients to calculate the FRS, QRISKII, HeartScore and ASCVD, respectively. After a mean follow up of 6.7±4.7 years, 30 patients (13.2%) experienced a CVD event (CVD +group). At baseline, the CVD +group was significantly older (57.8±12.0 vs 47.6±11.2 years;  $p<0.001$ ), with a higher prevalence of diabetes (26% vs 12%;  $p<0.021$ ), had higher systolic blood pressure (SBP: 142±22.0 vs 128

±19.6 mmHg;  $p<0.001$ ) and higher triglycerides (TG: 1.9±1.3 vs 1.4±0.8 mmol/L,  $p=0.027$ ). All CVD risk scores were significantly higher in the CVD +group (FRS: 18.3±13.1 vs 8.9±8.7,  $p<0.001$ ; QRISKII: 11.9±8.6 vs 4.9±5.0,  $p<0.001$ ; HeartScore: 2.3±2.1 vs 0.9±1.3,  $p=0.001$ ; ASCVD: 14.5±12.8 vs 4.8±5.2,  $p=0.001$ ). AUC for FRS, QRISKII, HeartScore and ASCVD were 0.74 (0.64–0.83,  $p<0.001$ ), 0.76 (0.66–0.86,  $p<0.001$ ), 0.72 (0.62–0.83,  $p<0.001$ ), and 0.77 (0.67–0.86,  $p<0.001$ ), respectively. In total, 76 (33.5%), 9(4.0%), 7 (3.1%) and 47 (25.0%) patients were classified as high CVD risk according to FRS >10%, QRISK II>20%, HeartScore >5% and ASCVD >7.5% respectively. In the CVD +group, those identified as high risk were only 63% (by FRS), 20% (by QRISK2), 13.3% (by HeartScore) and 46% (by ASCVD) (figure 1a). By applying the EULAR multiplication factor, 80%, 36%, 26.67% and 56.7% of the patients with CVD +were reclassified as high risk (figure 1b).



**Abstract SAT0309 – Figure 1**

**Conclusions:** All CVD risk scores significantly underestimated CVD risks among PsA patients. This study demonstrated for the first time that adaptation of the EULAR recommendation only improved the accuracy of FRS to a moderate level.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.6074

### SAT0310 THE ASSOCIATIONS OF SERUM IL18 AND OSTEOPROTEGERIN (OPG) LEVELS WITH THE LIPID PROFILE IN PSORIATIC ARTHRITIS (PSA) PATIENTS

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**Background:** We have previously found that IL-18 and OPG serum concentrations are correlated with cardiovascular (CV) risk in psoriatic arthritis but not in ankylosing spondylitis (AS) patients.<sup>1</sup>

**Objectives:** To investigate whether in PsA patients the association of OPG and IL-18 with CV risk is mediated by an impact of these cytokines on lipid profile changes.

**Methods:** 49 patients with PsA (25 M/24 F) with (n=10) and without (n=39) coronary heart disease (CHD), and 25 sex and age matched (mean age 44,4 vs 43,4 years) patients with AS were enrolled. Disease activity was measured by DAPSA (25,17±19,9) in PsA group and by BASDAI (5,37±2) and ASDAS- CRP (3,18±1) in AS group. The lipid profile (triglycerides – TG, total cholesterol – tChol, low- and high-density lipoprotein – LDL and HDL, respectively), systemic inflammation markers and cytokines (OPG, IL-18) were measured in patients serum samples. Atherogenic index (AI=tChol/HDL) was calculated. Statistical analysis was performed using Mann-Whitney U-test and Spearman's Rank test. Data are expressed as mean values.

**Results:** Patients with PsA presented more atherogenic lipid profile than AS patients because of their higher TG levels (153 vs 126,6 mg/dl;  $p=0,05$ ) and AI values (3,83 vs 3,24;  $p=0,05$ ) while lower HDL concentrations (51,6 vs 61,4 mg/



dl;  $p=0,04$ ). Compared to AS group, PsA patients were characterised by higher IL-18 (235 vs 208 pg/ml;  $p<0,05$ ) but lower OPG (815 vs 1660 pg/ml;  $p<0,05$ ) serum levels. In PsA patients without CHD, serum OPG positively but moderately correlated with LDL ( $r=0,3$ ;  $p=0,05$ ), TG ( $r=0,43$ ;  $p=0,007$ ) and AI ( $r=0,45$   $p=0,004$ ). Moreover, in this PsA patients subgroup we confirmed previously observed<sup>1</sup> inverse correlation of IL-18 with HDL levels ( $r=-0,34$ ;  $p=0,05$ ) and positive correlation of this cytokine with both TG levels ( $r=0,37$ ;  $p=0,04$ ) and AI values ( $r=0,53$ ;  $p=0,002$ ). Interestingly, similar but stronger associations of IL-18 with HDL levels ( $r=-0,88$ ;  $p=0,004$ ) and AI values ( $r=0,88$ ;  $p=0,004$ ) were presently found in PsA patients with accompanied CHD. Consistently with our previous report,<sup>1</sup> we failed to find any correlations between CV risk, lipid profile, and tested cytokines serum concentrations in patients with AS.

**Conclusions:** We report that in PsA, but not AS, patients serum IL-18 and OPG concentrations are correlated with an altered and pro-atherogenic lipid profile. These associations are stronger in patients with concomitant CHD. Thus, present results explain partially the way by which these cytokine contribute to CV complications in PsA.

#### REFERENCE:

- [1] Kontny E, et al. Association of serum osteoprotegerin and IL-18 concentrations with cardiovascular risk in ankylosing spondylitis and psoriatic arthritis. *Ann Rheum Dis* 2017;76(suppl 2):1310–1311 AB0733.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.4647

SAT0311

#### PREVALENCE AND FACTORS RELATED TO INAPPROPRIATELY HIGH LEFT VENTRICULAR MASS IN PATIENTS WITH PSORIATIC ARTHRITIS WITHOUT OVERT CARDIAC DISEASE

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**Background:** Early cardiovascular (CV) involvement has been found in patients with psoriatic arthritis (PsA). These patients may have a high prevalence of subclinical left ventricular (LV) dysfunction, even without established CV disease and in the absence of traditional CV risk factors. However, currently, the factors associated with LV dysfunction in PsA are unknown. Patients with inflammatory disorders are exposed to the development of excessive left ventricular mass disproportionate to the need to compensate left ventricular load, a condition named 'inappropriately high left ventricular mass' (iLVM). Previously, we have shown that iLVM is associated with unfavourable prognosis in patients with rheumatoid arthritis independent of traditional CV risk factors.

**Objectives:** In this cross-sectional study, we assessed the prevalence and factors associated with iLVM in a cohort of patients with PsA and tested the hypothesis that PsA is *per se* related to iLVM.

**Methods:** We evaluated 101 non-institutionalised patients >18 years of age diagnosed with PsA according to CASPAR criteria and consecutively recruited between March 2014 and December 2016. All PsA patients were free of symptoms or signs of cardiovascular disease. Patients with PsA were compared with 101 controls matched for age, sex, BMI, prevalence of hypertension and diabetes. Left ventricular chamber dimensions and wall thicknesses were measured according to the American Society of Echocardiography guidelines and predicted LVM was calculated using a validated equation considering height, sex and left ventricular work. iLVM was defined as measured/predicted LVM ratio above the 95% percentile of a reference population of healthy controls.<sup>1</sup>

**Abstract SAT0311 – Table 1.** Variables significantly related to iLVM in the entire study population (101 patients with PsA and 101 matched controls).

Predictors	OR	95% CI	P value
Psoriatic arthritis	6.91	2.80–17.06	<0.001
Waist circumference	1.04	1.00–1.07	0.047
Dyslipidemia	0.85	0.39–1.89	0.696
Hypertension	1.29	0.56–2.96	0.547
Diabetes mellitus	2.42	0.60–9.79	0.214
Age	1.02	0.98–1.07	0.291
Sex (male)	1.27	0.57–2.84	0.559

**Results:** iLVM was detected in 58% of patients with PsA and 18% of controls ( $p<0,001$ ). In multivariable logistic regression analysis considering only patients with PsA, the variables independently associated with iLVM were left ventricular

systolic dysfunction (LVSD) measured as mid-wall shortening and concentric left ventricular geometry. In multiple regression analyses considering the entire study population (patients with PsA and matched controls), the diagnosis of PsA was significantly associated with iLVM independent of traditional cardiovascular risk factors (OR 6.91, 95% CI 2.80–17.06,  $p<0,001$ ; table 1).

**Conclusions:** More than 50% of patients with PsA have a disproportionate increase in their LVM. An inappropriately high LVM in PsA is associated with LV systolic dysfunction and LV concentric geometry.

#### REFERENCE:

- [1] Cioffi G, Viapiana O, Ognibeni F, Dalbeni A, Giollo A, Adami S, Gatti D, Russo G, Barbati G, Cherubini A, Di Lenarda A, Rossini M. Prevalence and factors related to inappropriately high left ventricular mass in patients with rheumatoid arthritis without overt cardiac disease. *J Hypertens* 2015;33:2141–2149.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.2953

SAT0312

#### INCIDENCE OF INFECTIONS IN CLINICAL TRIALS OF TILDRAKIZUMAB FOR MODERATE TO SEVERE CHRONIC PLAQUE PSORIASIS

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**Background:** Risk of infections is a concern with cytokine inhibitor treatments.

**Objectives:** This analysis assessed infections during phase 2 and 3 trials of tildrakizumab (TIL), a high-affinity, humanised, immunoglobulin G1/κ monoclonal antibody against IL-23p19 under development for moderate to severe chronic plaque psoriasis.

**Methods:** Patients were randomised in P05495 (phase 2; NCT01225731), reSURFACE 1 (phase 3; NCT01722331), and reSURFACE 2 (phase 3; NCT01729754). In Part 1 (Weeks 1–16) of P05495, patients received subcutaneous (SC) TIL 5, 25, 100, or 200 mg or placebo (PBO) at Weeks 0 and 4 and were rerandomized to various TIL doses in Part 2 (Weeks 16–52). In Part 1 (Weeks 1–12) of reSURFACE 1 and 2, patients received SC TIL 200 mg, TIL 100 mg, or PBO at Weeks 0 and 4. Patients were rerandomized in Part 2 (Weeks 12–28) and Part 3 (Weeks 28–64 or –52 in reSURFACE 1 and 2, respectively). Etanercept (ETN) 50 mg was an active control in Parts 1–2 of reSURFACE 2. Treatment-emergent adverse event (AE) data pools (n=2081) for the PBO-controlled and full trial periods (52 weeks for P05495/reSURFACE 2; 64 weeks for reSURFACE 1) were analysed. Severe infections met the regulatory definition of a serious AE or required intravenous antibiotics.

**Results:** In the PBO-controlled period, incidences of infections were comparable for TIL 100 mg and 200 mg (23% and 22%, respectively) and PBO (23%); all were comparable with ETN (24%). Incidences of severe infections were low for all treatment groups (range, 0.0%–0.3%; TIL  $p \geq 0.6$  vs PBO). In the full trial period, exposure-adjusted rates (patients/100 patient-years) for infections with TIL 100 mg and 200 mg (48.9 and 52.6, respectively) were lower than with PBO and ETN (79.5 and 86.0, respectively). Exposure adjusted rates for severe infections were 1.10, 1.61, 1.96, and 0.91 for TIL 100 mg, TIL 200 mg, ETN, and PBO, respectively. In total, 33 severe infections were identified (respiratory: TIL 100 mg, 4 events; TIL 200 mg, 2 events; ETN and PBO, 0 events; skin: TIL 100 mg, 3 events; TIL 200 mg, 6 events; ETN, 2 events; PBO, 3 events; gastrointestinal: TIL 100 mg, 4 events; TIL 200 mg, 5 events; ETN and PBO, 0 events; urinary tract: TIL 200 mg, 1 event; ETN, 1 event; TIL 100 mg and PBO, 0 events). One patient had bone tuberculosis (TIL 200 mg; original purified protein derivative test was negative); 1 sepsis event (TIL 200 mg) occurred months after ending TIL treatment.

**Conclusions:** Infection rates with TIL treatment were low and comparable to PBO and ETN during the PBO-controlled period. By Weeks 52/64, exposure-adjusted rates remained low for all groups.

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SAT0313

### LIPID PROFILE OF PSORIATIC ARTHRITIS PATIENTS. A FIVE-YEAR STUDY

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**Background:** Psoriatic arthritis (PsA) is an inflammatory arthritis associated with psoriasis. Many studies have shown alterations in lipid profile of PsA patients and an association with increased cardiovascular risk.

**Objectives:** To evaluate the changes of lipid profile in PsA patients treated with conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs) and/or with biological DMARDs (bDMARDs) in a five-year period.

**Methods:** We studied 254 patients diagnosed with PsA according to CASPAR and ASAS (for those with axial disease) criteria. Patients were followed up at pre-defined time points [baseline, 24 weeks (wks), 48 and 240 wks after initiation of treatment. We recorded levels of Total Cholesterol (CHOL), Low Density Lipoproteins (LDL), High Density Lipoproteins (HDL) and Triglycerides (TGL). The disease activity was assessed by using Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI), disease activity score-28 (DAS) -C-Reactive Protein (CRP), DAS28-erythrocyte sedimentation rate (ESR), Health Assessment Questionnaire (HAQ), and inflammatory marker CRP and ESR. Patients were categorised in three treatment groups: patients treated with bDMARDs: anti-tumour necrosis factor alpha (TNF $\alpha$ ) agents, patients treated with csDMARDs and combined therapy (bDMARDs and csDMARDs). Disease Phenotype and epidemiological features of PsA patients were also recorded.

**Results:** There were 137 male and 117 female patients. The (Mean  $\pm$ SD) age of the patients was 56,11 $\pm$ 14,64 years and the body mass index (BMI) was 27,86  $\pm$ 5,12. Thirty-nine per cent of the patients presented as asymmetric oligoarthritis, 25,6% as symmetric polyarthritis while 27,6% had axial involvement with or without peripheral arthritis. Total CHOL and LDL levels were significantly associated with disease duration ( $p < 0,05$ ) while TGL and HDL were not significantly correlated. We found that HDL levels were significantly correlated with disease activity through time. More specific lower disease activity was associated with higher HDL levels for all disease activity scores and CRP at all time points ( $p < 0,05$ ). The significance was lost only for ESR. No association was found between the HDL levels and the different therapeutic option used. The rest of lipid profile levels did not show statistical significant association with disease activity at any time point for all disease activity indexes, including CRP and ESR.

**Conclusions:** Lipid profile of PsA patients seems to improve with better control of disease activity. More specifically high HDL levels are associated with low disease activity and these changes appear to be independent of the therapeutic choices.

**Disclosure of Interest:** None declared

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SAT0314

### TO DESCRIBE AND CHARACTERISE THE PATIENT GROUP DEFINED AS COMPLEX IN A JOINT RHEUMATOLOGY/DERMATOLOGY CLINIC (PAIDER)

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**Objectives:** To describe and characterise the patient group defined as complex in a joint Rheumatology/Dermatology clinic (PAIDER).

**Methods:** We performed a retrospective chart review of patients evaluated between May 2012 and November 2017 at a weekly joint Rheumatology/Dermatology clinic at Hospital de Sant Pau (Autonomous University of Barcelona), Spain. We reviewed the medical records for demographic information, source of referral, complexity, cardiovascular risk factors and the number of visits. Complexity or complex patient was defined by at least one of the following characteristics: liver disease, neoplastic disease, psychiatric disorders, communication difficulties, adverse drug reactions to previous treatment, or paradoxical effects of biological therapy. The degree of complexity was a number (from 1 to 6) resulting from the sum of the previous characteristics. A descriptive analysis was carried out and the correlation between variables was studied through the application of nonparametric tests. The statistical package SPSS v. 21 was used to analyse the data.

**Results:** 494 patients were evaluated (52% women) with a total of 1110 visits. The mean age was 53 years. Patients were referred from Rheumatology, Dermatology, primary care physicians and other specialties in 47%, 40%, 6.5% and 5.5% of cases, respectively. The average number of visits per patient was 2.25.

164 patients (33%) were defined as complex with a total of 546 visits. 48.8% were women. The mean age was 55 years. They were referred from Rheumatology, Dermatology, primary care physicians and other specialties in 50.6%, 35.4%, 7.3% and 6.7% of cases, respectively. The mean number of following-up visits for the complex patients was 3.33.

The features that defined complexity and the number of visits required are shown in table 1.

Complexity features	Number of patients	Visits Mean $\pm$ SD
Liver disease	47/164 (28.7%)	3.6 $\pm$ 3.7
Psychiatric disorder	47/164 (28.7%)	3.4 $\pm$ 4.7
Adverse drug reactions	46/164 (28%)	4.7 $\pm$ 5.2
Paradoxical effects of biological therapy	37/164 (22.6%)	5.2 $\pm$ 5.7
Neoplastic disease	27/164 (16.5%)	1.8 $\pm$ 1.5
Communication difficulties	19/164 (11.6%)	4.1 $\pm$ 4.9

The number of visits according to the degree of complexity is shown in table 2.

Degree of complexity	Number of patients	Visits Mean $\pm$ SD
1	120/164 (73.2%)	2.8 $\pm$ 2.9
2	32/164 (19.5%)	4.1 $\pm$ 4.1
3	10/164 (6.1%)	6.4 $\pm$ 7.3
4	1/164 (0.6%)	1
5	1/164 (0.6%)	1
6	0/164 (0%)	0

The complexity features that had a significant correlation with the number of visits were liver disease ( $p < 0.001$ ), serious adverse effects to previous treatments ( $p < 0.001$ ) and paradoxical effects of biological therapy ( $p < 0.001$ ). The degree of complexity was also correlated with the number of visits (Spearman's Rho=0.262,  $p < 0.001$ ).

**Conclusions:** A third of the patients visited in our joint clinic were defined as complex, although the great majority showed a low level of complexity. Of all the features used to define complexity, only a few were associated with a greater number of visits. However, the degree of complexity of the patients was associated with an increased number of visits.

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SAT0315

### ABATACEPT IN PSORIATIC ARTHRITIS: A SINGLE CENTRE, PLACEBO-CONTROLLED, CROSSOVER STUDY IN 20 PATIENTS; A PILOT PROTEOMIC FEASIBILITY STUDY

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**Background:** Psoriatic arthritis (PsA) is a multifaceted inflammatory disease that affects approximately 0.25% of the global population<sup>1</sup>. A range of disease modifying drugs has been used to treat PsA including Abatacept. Unfortunately, not all PsA patients respond to Abatacept treatment and some patients may be intolerant, thus there is an urgent need for the improved selection of patients who are likely to respond Abatacept treatment.

**Objectives:** This pilot project seeks to demonstrate the potential with which MS based proteomics strategies might be used to discover proteins that may discriminate responders from non-responders to treatment with Abatacept. Using synovial samples collected at baseline and a label-free nLC-MS/MS strategy, candidate proteins were identified. These proteins together with other proteins identified in previous studies were further evaluated by developing multiplexed MRM assays to quantify the proteins both before and during Abatacept treatment (at 2 and 6 months).

**Methods:** Baseline samples from 6 patients were prepared according to the FASP protocol and analysed by Q-Exactive. MS data was analysed using MaxQuant (v. 1.4.1.2.) and Perseus (v. 1.5.0.8). For the evaluation of candidate proteins Skyline (v. 3.7.0.11317) was used to develop multiplexed MRM assays for these newly identified proteins and to analyse the MRM data acquired on high sensitivity triple quadrupole mass spectrometer (Agilent 6495).

**Results:** 41 proteins were shown to be differentially expressed at baseline between responders (n=5) and the non-responder (n=1). Of these proteins, 15 were elevated and 26 were reduced in the non-responder. A sub-set of the candidate proteins identified here (n=41) and some proteins identified in our previous PsA related studies<sup>2</sup> was used to develop an MRM assay targeting total 114 proteins. The MRM assay was developed using our stringent MRM assay standards. Six candidate proteins, ANXA1, ANXA2, S100A10, LMNA, CADH5 and MYL6 have been shown to be differentially expressed in synovial samples collected at 2 months when compared to 6 months. A further 5 proteins, ANXA5, RS18, TAGL, TRFL and HPT were differentially expressed between responders and non-responder at the 2 month time point but most importantly, these five proteins have shown a similar pattern of expression following four months of Abatacept treatment.

**Conclusions:** Although the small number of patient samples in this pilot study limits the biological significance of these findings, the data highlights some of the significant advantages of unbiased LC-MS/MS protein discovery and of multiplexed MRM assays. These advantages include reproducible and robust coverage of a large number of proteins in small synovial tissue samples and a workflow that supports rapid development of optimised multiplexed assays targeted to proteins of interest.

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SAT0316

### RAPID AND SUSTAINED IMPROVEMENTS IN BOTH SKIN AND MUSCULOSKELETAL SYMPTOMS CORRELATES WITH IMPROVED QUALITY OF LIFE IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS

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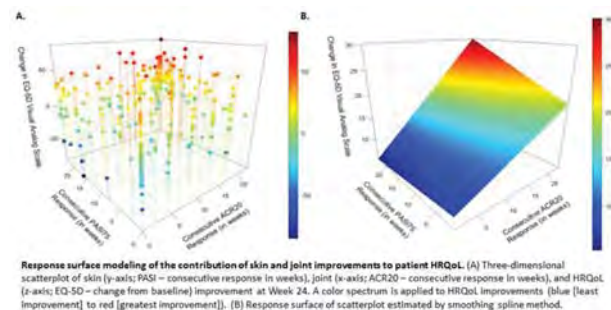
**Background:** Psoriatic arthritis (PsA) is a chronic, systemic, autoimmune, inflammatory arthritis condition commonly associated with psoriasis. Several biologic

therapies exist for the treatment of PsA, with varying degrees of efficacy and onset of action.

**Objectives:** The objective of this analysis was to examine whether there is additional value to a patient's overall quality of life if efficacy is achieved early during treatment and sustained.

**Methods:** Data were analysed from an integrated database of 2 double-blind, phase III SPIRIT trials investigating the efficacy and safety of ixekizumab (IXE), a high-affinity monoclonal antibody selectively targeting interleukin-17A, for patients with active PsA. The integrated database consisted of patients who were biologic-naïve (SPIRIT-P1, NCT01695239) or who had an inadequate response or were intolerant to tumour necrosis factor inhibitors (SPIRIT-P2; NCT02349295). Patients were randomised to placebo (n=224) or 80 mg IXE every 4 (n=229) or 2 weeks (n=226) after a 160 mg starting dose. Patients included in this post-hoc analysis had baseline  $\geq 3\%$  body surface area (BSA) and at least one visit with a Psoriasis Area and Severity Index (PASI) 75 and American College of Rheumatology (ACR) 20 response; all treatment groups were combined. During the first 24 weeks of the trial, health-related quality of life (HRQoL) was measured by Short Form-36 Health Survey (SF-36) domain scores, the EuroQoL 5 Dimensions Visual Analogue Scale (EQ-5D VAS), and the Work Productivity and Activity Impairment-Specific Health Problem (WPAI-SHP) activity impairment domain. Change in HRQoL at Week 24 was modelled using a response surface model with duration of consecutive PASI and ACR responses and their interaction as independent variables. Missing data were imputed using last observation carried forward and non-responder imputation for continuous and categorical endpoints, respectively.

**Results:** Of the 679 placebo- and IXE-treated patients in the SPIRIT trials, 215 (31.7%) had baseline  $\geq 3\%$  BSA and  $\geq 1$  PASI75 and ACR20 response. Longer consecutive ACR20 responses correlated positively with greater HRQoL improvements, as measured by the EQ-5D VAS (figure 1). Patients with a longer consecutive number of both ACR20 and PASI75 responses had the highest improvements in EQ-5D VAS. This was consistent with 7 of 8 SF-36 domains, as well as the WPAI-SHP activity impairment domain (data not shown).



Abstract SAT0316 – Figure 1

**Response surface modelling of the contribution of skin and joint improvements to patient HRQoL.** (A) Three-dimensional scatterplot of skin (y-axis: PASI – consecutive response in weeks), joint (x-axis: ACR20 – consecutive response in weeks), and HRQoL (z-axis: EQ-5D – change from baseline) improvement at Week 24. A colour spectrum is applied to HRQoL improvements (blue [least improvement] to red [greatest improvement]). (B) Response surface of scatterplot estimated by smoothing spline method.

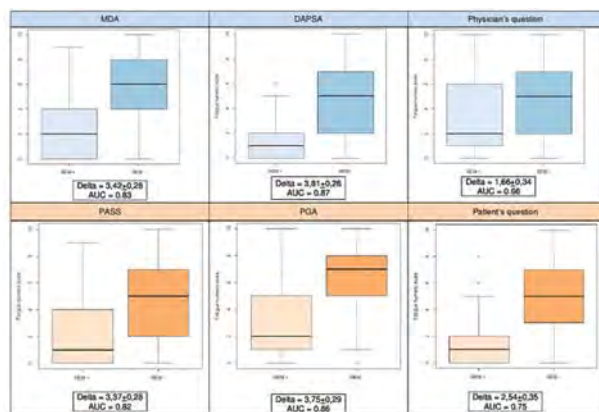
**Conclusions:** Early and sustained improvements in the symptoms of PSA correlated positively with improved HRQoL. The greatest HRQoL improvements were achieved when both skin and musculoskeletal symptoms improved early and were sustained.

**Disclosure of Interest:** A. Kavanaugh Consultant for: Eli Lilly and Company, J. Birt Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, C.-Y. Lin Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, O. Benichou Employee of: Eli Lilly and Company, M. Hufford Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, A. B. Gottlieb Grant/research support from: Janssen, Incyte, Consultant for: Janssen Inc.; Celgene Corp., Bristol Myers Squibb Co., Beiersdorf, Inc., Abbvie, UCB, Novartis, Incyte, Lilly, Reddy Labs, Valeant, Dermira, Allergan, Sun Pharmaceutical Industries

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**Conclusions:** Fatigue levels were relatively high in these PsA patients whose disease was often well-controlled. Fatigue was lower in patients in remission, according to all definitions of remission; the remission definition with best known-groups validity for fatigue was DAPSA remission. Moreover both composite measures perform better than the physicians opinion of remission. These elements may be important in a context of shared decision-making.

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#### SAT0319 DESCRIPTION OF MUSCULOSKELETAL SYMPTOMS IN A COHORT OF PATIENTS WITH PSORIASIS

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**Background:** The BIOMarkers of COMorbidities (BIOCOM) in Psoriasis (Pso) study is a longitudinal study which aims to identify clinical, genetic or protein biomarker features associated with the development of co-morbidities, notably Psoriatic Arthritis (PsA) in patients with Pso. Pso usually precedes the development of PsA with an average interval of 10 years. Thus, Pso patients are an ideal group in which to study the early events in the evolution to PsA.

**Objectives:** Herein we describe the baseline clinical features in this BIOCOM cohort. Based on these features, we categorise patients into groupings which may be helpful during long-term follow-up.

**Methods:** Patients are being recruited from the dermatology clinics at St. Vincent's University Hospital, Dublin. Inclusion criteria included a diagnosis of Pso with disease duration of less than 10 years and an age of 18 years or older. Patients with another serious active medical illness, a previous diagnosis of inflammatory arthritis or those who were receiving systemic immunosuppressant therapy for Pso were excluded

Following recruitment, patients were assessed for musculoskeletal (MSK) signs or symptoms: questionnaire detailing history of any MSK complaints including inflammatory back pain, full physical examination including evidence of tender or swollen joints and enthesal tenderness (using the Leeds Enthesitis Index) and routine blood testing including inflammatory markers.

If patients had any MSK findings they underwent routine radiographs, MRI scanning or ultrasound scanning as indicated. Patients were then categorised using all information available as follows: Pso only; Pso+: MSK signs or symptoms but insufficient for diagnosis of PsA; PsA (CASPAR); Diagnosis of PsA meeting CASPAR criteria; Other Rheumatic Disease.

**Abstract SAT0319 – Table 1.** Breakdown of Features of Inflammatory Articular Disease

MSK Finding(s)	No. of Patients (total 96)
Tender or Swollen Joint(s) (T/S J) only	41
Enthesitis (E) only	12
Inflammatory Back Pain (IBP) only	10
T/S J and E	20
T/S J and IBP	3
E and IBP	2
T/S J, E and IBP	8

Of these 96 patients, 79 patients had some additional imaging studies.

**Results:** To date 190 patients with Psoriasis have been recruited. Of those, 9 were excluded due to a diagnosis of Pso >10 years previously. One was excluded due to a previous diagnosis of JIA

Of the remaining 180 patients: 106 were male (58.9%). Mean age was 41.5 ±14.8 years. Average duration of Pso: 6.1±2.9 years.

On examination: 126 (70%) had psoriatic nail disease (pitting, ridges or onycholysis).

84 patients had no musculoskeletal signs or symptoms. The remaining 96 patients had at least one musculoskeletal finding as outlined in table 1 below.

**Abstract SAT0319 – Table 2.** shows how patients were subsequently categorised based on their history, clinical examination, laboratory blood results and imaging.

Breakdown of Diagnoses of BIOCOM patients at baseline (180)

Pso only	84
Pso+	64
PsA (CASPAR)	7
Other Rheumatic Disease	25

**Conclusions:** Analysis of patients recruited to date for the BIOCOM-Pso study shows that at baseline at least one third of patients with Pso had non-specific MSK signs and symptoms. Previous studies suggest these patients may be more likely to subsequently develop PsA. By following this cohort prospectively, we hope to better characterise which features are predictive of the development of PsA in patients with Pso.

**Disclosure of Interest:** None declared

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#### SAT0320 RELIABILITY ANALYSIS OF THE MADRID SONOGRAPHIC ENTHESIS INDEX (MASEI) AND DIFFERENT DOPPLER SUBGROUPS IN PSORIATIC ARTHRITIS

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**Background:** Enthesitis is the cornerstone of spondyloarthritis, and ultrasound (US) indexes have emerged in the last years being the Madrid Sonographic Enthesis Index (MASEI) one of the more widely used.

**Objectives:** To evaluate the reliability of MASEI and different entheses power doppler (PD) definitions in Psoriatic Arthritis (PsA).

**Methods:** 27 consecutive non selected PsA patients were included. An US expert rheumatologist performed the MASEI examination using a MyLab 70 XVG machine, Esaote, Genova, Italy, with a greyscale (GS) 13 MHz probe and 7.1 MHz power Doppler (PD) frequency, PRF 750 Hz and 60 Gain. US images and 3–5 s videos were obtained in transversal and longitudinal views for further reliability analysis. The inter-reader reliability analysis was performed by three readers and true US result was the consensus of at least two of them. In addition to the PD item of MASEI (defined as signal in bone profile or intratendon or bursa on the entheses area), three other PD definitions were evaluated as present or absent: PD OMERACT (PD signal at entheses ≤2 mm to the bone profile), PD bursa (PD signal inside bursa) and PD tendon (PD signal in the entheses tendon >2 mm from the bone profile). Intraclass correlation coefficient (ICC) estimations and 95% confident intervals were calculated for the reliability analysis of MASEI and PD subgroups based on a mean-rating (k=3), absolute-agreement, two-way mixed effect model. Cohen's Kappa test was used for analysis of MASEI's items reliability. SPSS statistical package version 20 (SPSS Inc, Chicago, IL) was used.

**Results:** Inter-reader reliability of MASEI and PD subgroups is shown in table 1. PD bursa showed the lowest reliability. MASEI, PD MASEI, PD OMERACT and PD tendon showed good to excellent reliability, being PD tendon the best one. table 2 shows reliability data of each MASEI lesion in each entheses included in the index. Best agreement percentages and kappa values were found in erosions and PD with mainly good to excellent data, while the worst ones were found in calcifications with poor to moderate values.

**Abstract SAT0320 – Table 1.** Inter-reader reliability of MASEI and PD subgroups. Scores expressed as mean±SD for each reader.

	Reader 1	Reader 2	Reader 3	ICC	95% CI
<b>MASEI</b>	28,52 ±13,43	31,89 ±13,99	31,30 ±14,14	0922	0,852– 0962
<b>PD MASEI</b>	6,44±5,80	6,89±6,43	6,78±5,43	0921	0,851– 0962
<b>PD OMERACT</b>	1,25±1,32	1,41±1,65	1,11±1,39	0895	0,802– 0949
<b>PD BURSA</b>	0,30±0,67	0,18±0,56	0,11±0,42	0776	0,576– 0891
<b>PD TENDON</b>	1,96±1,74	2,15±2,09	2,22±1,82	0934	0,876– 0968

**Abstract SAT0320 – Table 2.** Inter-reader reliability and agreement analysis of MASEI components. All items were categorised as yes/no. N/A not applicable since one of the lectors offers the same result for all cases, so kappa can't be calculated in this item due to sparse differences between lectors. N/B enthesis without bursa.

		Abnormal tendon structure	Thickened tendon	Erosion	Enthesis calcification	Enthesis PD	Bursitis
Triiceps tendon enthesis	Mean kappa	0.68 ± 0.19	0.68 ± 0.19	0.68 ± 0.19	0.57 ± 0.19	0.62 ± 0.19	N/A
	Mean agreement	81.95%	86.42%	86.25%	80.25%	85.04%	
Quadriceps tendon enthesis	Mean kappa	0.52 ± 0.16	0.58 ± 0.16	0.60 ± 0.16	0.49 ± 0.15	0.61 ± 0.16	N/A
	Mean agreement	76.55%	79.01%	76.69%	70.69%	82.71%	
Proximal patellar ligament enthesis	Mean kappa	0.50 ± 0.14	0.47 ± 0.13	0.47 ± 0.13	0.23 ± 0.09	0.72 ± 0.11	N/A
	Mean agreement	77.77%	83.95%	88.89%	39.03%	93.83%	
Distal patellar ligament enthesis	Mean kappa	0.25 ± 0.13	0.49 ± 0.13	0.60 ± 0.13	0.43 ± 0.12	0.80 ± 0.09	N/A
	Mean agreement	60.25%	81.88%	100%	77.77%	85.04%	95.83%
Achilles tendon enthesis	Mean kappa	0.47 ± 0.14	0.79 ± 0.09	0.93 ± 0.04	0.49 ± 0.14	0.81 ± 0.08	0.78 ± 0.13
	Mean agreement	72.84%	91.64%	96.77%	81.48%	92.99%	83.83%
Plantar aponeurosis enthesis	Mean kappa	0.27 ± 0.11	0.52 ± 0.09	0.60 ± 0.10	0.11 ± 0.05	N/A	N/A
	Mean agreement	72.84%	87.04%	100%	45.68%	98.77%	

**Conclusions:** MASEI has demonstrated to be a reliable tool in PsA. Erosions and PD showed the best reliability values. Evaluating different definitions of enthesis PD, signal in the tendon was the most reliable one, followed with minimal differences by PD MASEI and PD OMERACT, and in last place PD bursa.

**Disclosure of Interest:** None declared

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**Abstract SAT0321 – Table 1.** Enthesitis and Dactylitis Resolution from the Integrated SPIRIT-P1 and SPIRIT-P2 Dataset (Week 24)

	PBO	IXEQ4W	IXEQ2W
LEI=0	26/126 (21%)	53/136 (39%)*	49/141 (35%)*
Lateral epicondyle=0	24/79 (30%)	39/85 (46%)*	39/86 (45%)*
Medial femoral condyle=0	23/79 (29%)	41/92 (45%)*	45/100 (45%)*
Achilles tendon insertion=0	19/64 (30%)	37/75 (49%)*	38/74 (51%)*
LDI-B=0	10/42 (24%)	52/67 (78%)*	30/46 (65%)*

Data presented as n/N (%). N=patients with baseline enthesis (LEI>0), depicted enthesal points, or dactylitis (LDI-B=0); n=responding patients \*p<05,\*\*p<001

**Conclusions:** Treatment with IXE resulted in significant improvement in enthesitis and dactylitis in patients with pre-existing enthesitis or dactylitis. Resolution of enthesitis symptoms was associated with improvements in patients' function and HRQoL.

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**SAT0321 IXEKIZUMAB TREATMENT SIGNIFICANTLY IMPROVES ENTHESITIS AND DACTYLITIS IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS: RESULTS FROM THE SPIRIT TRIALS**

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**Background:** Psoriatic arthritis (PsA) is a chronic inflammatory disease with heterogeneous musculoskeletal manifestations including enthesitis and dactylitis. Ixekizumab (IXE), an interleukin-17A antagonist, is approved in the USA for the treatment of PsA including patients with pre-existing enthesitis or dactylitis.

**Objectives:** To investigate the impact of IXE treatment on the resolution of enthesitis or dactylitis and whether such improvements were associated with improved function and health-related quality of life (HRQoL).

**Methods:** Patients with active PsA who were biologic-naïve (SPIRIT-P1; NCT01695239) or with prior inadequate response to tumour necrosis factor inhibitor(s) (SPIRIT-P2; NCT02349295) were randomised to placebo (PBO) or 80 mg IXE every 4 weeks (IXEQ4W) or 2 weeks (IXEQ2W), after a 160 mg starting dose. All patients who were inadequate responders at Week 16 received rescue therapy (changes in background therapy). Leeds Enthesitis Index (LEI), Leeds Dactylitis Index-Basic (LDI-B), Health Assessment Questionnaire Disability Index (HAQ-DI), and EuroQoL-5D Visual Analogue Scale (EQ-5D VAS) were measured at Week 24. Missing data or data from inadequate responders were considered non-response or imputed with last observation carried forward for categorical and continuous measures, respectively. Statistical comparisons between PBO and IXE treatment groups were performed with a logistic regression model using Wald's test with treatment and study as factors. In post hoc-analyses, associations between enthesitis and dactylitis with HAQ-DI and EQ-5D VAS are based on an ANCOVA model adjusting for study and Disease Activity of Psoriatic Arthritis (DAPSA).

**Results:** In the integrated SPIRIT-P1 and -P2 dataset (n=679), 403 patients (59% of total) had baseline enthesitis (LEI >0) with a mean 2.9 LEI score, and 155 patients (23% of total) had baseline dactylitis (LDI-B >0) with a mean 56.4 LDI-B score. Relative to PBO, IXE treatment resulted in significantly higher resolution of enthesitis (SPIRIT-P1) and dactylitis (SPIRIT-P1 and -P2) after 24 weeks.<sup>1,2</sup> In the integrated SPIRIT-P1 and -P2 dataset, both IXEQ4W and IXEQ2W had significantly higher enthesitis and dactylitis resolution than PBO treatment at Week 24 (Table). In ad-hoc analysis, IXE treatment had significantly higher resolution of enthesitis compared to PBO at the enthesal points comprising the LEI score (Table). For all PBO- and IXE-treated patients at Week 24, least squares mean (SE) HAQ-DI changes from baseline were -0.44 (0.05) and -0.25 (0.03); p<0.01 for patients who did and did not resolve enthesitis, and -0.41 (0.06) and -0.31 (0.07); p=0.34 for patients who did and did not resolve dactylitis. Corresponding EQ-5D VAS improvements were 12.3 (2.2) and 5.8 (1.5); p=0.02 for patients who did and did not resolve enthesitis, and 10.8 (2.8) and 9.8 (3.5); p=0.83 for patients who did and did not resolve dactylitis.

**SAT0322 THE EFFECT OF GUSELKUMAB ON DACTYLITIS: RESULTS FROM A PHASE 2 STUDY IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS**

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**Background:** In a Phase 2 study, Guselkumab (GUS) was shown to be safe and effective in patients (pts) w/active psoriatic arthritis (PsA).

**Objectives:** To evaluate the effect of GUS on dactylitis in a subset of pts w/dactylitis at baseline (BL) in the phase 2 PsA study of GUS.

**Methods:** Pts w/active PsA and ≥3% body surface area of plaque psoriasis, despite current or previous treatment, were randomised 2:1 to receive 100 mg subcutaneous GUS at wks 0, 4 then every 8 weeks (wks, q8w) or placebo (PBO) during a 24wk double-blind treatment period. At wk16, pts w/<5% improvement in swollen and tender joint counts early escaped (EE). At wk24, the PBO group crossed over to receive GUS (wks 24, 28 then q8w) (PBO→GUS) and the GUS group continued receiving GUS (GUS→GUS) through wk44. Dactylitis was assessed by scoring each digit from 0–3 (0=absent, 1=mild, 2=moderate, 3=severe), for a combined score of 0–60. Sensitivity analysis of change from BL through wk24 in dactylitic digits was performed (combined score 20). Dactylitis scores during the 24-wk double-blind treatment was analysed using LOCF imputation for missing data and EE. Dactylitis after wk24 was evaluated using observed data.

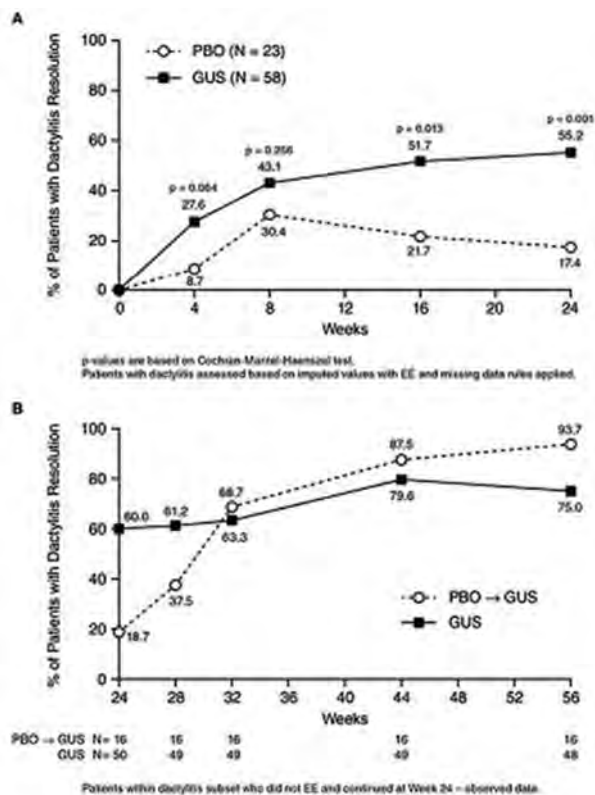
**Results:** Of 149 pts, 81 presented w/dactylitis at BL (PBO n=23, mean[SD]=3.9 [3.01]; GUS n=58, mean[SD]=6.5 [6.15]) and 66 continued to the active treatment period (PBO→GUS n=16; GUS→GUS n=50). The dactylitis subset was similar to the overall population in BL characteristics except for higher median values for # of swollen joints, # of tender joints, and CRP. At wks 16 and 24, the GUS group had a significantly greater reduction in the dactylitis score (wk24 mean [SD] change from BL, PBO: -0.4 [6.06]; GUS: -3.8 [4.93]; p=0.006) and a greater% of pts w/dactylitis resolution, compared to the PBO group (figure 1). Consistent results were obtained w/the # digits w/dactylitis (wk24 mean [SD] change from BL, PBO: -0.2 [3.04]; GUS: -2.1 [2.21]; p=0.003). Improvement in dactylitis seen at wk24 was maintained in the GUS→GUS group (wk56: mean[SD] change from BL=-5.5 [4.84], 75% of pts w/resolution) and the values for the PBO→GUS group (wk56: mean[SD] change from BL=-4.4 [3.50], 93.7% of pts w/resolution) approached those of the GUS→GUS group. Improvement in dactylitis was greater in ACR20/ACR50 responders vs non-responders in GUS-treated patients (Table



1) and was significantly correlated with improvement in TJC ( $R=0.38$ ,  $p=0.004$ ), SJC ( $R=0.50$ ,  $p<0.0001$ ), and HAQ-DI score ( $R=0.33$ ,  $p=0.013$ ).

**Abstract SAT0322 – Table 1.** Change in Dactylitis Score in ACR20/50 and PASI75 Responders and Non-responders

	Mean (SD) change from BL in Dactylitis Score at Wk24		
	Non-responders	Responders	p-value
ACR 20	-1.76 (7.595), n=21	-4.94 (4.666), n=36	0.044
ACR 50	-2.44 (6.213), n=36	-6.05 (5.133), n=21	0.027
PASI 75	-4.00 (2.858), n=13	-3.70 (6.736), n=44	0.924



**Figure 1.** Proportion of Patients with Dactylitis Resolution over Time

**Conclusions:** GUS is efficacious in resolving symptoms of dactylitis in pts w/ active PsA. This effect on dactylitis is correlated with improvement in joint symptoms and physical function.

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### SAT0323 ADVERSE DRUG REACTIONS RELATED TO DISEASE-MODIFYING DRUGS (DMARD) IN PSORIATIC ARTHRITIS PATIENTS IN DAILY CLINICAL PRACTICE

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**Background:** Psoriatic arthritis (PsA) benefits from DMARDs and to know more about the adverse drug reactions (ADRs) represent an advance for the management and safety of these patients in clinical practice.

**Objectives:** To evaluate the discontinuation due to ADRs of DMARDs used in PsA patients and to analyse the possible associated factors.

**Methods:** Retrospective longitudinal observational study. **Subjects:** inception cohort of patients from January 2010 to December 2014 and followed up to December 2016, diagnosed with PsA according to ICD-10 code. **Main outcome:** discontinuation of conventional synthetic DMARDs (csDMARDs) and biological originator DMARDs (boDMARDs) due to ADR (moderate: drug suspension regardless of the repercussions, severe: hospital admission required or death). **Covariables:** sociodemographic and clinical. **Statistical analysis:** To estimate DMARDs discontinuation rates, survival techniques were used, expressing the incidence rate (IR) per 100patients\*year with their respective CI at 95%. Multivariate Cox regression models were performed to analyse the factors associated with DMARDs discontinuation due to ADRs and results were expressed in Hazard ratio(HR) and 95% CI.

**Results:** 191 patients were included, with a follow-up of 379.70 Patients\*year. 50.3% were male, mean age at diagnosis was 50±14.6 years old. 46.6% of the patients had a history of cutaneous psoriasis. HLA-B27 was positive in 20% of patients. Throughout the follow-up, all patients received csDMARDs and 23 used boDMARDs. Methotrexate(MTX) was the most used drug 69.7%. 30% were on combination therapy, the most frequent was antiTNF +MTX. There were 44 discontinuations due to ADRs, IR 11.59 [8.62–15.57] and 3 were severe, requiring hospital admission (two infections and one cancer), no deaths were recorded. Among the most frequent causes of discontinuation related to ADRs were digestive intolerance 32%, nonspecific manifestations 11%, infections 9% and abnormal transaminase levels 9%. Table1 shows the DMARDs discontinuation rates due to ADRs. In the final discontinuation model related with ADRs (Table2), we observed that distress, high disease activity, corticosteroids at diagnosis and combination therapy were associated with a higher rate of discontinuation.

Table1	Patients*years	Events (n)	IR	95% CI
MTX	243.46	23	9.45	
Salazopyrine	84.80	14	16.51	
Leflunomide	21.83	10	27.48	
Antimalarials	25.34	8	15.78	
boDMARDs	57.56	5	8.69	
Combination therapy	101.76	16	15.72	

Table2	HR	95% CI	P
Women	1.38	0.61–3.09	0.436
Age at diagnosis	0.97	0.94–1.00	0.103
Distress level	3.78	1.85–7.71	0.000
C Reactive protein ≥1.05 gr/dL	2.31	1.02–5.20	0.043
corticosteroids at diagnosis	2.66	1.10–6.40	0.029
Combination therapy	2.23	1.14–4.38	0.020
boDMARD	0.32	0.08–1.27	0.105
MTX vs rest of DMARD	0.42	0.19–0.92	0.032

**Conclusions:** The discontinuation rate due to ADRs was 11.59, although most of them did not have an important clinical impact. We have found some psychological, clinical and treatment factors that can modify the DMARDs survival on PsA patients. We also observed that MTX, seems to be safe in the treatment of PsA, presenting the lowest probability of suspension related to ADRs compared with the rest of treatments.

**Disclosure of Interest:** None declared

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SAT0324

**CERTOLIZUMAB PEGOL PROVIDES SUSTAINED REMISSION AND MINIMAL DISEASE ACTIVITY IN PATIENTS WITH PSORIATIC ARTHRITIS OVER 4 YEARS' TREATMENT**

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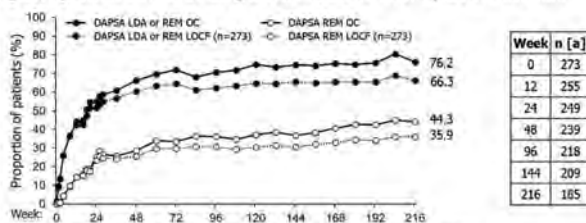
**Background:** Disease Activity Index for Psoriatic Arthritis (DAPSA)<sup>1</sup> and the minimal disease activity (MDA) criteria<sup>2</sup> are instruments recommended for evaluating disease activity in psoriatic arthritis (PsA). The RAPID-PsA trial (NCT01087788) has demonstrated the sustained efficacy of certolizumab pegol (CZP) across the spectrum of PsA symptoms.<sup>3,4</sup>

**Objectives:** To report the proportion of CZP-treated patients (pts) achieving DAPSA remission (REM), DAPSA low disease activity (LDA), MDA (fulfilling ≥5/7 MDA criteria), and very low disease activity (VLDA; fulfilling 7/7 MDA criteria) over 216 weeks (wks) in RAPID-PsA.

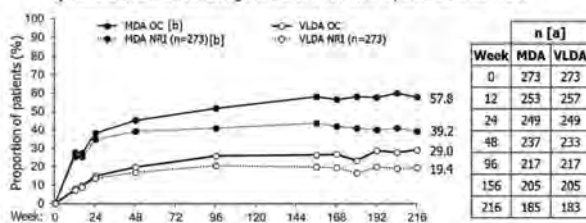
**Methods:** RAPID-PsA was double-blind and placebo-controlled to Wk24, dose-blind to Wk48, and open-label (OL) to Wk216. Pts had active PsA and had failed ≥1 disease modifying anti-rheumatic drug. Data for pts randomised to CZP at Wk0 (200 mg every 2 wks or 400 mg every 4 wks, following a 400 mg loading dose at Wks0, 2, 4), who continued their assigned dose in the OL period, are presented as observed case and with imputation (figure 1). Outcomes reported are DAPSA (the sum of tender and swollen joint counts [TJC 68; SJC 66], pt global and pain assessment [10 cm visual analogue scale], and C-reactive protein levels [mg/dL]), and pts achieving: 1) DAPSA LDA (DAPSA >4 and ≤14); 2) DAPSA REM (DAPSA ≤4); 3) MDA (fulfilling ≥5/7 MDA criteria); and 4) VLDA (fulfilling 7/7 MDA criteria), to Wk216. Pts withdrawing from the study between scheduled visits had their final observed assessment values assigned to the next scheduled visit timepoint.

**Results:** Of 409 pts randomised; 273 received CZP from Wk0, of whom 248 (90.8%) completed Wk24, 237 (86.8%) completed Wk48, and 183 (67.0%) completed Wk216. The mean (SD) baseline DAPSA was 44.8 (22.9). Of pts completing Wk24, 29.7% (74/249) achieved LDA; 25.3% (63/249) REM; 38.2% (95/249) MDA; and 14.9% (37/249) VLDA. At Wk216, 31.9% (59/185) achieved LDA; 44.3% (82/185) REM; 57.8% (107/185) MDA; and 29.0% (58/183) VLDA (figure 1).

**Figure: A) Patients with PsA achieving DAPSA LDA and REM over 4 years' CZP treatment**



**B) Patients with PsA achieving MDA and VLDA over 4 years' CZP treatment**



Data shown for the Randomized Set, for pts on either dose regimen. OC proportions are calculated as the number achieving the target relative to the number of pts assessed at that timepoint. Missing values were imputed using LOCF for DAPSA and NRI for MDA criteria. [a] Number of patients with an observed value at the scheduled visit timepoint; [b] The proportion of pts achieving MDA (≥5/7 criteria) shown includes those achieving VLDA (7/7 MDA criteria). CZP: certolizumab pegol; DAPSA: Disease Activity Index for Psoriatic Arthritis; DAPSA LDA: DAPSA low disease activity (>4 and ≤14); DAPSA remission: DAPSA REM (≤4); LOCF: last observation carried forward; MDA: minimal disease activity; NRI: non-responder imputation; OC: observed case; PsA: psoriatic arthritis; pt: patient; VLDA: very low disease activity.

**Abstract SAT0324 – Figure 1. A) Patients with PsA achieving DAPSA LDA and REM over 4 years' CZP treatment. B) Patients with PsA achieving MDA and VLDA over 4 years' CZP treatment**

**Conclusions:** A substantial proportion of pts who completed the 4 year study achieved disease inactivity targets: ~75% achieved DAPSA LDA or REM, almost 60% achieved MDA, and half of those also achieved VLDA.

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SAT0325

**COMPARATIVE ANALYSIS OF GENDER DIFFERENCES, HLA-B27 STATUS AND SKIN LESION SEVERITY IN EARLY AXIAL AND PERIPHERAL PSORIATIC ARTHRITIS PATIENTS**

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**Background:** Clinical features of axial involvement in psoriatic arthritis (PsA) had been studied before only at advanced stages. Skin lesion severity, HLA-B27 status and gender-specific differences in early PsA patients with axial involvement hadn't been sufficiently studied.

**Objectives:** To compare clinical features of two early peripheral PsA patient populations – with and without axial involvement.

**Methods:** 95 patients (pts) (M/F=47/48) with early PsA according to CASPAR criteria were included; all pts had peripheral arthritis for ≤2 years; no inflammatory back pain (IBP) pts were specially selected. Mean age 36.5±10.7 years, disease duration 12.2±10.3 mo, disease activity indexes DAS=4.0±1.4, DAS28=4.2±1.1, BASDAI=4.5±1.6 (in pts with axial involvement); patient's global disease activity (PGA) VAS 56.9±17.1. All pts were evaluated for the presence of inflammatory

back pain (IBP) by ASAS criteria. The examination included X-ray of sacroiliac joints (SIJs) (pelvic radiographs), HLA B27 antigen status; magnetic resonance imaging (MRI) of SIJs was performed in 79 pts, regardless of the presence of IBP, on Signa Ovation 0,35T. Bone marrow oedema on MRI (STIR) was considered as active MRI sacroiliitis (MRI-SI). Radiographic sacroiliitis (R-SI) was considered according to New York criteria (unilateral grade  $\geq 3$  or bilateral grade  $\geq 2$ ). X-ray and MRI results were evaluated by an independent reader. IBP was observed in 63 cases (66.3%), MRI-SI in 28 of 79 (35.4%) examined cases, R-SI in 29 cases (30.5%). Pts were split into two groups (gr.): those with axial involvement (axPsA), that is with IBP and/or R-SI and/or MRI-SI; and those without axial involvement (having only peripheral PsA [pPsA]). The axPsA gr. included 65 (68.4%) cases, the pPsA gr. – 30 (31.6%) cases. Skin lesion severity was evaluated in terms of body surface area (BSA) affected and Psoriasis Area Severity Index (PASI). When BSA was  $\geq 3\%$ , PASI was calculated.  $PASI \geq 11$  indicates moderate and severe psoriasis.

**Results:** The following significant differences were revealed between gr. axPsA and gr. pPsA: **gender-related ones:** in gr. axPsA men-to-women ratio was 60.0% to 40.0%, while in gr. pPsA it was 26.7% to 73.3% ( $p=0.003$ ); **age-related ones:** mean age of gr. axPsA was  $33.9 \pm 9.6$  years, while of gr. pPsA it was  $41.7 \pm 10.6$  years ( $p=0.0007$ ); **in disease duration:** in gr. axPsA it was  $10.3 \pm 8.7$  mo. which was less than gr. pPsA  $16.1 \pm 11.7$  mo. ( $p=0.008$ ); **in HLA-B27 antigen status:** in gr. axPsA it was positive in 47.6% of pts. while in gr. pPsA in 23.3% of pts. ( $p=0.02$ ); **in PGA:**  $58.4 \pm 17.3$  mm in gr. axPsA, and  $49.8 \pm 16.7$  mm in gr. pPsA ( $p=0.02$ ); **in skin lesions' severity:** it was higher in gr. axPsA: BSA median was 3.0 [1.0–9.0] in gr. axPsA and 1.0 [0.2–3.0] in gr. pPsA ( $p=0.007$ ), and PASI median was 15.6 [6.6–55.2] in gr. axPsA and 6.0 [0.0–7.2] in gr. pPsA ( $p=0.006$ ).

**Conclusions:** Axial involvement in early PsA patients is significantly more frequent in males and in pts with positive HLA-B27 antigen status. Axial involvement is associated with high patient-reported disease activity and severe skin lesion. These findings may have a positive impact on diagnosis of axial disease, as well as on the selection of the best therapeutic strategy.

**Disclosure of Interest:** None declared

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SAT0326

#### DURATION OF REMISSION AND MINIMAL DISEASE ACTIVITY AFTER STARTING AND DISCONTINUATION OF BIOLOGIC (B) DMARDS IN EARLY PSORIATIC ARTHRITIS PATIENTS TREATED ACCORDING TO TREAT-TO-TARGET STRATEGY (RESULTS OF AN OPEN-LABEL REMARCA STUDY)

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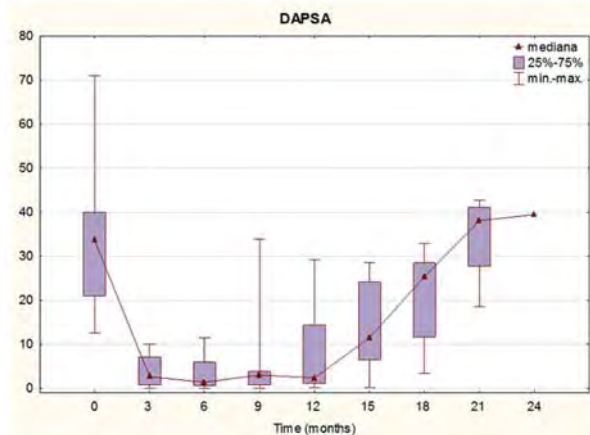
**Background:** The main goal of treat-to-target (T2T) strategy in psoriatic arthritis (PsA) is achievement of remission (REM) or minimal disease activity (MDA). There is limited data concerning the duration of REM/MDA after starting and discontinuation of bDMARDs in early (E) PsA patients (pts).

**Objectives:** to investigate the timing and duration of REM/MDA after starting and discontinuation of bDMARDs therapy in EPsA pts treated according to T2T strategy.

**Methods:** 34 (M-18/F-16) pts with active EPsA according to the CASPAR criteria non-responder to methotrexate (MTX) subcutaneous treatment, bDMARD-naïve were included; mean age  $38 \pm 11$  years, PsA duration  $12 \pm 10$  months (mon.), psoriasis duration  $89.8 \pm 91.1$  mon., median Disease Activity index for Psoriatic Arthritis (DAPSA)  $33.55 [28.34–41.77]$ . All pts started bDMARDs: Adalimumab (21 pts), Certolizumab pegol (3 pts), Etanercept (2 pts), Ustekinumab (8 pts)  $\pm$  MTX. The median duration of bDMARDs treatment was 9 [6.5–15], Min 3 mon. – Max 24 mon. The bDMARDs treatment was stopped due to an individual inefficiency, loss of efficacy or non-medical reasons. At baseline and every 3 mon. all pts underwent assessment of PsA activity by DAPSA and MDA criteria (tender joint count  $\leq 1$ , swollen joint count  $\leq 1$ , PASI  $\leq 1$  or BSA  $\leq 3$ , patient pain global assessment VAS  $\leq 15$ , patient's global disease activity VAS  $\leq 20$ , HAQ  $\leq 0.5$ , enthesitis count  $\leq 1$ ). The proportion of pts who achieved REM by DAPSA  $\leq 4$  and MDA (5 of 7 cutpoints) at least once, as well as timing and duration of REM/MDA after starting and cessation of bDMARDs were performed. Pts reports about a flare coming, close to the scheduled time of assessment, was taken into account.  $M \pm SD$ , Me [Q75; Q50], (%) were calculated. All  $p < 0.05$  were considered to indicate statistical significance.

**Results:** By the 24 mon. of the study REM by DAPSA and MDA was reached at least once by 27 (79%) and 28 (82%) out of 34 pts, accordingly. Mean timing of REM by DAPSA and MDA after starting of bDMARDs was  $5.8 \pm 3.2$  and  $4.0 \pm 1.9$  mon., accordingly. During the observation 19 out of 27 pts (70.4%) had stopped bDMARDs due to different reasons. 8 out of 27 pts (29.6%) continued the treatment and had REM according to DAPSA by the end of the study. After cessation of bDMARDs flares by DAPSA were seen in 12 out of 19 pts (63.2%) with the mean duration of REM  $5.8 \pm 2.3$  mon. (Fig 1.). The loss of MDA was seen in 12 out of 20 pts (60%) with the mean duration of MDA  $6.2 \pm 3.0$  mon. Pts reports about

the time of PsA symptoms flares was  $3.5 \pm 3.4$  mon. 5 out of 34 pts (15%) loss the efficacy after  $12.0 \pm 4.7$  mon. of bDMARDs treatment.



**Abstract SAT0326 – Figure 1.** Dynamics of DAPSA after starting and discontinuation of bDMARDs therapy in EPsA.

**Conclusions:** Most EPsA pts treated with bDMARDs according to T2T strategy achieved REM and MDA within 5 mon. Flares after bDMARDs discontinuation within 6 mon were found in more than a half of pts. according to PsA activity indices and within 3 mon. by pts reports. REM and flare timing after bDMARDs therapy discontinuation indicate that further studies concerning optimal management PsA pts by bDMARDs are needed.

**Disclosure of Interest:** None declared

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SAT0327

#### BASELINE CHARACTERISTICS AND REASONS FOR APREMILAST PRESCRIPTION IN A LARGE ITALIAN COHORT OF PSORIATIC ARTHRITIS PATIENTS

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**Background:** There are no real-world data for the profiling of patients with psoriatic arthritis (PsA) receiving the phosphodiesterase-4 inhibitor apremilast.

**Objectives:** To retrospectively evaluate the baseline characteristics and the reasons for apremilast prescription in a large Italian multicenter cohort of PsA cases (Real-life APremilast for Psoriatic arthritis Evaluation Registry, RAPPER).

**Methods:** Data were retrospectively extracted from the RAPPER registry which includes all PsA cases treated with apremilast in 11 Italian tertiary rheumatology centres between January 2017 and December 2017. Descriptive analysis of baseline characteristics of study population included demographics, previous treatments before apremilast, pattern of PsA involvement, disease activity indices, and prevalence of comorbidities (computed by the Rheumatic Disease Comorbidity Index [RDCl]). Reasons for apremilast choice were also analysed.

**Results:** We studied 97 patients with PsA (61% women; mean  $\pm$  standard deviation, SD) age  $56.7 \pm 11.9$  years; mean disease duration  $10 \pm 13.1$  years) who received apremilast as first-line targeted disease modifying drug (51.5%) or after the failure of at least one biologic agent (48.5%). In 75%, 33%, 11%, and 63% of patients there were articular (57% asymmetric oligoarthritis; mean Disease Activity in Psoriatic Arthritis [DAPSA]  $22.55 \pm 11.55$ ), enthesal (mean Leeds Enthesitis Index [LEI]  $2.63 \pm 1.42$ ), axial (mean Bath Ankylosing Spondylitis Disease Activity Index [BASDAI]  $6.02 \pm 2.40$ ), and skin/ungueal (mean body surface area [BSA]  $1.71 \pm 3.44$ ) involvement, respectively. Two thirds (64%) of patients had at least one comorbidity (mean RDCl  $1.20$ ) and the prevalence of conditions is reported in table 1. The main reasons for apremilast prescription were contraindication to biologic agents (66%), lack of poor prognostic factors (35%), comorbidities (34%),



risk of infections (33%), and history of malignancy (22.6%), whereas a preference for an oral drug drove the choice only in 7% of patients.

Abstract SAT0327 – Table 1. baseline prevalence of comorbidities

COMORBIDITY	PREVALENCE (n=97)
Hypertension	34%
History of malignancy	22%
Fibromyalgia	15%
Latent tuberculosis	14%
Liver disease	14%
Lung disease	13%
Dyslipidemia	12%
Diabetes	11%
Depression	10%
HBV/HCV infection	9%
Osteoporosis	8%
Hematological disorders	7%
Cardiovascular disease	7%
Gastrointestinal disorders	3%
Neurological disorders	3%

**Conclusions:** Based on our analysis, apremilast is mainly used in PsA with oligoarthritis, enthesitis, mild skin involvement, and low risk of disease progression, carrying comorbidities (especially history of infections and malignancies) with contraindications to the use of biologic drugs.

#### REFERENCE:

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#### SAT0328 WEIGHT-LOSS IMPROVES DISEASE ACTIVITY IN OBESE PATIENTS WITH PSORIATIC ARTHRITIS

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**Background:** Obesity is over-represented in patients with psoriatic arthritis (PsA) and associated with increased risk of getting the disease, higher disease activity, poorer effect of treatment and in addition cardiovascular co-morbidity.

**Objectives:** The aim of this study was to determine the effects of weight-loss treatment on disease activity in patients with PsA and obesity

**Methods:** Patients with PsA (Caspar criteria) and obesity (body mass index BMI  $\geq 33$  kg/m<sup>2</sup>) were recruited from three Rheumatology clinics in the Western Sweden. Weight-loss treatment with Very Low Energy liquid Diet (VLED), which comprises a daily energy intake of 640 kcal, was given during 12–16 weeks, depending on BMI. The first strict period was followed by a structured reintroduction of an energy restricted diet during 18 weeks. The treatment was given within the framework of a structured program including support and medical follow-up at the Obesity Unit at Sahlgrenska University Hospital.

Treatment with DMARDs and biologics was held constant from 3 month before baseline until 6 months after baseline. The patients were assessed with 66/68 joints count, back-mobility tests, body surface area (BSA), questionnaires, ESR, CRP and BMI at baseline, 3 and 6 months. The number of patients reaching Psoriatic Arthritis Response Criteria (PsARC) and Minimal Disease Activity (MDA) was calculated.

**Results:** Totally 41 PsA patients, median age 54 (IQR 48–62) years, 63% women were included. The median weight-loss was 18.7 (IQR 14.6–26.5) kg. BMI decreased from median 35.2 (34.1–38.1) to 29.7 (26.2–31.5) kg/m<sup>2</sup>. A majority of the disease activity parameters improved significantly (Table). Totally 16 patients (39.0%) reached PsARC and the number of patients with MDA increased from n=12 (29%) to n=22 (54%), p<0.001 between baseline and the 6 months visit.

**Conclusions:** Weight-loss treatment with VLED had significant positive effects on disease activity in joints, entheses and skin in patients with PsA and obesity.

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declared, S. Björkman: None declared, B. Eliasson: None declared, I. Larsson: None declared

n=41	BASELINE Median (IQR)	6 MONTHS Median (IQR)	p-value
Tender joints 68, score	4 (1–14)	2 (0–6.5)	<0.001
Swollen joints 66, score	0 (0–1)	0 (0–0.5)	0.021
Leeds enthesitis index	2 (0–4)	0 (0–3)	0.001
BSA,%	0,75 (0–2.25)	0,25 (0–1.25)	0.014
BASMI, score	2,8 (1,8–3,6)	2,8 (2,0–3,4)	0,664
CRP	4,0 (2,0–8,5)	2,0 (1,0–6,5)	0,041
ESR, mm/h	12,0 (5,5–18,0)	14 (6,0–27,5)	0,008
VAS Pain, mm	30 (17–62)	20 (5,0–56,5)	0,005
VAS Global health, mm	33 (17,5–57,3)	14 (6–51)	0,002
VAS Fatigue, mm	55 (21–66)	30 (8–44)	0,001
HAQ, score	0,63 (0,13–1,0)	0,25 (0–0,63)	<0,001
DAS-28, score	2,62 (1,92–4,02)	2,44 (1,97–3,69)	0,013

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#### SAT0329 FIBROMYALGIA IN PATIENT WITH PSORIATIC ARTHRITIS: RELATIONSHIP WITH ENTHESOPATHY, SLEEP, FATIGUE AND QUALITY OF LIFE

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**Background:** Fibromyalgia is a syndrome characterised by musculoskeletal pain, sleep disturbance and fatigue. Fibromyalgia commonly accompanies rheumatic diseases. Enthesopathy seen in psoriatic arthritis (PsA) patients may have effect on fibromyalgia.

**Objectives:** To evaluate relationship of fibromyalgia with enthesopathy, sleep, fatigue and quality of life in patients with psoriatic arthritis.

**Methods:** The psoriatic arthritis patients according to CASPAR criteria were included into the study. Fibromyalgia diagnosis was based on 2010 ACR criteria. Demographic (age, gender, marital status, education, body mass index) and clinical parameters (disease duration, comorbidities, Moll-white classification of PsA) were noted. Disease activity and enthesopathy were evaluated with Disease Activity Score-28 (DAS-28) and Maastricht Ankylosing Spondylitis Enthesitis Score (MASES), respectively. Functional assessment scales in this study were Psoriatic Arthritis Quality of Life (PsAQoL), Pittsburgh Sleep Quality Index (PSQI), Multidimensional Assessment of Fatigue (MAF), Fibromyalgia Impact Questionnaire (FIQ) was used to assess functional status of fibromyalgia. The difference in mean scores between fibromyalgia and the patients without fibromyalgia were analysed with Mann-Whitney U test. Spearman correlation coefficient (rho) was used for correlations between functional parameters. p<0.05 was accepted as significant.

**Results:** We enrolled 50 PsA patients (32 female, 18 male) with a mean age 49.6 years (SD: 10.4) and mean disease duration 90.2 months (SD: 90.8). Thirty-two patients (64% of PsA patients) fulfilled ACR criteria for fibromyalgia. The mean scores of MASES, PSQI, MAF and PsAQoL were significantly higher in patients with fibromyalgia (p<0.05). The correlations between FIQ and other functional parameters were as follows; MASES (rho=0.73, p<0.0005), PSQI (rho=0.56, p<0.0005), MAF (rho=0.63, p<0.0005), PsAQoL (rho=0.69, p<0.0005). There was no significant correlation between FIQ and disease duration (p>0.05). Weak correlation was existing between FIQ and DAS-28 (rho=0.30, p=0.03).

Abstract SAT0329 – Table 1. Clinical characteristics of patients (n=50)

	Min-Max	Median (SD)	Lower-Upper Quartiles
DAS-28	1,20–5,60	2,60 <sup>1,18</sup>	1,99–3,50
MASES	0–13	3,00 <sup>4,84</sup>	0,00–10,00
PSQI	0–14	6,00 <sup>4,50</sup>	2,00–11,00
PSAQOL	0–20	6,00 <sup>5,79</sup>	1,75–11,25
MAF	1–45,80	27,25 <sup>14,98</sup>	10,75–37,75
FIQ	0–92,82	32,25 <sup>26,54</sup>	10,75–52,73

DAS-28: Disease activity score-28, MASES: Maastricht Ankylosing Spondylitis Enthesitis Score, PSQI: Pittsburgh Sleep Quality Index, PSAQOL: Psoriatic Arthritis Quality of Life, MAF: Multidimensional Assessment of Fatigue, FIQ: Fibromyalgia Impact Questionnaire, SD: Standart Deviation

**Conclusions:** Coexistence of fibromyalgia in PsA patients is associated with presence of enthesopathy, poor quality of life, sleep disturbance and fatigue. It is an important aspect to diagnose and treat fibromyalgia in PsA patients for comprehensive treatment.

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**SAT0330 CHANGES IN LYMPHOCYTES AND LYMPHOCYTE SUBSETS IN TOFACITINIB-TREATED PATIENTS WITH PSORIATIC ARTHRITIS**

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**Background:** Tofacitinib is an oral Janus kinase (JAK) inhibitor for the treatment of psoriatic arthritis (PsA). Cytokines involved in lymphocyte development, function and homeostasis signal through JAKs, and reductions in mean lymphocyte count over time have been reported in tofacitinib-treated patients (pts) with rheumatoid arthritis.<sup>1</sup>

**Objectives:** To characterise the effects of tofacitinib on absolute lymphocyte counts (ALCs) and lymphocyte subset counts (LSCs) in pts with PsA.

**Methods:** Data were pooled from 2 placebo (PBO)-controlled, double-blind, Phase 3 studies (OPAL Broaden [12 months; NCT01877668]; OPAL Beyond [6 months; NCT01882439]). Pts had active PsA and inadequate response to  $\geq 1$  conventional synthetic DMARD (OPAL Broaden) or to  $\geq 1$  tumour necrosis factor inhibitor (OPAL Beyond). Pts were randomised to tofacitinib 5 mg twice daily (BID), tofacitinib 10 mg BID, adalimumab 40 mg subcutaneous injection once every 2 weeks (active control; OPAL Broaden only) or PBO. PBO pts advanced in a blinded manner to tofacitinib 5 or 10 mg BID at Month (M)3. ALCs and LSCs were collected every 3 months as part of safety monitoring procedures in the Phase 3 studies (any abnormalities were confirmed upon retesting). Median ALCs and LSCs are reported up to M6. Incidence rates (pts with event/100 pt-years) for serious infections (SIs) were assessed by confirmed (two sequential measurements) ALC categories ( $\geq 2.0$ ,  $<2.0$ – $1.5$ ,  $<1.5$ – $1.0$  and  $<1.0$ – $0.5 \times 10^3/\text{mm}^3$ ) up to M12.

**Abstract SAT0330 – Table 1.** Median (range) absolute lymphocyte counts and lymphocyte subset counts up to Month 6, pooled across OPAL Broaden and OPAL Beyond

	Tofacitinib 5 mg BID N=238	Tofacitinib 10 mg BID N=236	Adalimumab 40 mg SC Q2W <sup>a</sup> N=106	Placebo <sup>b</sup> N=236
<b>ALC (<math>\times 10^3/\text{mm}^3</math>)</b>				
Baseline	1.74 (0.78–5.24)	1.71 (0.72–4.20)	1.62 (0.79–3.20)	1.69 (0.60–3.78)
Month 3	1.71 (0.60–4.38)	1.75 (0.47–4.74)	1.96 (1.11–3.80)	1.69 (0.65–3.45)
Month 6	1.68 (0.22–4.42)	1.68 (0.55–4.51)	1.88 (0.87–4.69)	–
<b>Total T cells: CD3+ (<math>\times 10^3/\text{mm}^3</math>)</b>				
Baseline	1.32 (0.48–3.88)	1.35 (0.44–3.60)	1.27 (0.43–2.73)	1.28 (0.26–3.04)
Month 3	1.30 (0.41–4.45)	1.33 (0.49–3.18)	1.44 (0.62–3.04)	1.35 (0.34–2.69)
Month 6	1.25 (0.28–3.66)	1.33 (0.26–3.30)	1.47 (0.71–4.08)	–
<b>T-helper cells: CD4+ (<math>\times 10^3/\text{mm}^3</math>)</b>				
Baseline	0.88 (0.32–3.24)	0.87 (0.26–2.68)	0.78 (0.32–2.04)	0.84 (0.08–2.54)
Month 3	0.88 (0.29–3.77)	0.90 (0.32–2.30)	0.93 (0.28–2.15)	0.87 (0.22–2.15)
Month 6	0.84 (0.22–2.64)	0.91 (0.20–2.58)	0.91 (0.44–2.60)	–
<b>Cytotoxic T cells: CD8+ (<math>\times 10^3/\text{mm}^3</math>)</b>				
Baseline	0.41 (0.10–1.40)	0.40 (0.08–1.03)	0.39 (0.07–1.16)	0.41 (0.06–1.32)
Month 3	0.38 (0.08–1.43)	0.38 (0.09–1.08)	0.44 (0.09–1.17)	0.43 (0.07–1.18)
Month 6	0.37 (0.05–1.20)	0.36 (0.04–1.32)	0.50 (0.12–1.57)	–
<b>B cells: CD19+ (<math>\times 10^3/\text{mm}^3</math>)</b>				
Baseline	0.21 (0.00–1.48)	0.20 (0.00–1.30)	0.18 (0.01–0.62)	0.21 (0.00–1.15)
Month 3	0.27 (0.01–1.08)	0.30 (0.01–1.42)	0.27 (0.02–0.99)	0.22 (0.01–0.93)
Month 6	0.26 (0.01–1.32)	0.28 (0.00–1.22)	0.26 (0.02–0.95)	–
<b>NK cells: CD16+56+ (<math>\times 10^3/\text{mm}^3</math>)</b>				
Baseline	0.23 (0.06–1.39)	0.22 (0.06–0.94)	0.22 (0.03–0.60)	0.20 (0.04–0.75)
Month 3	0.20 (0.04–0.79)	0.18 (0.03–0.75)	0.22 (0.05–0.66)	0.22 (0.03–0.71)
Month 6	0.19 (0.04–0.83)	0.19 (0.04–1.09)	0.25 (0.05–0.75)	–

<sup>a</sup>OPAL Broaden only; <sup>b</sup>Placebo-controlled period was 3 months

ALC, absolute lymphocyte count; BID, twice daily; N, number of patients with observations at baseline; Q2W, once every 2 weeks; SC, subcutaneous

**Results:** The analysis included 816 pts: tofacitinib 5 mg BID, n=238; tofacitinib 10 mg BID, n=236; adalimumab, n=106; PBO, n=236. Up to M6, minimal decreases in median ALC were observed in pts who received tofacitinib 5 mg BID, tofacitinib 10 mg BID or PBO (up to M3 only) (Table). LSCs, including total T

cells (CD3+), cytotoxic T cells (CD8+) and NK cells (CD16 +56+), showed a similar trend to ALC for both tofacitinib doses and PBO (Table), with minimal decreases over 6 months. B cells (CD19+) showed numerical increases across treatments. Percentage changes from baseline in LSCs at M6 showed a generally similar pattern to absolute values. In adalimumab-treated pts, ALCs and all LSCs increased over 6 months. Up to M6, no pts receiving tofacitinib or adalimumab had confirmed ALC  $<0.5 \times 10^3/\text{mm}^3$ ; 1 pt receiving PBO had a confirmed ALC  $<0.5 \times 10^3/\text{mm}^3$  over 3 months, resulting in discontinuation from the study before advancing to active treatment. Up to M12, SIs were reported in 7 tofacitinib- (including 2 pts who advanced from PBO) and 1 adalimumab-treated pt; of these, 1 SI (PBO advanced to tofacitinib) occurred  $>6$  months after treatment initiation. There was no trend that suggested an increased risk of SIs in any ALC category (data not shown).

**Conclusions:** Up to M6 in tofacitinib-treated pts with active PsA, minimal changes in ALCs and LSCs were observed. Although incidence of SIs did not appear to be related to ALC, conclusions are limited by the small number of events.

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**SAT0331 INFLAMMATORY MARKERS AND ADIPOKINES RELATED TO CARDIOVASCULAR RISK AND METABOLIC COMORBIDITIES IN PSORIATIC ARTHRITIS. IN VIVO EFFECTS OF APREMILAST**

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**Objectives:** 1) To evaluate the role of inflammatory mediators and adipokines in the cardiovascular risk profile and the metabolic comorbidities associated with psoriatic arthritis (PsA). 2) To evaluate the effect of apremilast in the adipocytokine pattern, metabolic components and endothelial dysfunction in patients with PsA and metabolic syndrome (MetSyn).

**Methods:** 55 PsA patients and 30 age and gender-matched healthy donors (HD) were analysed. An extensive clinical analysis including body index mass, lipid profile, HOMA-IR and intra-arterial blood pressure was performed. Endothelial function was measured through post occlusive hyperemia using Laser-Doppler. Different proinflammatory cytokines (TNF $\alpha$ , IL1b and IL6), vascular adhesion molecules (VEGF and E-Selectin) and adipokines (adiponectin, leptin, resistin and visfatin) were analysed on serum by ELISA. Ten biological-naïve patients with PsA having metabolic syndrome were given apremilast 30 mg twice daily for 6 months. All the measures were carried out at basal, week 4 and week 24 after apremilast treatment.

**Results:** The prevalence of metabolic comorbidities such as MetSyn, obesity and insulin resistance (IR) was significant higher in PsA compared to HD. PsA patients had impaired endothelial function showed by a reduced peak flow and hyperaemia area and increased levels of VEGF and E-Selectin in serum. The levels of

adipocytokines were significantly higher in PsA compared to HD. The body mass index values were significantly correlated with the clinical inflammatory parameters (CRP and ESR) and activity of the disease (swollen joints count and DAS28). Increased levels of HOMA-IR also correlated with DAS28, clinical and serological inflammatory markers, and diverse adipokines. Elevated levels of cytokines correlated with the activity of the disease and lipid alterations.

Significant improvements in efficacy outcomes, including DAS-28 using erythrocyte sedimentation rate (ESR), tender and swollen joint count, Visual Analogue Scale (VAS), enthesitis and morning stiffness severity, were observed with apremilast at week 4. No changes on BMI were noticed. A significant reduction of intra-arterial blood pressure was evidenced since the first 4 weeks. Serum levels of Apolipoprotein A and B, insulin and HOMA-IR values were also significantly reduced after 24 weeks of treatment. Endothelial dysfunction was significantly restored shown by an increase of the peak flow and hyperaemia area and decreased adhesion molecules in serum. Levels of interleukins and adipokines were also modulated after apremilast treatment.

#### Conclusions:

- PsA is associated with an increase in inflammatory cytokines and adipokines, alongside with an endothelial dysfunction. These alterations are related to the disease activity and the presence of metabolic comorbidities such as insulin resistance or obesity, contributing to the burden of cardiovascular disease risk.
- Apremilast might reduce IR, inflammation, hypertension, lipids and endothelial dysfunction, parameters strongly involved in cardiovascular disease.

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SAT0332

#### A HIGH-DIMENSIONAL APPROACH TO DISSECTING THE ROLE OF THE TISSUE MICROENVIRONMENT IN SHAPING THE IMMUNE RESPONSE IN PSORIATIC ARTHRITIS

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**Background:** Psoriasis (Ps) currently inflicts 2%–3% of the population globally and one-third of patients have psoriatic arthritis (PsA). Up to 30% of PsA patients with active psoriasis (Ps) do not respond adequately to any treatment. Understanding the immune mechanisms contributing to the initiation and disease progression of PsA and Ps is crucial for devising novel therapeutic strategies.

**Objectives:** To address the current unmet clinical need and bridge the knowledge gap in the pathogenesis underlying PsA/Ps, we perform transcriptomic analyses of the skin microenvironment and deep immunophenotyping of immune cells from PsA patients with active disease. We hypothesise that the interaction between the tissue microenvironment and the peripheral immune system dictates the immune response that impacts upon the development and progression of PsA/Ps. This multi-dimensional strategy will also enable the distillation of immune cell subsets in the periphery that can potentiate pathogenic responses in the microenvironment.

**Methods:** Total RNA was extracted from skin punch biopsies of lesional and morphologically normal sites from 7 patients with active disease. RNASeq was performed to decipher the transcriptomes of the skin punch biopsies. Peripheral Blood Mononuclear Cells (PBMCs) from 17 PsA patients and 12 healthy donors were stimulated with PMA-Ionomycin, stained with 37 phenotypic T cells markers and interrogated with the CyTOF platform. Dimensional reduction and unsupervised clustering analyses were performed with Multi-dimensional Automated Reduction and Visualisation (MARVis).

**Results:** Transcriptomic analysis of skin punch biopsies of psoriatic and morphologically normal sites revealed a gene signature in lesional skin that promotes the infiltration of multiple immune cell subsets into the microenvironment. The expression of chemokine genes such as CXCL8, CCL4, and CCL20 suggests a role for the accumulation of neutrophils, monocytes, natural killer (NK) cells and lymphocytes in the establishment of a pro-inflammatory microenvironment that is perpetuated by the presence of TNF and IFN $\gamma$ .

Examination of the immune landscapes of PsA patients highlights multiple perturbations in various immune cell subsets. Specifically, we observed declines in CD8 +CD161+TCRV $\alpha$ 7.2+Mucosal Associated Invariant T (MAIT), CD4 +CD45RO+CXCR5+TFH as well as CD45RO+Tbet+IFN $\gamma$ +TNF $\alpha$ +IL17A +memory TH1 cells in PsA patients. This decline is potentially attributed to the trafficking of these immune cell subsets into the microenvironment in response to chemokine signals. Conversely, we observed enrichments of CD56 +Tbet

+GranB +IFN $\gamma$ +NK and activated CD4 +CD127+CCR7+CD69+effector T cells in PsA patients that can contribute to the pathogenic immune response.

**Conclusions:** Our multi-dimensional approach resolves the complex interactions between the tissue microenvironment and the peripheral immunome that shapes the immune response and dictates the cellular composition in lesional skin. These findings possess translational value and will facilitate the identification of novel immune therapeutic targets.

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SAT0333

#### DRUG SURVIVAL ON FIRST TNF INHIBITORS IN PATIENTS WITH PSORIATIC ARTHRITIS: COMPARISON ACROSS ETANERCEPT, ADALIMUMAB, GOLIMUMAB AND INFLIXIMAB

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**Background:** It is commonly accepted that additional methotrexate (MTX) does not increase efficacy for treatment with TNF in psoriatic arthritis (PsA) but concomitant MTX has been also associated with increased drug survival in register studies. However, the role of MTX comedication in PsA is still unclear.

**Objectives:** We aim was to evaluate TNF- $\alpha$  inhibitor (TNFi) persistence when used as first -line biologic therapy for the management of PsA naïve to biologic and determine features of patients as MTX comedication that are associated with TNFi persistence.

**Methods:** A ambispective longitudinal observational multi-centre cohort study was performed on all patients with PsA starting first TNFi therapy (etanercept, adalimumab, golimumab and infliximab) between 01/JUN/2003 and 01/12/2015. Demographic and clinical data, concomitant treatment with MTX, were compared with TNFi persistence, using Kaplan-Meier survival and Cox regression analysis.

**Results:** Were included 468 patients starting treatment with etanercept (242), adalimumab (120), golimumab<sup>31</sup> and infliximab (75); 235 receiving TNFi as monotherapy (50.2%) and 233 receiving concomitant MTX (49.8%). Mean age was 53.3 $\pm$ 12.6 years (men 53.3 $\pm$ 12.9 and women 53.2 $\pm$ 12.3, p=0.928) and 55.2% were men. Obesity (BMI  $\geq$ 30) was similar in patients with or without persistence on treatment: 30.39 (13.32) vs 29.20 (5.44), p=0.355). At 60 months of follow-up 50.6% of patients persisted with TNFi therapy (55.8% with etanercept, 50.0% with adalimumab, 29.3% with infliximab and 67.7% with golimumab). Infliximab had the lowest retention rate (p=0.006). Drug survival analyses had not differences between patients receiving co-medication or not (p=0.849). In the Cox regression analysis lack of concomitant MTX and gender female were predictors of discontinuation of TNFi (0.014).

**Conclusions:** At 60 months infliximab had the lowest percentage of treatment continuation compared with etanercept, adalimumab and golimumab. Patients with PsA who are female and have not concomitant treatment with MTX could have lower TNFi persistence.

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SAT0334

#### CLINICAL AND SONOGRAPHIC ANALYSIS OF PSORIATIC PATIENTS WITHOUT MUSCULOSKELETAL COMPLAINTS. PRELIMINARY RESULTS OF A PROSPECTIVE STUDY: THE PRE-APS COHORT

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**Background:** Early diagnosis in psoriatic arthritis (PsA) is mandatory in order to initiate early therapy and prevent disability. Around 20% of patients with Psoriasis (PsO) routinely visited in Dermatology departments have PsA previously undiagnosed.



**Objectives:** The aim of this study is to evaluate the presence of inflammation by clinical examination and ultrasound in joints and entheses of patients with PsO without musculoskeletal symptoms.

**Methods:** Patients with PsO under topic or PUVA therapy without musculoskeletal symptoms were referred to our Arthritis Unit. Clinical and demographic data were collected. The patients were evaluated for Body Surface Area (BSA), Swollen Joint Count (SJC) (66 joints), Tender Joint Count (TJC) (68 joints) and enthesitis (MASES). Psoriatic Arthritis Impact of Disease tool questionnaire (PsAID) and Psoriasis Epidemiology Screening tool questionnaire (PEST) were used to assess the impact of the disease. A comprehensive ultrasound evaluation of 46 joints and 12 entheses was made (ESAOTE MylabTwice, 12–18 Mhz probe). Enthesitis score was calculated using the Madrid Sonographic Enthesitis Index (MASEI) and a total score for synovitis (synovial hypertrophy and Power Doppler) was also calculated.

**Results:** 42 patients were included. 20 patients were female (48%), mean age (SD) was 48.3 y (14.6) and disease duration was 17.9 y (15.9). Mean BMI was 24.6 (5.2) and BSA 5 (8.7). 13 out of 42 (31%) had severe PsO (systemic treatment or BSA >10% at any time of evolution). 4 patients (9.5%) had Power Doppler signal and 2 (4.8%) fulfilled criteria for ultrasound-defined active synovitis (SH  $\geq 2$  + PD) despite no signs or symptoms of musculoskeletal disease. However, although structural alterations such as calcifications and enthesophytes were frequent, no PD was found at any entheses.

In the univariate analysis, higher BMI ( $p=0.013$ ), weight ( $p=0.010$ ), waist ( $p=0.033$ ) and hip ( $p=0.014$ ) circumferences were significantly associated with severe PsO. In the same way, CRP serum levels were also significantly higher in patients with severe PsO ( $p=0.027$ ). A strong trend was found between higher MASEI scores and onychopathy ( $p=0.09$ ).

pan>

**Conclusions:** Patients with PsO under topic or PUVA therapy without musculoskeletal symptoms have a low prevalence of findings in the joints and entheses ultrasound evaluation. Of note, 9.5% of PsO patients had subclinical synovitis defined as PD. No changes in those finding were found in a short follow-up (6 months) in these patients. A higher number of patients would be necessary to have strong results. These patients will be followed in order to confirm if they develop Psoriatic Arthritis.

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SAT0335

### SECUKINUMAB PROVIDES RAPID AND SUSTAINED RESOLUTION OF ENTHESITIS IN PSORIATIC ARTHRITIS PATIENTS: POOLED ANALYSIS OF TWO PHASE 3 STUDIES, FUTURE 2 AND FUTURE 3

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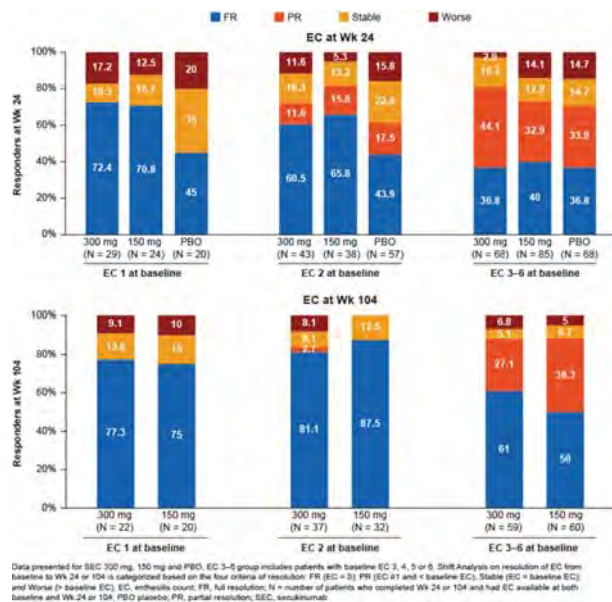
**Background:** Enthesitis, one of the key features of psoriatic arthritis (PsA), shows chronicity in 50–70% of affected patients (pts).<sup>1</sup> Secukinumab (SEC), a fully human monoclonal antibody that selectively neutralises IL-17A, provided significant and sustained improvement in the signs and symptoms of active PsA, with sustained resolution of enthesitis in Phase 3 studies.<sup>2,3</sup>

**Objectives:** Comprehensive *post-hoc* analysis to evaluate the effect of SEC on resolution of enthesitis count (EC; defined by Leeds Enthesitis Index) in PsA pts using pooled data from two Phase 3 studies, FUTURE 2 (NCT01752634) and FUTURE 3 (NCT01989468).

**Methods:** SEC and placebo (PBO) were administered weekly during the first 4 weeks (wks) followed by subcutaneous maintenance dosing every 4 weeks thereafter (PBO until Wk 16/24). The results are reported only for SEC 300 and 150 mg (approved doses). Pts with baseline (BL) enthesitis (BLE) or without BLE (No BLE) were included. Evaluation through Wk 104 included: time to first resolution of enthesitis (i.e. EC=0); shift analysis of BL EC (1, 2 or 3–6) to full resolution (FR) and partial resolution (PR; reduction of EC) at Wks 24 and 104; and number of new enthesitis sites developed in No BLE pts. Individual status over time with respect to resolution of EC was also determined by heat map analysis using last observation carried forward. Data are as observed in the overall population; time to first resolution of enthesitis was analysed in the overall population and by prior use of tumour necrosis factor inhibitor (TNFi-naïve and -inadequate responders [IR]).

**Results:** A total of 466 pts had BLE with a mean EC of 3.1±1.6, and 246 pts had no BLE. Median days to resolution of EC in BLE pts for SEC 300, 150 mg and PBO groups were 57, 85 and 167 in overall population; 57, 85 and 120 in TNFi-naïve pts; and 92, 82 and 169 in TNFi-IR pts, respectively. In pts with BL EC=1/2,

72%/61% (SEC 300 mg), 71%/66% (SEC 150 mg) and 45%/44% (PBO), respectively, achieved FR at Wk 24, with FR in SEC groups sustained or increased to 77%/81% (SEC 300 mg) and 75%/88% (SEC 150 mg) at Wk 104. In BL EC=3–6, 81% (SEC 300 mg), 73% (SEC 150 mg) and 71% (PBO) of pts achieved FR and PR at Wk 24, with an increase of FR and PR to 88% (in both SEC 300 and 150 mg) at Wk 104 (figure 1). A total of 89% of pts with No BLE did not develop enthesitis by Wk 104. Heat map analysis showed that SEC-treated pts at individual level had more resolution of EC than PBO pts at Wk 24.



Abstract SAT0335 – Figure 1. Shift Analysis of EC from Baseline to Wk 24 or 104

**Conclusions:** Time to resolution of enthesitis was earlier with SEC than PBO in the overall population, with faster resolution observed in TNFi-naïve than TNFi-IR pts. Majority of SEC-treated pts with BL EC=1/2 had FR by Wk 24, with further an improvement by Wk 104. In pts with BL EC=3–6, greater improvement was observed with SEC 300 mg vs PBO in the proportion of pts with FR and PR of enthesitis at Wk 24; further improvements were observed in both SEC groups at Wk 104.

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SAT0336

### MEASUREMENT PROPERTIES OF THE MINIMAL DISEASE ACTIVITY CRITERIA FOR PSORIATIC ARTHRITIS

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**Background:** Psoriatic arthritis (PsA) is a heterogeneous inflammatory joint disease, which generally occurs in combination with psoriasis. Key defining features include joint inflammation, psoriasis, nail changes, axial disease, dactylitis, and enthesitis. A composite endpoint that captures all aspects of the disease is critical to understanding disease activity. Recognising the need for a measure of acceptable disease status that equates to a clinically meaningful outcome for patients, the Group for Research and Assessment of Psoriasis and PsA followed methodology from Outcome Measures in Rheumatology to develop the Minimal Disease Activity (MDA) criteria.<sup>1</sup> Since initial publication of the MDA criteria, which consist of physician and patient-reported measures, they have been used in a number of randomised controlled trials (RCTs) and long-term observational studies (LOS). These studies provide an opportunity to systematically evaluate the measurement properties of the MDA.

**Objectives:** To examine evidence of the validity and the ability of the MDA to detect change in published PsA studies.

**Methods:** A targeted literature review was conducted in MEDLINE and EMBASE to identify publications that provided evidence of the validity or ability of the MDA criteria to detect change. LOS that reported data without a comparator and studies that examined the relationship between achievement of MDA and baseline variables were excluded. Abstracts of conference proceedings were included if they reported on phase 3 results not yet formally published. Relevant data were extracted and summarised in tabular format, and reviewed by an independent investigator.

**Results:** 20 publications were identified that met inclusion criteria. In both LOS and RCTs, patients in MDA consistently had decreased inflammatory markers (ie CRP), decreased radiographic joint erosions and progression of structural damage over time, and reported less disease impact on patient-reported outcomes. The consistency of these findings in both LOS and RCTs provide support for the validity of the MDA. Nine RCTs demonstrated superior efficacy to the respective comparator arm. All nine of these RCTs also reported a significantly greater percentage of patients in the active treatment arms met MDA criteria vs. Placebo. These results provide support for the ability of the MDA to detect between-subjects change. Two LOS were also identified that reported on the association with achievement in MDA following initiation of treatment with bDMARDs. demonstrated a significant likelihood of patients beginning treatment with bDMARDs to meet MDA after 4, 6, and 12 months of treatment, providing support for the MDA to detect change in a real-world setting.

**Conclusions:** Published evidence indicates that the MDA is a validated measure with the ability to detect change in PsA patients. The MDA criteria offer a practical, holistic, and clinically meaningful endpoint for patients and clinicians to assess the impact of specific treatment interventions on PsA disease activity.

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SAT0337

### BIOLOGIC DMARDS AND PSORIATIC ARTHRITIS IN EUROPE IN 2016/2017: CHARACTERISTICS OF PATIENTS STARTING TNF-INHIBITORS OR USTEKINUMAB IN THE ONGOING PSABIO OBSERVATIONAL COHORT STUDY

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**Background:** The PsABio study (ClinicalTrials.gov Id: NCT02627768) was developed to evaluate the efficacy, tolerability and persistence of TNF inhibitors (TNFi) and ustekinumab (UST) for patients with psoriatic arthritis (PsA) starting 1 st, 2nd or 3rd line biologic disease-modifying antirheumatic drugs (bDMARDs) in real-world routine care.

**Objectives:** In this interim analysis, the objective was to describe the profile of patients starting either UST or TNFi in routine clinical care in 8 European countries.

**Methods:** Between Dec 2015 and, Aug 2017 patients were enrolled in Italy, Greece, Russia, France, United Kingdom, The Netherlands, Spain and Belgium and had valid baseline data available. Descriptive baseline characteristics for the UST and TNFi cohorts were compared.

**Results:** 563 consecutive patients were analysed (278 UST- and 285 TNFi-treated patients): mean (SD) age 49.3 (12.4) years, disease duration 7.2 (7.5) years; 49.6% were men and most had polyarticular disease (Table). Among comorbidities, cardiovascular disease (38.9%) and obesity (30.4%) were most frequent; 11.5% had anxiety or depression. 25.6% of patients were current smokers. TNFis were more often given as 1 st line bDMARD than UST (56.8% vs 39.2%). For patients receiving their 1 st bDMARD, the prevalence of concomitant conventional synthetic (cs) DMARDs at baseline was: UST: 46.8% (39.5% methotrexate [MTX]) and TNFi: 53.7% (39.5% MTX). Among 166 patients who received a 2nd or 3rd bDMARD and had no ongoing csDMARDs at baseline, 66.3% received UST and 33.7% received TNFi. The most prescribed TNFi were etanercept (34.0%), adalimumab (25.3%) and golimumab (19.6%); 12.6% were TNFi biosimilars. The majority of patients on UST received the recommended dose, although 27.8% (10/36) of patients >100 kg started with 45 mg every 3 months. Disease activity was moderate to high with more axial, skin and nail involvement in the UST group.

**Abstract SAT0337 – Table 1.** Baseline characteristics for all patients and by bDMARD in PsABio as of August 2017. Values are mean (SD), if not otherwise indicated.

	UST (n=278)	TNFi (n=285)	All (n=563)
Age, yrs	49.9 (12.2)	48.8 (12.6)	49.3 (12.4)
Disease duration since diagnosis, yrs	7.7 (7.6)	8.7 (7.4)	7.2 (7.5)
Sex (male), %	47.8	51.2	49.6
Comorbidities (all), %	62.9	55.4	59.1
Cardiovascular comorbidity, %	40.8	37.2	38.9
PsA subtype: %			
oligo	25.6	28.5	27.0
poly	63.0	61.6	62.3
axial (isolated or combined with other subtype)	35.1	27.8	32.6
Enthesitis present, %	47.6	47.9	47.8
Leads Enthesitis Index	2.6 (1.4)	2.5 (1.3)	2.6 (1.4)
Dactylitis present, %	20.1	21.8	21.0
BSA, %			
<3%	36.3	50.4	43.3
3%–10%	35.0	33.2	34.1
>10%	28.8	16.4	22.6
Nail disease, %	43.5	37.2	40.3
DAS28	4.3 (1.2)	4.1 (1.3)	4.2 (1.3)
DAPSA	33.6 (21.1)	31.9 (18.9)	32.7 (20.0)
Swollen Joint Count (66)	5.9 (7.8)	5.6 (6.3)	5.8 (7.1)
Tender Joint Count (68)	12.6 (12.7)	11.4 (10.2)	12.1 (11.5)
CRP (mg/dl), median (IQR)	0.7 (0.3, 1.6)	0.7 (0.3, 1.8)	0.7 (0.3, 1.6)

**Conclusions:** European PsA patients starting bDMARDs in 2016/2017 frequently presented with moderate to high disease activity, and overlapping subtypes of PsA, mainly polyarticular disease. Comorbidities, predominantly



cardiovascular, were common. Compared to patients treated with TNFi, UST was more often given as 2nd or 3rd line bDMARD and in patients with more axial and skin disease. Among patients who switched to a 2nd or 3rd line bDMARD, those not on concomitant csDMARDs preferentially received UST.

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SAT0338

#### PREDICTION OF CARDIOVASCULAR EVENTS IN PATIENTS WITH PSORIATIC ARTHRITIS: PERFORMANCE OF FIVE RISK ALGORITHMS IN AN ITALIAN BICENTRIC STUDY

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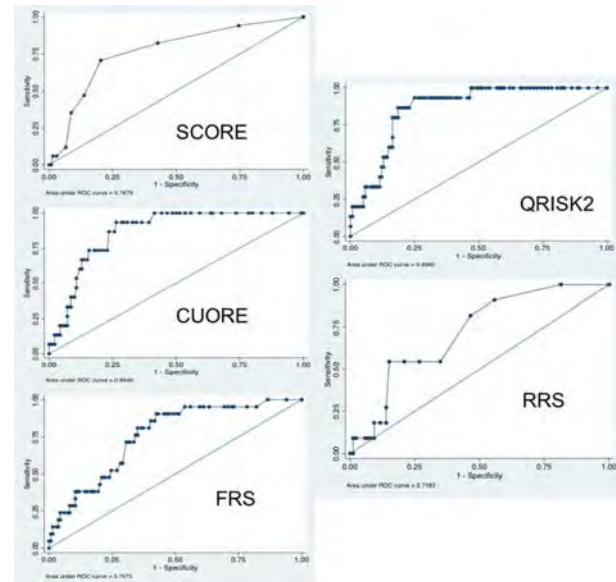
**Background:** The burden of cardiovascular (CV) risk in patients with psoriatic arthritis (PsA) is increased. Prediction of CV risk and consequent preventive strategies play a pivotal role in management of PsA. Recently, EULAR recommendations suggested to use a multiplication by the factor of 1.5 of original CV risk algorithms in patients with rheumatoid arthritis and other inflammatory arthritis.<sup>1</sup>

**Objectives:** To evaluate the performance and calibration of five original and adapted according to EULAR recommendations CV risk algorithms in PsA: SCORE, CUORE, Framingham Risk Score (FRS), QRISK2, and Reynold's Risk Score (RRS).

**Methods:** Prospectively collected data from two Central-Southern Italian cohorts of patients with an history of PsA of almost 10 years at November 2017 and without a personal history of CV disease (CVD) at baseline has been used. The primary outcome was the first CV event: sudden cardiac death, coronary artery diseases (CAD) (stable and unstable angina pectoris, myocardial infarction), cerebral vascular accident (CVA), transient ischaemic attack (TIA), peripheral artery disease (PAD) and heart failure (HF). Discriminatory ability for CV risk prediction was evaluated by the area under the receiver operating curve (ROC). Calibration between predicted risk and observed events was assessed by Hosmer-Lemeshow (HL) tests and calibration plots. Fisher's exact test has been used for analysis of contingency table 1, while Mann-Whitney test has been used to compare ranks. Sensibility, specificity, and odds ratio were calculated for low-to-intermediate risk cut-off (1% for SCORE, 10% for all the other algorithms) and for intermediate-to-high risk cut-off (5% for SCORE, 20% for all the other algorithms).

**Results:** 155 patients (57±10.57 years) were enrolled with an observation of 1550 patient/year. During follow-up, 21 patients had a CV event (1.35 events per 100 patient/years): 8 cases of myocardial infarction or unstable angina pectoris, 3 cases of stable angina pectoris, 2 cases of TIA, 4 cases of PAD, 4 cases of HF. No fatal events were reported. Area under the ROC were 0.7679 (95% CI 0.64768 to 0.88812), 0.864 (95% CI 0.79675 to 0.93278), 0.7575 (95% CI 0.65784 to

0.85708), 0.8660 (95% CI 0.79428 to 0.93772), and 0.7183 (95% CI 0.57795 to 0.85862) for SCORE, CUORE, FRS, QRISK2, and RRS, respectively, suggesting fair to good discriminative ability between patients with or without a CV event (figure 1). HL tests demonstrated poor model fit (p<0.05) for SCORE, CUORE, and RRS, but not for FRS and QRISK2 (p>0.05). Discriminative ability and calibration were not improved by adaption of the algorithms according to EULAR indications. A large amount of patients who experienced a CV event was at "low risk" (minimum 17.6% for SCORE and maximum 81.8% for RRS) or at "low-intermediate" risk (minimum 52.9% for SCORE and maximum 95.2% for FRS).



**Conclusions:** Adaption of the CV risk algorithms according to EULAR indications did not provide improvement in discriminative ability and calibration in patients with PsA from Centre and South of Italy. In PsA, an excess of CV events has been observed in patients at "low risk" or "low-intermediate risk".

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SAT0339

#### IMPACT OF ALTERNATE MECHANISM OF ACTION BIOLOGICS ON TUMOUR NECROSIS FACTOR INHIBITOR (TNF) PRESCRIBING IN PSORIATIC ARTHRITIS: RESULTS FROM A NATIONAL PATIENT CHART AUDIT

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**Background:** Tumour Necrosis Factor-inhibitor (TNF) therapy has long been the standard of care for adult patients diagnosed with moderate to severe psoriatic arthritis (PsA), though several new biologics and small molecules have recently received FDA approval for the treatment of PsA.

**Objectives:** This research sought to understand the extent to which biologics and small molecules with a different mechanism of action (MOA) have been adopted for the treatment of PsA and their impact on the use of well-established TNFs in the United States.

**Methods:** We conducted a retrospective chart review of patients diagnosed with PsA (n=1,008), who had switched from one biologic therapy or apremilast to another in the prior twelve weeks. Data were collected in April 2017 and included clinical and non-clinical patient demographics, as well as physician demographics and attitudinal survey responses. This study was a non-longitudinal trending analysis to a 2016 audit following the same methodology.

**Results:** 78% of the participating rheumatologists reported recent changes to the management of their patients with PsA. The two most commonly recalled treatment shifts were: more aggressive use of biologics in general and an increased use non-TNF agents for the treatment of PsA. With increased treatment options, US rheumatologists are switching patients more frequently and faster than previously recorded. In 2017, US rheumatologists reported that, over the course of a year, 29% of their biologic and apremilast treated patients are switched to a



different brand, a figure significantly up from 2016 (25%). Furthermore, a higher percent of the audited switched patients occurred within six months of initiating the prior agent compared to the prior year (56% vs. 40%).

In 2017, switching between TNF agents significantly decreased from 52% in 2016 to 41% in 2017, and switches from a TNF to an alternate MOA biologic significantly increased from 13% to 20%, respectively. The growth in the switching share of alternative MOAs was driven primarily by increased use of secukinumab, an Interleukin-17 inhibitor approved in January 2016. While most of the secukinumab patients originated from TNF inhibitors, ustekinumab switching share was also impacted. Indeed, rheumatologists indicated that 33% of the patients switched to secukinumab in 2017 would have been placed on ustekinumab if secukinumab had not been available.

**Conclusions:** Increased biologic and small molecule options for the treatment of PsA has resulted in US rheumatologists switching patients more frequently and faster than in the past. Though TNF inhibitors remain the predominant mechanism of action for the treatment of PsA, the introduction of secukinumab has had a direct impact on the PsA switching environment in 2017 and recent approvals in the form of tofacitinib, ixekizumab, and abatacept are hypothesised to further impact the PsA switching environment in 2018.

#### REFERENCE:

- [1] RealWorld DynamixTM: Biologic and Apremilast Switching in Psoriatic Arthritis 2017.

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SAT0340

#### PSA-DISK, A NOVEL VISUAL INSTRUMENT TO ASSESS THE BURDEN OF DISEASE IN PSORIATIC ARTHRITIS PATIENTS

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**Background:** The assessment of joint disease in psoriasis (PsO) patients is paramount, particularly where consensus among dermatology and rheumatology specialists is necessary.

**Objectives:** To evaluate the prevalence of psoriatic arthritis (PsA) in PsO patients and assess how a novel 16-item visual instrument (PsA-Disk) correlates with the disease and its clinical manifestations.

**Methods:** Data were prospectively collected from 8 dermatological/rheumatological centres across Italy. During their first dermatological visit, patients completed both PEST (Psoriasis Epidemiology Screening Tool) and PsA-disk questionnaires. Rheumatological visit was performed in order to confirm presence/absence of PsA. Clinimetric and disease activity variables were recorded.

**Results:** From a total of 239 PsO patients, 120 (50.2%) patients were diagnosed with PsA. More PsA-positive patients had nail PsO (54.2% vs. 42%, p=0.05) and a PEST score  $\geq 3$  vs. PsA-negative patients (77.5% vs. 37.8%, p<0.001). PsA-positive patients presented with significantly higher ESR (21.9 $\pm$ 17.1 vs. 15.9 $\pm$ 10.2 mm/h, p=0.041), NAPS1-feet (10.2 $\pm$ 9.7 vs. 3.9 $\pm$ 7.8, p=0.002), NAPS1-(hands+feet; 9.3 $\pm$ 6.8 vs. 4.6 $\pm$ 7.9, p=0.007), and PsA-Disk scores (73.9 $\pm$ 32.1 vs. 58.1 $\pm$ 39.8, p<0.001) vs. PsA-negative patients. PsA-patients with axial involvement had higher PsA-Disk scores (86.7 vs. 72.5, p=0.088) as well as patients with knee arthritis (98.4 vs. 71.5, p=0.006). PsA-Disk scores were also positively correlated with number of swollen (r=0.2, p<0.05) and tender joints (r=0.24, p=0.021), patient- (r=0.4, p<0.001) and physician-pain-VAS (r=0.33, p<0.001), PGA-VAS (r=0.23, p=0.025), physician-HAQ (r=0.38, p=0.011), DAS-44 (r=0.25, p=0.023) and DAPSA scores (r=0.31, p=0.005) (figure 1A). Examples of the powerful visual use of this instrument can be seen in figure 1B.

**Abstract – Figure 1.** [A] Correlation between clinical variables and PsA-Disk score in PsA+ patients.

Figure 1 [A] Correlation between clinical variables and PsA-Disk score in PsA+ patients.

Clinical characteristic	N	Mean $\pm$ SD	Coefficient (r)	P-value
Time to diagnosis PsA (years)	75	1.7 $\pm$ 5.6	0.14	N.S.
CRP (mg/dL)	198	5.5 $\pm$ 13.2	0.068	N.S.
ESR (mm/h)	232	21.9 $\pm$ 17.3	0.013	N.S.
N. swollen joints	305	3.2 $\pm$ 4.3	0.2	0.05
N. tender joints	305	6.8 $\pm$ 7.7	0.24	0.021
Pain-VAS – patients assessment	304	6.7 $\pm$ 7.4	0.4	<0.001
Pain-VAS – physicians assessment	304	4.7 $\pm$ 7.5	0.33	<0.001
PGA-VAS	305	5.8 $\pm$ 7.2	0.23	0.025
HAQ	43	0.9 $\pm$ 0.5	0.38	0.012
BASMI	23	4.9 $\pm$ 3.3	0.27	N.S.
DAS-44	49	2.7 $\pm$ 1.3	0.25	0.029
CPGA	49	5.4 $\pm$ 2.2	0.38	N.S.
DAPSA	86	28.8 $\pm$ 11.5	0.31	0.005

ESR=erythrocyte sedimentation rate; CRP=C-reactive protein; HAQ=Health Assessment Questionnaire; NAPS1=Number of Active Psoriatic Sites (1-6); Pain-VAS=Visual Analogue Scale for Pain; PGA=Physician Global Assessment; DAS=Disability Score; CPGA=Clinical Psoriasis Global Assessment; DAPSA=Definition of Psoriatic Arthritis Score.

\*Statistically significant (p<0.05)

\*\*Statistically significant (p<0.01)

\*\*\*Statistically significant (p<0.001)

\*\*\*\*Statistically significant (p<0.0001)

N.S.=Not Significant

Figure 1 [B]



**Conclusions:** PsA-Disk is a novel instrument helping both dermatologist and rheumatologist in the rapid assessment PsA, facilitating in the timely therapeutic management of these patients.

**Disclosure of Interest:** None declared

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SAT0341

#### EFFICACY AND SAFETY OF IXEKIZUMAB IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS AND PREVIOUS INADEQUATE RESPONSE TO TNF INHIBITORS: 52-WEEK RESULTS FROM A PHASE 3 STUDY

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**Background:** Ixekizumab (IXE) is a high affinity monoclonal antibody that selectively targets interleukin-17A. In patients with active psoriatic arthritis (PsA) who had an inadequate response to tumour necrosis factor inhibitors (TNFi), IXE was superior to placebo (PBO) in improving the signs and symptoms of PsA after 24 weeks of treatment (SPIRIT-P2; NCT02349295).<sup>1</sup>

**Objectives:** The objective of this study is to report the Week 52 interim efficacy and safety findings of IXE treatment during the Extension Period (EP) of SPIRIT-P2 (Weeks 24–156).

**Methods:** SPIRIT-P2 is a Phase 3, multicenter, double-blind study. All 363 patients had an inadequate response to one or two TNFi or were intolerant to TNFi. During the Double-Blind Treatment Period (DBTP; Weeks 0–24), patients were randomly assigned 1:1:1 to subcutaneous administration of either 80 mg IXE every 4 weeks (Q4W; n=122) or every 2 weeks (Q2W; n=123) following a 160 mg starting dose at Week 0, or PBO (n=118). Of these, 310 patients completed the DBTP and entered the EP (Weeks 24–156). Patients randomised to IXE at Week 0 continued the same dose regimen in the EP. PBO patients were re-randomised (1:1) to IXE Q4W or Q2W at Week 16 (inadequate responders) or 24. In this interim analysis, efficacy (up to Week 52) and safety (up to Week 156) were analysed using the EP population, defined as all patients who received at least 1 dose of study drug in the EP. Missing values were considered non-response for categorical data and were imputed by modified baseline observation carried forward for continuous data.

**Results:** In the DBTP, a significantly higher percentage of patients achieved ACR20 at Week 24 with IXE Q4W (53%) or Q2W (48%) than with PBO (20%).<sup>1</sup> For patients who entered the EP, the mean age was 52 years, 47% were male, the mean time since PsA onset was 12 years, and mean tender and swollen joint counts at baseline (Week 0) were 23 and 12, respectively. For EP patients who were initially randomised to IXE Q4W or Q2W during the DBTP, ACR20 responses at Week 52 were 68% and 59%, respectively. For patients treated with PBO during the DBTP and re-randomised to IXE Q4W or Q2W during the EP, ACR20 responses at Week 52 were 61% and 50%, respectively. Additional efficacy measures are depicted in the Table. The frequency of adverse events (AEs) in the EP is presented in the Table; the majority were mild or moderate in severity. Serious AEs occurred in 15 patients, and one death occurred in the EP population: a myocardial infarction in a PBO/IXE Q2W patient 502 days after starting IXE.

**Abstract SAT0341 – Table 1.** Efficacy and safety results of an interim analysis of the extension period population of SPIRIT-P2.

	IXE Q4W (N=111)	IXE Q2W (N=107)	PBO/IXE Q4W (N=46)	PBO/IXE Q2W (N=46)
<b>Week 52 Responder Rate, n/N (%), NRI</b>				
ACR 20	75/111 (68)	63/107 (59)	28/46 (61)	23/46 (50)
ACR 50	51/111 (46)	41/107 (38)	20/46 (44)	16/46 (35)
ACR 70	32/111 (29)	22/107 (21)	11/46 (24)	7/46 (15)
MDA	42/111 (38)	29/107 (27)	14/46 (30)	13/46 (28)
LEI (0) <sup>a</sup>	32/61 (53)	30/73 (41)	13/24 (54)	12/29 (41)
LDI-B (0) <sup>b</sup>	21/26 (81)	11/16 (69)	7/7 (100)	2/6 (33)
PASI75 <sup>c</sup>	41/62 (66)	37/57 (65)	19/25 (76)	15/31 (48)
PASI90 <sup>c</sup>	34/62 (55)	27/57 (47)	18/25 (72)	14/31 (45)
NAPSI (0) <sup>d</sup>	41/81 (51)	24/67 (36)	10/29 (34)	9/25 (36)
<b>Week 52 Mean (SD) Change from Baseline, mBOCF</b>				
HAQ-DI	-0.4 (0.5)	-0.4 (0.5)	-0.4 (0.4)	-0.2 (0.5)
DAS 28-CRP	-2.2 (1.5)	-1.9 (1.3)	-2.0 (1.3)	-1.6 (1.3)
<b>Safety Overview (Weeks 24-156), n (%)</b>				
TEAE	79 (71)	68 (64)	32 (70)	27 (59)
SAE	6 (5)	4 (4)	2 (4)	3 (7)
Discontinued due to AE	2 (2)	8 (8)	0 (0)	2 (4)

For efficacy analyses, baseline was defined as assessment recorded on or prior to Week 0. For analyses of TEAEs, baseline was defined as AEs that started prior to the study drug injection at Week 24. <sup>a</sup>Assessed only in patients with enthesitis and LEI >0 at baseline; <sup>b</sup>Assessed only in patients with dactylitis and LDI-B >0 at baseline; <sup>c</sup>Assessed only in patients with psoriatic lesions ≥3% of BSA at baseline; <sup>d</sup>Assessed only in patients with fingernail psoriasis at baseline. Abbreviations: ACR20/50/70=20/50/70% improvement in the ACR; ACR=American College of Rheumatology; BSA=body surface area; DAS28-CRP=Disease Activity Score based on a 28 joint count with C-reactive protein; HAQ-DI=Health Assessment Questionnaire-Disability Index; LDI-B=Leeds Dactylitis Index-Basic; LEI=Leeds Enthesitis Index; mBOCF=modified baseline observation carried forward; MDA=minimal disease activity; NAPSI=Nail Psoriasis Severity Index; NRI=nonresponder imputation; PASI75/90=Psoriasis Area and Severity Index 75/90; SAE=serious adverse event; TEAE=treatment-emergent adverse event

**Conclusions:** IXE demonstrated sustained improvement in the signs and symptoms of PsA across treatment groups during the EP. The safety profile of IXE observed in the EP population was consistent with the safety profile of the intent-to-treat population in the DBTP of SPIRIT-P2.<sup>1</sup>

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#### SAT0342 INFLAMMATORY BACK PAIN IN PSORIATIC ARTHRITIS IS SIGNIFICANTLY MORE RESPONSIVE TO CORTICOSTEROIDS COMPARED TO BACK PAIN IN ANKYLOSING SPONDYLITIS: A PROSPECTIVE, OPEN-LABELLED, CONTROLLED PILOT STUDY

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**Background:** Inflammatory spinal disease is one of three inflammatory musculoskeletal manifestations which frequently occur in PsA. There is very limited data about the axial involvement in PsA, especially as regards treatment, with

treatment guidelines based largely on data from AS trials. The efficacy of corticosteroids in PsA patients with inflammatory back pain has not been studied to date. **Objectives:** In this controlled trial, we aimed to investigate the comparative performance of corticosteroids for active axial-PsA (AxPsA) versus those with active AS.

**Methods:** PsA patients (fulfilling CASPAR criteria), and AS as per the 1984 Modified New York Criteria, were suitable for inclusion. Among them, patients with active AxPsA and active AS (naïve to biologic therapies) were recruited. The active disease was defined as patients with inflammatory back pain, with spinal pain score of ≥4 and BASDAI score ≥4 despite taking NSAIDs. Furthermore, only those AxPsA and AS patients with an MRI proven sacroiliac joint bone marrow oedema (MRI of sacroiliac joints performed within the 6 months prior to recruitment) were considered for inclusion. Hence, all recruited patients with AxPsA and AS had not only clinically active disease, but also had bone marrow oedema on MRI of sacroiliac joints. Moreover, we recruited a control group of non-inflammatory lower back pain. All patients received a single, intra-muscular dose of depot corticosteroid injection (Triamcinolone Acetonide 80 mg) at baseline. The intra-muscular corticosteroid option was used to overcome any drug compliance issues. Clinical outcome assessments were made at following time points: baseline, week-2, and week-4. The primary efficacy end point was the mean change in Ankylosing Spondylitis Disease Activity Score (ASDAS) at week-2. Key secondary outcome were the mean change of BASDAI, BASFI and ASQoL at week-2 and week-4.

**Results:** In total, 40 patients were recruited – AxPsA=15, AS=15, control=10. At week-2 following corticosteroid treatment, patients with AxPsA had significantly higher improvements in the mean ASDAS compared to patients with AS (1.43 ±0.39 vs. 1.03±0.30, p=0.004), and the same was the case when compared to controls (p<0.001, table-2, figure-1). At week-4, AxPsA patients also showed significantly higher improvements in the mean ASDAS compared to both AS patients (1.09±0.32 vs. 0.77±0.27, p=0.007) and controls (p<0.001). Similarly, the mean BASDAI, VAS spinal pain score, ASQoL and BASFI improved significantly among AxPsA patients compared to AS patients and controls at week-2, with this trend also largely maintained at week-4

**Conclusions:** Axial inflammation in PsA potentially responds significantly better to corticosteroids than in patients with AS. This furthers the argument and adds to the growing evidence that AxPsA and AS are distinct entities. Future studies should further investigate the use of corticosteroids and of sDMARD usage among patients with active IBP in PsA.

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#### SAT0343 CARDIOVASCULAR DISEASE RISK IN CLINICAL SUBTYPES OF PSORIATIC ARTHRITIS

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**Background:** Patients with psoriatic arthritis (PsA) have been shown to be at increased risk of developing cardiovascular disease (CVD), with one recent meta-analysis demonstrating an increased CVD risk of 43% compared to the general population. However PsA is a heterogeneous disease consisting of five different clinical subtypes. It is not known whether the risk of CVD varies between different PsA subtypes.

**Objectives:** To determine whether particular subtypes of PsA are associated with an increased risk of cardiovascular disease.

**Methods:** 114 patients with PsA attending the University Hospital of Wales were asked to complete a questionnaire about their cardiovascular risk factors. Anthropometric and biochemical measurements, including blood pressure, body mass index (BMI), C-reactive protein (CRP) and cholesterol, were also performed. Patients were grouped into one of the five PsA subtypes as described by Moll and Wright. The QRISK2 algorithm was used to determine the 10 year risk of developing CVD for each patient. Multivariate analyses using linear and logistic regression with QRISK2 score and QRISK2 score >10% as dependent variables were conducted and adjusted for known cardiovascular risk factors.

**Results:** Symmetrical polyarthritis was the most common subtype, no patients had arthritis mutilans. There were no statistically significant differences between the subtypes with regards to age, gender, BMI, blood pressure, smoking status, cholesterol or CRP. Statistically significant differences were found between the subtypes using Chi-square (χ<sup>2</sup>) tests for QRISK2 score >10% (p=0.031) as well as the presence of existing cardiovascular disease, diabetes mellitus and cholesterol lowering treatment (p=0.021, 0.021 and 0.037 respectively). The table 1 below lists the number of patients by subtype and these variables.

	Asymmetrical/ oligo-articular	Distal interphalangeal (DIP) predominant	Spinal predominant	Symmetrical polyarthritis
n (out of 100)	24	9	13	68
Age (mean±SD)	51.3±15.0	61.4±7.8	58.8±13.7	50.7±15.2
Male (n,%)	14 (58.3)	5 (55.6)	6 (46.2)	32 (47.1)
Presence of cardiovascular disease (n,%)*	1 (4.2)	0 (0)	3 (23.1)	1 (1.5)
History of diabetes mellitus (n,%)*	6 (25.0)	2 (22.2)	3 (23.1)	3 (4.4)
On cholesterol- lowering treatment (n, %)*	4 (16.7)	1 (11.1)	6 (46.2)	9 (13.2)
QRISK2 risk score (mean±SD)	12±12.3	15.1±8.5	18.8±13.9	11.1±13.3
Those with QRISK2 risk score>10% (n,%)*	9 (37.5)	7 (77.8)	8 (61.5)	23 (33.8)

\*denotes p<0.05

**Conclusions:** PsA patients with symmetrical polyarthritis appear to have the lowest risk of developing CVD. This subtype also had a significantly lower proportion of patients with coexisting diabetes mellitus. Patients with the distal interphalangeal (DIP) subtype are more likely to have existing CVD and be on cholesterol-lowering medications. Patients with the DIP and spinal predominant subtypes of PsA are also more likely to have a QRISK2 score of greater than 10% compared to the other PsA subtypes, suggesting they are more likely to develop CVD and may consequently need closer monitoring and management of CVD risk factors.

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**SAT0344 THE EFFECT OF GUSELKUMAB ON ENTHESITIS: RESULTS FROM A PHASE 2 STUDY IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS**

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**Background:** In a Phase 2 study, Guselkumab (GUS) was shown to be safe and effective in patients (pts) w/active psoriatic arthritis (PsA) w/meaningful improvements in enthesitis.

**Objectives:** To evaluate the effect of GUS on enthesitis in a subset of pts w/ enthesitis at baseline (BL) from the phase 2 PsA study of GUS.

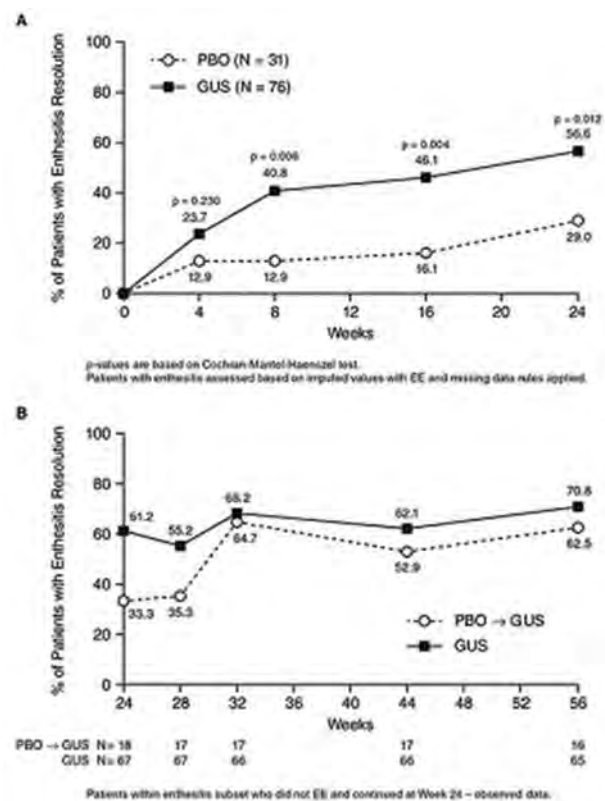
**Methods:** Pts w/active PsA and ≥3% body surface area of plaque psoriasis, despite current or previous treatment, were randomised 2:1 to receive 100 mg subcutaneous GUS or placebo (PBO) at weeks (wks) 0, 4, then every 8 wks (q8w) during a 24-wk double-blind treatment period. At wk16, pts w/<5% improvement in swollen and tender joint counts early escaped (EE) to open-label ustekinumab. At wk24, the PBO group crossed over to receive GUS at wks 24, 28 then q8w (PBO→GUS) and the GUS group continued receiving GUS (GUS→GUS) through wk44. Enthesitis was assessed using the Leeds enthesitis index (LEI). Enthesitis scores during the 24-wk double-blind treatment was analysed using LOCF imputation for missing data and EE. Enthesitis after wk24 was analysed using observed data.

**Results:** Of 149 total pts w/active PsA, 107 (72%) presented w/enthesitis at BL (PBO n=31, mean [SD] LEI=2.6 [1.48], median [range]=2.0;<sup>1</sup>; GUS n=76, mean (SD) LEI=2.7 [1.54], median [range]=2.0<sup>1</sup>; and 85 continued at Wk24 (PBO→GUS n=18; GUS→GUS n=67). Except for higher tender/swollen joint counts and CRP, BL characteristics of the enthesitis subset was similar to the overall population. GUS significantly reduced the LEI by wk8 (mean [SD] change from baseline, PBO: -0.4 [1.59]; GUS: -1.2 [1.65]; p=0.037), and through wk24

(mean [SD] change from baseline, PBO: -0.7 [1.53]; GUS: -1.5 [1.81]; p=0.045). GUS also significantly increased the% of pts w/enthesitis resolution (figure 1). After wk24, the PBO→GUS group achieved rapid, sustained resolution (wk56: mean[SD] change from BL=-2.1 [1.65]; 62.5% of pts w/resolution), similar to GUS→GUS group (wk56: mean[SD] change from BL=-1.9 [1.59], 70.8% of pts w/resolution). Improvement in enthesitis was observed at each enthesitis site assessed, and was greater in ACR20 (Table) responders vs non-responders in GUS-treated patients and was correlated w/improvement in tender (R=0.37, p=0.001) and swollen (R=0.27, p=0.020) joint counts, physician's (R=0.47, p<0.0001) and patient's global assessment of disease activity (R=0.32, p=0.005), and SF36 PCS (R=0.27, p=0.02) and MCS (R=0.35, p=0.002).

**Abstract SAT0344 – Table 1.** Change in LEI in ACR20/50 and PASI75 Responders and Non-responders

	Mean (SD) change from BL in LEI at Wk24		
	Non-responders	Responders	p-value
ACR 20	-0.93 (2.054), n=28	-2.06 (1.660), n=47	0.002
ACR 50	-1.55 (2.190), n=49	-1.81 (1.132), n=26	0.057
PASI 75	-1.25 (1.138), n=12	-1.71 (1.995), n=63	0.524



**Abstract SAT0344 – Figure 1.** Proportion of Patients with Enthesitis Resolution over Time

**Conclusions:** GUS treatment produces rapid and sustained improvement of enthesitis in pts w/active PsA, which correlates w/improvement in joint symptoms and patient-reported outcomes.

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**SAT0345 QUALITY INDICATORS IN THE CARE OF PSORIATIC ARTHRITIS**

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**Background:** In 2016, members of GRAPPA in collaboration with KPMG LLP (UK) conducted a study to benchmark care in psoriatic arthritis (PsA). Challenges in the care of patients with PsA were identified but a key finding was that centres do not usually have processes in place to measure the impact of improved quality of care.<sup>1</sup>

**Objectives:** To identify quality of care indicators to enable PsA caregivers to assess and monitor the outcomes of specific initiatives aimed at improving care in four focus areas. The focus areas are aligned to key patient pathway challenges: 1) Shorten time to diagnosis, 2) Improve multi-disciplinary collaboration, 3) Optimise disease management and 4) Improve disease monitoring.

**Methods:** 1. Structured review literature to obtain a longlist of 100 potential indicators across 4 focus areas. Search strategy used specific terms related to quality measures in PsA, adjacent and other chronic diseases. 80+publications were reviewed and rated based on relevance to four focus areas. 2. Survey expert rheumatologists and dermatologists representative of different healthcare systems to review the longlist and identify the most meaningful and feasible indicators for use in day to day practice. 3. Consensus discussion among the experts to identify shortlist of indicators based on pre-defined selection criteria. Key criteria for the Indicators were: <sup>1</sup> support improvement of patient care <sup>2</sup> evidence-based, <sup>3</sup> measurable, and <sup>4</sup> feasible. 4. Electronic group discussion among the experts to refine definitions of shortlisted indicators and targets.

**Results:** The expert group arrived at a consensus with a shortlist of 8 quality indicators across each focus area.

Domain (Indicator, Target). 1. *Shorten time to diagnosis* (a) Average duration from presentation to HCP to confirmed PsA diagnosis. Less than 6 months<sup>2</sup> (b)% of patients with Psoriasis who receive a PsA screening test Annually<sup>3</sup>. 2. *Improve multidisciplinary collaboration* (a) Multidisciplinary PsA assessment is available (Y/N)<sup>4</sup> (b) Does the centre provide suitable training for HCPs, nurses etc. to increase awareness of PsA disease symptoms (Y/N)<sup>5</sup> 3. *Optimise disease management* (a) Average number of PsA evaluations done by HCP per patient in a year<sup>6</sup> 1–2 annually (b)% PsA patients on whom T2T strategy is applied<sup>7</sup> 4. *Improve disease monitoring* (a)% of PsA patients who received full disease assessment for co-morbidities, e.g. co-morbidity index at least once every year<sup>8</sup> (b) Availability of short-term unscheduled appointments (Y/N)<sup>9</sup> Max. 2 weeks.

**Conclusions:** 8 quality indicators in 4 areas of practice have been defined. The respective targets are evidence based, feasible, measurable and meaningful for patients.

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**SAT0346 CLINICALLY MEANINGFUL IMPROVEMENT IN SKIN AND NAIL PSORIASIS IN BIO-NAÏVE ACTIVE PSORIATIC ARTHRITIS PATIENTS TREATED WITH INTRAVENOUS GOLIMUMAB: RESULTS THROUGH WEEK 24 OF THE GO-VIBRANT STUDY**

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**Background:** GO-VIBRANT was a Ph3 trial of IV golimumab (GLM) in adult pts w/active PsA.

**Objectives:** To evaluate improvement in skin, nail psoriasis and Dermatology Life Quality Index (DLQI) w/IV GLM.

**Methods:** Adult bio-naïve PsA pts w/active disease (≥5 swollen and tender joints, CRP ≥0.6 mg/dl, active plaque PsO or documented history, and despite treatment w/csDMARDs and /or NSAIDs) were randomised to IV GLM 2 mg/kg at wks0, 4, and q8wks thereafter or PBO at wks0, 4, 12, and 20 w/crossover to GLM at wk24. Pts w/≥3% body surface area (BSA) PsO at baseline (BL) were assessed using Psoriasis Area and Severity Index (PASI, 0–72) 75/90/100% and modified Nail Psoriasis Severity Index (mNAPSI, 0–130) at BL, wks14 and 24 (in pts w/ mNAPSI>0 at BL). DLQI was assessed at BL, wks8, 14 and 24.

**Results:** 394 pts (PBO:n=198;GLM:n=196) had ≥3% BSA PsO at BL; 76.5% had mNAPSI >0 at BL (mean 18.6). Pts on GLM achieved a greater PASI75 response vs PBO (59.2% vs 13.6%, p<0.001) at wk14 and wk24 (64.8% vs 13.1%, p<0.001). At wk14, pts on GLM achieved greater PASI 90/100 responses vs PBO (39.3/16.8% vs 6.6/4.5%; p<0.001 for all) and at wk24 (42.9/25.5% vs 7.6/5.6%; p<0.001 for all) (table 1). At wk14, similar proportions of pts in GLM grps, regardless of BL MTX use, achieved PASI 90/100 responses. At wk24, greater proportions of pts on GLM+MTX and GLM only achieved PASI100 vs PBO (+MTX:30.5% vs 7%, p<0.001; -MTX:15.4% vs 1.8%, p<0.010) (table 1). Mean decrease (improvement) from BL in mNAPSI score was greater in GLM vs PBO (-9.6 vs -1.9, p<0.001) at wk14 and wk24 (-11.4 vs -3.7, p<0.001). At wk8, mean decrease (improvement) from BL in DLQI was greater in GLM vs PBO (-7.2 vs -1.7, p<0.001), at wk14 (-7.7 vs -1.8, p<0.001) and wk24 (-8.1 vs -1.9, p<0.001). At wk14, 55.1% of pts treated w/GLM achieved a PASI50 response and improvement in DLQI ≥5 vs 7.1% treated w/PBO (p<0.001) and at wk24, 59.2% vs 8.1% (p<0.001).

**Abstract SAT0346 – Table 1.** Change from Baseline in PASI 90/100 Through Wk24

	Wk14		Wk24	
	PBO	GLM	PBO	GLM
Pts evaluable for improvement fr/BL in PASI, n	198	196	198	196
PASI 90 (%)	6.6	39.3	7.6	42.9
% Diff (95% CI)		32.7 (25.10, 40.40)*		35.3 (27.52, 43.16)*
PASI 100 (%)	4.5	16.8	5.6	25.5
% Diff (95% CI)		12.3 (6.34, 18.30)*		20.0 (13.22, 26.85)*
+BL MTX, n	142	131	142	131
PASI 90 (%)	7.7	41.2	9.2	45.8
% Diff (95% CI)		33.5 (23.97, 42.98)*		36.6 (26.88, 46.41)*
PASI 100 (%)	5.6	17.6	7.0	30.5
% Diff (95% CI)		11.9 (4.39, 19.46)**		23.5 (14.55, 32.43)*
- BL MTX, n	56	65	56	65
PASI 90 (%)	3.6	35.4	3.6	36.9
% Diff (95% CI)		31.8 (19.21, 44.41)*		33.4 (20.65, 46.05)*
PASI 100 (%)	1.8	15.4	1.8	15.4
% Diff (95% CI)		13.6 (4.17, 23.03)***		13.6 (4.17, 23.03)***

\*p<0.001; \*\*p=0.002; \*\*\*p=0.010

**Abstract SAT0346 – Table 2.** Change from Baseline in mNAPSI Through Wk24

	Wk14		Wk24	
	PBO	GLM	PBO	GLM
Pts (mNAPSI>0) evaluable for change fr/BL, n	170	197	170	197
Mean (SD)	-1.9	-9.6 (15.71)	-3.7	-11.4 (16.38)
LS Mean diff (95% CI)	(13.05)	-8.4 (-10.71, -6.05)*	(14.45)	-8.4 (-10.82, -6.01)*

\*p<0.001

**Conclusions:** As early as wk14, IV GLM demonstrated clinically meaningful improvements in skin PsO irrespective of MTX use and nail PsO. Improvement in DLQI was seen as early as wk8, w/continued improvement at wks14 and 24.

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### SAT0347 BASELINE CHARACTERISTICS OF PATIENTS WITH PSORIATIC ARTHRITIS INITIATED ON APREMILAST IN THE CORONA PSORIATIC ARTHRITIS/SPONDYLOARTHRITIS (PSA/SPA) REGISTRY

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**Background:** Apremilast (APR) is an oral phosphodiesterase 4 inhibitor approved for the treatment of adult patients with active psoriatic arthritis (PsA) and psoriasis.

**Objectives:** To characterise demographics, disease activity and duration, concomitant therapy, quality of life, and prior comorbidities among patients with PsA who initiated APR in the Corona Psoriatic Arthritis/Spondyloarthritis (PsA/SpA) registry, an independent, prospective, US observational cohort.

**Methods:** Adult patients  $\geq 18$  years of age with PsA who were reported initiating APR in the Corona PsA/SpA registry between May 2014 and September 2017 were included in the analysis. Descriptive statistics were calculated for patients' clinical characteristics and disease assessments at the index visit. The index visit was defined as the Corona visit when APR initiation was reported. If the patient started a drug between 2 Corona visits, the measures/outcomes from a prior visit were imputed to replace the missing values.

Clinical Characteristics and Disease Assessments of PsA/SpA Patients at the Index Visit		
Characteristic	n*	Mean (SD)
Swollen joint count (0-66)	136	2.7 (4.43)
Tender joint count (0-68)	136	7.2 (11.56)
PhGA (VAS 0-100 mm)	135	22.1 (18.82)
PGA (VAS 0-100 mm)	134	54.2 (26.45)
Dactylitis count (1-20)	14/138	2.6 (2.21) <sup>‡</sup>
SPARCC/Leeds Enthesitis Index (1-16)	34/138	4.2 (3.05) <sup>‡</sup>
DAS-28 (CRP) (0-10)	67	3.1 (1.04)
CDAI (0-76)	128	13.9 (9.57)
cDAPSA (0-154)	128	20.7 (15.07)
HAQ-S (0-3)	135	0.95 (0.69)
BASDAI (0-10)	126	5.4 (2.53)
Morning stiffness (VAS 0-100 mm)	134	54.4 (28.26)

\*Number of patients with data for the given assessment. <sup>‡</sup>Assessed among patients with dactylitis (n=14) or enthesitis (n=34) at baseline.  
PhGA=Physician's Global Assessment of Disease Activity; PGA=Patient's Global Assessment of Disease Activity; VAS=visual analog scale; SPARCC=Spondyloarthritis Research Consortium of Canada; DAS-28-28=joint count Disease Activity Score; CRP=C-reactive protein; CDAI=Clinical Disease Activity Index; cDAPSA=Clinical Disease Activity Index for Psoriatic Arthritis; HAQ-S=Health Assessment Questionnaire for Spondyloarthritis; BASDAI=Bath Ankylosing Spondylitis Disease Activity Index.

**Results:** Among 138 patients included in the analysis, mean (SD) age was 56<sup>12</sup> years, mean (SD) BMI was 33,<sup>7</sup> 62% were female, 66% were previously on a non-biologic DMARD (nbDMARD) and 79% had prior biologic use; 62% were on APR monotherapy. Of the APR initiators, the number of patients receiving concomitant methotrexate, nbDMARD, TNF inhibitor, and non-TNF inhibitor were 32 (23%), 41 (30%), 6 (4%), and 4 (3%), respectively. Pertinent comorbidities included diabetes mellitus (22%), metabolic syndrome (22%), cancer (18%), cardiovascular disease (17%), and congestive heart failure (0.7%). Patients reported a mean (SD) of 13<sup>10</sup> years for PsA symptoms and a mean (SD) of 10<sup>9</sup> years since PsA diagnosis. Of the 94 patients with data available for evaluation, 14% met criteria for minimal disease activity while 1% met criteria for very low disease activity. Most patients had moderate or low levels of disease activity, respectively: CDAI (48% and 35%), cDAPSA (47% and 34%), and DAS-28 (CRP) (37% and 21%). Of note, 82% of patients had <5 swollen joints and 63% had <5 tender joints. Mean HAQ-S (0-3) was 0.95 and BASDAI (0-10) was 5.4 (Table). Patients demonstrated a substantial burden of disease with a mean fatigue score (0-100) of 55 and mean overall pain score (0-100) of 55, and 81% reported stiffness lasting >30 min. Additionally, mean baseline work productivity and activity impairment (WPAI) subscale scores

indicated limitations on absenteeism (8%), presenteeism (25%), work productivity loss (26%), and activity impairment (40%).

**Conclusions:** The population of patients with PsA treated with APR in the Corona PsA/SpA registry exhibited low to moderate disease activity and were substantially impacted, as evidenced by patient-reported outcomes (pain, fatigue, stiffness, and productivity). Future analyses on this cohort will provide more insight into patient characteristics and treatment patterns in this population, as well as long-term efficacy and safety information for PsA patients treated with APR.

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### SAT0348 SAFETY OF IXEKIZUMAB IN PATIENTS WITH PSORIATIC ARTHRITIS: RESULTS FROM A POOLED ANALYSIS OF THREE CLINICAL TRIALS

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**Background:** Ixekizumab (IXE), a high affinity monoclonal antibody that selectively targets interleukin-17A, has been shown to be superior to placebo (PBO) in improving signs and symptoms of psoriatic arthritis (PsA) in Phase 3 trials<sup>1,2</sup>.

**Objectives:** To assess the safety of IXE in patients with active PsA using data pooled from 3 (SPIRIT-P1, -P2, and -P3) Phase 3 trials.

**Methods:** SPIRIT-P1<sup>1</sup> and -P2<sup>2</sup> are double-blind trials; patients were randomised to PBO, adalimumab (ADA; active reference arm; SPIRIT-P1 only),<sup>1</sup> or 80 mg IXE every 4 (Q4W) or 2 (Q2W) weeks. PBO and ADA patients were re-randomised to either IXEQ4W or IXEQ2W for the open-label extension period (Weeks 24–156); patients who initially received IXE remained on their original dose. SPIRIT-P3 is an open-label (Week 36–64) trial where patients received IXEQ2W followed by a randomised withdrawal period. In all the 3 trials, patients received a 160 mg loading dose of IXE. Safety data were integrated from all IXE-treated patients (defined as all patients receiving  $\geq 1$  dose of IXE) included in SPIRIT-P1, -P2, and -P3. Exposure-adjusted incidence rates (IRs) per 100 patient-years (PY) were reported for adverse events (AEs).

**Results:** Overall, 1118 patients received IXE (total exposure=1373.4 PY). Four deaths (0.3/100PY) were reported (cerebrovascular accident, cardio-respiratory arrest, drowning, and pneumonia) (Table). The most common treatment-emergent AEs (TEAEs) were injection-site reaction (ISRs), upper respiratory tract infection, and nasopharyngitis; IRs for TEAEs, including ISRs, decreased over-time. There was no clinically meaningful increase in IRs of serious AEs, infections, serious infections, hypersensitivity, and major adverse cardiovascular events (MACE) with longer IXE exposure (Table). IR for serious infections was low (1.2/100PY). Serious infections included pneumonia (0.2/100PY), lower respiratory tract infection, and esophageal candidiasis (0.1/100PY each). No case of active tuberculosis (TB) was reported, but 1 case of latent TB was deemed as serious due to hospitalisation for testing to exclude active TB. Opportunistic infections were limited to oral and esophageal *Candida* and localised herpes zoster. There were no reports of deep organ or bloodstream *Candida* infections. No anaphylaxis was reported, but 1 patient (0.1/100PY) experienced angioedema. No patient had infections temporally associated with Grade  $\geq 2$  neutropenia. Nine patients (0.7/100PY) had MACE. One case (0.1/100PY) each of Crohn's disease (with prior history of irritable bowel syndrome) and ulcerative colitis were reported. However, none of the 12 patients with pre-existing inflammatory bowel disease experienced an exacerbation with IXE.

**Abstract SAT0348 – Table 1.** Exposure-Adjusted Incidence Rate of TEAEs at 12-Week Intervals up to Week 96 (All PsA Ixekizumab Exposures Integrated Analysis Set: SPIRIT-P1, SPIRIT-P2, and SPIRIT-P3).

	Week 0-12 N=1119	Week 12-24 N=1061	Week 24-36 N=992	Week 36-48 N=777	Week 48-60 N=525	Week 60-72 N=446	Week 72-84 N=377	Week 84-96 N=315
Deaths	0.4 (0.1, 2.9)	0.9 (0.0, 5.4)	0.5 (0.1, 3.4)	0.6 (0.0, 6.0)	0.9 (0.1, 6.3)	0.6 (0.0, 5.0)	1.3 (0.2, 9.3)	2.0 (0.0, 12.2)
TEAEs	225.8 (207.9, 245.4)	180.7 (164.0, 198.4)	185.9 (168.3, 205.3)	127.7 (117.9, 139.4)	153.3 (131.8, 178.4)	117.9 (97.7, 142.2)	106.5 (85.7, 132.4)	102.5 (80.7, 130.2)
SAEs	7.7 (4.9, 12.0)	9.8 (6.5, 14.7)	4.3 (2.2, 8.3)	4.5 (2.0, 10.0)	10.0 (5.8, 18.1)	9.7 (5.1, 18.7)	15.8 (9.0, 27.8)	10.7 (5.1, 22.5)
Infections	81.2 (72.6, 95.4)	80.8 (70.1, 93.2)	101.1 (88.1, 115.7)	79.2 (65.5, 95.8)	74.8 (60.3, 92.9)	31.9 (19.1, 58.0)	46.0 (33.0, 64.1)	36.7 (24.6, 54.8)
Infusions	78.8 (58.2, 90.7)	34.0 (27.2, 42.4)	23.5 (17.7, 31.1)	20.2 (13.8, 29.4)	18.4 (10.4, 28.1)	6.5 (2.8, 14.4)	7.6 (3.5, 17.0)	7.8 (3.2, 18.4)
Hypersensitivity*	11.3 (7.8, 16.4)	4.0 (1.8, 11.7)	4.0 (1.3, 11.0)	7.5 (4.0, 13.0)	1.8 (0.5, 7.3)	3.2 (0.5, 8.6)	1.9 (0.2, 9.3)	4.1 (2.3, 14.3)
MACE	0.4 (0.1, 3.0)	0.4 (0.1, 1.9)	0.5 (0.1, 1.4)	0.9 (0.0, 4.0)	0.7 (1.3, 2.7)	0.0 (0.0, 0.0)	2.6 (0.7, 10.5)	0.6 (0.0, 15.3)

All data are IRs (95% confidence intervals) unless otherwise specified. \*Potential hypersensitivity events were defined by the adverse event within hypersensitivity SMOO excluding local injection site reactions.  
Abbreviations: DIP, inflammatory bowel disease; IR=incidence-adjusted incidence rates per 100 patient-years; ISR=injection site reactions; MACE=major adverse cardiac event; N=total number of patients analyzed at each time point; SAEs=serious adverse events; TEAEs=treatment emergent adverse events.

**Conclusions:** The safety profile of IXE in patients with PsA is consistent with previous reports as derived from the analysis of the three SPIRIT trials from a large cohort of patients. No new safety signals were identified with longer IXE treatment exposure.

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**SAT0349 A NOVEL SCORING SYSTEM TO DIFFERENTIATE PSORIATIC ARTHRITIS FROM NODAL OSTEOARTHRITIS ON PLAIN-FILM RADIOGRAPHS**

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**Background:** Differentiating Psoriatic Arthritis (PsA) and Nodal Osteoarthritis (NOA) in patients with interphalangeal joint (IPJ) involvement is often challenging.<sup>1-3</sup> Yet, the distinction is important to make, especially as the treatment for these conditions is vastly different. Here we present a novel scoring system based on identifying often subtle but characteristic radiographic features of both conditions on bilateral hand plain-film radiographs.

**Objectives:** To describe the key radiographic discriminating features that underpin a new scoring system aimed primarily to differentiate PsA from NOA.

**Methods:** The initial scoring methodology was tested through blind analysis and scoring of 99 bilateral hand radiographs of patients with a confirmed clinical diagnosis of PsA, NOA and RA.<sup>4</sup> In this initial study, anonymised radiographs were read by a Musculoskeletal Radiologist blinded to all clinical information. The reader correctly identified the clinical diagnosis in 100% of radiographs. The analysis method was taught to 3 specialist trainees, in a 1 hour training session. They assessed the same radiograph series with an accuracy of 67%–88%.

We refined the radiograph analysis method to develop a scoring system by developing weighted scores for different PsA arthropathic features. These include peri-articular erosions and new bone formation (NBF), reduced joint space, soft tissue

oedema and asymmetry of findings. Osteoarthritis features included marginal osteophytes, subchondral sclerosis/cysts and reduced joint space.

**Results:** All bilateral interphalangeal joints and 1 st metacarpophalangeal (MCP) joint are assessed – (20 joints in total). First carpo-metacarpal joint changes were more common in NOA, but had little discriminatory value. Periarticular erosion and NBF are the key indicators and either feature must be present on the radiographs. Asymmetry of the findings and soft tissue oedema are also included.

Each radiographic feature is scored between 0 and 2 (0=normal, 1=mild/moderate, 2=severe). The scoring system allows the identification of PsA features, even in the presence of background NOA. This scoring system is currently undergoing validation.

**Conclusions:** This radiographic interpretation and scoring system provides a clear framework with key discriminators and relative major and minor weighting. Once validated, it could be taught and used as a readily available, low-cost imaging tool, by both radiologists and non-radiologists alike.

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**SAT0350 CONTENT AND FACE VALIDITY AND FEASIBILITY OF FIVE CANDIDATE INSTRUMENTS FOR PSORIATIC ARTHRITIS RANDOMISED CONTROLLED TRIALS: RESULTS FROM THE PSA OMERACT CORE SET WORKSHOP AT THE GRAPPA 2017 ANNUAL MEETING**

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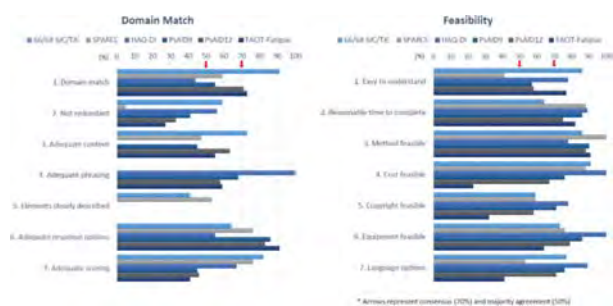
**Background:** The Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) – Outcome Measures in Rheumatology (OMERACT) Psoriatic Arthritis (PsA) Core Set working group is developing a core instrument set to guide selection of outcome measures (instruments) for PsA randomised controlled trials (RCTs) and longitudinal observational studies (LOS). Candidate instrument measurement properties are being appraised in systematic literature reviews by working group members.

**Objectives:** Appraise the content and face validity (domain match) and feasibility of PsA instruments with GRAPPA stakeholders using the OMERACT Filter 2.1 instrument selection process<sup>1</sup>.

**Methods:** The PsA Core set workshop held at the GRAPPA 2017 annual meeting comprised an introductory plenary session and breakout group discussions. Working group members facilitated six breakout groups, with two patient research partners (PRPs) per group, discussing pre-selected domain-instrument pairs. Participants individually reviewed the instrument(s). After group discussion, they completed anonymised paper-based OMERACT questionnaires examining domain match and feasibility, with votes for each aspect of domain match and feasibility centralised by instrument. A final vote (show of hands) on whether the assigned instrument met the requirements for domain match and feasibility using the OMERACT traffic-light scoring system was taken. Consensus was defined as more than 70% agreement, and majority as more than 50% agreement within a group. Consensus represents stronger evidence than majority agreement.

**Results:** There were 145 participants across all breakout groups and 116 returned completed questionnaires. Anonymized votes are summarised across groups and instruments in figure 1. More than 70% in the respective breakout groups endorsed the PsA instrument 66 swollen and 68 tender joint count (66/68 SJC/TJC) as a good match with the target domain of arthritis, a subset of MSK disease activity, FACIT-Fatigue as a good match with fatigue, and PsAID12 as a good match with HRQoL. There was consensus or majority agreement for all feasibility questions for the 66/68 SJC/TJC, HAQ-DI and PsAID9 and PsAID12. For the SPARCC enthesitis index only one item in both domain match and feasibility did not reach majority agreement.





**Abstract SAT0350 – Figure 1.** GRAPPA stakeholders' ratings for OMERACT domain match and feasibility for 6 PsA instruments

**Conclusions:** The first two steps of the OMERACT Filter 2.1 instrument selection process for five candidate instruments have been completed. The first set of candidate instruments selected to undergo the next phase of the OMERACT Filter 2.1, construct validity and discrimination appraisal are 66/68 SJC/TJC, SPARCC enthesitis index, PsAID9, PsAID12, HAQ-DI and FACIT-Fatigue. Additional PsA instruments will undergo the OMERACT selection process.

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#### SAT0351 VERY LOW DISEASE ACTIVITY, DAPSA REMISSION, AND PATIENT-ACCEPTABLE SYMPTOM STATE IN PSORIATIC ARTHRITIS

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**Background:** The goal of treatment in psoriatic arthritis (PsA) according to the T2T strategy is remission, or at least, a low disease activity state<sup>1</sup>. Currently there is no clear agreement on how to measure these treatment goals.

**Objectives:** To explore the relationship between very low disease activity (VLDA) state, according to the MDA 7/7 criteria<sup>2</sup>, and DAPSA remission<sup>3</sup>, as well as its association with the impact of the disease evaluated by the PsAID questionnaire<sup>4</sup>, in patients with PsA in routine clinical practice.

**Methods:** Post-hoc analysis of the MAAPs study<sup>5</sup>. We included patients who met CASPAR criteria, with at least one year of disease evolution, and treated with biological and/or synthetic DMARDs according to the usual clinical practice in Spain. Patients were considered in VLDA if they met 7/7 of the MDA criteria, and in DAPSA/cDAPSA remission (this last without CRP) if they had a value  $\leq 4$ . A PsAID  $< 4$  represented a patient-acceptable symptom state (PASS). The frequency of these states and kappa ( $\kappa$ ) agreement between them were analysed.

**Results:** Of the 227 patients included in the original study, 26 (11.5%), 52 (30.6%), 65 (36.9%) and 125 (55%) were in VLDA, DAPSA remission, cDAPSA remission, and PASS, respectively. There was a moderate agreement between VLDA and DAPSA remission ( $\kappa=0.52$ ) or the cDAPSA remission ( $\kappa=0.42$ ). Patients in VLDA had a lower impact of the disease measured by PsAID [mean total score (SD): VLDA 1.1 (1.2); DAPSA remission 1.3 (1.5); cDAPSA remission 1.7 (1.6)]. There was a moderate agreement between DAPSA remission or cDAPSA remission and PASS ( $\kappa=0.55$  and  $\kappa=0.58$  respectively), while fair agreement was found between VLDA and PASS ( $\kappa=0.18$ ).

**Conclusions:** About one third of this series reached DAPSA remission, while only 11.5% reached VLDA state. On the other hand, more than half were in PASS situation. Agreement between VLDA and DAPSA was moderate. Although the MDA 7/7 criteria seem to be more stringent criteria for assessing remission, DAPSA remission shows better agreement with PASS. DAPSA and VLDA would be adequate treatment targets in daily practice.

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#### SAT0352 PREVALENCE AND CHARACTERISTICS OF CORONARY DISEASE AND CARDIOVASCULAR RISK FACTORS IN A COHORT OF PATIENTS WITH PSORIATIC ARTHRITIS

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**Background:** We performed a descriptive study of our patients with psoriatic arthritis (PsA) over 40 years old, attending to the presence of coronary disease and cardiovascular risk factors in each group of treatment (DMARDs vs biologic therapy).

**Methods:** Patients older than 40 years, diagnosed with psoriatic arthritis attending clinics at the Department of Rheumatology were analysed to determine how many of them presented coronary disease. The following information was recorded: age, sex, disease duration and age at the coronary event, HLA-B27 positivity, hypertension, type II diabetes and hyperlipidemia, on medical records and discharge reports for each patient.

**Results:** All 137 patients were identified from an electronic database. We found a male predominance: 57% versus 43% of women. Mean age  $57.05 \pm 10.6$  years. Of the 137 patients, 82% had only peripheral arthritis, while 18% also showed axial involvement. With regard to the latter subgroup, 16% patients had a positive HLA-B27 test, 56% were HLA-B27 negative and 28% showed lack of HLA-B27 test. Almost all patients (87%) were in DMARDs therapy, while 31% received biologic therapy: etanercept 42%, secukinumab 16%, adalimumab 12%, ustekinumab 12%, infliximab 9.5%, golimumab 4.7% and certolizumab 2%. About 7% of patients didn't receive DMARDs neither biologic therapy, because of intolerance. Results regarding to cardiovascular risk factors, and coronary disease are as follows:

	DMARD therapy	Biologic therapy ( $\pm$ DMARDs)
Arterial Hypertension	43%	26%
Diabetes	19.5%	7%
Hyperlipidemia	47.5%	38%
Coronary disease	10.9%	2.4%

In DMARD subgroup, we found 6 myocardial infarction (all of them revascularized) and 3 angina, versus 1 myocardial infarction in biologic subgroup.

**Conclusions:** There is solid epidemiologic evidence linking PsA to cardiovascular risk factors and an increased risk of developing cardiovascular disease<sup>1</sup>. Furthermore, over the past two decades it has become increasingly clear that chronic inflammation is an independent risk factor for cardiovascular events. In our study the ratio of ischaemic heart disease for patients with PsA in DMARD therapy is four times higher than that of biologic treatment group. This may be due to the greater percentage of cardiovascular risk factors in the first group, although, the cardioprotective effect of biologic therapies, must be taken into account, as there are some studies that show association between anti-TNF and significant reduction in carotid IMT<sup>2</sup>. Proper management of cardiovascular risk requires aggressive control of disease activity.

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**Disclosure of Interest:** None declared

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**SAT0353 GEOGRAPHICAL DIFFERENCES IN PSORIATIC ARTHRITIS: A TRANSATLANTIC COMPARISON**

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**Background:** The environmental and genetic factors play a crucial role in the pathogenesis of psoriatic arthritis (PsA) which may cause a difference in disease characteristics for patients from different geographical regions.

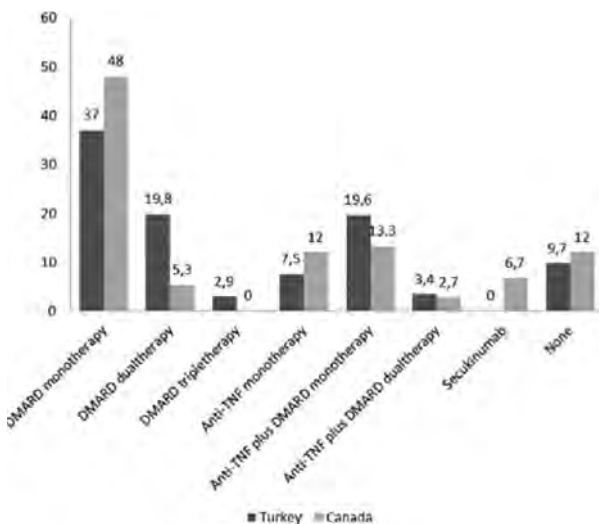
**Objectives:** The aim of the study was to explore the disease characteristics, treatment choices and comorbidities in patients with PsA in different countries to see the impact of geographic factors.

**Methods:** PsArt-ID (Psoriatic Arthritis- International Database) is a prospective, multicentre registry in PsA, which was initially developed in Turkey in 2014, with participation of Canada since 2015 and Italy since 2017. Patients with PsA are consecutively registered to this registry with the aim of investigating the real-life data. Patient characteristics across Turkey (n=1283) and Canada (n=119) are compared for this analysis.

**Abstract SAT0353 – Table 1.** The demographics and clinical characteristics in two countries

	TURKEY	CANADA	p value
Female*	827/1283 (64.5)	60/119 (50.4)	<b>0.002</b>
Age (years)	47 (36–56.7)	49 (34–61)	<b>&lt;0.001</b>
BMI (kg/m <sup>2</sup> )	27.47 (24.5–31.2)	29 (23.7–33.5)	<b>0.013</b>
At onset age for PsA	36 (29–49.7)	39 (30–48)	0.058
Smoking (package/years)	10 (3–19.7)	14.5 (5–26.25)	<b>0.007</b>
Education years	8 (5–12)	15 (13–16)	<b>&lt;0.001</b>
SJC	2 (1–5)	2 (1–7)	0.461
TJC	4 (2–8)	6.5 (2–17)	0.340
TEP	2 (1–2)	1 (1–2)	<b>0.021</b>
BSA	5 (1–13.75)	1 (0–5)	<b>&lt;0.001</b>
BASDAI	37 (20–54)	38 (22–58)	<b>0.027</b>
PT GA	45 (20–60)	31 (12–70)	<b>&lt;0.001</b>
PGA	30 (20–50)	34 (18–66)	<b>&lt;0.001</b>
Pain VAS	40 (20–60)	33 (18–78)	<b>&lt;0.001</b>

TJC: tender joint counts; TEP: tender enthesal points; BSA: body surface area; PTGA: patient global activity; PGA: physician global activity. All data were given n/total n (percentage (%))\* or median (first-third percentiles).



**Abstract SAT0353 – Figure 1.** The distribution of the treatment choices in Turkey and Canada, excluding patients with new diagnosis at the time of recruitment. DMARD: Disease-modifying anti-rheumatic drug; anti-TNF: anti-tumour necrosis factor. All data were given n/total n (percentage (%)).

**Results:** Canadian patients were older at the time of recruitment (Table). They also were more frequently smokers, had higher duration of education and higher BMI than patients in Turkey. Patients in Canada had more frequent polyarthritis (66.7% vs 39.6%, p<0.001), DIP joint disease (34.2% vs 16%, p<0.001), dactylitis (38.1% vs 29%, p=0.037) nail involvement (55.9% vs 45.7%, p=0.008) and higher number deformed joints (29.3% vs 20.7%, p=0.035) whereas Turkish patients had oligoarthritis more often (37.6% vs 24.8%, p=0.016). For disease activity, tender and swollen joint counts were similar for whereas the skin activity was higher in Turkish patients. There were no major differences between countries regarding treatment choices with similar frequencies of patients on biologic therapies (34.5% vs 30.2%, p=0.339) (figure 1). Although the numbers were very low, there was more frequent cancer in Canada than Turkey (4.3% vs 1.4%, p=0.022) whereas all the other comorbidities were similar.

**Conclusions:** Geographical differences have impacts on the disease features in PsA, which may be due to genetic, environmental and cultural differences. The treatments are comparable suggesting a similar approach by the physicians.

**Disclosure of Interest:** None declared

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**SAT0354 THE WORK PRODUCTIVITY AND ACTIVITY INDEX SPECIFIC HEALTH PROBLEM (WPAI-SHP) AND ITS ASSOCIATION WITH PSORIATIC ARTHRITIS (PSA) ACTIVITY BY DISEASE ACTIVITY INDEX FOR PSORIATIC ARTHRITIS (DAPSA) IN ROUTINE CARE: DATA OF THE RUSSIAN PSORIATIC ARTHRITIS REGISTRY (RU-PSART)**

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**Background:** Psoriatic arthritis (PsA) can lead to impaired physical function and work productivity due to chronic inflammation. The goal of PsA treatment is minimal disease activity (MDA) or Remission/Low Disease Activity (REM/LDA) attainment by DAPSA. But there is limited data about the association between PsA activity and work productivity in routine care. The Russian Psoriatic Arthritis Registry (RU-PsART) collected data from 25 rheumatology clinics in the Russian Federation regions.

**Objectives:** evaluate the association between attainment of REM/LDA by DAPSA and the WPAI-SHP in PsA pts in routine care.

**Methods:** 294 (M/F=133/161) pts with PsA, diagnosed according to CASPAR criteria, mean age 41.2±1.9 (Min 21 – Max 72) years (yrs.), PsA duration 6.1±5.3 (Min 0 – Max 31) yrs., psoriasis duration 13.6±10.7 (Min 0.2 – Max 54.8) yrs. were included in the RU-PsART after signing consent participation forms. Pts underwent evaluation of PsA activity by DAPSA and considered REM≤4, LDA≤14, moderate disease activity (MDA) ≤28, high disease activity (HDA) >28 at baseline. 175 out of 294 pts fulfilled WPAI-SHP. DAPSA and WPAI-SHP at the same time were available in 135 out of 175 pts. 87 out of 135 patients were able to work and operate. At the time of evaluation 82 out of 135 pts were taking sDMARDs, 19 out of 135 pts were missing. Overall work impairment, daily activity impairment, absenteeism and presentism were calculated. M±SD,%, ORs with 95% CI were performed. All CI >1 were considered to indicate statistical significance.

**Results:** Daily activity impairment was found in 91 out of 135 pts (67%), overall work impairment – in 64 out of 87 pts (74%), presentism – in 47 out of 87 pts (49%), absenteeism – in 31 out of 87 pts (36%). 40 pts out of 135 (29.6%) had REM/LDA and 95 out of 135 pts (62.9%) had MDA/HAD by DAPSA accordingly at the time of the assessment. Among pts with MDA/HAD daily activity impairment, overall work impairment, presentism and absenteeism were seen in significantly more cases compared to pts with REM/LDA – in 69 out of 95 pts (73%) and in 22 out of 40 pts (55%), OR 2.17 [1.0–4.69]; in 54 out of 62 pts (87%) and in 10 out of 25 pts (40%), OR 10.13 [3.40–30.16]; in 38 out of 62 pts (38%) and in 9 out of 25 pts (36%), OR 2.81 [1.07–7.38]; in 30 out of 62 pts (48%) and in 1 out of 25 pts (4%), OR 22.5 [2.86–176.80] accordingly (Fig.1).



**Abstract SAT0354 – Figure 1.** Interrelation between WPAI-SHP and PsA activity by DAPSA. ORs with 95% CI.

**Conclusions:** Work disability is commonly found in PsA pts in routine care. REM/LDA status by DAPSA was associated with less disability and better work productivity.

**Disclosure of Interest:** None declared

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SATURDAY, 16 JUNE 2018

## Crystal diseases, metabolic bone diseases and bone diseases other than osteoporosis

### SAT0355 THE VALIDITY OF GOUT DIAGNOSIS IN PRIMARY AND SECONDARY CARE – RESULTS FROM A PATIENTS SURVEY

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**Background:** Gout affects 1%–2% of adults worldwide being the most common inflammatory arthritis and usually managed in primary care. The gold standard for definitive diagnosis of gout is the presence of monosodium urate crystals (MSU) in joints or tissues and the latest classification criteria from ACR-EULAR also have this as a central item. Microscopy is however seldom performed in primary care today. Although not intended as diagnostic there are several classification criteria, such as the Mexico and the Netherlands criteria that do not include microscopy.

**Objectives:** The aim of this study was to validate the diagnosis of gout in primary and secondary care according to the Mexico and the Netherlands criteria and items thereof through a patient survey.

**Methods:** All patients above 18 with an ICD10-diagnosis of gout at a visit in primary and secondary care<sup>Jan 2015</sup> through February 2017) were identified from 12 primary care centres and one rheumatology clinic within the Western Sweden Health Care Region. They were sent a questionnaire regarding comorbidities, demographics and gout characteristics. To test the validity of their gout diagnosis, questions of the two gout classification criteria Mexico and the Netherlands were posed. Self-reported knowledge about having gout, was included as an anchor point for the diagnosis. Positive predictive values (PPV) were calculated for these definitions. Structured telephone interviews collecting similar information were performed in 10% of non-responders. The ACR/EULAR criteria was not used, since it includes identification of MSU crystals and imaging as central items.

**Abstract SAT0355 – Table 1.** Positive predictive values for different classification criteria, anchor points for gout diagnosis and common items of classification criteria

Definitions used for gout diagnosis	Primary care (n=784)	Secondary care (n=84)
Netherlands $\leq$ 4, n(%)	57 (7.7)	3 (3.8)
Netherlands $\geq$ 8, n(%)	522 (70.7)	62 (78.5)
Mexico_score $\geq$ 4, n(%)	548 (74.2)	64 (82.1)
Self-reported gout diagnosis (%)	691 (90.2)	78 (94.0)
<b>Selected items (self-reported) from classification criteria</b>		
Hyperuricemia, n(%)	320 (41.8)	55 (66.3)
Men, n(%)	629 (80.2)	62 (73.8)
MI§ or Stroke or Hypertension, n(%)	598 (78.1)	70 (84.3)
Tophus, n(%)	107 (14.1)	26 (31.3)
Any MTP1 attack, n(%)	472 (62.4)	39 (47.6)
Swollen and red joint at attack, n(%)	583 (76.7)	77 (92.8)
Individual joints ever involved in attacks:		
1 joint, n(%)	205 (27.1)	3 (3.7)
>1 joints, n(%)	471 (60.1)	73 (86.9)

§ Myocardial infarction

**Results:** 1589 individuals with a gout diagnosis were identified. 868 (54.6%) individuals responded. Mean age was 71 years and the proportion of men was 80%.

89% of secondary care patients had ever been treated with Allopurinol compared to 71% in primary care. The PPVs ranged from 78.5% to 94%, in secondary care, being lowest for the Netherlands criteria and highest for self-reported gout (table 1). Corresponding PPVs were marginally lower in primary care (but still over 70% for all criteria). Similar results were found among those interviewed by telephone (not shown).

**Conclusions:** The majority of patients diagnosed with gout in both primary and secondary care have had clinical symptoms compatible with the Netherlands and Mexico criteria for gout. Diagnoses of gout identified through health care registers is therefore a valid and useful tool for epidemiological research. Patients with gout in secondary care reported more features of gout than patients in primary care.

**Disclosure of Interest:** None declared

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### SAT0356 FACTORS INFLUENCING TOPHUS RESOLUTION IN PATIENTS WITH PERSISTENT URATE LOWERING RESPONSES TO PEGLOTICASE

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**Background:** Pegloticase is a recombinant mammalian uricase conjugated to polyethylene glycol approved for treatment of chronic refractory gout. It profoundly decreases serum urate levels and also causes rapid resolution of tophi. However, there is considerable heterogeneity in the velocity of tophus resolution.

**Objectives:** To assess factors that may influence the velocity of tophus resolution in subjects with persistent lowering of serum urate levels.

**Methods:** This analysis used results from two randomised controlled trials (RCT) of 6 months duration.<sup>1,2</sup> Tophus assessment was carried out using Computer-Assisted Photographic Evaluation in Rheumatology (CAPER) methodology.<sup>3</sup> Photographs of hands and feet and two other area of visually apparent tophi were taken and assessed for total tophus area and also resolution of tophi in response to therapy. Subjects were defined as responders based upon maintenance of serum urate <6 mg/dL during intensive monitoring periods after 3 and 6 months of treatment. Subject factors evaluated for a relationship with velocity of tophus resolution included age, body mass index, gender, race, and tophus location. Additionally, results for pegloticase responders were subdivided into tertiles on the basis of baseline tophus burden; low (total baseline tophus area <668 mm<sup>2</sup>), medium (baseline tophus burden 688–1690 mm<sup>2</sup>), and high (baseline tophus burden >1690 mm<sup>2</sup>), and the velocity of tophus resolution was determined for each of these groups.

**Results:** The mean measured total tophus area at baseline was 585.8 mm<sup>2</sup> for biochemical responders and complete resolution of all tophi photographed was achieved by 34.8% of this group during the RCT. The velocity of tophus resolution for the pegloticase responders was 60.1 mm<sup>2</sup> per month. Clinical features including age, body mass index, gender, race, and tophus location did not significantly influence the velocity of tophus resolution. The mean (standard deviation [SD]) baseline tophus areas at baseline were 419.4 mm<sup>2</sup> (202.4) for subjects with low baseline tophus burden, 1176.9 mm<sup>2</sup> (238.7) for those with moderate tophus burden, and 4260.4 mm<sup>2</sup> (2784.9) for those with high baseline tophus burden. The mean (SD) velocity of tophus resolution was 28.7 mm<sup>2</sup>/month (13.6) for patients with low baseline tophus burden, 60.2 mm<sup>2</sup>/month (53.5) for those with moderate baseline tophus burden, and 89.5 mm<sup>2</sup>/month (38.7) for those with high baseline tophus burden. Even though the velocity of resolution was greater for those with a larger tophus burden, the time required for complete tophus resolution was substantially less for those with a smaller tophus burden. The projected times to resolution of all visualised tophi determined by linear regression analysis were 6.98, 7.14 and 12.02 months for the subjects with low, medium and high baseline tophus burden (p<0.0001, p<0.0001, p=0.048), respectively.

**Conclusions:** Pegloticase treatment causes a rapid resolution of tophi in biochemical responders and the rate of decrease is not significantly associated with age, body mass index, gender, race, or tophus location. However, the rate of tophus resolution is inversely correlated with the total tophus burden at the beginning of treatment.

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SAT0357

### COMPLIANCE AND PERSISTENCE TO URATE LOWERING THERAPY FOR THE TREATMENT OF GOUT AND HYPERURICEMIA: A RETROSPECTIVE ANALYSIS OF MEDICATION PRESCRIPTION RECORDS

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**Background:** Hyperuricemia is the predominant risk factor for gout, a common crystal-induced disease, manifested as an acute inflammatory arthritis. Urate lowering therapy (ULT) is an effective and recommended life-long treatment for lowering and managing serum urate levels in gout patients.<sup>1</sup> However, recurrent attacks of gouty arthritis are commonly observed in practice, even during long-term ULT.<sup>2</sup> This is often attributed to poor medication adherence and continuance.<sup>3</sup> Gaining insight into the dispensing patterns and medication adherence of ULT, provides a reflection of the current gout care delivered by health professionals.

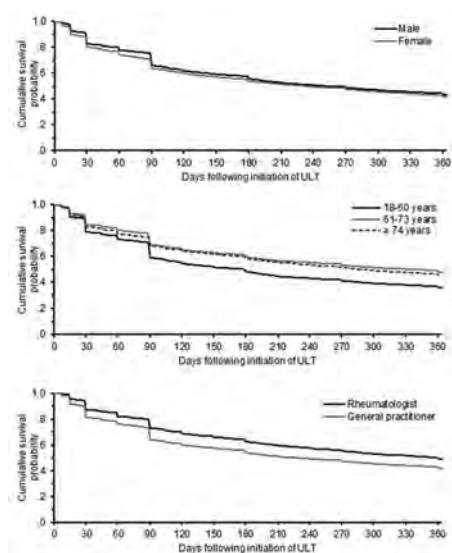
**Objectives:** To examine the levels of compliance and persistence to commonly prescribed ULT for the treatment of hyperuricemia and gout in the Netherlands.

**Methods:** Anonymous medication prescription records were obtained from IQVIA's longitudinal prescription database in The Netherlands, containing ULT dispensing data (allopurinol, febuxostat and benzbromarone) from November 2013 to July 2017. Compliance to ULT was determined by calculating the proportion of days covered (PDC) over a period of 12 consecutive months. Good compliance was defined as a PDC $\geq$ 0.80. Persistence over 12 months was evaluated by determining the time to discontinuation, without surpassing a refill gap of >30 days. The association of PDC and persistence with age, gender and first prescriber were examined using beta regression- and cox-regression models, respectively.

Abstract SAT0357 – Table 1. Variables associated with PDC

	Univariate analyses			Multivariate analyses <sup>1</sup>		
	Gender	Age	Prescriber	Gender	Age	Prescriber
$\beta$ -coefficient	-0.044*	0.011**	0.336**	-0.127**	0.012**	0.348**
SE	0.014	<0.000	0.015	0.014	<0.000	0.015
Pseudo R <sup>2</sup>	<0.000	0.011	0.011	0.024	0.024	0.024

<sup>1</sup> Model: PDC~gender+ age+prescriber. \*p<0.01; \*\*p<0.001; SE, standard error; PDC, proportion of days covered.



Abstract SAT0357 – Figure 1. Survival curves of persistence of ULT drugs one year after initiation of treatment.

**Results:** In total, 45 654 patients were identified meeting the enrollment criteria, of which 76.1% were male. The initial ULT drug prescribed most frequently among general practitioners and rheumatologists was allopurinol 100 mg, 75.9% and 72.1%, respectively. In total, 51.7% of the cases had good compliance after one year. The median time to discontinuation was 248 days, and after one year 42.7%

of the cases were still persistent. In general, men, older patients and patients whose first prescriber was a rheumatologist were more persistent, and had a higher PDC, although effect sizes were modest (table 1 and **Abstract SAT0357 – figure 1**).

**Conclusions:** Our results show that medication adherence to ULT after one year is suboptimal, considering that current guidelines recommend ULT as a life-long treatment. Future studies addressing the reasons for treatment cessation and improving treatment adherence are warranted.

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SAT0358

### DIABETES AND GOUT: REAL-WORLD EVIDENCE EVALUATING PATIENT CHARACTERISTICS, TREATMENT PATTERNS, AND HEALTH CARE UTILISATION

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**Background:** Gout and type 2 diabetes mellitus (T2DM) are common in the United States (US), but little is known about potential associations of T2DM and hyperuricemia/gout with clinical outcomes. This study examined variations in gout severity, management, and health care utilisation among gout patients with and without T2DM.

**Methods:** Data were assessed from a survey of US physicians and patient chart audits. Participating physicians managed the care of  $\geq$ 50 patients with gout annually; chart audits were of their last 5 consecutive adult patients with confirmed gout. Gout severity was measured by physician global assessment, flares, organ/joint damage, and tophi. Treatment characteristics, presence of clinician-confirmed T2DM, and socio-demographics were identified. Descriptive and multivariate (stepwise logistic regression) statistics analysed the differences among gout patients with and without clinician-confirmed comorbid T2DM and assessed urate-lowering therapy (ULT) use and gout control.

**Results:** Overall, 1159 charts of patients with gout were abstracted (246 with T2DM, 913 without T2DM; 81% male; 71% Caucasian); the proportion of patients aged  $\geq$ 61 with gout was greater for those with T2DM than without T2DM (69% vs 31%; p<0.01). Patients with gout and T2DM had longer mean duration of gout (63 vs 41 months), were more likely to have tophi (37% vs 20%), joint damage (24% vs 13%), and clinician-rated severe gout (27% vs 13%) than those without T2DM (all p<0.01). Patients with gout and T2DM were also more likely to receive ULT than those without T2DM (86% vs 71%; p<0.01), and among those patients with gout and T2DM receiving allopurinol, mean daily doses were not significantly different (321 mg vs 298 mg; p=0.17). Gout patients with T2DM were more likely to have additional comorbidities (cardiovascular disease, kidney disease, COPD, depression, diabetes, hyperlipidemia, hypertension, obesity, prostate problems [men]) and have chronic pain than those without T2DM (all p<0.05). On average, gout patients with T2DM vs. those without T2DM reported more office visits (4.1 vs 3.5), were more likely to have an emergency department visit (17% vs 9%) and were more likely to have a hospitalisation (5% vs 2%) (all p<0.01). In both groups, ULT use was associated with better gout control, but the specific factors predictive of ULT use and disease control varied between those with and without T2DM.

**Conclusions:** Gout patients with T2DM were more likely to have a greater impact on health system utilisation and spending, with additional comorbidities and more severe gout than those without T2DM. These data suggest that patients with gout and T2DM constitute a less healthy group in need of careful monitoring and more aggressive gout management.

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### SAT0359 EVOLUTION OF RENAL FUNCTION IN GOUT AFTER NORMALISATION OF SERUM URIC ACID LEVEL

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**Background:** Chronic kidney disease (CKD) is one of the main causes of mortality in gout. In addition, hyperuricemia can contribute to the decrease of renal function.

**Objectives:** The aim of this study was to evaluate the evolution of renal function after reducing serum uric acid (sUA) level to therapeutic target in gout, and to identify the factors that might influence this evolution.

**Methods:** Patients with gout were followed at a single university-based hospital. They were free of urate lowering therapy (ULT) and had an estimated glomerular filtration rate (eGFR) higher than 15 ml/min. Renal function was measured at start of ULT and when sUA was reduced below 360 µmol/L (or 6.0 mg/dL). ULT was allopurinol or febuxostat at the choice of clinician.

**Results:** In this retrospective study, 63 patients (pts) were included with an initial mean sUA level of 541 µmol/l (±86). Overall 42 pts were treated with allopurinol and 21 with febuxostat for an average length of 278 days (±185). After ULT, mean eGFR differed significantly: +2.6 [IC95%: -0.279; 5.484; p=0.08], +3 [IC95%: 0.167; 5.794; p=0.04] and +2.7 [IC95%: 0.490; 4.960; p=0.02] ml/min/1.73 m<sup>2</sup> depending on the calculation method, Cockcroft-Gault (C-G), MDRD and CKD-EPI, respectively. eGFR improvement was statistically significant, p=0.04, 0.02 et 0.01, respectively. Initial eGFR >45 ml/min/1.73 m<sup>2</sup> was associated with a better outcome of eGFR expressed in percentage: +4.7% vs -7.3% (p=0.02), +6.3% vs -4.9% (p=NS), +6.2% vs -5.3% (p=0.03) according to the calculation method, C-G, MDRD and CKD-EPI, respectively. We also found a better evolution of renal function when patients were treated with allopurinol compared to febuxostat, but confounding bias might have occurred since their mean eGFR was also better. In contrast, neither sex, BMI, presence of hypertension nor diabetes showed any significant effect on eGFR improvement.

**Conclusions:** Renal function was significant different after normalisation of sUA in gout patients. We observed an improvement of eGFR which is consistent with recent studies. Interestingly, when initial renal function was at CKD IIIa level or higher (eGFR >45 ml/min/1.73 m<sup>2</sup>), renal outcome was even better. It strengthens the rationale to treat high sUA as soon as possible.

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### SAT0360 A SUMMARY OF CLINICAL EVIDENCE FOR COMMONLY USED URICOSURICS FOR GOUT IN EUROPE

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**Background:** Uricosurics (benzbromarone, probenecid, or sulfipyrazone) are recommended for second-line treatment of gout if treatment target cannot be achieved with allopurinol or if allopurinol cannot be tolerated. While some uricosurics have been available since the 1970s, only two head-to-head trials have been conducted, both of which compared benzbromarone with probenecid. A new uricosuric, lesinurad, has recently been developed, but also has no head-to-head data against current uricosurics. There is therefore a need to compare the efficacy of uricosurics relative to each other via network meta-analysis (NMA), which requires high-quality evidence from well conducted trials, and also for evidence-based recommendations.

**Objectives:** To identify and assess the quality of the randomised controlled trial (RCT) evidence for uricosurics currently licensed for the treatment of gout, and to assess the feasibility of developing an NMA based on these trials.

**Methods:** A systematic review was conducted to identify RCT evidence for uricosurics, followed by an assessment of the quality of the comparisons possible based on this evidence using the GRADE system. This assessment was then used in a feasibility assessment for NMA based on the comparability of the trials in terms of population, comparators, and outcomes.

**Results:** In total, 21 publications reporting on 13 unique studies were identified by the SR, two of which had no common comparator arm with other trials and were excluded from further assessment. Eleven studies were included in the quality assessment informing comparisons between treatments for two outcomes: proportion of patients achieving sUA <6 mg/dL (or 0.36 mMol/L) and change from baseline in sUA. Issues with two or more elements of the methodological quality of the studies were present in all comparisons other than lesinurad plus allopurinol vs placebo plus allopurinol, including open-label design, incomplete reporting and sparse data mainly of safety assessment, and inadequate randomisation. The outcomes assessed in these RCTs were generally comparable across trials, but follow-up time ranged from 1 week to a mean of 19.6 months and few trials reported data at the same endpoint. In addition, line of therapy was unclear/not reported in four trials, with uricosurics used in a first-line population in two trials. The final GRADE quality rating was 5 (high) for lesinurad plus allopurinol vs placebo plus allopurinol and -1 to 1 (very low) for all other comparisons (febuxostat plus lesinurad was not included in comparisons). Based on this assessment, it was concluded that a NMA or other statistical comparison is not possible because of substantial heterogeneity between trials for methodological quality, outcomes, and population.

**Conclusions:** The quality of the randomised controlled trial evidence supporting the use of uricosurics other than lesinurad for gout is poor, and there is substantial heterogeneity in reported follow-up times and study populations. It is therefore not possible to make valid comparisons between these treatments based on this data, which may have implications for decision-makers in assessments of future treatments for gout.

**Disclosure of Interest:** None declared

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### SAT0361 TRABECULAR BONE SCORE IN OSTEOGENESIS IMPERFECTA. IS IT USEFUL?

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**Background:** The trabecular Bone Score (TBS) is a novel gray-level textural analysis measurement that can be applied to DXA images to estimate trabecular microarchitecture and has been shown to be related to direct measures of bone microarchitecture and fracture risk. Osteogenesis imperfecta (OI) is a congenital bone disease characterised by a low bone mineral density (BMD) and poor bone quality and strength. The usefulness of TBS in OI has been scarcely evaluated.

**Objectives:** To analyse the clinical usefulness of TBS determination in patients with OI and its relation with anthropometric and clinical features (especially concerning skeletal fractures and BMD results).

**Methods:** Twenty-four patients (18 F:6 M) with OI with a mean age of 38±15 years<sup>19-63</sup> attending a Metabolic Bone Disease Unit were included. The clinical reports of the patients were reviewed, with especial attention to the clinical features (weight, height and body mass index [BMI]), previous fractures, disease severity, associated mutations and treatments received. Lumbar spine (LS), total hip (TH), and femoral neck (FN) BMD were measured using DXA equipment (Lunar) in all patients. TBS was analysed in LS, and the results were classified in three categories<sup>1</sup>: TBS >1.310 (normal), TBS 1.230-1.310 (partially degraded microarchitecture), TBS <1.230 (degraded microarchitecture). TBS values were compared with a healthy control group of similar age and gender.

**Results:** 5/24 patients (21%) had a degraded microarchitecture, 4 (17%) a partially degraded microarchitecture and 15 (63%) normal TBS. All patients with TBS <1.230 were over 40 years old. 21/24 patients had a previous history of multiple fractures. Regarding BMD, 54% of the patients had osteoporosis, 42% osteopenia and one had normal values. Most patients had a mutation in the COL1A1 gene (63%). A correlation was observed between TBS and age (r=-0.5, p=0.006) and LS BMD (r=0.5, p=0.014), showing a trend to significance with BMI (r=-0.4, p=0.058). No significant differences were observed on comparing TBS in patients and controls (1.321 vs. 1.391, p=N .S.).

**Conclusions:** TBS measurement does not seem to be useful for evaluating bone strength in patients with OI. Despite most patients presenting a history of multiple fractures, only 21% showed degraded microarchitecture with TBS.

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SAT0362

### PERFORMANCE OF THE 2015 ACR/EULAR CLASSIFICATION CRITERIA FOR GOUT IN KOREAN PATIENTS PRESENTING WITH ACUTE ARTHRITIS

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**Background:** A definite diagnosis of gout requires the detection of monosodium urate (MSU) crystals in synovial fluid or tissue. However, the procedure involved is invasive and often not available in acute or primary care settings. Therefore, several alternate sets of classification criteria for gout have been developed.

**Objectives:** This study was undertaken to assess the performance of the 2015 American College of rheumatology (ACR)/European League Against Rheumatism (EULAR) classification criteria for gout and to compare its performance to previous sets of criteria including the New York, American Rheumatism Association (ARA) 1977 and Mexico criteria, in Korean patients presenting with acute arthritis.

**Methods:** Patients with acute arthritis who attended rheumatology clinics and underwent arthrocentesis were enrolled in the study, during February 2017 and December 2017. The gout group included patients with MSU crystals in synovial fluid or tissue, as assessed by an experienced rheumatologist or pathologist. Since the presence of MSU crystals alone is sufficient to fulfil the criterion for gout according to the 2015 ACR/EULAR classification, New York, ARA 1977 and Mexico criteria, this criterion is considered to have a 100% sensitivity in the gout group by our definition. Therefore, we excluded positive MSU crystal results in these four criteria sets to avoid a case of circular reasoning.

**Results:** A total of 116 gout patients (as determined by the presence of MSU crystals) and 71 non-gout patients participated in the study. The number of male patients in the gout group (94.8%) was higher than that in non-gout group (15.1%). The mean ( $\pm$ SD) age of the patients was 58.4 ( $\pm$ 15.0) and 64.5 ( $\pm$ 13.3) years in the gout and non-gout group, respectively.

The sensitivity, specificity, positive predictive value and negative predictive value of the criteria sets were 87.1%, 100%, 100% and 73.2% respectively (area under the curve, AUC 0.975) for the 2015 ACR/EULAR classification criteria, 71.5%, 97.2%, 97.6% and 67.6% (AUC 0.960) for the clinical-parameters-only version of the 2015 ACR/EULAR classification criteria, 68.1%, 81.7%, 85.9% and 61.0% (AUC 0.784) for the New York criteria, 77.6%, 81.7%, 87.4% and 69.0% (AUC 0.878) for the ARA 1977 criteria, and 87.9%, 63.4%, 79.7% and 76.3% (AUC 0.878) for the Mexico criteria.

To determine the performance of the existing criteria sets for gout without relying on the detection of MSU crystals, we also calculated the performance of the criteria assuming an absence of both positive and negative crystal test results. By this parameter, the sensitivity of the 2015 ACR/EULAR classification criteria was 77.6%, specificity was 84.8%, positive predictive value was 89.1%, and negative predictive value was 69.8% (AUC 0.918). The performance of the New York, ARA 1977 and Mexico criteria did not change.

**Conclusions:** The performance of the 2015 ACR/EULAR classification criteria for gout was better than that for the New York, ARA 1977 and Mexico criteria in Korean patients presenting with acute arthritis. When an MSU crystal identification test is not available, 2015 ACR/EULAR classification criteria for gout could be a useful option in the diagnosis of gout in Korean patients presenting with acute arthritis.

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SAT0363

### ARE "TARGET-URATE" AND REMISSION CRITERIA POSSIBLE IN SEVERE GOUT? A REAL LIFE EXPERIENCE IN A COHORT

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**Background:** Gout remission, quality of life and disability improvement are the main objectives of chronic treatment. Gout T2T goal is to achieve and maintain target urate <6 mg/dL and <5 mg/dL (TU) in severe gout (SG).

**Objectives:** To determine in a cohort of gout patients, SG frequency, associated factors, percentage of patients achieving TU and remission criteria.

**Methods:** Patients with gout (ACR-EULAR) from GRESGO cohort were included and evaluated at baseline and bi-annually. At baseline visit, information about gout, life style changes and treatment were discussed with the patients and relatives. Prescription for gout and associated diseases was according to published guides and available drugs. Measures: demographic, clinical and biochemical. HAQ, EUROQoL, VAS-pain and global health. SG: $\geq$ 5 tophi and/or intradermal

tophi. TU:sUA <6 mg/dL and <5 mg/dL; remission according to published proposal (de Loutour H/2016). This protocol was approved by the local IRB, all patients signed informed consent. Statistical analysis: t test, X2, Friedman, multi-ple-correlation and multivariable analysis.

**Results:** At baseline visit 500 gout patients were included, (221/44% with SG and 279/56% non-SG). Males 97%, all received individualised ULT treatment (allopurinol and/or probenecid). The whole group, improved significantly during follow-up in urate, flares, tophus burden, HAQ, pain, EUROQoL and renal function. SG patients were significantly: younger at onset, with lower educational level, socioeconomic status, more laboral absenteeism. Also, had longer disease duration and significant differences in all clinical variables related to severity:>joint count, >index tophi size, >% lithiasis,>HAQ score,>EUROQoL and<MDRD, all these outcomes improved significantly during follow-up. In multivariate analysis, disease duration (p0.008) and flares/years (p0.055) persist significantly associated to SG at baseline. SG patients received significantly higher allopurinol doses (>600 mg/day) and required more frequently glucocorticoids. Eleven patients died, 1 year after baseline ~50% patients were lost. Among those that continued, target urate <6 mg/dL was possible in only 50%–70% of the patients followed for 3–5 years. Less than 50% of patients achieved TU<5 mg/dL during long follow-up. There were no significant differences in most percentages of TU 6 or 5 mg/dL between SG VS non-SG patients (see table 1). Although, both groups improved significantly in all clinical outcomes. Remission definition require none tophi and at least 12 months follow-up, it was observed in 9.4% of non-SG patients.

**Percentage of patients achieved TU:** (\*significant differences)

TU<6 mg/dL<5 mg/dL

	SG %	Non- SG %	SG %	Non- SG %	N
Baseline	12	16	1	8	500
6	21	24	11	15	329
12	35	44	16	22	254
18	53	55	28	26	208
24	58	52	37*	24	189
30	56	51	32	28	152
36	58	59	38	34	131
42	70	58	38	30	94
48	73*	50	35	27	81
54	63	54	0	0	53
60	53	43	42	19	40

**Conclusions:** In our population, SG is very frequent and associated with younger age at onset, low socioeconomic and educational level, longer duration and severe disease. Although they receive more intense treatment according to availability, TU and remission criteria are seldom observed and very difficult to achieve. Earlier diagnosis, intensive and adequate treatment should change these results.

**Disclosure of Interest:** None declared

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SAT0364

### HIGH PREVALENCE OF ENTHESTOPATHIES IN PATIENTS WITH X-LINKED HYPOPHOSPHATEMIA

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**Background:** X-linked hypophosphatemia (XLH) is a rare genetic disease (incidence 1/20 000) due to mutations in the *PHEX* gene. The genetic defects is associated with high level of FGF23 leading to impaired renal phosphate reabsorption and 1,25(OH)vitaminD synthesis. Most patients are diagnosed at walking age because of lower limb deformities and rickets. In adulthood, patients complain of musculoskeletal pain in relation to bone lesions (pseudofractures, osteomalacia) and joint involvement but also ossification of entheses. The latter is a strong determinant of the altered quality of life in this population.

**Objectives:** The aim of this work was to describe the structural bone and joint involvement of the entire skeleton in a large cohort of adult patients with XLH.

**Methods:** The study was prospectively conducted in symptomatic adult XLH patients in the context of the systematic evaluation at the French reference centre for rare diseases of calcium and phosphate metabolism. 81 of the 136 patients included between June 2011 and December 2017 had full body x-rays performed with the EOS low-radiation system. Two trained readers performed a standardised analysis of radiographs with a reading grid including the collection of ossifications of the anterior and lateral vertebral ligament, iliac crests, ischial sites, cotyles and achilles tendons; osteophytes on the spine and hip osteoarthritis; and sacroiliac joint aspect.

**Results:** Of the 81 patients, 55 are women (68%), mean age 42.4 $\pm$ 13.6 years, diagnosed on average at the age of 11 years. 63 (78%) patients were treated during childhood with phosphate and/or vitamin D supplementation. At the time of study, 41 (50.6%) were still upon phosphate supplements and/or vitamin D



analogues, 32 (40%) were taking analgesics, although 65 (80%) suffered from pain (71% articular pain, 22% bone pain and 20% enthesitic pain). Of the 81 patients, 71 (88%) presented with structural damage including 44 (63%) with syndesmophytes or ossifications. The average number of syndesmophytes/ossifications was 4.1±2.6 per patient in this subgroup. Most of them were localised at the cervical spine (82%) and the lumbar spine (62%). In addition, these ossifications were fine in 59% (syndesmophytes-like) and coarse in 41%. The other localizations were the ischial region (40%), iliac crests (37%) and the cotyles (90%). Calcanei were visible on 52 radiographs and showed coarse ossifications for 22 of them (42%). 46 patients (65%) had already hip osteoarthritis and 26 (37%) had at least one osteophyte on the spine mainly on the thoracic spine (58%). We found complete ankylosis of sacro-iliac joints in 12 patients (17%).

**Conclusions:** This observational study shows that 88% of adult XLH patients have structural damages and at least one ossification on the spine and/or on periarthral joint (specially on the cotyles). Of importance, these ossifications were as frequent and as severe in patients not treated with phosphate and vitamin D analogues than in untreated patients. Knowing that this disease can be misdiagnosed and eventually diagnosed only at the adult age, attention must be paid to ossification of the entheses, in particular of the common anterior vertebral ligament and Achilles tendons. The mechanisms of formation of these enthesopathies remain to be determined.

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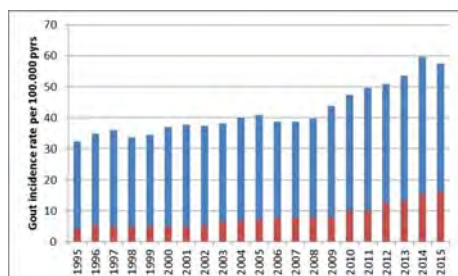
### SAT0366 SECULAR TRENDS IN THE INCIDENCE AND PREVALENCE OF GOUT IN DENMARK FROM 1995–2015: A NATIONWIDE REGISTER-BASED STUDY

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**Background:** Gout is perceived as the most prevalent inflammatory arthritis in the western world – but with great regional and ethnical variation. The incidence and prevalence is thought to be increasing but it's based on few population studies with limited calendar time periods.<sup>[1]</sup> We took advantage of the unique Danish health registries to examine the incidence and prevalence of gout in a nationwide cohort covering the last two decades.

**Objectives:** To examine temporal trends in the incidence and prevalence of gout in the adult Danish population.

**Methods:** Using the nationwide Danish National Patient Registry (DNPR), we calculated the incident rate of hospitalised gout patients (per 1 000 000 person-years) within each 1 year period from 1995 to 2015, and prevalence of gout requiring hospitalisation in 2000 and 2015. Additionally, the age- and gender-specific incidence rates of gout from 1995 to 2015 were calculated. Incidence rates were standardised according to the NORDCAN standard population. Confidence intervals (CI) were calculated according to a Poisson distribution. Both incidence rates based on diagnosis from all specialties and rheumatologists, respectively, were calculated.



**Results:** In the 20 year study period we identified 45 685 newly diagnosed cases of gout. We found an increase in overall incidence, from 32.26/100,000 [95%CI 30.7 to 33.1] in 1995 to 57.5/100,000 [95%CI 55.6 to 59.5] in 2015 (p<0.001). The age and sex specific incidence rates increased progressively with increasing age among both sexes, most markedly in patients aged >60 years. Similar trends were observed for cases diagnosed at rheumatology departments. We likewise observed an increase in the prevalence of gout from 0.29% [95%CI 0.29 to 0.30] in 2000 to 0.68% [95%CI 0.68 to 0.69] in 2015.

**Conclusions:** We found a 1.8-fold increase in the incident rate of hospitalised gout patients in the period 1995–2015 in Denmark among both men and women. Similarly we found a 2.2-fold increase in the prevalence from 2000 to 2015. Further research is needed to elucidate the causes underlying the observed increase in the burden of gout in Denmark

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### SAT0366 SERUM URIC ACID INCREASES AFTER ABROGATION OF SYSTEMIC INFLAMMATION BY TNF INHIBITION

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**Background:** In patients with gout, the serum uric acid (SUA) is usually lower during acute gouty attacks than during intercritical periods. It has been suggested that systemic inflammatory response can cause this phenomenon.

**Objectives:** We aimed to investigate whether SUA levels are associated with levels of pro-inflammatory cytokines in patients with systemic autoimmune rheumatic diseases: rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriatic arthritis (PsA) and juvenile idiopathic arthritis (JIA) and whether the initiation of a therapy with TNF inhibitors (TNFi) would change levels of SUA.

**Methods:** A cohort of 128 patients with clinically active chronic inflammatory rheumatic disease (44 with RA, 45 with AS, 23 with PsA, 16 with JIA) and CRP ≥10 mg/L was recruited in the Institute of Rheumatology, Prague. SUA, CRP, creatinine, MCP-1, IFN-α2, IFN-γ, IL-1β, IL-6, IL-8, IL-10, IL-12, IL-17a, IL-18, IL-23, IL-33 and TNF-α were measured in serum before and after 3 months of treatment with TNFi. We employed bead-based immunoassays to quantify the cytokines and retrieved demographic data, BMI and co-medications. We present the data as mean ± standard deviation or mean and 95% CI.

**Results:** SUA was significantly lower before initiation of TNFi (288.5±78.7 μmol/l) than after 3 months of treatment (307.7±81.7 μmol/l, p=0.0002). The level of CRP (38.9±30.3 vs 5.0±7.6 mg/L, p<0.0001), IL-6 (172.8±339.0 vs 24.2±32.5 pg/ml, p<0.0001) and MCP-1 (1062±554.7 vs 959.2±508.9 pg/ml, p=0.015) significantly decreased during treatment. When we grouped our patients according to sex and diagnosis, the SUA levels significantly increased in the male patients (311.4±79.5 vs 343.9±74.3 μmol/l, p<0.0001), patients with AS (298.4±70.0 vs 326.4±73.1 μmol/l, p=0.0009) and with PsA (302.6±75.3 vs 334.6±74.3 μmol/l, p=0.033), but not in patients with RA or JIA. There was no correlation between the magnitude of the change of SUA, CRP and pro-inflammatory cytokines or the reported use of NSAIDs. However, when we classified our cohort according to increase or decrease of SUA after initiation of TNFi, we observed statistically significant differences in the changes of IL-1β (1.5, -10.8 vs 13.9, vs 29.4, 5.4 to 53.1 pg/ml, p=0.023), IL-23 (0.7, -40.0 to 41.3 vs 102.0, 5.5 to 198.6 pg/ml, p=0.023), IL-33 (-1.2, -26.7 to 24.3 vs 48.8, 3.8 to 93.9 pg/ml, p=0.039) and TNF-α (-0.8, -6.1 to 4.5 vs 10.5, -0.4 to 21.32 pg/ml, p=0.037) between these two groups.

**Conclusions:** We have shown that abrogation of systemic inflammation by TNFis results in an increase in the levels of SUA within 3 months, especially in male patients with AS or PSA. Our results support the hypothesis that systemic inflammation is associated with a decrease in SUA concentrations. The mechanism remains elusive. However, IL-1β, IL-23, IL-33 and TNF-α are candidate players. The difference between the male and female patients argue for a role of the sex hormones. We cannot exclude the possibility that an underreported differential in the use of NSAIDs, known for their uricosuric effect, may have partly biased our observations.

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SAT0367

### PATIENTS HOSPITALISED WITH GOUT AS MAIN DIAGNOSIS: COSTS AND EFFICIENCY ACCORDING TO HOSPITAL DEPARTMENTS

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**Background:** Gout is the most common inflammatory articular disease in adults concerning a 1%–2% of the general population, and even a 4%–5% in older than 70 years. Recently, it has been reported an increase of the prevalence of gout, especially in developed countries.

**Objectives:** The main objective of this study is to describe the clinical and epidemiological characteristics of gout hospitalised patients in Spain (as the main reason of admission) and the economic outcomes of its management by the main care departments in charge when this disease is the principal diagnosis.

**Methods:** The main objective of this study is to describe the clinical and epidemiological characteristics of gout hospitalised patients in Spain (as the main reason of admission) and the economic outcomes of its management by the main care departments in charge when this disease is the principal diagnosis.

**Results:** From the whole 192.037 patients we have with gout diagnosis we performed a sub-analysis of 10.512 patients with gout as the main cause of hospitalisation, from which the 85.9% are males. The admission number for this cause has remained constant or with a slight increase, with an average of 956 patients per year (equivalent to a 5.5% of gout total admissions). The average male age was 64.02 years (standard deviation (SD) 14.43) and 73.9 years (SD 13.69) for women ( $p < 0.001$ ). When comparing patients with gout as main cause of admission against patients hospitalised by other causes, with gout as a secondary diagnosis. The former ones showed a significant lower percentage of comorbidities (type 2 diabetes, congestive heart failure, acute myocardial infarction and cerebrovascular disease).

Regarding the average of hospital stay of these patients, it was  $6.71 \pm 6.8$  days with an average cost of  $3471 \pm 2678$  €. Three medical specialities (Internal Medicine with 3852 hospital admissions (36.6%), Rheumatology with 2600 (24.7%) and Traumatology with 2033 (19.3%)), attended to an 80.6% of the total gout patients as main diagnosis for admission. It was noticed that the hospital stay was lower in the Traumatology Department with an average of  $4.85 \pm 6.78$  days compared with the Rheumatology and Internal Medicine departments, which had an average of  $6.52 \pm 5.65$  days and  $7.76 \pm 6.83$  days respectively. However, it was found the lowest cost in the Rheumatology Department, with an average of 2892 €.

**Abstract SAT0367 – Table 1.** Average stay and costs by clinical departments: in gout as main diagnosis hospitalised patients.

	Internal Medicin	Rheumatology	Traumatology
Number (%)	3852 (36.6%)	2600 (24.7%)	2033 (19.3%)
Average hospital (SD) days	7.76 (6.83)	6.52 (5.65)	4.85 (6.78)
Cost (SD) €	3549 (1796)	2892 (1806)	3715 (2541)

SD=standard deviation

**Conclusions:** Only 24.7% of hospitalised patients with gout as main diagnosis are attended by Rheumatology Departments. However, Rheumatology was the most efficient clinical department in the care of this pathology. This conclusion should be considered in order to improve the management of gout in the health system

**Disclosure of Interest:** None declared

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SAT0368

### ROLE OF JOINT ULTRASONOGRAPHY IN PATIENTS WITH GOUT STARTING TREATMENT WITH FEBUXOSTAT

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**Background:** Gout is the most prevalent arthritis globally, it is due to monosodium urate (MSU) crystals deposit on tissues, mainly in joints and periarticular structures. Although the main clinical pattern in gout is monoarticular, many patients suffer from oligo/polyarticular disease. Due to the information obtained

through imaging tests such as ultrasonography (US), we know that the extent of MSU deposits are greater than we expected in many occasions, affecting clinically silent joints. Musculoskeletal US is a key tool due to its accessibility and safety, it determines accurately the current extent of deposits and joint involvement in gout, which may condition therapeutic changes.

**Objectives:** To evaluate the influence of articular US for clinical practice in Rheumatology when initiating treatment with febuxostat in patients with gout, determining the degree of crystalline deposit and articular ultrasonographic involvement.

**Methods:** Observational cross-sectional study of 129 patients diagnosed with gout (ACR criteria), treated with febuxostat (14 due to renal disease, adverse reaction/intolerance to allopurinol, and 115 due to non-response to allopurinol). One month after the onset of treatment, US examination was performed following the protocol proposed by Peiteado *et al*<sup>1</sup>, determining the number of joints with signs of gout (double contour, hyperechoic aggregates) and acute inflammatory activity (Doppler). Other variables were analysed: age, sex, hypertension, diabetes, dyslipidemia, chronic kidney disease, time of disease evolution and clinical pattern of joint involvement.

**Results:** 115 patients with febuxostat (112 men and 3 women), with a mean age of  $57 \pm 13$  years and mean of disease evolution  $14 \pm 10$  years. 59 patients had monoarticular clinical pattern, 46 oligoarticular and 10 polyarticular. US involvement: we observed acute inflammatory activity by Doppler in 47 patients (40.86%), microcrystalline aggregates in 90 patients (78.26%) and double contour sign in 53 patients (42.08%). The mean uricemia at the time of the joint ultrasound examination was  $7.4 \pm 1.8$  g/dl. Of the 94 patients with uric acid levels  $> 6$  mg/dl, 72 presented extensive US involvement (76.59%), whereas of the 21 patients with levels  $\leq 6$  mg/dl, US involvement was observed in 18 (85.71%). From the observed variables, none was a risk predictor for joint involvement in binomial logistic regression model. Uricemia presented OR=0.83 CI (0.6–1.1)

**Conclusions:** US quantification of MSU deposits can significantly condition the intensity of uricemia-reducing treatment regardless of serum uric acid levels. In this study, patients with non-target uricemia did not present a greater joint affection evaluated by US, however, those with  $< 6$  mg/dl, did present more affection than might be expected. US examination of joints allows a more precise individualization of the treatment in gout and should be incorporated to the periodic evaluation of these patients to optimise their prognosis

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SAT0369

### COMPARISON OF RISK FACTORS FOR CARDIOVASCULAR DISEASES IN PTS WITH CPPD GOUT AND OSTEOARTHRITIS

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**Background:** The data on rates of comorbidities and risk factors for cardiovascular disease in CPPD is insufficient.

**Objectives:** To compare the rates of cardiovascular diseases, risk factors and the risk of death from cardiovascular disease in pts with CPPD, OA and gout.

**Methods:** The study included 488 patients: 232 CPPD (111 m and 121 f) pts, 60 OA (19 m and 41 f) pts and 196 (169 m and 27 f) gout pts. The OA diagnosis was established based on ACR criteria, the CPPD diagnosis – on McCarty criteria, and gout diagnosis – on the detection of monosodium urate crystals in synovial fluid. The mean age in CPPD pts was  $57.6 \pm 18.2$  y., OA pts –  $57.5 \pm 8.5$  y., and gout pts –  $52.7 \pm 12.2$  y. Serum levels of cholesterol, glucose, uric acid, and hsCRP were obtained in all pts, and thorough evaluation for cardiovascular diseases was performed as well as including SCORE (Systematic COronary Risk Evaluation) scale assessment. Statistica 10.0, and Biostatistics were used for statistical data processing. Differences were considered to be statistically significant at  $p < 0.05$ .

**Results:** Obtained data are presented in table 1. High or very high risk of cardiovascular death (SCORE scale) was identified in 47.8% of CPPD pts, was comparable to that in gout pts (48.9%) and exceeded the same in OA pts (33%) ( $p < 0.05$ ). Higher probability of myocardial infarction (MI), chronic heart failure (CHF), chronic kidney disease stage  $\geq 2$  (CKD) and higher mean serum CRP levels were established in CPPD and gout patients as compared to OA pts. There was no difference in rates of stroke, thrombosis, arterial hypertension (AH), ischaemic disease (ICD), diabetes mellitus (DM 2), or in average glucose and cholesterol levels between CPPD, OA and gout pts. Average serum levels of uric acid were higher in patients with gout.

**Abstract SAT0369 – Table 1.** Comparative rates of cardiovascular diseases, risk factors and SCORE values in patients with CPPD, gout and OA

Parameter	CPPD (n=232)	Gout (n=196)	OA (n=60)
hsCRP, mg/l	16.1±8.43*	34.3±24.8***	4.2±2.18
UA, µmol/l	350.8 ±115.8	504.0±136.8**	313.0 ±71.4
Glucose, mmol/l	5.3±1.2	6.1±1.21	4.3±1.2
Cholesterol, mmol/l	6.1±1.17	5.44±1.19	5.1±1.14
AH, n (%)	145 (62.5)	144 (73.4)	41 (68.3)
ICD, n (%)	64 (27.6)	38 (19.3)	21 (35.0)
CHF, n (%)	27 (11.6)*	16 (8.1)*	3 (5.0)
MI, n (%)	9 (3.8)*	13 (8.1)*	0
Stroke, n (%)	2 (0.8)	13 (8.1)	5 (8.3)
Thrombosis, n (%)	9 (3.8)	2 (1.0)	3 (5.0)
CKD≥2 stage, n (%)	17 (7.3)*	28 (14.3)*	0
DM 2, n (%)	24 (10.3)	36 (18.3)	12 (20.0)
SCORE, (%)	5.37±4.29	5.17±4.54	4.58±3.99
High and very high SCORE values (>5%), n (%)	111 (47.8)*	96 (48.9)*	20 (33.3)

\*p&lt;0.05 between CPPD and OA; gout and OA, \*\*p&lt;0.05 between CPPD and gout

**Conclusions:** Cardiovascular risk in CPPD pts may be underestimated and suggests the need for further research.**Disclosure of Interest:** None declared

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SAT0370

**ASSOCIATION OF RENAL DYSFUNCTION AND DEVELOPMENT OF TOPHI IN SUBJECTS WITH CHRONIC REFRACTORY GOUT AND RESPONSE TO TREATMENT WITH PEGLOTICASE**N.L. Edwards<sup>1</sup>, J. Singh<sup>2</sup>, O. Troum<sup>3</sup>, A. Yeo<sup>4</sup>, P. Lipsky<sup>5</sup>. <sup>1</sup>University of Florida, Gainesville; <sup>2</sup>University of Alabama at Birmingham, Birmingham; <sup>3</sup>University of Southern California, Los Angeles; <sup>4</sup>Horizon Pharma, Lake Forest; <sup>5</sup>AMPEL BioSolutions LLC, Charlottesville, USA**Background:** Many, but not all patients with chronic refractory gout develop tophi; and the factors that govern tophus formation are not known. To address this question, we assessed subjects enrolled in the pivotal trials of pegloticase, a mammalian recombinant uricase conjugated to polyethylene glycol that is approved for the treatment of gout refractory to conventional oral urate lowering therapy.**Objectives:** To determine the factors associated with the presence of tophi in patients with chronic refractory gout.**Methods:** This analysis used results from two pivotal randomised controlled trials (RCTs)<sup>1,2</sup> to assess the clinical characteristics of subjects with chronic refractory gout and effects of treatment with pegloticase. Overall, 73% of the subjects in these trials had clinically apparent tophi at baseline and 27% did not. Demographic features of these subjects were assessed and renal function was evaluated by measurement of estimated glomerular filtration rate (eGFR). Subjects were treated with pegloticase, 8 mg every other week (q2w) in a 6 month RCT and then followed for up to 3 years in an open label extension (OLE).**Results:** The analysis included subjects with chronic refractory gout, 154 with tophi at baseline and 57 without tophi. Chronic refractory gout subjects in the two groups were generally similar at baseline, but with a difference in disease duration: 16.3 years for tophaceous subjects vs 11.7 years for subjects without tophi (p=0.007). There were no significant differences in most comorbidities for the two groups. However, eGFR was significantly lower in the subjects with tophi (85.2 mL/min) vs those without tophi (116.5 mL/min) (p=0.001). The frequency of tophi increased in subjects with lower eGFR values (Table). Six months of treatment with pegloticase (8 mg q2w) in a subgroup of subjects resulted in complete or partial resolution of at least one tophus with no increase in others in 74% of subjects, but had no significant effect on renal function measured by eGFR (78.8 mL/min vs 84.2 mL/min, n=51, p=0.7). Continued treatment with pegloticase in the OLE further decreased the burden of tophi, but had no significant effect on renal function measured by eGFR (75.7 mL/min, p=0.6).**Abstract SAT0370 – Table 1**

Baseline eGFR (mL/min)	Non-tophaceous (n=57)	Tophaceous (n=154)
≥90 (n=97)	33 (34.0%)	64 (66.0%)
60 to <90 (n=54)	16 (29.6%)	38 (70.4%)
30 to <60 (n=43)	5 (11.6%)	38 (88.4%)
15 to <30 (n=17)	3 (17.6%)	14 (82.4%)

p=0.0094, Cochran-Mantel-Haenszel chi square test

**Conclusions:** These results indicate that chronic refractory gout patients may present with or without clinically apparent tophi. A significant association was

noted between the presence of renal dysfunction measured by eGFR and the frequency with which chronic refractory gout patients manifested tophi. Pegloticase treatment markedly decreased the tophus burden, but in this analysis did not improve renal function. These results suggest that renal failure may predispose patients to tophus formation, whereas the resolution of tophi in this analysis did not appear to improve renal function.

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SAT0371

**FACTORS ASSOCIATED WITH ALLOPURINOL ADHERENCE AND TREATMENT OUTCOME AMONG GOUT PATIENTS**

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**Background:** A serum uric acid (SUA) level of <6.0 mg/dL has been widely accepted as the therapeutic target for patients with gout. Recent studies implicate allopurinol nonadherence as a major barrier to achieving this target. However, factors that could affect this medication adherence are not clearly identified.**Objectives:** To identify factors associated with allopurinol adherence and SUA goal attainment in gout patients.**Methods:** This study identified patients aged 18 years or older with a diagnosis of gout by 1977 ARA classification criteria for gout, received at least 1 month of allopurinol, and attended out-patient clinics of Phramongkutklao hospital from Jul 2016–Sep 2017. Allopurinol adherence was defined as Medication Taking Behaviour for Thai patient (MTB-Thai) scores >21 points. Patient characteristics, comorbidities, concomitant medications, prescriber specialty, number of gout attack and SUA were examined. Multivariate logistic regression was used to examine factors associated with allopurinol adherence and SUA target, defined as SUA <6.0 mg/dL.**Results:** A total of 226 patients with gout was included. Approximately half of patients (43.4%) were adherent, whereas only one-third of them achieved SUA target (29.2%). Factors associated with allopurinol adherence in the multivariate analysis included disease duration (>1 year) (odds ratio [OR] 0.1, 95% confident interval [CI]: 0.05–0.21), history of gout attack (>2 times/year) (OR 0.14, 95% CI: 0.08–0.27), and prescriber specialty (rheumatologist) (OR 2.64, 95% CI: 1.28–5.43). Factors associated achieved SUA goal in the multivariable analysis included history of gout attack (>2 times/year) (OR 0.21, 95% CI: 0.1–0.42), prescriber specialty (rheumatologist) (OR 2.01, 95% CI: 1.31–4.13), allopurinol dose escalation (OR 2.11, 95% CI: 1.17–3.79), current allopurinol dosage (>100 mg/day) (OR 2.02, 95% CI: 1.11–3.65), and allopurinol adherence (OR 13.6, 95% CI: 6.52–28.39).**Conclusions:** Among patients with gout receiving allopurinol in our study, 70.8% did not reach the SUA goal and 56.6% of patients were non-adherent. Allopurinol adherence was strongly associated with SUA goal attainment. The only modifiable factor associated with allopurinol adherence was prescriber specialty, whereas, modifiable factors associated with SUA goal attainment were prescriber specialty, allopurinol dose escalation, and current allopurinol dosage. Appropriate dose escalation and rheumatology referral could be important factors to consider in efforts aimed at optimising gout treatment outcomes.**Disclosure of Interest:** None declared

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SAT0372

### INCREASED CAROTID INTIMA-MEDIA THICKNESS IN HYPERURICEMIC INDIVIDUALS MAY BE EXPLAINED BY HYPERHOMOCYSTEINEMIA ASSOCIATED WITH RENAL DYSFUNCTION

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**Background:** Both hyperuricemia and hyperhomocysteinemia are known to be associated with the deterioration of vascular endothelial function and are regarded as important risk factors for atherosclerotic vascular diseases. However, there has been no report about the relationship between homocysteine (Hcy) and atherosclerosis in patients with hyperuricemia.

**Objectives:** In this study, we evaluated the relationship between the carotid IMT and various clinical parameters including renal function and serum Hcy level in patients with hyperuricemia, and investigated the possible mechanism of how hyperuricemia is related with the increase of carotid IMT.

**Methods:** A total of 1228 subjects who visited the health promotion centre of hospital were enrolled in this study. All subjects completed both carotid ultrasonography and laboratory measurement, including serum Hcy levels and renal function. Serum Hcy levels were measured by a competitive immunoassay using direct chemiluminescent. Carotid IMT was evaluated by B-mode carotid ultrasonography.

**Results:** Hyperuricemic patients showed higher carotid IMT values compared with normouricemic patients (1.12±0.64 mm vs. 1.02±0.50 mm, p=0.043). The serum Hcy levels were significantly higher in the hyperuricemic group than in the normouricemic group (13.39±4.42 µmol/L vs. 11.69±3.65 µmol/L, p<0.001). In patients with hyperuricemia, serum uric acid levels were negatively correlated with estimated glomerular filtration rates (eGFR) ( $\gamma=-0.334$ , p<0.001), and eGFR were negatively correlated with serum Hcy levels ( $\gamma=-0.490$ , p<0.001). Carotid IMT was correlated with serum Hcy levels ( $\gamma=0.196$ , p=0.008), and atherosclerotic changes of carotid artery measured by carotid ultrasonography increased 1.09-fold (OR, 95% CI 1.006–1.185, p=0.036) per 1 µmol/L difference in serum homocysteine levels. In multivariate linear regression analysis, carotid IMT was affected by reduced eGFR ( $\beta=-0.263$ , p=0.002).

**Conclusions:** Carotid IMT was higher in patients with hyperuricemia than in normouricemic individuals. This study suggests that impairment of the renal function in patients with hyperuricemia may induce the increase in carotid IMT via increased serum Hcy levels.

**Disclosure of Interest:** None declared

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SAT0373

### PREVENTING A LARGE MAJORITY OF INCIDENT GOUT CASES BY MODIFYING KEY RISK FACTORS: FINDINGS FROM A PROSPECTIVE COHORT OF 44,629 MEN OVER 26 YEARS

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**Background:** Many modifiable risk factors have been found to be independently associated with the risk of developing gout, including dietary factors (e.g., intakes of red meat and fructose), adiposity, alcohol intake, and diuretic use. Conversely, healthy dietary patterns (e.g., Dietary Approaches to Stop Hypertension [DASH]) and a high intake of vitamin C have been shown to be independently associated with lower gout risk. However, the potential combined impact of these factors on the risk of developing gout is unknown.

**Objectives:** We aimed to estimate the proportion of incident gout cases that could theoretically be avoided through the simultaneous adoption of multiple low-risk behaviours, including low body mass index (BMI), consumption of a DASH-style eating pattern, no alcohol intake, vitamin C supplementation, and no diuretic use.

**Methods:** From 1986 to 2012, we prospectively followed 44 629 men free from gout at baseline in the Health Professionals Follow-up Study. Lifestyle, anthropometric, and medical information was collected at baseline and updated biennially. Dietary data were obtained using validated food frequency questionnaires at baseline and approximately every 4 years during follow-up. We ascertained incident cases of gout using the American College of Rheumatology survey criteria for gout. We defined low-risk groups according to combinations of the following

five factors: a low BMI (<25 kg/m<sup>2</sup>), adherence to a DASH-style diet, no alcohol intake, vitamin C supplementation ( $\geq 1500$  mg), and no diuretic use. Cox proportional hazard regression models were used to estimate the association of each risk factor with the development of gout and calculate the population attributable risk percent (PAR%).

**Results:** During 9 50 086 person-years of follow-up, incident gout developed in 1687 participants. All five modifiable risk factors were independently associated with incident gout. Obesity was the single most important predictor of gout; all other risk factors were also associated with a statistically significant increased risk of gout, even after adjustment for BMI. As compared with the rest of the cohort, men in the low-risk group (comprised of all five low-risk factors; 4.4% of men) had a relative risk of gout of 0.30 (95% confidence interval [CI], 0.12 to 0.72) (table 1). Accordingly, the PAR% for all five risk factors combined was 70% (table 1). The PAR% for four and three risk factors was 64% and 50%, respectively (table 1).

**Abstract SAT0373 – Table 1.** Relative and Population Attributable Risks of Gout for Groups Defined by Combinations of Modifiable Risk Factors

	Percentage of Men (%)	Number of Gout Cases	Relative Risk (95% CI)	PAR%
3 factors in low-risk category <sup>a</sup>	11.0	24	0.49 (0.33, 0.74)	50
4 factors in low-risk category <sup>b</sup>	10.3	15	0.35 (0.21, 0.59)	64
5 factors in low-risk category <sup>c</sup>	4.4	5	0.30 (0.12, 0.72)	70

Abbreviations: BMI, body mass index. CI, confidence interval. DASH, Dietary Approaches to Stop Hypertension. PAR%, Population attributable risk percent.

Relative risks were adjusted for total energy intake, coffee intake, and histories of renal failure and hypertension.

<sup>a</sup>Low BMI, highest quintile of DASH diet score, and no alcohol intake.

<sup>b</sup>Low BMI, highest quintile of DASH diet score, no alcohol intake, and no diuretic use.

<sup>c</sup>Low BMI, highest quintile of DASH diet score, no alcohol intake, no diuretic use, and vitamin C supplementation.

**Conclusions:** Five modifiable risk factors accounted for 70% of incident gout cases in this large prospective cohort of male health professionals. Assuming a causal relation, our findings support the hypothesis that the vast majority of cases of gout could be prevented by modifying key risk factors.

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**Disclosure of Interest:** None declared

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SAT0374

### LESINURAD (LESU) ADJUNCTIVE THERAPY WITH ALLOPURINOL (ALLO) IN PATIENTS NOT RESPONDING TO ALLO MONOTHERAPY: POOLED POST HOC SAFETY AND EFFICACY ANALYSIS IN A PATIENT SUBGROUP USING CONCOMITANT DIURETICS AT SUBLINE (BL)

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**Background:** LESU is approved as adjunctive therapy in combination with xanthine oxidase inhibitors (XOI) for gout PT not responding to XOI alone<sup>1</sup>. Gout PT often have hypertension (HT) for which diuretics especially thiazide and thiazide-like diuretics (TTLD) are prescribed. TTLD contributes to hyperuricemia<sup>2</sup> by acting on OAT4 transporter, which is inhibited by LESU.

**Objectives:** To assess the efficacy and safety of LESU+ALLO in the subgroup of PT using concomitant diuretics at BL in CLEAR 1 and CLEAR 2, two randomised, double-blind, placebo-controlled Phase 3 studies that evaluated LESU200/400 mg daily in combination with ALLO vs ALLO+placebo.<sup>3&4</sup>

**Methods:** Data from both trials of 1,213 PT, was pooled and PT group using diuretics at baseline was compared to non-users with respect to sUA target and TEAE.

**Results:** Totally 221 PT received diuretics, >90% due to HT and ~80% being TTLD. In both groups, LESU +ALLO doubled the number of PT reaching sUA target of <6.0 mg/dL vs ALLO +PBO at month 6 (m-6) and 12 (m-12) (table 1). At m-12, the response rate in PT receiving TTLD was 60.8%, 61.5% in the LESU 200 and 400 mg group, and 26.6% in the ALLO alone group, and 47.5%, 50.5%, and 25.7% in PT not receiving TTLD respectively. The safety profile was comparable

except for transient and reversible serum creatinine elevations in the LESU groups. (table 1).

Abstract SAT0374 – Table 1

Variable	Group receiving Diuretics			Group not receiving Diuretics		
	PBO	LESU	LESU	PBO	LESU	LESU
	+ALLO	200 mg	400 mg	+ALLO	200 mg	400 mg
	[n=64]	+ALLO	+ALLO	[n=343]	+ALLO	+ALLO
		[n=79]	[n=78]		[n=326]	[n=323]
<b>Efficacy</b> , proportion of PT achieving [number (%)]:						
sUA<6.0 mg/dL at m-6	19 (29.7)	48 (60.8)†	57 (73.1)*	85 (24.8)	174 (53.4)*	195 (60.4)*
sUA<6.0 mg/dL at m-12	17 (26.6)	48 (60.8)*	48 (61.5)*	88 (25.7)	155 (47.5)*	163 (50.5)*
<b>Safety</b> , proportion of PT reporting [number (%)]:						
Any TEAEs	45 (70.3)	62 (78.5)	65 (83.3)	239 (69.7)	237 (72.7)	252 (78.0)
←Serum creatinine by ≥1.5	2 (3.1)	2 (2.5)	11 (14.1)	5 (1.5)	17 (5.2)	47 (14.6)

† p=0.0003, \*p<0.0001 versus PBO+ALLO (Cochran-Mantel Haenszel test)

**Conclusions:** LESU +ALLO doubled the number of PT reaching sUA target of <6.0 mg/dL at m-6 and sustained at m-12, irrespective of TTLD use. Adjunctive therapy with LESU +ALLO is safe and efficacious even in PT subgroups using concomitant TTLD.

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#### SAT0375 IMPACT OF FEBUXOSTAT ON RENAL FUNCTION AMONG GOUT PATIENTS WITH DIFFERENT RENAL FUNCTION

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**Background:** Febuxostat is a new xanthine oxidase inhibitor which is effective in the treatment of hyperuricemia. Its use in people with different levels of renal function has not been thoroughly assessed.

**Objectives:** To assess the risk of renal function deterioration in gout patients using febuxostat and compare it with patients using allopurinol and other uricosuric agents.

**Methods:** We included 5882 adult patients with gout diagnosed between 2012 and 2015. We divided patients into three groups by usage of urate-lowering drugs used (allopurinol, febuxostat and uricosuric agents including benzbromarone, probenecid and sulfipyrazone). The primary outcome was a progress of one chronic kidney disease (CKD) stage. The index date was the first date of urate-lowering drugs used. We follow each patient to the date of event, death, switch to other drug or the end of the study. The Cox proportional hazards model was used to estimate the adjusted hazard ratios (HRs), adjusted for age, sex, baseline eGFR, baseline serum urine acid, comorbidity, co-medication.

**Results:** The incident rate of the renal function deterioration was 2.37 (95% CI, 1.75–3.14) per 1000 person-days in allopurinol users, 1.54 (95% CI, 1.30–1.81) per 1000 person-days in febuxostat users and 1.43 (95% CI, 1.32–1.56) per 1000 person-days in uricosuric agent users. The HRs of progression of CKD stage in febuxostat and uricosuric agent users were 0.98 (95% CI, 0.70–1.38) and 0.80 (95% CI, 0.59–1.09) compared with allopurinol. Among febuxostat users, the HRs were 1.80 (95% CI, 0.85–3.98) in patients with an estimated glomerular filtration rate (eGFR) ≥90 ml/min/1.73 m<sup>2</sup>, 1.06 (95% CI, 0.56–2.03) for patients with an

eGFR 60–89 ml/min/1.73 m<sup>2</sup>, 0.78 (95% CI, 0.45–1.42) for patients with an eGFR 30–59 ml/min/1.73 m<sup>2</sup> and 0.73 (95% CI, 0.22–3.52) for patients with an eGFR 15–29 ml/min/1.73 m<sup>2</sup>. Among uricosuric agent users, the HRs were 0.94 (95% CI, 0.52–1.88) in patients with an eGFR ≥90 ml/min/1.73 m<sup>2</sup>, 0.88 (95% CI, 0.55–1.50) in patients with an eGFR 60–89 ml/min/1.73 m<sup>2</sup>, 0.71 (95% CI, 0.41–1.28) in patients with an eGFR 30–59 ml/min/1.73 m<sup>2</sup> and 0.71 (95% CI, 0.19–3.62) in patients with an eGFR 15–29 ml/min/1.73 m<sup>2</sup>.

**Conclusions:** Renal function deterioration is not uncommon after initiation of urate-lowering treatment and febuxostat has a similar renal safety profile as allo-purinols and uricosuric agents.

**Disclosure of Interest:** None declared

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#### SAT0376 THE INCIDENCE, PREVALENCE AND USE OF URATE LOWERING AGENTS IN HONG KONG: A POPULATION STUDY FROM 2006 TO 2016

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**Background:** The prevalence of gout has increased significantly over the past decade, especially in developed countries and Oceanic populations. The estimated prevalence of gout in the US, Canada and European countries was 3%. Asian countries, except Taiwan, were considered to have a lower prevalence of gout due to differences in ethnicity and lifestyle.

Since there are no recent epidemiological data on gout in Hong Kong, we conducted this population study to determine the incidence and prevalence of gout in Hong Kong as well as the utilisation of urate lowering agents among patients with gout.

**Objectives:** To determine the incidence, prevalence of gout and use of urate lowering agents in Hong Kong

**Methods:** Data were retrieved from the Clinical Data Analysis and Reporting System (CDARS) of the Hospital Authority. The Hospital Authority is the only public healthcare provider in Hong Kong. Since treatment is heavily subsidised and available to all residents, it covers more than 90% of all medical care for the general population in Hong Kong.

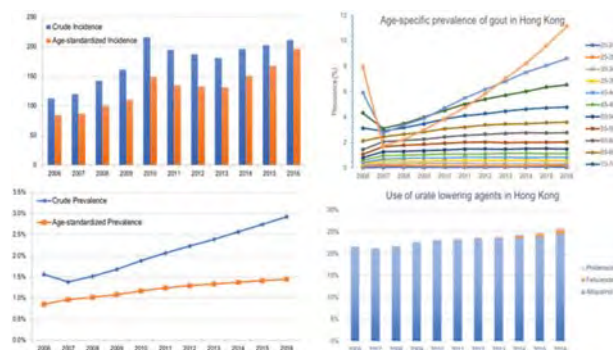
Clinical data including demographic, diagnosis of gout, serum urate levels and prescriptions of urate lowering agents were retrieved from CDARS from 2006 to 2016. For inclusion, subjects must have attended any out-patient clinics or accident and emergency department (with or without hospitalisation) in 2005. Subjects with a diagnosis of gout who died before 2006 were excluded. All subjects were followed until the cut-off date or death.

Gout was defined as the physician diagnosis and coding in CDARS. The serum urate levels achieved after prescribing urate lowering agents were the means of all serum urate levels 6 months after prescriptions.

Results were analysed by R statistics version 3.3.3. with package 'prevalence' version 0.4.0.

**Results:** 2741862 participants were included in the analysis. Both the incidence and prevalence of gout in Hong Kong have increased over the past 10 years. In 2016, the crude and age-standardised prevalence of gout were 2.92% and 1.44%, respectively. 6.26% of the general population aged 80 years or older was diagnosed to have gout.

Despite the increase in incidence and prevalence of gout in Hong Kong, the utilisation of urate lowering agents remained low. In 2016, only 25.55% of patients with gout were prescribed urate lowering agents. More importantly, only 35.8% of those could achieve the therapeutic target of serum urate level <6 mg/dL.



**Conclusions:** Population ageing has led to increases in incidence and prevalence of gout in Hong Kong. In 2016, the crude prevalence of gout in Hong Kong was 2.92%, which is similar to figures reported in western countries. Despite an

increase in prevalence of gout, the utilisation of urate lowering agents remained low. Only 1 in 4 patients with gout were prescribed urate lowering agents.

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SAT0377

#### THE BURDEN OF MONOSODIUM URATE CRYSTALS ASSESSED BY DUAL-ENERGY CT AND ULTRASONOGRAPHY IS NOT CORRELATED TO CARDIOVASCULAR RISK

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**Background:** Gout is associated with higher cardiovascular risk and increases with disease severity. It is not clear if the monosodium urate (MSU) crystal burden is associated with traditional cardiovascular risk factors.

**Objectives:** The objective of this study was to explore the relationship between the extent of MSU deposition assessed with ultrasonography (US) and dual-energy CT (DECT) and cardiovascular risk.

**Methods:** Gout patients naive of urate lowering therapy were included in this cross-sectional study to undergo DECT scans for the assessment of total MSU volume deposition of the knees and feet, and US to evaluate the number of joints with the double contour (DC) sign among the femoro-patellar, talo-crural and first metatarsophalangeal joints. Participants were screened for traditional cardiovascular risk factors and levels of the ACC/AHA 10 year-risk for heart disease or stroke was calculated. The primary endpoint was the Spearman correlation coefficient  $\rho$  between DECT MSU volume and cardiovascular risk.

**Results:** A total of 50 patients predominantly male (46/50) aged 62.6 years ( $\pm 14.1$ ) were included. Participants had gout duration of 9.5 years ( $\pm 11.8$ ), had experienced 4.1 flares ( $\pm 6.3$ ) over the past year, had serum urate (SU) levels of 8.1 mg/dL ( $\pm 2.3$ ), and 35/50 had at least one US tophus of 1.5 cm<sup>3</sup> ( $\pm 1.8$ ). The volume of MSU deposits with DECT was 3.9 cm<sup>3</sup> ( $\pm 11.2$ ) for the feet and 2 cm<sup>3</sup> ( $\pm 4.4$ ) for the knees. Overall, 28 patients presented with the metabolic syndrome. Correlations between DECT volumes of MSU deposits of the knees, feet, and knees+feet were poor with  $\rho$  respectively of 0.23, 0.03 and 0.21. There was no correlation between the number of joints with the DC sign and cardiovascular risk ( $\rho$  of 0) and the correlation was poor with SU levels ( $\rho=0.09$ ). Patients with the metabolic syndrome had similar DECT volume of MSU deposits than those without ( $p=0.29$ ).

**Conclusions:** This study suggests that the association of gout with traditional cardiovascular risk factors is not related to the extent of the monosodium urate crystal burden.

**Disclosure of Interest:** None declared

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SAT0378

#### THE TREND OF TREG AND TH17 CELLS CHANGES IN P2X7R-REGULATED ACUTE GOUTY ARTHRITIS MODEL RATS

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**Background:** ATP may be the second causative signal for the onset of gout, which acts on P2  $\times$  7R to regulate the development of acute gouty arthritis.<sup>1</sup> Both regulatory T cells and Th17 cells are important in the development and progression of inflammatory diseases.<sup>2</sup>

**Objectives:** To investigate the effect of P2  $\times$  7R on Treg and Th17 cells in acute gouty arthritis model of rats and its role in acute gouty arthritis.

**Methods:** Eighty male SD rats were randomly divided into three groups: After establishment of acute gouty arthritis model, rats were given P2  $\times$  7R agonist ATP, P2  $\times$  7R inhibitor BBG and PBS, respectively. The rats were sacrificed at 6 hour, 12 hour, 24 hour, 48 hour and 72 hour after treatment. The spleens of the rats were grinded and the expression of Treg and Th17 cells were detected by flow cytometry. Comparison the levels and the ratio of Treg and Th17 cells at the different time points.

**Results:** (1) The expression levels of Treg and Th17 in the spleen: After treatment at 12 hour, The expression levels of Treg and Th17 in the ATP group were significantly higher than that in the BBG and control groups ( $p=0.001$ ,  $0.021$ ;  $p=0.01$ ,  $0.025$ ); The expression levels of Treg and Th17 in control group were higher than that in BBG group ( $p=0.021$ ,  $0.044$ ); There were no significant differences in the three groups at 72 hour after treatment ( $p=0.052$ ,  $0.116$ ). (2) The expression trend of Treg and Th17 in different time points: the level of Treg was increased at 6 hour, but decreased gradually at 12 h, 24 hour and then increased at 48 hour again; The level of Th17 was increased at 6 hour, 12 h and 24 hour, but decreased gradually at 48 hour, 72 hour. (3) The ratio of Treg/Th17 gradually decreased in the first three time points, increased at 48 hour and 72 hour in three groups. The ratio of Treg/Th17 in ATP group was lower than that in BBG group and control group at 12 hour, with significant difference ( $p<0.05$ ). But at other four time points, the ratios were no significant differences among the three groups.

**Conclusions:** Activation of P2  $\times$  7R decreased the ratio of Treg/Th17 in acute gouty arthritis rat model that showed an acute change trend along with the time, suggesting that P2  $\times$  7R-regulated the ratio of Treg/Th17 cells affected acute gouty arthritis.

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SAT0379

#### VACUUM-ASSISTED CLOSURE VERSUS CONVENTIONAL WOUND CARE IN THE MANAGEMENT OF CHRONIC ULCERS IN PATIENTS WITH TOPHACEOUS GOUT: A PROSPECTIVE ANALYSIS

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**Background:** With the rising epidemic of gout, an increasing number of patients suffer from chronic ulcers associated with tophaceous gout in China, causing poor quality of life and disability. Such ulcers are very difficult conditions to deal with. Vacuum-assisted closure (VAC) has been proved to be effective in treating a variety kinds of wounds such as diabetic foot ulcers. However, its use in chronic ulcers associated with tophaceous gout has seldom reported.

**Objectives:** In the present study, we evaluated the use of VAC in the treatment of chronic ulcers associated with tophaceous gout in comparison to conventional wound care (CWC).

**Methods:** We performed a 12 week prospective study that included 13 patients treated with VAC and 14 patients treated with CWC. We collected the clinical outcomes of these patients and data from a satisfaction survey. Chronic ulcers were treated until wound closure, or until the end of 12 weeks. Study will discontinue when the ulcer worsens or remains unchanged by the end of week 4.

**Results:** Granulation tissue appeared in 12 (92.31%) patients by the end of week 2 in the VAC group, while it appeared in 6 (42.86%) patients by that time in the CWC group ( $p=0.013$ ). 100% granulation was achieved in 11 (84.62%) patients by the end of week 8 in the VAC group as compared to 5 (35.71%) patients by that time in the CWC group ( $p=0.018$ ). By the end of week 12, decreasing in wound size was achieved in 12 (92.31%) patients in the VAC group, while it was achieved in 10 (71.43%) patients in the CWC group ( $p=0.326$ ). Among them, wound closure was achieved in 9 (69.23%) patients in the VAC group, while it was achieved in 3 (21.43%) patients in the CWC group ( $p=0.021$ ). None developed local infection in both groups during the treatment. More patients in the VAC group were satisfied with treatment as compared to the CWC group.



SATURDAY, 16 JUNE 2018

## Infection-related rheumatic diseases

SAT0380

## PANLAR-ACCAR RECOMMENDATIONS ON DIAGNOSIS AND TREATMENT OF CHIKUNGUNYA-RELATED INFLAMMATORY ARTHROPATHIES IN LATIN AMERICA

P. Monge<sup>1</sup> on behalf of PANLAR-ACCAR Consensus Group in Chikungunya in Latin America, A.M. Sapag<sup>2</sup>, I.Y. Moreno<sup>3</sup>, R.A. Montúfar<sup>4</sup>, V. Khoury<sup>5</sup>, P. Camilo<sup>5</sup>, R.E. Rivera<sup>6</sup>, J.C. Rueda<sup>7</sup>, D. Jaramillo-Arroyave<sup>8</sup>, J. Londoño<sup>9</sup>, M.C. Ruiz<sup>10</sup>, F. Fernández-Castillo<sup>11</sup>, M. Quintero<sup>12</sup>, Y. Fuentes<sup>13</sup>, J.L. Aguilar<sup>14</sup>, C. V. Caballero-Urbe<sup>15</sup>, H. Sandoval<sup>16</sup>, C. Pineda<sup>16</sup> on behalf of Pan-American League of Associations for Rheumatology (PANLAR), in collaboration with the Central American, Caribbean and Andean Rheumatology Association (ACCAR by its Spanish acronym). <sup>1</sup>Asociación Costarricense De Reumatología, San Jose, Costa Rica; <sup>2</sup>Sociedad Boliviana de Reumatología, Santa Cruz, Bolivia, Plurinational State Of; <sup>3</sup>Sociedad Panameña de Reumatología, Panama City, Panama; <sup>4</sup>Asociación Salvadoreña de Reumatología, San Salvador, El Salvador; <sup>5</sup>Sociedad Dominicana de Reumatología, Santiago, Dominican Republic; <sup>6</sup>Asociación Guatemalteca de Reumatología, Guatemala City, Guatemala; <sup>7</sup>Asociación Colombiana de Reumatología, Chia; <sup>8</sup>Asociación Colombiana de Reumatología, Medellín; <sup>9</sup>Asociación Colombiana de Reumatología, Bogotá, Colombia; <sup>10</sup>Sociedad Venezolana de Reumatología, Maracay; <sup>11</sup>Sociedad Venezolana de Reumatología, Barquisimeto; <sup>12</sup>Sociedad Venezolana de Reumatología, Mérida; <sup>13</sup>Sociedad Venezolana de Reumatología, Ciudad Bolívar, Venezuela, Bolivarian Republic Of; <sup>14</sup>Sociedad Peruana de Reumatología, Lima, Peru; <sup>15</sup>Asociación Colombiana de Reumatología, Barranquilla, Colombia; <sup>16</sup>Instituto Nacional de Rehabilitación, México City, Mexico

**Background:** Although mortality rates related with Chikungunya (CHIK) outbreaks into Latin America's endemic-dengue rural and new urban regions are low, dealing with symptoms and sequelae can produce both a significant burden of disease and diminish quality of life — from many months to years — after the acute phase of infection, with a significant impact on public and individual health.

**Objectives:** The aim of this work was to establish a PANLAR-ACCAR consensus on diagnosis and treatment of CHIK-related inflammatory arthropathies transmitted by *Ae. Aegypti* and *Ae. Albopictus* in Latin America (LA).

**Methods:** Based on the Consensus Development Conference format, a panel of ACCAR rheumatologists (n=10) took part in this PANLAR initiative. Experts voted recommendations from a previous content analysis of the medical literature on CHIK, four subsequent topic's Conferences and a workshop. Consensus represents the majority agreement (≥80%) achieved for each recommendation.

**Results:** The panel reach four overarching principles: 1) CHIK virus (CHIKV) is a re-emergent virus transmitted by two species of mosquitoes: *Ae. Aegypti* and *Ae. Albopictus*; 2) CHIKV caused massive outbreaks in LA; 3) Chronic CHIKV infection produces an inflammatory joint disease that in some cases can last several months to years, and 4) Currently, there are no vaccines or antivirals available for CHIKV infections.

**Conclusions:** PANLAR-ACCAR achieve 13 recommendations on CHIK categorised in three groups: 1) epidemiology and clinical manifestations; 2) diagnosis, and 3) treatment, representing the consensus agreement from the panel's members.

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**Disclosure of Interest:** None declared

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Figure 1. A 57-years old man, who suffered from ulcers associated with tophaceous gout for around 3 months, was successfully treated with VAC therapy.

**Abstract SAT0379 – Figure 1.** A 57-years old man, who suffered from ulcers associated with tophaceous gout for around 3 months, was successfully treated with VAC therapy.



Figure 2. A 35-years old man, who suffered from ulcers associated with tophaceous gout for around 6 months, was successfully treated with VAC therapy.

**Abstract SAT0379 – Figure 2.** A 35-years old man, who suffered from ulcers associated with tophaceous gout for around 6 months, was successfully treated with VAC therapy.

**Conclusions:** Our preliminary study suggests that VAC therapy is effective and safe in treating chronic ulcers associated with tophaceous gout and appears to be superior to CWC therapy. Large-scale studies are needed to further evaluate the efficacy and safety of the VAC therapy in the treatment of chronic ulcers associated with tophaceous gout.

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SAT0381

### NEUTROPHIL-RELATED BIOMARKERS DISCRIMINATE SEPTIC ARTHRITIS FROM OTHER INFLAMMATORY ARTHRITIDES: DATA FROM THE BOSSA TRIAL

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**Background:** Septic arthritis is a life threatening purulent invasion of a joint by an infectious agent which produces arthritis. If untreated, septic arthritis causes structural damage to the joint. Unfortunately no relevant biomarkers are available for the diagnosis of this disabling condition. We aimed at determining whether calprotectin (S100A8/A9) and Human neutrophil alpha-defensins (HNP1-3) could discriminate septic from other inflammatory arthritides

**Objectives:** We aimed at determining whether calprotectin (S100A8/A9) and Human neutrophil alpha-defensins (HNP1-3) could discriminate septic from other inflammatory arthritides

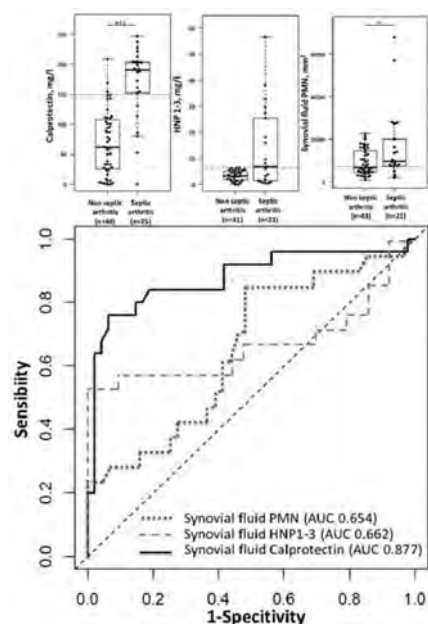
**Methods:** Patients joint effusions for which septic arthritis was suspected were prospectively collected in Grenoble Hospital. Patients with inflammatory synovial fluid (*i.e.* with white blood cell >2000/mm<sup>3</sup> and >80% polymorphonuclear neutrophils (PMN)) were included in this trial. Diagnosis of septic arthritis was retained if bacteria were cultured from inflammatory synovial fluid and/or blood samples. Diagnosis of pseudo gout was retained when pyrophosphate calcium crystals were observed in inflammatory synovial fluid. Diagnosis of rheumatoid arthritis was retained according to rheumatologist opinion.

C Reactive protein (CRP), both neutrophil-related proteins calprotectin and human neutrophil alpha-defensins (HNP1-3) levels were assessed in synovial fluids.

Threshold for biomarkers were determined by ROC curve analysis. Sensibility, Specificity, Positive (PPV) and Negative (NPV) Predictive Values at a pre specified threshold were calculated. Biomarkers with  $p \leq 0.05$  were included into a multivariate model. Multivariate logistic regression with stepwise selection was performed to build the final combined model.

**Results:** A total of 74 patients were included: septic arthritis (n=26), pseudo gout (n=28) and Rheumatoid arthritis (n=20). Patients with septic arthritis group were more likely to be male (69% vs. 31%,  $p=0.030$ ), were younger (median age (range) 65.5 (27-84) vs. 72.5 (33-91),  $p=0.047$ ), displayed higher synovial fluid PMN count (9,600 (1,800-68000) vs. 6560 (750-22500,  $p=0.047$ ), LR+12.2 and LR- 0.26.

Calprotectin was significantly increased in patients with septic arthritis (190 (0.1-247) vs. 62 (0-208) mg/L,  $p<0.001$ , figure 1) whereas only a trend of an HNP1-3 rise was shown in arthritis septic (6.8 (0.5-56.6) vs. 3.4 (0.1-6.4) mg/L,  $p=0.050$ ). Optimal Thresholds for calprotectin, HNP1-3, and synovial fluid PMN were respectively 150 mg/L, 6.5 mg/L and 7000/mm<sup>3</sup>.



In the multivariate model, including calprotectin, HNP1-3, synovial fluid PMN count and gender, calprotectin was the only biomarker discriminating septic arthritis from non-septic inflammatory arthritides with 76% sensitivity, 94% specificity, 86% PPV and 88% NPV.

**Conclusions:** Our data show here that synovial fluid calprotectin is a relevant biomarker to discriminate septic arthritis from other inflammatory arthritides. This biomarker should be tested in an independent cohort.

**Acknowledgements:** The authors thank Sylvie Papacatzis for her help in the study.

**Disclosure of Interest:** None declared

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SAT0382

### UTILITY OF NEUTROPHIL CD64 & SERUM TREM-1 IN DISTINGUISHING BACTERIAL INFECTION FROM DISEASE FLARE IN SLE AND ANCA ASSOCIATED VASCULITIS

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**Background:** Treating physician is challenged to differentiate between disease activity vs. infection as to the cause of fever in patients with SLE and ANCA associated vasculitis (AAV). Presently, there is no biomarker to reliably differentiate between them.

**Objectives:** We aimed to determine the usefulness of CD64 (FcγR1) expression on neutrophils and sTREM-1 (soluble triggering receptor expressed on myeloid cells) in serum in distinguishing bacterial infection from disease flare in SLE and AAV.

**Methods:** 20 healthy controls and patients of SLE and AAV admitted to our unit either with disease flare or bacterial infection were recruited over a period of 1 year. Neutrophil CD64 expression was measured by flow cytometry and sTREM-1 by ELISA from blood samples collected on the day of admission.

**Results:** Among the 76 patients included in the study 51 (SLE-35 and AAV-16) had disease flare while 25 (SLE-21 and AAV-4) had infection. 72% had fever at presentation. The percentage of neutrophils with CD64 expression and their mean fluorescence intensity in patients with infection were significantly ( $p<0.05$ ) higher as compared to those without infection and controls (Table-1). The sensitivity and specificity of CD64 expression on neutrophils to diagnose bacterial infection (using a cut off value of 30%) was 85% and 84%, respectively. Whereas, the sensitivity and specificity of procalcitonin was 75% and 85% respectively. There was no significant difference in soluble TREM-1 levels between the two groups. Total leucocyte count (TLC), ESR, CRP, C3, C4 levels were not significantly different between disease flare and infection group. On subgroup analysis (Table-2) patients of SLE with infection had a higher CRP, TLC and Procalcitonin compared to those with disease flare ( $p<0.5$ ). ROC curves are depicted in figure 1.

**Table-1-** Comparison of various parameters between healthy controls, patients with active disease and infection

Characteristic	Active disease (n=51)	Infection (n=25)	Healthy controls (n=20)
CD64 expression on neutrophils (%)	7.7 (2.6-13)	68.8 (56.9-86.5)*	7.05 (1.4-9.5)
Mean fluorescence intensity of CD64	456 (20-986)	1037 (229-1828)*	99.5 (54.7-140.7)
sTREM-1 (pg/ml)	1184 (717-1609)**	899 (531-1284)**	255.1 (95.1-634.8)
Procalcitonin (pg/ml)	157.7 (115.1-209.3)**	301 (141.8-339.3)*	77.6 (61-101.8)
Total leucocyte count (cells/mm <sup>3</sup> )	9700 (4600-12400)	10750 (6000-15000)	-
CRP (mg/L)	1.9 (0.86-6.05)	5.4 (1.83-8.9)	-
ESR (mm/hr)	70 (30-103)	75 (55-110)	-

\* $p<0.05$  vs. active disease group and healthy controls

\*\* $p<0.05$  vs. healthy controls

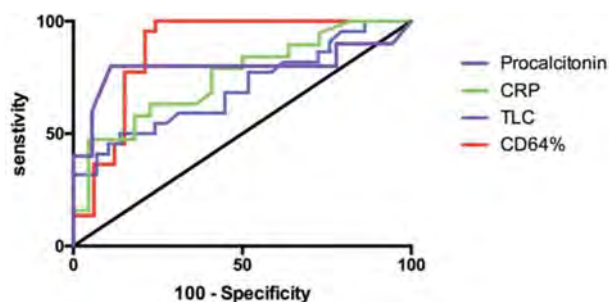
All values expressed as median (25th-75th Interquartile range)

**Abstract SAT0382 – Table 2.** Subgroup analysis of patients with SLE and ANCA associated vasculitis

Variable	SLE with active disease (n=35)	SLE with Infection (n=21)	AAV with active disease (n=16)	AAV with infection (n=4)
CRP (mg/dl)	1.3 (0.39-2.3)	5.54 (1.8-9.2)*	7.3 (2.64-10.5)	11.7 (2.08-20.85)
TLC (cells/mm <sup>3</sup> )	6400(3400-9500)	11 000(5925-16650)*	12 200(10550-20400)	12 000(10,300-20100)
nCD64 (%)	9.42 (3-13.7)	69.4 (59-87.1)*	4.25 (2.27-8.5)	76 (42.5-80.9)
Procalcitonin (pg/ml)	174 (101-204)	316 (231-345)*	172 (127-257)	104 (86-356)

\* $p<0.05$  vs. SLE with disease flare

All values expressed as median (25th-75th Interquartile range)



Abstract SAT0382 – Figure 1. ROC analysis of various parameters in patients with underlying SLE

**Conclusions:** CD64 expression on neutrophils is helpful in differentiating bacterial infection from disease flare in patients with SLE and AAV.

**Disclosure of Interest:** None declared

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### SAT0383 RHEUMATOLOGICAL DISORDERS FOLLOWING CHIKUNGUNYA INFECTION – A RETROSPECTIVE STUDY OF 882 CASES FROM NEW DELHI

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**Background:** Chikungunya virus (CHIKV) is notoriously arthritogenic and is known to cause a wide spectrum of rheumatological disorders.

**Objectives:** To study the Rheumatological Manifestations of CHIKV Infection.

**Methods:** Record of 1641 consecutive patients who presented to the outpatient department (OPD) with history of chikungunya infection (fever, joint pains±rash) during the period of 1 st July 2016 to 31 st October 2016 were checked and recruited from private hospital, camps and clinic from urban and suburban population from 1 st February to 31 st December 2017. The study cohort was subjected to laboratory tests – serum IgM, IgG and RT-PCR for chikungunya virus. Those patients who tested positive for  $\geq 1$  lab tests were included in the study. Of the 1641 patients, 408 patients either refused the lab tests or were lost to follow up. Of the remaining 1233 patients, 882 (71.53%) patients tested positive for  $\geq 1$  lab tests and 351 (28.47%) tested negative for all the 3 lab tests. These patients were classified into rheumatological disorders as per validated criteria.

**Results:** We studied 882 consecutive patients of chikungunya infection with some rheumatological manifestations. Mean age of study cohort was 53.64  $\pm$  15.82 years with male:female of 398 (45.12%):484(54.88%). Mean disease duration of post CHIKV infection was 08.45 $\pm$ 3.64 months. Serologically, isolated serum IgM CHIKV was positive in 128 (14.51%) patients, IgG CHIKV in 340 (38.54%) patients and RT-PCR CHIKV in 223 (25.28%) patients. Combination of serum IgG and IgM CHIKV both were positive in 62 (7.03%), IgM and RT-PCR CHIKV 49 (5.55%) and IgG and RT-PCR CHIKV in 40 (4.54%) patients. All the 3 serum IgM, IgG and RT-PCR CHIKV were positive in 50 (5.67%) patients.

Of these 882 patients, 143 (16.21%) patients had rheumatological disorder prior to CHIKV infection which flared up after the infection. Of the 143 patients, 69 (48.25%) had osteoarthritis (OA) knee, 29 (20.27%) had mechanical low back ache, 12 (8.39%) cervical spondylitis, 10 (6.99%) had rheumatoid arthritis (RA), 7 (4.89%) each adhesive capsulitis and ankylosing spondylitis (AS), 3 (2.1%) psoriatic arthritis (PsA), 2 (1.4%) each had SLE, dequervian tenosynovitis and granulomatous with polyangitis.

Remaining 739 patients presented with various rheumatological disorders, most common of which was post chikungunya polyarthralgias in 568 (76.86%) patients. Of the 739 patients, 40 (5.4%) patients developed new onset OA knee, 38 (5.14%) met ACR/EULAR 2010 criteria for RA, 28 (3.78%) met modified New York criteria for AS, 29 (3.92%) developed undifferentiated arthritis, 17 (2.3%) patients developed various enthesitis and tenosynovitis, 1 (0.14%) patients fulfilled ACR 1997/SLICC 2012 criteria for SLE, 20 (2.7%) patients fulfilled ACR 2010 criteria for fibromyalgia, 5 (0.67%) patients fulfilled CASPAR criteria for PsA, 3 (0.4%) patients fulfilled 2015 classification criteria for Gout.

Family history of RA was present in 4 (10.52%) patients and AS in 9 (32.1%) patients. Co-morbidities as hypothyroid were present in 132 (17.86%) patients, hypertension in 88 (11.90%) and diabetes mellitus in 168 (22.73%) patients. Limitation of study – This study was not community based and only those patients who had persistent symptoms were recruited. Those patients whose symptoms of CHIKV infection subsided were not included.

**Conclusions:** CHIKV is a worldwide epidemic which precipitates chronic inflammatory rheumatological diseases.

**Acknowledgements:** Nil

**Disclosure of Interest:** None declared

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### SAT0384 EVOLVING PATTERNS OF REACTIVE ARTHRITIS

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**Background:** Reactive arthritis (ReA) seen by rheumatologists may be changing in frequency (less common) and severity (less than full triad of symptoms and less chronic ReA). Epidemiologic changes in ReA could be due to less food borne illness, cleaner water, and possibly more rapid treatment of sexually transmitted diseases or for other unknown reasons.

**Objectives:** To understand rheumatologists' perspectives about changes in frequency, severity, and manifestations of ReA.

**Methods:** After obtaining ethics approval, 548 members of the Canadian Rheumatology Association (CRA) were surveyed via email with a reminder email. There were 6 groups of questions: demographic information, views from respondents regarding the prevalence of ReA (including acute, recurrent, and chronic), tests ordered to investigate suspected ReA, treatments prescribed for ReA, causes of ReA in their practices, and perspectives on changes in the incidence, severity and causes of ReA over time. Descriptive statistics were used to analyse the data. Results were by physician report and were not confirmed by chart audits.

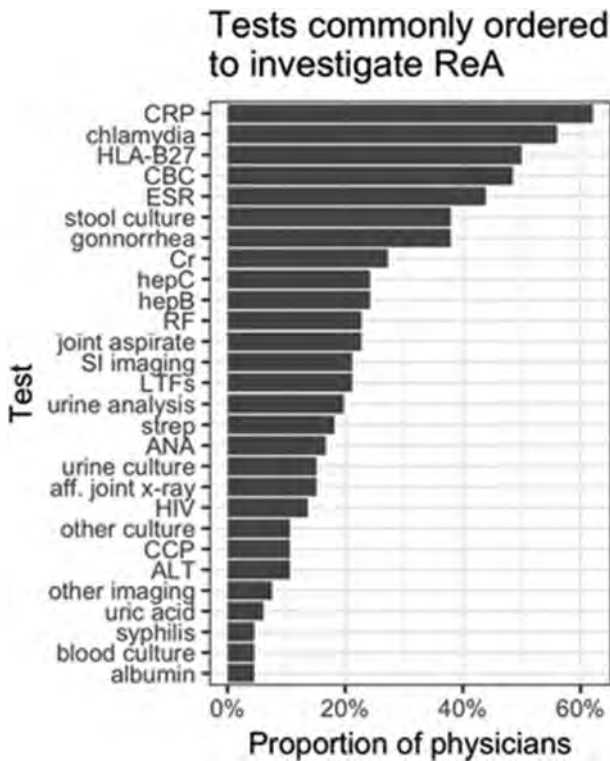
**Results:** Sixty-six rheumatologists completed the survey (15.5% response rate). The results of the survey indicated that 47% of rheumatologists believed that the incidence of ReA is declining, compared to 6% who thought it was increasing; and that the common causes may be changing (39% agreed/strongly agreed with a mean 3.4/5 on the Likert scale).

Acute, chronic, and recurrent ReA were all perceived to have similar frequencies in their practices. In terms of presentation, asymmetric oligoarthritis occurred in the majority of ReA seen by those surveyed (78%). Full triad ReA (arthritis, conjunctivitis, urethritis) was thought to occur in 21% of ReA cases, and patients with conjunctivitis were very likely to exhibit the rest of the triad. Similarly, patients with recurrent ReA were more likely to exhibit the full triad (43%) compared to acute or chronic ReA (14%). Rheumatologists believed that the infectious cause of ReA was found in only 35% of cases. The data indicate that the most common cause of ReA was 'unknown' infectious organisms, followed by gastrointestinal (GI) infections and sexually transmitted infections (STIs).

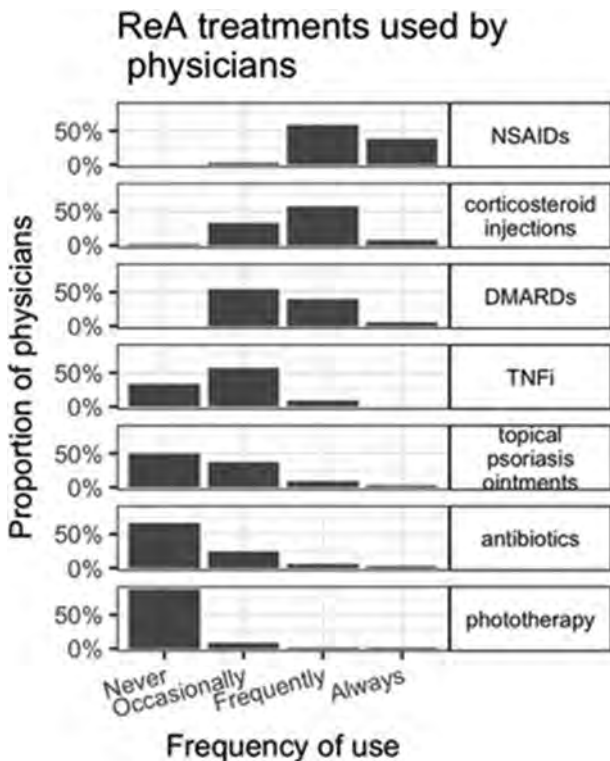
Multiple tests were ordered to investigate ReA. The three most common investigations ordered by respondents included testing for chlamydia (66%), C-reactive protein (CRP) (62%), and human leukocyte antigen (HLA-B27) (50%). Imaging was ordered by 39% of respondents with sacroiliac (SI) joint imaging ordered by 21%, X-rays of the affected joints by 15%, and other imaging by 7.5%. Figure 1 shows these results.

Treatments used for ReA varied, as shown in figure 2. The most common treatments for ReA were nonsteroidal anti-inflammatory drugs (NSAIDs) (97% frequently or always used), intra-articular corticosteroid injections (65% frequently or always used), and disease-modifying antirheumatic drugs (DMARDs) (45% frequently or always used). Sixty-six percent said they used tumour necrosis factor alpha inhibitors (TNFi) at least occasionally in chronic ReA.





Abstract SAT0384 – Figure 1



Abstract SAT0384 – Figure 2

**Conclusions:** Respondents tended to believe that ReA may be decreasing and the causes may be changing. In most cases the causative organism was thought to be unknown followed by GI and STIs. Interestingly, full triad ReA was thought to be linked with recurrent ReA. The results suggest several avenues for exploring clinical and epidemiological relationships in ReA.

**Disclosure of Interest:** None declared

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**SAT0385** **MULTIPLE INFECTION IS INDEPENDENTLY RELATED TO DEATH IN ADULT PATIENTS WITH HEMOPHAGOCYTIC SYNDROME: ETIOPATHOGENICALLY-DRIVEN MULTIVARIATE ANALYSIS IN 151 PATIENTS**

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**Objectives:** To characterise the etiologies and clinical features at diagnosis of patients with hemophagocytic lymphohistiocytosis (HLH) and correlate these baseline features with survival using an etiopathogenically-guided multivariate model.

**Methods:** The HLH Study Group of the Spanish Group of Autoimmune Diseases (GEAS) was formed in 2013 with the aim of collecting a large series of Spanish adult patients with HLH with substantial experience in the management of patients with systemic diseases. By October 2017, the database included 151 consecutive patients who fulfilled at least 5 of the 8 criteria proposed by the Histiocytosis Society in 2004.

**Results:** The cohort consisted of 151 patients (91 male, mean age 51.4 years). After a mean follow-up of 17 months, 80 (53%) patients died. With respect to the HLH-dependent variables, adenopathies (HR 0.63, p=0.040), low platelets (HR 3.39, p=0.008), leukopenia (HR 1.81, p=0.047), severe hyponatremia (HR 1.61, p=0.042), disseminated intravascular coagulation (HR 1.87, p=0.034), bacterial infection (HR 1.99, p=0.025), mixed microbiological infections (HR 3.42, p=0.008) and >1 infectious trigger (HR 2.95, p=0.003) were associated with death. Time-to-event analyses for death identified a worse survival curve for patients with neoplasia (p<0.001), mixed microbiological (p=0.019) and >1 (p=0.011) infections and glucocorticoid monotherapy (p=0.021). After adjusting for confounding variables, platelets<100,000/mm<sup>3</sup> (HR 2.64), severe hyponatremia (HR 1.88), >1 infectious trigger (HR 3.43) and mixed microbiological infection (HR 2.96) remained significant. Multivariate Cox proportional hazards regression analysis identified >1 infectious trigger (HR 2.60, 95% CI 1.16 to 5.84) as the only variable independently associated with death.

**Conclusions:** The mortality rate of adult patients diagnosed with HLH exceeds 50%. Infection with >1 microbiological agent was the only independent variable associated with mortality irrespective of the underlying disease, epidemiological profile, clinical presentation and therapeutic management.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.4112

**SAT0386** **ADJUDICATION OF INFECTIONS FROM THE PHARMACOVIGILANCE IN JUVENILE IDIOPATHIC ARTHRITIS PATIENTS (PHARMACHILD) TREATED WITH BIOLOGIC AGENTS AND/OR METHOTREXATE: UPDATE ON RESULTS WITH A FOCUS ON OPPORTUNISTIC INFECTIONS**

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**Background:** Pharmachild is a pharmacovigilance registry on children with JIA treated mainly with biologics±methotrexate (MTX). Little evidence exists in literature about the role of JIA or its immunosuppressive therapy in determining infections, especially caused by opportunistic pathogens.

**Objectives:** To provide an update on opportunistic infections (OI) revised by an independent Safety Adjudication Committee (SAC) (3 paediatric rheumatologists and 2 paediatric infectious disease specialists).

**Methods:** The participating centres were asked to report all infections encountered by their JIA patients. PRINTO and the medical monitor (MM) classified events based on MedDRA dictionary. Moderate/serious/severe/very severe infections were then revised blindly by the SAC, who was asked to answer 6 questions. The events with consensus of at least 3/5 experts on the first 3 questions ('Is this an infection?', 'Is it common?', 'Is it opportunistic?') were retained for the analysis. With referral to the recommendations by Withrop *et al.*<sup>1</sup>, for the first time a list of OIs in children with JIA on immunosuppressive therapy was elaborated and approved by consensus, through three Delphi steps. Finally, we compared the OI list defined by the SAC to the list of OI approved by the specialists.

**Results:** A total of 772 safety events related to 634 patients were submitted to the SAC. 689 (89.2%) events received consensus among the experts on the 3 questions and, of these, 682 (99.0%) were considered as infections, corresponding to 153 different Preferred Terms (PT), according to MedDRA dictionary. Among the 682 infections, 603 (88.4%) were defined by the experts as common and 119 (17.4%) as opportunistic. For 92 (60%) of the 153 PT, the MM and SAC used the same PT, while the remaining 40% was adjudicated by a third examiner, who analysed again the case reports and assigned the PT which was the most appropriate taking into account the experts' opinion. Among the final number of infections emerged that herpes viral, respiratory and EBV infections were the most frequent (Table). Analysing the infections by PT (n=149), the experts adjudicated: 22 as OI, 119 as not OI, 8 discordant. Comparing the experts' adjudication with the approved list of OI by PT, there was full agreement for the 22 PT classified as OI, while 19/117 (16.2%) PT resulted in the list, but were not classified as OI by the experts.

Abstract SAT0386 – Table 1. The most frequent HLT for the 682 infections with agreement of at least 3/5 experts on the first questions. (N: number of infections)

HLT	N	%
Herpes viral infections	265	38.9
Lower respiratory tract and lung infections	49	7.2
Upper respiratory tract infections	44	6.5
Epstein-Barr viral infections	38	5.6
Abdominal and gastrointestinal infections	32	4.7
Tuberculous infections	29	4.3
Bacterial infections NEC	27	4
Infections NEC	19	2.8
Ear infections	18	2.6
Candida infections	17	2.5
Influenza viral infections	14	2.1
Streptococcal infections	14	2.1
Salmonella infections	9	1.3
Urinary tract infections	9	1.3
Cytomegaloviral infections	8	1.2
Molluscum contagiosum viral infections	7	1
Papilloma viral infections	7	1
Sepsis, bacteraemia, viraemia and fungaemia	7	1
Campylobacter infections	5	0.7
Staphylococcal infections	5	0.7
Viral infections NEC	5	0.7
Escherichia infections	4	0.6
Pneumocystis infections	4	0.6
Skin structures and soft tissue infections	4	0.6

**Conclusions:** Our analysis showed a significant number of OI in JIA patients on immunosuppressants and provided an approved document stating the most frequent OI in children with JIA. The most frequent opportunistic pathogens resulted herpes virus, excluding varicella, and mycobacteria, but the list of definite and probable OIs needs to be validated/revised with the analysis of future datasets.

**REFERENCE:**

[1] Winthrop, et al. Ann Rheum Dis 2015;74:2107–16.

**Disclosure of Interest:** None declared

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SAT0387

**DESCRIPTIVE ANALYSIS OF LEISHMANIASIS CASES IN THE FUENLABRADA OUTBREAK (SPAIN) ASSOCIATED WITH THE USE OF BIOLOGICAL THERAPY**

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**Background:** Protozoan parasites of the genus Leishmania can cause opportunistic infections in patients using anti-tumour necrosis factor (anti-TNF) agents, and some authors recommend serological tests for leishmaniasis before using them. An outbreak of cutaneous and visceral leishmaniasis (CL,VL) occurred in the Fuenlabrada area (Spain) in 2010–2012. Some patients were on anti-TNF treatment.

**Objectives:** We aimed to explore leishmaniasis related to biological therapies in the literature, and to obtain data on leishmaniasis cases in patients using anti-TNFs referred to our Department of Infectious Diseases

**Methods:** Literature search of leishmaniasis cases in patients using biological therapies, and to realise descriptive analysis of the clinical features of patients treated with anti-TNFs in our outbreak.

**Results:** Cases detected in the literature, included our cases, are listed in table 1. In our outbreak of Leishmaniasis, 127 VL and 194 CL cases were detected. Six patients were using anti-TNFs: 2 presented with VL and were using etanercept (33.3%) and 4 using other anti-TNFs had CL (66.6%). (table 2) These results do not coincide with the total data (table 1): CL 55.2%, VL 44.8%, 17 ADA (44.7%), 16 IFM (42.1%), 4 ETN (10.5%), 1 CTZ (2.7%). There are not more cases described with another biologic therapies at the present time.

Abstract SAT0387 – Table 1

Pathology	Cutaneous Leishmaniasis	Visceral leishmaniasis
Rheumatoid Arthritis	4 ADA, 2 IFM, 1 CTZ	4 ADA, 4 IFM, 2 ETN
Psoaric Arthritis	4 ADA, 1 IFM	1 ADA, 2 ETN
Ankylosing spondylitis	3 IFM, 3 ADA	2 IFM
Undifferentiated Arthritis		1 IFM
Giant cell arteritis		1 IFM
Psoaric	1 ADA, 2 IFM	

Table 2

Hospital	Sex	Age	Condition	Anti-TNF	CL/VL	Other treatment	Clinical details
HUIL	M	47	RA	CTZ	CL	MTX, folate acid.	Prior anti-TNF agents: -
HUP	M	54	PSA	ETH	VL	MTX, SSZ (prior discontinued)	- Infliximab (secondary loss of efficacy)
HUP	F	51	PSA	ADA	CL	Prior: EFA, ETH, MTX, SSZ (prior discontinued)	Prior anti-TNF agents: EFA, ETH (diverse event)
HUP	F	54	RA	ADA	CL	MTX (discontinued)	Non-healing granulomatous disease
HUP	M	32	PSO (not rheum.)	IFM	CL	MTX, CSA, 4-cortem	
HUP	F	55	RA	ETH	VL	MTX, FRD	ETH and MTX discontinued 1 month before myelodysplasia diagnosis

HTL: Hospital Universitario; HUP: Hospital Universitario de Fuenlabrada; RA: Rheumatoid arthritis; CL: cutaneous leishmaniasis; VL: Visceral leishmaniasis; PSA: Psoriasis; ADA: adalimumab; CTZ: etanercept; EFA: efalizumab; ETH: etanercept; MTX: methotrexate; FRD: granulomatous fistulizing dermatitis; CSA: Cyclosporine A

**Conclusions:** This preliminary detection of leishmaniasis in patients using anti-TNFs is aimed at examining the safety of TNFα inhibitors in areas where Leishmania is endemic. This is a small series, but the largest described to date. Our preliminary results suggest that the use of either TNFα receptor or other anti-TNFs has the same probability of triggering the disease but etanercept seems to be associated with fewer, although more severe, cases of VL. Nevertheless, adding all the cases, Table number 1, ADA e IFM are the 86.8% of the Leishmaniasis, but perhaps will be due to this therapies are combined and of the most prevalent use. On the other hand, no leishmaniasis cases related to IBD treatment have been described in the literature, suggesting possible involvement of therapies concomitant with the use of anti-TNF with MTX. We detected 3 additional cases of VL and 1 CL using MTX without anti-TNFs. Serological tests for leishmaniasis before using anti-TNFs might not be useful.

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SAT0388

### FACTORS ASSOCIATED WITH THE PERSISTENCE OF ARTICULAR SYMPTOMS IN PATIENTS WITH CHIKUNGUNYA FEVER – CHIKBRASIL COHORT

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**Background:** Chikungunya Fever (CHIK) may evolve chronically with joint impairment, often disabling, which leads to a functional and quality of life impact. The CHIK outbreak in Brazil began in 2015, reaching its peak in 2016, particularly in the Northeast of the country, with 2 35 136 reported cases. Since this is the first epidemic of CHIK in Brazil, data on persistent post-acute joint disease are scarce, and this knowledge is of fundamental importance in defining the long-term impact of the disease.

**Objectives:** To evaluate factors associated with persistence of the joint symptoms in CHIK patients.

**Methods:** The CHIKBRASIL cohort is a prospective, multicenter, observational study, conducted in six research rheumatology centres from the Northeast of Brazil, and has enrolled CHIK patients with joint manifestations since April 2016. Data from 207 patients followed up to December 2017 were analysed.

**Results:** The mean age was 54.7 years, most female (90.3%); 39.1% of the patients had a diagnosis of previous rheumatic disease (49.4% osteoarthritis). The most frequent initial clinical manifestations were arthralgia (98.1%), fever (95.6%), morning stiffness (92.3%) and arthritis (88.9%). The first evaluation with the rheumatologist occurred at a median time of 12 weeks after the onset of symptoms; at this time the median PGA of disease by the patient was 7 and by the physician was 6; the median number of painful joints was 8 and of swollen joints was 3% and 75.5% of the patients had arthritis. After a median follow-up time of 37 weeks, there was complete improvement of joint symptoms in 21.7% and 18.9% of cases reported little or no improvement. The persistence of arthralgia was reported by 76.7% and arthritis by 28.1% of the patients. A significant association was found between the persistence of arthritis and the physician's general VAS (p=0.02), number of painful (p=0.002) and swollen (p=0.001) joints, besides knees (p=0.009), proximal interphalangeal (p=0.07), metacarpophalangeal (p=0.022), elbow (p=0.026) and wrist oedema (p=0.003) at the first consultation). With regard to the persistence of joint pain, associations were found with a higher initial morning stiffness time (p=0.011), shoulder tendinopathy (p=0.019) and tarsal pain. The factors associated with no complete improvement after the follow-up period were tarsal pain (0.021) and shoulder tendinopathy.

**Conclusions:** In the Brazilian CHIK patients, the percentage of persistence of joint manifestations is high after 24 weeks, with a considerable number of patients maintaining arthritis, similar to other countries in Latin America.<sup>2</sup> Significant associated factors were more severe initial symptoms, polyarthritis, polyarthralgia, shoulder tendinopathy and tarsal pain.

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SAT0389

### MRI PREDICTIVE FACTORS FOR POSITIVE CT-GUIDED BIOPSY IN SUSPECTED SEPTIC SPONDYLODISCITIS

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**Background:** Septic spondylodiscitis is an infection involving intervertebral disc and adjacent vertebral endplates that could lead to neurological complications. Magnetic resonance imaging (MRI) is the main imaging modality to suspect spondylodiscitis. However, MRI features predictive for septic spondylodiscitis are still lacking.

**Objectives:** To assess the MRI features associated with microbial pathogen detection by CT-guided biopsy among patients with suspected septic spondylodiscitis.

**Methods:** Between May 2007 and July 2017, we retrospectively analysed patients who underwent MRI and CT-guided biopsy for suspicion of septic spondylodiscitis. Baseline clinical and biological characteristics were collected. MRIs were analysed by one physician blinded to clinical data. The following MRI features were assessed when available: oedema or contrast-enhancement of intervertebral disk, adjacent vertebrae, epidural and paravertebral space, presence of abscess and paravertebral oedema size. A positive biopsy was defined by pathogen identification on culture or by direct microscopy examination.

**Results:** Fifty-one patients (54.9% of males, mean  $\pm$ SD age of 59.2 $\pm$ 19.1 years) were analysed. Lumbar spine (n=38) was the most affected site. A total of 26 (51%) patients had a CT-guided biopsy positive for a bacterial pathogen, mainly *mycobacterium tuberculosis* (n=7) and *staphylococcus aureus* (n=7). Disc size reduction, more than 50% of endplate oedema, loss of intradiscal cleft and abscess were the MRI findings associated with detection of bacterial pathogen by biopsy with a frequency of 100%, 92%, 81% and 50%, respectively. Size of paravertebral oedema was statistically higher in positive CT-guided biopsy than those negative (20.5 $\pm$ 12.6 vs. 11.0 $\pm$ 9.8 mm, p=0.004). The highest specific MRI finding for bacterial pathogen detection was the presence of paravertebral abscess (80%).

**Abstract SAT0389 – Table 1.** Characteristics of the patients (n=51)

Male sex, n (%)	28 (54.9)
Age, mean $\pm$ SD years	59.2 $\pm$ 19.13
Symptoms duration, mean $\pm$ SD days	91.7 $\pm$ 86.58
Fever, n (%)	12 (23.5)
Altered general health status, n (%)	21 (41.2)
Back pain, n (%)	45 (88.2)
Positive blood culture, n (%)	10 (19.6)
C-reactive protein, mean $\pm$ SD mg/L	79.6 $\pm$ 79.0
Neurological complications, n (%)	13 (25.5)

**Abstract SAT0389 – Table 2.** MRI features according to bacterial pathogen detection by CT-biopsy

	Positive CT-biopsy (n=26)	Negative CT-biopsy (n=25)	p
Endplate oedema, n (%)	26 (100)	24 (96)	0.98
>50% of endplate oedema, n (%)	24 (92)	17 (68)	0.029
Disc oedema (n=45) n (%)	25 (96.2)	20 (80)	0.145
Loss of intradiscal cleft (n=30) n (%)	21 (80.8)	9 (36)	0.001
Epiduritis (n=30) n (%)	19 (73.1)	11 (44)	0.067
Paravertebral oedema (n=46) n (%)	23 (88.5)	23 (92)	0.317
Paravertebral infiltrate size, mean $\pm$ SD mm	20.5 $\pm$ 12.6	11.0 $\pm$ 9.8	0.004
Abscess (n=17) n (%)	13 (50)	4 (16)	0.025
Endplate erosion (n=40) n (%)	23 (88.5)	17 (68)	0.528
Disc size reduction (n=47) n (%)	26 (100)	21 (84)	0.034

**Conclusions:** Our study showed that loss of intradiscal cleft, abscess and a large endplate oedema were the best predictive factors for a positive CT-guided biopsy. Size of paravertebral oedema is also associated with detection of bacterial pathogen. Physician must be aware of these MRI findings to better determine which patients should have a CT-guided biopsy.

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SAT0390

### CLINICAL SPECTRUM OF CHIKUNGUNYA EPIDEMIC-OBSERVATIONAL STUDY FROM A TERTIARY REFERRAL CENTRE IN CENTRAL INDIA

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**Background:** Chikungunya virus is an alphavirus, family Togaviridae. Chikungunya fever is a mosquito born disease transmitted to humans by the bite of infected *Aedes aegypti* mosquitoes. An outbreak of chikungunya virus is currently ongoing in many Asian countries since January 2005. The recent outbreak and epidemic of Chikungunya fever in our state reflect the survival capability and tenacity of mosquitoes that continues to be man's biggest foes. An Observational study was conducted to evaluate epidemiological, virological and clinical features of chikungunya fever in patients presenting with acute febrile illness in our state of madhya pradesh.

**Objectives:** To observe the clinical features and laboratory parameters of patients coming with Chikungunya coming to our referral setup during the three months of epidemic presenting from 1 st July to 30th September 2017.



**Methods:** We included all patients (n=325) presenting to us from age 16 years with acute history (<7 days) of fever with joints pain. They were assessed for demographic characteristics, pattern of joints involvement, systemic manifestations, lab parameters, and chikungunya virus positivity. All these parameters were observed according to age and sex and both clinical as well as laboratory markers were studied. We excluded 29 patients, twenty one had past history of inflammatory joint pain and rest had positive virology for dengue virus.

**Results:** We included 325 patients in which Males (M) were 140 and Females (F) were 185, F:M ratio of 1:0.75). The distribution of patients according to age was quite similar across all age groups. Small joints involvement in total of 287 patients (M:40.4%, F:59.6%), axial involvement in 219 patients (M:36.1% and F:67.6%), knee joint involvement in 285 patients (M:41.1% and F:58.9%), ankle pain in 285 patients (M:42.8% and F:57.2%), early morning stiffness was seen in 308 patients (M:44.8% and F:55.19%), eyes involvement in 53 patients (M:35.8% and F:64.2%), Neurological manifestations in 134 patients (M:43.3% and F:56.7%), stomatitis and oral ulcers in 85 patients (M:45.9% and F:54.1%), retrobulbar pain occurred in 73 patients (M:45.2% and F:54.8%), rashes were seen in 47 patients (M:59.6% and F:40.4%). Forty two patients (12.9%) had history of Diabetes (F:73% and M:26%) and 31 patients (9.5%) were hypothyroid with female predominant (100%). Urea and creatinine was also raised (n=18). Rheumatoid factor was positive in 19 patients (M:42.1% and F:57.9%). IgM Chikungunya was positive in 202 patients (M:46.04% and F:53.96%), and out of those 65 patients in which it was negative, we did RT-PCR in 18 patients due to unaffordability being a major factor and we found that RT-PCR came out positive in 15 patients. The mean ESR in males was 41.76±19.98, in females it was 53.66±24.66, mean CRP in males was 29.84±19.61 and in females it was 40.74±25.94.

**Conclusions:** We conclude that Chikungunya is a multisystem disease affecting both genders. In our setup, we observed it affected females more and seropositivity for chikungunya was seen in around half of the patients presenting with signs and symptoms. PCR test is more reliable for confirmation. Skin rashes with neurological symptoms, severe pain causing disability and dependence on others for personal care were main complaints. No mortality was reported in our study.

**Disclosure of Interest:** None declared

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### SAT0391 MUSCULOSKELETAL MANIFESTATIONS OF CHIKUNGUNYA FEVER IN ELDERLY PATIENTS – CHIKBRASIL COHORT

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**Background:** Elderly patients with Chikungunya virus (CHIKV) infection may exhibit atypical and more severe clinical manifestations in the acute phase,<sup>1</sup> but little is known about these patients progress in the chronic phase of the disease.

**Objectives:** To describe the chronic clinical course of CHIKV infection in Brazilian elderly patients.

**Methods:** The CHIKBRASIL is a prospective, multicenter, observational cohort, conducted in six research rheumatology centres from the Northeast of Brazil, and has enrolled CHIK patients with joint manifestations since April 2016.<sup>2</sup> Data from 353 patients followed up to December 2017 were analysed, divided into two groups: the elderly (age ≥60 years) and not elderly.

**Results:** Of the 353 cases, 124 were elderly (35,1%), mean age was 67.1 years (±5.6), 81.5% women. Patients in the elderly group had a higher frequency of comorbidities, such as systemic arterial hypertension (p<0.0001), diabetes mellitus (p<0.001) and hyperlipidemia (p=0.0003). The median time of disease was 26 weeks, most of them were in the chronic phase of the disease (61.3%). With respect to initial clinical manifestations, no significant differences were observed between the groups, except for fatigue, which occurred more often in the non-elderly group (p=0.036). In general, the elderly group presented a lower frequency of absence at work (0.000), lower limb oedema (0.006) and less prescription of methotrexate (p=0.048). In addition, it was also observed that older patients had a lower mean of the number of painful joints (10.2±1.7), but without statistical difference (p=0.0655). After a median follow-up time of 27.5 weeks, the number of patients who presented complete improvement was higher in the non-elderly group (p=0.07), but without differences between the number of tender and swollen joints, persistence of arthralgia or arthritis in the two groups. No association was observed between the presence of comorbidities and the clinical evolution of the patients.

**Conclusions:** Despite the risk of a more severe evolution at the onset of CHIKV infection, elderly patients present a similar clinical course to the non-elderly in the chronic phase, apparently with less severity. However, such group is a high-risk

population with an important number of comorbidities. In all stages of the disease, especially in the acute phase, strict clinical supervision is recommended regarding the use of drugs and increased risk of complications.

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### SAT0392 THE RELEVANCE OF SERUM PROCALCITONIN QUANTIFICATION FOR DIFFERENTIAL DIAGNOSIS OF INFECTIONS AND RHEUMATIC DISEASES

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**Background:** Assessment of procalcitonin (PCT) serum levels is of great interest in current rheumatology practice, due to clinical and laboratory similarity of acute systemic rheumatic diseases (RDs) and acute infectious process, and because of low diagnostic yield of conventional ESR, CRP and WBC in active RDs.

**Objectives:** To evaluate the relevance of PCT as a specific marker of generalised and local infections in patients with RDs.

**Methods:** Medical records of 134 in-hospital patients (mean age 40,6±19,5) admitted to VA Nasonova Research Institute of Rheumatology for examination and treatment were analysed in this retrospective study. Serum PCT concentration was measured using quantitative electrochemiluminescence method, Cobas E 411 analyzer (Roche, Switzerland). The infectious process was diagnosed in 75 pts, generalised – in 4, and local – in 71. Based on the severity of fever and intoxication local infections were divided into mild – 41 cases, and severe – 30 cases.

**Results:** The PCT level reached >2.0 ng/mL in 3 of 4 cases in generalised infection. In population with severe local infections (n=30) the PCT concentration exceeded the threshold and amounted to 0.60 ng/mL [0.19; 1.84], while in pts with mild infection (n=41) it was 0.13 ng/mL [0.08; 0.25] (table 1). PCT levels positively correlated with ESR, CRP, white blood cell count, and SLE activity according to SLEDAI index in this retrospective study. Maximal PCT levels were found in adult-onset Still's disease (ASD) pts with high activity of rheumatic process without underlying infection – 0.26 [0.10; 0.61] ng/mL. The test's sensitivity and specificity in generalised/severe local infections group (n=34) were 60% and 82,5%, respectively, with a threshold value of 0.4 ng/mL.

**Abstract SAT0392 – Table 1.** PCT values in different groups of patients, n (%)

PCT level, ng/mL	Generalised infection (n=4)	Local infection		No infection	
		Severe (n=30)	Mild (n=41)	Still's disease (n=6)	Totally (n=59)
≤ 0,05	-	1 (1,33)	4 (9,76)	-	12 (20,34)
0,05–0,1	-	2 (6,67)	13 (31,71)	1 (16,67)	19 (32,20)
0,1–0,25	-	5 (16,67)	13 (31,71)	2 (33,33)	16 (27,12)
0,25–0,5	1 (25)	6 (20,0)	6 (14,63)	1 (16,67)	6 (10,17)
0,5–2,0	0	11 (36,67)	5 (12,20)	2 (33,33)	6 (10,17)
2,0–10,0	1 (25)	3 (10,0)	-	-	-
>10,0	2 (50)	2 (6,67)	-	-	-
Me [25-ii; 75-ii percentiles]	5,30 <sup>1,63; 9,06*</sup>	0,60 [0,19; 1,84] <sup>†</sup>	0,13 [0,08; 0,25] <sup>‡</sup>	0,26 [0,10; 0,61] <sup>§</sup>	0,09 [0,06; 0,19] <sup>¶</sup>

p < 0,05.

**Conclusions:** PCT quantification is a sensitive and specific method for differential diagnosis of serious bacterial infections in patients with different activity of systemic RD. ASD seems to be the exception, as it was associated with PCT increase in the absence any infection. Further studies are needed to determine PCT thresholds for different RDs.

**Disclosure of Interest:** None declared

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**SAT0393 DEVELOPMENT OF A SCORE FOR THE DIAGNOSIS OF INFECTIOUS ARTHRITIS IN DIFFICULT TO PUNCTURE JOINTS**

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**Background:** In previous studies, we have demonstrated the benefit of the determination of serum procalcitonin in the diagnostic discrimination between gouty and an infectious monoarthritis. On the other hand, the utility of this analyte has been suggested in the diagnostic study of monoarthritis in which the obtention of joint fluid for lab analysis is difficult or impossible in the immediate term.

**Objectives:** The objective of this study is to perform the validation of a score to determine the diagnosis of Native Joint Septic Arthritis (ASAN) in difficult to puncture joints.

**Methods:** A logistic regression study was conducted using 37 cases of ASAN (sternoclavicular, acromioclavicular, coxofemoral, intratarsal, and metatarsophalangeal) and 160 of non-infectious arthritis diagnosed as such between 2013 and 2016 by microbiological criteria, the presence of crystals or absence of both situations. The explanatory variables were: Three age strata, three CRP levels, three strata of PCT figure, immunomodulation/immunosuppression condition, two strata of time of evolution, the presence of fever and neutrophilia. After a forward modelling, a test validation study was performed using the modelling coefficients as a weight reference for each value of the score.

**Results:** The only variables that overcame the forward modelling were PCT, temperature, immunosuppression and time of evolution. Using the reference coefficients (table 1), validation tests were performed by means of the ROC curve. According to the presented curve, a sensitivity of 86.6% and specificity of 95.8% is reached if the total score reaches or exceeds 5pts (Strata of PCT 6, 4 and 2, and 2 points by any of the remaining three considerations). The total area under the curve was 0.926.

**Abstract SAT0393 – Table 1.** Results of the multivariable logistic regression backward modelling.

Variable	Coef.	E.E.	Wald	p-value	R
PCT > 1.4ng/ml.	5.8412	1.0231	32.5971	<0.0001	0.4010
PCT <1.0 – 1.4ng/ml.>	5.2632	1.9117	7.5798	0.0059	0.1712
PCT <0.5 – 1.0ng/ml.>	4.6626	1.7378	7.1985	0.0073	0.1653
Body temp > 38.0°C	2.1119	0.8883	5.6524	0.0174	0.1385
Immunomodulation	1.9623	0.9473	4.2911	0.0383	0.1097
Time of onset <72h	1.6565	0.7649	4.6897	0.0303	0.1189

**Conclusions:** Taking into account the high specificity achieved, we the authors propose the use of the present score to exclude ASAN in situations in which access to synovial fluid is difficult or technically not feasible.

**Disclosure of Interest:** None declared

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**SAT0394 IMMUNOGENICITY AND SAFETY OF 23-VALENT PNEUMOCOCCAL VACCINE IN RA PATIENTS: RESULTS OF A 4- YEAR FOLLOW UP STUDY**

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**Background:** Comorbid infections have significant impact on morbidity and mortality, especially in autoimmune diseases. Prevention of infection is an integral part of supervision of these patients.

**Objectives:** To investigate immunogenicity and safety of 23-valent polysaccharide pneumococcal vaccine in patients with rheumatoid arthritis (RA) treated with diseases modifying anti rheumatic drugs (DMARDs) and biologic diseases modifying anti rheumatic drugs (bDMARDs).

**Methods:** The study included 110 patients (females–81 (73.6%), males–29 (26.4%), aged 23–76 y), 79 RA pts and 31 controls with  $\geq 2$  recent episodes of upper respiratory tract infections (bronchitis, pneumonia). 52 RA pts were treated with methotrexate (MT), 14 – with leflunomide (Lef), 13– with TNF-  $\alpha$  inhibitors +MT. One dose (0,5 ml) of 23-valent polysaccharide pneumococcal vaccine was administered subcutaneously without discontinuing MT/Lef or 28–30 days prior to initiation of TNF-  $\alpha$  inhibitors. Control visits were scheduled as follows: at baseline (Visit I), and in 1, 3, and 12 months after immunisation. 39 out of 110 pts were followed for 24 months, 23 pts – for 36 months, and 16 pts – for 48 months. Standard clinical examination and lab tests were performed at each visit. Levels of serum antibodies (AB) to Pneumococcal capsular polysaccharide were measured with VacciZyme™ PCP IgG 2 panels (The Binding Site Group Ltd, Birmingham, UK). Coefficient of post-immunisation response (CPR) was determined for each patient as the ratio of AB levels at Visits II, III, IV, V, VI and VII to AB level at Visit I.

**Results:** There were no documented clinical or radiological symptoms of bacterial pneumonia in a single patient during the FUP. CPR dynamics in RA pts on different therapeutic regimens and in the controls is shown in the table 1.

**Abstract SAT0394 – Table 1.** CPR dynamics in RA pts and the controls during 1-year FUP, M $\pm$  $\sigma$ .

	Visit II (1 month)	Visit IV (12 month)	Visit V (24 month)	Visit VI (36 month)	Visit VII (48 month)
RA patients	2,33* [1,6;3,8]	2,64* [2,03;6,39]	3,07* [1,56;6,18]	1029 [0,74;1,32]	2,08* [0,69;3,80]

\*p<0,05

Pronounced positive immune reaction to the study vaccine was documented in all RA patients on different therapeutic regimens as significant CPR incremental growth. The proportion of responders to the vaccine reached 61% among RA pts. *Significant* decrease of RA activity according to DAS28 scores in RA pts (4,32 and 3,31 at Visits I and IV, respectively, p<0,001) demonstrates absence of any negative effect of vaccination on disease activity. There was a trend to weakening of post-vaccination response in 3 years, although significantly high level of post-immunisation response still persisted after 4 years of FUP. Not a single case of pneumococcal infection was ever documented during 4 years FUP, although one case of interstitial viral pneumonia was registered in 6 month after immunisation. Not a single vaccination-related RA exacerbation episode was documented during the FUP.

**Conclusions:** Therefore obtained results are indicative of sufficient immunogenicity, good safety and efficacy of 23-valent pneumococcal vaccine in RA pts on different therapeutic regimens.

**Disclosure of Interest:** None declared

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**SAT0395 ASSESSMENT OF EFFICACY AND SAFETY OF A TRIVALENT SPLIT-VIRUS INFLUENZA VACCINE IN PATIENTS WITH RHEUMATIC DISEASES**

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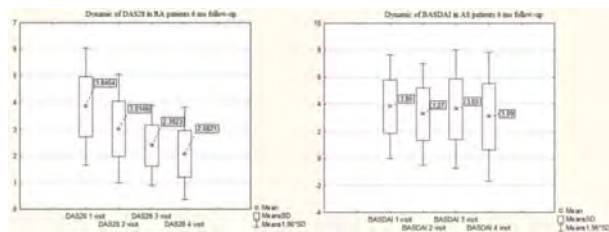
**Background:** In current rheumatology practice concurrent infections produce significant negative impact on patients' morbidity, mortality and quality of life, especially in cases of systemic connective tissue diseases. Based on WHO estimations the annual incidence of influenza in adult population amounts to 5%–10% worldwide. Influenza can lead to hospitalisation (3 to 5 million cases per year) and even death (250–500 thousand cases per year). Flu and its complications rates are higher in patients with rheumatic diseases (RD) as compared to general population. Therefore, prevention of influenza should be viewed as integral part of RD population management.

**Objectives:** To study the safety and efficacy of inactivated split-virus influenza vaccine in patients with rheumatoid arthritis (RA), ankylosing spondylitis (AS), and systemic sclerosis (SS) treated with diseases modifying anti rheumatic drugs (DMARDs) and biologic diseases modifying anti rheumatic drugs (bDMARDs).

**Methods:** 133 subjects (97 females and 36 males, aged 22–82 y) with recent acute respiratory viral infections (ARVI) and flu episodes in medical records were enrolled, including 52 RA patients, 34 AS patients, 7 SS patients and 40 healthy volunteers as the control group.

39 RA pts received methotrexate (MTX), 12 – TNF $\alpha$  inhibitors+MTX, 8 – leflunomide, 2 – abatacept, 2 – sulfasalazine, 1 – tofacitinib +MTX. 19 AS patients were treated with nonsteroidal anti-inflammatory drugs (NSAIDs), 15 –with TNF $\alpha$  inhibitors. The RD duration ranged from 2 months to 46 years. All participants were injected subcutaneously with one dose (0.5 ml) of the "Vaxigrip" vaccine containing the actual influenza virus strains with ongoing therapy. The control visits were scheduled at baseline, and in 1, 3 and 6 months after vaccination (Visits 0, 1, 2 and 3, respectively). Standard clinical and laboratory tests were performed during each visit.

**Results:** Vaccine tolerability was good in 103 participants (77.4%). Post-vaccination pain, swelling and redness of the skin up to 2 cm in diameter were registered in 20 cases (15%), low-grade fever, myalgia and malaise were documented in 10 cases (7.5%). There was no causal relationship between these reactions and principal therapy, therefore, no modifications of therapeutic regimens were required, and complete resolution occurred within 24 hours without additional interventions. No RD exacerbations or emergence of *de novo* autoimmune disorders were observed during the FUP. At baseline mean pts' DAS28 and BASDAI scores were 3.56 and 3.85, improving up to 1.99 and 3,09, respectively, 6 mo post-vaccination. For the entire FUP there were no cases of influenza or influenza-like illness registered.



**Conclusions:** Therefore, the preliminary results show good tolerability and efficacy of inactivated split-virus influenza vaccine in RA, AS, and SS patients. Future studies on larger patients' populations are warranted for more complete evaluation of vaccine safety and efficacy.

**Disclosure of Interest:** None declared

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### SAT0396 THE RISK FACTORS OF SERIOUS INFECTION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Although life expectancy has improved for many rheumatoid arthritis (RA) patients, serious infection is one of the major causes of mortality. Undernutrition is widely known to be a risk factor for infection; however, the association between undernutrition and infection in RA patients is not well known.

**Objectives:** The aim of this study was to identify the risk factors associated with infection requiring hospitalisation in RA patients.

**Methods:** We retrospectively analysed data obtained from 74 patients with RA (male, n=21; female, n=53; age 74.7±12.6), who were admitted to our hospital between 2016 and 2017 for infection (infection group). Among the patients who experienced multiple infections during this time, only the first infection was included in this study. We also recruited control RA patients (n=222) who were matched for age, gender and disease duration, with a match ratio of 1:3 (non-infection group). The details of the patients' infections, clinical characteristics (including nutritional conditions), and RA treatment were obtained from their clinical records. The nutritional condition was assessed based on the body mass index (BMI), serum albumin (Alb) level, total lymphocyte count (TLC), haemoglobin (Hb) level, controlling nutrition status (CONUT) score, and prognostic nutritional index (PNI). Differences between each group were compared using a nonparametric Wilcoxon's rank sum test for continuous variables and Fisher's exact test for categorical variables. Multiple regression analyses were performed to determine the factors associated with the development of serious infection. We selected seven candidate factors: Steinbrocker's classification (Stage)≥III, BMI≥18.5, CONUT score ≥5, DAS28-ESR≥3.2, use of methotrexate, use of prednisolone, use of biologics.

**Results:** The respiratory tract was the most frequent site of infection (n=33, 44.6%), followed by the urinary tract (n=14, 18.9%), skin (n=13, 17.6%), bones and joints (n=5, 6.8%), and gastrointestinal tract (n=3, 4.1%). Seven patients died during hospitalisation for infection, in spite of treatment. Relative to the non-infection group, the BMI (20.9±4.1 vs. 22.0±3.4, p=0.036), Alb (3.3±0.7 vs. 3.9±0.4 g/dL, p<0.001), TLC (1190±574 vs. 1328±526/μL, p=0.008), Hb (11.1±1.9 vs. 12.3±1.5 g/dL, p<0.001), and PNI (55.4±8.0 vs. 60.4±8.0, p<0.001) values were significantly lower, and the CONUT score (4.1±2.7 vs. 1.9±1.5, p<0.001) was significantly higher in the infection group. In addition, the DAS 28-ESR (3.5±1.2 vs. 2.9±1.1, p=0.001), dose of prednisolone (4.6±3.4 vs. 2.3±2.3, p<0.001), and rate of biologics usage (33.8 vs. 21.2%, p=0.041) were higher, while the dose of methotrexate (1.6±3.2 vs. 3.2±4.0, p=0.002) was lower in the infection group. The multiple regression analysis revealed that the CONUT score (odds ratio [OR], 62.9; 95% credible interval [CrI], 7.9 to 500.0), use of prednisolone (OR, 6.7; CrI, 2.2 to 20.7), and use of biologics (OR, 3.9; CrI, 1.7 to 9.3) were significant risk factors for serious infection.

**Conclusions:** Multiple factors were found to be associated with infection in RA patients. The improvement of nutrition may have a beneficial effect with regard to the prevention of infection during the care of RA patients.

**Disclosure of Interest:** None declared

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### SAT0397 SAFETY AND IMMUNOGENICITY OF 23-VALENT PNEUMOCOCCAL VACCINE IN SLE PATIENTS

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**Background:** Immunisation with pneumococcal vaccine is the key prophylactic measure to protect patients with systemic lupus erythematosus (SLE) against severe respiratory infections.

**Objectives:** To study the efficacy and immunogenicity of 23-valent polysaccharide pneumococcal vaccine in SLE pts.

**Methods:** The study included 30 SLE pts, 27 females, 3 males, aged 19–62 y, the follow up (FUP) was 12 mo. Disease activity at vaccination was high – in 1 patient, moderate – in 4 pts, and low – in 20 pts; drug-induced remission – in 5. Therapy: 29 pts were on glucocorticoids (GCs), 23 – on hydroxychloroquine, 14 – on cytostatic (CS) drugs, 9 – on biologic diseases modifying anti rheumatic drugs (bDMARDs): 4 – on rituximab, and 5 – on belimumab. One dose (0,5 mL) of 23-valent polysaccharide pneumococcal vaccine was administered subcutaneously. Standard clinical examination and lab tests were performed, and vaccine immunogenicity was determined by measuring antibody (AB) levels against *Streptococcus pneumoniae* (VaccZyme™ PCP IG 2 panels (The Binding Site Ltd, Birmingham, UK)) at control visits.

**Results:** Local injection site reactions of varying intensity were registered in 19 (63,3%) pts, lasting from 2 to 7 days. One patient developed an immediate hypersensitivity reaction – the Arthus phenomenon-type. All accompanying symptoms completely resolved within 7 days with the intake of antihistaminic drug and local use of GCs. Mean (Me (25,75 percentiles)) SLEDAI scores for SLE activity prior to and 1 year after vaccination did not differ significantly: 2 (2;4) and 2 (0;4), respectively. Mean values of SLE immunological activity parameters (a-dsDNA, C3 and C4 components of the complement) also did not differ significantly, with a visible trend for a-dsDNA reduction and complement components increase: C3 (0,86 (0,81;1,07) and 0,93 (0,86;1,05)); C4 (0,16 (0,13;0,19) and 0,18 (0,13;0,19), respectively. (table 1)

**Abstract SAT0397 – Table 1.** Dynamics of immunological activity parameters (Me) and SLE SLEDAI (Me) scores prior to and after the vaccination (12 mo).

FUP	A-dsDNA <20	C3 0,9–1,8	C4 0,1–0,4	SLEDAI
Visit 1 (baseline)	21,3 (4,7; 48,4)	0,86 (0,81;1,07)	0,16 (0,13;0,19)	2 (2;4)
Visit 2 (1 mo)	25,0 (4,7; 48,4)	1,1 (0,9; 1,2)	0,17 (0,13; 0,19)	2 (0;4)
Visit 3 (3 mo)	20,9 (8,2; 34,5)	0,91 (0,8; 1,0)	0,17 (0,14; 0,2)	2 (2;4)
Visit 4 (12 mo)	18,7 (8,7;68,7)	0,93 (0,86;1,05)	0,18 (0,12;0,19)	2 (0;4)

There were no SLE exacerbations with definite casual relationship with the vaccination. Significant increase (≥2 fold vs the baseline values) of AB levels against *S.pneumoniae* polysaccharides was documented in 25 (83,3%) pts 1 mo post-vaccination. High AB titers still persisted 1 year post-vaccination in 19 (63,3%) pts (responders). More than 2-fold increase of anti-*S.pneumoniae* AB concentrations was not maintained by the end of FUP (12 mo) in 11 (36,7%) «non-responders». 7 (63,6%) out of them were treated with GEBA (4-rituximab, 3 – belimumab). 2 (10,5%) pts out of 19 «responders» were also treated with GEBA (belimumab). The difference was statistically significant, p=0008.

**Conclusions:** Obtained results demonstrate the safety and immunogenicity of 23-valent pneumococcal vaccine in SLE patients during one year FUP. The negative effect of bDMARDs on post-vaccination response was noticed. Future studies of vaccine efficacy and safety are needed in larger SLE populations.

**Disclosure of Interest:** None declared

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### SAT0398 SPINE IMMOBILISATION AND NEUROLOGICAL COMPLICATIONS IN VERTEBRAL OSTEOMYELITIS: RESULTS FROM A MULTICENTER PROSPECTIVE STUDY

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**Background:** Neurological complications of vertebral osteomyelitis (VO) can be serious. In a previous work,<sup>1</sup> we showed that they occur in up to 40% of the



patients. Bed rest and spine immobilisation by bracing is prescribed to decrease pain but also to prevent those complications. There is currently no consensus about the best immobilisation protocol to follow in VO. French guidelines recommend bracing for all patients whereas recently published American recommendations did not even mention spine immobilisation.

**Objectives:** To describe the type and duration of prescription of spine immobilisation during VO.

**Methods:** A prospective multicenter study was performed in 7 French centres. All patients with VO were followed prospectively: neurological complications, imaging findings, type and duration of immobilisation were reported. We present here the data of our study after 3 months of follow-up.

**Results:** To date, 79 patients completed 3 months follow-up. Median age was 67 ±15 years old with 66% of males. Median duration of symptoms before diagnosis was 27 days, IQR. 11–40 37 patients (47%) had staphylococcal infection.

35% of the patients had an abnormal neurological exam at baseline: 18 patients (23%) had minor neurological signs (sensory loss, radiculopathy or pyramidal syndrome), and 10 (12%) had major neurological signs (motor deficit or cauda equine syndrome). During hospital stay, 5 patient developed major neurological signs (median 5 days after diagnosis) and 7 minor neurological signs (median 6 days after diagnosis). Half of the patients with abnormal neurological exam at baseline had functional sequelae at 3 months. On MRI, 17% of patients had epidural phlegmon, 20% had anterior effacement of subarachnoid space, and 16% had involvement of cervical spine. All these MRI signs were significantly associated with major neurological complications ( $p=0.004$ ,  $p=0.004$  and  $p=0.002$ , respectively).

Median duration of bed rest was 9 days (IQR 7–18). Overall, only 60% of patients have been immobilised by bracing (90% of rigid bracing). Median duration of prescription was 8 weeks, IQR. 6–12 Patients who did not receive spine immobilisation had all a lumbar involvement, a normal neurological examination at baseline. None of them developed secondary neurological complications. They were no significant difference in age (72±16 versus 65±15 years old), sex or duration of the symptoms between patients who have been immobilised or not.

**Conclusions:** Neurological complications occurred in 35% of our patients as published in previous VO cohort. Interestingly, 40% of our patients were not treated with bracing. They all had lumbar involvement and normal initial neurological examination. None of them developed secondary neurological complications. Bed rest without bracing might be the best therapeutic option for these patients, preventing the morbidity associated with bracing.

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**Disclosure of Interest:** None declared

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#### SAT0399 CHIKUNGUNYA FEVER IN KARACHI: CLINICAL AND LABORATORY FEATURES AND FACTORS ASSOCIATED WITH PERSISTENT ARTHRALGIA

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**Background:** Chikungunya virus (CHIKV) is an alphavirus transmitted by mosquito vectors.<sup>1</sup> Acute infection lasts for 1–10 days and is characterised by abrupt onset of fever and severe arthralgia. Painful polyarthralgia is the symptom causing serious economic and social impacts on individuals and the affected communities.<sup>2</sup> In a study conducted by Schilte C et al, 60% of CHIKV-infected patients suffered from arthralgia, 36 months after acute infection.<sup>3</sup> Non-salicylate analgesics and non-steroidal anti-inflammatory drugs (NSAIDs) are most commonly used for symptomatic relief.<sup>4</sup> There is lack of local data on CHIKV and its after effects. By determining the clinical and laboratory features associated with CHIKV and persistent arthralgia, it will help us in early diagnosis, and improved outcomes in our population.

**Objectives:** To study clinical and laboratory features associated with persistent arthralgia in patients with chikungunya fever

**Methods:** This observational study was conducted at the Rheumatology Clinic of Liaquat National Hospital, Karachi. It comprised of collected data of patients who presented with arthralgias and positive chikungunya serology. Detailed history, examination and laboratory investigations were recorded in a pre-designed structured proforma and SPSS21 was used for statistical analysis.

**Results:** We had 52 patients out of which 28.8% were males and 71.2% were female, mean age being 45±5 years. Mean duration of arthralgia was 2.6 months. Pre-existing rheumatologic conditions were RA in 1.9% while SLE in 1.9% of the patients. Out of the total 9.6% were hospitalised due to complications like encephalitis, septic arthritis. Symmetrical arthralgia and asymmetrical was described

in 76.9% and 23.1% of cases respectively. Small joint involvement was in 21.2%, large joint in 20.8% while both small and large involvement was seen in 48.1% of patients. Morning stiffness of greater than ½ hour was described in 63.5% of cases. Elevated ESR, CRP was seen in 69.2% and 59.6% cases, respectively. Patients were either given NSAIDs (34.6%), steroids (57.7%), or both (7.7%). Steroid was usually given in the form of a single intra muscular methylprednisolone 120 mg dose. In total 85.7% of patients improved after receiving steroids. While in group receiving NSAIDs only, improvement was seen 7.1% of total cases, and persistent arthralgia was seen in 88.9% of same group.

**Conclusions:** Chikungunya viral arthralgia has constituted a major disease and socioeconomic burden in our society in a relatively short span of time. Studies including our show it to be a great mimicker of inflammatory arthritis, and stresses the need to differentiate it, as history, clinical examination and lab parameters show quite similarity. Prompt treatments through steroids have shown great response in symptoms.

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#### SAT0400 INFECTIOUS SPONDYLODISCITIS: 7-YEAR ANALYSIS OF CLINICAL AND PROGNOSTIC VARIABLES IN A TERTIARY HOSPITAL

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**Background:** Spondylodiscitis is an infectious disease of the vertebral body and intervertebral space, the early diagnosis and treatment are essential to give the patient the best chance of a good outcome, but these are often delayed because it tends to present nonspecific manifestations.

**Objectives:** To analyse cases of Spondylodiscitis and identify poor prognosis variables.

**Methods:** A retrospective observational study, included all adult patients with confirmed infectious spondylodiscitis between January 2010 and December 2017. Demographic features, concurrent disease, clinical history, laboratory findings, microbiological diagnosis, radiological data and clinical outcome were compiled from the clinical history management software. Statistical analysis was performed with the software R (version 3.3.2).

**Results:** We included 87 patients with a mean age of 62.05 (16.94) years old. Males predominated (69%). Almost 31% patients presented of a level of immunosuppression (immunosuppression treatment, cirrhosis, HIV infection, solid organ transplantation). The average time with axial pain was 74 (87.65) days. Mean length of hospital stay was 34.24 (34.3) days and readmission rate was 34.9%. Most of patients showed high CRP levels at their admission, with an average value of 88.92 (84.58) mg/L, it was not correlated with worse prognosis. Underlying endocarditis proportion was 11.5%. Blood cultures were positive in 29 patients (33,3%), it was correlated with hospital stay ( $p=0,03$ ). 51 patients had punction-aspiration and intervertebral biopsy with microbiologic findings diagnosis in 30 patients (58.8%): 42.5% patients had an identifiable gram +bacteria (37,8% *Streptococcus* genere), 13.7% a Gram- bacteria, *Mycobacterium tuberculosis* in 8% and fungi infection (all *Candida spp.*) in 3.4%. 38% of patients showed vertebral destruction on MRI; 17.4% cord compression and developed neurological complications (8 of them paraparesis). 18.4% of patients required further surgical procedures. Furthermore, vertebral destruction was statistically correlated with epidural abscess ( $p=0,006$ ). Almost 6% of patients died in the following year after diagnostic.

**Conclusions:** Delay in diagnosis is an important issue in Spondylodiscitis patients. Higher complications rates are mainly in relation to greater vertebral destruction. Underlying infectious endocarditis was described in a small proportion of patients in contrast to other studies. Presence of epidural abscess was also

correlated with vertebral destruction, for this reason, patients with this finding should be more carefully follow-up.

**Disclosure of Interest:** None declared

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#### SAT0401 RISK OF HOSPITAL ADMISSION DUE TO SEVERE INFECTION IN PATIENTS UNDER TREATMENT WITH ANTI-TNF DRUGS: DATA FROM A LOCAL REGISTRY

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**Objectives:** To Know characteristics of patients treated with anti-TNF, who suffered infections that forced hospital admission.

**Methods:** Prospective observational study in patients treated with anti-TNF, during 1/1/2000 to 12/31/2017, followed up in the Rheumatology Section. General data of patients (age, gender), of disease (diagnosis and time of evolution, type of anti-TNF, time in anti-TNF, concomitant treatment with DMARD), regarding the presence of severe infection, defined as infection that required hospital admission (time in anti-TNF to infection, location of infection, days of admission, mantoux/IGRAS and vaccinations prior to the start anti-TNF treatment) was collected. The admission decision was made by Emergency Department of centre or Rheumatology.

**Results:** Of 442 patients with anti-TNF, 44 (9.6%) patients had at least one hospital admission due to severe infection. 59% were women, with mean age 64±16.72 years,<sup>22-88</sup> 21.25±4.02 years of disease evolution. A mantoux/IGRAS was performed prior anti-TNF. Diagnosis was: rheumatoid arthritis (RA): 25 (57%), ankylosing spondylitis (AS): 12 (27%), psoriatic arthritis (PSA): 5 (11%) and juvenile idiopathic arthritis (JIA): 2 (5%). The mean time of treatment with anti-TNF is 5.6 ±4.5 years. Adalimumab received 24 (55%) patient, infliximab 8 (18%) patients, etanercept 6 (14%) patients, golimumab 5 (11%) and 1 (2%) certolizumab.

Of the 55 confirmed infections: non-pneumonic infection in 13 (24%) patients, pneumonia: 10 (18%), septic arthritis: 6 (11%), septic shock and/or bacteremia: 6 (11%), abscess: 4 (7%), urinary infections: 4 (7%), cellulitis: 3 (5%), cutaneous leishmaniasis: 3 (5%), acute gastroenteritis: 2 (4%), surgical wound infection: 1 (2%), cutaneous infection: 1 (2%), Septic bursitis: 1 (2%), gonorrhoea: 1 (2%). The mean time of hospital admission was 9.76 days. Three (7%) patients presented the infection within a year of starting treatment.

The rate of severe infection x100 patients/year of exposure is 2.01 (1.47–2.67). The odd ratio of admission for infection of 3.67 (1.11–4.87, p=0.03). The risk of admission for infection in patients with peripheral arthritis (RA, PSA, JIA) is 2.42 (1.21–3.11) times higher than in patients with AS (p=0.012).

In the table 1, the Odd ratio of income for infection distributed by anti-TNF drug is shown.

Anti-TNF	N° patients	Odds ratio (IC 95%)
Infliximab	101	8.01 (4.99–12.05)
Golimumab	82	5.68 (2.95–9.73)
Certolizumab	33	3.25 (0.54–10.03)
Adalimumab	239	3.03 (2.08–4.22)
Etanercept	188	2.44 (1.48–3.76)

**Conclusions:** 1. The severe infection rate x100 patients/year of exposure is 2.01 and the prevalence is 9.6%. 2. The majority of severe infection occurred late, after more than 1 year of treatment. 3. The most frequent infection were those of respiratory origin, followed by sepsis or bacteremia and septic arthritis. 4. Etanercept has presented the lowest rate of severe infection. 5. Patients with AS have a lower risk of severe infection than patients with chronic peripheral arthritis.

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**Disclosure of Interest:** None declared

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#### SAT0402 LEISHMANIASIS IN PATIENTS ON TUMOUR NECROSIS FACTOR INHIBITORS TREATMENT

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**Background:** Tumour necrosis factor (TNF) plays a major role in defense against leishmaniasis. Despite wide use of TNF $\alpha$  inhibitor (anti-TNF) for several diseases, leishmaniasis has been a rare infectious complication so far in these patients. Recently, an increased incidence has been noted.

**Objectives:** To describe a recent multicenter case series of leishmaniasis in patients with chronic inflammatory diseases treated with anti-TNF.

**Methods:** We reviewed the clinical history of a multicentric series of patients with chronic inflammatory diseases treated with anti-TNF, who were diagnosed with leishmaniasis between January 2013 and December 2017. Patients came from Rheumatology, Digestive and Dermatology departments of several hospitals in Valencia<sup>2</sup> and Cataluña<sup>1</sup> region. Demographic (age, sex) and clinical (inflammatory disease, comorbidities, current treatment, year of infection and leishmaniasis form) variables were collected. Anti-TNF withdrawal, subsequent reintroduction and recurrence rate were recorded in two hospitals. Biologic drug dispensation trends from 2013 to 2016 and epidemiological data published by the Regional Ministry of Health of Valencia for the area where cases were most incident were analysed.

**Results:** 25 cases of leishmaniasis in patients treated with immunomodulators were identified: 7 on DMARD, 1 on tocilizumab and 17 on anti-TNF (7 infliximab, 4 adalimumab, 3 golimumab, 2 certolizumab, 1 etanercept). Regarding patients on anti-TNF, 2 cases were collected in 2014, 4 in 2015, 4 in 2016 and 7 in 2017. Three patients developed the visceral form, 13 the cutaneous form and 1 presented visceral and cutaneous involvement. Seven patients were males and 10 females, with an average age of 50 (SD14) years. One patient presented rheumatoid arthritis, 4 psoriatic arthritis, 1 undifferentiated spondyloarthritis, 2 ankylosing spondylitis, 1 uveitis, 6 Crohn's disease and 2 ulcerative colitis. Six patients presented other chronic disease (1 latent tuberculosis, 1 pyoderma gangrenosum, 1 psoriasis and 3 diabetes mellitus). In two hospitals (15 patients), anti-TNF treatment was withdrawn in 10 cases, and it was reintroduced after treating the infection in 5 cases. No infection recurrences have been identified. Focusing on the area with the highest incidence of cases, despite the increase in anti-TNF use over the last years, its consumption was not parallel to the rise of leishmaniasis cases reported.

**Conclusions:** the disproportionate increase of leishmaniasis cases in patients with anti-TNF suggests the necessity to investigate and control other possible factors involved.

**Disclosure of Interest:** None declared

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#### SAT0403 BLOOD B CELL SUBSET PROFILE DISTURBANCE IN WHIPPLE'S DISEASE

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**Background:** Technological advances have improved phenotypical characterisation of blood cells, and flow cytometry is currently used in haematology, infectious disease, systemic auto-immune diseases. Abnormalities of blood B cell subset profile might provide a useful diagnostic tool in systemic auto-immune diseases, especially for primary Sjögren's Syndrome<sup>1</sup> in which the activated B cells to memory B cells ratio is increased. Nevertheless, we observed that some patients suffering from chronic infection had lymphocytes disturbances similar to those observed in primary Sjögren's Syndrome.

**Objectives:** Whipple's disease (WD) is a rare, systemic, disease caused by intracellular gram positive bacterium, *Tropheryma Whipplei* (TW). No previous study evaluated the role of B cells in WD. The aim of this study was to analyse whether the circulating blood B cell subset disturbances is characteristic of WD.

**Methods:** We collected characteristics of all patients coming for inflammatory rheumatism in our rheumatology department between April 2010 and December 2016. All of them had systematically routine examination, immunological tests, lymphocyte subsets in peripheral blood by flow cytometric analysis. We selected among this population those patients who also had PCR for *TW* for suspicion of WD, and compared the distribution of lymphocyte subsets of those with and without WD. Then, we evaluated their diagnostic value for WD using a ROC curve.

**Results:** Among 3494 patients with inflammatory rheumatism, 121 patients (212 visits) had a suspicion of WD and the diagnosis of WD was retained by an expert rheumatologist for 9 (7.4%) (22 visits). T cells and NK cells were not different whereas percentage of circulating memory B cells (IgD<sup>+</sup>CD38<sup>low</sup>) was lower (18.0%±9.7% vs 26.0±14.2%,  $p=0.041$ ) and the ratio of activated B cells to memory B cells higher (4.4±2.0 vs 2.9±2.2,  $p=0.023$ ), in patients compared with controls. More precisely, the analysis of the frequency of peripheral blood B cells showed that IgD<sup>+</sup>CD27<sup>-</sup> naïve B cells were higher (66.2%±18.2% vs 54.6±18.4%,  $p=0.047$ ) and IgD<sup>+</sup>CD27<sup>+</sup> switched memory B cells lower (13.3%±5.7% vs 21.4±11.9%,  $p=0.023$ ), in patients compared with the controls. The best diagnostic value was obtained for the IgD<sup>+</sup>CD27<sup>-</sup> naïve B cells (cut off 70.5, sensitivity 73%, specificity 80%).

**Conclusions:** Our study provides data on blood B cells disturbances and a first step towards understandings of immunological abnormalities in WD. These disturbances provide guidance for diagnosis and allow physiopathological hypothesis.

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#### SAT0404 CLINICAL CHARACTERISTICS AND OUTCOME AFTER TREATMENT OF A NATIONAL COHORT OF PCR-POSITIVE LYME ARTHRITIS

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**Background:** Lyme arthritis (LA) is a disseminated *Borrelia* infection whose prevalence is lower in Europe than in the USA, probably because of difference in *Borrelia* species ecology. Few data concerning treatment efficacy and long-term outcome of LA in Europe are available.

**Objectives:** The aim of our study was to describe clinical characteristics and treatment outcomes of a national cohort of patients with LA confirmed with synovial fluid PCR.

**Methods:** We conducted a retrospective observational study using the French Borrelia reference centre database. Patients presenting with a PCR positive for *Borrelia* DNA in their synovial fluid between 2011 and 2016 were included. PCR-positive patients were offered by their referring physician to participate to a standardised telephonic interview. Patients' medical files were also retrieved. The main objectives were to describe patient characteristics, disease presentation and outcomes after antibiotic treatment.

**Results:** Between 2011 and 2016, among 358 synovial fluids tested at the national reference centre, 38 were positive for *Borrelia* DNA. Among these patients, 35 were contacted (3 missing contact information). Median age was 36 years with 31% minors and 63% men. Tick exposure was reported by 88% patients whereas tick bite and erythema migrans were only reported in 40% (10/25) and 14% (3/21), respectively. The presentation was monoarticular in 91% (32/35) cases and oligoarticular in others. The knee was involved in 97% (34/35) cases and 21% presented fever. The diagnosis was often delayed with a median time from symptom onset to diagnosis of 3 months (range 1 to 112). The serology performed before or at the time of the PCR testing was IgG positive in all cases but only in IgM positive in 40%. All positive IgG serologies were also positive with Western-Blot. In the synovial fluid, the identified species of *Borrelia* were *B. burgdorferi sensu stricto*, *B. garinii* and *B. afzelii* in 54%, 29% et 17% of cases, respectively. Antibiotics prescribed were mostly doxycycline and ceftriaxone in 17 and 9 patients, respectively, sometime in combination. Follow-up data were available for 26 patients with a median follow-up time of 27 months (range 1–73). Full recovery was reported by 62% patients whereas 6 presented persistent non-inflammatory articular pain of the affected joint. One patient reported a chronic pain syndrome without objective sign of persistent infection (including a negative synovial fluid PCR). Three patients developed chronic inflammatory arthritis leading to the introduction of DMARDs.

**Conclusions:** Our study reports original data on Lyme arthritis in France. Treatment outcomes are usually good but a significant proportion of patients may develop chronic inflammatory arthritis.

**Acknowledgements:** All clinicians participating the study.

**Disclosure of Interest:** None declared

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#### SAT0405 FINDINGS OF A COHORT OF PATIENTS WITH CHIKUNGUNYA IN A COLOMBIAN POPULATION

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**Background:** Chikungunya virus is a Togaviridae family virus transmitted by mosquitoes, which generates febrile syndrome with joint pain. It has been widely studied for the findings of chronic inflammatory polyarthropathy similar to rheumatoid arthritis. In Colombia, an epidemic occurred between 2014 and 2015, which was studied in several cities. International meta-analyses have shown a prevalence of 32.13% in the follow-up cohorts greater than 18 months. At present, this issue has gained a new opportunity due to the appearance of new outbreaks in Italy and France, after 10 years of the first epidemic.

**Objectives:** To compare the clinical findings of a cohort of patients with Chikungunya in the subacute phase and the chronic phase.

**Methods:** Follow-up of 70 patients who attended Chikungunya in a Colombian population who were evaluated in person by a rheumatologist, initially at 40 days after the disease and after two years.

**Results:** The average age of the study participants was 59.88 years, being more frequent in women with 78.6% of the cases. 40% of the cases were older than 65 years, with the older adult population being a representative part of the cases. The history of osteoarthritis occurred in 11.7% of cases. There was no history of systemic lupus erythematosus.

The most frequent symptoms presented at the first visit (outbreak context) were as follows, in order: Joint pain (71.4%), morning stiffness (48.6%), Metacarpophalangeal compression test (51.2%). The most frequent symptoms in the second visit (two years after the outbreak) were: joint pain (74.2%), morning stiffness (21.4%) and metacarpophalangeal compression test (17.1%).

At the time of the second visit, the clinical findings were classified by diseases, according to the rheumatologist's assessment as follows: Post-Chikungunya polyarthropathy (17.1%), Fibromyalgia (10%), Carpal tunnel syndrome (17.1%), Osteoarthritis of knees (32.8), osteoarthritis of distal interphalangeal (20%), painful shoulder syndrome (17.1%), tenosynovitis (18.6%), gout (1.4%), sequelae of fracture of hip (1.4%), lateral epicondylitis (1.4%). 28.5% of the cases had no diagnosis of rheumatological pathology. Of the total cases, only 24.3% (17 people) had symptoms for more than 6 weeks.

**Conclusions:** Chikungunya virus infection increases the prevalence of joint and extra-articular rheumatological diseases in the Colombian population evaluated.

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#### SAT0406 CHIKUNGUNYA VIRUS AND THE RHEUMATOLOGY: OBSERVATION OF 76 CASES DURING AN EPIDEMIC IN BRAZIL

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**Background:** Chikungunya fever is caused by a virus of the family Togaviridae and the genus Alphavirus. The first epidemic occurred in Africa in 1952, transmitted by mosquitoes of the genus *Aedes*. In Brazil, the first cases were registered in 2014. Clinical manifestations include fever, polyarthralgia, joint oedema, arthritis and morning stiffness.

Diagnosis is confirmed by IgM/IgG serology for Chikungunya. The persistence of joint symptoms for a long time is an important feature of the disease.



**Objectives:** To evaluate the prevalence of rheumatologic manifestations in 76 patients with Chikungunya infection, during an epidemic occurred in 2016 in the city of Rio de Janeiro, Brazil.

**Methods:** To evaluate the prevalence of rheumatologic manifestations in 76 patients with Chikungunya infection, during an epidemic occurred in 2016 in the city of Rio de Janeiro, Brazil.

**Results:** Females were the most prevalent: 65 patients (85,5%); male sex: 11 (14,5%). The mean age of the patients was 57,17 years, The youngest at age 24 and the oldest 87 years old. The time between the onset of symptoms and the first consultation with a rheumatologist ranged from 11 days to the highest period of 40 weeks. Among articular symptoms, polyarthralgia occurred with higher prevalence (39 patients, 51,31%), affecting wrists, ankles, shoulders, knees and hands. Twenty six patients had arthritis (34,21%), Tendinopathy in 27 regions, being more common in shoulders, ankles and wrists and including De Quervain. Paresthesias occurred in 7 patients, prevailing carpal tunnel syndrome and one patient presented dactylitis. Symptoms persisted for months in all patients.

**Conclusions:** Chikungunya is an endemic disease in Brazil, with severe joint manifestations and chronic symptoms. Often there is delay in starting treatment with rheumatologist, resulting in worsening of the clinical picture.

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**Disclosure of Interest:** None declared

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#### SAT0407 MYCOBACTERIAL INFECTIONS IN A RHEUMATOLOGY UNIT OF A TERTIARY HOSPITAL

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**Background:** Many treatments for rheumatic diseases, especially the new ones such as anti-TNF or anti-IL6 therapies, are known to increase the risk of tuberculosis (TB) and nontuberculous mycobacterial (NTM) infections.

**Objectives:** To determine the incidence of mycobacterial infections in patients of the rheumatology unit in our hospital.

**Methods:** We retrospectively reviewed the results of microbiological studies for the detection of mycobacteria requested for patients of the Rheumatology service in our hospital from January 1, 2008 to October 1, 2017. We reviewed the clinical histories of the patients in whom a positive result was obtained. Different clinical and microbiological parameters were collected: age, gender, type of sample, isolated germ, infection location, antimicrobial treatment, main basal disease and immunosuppressive treatment received at the time of sampling.

**Results:** We reviewed 719 samples from 311 patients. The 28 samples that were positive for mycobacteria corresponded to 16 patients (50% males, with a mean age of 58.6 years). *M. avium complex* (MAC) was isolated in 10 patients, *M. tuberculosis complex* (MTB) in 4 patients and *M. goodii* in two cases. Seven clinical infections occurred (5% of the total studied patients), 4 due to MTB and 3 to MAC. The predominant involvement was pulmonary (5 patients, one of them also with spondylodiscitis); one patient had infectious oligoarthritis with cutaneous involvement and another patient lymph node involvement. Six of the 7 patients with mycobacterial infection were receiving chronic treatment with prednisone (or equivalent dose of corticosteroids)>5 mg/day (85.71%). In two of them adalimumab was associated, and methotrexate in other two.

**Conclusions:** The incidence of mycobacterial infections in patients with rheumatic diseases has increased, coupled with prolonged corticosteroid therapy – sometimes at high doses – and biological therapies. In our unit, an incidence of mycobacterial infections of 5% has been observed in the last 10 years. Most of the patients with clinical infection were under treatment with prednisone (or equivalent dose of corticosteroids)>5 mg/day. We conclude that the need for chronic corticosteroid therapy should be balanced carefully in each patient, trying to reduce the dose and/or suspend it as soon as possible.

**Disclosure of Interest:** None declared

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#### SAT0408 SAFETY OF CONCOMITANT TREATMENT WITH DENOSUMAB AND OTHER BIOLOGICAL DRUGS

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**Background:** Denosumab (DB) is a monoclonal antibody to RANK ligand that, like all biological drugs, can be associated with an increased risk of infections. However, there are few studies concerning the risk of infection in these patients treated concomitantly with DB and other biologic drugs.

**Objectives:** This study aims at determining whether the treatment with biological drugs and DB combined is associated with an increased risk of adverse effects in patients with autoimmune diseases.

**Methods:** Retrospective observational study of patients treated with DB combined with other biological drugs at the Hospital of León between 2010–2017. For proper patient selection, the data obtained from the medical prescription program of primary care and the data from the registry of outpatients and walk-in patients of hospital pharmacy were cross-referenced.

To determine the increased risk, a control group of patients treated both with bisphosphonates (BF) and with biological agents was selected.

The data collected in both groups were: age, sex, diagnosis, comorbidities and other prescribed drugs. Infection, tumour or other adverse effects appeared three months, six months, one year and two years after starting the concomitant treatment. When performing the statistical analysis, it was analysed the time elapsed until the first adverse effect appeared.

**Results:** A total n of 28 patients was registered. 16 were treated with BF and biological agents, and 12 were treated with DB and other biological drugs. The prevalence of women was higher in both groups (87.5% BF, 91.7% DB). The mean age at the beginning of the concomitant treatment was similar, being 69.1±8.5 years in the BF group and 69.7±7.1 years in the DB group. All patients treated with DB were diagnosed with RA. Regarding the comorbidities, it seems that those patients treated with DB had fewer CVRF than those treated with BF (68.8% HBP in BF versus 50% in DB, 37.5% dyslipidaemia in BF versus 33.3% in DB). The biological drugs prescribed to be used concomitantly with DB were: 49.7% anti-TNF $\alpha$ , 33.3% rituximab, 8.3% abatacept and 8.3% tocilizumab.

In addition, there were no significant differences regarding the application time of the concomitant treatment with biological agents in the BF (35.7±26.7 months) and DB (58.6±43.7 months) groups; being in both groups similar. By comparing both groups, it is observed that those patients treated concomitantly with DB and other biological drugs, have more infections and these appear earlier in time than in patients treated with BF and biological agents (p<0.005). Only one patient in the DB group had a tumour of pulmonary nature as an adverse effect.

There were no differences in the appearance of adverse effects in patients with other comorbidities or concomitant treatments.

**Conclusions:** It seems that the treatment of DB combined with other biological drugs is associated with a greater number of adverse effects, mainly caused by infections, and having an earlier appearance.

More studies and a larger sample would be necessary to confirm this association and to be able to prove the relationship between comorbidities and the use of other concomitant drugs with the appearance of adverse effects.

**Disclosure of Interest:** None declared

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#### SAT0409 AEROCOCCUS URINAE: FIRST REPORT OF SEPTIC OLIGOARTHRITIS AND SYSTEMATIC REVIEW OF AN EMERGING GERM IN MUSCULOSKELETAL INFECTIONS

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**Background:** Aerococcus are a bacteria not generally included in lists of musculoskeletal infections (MSK-I). They have been misidentified using standard techniques and can be detected by the sequencing of 16S rRNA (16S rDNA-PCR). Matrix-assisted laser desorption ionisation time-of-flight mass spectrometry (MALDI-TOF MS) has shown to be reliable.<sup>1</sup>

**Objectives:** To describe and analyse all documented cases of musculoskeletal infections caused by *Aerococcus* *urinae* and other *Aerococcus* sp.

**Methods:** In the framework of the study of a 63-years-old man with septic oligoarthritis caused by *Aerococcus* *urinae* (AU) (isolated in 2 synovial fluid samples), a systematic review was conducted to analyse all documented cases of aerococcal MSK-I (until December 2017); other manifestations of interest present in our case were also considered.

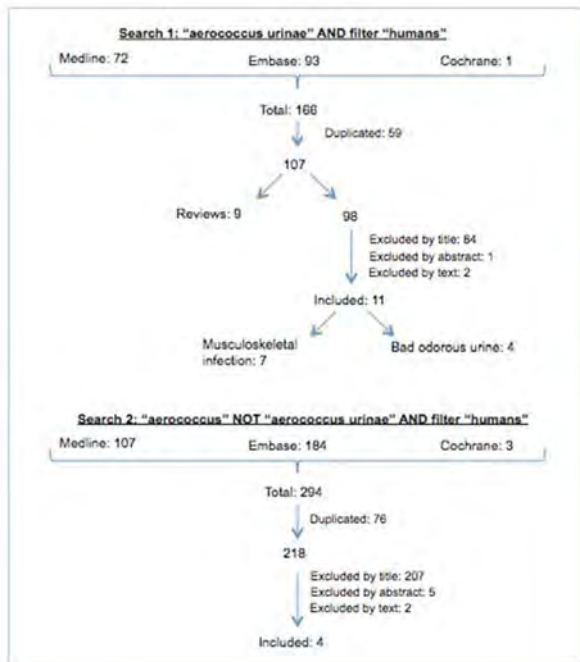
**Results:** A total of 166 articles were obtained for the term "Aerococcus urinae" and 294 for "Aerococcus" NOT "Aerococcus urinae" (both with filter "humans") (figure 1). Of them, 15 articles (16 cases) were selected and analysed:

- 8 AU MSK-I cases (our case is the 9th involving a MSK-I):
- 6 cases of spondylodiscitis (66%), 1 hip abscess, 1 septic arthritis in a prosthetic hip and our case with septic oligoarthritis.
- 66% were male and 77% were 60 years or older.
- 77% presented previous urinary tract disease, 55% previous urinary tract invasive procedures and 44% prostatic disease.
- AU was isolated in 4 of 6 cases that reported blood cultures and 2 of 4 cases with reported echocardiography presented infectious endocarditis.
- AU was not isolated in any of the 5 cases that reported urine cultures.
- 100% of cases were diagnosed after 2002 and 78% after 2010; 56% of them were diagnosed by **16 s rDNA PCR or MALDI-TOF MS** while a 33% did not provide enough information on the identification method used.

4 cases of AU with bad odorous urine (symptom present in our case): all were healthy paediatric boys that presented AU in urinary cultures without other associated symptoms; 100% were diagnosed after 2010 and 75% of them by **16 s rDNA PCR or MALDI-TOF MS**.

4 cases of *Aerococcus viridans* MSK-I: 2 spondylodiscitis, 1 knee arthritis and 1 case of hip septic arthritis; none was diagnosed via the methods previously described.

The analysed cases and previous reviews that report other AU invasive infections describes good response to beta-lactams and a synergistic effect with aminoglycoside. Our case was treated with intravenous Ampicillin (4 weeks) followed by oral Ciprofloxacin (7 weeks), due to a better bone penetration than oral beta-lactams.



Abstract SAT0409 – Figure 1. Flowchart.

**Conclusions:** – Similarly as in other invasive infections, AU **MSK-I** are more frequent in older males with previous urinary tract disease.

- The recent increased identification of AU **MSK-I** may well correlate with an increasing use of **MALDI-TOF MS** in clinical laboratories.<sup>1</sup>
- Despite its limitations, this systematic review summarises the only data available to date on aerococcus MSK-I and also suggest the likelihood of more frequent diagnosis in the near future.

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#### SAT0410 CHARACTERISTICS OF ABSCESSES DURING BRUCELLAR SPONDYLODISCITIS

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**Background:** Spondylodiscitis is a frequent and important complication of brucellosis. The occurrence of abscesses is common

**Objectives:** The aim of this study was to determine the characteristics of these collections and if there is an association between the diagnostic delay and their occurrence

**Methods:** we conducted a retrospective study of 27 patients admitted for Brucella spondylodiscitis over a period of 17 years [2000 and 2016]. Etiological diagnosis was made on a positive Wright agglutination test. All patients underwent a cross sectional imaging: spinal CT (13 cases) and/or spinal MRI (24 cases).

**Results:** twenty seven patients were included. Ten women and 17 men aged from 33 to 75 years. The most common symptoms were spinal pain (96,3%) and radiculargia (44,4%). The most frequently involved segments were the lumbar spine (59,3%) and the dorsal spine (18,5%). Three patients (11,1%) suffered from cervical spondylodiscitis. The physical examination showed no paravertebral swelling or neurological abnormalities. Seventeen patients had abscesses on the cross sectional imaging (63%). Epidural fluid collections were revealed in 10 cases (37%). Nine patients had psoas abscesses (33,3%) with a bilateral involvement in 3 cases (11,1%). Less frequently, a prevertebral (18,5%), peri-vertebral (18,5%) and intradiscal collections (3,7%) were detected. A statistically significant positive association was found between a longer diagnosis delay and the presence of abscess on spinal MRI (p=0.036).

**Conclusions:** Epidural and paravertebral abscesses during Brucellar spondylodiscitis are frequent, especially if the diagnosis is delayed. However, they are rarely associated with neurological damage and must be sought consistently on the MRI

**Disclosure of Interest:** None declared

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#### SAT0411 INVESTIGATIONS FOR THE DIAGNOSIS OF SEPTIC ARTHRITIS IN THE ACUTE SETTING. RESULTS FROM A SINGLE TERTIARY CENTRE OVER 5 YEARS

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**Background:** Septic arthritis is a rheumatologic emergency associated with significant morbidity and mortality<sup>1</sup>. Timely and accurate diagnosis in the emergency department is essential for early medical and surgical involvement.

**Objectives:** To examine the predictive value of investigations used to diagnose septic arthritis in the acute setting.

**Methods:** A retrospective chart review was conducted on all patients referred from the emergency department to the orthopaedic surgery service with a potential diagnosis of septic arthritis between June 2010 and December 2015 at the Austin Hospital in Melbourne, Australia. Data was collected regarding demographic details, risk factors, pathology results, antibiotic prescribing, joint aspirate and theatre samples.

**Results:** The study included 126 patients with 132 emergency department presentations involving 141 joints. The median age of patients was 70 (IQR 52.3–79.8); 86 (68.3%) were male. The most common joints involved were the knee (49.6%) and hip (17.7%). In 88 of the 132 presentations (67%), culture of the synovial fluid was positive. 19 of these 88 (22%) culture positive presentations had no classical risk factors for septic arthritis (joint prosthesis, previous septic arthritis, immunosuppressed, previous joint disease, intravenous drug use). 12 of the 88 (13%) culture positive patients had symptoms for longer than 4 weeks on presentation in contrast to 2 of the 44 (5%) in culture negative group. There were 8 presentations with multiple joints involved. None of these presentations were in the culture positive group. There was no evidence of a relationship between WCC and culture status (p=0.56) or CRP and culture status (p=0.64), either singly or when combined. There were 94 joint aspirations performed in 132 presentations. 30 (32%) joint aspirations required ultrasound guidance. 42 (45%) joint aspirations had antibiotics administered prior to sample collection. In the culture positive presentations 25 (28.4%) did not have a joint aspirate performed prior to surgical washout. Crystals were seen in 19 (30.2%) culture positive patients. 26 (29.5%) culture positive presentations had no growth on aspirate culture but had positive theatre cultures.

**Conclusions:** While septic arthritis is a common emergency presentation, there are few useful non-invasive diagnostic tests. Although risk factors aid in stratifying risk, duration of symptoms and inflammatory markers are poor differentiators. Neither the presence of crystals nor the absence of growth on aspirate culture exclude septic arthritis.

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**Disclosure of Interest:** None declared

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**SAT0412 TUBERCULOSIS REACTIVATION DURING BIOLOGICAL THERAPY**

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**Background:** With the increasing use and wide variety of biological therapies, there is a concomitant increase in concern for associated opportunistic infections, especially for *Mycobacterium tuberculosis*.<sup>1</sup>

**Objectives:** The aim of this study was to identify patients who have developed tuberculosis (TB) reactivation during treatment with a biological agent.

**Methods:** We included patients treated with biological agents in a tertiary Department of Rheumatology who had developed TB and were registered in the national registry for biological therapy. Demographic (urban or rural environment), clinical, therapeutic (biologic agent used) and comorbidities data were retrieved from the database.

**Results:** The database included 505 patients: 314 patients with rheumatoid arthritis (RA), 129 patients with ankylosing spondylitis (SA) and 62 patients with psoriatic arthritis (PsA).

Prior to the start of biological therapy, tuberculosis screening for latent infection was conducted in all patients. Eight patients (1,58%) were identified as being diagnosed with TB reactivation during biological therapy: 5 RA and 3 SA patients. Two had positive tuberculin test (TST) at baseline and required chemoprevention therapy prior to the initiation of the biological agent (respecting the preexisting guidelines).

Demographic data shows 62.5% patients from urban areas, 50% female and 50% male. Regarding comorbidities, one patient had biapical pachypleuritis (probably TB sequelae), antiphospholipid syndrome and pulmonary hypertension; one had chronic kidney failure and inflammatory bowel disease. The other six patients had minor comorbidities.

62,5% of patients were treated with oral corticosteroids combined with DMARDs. Four patients have been treated with infliximab, three with adalimumab and one with etanercept.

The average time to TB reactivation was 19.6 months (range 2 months to 52 months). Patients who had TB reactivation after two months of biologic therapy were treated with infliximab.

Four patients had developed pulmonary TB; one case was described as a miliary complicated with bacillary peritonitis (peritoneal biopsy). One patient had developed lymph node TB (lymph node biopsy) and one TB of the wrist (switch therapy was not chosen yet).

One particular case was of a patient that had developed TB meningitis with lymphadenitis and a compressible tuberculoma with spastic paraparesis. Switching of biological agent was chosen in 5 patients without another reactivation of tuberculosis. The biological agents chosen in 40% was rituximab, 20% was etanercept, 20% was adalimumab and 20% was infliximab.

**Conclusions:** Pulmonary and extrapulmonary TB reactivation equally occurred during anti TNF therapy. In some cases, reactivation of tuberculosis occurred even with chemoprevention.

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**Disclosure of Interest:** None declared

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**SAT0413 THE TREND OF INCIDENCE RATE, FREQUENCY, OUTCOMES AND HLA PHENOTYPE OF REACTIVE ARTHRITIS AND UVEITIS IN JAPANESE PATIENTS WITH BLADDER CANCER FOLLOWING INTRAVESICAL BCG THERAPY: A 20-YEAR, TWO-CENTRE RETROSPECTIVE STUDY**

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**Background:** Intravesical instillation of Bacillus Calmette-Guerin (iBCG) is used as an effective immunotherapy of bladder cancer. However it may have, as adverse event, a reactive arthritis (ReA) and the frequencies are known as about 0.5% to 1% in Western countries.

**Objectives:** To evaluate the trend of incidence rate, frequency and HLA phenotype of reactive arthritis (ReA), uveitis and other adverse events in Japanese patients with bladder cancer following iBCG therapy.

**Methods:** The clinical findings of Japanese patients who received iBCG (n=555 [250 and 305 in Kochi Medical School Hospital and Kurashiki Medical Centre, respectively]) for bladder cancer from March 1997 to February 2017 were retrospectively assessed, with specific attention to patients with ReA and uveitis. HLA phenotypes of patients with ReA were also looked. Moreover, iBCG-induced ReA diagnosed from 1997 to 2007 were compared with that from 2007 to 2017. Finally, outcomes of ReA patients were also evaluated.

**Results:** Patients' mean age was 72±10 years and male/female ratio was 438/117. Fever, haematuria, and dysuria were presented in 91/555 (16.4%), 121/555 (21.8%), and 196/555 (35.3%), respectively of all enrolled patients. Of the 555 cases, ReA and uveitis were revealed in 11/555 (2.0%) and 4/555 (0.7%). The protocol of iBCG therapy was stable over the 20 years. Notably, HLA-B27, -B35, -B39 and -B51 positivity was more frequent in ReA patients (9.1%, 36.3%, 36.3% and 63.6%, respectively) (p<0.05) than in healthy subjects without ReA (0.3%, 8.3%, 4.0% and 9.1%, respectively). All 4 cases with uveitis had ReA, and showed positive HLA-B27 (25%), -B39 (50%) and -B51 (25%). Moreover, the overall incidence of iBCG-ReA was not different between from 1997 to 2007 and 2007 to 2017. Finally, all ReA patients did not progress to chronic type and spondyloarthritis (SpA) as outcomes.

**Conclusions:** The 2.0% iBCG-induced ReA frequency in Japanese patients exceeds that in Western countries, and its incidence has been stable and all ReA did not progress chronic type and SpA over the last 20 years. HLA phenotype, especially HLA-B51 and -B39 alleles in addition to -B27, may be a risk factor in iBCG-induced ReA in Japanese patients.

**Disclosure of Interest:** None declared

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SATURDAY, 16 JUNE 2018

**SLE, Sjögren's and APS – clinical aspects (other than treatment)**

**SAT0414 DEVELOPMENT OF MALIGNANCY IN KOREAN SJÖGREN'S SYNDROME PATIENTS; WHOLE NATIONAL HEALTH INSURANCE DATA BASED ANALYSIS**

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**Background:** Though ocular and oral dryness are the main symptoms of Sjögren's syndrome, extraglandular manifestations including lymphoma were also developed. However, prevalence of Sjögren's syndrome was too low, most studies about lymphoma and malignancy were done on a small-scale.

**Objectives:** For more large-scale research about development of malignancy in Sjögren's syndrome, we analysed this with whole Korean National Health Insurance data which include more than 95% of the population of the Republic of Korea.

**Methods:** We compared the incidence of malignancy in newly diagnosed Sjögren's syndrome patients from 2004 to 2015 with age-sex matched controls and calculated hazard ratio (HR) with multiple Cox's model.

**Results:** Among 198,872 Sjögren's syndrome patients, cancer developed in 9883 patients (5% of newly diagnosed Sjögren's syndrome patients) after diagnosed Sjögren's syndrome. The duration from diagnosis of Sjögren's syndrome to development of malignancy was 5.4 year and their mean age was 55.2 years old. Malignancy incidence was higher in men, increased with age from the forties. It was also higher in patients who smoking or smoked, drinking more than 3times a week, and having history of malignancy (HR; 1.588, 95% CI; 1.405–1.794). The



most common malignancy in patients with Sjogren's syndrome was thyroid cancer. The risk of overall malignancy was not higher than that of the control. However, the incidence of prostate cancer (HR; 1.339, 95% CI; 1.076~1.667), thyroid cancer (HR; 1.320, 95% CI; 1.093~1.594) and lymphoma (HR; 1.620, 95% CI; 1.066~2.462) were higher and hepatocellular carcinoma (HR; 0.591, 95% CI; 0.455~0.767) was lower than that of control. Lymphoma developed in 305 patients (3.1% of total malignancy); 10 cases of Hodgkin lymphoma, and 290 cases of non-Hodgkin lymphoma. Gender, age, smoking, drinking, body mass index, fasting blood glucose, and proteinuria were not significantly different from the control group in lymphoma development.

**Conclusions:** Sjogren's syndrome patients' overall malignancy risk was not higher than that of control group. However, risk of lymphoma, prostate cancer, and thyroid cancer was higher than control group.

**Disclosure of Interest:** None declared

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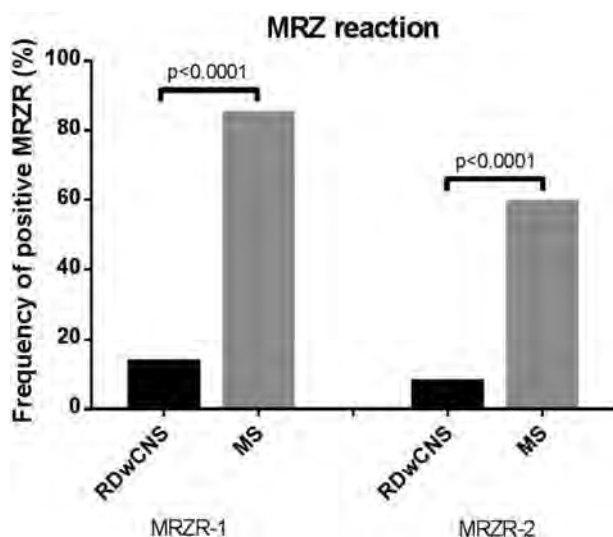
**SAT0415 THE MRZ REACTION HELPS TO DISTINGUISH RHEUMATOLOGIC DISORDERS WITH CENTRAL NERVOUS INVOLVEMENT FROM MULTIPLE SCLEROSIS**

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**Background:** Some rheumatologic disorders (RD) may initially manifest with central nervous system (CNS) affection, mimicking the clinical, magnetic resonance imaging, and cerebrospinal fluid (CSF) findings of multiple sclerosis (MS). Vice versa MS might be difficult to separate from some RD because of the presence of autoantibodies (e.g. ANA) in up to 50%. The MRZ reaction (MRZR), composed of the three respective antibody indices (AI) against measles, rubella, and varicella zoster virus, has been found positive frequently in MS patients. However, it is unclear whether the MRZR is helpful to distinguish rheumatologic disorders with CNS involvement (RDwCNS) from MS.

**Objectives:** To investigate the MRZ reaction as a diagnostic tool to distinguish patients with RDwCNS from patients with MS.

**Methods:** The MRZR was evaluated in 35 patients with RDwCNS and compared to 70 sex- and age- matched MS patients. An AI result  $\geq 1.5$  was indicative for intrathecal IgG production against the respective pathogen. Two previously established stringency levels, MRZR-1 ( $\geq 1$  of 3 AIs positive) and MRZR-2 ( $\geq 2$  of 3 AIs positive), were applied. CNS involvement of RDwCNS was defined as clinical manifestation with neurological symptoms and signs of inflammation in CSF analysis and/or cerebral/spinal magnetic resonance imaging (MRI). MRZR results were compared using the Fisher's exact test with  $p < 0.05$  for statistical significance.



**Abstract SAT0415 – Figure 1.** Frequency of positive MRZ reaction (MRZR-1 and MRZR-2) in patients with RDwCNS compared to MS patients.

**Results:** Within the RDwCNS group, 31 patients suffered from systemic lupus erythematosus, four had a small vessel vasculitis. In both groups 77.1% were female, mean age ( $\pm$ SD) was 43.2 years ( $\pm$ 18.7) in RDwCNS and 47.5 years

( $\pm$ 7.8) in MS ( $p = .n.$ ). All RDwCNS patients showed clinical symptoms indicative for CNS involvement and signs of inflammation in CSF analyses and/or MRI of the brain. In 52 MS patients autoantibody screening was performed. 42% were positive for ANA ( $n=20$ ) or ANCA ( $n=2$ ) in indirect immunofluorescence. Only 14.3% of RDwCNS patients had a positive MRZR-1 compared to 85.7% within the MS group ( $p < 0.0001$ ). The more specific MRZR-2 was positive in 60% of the MS patients compared to only 8.5% of the RDwCNS patients ( $p < 0.0001$ ). By using a higher threshold of  $>2.0$  for a positive AI, the prevalence of positive MRZR-2 dropped to 5.7% ( $n=2$ ) in the RDwCNS group compared to 54.3% ( $n=38$ ) in the MS group ( $p < 0.0001$ ). Oligoclonal bands were found in 94.3% of the MS and 28.6% of the RDwCNS patients ( $p < 0.0001$ ).

**Conclusions:** Considering the high specificity of the MRZR-2 for MS confirmed in this study, this laboratory test may be a helpful diagnostic tool to distinguish RDwCNS from MS.

**Disclosure of Interest:** None declared

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**SAT0416 LIFE-THREATENING PRIMARY SJÖGREN SYNDROME: CLINICAL CHARACTERISATION AND OUTCOMES IN 1535 PATIENTS (GEAS-SS REGISTRY)**

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**Objectives:** To analyse the clinical features and outcomes of patients presenting with life-threatening systemic disease in a large cohort of Spanish patients with primary Sjogren syndrome (SjS).

**Methods:** The GEAS-SS multicenter registry was formed in 2005 with the aim of collecting a large series of Spanish patients with primary SS. By January 2018, the database included 1535 consecutive patients fulfilling the 2002/2016 criteria. Life-threatening systemic disease was defined as an activity level scored as "High" in at least one ESSDAI domain.

**Results:** 209 (14%) were classified as presenting with a life-threatening systemic disease: 194 presented one ESSDAI domain classified as high, 14 two domains and only one presented three high activity domains. The high-ESSDAI domains included lymphadenopathy in 78 (37%) cases, CNS in 28 (13%), PNS in 25 (12%), pulmonary in 25 (12%), renal in 22 (10%), cutaneous in 18 (9%), articular in 18 (9%), haematological in 7 (3%) and muscular in 4 (2%); the most frequent clinical presentations in each domain were, respectively, parotid lymphoma ( $n=41$ ), focal neurological deficit ( $n=20$ ), ganglionopathy ( $n=11$ ), usual interstitial pneumonitis ( $n=9$ ), renal failure ( $n=11$ ), ulcerated cutaneous vasculitis ( $n=9$ ), symmetric polyarthritis ( $n=17$ ), severe thrombocytopenia ( $n=3$ ) and severe myositis ( $n=3$ ). With respect to therapeutic approach, 144 (69%) required glucocorticoids, 65 (31%) immunosuppressive agents and 42 (20%) biological therapies. During the follow-up, 36 (17%) patients died, mainly due to lymphoma ( $n=16$ ), pulmonary fibrosis ( $n=5$ ), end-stage renal failure ( $n=4$ ), CNS progressive disease ( $n=3$ ) and systemic vasculitis ( $n=3$ ).

**Conclusions:** A 14% of patients with primary SjS develop a potentially life-threatening systemic disease (mainly lymphoma, but also severe internal organ involvements including nervous system, the lungs and the kidneys). This subset of patients requires intensive therapeutic management with a mortality rate of nearly 20% of cases.

**Disclosure of Interest:** None declared

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**SAT0417 PREDICTIVE VALUE OF FETAL UMBILICAL ARTERY DOPPLER IN PRETERM BIRTH IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS**

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**Background:** Pregnancies in women with systemic lupus erythematosus (SLE) resulted in an increase of preterm birth. The predictive value of fetal umbilical artery Doppler examinations for adverse pregnancy outcomes has been reported, while not widely be assessed in SLE pregnant women.

**Objectives:** To examine the predictive value of the fetal umbilical artery Doppler on preterm birth in pregnant women with SLE.

**Methods:** A fetal Doppler ultrasound examination was performed on all fetuses during the third trimester (28–36 weeks of gestation). The Doppler flow parameters of umbilical arteries were recorded, including pulsatility parameter (PI), resistance index (RI), the peak value of umbilical arteries at end-systole (Vmax, also abbreviate as S) and the peak value of umbilical arteries at end-diastole (Vmin, also abbreviate as D). The value of S/D was automatically calculated. The clinical data from 160 live births of SLE patients were analysed retrospectively.

**Results:** The mean age of SLE patients at pregnancy was (29.7±3.7) years old (20–37). Totally, 52 patients (32.5%) were preterm births and 76 (47.5%) were fullterm births without any other adverse pregnancy outcomes. The rate of preterm birth before 34 weeks was 26.9% and the number changed to 73.1% for those preterm deliveries after 34 weeks. Iatrogenic preterm birth was the most common cause of preterm birth (30 cases), followed by spontaneous preterm birth (12 cases) and preterm premature rupture of membranes (10 cases). The pulsatility index (PI), resistance index (RI) as well as S/D value of SLE patients with pre-term delivery was higher than that of patients with full-term delivery ( $p < 0.05$ ). The area below the ROC curve for PI, RI and S/D was 0.6 (95%CI 0.5–0.7), 0.7 (95%CI 0.6–0.8) and 0.6 (95%CI 0.5–0.7), respectively. PI with cut-off value of 1.0 indicated the highest risk of preterm birth, with sensitivity of 34.6% and specificity of 84.2%. Regarding 0.7 as the cut-off value for RI to predict preterm birth, the sensitivity was 50.0% and the specificity was 81.6%. The optimal cut-off value for S/D was 2.8, at which sensitivity (50.0%) and specificity (81.6%) had the best combination.

**Conclusions:** Pregnancies in lupus still had an increased risk of preterm birth. Umbilical artery Doppler was a useful monitoring measure for preterm birth in lupus pregnancies.

**Disclosure of Interest:** None declared

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**SAT0418 CAN THE AUTOMATED NEUROPSYCHOLOGICAL ASSESSMENT METRICS (ANAM) PREDICT COGNITIVE IMPAIRMENT COMPARED TO A COMPREHENSIVE NEUROPSYCHOLOGICAL BATTERY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)?**

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**Background:** The diagnosis of cognitive impairment (CI) is often delayed requiring use of a comprehensive battery (CB). The Automated Neuropsychological Assessment Metrics (ANAM) is a computerised tool that can be used to screen for CI.

**Objectives:** To determine the ability of ANAM (v4) GNS Battery to predict CI in patients with systemic lupus erythematosus (SLE).

**Methods:** SLE patients (n=98), aged 18–65 years, attending a single centre between July 2016–April 2017 were recruited. Participants were administered the ANAM and CB on the same day. ANAM throughput scores were used to provide an estimate of cognitive efficiency. Patient scores on the ANAM and CB were compared to a normative sample of age and gender-matched healthy controls. The CB evaluates the following major cognitive domains: manual motor speed and dexterity, simple attention and processing speed, visual-spatial construction, verbal fluency, learning and memory (visuospatial and memory), and executive

functioning (untimed and timed). ANAM evaluates the following major cognitive domains: attention and processing speed, memory, visual-spatial processing, executive functioning, abstract language function and fine motor processing. CI was operationalized on the CB and ANAM as a z-score of  $\leq -1.5$  on  $\geq 2$  domains or a z-score  $\leq -2.0$  on  $\geq 1$  domains, or either.

The performance of ANAM was compared against the CB using different CI definitions. Descriptive analysis was used to determine prevalence, sensitivity (Sn), specificity (Sp), Positive Predictive Value (PPV) and Negative Predictive Value (NPV).

**Results:** Of the 98 patients (90.8% female), the mean age at SLE diagnosis was 28.5±10.2 and disease duration at enrolment was 15.5±10.0 years. Prevalence of CI using CB ranged between 40.0%–44.8% ( $z \leq -1.5$  on  $\geq 2$  domains and  $z \leq -2.0$  on  $\geq 1$  domains, respectively) and 55.2% for either. Prevalence of CI using the ANAM ranged between 30.8%–39.3% ( $z \leq -1.5$  on  $\geq 2$  domains and  $z \leq -2.0$  on  $\geq 1$  domains, respectively) and 43.0% for either.

ANAM Sn/Sp was 52/73% and PPV/NPV was 70/55% [based on  $z \leq -1.5$  on  $\geq 2$  domains or  $z \leq -2.0$  on  $\geq 1$  domains for ANAM and CB (corresponding for A+B and E+F in table 1)].

**Abstract SAT0418 – Table 1.** Performance of ANAM against the CB

	Definitions of CI	Comprehensive Battery (CB)			
		$z \leq -1.5$ on $\geq 2$ domains		$z \leq -2.0$ on $\geq 1$ domains	
		E Sn/Sp PPV/NNV	F Sn/Sp PPV/NNV	E+F Sn/Sp PPV/NNV	
ANAM	$z \leq -1.5$ on $\geq 2$ domains	A	45/81%	37/76%	37/80%
		B	62/68%	55/61%	69/51%
	$z \leq -2.0$ on $\geq 1$ domains	B	55/76%	49/72%	50/80%
		A	61/71%	58/65%	75/57%
	+B	55/69%	51/67%	52/73%	
			55/64%	55/64%	70/55%

Sn sensitivity; Sp specificity; PPV Positive Predictive Value/NPV Negative Predictive Value

**Conclusions:** ANAM is a promising tool for the assessment of CI in SLE. Future studies are required to determine if the sensitivity of the ANAM can be improved against the current CB.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.5573

**SAT0419 RENAL AND OVERALL SURVIVAL ANALYSIS IN A COHORT OF PATIENTS WITH LUPUS NEPHRITIS WITH UP TO 40 YEARS OF FOLLOW UP**

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**Background:** Although the prognosis has improved in the last decades, Lupus patients still have a 3-fold increase in mortality, compared with the general population. Lupus nephritis (LN) is one of the most severe manifestations of this complex systemic disease, occurring in up to 60% of patients.

**Objectives:** 1) To obtain the overall and renal survival curves for a LN cohort; 2) To investigate factors affecting survival; 3) To identify the causes of death in this cohort.

**Methods:** Single-centre retrospective observational study, including all patients with biopsy-proven LN, followed at UCLH Rheumatology department from 1975 to 2017. Individual clinical files were reviewed to obtain demographic, clinical, laboratory and pathological data. We also recorded data on treatment with corticosteroids, immunosuppressants and antimalarials. We analysed overall survival and renal survival through the Kaplan-Meier method. COX regression analyses were conducted to investigate possible predictors of shorter survival. Significance level was defined at 0.05.

**Results:** 209 patients were included (table 1). Cumulative survival at 5, 10, 15 and 20 years after the diagnosis of LN was 92%, 86%, 81% and 76%, respectively. Main causes of death were infection (29%), malignancy (21%) and cardiovascular (21%). Regarding progression to end-stage renal disease (ESRD), cumulative renal survival at 5, 10, 15 and 20 years was 94%, 86%, 79% and 72%, respectively. Table 2 shows the predictors of shorter survival identified for this

cohort. Image 1 represents the Kaplan-Meier curves according to the factors affecting renal survival.

**Abstract SAT0419 – Table 1.** Characterisation of the UCLH cohort of Lupus Nephritis patients

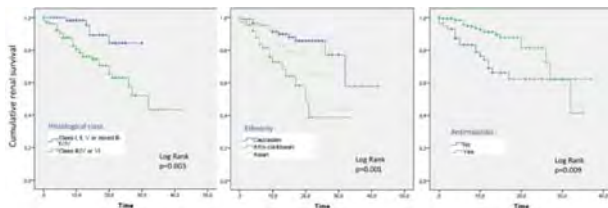
		ISN/RNP 2003 classification						Total
		I	II	III	IV	V	VI	
Total, N		2	18	38	97	38	2	209
Sex	F, N (%)	2	18	35	88	33	2	189 (90.4)
	M, N (%)	0	0	3	9	5	0	20 (9.6)
Ethnicity	Caucasian, N (%)	1	8	19	48	12	1	92 (44)
	Afro-Caribbean, N (%)	1	7	9	26	18	1	68 (32.5)
	Asian, N (%)	0	3	10	23	8	0	49 (23.4)
ESRD, N (%)		0	0	8	26	3	1	40 (19)
Deaths, N (%)		0	2	9	21	4	1	38 (18)
Age LN diagnosis, mean±SD		28.68±11.81						
Time FU since LN, mean±SD		12.95±8.96						

ISN/RNP: International Society of Nephrology and Renal Pathology Society; F: females; M: males; ESRD: end-stage renal disease; LN: Lupus nephritis; FU: follow-up.

**Abstract SAT0419 – Table 2.** Final models for predictors of shorter survival.

Multivariable COX regression	HR [95% CI] p
<b>Overall survival</b>	3.002 [1.461–6.171] 0.003
ESRD	
No antimalarials	2.942 [1.430–6.052] 0.003
Ethnicity (Afro-Caribbean)	2.656 [1.250–5.642] 0.011
Age at LN diagnosis	1.039 [1.012–1.067] 0.004
<b>Renal survival</b>	4.424 [1.542–12.695] 0.006
Histological class (III, IV or VI)	
Ethnicity (Afro-Caribbean)	3.727 [1.691–8.218] 0.001
No antimalarials	2.482 [1.237–4.982] 0.011

HR: hazard ratio; ESRD: end-stage renal disease; LN: Lupus nephritis



**Conclusions:** Cumulative survival rates and causes of death for this cohort are comparable with other cohorts of LN. ESRD confers the higher risk for death; African or Caribbean ethnicities and not taking antimalarials predict shorter overall and renal survival among these patients.

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**Disclosure of Interest:** None declared

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#### SAT0420 INCREASED RESISTANT HYPERTENSION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A RETROSPECTIVE COHORT STUDY

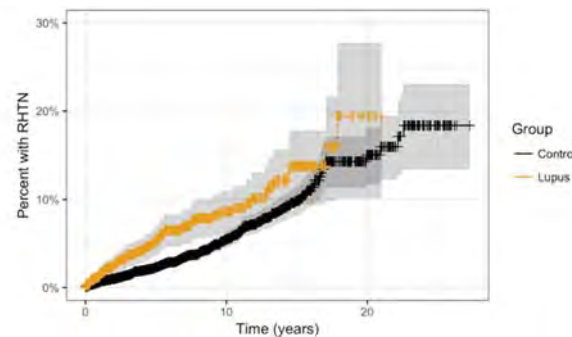
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**Background:** Resistant hypertension (RHTN) is characterised by blood pressure that remains  $\geq 140/90$  mmHg despite concurrent use of 3 antihypertensive drugs. In the general population, RHTN is associated with a 47% increased risk of cardiovascular events.<sup>1</sup> Patients with systemic lupus erythematosus (SLE) have increased cardiovascular risk; however, no research has addressed the incidence, prevalence, or risk factors associated with RHTN in patients with SLE.

**Objectives:** To compare the risk of RHTN in patients with SLE and frequency-matched controls without SLE; to define factors associated with RHTN in patients with SLE.

**Methods:** We used a validated algorithm (94% PPV) to identify patients with SLE from the electronic health records (EHR) at an academic medical centre.<sup>2</sup> We established a control cohort matched by age, race, and sex with a 5:1 control-case ratio. Follow-up began at first ICD9 code for SLE (cases) or first ICD9 code (controls) and continued until RHTN diagnosis or last note. RHTN diagnosis required either the simultaneous use of 3 antihypertensive drugs and a mean blood pressure  $\geq 140/90$  mm Hg in the following 6 months, or the use of  $\geq 4$  antihypertensive drugs simultaneously. We used logistic regression and Cox proportional hazards (CPH) models to compare risk of RHTN between groups, with CPH performed on incident cases only.

**Results:** We studied 1044 patients with SLE and 5241 controls (median age 42, [31–54] 90% female and 70% Caucasian). Of the total cohort, RHTN developed in 106 SLE patients (10%) and 278 controls (4%). The incidence rate of RHTN was 14.7 cases/1000 person-years in SLE patients compared to 7.4 in controls [HR 1.66, 95% CI, 1.25–2.21] (figure 1). In logistic regression models, RHTN was associated with older age, black race, male gender and end stage renal disease (ESRD). Patients with SLE had a higher risk of RHTN when adjusted for age, sex, race, calendar year, and ESRD [HR 1.53, 1.15–2.05]. In an analysis among SLE patients, RHTN was associated with mortality in an unadjusted model [HR 3.38, 2.20–5.18]. This association remained when age, sex and race were added to the model [HR 2.58, 1.65–4.03], but when ESRD, calendar year and creatinine were included, the association was no longer significant [HR 1.51, 0.91–2.51].



**Abstract SAT0420 – Figure 1.** Cumulative Incidence of RHTN in SLE versus Control Cohort

Log rank test:  $p=0.000391$

**Conclusions:** Patients with SLE have a higher risk of RHTN compared to frequency-matched controls. RHTN is an important comorbidity for clinicians to recognise in SLE, as it is associated with a 3.3-fold higher risk of mortality.

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[2] Barnado A, et al. *Arthritis Care Res* 2017;69(5):687–693.

**Acknowledgements:** VUMC's Synthetic Derivative supported by institutional funding and by the CTSA grant ULTR000445 from NCATS/NIH. CTSA awaUL1TR000445 from NCATS, The Rheumatology Research Foundation, Lupus Research Alliance and K-23 award from the NIAMS.

**Disclosure of Interest:** None declared

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#### SAT0421 LONG-TERM IMMUNOGENICITY OF A QUADRIVALENT HUMAN PAPILLOMAVIRUS VACCINE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Objectives:** To report the 5 year immunogenicity of a quadrivalent human papillomavirus (HPV) vaccine (GARDASIL) in patients with systemic lupus erythematosus (SLE).

**Methods:** Female SLE patients and healthy controls, aged 18–35 years, who received GARDASIL in the year 2011 and sero-converted 12 months post-vaccination were followed for the persistence of immunogenicity at 5 years. Antibodies to HPV serotypes 6,11,16,18 were repeated at 5 years using an IgG immunoassay developed on a Luminex microsphere platform (total IgG LIA; Merck Research Laboratory). The rate of sero-reversion was compared between



patients and controls. Factors associated with sero-reversion of the anti-HPV antibodies were studied by statistical analyses.

**Results:** 50 SLE patients (age 25.8±3.9 years) and 50 controls (25.8±3.9 years) were vaccinated with Gardasil in 2011. The sero-conversion rates of anti-HPV serotypes 6,11,16 and 18 in patients and controls were 82%, 89%, 95%, 76%, and 98%, 98%, 98%, 80%, respectively, at month 12 post-vaccination. Among those subjects who sero-converted and were available for follow-up, persistence of the antibodies to HPV serotypes 6,11,16 and 18 at 5 years was present in 24/27 (89%), 26/31 (84%), 32/34 (94%), 24/25 (96%) of the SLE patients and 32/33 (97%), 32/33 (97%), 32/32 (100%) and 23/24 (96%) of the controls, respectively. Moreover, antibody titers to HPV serotypes 6 and 16 at 5 years were significantly lower in SLE patients than controls. Seven (21%) SLE patients had sero-reversion of any one of the four anti-HPV antibodies (6,11,16 or 18) at year 5 post-vaccination. Patients who sero-reverted had received a significantly higher cumulative dose of prednisolone (13.0±5.34 vs 4.63±4.59 grams;  $p=0.002$ ), mycophenolate mofetil (1050±1180 vs 238±49.5 grams;  $p=0.007$ ) and tacrolimus (375±580 vs 268±1180 mg;  $p=0.03$ ) during the 5 year follow-up than those with persistence of immunogenicity. These sero-reverted patients had also received a non-significantly higher cumulative dose of cyclophosphamide (1.97±5.22 vs 0.43±2.24 grams;  $p=0.27$ ). In addition, sero-reverted patients had more SLE flares in the 5 year follow-up period compared to those with persistence of immunogenicity (3.14±1.21 vs 1.89±1.28;  $p=0.03$ ). Among 64 flares in patients with persistent anti-HPV antibodies and 26 flares in those with sero-reversion, renal flares occurred more frequently in the latter group of patients (16% vs 38%;  $p=0.02$ ).

**Conclusions:** Immunogenicity of the quadrivalent HPV vaccine was retained in 79% of SLE patients at 5 year post-vaccination. Antibody titers to HPV serotypes 6 and 16 were significantly lower in SLE patients than controls. Patients who had more SLE flares, especially renal flares, and had received higher cumulative doses of glucocorticoids, mycophenolate mofetil and tacrolimus were more likely to have sero-reversion of one or more anti-HPV antibodies. Re-vaccination of these patients should be considered.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.4332

**SAT0422** **INDIRECT PATHOGENIC ROLES OF CEREBROSPINAL FLUID ANTI-U1RNP ANTIBODIES IN THE PRESENCE OF ANTI-NR2 ANTIBODIES IN PATIENTS WITH NEUROPSYCHIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS**

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**Background:** Autoantibodies (auto Abs) and inflammatory mediators (IMs) in cerebrospinal fluid (CSF) may be involved in the pathogenesis of neuropsychiatric systemic lupus erythematosus (NPSLE). Previous studies indicated that anti-N-methyl *D*-aspartate receptor NR2 subunit (NR2) Abs have a pathogenic role in NPSLE by BBB disruption.<sup>Hirohata S, et al. Arthritis Res Ther. 2014</sup> We also reported the association between NPSLE and CSF-anti-U1RNP Abs (Sato, et al, A and R, 2010).

**Objectives:** In the present study, synergistic effects of these auto Abs, their associated IMs, and blood brain barrier (BBB) permeability are determined in NPSLE patients.

**Methods:** CSF samples were collected from 69 of NPSLE patients at their acute phase and 13 of non-NPSLE control after obtaining the written informed consent. CSF anti-NR2 and anti-U1RNP Abs were determined by ELISA. CSF IL-6, IL-8, and monokine induced by IFN- $\gamma$  (MIG) were measured by quantitative multiplex cytokine analysis. BBB permeability was evaluated by albumin quotient (Qalb).

**Results:** 1) CSF IL-6 levels were higher in CSF anti-NR2 Ab +ve (70±178 pg/mL) than in -ve (11±32,  $p=0.02$ ) patients and in controls (16±40,  $p=0.003$ ) and positively correlated with anti-NR2 Ab titer ( $r=0.42$ ,  $p=0.003$ ). Anti-U1RNP Ab positivity was not associated with CSF IL6 elevation. 2) CSF IL-8 levels were higher in CSF anti-U1RNP Ab +ve than in -ve (270±862 vs. 52±177 pg/mL,  $p=0.04$ ) patients. Anti-NR2 Ab positivity was not involved in CSF IL8 elevation. 3) CSF MIG levels were more elevated in both CSF anti-NR2 +ve (4483±11845 pg/mL,  $p=0.04$ ) and anti-U1RNP Ab +ve (5519±13504,  $p=0.03$ ) patients than in controls (115±125). 4) All the patients were divided into 4 groups: CSF anti-NR2 +ve/anti-U1RNP+ve (double positive [DP], n=9), anti-NR2 +ve/anti-U1RNP -ve (aNr2, n=15), anti-NR2 -ve/anti-U1RNP+ve (aU1RNP, n=9), and anti-NR2 -ve/anti-

U1RNP -ve (double negative [DN], n=36). In comparison between DP and aNr2 groups, anti-U1RNP Abs had a synergistic effect on CSF IL-6 elevation (150±260 vs. 18±44 pg/mL,  $p=0.03$ ) that is not directly associated with anti-U1RNP Ab positivity. In comparison with aNr2 group, both CSF IL-8 (543±1198 vs. 43±102 pg/mL,  $p=0.04$ ) and MIG (10104±17 748 vs. 1111±2584 pg/mL,  $p=0.03$ ) levels, which were positively correlated with CSF anti-U1RNP Ab titer, were more elevated in DP group. 5) Qalb was positively correlated with CSF IL-8 ( $r=0.51$ ,  $p<0.0001$ ) and MIG ( $r=0.44$ ,  $p=0.0003$ ), suggesting that CSF anti-U1RNP Ab positivity is involved in the BBB disruption. Actually, Qalb ( $\times 10^3$ ) tended to be higher in DP than in aNr2 group (13±9 vs. 9±8,  $p=0.06$ ) and CSF anti-NR2 Ab titer appeared to be more elevated in DP than in aNr2 group (81±47 vs. 57±21,  $p=0.06$ ).

**Conclusions:** The present study suggested that anti-NR2 and U1RNP Abs have synergistic effects on CSF IL-6 elevation in patients with NPSLE. CSF IL-6 level was associated with anti-NR2 Ab titers, which depend on BBB permeability. CSF anti-U1RNP Ab-mediated IL-8 and MIG elevation may induce BBB disruption followed by anti-NR2 Ab penetration into CSF.

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- [2] Yokoyama T, Fujii T, et al. Lupus 2014;23:635.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.3033

**SAT0423** **MOLECULAR PROFILES ASSOCIATE WITH CLINICAL DISEASE ACTIVITY AND INFORM PATIENT SUBSETTING IN ADULT SYSTEMIC LUPUS ERYTHEMATOSUS**

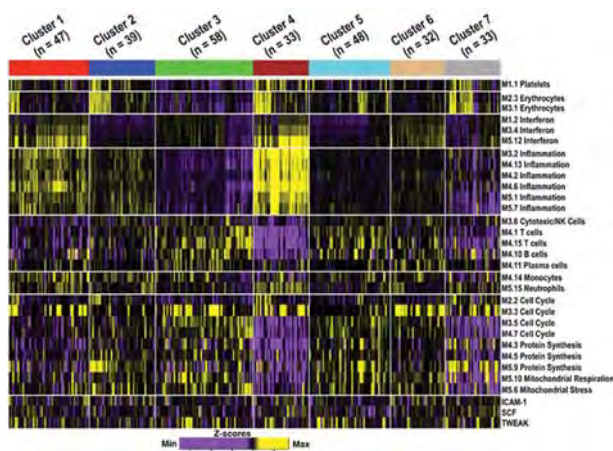
J.M. Guthridge, R. Lu, C. Arriens, T. Aberle, S. Kamp, M.E. Munroe, T. Gross, W. DeJager, S.R. Macwana, R.L. Bourn, S. Apel, H. Chen, E.F. Chakravarty, A. Thanou, J.T. Merrill, J.A. James. Arthritis and Clinical Immunology, Oklahoma Medical Research Foundation, Oklahoma City, USA

**Background:** Systemic lupus erythematosus (SLE) is characterised by remarkable clinical and pathophysiological diversity, hindering diagnosis, treatment and treatment development. Subsetting of patients based upon clinical presentations alone has not identified homogeneous groups of patients best treated with a directed therapeutic.

**Objectives:** To cluster SLE patients into more homogeneous subsets with common molecular pathway signatures, and to assess the clinical, therapeutic, and demographic features enriched in each cluster.

**Methods:** Serial or single plasma, serum and RNA samples (n=290) were collected from 198 SLE patients who met ACR classification. Disease activity was assessed by modified SLEDAI-SLEDAI at an average of 17 visits per patient. Transcriptional co-expression signature module scores were calculated from Illumina Beadchip Microarray gene expression data for 29 immune pathway related modules. Plasma soluble mediators (n=23) and 12 antinuclear autoantibodies (anti-dsDNA, chromatin, ribosomal P, Sm, Sm, SmRNP, RNP, Ro/SSA, La/SSB, centromere B, Scl-70 and Jo-1) were assessed by multiplex bead-based assay and ELISA. Spearman correlations were used for univariate and multivariate analysis using R. Patients were clustered on module signature scores and soluble mediators using random forest and tSNE.

**Results:** SLEDAI scores strongly correlated with interferon modules and were modestly correlated with plasmablast and select cell cycle signatures in this adult lupus collection. SLEDAI scores also correlated with soluble levels of IFN $\alpha$ , IL21, IL1 $\alpha$ , IL17A, IP10 and MIG. Random forest defined seven clusters of SLE patients with unique molecular phenotypes based upon gene co-expression module signatures and soluble mediators. Inflammation and interferon (IFN) signatures were elevated in Clusters 1 (moderately) and 4, with decreased T cell signatures in Cluster 4. The other clusters had lower IFN and inflammation signatures, but differed in their monocyte, plasmablast and T cell signatures. Clusters 1 and 4 had the highest SLEDAI scores, with high rates of anti-dsDNA, low complement, proteinuria and hematuria; these features were also prominent in Cluster 3, which lacked the IFN and inflammation signatures. Cluster 6 had the highest plasmablast module score, highest IL1 $\alpha$  levels, and SLEDAI scored rashes, but only moderate IFN and inflammation module scores. Cluster 2 had higher rates of SLEDAI scored alopecia, a slightly elevated inflammation signature, but lower interferon signature and lower soluble mediator levels.



Abstract SAT0423 – Figure 1. Modular transcriptional score profiles of seven SLE clusters

**Conclusions:** SLE subsets can be distinguished by a range of molecular profiles encompassing IFN, T cell, neutrophil, plasmablast, and inflammation co-expression signatures, as well as soluble mediators that vary with disease activity. Prospective longitudinal studies of these molecular profiles may inform clinical trial design and personalised disease management.

**Acknowledgements:** This work was supported in part by grants from the National Institutes of Health: U19AI082714, U01AI101934, U54GM104938, and P30AR053483.

**Disclosure of Interest:** None declared

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**SAT0424** **COMPLEMENT C4 GENE COPY NUMBER VARIATIONS BESTOW LARGE RANGES OF SERUM C4 PROTEIN LEVELS IN CHINESE PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) AND CONTRIBUTE TO ORGAN AND CARDIOVASCULAR DAMAGES OVER TIME**

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**Background:** Human SLE is characterised by fluctuating serum levels of complement proteins. There are frequent copy number variations (CNVs) of complement C4A and C4B genes among different individuals. Previously, we demonstrated that C4A deficiency is a strong genetic risk factor for SLE.

**Objectives:** To investigate how CNVs of C4 contribute to the great variability of C4 serum levels and how deficiencies of C4A or C4B modulate the clinical presentations, including organ damage, of SLE.

**Methods:** Our study population included 499 patients from Hong Kong, who fulfilled  $\geq 4$  of the 2013 ACR/SLICC criteria for SLE. Among them 93% were women, the mean age of SLE onset was  $32.8 \pm 13.0$  years, and SLE duration was  $14.4 \pm 7.6$  years. Gene copy numbers (GCNs) of total C4 (C4T), C4A and C4B were determined by real-time PCRs. Serial serum levels over the past 5 years for C4 and C3 of each patient were retrieved through the laboratory data registry system. Serum C4 and C3 levels are shown as mg/100 ml (unit). Clinical manifestations and organ damage of SLE were correlated with CNVs of C4 genes and serum levels. Continuous data between groups were compared by t-tests and categorical data by  $\chi^2$  analyses. Logistic regression was used to calculate odds ratios (ORs) and 95% confidence intervals for effects of C4 CNVs on cumulative clinical manifestations of SLE and accrued organ damage, adjusted for durations of disease.

**Results:** Serum levels for C4 varied from 1–84 units (Median: 17) and for C3 from 8–314 units (Median: 86). There was a very strong correlation between C4 and C3 protein levels ( $R=0.70$ ,  $p=5.3 \times 10^{-75}$ ). The GCN of C4T varied between 2 and 9 with a median of 4 copies (54%), followed by 2 and 3 copies (21%). Each additional gene copy correlated to an increase of 4 and 6 units for the mean and maximum serum C4 levels, respectively. A higher GCN of C4T ( $\geq 3$  vs  $<3$ ) was protective against the development of neuropsychiatric disorder over time [OR 0.45 (0.21–0.98),  $p=0.04$ ]. A high GCN of C4L ( $\geq 3$  vs  $<3$ ), or the absence of C4S (GCN=0), was negatively associated with the occurrence of thrombocytopenia

[OR 0.64 (0.42–0.97),  $p=0.04$ ]. A high GCN of C4B was associated with damage to any organ [OR 1.76 (1.05–2.93),  $p=0.03$ ], but a high GCN of C4A ( $\geq 3$  vs  $<3$ ) was associated with cardiovascular damage [OR 2.30 (1.06–5.00),  $p=0.04$ ]. Among the SLE patients studied, 18.3% had persistently low levels of C4 (mean  $\leq 10.0$  units). These patients mostly had GCNs of C4T=2 or 3 [OR 4.02 (2.47–6.56),  $p=4.7 \times 10^{-8}$ ], or C4B=0 or 1 [OR 3.06 (1.89–4.96),  $p=9.0 \times 10^{-6}$ ]. Patients with persistently low C4 levels had increased prevalence of mucosal ulceration [OR 2.09 (1.15–3.78),  $p=0.02$ ], lymphopenia [OR 1.76 (1.01–3.05),  $p=0.045$ ] and gastrointestinal disorders [OR 2.52 (1.31–4.84),  $p=0.005$ ].

**Conclusions:** CNVs of C4 genes confer great variability of serum C4 levels among SLE patients. While C4A deficiency contributes to genetic predisposition of SLE, persistently low levels of serum C4 among patients were strongly correlated with low GCN of total C4 and C4B deficiency. Elucidating C4-CNVs may have prognostic significance of SLE as high GCNs of C4B and C4A appeared to correlate with organ damage and cardiovascular disease, respectively.

**Disclosure of Interest:** None declared

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**SAT0425** **PHENOTYPING PRIMARY SJÖGREN'S SYNDROME (PSS) BY USING SALIVARY GLAND ULTRASONOGRAPHY: A STEP FORWARD TO INDIVIDUALISED THERAPIES**

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**Background:** Salivary gland ultrasonography (SGUS) has recently appeared as a useful tool to non invasively assess major salivary glands inflammation and damage in primary Sjögren's syndrome (pSS). To date, relatively few studies have evaluated the usefulness of SGUS in characterising different disease phenotypes ultimately providing information on which patients might be most likely to benefit from specific interventions.

**Objectives:** to explore whether SGUS may be useful in identifying different clinical-serological and histopathological phenotypes of pSS, ultimately allowing individualised treatments.

**Methods:** Sonographic data were retrieved from a large monocentric cohort of pSS patients. The echostructure of each gland on B-mode images was graded on a 5-point scale (0–4), and a SGUS score  $\geq 2$  was defined as pathological. Hypo-anechoic areas in the glands were defined as isolated ( $<25\%$  of the surface), localised (25%–50%) and diffuse-scattered ( $>50\%$ ). The biggest hypo or anechoic area in each gland was measured. SGUS was repeated in 150 pSS patients at least twice over a median follow up of 24 months. All the patients received a complete rheumatological assessment: disease activity was measured by the EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI), histopathological evaluation included the assessment of the focus score (FS) and the reporting of the number of germinal centre (GC)-like structures.

**Results:** We included in this study 311 patients (300 F: 11 M; median age=58 years (IQR, 49–69)) and median disease duration of 3 years (IQR 0–9). Out of them 136/311 (43.7%) had a SGUS score  $<2$  with none or isolated hypo-anechoic areas in their glands. Localised areas were detected in 87/311 (28%) pSS patients and diffuse-scattered areas in 88/311 (28.3%). Patients with none or isolated hypo-anechoic areas tended to be older ( $p=0.06$ ) and presented a significantly lower FS, a lower ESSDAI and a higher unstimulated salivary flow rate when compared to the other pSS patients ( $p<0.001$ ). Patients with localised or diffuse-scattered echographic pattern were more frequently seropositive for anti-Ro/SSA, anti-La/SSB and rheumatoid factor, presented more frequently hypergammaglobulinemia and low C3/C4 levels and had a higher frequency of GC-like structures in their biopsies ( $p<0.001$ ). Patients with diffuse-scattered hypo-anechoic areas presented the highest disease activity, in particular in the ESSDAI glandular, cutaneous and haematological domains. Notably, the SGUS score did not change over the time in patients who underwent repeated SGUS evaluations. Out of 136 patients with a SGUS score  $<2$ , 58 underwent additional SGUS evaluations over the follow-up. The SGUS was unchanged in all the cases and still associated with a low systemic disease activity.

**Conclusions:** This study highlighted the potential usefulness of SGUS in phenotyping pSS subsets. Patients with none or isolated hypoechoic areas in their glands are likely to present a low systemic disease activity during the disease course, being therefore candidate to less aggressive treatments. By contrast, patients with highest SGUS scores tend to present a more active systemic involvement and are candidate to receive a more aggressive therapy.

**Disclosure of Interest:** None declared

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**SAT0426 SERUM URIC ACID LEVELS PREDICT DAMAGE ACCRUAL IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS**

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**Background:** Serum uric acid levels have been reported as predictors of cardiovascular and renal morbidity,<sup>1</sup> and, of increasing the risk of renal damage in systemic lupus erythematosus (SLE) patients.<sup>2</sup> However, their role as predictors of global damage accrual in SLE patients has not been determined.

**Objectives:** To determine whether uric acid levels predict new damage in SLE patients.

**Methods:** This is a longitudinal study of SLE patients from a single centre cohort which started in 2012. Visits were performed every six months. Patients with at least two visits were included. Demographic and clinical characteristics as well as treatment were recorded at every visit. Disease activity was ascertained with the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI), and damage with the Systemic Lupus International Collaborating Clinics (SLICC)/American College of Rheumatology (ACR) damage index (SDI). Prednisone use was recorded as current daily dose and time of exposure. Immunosuppressive drugs and antimalarial use was recorded as current, past or never. All variables were ascertained at baseline, with the exception of new damage which was assessed at the subsequent visits. Univariable and multivariable Cox-regression models were performed to determine the impact of uric acid levels on the risk of new damage. Multivariable models were adjusted for age at diagnosis, disease duration, socioeconomic status, SLEDAI, SDI, comorbidities and use of prednisone, immunosuppressive drugs and antimalarials.

**Results:** Two hundred and thirty-seven patients were evaluated. The mean (SD) age at diagnosis was 35.9 (13.1) years, 220 patients (92.8%) were female, nearly all were Mestizo, disease duration was 7.3 (6.6) years. The mean SLEDAI and SDI were 5.1 (4.2) and 0.9 (1.3), respectively. The Charlson comorbidity index was 0.5 (0.9). Uric acid levels were 4.5 (1.4) mg/dl. The mean current prednisone dose 7.1 (6.4) mg/d. The duration of exposure to prednisone was 6.9 (6.2) years. Follow-up time was 3.1 (1.3) years. One hundred and twelve (47.3%) patients accrued damage during the follow-up. In univariable and multivariable analyses, uric acid levels predicted new damage [HR=1.14 (95% CI 1.01–1.28); p=0.026 and HR=1.16 (95% CI 1.00–1.34); p=0.043, respectively].

**Conclusions:** Higher uric acid levels predicted the development of new damage in our SLE patients.

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**SAT0427 PREDICTIVE VALUE OF FETAL UMBILICAL ARTERY DOPPLER IN ADVERSE PREGNANCY OUTCOMES IN PATIENTS WITH LUPUS NEPHRITIS**

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**Background:** Compared with the general population, patients with lupus nephritis (LN) are still at high risk of adverse pregnancy outcomes (APOs), including fetal loss, preterm birth and intrauterine growth retardation (IUGR). Umbilical artery is particularly important for placental perfusion and fetal development. Increased umbilical artery resistance could be traced by Doppler velocimetry, which could be used as a screening tool for placenta-related diseases. However, the predictive value in HDP of lupus pregnancies has not been widely assessed.

**Objectives:** To examine the predictive value of the fetal umbilical artery Doppler on adverse pregnancy outcomes (APOs) in pregnant women with lupus nephritis (LN).

**Methods:** The clinical data of 158 LN pregnant patients from the First Affiliated Hospital of Sun Yat-sen University were analysed retrospectively.

**Results:** Totally, 119 were diagnosed before pregnancy and 39 were newly diagnosed during pregnancy. One or more APOs occurred in 74.7% of patients with LN and 40 (25.3%) were without any APOs. Fifty-four of pregnancies (12.3%) resulted in fetal loss. A total of 55 pregnancies were preterm birth, 24 were IUGR, 14 were fetal distress and 9 were neonatal lupus. Doppler pulsatility index (PI), resistance index (RI) as well as S/D value were significantly higher in the APOs groups than in the patients without APOs (p<0.05). The area below the receiver operating characteristic (ROC) curve for PI, RI and S/D all was 0.7 (95%CI 0.6–0.8). PI with cut-off value of 0.9 indicated the highest risk of APOs, with sensitivity of 28.3% and specificity of 97.2%. Regarding 0.6 as the cut-off value for RI to predict APOs, the sensitivity was 45.7% and the specificity was 80.6%. The optimal cut-off value for S/D was 2.5, at which sensitivity (39.1%) and specificity (90.0%) had the best combination.

**Conclusions:** Pregnancies in LN were more prone to pregnancy loss and preterm birth. Umbilical artery Doppler was a useful monitoring measure for APOs in pregnancies of LN.

**Disclosure of Interest:** None declared

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**SAT0428 ASSOCIATION BETWEEN ORGAN DAMAGE AND HEALTH-RELATED QUALITY OF LIFE IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE): A SYSTEMATIC REVIEW**

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**Background:** Organ damage in SLE is associated with increased morbidity and mortality. The comorbid burden of SLE involves various organ systems and may be associated with pain, fatigue, difficulty with daily activities (including school and work), and emotional well-being, all contributing to high rates of disability.

**Objectives:** We conducted a systematic literature review evaluating association between SLE-related organ damage and health-related quality of life (HRQOL).

**Methods:** A systematic literature search (January 2000–February 2017) of PubMed, EMBASE, Cochrane Library, and Latin American and Caribbean Health Sciences Literature was conducted to identify studies evaluating association between organ damage (measured by SLICC/ACR Damage Index [SDI]) and HRQOL for adults with SLE. Instruments examined include the Short Form 36 (SF-36: Physical Component Summary [PCS] and Mental Component Summary [MCS], 15 studies); EuroQol 5 Dimensions Questionnaire (EQ-5D) and Fatigue Severity Scale (FSS, 2 studies each); and the LupusQoL, Multidimensional Fatigue Inventory (MFI), Quality of Life Questionnaire of the European Foundation for Osteoporosis (QUALEFFO), and WHO Quality of Life Scale (WHOQOL-BREF) (1 study each).

**Results:** From 10 420 articles screened, 20 studies were included (3 prospective cohort studies, 17 cross-sectional studies). The 3 prospective studies evaluated HRQOL by the SF-36, 2 of which modelled SDI as a binary variable. For patients without damage at baseline, any damage accrual over 2 years was associated with a 5.5-fold increased risk of decreased HRQOL compared with those who did not develop new damage (SF-36 overall relative risk [RR] 5.5 [95% CI: 1.1–26.6; p=0.03]). A similar trend toward increased risk of decreased HRQOL was observed with PCS: RR 2.5 (95% CI: 0.6–10.0; p=0.19); and MCS: RR 4.6 (95% CI: 0.9–22.8; p=0.06). Any damage at baseline was associated with 67% decreased odds of achieving minimum clinically important improvement in SF-36 PCS: odds ratio [OR] 0.33 (95% CI: 0.13–0.85; p=0.02). However, no association was observed for MCS. When SDI was modelled as a continuous variable, increasing damage was associated dose-dependently with decreased SF-36 PCS compared with SDI=0; SDI 1: –2.64, p<0.001; SDI 2: –2.86, p=0.003; SDI 3: –5.94, p<0.001; SDI 4: –6.35, p<0.001; and SDI 5+: –8.11, p<0.001. In cross-sectional evaluations, increasing SDI was modestly correlated with decreased HRQOL: SF-36 correlation coefficient score range: –0.12 to –0.30; SF-36 regression coefficient score range: –0.011 to –4.65; LupusQoL correlation coefficient –0.31, p<0.01; and WHOQOL-BREF regression coefficient –0.06, p=0.57. Increasing fatigue displayed weak correlation with damage: FSS correlation coefficient range: 0.04 to 0.15.

**Conclusions:** Organ damage was associated with decreased HRQOL in most studies evaluated. This review determined heterogeneity in HRQOL instruments and methodology across studies. Improving construct validity of instruments and



consistent evaluation will improve the ability to estimate the burden of SLE and enhance efforts to improve HRQOL in SLE.

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SAT0429

#### HOW PHENOTYPE OF THE SMALL FIBRE NEUROPATHY (SFN) IN PRIMARY SJÖGREN SYNDROME (PSS) DIFFERS FROM OTHERS CAUSES OF SMALL FIBRE NEUROPATHY?

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**Background:** Small fibre neuropathy (SFN) is a peripheral neuropathy characterised by neuropathic pain associated with normal routine nerve conduction study but rarefaction of intraepidermal nerve fibres (IEFN). Primary Sjögren Syndrome (pSS) is one of the many etiology of SFN.

**Objectives:** To compare phenotype of SFN in pSS, transthyretin (TTR) familial amyloidosis and idiopathic SFN. To describe evolution of SFN in pSS.

**Methods:** All patients referred since October 2012 with a biopsy-proven SFN associated with either pSS (ACR/<sup>EULAR</sup> 2016 criteria), TTR-amyloidosis or idiopathic were included in this monocentric retrospective study. Diagnosis of SFN was confirmed by normal nerve conduction study and abnormal lower limb skin biopsies. All patients undergo standardised diagnosis procedures during an out-patient day-clinic, pSS patients were further followed and undergo a second evaluation. Characteristics of SFN were compared between 3 groups: pSS, TTR-amyloidosis and idiopathic, and outcome of pSS associated SFN was analysed.

**Results:** We included 15 patients with pSS (13 (86.7%) women, median age: 56 years [IQR:46.5–63.5], 7 (46.7%) anti-SSA positive, 12 (80%) focus score  $\geq 1$ , 17 with TTR-amyloidosis (7 (41.2%) women, median age: 47 years<sup>35–56</sup>) and 11 with idiopathic SFN (7 (63.6%) women, median age: 47 years [36–56.5]). Patients with pSS had a median ESSDAI of 5.5–8. One had monoclonal gammopathy, 5/13 (38.5%) rheumatoid factor, 2/13 (15.4%) hypergammaglobulinemia and none had cryoglobulin. Time from first neurologic symptoms to diagnosis of SFN was significantly higher for pSS (29 months [8.5–65]) and idiopathic group (35 months [11.5–65]) than for TTR group (6 months [0–15]). Clinical presentation was length dependant in only 2 (13.3%) patients with pSS compared to 10 (58.8%) in TTR amyloidosis ( $p=0.01$ ) and 2 (18.2%) in idiopathic group ( $p=1$ ). A “patchy” presentation (defined by asymmetrical and/or proximal symptoms involving limb, trunk and/or face), was significantly more frequent in pSS than in TTR amyloidosis (7 (43.7%) vs. 1 (5.9%);  $p=0.01$ ). This more frequent non-length dependant course was confirmed on skin biopsies with an IEFN at proximal site <IEFN at distal site in 7/14 (50%) pSS patients compared to 2/15 (13.3%) in TTR ( $p=0.05$ ) and 1 (9.1%) in idiopathic ( $p=0.04$ ) groups. Lauria score was significantly higher in pSS than in TTR, (5 [4–7.5] vs. 2.2–5  $p=0.007$ ), mainly due to items of sicca symptoms ( $n=14/15$ ) and peripheral limb pain ( $n=13/15$ ). Ten patients with pSS have been reassessed with a median follow up of 31 months [16.5–53.5]. At reassessment, the Lauria score did not significantly differ (6<sup>5–7</sup>) from initial score, patchy presentation was still predominant 5 (50%). Patients did not evolve through large fibre neuropathy, except one patient who had received a neurotoxic chemotherapy by platin for ovarian cancer, between the 2 evaluations.

**Conclusions:** pSS patients with SFN had a low frequency of serum B cell activation biomarkers. Compared to other causes of SFN, in pSS SFN was characterised by a more frequent non-length dependant and patchy presentation and a higher Lauria score. After a median follow-up of 31 months, SFN in pSS were stable in the time and did not evolve through large fibre neuropathy.

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SAT0430

#### ASSESSMENT OF ACR AND SLICC CLASSIFICATION CRITERIA IN THE ASIA PACIFIC LUPUS COLLABORATION COHORT

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**Background:** Patients with systemic lupus erythematosus (SLE) are commonly assessed using the classification criteria developed by the American College of Rheumatology (ACR), or more recently by the Systemic Lupus International Collaborating Clinics (SLICC). Although SLE is highly prevalent and severe in Asians, no comparison of patients meeting these criteria in predominantly Asian SLE patients has been performed.

**Objectives:** To compare patients meeting the ACR and SLICC classification criteria in the Asia Pacific Lupus Collaboration (APLC) cohort.

**Methods:** All patients fulfilled either the ACR (1997) criteria ( $\geq 4$  of 11 items) or SLICC criteria ( $\geq 4$  of 17 items, including  $\geq 1$  clinical and  $\geq 1$  immunologic criteria, or biopsy-proven lupus nephritis (LN) +  $\geq 1$  immunological criterion), evaluated at enrolment. Demographic and clinical data were compared using Kruskal Wallis (for medians) chi-squared (proportions) tests.

**Results:** 1735 patients were studied with a median (IQR) (range) follow up of 795 [532, 1087] (0, 1443) days. 1716 (98.9%) and 1668 (96.1%) patients met SLICC and ACR criteria respectively. 1649 (95%) patients met both criteria, 67 (3.9%) patients met SLICC criteria only and 19 (1.1%) patients met ACR criteria only. Patients in ACR-only and SLICC-only groups were significantly older than those who met both criteria (ACR-SLICC group); ACR-only patients had longer observation period (table 1), 15/67 SLICC-only patients had non-scarring alopecia, which is not an ACR item, and 14 had LN with  $\geq 1$  immunologic criterion. Discrepancies between the 19 ACR-only patients and the ACR-SLICC group were predominantly observed in the immunological criteria. Both ACR-only and SLICC-only patients had lower SLEDAI-2k score at recruitment when compared to ACR-SLICC group, and a fewer SLICC-only patients were in flare (table 1). During the observation period, SLICC-only patients had the lowest time-adjusted mean (TAM) SLEDAI-2k and prednisolone dose; lowest proportions of flares and damage accrual, and highest proportion of patients achieving Lupus Low Disease Activity State (LLDAS) at least once. In contrast, ACR-only patients had the highest proportion of patients experiencing flares and least proportion of achieving LLDAS (table 1).

	ACR & SLICC n=1649	ACR only n=19	SLICC only n=67	p-value
<b>Demographics</b>				
Age at enrolment (years)	40 (31, 50)	50 (37, 59)	46 (34, 55)	0.003
Study observation period (years)	2.2 (1.5, 3.0)	3.4 (2.4, 3.5)	2.1 (1.7, 2.8)	0.005
Females, n (%)	1533 (93.0%)	18 (94.7%)	64 (95.5%)	0.7
<b>Clinical indications at recruitment</b>				
PGA	0.5 (0.2, 1.0)	0.5 (0.2, 0.8)	1.0 (0.3, 1.2)	0.09
SLEDAI-2k score	4.0 (2.0, 6.0)	2.0 (0.0, 4.0)	2.0 (1.0, 4.0)	0.03
Mild/mod./severe flare, n (%)	272 (16.5%)	4 (21.1%)	3 (4.5%)	0.03
Organ damage, n (%)	679 (41.2%)	10 (52.6%)	25 (37.3%)	0.5
In LLDAS, n (%)	769 (46.7%)	7 (36.8%)	39 (58.2%)	0.12
<b>Longitudinal clinical indications</b>				
Time adjusted mean PGA	0.4 (0.2, 0.8)	0.4 (0.2, 0.6)	0.5 (0.2, 0.9)	0.7
Time adjusted mean SLEDAI	3.4 (1.5, 5.4)	2.6 (1.0, 5.3)	2.0 (1.3, 4.0)	0.009
Time adjusted mean prednisolone (mg)	5.0 (2.1, 8.9)	4.1 (2.5, 8.9)	3.0 (0.0, 6.6)	0.004
Mild/mod./severe flare ever, n (%)	954 (57.9%)	12 (63.2%)	21 (31.3%)	<0.001
Damage accrual, n (%)	241 (14.6%)	3 (15.8%)	6 (9.0%)	0.4
LLDAS ever, n (%)	1282 (77.7%)	12 (63.2%)	58 (86.6%)	0.07

**Conclusions:** We observed a high overlap between the two classification criteria, but the use of both criteria captured a larger cohort overall. In this cohort, patients meeting SLICC but not ACR criteria had less active disease.

**Disclosure of Interest:** None declared

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SAT0431

### THE ACR-EULAR CLASSIFICATION CRITERIA IN PRIMARY SJÖGREN'S SYNDROME: THE CONTRIBUTING ROLE OF ULTRASOUND

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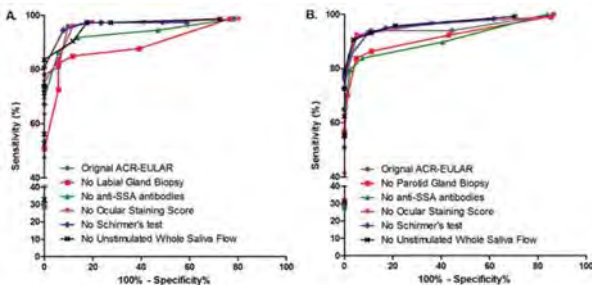
**Background:** Salivary gland ultrasound (SGUS) is cheap, non-invasive and easy to perform in an outpatient setting. The ACR-EULAR criteria were recently developed to reach international consensus regarding the classification of primary Sjögren's syndrome (pSS), but SGUS is not yet included as a classification item.

**Objectives:** To assess the performance of the ACR-EULAR criteria when salivary gland ultrasound (SGUS) replaces current items, in a large cohort of patients clinically suspected or diagnosed with pSS in daily clinical practice.

**Methods:** Included were all consecutive outpatients who underwent SGUS between October 2014 and July 2017 and had a complete data-set on all ACR-EULAR items. Classification according to the criteria was determined separately in patients who were subjected to a labial or parotid gland biopsy. For SGUS, the average score for hypoechogenic areas in the parotid and submandibular glands on one side was applied (range 0–3)<sup>1</sup>. The optimal cut-off value for our SGUS score was determined using ROC analysis. Clinical diagnosis by the treating physician was used as gold standard. Area under the curve (AUC), absolute agreement, sensitivity and specificity of the original and adjusted ACR-EULAR criteria sets were determined.

**Results:** Of the 363 consecutive patients, 243 patients had a complete data-set, of whom 147 patients were diagnosed with pSS. Accuracy of SGUS to predict clinical diagnosis was good, with an AUC of 0.860 and optimal cut-off value of  $\geq 1.5$ . When applying a weight of 1 point for a positive SGUS, the cut-off value of the ACR-EULAR criteria to discriminate between pSS and non-pSS remained 4, irrespective of the type of biopsy used.

In patients who underwent a labial gland biopsy (n=124), the original ACR-EULAR criteria showed an AUC of 0.965 (figure 1A). Absolute agreement with clinical diagnosis was 94.4%, sensitivity was 95.9% and specificity was 92.2%. When SGUS replaced the labial gland biopsy, absolute agreement was 87.9%, sensitivity was 82.2% and specificity was 96.1%. When SGUS replaced anti-SSA antibody status, absolute agreement was 89.5%, sensitivity was 86.3% and specificity was 94.1%. When SGUS replaced the ocular staining score (OSS), Schirmer's test or unstimulated whole saliva flow (UWS), absolute agreement varied between 89.5%–93.5%, sensitivity varied between 90.4%–95.9% and specificity varied between 88.2%–92.2%. In patients who underwent a parotid gland biopsy (n=198), similar results were found (figure 1B).



**Abstract SAT0431 – Figure 1.** Ultrasound replacing current ACR-EULAR items in patients who underwent a labial gland biopsy (A) or a parotid gland biopsy (B).

**Conclusions:** SGUS cannot be used as a replacement for salivary gland biopsy or anti-SSA antibody status in the ACR-EULAR criteria because of a substantial reduction in sensitivity. For diagnostic purposes, a high sensitivity is preferred over a high specificity.

Replacement of the OSS, Schirmer's test or UWS by SGUS only resulted in negligible changes in accuracy of the ACR-EULAR criteria. With SGUS being able to replace one of these function tests, clinicians are offered more options that could lead to fulfilment of the ACR-EULAR criteria.

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[1] Mossel, et al. Ann Rheum Dis 2017; Published online first at December 12.

**Disclosure of Interest:** None declared

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SAT0432

### MEMBRANOUS VERSUS PROLIFERATIVE LUPUS NEPHRITIS: TWO DIFFERENT DISEASES?

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**Background:** Lupus nephritis (LN) is currently classified according to the 2003 International Society of Nephrology/Renal Pathology Society (ISN/RPS) classification system, which is based on histology. Most patients have proliferative lupus nephritis (PLN), which has been the most studied type of LN. Membranous lupus nephritis (MLN) is less frequent, accounting for 10%–20% of the cases. In some patients there is a combination of the two types.

**Objectives:** To compare MLN and PLN with respect to demographic, clinical and laboratory characteristics.

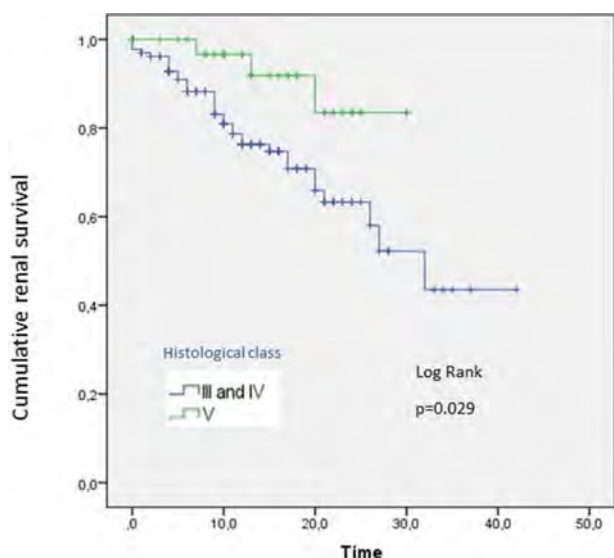
**Methods:** Single-centre retrospective observational study. All patients with biopsy-proven proliferative (class III and IV), membranous (class V) and mixed (class III or IV+V) LN (according to the 2003 ISN/RPS classification), followed at UCLH Rheumatology department from 1975 to 2017, were included. Individual clinical files were reviewed to obtain demographic, clinical, laboratory and pathological data. We also recorded data on treatment with corticosteroids, immunosuppressants and antimalarials. We compared groups using Pearson's chi-squared test for qualitative variables and Mann-Whitney test for quantitative variables. Renal survival was analysed through the Kaplan-Meier method. Significance level was defined at 0.05.

**Results:** 187 patients were included (table 1). Age at diagnosis was not significantly different between groups (p=0.474). The groups differ regarding ethnicity – higher proportion of Caucasians with PLN versus higher proportion of Afro-Caribbeans with MLN. Patients with MLN present with higher C3 levels and significantly lower anti-dsDNA levels than the ones with proliferative changes. Thirty-four patients with PLN, 3 with MLN and 2 with mixed nephritis, progressed to end-stage renal disease. Cumulative renal survival rates at 5, 10, 15 and 20 years were 91, 81, 75% and 66% for PLN and 100, 97, 92% and 84% for MLN, respectively (Image 1).

**Abstract SAT0432 – Table 1.** Comparison between the three groups of patients

		Class III and IV	Class V	III+V or IV+V	p
<b>Total, N</b>		135	38	14	
<b>Sex</b>	<b>F, N (%)</b>	123 (91)	33 (87)	11 (79)	0.303
	<b>M, N (%)</b>	12 (9)	5 (13)	3 (21)	
<b>Ethnicity</b>	<b>Caucasian, N (%)</b>	67 (50)	12 (32)	3 (21)	<b>0.044</b>
	<b>Afro-Caribbean, N (%)</b>	35 (26)	18 (47)	6 (43)	
	<b>Asian, N (%)</b>	33 (24)	8 (21)	5 (36)	
<b>uPCR at LN diagnosis, median; IQR</b>		261.5; 372	254.0; 276	143.0; 195	0.663
<b>Creatinine at LN diagnosis, median; IQR</b>		73.5; 40	54.5; 17	73; 58	0.106
<b>Albumin at LN diagnosis, median; IQR</b>		32.5; 13	31; 9	35; 4	0.624
<b>C3 at LN diagnosis, median; IQR</b>		0.61; 0.34	0.81; 0.57	0.64; 0.32	<b>0.002</b>
<b>Anti-dsDNA at LN diagnosis, median; IQR</b>		863.0; 1616.75	80; 149.5	296; 242	<b>0.000</b>
<b>Ever Low C3, N (%)</b>		107 (80)	35 (92)	11 (79)	0.203
<b>Ever anti-dsDNA positive, N (%)</b>		111 (83)	32 (84)	12 (86)	0.950
<b>Ever anti-Sm positive, N (%)</b>		25 (19)	16 (42)	6 (43)	<b>0.004</b>
<b>Ever anti-RNP positive, N (%)</b>		42 (31)	19 (50)	8 (57)	<b>0.030</b>
<b>Ever anti-Ro positive, N (%)</b>		54 (40)	16 (42)	10 (71)	0.081
<b>Ever anti-La positive, N (%)</b>		21 (16)	3 (8)	4 (29)	0.168
<b>Use of antimalarials, N (%)</b>		82 (66)	27 (73)	9 (69)	0.732
<b>Use of immunosuppressants, N (%)</b>		121 (95)	35 (95)	14 (100)	0.669
<b>Use of corticosteroids, N (%)</b>		125 (97)	36 (95)	13 (93)	0.668

F: females; M: males; uPCR: urinary protein-creatinine ratio; LN: Lupus nephritis; FU: follow-up



**Conclusions:** In spite of presenting in the context of the same autoimmune systemic disease, PLN and MLN appear to be very different entities, showing significant differences regarding serologic profiles and renal survival.

**Disclosure of Interest:** None declared

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SAT0433

#### APPLICATION OF THE DORIS ALGORITHM FOR THE DEFINITION OF DISEASE REMISSION OVER A 2-YEAR PERIOD IN A COHORT OF ITALIAN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Systemic Lupus Erythematosus (SLE) is characterised by a fluctuating course. To achieve sustained remission is the ultimate goal of maintenance treatment. However remission is difficult to define in SLE. In 2014, an international Task Force named DORIS proposed four definitions of remission.<sup>1</sup>

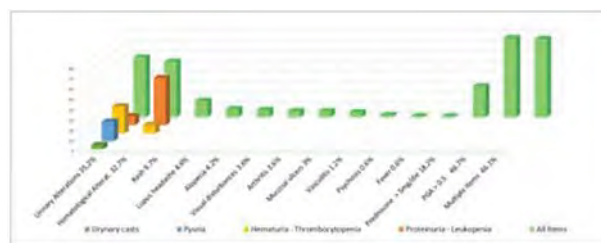
**Objectives:** Aim of this study was to evaluate the performance of the DORIS algorithm in comparison to the remission status as defined by clinical judgement and to identify the frequency of remission as determined by DORIS for each clinical disease pattern.

**Methods:** Monocentric retrospective study. Among all SLE patients followed at the Lupus Clinic between 2014 and 2016, we enrolled patients fulfilling the SLICC<sup>2012</sup> criteria who were visited at least once in 2016 and who had at least 5 biannual medical examinations in the previous 2 years. Definitions of remission according to DORIS, Clinical Remission, and disease patterns are reported in table 1.

**Results:** 101 SLE patients were enrolled for this study (94% female, mean age 45 years). 17.8% of patients were in remission in all the 5 time-points, vice versa 29.7% of patients never got into remission. 17.8% of patients have been in remission for 24 months, while 21.8% of patients less than 6 months. Mean duration of DORIS remission was 7.96 months. The most prevalent disease pattern were RR (41.6%) and CQ (41.6%), while CA pattern was present in 16.8% of patients. DORIS remission was most frequently achieved in CQ pattern (65.2% of visits), less frequently in CA (5.9%). 294 visits out of 505 (58%) were defined as "non-remission" according to DORIS. cSLEDAI above zero was the item that most frequently accounted for "non-remission", particularly urinary and haematological (as reported in figure 1). In 229 (43.3%) visits there was a disagreement between DORIS and clinical judgement: the reasons for discordant results were respectively: a) self-management of steroids dosage and precautionary increase of steroids in the suspect of a flare in 7.1%; b) cSLEDAI >0 in 27.2%, PGA ≥ 0.5 in 12.6%, more than one of these items in 53.1%.

**Abstract SAT0433 – Table 1.** Definition of Remission according to Doris, Definition of Clinical Remission according to Clinical judgement; Definition of disease pattern. PGA: Physician Global Assessment; cSLEDAI: clinical SLEDAI

Definition of Remission	Clinical Items		Treatment		
	cSLEDAI	PGA	Daily dose of prednisone	Antimalarials	Immunosuppressants/ Biologics
Remission "off treatment"	= 0	< 0.5	0	yes	no
Remission "on treatment"	= 0	< 0.5	≤ 5 mg	yes	yes
No Remission	≠ 0	≥ 0.5	≥ 5 mg	yes	yes
<b>Definition of Clinical judgement of Remission</b>	Absence of any increase in corticosteroids dosage or any change in immunosuppressants				
<b>Definition of disease patterns</b>					
Chronic active (CA)	Persistent disease activity over time with a cSLEDAI ≥ 1 in each visit for at least one year				
Relapsing-remitting (RR)	Characterised by periods of disease activity with cSLEDAI ≥ 1 interspersed with periods of disease inactivity with cSLEDAI = 0 in different visits for at least one year				
Clinical quiescent (CQ)	Defined as absence of disease activity with a cSLEDAI = 0 for at least one year				



**Abstract SAT0433 – Figure 1.** Items are responsible of disagreement between DORIS and Clinical definition of Remission

**Conclusions:** Nearly 40% of the visits displayed a disagreement between clinical judgement of remission and DORIS remission. This may be attributable mainly to a different approach in evaluating patients: longitudinal by clinical judgement and cross-sectional by DORIS. As compared to clinical judgement of remission, the DORIS definition is not designed to capture "low disease activity", particularly patients who carry a PGA between 0.5 and 1 and those who require a medium dosage of steroids in the frame of a CA pattern.

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**Disclosure of Interest:** None declared

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SAT0434

#### PARTICIPATION IN SYSTEMIC LUPUS ERYTHEMATOSUS – A CROSS-SECTIONAL ANALYSIS OF THE LULA-COHORT IN GERMANY 2015

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**Background:** Participation of chronically ill patients can be permanently and severely impaired. In a heterogeneous disease like systemic lupus erythematosus (SLE), various influencing factors such as disease activity, damage, concomitant diseases, but also detrimental effects due to the psychological burden must be considered.

**Objectives:** Our objective was to assess the current state of participation in a representative sample of German patients with SLE and evaluate the impact of demographic and clinical factors.

**Methods:** The Lupus erythematosus long-term study (LuLa-Study), a nationwide longitudinal study among German Caucasian patients with SLE, is being



conducted annually by a self-reported questionnaire since 2001. Inclusion criteria are a diagnosis of SLE and returning the completed paper questionnaire. Amongst others medication, comorbidities, health-related quality of life (HRQoL, Short-Form-12), and disease activity (Systemic Lupus Activity Measure) are surveyed. In the year 2015 we additionally inquired about participation using the "Index zur Messung von Einschränkungen der Teilhabe" (IMET; Index for measuring limitations of participation) that was developed on the basis of the International Classification of Functioning, Disability and Health (ICF), as well as depression (Centre for Epidemiologic Studies Depression Scale), and pain coping (Pain Related Self statements scale).

A multiple linear regression was run to predict overall impairment and impairment in the individual subdomains (dependent variables). Age, disease duration, number of comorbidities, pain, disease activity, catastrophizing, coping, depression, physical functioning, and physical and mental HRQoL were entered into our model as candidates for the independent variables. Variable selection was accomplished by a stepwise approach based on Akaike information criterion (AIC).

**Results:** The questionnaire was completed by 579 patients (response rate 89.2%). Only 48 (8.3%) reported no impairment of participation by their disease. Most limitations were reported in the domains 'stress and extraordinary strains' (56.3% reported moderate to high impairment) and 'sex life' (48.7%), whereas 'common activities of daily life' (21.1%) and 'close personal relationships' (26.5%) seemed to be limited less frequently.

Depression, physical functioning, and physical and mental HRQoL predicted overall participation (F-test,  $p < 0.0001$ ).

Depression, physical functioning, and physical HRQoL predicted also most of the participation subdomains whereas age, disease duration, no. of comorbidities, disease activity, pain, and pain coping behaviour impacted only individual subdomains.

**Conclusions:** Limitations of participation are common in SLE patients and affect different areas of life. In order to improve participation, it is of great importance to maintain, respectively improve physical and mental quality of life, physical functioning, and depression. The direction of causality cannot be proved beyond reasonable doubt in this cross-sectional analysis. Additional longitudinal studies are necessary.

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#### SAT0435 PLASMA PTX3 LEVELS CORRELATE WITH SYSTEMIC LUPUS ERYTHEMATOSUS ACTIVITY AND ARE INFLUENCED BY CORTICOSTEROIDS

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**Background:** Systemic lupus erythematosus (SLE) is an autoimmune disease characterised by a variable involvement of multiple organs and tissues. Acute and/or chronic vascular inflammation is not uncommon in patients with SLE and can significantly affect patient quality of life and survival. Specific markers of vascular inflammation in SLE are lacking. Pentraxin-3 (PTX3) is an evolutionarily conserved pattern recognition receptor expressed by multiple cell lines and is growingly recognised as a marker of the vessel response to injury. Glucocorticoids are known inducers of PTX3 in most tissues. The role of PTX3 as a biomarker in SLE is discussed.

**Objectives:** To assess the potential informative role of PTX3 as a biomarker in patients with SLE with and without current or previous vasculitic manifestations and with active or quiescent disease.

**Methods:** We enrolled 55 adult patients with SLE for a total of 60 samples. Samples were classified as taken from patients with active disease (SLE disease activity index, SLEDAI,  $\geq 4$ ) with or without active vasculitis and from patients with quiescent disease (SLEDAI  $< 4$ ). Further stratification was performed according to a history of lupus vasculitis. Five patients were bled twice under different conditions. Plasma PTX3 was measured by ELISA. Non-parametric tests were employed to compare PTX3 levels among groups.

**Results:** PTX3 plasma levels were slightly but not significantly more elevated in patients with active vasculitis. PTX3 levels correlated with SLEDAI in the whole set of patients ( $p = 0.007$ ) and in those who were off corticosteroids ( $p < 0.001$ ), but

not in patients receiving prednisone. PTX3 levels correlated with the dose of prednisone ( $p < 0.001$ ). Patients with  $> 1$  moderately-to-highly active (A, B) British Isles Lupus Assessment Group (BILAG) domain had significantly higher PTX3 levels than those with more limited disease activity extent ( $p = 0.041$ ). PTX3 also correlated with a 0.0–3.0 physician global assessment scale (PGA), with patient-reported visual analogue scale, and inversely with C4 levels ( $p = 0.004$ ,  $p = 0.013$ ,  $p = 0.001$  respectively). There was no significant correlation with age or disease duration nor with C-reactive protein (CRP). Similar to PTX3, CRP was higher in patients with  $> 1$  A/B BILAG domain ( $p = 0.004$ ), but did not correlate with SLEDAI or prednisone dose. Repeated samples showed a high intra-individual variability for PTX3, which unpredictably correlated with disease activity and prednisone dosage.

**Conclusions:** Our data suggest that PTX3 is a marker of active disease extent rather than vascular inflammation in SLE and it shares this behaviour with CRP, another member of the pentraxin family. Nonetheless, PTX3 also specifically correlate with monoparametric indexes of activity such as SLEDAI. A high intra-individual variability and the effect of corticosteroids constitute potential limitations to future diagnostic applications of PTX3 in SLE.

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**Disclosure of Interest:** None declared

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#### SAT0436 TRANSJUGULAR RENAL BIOPSY: A SAFE AND EFFECTIVE WAY TO PERFORM RENAL BIOPSY IN SYSTEMIC LUPUS ERYTHEMATOSUS AND ANTIPHOSPHOLIPID ANTIBODY SYNDROME PATIENTS TREATED WITH ANTI-THROMBOTIC DRUGS – A MONOCENTRIC EXPERIENCE OF 256 PROCEDURES

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**Background:** Renal biopsy is the cornerstone of Lupus nephritis (LN) management. However, transcutaneous renal biopsy (TCRB) is hampered by the antithrombotic treatment frequently prescribed in Systemic Lupus Erythematosus (SLE) and Antiphospholipid Antibody Syndrome (APS). Transjugular renal biopsy (TJRB) offers an attractive alternative for patients at increased risk of bleeding.

**Objectives:** The primary objective of the study was to describe the safety and the diagnostic performance of TJRB in SLE and APS.

**Methods:** A retrospective review of SLE and/or APS patients who consecutively underwent a renal biopsy in our department between January 2004 and October 2016 was performed. Biopsies were divided into four groups: TCRB, TJRB with aspirin treatment (aspirin TJRB), TJRB with anticoagulant treatment (anticoagulant TJRB), and TJRB without anti-thrombotic drug (no-antithrombotic TJRB). Major complications were defined as decrease, haemostasis nephrectomy, renal artery embolization, blood transfusion, sepsis and vascular thrombosis. Minor complications were defined as gross haematuria, renal hematoma and arteriovenous fistula.

**Results:** Fifty-four TCRB and 256 TJRB were analysed – 69 aspirin TJRB, 68 anticoagulant TJRB and 119 no-antithrombotic TJRB. Major complications rate was 1.9% for TCRB and 2.0% for TJRB ( $p = 1$ ). One patient in the TJRB group suffering from catastrophic antiphospholipid syndrome (CAPS) died suddenly 6 weeks after the biopsy. No patient died of bleeding complication. One patient in the anticoagulant TJRB group required a renal artery embolization and blood transfusion. Four other patients required blood transfusion (1 in the TCRB group, 1 in the aspirin TJRB group and 2 in the anticoagulant TJRB group). Minor complications rate was 1.9% for TCRB and 7.8% for TJRB ( $p = 0.2$ ).

Among the 256 TJRB, the rate of complication (major or minor) was higher for patients with glomerular filtration rate CKD-EPI  $< 30$  mL/min (6/24 [25%]) compared to patients with GFR  $> 30$  mL/min (16/232 [7%],  $p < 0.01$  using the Chi-2 test). Age over 40, blood pressure  $> 140/90$  mmHg, APS or positive

antiphospholipid biology without APS, Prothrombin Time<50%, activated Partial Thromboplastin Time ratio >1.2, platelets<50 G/L and biopsied kidney size were not associated with a higher rate of complications.

The number of glomeruli sampled and the performance of the biopsy to establish a histologic diagnostic were similar in the 4 groups.

**Conclusions:** TJRB provides diagnostic yield and safety similar to those of TCRB. It should be considered as a first intention procedure for SLE and APS patients at risk of bleeding.

**Disclosure of Interest:** None declared

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SAT0437

#### INITIAL MANIFESTATIONS OF CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS: RESULTS OF SINGLE CENTRE RETROSPECTIVE STUDY

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**Background:** Approximately 10%–20% of patients (pts) with SLE develop lupus before 18 years old. Childhood-onset SLE (cSLE) usually has more aggressive course. The achievement of medication-free remission in adulthood is extremely rare in cSLE and quality of life remains compromised.

**Objectives:** To establish the specific features of cSLE at disease onset by the retrospective study in single centre.

**Methods:** 216 pts with cSLE who were hospitalised in our centre from 1992 to 2017 were included in retrospective study. Diagnosis of SLE was reviewed according to 2012 SLICC criteria. Clinical, haematological and immunological manifestations of SLE were evaluated. SLEDAI 2K was used for disease activity assessment.

**Results:** 12.9% of cSLE pts were boys (girls to boys ratio was 6.7:1). The triggering factor was found in 29% pts: solar exposure – in 51%, previous infection – in 19%, stressful situation – in 12%, vaccination – in 10%, menarche – in 5%, high physical activity – in 3%. Only 9.2% of patients initially had SLE diagnosis, 1.4% had discoid lupus erythematosus as an initial diagnosis, 21% – different infections, 11.2% – allergic diseases, 6.3% – nephritis, 33.6% – various rheumatic diseases (16.8% – juvenile idiopathic arthritis), in remaining 17.3% cases the information about initial diagnosis was missing. The median age at the onset was 13.7 y (10.8; 15.05); the median disease duration at the time of cSLE verification was 6 months.<sup>2; 14</sup> In 33.4% pts cSLE was verified after 1 year disease duration, in 15.3% – after 3 years. The most common feature was arthritis – in 71.4%. Fever observed in 68.5% pts at the onset, significant weight loss – in 29.4%. 64% pts had acute cutaneous lupus at the onset, 42.4% – chronic cutaneous lupus, 17.7% – oral and nasal ulcers, 22.2% – non-scarring alopecia, 31% – serositis, 56.6% – renal involvement, 21.2% – neuropsychiatric disorder. The Coombs' positive hemolytic anaemia was found in 15.8% pts, leucopenia/lymphopenia – in 52.2%, thrombocytopenia – in 23.6%. ANA were detected in 100% pts, anti-dsDNA – in 83.3%, anti-Sm – in 29.2%, antiphospholipid antibodies – in 7.3%, hypocomplementemia – in 49.0%, positive direct Coombs test out of hemolytic anaemia – in 13.5%. Macrophage activation syndrome at the onset was documented in 3.4% pts. Median disease activity by SLEDAI at the time of cSLE verification was 13.7 scores,<sup>8;20</sup> maximum – 42.

**Conclusions:** cSLE presentation with non-specific general and constitutional manifestations in the majority of cases misled to erroneous interpretation of the condition as infectious or allergic disease in 1/3 of all cases. A monosymptomatic manifestation at the onset, such as arthritis, skin lesion or hematologic disorders, can lead to late diagnosis and very high activity at the moment of start therapy. Specific features of cSLE must be suspected in all cases of arthritis with skin lesions and/or any haematological manifestations, even non-specific.

**Disclosure of Interest:** None declared

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SAT0438

#### INCREASED RISK OF DEPRESSION IN PATIENTS WITH CUTANEOUS LUPUS ERYTHEMATOSUS AND SYSTEMIC LUPUS ERYTHEMATOSUS: A DANISH NATIONWIDE COHORT STUDY

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**Background:** Quality of life is considerably impaired in patients with systemic lupus erythematosus (SLE) as well as in patients with cutaneous lupus erythematosus (CLE). In patients with SLE, prevalence estimates of depression ranges considerably,<sup>1</sup> while the prevalence of depression in CLE remains severely understudied. Data on the actual risk of depression in adults after being diagnosed with CLE or SLE remain scarce.

**Objectives:** To examine whether patients with SLE or CLE have increased risk of depression.

**Methods:** In this nationwide observational cohort study, we included patients ≥18 years with a first-time diagnosis of SLE or CLE between 2000–2015 identified in the Danish National Patient Register matched with people from the general population in Denmark in a 1:10 ratio. After linkage to various national Danish health registers analyses of risk for depression and antidepressant use were performed in Cox regression models adjusted for age, sex, socio-economic status, smoking, alcohol abuse, prior depression, and prior antidepressant use.

**Results:** A total of 3489 patients with lupus erythematosus and 34 890 people from the general population were included. The adjusted hazard ratios (HRs) of depression were 1.87 (95% CI, 1.37–2.55) and 2.15 (95% CI, 1.66–2.77) for patients with CLE and SLE, respectively, compared to the general population. The adjusted HRs of antidepressant use were 1.36 (95% CI 1.22–1.51) and 1.76 (95% CI 1.62–1.91) for patients with CLE and SLE, respectively. The risk of depression was more pronounced in patients diagnosed <50 years of age; adjusted HR=2.88 (95% CI, 1.77–4.69) for CLE and HR=2.33 (95% CI, 1.56–3.49) for SLE. Also a high risk of depression was observed for men with CLE (HR 2.59, 95% CI, 1.24–5.42) and SLE (HR 2.23, 95% CI, 1.11–4.48). Neither CLE or SLE were associated with increased risk of death from suicide.

**Abstract SAT0438 – Table 1.** Crude and adjusted hazard ratios for depression and antidepressant use in patients with lupus erythematosus compared with the general population

	Crude HR	(95% CI)	P-value	Adjusted HR*	(95% CI)	P-value
<b>Depression</b>						
CLE	2.34	(1.71–3.18)	<0.0001	1.87	(1.37–2.55)	0.0001
SLE	2.33	(1.81–3.01)	<0.0001	2.15	(1.66–2.77)	<0.0001
<b>Antidepressant use</b>						
CLE	1.61	(1.45–1.79)	<0.0001	1.36	(1.22–1.51)	<0.0001
SLE	1.94	(1.78–2.10)	<0.0001	1.76	(1.62–1.91)	<0.0001

\* Adjusted for age, sex, smoking, alcohol abuse, socio-economic status, prior depression, and prior antidepressant use.

CI, confidence interval; CLE, cutaneous lupus erythematosus; HR, Hazard Ratio; SLE, systemic lupus erythematosus.

**Conclusions:** The risk of depression was significantly increased in patients with SLE or CLE. We recommend that rheumatologists and dermatologists are aware of the increased risk of depression in patients with SLE or CLE.

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**Disclosure of Interest:** None declared

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SAT0439

#### DIFFERENTIAL LEVELS OF NOVEL AND CLASSIC ANTIPHOSPHOLIPID ANTIBODIES AMONG PATIENTS WITH PRIMARY ANTIPHOSPHOLIPID SYNDROME AND SYSTEMIC LUPUS ERYTHEMATOSUS

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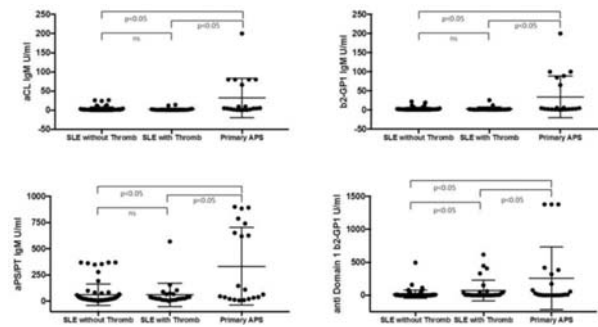
**Background:** High levels of antiphospholipid antibodies (aPL) are associated predominantly with a higher risk of thrombosis, however, information about differential levels according underlying diagnosis is less well known.

**Objectives:** Our aim was to compared serum levels of 2 novel aPL (anti-phosphatidylserine/prothrombin (PS/PT) antibodies and anti domain 1 against β2 glycoprotein I (anti-D1 B2GP1)) and "classic" (anticardiolipin, aCL and anti B2GP1 antibodies) among patients with primary APS, SLE with and without thrombosis

**Methods:** In this cross-sectional study, Anti-D1 B2GP1 antibodies were tested using a chemiluminescent immunoassay (QUANTA Flash, Inova Diagnostics). In

addition, anti PS/PT (IgG and IgM), aCL (IgG and IgM) and anti B2GP1 (IgG and IgM) were measured at the same time by ELISA techniques (QUANTA Lite, Inova Diagnostics). Lupus anticoagulant was detected according to the guidelines of the International Society on Thrombosis and Haemostasia. Differences in mean values between groups were analysed with the Mann-Whitney U test for comparison of 2 groups

**Results:** One hundred and seventy three patients were included, 87% of patients were female with a mean age of 33±12 years. 150 patients had SLE and 23 patients primary APS. Fifty five (31%) out of 177 had history of thrombosis and 41 (23%) of pregnancy losses. Levels of IgM aCL, IgM B2GP1, IgM Anti PS/PT and total antibodies against Anti-D1 B2GP1 were significantly higher in patients with primary APS than in patients with SLE and thrombosis (see figure 1). IgG anti PS/PT (75.9±91.3 vs 27.4±39.3 IU, p<0.001) and total anti-D1 B2GP1 (65.2±152 vs 16.4±65.1 IU, p<0.001) were significantly higher in patients with SLE with thrombosis than in patients with SLE without thrombosis. Obstetric morbidity (66.7% vs 21.7%, p=0.016) and *livedo reticularis* (22% vs 0%, p>0.07) were more common in patients with primary APS than SLE with thrombosis. No significant differences were found in terms of thrombotic events among both groups



**Abstract SAT0439 – Figure 1.** aPL levels according diagnosis (IgM for aCL, anti B2GP1 and anti PS/PT and total antibodies against Anti-D1 B2GP1)

**Conclusions:** Patients with primary APS have significant higher serum levels of anti PS/PT and anti-D1 B2GP1 antibodies and “classic” aPL (aCL and anti B2GP1) antibodies than patients with SLE with thrombosis. Whether if these titers are useful to differentiate patients with primary and secondary APS requires further analysis in prospective studies.

**Acknowledgements:** Anti D1- B2GP1 antibodies antibodies were provided by Inova, Werfen, Colombia

**Disclosure of Interest:** J. A. Gómez-Puerta Speakers bureau: Werfen/Inova, T. Urrego: None declared, A. Hernández: None declared, S. Ruiz: None declared, S. M. Osorno: None declared, C. Rua: None declared, J. Duque Botero: None declared, A. Vanegas-García: None declared, C. H. Muñoz: None declared, L. A. González: None declared, G. Vásquez: None declared

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**SAT0440 PHENOTYPIC FEATURES AND PREDICTORS OF THE CLINICAL SEVERITY OF KERATOCONJUNCTIVITIS SICCA AND SALIVARY GLAND DYSFUNCTION IN PATIENTS WITH SJÖGREN'S SYNDROME: A LONGITUDINAL ANALYSIS OF THE KISS COHORT**

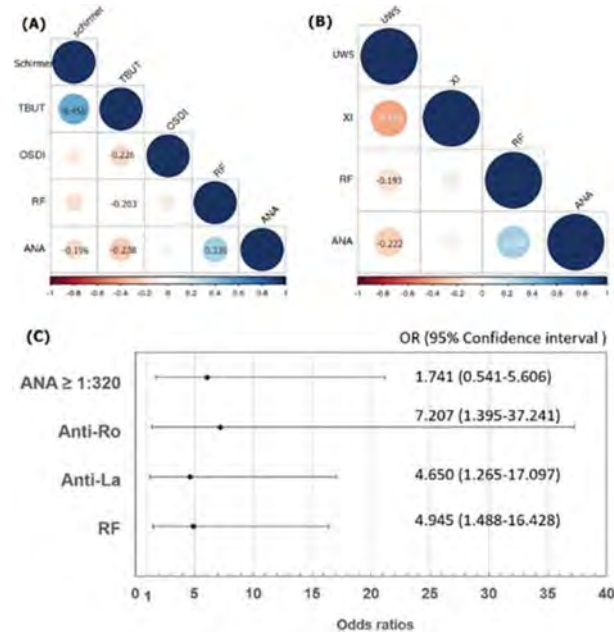
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**Background:** Hyposecretion of tears and saliva is the main phenotype of primary Sjögren's syndrome (PSS). However, the prevalence and degree of ocular and oral involvement in PSS is highly variable.

**Objectives:** The aims of this study were 1) to investigate oral and ocular signs and changes in primary SS patients, and 2) to explore possible predisposing factors for moderate to severe oral or ocular signs in primary SS.

**Methods:** We analysed 140 participants from the Korean Initiative of PSS cohort who completed a two-year follow-up oral and ocular sign test. The severity of keratoconjunctivitis sicca (KCS) was determined by the Schirmer I test (Moderate-to-severe [MS], ≤5 mm/5 min; mild [Mi], >5 mm/5 min). Salivary gland dysfunction (SGD) was determined by unstimulated whole salivary flow rate (UWS) (MS, UWS <0.1 ml/min; Mi ≥0.1 ml/min). Subgroups were divided into three groups according to the severity of KCS and SGD: MS-KCS/MS-SGD, MS-KCS/Mi-SGD, and Mi-KCS/MS-SGD group. We analysed the severity of changes in KCS and SGD during the follow-up period.

**Results:** Among the 140 participants enrolled in this study, 108 (61%) were placed in the MS-KCS/MS-SGD group, 17 (24%) were in the MS-KCS/Mi-SGD, 15 (16%) were in the Mi-KCS/MS-SGD at the two-year follow-up. The MS-KCS/Mi-SGD group was younger than the other two groups, had a lower xerostomia inventory, and lower level of β2 microglobulin. Participants in the Mi-KCS/MS-SGD group had less hyperimmunoglobulinemia, rheumatoid factor (RF), antinuclear antibodies, anti-Ro, and anti-La antibodies. Older patients and those with positive RF, anti-Ro, or anti-La antibodies at baseline were more likely to have moderate to severe KCS at the two-year follow-up.



**Conclusions:** Patients with PSS and positive RF, anti-Ro, or anti-La antibodies at baseline may benefit from regular ophthalmology exams, even if they do not have KCS at baseline or dry eye symptoms.

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**SAT0441 PREDICTIVE VALUE OF ANTIPHOSPHOLIPID ANTIBODIES IN THE ACUTE PHASE OF DEEP VEIN THROMBOSIS**

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**Background:** Deep vein thrombosis (DVT) is frequent and potentially life threatening disease with tendency to recur. Anticoagulant treatment of the first episode of DVT usually lasts 3 months. Antiphospholipid syndrome (APS) is an important cause of DVT. However, the APS can be confirmed only 24 weeks after DVT according to the current APS classification criteria.<sup>1</sup> Thus, undiagnosed APS patients, who cease anticoagulant therapy after 3 months, might be exposed to a greater risk for recurrent venous thromboembolism. Studies evaluating the significance of positive antiphospholipid antibody (aPL) test in the acute phase of DVT are lacking.

**Objectives:** To evaluate whether positive aPL test at the time of acute DVT diagnosis is predictive of APS.

**Methods:** Patients with acute DVT were included into a 24 month prospective study. All patients were given anticoagulants. aCL IgG/IgM and anti-β2GPI IgG/IgM/IgA antibodies were determined by our in-house ELISA<sup>2</sup> at inclusion and then every 4 weeks for the first 24 weeks. The last aPL measurement was performed 24 months after inclusion into the study. APS was confirmed if a patient tested positive (medium or high positive aCL and/or presence of anti-β2GPI) 12 and 24 weeks after DVT. Lupus anticoagulants (LA) were tested after cessation of anticoagulation.

**Results:** 196 patients (111 male, 85 female, age 54±2 years) included in the study had aPL titer assessed at least 5 times. Ultimately, 20/196 (10.2%) patients fulfilled APS classification criteria. Among these, 15/20 (75%) patients had medium or high titer aPL at the time of acute DVT (1 of them had double positive aPL and 2 of them had multiple positive aPL at first aPL determination). Two patients (10%) had low positive aCL IgG and one had low titer aCL IgM. Two patients (10%) were negative for aPL, but had later fulfilled APS criteria due to positive LA. APS was not established in 176/196 (89.8%) patients. Among these, 146/176 (83%) patients were negative for aPL at inclusion, while 30/176 (17%) had low titer aCL IgM or aCL IgG. Altogether, diagnostically important aCL IgG/IgM and/or anti-β2GPI titer at the time of acute DVT had 83% specificity and 90.5% sensitivity for APS. Isolated low titer aCL IgG were more frequent in patients with APS than in patients without APS ( $\chi^2=125.6$ ;  $p<0.001$ ). Completely negative aCL IgG/IgM and anti-β2GPI in the acute phase of DVT had a negative predictive value of 98.6%.

**Conclusions:** Here we show that in acute phase of DVT, positive medium or high titer aCL IgG/IgM or anti-β2GPI is suggestive of APS. In these patients continuation of anticoagulation beyond the initial 3 months should be considered. Patients with negative aPL in the acute phase of DVT do not need further aPL testing; however, LA should be determined. Low aPL titre at the time of acute DVT deems further testing imperative.

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**Disclosure of Interest:** None declared

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**SAT0442 RISK FACTORS FOR HEART VALVE DISEASES IN PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME**

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**Background:** Antiphospholipid syndrome (APS) patients are known to be at a high risk of heart valve diseases (HVDs), however, risk factors of HVDs in APS patients is unclear.

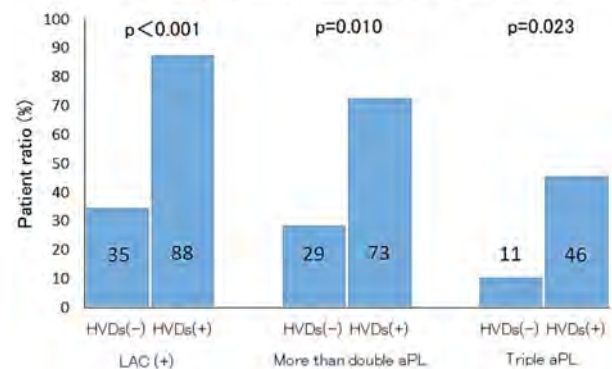
**Objectives:** The purpose of this study is to elucidate risk factors for HVDs in patients with APS.

**Methods:** We reviewed consecutive APS patients diagnosed according to the Sydney criteria in 2006 who had been followed in Keio University Hospital in October 2017. The presence of HVDs was identified by the latest transthoracic and/or transesophageal echocardiography. HVDs were defined any kind of valve diseases such as mitral valve regurgitation (MR) and stenosis more than mild degree, aortic valve regurgitation (AR) and stenosis more than mild degree and Libman-Sacks endocarditis. Antiphospholipid antibodies (aPLs) included lupus

anticoagulant (LA), anticardiolipin antibodies (aCL), and anticardiolipin β2-glycoprotein I complex antibodies (aCL-β2GPI). We divided the patients into two groups by the presence of HVDs, and evaluated the risk factors of them.

**Results:** Fifty-five APS patients were identified. Among them, 43 patients underwent echocardiography and enrolled in the analysis. Six patients were primary APS, 36 were secondary APS with systemic lupus erythematosus, and one with Sjögren syndrome. HVDs were detected in 26 (60.5%) patients including 20 patients with MR, 8 patients with AR and a patient with Libman-Sacks endocarditis. The use of prednisolone, miscarriage episodes and the presence of arterial or venous thrombosis in patients with HVDs did not differ from those without HVDs. Immunologically, there was no significant difference in anti-double-stranded DNA antibody, anti-Smith antibody, anti-ribonucleoprotein antibody, anti-SSA/La antibody and anti-SSB/Lo antibody between patients with or without HVDs. While the positivity of aCL or aCL-β2GPI was not different between patients with HVDs and those without, positive LA was much higher in patients with HVDs and in patients with MR than those without (88.5% vs 35.3%,  $p<0.01$ ; 85.0% vs 52.2%,  $p=0.027$ , respectively). In addition, patients with HVDs had double and triple positive tests of aPLs significantly more frequently than those without HVDs ( $p=0.010$  and  $p=0.023$ , respectively[Y1]). Hospitalisation risk in patients with HVDs because of heart failure or syncope were 0.011/patient year.

**The proportions of positive aPLs in APS patients with HVDs and without them.**



**Conclusions:** Positive LA test and positivity for 2 or more tests of aPLs are risk factors for HVDs in patients with APS. Regular monitoring cardiac ultrasonography is needed in those patients.

**Disclosure of Interest:** None declared

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**SAT0443 DIAGNOSTIC AND PREDICTIVE EVALUATION USING SALIVARY GLAND ULTRASONOGRAPHY IN PRIMARY SJOGREN'S SYNDROME**

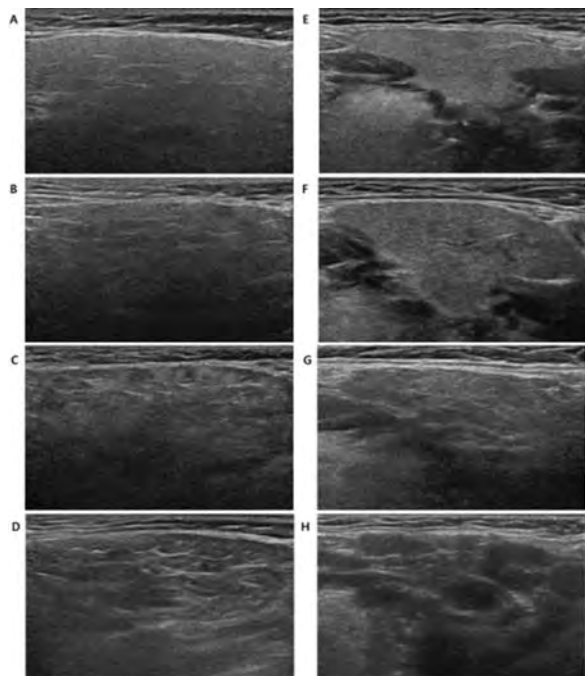
K.-A. Lee, S.-H. Lee, H.-R. Kim. *Konkuk University Medical Center, Seoul, Korea, Republic Of*

**Background:** There is an increasing need for alternative, non-invasive and reliable diagnostic tools with the potential to improve and simplify the diagnostic process for primary Sjogren's syndrome (pSS). The main advantage of salivary gland ultrasonography (SGUS) is the direct visualisation of structural abnormalities of the salivary glands. Despite these advantages of SGUS, a number of obstacles remain. Different SGUS scoring systems in B-mode were used in previous studies. The diagnostic usefulness of Doppler analysis and glandular size measurement has not been established. Indeed there is no proven prognostic factor for glandular damage in pSS, although a number of studies have revealed the risk factors for lymphoma.

**Objectives:** We aimed to assess the diagnostic value of SGUS as a single test for the detection of pSS in an integrated manner. We assessed the diagnostic accuracy of three SGUS parameters: the ultrasound (US) grey-scale scoring system, glandular volume measurement, and intraglandular power Doppler US. The secondary aim was to examine the prognostic factors for severe structural changes in major salivary glands based on the SGUS scoring system.

**Methods:** Patients with pSS (n=94) and idiopathic sicca syndrome (n=44) were evaluated using the SGUS 0–48 scoring system, which comprises five parameters: parenchymal echogenicity, homogeneity, hypoechoic areas, hyperechoic reflections, and clearness of posterior borders (figure 1). The salivary gland volume and intraglandular power Doppler signal (PDS) were also assessed. A multivariate linear regression analysis was performed to determine the factors associated with SGUS score.

**Results:** Patients with pSS showed a significantly higher SGUS score than controls [median (IQR): 24.5 (13.0) vs 6 (3.75),  $p < 0.001$ ]. An SGUS cut-off of  $\geq 14$  had a sensitivity of 80.9% and a specificity of 95.5% for the diagnosis of pSS. There were no significant differences in the measured volumes and PDS between pSS patients and controls. The SGUS score correlated with unstimulated salivary flow rate (USFR), serum rheumatoid factor and IgG. Double seropositivity with anti-Ro/SS-A and anti-La/SS-B ( $\beta = 6.060$ ,  $p = 0.001$ ) and USFR ( $\beta = -1.913$ ,  $p < 0.001$ ) were independently associated with the SGUS score.



**Conclusions:** The SGUS scoring system is a valuable diagnostic method for pSS. Double seropositivity of anti-Ro/SS-A and La/SS-B is an independent predictive factor for structural damage of the salivary glands.

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**Disclosure of Interest:** None declared

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SAT0444

#### INCIDENCE AND PREDICTORS OF IMMUNOSUPPRESSANT DISCONTINUATION AND RISK OF SUBSEQUENT FLARE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Prolonged treatment with immunosuppressants (IS) has been associated with long-term complications in Systemic Lupus Erythematosus (SLE); however, few data on IS discontinuation in remitted patients are available to date.

**Objectives:** We conducted an observational study to describe the proportion of SLE patients who discontinued IS and to assess the potential predictors of a subsequent flare.

**Methods:** We used data from Padua Cohort, which includes 454 SLE patients followed up from 1990 to 2017. Patients treated with IS over the disease course who discontinued IS and seen at least once in 2017 were studied. Reasons for discontinuation were: remission (defined by clinical SLE disease activity Index=0) or poor compliance/intolerance. Flares were defined according to SLEDAI Flare

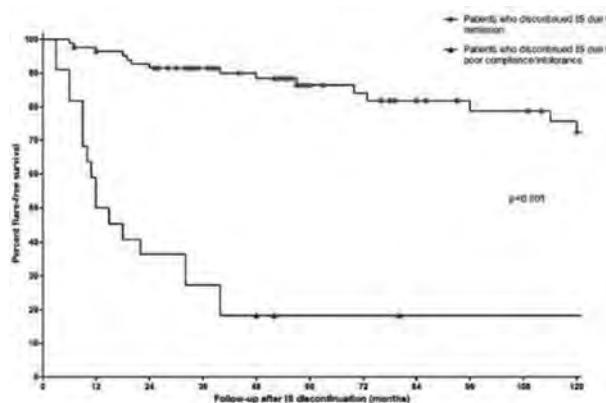
Index. Predictors of a subsequent flare were analysed by multivariate logistic regression analysis.

**Results:** Eligible patients who were ever treated with IS were 297. IS were discontinued in 106 patients (35.7%): mycophenolate (50, 47.2%), azathioprine (27, 25.5%), cyclophosphamide (11, 10.4%), methotrexate (10, 9.4%), cyclosporine (8, 7.5%). Mean  $\pm$ SD follow-up duration after IS withdrawal was  $82 \pm 64$  months (range 6–320).

83 out of 106 patients (78.4%) discontinued IS due to remission (mean remission duration at IS discontinuation  $39 \pm 28$  months), and 23 (21.6%) due to poor compliance/intolerance. Among remitted patients, 18 (78.3%) experienced a flare after IS discontinuation (9/55 patients with nephritis, 5/10 with arthritis, 2/9 with skin involvement, 1/3 with neuroSLE, 1/4 with haematological involvement) after a mean of  $65 \pm 52$  months (range 6–180). Conversely, in patients with poor compliance/intolerance, 17 relapsed (73.9%) after a mean of  $22 \pm 16$  months. Flare-free 10 year-survival rate was higher in patients who discontinued IS due to remission than to poor compliance/intolerance ( $p < 0.001$ , figure 1).

In patients who discontinued IS due to remission, a shorter duration of remission at IS discontinuation was associated with disease relapse ( $p = 0.006$ ). Patients who were on IS due to nephritis had a lower risk of flare after IS discontinuation compared with patients with other manifestations (16.4% vs 32.1%, OR 0.58, 95% CI 0.32–0.98,  $p = 0.049$ ); patients with arthritis were those who were more likely to flare (OR 4.61, 95% CI 1.16–18.29,  $p = 0.035$ ). Positive anti-SSA/SSB (OR 0.45, 95% CI 0.26–0.78,  $p = 0.012$ ) and antimalarials intake after IS discontinuation (OR 0.22, 95% CI 0.07–0.73,  $p = 0.015$ ) were associated with a lower risk of flare. No clinical features over the disease course were associated with flare occurrence.

At multivariate analysis, antimalarial use was the strongest protective factor against flares after IS discontinuation (OR 0.22, 95% CI 0.05–0.85,  $p = 0.029$ ).



**Abstract SAT0444 – Figure 1.** Free-flare 10 year survival in the cohort.

**Conclusions:** In our cohort, one third of patients treated with IS discontinued the drug during the follow-up, in most cases due to a prolonged remission. Patients who discontinued IS due to remission had a higher free-survival rate than those who discontinued these drugs due to poor compliance/intolerance. The use of antimalarials after IS discontinuation was independently associated with a significant decrease in the risk of flare. IS discontinuation in patients with arthritis requires particular caution.

**Disclosure of Interest:** None declared

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SAT0445

#### THE CORRELATION BETWEEN THE TYPE OF CELLS IN MINOR SALIVARY GLANDS INFILTRATES AND THE SELECTED IMMUNOLOGICAL, CLINICAL AND LABORATORY PARAMETERS, IN PRIMARY SJOGREN'S SYNDROME PATIENTS WITH HISTORY OF EPSTEIN – BARR VIRUS INFECTION

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**Background:** The number of inflammatory mononuclear cell foci is crucial in primary Sjogren's syndrome (pSS) diagnosis, with their cellular composition changing in subsequent inflammation stages. The Epstein -Barr virus (EBV) infection is believed to play a role in the pathogenesis of pSS.

**Objectives:** Establishing the correlation of selected clinical, immunological and laboratory parameters with cellular composition of minor salivary glands infiltrations.

**Methods:** 41 pSS patients, 34 female (83%), 7 men (17%), average age 52 y.o, SD=15, with history of EBV infection, divided into two age groups (45<:>45). The diagnostics: white blood count (WBC), rheumatoid factor (RF), erythrocyte sedimentation rate (ESR), CRP, serum concentration of  $\gamma$ -globulins, antinuclear antibodies ANA(IF); anti-SS-A and anti-SS-B antibodies (semi-quantitative immunoblotting evaluation), standard ELISA assays of serum cytokines levels (BAFF, APRIL, FLT-3L, LT- $\alpha$ , IL-21), minor salivary gland biopsy with the histopathological evaluation (focus score-FS), immunochemistry assessment of the CD3 +, CD4 +, CD19 +, CD21 +, CD35 +cells presence, ocular tests: Schirmer's test and ocular staining score (OSS); ELISA assay of antibodies against EBV specific proteins (viral capsid antigen, early antigen and Epstein-Barr nuclear antigen), ESSDAI evaluation. The Bioethics Committee approval was obtained. Statistic: U Mann-Whitney test and Spearman correlation coefficient with statistical significance set at  $p < 0.05$ .

**Results:** In infiltrates CD3 +, CD4 +and CD19+cells dominated, WBC negatively correlated with CD 35+cells ( $\rho = -0.323$ ). CD3 +and CD4+absolute cell count correlated positively with anti-SS-A antibodies, but not with ANAs and anti-SS-B antibodies. The CD19 +, CD3 +and CD4+absolute cell count correlated positively with the serum LT- $\alpha$  concentration (respectively  $\rho = 0.349, 0.488, 0.483$ ) and moderately negatively with Schirmer test, but not with OSS. There were no differences in FS grade between age groups. In the younger group all cell types were found, including CD21 + ( $p = 0.042$ ) and CD35 + ( $p = 0.036$ ); the older subgroup lacked dendritic cell markers. The ESSDAI positively correlated with CD3 +, CD4 +, CD19 +and CD21+cells (respectively  $\rho = 0.320, 0.329, 0.28, 0.241$ ).

**Conclusions:** a) Leukopenia may be associated with the dendritic cells (CD35 +) presence in the disease subsequent stage. b) The positive correlation of mononuclear cells with LT- $\alpha$  confirms the LT- $\alpha$  effect on the immune response in peripheral lymphatic organs and on T and B lymphocytes. c) The presence of CD21 +and CD 35+cells observed in younger group, may indicate an active and early phase of inflammation and the activity of both T and B-lymphocytes and dendritic cells. d) The positive correlation ESSDAI with all studied cell types confirms the observation, that organ-related complications correlate with inflammatory activity expressed in mononuclear cell infiltrates. e) The effect of EBV reactivation/previous infection on FS, CD3 +, CD4 +, CD19 +, CD21 +, CD35 +was not demonstrated.

**Disclosure of Interest:** None declared

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SAT0446

#### SERUM CONCENTRATIONS OF 25-HYDROXYVITAMIN D AND METABOLIC SYNDROME AND ITS COMPONENTS IN NONDIABETIC SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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**Background:** Increasing evidence has suggested a protective role of vitamin D in the metabolic syndrome (MetS). However, studies addressing this issue are limited in systemic lupus erythematosus (SLE).

**Objectives:** We examined the relationship between serum 25-hydroxyvitamin D (25(OH)D) status and MetS in nondiabetic SLE patients.

**Methods:** Cross-sectional analyses of the relationship between concentrations of 25(OH)D, MetS, and its components were made in 160 nondiabetic SLE women. MetS was defined according to the NCEP-ATP III criteria. Serum 25(OH)D was measured by chemiluminescent immunoassay. Serum 25(OH)D levels were categorised into quartiles (<16.6, 16.6–21.1, 21.2–26.3,  $\geq 26.4$  ng/ml).

**Results:** A total of 79 (49.3%) of SLE women had MetS. Without adjusting for BMI or smoking, the odds of having MetS decreased according to increasing quartiles of vitamin D levels ( $P$  for trend=0.036). The odds ratio (OR) of having MetS was 0.39 (95% confidence interval: 0.16–0.97,  $p = 0.043$ ) for the highest vs. the lowest quartile of vitamin D levels when adjusted by age. The crude OR of having elevated hypertriglyceridemia decreased according to increasing quartiles of

vitamin D levels ( $P$  for trend=0.036). However, further adjustments for BMI and smoking removed the inverse association between vitamin D status and MetS and its individual components (Table).

**Table.** Multivariable-adjusted OR (95%) for metabolic syndrome according to categories of serum 25(OH)D

	Quartiles of 25(OH) ng/ml				P value
	Q1	Q2	Q3	Q4	
<b>Number of subjects</b>	40	41	38	41	
Median 25 (OH) ng/ml	14.9	19.2	23.3	29.2	
<b>Metabolic syndrome</b>	24 (60)	21 (51.2)	18 (47.3)	16 (39.0)	
Crude OR (95% CI)	1.0	0.57 (0.23–1.38)	0.54 (0.21–1.33)	0.38 (0.15–0.94)	0.036
Adjusted OR (95% CI)*	1.0	0.56 (0.23–1.38)	0.53 (0.21–1.38)	0.39 (0.16–0.97)	0.043
Adjusted OR (95% CI)†	1.0	0.59 (0.22–1.60)	0.69 (0.25–1.91)	0.49 (0.17–1.34)	0.162
Adjusted OR (95% CI) ‡	1.0	0.59 (0.22–1.60)	0.69 (0.25–1.91)	0.49 (0.17–1.34)	0.163
<b>Triglycerides <math>\geq 150</math> mg/dl (n,%)</b>	25 (62.5)	25 (60.9)	18 (47.3)	16 (39.0)	
Crude OR (95% CI)	1.0	0.93 (0.38–2.69)	0.48 (0.19–1.20)	0.38 (0.15–0.94)	0.036
Adjusted OR (95% CI)*	1.0	0.92 (0.37–2.29)	0.46 (0.18–1.16)	0.40 (0.16–1.00)	0.050
Adjusted OR (95% CI) †	1.0	1.06 (0.40–2.82)	0.57 (0.21–1.54)	0.49 (0.18–1.32)	0.161
Adjusted OR (95% CI) ‡	1.0	1.07 (0.40–2.85)	0.58 (0.21–1.58)	0.49 (0.18–1.32)	0.492

\* Adjusted by age, † Adjusted by age and BMI, ‡ Adjusted by age, BMI and smoking

**Conclusions:** In nondiabetic SLE women with mild activity, the potential inverse relationship between vitamin D status and MetS may be attributable to the joint effects of individual obesity and smoking. Prospective studies are necessary to better determine the role of 25(OH)D in the incidence of MetS in SLE patients.

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SAT0447

#### VALIDATION OF THE 2017 ACR/EULAR CLASSIFICATION CRITERIA OF SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Two major classification criteria have been used in the clinical trials of systemic lupus erythematosus (SLE). One is American College of Rheumatology (ACR) criteria first developed in 1982 and revised in 1997 (1997 criteria)<sup>1</sup>, and the other is Systemic Lupus International Collaborating Clinics (SLICC) criteria developed in 2012 (2012 criteria)<sup>2</sup>. In the ACR annual meeting on November 2017, the new classification criteria of SLE (2017 criteria) were proposed, aiming for better specificity and sensitivity. They were made based on the agreement of expert panel<sup>3</sup>, and have not been validated in the real-world practice.

**Objectives:** The objective of the study is to evaluate the sensitivity of 2017 criteria when applied to real SLE cases.

**Methods:** We retrospectively reviewed the electronic medical record of the consecutive 100 patients who visited St. Luke's International Hospital, a tertiary care centre in Tokyo, Japan, searching back from November 13, 2017. Patients were included if they are clinically diagnosed as having SLE with board-certified doctors, and excluded if they complicated with other autoimmune disease or if they



are under 18-year-old. Each patient was evaluated if he or she satisfied the 1997, 2012, or 2017 criteria.

**Results:** Among the 100 cases, 9 were male and 91 were female, with wide range of age;<sup>18-88</sup> mean 44.5-year-old). Asian accounted for 98%, with Hispanic 1%, and Caucasian 1%.<sup>†</sup> The sensitivity of 1997, 2012, 2017 criteria are, 97%, 99%, 87% respectively. The positivity rate of each domain in the 2017 criteria was shown in table 1. The total score that the patients got in the 2017 criteria ranged from 12 to 44 (mean: 27.3). All the cases who were classified as non-SLE in the 2017 criteria had anti-nuclear antibody (ANA) <80; all of them scored more than 10 points.

**Abstract SAT0447 – Table 1.** Validation of the 2017 SLE classification criteria using clinically diagnosed 100 SLE cases.

Item (point)	Positivity (%)
<b>Entry Criteria</b>	
ANA ≥80 (required: no point)	87.0
<b>Constitutional Domain</b>	
Unexplained fever >38.3° C (2)	47.0
<b>Muco-Cutaneous Domain</b>	
Non-scarring alopecia (2)	48.0
Oral ulcers (2)	27.0
SCLÉ or DLE (4)	42.0
ACLE (6)	70.0
<b>Arthritis Domain</b>	
Synovitis or tenderness in ≥2 joints or tenderness and ≥30 minutes of morning stiffness (6)	79.0
<b>Neurologic Domain</b>	
Delirium (2)	0
Psychosis (3)	4.0
Seizure (5)	7.0
<b>Serositis Domain</b>	
Pleural or pericardial effusion (5)	29.0
Acute pericarditis (6)	0

<b>Hematological Domain</b>	
Leukopenia (3)	77.0
Thrombocytopenia (4)	26.0
Autoimmune hemolysis (4)	14.0
<b>Renal Domain</b>	
Proteinuria >0.5g / 24 hours (4)	64.0
Renal biopsy with Class II or V lupus nephritis (8)	12.0
Renal biopsy with Class III or IV lupus nephritis (10)	17.0
<b>Antiphospholipid Domain</b>	
aCL (IgG) >40 GPL units, anti-β2-GPI >40 units, or lupus anticoagulant positive (2) †	17.0
<b>Complement Proteins Domain</b>	
Low C3 or Low C4 (3)	40.0
Low C3 and Low C4 (4)	40.0
<b>Highly Specific Antibodies Domain</b>	
Anti-dsDNA antibody (6)	74.0
Anti-Smith antibody (6) ‡	28.0
<b>Rate of the patients classified as SLE (ANA ≥80 and got ≥10 points overall)</b>	
	87.0

†N/A in 3, ‡N/A in 1.  
 Abbreviations: ACLE, acute cutaneous lupus erythematosus; ANA, anti-nuclear antibody; anti-CL, anti-cardiolipin antibody; DLE, discoid lupus erythematosus; N/A, not available; SCLÉ, sub-acute cutaneous lupus erythematosus; SLE, systemic lupus erythematosus.

†N/A in 3, ‡N/A in 1.  
 Abbreviations: ACLE, acute cutaneous lupus erythematosus; ANA, anti-nuclear antibody; anti-CL, anti-cardiolipin antibody; DLE, discoid lupus erythematosus; N/A, not available; SCLÉ, Sub-acute cutaneous lupus erythematosus; SLE, systemic lupus erythematosus.

**Conclusions:** 2017 criteria for SLE accomplished modestly high sensitivity in the real-world practice, but not as high as 1997 and 2012 criteria. They possibly miss-classify the real SLE cases as non-SLE, especially if patients have low titer (<80) of ANA.

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**SAT0448 REPORT OF 86 CASES OF CONGENITAL HEART BLOCK: DATA FROM THE ITALIAN REGISTRY (LU.NE REGISTRY)**

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**Background:** Cardiac neonatal lupus is due to placental transfer of maternal anti-Ro/SSA and anti-La/SSB autoantibodies to the fetus and mainly includes congenital heart block (CHB) and dilated cardiomyopathy. The prevalence of CHB has been estimated as 1%–2% in anti-Ro/SSA women while the recurrence rate is 16%–19%.<sup>1</sup> This condition is associated with a high rate of fetal/neonatal mortality and in the majority of cases requires pacemaker pacing.<sup>2–6</sup>

**Objectives:** The rarity of this condition requires the establishment of collaborative registries in order to improve our knowledge. Here we report the data of the ongoing Italian Registry of the autoimmune congenital heart block (Lu.Ne), which was created in 2016

**Methods:** The aim was to collect retrospective and prospective pregnancies complicated with CHB in patients with antibodies. Data regarding demography, treatment, maternal and neonatal outcome and follow-up were collected through an online electronic datasheet prepared in a Research Electronic Data Capture platform.

<b>Maternal demography</b>	<b>n=82</b>
<b>Maternal Diagnosis at CHB detection</b>	
Undifferentiated Connective Tissue Disease	26 (31.7)
Sjogren Syndrome	16 (19.5)
Systemic Lupus Erythematosus	4 (4.8)
Carriers Ro/SSA	18 (21.9)
Carriers Ro/SSA+La/SSB	15 (18.4)
Other	3 (3.7)
<b>Autoantibodies profile</b>	
Anti-Ro/SSA	78 (95)
Anti-La/SSB	47 (53)
<b>Pregnancy Outcome</b>	
Live birth	71 (82.5)
Intrauterine fetal death/termination of pregnancy	15 (17.5)
<b>CHB detection</b>	
In utero	81 (94.2)
Neonatal	5 (5.8)
Mean week of detection of CHB (±SD)	22.4±8.5
<b>CHB degree</b>	
II degree	17 (19.7)
III degree	59 (68.7)
II-III intermittent	4 (4.6)
Other/unknown	5 (5.8)
<b>Therapy after in utero CHB detection</b>	
<b>n=81</b>	
Fluorinated steroids	45 (55)
Intravenous Immunoglobulins	19 (23)
Plasma-exchange	18 (22)
<b>Postnatal outcome of liveborns with CHB</b>	
<b>n=71</b>	
At birth/Neonatal Pacemaker implantation	27 (38)
Neonatal death	3 (4.4)
Later Pacemaker implantation	23 (32.4)
Infant/childhood death	2 (3.2)

**Results:** Eighty-six cases of CHB were collected in 82 women with 85 pregnancies that occurred between 1969–2016. CHB was mostly detected in utero (81

cases, 90.6%) with 5 neonatal CHB. Demographic description of the mothers, pregnancy outcomes and treatment are reported in table 1. Child mortality was observed in 22 (25.5%) cases: 12 fetal, 5 termination of pregnancy and 5 postnatal. Maternal and fetal risk factors for fetal mortality were analysed and, at univariate analysis, factors associated with death were an earlier detection of CHB (20.9  $\pm$  0.9 weeks vs 24.8  $\pm$  5.4 weeks;  $p=0.007$ ), hydrops ( $p=0.002$ ; OR=11.3; CI95% 1.84–69.2) and pericardial effusion ( $p=0.025$ ; OR >100; CI95% 2.88 > 100).

**Conclusions:** The Lu.Ne registry is an ongoing project aiming at collecting all Italian CHB. Our data showed similar rate of fetal/neonatal death and of PM implantation previously reported. We confirmed that hydrops and pericardial effusion are risk factors for fetal death. A peculiarity of our cohorts is that the majority of the mothers (59%) had an established diagnosis of systemic autoimmune disease at CHB detection. This is in contrast with other registries showing that usually CHB was incidentally detected in healthy women and related to the recruiting Centres all belonging to Rheumatology Society. The collection of cases from Gynaecological and Paediatric Centres, planned in the next months, will complete our analysis

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#### SAT0449 JUVENILE ONSET SYSTEMIC LUPUS ERYTHEMATOSUS OUTCOME IN ADULTHOOD: A MONOCENTRIC RETROSPECTIVE COHORT

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**Background:** Outcome of juvenile-onset SLE (j-SLE) during adulthood is poorly described.

**Objectives:** To report adult outcome of j-SLE and compare SLE course during childhood and adulthood.

**Methods:** j-SLE was defined as a SLE fulfilling ACR criteria and diagnosed before the age of 16 years. Mac Nemar test for paired nominal data and Wilcoxon signed rank test for paired data were used.

**Results:** One hundred and six patients j-SLE (88 women and 18 men, female to male ratio: 4.9), mean age at diagnosis: 12.3 years were followed during a mean duration of 13.8 years, from childhood (mean: 4 years) to adulthood (mean: 10.3 years). 97.2% patients received corticosteroids (with intravenous pulses for 50.9%) and 77.3% immunosuppressant drugs. 105 (99%) patients received anti-malarial drugs.

Clinical manifestations of the first flare were: arthritis (67.9%), cutaneous (57.5%), nephritis (23.6%), fever (17.9%), hematologic: ITP, AIHA (15%). Neuropsychiatric manifestations were found in 6.6%. Digestive involvement was only present in 6% of cases. According to the revised SELENA FLARE INDEX (SFI), the first flare was severe for half of the patients (n=55).

Disease course during adulthood had two patterns: 82 patients (77.3%) had at least one SLE flare and 24 (22.6%) a sustained remission. Mean follow up was however significantly higher in the relapsing group (15 years vs 9.8 years,  $p=0.0014$ ). No difference was found between these 2 groups for first flare severity and clinical manifestations during childhood.

Significantly more cutaneous (61.3 vs 42.4%,  $p=0.003$ ), musculoskeletal (75.5 vs 59.4%,  $p=0.007$ ), neuropsychiatric (10.4 vs 3.8%,  $p=0.035$ ), or hematologic manifestations like AIHA (9.4 vs 2.8%,  $p=0.039$ ) or ITP (26.4 vs 10.4%,  $p=0.001$ ), and fever (32.1 vs 3.7%,  $p<0.001$ ) were observed during childhood than during adulthood. Nephritis occurred at similar frequencies in childhood and adulthood (34.9% and 30.2% respectively). Half of adulthood nephritis were relapses of j-SLE nephritis.

At the end of the survey mean global SLICC damage index (SDI) was 0.64. Mean childhood SDI was lower than mean adulthood SDI (0.21 vs 0.45,  $p=0.016$ ). However mean adult follow up was significantly longer. Mean SDI increase per year was similar during childhood and adulthood (0.053 vs 0.049 respectively,  $p=0.563$ ).

13 patients (12.3%), had musculoskeletal damage occurring more frequently during adulthood than childhood (11 vs 2,  $p=0.022$ ), specially avascular necrosis (8 vs 0,  $p=0.008$ ). 5 (4.7%) patients had a renal damage that occurred mostly during adulthood (n=4). Ocular damage was present for 9 (8.5%) patients. Premature gonadal failure occurred for 5 women (5.7%). Among the 88 women 19 had 32 pregnancies, leading to 22 births.

**Conclusions:** Damage accrual seems to increase at the same pace during childhood and adulthood. SDI was low at the end of the survey. This could reflect a protective role for HCQ, more immunosuppressant use with lower dose of steroids. Juvenile SLE nephritis are at high risk of relapsing during adulthood raising the issue of duration of immunosuppressive treatment.

**Disclosure of Interest:** None declared

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#### SAT0450 ESTIMATING DURATION OF RESPONSE IN SYSTEMIC LUPUS ERYTHEMATOSUS TRIALS

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**Background:** The primary endpoint in SLE trials is usually response to therapy at a landmark visit. However, during a trial, patients may alternate between response and non-response states. Duration of response would therefore be important to assess, but the optimal approach for estimating response duration has not been determined. Analysing response duration only among responders at a landmark visit can result in selection bias. Drop-outs and missed visits further complicate estimation of response duration.

**Objectives:** To quantify response duration and assess baseline predictors of transitions into and out of response in SLE patients receiving standard of care (SoC) by fitting a multi-state Markov (MSM) model.

**Methods:** Data on 759 SLE patients with active disease (SLEDAI  $\geq 6$  at entry) randomised to SoC in 52 week trials was obtained from the Collective Data Analysis Initiative (CDAI) database of the Lupus Foundation of America. The following monthly response endpoints (without medication stipulations) were analysed: SRI-4, SRI-5, SRI-6, and BICLA. A MSM model allowing for bi-directional transitions between response and non-response states was fit to estimate the probability of being in response at 52 weeks, average duration of response (sojourn time) and mean total time in response. Predictors of attainment and loss of SRI-5 response were also identified.

**Results:** Based on the MSM model, the probability of being in response at 52 weeks ranged from 42% (SRI-6) to 61% (SRI-4), higher than conventional 52 week landmark response rates that assume non-response for missing data. The estimated mean duration of response ranged from 20.4 weeks (BICLA) to 31.5 weeks (SRI-4). Mean total time in response over 52 weeks based on all patients was 16.4–24.8 weeks. After adjusting for baseline SLEDAI score, patients with lower anti-dsDNA titers were more likely to achieve and maintain SRI-5 response ( $p<0.001$ ). Younger age ( $p<0.001$ ) and higher protein/creatinine ratio ( $p<0.001$ ) were associated with higher frequency of SRI-5 response but also shorter response duration. Response duration was also shorter in patients who were non-White ( $p<0.001$ ), had longer history of disease ( $p=0.03$ ), and lower lymphocyte count ( $p=0.001$ ) at baseline.

Responder index	Landmark response rate at 52 weeks	Probability in response at 52 weeks from MSM (95% CI)	Mean sojourn time in response (95% CI)	Mean total time in response (95% CI)
SRI-4	45.5% (95% CI 42.3%–49.5%)	61.0% (95% CI 58.3%–63.5%)	31.5 weeks (95% CI 28.5–34.6)	24.8 weeks (95% CI 23.7–25.9)
SRI-5	33.6% (95% CI 30.2%–37.1%)	43.0% (95% CI 40.8%–46.3%)	25.7 weeks (95% CI 23.1–28.7)	17.7 weeks (95% CI 16.1–19.1)
SRI-6	32.5% (95% CI 29.2%–36.0%)	41.7% (95% CI 38.8%–44.7%)	24.3 weeks (95% CI 21.9–27.1)	16.4 weeks (95% CI 15.3–17.5)
BICLA	38.9% (95% CI 33.4%–47.7%)	50.2% (95% CI 47.1%–53.5%)	20.4 weeks (95% CI 18.1–23.0)	21.3 weeks (95% CI 19.7–22.5)

**Conclusions:** Factors associated with greater disease severity were consistently associated with shorter response duration on SoC, despite exhibiting variable effects on the probability of achieving response at a given time. Response duration might therefore provide a more discriminating measure to distinguish effective investigational treatments from background SoC, although this remains to be tested. Multi-state models make better use of complex longitudinal clinical trial data and provide a more comprehensive view of the response profile and the role of patient characteristics in different aspects of response.

**Disclosure of Interest:** None declared

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**SAT0451 DISEASE COURSE PATTERNS IN SYSTEMIC LUPUS ERYTHEMATOSUS**

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**Background:** Previous studies described three patterns of disease activity over time in systemic lupus erythematosus (SLE), namely long quiescent, relapsing remitting and persistently active. However, they enrolled prevalent patients, many of whom in the late stages of the disease. As such, the patterns of disease course since diagnosis are not known.

**Objectives:** The aim of the present study was to assess the prevalence and characteristics of such patterns over 10 years of follow-up in an inception cohort.

**Methods:** The inception patients of a large lupus cohort (enrolled within 18 months of diagnosis, n=883), with at least 10 years of follow-up and no time interval >18 months between consecutive visits, were investigated. Monophasic (M) pattern was defined as a clinical SLEDAI-2K=0 [serology (anti-dsDNA antibodies and C3/C4 levels) excluded], achieved within five years since enrollment and maintained for ≥10 years after that. Relapsing-remitting (RR) pattern was defined based on ≥2 remission periods (a remission period equals two consecutive visits with a clinical SLEDAI-2K=0), while patients with no remission were categorised as persistently active (PA). Descriptive and regression analyses were used to compare the different groups regarding cumulative damage at 10 years, mortality and flare rate beyond 10 years.

**Results:** Of 267 patients who fulfilled the inclusion criteria, 27 (10.1%) were monophasics, 180 (67.4%) RR and 25 (9.4%) PA. Thirty-five patients (13.1%) had only one remission period ("hybrid"). There were no significant differences regarding the demographic, clinical, immunological and therapeutic characteristics among groups at enrollment. At 10 years, PA patients had received significantly more glucocorticosteroids [39.4±24.3 g vs. 16.6±10.7 g and 27.3±18.4 g for the M and RR groups, p<0.001] and accumulated significantly more damage [SLICC/DI=2.36±1.6 vs. 0.93±1.07 and 1.22±1.33, respectively, p<0.001]. A trend for higher mortality was observed in the PA patients [24% vs. 13.3% and 11.1% for the RR and M patients respectively, p=0.22] whereas death occurred earlier [18.4±4.4 vs. 20.1±7.2 and 24±4.1 years, p=0.11]. Beyond 10 years, the annual flare rate was higher for the PA and RR patients as compared to the monophasics [0.50±0.40 vs. 0.47±0.57 vs. 0.10±0.18 respectively, p<0.001]. Multinomial regression analysis for group membership showed Black race [OR=2.78, 95% CI=1.05–7.31, p=0.039] and higher adjusted mean SLEDAI-2K over the first two years [OR=1.21, 95% CI=1.11–1.32, p<0.0001] to be associated with a more severe disease course.

**Conclusions:** Approximately 70% of lupus patients followed a relapsing remitting course from diagnosis onwards, while 10% displayed a monophasic and another 10% a persistently active course. Black race and more severe disease over the first two years were associated with a worse disease course.

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**SAT0452 ENDOTHELIUM DYSFUNCTION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS WITH AND WITHOUT NEPHRITIS**

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**Background:** Organ-specific manifestations in systemic lupus erythematosus (SLE) are highly influenced by the inherent characteristic of the vasculature<sup>(1)</sup> Endothelial dysfunction might have significant roles in the pathogenesis of glomerular diseases. CD31 or platelet endothelial cell adhesion molecule-1 is known to have roles in angiogenesis, platelet function, thrombosis, and regulation of leukocyte migration through vascular walls<sup>(2)</sup>

**Objectives:** to assess the endothelium dysfunction in SLE patients (pts) and to determine its association with lupus nephritis (LN)

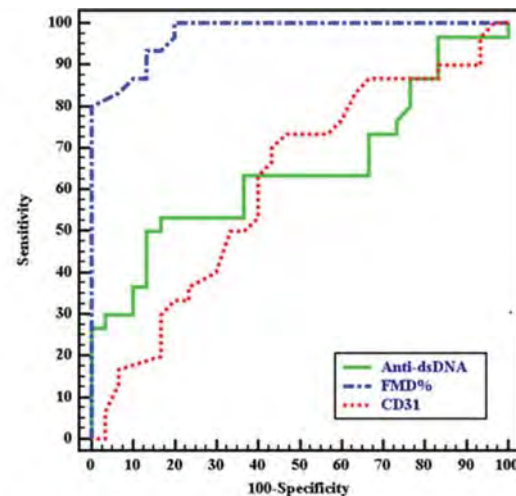
**Methods:** Study included 60 pts with SLE fulfilling the SLICC criteria for classification of SLE: 30 with(LN), 30 SLE without LN and 10 matched healthy controls. Routine laboratory tests, lipid profile, renal functions, titres of autoantibodies [ANA, anti ds-DNA, anticardiolipin antibodies ACL(IgM, IgG), flowcytometry to detect PECAM-1/CD31, doppler ultrasound to detect FMD of the brachial artery and SLEDAI were done to all SLE pts. Pts with diseases known to affect endothelial function: smoking, DM, essential HTN, known CAD were excluded

**Results:** Correlation between FMD% and different parameters are shown in table 1. There was a statistical significant positive relation between CD31 and urea in LN(p=0.014), non LN(p=0.014), total SLE pts(p<0.001), creatinine in non LN group

(p=0.025), 24 hour protein in LN(p<0.001), non LN(p<0.001) and total SLE pts (p<0.001), cholesterol in LN(p<0.001), non LN(p=0.001) and total SLE pts (p<0.001), LDL in LN(p=0.001), non LN(p=0.009) and total SLE pts(p<0.001), TG in total pts(p=0.048), anti-dsDNA in LN(p=0.024) and total SLE pts(p=0.008), SLEDAI in LN(p=0.001) and total SLE pts(p<0.001).

	LN		FMD%		Total patients	
	r	p	r	p	r	p
<b>Demographic data</b>						
Age	0.033	0.862	0.275	0.141	0.057	0.666
D. duration	-0.730	<0.001	-0.574	0.001	-0.332	0.010
<b>Renal function</b>						
Urea	-0.771	<0.001	-0.689	<0.001	-0.731	<0.001
Creatinine	-0.084	0.657	0.196	0.300	-0.324	0.012
Creatinine clearance	0.084	0.660	-0.024	0.898	0.200	0.126
24 hour Urine protein	-0.543	0.002	-0.392	0.032	-0.631	<0.001
<b>Lipid profile</b>						
Cholesterol	-0.438	0.016	-0.534	0.002	-0.530	<0.001
LDL	-0.837	<0.001	-0.779	<0.001	-0.766	<0.001
Triglyceride	-0.252	0.179	0.086	0.652	-0.468	<0.001
<b>Immunological profile</b>						
Anti DNA	-0.517	0.003	-0.648	<0.001	-0.565	<0.001
SLEDAI	-0.792	<0.001	-0.853	<0.001	-0.676	<0.001

Fig 1 The performance of FMD to detect LN was better than anti-dsDNA and than CD31, where FMD was 80% sensitive and 100% specific at cut off point >189 >49%


**ROC curve for anti-dsDNA, CD31 % and FMD % to detect LN in SLE pts**

**Abstract SAT0452 – Figure 1.** ROC curve for anti-dsDNA, CD31% and FMD% to detect LN in SLE pts

**Conclusions:** Endothelial dysfunction is the first step in the atherogenic process. FMD and CECs may be used as markers for endothelial dysfunction in SLE. FMD correlated with proteinuria and may be used as an early marker for LN. CECs may play a role in atherosclerosis, vasculitis and LN

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**SAT0453 ASSOCIATION OF COMORBID PULMONARY CONDITIONS WITH PATIENT-REPORTED OUTCOMES IN SYSTEMIC LUPUS ERYTHEMATOSUS**

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**Background:** Risk of chronic obstructive pulmonary disease (COPD) and allergic conditions, including asthma (AM), is elevated among SLE patients.<sup>1</sup> Both AM and COPD negatively affect quality of life measured through patient-reported outcomes (PROs). Little research has examined the impact of AM and COPD on PROs in SLE, independent of SLE disease status.

**Objectives:** Determine the impact of AM/COPD on PROs in SLE, concurrently and longitudinally.

**Methods:** Data from 2 large, longitudinal, observational cohorts were examined (Lupus Outcomes Study, LOS: n=796; National Data Bank for Rheumatic Diseases, Forward: n=2804). AM and COPD were determined at study entry by self-report. PROs included validated scales or items measuring physical functioning, fatigue, pain, cognitive function, depressive symptoms and global severity, although the cohorts included different PROs (Table). Multiple regression analyses examined differences between subjects with and without AM/COPD cross-sectionally, controlling for age, sex, race, lupus duration, education, income, obesity, smoking, other comorbid conditions, and presence or history of renal involvement, clotting disorder or seizures. Longitudinal analyses examined PROs at 3 years (yrs) of follow-up, controlling for covariates above as well as baseline PRO values.

**Results:** LOS cohort was 92% female, mean age 47 years, 70% white, 42% ever smokers, mean lupus duration 13 years. Forward cohort was 94% female, mean age 51 years, 87% white, 38% ever smokers, mean lupus duration 16 years. 36% of LOS and 30% of Forward reported AM/COPD at study entry, compared to COPD prevalence of 7%<sup>2</sup> and AM prevalence of 9.7%<sup>3</sup> among US women. In cross-sectional analyses (Table), AM/COPD were associated with significantly worse scores on all PRO measures, except depressive symptoms (LOS). Longitudinal results were similar: AM/COPD were associated with worse scores on all PROs except SF-36 PF and Fatigue in LOS.

Table. Multivariate Regression Analyses

	PRO variables	Cross-sectional	Longitudinal
LOS	SF-36 Physical Function (PF) <sup>†</sup>	-9.2 (<0.0001)*	-1.8 (0.26)
	SF-36 Fatigue	6.6 (<0.0001)	2.4 (0.09)
	CESD	1.5 (0.10)	1.7 (0.04)
Forward	MOS Cognitive <sup>†</sup>	-6.6 (<0.0001)	-3.3 (0.01)
	HAQ II	0.2 (<0.0001)	0.2 (<0.0001)
	Fatigue (0-10)	0.7 (<0.0001)	0.8 (<0.0001)
	PHQ8	2.0 (0.01)	1.9 (0.006)
	Pain (0-10)	0.8 (<0.0001)	0.8 (<0.0001)
	Trouble thinking or remembering	1.5 (1.2-1.8)	1.2 (1.0-1.5)
	Global severity (0-10)	0.5 (<0.0001)	0.6 (<0.0001)

\*Beta (p value) from multiple linear regression analyses, except Forward 'trouble thinking or remembering', which is odds ratio (95% CI)

<sup>†</sup>Lower scores=worse status. Otherwise, higher scores=worse status  
CESD=Centre for Epidemiologic Studies Depression scale; HAQ=Health Assessment Questionnaire; PHQ8=Patient Health Questionnaire depression inventory

**Conclusions:** AM/COPD are more common in SLE than the general population and are independently associated with worse outcomes on a wide range of PROs, even after controlling for sociodemographic and lupus characteristics. Findings suggest that physicians should screen for pulmonary comorbidities and ensure adequate treatment for these conditions. Future analyses of PROs in SLE should include AM/COPD as important comorbid conditions.

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**SAT0454 IN PRIMARY SJÖGREN'S SYNDROME BLOOD CD180-NEGATIVE B CELLS ARE INCREASED IN PATIENTS WITH HIGH SYSTEMIC DISEASE ACTIVITY**

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**Background:** CD180, a related member of the Toll-like receptor family, seems to be underexpressed at the plasma membrane in circulating B cells of auto-immune disease (systemic lupus especially),<sup>1</sup> and is lost in various B-cell lymphomas except marginal zone lymphomas (MZL), the most severe complication of primary Sjögren's Syndrome (pSS).<sup>2</sup>

**Objectives:** To define the expression of CD180 at the plasma membrane of circulating B cells of pSS and determine its association with systemic disease activity.

**Methods:** The expression of CD180 at the plasma membrane of circulating B cells was studied by flow cytometry, in 69 successive patients with pSS, in comparison to patients with systemic lupus (SLE) (n=7) and healthy controls (n=28).

**Results:** The cohort of pSS was composed of 65 women for 4 men, median age of 59 years.<sup>25-89</sup> Median clinESSDAI was 2 [0-18], 46 patients with a clinESSDAI >0 (low disease activity), 18 patients with a clinESSDAI >5 (moderate disease activity) and 6 patients ≥14 (high disease activity). The more frequently involved domains of the ESSDAI were biological (39%, n=27), glandular (32%, n=22), articular (20%, n=14), and peripheral neurological (9%, n=6) domains. Forty patients were anti-SSA+, 16 anti-SSA and anti-SSB+. 18 had a hypergammaglobulinemia, 17 a hypocomplementemia, 7 a cryoglobulinemia, 18 a rheumatoid factor and 9 a lymphopenia.

**- CD180-negative B cells in pSS, SLE and controls**

The proportion of total lymphocytes, B cells, T cells, NK cells or CD180-negative B cells (0.85% vs 0.95%, p=0.64) was not significantly different between pSS patients and healthy controls.

Patients with SLE had significantly fewer lymphocytes (860 vs 1544, p=0.0012), B cells and T cells than those with pSS (p=0.023 and p=0.0016); CD180-negative B cells tended to have a higher proportion in SLE than in pSS patients (1.9% vs 0.85%, p=0.055).

**- Increase of CD180-negative B cells in patients with pSS and high systemic disease activity**

CD180-negative B cells subset was significantly higher in patients with high systemic disease activity (2.55% CD180-negative B cells in patients with clinESSDAI ≥14 vs 0.8% in patients with clinESSDAI <14, p=0.036). CD180-negative B cells subset was also significantly higher in patients with anti-SSA and anti-SSB+ (1.9% vs 0.8%, p=0.0082) and in patients with markers of B-cell activation: hypergammaglobulinemia (1.7% vs 0.75%, p=0.034), hypocomplementemia (2.1% vs 0.8%, p=0.0021), cryoglobulinemia (4.6% vs 0.8%, p=0.0097), presence of rheumatoid factor (1.7% vs 0.7%, p=0.015).

**Conclusions:** Blood CD180-negative B cells are increased in pSS patients with high systemic disease activity or in immunologically active pSS. Functionality of CD180 and the prognostic interest of CD180 staining on blood B cells to predict lymphoma in pSS patients, have now to be studied.

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**SAT0455 CLINICAL AND IMMUNOLOGICAL CHARACTERISTICS OF PATIENTS WITH SUSPECTED SJÖGREN SYNDROME AND ANTI-RO52 POSITIVE ANTIBODIES**

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**Background:** Anti-Ro52 antibodies have been described in patients with Sjögren syndrome (SS) but there are limited data on their significance, and they are not included in the diagnostic criteria of SS.

**Objectives:** To analyse the clinical and immunological characteristics of patients with suspected SS and positive anti-Ro52 antibodies, and to assess the diagnostic value of this antibodies.

**Methods:** retrospective study of all patients evaluated at our Department between January 2000 and January 2016 for possible SS in which anti-Ro52 abs. were determined. Patients were classified as having SS, according to the 2002

European-American Consensus Group (EACG) criteria. Statistical analysis was performed using the SPSS vs.20 package

**Results:** 348 patients (331 women), mean age at diagnosis 56.12±14.19 years (range 22–92), with possible SS were analysed. All patients met the European criteria for SS diagnosis, and 242 the EACG criteria. AAN were positive in 345 (99.4%) patients, RF in 169 (48.4%), anti-Ro60/SSA in 188 (54%), and anti-La/SSB in 11 (32%). Anti-Ro52 abs. were positive in 173 (49.7%) patients: 162 women, 11 men. Of these patients, 154 (89%) also had anti-Ro60/SSA positive abs., 103 (59.5%) anti-La/SSB abs., and 117 (67.6%) positive RF. Anaemia, leukopenia, lymphocytopenia and hypergammaglobulinemia, were significantly more frequent in patients with anti-Ro52 positive abs. The presence of anti-Ro52 abs. was significantly related to the development of lung fibrosis (OR 2.42, 95% CI 1.23–4.75, p=0.007), peripheral neuropathy (OR 2.53, 95% CI 1.1–5.95, p=0.022), arthritis (OR 1.95, 95% CI 1.2–3.35, p=0.016) and parotitis (OR 3.04, 95% CI 1.75–5.3, p<0.001). A total of 160/173 (92.5%) patients with anti-Ro positive abs. met the EACG criteria. When we analysed the 13 patients with anti-Ro52 positive abs., which did not meet the AECG criteria, these patients presented severe salivary gland scintigraphic involvement, positive ocular test for dry eyes, more hypergammaglobulinemia (OR 6.67, 95% CI 1.95–22.8, p=0.003), more peripheral neuropathy (OR 13.8, 95% CI 2.1–92.7, p=0.0012), more lung fibrosis (OR 13.95, 95% CI 2.1–93.7, p=0.012), and more risk of lymphoma development (OR 16.72, 95% CI 1.4–199.8, p=0.039), than patients with suspected SS who did not meet the AECG criteria and who had negative anti-Ro52 abs.

**Conclusions:** in our series most patients with anti-Ro52 positive antibodies had also anti-Ro60/SSA positive antibodies and met the AECG criteria. However, there were 13 patients with positive anti-Ro52 abs., which did not meet the AECG criteria. These patients showed similar characteristics to those with positive anti-Ro52 abs. and AECG criteria, and had more risk to develop peripheral neuropathy, lung fibrosis and lymphoma. Our results support that anti-Ro52 antibodies should be included in the diagnostic criteria for SS.

**Disclosure of Interest:** None declared

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## SAT0456

**THE INCIDENCE OF CARDIOVASCULAR EVENTS IN ITALIAN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IS LOWER THAN IN NORTH EUROPEAN AND AMERICAN COHORTS: IMPLICATION OF DISEASE-ASSOCIATED AND TRADITIONAL RISK FACTORS AS EMERGED BY A 16-YEAR RETROSPECTIVE GIRRCS STUDY**

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**Background:** Cardiovascular (CV) disease is the leading cause of premature death among Systemic Lupus Erythematosus (SLE) patients<sup>1</sup>. Several studies have analysed the incidence of CV events in SLE patients. However, the majority of them have been conducted in American and North European countries 2–7. At the best of our knowledge, no studies in Italy have considered cumulative incidence and incidence rate of CV events in Italy.

**Objectives:** The present study is devoted to estimate the incidence of a first ever CV event in Italian lupus patients from five rheumatologic tertiary units from North, Centre and South Italy and to search for features associated with and potentially causative of the detected differences.

**Methods:** Clinical charts of SLE patients consecutively admitted to five Italian rheumatologic centres from November 1 st 2000 and December 31 st 2016 were retrospectively studied. Patients selected were free of CV events at baseline. CV cumulative incidence was evaluated as the proportion of patients who experienced a new CV event over the follow up period. CV incidence rate was expressed as the number of events in the cohort divided by the total number of

years at risk. Our incidence was compared with that detected in the Italian general population and those reported in SLE cohorts from other countries.

**Results:** The median duration of follow-up was 6 years (IQR=3–11). During the observational period, 39(cumulative incidence=7.6%) of the 511 patients had a first CV event with an incidence rate of 10.4/1000 person-years i.e. 12 times higher than in the general population. The CV cumulative incidence detected in our Italian cohort was similar to that reported in the Spanish cohort, but lower than those from North European and American cohorts. The Italian cohort differed from other SLE cohorts in some traditional risk factors (smoke, hypertension, dyslipidemia) and treatment with aspirin and hydroxychloroquine.(table1)

**Abstract SAT0456 – Table 1.** Comparison of characteristics among patients from different SLE cohorts (values in bold are statistically significant at an alpha of 0.05).

	Our cohort N=511	Spain <sup>1</sup> N=3648	Sweden <sup>2</sup> N=182	Baltimore <sup>3</sup> N=1874	PROFILE <sup>4</sup> N=1333	MESA <sup>5</sup> N=70	p value
Male gender (n,%)	367; 71	353; 9.7	18; 10	136; 7.2	127; 9.5	13; 18.5	<b>0.004</b>
Age, years (median, IQR) (mean, SD)	39 (31–46) 45, 12.6	45 (35–56) -	45 (31–53) -	- 37, 12	- 35, 7.12.9	52	
Ethnicity							
White European(n,%)	511; 100	3300;	171; 94	0	0	0	
White Americans(n,%)	0	304	0	840; 48.5	85; 97	0	
Black n,%)	0	18; 5.1	0	472; 36.8	0	0	
Asians(n,%)	0	8; 0.2	1; 0.5	0	0	0	
Hispanics(n,%)	0	21; 0.6	0	241; 18.1	0	0	
Other (n,%)	0	0	0	0	29; 0.6	2.5	
Smokers (n,%)	135; 26.6	1350;	92; 51	215; 16.1	37; 52.9	17; 24	<b>&lt;0.0001</b>
Hypertension (n,%)	101; 19.9	370;	54; 30	667; 51.5	17; 24	17; 24	<b>&lt;0.0001</b>
Dyslipidemia (n,%)	111; 21.6	1100;	75; 41	30.1	9; 13	9; 13	<b>&lt;0.0001</b>
Diabetes (n,%)	18; 3.1	179; 4.9	4; 2	-	5; 7	5; 7	<b>&gt;0.05</b>
HCG(n,%)	451; 88.0	2878;	52; 29	1075; 80.6	52; 75	52; 75	<b>&lt;0.0001</b>
Aspirin(n,%)	302; 59.5	78.9	34; 19	382; 28.6	382; 28.6	382; 28.6	<b>&lt;0.0001</b>
CV events(n,%)	39; 7.6	205; 7.4	24; 13	134; 7	123; 9.8	17; 24	<b>&lt;0.0001</b>
First CV event	Yes	Yes	Yes	Yes	Yes	No	
Mean follow-up (years)	6	-	8.3	-	6.4	7.7	
Person-years	3721	-	-	9485	-	540	
Incidence rate (1000p-y)	10.4	-	-	14.1	-	31.4	

**Conclusions:** Our study confirmed the increased CV risk in SLE compared with the general population. However, the incidence of CV events in our SLE series was lower than that detected in North European and American lupus cohorts. These disparities could be ascribed to the differences in the prevalences of traditional CV risk factors among the distinct cohorts. Nevertheless, our CV cumulative incidence was very similar to that detected in the Spanish cohort, despite their higher frequency of traditional risk factors. For this evidence, the geographic (Mediterranean) origin deserve to be considered. On the other hand, the slight difference detected between our series and Baltimore cohort<sup>2</sup>(where patients were examined every 3 months) underlines the need of a strict follow-up of the SLE patient.

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**SAT0457 SJÖGREN BIG DATA PROJECT, THE FIRST EXAMPLE OF DATA SHARING IN AUTOIMMUNE DISEASES: ANALYSIS OF 10475 WORLDWIDE PATIENTS**

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**Objectives:** To take a "high-definition" picture of the main features of primary Sjögren syndrome (SjS) following a worldwide data-sharing cooperative merging of international clinical SjS databases.

**Methods:** The Big Data Sjögren Project Consortium is an international, multi-centre registry created in 2014 including leading clinical centres in SjS of the 5 continents that shared a harmonised data architecture and conducted cooperative online efforts to refine collected data of primary SjS patients fulfilling the 2002 classification criteria.

**Results:** By January 2018, the participant centres had included 10 475 patients from 22 countries, including 7637 (73%) patients from Europe, 1420 (14%) from America, 1186 (11%) from Asia, 167 (1.4%) from Australia and 65 (0.6%) from Africa. The cohort included 9781 (93%) women and 694 (7%) men, with a mean age at diagnosis of primary SjS of 53 years. The frequencies of fulfilment of the 2002 criteria were 92% for dry eye, 94% for dry mouth, 83% for abnormal ocular tests, 82% for positive minor salivary gland biopsy, 78% for abnormal oral diagnostic tests and 76% for positive anti-Ro/La antibodies. The frequency of positive immunological markers at diagnosis was 79% for ANA, 73% for anti-Ro, 49% for RF, 45% for anti-La, 13% for low C3 levels, 14% for low C4 levels and 7% for cryoglobulins.

**Conclusions:** International data sharing-based projects merging disperse clinical registries may be essential tools to increase current knowledge and to improve patient care in specific systemic autoimmune diseases.

**Disclosure of Interest:** None declared

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**SAT0458 URINE SOLUBLE UROKINASE PLASMINOGEN ACTIVATOR RECEPTOR AS A POTENTIAL BIOMARKER OF LUPUS NEPHRITIS ACTIVITY**

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**Background:** Over the recent years, soluble urokinase plasminogen activator receptor (suPAR) has been described as a valuable indicator of the activation state of the immune system. Our previous work supported that suPAR might be an objective marker for identifying systemic lupus erythematosus (SLE) patients with active disease. Urokinase plasminogen activator receptor (uPAR) expression is also induced in podocytes during renal diseases such as focal segmental

glomerulosclerosis (FSGS). In addition, levels of suPAR were found to be elevated in paediatric and adult patients with FSGS. Current noninvasive laboratory and clinical measures of lupus nephritis (LN) activity are not sensitive or specific enough to reliably measure the course of LN. Improved, noninvasive biomarkers are needed to accurately detect LN activity.

**Objectives:** To evaluate suPAR in urine as a potential biomarker of renal system-specific disease activity in SLE.

**Methods:** A prospective follow-up study was designed. 14 SLE patients with newly diagnosed LN and 31 healthy individuals were enrolled in this study. LN was the leading symptom of all SLE patients. Further organ involvements including arthritis, leucopenia, serositis, fever and rash also occurred at the time of LN diagnosis. 12 out of 14 LN were confirmed by renal biopsy. Urine samples were taken before the initiation of LN induction therapy, and monthly thereafter (6 to 11 times). Global and renal disease activity were defined using the SLE Disease Activity Index 2000 (SLEDAI-2K) and the SLEDAI-2K renal domain score. suPAR concentrations in the urine were measured with the suPARnostic Flex ELISA assay. Non-parametric testing was used for statistical analysis, including the Kruskal-Wallis test and the Mann-Whitney U test.

**Results:** All urine suPAR levels were elevated in SLE patients with active LN compared with patients with resolved LN and healthy controls (21.75 vs 4.93 and 5.09 ng/mL, respectively, p<0.0001). suPAR levels were higher measured before than after the initiation of LN induction therapy in patients before resolution of active LN (29.46 vs 21.07 ng/mL, p=0.0122). Prospective follow-up measurements also suggested that urine suPAR levels raised again in patients with a relapse of LN according to SLEDAI-2K renal domain score (n=3; 5.45 vs 15.19 ng/mL, p=0.0127).

**Conclusions:** Urine suPAR is a promising LN activity biomarker, given its isolated elevation in urine in active LN and pronounced decrease with LN improvement. It may potentially become a more convenient alternative to renal biopsy, the current gold standard of LN activity monitoring.

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**SAT0459 OCCURRENCE OF LYMPHOMA IN SYSTEMIC LUPUS ERYTHEMATOSUS: A CASE-SERIES OF 38 PATIENTS**

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**Background:** Patients with systemic lupus erythematosus (SLE) are at higher risk than the general population of developing lymphoma. Relatively little is known about the risk factors, the treatment and the outcome of lymphoma in SLE.

**Objectives:** We aimed to describe a cohort of patients suffering from lymphoma in the setting of SLE and to study the risk factors of developing this complication.

**Methods:** We collected clinical data of SLE patients with confirmed lymphoma in a multicentric and retrospective study. SLE patients were eligible for the study if they fulfilled at least 4 of the 1997 ACR criteria for SLE. Exclusion criteria were HIV or C hepatitis infection.

**Results:** We included 38 patients (34 women and 4 men) coming from 10 different French University Hospitals. The lymphoma occurred after the diagnosis of SLE for 35 patients, with a median (range) time of 8.8 years (0–39). In their past or present medical history, 11 (29%) had a haematological involvement (5 immune thrombocytopenias, 4 autoimmune hemolytic anemias and 2 patients with both). Nine patients (24%) had associated Sjögren syndrome. 22 patients (58%) had a polyclonal hypergammaglobulinemia. Before the occurrence of the lymphoma, 18 patients (47%) had received an immunosuppressant during a median (range) period of 67 months. 6–195 17 patients had an indolent B cell lymphoma (IBCL), 14 a high-grade B cell lymphoma (11 diffuse large B cell lymphoma [DLBCL]; 2 a primary DLBCL of the central nervous system; and 1 an iatrogenic immunodeficiency-associated lymphoproliferative disorder), 5 a Hodgkin's disease (HD), and 2 a T cell lymphoma. The EBER *in situ* hybridization stain was positive in 7 of the 13 patients assessed (3/3 HD, 3/7 DLBCL and 1/2 IL) and was not associated with the immunosuppressant prescription. The median (range) of the survey after the lymphoma was 28.5 month (0–235.1). The 14 DLBCL patients except 1 were treated with chemotherapy: 4 died, 9 were in complete remission and 1 was in progression. Regarding the 17 IBCL, 9 patients were treated with chemotherapy, 2



patients with surgery, 1 patient with radiotherapy and 5 patients were not treated: 3 patients had to short follow-up or were lost, 1 died, 2 developed a DLBCL, 4 were stable and 7 were in complete remission. The 5 HL were treated with chemotherapy and all were in complete remission.

**Conclusions:** IBCL and DLBCL were the most common type of lymphomas in SLE patients. Data suggest a role for EBV but not for exposition to immunosuppressant in the pathogenesis of SLE-associated lymphoma. The outcome of lymphoma in the setting of SLE seems not different from the outcome of lymphoma in the general population. A case-control study is ongoing to study the risk factors associated with the occurrence of lymphoma in SLE

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SAT0460

#### LONG-TERM IMMUNE PROTECTION FOLLOWING PNEUMOCOCCAL 13-VALENT/23-VALENT POLYSACCHARIDE VACCINE IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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**Background:** Systemic lupus erythematosus (SLE) patients are at increased risk for *Streptococcus pneumoniae* infection. Although pneumococcal vaccination is an attractive method to prevent invasive pneumococcal infection, vaccination coverage remains dramatically low in SLE. Moreover, the efficacy of vaccination may be reduced in SLE patients and sequential pneumococcal vaccination using new conjugated pneumococcal vaccines in combination with 23-valent pneumococcal polysaccharide vaccine (PPV23) is now advocated.

**Objectives:** We aimed to determine the efficacy of the prime-and-boost vaccination strategy using the 13-valent pneumococcal conjugate (PCV13) and 23-valent polysaccharide (PPV23) vaccines in SLE.

**Methods:** Consecutive SLE patients admitted from April to December 2015 in our daycare hospital unit (Paris, France) were enrolled to receive PCV13 vaccine followed by PPSV23 vaccine 8 weeks later. Immune protection, defined by an antigen-specific IgG concentration  $\geq 1.3$   $\mu\text{g/mL}$  for at least 70% of 7 pneumococcal serotypes (4, 6 B, 9 V, 14, 18 C, 19 F, 23 F), was assessed at baseline, 2 and 12 months. The primary endpoint was immune protection 12 months (long-term) after PCV13 shot.

**Results:** 37 consecutive adult SLE patients admitted in our daycare hospital unit (Department of Internal Medicine, Bichat Hospital, Paris, France) were screened for pneumococcal vaccination. Among them, 8 patients refused to be vaccinated, 7 patients accepted the vaccination but refused to complete the 12 months immune response follow up and 1 patient had already been vaccinated against pneumococcal infection. Eventually, 21 (40<sup>25-75</sup> years; 85.7% female) SLE patients were included in the study and received the sequential PCV13/PPV23 pneumococcal vaccines. Only 12 patients (57.1%) reached the primary endpoint. Nine patients had no long-term protection with a seroconversion that never (n=4, not protected, NP) or only transiently (n=5, short-term protected, STP) occurred. B-cells defects and immunosuppressive treatment were associated with the NP status. A lower IgG2 serum level and a higher ratio of pre-germinal/post-germinal centre B cells were associated with the STP status. The serotype 19 F IgG titer measured 2 months after PCV13 had the best ability (sensitivity of 100% [95% CI: 47.8–100]; specificity of 91.7% [95% CI: 61.5–99.8]) to predict long-term protection.

**Conclusions:** The benefit of sequential PCV13/PPV23 vaccination in SLE is limited. Several factors are associated with long-term immune protection and may help to design selective schedule strategy and/or new vaccines.

**Disclosure of Interest:** None declared

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SAT0461

#### ULTRASONOGRAPHY OF SALIVARY GLANDS IN PRIMARY SJOGREN'S SYNDROME AND ASSOCIATION WITH DISEASE ACTIVITY, SEROLOGICAL MARKERS AND BIOPSY OF MINOR SALIVARY GLANDS

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**Background:** Parenchymal inhomogeneity of the salivary glands (SG) is the most relevant ultrasonographic (US) feature for diagnosis primary Sjogren's syndrome (pSS).

**Objectives:** To analysis parenchymal echostructure of SG in patients with established pSS and association USSG score with disease activity, serological markers and biopsy of minor salivary glands (MSG).

**Methods:** This study included 205 pSS patients (mean age 53.9 $\pm$ 11.5, disease duration 5.6 years) and 87 healthy controls (mean age 52.3 $\pm$ 14.7). All pSS patients fulfilled the AECG diagnostic criteria. The disease activity was evaluated by EULAR SS disease activity index (ESSDAI), Sjögren's Syndrome Disease Damage Index (SSDDI) and EULAR Sjogren's syndrome patient reported index (ESSPRI). The presence of ANAs assessed by indirect immunofluorescence assay on Hep-2 cells, anti SSA and anti SSB (commercial ELISA kit) and RF (nephelometry). The parotid and submandibular glands on both sides were examined by US using a GE LogiqE9 with a linear high-frequency transducer (6–15 MHz). Inhomogeneity of the SG were graded according to the De Vita scoring system. Grading 0 was for a homogeneous gland, 1 for mild inhomogeneity, 2 for evident inhomogeneity and 3 for a grossly inhomogeneous gland. The global SGUS score (0–6) was the sum of the scores of each pair of SG. Statistical analysis was performed by SPSS v19. Data were compared using *t*-test,  $\chi^2$  test and Mann-Whitney U test. The diagnostic accuracy of inhomogeneity was evaluated by area under the receiver operating characteristics curves (AUC-ROC). A multivariate linear regression analysis was performed to determine the factors associated with SGUS score.

**Results:** Xerophthalmia and xerostomia were presented in 185/205 (90.2%) and 186/205 (91.2%), respectively. According to ESSDAI, the majority of pSS patients 88/205 (43%) had moderate disease activity. Seventy-eight per cent of pSS patients were anti-SSA positive, 44% anti-SSB positive. Biopsy of MSG was positive in 140/172 (81.4%) pSS patients. US abnormalities were established in 197/205 (96%) pSS patients and in 16/85 (18%) controls ( $p < 0.0001$ ). The median SGUS was significantly higher in pSS patients in comparison with control group [median (range) 4 (0–6) vs. 0 (0–2),  $p < 0.0001$ ]. The diagnostic accuracy of parenchymal inhomogeneity was high, AUC-ROC 0.89 (0.02) with cut-off  $\geq 2$  (Sp 89.5%, Sn 89.3%). Out of 197 pSS patients with abnormal findings, the most patients had US score 4 (47%), while 81% in control group had score 0. After adjustment for potential confounders variables, dry mouth ( $B=1.192$ ,  $\beta=1.542$ ;  $p=0.04$ ), ESSDAI ( $B=0.184$ ,  $\beta=1.203$ ;  $p=0.008$ ) and biopsy of MSG ( $B=1.006$ ,  $\beta=2.735$ ;  $p=0.05$ ) were significantly associated with advanced US changes of SG. Dry eyes, SSDAI, ESSPRI and serological markers were not associated with USSG score ( $p > 0.05$ ).

**Conclusions:** Our findings confirmed that parenchymal inhomogeneity of the salivary glands is the reliable feature for primary Sjogren's syndrome. Presence of xerostomia, objective disease activity assessed by ESSDAI and pathological findings of biopsy of minor salivary glands had predictive value for advanced US change of salivary glands.

**Disclosure of Interest:** None declared

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SAT0462

#### PD-1+CXCR5-CD4+ T CELLS MAY PLAY AN IMPORTANT ROLE IN THE SEVERITY OF SYSTEMIC ERYTHEMATOSUS LUPUS

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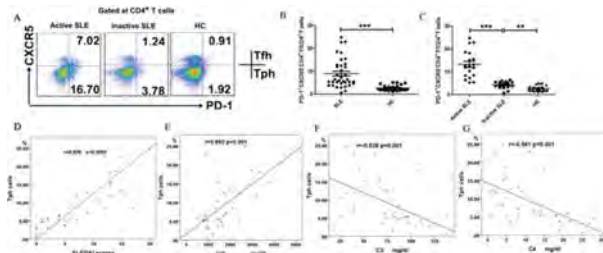
**Background:** CD4<sup>+</sup> T cells are central mediators in specific autoimmune diseases; however, it remains challenging to define their key effector functions in systemic erythematosus lupus (SLE), a chronic immune-mediated damage to the whole system. Programmed death 1 (PD-1), a negative T cell regulator to maintain peripheral tolerance, induces negative signals to T cells during interaction with its ligands. PD-1<sup>+</sup>CD4<sup>+</sup>T cells could be divided into PD-1<sup>+</sup>CXCR5<sup>+</sup>CD4<sup>+</sup>T peripheral helper cells and PD-1<sup>+</sup>CXCR5<sup>+</sup>CD4<sup>+</sup>T (Tfh) cells according to CXCR5 expression. PD-1<sup>+</sup>CXCR5<sup>+</sup>CD4<sup>+</sup>T peripheral helper (Tph) cells were proven to promote B cell responses and antibody production in rheumatoid arthritis Rao DA, Nature, 2017.<sup>1</sup> Tfh cells were required for the generation of most memory B cells and long-lived plasma cells in SLE. However, what the role of Tph cells in the pathogenesis of SLE was unknown.

**Objectives:** We assessed that whether Tph cells were associated with clinical profiles of patients with SLE.

**Methods:** This cohort study included 36 patients with SLE from the Division of Rheumatology, the first Affiliated Hospital, college of medicine, Zhejiang University. All SLE patients fulfilled the American College of Rheumatology revised classification criteria. 26 Age- and sex-matched healthy individuals had no connective tissue disorders, neoplasms or current infections. Here we used flow cytometry to analyse PD-1<sup>+</sup>CXCR5<sup>+</sup>CD4<sup>+</sup>T cells in peripheral blood from patients with SLE. Correlation between Tph cells and other parameters was investigated by Spearman's correlation coefficient test, and comparisons between groups were performed using nonparametric Mann-Whitney test.

**Results:** Firstly, we revealed a markedly expanded population of Tph cells (8.95  $\pm$  6.35 vs. 2.67  $\pm$  1.22,  $p < 0.0001$ ) in the circulation of patients with SLE (n=36),

compared to healthy controls ( $n=26$ ) (figure 1a, b). And Tph cells were much higher in active group than those in inactive group ( $13.21\pm 5.96$  vs.  $4.19\pm 1.59$ ,  $p<0.0001$ ) (figure 1a, c). Secondly, like Tfh cells ( $r=0.611$ ,  $p<0.0001$ ), Tph cells ( $r=0.829$ ,  $p<0.0001$ ) were significantly associated with SLEDAI scores (figure 1d). Tph cells were associated with IgG ( $r=0.650$ ,  $p<0.001$ ) (figure 1e), C3 ( $r=-0.528$ ,  $p=0.001$ ) (figure 1 f), C4 levels ( $r=-0.561$ ,  $p=0.001$ ) (figure 1 g), but not ESR, CRP, IL-2, IL-6, TNF- $\alpha$ , IFN- $\gamma$ , and IL-17A levels. Furthermore, Tph cells were much higher in lupus patients with arthritis ( $17.71\pm 10.05$  vs.  $11.14\pm 6.84$ ,  $p=0.045$ ), in skin mucous group ( $18.71\pm 6.08$  vs.  $10.32\pm 7.32$ ,  $p=0.004$ ), in pleuritis ( $20.60\pm 8.87$  vs.  $11.40\pm 7.24$ ,  $p=0.025$ ), in pericarditis group ( $26.65\pm 0.21$  vs.  $11.58\pm 7.25$ ,  $p=0.006$ ), in group with haematological involvement ( $15.51\pm 7.76$  vs.  $8.97\pm 6.58$ ,  $p=0.010$ ), when compared to patients without relevant symptoms.



**Conclusions:** Our data suggest that increased Tph cell proportions seem to have an important role in lupus disease development.

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SAT0463

#### OLFACTORY IMPAIRMENT IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME AND ITS CORRELATION WITH ORGAN INVOLVEMENT AND IMMUNOLOGICAL ABNORMALITIES

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**Background:** Recent findings suggest that autoimmune disorders predispose to a diminished capacity to smell. This has been shown for patients with systemic lupus erythematosus as well as for patients with rheumatoid arthritis. However, this problem has not received much attention in primary Sjögren's syndrome (pSS).

**Objectives:** The aim of the study was to assess the olfactory functions of patients with primary Sjögren's syndrome and to correlate these findings with their disease activity.

**Methods:** Fifty-two patients with primary SS and 52 age- and sex-matched healthy control subjects underwent clinical and laboratory examination. Olfactory functions were evaluated using olfactory function assessment by computerised testing including the three stages of smell: threshold, identification and memory of the different odours. The disease activity was assessed by the EULAR SS Patient Reported Index (ESSPRI) and the EULAR SS Disease Activity Index (ESSDAI).

**Results:** All the olfactory scores (odour threshold, odour memory and identification) in patients with pSS were significantly below the scores in the control group (all  $p<0.001$ ). Multivariable regression analysis revealed that smell threshold score correlated negatively with ESSPRI and ESSDAI (adjusted  $R^2=0.381$ ,  $p<0.05$ ). Smell threshold score was decreased in pSS patients with anti-SSA antibody compared with those without ( $p<0.05$ ). Total smell scores were significantly reduced in patients with thyroid involvement ( $p<0.01$ ).

**Conclusions:** Our findings indicate that olfactory functions are impaired in pSS patients. There was close correlation between olfactory dysfunction with disease severity and serological abnormalities. Therefore, imperative that physicians should make their patients to be aware of these sensory dysfunctions and educate them on methods to cope with it for better quality of life.

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SAT0464

#### COMPARISON OF DISEASE ACTIVITY SCORES PREDICTING MORTALITY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN COLOMBIA

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**Background:** Systemic lupus erythematosus (SLE) is a disease with multisystem involvement. Throughout history, different activity indices have been developed trying to identify patients who have the flare of the disease. These indexes measure different aspects of the disease. Among the most recognised score is SLEDAI 2 K. Others that had been evaluated is the SLEDAI MEX and the ECLAM. The performance of the measurement of the SLEDAI 2 K is more expensive because of the number of variables evaluated. ECLAM score and the SLEDAI MEX have less number of variables and therefore costs are minor. <sup>1, 2, 3</sup>

**Objectives:** To compare the predictive capacity of mortality of three different scores of disease activity (SLEDAI 2 K, SLEDAI MEX, and ECLAM) in a Colombian population with SLE.

To compare the predictive capacity of mortality of three different scores of disease activity (SLEDAI 2 K, SLEDAI MEX, and ECLAM) in a Colombian population with SLE.

**Methods:** Cross-sectional study, in which descriptive analysis with measures of frequency, central tendency and dispersion were made. Subsequently, mortality prediction analysis of the three scales was performed through the evaluation of the ROC curve. Analysis of classification statistics was done.

**Results:** A total of 200 patients with SLE were included, with mortality of 11%. The averages of disease activity were: for SLEDAI 2 K was 14.5 with standard deviation (SD) of 9.7, for SLEDAI MEX 9.26 with SD of 5.93 and for ECLAM 4.39 with SD of 2.28. The area under the curve of the ROC curves was 0.9082, 0.9206 and 0.8917 for the scales SLEDAI 2 K, SLEDAI MEX and ECLAM respectively. Regarding classification statistics, a sensitivity of 36.3% was found for the SLEDAI 2 K scale, specificity was 97.7%, positive predictive value 66.6, negative predictive value 92.5% and correct classification of 91%. For the SLEDAI MEX scale were: Sensitivity 50%, specificity 96.6%, positive predictive value 64.7%, negative predictive value 93.9% and correct classification of 91.5%. Finally, for the ECLAM scale, it was obtained the following results: sensitivity 9.09%, specificity 98.88%, positive predictive value 50%, negative predictive value 89.8% and correct classification in 89%.

**Conclusions:** It can be observed that the predictive capacity for mortality in the patients evaluated is good with the three different scales. The sensitivity found for the three scales is not optimal for making a promptly medical decision, so later it will be necessary the formulation of a new index in which higher number of patients with SLE can be detected with death risk. An additional relevant result is that the SLEDAI MEX activity index has a similar performance than the SLEDAI 2 K activity index for predicting mortality, with the advantage of being a practical index easy to apply and a lower cost of the evaluation.

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SAT0465

**CLINICAL MANIFESTATIONS AND PROGNOSIS OF SLE WITH CLINICALLY SIGNIFICANT ANTIPHOSPHOLIPID ANTIBODIES**

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**Background:** Antiphospholipid antibodies (aPLs) have been described in 20% >40% of SLE patients, with 50%>70% of patients with SLE and aPL showing the clinical features of APS after 20 years of follow-up<sup>1</sup>. It assumes that aPLs-positive SLE patients would have a more severe clinical phenotype and worse prognosis than those without aPLs.

**Objectives:** We decided to investigate the clinical manifestations and prognosis of SLE with clinically significant aPLs in a multiple centre SLE cohort.

**Methods:** A follow-up study to investigate the prognosis of SLE, has been conducted in 26 centres across Jiangsu province as described before<sup>2</sup>. SLE patients fulfilled ACR/SLICC criteria. Patients who had ever recorded first admissions and detected aPLs during the 1999±2009 decade were followed and checked for their survival status in 2015. Clinically significant aPL were defined as: positive LA test, aCL IgG/IgM antibodies>99 th percentile and/or aβ2GPI>99 th percentile on two or more occasions at least 12 weeks apart.

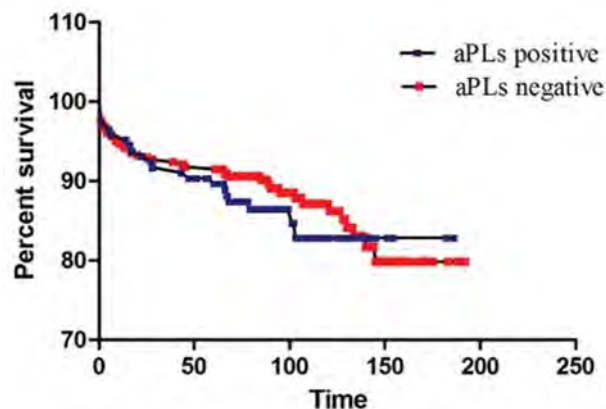
**Results:** 1) Among 1372 SLE patients, 495 patients was reported the aPLs minutely, and 146 cases was with clinically significant aPLs. Compared with aPLs negative SLE patients, the proportion of men, and the rates of oral ulcer, neuropsychiatric involvement, dsDNA, antinuclear antibody and C3 were significantly higher in aPLs positive SLE. (table 1)

	aPLs positive n=146	aPL negative n=349	P
Gender (male)	5	32	0.017
Oral ulcer	29	44	0.047
Thromboembolism	16	18	0.031
Neuropsychiatric	14	20	0.000
C3 decrease	119	248	0.015
Anaemia	109	214	0.005
ANA positive	138	317	0.048
Anti dsDNA positive	83	169	0.009

2) There were 20 deaths in aPLs positive SLE group and 52 deaths in aPLs negative SLE group during the average follow up of 7.38±0.56 years and 7.54±0.0.47 years respectively. There was no significant difference in survival curves by Kaplan Meier survival analysis (p=0.776). (Picture 1)

3) Multivariate Cox regression analysis revealed that long time of diagnosis (HR 4.205, p<0.05), SDI>1 in admission (HR 11.982, p<0.01), neuropsychiatric involvement (HR 2.826, p<0.05), and increased serum creatinine (HR 8.403, p<0.01) were independent predictors of mortality. (table 2)

factors	Univariate			Multivariate		
	HR	95% CI	P	HR	95% CI	P
Time of diagnosis>1 year	5.26	2.24–12.32	0	4.20	1.06–16.56	0.04
SDI≥1 on admission	4.37	1.67–11.40	0.003	11.98	2.85–50.25	0.001
Neuropsychiatric	4.52	1.89–10.84	0.001	2.82	1.01–7.85	0.048
Increased serum creatinine	4.39	1.87–10.30	0.001	8.40	2.20–32.04	0.002



**Conclusions:** In this study, we observed that around one-third of patients had clinically significant aPLs, and such autoantibody positivity was associated with a different clinical and serological profile. However, the mortality between aPLs

positive and negative SLE patients had no significant difference. SLE patients presented with vital organ damages rather than active disease at initial hospitalisation are likely to have a poor outcome, especially neuropsychiatric involvements and renal insufficiency.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.5540

SAT0466

**SERUM VITAMIN D DEFICIENCY IS ASSOCIATED WITH ACTIVE RENAL DISEASE IN SYSTEMIC LUPUS ERYTHEMATOSUS**

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**Objectives:** 25-hydroxyvitamin D (25(OH)D) deficiency is common in systemic lupus erythematosus (SLE) as well as chronic kidney disease. In this study, we investigated the association of 25(OH)D deficiency and renal involvement in SLE patients.

**Methods:** Two hundred seventy-two SLE patients and 138 control subjects were enrolled; 102 patients with active nephritis, 42 patients with inactive nephritis, and 128 patients with non-renal disease. Serum 25(OH)D levels were measured, and clinical and laboratory data were obtained from medical records.

**Results:** Mean serum 25(OH)D levels were significantly lower in SLE patient than control subjects (19.6 ng/ml versus 21.7 ng/ml, p=0.006). Out of 272 patients, 61.8% were vitamin D deficient (defined as <20 ng/ml). Patients with active nephritis had lower serum 25(OH)D levels (16.9 ng/mL) than patients with inactive nephritis (20.2 ng/mL) and without nephritis (21.5 ng/mL) (p=0.030, p<0.001), but there was no difference between the inactive nephritis and non-renal disease. Moreover, serum 25(OH)D levels were positively correlated with complement C3 ( $\gamma=0.135$ , p=0.026) and C4 ( $\gamma=0.159$ , p=0.009), but inversely with anti-dsDNA antibody level ( $\gamma=-0.156$ , p=0.010). Analysis of receiver operating characteristic curve for differentiating active nephritis and non-renal disease revealed an area under the curve (AUC) of 0.676, which is better than those of anti-dsDNA antibody (AUC=0.585, p=0.038) and complement C3 (AUC=0.509, p=0.001), C4 (AUC=0.538, p=0.008).

**Conclusions:** Vitamin D deficiency is more common in SLE patients with active nephritis, and its level could be a potential marker for active renal disease in SLE. A prospective cohort study is needed to further elucidate the causal relationships over time.

**Disclosure of Interest:** None declared

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SAT0467

**CEREBRAL VENOUS THROMBOSIS OCCURRENCE IN SYSTEMIC LUPUS ERYTHEMATOSUS WITHOUT ANTIPHOSPHOLIPID ANTIBODY SYNDROME: A MONOCENTRIC SERIE OF 10 CASES**

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**Background:** Cerebral venous thrombosis (CVT), which includes cerebral vein and dural sinus thrombosis, is a rare disorder that can lead to significant morbidity and mortality. Its occurrence in SLE in the absence of APS has been rarely reported. In this study we aimed to describe a cohort of SLE patients suffering from CVT without APS.

**Methods:** We collected retrospectively clinical and biological data of patients with confirmed CVT in the Pitié-Salpêtrière cohort of SLE (n=1352 patients). Patients fulfilled ACR SLE criteria. The diagnosis of CVT was confirmed by brain imaging studies. Exclusion criteria were patient with a lupus anticoagulant or IgG/IgM anti-cardiolipin antibodies or anti-β2 glycoprotein-1 abs. We searched on PUBMED database for case report of this association published in English until 31 August 2017. Lupus flares were defined according the SELENA Flare instrument.

**Results:** We included 10 patients (8 women and 2 men). The median (range) age at diagnosis of CVT was 28 years.<sup>9-53</sup> The CVT occurred with a median delay of 4



years (0–11) after the diagnosis of SLE. At the time of the CVT diagnosis: no patients had a past medical history of thrombotic event or miscarriage or foetal loss; 7 patients had a lupus flare (5 lupus nephritis [1 class I, 1 class V, 2 class IV and 1 class III+V], 4 immune thrombocytopenia, 2 autoimmune hemolytic anaemia, 3 cutaneous lupus, 1 serositis and 1 arthritis); 7 patients were treated with corticosteroids, 4 with hydroxychloroquine and 4 with immunosuppressive drugs. Other potential precipitating factors of CVT were: 2 nephrotic syndromes, 2 anaemia and 1 hyperhomocysteinemia. CVT was symptomatic for 9 patients: 8 headaches, 3 epilepsy and 1 sensitive-motor deficit. The diagnosis of CVT was confirmed by magnetic resonance imaging (MRI) for 9 patients and cerebral angiography for 1 patient. The median delay between the onset of clinical symptoms and the diagnosis of thrombosis was 10 days.<sup>3–37</sup> Nine patients presented a single localisation of CVT (superior longitudinal or lateral or cavernous sinus, or cortical cerebral vein). Only 1 patient had thrombosis of both lateral and sigmoid sinus. Cerebral infarction or haemorrhage was seen for 2 patients. Corticosteroids and immunosuppressant treatment were increased or introduced because of a concomitant lupus flare for 2 patients. All patients were treated with heparin followed by vitamin K antagonists for 7 patients or apixaban for 2 patients. One patient received long-term heparin. After a median survey of 19.5 (1–120) months: anti-coagulant drugs were stopped for 6 patients; recanalisations were complete in 7 of the 7 patients assessed on brain MRI; no patient had a residual neurological damage; only 1 patient had a new vascular event in the form of a brain haemorrhage. In addition to these 10 cases we found 17 cases from a literature review.

**Conclusions:** CVT is a rare event in SLE in absence of APS. In our cohort SLE was often active at the time of the CVT occurrence. Most of the CVT were limited in extension and severity. The outcome on anticoagulant treatment was favourable without residual neurological damage. The occurrence of CVT in SLE is not an indication by itself to increase or to introduce corticosteroids or immunosuppressive drug.

**Disclosure of Interest:** None declared

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SATURDAY, 16 JUNE 2018

## Scleroderma, myositis and related syndromes

### SAT0468 SCLERODERMA -INTERSTITIAL LUNG DISEASE: DOES MAINTENANCE THERAPY MAKE A DIFFERENCE

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**Background:** Interstitial lung disease (ILD) is the commonest cause of death among Scleroderma (SSc) patients. The evidence regarding efficacy of cyclophosphamide (CYC) in SSc-ILD results mainly from two high-quality RCTs.<sup>1,2</sup> In the scleroderma lung study 1, after 12 months of therapy with oral CYC, a significant difference in mean forced vital capacity (FVC) was noted favouring CYC group. However, the effect waned off by the end of 24 months of follow up, indicating that maintenance therapy might help in preserving the initial benefits.<sup>3</sup>

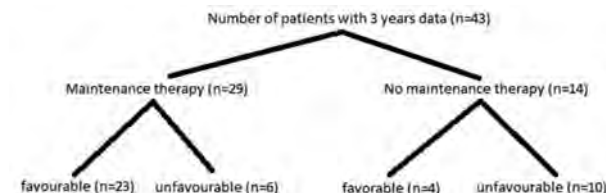
**Objectives:** To study the long-term effect of maintenance therapy in SSc related interstitial lung disease (SSc-ILD)

**Methods:** This is a retrospective data analysis of forty-three patients with SSc-ILD divided into two groups, those who received maintenance therapy with either mycophenolate (MMF) or azathioprine (AZA) and the other group without any maintenance therapy following CYC induction. Response to treatment was classified as improved ( $\geq 10\%$  increase in FVC from baseline), stable (change in FVC of 0%–10% from baseline) and worsened ( $\geq 10\%$  decrease in FVC or fall of FVC to  $< 40\%$  of predicted). Results were expressed as percentages for categorical variables and mean with standard deviation (SD) for continuous variables. Chi square test was used for comparison of responses between two groups of patients. Following induction patients were divided into groups: those They were assessed at three years.

**Results:** Baseline characteristics of the study population are shown in table 1. Maintenance therapy was given in 29 (67.4%) patients and among them favourable outcome (improve +stable) was noted in 23 (79.3%) patients and unfavourable outcome was noted in 6 (20.7%) patients. Fourteen (32.6%) patients did not receive maintenance therapy and among them, favourable outcome was noted in 4 (28.6%) patients and unfavourable outcome in 10 (71.4%) patients. This difference in the rates of favourable outcome between both the groups was statistically significant ( $p=0.001$ ). Figure 1 summarises the response rates of the patients of these two groups.

**Abstract SAT0468 – Table 1.** Baseline characteristics of the patients (n=43)

Characteristic	Maintenance group (n=29)	No maintenance group (n=14)
Females (%)	93	85.7
Mean age in years(SD)	40.9 ( $\pm 10.9$ )	42 ( $\pm 10.5$ )
Type of Scleroderma		
Limited cutaneous (%)	44.8	57.1
Diffuse cutaneous (%)	55.1	42.9
ANA positivity (%)	75.9	78.6
PAH (%)	34.5	28.6
Mean FVC (SD)	57.6 ( $\pm 13$ )	55.6 ( $\pm 15.2$ )



**Conclusions:** Maintenance therapy up to 3 years (either with AZA or MMF) following IV-CYC induction, resulted in a favourable outcome and helps in preserving the initial beneficial effects achieved with IV CYC.

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**Disclosure of Interest:** None declared

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### SAT0469 “INTERSTITIAL LUNG DISEASE IN IDIOPATHIC INFLAMMATORY MYOPATHIES: ULTRASOUND ASSESSMENT OF PLEURAL IRREGULARITIES AND COMPARISON WITH HIGH RESOLUTION COMPUTED TOMOGRAPHY”

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**Background:** Interstitial Lung Disease (ILD) is one of the most frequent and significant extra-muscular manifestations in Idiopathic Inflammatory Myopathies (IIM). Although high resolution computed tomography (HRCT) remains the gold standard technique for the evaluation of ILD, during the last years several authors proposed ultrasound (US) quantification of pleural irregularities (PIs) as a possible method to detect lung involvement in IIM patients.

**Objectives:** The objective of our study was to evaluate the prevalence of PIs and to compare the results obtained to the data provided by HRCT.

**Methods:** Thirtyseven patients (24 females, 13 males, mean duration of the disease 5.21 $\pm$ 7.6 and median age 62.24 $\pm$ 1.8 years) with a diagnosis of IIM according to Bohan and Peter criteria (17PM, 16DM, 1MCI, 3overlap syndromes) who required HRCT evaluation were enrolled. All patients underwent rheumatological clinical evaluation, including dyspnoea measurement by means MRC scale and disease activity assessment according to IMACS criteria (muscle enzymes, MMT8, VAS, HAQ, MYOACT). Patients were also asked to complete Patient Reported Outcome (PRO) questionnaires as Leicester Cough Questionnaire (LCQ). All the patients underwent a thoracic US evaluation in 53 anterior and posterior thoracic areas by Esaote MyLab Gold ultrasound device with 8–18 MHz

linear probe. We evaluated the aspect of the pleural profile assigning each space a score according to a 3 points scale (regular=0, mild irregularity=1, irregularity=2) and summed the score in each space to obtain the PIs total score. HRCT was assessed by an expert radiologist to obtain a semiquantitative evaluation of parenchymal involvement by Warrick score. In a subgroup of patients, thoracic US was repeated by the same operator after two days from the first evaluation and by a second operator to evaluate the intrareader and interreader agreement of the technique.

**Results:** The PIs total score obtained with lung US ( $24.70 \pm 13.66$ ) was higher in patients with thoracic crackles at clinical examination ( $p=0.008$ ) and in patients with positivity for antisynthetase autoantibodies, particularly anti-Jo1 ( $p<0.001$ ). A positive correlation was found between PIs total score and MYOACT total score ( $r=0.36; p=0.027$ ), instead a negative one was found with LCQ score ( $r=-0.56; p=0.009$ ). Interestingly, a good correlation between PIs total score and the Warrick score ( $r=0.65; p<0.001$ ) was found. From the analysis of ROC curve, we demonstrated that a cut-off of PIs total score  $<18.5$  might be able to identify all patients with HRCT abnormalities (sensitivity 100%). Lung US was repeatable (inter-reader reliability:  $\alpha=0.916$ ) and reproducible (intra-reader reliability:  $\alpha=0.945$ ).

**Conclusions:** The US PIs total score is strictly correlated to clinical, serological and HRCT parameters and as the lung US is a non-invasive and relatively inexpensive technique, the results of our study suggest a possible role of this method in the screening of lung involvement in IIM patients. Follow up studies in a larger cohort of IIM patients are required.

**Disclosure of Interest:** None declared

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#### SAT0470 MYOSITIS, OFTEN SUSPECTED, IS ACTUALLY RARE IN PRIMARY SJÖGREN'S SYNDROME: DATA FROM THE FRENCH COHORT ASSESS

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**Background:** Myositis prevalence in primary Sjögren's syndrome (pSS) and whether it is associated with peculiar extra-muscular involvement and/or a biological profile is unknown.

**Objectives:** To refine prevalence and characteristics of patients with pSS and myositis.

**Methods:** In the national multicenter prospective cohort ASSESS (395 patients with pSS with a 5 year-prospective follow-up), patients with suspected myositis were identified. Their charts were reviewed and the patients were compared with the rest of the cohort.

**Results:** Myositis was suspected in 38 patients (2 men, 36 women, 58<sup>29-78</sup> yr old) because of myalgia and/or exercise intolerance ( $n=38$ ) along with high blood CK level ( $n=28$ ). As compared with the rest of the cohort, they had higher patient-reported signs including pain VAS, dryness VAS and patient reported index ESSPRI (6.3 vs 5.3,  $p=0.007$ ). In contrast, proportion of systemic involvements (76.3% vs 70.9%,  $p=0.57$ ) and systemic disease activity measured by the ESSDAI, without taking the muscular domain into account (2 vs 3,  $p=0.93$ ), were not different from patients without suspected myositis. Demographic characteristics and disease duration were also similar.

Electromyographic recording and/or muscle histology performed in these 38 patients objective muscular involvement in only 4 patients (1% of the cohort).

- Three patients were diagnosed with inclusion body myositis (sIBM). Accordingly, age at first sign was 49 years, 49-60 muscle disease had progressive onset as suggested by the 11 years<sup>1-28</sup> delay between first muscle sign and diagnosis. CK level was  $<1000$  U/L. Immunomodulatory drugs had no effect on myositis, even though methotrexate, IVIg and rituximab were most frequently given than in patient without myositis (respectively 50% vs 12.4%; 75% vs 1.8% and 75% vs 4.9%;  $p<0.0001$ ).

- One pSS patient with myositis was a 39 years old woman with polymyositis. She developed proximal muscle weakness, CK was 750U/L and muscle biopsy found endomyosial infiltrate. Muscle force and CK level normalised with immunomodulatory drugs.

Compared to the rest of the cohort, patient with myositis had longer disease duration at inclusion (15 vs 5 year,  $p=0.01$ ) and tended to be younger at pSS diagnosis (41.5 vs 53 year,  $p=0.07$ ). They had more frequent history of systemic manifestations (100% vs 65.0%,  $p=0.011$ ) but ESSDAI at baseline (2 vs 3,  $p=0.56$ ) and the

biological characteristics were not different from patients without myositis. In contrast with the patients with suspected but not confirmed myositis, patient-reported signs (i.e. fatigue, pain, dryness and ESSPRI score) were similar to patients without myositis.

**Conclusions:** Myositis is frequently suspected in patients with pSS, especially when patients-reported signs are particularly disabling. Myositis occurs very infrequently (1% of the cohort), in patients with longer disease duration. sIBM was the most predominant subset of myositis in the present study.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.2945

#### SAT0471 ABNORMAL NAILFOLD CAPILLAROSCOPIC PATTERNS ARE COMMON IN UNDERWEIGHT SUBJECTS WITH RAYNAUD'S PHENOMENON

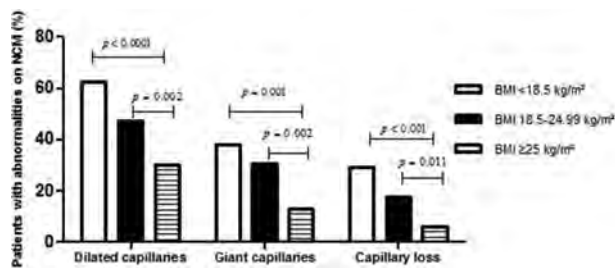
A. Eman Abdulle<sup>1</sup>, A.M. van Roon<sup>1</sup>, M.M. Habing<sup>1</sup>, A.J. Stel<sup>2</sup>, A.J. Smit<sup>1</sup>, H. van Gooij<sup>3</sup>, D.J. Mulder<sup>1</sup>. <sup>1</sup>Dept. of Internal medicine, div. Vascular Medicine; <sup>2</sup>Dept. of Rheumatology and Clinical Immunology; <sup>3</sup>Dept. of Pathology and Medical Biology, Section Pathology, University of Groningen – University Medical Centre Groningen., Groningen, Netherlands

**Background:** Despite the extensive research on this subject, the exact pathogenesis of RP still remains incompletely understood. The current view on this rather complex phenomena is that the imbalance between vasoconstriction and vasodilatation is purely functional and that structural vascular changes do not occur in PRP patients. Although RP is a frequently occurring problem in underweight patients, microvascular changes have never been (structurally) investigated.

**Objectives:** The aim of the current study was to investigate the relationship between microvascular abnormalities and body mass index (BMI) in subjects with Raynaud's phenomenon (RP), without an underlying connective tissue disease.

**Methods:** Nailfold capillaroscopic patterns (NCP) were retrospectively assessed in 352 RP patients, without an underlying systemic disease (e.g. negative serology tests, and no signs of organ involvement). Patient characteristics were obtained and patients were divided by BMI category: underweight (BMI  $<18.5$  kg/m<sup>2</sup>), normal weight (BMI 18.5–24.99 kg/m<sup>2</sup>), and overweight (BMI  $\geq 25$  kg/m<sup>2</sup>). Patterns were deemed abnormal if the mean capillary count was  $<20$  per 3 mm, or mean number of dilated capillaries per finger was  $>3$ , or any giant capillaries were observed.

**Results:** Approximately 70% of the underweight patients showed an abnormal NCP. This was irrespective of age and smoking behaviour. Underweight RP patients had the highest mean count of dilated capillaries (5.14 for BMI  $<18.5$  kg/m<sup>2</sup>; 4.17 BMI for 18.5–24.99 kg/m<sup>2</sup>; 2.61 for BMI  $\geq 25$  kg/m<sup>2</sup>,  $p=0.002$ ) and giant capillaries (1.01 for BMI  $<18.5$  kg/m<sup>2</sup>; 0.48 BMI 18.5–24.99 kg/m<sup>2</sup>; 0.23 BMI  $\geq 25$  kg/m<sup>2</sup>,  $p=0.024$ ). However capillary loss was not found to be significantly different ( $p=0.458$ ). Furthermore, mean number of capillaries ( $r=0.260$ ,  $p<0.001$ ), mean number of dilated capillaries ( $r=-0.225$ ,  $p<0.001$ ) and mean number of giant capillaries ( $r=-0.221$ ,  $p<0.001$ ) were found to be associated with BMI.



**Conclusions:** Our findings indicate NCP abnormalities are more frequently observed in underweight individuals, indicating that microvascular changes may occur independently of an underlying connective tissue disease. These findings may alert clinicians that (perivascular) adipose tissue may play a crucial role in the occurrence of Raynaud's phenomenon.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.7149

SAT0472

### ULNAR OCCLUSION IS A MARKER OF GLOBAL VASCULAR DAMAGE IN SYSTEMIC SCLEROSIS: RESULTS FROM A MONOCENTRIC PROSPECTIVE STUDY OF 99 PATIENTS

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**Background:** Macrovascular damages of systemic sclerosis (SSc) were poorly investigated, and the link between macrovasculopathy and microvasculopathy of SSc, cardiovascular disease, and mortality remain unclear.

**Objectives:** To evaluate if macrovascular damage in SSc predicts the occurrence of new digital ulcers (DU), cardiovascular events and mortality, and to further assess the relationship between micro and macrovascular damages in SSc.

**Methods:** All consecutive SSc patients followed in our SSc National Reference Centre, who underwent an arterial doppler ultrasonography (aDUS) of the upper limbs, were included and prospectively followed up until October 2017. Inclusion criteria were: 1) adults; 2) a diagnosis of SSc according to 2013 ACR/EULAR criteria; 3) aDUS performed in our vascular exploration department.

**Results:** Ninety-nine SSc patients were included. Median follow-up duration was 35 (IQR, 21 to 39) months. Macrovascular damages mainly affected ulnar arteries, with ulnar artery occlusion (UAO) in 28 (28.3%) patients (bilateral 60.7%). New DU occurred in 26 (27.1%) patients, new cardiovascular event in 10 (10.4%) patients, and 11 patients died during the study period. Interestingly, UAO was not associated with traditional cardiovascular risk factors (except dyslipidemia) nor with history of cardiovascular diseases, and was not predictive of new cardiovascular events. Conversely, UAO was associated with makers of microvascular damages, such as late nailfold capillaroscopy pattern (33.3% vs 6.8%; OR=6.88, 95% CI=1.76 to 26.82; p=0.03) and was predictive of new ischaemic DU (44.5% vs 24.8%; HR=2.23, 95%CI=1.02 to 4.86; p=0.037), pleading for a SSc specific vasculopathy.

**Conclusions:** Our study confirms that macrovascular damages are frequent in SSc patients and mainly affect ulnar arteries. Interestingly, UAO was associated with severe microvasculopathy, but not with markers of cardiovascular diseases.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.3141

SAT0473

### CLINICAL AND ECHOCARDIOGRAPHIC ASSOCIATES OF ALL-CAUSE MORTALITY AND CARDIOVASCULAR OUTCOMES IN PATIENTS WITH SYSTEMIC SCLEROSIS

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**Background:** Cardiac events are an important cause of mortality in Systemic Sclerosis (SSc), but its diagnosis remains challenging. Left ventricular global longitudinal strain is a novel parameter derived from speckle tracking echocardiographic analysis which has been proposed to identify patient at higher risk of cardiac events.

**Objectives:** We aimed to identify clinical and echocardiographic (including GLS) parameters associated with all-cause mortality and cardiovascular events in SSc patients.

**Methods:** 408 SSc patients (344 females, age 54±14 years.) were prospectively evaluated at baseline and follow-up (FU time 3.3 years. [IQR 1.8 to 5.5]). Cardiovascular events included: heart failure, cardiac infarction, coronary interventions, device implantation, arrhythmias, cerebral infarction, peripheral ischaemic vascular disease.

**Results:** All-cause mortality (n=37) or cardiovascular events (n=57) occurred in 84 patients. At baseline, these patients were older (59±14 vs. 53±14 years., p<0.001), more often male (24 vs. 13%, p=0.018), more often had skin pigment changes (21 vs. 5%, p=0.011), coronary artery disease (11 vs. 3%, p=0.001), holter abnormalities (45 vs. 24%, p≤0.001), increased ESR (24 [IQR 14 to 46] vs. 11 [IQR 6 to 25], p<0.001), worse NT-proBNP (151 [IQR 60 to 644] vs. 82 [IQR 51 to 145] ng/L, p<0.001), worse lung function test results (FVC 92±19 vs. 104%±21%,

p<0.001; DLCO 55±17 vs. 70%±19%, p<0.001), worse left ventricular diastolic function (E/E-prime ratio 9.9 [IQR 6.7 to 10.2] vs. 7.8 [IQR 6.4 to 9.7], p<0.001), higher systolic pulmonary artery pressure (31±12 vs. 25±7 mmHg, p<0.001) and lower GLS (-18.8 [IQR -20.3 to -19.5] vs. -21.1 [IQR -22.1 to -20.0]%, p<0.001). In a multivariate cox-regression analyses, age (HR 1.029, 95% CI 1.006 to 1.052), female sex (HR 0.527, 95% CI 0.302 to 0.922), NT-proBNP (HR 1.000, 95% CI 1.000-1.001), DLCO (HR 0.973, 95% CI 0.961-0.986) and GLS (HR 1.281, 95% CI 1.172-1.399) were independently associated with outcome. After dividing patients into groups according to median GLS (-20.9%) and elevated NT-proBNP (>200 ng/L), survival rates were lower and cardiovascular events increased when GLS was impaired and worsened when NT-proBNP was elevated (Log-rank p<0.001).

**Conclusions:** In SSc patients, next to age, DLCO and NT-proBNP, GLS strongly associates with all-cause mortality and cardiovascular events, indicating that these parameters reflect relevant cardiac involvement in SSc, and as such can contribute to risk stratification and patient management.

**Disclosure of Interest:** None declared

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SAT0474

### RACIAL DIFFERENCES IN SSC DISEASE PRESENTATION: A EUROPEAN SCLERODERMA TRIALS AND RESEARCH GROUP STUDY

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**Background:** Genetic and environmental factors play a significant role in systemic sclerosis (SSc). African Americans are known for a higher SSc incidence, an earlier age of onset, and a greater frequency of interstitial lung disease and pulmonary hypertension (PH) compared to white patients. Data on blacks mostly stem from African Americans and studies on SSc in Asians are mostly from outside Asia and lack direct comparison with other racial groups.

**Objectives:** We aimed to evaluate differences of SSc presentations between white, Asian and black patients.

**Methods:** Characteristics of self-reported white, Asians or black SSc patients from the EUSTAR cohort were compared across racial groups; survival and multiple logistic regression analyses were used to adjust for age, sex, disease duration and antibody status.

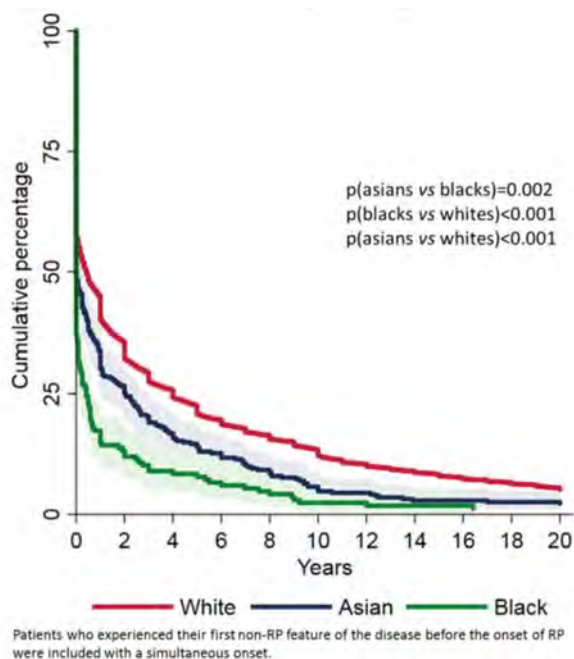
**Results:** 9162 white, 341 Asian and 181 black patients were included. Of the Asian patients 208 stem from within Asia and 133 from 34 centres outside Asia; of the black patients 65 stem from within Africa and 116 from 35 centres outside Africa.

Asian and black patients were on average 10 years younger than white patients (p<0.001). Black patients developed the first non-Raynaud's phenomenon (RP) feature of SSc faster than Asian and white patients (all p<0.01; figure 1) also after adjustment (hazard ratio (HR)[blacks] 1.4, p<0.001; HR[Asians] 1.1, p=0.13 vs whites).

Among ANA specificities, ACA predominated in white patients (whites: 40%, Asians: 16%, blacks: 10%; p<0.001) and Scl-70 in Asian patients (whites: 34%, Asians: 46%, blacks: 32%; p<0.001). The prevalence of diffuse skin involvement was similar in Asian (28%) and white patients (27%), but more common in black patients univariately (59%; p<0.001); however in multivariable analysis Asian patients were less likely to have diffuse SSc than white patients (OR 0.6, p=0.001) while black patients were more likely (OR2.9, p<0.001).

The prevalence of PH (defined as PAPsys >40 mmHg as estimated by echocardiography) was similar in the three groups (whites: 13%, Asians: 17%, blacks: 14%; p=0.10); however multivariably, Asians were more likely to have PH (OR [Asians] 2.0, p<0.001, OR[black] 1.5, p=0.13 vs whites). Asians had a higher prevalence of an impaired diffusing capacity for carbon monoxide (DLCO;<80% of predicted; 84%) than black (72%) or white patients (69%, p<0.001) also in multivariable analysis (OR[Asians] 3.0, p<0.001; OR[blacks] 1.2, p=0.36 vs whites). Both, Asians (43%) and black patients (58%), had a higher prevalence of a reduced forced vital capacity (FVC;<80% of predicted) compared to white patients (23%, p<0.001) univariably and multivariably (OR[Asians] 2.4, p<0.001; OR[blacks] 4.0, p<0.001 vs whites).





**Abstract SAT0474 – Figure 1.** Kaplan-Meier curves with 95% CI of the first non-RP feature after RP onset according to racial group.

Patients who experienced their first non-RP feature of the disease before the onset of RP were included with a simultaneous onset.

**Conclusions:** Several clinical and serological differences were evident between the three racial groups. Asians had high prevalences of Scl-70, PH and of a reduced FVC. Black patients in contrast had fast disease onset and a high prevalence of diffuse skin involvement.

**Disclosure of Interest:** None declared

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SAT0475

**ANTI-MDA5 (+) CLINICALLY AMYOPATHIC DERMATOMYOSITIS-ASSOCIATED RAPIDLY PROGRESSIVE INTERSTITIAL LUNG DISEASE: ROLE OF HEMOPERFUSION WITH POLYMYXIN**

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**Background:** Patients with clinically amyopathic dermatomyositis (CADM) with MDA5 positive autoantibodies may develop a severe pulmonary syndrome with rapidly progressive interstitial lung disease (RP-ILD) with a bad prognosis and high mortality.

**Objectives:** To analyse the efficacy of a therapeutic protocol that includes hemoperfusion with polymyxin B (PMX-HP) in addition to immunosuppressive treatment with tacrolimus and glucocorticoids, plasmapheresis and intravenous immunoglobulin (IVIG).

**Methods:** We retrospectively analysed 12 (10 male) patients diagnosed with anti-MDA5 (+) CADM associated RP-ILD between 1983 and 2018. Anti-MDA5 antibodies were determined by ELISA and confirmed by blot. RP-ILD was defined as a worsening of radiologic interstitial changes with progressive dyspnoea and hypoxemia within 1 month after the onset of respiratory symptoms. From 2014 to 2018, patients (Group 1) were treated with the following protocol: pulses of methylprednisolone (500 mg/day for 3 consecutive days), tacrolimus 2 mg/12 hour, PMX-HP (Toraymyxin 20R, Toray Medical Co., Tokyo, Japan) at a flow of 100 ml/

h for 3 hour once daily on two successive days, and a plasmapheresis scheme with replacement of 3.5 l of seroalbumin 5% followed by IVIG infusion (0.4 mg/kg) during 3 consecutive days and then in alternate days for 7 days more. A comparison was performed with anti-MDA5 (+) CADM associated RP-ILD patients from a historical group (Group 2). PaO<sub>2</sub>/FiO<sub>2</sub> (P/F) ratio was measured before and after PMX therapy. A composite endpoint that included mortality due to respiratory failure or lung transplantation was defined. Differences between pre- and post-PMX P/F values were evaluated using paired sample t-test.

**Results:** Mean (SD) age at diagnosis was 49 (3.5) yrs, with a mean (SD) follow-up of 13 (3.9) months. Comparison between both Groups showed that 3 out of 6 (50%) patients from the Group 1 in comparison with 5 out of 6 (83.3%) from the historical group (Group 2) reached the composite endpoint. Mean (CI 95%) values of P/F after PMX treatment showed a significantly improvement when compared with the pre-PMX values (240 [85–396] vs. 125, <sup>60–189</sup> p=0.038)

**Conclusions:** Our protocol seems to be useful at some extent in anti-MDA5 (+) CADM associated RP-ILD patients. A transient but significant improvement can be attributed to PMX-HP. Adsorption and elimination of inflammatory cytokines, mediators and activated leukocytes, as well as anti-MDA5 antibodies could be the rationale of its efficacy.

**Disclosure of Interest:** None declared

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SAT0476

**INCIDENCE, PREVALENCE, MORTALITY AND PERFORMANCE OF THE ACR/EULAR 2013 CLASSIFICATION CRITERIA IN PHYSICIAN DIAGNOSED SYSTEMIC SCLEROSIS: RESULTS FROM A POPULATION BASED US COHORT (1980–2016)**

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**Background:** Systemic Sclerosis (SSc) is a complex and heterogenous chronic inflammatory disease characterised by widespread fibrosis of the skin and visceral organs, microvascular injury and evidence of immune system activation. Diagnosis can be challenging in the absence of specific laboratory markers or diagnostic criteria.

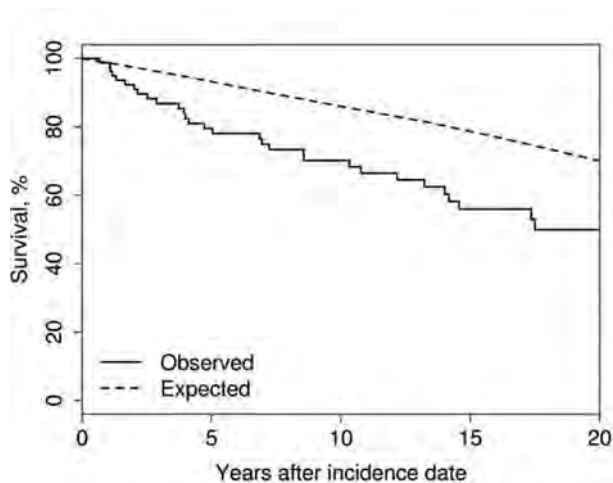
**Objectives:** To determine the incidence, prevalence and mortality of physician diagnosed SSc in a population based US cohort and evaluate the performance of the ACR/EULAR 2013 Classification criteria in comparison to the 1980 ACR criteria in classifying patients with SSc.

**Methods:** Medical records of patients with a diagnosis or suspicion of SSc in Olmsted County, Minnesota from January 1, 1980 to December 31, 2016 were reviewed to identify incident cases of SSc (defined by physician diagnosis). Prevalent cases of SSc in Olmsted County on January 1, 2015 were also identified. Incidence and prevalence rates were age and sex adjusted to the 2010 US white population. Survival rates were compared with the expected rates in the population of Minnesota. Fulfilment of the 1980 and 2013 classification criteria was ascertained.

**Results:** A total of 79 incident cases of SSc from 1980 through 2016 and 49 prevalent cases on Jan 1, 2015 were identified. Of these, 71 (90%) were females, 68 (87%) were caucasians, age at diagnosis 55.8±15.9 years (mean ±SD). The overall age- and sex- adjusted annual incidence for 1980–2016 was 2.7 (95% C.I. 2.1–3.3) per 1 00 000 population. The age-adjusted incidence was 4.6 (95% CI: 3.5–5.7) per 1 00 000 for females and 0.6 (95% CI: 0.2–1.1) per 1 00 000 for males, with no change in incidence over time. The age- and sex-adjusted prevalence on January 1, 2015 was 47.4 (95% CI: 34.1–60.7) per 1 00 000 population.

64 of 79 (81%) patients fulfilled the 2013 classification criteria, while only 48% fulfilled the 1980 criteria. All but 1 patient that fulfilled the 1980 criteria, also fulfilled the 2013 criteria. All 79 patients had Raynaud's, 38 had cardiopulmonary involvement (pulmonary artery hypertension and/or interstitial lung disease), 33 had digital ulcers/pitting scars, 66 had telangiectasias and 69 had sclerodactyly. 66 patients had limited cutaneous SSc, 11 had diffuse cutaneous SSc and only 2 had Sine scleroderma. 39 patients had a positive autoantibody for SSc: anti-centromere in 29, anti Scl-70 in 8 and anti RNA-polymerase III in 2.

Mortality among SSc patients was significantly higher in comparison to the general population (standardised mortality ratio, 2.24; 95% C.I., 1.52–3.18). Figure 1 demonstrates survival of 79 Olmsted County residents with incident SSc compared to expected rates from Minnesota life tables (observed: solid line; expected dashed line).



**Conclusions:** The average incidence of SSc in this population-based US cohort was 2.7 per 1 00 000 population with no change in incidence over the 36 year period of study. The new 2013 classification criteria perform significantly better than the 1980 criteria, but failed to classify 19% of patients in this cohort. Overall survival of patients with SSc is worse than the general population with no evidence of improved survival over time, indicating an unmet need for early diagnosis and more aggressive management.

**Disclosure of Interest:** None declared

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SAT0477

#### INTENSIFIED B-CELL DEPLETION THERAPY IN PROGRESSIVE SYSTEMIC SCLEROSIS PATIENTS: 24 MONTHS FOLLOW-UP

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**Background:** Systemic sclerosis (SSc) is a connective tissue autoimmune disease with systemic involvement and a serious medical condition with a high rate of mortality, especially due to interstitial lung disease (ILD). The exact pathophysiology is still unclear, but B cells seem to play a crucial role in the initiation and the progression of the disorder.<sup>1</sup> Therefore, the use of Rituximab (RTX) might have a rational in the treatment of SSc.

**Objectives:** We aimed to investigate the outcomes of SSc patients treated with RTX after a follow-up of 24 months.

**Methods:** We retrospectively collected data from SSc patients<sup>2</sup> resistant or intolerant to previous therapies, treated with intensified B-depletion therapy, between 2013 and 2016. Therapeutic protocol comprehends: RTX 375 mg/sm on days 1, 8, 15, 22, and two more doses after one and two months, associated with two intravenous administrations of 10 mg/kg of cyclophosphamide and three methylprednisolone pulses (15 mg/kg) followed by oral prednisone (0.8 mg/kg/day, rapidly tapered to 5 mg/day by the end of the 3rd month after RTX).

**Results:** The study included 20 SSc patients (18 females and 2 males; mean age 66.7±11.0 years). Patients presented with severe multiorgan involvement: ILD (19/20, 95%), pulmonary hypertension (12/20, 60%), and skin thickening (17/20, 85%). After a follow-up of 24 months, we observed a decrease in the levels of NT-proBNP (mean baseline: 385.4±517, mean at 24 months: 283±648, p<0.05), and in the Modified Rodnan Skin Score (mRSS) (mean mRSS baseline: 14.4±10.5, mean after 24 months of follow-up: 12.9±10, p<0.05). Four out of 19 (21%) patients experienced a significant improvement of ILD, as assessed by high-resolution computed tomography, while in 12/19 (63%) patients the intensified B-cell depletion therapy was associated with a stabilisation of the imaging features with no sign of progression. Three out of 19 (16%) patients showed a deterioration of the ILD.

Patients showed no significant decrease in forced vital capacity (FVC) (mean baseline FVC: 93.6±19.3, mean after 24 months of follow-up: 92.2±23.3), no significant decrease in forced expiratory volume in one second (FEV1) (mean baseline FEV1: 89.5±15.6, mean FEV1 at 24 months: 87±21.2), no significant decrease in diffusing capacity (DLCO) (mean baseline DLCO values: 58.8±8.6, mean at 24 months: 60.3±14), no significant change in the ejection fraction (EF)

(mean baseline EF values: 62.8±6.4, mean EF values at 24 months: 58.6±7.1) and in pulmonary artery pressure (PAP) (mean baseline PAP: 30.2±10.5, mean at 24 months: 31.1±11.05).

**Conclusions:** Despite recent advances in the treatment of SSc, ILD heavily affects prognosis and life expectancy of these patients. Our data suggest that the intensified B-depletion therapy protocol might represent a promising tool for the management of SSc in terms of controlling the progression of the disease, especially when considering pulmonary and skin manifestations. Further prospective studies are needed in order to confirm our results.

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**Disclosure of Interest:** None declared

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SAT0478

#### DISEASE-SPECIFIC AUTOANTIBODIES ASSOCIATE WITH REMARKABLY DIFFERENT RISK OF DEVELOPMENT OF SIGNIFICANT LUNG FIBROSIS IN SYSTEMIC SCLEROSIS

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**Background:** Pulmonary fibrosis (PF) is an important complication of systemic sclerosis (SSc), being a leading cause of disease related death. Some studies suggest that the timing of PF development differs between patients with different autoantibodies.

**Objectives:** We set out to assess a large single-centre SSc cohort, focusing on the timing of clinically significant PF (csPF), and to compare this within subgroups with different disease-specific autoantibodies, in particular anti-centromere antibody (ACA), anti-topoisomerase I antibody (ATA) and anti-RNA polymerase antibody (ARA).

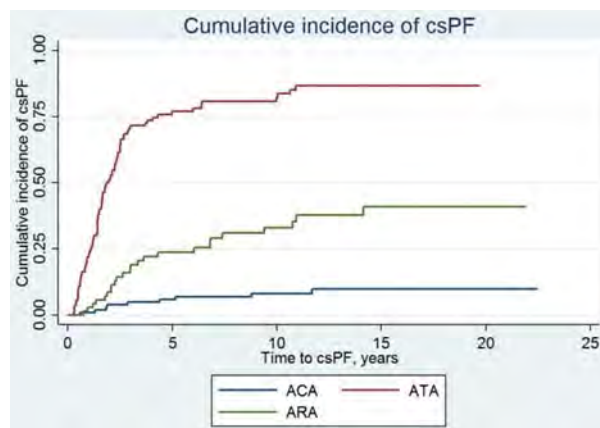
**Methods:** Patients with confirmed SSc and information on autoantibodies were included. PF was confirmed on high-resolution CT and defined as clinically significant based on at least one of the following: FVC <70%; a drop in FVC >15%; DLCO<70% with no pulmonary hypertension (PH) present; or a drop in DLCO>15% with no PH. Only subjects who had first available lung function test result within the first 3 years from onset were included. 1-Kaplan-Meier (1 KM) estimation was used to calculate cumulative incidence of csPF. To assess the timing of highest rates of csPF development, hazard rates were calculated within intervals of 12 months over the follow-up.

**Results:** A total of 450 subjects, 75 (16.7%) male, mean age of onset 47.4 years, were included in the study. Of those 225 (50%) had diffuse cutaneous SSc, 105 (23.3%) carried ACA, 113 (25.1%) ATA and 72 (16%) ARA. Mean follow-up was 12 years, interquartile range 8–16 years. Over the entire follow-up period, 196 (43.6%) of the subjects developed csPF.

Using 1 KM estimation, for the whole cohort, over the first 20 years of disease, approximately half of the patients developed csPF. Three quarters of the patients who developed csPF had reached this endpoint by 5 years (38.2%) with much lower incidence thereafter (at year 10, 15 and 20%—43%, 47% and 49.6%, respectively).

Analysis within subgroups showed that, ACA was associated with a very low risk of csPF development (cumulative incidence of 5.9%, 8.1%, 9.8% at 5, 10 and 15 years from SSc onset). On the other hand, ATA +patients had a remarkably high risk of csPF development, which ultimately occurred in the majority of cases, with cumulative incidence of 77.6% at 5 years, 82.7% at 10 years and 87.1% at 15 years. Rates of csPF development among ARA+patients were higher than those in ACA+, but still much lower than ATA+, and even after 20 years of follow-up, the cumulative incidence of csPF among them was less than a half of that among ATA +patients (23.7%, 33% and 41% at years 5, 10 and 15, figure 1).

The hazard of csPF among ACA +patients was highest in the second year from SSc onset (3%) and in the subsequent years varied between 0% and 1.8%. On the other hand, among ATA +patients hazard of csPF was 28.3% in year 1, 44.9% in year 2, peaked at 52.5% in year 3 and went down sharply thereafter. Although hazard was much lower among ARA+patients, this still peaked at year 3 (2.8%, 6.1% and 12.1% at year 1, 2 and 3 respectively) and declined after.



**Conclusions:** Our analysis demonstrates that csPF is a complication that tends to develop early in the disease course. Although the overall risk of csPF differs by antibodies, it is highest at around 3 years from disease onset and goes down thereafter. This can be used to inform organ disease monitoring and clinical trials recruitment.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.7089

**SAT0479 LASER SPECKLE CONTRAST ANALYSIS: A PILOT STUDY AND SYSTEMATIC LITERATURE REVIEW OF RELIABILITY OF THE QUANTITATIVE ASSESSMENT OF PERIPHERAL BLOOD PERFUSION IN SYSTEMIC SCLEROSIS**

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**Background:** Microvasculopathy is an important feature of systemic sclerosis (SSc), making its assessment a key issue in SSc clinical research. Nailfold videocapillaroscopy (NVC) is a valuable tool to detect and classify microvascular structural alterations. In contrast, laser speckle contrast analysis (LASCA), a non-invasive microvascular imaging tool, has been proposed as an objective technique to dynamically evaluate the peripheral blood perfusion (PBP).

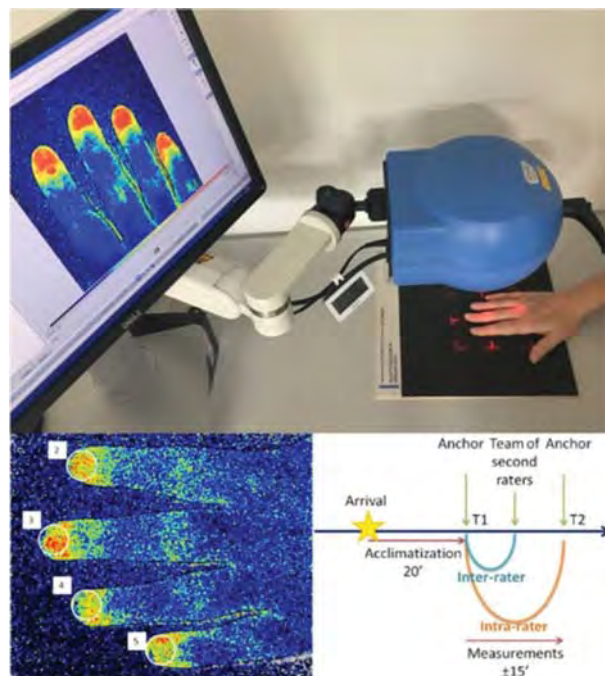
**Objectives:** The specific objectives were 1) to perform a pilot study to investigate as first both the intra- and inter-rater reliability of LASCA in an unselected SSc cohort and descriptively in healthy subjects (HS) and 2) to identify the available literature on the reliability of LASCA in SSc by a systematic literature review.

**Methods:** First, a pilot study was performed to assess the reliability of LASCA to measure the PBP at the level of the fingers in an unselected cohort SSc patients and descriptively in HS. Intra-rater reliability was assessed by having a first anchor rater performing the measurements at 2 time-points (within 15 min) and inter-rater reliability by subsequently having the first anchor rater and a team of 3 s raters performing the measurements in 15 SSc and 30 HS (see figure 1). As external validation, the measurements were repeated with a second anchor rater in a distinct cohort of 15 SSc patients. Reliability was described by calculating the intraclass correlation coefficient (ICC).

The systematic search was performed to identify relevant full-text articles in PubMed, EMBASE and Web of Science. All retrieved articles were screened on title, abstract and full-text level, reference lists were additionally searched.

**Results:** Thirty SSc patients (5 men, 25 women; mean age 52±17 y; 1LSSc, 25LcSSc, 4DcSSc; 14 vasodilatory therapy) and 30 HS (8 men, 22 women; mean age 33±11 y) underwent LASCA measurements. ICC for intra-rater reliability of the first anchor was 0.95 (95% CI 0.86–0.98) in SSc and 0.93 (95%CI 0.83–0.97) in HS, the ICC for inter-rater reliability was 0.97 (95%CI 0.90–0.99) in SSc and 0.93 in HS. Intra- and inter-rater reliability of anchor 2 was 0.78 (95%CI 0.46–0.92) and 0.87 (95%CI 0.67–0.96) respectively.

The systematic search identified 64 unique articles, of which 12 were eligible for full-text review. Two additional references were identified through a reference search of retrieved articles. Only 1 of the 14 selected references that met the inclusion criteria documented reliability as outcome and was included in the final analysis. This pilot study by Lambrecht et al measured the PBP at the level of the fingertips and reported ICC values varying from 0.82–0.91 for the dorsal and 0.74–0.86 for the volar fingertips.



**Conclusions:** The body of knowledge regarding intra- and inter-rater reliability of LASCA in SSc is very limited. Only one manuscript reporting very good inter-rater reliability of PBP measurements of the distal fingertips by LASCA could be withheld. These results could be confirmed by our pilot study. In addition, we demonstrated excellent intra-rater reliability of LASCA measurements for the evaluation of the PBP of the hands in SSc patients and HS.

**Disclosure of Interest:** None declared

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**SAT0480 EVALUATION OF STANDARDISED TEACHING OF MODIFIED RODNAN SKIN SCORE ASSESSMENT IN SYSTEMIC SCLEROSIS**

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**Background:** The modified Rodnan skin score (mRSS) is a standard outcome measure for skin involvement in systemic sclerosis (SSc) clinical trials. Training assessors reduces variability in mRSS measurement.

**Objectives:** Our objective is to report the inter- and intra-observer variability of mRSS scoring using newly developed standardised training guidelines by the Scleroderma Clinical Trials Consortium (SCTC).

**Methods:** Two SSc experts (DK/AL), 2 facilitators, 52 rheumatology trainees and 8 SSc patients fulfilling the 2013 American College of Rheumatology criteria participated in a SSc skin scoring workshop. Eight SSc patients were examined by 2 SSc experts and facilitators together and consensus scores reached. All trainees attended a talk on mRSS skin scoring by an SSc expert (DK), followed by a video and live demonstration by an expert examining a patient exhibiting different aspects of skin scoring. Each trainee subsequently performed mRSS scoring on 4 SSc patients independently. This concluded the teaching session for mRSS scoring. The mRSS scoring for each trainee was compared to the consensus expert mRSS, and a score of ≤5 in 3 out of 4 patients is considered acceptable inter-observer variability, as determined by SCTC guidelines.

Two days after training, 12 trainees, 2 facilitators and 2 experts re-assessed independently the mRSS of 2 SSc patients whom they had examined previously. The repeat day 2 mRSS score for each trainee was compared to the baseline mRSS score, and a score of ≤3 is considered acceptable intra-observer variability.

We computed the inter- and intra-observer variability using a linear mixed model with an intercept term and random effects for patient, rater and patient by rater with the following values representing the degrees of agreement: <0 –poor; 0–0.20 –slight; 0.21–0.40 –fair; 0.41–0.60 –moderate; 0.61–0.80 –substantial; and 0.81–1.00 –almost perfect agreement.

**Results:** For the first group of assessors involving 52 trainees, 65.4% of them achieved acceptable inter-observer variability, with inter-observer variability of





activity and depression. Full names of questionnaires are listed in the table 1. Data are presented as mean  $\pm$  SEM.

**Results:** Compared to HC, patients with SSc had significantly higher prevalence and greater severity of sexual dysfunction (FSFI, BISF-W: in all subscales as well as total scores), dysfunction of pelvic floor (PISQ-12, PFIQ7), and worse sexual quality of life (SQoL-F) (table 1). Worse scores in SSc patients were associated with higher disease activity [ESSG activity index: SQoL-F ( $r=-0.364, p=0.0443$ ), PFIQ7-gynaecological subscale ( $r=0.492, p=0.0036$ )], greater fatigue [all three questionnaires FSS/FIS/MAF correlated negatively with FSFI, BISF-W], more severe depression [BDI-II: FSFI ( $r=-0.553, p=0.0002$ ), BISF-W ( $r=-0.514, p=0.0007$ ), PFIQ7 ( $r=0.495, p=0.0010$ )], deteriorated quality of life [SHAQ: FSFI ( $r=-0.536, p=0.0003$ ), BISF-W ( $r=-0.563, p=0.0001$ ), SQoL-F ( $r=-0.338, p=0.0382$ ), PISQ-12 ( $r=0.563, p=0.0051$ ), PFIQ7 ( $r=0.380, p=0.0142$ )], and worse ability to perform physical activities [HAP: FSFI ( $r=0.407, p=0.0082$ ), BISF-W ( $r=0.409, p=0.0078$ )].

Questionnaire: score range	Systemic sclerosis (n=41)	Healthy controls (n=41)	p-value
FSFI: Female Sexual Function Index: 2(worst)–36(best)	15.2 $\pm$ 1.7	25.0 $\pm$ 1.7	$p<0.0001$
BISF-W: Brief Index of Sexual Function for Women: –16(worst)–75(best)	17.5 $\pm$ 2.8	29.7 $\pm$ 2.8	$p=0.0027$
PISQ-12: Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire short form: 0(best)–48(worst)	13.9 $\pm$ 0.9	8.5 $\pm$ 0.7	$p<0.0001$
PFIQ7: Pelvic Floor Distress Inventory Questionnaire – short form 7: 0(best)–300(worst)	26.4 $\pm$ 5.9	7.1 $\pm$ 2.2	$p=0.0092$
SQoL-F: Sexual Quality of Life Questionnaire – Female: 0(worst)–100(best)	56.7 $\pm$ 3.9	78.8 $\pm$ 3.3	$p<0.0001$
FSS: Fatigue Severity Scale: 9(best)–63(worst)	40.7 $\pm$ 2.2	6.9 $\pm$ 1.0	$p<0.0001$
FIS: Fatigue Impact Scale: 0(best)–160(worst)	59.2 $\pm$ 4.9	28.8 $\pm$ 4.3	$p<0.0001$
MAF: Multidimensional Assessment of Fatigue Scale: 1(best)–50(worst)	26.0 $\pm$ 1.6	13.6 $\pm$ 1.3	$p<0.0001$
BDI-II: Beck's Depression Inventory II: 0(best)–63(worst)	14.2 $\pm$ 1.3	4.8 $\pm$ 0.8	$p<0.0001$
HAP: Human Activity Profile–adjusted activity score: 0(worst)–94(best)	49.4 $\pm$ 3.7	81.1 $\pm$ 1.5	$p<0.0001$
HAQ: Health Assessment Questionnaire: 0(best)–3(worst)	0.9 $\pm$ 0.1	0.1 $\pm$ 0.0	$p<0.0001$

**Conclusions:** Women with SSc reported significantly impaired sexual function, sexual quality of life and pelvic floor function than age-matched healthy controls. Worse scores in SSc were associated with disease activity, physical activity, fatigue, depression and quality of life.

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**Disclosure of Interest:** None declared

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#### SAT0484 PERFORMANCE OF THE 2017 EULAR/ACR CLASSIFICATION CRITERIA FOR INFLAMMATORY MYOSITIS AND THEIR MAJOR SUBGROUPS IN THE REMICAM (REGISTRY OF INFLAMMATORY MYOPATHIES IN THE MADRID COMMUNITY)

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**Background:** A collaborative EULAR/ACR Project has developed new criteria for inflammatory myopathies(IM) and their subgroups<sup>1</sup>

**Objectives:** To analyse agreement between the 2017 IM classification criteria and the Bohan and Peter(BP) criteria in REMICAM cohort<sup>2</sup>

**Methods:** All patients were included. New criteria were applied to obtain classification as: possible(Pos), probable(Pro) and definitive(Def) IM, and subclassification in 6 subgroups: polymyositis(PM), dermatomyositis(DM), juvenile DM(JDM), amiodopathic DM(ADM), inclusion body myositis(IBM) and juvenile myositis(JM). The 7 subgroups in REMICAM were harmonised to fit the 6 subgroups of the 2017 criteria. Agreement between 2017 and BP criteria was analysed in classification/subclassification, calculating the weighted kappa value (k). Subanalysis including only patients with available data on the muscle strength items required for the 2017 criteria, and in those having also muscle biopsy data, were conducted.

**Results:** From 479 REMICAM patients, 477 (99.6%), fulfilled BP criteria (5.9% Pos, 26.8%Pro, 67.4%Def) and 431 (89.9%) 2017 criteria (2.5%Pos, 21.8%Pro, 65.7Def). Global agreement between both criteria was 89.5%. Agreement

between subtypes (Pos, Pro, Def) was low ( $k=0.15$ ). When 399 patients with muscle strength data, and 243 with muscle biopsy data were analysed, results were similar ( $k=0.17$ ). Disagreement was mainly seen in Pos/Pro subtypes with BP criteria, since 60% classified as Def when the 2017 criteria were applied. Agreement in the different subgroups of IM (PM, DM, JDM, ADM, IBM, JM) between both criteria was very high ( $k=0.94$ ).

**Conclusions:** The new 2017 EULAR/ACR criteria for IM classification show good agreement with BP criteria in the REMICAM cohort. New criteria classify 60% of Pos/Pro patients by BP criteria, as Def, and show very high agreement between IM subgroups. Validation studies are needed, but our results in this large cohort suggest the 2017 criteria might be useful for clinical trials and research in IM.

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**Disclosure of Interest:** None declared

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#### SAT0485 WHAT IS THE EFFECT OF CYCLOPHOSPHAMIDE IV PULSE THERAPY IN PATIENTS WITH DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS ON SKIN INVOLVEMENT: AN OBSERVATIONAL STUDY

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**Background:** Patients with systemic sclerosis who have proximal skin involvement are classified as diffuse cutaneous systemic sclerosis (DcSSc). Patients with progressive skin involvement have worse prognosis due to internal organ involvement. Treatment options of these patients consist among others of cyclophosphamide iv pulse therapy (iv CYC).<sup>1</sup> Recent studies show significant improvement of skin thickening in patients treated with CYC orally,<sup>2</sup> but the effect of iv CYC on skin involvement remains unclear.

**Objectives:** To examine the extent of skin involvement during 12 monthly iv CYC (750 mg/m<sup>2</sup>) in DcSSc and to identify factors that predict response to therapy.

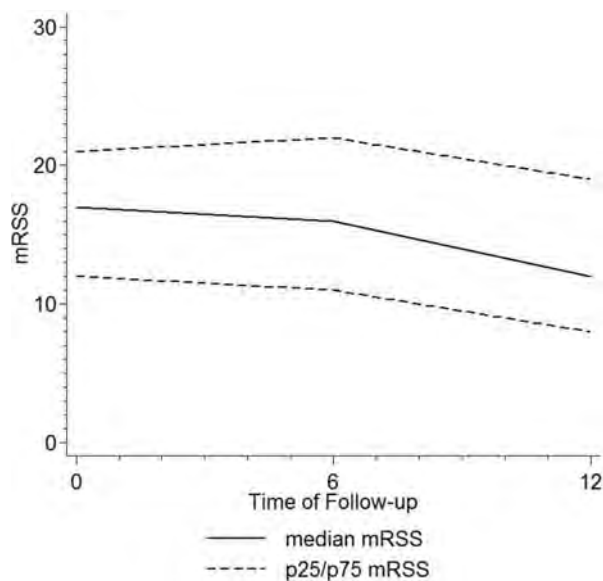
**Methods:** Patients with DcSSc receiving iv CYC between 2004 and 2016 were included if they received at least 6 pulses. Skin involvement was assessed with the modified Rodnan Skinscore (mRSS) at baseline, month 6, 12, 24 and 36 by the same trained rheumatologist as part of routine care. Data of patients with the baseline measurement and at least one follow up measurement were included in the study. Missing mRSS data were imputed using multiple imputation by chained equation. Patients were classified as responders if the mRSS decreased at least 5 points and 25% from baseline at month 12. A prediction model for response at 12 months was created using backwards logistic regression considering baseline variables and response at 6 months as possible predictors.

**Results:** A total of 99 patients were included. The mean improvement of mRSS over time was  $-4.05$  (95% CI  $-5.53$  to  $-2.55$ ) (figure 1). 43% of patients had a response according to the response criteria.

**Abstract SAT0485 – Table 1.** Demographic and clinical characteristics of responders and non-responders

	Responders at 12 months (n=40)	Non-responders at 12 months (n=51)
Age, mean (sd)	52 (14)	54 (13)
Female gender, n (%)	19 (48%)	19 (37%)
Baseline mRSS, median (IQR)	13 (9–21)	19 (15–24)
Disease duration (months), median (IQR)	3 (1–12)	6 (2–18)
infusions completed, n (%)	37 (93%)	37 (73%)
12	3 (8%)	14 (27%)
$\geq 6$ and $<12$		
Antibodies	12 (30%)	19 (37%)
-ANA	24 (60%)	29 (57%)
-Anti-topoisomerase		
Response at 6 months	17 (46%)	1 (2%)

In univariate prediction models, baseline mRSS (OR 1.06,  $p=0.024$ ), response at 6 months (OR: 37.45,  $p<0.001$ ) and completed treatment (yes/no) (OR: 4.108,  $p=0.033$ ), were significant predictors of response at 12 months. For the last variable it should be mentioned that some patients who did not achieve a response at month 6 did not continue iv CYC for that reason.



Abstract SAT0485 – Figure 1. mRSS course of all patients during iv CYC

**Conclusions:** This study shows that only 43% of the treated DcSSc patients experienced clinical important improvement of skin involvement following iv CYC. Response at month 6 is the best predictor for response on month 12. This could imply that at this time point, counselling about other available treatment options, should be considered in those patients.

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**Disclosure of Interest:** None declared

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#### SAT0486 MYELOABLATION FOLLOWED BY AUTOLOGOUS STEM CELL RESCUE LEADS TO NORMALISATION OF SERUM IL-6 LEVELS IN PATIENTS WITH SYSTEMIC SCLEROSIS

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**Background:** In the randomised Scleroderma: Cyclophosphamide or Transplantation (SCOT) trial, myeloablation followed by autologous hematopoietic stem cell transplantation (HSCT) led to improved clinical outcomes compared to monthly cyclophosphamide (CYC) treatment in systemic sclerosis (SSc).<sup>1</sup> Moreover, there is emerging evidence on the role of the Th2 cytokine, interleukin 6 (IL-6) in SSc pathogenesis, and clinical trials targeting the IL-6 pathway have been completed.<sup>2</sup>

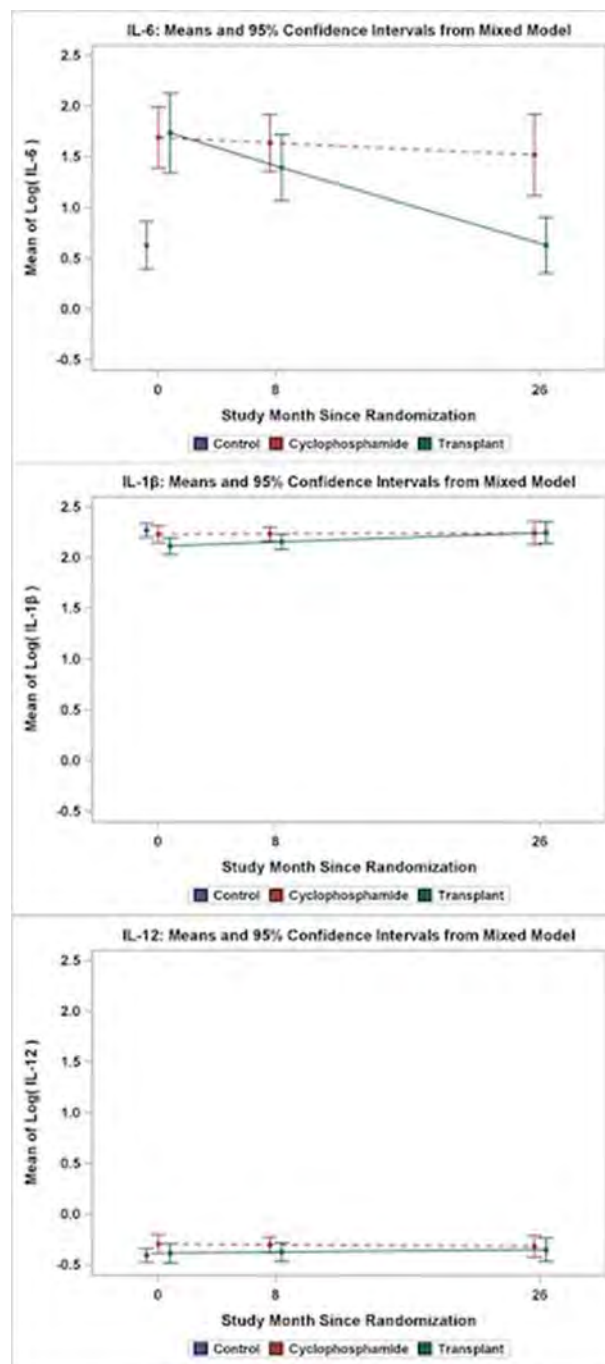
**Objectives:** To investigate the association of IL-6 with baseline clinical features and to examine its longitudinal changes in the treatment arms of the SCOT trials.

**Methods:** The SCOT trial enrolled 75 subjects with diffuse SSc, 65 (HSCT=31, CYC=34) subjects with a mean disease duration of 2.2 years were analysed; 65 age and gender matched controls were also investigated. All available serum samples at the baseline (n=65), 8- (n=55) and 26- (n=45) month visits were included. IL-6 was determined using ultra-sensitive Simoa assay. For purposes of comparison, prominent, pro-inflammatory Th1 cytokines, Interleukin 1 $\beta$  (IL-1 $\beta$ ), interleukin 12 (IL-12), and interferon gamma (IFN- $\gamma$ ) were determined by Rule

Based Medicine multiplex assays. The serum IFN- $\gamma$  levels were in undetectable range in the majority of patient and control samples. Therefore, the comparative analysis focused on IL-1 $\beta$  and IL-12.

**Results:** Serum IL-6 was higher in SSC patients than controls (fold change=1.62,  $p<0.001$ ). At the baseline visit, IL-6 positively correlated with hsCRP ( $r_s=0.56$ ,  $p<0.001$ ) and modified Rodnan Skin Score ( $r_s=0.26$ ,  $p=0.037$ ) and showed an inverse relationship with disease duration ( $r_s=-0.26$ ,  $p=0.037$ ), while it did not have a significant correlation with forced vital capacity ( $r_s=-0.19$ ,  $p=0.126$ ). Moreover, no significant correlations were observed with IL-1 $\beta$  and IL-12.

A comparison of regression lines revealed a significant decrease in serum IL-6 levels in the HSCT arm relative to CYC ( $p=0.0004$ ). By 26 months, the HSCT arm no longer showed upregulation of serum IL-6 relative to controls while the CYC arm remained upregulated. In contrast, time trends for IL-1 $\beta$  and IL-12 did not differ significantly between arms ( $p$ -values=0.161 and 0.456, respectively). (figure 1).



**Conclusions:** The Serum IL-6 levels decreased significantly 26 months after HSCT, while the two Th1, proinflammatory cytokines did not show similar



changes. This finding supports the notion that this treatment modality normalises specific serum protein imbalances implicated in SSc pathogenesis.

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**Disclosure of Interest:** None declared

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SAT0487

#### A COHORT STUDY OF MACROVASCULAR INVOLVEMENT IN PATIENTS WITH SYSTEMIC SCLEROSIS

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**Background:** It is well known that systemic sclerosis (SSc) affects microvessels, but data on macrovascular involvement are still lacking or debatable.

**Objectives:** Aim of this study was to estimate the prevalence of atherosclerotic plaques and their possible determinants in a large cohort of SSc patients.

**Methods:** One-hundred and four outpatients with SSc were enrolled. Data about disease characteristics and cardiovascular risk factors (diabetes, hypertension, dyslipidemia, smoke) were collected and patients underwent a full ecocolor Doppler ultrasonography of arteries of the neck and lower limbs (LL).

**Results:** Mean age of our cohort was 62±13 years and 17 (16.3%) patients were male. Seventy patients (67.3%) had a limited subset and the mean disease duration was 12.7±6.8 years. A previous history of digital ulcers was found in 27 cases (26.0%). Thirty-eight patients (36.5%) were on ongoing or previous treatment with immunosuppressive drugs.

Regarding cardiovascular risk factors, 22 (21.2%) had hypertension, 7 (6.7%) diabetes, 52 (50%) dyslipidemia and 45 (43.3%) were active or past smokers. Fifty-seven (54.2%) patients had plaques at carotids, 1 (1%) at LL and 37 (35.9%) at UL. Prevalences were higher in older patients, as expected.

Patients with carotid plaques were older ( $p<0.001$ ), with hypertension ( $p=0.057$ ), a limited disease subset ( $p=0.005$ ), a more severe disease according to Medsger severity score (0.048), worse renal function ( $p=0.012$ ), higher glucose blood levels ( $p<0.001$ ), homocysteinemia ( $p=0.006$ ) and ESR ( $p=0.004$ ) and less often on immunosuppressors ( $p=0.048$ ) but more often on steroids ( $p=0.050$ ). Patients with LL plaques were older ( $p<0.001$ ), male ( $p=0.003$ ), treated with statins ( $p=0.056$ ), with a worse renal function ( $p=0.001$ ), higher glucose blood levels ( $p=0.038$ ) and homocysteinemia ( $p=0.006$ ).

In multivariate analysis with all variables with a  $p<0.010$  in univariate, patients with carotid plaques were found to be older ( $p=0.003$ ) and with a limited disease subset ( $p=0.012$ ; OR 5.6, CI95% 1.5 to 21.5). These data were confirmed even after correcting also for other well-known risk factors for atherosclerosis. No variables were found to be statistically different between patients with and without LL plaques.

**Conclusions:** in this study we performed one of the most complete evaluation of macrovascular involvement in one of the most numerous cohort of SSc patients present in literature. The prevalence of carotid and LL plaques did not seem to be higher in SSc patients as compared to what reported in healthy subjects. Intriguing is that patients with limited disease have an increased risk of having carotid plaques even after correcting for possible confounders.

**Disclosure of Interest:** None declared

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SAT0488

#### ORGAN INVOLVEMENT AND ILD PROGRESSION IN SCLERODERMA PATIENTS WITH ANTI-TOPOISOMERASE I SPECIFICITY AND LIMITED CUTANEOUS FORM

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**Background:** The great variability of clinical manifestations in systemic sclerosis (SSc) yields the need of defining prevalence and progression of organ

involvement in the different subsets of the disease. Despite the classical association between anti-topoisomerase-I (SCI70) positivity with diffuse cutaneous SSc (dSSc), and anti-centromere (ACA) with limited cutaneous SSc (lSSc), a population of patients with anti-SCI70 and lSSc has been described.<sup>1</sup> Interstitial lung disease (ILD) is nowadays the leading cause of mortality in SSc; its progression can range from a self-limiting form to a rapidly progressive lung involvement, despite immunosuppressive treatment.

**Objectives:** The aim of our study was to evaluate the prevalence of different organ involvement in three groups of patients: ACA-lSSc, SCI70-dSSc e SCI70-lSSc. Our second endpoint was to investigate possible differences in ILD onset and progression between SCI70-lSSc and SCI70-dSSc patients.

**Methods:** Consecutive 260 patients attending the Rheumatology Unit of Padova University of Padova were included and retrospectively evaluated. Clinical, biochemical and functional parameters concerning pulmonary, cardiac and articular involvement were collected in all patients, with an average follow-up time of 15 years. As for lung involvement, spirometric indices (FVC e DLCO) and HRCT at ILD onset and at last follow up were considered (median ILD duration 8 years<sup>4,12</sup>). Time between SSc onset and ILD first evidence was defined as "scleroderma free ILD". ILD grading was determined according to Kazerooni score. ILD progression was defined as either an HRCT score worsening of at least 2 points, or as a significant progression of spirometric indices (10% and 15% for FVC and DLCO respectively).<sup>2</sup>

**Results:** 150 patients with ACA-lSSc, 58 with SCI70-dSSc and 52 with SCI70-lSSc were included in the study. SCI70-lSSc patients presented more often with pulmonary and articular involvement with respect to ACA-lSSc patients (50% vs 6.9% and 42.9% vs 23.6% respectively), and less often compared to SCI70-dSSc. In SCI70-lSSc, cardiac and gastrointestinal involvement, BEV and digital ulcers were less prevalent with respect to SCI70-dSSc ( $p<0.05$ ). SCI70-lSSc patient had a longer "scleroderma free-ILD" compared to SCI70-dSSc. At ILD onset pulmonary function was worse in SCI70-dSSc group than in SCI70-lSSc group ( $p=0.02$  e  $p=0.009$  for FVC e DLCO respectively), even in the absence of a significant difference between HRCT scores (12.73±5.25 vs 10.25±4.93,  $p=0.284$ ). Total ILD progression was significantly higher in SCI70-dSSc ( $p<0.0001$ ).

**Conclusions:** Our study shows that SCI70-lSSc patients appeared to have a different prevalence of targeted organ involvement and ILD progression with respect to both SCI70-dSSc and ACA-lSSc. Since the correct classification of SSc patients is extremely important in view of a tailored treatment, our data suggest that it could be worth to identify patients with SCI70 and limited cutaneous form as a different and specific subset.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.7232

SAT0489

#### ASSESSMENT OF PERSISTENT ORGAN DAMAGE ACCORDING TO IMACS (INTERNATIONAL MYOSITIS ASSESSMENT AND CLINICAL STUDIES) MYOSITIS DAMAGE INDEX IN 92 PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOSITIS

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**Background:** Number of work regarding long term organ damage caused by idiopathic inflammatory myopathies (IIM) and risk factors associated with organ damage have been understudied and never reported from Turkey; recently a new tool as developed for that purpose.

**Objectives:** In this study we aimed to evaluate by long term organ damage and risk factors, associated with these prospectively in IIM patients.

**Methods:** IIM patients (n=110) who has been followed up for at least six month by our clinic and fulfilling Bohan and Peter criteria were recruited. Demographic data, clinical and serological features, treatment and final clinical tatus was recorded. IMACS Myositis Damage Index (MDI) was determined twice in 92 patients (71% female) at the time of diagnosis from the records and at the at last clinical visit prospectively.

**Results:** Mean age of the 92 patients during the diagnosis was 46±14.7. Out of 92 patients 69% had dermatomyositis, 23% had polymyositis, 8% had necrotizing

autoimmune myopathy and inclusion body myositis. Mean follow up was 82 months. Frequencies of dysphagia, respiratory muscle involvement and interstitial lung disease were 29.5;34% respectively. Twenty-one percent of the patients had associated malignancy. The mean daily prednisolone dosage and total amount was 7.5 mg/day and 9000 mgs. Mortality was 13%. Initial mean MDI at the time of diagnosis was 1.6±3.0 (range, 0–14) and the last DMI score recorded was 6.1±4.7 (range, 0–21). After the last assessment the proportion of patients without damage was 8% and whose score was 4 were 37%. The last DMI score was significantly higher than the first DMI score ( $p<0.001$ ). The last DMI in females and patients with calcinosis were significantly high ( $p=0.002$ ;  $p=0.007$ ). The last DMI score and disease duration were weakly correlated ( $r=0.35$   $p=0.001$ ). A moderately significant correlation was found between the last DMI score, the duration of glucocorticoid use and the total dose used ( $r=0.48$   $p<0.001$ ;  $r=0.45$   $p<0.001$ ).

**Conclusions:** Our long term follow up data showed that persistent organ damage assessed by DMI and mortality were high in patients with IIM and over half of patients developed severe damage. Organ damage was detected in some patients at presentation and DMI scores were significantly increased during the follow up. DMI scores were found high in females and in patients with calcinosis. There were significant correlation between disease duration, the duration of glucocorticoid use, the total dose used and DMI scores. Current treatments and strategies have been insufficient at improving the prognosis of patients with IIM and new treatment strategies and drugs are needed.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.4872

#### SAT0490 INCIDENCE AND PREVALENCE OF SYSTEMIC SCLEROSIS IN AN ITALIAN ALPINE VALLEY DURING A 18-YEAR LONG PERIOD

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**Background:** Not much information is available on the variations in the incidence and prevalence of Systemic Sclerosis (SSc) over time.

**Objectives:** To investigate the epidemiology of SSc in Valcamonica, an Alpine valley in northern Italy (Brescia Province, Lombardy region), during a 18-year-long period.

**Methods:** All patients with diagnosis of SSc living in Valcamonica between 1999 and 2016 were identified by capture/recapture method using: 1) clinical databases of the only secondary Rheumatology Unit present in the valley (Esine Hospital), and of the only tertiary referral centre for this area (Spedali Civili, Brescia); 2) administrative data (ASST Valcamonica, Esine), extracting all records with the ICD-10 code for SSc (710.1). Clinical charts were reviewed and patients included in the analysis when either the 1980 ARA or the 2013 ACR/EULAR classification criteria for SSc were satisfied. Incidence was calculated using the number of new cases observed as the numerator, and the Valcamonica population as the denominator for each year; to study temporal changes, mean yearly incidence during 3 different 6 year intervals was calculated (table 1). Prevalence rates were estimated at 4 different time points dividing the number of living patients by the number of individuals in the population (table 2). Survival, incidence and prevalence rates were expressed with 95% confidence intervals. Incidence and prevalence rates observed in different periods were compared using ANOVA test. Demographic data were expressed as the medians (IQR).

**Results:** General population with age over 14 years living in Valcamonica varied during the evaluated period between 85 168 (1999) and 91 245 inhabitants (2011). Fifty-six patients with SSc fulfilling the 2013 ACR/EULAR criteria, and in 68% of them also the 1980 ARA criteria were identified (Female 85.7%, Male:

14.3%; Caucasian: 96.4%, African 3.6%; age at diagnosis: 58;<sup>47–80</sup> deaths: 13 (8 because of SSc); survival: at 5 years: 89.4% (76.2–95.5), at 10 years: 84.4% (69.9–92.3); diffuse SSc: 17.9%, limited SSc: 82.1%; anticentromere: 62.3%, anti-topoisomerase I (topo I): 20.8%, anti-RNA polymerase III (RNAP3): 5.4%; anti-topo I and RNAP3: 1.9%; Anti-Th/To: 1.9%; interstitial lung disease: 23.1%; group 1 pulmonary arterial hypertension 19.6%; renal crisis 5.4%). No significant variation of incidence was observed during the period of time evaluated in the study (table 1). Analysis of prevalence revealed a continuous increase of the disease using both the 1980 ARA criteria or 2013 ACR/EULAR criteria ( $p<0.001$  for both comparisons; table 2). The prevalence on 2016 was 50.9 per 1 00 000 persons aged >14 years, one of the highest ever recorded by SSc epidemiology studies. However, notably, the prevalence in Valcamonica during the first years of the 21 st century was similar to that reported by previous other studies performed in Italy in the same years.<sup>1–2</sup>

**Abstract SAT0490 – Table 1.** Incidence of SSc in Valcamonica expressed as cases per 100,000 adults aged over 14-years

SEX	STUDY PERIOD	MEAN POPULATION >14 YEARS	NEW CASES	INCIDENCE (CI 95%)
MALE AND FEMALE	1999-2004	86,205.5	12	2.3 (1.2-4.1)
	2005-2010	89,448.5	14	2.6 (1.4-4.4)
	2011-2016	90,843	16	2.9 (1.7-4.8)

**Abstract SAT0490 – Table 2.** Estimates of the prevalence of SSc in Valcamonica expressed as cases per 100,000 adults aged over 14-years

SEX	YEAR	POPULATION >14 YEARS	LIVING CASES	PREVALENCE (CI 95%)
MALE AND FEMALE	1999	85168	14	16.4 (9-27.6)
	2005	88011	26	29.5 (19.3-43.3)
	2011	91245	37	40.6 (28.6-55.9)
	2016	90441	46	50.9 (37.2-67.8)
FEMALE	1999	43755	13	29.7 (15.8-50.8)
	2005	44751	22	49.2 (30.8-74.4)
	2011	46149	31	67.2 (45.7-95.3)
	2016	45868	42	91.6 (66-123.8)
MALE	1999	41413	1	2.4 (0-13.5)
	2005	43260	4	9.3 (2.5-23.7)
	2011	45096	6	13.3 (4.9-29)
	2016	44573	4	9 (2.5-23)

**Conclusions:** Although the incidence of SSc did not change significantly over time in this area, the disease prevalence constantly increased, with recruitment of new cases exceeding the number of deaths.

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**Disclosure of Interest:** None declared

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SAT0491

### CLINICAL FEATURES AND COMPLICATIONS IN A LARGE INTERNATIONAL COHORT OF ANTIMDA5 PATIENTS: A CHALLENGE FOR THE FUTURE

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**Background:** Anti-MDA5 antibodies are a known set of antibodies observed mainly in dermatomyositis, typically associated with cutaneous involvement, presence and often rapid progression (RP) of interstitial lung disease (ILD) and amyopathic muscle involvement. Despite the increased attention, described cohorts involves only a limited number of cases

**Objectives:** to define clinical characteristics of a large cohort of anti-MDA5 antibodies positive patients

**Methods:** Retrospective assessment of anti-MDA5 positive patients from centres referring to our group

**Results:** 82 anti-MDA5 positive cases (56 females) were collected. In median: onset age was 44 Y (IQR 22.57), diagnostic delay 4 Mo (IQR 1–10), follow-up 13 Mo (IQR 3–43). Fifty-three patients had ILD, that was RP in 24 cases (15 at ILD onset, 9 after ILD onset). Fifteen ILD patients were admitted in Intensive Care Unit (ICU): 4 were treated with Extracorporeal-Membrane-Oxygenation, 7 with mechanical-invasive and 2 with mechanical-non-invasive ventilation. Forty-nine patients had muscle involvement (39 symptomatic), 42 arthritis, 54 cutaneous involvement, 9 history of malignancy. Twelve patients died (ILD=7, ILD and sepsis=3, neoplasia=1, not specified=1), 7 of those in ICU

**Conclusions:** In our cohort, ILD was the most frequent finding. A RP of ILD was common, occurring also in ILD with symptomatic/chronic onset. The low rate of survival in ICU raised the problem of follow up and early treatment of ILD. In our cohort arthritis was common and muscle involvement mainly symptomatic. Finally, the high percentage of observed malignancies suggests a careful neoplastic screening and follow up

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SAT0492

### PREVALENCE OF THE METABOLIC SYNDROME IN PATIENTS WITH SYSTEMIC SCLEROSIS

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**Background:** The metabolic syndrome is an independent risk factor for ischaemic heart disease. Patients with systemic lupus erythematosus have an increased prevalence of the metabolic syndrome.<sup>1</sup> There are no controlled studies of the metabolic syndrome in patients with SSc.

**Objectives:** To compare the prevalence of the metabolic syndrome in patients with SSc and controls and to evaluate its relationship to activity and severity of disease.

**Methods:** Methods: 50 consecutive patients with SSc (45 female, median age 48; range 20–72) and 50 controls (patients with fibromyalgia) (45 female, median age 46; range 25–72) were studied. The prevalence of the metabolic syndrome was compared in patients and controls using the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATPIII): central obesity: waist: 102 cm in men and 88 cm in women;<sup>2</sup> hypertriglyceridaemia:>150 mg/dl;<sup>3</sup> low HDL, 40 mg/dl in men and 50 mg/dl in women;<sup>4</sup> high blood pressure:>130/85 mm Hg or use of drugs for high blood pressure; and<sup>5</sup> high fasting glucose >110 mg/dl, and associations with activity and severity of the disease were examined.

**Results:** The metabolic syndrome was present in 24% of patients and in 30% of controls subjects (p>0.05). Among patients with SSc, the metabolic syndrome was significantly associated with higher value of ESR (ESR >30) (5/7 vs 4/34; p=0.027). Neither disease activity nor severity scores were associated with the metabolic syndrome

**Conclusions:** Patients with SSc have a lower prevalence of the NCEP-ATPIII-defined metabolic syndrome than controls. This result may help to justify the coronary prevalence in SSc patients similar to that of the general population.<sup>2–3</sup>

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SAT0493

### PLASMA LEVELS OF HSP90 ARE INCREASED IN INTERSTITIAL LUNG DISEASE AND SKIN FIBROSIS IN PATIENTS WITH SYSTEMIC SCLEROSIS

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**Background:** Our previous study demonstrated that Heat shock protein 90 (Hsp90) is overexpressed in the skin of patients with systemic sclerosis (SSc), in cultured SSc fibroblasts and preclinical models of SSc in a TGF- $\beta$  dependent manner. We showed that Hsp90 is a regulator of TGF- $\beta$  signalling and its inhibition prevents the stimulatory effects of TGF- $\beta$  on collagen synthesis and dermal fibrosis in three preclinical models of SSc<sup>1</sup>.

**Objectives:** The aim of this study was to evaluate Hsp90 in the circulation of SSc patients and characterise its potential association with skin changes and SSc-related features.

**Methods:** A total of 91 patients (78 females; mean age 52.7; disease duration 6.0 years; diffuse cutaneous (dc)SSc/limited cutaneous (lc)SSc=38/53) who met the ACR/EULAR 2013 classification criteria for SSc and 85 age-/sex- matched healthy individuals were included. Plasma Hsp90 was measured by ELISA (eBioscience, Vienna, Austria). Data are presented as median (IQR, 25.–75. percentile).

**Results:** Plasma Hsp90 levels were increased in SSc patients compared to healthy controls [12.5 (9.6–17.9) vs. 9.9 (7.9–12.6) ng/mL, p=0.001], but no difference between lcSSc and dcSSc was detected [13.1 (9.4–18.1) vs. 11.5 (9.5–17.5) ng/mL, p=0.316]. Hsp90 levels in all patients positively correlated with CRP



( $r=0.313$ ,  $p=0.006$ ). Furthermore, Hsp90 was increased in patients with interstitial lung disease (ILD) compared to those without ILD [12.8 (10.2–17.9) vs. 10.3 (8.6–16.6) ng/mL,  $p=0.045$ ] and was negatively associated with functional parameters of ILD: FVC ( $r=-0.299$ ,  $p=0.011$ ), FEV1 ( $r=-0.256$ ,  $p=0.031$ ), DLCO ( $r=-0.303$ ,  $p=0.009$ ) and SpO<sub>2</sub> ( $r=-0.317$ ,  $p=0.038$ ). In addition, only in patients with dcSSc, Hsp90 levels positively correlated with the mRSS ( $r=0.437$ ,  $p=0.006$ ). Hsp90 concentrations were not significantly affected by other main clinical parameters of SSc.

**Conclusions:** We demonstrated higher plasma levels of Hsp90 in SSc patients compared to healthy controls. Concentrations of extracellular Hsp90 increase with higher inflammatory activity, with deteriorated lung functions in ILD and also with the extent and severity of the skin involvement in patients with diffuse cutaneous SSc. These data further highlight the role of Hsp90 as a significant regulator of fibroblast activation and tissue fibrosis in SSc.

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**Disclosure of Interest:** None declared

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SAT0494

#### CLINICAL AND ELECTROPHYSIOLOGICAL DIAGNOSIS OF SYMMETRICAL POLYNEUROPATHY IN SYSTEMIC SCLEROSIS: STUDY FROM A SINGLE TERTIARY CENTRE IN MALAYSIA

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**Background:** Peripheral neuropathy (PN) in systemic sclerosis (SSc) is an under recognised non-lethal burden with its prevalence between 0.01% to 28%<sup>1</sup>. Previous studies have been limited by small sample size, variable diagnostic criteria and different populations studied.

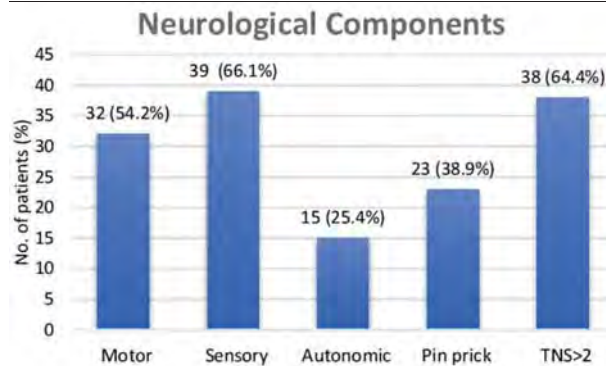
**Objectives:** The aim of this study is to determine the prevalence of symmetrical PN in SSc patients and to identify the associated factors that can predispose to PN in SSc.

**Methods:** 59 SSc patients from University Malaya Medical Centre participated in this cross-sectional study. Clinical symptoms/signs of PN were assessed using modified Total Neuropathy Score (TNS). Nerve conduction studies (NCS) were carried out on the upper and lower limbs. Diagnosis of symmetrical polyneuropathy was defined as combined TNS score  $\geq 2$  and abnormal NCS parameters in at least 2 nerves including the sural<sup>2</sup>. Focal neuropathy was defined as abnormal NCS of a nerve other than the sural nerve (radial, median, ulnar, common peroneal).

**Results:** Majority were females (54, 91.5%) and had limited cutaneous SSc (44, 74.6%). Mean age was 55.7 (SD  $\pm 13.1$ ) years while mean duration of disease (non-Raynaud's disease onset) was 8.74 years (SD  $\pm 8.09$ ) (range 1 to 44 years). Out of 59 patients, 38 (64.4%) had TNS  $\geq 2$ . On NCS, 17 (31.5%) and 12 (22.2%) had findings of symmetrical polyneuropathy and focal neuropathy respectively. A total of 14 (23.7%) SSc patients were diagnosed to have symmetrical polyneuropathy. Lower haemoglobin level was significantly associated with symmetrical polyneuropathy ( $p=0.047$ ) after adjustment for potential confounding variables. Serum vitamin B12 was normal in all subjects with symmetrical polyneuropathy. No correlation was seen in SSc related comorbidities (diabetes mellitus and kidney disease), serum fasting blood sugar, creatinine and MCV, as well as disease markers such as skin fibrosis (MRSS skin score), specific organ manifestations, Raynaud's or vasculopathy, SSc specific auto-antibodies and treatment received.

Demography	No polyneuropathy n=45 (76.3%)	Polyneuropathy n=14 (23.7%)	p value
Mean age (y.o $\pm$ )	53.6 $\pm$ 13.22	62.57 $\pm$ 10.69	<b>0.025</b>
Sex			0.325
Female	45 (76.3)	14 (23.7)	
Male	5 (100)	0 (0)	
BMI kg/m <sup>2</sup> (mean)	22.9 $\pm$ 5.94	21.0 $\pm$ 5.13	0.736
Diffuse SSc	10 (22.2)	4 (28.5)	0.722
Limited SSc	35 (77.7)	10 (71.4)	0.316
MRSS score (mean)	10.29 $\pm$ 8.02	8.36 $\pm$ 4.23	0.594
SSc duration (mean)	8.97 $\pm$ 8.78	8.00 $\pm$ 5.51	0.803
Haemoglobin (mean) (g/L)	12.36 $\pm$ 1.33	11.2 $\pm$ 1.25	<b>0.010</b>
MCV <sub>&gt;97</sub> (fl)	4 (8.9)	3 (21.4)	0.175
Creatinine (median) (umol/L)	55 $\pm$ (IQR 45–60)	61.5 $\pm$ (IQR 49–75)	0.111

Fasting blood sugar (mean) (mmol/L)	4.32 $\pm$ 1.16	5.67 $\pm$ 2.46	0.095
ESR (mean) (mm/hr)	33.7 $\pm$ 20.65	44.23 (19.6)	0.068



**Conclusions:** The prevalence of PN in a Malaysian SSc cohort is similar to other studies (23.7%). Lower haemoglobin level was significantly associated with symmetrical polyneuropathy in SSc.

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SAT0495

#### PLASMA D-DIMER CONCENTRATION, MACROVASCULAR DISEASE AND MORTALITY IN PATIENTS WITH SYSTEMIC SCLEROSIS

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**Background:** Plasma d-dimer (DD) has proven to be a reliable marker of a systemic prothrombotic state and its measurement might be helpful in predicting cardiovascular events and even mortality across a broad variety of diseases. An association between high levels of DD and macrovascular disease, diffuse cutaneous involvement and active disease has been suggested in patients with SSc.

**Objectives:** To determine the usefulness of DD measurement as a marker of macrovascular disease and mortality in patients with SSc. To explore its relation with other features and biomarkers of SSc.

**Methods:** Descriptive ambispective observational study. We included, consecutively from 2010 to 2015, SSc patients controlled in a tertiary hospital. We gathered demographic, clinical, and analytical variables, including DD levels measured by turbidimetric immunoassay (ACL TOP 700 CTS, Werfen Spain). Other variables were collected retrospectively from the electronic medical record. We explored the extracranial branches of the carotid artery (ESAOTE MyLab XV70, 7–12 MHz linear probe, software <sup>RF</sup>QIMT) measuring intima media thickness (IMT) by radiofrequency, and the presence of atheroma plaques, as per the Mannheim consensus, was registered. The *ankle-brachial index (ABI)* was measured by a Vascular Surgeon. We considered an IMT > 900  $\mu$  and/or presence of atheroma plaque and/or an ABI < 0.9 as macrovascular damage. We prospectively collected mortality until dec-2017. Statistical analysis was performed using SPSS 17.0 software.

**Results:** 115 patients were included consecutively, of which finally 100 were studied (91 women, 9 men), with a mean age of 60.2 years (SD 15). Mean SSc evolution time was 13.9 years (SD 11.2). LSSc was most frequently diagnosed (50%), followed by DSSc (18%), SSc without scleroderma (17%), overlap syndrome (9%) and pre-SSc (6%). 37% of patients were hypertensive, 45% dyslipidemic, and 7% were diabetic. Overall, 40% had macrovascular damage. The mean values of DD were 437.6 ng/mL (SD 683.5), 60% of the patients having levels of DD (>250 ng/mL). During follow up, there were 16 deaths, 50% due to vascular events. Baseline high levels of plasma DD were associated to macrovascular damage and ischaemic digital ulcers, together with advanced age, arthritis, inflammation biomarkers, HTA, sPAP, lower DLCO% and coexistence of

an inflammatory disease (overlap, infection, neoplasia), and showed a tendency to an association with mortality. This association became statistically significant when considering DD plasma levels as a quantitative variable ( $p < 0.001$ ) and remained significant after adjustments (age, coexistence of an inflammatory disease) ( $p = 0.003$ ).

**Conclusions:** DD plasma levels are associated with macrovascular involvement and can be helpful in predicting medium-term mortality in our SSC patients. Levels of plasma DD can be modified by systemic inflammation.

**Disclosure of Interest:** None declared

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#### SAT0496 INCIDENCE, CARDIOVASCULAR EVENTS AND MORTALITY OF ADULT INFLAMMATORY MYOPATHIES IN SOUTH KOREA: A NATIONWIDE POPULATION-BASED STUDY

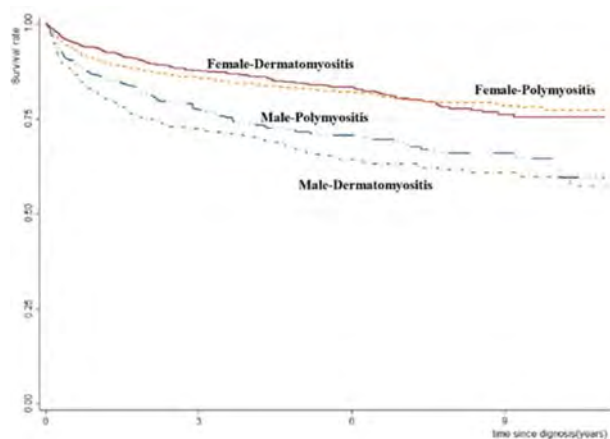
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**Background:** The inflammatory myopathies (IMs), including dermatomyositis (DM) and polymyositis (PM), are rare autoimmune diseases characterised by progressive proximal muscle weakness, elevated muscle enzyme and various organ involvement. Studies on epidemiology and mortality of IMs at the national level are rare.

**Objectives:** We conducted a nationwide population study of incidence, cardiovascular events (especially acute myocardial infarction, ischaemic stroke, haemorrhagic stroke) and survival of IMs in South Korea over the course of 11 years.

**Methods:** We used data from the Rare Intractable Disease (RID) registry and Health Insurance Review and Assessment (HIRA) service, which include information on all IMs patients diagnosed based on uniform criteria between 2005 and 2015. Survival data from Statistics Korea linked to HIRA-RID database were used in our survival analysis.

**Results:** In this study, total incident cases between 2005 and 2015 were 3014 (1,860 DM patients, 1,154 PM patients) and the mean annual incidence rate was  $7.16/10^6/\text{year}$  (DM was  $4.42/10^6/\text{year}$ , PM was  $2.74/10^6/\text{year}$ ). The female to male ratio of DM was 2.2:1 and that of PM was 1.9:1. Cardiovascular events occurred in 155 patients during the study period. Of the patients with DM, 25 were diagnosed with AMI (SIR 1.3, 95% CI 0.9–1.9), 39 with ischaemic stroke (SIR 1.4, 95% CI 1.0–1.9), 18 with haemorrhagic stroke (SIR 1.3, 95% CI 0.8–2.0). The results of PM were similar with those of DM. Of 155 patients, 63 (40.6%) died and had a high mortality rate. 640 of 3014 patients with IMs died during the study period; 290 and 350 were male and female, respectively. The survival curve for IMs is shown in Fig.1. The DM patients showed a 5 year survival rate (YSR) of 76.8%, and a 10-YSR of 68.9%, and the PM patients showed a 5-YSR of 79.3% and a 10-YSR of 68.3%.



**Abstract SAT0496 – Figure 1.** Survival curves of dermatomyositis and polymyositis

**Conclusions:** This is the first study of incidence and mortality of IMs over 3000 cases by the national registry in South Korea. In this nationwide population-based study of IMs, we found still high mortality and low survival and increased cardiovascular events related mortality compared than general population.

**Disclosure of Interest:** None declared

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#### SAT0497 FOLLOW-UP OF DISEASE ACTIVITY IN HUNGARIAN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHY

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**Background:** Assessing disease activity in patients with myositis is an important goal. A method called Disease Activity Core Set Measures was established by International Myositis Assessment and Clinical Studies Group (IMACS) for evaluating activity of myositis. This assesses the manifestations of myositis which are thought to be reversible that result directly from the inflammatory process.

**Objectives:** In this prospective study authors aimed to monitoring disease activity in Hungarian myositis patients treated at the Autoimmune Outpatient Clinic, Department of Clinical Immunology, University of Debrecen. First, disease activity data of poly (PM) – and dermatomyositis (DM) patients were compared. Secondly, by patients with active disease, the correlations between the components of Disease Activity Core Set Measures were studied.

**Methods:** During the three-year follow-up period, at every single visit, authors evaluated disease activity using factors of Disease Activity Core Set Measures and patients filled Health Assessment Questionnaire (HAQ). Only those patients who appeared at least three times during the follow-up period were selected. Statistical analysis was made using SPSS 17.0 statistical software.

**Results:** Collection of data from 219 patients (age: 44.93 years, female: male ratio 2.98:1) happened in a total of 1101 outpatient visits. The 107 PM patients had statistically significant higher physician and patient visual analogue (VAS) and myositis disease activity assessment tools scores than the 61 DM patients, with the exception of cardiovascular disease activity. Activity of skin lesions was significant higher in DM patients. By the 44 patients, who had an active disease, the MMT scores gave significant negative correlations with HAQ scores ( $R = -0.536$  and  $p < 0.001$ ) and CK levels ( $R = -0.387$  and  $p < 0.001$ ). The physician and patient VAS gave strong negative correlations with MMT scores ( $R = -0.714$  and  $p < 0.001$  and  $R = -0.730$  and  $p < 0.001$ , respectively) and positive correlations with HAQ scores and CK levels (physician VAS vs. HAQ  $R = 0.691$  and  $p < 0.001$ ; patient VAS vs. HAQ  $R = 0.629$  and  $p < 0.001$ ; physician VAS vs. CK  $R = 0.622$  and  $p < 0.001$ ; patient VAS vs. CK  $R = 0.615$  and  $p < 0.001$ ).

**Conclusions:** As far as we know, this is the first study which compares the activities of PM and DM patients based on the IMACS system. According to our data, we can conclude that PM patients had more severe muscle symptoms and extra-muscular manifestations. Secondly, as seen in other previous studies, calculations in patients with active myositis showed a clear correlation between the most important components of Disease Activity Core Set Measures.

**Disclosure of Interest:** None declared

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#### SAT0498 ABNORMAL ELECTROCARDIOGRAPHIC FINDINGS IN A SCANDINAVIAN COHORT OF PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES

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**Background:** Idiopathic inflammatory myopathies (IIMs) are characterised by progressive muscle weakness and muscle fatigue. IIMs frequently appear with other organ involvement, e.g. the heart. Cardiac affection is often subclinical but associated with poor prognosis which makes early detection critical.

Presence of autoantibodies is common in IIMs and autoantibodies are important biomarkers to confirm the diagnosis of IIMs. Autoantibodies may even predict organ involvement, e.g. the common myositis specific autoantibody anti-Jo1, which is a marker of lung involvement. So far, an autoantibody predicting cardiac involvement has yet to be identified.

**Objectives:** The aim of this study was to identify and estimate presence of cardiac involvement detected by electrocardiography (ECG) and to evaluate possible associations between ECG changes and autoantibodies in a Scandinavian cohort of patients with IIMs.

**Methods:** In a Scandinavian cross-sectional study, 241 patients with polymyositis (PM), dermatomyositis (DM), or inclusion body myositis (IBM) and 48 healthy controls (HCs) were investigated by ECG, basic cardiovascular assessments, and

autoantibody profile including myositis specific autoantibodies (MSAs) and myositis associated autoantibodies (MAAs).

**Results:** Compared to HCs, patients with IIMs more frequently had prolongation of QTc ( $p=0.037$ ) and QRS ( $p=0.031$ ). All patient groups had significantly longer QTc and QRS duration than HCs. In multivariate regression analysis of patients with IIMs, increased CRP ( $p=0.006$ ) was associated to increased QTc. Pooled data for patients with IIMs and HCs showed an association between diagnosis of IIM and increased QTc duration ( $p<0.001$ ). An association between presence of any MAA and QRS duration appeared in patients with IIMs ( $p=0.019$ ). In pooled data for patients with IIMs and HCs, diagnosis of IIM was associated with QRS duration ( $p=0.001$ ).

Table: Multivariate regression analyses of explanatory factors for QTc duration (ms)

Risk factor	OR	95% CI	P-value	OR	95% CI	P-value
Gender, male	0.46	0.28 0.75	0.002	0.46	0.29 0.72	0.001
Age at inclusion, per year	1.02	0.99 1.04	0.068	1.02	1.00 1.04	0.047
Hypertension, no vs. yes	1.63	0.93 2.86	0.086	1.58	0.97 2.60	0.069
Former/present smoker, no vs. yes	1.35	0.84 2.17	0.213	1.57	1.02 2.41	0.041
Increased CRP, no vs. yes	2.17	1.25 3.75	0.006	1.98	1.15 3.40	0.013
BMI, kg/m <sup>2</sup>			NS			NS
Dyspnea (NYHAI-IV), no vs. yes			NS			NS
Presence of MSAs/MAAs, no vs. yes			NS	NA	NA	NA
HAQ (Health Assessment Questionnaire), 0–3			NS	NA	NA	NA
IIM, no vs. yes	NA	NA	NA	4.11	2.21 7.63	<0.001

**Conclusions:** Patients with IIMs, no matter of clinical subgroup, had a higher occurrence of cardiac abnormalities detected by ECG than HCs. Increased CRP and presence of any MAA were associated with increased QTc and QRS duration, respectively. These results support our notion of possible associations between inflammation and autoimmunity and cardiac affection in patients with IIMs. There is now a pressing need to set up a larger prospective study to validate the present findings.

**Disclosure of Interest:** None declared

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#### SAT0499 ASSOCIATION BETWEEN SYSTEMIC SCLEROSIS AND OTHER SYSTEMIC AUTO-IMMUNE DISEASES: STUDY IN TWO UNIVERSITY HOSPITALS COHORTS

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**Background:** Association between systemic sclerosis (SSc) and another autoimmune systemic disease (AISD) in the same patient seems to be more frequent than each disease's prevalence would explain.

**Objectives:** The aim of our work was to describe patients presenting an overlap syndrome from 2 french cohorts and to compare their characteristics with patients presenting SSc alone.

**Methods:** This was a retrospective observational study conducted in two french auto-immune diseases reference centre (Strasbourg and Bordeaux). Patients responding to the 2013 ACR-EULAR scleroderma classification criteria for SSc were screened for concomitant AISD. Patients satisfying 2010 ACR-EULAR diagnostic criteria for rheumatoid arthritis (RA) and/or 2016 ACR-EULAR classification criteria for Gougerot-Sjögren syndrome (GSS) and/or 2012 SLICC systemic lupus erythematosus (SLE) classification criteria were included in our study. Patient, disease, and treatment characteristics were retrospectively retrieved from medical records and were compared to a SSc control cohort for Bordeaux University Hospital.

**Results:** A population of 534 SSc patients was studied. Thirty-four (6.4%) patients were identified as having overlap syndrome. There was 21 (62%, prevalence 3.9%) patients with RA, 14 (41%, prevalence 2.6%) with GSS and 4 (12%, prevalence 0.7%) with SLE (5 patients had 2 AISD).

There were 24 (71%) patients with limited cutaneous SSc. Median Rodnan was 6 (extreme 0–42), 13 (38%) patients had interstitial pneumonia and 9 (26%) presented lung fibrosis. Three patients had pulmonary arterial hypertension (PAH) confirmed with catheterism. Seventeen patients (50%) had anti-centromere Ab, 11 (32%) had anti-Scl70 Ab whereas none had anti-RNA-polymerase III Ab (investigated in 24 patients).

Concerning RA patients, 17 (81%) were ACPA-positive and 17 (81%) had erosive disease. Only 6 (29%) were in remission according to Boolean criteria and 13 (62%) had a DAS28-CRP $\leq$ 3.2 suggesting difficult-to-treat RA. Patients with GSS

all presented sicca syndrome, 8 (57%) had a Chisholm grade  $\geq$ 3 on accessory salivary gland biopsy and 12 (86%) had positive anti-SSA Ab. In patients with SLE, 3 (75%) had positive anti-DNA Ab and one had a grade IV kidney disease. Three (75%) patients with SLE had a SLICC organ-damage score  $\geq$ 5 suggesting severe SLE.

Compared with our control cohort, patients with overlap syndrome had higher frequency of corticosteroid, immunosuppressive and biologic therapy use (85.3% vs 45%; 70.6% vs 31.3%; 52.9 vs 3.8%;  $p<0.0001$  for all comparisons).

**Conclusions:** Association of SSc and another auto-immune systemic disease is present in more than 6% of patients. These patients might have a more severe disease than usual SSc patients requiring prompt diagnosis and adequate treatment.

**Disclosure of Interest:** None declared

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#### SAT0500 MYOCARDIAL INVOLVEMENT AT MAGNETIC RESONANCE IN PATIENTS WITH SYSTEMIC SCLEROSIS AND MINOR ARRHYTHMIAS: ASSOCIATION WITH CLINICAL FEATURES AND IMPACT OF TREATMENT

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**Background:** Systemic sclerosis (SSc) is an autoimmune fibrotic disease characterised by variable clinical manifestations based on the predominant organ involvement. With the exceptions of acute fulminant myocarditis with pericardial effusion and heart failure, myocardial involvement in SSc is clinically silent until arrhythmias appear, while representing the major cause of sudden death or atrio-ventricular (AV) blocks in SSc. There are no reliable screening algorithm to discriminate myocardial involvement nor established treatments.

**Objectives:** To identify early/clinically silent myocardial involvement in SSc and define a possible treatment.

**Methods:** We used Holter electrocardiography (ECG) to investigate our cohort of patients with SSc ( $n=221$ , all fulfilling the ACR classification criteria) for ventricular ectopic beats (VEB)/AV blocks/unexplained tachycardia as sensitive signs of myocardial involvement. In 24 patients (women 23%–95.8%, anti-centromere-ACA 16%–66.6%, anti-topoisomerase-aScl70 3%–12.5%, anti-RNA polymerase III 3%–12.5%, anti-Ku 2%–8.3%, limited skin disease-ISSc 12%–50%, diffuse skin disease 5%–20.8%, *sine scleroderma* 7%–29.2%, median age 66.5 years, IQR 57.8–72.5), never treated with anti-fibrotic agents, we performed heart magnetic resonance (hMR) searching for myocardial oedema (on T2 STIR sequences, using the signal ratio between myocardium and skeletal muscle with a cut-off value of  $\geq 1.9$  for oedema) or fibrosis (presence of any late gadolinium enhancement (LGE) with intramyocardial or subepicardial pattern). Patients with myocardial oedema at hMR were treated with mycophenolate mofetil (MMF) 2 g/day or with azathioprine (AZA) 100 mg/day and underwent a control hMR after six months.

**Results:** In 10/24 (42%) of the SSc cases with Holter ECG alterations (8 VEB, 1 tachycardia, 1 type II AV block) we observed SSc myocardial involvement at hMR. In more detail, 6 patients had myocardial oedema at T2 STIR sequences (including cases as follows: 1 aScl70-positive with ISSc and lung fibrosis, 2 ACA-positive with ISSc, 3 ACA-positive *sine scleroderma*), and 4 only fibrosis (1 Scl70-positive with ISSc and lung fibrosis, 1 ACA-positive with ISSc, 1 ACA-positive *sine scleroderma*, 1 anti-Ku-positive *sine scleroderma*). At 6 months of medical treatment, myocardial oedema disappeared in 3 patients treated with AZA and in 1 treated with MMF, the additional 2 patients are still receiving MMF treatment at the time of analysis.

**Conclusions:** We observed that 42% of patients with SSc and minor arrhythmias on 24 hour Holter ECG have clinically silent myocardial involvement at hMR; those with potential reversible disease (oedema rather than fibrosis) favourably respond to immunosuppressants. Detectable serum ACA and the absence of skin involvement are over-represented in this subgroup of patients.

**Disclosure of Interest:** None declared

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#### SAT0501 EARLY VERSUS LATE-ONSET SYSTEMIC SCLEROSIS: ARE THERE CLINICAL AND IMMUNOLOGICAL DIFFERENCES?

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**Background:** The clinical course of Systemic Sclerosis (SSc) depends on subtype, organ involvement and age. Peak age at onset of SSc is between 30 and 50



years, although SSc may also start in both young and elderly patients. Few data have been reported on patients suffering from late-onset SSc.

**Objectives:** To characterise clinical and immunological features of early and late-onset SSc in a tertiary referral hospital.

**Methods:** We analysed data from 178 patients followed at our SSc clinic. All the patients fulfilled the ACR/EULAR 2013 classification criteria for SSc or the LeRoy's criteria for the classification of early SSc.

Based on the mean of age of onset of the whole series (50±15 years), ages extremes were defined as younger than 35 versus older than 65 years of age at onset. Disease characteristics as well as clinical and immunological features were evaluated.

**Results:** The early and the late-onset groups included 35 and 31 patients, respectively. Patients' current mean age was 42.8±14.1 vs. 75.8±6.2 with a mean disease duration of 14.5±14.7 vs. 4.3±4.6 years. The most common first manifestation of disease was Raynaud phenomena followed by arthritis/inflammatory arthralgia, in both groups. However, the time between clinical onset and SSc diagnosis was higher in the late-onset group (p=0.034). A higher number of diffuse and pre-SS was observed in the early group but this difference didn't prove statistically significant. There was a higher prevalence of centromere antibodies in the late-onset group (p=0.001). Clinical manifestations and target-organ damage didn't differ between groups, except for a higher prevalence of heart conduction abnormalities in the late-onset group (p=0.02). In multivariate analyses, age alone (OR=1.04; 95% CI 1.0, 1.1), but not disease duration (OR=0.99; 95% CI 0.9–1.0), was an independent predictor for the presence of heart conduction abnormalities.

**Abstract SAT0501 – Table 1.** Demographic, clinical and immunological features of Early and Late-Onset SSc Patients. Abbreviations: yr = years; SSc = Systemic Sclerosis. \* confirmed by esophageal manometry. \*\* Based on pulmonary function tests with diffusing capacity of lung for carbon monoxide. \*\*\* Diagnosed with echocardiography and confirmed by right heart catheterization wherever available.

	Early-Onset Group (≥ 35 yr), n=35	Late-Onset Group (≥ 65 yr), n=31	P
Sex (male:female)	6:29	5:26	0.912
Age at diagnosis (yr)	28.3 ± 5.4	71.4 ± 4.7	<0.001
Time until diagnosis (yr)	4.3	8.5	0.034
First manifestation (%)			
- Raynaud	82.9	82.1	0.061
- Arthritis/Arthralgia	14.3	20.7	0.499
Type of SSc (%)			
- Pre-SSc	37.1	25.8	0.324
- Limited	34.3	41.9	0.523
- Diffuse	22.9	12.9	0.295
Capillaroscopy pattern (%)			
- SSc specific	51.7	52.9	0.936
- Unspecific	31.0	41.2	0.486
- Normal	17.2	5.9	0.270
Raynaud phenomena (%)	100	92.9	0.113
Digital ulcers (%)	48.5	30.8	0.169
Arthritis/arthralgia (%)	63.6	44.4	0.137
Esophageal involvement (%) <sup>*</sup>	31.2	33.3	0.865
Interstitial lung disease (%) <sup>**</sup>	28.1	26.9	0.919
Pulmonary arterial hypertension (%) <sup>***</sup>	12.5	29.6	0.103
Heart conduction alteration (%)	18.8	48.1	0.016
Anticentromere antibodies (%)	45.7	87.1	<0.001
Anti-Scl 70 antibodies (%)	17.1	3.2	0.067
Anti-nuclear antibodies (%)	94.3	100	0.401

**Conclusions:** In line with findings from other studies, late-onset SSc shows a distinct clinical and immunological presentation. The present study confirms that late-onset is associated with longer diagnostic delay, positive centromere and heart conduction abnormalities. These observations may be due to age and potential age-associated confounders, rather than the disease itself. Knowledge of these different characteristics can help to improve the management of the disease.

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SAT0502

#### COMPARISON OF THE CREATININE-BASED AND THE CYSTATIN C-BASED ESTIMATED GLOMERULAR FUNCTION (EGFR) IN PATIENTS WITH SYSTEMIC SCLEROSIS PATIENTS

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**Background:** Kidney involvement is common in systemic sclerosis (SSc) and proteinuria or renal crisis are associated risk factors for increased mortality in SSc.

For the measurement of the kidney function (glomerular filtration rate, GFR) the creatinine-based estimation formula of the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) and the Modification of Diet in Renal Diseases (MDRD)-formula are commonly used.

Cystatin C has a higher diagnostic sensitivity to show a reduction of GFR. As it is not being influenced by muscle mass or diet it has advantages over the creatinine-based measurements.

**Objectives:** Comparison of the creatinine-based and cystatin C-based eGFR in systemic sclerosis patients.

**Methods:** Single-centre, retrospective analysis of SSc patients between 2015–2017 which were parallel tested for serum creatinine and cystatin C.

108 patients (78 females, 30 males), 21 patients with diffuse systemic sclerosis (dcSSc), 76 patients with limited systemic sclerosis (lcSSc) and 11 patients with overlap syndrome. Medium age 58,8 (±16,1 years), age span 17–83 years.

For the calculation of the estimated glomerular filtration rate (eGFR) the following formulas were used: MDRD-Study Equation, CKD-EPI Creatinine Equation 2009. CKD-EPI Cystatin C Equation 2012

**Results:** The mean eGFR according to the CKD-EPI Creatinine Equation was 84,4 ml/min (±23,5), according to the MDRD formula it was 80,24 ml/min (±22,8) (p<0,001) and 65,3 ml/min (±21,7) (p<0,001) when the CKD-EPI Cystatin C Equation was used. According to the KDIGO stages of chronic renal impairment a stage G2 (eGFR <90 ml/min) was present in 39,8% of the patients (43/108) using the CKD-EPI Creatinine Equation, in 47,2% (51/108) using MDRD and in 48,1% (52/108) using the CKD-EPI Cystatin C Equation.

A relevant chronic kidney impairment stage G3 (eGFR <60 ml/min) or higher was present in 14,8% of the patients (16/108) calculated by CKD-EPI Creatinine Equation, in 17,6% (19/108) of the patients according to MDRD Equation and in 38,8% (42/108) according to CKD-EPI Cystatin C Equation.

Patients with a higher difference (>18 ml/min) between creatinine-based and cystatin C-based eGFR did not differ in age, body mass index (BMI) or disease subset from patients with a lower difference but a higher difference occurred significantly more often in men (p=0,012).

**Conclusions:** Many patients with SSc showed a significant difference using cystatin C for the calculation of GFR compared to the creatinine-based formulas. As reduced muscle mass is common in SSc this could be due to sarcopenia in the context of the underlying disease. Early detection of impaired kidney function might be useful to monitor disease progress and is important for the management of immunosuppressive drugs like methotrexate and cyclophosphamide which are commonly used in the disease but need to be adjusted to the renal function.

A prospective study with measurement of GFR and comparison of different formulas in this patient population seems necessary.

**Disclosure of Interest:** None declared

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SAT0503

#### ASSESSMENT OF PROSTANOIDS (ILOPROST, ALPROSTADIL) EFFICACY IN TREATMENT OF ULCERS IN PATIENTS WITH SYSTEMIC SCLEROSIS

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**Background:** The prostanoids are currently regarded as the most effective agents in treatment of ischaemic lesions in patients with rheumatic diseases. However, the efficacy of Alprostadil is underexplored, especially in comparison with Iloprost.

**Objectives:** To evaluate the efficacy of Alprostadil (Vazaprostan®) and Iloprost (Ilomedin®) in treatment of digital ulcers in SSc pts using modern assessment tools (questionnaires and designated forms) of digital ulcers.

**Methods:** This 1 year study included 42 patients with systemic scleroderma (SSc) aged >18 y, having digital ulcers. Standard evaluation procedures and questionnaire to assess therapy, as well as scales and questionnaires for assessment of digital ulcers were used at baseline and after 12 months. The therapeutic regimens were as follows: Alprostadil at 20 mg/kg i/v drip rate infusion during 10 days, 1 course in 6 mo (totally 2 courses). Iloprost at 20 mg/kg i/v via infusion pump during 5 days each 3 months (totally 2 courses).

The following questionnaires/forms to evaluate the therapy of digital ulcers were used: 1/VAS for pain assessment, 2/SSc-HAQ, 3/Cochin hand function scale, 4/ the total hand pain score, 5/global patient's assessment of ulcers, 6/global

physician's assessment of ulcers, 7/patient's evaluation of changes in ulcers, 8/ physician's evaluation of changes in ulcers 9/number of digital ulcers.

The patients were evaluated after the drug infusion and 1 year later. Clinical and demographic characteristics of patients treated with vasoactive drugs are presented in table 1.

**Results: Table 1.** Clinical and demographic characteristics of patients with digital ulcers

	llovedin <sup>®</sup>	Vazaprostan <sup>®</sup>
N	22	20
Females (%)	100	90
Age	46.7 (±9.9)	41.9 (±12.9)
Diffuse SSc (%)	36.4	14.3
SSc duration (yy)	12.9	10.8
N of ulcers (baseline)	3.3 (±2.2)	1.7 (±1.03)

\*Mean ±SD

**Results:** The results obtained show improvement of ischaemic lesions in both groups.

The comparison of results speaks in favour of Vasoprostan vs llovedin in terms of significant pain reduction, table 2.

**Abstract SAT0503 – Table 2.** Comparative characteristics of scores and values from different assessment tools in groups treated with Vasoprostan and llovedin (post-treatment).

	llovedin <sup>®</sup>	Vazaprostan <sup>®</sup>
HAQ-SSc	1.49	1.18
HAQ	1.22	1.18
Cochin score	16.38	22
VAS	46.61*	27.12*
Physicians Global assessment	3.8	3.5
patients Global assessment	4.61	3.75
Ulcers N	3.07	1.16

\*p<0.05

**Conclusions:** It should be noted that certain degree of positive dynamics in healing of ulcers was established by practically all assessment tools. VAS looks like the most sensitive tool in evaluation of pain. Of importance is the fact, that despite marked ischaemic lesions and digital ulcers, the Cochin score reflecting hand functional capacity did not exceed average values at baseline and did not change significantly post-treatment.

**Disclosure of Interest:** None declared

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#### SAT0504 THE ASSOCIATION OF MYOSITIS SPECIFIC ANTIBODIES IN PATIENTS WITH INFLAMMATORY MYOSITIS: PRELIMINARY DATA IN INDIAN PATIENTS

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**Background:** Studies in Autoimmune Inflammatory Myositis (AIM) have shown that certain antibodies have a role in the diagnosis and prognosis of patients with myositis. This ongoing study presents the preliminary data of 48 patients of Indian AIM.

**Abstract SAT0504 – Table 1.** Myositis Antibody distribution according to clinical features.

	Proximal muscle weakness (%) (n=46)	Pharyngeal muscle weakness (%) (n=17)	Rash (%) (n=28)	Mechanic hands (%) (n=5)	Raynaud's (%) (n=11)	Digital Ulcer (%) (n=2)	Arthritis (%) (n=13)	ILD (%) (n=11)	Total (n=48)
<b>Myositis Specific Antibodies</b>									
MI-2	6 (13)	2 (11.7)	6 (21.4)	0	1 (9)	0	1 (7.6)	0	6 (12.5)
JO-1	4 (8.6)	1 (5.8)	3 (10.7)	3 (60)	2 (18.1)	0	3 (23)	4 (36.3)	5 (10.4)
NON JO-1 ARS (PL-7)	1 (2.1)	0	2 (7.1)	0	2 (18.1)	0	0	1 (9)	2 (4.1)
SRP	2 (4.3)	0	0	0	0	0	0	1 (9)	2 (4.1)
MDA-5	0	0	1 (3.5)	1 (20)	1 (9)	1 (50)	1 (7.6)	0	1 (2)
NXP2	1 (2.1)	1 (5.8)	1 (3.5)	0	0	0	0	0	1 (2)
TIF1 $\gamma$	1 (2.1)	0	0	0	0	0	0	1 (9)	1 (2)
SAE1	0	0	0	0	0	0	0	0	0
SAE2	0	0	0	0	0	0	0	0	0
<b>Myositis Associated Antibodies</b>									
RO52	14 (30.4)	4 (23.5)	10 (35.7)	4 (80)	6 (54.5)	1 (50)	3 (23)	5 (45.4)	16 (33.3)
PM SCL	1 (2.1)	0	0	0	0	0	0	1 (9)	1 (2)
RNP	2 (4.3)	1 (5.8)	1 (3.5)	0	2 (18.1)	1 (50)	2 (15.3)	2 (18.1)	2 (4.1)
Ku	0	0	0	0	0	0	0	0	0

**Objectives:** To study the prevalence of Myositis specific and Myositis Associated antibodies (MSA and MAA respectively) in Indian patients with AIM and to correlate these antibodies with clinical features.

**Methods:** All consecutive patients with Inflammatory myositis (satisfying the Bohan and Peter criteria, 1975 attending the Rheumatology and Clinical Immunology department of Medanta hospital from November 2016 to October 2017 were included prospectively and divided into groups as Dermatomyositis (DM), Polymyositis (PM), CTD associated myositis (CTD-M), Cancer associated myositis (CAM) and Juvenile Myositis (JM). Their clinical data and sera were collected after obtaining informed consent. Sera was analysed for IgG antibodies against Jo-1, PL-7, PL-12, E.J, SRP, Mi-2, MDA-5, TIF1 $\gamma$ , SAE1, SAE2, NXP2 and SSA/RO52kD using the microELISA technique (BlueDriver Dot Myositis<sup>12</sup> SAE IgG kit). Their ENA was also recorded (Blue DriverQuantrix-ANA25 Screen IgG kit d-tek). Results were read by the BlueScan scanner and value  $\geq 10$  were considered positive. The study was approved by the Ethics committee of Medanta hospital.

**Results:** There were 48 patients in the cohort (M:F=12:36) with the mean age of 41.3 years and a median disease duration of 30 months. Nineteen of them were DM, 19 were PM, 5 were CTD-M, 2 were CAM and 3 were JM. 58.3% were ANA positive and MSA were positive in 37.5% of the cohort, MSA being mutually exclusive. Antibodies against Mi-2 were present in 6 patients (12.5%), Jo-1 antibodies in 5 (10.4%), 2 (4.1%) patients each had PL-7 and SRP antibodies. One patient (2%) each had MDA-5, NXP2 and Tif1 $\gamma$  antibodies. MAAs were seen in 39.5% of the cohort with antibodies against Ro, RNP and PM- Scl seen in 16 (33.3%), 2 (4.1%) and 1 (2%) respectively. Mi-2 antibodies were seen only in DM and JM group. The lone patient who had MDA-5 antibody had amyopathic DM. Malignancy screening was negative in NXP2 and TIF1 $\gamma$  antibody positive patients.

**Conclusions:** MSA were present in almost 40% of the cohort. Mi-2 antibodies were associated with rash and none had ILD whereas Jo-1 antibodies were associated with mechanic hands, arthritis and ILD. With further recruitment of patients in this ongoing study, we hope to get more robust data in future.

**Disclosure of Interest:** None declared

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#### SAT0505 COMPARISON OF LONG-TERM CYCLOPHOSPHAMIDE (CY) AND MYCOPHENOLATE MOFETIL (MMF) EFFICACY AND SAFETY IN PATIENTS WITH SYSTEMIC SCLEROSIS (SSC) AND INTERSTITIAL LUNG DISEASE (ILD)

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**Background:** CY is considered to be the drug of choice for ILD therapy in patients with SSc. However, based on published evidence, only temporary and modest improvement of pulmonary fibrosis is usually achieved, therefore search for new more effective and safe agents is ongoing, with specific attention given to MMF.

**Objectives:** To compare CY and MMF effects on SSc clinical manifestations and activity, and safety of both agents in an open prospective non-randomised study.

**Methods:** The study included patients with a documented SSc diagnosis and ILD signs based on HRCT data. All patients were treated with immunosuppressants in combination with low and medium doses of glucocorticoids. 36 pts (mean age 47  $\pm$  12 years, m/f 1/1,1, SSc duration 5.0 $\pm$ 4.8 years, diffuse/limited – 1/1,6) were administered parenteral CY during 12 $\pm$ 6 months, with a cumulative dose of 10.6  $\pm$  5 g. 45 pts (mean age 49 $\pm$ 13 years, m/f – 1/10, SSc duration 7.6 $\pm$ 6.3 years, diffuse/limited – 1/1,3) were administered MMF at 2 g/day during 13 $\pm$ 2 months. The

following parameters were monitored during the study: FVC%, DLC%, modified skin score (), activity index (EScSG), gastrointestinal tract symptoms, left ventricle ejection fraction, presence of diastolic ventricle dysfunction, PASP (Echo-CG), heart rhythm and conduction disorders (ECG), count of digital ulcers and necroses.

**Results:** MMF therapy led to a significant reduction of the mRSS (7.5±6.9 and 4.8±3.9, p=0.0006), EScSG (1.9±1.5 and 1.22±0.9, p=0.005), number of patients with heart conduction disorders (13/29% and 5/11%, p=0.03).

The FVC improvement by ≥10% was documented in 6 (13%) pts, and DLCO – in 3 (7%); while worsening was observed in 4 (9%), and 2 (4%) cases, respectively. Mean FVC (90.3±20.8 and 92.2±21, p=0.09), and DLCO (52.2±17.4 and 51.9 ±17, p=0.86) values did not change significantly.

CY therapy resulted in significant FVC increase (80.5±20.1 and 85.9±20.5; p=0.034), reduction of EScSG (2.8±2 and 1.4±1.2, p=0.0002) and mRSS (11,2 ±9,8 and 7.9±6,8, p=0.009). ≥10% FVC increase was observed in 11 (31%) pts, which was significantly more than in MMF group (p=0.043). FVC loss was noticed in 2 (5.6%) cases. The median FVC increase was 5.4% (25th%=-0.6, 75th% =12.3). ≥10% DLCO improvement and worsening was observed in 2 (6.7%) pts. The mean DLCO values (53,5±16,2 and 54.4±15,5) did not change significantly.

The other parameters monitored did not show significant deviations during the observation period.

Drug tolerability was better in MMF group: the rate of adverse drug reactions was significantly lower in MMF group (12/27%), compared to CY group (19/53%), p=0.03.

**Conclusions:** Both drugs effectively reduced mRSS and EScSG in SSc patients. However, CY more often led to a clinically significant increase in FVC, in contrast to MMF, mostly contributing to stabilisation of FVC. The obtained results justify a differentiated approach to SSc pharmacotherapy depending on disease severity. A CY induction therapy should be considered as appropriate practice in patients with more severe pulmonary disease. A MMF induction therapy should be considered in SSc patients with cardiomyopathy and mild pulmonary disease, with poor CY tolerability. In other cases, MMF should be used for maintenance therapy after induction with CY.

**Disclosure of Interest:** None declared

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#### SAT0506 SSC IN OLDER AGE: FREQUENT AND WITH A DIFFERENT PHENOTYPE. DATA OF THE GERMAN NETWORK FOR SYSTEMIC SCLEROSIS

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**Background:** Systemic sclerosis (SSc) is a very heterogeneous multisystem connective tissue disease. The majority of affected patients develop initial clinical symptoms between the age of 30 to 50 years. It is not known whether an ageing population affects the clinical phenotype of SSc.

**Objectives:** To investigate the relationship of the age at disease onset and clinical characteristics in SSc patients using the registry of the German Network for Systemic Scleroderma.

**Methods:** Clinical data of the patient registry, currently including 4021 patients, were evaluated. Three age ranges at disease onset (<40 years, 40–60 years, and >60 years) were correlated with clinical characteristics.

**Results:** Among all SSc patients, 27% of patients developed first non-Raynaud symptoms at the age <40 years, while 44% developed SSc between 40–60 years, and 29% were older than 60 years of age. In particular, SSc patients with disease onset >60 years developed significantly (p<0.001) more often the lcSSc subtype (71.1%), anti-centromere antibodies (45.8%), had a significantly lower modified Rodnan Skin Score (mRSS) (7.8±8.1), more often pulmonary hypertension (PH) (17.4%), a significantly lower mean DLCO level (69.7%±21.5) and less often digital ulcerations (20.2%). However, a significant difference for lung fibrosis, heart or kidney involvement could not be observed. The more progressive subsets (dcSSc

and SSc overlap syndromes) are found significantly more often at younger ages (p<0.001).

**Conclusions:** In this registry, nearly one third of patients developed SSc at an age above 60 years. These are mostly of the limited cutaneous subtype with frequent PH. These findings have an important influence on recommendations on diagnosis and therapy of SSc.

**Disclosure of Interest:** None declared

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#### SAT0507 IMPLANTABLE LOOP RECORDER CAN SCREEN FOR INCIDENTAL SIGNIFICANT ARRHYTHMIAS IN SCLERODERMA, WITH CARDIAC MRI ECV AND TROPONIN BIOMARKER, USEFUL FOR RISK STRATIFICATION

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**Background:** Cardiac involvement and in particular conduction abnormalities represent a significant cause of morbidity and mortality in patients with systemic sclerosis (SSc). No studies assessed the value of implantable loop recorder (ILR) for early detection of arrhythmias in asymptomatic patients with SSc; or whether cardiac magnetic resonance (CMR) features associate with arrhythmias.

**Objectives:** To assess the prevalence of conduction abnormalities over a 3 year period using an ILR (REVEAL) and evaluate relationship with disease phenotype, cardiac biomarkers and CMR in SSc patients.

**Methods:** 20 patients (pts) with ACR/EULAR criteria for SSc, with no history of cardiovascular (CV) disease and ≤1 CV risk factor had 3T CMR with late gadolinium enhancement (LGE) and T1 mapping for ECV quantification. An ILR was then inserted, for 3 years follow-up. ILR data were downloaded every 3 months. Serum cardiac biomarkers were also measured at the initial visit.

**Results:** 19 pts had available ILR data; 12 (63%) females, median (SD) age 53 (12, 6 (32%) diffuse SSc(dcSSc), 6 (32%) ACA+, 4 (21%) Scl70+, 8 (42%) history of interstitial lung disease (ILD) and 7 (36%) history of digital ulcers (DU). 14/19 had any ILR abnormalities, 8/14 significant arrhythmias: 1 complete heart block; 2 non-sustained ventricular tachycardia (NSVT), and 5 atrial arrhythmias (1 atrial flutter, 1 AF, 1 SVT, 1 AF and SVT and 1 AF followed by atrial flutter and SVT). Of these 8 pts, 4 had dcSSc, 2 Scl70+, 4 ACA+, 3 with ILD and 3 DU history. All 3 patients with severe arrhythmias (NSVT/CHB) were dcSSc, 2 Scl70+, 2 males. Management comprised 1 permanent pacemaker implantation, 3 antiarrhythmic treatment, 1 anticoagulation. 15 pts had CMR. The 8 pts with significant arrhythmia appeared to have higher ECV, LV mass, and LVEF% (table 1). LGE was observed in 1 (NSVT), of a total of 5/15 with LGE. HsTnI was considerably higher in those with significant arrhythmias (mean diff. (95% CI) 117 (-10, 245)). NTproBNP [(mean diff. (95% CI) 92 (-30, 214)] also appeared greater in those with significant arrhythmias. There was no difference in CK levels between the two groups.

CMR baseline	ILR significant arrhythmias, all years n=6 Mean(SD)	ILR no significant arrhythmias n=9 Mean(SD)	Mean difference [95% CI]
ECV%	32 <sup>(2)</sup> n=5	29 <sup>(4)</sup> n=9	2 [-2,6]
LVEDV/BSA (ml/m <sup>2</sup> )	84 <sup>(16)</sup>	83 <sup>(20)</sup>	1 [-21, 22]
LVEF%	62 <sup>(4)</sup>	59 <sup>(5)</sup>	2 [-3,8]
LV mass/BSA(g/m <sup>2</sup> )	46 <sup>(7)</sup>	44 <sup>(14)</sup>	2 [-10, 15]
LVSV/BSA(ml/m <sup>2</sup> )	51 <sup>(8)</sup>	49 <sup>(11)</sup>	2 [-9, 13]
LVESV/BSA(ml/m <sup>2</sup> )	33 <sup>(9)</sup>	34 <sup>(10)</sup>	-2[-13, 9]
Distensibility (10 <sup>-3</sup> mmHg <sup>-1</sup> )	5 (4)	4 (2)	0.4 [-3, 4]
Torsion °	12 <sup>(6)</sup> n=5	14 <sup>(5)</sup> n=8	-2[-8, 5]
LGE	N 1/5	N 4/9	

**Conclusions:** This pilot study demonstrates the ability of ILR to detect life-threatening arrhythmia in asymptomatic SSc pt. The data suggest CMR ECV (but not LGE) and cardiac biomarkers, in particular hsTnI (indicating subclinical myocardial injury) may be able to identify at risk pts that would benefit from ILR screening. Future studies can inform a risk model, and provide insight into the pathogenesis of SSc associated arrhythmias.

**Disclosure of Interest:** None declared

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SAT0508

### ACE-INHIBITORS IN ARTERIAL HYPERTENSION IN SSC PATIENTS DISPLAY A RISK FACTOR FOR SCLERODERMA RENAL CRISIS – A EUSTAR ANALYSIS

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**Background:** Scleroderma renal crisis (SRC) represents a rare but life-threatening manifestation in systemic sclerosis (SSc). Survival remains poor despite therapeutic use of ACE inhibitors (ACEi). Factors influencing the risk of SRC are not well characterised. In particular, ACEi are discussed as promoting but also as protecting SRC.

**Objectives:** To investigate the effect of ACEi on SRC incidence in prospectively collected data of a cohort of SSc patients.

**Methods:** EUSTAR database analysis with focus on arterial hypertension, antihypertensive medication and glucocorticoids. Subgroup analysis of a dataset with defined documentation of medication from January 2009 until November 2017.

**Results:** Out of 14'524 patients in the database we identified 7'648 patients with at least one follow-up after 2009. 102 patients developed SRC in 27'450 person-years (py), representing an incidence of 3.72 (3.06–4.51) per 1'000 py. In a multi-variable time-to-event analysis adjusted for age, sex, disease severity and onset, arterial hypertension, tendon friction rubs, SCL70 and ACA positivity, 78 of 6083 patients developed SRC. Herein, use of ACEi displayed an increased risk for the development of SRC with a hazard ratio (HR) of 2.07 (95% confidence interval (CI):1.28–3.36). Calcium channel blockers (CCB), angiotensin receptor blockers, endothelin receptor antagonists and glucocorticoids did not influence SRC incidence. Medication strategies were not altered after renal crisis. Cumulative mortality 5 years after renal crisis was 18.6% (95% CI: 13.0%–26.3%).

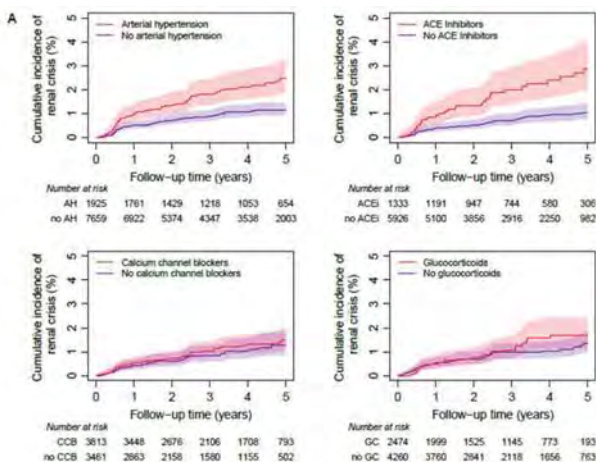


Figure (A) Cumulative incidence plots for scleroderma renal crisis (SRC) depending on whether patients have arterial hypertension (AH), or are treated with ACE inhibitors (ACE), Calcium channel blockers (CCB) or Glucocorticoids (GC).

**Conclusions:** This EUSTAR analysis supports the notion that ACEi should be avoided in arterial hypertension in SSc patients. Alternative antihypertensive drugs as CCB might be preferred.

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SAT0509

### HOW MONEY SHOULD BE SPENT: PATIENTS PERSPECTIVES ON SCLERODERMA RESEARCH FUNDING

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**Background:** Scleroderma (systemic sclerosis, SSc) is an autoimmune disease that can affect blood vessels, skin and various organs, causing Raynaud's phenomenon, thickening of skin, gastro-oesophageal reflux and lung fibrosis. Despite remarkable improvements and innovations in management for SSc, leaders in the field continue to believe there is scope for more.<sup>1</sup> Patients' opinions on future research into the condition and its management, can provide valuable insight on how to shape its prospects and improve outcomes, and how research funding should be best directed.<sup>2</sup>

**Objectives:** To determine if doctors and patients with scleroderma agree on where future scleroderma research should be focussed.

**Methods:** 25 patients with scleroderma and 10 doctors were given questionnaires that asked them to rank 12 issues in order of importance, with a view to directing future Scleroderma research and funding. The highest ranked issue was appointed a score of 12, and the lowest ranked appointed a score of 1. The mean scores were calculated, and compared for concordance using ANOVA testing.

All patients had been admitted for elective Iloprost infusions at Royal Free Hospital and varied in age and gender. The clinicians were of varied levels from FY1-consultant, and all worked in the Rheumatology team at Royal Free.

**Results:** Patients ranked the issue of "managing Raynaud's symptoms" as the most important, which is significantly different to how clinicians viewed it – patients gave it a ranking 9.8 compared to only 4.9 from clinicians ( $p < 0.005$ ). However, doctors placed more value on "avoiding organ involvement" (10.4 from clinicians and 7.67 from patients ( $p < 0.005$ )).

Patients and clinicians, however, agreed about the least important issues, scoring "medication side effects" 3.6 and 3.1 respectively, "social and psychological support" 3.7 and 4.0, and "family planning and genetics" 3.8 and 3.6. They also agreed that research should be targeted at finding "new treatments that stop disease progression" which scored highly in both groups (9.7 in patients, 10.5 in clinicians).

**Conclusions:** Patients appear to feel that Raynaud's symptoms are affecting their quality of life in a way that is not being appreciated as important by clinicians. This may be due to ineffective communication between them, perhaps due to the time constraints of appointments.

Contrastingly, doctors are more concerned about avoiding organ involvement compared to patients, perhaps as they are more aware that organ involvement has a much greater effect on prognosis. However, both patients and clinicians were equally committed to investigating mechanisms of this disease.

Overall, these findings between doctors and patients should not just be a point of focus for future funding and research. It can be used to identify where there are differences in expectations during clinical encounters, and therefore allow us as clinicians to tailor our agenda to better meet the needs of our patients, which would likely improve the patient-doctor relationship, enhancing communication in clinic appointments.

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**SAT0510 CUTANEOUS MANIFESTATIONS IN IDIOPATHIC INFLAMMATORY MYOPATHIES: FACTORS ASSOCIATED WITH CALCINOSIS**

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**Background:** Calcinosis is a cutaneous manifestation that produces disability and complications in patients with idiopathic inflammatory myopathies (IIM). Studies about associated factors are limited.

**Objectives:** To investigate cutaneous manifestations and factors associated with calcinosis in patients with IIM from the REMICAM registry.

**Methods:** A multicenter retrospective study (1980–2014) was performed. Patients were classified as primary dermatomyositis (DM), primary polymyositis (PM), cancer associated myositis (CAM), overlap myositis (OM), inclusion body myositis, immune-mediated necrotising myopathy (IMNM) and juvenile myositis (JuM). A description of the cutaneous manifestations in each subgroup of IIM was done. The associations between calcinosis and demographic data, clinical characteristics, antibodies and treatments were analysed independently for JuM and adult IIM.

**Results:** 479 patients were included, of whom 49 (10%) had calcinosis with the following distribution: 27 JuM (55%), 9 DM (18%), 9 OM (18%), 3 PM (6%) and 1 IMNM (2%). Non-characteristic cutaneous manifestations were more prevalent in DM, OM, CAM and IMNM. At multivariate analysis, disease duration (OR=2; p=0.016), immunoglobulin treatment (OR=5.68; p=0.036) and immunosuppressants (OR=8.94; p=0.01) were associated with calcinosis in JuM. In addition, dysphagia (OR=21.3; p=0.008), positivity for anti-PM-Scl (OR=34.1; p=0.01), baseline ESR (OR=1.05; p=0.04) and interstitial lung disease (OR=10.2; p=0.039) were associated with calcinosis in adult.

**Conclusions:** Our results suggest that factors associated with calcinosis might be different in adult and juvenile myositis, but in both cases, they are related to more severe disease.

**Disclosure of Interest:** None declared

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**SAT0511 PRACTICAL SUGGESTIONS ON INTRAVENOUS ILOPROST IN RAYNAUD'S PHENOMENON AND DIGITAL ULCER SECONDARY TO SYSTEMIC SCLEROSIS: SYSTEMATIC LITERATURE REVIEW AND EXPERT CONSENSUS**

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**Background:** Raynaud's phenomenon (RP) and digital ulcer (DU) are prominent features of SSc. According to the 2017 EULAR recommendations, intravenous (IV) iloprost (ILO) may be used for RP and DU after failure of oral therapies. Where available, IV ILO is indicated in RP secondary to systemic sclerosis (SSc) for 3–5 days with no other advice about the regimen (dosage, duration and frequency).

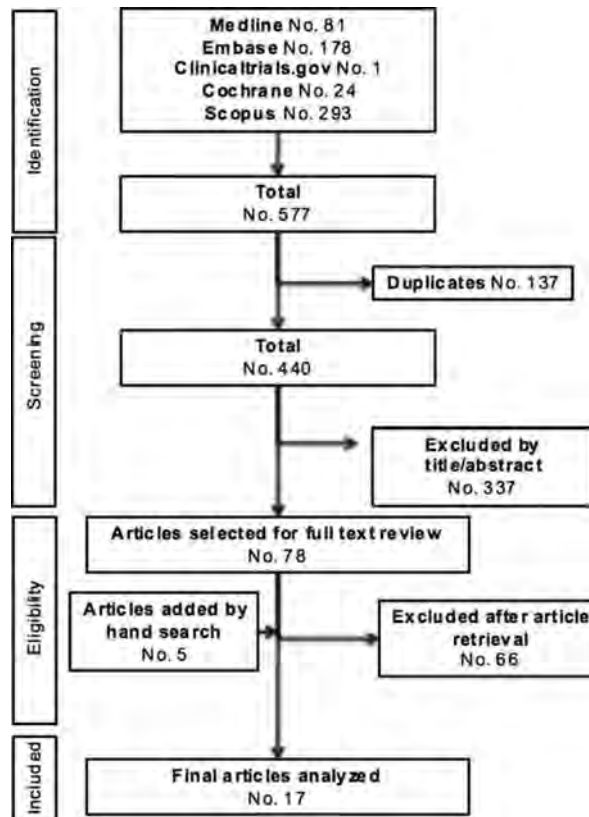
**Objectives:** To provide a systematic review focused on IV ILO use in SSc RP and DU and to perform a meta-analysis. In the case of lack of data, a Delphi consensus was performed to provide practical suggestions about ILO usage in SSc RP and DU and to propose a research agenda for future studies.

**Methods:** The systematic review of the literature on IV ILO in SSc patients complicated by DU and RP was performed according to PRISMA guidelines and the meta-analysis to the GRADE system. A three-step web-based Delphi consensus was designed if not enough data were available from the literature.

**Results:** The review flow process is outlined in figure 1. The meta-analysis could not be performed due to insufficient literature data about dosage, regimen and frequency of IV ILO. Therefore, a three-round Delphi exercise was performed to

identify and establish a consensus about IV ILO use in SSc RP and DU. Expert consensus was reached at the third step for the following items:

- Severe or refractory to oral therapy RP, IV ILO 0.5 and 2.0 ng/kg/min, 1–3 days monthly.
- DU healing, IV ILO 0.5 and 2.0 ng/kg/min up to the maximum tolerated dose the first day of therapy, 1–3 days monthly.
- DU prevention, IV ILO 0.5 and 2.0 ng/kg/min, 1 day monthly.
- Research agenda: trials for head-to-head comparison and for regimen assessment.



**Conclusions:** IV ILO is currently available in some countries with the approved indication only for RP-SSc for 3–5 days. Our data, based on expert consensus, suggest a 1–3 days monthly regimen for RP and DU healing and 1 day monthly for DU prevention. These suggestions may allow clinicians to decide how to personalise the IV ILO therapy according to patients' needs. Although these suggestions are intended for clinical setting use, it will be necessary to formally validate the present suggestions in future clinical trials.

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**Disclosure of Interest:** None declared

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**SAT0512 SAFETY AND EFFICACY OF LENABASUM IN REFRACTORY SKIN-PREDOMINANT DERMATOMYOSITIS SUBJECTS TREATED IN AN OPEN LABEL EXTENSION OF TRIAL JBT101-DM-001**

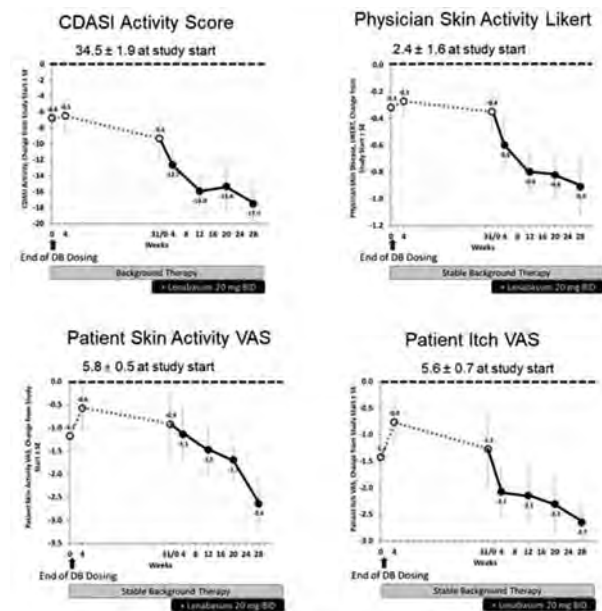
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**Background:** Lenabasum (aka anabasum, JBT-101) is a selective cannabinoid receptor type 2 agonist that activates resolution of innate immune responses. It is a synthetic, oral, non-immunosuppressive small molecule. Lenabasum showed acceptable safety and tolerability and evidence of clinical benefit in 22 subjects with refractory, skin-predominant dermatomyositis (DM) in Phase 2 trial JBT101-DM-001 (NCT02466243).

**Objectives:** This study evaluated safety and efficacy of open-label dosing of lenabasum in moderately-to-severely active skin-predominant DM in subjects who were refractory to or intolerant of hydroxychloroquine treatment.

**Methods:** Subjects who completed the double-blind placebo-controlled (DBPC) part of JBT101-DM-001 with 12 weeks of active dosing and 4 weeks of safety follow-up were eligible to receive lenabasum 20 mg BID in an open-label extension (OLE). Safety and efficacy evaluations were done at Week 4 after the start of OLE, then every 8 weeks thereafter.

**Results:** 20/22 (91%) eligible subjects enrolled in the OLE and 17/20 (85%) were on baseline immunosuppressive drugs. There was a mean interval of 31 weeks (range 4–92 weeks) from the end of active DBPC dosing and the start of the OLE, during which time subjects remained on background medications prior to adding lenabasum in the OLE. At the time of OLE data cut-off, no subjects had discontinued, all 20 subjects in the OLE completed visits through Week 12 and 11 subjects completed visits through Week 28. During the 28 weeks of OLE dosing, adverse events (AEs, n=30) occurred in 14/20 (70%) subjects. Only 1 subject had a moderate AE, all other AEs were mild. Four (20%) subjects had AEs considered related to lenabasum. The only AE that occurred in more than 1 subject was DM flare (n=2, 10%). During the OLE, there was improvement from the beginning of the OLE dosing and from the study start in Cutaneous Dermatomyositis Activity and Severity Index (CDASI) Activity score and physician Likert assessments of global disease activity, skin disease activity and extramuscular disease activity. Similarly, there were improvements in multiple patient-reported outcomes, including patient 10 cm VAS scores of global disease activity, skin disease activity, itch and pain, as well as the Skin-dex-29 symptoms domain and PROMIS-29 physical function, fatigue, pain interference, and anxiety domains. Selected efficacy outcomes are shown in figure 1 as change from study start during two periods: 1) "off treatment" from the end of active DBPC dosing to the start of OLE, dotted line; and 2) OLE dosing, solid line.



Abstract SAT0512 – Figure 1. Mean change from Baseline ± SE in Selected Efficacy Outcomes

**Conclusions:** Lenabasum continues to have a favourable safety and tolerability profile in the OLE of the Phase 2 trial JBT101-DM-001 with no severe or serious AEs or study discontinuations related to lenabasum. The CDASI activity score and multiple other physician and patient-reported outcomes improved from study start and start of the OLE, although open-label nature of dosing with lenabasum is acknowledged. These data support further testing of lenabasum for the treatment of DM.

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**SAT0513 PROGRESSIVE SKIN FIBROSIS IS ASSOCIATED WITH A DECLINE IN LUNG FUNCTION AND POORER SURVIVAL IN PATIENTS WITH DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS: A EUROPEAN SCLERODERMA TRIALS AND RESEARCH (EUSTAR) ANALYSIS**

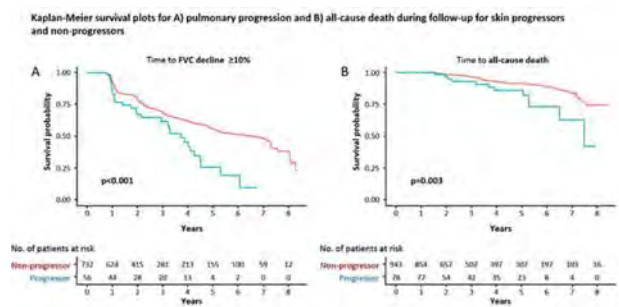
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**Background:** Short disease duration and low baseline modified Rodnan skin score (mRSS) have been identified as independent predictors of progressive skin fibrosis in patients with diffuse cutaneous systemic sclerosis (dcSSc) using the EUSTAR database.<sup>1</sup> However, whether worsening of skin fibrosis is an appropriate surrogate marker for new-onset or deterioration of visceral organ disease and overall survival in dcSSc has been questioned.

**Objectives:** To determine whether progressive skin fibrosis is associated with visceral organ progression and mortality in dcSSc patients during follow-up.

**Methods:** We performed a survival analysis of the EUSTAR database including patients with dcSSc, fulfilling the ACR 1980<sup>2</sup> criteria, with baseline mRSS ≥ 7 in 2009 or later, valid mRSS at 12±3 months after baseline and ≥ 1 available annual follow-up visit. Progressive skin fibrosis was defined as an increase in mRSS >5 units and ≥25% from baseline to 12±3 months later. Disease outcome was defined as occurrence of one of the following new events during follow-up based on expert group consensus: relative decrease in forced vital capacity (FVC) ≥10%; left ventricular ejection fraction (LVEF) <45% or relative decrease in LVEF >10% for patients with baseline LVEF <45%; pulmonary hypertension globally judged on echocardiography by the treating physician; renal crisis; all-cause death. The association between skin progression and disease outcomes over follow-up was evaluated by Kaplan–Meier analysis, log-rank test and multivariate Cox regression. Multiple imputation was used to handle missing values.

**Results:** Among 1021 eligible dcSSc patients, 78 (7.6%) had progressive skin fibrosis within 1 year (defined as progressors). The median follow-up period was 3.4 years. Survival analyses indicated that skin progressors had a significantly higher probability of FVC decline ≥10% (53.6% vs 34.4%; p<0.001) and all-cause death (15.4% vs 7.3%; p=0.003) than non-progressors (figure 1). These significant associations between skin progression and FVC decline and all-cause death were also observed in the subgroup of patients with either baseline mRSS ≤22/51 or disease duration ≤15 months. Multivariate Cox regression confirmed that skin progression was independently associated with FVC decline ≥10% (HR 1.79, 95% CI 1.20 to 2.65) and all-cause death (HR 2.58, 95% CI 1.31 to 5.09).



Abstract SAT0513 – Figure 1. Kaplan-Meier survival plots for A) pulmonary progression and B) all-cause death during follow-up for skin progressors and non-progressors

**Conclusions:** In patients with dcSSc, progressive skin fibrosis within 1 year is associated with a decline in lung function and worse survival over follow-up. This evidence-based finding is helpful for cohort enrichment in clinical trials for both skin and lung fibrosis, and for risk stratification in clinical practice.

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#### SAT0514 MRI – GUIDED THERAPY FOR SYSTEMIC SCLEROSIS ASSOCIATED MYOSITIS

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**Background:** Muscle involvement in systemic sclerosis (SSc) has a significant impact on morbidity, functional capacity, and mortality. The muscle histopathology is heterogeneous including inflammatory and fibrotic changes. Currently there are no satisfactory means to diagnose inflammatory myopathy in SSc pts with normal creatine kinase (CK) and to assess the response to therapy.

**Objectives:** Our aim was to evaluate whether muscle magnetic resonance imaging (MRI) might be a tool to diagnose inflammatory myopathy in SSc patients (pts) and to assess the effect of muscle oriented- immunomodulatory therapy.

**Methods:** We retrospectively analysed the clinical data of 290 consecutive SSc pts seen at our centre between the years 2012–2017. Our cohort is part of the EUSTAR registry (centre 042). Pts with muscle weakness as defined by the Medsger muscle severity score of  $\geq 1$  and at least one MRI study were included. Clinical data analysis included SSc subtype, disease duration, modified Rodnan skin score (mRSS), Medsger muscle severity score, CK, autoantibody profile, MRI and immunomodulatory treatment.

**Results:** 26 pts with muscle weakness answered the criteria of Medsger muscle severity score of  $\geq 1$  MRI data were available, in 17 of the pts. Muscle oedema and fasciitis were seen in MRI in 13 pts (10 diffuse subset, median: age 40, disease duration 1.25 years, mRSS 13.5). MRI was normal in 4 pts (2 diffuse SSc, median: age 50 years, disease duration 6 years, mRSS 4). CK was normal in 10 pts with pathologic MRI. Anti-topoisomerase was positive in 6 pts, RNA polymerase 3 – in 3 pts, anti-centromere – in 2 pts and 6 pts were only ANA positive. Muscle biopsy results were available in 4 pts: Biopsy was compatible with myositis in 3 pts with pathologic MRI and revealed fibrosis in 1 pt with normal MRI. 14 pts received immunomodulatory treatment: rituximab (3 pts), rituximab and intravenous immunoglobulins (IVIG) (3 pts), IVIG and methotrexate/azathioprine/mycophenolate mofetil.<sup>8</sup> A second MRI was performed in 6 pts with first pathologic MRI, after 12 months of treatment. Significant regression of muscle oedema and per fasciitis was observed in 5 pts and correlated with clinical amelioration, with improvement of muscle strength. No clinical and imaging improvement occurred in one patient, despite the treatment. No change in muscle strength was seen in the patient with normal MRI and evidence of fibrosis on muscle biopsy, although the skin score improved.

**Conclusions:** MRI might serve as a non-invasive tool for diagnosis of inflammatory myopathy in SSc pts with early disease, Medsger muscle severity score of  $\geq 1$  and normal CK and for assessment of treatment efficacy.

**Disclosure of Interest:** None declared

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#### SAT0515 CLINICAL CHARACTERISTICS OF PATIENTS WITH CANCER-ASSOCIATED MYOSITIS COMPLICATED BY INTERSTITIAL LUNG DISEASE

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**Background:** Cancer-associated myositis (CAM) is believed to be rarely complicated by interstitial lung disease (ILD), and, thus, detailed clinical characteristics of CAM in patients with polymyositis (PM)/dermatomyositis (DM)-associated ILD are not well known.

**Objectives:** To clarify the incidence, risk factors, and impact on survival of malignancy in patients with PM/DM-associated ILD, using a large cohort data.

**Methods:** We used 497 patients with PM/DM-associated ILD enrolled in a multi-centre retrospective cohort of incident cases from 44 institutions across Japan (JAMI). CAM was defined as malignancy diagnosed within 3 years before or after PM/DM diagnosis. Demographic data and clinical characteristics were recorded at the time of diagnosis, and follow-up survival and malignancy data were collected prospectively.

**Results:** Thirty-two patients with CAM (6.4%) were identified. Patients in the CAM group were older (64.3 vs 55.1 years,  $p < 0.001$ ), had shorter disease duration at onset (4.1 vs 7.0 months,  $p = 0.01$ ), and presented with arthritis less frequently (24.1 vs 48.5%,  $p = 0.01$ ), in comparison with those with non-CAM group. All patients with CAM were older than 40 years, and the proportion of CAM increased along with the age. Patients who were  $\geq 59$  years at diagnosis and lacked arthritis were at 12 times higher risk for concomitant malignancy than those without such features (figure 1). Frequencies of autoantibodies, including anti-MDA5, anti-ARS, and anti-TIF1gamma, were not different between the groups. In 19 patients (59%), malignancy was diagnosed within 3 months before or after PM/DM diagnosis. Eleven CAM patients were died, and cause of deaths included ILD in 6 and malignancy in 5. Survival analysis by Kaplan-Meier method demonstrated that CAM patients had a poorer survival than did non-CAM patients ( $p = 0.016$ ).

**Conclusions:** In patients with PM/DM-associated ILD, older age at diagnosis and lack of arthritis are predictors for concomitant malignancy, which leads to a reduced survival.

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SATURDAY, 16 JUNE 2018

#### Vasculitis

#### SAT0516 TWO DISTINCT SUBSETS OF LOW DENSITY GRANULOCYTES IN ANCA ASSOCIATED VASCULITIS

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**Background:** Low density granulocyte (LDG), a proinflammatory population of neutrophils, was first described in systemic lupus erythematosus (SLE) and has

been shown to contribute to lupus pathogenesis. It has been suggested that LDGs have a pathogenic role in ANCA associated vasculitis (AAV) based on the data of gene expression signature in AAV and the ability of excessive neutrophil extracellular traps (NETs) formation by LDGs in AAV. However, more detailed analysis of LDG in AAV patients has not been reported.

**Objectives:** In this study we investigated the characteristics of LDG in AAV patients using flow cytometry and proteomics approach and examined the correlations with disease activity.

**Methods:** We examined the presence of LDGs in peripheral blood of 10 AAV patients before treatment and followed them for 4 months with immunosuppressive therapy. Normal-density granulocytes (NDGs) were isolated by dextran sedimentation and PBMCs were isolated by Ficoll gradient. LDGs were assessed using cell surface expression of CD14 and CD15 by flow cytometry and isolated by magnetic bead procedure from PBMCs. We performed comparative proteomic analysis among LDGs and autologous NDGs and healthy controls (HC)-NDGs.

**Results:** LDG frequencies were 9.8-fold higher in AAV patients before treatment relative to HC. There were two distinct populations of LDGs showing different cell surface expressions of CD10, CD14, and CD15 in AAV patients. One population of LDGs was mainly CD10 positive and another one was CD10 negative. Although the frequency of CD10 positive-LDG decreased along with decrease of disease activity, the frequency of CD10 negative-LDG increased in 4 months (17.9-fold higher than before treatment). Comparative proteomic analysis revealed these two populations of LDGs were distinct from each other and had common differences from autologous NDGs and HC-NDGs.

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**Conclusions:** We identified two distinct subsets of LDGs in AAV. It is possible that they play different roles in the pathogenesis of AAV.

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SAT0517

#### GENDER DIFFERENCES INFLUENCES CLINICAL PRESENTATION AND VASCULAR PATTERN IN PATIENTS WITH TAKAYASU ARTERITIS: AN ITALIAN MONOCENTRIC STUDY

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**Background:** Takayasu arteritis (TA) is a large-vessel vasculitis affecting aorta and its major branches<sup>1</sup>. Vascular inflammation may cause luminal narrowing, occlusion or aneurysms<sup>2</sup>. TA affects more frequently young women, but occurrence in patients >40 years is not rare. Female:male ratio is 9:1<sup>3</sup>

**Objectives:** To compare age at disease onset, age at diagnosis and diagnostic delay between male and female Italian TA patients from our cohort. To compare symptoms presentation and vascular involvement

**Methods:** Data from 10 male and 104 female TA patients (fulfilling ACR criteria) from our tertiary centre were retrospectively collected. Age at diagnosis, age at first symptom onset, diagnostic delay, signs and symptoms subsequently attributed to TA, and arteries involved before the diagnosis were compared. Non-parametric statistical tests were used

**Results:** In male patients mean age at diagnosis was 33.5±14.64 years and mean age at onset was 25.8±13.01 years. In female patients mean age at diagnosis was 36.26±12.6 years and mean age at onset was 31±13.1 years. The differences not being statistically significant. The highest percentage of male patients disease onset was <18 years (40%), in female patients it was between 18–40 years (61.5%). Mean diagnostic delay was 92.9±80.78 months in male and 63.03

±85.63 in female patients (p=0.050). Features at disease onset are summarised in table 1. Frequency of limbs claudication was not significantly different in the two groups (50% vs 56.7%), 10% of male patients had upper limbs claudication, compared to 43.3% of female patients, p=0.047. Arterial hypertension was more frequent in male patients (70% vs 35.6%, p=0.044). Acute coronary syndrome was more frequent in male patients (30% vs 5.8%, p=0.031). Frequency of cardiovascular risk was not significantly different in the two groups (40% vs 32.7%). Coronary angiography was more frequently performed in male patients (30% vs 2.9%, p=0.009). At disease onset, compared to female patients, male patients coronary (30% vs 6.7%, p=0.042), iliac (50% vs 15.4%, p=0.018) and femoral arteries (40% vs 6.6%, p=0.008) were more frequently involved. In female patients subclavian arteries were more frequently involved (72% vs 40%, p=0.066).

Signs/symptoms	N°male patients (%)	N°female patients (%)	P-value
Constitutional symptoms	5 (50)	61 (58.7)	0.740
Arthralgias	3 (30)	28 (26.9)	1
Carotidynia	1 (10)	25 (24.0)	0.451
Syncope/vertigo	2 (20)	22 (21.2)	1
Neurological signs	1 (10)	8 (7.7)	0.576
Overall limbs claudication	5 (50)	59 (56.7)	0.746
Upper limbs claudication	1 (10)	45 (43.3)	<b>0.047*</b>
Lower limbs claudication	5 (50)	25 (24.0)	0.125
Arterial hypertension	7 (70)	37 (35.6)	<b>0.044*</b>
Discrepancy in BP	1 (10)	29 (27.9)	0.287
Reduced/absent pulses	3 (30)	46 (44.2)	0.511
Vascular bruits	4 (40)	32 (30.8)	0.723
Angina abdominis	0 (0)	16 (15.4)	0.353
Chest pain	3 (30)	9 (8.7)	0.071
Acute coronary syndrome	3 (30)	6 (5.8)	<b>0.031*</b>
Serositis	0 (0)	7 (6.7)	1

**Conclusions:** Male patients with TA have more frequent involvement of the coronary arteries and of the iliac and femoral arteries. As a consequence, they suffer more frequently acute coronary syndrome and lower limbs claudication. Besides, they have more frequently arterial hypertension

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SAT0518

#### THE ROLE OF LEFLUNOMIDE IN THE TREATMENT OF GIANT CELL ARTERITIS

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**Background:** Glucocorticoids (GC) have been the mainstay treatment in giant cell arteritis (GCA) for decades. Recently tocilizumab and abatacept have been proven to be effective alternatives to glucocorticoids. However, not all GCA patients are eligible for a biologics.

**Objectives:** We aimed to evaluate the role of leflunomide (LEF) as a steroid sparing agent in GCA.

**Methods:** This prospective observational study included newly diagnosed GCA patients followed at least 48 weeks at a single secondary/tertiary rheumatology centre.

Patients were treated with GC in line with the EULAR recommendations.<sup>1</sup> In short, patients with uncomplicated GCA initially received oral methylprednisolone (MP) 32–48 mg qd, while those with ischaemic complications or large vessel disease first received MP 250 mg on 3 consecutive days intravenously, followed by oral MP. MP tapering was started 2–4 weeks after treatment initiation slowly to 4 mg qd which was continued for at least 6 months. At week 12, LEF 10 mg qd was recommended as an add-on therapy to those GCA patients without contraindications for it. The final decision to add LEF was patient dependent. Follow-up visits with predetermined clinical and laboratory tests were performed 4, 12, 24, 48, 96 and 144 weeks after diagnosis. In patients who relapsed during the MP tapering unscheduled visits were arranged and treatment was adjusted (GC dose was

increased and LEF 10 mg or LEF dose increase to 20 mg or alternative steroid sparing agent in case of LEF ineffectiveness recommended). The number of relapses and a cumulative GC dose during follow-up were recorded.

**Results:** Between July 2014 and December 2016 we identified 76 (65.8% female, median (IQR) age 73.7 (66.1–78.8) years) new GCA cases with a follow-up of at least 48 weeks (median (IQR) 75<sup>51–104</sup> weeks). 30/76 patients (39.5%) received LEF at W12 ("LEF" group), the others continued with GC only. During the follow-up 22 patients relapsed, 4 in "LEF" group (13.3%) and 18 (39.1%) in "GC only" group. The difference was statistically significant ( $p=0.02$ ; NNT 3.9 (95%CI 2.2–17.4)). Furthermore, 17/30 GCA cases (56.7%) in "LEF" group managed to stop GC at W48 (with 1 relapse (5.9%) shortly afterwards), but none in GC only group. Patients tolerated LEF relatively well. Adverse events (AEs) were usually mild. 8/30 patients (26.7%) discontinued LEF (1 due to ineffectiveness and 7 due to one/more AEs – hair loss developed in 4/7 cases, diarrhoea in 2/7 patients, weight loss in 2/7 cases, and elevated transaminases in 1/7). The occurrence of infections requiring antibiotics and/or hospital admission was lower in LEF group compared to "GC only" group (10% vs. 26.5%).

**Conclusions:** We found in our prospective observational study in GCA a steroid sparing action and a rather good tolerability of LEF.

**Disclosure of Interest:** None declared

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SAT0519

### INTERSTITIAL LUNG DISEASE IN ANCA-ASSOCIATED VASCULITIS PATIENTS: COMPARISON WITH IDIOPATHIC PULMONARY FIBROSIS AND INTERSTITIAL PNEUMONIA WITH AUTOIMMUNE FEATURES

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**Background:** Patients with ANCA-positive vasculitis may develop interstitial lung disease (ILD), it is an uncommon but increasingly recognised manifestation. Clinical characteristics and prognosis are not well known in these patients. The largest report to date is from East Asia describing microscopic polyangiitis (MPA) as the most common association with ILD.

**Objectives:** To describe the clinical manifestations and response to therapy of patients with AAV and ILD compared with patients with idiopathic pulmonary fibrosis (IPF) and interstitial pneumonia with autoimmune features (IPAF)

**Methods:** We conducted a retrospective 10 year chart review at the Mayo Clinic Florida, including patients with confirmed diagnoses of both AAV and ILD done by expert rheumatology and pulmonology clinical evaluations. Clinical characteristics of ANCA-ILD in 24 patients were compared to 29 patients with idiopathic pulmonary fibrosis (IPF) and 22 patients with interstitial pneumonia with autoimmune features (IPAF), which were confirmed by applying the IPF diagnostic criteria based on the most recent ATS guidelines and IPAF criteria defined by Fischer and colleagues, respectively.

**Results:** We identified 24 ANCA-ILD patients. 14 patients had MPA, 12 patients had granulomatosis with polyangiitis (GPA), and 2 patients had eosinophilic granulomatosis with polyangiitis (EGPA). 54% were female and mean age was 70. In half of the ANCA-ILD patients, vasculitis presented prior to ILD, mainly MPA, 36% of patients presented with ILD first, most of them with GPA. The rest presented with ILD and vasculitis at the same time. Usual interstitial pneumonia (UIP) was the most common radiographic pattern. Honeycombing was more common in MPA compared to GPA patients. Ground glass opacity was present in 5 (63%) of GPA and in 5 (36%) of MPA patients. Most MPA patients had positive anti-MPO antibody and p-ANCA. Only one GPA patient had positive anti-MPO antibody and two were p-ANCA positive. The majority of the GPA patients were positive for anti-proteinase-3 antibody and c-ANCA. The mainstay of treatment was corticosteroids. Rituximab was used in 14 patients. The decline in functional vital capacity (FVC) and diffusing capacity (DLCO) was most marked in IPF group, followed by ANCA-ILD and then the IPAF group ( $\Delta$  FVC,  $-0.5$ ,  $-0.5$ , and  $0.3$  L/s;  $\Delta$  DLCO,  $-3.7$ ,  $-3.6$ , and  $-0.1$ , respectively). In a similar manner, survival was poorest in IPF, followed by ANCA-ILD and was best in the IPAF group.

**Conclusions:** This is, to our knowledge, the largest case series of clinically confirmed AAV with ILD in North America. Sizable number of GPA with c-ANCA positive patients presenting concomitant ILD is a novel observation for the clinical characteristics of ANCA-ILD that contradicts previous epidemiology of ANCA-ILD. Our data is also of value by adding prognostic information in an era of newer therapeutics, such as rituximab. In addition, the intermediate prognosis of ANCA-ILD, between IPF and IPAF, is very interesting especially after the new classification IPAF.

**Disclosure of Interest:** None declared

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SAT0520

### ANTI-IL6-RECEPTOR TOCILIZUMAB IN REFRACTORY UVEITIS ASSOCIATED TO EXTRAOCULAR MANIFESTATIONS IN PATIENTS WITH BEHÇET'S DISEASE. MULTICENTER STUDY OF 11 PATIENTS

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**Objectives:** To assess the efficacy of Tocilizumab (TCZ) in refractory uveitis associated to extraocular manifestations due to Behçet's disease (BD).

**Methods:** Multicenter study of patients with BD refractory to standard systemic treatment (conventional immunosuppressive drugs and/or anti-TNF- $\alpha$  agents).

**Results:** We studied 11 patients (7 men/4 women) (20 affected eyes); mean age 38.4 $\pm$ 20.4 years. Uveitis was bilateral in 9 patients. The pattern of ocular involvement was: panuveitis (n=8; with retinal vasculitis in 4), anterior uveitis (n=2) and posterior uveitis (n=1). Cystoid macular oedema (CME) was present in 7 patients. The clinical course was recurrent (n=7) or chronic (n=4). Apart from the visual complications, at TCZ onset the following extraocular manifestations were present: oral and/or genital ulcers (n=7), arthritis (n=4), folliculitis/pseudofolliculitis (n=4), erythema nodosum (n=2), livedo reticularis (n=1), intestinal affection (n=1), and neurological involvement (n=2).

Before TCZ, they had received systemic corticosteroids, conventional immunosuppressive drugs and biologic agents, adalimumab (n=8), infliximab (n=4), golimumab (n=3), canakinumab (n=1), or etanercept (n=1). TCZ was used in monotherapy or combined with conventional immunosuppressive drugs at 8 mg/kg/iv/4 weeks (n=10) or 162 mg/sc/week (n=1). TCZ yielded rapid and maintained improvement in all ocular parameters (TABLE). After a mean follow-up of 9.5 $\pm$ 8.05 months using TCZ, all patients experienced ocular improvement, with complete remission in 8 of them. However, TCZ was only effective in 3 of the patients with extraocular manifestations. This biologic agent had to be withdrawn in 2 cases, 1 due to a severe infusion reaction and 1 due to arthritis impairment.

**Abstract SAT0520 – Table 1.** Epidemiological and clinical characteristic of the sample.

Case	Sex / Age (years)	Ocular pattern and course	Extraocular manifestations	Extraocular manifestations with no response to TCZ
1	Male/27	Anterior posterior uveitis + unilateral CME	Oral ulcers, arthropathy, white nodules (nodules on skin, ankles, elbows)	---
2	Female/32	Anterior uveitis + unilateral CME	Oral and genital ulcers, erythema nodosum	Oral and genital ulcers, erythema nodosum
3	Male /33	Anterior uveitis/papillitis + unilateral CME	Psoriasis, arthritis	---
4	Male /38	Anterior uveitis + retinal vasculitis	Oral ulcers, skin ulcers	Oral ulcers, skin ulcers
5	Female/37	Anterior uveitis + retinal vasculitis + bilateral CME	Oral ulcers	Arthropathy
6	Male /33	Anterior uveitis + retinal vasculitis + unilateral CME	Oral ulcers, skin ulcers, folliculitis	Oral and genital ulcers, folliculitis
7	Female/22	Anterior uveitis + bilateral CME	None	---
8	Male /39	Anterior uveitis + retinal vasculitis + unilateral CME	Oral and genital ulcers, white, skin ulcers	Oral and genital ulcers, skin ulcers
9	Male /30	Anterior uveitis	Oral and genital ulcers, hemorrhagic stroke, erythema nodosum	Hemorrhagic stroke
10	Female/41	Anterior uveitis	Oral and genital ulcers, arthritis, erythema nodosum, arthropathy, erythema nodosum, arthropathy	Oral and genital ulcers, arthritis, erythema nodosum, arthropathy
11	Male /38	Anterior uveitis	Oral ulcers, arthritis	Oral ulcers, arthritis

Abbreviations: CME, cystoid macular oedema; MRI, magnetic resonance imaging; TCZ, tocilizumab.

#### Abbreviations:

CME, cystoid macular oedema; MRI, magnetic resonance imaging; TCZ, tocilizumab.

**Conclusions:** TCZ appears to be useful in highly refractory BD-related uveitis. However, there are controversial results regarding its efficacy in the treatment of extraocular manifestations of BD.

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SAT0521

**A PROSPECTIVE OBSERVATIONAL STUDY ON THE SAFETY AND EFFICACY OF INFliximab-BIOSIMILAR IN PATIENTS WITH TAKAYASU'S ARTERITIS (TAKASIM): PRELIMINARY DATA**

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**Background:** Takayasu arteritis (TA) is a large-vessel vasculitis<sup>1</sup>. Treatment is mainly based on steroids, but in approximately 50% of patients a disease-modifying antirheumatic drug (DMARD) is required<sup>2</sup>. Anti-TNF $\alpha$  agents are recommended for steroid tapering despite DMARDs<sup>3</sup>. Infliximab-originate (IFX-O) is a chimeric monoclonal antibody against TNF $\alpha$  effective in TA patients. Infliximab-biosimilar (IFX-B) is an immunoglobulin-G1 chimeric human-murine monoclonal antibody biosimilar to IFX-O.

**Objectives:** To assess safety and efficacy of IFN-B in TA patients requiring anti-TNF $\alpha$  therapy.

**Methods:** 30 TA patients, diagnosed according to ACR criteria at our tertiary centre, will be recruited from our cohort. Both biological therapy-naïve and IFX-O treated patients will be eligible. Disease activity will be assessed 6-monthly by means of magnetic resonance angiography (MRA) and 18 F-fluorodeoxyglucose (FDG) PET/CT. ITAS2010 and ITAS-ESR/CRP will be obtained 6-monthly. Baseline was defined as the time of IFX-B start. Non parametric statistical tests were used.

**Results:** At January 2018, 19 patients (18 female, 1 male) were included. 12 patients have been on IFX-B for at least 6 months. Median age at baseline was 45 years (range 25–70). At recruitment median disease duration was 52 months (range 24–180), all patients were on IFX-O. Median time on IFX-O at baseline was 35 months (range 14–150). 3 patients had been previously treated with other biologics: tocilizumab,<sup>1</sup> adalimumab.<sup>1</sup> 18/19 patients (94.7%) were on concomitant steroid therapy (mean dose 5 $\pm$ 1.8 mg). It was significantly reduced to a mean dose of 4 $\pm$ 1.7 mg (p=0.043) at month 6. 15/19 patients (78.9%) were also on DMARDs, kept unchanged throughout treatment. 1 patient on IFX-B was switched to a different therapy because of poor disease control with both IFX-O and IFX-B. Mean IFX-B dose at baseline was 6.92 $\pm$ 1.76 mg/kg. Mean IFX-B dose at month 6 was 7.42 $\pm$ 2.19 mg/kg. IFX-B dose was increased in 5 patients. Mean time interval between IFX-B infusions was kept unchanged (5.79 $\pm$ 0.63 weeks). Mean CRP and ESR were 3.28 $\pm$ 2.64 mg/L and 19.68 $\pm$ 9.94 mm/1 hour at baseline and 3.4 $\pm$ 3.12 mg/L and 20.53 $\pm$ 14.06 mm/1 hour at month 6, the difference not being statistically significant. Mean ITAS2010 and ITAS-ESR/CRP were 7.6, 8.2 and 8 at baseline and 6.1, 6.8 and 6.3 at month 6, the difference not being statistically significant. At month 6 PET/CT showed no disease progression in all patients and MRA disclosed disease stability in 8/12 (66.7%), progression in 3/12 (25%) and improvement in 1 (8.3%) patient. No patient experienced side effects during infusion. 11/19 patients (57.9%) experienced low-grade side effects related to TNF $\alpha$  blockade. 6 patients experienced upper airway infection, 3 herpes simplex reactivation, 1 viral gastroenteritis, 1 vaginal candidiasis. No modification of IFX-B therapy was required.

**Conclusions:** Our preliminary data suggest that IFX-B is as effective and safe as IFX-O in TA patients.

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SAT0522

**VASCULAR AND JOINT INFLAMMATION ARE NEGATIVELY CORRELATED IN PATIENTS WITH POLYMYALGIA RHEUMATICA, GIANT CELL ARTERITIS AND FEVER OF UNKNOWN ORIGIN**

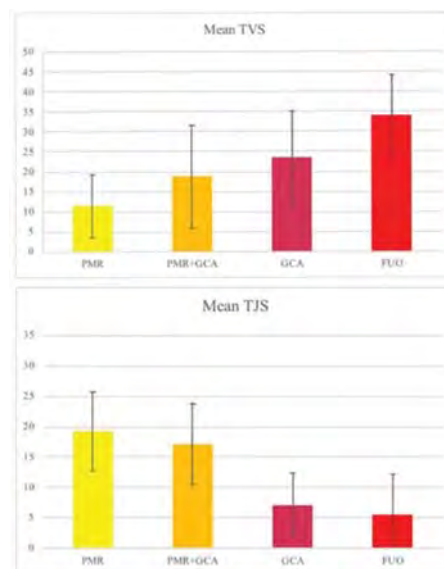
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**Background:** 18 F-Fluorodeoxyglucose positron emission tomography (PET) reveals the presence of large vessel vasculitis (LVV) in 30%–40% of patients with apparently isolated polymyalgia rheumatica (PMR), in 70%–80% of patient with giant cell arteritis<sup>1</sup> and in about 20% of patient with fever of unknown origin (FUO)<sup>2</sup>, suggesting that these conditions may be different clinical manifestations of the same entity.

**Objectives:** To evaluate and compare the patterns of vascular and joint uptake in patients with PMR, GCA, and FUO.

**Methods:** Consecutive patients with a diagnosis of PMR, GCA or FUO underwent a thorough clinical examination and a PET/CT scan. Arterial and joint uptake of FDG were scored relative to liver uptake with a 4-point scale. The values of each district examined were summed to obtain a total vascular score (TVS) and a total joint score (TJS). A semi-quantitative analysis of FDG uptake was carried out. Arterial FDG uptake was quantified by calculating the mean standardised uptake value (SUV) within each region of interest (ROI) and the results expressed as the ratio between mean SUV value of each ROI and the blood-pool (SUV/BP). To assess joint metabolism, CT-based ROIs were bilaterally drawn on joint and bursal spaces.

**Results:** One hundred and thirty-one patients were included, 89 females and 42 males, with a median age of 74 years (range 47–92). Ninety-seven patients were diagnosed as PMR, 13 as GCA, 16 with both PMR and GCA and 5 patients presented with FUO. FUO patients showed a higher mean arterial SUV in comparison to PMR (0.77 vs. 1.15, p=0.004) and GCA patients (0.81 vs 1.15, p=0.052). Similar and more striking results were obtained using visual scoring. FUO patients showed always increased uptake in the large vessels. PMR patients showed statistically lower TVS than GCA +PMR, GCA and FUO patients. Patients with PMR showed a statistically significant higher mean joint SUV than GCA patients (p=0.01). The highest mean articular uptake was shown by PMR patients and the lowest by FUO patients. Mean TJS of PMR patients was significantly higher than that of GCA and FUO patients (p<0.001). TVS and TJS correlated negatively (p=0.01), as did mean vascular SUV and mean joint SUV (p=0.001).



**Conclusions:** Although patients with diseases different from PMR were few, our PET/CT study support the view that there is a continuum in the intensity of inflammation, with FUO >GCA>PMR+GCA> PMR for vessels, and the opposite for joints. Vascular and joint inflammation were negatively correlated. Our data support the view that similarities exceed differences in these conditions, with clinical features depending from the relative contribution of vessel and joint involvement.

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SAT0523

## EVOLUTION OF VISUAL AFFECTATION IN PATIENTS WITH GIANT CELL ARTERITIS TREATED WITH TOCILIZUMAB

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**Background:** Giant cell arteritis (GCA) is a large vessel vasculitis that has a special predilection for extracranial branches of the external carotid artery. Among its most fearsome complications is visual affectation. Tocilizumab (TCZ) is a monoclonal antibody directed against the interleukin 6 receptor that has shown utility in the treatment of GCA.

**Objectives:** Our aim was to assess the evolution of visual clinic in patients with GCA treated TCZ.

**Methods:** Retrospective multicentre study of 20 GCA patients with visual involvement treated with TCZ. The efficacy of this drug on visual symptoms was evaluated.

**Results:** We evaluated 20 patients (14 women and 6 men) with a mean age  $\pm$ SD of  $73.7 \pm 10.1$  years with GCA and visual symptoms. In total there were 23 affected eyes. The symptoms reported were: unilateral blindness (n=6), unilateral blurred vision (n=6), unilateral amaurosis fugax (n=3), unilateral hemianopsia (n=2), bilateral blindness (n=1), bilateral blurred vision (n=1), bilateral hemianopsia (n=1). Before starting treatment with TCZ all patients had received high doses of prednisone, with a mean  $\pm$ SD of  $54.2 \pm 13.8$  mg/day (range of doses: 40–80 mg/day). In addition, 9 of them also received intravenous corticosteroid boluses. In addition, 13 patients received traditional immunosuppressants: methotrexate (MTX) (n=12), cyclophosphamide (n=2), leflunomide (n=1) and azathioprine (n=1). Regardless of corticosteroids, TCZ was administered as monotherapy in 14 patients, while in 6 it was administered in combination with MTX. The TABLE shows the evolution of the visual affectation of these patients. Throughout a median follow-up [RIC] of 9<sup>4</sup>–18 months, none of the 7 patients who had a blindness regained vision. The 2 patients who presented unilateral hemianopsia recovered vision. The patient with bilateral hemianopsia and the patient with bilateral blurred vision experienced a partial improvement. The rest of the patients achieved a complete recovery.

	Month 1 n=20	Month 3 n=14	Month 6 n=10	Month 12 n=5
<b>Visual improvement after starting TCZ, n (%)</b>				
Complete improvement:	6 (30)	5 (35.7)	5 (50)	1 (25)
Partial improvement:	2 (10)	3 (21.4)	0 (0)	0 (0)
No improvement:	12 (60)	6 (42.8)	5 (50)	4 (75)

**Conclusions:** Although TCZ seems to be also useful in the treatment of visual manifestations of ACG, once blindness is established, it does not seem to be effective.

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SAT0524

## THE ROLE OF POLYMORPHISMS OF HEMOSTASIS GENES IN VENOUS THROMBOEMBOLIC EVENTS IN ANCA-ASSOCIATED VASCULITIDES

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**Background:** The role of polymorphisms of hemostasis genes in venous thromboembolic events in ANCA-associated vasculitides.

**Objectives:** To evaluate the role of polymorphisms of hemostasis genes in the risk of VTEs in AAV patients and to the clinical features of AAV.

**Methods:** We studied 85 patients with AAV [69 with granulomatosis with polyangiitis (GPA), 11 with microscopic polyangiitis (MPA), 5 with eosinophilic granulomatosis with polyangiitis (EGPA)] diagnosed according to CHCC 2012 classification. There were 34 males and 51 females, aged of 55<sup>45;63</sup> years. Duration of follow-up was 74.0 (36.5;120.3) months. Coagulation genes polymorphisms MTHFR 677 C/T (rs1801133), FV 1691 G/A (rs6025), FII 20120 G/A (rs1799963), FGB 455 G/A (rs1800790), PAI-1 675 5G/4G (rs1799889), ITGA2 807 C/T (rs1126643), ITGB3 1565 T/C (rs5918), FVII 10976 G/A (rs6046), FXIII 103 G/T (rs5985) were evaluated by real time polymerase chain reaction. VTEs (deep vein thrombosis, pulmonary embolism) were identified by ultrasonography and chest computed tomography, respectively. We used score system, according to which the presence of each minor allele was assigned one point.

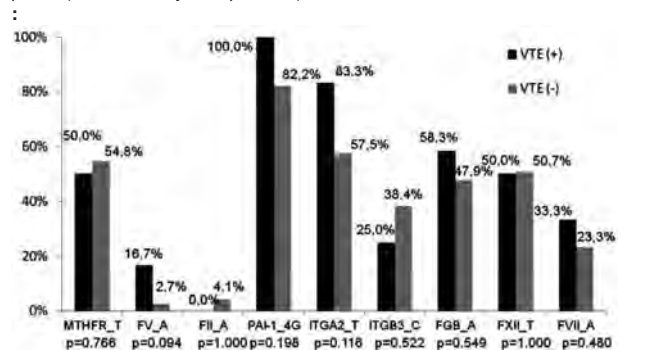
**Results:** We retrospectively detected 12 (14.1%) VTEs in 85 patients with AAV, including 5 (7.2%) in GPA, 4 (36.4%) in MPA and 3 (60.0%) in EGPA. There were no significant differences in the prevalence of alleles of the each gene in patients with and without VTE (figure 1). However, the combination of integrin A2 (ITGA2 807 C/T), plasminogen activator inhibitor-1 (PAI-1 675 5 G4G), fibrinogen (FGB 455 G/A) and FV<sup>FV 1691</sup> G/A) polymorphisms was associated with a significantly higher occurrence of VTE in patients with AAV (p=0.007) (table 1).

**Abstract SAT0524 – Table 1.** The prevalence of minor alleles of ITGA2 807 C/T, PAI-1 675 5G/4G, F5 1691 G/A, FGB 455 G/A in patients with and without VTE

Minor allele sum score	VTE (n=12)	No VTE (n=73)
0	0 (0%)	4 (5.5%)
1	1 (8.3%)	17 (23.3%)
2	3 (25.0%)	34 (46.6%)
3	8 (66.7%)	18 (24.7%)
4	0 (0%)	0 (0%)
Median sum score*	3.0 (2.0;3.0)*	2.0 (1.0;2.5)*

\*p=0.007

We observed a higher risk of lung involvement in carriers of methylenetetrahydrofolate reductase gene (MTHFR 677 C/T) polymorphism (p=0.007, OR 4.305 (95% CI 1.55 to 11.98), and an earlier AAV onset in patients with FXIII 103 G/T polymorphism (47.0 vs 50.0 years, p=0.049)



**Abstract SAT0524 – Figure 1.** Rates of minor alleles in patients with and without VTE

**Conclusions:** The combination of several genetic polymorphisms of hemostasis system is associated with an increased prevalence of VTE in AAV patients. The association between MTHFR 677 C/T and FXIII 103 G/T alleles and clinical features of AAV warrants further studies in the larger cohorts of patients.

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SAT0525

### AN UPDATE ON PULMONARY ARTERY INVOLVEMENT IN BEHCET'S SYNDROME: MORE PULMONARY ARTERY THROMBOTIC DISEASE AND A BETTER OUTCOME

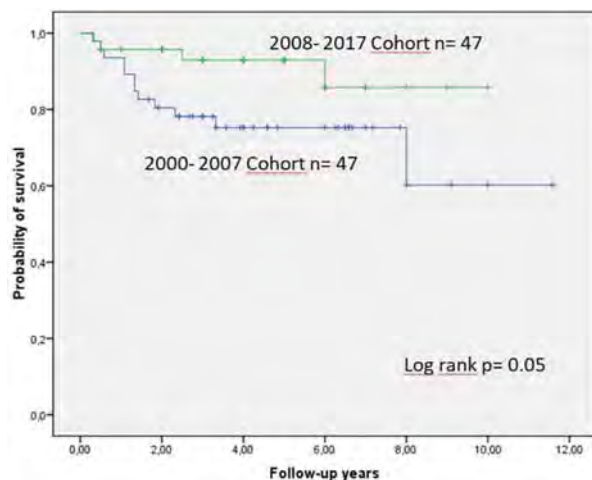
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**Background:** Pulmonary artery involvement (PAI) is the most common form of arterial involvement in Behçet's syndrome (BS) and is a well-known cause of mortality and morbidity. A previous survey<sup>1</sup> by our group had analysed the clinical characteristics and outcome of 47 pts with PAI registered between 2000–2007 and shown that: 1. the overwhelming male predominance was decreasing; 2. 1/4th of the pts had isolated pulmonary artery thrombosis (PAT); and 3. the mortality rate was 26% after a mean follow-up of 7 years. Recently we had the impression that female/male ratio was perhaps increasing, we are becoming to see more pts with isolated PAT and that we started to use more biologics.

**Objectives:** This survey was done to look at these assumptions formally in a recent group of BS pts with PAI.

**Methods:** We reviewed the records of about 3390 pts with BD who were registered at our multidisciplinary BS clinic between Jan 2008 and Jan 2018. From this group we identified 47 (42 M/5 F) pts who were diagnosed with PAI and recorded all information regarding clinical characteristics, outcome, radiological studies and medical or surgical treatment.

**Results:** The prevalence of pts with PAI decreased from 1.9% to 1.4% in the recent cohort. The M/F ratio, the mean age at the onset of PAI were similar across 2 cohorts. The frequencies of other vascular involvement were almost similar to that observed in the previous cohort. However, there were more pts with neurological disease (parenchymal) in the recent cohort. As usual, PAT or PAA were mostly bilateral and involved descending lobar arteries. On the other hand, types of PAI involvement at presentation had changed substantially: those with isolated PAT reached a share of 45%. Forty-five (96%) pts received cyclophosphamide (Cy) pulses for a mean of 6±4 courses, which was significantly shorter compared to that observed in the previous cohort. A total of 23 (49%) pts received infliximab because of relapsing course, side effects or unresponsiveness to Cy for a mean follow-up of 8±4 mo while only 2 pts received anti-TNF's in the older cohort. 4 pts had lung surgery. These were lobectomies in 3 pts due to giant rapidly progressing aneurysms and cavectomy in 1. Bronchial artery embolization was done in 3 pts because of refractory hemoptysis. By Jan 2018 the outcome of information was available on 45/47 pts: 4 pts (all male) (8%) had died, 2 were lost to follow-up after 12 and 16 mo of follow-up and the remaining were alive after a median follow-up of 5 [IQR:3–9] years. The causes of deaths were massive hemoptysis in 3, severe pulmonary hypertension in 1. As shown in the figure, the survival has improved significantly in the recent yrs.



**Conclusions:** The surveys of 2 consecutive cohorts showed that the prevalence of PAI perhaps mildly decreased, isolated PAT type of involvement was with considerably higher frequency and the outcome was getting better. Cy is still the first agent in these pts however its duration of use became much shorter and anti-TNF's mainly infliximab was used in about half of the cohort. The survival seems to have improved significantly. This could have been due to a decreased severity of the type of PAI, with isolated PAT becoming the most frequent type, or a better management.

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**Disclosure of Interest:** None declared  
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SAT0526

### IS RELAPSE RATE OF GIANT CELL ARTERITIS IN REAL-LIFE EXPERIENCE LOWER THAN IN THE CONTROLLED TRIALS? RESULTS OF A RETROSPECTIVE, MULTI-CENTRE COHORT STUDY

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**Objectives:** Corticosteroids (CS) are accepted as the standard first-line treatment for giant cell arteritis (GCA). However, controlled trials of tocilizumab and abatacept demonstrated relapse rates of up to 70%–80% in patients on CS-only protocols in 12–24 months. Though level of evidence is low and not suggested by guidelines (except for methotrexate), conventional immunosuppressives (ISs) are also commonly used. We aimed to assess the relapse rates in patients with GCA in routine practice, retrospectively.

**Methods:** We assembled a retrospective cohort of patients with GCA from Turkey. All data was abstracted from records. Relapse was defined as any new manifestation or increased acute-phase response leading to the change of the CS dose or use of a new therapeutic agent by the treating physician.

**Results:** The study included 156 (F/M: 95/61) patients with GCA (table 1). The mean age at disease onset was 67.8±9.1 years. Polymyalgia Rheumatica was also present in 48 (30.8%) patients. Diagnosis was proven histopathologically in 99 patients. All patients received 1 mg/kg/day CS for remission induction, additional CS pulses were given to 36 (23.1%) patients. Conventional ISs including methotrexate and azathioprine were used in 89 (56.1%) and 26 (16.6%) patients respectively, while 10 (6.4%) patients received biologic treatments (8 tocilizumab, 2 etanercept). Forty-four (28.2%) patients used only CS during follow-up. Follow-up of at least 6 months was available for 132 patients, and median follow-up duration was 35 (6–268) months. Relapses occurred in 27 (20.5%) patients during follow-up. Mortality rate was 7.5% (n=10) during follow-up. VDI score was 2.4±1.7. Main causes of damage were related to CS treatments such as cataract, osteoporosis and diabetes mellitus.

	Giant Cell Arteritis (n=156)
Manifestations of systemic inflammation, n/156 (%)	
Anemia (<12 mg/dl for female, <13 mg/dl for male)	94 (60.2%)
Erythrocyte Sedimentation Rate (mm/hour) *	84.6 ± 30.1
C-reactive protein (mg/l) *	84.8 ± 65.3
Malaise	132 (84.6%)
Weight loss	72 (46.1%)
Fever	35 (22.4%)
Stiffness and/or pain muscles and joints	48 (30.8%)
Manifestations of Vascular Ischemia, n /156 (%)	
Headache	144 (92.3%)
Scalp Tenderness	78 (50%)
Jaw Claudication	57 (36.5%)
Ocular Symptoms	72 (46.2%)
Extremity Claudication	14 (8.9%)
Neurological Manifestations	14 (9%)

**Conclusions:** In this first multi-centre series of GCA from Turkey, we observed that only one fifth of patients had relapses during a mean follow-up of 35 months. This lower relapse frequency suggests a different clinical spectrum in routine



practice compared to patients included in controlled trials. Our results also suggest that there is a clear need for a steroid sparing agent in patients with GCA, that is a older aged population prone to CS side effects.

**Disclosure of Interest:** None declared

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SAT0527

### RITUXIMAB PRESCRIPTION PATTERNS AND EFFICACY IN THE INDUCTION TREATMENT OF ANCA-ASSOCIATED VASCULITIS IN A BELGIAN MULTICENTRIC COHORT

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**Background:** The RAVE trial has revolutionised the induction treatment of ANCA-Associated Vasculitis (AAV, including GPA, granulomatosis with polyangiitis and MPA, microscopic polyangiitis), by demonstrating non-inferiority of rituximab compared with cyclophosphamide<sup>1</sup>.

**Objectives:** To study AAV patients' characteristics, rituximab prescription practices and efficacy in AAV induction treatment in 4 Belgian university hospitals. The patient population, selected according to the Belgian reimbursement criteria, is relatively homogeneous and comparable to the one of RAVE trial.

**Methods:** 57 patients, receiving rituximab as AAV induction therapy since May 2014, were enrolled in an observational retrospective multicenter trial involving 4 Belgian university hospitals. We have focused on the type of AAV (GPA/MPA), ANCA specificity (anti-PR3/MPO), prescriber's speciality, used reimbursement criteria, organ involvements, severity of the flares (according to BVAS-WG definition) and finally rituximab efficacy in AAV induction treatment by considering the RAVE primary (complete remission without prednisone) and secondary (complete remission with prednisone <10 mg, rates of relapses) outcomes at 6, 12, 18 and 24 months.

**Results:** The most frequent subtype of AAV was GPA (84%). The main indication was relapsing disease (54.4%), followed by contra-indication to cyclophosphamide (38.6%). 66.7% of the patients reached complete remission with prednisone <10 mg at 6 months, and 55.3% at 12 months, 40% at 18 months, 25% at 24 months respectively. In the "severe disease" subgroup, 73% reached complete remission with prednisone <10 mg at 6 months, 58.8% at 12 months, 50% at 18 months and 32% at 24 months. The rates of complete remission without steroids were very low at 6, 12, 18 and 24 months (between 0%–6%) but our patients were not asked to follow a glucocorticoid tapering scheduled for complete withdrawal of prednisone after 6 months and were usually maintained under low-dose prednisone. Relapse rates were high between 18 and 24 months both in the total group and in the severe disease subgroup (due to the fact that rituximab is not reimbursed for maintenance treatment in Belgium). The subtype of ANCA was not predictive of the risk of relapse.

**Conclusions:** Our results confirm – in a "real-life" cohort of patients selected according data of RAVE trial – those of RAVE regarding complete remission rates at 6 months with prednisone 10 mg/j. The high prevalence of relapses – in particular after 18 months – underlines the need to optimise maintenance treatment after an induction treatment with rituximab.

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**Disclosure of Interest:** None declared

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SAT0528

### EFFECTIVENESS OF REMISSION-INDUCTION THERAPY WITH CONCOMITANT CYCLOPHOSPHAMIDE AND GLUCOCORTICOID FOR MICROSCOPIC POLYANGIITIS AND GRANULOMATOSIS WITH POLYANGIITIS IN JAPAN: A PROPENSITY SCORE MATCHED ANALYSIS OF TWO NATIONWIDE PROSPECTIVE COHORT STUDIES

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**Background:** Although concomitant use of cyclophosphamide (CYC) with glucocorticoids (GC) is considered to be one of the standard remission-induction therapies for antineutrophil cytoplasmic antibody (ANCA) associated vasculitis over 30 years, there are few reports about clinical efficacy or effectiveness of CYC.

**Objectives:** To evaluate effectiveness and safety of concomitant CYC as remission induction therapy in Japanese patients with microscopic polyangiitis (MPA) and granulomatosis with polyangiitis (GPA) using data sets from two nationwide prospective cohort studies.

**Methods:** Newly diagnosed MPA and GPA patients treated with GC with or without CYC for remission-induction therapy were enrolled. The patients treated with other immunosuppressants or plasma exchange were excluded. A propensity score for the use of CYC was estimated using age, types of AAV, serum creatinine level, Birmingham Vasculitis Activity Score (BVAS), and initial GC dosage at baseline. After propensity score matching at 1:1, remission, overall survival, and end-stage renal disease (ESRD)-free survival rates, Vasculitis Damage Index (VDI), and incidence of serious infection within 6 months were compared between patients treated with and without concomitant CYC.

**Results:** Of enrolled 327 patients, concomitant CYC was used in 119 (36%) patients during the initial 3 weeks of treatment. After propensity score matching, 95 patients with concomitant CYC (CYC group) and 95 controls (non-CYC group) were selected. Demographics, baseline characteristics and treatments were balanced between the two groups except for myeloperoxidase ANCA positivity (Table). The remission within 6 months was achieved in 85% in both groups. The survival and ESRD-free survival rates were also similar between the two groups (log-rank test;  $p=0.77$  and  $1.0$ , respectively). Median VDI at the time of last observation did not differ between the two groups (CYC, 3 [interquartile {IQR}: 2–4]; non-CYC, 2 [IQR:1–3],  $p=0.26$ ). The accumulated GC dosage of the CYC-group from 3 to 24 months was lower than the non-CYC group, the GC-related damage did not differ (CYC, 1 [IQR: 0–2]; non-CYC, 0 [IQR:0–2],  $p=0.69$ ).

**Table.** Comparison of patients treated with concomitant cyclophosphamide and with glucocorticoid alone

Variables at baseline and treatments	Cyclophosphamide users (n=95)	Non-users (n=95)	p-value
Male/female, n	51/44 (46%)	60/35	0.24
Age, years	70 (65–78)	71 (62–75)	0.92
GPA/MPA	26/69	27/68	1.0
Myeloperoxidase ANCA, n (%)	78 (82)	89 (94)	0.02*
Proteinase-3 ANCA, n (%)	17 (18)	8 (8)	0.15
Serum creatinine, mg/dL	1.2 (0.8–3.2)	1.1 (0.7–2.5)	0.39
C-reactive protein, mg/dL	7.5 (2.3–12.6)	7.2 (2.1–11.7)	0.35
BVAS	15 (12–20)	16 (12–21)	0.99
Interstitial lung disease, n (%)	38 (40)	37 (49)	0.55
Glucocorticoid (mg/kg/day) <sup>d</sup>	0.83 (0.72–0.97)	0.83 (0.67–0.99)	0.89

Values expressed as a number of patients (%) or median (interquartile). \* $p<0.05$ .

**Conclusions:** In Japanese patients with MPA and GPA, concomitant CYC could not show any benefits on clinical outcomes within 24 months. Dosage and treatment duration of CYC, as well as tapering methods of GC, could be confounding factors. Longer observation may be necessary to confirm the effectiveness of CYC as GC sparing agent.

**Disclosure of Interest:** None declared

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SAT0529

**SHORT-TERM EFFICACY AND SAFETY OF BIOSIMILAR RITUXIMAB IN PATIENTS WITH SYSTEMIC VASCULITIDES**

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**Objectives:** To study efficacy and safety of biosimilar (intended copy) rituximab (Acellbia, BIOCAD) in patients with systemic vasculitides.

**Methods:** We enrolled in our case series all consecutive patients with systemic vasculitides diagnosed according to CHCC2012 and ACR criteria (if applicable) who were treated with biosimilar rituximab since 2015. Activity of vasculitis was evaluated using BVAS3. CD19+ B-cells count was measured by standard method. Patients received intravenous rituximab at a 500 mg dose (four weekly infusions for remission induction or two weekly every 6 months infusions for maintenance treatment).

**Results:** In total, 45 patients were treated with biosimilar rituximab (29 GPA, 12 MPA, 1 EGPA, 2 cryoglobulemic vasculitis, 1 rheumatoid vasculitis). In 12 patients (7 GPA, 3 MPA, 1 CryoVas, 1 RheumVas), rituximab was administered for induction of remission due to high activity and relapsing course of vasculitis and low efficacy of previous treatment. 33 patients (22 GPA, 9 MPA, 1 EGPA, 1 CryoVas) received rituximab for maintenance of remission. Median duration of follow-up was 12 months.<sup>6-26</sup>

At 1 and 3 months, all patients achieved B-cell depletion. At 6 months, B-cell repopulation was shown in 9 patients (20%). Remission induction therapy with rituximab resulted in decrease of median BVAS from 16 10–24 to 1 (0–4) at 3 months and to 0 (0–2) at 6 months. At 3 and 6 months, median prednisone dose was tapered from 50 mg 35–80 to 25 mg 15–40 and 10 mg, 5–20 respectively.

In patients who received rituximab for maintenance treatment, median BVAS showed no disease activity (0–1) both at baseline and at 3 or 6 months. At baseline and at 3 months median doses of prednisolone were 5 mg (0–7.5) and 5 mg (0–5). At 6 months, it was reduced to 2.5 mg (0–5). Biosimilar rituximab had acceptable safety profile. Adverse events included mild infusion reaction,<sup>2</sup> urinary<sup>3</sup> and bronchopulmonary<sup>5</sup> infections which required intravenous antibiotics (median 4 months after infusions), hypogammaglobulinemia<sup>2</sup> that persisted for at least 12 months and 1 case of late-onset neutropenia in 8 months.

**Conclusions:** Biosimilar rituximab showed high efficacy and acceptable safety in patients with systemic vasculitides.

**Disclosure of Interest:** None declared

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SAT0530

**CLINICAL FEATURES ASSOCIATION WITH HLA-B ALLELIC TYPES (B27, B51) IN KOREAN PATIENTS OF BEHCET'S DISEASE**

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**Background:** The recurrent oral ulcer frequently occur as a first clinical manifestation of Behcet's disease (BD), but BD is characterised by considerable phenotypic variation, comprising a myriad of manifestations, e.g. recurrent genital ulcers and skin, joint, eye, vascular and/or CNS involvement. BD is well known to be associated with HLA-B51 antigen. HLA B27 antigen is famous for association with spondyloarthritis. But BD is also observed in HLA B27 positive patients.

**Objectives:** The aim of this study was to clarify the clinical features association with HLA-B antigens (B27, B51) in Korean patients of Behcet's disease.

**Methods:** We genotyped HLA-B alleles in 433 patients who showed recurrent oral ulcer. The diagnosis of BD was determined according to revised international study group criteria. Among them, 126 patients of BD were included. The genotyping was performed using 66 sets of sequence specific DNA probe (PCR-SSP). The clinical feature was assessed according to HLA B allele in the patients diagnosed with BD.

**Results:** HLA-B51 allele frequency was more frequent in both 126 BD patients and 433 total patients and the frequency was 40 (31.7%) and 110 (25.4%) respectively. Among the HLA B51 +BD patients (n=40), similar gender ratio was observed (Male 52.5%, Female 47.5%) and clinical features of diagnostic criteria were dominant. Among the HLA B27 +BD patients (n=17), genital ulcer and skin lesions were dominant. HLA B27 +B51+BD patient was one and clinical features were genital ulcer, skin lesion and arthritis.

**Conclusions:** The specific clinical features of BD were observed in HLA-B51 +BD patients. In HLA B27 +BD patients, genital ulcer and skin lesions were

more observed. The study about clinical features associated with HLA-B allele (B27, B51) in spondyloarthritis patients is also needed.

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SAT0531

**ACUTE PHASE REACTANT LEVELS AND PREDNISONE DOSES AT DISEASE FLARE IN PATIENTS WITH GIANT CELL ARTERITIS: PROSPECTIVE DATA FROM THE GIACTA TRIAL**

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**Background:** The relationship between acute phase reactant levels and giant cell arteritis (GCA) disease flares is not known, particularly in the era of interleukin-6 receptor blockade with tocilizumab (TCZ). Prednisone doses at which GCA flares can occur have not been studied thoroughly in prospective clinical trials.

**Objectives:** Investigate prednisone doses and acute phase reactant levels at the time of disease flare in patients with GCA.

**Methods:** Secondary analyses of prednisone doses, C-reactive protein (CRP) levels, and erythrocyte sedimentation rate (ESR) were performed for patients who experienced GCA flare after achieving remission during 52 weeks of treatment with TCZ-weekly or -every-other-week+26 week prednisone taper (TCZ-QW or TCZ-Q2W) or placebo +26 week or 52 week prednisone taper (PBO+26 or PBO+52). The last CRP and ESR values before first disease flare were used if values on the day of first flare were missing. Analyses are descriptive and were performed post hoc.

**Results:** GCA flare after remission was reported in 23% (23/100) of TCZ-QW patients, 26% (13/50) of TCZ-Q2W patients, 68% (34/50) of PBO +26 patients, and 49% (25/51) of PBO +52 patients.<sup>1</sup> Median CRP levels and ESR at the time of flare were lower in the TCZ groups than in the PBO groups (Table). In the TCZ groups, 92% (33/36) of flares were associated with normal CRP levels ( $\leq 1$  mg/dL) and 89% (32/36) were associated with normal ESR values ( $< 30$  mm/h). In the PBO groups, 34% (20/59) of flares were associated with normal CRP values and 31% (18/59) with normal ESR. Median (min–max) prednisone doses at the time of disease flare in the combined TCZ and combined PBO groups were 5.5 (0.0–310.0) and 9.0 (0.0–55.0) mg/day, respectively. Among 149 patients in the TCZ groups, 10 (7%) had disease flares while receiving prednisone doses greater than 10 mg/day, accounting for 28% of all disease flares in the TCZ groups. Among 101 patients in the PBO groups, 23 (23%) had disease flares while receiving prednisone doses  $> 10$  mg/day, accounting for 39% of all disease flares in the PBO groups. Thus, 33 of the 95 disease flares in GiACTA (35%) occurred while the patient was receiving  $\geq 10$  mg/day prednisone.

**Abstract SAT0531 – Table 1.** Prednisone doses and acute phase reactants at GCA flare

	TCZ-QW N=100	TCZ-Q2W N=49	PBO+26 N=50	PBO+52 N=51
Patients who experienced flare, n (%) <sup>a</sup>	23 (23)	13 (27)	34 (68)	25 (49)
Median (min-max) prednisone dose at flare, mg	7.0 (0.0–30.0)	2.0 (0.0–310.0)	6.5 (0.0–55.0)	10.0 (2.0–40.0) <sup>a</sup>
Patients who experienced first flare while on prednisone dose, mg/day, n (%) <sup>a</sup>				
0	5 (5.0)	4 (8.0)	9 (18.0)	0
1–5	5 (5.0)	4 (8.0)	7 (14.0)	5 (9.8)
>5–10	5 (5.0)	3 (6.0)	4 (8.0)	10 (19.6)
>10–20	5 (5.0)	1 (2.0)	9 (18.0)	8 (15.7)
>20–30	3 (3.0)	0	2 (4.0)	0
>30–40	0	0	2 (4.0)	1 (2.0)
>50–60	0	0	1 (2.0)	0
>60	0	1 (2.0)	0	0
Median (min-max) CRP, <sup>b</sup> mg/L	0.4 (0.2–93.2)	1.0 (0.2–18.1)	23.1 (1.4–119.0)	17.3 (0.2–122.0)
Flare patients with elevated CRP, <sup>c</sup> n (%) <sup>c</sup>	1 (4)	2 (15)	22 (65)	17 (68)
Median (min-max) ESR, <sup>d</sup> mm/h	5.0 (0.0–80.0)	5.0 (1.0–43.0)	51.0 (8.0–140.0)	39.0 (4.0–138.0)
Flare patients with elevated ESR, <sup>e</sup> n (%) <sup>e</sup>	1 (4)	3 (23)	27 (79)	14 (56)

<sup>a</sup>Percentage based on N. <sup>b</sup>Normal  $\leq 10$  mg/L. <sup>c</sup>Percentage based on n who experienced flare. <sup>d</sup>Normal  $< 30$  mm/h. <sup>e</sup>n=24

**Conclusions:** Acute phase reactants are not reliable correlates of disease flare in TCZ-treated patients, but approximately one-third of all PBO +prednisone patients also had normal acute phase reactants at the time of disease flare. Median prednisone dose at the time of disease flare for TCZ-treated patients was numerically lower than that of patients treated with PBO +prednisone. One-third of all disease flares in GACTA occurred while the patient was receiving  $>10$  mg/day prednisone.

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### SAT0532 TREATMENT WITH METHOTREXATE AND RISK OF ISCHAEMIC RELAPSES IN PATIENTS WITH GIANT CELL ARTERITIS IN CLINICAL PRACTICE

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**Background:** Clinical trials show the efficacy of Methotrexate (MTX) in giant cell arteritis (GCA). It is necessary to corroborate these results in real life.

**Objectives:** To assess the incidence and the risk of ischaemic relapses in GCA patients treated with and without Methotrexate (MTX) in clinical practice.

**Methods:** Retrospective longitudinal observational study. **Subjects:** patients treated at the Rheumatology Service of the Hospital Clínico San Carlos with the diagnosis of GCA. They were included from the date of diagnosis (January 1991 to September 2013) and followed-up until lost of follow up or Sept-2014. **Main outcome:** relapses by isquem event (RIE): Presence of mandibular claudication, visual manifestations (blurred vision, diplopia, transient or permanent loss of vision), cerebrovascular accident, ischaemic heart disease or claudication of limbs, after having achieved an objective improvement, associated with an

increase in the erythrocyte sedimentation rate (ESR) and the need to increase corticosteroids (at least 10 mg over the previous dose). **Independent variable:** exposure to MTX over time. **Secondary variables:** sociodemographic, clinical and treatment. **Statistical analysis:** RIE rates were assessed by survival techniques, expressing the incidence per 100 patients\*year with their 95% confidence interval [CI]. The influence of MTX on the RIE was analysed by multivariate Cox regression models. Results were expressed as Hazard ratios (HR) with their respective CI.

**Results:** 168 patients were included with a follow-up of 675.59 patients\*year. 80.36% were women (mean age: 76.77 $\pm$ 7 years). The most prevalent comorbidities were arterial hypertension (64%), dyslipidemia (34%), cardiovascular pathology (30%) and polymyalgia rheumatica (13.77%). The most common clinical symptom at diagnosis was headache (87.43%), systemic involvement (55%) and polymyalgia rheumatica (49.70%). The ESR was 78 $\pm$ 30.85 mmHg and Hb of 12.06 $\pm$ 1.58 mg/dL. 46.39% had a positive biopsy. 64% were on MTX (mean dose: 10 mg) at any time during the follow-up, from those 68% started MTX in the first 4 weeks after diagnosis. The mean dose of corticosteroids was 50.72 $\pm$ 15.46 mg. There were 21 relapses by ischaemic events (12.5%), with an incidence of 3.1 [2.02–4.77]. The median time to first RIE was 0.4 [p25–75: 0.4–5.1] years. The incidence of RIE in patients exposed to MTX was 1.92 [0.8–4.62], whereas in those without MTX was 3.84 [2.36–6.28]. The incidence of RIE in women was 3.44 [2.17–5.46] and in men was 1.97 [0.6–6]. In the multivariate analysis after adjusting for age, sex, disease activity and calendar time, exposure to MTX had less risk of relapse by ischaemic event compared to those without MTX (HR 0.3 [0.096–0.99]; p=0.048).

**Conclusions:** The frequency of RIE was 12.5%. The incidence of RIE was 3% patients-year. With the results observed in this study, the use of MTX seems to decrease the risk of relapses by ischaemic event.

**Disclosure of Interest:** None declared

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### SAT0533 POLVAS – RETROSPECTIVE REGISTRY OF POLISH PATIENTS WITH ANCA-ASSOCIATED VASCULITIDES

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**Background:** Vasculitides are a heterogeneous group of rare diseases with unknown etiology and the clinical spectrum ranging from life-threatening systemic disease to minor isolated skin changes. Present nomenclature and definitions of systemic vasculitides have been proposed in 2012 at the International Chapel Hill Consensus Conference.<sup>1</sup> Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitides (AAV) belong to the small to medium-size vessel systemic diseases comprising granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) and eosinophilic granulomatosis with polyangiitis (EGPA).

**Objectives:** We decided to retrospectively analyse a large cohort of Polish AAV patients coming from referral centres – members of the Scientific Consortium of the Polish Vasculitis Registry (POLVAS).<sup>2,3</sup>

**Methods:** We conducted a systematic multicenter retrospective study of adult patients diagnosed with AAV between Jan 1990 and Dec 2016. Patients were enrolled to the study by 9 referral centres (14 clinical wards: – rheumatology – 10, nephrology – 2, metabolic diseases – 1, clinical immunology – 1) from 7 Voivodships populated by 22.3 mln inhabitants (58.2% of the Polish population). Patient data have been collected according to the uniform protocol in the POLVAS registry.

**Results:** Distribution of AAV in the Polish population resembles that of north European cohorts.<sup>4</sup> In POLVAS registry 417 (66.7%) patients were diagnosed with GPA, 106 (17.0%) with MPA and 102 (16.3%) with EGPA. Male-to-female ratios were almost 1:1 for GPA (210/207) and MPA (54/52), but EGPA was twice more frequent among women (34/68). Clinical manifestations and organ involvement were analysed both by clinical phenotype (GPA, MPA, EGPA) and ANCA specificity (anti-PR3+, and anti-MPO+). Analysis by ANCA specificity showed no apparent difference as compared to phenotype analysis. Clinical manifestations



of different AAV in the Polish population seems very similar to other European countries.

	GPA	MPA	EGPA	
Number	417	106	102	
Male/female	210/207	54/52	34/68	*,§
Mean (median) age (yrs.); range	48,9 (51,4) <sup>13-80</sup>	61,5 (63,7) <sup>19-85</sup>	44,6 (44,5) <sup>9-85</sup>	*,§
Organ involvement				
General n (%)	355 <sup>(85,1)</sup>	83 <sup>(78,3)</sup>	87 <sup>(85,3)</sup>	NS
Skin n (%)	140 <sup>(33,6)</sup>	24 <sup>(22,6)</sup>	51 <sup>(50)</sup>	*,§
Eye n (%)	114 <sup>(27,3)</sup>	4 (3,8)	6 (5,9)	*,§
ENT n (%)	315 <sup>(75,5)</sup>	18 <sup>(17,0)</sup>	82 <sup>(80,4)</sup>	*,§
Respiratory n (%)	315 <sup>(75,5)</sup>	60 <sup>(56,6)</sup>	100 <sup>(98,0)</sup>	*,§
Heart n (%)	55 <sup>(13,2)</sup>	11 <sup>(10,4)</sup>	43 <sup>(42,2)</sup>	*,§
GI n (%)	46 <sup>(11,0)</sup>	12 <sup>(11,3)</sup>	25 <sup>(24,5)</sup>	*,§
Renal n (%)	252 <sup>(60,4)</sup>	101 <sup>(95,3)</sup>	25 <sup>(24,5)</sup>	*,§
Urinary n (%)	8 (1,9)	3 (2,8)	0	NS
CNS n (%)	45 <sup>(10,8)</sup>	2 (1,9)	8 (7,8)	*,§
Neurological n (%)	75 <sup>(18,0)</sup>	20 <sup>(18,9)</sup>	50 <sup>(49,0)</sup>	*,§

p<0,05; # – GPA vs MPA, \* – GPA vs EGPA, § – MPA vs EGPA

**Conclusions:** This is the first multicenter retrospective study of the Polish patients suffering from with AAV. Demographic characteristics and disease manifestations of AAV patients in POLVAS registry follow the same pattern as those from other European countries.<sup>4</sup>

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SAT0534

#### ANNUAL INCIDENCE OF GIANT CELL ARTERITIS IN URBAN AND RURAL AREAS IN WESTERN NORWAY 1972–2012

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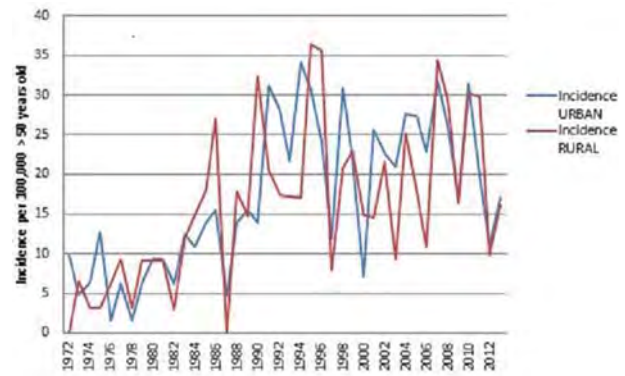
**Background:** Giant cell arteritis (GCA) is the most common vasculitis in adults. The etiology is not fully understood, and environmental factors which may influence the incidence are poorly investigated.

**Objectives:** To determine the potential influence of rural or urban residence on the incidence of GCA during a 41 year period.

**Methods:** Hospital-based retrospective cohort study including patients diagnosed with GCA in Bergen Health Area during 1972–2012. Patients were identified through computerised hospital records using the International Classification of Diseases (ICD)-coding system. Clinical information was extracted by review of the patients' medical journals. The patients' residential address was obtained from the population register in Norway. Municipalities were classified as urban (code 1 and 2) or rural (code 3 thru 6) using the <sup>Statistics Norway 2017</sup> classification of centrality. The background population data was obtained from Statistics Norway ([www.ssb.no](http://www.ssb.no)). Wilcoxon signed-rank test was used for statistical comparison.

**Results:** The inclusion process have been published previously.<sup>1</sup> For the computing of incidence 743 patients were included. Among these there were 536 (72%) females (mean age 73.4 years, SD 8) and 207 (28%) males (mean age 72.6, SD 9). 493 patients (66%) had a positive temporal artery biopsy. 484 patients (65%) had a residential address in a municipality classified as urban and 259 (35%) in a rural municipality. The number of inhabitants (aged ≥50 years) in urban areas (i.e. city of Bergen) was 60 910 in 1972 and 81 972 in 2012. The corresponding number of inhabitants in rural areas was 30 320 and 51 401.

The overall annual cumulative incidence of GCA was 16.7 (95% CI 15.5–18.0) per 100 000 persons ≥50 years. The mean annual incidence for urban municipalities was 17.1 (95% CI 15.9–18.4) per 100 000 ≥50 years. The corresponding incidence for rural areas was 16.1 (95% CI 14.9–17.3), p=0.46. With regards to biopsy-proven GCA, the overall annual incidence was 11.2 (95% CI 10.2–12.3). In urban and rural areas, the incidence of biopsy-proven GCA was 11.7 (95% CI 10.6–12.7) and 10.4 (95% CI 9.4–11.4) respectively, p=0.10. There were large fluctuations in annual incidence in both urban and rural areas (figure 1).



**Conclusions:** Annual cumulative incidence of GCA was slightly higher in urban than in rural areas in our study, but the difference was not statistically significant. This is in contrast to a previous study, which found GCA more prevalent in urban than in rural populations.<sup>2</sup> Further studies are required to determine whether there is a true difference in incidence of GCA in urban versus rural populations, and whether or not exposures to environmental factors may be involved in GCA pathogenesis.

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SAT0535

#### EULAR 2018 CORE SET OF DATA TO BE COLLECTED IN GIANT CELL ARTERITIS REGISTRIES AND DATABASES VIEWPOINTS FROM A EULAR TASK FORCE

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**Background:** Giant cell arteritis (GCA) represents the most common form of primary vasculitis and can be associated with severe and potentially life-threatening complications. Due to its low prevalence, systematically collected data on course and outcome of this disease are scarce.

**Objectives:** The aim of this EULAR Task Force was to identify a core set of data items which can easily be collected from clinicians and facilitates examination of disease course and outcome.

**Methods:** A multidisciplinary EULAR task force group of 20 experts including rheumatologists, epidemiologists and patient representatives was assembled and breakout groups formed for a meeting at which items from a previously compiled collection of core parameters for a GCA registry were evaluated. Results were presented to the other group members following a structured process for discussion and consensus finding. The meeting was followed by several rounds of discussions to achieve consensus.

**Results:** A total of 95 items were identified, subdivided into the following categories: General, Demographics, GCA-related signs and symptoms, Other medical conditions, and Treatment. Suitable instruments and assessment intervals were determined for documentation of each item. To facilitate implementation of the recommendations in both primary care and scientifically oriented registers, a minimum core set of parameters was distilled, with supplemental items that can be added optionally depending on the designated purpose of individual registers.

**Abstract SAT0535 – Table 1.** A minimum core set of parameters to be collected in giant cell arteritis registries and databases

Item	Instrument
<b>General</b> <sup>1,2</sup>	
visit date	date
<b>Demographics</b>	
age <sup>3</sup>	date of birth
<b>GCA-related Signs &amp; Symptoms</b> <sup>4,5</sup>	
cranial <sup>6</sup>	
ocular involvement	
permanent partial visual loss / blindness	y/n (examination)
transient visual loss (amaurosis fugax)	y/n (interview)
scotopia	y/n (interview)
headache	y/n (interview)
<b>Treatment</b> <sup>7</sup>	
glucocorticoids <sup>8,9</sup>	
current GC use	mg per day in prednisone equivalent; route of administration
tapering ongoing	y/n
recent GC use	
continuous (> 3 months) intake	y/n (interview)
immunosuppressants	
conventional synthetic DMARDs	current medication <sup>10,11</sup>
biological DMARDs	historical treatment <sup>12</sup>
	current medication <sup>13,14</sup>

<sup>1</sup> record at baseline  
<sup>2</sup> record during follow-up  
<sup>3</sup> report with date in case it occurs  
<sup>4</sup> record every 3-6 months; acute changes need to be recorded whenever they occur (e.g. new medication, imaging finding, osteoporotic fracture)  
<sup>5</sup> record every 6-12 months; acute changes need to be recorded whenever they occur (e.g. new medication, imaging finding, osteoporotic fracture)  
<sup>6</sup> record annually; acute changes need to be recorded whenever they occur (e.g. new medication, imaging finding, osteoporotic fracture)

**Conclusions:** This core set intends to ensure that data from different GCA registries and databases can be compared for the dual purposes of clinical research and improving clinical care, thereby facilitating collaborative analyses.

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#### SAT0536 MULTIPLE RELAPSES IN PATIENTS WITH GIANT CELL ARTERITIS

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**Background:** Glucocorticoids (GC) remain the mainstay of treatment for patients with GCA. However, relapses and recurrences (events) occurred in 34% to 74.5%

of the patients.<sup>1-3</sup> Most studies compared mainly patients with disease relapses/recurrences to whom without any.

**Objectives:** To compare patients who had multiple events to those who presented only one in order to identify characteristics and predictive factors of multiple events in patient with GCA

**Methods:** From 1976 to 2016, we collected prospectively clinical, laboratory, and pathological data, and the treatments and outcomes, of consecutive patients who were diagnosed to have GCA based ACR classification criteria. We compared these data in patients who had more than one event (group 1), either a relapse or a recurrence, to those who had only one (group 2). Relapse was defined as occurrence of clinical symptoms and/or inflammatory parameters, attributable to GCA, which required increased medication during follow-up i.e. under GC therapy while new disease activity after a period of remission was defined as a recurrence.

**Results:** We included 494 patients for whom data was collected. Forty-seven patients were excluded from our cohort due to lack of data. Among the 447 patients, 228 (51%) presented at least one event. Mean age of this population was 73,3±7 years with female predominance (70%). The median follow-up was 75±55 months. Among these patients 139 (61%) had only one event while 89 (39%) presented more than one. The total number of events was 477 of which 89 recurrences. Events occurred during the first year of treatment in 74% of patients. The majority of these events occurred with a mean prednisone dose of 12.8 ±9 mg/day (median dose 10 mg/d). In univariate analysis, significant differences between both groups is illustrated in table 1. Multivariate analysis showed that ear pain and an elevated ESR were predictive factors of multiple events (OR: 2,45 and 1,93; p=0,04 and p=0,03 respectively). We also found that this risk is lower in patients over 80 years-old (OR: 0,35, p=0,008)

**Abstract SAT0536 – Table 1**

Characteristic	Group 1 (>1; n=89)	Group 2 (=1; n=139)	P
Age (years)	72,67	75,34	0.011
Cough (%)	20,7	10,9	0.042
Ear pain (%)	19,5	9,4	0.029
PMR (%)	11,3	4,3	0.041
Duration of CS (m)	53,7	26,3	0.0001
Complications of CS(%)	28,4	16	0.024
Steroid sparing treatment (%)	30,7	17,8	0.024
Remission(%)	35,6	62,1	0.0001
Death(%)	23,8	36,4	0.046

**Conclusions:** Patients with more than 1 event represent 7% to 46% of patients with event<sup>1-3</sup> which is consistent with our study (39%). The event occurred most often during the first year of GC therapy in our cohort (74% of patients) while it affects 24% to 50% of patients in other series for the same period.<sup>1-3</sup> This difference could be explained by the heterogeneity of GC protocols. We did not found any positive correlation with hypertension, diabetes, and deep vein thrombosis that seemed to be more frequent in patients with multiple events.<sup>2</sup> In our study, this group of patients appeared younger and presented more often with cough, ear pain, and polymyalgia rheumatica that preceded GCA. Logically, in these patients, corticosteroid therapy was longer and the use of GC-sparing agent was more common. Although getting remission was more difficult in these patients, the long-term prognosis is not poor.

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**Disclosure of Interest:** None declared

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#### SAT0537 IS BALANCE AFFECTED IN BEHCET'S DISEASE AND WHAT ARE THE FACTORS THAT EFFECT THE BALANCE?

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**Background:** Behcet's Disease (BD) is a multisystem vasculitis that has a broad range of manifestations. Balance as a complex task may be affected in BD and this may cause postural instability and fall risk.

**Objectives:** The aim of this study was to determine the fall risk in cases with BD with an objective computerised technique and to evaluate the potential related risk factors for falls in these cases.

**Methods:** After calculating sample size as 24 (with%95 confidence interval and± %5 standard deviation), 30 patients with BD (according to The Behcet's

Syndrome International Study Group Criteria) and 30 healthy controls were included. Cases who were not able to tolerate posturography, with a history of orthopaedic surgery and with known balance problems were excluded. The age, gender, disease duration, anamnesis of falls (last 12 months), fear of falling (yes/no) and drugs used were recorded. Also disease activity (with Behçet's Disease Current Activity Form; BDCAF) and fall efficacy (with Tinetti's Falls Efficacy Scale) were evaluated. Fall risk analysis was performed by Tetrax Interactive Balance System which is a computerised posturography device. By this method, fall risk is obtained as a numeric value (0–100) and as ranges indicating low, moderate or high risk of fall. We investigated age, gender, disease duration, fall anamnesis, fear of falling, drug usage, fall efficacy, disease activity as possible related factors to fall risk. Mann–Whitney U, chi square and Spearman correlation tests were used for statistical analysis.

**Results:** The mean ages of the cases and controls were 35,17±9,48 and 33,03±11,813 years, respectively. Symptom duration of the cases was 7,70±6,613 years. 7 cases (23,3%) had anamnesis of falls during the last 12 months, whereas only 8 control (26,7%) had this anamnesis ( $p>0.05$ ). Fear of falling was reported by 43,3% of the cases and 40% of the controls ( $p>0.05$ ). There was no significant difference between case and control groups in terms of FES-I scores (15,97±9,257 and 12,53±3048 respectively;  $p=0,599$ ). With the computerised system used, significantly higher fall risk results were recorded in patients with BD than the controls (50,40±24 710 and 23,13±11,811, respectively;  $p<0,001$ ). Low, moderate and high fall risks were recorded as 30%, 33,3% and 36,7% of the cases and 70%, 30% and 0% of the controls and this distribution was also significantly worse in cases than controls ( $p<0,05$ ). No significant correlation was found between fall risk and other factors including age, gender, disease duration, fall anamnesis, fear of falling, drug usage, disease activity except arthralgia which was significantly correlated with fall risk assessment in cases ( $p<0,05$ ).

**Conclusions:** With an objective computerised technique, fall risk was found to be higher in cases with BD than controls in our study. The higher fall risk in these patients seems to be affected by joint involvement. An increased awareness of the potential fall risk and future studies investigating the possible coexisting balance problems in BD may contribute to the management.

**Disclosure of Interest:** None declared

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SAT0538

#### AORTIC INVOLVEMENT IN RELAPSING POLYCHONDRIITIS: A SYSTEMATIC REVIEW

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**Background:** Aortic involvement (AI) is an important complication of relapsing polychondritis (RP). Current literature is based on case reports and small case series.

**Objectives:** To delineate the clinical characteristics and outcome of AI in RP through a systematic literature review (SLR).

**Methods:** The SLR covered all English articles retrieved with relevant keyword combinations listed in PubMed until October 2017. Initially the titles and abstracts were screened by two investigators and articles considered to be relevant (involvement of the aorta and the aortic valve) were identified. Data extraction was done by the same investigators.

**Results:** The SLR revealed 352 papers of which 162 were discarded at the first step and a further 114 after full reading. After excluding 5 articles reporting on the same patient, we finally had 71 papers reporting 97 patients. The sex distribution was identifiable in 79 patients of whom 39 were men and 40 were women. The median age at the first symptom of RP was 31.5 years [IQR:24–43 years], the median age at RP diagnosis was 36 years [IQR: 28–43 years]; median age at the diagnosis of AI was 37 years [IQR:29–49 years]. Median duration from first RP diagnosis to AI diagnosis was less than 1 year [Range:0–21]. AI was the presenting symptom in 3 patients.

Seventy patients (73%) had involvement of thoracic aorta and 16 (23%) had involvement of the abdominal aorta. Other involved arteries were: coronary (8 patients), subclavian (5 patients), renal (3 patients), iliac (3 patients) and others (8 patients). Two patients had neurologic and renal involvement, respectively.

The most common symptoms were dyspnea (40%), followed by chest pain (13%), abdominal pain (13%) and fever (9%).

The diagnosis of AI was made during surgery in 6 patients and with different radiologic methods ranging from chest x-ray to PET-CT.

All patients excluding 1 received corticosteroids either alone or in combination with classical immunosuppressives (cyclophosphamide, azathioprine, methotrexate, mycophenolate-mofetil) or biologics (infliximab, tocilizumab, adalimumab).

The majority of the patients (53/87 patients (61%) underwent surgery including aortic graft replacement, coronary by-pass, aortic valve or mitral valve replacement operations.

16 patients died after a median follow up of 24 [IQR:11–43] months. The reasons for deaths were mainly vascular (acute myocardial infarction, heart failure,

cardiovascular operation, abdominal aorta dissection, aortic rupture and acute aortic valvular dysfunction).

Information on follow-up was known in 30 patients for a median of 18.5 months [IQR 10–48 months].

**Conclusions:** AI is less frequently recognised but prognostically important complication of RP. Thoracic aorta is the most frequently involved site. Surgery is needed in the majority of patients. Medical treatment is empirical and is based on glucocorticoids and immunosuppressives including biologic agents. Despite treatment, mortality is high (18% during a median of 24 months).

**Disclosure of Interest:** None declared

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SAT0539

#### THE FREQUENCY OF RECURRENT ORAL ULCERS IN FAMILY MEMBERS OF PATIENTS WITH BEHÇET'S DISEASE

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**Background:** It is unknown whether the observed geographic disparities in Behçet's Disease (BD) occurrence reflect primary genetic susceptibility or environmental influences within specific populations. Family aggregation studies may help to discriminate between environmental and genetic components but there are no large family surveys.

**Objectives:** The aim of this study was to contribute to a better understanding of the genetic aspect of familial aggregation studies in Turkey.

**Methods:** The study group consisted of siblings and children of 133 unrelated consecutive patients followed up at the BD outpatient clinic in FSM Hospital, Istanbul. Surveyed individuals were interviewed via telephone regarding if they had ever suffered from recurrent oral ulcerations (ROU). Children less than ten years old were surveyed via discussion with their parents. Symptoms and signs of Behçet's disease in family members were also interviewed via telephone. Subjects experience ROU, at least three episodes in one year, were invited to attend further examination, and also were asked whether anyone in their family had BD.

**Results:** Total 133 patients with BD (86 F, 47 M, respective mean ages: 39.9±11.7, 43.9±10.4 years) had 271 children (137 F, 134 M) and 642 siblings (319 sisters, 323 brothers, respective mean ages: 42.1±13.6, 40.7±14.4 years). All 642 siblings were contacted by telephone: 62 siblings (33 F, 29 M, respective mean ages: 17.9±9.8, 18.2±9.9 years) and 84 children (63 F, 21 M) had positive ROU history. All probands were invited, only 36% family members attended. Apart from patients with BD, 146 family members had ROU (14%). The estimated ROU rate among siblings and children was 9.6%, and 31% respectively. Among members there were 13 patients with BD (2 fathers, 1 mother, 2 children, 3 brothers, 5 sisters). Eleven of these were diagnosed at another centre. We identified 2 additional patients who met ISG criteria during the survey. Only five spouses had ROU (0.5% of members).

**Conclusions:** In a study from Istanbul, ROU was reported as 9.5% in the general population. In our previous study, that was conducted in an area that was reported as having the lowest prevalence rate of BD, this was estimated as 2.1% in the general population. The ROU rate in the current study for total family members was 16%, and 31% for children, which was higher than in the general population. The rate of patients with BD in the studied cohort, apart from previously diagnosed patients, were 140 per 10,000 while the reported prevalence rates changed regionally between 20 per 10,000 and 42 per 10,000 in Turkey. These findings suggest that BD risk is primarily influenced by genetics rather than environmental conditions. Familial aggregation supports a genetic background for BD

**Disclosure of Interest:** None declared

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SAT0540

#### TREATMENT WITH INTRAVENOUS IMMUNOGLOBULIN IN THE VASCULITIS ANCA POSITIVE. 27 CASES STUDIED IN A SINGLE REFERENCE CENTRE

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**Objectives:** Intravenous immunoglobulins (IGIV) is a therapeutic alternative in vasculitis ANCA+ specially in cases of refractory or superinfection. We study the efficiency and safety in the short and long term of the IGIV in the vasculitis ANCA.

**Methods:** Descriptive and observational study of 27 patients with vasculitis ANCA from a reference tertiary hospital. We analysed the treatments received, the clinical and analytical variables and the indexes of activity and evolution (TABLE). Birmingham Vasculitis Activity (BVAS) was the activity index used, and for prognosis Five Factory Score (FFS). Results are indicated as mean ±SD when



there is a normal distribution, or as median [25–75 IQR] when there is an usual one.

**Results:** 27 patients were analysed (14 W/13 M). At the beginning of the IGIV the average age was 57.8±15.98 and the vasculitis average development was 1.29 ±0.68. The vasculitis ANCA subtypes were: **a)**granulomatosis with polyangiitis (n=14; 51.8%), **b)**microscopic polyangiitis (n=9; 33.3%), **c)**eosinophilic granulomatosis with polyangiitis (n=2; 7.4%), **d)**pulmonary-renal syndrome with ANCA positive (n=1; 3.7%) and **e)** indeterminate vasculitis ANCA positive (n=1, 3.7%). Previously to the treatment with IGIV, apart from steroids, they also received: cyclophosphamide (n=12, 44.4%), metotrexate (n=6, 22.2%), infliximab (n=5, 18.5%), rituximab (n=4, 14.8%), azathioprine (n=3, 11.1%), mycophenolate (n=3, 11.1%) and plasmapheresis (n=1; 3.7%).

Refractionness (n=18) and suspicious of infection (n=9) were the reasons for the application of IGIV. The IGIV guideline was 0.4 g/kg/day for 5 consecutive days. 66.6% received methylprednisolona IV concomitant (0.5–1 g/day for 3 days). After a follow-up of 80±68.4 months we observed clinical and analytical improvement, as well as, in the activity indexes (TABLE). The majority of the side effects were lower and IGIV was suspended in just one patient due to severe effects of congestive heart disease.

	Initial (n=27)	1 month (n=22)	3 months (n=22)	6 months (n=22)	1 year (n=22)	2 years (n=22)	Last visit (n=22)
<b>Class, n (%)</b>							
Constitutional symptoms	34 (88.8%)	4 (14.8%)	4 (14.8%)	1 (3.7%)	3 (9%)	1 (3.7%)	0 (0%)
Weight	5 (11.1%)	0 (0%)	0 (0%)	2 (7.3%)	1 (3.7%)	0 (0%)	0 (0%)
ORL	7 (25.9%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (7.4%)	3 (11.1%)
Pulmonary	10 (34.8%)	0 (0%)	0 (0%)	1 (3.7%)	0 (0%)	4 (14.8%)	1 (3.7%)
Arteries	4 (11.8%)	0 (0%)	0 (0%)	1 (3.7%)	1 (3.7%)	0 (0%)	1 (3.7%)
Renal	25 (82.7%)	10 (39.6%)	10 (39.6%)	12 (45.5%)	13 (45.5%)	10 (37%)	12 (44.4%)
Cardiac	4 (11.4%)	1 (3.7%)	1 (3.7%)	2 (7.4%)	2 (7.4%)	1 (3.7%)	1 (3.7%)
Skin	5 (14.8%)	1 (3.7%)	2 (7.4%)	1 (3.7%)	2 (7.4%)	0 (0%)	0 (0%)
DMC	2 (4.8%)	1 (3.7%)	4 (14.8%)	2 (7.4%)	2 (7.4%)	2 (7.4%)	0 (0%)
Arterial	4 (11.4%)	1 (3.7%)	1 (3.7%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
<b>Laboratory, mean±SD</b>							
VSG (mm/h)	66.14 <sup>±</sup> 36.38	61.27 <sup>±</sup> 30.28	58.49±35.87	53.19 <sup>±</sup> 27.83	55.72 <sup>±</sup> 21.18	53.94±30.38	49 <sup>±</sup> 15.36
PCR (mg/dl)	12.36 <sup>±</sup> 16.44	8.83±5.15	1.87 <sup>±</sup> 3.63	4.07 <sup>±</sup> 12.29	10.56±22.39	8.79 <sup>±</sup> 4.33	8.27 <sup>±</sup> 26.94
Creatinine (mg/dl)	1.07 <sup>±</sup> 4.88	1.07 <sup>±</sup> 1.26	1.07 <sup>±</sup> 0.43	1.35±2.63	1.24±0.83	1.37 <sup>±</sup> 0.83	1.19±0.82
Urea (mg/dl)	74 <sup>±</sup> 44.21	61.27 <sup>±</sup> 33.48	53.84±17.81	65.3 <sup>±</sup> 23.43	57.85 <sup>±</sup> 30.64	58.36 <sup>±</sup> 40.81	61.23±29.33
Proteins 24h (mg)	843.77 <sup>±</sup> 1882.31	844.27±1138.25	867.28±1211.74	474 <sup>±</sup> 1564.36	333.47±274.68	259.42±475.76	512±548.88
Triglycer. (mg/dl)	52.87 <sup>±</sup> 22.85	21.87 <sup>±</sup> 47.36	14.52±28.5	6.18 <sup>±</sup> 18.34	3.87 <sup>±</sup> 13.83	4.17 <sup>±</sup> 13.83	3.14 <sup>±</sup> 17.36
<b>Indexes of activity/Progress</b>							
BIAS	4.92	6.07	2.82	2.56	1.42	1.15	NA <sup>†</sup>
FTS	0.85	0.58	0.77	0.45	0.45	0.38	NA <sup>†</sup>

**Conclusions:** IGIV seems to be an effective and secure therapy in the treatment of vasculitis ANCA.  
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**Disclosure of Interest:** None declared  
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**SAT0541** **INCIDENCE OF LARGE VESSEL GCA IN NORTHERN ITALY DURING A 12-YEAR PERIOD (2005–2016)**

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**Background:** There are no studies regarding the incidence of large vessel GCA (LV GCA).

**Objectives:** To investigate the incidence of LVGCA in the Reggio Emilia Area from 2005 through to 2016.

**Methods:** All patients with incident large vessel GCA diagnosed between 1 January 2005 and 31 December 2016 and living in the Reggio Emilia area, were identified by capture and re-capture checking of computerised discharge diagnosis codes (ICD10) and using outpatients databases from rheumatology, internal medicine, surgery, pathology, imaging departments of Reggio Emilia Hospital as well as by examining the Reggio Emilia district database for rare diseases. To be included in the study, patients must satisfy the following 2 criteria: Age at disease onset ≥50 years; evidence of large-vessel vasculitis by angiography, MRA, CTA, PET/CT and/or ultrasonography. We included in the study also patients associating biopsy proven GCA with evidence of LVV. We also evaluated the incidence of biopsy proven GCA without LV in same time period.

**Results:** There were 93 incident cases of LV GCA (66 women, 71%) during the 12 year study period; Mean ±SD age at diagnosis was 72±9 years. Incidence per 1 00 000 persons aged ≥50 years was 3.78 (95% confidence interval [95% CI 3.01, 4.55]). In particular incidence was 1.60 in LV GCA with biopsy proven GCA and 2.18 in LV GCA not biopsy proven GCA (pts biopsy negative and pts in which the biopsy had not been performed). Incidence was significantly higher in women (4.89 [95% CI 3.69, 6.09]) than in men (2.50 [95% CI 1.56, 3.45]) (p<0.0006). The highest incidence in women was observed in the 70–79 years age group (7.72 [95% CI 4.89, 11.58]) while in men the peak of incidence was in the 80–89 age group (4.23 [95% CI 2.50, 8.45]). A progressive increase in total incidence rates was observed during the 4 three years periods from 3.13 (2005–2007) to 4.85 (2014–2016). The incidence per 1 00 000 persons aged ≥50 years of GCA

biopsy proven without LV during the 12 year study period was 4.48 [95% CI 2.22, 9.45].

**Conclusions:** The incidence of LV GCA in the Reggio Emilia area 100.000/aged >50 was 3.78 and it was lower than that of patients with biopsy proven GCA without LV; the incidence of LV GCA was significantly higher in women and increased during the study period.

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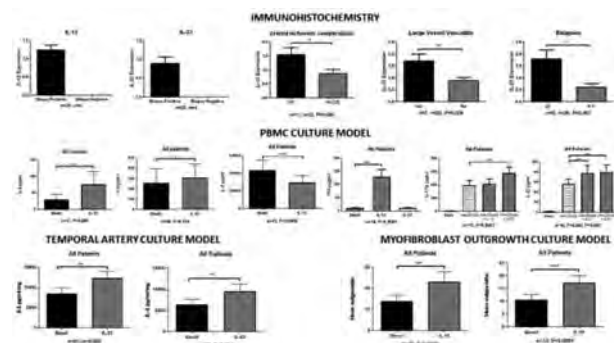
**SAT0542** **INTERLEUKIN-12 AND INTERLEUKIN-23 ARE KEY PATHOGENIC PLAYERS IN GIANT CELL ARTERITIS**

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**Background:** Giant cell arteritis (GCA) is the most common form of systemic vasculitis; the pathogenesis is unclear. Current evidence suggests both the T<sub>H</sub>1 and T<sub>H</sub>17 pathways are important but the proximal initiators and effector cytokines are unknown. IL-12 and IL-23 secreted by dendritic cells are hypothesised as stimulators of these pathways. We have previously reported the efficacy of IL-12/23 blockade with ustekinumab in refractory GCA in a prospective clinical trial.

**Objectives:** To assess the role of IL-12 and IL-23 in GCA pathogenesis.  
**Methods:** IL-12 and IL-23 were quantified by immunohistochemistry in temporal artery (TA) biopsies. TA explant, peripheral blood mononuclear cell (PBMC) and myofibroblast outgrowth culture models were established from patients with GCA and disease controls. PBMCs and TA explants were cultured for 24 hours in the presence or absence of IL-23 (10 ng/ml) or IL-12 (50 ng/ml). Gene expression was quantified by Real-time PCR and cytokine secretion by ELISA. Myofibroblast outgrowths were assessed following 28 days culture and quantified by counting the number of outgrowths/high-power field (hpf).

**Results:** Immunohistochemistry demonstrated IL-12p35 and IL-23p19 in inflammatory cells in TA biopsies (n=33). IL-12p35 and IL-23p19 were only detected in positive TA biopsies. IL-12p35 was increased in those with cranial ischaemic complications (p=0.026) and those with large vessel vasculitis (p=0.006). IL-23p19 was increased in those with two or more relapses (p=0.007). In cultured PBMCs, IL-12 stimulation increased IL-6 (n=17, p=0.009), IL-22 (n=16, p=0.003), and IFN-γ (n=14, p=0.0001) secretion and decreased IL-8 (n=15, p=0.0006) secretion, while IL-23 stimulation increased IL-6 (n=40, p=0.029), IL-22 (n=16, p=0.001), IL-17A (n=16, p=0.0003) and IL-17F (n=9, p=0.012) secretion. In the TA explant culture model, IL-23 stimulation increased gene expression of IL-8 (n=13, p=0.0001) and CCL-20 (n=9, 0.027) and protein expression of IL-6 (n=61, p=0.002) and IL-8 (n=60, p=0.004). IL-12 stimulation (n=14) had no effect; however, IFN-γ and IL-17A were not detectable in this model. IL-12 (n=20, p=0.0005) and IL-23 (n=33, p<0.0001) stimulation increased the quantity of myofibroblast outgrowths from TA biopsies. In all experiments there were no significant differences between biopsy positive GCA, biopsy negative GCA, and disease controls.



**Conclusions:** IL-12 and IL-23 play central and distinct roles in stimulating inflammatory and proliferative pathways in GCA. Our results were consistent in patients with biopsy positive and negative GCA, and in disease controls, suggesting that IL-12 and IL-23 play proximal roles in inducing these pathways.

**Disclosure of Interest:** None declared  
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**SAT0543** QUALITY OF LIFE IN BEHÇET'S SYNDROME: THE ROLE OF PATIENT REPORTED OUTCOME

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**Background:** Behçet's syndrome (BS) is a systemic vasculitis, typically characterised by recurrent oro-genital ulcers, ocular inflammation and skin manifestations; articular, vascular, gastro-enteric and neurological involvement may also occur. The complex pattern of BS profile can effect negatively on patients' quality of life.

**Objectives:** The primary aim of this study was to explore the role of quality of life in BD patients by means of patient reported outcome (PRO); the secondary aim was to study any correlation between disease activity and quality of life.

**Methods:** The study enrolled 130 patients (71 M, 59 F), all fulfilling the International Study Group (ISG) criteria for BS. Their mean age was 42±8 years, 18–77 while the mean age at disease onset was 11±4 years 5–18 and the mean follow-up of 8±2 years. Disease activity was evaluated by means of the Behçet's Disease Current Activity Form (BDCAF), while Short-form-36 (SF-36) was used to evaluate quality of life. Disease activity was compared with the global SF-36 score and with each dimension, that includes: physical functioning, physical disability, body pain, general health, vitality, social functioning, emotional disability, mental health. The statistical analysis was performed using Student t-test, Mann-Whitney-U test, ANOVA and Pearson correlation

**Results:** At time of evaluation, according BDCAF, 51 BS patients (39%) had clinically active disease (36 muco-cutaneous involvement, 21 ocular involvement 10 joint involvement, 6 neurological involvement, 4 gastro-enteric). As expected, the overall SF-36 scores were significantly lower in patients with clinically active disease. Moreover, female BS patients had statistically significant lower scores in all SF-36 domains compared with male patients. When each domain of SF-36 was evaluated, we found that physical disability (p=0.004), body pain (p=0.006), general health (p=0.001), and vitality (p=0.001) were significantly lower in patients with disease activity. Notably, vitality (p=0.001), physical disability (p=0.004), social functioning (p=0.001), emotional disability (p=0.003) and mental health (p=0.001) were significantly lower in patients with muco-cutaneous active disease, compared with the other patients with active disease.

**Conclusions:** The clinicians who take care of any chronic disease would like to correctly know the current status of a patient to manage him properly. In this regard, the combination data of PRO measures and disease activity have been demonstrated to add more information compared to the evaluation of disease activity alone. These consideration suggest that the correct assessment of BS needs a multi-dimensional approach, that fairly includes disease activity, disease damage and quality of life

**Disclosure of Interest:** None declared

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**SAT0544** COMPARING THE CLINICAL PROFILE OF ADULTS AND CHILDREN WITH BEHÇET'S SYNDROME IN THE UK

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**Background:** Behçet's syndrome (BS) is a rare multi-system inflammatory disorder and most commonly presents in young adults. Clinical phenotypic variance across geographical regions is recognised but there has been no UK publication assessing UK BS patients' variance by age groups. BS is primarily a clinical diagnosis, and there is significant diagnostic delay in the UK. Exploration of the phenotype in UK adults and children may help clinicians diagnose BS more effectively.

**Objectives:** Describe and compare the clinical features of adults and children with BS in a UK population.

**Methods:** We examined and compared two cumulative databases of clinical features of BS patients. The paediatric database was collected Great Ormond Street Hospital for Children, London (n=46). The adult database was collected at the Hammersmith Hospital, London (n=560).

**Results:** Oral ulcers were common for both paediatric (97.8%) and adult (96.6%) populations. Genital ulceration also did not differ between paediatric (73.9%) and adult (75.7%) groups. Eye involvement was rare in children (4.3%) versus adults (37%) (p<0.001). Skin involvement was more common in the adult cohort (55.4% vs. 21.7%, p<0.001). There was a trend towards increased vascular involvement in adults (17.5%) versus children (6.5%). The children had higher gastrointestinal involvement compared to adults (21.7% vs. 4.5%, p<0.001)

**Conclusions:** Paediatric BS patients displayed less ocular and skin manifestations compared to the adult BS patients. The BS UK phenotype differs from international cohorts. This information will be valuable in helping clinicians diagnose BS in UK adult and paediatric populations.

**Disclosure of Interest:** None declared

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**SAT0545** GIANT CELL ARTERITIS AND HEMATOLOGIC MALIGNANCIES: A REAL-LIFE EXPERIENCE

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**Background:** Giant cell arteritis (GCA), also known as temporal arteritis, is a vasculitis of large and medium-sized vessels, which commonly involves the extracranial branches of the carotid artery. There are conflicting evidence regarding the association between GCA and both solid and hematologic malignancies.<sup>1-4</sup>

**Objectives:** To assess the coexistence rate of GCA and hematologic malignancies.

**Methods:** This cross-sectional study was performed utilising the database of Israel's largest healthcare association, Clalit Health Services (CHS). All patients with previously documented diagnosis of GCA were included, as well as age- and sex-matched controls without GCA. The proportions of Hodgkin's lymphoma, Non-Hodgkin's lymphoma and multiple myeloma were compared between patients and controls. Univariate analysis was compared using chi-square test for categorical variables and student's t-test for continuous variables. A multivariable logistic regression model was built to assess the covariates associated with each Non-Hodgkin's lymphoma, the hematologic malignancy with the highest number of patients.

**Results:** The study included 5,663 GCA patients and 28 308 controls with a mean age of 71 and 68.3, respectively. Both groups consisted of 69.8% females. Multiple myeloma was observed in 27 GCA patients (0.48%) and 53 controls (0.19%), crude OR=2.56 p<0.001. Hodgkin's lymphoma was observed in 19 GCA patients (0.34%) and 41 controls (0.14%), crude OR=2.33 p=0.004. Non-Hodgkin's lymphoma was observed in 64 GCA patients (1.13%) and 164 controls (0.58%), crude OR=1.96 p<0.001. Multivariable logistic regression model adjusting for age and gender found GCA as independently associated with Non-Hodgkin's lymphoma (adjusted OR 1.96, p<0.001).

Characteristic	No GCA n=28 308	GCA n=5663	OR	p.ratio
Age	68.3±27.4	71.0±15.6	1.00	<0.001
Gender: Female	19 767 (69.8%)	3954 (69.8%)	1.00	0.991
BMI	28.2±5.91	28.1±5.60	1.00	0.081
Socioeconomic status:				
Low	5443 (36.8%)	1970 (34.9%)	Ref.	Ref.
Medium	6241 (42.2%)	2339 (41.4%)	1.04	0.330
High	3093 (20.9%)	1336 (23.7%)	1.19	<0.001
Multiple Myeloma	53 (0.19%)	27 (0.48%)	2.56	<0.001
Hodgkin's Lymphoma	41 (0.14%)	19 (0.34%)	2.33	0.004
Non-Hodgkin's Lymphoma	164 (0.58%)	64 (1.13%)	1.96	<0.001

**Conclusions:** GCA patients have higher rate of hematologic malignancies compared to controls. The association with Non-Hodgkin's lymphoma is the most prominent, and proper screening methods should be applied for early detection and treatment.

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**SAT0546** **SENSORINEURAL HEARING LOSS IN TAKAYASU'S ARTERITIS**

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**Background:** Sensorineural hearing loss has been reported to be increased in several chronic autoimmune and non-autoimmune diseases such as systemic lupus erythematosus (SLE), progressive systemic sclerosis, rheumatoid arthritis, small vessel vasculitides, ankylosing spondylitis and Behçet's syndrome. We had sporadically noted several degrees of sensorineural hearing loss among our Takayasu's arteritis (TA) patients. While some revealed this in their past history, others had relapsing attacks of hearing loss independent of or associated with vascular relapses.

**Objectives:** We formally investigated the frequency and type of hearing loss among TA patients and suitable controls.

**Methods:** The study was done in two parts. In the first part, consecutive TA and SLE patients seen at outpatient clinic along with apparently healthy controls were administered a standardised questionnaire that assessed hearing loss, tinnitus, and episodic vertigo. In the second part, previously registered TA and SLE patients for another study were called to specifically for otological examination and audiometry tests that included pure-tone air and bone conduction, speech audiometry and acoustic reflex threshold test.

**Results:** In the first part, 73 patients with TA, 107 patients with SLE and 133 healthy controls were studied as shown in table 1. The frequency of those with hearing deficit/loss, tinnitus and vertigo were significantly more common among both TA and SLE patients (table 1). While the frequency of those with hearing deficit/loss was similar in TA and SLE, those with tinnitus and vertigo were significantly more common in TA.

In the second part, 50 patients with TA, 22 patients with SLE and 32 healthy controls were studied as shown in table 2. Audiometry tests revealed that several degrees of hearing loss were present in 36% of the patients with TA, 18% of the patients with SLE and 6.3% of the healthy controls ( $p < 0.05$ ). This was mostly due to sensorineural hearing loss in TA patients (13/18) and high-frequency type was the most common pattern. Moreover, those TA patients with sensorineural hearing loss did not show any specific vascular pattern.

**Abstract SAT0546 – Table 1.** Results of the questionnaire survey

	Takayasu's arteritis (n=73)	SLE (n=107)	Healthy controls (n=133)	p value
Mean age	43.7±11.0	44.0±10.3	42.5±8.3	
Disease duration, med [IQR]	7 <sup>3-12</sup>	8 <sup>3-11</sup>	NA	
Hearing deficit/loss, n (%)	20 (27.4)	21 (19.6)	4 (3.0)	<b>0.001</b>
Tinnitus, n (%)	37 (50.7)	34 (31.8)	16 (12.0)	<b>0.001</b>
Vertigo, n (%)	39 (53.4)	38 (35.5)	19 (14.3)	<b>0.001</b>

	Takayasu's arteritis (n=50)	SLE (n=22)	Healthy controls (n=32)	p value
Mean (SD) age	41.3±8.9	42.1 ±10.3	41.1±0.8	NS
Disease duration, med [IQR]	6 <sup>4-11</sup>	7 <sup>3-11</sup>	-	NS
Hearing loss, n (%)	18 (36.0)	4 (18.1)	2 (6.3)	<0.05
Sensorineural type, n (%)	13 (26.0)	2 (9.0)	1 (3.1)	
Conductive type, n (%)	5 (10.0)	2 (9.0)	1 (3.1)	

**Conclusions:** We are unaware of previous surveys of sensorineural hearing loss in TA. Our study shows that audiovestibular system is considerably affected in TA, similar to that observed in SLE. The fact that there was no clear vascular pattern among patients with hearing loss, suggest that small vessel vasculitis was probably the cause of this hearing loss.

**Disclosure of Interest:** None declared

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**SAT0547** **PROGNOSTIC NUTRITIONAL INDEX FOR ESTIMATING BIRMINGHAM VASCULITIS ACTIVITY SCORE IN ANCA-ASSOCIATED VASCULITIS**

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**Background:** The prognostic nutritional index (PNI), which was first introduced by Onodera et al., is calculated based on the serum albumin level and total lymphocyte count in the peripheral blood. It is proposed to be a parameter to reflect immunonutritional status, however, it is also known that albumin and lymphocyte count may decrease in proportion to inflammatory burdens in autoimmune diseases.

**Objectives:** We investigated whether PNI at diagnosis can be used for estimating BVAS at diagnosis in antineutrophil cytoplasmic antibody (ANCA) associated vasculitis (AAV) patients.

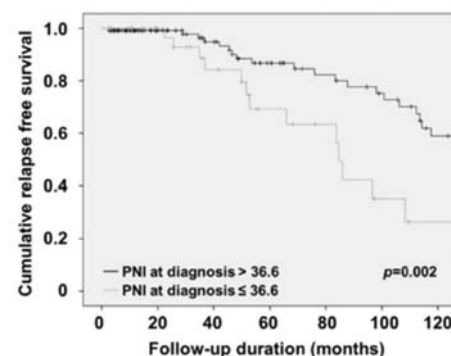
**Methods:** We retrospectively reviewed the medical records of 160 patients with AAV. We calculated Birmingham vasculitis activity score (BVAS). We collected laboratory results including erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), while blood cell, lymphocyte and platelet counts and serum albumin. Prognostic nutritional index (PNI) was calculated by  $(10 \times \text{serum albumin (g/dl)} + 0.005 \times \text{lymphocyte count (mm}^3))$ . The association was assessed linear regression analyses. The optimal cut-off of PNI for predicting relapse was set at 36.6. Comparison of cumulative relapse free survival was analysed by the Kaplan-Meier survival analysis.

**Results:** The mean age at diagnosis was 55.2 years and 48 patients were male. Eighty-five patients had MPA, 41 patients had GPA and 34 patients had EGPA. The mean BVAS and PNI at diagnosis were 11.9 and 43.4. Forty-three patients experienced relapse of AAV. In univariable linear regression analysis, BVAS was positively correlated with ESR and CRP and was negatively correlated with lymphocyte count, serum albumin level and PNI. In multivariable analysis, BVAS was the most significantly associated with only PNI (standardised  $\beta = -0.296$ ). Patients having PNI at diagnosis  $\leq 36.6$  exhibited significantly lower cumulative relapse free survival rate than those having PNI at diagnosis  $> 36.6$  ( $p = 0.002$ ).

**Abstract SAT0547 – Table 3.** Univariable linear regression analysis of BVAS and continuous variables in 160 patients with AAV

	Univariable analysis		
	Regression Coefficient (Crude B)	Correlation Coefficient (R=β)	p value
<b>Demographic data at diagnosis</b>			
Age (year old)	0.027	0.053	0.504
<b>Acute reactants at diagnosis</b>			
ESR (mm/hr)	0.044	0.218	0.006
CRP (mg/L)	0.023	0.169	0.033
<b>Laboratory results reflecting inflammation at diagnosis</b>			
White blood cell count (/mm <sup>3</sup> )	0.000	0.104	0.189
Lymphocyte count (/mm <sup>3</sup> )	-0.002	-0.214	0.007
Platelet count (x1,000/mm <sup>3</sup> )	0.003	0.060	0.449
Serum albumin (g/dL)	-2.557	-0.262	0.001
<b>PNI</b>	<b>-0.252</b>	<b>-0.307</b>	<b>&lt;0.001</b>

BVAS: Birmingham vasculitis activity score; ANCA: antineutrophil cytoplasmic antibody; AAV: ANCA associated vasculitis; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; PNI: prognostic nutritional index.



**Abstract SAT0547 – Figure 2.** The association of PNI at diagnosis with relapse of AAV during the follow-up. We selected the optimal cut-off of PNI at 36.6, divided patients into two groups according to the cut-off and conducted Kaplan-Meier survival analysis. Patients having PNI at diagnosis  $\leq 36.6$  exhibited significantly lower cumulative relapse free survival rate than those having PNI at diagnosis  $> 36.6$  ( $p = 0.002$ ). PNI: prognostic nutritional index; AAV: antineutrophil cytoplasmic antibody.



**Conclusions:** PNI at diagnosis can be used to estimate BVAS at diagnosis and PNI at diagnosis  $\leq 36.6$  may predict relapse during the follow-up in AAV patients.

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SAT0548

#### PROGNOSTIC FACTORS FOR INTERSTITIAL LUNG DISEASE WITH MICROSCOPIC POLYANGIITIS

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**Background:** Many cases of interstitial lung disease (ILD) complicated by microscopic polyangiitis (MPA) show the UIP pattern on chest HRCT, being similar to idiopathic pulmonary fibrosis (IPF/UIP), and the associated prognosis is poor compared with that of MPA without ILD.<sup>1</sup> However, the details have not been fully clarified.

**Objectives:** Prognostic factors of MPA-ILD sufficiently treated with immunosuppressive therapy were investigated.

**Methods:** Of consecutive patients with MPA who received inpatient treatment at our hospitals between 2001 and 2016, MPO-ANCA-positive patients who met the 2007 EMEA classification criteria and had concomitant ILD on HRCT were selected as the subjects. Using the clinical data and HRCT fibrosis score,<sup>2</sup> the outcome and prognostic factors were retrospectively investigated.

**Results:** The subjects were 65 patients with MPA-ILD, 31 and 34 patients were male and female, respectively, and the median age (interquartile range) was 73<sup>67–76</sup> years old. At the time of treatment initiation, MPO-ANCA was 129 (50.9–359) EU; KL-6, 461 (289–665) U/mL; Aa-DO2, 25.1 (15.6–34.2);%FVC, 81.2 (67.8–93.9)%; and%DLco/VA, 62.7 (45.3–73.2)%. On HRCT, the UIP and non-UIP patterns were observed in 44 and 21 patients, respectively. In treatment, prednisolone was administered to 63 patients, immunosuppressants were used in 55 patients, and blood purification therapy was concomitantly administered to 9 patients. MPO-ANCA on the final follow-up was lower than the detection sensitivity in 56 patients. The outcome was death in 23 patients, and the 5- and 10 year survival rates after treatment initiation were 69.8% and 51.1%, respectively (acute exacerbation of interstitial pneumonia: 5 patients, infection and alveolar haemorrhage: 3, infection: 1, pneumothorax: 1, lung cancer: 2, pulmonary hypertension: 1, sudden death: 4, heart failure: 2, renal failure: 2, cerebral haemorrhage: 1, intestinal haemorrhage: 1). Regarding lung disease-related death, the age (p=0.018),%FVC (p=0.026), HRCT fibrosis score (p<0.001), CPFE (p=0.004), decreased lung volume (p=0.041), and honeycombing (p=0.051) were extracted on univariate analysis, and the HRCT fibrosis score was significant on multivariate analysis (p=0.001): The prognosis of patients with a fibrosis score of 19% or higher was significantly poor.

**Conclusions:** Many MPA-ILD patients showed the UIP pattern, but their prognosis was better than that of previously reported IPF/UIP patients, suggesting that early immunosuppressive therapy is effective. However, expansion of fibrosis was included in the factors indicating a poor prognosis, suggesting the limit of immunosuppressive therapy.

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SAT0549

#### AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT) FOR ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODY (ANCA)-ASSOCIATED VASCULITIS (AAV) – A EBMT RETROSPECTIVE SURVEY

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**Background:** ANCA-associated vasculitides (AAV) are chronic autoimmune diseases, which can present with life-threatening multi-system involvement. Despite the use of rituximab and other available modern biologic therapies some patients with AAV develop severe and refractory courses of disease.

**Objectives:** The aim of this study was to analyse outcomes of autologous hematopoietic stem cell transplantation (HSCT) for refractory AAV

**Methods:** Adults receiving HSCT for AAV and whose data were registered within the EBMT Autoimmune Disease Working Party (ADWP) were identified retrospectively through the EBMT database. Treating physicians were surveyed to produce a retrospective evaluation of outcomes.

**Results:** 7 patients underwent HSCT primarily for AAV between 1999–2014 in 6 centres across Europe. 5 females and 2 males were transplanted; 6 had a diagnosis of granulomatosis with polyangiitis (GPA) and 1 eosinophilic granulomatosis with polyangiitis (EGPA). Median age was 39 years (range 32–55 years). Patients had received 4–6 prior lines of therapy, including cyclophosphamide (CYC, with median cumulative dose of 80 g) and steroids in every case, and rituximab in 4 cases. Stem cell source was peripheral blood in every case; CD34-selection was performed in 4 cases, mean CD34<sup>+</sup> cell dose was 4.2 × 10<sup>6</sup>/kg (range 0.6–7.9 × 10<sup>6</sup>/kg). Conditioning regimen was CYC/ATG in 5 patients and CYC in 2 patients. Median follow-up was 86 months (range 1–204 months). Transplant-related mortality (TRM) occurred in 2 causes. All but one patient went into remission but 3 later relapsed at 6, 12 and 36 months, respectively, and required further treatment for disease control. At time of last clinical follow-up, 3 patients had drug-dependent partial response; 1 had drug-dependent complete remission and 1 had drug-free complete remission.

**Conclusions:** Outcomes of HSCT for these heavily pre-treated AAV patients were variable. Only 1 patient achieved drug-free complete remission and TRM was observed in a quarter. Nevertheless, HSCT had the potential to stabilise AAV in patients who initially failed to respond to conventional therapies. These data do not support HSCT for advanced stage ANCA-positive vasculitis, although it may have a place as salvage treatment in otherwise refractory patients. As for other autoimmune diseases, HSCT may provide better outcomes when performed at early stage of disease. Overall, HSCT should only performed in clinical trial settings in experienced centres.

**Disclosure of Interest:** None declared

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SAT0550

#### HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH GIANT CELL ARTERITIS TREATED WITH TOCILIZUMAB IN A PHASE 3 RANDOMISED CONTROLLED TRIAL

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**Background:** Superior rates of sustained glucocorticoid (GC)-free remission were shown in patients with giant cell arteritis (GCA) treated with weekly or every-other-week (wk) subcutaneous tocilizumab (TCZ) 162 mg +26 wk GC taper for 52 wks compared with placebo +26 wk or 52-wk GC taper (PBO +26 or PBO +52) in the GiACTA trial. Statistically significant improvements in SF-36 Physical Component Summary (PCS) scores were reported for weekly TCZ vs PBO +52 and in patient-reported global assessment of disease activity for both TCZ groups vs both PBO groups.<sup>1</sup>

**Objectives:** To report further analysis of patient-reported outcomes (PROs) in GiACTA.

**Methods:** Analyses of SF-36 PCS and Mental Component Summary (MCS), SF-36 domains, and Functional Assessment of Chronic Illness Therapy (FACIT)-fatigue compared patients treated with weekly TCZ (n=100) vs PBO +26 (n=50);

not shown) or PBO +52 (n=51) for 52 wks based on reported data, including all responders as well as patients with post-escape data following flare.  
**Results:** Improvements in SF-36 PCS and MCS scores, 6 of 8 SF-36 domains, and FACIT-Fatigue at wk 52 were significantly greater with weekly TCZ vs PBO +52 (p<0.01) (table 1, figure 1). At wk 52, mean scores met or exceeded age/gender (A/G)-matched normative scores in the weekly TCZ group; higher proportions of patients reported scores exceeding A/G norms in SF-36 PCS and MCS, all SF-36 domains, and FACIT-Fatigue (Table) compared with PBO groups. The median cumulative prednisone dose over 52 wks was lower with weekly TCZ (1862.0 mg) vs PBO +26 (3296.0 mg) or PBO +52 (3817.5 mg) (p<0.01).

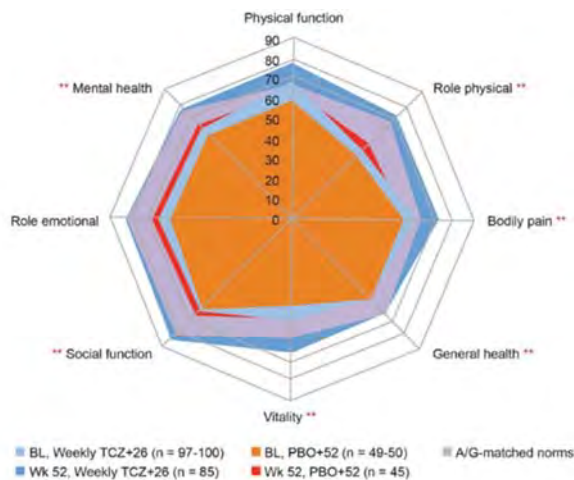
Table. Change From Baseline to Wk 52; mean score (% ≥A/G norms)

	Weekly TCZ+26 n=100			PBO+52 n=51		
	Baseline	Wk 52	LSM Δ	Baseline	Wk 52	LSM Δ
<b>PROs (A/G norms)</b>						
PtGA	43.61	24.36	-17.14	47.78	35.44	-7.56
FACIT-Fatigue (40.0)	36.05 (43.4)	42.08 (73.8)	5.30 <sup>a</sup>	31.42 (32.7)	32.62 (35.6)	-0.42
SF-36 PCS (50.0)	43.10 (23.7)	47.75 (43.5)	4.18 <sup>a</sup>	41.12 (20.4)	41.24 (22.2)	-0.40
SF-36 MCS (50.0)	42.77 (33.0)	51.64 (60.0)	8.10 <sup>a</sup>	40.45 (34.7)	44.86 (40.0)	1.89
<b>SF-36 Domains (A/G norms)</b>						
Physical function (67.56)	69.10 (60.0)	78.28 (78.8)	6.83	59.40 (42.0)	65.44 (55.6)	2.68
Role physical (69.44)	49.56 (25.0)	73.75 (56.5)	20.64 <sup>a</sup>	45.38 (28.0)	53.89 (33.3)	4.46
Bodily pain (64.52)	61.93 (41.0)	73.25 (65.9)	10.89 <sup>a</sup>	55.67 (34.7)	56.27 (31.1)	-2.87
General health (66.49)	55.00 (25.8)	65.81 (57.6)	9.06 <sup>a</sup>	55.69 (36.0)	52.29 (22.0)	-4.05
Vitality (58.65)	50.19 (33.3)	66.13 (68.2)	15.69 <sup>a</sup>	42.38 (28.0)	49.17 (33.3)	3.53
Social function (81.49)	64.25 (29.0)	84.71 (63.5)	17.35 <sup>a</sup>	63.00 (40.0)	67.50 (40.0)	2.34
Role emotional (82.08)	66.38 (43.0)	82.45 (62.4)	13.37	60.33 (36.0)	69.63 (46.7)	3.53
Mental health (77.16)	64.04 (32.3)	77.94 (52.9)	12.54 <sup>a</sup>	59.10 (24.0)	66.33 (31.1)	3.13

LSMΔ, least squares mean change from baseline to wk 52; PtGA, patient-reported global assessment.

All analyses based on observed data (post-escape data included).

<sup>a</sup>p<0.01 vs PBO+52.



\*\*p < 0.01 vs PBO+52.  
 A/G, age/gender; BL, baseline.

**Abstract SAT0550 – Figure 1.** SF-36 Domains at BL and Week 52. \*\*p<0.01 vs PBO+52. A/G, age/gender; BL, baseline.

**Conclusions:** Patients with GCA treated with weekly TCZ 162 mg and a 26-wk GC taper reported statistically significantly greater improvements in health-related quality of life and fatigue that exceeded normative values compared with those receiving 52-wk GC taper alone, in part ascribed to lower steroid doses.

**REFERENCE:**

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**Disclosure of Interest:** V. Strand Consultant for: AbbVie, Amgen, AstraZeneca, BMS, Boehringer Ingelheim, Celgene, Celltrion, CORRONA, Crescendo, EMD Serono, Genentech/Roche, GSK, Janssen, Lilly, Merck, Novartis, Pfizer, Protogen, Regeneron, Samsung, Sandoz, Sanofi, UCB, S. Dimonaco Employee of: Roche, K. Tuckwell Shareholder of: Roche, Employee of: Roche, M. Klearman Employee of: Genentech, N. Collinson Employee of: Roche, J. H. Stone Grant/research support from: Roche, Genentech, Xencor, Consultant for: Roche, Genentech, Xencor

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**SAT0551 LEG ULCERS IN BEHCET'S SYNDROME: AN OBSERVATIONAL SURVEY IN 24 PATIENTS**

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**Background:** Formal experience with leg ulcers in Behçet's syndrome (BS) is limited. It is a rare complication that can be seen during the course of mainly pts with the post-thrombotic syndrome. They can be difficult to manage and may cause disability leading to unemployment and severe impairment in quality of life.

**Objectives:** In this observational survey, we aimed to describe clinical characteristics of pts with leg ulcers.

**Methods:** A total of 24 pts (23 M/1 F) that were seen at our multidisciplinary BS clinic between May 2016-Jan 2018 were evaluated with the help of a standardised questionnaire. Venous Doppler US and if necessary abdominal CT were used to evaluate localization of venous involvement. Biopsies were done if needed. Medical and other interventional treatments were recorded.

**Results:** The mean age at disease onset was 27.5±7.1 years. The median duration between the disease onset and ulcer development was 4.0 [2.5–11.5] years. The median follow-up was 7.8 [IQR: 2.9–14.2] years. Eleven (46%) were unemployed due to the leg ulcer. Venous involvement was present in 20 pts (83%). Lower extremity vein thrombosis was shown in all these 20 pts. It was mostly bilateral (15/20). Femoral veins were the most commonly involved (18/20), followed by popliteal veins (14/20), v. saphena magna or v. saphena parva (7/20), iliac veins or inferior vena cava (8/20). The same 9/20 pts had other large vessel involvement such as pulmonary artery (n=5) or dural sinus thrombosis (n=3). Four pts did not have any venous thrombosis or insufficiency. Histopathologic studies could be done in 3 and showed necrotizing vasculitis in 2 and venous stasis in the 3rd. Twelve pts (50%) had solitary ulcers and 12 had 2 or more. We observed a total of 34 ulcers in 24 pts. They were mostly found around the medial malleolus (15/34) and anterior surface of the tibia (14/34). Five pts had leg ulcers at unusual places such as lateral malleolus (n=2), popliteal fossa (n=1) and posterior surface of the tibia (n=2). Immunosuppressive agents including azathioprine, cyclophosphamide, interferon alpha, infliximab, and corticosteroids were used. Bed rest was advised to almost all. Iloprost infusions were given in 13 (54%) for a median duration of 6 mo. Additionally, larvae of *Lucilia sericata* were tried in 9 pts. Skin graft insertion was used in 2 pts, however, was successful in 1. We observed that in 11 (46%) pts 17 ulcers healed in median 24 mo [IQR:9–78]. In the remaining 13 (54%) pts 17 ulcers stayed as unhealed for a median 7 years [IQR:5–11], despite all interventions and medical treatment. We saw the mean age at BS onset was significantly younger (24.4±5.4 vs 30.4±7.3 years; p<0.05) and the median time between disease onset and ulcer development was significantly shorter (3 [IQR:1–4.5] vs 10 [IQR:4–14] years, p<0.05) in pts with healed ulcers compared to those with unhealed ulcers. There were no apparent associations with the type of management and the severity of venous involvement.



**Conclusions:** Leg ulcer develops mainly due to venous disease in the lower extremities. Peripheral arterial occlusive disease seems to be rarely involved. It may cause unemployment in 46% and be resistant to treatment in 54% of the cases. Ulcers that appear early during the disease course heal faster and is more responsive to treatment.

**Disclosure of Interest:** None declared

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SATURDAY, 16 JUNE 2018

## Osteoarthritis

SAT0552

### BASILINE PREDICTORS OF UPPER LEG MUSCLE STRENGTH OVER 2 AND 4 YEARS IN SUBJECTS WITH KNEE OSTEOARTHRITIS: DATA FROM THE OSTEOARTHRITIS INITIATIVE

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**Background:** Muscle weakness is common in patients with knee osteoarthritis (OA). Muscle weakness negatively impacts future functional status, and has been linked to symptomatic and radiographic progression of knee OA. Limited information is available on the course of muscle strength over time in these patients.

**Objectives:** The aim of the present study is to (i) analyse the course and (ii) to identify baseline predictors for upper leg muscle strength over time in subjects with knee OA.

**Methods:** Data were obtained from the progression cohort of the Osteoarthritis Initiative (OAI) database. Upper leg muscle strength (in N/kg) was measured at baseline, 24 months and 48 months. Potential baseline predictors were demographic factors (age, gender, race, body height, body weight), metabolic factors (body mass index (BMI)), nutrition and vitamin related factors (dietary protein intake, dietary energy intake, vitamin D use, glucosamine use), lifestyle related factors (alcohol consumption, smoking, physical activity), OA-specific factors (KL grade, knee alignment, effusion, pain, pain medication use) and health related factors (comorbidities and depression). Univariable and multivariable mixed model analyses were performed to analyse the course and to identify baseline predictors for muscle strength over time.

**Results:** A total of 1390 subjects with knee osteoarthritis were included. The majority of the subjects were female (57.1%), mean  $\pm$ SD for age was 61.4  $\pm$ 9.1 and mean  $\pm$ SD for body mass index was 30.2  $\pm$ 4.9. All subjects had frequent knee symptoms and radiographic tibiofemoral knee OA (Kellgren en Lawrence score  $\geq$  2) at baseline. Muscle strength was significantly lower at 24 months and 48 months compared to baseline; there was no difference between 24 and 48

months. Older age, being female, higher BMI, being non-Caucasian, lower protein intake (g/kg bodyweight), higher dietary energy intake, alcohol consumption, less physical activity valgus malalignment, higher score on the WOMAC pain subscale and the use of pain medication at baseline were predictors of lower muscle strength over time.

**Conclusions:** Muscle strength decreased over time between baseline and 24 months, but not between 24 and 48 months, which may be attributed to reaching a plateau or to other reasons. In the present study a number of demographic factors, metabolic factors and factors related to nutrition and vitamins, lifestyle and knee OA were found to be predictive for decreased muscle strength over time. This set of baseline factors can be used to identify patients with knee OA at risk for decline of muscle strength over time. External validation of our model is needed.

**Disclosure of Interest:** None declared

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SAT0553

### CHONDROCALCINOSIS OF THE KNEE AND THE RISK FOR KNEE OR HIP OSTEOARTHRITIS PROGRESSION: DATA FROM THE KHOALA COHORT

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**Background:** Cross-sectional studies repeatedly found that chondrocalcinosis (CC) is associated with osteoarthritis (OA). However, whether CC worsens pre-existing knee or hip OA is unclear.

**Objectives:** We conducted this study to assess the impact of knee CC on the risk of 1) incident joint replacement surgery, 2) worsening of pain or function and 3) radiographic progression in patients with symptomatic knee OA.

**Methods:** The KHOALA cohort is a French multicenter population-based cohort of 878 patients with symptomatic knee and/or hip OA (ACR criteria), aged 40–75 years. Patients were followed annually by self-reported questionnaires and by clinical examination and radiography at baseline (year 0), years 3 and 5. Only patients with knee OA were kept for this analysis. CC, defined by the presence of calcium deposits within hyaline or fibro-cartilage on knee radiograph (anteroposterior view), was recorded as present or absent. We used Cox proportional-hazard regression modelling to estimate the local or systemic impact of CC at one knee (index knee) on the 5 year risk of incident total knee replacement (TKR) at the index knee or incident total hip or knee joint replacement (TJR), respectively. In the subgroup of patients without incident TJR during follow-up, logistic regression was performed to assess whether CC was associated with the worsening of Western Ontario and McMaster Universities Arthritis Index (WOMAC) for OA pain or function, or with radiographic progression as defined by a change in Kellgren and Lawrence (KL) grade, between years 0 and 5.

**Results:** Among the 656 patients included (mean  $\pm$ SD age 62.2 $\pm$ 8.5 years; 70.3% females), 93 (14.2%) had CC in at least one knee at baseline. As compared with patients without CC, those with CC were older (64.3 $\pm$ 9.6 vs 61.9 $\pm$ 8.2 years; p=0.009), had longer disease duration (16.4 $\pm$ 10.5 vs 13.0 $\pm$ 7.6 years; p<0.001) and lower body mass index (29.1 $\pm$ 5.3 vs 30.5 $\pm$ 6.3 kg/m<sup>2</sup>; p=0.047). Patients with/without CC did not differ in baseline pain (7.1 $\pm$ 4.3 vs 6.6 $\pm$ 3.8; p=0.26) and function (22.2 $\pm$ 14.7 vs 20.7 $\pm$ 13.5; p=0.32) scores, or KL grade (p=0.69). Overall, 105 (16.0%) and 91 (13.9%) patients underwent TJR and TKR of the index knee, respectively, during follow-up. The presence of CC at one knee did not affect the risk of TKR in the same index knee (HR=1.0; 95% CI 0.6 to 1.8), or risk of TJR (HR=0.9; 95% CI 0.5 to 1.6). In patients without incident TJR surgery (n=551), the presence of CC did not affect the risk of worsened WOMAC pain/function scores or KL grade at year 5.

**Conclusions:** In a population-based cohort of symptomatic knee OA, the presence of CC in the knee did not affect the risk of subsequent TKR or TJR, nor clinical or radiographic outcomes at 5 years. These results suggest that CC is not a risk factor for worsening clinical or structural outcomes in knee OA.

**Disclosure of Interest:** None declared

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SAT0554

### PREOPERATIVE PHYSICAL FUNCTION INFLUENCES ON STAIR CLIMBING ABILITY 1 MONTH AFTER TOTAL KNEE ARTHROPLASTY

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**Objectives:** This study was undertaken to identify preoperative physical performance factors predictive of stair climbing ability 1 month following total knee arthroplasty.



**Methods:** In this prospective cohort study, we assessed a total of 84 patients (8 males and 76 females; average age 72.0±6.0 years) who underwent a primary unilateral total knee arthroplasty (TKA). Before and 1 month after TKA, patients completed physical performance tests including stair climbing test (SCT), 6 min walk test (6MWT), timed up and go test (TUG), isometric knee flexor and extensor strength of the surgical and non-surgical knees, and instrumental gait analysis for spatiotemporal parameters. Self-reported disease-specific physical function measured by using the Western Ontario McMaster Universities Osteoarthritis Index (WOMAC) and self-reported quality of life measured by using Euro QOL five dimensions (EQ-5D) questionnaire.

**Results:** In the bivariate analyses, the postoperative SCT-ascent had a significant positive correlation with the SCT-ascent ( $r=0.29$ ,  $p=0.01$ ), SCT-descent ( $r=0.28$ ,  $p=0.01$ ), TUG ( $r=0.37$ ,  $p<0.01$ ), preoperative age ( $r=0.25$ ,  $p=0.02$ ), and a significant negative correlation with the preoperative 6MWT ( $r=-0.33$ ,  $p<0.01$ ), peak torque (PT) extensor of surgical knee ( $r=-0.29$ ,  $p=0.01$ ), PT flexor of surgical knee ( $r=-0.26$ ,  $p=0.02$ ), PT extensor of the non-surgical knee ( $r=-0.26$ ,  $p=0.02$ ), PT flexor of the nonsurgical knee ( $r=-0.25$ ,  $p=0.02$ ). The postoperative SCT-descent had a significant positive correlation with the SCT-ascent ( $r=0.28$ ,  $p=0.01$ ), SCT-descent ( $r=0.40$ ,  $p<0.01$ ), TUG ( $r=0.38$ ,  $p<0.01$ ), preoperative age ( $r=0.27$ ,  $p=0.01$ ), WOMAC function ( $r=0.30$ ,  $p<0.01$ ), and a significant negative correlation with 6-MWT ( $r=-0.33$ ,  $p<0.01$ ), PT extensor of surgical knee ( $r=-0.23$ ,  $p=0.04$ ), PT flexor of surgical knee ( $r=-0.24$ ,  $p=0.03$ ), PT extensor of the nonsurgical knee ( $r=-0.25$ ,  $p=0.03$ ), PT flexor of the nonsurgical knee ( $r=-0.23$ ,  $p=0.03$ ). In the linear regression analyses, the postoperative SCT-ascent had a significant positive correlation with the preoperative TUG ( $\beta=0.28$ ,  $p<0.01$ ), PT extensor of surgical knee ( $\beta=-0.23$ ,  $p=0.03$ ) and the postoperative SCT-descent had a significant positive correlation with preoperative SCT-descent ( $r=0.28$ ,  $p=0.01$ ), and the age ( $\beta=0.20$ ,  $p=0.04$ ).

**Conclusions:** This study demonstrated that preoperative physical function influenced on postoperative stair climbing ability 1 month after TKA. Using variables easily measured before surgery, it may be possible to predict with good accuracy for postoperative stair climbing ability. In addition, these results could be of importance in determining variable preoperative rehabilitation strategies to improve stair climbing ability, especially focusing on balance, endurance and strengthening exercises.

**Disclosure of Interest:** None declared

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**SAT0555 ON THE WAY TO KNEE REPLACEMENT: TRAJECTORY AND CORRELATION OF KNEE OA MRI CARTILAGE THICKNESS, RADIOGRAPHIC JOINT SPACE WIDTH, AND WOMAC KNEE PAIN IN THE OAI**

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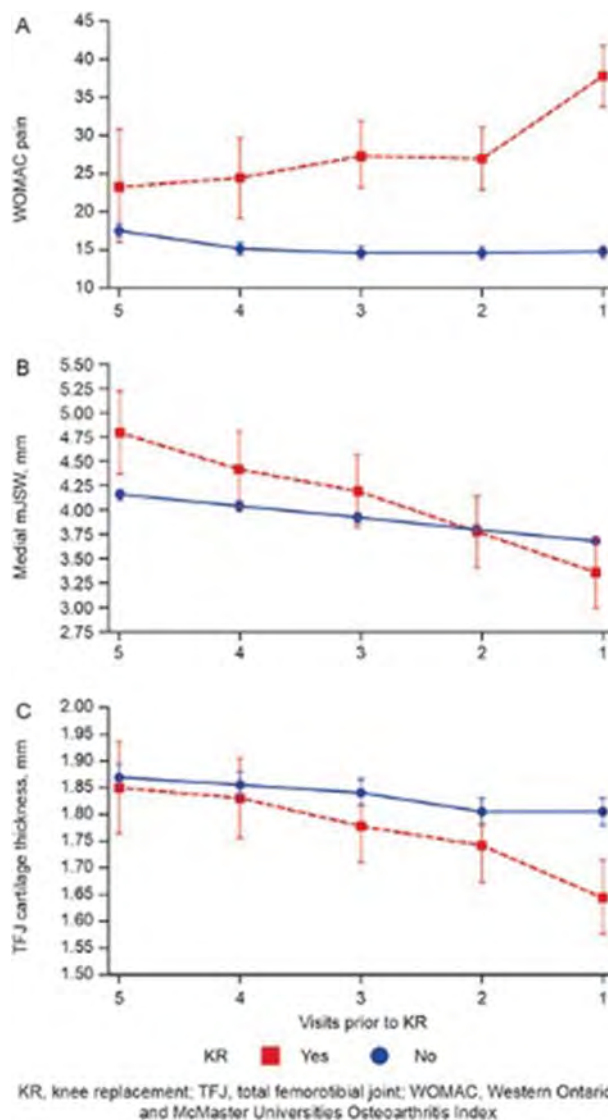
**Background:** Symptoms and structure are both important outcomes in osteoarthritis. However, prior knee osteoarthritis studies have found either poor or no correlation between structural and symptom outcomes.

**Objectives:** 1) Estimate the trajectory of mean WOMAC pain scores, medial minimum JSW (mJSW), and quantitative total tibiofemoral joint (TFJ) cartilage thickness in the five years leading up to knee replacement (KR), in KR case and control knees; 2) Estimate the correlation between change in WOMAC pain scores and change in structural measures prior to KR.

**Methods:** Osteoarthritis Initiative participants with at least one knee that met common eligibility criteria for DMOAD RCTs up to the 4 year follow-up visit were selected for analysis. Eligibility criteria included Kellgren and Lawrence grade of 2 or 3, medial mJSW  $\geq 2.5$  mm, and knee pain at its worst in the past 30 days (4–9 on a 10-point scale, or 0–3 with pain medication). Quantitative MRI (qMRI) cartilage thickness across the TFJ was measured on 3 Tesla MRI. Medial mJSW was measured on fixed flexion weight-bearing radiographs. WOMAC questionnaires were administered annually, and pain scores were scaled 0–100. Mean pain scores and structural measures at each annual visit were estimated with 95% confidence intervals (CI) using mixed effects models. Correlations between changes in structure and WOMAC pain scores were estimated using Spearman correlation coefficients ( $r$ ), with negative coefficients indicating a correlation between loss of cartilage and increase in pain.

**Results:** WOMAC scores and medial mJSW measures were available for 91 cases (KR knees) and 1833 controls, with knees contributing an average of 4.5 WOMAC observations and 3.7 medial mJSW observations to the longitudinal analysis. TFJ cartilage thickness measures were available in 86 cases and 524 controls, with knees contributing an average of 3.1 observations. Over 4 years of

observation, among knees that went on to KR, the greatest annual change in mean WOMAC pain (10.8; 95% CI: 7.2, 14.4) and cartilage thickness ( $-0.100$  mm; 95% CI:  $-0.118$ ,  $-0.082$ ) occurred between the two visits most proximal to KR, while the decrease in mean medial mJSW in the final year ( $-0.408$ ; 95% CI:  $-0.545$ ,  $-0.270$ ) was similar to the rate of loss in prior years (figure 1). Average pain and structure was relatively stable among knees that did not undergo KR. Estimated correlation was moderate between one year change in WOMAC pain and TFJ cartilage thickness among case knees over the year prior to KR ( $n=52$ ,  $r=-0.46$ ), with lower correlations at earlier time points based on a more limited sample. Among control knees, the estimated correlation between annual change in WOMAC pain and structure was negligible at all time points ( $r<0.1$ ).



**Conclusions:** Loss of TFJ cartilage thickness and pain progression were most pronounced over the year prior to knee replacement. Over this time frame, pain progression was moderately correlated with loss of TFJ cartilage, though not with loss of medial mJSW.

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SAT0556

### COST-EFFECTIVENESS OF A BLENDED PHYSIOTHERAPY INTERVENTION IN PATIENTS WITH HIP AND/OR KNEE OSTEOARTHRITIS: A CLUSTER RANDOMISED CONTROLLED TRIAL

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**Background:** Physiotherapy, consisting of education, graded activity and exercises, is effective in improving levels of physical functioning and pain in patients with osteoarthritis (OA) of hip and/or knee. Blended physiotherapy, in which physiotherapy sessions and an online application are integrated, might support patients in taking an active role in the management of their condition and may reduce disease related costs. Recently, the blended physiotherapy intervention e-Exercise was developed.<sup>Bossen 2016</sup> E-Exercise is an integration of five face-to-face physiotherapy sessions with an online application consisting of information-, exercise-, and a graded activity module.

**Objectives:** To evaluate the cost-effectiveness of e-Exercise compared to usual physiotherapy in patients with OA of hip and/or knee, from the societal as well as the healthcare perspective.

**Methods:** This economic evaluation was conducted alongside a 12 month cluster randomised controlled trial, in which 108 patients received e-Exercise and 99 patients received usual physiotherapy. Clinical outcome measures were quality-adjusted life years (QALYs) according to the EuroQol (EQ-5D-3L), physical functioning (HOOS/KOOS) and physical activity (Actigraph Accelerometer). Costs were measured using self-reported questionnaires. Missing data were multiply imputed and bootstrapping was used to estimate statistical uncertainty.

**Results:** Total societal costs and total healthcare costs did not significantly differ between groups. Intervention costs ( $\Delta C$  € -202; 95% CI: -286 tot -120) and medication costs ( $\Delta C$  € -151; 95%: -340 tot -52) were significantly lower in e-Exercise compared to usual physiotherapy. No significant differences in effectiveness were found between groups (QALYS (0-1): B=0.01; 95% CI: -0.03 till 0.04; HOOS/KOOS (0-100): B=1.49; 95% CI: -4.70 till 0.69; Accelerometer (min/dag): B=-3.46; 95% CI: -11.66 till 4.73). For physical functioning and physical activity, the maximum probability of e-Exercise being cost-effective compared to usual physiotherapy was moderate (<0.82) from both perspectives. For QALYs, the probability of e-Exercise being cost-effective compared to usual physiotherapy was 0.68/0.84 at a willingness to pay of € 10.000,- and 0.70/0.80 at a willingness to pay of € 80.000,- per gained QALY, from respectively the societal and the healthcare perspective.

**Conclusions:** E-Exercise itself was significantly cheaper compared to usual physiotherapy in patients with hip and/or knee OA, but not cost-effective from the societal- as well as healthcare perspective. The decision between both interventions can be based on the preferences of the patient and the physiotherapist.

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**Disclosure of Interest:** None declared

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SAT0557

### 10-YEAR TRAJECTORIES OF PAIN IN EARLY KNEE AND HIP OSTEOARTHRITIS; THE CHECK STUDY

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**Background:** Osteoarthritis (OA) is one of the leading causes of chronic pain worldwide. Yet, relatively little is known about the trajectories of pain in early knee and hip OA.

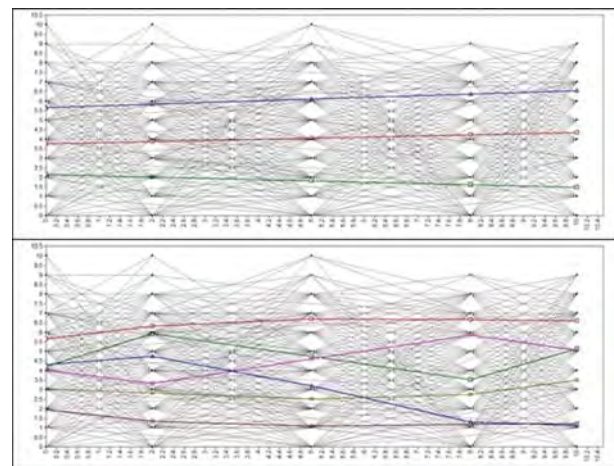
**Objectives:** To determine subgroups of patients with homogenous patterns of pain over 10 years follow-up, among patients with early hip and/or knee complaints in primary care.

**Methods:** Data from the CHECK cohort (Cohort Hip and Cohort Knee) were used. For this cohort, 1002 patients between 45 and 65 years at or within 6 months from their first consultation at a general practitioner for symptoms of their hips and/or knees, were included and followed for 10 years. A numeric rating scale (NRS) for perceived pain was obtained at baseline and after 2, 5, 8 and 10 years, or until total joint replacement. Using these longitudinal data, subgroups of patients with comparable trajectories over time were identified using Latent Class Growth Analysis (LCGA). Models with 3 to 6 classes when using linear, cubic and quadratic trajectories were evaluated using Mplus software.

**Results:** At baseline, the 998 subjects (79% women) with  $\geq 2$  NRS data points available had a mean age of 55.9 $\pm$ 5.2 years and a mean BMI of 26.2 $\pm$ 4.0 kg/m<sup>2</sup>. In total, 410 patients reported knee pain only (41%), 173 hip pain only (17%), and 415 reported both knee and hip pain (42%) at baseline. On a joint level, 156 knees and 160 hips had KL-grade  $\geq 2$  at baseline.

The by LCGA derived models of 3 groups with a linear trajectory and of 6 groups with a cubic trajectory resulted in comparable goodness of fit indicators (Bayesian Information Criteria 17 991 vs. 17927, Akaike Information Criteria 17 927 vs. 17761, and entropy 0.694 vs. 0.683 for the 3 and 6 group models, respectively). Both models and the corresponding trajectories are presented in the figure 1. In the 3 group model, the 'high pain trajectory' (group 2, blue line, n=206) contained most patients with knee and hip complaints (53%), females (84%), TJR (21%), and the highest mean BMI (27.6 $\pm$ 4.6). The 'low pain trajectory' (group 3, green line, n=441) contained most patients with only hip (19%) and only knee (48%) complaints, and the lowest mean BMI (25.3 $\pm$ 3.6).

In the 6 group model, the 'always high pain trajectory' (group 1, red line, n=176) contained most females (86%) and TJR (24%), and the highest mean BMI (27.7 $\pm$ 4.7). The 'always low pain trajectory' (group 5, brown line, n=289) contained most patients with only knee complaints (51%) and the lowest mean BMI (25.0 $\pm$ 3.4). The 'decreasing pain trajectory' (group 2, blue line, n=37) contained most patients with only hip complaints (22%). The 'fluctuating high pain trajectories' (groups 3 (n=88) and 4 (n=142), green and pink lines) contained most females (3:83% and 4:86%), and patients with knee and hip complaints (3:61% and 4:44%).



**Conclusions:** The 6 group model identified more extreme groups with lower minimal and higher maximal prevalence of the presented clinical characteristics. In the end, the conclusion drawn from the two models appear similar; Patients presenting with both knee and hip complaints had less favourable pain trajectories over the following 10 years and the number of total joint replacements was the highest in the groups always reporting high pain scores.

**Disclosure of Interest:** None declared

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SAT0558

### PHARMACOTHERAPY OF OBESITY IN PATIENTS WITH KNEE OSTEOARTHRITIS AND METABOLIC SYNDROME

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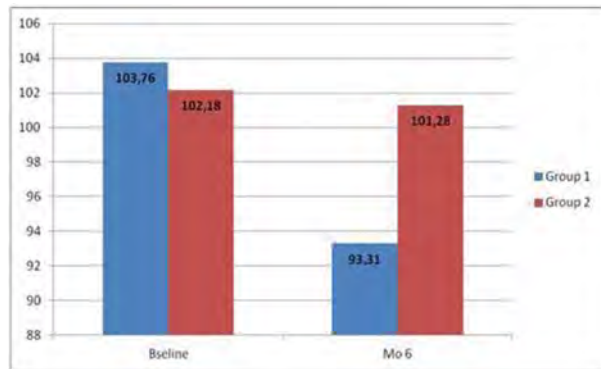
**Background:** Osteoarthritis (OA) is one of most common diseases of locomotor system. Different OA phenotypes are currently identified, including metabolic OA associated with meta-inflammation induced by obesity and metabolic syndrome.

**Objectives:** To assess orlistat pharmacotherapy in patients with knee OA (KOA) and metabolic syndrome.

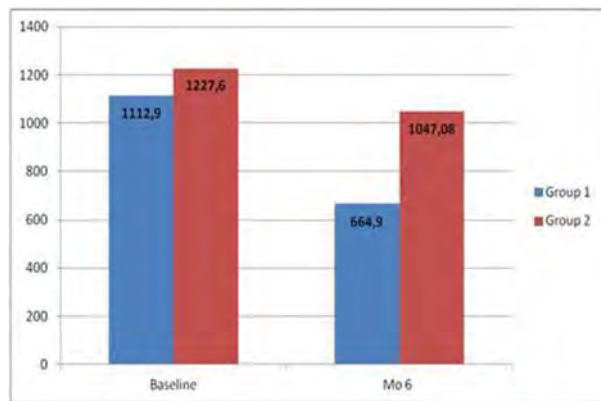
**Methods:** 50 female patients with Kellgren-Lawrence stage II-III KOA were randomised into 2 equal groups in a 6 months study. All pts were administered lifestyle

changes by increasing physical activity and limiting calories (1200 kcal), and patients from Group 1 were additionally treated with orlistat 120 mg 3 times a day. WOMAC and EQ-5D scores and anthropometric data were regularly obtained during the study; biochemistry panel (lipid profile, glucose, CRP), leptin and interleukin-6 were assessed at baseline and at Mo 6.

**Results:** Metabolic syndrome (MS) was diagnosed at baseline in 41 patients. Following orlistat therapy pts from Group 1 managed to reduce their body weight by 10,07% ( $p<0,05$ ; Fig 1), and waist circumference (WC) by 7,5% ( $p<0,05$ ), improving the clinical course of OA: total WOMAC score was reduced by 55% ( $p<0,05$ ; Fig 2), and EQ-5D quality of life was improved by 44% ( $p<0,05$ ). Patients from Group 2 lost only 0,88% of their body weight versus the baseline, and reduced WC by 1%, without changes in EQ-5D scores. MS lab parameters – lipid profile and glucose – did not change significantly after orlistat treatment in Group 1. Patients from Group 2 showed significant increase in total cholesterol ( $p<0,05$ ) after 6 months of dieting and exercising, revealing direct correlation between raised LDL and triglycerides levels and total WOMAC scores. CRP dropped by 23,74% ( $p>0,05$ ) in Group 1. More pronounced decrease of CRP was observed in pts losing more than 10% of their body weight ( $p=0,07$ ). Statistically significant decrease in leptin and IL-6 levels was documented in pts with orlistat-induced significant weight loss ( $p<0,05$ ).



Abstract SAT0558 – Figure 1. Body mass reduction (kg,  $p<0,05$ ).



Abstract SAT0558 – Figure 2. Dynamics of total WOMAC score ( $p<0,05$ ).

**Conclusions:** Abdominal obesity is considered to be the major component of MS and key risk factor for the development and progression of knee OA. Our study demonstrates that induced by orlistat, diet and exercise weight loss by >10% improves the clinical course of KOA and patient’s quality of life, reduces activity of inflammation and improves key parameters of metabolic syndrome. Therefore, KOA and MS therapeutic strategies should include pharmacotherapy of obesity in patients who fail to lose weight with the diet and physical exercise only.

**Disclosure of Interest:** None declared

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**SAT0559 SYSTEMATIC LITERATURE REVIEW (SLR) FOR THE 2018 UPDATE OF THE EULAR MANAGEMENT RECOMMENDATIONS FOR HAND OSTEOARTHRITIS (OA)**

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**Background:** As part of the update of the EULAR management recommendations an SLR of available evidence for hand OA treatment was performed.

**Objectives:** To inform the task force of an overview of available evidence for the efficacy and safety of all non-pharmacological, pharmacological and surgical interventions for hand OA.

**Methods:** We searched Medline, EMBASE, Cochrane Central, and 2016–2017 conference abstracts until June 2017 for (randomised) controlled trials or Cochrane reviews. Observational studies with a comparator were included to assess safety, or effects of surgical interventions. Main efficacy outcomes were pain, function, and hand strength. Risk of bias was assessed. Meta-analysis was performed if possible.

**Results:** Of 7036 records, 127 references were included, of which 50 studies concerned non-pharmacological, 64 concerned pharmacological, and 12 concerned surgical interventions. Most trials were published after 2007. Many studies were at high risk of bias, mainly due to inadequate randomisation or lack of blinding. Overall, effect sizes of effective therapies were small. Beneficial non-pharmacological treatments for pain relief include hand exercise, and prolonged splinting of the thumb base (Table). A single trial showed that assistive devices had no effect on pain, but led to functional improvements (mean difference (MD) –0.3, 95% confidence interval (CI) –0.6;0.01 on AUSCAN function, range 1–5). Topical and oral non-steroidal anti-inflammatory drugs (NSAIDs) proved equally effective for pain relief (Table), while topical NSAIDs led to less adverse events (e.g., risk ratio for withdrawals due to adverse events 0.15, 95% CI 0.03;0.63). Single trials demonstrated beneficial effects for other pharmacological interventions, including chondroitin sulphate, and intra-articular (i.a.) glucocorticoid injections in interphalangeal joints (Table). Compared to placebo, no beneficial effects were demonstrated for i.a. glucocorticoid or hyaluronic acid injections in the thumb base, hydroxychloroquine, or tumour necrosis factor inhibitors (Table). In two trials, structure modification was the primary outcome measure, though no disease-modifying properties were found in these studies. In a Cochrane review no surgical intervention for thumb base OA appeared more effective than another, although in general, more complex procedures led to more complications.

Abstract SAT0559 – Table 1. Effect on pain of main non-surgical interventions for hand OA from controlled trials.

Intervention	Control	N patients (studies)	Duration	OA type or location	RoB	Difference?	Effect estimate [95% CI]
<b>Non-pharmacological interventions</b>							
Hand exercise	No exercise	381 (5)	12 w	-	High	Intervention better	SMD -0.27 [-0.47, -0.07]
Joint protection	No joint protection	257 (1)	26 w	-	High	No	MD -0.79 [-1.7, 0.12] on AUSCAN pain (range 0-20)
Thumb splint	Usual care or no intervention	221 (4)	4-8 w	CMC	High	No	MD -2.9 [-12.2, 6.3] on 100 mm VAS
		137 (2)	13-52 w	CMC	High	Intervention better	MD -37.4 [-25.6; -49.2] on 100 mm VAS
Long thumb splint (MCP + CMC joint)	Short thumb splint (only CMC joint)	189 (3)	2-12 w	CMC	High	No	MD -0.85 [-5.1, 3.4] on 100 mm VAS
DIP splint	No intervention	28 (1)	12 w	DIP	High	No	Median difference -6.5 [range -7.5, 5, p-value 0.53] on 10 cm VAS
<b>Assistive devices</b>							
Information provision	No intervention	70 (1)	12 w	-	High	No	MD 0.4 [-0.8, 0.8] on 100 mm VAS
<b>Pharmacological interventions</b>							
Topical NSAID	Topical placebo	389 (1)	8 w	-	Low	Intervention better	MD -5.9 [-11.7, -0.08] on 100mm VAS
Topical NSAID	Oral NSAID	381 (2)	3 w	"distal hand" IP OA	Low	No	SMD -0.09 [-0.27, 0.17] (1 trial, n=323)
Oral NSAID	Placebo	699 (3)	2-4 w	-	Low	Intervention better	SMD 0.40 [0.20, 0.60] (2 trials, n=654)
Chondroitin sulphate	Placebo	362 (1)	28 w	-	Low	Intervention better	MD -8.7 [-9.8; -7.6] on 100mm VAS
I.a. glucocorticoids	I.a. placebo	208 (3)	28 w	CMC	Low/unclear	No	MD -8.6 [-13.0, -4.2] on 100mm VAS (2 trials, n=166)
I.a. glucocorticoids	I.a. placebo	80 (1)	12 w	IP	Low	Intervention better	MD -18.0 [-31.5; -2.4] on 100mm VAS
I.a. hyaluronic acid	I.a. placebo	239 (3)	28 w	CMC	Unclear	No	MD 5.3 [-9.2, 21.8] on 100mm VAS (1 trial, n=128)
Hydroxychloroquine	Placebo	503 (3)	24-52 w	-	Unclear	No	MD 2.9 [-3.8, 8.2] on 100mm VAS (2 trials, n=307)
TNF inhibitor	Placebo	233 (3)	24-52 w	CMC/OA	Low	No	MD -4.9 [-12.5, 2.8] on 100mm VAS (2 trials, n=178)

**Conclusions:** The number of trials in hand OA has steeply increased over the last decade, providing evidence for several therapeutic options for symptom relief, though no disease-modifying drugs have yet been found. High-quality trials investigating often used analgesics like paracetamol are needed.

**Disclosure of Interest:** None declared

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SAT0560

### FROM A 2-YEAR MULTICENTRE CLINICAL TRIAL IN KNEE OSTEOARTHRITIS, A METABOLOMIC ANALYSIS REVEALS THAT OVER ACTIVATION OF THE CONVERSION PATHWAY OF PHOSPHATIDYLCHOLINE TO LYOPHOSPHATIDYLCHOLINE IS ASSOCIATED WITH KNEE CARTILAGE VOLUME LOSS OVER TIME

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**Background:** While progression of osteoarthritis (OA) is variable, no tools yet exist to predict disease course.

**Objectives:** To identify, using a metabolomic approach, serum marker(s) for predicting knee cartilage volume loss over time measured by magnetic resonance imaging (MRI) in a 24 month Phase III clinical trial in patients with symptomatic knee OA.

**Methods:** 139 knee OA patients who completed the clinical trial according to protocol were selected from a 24 month DMOAD trial studying the effect of licofelone versus naproxen. MRI was performed at baseline and 24 months. Targeted metabolomic profiling was performed on serum collected at baseline. Metabolite ratios as proxies for enzymatic reaction were calculated and used in the analysis. The levels of 186 metabolites were measured and 152 met the quality control requirements. The metabolite concentrations were standardised using the Z-score. 21 952 pair wise metabolite ratios were analysed. A metabolome-wide significance level of  $\alpha=2.3 \times 10^{-5}$  was defined after correcting multiple testing with the Bonferroni method. Univariable and multivariable analyses adjusted for age, sex, BMI and treatment were performed. Gene expression analysis of human OA articular cartilage (n=32) and subchondral bone (n=39) tissues from total joint replacement, and controls (non-OA) from individuals having a fracture (n=21; n=9, respectively) was done to further explore the potential metabolic pathway(s).

**Results:** Data revealed that the baseline ratio of the metabolite lysophosphatidylcholine 18:2 (lysoPC 18:2) to phosphatidylcholine 44:3 (PC44:3) was associated with the cartilage volume loss in the lateral compartment (univariable,  $b=-0.21 \pm 0.04$ ,  $p=8.53 \times 10^{-7}$ ; multivariable,  $b=-0.18 \pm 0.04$ ,  $p=9.5 \times 10^{-6}$ ). Further experiments demonstrated that the lysoPC 18:2/PC44:3 ratio was also significantly ( $r=0.31$ ,  $p=0.0002$ ) correlated with an articular degradation marker, COMP. The data of the increased lysoPC 18:2 to PC44:3 ratio involve a conversion pathway of PC to lysoPC which is catalysed by a phospholipase A2 (PLA2), suggesting a higher activity of PLA2. Data demonstrated that in both human cartilage and subchondral bone tissues, a PLA2, PLA2 group 5 (PLA2G5), was markedly over-expressed in OA cartilage and subchondral bone compared to these non-OA tissues (445% and 158% increase, respectively, all  $p<0.02$ ). Interestingly, in these tissues TNF- $\alpha$  was also upregulated ( $p=0.007$ ;  $p=0.06$ , respectively), and positively correlated with PLA2G5 ( $r=0.71$ ,  $p=0.02$ ).

**Conclusions:** Our data suggest that the ratio of lysoPC 18:2/PC44:3 is predictive of greater risk of cartilage loss in OA. We speculate that this specific conversion pathway may produce a bioactive molecule like oleoylethanolamide (OEA), which has been demonstrated to bind to a novel cannabinoid receptor, GPR119, thus could be a novel therapeutic target for OA treatment.

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SAT0561

### MITOCHONDRIAL BACKGROUND INFLUENCES THE JOINT EVOLUTION IN A CONPLASTIC MOUSE MODEL OF AGEING

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**Background:** Several studies showed interesting associations between mtDNA haplogroups and different OA-related features, including prevalence, incidence or progression of the disease<sup>1-3</sup>. The use of conplastic animals-individuals with the same nuclear genome but different mtDNA variants-provides an accurate tool to study the influence of the mitochondrial background in the ageing process<sup>4</sup>.

**Objectives:** To study the influence of mtDNA variation in the degree of joint deterioration of the knees of aged animals using a conplastic mouse model of ageing

**Methods:** mtDNAs from C57BL/6 and NZB/OlaHsd mice were used. These mtDNAs differ by 12 missense mutations, 4 tRNAs mutations, 8rRNAs mutations and 10 non-coding region mutations. Then, a conplastic mouse strain was developed with the C57BL/6 nuclear genome and the NZB/OlaHsd mtDNA (BL/6<sup>NZB</sup>) to compare with the original C57BL/6 strain (BL/6<sup>C57</sup>) in animals of 25 and 75 weeks. A total of 38 limbs from 19 mice were processed to perform histologic analyses: 8 BL/6<sup>NZB</sup>25 w, 10 BL/6<sup>NZB</sup>75 w, 10 BL/6<sup>C57</sup>25 w and 10 BL/6<sup>C57</sup>75 w.

**Results:** Mankin score data showed significantly increased values in all knees from both strains at 75 w compared with 25 w ( $p<0.001$ ), confirming the ageing of the joint. When 75 w mice were selected (table 1), the BL/6<sup>C57</sup> strain showed a significantly increased score in whole joint ( $p=0.038$ ), femoral condyles ( $p=0.021$ ) and medial femoral condyle ( $p=0.015$ ) than BL/6<sup>NZB</sup> strain. Safranin-O/Fast-green ratio value at 75 w was higher in the medial compartment of BL/6<sup>NZB</sup> compared with BL/6<sup>C57</sup> (both tibial plateau and femoral condyle); however, only the differences detected in the medial compartment of the tibial plateau reached the statistical significance ( $p<0.001$ ), whilst the differences detected in the femoral condyle borderline the statistical significance ( $p=0.091$ ).

The width of the epiphyseal plate was analysed in both tibia and femur bones. The results showed significantly decreased values in BL/6<sup>C57</sup> at 75 w compared with the same strain at 25 w in tibial plateau ( $p<0.001$ ) and femoral condyle ( $p=0.049$ ); however, these differences were not observed in animals belonging to BL/6<sup>NZB</sup> strain. In addition, the BL/6<sup>C57</sup>75 w strain also showed significantly lower values in tibial plateau than BL/6<sup>NZB</sup> strain at the same age ( $p=0.032$ )

**Abstract SAT0561 – Table 1.** Mankin score grading of cartilage destruction in conplastic mice BL/6<sup>C57</sup> and BL/6<sup>NZB</sup> at 75 w

	LTP	LFC	MTP	MFC	TP	FC	Med comp	Lat comp	Whole joint
BL/6 <sup>C57</sup>	5,80	4,40	4,67	6,00	10,44	10,37	10,14	10,20	19,71
BL/6 <sup>NZB</sup>	$\pm 1,81$	$\pm 1,07$	$\pm 2,06$	$\pm 1,07$	$\pm 3,43$	$\pm 1,85$	$\pm 3,02$	$\pm 2,39$	$\pm 4,57$
BL/6 <sup>C57</sup>	5,00	4,38	4,40	4,44	9,40	8,71	8,44	9,13	17,43
BL/6 <sup>NZB</sup>	$\pm 2,11$	$\pm 0,92$	$\pm 2,12$	$\pm 1,24^*$	$\pm 1,78$	$\pm 1,70^*$	$\pm 2,60$	$\pm 1,55$	$\pm 1,72^*$

LTP: lateral tibial plateau; LFC: lateral femoral condyle; MTP: medial tibial plateau; MFC: medial femoral condyle; TP: tibial plateau; FC: femoral condyle; Med comp: medial compartment; Lat comp: lateral compartment; \* $p<0,05$  with respect to BL/6<sup>C57</sup>

**Conclusions:** This study demonstrates the functional impact of mtDNA variation in the process of joint deterioration associated to ageing, leading to consider the mtDNA as a potential therapeutic target in osteoarthritis associated to ageing

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SAT0562

### HIP SHAPE PREDICTS KNEE OSTEOARTHRITIS OUTCOMES OVER A DECADE IN OLDER-ADULTS

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**Background:** Various hip shapes may be important as a risk factor for development and progression of knee osteoarthritis, due to the biomechanical link between the two joints.

**Objectives:** This study aims to identify the relationship between hip morphology and structural and clinical osteoarthritis outcomes in the knee over 10.7 years, in older-adults.

**Methods:** 377 community-dwelling older-adults aged 50–80 years were studied. At baseline, dual-energy X-ray absorptiometry images of the left hip were obtained and hip shapes were described using mode scores from an 85-point statistical shape model. MRI scans were conducted at baseline and a mean follow-up of 10.7(SD:0.67) years later, to assess right knee tibial cartilage volume and bone-marrow lesions(BMLs). Knee pain was assessed using Western Ontario and McMaster Universities Osteoarthritis Index(WOMAC). Knee replacement(KR) data were obtained by data linkage to the Australian Orthopaedic Association National Joint Replacement Registry. Linear mixed-effects, log-binomial models

and survival analysis, were used to investigate associations between hip shape modes and change in cartilage volume, incident BMLs, worsening knee pain and left KR respectively. All models were adjusted for baseline age, sex, BMI, knee injury or surgery and hip radiographic osteoarthritis (ROA), while the KR model was additionally adjusted for WOMAC pain and knee ROA.

**Results:** Ten hip shape modes were identified, describing 78% of the total shape variance in descending order from mode 01 (31% variance) to mode 10 (1.82% variance). Hip shapes with a larger greater trochanter (mode 07) were associated with lower knee cartilage volume loss (Beta:2.14, 95% CI:0.07,4.21), while a shorter and narrower femoral neck shape (mode 09) was related to increased volume loss (Beta:-3.86, 95% CI:-6.16,-1.56). Increasingly non-spherical femoral head (mode 04) was associated with an increased risk of incident BMLs (RR:1.19, 95% CI:1.07,1.34). Those with a longer, wider femoral neck and a larger femoral head (mode 01) had an increased risk of worsening knee pain (RR:1.33, 95% CI:1.09,1.61), whereas those with a smooth curving upper femoral neck (mode 09) had a lower risk of worsening knee pain (RR:0.78, 95% CI:0.67,0.90). A larger greater trochanter and wider femoral neck shape (mode 08) was associated with an increased risk of KR (RR:1.73, 95% CI:1.18,2.52), while increasing acetabular coverage (mode 10) was associated with a lower risk of KR (RR:0.54, 95% CI:0.36,0.8).

**Conclusions:** Hip shape variations were associated with significant MRI-based and clinical outcomes in knee over 10.7 years, possibly due to biomechanical, lifestyle or other factors related to both joints. These results suggest that hip shape may play an important role in the onset and progression of knee osteoarthritis over time.

**Disclosure of Interest:** None declared

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SAT0563

#### IDENTIFICATION AND VALIDATION OF PHYSICAL ACTIVITY PHENOTYPES FOR KNEE OSTEOARTHRITIS: A POPULATION-BASED COHORT STUDY

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**Background:** The identification of phenotypes to reduce heterogeneity of characteristics is important in understanding the development and progression of knee osteoarthritis.

**Objectives:** This study aimed to identify physical activity (PA) phenotypes and to investigate the association of these phenotypes with tibial cartilage volume, bone marrow lesions (BMLs) and knee replacements (KR) over 10.7 years.

**Methods:** 1046 community-dwelling older adults aged 50–80 years were studied. At baseline, PA was measured by pedometers (steps/day), knee pain was assessed using Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and body mass index (BMI) was determined utilising objective weight and height measures. MRI scans were conducted at baseline and 10.7 years to assess tibial cartilage volume and BMLs. The incidence of KR was determined by data linkage to the Australian Orthopaedic Association National Joint Replacement Registry. Latent class analysis was used to determine 'PA phenotypes' based on PA, BMI and WOMAC pain at baseline. Linear mixed-effects models and log-binomial models were used to estimate the associations between the identified PA phenotypes with change in cartilage volume, incident BMLs, and KR surgery over 10.7 years. All models were adjusted for age, sex, and history of knee injury or surgery, while the KR model was additionally adjusted for the prevalence of knee radiographic osteoarthritis.

**Results:** Three PA phenotypes were identified: Class 1: Normal/overweight participants with low levels of PA and low pain (42%); Class 2: Obese participants with low levels of PA and high pain (26%); Class 3: Normal/overweight participants with high levels of PA and low pain (32%). Mean cartilage volume loss over 10.7 years was 465±231 mm<sup>3</sup>. 221 participants had an incident BML while 74 had an incident KR. Class 2 participants had greater cartilage volume loss over 10.7 years (Beta: -79.9, 95% CI -135.8,-23.9) and, had a higher risk of KR (RR 2.36, 95% CI 1.20, 4.67) compared to Class 1 participants. Class 3 was not associated with cartilage volume loss (Beta: -36.2, 95% CI -86.6, 14.1) or risk of KR (RR 0.86, 95% CI 0.40, 1.84) compared to Class 1. Similarly, PA phenotypes were not associated with incident BMLs (Class 2: RR 1.15, 95% CI 0.88, 1.50; Class 3: RR 1.19, 95% CI 0.93, 1.54; compared to Class 1).

**Conclusions:** Our findings support the existence of homogeneous PA profiles, and suggest that PA interacts with body weight and knee pain and has long-term impacts on osteoarthritis outcomes.

**Disclosure of Interest:** None declared

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SAT0564

#### EFFECTS OF EDUCATION AND INCOME ON PREVALENCE, INCIDENCE, AND PROGRESSION OF RADIOGRAPHIC KNEE OSTEOARTHRITIS: AN ANALYSIS OF THE OSTEOARTHRITIS INITIATIVE DATA

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**Background:** Low socioeconomic status (SES) is one of the strongest predictors of morbidity and mortality from many chronic diseases including cardiovascular diseases, obesity, and diabetes.<sup>1</sup> There is insufficient data regarding impact of SES on knee osteoarthritis (OA).

**Objectives:** To evaluate the associations between education, income levels and prevalence, incidence, and progression of radiographic knee OA

**Methods:** For the current analysis we used data from the publicly available Osteoarthritis Initiative (OAI) database. The education status of the participants was dichotomized into either low/moderate or high educational attainment. The income status was dichotomized using 50 K US threshold. A baseline sample was used to analyse the impact of SES on knee OA prevalence (prevalence sample). To evaluate the effects of SES on knee OA incidence and progression we analysed the samples of OAI participants with KL <2 at baseline (incidence sample) and OAI participants with JSN <3 at baseline (progression sample), respectively. We used logistic regression models to assess the association between SES and prevalence and incidence of radiographic knee OA (defined as KL2 and JSN or joint replacement), and disease progression (defined as increase in semiquantitative JSN or a new knee replacement). Generalised estimating equations (GEE) were used to adjust for the correlation between knees. The models were adjusted for multiple covariates including age, race, and body mass index.

**Results:** Prevalence, incidence, and progression samples consisted of 4371 participants (8741 knees), 2268 participants (4535 knees), and 3950 participants (4013 knees), respectively.

Higher education attainment and higher income were associated with decreased prevalence of the knee OA in the crude analyses. After adjustment for confounders these associations became insignificant (Table). There was no effect of SES on incidence and progression of the knee OA.

Table

	Prevalence			
	Unadjusted OR (95% CI)	P value	Adjusted OR (95% CI)	P value
Education	0.8 (0.7–0.9)	<0.001	1.05 (0.9–1.18)	0.48
Income	0.71 (0.64–0.8)	<0.001	1 (0.87–1.4)	0.97

OR – odds ratio, CI – confidence interval

**Conclusions:** Higher levels of education and income are linked with decreased prevalence of radiographic knee OA. Lack of this association after adjustment suggests confounding or mediating effects of other risk factors. Future studies are needed to delineate the precise mechanisms of how SES impact knee OA.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.3424

SAT0565

#### ADJUSTING FOR THE INTRA-ARTICULAR PLACEBO EFFECT IN KNEE OSTEOARTHRITIS THERAPIES

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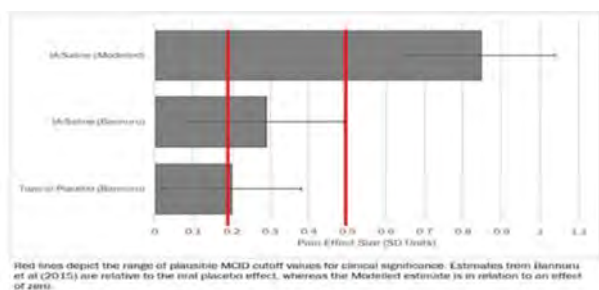
**Background:** Currently, there is a large debate regarding the appropriateness of intra-articular (IA)-saline injection as a "placebo" comparator in knee osteoarthritis (OA) trials and meta-analyses. There is substantial evidence to suggest that the injection of saline into the joint is not without treatment effect.

**Objectives:** This study aimed to assess the current literature's estimates of the IA-saline treatment effect against a range of appropriate minimal clinically important difference (MCID) values to identify if IA-saline provides a therapeutic effect that is not indicative of a null-effect.

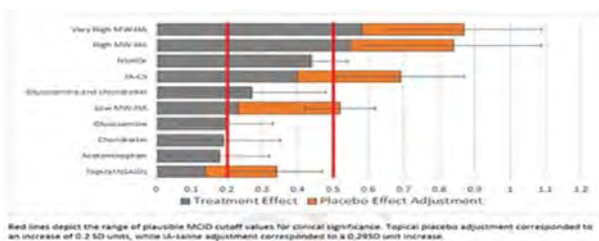
**Methods:** The treatment effect estimates of IA-saline and topical placebo for knee OA pain, relative to oral placebo, were derived from a published network meta-analysis Bannuru et al, 2015 and compared across a range of plausible

MCID values. Effect estimates of pharmacologic knee OA treatments were also extracted from recent high-quality meta-analyses, and the effect of IA-saline or topical placebo was used as an adjustment for meta-analyses that used IA-saline or topical placebo as a comparator, respectively. This was done to estimate the therapeutic effect of these treatment options when compared to a truly null treatment option, as IA-saline has been shown to not be a null-effect intervention. The unadjusted and adjusted treatment effect values were compared across an MCID value range of 0.2 to 0.5 standard deviation units representing an effect size range. This range was used to determine if the adjustment for the effect of IA-saline would affect the potential clinical interpretation of the previously published meta-analysis results.

**Results:** IA-saline provides a therapeutic benefit that is potentially clinically meaningful to patients based on a range of MCID values (figure 1). Across the same range of MCID values, the effects of high molecular weight IA-hyaluronic acid products and IA-corticosteroid treatments were not conclusively clinically significant. However, when reassessing these treatments while accounting for the treatment effect of IA saline, they were found to have a clinically significant effect at the strictest MCID value (figure 2).



**Figure 1.** Effects of Topical Placebo and IA-Saline in Comparison to the MCID Threshold Range



**Figure 2.** Pain Effect Estimates Adjusted for Placebo Effect Estimate (from Bannuru et al [2015])

**Conclusions:** The use of IA-saline as a placebo treatment within RCTs of IA injectable therapies is inappropriately underestimating the true effect of these treatments. When the potential therapeutic effect that IA-saline demonstrates is accounted for, these IA therapies show a considerably larger therapeutic effect.

**REFERENCE:**

[1] Bannuru RR, et al. Ann Intern Med 2015;163:365–372.

**Disclosure of Interest:** I. Simsek Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, T. Phalen Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, A. Bedenbaugh Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, M. Phillips Grant/research support from: Samumed, LLC, J. Tambiah Shareholder of: Samumed, LLC, Employee of: Samumed, LLC  
**DOI:** 10.1136/annrheumdis-2018-eular.3820

**SAT0566 ASSOCIATIONS OF OSTEOCLASTS AND MACROPHAGES IN SUBCHONDRAL BONE WITH SYMPTOMS IN PEOPLE WITH KNEE OA**

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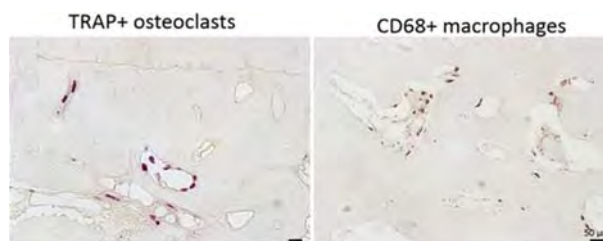
**Background:** Knee pain is a major source of disability and reason for hospital visits in patients with knee OA, but the pain pathophysiology is incompletely

understood. Recent accumulating clinical evidence indicates that subchondral bone plays a role in generating joint pain in OA<sup>1</sup>. Subchondral bone marrow lesions (BMLs) detected on magnetic resonance imaging (MRI) in knee OA are strongly associated with pain<sup>1</sup>. In human OA histology, bone turnover and osteoclast numbers in subchondral bone were increased<sup>2</sup>. Inflammatory CD68-positive macrophages have been detected in bone marrow compartments of subchondral bone tissue from tibial plateaux of OA knees<sup>3</sup>. However, the relevance of osteoclasts and macrophage infiltration in subchondral bone to knee OA symptoms has not been clarified.

**Objectives:** To identify osteoclast and macrophage infiltration in subchondral bone associated with symptomatic knee OA, by comparing cases with similar macroscopic chondropathy, half of whom had sought help for knee pain and undergone total knee replacement (TKR) surgery (symptomatic chondropathy), the other half of whom had not sought help for knee pain but had died from unrelated illness (asymptomatic chondropathy).

**Methods:** Medial tibial plateaux were obtained from people undergoing TKR for OA (symptomatic chondropathy), and from post-mortem (PM) cases matched for similar macroscopic chondropathy scores (asymptomatic chondropathy). Samples were histologically graded for chondropathy, subchondral fibrovascular or macrophage infiltration, and TRAP-positive osteoclasts were quantified (figure 1).

**Results:** Patient demographics are shown in table 1. Total Mankin score showed similar values between the two groups (Table 2). The number of osteoclasts in symptomatic chondropathy cases was significantly higher than in asymptomatic chondropathy cases (table 2). This difference remained significant (p<0.05) after adjusting for age by logistic regression analysis. However, there was no significant difference in macrophage densities between symptomatic and asymptomatic chondropathy groups (Table 2).



**Abstract SAT0566 – Figure 1.** Representative photomicrographs of TRAP-positive osteoclasts and CD68-positive macrophages in subchondral bone.

**Abstract SAT0566 – Table 1.** Patient demographic data.

	PM Asymptomatic chondropathy	TKR Symptomatic chondropathy	p
Number	31	31	
Male/Female	19/12	16/15	0.442
Years (mean ± SD, median (IQR))	75 ± 11 74(68, 84)	65 ± 10* 67(56, 73)	0.001
Revised SFA score (mean ± SD, median (IQR))	69 ± 17 74 (68, 84)	69 ± 17 76(57,79)	0.955
Grade IV chondropathy score (mean ± SD, median(IQR))	30 ± 27 30(0, 50)	30 ± 27 30(0, 48)	0.943

SFA, Systeme Franc, ise D'Arthroscopie

\* : p<0.05 by Mann-Whitney U test

SFA; Sytème Franc, also D'Arthroscopic

\*; p<0.05 by Mann-Whitney U test

**Abstract SAT0566 – Table 2.** Histopathological characteristics.

	PM Asymptomatic chondropathy	TKR Symptomatic chondropathy	p
Total Mankin score (mean ± SD, median (IQR))	8.8 ± 2.7 8 (7, 11)	9.1 ± 2.4 9 (7, 11)	0.755
Fibrovascular tissue(n)	14	11	0.437
Osteoclasts (number / cm)	1.1 ± 3.2 0 (0, 0.8)	3.3 ± 5.7* 1.0 (0, 2.7)	0.019
CD68+ macrophages grading(0-2) (mean ± SD, median (IQR))	1.13 ± 0.76 1 (1, 2)	1.06 ± 0.51 1 (1, 1)	0.626

\* : p<0.05 by Mann-Whitney U test

\*; p<0.05 by Mann-Whitney U test



**Conclusions:** Our results showed that not macrophages but osteoclast infiltration in subchondral bone were associated with symptomatic knee OA. Osteoclasts release protons that generate a local acidosis, which might be a potent activator of nociceptors leading to increased pain signaling<sup>4</sup>. Increased osteoclast activity might be key features associated with bone pain in knee OA.

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SAT0567

#### THE LEADING RISK FACTORS FOR DEVELOPING INTENSIVE PAIN SYNDROME IN THE KNEE JOINTS IN PATIENTS WITH OSTEOARTRITIS

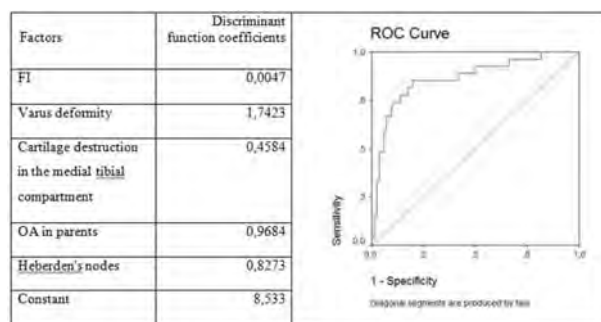
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**Background:** Intensive pain is one of key predictors of OA progression, although it remains unclear which key factors are responsible for the development of intensive pain.

**Objectives:** To study the risk factors for developing intensive knee pain in OA pts in a multicenter prospective study.

**Methods:** A prospective 5 year study included 185 female-patients from 6 RF territorial entities aged 40–75 y. with confirmed knee OA (ACR criteria), stages I-III (Kellgren J.-Lawrence J), who signed an informed consent. Mean age was 59 ± 8,1 y., the age at knee pain onset was 49 ± 8,7 y., and average OA duration was 11 ± 8,4 y. Individual annual medical file included patient's anthropometric parameters, case history, clinical examination findings, evaluation of knee pain intensity by VAS, WOMAC scale, the knee joint status, comorbidities and therapeutic modalities used during the follow up period. Instrumental diagnostic methods included plain radiography of knee joints, dual energy X-ray absorptiometry (DEXA) of the lumbar spine, femoral neck and of subchondral bone of the hip and tibia, ultrasonography (US) and MRI examination of knee joints. Stage II of knee OA was documented in 135 (73%) out of 185 pts, and stage III – in 50 (27%). Statistica 10.0 and SPSS 15.0 packages were used for statistical analysis.

**Results:** Based on pain intensity pts were divided into two groups: Group I – pts with more intensive pain (>70 mm VAS) – 16,8%, and Group II – pts with less intensive knee pain (<70 mm VAS) – 83,2%. Both groups were comparable in terms of age 58,8 ± 7,68 vs 61,06 ± 5,91 y., and disease duration 10<sup>(5–17)</sup> vs 12<sup>(6–18)</sup> y. Although, pts from Group I had statistically significantly higher body weight 82,7 ± 13,8 vs 74,8 ± 12 kg ( $p=0,002$ ), higher pain estimations by WOMAC 374<sup>(348–382)</sup> vs 225<sup>(172–268)</sup> mm ( $p<0,0001$ ), stiffness 100<sup>(80–125)</sup> vs 80<sup>(60–110)</sup> mm ( $p=0,01$ ), FI 1102 (970–1238) vs 820(646–935) mm ( $p<0,0001$ ) and total WOMAC 1541 (1462–1702) vs 1130(880–1291) mm ( $p<0,0001$ ). Besides, pts from Group I had greater percentages of varus knee deformity – 80,6% vs 29,2% (RR=2,76, 95% CI 2,04–3,73,  $p<0,0001$ ) and of H.valgus 87,1% vs 59,1% (RR=1,47, 95% CI 1,22–1,78,  $p=0,002$ ). MRI showed higher rate of bone marrow oedema in medial tibia in Group I: 51,9% vs 31,1% (RR=1,67, 95% CI 1,07–2,59,  $p=0,03$ ) compared to pts from Group II with less pronounced pain. A multivariate (discriminant) analysis showed that the most important risk factors for developing intensive knee pain in OA pts were: significant functional impairment, presence of knee varus deformity and Heberden's nodes, cartilage abnormalities (MRI finding) in medial tibial compartment, familial OA. A model capable of predicting development of intensive knee pain in an individual patient with high accuracy (area under the ROC-curve 0910 (95% CI 0,860–0,961) has been developed based on identified RF and their coefficients. Model accuracy is 87%.



**Conclusions:** In a prospective multicenter study, using comprehensive instrumental modalities (knee radiography, ultrasonography, MRI and BMD of peripheral bones and subchondral hip and tibia) it has been demonstrated that intensive knee pain (>70 mm VAS) is caused by excessive functional impairment, presence of knee varus deformity, Heberden's nodes, OA in parents, and cartilage destruction in the medial tibial compartment.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.4639

SAT0568

#### EFFECT OF DIACERIN VS GLUCOSAMINE-CHONDROITIN ON DISEASE PROGRESSION, AND MEASURES OF FUNCTION IN PERSONS WITH KNEE OSTEOARTRITIS: A 2-YEAR RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

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**Background:** Globally, the incidence of knee osteoarthritis (KOA) is increasing. The treatments available for many years have included both pharmacological and non-pharmacological modalities.

**Objectives:** To examine whether Diacerein is more effective than glucosamine-chondroitin or a placebo in slowing disease progression, physical functioning and/or pain in patients with mild-moderate knee osteoarthritis

**Methods:** In a double-blind RCT, 322 Pakistani patients between 40–65 years with mild to medium KOA (Kellgren-Lawrence Grading 2 or 3) and a history of knee pain >6 months were randomised to receive Diacerein (50 mg twice daily) or Glucosamine-chondroitin (1200 mg twice daily) or a placebo (twice daily) for 2 years. All groups received exercise, diet and pain management counselling. Participant's general health and knee condition was assessed at baseline, 6-, 12-, 18- and 24 months using Short Form<sup>36</sup> Health Survey (SF 36) and WOMAC Index respectively. The Cartilage Oligomeric Matrix Protein (COMP) test was carried out at baseline, 12- and 24 months to assess progression of Knee OA. Improvement was considered at least a 10 point increase in SF36 score from baseline; a 10 point decrease in WOMAC and a 1 unit decrease in COMP.

**Results:** Participants with complete data at the end of year 1 (n=226) and year 2 (n=191) were analysed. At baseline, no significant differences were found in the distribution of gender, age, BMI, COMP levels, SF36, WOMAC scores as well as KL grade levels. Compared to baseline, at year 1 and 2 follow-up, participants in the Diacerein group had statistically significant improvement in their ability to work and other physical activities in comparison with those in the other 2 groups. By the end of year 2, social functioning improved in the Diacerein group as compared to those in the Glucosamine-Chondroitin (GC) group. Compared to placebo group, social functioning improved in the Diacerein group. A greater proportion of GC and placebo group participants reported reduction in their fatigue levels than those in the Diacerein group ( $p$  value=0.007). Using the SF36 scale, in comparison to baseline, improvements were made in all the groups albeit with no between group differences for physical functioning, emotional well-being, and general health. Using the WOMAC index, improvement occurred in all its domains of pain, stiffness and physical functioning, but statistically larger proportion of stiffness reduction took place in the GC group.

**Abstract SAT0568 – Table 1.** Status (% of patients) of functionality in participants at end of Year 1 and Year 2 compared to baseline

	Yr compared to BL	Diacerein <sup>a</sup>	Glucosamine-Chondroitin <sup>b</sup>	Placebo <sup>b</sup>	P-value
<b>General Health - SF-36 Scales</b>					
Role limitation due to physical health	Yr1	Improved (89.6%) <sup>c,c'</sup>	Improved (75.3%)	Improved (75%)	0.04 <sup>c</sup>
	Yr2	Improved (91.8%) <sup>c,c'</sup>	Improved (75%)	Improved (80.3%)	0.04 <sup>c</sup>
Fatigue	Yr1	Decreased (66.2%)	Decreased (80.8%) <sup>c'</sup>	Decreased (86.8%) <sup>c'</sup>	0.007 <sup>c</sup>
	Yr2	Decreased (73.8%)	Decreased (78.1%)	Decreased (69.7%)	0.55
Social functioning	Yr1	Improved (70.1%) <sup>b</sup>	Improved (92.2%)	Improved (72.4%)	0.20
	Yr2	Improved (67.2%) <sup>b</sup>	Improved (45.3%)	Improved (60.6%) <sup>b</sup>	0.04 <sup>c</sup>
Pain	Yr1	Decreased (58.4%)	Decreased (71.2%) <sup>c'</sup>	Decreased (53.9%)	0.08
	Yr2	Decreased (54.1%)	Decreased (45.3%)	Decreased (48.5%)	0.61
<b>Clinical Criteria - WOMAC Scales</b>					
Pain <sup>d</sup>	Yr1	Decreased (83.1%)	Decreased (88.6%)	Decreased (80.8%)	0.33
	Yr2	Decreased (81.8%)	Decreased (91.7%) <sup>c,c'</sup>	Decreased (78.9%)	0.09
Stiffness	Yr1	Decreased (68.9%)	Decreased (71.9%)	Decreased (69.7%)	0.93
	Yr2	Decreased (68.9%)	Decreased (71.9%)	Decreased (69.7%)	0.93
Physical functioning	Yr1	Improved (97.4%)	Improved (97.2%)	Improved (98.7%)	0.80
	Yr2	Improved (98.4%)	Improved (98.4%)	Improved (98.5%)	0.99
Biochemical Criteria: Comp	Yr1	Decreased (45.5%)	Decreased (53.4%)	Decreased (60.5%) <sup>c</sup>	0.17
	Yr2	Decreased (47.5%)	Decreased (43.5%)	Decreased (50%)	0.76

Significant differences between groups in superscript where a)Diacerein, b)Glucosamine-Chondroitin, c)Placebo  
<sup>c</sup>p-value<0.05; <sup>c'</sup>p-value<0.10; Chi-square/Fisher-exact test  
<sup>b</sup>At yr 2 patients showed a 100% decrease in pain levels

**Conclusions:** In the first placebo-controlled trial assessing the effect of Diacerein versus GC, improvements occurred for all 3 criteria: general health, clinical and biochemical. A larger proportion of Diacerein participants improved their physical role limitation and social functioning in comparison to the other groups. Fatigue reduction was not the highest in the Diacerein group but that could be attributed to their increased physical and social functioning. Using the WOMAC scale, improvement in pain, stiffness and physical functioning occurred in all the groups indicating that perhaps the role of non-pharmacological interventions such as diet, exercise and pain management needs to be further explored. Biochemical COMP levels decreased in half the participants in comparison to baseline in all groups.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.1656

## SAT0569 IMPACT OF BARIATRIC SURGERY ON RHEUMATIC DISEASES: A SYSTEMATIC REVIEW AND META-ANALYSIS

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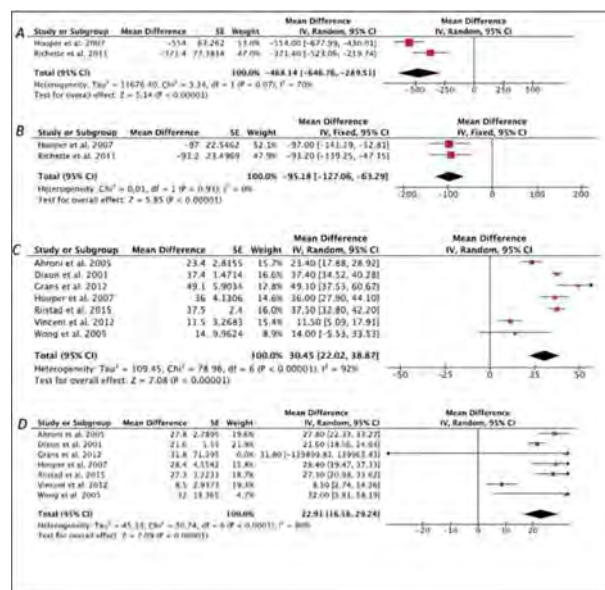
**Background:** Obesity increases the incidence of rheumatic diseases.<sup>1-3</sup> Bariatric surgery (BS), is known to improve obesity-related comorbidities.<sup>4</sup>

**Objectives:** The aim of our study was to assess current literature on the impact of BS on rheumatic diseases.

**Methods:** We systematically searched literature (via Pubmed, Embase, Cochrane library and abstracts from recent ACR and EULAR meetings) for studies evaluating the effects of BS on musculoskeletal disorders and, more precisely, on auto-immune inflammatory rheumatic disorders (AIRD), osteoarthritis and gout. Whenever methodologically feasible and relevant, a meta-analysis was performed with Review Manager Software, with random effects models in case of heterogeneity. Data were extracted by one investigator and independently checked by another.

**Results:** The literature search revealed 399 articles of potential interest, and further examination resulted in 119 studies included in systematic review (SR) and 24 studies fulfilling required criteria for preplanned meta-analysis. According to SR, BS seems to improve AIRD outcomes with notably 1 study on rheumatoid arthritis showing improvement in disease activity scores after BS and 2 studies showing a reduced incidence of psoriatic arthritis in patients who had BS compared to either general population or patients with psoriasis. Studies on patients

with musculoskeletal disorders (mainly osteoarthritis but also undefined musculoskeletal pain) showed an improvement of physical function and pain after BS with pooled mean difference of -468.1 (95% confidence interval [95% CI] -646.8; -289.5) for WOMAC function score, -95.2 [-127.1; -63.3] for WOMAC pain score, 30.5 [22.0; 38.9] for SF36 physical function score, 22.9 [16.6; 29.2] for SF36 bodily pain score (figure 1). Meta-analysis on osteoarthritis surgical management (hip or knee arthroplasty) did not show significant differences between patients who had undergone BS and obese patients without previous BS: pooled Odds ratio (OR) for incidence of orthopaedic reoperation was 1.4 [0.88; 2.3] and pooled OR for incidence of post-operative prosthesis infection was 0.91 [0.53; 1.6]. Hyperuricemia frequency (effect size 0.83 [0.79; 0.87]) and uric acid levels (mean difference -1.5 [-2.0; -0.94]) were significantly decreased after BS. Two studies showed a decrease in gout flares after BS.



**Abstract SAT0569 – Figure 1.** Forest plot for the mean difference between before and after BS for WOMAC function (A), WOMAC pain (B), SF36 physical function (C) and SF36 bodily pain (D) in musculoskeletal disorders

**Conclusions:** Despite heterogeneity, our study supports the benefit of BS on several parameters for obese patients presenting with rheumatic diseases.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.5686

**SAT0570 RESTING-STATE FMRI BRAIN CONNECTIVITY IN HAND OSTEOARTHRITIS**

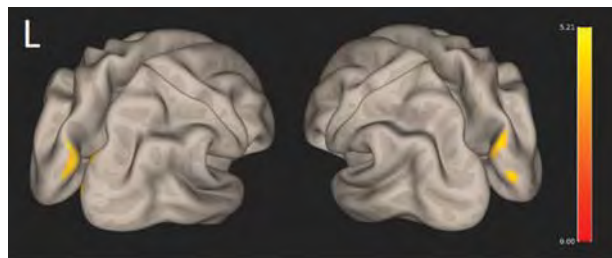
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**Background:** Studies indicate brain grey matter volumetric changes are associated with chronic pain. In people with painful hand osteoarthritis (OA), grey matter volume reductions have been identified in the anterior cingulate cortex (ACC): a key pain-processing region.<sup>1</sup>

**Objectives:** We hypothesised that people with hand OA would have alterations in resting-state functional connectivity networks involving the ACC and other pain-processing brain regions relative to non-OA controls. Furthermore, we hypothesised that treatment with centrally-acting analgesics (pregabalin or duloxetine) would result in connectivity changes in these brain regions.

**Methods:** Resting-state functional MRI (fMRI) of the brain was performed on hand OA participants (n=28) before and after 12 weeks of treatment with duloxetine, pregabalin or placebo, and compared to non-OA participants (n=11) from the same age range (40–75 years). Scans of 7 hand OA participants and 1 control were excluded due to excessive movement artefact. Seed-based correlation analyses were performed using the CONN toolbox<sup>2</sup> to evaluate differences in functional connectivity of networks involving the ACC, insular cortices and thalami between patients and controls, and between pre- and post-treatment states.

**Results:** Relative to non-OA controls, hand OA participants had increased functional connectivity at baseline between the ACC and the cuneil, occipital poles, lateral occipital cortices and precuneus ( $p=0.00054$ , FDR-corrected for multiple comparisons; MNI coordinates  $x=-4$ ,  $y=-86$ ,  $z=+40$ ; 513 voxels) (figure 1). No differences in baseline functional connectivity were seen in the insular cortices or thalami. After treatment, altered functional connectivity was identified between the left thalamus and the ACC and paracingulate gyri ( $p_{FDR}=0.038$ ; MNI coordinates  $x=+2$ ,  $y=+36$ ,  $z=+24$ ; 138 voxels). Pairwise comparisons between treatment cohorts suggested that this represented a reduction in connectivity with pregabalin relative to duloxetine, without reaching statistical significance ( $p_{FDR}=0.062$ ). No significant treatment-associated connectivity changes were evident between duloxetine and placebo, or pregabalin and placebo.



**Abstract SAT0570 – Figure 1.** Seed-based correlation analysis demonstrating increased baseline functional connectivity between the ACC and the cuneil, occipital poles, lateral occipital cortices and precuneus in hand OA participants, relative to non-OA controls.

**Conclusions:** We have shown that people with painful hand OA have altered functional connectivity networks involving the ACC. In conjunction with previous findings of volumetric changes in this pain-processing brain region, this strongly supports the role of maladaptive neuroplasticity and central sensitisation in hand OA pain. Larger studies are required to better confirm if treatment with centrally-acting analgesics leads to connectivity changes in these brain regions.

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**SAT0571 THE RADIOLOGICAL, CLINICAL AND FUNCTIONAL PROPERTIES OF HAND OSTEOARTHRITIS AND THEIR RELATION WITH RADIOLOGICAL FINDINGS IN A TURKISH POPULATION: TLAR-OA STUDY**

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**Objectives:** To evaluate the radiological, clinical and functional properties of hand osteoarthritis and to assess their relationship in a Turkish population.

**Methods:** The subjects with hand OA recruited into the study from the multi-centre national osteoarthritis cohort by the Turkish League Against Rheumatology (TLAR-OA). The demographic characteristics, body mass index (BMI), smoking, finger ratio, (2nd to 4th finger length), grip strengths with Jamar dynamometer, hand pain duration (month), hand pain severity (visual analogue scale; 0–100 mm) were evaluated. The radiological stage of hand OA was assessed according to the Kellgren Lawrence OA staging. The highest stage among the joints involvement was noted as the OA stage of the hand. The functional disability concerning to hand involvement was assessed with Duruöz Hand Index (DHI). The SPSS 24.0 statistical package was used for analysis. The descriptive analysis was performed for all parameters. Spearman's correlation coefficient was used to assess the relation between quantitative variables.

**Results:** A total of 364 subjects (330 female, 34 male) from 15 centres with mean of age 62.96 (SD: 10.22) were recruited into the study. The mean of BMI was 29.54 (SD: 4.51) and the percentage of smoking person was 6.3%. The mean of 2nd finger to 4th finger ratio of the patients was 0.96 (SD: 0.05). The mean of grip strengths of the right hand and left hand were respectively 15.55 kg (SD: 12.88) and 14.13 kg (SD: 11.39), which is lower than normal population.<sup>1</sup> The median pain duration of hand was 24 months (min-max: 1–480 months). The mean VAS score of pain was 5.05 (SD: 2.33). The mean DHI score was 16.82 (SD: 15.53). The patients' radiological OA involvement stages (2,3 and 4) of right and left hands were respectively 26.1% and 23.6% (stage 2); 22.5% and 20.9% (stage 3); 13.2% and 12.4% (stage 4) according to the Kellgren Lawrence scoring. The radiological stages of right and left hands respectively had poor correlation with VASpain ( $\rho=0.152$ ,  $p=0.010$ ;  $\rho=0.158$ ,  $p=0.009$ ); low but significant correlations with Duruöz Hand Index ( $\rho=0.257$ ,  $p<0.0001$ ;  $\rho=0.267$ ,  $p<0.0001$ ) and low but significant correlations with the duration of pain ( $\rho=0.231$ ,  $p<0.0001$ ;  $\rho=0.181$ ,  $p=0.003$ ). There were no significant correlations between the radiological stage of hand OA and BMI, finger ratio, grip strength ( $p>0.05$ ).

**Conclusions:** Although the subjects with hand OA had pain, low grip strength and hand disability; the radiological findings had meaningful relations with only functional involvement and pain duration in our population.

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SAT0572

### INITIAL STRUCTURAL RESPONSE PREDICTS LONG-TERM SURVIVAL OF KNEE JOINT DISTRACTION AS A TREATMENT FOR KNEE OSTEOARTHRITIS

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**Background:** In relatively young patients with end-stage knee osteoarthritis (OA), total knee arthroplasty (TKA) comes with the risk of revision surgery<sup>1</sup>. Knee joint distraction (KJD) is a joint preserving surgery technique, which has been shown to provide clinical and structural improvement for at least five years<sup>2</sup> and postpones the need for TKA.

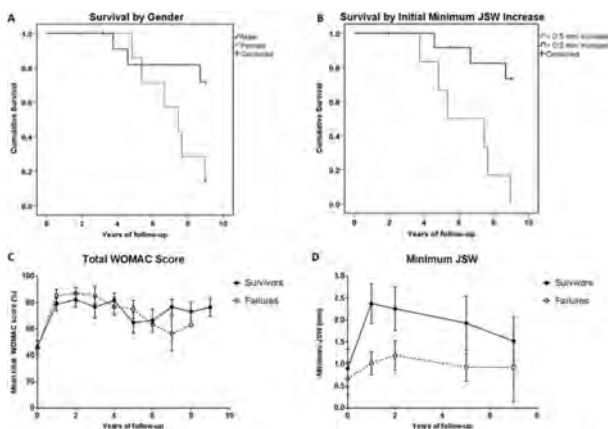
**Objectives:** To evaluate long-term clinical and structural results and identify characteristics predicting survival of the native knee joint after KJD.

**Methods:** End-stage tibiofemoral OA patients (n=20; age <60 years) indicated for TKA were treated with KJD. WOMAC questionnaires (100 best) and VAS pain scores (0 best) were used for clinical evaluation at baseline and every year after treatment, up to 9 years. Minimum and mean joint space width (JSW) and mean bone density of the most affected compartment (MAC) were measured using KIDA software on standardised radiographs (baseline and 1, 2, 5 and 7 years after treatment). The mean cartilage thickness of the MAC was measured on MRI scans (baseline and 1, 2 and 5 years after treatment). Survival after treatment was analysed (failure defined by TKA). Prediction of KJD survival was studied by logistic regression analyses.

**Results:** Three patients withdrew consent. Survival 9 years after treatment was 48%. Survival percentages differed significantly for gender (women 14%, men 70%; p=0.035; figure 1A) and for increase in minimum JSW in the 1st year (<0.5 mm increase 0%, >0.5 mm increase 72%; p=0.002; figure 1B).

Survivors reported clinical improvement compared to baseline:  $\Delta$ WOMAC+29.9 points (95% CI +16.9 to +42.9; p=0.001; figure 1C),  $\Delta$ VAS -46.8 mm (95% CI -31.6 to -61.9; p<0.001). In addition, a significant increase of the minimum JSW (+0.62 mm; 95% CI +0.13 to +1.11; p=0.020; figure 1D) was found after 7 years. No significant changes were found for the mean JSW (+0.36 mm; 95% CI -0.85 to +1.57; p=0.505). In patients whose treatment failed over time, last reported clinical scores were still improved compared to baseline:  $\Delta$ WOMAC+20.5 points (95% CI -1.8 to +42.8; p=0.067; figure 1C),  $\Delta$ VAS -25.4 mm (95% CI -3.2 to -47.7; p=0.030). In contrast, the minimum JSW (+0.22 mm; 95% CI -0.15 to 0.58; p=0.205) and mean JSW (+0.21 mm; 95% CI -1.08 to 1.51; p=0.712) at the last reported time points were no longer increased.

Gender and minimum JSW increase after 1 year predict survival of the native knee joint after 9 years (OR of 14 and 0.02; both p<0.046). The 1 year bone density decrease and mean cartilage thickness increase had a tendency to be predictive (OR of 1.38 and 0.01; both p<0.090).



**Abstract SAT0572 – Figure 1.** Long-term response after treatment with knee joint distraction. (A) Kaplan-Meier survival curves by gender, men (n=11) versus women (n=9), and (B) by increase in minimum joint space width one year after treatment, less than 0.5 mm increase (n = 7) versus more than 0.5 mm increase (n = 13). (C) Total WOMAC score change over nine years and (D) minimum joint space width change over seven years, separated by survivors and patients whose treatment failed within nine years. Mean values  $\pm$ SEM are given.

**Conclusions:** Joint distraction for end-stage knee OA shows long-lasting clinical and structural improvement with a survival of 48% at 9 years. Clinical scores in patients failing treatment were still improved compared to baseline and cannot

fully explain the subsequent TKA surgery. Positive predicting factors for survival of the native knee are male gender and a larger initial increase in minimum JSW (both, 70% survival at 9 years). Potentially, an initial decrease in bone density and an increase in mean cartilage thickness are predictive as well.

Overall, the initial structural response after KJD appears to be important for long-term success of the treatment.

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SAT0573

### PROGRESSION OF PAIN, STIFFNESS, FUNCTION CHANGES, AND ULTRASOUND DETECTED SYNOVITIS AND OSTEOPHYTE FORMATION IN PATIENTS WITH HAND OSTEOARTHRITIS OVER THREE YEARS

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**Background:** Hand osteoarthritis (HOA) is a common and frequent cause of pain. HOA is a heterogeneous group of disorders with two main subsets including non-erosive and erosive disease. Few studies demonstrated inflammatory ultrasound changes and more severe clinical symptoms in patients with erosive compared with non-erosive disease, however the results are inconsistent.

**Objectives:** The aim of this study was to evaluate progression of pain, stiffness, physical impairment and ultrasound features in patients with erosive and non-erosive HOA in a three years longitudinal study.

**Methods:** Consecutive patients with symptomatic HOA fulfilling the American College of Rheumatology (ACR) criteria were included in this study. Joint pain and swelling were assessed. Pain, joint stiffness and disability were assessed by the Australian/Canadian OA hand index (AUSCAN). Radiographs of both hands were examined, and erosive disease was defined by at least one erosive interphalangeal joint. Synovial hypertrophy and power Doppler signal (PDS) were scored with ultrasound. Synovitis was graded on a scale of 0–3 and osteophytes were defined as cortical protrusions seen in two planes. Patients were examined at baseline and at the first, second and third year of follow up.

**Results:** Altogether, 97 patients (7 male) with symptomatic nodal HOA were included in this study and followed between April 2012 and January 2018. Out of these patients, 57 had erosive disease. The number of painful and clinically swollen joints (p<0.05) was significantly higher in patients with erosive compared with non-erosive disease at baseline. The number of painful and clinically swollen joints fluctuate over the second and third year of follow up, but it still remains statistically higher (p<0.01) at the third year of follow up in patients with erosive disease.

According to the AUSCAN, patients with erosive disease had more pain (p<0.05) and stiffness (p<0.01) at baseline. Pain and stiffness, but not function, worsened in patients with erosive compared with non-erosive disease after second year (p<0.01). Pain (p<0.01), stiffness (p<0.05) and also function (p<0.01) worsened in patients with erosive disease at the third year of follow up.

US-detected pathologies such as gray-scale synovitis (p<0.001), intensity of PDS (p<0.01) and number of osteophytes (p<0.01) were significantly higher in patients with erosive disease at baseline. There were improvements in gray-scale synovitis total score and intensity of PDS in patients with non-erosive disease while patients with erosive disease worsened after the second and third year of follow up (p<0.01). On the other hand, the progression of US-determined osteophyte formation was observed in both groups after the second year of follow up but were significantly higher in patients with erosive compared with non-erosive disease after the third year of follow up (p<0.05).

**Conclusions:** The findings of this study show that pain and number of clinically swollen joints associated with US-detected synovial changes and osteophyte formation is more severe in patients with erosive HOA than in patients with non-erosive disease. In addition, osteophyte formation is more likely to progress independent of synovial inflammation.

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**SAT0574 SENSITISATION AND PAIN SEVERITY IN PATIENTS WITH HAND OSTEOARTHRITIS**

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**Background:** Sensitisation, a hyperexcitability of nociceptive pathways, contributes to pain severity in patients with knee osteoarthritis, but this association has not yet been examined in patients with hand osteoarthritis (HOA).

**Objectives:** This study explored the occurrence of central and peripheral sensitisation in patients with HOA and the relationship between sensitisation and hand pain severity.

**Methods:** Three hundred subjects (89% women) with clinical and/or ultrasound-verified HOA were included in this cross-sectional study. Hand pain severity was assessed with the numeric rating scale (0–10 NRS) of hand pain during the last 24 hours, the pain subscale (0–20) of the Australian/Canadian (AUSCAN) hand index and a modified version (0–42 scale) of the Intermittent and Constant Osteoarthritis Pain (ICOAP) questionnaire.

Pressure pain thresholds (PPT) were measured with an algometer at two sites: dorsum of the OA finger joint reported to be most painful to test peripheral sensitisation, and at a remote site (mid-portion of tibialis anterior) to test widespread hyperalgesia. Temporal summation (TS), the increase in perceived pain to repetitive noxious stimuli reflecting central sensitisation, was assessed with a mechanical probe at the right wrist. First, probes with increasing weight (32, 64, 128, 256 or 512 mN) were applied at the wrist until the patients reported pain of at least 4/10. The selected probe was applied to the wrist ten times at 1 Hz. Subjects reported NRS pain on the first, fifth and tenth touch. The magnitude of enhanced TS was defined as TS-Δ: highest pain value of fifth or tenth touch minus the first pain value.

Subjects were categorised into sex-specific PPT tertiles. We then used linear regression to analyse whether PPT tertiles and TS-Δ were associated with pain severity with and without adjustments for age, sex, BMI, use of analgesics (NSAIDs, acetaminophen and opioid-like drugs) and several psychosocial factors (highest degree of completed education (1–7 scale), sleep disturbance (0–4 scale), the Pain Catastrophizing Scale (PCS) and the Hospital Anxiety and Depression Scale (HADS)).

**Results:** Median age was 61 (IQR 57, 67) years, symptom duration 6 (IQR 3, 13) years, and mean body mass index (BMI) was 26.5 (SD 4.9) kg/m<sup>2</sup>. Median TS-Δ among the participants was 1 (IQR 0, 2) and TS-Δ of 2 or more was found in 41%. Subjects in the lowest PPT tertile of their painful OA joint and tibialis anterior reported more hand pain than subjects in the highest PPT tertile. Unadjusted, the relation of PPT to NRS and ICOAP were statistically significant, and for the tibialis anterior only, it was also significantly associated with AUSCAN. After adjusting for potential confounders, the relationships were only statistically significant for NRS (Table).

We found positive adjusted associations between increasing TS-Δ and NRS (beta 0.18, 95% CI 0.04, 0.32) and ICOAP (beta 0.63, 95% CI –0.16, 0.3), but not for AUSCAN pain (beta 0.12, 95% CI 0.11, 1.16).

**Abstract SAT0574 – Table 1.** Pain severity across different levels of pressure pain thresholds.

	NRS	AUSCAN Pain	ICOAP
PPT- tertiles	Mean (SD)	Mean (SD)	Median (IQR)
Highest (ref.)			
Painful OA joint	3.48 (2.15)	7.87 (4.00)	9 (4, 17)
Tibialis anterior	3.06 (2.00)	7.31 (3.90)	9 (4, 14)
Middle			
Painful OA joint	3.49 (2.27)	8.08 (4.20)	10 (5, 15)
Tibialis anterior	3.59 (2.13)	8.01 (3.88)	11 (4, 15)
Lowest			
Painful OA joint	4.35 (2.32) *	8.72 (3.98)	14 (7, 22)
Tibialis anterior	4.65 (2.40) *	9.24 (4.21)	15 (8, 23)

Adjusted for age, sex, BMI, use of analgesics, education level, degree of sleep disturbance, PCS and HADS. \*Level of significance p<0.05.

**Conclusions:** In patients with HOA, sensitisation, as reflected by lower PPTs and enhanced TS, was significantly associated with greater pain severity. Future studies are needed to explore whether sensitisation is a result of OA pathology or traits of certain patients, and whether treatments aiming to reduce sensitisation might reduce pain in patients with HOA.

**Disclosure of Interest:** None declared

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**SAT0575 SAFETY AND EFFICACY OF LUTIKIZUMAB (ABT-981), AN ANTI-INTERLEUKIN-1 ALPHA/BETA DUAL VARIABLE DOMAIN (DVD) IMMUNOGLOBULIN, IN SUBJECTS WITH KNEE OSTEOARTHRITIS: RESULTS FROM THE RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PARALLEL-GROUP PHASE 2 TRIAL**

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**Background:** Animal studies suggested that inhibiting IL-1α/β with lutikizumab (formerly, ABT-981) may reduce pain and slow structural progression in OA.

**Objectives:** This study (NCT02087904; ILLUSTRATE-K) assessed the safety and efficacy of lutikizumab in subjects with knee OA.

**Methods:** Subjects (n=350; 347 analysed) with Kellgren-Lawrence (KL) grade 2–3 knee OA, synovitis on MRI or US, and visual analogue scale knee pain score 4–8 (range, 0–10) were randomised to receive placebo (PBO) or lutikizumab 25, 100, or 200 mg subcutaneously (sc) every 2 wk (E2W) for 50 wk. The primary endpoints were change from baseline (BL) in WOMAC pain at wk 16 and change from BL in MRI synovitis at wk 26. Other endpoints included WOMAC function and OMERACT/OARSI response (wk 16, 26, and 52) MRI cartilage volume (wk 26 and 52), and x-ray joint space narrowing (JSN) (wk 52).

**Abstract SAT0575 – Table 1.** Changes From Baseline in Efficacy Endpoints (LOCF)

Signs and Symptoms Endpoints (LOCF data)	PBO (n=85)	Week 16 LUTIKIZUMAB, mg sc E2W			Week 52 LUTIKIZUMAB, mg sc E2W			
		25 (n=88)	100 (n=84)	200 (n=88)	PBO (n=85)	25 (n=88)	100 (n=84)	200 (n=88)
WOMAC pain (0–50)	-8.9	-9.2	-11.8	-10.1	-11.0	-12.1	-12.2	
P value vs PBO		0.834	0.050*	0.415	0.500	0.180	0.137	
WOMAC function (0–170)	-28.7	-29.8	-36.3	-32.1†	-32.9	-36.1	-39.7†	
P value vs PBO		0.818	0.109	0.465	0.558	0.295	0.218	
OMERACT/OARSI response, %	60.0	67.0	72.6	65.5†	70.6	69.3	71.4	
P value vs PBO		0.311	0.080	0.435	0.824	0.964	0.783	
Structural Endpoints (observed data)								
		Week 26 LUTIKIZUMAB, mg sc E2W			Week 52 LUTIKIZUMAB, mg sc E2W			
Endpoint	PBO	25	100	200	PBO	25	100	200
WORMS synovitis effusion volume	0.07	-0.01	-0.08	-0.07	-0.05	-0.05	-0.06	-0.01
n	70	76	70	75	59	66	62	66
P value vs PBO		0.384	0.095	0.106	0.967	0.203	0.692	0.692
Effusion volume, ml	0.03	0.26	-1.04	-1.49	-1.90	1.17	-0.67	-1.53
n	60	69	67	68	53	60	60	58
P value vs PBO		0.897	0.542	0.385	0.154	0.569	0.973	0.973
Synovial membrane thickness, mm	-0.05	0.01	-0.08	0.01	-0.07	-0.04	-0.05	-0.02
n	59	65	59	63	50	59	55	53
P value vs PBO		0.145	0.520	0.139	0.474	0.637	0.221	0.221
Cartilage volume, mm <sup>3</sup>								
n	58	65	53	66	49	57	50	56
Total	-526.0	-325.5	-323.4	-359.0	-557.0	-598.7	-554.3	-583.1
P value vs PBO		0.392	0.948	0.523	0.534	0.970	0.713	0.713
Medial	-166.9	-139.3	-163.1	-153.7	-288.8	-317.3	-268.7	-310.9
P value vs PBO		0.804	0.904	0.655	0.303	0.670	0.599	0.599
Lateral	-159.8	-166.3	-158.0	-204.1	-270.7	-280.9	-287.9	-271.1
P value vs PBO		0.860	0.969	0.239	0.820	0.711	0.992	0.992
JSN, mm								
n	–	–	–	–	58	70	64	68
Medial	–	–	–	–	0.00	-0.18	-0.11	-0.06
P value vs PBO	–	–	–	–	0.017*	0.148	0.415	0.415
Lateral	–	–	–	–	-0.16	0.14	-0.07	0.04
P value vs PBO	–	–	–	–	0.005*	0.418	0.065	0.065

Data are least squares means unless otherwise noted. LOCF, last observation carried forward; PBO, placebo, sc, subcutaneous. \*P<0.05 vs PBO. Continuous variables compared with analysis of covariance (ANCOVA) with treatment, age, and KL grade as main factors and baseline as covariate. Categorical variables compared with Cochran-Mantel-Haenszel test with age group and KL grade as stratification factors. †Data missing for 1 subject.

**Results:** BL demographics and disease characteristics were balanced (KL grade 3, 36.0%–38.8%; mean WOMAC pain (scale 0–50), 26.2–28.4). The primary endpoint of WOMAC pain at wk 16 improved significantly, compared with PBO, with lutikizumab 100 mg (p=0.050), but not 25 mg (p=0.834) or 200 mg (p=0.415). WOMAC pain reduction in all lutikizumab groups was sustained from wk 16 to 52, but differences between lutikizumab and PBO for WOMAC pain and other key signs and symptoms were not significant (table 1). Synovitis-related imaging, cartilage volume endpoints, and JSN were similar between lutikizumab and PBO groups at wk 26 and 52. Lutikizumab was well tolerated; serious adverse events (SAEs), treatment-related SAEs, and infections and serious infections were similar with lutikizumab vs PBO. Injection site reactions, grade 2/3 neutropenia, and discontinuations due to neutropenia were more frequent with lutikizumab vs PBO. Lutikizumab exposures reached steady state after wk 6 and were stable



through wk 52. Pharmacodynamic responses (neutrophil and high-sensitivity CRP levels) plateaued at the 100 mg dose and data were similar at 200 mg. The low immunogenicity to lutikizumab did not meaningfully affect outcomes.

**Conclusions:** Lutikizumab was generally well tolerated and met the primary endpoint of reduction in WOMAC pain at wk 16 compared with placebo at a dose of 100 mg, but not at 25 mg or 200 mg; cartilage thickness, synovitis, and other structural endpoints were similar between lutikizumab and PBO.

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SAT0576

#### BIOMARKERS PREDICTIVE OF PAIN IMPROVEMENT IN KNEE OSTEOARTHRITIS SUBJECTS TREATED WITH THE ANTI-IL-1 ALPHA/BETA DUAL VARIABLE DOMAIN IMMUNOGLOBULIN LUTIKIZUMAB (ABT-981)

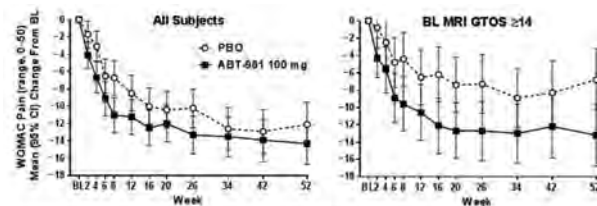
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**Background:** Development of disease-modifying drugs for OA has been challenging, partly due to lack of predictive biomarkers.

**Objectives:** Our primary objective was to identify baseline (BL) biomarkers predicting greater treatment effects on WOMAC pain among knee OA subjects in the lutikizumab (formerly ABT-981) ILLUSTRATE-K trial (NCT02087904).

**Methods:** Subjects (n=347) with Kellgren-Lawrence (KL) grade 2-3 knee OA, synovitis on MRI or ultrasound, and knee pain score 4-8 (range, 0-10) were randomised to placebo (PBO) or lutikizumab 25, 100, or 200 mg subcutaneously every 2 wk for 52 wk. The primary endpoints were change from BL (CFB) in WOMAC pain at wk 16 and CFB in MRI synovitis at wk 26. Demographics, patient-reported outcomes (WOMAC, ICOAP, global assessment [PGA]), x-ray joint space width, and Whole Organ MRI Score (WORMS) were determined at BL. The Patient Rule Induction Method, Sequential Batching, and the Adaptive Index Model were used to identify BL predictive biomarkers and OA subsets with greater lutikizumab treatment effects. Continuous efficacy endpoints were assessed using ANCOVA with treatment, age group, and KL grade as main factors and BL measurements as covariates with LOCF imputation for WOMAC pain.

**Results:** WORMS Global Total Osteophyte Score (GTOS), which semi-quantitatively summates osteophyte severity from 14 regions of the knee, identified a subset of subjects with a greater lutikizumab treatment effect vs PBO; the optimal GTOS cutoff for discriminating treatment effects was 14 (figure 1). Among subjects with a GTOS  $\geq 14$ , the PBO WOMAC pain response was markedly reduced and only marginally improved for ABT-981. At wk 16, among subjects with GTOS  $\geq 14$ , the standardised mean difference (95% CI) of WOMAC pain for the lutikizumab 100 mg dose group vs PBO was  $-0.62$  ( $-0.16$  to  $-1.09$ ) vs  $-0.30$  ( $0$  to  $-0.61$ ) for all subjects. Compared with the total study population, the 41% of subjects with GTOS  $\geq 14$  not only had a greater ABT-981 treatment effect vs PBO on WOMAC pain, but also other measures of OA symptoms. BL systemic markers of synovitis (serum C1M and C3M) and potential markers of macrophage activation by IL-1 (serum alkaline phosphatase) were positively associated with greater lutikizumab treatment effects vs PBO but to a lesser extent than GTOS. Other data supported the robustness of the GTOS predictive marker because 1) a priori, KL grade was used to stratify subjects, 2) subject characteristics were balanced and 3) osteophyte formation is directly linked with synovial macrophage numbers in humans and OA synovial macrophages are the predominant source of IL-1, which is an important mediator of pain.



ABT-981	BL and LS Mean Change From BL (P Value) in WOMAC Pain at Weeks 16, 26, and 52 for ABT-981 vs PBO (LOCF)							
	All Subjects				BL MRI GTOS $\geq 14$			
	BL	Wk 16	Wk 26	Wk 52	BL	Wk 16	Wk 26	Wk 52
25 mg	27.1	-0.3 (0.834)	-0.6 (0.664)	-1.1 (0.500)	29.7	-2.2 (0.345)	-1.6 (0.521)	-4.6 (0.084)
100 mg	28.3	-2.9 (0.050)	-2.7 (0.075)	-2.2 (0.186)	28.2	-6.0 (0.010)	-5.4 (0.027)	-5.4 (0.013)
200 mg	27.1	-1.2 (0.415)	-2.4 (0.107)	-2.3 (0.157)	26.2	-4.6 (0.039)	-5.5 (0.024)	-6.6 (0.020)

Abstract SAT0576 – Figure 1

**Conclusions:** The GTOS biomarker predicted improvement of knee OA pain and other symptoms with lutikizumab treatment. We hypothesise that subjects with more severe osteophytes may have had more inflammation-dependent pain that was less responsive to PBO, suggesting that IL-1 inhibitors should be studied further as a treatment for knee OA symptoms in this subset of patients.

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**Disclosure of Interest:** S. Feng Shareholder of: AbbVie, Employee of: AbbVie, S. Chen Shareholder of: AbbVie, Employee of: AbbVie, L. Wang Shareholder of: AbbVie, Employee of: AbbVie, C. Peterfy Shareholder of: Spire Sciences, Inc. (which provides imaging services for clinical trials to multiple pharmaceutical companies), Employee of: Spire Sciences, Inc. (which provides imaging services for clinical trials to multiple pharmaceutical companies), V. Kraus Consultant for: AbbVie, R. Kamath Shareholder of: AbbVie, Employee of: AbbVie, L. Zhang Shareholder of: AbbVie, Employee of: AbbVie, Y. Luo: None declared, L. Cui Shareholder of: AbbVie, Employee of: AbbVie, J. Medema Shareholder of: AbbVie, Employee of: AbbVie, M. Levesque Shareholder of: AbbVie, Employee of: AbbVie

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SAT0577

#### EVALUATION OF SARCOPENIA MULTIDimensionALLY IN PATIENTS WITH KNEE OSTEOARTHRITIS

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**Background:** Osteoarthritis(OA) is a noninflammatory chronic degenerative disease.The rate of development of sarcopenia has been increased in patients with OA.

**Objectives:** In this study,we evaluated the presence of sarcopenia multidimensionally in patients with knee osteoarthritis (OA) using clinical,ultrasonographic and biochemical parameters,and in this respect, it was aimed to investigate the relation between OA and sarcopenia and to identify the most practical,easily accessible and inexpensive method for investigating sarcopenia.

**Methods:** 102 patients with clinical and radiological diagnosis of knee osteoarthritis and 33 healthy control subjects were included in the study.A total of 135 subjects were evaluated by the European Working Group on Sarcopenia in Older People (EWGSOP) for the diagnosis of sarcopenia.The first group consists of (OA) patients with sarcopenia, the second group consist of OA patients without sarcopenia and the third group is controls subjects.Dual-X-ray absorptiometry (DEXA) is used to measure Body composition parameters and muscle mass measurements, isometric muscle strength evaluations, hand grip strength and walking speeds for diagnosis of sarcopenia. Short form -36 (SF-36) The Nutritional Assessment-short form (MNA), the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), the International Physical Assessment Questionnaire Short Form (IPAQ-SF) and the Centre for Epidemiologic Studies Depression Scale (CES-D scale) were administered to every patients.

**Results:** The mean age of the group with sarcopenia was statistically higher than the other two groups ( $p < 0.001$ ). The weight, body mass index (BMI), waist circumference, upper mid-arm circumference, thigh and leg circumference of osteoarthritis (OA) patients with sarcopenia were statistically lower than those of non-sarcopenic and control group ( $p < 0.01$   $p < 0.001$ ).Body composition parameters results showed that sarcopenic patients had statistically lower values as fat mass, lean body mass and Skeletal Muscle Index ( $p < 0.001$ ,  $p = 0.001$ ,  $p < 0.001$ , respectively) than those of non-sarcopenic and control group.It was determined that body composition values measured with DEXA, ultrasonographic measures,



isokinetic muscle strength assessment, hand grip strength and gait speed had predictive values for sarcopenia.

**Abstract SAT0577 – Table 1.** Baseline features of the patients of knee Osteoarthritis and healthy controls

	Group 1	Group 2	Group 3	p
<b>Age</b>	67.08±2.02 (64-69) <sup>a</sup>	60.31±4.71 (50-70)	59.76±5.16 (52-69)	<0.001 <sup>c</sup>
<b>Body mass index</b>	23.24±3.34 (18.4-29.3) <sup>b</sup>	32.82±5.44 (20.8-61.6)	29.22±3.20 (22.6-35.9)	<0.001
<b>Mid-Upper Arm Circumference</b>	22.17±4.00 (18-32) <sup>b</sup>	33.37±5.04 (21-57)	32.18±4.33 (26-43)	<0.001
<b>Calf circumference</b>	31.92±2.68 (25-35) <sup>b</sup>	40.52±6.30 (32-63)	40.85±6.46 (32-57)	<0.001
<b>Gait speed</b>	09.36±0.1 (0.82-1.12) <sup>a</sup>	0.61±0.18 (0.36-1.5)	0.6±0.14 (0.36-0.9)	<0.001
<b>Hand grip strength (right)</b>	13.58±2.94 (7-17) <sup>a</sup>	20.69±5.38 (8-38)	21.94±5.72 (12-38)	<0.001

mean±standard deviation

<sup>a</sup> A statistically significant difference was found between the post-hoc bilateral comparative "sarcopenic" group (p < 0.017)

<sup>b</sup> A statistically significant difference was found between the post-hoc bilateral comparative "non sarcopenic" group (p < 0.017)

<sup>c</sup> A statistically significant difference was found between the post-hoc bilateral comparative "healthy control" group (p < 0.017)

**Conclusions:** We found that patients with sarcopenic OA were older, weaker, less powerful, undernourished, and restricted in their level of physical activity in the study in which we identified sarcopenia as approximately 12% in patients with osteoarthritis. Among the methods of determining sarcopenia, ultrasound becomes prominent with its practical, cheap and easily accessible features. We think that our results will increase the awareness of the presence of sarcopenia in OA patients.

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#### SAT0578 PATELLAR TENDON ENTHESIS ABNORMALITIES AND THEIR ASSOCIATION WITH KNEE PAIN AND STRUCTURAL ABNORMALITIES IN OLDER ADULTS

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**Background:** The patellar tendon works together with the quadriceps tendon to enable knee flexion and straightening. Its attachment site (enthesis) is at risk of micro damage and degeneration. Recent studies suggest that enthesitis abnormalities are associated with development of osteoarthritis.<sup>1, 2</sup> However, no studies have assessed the presence of patellar enthesitis abnormalities in older adults and its association with osteoarthritis outcomes.

**Objectives:** To describe the associations of patellar tendon enthesitis (PTE) abnormalities visible on magnetic resonance (MR) images; and knee pain, physical function limitations, osteoarthritic structural abnormalities cross-sectionally and longitudinally over 10.7 years.

**Methods:** PTE abnormalities were defined as presence of abnormal bone signal and/or bone erosion. They were measured on T2-weighted fat suppressed fast spin echo MR images at baseline in 961 community-dwelling older adults and followed for 10.7 years. Knee pain and physical function limitation score were assessed using WOMAC. Bone marrow lesions (BMLs), cartilage volume and defects, tibial bone area, and infrapatellar fat pad (IPFP) area were assessed using validated methods. Associations were assessed using hurdle, log binomial, linear, and mixed models, after adjusting for confounders.

**Results:** 20% of participants had bone signal and/or erosion at PTE. Cross-sectionally, presence of PTE abnormalities were associated with greater intensity of pain while going up and down stairs ( $\beta=0.22$  (95% CI; 0.03, 0.41)), greater risk of having a femoral BML (RR=1.46 (1.22, 1.90)), greater lateral tibial bone area ( $\beta=25.95$  (1.00, 50.91)), smaller IPFP area ( $\beta=-0.26$  (-0.46, -0.05)), and a worse tibial cartilage defects cross sectionally (RR=1.70 (1.16, 2.47)), after adjustment of demographic and structural confounders. Longitudinally, PTE abnormalities at baseline predicted an increased risk of deleterious changes in tibial BML size (RR=1.52 (1.12, 2.05)) but not clinical symptoms, and other structural changes over 10.7 years.

**Conclusions:** Patellar tendon enthesitis abnormalities are common in the elderly. The presence of cross-sectional but not longitudinal associations suggests they commonly co-exist with other knee structural abnormalities, but that they are not be a major player in symptom development or structural changes, excepting tibial BMLs.

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#### SAT0579 PRESENCE OF AUTOANTIBODIES IN EROSIIVE HAND OSTEOARTHRITIS AND ASSOCIATION WITH CLINICAL PRESENTATION

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**Background:** One of the most prevalent clinical phenotype of osteoarthritis (OA) is hand OA (HOA), which in some patients can evolve to erosive HOA. In erosive HOA central erosions and subchondral destruction are seen, and imaging studies have indicated that in erosive HOA hand joints display more inflammatory signs than in non-erosive HOA.

Autoantibodies directed against post-translationally modified proteins, such as citrullinated (ACPA) and carbamylated (anti-CarP antibodies) proteins, are a hallmark of rheumatoid arthritis (RA), and are associated with more severe joint damage and inflammation. Interestingly, these antibodies are present in a small subset of SLE patients as well, in which they associate with bone erosions. This suggests the possible involvement of autoantibodies in inflammation and joint damage in other conditions than RA. Therefore, we hypothesised that autoantibodies are present in HOA and associate with erosive disease.

**Objectives:** To investigate whether three RA-associated antibodies, Rheumatoid Factor (RF), ACPA and anti-CarP antibodies, are present in hand OA and associate with erosive OA.

**Methods:** Anti-CarP IgG, ACPA IgG and RF IgM were measured by ELISA in baseline sera of HOA patients from 3 cohorts: HOSTAS (n=510, mean age 61.0 years, 85.7% women, 27.2% EOA), ECHO (n=47, mean age 63.4 years, 89.4% women) and EHOA (n=23, mean age 57.1 years, 73.9% women), and in sera of healthy controls (HC; n=196, mean age 44.1 years, 51.0% women). The prevalence of autoantibodies was compared between HOA and HC and between erosive and non-erosive HOA. In HOSTAS, hand radiographs were scored (Kellgren-Lawrence, OARSI osteophyte and joint space narrowing scores) and C-reactive protein (CRP) levels, representing inflammation, were assessed. Groups were compared using non-parametric tests.

**Results:** In both ECHO and EHOA cohorts, only one patient was positive for RF IgM and none were positive for ACPA IgG. In all three cohorts, a low prevalence of anti-CarP IgG was detected and this was not different between HOA patients and HC (6.6% vs 3.6%, p=0.12). Moreover, in HOSTAS, the prevalence of all tested autoantibodies was low and not significantly different from HC (anti-CarP 7.1% vs 3.6%, p=0.08; ACPA 0.8% vs 1.5%, p=0.37; RF 6.1% vs 4.1%, p=0.30). Likewise, no difference was found between erosive and non-erosive HOA (anti-CarP 7.2% vs 7.1%, p=0.94; ACPA 0.7% vs 0.8%, p=0.92; RF 4.3% vs 6.5%, p=0.36). Radiographic damage and CRP levels were similar in anti-CarP positive vs negative, and RF positive vs negative HOSTAS patients.

**Conclusions:** The prevalence of autoantibodies is similar in HOA patients and healthy controls. Moreover, these autoantibodies are not associated with erosive disease, structural damage or inflammation in HOA patients, indicating that another mechanism is driving erosive disease.

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SAT0580

#### ASSOCIATION OF CHILDHOOD AND ADULTHOOD ADIPOSITY MEASURES WITH KNEE CARTILAGE THICKNESS, CARTILAGE VOLUME AND BONE AREA IN YOUNG ADULTS

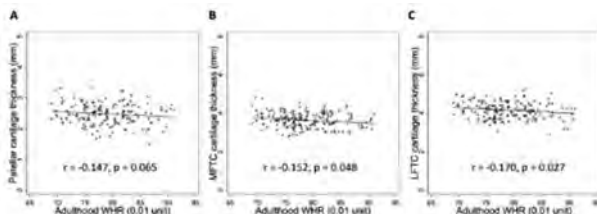
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**Background:** Adiposity is associated with increased risk of knee osteoarthritis (OA); cartilage thickness, cartilage volume and subchondral bone area are established biomarkers in knee OA. However, there are no studies describing the effects of adiposity during early life on knee cartilage and bone morphology in adulthood.

**Objectives:** To describe the longitudinal associations between adiposity measures in childhood and adulthood and knee cartilage thickness, cartilage volume and subchondral bone area in young adults.

**Methods:** 186 participants from the Australian Schools Health and Fitness Survey of 1985 (aged 7–15 years) were followed up 25 years later (aged 31–40 years). Childhood measures (weight, height, waist circumference and hip circumference) were collected in 1985, and corresponding adulthood measures were collected during 2004–2006. Body mass index (BMI) and waist-hip ratio (WHR) were calculated. Participants underwent knee magnetic resonance imaging (MRI) during 2008–2010, and cartilage thickness, cartilage volume and subchondral bone area were measured using a quantitative approach (Chondrometrics 3.0, Germany). Multivariable linear regressions were used to examine the above associations.

**Results:** Among 186 participants (48.4% females), 7.6% were overweight in childhood, and 42.1% in adulthood. There were no significant associations between childhood adiposity measures and adulthood knee cartilage and bone morphological measures; the same applied to adulthood BMI and overweight. However, adulthood WHR was negatively associated with cartilage thickness in the patella ( $\beta$   $-0.009$  mm/0.01 unit, 95% confidence interval (CI)  $-0.019$  to  $0.001$ ,  $p=0.065$ ), the medial femorotibial compartment (MFTC) ( $-0.011$ ,  $-0.022$  to  $0.000$ ,  $p=0.048$ ) and the lateral femorotibial compartment (LFTC) ( $-0.013$ ,  $-0.025$  to  $-0.002$ ,  $p=0.027$ ), with cartilage volume in the patella ( $\beta$   $-21.85$  mm<sup>3</sup>/0.01 unit, 95% CI  $-37.77$  to  $-5.93$ ,  $p=0.007$ ), the MFTC ( $-14.17$ ,  $-29.53$  to  $1.19$ ,  $p=0.070$ ) and the LFTC ( $-23.87$ ,  $-42.18$  to  $-5.57$ ,  $p=0.011$ ), and with subchondral bone area in the patella ( $\beta$   $-4.69$  mm<sup>2</sup>/0.01 unit, 95% CI  $-8.26$  to  $-1.12$ ,  $p=0.010$ ) and the LFTC ( $-4.76$ ,  $-9.47$  to  $-0.06$ ,  $p=0.047$ ), but not the MFTC.



**Abstract SAT0580 – Figure 1.** Scatter plots and linear regression lines for associations between adulthood WHR and knee cartilage thickness (A: patella; B: MFTC; C: LFTC).

Linear regression lines are from models adjusted for adulthood age, duration of follow-up, gender and adulthood knee injury. WHR, waist-hip ratio; MFTC, medial femorotibial compartment; LFTC, lateral femorotibial compartment.

**Conclusions:** Childhood adiposity measures did not predict adulthood knee cartilage and bone morphological measures. However, adulthood WHR, but not BMI or overweight status, was negatively associated with cartilage thickness, cartilage volume and subchondral bone area, suggesting central obesity may affect knee structures in young adults.

**Disclosure of Interest:** None declared

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SAT0581

#### PREDICTIVE FACTORS OF RESPONSE TO A SINGLE INJECTION OF MANNITOL-MODIFIED CROSS-LINKED HYALURONIC ACID (HANOX-M-XL) IN PATIENTS WITH TRAPEZIOMETACARPAL OSTEOARTHRITIS. RESULTS OF A MULTICENTRE PROSPECTIVE OPEN-LABEL PILOT STUDY (INSTINCT TRIAL)

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**Background:** Viscosupplementation is likely effective to alleviate pain and improve function in patients suffering from rhizarthrosis. However no study has been focused on the predictors of efficacy of the treatment.

**Objectives:** To search predictive factors of success or failure 3 months after a single intra-articular injection of a mannitol-modified hyaluronic acid (HA) viscosupplement, in patients suffering from trapeziometacarpal (TMC) osteoarthritis (OA).

**Methods:** Patients with symptomatic TMC OA were included in a 3 month prospective multicentre open-label trial. To be included in the study patients must have symptomatic TMC OA, not adequately relieved by analgesics/NSAIDs therapy and/or by the use of a thumb splint. Before treatment all patients must have had plain radiographs with the Kapandji incidences, for the Dell radiological grade assessment. (1 to 4). Primary endpoints were the variation between injection (D0) and day 90 (D90) of the thumb pain measured on 11 point-Likert scale (0 to 10) and the patient's self-assessment of efficacy (0 to 3). Treatment consisted in a single injection of 0.6 to 1 ml of HANOX-M-XL, a viscosupplement made of a cross-linked HA of high molecular weight, from biofermentative origin, combined with mannitol. All injections were performed under fluoroscopic or ultrasound guidance. Predictive factors of pain decrease were studied in univariate and multivariate analysis. All statistical tests were carried out two tailed at the 5% level of significance.

**Results:** 122 patients (76% females, mean age 60, mean disease duration 36 months) were included and 120 (98%) were assessed at 3 months. 23% of the TMC OA were grade 1 according to Dell classification, 36.8% grade 2, 36.8% grade 3 and 3.5% grade 4. At D0, the average (SD) pain level was  $6.5 \pm 1.6$  without significant difference between Dell groups ( $p=0.21$ ). At day 90, pain decreased from  $6.5 \pm 1.6$  to  $3.9 \pm 2.5$  (Difference  $-2.7 \pm 2.5$ ;  $-42\%$ ;  $p<0.0001$ ) without significant difference depending on the Dell grade ( $p=0.055$ ), despite a seemingly smaller number of responders in stage 2 patients. The average analgesic consumption decreased in more than one out of two patients. In univariate analysis, the clinical response was significantly worse in patients taking NSAIDs at baseline ( $p=0.012$ ), but this difference no longer reached the significance threshold in the multivariate analysis. In multivariate analysis no predictor of response was identified. There was no safety issue. All AEs (11%) were transient increase of pain during or following HA administration and resolved without sequel within 1 to 7 days.

**Conclusions:** This study, of the largest cohort of patients treated with viscosupplementation in TMC OA, suggests that a single course of HANOX-M-XL injection is effective in relieving pain, without safety concern. Interestingly patients with the more advanced stages of OA seemed to benefit the treatment as well as those with less advanced OA.

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**SAT0582 BONE MARROW LESION TYPE AND PAIN IN KNEE OSTEOARTHRITIS**

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**Background:** Bone marrow lesions (BMLs) have been associated with pain in observational studies of knee OA. The aim of this study was to determine whether type of BML (subchondral, with and without regions of well-defined high post-contrast signal, and ligament-based) were associated with knee symptoms.

**Objectives:** To assess the association between bone marrow lesion volume, including sub-types, and pain in symptomatic knee OA.

**Methods:** Data were collected on a sub-sample of participants who were part of the UK VIDEO study<sup>1</sup>; a 3 year multicentre randomised placebo-controlled trial of vitamin D therapy in patients with symptomatic knee OA. Those recruited to one of the participating centres (Southampton) had contrast enhanced MR imaging (CE-MRI) of the index knee performed at one or more annual visits. BML volume was assessed by segmentation of sagittal T1-weighted fat-suppressed post-contrast scans. BMLs were categorised by type (subchondral/ligament-based) and by the presence/absence of regions of well-defined high post-contrast signal (for the subchondral BMLs only). As part of the trial, subjects completed the WOMAC questionnaire which included questions on pain, function and stiffness. We used random-effects multiple linear panel regression, adjusting for variance between follow-up visits to explore the relationship between BML volume and the WOMAC pain and function subscales. This approach is preferred over cross-sectional analyses, as it makes use of all available observations from study visits, and controls for within-patient correlations appropriately.

**Results:** In this analysis, we included 50 subjects who had had a baseline MRI and at least one other MRI performed. The mean age of the subjects was 63.3 (SD  $\pm$ 6.5) years and 74% were female. After adjusting for variation between visits, there was no significant association between total BML volume and WOMAC pain when the BMLs were stratified by type; total subchondral BML volume ( $b=41.5$  mm<sup>3</sup>; 95% CI  $-19.35$  to  $102.37$ ) or total ligament-based BML volume ( $b=9.1$  mm<sup>3</sup>; 95% CI  $-6.39$  to  $24.59$ ). Further, we did not observe an association between pain and volume of subchondral BMLs with or without regions of well-defined high post-contrast signal; (i) total mixed subchondral oedema-like BMLs containing regions of well-defined high signal ( $b=39.45$  mm<sup>3</sup>; 95% CI  $-3.93$  to  $82.83$ ) or (ii) subchondral oedema-like BML volume ( $b=-4.16$  mm<sup>3</sup>; 95% CI  $-53.49$  to  $45.18$ ), after adjusting for variation between visits. There was, however, a significant association between the volume of subchondral regions of well-defined high signal and both WOMAC pain ( $b=2.19$  mm<sup>3</sup>; 95% CI  $0.88$  to  $3.49$ ) and function ( $b=1.61$  mm<sup>3</sup>;  $0.37$  to  $2.84$ ).

**Conclusions:** In this analysis, an increased volume of regions of well-defined high signal intensity on post-contrast scans within subchondral BMLs was associated with knee pain and function.

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**SAT0583 THE IMMEDIATE EFFECT OF A SOFT KNEE BRACE ON DYNAMIC KNEE INSTABILITY IN PERSONS WITH KNEE OSTEOARTHRITIS**

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**Background:** Wearing a soft knee brace has been shown to reduce self-reported knee instability in persons with knee osteoarthritis (OA).<sup>1</sup> There is a need to assess whether a soft knee brace has a beneficial effect on objectively assessed dynamic knee instability as well.

**Objectives:** The aims of the study were: (i) to evaluate the immediate effect of a soft knee brace on dynamic knee instability, and (ii) to assess the difference in effect between a tight and a non-tight knee brace in persons with knee OA.

**Methods:** A within-subject cross-over design was used, comparing wearing a soft knee brace with not wearing a soft knee brace, and comparing wearing a tight

brace (standard fit) with wearing a non-tight brace (one size larger). The order of brace type was randomised. Participants walked, both without and with the brace, on a treadmill, which is integrated in the GRAIL system, placed in a virtual reality environment (GRAIL system, MOTeKForce Link, The Netherlands). Participants were subjected to two tasks: (i) level walking and (ii) walking with mechanical perturbations on the treadmill. Mechanical perturbations on the treadmill comprised five lateral and five medial translations (2 cm displacements) of the treadmill belts occurring during 20%–50% of the gait cycle. During the walking trials, 3D movement of the lower legs, pelvis and trunk were captured via markers on anatomical landmarks at 100 Hz using a motion-capture system (Vicon, Oxford, United Kingdom). The outcome measure was dynamic knee instability, expressed by the Perturbation Response (PR), i.e. a biomechanics based measure reflecting deviation in the mean knee varus-valgus angle after a controlled mechanical perturbation, standardised to the mean (standard deviation) varus-valgus angle during level walking. Lower PR values indicate less deviation in the mean varus/valgus angle. Linear mixed-effect model analysis was used to evaluate the effect of a brace on dynamic knee instability.

**Results:** Thirty-eight persons with knee OA and self-reported knee instability from the Amsterdam Osteoarthritis Cohort participated in the study. Wearing a brace significantly reduced the PR compared to not wearing a brace ( $p<0.05$ ). The PR value reduced from 0.48 when not wearing a brace to 0.32 when wearing a brace. This means that wearing a brace resulted in a reduction of 33% in dynamic knee instability compared to not wearing a brace. There was no difference between a non-tight and a tight brace ( $p>0.05$ ).

**Conclusions:** This study is the first to report that wearing a soft brace results in an improvement of objectively assessed dynamic knee instability, beyond the previously reported subjective improvement.

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**SAT0584 CLINICAL VALIDATION OF TWO PANELS OF BIOMARKERS TO PREDICT SYMPTOMATIC DRUGS RESPONSE IN KNEE OA**

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**Background:** The prediction of drug responses based on the analysis of multiple clinical variables and *omics* data is mandatory for accomplishing the promise of precision medicine in rheumatology.

**Objectives:** Integrating clinical-radiological-analytical variables and proteomics data for predicting patient's response to different treatments, in order to optimise therapeutic outcomes in OA.

**Methods:** A panel of 10 serum proteins potentially useful to predict OA patient's response was qualified using ELISA Kits in the whole Multicentre Osteoarthritis interVENTion trial with Sysadoa (MOVES) cohort. Patients were classified as responders (R) and non-responders (NR), either to Chondroitin sulfate/Glucosamine hydrochloride (CS+GH; Droglican, Bioiberica, Spain) or Celecoxib, after 6 months of treatment. Logistic regression analyses, adjusted by confounder variables previously reported as significant in bivariate approaches, were used to analyse the contribution of the measured proteins to our prediction models of drug response in knee OA. Appropriate receiver-operating-characteristics (ROC) curves were also calculated.

**Results:** In the *discovery phase* of the study, two different panels of putative predictive biomarkers useful to stratify OA patients according to their unique protein profiles was identified by shotgun proteomics ( $n=80$ ). In the *verification phase*, the panel of 6 proteins specific for Droglican treatment (APOA2, APOA4, APOH, ITIH1, C4BPa and ORM2), and the panel of 4 proteins specific for Celecoxib treatment ( $\alpha$ 2HS, SHBG, CD5L and TSP1) were verified in a larger cohort of OA patients ( $n=262$  for CS+GH group and  $n=244$  for Celecoxib group) by ELISA assays. In the *qualification phase*, the sensitivity and specificity of a panel of 4 validated proteins (ORM2, APOA2, ITIH1, and TSP1) were tested in blind in the whole MOVES cohort at baseline ( $n=506$ ). In CS+GH group, only ORM2 levels were significantly lower in responders compared to non-responders (R: 192.8 ug/mL vs NR: 261.6 ug/mL;  $p=0.042$ ), while no statistically significant differences were found in the Celecoxib group. Five clinical and two analytical parameters recorded at baseline significantly influence patients' response regardless of treatment. Notably, if we include ORM2 as covariate, we found a specific interaction



between response to CS+GH and baseline protein levels ( $p=0.007$ ) thus increasing the power of our prediction model (ROC up to 0,843). In the Celecoxib group, non parametric analysis showed increased levels only of TSP1 at baseline in responders compared to non-responders (R: 363,03±104,83 ng/mL vs NR: 331,95 ±92,59 ng/mL;  $p=0.041$ ), while no statistically significant differences were found for this protein in the CS+GH group. When we include in the regression model 4 predictive variables (2 clinical and 2 analytical) and TSP1 as covariate, we found a specific interaction between response to Celecoxib and baseline protein levels ( $p=0.045$ ) thus increasing the predictive power of this model (ROC up to 0,749).

**Conclusions:** Combining clinical and analytical parameters, we clinically validated (qualified) 2 panels of biomarkers that could efficiently predict OA patients' response to CS+GH with an accuracy of 84,3% or to Celecoxib with an accuracy of 74,9%.

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### SAT0585 DECREASED SYNOVIAL LEVELS OF DICKKOPF-1 ARE ASSOCIATED WITH RADIOLOGICAL PROGRESSION IN KNEE OSTEOARTHRITIS PATIENTS

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**Background:** Dickkopf-1 (Dkk-1) is a direct inhibitory ligand of Wnt  $\beta$ -catenin signalling pathway that act through binding to low-density lipoprotein (LDL) related proteins (LRP5/6) receptors. Dkk-1 is considered an important mediator of cartilage homeostasis and skeletal remodelling.<sup>1</sup>

**Objectives:** This study aimed to measure serum and synovial fluid (SF) levels of Dkk-1 in patients with early primary knee osteoarthritis (KOA) and to examine the relationship between these levels and the clinical and functional parameters as well as radiological progression of KOA

**Methods:** We measured Dkk-1 in the serum ( $n=48$ ) and SF samples ( $n=22$ ) from 48 early KOA patients and in the serum from healthy control ( $n=30$ ). Body mass index (BMI), numerical rating scale of pain (NRS) and The Western Ontario Mc Master scale (WOMAC) were recorded. Plain radiographs using Osteoarthritis Research Society International (OARSi) atlas to assess joint space narrowing (JSN)<sup>2</sup> and musculoskeletal ultrasound examination (MSUS) were performed at baseline and after 24 months to assess radiological progression. Radiological progression was considered if there is more than 2 points increase in JSN score or transition to higher grade in MSUS examination<sup>3</sup> at the 24 months follow up period compared to baseline grade.

**Results:** SF Dkk-1 levels were significantly decreased (mean  $\pm$ SD 115.05  $\pm$ 34.2 pg/ml) compared to their paired serum levels (mean  $\pm$ SD 969.82  $\pm$ 365.72 pg/ml),  $p<0.001$  in KOA patients. There was no significant difference in serum Dkk-1 levels between KOA patients and healthy controls (mean  $\pm$ SD 988.77 $\pm$ 385.19 pg/ml and 1084.73 $\pm$ 408.38 pg/ml respectively), the SF concentrations of Dkk-1 significantly correlated with the baseline thickness of the cartilage on the medial condyle (0.53,  $p<0.05$ ) but not on the lateral condyle of the femur ( $r=0.11$ ,  $p>0.05$ ), there was no significant correlation between serum Dkk-1 and baseline cartilage thickness on medial and lateral condyles ( $r=-0.13$  and  $-0.09$  respectively,  $p<0.05$ ). Patients in the least quartile of SF Dkk-1 had an increased risk of radiological progression with plain radiography and MSUS (age, sex and BMI adjusted RR 2.1 and 3.4, 95% CI respectively).

**Conclusions:** Osteoarthritis patients have significantly lower synovial levels than serum levels of Dickkopf-1 that were obviously associated with radiological progression on plain radiography and MSUS suggesting that it could be a useful marker to reflect OA severity and implies a possible role in the pathogenesis of OA.

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### SAT0586 RESULTS FROM A 52 WEEK RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PHASE 2 STUDY OF A NOVEL, WNT PATHWAY INHIBITOR (SM04690) FOR KNEE OSTEOARTHRITIS TREATMENT

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**Background:** Knee osteoarthritis (OA) is characterised by pain, disability and joint deformity due to articular cartilage degradation and bone remodelling. Wnt signalling is involved in these cellular processes. SM04690, a small molecule Wnt pathway inhibitor, is in development as a potential disease modifying OA drug (DMOAD) for knee OA.

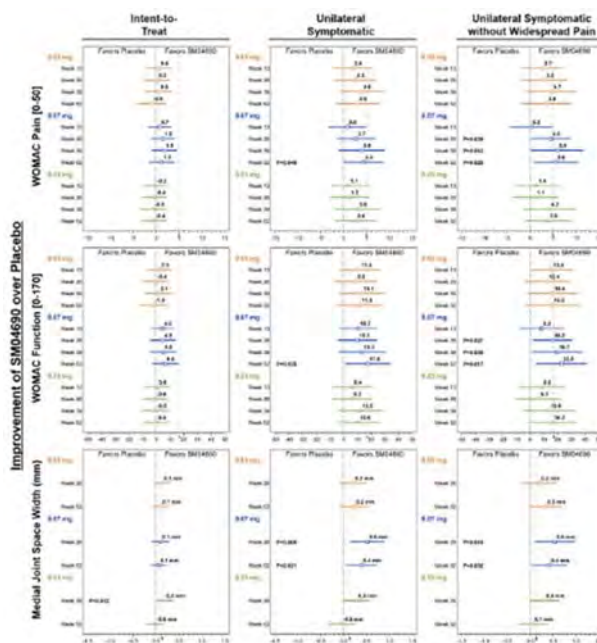
**Objectives:** A phase 2, multicenter, 52 week, placebo-controlled (PBO) trial was conducted to identify a target population, determine optimal dose and assess safety.

**Methods:** Knee OA subjects, Kellgren-Lawrence (KL) grades 2–3, received a single 2 mL injection of SM04690 0.03 mg, 0.07 mg, 0.23 mg or PBO in target (most painful) knee. WOMAC Pain and Function were assessed (Weeks 0, 4, 13, 26, 39, 52) and fixed flexion radiographs (QuAP positioned; Weeks 0, 26, 52) assessed medial joint space width (mJSW). Analysis of covariance adjusted for baseline was conducted using multiple imputation for missing data. Exploratory subgroups included: 1) unilateral symptomatic subjects (pre-specified; determined by history and examination) and 2) unilateral symptomatic subjects without comorbid pain (post-hoc; Widespread Pain Index  $\leq 4$ , Symptom Severity  $\leq 2$  [WP-]).

**Results:** 455 subjects (mean age 60.3 [ $\pm 8.7$ ] years, BMI 29.9 [ $\pm 4.6$ ] kg/m<sup>2</sup>, female 58.9%, KL grade 3 [64.4%], unilateral symptomatic OA [36.0%]) were enrolled, 91% with radiographic bilateral OA. Seventeen serious adverse events, all unrelated to SM04690, were reported.

The primary endpoint of Week 13 change from baseline in WOMAC Pain was not met. In ITT, at all timepoints, minimal clinically important differences ( $>10\%$  full range) in WOMAC Pain and Function compared to baseline were seen in all groups. In 0.07 mg unilateral symptomatic subjects, at 52 weeks, WOMAC Pain (4.4,  $p=0.049$ ), and Function (17.5,  $p=0.035$ ) were significantly improved compared to PBO. In 0.07 mg unilateral symptomatic WP- subjects at Weeks 26, 39, and 52, WOMAC Pain (4.6,  $p=0.039$ ; 5.9,  $p=0.042$ ; and 5.6,  $p=0.025$ , respectively) and Function (16.3,  $p=0.027$ ; 19.7,  $p=0.035$ ; and 22.8,  $p=0.017$ , respectively) were significantly improved compared to PBO (**Abstract SAT0586 – figure 1**).

At 26 and 52 weeks, 0.07 mg unilateral symptomatic (0.5 mm,  $p=0.006$  and 0.4 mm,  $p=0.021$ , respectively) and 0.07 mg unilateral symptomatic WP- (0.5 mm,  $p=0.016$  and 0.4 mm,  $p=0.032$ , respectively) subgroups demonstrated significant increases from baseline in mJSW compared to PBO (figure 1).



**Abstract SAT0586 – Figure 1.** Ladder plots depicting mean improvement (and 95% confidence intervals) of SMO4690 over placebo adjusted for baseline.

**Conclusions:** A target subgroup of unilateral symptomatic knee OA subjects and potential optimal dose (0.07 mg) of SM04690 were identified. Clinical and radiographic outcomes suggested that SM04690 has potential as a DMOAD, especially in subjects with unilateral symptomatic WP- knee OA. Further studies are ongoing.

**Disclosure of Interest:** Y. Yazici Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, T. McAlindon Grant/research support from: Samumed, LLC, Consultant for: Samumed, LLC, Astellas, Flexion, Pfizer, Regeneron, Seikugaku, A. Gibofsky Shareholder of: AbbVie, Amgen, Johnson and Johnson, GSK, Regeneron, Consultant for: AbbVie, Pfizer, Horizon, Iroko, Celgene, Novartis/Sandoz, Samumed, LLC, Speakers bureau: AbbVie, Celgene, Pfizer, N. Lane Consultant for: Samumed, LLC, D. Clauw Consultant for: AbbVie, Astellas, Cerephex, Eli Lilly, Forest Laboratories, Johnson and Johnson, Merck, Pfizer, Purdue, Samumed, LLC, Theravance, Tonix, UCB, Williams and Connolly LLP, Zynerba, C. Swearingen Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, A. DiFrancesco Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, J. Tambiah Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, M. Hochberg Consultant for: Bioberica, EMD Serono, Novartis Pharma AG, Plexikon, Pfizer, Proximagen, Regeneron, Samumed, LLC, Theralogix LLC  
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SATURDAY, 16 JUNE 2018

## Other orphan diseases

### SAT0587 MAJOR SALIVARY GLANDS ULTRASONOGRAPHY IN DIFFERENTIAL DIAGNOSIS OF IGG4-RELATED DISEASE AND PRIMARY SJOGREN'S SYNDROME

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**Background:** IgG4-related disease (IgG4-RD) is a group of fibro-inflammatory immunomediated conditions with IgG4 overexpression in the serum and affected tissues in the majority of patients. Major salivary and lacrimal glands are the most frequently affected sites in IgG-RD. Moderate sicca symptoms can be present as well thus requiring differential diagnosis with primary Sjogren's syndrome (pSS). Major salivary glands ultrasonography (sUS) has been reported as an effective diagnostic tool in pSS.

**Objectives:** To evaluate the difference in sUS score in pSS and IgG4-RD patients

**Methods:** 15 patients with IgG4-related sialoadenitis consecutively admitted to our clinic and 28 with pSS underwent sUS. Parenchymal echogenicity, homogeneity, hypoechogenic and hyperechogenic areas and clearness of salivary gland border were scored according to the Hocevar scoring system (cut-off – 15 points). Statistical analyses were performed using MEDCALC program. Median values of the sUS score and Mann-Whitney U-test were used to evaluate differences in total ultrasound score between patients in two groups.

**Results:** All patients with IgG4-related sialadenitis and pSS had some sUS abnormalities. The most frequent feature in IgG4-RD were: the presence of hypoechotic lesions in major salivary glands (53% of patients) or diffuse salivary gland parenchyma hypoechogenicity (27% of patients) and multiple intraglandular lymph nodes (66.7% of patients). Median value of sUS score in IgG4-RD group was 12 points and in pSS group – 22 points. The difference was significant (Mann-Whitney U-test 60.5,  $p < 0.05$ ).

**Conclusions:** Although different US-changes are frequently seen in IgG4-RD patients, sUS Hocevar score seems to be a rather reliable tool to differentiate IgG 4-related sialoadenitis and pSS.

**Disclosure of Interest:** None declared

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### SAT0588 RHEUMATOLOGIC IMMUNE-RELATED ADVERSE EFFECTS OF CHECKPOINT INHIBITOR THERAPY: A SINGLE CENTRE COHORT OF 29 PATIENTS

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**Background:** Immune checkpoint inhibitors for advanced malignancy are associated with a wide range of autoimmune phenomena known as immune-related

adverse effects (irAEs).<sup>1</sup> Knowledge of irAEs resembling rheumatologic diseases is limited to case reports and small case series, and there are currently no specific guidelines on how to diagnose or manage these patients.

**Objectives:** To describe the prevalence, clinical presentation, and management of patients with rheumatologic irAEs from checkpoint inhibitor therapy.

**Methods:** We retrospectively studied all patients who received a checkpoint inhibitor for any malignancy at Mayo Clinic Rochester, Minnesota between January 1 st, 2011 and November 1 st, 2017. From these patients we identified those with possible rheumatologic irAEs using diagnostic codes, search terms, and the presence of specific laboratory testing.

**Results:** Of the 1216 patients who received any checkpoint inhibitor, we identified 29 who were clinically diagnosed with a rheumatologic irAE. The diagnosis was confirmed by a rheumatologist in all but 3 cases. Mean follow up time from irAE diagnosis was 1.5 years ( $\pm 1.1$ ). Seven patients had a pre-existing autoimmune disease with one of these being a rheumatologic disease (Giant-cell arteritis). irAEs included inflammatory arthritis,<sup>15</sup> sicca syndrome,<sup>3</sup> systemic sclerosis,<sup>3</sup> myositis,<sup>3</sup> vasculitis,<sup>3</sup> spondylitis,<sup>1</sup> and polymyalgia rheumatica.<sup>1</sup> Only one irAE represented a disease flare. Mean time from initiation of checkpoint inhibitor therapy to onset of irAE symptoms was 15.0 weeks ( $\pm 10.8$ ). 24 patients (83%) were treated with corticosteroids and 8 patients (28%) received additional therapy with disease modifying drugs. Mean treatment duration for these 24 patients was 19.5 weeks ( $\pm 21.7$ ), and 8 patients (33%) had complete symptom resolution within the study period. Rheumatologic irAEs resulted in discontinuation of checkpoint inhibitor therapy in 7 patients (24%).

Abstract SAT0588 – Table 1. Clinical Features

Rheumatologic irAEs	29 total
Inflammatory arthritis	15
Sicca syndrome	3
Systemic sclerosis	3
Myositis	3
Vasculitis	3
Spondylitis	1
Polymyalgia rheumatica	1
Treatment	
Prednisone only	16
Prednisone plus biologics	8
No treatment	5
Starting prednisone dose, MG, mean (St. Dev)	47 (26)
Weeks on prednisone, mean (St. Dev)	15 (11)
Weeks to symptom onset, mean (St. Dev)	15 (11)
Sedimentation rate, mean (St. Dev)	39 (30)
C-reactive protein, mean (St. Dev)	49 (57)
Diagnosed by rheumatologist	26 (90%)
Positive autoimmune serologies	4 (14%)
Flare of existing autoimmune disease	2 (7%)
Comorbid non-rheumatologic irAEs	19 (66%)

**Conclusions:** Our study represents one of the largest cohorts of rheumatologic irAEs to date. Most patients required long courses of treatment with only a minority achieving complete symptom resolution. Prospective, multicenter studies are necessary to determine the optimal management of these emerging disorders.

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SAT0589

### MUSCULOSKELETAL MANIFESTATIONS OCCUR PREDOMINANTLY IN PATIENTS WITH OLDER ONSET FAMILIAL MEDITERRANEAN FEVER

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**Background:** Our previous nation-wide survey showed the clinical manifestations and prevalence of Japanese Familial Mediterranean Fever (FMF) patients. However, the clinical differences between young-onset FMF (YOFMF), adult-onset FMF (AOFMF), and late-onset FMF (LOFMF) have not been yet clarified.

**Objectives:** We sought to compare between the clinical profile of patients with AOFMF, LOFMF and YOFMF and to determine the clinical characteristics of them.

**Methods:** We enrolled consecutively 395 patients in 2006–2017. Mutation detection in exons 1, 2, 3, and 10 of the *MEFV* gene was performed. We defined YOFMF, AOFMF and LOFMF as the onset of FMF <20, 20–39 and ≥40 years of age, respectively. We compared clinical manifestations and mutations in *MEFV* gene among these three groups.

**Results:** The median age at the onset of YOFMF, AOFMF and LOFMF were 12.5, 28 and 51 years old respectively. A family history of FMF and a mutation in exon 10 of the *MEFV* gene were significantly more frequent in groups with younger onset ([YOFMF 28%, AOFMF 17%, LOFMF 12%; p<0.01], [YOFMF 51%, AOFMF 33%, LOFMF 19%; p<0.001], respectively). In the accompanying manifestations during the attacks, abdominal pain and chest pain were significantly more frequent in groups with younger onset ([YOFMF 64%, AOFMF 56%, LOFMF 30%; p<0.001], [YOFMF 45%, AOFMF 33%, LOFMF 24%; p<0.01], respectively), whereas arthritis and muscle pain were significantly more frequent in groups with older onset ([YOFMF 32%, AOFMF 48%, LOFMF 62%; p<0.001], [YOFMF 8%, AOFMF 18%, LOFMF 26%; p<0.01], respectively). There was no significant difference in the response to colchicine among the three groups.

	YOFMF (n=182)	AOFMF (n=115)	LOFMF (n=90)	P value		
				YOFMF vs AOFMF vs LOFMF	YOFMF vs Others	Others vs LOFMF
Thoracic pain	82/182(45%)	38/115(33%)	22/90(24%)	0.0025	0.0015	0.0060
Abdominal pain	117/182(64%)	64/115(56%)	27/90(30%)	<0.0001	0.0001	<0.0001
Arthritis	58/182(32%)	55/115(48%)	56/90(62%)	<0.0001	<0.0001	<0.0001
Myalgia	13/161(8%)	16/91(18%)	17/65(26%)	0.0014	0.0012	0.0051
Erysipelas-like erythema	18/182(10%)	16/115(14%)	17/90(19%)	0.11	0.10	0.08
Headache	25/161(16%)	18/91(20%)	10/65(15%)	0.65	0.65	0.85

**Conclusions:** Our results suggest that older onset FMF had a lower percentage of mutations in exon10 of the *MEFV* gene and predominantly presented arthritis and muscle pain during the attacks. It is thus important to distinguish them from other inflammatory diseases such as gout, adult Still's disease, and infectious arthritis.

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SAT0590

### LONG-TERM EFFICACY AND SAFETY OF ADALIMUMAB BY AETIOLOGY IN PATIENTS WITH NON-INFECTIOUS UVEITIS IN THE VISUAL III TRIAL

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**Objectives:** To evaluate the long-term safety and efficacy of adalimumab in patients with non-infectious intermediate, posterior, or panuveitis, across different disease etiologies.

**Methods:** Adult patients in the Phase III VISUAL I/II trials, who met treatment failure (TF) criteria or who completed the study without TF, were eligible to enter the Phase III open-label extension study, VISUAL III, wherein patients received adalimumab 40 mg every other week. In this exploratory analysis, endpoints were analysed by six uveitis etiologies: i) idiopathic/other (IO), ii) birdshot chorioretinopathy (BCR), iii) multifocal choroiditis and panuveitis (MCP), iv) Vogt-Koyanagi-Harada syndrome (VKH), v) sarcoidosis, vi) Behçet's disease (BD). Endpoints assessed through Week 78 of treatment were proportion of patients with: no active inflammatory lesions in both eyes; anterior chamber (AC) cell grade ≤0.5 +in both eyes; vitreous haze (VH) grade ≤0.5 +in both eyes; and quiescence (defined as no active inflammatory lesions AND AC cell grade ≤0.5 + AND VH grade ≤0.5+). Mean best corrected visual acuity (BCVA) was also assessed. Missing data were reported using non-responder imputation for categorical endpoints and last observation carried forward for continuous variables. Adverse events (AEs) were collected from the first adalimumab dose in VISUAL III through the interim cut-off date of Oct 31, 2016.

**Results:** Of 371 patients included in the intent-to-treat analysis, disease etiology subgroups were (n[%]): IO (155 [41.8]); BCR (51 [13.7]); MCP (14 [3.8]); VKH (72 [19.4]); Sarcoidosis (52 [14.0]); BD (27 [7.3]). The proportion of patients achieving quiescence improved over time in all uveitis etiologic subgroups: IO 28.4%/63.9% (Week 0/Week 78), BCR 43.1%/64.7%, MCP 35.7%/50.0%, VKH 37.5%/63.9%, sarcoidosis 32.7%/69.2%, and BD 44.4%/74.1%. The proportions of patients with no active inflammatory lesions, AC cell grade ≤0.5+, or VH grade ≤0.5+, showed moderate increases or decreases between Weeks 0 and 78 within specific etiology subgroups; percentage ranges across all subgroups at Weeks 0/78, were 60.8–87.5/57.1–78.8% (no active inflammatory lesions), 47.2–92.2/50.0–77.8% (AC cell grade ≤0.5+), and 42.9–72.2/57.1–77.8% (VH grade ≤0.5+), respectively. Improvement or maintenance of mean BCVA was observed over time across the etiologic subgroups. AE rates were consistent with the VISUAL I and II trials.

**Conclusions:** Adalimumab increased the percentage of patients achieving quiescence and improved or maintained visual acuity at Week 78 of the VISUAL III study, with consistent results across uveitis etiologic subgroups. No new safety signals were detected with long-term adalimumab treatment.

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SAT0591

### DEMOGRAPHIC AND CLINICAL FEATURES OF FAMILIAL MEDITERRANEAN FEVER PATIENTS

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**Background:** Familial Mediterranean Fever (FMF) is an autosomal recessive genetic disorder that causes recurrent episodes of fever, polyserositis, arthritis, skin eruptions.

**Objectives:** In this study, we aim to present clinical and demographic features of FMF patients followed up in our clinic.

**Methods:** The clinical, demographic, genetic features and managements of 402 FMF patients (fulfilling Tel-Hashomer Diagnostic Criteria) were analysed.

**Results:** The mean age was 36.8±11.2 years, mean diagnosis age was 28±11.9 years, and mean disease duration was 189.2±124.5 months, mean duration between onset of disease and onset of treatment was 93.6±104 months. Consanguineous marriage was detected in 7%<sup>29</sup> patients. Fever and abdominal pain both were initial symptoms in 72% of the patients, while 7% of them had chest pain, 4% had only fever, 15% had arthritis, 1% had erysipelas-like erythema and 1.5% had inflammatory back pain as the first symptom of FMF (table 1).

Eight patients (2%) were suffered from chronic kidney disease and 2 of them were on dialysis programme. Amyloidosis were identified in 14 patients (3.5%) with biopsy.

At least one mutation of *MEFV* gene was detected in 78% patients There was no mutation in 8% patients. In 15% patients, *MEFV* gene analysis could not be done. The most frequent mutation was M694V mutation and its allel frequency was 54%; the frequency of V726A, M680I, E148Q, R761H and A744S allels mutation



were 11%, 7%, 7%, 2%, 1%, respectively. The frequency of compound mutation was 38%, and the most common compound mutation was M694V+R202Q (11%). There was significantly relationship between M694V mutation and arthritis, erysipel-like erythema, proteinuria, sacroiliitis (table 2). Amyloidosis was more frequent in patients who had M694 homozygous mutation. Mean age of disease onset was lower in patient who had M694V homozygous mutation than M694V heterozygous mutation ( $p < 0.001$ ).

**Abstract SAT0591 – Table 1.** Demographical and Clinical Features of FMF Patients

n=402	n(%)
Gender Female	241 (60)
Male	161 (40)
Fever	299 (75.5)
Abdominal Pain	347 (86)
Erysipel-like erythema	54 <sup>13</sup>
Chest pain	83 (21)
Positive family history	174 (43)
Appendectomy	96 <sup>24</sup>
Amyloidosis	14 (3.5)
Chronic kidney disease	8 (2)
Inflammatory back pain	63 <sup>16</sup>
Arthritis	129 (32)
Hip pain	27 (7)
Heel pain	30 (7.5)
Uveitis	4 (1)
Sacroiliitis	44 <sup>11</sup>
Biological treatment	16 <sup>4</sup>

**Abstract SAT0591 – Table 2.** Relationship between M694V mutation and clinical findings

N(%)	Negative	Heterozygous	Homozygous	P
Fever	75 (60)	80 (62)	67 (75)	0,0503
Abdominal pain	107 (85,6)	107 (82,9)	79 (88,8)	0,487
Erysipel-like erythema	5 (4)	13 (10,1)	19 (21,3)	<b>0,0003</b>
Chest pain	21 (16,8)	24 (18,6)	20 (22,5)	0,0575
Myalgia	2 (1,6)	5 (3,9)	3 (3,4)	0,535
Arthritis	32 (25,6)	34 (26,4)	41 (46,1)	<b>0,002</b>
Sacroiliitis	11 (8,8)	12 (9,3)	19 (21,3)	<b>0,0096</b>
Amyloidosis	4 (3,2)	0 (0)	10 (11,2)	N/A
Proteinuria	7 (5,6)	5 (3,9)	18 (20,2)	<b>0,000</b>

**Conclusions:** Tight control and sustained management are important in FMF to protection from amyloidosis. Similar to literature, the most frequent mutation was M694V mutation, and there was significantly relationship between M694V mutation and arthritis, erysipel-like erythema<sup>(1)</sup>, proteinuria, sacroiliitis<sup>(2)</sup> in our study.

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#### SAT0592 HRCT PULMONARY MANIFESTATIONS IN PATIENTS WITH SYNOVITIS, ACNE, PUSTULOSIS, HYPEROSTOSIS, AND OSTEITIS (SAPHO) SYNDROME

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**Background:** Synovitis, acne, palmoplantar pustulosis, hyperostosis and osteitis syndrome (SAPHO) is a rare syndrome that affects the skin, bones and joints.<sup>1</sup> SAPHO syndrome shares a variety of features with the seronegative spondyloarthropathies (SpAs), such as psoriatic arthritis (PsA).<sup>1</sup> While the extra-articular manifestations of PsA are well defined, the systemic involvements of SAPHO syndrome are only reported occasionally.<sup>2</sup> Previous cases of accompanied pleural effusion<sup>3, 4</sup> and organising pneumonia<sup>5</sup> were reported. In clinical work, we observed that pulmonary lesions progressed when diseases aggravated.

However, the relationship between pulmonary manifestations and diseases activity remains unclear.

**Objectives:** This study is to explore the pulmonary comorbidity with SAPHO syndrome.

**Methods:** Pulmonary HRCT images were reconstructed from whole-spine CT images in 67 SAPHO patients. HRCT images of 58 healthy controls were obtained and reviewed. Pneumonia and tuberculosis were excluded. We investigated the presence of different HRCT images findings with detailed examinations.

**Results:** In detailed HRCT evaluations, abnormalities were identified in 45 of all patients. We found stripe in 29 (43.3%) cases, patchy shadows in 22 (32.8%), ground-glass opacity in 11 (16.4%), pleural thickening in 9 (13.4%), solitary nodule in 6 (9%), bronchiectasis in 3 (4.5%), pulmonary bulla in 2 (3%), multiple nodules in 1 (1.5%), and interstitial change in 1 (1.5%). Compared with healthy controls, SAPHO patients have significantly higher rate of patchy shadows while significantly lower percentage of nodules (especially multiple nodules), although the overall rates of abnormal HRCT findings are similar.



**Abstract SAT0592 – Figure 1.** HRCT images in 3 SAPHO patients. A: Ground glass opacities (arrows); B: Solitary nodule (arrow); C: Interstitial change (arrow).

**Conclusions:** Our study was the first to study HRCT pulmonary changes in SAPHO patients. SAPHO patients have significantly higher percentage of patchy shadows and significantly lower rate of pulmonary nodules than healthy controls. BASDAI and age are possible good predictors for abnormal HRCT pulmonary findings.

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#### SAT0593 PROGRESSIVE FIBROSING INTERSTITIAL LUNG DISEASE (PF-ILD) IN PATIENTS WITH AUTOIMMUNE RHEUMATIC DISEASES

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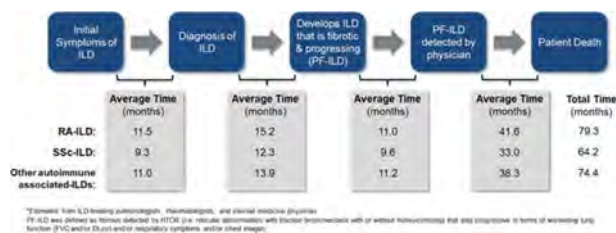
**Background:** Interstitial lung disease (ILD) associated with autoimmune conditions is among the most challenging aspect of care for patients with rheumatic diseases. While idiopathic pulmonary fibrosis (IPF) is the classic fibrosing ILD, some patients with differing clinical ILD diagnoses including autoimmune associated-ILD can develop a progressive fibrosing phenotype. This phenotype is characterised by progressive pulmonary fibrosis, worsening respiratory symptoms, declining lung function, resistance to immunomodulatory therapies and early mortality. There are limited data available on current practice in diagnosis, management and treatment of PF-ILD in patients with autoimmune rheumatic diseases.

**Objectives:** To investigate the patient journey in patients with autoimmune rheumatic diseases and PF-ILD.

**Methods:** Twenty-two ILD experts from Germany, Japan, UK and the US participated in a 1 hour interview. Physicians who spend  $\geq 75\%$  of their professional time managing patients and in whose caseload  $\geq 10$  patients had PF-ILD in the

past year completed an online survey. Physicians (243 pulmonologists, 203 rheumatologists, 40 internal medicine physicians) from the US, Japan, Germany, France, Italy, Spain and UK participated. ILD prevalence and treatment patterns in the US were analysed based on insurance claims from patients with  $\geq 2$  claims with an ILD diagnosis between 2014 and 2016 (ICD-9/10 codes) and  $\geq 1$  visit to a pulmonologist in the 3 years.

**Results:** Analysis of US claims identified 21 592 patients with autoimmune ILD. Rheumatoid arthritis ILD (RA-ILD) and systemic sclerosis ILD (SSc-ILD) were the most prevalent ILDs across all autoimmune rheumatic diseases. The course of the patient journey is summarised (figure 1). Most patients with autoimmune-associated ILD initially present to a rheumatologist or a primary care doctor. Both pulmonologists and rheumatologists play a key role in detection and diagnosis of ILD; however US claims data suggest that the former are more likely to make the diagnosis. Although there is significant inter-patient variation, diagnosis of ILD is estimated to take approximately 9–12 months after symptoms develop. In general ILD is diagnosed earlier in SSc. Management of patients with autoimmune-associated ILD is typically multidisciplinary, involving both a rheumatologist and a pulmonologist. The physician survey suggested that 24%–31% of patients with autoimmune-associated ILD develop PF-ILD; detection can take up to 1 year. The majority of physicians use corticosteroids as a first line treatment across autoimmune rheumatic diseases; cyclophosphamide and mycophenolate mofetil were the second and third first line option for SSc-ILD. Physicians estimate the total disease course in patients with autoimmune-associated PF-ILD to be approximately 5–7 years.



**Abstract SAT0593 – Figure 1.** Physician\* Estimated PF-ILD Disease Course in patients with autoimmune rheumatic diseases

**Conclusions:** Physicians who manage patients with autoimmune diseases estimate that 24%–31% develop PF-ILD. Delayed referral to a pulmonologist or rheumatologist is likely to delay diagnosis and management of PF-ILD. Life expectancy for these patients is believed to be similar to patients with IPF. There is an unmet need for treatments that slow or stabilise disease progression of PF-ILD.

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**SAT0594 WHICH ONE IS MORE VALUABLE FOR DIAGNOSIS OF ADULT ONSET STILL'S DISEASE? SOLELY NEUTROPHILIA OR LEUKOCYTOSIS WITH NEUTROPHILIA?**

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**Background:** Adult onset Still's disease (AOSD) is a rare, auto-inflammatory disease that has unknown etiology and poorly defined pathogenesis. To date, there are several classification criteria, available for AOSD, but most commonly used one is proposed by Yamaguchi et al.<sup>1</sup> One of the major items of this set of criteria is leukocytosis with neutrophilia.

**Objectives:** To usefulness of solely neutrophilia instead of leukocytosis with neutrophilia for the Yamaguchi criteria.

**Methods:** Sixty-one AOSD patients followed at Hacettepe University department of rheumatology were included to analysis. Diagnosis of AOSD was based on physicians' decision, but Yamaguchi criteria was applied for all patients, as well. Complete blood test with differential was noted at the time of diagnosis of AOSD. One of the major criteria of Yamaguchi criteria was "leukocytosis with neutrophilia (defined as more than 80% of leukocytes would be granulocyte)". Leukocytosis [ $>10000/\text{mm}^3$  x1000] and neutrophilia [(6400/ $\text{mm}^3$ ) x1000] were defined according to normal upper limits of our laboratory. To compare with Yamaguchi criteria, neutrophil/leukocyte ratio for all patients were calculated. Descriptive statistics for non-normally distributed countable data were given as median and interquartile range (Med [IQR]).  $p < 0,05$  was considered as statistically significant.

**Results:** Total 61 patients (46 (75%) female) were recruited. Prevalence of major and minor Yamaguchi criteria were as follow: fever in all patients, arthralgia in 58 (95%) patients, rash in 43 (71%) patients, sore throat in 48 (79%) patients, lymphadenopathy and/or splenomegaly in 23 (38%) patients, absence of RF and ANA in 58 (96%) patients, elevated liver enzymes in 47 (77%) patients. Median leukocyte and neutrophil count were 13.5 (IQR;10.1–18,9) x 1000/ $\text{mm}^3$ , 12 (IQR;7.2–17.6) x 1000/ $\text{mm}^3$ , respectively. "Neutrophilia >UNL" was significantly more prevalent than "leukocytosis with neutrophilia >80%" (51 (83,6%) vs. 37 (60,6%),  $p < 0,001$ ). Overall, 14 (23%) patients would have one more positive major criteria if "neutrophilia >UNL" would be used instead of "leukocytosis with neutrophilia >80%". When current Yamaguchi criteria (including leukocytosis with neutrophilia >80%) applied to patients with AOSD, 57 (93,5%) of 61 patients were met the criteria. However, when "neutrophilia >UNL" was used instead of "leukocytosis with neutrophilia >80%", all patients were met the revised criteria.

**Conclusions:** As all patients who had leukocytosis also had neutrophilia but it was not vice versa. In other words, choosing "leukocytosis with neutrophilia >80%" instead of "neutrophilia >UNL" can underdiagnose AOSD approximately in 7% of patients according to Yamaguchi criteria. Moreover, Physicians should be keep in mind that reactive hemophagocytosis may influence the count of leukocyte. Consequently, using "neutrophilia >UNL" as a criteria instead of "leukocytosis with neutrophilia >80" may be more appropriate for the diagnosis of AOSD in real life.

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**Disclosure of Interest:** None declared

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**SAT0595 ANALYSIS OF RECURRENCES AFTER SUSPENSION OF IMMUNOSUPPRESSIVE TREATMENT IN NON-INFECTIOUS UVEITIS**

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**Background:** Uveitis is the most common ocular inflammatory disease. According to the classification, non-infectious uveitis 70% of the total, presenting a chronic course and with it, an increased risk of complications. The phased therapeutic approach in ophthalmology is well established and is based on the efficacy of synthetic and biological immunosuppressive therapy.<sup>1</sup> However, we do not have evidence-based protocols that allow us to know how long to maintain them, or when to interrupt them.

**Objectives:** The main objective is to evaluate the free time without ocular inflammatory activity after the withdrawal of the synthetic and/or biological immunosuppressive treatment in patients with non-infectious uveitis.

As secondary objectives are collected the epidemiological and clinical characteristics, the distribution of the different immunosuppressive drugs employed and

analysed the cases of recurrence after the interruption of treatment, and the need of reintroduction.

**Methods:** A retrospective cohort multicenter study was conducted in patients with a diagnosis of non-infectious uveitis followed in a multidisciplinary unit, that after two or more years of ocular and extraocular inactivity, the immunosuppressive treatment was suspended. It was defined inactive uveitis as cell Tyndall 0 in anterior and vitreous chamber, as well as the absence of other signs of active inflammation (retinal infiltrates, choroid and vasculitis and/or papillitis with angiographic leakage).

Demographic characteristics, anatomical location and laterality of the uveitis, visual acuity at the beginning and end of the study and the drugs used were recorded.

**Results:** We analysed 48 patients with an average age at the onset of immunosuppressive treatment of 39.3 years ( $\pm 16$  years). 85.4% of the uveitis were bilateral. The main diagnoses are described in table 1. In 56.3% of cases a single immunosuppressant was used. Cyclosporine was the most employed (72.9%) and methotrexate was the most used in monotherapy (83.3%). 83% of patients received corticosteroids and 12% treatment with Infliximab. The mean duration of immunosuppressive treatment was 6.9 years ( $\pm 5$ , 7 años). The percentage of total and ocular recurrence was 37.5% and 31.25% respectively. The mean duration of follow-up after treatment suspension was 4.3 years ( $\pm 4.5$  years), being more than 1 year in 77.1% of patients. We found that 75% of patients remained free of recurrence at least 27 months. The administration of two or more immunosuppressive drugs proved to be a risk factor for recurrence ( $p=0,048$ ) and reintroduction of treatment after it ( $p=0,008$ ), which was performed in 39% of the ocular recurrences. Visual acuity did not suffer variation in 78.6% of recurrences and 80.3% of those that did not recur.

Abstract SAT0595 – Table 1-. Main diagnoses

Diagnosis	Female (n=29)	Male (n=19)	All (n=48)
Idiopathic uveitis (n=13)	7 (53,8%)	6 (46,2%)	13/48 (27%)
Juvenil idiopathic arthritis (n=1)	1 (100%)	0 (0%)	1/48 (2,08%)
Multifocal Choroiditis with Panuveitis (n=1)	0 (0%)	1 (100%)	1/48 (2,08%)
Serpiginous choroiditis (n=3)	1 (33,3%)	2 (66,7%)	3/48 (6,25%)
Behçet disease (n=10)	4 (40%)	6 (60%)	10/48 (20,83%)
Birdshot Retinochoroidopathy (n=5)	3 (60%)	2 (40%)	5/48 (10,41%)
Inflammatory bowel disease (n=1)	1 (100%)	0 (0%)	1/48 (2,08%)
Multiple sclerosis (n=3)	3 (100%)	0 (0%)	3/48 (6,25%)
Ankylosing spondylitis (n=1)	0 (0%)	1 (100%)	1/48 (2,08%)
HLA27 positive (n=1)	1 (100%)	0 (0%)	1/48 (2,08%)
Pars planitis (n=2)	1 (50%)	1 (50%)	2/48 (4,16%)
Sarcoidosis (n=5)	5 (100%)	0 (0%)	5/48 (10,41%)
Vogt-Koyanagi-Harada (n=2)	2 (100%)	0 (0%)	2/48 (4,16%)

**Conclusions:** In our cohort, patients with no ocular inflammatory activity for at least two years could benefit from the suspension of immunosuppressive treatment without a visual risk. The use of one or more immunosuppressive drugs has been identified as a risk factor for recurrence.

#### REFERENCE:

[1] Update on the principles and novel local and systemic therapies for the treatment of non-infectious uveitis. *Inflamm Allergy Drug Targets* 2013;12 (1):38–45.

**Disclosure of Interest:** None declared

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SAT0596

#### THORACIC INVOLVEMENT AT DIAGNOSIS DRIVES A DIFFERENTIATED CLINICAL PRESENTATION OF SARCOIDOSIS: ANALYSIS OF 1245 PATIENTS (SARCOGEAS-SEMI)

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**Objectives:** To analyse whether thoracic involvement at diagnosis is associated with a specific clinical presentation of sarcoidosis.

**Methods:** The SARCOGEAS-SEMI is a nationwide registry of patients with sarcoidosis. Radiographic stages at diagnosis were classified as stage 0 (normal), stage I (only bilateral hilar lymphadenopathy -BHL-), stage II (BHL +pulmonary infiltrates), stage III (only infiltrates) and stage IV (fibrosis).

**Results:** The cohort consisted of 1245 patients (722 women, 523 men, mean age at diagnosis 47 years). Pulmonary imaging data at diagnosis was available in 1230 patients including 395 (32%) with stage I, 500 (40%) with stage II, 195 (16%) with stage III and 42 (3%) with stage IV. Patients with no thoracic involvement (stage 0) were more frequently women (73% vs 56%,  $p=0.002$ ), older (52.1 vs 46.8 years,  $p=0.001$ ) and had a higher frequency of skin (54% vs 34%,  $p<0.001$ ) and neurological (14% vs 6%,  $p=0.004$ ) involvements in comparison with those with stages I-IV. Patients without ILD (stage I) were more frequently women (61% vs 54%,  $p=0.031$ ), had a higher frequency of fever (27% vs 19%,  $p=0.002$ ), skin (43% vs 29%,  $p<0.001$ ) and salivary gland involvement (8% vs 3%,  $p=0.001$ ), and a lower frequency of respiratory symptoms (37% vs 54%,  $p<0.001$ ) and liver involvement (9% vs 16%,  $p=0.001$ ) with respect to those with ILD (stages II-IV).

**Conclusions:** A specific clinical and epidemiological pattern of disease presentation was found in patients with no thoracic involvement and in those presenting with interstitial lung disease at diagnosis.

**Disclosure of Interest:** None declared

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SAT0597

#### NEW AUTOINFLAMMATORY PHENOTYPE MANIFESTING AS HYPOCOMPLEMENTEMIC URTICARIAL VASCULITIS AND ASSOCIATED WITH HOMOZYGOUS AGBL3 VARIANT

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**Background:** Autoinflammatory disorders are primarily associated with inborn errors of the innate immune system, but some of them are also developing autoimmune features.

**Objectives:** To define a new autoinflammatory phenotype in a patient with inflammatory attacks manifesting as hypocomplementemic urticarial vasculitis and to identify responsible gene/pathway.

**Methods:** Clinical manifestations of the index case and his family history were carefully searched and blood samples were collected from the index case and his both parents. Genomic variations were screened by whole exome sequencing,



and a systematic search was carried out specifically for identification of deleterious genetic variants in genes involved in novel inflammatory pathways.

**Results:** The index case was coming from a consanguineous family of Assyrian origin, who is now 22-year-old male. He presented to our outpatient clinic with recurrent attacks of fever, urticarial rash on the extremities and trunk, conjunctival injections and arthralgia, without a trigger or more frequently following an infection. His attacks started when he was 13, and two to three days lasting attacks recurred more frequently during warm weather conditions or following hot baths. He had highly elevated CRP and ESR during attacks, but his acute phase response did not return to normal values in between the flares. Low C3 and C4 values were also observed during asymptomatic periods. His ANA test became positive during the course of his disease, with an increasing titer in the last year. He responded partially to corticosteroids as well as canakinumab and anakinra treatments, and he is currently on low dose steroids and 100 to 200 mg/day anakinra. Whole exome sequencing revealed a deleterious homozygous c.769C>T mutation in AGLB3 (ATP/GTP binding protein-like 3) gene, which results in early termination of the protein (p.Gln257Ter) and deletion of the functional carboxypeptidase domain. This protein belongs to metalloproteinases that mediate both deglutamylation and deaspartylation of target proteins. AGLB3 is suggested to catalyse the deglutamylation of polyglutamate side chains, especially in proteins such as tubulins. Also, STRING search revealed the interaction of AGLB3 with complement regulatory proteins, such as CD46, CD55, and CD59, which are potent inhibitors of the complement membrane attack complex. We searched databases from Turkey and other sources including 1000 Genomes Project data, and we could not identify this variant in other individuals.

**Conclusions:** This study identifies the AGLB3 metalloproteinase gene as a potential autoinflammatory gene involved in a novel pathway and possibly associated with hypocomplementemic urticarial vasculitis phenotype. Previously, DNASE1L3 mutations have been associated with hypocomplementemic urticarial vasculitis and systemic lupus erythematosus phenotype. The loss of function mutation in the AGLB3 may result in a potent innate inflammatory response as well as autoimmunity through a new pathway, which is resulting in lower complement levels and ANA positivity along with recurrent inflammatory episodes. This complex phenotype explains a partial response to the IL-1 blockade, and further studies in patients/families with a similar phenotype are needed.

**Disclosure of Interest:** None declared

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SAT0598

#### SYSTEMATIC LITERATURE REVIEW ON THE EFFICACY AND SAFETY OF IMMUNOMODULATORY DRUGS IN PATIENTS WITH NONINFECTIOUS INTERMEDIATE AND POSTERIOR UVEITIS, PANUVEITIS AND MACULAR OEDEMA

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**Background:** Posterior segment uveitis (PSU) is a sight-threatening condition

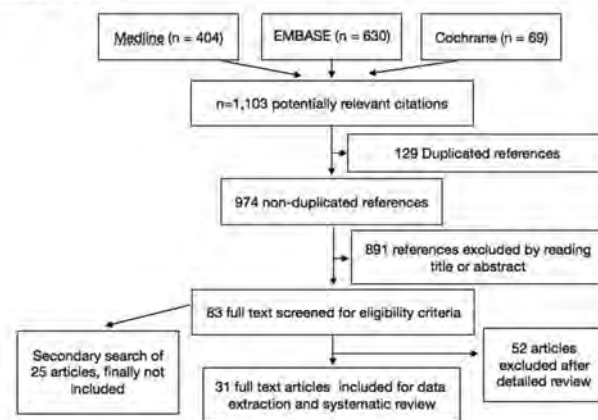
**Objectives:** To perform a systematic review of the literature on the use of immunomodulatory drugs in adult patients with non-infectious and non-malignant PSU including intermediate (IU) and posterior uveitis (PU), panuveitis (PanU) and macular oedema (ME).

**Methods:** Search strategies were designed for Medline, Embase, and Cochrane Library for articles with clinical, safety or cost-effectivity data up to, Jan 2017 followed by secondary search from their bibliography. Quality was assessed (Jadad/Oxford)

**Results:** From 1103 articles, 31 moderate quality clinical trials (CT) were selected, prospective/retrospective, with variability in mean duration, No. and patients' characteristics. PSU was treated with synthetic DMARDs methotrexate (MTX), azathioprine (AZA), cyclosporine A (CsA), cyclophosphamide (CyC), tacrolimus, sirolimus, micophenolate (MMF) and interferon  $\beta$ , and biologic DMARDs ranibizumab, daclizumab, rituximab (RTX), secukinumab, adalimumab (ADA), bevacizumab and infliximab (IFX) at usual dosages. Most common measures: visual acuity (VA), macular thickness and vitreous haze. MTX vs.MMF, was effective in IU, PU and PanU, with no differences in efficacy and adverse events (AEs), neither in Vogt-Koyanagi-Harada. MTX was effective with RTX, and SC was inferior to IFN $\beta$  with lower rate of AEs in IU with cistoid ME (CME). CsA did not show efficacy vs. placebo (pbo), with more neurological AEs. Tacrolimus vs. CsA was safer with similar efficacy, and CsA was useful with no differences vs.

prednisone (pred) or vs.CsG, and similar vs.CYC at 2 y in Behçet PSU. CsA +pred + ketoconazole combined showed additional benefits. CYC+AZA were effective in PU, except for VA and retinal vasculitis, with no differences vs. RTX +MTX. CYC was useful in serpinginoid vasculitis  $\pm$ dexamethasone. ADA was useful in IU, PU and PanU vs. pbo. IFX in Behçet PSU, was more effective vs. prednisolone +CsA + AZA/MTX. Intravitreal ADA and IFX did not show any benefit. Secukinumab vs. pbo did not prevent recurrences. In another RCT, IV route showed a higher response rate vs.SC for 30 mg/kg, with similar rate of EAs. Intravitreal bevacizumab was effective in multifocal choroiditis and CME. Intravitreal ranibizumab was useful in pigmentary retinitis +CME. Daclizumab in Behçet PSU did not show benefit vs. pbo. Tacrolimus as 2nd line in PU was effective  $\pm$ pred. Intravitreal and subconjunctival sirolimus were effective in IU, PU and PanU in vitreal haze but not VA and ME, improving functional scores

#### Studies flow chart



**Conclusions:** 1 Moderate quality of evidence

2 Variability in patients, definitions and outcomes

3 Systemic DMARDs MTX, MMF, CsA, CyC, tacrolimus, sirolimus, MMF and IFN $\beta$  were useful in PSU;AZA in combination

4 Biologic DMARDs ADA, IFX (systemic), ranibizumab, bevacizumab (intravitreal) were useful, daclizumab did not show efficacy. Possible efficacy of secukinumab

5 Intravitreal anti-TNF (ADA,IFX) were not useful

**Disclosure of Interest:** None declared

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SAT0599

#### IDIOPATHIC GRANULOMATOUS MASTITIS MAY RESPOND WELL TO COMBINATION OF IMMUNOSUPPRESSIVES AND GLUCOCORTICOIDS

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**Background:** Idiopathic granulomatous mastitis (IGM) is a rare inflammatory disease of breast. Corticosteroids (CS) and immunosuppressive agents constitute treatment alternatives other than surgery.

**Objectives:** To evaluate the clinical characteristics and treatment responses of IGM patients followed up in our clinic.

**Methods:** The medical records of 70 IGM patients who were referred to Hacettepe University Rheumatology Clinic were examined. Forty-four patients who had at least one visit in the last 2 years were included in the analysis. Demographic, clinical and laboratory characteristics of the patients, treatments, clinical and/or ultrasonographically measured lesion sizes at the time of diagnosis and at the last follow-up were recorded. Complete and partial response in the last control visit were defined as  $\geq$ 50% and <50% decrease in the lesion size, respectively. Lesions which are stable or increasing in size was accepted as unresponsive. Increase in the drug dose by the clinician or increasing of the lesion size during follow-up were considered as relapse.

**Results:** Median age was 35.7 (24.3–57.2) years and median symptom duration was 2.5 (0.2–54.1) months at baseline. Palpable mass (90.9%) and breast pain (88.1%) were the most common symptoms. Skin fistules and axillary lymphadenopathy were present in 16 (37.2%) and 15 (34.1%) patients, respectively. Erythema nodosum was seen in 5 (11.4%) patients during follow-up. The median follow-up duration was 10.5 (1.05–99.6) months. CS monotherapy and combination of CS and immunosuppressive were used in 3 (7.8%) and 38 (86.4%) patients, respectively. Three patients were followed up without treatment. The first immunosuppressive agent was methotrexate (MTX) in 32 patients (84.2%) and

azathiopurine (AZA) in 6 patients (15.7%). In one patient, MTX was switched to AZA due to hepatotoxicity. Treatment regimens and responses of the patients are summarised in table 1. IGM lesions disappeared in 24 patients at the end of follow-up. In two patients who were on MTX and KS, surgical excision was required because of unresponsiveness. Among relapsed patients (n=5), 2 patients were on MTX and KS, 1 patient was on AZA and KS and 2 patients were on KS at the time of relapse. In one patient, relapse was observed 1 year after cessation of MTX and KS.

**Abstract SAT0599 – Table 1.** First line treatments and responses at last follow-up visit\*

	MTX+CS (n=32)	AZA+CS (n=6)	CS (n=3)	Observation (n=3)
Age <sup>a</sup> , years	36.1 (25.6-50.3)	33.8 (28.2-39.9)	28.9 (24.3-57.2)	29.4 (29.4-37.1)
Follow-up duration <sup>a</sup> , months	8.3 (1.5-54.4)	26.0 (13.8-99.5)	9.6 (3.0-35.8)	8.6 (1.0-13.4)
Duration of immunosuppressive treatment <sup>a</sup> , months	7.3 (0.9-28.2)	12.9 (8.2-27.3)	-	-
Immunosuppressive dose <sup>a</sup>	15 (10-15)	150 (100-150)	-	-
Duration of CS treatment <sup>a</sup> , months	7.0 (0.9-25.6)	13.7 (1.9-99.5)	2.5 (2.0-9.6)	-
Initial CS dose <sup>a</sup> , mg	30 (10-40)	20 (10-30)	20 (10-30)	-
CS dose at last control visit <sup>a</sup> , mg	7.5 (0-30)	0 (0-10)	10 (10-15)	-
Patients who discontinued CS, n (%)	12 (37.5)	3 (50.0)	-	-
Response to treatment				
Unresponsive, n (%)	5 (17.2)	1 (16.7)	-	-
Partial response, n (%)	1 (3.4)	-	1 (33.3)	-
Complete response, n (%)	23 (79.2)	5 (83.3)	2 (66.7)	2 (66.7)

\*Lesion size at last follow-up visit was available in 40 patients

<sup>a</sup>Values are given as median (min-max)

<sup>a</sup>Treatment doses are presented as mg/week for MTX and mg/day for AZA.

**Conclusions:** In a case series previously published by our study group, the efficacy of the combined use of KS and immunosuppressants in IGM treatment was retrospectively studied.<sup>1</sup> In this study, the efficacy of immunosuppressive therapy has been demonstrated with prospective approach.

#### REFERENCE:

[1] Konan A, et al. *Breast Care* 2012;7:297-301.

**Disclosure of Interest:** None declared

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#### SAT0600 MULTICENTRIC RETICULOHISTIOCYTOSIS (1980-2017): CLINICAL CORRELATES, TREATMENT OUTCOMES & ASSOCIATION WITH AUTOIMMUNITY & MALIGNANCY

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**Background:** Multicentric reticulohistiocytosis (MRH) is a rare systemic disease characterised by papulo-nodular skin eruptions and a rapidly progressive, deforming arthritis. It can mimic rheumatic disorders such as rheumatoid arthritis or dermatomyositis. Immunosuppression is often helpful, but challenging due to the association of MRH with malignancy.

**Objectives:** To examine the clinical correlates and outcomes of MRH and its association with malignancy and other autoimmune conditions

**Methods:** A retrospective review of all patients with MRH treated at our institution between 01/01/1980 and 04/30/2017 was performed. Demographics, clinical features, laboratory tests, imaging findings, histopathology, treatments and outcomes were abstracted. Data on autoimmune disorders and malignancies before and after MRH diagnosis were collected.

**Results:** We identified 24 patients with MRH (58% female, 75% Caucasian, mean age at diagnosis 52 y). Median length of follow up was 2.3 y. All patients had confirmed diagnosis by histopathology (23 skin, 7 synovial). All patients had cutaneous and articular involvement. Nodular skin lesions were noted in 96% patients (periungual area and dorsal hand in 87%, periarticular 61% [around DIP 42%, PIP 25%, MCP 8%], face 54%, arms 42%, back 29%, neck 21%, legs 21%, ears 12%, scalp 12%). Mucosal nodules were noted in 30%. Regarding articular involvement, 22 (92%) had arthralgia, 21 (88%) patients had joint swelling, and 13 (54%) had synovitis. Frequency of joint involvement was upper extremity PIP (29%) > upper extremity DIPs, MCPs, wrist > MTPs, Toes > Knees > Elbows. Radiographic erosions were noted in 67% patients. Constitutional symptoms included fatigue,<sup>15</sup> unintentional weight loss,<sup>10</sup> lymphadenopathy<sup>4</sup> and pruritis.<sup>11</sup> Systemic features included dysphagia,<sup>5</sup> photosensitivity,<sup>4</sup> dry eyes,<sup>3</sup> pericarditis<sup>2</sup> and pleuritis.<sup>1</sup> Several patients had positive autoimmune serologies: ANA,<sup>8</sup> RF,<sup>5</sup> Anti-CCP,<sup>3</sup> SS-A,<sup>3</sup> SS-B,<sup>2</sup> Anti-DsDNA.<sup>1</sup> A third of patients had concomitant autoimmune disorders: inflammatory arthritis,<sup>3</sup> Sjögrens,<sup>1</sup> chronic focal glomerulonephritis,<sup>1</sup> JRA,<sup>1</sup> psoriasis,<sup>1</sup> myasthenia gravis and ITP.<sup>1</sup> A third of patients (8/24) had malignancy: malignant melanoma,<sup>3</sup> basal cell carcinoma,<sup>2</sup> and 1 each with ovarian carcinoma, squamous cell carcinoma lung, peritoneal

adenocarcinoma, and endometrial carcinoma. Most patients were treated with systemic glucocorticoids<sup>15</sup> and oral DMARDs<sup>13</sup>: methotrexate,<sup>8</sup> cyclophosphamide,<sup>10</sup> chlorambucil<sup>2</sup> and cyclosporine.<sup>1</sup> Biologics were used in 4 patients (1 infliximab, 2 etanercept, 1 adalimumab). Only 2 patients had complete resolution of their symptoms, while majority showed only partial improvement. 10 (44%) patients developed joint deformities involving: wrist,<sup>4</sup> MCP,<sup>4</sup> PIP,<sup>7</sup> DIP,<sup>4</sup> knee<sup>2</sup> and MTP.<sup>3</sup> None had arthritis mutilans. 75% patients were alive at last follow up.



**Conclusions:** To our knowledge, this is the largest series of MRH patients from a single institution, highlighting the rarity of the condition, and an unmet need for treatment options that can allow sustained disease remission. We emphasise the need for histopathology to distinguish it from mimicking rheumatic conditions and initiating early aggressive treatment to potentially prevent deforming joint disease. A high vigilance for malignancy and other autoimmune diseases is necessary.

**Disclosure of Interest:** None declared

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#### SAT0601 ANTI-IL6-RECEPTOR TOLICIZUMAB IN GRAVES' ORBITOPATHY. MULTICENTER STUDY OF 29 PATIENTS

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**Objectives:** To assess the efficacy of Tocilizumab (TCZ) in refractory thyroid associated orbitopathy (TAO) due to Grave's disease.

**Methods:** Multicenter study of 29 patients with TAO refractory to conventional immunosuppressive therapy.

**Results:** We studied 29 patients (58 eyes) (23 women/6 men); mean age at diagnosis 48.79±12.39 years. Besides oral corticosteroids and before the onset of TCZ, patients had been treated with pulses of intravenous methylprednisolone (n=24), methotrexate (n=2) and other drugs (methimazole in 4 cases, leflunomide in 1, selenium in 9). Urgent decompressive surgery had to be performed in 2 patients.

According to the classification of severity of the EUGOGO group (European Group on Graves' Orbitopathy) using the clinical activity score (CAS), before TCZ onset patients whose data were available had severe (n=14 eyes) or moderate

(n=22 eyes) disease. Moreover, patients presented exophthalmos (n=30 eyes), strabismus (n=17 eyes), muscle fibrosis (n=15 eyes) and dysthyroid optic neuropathy (n=1).

TCZ was used in monotherapy (n=27) or combined with methotrexate (n=2) at 8 mg/kg/iv/4 weeks (n=24) or 162 mg/sc/week (n=5). TCZ yielded rapid and maintained improvement in all ocular parameters (TABLE).

After a mean follow-up of 8.96±7.55 months using TCZ, all patients experienced ocular improvement, with TCZ withdrawal in 16 cases due to complete remission (n=5) or stability of ocular inflammation (n=11). Only 4 adverse effects were observed (neutropenia, external otitis, otitis media, costal osteitis).

**TABLE.** Improvement of ocular parameters with TCZ therapy. Data are expressed as mean ±SD or median[IQR].

	BASAL	1 WEEK	2 WEEKS	1 MONTH	3 MONTHS	6 MONTHS	1 YEAR
<b>VA</b>	0.7 [0.5–1]	0.7 [0.6–1]	0.8 [0.7–1]	0.85 [0.7–1]	1 [0.9–1]	1 [0.7–1]	1 [0.8–1]
<b>IOP</b>	19.22 ±4.20	17.25 ±1.90	16.75 ±2.31	18.23 ±5.00	17.39±3.51	16.52±3.56	16.00 ±3.41
<b>CAS</b>	4.97 ±1.72	4.85 ±2.95	-	3.40±2.28	2.34±1.71	1.29±1.12	1.11 ±0.85

VA=visual acuity; IOP=intraocular pressure; CAS=clinical activity score (0/7 at baseline, 0/10 in the rest of time measures).

**Conclusions:** TCZ appears to be useful in TAO treatment.

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SAT0602

#### CLINICAL SIGNIFICANCE OF AUTOANTIBODY POSITIVITY IN IDIOPATHIC PULMONARY FIBROSIS

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**Background:** Recently, the concept of interstitial pneumonia with autoimmune features (IPAF) was proposed by the American Thoracic Society.<sup>1</sup> The serologic domain of IPAF is composed of antibodies to extractable nuclear antigens, cyclic citrullinated peptide antibody, a high titer of rheumatoid factor, and a high titer of antinuclear antibody. However, the clinical significance of the serologic domain of IPAF has not yet been evaluated in idiopathic pulmonary fibrosis (IPF).

**Objectives:** To investigate the clinical significance of autoantibody positivity in IPF.

**Methods:** We retrospectively reviewed the records of 528 patients who met the ATS/ERS/JRS/ALAT diagnostic criteria for IPF at a tertiary hospital from January 2007 through March 2014. Patients treated with pirfenidone or nintedanib, an established IPF treatment regimen, were excluded. All patients were divided into the following 3 groups: autoimmune IPF (n=153), patients with autoantibodies that met the criteria for the IPAF serologic domain; incomplete autoimmune IPF (n=68), patients who did not completely meet the criteria for the IPAF serologic domain; lone IPF (n=307), patients without autoantibodies. Multivariate Cox proportional hazards models with backward elimination were used to investigate the risk factors for mortality.

**Results:** The 5 year mortality rates were as follows: autoimmune IPF group, 54.9% (n=84, 3.4 years after diagnosis [median; IQR=1.9–5.0]); incomplete autoimmune IPF group, 64.7%; lone IPF group, 58.6% (n=180, 2.9 years after diagnosis [median; IQR=1.6–4.9]). Independent risk factors for mortality on multivariable analysis in the overall IPF patient population included age at diagnosis (adjusted hazard ratio (HR) 1.028, p=0.002), autoimmune IPF (adjusted HR 0.747, p=0.050), baseline SaO<sub>2</sub> in the 6 min walking test (6MWT, adjusted HR 0.973, p=0.012), baseline distance in the 6MWT (adjusted HR 0.998, p=0.001), baseline forced vital capacity (adjusted HR 0.977, p<0.001), and diffusing capacity of the lungs for carbon monoxide (DLCO) (adjusted HR 0.979, p<0.001). In the autoimmune IPF group, use of glucocorticoid (not for management of acute exacerbation, adjusted HR 1.971, p=0.029), use of immunosuppressants (adjusted HR 0.343, p=0.002), baseline distance in 6MWT (adjusted HR 0.998, p=0.032), and baseline DLCO (adjusted HR 0.975, p=0.003) were independent risk factors for mortality on multivariable analysis.

**Abstract SAT0602 – Table 1.** Risk factors associated with mortality in autoimmune IPF patients

Characteristics	Hazard Ratios	Multivariable analysis		P-value
		LB	UB	
Use of glucocorticoid (not for acute exacerbation management)	1.971	1.073	3.622	0.029
Use of immunosuppressants	0.343	0.175	0.674	0.002
Baseline distance in 6MWT	0.998	0.996	1.000	0.032
Baseline FVC	0.984	0.966	1.002	0.081
Baseline DLCO	0.975	0.959	0.991	0.003

6MWT = 6-minute walking test; FVC = forced vital capacity; DLCO = diffusing capacity of the lung for carbon monoxide.

**Conclusions:** Our results suggest that positive autoimmunity might be a favourable factor for 5 year mortality in IPF patients compared to those without autoimmunity, and the use of immunosuppressants could be associated with improved mortality in autoimmune IPF patients.

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SAT0603

#### CAN HOMOZYGOUS OR HETEROZYGOUS MEFV MUTATIONS LEAD TO DIFFERENT PRESENTATION OF FAMILIAL MEDITERRANEAN FEVER?

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**Background:** Although some patients with familial Mediterranean (FMF) have heterozygous mutations for MEFV gene, there is a debate about whether heterozygosity for MEFV mutations in FMF might be responsible for disease symptoms or not.

**Objectives:** To evaluate differences between the patients with FMF having homozygous (Hom) or heterozygous (Het) MEFV mutations in terms of clinical features and severity of the disease as well as concomitant disorders.

**Methods:** We included 259 unrelated patients (female: 143, male: 116; mean age: 33.5±12 years) who were clinically diagnosed as having FMF and who met the Tell-Hashomer's diagnostic criteria. The presence of MEFV mutations was investigated in exon 2,3,5 and 10 by multiplex-PCR reverse hybridization method. All clinical manifestations and their features were revised. All the patients were questioned for the presence of concurrent disorders, and the medical records of these patients were revised retrospectively. A previous diagnosis of a concomitant disease was taken into consideration if it met the relevant criteria.

**Results:** In 12 of 259 patient, MEFV mutation analysis was not performed. No mutation was not determined in 8 FMF patients (3.2%). Hom mutation was found in 79 patients with FMF (31.9%), Het plus compound heterozygotes (cHet) in 160 FMF patients (64.7%). Early onset and early diagnosis of FMF were found in Hom group compared to Het plus cHet group (8.4 years vs 13.6 years; 23.3 years vs 28.6 years, p<0.0001, respectively). The number of patients with a higher severity score was significantly higher in hom group than Het plus cHet group (p<0.001). No significant difference was found between Hom and Het plus cHet group in terms of clinical features except for erysipelas like erythema (ELE) (p<0.0001). Concomitant disorders were as follows: ankylosing spondylitis (AS) 24 (9.3%), amyloidosis 13 (5%), Behcet's disease 8 (3%). Amyloidosis (9 vs 4) was significantly higher in Hom group than Het plus cHet group (p<0.01).

**Conclusions:** The presence of homozygous MEFV mutations in contrast to Het mutations creates a tendency for early onset of the disease, early diagnosis, frequent ELE and amyloidosis and severe disease phenotype.

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**SAT0604 SECONDARY HEMOPHAGOCYTIC SYNDROME: RETROSPECTIVE STUDY ACCORDING TO THE UNDERLYING DISEASE**

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**Background:** Secondary Hemophagocytic Syndrome (SHS) is associated with Hematologic (HO), Autoimmune (AI) diseases [such as Systemic Lupus Erythematosus (SLE) or Adult's Still Disease (ASD)] and in a lower frequency with Infections (Inf.) and Tumours (Tum.).

**Objectives:** Describe the demographic and underlying disorders during hospital admission of patients with SHS during the period December/2005-January/2018.

**Methods:** A retrospective search of patients diagnosed with SHS and bone marrow biopsy (B.M.O.) with hemophagocytosis was performed. Patients were grouped in: AI, HO, Inf, Tum. and SHS without cause (wc). The variables were: sex, age, diagnosis of the underlying disease, fever, organomegaly, laboratory findings, days of hospital stay, days from admission to B.M.O. and mortality.

**Results:** A total of 27 patients were found. table 1 shows the characteristics of the groups. AI □ diseases found were: 5 SLE, 2 ASD, 1 Rheumatoid Arthritis and 1 Sclerosing Disease Related to IgG4. The HOs were: 4 Myelodysplastic Syndrome, 3 Non-Hodgkins Lymphomas, 2 Acute Leukemias, 1 Extranodal Lymphoma of Natural Killer Cells (NKC) and 1 Gastric Plasmocytoma. Inf. were: 1 infection of *Pneumocystis* in the recent diagnosis of HIV and Gastroenteritis by *Campylobacter jejuni*. One Tum. in a patient with Glioblastoma multiforme who received temozolomide. During the follow-up no recurrence of SHS was observed. The sCD25 and cytolytic activity of the NKC were not done.

Abstract SAT0604 – Table 1

	All (n=27) (P25-P75 or%)	AI (n=9) (P25-P75 or%)	HO (n=11) (P25-P75 or%)	Inf. (n=2) (P25-P75 or%)	Tum. (n=1)	SHSwc (n=4) (P25-P75 or%)
Years	57 (40–70)	40 (30–56)	67 (57,4–72,5)	46 (38–23)	78	64 (55–72)
Female sex	15 (56)	7 (77)	3 (27)	1 (50)	0	4 (100)
Debut of the underlying diseases	16 (59)	6 (67)	4 (36)	2 (100)	0	4 (100)
Days of hospital stay	35 (20–62)	26 (10–38)	60 (40–91)	23 (20–27)	28	38 (20–56)
Days from admission to B.M.O.	16 (10–30)	12 (5–16)	24 (13–37)	14 (13–16)	13	42 (28–49)
Fever	27 (100)	9 (100)	11 (100)	2 (100)	1	4 (100)
Organomegaly	16 (59)	5 (55,5)	8 (72,7)	2 (100)	0	1 (25)
Haemoglobin (mg/dl)	7 (6,4–7,7)	7,3 (6,7–8,3)	6,6 (6–7,2)	7,6 (7,4–7,7)	8,6	7 (6,7–8)
Platelets (10 <sup>3</sup> /ul)	12 <sup>(5–32)</sup>	17,3 (12–72)	4 (0,6–15)	9,5 (9–10)	5	93 (34–165)
Leukocytes (/ul)	1200 (340–2715)	1860 (1400–3340)	170 (20–685)	2050 (1530–2570)	480	4170 (3343–5135)
Neutrophils (/ul)	580 (0–1280)	890 (650–1130)	0 (0–190)	1160 (580–1740)	230	2190 (1285–3453)
Triglycerides (mg/dl)	341 (241–422)	411 (254–417)	340 (275–367)	373 (323–422)	149	418 (279–520)
Fibrinogen (mg/dl)	172 (117–381)	297 (116–450)	147 (139–321)	214 (214–2014)	117	172 (127–224)
Ferritin (ug/L)	15300 (5015–28729)	13225 (4864–15359)	16751 (15664–47537)	10347 (10051–10642)		14766 (3840–25757)
Oxalacetic glutamic transaminase (UI/l)	144 (74–399)	402 (325–1080)	91 (72–187)	79 (51–106)	54	127 (91–315)
Transaminase aspartate aminotransferase (UI/l)	177 (65–342)	437 (325–596)	108 (88–255)	133 (83–184)	88	103 (28–232)
Lactate dehydrogenase (UI/l)	721 (494–976)	845 (708–959)	638 (339–1133)	597 (519–674)	426	786 (497–1797)
Mortality	11 (4)	1 (11)	7 (37)	1 (50)	0	2 (50)

**Conclusions:** Patients with SHS to HO disease had a high mortality and a longer hospital stay compared to the rest of the groups. Practically all patients met all

diagnostic criteria, the most frequent were fever, pancytopenia and hyperferritinemia.

**Disclosure of Interest:** None declared

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**SAT0605 THE PRESENCE OF UVEITIS PREDICTS THE RESPONSE TO THE INTERLEUKIN (IL)-1 INHIBITORS ANAKINRA AND CANAKINUMAB IN BEHÇET'S DISEASE**

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**Background:** In recent times IL-1 inhibition has been proposed as an intriguing therapeutic option in Behçet disease (BD) patients with multi-drug resistant manifestations.<sup>1</sup> However, despite the good clinical results obtained during the last years, cases of BD nonresponsive to anakinra (ANA) and canakinumab (CAN) have also been identified. This evidence has induced to suspect the existence of specific subsets of patients characterised by a more pronounced IL-1 driven pathogenesis.<sup>2,3</sup>

**Objectives:** To identify predictive factors of response to interleukin (IL)-1 inhibition among demographic, clinical and therapeutic data in patients with (BD).

**Methods:** BD patients treated with ANA or CAN were enrolled. Patients were divided into 2 groups according to the clinical response: group 1 included subjects showing a treatment duration of at least 52 weeks and no secondary inefficacy during the first follow-up year; the remaining patients were included in the group 2. Demographic, clinical and therapeutic data were analysed to identify significant differences between groups.

**Results:** Eighteen patients (50%) were included in group 1 and 18 (50%) in group 2. A better response to IL-1 inhibitors was significantly more common among patients with BD-related uveitis (p=0.006) and patients with a longer disease duration (p=0.03).

**Conclusions:** IL-1 blockade is effective in BD, especially in the subset of patients presenting ocular involvement and in those with long-lasting disease.

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**SAT0606 DISEASE MODIFYING ANTI RHEUMATIC DRUGS IN THE TREATMENT OF SAPHO SYNDROME: SYSTEMATIC LITERATURE ANALYSIS**

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**Background:** SAPHO (Synovitis Acne Pustulosis Hyperostosis Osteitis) Syndrome is a rare, heterogeneous clinical entity with cutaneous and osteoarticular expression. The therapeutic management is not codified and there is no validated evaluation tool for SAPHO syndrome.

**Objectives:** To perform a systematic analysis of the literature in order to evaluate the effects of DMARDs in SAPHO syndrome.

**Methods:** Bisphosphonates, conventional and targeted synthetic DMARDs, anti-TNF alpha, and other biologics have been subjected to advanced Pubmed research. Treatment was considered effective when the patient validated the response criteria defined in the study or if at least partial benefit was obtained for a minimum of three months. The different treatments were ranked according to their effectiveness rate in three interest groups and then grouped by therapeutic class to determine an overall response rate. These rates led to the calculation of an efficacy index weighted by the number of patients treated in the subgroup (molecule or therapeutic class) compared to the total number of patients in our study.

**Results:** Treatment efficacy was evaluable in 284 of the 292 patients analysed. The clinical presentation of cases was reported in 205 patients for osteoarticular

involvement, and 193 for cutaneous involvement. The group of treatments that most often induces a therapeutic response (in more than 75% of cases) includes lbandronate, Etanercept, Anakinra, Infliximab, Pamidronate and Adalimumab. Pamidronate, which represents the largest subpopulation in our study, has the highest weighted index of efficacy. Zoledronic acid, Leflunomide, Ustekinumab and Methotrexate have less often induced a therapeutic effect (efficacy between 50% and 75%) and Sulfasalazine and Secukinumab have response rates of less than 30%. In total, bisphosphonates and TNF alpha antagonists have efficacy rates of 87.77% and 85% respectively. The weighted index, more than twice as high for bisphosphonates (42.96 versus 17.96), reflects the predominant use of these in SAPHO syndrome, with most often a beneficial effect. Conventional and synthetic targeted DMARDs and other biological treatments are less often effective in our study, with response rates of 47% and 58% respectively. The frequencies of each clinical manifestation were in agreement with the data of the literature. There was no clear clinical profile of a good responder to a particular treatment.

Therapeutic class	Number of patients	Number of responders	Efficacy rate (%)	Weighted index
Bisphosphonates	139	122	87,77	42,96
Conventional DMARDs	68	32	47,06	11,27
Synthetic targeted drugs	0	NA	NA	NA
Anti TNF alpha	60	51	85	17,96
Other biologics	17	10	58,82	
TOTAL	284	215	75,82	NA

**Conclusions:** This work made it possible to rank the different DMARDs used in the SAPHO syndrome. Anti TNF alpha and Pamidronate are the treatments that seem to bring the higher benefit.

**Disclosure of Interest:** None declared

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#### SAT0607 DRUGS USED OFF LABEL IN A RHEUMATOLOGY SERVICE OF A TERTIARY HOSPITAL

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**Background:** The use of drugs off-label (DOL) is not uncommon in Rheumatology daily clinical practice for the treatment of patients with immune-mediated inflammatory diseases (IMID).

**Objectives:** To analyse the use of DOL requested by the Rheumatology Service.

**Methods:** We reviewed the medical records of all patients registered in the DOL database of the Hospital Pharmacy Service between July 2009 and March 2017. The following variables were collected: date of approval and start of the drug, physician, disease, reason for indication, sex and age of the patients, response to treatment according to the global assessment of the responsible physician, date and reason of withdrawal. A descriptive study of the variables collected through STATA 12 is carried out.

**Results:** 225 DOL were requested for a total of 174 patients. Women were 78.7%, with an average age of 56.5 years (sd 1.15). In most patients (77%) a single drug was requested. In 37 patients were requested between two (16.4%) and seven drugs (0.5%). The indications of the DOL in our database were: connective tissue diseases (CTD: 46.6%), vasculitis (23%), rheumatoid arthritis (RA: 5.2%) and spondyloarthritis (SPA:8%). Other diseases (17.2%) are included in two heterogeneous groups classified according to their etiology (autoimmune (8.6%) or not (8.6%).

39.5% of the drugs requested were conventional synthetic DMARDs (csDMARDs), 38.2% biological DMARDs (bDMARDs), 7.5% were antivirals, 2.6% vasodilators and 12% other drugs.

Conventional synthetic DMARDs (csDMARDs) represented 39.5% of request, biological DMARDs (bDMARDs) 38.2%, antiviral drugs 7.5%, vasodilator drugs 2.6% and other drugs 12%.

Tables 1 and 2 show csDMARDs and bDMARDs respectively, according to the indication.

The effectiveness of the DOL was variable, ranging between 0% and 76.5%. The most effective were antiviral drugs, used to treat viral infections in immunosuppressed patients (76.5%), tocilizumab (72.2%) and rituximab (61.1%). By contrast, the least effective were anakinra (0%) and TNF blockers (31.8%). The csDMARDs group had an effectiveness of 53.9% (Mycophenolate stands out with 75% effectiveness).

The disease groups that responded best to DOL therapy were connective tissue and vasculitis, with 58% and 53.7% of effectiveness.

**Abstract SAT0607 – Table 1**

	RA	CTD	SPA	VASCULITIS	OTHERS <sup>1</sup>
APREMILAST(%)	0	0	50	0	0
CYCLOPHOSPHAMIDE (%)	28.6	1.9	0	0	16.7
CYCLOSPORINE(%)	14.3	7.7	0	4.6	16.7
LEFLUNOMIDE(%)	0	1.9	50	45.5	16.7
MYCOPHENOLATE(%)	42.9	86.5	0	50	50
TACROLIMUS(%)	14.3	1.9	0	0	0

**Abstract SAT0607 – Table 2.**

	RA	CTD	SPA	VASCULITIS	OTHERS <sup>1</sup>
ABATACEPT (%)	0	0	7.7	3.9	16.7
ANAKINRA(%)	0	0	0	0	25
TNF blockers (%)	0	6	53.9	30.8	41.7
RITUXIMAB(%)	0	87.9	0	26.9	0
TOCILIZUMAB (%)	100	3	23.1	38.5	16.7
USTEKINUMAB (%)	0	0	15.4	0	0

<sup>1</sup>Others: other diseases mediated by immune mechanisms

**Conclusions:** Rheumatic diseases for which DOL is most commonly requested are connective tissue and vasculitis, as a consequence of the absence of specific indications for these pathologies. In our experience, rituximab is a good option in the treatment of connective tissue diseases, which contrasts with the results of some clinical trials. Tocilizumab is a good therapeutic option in the treatment of vasculitis, a group that includes Giant Cell Arteritis, as recently confirmed with its approval for this indication.

**Disclosure of Interest:** None declared

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#### SAT0608 HOW TO DIFFERENTIATE ADULT ONSET STILL'S DISEASE FROM OVERALL OTHER CAUSES OF FEVER OF UNKNOWN ORIGIN: RESULTS OF A PROSPECTIVE STUDY FROM A TERTIARY REFERRAL CENTRE

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**Background:** Adult onset Still's disease (AOSD) is a rare, auto-inflammatory disease that commonly presents as fever of unknown origin (FUO), and most common rheumatologic cause of FUO. Clinical and/or laboratory parameters that can discriminate AOSD from other causes of FUO need to be clarified in current literature.

**Objectives:** To determine clinical and/or laboratory parameters that help to differentiate AOSD from other causes of FUO and demonstrating a clinician-friendly algorithm for this purpose.

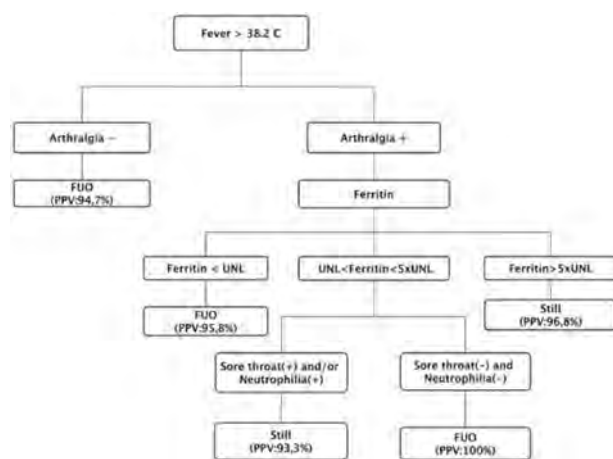
**Methods:** Data from patients who admitted to Hacettepe University Hospitals, inpatient sections of department of internal medicine with the complaint of FUO, who eventually had a certain diagnosis, collected prospectively during 30 months. AOSD patients followed at Hacettepe University department of rheumatology were included. Clinical and laboratory data were collected at the time of diagnosis of AOSD and time of admission of patients with FUO.

**Results:** Total 156 patients (n=69, for AOSD; n=87, for FUO) were included. FUO group were also divided into three subgroups: rheumatologic (n=31, 35.6%), infectious (n=28, 32.2%) and malignant (n=28, 32.2%) causes. While 51 (74%) patients were female in AOSD group, 43 (49.4%) patients were female in FUO group (p=0.03). Frequency of rash, arthralgia, arthritis, sore throat, fever at night (p<0.001 for each), history of hemophagocytosis (p=0.037) were significantly higher in AOSD group. Fever peak number equal and/or higher than 3, presence of lymphadenopathy (p=0.002 and p=0.001, respectively) were significantly higher in FUO group. While leukocytosis, neutrophilia, thrombocytosis, hyperferritinemia, higher lactate dehydrogenase and complement 3 levels (p<0.001 for each) were significantly more frequent in AOSD group, albumin levels lower than 3 g/dl and positive rheumatoid factor (p=0.009 and p=0.002, respectively) were significantly more frequent in FUO group. Results of univariate and multivariate analysis are given in table 1. Algorithm for discrimination of AOSD and FUO is given at **Abstract SAT0608 – figure 1.**

**Abstract SAT0608 – Table 1.** Results of univariate and multivariate analysis

Variables	Univariate Analysis			Multivariate Analysis		
	Odds Ratio	Confidence Interval	p value	Odds Ratio	Confidence Interval	p value
<b>Favours Still's</b>						
Fever at night	7,66	3,53–16,5	<0001			
Rash	10,08	4,80–21,2	<0001	31,3	3,6–271,9	<b>0002</b>
Arthritis	6,58	3,09–14,01	<0001			
Arthralgia	36	10,46–123,8	<0001	158,1	4,3–5755,8	0006
Sore throat	27,72	11,58–66,33	<0001	20,8	2,8–154,7	0003
Hemophagocytosis	4,79	0,96–23,89	0079			
Neutrophilia	10,87	4,90–24,13	<0001	18,4	2,6–132,3	0004
Ferritin ≥ 5 x UNL	4,88	2,34–10,16	<0001	132,8	7,1–2502,9	0001
LDH	7,12	2,35–21,59	<0001	6,2	0,76–50,9	0087
C3	3,20	1,47–7,00	0003			
Female	2,90	1,46–5,73	0002			
<b>Favours FUO</b>						
Pleuritis	2,04	0,68–6,12	0,19			
Fever peak number ≥ 3	3,66	1,16–11,52	0019	69	2,2–2114,4	0015
Lymphadenopathy	3,39	1,72–6,79	<0001			

UNL: Upper normal limit (for ferritin: 336 ng/ml)



**Conclusions:** Presence of arthralgia, hyperferritinemia, sore throat and neutrophilia strongly favour AOSD in patients presenting as FUO. This study demonstrates a clinician-friendly algorithm for the first time in current literature.

**Disclosure of Interest:** None declared

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**SAT0609** **VENOUS VESSEL WALL THICKNESS IN LOWER EXTREMITY IS INCREASED IN MALE BEHCET'S DISEASE PATIENTS WITH AND WITHOUT VASCULAR INVOLVEMENT**

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**Background:** Vascular involvement is seen in up to 40% of the patients with Behcet's Disease (BD), especially in young males and is one of the major causes of mortality and morbidity. Lower extremity vein thrombosis due to vascular inflammation is the most frequent form of vascular involvement in BD. Recently, assessment of vessel wall thickness (VWT) and venous dilatation by US is suggested to be valuable in patients with vascular inflammation.

**Objectives:** In this study, we investigated whether vessel wall thickness or dilatation is present in young male BD patients prone to venous vascular disease.

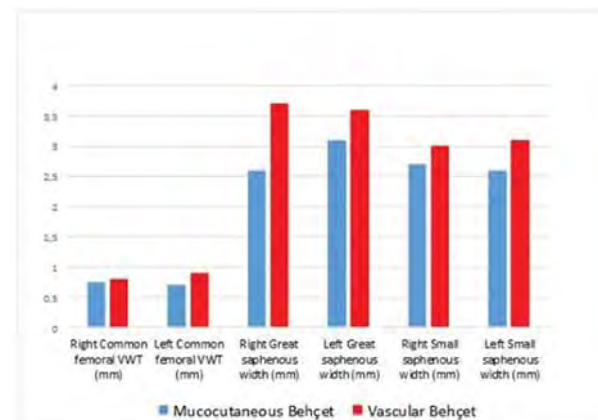
**Methods:** Thirty male patients with BD without major organ involvement and 29 male patients with Vascular BD (VBD) followed in Marmara University Behcet's Clinics, 24 healthy male controls and 27 male patients with Ankylosing Spondylitis (AS) were included the study. Bilateral lower extremity venous doppler ultrasonography (US) was performed by an experienced radiologist blinded to cases. No patients except VBD were under immunosuppressive treatment. Bilateral common femoral vein (CFV) wall thickness and great/small saphenous vein dilatations were examined. Behcet Syndrome Activity Score (BSAS) was used for the general assessment of disease activity. In 10 patients, CFV wall thickness was measured by 2 different radiologist (RE, RA) in the same day to calculate "inter-observer reliability". Correlation between radiologists was good. (r=0.765, p<0.001).

**Results:** The mean disease duration was 9.1±6 years in patients with BD. BSAS score was 24±17. All venous measurements were significantly higher in BD compared to AS and healthy controls (p<0.001 for all, table 1). When we compared mucocutaneous BD and VBD, all measurements of patients with VBD were higher than mucocutaneous BD. But only left CFV thickness and width of right great saphenous vein reached the statistical significance (p<0.001, an p=0.028, respectively, figure 1). There were no correlations between BSAS, acute phase reactants and venous wall measurements.

**Abstract SAT0609 – Table 1.** Venous wall measurements of lower extremity in study groups.

	Behçet's Disease (n=59)	Ankylosing Spondylitis (n=27)	Healthy Controls (n=24)	P Value
Age, years	32.5 (23–42)	32 (20–37)	27.5 (25–42)	0.023
Body Mass Index (kg/m <sup>2</sup> )	25.1 (18–33)	25 (18–32)	23.8 (20–29)	0.213
Right Common femoral VWT (mm)	0.8 (0.04–1.8)	0.3 (0.1–0.6)	0.25 (0.06–0.4)	<b>&lt;0.001</b>
Left Common femoral VWT (mm)	0.8 (0.3–1.6)	0.3 (0.1–0.5)	0.2 (0.04–0.6)	<b>&lt;0.001</b>
Right Great saphenous width (mm)	3.1 (0–6.4)	2.5 (1.1–3.5)	2.1 (1.3–3.5)	<b>&lt;0.001</b>
Left Great saphenous width (mm)	3.1 (0–7.4)	2.6 (0.3–4.8)	2.4 (1.6–3.6)	<b>&lt;0.001</b>
Right Small saphenous width (mm)	2.8 (0–5.3)	1.7 (1–3.1)	1.4 (0.9–3.7)	<b>&lt;0.001</b>
Left Small saphenous width (mm)	2.7 (0–5.2)	1.8 (1.1–3.4)	1.6 (0.8–3.6)	<b>&lt;0.001</b>

VWT: Venous wall thickness



**Abstract SAT0609 – Figure 1.** Venous Vessel Assessments of patients with Mucocutaneous Behçet and Vascular Behçet

**Conclusions:** In our study, an increased venous vessel wall thickness in lower extremity was shown in male BD patients with or without vascular involvement. As a similar change was not observed in controls, we think, increased VWT might be an early sign of venous inflammation in patients with BD rather than a result of non-specific systemic inflammation.

**Disclosure of Interest:** None declared

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**SAT0610** **A DECLINING TREND IN FREQUENCY OF SECONDARY AMYLOIDOSIS IN BEHCET'S SYNDROME**

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**Background:** A decline in the frequency of AA amyloidosis secondary to rheumatoid arthritis and infectious diseases has been reported. This is probably due to more effective treatment strategies. We had previously reported that although amyloidosis occurs in less than 0.5% of BS patients, it is one of the leading causes of death.<sup>1–3</sup> We had an impression that the frequency of amyloidosis is decreasing among our patients with BS.

**Objectives:** We aimed to determine the change in the frequency of AA amyloidosis over years in BS pts in addition to elaborating on clinical characteristics and outcomes.



**Methods:** We performed a chart review to identify all pts with amyloidosis in our BS centre since 1976. We noted demographic characteristics, BS manifestations, age at BS and amyloidosis diagnosis, treatment modalities of these pts. Our endpoints were death and end stage renal disease (ESRD) requiring renal replacement therapy. The prevalence of amyloidosis was calculated separately for two periods (pts registered between 1976–2000 and 2000–2017)

**Results:** Among our 9410 BS pts, 27 (0.29%) had amyloidosis. We identified 24 pts with amyloidosis among the 3820 pts in the earlier cohort and 3 additional amyloidosis among the 5590 pts in the recent cohort. The frequency of AA amyloidosis had declined from 0.62% to 0.054% in the recent cohort. M/F ratio was 22/5 and mean age at BS diagnosis was 29.5±7.4 years. Twenty-two (82%) of the pts with amyloidosis had major organ involvement (vascular involvement in 15, eye involvement in 13 and neurologic involvement in 2). Five (18%) of 27 pts had only mucocutaneous involvement. AA amyloidosis was diagnosed after a mean duration of 9.8±6.7 years (mean age at amyloidosis: 39.3±9.3 years) and was confirmed with renal biopsy in 14 pts and rectal biopsy in 13. Eight pts had non-nephrotic range proteinuria at amyloidosis diagnosis. After amyloidosis diagnosis, 24 pts continued their previous immunosuppressives and colchicine. Two of these 24 were on anti-TNFs at AA diagnosis. Biologics were initiated in 3 pts who were most recently diagnosed to have amyloidosis, anti-TNFs in 2 and tocilizumab in 1. Fourteen (52%) pts had died after a median follow-up of 3 (IQR:1–8.75) years, 3 were lost to follow-up just after amyloidosis diagnosis and 10 (37%) are still alive after a median follow up of 16 (IQR:10–23) years. The reasons for death were infections in 5, related to ESRD in 5, subarachnoid haemorrhage, gastric adenocarcinoma, liver cirrhosis and iatrogenic bowel perforation in 1 patient each. 10 (71%) of these 14 pts had developed ESRD before their deaths. Overall, 15/27 pts developed ESRD after a median follow-up of 3.5 (IQR:1.25–6.5) years after amyloidosis diagnosis. 5 of them had renal transplantation, all but 1 are still alive after 3, 4, 6, and 12 years.

**Conclusions:** AA amyloidosis appears to be a rare, but fatal complication of BS. Around 50% of patients died after a median follow-up of 3 years after amyloidosis. This study showed a decreasing trend of AA amyloidosis due to BS similar to that observed in other inflammatory and infectious causes. The shorter follow-up duration may be contributing for the lower prevalence of AA amyloidosis in the recent cohort.

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**Disclosure of Interest:** None declared

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SAT0611

#### CANAKINUMAB USE IN ADULT FAMILIAL MEDITERRANEAN FEVER PATIENTS: A LARGE SINGLE CENTRE EXPERIENCE

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**Background:** IL-1 blocking agents have been shown to be effective in the prevention of attacks in colchicine resistant FMF (crFMF) patients. Canakinumab is FDA approved long acting recombinant IL-1 receptor antagonist for use in crFMF patients which is available for off label use in Turkey. Herein, we aimed to share our real life single centre experience for use of canakinumab in adult crFMF patients.

**Methods:** Data was derived from Gazi FMF cohort which was established in year 2010. From that date patients with FMF who were diagnosed according to the Tel Hashomer criteria were registered. Co-morbidities, detailed attack characteristics, type, duration, severity, treatments, laboratory parameters and impact of FMF on their life in terms of quality of life and work productivity were recorded either by FMF diary or a mobile phone application (FMF AIDD free to download from App-Store and android market). A retrospective cohort analysis was made from records of patients who were treated with canakinumab.

**Results:** Eighteen adult crFMF patients (%61 female) treated with canakinumab were enrolled in this study. The median age was 31<sup>24–58</sup> years and the median disease duration was 28<sup>16–40</sup> years. All patients harbour homozygous or compound heterozygous exon 10 *MEFV* mutations. Treatment reasons for canakinumab were colchicine resistance (n=14) and amyloidosis (n=4). In three patients canakinumab was initiated directly, while in 15 it was switched from anakinra (seven was allergic to anakinra, one patient had significant leukopenia, in six fail to control attacks). The median duration of canakinumab use was 8 (min 1- max 22) months. In two patients canakinumab was used as 300 mg/monthly, and in

remaining as 150 mg/monthly. Pre- and post-canakinumab periods of patients were compared (Table). Patient reported attack severity (p<0.01), duration (p<0.01), frequency (p<0.01), C-reactive protein (CRP) (p<0.01) and erythrocyte sedimentation rates (p<0.01) were significantly improved while serum creatinine and alanine aminotransferase (ALT) levels remained same (p=0.2, p=0.35, respectively). Canakinumab achieved complete disease remission in 5 patients. Side effects requiring discontinuation of canakinumab were observed in none of patients.

**Table.** Comparison of attack characteristics of 18 Adult crFMF patients before and after canakinumab

	Colchicine	Colchicine +canakinumab	P
Attack severity, VAS	8,5 (5–10)	3,5 (0–10)	<0,01
Attack duration, hours	108 (48–144)	24 (0–96)	<0,01
Attack frequency*	6 (1–10)	1 (0–3)	<0,01
CRP, mg/L	35,8 (3,8–85,0)	4,2 (2,45–55)	<0,01
ESR, mm/h	38 (11–67)	12 (3–44)	<0,01
Serum creatinine	0,66 (0,40–3,00)	0,70 (0,43–3,00)	0,20
ALT	20 (10–55)	19 (9–70)	0,35
Treatment duration, months	204 (48–456)	8 (1–22)	

\*Attack frequencies adjusted for 3 months intervals. VAS: visual analogue scale, CRP: C-reactive protein, ALT: alanine aminotransferase, ESR: erythrocyte sedimentation rate

**Conclusions:** Canakinumab is effective in the prevention of attacks with a favourable safety profile.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.7283

SAT0612

#### THE EFFICACY OF CALCINEURIN INHIBITORS IN PATIENTS WITH ADULT-ONSET STILL'S DISEASE: SINGLE-CENTRE HISTORICAL COHORT STUDY

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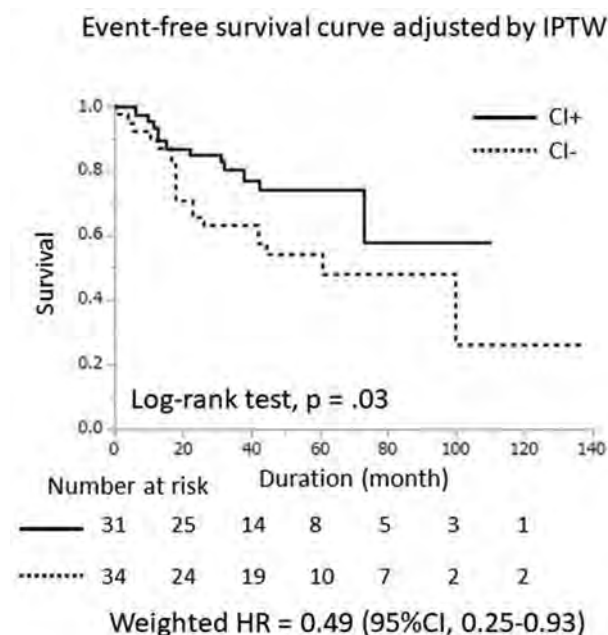
**Background:** Adult-onset Still's disease (AOSD) is a systemic inflammatory disorder generally responsive to corticosteroid therapy, whereas refractory AOSD is often encountered that not controlled by corticosteroid monotherapy. In such cases, methotrexate and biologics including TNF- $\alpha$ , IL-1, or IL-6 inhibitors are used.<sup>1</sup> However, more treatment options are required for refractory AOSD patients who are intolerant to methotrexate or biologics. Calcineurin inhibitors downregulate T cell activation through inhibiting IL-2 transcription and signal transduction. Therefore, calcineurin inhibitors are reasonable therapeutic medication for AOSD since T cells and subsequently activated macrophages play a pathophysiological role in AOSD.<sup>2</sup> Nevertheless, only a few case series have indicated effects of calcineurin inhibitors in clinical practice.

**Objectives:** To evaluate the efficacy of calcineurin inhibitors in patients with AOSD.

**Methods:** This is a single-centre historical cohort study comprised of the consecutive patients with AOSD according to Yamaguchi classification criteria, who were attending our Rheumatology Department between January 2000 and December 2016. The primary endpoint was set as the time from the initiation of treatment to event defined as death of any causes, relapse of AOSD requiring an increase of corticosteroid dose, or serious adverse effects. Secondary endpoints were set as the minimum dose of corticosteroid, persistency rate of calcineurin inhibitors, and safety. Based on the recurrent event data analysis, these endpoints were evaluated for each event. We divided the events into two groups according to the treatment that included calcineurin inhibitors (CI+) or conventional therapy without calcineurin inhibitors (CI-), and compared them after adjustment using inverse probability of treatment weighting (IPTW) methods.

**Results:** Forty-two patients (31 female and 11 male) were enrolled in this study. Mean age was 41 year-old, and median follow-up period 38 months. Thirty-one events in 21 patients were treated with therapeutic regimen including calcineurin inhibitors (CI+, cyclosporine: 7, tacrolimus: 24), and 34 events in 25 patients were treated with the conventional therapy excluding calcineurin inhibitors (CI-). After adjustment, the CI +group had significantly longer event-free survival than the CI-group (figure 1). The weighted hazard ratio (HR) was 0.49 (95% CI, 0.25–0.93, p=0.03). In addition, the CI +group had lower doses of corticosteroid (3.5 vs 6.1 mg/day, p=0.03) when the events occurred. The persistency rate of

calcineurin inhibitors was 92% at 5th year. Serious infection occurred in four patients (19%) in the CI+ group, and one of them had a fatal course.



**Conclusions:** Our retrospective analysis suggested that calcineurin inhibitors could be an additional option for AOSD and further prospective studies were desired.

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**Disclosure of Interest:** None declared

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#### SAT0613 INCREASED SERUM LEVEL OF IL-36 RECEPTOR ANTAGONIST IS ASSOCIATED WITH ACTIVE DISEASE IN PATIENTS WITH ADULT-ONSET STILL'S DISEASE

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**Background:** Adult onset Still's disease (AOSD) is an inflammatory disorder which was associated with varying level of pro-inflammatory cytokines. However, the role of natural anti-inflammatory molecules has not been evaluated to date. Interleukin (IL) 1 cytokine family is closely related to clinical presentations, disease activity and thus is a target for treatment of AOSD. IL-36 receptor antagonist (Ra) is an anti-inflammatory molecule, but its clinical significance has not been studied in AOSD patients.

**Objectives:** To figure out the role of IL-36Ra in monitoring disease activity in patients with AOSD.

**Methods:** The number of 49 AOSD patients meeting Yamaguchi criteria were recruited. Each patient was serially monitored following clinical course of flare and remission, which presented at least 2 points of change in modified Pouchot's score. They were divided into two groups by clinical courses, which were predominant systemic symptoms or arthritis. We compared erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), ferritin as disease activity markers between flare and remission. Serum levels of inflammatory cytokines, IL-18, IL-37, and IL-36Ra were measured by enzyme-linked immunosorbent assay (ELISA) in each clinical state of AOSD patients.

**Results:** Forty-nine patients with AOSD were included in this study; 40 were women (81.6%) and 9 were men (18.3%), with mean age of  $49.08 \pm 14.17$  years old. The mean duration of follow-up was  $6.44 \pm 3.87$  years, and mean difference of modified Pouchot's score was  $5.37 \pm 1.98$  between remission and flare. The number of 33 (67.4%) patients had presented systemic symptoms predominantly, while 16 (32.7%) presented arthritis more frequently in their clinical course. In flare state of AOSD, overall inflammatory markers were elevated, including cytokines

of IL-18 and IL-37. The serum level of IL-36Ra was  $164.04 \pm 169.03$  pg/mL in active state, compared to  $125.36 \pm 452.0$  in inactive state of AOSD patients ( $p < 0.001$ ). IL-36Ra presented positive correlation with modified Pouchot's score and inflammatory markers, including CRP ( $r = 0.286$ ,  $p < 0.01$ ), ferritin ( $r = 0.225$ ,  $p < 0.05$ ) and IL-37 ( $r = 0.353$ ,  $p < 0.01$ ), but was not with level of IL-18 and ESR in active AOSD. Distribution of IL-36Ra level was analysed by each clinical course, however, there was no significant difference in level of IL-36Ra by clinical presentations stratified with predominance of arthritis.

**Abstract SAT0613 – Table 1.** Comparison of serum IL-36Ra levels in active AOSD patients with other markers for disease activity

	Modified Pouchot's score	ESR	CRP	Ferritin	IL-18	IL-37
IL-36Ra	0.295 <sup>a</sup>	0.086	0.286 <sup>b</sup>	0.225 <sup>a</sup>	0.095	0.353 <sup>a</sup>

Correlation coefficient was presented by each inflammatory markers; <sup>a</sup>  $p < 0.05$ , <sup>b</sup>  $p < 0.01$

**Conclusions:** Serum IL-36Ra level was significantly increased in active AOSD patients compared to inactive AOSD patients, presenting positive correlation with other inflammatory markers. In patients with AOSD, level of IL-36Ra might be another potential serologic marker to estimate disease activity, especially active state of the disease.

**Disclosure of Interest:** None declared

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#### SAT0614 NEW VARIANT IN THE IL1RN-GENE ASSOCIATED WITH LATE ONSET AND ATYPICAL PRESENTATION OF DIRA

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**Background:** Deficiency of the interleukin-1 receptor antagonist (DIRA) is an autoinflammatory disease characterised by severe systemic inflammation with bone and skin involvement present in the first days of life.

**Objectives:** We report a novel variant in the *IL1RN*-gene associated an atypical phenotype of DIRA.

**Methods:** A 3 year-old Caucasian boy presented with recurrent monthly episodes of fever and fatigue, associated with lymphadenopathy, pericarditis, pleuritis, pancreatitis, and arthritis involving sacroiliac, hip, knee and ankle joints in the absence of any skin involvement. Symptoms had started at age one and had progressed over time to life-threatening episodes requiring intensive care therapy. Throughout, inflammatory parameters including ESR, CRP, SAA, S100A8/9, leukocytes, and platelets were highly elevated. Treatment with colchicine and steroids improved symptoms, however did not prevent flares. Immune deficiencies were ruled out; genetic testing for FMF, CAPS, TRAPS, HIDS and DITRA did not reveal variants in the associated genes.

**Results:** Whole exome sequencing detected a novel homozygous stop variant c.62C>G; p.Ser21\* in the *IL1RN* gene (NM\_173842.2). Mother, father and brother are heterozygous for the same variant. In addition, three variants of unknown significance were identified in the patient's *PCGF5*, *CPA1* and *SPTA1* genes. Functional studies revealed only marginal secretion of IL-1RA in the patient's unstimulated leucocytes and after stimulation with IL-1 $\beta$  and LPS, confirming the disease-causing nature of the variant. Subsequently, IL-1 inhibition with anakinra at 2 mg/kg/d was started resulting in complete resolution of clinical symptoms, normal inflammatory markers and dramatically improved energy levels. Intolerance to daily subcutaneous injections prompted a switch to canakinumab at 4 mg/kg/4 weeks. However patient's and mothers assessment of disease activity was inferior on canakinumab compared to anakinra. After four months a flare appeared and lead to return to anakinra.

**Conclusions:** This is the first report of the novel c.62C>G; p.Ser21\* variant in the *IL1RN*-gene primarily causing severe serositis in a homozygous carrier, while heterozygous family members were completely symptom free. Skin disease, one of the most prominent features in other patients with DIRA was not observed in this patient, while IL-1 inhibition was likewise effective.

Pathogenic variants in all reported DIRA patients so far affect all 4 isoforms of IL-1RA.<sup>1</sup> The different phenotype in the patient reported here, may be due to the selective loss of secreted IL1RN.

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**Disclosure of Interest:** J. Kuemmerle-Deschner Grant/research support from: Novartis, SOBI, Consultant for: Novartis, SOBI, K. Hoertnagel: None declared, S. Schlipf: None declared, S. Hansmann: None declared, A. Hospach: None declared, X. Liu: None declared, S. Benseler: None declared, A. Weber: None declared

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**SAT0615 SYMPATHETIC JOINT EFFUSION IN AN URBAN HOSPITAL**

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**Background:** Sympathetic joint effusion (SJE) or sympathetic synovial effusion (SSE) is a rheumatologic entity that has not been well defined in the medical literature. It is a non-inflammatory synovial fluid collection that is associated with infection or inflammation of an adjacent anatomic structure.<sup>1</sup> The epidemiology and clinical characteristics of SJE/SSE are largely unknown. This knowledge gap has led to a lack of recognition and misdiagnosis by clinicians.

**Objectives:** Our study aimed to determine incidence, demographic information, and describe the clinical characteristics and potential triggering conditions for this presumptive reactive phenomenon.

**Methods:** We conducted a study of patients >18 years of age hospitalised at Temple University Hospital (TUH) between January 31, 2010 and December 10, 2016 who underwent diagnostic arthrocentesis for painful effusions. Individuals with synovial fluid white blood cell count (WBC) in the normal range of 200 WBC/mm<sup>3</sup> or less were included. Patients with both non-inflammatory and inflammatory range synovial fluid of greater than 200 WBC/mm<sup>3</sup> were excluded to limit confounders. Demographic and clinical data of 72 patients were included for detailed analysis.

**Results:** SJE/SSE was seen in 80/882 hospitalised patients (incidence of 9%). Seventy-two patients fulfilled inclusion criteria for detailed chart review. Demographic information revealed: male 46/72 (64%), female 26/72 (36%), African-American 38/72 (53%), Caucasian 16/72 (22%), Hispanic 10/72 (14%), undefined and other 8/72 (11%). Onset was typically acute, with 45/72 (63%) of patients developing symptoms within six days of arthrocentesis. All patients (100%) with SJE/SSE presented with painful effusion, and a minority had physical findings of warmth 23/72 (32%) or erythema 12/72 (17%). Interestingly, nearly a third of patients 21/72 (29%) were misdiagnosed with crystal or septic arthritis based solely on clinical exam, and empiric treatment was often administered prior to arthrocentesis. The most commonly affected joint was the knee 61/72 (85%), followed by the elbow 5/72 (7%), shoulder 3/72 (4%) and hip 3/72 (4%). Identifiable pathology in the affected limb was found in 29/72 (40%) of patients. Infection was the most common etiology, found in 17/29 (59%) of patients, and included cellulitis, abscess, osteomyelitis, septic bursitis, myositis, and necrotizing fasciitis. The majority of cases of SJE/SSE 23/29 (79%) were associated with concomitant infection, DVT or intramuscular hematoma in the affected limb which required specific therapeutic interventions.

**Conclusions:** Sympathetic joint effusion or sympathetic synovial effusion (SJE/SSE) is relatively common in hospitalised patients. SJE/SSE may be a sentinel sign for a more serious disorder affecting the same limb. Clinicians should maintain a heightened index of suspicion for SJE/SSE. A search for underlying infection, venous thrombosis, and intramuscular hematoma in the affected limb is warranted when encountering acute painful joint effusion with normal range synovial fluid WBC count.

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**SAT0616 TEN-YEAR RETENTION RATE OF INFLIXIMAB IN PATIENTS WITH BEHÇET'S DISEASE-RELATED UVEITIS**

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**Background:** To date, a few studies have reported the long-term efficacy of Infliximab (IFX) in Behçet's disease (BD)-related uveitis.<sup>1,2</sup> Nevertheless, it is known that TNF- $\alpha$  inhibitor drugs may lose their efficacy over time due to the formation of anti-drug antibodies, causing secondary failure and influencing the retention rate of these agents.<sup>3</sup> In this regard no previous study has specifically investigated IFX retention-rate in BD-related uveitis.

**Objectives:** To evaluate the 10 year drug retention rate of IFX in BD-related uveitis, the effect of a concomitant use of disease modifying anti-rheumatic drugs (DMARDs) on drug survival and differences according to the lines of biologic treatment.

**Methods:** Cumulative survival rates were studied using the Kaplan-Meier plot, while the Log-rank (Mantel-Cox) test was used to compare survival curves.

**Results:** Forty patients (70 eyes) were eligible for analysis. The drug retention rates at 12-, 24-, 60- and 120 month follow-up were 89.03%, 86.16%, 75.66% and 47.11% respectively. No differences were identified according to the use of concomitant DMARDs ( $p=0.20$ ), while a statistically significant difference was observed in relation to the different lines of IFX treatment ( $p=0.014$ ). Visual acuity improved from baseline to the last follow-up visit ( $p=0.047$ ) and corticosteroids-sparing effect was observed ( $p<0.0001$ )

**Conclusions:** IFX retention rate in BD-uveitis is excellent and is not affected by concomitant DMARDs

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**SAT0617 COMORBIDITY IN PATIENTS AFFECTED BY AVASCULAR NECROSIS OF THE FEMORAL HEAD AND IMPACT OF COEXISTENT DISEASES ON CONTRALATERAL JOINT INVOLVEMENT**

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**Background:** Avascular necrosis (AN) represents a significant problem of modern rheumatology. The highest incidence of this disease is in able-bodied men. The risk of disability among patients with avascular necrosis of the femoral head (ANFH) is high, especially in case of bilateral process, as AN tends to progress steadily and results in osteoarthritis due to untimely diagnosis. Patients with AN can be affected by other coexistent diseases, that can influence the disease presentation and management.

**Objectives:** This study aimed to analyse the prevalence and pattern of comorbidities in patients affected by ANFH and to determine if there is a differential pattern of comorbidities in patients with bilateral and unilateral ANFH.

**Methods:** This was a cross-sectional study, comprising 102 adult patients, aged 48,<sup>38–58</sup> with a diagnosis of ANFH according to Ficat and Arlet criteria. Sociodemographic, anthropometric, clinical parameters of interest were collected from medical records. In order to characterise the burden of coexisting diseases or conditions Charlson Comorbidity Index was calculated. The data obtained were processed with STATISTICA 10.0 using descriptive and nonparametric statistics.

**Results:** Among a total of 102 patients, a significant prevalence of comorbidities (86,27%) was found. 78,85% of all patients suffered from 2 or more coexistent conditions. The most prevalent comorbidities were: cardiovascular diseases



(CVD) (53,92%), including hypertension (50,0%) and atherosclerosis (34,31%), endocrine and metabolic disorders (66,67%), including hypercholesterolemia (65,70%) and obesity (32,35%), diseases of the digestive system (30,39%), dorsopathies (22,55%). The number of comorbidities was associated with age ( $p=0,42$ ,  $p<0,001$ ) and body mass index ( $p=0,29$ ,  $p<0,001$ ).

In patients with bilateral ( $n=44$ ), compared with those affected by unilateral ANFH ( $n=58$ ), prevalence of younger age (43,5 (36–51) vs. 54,<sup>43–62</sup>  $p<0,01$ ) and male gender (odds ratio (OR) 2,99 (95% confidence interval (CI) 1,28–6,99),  $p<0,05$ ) were detected. A history of (CVD) was more frequent in patients with unilateral ANFH (63,79% vs. 40,91%, OR 3,62 (95%CI 1,67–7,88),  $p<0,05$ ), as well as hypertension (62,07% vs. 34,09%, OR 3,16 (95%CI 1,40–7,17),  $p<0,01$ ). Patients with unilateral ANFH were more likely to have higher number of comorbidities (3,80<sup>1,17–6,43</sup> vs. 2,89 (0,73–5,05)) and Charlson Comorbidity Index (0,72 (0,43–1,47) vs. 0,52 (0,43–1,87)).

**Conclusions:** ANFH is associated with high prevalence of comorbidities, especially CVD.

CVD, including hypertension, were more likely to be found in patients with unilateral ANFH, as well as higher comorbidity burden. It can be explained by the fact that patients with CVD received treatment according to national guidelines, including antihypertensive drugs, anticoagulants, statins, etc. This indicates that performing secondary prevention of CVD can be important in both CVD and ANFH, as such treatment can influence on intraosseous blood circulation in the contralateral joint.

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#### SAT0618 RELATIONSHIP BETWEEN ARTERIAL STIFFNESS AND DISEASE DURATION IN BEHCET'S DISEASE

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**Background:** There are few studies in the literature investigating arterial stiffness in Behcet's Disease (BD). The association of arterial stiffness with duration of disease is unknown.

**Objectives:** The aim of this study is to compare arterial stiffness by assessing pulse wave velocity (PWV) and augmentation index (AI) measurements in healthy controls (HC) and patients diagnosed as BD with low and high disease duration.

**Methods:** Seventy BD patients and 40 HC without diabetes mellitus, Hypertension or chronic renal failure were included in the study. Patients with BD who were diagnosed within 12 months were taken to the group with low disease duration (LDD) and the others to the group with high disease duration (HDD). Demographic data and lipid parameters of all participants were recorded and PWV and AI measurements were made from brachial artery. The clinical characteristics of the patients with BD were recorded and the Behcet's Syndrome Activity Scale (BSAS) questionnaire was filled in for all patients with BD. Findings were compared between LDD, HDD and HC groups.

**Results:** Age, gender and body mass indexes were not statistically different between groups ( $p=0.134$ ,  $p=0.948$ ,  $p=0.929$  respectively). Augmentation index and PWV measurements were different between groups ( $p=0.014$ ,  $p=0.024$  respectively). In the HDD group, both PWV and AI were significantly higher than HC ( $p=0.013$ ,  $p=0.006$  respectively). In LDD group AI was significantly higher than HC however PWV was not ( $p=0.047$ ,  $p=0.919$  respectively). There was moderate correlation between PWV and disease duration (Rho:0.393;  $p<0.001$ ) and there was no correlation between AI and disease duration ( $p=0.287$ )

**Abstract SAT0618 – Table 1.** Demographic data, parameters of arterial stiffness, lipid parameters in all participants and disease duration, BSAS scores in patients with BD.

	Healthy controls (n=40)	The time since the diagnosis of BD		P
		LDD <sup>1</sup> (12 months ≤) (n=32)	HDD <sup>2</sup> (12 months <) (n=38)	
Age (year)	38.35±8.99	37.16±8.89	41.37±9.38	0.134
Gender (f/m)	23/17	20/12	19/19	0.948
BMI <sup>3</sup> (kg/m <sup>2</sup> )	26.55±5.65	26.33±3.68	26.22±4.38	0.929
BSAS <sup>4</sup> (0-100)		42.97±21.59	42.87±22.83	0.985
Disease duration (month)		0 (0-6.7)	120 (36-186)	<0.001
Augmentation index (%)	22.53±7.80	26.63±9.72	28.87±11.24	0.014
Pulse wave velocity (m/s)	5.75 (5.3-6.4)	5.8 (5.3-6.5)	6.6 (5.6-7.0)	0.024
LDL (mg/dl)	124.25±29.99	114.89±29.41	115.80±27.78	0.593
T. Cholesterol (mg/dl)	204.25±36.80	191.82±42.66	188.80±29.62	0.426
Triglycerides (mg/dl)	105.62±35.46	127.82±77.22	125.40±58.38	0.507
HDL (mg/dl)	54.75±10.34	52.35±13.62	47.65±10.71	0.182

LDD: Low disease duration, HDD: High disease duration, BMI: Body mass index, BSAS: Behcet Syndrome Activity Scale, BD: Behcet Disease

**Conclusions:** The augmentation index is higher in patients with BD than HC regardless of the duration of the disease. Pulse wave velocity does not increase in the early period of the disease in patients with BD but increases with prolonged disease duration.

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#### SAT0619 ASSOCIATIONS BETWEEN CLINICAL MANIFESTATIONS OF BEHCET'S SYNDROME AND WORK OUTCOMES: RESULTS FROM A UK CROSS-SECTIONAL ANALYSIS

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**Background:** Behcet's syndrome (BS) is a multi-systemic auto-inflammatory disease which exhibits significant heterogeneity in clinical manifestations, including orogenital ulceration, skin rash, arthralgia and ocular, venous, gastro-intestinal and neurological involvement. BS affects adults of working age, usually presenting between 20–40 years,<sup>1</sup> and can therefore have a significant impact on work. The association between individual and cumulative clinical manifestations of BS on employment status has not previously been assessed.

**Objectives:** To 1) describe demographics, clinical manifestations, work outcomes and use of unemployment benefits in a UK BS cohort and 2) to explore the relationship between individual and cumulative manifestations of BS and work outcomes.

**Methods:** A cross sectional analysis was performed using the Liverpool Behcet's Centre of Excellence clinical database. Inclusion criteria were clinical characteristics meeting International Criteria for Behcet's Disease (ICBD) diagnostic criteria and recorded employment data. Patients meeting ICBD but thought unlikely to have BS on clinical review by our multi-disciplinary team were excluded. Demographics, clinical manifestations, work outcomes and use of employment related benefits were described. A binomial variable 'Out of work' was generated and defined as unemployment, sickness absence, or patients marked as retired but of working age, a carer or a homemaker if the patient had to stop work due to BS. Associations between Out of work and: 1) individual clinical manifestations of BS, and 2) number of clinical BS manifestations, were explored using multivariate logistic regression adjusted for age, gender, mean EQ5D score and socio-economic status. Odds ratios (OR) and 95% confidence intervals were calculated.

**Results:** 120 patients met inclusion criteria. Mean age was 41.1 years and 33 patients (28%) were male. The minimum number of clinical manifestations were two in order to meet ICBD; the frequencies were 100% oral ulceration, 94% genital ulceration, 71% arthralgia, 43% skin rash and 20% ocular, 7% neurological, 6%

vascular and 5% gastro-intestinal involvement. 37 patients (31%) were out of work with 44 patients (37%) claiming employment related benefits. With regard to individual clinical manifestations, ocular disease had a statistically significant increased risk for being out of work when assessed alone with OR 2.84 (95% CI 1.13, 7.13) but lost statistical significance when analysed in the multivariate model: OR 2.45 (95% CI 0.70, 8.60). With regard to cumulative clinical manifestations, patients with four or more clinical manifestations of BS had a statistically significant increased risk of being out of work with OR 5.57 (95% CI 1.33, 23.27) in comparison to patients with two manifestations in the multivariate model.

**Conclusions:** This study has highlighted the significant burden of BS on work outcomes in this UK cohort. In particular, four or more cumulative BS manifestations were independently associated with being out of work in this young cohort. Further work is required to identify whether education or intervention in the workplace can help prevent disease related job loss in BS.

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SAT0620

#### FURTHER EVIDENCES OF SECONDARY AMYLOIDOSIS IN ALKAPTONURIA

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**Background:** Alkaptonuria (AKU) is an ultra-rare inborn error of metabolism due to a deficient activity of homogentisate 1,2-dioxygenase. Patients suffer from a severe arthropathy. Evidence was provided on the presence of a secondary serum amyloid A (SAA)-based amyloidosis. Here a complete microscopic and ultrastructural analysis of different AKU tissues, taken from six differently aged patients, is presented.

**Objectives:** SAA amyloidosis is a complication in AKU, making the detection of amyloid deposits at an early phase, important for treatment. We present a study of tissues from patients of different age and relevance of symptoms, providing a detailed overview of AKU amyloidosis.

**Methods:** Different tissues were obtained from a cohort of 6 AKU patients: 4 M (63,68,42,44 y) and 2 F (66,71 y) with different severity of symptoms. Histology and amyloid were investigated. A complete microscopic and ultrastructural analysis is presented and patient features as radiological examination, mild-to-severe degenerative changes as joint space narrowing, cartilage irregularities, sub-chondral sclerosis or peripheral osteophytes and linear intervertebral disk calcifications were reported. SAAserum levels and other serological markers were measured too. Specimens were analysed by Congo Red, Immunofluorescence, Transmission Electron Microscopy.

**Results:** The analysis of all AKU specimens confirmed the massive presence of amyloid fibrils even in young patients. Alterations in collagen composition, strictly associated to amyloid bundles deposition, were observed especially in labial salivary gland, cartilage, tendons and infrapatellar fat pad. Histological analysis showed depletion of glycosaminoglycans in young patients, whereas, at light microscopy, calcification and fibrillation were observed only in elderly patients. Immunofluorescence assessed undoubtedly the presence of SAA in amyloid deposits in AKU, and we reported for the first time the finding of amyloid deposition in young AKU patients and in less common regions.

**Conclusions:** We provide the first detailed overview of amyloidosis in AKU. Overall, our findings depicted a novel biological framework underlining the pathological role of amyloidosis in several AKU tissues. Furthermore, we found that degradation of extra-cellular matrix AKU is not limited to elderly. The clinical burden of AKU may notably increase, since amyloidosis was found even in young AKU patients, whereas degeneration of cartilage and tendons was limited to older subjects.

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SAT0621

#### CLINICAL SIGNIFICANCE OF INTERLEUKIN-18 AND INTERLEUKIN -6 ON DISEASE COURSE OF ADULT-ONSET STILL'S DISEASE

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**Background:** Innate pro inflammatory cytokines interleukin (IL)–6 and IL-18 are critical for perpetuating the inflammatory processes in adult-onset Still's disease (AOSD),<sup>1</sup> and macrophage activation syndrome (MAS).<sup>2</sup>

**Objectives:** To assess the role of IL-6 and IL-18 in the pathogenesis of (AOSD) and MAS, and to investigate the clinical significance of serum cytokine profile with IL-6 and IL-18 in (AOSD) and MAS,

**Methods:** we analysed the serum IL-6 and IL-18 in patients with (AOSD) and compared them with the clinical features of (AOSD) 51 patients with (AOSD) including 17 patients with MAS were analysed. Levels of IL-6 and IL-18 were quantified in serum by enzyme linked immune sorbent assay. Results were compared with clinical features of (AOSD).

**Results:** Two distinct Adult Still's disease patient subsets based on their serum IL-6 and IL-18 levels were identified: an IL-18 dominant (IL-18/IL-6 1000) and an IL-6 dominant (IL-18/IL-6 1000). The IL-6 dominant subset had a significantly greater number of joints with active disease and higher serum levels of matrix metalloproteinase-3, whereas the IL-18-dominant subset was more likely to develop MAS. The cut off value of serum IL-18 to predict the development of MAS was 52000 pg/ml with 87.3% of sensitivity and 79.3% of specificity. The patients with IL-18 dominant pattern were likely to have monophasic or polycyclic disease course, whereas the patients with IL-6 dominant pattern were likely to have persistent disease course. Serum IL-18 levels in patients achieved remission decreased to the levels <1,000 pg/mL in inactive phase and normalised in remission phase. In contrast, serum IL-18 levels in patients experienced relapse during withdrawal of steroid within 12 months after disease onset demonstrated a sustained elevation of serum IL-18 levels >1,000 pg/mL during the inactive phase

**Conclusions:** Two subsets of patients with (AOSD), one which is prone for arthritis and another with prone for MAS, can be identified on the basis of their serum IL-6 and IL-18 levels. These two subsets appear to be characterised by certain distinct clinical features. Monitoring the cytokine profile with IL-18 and IL-6 might be useful to predict disease course. Furthermore, serum IL-18 levels reflect the biological activities of the immune system in (AOSD) and may predict the development of MAS and the prognosis of Adult Still's disease

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SAT0622

#### HIGH DOSE INTRAVENOUS METHYLPREDNISOLONE INDUCES RAPID IMPROVEMENT IN SEVERE UVEITIS: A MULTICENTER STUDY OF 129 PATIENTS

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**Background:** In uveitis rapid and effective remission-inducing therapy is mandatory to avoid irreversible damage.

**Objectives:** To evaluate the efficacy and safety of high-dose intravenous methylprednisolone (IVMP) pulse therapy in uveitis.

**Methods:** Multicentre study of 129 patients (203 eyes) with uveitis who received IVMP. The underlying diseases were: Idiopathic (n=30), Vogt Koyanagi Harada,<sup>29</sup> Behçet disease,<sup>19</sup> Sarcoidosis,<sup>6</sup> Multifocal Choroidopathy,<sup>4</sup> Birdshot chorioretinopathy,<sup>2</sup> Acute posterior multifocal placoid pigment epitheliopathy,<sup>1</sup> Granulomatosis with polyangiitis,<sup>2</sup> Aortitis,<sup>1</sup> Immune thrombocytopenic purpura,<sup>1</sup> Rheumatoid arthritis,<sup>2</sup> Axial Spondylitis,<sup>6</sup> Psoriatic arthritis,<sup>2</sup> Juvenile Idiopathic Arthritis,<sup>1</sup> Thrombophilia synd.,<sup>1</sup> Eales Disease,<sup>2</sup> Sympathetic Ophthalmia,<sup>2</sup> Multiple Sclerosis,<sup>2</sup> Relapsing Polychondritis,<sup>1</sup> Cogan's synd.,<sup>1</sup> Sjögren synd.,<sup>2</sup> Crohn's disease,<sup>1</sup> Reactive arthritis,<sup>1</sup> Toxic oil synd. and brain ischemia,<sup>1</sup> Raynaud's Disease and brain ischemia,<sup>1</sup> Pseudotumor,<sup>1</sup> Cataract surgery,<sup>1</sup> Herpes Simplex,<sup>1</sup> Varicella Zoster-associated acute retinal necrosis,<sup>1</sup> *T.pallidum*<sup>2</sup> and *M.*

*tuberculosis*.<sup>1</sup> The inflammatory ocular patterns were: panuveitis (66), posterior uveitis (PU),<sup>31</sup> intermediate uveitis (IU),<sup>5</sup> anterior uveitis (AU),<sup>12</sup> AU and PU,<sup>2</sup> AU and IU,<sup>1</sup> IU and PU,<sup>1</sup> exudative retinal detachment,<sup>3</sup> vasculitis,<sup>4</sup> pseudotumor,<sup>1</sup> scleritis<sup>2</sup> and sclero-uveitis.<sup>1</sup> Bilateral ocular involvement was observed in 74 cases. Patients were assessed at basal visit and day 2–5, 7, 15 and 30 after IVMP. The main outcome variable was best corrected visual acuity (BCVA), the degree of inflammation of the anterior chamber and vitreous, and macular thickness (macular oedema defined by OCT >300  $\mu$ m). The results are expressed as mean  $\pm$ SD for normally distributed variables, or as median [interquartile range] when are not. Comparison of continuous variables was performed using the Wilcoxon test.

**Results:** We studied 74 ♀/55 ♂; mean age 42 $\pm$ 14.3 years. IVMP dose ranged from 40–1000 mg/day for 3–5 consecutive days. Prior to IVMP, cycloplegic and corticosteroid eye drops were used in all cases. Improvement was faster among patients with inflammation in anterior chamber and vitritis than in BCVA, CME, retinitis and retinal vasculitis (TABLE). Total remission was achieved in 19.4% of the 129 patients after IVMP. In 126 of the patients continued with oral corticosteroids and 4 received an intraocular dose of steroids. These immunosuppressive drugs were added: Methotrexate (52), Cyclosporine A,<sup>48</sup> Azathioprine<sup>40</sup> and others.<sup>5</sup> In a few cases biological therapy (64) was administered afterwards. In general, acute respiratory infection was the side-effect most frequent.

Abstract SAT0622 – Table 1

	Affected eyes	Affected eyes after high-dose IVMP (%)				
	baseline	Day 2.3	Day 7	Day 15	Day 30	
BCVA, mean $\pm$ SD	0.47 $\pm$ 0.35	0.56 $\pm$ 0.34*	0.61 $\pm$ 0.33*	0.68 $\pm$ 0.31*	0.75 $\pm$ 0.3*	
Anterior chamber cells (median [IQR])	0.75 [0-4]	0 [0-4]*	0 [0-4]*	0 [0-3]*	0 [0-2]*	
Vitritis (median [IQR])	0 [0-5]	0 [0-5]*	0 [0-4]*	0 [0-3]*	0 [0-3]*	
OCT (microns) mean $\pm$ SD	465.36 $\pm$ 189.1	366.49 $\pm$ 159.7*	346.49 $\pm$ 150.9*	308.2 $\pm$ 120.06*	281.79 $\pm$ 107.6*	
Choroiditis/Chorioretinitis n. (%)	59 (23%)	51 (20%)	33 (13%)	23 (9%)	16 (6%)	
Retinitis n. (%)	86 (34%)	74 (29%)	70 (27%)	46 (18%)	21 (8%)	
Retinal vasculitis n. (%)	66 (26%)	58 (23%)	52 (20%)	36 (14%)	16 (6%)	
Synechiae n. (%)	39 (15%)	32 (12%)	30 (12%)	30 (12%)	33 (13%)	
Cystoid macular edema (CME) n. (%)	83 (33%)	68 (27%)	57 (22%)	41 (16%)	20 (8%)	

\*p < 0.05 compared with basal

**Conclusions:** High-dose IVMP pulse therapy is beneficial in the prompt control of severe uveitis and it is well tolerated.

**Disclosure of Interest:** None declared

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## SAT0623 CLINICAL FEATURES AND TREATMENT OF IDIOPATHIC RECURRENT ACUTE PLEURO-PERICARDITIS

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**Background:** Idiopathic recurrent acute pleuro-pericarditis (IRAP) is an increasingly recognised autoinflammatory disease comprising post-pericardiotomy-syndrome, recurrent pericarditis and post-myocardial-infarction-syndrome. Different autoimmune mechanisms were discussed in the past. Recently, IRAP is considered as an autoinflammatory disease. Therapeutic options comprise colchicine, prednisolone and interleukin (IL)–1beta blockingagents.

**Objectives:** to investigate whether idiopathic and post-interventional pleuro-pericarditis represent a clinical spectrum and to identify treatment options.

**Methods:** This study analyses demographic, clinical and laboratory features of post-interventional and idiopathic pleuro-pericarditis and adult onset Still's disease (AOSD) as a reference. Patients with infectious disease, connective tissue disease, chronic heart failure, renal failure and other non-exsudative effusions were excluded from this analysis. Patients with IRAP were treated with colchicine, prednisolone and IL1 $\beta$  blocking agents.

**Results:** Between 2005 and 2017 66 cases of idiopathic and post-interventional pleuro-pericarditis were identified and compared to 83 cases of AOSD. Clinical and laboratory features suggest that idiopathic and post-interventional pleuro-pericarditis represent a clinical spectrum which is identical with IRAP.

Prednisolone was started with 25 mg to 125 mg and tapered to less than 7 mg or discontinued if not effective. 47 of 66 patients (71%) were treated with prednisolone and 10/47 (21%) were in remission with no need of any further therapeutically escalation.

Colchicine was given to 44/66 patients (67%) and 29/44 (66%) were in complete remission.

Four of 66 patients (6%) did not respond or had contraindications against colchicine or prednisolone and were treated with anakinra. Of these patients 4/4 (100%)

were in remission. During the follow-up period of 20 patient\*months 2 of 4 patients maintained the remission with anakinra every 2nd day and two patients discontinued anakinra and remained in remission.

**Conclusions:** 1. post-pericardectomy-syndrome, post-myocardial-infarction-syndrome and idiopathic recurrent pericarditis represent a clinical spectrum of autoinflammatory diseases.

2. treatment options comprise colchicine as a first-line therapy, prednisolone and anti-IL1 blocking agents.

**Acknowledgements:** none.

**Disclosure of Interest:** None declared

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## SAT0624 INCIDENCE AND BASELINE CHARACTERISTICS OF RELAPSE OR EXACERBATION IN PATIENTS WITH PULMONARY SARCOIDOSIS: A SINGLE CENTRE LONG-TERM OBSERVATIONAL COHORT STUDY

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**Background:** Sarcoidosis is a systemic granulomatous disease that can affect multiple organs. Lung involvement is particularly common, occurring in more than 90% of patients.<sup>1</sup> However, spontaneous remission of pulmonary sarcoidosis is often observed within 2 years.<sup>2</sup> Factors reported to indicate a poor prognosis in pulmonary sarcoidosis include chest radiographic stage, skin involvement, age over 40 years and smoking history.<sup>3, 4</sup> To date, however, no study has comprehensively described factors of relapse and exacerbation and characteristics of untreated patients with favourable outcomes over a long-term period of more than 2 years.

**Objectives:** The aim of study was to identify the incidence and baseline characteristics of relapse and exacerbation in patients with pulmonary sarcoidosis over a long-term period.

**Methods:** One hundred- and three patients who visited our division of Hachinohe Red Cross Hospital between January 2007 and December 2016 and were clinically diagnosed as having pulmonary sarcoidosis were enrolled. The incidence and characteristics of relapse or exacerbation were prospectively calculated and statistically analysed using clinical, laboratory and imaging data collected from medical records.

**Results:** Of 103 patients, 79% were women and mean age at diagnosis was 50.1  $\pm$  16.4 years. Mean observation period was 9.8 $\pm$ 8.6 years. The number of patients with previously reported short-term prognostic factors were as follows: chest radiographic stage (Stage 0, n=7; Stage I, n=32; Stage II, n=36; Stage III, n=18; Stage IV, n=10), skin involvement (n=9), age over 40 years old (n=73), and smoking history (n=38). Overall relapse or exacerbation was 22.3% (n=23) and mean period to relapse or exacerbation was 8.7 $\pm$ 8.3 years. We then analysed the 69 patients who were observed for more than 5 years, and identified relapse or exacerbation within 5 years in 9 patients. Comparison of characteristics at diagnosis between the relapse or exacerbation group and spontaneous group showed that the relapse or exacerbation group had a significantly elevated frequency of bilateral hilar lymphadenopathy, disease duration, ocular involvement, cardiac involvement, and oral glucocorticoid use at diagnosis (p=0.014, 0.027, 0.019, 0.035, and 0.0043, respectively). On stratification, the number of risk factors was positively and significantly associated with the cumulative ratio of relapse or exacerbation (p=0.048).

**Conclusions:** Our long-term observational cohort study newly identified the incidence and baseline characteristics of relapse or exacerbation in patients with pulmonary sarcoidosis over a long-term period. Scoring the number of the factors at baseline may facilitate the prediction of relapse or exacerbation.

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**SAT0625 SARCOIDOSIS IS ASSOCIATED WITH AN INCREASED RISK OF GASTROINTESTINAL EVENTS: A POPULATION-BASED RETROSPECTIVE COHORT STUDY 1976–2013**

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**Background:** An increased risk of gastrointestinal (GI) diseases has been observed in several chronic inflammatory disorders but the risk in patients with sarcoidosis is not known.

**Objectives:** This study was undertaken to characterise the risk of GI diseases in patients with sarcoidosis.

**Methods:** A population-based cohort of 345 incident cases of sarcoidosis among Olmsted County, Minnesota residents in 1976–2013 was identified from a comprehensive medical record-linkage system. Diagnosis was confirmed by individual medical record review. A cohort of 345 sex and age-matched comparators was also identified from the same underlying population. Medical records of both groups were reviewed for GI diseases. Cox models adjusted for age, sex and calendar year were used to compare the rate of development of GI diseases between the groups.

**Results:** GI events occurred in 101 cases and 63 comparators, corresponding to an adjusted hazard ratio (HR) of 1.90 (95% confidence interval [CI] 1.38–2.61). Patients with sarcoidosis had an increased risk for both upper (HR 1.90; 95% CI 1.27–2.83) and lower GI events (HR 1.97; 95% CI 1.27–3.05) relative to comparators. By disease type, patients with sarcoidosis had a significantly elevated risk of upper GI ulcer, upper GI haemorrhage and diverticulitis (**table 1**).

Comorbidity	Number of events prior to index date	p-value	Number of events after index date	Cumulative incidence at 10 years for non-sarcoidosis subjects (±SE)	Cumulative incidence at 10 years for sarcoidosis patients (±SE)	Hazard ratio (95% CI)	p-value
<b>Upper GI diagnoses</b>							
Upper ulcer	21/19	0.87	11/27	1.9 (0.2, 3.6)	4.5 (2.0, 6.8)	2.56 (1.27, 5.17)	0.009
Upper bleed	6/14	0.11	14/29	0.9 (0.0, 2.0)	4.4 (1.9, 6.9)	2.36 (1.24, 4.47)	0.009
Upper perforation	2/0	0.50	0/1	–	–	–	–
Upper obstruction	1/3	0.62	7/8	1.4 (0.0, 2.7)	0.3 (0.0, 0.9)	1.20 (0.43, 3.32)	0.72
Esophagitis	7/4	0.55	18/27	3.6 (1.4, 5.8)	5.4 (2.7, 8.1)	1.58 (0.87, 2.88)	0.13
Esophageal varices	0/3	0.25	1/6	0.0 (0.0, 0.0)	0.7 (0.0, 1.8)	6.51 (0.78, 54.16)	0.083
<b>Lower GI diagnoses</b>							
Lower ulcer	2/1	1.0	2/7	0.6 (0.0, 1.4)	1.4 (0.0, 2.8)	3.51 (0.73, 16.92)	0.12
Lower bleed	5/3	0.72	12/15	1.8 (0.2, 3.3)	2.9 (1.0, 4.8)	1.32 (0.62, 2.82)	0.48
Lower perforation	0/0	–	2/1	–	–	–	–
Lower obstruction	0/2	0.50	1/2	–	–	–	–
Diverticulitis	3/2	1.0	9/18	0.4 (0.0, 1.1)	2.3 (0.6, 4.0)	2.29 (1.03, 5.10)	0.043
Ischaemic colitis	2/0	0.50	3/7	0.0 (0.0, 0.0)	0.6 (0.0, 1.5)	2.38 (0.61, 9.26)	0.21
Infectious colitis	1/5	0.22	7/13	0.6 (0.0, 1.5)	2.9 (0.9, 4.9)	1.99 (0.79, 5.00)	0.14

**Conclusions:** Patients with sarcoidosis have a higher risk of both upper and lower GI events compared with subjects without sarcoidosis.

**Disclosure of Interest:** None declared

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**SAT0626 ANAKINRA TREATMENT IN REFRACTORY CASES OF ADULT-ONSET STILL DISEASE: CASE SERIES**

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**Background:** Despite methotrexate and steroid treatment, in cases of Adult-onset Still's disease (AOSD) it is usually difficult to maintain clinic stability. In refractory cases, Anakinra treatment has been reported to be efficacious.<sup>1</sup>

**Objectives:** In this retrospective review, it is aimed to evaluate the AOSD cases treated with anakinra in our centre.

**Methods:** Fourteen AOSD patients (11 female, 3 male) who were being followed in our outpatient clinic were reviewed retrospectively. The demographic characteristics, pre- and post-treatment clinical findings were reported.

**Results:** The mean follow-up period of the patient population was 33.5±30.07 months (mean ±SD). Initial prednisolone dose was 37.3 mg/day. Except for one, all of our patients were exposed to methotrexate before being treated with anakinra. This patient was being treated with cyclosporine instead, since she had concomitant Macrophage Activation Syndrome. The other medications, the patients were previously treated with, were Etanercept (n=2), Tocilizumab (n=3), Infliximab (n=1) and Adalimumab (n=1).

All patients were on 100 mgs of Anakinra, daily, except for the one treated with 200 mg/day. The mean duration of Anakinra therapy was 11.4 months. Among 7 patients in whom anakinra therapy was terminated, 1 had drug induced urticaria, 1 was primary irresponsive, 4 were secondary irresponsive and the other had severe pneumonia. Primary irresponsiveness is the lack of response to the therapy since the drug was first introduced, whereas in secondary irresponsiveness the case responds to the medication for a while and starts to flare again after asymptomatic-free period on the medication. Among 14, 7 of our patients are still on 100 mg/d Anakinra.

The mean level of C reactive protein (CRP) measures was reduced from 64.38 ±61.95 mg/L to 34.3±24.3 mg/L with Anakinra therapy (p=0.003). Similarly, mean Erythrocyte Sedimentation Rate (ESR) was dropped to 33±22 mm/h from 59 ±35 mm/h by the help of the therapy (p<0.001). Among patients who primarily responded Anakinra therapy the mean Ferritin measures dropped to 427.25 ng/ml from 910 ng/ml (p=0.006). On the other hand, the Ferritin level was not significantly reduced in patients who did not respond Anakinra. The mean Patient reported Global Visual Analogue Scale (PG-VAS) score was also decreased to 3.83±4.7 from 9.5±0.07 following the therapy (p<0.001). Unfortunately, one of our 7 patients who were followed in remission under Anakinra died of an unknown etiology.

**Conclusions:** Adult-onset Still's disease is a challenging disorder, lacking a sufficient long-time clinical control. In order to obtain a full remission, various efforts have been spent so far. One of these approaches is to treat refractory cases with Anakinra, an IL-1 blocking agent. According to our clinical experience we state that, anakinra has a relatively high efficacy in controlling refractory cases.

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**Disclosure of Interest:** None declared

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**SAT0627 FABRY DISEASE: DIAGNOSTIC ERRORS IN RHEUMATOLOGY PRACTICE**

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**Background:** Fabry disease (FD) is a rare X-linked storage disease resulting from the deficient activity of the lysosomal α-galactosidase A (AGAL) and leading to a progressive accumulation of glycosphingolipids in a wide range of cell types throughout the body, including kidney, heart and nervous system. Certain manifestations of FD can mimic those of rheumatic diseases.

**Objectives:** To evaluate the occurrence and the possible causes of diagnostic errors in patients with FD in rheumatology practice.

**Methods:** We retrospectively studied the medical records of 82 adult patients with definite FD (low or absent AGAL activity, pathogenic mutation in the GLA gene, typical clinical symptoms in patient and/or his relatives, results of kidney biopsy). There were 55 males and 27 females aged of 18 to 69 years (median 38<sup>29</sup>, 48<sup>48</sup> years).

**Results:** Seventy two of 82 patients (87.8%) had a history of classic phenotype of FD from childhood or adolescence. The typical manifestations included neuropathic pain that was related to heat and fever (65/82; 79%), angiokeratoma (37/

82; 45%), anhidrosis/hypohidrosis (44/82; 53.6%), and cornea verticillata (40/62; 64.5%). However, there was a significant delay to diagnosis of up to 51 years (median 18<sup>9</sup>; 27 years). Moreover, diagnosis was established by nationwide screening in dialysis units in 22/82 (26.8%) patients or by family screening in 34/82 (41.4%) patients. At the time of diagnosis, patients usually presented with a clinical picture of systemic disease with mild to moderate proteinuria with or without impairment of kidney function (70/82; 85.4%), left ventricular hypertrophy (56/82; 68.3%), white matter lesions on brain MRI (38/72; 52.8%), and/or a history of stroke (15/82; 18.3%). Twenty six of 82 patients (31.7%) previously had at least one diagnosis of rheumatic disease (Table 1). The common causes for referral to rheumatologist were skin rash and neuropathic pain. In 6 of 26 patients (23.1%), the latter was initially misdiagnosed as joint pain. The possible causes of diagnostic errors included also 'genuine' arthralgia (6/26; 23.1%), episodes of unexplained fever (13/26; 50%), Raynaud phenomenon (2/26; 7.7%), and the laboratory markers of inflammation (11/26; 42.3%).

**Abstract SAT0627 – Table 1.** 'Rheumatic' diagnoses in Fabry patients

Misdiagnoses	Number of patients
Vasculitis*	6 (7.3%)
Arthritis**	5 (6.1%)
Osler-Weber-Rendu disease	4 (4.9%)
Rheumatic fever	4 (4.9%)
Systemic lupus erythematosus	3 (3.7%)
Familial Mediterranean fever	1 (1.2%)

Note: \*Vasculitides included IgA-vasculitis, Behcet disease, etc. \*\*Arthritides included rheumatoid arthritis, juvenile rheumatoid arthritis and osteoarthritis.

**Conclusions:** Practicing rheumatologists should be aware of FD, given a high occurrence of diagnostic errors. The clues to correct diagnosis include a history of typical symptoms (i.e. neuropathic pain, angiokeratoma, hypohidrosis) from childhood or adolescence and/or the presence of typical manifestations in family members. Notably, FD can initially present as an autoinflammatory disorder with episodes of joint pain and unexplained fever associated with the laboratory markers of inflammation.

**Disclosure of Interest:** None declared

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#### SAT0628 A RETROSPECTIVE OBSERVATIONAL STUDY OF AZATHIOPRINE MAINTENANCE THERAPY ON BEHCET'S DISEASE WITH VASCULAR INVOLVEMENT

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**Background:** Vascular disease which has potential to involve both arteries and veins of all size is one of the major causes of mortality and morbidity in Behçet's disease (BD). There is no controlled studies for the immunosuppressive (IS) therapy in vascular involvement of BD. For the induction and/or maintenance therapy, azathioprine (AZA) is widely used as a corticosteroid tapering IS agent in vascular BD although there are many different clinical presentation.

**Objectives:** The purpose of this study to investigate relapse rate and the clinical factors affecting it during AZA maintenance therapy.

**Methods:** Consecutive BD patients with a documentation for arterial or venous involvement were evaluated from two rheumatology centre between January-September 2017. Patients who have been treated for at least 3 months after the complete or partial remission were included to study. The baseline clinical and laboratory findings, treatment protocol, first vascular relapse time and adverse events were obtained medical records. Long-term outcome and factor associated with vascular relapse were assessed.

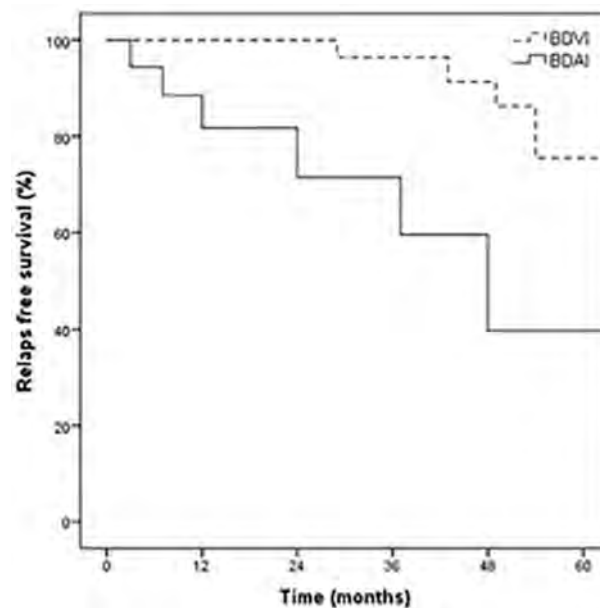
**Results:** Totally 78 patients were included to the study and majority of them [59 (%75.6)] was male. The mean age  $\pm$ SD of the patients was 37.5 $\pm$ 9 years. Clinical characteristics of patients are seen in table 1. The median duration of maintenance therapy with AZA was 25 (min 3- max 144) months and the mean dose  $\pm$ SD of AZA was found as 1.7 $\pm$ 0.3 mg/kg/day. AZA was withdrawn in 4 (% 5.1) patients because of adverse events. Twenty patients (%25.6) were receiving anti-coagulant therapy. Vascular relapse was observed in 14 (%17.9) patients. In relapsing group, arterial involvement and uveitis was higher statistically ( $p=0.014$  and  $0.045$  respectively). In regression analysis, arterial involvement was independent risk factor for relapse ( $p=0.016$ ). The percentage of relapses

was calculated as %39 (7/18) in patient subgroup with arterial involvement. Relapse free survival rates according to involving vessel were seen in figure 1.

**Abstract SAT0628 – Table 1.** Clinical characteristics of vascular Behçet's Disease (n=78)

The mean age $\pm$ SD	37.5 $\pm$ 9.2
Male gender n (%)	59 (76)
Genital ulcer n (%)	49 (63)
Skin lesions n (%)	44 (57)
Paterji positivity n (%)	29 (38)
Uveitis n (%)	17 (22)
Musculoskeletal involvement n (%)	15 (20)
CNS involvement n (%)	1 (1.2)
GIS involvement n (%)	1 (1.2)
Venous involvement n (%)	67 (86)
Arterial involvement n (%)	18 (24)

SD: Standart deviation, CNS: Central nervous system, GIS: Gastrointestinal system



**Abstract SAT0628 – Figure 1.** Relapse free survival rates according to involving vessels in patients with Behçet's disease (BD) by using Kaplan-Meier method (BDVI: Behçet's disease with venous involvement, BDAI: Behçet's disease with arterial involvement,  $p=0.001$  by log-rank test).

**Conclusions:** According to our study, AZA is seen as safe in maintenance therapy of BD with vascular involvement, however it can be said that the relapse rate is not favourable especially in patients with arterial involvement. Vascular involvement is considered as related to endotel inflammation resulting BD activity and the effect of anti-coagulant therapy is still controversial. TNF inhibitors or other immunosuppressant may be alternative to AZA for maintenance therapy with the support of randomized-controlled studies.

**Disclosure of Interest:** None declared

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#### SAT0629 IGG4 RELATED CASTLEMAN'S DISEASE OR "SECONDARY" IGG4 RELATED DISEASE OF MULTICENTER CASTLEMAN'S DISEASE?

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**Background:** It's widely accepted that a diagnosis of IgG4-related disease (IgG4-RD) can be made under a premise of rule out a series of disease including Castleman's disease (CD). Clinically, the two diseases may share similar clinical manifestations, such as multiple organ involvement. Pathologically, in some cases with CD, IgG4 positive plasma cell infiltrations are also evident. Otherwise, IgG4-RD may pathologically exhibits CD-like feature.<sup>1-3</sup>

**Objectives:** When the histopathology coincides with the diagnosis of both IgG4-RD and CD, it is hard to depart the two disease entity utterly. It's unknown whether it is IgG4 related CD or "secondary" IgG4-RD of multicentric CD, here we call it IgG4-CD provisionally. To our knowledge, no comparative study of IgG4-CD and IgG4-RD has yet been published. In this study, we aim to review the clinical feature of IgG4-CD.

**Methods:** This study is based on a retrospective analysis of a prospectively acquired database. IgG4-CD were defined histopathologically in patients who fulfilled the diagnosis of both IgG4-RD and CD. Forty five definite IgG4-RD patients were recruited as control. Clinical features including organ involvement, serum IgG4, IgG, IgE, ESR and CRP levels of all the participants were collected and analysed statistically.

**Results:** Fifteen patients (2.8%) out of 534 patients with IgG4-RD in China's largest prospective IgG4-RD and Mimicry cohort fulfilled the definition of IgG4-CD. There were 14 males and 1 female, mean age was 47±18 years, and the median disease duration before diagnosis was 12 (1–132) months. Eight patients have allergic history. IgG4-CD patients had more lymph node involvement (100% vs 57.8%,  $p<0.01$ ), while IgG4-RD patients had more submandibular (33.3% vs 77.1%,  $p<0.01$ ) and parotid gland (13.3% vs 40.9%,  $p<0.05$ ) affected. IgG4-CD patients had significantly higher levels of ESR (mm/h), CRP (mg/L), IgG (g/L), IgG1 (g/L), IgG3(g/L), IgG4(mg/dL), and IgE (g/L) [76.50 (5.00–129.00) vs 17.00 (2.00–89.00), 5.39 (0.54–134.00) vs 1.6 (0.08–113.74), 35.28 (9.76–69.00) vs 19.36 (7.46–61.00), 11.2 (6.84–41.00) vs 8.07 (4.08–16.70), 1.55 (0.19–3.20) vs 0.53 (0.09–2.00), 1590.00 (133.00–6420.00) vs 1070.00 (152.0–6100.00), 807.5 (215.00–2967.00) vs 214.00 (20.40–2437.00), respectively.  $p<0.05$ ). Except for one patient refused to receive drug therapy untreated, the remaining patients with IgG4-CD all received glucocorticoid (GC) treatment. Patients with multi-organ involvement or in severe inflammatory condition were treated with both GC and immunosuppressive agents, those who with active disease but resistant to above regimen accepted biologics such as rituximab. All patients with IgG4-CD exhibited favourable outcomes.

**Conclusions:** Both IgG4-RD and CD can involve multiple organs. There are a small group of patients who had clinical and pathological characteristics of both CD and IgG4-RD showed better clinical outcome. Long-term prognosis of these patients, the relationship of CD and IgG4-RD are waiting to be further elucidated.

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SATURDAY, 16 JUNE 2018

## Diagnostics and imaging procedures

SAT0630

### AGREEMENT BETWEEN PATIENT-REPORTED SWOLLEN AND TENDER JOINTS, CLINICAL EXAMINATION AND SYNOVITIS DETECTED BY ULTRASONOGRAPHY IN RHEUMATOID ARTHRITIS PATIENTS AT THE TIME OF PATIENT-REPORTED FLARE

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**Background:** In Rheumatoid Arthritis (RA), patient-reported tender joints (PrTJ) correlate better with clinical examination than patient-reported swollen joints (PrSJ).<sup>1</sup> Clinical examination has inferior sensitivity to detect synovitis compared to ultrasonography (US).<sup>2</sup> However, data is sparse about these findings at the time of patient-reported flare (PRFI).

**Objectives:** To investigate agreement between PrSJ, PrTJ, clinically detected swollen and tender joints (cSJ and cTJ), and inflammation by Colour Doppler (CD) US in RA patients at the time of PRFI.

**Methods:** 80 consecutive rheumatoid-factor and/or anti-cyclic citrullinated peptide antibody positive RA patients with DAS28-CRP<3.2 and no swollen joints at baseline were during a one-year follow-up period requested to contact the hospital in case of a hand flare according to patients' perspective. At the flare visit, patients indicated PrSJ and PrTJ, and underwent examination for cSJ and cTJ, and US of

bilateral wrists (wrist joints and six extensor tendon compartments), 1–5 metacarpophalangeal joints (MCP) and 1–5 proximal interphalangeal joints (PIP). CD synovitis and tenosynovitis were graded 0–3 according to EULAR/OMERACT scoring system<sup>3</sup> and joints and tendon sheaths with CD ≥ 1 were considered positive. Percentage agreement and Cohen's kappa were calculated between PrSJ, PrTJ, cSJ, cTJ and CD in joints and tendon sheaths.

**Results:** Thirty-six percent (29/80) of the RA patients reported a hand flare (69% female, mean age 65 years, median DAS28-CRP 1.8, at baseline). At flare, mean (±SD) number of PrSJ, cSJ, PrTJ, cTJ and CD positive joints were 2.7 (2.86), 1.5 (1.02), 4 (3.04), 4 (3.46) and 1.8 (1.31), respectively. For swelling, there was slightly superior agreement with CD for cSJ than for PrSJ, except for wrist tenosynovitis where patients agreed more frequently with CD than clinical examination did (table 1). Highest percentage agreement was seen for PIP, followed by MCP. Agreement, as assessed by kappa, was poor to fair, ranging from –0.009 to 0.33. Swelling in MCP and PIP joints, by patients and clinicians, and swelling in the wrist by clinician showed better agreement with CD than tenderness did.

**Abstract SAT0630 – Table 1.** Concordance between patient-reported and clinically examined swollen and tender joints versus CD at the time of patient-reported flare

Joint	No of joints examined	Comparison between	++	+/+	+/-	-/-	% agreement
Wrist	n=58	Clinical swelling vs CD synovitis	6	10	11	31	64
		Clinical swelling vs CD tenosynovitis	4	12	4	38	72
		Patient-reported swelling vs CD synovitis	5	13	12	28	57
		Patient-reported swelling vs CD tenosynovitis	6	12	2	38	76
		Clinical tenderness vs CD synovitis	5	11	12	30	60
		Clinical tenderness vs CD tenosynovitis	4	12	4	38	72
		Patient-reported tenderness vs CD synovitis	5	11	12	30	60
		Patient-reported tenderness vs CD tenosynovitis	5	11	3	39	76
MCP	n=290	Clinical swelling vs CD synovitis	0	18	27	245	85
		Patient-reported swelling vs CD synovitis	3	34	24	229	80
		Clinical tenderness vs CD synovitis	7	47	20	216	77
		Patient-reported tenderness vs CD synovitis	4	45	25	218	77
PIP	n=290	Clinical swelling vs CD synovitis	0	8	9	273	94
		Patient-reported swelling vs CD synovitis	0	19	9	262	90
		Clinical tenderness vs CD synovitis	3	30	6	251	88
		Patient-reported tenderness vs CD synovitis	1	38	8	243	84

CD: Colour Doppler; MCP: metacarpophalangeal joint; PIP: proximal interphalangeal joint.

**Conclusions:** Thirty-six percent of the RA patients reported flares in the hand during one year follow-up. Numbers of joints affected by swelling, tenderness or positive CD sign were low. Limited concordance between US, patient-reports and clinical examination suggests that these domains reflect different and potentially complementary aspects of inflammation in patient-reported flare.

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SAT0631

**LACK OF ASSOCIATION BETWEEN CLINICAL AND ULTRASOUND MEASURES OF DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS/CLINICAL REMISSION: A CROSS-SECTIONAL ANALYSIS**

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**Background:** Ultrasound (US) measures of synovitis and tenosynovitis have been shown to persist in patients with rheumatoid arthritis (RA) who achieve clinical remission.

**Objectives:** To assess the prevalence of such US findings in RA clinical remission, and analyse whether the US abnormalities found in this group of patients could be predicted by their clinical parameters.

**Methods:** Patients with established RA (1987 or 2010 diagnostic criteria) in clinical remission (DAS28-CRP<2.4) on conventional synthetic disease-modifying anti-rheumatic drugs (DMARDs) were recruited as part of the Biomarkers of Remission in Rheumatoid Arthritis (BioRRA) Study. Patients who had received systemic glucocorticoids in the past 3 months were excluded. All patients underwent baseline clinical assessment followed by a 7-joint US scan (Backhaus et al). US assessment was performed by the same operator (KB) blinded to disease activity score. Synovial Power Doppler (SPD) and greyscale (SGS) change were measured using a 4-point semi-quantitative scale (0–3); tendon GS (TGS) and erosions were classified as either present<sup>1</sup> or absent (0). Intra- and inter-rater scoring agreement was good (Cohen’s kappa 0.72 and 0.61 respectively). The association between individual dependent variables (SPD, SGS, TGS, and erosions) and clinical parameters was assessed by multivariate ordinal logistic regression, with Benjamini-Hochberg adjustment for multiple testing.

**Results:** 66 patients with RA in remission (median disease duration 6 years, median age 66 years) were included in the analysis. US abnormalities were common in both DAS28-CRP and ACR<sup>EULAR 2011</sup> Boolean remission (table 1). Seven associations were significant at the unadjusted p<0.05 level (figure 1). Only two associations remained statistically significant after multiple test correction, namely those of disease duration and TJC with higher and lower erosion scores respectively (table 2).

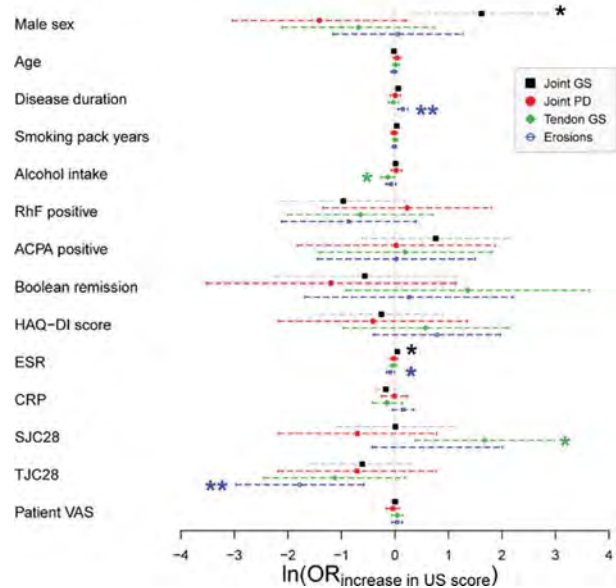
Abstract SAT0631 – Table 1.

Criterion	US parameter	Remission Definition		p (χ <sup>2</sup> )
		DAS28-CRP<2.4 (n=66)	ACR/EULAR Boolean (n=40)	
n (%) patients with total score ≥1	SPD	17 (26)	10 (25)	0.931
	SGS	66 (100)	40 (100)	n/a
	TGS	29 (44)	17 (43)	0.885
	Erosions	45 (68)	25 (63)	0.549
n (%) patients with any joint score ≥2	SPD	8 (12)	6 (15)	0.671
	SGS	48 (73)	27 (68)	0.566

Abstract SAT0631 – Table 2.

US score	Clinical parameter	Odds ratio (OR) increase in US score	95% CI	Unadjusted multivariate p value	Adjusted multivariate p value
SGS	Male sex	5.04	1.47–17.26	0.010	0.139
	ESR (mm/hr)	1.05	1.00–1.09	0.038	0.245
TGS	SJC28	5.37	1.46–19.72	0.011	0.159
	Alcohol intake (units/week)	0.88	0.77–1.00	0.044	0.307
Erosion	Disease duration (years)	1.16	1.06–1.27	0.002	<b>0.024</b>
	TJC28	0.17	0.05–0.56	0.004	<b>0.025</b>
	ESR (mm/hr)	0.92	0.85–0.99	0.022	0.101

Multivariate p < 0.005: \* Unadjusted, \*\* Adjusted



**Conclusions:** We demonstrate considerable subclinical US findings in RA patients in clinical remission, even when remission is defined using the more stringent ACR/EULAR Boolean criteria. Patients with longer disease duration and fewer tender joints had more joint erosions, though no other significant associations were seen after multiple test correction. Most strikingly SPD, which portends a poor prognosis, failed to show significant association with any of the clinical parameters. Our results suggest that clinical and ultrasound examinations may serve complementary, rather than duplicative, roles in the assessment of RA remission.

**REFERENCE:**

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**Disclosure of Interest:** None declared

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SAT0632

**ULTRASOUND IN THE MANAGEMENT OF RHEUMATOID ARTHRITIS USING A NOVEL PRAGMATIC ALGORITHM: A MULTICENTRIC OBSERVATIONAL STUDY**

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**Background:** Recently, novel algorithms for the pragmatic use of US in the management of RA patients were published in order to guide US use in various clinical scenarios.

**Objectives:** To evaluate the performance of the 2016 algorithm<sup>1</sup> proposed for evaluation of therapeutic response and its potential to contribute in decision-making.

**Methods:** Multicentric (5 centres), cross-sectional and observational study. Inclusion criteria: Patients older than 18 years old, RA diagnosis (ACR/EULAR criteria), receiving stable doses of conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) for the last six months. Exclusion criteria: use of biological DMARDs, severe articular deformities. Patients were submitted to clinical examination, CDAI (Clinical Disease Activity Index) was recorded and US examination performed by trained rheumatologists blinded to CDAI results. The following joints were examined: wrists, metacarpophalangeal (2 and 3), proximal interphalangeal (2 and 3) and metatarsophalangeal (2 and 5), in addition to any symptomatic joint. Synovitis was determined according to OMERACT. Joint distension (grey scale, GS) and Power Doppler (PD) graded on semiquantitative scale: absent=0, mild=1, moderate=2, intense=3. Total individual GS and PD scores were calculated by the sum of each joint scores. Therefore, each participant had two separate scores (GS and PD).

**Results:** 139 patients were included: 93% women, RF positive in 66%, age=57 ±11 [mean ±SD]yr, disease duration=10±8 year. Almost half (47.5%, n=66) of the patients had moderate/high disease activity, CDAl=20.65±10.66[mean ±SD]; while 52.5%(n=73) were in low activity/remission, CDAl=4.43±3.24.**US:** of the 66 patients with moderate/high disease activity, 26 patients (39.3%) presented negative PD and lowGS score: 5.11±2.67[mean ±SD]vs.40 patients with positive PD(PD=4.93±4.9)and a higher GS score (11.6±6.29, p<0.0001). CDAl in positive and negative PD subgroups was similar: mean (SD) values 21.81±11.32 vs. 18.86±9.02, p=0.13.Regarding CDAl low activity/remission group, 74% had negative PD, GS=4.5±3.6 and 5 (6.85%) were in US remission. Of these 5 patients, only one was in CDAl remission. From 26 patients in clinical remission, 4 (15.4%) patients had positive PD and GS score greater than 5, one was in US remission and the remaining (80.8%)presented negative PD but mild GS score.

**Conclusions:** Our study confirms that patients in CDAl remission may present active synovitis upon US exam. Likewise, patients with US remission may present falsely elevated clinical metrics possible due to the influence of other non-inflammatory comorbidities. Similarly in patients with moderate/high disease activity, US can alert to the possibility of other factors adding to high clinical scores. The US contributed to differentiate both clinical scenarios, with potential to optimise the therapeutic approach.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.5334

#### SAT0633 ULTRASOUND PREDICTIVE VALUE IN PREARTHRTIS. A PROSPECTIVE LONGITUDINAL STUDY

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**Background:** Inflammatory arthritis have a period of subclinical disease before the development of synovitis. It is necessary to know adequately the characteristics of this period to identify serological/imaging markers that recognise patients at risk of developing inflammatory arthritis.

**Objectives:** To describe the clinical characteristics and ultrasound (US) findings in "pre-arthritis" phases. To investigate the association of the US parameters with clinical or laboratory parameters.

**Methods:** Prospective longitudinal study of a cohort of patients with suspicious joint pain (predominance in nights or mornings, improving at day or with movement, or with morning stiffness >30') of less than 1 year of evolution and involvement of at least one small joint of hands or feet. Patients with clear synovitis, previously treated with DMARDs/steroids, or those with a diagnosis of fibromyalgia or osteoarthritis were excluded. The number of painful and swollen joints (PJC, SJC) and laboratory parameters were evaluated. A blind and extensive ultrasound examination (US) was performed with a MyLabTwice (Esaote) equip with a 5–13 MHz probe for grayscale (GS) and Power Doppler (PD). We assess the presence of synovitis in GS, PD (0–3) and erosions in 36 joints (radio- Carpal, Inter-carpal, 1 st –5th MCP and IPP, 2nd –5th MTP, elbow, shoulder and knee bilaterally) and 14 tendon compartments (2nd, 4th, 6th wrist extensor tendon compartments, 3rd and 4th finger flexor tendons, posterior tibial and fibularis tendons). In addition, an overall score of EG and PD in the cohort is calculated. Statistics analysis was made by mean ±SD or median (IQR), and comparison was made by t- Student test (quantitative parameters) and non parametric test (qualitative) (p<0.05).

**Results:** 20 patients were included, 95% women (60% non-smokers). Symptoms duration was 8±3 months. PJC median was 6 (RIC 2–9), without swollen joints in any case. ACPA and/or RF were positive in 6 patients (30%). ESR and/or RCP were elevated in 6 patients (30%). In the following 12 months, 45% of patients improved clinically, and 6 patients (30%) developed rheumatoid arthritis (RA). US results are exposed in the table 1, showing the number and percentage of patients with presence [≥1] of synovitis in GS, PD and erosions at different locations. The mean overall PD score was significantly higher in patients who will evolve to RA (9.1±2.8 vs 2.7±1.9, p<0.01) and in those with US erosions (10±1.4 vs 4.3±3.5, p<0.05). In addition, the mean overall GE score was higher in the RA group (9.1 ±2.8 vs 2.7±1.9, p<0.01) No significant differences were found between patients with or without acute phase reactants or positive RF/ACPA.

	GE=1 (n;% patients)	PD=1 (n;% patients)	Us erosion (n;% patients)
Wrist	17 (85%)	17 (85%)	0
MCP	15 (75%)	9 (45%)	0
IFP	13 (65%)	8 (40%)	0
Elbow	0	1 (5.5%)	0
Shoulder	0	0	0
MTP	13 (65%)	4 (20%)	2 (16.6%)
Knee	7 (37%)	4 (20%)	0
Wrist extensor tendons (n=18)	7 (39%)	3 (17%)	-
Finger flexor tendons (n=18)	3 (17%)	3 (17%)	-
Posterior tibial tendon	5 (28%)	2 (11%)	-
Fibularis tendons	0	1 (5.5%)	-
Global score*	9.2±4.9	5.3±3.8	0.1±0.3
*mean±DS			
Patients affected%	20 (100%)	19 (95%)	2 (10%)

**Conclusions:** In patients with pre-arthritis, Doppler scores were significantly higher among those with US erosions and those who evolve to RA. This results demonstrate the usefulness of US to predict the development of clinical arthritis in patients with inflammatory pain without synovitis

**Disclosure of Interest:** None declared

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#### SAT0634 DOES THE PRESENCE OF MRI-DETECTED OSTEITIS AT DIAGNOSIS WITH RHEUMATOID ARTHRITIS LOWERS THE RISK FOR ACHIEVING DMARD-FREE SUSTAINED REMISSION? – RESULTS OF A LONGITUDINAL STUDY

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**Background:** Although infrequent, some rheumatoid arthritis (RA)-patients achieve disease-modifying antirheumatic drug (DMARD)-free sustained remission. Absence of RA-specific auto-antibodies, such as anticitrullinated protein antibodies (ACPA) are known to be associated with this outcome, but furthermore mechanisms underlying the chronic nature of RA are largely unknown.

**Objectives:** Magnetic resonance imaging (MRI)-detected bone marrow oedema (BME, osteitis) strongly predicts erosive progression and is associated with ACPA-positivity. Therefore, we hypothesised that presence of MRI-detected osteitis is also predictive of not achieving DMARD-free sustained remission and that the presence of osteitis mediates the association between ACPA and DMARD-free sustained remission.

**Methods:** A 1.5T unilateral hand and foot MRI was performed at disease presentation in 238 RA-patients, evaluating BME, synovitis and tenosynovitis (summed in MRI-inflammation score). The median follow-up duration was 3.8 years. DMARD-free sustained remission, defined as the absence of clinical synovitis after DMARD-cessation that persisted during the total follow-up, was assessed. Associations between the different MRI-detected inflammatory features and this outcome were studied. A mediation analysis was performed to study whether the presence of BME mediated the association between ACPA and DMARD-free sustained remission. Finally, patterns of MRI-detected inflammation (including type, severity and location) with regard to DMARD-free sustained remission were studied using partial least squares (PLS) regression.

**Results:** Forty-six (19.3%) patients achieved DMARD-free sustained remission. ACPA-positivity associated independently with remission (HR 0.16, 95% CI 0.06–0.39). In contrast, no associations were observed between MRI-detected BME (HR 0.99, 95% CI 0.94–1.03), or other MRI-inflammatory features, and achieving DMARD-free sustained remission. Thus, the presence of BME did not mediate the association between ACPA and DMARD-free sustained remission. Furthermore, PLS regression revealed that patients who did or did not achieve remission could not be distinguished by patterns of MRI-detected inflammation.

**Conclusions:** At disease presentation, osteitis, as well as other MRI-detected inflammatory features, were not associated with achieving DMARD-free sustained remission over time. The data indicate that imaging predictors for joint damage and disease persistence differ. The processes mediating RA chronicity remain largely unsolved.

**Disclosure of Interest:** None declared

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SAT0635

### MAGNETIC RESONANCE IMAGING OF THE CERVICAL SPINE IN PATIENTS WITH RHEUMATOID ARTHRITIS AND ANKYLOSING SPONDYLITIS PRESENTING WITH CHRONIC NECK PAIN – A SYSTEMATIC COMPARISON OF CLINICAL ASSESSMENTS

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**Background:** Despite the differences in pathogenesis, neck pain associated with functional limitation and impaired mobility of the cervical spine is a frequent clinical symptom of patients with rheumatoid arthritis (RA) and ankylosing spondylitis (AS).

**Objectives:** To directly compare inflammatory and structural findings obtained by magnetic resonance imaging (MRI) in patients with RA and AS who present with chronic neck pain, and to correlate MRI findings with clinical measurements.

**Methods:** A total of 120 patients (60 RA and 60 AS) were consecutively included in the study if they had chronic neck pain (duration >3 months). All patients had clinical examinations for neck function and mobility and were asked to fill in disease specific questionnaires. They also had laboratory examinations (CRP, ESR) and MRI of the cervical spine (CS) using contrast-enhanced MRI sequences (T1 pre- and post-Gadolinium, sagittal and axial images). A total of 107 patients (59 RA with 295 and 48 AS with 240 vertebral segments) could be finally evaluated. An experienced rheumatologist examined all patients blinded to diagnosis and MR images. In addition, two experienced readers blinded to patients' diagnosis and clinical assessments evaluated the MRIs by describing the anatomical structures of the CS (vertebral body, intervertebral disc, facet joints) and the pattern of inflammatory activity in the bone marrow (vertebral edges vs. vertebral endplates).

**Results:** The RA group included more females (66.1%) and older patients (58.6 ±11.4 years) in comparison to AS (68.8% males, mean age 47.9±13.1 years), while there were no differences in the duration of neck pain. AS patients reported higher mean levels of neck pain on a 0–10 numerical rating scale (5.0±3.6) as compared to RA patients (3.0±3.1) (p=0.003), while the Northwick pain questionnaire didn't reveal any differences. There were numerically more patients with AS (n=11, 22.9%) than RA (n=9, 15.3%) (p=0.166) with bone marrow oedema (BME) at the vertebral edges. The majority of lesions was located in the lower CS. In contrast, more patients with RA (n=18, 30.5%) than AS (n=3, 6.3%) had erosive osteochondrosis with endplate BME (p=0.002). Atlantoaxial synovitis was found in only 1 patient with RA (1.7%), while inflammatory changes around the dens axis were found in 2 (3.4%) and atlantodental synovitis in 5 (8.5%) RA patients but not in AS patients. In comparison, erosive changes in the dens axis region were found in 3 RA (5.1%) vs. 2 AS (4.1%) patients. No major differences related to the presence of facet joint osteoarthritis was found (78% in RA vs. 65% in AS). The prevalence of facet joint osteoarthritis was the only imaging finding correlating with clinical symptoms: r=0.259 (p=0.049) for RA and r=0.416 (p=0.003) for AS, respectively. Similarly, only facet joint osteoarthritis correlated with restriction of cervical rotation in patients with AS (r=0.471, p=0.001).

**Conclusions:** Both BME and chronic changes of the lower part of the CS but not of the atlantoaxial region are seen in patients with RA and AS who present with chronic neck pain. The pattern of BME involvement in patients with RA vs. AS was different. Facet joint osteoarthritis was the only imaging finding that correlated with the magnitude of neck pain, in AS it also correlated with impaired cervical rotation.

**Disclosure of Interest:** None declared

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SAT0636

### REPEATABILITY OF MRI DIFFUSION WEIGHTED IMAGING OF SACROILIAC JOINTS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS AND HEALTHY SUBJECTS

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**Background:** Bone marrow oedema (BME) localised in sacroiliac joints (SIJ) as assessed by Short Tau Inversion Recovery (STIR) or T2 weighted fat saturated (T2w FS) sequences is one of the two cornerstones in the classification criterion for axial spondyloarthritis (SpA). Since Diffusion Weighted Imaging (DWI) can quantify water diffusion by measuring the Apparent Diffusion Coefficient (ADC), DWI may potentially be an alternative or supplementary imaging method to STIR or T2w FS.<sup>1</sup>

**Objectives:** The purpose was to measure the repeatability of (ADC) in a standardised Region-of-Interest (ROI) setting in healthy subjects and in active and chronic SpA patients and to compare the subjects.

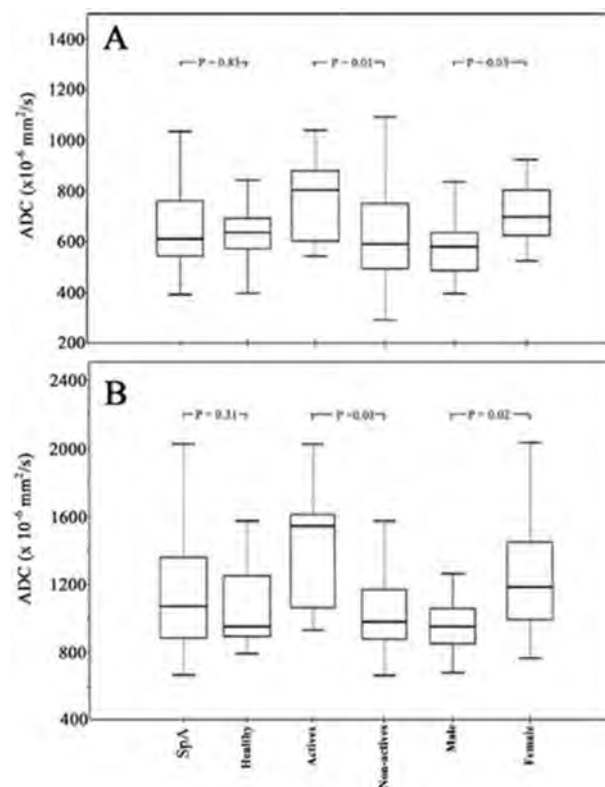
**Methods:** SpA patients and sex- and age- matched healthy subjects were examined twice within 7±2 days in the same MRI unit. Short Tau Inversion Recovery (STIR), T1 weighted and DWI sequences were performed in the semi-coronal plane. ADC map was calculated on basis of 4 b values: 0; 50; 500; 800. On each

consecutive slice in the cartilaginous compartment the SIJ was divided into four quadrants. From the joint surface a 5 mm deep ROI was drawn. In all ROIs median and 95th percentile ADC values were measured. Intraclass Correlation Coefficients (ICC) were measured to assess repeatability, and unpaired T tests to compare subgroups. Actives were defined as BME on STIR and non-actives as no BME on STIR.

**Results:** 25 SpA patients and 24 healthy subjects were enrolled. For all subjects inter-reader ICC was 0.66 and intra-reader ICC 0.92 for the median ADC and 0.57 and 0.74 for the 95th percentile ADC. In SpA patients, healthy subjects, females, males, actives and non-actives Inter-reader ICC was 0.79, 0.27, 0.42, 0.72, 0.78 and 0.52 for the median ADC and 0.74; 0.73, 0.68, 0.60, 0.88, 0.64, and 0.64 for the 95th percentile. Intrareader ICC was excellent for median ADC and good to excellent for 95th percentile ADC (table 1). Significant differences in median (figure 1A) and 95th percentile (fig 1B) ADC were measured between females versus males (p=0.03; p=0.02) and actives versus non-actives (p=0.01; p=0.01) but not in patients versus healthy controls.

**Abstract SAT0636 – Table 1.** Intraclass correlation coefficient (ICC) for median ADC and 95th percentile ADC measurements in subgroups.

	Inter Reader ICC	Inter Reader ICC	Intra Reader ICC	Intra Reader ICC
	(95% CI) Median ADC	(95% CI) 95th percentile ADC	(95% CI) Median ADC	(95% CI) 95th percentile ADC
All subjects	0.66 (0.46;0.80)	0.57 (0.33;0.73)	0.92 (0.86;0.95)	0.74 (0.58;0.85)
SpA	0.79 (0.58;0.90)	0.69 (0.40;0.85)	0.92 (0.82;0.96)	0.73 (0.47;0.87)
Healthy	0.27 (-0.17;0.61)	0.13 (-0.30;0.51)	0.95 (0.88;0.98)	0.68 (0.39;0.85)
Female	0.42 (0.01;0.71)	0.45 (0.04;0.73)	0.87 (0.72;0.94)	0.60 (0.24;0.81)
Male	0.72 (0.45;0.87)	0.63 (0.31;0.82)	0.93 (0.86;0.97)	0.88 (0.75;0.94)
BME on STIR	0.78 (0.16;0.96)	0.75 (0.08;0.95)	0.92 (0.59;0.99)	0.64 (-0.12;0.93)
No BME on STIR	0.52 (0.24;0.71)	0.29 (-0.03;0.55)	0.93 (0.87;0.96)	0.69 (0.48;0.82)



**Conclusions:** ADC seems a reliable parameter in SpA patients but not in healthy subjects. Our data encourage further studies of ADC measurements for discrimination of SpA patients with or without active inflammation.

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SAT0637

### RADIOGRAPHIC AND MRI DETECTED SACROILIITIS IS MORE OFTEN OBSERVED IN PATIENTS WITH LUMBOSACRAL TRANSITIONAL VERTEBRA IN THE DESIR COHORT

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**Background:** Lumbosacral transitional vertebra (LSTV) is a congenital anomaly of the lumbosacral transition reported in 16% to 36% of the general population. One study reported low clinical relevance of LSTV in the early diagnosis of axial spondyloarthritis (axSpA), but data remains scarce.

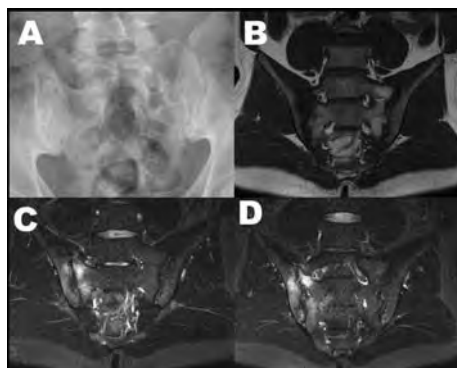
**Objectives:** Our objectives were to evaluate the association of LSTV with sacroiliitis on conventional radiographs (CR) and magnetic resonance imaging (MRI) in a population with inflammatory back pain (IBP) suspected of axSpA.

**Methods:** Baseline pelvic and lumbar CR of DESIR cohort patients (18–50 years, IBP ≥ 3 months but < 3 years and suspicion of axSpA) were analysed by readers blinded to clinical and other radiologic information. Baseline sacroiliac joint MRI had been read for sacroiliitis according to the ASAS definition. Radiographic sacroiliitis was defined according to the modified New York classification (mNYC). Unilateral sacroiliitis was defined as at least grade 2 according to the mNYC. LSTV were defined on radiographs, according to Castellvi classification: 0 normal; 1 enlarged transverse processes (a=unilateral, b=bilateral); 2 pseudo-articulation with the sacral bone (a=unilateral, b=bilateral); 3 fusion with the sacral bone (a=unilateral, b=bilateral); 4 pseudo-articulation on one side and fusion on the other. Imaging data collected at inclusion were compared in patients with LSTV versus patients without using Chi-square test or exact Fischer's test when appropriate.

**Results:** 688 patients with available CR enabling LSTV analysis were studied, 47% were men, mean age was 33 years, 64% fulfilled ASAS criteria. Among the 688 patients 29.1% presented LSTV. Number and percentages of patients with different classes of LSTV are presented in Table I. Patients with LSTV had more often sacroiliitis on CR than patients without, respectively 27% and 19% (p=0.013). Patients with LSTV had more often sacroiliitis on MRI (figure 1) than patients without, respectively 39% and 29% (p=0.019). Presence of fusion on the right transverse process was associated with both right (p=0.001) and left (p=0.001) sacroiliitis on CR. Presence of fusion on the left transverse process was associated with sacroiliitis in CR on both right (p=0.006) and left (p=0.001) sides.

Table I: Prevalence of LSTV in the DESIR cohort (for stage 4, laterality is for the fusion)

Castellvi	Laterality	Number (%)
I a (Mega-apophysis)	Right	26 (3.8)
	Left	28 (4.1)
I b		76 (11.0)
II a (New articulation)	Right	13 (1.9)
	Left	7 (1.0)
II b		12 (1.7)
III a (Fusion)	Right	3 (0.4)
	Left	4 (0.6)
III b		21 (3.0)
IV (New articulation and fusion)	Right	3 (0.4)
	Left	7 (1.0)



**Abstract SAT0637 – Figure 1.** A case of LSTV (class 4 from Castellvi classification) associated to CR (A) and MRI. T1 weighted sequence is shown in B and STIR weighted sequence in C and D.

**Conclusions:** LSTV is observed in 29.1% of patients from the DESIR cohort, as reported in the literature and is associated with sacroiliitis on conventional radiography and MRI. Further study is mandatory to understand if this is based on mechanical stress or AxSpA and to assess the potential bias of LSTV in axSpA diagnosis.

**Disclosure of Interest:** None declared

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SAT0638

### ULTRASONOGRAPHY THE PREVALENCE OF MONOSIDIUM URATE CRYSTAL DEPOSITION IN PATIENTS WITH CALCIUM PYROPHOSPHATE DEPOSITION DISEASE: ASSOCIATION WITH LABORATORY, RADIOGRAPHIC PARAMETERS AND MICROSCOPY OF SYNOVIAL FLUID

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**Background:** An association between gout and chondrocalcinosis is well known. Our objectives were to first, to determine by ultrasonography (US) the prevalence of monosodium urate (MSU) crystal deposition in patients (pts) with calcium pyrophosphate deposition disease (CPPD) and second, to investigate the relationship between serum urate (SU), synovial fluid (SF) examination, radiographic and US findings.

**Methods:** Eighty five pts (52% – men) with CPPD disease [McCarty criteria; median age 58.5 (range 50.5–65) years] were enrolled. SU levels were obtained during the follow-up period. US examination (Logiq 9, GE, 9 MHz probe) was performed by one sonographer, blind to clinical and laboratory data. Hyaline cartilages of the knees, II-V metacarpophalangeal and I metatarsophalangeal joints were evaluated for the “double contour” (DC) sign as evidence of MSU crystal deposition.<sup>1,2</sup> SF analyses under polarised microscopy were obtained at each time of US assessment. X-ray of knee joints was performed in all pts. We assessed joint space narrowing, osteophytes, presence of osteosclerosis and cyst in the tibiofemoral (TF) and patellofemoral (PF) compartments, radiographic evidence of knee osteoarthritis (OA, Kellgren and Lawrence (KL) criteria grade ≥ 2 in the medial and/or lateral TF compartment).

**Results:** 44% (38/85) pts had PFOA, 19% (16/85) had TFOA and combined PFOA and TFOA in 10.5% (9/85). Thirty-five of 85 (41%) pts had a SU level of > 6 mg/dl [7.9 (7.7–8.3) mg/dl]. Among them 60% (21/35) were performed US assessment of the joints. The prevalence of the DC sign was found in at least one articular site in 17 of 21 (81%) cases. SU levels were positively correlated with presence of the DC sign in joints (Spearman's r=0.532, p<0.05), PFOA (r=0.291, p<0.05). The MSU crystals from SF aspirates were received in 4 of 17 (23.5%) cases.

**Conclusions:** This study confirmed that the US DC sign in joints significantly correlate with a SU level and may be of use as a non-invasive tool in reflecting changes of uricemia in pts with crystal-associated synovitis. Hyperuricemia in pts with CPPD was associated with PFOA disease pattern.

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SAT0639

### INTEROBSERVER AGREEMENT OF THE OMERACT ULTRASONOGRAPHIC CRITERIA FOR THE DIAGNOSIS OF CALCIUM PYROPHOSPHATE DEPOSITION DISEASE AT THE WRIST, AMONG PANEL OF RADIOLOGISTS AND RHEUMATOLOGISTS

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**Background:** The OMERACT ultrasound (US) task force subdivision “US in CPPD” has created definitions for US identification of crystal deposits in joints and

tested interobserver agreement for several joints<sup>1</sup>. The knee and the wrist were the most reliable sites for assessing CPPD.

**Objectives:** To assess whether the high level of inter-observer agreement of US for the detection of Calcium Pyrophosphate Deposition Disease (CPPD) in the triangular fibrocartilage complex (TFCC) of the wrist found by the experienced rheumatologists of the OMERACT group<sup>2</sup> could be reproduced in real life

**Methods:** The OMERACT US criteria for identification of CPPD were utilised for this exercise on pre-recorded static images using a dichotomous score among several radiologists (n=2) and rheumatologists (n=5) with varying level of experience in musculoskeletal ultrasonography (range: 2–10 years). Firstly, the same 15 US images of the wrist that had been evaluated by the OMERACT panel were sent for evaluation to the local participants in order to calculate the inter-observer agreement. Secondly, 22 additional wrist US images extracted from locally performed examinations, in patients with a high suspicion of CPPD arthritis were evaluated. These local US examinations were performed in real life conditions, by different operators, on different machines and without prior standardisation of the procedure. For comparison, interobserver of wrist radiographs was also evaluated for all local patients

**Results:** The mean overall agreement and kappa values on the OMERACT panel US images were 0.89 and 0.78 respectively. These values are similar to those obtained previously by the OMERACT panel during the web exercise with the same images (0.80 and 0.68 respectively). The interobserver agreement was lower with the local US images (0.70 and 0.49 respectively), probably due primarily to the absence of strict standardisation of US procedure and inferior image quality. For comparison, the performance on the local radiographs was similar (0.70 and 0.47 respectively).

**Conclusions:** Our results confirm that the new OMERACT US definitions for assessing wrist CPPD are reliable when applied to pre-recorded static images. Scanning technique and standardisation of the procedure appear to be an important aspect with regards to the assessment of CPP deposition at the wrist.

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**Disclosure of Interest:** None declared

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#### SAT0640 WHOLE BODY-MRI IN AXIAL SPONDYLOARTHRITIS (AXSPA): DIFFUSION WEIGHTED IMAGING (DWI) OUTPERFORMS THE STIR SEQUENCE

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**Background:** None

**Objectives:** To compare the diagnostic value of DWI and STIR sequences as part of WB-MRI studies in AxSpA patients.

**Methods:** 20 consecutive patients (P) with confirmed diagnosis of active AxSpA and 20 controls (C) referred for metastatic cancer screening were investigated with identical WB-MRI protocols including DWI and STIR images. Two independent observers recorded the presence of "lesions" (high signal intensity foci on STIR and high b-value DWI images) in 17 anatomic areas; making a 17-point "area score" and a calculated 40-point "lesion score". Both were tested for correlation with clinical and biological parameters.

**Results:** In P, the "lesion score" was significantly higher with DWI than with STIR (p<0.025). The most experienced observer had higher DWI lesion scores, suggesting a learning effect. The lesion score and some anatomic areas could discriminate P from C. For this purpose, DWI had a higher AUC than STIR (AUC=99.9, CI: 99.5–1.00 vs AUC=95.8, CI: 90.9–1.00). For a trained MRI observer using DWI, a lesion score threshold of >4 had 100% sensitivity and 95% specificity. With STIR, a threshold of >3 had 85% sensitivity and 90% specificity. The area score AUC was significantly lower with STIR than with DWI (p=0.0233), but no satisfactory area score threshold was identified. The most frequently involved areas were the spine and hip entheses in C, the spine and SIJ in P. Manubrio- and chondro-sternal joint involvement was specific for AxSpA. The lesion score was positively correlated with ASDAS-CRP and (log) CRP.

**Conclusions:** DWI is a promising alternative to STIR in WB-MRI studies for the detection of active lesions in AxSpA. Training may be necessary. The involvement of specific anatomic areas could distinguish P from C.

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#### SAT0641 PERFORMANCE AND AGREEMENT OF DIFFERENT OPERATORS AND HISTOLOGICAL TECHNIQUES FOR THE ASSESSMENT OF GERMINAL CENTRES IN MINOR SALIVARY GLANDS IN PRIMARY SJÖGREN'S SYNDROME

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**Background:** A standardisation of minor salivary gland (MSG) histopathology in primary Sjögren's syndrome (pSS) has been recently proposed by the EULAR study group on Sjögren's syndrome. Although there is strong agreement that germinal centres (GCs) should be routinely identified, due to their prognostic value, a consensus regarding the best protocol is still lacking.

**Objectives:** Aim of this study was to compare the performance of different histological techniques and operators with variable experience in MSG histopathology to identify GCs in pSS MSGs.

**Methods:** MSG biopsies from 50 pSS patients were studied. Three blinded operators (expert rheumatologist, expert pathologist and rheumatologist with scarce experience on MSG histopathology) scored one slide stained with haematoxylin and eosin (H and E). Consecutive slides were processed by immunofluorescence and immunohistochemistry to assess CD3/CD20, CD21 and Bcl-6 expression.

**Results:** Overall, the prevalence of GC in MSG specimens (namely the presence of at least one focus positive for at least one operator or histological technique) ranged between 26% and 52%. By separate assessment of 225 foci, the best agreement was between H and E-stained sections evaluated by the expert rheumatologist and CD3/CD20 segregation (Cohen's kappa=0.72). In the foci with CD21 positivity, the agreement with the expert rheumatologist further increased (Cohen's kappa=0.75). Among the 3 methods employed, the best agreement was observed between B/T-cell segregation and the positivity for CD21 staining (0.84). The absence of Bcl-6 in a focus does not necessarily rule out the presence of the GC detected with other stainings.

**Conclusions:** GC assessment on H and E-stained sections should be performed with caution, as it is dependent on the background and expertise of the operator. The combination of H and E with CD3/CD20 and CD21 staining should be recommended as it is reliable, feasible, able to overcome the bias of operator experience and easily transferrable into routine practice.

**Disclosure of Interest:** None declared

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#### SAT0642 A CAD SYSTEM IN HEP-2 IIF READING: A MULTICENTRE STUDY

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**Background:** The indirect immunofluorescence (IIF) on HEP-2 cells is the recommended technique for anti-nuclear antibodies (ANA) detection. Automation of IIF image reading can provide a reliable basis for cost-effective serological diagnostics. Computer-aided diagnosis (CAD) tools based on digital imaging reading can help us to overcome the reader subjectivity. In a recent work<sup>1</sup> we assessed the inter-observer variability using digital images showing the 74.1% of agreement. It improved using "ground truth" as gold standard.

**Objectives:** To compare classification accuracy between readings provided by expert readers belonging to three different laboratories and those automatically returned by CAD.

**Methods:** We acquired 1771 images from 583 consecutive sample with an acquisition unit using HEp-2 cells (MBL) at 1:80 screening dilution. Each image was blindly classified as positive, negative, or weak positive by two experienced physicians, with more than ten years of experience in IIF, for each of the three laboratories. We obtained gold standard on the basis of annotations provided by expert physicians. We described a CAD system for HEp-2 classification that relies upon features provided by a deep neural network architecture, namely an Invariant Scattering Convolutional Network (Scatnet). We therefore compared human readings with automatic classification provided by a CAD.

**Results:** The dataset contains 215 positive samples, 136 weak positive, 219 negative. The CAD-system classification and experts showed a sensitivity of 93% vs 92.9%, 79.4% vs 74.5%, and 92.2% vs. 92.8% on positive, negative and weak positive, respectively (Fig 1). The CAD-system obtained an accuracy of 89.5%, slightly better than average experts' classification (88.5%) and, interestingly, it better recognised the weak positive samples.

Fig1

Sensitivity	CAD	Experts
Positive	0.930	0.929
Weak positive	0.794	0.745
Negative	0.922	0.928
<b>Positive Predictive Value</b>		
Positive	0.939	0.933
Weak positive	0.777	0.779
Negative	0.927	0.913

**Conclusions:** Solid gold standard is essential for use CAD systems in routine work lab. The CAD-system classification and the 3 experts have provided comparable results. Laboratories' agreement improves using digital images and comparing each single human evaluation to a potential reference data and for this reason nowadays the CAD system should be considered a reliable tool of standardisation reducing the inter-laboratory variability.

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SAT0643

#### ULTRASOUND ABNORMALITIES IN WRIST, MCP2 AND MTP5 ARE MOST DISCRIMINATIVE IN PREDICTING ARTHRITIS DEVELOPMENT IN SEROPOSITIVE ARTHRALGIA PATIENTS

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**Background:** Seropositive arthralgia patients are at risk of developing rheumatoid arthritis (RA). Ultrasound (US) might be used to further predict which seropositive individuals will progress to RA. However, the value of US in the prediction of RA is still a point of debate, mainly due to the use of different scoring systems and compositions of joints in US protocols in literature.

**Objectives:** To investigate which joints are most discriminative in predicting arthritis development in seropositive arthralgia patients.

**Methods:** We included 174 seropositive patients with arthralgia, but without clinical arthritis. US was performed at baseline in 16 joints: bilateral metacarpal phalangeal (MCP) 2 and 3, proximal interphalangeal (PIP) 2 and 3, wrist and metatarsal phalangeal (MTP) joints 2, 3 and 5. Images were scored for grey-scale (GS) synovitis and Power Doppler (PD) on a scale of 0–3. Grades  $\geq 2$  for GS synovitis and grades  $\geq 1$  for PD were regarded as abnormal. Clinical arthritis development was assessed in any of 44 joints during yearly follow-up or during an

unscheduled visit in case of progression of symptoms. Patients were followed until clinical arthritis development or for a maximum of 5 years.

**Results:** In a total of 2784 joints that were imaged, 112 showed GS synovitis and 14 PD. The majority of GS synovitis was present in MTP2 and MTP3 joints (56 (50%) and 32 (29%), respectively), followed by wrists (15 (13%)), MCP3 (4 (4%)), MTP5 (3 (3%)), MCP2 (2 (2%)) and none in PIPs. Out of 14 joints with PD, 7 were wrists, 3 MTP5, 2 MCP2 and 2 PIP3. Fifty-one (29%) of the patients developed clinical arthritis in at least one joint after a median follow-up of 12 (interquartile range 6–23) months. For GS synovitis, the wrist, MCP2 and MTP5 were most discriminative in predicting clinical arthritis development (12/15 (80%) of patients with GS synovitis in wrist developed clinical arthritis, 3/3 (100%) in MTP5 and 2/2 (100%) in MCP2). MTP2 and 3 were least discriminative (<27%). No substantial differences were found between left and right joints. No clear association with clinical arthritis development was found in the limited number of joints that had positive PD.

**Conclusions:** Wrist, MCP2 and MTP5 joints (although numbers were small) showed the highest predictive value for development of clinical arthritis in any of 44 joints. Although most GS synovitis was observed in MTP2 and 3, predictive value of MTP2 and 3 joints for development of clinical arthritis was low. These results indicate that the choice of joints in the US protocol may influence the predictive value of ultrasound in predicting clinical arthritis development in seropositive arthralgia patients.

**Disclosure of Interest:** None declared

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SAT0644

#### T1RHO MAPPING IN THE ASSESSMENT OF ARTICULAR CARTILAGE INTEGRITY OF THE KNEE IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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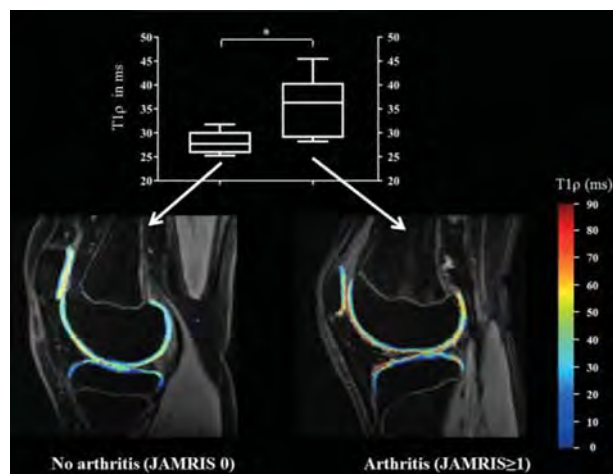
**Background:** Early detection of microstructural damage to cartilage of patients with juvenile idiopathic arthritis (JIA) might prevent irreversible cartilage damage by timely treatment and follow-up of cartilage microstructure. New, quantitative MRI sequences such as T1 $\rho$  are possibly able to detect pre-erosive cartilage damage by quantifying proteoglycan (PG) loss of cartilage<sup>1-4</sup>.

**Objectives:** To study feasibility of T1 $\rho$  mapping for assessment of articular cartilage integrity in children with JIA and study correlation between T1 $\rho$  relaxation time and the Juvenile Arthritis MRI score (JAMRIS)<sup>5</sup> for disease activity.

**Methods:** After IRB approval and informed consent, the knee of patients with JIA or suspected JIA was imaged at 3T MRI using T2, pre and post contrast T1 and a sagittal T1 $\rho$  sequence with 400 Hz and spin lock time of 5, 10, 20, 40 and 50 ms. A region of interest (ROI) was drawn in articular cartilage of the knee on the T1 $\rho$  images, resulting in a mean T1 $\rho$  value of articular cartilage per patient. Using regular T2W and T1W pre and post contrast scans, JAMRIS was assigned to discriminate inflamed knees (JAMRIS  $\geq 1$ ) from non-inflamed knees (JAMRIS 0). In SPSS, Mann-Whitney U test and Spearman correlation coefficient were used to compare the mean T1 $\rho$  value between patients with and without arthritis on MRI and to correlate T1 $\rho$  values with JAMRIS score. ROI drawing was performed twice in 5 subjects. Intraclass correlation coefficient (ICC) was used to study intra-reader reliability.

**Results:** Of all 13 patients (median age 13.7 years), 7 patients had inflammation in the knee. No cartilage lesions were observed on standard MRI sequences. Acquisition of the T1 $\rho$  was successful and without artefacts in 100% of the children. Patients with inflammation in the knee showed a significantly longer T1 $\rho$  value than patients without inflammation in the knee: 36.3 ms (IQR 29.0–40.4) versus 27.7 ms (IQR 25.8–30.2),  $p=0.02$ . Correlation between T1 $\rho$  value and JAMRIS score was 0.76 ( $p=0.003$ ). Repeatability of ROI drawing was characterised by ICCs  $>0.99$ ,  $p<0.05$ .





**Conclusions:** This pilot study indicates that, even in the absence of cartilage erosions, significant differences are seen in cartilage integrity with higher  $T1\rho$  relaxation times in patients with knee arthritis. This might indicate loss of glycosaminoglycan content in active synovitis of the knee. Thus, our pilot data suggest that  $T1\rho$  could serve as an imaging biomarker for cartilage integrity, ultimately aiming to prevent irreversible cartilage damage and long-term disability in this young JIA population.

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SAT0645

#### DIAGNOSTIC ACCURACY OF SERUM AUTOANTIBODIES MULTI-TESTING IN RHEUMATOID ARTHRITIS AND ECONOMIC CONSEQUENCES ACROSS EUROPE

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**Background:** Rheumatoid arthritis (RA) diagnosis requires interpretation of a combination of clinical, laboratory and imaging investigations. In RA, the consequences of incorrect serology test results are particularly important: patients with False Positive results (FPs) are initially managed as RA patients, bringing about extra costs until a correct diagnosis is made.

**Objectives:** The first aim of the study was to evaluate the diagnostic performance of RF-IgA, RF-IgM, and CCP, used alone or in multi-testing parallel or sequential combinations. The secondary goal focused on the economic consequences of serology FPs in selected European countries.

**Methods:** 190 established RA patients and 197 controls (either affected by other conditions or healthy donors) were used to assess the diagnostic performance of mono- and multi-serology testing in PC; both testing in Primary Care (PC) and in Secondary Care (SC) settings were considered.

For the secondary objective, a 12 month Markov model simulated, from the National Health Services perspective, 1.000 RA-suspected individuals tested in PC and SC with mono- or multi-testing. Costs come from the published literature. The European countries included in the analysis were the United Kingdom, Austria, Belgium, Denmark, France, Germany, Italy, the Netherlands, Portugal, Spain and Sweden. Uncertainty was addressed with sensitivity analysis.

**Results:** The mono-testing diagnostic performance was:

- RF-IgA: sensitivity [95% CI]=40.5% [33.5%, 47.9%], specificity=92.4% [87.8%, 95.7%];
- RF-IgM: sensitivity=59.0% [51.6%, 66.0%], specificity=89.3% [84.2%, 93.3%];
- CCP: sensitivity=59.5% [52.1%, 66.5%], specificity=96.5% [92.8%, 98.6%].

In multi-testing, defining a “positive result” as “positivity to at least one test” increased sensitivity; “positivity to all the tests” increased specificity. In a PC scenario:

- parallel testing:
  - o using CCP and RF-IgM increased specificity to 99.5% [97.2%, 100.0%];
  - o the three tests used simultaneously maximised specificity (100.0% [98.1%, 100.0%]), but reduced sensitivity to 35.8% [29.0%, 43.1%];
- sequential testing: testing positive to both RF-IgA and RF-IgM followed by CCP testing led to 90.7% [81.7%, 96.2%] sensitivity and to 100.0% [54.1%, 100.0%] specificity.

With respect to mono-testing, multi-testing options reduced the number of FPs. Therefore, in each of the countries considered, multi-testing allowed for important cost savings due to reduced clinical procedures and resource utilisation of FPs.

**Conclusions:** Multi-serology testing improve the diagnostic accuracy of the individual RF-IgA, RF-IgM and CCP tests. Optimal multi-testing combinations minimise the number of FPs, thus reducing avoidable costs to the National Health Services. Consequently, multi-testing for RA demonstrates superior value from patient and payer perspective.

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SAT0646

#### DEVELOPMENT AND VALIDATION OF A DEEP LEARNING ALGORITHM FOR CLASSIFYING ANTINUCLEAR ANTIBODY PATTERNS IN INDIRECT IMMUNOFLUORESCENCE IMAGES

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**Background:** Antinuclear antibody (ANA) is a valuable test in the evaluate for a variety of autoimmune diseases. It can be detected using immunofluorescence (IIF) which yield both serum titers and also staining patterns. The manual titration of ANA is laborious and evaluation of staining patterns by a microscope requires experts to make correct classification. Deep learning is a collection of computational methods that enable an algorithm to ‘learn’ from a large set of data to acquire ‘skills’ that are characteristic of human intelligence, for example, complex pattern recognition. Application of these methods to ANA pattern classification requires further assessment and validation.

**Objectives:** To train a deep convoluted neural network to create an algorithm for automated classification of ANA patterns in images of indirect immunofluorescence.

**Methods:** We construct a deep convoluted neural network based on inception V3. The model adopted a deep learning architecture with 21 layers and ANA images were used to train to detect speckled, homogenous, nucleolar, centromere, dense fine speckled, cytoplasmic and mitochondrial patterns. The data were collected from rheumatology patients from June 2016 to October 2017. We validate the performance of the model using a separate set of images.

**Results:** Our data set consisted of 81822 ANA images from 8839 patients. The overall accuracy was 99.46% after 200 epochs of iteration using the training dataset (65 458 images) and the accuracy was 96.33% using the validation dataset (16.64 images). The sensitivity was 97.1% for speckled pattern, 91.4% for homogenous pattern, 97.1% for nucleolar pattern, 97.1% for centromere pattern, 97.2% for cytoplasmic pattern, and 100% for both dense fine speckled and mitochondrial patterns. The specificity was also good, ranged between 97.1% and 100%.

**Conclusions:** In this study, an algorithm based on deep convoluted neural network had high sensitivity and specific for detecting specific ANA patterns. Further research is needed to determine the feasibility to deploy the technology in routine clinical works to assist rheumatologists to interpret ANA.

**Disclosure of Interest:** None declared

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SAT0647

### PREDICTIVE FACTORS OF POSITIVE POSITRON EMISSION TOMOGRAPHY FOR DIAGNOSING AORTITIS IN PATIENTS WITH POLYMYALGIC SYNDROME

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**Background:** Isolated non-infectious aortitis is a potentially serious condition whose diagnosis is often delayed due to the non-specific nature of its symptoms. Most of the patients initially present with polymyalgic syndrome associated with atypical symptoms. Nowadays, <sup>18</sup>F-FDG PET/CT scan is the best tool for early detection of aortitis. However, it is a complex and expensive technique. Thus, we should make an effort to select those patients who will benefit the most from this procedure. Unfortunately, we have no data about which factors may improve the probability of a positive diagnosis of aortitis using this imaging technique.

**Objectives:** Our aim was to evaluate, in patients with polymyalgia rheumatica (PMR), the predictive factors for a positive <sup>18</sup>F-FDG PET/CT scan, in order to make an early diagnosis of aortitis and optimise the use of this technique.

**Methods:** Retrospective study on 97 patients with PMR who had undergone an <sup>18</sup>F-FDG PET/CT scan between January 2010 and August 2017 with a high clinical suspicion of aortitis. Only patients with polymyalgic syndrome without any other underlying disease were included. We considered two groups: **a)** Classic PMR: patients who fulfilled the 2012 EULAR/ACR criteria; and **b)** Atypical PMR: patients with symptoms resembling PMR but did not fulfil the 2012 EULAR/ACR criteria. Distribution of categorical variables was compared by the Pearson Chi-squared test or Fisher exact test. Quantitative variables were analysed using the Student t test or MannWhitney U test as appropriate. An adjusted logistic regression model was built to assess the best set of predictive factors for a positive PET scan in both groups of patients.

**Results:** <sup>18</sup>F-FDG PET/CT scans were performed in 97 patients due to clinical suspicion of aortitis, being positive in 60 (61.9%). Patients (60 women/37 men) had a mean age of 68.4±10.7 years. Fifty-one (52.6%) had classic PMR and 46 (47.4%) atypical PMR. In patients with classic PMR, the best set of predictors for a positive PET/CT scan were lower limb pain (OR=8.4, 95% CI 2.0–35.1; p=0.004) and low back pain (OR=7.6, 95% CI 1.3–45.5, p=0.027), once adjusted for age, sex and current tobacco use. In atypical PMR patients, only the pelvic girdle affection (OR: 5.0, 95% CI 1.3–19.5; p=0.002) was significantly associated with a positive PET/CT scan, in the logistic adjusted model.

Abstract SAT0647 – Table 1

	PMR (n=97)					
	Classic PMR (n=51)			Atypical PMR (n=46)		
	Positive PET/CT (n=29)	Negative PET/CT (n=22)	P	Positive PET/CT (n=31)	Negative PET/CT (n=15)	P
Sex (women), n (%)	20 (69.0)	13 (59.1)	0.47	18 (58.1)	9 (60.0)	0.80
Age (years), mean ±SD	72.8 ± 8.8	75.2 ± 8.0	0.32	62.5 ± 9.1	62.4 ± 11.8	0.97
Recurrence of polymyalgic symptoms						
Neck pain, n (%)	6 (20.7)	4 (18.2)	0.99	3 (9.7)	2 (13.3)	0.71
Shoulder girdle, n (%)	17 (58.7)	15 (68.2)	0.45	12 (38.7)	10 (66.7)	0.076
Pelvic girdle, n (%)	19 (65.5)	11 (50.0)	0.27	29 (94.5)	4 (26.7)	0.016
Morning stiffness, n (%)	4 (13.4)	6 (27.3)	0.06	3 (9.7)	2 (13.3)	0.99
Atypical symptoms						
Inflammatory low back pain, n (%)	10 (34.5)	3 (13.6)	0.09	11 (35.5)	3 (20.0)	0.33
Diffuse lower limb pain, n (%)	17 (58.0)	8 (36.4)	0.004	17 (54.8)	8 (53.3)	0.35
Asthenia, n (%)	9 (31.0)	6 (27.3)	0.77	3 (9.7)	4 (26.7)	0.19
Hyporexia, n (%)	2 (6.9)	6 (27.3)	0.05	3 (9.7)	3 (20.0)	0.38
Weight loss, n (%)	4 (13.0)	6 (27.3)	0.30	5 (16.1)	4 (26.7)	0.45
Laboratory abnormalities						
Anemia, n (%)	11 (37.1)	12 (54.5)	0.24	8 (25.8)	5 (33.3)	0.73
CRP > 6 mg/l, n (%)	3 (10.3)	4 (18.2)	0.35	5 (16.1)	2 (13.3)	0.77
ESR > 40 mm, n (%)	12 (41.4)	12 (54.5)	0.57	16 (51.6)	8 (53.3)	0.81
Treatment response						
Lack of improvement with 15 mg of PD, n (%)	5 (17.2)	4 (18.2)	0.99	5 (16.1)	3 (20.0)	0.95

**Conclusions:** We have found that, in patients with classic PMR, the presence of diffuse lower limb pain and inflammatory low back may have clinical relevance when requesting a PET/CT scan due to aortitis suspicion. On the other hand, in patients with atypical PMR, only the presence of pain in the pelvic girdle seems to be a predictive factor for a positive result in PET/CT scan.

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SAT0648

### COXALGIA IN HEMOPHILIC PATIENTS. SONOGRAPHIC EVALUATION OF A NOT TARGET JOINT

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**Background:** Spontaneous bleeding in haemophilia shows a predilection for joints, and repeated hemarthrosis induce synovial inflammation, cartilage degeneration and bone damage, leading to hemophilic arthropathy. The hip is not a target joint and its involvement is not easy to be distinguished from other conditions which may provoke pain referred to the hip.

**Objectives:** Aim of the study was to analyse the different sonographic findings related to different pain producing conditions.

**Methods:** Thirty patients with haemophilia A and monolateral coxalgia were examined. Sonographic exam (US) was performed in all patients by Esaote equipment My Lab 70 with linear probe 4–13 MHz and power Doppler. The iliopsoas muscle and its bursa, the greater trochanteric bursa, and the hip joint were analysed. Sonographic findings in the joint were scored (score ranging from 0 to 21) for effusion, bone remodelling, cartilage damage, synovial hypertrophy, hemosiderin, osteophytes, hemarthrosis, erosion and fibrotic septa. The World Federation of Haemophilia (WFH) orthopaedic joint scale score and the radiologic Pattersson score were evaluated in all patients.

**Results:** US showed effusion in 20 hip joints (67%), bone remodelling in 18 (60%), cartilage damage in 10 (33%), synovial hypertrophy in 12 (40%), hemosiderin in 4 (13%), osteophytes in 7 (23%), hemarthrosis in 10 (33%) with power Doppler activity (>3 flags). In no patient erosion or fibrotic septa were observed. Fifteen out of 30 joints showed US score ≤5, and 15 US score >5. In 8 patients a hematoma of iliopsoas muscle was present, in two patients great trochanteric bursitis was detected. WFH mean score value was 39.5 (range 12–57) and the mean Pattersson score value was 10.4 (range 6–12).

**Conclusions:** Surprisingly, in most cases (67%) coxalgia was not related to trochanteric bursitis or iliopsoas muscle involvement but was due to hemophilic arthropathy of the hip which is not a target joint. Moreover, power Doppler allowed to detect hemarthrosis in 33% of patients, supporting the hypothesis that vascular changes and remodelling in haemophilia are associated with bleeding and joint damage<sup>1</sup>.

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SAT0649

### CORRELATION BETWEEN CLINICAL MANIFESTATIONS AND <sup>18</sup>F-FDG UPTAKE IN PATIENTS WITH POLYMYALGIA RHEUMATICA

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**Background:** Polymyalgia rheumatica (PMR) is an inflammatory disease characterised by pain and stiffness of the neck, shoulder and pelvic girdles. It can also be accompanied by other non-specific symptoms such as inflammatory low back pain, diffuse lower limb pain and constitutional syndrome. The role of <sup>18</sup>F-FDG PET/CT is increasing in the diagnosis of PMR but it remains unknown if there is a correlation between clinical symptoms and <sup>18</sup>F-FDG uptake.

**Objectives:** Our aim was to assess if the localization of pain of patients with PMR correlates with <sup>18</sup>F-FDG uptake in the corresponding region of interest.

**Methods:** Retrospective study of 75 patients with PMR and their respective PET/CT scans from a referral centre. PMR diagnosis was based on 2012 EULAR/ACR criteria.

**Results:** We evaluated 75 patients (27 men and 48 women) with a mean age ±SD of 68.2±10.7 years. A PET/CT was performed in all of them. Pattern of <sup>18</sup>F-FDG uptake in patients with different clinical manifestations were summarised in the TABLE. Twenty-two out of thirty-three patients (66.7%) with <sup>18</sup>F-FDG uptake in sternoclavicular joints had shoulder girdle pain. In all patients with morning

stiffness (n=11) an increase of  $^{18}\text{F}$ -FDG uptake in shoulders was observed. Twenty-three patients of thirty-two patients (71.8%) with  $^{18}\text{F}$ -FDG uptake in hips had pelvic girdle pain. The remaining localizations of  $^{18}\text{F}$ -FDG uptake in PET/CT scans did not show significant correlations with clinical symptoms.

Clinical manifestation/location of FDG uptake	F-FDG uptake		
	Positive, n/N (%)	Negative, n/N (%)	P
<b>Shoulder girdle pain (n=40)</b>			
Shoulder	27/45 (60.0)	13/30 (43.3)	0.16
Sternoclavicular joints	22/33 (66.7)	18/42 (42.9)	<b>0.04</b>
Cervical interspinous bursae	6/9 (66.7)	34/66 (51.5)	0.49
<b>Neck pain (n=12)</b>			
Shoulder	8/45 (17.8)	4/30 (13.3)	0.61
Cervical interspinous bursae	2/9 (22.2)	10/66 (15.5)	0.63
<b>Morning stiffness (n=11)</b>			
Shoulder	11/45 (24.4)	0/30 (0.0)	<b>0.002</b>
Sternoclavicular joints	7/33 (21.2)	4/42 (9.5)	0.20
Cervical interspinous bursae	3/9 (33.3)	8/66 (12.1)	0.12
<b>Pelvic girdle pain (n=42)</b>			
Hips	23/32 (71.8)	19/43 (44.2)	<b>0.02</b>
Lumbar interspinous bursae	18/29 (62.1)	24/46 (52.2)	0.40
Subtrochanteric bursae	11/20 (55.0)	31/55 (56.4)	0.92
Ischial tuberosities	10/19 (52.6)	32/58 (57.1)	0.73
Pubic symphysis	3/4 (75.0)	30/71 (54.9)	0.63
<b>Inflammatory low back pain (n=20)</b>			
Hips	10/32 (31.3)	10/43 (23.3)	0.44
Lumbar interspinous bursae	10/29 (34.5)	10/46 (21.7)	0.22
Ischial tuberosities	3/19 (15.8)	17/56 (30.4)	0.26
Subtrochanteric bursae	7/20 (35.0)	13/55 (23.6)	0.33
Pubic symphysis	3/4 (75.0)	17/71 (23.9)	0.06
<b>Diffuse lower limb pain (n=35)</b>			
Knees	16/33 (48.5)	19/42 (45.2)	0.78
Subtrochanteric bursae	8/20 (40.0)	27/55 (49.1)	0.49
Ischial tuberosities	9/19 (47.4)	26/56 (46.4)	0.94
Hips	15/32 (46.9)	20/43 (46.5)	0.98

**Conclusions:** In patients with PMR, the presence of shoulder girdle pain seems to correlate with  $^{18}\text{F}$ -FDG uptake in sternoclavicular joints, morning stiffness with  $^{18}\text{F}$ -FDG uptake in shoulders and pelvic girdle pain with  $^{18}\text{F}$ -FDG uptake in hips. No other significant correlations were found between any other symptom and  $^{18}\text{F}$ -FDG uptake.

**Disclosure of Interest:** None declared

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### SAT0650 MUSCULOSKELETAL ULTRASOUND IN FIRST DEGREE RELATIVES OF RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Preclinical phase of rheumatoid arthritis (RA) is characterised by a state of autoimmunity and inflammation. MSUS is known for its ability to detect subclinical synovitis, but changes in first degree relatives (FDR) are not yet defined.

**Objectives:** To investigate the presence of abnormal MSUS findings in FDR of RA who are free of clinical disease.

**Methods:** Study included 20 RA patients, and 25 of their FDR without evidence of arthritis. All were subjected to full history taking with special emphasis on joint symptoms, and joint examination. Measurements of ESR, CRP, RF and anti-CCP were performed in all and MSUS scan using the 7 joint ultrasonography (US7) score<sup>1</sup>

**Results:** Mean age in FDR 33.1±13.4 years, and in RA was 39.50±13.43 years with a mean disease duration of 11.95±8.36 years. All RA (100%) had symmetrical, polyarthralgia and/or arthritis, mostly involving small joints of hands and feet. 8/25 FDR (32%) had arthralgia that included different joints. While 17/25 FDR (68%) were asymptomatic. None of FDR had arthritis as it was an exclusion criteria. MSUS findings were detected in 16/20 (80%) RA and in 10/25 (40%) FDR. Of whom 3/10 FDR (12%) had arthralgia and 7/10 (28%) were asymptomatic. Synovitis was the commonest MSUS finding in RA (n=16, 80%), and in their FDR (n=10, 40%). Tenosynovitis was present in 5 (25%) RA and only one (4%) FDR. Erosions were detected in 9 (45%) of RA and one (4%) FDR in the 2nd MCP. In RA the wrist was most common joint to be involved on MSUS (n=14, 70%), followed by 2nd MCP and 2nd MTP joints in 11 (55%), 5th MTP joint in 8 (40%), 3rd MCP joint in 6 (30%), 2nd PIP joint in 4 (20%), with least involvement in the 3rd PIP joint in 3 (15%) of RA. In FDR the wrist was also the most commonly involved joint on MSUS and 2nd MTP joint in 6 (24%), followed by 2nd MCP joint in only 1 (4%). Whereas, the 3rd MCP, 2nd and 3rd PIPs and 5th MTP joints were spared.

US7 score in RA and FDR are shown in table 1. US7 erosion score correlated significantly with disease duration in RA. Anti-CCP significantly correlated with all parameters of US7 and RF with the tenosynovitis GS (grey scale) score. While, in FDR there was no statistical significant correlation between US7 score with any of the inflammatory or seromarkers.

**Abstract SAT0650 – Table 1.** US7 Joint score in RA and FDR

US7 score	RA (n=20)	FDR (n=25)	P
Synovitis GS	5.15±4.26	0.64±1.04	<0.001*
Synovitis PD	2.05±2.54	0.24±0.83	0.003*
Tenosynovitis GS	0.35±0.75	0.04±0.20	0.040*
Tenosynovitis PD	0.30±0.80	0.0±0.0	0.048*
Erosions	1.60±3.10	0.04±0.20	0.001*
Total score	9.45±7.21	0.96±2.01	<0.001*

Shown values are mean ±SD. p: p values for Mann Whitney test for comparing between the two groups\*. Statistically significant at p<0.05

**Conclusions:** This study confirms the presence of inflammatory synovial changes in FDR of RA who are free of clinical disease. This strengthens the concept of FDR as pre-RA. US7 score is a useful screening tool to identify subclinical synovitis in at-risk individuals. While in RA, US7 score is significantly correlated to disease duration and autoantibodies. More long term studies on FDR are needed for establishing the predictive value of abnormal MSUS findings for the development of persistent arthritis.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.2349

### SAT0651 CAROTID ULTRASOUND IN PATIENTS WITH ARTHRITIS: ¿IN WHICH PATIENTS DOES IT RE-STRATIFY CV RISK?

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**Objectives:** To explore in which patients with inflammatory rheumatic disease, the findings in a carotid ultrasound result in a change in cardiovascular (CV) risk stratification as compared to the CV risk measured with the SCORE index.

**Methods:** Longitudinal prospective study in patients included in a program geared at CV risk factor screening followed by optimisation of their treatment. Patients with rheumatoid arthritis (RA), spondyloarthritis (SpA) and psoriatic arthritis (PsA) were included in the program. In a nurse-led single-visit, the existence and adequate control of classic CV risk factors were recorded. SCORE index was calculated and then modified according to EULAR recommendations. CV risks was stratified according to European guidelines. A carotid ultrasound was performed in patients with a low, intermediate or high-risk stratification in order to assess intimal-media thickness (IMT) and plaques. If plaques were detected, CV risk was re-stratified to very high risk.

From this program, patients who had completed the baseline evaluation and the carotid ultrasound were selected. The characteristics of patients with findings in carotid ultrasound that allowed re-stratification to those without these findings were compared.

**Results:** A total of 181 patients have completed the baseline work-up, including the carotid ultrasound. 122 (67%) of the patients were women with a mean age of 55 (±11) years of age. Included patients had RA (n=96, 53%), SpA (n=37, 20%) or PsA (n=48, 27%).

A diagnosis of DM was performed in 19 (10%), hypertension in 78 (43%) and hypercholesterolemia in 92 (51%); 38 (21%) were active smokers and 63 (35%) were obese (BMI >30). Mean SCORE index (modified according to EULAR recommendations) was 2.4 (±1.7). Risk stratification before ultrasound was 145 (80%) patients with intermediate risk and 36 (20%) with high risk.

Carotid ultrasound imaging showed plaques in 43 patients (bilaterally in 14). In these, risk was re-stratified as very high risk. Overall, 11 patients showed a thickening of IMT; all presented plaques as well. Final risk stratification after including



the carotid ultrasound findings showed 110 patients with intermediate risk, 28 with high risk and 43 with a very high risk.

In table 1, the characteristics of the 43 patients whose carotid ultrasound findings resulted in a risk re-stratification vs the 138 with no risk modification.

	Risk modification due to pathologic carotid ultrasound (n=43)	No risk modification due to pathologic carotid ultrasound (n=138)
Sex (Woman)	32 (74%)	90 (65%)
Age (years)	58.1 (±9)	53.5 (±12)*
Disease	28 (65%)	68 (49%)
RA (n=96)	6 (14%)	31 (22%)
SpA (n=37)	9 (21%)	39 (28%)
PsA (n=48)		
DM	4 (9%)	15 (11%)
High blood pressure	24 (56%)	54 (39%)
Hypercholesterolemia	30 (70%)	59 (43%)*
Smoker	12 (28%)	26 (19%)
Obesity	31 (72%)	87 (63%)
Modified SCORE	2.7 (±1.6)	2.3 (±1.7)

\*p<0.05 between group comparison

**Conclusions:** Patients with risk modification due to carotid ultrasound findings were older and were more frequently hypercholesterolemic. Performing a carotid ultrasound in these patients seems to offer especially relevant information.

**Disclosure of Interest:** None declared

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SAT0652

#### STUDY OF NAIL UNIT WITH ULTRASONOGRAPHY IN SEVERAL RHEUMATOLOGICAL CONDITIONS: A CROSS SECTIONAL STUDY OF DISTAL INTERPHALANGEAL JOINT AND NAIL

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**Background:** The ultrasonography (US) is a feasible technique when you refer to the peripheral small joints and also to the nail.<sup>1</sup> DIP joints are not only affected by inflammatory disease and a more frequent condition is osteoarthritis (OA). The bone and synovial changes due to this condition are very similar to the ones of PSA especially regarding osteoproliferative lesions.

**Objectives:** The aim of our study was exploring through imaging the changes of nail and entheses of extensor tendon of the finger in inflammatory and degenerative conditions in order to find structural differences of nail and DIP.

**Methods:** This is an observational study on PSO, PSA, RA or OA patients. A control group of 50 healthy volunteers was used for comparison. Diagnosis was based on clinical or scientific criteria, such as CASPAR or EULAR/ACR were applicable. The study sample included 203 individual. The ultrasonographers were blind to clinical data and diagnosis of the patient. The ultrasound examination was done with a GE Logiq S8. The structural alterations of the plate were evaluated using a semiquantitative score for the magnitude of the alteration. The score provides values from 0 (no alteration) to 3 (severely altered). A semiquantitative approach was also used for evaluation of the power Doppler signal.

**Results:** The study sample was composed by 51 patients affected by PsA, 31 affected by PSO group, 37 subjects with RA, 34 with OA and 50 HC. The analysis of nail bed PDUS revealed an unusual trend for patients affected by OA who showed a prevalence of lesions of every grade but a lower rate of normal cases. The evaluation of the PDUS of the entheses revealed that patients affected by PsA have an increased rate of PDUS signal at the entheses of the extensor tendon. Considering nail plate HC showed a strong difference (p value<0.001) vs all groups except for patients affected by RA. Regarding nail bed thickness HC showed difference only if compared with PSA or OA group. P values are reported in table 1.

		PSO	PSA	RA	OA	HC
Nail plate Thickness	PSO	//	0.99	0.021	0.99	<0.001
	PSA	0.99	//	0.002	0.99	<0.001
	RA	0.021	0.002	//	0.06	0.06
	OA	0.99	0.99	0.06	//	<0.001
	HC	<0.001	<0.001	0.06	<0.001	//
Nail bed Thickness	PSO	//	0.99	0.003	<0.001	0.15
	PSA	0.99	//	<0.001	<0.001	0.002
	RA	0.003	<0.001	//	0.69	0.12
	OA	<0.001	<0.001	0.69	//	0.012
	HC	0.15	0.002	0.12	0.012	//

**Conclusions:** The data support the concept that nail entheses unit is in some way involved in different pathological conditions. No exclusive feature belongs only to one or another disease, but the data provided suggested that peculiar lesions might be found only in certain disease and in certain structures, like the entheses.

The US of the nail should be considered as one of the possible and promising approach in the study of these structures.

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SAT0653

#### RELATIONSHIP BETWEEN CARDIAC VALVULAR CALCIFICATION, CAROTID ATHEROSCLEROSIS, AND CORONARY CALCIFICATION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** The prevalence and relationship of VC with arterial atherosclerosis in patients with rheumatoid arthritis (RA) is under-investigated.

**Objectives:** investigate the prevalence of VC in patients with RA and its relationship with carotid atherosclerosis (CA) and coronary artery calcification (CAC).

**Methods:** Study population was consisted of 128 adult patients (65.6% women, age 55<sup>43</sup>;61 years) with RA according to ACR/EULAR criteria (disease duration 6<sup>5</sup>;18 month) with moderate/high RA activity (DAS28 5.3 [5.0; 6.1]). Arterial hypertension (AH) was found in 64%, ischaemic heart disease (IHD) – in 14%, dyslipidemia – in 54.7%, smoking – in 20.3%, diabetes mellitus type 2 – in 7%, myocardial infarction – in 1.6%, stroke – in 1.6%. Cardiac VC was evaluated by transthoracic echocardiography; CAC scoring was done with 32-row scanner by standard Agatston method; CA was evaluated with duplex ultrasound.

**Results:** Patients were divided on 3 groups depending on valve condition: normal (34.3%); leaves thickening (30.5%); VC (35.25%). The VC group consisted of isolated mitral VC – in 11%, isolated aortic VC – in 51%, calcification of both valve – in 38%. Mitral regurgitation (3 degree) was detected in 0.8% patient, mitral stenosis (mild) – 0.8%, aortic regurgitation (1 degree) – in 25%, aortic stenosis (mild) – in 0.8%. Age, BMI, SBP and frequency of AH, IHD, CA, CAC significant increased from 1 to 3 group (p<0.05). There was no significant difference in the sex, lipid levels, Rg-stage, RA duration and level of parameters of RA activity (DAS28, CRP, ESR) between investigated groups.

	Normal valve (n=44)	Thickening (n=39)	Calcification (n=45)
Age	39.5 <sup>29</sup> ;51	56.5 [51.5;62]	60 <sup>57</sup> ;67 *
BMI	23.4 [21.4;28.6]	26.3 [23.7;29.3]	27.2 <sup>25</sup> ;31 *
SBP	120 <sup>100</sup> ;130	120 <sup>110</sup> ;134	130 <sup>120</sup> ;140 *
AH	19 (43.2)	23 (59)	40 (88.9) *
IHD	1 (2.3)	6 (15.4)	11 (24.4) *
CA	12 (27.3)	30 (77)	39 (86.7) *
CAC	8 (18.2)	16 (41)	32 (71.1) *

Note: Data are expressed as median [25 percentile;75 percentile] for continuous variables and as a number (%) for the categorical variables. \* Difference for trend (p<0.05)

**Conclusions:** Among RA patients, more than half have a modified valve structure and in 1/3 of them VC. The presence of VC is correlated with traditional cardiovascular risk factors, but not with lipid levels, activity and severity of RA. The probability of CA and CAC presence is significantly increased when there is VC.

**Disclosure of Interest:** None declared

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SAT0654

#### ASSOCIATION OF PREDNISONE AND ANTIMALARIALS AND ECHOCARDIOGRAPHIC FINDINGS IN ASYMPTOMATIC CARDIOVASCULAR PATIENTS WITH SLE

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**Background:** Systemic lupus erythematosus (SLE) is an autoimmune inflammatory disease that presents with increase of cardiovascular risk. Echocardiogram can detect morphofunctional cardiac changes and predict clinical outcomes in patients with SLE<sup>1</sup>.

**Objectives:** To evaluate echocardiographic morphofunctional parameters in women with SLE, using conventional echocardiogram and to relate the echocardiographic findings to disease-related factors and therapeutics.

**Methods:** We have selected 51 women with SLE, without cardiovascular symptoms, under regular medical follow-up. Patients who had limitations to do echocardiography, smokers, and those with a creatinine level higher than 1.5 mg/dL were

excluded. 51 patients were divided into two groups, patients with SLEDAI <6 (n=30) and with SLEDAI ≥6 (n=21). They were submitted to clinical evaluation, laboratory tests and a traditional echocardiogram.

**Results:** Patients presented an average age of 34.5 years and average time of diagnosis of SLE of 7.2 years. In the comparison between groups, patients with SLEDAI ≥6 had a higher daily dose of prednisone (p=0.0016), more hospitalizations in the last 12 months (p=0.0173), and a higher cumulative dose of pulse therapy with methylprednisolone (p=0.008). Patients with SLEDAI <6 had a longer average time of antimalarials (AM) use (p=0.0309). Regarding the echocardiographic parameters, group with SLEDAI ≥6 presented greater left ventricular mass (LVM, p=0.0156), thickness of ventricular septum (p=0.0106) and left ventricular posterior wall (LVPW, p=0.0273). In multivariate analysis the LVM presented a positive association with age (p=0.0160), current daily dose of prednisone (p=0.0009) and time of AM use (p=0.0026),  $r^2$  0.3625. Regarding the thickness of the interventricular septum, there was a positive association with age (p<0.0001), current dose of prednisone (p<0.0001), SLEDAI (p=0.02), SLICC (p=0.0093) and pulse with methylprednisolone (p=0.0062), with  $r^2$  0.6983. There is a positive association of daily dose of prednisone with the parameters LVPW, LVM and septum thickness and AM was a predictor of greater LVM.

**Conclusions:** Several factors may contribute to cardiac morphofunctional changes in SLE. Ventricular hypertrophy in asymptomatic cardiovascular patients was not related to the use of prednisone or time of AM use in other studies, however these factors should be taken into account. There are no adequate study designs in literature to evaluate the effect of high doses of corticosteroids and time of AM use on cardiac morphology and function. AM induced cardiomyopathy is a rare, probably under-recognised, complication of prolonged AM treatment, it presents as a hypertrophic, restrictive cardiomyopathy with or without conduction abnormalities. Early recognition and drug withdrawal are critical with a survival rate of almost 55%. Longitudinal studies are needed to determine the effect of prednisone and AM use in subclinical echocardiographic findings to avoid unfavourable cardiovascular outcomes.

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**Disclosure of Interest:** None declared

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SAT0655

#### MYOSITIS AND FASCIITIS BY MAGNETIC RESONANCE IMAGING IN RECENT-ONSET POLYMYALGIA RHEUMATICA AND EFFECT OF TOCILIZUMAB THERAPY

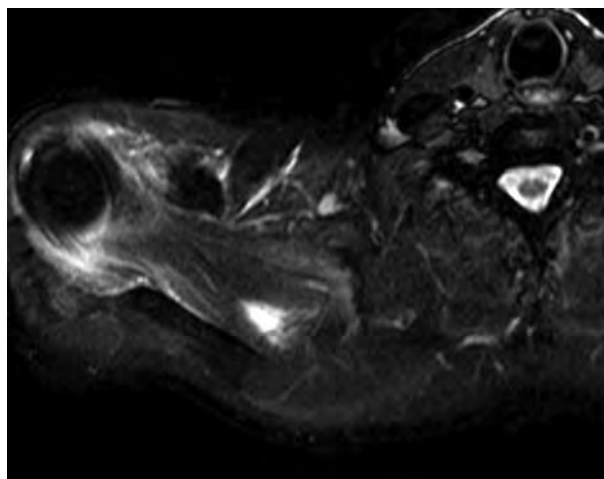
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**Background:** In everyday practice, myofascial lesions are not usually evaluated on MRIs obtained for patients with PMR.

**Objectives:** To assess the prevalence of myofascial inflammatory lesions visible by magnetic resonance imaging (MRI) and their changes after tocilizumab therapy in active polymyalgia rheumatica (PMR).

**Methods:** We conducted a post hoc analysis of data from the TENOR study of tocilizumab monotherapy in PMR.<sup>1</sup> The 18 patients each received tocilizumab injections at weeks 0, 4, and 8. The shoulder and pelvic girdles were assessed at baseline then at weeks 2 and 12 using T1- and T2-STIR-weighted MRI. Radiologists blinded to patient data assessed each muscle group for myositis and fasciitis on baseline, week-2, and week-12 MRIs. Reproducibility was estimated by having two radiologists assess the week-2 MRIs of 13 patients then computing the kappa coefficient.

**Results:** For myofascial lesion detection, intraobserver reproducibility was almost perfect ( $\kappa=0.890$ ) and interobserver reproducibility was substantial ( $\kappa=0.758$ ). At baseline, all patients had at least one inflammatory myofascial lesion (example on right shoulder fig 1); sites involved were the shoulder in 10 (71.4%) patients, hip in 13 (86.7%), ischial tuberosity in 9 (60.0%), and pubic symphysis in 12 (80.0%). Sites involved at week 12 were the shoulder in 8 (53.3%) patients, hip in 5 (33.3%), ischial tuberosity in 1, and pubic symphysis in 3 (20.0%). At week 12, of 103 muscle groups studied in all, 43 (41.7%) had no inflammatory lesions, compared to 33 at baseline (Mac Nemar; p<0.001) but some areas seemed to be more responsive to tocilizumab compared to other areas. Improvements were noted in 66 (64.1%) muscle groups, worsening in 2 (1.9%), no change in 35 (34.0%).



**Conclusions:** Myositis and fasciitis are common in recent-onset PMR and improve during tocilizumab therapy. They could be used for the diagnosis in routine practice and as criteria of outcome evaluation.

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**Disclosure of Interest:** J. P. Laporte: None declared, F. Garrigues: None declared, A. Huwart: None declared, S. Jousse-Joulin: None declared, T. Marhadour: None declared, D. Guellec: None declared, D. Cornec: None declared, V. Devauchelle-Pensec: None declared, A. Sarau: Grant/research support from: Chugai, Speakers bureau: Chugai

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SAT0656

#### CIRCULATING MIR-99B-5P IS A MARKER OF INFLAMMATION AND STRUCTURAL DAMAGE ON MRI IN EARLY RHEUMATOID ARTHRITIS

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**Background:** Expression of several miRNAs occurs in the plasma and synovial fluid of patients with established rheumatoid arthritis (RA). We found that microRNA-143-3 p (miR-143-3 p), miR-145-5 p, and miR-99b-5p expression was associated with greater erosion volume in early RA (ERA)<sup>EULAR 2018</sup>-abstract no 1980). Whether these miRNAs are associated with bone erosion and joint inflammation on magnetic resonance imaging (MRI) is unknown.

**Objectives:** To determine whether plasma cell-free circulating miRNAs are associated with (a) bone erosion and (b) inflammation severity on MRI in patients with ERA.

**Methods:** 66 ERA patients were recruited at presentation for this cross-sectional study. 60 of these 66 patients (90.9%) were treatment naïve. MRI of the most severely affected wrist was performed in all patients. The degree of bone damage (i.e. erosions), bone inflammation (osteitis) and soft tissue inflammation (synovitis/tenosynovitis) was scored on MRI (a) semi-quantitatively using the Rheumatoid Arthritis MRI score (RAMRIS) for scoring the severity of erosions, bone marrow oedema, synovitis and tenosynovitis; and (b) quantitatively by measuring synovial and tenosynovial volume (mm<sup>3</sup>). The three most dysregulated miRNAs (miR-143-3 p, miR-145-5 p, and miR-99b-5p) identified in our previous ERA study were validated by TaqMan<sup>®</sup> qRT-PCR in all patients.

**Results:** Expression of miR-99b-5p was higher in ERA patients with erosions (1.28±0.61) on MRI than those without erosions (0.23±0.43, p<0.05). Subdivided according to mean RAMRIS synovitis score (5.69), miR-99b-5p expression was higher in ERA patients with relatively more synovitis (0.75±1.24) on MRI than those with relatively less synovitis (0.34±1.14, p<0.05). Bone marrow oedema or tenosynovitis on MRI were not found to be associated with specific miRNA expression. Expression of miR-99b-5p did, however, correlate with synovial (r=0.443, p=0.018) and tenosynovial volume (r=0.423, p=0.025) on MRI. Linear regression analysis revealed miR-99b-5p expression to be independently associated with both increased synovial volume (B=15.65, 95% CI 3.42–27.89,

p=0.014) and increased tenosynovial volume (B=7.39, 95% CI 0.41~14.38, p=0.039) (Table).

Table 1 Univariate and multivariate analysis for factors associated with synovial volume and tenosynovitis volume at baseline in all ERA patients

Table Univariate and multivariate analysis for factors associated with synovial volume and tenosynovitis volume at baseline in all ERA patients

	Univariate			Multivariate		
	B	95%CI	P value	B	95%CI	P value
Age	0.79	0.09-1.50	0.026			
Sex	0.23	-0.043-0.51	0.098			
Dj	6.58	1.53-11.64	0.011			
DAS28-CRP	14.22	5.25-23.18	0.002			
miR-99b-5p	16.15	2.98-29.32	0.018	15.65	3.42-27.89	0.014

Dj: damage joint count; DAS 28: Disease Activity Score 28

	Univariate			Multivariate		
	B	95%CI	P value	B	95%CI	P value
Age	0.51	0.10-0.92	0.016			
Sex	0.47	-0.07-0.94	0.054			
Tj	1.07	0.044-2.10	0.042			
DAS28-CRP	5.86	0.42-11.30	0.035			
miR-99b-5p	7.36	-10.05-13.71	0.025	7.39	0.41-14.38	0.039

Tj: Tender joint count; DAS 28: Disease Activity Score 28

**Conclusions:** Increased cell-free circulating miR-99b-5p is associated with increased synovial and tenosynovial volume as well as more severe bone erosion in ERA patients at presentation. Whether it may serve as a biomarker for monitoring the progression of synovitis and damage would need to be addressed in prospective studies.

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**Disclosure of Interest:** None declared

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#### SAT0657 MICROWAVE RADIOMETRY-DERIVED THERMAL CHANGES OF SACROILIAC JOINTS AS A BIOMARKER OF SACROILIITIS IN PATIENTS WITH SPONDYLOARTHRITIS

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**Background:** Microwave Radiometry (MR) is a rapid, easy-to-perform, non-invasive method that detects in-depth tissue temperatures. In a proof-of-concept study we found that an increased knee joint temperature detected by MR reflects the presence of subclinical synovial inflammation in patients with rheumatoid arthritis.<sup>1</sup>

**Objectives:** To test the hypothesis that MR-derived increased temperature of sacroiliac (SI) joints is a biomarker of local inflammation in patients with axial spondyloarthritis (SpA) in a cross-sectional study.

**Methods:** Sixty patients with SpA (32 with ankylosing spondylitis, 24 with psoriatic arthritis, 4 with enteropathic arthritis) underwent clinical and laboratory assessments, magnetic resonance, X-ray imaging, and MR measurements of SI joints. All MR measurements were performed by a physician who was blinded to the clinical evaluations. Patients were classified as having active sacroiliitis (pain and/or tenderness and/or bone marrow oedema on magnetic resonance, n=23), inactive sacroiliitis (n=19), whereas signs/symptoms of a present/past SI joint involvement were absent in the remaining 18 patients. Twenty five age-matched healthy individuals served as controls. Three MR measurements were performed along each SI joint and a number was calculated for each patient denoting the difference ( $\Delta T$ ) in temperature between the warmest point in either SI joint and a control point, which was the iliac bone.

**Results:** A lower  $\Delta T$ , indicative of a warmer joint, was found in patients with either active or inactive sacroiliitis compared to patients without sacroiliitis [mean (SD)  $\Delta T$  of 0.1 (0.5) vs. 0.6 (0.5), respectively, p=0.001] or healthy controls [mean (SD)

$\Delta T$  of 0.60 (0.55), p=0.003]. A warmer SI joint was not significantly associated with the presence of local tenderness or pain, the patient visualised analogue pain scale for SI joints, the BASDAI score, the New York radiological grading of SI lesions, or C-reactive protein levels. Notably, all 20 patients with increased SI joint temperature ( $\Delta T < 0.05$ , which was the mean  $\Delta T$  value minus one SD in healthy controls) had either symptoms/signs of sacroiliitis or imaging confirmed sacroiliitis even in the absence of clinical findings. Receiver operating analysis showed that a  $\Delta T$  cut-off of 0.35 could discriminate with a sensitivity of 78% and specificity of 74% patients with sacroiliitis from those without, or from healthy controls (both p=0.001); sensitivity reached 100% for  $\Delta T$  values equal or lower than 0.05.

**Conclusions:** MR-derived increased in-depth temperature indicative of local inflammation of SI joints may serve as an additional diagnostic marker in axial SpA

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.6564

SAT0658

#### QUANTITATIVE ANALYSIS OF JOINT STRUCTURE BY HR-pQCT IN PATIENTS WITH RHEUMATOID ARTHRITIS: CORRELATION BETWEEN CARTILAGE LOSS AND BONE DETERIORATION

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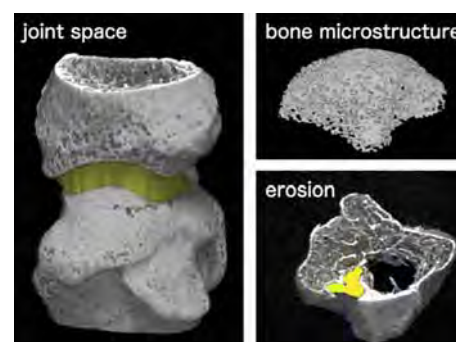
**Background:** HR-pQCT is a high-resolution CT dedicated to human extremities. It has been used for the study of rheumatoid arthritis (RA) in recent years, enabling quantitative analysis of bone erosion, bone microstructure, and joint space.

**Objectives:** The purpose of this study is to investigate a correlation between cartilage loss and bone deterioration (juxta-articular osteoporosis and erosion) in patients with RA by HR-pQCT.

**Methods:** Twenty patients with RA (70±8 years, 15 female, 5 male) participated in this study. The second and third MCP joints were scanned by second-generation HR-pQCT (XtremeCT II, Scanco Medical, Switzerland) at the voxel size of 61  $\mu\text{m}$ .

The following parameters were measured semiautomatically using dedicated software (TRI/3D-BON, Ratoc System Engineering, Tokyo) based on previous studies<sup>1-3</sup>. 1) Average joint space width (ave-JSW) of MCP joints, 2) bone microstructure of metacarpal head: volumetric bone mineral density (vBMD), trabecular thickness (Tb.Th), trabecular number (Tb.N), and structure model index (SMI), 3) total volume of erosions (ER-volume) on the metacarpal head.

**Results:** Ave-JSW of MCP joints was 1.47 (1.00-1.89) mm. vBMD of the metacarpal head was 131.4 (54.3-263.5)  $\text{mg}/\text{cm}^3$ , Tb.Th was 213.1 (166-329.3)  $\mu\text{m}$ , Tb.N was 0.95 (0.69-1.50)/mm, and SMI was 1.68 (0.65-2.52). The total number of erosions was 31, and an average number of erosions on each metacarpal head was 0.9 (0-4). Total ER-volume on the metacarpal head was 1.96 (0-16.7)  $\text{mm}^3$ . Ave-JSW had significant correlations with vBMD, SMI and ER-volume (R=0.37, -0.40, -0.42, p<0.05).



**Conclusions:** Cartilage loss was correlated with juxta-articular osteoporosis and bone erosion in RA patients. Quantitative evaluation of total joint structure (joint space, bone microstructure, and erosion) by HR-pQCT would be useful for the pathophysiological research and drug development of RA.

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SAT0659

### IS SYNOVIAL HYPERTROPHY WITHOUT DOPPLER ACTIVITY IN RHEUMATOID ARTHRITIS JOINTS SENSITIVE TO CHANGE? – RESULTS OF A LONGITUDINAL ULTRASOUND STUDY

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**Background:** Ultrasound (US) is used to assess diseases activity in rheumatoid arthritis (RA). Grey scale (GS) US shows the synovial hypertrophy (SH) and Doppler the amount of hyperemia which is believed to reflect disease activity. Some joints with SH may have no Doppler activity despite the use of high-end US equipment and these joints are generally believed to be inactive without potential to change.

**Objectives:** The aim was to investigate if joints with SH but no Doppler activity is sensitive to change during treatment with biological DMARD (bDMARD) in RA patients.

**Methods:** RA patients initiating or changing bDMARD treatment were included. US examination was performed at baseline, 3 and 6 months using Siemens Antares US equipment with Doppler settings for slow flow.

36 joints were evaluated at each visit. SH and Doppler activity was graded from 0–3 according to the US atlas by Hammer et al.<sup>(1)</sup> The GS score for SH in joints without Doppler activity was registered for the individual joints using GS SH  $\geq 1$  as threshold. The changes were compared to changes in SH in joints with Doppler activity.

**Results:** 151 patients (82.8% women, 80.1% seropositive for anti-CCP) were included, with a mean (SD) age 51.4 (13.2) years, disease duration 9.9 (7.9) years. At baseline, 50.7% used prednisolone (mean (SD) 5 mg (4.68)).

The patients had a mean (SD) baseline DAS28 of 4.5 (1.5). At baseline 23% of the joints had SH without Doppler activity and 23% of the joints had SH with Doppler activity.

Doppler-negative joints had overall lower grades of SH (mean 1.2) than Doppler-positive joints (mean 2.2) at baseline using GS SH  $>1$  as cut-off. The improvement in SH was similar in Doppler-positive and Doppler-negative joints but when adjusting for the baseline score of SH, Doppler-negative joints had a higher tendency towards decrease than Doppler-positive joints for all grades (3 months:  $p < 0.0001$ ; 6 months = 0.0006).

A weak correlation was found to changes in DAS 28(crp) (Doppler-negative joints: 0.27 ( $p = 0.001$ ) and 0.18 ( $p = 0.03$ ) at 3 and 6 months respectively – Doppler-positive joints: 0.25 ( $p = 0.004$ ) and 0.33 ( $p = 0.0002$ ) at 3 and 6 months respectively).

**Conclusions:** SH in joints without Doppler activity improves during bDMARD, i.e. is sensitive to change. Thus, SH without Doppler activity is not a sign of inactive disease. These findings document that both Doppler and SH should be evaluated when assessing disease activity by US.

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**Disclosure of Interest:** None declared

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SAT0660

### CLINICAL SIGNIFICANCE OF ANTI-RA33 AUTOANTIBODIES IN RHEUMATOID ARTHRITIS

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**Background:** Recently heterogeneous nuclear ribonucleoproteins (hnRNPs) were identified as antigenic targets for autoantibodies in RA. Autoantibodies to RNP B1, B2 and heterogeneous complex A2/b are the most studied and are referred to as "antigen RA33". Clinical value of anti-RA33 in RA continues to be studied, so the question is about the diagnostic and pathogenetic significance of these autoantibodies in patients with RA remains open.

**Objectives:** The aim of this study was to investigate the frequency of occurrence of anti – RA33y patients with RA and compare them with clinical manifestations and immunological parameters of disease.

**Methods:** The study included 139 patients with RA. The diagnosis was verified according to the classification criteria of ACR/<sup>EULAR 2010</sup> Autoantibodies to RNP B1 IgG was assessed in samples of blood serum by enzyme immunoassay (ELISA; Medipan AG, Germany). Anti-CCP, RF and antibodies to Sa-antigen (anti-Sa) was evaluated by ELISA according to the manufacturer's instructions (Euroimmun AG company, Germany). The results were expressed in relative units (U/ml). Statistical data processing was carried out using the software Statistica 7.0 (StatSoft, USA) and Medcalc 12.5.0.0 (USA), including standard methods of parametric and nonparametric analysis. Differences were considered significant at  $p < 0.05$ .

**Results:** In our cohort of patients with RA, the incidence rate of RF IgM was 96.02%, anti-CCP – 81.75%, anti-Sa – 69.88%, anti-RA33 – 35.97% of patients. For further analysis of the clinical significance of anti-RA33 patients were divided into 2 groups: anti-RA33 positive and anti-RA33negative.

Positive and negative for anti-RA33 patients did not differ ( $p > 0.05$ ) by key characteristics, such as age, gender, duration of disease, and indicators of disease activity (CRP levels, DAS28, SDAI, CDAI). In contrast to the data obtained Maslyansky A. L. and co-authors the correlation relationship between the levels of anti-RA33 and indicators of disease activity as well as duration of disease has not been established. At the same time seronegative for anti-RA33 patients demonstrated a higher frequency of extraarticular manifestations ( $p < 0.05$ ).

When analysing the frequency of occurrence of anti-CCP, RF IgM, anti-Sa and anti-RA33 autoantibodies, there were no differences between the groups of seropositive and seronegative for anti-RA33. Correlation relationship between the levels of the investigated autoantibodies is not established.

**Conclusions:** Thus anti-RA33 is a perspective independent biomarker of RA, which has its own potential. The possible pathogenic significance of anti-RA33 as a biomarker of a more favourable course of the RA should be considered.

To clarify the diagnostic and pathogenic value of anti-RA33 further research with a large sample size, comparison of immunological data with genetic factors, the results of other laboratory and instrumental studies, clinical manifestations of the disease are required. The obtained data will allow us to more thoroughly study the pathogenesis of RA and contribute to the search for new therapeutic options.

**Disclosure of Interest:** None declared

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SAT0661

### MEASUREMENT OF THE INTIMA MEDIA THICKNESS OF TEMPORAL AND AXILLARY ARTERIES IN SUBJECTS WITH DIFFERENT RISKS OF CARDIOVASCULAR DISEASE: AN ULTRASOUND STUDY

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**Background:** The "halo sign" is considered the well known qualitative ultrasound (US) finding for the diagnosis of giant cell arteritis (GCA). Recently, the measurement of the intima-media thickness (IMT) of temporal and axillary arteries has been proposed as a potential complementary US biomarker. A cut-off for IMT of 0.42, 0.29, 0.34 and 1.0 mm for superficial temporal arteries, parietal and frontal branches and axillary arteries, respectively, has been suggested. In fact, other conditions, such as atherosclerosis, may determine an increase of the IMT.

**Objectives:** To measure the IMT of the temporal and axillary arteries in subjects with different risks of cardiovascular (CV) disease and to investigate the prevalence of IMT values greater than the reference cut-off values.

**Methods:** Consecutive patients older than 50 years without signs or symptoms and without a previous history of GCA or polymyalgia rheumatica, were included. The European Guidelines of CV disease prevention were used to define different categories of CV risk. The subjects were divided in two groups: a first group made up of subjects with very high or high risk of CV disease and a second group made up of subjects with moderate or low risk of CV disease. The US examination was performed with a My Lab Twice (Esaote S.p.A. Genoa, Italy). The temporal arteries (superficial temporal arteries, parietal and frontal branches) were evaluated using a 18–22 MHz probe, whereas the axillary arteries were studied using a 6–18 MHz probe.

**Results:** Eight hundred and eight arteries were evaluated in 101 subjects (mean age 66.1 SD 8.5, 73.3% females). Thirty-one subjects (30.7%) were classified with very high risk of CV disease, 7 (6.9%) with high risk, 34 (33.7%) with moderate risk and 29 (28.7%) with low risk. The IMT of the superficial temporal and axillary arteries were significantly higher in the group made up of subjects with very high or high risk of CV disease than in the group made up of subjects with moderate or low risk of CV disease (0.21 SD 0.82 vs 0.19 SD 0.86  $p < 0.013$ ; 0.54 SD 0.17 vs 0.48 SD 0.10  $p < 0.20$ ). The value of the IMT was higher than the reference cut-off in 13 out of 808 (1.61%) of the studied arteries (2 superficial temporal artery, 6 parietal branch, 4 frontal branch and 1 axillary artery), in at least one artery in 10 out 101 patients (10.1%). Of these 10 patients, 8 (98%) were classified as having very high or high risk of CV disease.

**Conclusions:** These preliminary results suggest that an increased value of IMT may be observed in patients with very high or high risk of CV disease. However, the IMT value was higher than the reference cut-off only in a limited number of the studied arteries.

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#### SAT0662 SCREENING RESEARCH OF ULTRASONOGRAPHIC PERIPHERAL ARTHRITIS AND ENTHESITIS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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**Background:** Some patients with inflammatory bowel diseases (IBD) such as ulcerative colitis (UC) and Crohn's disease (CD) develop spondyloarthritis (SpA). Conventionally, the assessment of affected joint count in patients with SpA was relied for the detection of swelling and tenderness in the joints and entheses by clinical physical examination. To date, high quality ultrasonography (US) can detect inflammatory condition in the joint and entheses more sensitively than clinical assessment.

**Objectives:** The aim of this study was to research the utility of US screening for detection of peripheral arthritis in patients with IBD.

**Methods:** Total 42 patients including 27 patients with UC and 15 patients with CD were consecutively included. HI VISION Ascendus (HitachiAloka Medical, Tokyo, Japan) was used with an 18 MHz linear array transducer. US examination was performed in MCP, PIP, DIP and wrist joints in both hand. Greyscale (GS) and power Doppler (PD) US were scored on a 0–3 semiquantitative scale for each joint. Moreover, the US assessment of entheses was performed. Lateral epicondyle, triceps entheses, the proximal and distal patella tendon entheses, Achilles tendon and fascia plantaris tendon entheses was scanned in both GS and PD assessment. Abnormal findings of entheses was defined structure, thickness, bur-sitis, erosion, calcification in GS and power Doppler signal.

**Results:** In the joint clinical assessment, 12 patients with UC and 7 patients with CD had joint symptoms. US active synovitis (GS Grade $\geq$ 2 · PD Grade $\geq$ 1) was found in 8 patients with UC and 6 patients with CD. The concordance rate between clinical findings and US findings was relatively low in UC and high in CD patients. In the enthesial clinical assessment, 9 patients with UC and 7 patients with CD had tenderness in any entheses. Active enthesitis in US was found in 16 patients with UC and 8 patients with CD. The concordance rate between clinical findings and US findings was relatively high and subclinical enthesitis was also found in many patients.

	UC (n=27)	CD (n=15)
Male (%)	9 (33.3%)	7 (46.7%)
Age (years)	46.1 $\pm$ 14.2	39.4 $\pm$ 11.6
Height (cm)	161.2 $\pm$ 8.4	163.1 $\pm$ 5.8
Weight (kg)	56.4 $\pm$ 17.4	56.0 $\pm$ 9.16
BMI	21.3 $\pm$ 4.9	21.0 $\pm$ 3.0
Duration of IBD (years)	13.3 $\pm$ 12.5	12.3 $\pm$ 9.7
Clinical peripheral joint symptom	12 (44.4%)	7 (46.7%)
Active US synovitis (GS $\geq$ 2, PD $\geq$ 1)	8 (29.6%)	6 (40.0%)
Clinical enthesial symptom	9 (33.3%)	7 (46.7%)
US enthesitis (any pathological findings)	16 (59.3%)	8 (53.3%)
Inflammatory back pain	12 (44.4%)	9 (60.0%)

**Conclusions:** The peripheral arthritis and enthesitis findings in patients with IBD was compared between clinical and US examination. The prevalence rate of sub-clinical synovitis was not high, thus US screening might not be useful in patients with IBD without arthritis symptom. However, the subclinical enthesitis was found in patients without any enthesial symptoms. US screening might be useful to detect subclinical enthesitis than clinical examination in patients with IBD.

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**Disclosure of Interest:** None declared

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#### SAT0663 A NEW OPERATOR INDEPENDENT AUTOMATIC TOOL FOR ACCURATE IDENTIFICATION OF VERTEBRAL FRAGILITY FRACTURES

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**Background:** Osteoporosis is a systemic skeletal disease characterised by a compromised bone resistance that predisposes a subject to an increased risk of fracture. In particular, vertebral fractures are the most common of all osteoporotic fractures. A common clinically-used method for vertebral fracture detection is vertebral morphometry, which is based on measurements of front (Ha), middle (Hm), and rear (Hp) heights of vertebral bodies in radiographic images. This method is quantitative and does not require specific operator skills, but its actual accuracy is affected by errors made during the time-consuming manual measurements.

**Objectives:** In this work we propose a fully automatic algorithm for morphometric measurement, whose final goal is to reduce errors due to manual and semi-automatic processes. Our automatic method identifies the vertebrae and their edges. Then, the algorithm measures the characteristic vertebra heights (Ha, Hm, Hp) and determines possible vertebral deformities.

**Methods:** The vertebral morphometry uses lateral X-ray images and it is based on height measurements of vertebral bodies:

$$Hp = ||P1 - P2||_2,$$

$$Ha = ||A1 - A2||_2,$$

$$Hm = ||M1 - M2||_2.$$

**Where:** Pi: rear vertebral corners;

Mi: middle vertebral points;

Ai: front vertebral corners.

The vertebral deformities can be determined as follows:

biconcave deformity:  $Hm/Hp < 0.80$ , crushing deformity:  $Hp/Hp(\pm 1) < 0.80$ , wedge deformity:  $Ha/Hp < 0.80$ .

The main problem in implementing our fully automatic algorithm was the correct placement of the six reference points for each detected vertebra. Our approach first combined literature-reported methods for the identification of vertebrae in X-Ray images, subsequent emphasise the vertebral borders. The four corners of the vertebra (Pi and Ai) were localised on the borders detected vertebra. While, the middle points Mi were positioned at equal distance from Pi and Ai.

**Results:** The performance tests were based on the comparison between the results coming from our automatic approach and those obtained from the manual measurements by an experienced radiologist. We analysed 100 conventional lateral radiographs. The following metrics were used: sensitivity and specificity in vertebra detection; errors in the localization of characteristic points and in the measurement of diagnostic parameters; correlation between manual and automatic measurements. The results of our method showed a sensitivity of 90.8% and a specificity of 99.0%. Average errors in the localisation of vertebral characteristic points were always smaller than 3 mm. Bland-Altman analysis documented a mean error in automatic measurements of diagnostic ratios of 0.01  $\pm$  0.15 (bias  $\pm$  2 SDs), while Pearson's correlation coefficient resulted  $r=0.71$  ( $p < 0.001$ ).

**Conclusions:** Obtained results of our method compared to the results obtained by a trained radiologist showed an acceptable low error rate, a very good performance in vertebra detection and the same diagnosis (normal, biconcave deformity, crushing deformity, and wedge deformity). Overall, the adopted method has a strong potential for an effective employment in clinical routine for fast and accurate diagnosis of vertebral fractures.

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**Disclosure of Interest:** None declared

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**SAT0664** **CARTILAGE DAMAGE QUANTITATIVELY ASSESSED BY MRI USING T2 MAPPING IN CCP-POSITIVE RA PATIENTS**

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**Background:** T2 mapping is a non-invasive quantitative MRI approach which reflects cartilage hydration and collagen integrity without using contrast enhancement. It is a sensitive tool to determine cartilage damage and is currently spreading into broader clinical application.<sup>1</sup>

**Objectives:** This study aimed to analyse biochemical changes in cartilage of Metacarpophalangeal (MCP) joints in patients with rheumatoid arthritis (RA) using T2 mapping in a 3 T MRI setting.

**Methods:** Thirty RA patients fulfilling the 2010 ACR/EULAR criteria were recruited. Image acquisition was performed using two surface coils in a 3 T MRI whole body scanner (VERIO; SIEMENS Healthcare).<sup>2</sup> We obtained high-resolution images of the 2nd and 3rd MCP joint. T2 maps were calculated using a pixel-wise, mono-exponential, non-negative least-squares-fit analysis. Region-of-interest (ROI) analysis was performed by dividing the cartilage into medial, central and lateral phalangeal (med, cent, lat P) and metacarpal (MC) area. ACPA positive patients were compared to ACPA negative patients. Statistical evaluation was performed by means of univariate ANOVA testing with random factors. A p-value < 0.05 was considered statistically significant. The study protocol was approved by the local ethics commission. Written informed consent was obtained from all patients

**Results:** Fourteen ACPA positive (3 male/11 female) and 16 ACPA negative patients (6 male/10 female) were included. Mean age, sex distribution and disease duration were comparable (age: 49.0±15.1 years (ACPA+) vs. 56.1±10.9 years (ACPA-), t=1.494, p=0.146; sex distribution:  $\chi^2$  (1)=0.918, p=0.338, disease duration: 7.9±7.3 years (ACPA+) vs. 3.9±3.8 years (ACPA-), U=69.0, Z=-1.799, p=0.072).

T2 values were significantly higher in the majority of the ROIs in ACPA-positive (+) RA patients compared to ACPA negative (-) patients with a statistical significance in five of the six ROIs.

T2 values in ms: MC med (+) 41.3±15.3 vs. (-) 29.6±7.4 p=0.010, cent (+) 43.8±14.6 vs. (-) 28.4±10.9, p=0.001, lat (+) 45.6±13.8 vs. (-) 32.0±8.6, p=0.008.

P: med (+) 30.3±14.6 vs. (-) 25.7±14.0, p=0.169, cent (+) 29.9±13.0 vs. (-) 22.5±10.1, p=0.014, lat (+) 37.0±15.9 vs. (-) 28.8±12.6, p=0.039.

**Conclusions:** T2 mapping is a clinically feasible non-invasive MR tool for cartilage evaluation of RA patients' MC joints. ACPA positive RA patients showed significantly increased T2 values compared to ACPA negative patients reflecting a more severe cartilage alteration despite comparable disease duration.

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**SAT0665** **SYNOVITIS AS A PREDICTOR OF EROSIONS IN THE HAND OSTEOARTHRITIS**

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**Background:** The formation of bone erosions in hand osteoarthritis (HOA) is the result of the association of destructive and inflammatory changes in the joint and leads to a more aggressive course of the disease. X-ray examination assesses destructive bone changes, but there is no possibility to assess the condition of periarticular tissues and inflammatory changes objectively. Visualisation of both

erosions and synovitis is possible during ultrasound examination of the hands. On the basis of this results it is possible to predict the further development of the disease.

**Objectives:** To determine the risk of erosion appearance and the features of progression in patients with hand osteoarthritis in a prospective study.

**Methods:** The study included 45 women which were 45–75 years old with the diagnosis of HOA, defined by criteria of the American College of Rheumatologists (ACR). 22 joints were examined at each patient by ultrasound: distal interphalangeal joints (DIP), proximal interphalangeal joints (PIP), joints of the thumb and 1 st carpo-metacarpal joint (1 st CMC). Ultrasound examination included multiplane gray-scale investigation of the listed above groups of joints. The presence and severity of synovial hypertrophy and effusion followed by evaluation of the degree of synovitis was determined in the B-mode; the quantity and the sizes of osteophytes and bone erosions were evaluated in a similar way. The vascularisation of synovial hypertrophy was estimated in the power Doppler ultrasound. The study was started in 2013. In 3 years the study was repeated. The results were processed with STATISTICA 10.0 software (StatSoft Inc. USA) using the methods of nonparametric statistics. For the description of communication of qualitative signs we used coefficient "odds ratio" OR and  $\chi^2$ . The results were recognised statistically reliable at value p < 0.05.

**Results:** The total number of hand joints was evaluated using ultrasound 990. In the primary examination 391 joints had synovitis, 46 joints had synovitis and erosion. In 3 years the number of joints with synovitis and the number of joints with synovitis and erosion increased up to 443 and 73 respectively. In 2016 among 73 joints with synovitis and erosion, 40 joints were with erosion against the background of synovitis 3 years ago, and only in the 8 joints erosion were revealed where was no synovitis. Thus the frequency of erosion detection in hand joints at repeated examination was higher in the cases the synovitis was detected at primary examination:  $\chi^2$  2=16.38 p=0.0001; OR 4.373, CI 95% 2.01–9.47.

**Conclusions:** The synovitis in hand joints is a prognostic adverse factor of erosions appearance and transformation in the erosive subtype of osteoarthritis. The possibility one-time visualisation of inflammatory and destructive changes allows using ultrasound investigation at primary and differential diagnostics, and dynamic evaluation.

**Disclosure of Interest:** None declared

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**SAT0666** **INFLAMMATION BEYOND CLINICAL REMISSION: ULTRASOUND AS A TOOL TO GUIDE US TO REMISSION**

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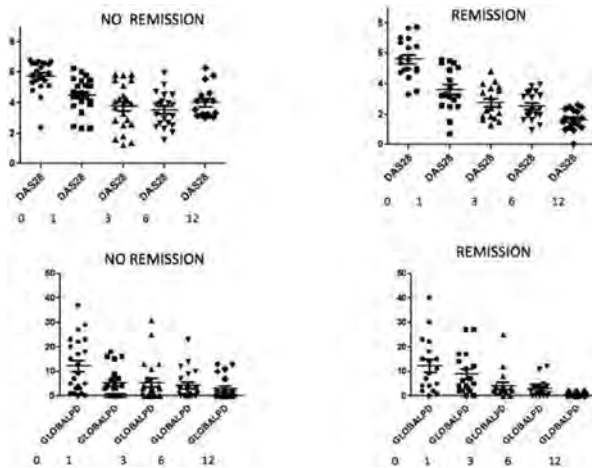
**Background:** Among patients with RA in remission, subclinical synovitis (SS) has a prevalence of 45% and is associated with an increased risk of clinical relapse and progression to structural damage. US is a sensitive and accessible tool for evaluating SS<sup>1,2,3</sup>.

**Objectives:** To analyse US as a tool for evaluating SS in RA patients treated with tocilizumab (TCZ), in order to assess remission, and from there on propose therapeutic tapering.

**Methods:** Multicenter, 1 year follow up study in 45 patients with RA treated with TCZ. The project was approved by Ethics Committees and all the patients gave their informed consent. At each visit: DAS28, SDAI, CDAI, mHAQ, US grey scale (GS) and Power Doppler (PD) parameters for 32 joints (J) and 28 tendons (T), with a semiquantitative scale from 0–3 points. A quantitative index was obtained for J and T in GS and PD and overall (EG + PD) for each patient/visit. SS was considered as the presence of synovitis with PD(+) ≥ 2. Our intra and interobserver kappa index was 0.8.

**Results:** A significant reduction of all clinical indexes and US variables was observed in all patients. Patients were divided into two groups: remission (R) and no remission (NR) according to whether they achieved DAS28 ≤ 2.6 at 12 months. Group R achieved DAS28 ≤ 2.6 after mo 3, whereas US showed SS (GS+, PD > 2) until mo 12. The final overall PD value in the R group was 0.6 (± 0.9).





**Conclusions:** A significant number of patients achieve clinical remission within a few months of starting TCZ. The R group, achieved a good EULAR response since mo 3; a progressive improvement in PD, persisted until mo 12. We consider that these findings refer to SS. From our data we consider that dose tapering should not be initiated until at least 9 months from the start of remission.

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#### SAT0667 IMPLEMENTATION AND ROLE OF MODERN MUSCULOSKELETAL IMAGING IN RHEUMATOLOGICAL PRACTICE IN EUROPE

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**Background:** Modern non-X-ray imaging methods are increasingly utilised by rheumatologists though the uptake and use of these techniques has developed very differently across Europe and there is limited data on their present impact in rheumatology for individual countries.

**Objectives:** To document the current implementation, role and training in modern musculoskeletal imaging techniques: musculoskeletal ultrasound (MSUS), magnetic resonance imaging (MRI), computed tomography (CT), and positron emission tomography (PET) among rheumatologists in the member countries of the European League Against Rheumatism (EULAR).

**Methods:** A EULAR Taskforce comprised of 9 rheumatologist experts in imaging developed English-language questionnaires for each imaging modality (CT, MRI, MSUS, PET) which were sent out to: national rheumatology societies of EULAR, national societies of the European Federation of Societies for Ultrasound in Medicine and Biology, the European Society for Magnetic Resonance Ultrasound in Medicine and Biology, as well as identified experts in the given modalities involved in research and/or training. The surveys were distributed via an online survey tool (SurveyMonkey). Simple descriptive and summary statistics were calculated from the responses.

**Results:** A total of 205 out of 395 experts replied to the surveys. More than 90% of MSUS experts had an MSUS unit in their department. The majority of responders reported having easy access to MRI, CT or PET (56%, 78% and 50% respectively). Suspicion of rheumatoid arthritis and peripheral spondyloarthritis were the main clinical indications for performing MSUS for diagnostic purposes. Suspicion of sacroiliitis and degenerative spine disease were the most common indications to perform MRI or CT for diagnostic purposes, while PET was mainly performed to

diagnose large vessel vasculitis and investigation of fever of unknown origin. When asked about the percentage of rheumatologists performing MSUS in their country 37% of experts reported less than 20%, 33% reported values between 20%–40% and 24% reported more than 40% (6%: unknown). The overwhelming majority (99%) of experts were certified in MSUS, while only 22% and 26% of experts in MRI and CT were certified in their techniques. Seventy-seven percent of responders reported that their national rheumatology societies organise MSUS courses, while courses in MRI or CT organised by the national rheumatology societies were less commonly reported (38% and 16% respectively).

**Conclusions:** Rheumatologists in Europe utilise modern imaging techniques, however access among the techniques and training offered is varied.

**Disclosure of Interest:** None declared

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#### SAT0668 ARTICULAR INVOLVEMENT IN CHRONIC HEPATITIS C INFECTION – A PRELIMINARY ULTRASOUND STUDY

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**Background:** Chronic hepatitis C is a public health issue. Extra-hepatic manifestations of this infection also include articular involvement, that sometimes mimics rheumatoid arthritis.

**Objectives:** Evaluation of potential articular involvement in patients diagnosed with chronic hepatitis C infection and possible correlations with biological abnormalities.

**Methods:** We evaluated 31 patients with chronic hepatitis C infection, using ultrasound (US) examination of both wrists and the second and fifth interphalangeal joints of the fingers. Then, we looked for possible correlations with various laboratory findings.

**Results:** 29% of patients were symptomatic (pain) at the time of the US examination.

10% of our patients had tenosynovitis of the extensor tendons, another 10% had active synovial hypertrophy (Doppler positive), 31.14% had inactive synovial hypertrophy, 20.9% had erosions and in 20% of them the US examination of the above mentioned joints was normal.

61.29% of patients having US abnormalities, where rheumatoid factor positive.

All patients with erosions and inactive synovial hypertrophy, 83.3% of those with active synovial hypertrophy and 67% of those with tenosynovitis where cryoglobulins positive.

We found low levels of C3 fraction of complement in 92.3 patients with erosions, 83.3 patients with active synovial hypertrophy, 84.2 patients with inactive synovial hypertrophy and 50% of patients with tenosynovitis.

In 85.7% of patients with active synovial hypertrophy, and 53.8% of patients with erosions, the C-reactive protein (CRP) levels were elevated.

No patient was diagnosed as also having rheumatoid arthritis

**Conclusions:** Even in asymptomatic patients with chronic hepatitis C infection, US examination of the wrists and of the second and fifth interphalangeal joints may reveal abnormalities. Certain types of these are probably correlated with the presence of cryoglobulins and possibly associated with CRP levels, C3 levels and rheumatoid factors positivity.

Further studies are needed to verify our finding

**Disclosure of Interest:** None declared

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#### SAT0669 99mTc-HDP SPECT/CT – A NEW METHOD IN EARLY DIAGNOSIS OF SACROILEITIS

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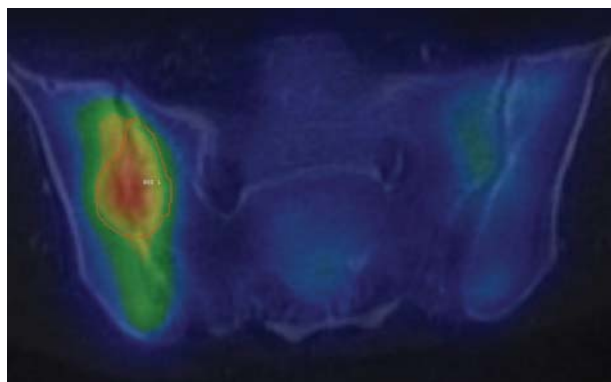
**Background:** 99Tc hydroxyl-diphosphonate SPECT-CT (HDP SPECT-CT) is a hybrid imaging technology, which is a new modality in the examination of the sacroiliac joint. It is a high resolution, low dose structural computer tomography scan fused with a functional metabolism recording. Our aim was to investigate whether it is comparable in sensitivity with MRI, to analyse quantitatively the radioisotope uptake, to assess its potential in the assessment of inflammatory activity, and in the diagnosis of spondylarthritis (SpA).

**Objectives:** Seventeen patients (9 women, 8 men, mean age 35 years) were involved into the study from July 2016. The patients were selected according the following clinical features: inflammatory type low back pain raising the suspicion of axial SpA,<sup>17</sup> elevated CRP level,<sup>6</sup> HLA-B27 positivity,<sup>8</sup> associated oligo- or

polyarthritis,<sup>5</sup> dactylitis,<sup>1</sup> enthesitis,<sup>1</sup> psoriasis,<sup>1</sup> uveitis<sup>1</sup> and inflammatory bowel disease.<sup>1</sup> All patients were therapeutic-naïve for glucocorticosteroids, DMARDs or TNF- $\alpha$  inhibitors.

**Methods:** First, we performed examination of the sacroiliac joint with X-ray, to exclude those patients, who already had radiographic lesions. Then an MRI was performed in the following sequences: T2-weighted STIR for the bone marrow oedema (BME) and T1-weighted sequence for the fat metaplasia (FM). The HDP SPECT/CT was used within one week to examine the sacroiliac joint. Thereafter, the MRI images were fused with HDP SPECT/CT images. On the MRI images the BME (active lesion) and FM (chronic lesion), on the CT scans the sclerotic lesions (SCL, chronic lesion) were drawn manually as volume of interest (VOI). Uninvolved cortical areas were drawn on the different modality slices as reference region (ref). Then, we determined the isotope (99mTc-labelled HDP) uptake of the different lesions and areas.

**Results:** Four active sacroileitis and five chronic sacroileitis without active lesions were diagnosed according to the MRI results. On the other 8 patient's sacroiliac joints images (MRI, scintigraphy, CT scans), no inflammation-related lesions were observed. The MRI and HDP SPECT-CT findings were 100% concordant. The isotope uptake of BME was the highest, the radioisotope uptake of sclerotic lesions was moderate, whereas the isotope uptake of FM lesions was not different from the HDP uptake of reference regions.



**Conclusions:** According to the initial results, the different MRI lesions have different isotope uptake, which suggests, that the HDP SPECT/CT can distinguish the early and chronic stage of axial SpA from chronic lesions. Thank to whole body imaging technique we can have further information about disease activity and extent. The presented data are the first of our prospective study, and examinations of new patients are still in progress and we plan to investigate our SpA patients in remission to explore the utility of this new method in subclinical activity assessment. We also plan to investigate the corner lesions of the spine to find other potential uses of the HDP SPECT-CT imaging in SpA.

**Disclosure of Interest:** None declared

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#### SAT0670 DYNAMIC THIOL/DISULFIDE HOMEOSTASIS AS A NOVEL OXIDATIVE MARKER IN BEHÇET'S DISEASE

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**Background:** Behçet's disease (BD) is a relapsing systemic inflammatory disorder of unknown etiology.<sup>1</sup>

**Objectives:** In this study, we aimed to evaluate the relationship between the thiol-disulfide balance and disease activity and organ involvement in BD.

**Methods:** One hundred fifty (150) patients with BD and 100 age-gender matched healthy controls were included in the study. Disease activity was assessed with the BD Current Activity Form (BDCAF) score. Serum levels of native thiol (NT), total thiol (TT), and disulfide were measured and the disulfide/native thiol, disulfide/total thiol and native thiol/total thiol levels were calculated for the patient and control groups.

**Results:** NT, TT, NT/TT values of the BD patients were significantly lower than those of the control group. The disulfide/NT, disulfide/TT values of BD patients were higher compared to the control group and the disulfide value of the BD group was slightly higher compared to the control group (table 1). No correlation was determined between thiol levels and disease activity and organ involvement in BD.

**Abstract SAT0670 – Table 1.** Laboratory results of the BD and the control group

	BD	HC	p
<b>Native Thiol (SH)(<math>\mu</math>mol/l)</b>	357.93 $\pm$ 76.65	453.01 $\pm$ 60.8	<b>0.000*</b>
<b>Total Thiol (<math>\mu</math>mol/l)</b>	398.57 $\pm$ 78.33	490.29 $\pm$ 58.48	<b>0.000*</b>
<b>Disulfide (<math>\mu</math>mol/l) (SS)</b>	20.32 $\pm$ 8.19	18.64 $\pm$ 7.87	<b>0.109</b>
<b>Disulfide/native thiol x100</b>	5.93 $\pm$ 2.76	4.25 $\pm$ 1.99	<b>0.000*</b>
<b>Disulfide/total thiol x100</b>	5.2 $\pm$ 2.13	3.86 $\pm$ 1.69	<b>0.000*</b>
<b>Native thiol/total thiol x100</b>	89.6 $\pm$ 4.26	92.28 $\pm$ 3.38	<b>0.000*</b>

\*p<0,05

**Conclusions:** In patients with Behçet's disease, the dynamic thiol-disulfide homeostasis balance shifted towards disulfide formation due to thiol oxidation. It may be used as a novel marker in BD because it is easy, practical, fully automated and relatively inexpensive.

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#### SAT0671 INITIAL DEVELOPMENT OF A WHOLE-BODY MAGNETIC RESONANCE IMAGING INFLAMMATION INDEX FOR ACTIVE DISEASE OF PERIPHERAL JOINTS AND ENTHESES IN PATIENTS WITH INFLAMMATORY ARTHRITIS

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**Background:** Magnetic resonance imaging (MRI) allows objective assessment of inflammation in peripheral joints and entheses. MRI scoring systems have until now focused on assessing specific parts of the musculoskeletal system in detail, e.g. the Rheumatoid Arthritis MRI Scoring System (RAMRIS), which is applied to wrist and metacarpophalangeal joints and adjacent tendon sheaths. The interest in a whole-body MRI approach is growing as modern MRI scanners now permit whole-body scanning within an acceptable time frame, and future improvements in MRI hardware and pulse sequences are expected to improve scan time and image resolution further.

**Objectives:** To develop a whole-body MRI scoring system for inflammation of peripheral joints and entheses and to investigate its feasibility and reliability.

**Methods:** Definitions of the key pathologies and locations for assessment have been agreed upon in the OMERACT MRI Working Group<sup>1</sup>. In a first round in June 2017, 9 readers (AJM/DG/FG/IE/MØ/PB/SJP/SK/WPM) scored MR images of 2 patients with spondyloarthritis using a draft web-based scoring system. Results were discussed and the scoring system was slightly modified. Hereafter, in a second round in October 2017, 14 MRI readers (3 musculoskeletal radiologist (IE/JLJ/RGL) and 11 rheumatologists with varying exposure to MRI (AJM/DG/FG/MS/MØ/PB/RP/SJP/SK/VF/WPM), scored 5 similar patients by the modified scoring system. Using a semiquantitative scale 0–3 (none/mild/moderate/severe), synovitis and osteitis were scored separately for 83 joints, and soft tissue inflammation and osteitis were scored separately for 33 entheses. Discrepancies between readers were discussed during an online meeting to obtain consensus, to train inexperienced readers, and to identify potential pitfalls when applying the scoring system.

**Results:** Inter-reader reliability was overall moderate for joint scores and poor for enthesis scores; however, among the 3 musculoskeletal radiologists, enthesis scores were as reliable as joint scores (Table). Reliability did not improve between the first and second round, possibly because patients with several very conspicuous inflammatory lesions were selected as cases in the first round.

**Abstract SAT0671 – Table 1.** Inter-reader reliability of scoring inflammation of peripheral joints and entheses (Cohen's kappa with squared weights for individual scores, ICC(3,1), agreement, for sum scores). All values are median (IQR; range) of all reader pairs (36 reader pairs for 9 readers, 91 reader pairs for 14 readers, 3 reader pairs for 3 readers [values for 3 reader pairs provided]).

	Kappa for osteitis scores (joints)	Kappa for synovitis scores (joints)	Kappa for osteitis scores (entheses)	Kappa for soft tissue inflamm. (entheses)	Kappa for all sites combined	ICC
First round (9 readers)	0.86 (0.81-0.90; 0.67-0.98)	0.63 (0.43-0.84; 0.26-0.94)	0.51 (0.27-0.63; 0.03-0.84)	0.36 (0.17-0.74; -0.08-0.92)	0.67 (0.62-0.75; 0.47-0.90)	0.64 (0.28-0.89; -0.26-1.00)
Second round (9 readers that had participated in first round)	0.61 (0.52-0.67; 0.36-0.80)	0.66 (0.61-0.70; 0.53-0.82)	0.33 (0.26-0.42; 0.02-0.69)	0.21 (0.12-0.31; -0.01-0.62)	0.53 (0.50-0.58; 0.42-0.70)	0.68 (0.60-0.82; 0.47-0.99)
Second round (all 14 readers)	0.48 (0.36-0.60; 0.10-0.80)	0.57 (0.45-0.66; 0.24-0.82)	0.32 (0.18-0.44; -0.06-0.80)	0.22 (0.12-0.35; -0.06-0.62)	0.47 (0.40-0.54; 0.25-0.72)	0.60 (0.30-0.75; -0.02-0.99)
Second round (3 musculoskeletal radiologists)	0.50 / 0.32 / 0.26	0.68 / 0.58 / 0.54	0.53 / 0.67 / 0.68	0.51 / 0.58 / 0.45	0.57 / 0.54 / 0.49	0.70 / 0.52 / 0.23

**Conclusions:** It is feasible to perform online multi-reader scoring exercises of whole-body MRI using a web-based scoring interface. MRI readers need to be further trained and calibrated in the semiquantitative scoring approach used to increase inter-reader reliability.

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**Disclosure of Interest:** None declared

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#### SAT0672 IS ULTRASOUND REMISSION ACHIEVABLE IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS?

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**Background:** In rheumatoid arthritis (RA) the "window of opportunity" has a crucial role for better long-term outcomes.<sup>1</sup> The ACR/EULAR remission criteria for RA are mostly represented by clinical parameters, while ultrasound (US) is not included.<sup>2</sup> However, in early diagnosed and early treated patients, who fulfil the remission criteria, residual US modifications can be identified.<sup>3</sup>

**Objectives:** The aim of this study was to investigate whether significant US-detectable differences between early RA (ERA) patients treated for one year and healthy controls (HC) are present.

**Methods:** We enrolled in this cross-sectional study consecutive patients with ERA at 1 year after having initiated RA disease-modifying (DMARD) therapy and who had received treatment following RA recommendations. Only patients who had fulfilled EULAR/ACR 2010 criteria for RA<sup>4</sup> and with symptoms duration of less than 1 year at treatment initiation were included. US exams were performed in 10 joints bilaterally (wrist, MCP II-V) by using both gray-scale and Doppler for evaluating synovitis was graded according to a semi-quantitative 4-point scale (0–3). A total US score for synovitis was calculated by adding the values recorded at each joint site. The presence of erosions was also recorded. Finally, US results obtained in patients were compared to those detected in HC.

**Results:** 84 subjects were enrolled – 45 ERA patients and 39 HC. In ERA patients the mean duration of symptoms prior to diagnosis was 3.5±3.5 months. The demographic, clinical and US data are reported in table 1.

**Abstract SAT0672 – Table 1.** Demographic, clinical and US data for ERA patients and HC [n (%), mean±SD or median (IQR)]

Parameters	ERA (n=45)	HC (n=39)	p
Gender (Female)	28 (62.2%)	25 (64.1%)	0.859
Age	56.16±19.91	46.59 ±12.93	0.003
VAS pain	19 (10.25–30)	0 (0–2)	<0.001
US score	4 (1.5–6.5)	1 (0–3)	<0.001
Erosions	23 (51.11%)	0 (0%)	<0.001

As expected, the values of visual analogue scale (VAS) for pain and of the total US score and the incidence of erosions were significantly higher in ERA patients than in HC. The values of the US score correlated with the presence of erosions ( $r_s=0.427$ ,  $p<0.001$ ) as well as with the values of acute phase reactants (CRP:  $r_s=0.539$ ,  $p=0.412$  and ESR:  $r_s=0.412$ ,  $p=0.005$ ), VAS of disease activity reported by patients ( $r_s=0.473$ ,  $p<0.001$ ) and physician ( $r_s=0.412$ ,  $p<0.001$ ).

**Conclusions:** Patients with RA, who had been early diagnosed and early treated, after 1 year of tight control had still US inflammatory and erosive changes compared to HC. US assessment gives an added value to clinical evaluation in ERA, for its capacity to detect residual inflammatory abnormalities, even under optimised treatment and consequent structural lesions.

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**Disclosure of Interest:** None declared

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#### SAT0673 MAGNETIC RESONANCE IMAGING IN THE DIAGNOSIS OF AXIAL SPONDYLOARTHRITIS: A SYSTEMATIC LITERATURE REVIEW

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**Background:** Magnetic resonance imaging (MRI) is an essential tool in the diagnosis and management of axial spondyloarthritis (axSpA). However, a recent survey showed variable practices in the use of MRI across the UK.<sup>1</sup> To inform a joint rheumatology and radiology consensus exercise aimed at standardising practice, we systematically reviewed the literature regarding the use of MRI in the diagnosis of axSpA.

**Objectives:** We aimed to answer three research questions:

1. How does the choice of anatomical region influence diagnostic performance?
2. How do MRI acquisition parameters influence diagnostic performance?
3. Which lesion, or combination of lesions, is most sensitive and specific for the diagnosis of axSpA?

**Methods:** MEDLINE (via Pubmed) and EMBASE (via Ovid) databases were searched using previously-reported terms.<sup>2</sup> These terms identified studies including adult patients with clinically suspected axSpA undergoing MRI, where a diagnosis of axSpA was used as an outcome and where patients with a negative test for SpA were used as controls. We included studies performed between January 2013 and March 2017, in addition to those included in a previous systematic literature review, which included all studies up to January 2013.<sup>2</sup> Search results were screened by title and abstract, and the included studies were subject to detailed review and quality assessment using the QUADAS-2 tool.<sup>3</sup>

**Results:** The combined search resulted in a total of 8114 studies; 34 of these were finally selected for inclusion.

Five studies evaluated the added value of spinal MRI over SIJ MRI alone, with variable results depending on the cohort.

Three studies addressed the effect of sequence choice on diagnostic accuracy, demonstrating comparable utility of fat-saturated T2-weighted (T2w) sequences and STIR imaging, and suggesting T2w Dixon imaging as a potential alternative



method for fat suppression. Three studies investigated the role of gadolinium in the SIJs, and overall found minimal added value.

Bone marrow oedema of the sacroiliac joint (SIJ) was found to be the most sensitive and specific lesion in the diagnosis of axSpA in seven studies. Sensitivity and specificity were increased by including other structural lesions, particularly bone marrow fat or erosions. Four studies addressed the utility of SIJ fat infiltration, demonstrating good sensitivity but relatively poor specificity. A number of studies addressing erosions, high T1 signal in the SIJ, fluid signal in the SIJ, ankylosis, sclerosis, capsulitis, backfill and vacuum phenomenon reported low to moderate diagnostic performance for these features. In the spine, four studies reported moderate sensitivity and specificity for corner inflammatory lesions, and four reported poor sensitivity and specificity for spinal fatty lesions.

Three studies evaluated agreement between observers for inflammatory and structural features. Agreement was best for the presence of oedema in the SIJs, but was poor for structural features. Agreement was weak to moderate for global diagnosis.

**Conclusions:** These results have informed the recommendations of a consensus group aiming to standardise practice around the use of MRI scans in the UK.

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**Disclosure of Interest:** None declared

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#### SAT0674 THE USE OF QUANTITATIVE MUSCLE ULTRASOUND AS A FOLLOW-UP TOOL IN INFLAMMATORY MYOSITIS AND DUCHENNE MUSCULAR DYSTROPHY IN CHILDREN

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**Background:** Ultrasound (US) can provide a painless and noninvasive tool for evaluation and follow up of muscle diseases especially in young children who may have restrictions in execution of muscle strength tests and functional scales.

**Objectives:** This study aimed to assess skeletal muscle structural status in children with Juvenile dermatomyositis (JDM) and Duchenne muscular dystrophy (DMD) using quantitative muscle US and to perform a longitudinal follow up of these changes over time and correlate these findings with clinical parameters, functional scales, biochemical and electromyographic tests.

**Methods:** This is a longitudinal study conducted on 35 subjects: 20 JDM patients and 15 DMD patients at baseline and after 12 months of follow-up. In all patients, Quantitative MSUS measurements was performed to the biceps brachii muscle (BB), the forearm flexors (FF), the rectus femoris muscle (RF), the tibialis anterior muscle (TA) according to a standard protocol.<sup>1</sup> The captured images were analysed offline for muscle thickness and echo intensity (EI) by means of computer-assisted grayscale histogram analysis. Manual muscle testing (MMT) was assessed and serum creatine kinase (CK) levels were measured. Also, Quantitative electromyography (QEMG) assessment was performed as BB and RF were studied on the most affected side with emphasis on motor unit potential (MUP) duration, area to amplitude ratio (AAR).

**Results:** In JDM patients, EI of the proximal muscles (BB and RF) at 12 months follow up (75.32±29.84 and 74.73±25.58 respectively) were highly significantly decreased compared to their baseline EI (127.18±50.62 and 100.68±33.65 respectively) (p<0.05). Also, EI of BB and RF at 12 months follow up showed statistically significant correlation with their MMT (r=-0.51, p<0.05), CK levels (r=0.42, p<0.05) and MUP duration (p<0.05). In DMD patients, EI of BB, RF and TA muscles at 12 months follow up (122.3±41.29, 132.55±41.38 and 136.75±38.02 respectively) were significantly increased compared to their baseline EI (116.7±42.65, 124±43.33 and 133.3±39.57 respectively, p<0.05). Also, EI of BB, RF and TA at 12 months follow up showed statistically significant correlation with their MMT (r=-0.67, -0.68 and -0.68 respectively, p<0.05), CK levels (r=0.77, 0.76 and 0.7 respectively, p<0.05), MUP duration (r=-0.73, -0.58 and -0.53 respectively, p<0.05) and AAR ratio (r=-0.79, -0.81 and -0.62 respectively, p<0.05). Logistic regression analysis showed that baseline EI were predictive of follow up MMT score in both JDM and DMD patients (p=0.03 and 0.01 respectively).

**Conclusions:** Quantitative muscle US is a sensitive, objective technique for measuring the presence and severity of muscle pathology in both JDM and DMD patients. EI is remarkably correlated with MMT, muscle enzymes and quantitative EMG suggesting that it could be a useful follow up tool to reflect disease severity and residual muscle damage.

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**Disclosure of Interest:** None declared

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#### SAT0675 SOLUBLE VASCULAR ADHESION MOLECULE-1 IS OVEREXPRESSED IN PATIENTS WITH VASCULITIS, RHEUMATOID ARTHRITIS AND ANKYLOSING SPONDYLITIS

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**Background:** Markers in rheumatology are in great demand in order to objectively diagnose the presence and activity of disease. CRP or ESR frequently are normal in many conditions. Vascular cell adhesion molecules mediate transendothelial migration. Several soluble isoforms can be measured in serum as marker for endothelial activation, for example in synovitis or vasculitis. We have recently shown that soluble vascular cell adhesion molecule-1 (sVCAM-1) is elevated in patients with positive antinuclear antibodies.<sup>1</sup>

**Objectives:** The objective of this study was to analyse sVCAM-1 in a set of several rheumatic diseases and compare them to age- and gender-matched healthy controls.

**Methods:** Cross sectional study with 223 patients with rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriatic arthritis (PsA) and different vasculitides. Patients were treated with routine immunosuppressive agents, where indicated. CRP (mean mg/l±SD, normal <5), ESR (mean mm/h±SD), standard clinical disease activity scores (mean ±SD) and sVCAM-1 (ng/ml±SEM) in serum, determined by ELISA, was analysed.

**Results:** Patients with RA (n=136) had a DAS28 of 2.54±0.83, a close to normal CRP of 6.43±10.52, ESR of 16.9±12.6 and sVCAM-1 levels of 225.40±20.35 vs. 158.90±7.32 (p=0.0025). Patients with vasculitis (n=20) had a mean BVAS of 24.85±10.68, CRP was 5.86±7.77 mg/dl, ESR 14.5±11.5 and sVCAM-1 levels were also significantly different as compared to HC with 358.20±68.91 vs. 122.60±14.62 (p=0.0013). Patients with AS (n=33) had a mean BASDAI of 4.16±2.40, a CRP of 4.06±4.67, ESR 12.0±8.8 and had sVCAM-1 levels of 291.30±51.91 vs. 144.60±34.01 (p=0.021). Patients with PsA (n=34) did not show significant changes.

**Conclusions:** sVCAM-1 might be an objective disease marker in patients with RA, vasculitis and AS. It might be more reliable than standard CRP, especially in vasculitis. Prospective studies are needed to determine if sVCAM-1 is a predictive marker of disease activity and perhaps specific for biologic treatment regimens.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.5850

#### SAT0676 ULTRASOUND DETECTED INFLAMMATION IN RHEUMATOID ARTHRITIS: ELUCIDATING THE RELATIONSHIP WITH CLINICAL MANIFESTATIONS AT THE WRIST

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**Background:** Tender and swollen joint counts are part of rheumatoid arthritis (RA) disease activity assessments. While subclinical synovitis is now a well-known entity, the relationship between tender and swollen joints and ultrasound (US) detected inflammation has not been well explored.

**Objectives:** To compare US detected inflammation (synovitis and/or tenosynovitis) with joint swelling and/or tenderness of the wrist, an important joint in RA. Tendons are included as tenosynovitis on US can be mistaken for joint involvement clinically.

**Methods:** Wrist outcome groups (Groups) 1–4 were identified: 1=S0 T0 (not swollen, not tender); 2=S0 T1 (not swollen but tender); 3=S1 T0 (swollen but not tender); 4=S1 T1 (swollen and tender). Power Doppler (PD) and grey-scale (GS) US were used to grade (a) synovitis semi-quantitatively (0–3) at the following joint recesses: dorsal radiocarpal and intercarpal, dorsal ulnocarpal and volar radiocarpal, and (b) tenosynovitis dichotomously (0=no, 1=yes) at the following tendon sites: extensor digitorum, extensor carpi ulnaris, and flexor digitorum. Scores on each wrist consisted of a PD score, a GS score and a combined (PD +GS) US (CUS) score. Positivity (+ve) for PD, GS and CUS scores was analysed using a generalised linear repeated measures mixed model with binary distribution and logit link. Scores were analysed using a general linear repeated measures mixed model assuming Gaussian errors. In both analyses, patients were modelled as random effects, and wrist (R/L) and follow up visit (baseline, 3 months) as fixed effects. Pairwise comparisons on +ve and scores were carried out among the 4 groups in the context of the models. P-values were not adjusted for multiple comparisons.

**Results:** 122 wrist assessments resulted from 32 RA subjects (87.5% female; 78.1% Chinese; mean (SD) disease duration of 42.8 (52.9) months) who either started or escalated on systemic corticosteroids and DMARDs. All subjects were assessed at baseline and 29 at 3 months. Significant differences among Group scores were: 4 vs 1 (PD, p=0.0031; GS, p=0.0159; CUS, p=0.0045), 4 vs 2 (PD, p=0.0176; GS, p=0.0160; CUS, p=0.0074), and 4 vs 3 (CUS, p=0.0374). Significant differences among +ve were: 4 vs 1 (PD, p=0.0007), 4 vs 2 (PD, p=0.0234), and 3 vs 1 (PD, p=0.0202). No significant Group differences were found for 2 vs 1 (for +ve and scores) and when comparing the 4 groups for GS +ve and CUS +ve. Table 2 shows the frequency distribution of patients by wrist and follow up. There were no significant effects attributable to differences in wrists or follow up visit (p-values all >0.05).

**Abstract SAT0676 – Table 1.** Analysis summary of ultrasound scores and positivity in the wrist.

Wrist Outcome Group <sup>1</sup>	LS Mean <sup>2</sup>	p-value comparison with			LS Mean Estimated Probability	p-value comparison with		
		S0T1	S1T0	S1T1		S0T1	S1T0	S1T1
PD score								
1=S0T0	0.56	0.7545	0.0712	0.0031**	0.21	0.3151	0.0202*	0.0007***
2=S0T1	0.68		0.2516	0.0176*	0.38		0.3378	0.0234*
3=S1T0	1.12			0.1003	0.56			0.052*
4=S1T1	1.55				0.79			
GS score								
1=S0T0	3.61	0.8195	0.3803	0.0159*	0.83	0.4937	0.3008	0.9963
2=S0T1	3.45		0.3544	0.0180*	0.91		0.9707	0.9984
3=S1T0	4.11			0.0549	0.90			0.9984
4=S1T1	5.05				1.00			
Combined US (PD+GS) score								
1=S0T0	4.22	0.9145	0.2063	0.0045**	0.83	0.4937	0.3008	0.9963
2=S0T1	4.12		0.2841	0.0074**	0.91		0.9707	0.9984
3=S1T0	5.21			0.0374*	0.90			0.9984
4=S1T1	6.60				1.00			
Combined US (PD + GS) positivity								
1=S0T0	4.22	0.9145	0.2063	0.0045**	0.83	0.4937	0.3008	0.9963
2=S0T1	4.12		0.2841	0.0074**	0.91		0.9707	0.9984
3=S1T0	5.21			0.0374*	0.90			0.9984
4=S1T1	6.60				1.00			

<sup>1</sup> Wrist Outcome Groups: 1=S0T0 (not swollen, not tender), 2=S0T1 (not swollen but tender), 3=S1T0 (swollen but not tender), 4=S1T1 (swollen and tender).  
<sup>2</sup> Least squares mean from general linear repeated measures mixed model with Gaussian error; patients modelled as random effects, wrist (R/L) and follow up visits (BL, 3mo) modelled as fixed effects. No significant differences between wrists (p<0.1886) or follow up visits (p<0.4106).  
<sup>3</sup> Least squares mean estimated probability using a generalised linear repeated measures mixed model with binary probability distribution and logit link; patients modelled as random effects, wrist (R/L) and follow up visits (BL, 3mo) modelled as fixed effects. No significant differences between wrists (p<0.3720) or follow up visits (p<0.5052).  
 Statistically significant \* p<0.05; \*\* p<0.01; \*\*\* p<0.001

**Abstract SAT0676 – Table 2.** Frequency distribution of subjects by follow-up and wrist

Wrist Outcome Group <sup>1</sup>	Baseline (N=32 subjects)		3-Months (N=29 subjects)	
	Left n (%)	Right n (%)	Left n (%)	Right n (%)
1=S0T0	7 (21.9)	6 (18.8)	7 (24.1)	8 (27.6)
2=S0T1	3 (9.4)	4 (12.5)	3 (10.3)	1 (3.4)
3=S1T0	9 (28.1)	9 (28.1)	11 (37.9)	10 (34.5)
4=S1T1	13 (40.6)	13 (40.6)	8 (27.6)	10 (34.5)

<sup>1</sup> Wrist outcome groups: 1=S0T0 (not swollen, not tender), 2=S0T1 (not swollen but tender), 3=S1T0 (swollen but not tender), 4=S1T1 (swollen and tender).

**Disclosure of Interest:** None declared

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SATURDAY, 16 JUNE 2018

**Epidemiology, risk factors for disease or disease progression**

**SAT0677 PREVOTELLA COPRI IN INDIVIDUALS AT RISK FOR RHEUMATOID ARTHRITIS**

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**Background:** *Prevotella spp.* have been identified as highly enriched in the intestinal microbiota of patients newly diagnosed with rheumatoid arthritis (RA), suggesting a role in the development of the disease.<sup>1</sup> Sequence homology between RA-specific autoantigens and proteins of *Prevotella copri* have been reported.<sup>2</sup> However, the role of these bacteria in the pathogenesis of the disease is not yet established.

**Objectives:** To determine the microbiome composition and prevalence of *Prevotella spp.* in different pre-clinical phases of RA, in a group of individuals at risk for RA, namely first degree relatives of patients with RA (RA-FDR).

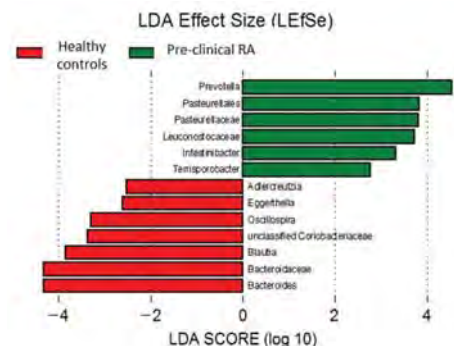
**Methods:** In an ongoing cohort study of RA-FDR, enrolling individuals without clinical evidence of RA at inclusion, we categorised individuals in the following groups: 'healthy controls': asymptomatic RA-FDR without any autoantibodies or symptoms associated with possible RA; 'pre-clinical RA': individuals with 'systemic autoimmunity associated with RA' defined by the presence of anti-citrullinated peptide antibodies (ACPA) or rheumatoid factor (RF) and/or symptomatic individuals with clinically suspect arthralgias or unclassified arthritis. Participants provided stool samples for microbiome analysis. We excluded subjects who had undergone antibiotic therapy within the last 3 months, with known history of inflammatory bowel disease and/or gastrointestinal tract surgery ever. Stool samples processing and microbial diversity culture-independent analyses were performed. After DNA extraction, the V4 region of the 16S rRNA gene was amplified using barcoded primers and sequencing was done on an Illumina MiSeq. Statistical analyses of community structures were performed.<sup>3</sup>

**Results:** Of the 134 participants enrolled, 51 were categorised as 'healthy controls' and 83 as 'pre-clinical RA'. table 1 shows the general characteristics of the two groups. The microbiota of 'pre-clinical RA' individuals was significantly altered compared to 'healthy controls', with abundance of specific bacteria, particularly an enrichment of *Prevotella spp.* (figure 1).

**Abstract SAT0677 – Table 1.** General characteristics of participants

Characteristics	Healthy controls n=51	Pre-clinical RA** n=83
Age, median (IQR)	55 (47–62)	58 (50–66)
Female sex, n (%)	39 (76)	74 (89)
Current Smoking, n (%)	12 (23)	16 (19)
Current Alcohol, n (%)	22 (46)	29 <sup>††</sup>
Body mass index, median (IQR)	24 (22–27)	24 (22–27)
Obesity, BMI≥30, n (%)	5 (10)	9 (11)
ACPA positivity, n (%)	0 (0)	38 (46)*
RF positivity, n (%)	0 (0)	28 (34)*
Shared epitope (1 or 2 copies), n (%)	32 (65)	42 (52)

\*p-value<0.05, Kruskal-Wallis test for continuous variables and Fisher's exact test for categorical variables. \*\*Pre-clinical RA group includes individuals with ACPA or RF positivity and/or with arthralgia or unclassified arthritis.



**Abstract SAT0677 – Figure 1.** Linear discriminant analysis (LDA) effect size (LEfSe) estimates the different relative abundance of bacteria in Healthy controls and Pre-clinical RA participants

**Conclusions:** Individuals at risk of RA who have developed systemic autoimmunity associated with RA and/or symptoms, have enrichment of *Prevotella spp* in comparison with healthy controls. Our findings support the hypothesis of a causal role of *Prevotella spp* in the development of RA, which could lead to future attempts to interfere with its intestinal colonisation during the preclinical stages of disease.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.5899

**SAT0678 SEASONALITY OF NEW EARLY INFLAMMATORY ARTHRITIS CASES: PRELIMINARY RESULTS FROM THE CANADIAN EARLY ARTHRITIS COHORT**

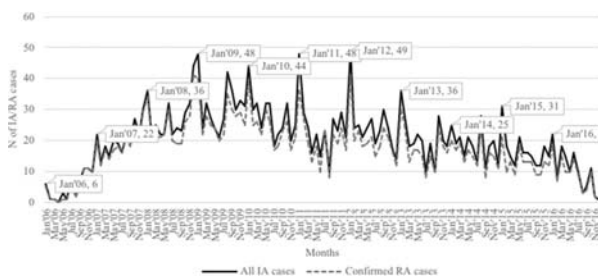
E. Kudaeva<sup>1</sup>, M. Speechley<sup>1</sup>, N. Klar<sup>1</sup>, O. Schieir<sup>2</sup>, S. Bartlett<sup>3</sup>, C. Hitchon<sup>4</sup>, G. Boire<sup>5</sup>, B. Haraoui<sup>6</sup>, E. Keystone<sup>7</sup>, D. Tin<sup>8</sup>, C. Thorne<sup>9</sup>, V. Bykerk<sup>10</sup>, J. Pope<sup>11</sup> on behalf of CATCH investigators. <sup>1</sup>Epidemiology and Biostatistics, Schulich School of Medicine and Dentistry, Western University, London; <sup>2</sup>Department of Epidemiology, University of Toronto Dalla Lana School of Public Health, Toronto; <sup>3</sup>Department of Medicine, McGill University, Montreal; <sup>4</sup>Department of Medicine, University of Manitoba, Winnipeg; <sup>5</sup>Department of Medicine, Universite de Sherbrooke, Sherbrooke; <sup>6</sup>Rheumatic Disease Unit, Institut de Rheumatologie, Montreal; <sup>7</sup>Division of Rheumatology, Mount Sinai Hospital, University of Toronto, Toronto; <sup>8</sup>Allied Health Professional Association; <sup>9</sup>Division of Rheumatology, Southlake Regional Health Centre, Newmarket; <sup>10</sup>Division of Rheumatology, Mount Sinai Hospital, University of Toronto, Toronto; <sup>11</sup>Division of Rheumatology, St. Joseph Health Care, Schulich School of Medicine and Dentistry, London, Canada

**Background:** Disease clustering suggests a possible environmental cause. However, confirming the causes of time-place clustering is challenging. Rheumatoid arthritis (RA) is an autoimmune disease that may be triggered by environmental factors: viral or bacterial infections can lead to RA via molecular mimicry, epitope spreading, B-cell-mediated pathway, bystander activation and via superantigens. Putative infections may also cluster.

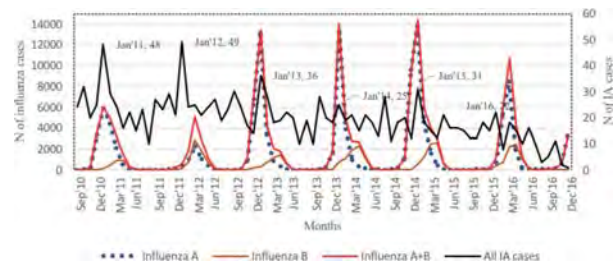
**Objectives:** To study the seasonal distribution of early inflammatory arthritis (IA) onsets in a Canadian sample, and potential relationships with influenza (flu) outbreaks.

**Methods:** Data from an incidence cohort of adults (>18 years) with early IA with <13 months symptom duration from the Canadian Early Arthritis Cohort (CATCH) enrolled between January 2007 – January 2017. Patient-reported date of symptom onset and physician-reported date of IA onset were used to estimate the monthly frequency of early inflammatory arthritis onsets. Monthly flu case frequencies from September 2010 – December 2016 were retrieved from the Public Health Agency of Canada’s FluWatch national surveillance system of confirmed influenza A and B cases. Time-series Poisson regression analyses were performed to assess the non-random covariance of IA and flu with different hypothesised time lags.

**Results:** A total of 2262 with early IA were included. Patient-reported IA onset was more frequent in winter months compared to other seasons (p=0.002), with peaks in January (figure 1). The ten-year aggregated data also showed January peaks of IA onset. There was a positive linear correlation between the number of IA and influenza A onsets (r=0.23, p=0.045), and almost no relationship between the number of IA and influenza B cases (p=0.87) (figure 2).



**Abstract SAT0678 – Figure 1**



**Abstract SAT0678 – Figure 2**

**Conclusions:** Our study provides novel information on the increased onset of IA in relation to seasonal influenza patterns in a Canadian population and adds to the existing literature supporting viral infections as a possible trigger to RA onset.

**Disclosure of Interest:** None declared

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**SAT0679 CIGARETTE SMOKING AND RISK OF BEHCET’S DISEASE: A CASE-CONTROL STUDY**

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**Background:** Behcet’s disease (BD) is a chronic inflammatory multisystem disease characterised by recurrent oral and genital aphthous ulcers, uveitis and skin lesions. Smoking play an important role in the development of inflammatory diseases.<sup>1</sup>

**Objectives:** BD is an inflammatory disease and smoking may have a role in its triggering. Although few studies reported association between smoking and clinical manifestations of BD, to the best of our knowledge, there is no research on the risk of developing BD in smokers.<sup>2–4</sup> This case-control study was conducted to investigate the association between smoking and the risk of BD.

**Methods:** We included 192 patients with BD and 822 healthy siblings of patient with BD and 373 age and sex matched healthy unrelated persons as control groups (table 1). Written informed consent was obtained from all the participants. Demographic data and smoking history of patients and their siblings were obtained by direct and in some cases by telephone interview with the participants. Demographic data and smoking history of healthy controls were obtained by direct interview. Current and former smokers were classified together as ever smokers for the purposes of this analysis. We carried out multivariate analyses with a logistic regression model with BD as the main outcome variable and smoking history as the main predictor variable. Models were adjusted for age, gender, marital status, educational status and pack-years.

**Results:** The patients with BD were more often ever smokers than healthy siblings of patients and healthy unrelated controls (table 1). However, pack-years of smoking in control groups were significantly more than the BD group. By multivariate logistic regression and after adjustment for age, sex, marital status and educational status (model 1), ever smoking was significantly associated with an increased risk of BD compared with never smoking. In comparison with healthy siblings and healthy unrelated persons who never smoked, the relative risk (RR) of developing BD was 1.43 and 1.51, respectively. After including pack year in multivariate analysis (model 2), the RR of developing BD in ever smokers increased to 2.23 and 2.01, respectively.

**Abstract SAT0679 – Table 1.** Demographic characteristics of participants

Variables	BD group (n=192)	Healthy sibling group (n=822)	P-value	Healthy unrelated control group (n=373)	P-value
Age (years)	38.9±10.6	39.3±11.3	NS	37.9±9.7	NS
Gender:			0.001		NS
Male	118 (61.5)	399 (48.5)		228 (61.1)	
Female	74 (38.5)	423 (51.5)		145 (38.9)	
Smoke status			0.01		0.025
Never-smoker	141 (73.4)	673 (81.9)		302 (81)	
Current smokers	43 (22.4)	138 (16.8)		58 (15.5)	
Past smokers	8 (4.2)	11 (1.3)		13 (3.5)	
Ever smokers	51 (26.6)	149 (18.1)		71 (19)	
Pack-years of smoking	11.19±8.8	17.79±11.4	0.003	14.19±10.7	0.007

Qualitative and quantitative variables were displayed as numbers (percentages) and means ±SD, respectively.

BD: Behcet’s disease; NS: non-significant



No significant differences were observed in the clinical manifestations of BD patients in ever smokers and never smokers. However, disease activity, at disease presentation and last visit in ever smokers was significantly more than never smokers.

**Conclusions:** Our data suggest that smoking is a significant risk factor for BD and genetic factors may play an important role in the developing of BD in smokers. We also show a particularly strong relationship between smoking with BD activity and response to treatment.

**Conflict of interest:** We have no potential conflict of interest.

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**Disclosure of Interest:** None declared

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### SAT0680 THE DEVELOPMENT AND VALIDATION OF INTERSTITIAL LUNG DISEASE PREDICTION MODELS IN THREE INTERNATIONAL MIXED CONNECTIVE TISSUE DISEASE COHORTS: THE NORWEGIAN MCTD COHORT, THE HUNGARIAN MCTD COHORT AND THE MCTD COHORT FROM MINNESOTA, US

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**Background:** Mixed Connective Tissue Disease (MCTD) is characterised by the presence of anti-RNP antibodies with clinical features also found in SSc, SLE and IIM. There is an ongoing debate of MCTD's position as a CTD. A substantial proportion of MCTD patients develop Interstitial Lung Disease (ILD).

**Objectives:** This study was conducted with the aims to explore the value of MCTD diagnosis and risk assessment by developing and validating ILD prediction models.

**Methods:** Multivariable logistic regression analyses were performed in 3 international MCTD cohorts. ILD prediction model development from clinical and laboratory parameters was performed in the Norwegian MCTD cohort (n=119). External validation of the models were performed in the Hungarian MCTD cohort (n=196) and the MCTD cohort from Minnesota, US (n=50). ILD was diagnosed by chest CT examination.

**Results:** The cohort characteristics are presented in table 1. An ILD prediction model including Pulmonary Function Test (PFT) results (table 2) and excluding PFT results was developed. The Hosmer-Lemeshow goodness of fit test (HL test) was. 31 and. 71 and the ROC was. 83 and. 78 respectively. The ILD prediction model including DLCO <60% was validated in the Hungarian MCTD cohort and showed good calibration and discrimination (HL test=0.95 and ROC=0.82). The ILD prediction model excluding PFT results showed good calibration and discrimination in both the Hungarian MCTD cohort (HL test=0.72 and ROC=0.80) and the MCTD cohort from Minnesota (HL test=0.96 and ROC=0.67).

**Abstract SAT0680 – Table 1.** Characteristics of the three MCTD cohorts

Characteristics	Norwegian MCTD cohort (n=119)	Hungarian MCTD cohort (n=196)	Minnesota MCTD cohort (n=50)	P- value
Male sex, N (%)	32 <sup>(24)</sup>	10 (5)	8 (16)	p<0.001
Age at diagnosis, yrs	34 (10)	36 (9)	48 (16)	p<0.001
Age at CT, yrs	44 (14)	41 (11)	48 (14)	p=0.001
ILD, N(%)	52 <sup>(39)</sup>	116(59)	14 <sup>(28)</sup>	p<0.001
DLCO<60% pred	28 (23)	67 (35)	NA	p=0.025
FVC<75% pred	18 (14)	97 (49)	NA	p<0.001

**Abstract SAT0680 – Table 2.** ILD prediction model including PFT results

	Univariable			Multivariable		
	HR	95% CI	P value	HR	95% CI	P value
<b>Sclerodactily</b>	<b>2.0</b>	<b>0.94–4.0</b>	<b>0.071</b>			
<b>RNP&gt;200</b>	<b>3.0</b>	<b>1.5–7.1</b>	<b>0.003</b>	<b>4.4</b>	<b>1.7–11.1</b>	<b>0.002</b>
<b>SR&gt;30</b>	<b>2.3</b>	<b>1.0–5.0</b>	<b>0.043</b>			
Male sex	1.6	0.71–3.5	0.268			
<b>Never arthritis</b>	<b>5.4</b>	<b>2.1–13.6</b>	<b>&lt;0.001</b>	<b>4.1</b>	<b>1.4–11.6</b>	<b>0.008</b>
<b>Pericarditis</b>	<b>2.2</b>	<b>0.8–6.1</b>	<b>0.117</b>			
<b>Agegroup at CT</b>						
<25 years						
26–35 years	1.0	0.2–4.5	0.953	1.8	0.3–9.8	0.504
36–45 years	2.6	0.6–	0.213	4.8	0.9–25.5	0.065
46–55 years	1.7	11.7.	0.513	2.9	0.5–14.7	0.210
56–65 years	2.3	4–7.4.	0.289	3.7	0.6–23.9	0.167
>65 years	6.0	5–10.8	0.048	13.0	1.6–	0.017
		1.0–35.4			107.3	

**Conclusions:** The cohorts have different characteristics. Despite these differences the ILD prediction models developed in the Norwegian MCTD cohort have shown external validity when assessed in the Hungarian MCTD cohort and the MCTD cohort from Minnesota. Risk factors of ILD in MCTD patients are high levels of anti-U1 RNP antibodies, absence of arthritis and increasing age. The successive ILD prediction across different MCTD cohorts strengthens the value of MCTD diagnosis and anti-RNP antibody detection in clinical practice.

**Disclosure of Interest:** None declared

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### SAT0681 THE CAUSAL ASSOCIATION BETWEEN CHILDHOOD AND ADULTHOOD BODY MASS INDEX AND OSTEOARTHRITIS: A MENDELIAN RANDOMIZATIONSTUDY

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**Background:** Childhood obesity is a strong predictor of adult obesity. Body mass index (BMI) has been associated with a dose-response increase in risk of osteoarthritis. However, studying causality in this association is difficult due to confounding factors

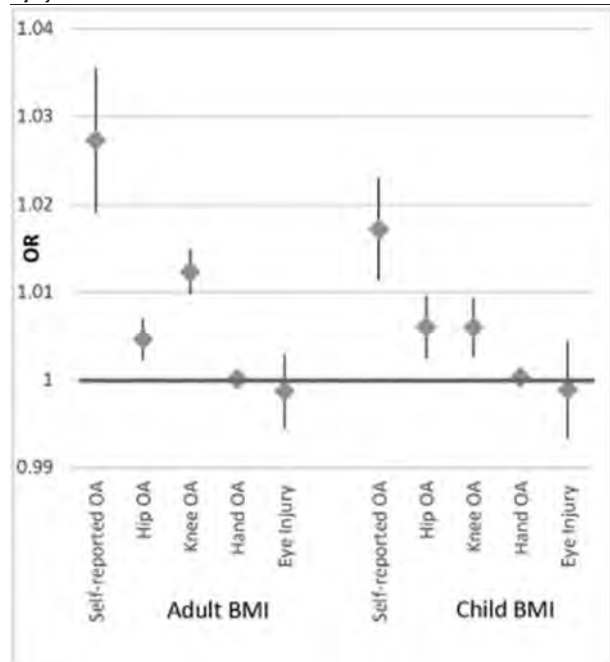
**Objectives:** To study the causal association of childhood and adult BMI on the risk of developing osteoarthritis using Mendelian Randomization (MR) methods

**Methods:** A two-step MR analysis was conducted. Exposures were determined by reviewing data from two genome-wide association study (GWAS) from >47,000 children describing 15 SNPs associated with childhood BMI, and another GWAS describing 97 SNPs related to BMI within 3 39 224 adults. For the

outcomes, data gathered from a GWAS analysing 3 37 000 unrelated individuals in the UK BioBank was used to assess the association between the SNPs of interest and self-reported osteoarthritis and ICD10 linked hospital data: knee, hip and first carpo-metacarpal joint osteoarthritis. Traumatic eye injury from the same cohort was used as a negative control. An inverse variance weighted meta-analysis estimator was used to test for association. In presence of heterogeneity, a weighted median approach was used and, when necessary, pleiotropy was controlled for using the MR Egger method. All analyses were performed using the TwoSampleMR package in R

**Results:** 14 and 91 SNPs associated with BMI in the childhood and adulthood were identified in the UK BioBank GWAS respectively. Association between childhood BMI and adult OA was seen for self-reported and hip and knee OA. Adult BMI also appeared associated with them [figure 1]. Conversely, no associations were found between BMI (either childhood or adult) and Hand OA risk. Finally, no relationship was seen between BMI and traumatic eye injury (negative control)

	Adult BMI		Child BMI	
	OR	95% CI	OR	95% CI
S-R OA	1.027	1.019–1.036	1.017	1.011–1.023
Hip OA	1.005	1.002–1.007	1.006	1.002–1.010
Knee OA	1.012	1.010–1.015	1.006	1.003–1.009
Hand OA	1.001	0.999–1.001	1.000	0.999–1.001
Eye Injury	0.999	0.994–1.003	0.999	0.993–1.004



**Conclusions:** Higher BMI in both childhood and adulthood overweight/obesity cause an excess in risk of knee and hip osteoarthritis. Whilst the effect of adult BMI seems stronger on knees, childhood BMI might impact both knee and hip osteoarthritis risk similarly. Age-specific associations should be treated with caution given significant overlap between loci associated with BMI across age ranges. In contrast, our findings contradict previous cohorts that found an association between overweight/obesity and hand osteoarthritis, which could be explained by confounding factors such as manual work or related socio-economic factors. The association between increased BMI and knee or hip osteoarthritis adds further impetus to strategies for the prevention of childhood and adult obesity in order to reduce subsequent disability.

**Disclosure of Interest:** None declared

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SAT0682

**“INCIDENCE AND REGIONAL VARIATION OF ANKYLOSING SPONDYLITIS AND SPONDYLOARTHRITIS 2000–2013: A NATIONWIDE COHORT STUDY”**

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**Background:** Spondyloarthritis is a group of inflammatory rheumatic diseases with Ankylosing Spondylitis (AS) as the major subgroup. Only a few studies worldwide have reported incidences of AS and their trend over time.

**Objectives:** To describe the incidences of Ankylosing Spondylitis (AS) and spondyloarthritis (SpA) in the Danish population in 2000–2013, at both national and regional level. To establish if there is a trend in incident cases over time and test if such a trend may be explained by use of MRI scans for diagnostic evaluation.

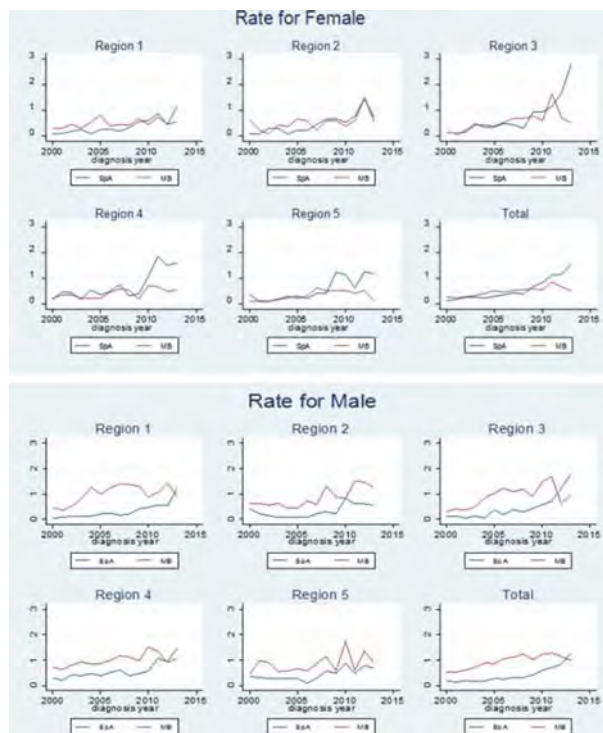
**Methods:** In the Danish National Patient Registry, we identified all patients with a valid Danish civil registration number who received an AS (ICD10:DM45) or SpA (ICD10:DM46) diagnosis during the time period from 1 January 2000 until 31 December 2013. Incident cases were identified and incidence rates described as rates per 1/100.000 of AS and SpA were calculated for each year. Variation among the five Danish regions were evaluated and correlated to the diagnostic use of MRI.

**Results:** We identified 3620 incident cases (AS: 2116, SpA: 1504). Males are overrepresented among AS incidents (58%–80%), both nationwide and regionally. The percentages of males with an AS diagnosis are stable throughout the time period (65%–69%). Females are overrepresented among SpA incidents nationwide and in most regions. In the Region of Southern Denmark, there is a small overrepresentation of males for both SpA and AS diagnoses (58%).

The number of nationwide AS incident cases increases between 2005 and 2009 from 534 (rate: 0.52) to 828 cases (0.82). During 2010–2013 the AS incidence decreased to 754 (0.94).

The number of SpA incident cases increased from 220 (0.21) in 2009 to 430 (0.43) in 2009 with an additional increase in incidence to 854 (1.06) in 2010–2013. The trend is the same throughout the five regions.

MRI was used for diagnostic purposes in only 10%–15% of the patients in 2002. In 2013 the number had increased to 95.0% of male patients and 94.3% of female patients diagnosed with AS and 98.5/98.1% of patients diagnosed with SpA.



**Conclusions:** In this Danish nationwide cohort, the incidence of AS increased during the years 2000–2004 and stabilised in 2005–2013 which is in line with previous studies exploring the trends of AS incidence.

The SpA incidence increased significantly during the years 2000 to 2013. This might be caused by the implementation of the ASA criteria in 2009, which included the “imaging arm”, and by increased access to MRI for diagnostic evaluation in patients with low back pain. This might lead to overestimation and/or misdiagnosis

of SpA because signs of inflammatory changes in the sacroiliac joint are a common finding in MRIs of low back pain patients.

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SAT0683

#### A NORTH-SOUTH WORLDWIDE GRADIENT IN SYSTEMIC ACTIVITY OF PRIMARY SJÖGREN SYNDROME: INCREASED SEVERE DISEASE IN PATIENTS FROM SOUTHERN COUNTRIES

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**Objectives:** To analyse the influence of geolocation on the clinical systemic presentation of primary Sjögren syndrome (SjS) at diagnosis.

**Methods:** The Big Data Sjögren Project Consortium is an international, multi-centre registry created in 2014. Centres were classified by continent, with an additional north-south sub-classification according to latitude (>or<50°N in Europe, equator >or<in America and >or<30°N in Asia). Systemic involvement at diagnosis was retrospectively scored using the ESSDAI.

**Results:** The highest baseline ESSDAI scores were reported from Southern vs Northern countries in Europe (7.2 vs 4.6, p<0.001), America (5.3 vs 3.5, p<0.001) and Asia (6.3 vs 3.9, p<0.001). In Europe, the frequency of activity in each domain was higher in Southern countries (in all domains except constitutional, p<0.001). In America, Southern countries had the highest frequencies of active patients in constitutional, articular, cutaneous, pulmonary, PNS and CNS domains (p<0.001 in all) and the lowest frequencies in lymphadenopathy (p=0.018) and biological (p<0.001) domains. In Asia, patients from China had the highest frequency of activity in glandular, articular, pulmonary, muscular, haematological and biological and those from India in lymphadenopathy, cutaneous, renal and PNS.

**Conclusions:** This study provides the first evidence for a strong influence of geolocation on the systemic phenotype of primary SjS at diagnosis. Geographical determinants should be considered as key variables when systemic disease is scored.

**Disclosure of Interest:** None declared

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SAT0684

#### APPENDICITIS AND THE RISK OF NEWLY DIAGNOSED SYSTEMIC SCLEROSIS: A NATIONWIDE, POPULATION-BASED, CASE-CONTROL STUDY IN TAIWAN

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**Background:** Previous studies suggested that patients with systemic sclerosis (SSc) had specific alterations in the gastrointestinal microbiota, including increased levels of pathobiont genera, such as Fusobacterium. Local expansion of Fusobacterium was also found in children with acute appendicitis. However, no prior study had explored the association between incident SSc and prior appendicitis.

**Objectives:** To explore the association between appendicitis and the risk of incident systemic sclerosis (SSc).

**Methods:** Using the 2003–2012 claims data of the entire population in Taiwan, we identified 1595 patients with a new diagnosis SSc (ICD-9-CM 710.1) validated by a thorough review of the original medical record from 2006 to 2012 as SSc cases. We also selected 15 950 individuals who never had a diagnosis of SSc during 2003–2012 matching SSc cases (1:10) for age, sex, and the year of index date from claims data of a one million representative Taiwanese population as non-SSc controls. The index date was defined the first date of SSc diagnosis in the SSc group and the first date of ambulatory visit for any reason in the control group. Using conditional logistic regression analysis, The association between appendicitis (ICD-9-CM 540–543) and the risk of incident SSc was tested by estimating odds ratios (ORs) with 95% confidence intervals (CIs) controlling for potential confounders, including Charlson comorbidity index, a history of periodontal disease (ICD-9-CM 523), salmonella infection (ICD-9-CM 003), and intestinal infection (ICD-9-CM 009). We also performed sensitivity analyses by varying the definition of appendicitis according to the status of receiving primary appendectomy.

**Results:** The mean ±SD age was 51±15 years in both cases and controls. The proportion of women was 77.5%. Appendicitis was identified in 17 (1.1%) of 1595 SSc cases and 81 (0.5%) of 15 950 non-SSc controls before the index date had a history of appendicitis. A significant association between appendicitis and the risk of SSc was demonstrated (OR, 2.03; 95% CI, 1.14–3.60) after adjustment for potential confounders. The association between appendicitis and SSc risk was still statistically significant using various definitions of tonsillitis based on the status of primary appendectomy.

	Univariate	Multivariate
	OR (95% CI)	OR (95% CI)
Appendicitis	2.11 (1.25–3.57)	2.03 (1.14–3.60)
Primary appendectomy	2.04 (1.17–3.57)	1.93 (1.06–3.54)
Appendicitis with primary appendectomy	2.07 (1.18–3.62)	1.97 (1.07–3.61)
Appendicitis or primary appendectomy	2.09 (1.23–3.53)	1.99 (1.13–3.53)

**Conclusions:** The present study reveals an association between SSc risk and a history of appendicitis.

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SAT0685

### TEMPERATURE AND SMALL PARTICULATE MATTER POLLUTION ARE ASSOCIATED WITH ORGAN SPECIFIC LUPUS FLARES: A SPATIO-TEMPORAL ANALYSIS

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**Background:** Understanding the role of environmental exposures in the development of SLE and their association with SLE activity may help identify modifiable risk factors and potential etiological mechanisms. Cluster detection is an essential tool in public health which has the goal of detecting anomalous clusters of disease cases.

**Objectives:** We performed a spatial-time cluster analysis of the Johns Hopkins Lupus cohort with the goal of identifying potential spatial-time clusters of SLE organ specific disease activity related to temperature changes and fine particulate matter pollution (PM2.5).

**Methods:** 1261 patients who fulfil 4 of the 11 American College of Rheumatology classification criteria for SLE and who had recorded home addresses were included in the analysis. Disease activity was expressed as Physician Global Estimate (PGA), and included rash, joint, serological, neural, renal, pulmonary, and haematological flare-ups. The area utilised in this analysis was a 350 kilometre radial buffer around the Johns Hopkins Lupus Centre. This area was considered due to the high and consistent density of study participants. The data ranged from January 1999 to February 2009. Average temperature and PM2.5 exposure over a period of 10 days prior to patient visit was obtained from the United States Environmental Protection Agency, and county level demographics were obtained from the US census. Univariate, multivariate, and multilevel models were built in order to study the association of these variables with lupus flare-ups. The models were adjusted for age, sex, income, racial distribution, and rural vs. urban patient residence.

**Results:** Rash (OR=1.0075 for 1 degree Fahrenheit(F) increase), neurologic (OR=1.0096 for 1 degree F increase), and joint (OR=1.011 for 1 degree F increase) flares were statistically significantly associated with an increase in temperature in univariate and multivariate analysis. Renal flares were negatively associated with increases in temperature (OR=0.996 for 1 degree F increase) in both univariate and multivariate analysis. Serositis flares were found to be associated in both univariate and multivariate analysis with increases in PM2.5 concentration (OR=1.024 for an increase of 1 ug/m<sup>3</sup>), as were hematologic flares (OR=1.019 for an increase of 1 ug/m<sup>3</sup>), and joint flares (OR=1.011 for an increase of 1 ug/m<sup>3</sup>). Maps were generated highlighting the study area and the flares. After adjusting for temperature and PM2.5, rash, neurologic, and renal flare-up clusters changed spatially and temporally, suggesting that the adjustment variables could be contributing causes to the original clusters of these kinds of flare-ups.

**Conclusions:** An increase in temperature was found to be significantly associated with skin, joint, and neurologic flares and inversely associated with renal flares, while increase in fine particulate matter pollution was significantly associated with serositis and hematologic flares. Spatiotemporal cluster adjustment for PM2.5 and temperature changed the neurologic, renal, and rash flare up clusters both spatially and temporally further supporting that these variables could be contributing causes to the original flare clusters. The clusters that remained unchanged indicate areas of unexplained variation that requires further study.

**Disclosure of Interest:** None declared

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SAT0686

### ARE MRI-DETECTED EROSIONS IN PATIENTS WITH UNDIFFERENTIATED ARTHRITIS PREDICTIVE FOR THE DEVELOPMENT OF RHEUMATOID ARTHRITIS? A LARGE LONGITUDINAL STUDY

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**Background:** Radiographic erosions are a clear hallmark of rheumatoid arthritis (RA) and the presence of radiographic erosions according to the EULAR definition is sufficient to classify patients as RA. Recently, the use of MRI has been recommended to detect erosions since it is more sensitive than radiography. To determine the specificity of MRI-detected erosions, we recently compared hand and foot MRI of patients presenting with RA with those of symptom-free persons and

patients presenting with other arthritides. This revealed that many MRI-detected erosions were not specific for RA but a few erosion features were identified as specific for RA. These were grade  $\geq 2$  erosions (defined as  $>10\%$  of bone eroded), erosions located in MTP5, and erosions located in MTP1 in persons aged  $<40$ . These results were derived by comparing patients that already received their final diagnosis. A clinically relevant question is whether MRI-detected erosions in patients presenting with undifferentiating arthritis (UA) are valuable in predicting future progression to RA.

**Objectives:** To determine whether MRI-detected erosions in patients presenting with UA are valuable in predicting future progression to RA.

**Methods:** 302 patients consecutively presenting with UA (not fulfilling the 2010-criteria) between 2010 and 2016 were studied. At baseline 1.5T MRI of the 2nd –5th metacarpophalangeal(MCP)- and 1st –5th metatarsophalangeal(MTP)-joints was performed. Erosions were scored according to the RAMRIS system by 2 readers (ICC  $>0.93$ ); an erosion was considered present if both readers scored  $\geq 1$ . First the presence of any MRI-detected erosion was evaluated. Then the presence of RA-specific erosions, defined as grade  $\geq 2$  erosions, erosions in MTP5 and erosions in MTP1 in persons aged  $<40$ , was evaluated. Patients were followed up for 1 year on the development of RA (according to the 2010-criteria) and/or on the start of DMARDs.

**Results:** Of the 302 UA-patients 144 (48%) developed RA and/or started DMARDs. MRI-detected erosions were observed in 57% of the 2010 UA-patients but their presence was not predictive for the development of RA (OR 1.3, 95% CI 0.8–2.0, PPV 50%). RA-specific erosions (either a grade  $\geq 2$  erosion, erosion in MTP5 and/or erosion in MTP1 in persons aged  $<40$ ) were present in only 8% of the 2010 UA patients and were also not associated with RA-development (OR 0.9 95% CI 0.4–1.9, PPV 44%). The observed PPVs were comparable to the prior risk of 48%. Similar findings were obtained when studying the individual RA-specific erosions separately.

**Conclusions:** MRI-detected erosions were frequently present in UA-patients. In contrast, RA-specific MRI-detected erosions were rare in UA. Since MRI-detected erosions were not associated with an increased risk on progression to RA, the present data indicate that evaluation of MRI-detected erosions is not prognostically relevant in UA-patients.

**Disclosure of Interest:** None declared

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SAT0687

### SILICONE BREAST IMPLANTS AND THE RISK OF AUTOIMMUNE DISEASES: REAL WORLD ANALYSIS

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**Background:** Previous reports have suggested an association between silicone breast implants (SBIs) and connective tissue disorders. However, several epidemiological studies have produced inconsistent results.

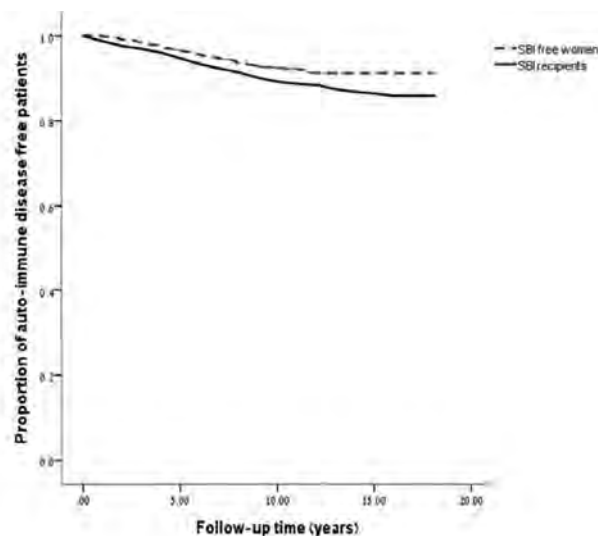
**Objectives:** To evaluate the association between SBIs and the most clinically relevant auto-immune diseases (ADs) using a large, population based database.

**Methods:** In this cross-sectional study, we used the computerised databases of Maccabi Healthcare Services (MHS) which include up to 20 years of data on 2 million members. Women with SBIs were identified by procedure and diagnosis codes, clinical breast examinations and mammography referrals. ADs were identified using the International Classification of Diseases 9th revision (ICD-9) codes. SBIs-free women were matched by age group and socio-economic status (SES) in a ratio of 1:4. Multivariable logistic regression and Cox's proportional hazards models were performed.

**Results:** We included 24,651 SBI recipients and 98 604 matched SBIs free women in our study. The association between SBIs and AD was significant ( $p<0.05$ ) (adjusted OR 1.21, 95% CI 1.17–1.26). The strongest association with SBIs (OR  $>1.5$ ,  $p<0.001$ ) was recorded for systemic sclerosis (SSc) and sarcoidosis (OR of 1.99 and 1.67, respectively). Similar results were calculated when analysis was limited to cancer free women. Multivariable Cox regression model yielded a HR of 1.45 (95% CI 1.21–1.73) for being diagnosed with at least one AD in women with SBI compared to those without.

Proportions and OR for ADs among SBI recipients in comparison to SBI-free women				
	SBI free women n=98,604 n (%)	SBI recipients n=24,651 n (%)	Unadjusted OR (95% CI)	Adjusted OR* (95% CI)
Any auto-immune disease	22 634 (22.95)	6510 (26.41)	1.20 (1.17–1.24)	1.21 (1.17–1.25)
Ankylosing spondylitis	155 (0.16)	41 (0.17)	1.06 (0.75–1.49)	1.24 (0.85–1.80)
Fibromyalgia/Chronic fatigue syndrome	6106 (6.19)	1997 (8.10)	1.34 (1.27–1.41)	1.33 (1.25–1.40)
Hyperthyroidism	2945 (2.99)	870 (3.53)	1.19 (1.10–1.28)	1.17 (1.07–1.27)
Hypothyroidism	10 870 (11.02)	2979 (12.08)	1.11 (1.06–1.16)	1.11 (1.05–1.16)
Multiple sclerosis	303 (0.31)	93 (0.38)	1.23 (0.97–1.55)	1.43 (1.12–1.82)
Psoriasis	4594 (4.66)	1293 (5.25)	1.13 (1.06–1.21)	1.13 (1.05–1.21)
Psoriatic arthritis	201 (0.20)	54 (0.22)	1.07 (0.80–1.45)	1.17 (0.85–1.61)
Rheumatoid arthritis	970 (0.98)	278 (1.13)	1.15 (1.00–1.31)	1.17 (1.01–1.36)
Sarcoidosis	187 (0.19)	93 (0.38)	1.99 (1.55–2.56)	1.95 (1.49–2.57)
Sjogren's syndrome	344 (0.35)	123 (0.50)	1.43 (1.17–1.76)	1.55 (1.24–1.94)
Systemic lupus erythematosus	457 (0.46)	117 (0.47)	1.02 (0.84–1.26)	1.03 (0.83–1.28)
Systemic sclerosis (Scleroderma)	242 (0.25)	101 (0.41)	1.67 (1.33–2.11)	1.63 (1.26–2.11)
Vasculitis	115 (0.12)	32 (0.13)	0.90 (0.61–1.33)	1.23 (0.80–1.89)

\*Adjusted for: age/socio-economic status/birth country/smoking status/breast cancer.



P-value from log rank test < 0.001

Note: SB = silicone breast implants

Abstract SAT0687 – Figure 1. Kaplan-Meier plot for diagnosis with an auto-immune among SBI recipients and SBI-free women (n=8906). P-value from log rank test <0.001. Note: SB=silicone breast implants

**Conclusions:** SBIs seems to be associated with higher likelihood of auto-immune disease diagnosis.

**Acknowledgements:** None

**Disclosure of Interest:** None declared  
**DOI:** 10.1136/annrheumdis-2018-eular.3886

**SAT0688 PROGRESSIVE DRIFT OF PATIENT POPULATIONS IN RHEUMATOID ARTHRITIS CLINICAL TRIALS OVER TIME**

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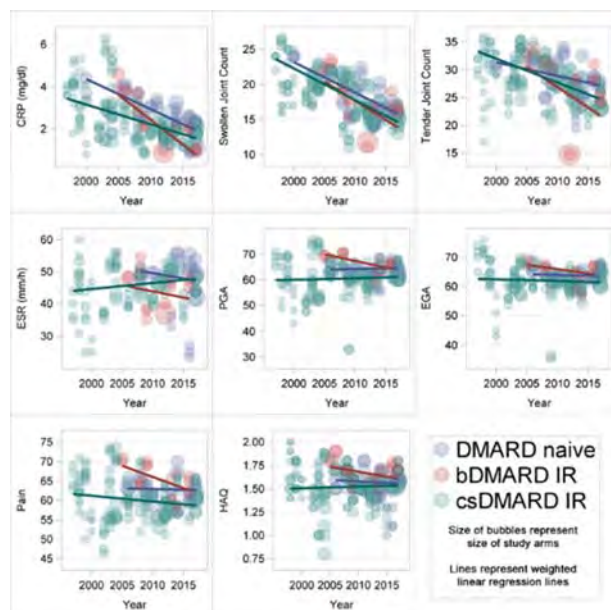
**Background:** Rheumatoid arthritis (RA) is among the most intensively studied chronic inflammatory musculoskeletal diseases. Over the past two decades numerous new compounds have been tested in RA. Although the results from any new clinical trial in RA is usually interpreted in the context of existing data from previous trials, it is not clear whether trial populations are necessarily historically comparable.

**Objectives:** To understand secular trends and drifts in characteristics of patient populations enrolled in RA clinical trials.

**Methods:** We performed a systematic literature review of randomised, controlled, double-blind trials, investigating biological therapies in RA. Reports were identified using PUBMED, EMBASE and the Cochrane Library. Populations were stratified into conventional disease modifying anti-rheumatic drug (cDMARD) naïve, cDMARD inadequate responders (IR), and biological DMARD IR. The following variables at baseline were extracted from reports: swollen and tender joint counts (SJC, TJC), pain, patient and evaluator global (PGA, EGA), acute phase measures (erythrocyte sedimentation rate, ESR and C-reactive protein, CRP), as well as the Health Assessment Questionnaire Disability Index (HAQ). In addition, we obtained the year of publication and the inclusion criteria of each trial. We then performed a mixed model meta-regression of year of publication on each of the mentioned baseline variables.

**Results:** Out of 697 abstracts selected for screening, 73 studies were chosen as relevant; 3 studies with mixed populations were excluded, resulting in 70 studies included for analysis. Table 1 shows the observed medians and quartiles for the baseline characteristics. Meta-regression showed a significant decrease of SJC ( $\beta = -0.415; p \leq 0.001$ ), TJC ( $\beta = -0.378; p \leq 0.001$ ), and CRP ( $\beta = -0.123; p \leq 0.001$ ) over the years (figure 1); for all other core set measures, there was no trend or significance. Inclusion criteria showed similar trends over time for SJC ( $\beta = -0.154, p \leq 0.001$ ), TJC ( $\beta = -0.243, p \leq 0.001$ ), and CRP ( $\beta = -0.065, p \leq 0.001$ ).

	DMARD NAIVE	csDMARD IR	bDMARD IR
<b>No of trials (n)</b>	13	48	9
<b>No of study arms (n)</b>	39	180	25
<b>No of patients (n)</b>	8894	23 752	4584
<b>Year of publication (YYYY)</b>	2014 (2009–2016)	2008 (2003–2012)	2013 (2008–2016)
<b>CRP (mg/dL)</b>	2.59 (2.27–3.26)	2.08 (1.67–3)	2.1 (1.08–3.11)
<b>ESR (mm/h)</b>	49.4 (42–52.8)	45.95 (40.2–49.9)	46.85 (39.2–48.2)
<b>Swollen Joints (0–66)</b>	16.65 (16–20.3)	17.95 (15.59–20.4)	17.1 (16.2–19)
<b>Tender Joints (0–68)</b>	28.05 (25.5–31)	28.1 (25.88–31.7)	28.75 (25.6–31.2)
<b>Patient global assessment (0–100)</b>	63.9 (61.8–66)	61 (58–65)	66.5 (63–69.7)
<b>Evaluator global assessment (0–100)</b>	63.6 (62–65.6)	62.05 (59.7–65)	66.45 <sup>62–67</sup>
<b>Patients pain assessment (0–100)</b>	62.5 (60.9–64.6)	60.29 (56.66–65)	65 (62–69)
<b>Health assessment questionnaire (0–3)</b>	1.54 (1.5–1.63)	1.51 (1.41–1.66)	1.7 (1.6–1.74)



**Conclusions:** There is a progressive drift towards lower number of swollen and tender joints and lower CRP-levels at trial entry of time, which is at least partly related to a similar trend in inclusion criteria for RA. The constancy of patient-reported outcomes suggests that the baseline activity is still perceived as similarly high. Differences in overall baseline inflammatory activity may pose a challenge for comparing newer with older trial results.

**Disclosure of Interest:** None declared

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SAT0689

#### THYMECTOMY IN PATIENTS WITH MYASTHENIA GRAVIS AND THE RISK OF AUTOIMMUNE RHEUMATIC DISEASES: A NATIONWIDE COHORT STUDY

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**Background:** Previous studies have shown myasthenia gravis (MG) and autoimmune rheumatic diseases (ARDs) share common pathogenetic mechanisms.

**Objectives:** Therefore, the present study investigated the possible relationship between MG and ARDs.

**Methods:** We analysed Taiwanese medical data from the Registry of Catastrophic Illness and identified patients with MG. From the entire general population data of the National Health Insurance Research Database, we randomly selected a comparison cohort that was frequency-matched by age (in 5 year increments), sex, and index date. We analysed the risk of ARDs by using a Cox proportional hazards regression model stratified by sex, age, and treatment.

**Results:** We enrolled 6478 patients with MG (58.03% women; mean age, 50.55 years) and 25 912 age- and sex-matched controls in the present study. The risk of total ARDs was 6.25 times higher in the MG cohort than in the non-MG cohort after adjustment for age and sex. Furthermore, the MG cohort was associated with a significantly higher risk of primary SS (pSS), SLE, and other ARD types (adjusted hazard ratios [HRs]: 15.84 [95% CI: 8.39–23.91]; 11.32 [95% CI: 5.04–25.429]; and 4.07 [95% CI: 1.31–12.62], respectively). MG cohort who received thymectomy had an increased risk of RA, pSS, and SLE (adjusted HRs: 4.41; 15.06; and 23.68, respectively).

**Conclusions:** The present nationwide cohort study revealed an association between MG and incident ARDs. MG cohort who received thymectomy had an increased risk of RA, pSS, and SLE. Future studies are needed to elucidate the underlying pathogenesis and to translate them into clinical therapeutic options.

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**Disclosure of Interest:** None declared

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SAT0690

#### THE ASSOCIATION BETWEEN SARCOIDOSIS AND ISCHAEMIC HEART DISEASE – A BIG DATA ANALYSIS

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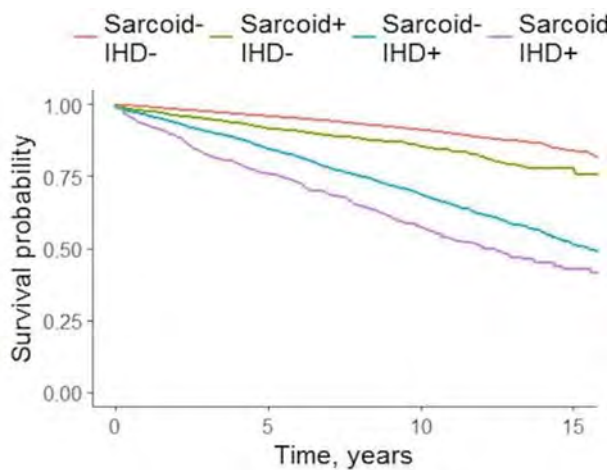
**Background:** Sarcoidosis is an inflammatory disease characterised by the hallmark sign of non-caseating granulomas<sup>1,2</sup>. In the past decade a consensus has formed regarding the pivotal role of inflammation in atherosclerosis<sup>3</sup>. Since this discovery the association between chronic inflammatory states and ischaemic heart disease was confirmed in several rheumatic diseases<sup>4</sup>. Therefore, the constant state of inflammation to which sarcoidosis patients are exposed might pose as a risk factor for ischaemic heart disease.

**Objectives:** The aim of this study is to assess the relation between sarcoidosis and Ischaemic heart disease and its prognostic significance.

**Methods:** Based on data from Clalit Health Services (CHS), Israel's largest health maintenance organisation, the medical records of 3993 sarcoidosis patients and 19 856 controls were acquired. Controls were matched to sarcoidosis patients according to age and sex. Chi-square and student t-tests were used in order to compare variables distribution in the cohort. Variables associated with ischaemic heart disease were assessed by logistic regression model. Log-rank test was performed for survival analysis, while Cox proportional hazards method was utilised to evaluate variables related to increased risk of all-cause mortality.

**Results:** Matched by sex and age – both sarcoidosis group and the control group were composed from 63% females with mean age being 56 years. Compared to the control group, sarcoidosis patients had a higher proportion of ischaemic heart disease, presenting with 856 (21.4%) cases whereas the control group had only 2999 cases (15.1%, p<0.001). The association between sarcoidosis and ischaemic heart disease was demonstrated by a multivariate analysis, (adjusted OR 1.503, 95% CI 1.361–1.660). A 15 year follow up revealed increased mortality among sarcoidosis patients – as 710 (17.8%) of sarcoidosis patients had passed away while 2121 (10.7%) deaths were reported in the control group (p<0.001). In a multivariate model, sarcoidosis patients were found to be in increased risk for all-cause mortality compared to the control group (adjusted HR 1.95, 95% CI 1.75–2.14).





**Conclusions:** Sarcoidosis is associated with an increased risk for ischaemic heart disease and all-cause mortality. Patients with co-morbidity of sarcoidosis and ischaemic heart disease should be treated accordingly.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.6887

SAT0691

#### ADHERENCE TO DISEASE-MODIFYING DRUGS IN CHRONIC INFLAMMATORY RHEUMATIC DISEASES: SEVERAL QUESTIONNAIRES, DIVERSE PATIENT CHARACTERISTICS AND SOME EFFICACIOUS INTERVENTIONS – A SYSTEMATIC LITERATURE REVIEW

D. Puyraimond-Zemmour, X. Romand, M. Lavielle, A. Molto, P. Gaudin, M. Soubrier, C. Beauvais, D. Wendling, E. Senbel, S. Pouplin, R.-M. Flipo, C. Richez, A. Sarau, L. Gutermann, M. Mézière, M. Dougados, L. Gossec. *Rencontres d'Experts 2017 Working Group, Paris, France*

**Background:** In chronic inflammatory rheumatic diseases (CIRDs), adherence to disease-modifying drugs (DMD) is only moderate. Non-adherence may lead to complications, unnecessary treatment switches and heightened costs. Physicians are often at a loss when faced with non-adherence.

**Objectives:** To obtain an overview of how to measure adherence, who to screen particularly (risk factors of non adherence) and interventions to enhance medication adherence to DMD in patients with CIRDs.

**Methods:** A systematic literature review was performed in Pubmed, Cochrane, Embase and websites in 2017. All english and french studies related to methods to measure non-adherence, risk factors regrouped in 5 domains according to World Health Organisation (patient characteristics, health status, treatments, socio-economic conditions and relations with caregivers and the health system) and interventions for non-adherence regrouped in 5 modalities (educational, behavioural, cognitive behavioural, multicomponent interventions or others) were selected. The scope was limited to CIRDs (i.e., rheumatoid arthritis (RA), spondyloarthritis (SpA), psoriatic arthritis (PsA), crystal-induced arthritis (CIA), connective tissue diseases (CTD), vasculitis and auto-inflammatory diseases), and to DMD (i.e., mainly conventional DMARDs, biologics and targeted synthetic DMARDs).

**Results:** After screening 1131 publications and 194 other documents, 231 relevant papers were analysed for measuring adherence (60% in RA, 8% in SpA, 6% in PsA, 11% in CIA and 15% in CTD), 117 for predicting non-adherence (55% in RA, 9% in SpA, 14% in gout and 22% in CTD) and 22 for improving adherence (72% in RA, 8% in SpA, 16% in systemic lupus and 4% in gout). Objective measurements of non-adherence included: delivery data (total number of use: n=92), pill counts (n=8), medication event monitoring system (n=9), blood level assessments (n=7). Subjective measurements included: patient global assessment (n=57), and 4 questionnaires. The most used questionnaire was the Morisky Medication Adherence Scale and the most widely validated in rheumatology were the Compliance Questionnaire on Rheumatology and the Medication Adherence Self-report Inventory. Around 100 predictive factors were identified. Polymedication, mood disorders, lack of information and poor physician-patient relationship were associated with lower adherence. Regarding management options for non-adherence, 13/22 studies were randomised controlled trials (1535 patients) and only 5 (38%) were positive (774 patients). Educational interventions were the most represented with the highest level of evidence: 8/13 trials (1017 patients) with 4/8 yielding positive results.

**Conclusions:** Despite the importance of medication adherence in CIRDs, this review revealed limitations in methods to measure non-adherence, a multiplicity of non-adherence risk factors and a relative lack of evidence on interventions to improve medication adherence. It's important to improve the assessment and optimisation of adherence in CIRDs.

**Acknowledgements:** AbbVie France funded this initiative but played no role in the points to consider.

**Disclosure of Interest:** None declared

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SAT0692

#### BREASTFEEDING IS NOT ASSOCIATED WITH ANTI-CITRULLINATED ANTIBODIES DEVELOPMENT IN INDIVIDUALS AT RISK FOR RHEUMATOID ARTHRITIS

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**Background:** 'Systemic autoimmunity associated with rheumatoid arthritis' (RA), is a pre-clinical stage preceding the onset of clinical RA, characterised by the presence of autoantibodies, such as anti-citrullinated protein antibodies (ACPA) or anti-carbamylated protein antibodies (antiCarP). Breastfeeding has been proposed as a protective factor for RA development,<sup>1</sup> but there are some controversies.<sup>2</sup> To establish the causal role of a putative risk factor, longitudinal studies are needed, in particular in the pre-stages of RA development.

**Objectives:** To study the association between breastfeeding and the development of systemic autoimmunity associated with RA.

**Methods:** This ongoing prospective study includes individuals genetically at risk of developing RA, namely first-degree relatives of RA patients (RA-FDR). Individuals without clinical evidence of RA were enrolled, and assessed yearly clinically and biologically. We included all RA-FDR women with available ACPA status (anti-CCP 2, 3.1 or 3.0) and information about breastfeeding. The primary outcome was ACPA positivity. The exposure of interest was breastfeeding and duration of breastfeeding (categorised as 0, 1–7 and ≥7 months). The presence of antiCarP was a secondary outcome. We used logistic regression to analyse univariable and multivariable associations.

**Results:** A total of 882 women were included, of which 57 (6%) were ACPA positive. The characteristics of ACPA positive and negative participants were balanced, except for an older age in ACPA positives (median 52 versus 45 years; table 1). In the univariable analysis, ACPA positivity was not significantly associated with breastfeeding (OR 1.5, p=0.16) or with breastfeeding duration (OR=1.8, p=0.14). In the multivariable analysis adjusted by age, smoking, number of pregnancies and years of education, there was a weak, but not significant, association between breastfeeding for more than 7 months and ACPA positivity (OR 2.16, p=0.10). Among 728 women with available antiCarP results, 70 (10%) were positive, of which 27 (40%) breastfed. Breastfeeding for more than 7 months was not significantly associated with antiCarP in univariable or multivariable analyses (OR 1.3, p=0.52 and OR 1.9, p=0.16, respectively).

**Abstract SAT0692 – Table 1.** General characteristics of RA-FDR women, n=882

Table 1. General characteristics of RA-FDR women, n=882		
	ACPA (+)	ACPA (-)
	57 (6%)	825 (94%)
<b>General characteristics</b>		
Age, years, median (IQR)	52 (47-60)	45 (34-54) *
Education, years, median (IQR)	14 (13-16)	14 (13-15)
Caucasian, n(%)	51 (90)	770 (93)
Body mass index, kg/m <sup>2</sup> , median (IQR)	24 (21-27)	23 (21-26)
Ever smoking, n(%)	32 (56)	378 (46)
Alcohol consumption, n (%)	43 (75)	651 (79)
Rheumatoid factor, n(%)	11 (19)	123 (15)
<b>Reproductive characteristics</b>		
Parous women, n(%)	38 (67)	465 (56)
Number of pregnancies, median (IQR)	2 (2-2)	2 (2-2)
Breastfeeding, [yes/no] n(%)	31 (54)	371 (45)
Breastfeeding, months, median (IQR)	1 (0-4)	0 (0-3)
0 month	26(46)	455(55)
1-7 months	22(39)	284(34)
≥7 months	9 (16)	86(10)

\*p-value &lt;0.05, univariable logistic regression.

**Conclusions:** Among women at risk of RA, breastfeeding was not associated with the presence of ACPA or antiCarP. Our results do not support a protective role of breastfeeding in the development of systemic autoimmunity associated with RA.

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**Disclosure of Interest:** None declared**DOI:** 10.1136/annrheumdis-2018-eular.5720
**SAT0693 GENETIC POLYMORPHISMS AND EFFICACY OF METHOTREXATE IN RHEUMATOID ARTHRITIS**

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**Background:** Methotrexate (MTX) is the DMARD of choice in the treatment of rheumatoid arthritis (RA). There is important variability in its therapeutic response. The identification of genetic factors related to the absorption, metabolism and action of MTX may facilitate a more efficient use.

**Objectives:** To study the effect of clinical characteristics and different single nucleotide polymorphisms (SNPs), related to the transport and metabolic pathways of MTX, on the therapeutic response of MTX in monotherapy in RA patients.

**Methods:** Observational study. Outcome variable: response to MTX (DAS-PCR <3.2). Study factors: SNPs of transport (ABCB1 C3435T), glutamine (GGH T16C and FPG G2782A), transmethylation (MTHFR C677T and MTHFR A1298C) and adenosine (AMPD1 C34T, ADA A534G, ITPA C94A). The association between SNPs and therapeutic response was analysed by logistic regression, assessing the allele independence (Hardy-Weinberg equilibrium) and interaction by sex. Different models of SNPs inheritance were analysed. Models were adjusted by the characteristics of the patient, of disease and of treatment. The haplotypes of the MTHFR SNPs (C677T and A1298C) were also analysed.

**Results:** Bivariate analysis showed lower probability of response with smoking (OR=0.37), erosions (OR=0.26), Mantoux (OR=0.20), disease activity (OR=0.08), previous DMARDs (OR=0.46) and doses of folic acid (OR=0.97), MTX (OR=0.87) and prednisone (OR=0.93), with higher response at a higher age at diagnosis (OR=1.05). In relation to the SNPs, the C/A genotype of the ITPA\_C94A decreases the probability of response (OR=0.48) according to an overdominant inheritance model, and the C/C genotype of MTHFR\_A1298C is also associated with a lower response according to a model of recessive inheritance (OR=0.18). An interaction between the GGH\_T16C SNP and sex was observed, so that the C/C genotype increases the possibility of response in women (OR=2.95), but not in men.

In the adjusted models, only the effect of genotype C/C of MTHFR\_A1298C is maintained (OR=0.14), irrespective of age, sex, smoking, alcohol, RF, anti-CCP, erosions, extra-articular manifestations, Mantoux, DAS28-CRP, previous

DMARDs, time to MTX, doses of folic acid, prednisone, MTX and route of administration. On the contrary, the association between the ITPA-C94A polymorphism and the response was not maintained nor the interaction effect of the C/C genotype of GGH\_T16C observed in bivariate analysis. Finally, the CC haplotype of the combination MTHFR C677T and MTHFR A1298C is associated with a decrease in the response (OR=0.55) in the adjusted models, so it is an effect independent of the control variables. No interaction effects were observed by sex.

**Conclusions:** Genetic polymorphisms related to the transport and metabolism of MTX have little effect on the therapeutic response, or at least much lower than other patient (smoking), disease (activity, erosions), or treatment (number of previous DMARDs) characteristics.

**Disclosure of Interest:** None declared**DOI:** 10.1136/annrheumdis-2018-eular.3047
**SAT0694 DETERMINANTS OF TRAJECTORIES OF MULTI-SITE PAIN IN KNEE OSTEOARTHRITIS: A 10.7-YEAR PROSPECTIVE STUDY IN OLDER ADULTS**

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**Background:** Pain in osteoarthritis (OA) is very common especially in elderly and commonly occurs at multiple sites. Multi-site pain (MSP) has been shown to be associated with more severe symptoms and worse health-related quality of life compared to single-site pain. Limited evidence exists about understanding the course of MSP and its determinants.

**Objectives:** To identify distinct trajectories of MSP over 10.7 years in an older population, and to examine risk factors for identified trajectories.

**Methods:** 1099 participants (mean age 63 years) from the population-based Tasmanian Older Adult Cohort study were recruited at baseline. 875, 768 and 563 participants attended years 2.6, 5.1 and 10.7 follow-up, respectively. Demographic, psychological, lifestyle and comorbidities data were obtained at baseline. Knee radiographic OA was assessed by X-ray at baseline. Group-based trajectory modelling was applied to identify distinct trajectories of MSP. Multi-nominal logistic regression was used for the analyses with adjustment for potential confounders.

**Results:** Three distinct MSP trajectories were identified: a group of participants with 'no MSP' (11%), a group with 'fluctuating MSP' (38%), and a group with 'persistent MSP' over time (51%). In multivariable analyses with the 'no MSP' trajectory as reference, emotional problems and comorbidity were significantly associated with both 'fluctuating MSP' and 'persistent MSP' trajectory. In addition, female sex, being obese and radiographic knee OA predicted the trajectory of 'persistent MSP' in the whole population. Results were similar with emotional problems (relative risk [RR]: 2.57 for 'fluctuating MSP' and 5.70 for 'persistent MSP', both p<0.05), being obese (RR: 3.80 for 'persistent MSP', p=0.007) and comorbidity (RR: 2.45, p=0.010) in either 'fluctuating MSP' or 'persistent MSP' trajectory in those with radiographic knee OA.

**Conclusions:** MSP trajectories appear stable once established and can be predicted by factors both peripheral and central in origin.

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**SAT0695 HOSPITALISATION RATES AMONG PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME: A POPULATION-BASED STUDY, 1995–2016**

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**Objectives:** To determine rates and primary discharge diagnoses of hospitalisation in a cohort of patients with incident primary Sjögren's syndrome (pSS) compared to the general population.

**Methods:** This was a retrospective population-based cohort study focused on Olmsted County, Minnesota. The pSS cohort consisted of patients with incident pSS in the 1976–2015 period and was compared with a cohort of individuals without pSS matched 3:1 for age, sex and calendar year, randomly selected from the same population. Hospitalizations in 1995–2016 were examined. Discharge diagnoses were categorised using the Clinical Classifications Software for ICD-9-CM.

**Results:** A total of 385 hospitalizations occurred in the 160 patients with pSS during 1592 person-years of follow-up. Among 466 comparators, there were 899 hospitalizations during 4660 person-years of follow-up, resulting in a significantly higher rate of hospitalizations in patients with pSS (rate ratio [RR]:1.25, 95% CI:1.11–1.41). Rates of hospitalisation were increased among patients with pSS for endocrine, nutritional and metabolic diseases and immunity disorders

(RR:1.82, 95% CI:1.08–2.98), diseases of the musculoskeletal system and connective tissue (RR:1.49, 95% CI:1.05–2.05), and for injuries and poisoning (RR:1.46, 95% CI:1.01–2.06). While not significantly increased overall, hospitalizations for diseases of the circulatory system were significantly increased in patients with pSS aged  $\geq 75$  years (RR:1.54, 95% CI: 1.11–2.11).

**Conclusions:** Patients with pSS experienced higher rates of hospitalisation than the general population. Hospitalizations for endocrine/metabolic disorders, diseases of the circulatory system, diseases of the musculoskeletal system and connective tissue disorders, and injuries were more common among patients with pSS than comparators.

**Disclosure of Interest:** None declared

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SAT0696

#### ASSOCIATIONS BETWEEN ANTIBIOTICS FOR NON-TUBERCULOUS MYCOBACTERIAL INFECTION AND INCIDENT SJÖGREN'S SYNDROME: A NATIONWIDE, POPULATION-BASED CASE-CONTROL STUDY

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**Background:** We recently reported an association between Sjögren's syndrome (SS) and prior nontuberculous mycobacterial (NTM) infection which was defined as having a diagnosis of NTM with concurrent combinational antibiotics therapy for NTM infection. However, whether the increased risk of SS was attributed to NTM infection or antibiotics used to treatment NTM infection was unknown.

**Objectives:** To address the association between use of antibiotics which can be used to treat NTM infection and the risk of newly diagnosed SS.

**Methods:** Using a nationwide, population-based, claims dataset, 5751 newly diagnosed SS were identified, and we further excluded those (n=198) having a history of confirmed or suspected mycobacterial infection to avoid the confounding effect of NTM infection-associated incident SS as we previously identified. A total of 5,553 SS cases were enrolled and compared them with 83 295 non-SS controls matched (1:15) for age, sex, and their year of first SS diagnosis date. The association between the risk of incident SS and antibiotics was determined by calculating odds ratios (ORs) with 95% confidence intervals (CIs) using conditional logistic regression analysis.

**Results:** After adjusting for potential confounders, the risk of SS was increased in patients treated with new macrolides (aOR 1.95, 95% CI 1.80–2.11), fluoroquinolones (aOR 1.52, 95% CI 1.41–1.64), and tetracyclines (aOR 1.69, 95% CI 1.59–1.79) compared with those in non-SS controls after adjusting for CCI, bronchiectasis and *Helicobacter pylori* infection. Notably, we found that the association was consistent among each antibiotic in these three groups of antibiotics. In contrast to these three groups of antibiotics, usage of amikacin was found to have a negative association with incident SS (aOR 0.68, 95% CI 0.53–0.87).

	Model A	Model B
	aOR (95% CI)	aOR (95% CI)
<b>New macrolide</b>		1.95 (1.80–2.11)
Clarithromycin	1.84 (1.69–2.01)	
Azithromycin	2.07 (1.71–2.51)	
<b>Aminoglycoside</b>		0.68 (0.53–0.87)
Amikacin	0.58 (0.41–0.81)	
Streptomycin		
Kanamycin	0.83 (0.58–1.19)	
<b>Fluoroquinolone</b>		1.52 (1.41–1.64)
Ofloxacin	1.15 (1.01–1.32)	
Ciprofloxacin	1.34 (1.17–1.54)	
Levofloxacin	1.50 (1.22–1.85)	
Moxifloxacin	1.43 (1.30–1.56)	
<b>Tetracycline</b>		1.69 (1.59–1.79)
Doxycycline	1.59 (1.49–1.70)	
Minocycline	1.48 (1.35–1.62)	

**Conclusions:** New macrolides, fluoroquinolones and tetracyclines were associated with a higher incidence of SS, whereas usage of amikacin had a negative correlation. These findings indicated the need for vigilance of SS in prescribing

these antibiotics to treat NTM and other infectious diseases and warrant further mechanistic studies.

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**Disclosure of Interest:** None declared

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SAT0697

#### ASSOCIATION BETWEEN TONSILLITIS AND NEWLY DIAGNOSED ANKYLOSING SPONDYLITIS: A NATIONWIDE, POPULATION-BASED, CASE-CONTROL STUDY

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**Background:** To date, two most commonly proposed environmental risk factors for ankylosing spondylitis (AS) include mechanical stress at the enthesis and infections. A recent Swedish study showed that childhood tonsillitis was associated with future development of AS. However, no Asian study has reported this association.

**Objectives:** To investigate the association between tonsillitis and the risk of newly diagnosed AS.

**Methods:** We used 2003–2012 data from the Taiwanese National Health Insurance Database to perform a nationwide, population-based, case-control study. We identified AS patients newly diagnosed from 2005 to 2012 as the study group and selected sex, age and the year of index date matched (1:6) non-AS individuals as controls. Using conditional logistic regression analysis after adjustment for potential confounders, including a history of periodontitis, appendicitis, and Charlson comorbidity index (CCI), we measured the association of AS risk with prior tonsillitis by calculating odds ratios (ORs) with 95% confidence intervals (CIs). Sensitivity analyses for the association between AS risk and tonsillitis were conducted by varying the definition of tonsillitis.

**Results:** We identified 37 002 incident AS cases and 2 22 012 matched non-AS controls. The risk of AS was associated with tonsillitis (OR, 1.80; 95% CI, 1.55–2.10) after adjustment for potential confounders. The association between AS risk and a history of tonsillitis remained significant by using various definitions of tonsillitis based on ICD9-CM Codes. Such associations were consistent across various subgroups stratified by age, sex, and a history of periodontitis or appendicitis.

**Conclusions:** The present study reveals an association between AS risk and prior tonsillitis.

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SAT0698

#### MORTALITY OF PATIENTS WITH DIAGNOSED RHEUMATOID ARTHRITIS (RA) IN GERMANY 2012: ANALYSIS OF CLAIMS DATA FROM 60 MILLION PEOPLE

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**Background:** Mortality data of RA patients in Germany are sparse. Recently, data on the prevalence and incidence of RA comprising about 75% of the German population became available.<sup>1</sup> In case of chronic diseases, it is possible to



**Abstract SAT0697 – Table 1.** Conditional logistic regression analyses for the association between covariates with AS risk

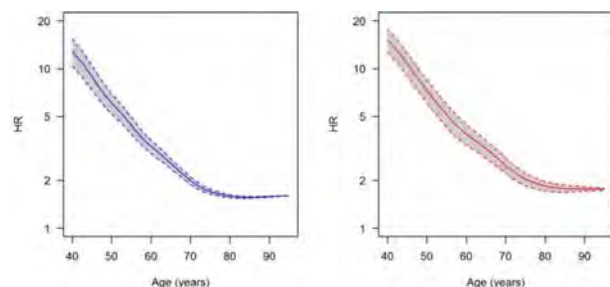
Covariate	Univariate	Multivariable	Multivariable	Multivariable	Multivariable	Multivariable	Multivariable	Multivariable
	analysis OR (95% CI)	aOR (95% CI)	aOR (95% CI)	aOR (95% CI)	aOR (95% CI)	aOR (95% CI)	aOR (95% CI)	aOR (95% CI)
Tonsillitis	1.96 (1.68–2.28)	1.80 (1.55–2.10)						
Chronic tonsillitis and adenoiditis	1.99 (1.38–2.86)		1.83 (1.26–2.64)					
Acute tonsillitis	1.96 (1.67–2.31)			1.81 (1.53–2.13)				
Tonsillectomy	1.89 (1.36–2.61)				1.66 (1.19–2.31)			
Tonsillitis with tonsillectomy	2.06 (1.33–3.19)					1.90 (1.22–2.97)		
Chronic tonsillitis and adenoiditis with tonsillectomy	1.90 (1.19–3.03)						1.73 (1.08–2.79)	
Acute tonsillitis with tonsillectomy	4.00 (1.13–14.18)							4.10 (1.15–14.63)
Periodontitis	1.42 (1.38–1.45)	1.32 (1.29–1.36)	1.32 (1.29–1.36)	1.32 (1.29–1.36)	1.32 (1.29–1.36)	1.32 (1.29–1.36)	1.32 (1.29–1.36)	1.32 (1.29–1.36)
CCI $\geq 1$	2.22 (2.15–2.29)	2.19 (2.12–2.26)	2.19 (2.13–2.26)	2.19 (2.12–2.26)	2.19 (2.12–2.26)	2.19 (2.13–2.26)	2.19 (2.13–2.26)	2.19 (2.13–2.26)
Appendicitis	1.36 (1.19–1.56)	1.31 (1.14–1.50)	1.31 (1.15–1.50)	1.31 (1.15–1.50)	1.31 (1.15–1.50)	1.31 (1.15–1.50)	1.31 (1.15–1.50)	1.31 (1.15–1.50)

estimate excess mortality of diseased people compared to non-diseased people if prevalence and incidence are known.

**Objectives:** To compute the mortality in RA patients in comparison to the population without RA in Germany, utilising claims data from 60 million people.

**Methods:** We used a mathematical relation between the age-specific prevalence, incidence and mortality to estimate the age- and sex-specific hazard ratio (HR) of mortality rates for patients with diagnosed RA compared to patients without RA.<sup>2</sup> Standardised mortality ratios (SMRs) for men and women were calculated using the sex-specific age distributions in Germany in 2012. In addition, we calculated years of lost life (YLL) for men and women aged 40 and 60 years with diagnosed RA.

**Results:** Estimation of sex-specific HR in the age range of 40 to 95 years is possible from the data in.<sup>1</sup> The age-specific HRs are elevated in both male and female RA patients (figure 1, left panel and right panel, respectively) with a particular increase in the younger. SMRs in the age range of 40 to 95 are 1.93 and 2.15 for men and women, respectively. YLL at age 40 are 12.0 and 7.5 years for men and women with RA, respectively. The associated YLLs at age 60 are 5.2 and 4.7 years.



**Abstract SAT0698 – Figure 1.** Age-specific HR for men (left) and women (right) in Germany 2012. Grey regions indicate the range of possible values.

**Conclusions:** Despite the limitation of the data source (claims data), an estimation of excess mortality in terms of the HR is possible and yields plausible results. The obtained SMRs are similar to comparable populations.<sup>3</sup> At age 40 men with RA suffer more from reduced life expectancy than women with RA. At age 60 the difference in YLL between men and women with RA is virtually vanished.

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#### SAT0699 PREDICTION OF CARDIOVASCULAR EVENTS IN RHEUMATOID ARTHRITIS PATIENTS USING A MULTI-BIOMARKER OF DISEASE ACTIVITY

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**Background:** The ACC/AHA recommends preventive strategies for patients with a high predicted risk of atherosclerotic cardiovascular disease (CVD). RA patients are at higher risk for CVD events, yet the role of systemic inflammation and the influence of traditional CVD risk factors is unclear with respect to risk prediction in RA.

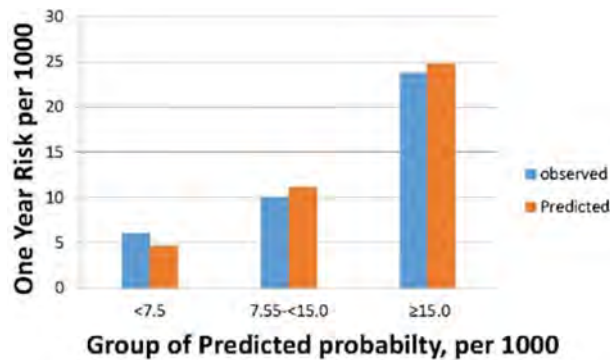
**Objectives:** A simple and accurate algorithm for predicting CVD event risk that includes systemic inflammation might help risk assessment for RA patients and optimise preventive care.

**Methods:** We derived a U.S. cohort of RA patients with multi-biomarker disease activity (MBDA) test results linked to Medicare claims data. Patients had to have  $\geq 1$  year baseline with Medicare coverage prior to the first MBDA test. Exclusions were past MI, PCI/CABG, stroke, or cancer. Follow-up ended at the earliest of 1) CVD event; 2) other than CVD cause of death; 3) loss of coverage; or 4) 12/31/2014. The composite CVD event comprised of incident MI, stroke or fatal CVD event, using validated algorithms. MBDA scores were grouped as low ( $<30$ ), moderate,<sup>30–44</sup> and high ( $>44$ ). Other predictors included demographics, healthcare utilisation, and comorbidities. Three separate models were developed using Cox regression. Model 1 included age, sex and race. Model 2 included age, sex, race, 9 comorbidities and CVD medication classes, plus interaction terms. Model 3 included age, sex, and race plus categorised MBDA score. We calculated the net reclassification index (NRI) for model 2 and 3 compared to model 1. We also plotted the observed vs. predicted probability of CVD event for each model, with risk categorised as low ( $<7.5$ ), moderate (7.5– $<15$ ) and high ( $\geq 15$ ) per 1000 person-years based upon annualised ACC/AHA cutpoints.

**Results:** A total of 15,757 RA patients were included; mean (SD) age 68.6 (10.8) years, 80% female, 80% white. A total 209 CVD events occurred in 14 843 person years (1.41/100 py). The median (IQR) follow up time was 0.84 (0.41, 1.27) year. The maximum event time was at 2.7 year. All models had reasonable discrimination and calibration; model 3 was better than models 1 and 2 and observed vs predicted risk is shown (figure 1). The sum of the absolute difference between observed and predicted probability was 0.56, 0.57 and 0.33 for models 1, 2 and 3 respectively.

Compared to model 1, model 2 resulted in a positive overall NRI of 0.214 (non-event NRI=0.173, event NRI=0.041); model 3 resulted in positive overall NRI of 0.279

(non-event NRI=0.092, event NRI=0.187), consistent with more accurate CVD event classification.



**Abstract SAT0699 – Figure 1.** Observed vs. Predicted One-Year CVD Risk per 1000 person-years in RA Patients, using only Age, Sex, Race, and MBDA score (Model 3)

**Conclusions:** Preliminary results from this analysis suggest that a simple algorithm consisting only of age, sex and race plus a multi-biomarker score can provide an accurate method to predict short term CVD risk in RA. Further validation with more extended time frames should improve the utility of this approach.

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SAT0700

#### THE RELATIONSHIP BETWEEN MUSCULOSKELETAL PAIN, INFLAMMATION AND DEPRESSION IN MEN

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**Background:** Up to 40% of persons with musculoskeletal (MSK) pain report depression. High sensitivity C-reactive protein (hsCRP), a sensitive marker of chronic low grade inflammation, is elevated in persons with MSK pain when compared to those who are pain free, and in those with MSK pain is positively associated with increasing pain severity. High levels of hsCRP are also associated with depression. Whether hsCRP is the mechanism linking MSK pain to depression has not been tested.

**Objectives:** To test the hypothesis that MSK pain predicts depression and the relationship would at least in part be explained by hsCRP.

**Methods:** 3309 men aged 40–79 in the multicentre European Male Ageing Study completed a postal questionnaire asking about MSK pain (classified as chronic widespread pain<sup>American College of Rheumatology 1990</sup> criteria) (CWP), some pain that was not CWP (SP), or no pain (NP) and depression (Beck Depression Inventory-II (BDI-II), score range 0–21). At a research clinic, fasting morning blood samples were shipped to one Centre where hsCRP was measured using a solid-phase, chemiluminescent immunometric assay with a sensitivity of 0.01 mg/dL. Covariates were date of birth, education level, body mass index (BMI), tobacco use, and frequency of alcohol consumption. Participants were followed up (mean 4.4 (SD 0.3) years) and completed the BDI-II. Linear regression tested the association between baseline pain and follow up BDI score (outcome), with adjustments for age, centre and baseline BDI. In a final model hsCRP and covariates were added and the impact on the relationship between pain and BDI-II examined. Results are expressed as  $\beta$  coefficients with 95% confidence intervals (CI).

**Results:** 2404 (72.7%) men had complete baseline and follow-up data. At baseline 1003 (41.7%) reported NP, 1205 (50.1%) SP, and 196 (8.2%) CWP. Mean (SD) age was 59.3 (10.6), CRP 0.41 (0.74) mg/l, and BDI 6.6 (6.2). Mean BMI was 27.8 (10.6), 30.1% were current smokers, 23.6% drank alcohol 5–7 days/week and 53.9% had gone on to further education. After adjusting for age, Centre and baseline BDI-II when compared to those with NP having SP ( $\beta=0.7$ , 95% CI (0.3, 1.1)) or CWP (1.3 (0.5, 2.0)) at baseline was associated with higher BDI-II scores at follow-up. Baseline hs-CRP did not predict follow up BDI-II (0.05 (-0.2, 0.3)). The relationship between SP (0.7 (0.2, 1.1)) or CWP (1.5 (0.7, 2.3)) and follow up BDI-II persisted after adjustment for hs-CRP and all covariates.

**Conclusions:** The excess rate of depression in men with MSK pain remains to be explained. A broader assessment of inflammatory markers (e.g. TNF- $\alpha$ , Interleukins, and IFN- $\gamma$ 1) may identify mechanisms linking MSK pain with subsequent depression.

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**Disclosure of Interest:** None declared

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SAT0701

#### PREGNANCY OUTCOME IS IMPROVED AND SIMILAR TO THAT OF THE GENERAL OBSTETRIC POPULATION IN PATIENTS WITH RHEUMATOID ARTHRITIS WHO FOLLOW THE “IDEAL CLINICAL PATHWAY” BEFORE AND DURING PREGNANCY

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**Background:** With the therapeutic advances of the last decades yielding to stable disease remission in the majority of patients, the goal of a successful pregnancy appears to be attainable for women affected by Rheumatoid Arthritis (RA). However, individual risk stratification and measures to minimise it (e.g. withdrawal and wash-out of teratogenic drugs) are essential for the management of pregnancy in RA.<sup>(1)</sup>

**Objectives:** This analysis aims to evaluate the adherence to a reference clinical pathway of diagnostic, pharmacological and follow-up management in women with RA, and the influence of the adherence to this pathway on the outcome of pregnancy.

**Methods:** Data were extracted from the Lombardy Region's (Italy) health databases for the period between 2004–2013. Patients with RA were identified through the chronic disease certification by rheumatologist (ICD9-CM code 714.0). Among these, women between the ages of 18 and 51 were selected. Data of controls from general population were also extracted. Conception has been approximated from the date of delivery or abortion. Seven healthcare quality indicators have been constructed: 1) screening of blood chemistry tests, 2) pre-conception musculoskeletal imaging, 3) pre-pregnancy antiphospholipid antibody tests, 4) ANA test and anti-ENA (antiRo/SSA) test, 5) no exposure or wash-out from teratogenic drugs (MTX/LEF); 6) no exposure to biological drugs; 7) rheumatological follow-up in outpatient visits. These 7 indicators were then summarised in 3 pathway indicators: 1) diagnostic pathway, 2) therapeutic pathway, 3) follow-up. The pregnancy outcome was defined on the basis of the DRG of complicated birth or abortion. Subanalysis on abortion was also done. The relationship between quality indicators and outcome variables was analysed using logistic models crude and adjusted for age and comorbidities, and the results presented as odds ratios (OR) and 95% confidence intervals (95% CI).

**Results:** 443 pregnancies of patients with RA were identified, with median age of 34 (IQR 31–37), median disease duration at conception of 3.8 years (IQR 1.83–6.19), 157 (35.4%) of which with unfavourable outcome pregnancy outcome, of which 115 pregnancy losses. The increase or decrease of risk for those who meet specific quality indicators and pathway indicators showed a better outcome for patients screened for autoantibodies and with no exposure or washout from MTX/LEF (Table). The comparisons of those who followed the ideal pathway or not compared to the general population showed a significant increase of risk only for patients not following the ideal pathway (Table).

Clinical pathway indicator	Overall Adjusted OR(95%CI)	Abortion Adjusted OR(95%CI)
Blood chemistry tests	0.99 (0.47-2.11)	0.78 (0.36-1.70)
Imaging	1.09 (0.72-1.65)	1.14 (0.72-1.81)
antiphospholipid antibody tests	0.56 (0.37-0.85)	0.34 (0.20-0.56)
ANA or anti-ENA	0.64 (0.42-0.96)	0.43 (0.27-0.68)
No exposure or wash out of MTX/LEF	0.52 (0.31-0.86)	0.44 (0.25-0.75)
No exposure to biological drugs	Not estimable	Not estimable
Rheumatological follow-up in outpatient visits	0.85 (0.56-1.28)	0.65 (0.40-1.04)
Diagnostic pathway	1.05 (0.46-2.38)	0.84 (0.36-1.98)
Therapeutic pathway	0.48 (0.29-0.80)	0.44 (0.25-0.75)
Follow-up	0.85 (0.56-1.28)	0.65 (0.40-1.04)
Ideal pathway	0.59 (0.37-0.95)	0.38 (0.21-0.67)
General population	Reference	Reference
Ideal pathway	0.89 (0.57-1.37)	0.70 (0.40-1.23)
No ideal pathway	1.48 (1.12-1.95)	1.81(1.31-2.49)

**Conclusions:** The optimal management of pregnancy (stratification of pre-conceptional obstetric risk, modulation of therapy) in women with RA is associated with a reduced risk of unfavourable pregnancy outcome, bringing back that risk to that expected for a general obstetric control population.

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- [1] Götestam Skorpen C, et al. The EULAR points to consider for use of anti-rheumatic drugs before pregnancy, and during pregnancy and lactation. *Ann Rheum Dis* 2016 May;75(5):795–810.

**Disclosure of Interest:** None declared

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#### SAT0702 INFLUENCE OF OBESITY AND GENDER ON DRUG EFFECTIVENESS IN RHEUMATOID ARTHRITIS DEPENDS ON THE OUTCOME CONSIDERED

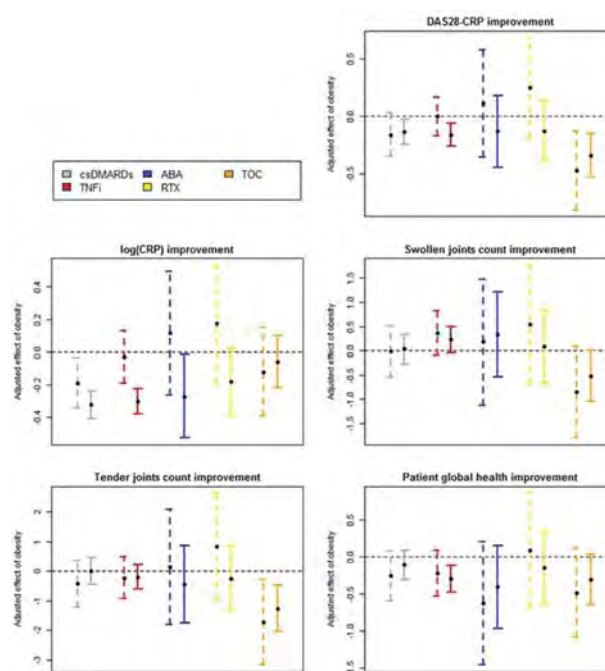
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**Background:** While effectiveness of TNF inhibitors (TNFi) and, to some extent, tocilizumab (TOC), has been shown to be affected by obesity in patients with rheumatoid arthritis (RA), no such effect has been found for abatacept (ABA) and rituximab (RTX). Also, it remains unresolved whether gender is an effect modifier for obesity, e.g. due to different body fat distributions in men and women.

**Objectives:** Assess whether obesity affects drug effectiveness of common DMARDs, taking into account potential differences between sexes. As measures for effectiveness, the degree of improvement regarding DAS28-CRP as well as its components after 6 months of treatment were considered.

**Methods:** Data of 8,623 RA patients included since 2009 in the German observational cohort study RABBIT were analysed. Patients had to have a BMI  $\geq 18.5$  and at least 6 months of follow-up. Multiple imputation of missing values in outcomes was performed. The influence of obesity (BMI  $\geq 30$ ) on drug effectiveness was investigated by multiple linear regression, adjusting for age, baseline value of the outcome of interest, disease duration, prior bDMARD failure, glucocorticoid therapy, number of comorbidities, joint erosions, autoantibody status, and smoking habits.

**Results:** At baseline, obese patients were comparable to others in age (both mean 58 years) and gender (women: 75% vs. 74%). They were less likely to be seropositive (66% vs. 75%), had less erosions (40% vs. 52%) but more often  $\geq 3$  comorbidities (43% vs. 30%). With the exception of infliximab, around 90% of patients or more received the recommended drug dosage regardless of their weight (assuming a tolerance interval for norm in case of weight-dependent infliximab and tocilizumab dosages). For women treated with TNFi or csDMARDs as well as for patients treated with TOC, obesity had a negative influence on the improvement in DAS28-CRP after 6 months of treatment (figure 1). With the exception of patients treated with TOC, this influence seemed to be caused mostly by inflammation, while for joint swelling or pain no associations were observed. Men and women treated with TNFi differed significantly regarding the effect of obesity on the improvement of log(CRP) values.



**Abstract SAT0702 – Figure 1.** Influence of obesity on the RA disease course regarding the improvement in DAS28-CRP and its components after 6 months of treatment, as assessed by multiple linear regression. Shown are point estimates and 95% confidence intervals for obesity effects, separately for men (left, dashed line) and women (right, solid line) in five treatment groups.

**Conclusions:** The influence of obesity on drug effectiveness depends on the considered outcome and, to some extent, on gender. It may therefore be worthwhile to assess it separately for men and women.

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#### SAT0703 RACIAL DISPARITIES IN GOUT AND HYPERURICEMIA – A UNITED STATES GENERAL POPULATION STUDY

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**Background:** Although African-Americans (AAs) have a higher prevalence of risk factors for gout and hyperuricemia (e.g., hypertension, obesity, and chronic kidney disease [CKD]) than Whites, data on their disease burden of gout and hyperuricemia remains scarce.

**Objectives:** To examine potential racial/ethnic disparities in the prevalence of gout and hyperuricemia, using a nationally-representative sample of United States (US) adults over the past 10 years (The National Health and Nutrition Examination Survey [NHANES] 2007–16).

**Methods:** Using data from 26 332 participants aged  $\geq 20$  years (13 539 females and 12 793 males) from NHANES 2007–16, we calculated the age-standardised prevalence of gout and hyperuricemia by race/ethnicity. Gout was defined by report of a diagnosis by a health professional, and hyperuricemia as a serum urate  $>7.0$  mg/dL (0.42 mmol/L) from participants' blood samples. Logistic regression was used to adjust for covariates, while taking into account clusters and strata of the complex survey design of NHANES.

**Results:** The age-standardised prevalence of gout was 3.7% for Whites and 4.7% for AAs, with the age-standardised prevalence of hyperuricemia being 12.7% and 14.9% for Whites and AAs, respectively. Compared to Whites, AAs had a 65% higher odds of gout among females (age-adjusted OR, 1.65; 95% CI, 1.14 to 2.38) and a 31% higher odds of gout among males (age-adjusted OR,



1.31; 95% CI, 1.05 to 1.63). Further adjustment by body-mass index (BMI) attenuated these associations to non-significance for both sexes (table 1). AA females had a higher odds of hyperuricemia than White females (age-adjusted OR, 2.17; 95% CI, 1.72 to 2.73), but not males (age-adjusted OR, 1.08; 95% CI, 0.95 to 1.22; *P* for interaction=0.002) (table 1). Among females, this association attenuated after further adjustment for BMI, hypertension, CKD, type 2 diabetes mellitus, household income, and education, but remained significant (adjusted OR, 1.52; 95% CI, 1.19 to 1.95).

**Abstract SAT0703 – Table 1.** ORs of Gout and Hyperuricemia According Race/Ethnicity, NHANES 2007–16

	Gout		Hyperuricemia	
	Age-adjusted OR (95% CI)	Age and BMI-adjusted OR (95% CI)	Age-adjusted OR (95% CI)	Age and BMI-adjusted OR (95% CI)
<b>Female</b>				
White	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
African American	1.65 (1.14–2.38)	1.33 (0.92–1.92)	2.17 (1.72–2.73)	1.62 (1.27–2.05)
<b>Male</b>				
White	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
African American	1.31 (1.05–1.63)	1.24 (1.00–1.53)	1.08 (0.95–1.22)	1.02 (0.89–1.17)

**Conclusions:** These nationally-representative data indicate that AAs have a larger disease burden of gout and hyperuricemia than Whites, particularly among women. This burden appears to be at least partly due to a higher prevalence of risk factors for hyperuricemia in AAs.<sup>1</sup>

#### REFERENCE:

[1] Flegal KM, et al. *JAMA* 2016 Jun 7;315(21):2284–2291.

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#### SAT0704 COLLECTION OF ANTI-RHEUMATIC MEDICATION DATA FROM BOTH PATIENTS AND RHEUMATOLOGISTS SHOWS STRONG AGREEMENT IN A REAL WORLD CLINICAL COHORT: RESULTS FROM THE ONTARIO BEST PRACTICES RESEARCH INITIATIVE (OBRI)

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**Background:** Collection of Anti-Rheumatic Medication (ARM) information from both patients and rheumatologists is considered a strength for Rheumatoid Arthritis (RA) registries and cohorts. However, it is important to assess the agreement between these two data sources.

**Objectives:** We aimed to examine the agreement of ARM use, their administration routes, and start and stop dates between self-reports and rheumatologist reports in the Ontario Best Practices Research Initiative (OBRI).

**Methods:** Adult Patients enrolled in the OBRI who consented to both patient interviews and rheumatologist evaluations were included. Patients in the OBRI are interviewed every six months, while rheumatologist assessments are conducted as per routine care. For this analysis, we included patients who enrolled in OBRI on or after Sep 1 st 2010 and compared ARM use reports where rheumatologist visits and interviews occurred within 60 days of each other. ARM included conventional synthetic Disease-Modifying Antirheumatic Drugs (csDMARDs) and biologic DMARDs (bDMARDs). Cohens' Kappa statistics of agreement between the two data sources were calculated. Kappa values 0.61–0.80 were considered to represent good and 0.81–1.00 as very good agreement. To examine factors associated with agreement, a multivariate backward stepwise logistic regression was used to model the odds of agreement for ARM use. The agreement and absolute time gap (days) for starts and stops dates between self-reports and rheumatologist reports were also assessed and presented by median and interquartile range (IQR) in a subset analysis.

**Results:** 2154 patients (78.7% female) were included with a mean (SD) age at OBRI enrolment of 57.8 (12.6) year. Mean (SD) disease parameters were: disease duration: 8.4 years (9.9); DAS28: 4.2 (1.6); physician global: 4.0 (2.5); and health assessment questionnaire (HAQ) disability Index: 1.1 (0.8). For csDMARDs use, the prevalence was 74.2% based on self-reports and 76.6%

based on rheumatologist reports. The prevalence of bDMARDs use was approximately 20.0% based on both reports.

Overall agreement for ARM use between self-reports and rheumatologist reports was good. In the regression model, increased HAQ-pain index (OR: 0.66; 95% CI: 0.60–0.73) and physician global (OR: 0.95; 95% CI: 0.92–0.98) were significantly associated with the lower agreement. By contrast, post-secondary education (OR: 1.20; 95% CI: 1.02–1.40), and seeing an academic rheumatologist (OR: 1.47; 95% CI: 1.25–1.73) were significantly associated with the higher agreement between two data sources.

There was a good and very good agreement for reported administration route of bDMARDs and csDMARDs, respectively. The median absolute time gap (IQR) of start dates and stop dates for ARM use reported by two data sources was 7 days 1–27 and 19 days, 5–48 respectively.

**Conclusions:** The results of this analysis suggest that ARM reports from the two data sources have strong agreement in the OBRI. This agreement is even better for patients who have post-secondary education and are being treated by an academic rheumatologist.

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#### SAT0705 ASSOCIATION BETWEEN FRACTURE SITES IN PATIENTS WITH A HISTORY OF PARENTAL FRACTURE

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**Background:** Fragility fractures (FF) are fractures due to low energy force. Factors predisposing to FF in the general population include reduced bone mineral density (BMD), and family history of osteoporosis. FF most commonly occur in the vertebrae, proximal femur, and distal radius. Studies have demonstrated increased risk of FF in patients with decreased BMD and parental history of FF, particularly hip fracture.<sup>1,2</sup> Few data exist on the association between sites of fracture in patients with a history of parental fracture, especially whether they co-exist at several sites and if particular factors are associated with discrete sites.

**Objectives:** We aimed to find the correlation between sites of FF in patients with a history of parental fracture, and identify and examine the clinical association with any clusters of fractures.

**Methods:** 2094 patients with a history of parental FF and personal history of at least one FF, presenting for BMD estimation from their primary or secondary care practitioner, from 2006–2016, were included. Parameters recorded: height, weight, age at scan, average fat mass, site of fracture(s), smoking, alcohol, corticosteroid use, aromatase inhibitor use, Depo-Provera use, hormone replacement therapy (HRT), rheumatoid arthritis (RA), polymyalgia rheumatica (PMR), breast or prostate cancer, and coeliac disease.

Factor analyses with polychoric correlation matrices were applied to determine association between fracture sites. Any associations with Eigenvalues of more than one were then examined using a logistic model to analyse the effect of the above risk factors.

**Results:** Fracture sites with Eigenvalue of more than one (tibia/fibula, spine, ribs, pelvis) were compared to sites with least co-variability (humerus, forearm, femur). The two cohorts were significantly different in age; therefore, an age-adjusted model is reported below (table 1). Smoking, HRT, and increased age significantly impacted clustering of fractures in the tibia/fibula, spine, ribs, and pelvis, compared with clustering at the humerus, forearm, and femur.

**Abstract SAT0705 – Table 1.** Age-adjusted predictors of fracture for tibia/fibula/spine/ribs/pelvis vs. humerus/forearm/femur (\* denotes significance)

Variable/Fracture cluster	OR (95% CI)
Corticosteroid	0.878 [0.748–1.031]
Smoking	0.879 [0.779, 0.992] *
Alcohol	0.954 [0.808–1.127]
Rheumatoid arthritis	1.393 [0.928–2.092]
Polymyalgia rheumatica	0.907 [0.465–1.769]
HRT	0.635 [0.420, 0.961] *
Aromatase inhibitors	0.950 [0.772, 1.170]
Breast/prostate cancer	1.489 [0.610–3.636]
Gender	0.804 [0.589–1.096]
Age at scan (years)	1.011 [1.003, 1.019] *
Height (cm)	0.989 [0.978–1.000]
Weight (kg)	0.995 [0.989–1.000]

**Conclusions:** In this cohort of patients, there was overlap between all fracture sites, with significant clustering seen in fractures of the tibia/fibula, spine, ribs, and pelvis. After adjusting for age, predictors of fracture in this cluster were smoking, HRT and increased age. This indicates that risk factors for FF are different at different sites, and affects the association of fracture between sites. Further work validating this finding is currently underway.

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- [1] A family history of fracture and fracture risk: a meta-analysis. Bone [Internet]. Elsevier 2004 Nov 1 [cited 2017 Oct 27];35(5):1029–37.
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**Disclosure of Interest:** None declared

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#### SAT0706 INCIDENCE OF PSORIATIC ARTHRITIS IN GERMANY: ANALYSIS OF CLAIMS DATA FROM 65 MILLION PEOPLE FROM 2009 TO 2012

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**Background:** Epidemiological studies are important for understanding the etiology and burden of psoriatic arthritis (PsA). Currently, there are no data available about the incidence of PsA in Germany.

**Objectives:** This study aims to estimate the age-standardised incidence of diagnosed PsA for German men and women during 2009 to 2012.

**Methods:** Estimation of the incidence of a chronic disease from prevalence data is possible if information about the general mortality and excess mortality of diseased compared to non-diseased people are available in terms of the hazard ratio (HR).<sup>1</sup> Prevalence was extracted from the complete diagnosis data (in- and outpatient) from about 80% of the overall German population during 2009 to 2012. Diagnoses are based on claims data from all insurances of the German statutory health insurance (SHI) system. After determining the age-standardised sex-specific prevalence of PsA for each of the four years, the age-standardised incidence for men and women has been estimated. General mortality was obtained from the Federal Statistical Office of Germany. Since the HR is unknown in Germany, we use different scenarios motivated from a systematic review<sup>2</sup> in the range from 1.3 to 1.6.

**Results:** For each of the years from 2009 to 2012, a total of 127, 138, 146 and 156 thousand patients with diagnosed PsA were identified in about 65 million people from the SHI, respectively. The age-standardised prevalence increases from 1.8 to 2.1 per mil in men, and from 2.1 to 2.5 per mil in women. The estimated age-standardised incidence over the study period is shown in the figure 1. Over the study period, the incidence rate of PsA decreases for both sexes and the rate of men is lower than the rate of women. The average incidence rates are 11.5 and 14.5 per 100'000 person-years for men and women, respectively. This means that about 4700 men and 5900 women contract PsA each year. The impact of the different scenarios in HR is small.

**Conclusions:** These data from about 65 million people insured in the German SHI for the first time allow an estimation of the incidence of PsA in Germany. A selection bias is likely to be present, because the roughly 20% of the overall German population who could not included in the analysis (mainly privately insured people) are known to have other health risks. However, the results refer to the vast majority of the German population. The analysis cannot be adjusted for potential confounders other than age and sex (e.g., socio-economic position or presence of co-morbidities).

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**Disclosure of Interest:** None declared

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#### SAT0707 TRENDS IN THE INCIDENCE OF RHEUMATOID ARTHRITIS IN DENMARK FROM 1995–2016: A NATIONWIDE REGISTER-BASED STUDY

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**Background:** Previous studies have shown conflicting results regarding temporal trends in the incidence of rheumatoid arthritis (RA).

**Objectives:** To investigate annual incidence rates of RA in Denmark from 1995–2016 using nationwide health care registers, and to explore how these are affected by different case definitions of RA.

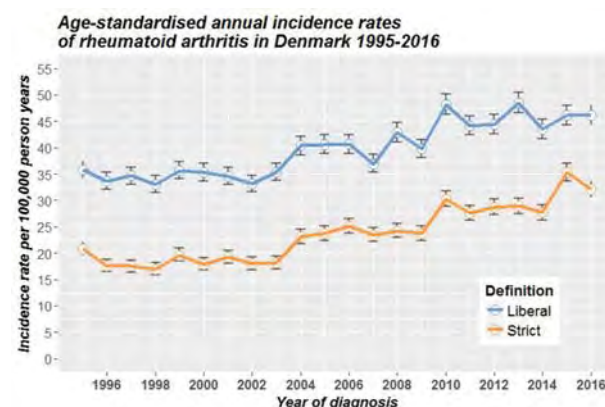
**Methods:** The Danish National Patient Register captures all in- and outpatient (since 1977 and 1994, respectively) contacts at private and public hospitals. Excluding prevalent cases (ICD-8: 712), and using two different case-definitions, we identified all incident RA patients (ICD-10 codes M05.1;3;8;9 and M06.0;8;9) aged  $\geq 18$  in each year from 1995–2016, and calculated annual age-standardised incidence rates (per 1 00 000 person years). We used the NORDCAN population for direct standardisation, and the number of adults alive in Denmark at the beginning of each year as the denominator. We furthermore calculated the age- and sex specific incidence rates during the period. **Strict case definition:** incident patients were required to have at least two in- or outpatient visits at a rheumatology- or general internal medicine clinic/department within 90 days with RA listed as the main diagnosis. **Liberal case definition:** patients with at least two in- or outpatient contacts listing RA as a main- or contributory diagnosis within 1 year.<sup>1</sup>

**Results:** We identified 26 090 and 43 080 patients using the Strict and Liberal case definitions, respectively. Patient characteristics according to choice of definition are presented in the Table. The overall incidence rates were 23.7/100,000 person years (23.4–23.9) using the Strict and 39.7/100,000 person years (39.4–40.1) using the Liberal definition. As seen from the figure 1, a slightly increasing trend in RA was observed from 1995 to 2016 independent of choice of case definition, and this increase was more pronounced in 2010.

The age-specific incidence rates were highest in women (Strict: 75/100,000 person years; Liberal: 134/100,000 person years) as well as men (Strict: 47/100,000 person years; Liberal: 81/100,000 person years) aged 70–79 years.

Table. Demographics and characteristics of rheumatoid arthritis patients diagnosed at hospitals in Denmark 1995–2016 according to case definition.

	Strict case definition	Liberal case definition
N	26 090	43 820
Mean (s.d) age at diagnosis	58.1 (15.2)	59.3 (15.5)
Females, n (%)	18 238 (70)	30 749 (70)
% with COPD	3.1	3.7
% with DM	3.3	3.8
% with CVD	7.2	8.4



**Conclusions:** We found a slightly increasing trend in the incidence rate of RA from 1995–2016. Further, we found that using the Liberal case definition, the overall and age- and sex specific incidence rates were remarkably similar to those reported from Sweden<sup>1</sup>, whereas the Strict definition resulted in lower incidence rates than previously reported from other countries.

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SAT0708

### WILLINGNESS TO PARTICIPATE IN RESEARCH AND REPRESENTATIVENESS OF AN ONLINE HEALTH COMMUNITY AND A PATIENT ORGANISATION POPULATION WITH RHEUMATOID ARTHRITIS

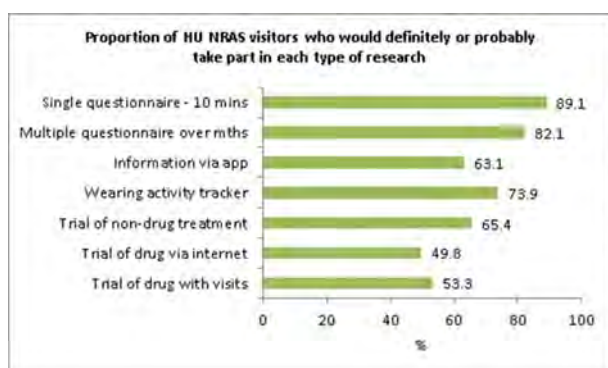
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**Background:** Studies requiring large numbers of participants usually recruit from hospital clinics or general practice registers. These recruitment methods are expensive, time consuming and often fail to reach recruitment targets. One method to overcome these limitations is to recruit patients directly through the internet or patient organisations. However it is not known how willing people would be to take part in different types of research and how representative participants would be of the target population.

**Objectives:** To describe: 1) the willingness of users of an online health community (HealthUnlocked.com (HU)) with rheumatoid arthritis (RA) to participate in research, 2) the representativeness of HU users and patient organisation members (National Rheumatoid Arthritis Society (NRAS)) with RA compared to the general RA population identified from a UK primary care research database (the Clinical Practice Research Datalink (CPRD)).

**Methods:** A pop-up survey was embedded on HU to determine users' willingness to participate in different types of research, demographics (age, gender, employment, postcode and ethnicity) and disease duration. NRAS provided a dataset of their members' demographics and disease characteristics. People with RA were identified from the CPRD, to represent the general RA population. Willingness and characteristics of those willing to take part in research was tabulated. The characteristics of HU users and NRAS members were compared to the characteristics of the RA cohort from CPRD.

**Results:** The HU survey was live for 74 days between May and August 2016 and had 1 00 112 pop-ups. 2647 people clicked on the pop-up, 900 people agreed to take part, 750 respondents had RA, of whom 135 did not provide age and gender resulting in 615 responses available for analysis. Over 80% of users were willing to complete questionnaires of different lengths, from a single questionnaire taking up to 1 min to complete, to multiple questionnaires over a number of months. 74% were willing to wear an activity tracker and 63% to use an app. Just over half (53%) were willing to take part in trials that involved visits to clinics (figure 1). Younger users were more willing to take part in all types of research, with 2% to 17% difference between those aged less than 65 years and those 65 years or over. Compared to those 65 years or over, 2% more of those aged less than 65 years were willing to complete multiple questionnaires over a number of months and 17% more were willing to provide information via an app. HU users were younger than NRAS and the general RA population (Age <55 years HU: 49%, NRAS: 23%, CPRD: 23%). Both HU and NRAS had more females, 88% and 85%, respectively, compared to CPRD 70%. A total of 61% HU participants were diagnosed in the years 2010–2016 compared to 25% in NRAS and 37% in CPRD.



**Conclusions:** Participants surveyed online show high rates of willingness to participate in research studies. While broadly representative of the general RA, they

were younger and more recently diagnosed and these population differences should be considered during study design.

**Disclosure of Interest:** None declared

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SAT0709

### SUBCLINICAL HEPATITIS C VIRUS INFECTION IN EGYPTIAN PATIENTS WITH RHEUMATOLOGIC DISEASES: A MULTI-CENTRE STUDY

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**Background:** Egypt has the highest prevalence of hepatitis C virus (HCV) in the world. In 2015, the prevalence of HCV RNA was found to be 7.0%.<sup>(1)</sup> The prevalence of HCV was studied in Rheumatoid arthritis in few studies,<sup>(2,3)</sup> but to our knowledge, no previous work studied it in other rheumatologic patients.

**Objectives:** This study aims at detecting the prevalence of subclinical HCV infection in different rheumatologic disease groups in Egypt.

**Methods:** Consecutive patients with different rheumatologic diseases from seven-geographically different- rheumatology departments were prospectively studied. None of the patients was known to have previous HCV infection. Patients' serum samples were screened for the presence of anti-HCV antibodies. Patients with positive serology were further evaluated for the presence of HCV ribonucleic acid by reverse transcriptase polymerase chain reaction (RT-PCR).

**Results:** 1454 rheumatic patients (1242 (85.4%) women, 212 (14.5%) men) with mean age[SD] of 43.7 [12.7] years were included in this study. Both anti-HCV serology and HCV RNA were positive in 124 patients (8.5%). Positive PCR for HCV was significantly higher in the age group of 40 to <60 years (p<0.0001) versus other age groups. No statistically significant difference in HCV PCR positivity was found in relation to gender, specific rheumatologic disease, comorbidities or disease duration among studied patients. AST and ALT serum levels were significantly higher in the HCV PCR positive patients (p<0.0001 and p=0.002 respectively).

Geographic area	Anti HCV PCR Positive No=124 (8.5%)	Total No. No=1454	P value P1
Assiut	48 (9.5%)	504 (34.7%)	0.947
Tanta	14 (6.9%)	202 (13.9%)	
AL-Behera	14 (9.6%)	146 (10.0%)	
Cairo	24 (6.9%)	346 (23.8%)	
Aswan	10 (8.2%)	122 (8.4%)	
Sharkeya	14 (10.4%)	134 (9.2%)	
<b>Diagnosed Diseases</b>			<b>P2</b>
-Rheumatoid arthritis	82 (8.4%)	974 (67.1%)	0.053
-Systemic Lupus erythrematosis	10 (5.1%)	196 (13.5%)	
-Scleroderma	0 (0.0%)	38 (2.6%)	
-Behcet's Disease	2 (3.7%)	54 (3.7%)	
-Crystal arthropathy	4 (8.7%)	46 (3.2%)	
-Others	26 (18.1%)	144 (9.9%)	
<b>Disease duration</b>			<b>P3</b>
<5 years	44 (8.1%)	546 (37.6%)	0.924
5–10 years	52 (9.0%)	578 (39.8%)	
>10 years	28 (8.5%)	330 (22.7%)	

Table (1): Number and percentage of positive HCV PCR and statistical significant differences among geographic areas (P1), among different diseases (P2), and between age groups(P3)

**Conclusions:** The detection of subclinical HCV infection in 8.5% of rheumatologic patients in Egypt with significant higher level in the middle age group, draws attention to the importance of screening for HCV in such population for early detection and intervention.

**Disclosure of Interest:** None declared

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**SAT0710 RISK ASSOCIATION FOR ANKYLOSING SPONDYLITIS USING A GENETIC RISK SCORE COMBINING 110 SNPS OF GENOME-WIDE SIGNIFICANCE IN THE POPULATION-BASED HUNT STUDY**

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**Background:** The genetic component of AS development is estimated to ~90%. About 20% of the known heritability for AS is attributed to *HLA-B27* and about 7.4% to 113 SNPs found in genome-wide association studies,<sup>1</sup> with a further ~60% of heritability determined by as yet unmapped variants.

**Objectives:** To evaluate whether a weighted genetic risk score (wGRS) developed based on the currently identified SNPs is predictive of AS in the Norwegian population-based Nord-Trøndelag Health Study (HUNT).

**Methods:** HUNT invited the entire adult population of Nord-Trøndelag county. We used data from HUNT2 (1995–97) and HUNT3 (2006–8). AS cases were diagnosed from hospital records using the Modified New York Criteria. Participants with other inflammatory arthritis were excluded, leaving 181 AS cases and 55 586 controls. Genotyping was performed with Illumina HumanCoreExome arrays. Imputation was performed with Minimac3 based on European ancestry data. Imputed or genotyped data were available for 110 (97%) of the 113 SNPs. We used rs4349859 to indicate *HLA-B27* carrier state (positive/negative). The wGRS was calculated by addition of risk alleles and weighting by the published OR from,<sup>1</sup> representing each person's carriage of all risk variants. Data were analysed using logistic regression. Four models were compared using AUC analysis: 1) the wGRS only; 2) *HLA-B27* only; 3) the wGRS and *HLA-B27*; 3) the wGRS, *HLA-B27*, age, gender, BMI, hypertension, and smoking (never/previous/present). HUNT had ethical approval and participants gave informed consent.

**Results:** At baseline, mean age for cases was 43 years, 61% were men and 87% were *HLA-B27* positive. The corresponding figures for controls were 46 years, 47% men and 12.7% *HLA-B27* positive. The mean wGRS was 14.37 (range: 10.93 to 17.41). The wGRS alone was associated with AS (OR=1.7 for one unit increase,  $p<0.001$ ), but had low discriminative ability (AUC: 0.62, 95% CI: 0.58–0.66). *HLA-B27* alone was also associated with AS (OR=48<sup>31-74</sup>),  $p<0.001$  and showed high discriminative ability (AUC: 0.88 (0.85–0.90)). AUC for the combined wGRS and *HLA-B27* model (0.89 (0.87–0.92)) was higher than for the univariate models ( $p<0.001$  vs. wGRS only;  $p<0.01$  vs. *HLA-B27* only). Further addition of age, gender, BMI, hypertension, and smoking to the combined model gave a small improvement (AUC: 0.91 (0.88–0.94),  $p=0.03$ ).

**Conclusions:** The wGRS was associated with AS, but had low predictive ability in a population-based setting. *HLA-B27* was a much better predictor. Addition of clinical variables only slightly improved prediction, in accordance with the high genetic component in AS pathophysiology. Discovery and inclusion of more genetic risk variants, epigenetic factors, other demographic factors, and interaction terms, in addition to more efficient statistical approaches such as genome-wide risk score development, could improve prediction. Study limitations are false positive- or -negative AS diagnoses and potential selection bias of participants in HUNT.

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**SAT0711 SENSE OF COHERENCE PREDICTS DEVELOPMENT OF CHRONIC WIDESPREAD PAIN OVER TIME**

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**Background:** Chronic musculoskeletal pain is a common condition that has become a great challenge for those affected and for the society. Although much is known about factors that are associated with chronic pain, there is less of knowledge on the influence of salutogenetic factors as measured by sense of coherence (SOC) on pain, especially over time.

**Objectives:** To investigate the associations between SOC, health status and chronic musculoskeletal pain in a general population followed over 13 years.

**Methods:** A cross-sectional and longitudinal cohort study, based on a postal survey at baseline 2003 and a follow-up survey in 2016, including a sample of 1850 subjects from the general population. SOC was measured by a short three item

questionnaire, SOC-3. Subjects were divided into three levels of SOC (low, moderate, high). Health status was measured by SF-36. Pain was reported on a pain mannequin with 18 predefined regions, and was categorised into three pain groups; no chronic pain (NCP), chronic regional pain (CRP), and chronic widespread pain (CWP). CWP was defined according to the ACR<sup>1990</sup> criteria for fibromyalgia. The results were controlled for age and gender, and where appropriate also for pain group.

**Results:** Subjects with high SOC at baseline reported higher mean scores in all eight SF-36 dimensions than those with moderate or low SOC ( $p<0.001$  for all dimensions). Those with high SOC also reported a higher prevalence of NCP (66% vs. 34%) and a lower prevalence of CWP (8% vs. 33%) than subjects with low SOC ( $p<0.001$ ). In the long term follow-up a report of high SOC significantly ( $p<0.001$ ) predicted a better outcome with regard to development and persistence of CWP. Subjects with NCP and high SOC at baseline were less likely to report CWP in the thirteen-year follow-up than those with low SOC (3.6% vs. 10%). For those with CWP at baseline, subjects with high SOC more often reported less chronic pain (NCP or CRP) at follow-up compared to those with low SOC (43.5% vs. 20.5%). When controlled for age, gender and pain, there were no significant differences in SF-36 at follow-up for subjects with different level of SOC at baseline.

**Conclusions:** High level of SOC predicted a lower risk to develop CWP over time, and a better prognosis for those with CWP at baseline. The findings suggest that it would be beneficial to develop methods and make efforts to strengthen SOC, both when meeting patients in the clinic and when making interventions on a national level.

**Disclosure of Interest:** None declared

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**SAT0712 EVALUATION OF STRUCTURAL DAMAGE IN PSORIATIC ARTHRITIS: A SYSTEMATIC LITERATURE REVIEW**

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**Background:** Measuring structural damage in psoriatic arthritis (PsA) is important since it is the ultimate goal of treatment.<sup>1</sup> Similar to rheumatoid arthritis (RA), structural damage in PsA is evaluated mainly on x-rays, but there is no consensus about the radiologic scoring method to use in trials. Usually scores from RA are used and modified so they can capture PsA specific features, such as distal interphalangeal (DIP) joints involvement, bone proliferation, periostitis, osteolysis etc.<sup>2</sup>

**Objectives:** The objective of this study was to analyse existing data on the definition and scoring methods of structural damage in studies on PsA.

**Methods:** A systematic literature review was performed. Studies evaluating structural damage in PsA were identified in Pubmed/Medline and Embase on 10th December 2017. Several synonyms for the main components (i.e. psoriatic arthritis, structural damage, radiologic progression) were used. No search limits were applied. Studies not assessing structural damage or not providing enough information on the definition of damage were not included, nor reviews, case-reports, letters. Descriptive statistics were used.

**Results:** In all, 3321 abstracts were identified of which 61 full length articles were included in the final analysis. The majority were observational studies (59%). Only 3 studies were on axial PsA (axPsA) and around 10% of the studies also had a control population, e.g., RA, osteoarthritis, spondyloarthritis and healthy individuals. In total, a median of 220 (minimum-maximum: 12–1077) patients were included. Most of the studies used the CASPAR criteria (63.9%). A wide majority of studies (80.3%) assessed progression of structural damage.

Structural damage was defined mainly radiographically (77%), followed by the clinical definition (24.6%) and to a lesser extent by other investigations: magnetic resonance imaging (8.2%), computer tomography (4.9%) and ultrasound (3.3%), respectively.

Radiologic assessment of peripheral damage included radiographs of hands and feet, but was very heterogeneous, with most of the studies using the scores “borrowed” from RA and modified for PsA. Hence, 97.8% of the studies using the radiographic evaluation of damage have adapted the scoring method so that it includes the DIP joints of hands and feet. The following elements were included in the radiographic scores: space narrowing 42 studies (93.3%), erosions 44 (97.8%), osteolysis 24 (53.3%), proliferation 12 (26.7%), periostitis 9 (20%), tuft resorption 14 (31.1%), pencil in cup 17 (37.8%), juxta-articular osteopenia/osteoporosis 4 (8.9%), subluxation 6 (13.3%), and ankylosis 5 (11.1%) (table 1). In axPsA radiographic damage was defined by sacroiliitis grades and spine damage, i.e., presence of syndesmozytes and scores such as BASRI-spine, mSASSS, RASSS and PASRI.

**Abstract SAT0712 – Table 1.** Frequency of specific psoriatic arthritis radiographic features

	Randomized control trials	Observational studies	Total number of studies (out of N=61)
Erosions	24 (54.5%)	20 (45.5%)	44
Space narrowing	24 (57.1%)	18 (42.9%)	42
Osteolysis	14 (58.3%)	10 (41.7%)	24
Pencil in cup	10 (58.8%)	7 (41.2%)	17
Tuft resorption	6 (42.9%)	8 (57.1%)	14
Proliferation	6 (50%)	6 (50%)	12
Periostitis	5 (55.6%)	4 (44.4%)	9
Subluxation	3 (50%)	3 (50%)	6
Ankylosis	2 (40%)	3 (60%)	5
Juxta-articular osteopenia/osteoporosis	0 (0%)	4 (100%)	4

**Conclusions:** Damage in PsA is usually evaluated radiologically. Although radiographic scores are almost always adapted for PsA in order to include DIP joints, the other PsA specific radiographic elements are not so frequently assessed. A more specific but also a feasible radiographic score for PsA damage to be universally used in studies is still needed. Further research on other methods of evaluating PsA damage is also needed since data is scarce.

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SAT0713

### INCIDENCE OF EROSIVE INTERPHALANGEAL OA IS STRONGLY ASSOCIATED WITH AGE, FEMALE GENDER, WHITE RACE, AND PRE-EXISTING HAND OA: DATA FROM THE OSTEOARTHRITIS INITIATIVE

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**Background:** Symptomatic erosive interphalangeal OA (SEIPOA) is differentiated from hand OA by the presence of central joint erosions and is more strongly associated with hand pain, disability and finger deformity. There are no specific treatments for SEIPOA and relatively little is known about its incidence and natural history.

**Methods:** We evaluated participants in the Osteoarthritis Initiative (OAI), a multicenter cohort study of 4796 adults with or at risk for symptomatic knee OA recruited at 4 clinical sites between February 2004 and May 2006, which included postero-anterior radiographs of one or both hands at baseline and at 48 months, as well as questions about joint pain including the hand (based on a homunculus where patients indicated left or right hand pain) and self-reported physician-diagnosed hand OA.

Trained readers scored the severity of OA in 16 joints of the dominant hand using the Kellgren Lawrence scale and classified presence of central erosions according to the OARS1 Atlas of radiographic features: 2nd-5th distal interphalangeal (DIP) joints, 2nd-5th proximal interphalangeal (PIP) joints, 1st-5th metacarpophalangeal (MCP) joints, thumb interphalangeal (IP) joint, thumb-base joints (i.e., first carpometacarpal (CMC-1) joint and the scaphotrapezium (ST) joint).

We classified erosive interphalangeal OA (EIPOA) based on presence of OA (KL  $\geq 2$ ) in at least one IP joint on two different fingers (excluding thumb base joints) with at least one with a central erosion and symptomatic erosive interphalangeal OA (SEIPOA) if there was also a report of hand pain.

Baseline characteristics were examined by incident SEIPOA and EIPOA using ANOVA for continuous variables and chi-square analysis for categorical variables. Odds ratios were calculated to estimate the strength of association with

incident SEIPOA. A p-value  $\leq 0.05$  was considered significant. All analyses were conducted with SAS 9.4.

**Results:** 3604 participants had hand radiographs at baseline and 48 months; 18 radiographs were not readable and 121 had prevalent SEIPOA at baseline, leaving 3465 individuals eligible for analysis. The average age was 60.8 years (sd=9.1), 56.1% were female, and 81.3% were white.

133 individuals (3.8%) developed incident SEIPOA over the 4 year observation period. They had greater burden of IP OA at baseline (1.9 vs. 6.2 joints, p<0.001) and were more likely to report a diagnosis of hand OA (13.0% vs. 42.9%, p<0.001) than those who did not develop SEIPOA. 97.7% of the incident SEIPOA occurred in hands with radiographic hand OA, vs. 2.3% in hands without radiographic OA. SEIPOA incidence was strongly associated with older age, female gender, white race, smoking, lower BMI and lower level of physical activity (Image 1). Results were similar for radiographic EIPOA with the exception of the association with hypertension.

	No SEIPOA (n=3332)	SEIPOA (n=133)	p-value	OR (95% CI)
Age, years (mean, sd)	60.6 (9.1)	66.6 (7.6)	<0.001	2.00 (1.66, 2.41)
Gender (n, %)			<0.001	
Female	1844 (55.3)	99 (74.4)		2.35 (1.58, 3.49)
Race/Ethnicity (n, %)			0.003	
White	2695 (80.9)	121 (91.0)		2.38 (1.31, 4.34)
Smoking Status (n, %)			0.007	
Ever smoked	1313 (39.4)	69 (51.1)		1.61 (1.14, 2.28)
BMI, kg/m <sup>2</sup> (mean, sd)	28.6 (4.8)	27.0 (4.2)	<0.001	0.69 (0.57, 0.84)
Waist Circumference > cut-point (n, %)	2404 (74.1)	110 (82.7)	0.025	1.68 (1.06, 2.64)
Diabetes (n, %)	219 (6.7)	11 (8.5)	0.436	1.29 (0.68, 2.42)
Hypertension (n, %)	1652 (49.6)	84 (63.2)	0.002	1.74 (1.22, 2.50)
PASE score (mean, sd)	166 (82.3)	137 (72.5)	<0.001	0.68 (0.56, 0.82)
# joints with OA sans TB (mean, sd)	1.9 (2.6)	6.2 (2.6)	<0.001	3.11 (2.67, 3.62)
MD diagnosed hand OA (n, %)	434 (13.0)	57 (42.9)	<0.001	5.01 (3.50, 7.16)

Note: OR's are calculated per SD for continuous variables

**Figure 1.** Comparison of baseline characteristics by incident SEIPOA group

**Conclusions:** Incidence of SEIPOA in older people is substantial and approximates that of rheumatoid arthritis. SEIPOA is strongly related to age, female gender, and white race, develops in the setting of pre-existing hand OA, and is somewhat associated with reduced BMI and lower level of physical activity.

**Disclosure of Interest:** None declared

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SAT0714

### IMPACT OF PM10 ON THE BURDEN OF RAYNAUD'S PHENOMENON SECONDARY TO SYSTEMIC SCLEROSIS

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**Background:** Raynaud's phenomenon (RP) is the most frequent manifestation of patients with systemic sclerosis (SSc) and it is responsible for significant morbidity. RP has been ranked by patients with SSc as the second most disturbing related-disease symptom.<sup>1</sup> It's well known that RP, defined as episodic digital ischemia characterised by pain, numbness and digital colour changes, is provoked by environmental factors such as cold temperature and smoking exposure.<sup>2</sup> No data are available on the impact of particulate matter (PM) exposure on SSc-RP severity.

**Objectives:** Our aim was to evaluate the association between PM with aerodynamic diameter  $\leq 10 \mu\text{m}$  (PM<sub>10</sub>) and SSc-RP severity.

**Methods:** We applied multivariable continuous ordinal regression model to evaluate the association between short-term exposure to PM<sub>10</sub> and a measure of RP severity (in terms of number and duration of RP attacks, numbness, pain, burning and tingling) as measured by a Visual Analogue Scale (VAS). The model was then adjusted by sex, intravenous prostacyclin therapy (alprostar or iloprost), SSc subtype, general health (GH) VAS and season. Daily PM<sub>10</sub> concentrations, from monitoring stations measured by Regional Environmental Protection Agency (ARPA Lombardia), were used to assign short-term exposure (mean of the 3 days preceding the evaluation) to each study subjects at his/her area of residence.

**Results:** We enrolled 87 consecutive patients with SSc-RP from September 2016 to February 2017. 88.5% were female, mean age was 61 years, median time from diagnosis was 14 years (q1-q3: 7–21 years), and 10% had diffuse cutaneous SSc. The median VAS severity was 5 mm (q1-q3: 2–7 mm). 43.7% were treated with prostacyclin therapy.

The model, performed as described above, estimated that for each 10  $\mu\text{g}/\text{m}^3$  increase in  $\text{PM}_{10}$  there is a worsening of 40% in RP VAS severity (OR 10  $\mu\text{g}/\text{m}^3 \approx 1.40$ ; 95% CI: 1.12–1.74).

**Conclusions:** To our knowledge a correlation between SSc-RP and air pollution as assessed by  $\text{PM}_{10}$  has never been published before. There is increasing evidence that a number of environmental factors are fundamental in the development and course of SSc.<sup>3</sup> These results support the need to perform exposome epidemiology studies, next to genomics, to fully reveal the underlying mechanisms of diseases.

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SAT0715

#### RISK FACTORS OF IMMUNE-RELATED ADVERSE EVENTS IN PATIENTS TREATED WITH ANTI-PD-1 ANTIBODY PEMBROLIZUMAB

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**Background:** Immune checkpoint inhibitors targeting cytotoxic T-lymphocyte-associated protein 4 and programmed cell death protein 1 (PD-1) have been

established as a novel standard treatment for various types of malignancies. However, these new class of drugs have led to increased immune-related adverse events (IrAEs) including rheumatic manifestations.

**Objectives:** To determine the risk factors of IrAEs in patients treated with anti-PD 1 antibody pembrolizumab.

**Methods:** A retrospective medical record review was performed to identify all patients who received at least one dose of pembrolizumab at Samsung Medical Centre, Seoul, Korea between June 2015 and December 2017. Three hundred and ninety two patients were identified. Multivariate logistic regression model was used to identify risk factors of IrAEs.

**Results:** The mean age was 59.7 $\pm$ 13.0 years (range, 18–95) and the median number of doses of pembrolizumab was 2 (IQR, 1.25–5). The primary malignancies included in the study were lung cancer (n=212, 54.1%), melanoma (n=74, 18.9%), lymphoma (n=53, 13.5%) and others (n=53, 13.5%). Sixty-seven (17.1%) patients experienced clinically significant IrAEs; most commonly dermatologic disorders (n=39, 9.9%), pneumonitis (n=11, 2.8%), musculoskeletal disorders (n=10, 2.6%), followed by endocrine disorders (n=7, 1.8%). Fourteen patients (3.6%) experienced serious IrAEs ( $\geq$ Grade 3). Most common serious IrAEs were pneumonitis (n=9, 2.3%). There were 4 deaths associated with IrAEs, all of which were due to pneumonitis. Multivariate logistic regression analysis showed that obesity was the risk factors of IrAEs in pembrolizumab-treated patients. Patients with a body mass index (BMI) of 25 or higher had a 3.65-fold higher risk of IrAEs compared with patients with a BMI between 18.5 and 22.9 (95% CI, 1.58 to 8.42).

**Conclusions:** To our knowledge, this is the first study to explore the risk factor for IrAE in patients undergoing modern cancer immunotherapy. Our study demonstrate that BMI is associated with an increased risk of IrAEs in patients treated with pembrolizumab. Further studies to investigate the potential mechanisms by which obesity raises IrAEs are needed.

**Disclosure of Interest:** None declared

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# Abstracts Accepted for Publication

## Genomics, genetic basis of disease and antigen presentation

AB0001

### ASSOCIATION OF DICKKOPF1-1 POLYMORPHISMS WITH RADIOLOGICAL DAMAGE AND PERIODONTAL DISEASE IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is an autoimmune disease that primarily affects the joints but also has extra-articular manifestations such as Periodontal Disease (PD). The Dickkopf-1 (DKK-1) may have an active role in the regulation of bone biology and patients with RA that carry genetic variants of DKK-1 have greater bone damage

**Objectives:** To investigate the polymorphisms of DKK-1 in patients with early RA (eRA) and its association with some rheumatic, radiological and periodontal variables.

**Methods:** A cross-sectional study in 63 patients with eRA according to the ACR/EULAR 2010 criteria and PD based on the AAP/CDC and Prevention criteria. Serum markers rheumatoid factor (RF), erythrocyte sedimentation rate (ESR), C reactive protein (CRP) and anticitrullinated peptide antibodies (APCAs) were evaluated. Patients selected were over 18 and less than 65 years old and were on treatment with conventional disease modifying antirheumatic drugs. Rheumatic activity was assessed by scales disease activity score 28 and simplified disease activity index. Radiographs of hands and feet were evaluated using the Sharp-van der Heijde (SvH) and Simple Erosion Narrowing Scores (SENS). DKK-1 polymorphisms as rs1896368, rs1896367 and rs1528873 were determined using the High resolution Melting technique (Bio-Rad). A bivariate analysis was performed to determine the variables associated between polymorphism to the presence of radiological and activity scores, diagnosis and severity of PD. A regression model was performed to confirm these associations.

**Results:** The mean age was 48.57±11.35 years, and 76.7% were female. 11.7% had a body mass index >30 kg/m<sup>2</sup>. 35% had an ESR >20 mm/h, and 56.7% had elevated CRP. RF >20 was observed in 61.7% of patients as were APCAs >20 in 43.3% of them. 30%, 42% and 1.6% of patients were homozygous for polymorphism rs1896367, rs1896368 and rs1528873 respectively. Individuals heterozygous for polymorphism rs1896367 had more frequent erosions (p=0.026) and joint space narrowing (JSN) (p=0.005) in the feet, and consequently higher SHS scores (p=0.016). These patients also had higher SENS scores (p=0.001) and more frequent erosions (p=0.02). In contrast, patients homozygous for polymorphism rs1896368 had less frequent JSN in hands and feet as assessed by SHS, as well as less presence of erosions based on the SENS scale. These findings were validated in the regression model (OR: 0.04, 95% CI:0.00–0.93;p<0.05). Finally, the presence of PD was associated with the homozygous expression of polymorphism rs1896367 (p=0.009) and the heterozygous expression of polymorphism rs1696368 (p=0.033).

**Conclusions:** DKK-1 polymorphisms can be associated with the presence of bone damage in patients with eRA and it could affect periodontal outcomes. While polymorphism rs1696367 seems to be associated with greater radiological compromise, polymorphism rs1696368 confers protection against bone damage in Colombian eRA patients.

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AB0002

### EFFECT OF COMMON POLYMORPHISMS IN THE METHOTREXATE PHARMACOKINETIC PATHWAY ON EFFICACY/ADVERSE EFFECTS AND METHOTREXATE POLYGLUTAMATE LEVELS IN RA

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**Background:** Measurement of erythrocyte methotrexate polyglutamate levels (MTX-glu<sub>n</sub>) are widely used to predict response and adverse effects to methotrexate in rheumatoid arthritis patients, but there are very few studies in which these levels were correlated with common polymorphisms in genes involved in methotrexate (MTX) pharmacokinetics. This preliminary study evaluated their utility in Asian Indian patients in a prospective study over 24 weeks.

**Objectives:** The objective of this study is to investigate the impact of seven common polymorphisms in genes involved in methotrexate (MTX) pharmacokinetics on response, adverse effects and methotrexate polyglutamate (MTXPG) levels in rheumatoid arthritis.

**Methods:** This study enrolled 117 RA patients who were treated prospectively with MTX for 24 weeks. Patients were categorised on the EULAR criteria into responders (good and moderate) and non-responders. Adverse effects were ascertained using a questionnaire. The following polymorphisms were ascertained using hydrolysis probes – rs1045642 (ABCB1 3435C>T), rs1128503 (ABCB1 1236C>T), rs10106 (FPGS 1994A>G), rs1544105 (FPGS G>A), rs11545078 (GGH 452C>T), rs3758149 (GGH -401C>T) and rs1051266 (RFC1 80G>A). RBC MTXPG1–5 levels were determined using HPLC at 4, 8, 16 and 24 weeks.

**Results:** There was a significant association of the GGH 452C>T CC genotype (OR 9.5, 95% CI 1.2 to 76.0) with response to MTX. On logistic regression, higher DAS28<sup>3</sup> at baseline and GGH 452CC genotype were significantly associated with response (table 1); the accuracy of the model was 75%. The FPGS 1994A>G GG genotype was associated with a significantly lower risk of adverse effects to MTX (Odds Ratio 0.3 (95% CI 0.1 to 0.6)). On logistic regression, FPGS 1994GG genotype and lower BMI were significant predictors for adverse effects with an accuracy of 66%. The other polymorphisms were not associated with response or adverse effects. None of the polymorphisms were associated with change in MTXPG levels.

**Conclusions:** GGH 452 CC genotype was found to be associated with response to MTX and FPGS 1994 A>G GG with a lower risk of adverse effects; however, not by change in MTXPG levels.

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AB0003

### A GALNT3 GENE MUTATION IN TWO SIBS WITH CHRONIC RECURRENT MULTIFOCAL OSTEOMYELITIS ASSOCIATED WITH HYPERPHOSPHATEMIC FAMILIAL TUMORAL CALCINOSIS

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**Background:** Chronic recurrent multifocal osteomyelitis (CRMO) is an uncommon inflammatory disease mostly affects the metaphyses of long bones. It can be distinguished from osteomyelitis by multifocality and recurrence. Hyperphosphatemic familial tumoral calcinosis (HFTC) is a rare genetic disorder characterised by increased re-absorption of phosphate through the renal proximal tubule leading to increased phosphate concentration and deposition of calcified deposits in cutaneous and subcutaneous tissues, as well as some visceral organs. HFTC is inherited in an autosomal recessive manner and is caused by mutations in three different genes, *FGF23*, *GALNT3* and *KLOTHO*. CRMO has been associated with some chronic inflammatory diseases such as inflammatory bowel disease, palmoplantar pustulosis and SAPHO syndrome. The association of CRMO and HFTC is extremely rare and only three patients have been described so far in the literature.

**Objectives:** To report the clinical, radiological and molecular findings of two sibs with CRMO associated with HFTC.

**Methods:** In this report, we present two siblings; offspring of consanguineous parents. They presented with spontaneous bony pains not responding to NSAID and later on, that developed tender hard masses. There were no similarly affected family members, and they had a non-affected sibling. Clinical, laboratory, pathological and radiological examination was performed. Mutational analyses of the *FGF23*, *GALNT3* and *KLOTHO* genes was carried out by Sanger sequencing of the entire coding region of each gene.

**Results:** Laboratory results including blood cultures and sensitivities were normal, apart from mildly elevated ESR. Serum calcium, 25(OH) vitamin D, renal functions, albumin, alkaline phosphatase, parathormone hormone, and phosphorous were normal apart from hyperphosphatemia in both siblings.

Initial x-rays revealed lytic lesions with a sclerotic margin. Follow up x-rays showed healing with sclerosis and hyperostosis. After developing the hard masses, x-rays showed calcified masses. Resection pathological analysis revealed non-neoplastic inflammatory bone growth with prominent periosteal and bone proliferation, it was free from any granulomatous or malignant changes. We suggested a provisional diagnosis of CRMO associated with HFTC. Molecular studies confirmed the diagnosis by identifying a known pathogenic mutation in the donor splice site of exon 8 of the *GALNT3* gene, c.1524+1G>A. The mutation was found in the homozygous form in the two sibs and both parents were heterozygous.

**Conclusions:** This study documents the first Egyptian family clinically diagnosed with CRMO associated with HFTC and confirmed by molecular studies, with the identification of a splice mutation in the *GALNT3* gene.

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AB0004

### PHARMACOGENETIC ASPECT OF METHOTREXATE, IN A GROUP OF COLOMBIAN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Methotrexate (MTX) as monotherapy or in combination, is the most commonly Disease-Modifying-AntiRheumatic-Drug (DMARDs) used in rheumatoid arthritis (RA). About 40% of patients do not respond to treatment or have adverse effects. The genetic variability could be responsible for this phenomenon. Different studies suggest associations between polymorphisms in the enzymes involved in the metabolic pathway of MTX with alterations in the efficacy and toxicity.

**Objectives:** Determine the polymorphisms of the enzymes involved in MTX metabolism in a group of Colombian patients.

**Methods:** 400 patients with RA over 18 years old, diagnosed according to the ACR/EULAR classification criteria, who consecutively attended an outpatient RA clinic between March 2015 and December 2016 were included. MTX efficacy was defined by DAS28 score  $\geq 3.2$ , liver toxicity by elevation of transaminases above three times the normal value, Haematological toxicity by: leukocytes <4,000, Hb <9.5, platelets <150,000, renal toxicity: creatinine >1.5. The single nucleotide polymorphisms (SNPs) studied were MTHFR C677T, MTHFR A1298C, ATIC C347G,

RFC1 G80A, FPGS-AG and DHFR-CT and were identified by the technique of polymerase chain reaction in real time (RT-PCR).

**Results:** The mean age of patients was 60.7±13.9 years, the duration of the disease was 13.2±10.9 years and 76% were women. A significant increase in the frequency of MTHFR C677T and A1298C SNPs (p=0.05 and p=0.048) were found in the responding patients compared to non-responders. The DHFR-CT and the ATIC C347G SNPs were significantly increased in patients with any toxicity to MTX (p=0.0095 and p=0.005 respectively). We did not find a significant difference between the polymorphisms studied with any specific toxicity.

Abstract AB0004 – Table 1

Polymorphisms	n	Activity (%)	Remission (%)	OR-95%(IC)	p
<b>MTHFR C677CC</b>	344	189	155	1.62 (1.0–2.68)	0.05
CC	81	37 (20)	44 (28)		
TT	263	152 (80)	111 (72)		
<b>MTHFR A1298</b>	381	219	162	1.74 (1.01–3.02)	0.048
AA	312	172 (79)	140 (86)		
TT	69	47 (21)	22 (14)		
<b>DHFR</b>	394	225	165	1.03(0–68–1.55)	0.484
CC	233	131 (58.2)	95 (57.6)		
TT	(58.3)	91 (40.5)	68 (41.2)		
	161				
	(25.8)				
<b>FPGS</b>	400	225	165	1.92 (0.69–1.41)	0.406
AA	137	74 (32.9)	57 (34.5)		
GG	(34.3)	151 (67.7)	108 (65.5)		
	263				
	(65.7)				

Abstract AB0004 – Table 2

Polymorphisms	n	Toxicity	OR-95%(IC)	p
<b>MTHFR C677CC</b>	316	81	1.31 (0.73-2.34)	0.21
CC	74	22		
TT	242	59		
<b>MTHFR A1298</b>	312	80	1.50 (0.71-3.16)	0.184
AA	261	70		
TT	51	10		
<b>DHFR</b>	313	81	1.93(1.13-3.30)	0.0095
CC	175	55		
TT	136	26		
<b>ATIC C347</b>	313	80	2 (1.2012-3.36)	0.005
CC	121	41		
GG	192	39		

**Conclusions:** The Colombian population has similar statistical data compared to the global studies regarding the association of SPNs with the efficacy and toxicity of methotrexate, however the polymorphisms associated with inefficiency in the literature are not replicated in our data. These SNPs could be established as biomarkers to the methotrexate response in terms of efficacy and toxicity in our Colombian population with RA.

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AB0005

### HLA CLASS II IN PARAGUAYAN IMMUNE-MEDIATED INFLAMMATORY PATIENTS

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**Background:** Immune-mediated inflammatory disease (IMID) is a concept used to describe a group of conditions that share common inflammatory pathways leading to systemic inflammation. The best-known genetic factor for IMID susceptibility is the human leukocyte antigen (HLA) haplotypes. Nowadays, there is a lack of information about HLA profile in Paraguayan patients with IMIDs.

**Objectives:** To identify HLA alleles associated with susceptibility to develop an IMID in Paraguayan patients controlled in a reference centre.

**Methods:** Paraguayan IMID patients were recruited from the Rheumatology Department of Hospital de Clínicas, Paraguay. IMID *HLA II* frequencies were compared with a control group of 50 unrelated individuals without disease and from the same geographic origin. Genotyping for HLA was performed using LumineX PCR technology. The association analysis with the IMIDs risk was performed using the chi-square allelic test.

**Results:** 249 IMID patients (95 lupus, 104 rheumatoid arthritis and 50 systemic sclerosis) were included. Of these 84.4% were women with an average age of 43.4 ( $\pm 14$ ). Comparing the haplotypes profiles for the 5 HLA class II genes between the patients and the healthy controls, in the risk association analysis, the association of the known risk allele was corroborated HLADRB1\*03:01 ( $p=2e-06$ , OR:14.97). A significant association was identified between the allele HLADRB1\*08:02 ( $p=0.0271$ , OR:0.13) and HLADRB1\*08:07 ( $p=0.0133$ , OR: 0.08). In the gene *HLADQA1*, 1 allele associated with the IMIDs were found, the HLADQA1\*04:01 ( $p=1.4e-05$ , OR: 0.06). In the *HLADPB1* gene 3 alleles associated with the IMIDs were identified: HLADPB1\*02:01 ( $p=4.2e-05$ , OR: 82.91), HLADPB1\*03:01 ( $p=2e-06$ , OR: 14.97), HLADPB1\*04:01 ( $p=1.5e-05$  OR: 34.55). Different associations between IMIDs and alleles was identify (table 1).

**Abstract AB0005 – Table 1.** List of associated alleles stratified by disease

ALLELE (Systemic Lupus Erythematosus Cohort)	P-value	OR
HLADQA1*02:01	0.0253	14
ALLELES (Rheumatoid Arthritis Cohort)		
	P-value	OR
HLADRB1*08:02	0.0367	0.11
HLADPB1*02:01	0.0003	54.62
HLADPB1*03:01	0.0010	7.92
HLADPB1*04:01	0.0001	29.69
HLADQA1*02:01	0.0467	0.24
HLADQA1*04:01	0.002	0.07
HLADPA1*02:01	0.0022	0.029
ALLELES (Scleroderma Cohort)		
	P-value	OR
HLADPB1*02:01	0.0003	82.33
HLADPB1*03:01	0.0094	8.44
HLADPB1*04:01	0.0001	47.50
HLADQA1*04:01	0.0013	0.06

**Conclusions:** In the genetic association analysis, already known associations have been replicated and new ones previously unpublished have been identified in Paraguayan IMIDs patients. This is the first genetic association study in IMID patients Paraguayan origin.

**Disclosure of Interest:** None declared

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AB0006

#### MIR-26A POLYMORPHISM IS ASSOCIATED WITH SUSCEPTIBILITY OF RHEUMATOID AND PSORIATIC ARTHRITIS

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**Background:** Serum levels of miR-26a has been reported to act as potential biomarker of rheumatic diseases.

**Objectives:** The aim of the study was to analyse the genetic variation and expression of miR-26a as potential diagnostic and/or prognostic markers of rheumatoid diseases.

**Methods:** The miR-26a polymorphism was examined in 111 patients with rheumatoid arthritis (RA), 86 patients with psoriatic arthritis (PsA) and 162 healthy blood donors that served as a control group. Genotyping for miR-26a rs7372209 was performed using a LightSNiP assay. For analysis of the miR-26a expression, RNA was isolated from sera of 15 RA patients (before and 3 months after anti-TNF treatment) and 10 controls (Nucleospin-miRNA Plasma; MACHEREY-NAGEL GmbH and Co. KG) followed by cDNA synthesis (TaqMan MicroRNA Reverse Transcription Kit; Applied BiosystemsTM by Life Technologies) and Real-time PCR amplifications with hsa-miR-26a TaqMan specific and U6 snRNA control primers for each probe. The results were analysed using the ( $\Delta\Delta C_t$ ) calculations.

**Results:** It was found that the presence of miR-26a TT genotype (rs7372209) more than 5 times increases the risk of RA (OR=5.28,  $p=0.003$ ) while the presence of CC homozygotes is associated with the risk of PsA (OR=1.77,  $p=0.037$ ).

There was no significant difference in the miR-26a serum levels between patients and controls. Also miR-26a serum levels did not significantly differed between RA patients before, 3 and 6 months after the implementation of biological therapy with TNF-alpha inhibitors.

**Conclusions:** These results imply that miR-26a rs7372209 allelic variants differentially affect the risk of rheumatoid and psoriatic arthritis while anti-TNF biological treatment seems not to affect the miR-26a expression in RA patients.

**Disclosure of Interest:** None declared

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AB0007

#### ASSOCIATION AT SYSTEMIC LEVELS OF CYTOKINE MRNAS AND PROTEIN QUANTITIES IN RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is an autoimmune inflammatory disease, characterised by chronic synovitis, bone and cartilage destruction, as well as systemic manifestation. In accordance with the pivotal role of cytokines in autoimmunity and their impact as biomarkers, we analysed gene expression at both mRNA and protein levels of several cytokines in peripheral blood of RA patients.

**Objectives:** The aim of the present study was to investigate the gene expressions at mRNA and protein levels of main pro-inflammatory (TNF- $\alpha$ , IL18, IL-12p40; IL-23, IL-6) and immunosuppressive (TGF- $\beta$ 1 and IL10) cytokines and transcription factor Foxp3 in peripheral blood of RA patients.

**Methods:** Total RNA from peripheral blood was isolated from 32 patients matching the ACR/EULAR 2010 criteria for RA and 27 healthy controls. Quantitative real-time polymerase chain reaction was performed for the 8 genes of interests, using the TaqMan detection system. Relative quantitative evaluation of mRNAs was performed by the comparative  $\Delta\Delta C_t$  method and results were presented as n-fold mean difference (RQ-relative quantity) of target genes relative to calibrator (healthy controls) after normalisation to the reference genes (GAPDH and 18srRNA). Serum quantities of cytokines were measured by ELISA.

**Results:** From studied pro-inflammatory cytokine genes, we found down-regulation in the following order: IL6 >TNFA>IL12B; up regulation of IL23A and no change in IL18 gene expression in RA patients group compared to healthy controls. For anti-inflammatory genes we detected significantly increased quantity for IL10 mRNA and no change for TGF $\beta$ 1 mRNA. The most profound down-regulation (more than 7-fold) was observed for IL6 gene ( $p<0.001$ ), while the serum level of the same cytokine was significantly increased as compared to the same controls. The similar tendency was observed in the expression of TNFA, which gene expression was approximately 2-fold down-regulated, whereas serum levels were increased. IL12B mRNA were slightly but not significantly decreased (RQ=0.709;  $p=0.169$ ) in RA patients. An upregulation of IL-23 was detected for IL23A gene (RQ=2.422,  $p=0.002$ ) and serum level of IL-23 as well.

TGF $\beta$ 1 mRNA levels were approximately equal in patients and controls in contrast to IL-10, which was upregulated in both mRNA (RQ=1.6;  $p=0.034$ ) and serum levels (over 6.6 fold;  $p<0.05$ ). In addition, mRNA expression of FoxP3, a master transcription factor for Treg subset was also down-regulated over 4-fold in RA patients ( $p<0.001$ ). A positive correlation was found between gene expression of IL6 with Foxp3, TNFA and TGF $\beta$ 1 in RA ( $r=0.744$ ,  $p=0.004$ ;  $r=0.6$ ,  $p=0.03$ ;  $r=0.556$ ,  $p=0.048$ , respectively).

**Conclusions:** Our results demonstrated significant differences in the expression of mRNA encoded cytokines and their protein quantities at systemic level of RA patients, mostly on IL-23, IL-6 and TNF-alpha.

**Disclosure of Interest:** None declared

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AB0008

#### CROSS-TALK BETWEEN BONE TURNOVER AND CARDIOVASCULAR DISEASE. ASSOCIATION OF MICRORNAs EXPRESSION, FRACTURE AND ABDOMINAL AORTIC CALCIFICATIONS

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**Background:** MicroRNAs (miRs) have emerged as pivotal epigenetic key actors of gene regulation and several miRs have been shown to be at the crossroads of angiogenesis and of bone turnover, taking part in the calcification process by acting on osteoblasts and osteoclasts.<sup>1</sup> Calcification of the aortic media is highly



regulated and involves numerous factors, including calcium deposal and other bone remodelling factors.<sup>2</sup>

**Objectives:** The objective of this study was to find a signature of miRs linked both to osteoporotic fracture risk and abdominal aortic calcification (AAC).

The first outcome was the link between miRs levels at baseline and incident osteoporotic fractures (IOF) during 20 years; the second outcome was the link between miRs levels at baseline and the increase in AAC during 17 years.

**Methods:** Post-menopausal women older than 50 years from the OFELY cohort (Os des Femmes de LYon) were selected if they had available serums at inclusion, and available data for each outcome.

3 miRs selected after literature review because of their impact on vascular calcification and bone turnover (miRs 26a-5p, 34a-5p, and 223-5 p) were measured at baseline. Bioassays of miRs was conducted with miRCURY Biofluids (Exiqon) extraction kit, TaqMan Life Technologies protocol, and QuantStudio 7 flex (Applied Biosystems) for RNA quantification. Results are expressed by relative quantification of Cycle threshold (Ct).

**Results:** A sample of 434 age-matched women (63 [57–72] years old), 50% with incident osteoporotic fracture during the 20 years of follow-up, was included. 183 women had available data to explore AAC; 93 had an increase in Kauppila score in 17 years (58 [55–61] years old), 90 did not (55 [53–58] years old).

No significant link was underlined between miRs and IOF (miR-26: 1.06 [0.85–1.27] vs 0.99 [0.85–1.17],  $p=0.07$ ; miR-34: 1.15 [0.53–1.87] vs 1.26 [0.60–2.07],  $p=0.35$ ; miR-223: 1.01 [0.68–1.43] vs 1.05 [0.72–1.56],  $p=0.32$ ).

No miR was significantly linked to an increase in AAC (miR-26: 1.09 [0.94–1.28] vs 1.10 [0.89–1.30],  $p=0.95$ ; miR-34: 0.78 [0.46–1.21] vs 0.73 [0.38–1.50],  $p=0.90$ ; miR-223: 0.97 [0.69–1.22] vs 0.78 [0.56–1.22],  $p=0.11$ ).

**Conclusions:** No association was observed between the 3 tested miRs and IOF or increase in AAC. Larger studies are necessary to select interesting epigenetic pathways reproducible on wider population.

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#### AB0009 GENETIC ASSOCIATION OF MITOCHONDRIAL DNA POLYMORPHISMS WITH BEHÇET'S DISEASE IN A KOREAN POPULATION

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**Background:** Behcet's disease (BD) is an inflammatory multi-genetic disorder with unknown etiology. In the previous study, we sequenced whole mitochondrial nucleotides from blood of 20 BD patients and 10 sex-, age-matched healthy controls, m.248A>G, m.709G>A, m.3970C>T, m.6392T>C, m.6962G>A, m.10310G>A, m.10609T>C, m.12406G>A, m.12882C>T, m.13928G>C, m.16129G>A, and m.16304T>C were more frequently observed in patients group than healthy control without statistical significance. While, m.304C>A, m.3010G>A, m.4883C>T, m.5178C>A, and m.14668C>T were more frequent in control group ( $p=0.008$ , 0.026, 0.007, 0.007, and 0.026, respectively). m.16182A>C, m.16183A>C, m.16189T>C were associated with uveitis ( $p=0.041$ , 0.022, and 0.014, respectively).

**Objectives:** We performed a follow-up study to validate these possible associations in larger groups.

**Methods:** Whole blood or buffy coat were collected from 98 BD patients from four university hospitals located in Chung-Cheong district of Republic of Korea, 196 age-, sex-matched healthy controls from Konyang University Hospital. Above mentioned 20 targeted mitochondrial DNA (mtDNA) genomes were analysed using MassARRAY<sup>®</sup> system (Agena Bioscience, Inc., San Diego, CA, USA) for m.709, m.3010, m.4883, m.6392, m.6962, m.10310, m.10609, m.12406, m.12882, m.13928, and m.14668; Sanger sequencing for m.248, m.304, m.5178, m.16129, m.16182, m.16183, m.16189, and m.16304; and TaqMan-based genotyping assay (Applied Biosystems, Foster City, CA, USA) for m.3970. Results were compared with the revised Cambridge Reference Sequence (rCRS). Chi square or Fisher's exact test were used to analyse association of mtDNA

alterations between groups and between mtDNA alterations and clinical/laboratory characteristics.

**Results:** Presence of m.248A>G, m.304C>A, m.709G>A, m.3010G>A, m.3970C>T, m.4883C>T, m.5178C>A, m.6392T>C, m.6962G>A, m.10310G>A, m.10609T>C, m.12406G>A, m.12882C>T, m.13928G>C, m.14668C>T, m.16129G>A, and m.16304T>C were not differentiated by the groups. However, m.16812A>C was more frequently observed in the patient group than control [22 (22.4%) vs. 24 (12.2%),  $p=0.061$ ], and it was significantly associated with HLA-B51 positivity ( $p=0.011$ ), arthralgia ( $p=0.043$ ) and methotrexate use ( $p=0.02$ ), and was not associated with uveitis in the follow-up study. Among clinical and laboratory characteristics in BD patients, thrombosis was more frequently observed in male patients than female patients [7 (22.6%) vs. 0 (0%),  $p<0.001$ ], and WBC counts were lower in female patients [3642.3±3413.6 vs. 5200.8±3912.7,  $p=0.048$ ].

Abstract AB0009 – Table 1

RCRS position	Alteration	BD (n=98)	HC (n=196)	p-value	OR* (95% CI)
248	A del	12 (12.2%)	23 (11.7%)	1.000	1.050 (0.499–2.209)
304	C>A	0 (0%)	0 (0%)	NA	NA
709	G>A	24 (24.5%)	35 (17.9%)	0.236	1.492 (0.929–2.686)
3010	G>A	19 (19.4%)	50 (25.5%)	0.307	0.702 (0.387–1.273)
3970	T>C	14 (14.3%)	19 (9.7%)	0.327	1.553 (0.743–3.246)
4883	C>T	25 (25.5%)	59 (30.1%)	0.494	0.795 (0.460–1.374)
5178	C>A	25 (25.5%)	59 (30.1%)	0.494	0.795 (0.460–1.374)
6392	T>C	14 (14.3%)	19 (9.7%)	0.327	1.553 (0.743–3.246)
6962	G>A	12 (12.2%)	18 (9.2%)	0.540	1.380 (0.636–2.993)
10310	G>A	16 (16.3%)	24 (12.2%)	0.434	1.398 (0.705–2.774)
10609	T>C	12 (12.2%)	16 (8.2%)	0.361	1.570 (0.711–3.463)
12406	G>A	12 (12.2%)	17 (8.7%)	0.447	1.469 (0.672–3.213)
12882	C>T	12 (12.2%)	16 (8.2%)	0.361	1.570 (0.711–3.463)
13928	G>C	14 (14.3%)	19 (9.7%)	0.327	1.553 (0.743–3.246)
14668	C>T	19 (19.4%)	49 (25.0%)	0.353	0.722 (0.398–1.310)
16129	G>A	23 (23.5%)	42 (21.4%)	0.804	1.124 (0.631–2.005)
16182	A>C	22 (22.4%)	24 (12.2%)	0.061	2.062 (1.089–3.906)
16183	A>C	32 (32.7%)	42 (21.4%)	0.092	1.766 (1.026–3.040)
16189	T>C	42 (42.9%)	64 (32.7%)	0.112	1.547 (0.939–2.548)
16304	T>C	15 (15.3%)	18 (9.2%)	0.170	1.787 (0.859–3.720)

**Conclusions:** We performed a follow-up study to validate possible associations between BD and 20 mtDNA alterations. m.16812A>C could be associated with BD and its several clinical or laboratory characteristics a Korean population.

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#### AB0010 EVALUATION OF SENSITIVITY TO DNA DAMAGING AGENTS AND EFFICIENCY OF DNA REPAIR IN HUMAN PERIPHERAL BLOOD MONONUCLEAR CELLS FROM PATIENTS WITH DERMATOMYOSITIS AND POLYMYOSITIS

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**Background:** Idiopathic inflammatory myopathies (IIM) being one of the connective tissue diseases are a group of diseases with not fully understood pathology. The common features are production of autoantibodies, abnormal immune response against self-antigens and inflammatory process leading to destruction of muscle cells and internal organ involvement. Patients with inflammatory myopathies have higher risk of developing cancers. One of the processes that can

attribute to increased risk of cancers can be genomic instability and impaired DNA repair.

**Objectives:** The aim of the study was to assess the processes of endogenous and exogenous DNA damage and its repair in patients with IIM as compared to healthy controls.

**Methods:** The study included 10 patients (9 men and 1 woman, mean age 46.6 ± 16.5) with idiopathic inflammatory myopathies (dermatomyositis or polymyositis) as well as 7 healthy control individuals (4 men and 3 women, mean age 33.8 ± 9.8). DNA damage and repair were investigated by the comet assay. To perform the comet assay human peripheral blood mononuclear cells (PBMCs) were isolated and incubated with tert-butyl hydroperoxide (t-BOOH) or bleomycin. Both compounds are common DNA damaging agents – t-BOOH induces oxidative DNA lesions whereas bleomycin induces also DNA double strand breaks (DSBs). To test the DNA repair capability, PBMCs were allowed to recover for 2 hour. The level of endogenous DNA lesions was also investigated.

**Results:** The levels of endogenous DNA damage were not statistically significantly different between tested groups (IIM-3.3±3.6% vs 3.2±3.8% in control;  $p=0.648$ ). The extent of the DNA damage induced by bleomycin (IIM-23.3 ± 19.5% vs 9.8±5.9% in control) as well as oxidative stress (IIM-14.7±16.2% vs 10.4±7.4% in control) was significantly higher in PBMCs derived from IIM patients than in healthy counterparts ( $p<0.001$ ). Kinetic curves of DNA repair are different but the background mechanism underlying observed differences in the repair curve between healthy subjects and patients need to be evaluated further.

**Conclusions:** Understanding the etiology of this phenomena in these diseases may provide insight into disease pathogenesis and explain the increased susceptibility of patients to malignancies. Finding the patients with increased DNA instability could potentially serve as a biomarker and indicate the group of patients who should be carefully screened for neoplasms.

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#### AB0011 EVALUATION OF SALIVARY MIRNAS IN PATIENTS AFFECTED BY SJÖGREN'S SYNDROME AND CORRELATION WITH CLINICAL AND ULTRASONOGRAPHIC OUTCOMES

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**Background:** It has been demonstrated that miRNAs expressed in PBMCs and salivary glands of patients affected by Sjögren's Syndrome (SS) could be involved in the epigenetic control of the disease.

**Objectives:** We aimed to compare the concentration of miRNA-146a/b, 16, 17–92 cluster and 181a in salivary and plasmatic samples collected from SS patients and healthy controls and to evaluate the associations with clinical, laboratory and ultrasound findings.

**Methods:** We collected plasmatic and salivary samples from 28 patients (27 females, mean age 64.4±10.1 years, mean disease duration 10.7±6.9 years) affected by primitive SS according to <sup>ACR</sup> 2012 and/or 2016 criteria and 23 matched healthy controls. In the group of patients, the following data were recorded: ESS-DAI and ESSPRI scores, anti-SSA and anti-SSB status and laboratory data, Schirmer's test, ultrasound scores of the four major salivary glands according to Cornec et al. and concomitant treatments. The following miRNA were extracted, retro-transcribed and quantified: miR16–5 p, miR17–5 p, miR18a–5p, miR19a–5p, miR19b–1–5 p, miR20a, miR92–5 p, miR146a–5p, miR146b–5p, miR181a–5p.

**Results:** The concentration of miRNAs evaluated in plasma and saliva did not significantly match both in patients and in controls, underlining a different modulation in their expression according to the corporeal district. In patients and controls miRNAs16, 17 and 20 were hyper-expressed and miRNA146b and 181 hypo-expressed in salivary samples compared to plasmatic ones. Salivary miRNAs 18a and 146a were hyper-expressed in patients and hypo-expressed in controls, when compared to plasmatic concentrations.

Comparing salivary and plasmatic patients' miRNAs concentrations to those of healthy subjects, plasmatic miRNA16 and 181a were significantly more expressed in patients than in controls (two-tailed Wilcoxon test and Student's T test for unpaired samples).

In SS patients, salivary miRNA 181 and 146a were significantly increased in older subjects ( $p=0.01$  and  $p=0.04$  respectively). Spearman's correlation revealed that salivary miRNA146b was significantly hyper-expressed in patients with worse ESSPRI scores ( $p=0.02$ ); on the contrary, salivary miRNA17, 146b and plasmatic miRNA17 were reduced in patients with higher scores at ultrasound evaluation ( $p=0.01$ ,  $p=0.01$  and  $p=0.04$  respectively). Plasmatic concentration of miRNA18a was increased in patients with less lachrymal production at Schirmer's test ( $p=0.01$ ) and plasmatic concentration of miRNA17 was reduced in patients with

higher ESR values ( $p=0.01$ ). Salivary miRNA18a was significantly increased in patients with anti-La/SSB ( $p=0.04$ ; Mann-Whitney U test for unpaired samples). Salivary and plasmatic miRNAs did not correlate with disease duration and concomitant therapies.

**Conclusions:** Our data show that the expression of salivary miRNAs 17, 18a and 146b may be altered in SS patients and associated with worse ultrasound and ESSPRI scores and anti-La/SSB positivity.

**Disclosure of Interest:** None declared

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#### AB0012 ALLELE AND GENOTYPE FREQUENCY OF SOME GENE POLYMORPHISMS DIFFERS IN VARIOUS JUVENILE IDIOPATHIC ARTHRITIS SUBTYPES

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**Background:** In spite of the fact that chronic arthritis has been the core of paediatric rheumatology, etiology and pathogenesis of juvenile idiopathic arthritis (JIA) are still unclear. It is important to ascertain genetic nature of such a heterogeneous disease.

**Objectives:** The aim of the study was to assess the role of some SNPs of six genes implicated in immune and inflammatory responses: *TNFA* (rs1800629, rs361525), *PTPN22* (rs2476601), *MIF* (rs755622, rs5844572), *TRAF/C5* (rs3761847), *CTLA4* (rs5742909, rs231775), *STAT4* (rs7574865); as well as homozygous deletions of xenobiotic biotransformation genes *GSTT1* and *GSTM1*.

**Methods:** 206 patients diagnosed with JIA (mean age 8.87±4.92), and 218 hospital controls with no signs of autoimmune or inflammatory diseases (mean age 13.88±2.72) were recruited for the study. The JIA patients were divided into subgroups according to IAR classification criteria; the majority of them (125 patients) had oligoarthritis, 42 children developed RF-negative polyarthritis and 27 patients were diagnosed with systemic arthritis. Genomic DNA was extracted from peripheral blood samples by means of the phenol-chloroform method. SNPs were genotyped using PCR-RFLP, Real-Time PCR or fragmental analysis.

**Results:** The allele frequencies for all SNPs in the hospital control group were similar to those in European populations. The allele and genotype frequency distribution for all SNPs was identical in patients and controls. However, when comparing distinct subtypes of JIA, *STAT4* polymorphism demonstrated higher frequencies of minor T allele (30.5% vs. 17.8%,  $p=0.01$ , OR=2.03, 95% CI [1.14–3.6] and G/T genotype (46.3% vs. 25.6%,  $p=0.03$ , OR=2.51, 95% [1.2–5.24]) in RF-negative polyarthritis than in oligoarthritis. On the contrary,  $\Delta$ *GSTT1* appeared to prevail in oligoarthritis (23.7% vs. 7.9% in RF-negative polyarthritis,  $p=0.03$ , OR=3.6, 95% CI [1.03–12.7]). As to systemic arthritis, it was shown, that minor G allele of *TRAF/C5* was more frequent in comparison with oligoarthritis ( $p=0.037$ , OR=2.43, 95% CI [1.05–5.6]).

**Conclusions:** The results obtained can be considered as evidence for distinct genetic nature of the different JIA subtypes.

**Disclosure of Interest:** None declared

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#### AB0013 EXPRESSION LEVELS OF MIR-124 IN THE PLASMA OF RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Micro-ribonucleic acids (microRNAs) comprise a class of small non-coding RNAs that regulate gene expression on post transcriptional level. Levels of miR-124 have been found to be decreased in rheumatoid arthritis (RA) synoviocytes and *in vivo* studies have shown that treatment with pre-miR-124 suppresses the progression of joint damage<sup>1</sup>.

**Objectives:** To evaluate the expression levels of miR-124–3 p in plasma of RA patients and to determine its possible role as biomarker for diagnosis and disease activity.

**Methods:** 34 RA patients according to the 1987 ACR criteria were included in the study. Expression levels of miR-124–3 p in the plasma were determined by PCR

(SYBR Green technology).  $2^{-\Delta\Delta Ct}$  method was used for analysis. 10 healthy donors were used as controls.

**Results:** Expression levels of miR-124-3 p were upregulated in the plasma of 33 (97.06%) of the patients when compared to controls. Receiver operating characteristic curve analysis was conducted in order to evaluate the diagnostic accuracy of the expression levels of the studied miRNA in the plasma. Area under the curve for miR-124-3 p was 0.879 (95% CI=0.740–1.00),  $p=0.303 \times 10^{-3}$ . When the relative quantification (RQ) cut value was 2.89, the sensitivity was 91.2% and the specificity was 80%. Levels of miR-124-3 p in plasma correlated with the diagnosis ( $p=0.106 \times 10^{-3}$ ), with markers of inflammation – ESR ( $p=0.0497$ ) and CRP ( $p=0.047$ ) as well as with the immunological activity – the presence of RF ( $p=0.007$ ), RF IgM ( $p=0.004$ ), RF IgG ( $p=0.004$ ), RF IgA ( $p=0.005$ ) and anti-CCP antibodies in the serum ( $p=0.025$ ).

**Conclusions:** In contrary to the literature data that report levels of miR-124 to be decreased in RA synovial fibroblasts we found increased expression of miR-124-3 p in the plasma of RA patients which might reflect the pathophysiological response to the inflammation, the effect of the treatment regimen or the presence of miR-124a gene promoter hypermethylation in the synovial tissue which might downregulate miR-124 locally.<sup>1,2</sup> To our knowledge this is the first study to evaluate the diagnostic accuracy of plasma levels of miR-124 in RA patients as well as the possibility of using miR-124 as biomarker for disease activity but larger set is needed to confirm these results in the clinical practice.

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#### AB0014 GENETIC INFLUENCE OF DIFFERENT MEASURE FOR TUMOUR NECROSIS FACTOR INHIBITORS RESPONSE IN RHEUMATOID ARTHRITIS

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**Background:** The genetic studies of tumour necrosis factor inhibitors (TNFi) response in patients with rheumatoid arthritis (RA) have largely relied on the changes in complex disease scores as a measure of treatment response. It is expected that genetic architecture of such complex score is heterogeneous and not very suitable for pharmacogenetic studies.

**Objectives:** We aimed to select the most optimal phenotype for TNFi response using heritability estimates using genome-wide association studies (GWAS) in the Korean population.

**Methods:** Disease Activity Scores based on 28 joint counts (DAS28) and Clinical Disease Activity Index (CDAI) were assessed at baseline, and after 6 months in 370 Korean RA patients who started TNFi due to moderate or high disease activity. Genotypes were generated on the Illumina HumanOmni2.5Exome array (2.5 million variants) in TNFi-treated Korean patients with RA. We estimated heritability using a linear mixed-modelling approach (GCTA) for the TNFi drug-response phenotype  $\Delta$ DAS28,  $\Delta$ CDAI and its separate components, such as  $\Delta$  swollen joint count (SJC),  $\Delta$  tender joint count (TJC),  $\Delta$  erythrocyte sedimentation rate (ESR),  $\Delta$  visual-analogue scale of general health (VAS-GH) and  $\Delta$  provider global assessment of disease activity (PrGA). Furthermore, a multivariate GWAS approach was implemented, analysing separate DAS28 and CDAI components simultaneously

**Results:** The highest heritability estimates were found for  $\Delta$ PrGA ( $h^2=0.76$ ) and  $\Delta$ TJC ( $h^2=0.73$ ); lower heritability was found for  $\Delta$ DAS28 ( $h^2=0.32$ ) with estimates for  $\Delta$ ESR ( $h^2=0.66$ ),  $\Delta$ SJC ( $h^2=0.62$ ),  $\Delta$ CDAI ( $h^2=0.60$ ) and  $\Delta$ VAS-GH ( $h^2=0.53$ ) (all  $p$ -value<0.005).

**Conclusions:** Our results indicate that multiple SNPs together explain a substantial portion of the variation in change in provider global assessment of disease

activity in TNFi-treated patients with RA. In conclusion, optimal phenotype based on heritability suggests the use of changes in clinical disease activity index (CDAI) including provider global assessment than DAS28 in pharmacogenetic study.

**Disclosure of Interest:** None declared

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#### AB0015 THE EFFECT OF RARE CODING VARIANTS ON RESPONSE OF TNF INHIBITORS TREATMENT IN RHEUMATOID ARTHRITIS

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**Background:** Although pharmacogenetic studies of TNF inhibitors (TNFi) response presented the estimates of high heritability, only few loci with suggestive weak common association as biomarkers for TNFi response have been identified.

**Objectives:** We aimed to identify novel functional rare variants associated with response to etanercept using targeted exon sequencing in Korea.

**Methods:** Disease activity scores were assessed at baseline and after 6 months in 156 Korean RA patients who started etanercept due to moderate or high disease activity. We analysed targeted exon sequencing data of 399 genes selected from a multifaceted approach. We conducted a single-marker association test (MAF  $\geq 1\%$ ) and a gene-based analysis [optimal sequence kernel association test (SKAT-O)] of rare variants (MAF <1%). In addition, we performed gene set analyses of TNF pathway genes.

**Results:** We identified that clinical factors seem to influence the therapeutic good response of etanercept including male, high disease activity score at baseline, BMI. After stringent quality control, we analysed 14 024 variants of 399 genes in 156 RA patients. We identified two novel significant functional SNPs [rs16942564, rs61734378 (exon of AKAP13)] associated with response to etanercept, surpassing study-wide significant threshold ( $p < 3.0 \times 10^{-5}$ ) in single variant association tests. Using a gene-based approach, we found two genes with nominal burden signals ( $p < 0.001$ ) which did not reach study-wide significance. In the gene set enrichment test, we found no evidence for enrichment of association at genes involved in the TNF pathway.

**Conclusions:** We were unable to identify rare coding variants with large effect of 399 targeted genes. Our study suggests that rare coding variants of RA risk associated genes do not contribute to heritability of response to etanercept therapy.

**Disclosure of Interest:** None declared

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#### AB0016 CHROMATIN LOCALIZATION OF SURVIVIN IN CD4+ T-CELLS OF PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Oncoprotein survivin emerged as an important player in the pathogenesis of rheumatoid arthritis (RA). Results of genome-wide study suggest that survivin may take part in transcription stimulation of the RA-specific genes.

**Objectives:** To identify and describe survivin-dependent differences in transcription pattern between CD4<sup>+</sup> T-cells of RA patients and healthy subjects focusing in particular on a subset of genes involved in maturation of Th1 and Th17 cells.

**Methods:** CD4<sup>+</sup> T-cells were isolated from PBMC of 3 RA patients and 5 non-smoking and 2 smoking healthy controls using a positive selection and activated by Pam3cys+Concanavalin A+LPS. Chromatin immunoprecipitation (ChIP) was done using rabbit polyclonal anti-Survivin, purified DNA was prepared into libraries using ThruPLEX (Rubicon) and sequenced using Hiseq 2000 (Illumina). Resulting fastq sequencing files were mapped to the human reference genome (hg38) using the STAR aligner. Peaks were associated with the closest transcription start site. Enriched peak regions ( $p < 10^{-5}$ ) were identified in survivin-ChIP samples above background ("input") using the Homer software. The peaks were analysed using gene ontology (GO) technique as implemented in GOrilla and GSEA software. The genes, scored high in RA and not present/low in any controls or vice versa were identified. The enriched GO groups were searched for presence of Th1/Th17 regulating genes.

**Results:** We identified 11 145 survivin-bound chromatin sequences. Out of them, GO technique indicated 770 genes in RA samples (7.3%) and 766 genes in healthy controls (19.5%) which were annotated and enriched (>log-5) in GO



terms. In the screening for genes regulating maturation of Th1/Th17 cells, CBLB, IRF1, STAT3, SGK1 and TNFSF14 were identified among the genes enriched in RA samples, while EGR3 and ETS1 were enriched only in healthy controls. Additionally, transcription factors Ezh2, Rad21, Ctp2 and Suz12 were identified as common for both RA and healthy groups genes, associated with significant GO enrichment.

**Conclusions:** This study confirms the role of survivin as a transcription mediator in CD4 +T cells and is suggested to influence multiple genes involved in RA pathology.

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#### AB0017 VITAMIN D LEVEL AND MIRNA 22 AND 125b GENE EXPRESSION IN BEHÇET'S DISEASE PATIENTS

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**Objectives:** To investigate serum levels of vitamin D and its effect on microRNA 22 and 125b gene expression in Behçet's disease (BD) patients and to evaluate their relation to clinical characteristics and disease activity.

**Methods:** Fifty-one BD patients and 45 matching controls were studied. Disease activity was assessed using BD Current Activity Form (BDCAF). Serum vitamin D3 was measured by ELISA. MicroRNAs were assayed by reverse transcription-quantitative polymerized chain reaction (RT-qPCR).

**Results:** Patients mean age was 34.3±8.6 years and disease duration 65.3±52.4 months. The BDCAF was 2.4±1.3. Vitamin D level was significantly lower (29.7 ±14.4 ng/ml) in patients than in control (40.1±17.8 ng/ml)(p<0.001) especially males (25.8±7.5 ng/ml) compared to females (48±23.7 ng/ml)(p<0.001). There was no relation between 25(OH)D levels and disease activity or with the presence of clinical manifestations. There was a 3.8±1.5 fold increase in miRNA125b while miR-22 showed no significant difference (0.38±0.46) but was significantly reduced in those receiving steroids (0.21±0.27) compared to those not (0.66±0.58) (p=0.003). There was no significant difference in the frequency of miR-22 or miR-125 expression according to the presence of clinical manifestations, medications received or disease activity. The fold change in miR-125b significantly correlated with vitamin D (r=0.54, p<0.001) but not with BDCAF (p=0.64).

**Conclusions:** Vitamin D level is decreased in BD patients and significantly correlated with the fold change of miR-125b especially in males thus representing a possible therapeutic target. The miR-22 expression did not change but was notably downregulated by steroids. Further longitudinal studies on a larger sample are recommended to validate the present results.

**Disclosure of Interest:** None declared

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#### AB0018 CLINICAL STATUS AND GENE EXPRESSION IN CLASS IV LUPUS NEPHRITIS

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**Background:** Lupus nephritis (LN) is one of the most frequent and serious complications in the patients with systemic lupus erythematosus. Several studies have identified risk factors for poor kidney prognosis in patients with SLE, including age, sex, hypertension, decreased estimated GFR (eGFR), proteinuria, and renal pathologic types.<sup>1</sup> Biopsy allows classifying the type of renal involvement, assessing its activity, and thus guiding the therapeutic behaviours. It has been shown that structural changes and inflammatory infiltrate associated with LN contribute to a hypoxic state which induces angiogenesis.<sup>2</sup> Herein, it was hypothesised that differential expression of angiogenic genes could classify Lupus

Nephritis Patients (LNP) with the same histological score but different "clinical status".

**Objectives:** To investigate if there is a differential angiogenic gene expression in biopsies of LNP under the same histological classification but different "clinical status" measured by eGFR.

**Methods:** Twenty four kidney biopsies samples classified according to ISN/RPS scoring system as Class IV from 24 LNP were divided into eGFR <60 ml/min (n=10, age: 31.00±10.93, range: 17–46) and eGFR >60 ml/min (n=14, age: 32.64 ±11.34, range: 21–64). RNA was isolated using TRIzol-Chloroform technique and then was reverse-transcribed using random primers. Gene expression level of pro-angiogenic factors: VCAM-1, VEGF, TGF-β and ANGPT-1 were evaluated using Quantitative Real Time PCR (QPCR). The threshold cycle (Ct) scores were averaged for calculations of relative expression values. The Ct scores were normalised by subtracting β2Microglobuline (β2M) control, or ΔCt=Ct<sub>gene</sub>-Ct<sub>β2M</sub>. To test for differential gene expression between groups, a two sample T-test was performed to compare the ΔCt in the two groups.

**Results:** ΔCt is inversely proportional to the gene expression level. Significant differences between groups was found in VEGF-A gene (p=0.0326), where the greatest expression corresponding to eGFR <60 ml/min group. However, there were not statistically significant differences in VCAM-1, ANGPT1 and TGF-β expression (table 1). Particularly TGF-β, a proangiogenic and profibrotic gene showed a uniform expression level in both groups.

**Abstract AB0018 – Table 1.** Levels of gene expression and laboratory parameters in eGFR <60 ml/min and eGFR >60 ml/min expressed as ΔCt values.

Gene	eGFR<60 ml/min	eGFR>60 ml/min	p value
	n=10	n=14	
VCAM-1	5,021±1768	6,248±3264	0,3165
VEGF-A	3,414±1161	4,651±1409	0,0326
TGF-β	6,168±1011	6,699±1351	0,3421
ANGPT1	10,330±2294	9,891±2113	0,5007

**Conclusions:** In the present cross-sectional study, increased levels of VEGF-A were observed in biopsies Class IV from LNP with eGFR <60 ml/min. These findings suggest a differential gene expression that may be associated with an impaired renal function, reflected by eGFR.

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#### AB0019 THE ROLE OF THE IL2-IL21 RS6822844 POLYMORPHISM IN THE PREDISPOSITION TO THE ERYTHROCYTE SEDIMENTATION RATE ELEVATION IN JUVENILE IDIOPATHIC ARTHRITIS

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**Background:** Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disorder in paediatrics.<sup>1</sup> The erythrocyte sedimentation rate (ESR) is one of the key measures of the JIA activity.<sup>2</sup> However, in some patients, even in the active disease period, the ESR is not elevated.<sup>3</sup>

**Objectives:** The aim of the study was to assess the relationship between the *IL2-IL21 rs6822844* locus polymorphic variants and a predisposition to the ESR elevation in JIA patients.

**Methods:** The study included 255 JIA patients from the Republic of Bashkortostan, Russia. The ESR was considered elevated if its value exceeded the upper limit of the normal range two or more times. Genotyping was performed by real-time PCR, statistical analysis – using the two-tailed Fisher exact test (p) and the odds ratio (OR) with a 95% confidence interval (CI).

**Results:** The girls/boys ratio was 65.88%/34.12%. The ESR elevation in the active disease period was seen in 70.98% of patients. When studying the *IL2-IL21 rs6822844* polymorphic locus, a marginal significance level was noted for the rarer occurrence of the GT genotype in patients with the elevated ESR (14.92%

vs. 25.68%,  $p=0.049$ , OR=0.508, 95% CI 0.258–0.985, compared with patients with the normal ESR, respectively). After stratification according to the sex, similar differences in the GT genotype frequencies were seen and even intensified only for female JIA patients (15.38% vs. 31.37%, respectively,  $p=0.022$ , OR=0.398, 95% CI 0.180–0.897). In addition, a significant increase in the GG genotype proportion and a tendency towards a decrease in the T allele proportion were observed in girls with the elevated ESR (GG: 83.76% vs. 68.63%,  $p=0.038$ , OR=2.358, 95% CI 1.058–5.110; T: 8.55% vs. 15.69%,  $p=0.057$ , compared with girls with the normal ESR, respectively).

**Conclusions:** In the present study, the association of the *IL2-IL21* rs6822844 locus polymorphic variants with a predisposition to the ESR elevation in female JIA patients was shown.

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#### AB0020 DIFFERENTIALLY EXPRESSED GENES IN SJGREN'S SYNDROME MICROARRAY

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**Background:** Sjogren's syndrome (SS) is a chronic autoimmune disease characterised by a decrease in the secretion of tears and saliva, and is considered to be a common rheumatic immunologic disease second only to rheumatoid arthritis. Patients with SS may have different prognosis or different reactions to the same treatment plan. Therefore, a more accurate and more practical predictor is needed to provide a basis for the individualised treatment of SS. Bioinformatics is a new approach. It applies bioinformatics methodology, tools, software and database to molecular mechanisms, new biomarkers and individualised treatment measures.

**Objectives:** In this study, gene expression data as the basis, combined with bioinformatics tools and literature mining methods, firstly analyses the expression differences between normal people and patients with parotid gland parotid Sjogren syndrome gene, a key pathway and further study the effect of SS involved in the occurrence and development of the application of protein interaction network screening key genes, pathogenesis help to clarify SS, and for the future of this disease and provide a new direction.

**Methods:** The expression profiles of mRNA in parotid gland of patients with Sjogren syndrome and normal parotid gland were obtained from the GEO database. A total of 24 patients with Sjogren's syndrome, 6 patients with dry mouth and dry eye symptoms and 25 patients without dry mouth and dry eye were enrolled in the study. 65 samples were collected. The GEO2R tool screened the parotid differentially expressed genes in the patients with SS compared with the healthy people, and the DAVID tool enriched the function and pathway of the gene. The STRING database constructs a network that differentially expresses the interaction of gene protein products and screening core genes.

**Results:** 24 upregulated genes and 147 down regulated genes were screened. KEGG enriched 5 pathways including cell adhesion, intestinal immune network IgA secretion, viral myocarditis pathway, rheumatoid arthritis pathway and leukocyte transendothelial migration. String protein interaction database was used to subcellular localization of differentially expressed gene protein products in parotid gland, and differentially expressed proteins were identified. The interaction network was constructed by Cytoscape software. The protein interaction network was constructed based on the 171 differentially expressed genes of SS, and the isolated and non interacting protein nodes were screened out. 108 upregulated gene encoded proteins were found to interact with each other, forming a complex network containing 390 interactions. The Degree>20 of the node is selected as the standard selection centre node, and 5 Hub genes are obtained. It is found that PTPRC, CD86, STAT1, FYN and LCP2 are key genes and may play an important role in the pathogenesis of Sjogren syndrome.

**Conclusions:** Above all, we used bioinformatics to find genes and critical pathways related to SS, which is expected to provide new molecular markers for the diagnosis and treatment of SS. It provides a new way of thinking for the treatment and prognosis of Sjogren syndrome.

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#### AB0021 A GENOME-WIDE SNP LINKAGE ANALYSIS SUGGESTS A NOVEL SUSCEPTIBILITY GENE FOR ANKYLOSING SPONDYLITIS

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**Background:** Ankylosing Spondylitis (AS) is a chronic, progressive and inflammatory disease, which is considered to be hereditary. However, the responsible molecular genetic determinants remain unidentified.

**Objectives:** To detect susceptibility gene(s) for AS by using an affected-only linkage analysis and high density single nucleotide polymorphism (SNP) in genome-wide manner.

**Methods:** All AS patients in three families of Cantonese were recruited. Their clinical material were collected by questionnaires. Genomic DNA derived from individual peripheral blood leukocytes was genotyped using Illumina HuamHap 610-Quad SNP Chip. Genotype data were generated using the Illumina BeadStudio 3.2 software. An affected-only linkage analysis was carried out using non-parametric and parametric linkage analysis. The customised allele frequencies were based on the 980 Cantonese healthy controls. SNP genetic map positions were interpolated as their physical positions in megabyte.

**Results:** 1. *Clinical data:* The mean age was 42.3±14.9 years (ranging from 18~62 years), mean age of onset was 23.8±7.4 years (ranging from 10~30 years), mean duration of affection was 17.0±13.0 years (ranging from 0.2~50.0 years), and the sex ratio of male to female was 2.5: 1. There was no Iritis and dactylitis, hip involvement (4, 19.05%), peripheral arthritis (4, 19.05%), inflammatory back pain (21, 100%) and HLA-B27 positive (20, 95.24%). 2. *Results of non-parameter linkage analysis:* The highest LOD value was found in chromosome 16, which reached 2.362. Although chromosome 6 was considered to be relative to the pathogenesis of AS, its LOD value was 1.499 and the range of the peak was located in 6 p21, where 96 SNPs (such as rs6930977) were included. 3. *Results of parameter linkage analysis:* The LOD value of chromosome 16 was 4.6807 and higher than that of other chromosomes which were less than 3 by the same analysis. A susceptibility locus was found in 16q12, spanning 88.5 Kb with LOD value above 3 (ranging: 51030764~51915940). 4. *Susceptibility genes:* According to the result of parameter linkage analysis in chromosome 16, seven genes (TOX high mobility group box family member 3 (TOX3), LOC643714, LOC146253, LOC100132440, LOC390730, LOC100128523 and chromodomain helicase DNA binding protein 9 (CHD9)) could be detected in the position where the LOD value exceeded 3. Interestingly, six SNPs could be found in CHD9 gene. Likewise, they were also found in another association analysis, which included 400 AS patients and 977 healthy controls. P value for SNP rs10153130 was 0.005879 (adjust  $p<0.05/6=0.00833$ ).

**Conclusions:** Genome-wide SNP linkage analysis in three AS families supports that a susceptibility locus for AS was found in 16q12, spanning 88.5 Kb with LOD value above 3 (ranging: 51030764~51915940).

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#### AB0022 FAMILY-BASED WHOLE-EXOME SEQUENCING REVEALS THE GENETIC BASIS OF RELAPSING POLYCHONDRIITIS

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**Background:** Relapsing polychondritis (RP) is a rare systemic disease, characterised by recurrent episodes of inflammation of cartilaginous tissues and other proteoglycan rich structures involving the cartilage of the ears, nose, larynx, tracheobronchial tree and cardiovascular system.<sup>1,2</sup> The susceptibility to RP has been reported to be significantly related to genetic factors.<sup>3,4</sup> However, family occurrence has yet to be reported and the responsible molecular genetic determinants hasn't been clearly elucidated.

**Objectives:** The purpose was to detect the susceptibility genes of RP through whole-exome sequencing (WES) in a Chinese family and deepen our understanding of the pathogenesis of RP.

**Methods:** A 32 year-old Chinese female proband with RP and her family in which only her mother was RP patient were recruited in the current study. The genomic DNA of 6 human subjects was extracted from the peripheral blood monocyte cells (PBMCs) and then identified gene allele mutations using WES. Candidate variants with low frequency (<0.1%) in general population and predicted deleterious on gene function were identified. Sanger sequencing was then used to validate the analysis results of WES and further validated the gene variants in 12 human subjects.

**Results:** 38 genes mutated were confirmed by WES among RP patients. Of them, 10 gene mutated were validated by Sanger sequencing, including Collagen Type XXII Alpha 1 Chain (COL22A1) rs200464636, folliculin (FLCN) NM\_144606: c.G838A: p.E280K, glycosylphosphatidylinositol anchor attachment 1 (GPA1) rs201424010, DNA ligase 3 (LIG3) rs761808558, RecQ like helicase 4 (RECQL4) rs757703895, ring finger protein 207 (RNF207) NM\_207396: c.T425C:p.I142T, coiled-coil domain containing 61 (CCDC61) rs777816675, Purkinje cell protein 2 (PCP2) rs144974437, tubulin alpha 3e (TUBA3E) rs749780020 and myosin heavy chain 15 (MYH15) NM\_014981: c.G4462A: p.A1488T.

**Conclusions:** This study confirms that coinheritance of multigene mutated may contribute to the susceptibility to RP. The candidate genes mutated we discovered are potential targets for in-depth functional studies.

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## Adaptive immunity (T cells and B cells) in rheumatic diseases

### AB0023 SEX-BASED DIFFERENCES IN ASSOCIATION BETWEEN CIRCULATING T CELL SUBSETS AND DISEASE ACTIVITY IN UNTREATED EARLY RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Genetic association studies strongly support the role of CD4<sup>+</sup> T cells in promoting RA pathology. In a cohort of untreated early RA patients, we recently demonstrated that the balance of helper T cell subsets in blood of ueRA patients is skewed towards Th2 cells relative to healthy controls.<sup>1</sup> RA has been shown to be a sexually dimorphic condition with current data suggesting that prevalence, disease course and treatment outcome varies between men and women.

**Objectives:** It is not known if sex-based disparities in immunological factors contribute to the disease process in rheumatoid arthritis (RA). Hence, we examined whether circulating T cell subset proportions and their association with disease activity differed in male and female patients with untreated early rheumatoid arthritis.

**Methods:** Proportions of T cell subsets were analysed in peripheral blood from 70 ueRA DMARD and prednisolone naïve patients with untreated early Rheumatoid arthritis (50 females and 20 males) and in 31 healthy age-matched controls. Broad analysis of helper and regulatory CD4<sup>+</sup> T cell subsets was done using flow cytometry. Disease activity in patients was assessed using DAS28, CDAI, swollen joint counts, tender joint counts, CRP and ESR.

**Results:** Multivariate factor analyses showed that male and female untreated early rheumatoid arthritis patients display distinct profiles of association between disease activity and circulating T cell subset proportions. In male, but not female, ueRA patients Th2 cells showed a positive association with disease activity and correlated significantly with DAS28-ESR, CDAI and tender joint counts. Likewise, proportions of non-regulatory CTLA-4<sup>+</sup> T cells associated positively with disease activity in male patients only, and correlated with DAS28-ESR. In contrast, there was a negative relation between Th1Th17 subset proportions and disease activity in males only. Proportions of Th1 and Th17 cells showed no relation to disease activity in either males or females. There were no significant differences in proportions of T cell subsets between the sexes in patients with untreated early rheumatoid arthritis.

**Conclusions:** In conclusion, our findings show sex-based differences in the association between T cell subsets and disease activity in ueRA patients, and that Th2 helper T cells may have a stronger role in the regulation of disease activity in male patients.

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### AB0024

### IGA-EXPRESSING BM PC ARE RESPONSIBLE FOR ENHANCED PHOSPHORYLATION OF BCR-ASSOCIATED KINASES AFTER BCR STIMULATION INDEPENDENTLY OF THEIR CD19 EXPRESSION

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**Background:** Plasma cells (PC) are considered key drivers of antibody mediated autoimmune diseases. Long-lived PC survive for years in their niches, preferentially in the bone marrow (BM) but also in inflamed tissues.<sup>1,2</sup> A subset of PC lacking expression of CD19 has been identified.<sup>3</sup> Better understanding of factors and pathways involved in survival and maintenance of long-lived PC is needed to find strategies to target PC in autoimmunity since targeting B cells or proliferating cells does not affect already existing PC.<sup>4</sup> B cell receptor (BCR) signalling is a critical mediator of B cell survival and it was shown before that IgA<sup>+</sup> and IgM<sup>+</sup> PC in the BM express a functional BCR suggesting a potential role for the BCR signalling pathway.<sup>5</sup>

**Objectives:** Expression of BCR associated molecules in BM PC and the response of CD19<sup>+</sup> and CD19<sup>-</sup> BM PC to BCR stimulation by anti-IgM/IgA/IgG was assessed to test whether these PC subsets are capable of responding to BCR mediated signals. We further investigated if the PC isotype has an impact on BCR signalling.

**Methods:** BM samples from patients undergoing routine total hip arthroplasty without systemic immune manifestations were stained for baseline expression of spleen tyrosine kinase (Syk) and Bruton's tyrosine kinase (Btk) as well as for the phosphosites pSyk (Y<sup>352</sup>) and pBtk (Y<sup>223</sup>). BM mononuclear cells have been isolated, stimulated with anti-IgM/IgA/IgG and the increase of fluorescence intensity of pSyk (Y<sup>352</sup>) and pBtk (Y<sup>223</sup>) was measured by intracellular flow-cytometric analyses. In some experiments, cells have been stimulated with anti-IgA alone and stained for the isotype additionally to the pPTK staining.

**Results:** Whole BM stainings revealed that both CD19<sup>+</sup> and CD19<sup>-</sup> PC express the PTKs Syk and Btk at baseline. Both PC subsets showed the ability to respond to BCR stimulation with enhanced phosphorylation of the PTKs with a clear trend to reduced responsiveness among CD19<sup>-</sup> PC. Ig staining revealed that IgA expression was identified on both membrane and intracellularly, whereas IgG was



only expressed intracellularly. Co-staining of IgA with pPTKs showed that IgA<sup>+</sup> PC in both subsets are responsible for enhanced PTK phosphorylation independently of CD19 expression.

**Conclusions:** CD19<sup>+</sup> and CD19<sup>-</sup> BM PC express kinases involved in BCR signaling and respond by enhanced phosphorylation of PTKs upon BCR stimulation with IgA-expressing cells being exclusively responsible for this increase. Further functional consequences of IgA expression in BM PC and autoimmunity remain to be delineated.

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#### AB0025 MTOR PATHWAY ACTIVATION IN LARGE VESSEL VASCULITIS

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**Background:** Mammalian target of rapamycin complex 1 (mTORC 1) drives the proinflammatory expansion of T helper (TH) type 1, TH17 cells and controls fibroblast proliferation, typical features of large vessel vasculitis (LVV) pathogenesis. Molecular pathways involved in arterial lesions of LVV are unknown.

**Objectives:** To analyse mTOR pathway activation in LVV (giant cell arteritis and Takayasu arteritis).

**Methods:** We evaluate pathway activation in the mTORC and the nature of cell proliferation in blood and vessels of patients with LVV compared non-inflammatory aorta by using double immunostaining, western blot and flow cytometry. Finally, using flow cytometry, we study the effect of rapamycin on T cells homeostasis in LVV compared to HD.

**Results:** Proliferation of both endothelial cells and vascular smooth-muscle cells was shown in vascular lesions in LVV. The vascular endothelium of proliferating aorta vessels from patients with LVV showed indications of activation of the mTORC1 pathway in endothelial cells (S6RP phosphorylation) compared to non-inflammatory aorta (45%<sup>24,48</sup> versus 10.4% [9.7;14.9] positive S6RP endothelial cells, p=0.03). In cultured vascular endothelial cells, sera from patients with LVV stimulated mTORC1 through the phosphorylation of S6RP. Activation of mTORC1 was also found in Th1 and Th17 cells both systemically and in the blood vessels. Patients with LVV exhibited a diminished S6RP phosphorylation in Tregs. Inhibition of mTORC1 pathway with rapamycin, increase Tregs and decrease effector CD4<sup>+</sup>IFN $\gamma$ <sup>+</sup>, CD4<sup>+</sup>IL17<sup>+</sup> and CD4<sup>+</sup>IL21<sup>+</sup> T cells in patients with LVV.

**Conclusions:** Our results suggest that the mTORC1 pathway is involved in the vascular lesions of LVV. Targeting mTORC pathway may represent a new therapeutic option in patients with LVV.

**Disclosure of Interest:** None declared

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#### AB0026 TLR9 STIMULATION OF ANERGIC HCV-ASSOCIATED ATYPICAL MEMORY B CELLS TRIGGERS RHEUMATOID FACTOR AUTOIMMUNITY BY THE TNF-A PATHWAY

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**Background:** Hepatitis C virus (HCV) infection contributes to the development of autoimmune disorders, but the mechanisms responsible for HCV-associated autoimmunity are not well understood.

**Results:** Here we show that TLR9 stimulation of atypical memory (AtM) B cells from patients with HCV-associated cryoglobulinemia vasculitis induce the secretion of IFN $\gamma$ , TNF $\alpha$  but not IL17A by CD4<sup>+</sup>CD25<sup>-</sup> effector T cells and stimulate their proliferation. Conversely, they reduce the proliferative capacity of CD4<sup>+</sup>CD25<sup>hi</sup>CD127<sup>low</sup>FoxP3<sup>+</sup> regulatory T cells. TLR9-stimulated AtM secrete TNF $\alpha$  and IgMs with rheumatoid factor activity. We identify a transcriptional

signature specific of TLR9-stimulated AtM, centred on TNF $\alpha$  overexpression. AtM B-cell expansions display intraclonal diversity of mutated IgM with features of antigen-driven maturation. AtM-derived antibodies possess rheumatoid factor activity, with each antibody clone targeting a unique epitope on the human IgG Fc region. AtM antibodies are neither polyreactive nor reactive to ubiquitous autoantigens and importantly, not cross-reactive against HCV antigens including NS3 and E2 proteins.

**Conclusions:** These data strongly suggest a central role for AtM in defective tolerance of HCV-CV patients through TLR9 reactivation of anergic AtM and production of IgM antibodies with rheumatoid factor activity.

**Disclosure of Interest:** None declared

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#### AB0027 SCREENING FOR ANTIBODY REACTIVITY IN EARLY AXIAL SPONDYLOARTHRITIS IDENTIFIES NOVEL ANTIGENIC TARGETS

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**Background:** Diagnosis of axial spondyloarthritis (axSpA) is challenging since clinical manifestations, such as inflammatory back pain, peripheral arthritis, enthesitis and inflammatory bowel disease, often overlap with other disorders. Despite the use of the genetic marker Human Leukocyte Antigen (HLA)-B27 in axSpA patients, an appropriate serological test is still lacking. Although antibodies are not considered to be a hallmark of axSpA, emerging evidence suggests plasma cells and antibodies to be involved in the disease course<sup>1</sup>.

**Objectives:** Our aim is to screen for antibodies reactive against antigenic targets in plasma of early axSpA patients which may potentially result in novel antibody biomarkers to improve axSpA diagnosis and can enhance the assessment of disease activity, prognosis and therapy response.

**Methods:** We applied Serological Antigen Selection (SAS), an unbiased and high-throughput antibody profiling procedure based on cDNA phage display. First, a cDNA phage display library was constructed from synovial hip tissue from 3 axSpA patients and screened for antibody reactivity in pooled plasma of early axSpA patients (n=10). By performing SAS, we identified antibodies in the axSpA plasma pool that were reactive against 104 different antigenic targets. These targets correspond to both known proteins and novel linear peptides. In a first validation, antibody reactivity against each of these 104 SAS-identified targets was determined in pooled plasma of additional early axSpA patients (n=50) and healthy controls (HC, n=30). Antigenic targets that showed highest reactivity in axSpA plasma pools were further validated in individual plasma samples of early axSpA patients (n=71) and HC (n=73) using phage enzyme-linked immunosorbent assay (ELISA).

**Results:** Increased antibody reactivity against 7 targets was found in pooled plasma of additional early axSpA patients. Further validation of these 7 antigenic targets in individual plasma samples revealed antibody reactivity in 39% of the early axSpA patients (28/71) compared with 21% of the HC (15/73). By forming a biomarker panel with 4 of these targets, specificity could be improved to 88% (9/73 HC) with only a slightly decrease in sensitivity (34%, 24/71).

**Conclusions:** We identified autoantibody reactivity to novel antigenic targets in early AS patients. In order to establish the true biomarker potential, antibody reactivity against our identified novel antigenic targets will be further validated in an independent cohort of axSpA patients, rheumatic controls and low back pain controls. Identification of antibody reactivity against novel antibody targets in early axSpA patients can contribute to novel biomarkers for an enhanced diagnosis and might provide more insight into the underlying disease pathology, resulting in novel treatment strategies and eventually improve disease outcome in axSpA patients.

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**AB0028** **ACTIVATED STROMAL CELLS INDUCE CCL20 RELEASE AND T CELL MIGRATION**

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**Background:** Although the role of IL-23/Th17 axis in psoriatic arthritis (PsA) is well known<sup>1</sup>, little data is available on the contribution of stromal cells to this pathway<sup>2</sup>. Enthesitis is a common feature of PsA and it may represent the site of onset<sup>3,4</sup>, suggesting tendon stromal cells (tenocytes) may have an initiating role in Th17 driven pathogenesis.

**Objectives:** To assess the ability of stromal cells to produce CCL20, a chemokine able to recruit Th17 cells, and to induce T cell migration.

**Methods:** Healthy tenocytes cultured from hamstring tendons and fibroblast-like synoviocytes (FLS) from PsA patients were stimulated with human recombinant IL-1 $\beta$  (1 ng/ml) and IL-17A (1, 10 and 100 ng/ml). Expression of CCL20 transcript and protein were assessed by quantitative PCR and ELISA, respectively. T cell migration assays were performed with magnetically enriched CD3<sup>+</sup> cells from peripheral blood of PsA patients and healthy controls using a Transwell system. Following incubation with conditioned media from stimulated stromal cells, the migrated cells were harvested and analysed via light microscopy and flow cytometry.

**Results:** Both tenocytes and FLS were able to produce CCL20 following stimulation with IL-1 $\beta$ . Furthermore, the addition of IL-17A induced a synergistic effect with IL-1 $\beta$ . Following cytokine stimulation, diseased stromal cells produced greater levels of CCL20 compared to stimulated healthy tenocytes. In addition, conditioned media from stimulated tenocytes promoted T cell migration, compared with supernatants from unstimulated tenocytes.

**Conclusions:** We have shown that tendon and PsA synovium stromal cells are able to produce CCL20 and induce T cell recruitment, suggesting a role in the chemotaxis of Th17 cells. The positive feedback observed with IL1 $\beta$  and IL-17A suggests a close relationship between stromal cells and Th17 cells.

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**AB0029** **CHARACTERISTIC PATTERNS OF HLA PRESENTATION AND T CELL DIFFERENTIATION IN ADULT-ONSET STILL'S DISEASE**

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**Background:** The role of T cells in AOSD pathogenesis remains controversial. In autoimmune and auto-inflammatory diseases, such as rheumatoid arthritis (RA) and Behçet's disease, a human leukocyte antigen (HLA)-restricted T cell response to antigen has been shown to affect disease progression, with several HLA alleles strongly associated with disease severity.

**Objectives:** In this study, we investigated the frequencies of cells presenting HLA-DP, DQ, and DR, as well as differentiated T cell populations including naïve and effector memory T cells in peripheral blood leukocytes (PBLs) of patients with AOSD. Frequencies of the markers were then compared based on clinical outcomes and disease activity, to better understand the role of these cell populations in the pathogenesis of AOSD.

**Methods:** This study enrolled 14 active AOSD patients, 20 rheumatoid arthritis (RA) patients, and 20 healthy controls (HC). The percentage of surface-stained cells presenting HLA-DP, DQ, and DR alleles, and the proportions of differentiated T cell populations in peripheral blood leukocytes (PBLs) were measured by flow cytometry.

**Results:** Patients with AOSD exhibited significantly higher percentages of lymphocytes presenting HLA-DP and HLA-DR, and lower percentages of cells presenting HLA-DQ, than patients with RA or HC. The proportions of CD4<sup>+</sup>, CD4<sup>+</sup>CCR7<sup>+</sup>, CD4<sup>+</sup>CD62L<sup>-</sup>, and CD8<sup>+</sup>CD62L<sup>-</sup> cells in PBLs were decreased in

patients with AOSD relative to patients with RA or HCs. In contrast, AOSD patients exhibited increased proportions of CD8<sup>+</sup> naïve T cells in whole blood relative to patients with RA or HC. The proportions of CD4<sup>+</sup> effector memory T cells, CD8<sup>+</sup> naïve T cells, and CD8<sup>+</sup> effector memory T cells in whole blood cells and CD4<sup>+</sup> effector memory T cell in lymphocytes were significantly associated with systemic score.

**Conclusions:** While the frequencies of CD4<sup>+</sup>, CD8<sup>+</sup>, CCR7<sup>+</sup>, CD4<sup>+</sup>CCR7<sup>+</sup>, CD4<sup>+</sup>CD62L<sup>-</sup>, and CD8<sup>+</sup>CD62L<sup>-</sup> cells were significantly decreased in patients with AOSD, the frequency of CD8<sup>+</sup> naïve T cells was elevated in patients with AOSD, and correlated with systemic score. Additional studies in a larger cohort of patients will be necessary to evaluate the role of these markers in the pathogenesis of AOSD.

**Disclosure of Interest:** None declared

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**AB0030** **TARGETING NF-KB SIGNALLING IN B CELLS: A POTENTIAL NEW TREATMENT MODALITY FOR ANCA-ASSOCIATED VASCULITIS**

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**Background:** The pivotal role of B cells in the pathogenesis autoimmune diseases such as ANCA-associated vasculitis (AAV) is well-established and further substantiated by beneficial therapeutic effects of rituximab (anti-CD20 B cell targeted therapy). However, this results in prolonged B cell depletion while long-lived plasma cells are not targeted. Thus, there is a need for novel therapeutics targeting the B-cell lineage in AAV. NF- $\kappa$ B signalling pathways that act downstream of various B cell surface receptors, including the B cell antigen receptor, CD40, BAFFR and TLRs, are crucially involved in B cell responses and may be suitable as novel targets.

**Objectives:** To identify whether inhibition of NF- $\kappa$ B signalling by novel pharmacological inhibitors is effective in targeting B cell responses in general and more specifically blocks (auto)antibody production and plasmablast differentiation in B cells from AAV patients.

**Methods:** PBMC and sorted B cells from AAV patients and healthy donors were cultured with T cell-dependent (anti-IgM +anti CD40+IL-21) and T cell-independent (CpG +IL-2) stimuli. NF- $\kappa$ B signalling was targeted in these cultures by small molecule inhibitors of NF- $\kappa$ B inducing kinase (NIK, non-canonical NF- $\kappa$ B signalling) and Inhibitor of  $\kappa$ B kinase  $\beta$  (IKK $\beta$ , canonical NF- $\kappa$ B signalling). Downstream NF- $\kappa$ B signalling and nuclear NF- $\kappa$ B translocation was determined by Western blot and confocal imaging. Effects on B cell proliferation and differentiation were determined by CFSE dilution assays and flow cytometric analysis of B cell markers. (Auto)antibody production was measured by ELISA.

**Results:** In B cells of AAV patients and healthy donors, targeting of NIK and IKK $\beta$  effectively inhibited downstream non-canonical or canonical NF- $\kappa$ B signalling, respectively. In a B cell stimulation assay, NIK and IKK $\beta$  inhibition significantly reduced T cell-dependent (anti-IgM +anti CD40+IL-21) and T cell-independent (CpG +IL-2) B cell proliferation. In addition, B cell differentiation towards plasmablasts (CD27<sup>+</sup>/CD38<sup>+</sup>) and functional antibody production was attenuated by both NIK and IKK $\beta$  inhibitors. Interestingly, the effects of NIK inhibition appeared to be B cell-specific as T cell proliferation was largely unaffected.

**Conclusions:** These data demonstrate that inhibition of NF- $\kappa$ B signalling in AAV B cells results in the modulation of various B cell responses. Ongoing studies will indicate whether targeting of NF- $\kappa$ B signalling in B cells may be an effective novel treatment modality for AAV.

**Disclosure of Interest:** None declared

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**AB0031** **DEEP IMMUNE-PROFILING OF CD4+ T CELLS IN BEHÇET'S DISEASE**

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**Background:** Functionality and immune-phenotypes of the human CD4<sup>+</sup> T-cell compartment in Behçet's disease (BD) are under-investigated, but several lines of evidence point to its relevance in the pathogenesis, progression and remission of the disease.

**Objectives:** We aimed to apply an unbiased single cell approach to assess protein expression levels of phenotypic and functional markers within the human CD4<sup>+</sup> T cell compartment in subjects with prototypical BD in order to identify cell populations of potential biologic relevance.

**Methods:** We determined single cell surface/intra nuclear expression levels of CD3, CD4, CD8, CD127, CD25, CD45RA, CCR7, FoxP3, HELIOS, Ki67, HLA-DR, CD38, CD39 in PBMC by flow cytometry and computed the representation of all mathematically possible cell populations within pre-defined starting populations. PBMC from BD subjects (n=13), healthy donors (HD) (n=25) and diseased subjects with non-BD auto-immune uveitis (n=11; VKH, Sarcoidosis, and HLA-B27 associated uveitis) were used. BD subjects met ISG criteria and were Arab or Chinese. 62% had pan-uveitis, 23% major vascular disease, and 7% parenchymal CNS disease. 46% were HLA-B51 carriers.

**Results:** Computation of all populations defined by CD127, CD25, CD45RA, CCR7, FoxP3, HELIOS, Ki67, HLA-DR within the CD4<sup>+</sup> T cell compartment yielded a total of 6560 (3<sup>8</sup>-1) cell populations out of which 45 reached a significance level of p<0.000001 in ANOVA testing to differentiate 3 groups (BD, non-BD uveitis, and HD). All of these populations comprised sub-types of the human regulatory T (Treg) cell compartment with a strong predominance of non-proliferating, non-activated, FoxP3<sup>+</sup>HELIOS<sup>+</sup> Treg carrying central-memory phenotypes (CD45RA<sup>-</sup>, CCR7<sup>+</sup>). Unpaired testing of BD vs non-BD revealed 43 distinct cell populations at a significance level of p<0.002 representing CD25<sup>+</sup> non-Treg; comparison of BD vs HD uncovered 58 populations at a significance level of p<0.0001 representing FoxP3<sup>+</sup>HELIOS<sup>+</sup> subpopulations, and non-BD vs HD identified 61 populations at p<0.001, comprising CD25<sup>+</sup>CD127<sup>+</sup> FoxP3<sup>+</sup>, but consistently HELIOS<sup>-</sup> cells. A separate analysis using CD38, CD39, CD227, TIGIT, CD45RA, CCR7 within the CD3<sup>+</sup>CD4<sup>+</sup>CD8<sup>-</sup>CD127<sup>+</sup>CD25<sup>+</sup> compartment that contains most human Treg, showed 48 populations (p<0.0001) in 3-way comparison pointing to high significance of TIGIT and CD226 staining Treg subpopulations, and 18 populations with differential expression of CD39<sup>+</sup> between BD and non-BD diseased subjects. TIGIT and CD226 co-expressing Treg (CD127<sup>+</sup>CD25<sup>+</sup>) subpopulations also reached significance (p<0.02) in a longitudinal paired analysis of 7 BD subjects in active vs inactive disease states, as did 56 out of 6560 populations within total CD4<sup>+</sup> T cells, mostly representing non-Treg cells in active BD.

**Conclusions:** Differential expression of CD4<sup>+</sup> Treg and non-Treg cells shapes the immune-phenotype of BD vs states of health and non-BD autoimmune diseases that have phenotypic overlap with BD (uveitis). The populations with the highest significance for differentiating BD from healthy states seem to exist within the HELIOS<sup>+</sup>FOXP3<sup>+</sup> compartment of non-activated, non-proliferating Treg, suggesting relevance of a true Treg phenotype. This is likely not specific to BD. Non-Treg CD25<sup>+</sup> cell populations seem more indicative of BD vs non-BD uveitic disease as well as of clinically active BD while populations with high CD39 expression may signify non-BD states of immune-mediated disease.

**Disclosure of Interest:** None declared

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AB0032

### B-CELL SUBPOPULATIONS IN NEWLY DIAGNOSED EORA AND YORA PATIENTS

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**Background:** B-cells are thought to have an important role in rheumatoid arthritis (RA). This is demonstrated by the success of B-cell depleting therapy as well as the negative prognostic value of anti-citrullinated protein antibodies (ACPA)<sup>1</sup>. However, the pathogenesis of the disease is unclear. Studies have suggested that there are differences in disease characteristics between elderly-onset RA patients (EORA, defined by disease onset at ≥60 years of age) and younger-onset RA patients (YORA, with disease onset <60 years of age).<sup>2</sup>

**Objectives:** Our aim was to study the B-cell subpopulations in newly diagnosed EORA and YORA patients. We investigated whether there were differences in B-cell subpopulations between the groups and whether there was a correlation between B-cell subpopulations and disease activity, autoantibody profile and inflammatory parameters in these two RA patient groups.

**Methods:** Treatment-naive EORA (n=29) and Yora (n=31) patients with newly diagnosed RA were included at their first visit to the Rheumatology clinic. The patients' clinical response (DAS28), autoantibodies and B-cells were assessed. Flow cytometry was used for the analysis of cellular surface markers on leukocytes in peripheral blood: CD19, CD27, CD24, CD27, CD38, PD-1, PD-L1, IgG,

IgD and IgM. Non-parametric tests were used for comparing groups and Spearman's test was used for correlation.

**Results:** We found a correlation between the ACPA titers and the frequency of the CD27<sup>+</sup> and CD27<sup>-</sup> memory B cell populations in EORA patients but not in YORA patients. This was further supported by a correlation of the ACPA titer and IgG<sup>+</sup> B cells in the EORA patients (r=0.7, p=0.003) and not in the YORA patients. There was neither a correlation between age and ACPA titer nor between age and memory B cell populations. We did not find any significant difference between the B cell subpopulations in the two patient groups.

**Conclusions:** Our results suggest that the memory B cell compartment in peripheral blood in EORA patients reflects the ACPA titer. This was not seen in the YORA patients. The mechanisms behind these findings need to be further elucidated.

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**Disclosure of Interest:** None declared

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AB0033

### B REGULATORY CELLS POSITIVELY CORRELATE WITH ANTIBODIES AGAINST SS-A RO52 IN SYSTEMIC SCLEROSIS

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**Background:** We and Japanese Investigators have shown that IL-10-producing regulatory B cells (B10 cells) are decreased in systemic sclerosis (SSc).<sup>1,2</sup> Contrary to the Japanese, we did not find a negative correlation between B10 cells and SSc-specific autoantibodies (autoabs) against centromere, Scl-70 or RNA polymerase III.<sup>3</sup> Since we found anti-Ro52 SS-A antibodies in approx. 30% of patients with SSc,<sup>4</sup> this being the 3rd most frequent autoantibody in this disease, we considered what is the relation of B10 cells with anti-Ro52 antibodies.

**Objectives:** We examined the number and function of Bregs in SSc in relation to anti-Ro52 autoabs.

**Methods:** Serum samples and PBMCs were collected from 40 SSc patients (15 anti-Scl-70, 20 anti-CEN and 5 anti-RNA pol III) and were further divided according to anti-Ro52-positivity into 22 anti-Ro52(+) and 18 anti-Ro52 (-). All serum samples were tested for the presence of disease-specific autoantibodies against Scl-70, CENP, RNA-pol, and against Ro52 using a line assay (Euroimmun Germany). The function of Bregs was determined by the ability to express IL-10 following activation with ODN 2006 (TLR-9). Percentages of transitional (CD19<sup>+</sup>CD24<sup>high</sup>CD38<sup>high</sup>) and memory (CD19<sup>+</sup>CD27<sup>+</sup>CD24<sup>high</sup>) Bregs were assessed by flow cytometry using fluorochrome conjugated antibodies (BD Biosciences).

**Results:** IL-10(+) Bregs (B10) were significantly elevated in SSc patients (6.7% ±2.6% n=15) with high-titre antibodies against Ro52 (mean anti-Ro52 arbitrary units AU >100; positivity cut-off AU >20) compared to patients (4.2%±1.9%, n=22) totally negative for Ro52 (mean AU <10) (p=0.03). Transitional Bregs were also significantly increased in all SSc patients tested positive for anti-Ro52 autoantibodies (7.5%±1.9%) compared to SSc patients negative for anti-Ro52 autoantibodies (3.7±0.8, p=0.02). Furthermore, transitional Bregs positively correlated with anti-Ro52 antibody levels (r<sup>2</sup>=0.39 p=0.01). In contrast, memory Bregs were not significantly different between anti-Ro52-positive (14.1%±2.7%) and -negative SSc patients (11.8%±2.2%) (p>0.05).

**Conclusions:** IL10-producing Bregs are higher in SSc patients with high anti-Ro52 antibodies and transitional Bregs correlated with antiRo52 antibodies in patients with SSc suggesting that this autoantibody could be a potential marker of Breg efficiency.

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AB0034

#### LOOKING FOR A SLE SIGNATURE ON PERIPHERAL B CELL SUBSETS: DOES A PREPONDERANT CD38 +PLASMA BLAST-SUBPOPULATION LACK CD73 AS A SIGN OF A DISTURBED ADENOSINE AXIS?

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**Background:** Systemic Lupus Erythematosus (SLE) is an autoimmune disorder characterised by polyclonal Bcell activation, production of dsDNA-autoantibodies and cytokines. Subsets of Bcells play a central role in SLE-pathogenesis. The inflammatory milieu is characterised by the accumulation of adenosine, which confers immunosuppressive effects.

**Objectives:** In SLE, the role of CD73, an enzyme involved in the extracellular generation of adenosine from ATP, is not well characterised. This study aimed to characterise expression of CD73 Bcell subsets of SLE-patients as compared to healthy controls (HC).

**Methods:** Bcell subsets were characterised from peripheral blood of 23 SLE patients attending the outpatient clinic at the Rheumatology Unit of University Hospital Düsseldorf and of 15 HC by FACS. All patients fulfilled the revised SLE-criteria of ACR and were randomly collected in clinical remission state (SLEDAI 1.1±1.9).

**Results:** By comparison of Bcell subsets between SLE and HC, CD38 was dominantly expressed by SLE-patients (SLE 74.2%±12.9% vs. HC 64.2%±12.2%; p(MWU)=0.018). Furthermore, SLE-patients showed an increase in CD19 +IgD CD27+CD38 high plasmablasts (SLE 2.1%±3.4% vs HC 0.4%±0.4%, p(MWU)<0.001). Furthermore, SLE-plasmablasts showed decreased CD73 expression as compared to HC(SLE 2.1%±1.9% vs HC 3.5%±2.2%; p(MWU)=0.034). SLE-Bcells revealed a trend towards an augmented CD38highCD138+plasmacell fraction (SLE 0.40%±0.5% vs HC 0.08%±0.07%; p=0.07), without any difference in CD73 expression. On the other hand, exhausted-memory B cell fraction (CD19 +IgD CD27-CD21-CD138-), showed an increased CD73 expression in SLE (SLE 13.7%±9.2% vs HC 6.2%±5.4%; p=0.004).

**Conclusions:** Our study confirms CD38 +plasmablasts as being increased in peripheral blood from SLE patients as compared to HC. Furthermore, the data reveal a deficiency for CD73 on SLE plasmablasts, which suggests a decreased anti-inflammatory capacity of SLE plasmablasts as compared to HC, supporting the notion of a disturbed adenosine axis in SLE. On the other hand, the enlarged CD73 +exhausted memory pool in SLE could point to an accelerated flow of CD73 +B cells into an exhausted B cell fraction. These findings support the hypothesis of dysregulation of the adenosine axis in SLE even in inactive SLE patients.

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AB0035

#### A PHYSIOLOGICAL NETWORK OF IGG AUTOANTIBODIES TARGETING G PROTEIN COUPLED RECEPTORS

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**Background:** Since the time when Paul Ehrlich conceived the term “horror auto-toxicus”, autoantibodies have been associated with the development of autoimmune diseases. However, several works have recently shown the presence of autoantibodies in sera from healthy subjects (n=489), who do not develop autoimmune diseases.

**Objectives:** Here, we report a network of immunoglobulin G (IgG) autoantibodies targeting G protein-coupled receptors (GPCRs), growth factors and growth factor-related molecules in sera from healthy subjects.

**Methods:** Autoantibody levels in sera were assessed using ELISA. Autoantibody network was analysed by exploratory factor analysis (EFA), dandelion plot method, hierarchical clustering, and multi-study factor analysis (MFA). We also reverse engineered autoantibody functions through *in silico* evaluation of autoantibody target interactions using STRING and gene ontology (GO). To test the autoantibodies functionality we assessed the *in vitro* production of IL-8 by PMBCs and neutrophil migration in response to IgG from healthy subjects as well as ETAR-immunised and control mice. Leukocyte cellularity to secondary immune organs was analysed comparing ETAR-immunised with control mice.

**Results:** Gender, age and the presence of pathological conditions (systemic sclerosis n=84, Alzheimer's disease n=91 and ovarian cancer n=207) changed correlations between the autoantibodies and their hierarchical clustering distribution. Notably, subjects at age below and above 65 years or with pathological conditions exhibited particular autoantibody hierarchical clustering signatures. In addition, females at age above 65 years, representing the group of subjects with higher risk to develop SSc, displayed the closest link to SSc in terms of autoantibody hierarchical clustering. Finally, autoantibody directed against the endothelin receptor type A (ETAR) showed an essential role in the autoantibody network by orchestrating neutrophil trafficking *in vitro* and in ETAR-immunised mice.

**Conclusions:** Our data provide a framework for the existence of a physiological network of autoantibodies and reveal a new paradigmatic view on these physiological molecules.

**Disclosure of Interest:** None declared  
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AB0036

#### ROLE OF PROGRAMMED DEATH-1 PATHWAY ON CD8+ T CELLS CYTOTOXICITY IN PRIMARY BILIARY CHOLANGITIS

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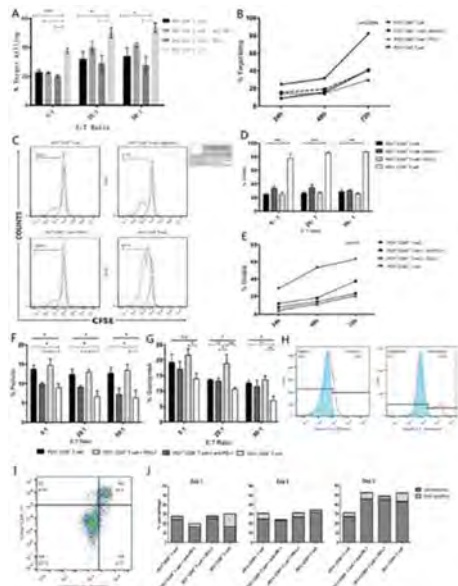
**Background:** Primary Biliary Cholangitis (PBC) is a chronic progressive autoimmune disease. It has been proven that there was abnormal activation of CD8 +T cells. Previous studies have shown that abnormal expression programmed death-1 (PD-1) and its ligand (PD-L1) in PBC. However, no study was found to confirm the abnormality of PD-1/PD-L1 pathway in CTL in PBC.

**Objectives:** To investigate the role of PD-1 and its ligand PD-L1 on CD8+ T cells cytotoxicity in the immunological mechanism of PBC.

**Methods:** The expression of PD-1 in peripheral CD8+ T cells of 69 patients diagnosed with PBC as well as 58 health controls (HC) was detected by flow cytometry. Plasma cytokines related to PD-1/PD-L1 pathway were detected by ELISA. The co-localization of PD-1 and CD-8, PD-L1 and CK19 in portal region in liver biopsy was analysed by immunofluorescence assay. Meanwhile, the relative gene expression of PD-1 regulatory pathway in CD8+ T lymphocytes were measured by RT-PCR. And co-culture of PD-1+ CD8+ CTL and HiBEC was done *in vitro* to detect the cytotoxicity, proliferation and cytokine expression of CD8+ CTL and the apoptosis of HiBEC.

**Results:** The proportion of peripheral PD-1+ CD8+ T cell decreased in PBC (12.0%±8.8%) than HC (19.9%±12.5%) (p<0.001). The plasma concentration of IL-10, IFN-γ and TGF-β in the PBC group were higher than that in HC (8.29±9.00 pg/ml v.s. 4.43±5.08 pg/ml, p=0.0066; 51.94±52.94 vs 26.71±26.26 pg/ml, p=0.0015; 1302.0±1972.8 pg/ml vs 205.8±298.9 pg/ml, p=0.0018, resp.). Compared with HC (n=19), *Tbet* gene expression in CD8+ T lymphocytes was increase

in PBC group (n=21) ( $0.82 \pm 0.76$  vs  $3.03 \pm 4.23$ ,  $p=0.028$ ). Immunofluorescence co-localization revealed that increased PD-1 positive cells in early PBC stage than late one, and less PD-L1 positive cells as well as PD-L1 and CK19 co-localised ones in PBC patients compared to HC. In the CTL and HiBEC co-culture system *in vitro*, the cytotoxicity of PD-1<sup>+</sup> CD8<sup>+</sup> T cells was weaker, with less proliferation and tendency of decreased production of IFN- $\gamma$  and TGF- $\beta$  compared to PD-1<sup>-</sup> CD8<sup>+</sup> T cells. Meanwhile, HiBEC apoptosis was relatively more in PD-1<sup>-</sup> CD8<sup>+</sup> T cells co-culture group. These effects could be antagonised by anti-PD-1 antibody and enhanced by PD-L1.



Abstract AB0036 – Figure 1

**Conclusions:** In PBC, the expression of Tbet is up-regulated in CD8<sup>+</sup> T cells, which leads to the down-regulated expression of PD-1 on. Meanwhile, the expression of PD-L1 in HiBEC may be down-regulated. The silenced PD-1/PD-L1 pathway caused more CD8<sup>+</sup> T cells proliferation, more related cytokines production and the enhanced CTL cytotoxic effects on HiBEC. PD-1/PD-L1 pathway functions as an important pathway in the immunological mechanism of PBC.

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#### AB0037 MIR-155 PROMOTES THE DIFFERENTIATION OF TH17 CELL BY TARGETING ETS-1 IN RHEUMATOID ARTHRITIS

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**Background:** MicroRNAs play important roles in arthritis. MiR-155 emerges as a central regulator of the immune response, but its function in autoimmune arthritis is poorly understood.

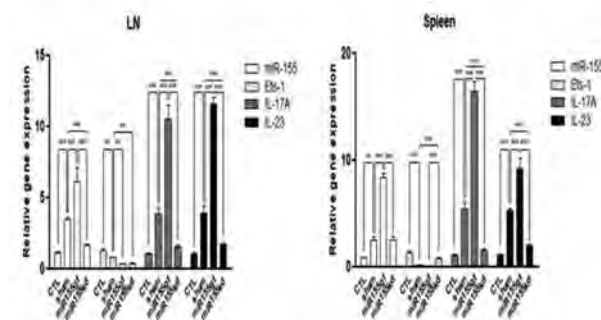
**Objectives:** To clarify the role of miR-155 in the balance of CD4<sup>+</sup>Th17 and Treg cell differentiations as well as how their mechanisms function in autoimmune arthritis.

**Methods:** CD4<sup>+</sup>T cells were *in vitro* isolated from DBA1 mice. The transfections of miR-155 mimics and miR-155 inhibitors in CD4<sup>+</sup>T cells were performed for

enhanced or knockdowns of miR-155 expression and RNA interference was applied to silence Ets-1 gene expression. In addition, we carried out *in vivo* experiments of enhanced miR-155 expression by lenti-virus mediated miR-155 (LV-miR-155) infection and silencing of miR-155 expression by lenti-virus-anti-miR-155 (LV-anti-miR-155) within our well-established type II collagen (CII)-induced arthritis (CIA) mice model. The ratios of IL-17<sup>+</sup> TH17 cells were analysed using flow cytometry (FCM). The expressions of some key autoimmune-response of genes including ROR $\gamma$ t, IFN-g, Ets-1, IL-17, IL-23, and Stat3 were further determined by (Taqman) Quantitative Real-time PCR and Western blotting. Initially n=6 per group if not indicated further; totally 6 groups in parallel per experiment. \* $p < 0.05$ , considered as significantly; \*\* $p < 0.01$ , considered as highly significantly.

**Results:** For the first time we showed that miR-155 may promote Th17 cell differentiation in RA pathogenesis. Firstly, we observed that miR-155 may significantly induce the expressions of some key autoimmune-response genes including ROR $\gamma$ t, IFN-g, IL-17, IL-23, and Stat3 but it significantly inhibited Ets-1 gene expression. 2ndly, miR-155 may in part modulates Th17 cell differentiation by targeting Ets-1 in that indeed the expression of miR-155 significantly co-related with disease index in CIA mice. Furthermore, the CIA mice with *in vivo* forced expression of miR-155 have significantly more Th17 cells (i.e. high ratio) and severe CIA disease index compared to their control CIA mice; strikingly, they also have a significantly higher expression of aforementioned autoimmune-response genes compared to their corresponding controls along with the response of Ets-1 exactly in a verse direction. Consistently, the CIA mice with *in vivo* knockdown of miR-155 expression resulted in significantly less Th17 cells and lesser severe CIA disease index compared to their control CIA mice. However, they have a significantly lower expression of above-mentioned autoimmune-response genes compared to their corresponding controls along with a response of Ets-1 in a verse direction (the data in part shown in Figure 1; sham=CIA treated with LV-nonspecific sequence).

**Conclusions:** For the first time our data show miR-155 has a critical role in Th17 differentiation and the RA pathogenesis via targeting the Ets-1. Although it warrants further investigations, miR-155 might be a promising therapeutic target for autoimmune diseases, esp. RA.



Abstract AB0037 – Figure 1

**Acknowledgements:** This work was supported by National Natural Science Foundation of China #81102266. All authors listed were either involved in conception and design, or acquisition, analysis and interpretation of data, and/or writing. Each author gave their final approval of this version.

**Disclosure of Interest:** None declared

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## Innate immunity in rheumatic diseases

#### AB0038 TBK1: A KEY REGULATOR AND POTENTIAL TREATMENT TARGET FOR INTERFERON POSITIVE SYSTEMIC LUPUS ERYTHEMATOSUS AND SYSTEMIC SCLEROSIS

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**Background:** Upregulation of type I interferons (IFN-I) is a hallmark of systemic autoimmune diseases like systemic lupus erythematosus (SLE) and systemic sclerosis (SSc). Three different receptor families are implicated in the induction of IFN-I production: Toll-like receptors (TLRs), RIG-like receptors (RLRs) and DNA-sensing receptors (DSRs). TANK-binding kinase (TBK1), is an important signalling hub downstream of RLRs and DSRs. TBK1 activates IRF3 and IRF7, leading

to IFN- $\gamma$  production and subsequent induction of interferon-stimulated genes (ISGs).

**Objectives:** To explore the potential of TBK1 inhibitors to downregulate IFN- $\gamma$  activation in SLE and SSc.

**Methods:** TBK1, IRF3, IRF7 and STAT1 were determined by qPCR in PAXgene samples and phosphorylated-TBK1 (pTBK1) was analysed by flowcytometry in plasmacytoid dendritic cells (pDCs) from IFN- $\gamma$  positive (IFNpos) patients. Peripheral blood mononuclear cells (PBMCs) from SLE and SSc patients and TLR7-stimulated PBMCs from healthy controls (HCs) were cultured with the TBK1 inhibitors BX795 followed by analysis of ISGs.

**Results:** Increased expression of TBK1, IRF3, IRF7 and STAT1 in whole blood and pTBK1 in pDCs was observed in IFNpos pSS, SLE and SSc patients compared to HCs. Upon treatment with BX795, PBMCs from IFNpos pSS, SLE, SSc and TLR7-stimulated HCs downregulated the expression of the ISGs MxA, IFI44, IFI44L, IFIT1 and IFIT3. The TBK1 inhibitor inhibited the secretion of IFN- $\gamma$  by TLR7-stimulated PBMCs from HCs.

**Conclusions:** TBK1 inhibition reduced expression of ISGs in PBMCs from IFNpos SLE and SSc patients indicating TBK1 as a potential treatment target.

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AB0039

#### IMMUNOSUPPRESSIVE EFFECT OF MESENCHYMAL STEM CELLS ON MONOCYTES DERIVED FROM PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Mesenchymal stem cells (MSCs) are a heterogeneous population of fibroblast-like progenitor cells that may be isolated and expanded from bone marrow, umbilical cord and other tissues. Moreover, MSCs display the capacity to self-renew and differentiate into various mesodermal cell lineages. They also have drawn considerable attention for their regenerative and immunosuppressive effects in a range of autoimmune diseases, which raises the question for their potential use as therapeutic tool in rheumatoid arthritis.

**Objectives:** In line with aforementioned and taking in mind that monocytes playing pivotal role in orchestrating immunological tolerance, we aimed to study the immunosuppressive effects of adipose tissue derived mesenchymal stem cells (AT-MSC) on monocytes derived from patients with rheumatoid arthritis (RA).

**Methods:** We enrolled 12 patients matching the ACR<sup>EULAR</sup> 2010 criteria for RA. AT-MSC were isolated and cultured according to well established protocols. ELISA was performed for testing the cytokines produced by AT-MSC (IL-1, IL-10, IL-4, IFN- $\gamma$ , IL-6, IL-8, CCL-5, RANTES, IL-17). Peripheral blood mononuclear cells (PBMCs) isolated from RA patients' samples were cultured in AT-MSC conditioned media and in control media. Flow cytometry was used for detection of monocytes markers (CD14, CD80, CD86, HLA-DR).

**Results:** Our results revealed considerable increase in number of cells expressing the myeloid lineage surface marker CD14 ( $p=0.026$ ) under the influence of AT-MSC medium. We further demonstrated decrease in percentage values of monocytes expressing HLA-DR ( $p=0.004$ ) and CD80/86 surface molecules ( $p=0.47$ ). Moreover, significant reduction in mean fluorescent intensity of HLA-DR surface expression ( $p=0.016$ ) was also demonstrated.

**Conclusions:** Our study unambiguously points out that under the impact of AT-MSC media monocyte development into dendritic cells was hampered and was also skewed into direction of accumulation of monocytes displaying more tolerogenic phenotype characterised by down regulation of HLA-DR and B7 complex (CD80/86) surface expression. Furthermore, antigen presentation alongside with expression of the co-stimulatory B7 complex and cytokine ambience forms a three-way signalling pathway responsible for T helper activation and proliferation and consequent antibody production by plasma cells. Hence, effects exerted by AT-MSC conditioned media on monocyte lineage development should not be neglected in the context of developing novel therapeutic approaches and strategies for treatment of RA.

**Disclosure of Interest:** None declared

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AB0040

#### TOLL-LIKE RECEPTOR 9 INFLUENCES INFLAMMATORY ARTHRITIS AND OSTEOCLASTOGENESIS

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**Background:** Release and insufficient removal of endogenous nucleic acids may be involved in triggering autoimmune reactions important in the initiation of systemic autoimmune diseases including rheumatoid arthritis (RA). Nucleic acid sensing molecules, such as the endosomal Toll-like receptors (TLRs) 7 and 9, have been linked to pathogenic autoimmune processes, but their role in RA is less clear. Data obtained in rats with pristane-induced arthritis (PIA) suggested involvement of TLR9 in the pathogenesis of this arthritis model<sup>1</sup>.

**Objectives:** To gain more insight into the role of TLR9 in autoimmune arthritis, TLR9 inhibition with specific oligodeoxynucleotide sequences (ODN)<sup>2</sup> was investigated in rats with PIA. To further investigate TLR9 involvement, streptococcal cell wall (SCW) arthritis was induced in TLR9<sup>-/-</sup> mice.

**Methods:** Arthritis was induced in mice with SCW lysates and in rats with the mineral oil pristane. Rats were treated with a TLR9 antagonist, starting before disease induction. Arthritis was scored using established scoring systems, inflammation and bone erosion were quantified by histological analysis. Levels of  $\alpha$ -1-acid-glycoprotein (AGP), rheumatoid factor (RF) and IL-6 in sera were analysed. The role of TLR9 in osteoclast differentiation and activation was investigated *in vitro*.

**Results:** In PIA, the TLR9 antagonist reduced arthritis severity by ~50%, which was accompanied by a reduction of AGP, IL-6 and RF. TLR9 inhibition led to reduced inflammation, bone erosion and cartilage degradation. Moreover, the T cell-dependent chronic phase of SCW arthritis was significantly suppressed in TLR9<sup>-/-</sup> mice. Remarkably, TLR7 and TLR9 mRNA levels strongly differed in the course of *in vitro* osteoclastogenesis. Whereas TLR7 expression did not change throughout osteoclastogenesis, expression of TLR9 was higher in precursor cells than in mature osteoclasts and stimulation with a TLR9 agonist (CpG) completely inhibited osteoclastogenesis.

**Conclusions:** Taken together, the results suggest a role for TLR9 in the T cell-dependent phases of PIA and SCW arthritis thus an important involvement of the DNA (CpG) recognising TLR9 in the initiation of autoimmune arthritis and during osteoclastogenesis. The precise role(s) of TLR9 in the different stages of arthritis needs to be further elucidated in future experiments.

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**Disclosure of Interest:** None declared

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AB0041

#### HETEROGENEITY OF THE TYPE I INTERFERON SIGNATURE IN RHEUMATOID ARTHRITIS MAY ACCOUNT FOR DIFFERENCES IN ITS CLINICAL RELEVANCE

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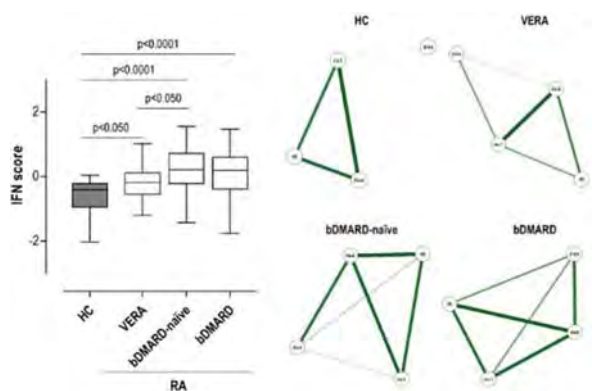
**Background:** increased expression of interferon-responding genes (IRGs), the so-called IFN signature, has been reported in rheumatoid arthritis (RA) in peripheral blood and synovial tissue. However, some controversy exists concerning its clinical relevance, since longitudinal changes of the IFN signature have been reported upon different treatments and a physiological diversification of the type I IFN signature among different conditions has been recently described. Additionally, the relevance of the IFN signature in the very early stage of RA is unknown.



**Objectives:** to evaluate (i) whether quantitative and qualitative differences in the activation of the IFN signature can be found in RA patients depending on the clinical stage and (ii) if these differences may be linked to a clinical relevance of the IFN signature.

**Methods:** expression of IFI44, IFI44L, IFI6 and MX1 was determined in peripheral blood in 98 RA patients and 28 controls. RA patients were classified into groups according to their clinical stage and treatments received: very early RA (VERA, recruited at onset and not exposed to any treatment), bDMARD-naïve (patients on csDMARD treatment) and bDMARD (patients on biological treatment, all anti-TNF $\alpha$  agents). An additional group of 13 RA patients candidate for TNF $\alpha$ -blockade was also recruited and samples were taken before and after anti-TNF $\alpha$  treatment. The associations among IRGs were evaluated by network and principal component analyses.

**Results:** all IRGs was increased in RA, although differences were noted among them. The IFN score was increased in all RA groups (VERA, bDMARD-naïve and bDMARD), but differences in their degree of activation and in the relationships among IRGs were observed. VERA patients exhibited a lower activation of the IFN signature and a distinct picture of the structure of the IRG network (figure 1) compared to both their established disease-counterparts and the HC group. The IFN score correlated the accumulated DAS28 over one year ( $r=0.593$ ,  $p=0.025$ ) and it was found to be a predictor of a good clinical outcome (EULAR good clinical response) in VERA (AUC=0.917,  $p=0.004$ ). However, no differences in the IFN score were observed between the bDMARD-naïve and bDMARD groups, but opposite associations with the clinical parameters were noted. Interestingly, the correlations among IRGs delineate different pictures between these two groups. The IFN score at baseline predicted poor clinical outcome upon TNF $\alpha$ -blockade. Although no absolute changes in the IFN score were found, TNF $\alpha$ -blockade shifted the associations among IRGs. These differences mirrored those found when comparing bDMARD-naïve and bDMARD groups.



Abstract AB0041 – Figure 1

**Conclusions:** a certain heterogeneity within the IFN signature can be recognised in RA, depending on the clinical stage. The structure of the IFN signature may be a potential explanation for the controversy in this field and may represent a limitation for its use as a clinical biomarker.

**Disclosure of Interest:** None declared

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AB0042

#### ESSENTIAL OIL EXTRACTED FROM CHAMAECYPARIS OBTUSA ATTENUATES THE SEVERITY OF COLLAGEN-INDUCED ARTHRITIS

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**Background :** *Chamaecyparis obtusa* (*C. obtusa*) is a tropical tree species found in Japan and the southern region of South Korea. Although the biological activities of essential oil extracted from *C. obtusa* (EOCO) are not yet fully understood, essential oil has been shown to have antibacterial activities and anti-inflammatory effects.

**Objectives:** We investigated the effect of essential oil extracted from *Chamaecyparis obtusa* on the development of collagen-induced arthritis (CIA), a well-characterised preclinical model of human RA.

**Methods:** DBA1/J mice were injected intraperitoneally with EOCO dissolved in dimethyl sulfoxide (DMSO) 3 times a week for 5 weeks after type II collagen (CII) immunisation. Arthritis severity was evaluated by clinical and histological parameters. Serum anti-CII antibody levels were assayed by ELISA. Interleukin-17 (IL-17) expressions in the joints were determined by immunohistochemistry. Effect of EOCO on Th17 cells and natural killer (NK) cells was analysed using flow cytometry.

**Results:** EOCO markedly reduced the clinical and histological severity of CIA. Serum anti-CII antibody levels and the expression of IL-17 in the joints were significantly lower in mice treated with EOCO than those treated with DMSO alone. EOCO inhibited the differentiation of Th17 cells in total splenocytes, not in isolated CD4<sup>+</sup> T cells, from mice. EOCO increased the production of granzyme B and perforin in NK cells.

**Conclusions:** Our data demonstrate a protective effect of EOCO on the development of CIA through the inhibition of Th17 cell differentiation. This effect may be related with NK cell activity enhanced by EOCO.

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AB0043

#### THE ELASTICITY PROPERTIES OF PROBIOTIC BACTERIA WALL ASSOCIATED WITH BENEFICIAL MODULATORY ACTIVITY ON INNATE IMMUNITY OF THE HOST

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**Background:** Probiotics have tremendous potential to develop healthy diets and integrated approach for immunity-related diseases treatment and prevention;<sup>1,2</sup> are effective actors in distant sites<sup>3</sup> with strong potential for applications in rheumatology. The cell wall of probiotic bacteria plays an essential role in many aspects of modulating beneficial immune response;<sup>4</sup> its elasticity properties associated with probiotic beneficial effects and can warrant to stratify strains on their modulatory activity on innate immunity to justify individualised and personalised approach for nutrition and prevention.

**Objectives:** The aim was to study the effect of lactic acid bacteria (LAB) and bifidobacteria strains on phagocytic system cells functional activity and immunoregulatory cytokines synthesis *in vitro* in regards to the bacteria surface properties as cell walls elasticity using atomic force microscopy (AFM).

**Methods:** We conducted experimental studies on BALB/c line mice 18–20 g weight using lyophilized strains of LAB – *Lactobacillus acidophilus* IMV B-7279, *L. casei* IMV B-7280, *L. delbrueckii* subsp. *bulgaricus* IMV B-7281 and bifidobacteria – *Bifidobacterium animalis* VKL, *B. animalis* VKB. We cultivated the macrophages received from the peritoneal cavity of mice by common method individually with the strains of LAB and bifidobacteria. We estimated the impact of LAB and bifidobacteria strains on the functional activity of peritoneal cavity macrophages using the conventional methods of study oxygen-dependent bactericidal activity, nitric oxide production, their effect on the immunoregulatory cytokines. We used AFM scanning to estimate bacteria cell walls elasticity.

**Results:** All strains demonstrated a stimulating effect on the functional activity of macrophages and ability to produce NO/NO<sub>2</sub> *in vitro*. Lactobacilli strains increased the production of IL-12 and IFN- $\gamma$  *in vitro*. The AFM demonstrated different degree of the cell walls elasticity in various strains of LAB and bifidobacteria. Among lactobacilli the most elastic cell wall was found in *L. delbrueckii* subsp. *bulgaricus* IMV B-7281, and among bifidobacteria – in *B. animalis* VKL, which induced the considerable activation of the phagocytes. Probiotic strains survival in

the macrophages depended on the elasticity of bacterial cell walls and on the time of their joint cultivation.

**Conclusions:** LAB and bifidobacteria strains stimulate immunomodulatory cytokines and active oxygen and nitrogen oxides compounds production in macrophages. Strains with a more elastic cell wall according to AFM data demonstrated higher resistance to intracellular digestion in macrophages and higher level of their activation. AFM might be considered as a fast and accurate method to assess parameters of probiotic strains cell wall to predict their beneficial immunomodulatory properties. Further large-scale preclinical research needed for future application in rheumatic diseases treatment and prevention.

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#### AB0044 HYPER IGD SYNDROME TREATMENT WITH HYDROXYCHLOROQUINE

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**Background:** Hyper IgD syndrome is a minor form of mevalonate kinase deficiency caused by a its gene mutation and considered an auto-inflammatory disease inherited in an autosomal recessive manner, characterised by periodic episodes of fever, arthralgia, lymphadenopathy, skin rash, headaches, and abdominal pain. These attacks can occur spontaneously or be triggered by infections. Treatment options include courses of NSAIDs, steroids, colchicine, statins, I.V immunoglobulin, Cyclosporine, anti-IL-1 agents (anakinra or canakinumab) and anti-TNF antagonist Etanercept, with transient response. To date, there is no report with long term hydroxychloroquine treatment<sup>1-3</sup>.

**Objectives:** To report a case of Hyper Ig-D syndrome with multiple recurrent episodes and successful treatment using Hydroxychloroquine alone.

**Methods:** We report a case of 36-year-old female, presented with a first manifestation at age 35 with fever and extended cellulitis of the left arm treated successfully with antibiotic, rapidly followed with urticarial rash involving the upper side of the body, face and upper limbs migratory type lasting less than 24 hours suspecting allergic reaction. She was under supportive treatment (anti-histaminic and low dose steroids) that improved her condition temporarily. She developed multiple recurrent similar episodes for 7 months with high grade fever up to 39°C, inflammatory polyarthralgia affecting small joints, recurrent left elbow erythematous plaque with few subcutaneous nodules, considered as panniculitis type lesion (Picture-1) along with urticarial rash. Series of tests were undertaken along with skin biopsy.

**Results:** Biopsy of the lesion showed intense deep dermal neutrophil infiltrates. CRP fluctuating between 50 to 95 mg/L during the episodes. Neutropenia (1.7 to 1.9), Normal findings for ANA and SSA antibodies, ACE, Lysozyme enzyme, C3 and C4. Other infectious work-up was negative including Quantiferon God test. Protein electrophoresis found hypergammaglobulinemia. The Ig-D level was 263 mg/L and on another occasion 313 mg/L (normal <153 mg/L), the samples were taken during flare up and after recovery. The patient was treated by Colchicine for more than 3 months without beneficial effect. A trial with hydrochloroquine 400 mg daily brought a progressive improvement with lesser episodes at 3rd month and no recurrences at 6 months. After one year of therapy the patient was symptomless on a lower dose 200 mg daily with completely normalised inflammatory markers.

**Conclusions:** We conclude that Hyper Ig-D syndrome can be treated by hydroxychloroquine. This is the first report in the literature conducting this treatment option that can bring attention for further case by case trials.



Abstract AB0044 – Figure 1

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#### AB0045 ACTIVATED RNASE L AS A NOVEL DISEASE ACTIVITY BIOMARKER IN PSORIATIC ARTHRITIS

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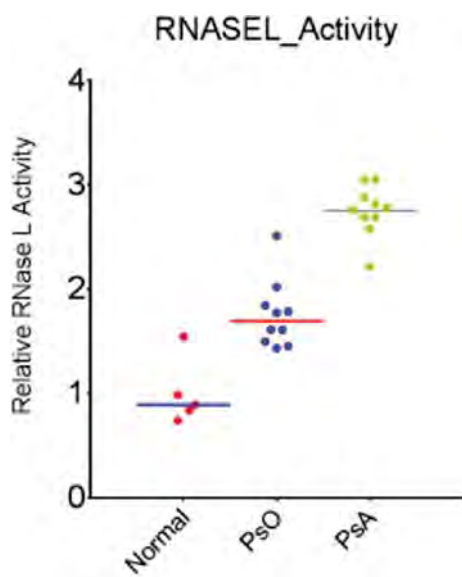
**Background:** Almost 60% of psoriasis (PsO) patients with psoriatic arthritis (PsA) are estimated to be untreated, undertreated or/and undiagnosed.<sup>1</sup> Delayed diagnosis leads to permanent joint damage causing major functional decline and diminished quality of life. However, in the absence of diagnostic biomarkers, the diagnosis of psoriatic arthritis is clinical and hence difficult to establish from non-rheumatologists.<sup>2</sup> Recent studies have demonstrated the upregulation of type I interferon (IFN)-inducible genes in paired peripheral blood cells (PBC) and synovial biopsies of patient with PsA.<sup>3</sup> Oligoadenylate synthetases (OAS) are type I IFN-stimulated family of proteins that are activators of the latent Ribonuclease L (RNase L) pathways. The OAS-RNase L system is a potent host antiviral IFN-responsive system that is completely inactive in normal conditions, but once activated mediates a broad array of pro-inflammatory cellular processes.<sup>4</sup>

**Objectives:**

1. To investigate the role of OAS–RNase L pathway in PsA;
2. To quantify the hypothesised increased OAS–RNase L activity.

**Methods:** To further explore the gene expression data, we developed a highly sensitive ELISA and fluorescence resonance transfer (FRET) assay to access and compare the RNase L activity in plasma and serum derived from PsA (n=10), PsO (n=10) patients or healthy control donors (n=5).

**Results:** We found that RNase L activity was 2–3 fold higher in PsO and 3–5 fold in PsA compared to normal control (figure 1). Consistent with the gene expression analysis of upregulated type I IFN inducible genes, we also observed amplification of the downstream pro-inflammatory pathway consisting of RNase L dimer (active) and the produced cleaved RNA, which further induce IFN- $\beta$  production and other inflammatory signalling.



Abstract AB0045 – Figure 1. RNASEL\_Activity

**Conclusions:** The proportionally increased activation of OAS/RNase L in psoriatic arthritis merits further investigation into this pathway as a potential disease activity biomarker. RNase L is an easily quantifiable enzyme that could categorise disease severity and progression in daily routine lab ordered by primary physician. The timely diagnosis is key to improved function and quality of life in PsA patients.

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**Disclosure of Interest:** None declared

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**AB0046** **TOFACITINIB IMPAIRS MONOCYTE-DERIVED DENDRITIC CELL DIFFERENTIATION IN RHEUMATOID ARTHRITIS AND PSORIATIC ARTHRITIS**

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**Background:** Tofacitinib (Pfizer) is an oral Janus kinase inhibitor, recently approved for the treatment of rheumatoid arthritis (RA). Although its mechanism

of action has been explored in circulating cells, in particular neutrophils and lymphocyte, its effect on dendritic cells development remains still to be elucidate. Monocyte-derived dendritic cells are a subset of inflammatory DC derived from circulating monocytes and have a key role in inflammation and infection.

**Objectives:** The aim of this project is to evaluate the effect of Tofacitinib on inflammatory monocyte-derived dendritic cells (Mo-DC) from RA and PsA patients, and in particular on the ability of monocyte to differentiate into dendritic cells, an important step in innate immunity.

**Methods:** Mo-DC were isolated from blood of RA and psoriatic arthritis (PsA) patients by magnetic separation. Monocyte were plated in presence/absence of GM-CSF/IL-4 cocktail for 7 days, to acquire immature dendritic cell phenotype. To evaluate the effect of Tofacitinib on Mo-DC differentiation, monocyte were treated with 1  $\mu$ M Tofacitinib (or DMSO as control) for 15 min prior to cytokine stimulation. CD209 (immature DC marker) and CD14 (monocyte marker) were evaluated by flow cytometry in the CD11c positive population. Phagocytosis was investigated by the analysis of dendritic cell uptake of soluble antigens through two different mechanisms: non-specific macropinocytosis (using Lucifer Yellow), and receptor-mediated endocytosis (using DQ<sup>TM</sup> Ovalbumin).<sup>1</sup> Western blot analysis was utilised for analysis of NOX5 and Actin protein expression on the total cell lysate.

**Results:** The pre-treatment of Mo-DC with Tofacitinib inhibited Mo-DC differentiation in RA and PsA patients, as shown by reduced CD209 surface marker expression, and a mirrored increase of CD14 marker. The decreased ability of monocyte to differentiate into dendritic cells was translated into a function impairment of phagocytosis ability, as observed by the decreased uptake of both DQ<sup>TM</sup> Ovalbumin (receptor-mediated endocytosis) and Lucifer Yellow (micropinocytosis) PsA cells treated with Tofacitinib. Low phagocytosis was observed in RA patients. NOX5 has previously been shown to play a key role in Mo-DC differentiation,<sup>2</sup> therefore we sought to investigate whether Tofacitinib could exert its effect on Mo-DC development through modulating NOX5. NOX5 protein expression was significantly decreased in Mo-DC pre-treated with Tofacitinib in PsA, and to a lesser extent in RA patients.

**Conclusions:** Together, these observations suggest a novel mechanism of action of Tofacitinib in RA and PsA, by inhibiting Mo-DC development, which may alter migration of DC to the joint and subsequent activation of the immune response.

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**Disclosure of Interest:** V. Marzaioli Grant/research support from: Project funded by Pfizer, M. Canavan: None declared, S. Wade: None declared, C. Low: None declared, D. Veale: None declared, U. Fearon: None declared  
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## Cytokines and inflammatory mediators

**AB0047** **EXPRESSION OF IFN TYPE I RESPONSIVE GENES IN A CARDIOVASCULAR DISEASE CONTINUUM OF RHEUMATOID ARTHRITIS**

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**Background:** Rheumatoid Arthritis (RA) patients have a prominent increase in cardiovascular disease (CVD) not fully explained by traditional risk factors<sup>1</sup>. Interferons type 1 (IFN-I) have been associated with premature CVD in SLE<sup>2</sup> and are implicated in several aspects of atherosclerosis and acute coronary syndromes<sup>3</sup>. A subpopulation of RA patients also display a peripheral blood IFN-I signature from 25% to 65%<sup>4</sup>, associated with clinical response to biologics<sup>5</sup>. The IFN-I signature association with CVD in RA remains unclear.

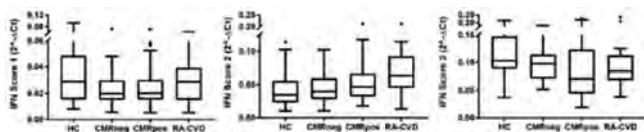
**Objectives:** To analyse expression of interferon type 1 response genes (ISGs) along a cardiac MRI (CMR) phenotyped CVD continuum in patients with RA.

**Methods:** PBMC samples from 94 RA patients and 21 healthy controls (HC) were obtained. RA patients were stratified based on CMR into: RA CMRneg (no CVD-



RA, n=13), RA CMRpos (subclinical CVD-RA, n=54), and RA with clinical CVD (defined as history of cerebrovascular disease or ischaemic heart disease) (RA-CVD n=25). qPCR of ISGs was performed using TaqMan Gene Expression Assays on Biomark (Fluidigm) with compatible reagents. Factor analysis of Ct values from 51 genes was used to create scores by calculating median dCt for genes loaded by each factor.

**Results:** RA cohort median (IQR) age 63 (13.3) yrs, 69% female, disease duration 148.7 (215.3) mths; HC age 43 (16.5) y, 62% female. Three IFN-I factors (IFN Score 1, 2, 3) were present in the dataset and were composed of 19, 21 and 7 genes respectively. The Jonckheere-Tepstra test showed significant increases in expression of Score 2 across the 4 groups ( $p=0.002$ ), consistent with a continuum, and multiplicity-corrected post-hoc analysis identified differences between HC and subclinical CVD ( $p=0.034$ ), HC and RA-CVD ( $p=0.004$ ); as well as between no CVD-RA and subclinical CVD-RA ( $p=0.034$ ); and subclinical CVD-RA with RA-CVD ( $p=0.029$ ). Scores 1 and 3 did not show consistent directional trends across all studied groups. In no CVD-RA expression of Score 1 and 2 positively correlated with CRP ( $\rho=0.744$ ,  $p=0.002$  and  $\rho=0.659$ ,  $p=0.010$  respectively). Score 1 with Low-Density Lipoproteins ( $\rho=0.527$ ,  $p=0.044$ ), Framingham 10y risk ( $\rho=0.595$ ,  $p=0.019$ ) and Score 3 with Pulse Wave Velocity ( $\rho=0.584$ ,  $p=0.022$ ). In subclinical CVD-RA score 3 expression negatively correlated with Left Ventricular mass ( $\rho=-0.381$ ,  $p=0.005$ ), in RA-CVD score 3 expression positively correlated with Glucose ( $\rho=0.724$ ,  $p=0.042$ ), Triglycerides ( $\rho=0.821$ ,  $p=0.023$ ) and Total Cholesterol/High-Density Lipoprotein ratio ( $\rho=0.505$ ,  $p=0.039$ ).



Abstract AB0047 – Figure 1

**Conclusions:** An IFN-I score (Score 2) emerged as a possible factor characterising progression along a CVD continuum in RA patients, from no CVD to subclinical and clinical CVD; also distinguishing between HC and RA with subclinical and clinical CVD. IFN-I is involved in metabolic disturbances associated with CVD development in RA. These results warrant further evaluation to confirm the findings in a larger cohort.

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**Disclosure of Interest:** None declared

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#### AB0048 SERUM CXCL13 LEVELS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND ITS CORRELATION TO DISEASE ACTIVITY AND LUPUS NEPHRITIS

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**Background:** Systemic lupus erythematosus (SLE) is a complex autoimmune disease that is characterised by the production of pathogenic autoantibodies against nuclear structures.<sup>1</sup> B lymphocyte chemoattractant (BLC) or CXC motif ligand 13 (CXCL13) play an important regulatory role of B1 and B2 cell trafficking for activation of autoreactive T helper cells.<sup>2</sup> CXCL13 can induce trafficking of the CXCR5<sup>+</sup> T lymphocyte subset designated as follicular helper T lymphocytes which are specifically involved in production of autoantibodies during the development of lupus.<sup>3</sup>

**Objectives:** To detect serum CXCL13 levels in SLE patients and determine its relation to the disease activity and lupus nephritis

**Methods:** The study included 32 SLE patients and 20 healthy individuals as a control group. Patients' group was further subdivided according to disease activity and renal involvement. Serum samples from all studied individuals were analysed for the concentrations of CXCL13 by ELISA.

**Results:** There was a high statistically significant increase ( $p<0.001$ ) in the mean of serum CXCL13 on comparing its levels in SLE patients [242 (121.5–855.6) pg/ml] versus control group [73.8 (22.8–120.3) pg/ml], and on comparing its levels in lupus nephritis patients [542.4 (171–855.6) pg/ml] versus other patients without lupus nephritis [212.9 (121.5–580.5) pg/ml]. Moreover, CXCL13 Concentrations were correlated with SLEDAI ( $r=0.771$ ,  $p<0.001$ ) and double-stranded DNA titres ( $r=0.374$ ,  $p<0.05$ ).

**Conclusions:** Our data suggest that CXCL13 has an important role in pathogenesis of SLE and lupus nephritis. Also, pharmacological regulation of CXCL13 and its receptor CXCR5 may be a useful therapy in lupus nephritis.

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**Disclosure of Interest:** None declared

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#### AB0049 EVALUATION OF CASPASE-3, CASPASE-9, CASPASE-14 AND PANNEXIN-1 LEVELS IN BEHÇET'S DISEASE

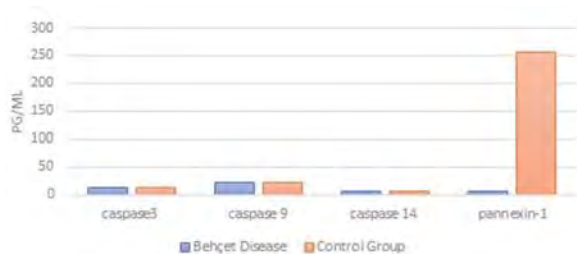
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**Background:** Behçet's disease (BD) is a rheumatic disease in which various systemic findings such as especially recurrent oral ulcers, and genital ulcers, eye involvement, skin lesions, gastrointestinal involvement, neurological involvement, vascular involvement and arthritis can be seen.<sup>1</sup> The pathogenesis of the disease has not yet been fully understood. Caspases play a central role in apoptotic signal transduction. They are cysteine bound aspartate specific proteases.<sup>2</sup> There are three main types of caspases, the initiator caspases, the effector caspases and the inflammatory caspases. Pannexin-1 is a high-conduction voltage-gated channel protein that is commonly found in many organs and tissues including sensory systems and both neuronal and non-neuronal cell types.<sup>3</sup>

**Objectives:** The aim of this study is to examine the role of initiator, effector and inflammatory caspases in BD and the levels of pannexin duct protein, which is thought to be active in inflammation in BD and to compare clinical findings with healthy individuals.

**Methods:** Between January 2017 – June 2017, forty-six patients diagnosed with BD admitting to Cumhuriyet University Medical Faculty, Department of Internal Medicine Rheumatology and forty-four healthy volunteers without any rheumatic, systemic and metabolic diseases enrolled in this study. Clinical findings of all patients were recorded. The blood from a peripheral vein using suitable blood tubes was withdrawn to measure serum caspase-3, caspase-9, caspase-14 and pannexin-1 levels. Blood tests were examined by Elisa method in Cumhuriyet University Department of Biochemistry.

**Results:** The mean serum caspase-3 level was measured as 12.04 (11.25–43.69) pg/ml in BD group and 12.1 (11.19–484.3) pg/ml in healthy control (HC) group. There was no statistically significant difference between two groups ( $p=0.143$ ). The mean serum levels of caspase-9 in the BD group were measured as 22 (5.14–29.33) pg/ml and 22.01 (11.23–850) pg/ml in the HC group. There was no statistically significant difference between the two groups ( $p=0.593$ ). The mean serum caspase-14 level was 6 (5.2–8.21) pg/ml in the BD group and 6.15 (5.7–353) pg/ml in the HC group. There was no statistically significant difference between the two groups ( $p=0.053$ ). The mean serum pannexin-1 levels were 6.36 (4.21–527.2) pg/ml in the BD group and 255.8 (5.38–2000) pg/ml in the HC. Serum pannexin-1 levels were statistically significant higher in the HC group ( $p<0.0001$ ) (figure 1).



**Abstract AB0049 – Figure 1.** Serum levels of caspase-3, caspase-9, caspase-14 and pannexin-1 in patients with behçet's disease and healthy controls

**Conclusions:** Serum caspase-3, caspase-9 and caspase-14 levels were not statistically significant different between BD and HC groups. Serum pannexin-1 levels were statistically significant lower in the BD group.

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AB0050

#### BIOMAP<sup>®</sup> PHENOTYPIC PROFILING OF TWO BATCHES OF ORIGINATOR ETANERCEPT REVEALS EQUIVALENT ACTIVITY SIGNATURES CONSISTENT WITH CONSERVED BIOLOGICAL ACTIVITY

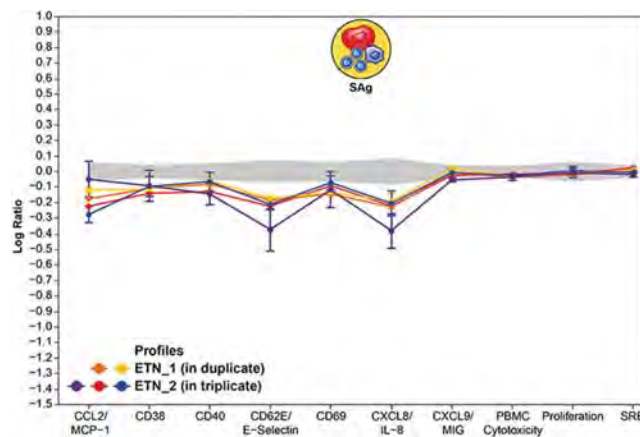
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**Background:** The BioMAP<sup>®</sup> platform is a complex human primary cell-based system for modelling tissue and disease states that is used to characterise drug activities based on the analyses of 148 clinically relevant biomarker readouts.

**Objectives:** To confirm that the BioMAP phenotypic signatures of two originator etanercept (ETN) samples remained comparable over time.

**Methods:** Two different ETN samples (ETN\_1 and ETN\_2) were independently profiled with a 5 year interval across a panel of 12 disease-relevant systems (3C and 4 hour [endothelial inflammation]; LPS [monocyte activation]; SAg [T cell activation]; BT [B cell activation]; BF4T and BE3C [epithelial inflammation]; CASM3C [vascular inflammation]; HDF3CGF, KF3CT, and MyoF [tissue remodelling, fibrosis]; Mphg [macrophage activation]). BioMAP systems consist of human primary cells or cocultures from healthy donors cultured in the presence of cytokines and growth factors. Protein levels, measured using immune-based methods or functional assays for cell viability and proliferation, were used to generate a BioMAP activity profile for each sample. ETN activities were annotated if they differed from the vehicle control and had an effect size >20%. The profiles of the 2 samples were compared using Pearson's correlation.

**Results:** BioMAP phenotypic profiling of ETN\_1 versus ETN\_2 samples at 10 µg/mL revealed similar signatures across 148 biomarkers in 12 disease-relevant systems. The Pearson's correlation coefficient was 0.781, which is above the determined threshold for mechanistic similarity ( $r \geq 0.7$ ). Key efficacy-related anti-inflammatory and immunomodulatory activities were commonly inhibited in multiple systems including tumour necrosis factor alpha (LPS and BT), interleukin (IL)-2 (BT), vascular cell adhesion molecule 1 (MyoF and Mphg), IL-8 (SAg and MyoF), and E-Selectin (SAg and Mphg). The profiles of ETN samples at 1 µg/mL in the SAg system modelling T cell activation responses also revealed statistically significant similarity in signatures ( $p < 0.01$ ) in both magnitude and direction across all biomarker activities (figure 1).



**Abstract AB0050 – Figure 1.** SAg system profile of ETN\_1 and ETN\_2 samples at 1 µg/mL.

**Conclusions:** The BioMAP phenotypic signatures of the ETN\_1 and ETN\_2 samples profiled in independent experiments using different primary cell pools remained comparable, which was consistent with conserved ETN mechanisms of action. The BioMAP platform represents a useful orthogonal approach for assessing ETN activity.

**Disclosure of Interest:** A. O'Mahony Employee of: Eurofins DiscoverX, E. L. Berg Employee of: Eurofins DiscoverX, H. Jones Shareholder of: Pfizer, Employee of: Pfizer, B. Fitzpatrick Shareholder of: Pfizer, Employee of: Pfizer, B. Hassett Shareholder of: Pfizer, Employee of: Pfizer, S. Vicik Shareholder of: Pfizer, Employee of: Pfizer, L. Marshall Shareholder of: Pfizer, Employee of: Pfizer, K. Roshak: None declared, E. Choy Grant/research support from: Novimmune, Pfizer, Roche, UCB, Consultant for: Abbott Laboratories, Amgen, Biogen, BMS, Celgene, Chugai Pharma, Eli Lilly, GSK, Hospira, Janssen, MedImmune, Napp, Novimmune, Novartis, Pfizer, Regeneron, Roche, R-Pharm, Sanofi

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AB0051

#### THE INFLUENCE OF ANTI-INFLAMMATORY LIPOXIN A4 ON GENERATION OF CYTOKINES BY PBMCs OF PATIENTS WITH PSORIATIC ARTHRITIS

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**Background:** Psoriatic arthritis (PsA) is affecting up to 40% of the patients with psoriasis. The pathogenesis of PsA is not completely understood. One of the hypothesis suggest that repeated micro injuries and trauma and lack of proper inhibition of inflammation lead to chronic inflammation spreading to surrounding tissue and other joints and ligaments. One of the mediators which lead to inhibition of inflammation in healthy conditions are derivatives of arachidonic acid – lipoxins.

**Objectives:** The aim of the study was to assess if the influence of lipoxin A4 on inhibition of synthesis of pro-inflammatory cytokines by peripheral blood mononuclear cells (PBMCs) of patients with psoriatic arthritis.

**Methods:** The study group consisted of 10 patients with psoriatic arthritis and 5 healthy controls. The peripheral blood mononuclear cells from patients with PsA and healthy controls were isolated and were stimulated with lipopolysaccharide (LPS) with or without 200 nM of lipoxin A4 for 24 hours. The supernatants were collected after 24 hour stimulation. The levels of IL-1b, IFN-gamma, TNF-alfa, MCP-1, IL-6, IL-8 and IL-33 were assessed by cytometric bead array system.

**Results:** Incubation of cells with LPS, increased production of all cytokines assessed either in patients with psoriatic arthritis or in healthy controls. In PBMCs from healthy controls incubation of cells with lipoxine A4 decrease production of proinflammatory cytokines (IL-1b, MCP-1, IL-8, IL-6, IL-33 and TNF-alfa;  $p < 0,05$ ). However in patients with psoriatic arthritis addition of lipoxine A4 did not inhibit LPS – induced proinflammatory cytokines release (IL-1b, MCP-1, IL-6, IL-8, IL-33 and TNF-alfa,  $p < 0,05$ )

**Conclusions:** Our study demonstrated that modulation of Inflammation by lipid mediators in patients with psoriatic arthritis is dysregulated.

**Disclosure of Interest:** None declared

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AB0052

### TREATMENT WITH BACTERICIDAL/PERMEABILITY-INCREASING PROTEIN REDUCES CRYSTAL-INDUCED INFLAMMATION AND COLLAGEN-INDUCED ARTHRITIS IN MICE

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**Background:** Bactericidal/permeability-increasing protein (BPI) is an antibacterial glycoprotein produced by polymorphonuclear cells (PMN). Although BPI has been detected in synovial fluid of patients with different type of arthritis, its effects in these diseases remain unexplored.

**Objectives:** To investigate the effects of BPI in mouse models of crystal-induced inflammation and collagen-induced arthritis (CIA).

**Methods:** Air pouches were raised on the backs of CD1 mice (n=14 per condition). 2 mg of calcium pyrophosphate (CPP) crystals in 1 ml of PBS were injected into the pouch in the presence or absence of 0.1 mg of BPI for 3 hour. Controls received 1 ml of PBS. After the sacrifice, pouch fluids were recovered by washing with 2 ml of PBS. Leukocyte count in lavage fluids was obtained using a hemocytometer and the PMN percentage was determined by May-Grünwald-Giemsa staining. CIA was induced in C57Bl/6 mice (n=12 per condition) by immunisation with collagen/complete Freund's adjuvant emulsion at days 0 and 21. Arthritis was monitored by measuring paw swelling with a calliper and scored (0–5) every 2 days. Arthritic mice (paw score=2) were intraperitoneally injected with 200 µl of BPI (50 µg/ml) or vehicle only (PBS). Treatment and arthritis evaluation were carried out twice a week for 2 month. At the experiment endpoints, mice were subjected to knee and ankle ultrasound (US) and then euthanized. Hind paws were processed for histological analysis to assess inflammation, pannus formation, cartilage and bone destruction in knee and ankle joints (score 0–5). IL-1β, IL-6, CXCL1 and TNF levels were measured by ELISA in pouch fluids and serum from collected blood.

**Results:** The injection of CPP crystals into the pouches induced leukocyte infiltration (26.27±4.14 × 10<sup>5</sup> cells/ml) comprising 73.5%±2.12% of PMN. IL-1β (80.99 ±3.65 pg/ml), IL-6 (892.90±28.14 pg/ml), CXCL1 (762.82±50.08 pg/ml) and TNF (52.70±0.49 pg/ml) were measured in lavage fluids. The co-injection of crystals and BPI inhibited leukocyte influx by 67% and PMN infiltration by 55% and, in turn, the levels of all assessed cytokines were reduced (46% IL-1β, 35% IL-6, 60% CXCL1, 64% TNF). CIA mice reached an arthritis score of 2 after 28–33 days and showed a progressive worsening of clinical signs that picked at day 49–56, and then improved only in BPI group. At the end of the experiment, hind paw swelling and scores were lower in BPI-mice (paw thickness=4.76±0.33 mm; score=4 ±0.5) than in controls (paw thickness=6.39±0.95 mm; score=5). US revealed synovial hypertrophy in all joints considered, but the presence of effusion only in knees of untreated animals. Power Doppler was positive in controls but not in BPI group. BPI decreased histological scores for pannus formation and inflammation by 3-fold, and for cartilage and bone destruction by 2-fold as compared to PBS-mice. CIA induction led to high levels of IL-1β (656.80±45.6 pg/ml), IL-6 (376.04 ±46.33 pg/ml), CXCL1 (834.08±68.8 pg/ml) and TNF (277.72±15.24 pg/ml), which were reduced with BPI treatment by 66%, 46%, 47% and 93%, respectively.

**Conclusions:** This study shows inhibitory effects of BPI on crystal-induced inflammation and CIA, suggesting a therapeutic potential of this protein for arthritis by down-regulating inflammatory process.

**Disclosure of Interest:** None declared

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AB0053

### A BIOASSAY TO MEASURE TGFβ ACTIVITY REVEALS DECREASED TGFβ ACTIVITY IN SSC SERUM

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**Background:** Systemic sclerosis (SSc) is a severe disease characterised by auto-immunity, vasculopathy and excessive fibrosis of connective tissues. The pathophysiology of SSc is still poorly understood, but its symptoms imply a role for dysregulated transforming growth factor β (TGFβ) signalling; e.g. this cytokine is known to regulate vascular and connective tissue biology. TGFβ circulates in blood in an inactive form bound to latency associated peptide and latent TGFβ binding proteins. This latent TGFβ first has to be activated before it can become bioactive. With the use of a bioassay, TGFβ's bioactivity can be measured in a complex mixture like serum, unlike with an ELISA which cannot take cellular activation processes into account.

**Objectives:** To determine the bioactivity of TGFβ in SSc serum compared to that of healthy control serum

**Methods:** Serum was collected of 10 SSc patients and 10 age and sex matched healthy controls. Primary human fibroblasts of 3 donors were

transduced with CAGA<sub>12</sub>-luc which produces luciferase in response to TGFβ/Smad3 or BRE-luc which produces luciferase in response to BMP/Smad1/5. These cells were treated with 10% serum for 16 hour and luciferase activity was measured. To activate all TGFβ, sera were treated with 4M HCl for 1 hour at RT, after which pH was normalised with 4M NaOH. Controls were treated with HCl and NaOH simultaneously. To verify that TGFβ signalling was measured in this reporter assay, sera were treated with anti-TGFβ1/2/3 for 1 hour at RT before use.

**Results:** Control sera significantly induced reporter activity by 4.5-fold. However, SSc sera only induced a 2.5-fold increase in luciferase activity, indicating significantly lower bioactivity of TGFβ (p<0.0001). This difference was not due to a difference in total TGFβ levels; after activation of all TGFβ both HC and SSc sera induced a similar 6-fold increase in signal strength. These data show that in HC sera approximately 75% of all TGFβ is bioactive compared to only 42% in SSc. Addition of anti-TGFβ1/2/3 inhibited all CAGA<sub>12</sub>-luc reporter activity (p<0.0001) of both HC and SSc serum, and of both acidified and not acidified sera (p<0.0001), showing that our bioassay is indeed TGFβ-dependent. To investigate if reduced bioactivity is a more general phenomenon we measured BMP activity. BMP proteins are structurally closely related to TGFβ and also circulate in inactive form. Both HC and SSc sera induced a similar 8-fold increase in BRE-luc activity, and this activity was increased to a 16-fold induction after acidification for both groups. BMPs in SSc sera are thus not less bioactive. This illustrates the uniqueness of our observation on TGFβ bioactivity.

**Conclusions:** TGFβ in SSc serum is less bioactive than in control serum whereas BMPs are not less bioactive.

**Disclosure of Interest:** None declared

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AB0054

### PDE4 INHIBITOR ATTENUATION OF IL-23 SECRETION FROM MONONUCLEAR CELLS

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**Background:** IL-23 is a cytokine heavily implicated in the immunopathology of both psoriasis and psoriatic arthritis. Emerging evidence suggest IL-36λ, a novel inflammatory cytokine which has been heavily implicated in psoriatic immunopathology, is able to stimulate the release of IL-23. 1–3 PDE4 inhibitors, which elevate cyclic AMP (cAMP) are known to exert anti-inflammatory effects by regulating transcription factors such as NF-κB. The PDE4 inhibitor, Apremilast has proved successful in treating both psoriasis and psoriatic arthritis with patients showing a decrease in inflammatory cytokine levels, including IL-23.<sup>4</sup> However, the ability and mechanism of PDE4 inhibitors to lower IL-23 secretion from immune cells induced by disease relevant stimuli is presently unknown. Additionally, any potential relationship between IL-36λ driven inflammation and potential PDE4 inhibition is yet to be determined.

**Methods:** Blood mononuclear cells from healthy patients, (n=5) were pre-treated with either the PDE4 inhibitor Rolipram or other compounds known to elevate cAMP levels, such as histamine and 8-bromo-cAMP. Cells were subsequently treated with either bacterial or fungal toll like receptor adjuvants (LPS and Mannan) or the novel psoriatic cytokine IL-36λ. IL-23 was subsequently measured in culture supernatants by ELISA and by intracellular IL-23p19 flow cytometry.

**Results:** LPS, Mannan and IL-36λ all induced IL-23 secretion which could be attenuated in a dose dependent manner by the PDE4 inhibitor, Rolipram. Other compounds also known to increase cAMP levels, histamine and 8-bromo-cAMP similarly were able to reduce IL-23 secretion from all stimuli.

**Conclusions:** This data suggests a direct link between PDE4 inhibition and reduced IL-23 secretion in circulating immune cells. Additionally, it provides insight into how IL36/IL-23/IL-17 driven inflammation may be reduced by PDE4 inhibitors in psoriasis and psoriatic arthritis.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.7287



AB0055

### HYDROXYCHLOROQUINE INHIBITS SOLUBLE CD154 PRODUCTION THROUGH CA<sup>2+</sup> AND PKC SIGNALLING PATHWAY

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**Background:** Over-expression of membranous CD154 and soluble CD154 (sCD154) in T lymphocytes is important in pathogenesis of autoimmune diseases. PKC pathway induces sCD154 production through promoting shedding of membranous CD154.

**Objectives:** Hydroxychloroquine (HCQ) has been used in the treatment of autoimmune diseases for decades. We sought to identify the effects of HCQ on sCD154 and a possibly regulatory mechanism.

**Methods:** CD4<sup>+</sup>T cells were isolated from the blood of healthy donor. After stimulated with ionomycin +PMA and various concentrations of HCQ, concentration of sCD154 in the medium, expression of membranous CD154, Ca<sup>2+</sup> pathway and PKC signalling pathway were assessed.

**Results:** HCQ attenuated intracellular sustained calcium storage release and membranous CD154 synthesis in activated T cells. Besides, HCQ inhibited PKC activation and subsequently shedding of membranous CD154.

**Conclusions:** HCQ inhibited production of sCD154 in activated T cells through suppressing Ca<sup>2+</sup> and PKC signalling pathway. These findings provide one of the mechanistic insights into HCQ treatment.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.3172

AB0056

### MEASUREMENT OF THE PRO-COAGULANT ACTIVITY OF MICROPARTICLES IN PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASES: PROSPECTIVE STUDY

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**Background:** Microparticles (MPs) are small membrane-bound vesicles that arise from activated and dying cells. Although the majority of MPs in the blood originate from platelets, all cells appear to be able to release MPs. Many studies have raised the implication of these MP in various processes: inflammation, thrombosis, angiogenesis. Previous studies reported inconsistent results in inflammatory rheumatic diseases. Studies have shown the correlation between the circulating MPs, platelet MPs and lymphocyte MPs in patients with spondyloarthritis (SpA) compared to control patients. For rheumatoid arthritis (RA), platelet MPs levels were correlated with DAS28.

**Objectives:** The aim of this study was to search a possible correlation between the disease activity and the pro-coagulant property of microparticles, potential indirect marker of inflammation.

**Methods:** The test used (STA Procoag PPL) is a standardised automated test. Results are expressed as coagulation times (in seconds). It is a functional test that provides information on the procoagulant potential of microparticles. The microparticles supply the phospholipids expressed on their membrane surface and the test provides calcium and factor Xa necessary to initiate coagulation: the shorter the coagulation time the greater the procoagulant activity of the phospholipids being studied, suggesting a higher number of MP.

This is a prospective, single-centre study, including 39 patients with spondyloarthritis (ASAS criteria), 37 with rheumatoid arthritis (ACR criteria) and 26 control patients (healthy subjects, osteoarthritis). All patients underwent STA Procoag PPL test, and we collected medical data: disease activity (BASDAI, BASFI,

DAS28vs and DAS28crp and HAQ), biological inflammation (VS, CRP), duration of disease, and current treatment.

**Results:** The *in vitro* clotting time of serum of patients with spondyloarthritis and rheumatoid arthritis compared with controls was not significantly different (p=0.23 and p=0.44, respectively). Regarding the activity scores of inflammatory rheumatic disease: BASDAI and BASFI, DAS28esr, DAS28crp and HAQ for patients with RA, no correlation between these data and coagulation time was found; the same goes for biological inflammation (ESR, CRP), duration and type of treatment (Nonsteroidal anti-inflammatory drugs, DMARDs, biologics).

Abstract AB0056 – Table 1

STA PPL	Controls (n=26)	SpA (n=39)	p	RA (n=37)	p
Mean±SD	62,70±11,58	66,48±12,77	p=0,23	65,25±13,54	p=0,44
BASDAI	r=0,0602	p=0,72	DAS28 esr	r=0,0230	p=0,17
BASFI	r=-0,125	p=0,45	DAS28 crp	r=0,151	p=0,37

**Conclusions:** In this study, there is neither difference in values of procoagulant activity of MPs between inflammatory rheumatic diseases and control subjects, nor correlation with their activity scores or biological inflammation.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.2581

AB0057

### DECREASED IRISIN LEVEL AS RISK FACTOR OF PATHOLOGICAL FRACTURES IN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Recent studies have been suggested that adipokines and myokines may be implicated in bone metabolism and pathogenesis of osteoporosis (OP).<sup>1</sup> Previous studies have revealed inverse correlation between irisin levels and vertebral fragility fractures, but no significant correlation was found between irisin and bone mineral density (BMD) as well as with lean weight. There is no previously published data about irisin levels in rheumatoid arthritis (RA) patients.<sup>2-4</sup>

**Objectives:** To investigate serum irisin levels in patients with RA.

**Methods:** We studied 170 people: 110 RA patients (mean age 53.58±12.32; hereinafter M±SD) and 60 healthy controls. All patients with RA were examined using dual-energy X-ray absorptiometry using LUNAR DPX-Pro densitometer. Osteoporotic fractures were confirmed by X-ray examination and/or by anamnesis data. All patients were passed through extensive clinical and laboratory examination, including N-terminal propeptide of procollagen type I, C-telopeptide of type I collagen, 25(OH)-vitamin D concentration. Serum irisin levels were measured by ELISA (BioVender test system, Cat №RAG018R).

**Results:** The mean concentration of irisin in RA group was 14.48±7.07 mg/ml, which was significantly lower than of healthy donors – 20.49±4.82 mg/ml (p<0,001). We subsequently divided all of RA patients into two groups: the first one (n=44) included patients with reduced serum irisin levels (below 10.85 mg/ml), and the second one (n=66) with normal irisin levels (above 10.85 mg/ml). The first group had significantly higher activity (DAS28), increased frequency of extra-articular manifestations, disease duration more than 5 years, class III of functional joints disability and lower levels of 25(OH)-vitamin D. We also observed higher incidence of pathological bone fractures in this group (p=0,047). There wasn't any significant correlation between serum irisin level and BMD at any localization, lean, or fat weight. We did not reveal any difference of bone turnover markers (serum C-terminal telopeptide of type I collagen, serum N-terminal propeptide of type I procollagen (P1NP)) between these groups.

**Conclusions:** We have therefore revealed relationships between decreased serum irisin levels, 25(OH)-vitamin D concentration and higher incidence of pathological bone fractures in RA patients. We found no connexion between serum irisin levels and BMD at any site and body composition. We could consequently suppose, that irisin levels may reflect bone quality or increased fall risk.

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**AB0058 IL2 DECREASE AND INCREASE OF IL10 AND INF1A ARE ASSOCIATED TO CLINICAL ACTIVITY IN SYSTEMIC LUPUS ERYTHEMATOUS PATIENTS**

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**Background:** Systemic lupus erythematosus (SLE) is an autoimmune disease characterised by deregulation of cytokine production. INF1A is a proinflammatory cytokine considered as a key molecule in the SLE etiopathogenesis, being responsible indirectly of IL10 upregulation. BLYS is involved in autoantibodies production and clinical activity in SLE, and its expression is regulated by other cytokines as IL10 and INF1A. IL2 is an anti-inflammatory cytokine in SLE, but its loss leads to the production of Th2 proinflammatory cytokines as IL4, IL5 and IL13.

**Objectives:** To analyse the association among inflammatory cytokine levels and clinical activity, as well as to identify a cytokine profile related to disease activity in SLE.

**Methods:** A cross-sectional, observational study of 142 patients diagnosed of SLE<sup>SLEICC 2012</sup> criteria, and 35 healthy controls, was performed. A complete blood-test and an interview were carried out to collect their clinical data. We analysed inflammatory cytokines serum levels by colorimetric methods. Biostatistical analysis with R was performed.

**Results:** Mean cytokine levels for the SLE patients and healthy controls are shown in the table 1.

**Abstract AB0058 – Table 1**

	SLE patients (pg/ mL)	Healthy controls (pg/ mL)
	Mean (SD)	Mean (SD)
IL2	4.34 (12.2)	4,96 <sup>4,5</sup>
IL4	58.65 (64.6)	89,05 <sup>70,18</sup>
IL5	18 (5.71)	7,33 <sup>8,59</sup>
IL10	12.29 (32.82)	1,92 <sup>3,67</sup>
IL13	44.97 (273.78)	42,85 <sup>93,05</sup>
IL21	3.18 (5.61)	2,82 <sup>3,35</sup>
INF1A	15.69 (24.59)	4,84 <sup>1,91</sup>
BLYS	2293.82 (6948.46)	1181,15 <sup>260,04</sup>

The mean clinical activity measured by SLEDAI was 5.91±5.06, and we observed a statistically significant association between high levels of IL10 and high clinical activity (p=0.001).

Statistical analysis indicates that complement consumption is associated with increased levels of IL10 (p=0.029), INF1A (p<0.001), IL4 (p=0.004), IL5 (p=0.009) and decreased levels of IL2 (p=0.045); or anti-DNA positivity is associated with increased levels of INF1A (p=0.002) and decreased levels of IL2 (p=0.045), IL4 (p=0.034) and IL5 (p=0.007).

Moreover, BLYS seems to have increased in patients with positive antiphospholipid antibodies and anti-DNA. IL10 is associated with ENAs positivity (p=0.022). In patients with other autoimmune disease associated with SLE, an increase of INF1A (p=0.008) and IL5 (p=0.044) is observed.

SLE patients were categorised by normal, low or high level of the eight cytokines. Despite the fact that no specific cytokine profile associated with clinical activity was observed, those patients with high SLEDAI score had increased levels of IL10 and INF1A and decreased levels of IL2 and IL21.

**Conclusions:** Our SLE patients displayed mainly IL10, INF1A and BLYS increased, and IL2 decreased. Although IL10 seems to be the cytokine which best fits to clinical activity in SLE, altered levels of INF1A, IL2, IL4, and IL5 are associated with complement consumption or anti-DNA positivity.

**Disclosure of Interest:** None declared

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**AB0059 FETUIN-A: CLINICAL AND LABORATORY ASSOCIATIONS IN WOMEN WITH RHEUMATOID ARTHRITIS**

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**Background:** Fetuin-A is an acute-phase protein with contradictory effects. It is well known that fetuin-A low levels are associated with calcification and higher risk of cardiovascular diseases and its level is downregulated by pro-inflammatory cytokines.<sup>1</sup> Nevertheless, it was shown, that fetuin-A induces synthesis of pro-inflammatory cytokines in adipocytes and macrophages.<sup>2</sup>

**Objectives:** To investigate the level of fetuin-A in women with rheumatoid arthritis (RA).

**Methods:** At baseline we measured fetuin-A level, femoral neck, total hip and L<sub>1-4</sub> BMD by DXA in 110 women with RA (mean age 54.5±12.6; hereinafter M±Std. dev.) and 30 healthy controls. Serum CRP and ESR were measured to assess inflammation. DAS28 was calculated to determine RA activity. The diagnosis of osteoporosis was set according to the recommendations of world health organisation – T-scores≤-2,5 for patients without glucocorticoid therapy in anamnesis, T-scores≤-1,5 for patients treated with glucocorticoid for 3 months in anamnesis or with an osteoporotic fracture in anamnesis. Fetuin-A in serum was determined by enzyme-linked immunosorbent assay.

**Results:** Mean concentration of fetuin-A in group with RA was 765,69 ±120,64 ug/ml, which was lower than of healthy controls – 812,95 ug/ml (p=0,0438). Secondary osteoporosis was revealed in 52 patients (47%) with RA with mean level of fetuin-A at 733,7±18,83 ug/ml vs. 794,36±12,83 ug/ml (p=0,0078) of 58 (53%) non-osteoporotic patients. Moderate negative correlations were observed between fetuin-A and DAS28 (r=-0,4334; p<0,001), fetuin-A and CRP (r=-0,3148; p<0,001), fetuin-A and ESR (p=-0,344; p<0,001). Mean concentrations of fetuin-A were significantly different between the subgroups with moderate (3,2≤DAS28<5,1) and high disease activity (5,1≤DAS28) of RA patients and healthy controls: 742,41±12,07 ug/ml vs. 812,95 ug/ml (p=0,0021) and 663,9 ±39,14 ug/ml vs. 812,95 ug/ml (p<0,001).

**Conclusions:** Our study confirms that lower levels of fetuin-A are associated with higher activity of RA and with the loss of bone mineral density.

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**Disclosure of Interest:** None declared

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**AB0060 MECHANISMS OF ACTION OF CHONDROITIN SULFATE AND GLUCOSAMINE IN MUSCLE TISSUE: IN VITRO AND IN VIVO RESULTS. A NEW POTENTIAL TREATMENT FOR MUSCLE INJURIES?**

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**Background:** Musculoskeletal injuries are the most common cause for severe, chronic pain and physical disability affecting hundreds of millions of people around the world and represent a major concern also in sports medicine. A preclinical study evaluated the impact of chondroitin sulfate (CS) and glucosamine (GLU) combination (both compounds used in the treatment of osteoarthritis) on muscle healing and force recovery. Although the mechanisms of action of the combination CS +GLU have been largely studied in articular tissue, its potential therapeutic effects for muscle healing remain still unknown.

**Objectives:** The aim of the present study is to elucidate the mechanisms of action responsible for this interesting benefit.

**Methods:** Human skeletal muscle biopsies were digested with Protease type XIV and the resulting tissue suspension were collected by centrifugation. The digested muscle pellet was then triturated to liberate the human satellite cells. Differential centrifugations were used to enrich the cell fraction. Cell suspension was then transferred onto cell-culture dishes in Growth media (DMEM/M-199 medium (3:1) with 10% FBS, 10 µg/ml insulin, 2 mM glutamine, 25 ng/ml fibroblast growth factor, and 10 ng/ml epidermal growth factor) and cells were expanded in a growing monolayer. The effect of CS+GLU treatment in primary human skeletal muscle

cells was evaluated in a cell proliferation assay. NF- $\kappa$ B intracellular levels were determined by Western Blot. TNF- $\alpha$  production was measured in culture medium supernatants by ELISA.

**Results:** An enhancement in cell proliferation was found in CS+GLU treatments at a concentrations of 100 and 200  $\mu$ g/ml, increasing 1,60-fold ( $p < 0.01$ ) and 2,04-fold ( $p < 0.001$ ), respectively, compared to untreated cells. In addition, myoblasts were then incubated with IL-6 (50 ng/ml) for 72 hour in order to induce an inflammatory environment. The results showed an IL-6 induced-reduction on cell proliferation in all groups, although the data did not reach statistical significance. Therefore, an IL-6 inhibitory effect on cell proliferation in human muscle cannot be ensured. We also measured the effect of the combined treatment CS+GLU on NF- $\kappa$ B activation and TNF- $\alpha$  production in human skeletal muscle cells in primary culture. Despite of TNF- $\alpha$  levels were undetectable in cell supernatants, preliminary data showed a slight reduction on NF- $\kappa$ B signalling pathway. Global gene expression profiles, measured by microarrays and GeneChip Human Gene 1.0 ST Arrays (Affymetrix), will also be analysed.

**Conclusions:** The mechanisms of action involved in the potential therapeutic effect described in an *in vivo* injured muscle model seem to be related with an increase in muscle cell proliferation, together with blocking NF- $\kappa$ B nuclear translocation and TNF $\alpha$  production. Although further investigation is required, these pre-clinical data suggests potentially positive effects of CS and GLU administration for the treatment of skeletal muscle injuries in sports medicine.

**Disclosure of Interest:** None declared

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### AB0061 SERUM IL-37 AS AN EFFICIENT BIOMARKER OF DISEASE ACTIVITY IN PATIENTS WITH ANKYLOSING SPONDYLITIS: POST-HOC ANALYSIS OF PLANETAS STUDY

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**Background:** IL-37 is an anti-inflammatory cytokine which belongs to IL-1 cytokine superfamily. Patients with ankylosing spondylitis (AS) also had a higher serum IL-37 concentration than controls, and were also associated with other inflammatory markers such as CRP, ESR, and BASDAI levels.<sup>1</sup> However, the relationship between serum IL-37 and disease activity after anti-TNF treatment has not been reported.

**Objectives:** To investigate the association of serum IL-37 level with disease activity in AS patients who were treated with infliximab.

**Methods:** Patients were recruited from the PLANETAS study (NCT01220518). Patients with active AS were treated with CT-P13 or infliximab originator. The serum levels of IL-37 were measured at week 0 and week 30 with specific ELISA. Other demographic, laboratory and clinical variables were evaluated simultaneously.

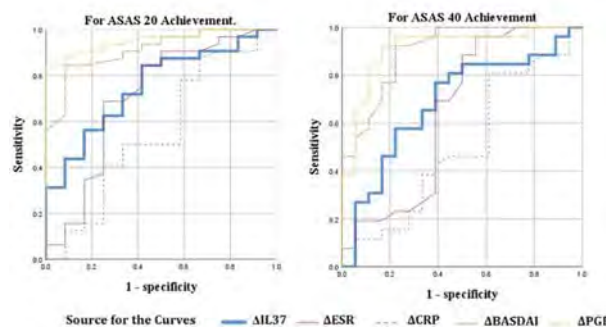
**Results:** Fifty patients with active AS (BASDAI  $> 4$ ) were analysed. The median age of patients was 40 years old [Interquartile range (IQR), 33.8–49.5], and the median BASDAI score was 6.7 (IQR 5.3–7.9). Compared to baseline, all measured clinical and laboratory parameters and serum IL-37 were significantly reduced. There was a statistically significant correlation between IL-37 and CRP, BASDAI at baseline, but not at week 30. Additionally, the differences ( $\Delta$ ) of parameters at baseline and at week 30 were assessed on their associations with other disease activity parameters. Delta IL-37 was significantly correlated with  $\Delta$ CRP,  $\Delta$ BASFI and  $\Delta$ BASDAI. The ROC curves of serum biomarkers for ASAS 20 achievement revealed that AUC value for  $\Delta$ IL-37 (AUC=0.74) was similar with  $\Delta$ ESR (AUC=0.71,  $p=0.64$ ) and superior than  $\Delta$ CRP (AUC=0.54,  $p < 0.01$ ). AUC value for  $\Delta$ IL-37 of ASAS 40 achievement was 0.66, which was similar with  $\Delta$ ESR (AUC=0.60,  $p=0.38$ ) and superior than  $\Delta$ CRP (0.46,  $p < 0.01$ ).

**Abstract AB0061 – Table 1.** Demographic & Clinical characteristics of analysed patients, comparing at baseline and at week 30.

Variables	At baseline	At week 30	P
Age	40.0 (33.8–49.5)	-	N/A
Female sex	7 (14%)	-	N/A
IL-37	105.1 (25.9–286.9)	44.5 (18.2–153.9)	$< 0.01$
ESR	35.0 (28.0–41.3)	7.5 (5.0–16.0)	$< 0.01$
CRP	158.1 (53.4–291.4)	20.0 (7.4–73.1)	$< 0.01$
BASDAI	6.7 (5.3–7.9)	3.3 (1.9–4.5)	$< 0.01$
BASMI	4.0 (3.0–5.0)	3.0 (2.0–4.0)	$< 0.01$
BASFI	6.6 (5.3–8.1)	3.3 (1.6–5.9)	$< 0.01$
PGD	70.5 (57.3–80.8)	33.0 (14.8–53.3)	$< 0.01$

**Abstract AB0061 – Table 2.** Correlations between IL-37 and other disease activity markers; at baseline and the differences between baseline and at week 30.

	At baseline			Difference between baseline and week 30		
	IL-37	ESR	CRP	$\Delta$ IL-37	$\Delta$ ESR	$\Delta$ CRP
IL-37		0.14	0.39**		0.24	0.36*
ESR	0.14		0.57**	$\Delta$ ESR	0.24	0.50**
CRP	0.39**	0.57**		$\Delta$ CRP	0.36*	0.50**
BASDAI	0.31*	0.31*	0.23	$\Delta$ BASDAI	0.32*	0.25
BASMI	0.05	0.09	0.16	$\Delta$ BASMI	-0.05	0.06
BASFI	0.20	0.36**	0.25	$\Delta$ BASFI	0.34*	0.35*
PGD	0.25	0.10	0.06	$\Delta$ PGD	0.16	0.28
						-0.06



**Abstract AB0061 – Figure 1.** Figure 1 ROC Curves of disease activity markers of ASAS 20 and ASAS 40 achievement.

**Conclusions:** Serum IL-37 levels are associated with BASDAI, patient's pain score, and CRP in active AS patients. Change in serum IL-37 level may serve as an efficient biomarker predicting the improvement of BASDAI and the achievement of ASAS 20 and 40 after anti-TNF treatment in AS patients.

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### AB0062 RECIPROCAL INTERACTION BETWEEN MACROPHAGE MIGRATION INHIBITORY FACTOR AND INTERLEUKIN-8 IN GOUT

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**Background:** Macrophage migration inhibitory factor is a proinflammatory, chemotactic, and tissue destructive cytokine.

**Objectives:** This study determined monosodium urate crystal-induced macrophage migration inhibitory factor production and its interaction with interleukin-8 in gout.

**Methods:** Peripheral blood, synovial fluid, and clinical data were obtained from 98 patients with gout. Synovial fluid and serum concentrations of macrophage migration inhibitory factor and interleukin-8 were measured. Synovial fluid monocytes and neutrophils were cultured with monosodium urate crystals and the cytokine production was determined. The signalling pathways involved were determined using signal inhibitors. The interaction between macrophage migration inhibitory factor and interleukin-8 was investigated.

**Results:** Synovial fluid macrophage migration inhibitory factor was higher in acute gout and that in serum was higher in patients with intercritical gout compared with controls. Synovial fluid macrophage migration inhibitory factor was positively correlated with synovial fluid leukocyte and neutrophil counts and interleukin-8. The expression of macrophage migration inhibitory factor was similar in synovial fluid neutrophils and monocytes, while interleukin-8 was higher in monocytes. Monosodium urate crystals induced macrophage migration inhibitory factor production in monocytes and interleukin-8 production in neutrophils. This effect was decreased by inhibiting Fc-gamma receptor 1 and toll-like receptor 4. Interleukin-8 increased macrophage migration inhibitory factor production in monocytes while macrophage migration inhibitory factor increased interleukin-8 production in neutrophils.



**Conclusions:** Macrophage migration inhibitory factor and interleukin-8 are highly produced in acute gout. Monosodium urate crystals induced macrophage migration inhibitory factor production in monocytes and interleukin-8 production in neutrophils with a reciprocal interaction between the two cytokines.

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AB0063

### HIGH-EFFICIENCY TRANSDUCTION OF MESENCHYMAL STEM CELLS BY AAV2/DJ VECTOR FOR THEIR POTENTIAL USE IN AUTOIMMUNE DISEASES

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**Background:** Mesenchymal stem cells (MSC), multipotential non-hematopoietic progenitors, can be isolated from various tissues and can modulate allogeneic immune cell responses. These properties make MSC as a promising potential treatment of autoimmune diseases.<sup>1</sup> Our previous studies have found that bone marrow-derived (BM)-MSC from systemic lupus erythematosus (SLE) patients are defective structurally and functionally,<sup>2</sup> treatment with modified and optimised MSC may bring a better effect on patients with autoimmune diseases. Most efforts have relied on adeno- and lentiviral vectors for delivering genes to MSC. Effective as these vectors may be, concerns regarding their immunogenicity and, in the case of lentivirus, the risk of insertional mutagenesis, have led to the pursuit of safer alternatives. Among these, adeno-associated virus (AAV) holds several advantages as a vector for human gene therapy. There are many serotypes of AAV available, and certain serotypes have been found to transduce specific cell types more efficiently than others.

**Objectives:** To determine the efficiency of different serotypes of AAV vectors for their ability to mediate transduction of different sources of MSC and assess whether AAV transduction affects MSC multipotentiality.

**Methods:** Serotypes 1, 2, 5, 6, 8, 9, PHP and DJ of AAV vectors were constructed in Viral Core, Boston Children's Hospital. The enhanced green fluorescent protein (eGFP) gene under transcriptional control of a CAG promoter was cloned into the AAV vector backbone. MSC derived from umbilical cord (UC), BM and amniotic fluid (AF) were isolated and approximately  $1 \times 10^5$  MSC were used for transductions with AAV vectors. eGFP expression was evaluated 3 days after transduction by fluorescence microscopy and flow cytometry. The capacity of MSC to differentiate *in vitro* was assessed.

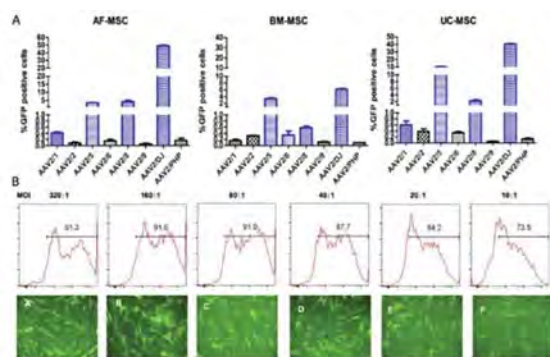


Fig1 A: the transduction efficiencies of AAVs (MOI=5:1) in AF-MSC, BM-MSC and UC-MSC. B: the transduction efficiencies of AAV/DJ in UC-MSC with different MOI.

**Abstract AB0063 – Figure 1.** A: the transduction efficiencies of AAVs (MOI=5:1) in AF-MSC, BM-MSC and UC-MSC. B: the transduction efficiencies of AAV/DJ in UC-MSC with different MOI.

#### Results:

- AAV serotype DJ vector was the most efficient in transducing MSC. AAV was added directly to the medium at 5 multiplicities of infection (MOI), 41% UC-MSC was transduced by AAV2/DJ, while the transfection is 0.47%, 0.3%, 10.5%, 0.3%, 1.84%, 0.06%, 0.16% by AAV2/1, AAV2/2, AAV2/5,

AAV2/6, AAV2/8, AAV2/9, AAV2/PHP (Fig 1A). Transduction efficiencies ranged from 73.5% for MOI 10% to 91.3% for MOI 320 in UC-MSC (Fig 1B).

- MSC derived from different tissues share a comparable level of transduction with the same AAV vector serotype. In our result, AAV2/DJ was the most efficient in transducing UC-MSC and AF-MSC.
- AAV2/DJ transduced MSC retained the same multipotential activity to differentiate into osteogenic and adipogenic lineage as comparable to untransduced cells.

**Conclusions:** AAV2/DJ vector can be used as a highly efficient tool to modify MSC *ex vivo* for therapeutic transplantation for autoimmune diseases.

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**Disclosure of Interest:** None declared

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AB0064

### ROLE OF IL-35 IN THE REGULATION OF IMMUNE RESPONSE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Interleukin 35 (IL-35) is a recently identified member of the IL-12 family of cytokines and represents a novel target for therapies of autoimmune, inflammatory, and infectious diseases, including rheumatoid arthritis (RA).<sup>Choi et al. 2015</sup>

IL-35 is a heterodimer consisting of EBV-induced gene 3 (EBI3) and IL-12 $\alpha$  chain p35 (Nakano et al. 2015). In contrast to other IL-12 cytokine family members, IL-35 appears to have anti-inflammatory and immunosuppressive properties mediated by induction of regulatory T and B cells; (Choi et al. 2015. Huang et al. 2017). In particular, IL-35 may play an important role in suppressing the inflammatory response by expanding regulatory T cells and in dampening the differentiation of Th17 cells (Niedbala et al. 2007).

**Objectives:** This study was designed to analyse effects of IL-35 on stimulated peripheral blood mononuclear cells (PBMC) and their subpopulations in RA patients and healthy controls.

**Methods:** PBMCs of 10 RA patients and 10 controls as well as CD14+ and CD4+ cells isolated from PBMCs using magnetic separation were cultured for 24 hours, and subjected to three conditions: no stimulation, stimulation with LPS (PBMC and CD14+) or stimulation with anti-CD3/anti-CD28 antibodies (PBMC and CD4+), and stimulation with added IL-35 (100 ng/ml). A panel of nine cytokines (IL-1 $\beta$ , IL-6, IL-8, IL-10, IL-12 (p70), IL-17a, IFN- $\gamma$ , MIP-1 $\beta$  and TNF) was analysed in the cell culture supernatants.

**Results:** RA patients had higher serum levels of IL-35 compared to healthy controls. A decreased secretion of IL-8 and increased secretion of TNF in the presence of IL-35 was observed *in vitro* in stimulated PBMCs of RA patients. In the control group, we observed an increased secretion of IL-6 by PBMCs and decreased secretion of IL-10 by T lymphocytes as a result of IL-35 addition to stimulated cells.

**Conclusions:** In this study, we found elevated serum levels of IL-35 in RA patients suggesting a possible involvement of IL-35 in the pathogenesis of RA. However, *in vitro*, the effect of IL-35 on stimulated immune cells was partially anti-inflammatory and partially pro-inflammatory, suggesting that the effect of IL-35 is pleiotropic and depends on the type and the state of the affected immune cell.

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**Disclosure of Interest:** None declared

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**AB0065** **N-CADHERIN IS DOWN-REGULATED BY DECOY RECEPTOR 3 IN SPECIFICALLY RHEUMATOID SYNOVIAL FIBROBLASTS**

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**Background:** Decoy receptor 3 (DcR3) is a secreted decoy tumour necrosis factor receptor and competitively binds and inhibits the TNF family including Fas ligand, LIGHT, and TL1A. We previously reported that DcR3 overexpressed in rheumatoid synovial fibroblasts (RA-FLS) stimulated by TNF $\alpha$  protects the cells from Fas-induced apoptosis.<sup>1</sup> We recently reported that DcR3 binds to TL1A expressed on RA-FLS resulting in the negative regulation of cell proliferation induced by inflammatory cytokines.<sup>2</sup> Further, we newly revealed the gene expression profiles in RA-FLS regulated by DcR3 by using microarray data analysis.<sup>3</sup> Among the genes in the profile, we demonstrated the possible involvement of tryptophan hydroxylase 1 down-regulated,<sup>4</sup> interleukin 12B up-regulated by DcR3<sup>5</sup> and centrosomal protein 70 kDa<sup>6</sup> in the pathogenesis of RA. The profiles also indicated that Cadherin 2/type 1/N-cadherin (CDH2) was up-regulated by DcR3 (fold change 1.93).<sup>3</sup> CDH2 has been reported to be associated with cell attachment and migration,<sup>7</sup> osteoblast differentiation,<sup>8</sup> and the proliferation of RA-FLS.<sup>9</sup> The hemophilic interaction of CDH2 suppresses the proliferation of RA-FLS through increasing the P27<sup>Kip1</sup> that inhibit cell-cycle progression.<sup>9</sup>

**Objectives:** In this study, we analysed CDH2 expression in RA-FLS stimulated with DcR3 in detail to reveal the involvement of CDH2 and DcR3 in the pathogenesis of RA.

**Methods:** Real-time polymerase chain reaction (real-time PCR). RA-FLS were stimulated with various concentration of DcR3-Fc or 1,000 ng/ml of IgG1, or left untreated in serum-free Opti-MEM for 12 hour. The relative expression levels of CDH2 mRNA were quantified by real-time PCR.

**Immunohistochemistry.**

Anti-CDH2 antibody was applied to frozen sections of synovial tissues from patients with RA or OA for overnight. After that, the expression of CDH2 protein was evaluated by immunohistochemical analysis.

**Results:** Real-time PCR demonstrated that DcR3-Fc significantly increased the expression of CDH2 mRNA in RA-FLS (104% with 10 ng/ml, 112% with 100 ng/ml, and 200% with 1000 ng/ml). Immunohistochemistry revealed that CDH2 was expressed more in the sublining layer of rheumatoid synovium than OA synovium.

**Conclusions:** In the gene expression profiles, we focused on CDH2 as the gene was highly up-regulated and belonged to major functional clustering categories; protein complex assembly, cell motility, regulation of transcription, cell membrane and glycosylation. In this study, we showed that the expression of CDH2 mRNA in RA-FLS was induced by DcR3 and that CDH2 was increased in the sublining layer of rheumatoid synovium. In this study, we demonstrated that DcR3 significantly induced CDH2 expression in RA-FLS. Considering the fact that CDH2 inhibits RA-FLS proliferation, DcR3 signalling may control the hyperplasia of RA synovium.

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**AB0066** **COMBINATION OF IL-10 AND IL-18 BUT NOT IL-6 AND IL-18 INDUCES IFN-GAMMA PRODUCTION AND SURFACE EXPRESSION OF TRAIL ON NK CELLS**

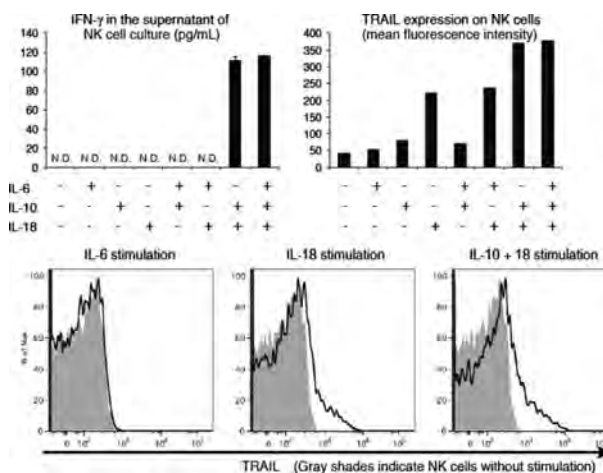
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**Background:** Adult-onset Still's disease (AOSD) is a systemic inflammatory disease, the cause of which is largely unknown. AOSD has been recently classified as one of the autoinflammatory diseases, in which innate rather than acquired immunity plays an important role. Serum IL-18 has been shown to be significantly high in AOSD patients.

**Objectives:** The aim of this study was to quantify the levels of multiple cytokines in the serum of AOSD patients, and compare the serum cytokine profile with that of healthy controls. We also attempted to evaluate the effects of the cytokines that were upregulated in the AOSD serum on natural killer (NK) cells, since NK cells are cells of innate immunity and IL-18 has been shown to enhance their cytotoxicity.<sup>1</sup>

**Methods:** We quantified the serum levels of 10 cytokines (IFN- $\alpha$ , IFN- $\gamma$ , IL-1 $\beta$ , IL-2, IL-4, IL-6, IL-10, IL-12p70, IL-17A and TNF- $\alpha$ ) in patients with AOSD and healthy controls using multiplex bead array assays and IL-18 using ELISA. We next sorted NK cells from peripheral blood mononuclear cells (PBMCs) of healthy controls, stimulated them *in vitro*, and quantified the level of IFN- $\gamma$  in the culture supernatant by ELISA and also assessed the surface expression level of tumour necrosis factor-related apoptosis-inducing ligand (TRAIL) on the cells.

**Results:** Compared to samples from healthy controls, the mean serum levels of IL-6 and IL-18 from AOSD patients were significantly higher. IL-10 was detectable in some of the patients. Originally, IL-18 was identified as a stimulator of IFN- $\gamma$  production<sup>2</sup>, however, serum IFN- $\gamma$  was below the detection limit. When NK cells were stimulated *in vitro* with IL-18 alone, the protein level of IFN- $\gamma$  in the culture supernatant was still below the detection limit. When we further added IL-6 and/or IL-10 to the culture, the combination of IL-10 and IL-18, but not IL-6 and IL-18, induced IFN- $\gamma$ . As IL-6 is a classic pro-inflammatory cytokine and IL-10 is considered to be an anti-inflammatory cytokine, this result was rather unexpected. Thus, we evaluated the expression of IL-6 and IL-10 receptors on NK cells and found that IL-10 receptors (IL-10R and IL-10R $\beta$ ) were present, but IL-6 receptors (IL-6R and gp130) were absent. We also assessed TRAIL expression on NK cells. Here, too, the combination of IL-10 and IL-18 induced TRAIL expression the most potently. Although a previous research showed that the combination of TLR3 and IL-18 signalling synergistically induced TRAIL on NK cells in an IFN- $\gamma$  dependent manner<sup>3</sup>, the addition of an anti-IFN- $\gamma$  antibody did not diminish the TRAIL expression.



**Abstract AB0066 – Figure 1**

**Conclusions:** A combination IL-10 and IL-18, not IL-6 and IL-18, induced the production of IFN- $\gamma$  and surface expression of TRAIL in NK cells. This TRAIL expression did not evidently depend on IFN- $\gamma$ . TRAIL was expected to be useful for the treatment of malignancy, but it turned out to be toxic to hepatocytes<sup>4</sup>. Since NK cells are rich in the liver and the abnormality of liver function is among the major symptoms in AOSD, we suggest that the combination of IL-10 and IL-18 may cause liver dysfunction by inducing TRAIL on NK cells in the liver.

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**Disclosure of Interest:** None declared  
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AB0067

### ALLOSTERIC RECEPTOR MODULATION OF A FREE FATTY ACID RECEPTOR TURNS NATURAL AGONISTS INTO POTENT ACTIVATORS OF THE SUPEROXIDE GENERATING NEUTROPHIL NADPH-OXIDASE

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**Background:** Short chain fatty acids are generated in the colon by bacterial fermentation of dietary fibres and serve as natural agonists for the free fatty acid receptor 2 (FFA2R/GPR43) which belongs to the large family of G-protein coupled receptors. We have earlier shown that acetate triggers an increase in the cytosolic concentration of free  $Ca^{2+}$  in neutrophils without any assembly/activation of the superoxide generating NADPH-oxidase (Mol Cell Biol. 2016 Sep 26;36(20):2583–95). Allosteric modulators bind to receptors at sites topographically distinct from the agonist/antagonist binding site and can regulate receptor functions positively or negatively.

**Objectives:** We undertook this study to determine whether an FFA2R selective modulator affects the neutrophil response induced by natural FFA2R agonists.

**Methods:** Neutrophils were collected from healthy blood donors. Release of superoxide anions generated by the assembled/activated NADPH-oxidase was recorded by sensitive isoluminol/HRP amplified chemiluminescence method. Intracellular  $Ca^{2+}$  transients were measured with FURA 2-AM labelled neutrophils.

**Results:** The allosteric modulator lacked a direct activating effect on neutrophils, but turned natural FFA2R agonists into potent activating agonists that triggered not only a transient rise in the cytosolic concentration of free  $Ca^{2+}$  ions but also an assembly of the NADPH-oxidase. The NADPH-oxidase activity induced by the combined effect of the allosteric modulator and the natural agonist acetate could be further increased in neutrophils treated with the pro-inflammatory cytokine TNF- $\alpha$ . The receptor selectivity was demonstrated through the inhibition of the neutrophil activity by the novel FFA2R antagonist CATPB. In addition, the allosteric modulator lacked effect on neutrophil responses triggered by a novel and selective agonist for the closely related GPR84, a receptor that recognises medium chain fatty acids.

**Conclusions:** Allosteric modulators that positively co-operate with natural FFA2R agonists and prime neutrophils in their response to such agonists may serve as good tools for further unravelling the physiological functions of the FFA2R and its involvement in various diseases. In this study, allosteric modulation of FFA2R is introduced as a receptor selective mechanism to prime neutrophils to produce increased amounts of reactive oxygen species.

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**Disclosure of Interest:** None declared  
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AB0068

### ALARMIN S100A8 AND S100A9 MODULATE THE INFLAMMATORY MICROENVIRONMENT IN EARLY TENDINOPATHY

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**Background:** Alarmins- also referred to as damage associated molecular patterns (DAMPs)- are endogenous molecules mobilised in response to tissue damage known to activate the innate immune system in the early stages of disease. The molecular mechanisms that regulate inflammatory and remodelling pathways

in tendinopathy are largely unknown therefore identifying early immune effectors is essential to understanding the pathology. S100A8 and S100A9 are constitutively expressed by cells of myeloid origin; under pathological conditions they are induced in other cell types in response to environmental triggers and cellular damage.

**Objectives:** Based on previous investigations we sought evidence of S100A8/A9 expression in human tendinopathy and thereafter, to explore mechanisms whereby S100 proteins may regulate release of inflammatory mediators and matrix synthesis in human tenocytes.

**Methods:** Torn supraspinatus tendon (established pathology) and intact subscapularis tendon (early pathology) biopsies were collected from patients undergoing arthroscopic shoulder surgery. Control samples of healthy hamstring tendon were collected from patients undergoing hamstring tendon ACL reconstruction. S100A8/A9 expression was analysed at transcript and protein level using quantitative RT-PCR and immunohistochemistry, respectively. Primary human tenocytes were cultured from hamstring tendon tissue. The *in vitro* effect of recombinant human S100A8/A9 on human tenocytes was measured using quantitative RT-PCR and release of inflammatory mediators was measured at protein level by ELISA.

**Results:** Immunohistochemical staining of tendinopathic tissues indicated the presence of S100A8 and S100A9 in tendinopathy with early diseased tissue displaying a distinct increase in S100A8 and S100A9 expression compared with control and established pathology. These findings were mirrored by data obtained at transcript level from both early and late pathology. Treating tenocytes with exogenous S100A8/9 significantly increased release of IL-6 and CCL2; however, no alterations in genes associated with matrix remodelling were observed at a transcript level.

**Conclusions:** The presence of S100A8 and S100A9 in early tendinopathic lesions suggests expression is upregulated in response to cellular damage. We have confirmed the presence of S100A8, S100A9, CCL2 and IL-6 in tendinopathy and propose that S100A8 and S100A9 participate in early pathology by modulating the stromal microenvironment and influencing the inflammatory profile of tenocytes. S100A8 and S100A9 may participate in a positive feedback mechanism involving enhanced leukocyte recruitment and release of pro-inflammatory cytokines from tenocytes that perpetuates the inflammatory response within the tendon in the early stages of disease. This, in turn, may contribute aberrant matrix remodelling and associated morphological deficiencies within the tendon. We propose S100A8 and S100A9 are active alarmins in early tendinopathy that indirectly influence matrix remodelling by perpetuating the stromal inflammatory environment. Selective targeting of DAMP signalling may offer novel therapeutic approaches in the management of human tendon disorders.

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**Disclosure of Interest:** None declared  
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AB0069

### INCREASED EXPRESSION OF SOLUBLE MIC-A IN THE SYNOVIAL FLUID OF RHEUMATOID ARTHRITIS PATIENTS

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**Background:** MIC-A (Major histocompatibility complex class I chain-related gene A)<sup>1</sup> is a transmembrane or soluble protein that interacts with the activating NKG2D receptor. MIC-A stimulates effector responses mediated by NK and CD8 +T cells under cellular stress conditions, like cancer or infections.<sup>2</sup> MIC-A is also associated with autoimmune diseases (such as rheumatic disorders) characterised by immune dysregulation triggered by environmental factors, and plays important roles in immune activation and surveillance.<sup>3</sup> In mice, various NKG2D ligands were discovered: Rae-1, H60 and MULT1 families.<sup>4</sup>

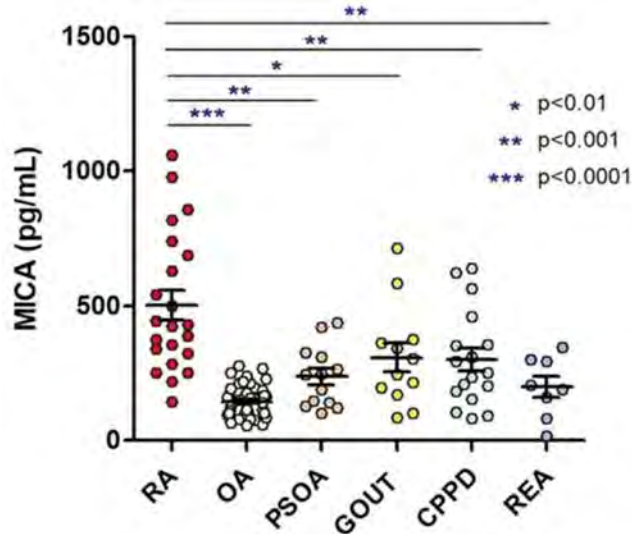
**Objectives:** This study aims at investigating the potential pathological relevance of soluble MIC-A (sMIC-A) protein in inflammatory rheumatic diseases involving articular structures in humans. The expression of orthologous NKG2D ligands in mouse models of experimental joint inflammation is also quantified.

**Methods:** We collected synovial fluid (SF) from 118 subjects: 22 Rheumatoid Arthritis (RA), 13 Psoriatic Arthritis (PSOA), 12 Gout Disease (GOUT), 18 Calcium



Pyrophosphate Deposition Disease (CPPD), 8 Reactive Arthritis (REA) and 45 Osteoarthritis patients. Gout and CPPD diseases were confirmed by the presence of crystals in SF. Clinical data were collected. The concentration of soluble MIC-A (sMIC-A), interleukin (IL)-1, IL-6 and IL-8 was measured by ELISA. Murine Rae-1, H60 and Mult1 transcripts were quantified by real-time quantitative PCR (RT-qPCR) in 3 models of joint inflammation: Serum Transfer Arthritis (STA), Collagen-induced arthritis (CIA) and Collagenase-Induced Osteoarthritis (CIOA).

**Results:** Significantly higher levels of sMIC-A were found in the synovial fluid of RA patients in comparison with all others diseases ( $p < 0.001$ , figure n.1). sMIC-A levels were correlated to white blood cell counts and levels of inflammatory cytokines IL-1, IL-6 and IL-8. Similarly, higher expression levels of Rae-1, H60 and Mult1 were found in chronic arthritis mouse models in comparison with osteoarthritic mice.



Abstract AB0069 – Figure 1

**Conclusions:** Our data identifies synovial sMIC-A as an important player in rheumatoid arthritis compared to other rheumatic diseases and osteoarthritis. Investigations in mouse models are in agreement with this finding

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#### AB0070 ADIPOKINES AND CYTOKINES IN THE PATHOGENESIS OF PSORIASIS AND METABOLIC DISORDERS

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**Background:** Psoriasis is a systemic immune-associated disease with a specific comorbidity. The manifestations of the metabolic syndrome in this category of

patients are changes that develop on systemic immune-associated inflammatory psoriatic process background and contribute to the progression of chronic inflammation.

**Objectives:** The aim of the study was determination of the main adipokines and cytokines content in the serum of peripheral blood, severity and activity of the disease in patients with psoriasis; clinical and laboratory evaluation of metabolic disorders. The interconnection between the production of adipokines and cytokines in psoriasis was analysed depending on the severity and activity of the psoriatic process and the nature of metabolic disorders.

**Methods:** Serum levels of adipokines (C-peptide, ghrelin, insulin, glucagon, leptin, visfatin, resistin, GIP, GLP-1 and PAI-1) and cytokines (IL-1 $\beta$ , IL-1ra, IL-2, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-12 (p70), IL-13, IL-15, IL-17, eotaxin, FGF-2, G-CSF, GM-CSF, IFN- $\gamma$ , IP-10, MCP-1, MIP-1 $\alpha$ , MIP-1 $\beta$ , PDGF-BB, RANTES, TNF- $\alpha$  and VEGF) were measured in 36 patients with moderate and severe psoriasis, psoriatic arthritis. There was control group of 15 basically healthy persons. Clinical and laboratory evaluation of metabolic disorders (BMI, dyslipidemia, carbohydrate metabolism disorders) and cardiovascular diseases was performed for all examined patients. The duration, severity and the amount of body surface area involved in psoriasis were evaluated in all patients using recommended indices (BSA, PASI).

**Results:** Patients with psoriasis showed an increase in the production of glucagon, leptin, visfatin, GLP-1 ( $p < 1.0E-03$ ) and a decrease in the level of C-peptide, insulin, GIP, PAI-1, resistin ( $p < 1.0E-06$ ) compared with the control group. The difference of ghrelin concentrations in both groups was not statistically significant. Patients with psoriasis showed an increase in the level of IL-1 $\beta$ , IL-1ra, IL-2, IL-4, IL-5, IL-6, IL-8, IL-9, IL-10, IL-12 (p70), IL-13, IL-15, IL-17, eotaxin, FGF-2, GM-CSF, IFN- $\gamma$ , IP-10, MCP-1, MIP-1 $\beta$  and TNF- $\alpha$  compared to control group ( $p < 0, 01$ ). Positive correlations between the level of adipokines and cytokines were revealed.

**Conclusions:** The obtained data allow us to define adipokines as mediators between immune and endocrine systems. The imbalance between the proinflammatory and anti-inflammatory effects of adipokines observed in psoriasis demonstrates lipid metabolism dysfunction as one of the possible provoking factors of chronic inflammation determining the severity of the underlying disease. According to the results of the study, the following biological adipokines and cytokines should be classified as early biological markers of severity of the psoriatic immune-associated inflammatory process, with all its comorbid risks: GLP-1, glucagon, leptin, visfatin, IL-1ra, IL-2, IL-4, IL-5, IL-6, IL-7, IL-8, IL-12, IL-13, IL-17, eotaxin, FGF-2, GM-CSF, IFN- $\gamma$ , IP-10, MCP-1, MIP-1 $\beta$ , TNF- $\alpha$ . The levels of adipokines and cytokines are probably the earliest biological markers in patients with metabolic syndrome and psoriasis, the control of adipokines and cytokines level can be used to optimise therapy.

**Disclosure of Interest:** None declared

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#### AB0071 EFFECTS OF CHONDROITIN SULPHATE AND GLUCOSAMINE ON INFLAMMATORY CYTOKINES IN MACROPHAGES

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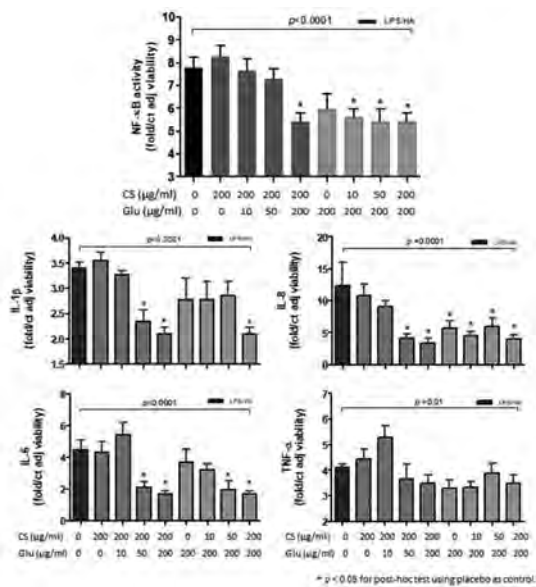
**Background:** The combination of pathogen-associated molecular patterns (PAMPs), such as lipopolysaccharide (LPS), and endogenous danger-associated molecular patterns (DAMPs), such as hyaluronan (HA) fragments, are known to be able to induce an inflammatory response from macrophages characterised by the release of pro-inflammatory cytokines<sup>1</sup>. We have previously shown that pharmaceutical grade chondroitin sulphate (CS), commonly used in the symptomatic treatment of osteoarthritis (OA), can attenuate the inflammatory response.

**Objectives:** To evaluate the synergistic effects of CS and glucosamine (GLU) in combination on LPS/HA mediated inflammatory responses of an immortalised human macrophage cell line (THP-1) and primary synovial fluid cells.

**Methods:** THP-1 monocyte cells were grown and differentiated into mature macrophages by the addition of 200 nM of phorbol 12-myristate 13-acetate (PMA) as previously described<sup>1</sup>. Cells were cultured with a physiologically achievable range of concentrations of CS and GLU (0, 10, 50, 200  $\mu$ g/ml of each, Bioibérica, S.A. U.) for 6 hours, then primed with physiologically relevant concentrations of LPS (10 ng/ml) (n=12/group). After 24 hours, cell culture media were replaced with serum free Opti-MEM supplemented with the previously mentioned concentrations of CS and GLU, LPS, and 10  $\mu$ g/ml HA fragments (ultra-low molecular weight, Lifecore). After a further 24 hours, supernatants were harvested for NF- $\kappa$ B activity and pro-inflammatory cytokine (IL-1 $\beta$ , IL-6, IFN- $\gamma$ , and TNF- $\alpha$ ) assessment. Cell viability was measured using PrestoBlue reagent. The human knee

primary synovial fluid cells were collected at the time of joint replacement and cultured with CS (200 µg/ml) and GLU (200 µg/ml), singly or in combination, with the addition of LPS and HA (n=2/group). After normalisation for cell viability, all results were expressed as fold change from the negative control (media only). One-way ANOVA with Dunnett's post-hoc test was performed using GraphPad Prism.

**Results:** CS and GLU in combination (200 µg/ml of each) significantly reduced NF-κB activity by 70% compared to the positive control group (LPS/HA only). Although CS (200 µg/ml) alone did not reduce NF-κB activity, the addition of the lower concentration of CS (10–50 µg/ml) to GLU (200 µg/ml) significantly reduced NF-κB activity compared with GLU (200 µg/ml) alone. Addition of lower concentrations of GLU (10–50 µg/ml) to CS (200 µg/ml) modestly reduced NF-κB activity (Fig 1). Similar trends were observed in secreted pro-inflammatory cytokines (IL-1β, IL-6, IFN-γ, and TNF-α); namely, CS and GLU in combination significantly attenuated the LPS/HA mediated pro-inflammatory responses (p<0.05) (Fig 1). Although, a diverse range of inflammatory responses to the LPS/HA activation was observed, constitutive pro-inflammatory cytokine production by primary synovial fluid cells was reduced by the combination of CS and GLU.



Abstract AB0071 – Figure 1

\*p<0.05 for post-hoc test using placebo as control.

**Conclusions:** Inflammatory reactions of THP-1 macrophages, induced by physiologically relevant concentrations of LPS and HA fragments, were suppressed synergistically by the combination of physiologically achievable concentrations of CS and GLU. A similar trend was observed in primary human synovial cells but further investigations are required. These data could explain, at least in part, the clinical efficacy of CS and GLU in combination observed in OA patients.

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#### AB0072 EVALUATION OF ANTI-INFLAMMATORY EFFECTS OF NAPROXEN SODIUM ON HUMAN OSTEOARTHRITIS SYNOVIAL CELLS

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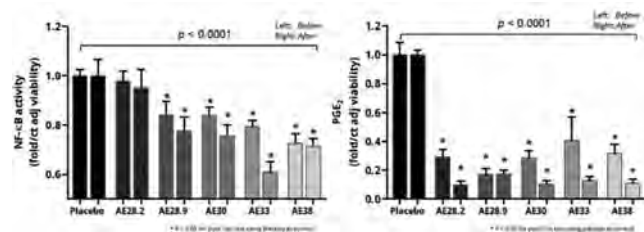
**Background:** Inflammation is increasingly recognised as an essential factor in the pathogenesis and progression of osteoarthritis (OA). Etarfolatide imaging for

activated macrophage quantification in knee joints confirms a high prevalence (~70%–80%) of joint inflammation in association with OA<sup>1</sup>. Naproxen sodium is a non-steroidal anti-inflammatory drug that is widely available over-the-counter (OTC) and has been shown to be effective in different pain models including OA<sup>2,3</sup>. Naproxen pre-treatment reduces inflammatory responses of chondrocytes. However, the effects of naproxen sodium on human OA synovial cells are not well known.

**Objectives:** Evaluate the ability of naproxen sodium to block the inflammatory responses and to reduce the activated inflammatory responses of a human monocyte cell line and primary human synovial fluid (SF) cells *in vitro*.

**Methods:** The immortalised human monocytic cell line, THP-1, was grown and differentiated into mature macrophages using phorbol 12-myristate 13-acetate as described previously<sup>4</sup>. Mature macrophages were treated with various concentrations of naproxen sodium two hours before or 24 hours after inducing an inflammatory reaction using lipopolysaccharide (LPS) and hyaluronan (HA) fragments (n=8/group). After a further 24 hours, the cell culture supernatants were assessed for NF-κB activity, pro-inflammatory cytokines (IL-1β, IL-6, IFN-γ, and TNF-α), and prostaglandin E<sub>2</sub> (PGE<sub>2</sub>). Cell viability was assessed using PrestoBlue reagent. Primary human SF cells were collected at the time of knee joint replacement for OA and treated 24 hours with naproxen sodium with and without the addition of LPS/HA (n=2/group). All results were expressed as fold change from the negative control (media only) after normalisation for cell viability. One-way ANOVA with Dunnett's post-hoc tests were done using GraphPad Prism.

**Results:** Compared to the placebo group, NF-κB activity of THP-1 cells was significantly reduced by as little as 28.9 mg/L naproxen sodium (corresponding to a trough plasma concentration achieved by a daily oral dose of 55 mg naproxen sodium) when added before or after the activation by LPS/HA (84% and 78% NF-κB activity reduction, respectively) (Fig1). When cells were treated before the activation with 33 mg/L naproxen sodium (corresponding to the concentration achieved by a 220 mg daily OTC dose), NF-κB activity was reduced 79% and IL-6 secretion was reduced by 77%. Cyclooxygenase enzyme activity, represented by PGE<sub>2</sub> production, was reduced to basal levels by as little as 28.2 mg/L naproxen sodium (p<0.05) when cells were treated either before or after the activation. Primary human SF cells treated with LPS/HA showed a striking increase in cytokine secretion ranging from 50-fold (IL-8) to 600-fold (IL-6). Cytokine production was reduced by naproxen sodium but a rebound phenomenon was observed for the highest concentration of 55/mg/L, which may indicate the cell stress response.



Abstract AB0072 – Figure 1

\*p<0.05 for post-hoc test using placebo as control.

\*p<0.05 for post-hoc test using placebo as control.

**Conclusions:** Naproxen sodium at low dose can both prevent and reduce inflammatory responses of a human monocytic cell line and primary human SF cells *in vitro*. These results highlight the potent activity of the OTC dose of naproxen sodium to dramatically reduce PGE<sub>2</sub>, NF-κB activity and cytokine production.

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AB0073

### EARLY MARKERS OF BONE – CARTILAGE RESORPTION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Systemic disorganisation of connective tissue with early metabolic disorder of its matrix is an inherent characteristic feature of rheumatoid arthritis (RA). The determination of the key extracellular matrix molecules in patients with early RA can adequately characterise a metabolism of connective tissue, stage of its destruction and the duration.

**Objectives:** to evaluate the significance of bone-cartilage resorption as an integral indicator of inflammatory-destructive processes in patients with early RA

**Methods:** We included 168 patients with early RA. The quantitative content and qualitative composition of glycosaminoglycans (GAG) in blood serum and excretion of GAG in urine were evaluated. Oxiprolin (OP) and its fractions (free OP), protein-bound (OPp) and hydroxyproline were determined in serum and urine. The presence of antibodies to the cyclic citrullinated peptide (ACPA) was studied, as well as the C-terminal telopeptides of serum collagen I (CTX).

**Results:** We identified the results of excretion of GAGs in urine depending on disease activity. And according to our data, in patients with low inflammatory process (IP) the level was  $6.31 \pm 1.09$  mg/g of creatinine (CR); moderate IP  $5.21 \pm 1.20$  mg/g of CR, and high disease activity  $6.53 \pm 0.96$  mg/g of CR. All these results were significantly higher in comparison with the control group by 55.9%, 29.1% and 67.7%, respectively. It means that GAG excretion rate did not depend on the stage of disease activity in patients with early RA, although even with a minimal IP it was significantly higher than normal. At the same time, the fractional composition of excreted GAGs in the urine in RA patients varied, as evidenced by a significant decrease in the sulfated GAGs content by 35% compared to the control group, although the differences between the groups were statistically unreliable.

CTX also proved to be 2.86 times higher than the level of healthy persons in whom the indicated index was 0.15 ng/ml.

In addition to a statistically significant increase of serum concentration of OP as compared to practically healthy persons, the qualitative composition of its fractions also changes, as evidenced by a significant elevation of OPp by 167.81%. No significant differences were found in the evaluation of OPfree and hydroxyproline

**Abstract AB0073 – Table 1.** Baseline demographic and clinical characteristics of RA patients, (n=168)

Characteristic		Value
Age, years		47,52±13,05
Gender	Male, n (%)	59 (35)
	Female, n (%)	109 (65)
Duration of symptoms, months		13,74±6,2
DAS28 (ESR)		5.9 (4.6-6.3)
ACPA positive, n (%)		102 (61)
Using GCs, n (%)		18 (11)
Using NSAIDs, n (%)		122 (73)
HAQ, points		1.3 (0.7-1.9)
RF positive, n (%)		83 (49)

#### Conclusions:

1. Progression of RA is accompanied by a progressive loss of the main functionally significant components of the extracellular matrix and manifested by a significant increase in the concentrations of proteoglycans and oxypoline.
2. The level of C-terminal telopeptides of type I of serum collagen – was elevated even in patients with early RA, indicating the activity of bone resorption processes.
3. The concentration and qualitative composition of blood serum GAGs adequately reflect the clinical symptoms of RA, being a sensitive integral

test that reliably indicates the severity of inflammatory and destructive changes.

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AB0074

### DAILY EXERCISE SUPPRESSES ACUTE PRO-INFLAMMATORY CYTOKINE EXPRESSION SYSTEMICALLY AND IL-1β LOCALLY IN A MURINE MODEL OF GOUT

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**Background:** Recent gout clinical practice recommendations/guidelines released by the ACR (2012) and the ACP (2017) do not address exercise as an interventional strategy; in contrast, the 2016 EULAR gout recommendations suggest that regular physical activity might decrease the excess mortality associated with chronic hyperuricemia. Referencing animal studies performed nearly a half century ago, many rheumatologists recommend resting the involved joints during an acute attack. However, recent evidence has demonstrated the anti-inflammatory effects of exercise in patients with rheumatic disease.

**Objectives:** The purpose of this study was to investigate the effects of exercise intensity on an immunological level in an animal model of gout by characterising pro-inflammatory cytokine expression.

**Methods:** BALB/C-Tg(NFκB-RE-luc)-Xen mice were exercised daily by treadmill walking (45 min/day) at low intensity (35% VO<sub>2</sub>max), moderate intensity (55% VO<sub>2</sub>max), and high intensity (75% VO<sub>2</sub>max). Following the 2 week training period, monosodium urate (MSU) crystal-mediated arthritis was induced by intra-articular injection of MSU crystals (0.5 mg) into the tibio-tarsal joint (ankle). At 16 hours post-MSU crystal injection, tissue was collected for immunohistochemistry (IHC) and both serum and synovial aspirates were processed to measure cytokine levels.

**Results:** Infiltrates consisted primarily of neutrophils and macrophages, as determined by IHC. The inflammatory responses were significantly reduced with low and moderate exercise when compared to either high intensity training or mice that were not exercised. Electrochemiluminescence detection assays quantifying the expression of a panel of pro-inflammatory cytokines showed that IL-2, IL-4, IL-5, IL-10, and IFN-γ were not detectable in the serum of MSU crystal-injected mice at levels greater than un-injected male/female controls. Furthermore, IL-12, CXCL1, TNF-α, and IL-6 expression was elevated in the serum with MSU crystal injection compared to un-injected counterparts, but this response was suppressed with low, moderate, or high intensity exercise training and undetectable in synovial aspirates. Conversely, IL-1β was not induced relative to un-injected controls systemically in the serum, but was increased locally in synovial aspirates. IHC staining of the ankle joint region for IL-1β confirmed this observation and further demonstrated a significant inhibition with low and moderate exercise relative to both high intensity training and non-exercised controls.

**Conclusions:** Our results demonstrate that daily exercise can have a measurable effect systemically in reducing pro-inflammatory cytokine expression in MSU crystal-mediated arthritis. Moreover, high-intensity exercise can suppress pro-inflammatory cytokine expression systemically, however, only low/moderate training suppressed the localised inflammatory response. Collectively, these data suggest a paradigm shift; emphasising physical activity in gout patients is potentially efficacious and warrants further investigation.

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AB0075

### INTRAAARTERIAL INJECTION OF HUMAN ADIPOSE-DERIVED MESENCHYMAL STEM CELLS (HAD-MSCS) ATTENUATES INFLAMMATION IN ACUTE ARTHRITIS MODEL

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**Background:** MSC are a potential therapeutic approach for the treatment of inflammatory diseases. Their anti-inflammatory role in both local and systemic diseases has been demonstrated in different experimental models and human diseases. Gouty arthritis is a systemic disease characterised by deposition of monosodium urate (MSU) crystals in soft tissues and joints. Frustrated phagocytosis of MSU crystals by resident leukocytes leads to NLRP3 inflammasome activation and subsequent amplification of inflammatory response resulting in severe tissue damage. MSCs are able to attenuate inflammatory response through different mechanisms, including NLRP3 inflammasome inhibition. Thus, MSCs could be a promising therapy for the attenuation of acute flares in gouty arthritis

**Objectives:** To study the antiinflammatory effect of hAD-MSCs in an acute gouty arthritis model

**Methods:** Acute gout flare was induced in 15 NZ rabbits by intra-articular injection of MSU crystals in both knees. 7 of these rabbits received a single dose of  $2.5 \times 10^6$  hAD-MSCs/kg, administered through the right femoral artery 1 hour after MSU injection (MSU+MSC group), while 8 animales were not treated (MSU group) This route of administration allowed the study of the effect of a direct MSC administration in the right knee synovial membrane (SM) in comparison to the contralateral knee, which received the cells after their vascular distribution through the organism. Inflammation was followed up measuring knee swelling and serum CRP. 4 healthy rabbits were simultaneously followed (Ctrl group). Animals were sacrificed 72 hour after MSU injections and SM were collected for further studies

**Results:** hAD-MSCs were able to attenuate joint swelling in both knees 24 hour after MSU injections, inducing a decrease in knee perimeter. Additionally, a significant decrease in serum CRP after 24 hour was observed in the treated group (Ctrl  $73 \pm 51$ ; MSU  $818 \pm 238^*$ ; MSU+MSC  $270 \pm 241$  mg/ml\*#;  $p < 0.05$  \*vs. Ctrl; # vs. MSU). Histopathological analysis showed that hAD-MSCs were able to significantly diminish SM inflammation after 72 hours of MSU injection (Krenn Score: Ctrl  $0.2 \pm 0.4$ ; MSU,  $5.6 \pm 2.3^*$ , MSU+MSC  $3.4 \pm 1.2^* \#$ ). SM vascularisation was reduced in treated animal (%CD31 +staining: Ctrl  $0.5 \pm 0.2$ ; MSU  $0.8 \pm 0.2^*$ ; MSU +MSC  $0.6 \pm 0.2^* \#$ ). hAD-MSC treatment also evoked a significant reduction of the inflammasome components in the SM: pro-IL1 $\beta$  (Ctrl  $0.9 \pm 0.2$ ; MSU  $1.5 \pm 0.5^*$ ; MSU+MSC  $1.1 \pm 0.2^* \#$ ), pro-caspase-1 (Ctrl  $1 \pm 0.6$ ; MSU  $3.5 \pm 3.1^*$ ; MSU+MSC  $1.4 \pm 0.5^* \#$ ), NALP3 (Ctrl  $1 \pm 0.3$ ; MSU  $2.9 \pm 2.1^*$ ; MSU+MSC  $1.4 \pm 0.7^* \#$ ). The synthesis of the pro-inflammatory cytokines COX-2 (Ctrl  $0.9 \pm 0.1$ ; MSU  $4.2 \pm 3.3^*$ ; MSU +MSC  $2.1 \pm 1.4^* \#$ ) and TNF $\alpha$  (Ctrl  $0.9 \pm 0.3$ ; MSU  $1.3 \pm 0.3^*$ ; MSU+MSC  $0.9 \pm 0.2^* \#$ ) were also reduced in the MSU+MSC animals, while TGF $\beta$  (Ctrl  $0.9 \pm 0.2$ ; MSU  $0.7 \pm 0.2^*$ ; MSU+MSC  $1.3 \pm 0.3^* \#$ ) and IL10 (Ctrl  $1.1 \pm 0.5$ ; MSU  $1.1 \pm 0.7^*$ ; MSU+MSC  $1.8 \pm 0.5^* \#$ ) were increased in comparison to MSU group. There were no differences between the direct and the indirect treatment, since both right and left SMS were equally damaged

**Conclusions:** Our data showed that a single dose of hAD-MSCs is able to modulate the inflammatory response in an acute gouty arthritis model in rabbit. Therefore, it is a promising therapeutic approach to attenuate gout flares, especially in patients with different comorbidities that complicate a conventional treatment

**Disclosure of Interest:** None declared

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AB0076

### JAK INHIBITOR BARICITINIB MODULATES HUMAN INNATE AND ADAPTIVE IMMUNE SYSTEM

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**Background:** Janus kinase (JAK), which constitutively binds to cytokine receptors, plays an important role in the cytokine signalling. While JAK is comprised of JAK1, JAK2, JAK3, and tyrosine kinase-2 (Tyk2), more than 40 types of cytokines transmit signals through JAK. After several clinical studies, baricitinib, a highly selective inhibitor of JAK1 and JAK2, has been approved recently for treatment of RA in Europe, Japan, and other countries. Although this drug is available orally due to its small molecular weight, it has comparable efficacy to the biological DMARDs (bDMARDs).

**Objectives:** The present study was designed to determine the effects of a highly-selective JAK1 and JAK2 inhibitor, baricitinib, on human immunocompetent cells, in order to establish the significance of JAK and the potential for baricitinib in the therapeutic armamentarium against immune-mediated diseases.

**Methods:** The effects of baricitinib and tofacitinib were evaluated using human monocyte-derived dendritic cells (MoDCs), plasmacytoid dendritic cells (pDCs), B cells and T cells.

**Results:** The expression of costimulatory molecules CD80/86 on MoDCs were induced 48 hours after LPS stimulation. Baricitinib concentration-dependently suppressed the expression of CD80/CD86. Inhibition of CD80/CD86 expression by tofacitinib was comparable to that induced by baricitinib. pDCs stimulated for 5 hours with CpG produced both TNF- $\alpha$  and IFN- $\alpha$ . Baricitinib reduced the proportion of these IFN- $\alpha$  producing pDCs in a concentration-dependent manner. On the other hand, TNF- $\alpha$  production was not affected by baricitinib. Baricitinib also suppressed the differentiation of B cells into plasmablasts by B cell receptor (BCR) and type-I IFN stimuli, and inhibited the production of IL-6 from B cells. Tofacitinib also suppressed BCR- and IFN- $\alpha$ -induced plasmablast differentiation and IL-6 production. However, neither baricitinib nor tofacitinib altered IgG production by B cells. Human CD4 +T cells proliferated after T cell receptor stimulation with anti-CD3 and anti-CD28 antibody; however, such proliferation was suppressed by baricitinib in a concentration-dependent manner. In addition, baricitinib inhibited Th1 differentiation after IL-12 stimulation and Th17 differentiation by TGF- $\beta$ 1, IL-6, IL-1 $\beta$  and IL-23 stimulation. Tofacitinib showed similar effects in these experiments. In naive CD4 +T cells, IFN- $\alpha$  and IFN- $\gamma$  induced phosphorylation of STAT1, which was inhibited by baricitinib as well as tofacitinib. Furthermore, IL-6-induced phosphorylation of STAT1 and STAT3 was also inhibited by JAK inhibitors.

**Conclusions:** The present study demonstrated that JAK inhibitors affect innate and adaptive immunity in humans. They can fine-tune various immune networks through a variety of mechanisms and seem suitable potential therapeutic agents for the treatment of diverse autoimmune diseases.

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AB0077

### HIGH-MOBILITY GROUP BOX 1 MEDIATED MONOSODIUM URATE CRYSTAL-INDUCED NLRP3 INFLAMMASOME ACTIVATION IN HUMAN MACROPHAGES

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**Background:** High-mobility group box 1 (HMGB1) was identified originally as a highly conserved non-histone DNA-binding factor and recently noted as a potent inflammatory mediator under inflammatory conditions.

**Objectives:** This study is to investigate the inflammatory cascade between HMGB1 protein and activation of NLRP3 inflammasome in human macrophage under uric acid-induced inflammation.

**Methods:** The study used human U937 macrophage cell line under stimulation with monosodium urate (MSU) crystal or HMGB1. Total reactive oxygen species (ROS) were measured by flow cytometry. Interleukin-1b (IL-1b), NLRP3, TXNIP, HMGB1, NF- $\kappa$ B, I $\kappa$ Ba, and caspase-1 protein expression was detected using western blotting. IL-1b, IL-18, caspase-1, and HMGB1 gene expression were assessed by quantitative real-time polymerase chain reaction. Intracellular HMGB1 expression was assessed by immunofluorescent staining with Mito-Tracker Red.

**Results:** MSU crystals induced HMGB1 and ROS production by activation of NF- $\kappa$ B signal pathway in human macrophages. HMGB1 mRNA expression was markedly attenuated under stimulation using TXNIP siRNA. Enhanced release of IL-1 was noted through increased HMGB1 expression and TXNIP-mediated NLRP3 inflammasome activation under stimulation of MSU. Combination of MSU and HMGB1 augmented NLRP3 inflammasome, compared to either MSU or HMGB1 stimulation.

**Conclusions:** This study demonstrated that HMGB1 is a crucial molecule for ROS-mediated TXNIP and NLRP3 inflammasome activation in uric acid-induced inflammation.

**Disclosure of Interest:** None declared

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**AB0078 SYSTEMIC AND LOCAL IL-17A AND MIR-223 LEVELS IN RHEUMATOID ARTHRITIS PATIENTS**

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**Background:** IL-17 is a proinflammatory cytokine, which overproduction promotes the autoimmune reaction in rheumatoid arthritis (RA). Recent studies have shown that IL-17 production in lymphocytes or its function could be regulated by miR-223 by targeting Roquin ubiquitin ligase or its receptors<sup>1–4</sup>.

**Objectives:** To examine a possible correlation between the expression levels of miR-223 and IL-17A in peripheral blood (PB) and synovial fluid (SF) of RA patients.

**Methods:** Expression levels of miR-223 were determined in matched PB and SF samples of RA patients by relative quantitation method 2<sup>-ΔΔCt</sup>. As reference control for normalisation RNU6B gene was used. Concentrations of IL-17A in matched serum and SF samples were determined by Human IL-17A ELISA kit (Gene probe, Diaclone). The results were compared to healthy control (HCs) as well as within the RA group.

**Results:** 58,73% of the RA patients showed overexpression of miR-223 in PB when compared to HCs (p=0.008) with AUC=0.673 (95 CI: 0.562/0.784), with 71.4% sensitivity and 46.9% specificity (p=0.006). miR-223 was overexpressed in 79.17% of RA SF (p=1.64 × 10<sup>-3</sup>) when compared to HCs SF with AUC=0.841 (95 CI: 0.724/0.958) with 87.5% sensitivity and 72.7% specificity (p=4.6 × 10<sup>-4</sup>). Within the RA group, SF miR-223 was underexpressed in 58.7% of the patients compared to its systemic levels. Levels of IL-17A were higher in RA SF compared to serum (8.645 pg/ml versus 0.315 pg/ml, p=0.012).

**Conclusions:** The difference between the systemic and local levels of miR-223 and IL17A in RA patients shows that the inflammatory disease process leads to their altered expression with a possible role of both molecules in the disease pathogenesis. The opposite changes in their systemic and local levels confirm the data about the possible role of miR-223 in regulating IL-17 function.

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**AB0079 ALFACALCIDOL SUPPLEMENTATION MODULATES CYTOKINE PRODUCTION IN PERIPHERAL BLOOD MONONUCLEAR CELLS CULTURE OF PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS**

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**Background:** Hormone D and its analogues display immunomodulatory activities that provide a beneficial effect in immunoinflammatory diseases. However, whether this hormone has an additive immunosuppressive effect when it is used with corticosteroids has not been investigated, although these agents are commonly used together.

**Objectives:** Testing the immunomodulatory *in vitro* effects of vitamin D analogue, alfacalcidol, in peripheral blood mononuclear cells (PBMC) cultures of patients with active rheumatoid arthritis (RA).

**Methods:** Sixteen patients with active RA were enrolled in the study. Patients PBMCs were isolated, stimulated with PMA/Ionomycin and cultivated for 48 hours at 37°C, 5% CO<sub>2</sub> in cell cultures medium with or without supplementation. *In vitro* effects of supplementation with alfacalcidol (concentration

10 nM), calcitriol (concentration 10 nM), methylprednisolone (concentration 400 nM) and cotreatment with alfacalcidol/methylprednisolone on cytokine production were studied. Stimulated production of cytokines IL-6, IL-17, IL-21, TNF-α, IL-4, IL-10, TGF-β and IFN-γ were determined in cell culture supernatant by standard ELISA method.

**Results:** *In vitro* alfacalcidol supplementation reduces the production of proinflammatory cytokines IL-17 (p=0.001), IL-21 (p=0.001), TNF-α (p=0.002) and IL-6 (p=0.4), and induce more intense anti-inflammatory cytokine production IL-4 (p<0.0001), IFN-γ (p=0.05), TGF-β (p<0.0001) and IL-10 (p=0.09), in PBMC cultures of patients with active RA. There was no significant difference between the effects of alfacalcidol and calcitriol, except decreased TGF-β production (p=0.535) after calcitriol supplementation. Methylprednisolone supplementation leads to a significant reduction of the IL-6 (p=0.002), IL-17 (p=0.0001), TNF-α (p=0.0001) and IL-4 (p=0.017) production, while increased production of IL-21, IL-10, IFN-γ didn't reach statistical significance. Cotreatment with alfacalcidol and methylprednisolone leads to additional, more significant reduction of IL-17 (p=0.0001) and TNF-α (p<0.0001) in PBMCs of patients with active disease.

**Conclusions:** Alfacalcidol, *in vitro*, showed a significant immunomodulatory effect through the specific inhibition of Th1- cytokine production, while Th2 cell response was enhanced – “Th2 switch”. Our results demonstrate that alfacalcidol has significant additive effects on glucocorticoid-mediated inhibition of Th1 cytokine production when combined with methylprednisolone. These findings demonstrate the potential use of alfacalcidol as an immunosuppressive agent when combined with corticosteroids in Th1, but not Th2, immune response.

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**AB0080 DIFFERENTIAL EFFECTS OF TR14 VERSUS DICLOFENAC ON PRO-RESOLVING LIPID MEDIATORS REVEALED BY RNASEQ**

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**Background:** Anti-inflammatory agents are used widely in treating numerous pain and inflammatory conditions. With a focus on the specialised pro-resolving mediators (SPM) pathways in cutaneous wound repair in mice, the therapeutic activities of Tr14 (Traumeel), a multicomponent/multitarget natural product, and diclofenac (NSAID), a non-selective cyclooxygenase (COX) inhibitor were compared. COX inhibitors can block the synthesis of prostaglandins and thromboxanes from arachidonic acid, and can have important effects on the synthesis of resolvins and protectins produced by similar enzymes from eicosapentanoic and docosahexanoic acid substrates. Differential effects were identified via transcriptome analysis (RNAseq).

**Objectives:** To compare the transcriptomic changes after administration of Tr14 or diclofenac in a mouse cutaneous wound healing model, with particular emphasis on the SPM pathways, which include resolvins and protectins.

**Methods:** After abrasive wounding, the wounds were treated with topical Tr14 (34 mg/ml) in combination with subcutaneous Tr14 injections (9.5 mg/ml), or with subcutaneous Tr14 injections only, or topical diclofenac at clinically relevant doses (2 mg/ml). Skin samples were analysed for RNA transcript profiling by RNAseq at specific times (12 hour, 24 hour, 36 hour, 72 hour, 96 hour, 120 hour, 192 hour) after injury. Differentially expressed genes (DEGs) were computed at each time point between diclofenac vs control or Tr14 vs control, using EdgeR.

**Results:** At early time points (12–36 hour), Tr14-treated wounds, and to a lesser extent diclofenac-treated wounds, showed marked induction of 3 lipoxigenase

enzyme mRNAs involved in SPM synthesis. Even more striking was a pronounced effect of Tr14 at 12–36 hours on Fpr1 and Fpr2 mRNAs, which are the transmembrane receptors for the SPM lipid mediators. Consistent with elevated levels of enzymes regulating SPM synthesis, and SPR receptors, there was a noticeable decrease in the mRNA levels of the p65/RelA subunit of NFkB at 72–96 hours. NFkB is a critical transcription factor in inflammation, regulating numerous cytokines and chemokines.

**Conclusions:** Tr14 and diclofenac had very different effects on the SPM synthetic pathway after cutaneous wounding. Tr14 stimulated mRNA levels of several key regulators of SPM synthesis, and had a marked effect on the mRNA levels of the SPM receptors. Tr14, *not* diclofenac, suppressed mRNA levels for NFkB subunit p65/RelA, which may explain some of the anti-inflammatory and proresolving properties of Tr14.

**Disclosure of Interest:** None declared

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AB0081

### LOW LIPOCALIN-2 IN SYSTEMIC LUPUS ERYTHEMATOSUS PREGNANCIES- A POSSIBLE MECHANISM FOR LOSS OF TOLERANCE

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**Background:** Lipocalin-2 (LCN2) has become increasingly relevant as a potential clinical biomarker of rheumatic diseases.<sup>1</sup> The biological role of LCN2 in the adaptive immunity is less understood. It has been shown that LCN2 can induce immune tolerance by upregulation of human leukocyte antigen G (HLA-G) expression and by expansion of T-regulatory cells.<sup>2</sup> LCN2-deficient mice have been found to be more susceptible to induction of autoimmunity.<sup>3</sup> Systemic lupus erythematosus (SLE) is a disease associated with loss of tolerance. Pregnancy complications seen in SLE are also regarded as a consequence of immune dysregulation. LCN2 might therefore play a role as an immune modulator in SLE-pregnancies.

**Objectives:** The study objective was to obtain a better understanding of immune regulation in pregnant women with SLE. In this study, we analysed serum LCN2 and clinical parameters in women with RA, SLE and healthy controls during pregnancy and postpartum.

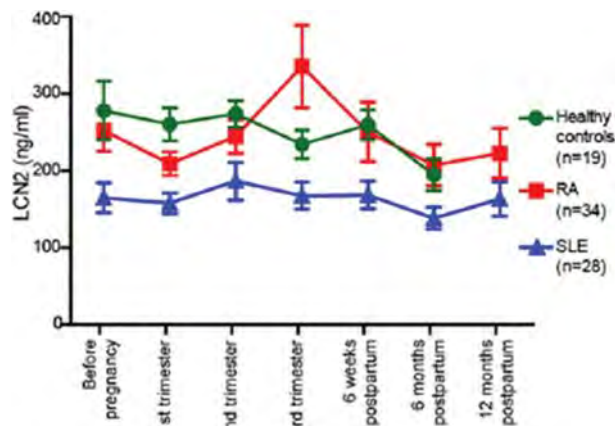
**Methods:** The Norwegian National Advisory Unit on Pregnancy and Rheumatic Diseases collects serum samples in a biobank from women with inflammatory rheumatic diseases. Samples were obtained before pregnancy, in each trimester and 6 weeks, 6 months and 12 months postpartum from pregnant women with SLE (n=28), RA (n=34) and healthy pregnant controls (n=19). A sandwich ELISA was used to measure LCN2 in the serum samples. The biobank database was linked to RevNatus, a Norwegian quality registry collecting comprehensive clinical data about these women.

**Results:** Our cohort of pregnant women with SLE and RA had low disease activity throughout pregnancy and 67%–95% used medication (table 1). LCN2 levels in serum samples from women with SLE were found significantly lower compared to samples from women with RA and healthy controls at all time-points (p<0.05) (graph).

Abstract AB0081 – Table 1. Disease activity and medication

	SLE patients			RA patients		
	1st trimester	2nd trimester	3rd trimester	1st trimester	2nd trimester	3rd trimester
<b>Disease activity</b>						
LAI-P Mean (range) [SD]	0,04 (0–0,25) [0,08]	0,02 (0–0,16) [0,05]	0,005 (0–0,08) [0,02]			
DAS28 Mean (range) [SD]				2,34 (1,79–3,91) [0,76]	2,57 (1,42–5,02) [1,06]	2,57 (1,79–4,90) [0,94]
<b>Medication</b>						
Prednisolone, receiving (%) (dose range [mg])	17 (2,5–7,5)	48 (2,5–7,5)	48 (2,5–10)	28 (2,5–10)	33 (2,5–15)	38 (2,5–12,5)
Other immunosuppressive receiving (>1*) (%)	96 (33)	91 (39)	95 (43)	67 (11)	76 (5)	80 (10)

\*>1: more than one of the following: SLE: hydroxychloroquine; azathioprine, RA: sulfasalazine, methotrexate, hydroxychloroquine, TNF inhibitors



Abstract AB0081 – Figure 1

**Conclusions:** Pregnant women with SLE had lower levels of LCN2 compared to pregnant women with RA and healthy controls. Our cohort of women had well controlled disease, making it likely that our findings represent inherent biological differences rather than effects of disease activity. Low LCN2 levels can be a possible mechanism for loss of tolerance seen in SLE patients during pregnancy.

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**Disclosure of Interest:** None declared

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AB0082

### CLINICALLY RELEVANT DISCREPANCIES BETWEEN DIFFERENT RHEUMATOID FACTOR ASSAYS

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**Background:** Accurate measurements of rheumatoid factors (RFs), autoantibodies binding IgG, are important for diagnosing rheumatoid arthritis (RA) and for predicting disease course. Worldwide, various RF assays are being used that differ in technique and target antigens.

**Objectives:** To study whether assay choice leads to clinically important discrepancies in RF status and level.

**Methods:** RF measurements using 4 commercial RF assays were compared in 32 RF<sup>+</sup> samples. Using ELISAs, the influence of the target antigen source—human IgG (hIgG) versus rabbit IgG (rIgG)—on measured RF levels was investigated in arthralgia patients and RA patients.

**Results:** Substantial discrepancies were found between RF levels measured in the four commercial assays. 6 samples (19%) with RF levels below or slightly above the cut-off in an rIgG-based assay were RF<sup>+</sup> in three assays using hIgG as the target antigen, some with very high levels. Direct ELISA comparisons of RF reactivity against hIgG and rIgG estimated that among 173 ACPA<sup>+</sup> arthralgia patients, originally RF negative in rIgG-based assays, up to 10% were single positive against hIgG. Monoclonal RFs binding to hIgG and rIgG or hIgG only supported these findings. In a cohort of 69 early RA patients, virtually all RF responses reacted with both targets, although levels were still variable.

**Conclusions:** The use of RF assays that differ in technique and target antigen, together with the different specificities of RF responses, leads to discrepancies in RF status and levels. This has important consequences for patient care if RA diagnosis and disease progression assessments are based on RF test results.

**Disclosure of Interest:** None declared

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AB0083

### LOCAL ICE CRYOTHERAPY DECREASES PROSTAGLANDIN-E<sub>2</sub>, NF-KB AND IL-6 SYNOVIAL LEVELS IN ARTHRITIC KNEES COMPARED TO CONTRALATERAL NON-TREATED JOINTS

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**Background:** Cryotherapy is widely used in rheumatic diseases, with a low level of evidence. Tissue mild hypothermia was reported to inhibit pivotal pro-inflammatory enzyme pathways such as COX-2/PGE<sub>2</sub> and NF-kB.

**Objectives:** We hypothesised that local cryotherapy (LC) might reduce joint inflammation through PGE<sub>2</sub> and NF-kB repression.

**Methods:** 47 patients suffering from non-septic knee arthritis were included (17 gout, 11 calcium pyrophosphate dehydrate crystal deposition diseases, 6 spondyloarthritis, 13 rheumatoid arthritis), taking no concurrent anti-inflammatory drug/DMARD. They were first randomised to receive local ice (30 min-N=16) or cold pulsed CO<sub>2</sub> (2 min – Cryo+ Cryonic-N=16) at 9 A.M and 5 P.M. Synovial fluid was collected just before the first cold application then 24 hours later (9 A.M). Synovial fluid IL-6, IL-1β, TNF-α, IL-17A, VEGF (Multiplex flow cytometry), NF-kB P65 (total/phosphorylated) and PGE<sub>2</sub> (ELISA) were measured and compared before and after 2 LC applications. Contralateral non-treated knees were then used as paired controls (in 16 other ice-treated patients).

**Results:** Synovial IL-6 significantly decreased after 2 LC applications (n=43 paired Wilcoxon:p=0.00015). This decrease was also significant in ice-treated subgroup (n=16 p<0.005) but not in CO<sub>2</sub>-treated patients (n=14;p=0.1). IL-1β and VEGF levels also decreased after treatment (n=44-p=0.02 and n=47-p=0.03) but not significantly in treatment subgroups. By contrast, IL-6 (n=13), IL-1β (n=15) and VEGF (n=15) didn't change in contralateral non-treated knees. LC had no significant effect on IL-17A nor TNF-α synovial levels. LC significantly reduced synovial NF-kB (n=38-p=0.04) and NF-kB-P levels (n=38-p=0.004). These levels were also significantly decreased in ice-treated patients (n=26-p=0.03 and 0.003) but not in CO<sub>2</sub>-treated patients (n=13). We observed no effect on the NF-kB levels in contralateral non-treated knees (n=12). NF-kB variations correlated significantly with IL-6 (Pearson's r=0.48-N=32 p<0.01) and VEGF (r=0.34-N=36-p=0.038) variations, and with the maximal skin temperature drop induced by LC (r=0.32-N=36-p=0.047). LC significantly reduced synovial PGE<sub>2</sub> (n=38-p=0.04), which was also significantly decreased in ice-treated patients (n=26-p=0.02) but not in CO<sub>2</sub>-treated patients (n=13). Conversely, we observed a significant increase in PGE<sub>2</sub> levels in contralateral non-treated knees (n=12-p=0.04), with a significant inter-class effect-size (weighted mean difference –1329 [–2232;–426] pg/mL-in 12 bi-arthritic patients).

**Conclusions:** Local ice cryotherapy applied twice during one day showed superior anti-inflammatory effects compared to local CO<sub>2</sub>, notably by reducing synovial IL-6 levels in arthritic knees. We also showed for the first time that this inhibitory effect on cytokine levels might be PGE<sub>2</sub> and NF-kB dependent, notably through significant inhibitory effects on the PGE<sub>2</sub> and (to a lesser extent) NF-kB pathways.

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**Disclosure of Interest:** None declared

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AB0084

### ELEVATED LEVELS OF IL-37 ARE ASSOCIATED WITH TOPHUS AND SUPPRESSED THE PRODUCTION OF INFLAMMATORY CYTOKINES IN PATIENTS WITH GOUT

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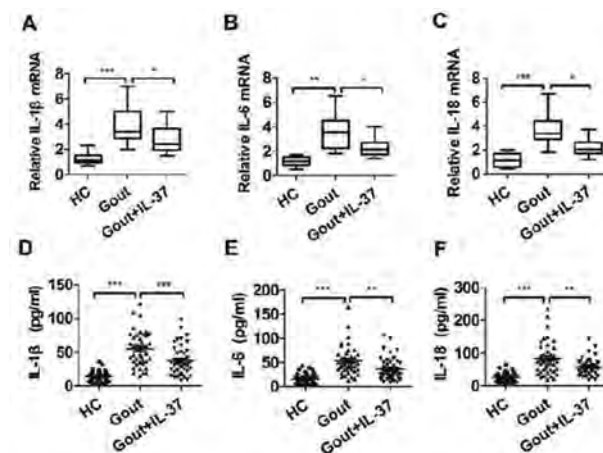
**Background:** IL-37 has been identified as a natural inhibitor of innate immunity. Although increasing evidence shows elevated IL-37 expression in various autoimmune diseases, its correlation with clinical symptoms in gout is still unclear.

**Objectives:** This study aims to determine the correlation between the levels of IL-37 and clinical indexes in gout patients, and to examine the inhibitory effect of IL-37 on pro-inflammatory cytokine including IL-1β, IL-6 and IL-18 from peripheral blood mononuclear cells (PBMC) of gout patients in culture.

**Methods:** Levels of serum IL-37 and concentrations of IL-1β, IL-6, IL-18 in cell culture from 42 patients with gout and 40 healthy controls (HCs) were measured by enzyme-linked immunoassay (ELISA). Moreover, the relative mRNA

expression of these cytokines in PBMCs was detected by real-time PCR (RT-PCR). The correlations between serum IL-37 levels and clinical values in gout patients were analysed by Spearman correlation test.

**Results:** Both protein and mRNA levels of IL-37 were higher in gout patients than healthy controls, especially in patients with tophus. Serum IL-37 levels of gout patients were positively correlated with C-reactive protein and uric acid. Furthermore, the expression of IL-1β, IL-6 and IL-18 in PBMCs from gout patients was significantly increased, which were markedly suppressed by IL-37 in culture.



**Abstract AB0084 – Figure 1.** IL-37 suppresses the expression of pro-inflammatory cytokines in PBMCs from gout patients

**Conclusions:** Serum levels of IL-37 are closely associated with clinical symptoms in gout patients and may represent a potential biomarker for the disease activity.

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AB0085

### THE MECHANISM OF TOTAL GLUCOSIDE OF PAEONY AND SINOMENINE ON THE PREVENTION OF ACUTE GOUT FLARES

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**Background:** The compliance of drug prevention for acute gout flares (GFs) during urate-lowering treatment (ULT) is very low. New preventive drugs of GFs during ULT is required. Our previous study found that the total glucoside of paeony (TGP), a traditional Chinese drug's extracts, has a good effect on the prevention and treatment for urate induced acute gouty arthritis (AGA) in rat.

**Objectives:** To explore the possible mechanism of TGP and Sinomenine (SIN) in the prevention and treatment of acute gouty arthritis.

**Methods:** Logarithmic growth phase of RAW264.7 cells were seeded into 96 well plate at a density of  $5 \times 10^4$ /mL. Cultured overnight in a humidified atmosphere of 5% CO<sub>2</sub> at 37°C. Then, the medium was changed to serum-free DMEM. Then divided into Control group (DMEM), Model group (DMEM +50 mg/L MSU), Colchicine group (DMEM +50 mg/L MSU +1 μmol/L Colchicine), TGP group (DMEM +50 mg/L MSU +40 mg/L TGP), SIN group (DMEM +300 μmol/L SIN), SIN +TGP group (DMEM +40 mg/L TGP +300 μmol/L SIN). The final volume of solution was 2 ml in each well, and each group had 3 wells, culturing for 24 hour in a humidified atmosphere of 5% CO<sub>2</sub> at 37°C. Then, culture supernatant was collected. NO level were detected by method of nitrate reductase, the level of IL-1β,

TNF- $\alpha$ , IL-8, MCP-1, MIF were detected by ELISA method. Western blot method was used to detect the expression of MyD88, NF- $\kappa$ B, ASC, and Caspase-1 in macrophages.

**Results:** The expression level of MyD88, NF- $\kappa$ B, ASC and Caspase-1 protein in macrophages of model group was significantly up-regulated, and the levels of IL-1 $\beta$ , TNF- $\alpha$ , IL-8, MCP-1, MIF and NO in the supernatant is increased significantly. TGP, SIN, TGP +SIN and Colchicine group compared with the model group, the expression of NF- $\kappa$ B, MyD88, ASC, Caspase-1 protein in macrophage and the level of IL-1 $\beta$ , TNF- $\alpha$ , IL-8, MCP-1, MIF and NO in supernatant were significantly decreased, the difference was statistically significant ( $p < 0.05$ ). TGP +SIN group compared with Colchicine group, the expression of inflammatory pathways proteins and the levels of inflammatory cytokines were no differenced ( $p > 0.05$ ) (table 1).

**Abstract AB0085 – Table 1.** Expression of major inflammatory cytokines and signalling pathway proteins (X $\pm$ S)

Group	N	IL-1 $\beta$ (pg/ml)	TNF- $\alpha$ (pg/ml)	MCP-1(pg/ml)	N	MyD88	NF- $\kappa$ B
Control	9	60.258 $\pm 5.159$	330.962 $\pm 15.046$	196.222 $\pm 17.696$	3	0.374 $\pm 0.017$	0.413 $\pm 0.059$
Model	9	115.360 $\pm 8.027^*$	638.118 $\pm 31.297^*$	568.332 $\pm 41.052^*$	3	0.831 $\pm 0.020^*$	0.871 $\pm 0.053^*$
Colch	9	78.561 $\pm 4.645^{\#}$	391.539 $\pm 21.616^{\#}$	339.777 $\pm 27.326^{\#}$	3	0.573 $\pm 0.024^{\#}$	0.568 $\pm 0.012^{\#}$
SIN	9	86.842 $\pm 5.758^{\Delta}$	461.174 $\pm 33.014^{\Delta}$	383.103 $\pm 26.296^{\Delta}$	3	0.674 $\pm 0.029^{\Delta}$	0.674 $\pm 0.012^{\Delta}$
TGP	9	93.200 $\pm 4.717^{\Delta\circ}$	466.507 $\pm 28.218^{\Delta\circ}$	421.988 $\pm 39.226^{\Delta\circ}$	3	0.699 $\pm 0.042^{\Delta\circ}$	0.777 $\pm 0.015^{\Delta\circ}$
SIN	9	79.902 $\pm 5.499^{\#}$	405.834 $\pm 20.824^{\#}$	343.728 $\pm 26.328^{\#}$	3	0.613 $\pm 0.026^{\#}$	0.575 $\pm 0.014^{\#}$

Note: \*  $P < 0.05$  vs Control; #  $p < 0.05$  vs Model;  $\Delta$   $p < 0.05$  vs Colchicine;  $\circ$   $p < 0.05$  vs SIN

**Conclusions:** The anti-inflammatory effect of Chinese herbal extracts (TGP and SIN) on the multiple targets of the inflammatory model may be one of its mechanisms of action for the prevention and control of acute gout flares.

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**Disclosure of Interest:** None declared

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## Cartilage, synovium and bone

### AB0086 TYPE II COLLAGEN AND GLYCOSAMINOGLYCAN TURNOVER IN BOVINE ARTICULAR CARTILAGE IS MODULATED BY LONG-TERM DYNAMIC COMPRESSION

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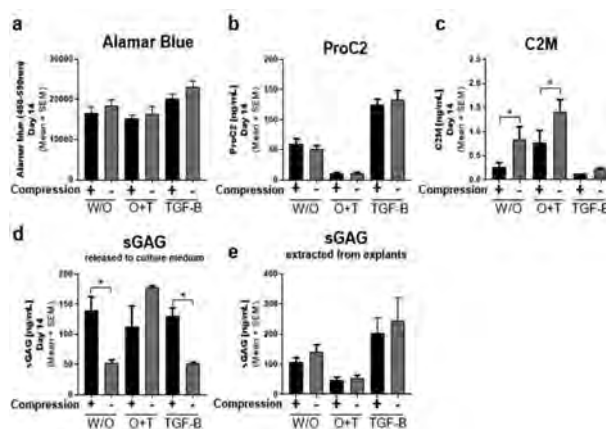
**Background:** Osteoarthritis (OA) patients suffer from progressive degradation of articular cartilage, to which there is no available treatment to block or reverse the catabolic mechanisms. Articular cartilage confers a biomechanical function in the joints, and in concordance chondrocytes have shown to be mechanosensitive. The effect of dynamic compression on cartilage extracellular matrix (ECM) could prove to be crucial for translational research in development and screening of new OA drug candidates.

**Objectives:** This study investigates the effect of long-term dynamic compression of a bovine articular cartilage *ex vivo* model through quantification of cartilage associated biomarkers.

**Methods:** Full depth bovine cartilage explants were cultured for 2 weeks. The explants were treated 3 times a week with either OSM [10 ng/mL] and TNF- $\alpha$  [2 ng/mL] (O+T), or TGF-B1 [50 ng/mL]. Untreated samples were included as negative controls (w/o). For each condition two groups were established; an unloaded group and a group compressed 3 times a week. Compression was applied using Electroforce 5500 (TA Instruments), in a sine wave with a maximum load per cycle of 1 MPa, at 1 Hz frequency for 1200 cycles. Metabolic activity was measured once a week using AlamarBlue. Biomarkers released to the supernatant were assessed using the following well-described ELISAs: formation of type II collagen was measured by ProC2, and MMP-degradation of type II collagen was

measured by C2M. Sulfated glycosaminoglycans (sGAG) released to media, and sGAG extracted from the explants on the last day using a 4 mM GuHCl solution were quantified using a 1,9-dimethylmethylene blue (DMB) assay.

**Results:** Compression of bovine explants significantly decreased release of C2M compared to unloaded samples in O-T and w/o groups with 42% and 48% respectively. ProC2 release was not affected by compression. Compression of w/o or TGF-b treated explants increased sGAG release with 195% and 152% relative to their unloaded controls. However, the total amount of sGAG extracted from the explants on the last day remained unchanged. Compression of the explants did not affect the metabolic activity.



**Abstract AB0086 – Figure 1**

**Conclusions:** Compression significantly reduced the degradation of type II collagen, which in combination with unaltered formation as measured by ProC2, may suggest suppression of the involved catabolic processes and increased deposition of type II collagen in the cartilage matrix. Furthermore, compression elevated the sGAG release without reduction in the explant GAG content, indicating an increased turnover of GAG. In conclusion, the cartilage ECM turnover is significantly modulated by dynamic compression. This method adds essential translational value to the continuous research addressing OA.

**Disclosure of Interest:** None declared

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### AB0087 SYNOVIAL TISSUE MACROPHAGES POLARISATION (M1, M2) IN PATIENTS WITH UNDIFFERENTIATED ARTHRITIS MEETING DIAGNOSTIC CRITERIA FOR RHEUMATOID ARTHRITIS OR PSORIATIC ARTHRITIS ALONG THE FOLLOW UP

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**Background:** Undifferentiated arthritis (UA) is defined as an inflammatory oligo- or polyarthritis that does not fulfill criteria for a definitive diagnosis. Earlier diagnosis would permit a better functional prognosis. Synovial tissue (ST) macrophages have been associated with disease activity, radiographic erosion and response to therapy in RA. Furthermore, it has been reported that M1 polarised macrophages predominate in RA synovitis, whereas M2 predominate in SpA synovitis.<sup>1</sup>

**Objectives:** To analyse polarised macrophages (M1 proinflammatory and M2 anti-inflammatory) in ST of patients with UA which evolved to RA or PsA, after a long follow-up, to explore their diagnostic value.

**Methods:** To determine the polarisation state of macrophages in ST obtained by arthroscopy from patients with UA that evolved to RA (UA-RA=8) or PsA (UA-PsA=9), the expression of proteins associated to GM-CSF-driven polarisation M1 (INHBA, TNF $\alpha$  and MMP12) and M-CSF-driven polarisation M2 (CD209) was assessed in ST CD163<sup>+</sup> macrophages. Patients with established RA (n=12) or PsA (n=10) were included as control. 4  $\mu$ m cryosections of ST in OCT were blocked for 10 min with 1% human immunoglobulins and incubated with primary (1–5  $\mu$ g/ml) and secondary antibodies. Imaging was performed with an inverted confocal microscope (SPE, Leica Microsystems) and glycerol immersion objective (ACS-APO 20x/NA 0.60). Single cell mean fluorescence intensity (MFI) was

assessed using ImageJ software (National Institutes of Health, Bethesda, MD, USA). At least three random fields were evaluated for each type of ST, quantifying the expression of INHBA, TNF- $\alpha$ , MMP12 and CD209 in all segmented CD163<sup>+</sup> macrophages. Macrophages density was normalised based on selected tissue area (mm<sup>2</sup>). After background subtraction, data were plotted using GraphPad software (GraphPad Software, La Jolla, CA, USA).

**Results:** CD163<sup>+</sup> sublining (SL) macrophages from UA-RA expressed abundantly the INHBA-encoded activin A, whereas TNF $\alpha$  and MMP12 were variably detected. Regarding the M-CSF-associated marker CD209, 2 populations of CD163<sup>+</sup> macrophages were found in the SL of UA-RA, CD163<sup>+</sup>CD209<sup>+</sup> and the other CD163<sup>+</sup>CD209<sup>-</sup>, with higher than 100 arbitrary units (au) for CD163<sup>+</sup>CD209<sup>+</sup> and lower than 100 au for CD163<sup>+</sup>CD209<sup>-</sup>. Similarly, INHBA, MMP12 and TNF $\alpha$  expression and 2 populations of CD209 were detected in CD163<sup>+</sup> macrophages from UA-PsA. Macrophage density was also found comparable between UA, with 650/mm<sup>2</sup> in UA-RA and 649/mm<sup>2</sup> in UA-PsA. Quantification of the above indicated markers in CD163<sup>+</sup>ST macrophages from established RA and PsA revealed similar levels of INHBA, TNF $\alpha$ , MMP12 and CD209 than those from UA-RA and UA-PsA.

**Conclusions:** This study shows for the first time that the polarisation state of ST CD163<sup>+</sup> macrophages in UA progressing to RA and PsA is similar to that of established RA and PsA in terms of INHBA, MMP12, TNF $\alpha$  and CD209 expression. Therefore, the inflammatory polarisation state of macrophages is similar in RA and PsA and it is already detected at the earlier steps.

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AB0089

#### HISTOPATHOLOGICAL CHANGE CAUSED BY BIOLOGICAL TREATMENT IN RHEUMATOID ARTHRITIS SYNOVIAL TISSUE

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**Background:** Multiple studies addressing the effects of biologics on the synovial tissue in rheumatoid arthritis (RA) patients have been reported. There are, however, few studies comparing histopathological changes in the synovial tissue in the same RA patients between before and after biologics treatment.

**Objectives:** We examined biologics impacts on RA synovial tissues based on pathological findings in them collected during surgeries for the same patient before and after biological drug usage.

**Methods:** Synovial tissues were collected from 34 RA joints before and after biologics. The average age and disease duration of the study subjects were 64.0 and 22.5, respectively. Synovial tissues were evaluated by hematoxylin. Histopathological changes in the synovial tissues were compared based on Rooney's score, and presence or absence of fibrinoid degeneration and proliferation of villi in the subsynovial tissue. We examined correlation between pathological findings in RA synovium and disease activity under biologics. Disease activity was assessed by CDAI. We examined the Histopathological changes in the Remission, Low disease activity group (RL group) and Moderate disease activity (M group). Etanercept, Infliximab, Tocilizumab, Adalimumab and Abatacept was used as biological drug for 18, 6, 5, 3 and 2 joints respectively.

**Results:** Rooney score between before and after biological usage improved from 28.4 to 12.0 showing significant difference. Significant improvement in Rooney score was observed in all items. Fibrinoid degeneration was observed in 29 cases (85.3%) and 6 cases (17.6%) before and after biologics treatment, respectively, demonstrating a significant reduction with biologics treatment. Proliferation of villi was observed in 32 cases (94.1%) and 11 (32.4%) before and after biologics treatment, respectively, demonstrating a significant reduction with biologics treatment. After biologics treatment, Rooney's score in RL group and M group were 10.4 and 15.3, respectively, showing a statistically significant difference. In addition, the M group had significantly higher scores in lymphoid follicle and lymphocyte infiltration compared to the RL group.

**Conclusions:** The study results demonstrated that biologics treatment significantly ameliorated inflammatory changes in the synovial lining layers and sublining layers. In addition, the results suggested that histopathological findings in the sublining layers reflected disease activity.

**Disclosure of Interest:** None declared

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AB0090

#### VERBASCOSIDE AND HYDROXYTYROSOL DOWNREGULATE STRESS-RELATED PATHWAYS IN HUMAN OSTEOARTHRITIC ARTICULAR CHONDROCYTES

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**Background:** Osteoarthritis (OA), is a leading cause of joint dysfunction and the disease is characterised by progressive destruction of the articular cartilage.<sup>1</sup> At the molecular level, degeneration of the cartilage is attributed to multifactorial events including oxidative stress, mitochondrial dysfunction, apoptosis and associated changes in inflammatory and catabolic gene expression.<sup>2</sup> Recent studies have revealed the essential role of plant-derived antioxidants in preventing pathological events observed in joint diseases by modulating redox signalling.<sup>3</sup>

**Objectives:** Here, we studied whether the polyphenolic compounds verbascoside and hydroxytyrosol exert chondroprotective effects by suppressing oxidative stress pathways and IL-1, IL-1 $\beta$ -converting enzyme (ICE) expression in human OA chondrocytes.

**Methods:** Chondrocytes were isolated from the joint cartilages of OA patients (grade 3–4) during total knee arthroplasty with the approval of Kecioren Training and Research Hospital, Clinical Research Ethics Committee (B.10.4.İSM.4.06.68.49), as described previously.<sup>4</sup> The alterations in cell counts, viability (MTT, NRU), proliferation (RTCA-iCELLigence System), reactive oxygen species (ROS) generation, stress-related signalling proteins and inflammatory progenitors ICE/caspase-1 (ELISA) were determined.

**Results:** Cell viability was increased at lower concentrations of hydroxytyrosol in OA chondrocytes (P1, 30th day). On the other hand, verbascoside treated cells did not show any difference in the activity of mitochondrial oxidoreductases by the MTT assay. However, both polyphenols significantly increased proliferation and reduced intracellular ROS generation in OA chondrocytes at lower concentrations. Although verbascoside has no effect on ICE/caspase-1, treatment with hydroxytyrosol downregulated ICE/caspase-1, indicating a potential anti-inflammatory effect. Both polyphenols modulated the activation of stress activated signalling pathways via p38 and JNK proteins.

**Conclusions:** At low concentrations the antioxidants hydroxytyrosol and verbascoside may have potential chondroprotective effects in OA.

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AB0091

#### MECHANICAL EXPOSURE AND DIACEREIN TREATMENT MODULATES INTEGRIN-FAK-MAPKS MECHANOTRANSDUCTION IN HUMAN OSTEOARTHRITIS CHONDROCYTES

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**Background:** Progression of osteoarthritis (OA) is characterised by destruction of articular cartilage, thickening of subchondral bone, and formation of osteophytes. The disease modifying OA drug (DMOAD) diacerein functions as a slow acting drug through anti-inflammatory, anti-catabolic, and pro-anabolic effects on cartilage and the synovial membrane. Mechanical loading of joint tissue directly affects the homeostasis of matrix degrading enzyme production and matrix repair.



**Objectives:** To explore the impact of diacerein and moderate mechanical stimulation on the anabolic metabolism of OA and non-OA chondrocytes, as well as on the integrin-FAK-MAPKs signal transduction cascade in these cells.

**Methods:** Mechanical stimulation was applied in terms of three different intensities by the Flexcell tension system. Influence on catabolic parameters such as MMPs, ADAMTS, and IL-6 were assessed by qPCR. Changes in phosphorylation of FAK, STAT3 as well as MAP kinases were verified by western blot analysis. Intracellular calcium was measured fluorimetrically using fura-2.

**Results:** Mechanical stimulation at moderate intensity (SM/SA) proved to be most efficient in terms of reducing production of matrix degrading enzyme and IL-6 expression. Treatment with diacerein by itself and diacerein in combination with SM/SA reduced phosphorylation of FAK and STAT3, which is more pronounced in OA cells. Pretreatment with diacerein for 7 days resulted in an increase in the sensitivity to Yoda1, the agonist for the mechanically activated ion channel Piezo1. However, in OA cells a significant reduction in Piezo1 expression was observed following treatment with diacerein.

**Conclusions:** Cyclic tensile strain can reduce matrix destroying enzymes, and when used in combination with diacerein, the activity of integrin signalling components is changed. The observed effects can be mainly attributed to diacerein's capacity to modulate STAT3 and Piezo1, which are both potential targets to prevent the progression of OA.

**Disclosure of Interest:** None declared

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#### AB0092 IL37 INHIBITS PROTEOGLYCAN LOSS IN HUMAN OA CARTILAGE: LINK BETWEEN IL37 AND MMP3

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**Background:** Glycosaminoglycans (GAGs) are essential for the pressure-resistant function of cartilage. During osteoarthritis (OA), GAGs are lost from cartilage. This loss impairs the functional and structural integrity of cartilage, thereby accelerating further cartilage damage. Proteoglycan degradation is mediated by enzymes such as MMP3, MMP13 and ADAMTS5.

**Objectives:** Recently we discovered that interleukin 37 (IL37) lowers the expression of these enzymes in human OA chondrocytes. The goal of this study was to investigate if IL37 protects against GAG loss in freshly obtained human OA explants.

**Methods:** Human cartilage was obtained from ten OA patients undergoing total knee or hip arthroplasty. Per condition 6 cartilage explants of 4 mm in diameter were used. Explants were incubated with recombinant IL37 (rhIL37) for up to 6 days. Every other day new rhIL37 was added. Additionally, an MMP3-inhibitor, or MMP13-inhibitor or ADAMTS5-inhibitor was added in the same protocol. Sulfated GAGs (sGAGs) were visualised by histology, and sGAG release in culture medium was quantified using 1,9-dimethylmethylene blue. To study sGAG synthesis, explants were incubated with rhIL37 followed by 4 hour labelling with <sup>35</sup>SO<sub>4</sub>. Alternatively, explants were pre-labelled for 4 hour with <sup>35</sup>SO<sub>4</sub> followed by incubation with rhIL37 to study sGAG degradation. Additionally, expression levels of proteoglycans and cartilage matrix degrading enzymes were measured by qPCR and Western Blot. Activity of MMP and ADAMTS enzymes was determined by measuring FFGV, ARGS and NITEGE neo-epitope levels in the supernatant of the cultures, using ELISA.

**Results:** Culturing human OA explants for up to 6 days, caused a reduction in GAG content as observed by loss of Safranin O staining. In addition, a release of sGAGs was measured in the supernatant of on average 17,5 µg/ml per mg cartilage. Incubation of cartilage explants with rhIL37 significantly reduced the release of GAGs. A maximal reduction of 24% was already observed with the lowest dose of rhIL37 (1 ng/ml). No effect of rhIL37 on the amount of incorporated <sup>35</sup>SO<sub>4</sub> was observed, indicating that rhIL37 does not alter the synthesis of GAGs. This is supported by the observation that rhIL37 does not affect the mRNA expression of the large proteoglycans and SLRPS. In contrast, we did find that rhIL37 significantly reduced the loss of <sup>35</sup>SO<sub>4</sub>-labelled GAGs from cartilage explants. In addition, rhIL37 reduced MMP3 and MMP13 protein expression and lowered both MMP and ADAMTS mediated degradation of proteoglycan fragments: FFGV neo-epitope and ARGS and NITEGE neo-epitopes, confirming that rhIL37 reduces active degradation of sGAGs. Lastly, to investigate which proteolytic enzyme contributes to the sGAG release in our culture system, a MMP3-, MMP13- or ADAMTS5-inhibitor was added to the explants. Strikingly, we found that only MMP3 inhibition mimicked IL37 function, suggesting that the effects of rhIL37 run via MMP3.

**Conclusions:** Our data show that rhIL37 reduces sGAG release of cartilage explants, indicating that IL37 supports cartilage matrix integrity. To our knowledge this is the first report demonstrating this anti-destructive effect of IL37 on freshly

obtained human OA cartilage explants. Possible these effects run via MMP3 because IL37 reduced MMP3 expression and only MMP3 inhibition results in similar effects as rhIL37 addition.

**Disclosure of Interest:** None declared

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#### AB0093 NATURAL POLYMER-BASED HYDROGELS FOR CARTILAGE REGENERATION

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**Background:** Cartilage is a tough, flexible tissue found throughout the body. It can become damaged because of a sudden injury, such as a sports injury, or gradual wear and tear (osteoarthritis). Injured articular cartilage has a poor regenerative capability, for this reason, tissue engineering may provide a fundamental therapeutic solution to repair cartilage injury.

Human articular cartilages are composed of dense extracellular matrix and chondrocytes. One of the major components in the extracellular matrix is hyaluronic acid. The combination of hyaluronic acid with other natural polymers to prepare hydrogel scaffolds may be potentially useful in many tissue engineering applications, including cartilage regeneration.

**Objectives:** We propose the synthesis of hydrogels based on hyaluronic acid and chitosan by a new strategy of synthesis using di-isocyanates to obtain an interpenetrated network of chitosan and hyaluronic acid.

**Methods:** Different kinds of hydrogels were synthesised using hyaluronic acid (Bioibérica, Spain), natural polymers (gelatine, chitosan) and stabilised with diisocyanates. The hydrogels were charged with chondroitin sulfate (Bioibérica, Spain).

**Morphological Characterisation:** The hydrogels were characterised by scanning electron microscopy and energy dispersive X-ray microscopy in order to study the morphology and the composition of the hydrogels.

**Hydrogel Swelling:** Dynamic swelling experiments were performed by placing discs of stabilised hydrogels in PBS at 37.0°C, and measuring their weight gain as a function of time.

**Biocompatibility:** Cytotoxicity *in vitro* assays (MTT) and cell adhesion tests (Alamar Blue) were performed on the hydrogels using different cell lines to corroborate the biocompatibility of the hydrogels.

**Results:** All the synthesised hydrogels presented a high interconnected porosity. The studied hydrogels swelled around 200%. After five hours equilibrium was reached and this equilibrium depended on the ratio hyaluronic acid/natural polymer increasing with the amount of hyaluronic acid present on the hydrogel. MTT assay indicated that the extracts collected at different times from the hydrogels were not cytotoxic and could be considered biocompatible. Cell adhesion assay demonstrated that the hydrogels supported cell adhesion and proliferation, and this behaviour was better on SC-loaded hydrogels.

**Conclusions:** Hydrogels based on hyaluronic acid and natural polymers are proposed as scaffolds for tissue engineering. The presence of interconnected porous and the good swelling properties, as well as the biocompatibility, represent a great advantage for application in cartilage regeneration. The addition of drugs or glycosaminoglycans is being studied to improve the cartilage regeneration.

**Disclosure of Interest:** None declared

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#### AB0094 POSITIVE EFFECTS OF CHIROPRACTIC MANIPULATION ON SUBCHONDRAL BONE MINERAL DENSITY, CARTILAGE DAMAGE AND SYNOVIAL INFLAMMATION IN OSTEOARTHRITIC RABBITS

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**Background:** Osteoarthritis (OA) is a degenerative joint disease characterised by the degradation and inflammation of cartilage and synovium with bone damage. Different approaches that decrease subchondral bone remodelling during OA have demonstrated to improve cartilage damage and synovial inflammation. Chiropractic is a therapeutic approach focused on the diagnosis, treatment and prevention of musculoskeletal disorders. Chiropractic manipulation (CM) is essentially manual, allowing the chiropractor to restore the normal range of motion and function of the joints, muscles, and ligaments. We have previously observed

that CM is able to increase subchondral bone mineral density (BMD) in an experimental model of osteoporosis<sup>1</sup>.

**Objectives:** To evaluate if CM could prevent the subchondral BMD alterations induced by OA, in association to an improvement in synovial membrane inflammation and cartilage damage in an OA model in rabbits.

**Methods:** Ten male New Zealand rabbits were submitted knee surgery to induce OA by transection of anterior cruciate ligament. CM was performed using the chiropractic adjusting instrument ActivatorV 3 times a week during 8 weeks as follows: Force 2 setting was applied onto the tibial tubercle of the rabbit right hind limb (CM-OA group), at an angle of 90°, whereas the corresponding left hind limb received a false manipulation (FM-OA group) consisting of ActivatorV firing in the air and touching the tibial tubercle. Three healthy animals were used as controls. Following sacrifice, tibiae and femora were removed for mCT and histological evaluation. Synovial inflammation was evaluated by Krenn's score and the protein presence of VEGF, MMP3 and CollagenVI in the synovial membrane was evaluated by western blot.

**Results:** In the OA rabbits, subchondral BMD decreased in relation to control animals (OA 4729±193 vs Control 5181±209 mg/cc), been partially reversed in the tibiae of OA rabbits with CM (TM-OA 5055±216 vs FM-OA 4404±170 mg/cc). Subchondral trabecular bone structural parameters were analysed by microCT and a significant decrease of bone volume/trabecular volume (BV/TV), trabecular number (TbN) and trabecular thickness (TbTh) was observed in the OA rabbits, while trabecular separation (TbS) increased compared to control animals. TM-OA group showed a significant improvement of these parameters compare to FM-OA group. TM-OA had lower cartilage damage compare to FM-OA (TM-OA 4±0,67 AU vs FM-OA 8±1,25 AU). TM-OA synovial membranes presented a total Krenn score lower than FM-OA joints (TM-OA 3±0,35 vs FM-OA 4.5±0,38 AU). OA synovial membranes showed higher levels of CollagenVI respect to control ones; TM-OA synovial membranes presented less expression of CollagenVI than FM-OA group (TM-OA 1.4±0,13 vs FM-OA 2.2±0,3 AU), been this associated with a decrease of both MMP3 (TM-OA 1.2±0,1 vs FM-OA 1.7±0,2 AU) and VEGF (TM-OA 1.2±0,14 vs FM-OA 1.9±0,26 AU).

**Conclusions:** These results support the hypothesis that CM may ameliorate subchondral BMD alterations induced by OA, in association to an improvement on synoviopathy and cartilage degradation.

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AB0095

#### ATTEMPT TO DEVELOP A CHIMERIC CO-CULTURE SYSTEM TO DIFFERENTIATE MOUSE OSTEOCLASTS BY CULTURING MOUSE PRECURSOR CELLS WITH HUMAN SYNOVIAL FIBROBLASTS

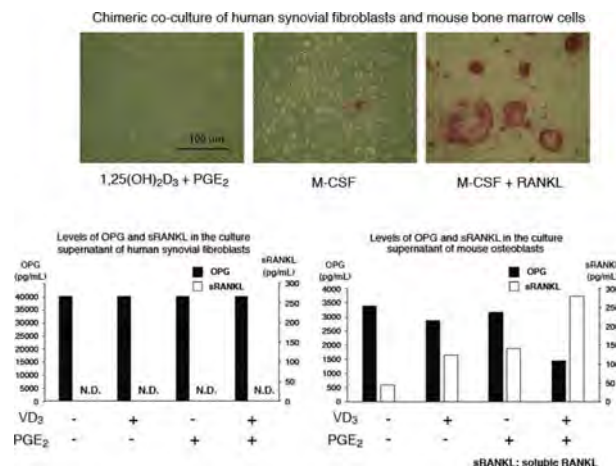
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**Background:** In rheumatoid arthritis (RA), inflammatory synovial tissue called the pannus proliferates and erodes the articular cartilage and bone in the affected joints. Osteoclasts, multinucleated cells of monocyte/macrophage lineage, are implicated in the bone destruction in RA. Thus, osteoclasts are considered an important therapeutic target in the prevention of the joint destruction. Mouse bone marrow cells differentiate into osteoclasts when co-cultured with osteoblasts or stromal cells in the presence of reagents such as 1,25-dihydroxyvitamin D<sub>3</sub> (1,25(OH)<sub>2</sub>D<sub>3</sub>) and prostaglandin E<sub>2</sub> (PGE<sub>2</sub>). There are no osteoblasts in the RA synovium, but there are fibroblasts and various inflammatory cells such as macrophages and lymphocytes. Thus, synovial fibroblasts may function as supporting cells for osteoclastogenesis in place of osteoblasts.

**Objectives:** The aim of this study was to establish a chimeric co-culture system of osteoclast differentiation using human synovial fibroblasts and mouse monocyte/macrophage lineage cells.

**Methods:** Synovial tissues were obtained from RA patients who underwent joint replacement surgery. Mouse osteoblasts were obtained from the calvariae of 2- or 3-day-old newborn C57BL/6 (B6) mice. Mouse bone marrow cells were prepared from femoral bones. Osteoclasts were visualised with tartrate-resistant acid phosphatase (TRAP) staining. The protein levels of RANKL and its decoy receptor, osteoprotegerin (OPG), in the culture supernatant were quantified using ELISA.

**Results:** We confirmed that mouse osteoclasts could be differentiated *in vitro* by culturing bone marrow cells in the presence of human M-CSF and RANKL. We then cultured mouse osteoclast precursors with human synovial fibroblasts in the presence of 1,25(OH)<sub>2</sub>D<sub>3</sub> and PGE<sub>2</sub>. The murine cells seemed to disappear in the course of the co-culture, whereas they survived when exogenous human M-CSF was added to the system. Interestingly, however, they did not become TRAP-positive multinuclear cells, suggesting that synovial fibroblasts do not provide a sufficient amount of the osteoclast differentiation factor, RANKL. Following these results, we used ELISA to quantify the level of human RANKL and OPG in the culture supernatant of synovial fibroblasts. Predictably, the level of RANKL was below the detection limit with or without the presence of 1,25(OH)<sub>2</sub>D<sub>3</sub> and/or PGE<sub>2</sub>. In contrast, that of OPG was very high, irrespective of the reagents added. We also quantified the levels of mouse RANKL and OPG in the culture supernatant of mouse osteoblasts. As expected, RANKL was detectable in this case. Interestingly, the level of OPG was very high and comparable to that of human OPG produced from synovial fibroblasts.



Abstract AB0095 – Figure 1

**Conclusions:** Synovial fibroblasts cannot be substituted for osteoblasts in a co-culture system of osteoclast differentiation. This is probably because synovial fibroblasts do not provide sufficient RANKL and M-CSF. Instead, they produce a large amount of OPG. This may be a mechanism by which ectopic osteoclastogenesis is inhibited. Thus, the osteoclasts observed in the pannus may be dependent on membrane-bound RANKL from other sources, like lymphocytes, or may be differentiated by stimulation with cytokines other than RANKL, such as TNF- $\alpha$  and IL-6.<sup>1,2</sup>

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**Disclosure of Interest:** None declared

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AB0096

#### EXPRESSION AND FUNCTION OF NEUROPEPTIDE Y RECEPTORS IN HUMAN ARTICULAR CARTILAGE: INFLUENCE OF GENDER AND OSTEOARTHRITIS

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**Background:** Elevated levels of neuropeptide Y (NPY) were reported in osteoarthritic (OA) joints<sup>1</sup>. No information exists regarding the role of NPY in OA joints, besides mediating or potentiating nociceptive transmission.

**Objectives:** To determine whether NPY receptors are present and functional in human chondrocytes, by evaluating the ability of NPY to activate important signalling pathways and to modulate autophagy, which was shown to be induced by this neuropeptide in hypothalamic neurons<sup>2</sup> and to be a crucial homeostatic mechanism in chondrocytes, whose reduction contributes to OA pathogenesis<sup>3</sup>.

**Methods:** Immunofluorescence for the NPY receptor subtypes, Y<sub>1</sub>, Y<sub>2</sub> and Y<sub>5</sub>, was performed in the human chondrocytic cell line, C28/I2, and in human cartilage sections obtained from multi-organ donors (4 males, 55–75 years old, mean=67.25, 3 females, 33–68 years old, mean=55.33) at the Bone and Tissue

Bank, University and Hospital Centre of Coimbra, with approval by the Ethics Committee. Phosphorylated levels of JNK, p38, ERK1/2, PKA, Akt and PKC and the levels of LC3B-I and II were evaluated by Western Blot of total cell extracts from C28/I2 cells.

**Results:** Immunoreactivity for Y<sub>1</sub>, Y<sub>2</sub> and Y<sub>5</sub> NPY receptors was observed in C28/I2 cells. In human cartilage, a positive signal was found for the Y<sub>2</sub> receptor in all samples while Y<sub>5</sub> receptor immunoreactivity was undetectable, regardless of disease state, gender and age of the donors. Y<sub>1</sub> receptor immunoreactivity was observed in male and female OA cartilage samples, as well as in those from non-OA females, but not in those from non-OA males. 50 nM NPY was sufficient to significantly increase the levels of phospho-JNK, -p38, -ERK1/2, -PKA, Akt and PKC with similar kinetics, but much slower than IL-1 $\beta$ . A 6 hour stimulation with 50 or 100 nM NPY decreased LC3B-I and II levels in comparison with untreated cells. In the presence of chloroquine (ChQ), NPY increased LC3B-II levels relative to those found in cells treated with ChQ alone, indicating an increased delivery of LC3B-II to the lysosome consistent with autophagy activation by NPY.

**Conclusions:** This study shows that distinct NPY receptor subtypes are present and functional in C28/I2 cells and in human chondrocytes *in situ* in the articular cartilage, strongly suggesting that non-neuronal cells and tissues of the joints, namely chondrocytes, are relevant as NPY targets. The presence of each receptor subtype seems to be determined by gender and, in males, also by the disease state. The role of age is unclear as most cartilage donors were aged >55 years old. Future studies will be addressed at further elucidating the role of NPY and its receptors in modulating male and female chondrocyte functions, both in health, ageing and osteoarthritis.

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AB0097

#### INDIVIDUAL FUNCTIONS OF THE HISTONE-ACETYLTRANSFERASES CBP AND P300 IN RHEUMATOID ARTHRITIS SYNOVIAL FIBROBLASTS

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**Background:** The close homologues cAMP-response element binding protein (CREB) binding protein (CBP) and p300 are writers of H3K27 histone acetylation marks found in active enhancers. In addition, their bromodomains are readers of acetylated lysine residues on histone tails and are subject of drug development for inflammatory and malignant diseases. CBP and p300 are widely accepted as redundant proteins and unique functions have not been investigated yet in depth.

**Objectives:** To analyse individual functions of CBP and p300 in rheumatoid arthritis synovial fibroblasts (SF).

**Methods:** SF were treated with the pan inhibitor I-CBP (1  $\mu$ M, 5  $\mu$ M), targeting the bromodomains of CBP and p300, in presence and absence of TNF- $\alpha$  (10 ng/ml) for 24 hour. The expression of CBP and p300 was silenced by transfection of antisense LNA gapmeRs (5 nM) in SF. Knockdown was verified by Western blotting. 24 hour after transfection cells were stimulated with TNF- $\alpha$  (10 ng/ml) for 24 hour. The mRNA expression of potential target genes was measured by quantitative Real-time PCR, using RPLP0 as an endogenous control. The protein expression of HOXD10 after CBP and p300 silencing was verified by Western blotting.

**Results:** I-CBP dose-dependently reduced the TNF- $\alpha$ -induced expression of MMP1 (p<0,05), MMP3, IL6 and IL8 in SF (n=3). Antisense LNA gapmeRs targeting CBP reduced the protein expression of CBP by 68,7% ( $\pm$ 12,9%, p<0,01, n=5) in unstimulated cells and by 89,7% ( $\pm$ 12,9%) in presence of TNF- $\alpha$ . The protein expression of p300 was reduced by 55,3% ( $\pm$ 29,8%, p<0,05, n=6) in unstimulated cells and by 62,7% ( $\pm$ 27,9%) in presence of TNF- $\alpha$  after transfection of LNA gapmeRs targeting p300. Silencing of CBP in SF (n=7) reduced the TNF- $\alpha$ -induced expression of IL6 (p<0,05), IL8 (p<0,05), MMP3 (p<0,05), as well as the basal (p<0,001) and the TNF- $\alpha$ -induced expression of MMP1 (p<0,05). In contrast, silencing of p300 induced the basal expression of IL6 (p<0,05), IL8 (p<0,01),

MMP1 (p<0,05), and MMP3 (p<0,05), as well as the TNF- $\alpha$ -induced expression of IL6 (p=0,078), IL8 (p=0,078), MMP1 (p<0,05) and MMP3 (p=0,063). Silencing of CBP in hand SF (n=4) reduced the expression of hand-specific HOX genes including HOXD10 (0,53 $\pm$ 0,10 fold; p<0,01), HOXD11 (0,76 $\pm$ 0,19 fold; p=0,098) and HOXA13 (0,75 $\pm$ 0,17 fold; p=0,063), whereas HOXA9, HOXA10 and HOXA11 were not affected. Silencing of p300 reduced the expression of HOXD10 (0,65 $\pm$ 0,24 fold; p=0,061), HOXD11 (0,45 $\pm$ 0,10 fold; p<0,01), HOXA10 (0,70 $\pm$ 0,14 fold; p<0,05) and HOXA13 (0,55 $\pm$ 0,19 fold; p<0,05). The down regulation of HOXD10 after silencing of CBP and p300 in hand SF was confirmed on protein levels by Western blotting.

Abstract AB0097 – Table 1

	CBP gapmeR	CBP gapmeR +TNF	p300 gapmeR	p300 gapmeR +TNF
MMP1	0,46 $\pm$ 0,17	0,41 $\pm$ 0,75	25,86 $\pm$ 26,82	1,96 $\pm$ 1,35
MMP3	0,97 $\pm$ 0,31	0,64 $\pm$ 0,35	2,60 $\pm$ 1,62	3,05 $\pm$ 2,89
IL6	1,21 $\pm$ 0,43	0,29 $\pm$ 0,17	4,51 $\pm$ 3,32	1,90 $\pm$ 1,20
IL8	8,27 $\pm$ 9,70	0,52 $\pm$ 0,20	207,8 $\pm$ 96,17	4,75 $\pm$ 2,67

**Conclusions:** Our results unravel opposing functions of CBP and p300 in regulating the TNF- $\alpha$ -induced expression of inflammatory and matrix-degrading target genes in SF. In addition, CBP and p300 likely contribute to the maintenance of a joint-specific gene expression in SF by regulating the expression of hand-specific HOX genes.

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AB0098

#### PEROXISOME PROLIFERATOR-ACTIVATED RECEPTOR-GAMMA COACTIVATOR-1B FACILITATES MIGRATION AND INVASION OF FIBROBLAST-LIKE SYNOVIOCYTES IN RHEUMATOID ARTHRITIS VIA ACTIVATION OF CANONICAL AND NON-CANONICAL NF-KB SIGNALLING PATHWAY

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**Background:** Fibroblast-like synovocytes (FLS) in rheumatoid arthritis (RA) manifest tumor-like properties including increased proliferation, prolonged survival, apoptosis resistance, adherence and invasiveness of adjacent tissues. Peroxisome proliferator-activated receptor-gamma coactivator-1 (PGC-1)  $\beta$  is a transcriptional coactivator which plays important roles in regulating energy metabolism and cytokine signalling pathways. Our previous study showed that elevated PGC-1 $\beta$  expressed in RA-FLS promoted their pro-inflammatory effect. However, the roles of PGC-1 $\beta$  on regulating migration and invasion of RA-FLS remains to be identified.

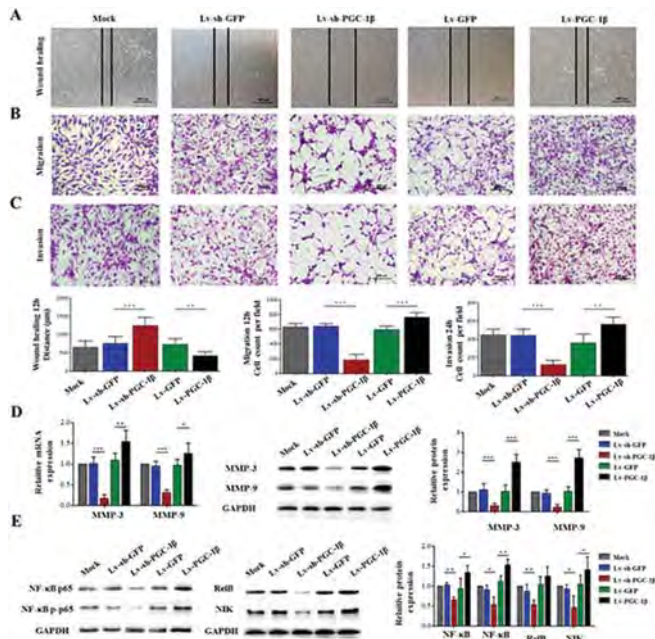
**Objectives:** To investigate the role of PGC-1 $\beta$  on regulating migration and invasion of RA-FLS and underlying mechanism.

**Methods:** Synovial tissues were obtained by closed needle biopsy from six patients with active RA and FLS were isolated and cultured. PGC-1 $\beta$  in RA-FLS was down-regulated or over-expressed by lentivirus with same vectors marked Lv-sh-GFP or Lv-GFP as negative controls. Effects of PGC-1 $\beta$  on migration and invasion capacity were detected by wound healing assays and transwell migration and invasion assays. The change of proteases in culture supernatants were detected by Proteome Profiler human protease array kit (R and D Systems, USA) and verified by qRT-PCR and western blot. The expression of key signalling molecules in canonical and non-canonical NF- $\kappa$ B signalling pathway was detected by western blot.

**Results:** Down-regulation of PGC-1 $\beta$  by Lv-sh-PGC-1 $\beta$  transfection inhibited migration and invasion of RA-FLS compared with Lv-sh-GFP transfection group (wound healing: 1252 $\pm$ 214 vs. 764 $\pm$ 184  $\mu$ m, p<0.001; migration: 184 $\pm$ 74 vs. 642 $\pm$ 32 cells/field, p<0.001; invasion: 124 $\pm$ 47 vs. 445 $\pm$ 67 cells/field, p<0.001), while



over-expression of PGC-1 $\beta$  promoted migration and invasion of RA-FLS (all  $p < 0.05$ , figure 1A-C). Down-regulation of PGC-1 $\beta$  in RA-FLS significantly decreased the expression of MMP-3 and MMP-9 in the culture supernatant which was measured by Proteome Profiler human protease array (MMP-3:  $p = 0.032$ , MMP-9:  $p = 0.037$ ). Further qRT-PCR and western blot analysis verified that both mRNA and protein expression of MMP-3 and MMP-9 in RA-FLS were significantly decreased compared with Lv-sh-GFP transfection group (all  $p < 0.05$ , figure 1D). Down-regulated PGC-1 $\beta$  in RA-FLS significantly suppressed the expression of NF- $\kappa$ B p65, NF- $\kappa$ B p-p65, RelB and NIK in protein level, while over-expression of PGC-1 $\beta$  promoted the expression of NF- $\kappa$ B p65, NF- $\kappa$ B p-p65, RelB and NIK (all  $p < 0.05$ , figure 1E).



**Abstract AB0098 – Figure 1.** Effects of PGC-1 $\beta$  on the migration and invasion capacity as well as proteases expression, canonical and non-canonical NF- $\kappa$ B signalling pathway activation in RA-FLS. **A–C** After down-regulation or over-expression of PGC-1 $\beta$ , wound healing and transwell assay showed the capacity of horizontal migration (A), vertical migration (B) and invasion (C) of primary RA-FLS. **D** After down-regulation or overexpression of PGC-1 $\beta$ , the expression of MMP-3 and MMP-9 was measured by qRT-PCR and western blot. **E** After down-regulation or overexpression of PGC-1 $\beta$ , the expression of NF- $\kappa$ B p65, NF- $\kappa$ B p-p65, RelB and NIK was measured by western blot. The data were representative as means  $\pm$  SD from six different RA patients. \* $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P < 0.001$ .

**Conclusions:** Our findings suggested that PGC-1 $\beta$  facilitates the migration and invasion capacity and MMP-3/9 expression in RA-FLS through activation canonical and non-canonical NF- $\kappa$ B signalling pathway.

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#### AB0099 ARTHROSCOPIC PECULIARITIES OF THE INFLAMMATORY PROCESS OF SYNOVIAL SHELL IN UROGENIC ARTHRITIS

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**Background:** In recent years there has been an increase in the incidence of reactive arthritis (ReA), associated with urogenital infection. Chronic synovitis of urogenital etiology is a nonspecific process, pathogenesis is very close to rheumatoid arthritis (RA), which complicates differential diagnosis. According to the literature, the inflammatory process in the synovial membrane (SM) supports the persistence of chlamydia, which reduces the effectiveness of standard anti-

inflammatory therapy of arthritis in patients with undifferentiated seronegative oligoarthritis, spondyloarthritis, RA.

**Objectives:** Arthroscopic assessment of the level of the inflammatory process in the synovial membrane, depending on the duration of the disease and the activity of the pathological process in patients with urogenital arthritis.

**Methods:** The study involved 39 patients with RA of urogenital etiology complicated by synovitis of knee joint (KJ) were examined; 23 of them were women and 16 men; mean age was  $35.5 \pm 38.0$  years. They received inpatient treatment at the Department of Traumatology and Orthopaedics of the 2nd TMA Clinic in 2014–2016 years. All these patients underwent diagnostic arthroscopy of KJ. Laboratory tests included enzyme-linked immunosorbent assay (ELISA) for TORCH infection, a polymerase reaction (PCR), determination of a rheumatic factor in synovial fluid and blood before and after treatment, arthroscopy of the joint.

**Results:** In arthroscopic examination in the acute phase (early period) of ReA, dull SM, vasodilation, and oedema are revealed, which is accompanied by an increase in the production of turbid synovial fluid (SF). On the surface of SM there are sections of fibrin filaments, expansion and hyperemia along the vessels. In the long-term (subacute phase) these violations partially disappear. The surface of the synovium can again become single-rowed, with moderate hyperemia of the vessels. The deposits of fibrin on the entire surface of SM can be significant. However, with reduced immunoreactivity of the organism, the reactive synovitis persists for a long time, and the chronic course of the pathological process leads to abundant deposits of fibrin masses and to the formation of villi in the form of large and flat petals. In some parts of the vascular vessels are pale, accompanied by disorganisation of the collagen frame of SM, which directly affects the cells of the articular cartilage.

**Conclusions:** Thus, reactive urogenital arthritis due to the persistence of an infectious agent is characterised by the polymorphism of the damage to the joint and cartilage of the joint. The arthroscopic changes revealed at various stages of the inflammatory process reflect the reactivity of the pathological process and determine the extent of the lesion. Arthroscopic examination of biopsy specimens of SM and cartilage allows to determine the dynamics of the disease, the degree of lesion, evaluate the effectiveness of the preventive and therapeutic measures being carried out, and also to determine the indications for joint synovcapsulectomy.

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#### AB0100 NEUROGENIC INFLAMMATION CHARACTERISED BY NERVE GROWTH FACTOR, TRKA AND SUBSTANCE P IS PREVALENT IN HUMAN FACET JOINT OSTEOARTHRITIS

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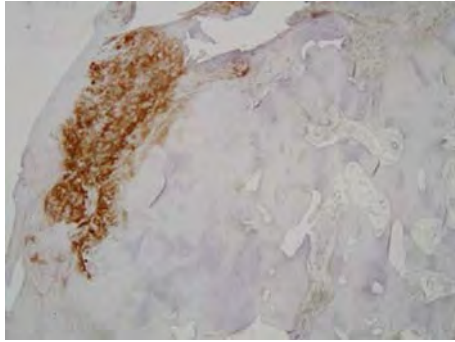
**Background:** Facet joint osteoarthritis (FOA) is a frequent cause of chronic low back pain and spinal stenosis. Neuron-derived molecules regulate pain sensation and inflammation. Nerve growth factor (NGF) is one of the most important mediators for this mechanism that is termed neurogenic inflammation.<sup>1</sup> Among many other effects, it regulates substance P (SP) expression as pivotal downstream peripheral pro-inflammatory molecule. Consequently, NGF inhibitors (NGFi) as a novel class of pain medication have shown significant efficacy in OA and to some extent also low back pain. However, it is unknown which tissue compartments in facet joints are involved in NGF signalling.

**Objectives:** To determine expression patterns of NGF, its high affinity transmembrane tyrosine kinase A (TrkA) receptor and SP in cartilage, subchondral bone marrow and capsular tissues of facet joints (FJ).

**Methods:** Dissected human FOA specimens of six donors were examined. OA severity was graded on HE-stained tissue sections. NGF, TrkA and SP expression was evaluated by immunohistochemistry with monoclonal antibodies. Similarly, new bone formation was assessed by staining for osteocalcin.

**Results:** FJ had low (n=2), high (n=2) and intermediate (n=2) inflammatory bone marrow infiltrates. NGF was strongly expressed in capsular tissue (figure, 40x),

focally in degenerated cartilage and differentially in FJ with active bone marrow infiltrates. TrkA was primarily found in all bone marrows and capsular tissues but not in cartilage. TrkA expression colocalized with osteocalcin in subchondral bone, indicating an association with new bone formation. SP strongly positive cells were found in the bone marrow, cartilage and synovial tissue of all FJ.



Abstract AB0100 – Figure 1

**Conclusions:** Here we define for the first time tissue compartments of the NGF axis in human FOA. The findings indicate that neurogenic inflammation is prevalent in different compartments of FOA. Based on these data NGFi might be efficient by targeting inflamed joint capsule or subchondral bone marrow as a source of pain. NGFi may thus have an impact on bone remodelling. Further studies are needed to more precisely examine this mechanism.

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#### AB0101 MESENCHYMAL STEM CELLS DERIVED FROM BONE MARROW, UMBILICAL CORD AND ADIPOSE TISSUE DO NOT HAVE THE SAME EFFECT ON HUMAN OSTEOARTHRITIC CARTILAGE

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**Background:** Osteoarthritis is a chronic debilitating disease characterised by degeneration of cartilage, synovitis and osteophytes formation.<sup>1</sup> This disease does not only affect aged people but it afflicts also young athletes where until today no medications has proven efficacy in stopping the progression of the disease and/or regenerate the loss of cartilage.<sup>2</sup> Recently cell therapy has attracted attention in many medical fields and especially in rheumatology and orthopaedic specialty. Stem cells due to their differentiation capacity, trophic and paracrine effects have been shown to serve as promising new modality in treating osteoarthritis.<sup>3,4</sup>

**Objectives:** Our objective in this study is to investigate the effect and mechanism of action of the three sources of stem cells; bone marrow derived stem cells (B-MSC), adipose derived stem cells (A-MSC) and umbilical cord stem cells (U-MSC) on osteoarthritic chondrocytes.

**Methods:** Mesenchymal stem cells were isolated from bone marrow, adipose tissue and umbilical cord from 5 different donors respectively and cocultured with human osteoarthritic chondrocytes obtained from 5 patients undergoing total knee arthroplasty. The effect autophagy was determined using flow cytometry analysis. Quantitative polymerase chain reaction (qPCR) and ELISA were used to measure the changes in the major factors playing a role in OA such as (a disintegrin and metalloproteinase with thrombospondin motifs-5(ADAMTS-5), Metalloproteinases (MMP-3, MMP13), tissue inhibitor of metalloproteinases (TIMP-1–2–3), Collagen, Cox-2, Il-6, the regulators of autophagy FOXO1, FOXO3, and LC3II and Beclin I in the tissues and cocultured media.

**Results:** In our study we found that the three stem cells sources increased significantly the proliferation of chondrocytes, and increased autophagy via increasing

Beclin 1 and LC3II, along with its regulators FOXO1, FOXO3 in human osteoarthritic chondrocytes with  $p < 0.05$ . Furthermore, the three sources of stem cells caused a dose dependent significant decrease in MMP-3, MMP-13, ADAMTS-5, IL-6, CCL20 and COX-2 with  $p < 0.05$ . Aggregan, collagen, TIMPs were also significantly increased by the co-culture of A-MSC, B-MSC, U-MSC.

**Conclusions:** These results suggest that stem cells could be a promising therapeutic target for the treatment of osteoarthritis.

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**Disclosure of Interest:** None declared

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AB0102

#### THE GINGER DERIVATIVE 6-SHOGAOL AS A TREATMENT IN OSTEOARTHRITIS. MODULATION OF CHONDROCYTE HYPERTROPHY AND MATRIX CALCIFICATION

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**Background:** Osteoarthritis (OA) is a complex joint disease characterised by a progressive loss of articular cartilage (AC), synovial inflammation and subchondral bone alterations. The latest theories of OA pathogenesis implicate the interplay between mechanical damage and chronic inflammation that has been associated to the activation of the innate immune system, intricately involved in the development of this low-grade inflammation. During the course of OA, Toll like receptor (TLR) activation has been related to the release of cytokines and inflammatory mediators, which further aggravate synovitis and AC damage.<sup>1</sup> In this scenario, hyaline chondrocytes seem to acquire a hypertrophic-like phenotype associated to AC degradation. 6-shogaol (6S), an effective anti-inflammatory Ginger derivative, is able to inhibit TLR4-mediated innate immune responses.<sup>2</sup>

**Objectives:** Our aim was to study the therapeutic benefit of 6-shogaol studying its anti-inflammatory effects in an OA mice model, and in the modulation of hypertrophic markers in chondrocyte cultures.

**Methods:** C57BL/6 male mice were randomly assigned to two groups: control (n=7) and OA (n=17). OA was induced by transection of the medial menisco-tibial ligament. Nine OA mice started receiving 6S (15 mg/kg/day; OA +6S) since surgery. After 8 weeks, animals were euthanized and joints were collected. Chondrogenic differentiation was induced *in vitro* in the pre-chondrogenic cell line ATDC5 in presence or absence of  $5 \times 10^{-6}$  M 6S. Gene expression of hypertrophic markers, as well as mineralization and proteoglycan synthesis were determined.

**Results:** Both synovial inflammation and AC damage were more severe in OA animals (Control:  $0.1 \pm 0.1$ ; OA:  $3.0 \pm 0$ ;  $p < 0.005$ , and Control:  $0.5 \pm 0.2$ , OA:  $5.4 \pm 0.6$ ;  $p < 0.005$ , respectively) with a significant reduction in OA+6S animals ( $2.4 \pm 0.2$ ;  $p < 0.05$  and  $2.6 \pm 0.5$   $p < 0.01$  vs. OA, respectively). Collagen X and MMP13 immunohistochemistry showed an increase in the AC of OA and OA-6S mice, while a significant reduction was found in 6S-treated mice (ColX: Control:  $0.13 \pm 0.03$ , OA:  $0.93 \pm 0.1$ ; OA-6S:  $0.43 \pm 0.1$ ;  $p < 0.05$  and MMP13: Control:  $0.35 \pm 0.1$ , OA:  $0.68 \pm 0.1$ , OA-6S:  $0.28 \pm 0.07$ ,  $p < 0.05$ ). Similar results were found in the synovium and meniscus for these two markers. 6S was able to significantly inhibit the expression of Collagen X, Ihh and MMP13 in ITS-stimulated cells after 14 and 21 days of culture. Furthermore, 6S prevented the increase in mineralization and proteoglycan synthesis in ITS-stimulated ATDC5 cells after 14 days of culture ( $p < 0.05$ ), as seen by Alizarin red and Alcian blue staining, respectively.

**Conclusions:** Our results showed that 6S significantly prevented cartilage degradation and synovial inflammation, in parallel to a reduction in the presence of hypertrophic markers in the cartilage of OA mice. *In vitro*, 6S inhibited the chondrogenic differentiation of ATDC5 cells. These results suggest that 6S could work as a good treatment in OA both inhibiting differentiation markers and reducing the severity of joint damage in an OA murine model.



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AB0103

### ESTABLISHMENT OF A HUMAN INDUCED PLURIPOTENT STEM CELL-LINE FROM PATIENTS WITH HAND OSTEOARTHRITIS

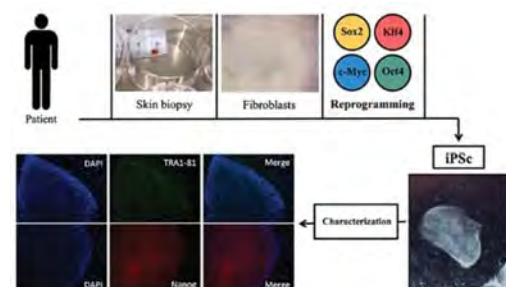
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**Background:** To date, there is no drug able cure such a prevalent disorder as it is hand osteoarthritis (OA). Cell therapies using stem cells have emerged as a promising strategy to explore and develop new treatments. Specifically, induced pluripotent stem cells (iPSc) are considered ideal tools not only for this purpose, but also for modelling the disease. The advantages of using an established iPSc line are unlimited cell source with regeneration capacity and chondrogenic differentiation potential. However, there are not many studies published generating iPSc from patients with hand OA.

**Objectives:** The aim of this study has been to generate an iPSc-line from human fibroblasts obtained from patients with radiographic hand OA, which can be useful for drug discovery, disease modelling and regenerative medicine applications.

**Methods:** Patients with radiographic hand OA and a healthy control were selected for the study. Using the explant culture technique, fibroblasts from 3 mm skin biopsies of these patients were isolated. These cells were histologically characterised and positivity for fibroblast markers was quantified. These cells were also karyotyped in order to confirm that chromosomal abnormalities did not exist before reprogramming. Four transcriptional factors were used for the reprogramming process: Oct4, Sox2, Klf4 and c-Myc. These were delivered using a non-integrative methodology that involves the use of Sendai virus. Cell lines obtained were clonally expanded over 20 passages and characterised for pluripotency markers by immunohistochemistry and RT-PCR, before and after reprogramming (figure 1). The best two clones of each one of the patients were selected according to the expression of the pluripotency markers to establish the cell-line.

**Results:** Cells were isolated from skin biopsies of two patients with radiographic hand OA and one healthy donor. Histological and immunohistochemical analyses showed that the 85%–95% of cells in the culture were fibroblasts, which presented a normal karyotype: 46, XX. Three weeks after reprogramming, embryonic stem cell-like colonies emerged in culture. These cells were positivity stained for alkaline phosphatase activity and the pluripotency markers Tra1–81 and Nanog. Alkaline phosphatase staining shows in blue the colonies correctly reprogrammed. Molecular analyses showed high relative expression levels of the endogenous pluripotency associated genes OCT4, SOX2, KLF4, NANOG and CRIPTO in the iPSc, but not in the no-reprogrammed fibroblasts. No presence of Sendai Virus-related genes was detected.



Abstract AB0103 – Figure 1

AB0104

### CARTILAGE-LIKE TISSUE GENERATION BY 3D-BIOPRINTING OF INDUCED PLURIPOTENT STEM CELLS IN A MODIFIED NANOCELLULOSE/ALGINATE BIOINK

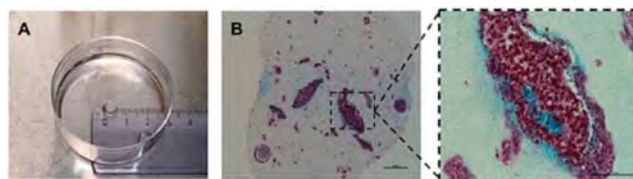
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**Background:** Today, several hundreds of million people all over the world are suffering from different joint disorders; like osteoarthritis (OA). Further, traumatic cartilage lesions can develop into OA. Recent studies indicate that human-derived induced pluripotent stem cells (iPSCs) can be 3D bioprinted and directed to form cartilage-like tissue, thus offering new approaches to treat cartilage lesions.<sup>N-guyen et al. 2017</sup> The advantages of using an established iPSc line are unlimited cell source with regeneration capacity and chondrogenic differentiation potential.

**Objectives:** The aim of this study was to improve the generation of cartilage-like tissue when 3D bioprinting of iPSCs by using molecularly modified nanocellulose/alginate bioink to resemble natural environment found in the tissue.

**Methods:** In this study the chondrocyte-derived iPSc line "A2B" was used (Borestrom et al. 2014). These cells were bioprinted in combination with a modified nanocellulose and alginate bioink. Constructs obtained after the 3D bioprinting were cultured in chondrogenic medium in order to stimulate chondrogenic differentiation. Cell number and viability inside the prints was studied and histological analyses of the 3D printed constructs were performed. Furthermore, expression of pluripotency and chondrogenic specific genes was assessed by Taqman qPCR before and after differentiation.

**Results:** After 3D bioprinting high cell viability was found inside the constructs. 3D printed constructs were positively stained for alcian blue van gieson (AB-vG) staining, showing proteoglycans presence inside the prints (figure 1B). Molecular analyses showed high relative expression levels of the pluripotency-related gene Oct4 before starting the differentiation protocol. Cells inside the constructs express chondrogenic specific genes, such as collagen type 2 and Sox9 after 6 weeks of differentiation. Moreover, 3D printed constructs showed cartilage-resembles (figure 1A).



Abstract AB0104 – Figure 1

**Conclusions:** The 3D printing of the iPSc and the *in vitro* generation of cartilage-like tissue was successfully achieved using the modified nanocellulose/alginate bioink. This approach could be use in the future to model OA disease and to perform screenings of different therapeutic compounds.

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**Disclosure of Interest:** None declared

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**AB0105** EFFECTS OF CARRAGEENAN INDUCED SYNOVITIS ON JOINT DAMAGE AND PAIN IN A RAT MODEL OF KNEE OSTEOARTHRITIS

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**Background:** Knee osteoarthritis (OA) is associated with ongoing pain and joint damage that can be punctuated by acute flares of pain and inflammation. Acute synovitis in normal knees might resolve without long-term detriment to joint function.

**Objectives:** We hypothesised that osteoarthritis is associated with impaired resilience to acute inflammation.

**Methods:** We induced synovitis by intra-articular injection of carrageenan into rat knees with or without meniscal transection-induced OA, and measured synovitis, weightbearing asymmetry (an index of pain behaviour), and joint damage up to 35 days after OA induction (23 days after carrageenan-injection).

**Results:** Intra-articular injection of carrageenan was followed by weightbearing asymmetry for 1 week, synovitis, indicated by a transient increase in knee diameter for 2 days after injection, and a more sustained (through day 23) increase in synovial macrophages, endothelial cell proliferation and vascular density compared with naïve controls. Meniscal transection was followed by weightbearing asymmetry and histological evidence of OA through day 35. Carrageenan-injection in OA knees was followed for 2 days by increased weightbearing asymmetry compared either to OA knees, or to carrageenan-injected, SHAM-operated knees. OA structural damage and synovitis at day 35 were greater after carrageenan injection on day 12 compared to saline-injected, MNX-operated knees, and compared to carrageenan-injected, SHAM-operated knees. Carrageenan injection alone did not induce OA in SHAM-operated knees.

**Conclusions:** OA knees were more sensitive to pain behaviour, inflammation and structural damage following an episode of acute inflammatory pain flare than were non-arthritic knees. Preventing inflammatory flares may be particularly important in preventing symptoms and long term joint damage in OA.

**Disclosure of Interest:** None declared

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**AB0106** FIBRIN-TRIGGERED CHONDROSYNOVIAL ADHESION AS A NOVEL MECHANISM OF CARTILAGE DAMAGE IN RHEUMATOID ARTHRITIS

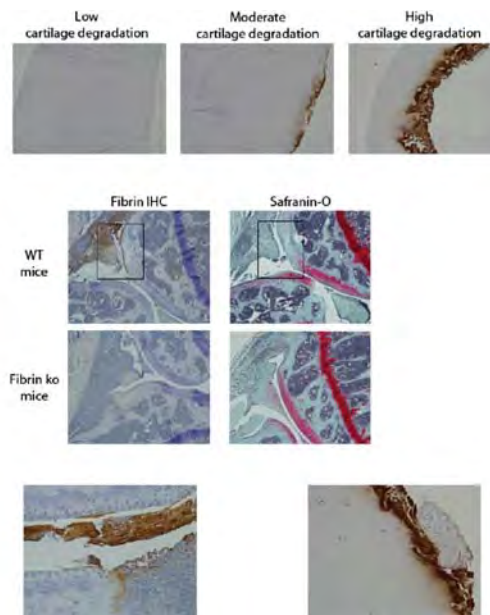
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**Background:** Synovial pannus infiltration and inflammatory cytokines production are the main factors responsible for cartilage damage in rheumatoid arthritis (RA). The crosstalk between inflammation and coagulation further amplifies and maintains chronic inflammation. Although synovial extravascular fibrin deposits in synovial fluid and synovial membranes being hallmarks of RA, there are no reports on direct fibrin deposition is widespread in RA, little is known about fibrin deposition and its relation to cartilage damage in RA.

**Objectives:** To investigate if fibrin deposition occurs in murine and human RA cartilage, and its relationship with cartilage degradation. Moreover, to determine the possible mechanism by which fibrin could play a role in the pathogenesis of RA.

**Methods:** Full-thickness cartilage explants were obtained from RA patients undergoing total knee replacement. Immunohistochemistry was performed on paraffin sections to study fibrin deposition, while Safranin-O staining was used to investigate cartilage damage. An *in vitro* model of chondrosynovial adhesion was established using primary human RA synoviocytes seeded on human RA cartilage explants. Adherent synoviocytes to cartilage were evaluated on H and E-stained histological sections and fibrin immunohistochemistry was performed on adjacent sections. Antigen induced arthritis (AIA) was induced in wild-type (WT) and fibrinogen knock-out mice and paraffin sections of knee joints assessed for fibrin deposition, cartilage damage, and chondrosynovial adhesion.

**Results:** In human RA cartilage, the extent of fibrin deposits positively correlated with the degree of cartilage degradation (figure 1). In WT mice, fibrin deposition was preferentially found on damaged cartilage and on cartilage areas in direct contact with synovial membrane (i.e chondrosynovial adhesions) (figure 2). In contrast, cartilage degradation and chondrosynovial adhesion were significantly lower in fibrin deficient mice (figure 2). Moreover, loss of superficial cartilage layers stained with fibrin was observed in regions of chondrosynovial adhesion (figure 3). Finally, in the *in vitro* model, synoviocytes were found to adhere to human OA cartilage, especially in severely damaged and fibrin-rich areas (figure 4).



**Abstract AB0106 – Figure 1**

**Conclusions:** Our results demonstrate that fibrin deposition on cartilage is highly associated with chondrosynovial adhesion and subsequent cartilage erosion in RA. We hypothesise that fibrin mediates chondrosynovial adhesion especially during joint resting periods (i.e night-time), leading to mechanical stripping of superficial cartilage layers following motion.

**Disclosure of Interest:** None declared

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**AB0107** INFLUENCE OF COBALT (II) + AND CHROMIUM (III)-IONS ON BONE FORMATION IN HUMAN OSTEOBLAST-LIKE CELLS IN-VITRO

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**Background:** Healthy bone is a result of the homeostasis between bone formation and resorption. The process of bone formation includes two major functions, which are the secretion of the organic matrix (mainly type I collagen) and the deposition of minerals into this matrix. This function of osteoblasts can be affected by numerous factors, as hormones, inflammation, mechanical load and other external stimuli.

In patients with artificial joint replacements, the release of particles or ions of cobalt and chromium ions from arthroplasties may exert local effects on the periprosthetic tissue leading to prosthesis loosening.

**Objectives:** It was the aim of the study to analyse the effect of Co<sup>2+</sup> and Cr<sup>3+</sup> ions on the capability of osteoblast-like cells to form bone.

**Methods:** Two human osteoblast-like cell lines MG63 and SaOs-2 were used to study the influence of Co<sup>2+</sup> and Cr<sup>3+</sup> ions on matrix secretion and mineralization. Cells (3 × 10<sup>5</sup>) were seeded in 2 ml DMEM (10% FCS) onto 12 well plates and stimulated with CoCl<sub>2</sub> and CrCl<sub>3</sub> in concentrations between 50–250 μM for 24 hours. Total RNA was extracted and changes of expression levels of collagen1A1 were analysed by real-time PCR. Secretion of collagen1 was analysed by Sirius Red staining (0.1% in water-saturated picric acid). After extraction of dye with 0.1N NaOH the absorption was measured at 540 nm.

For mineralization the cells were cultured for up to 4 weeks in DMEM (10% FCS) supplemented with 0.2 mM ascorbic acid, 10 nM dexamethasone and 10 mM glycerophosphate and different concentrations of Co<sup>2+</sup> and Cr<sup>3+</sup>. Calcium deposits were detected by 1% Alizarin Red S staining (pH 4.1), for quantification the dye was extracted using cetylpyridinium chloride, the absorption was determined at 562 nm.

**Results:** We observed that SaOs-2 cells, the more differentiated cells compared to MG63, exhibited a high potential for mineralization but secreted low amounts of collagen type 1. In contrast, MG63 cells produced high amounts of collagen1 and had a low potential for mineralization. When cultures were treated with Co<sup>2+</sup> and

Cr<sup>3+</sup>, we found that bivalent cobalt ions and trivalent chromium ions had different effects on osteoblasts. While Co<sup>2+</sup> reduced the secretion of collagen type 1 in osteoblast-like cells, Cr<sup>3+</sup> did not impair the collagen type 1 production. The secretion of this protein was partially attributable to a reduced gene transcription. In contrast, the mineralization was not impaired by Co<sup>2+</sup>. However, Cr<sup>3+</sup> at a concentration of 250 µM resulted in a decrease of mineralisation by 89% compared to controls. Even at the concentration of 50 µM a reduced mineralization by 34% was observed. The increase of the phosphate source resulted in an increased mineralization, suggesting that the capture of phosphate by Cr<sup>3+</sup> (formation of CrPO<sub>4</sub>), which is required for the mineralization could explain the inhibitory effect of chromium.

**Conclusions:** Our data suggest that Co<sup>2+</sup> and Cr<sup>3+</sup> ions affect bone formation at various stages of differentiation. While Co<sup>2+</sup> ions impair the formation of the bone organic matrix, Cr<sup>3+</sup> ions affect the deposition of inorganic minerals. Whether the inhibitory effect of chromium ions on the mineralization is caused by soluble Cr<sup>3+</sup> ions itself or by solid CrPO<sub>4</sub> needs to be clarified in further studies.

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**Disclosure of Interest:** None declared

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## Rheumatoid arthritis – etiology, pathogenesis and animal models

### AB0108 RELATIONSHIP BETWEEN PROGRANULIN AND MUSCULOSKELETAL ULTRASOUND IN RHEUMATOID ARTHRITIS

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**Background:** Progranulin (PGRN) is a pluripotent, secretory growth factor, mainly present in cells of the epithelium, central nervous system and immune system. PGRN known to directly regulate regulatory T cells and recently found to be upregulated in Rheumatoid Arthritis (RA) and related to its activity. No attempts was made to explore the relation between PGRN and RA activity measured by clinical and Ultrasound score (USS).

**Objectives:** To explore PGRN levels in the serum of patients with RA, and its correlation with disease activity assessed clinically combined by ultrasonography (USS).

**Methods:** RA patients: 52 RA patients were included in this study. They were consecutively recruited from the outpatient clinic of Rheumatology Department for regular follow-up at Fayoum University Hospitals. Patients were classified according to the 2010 ACR/EULAR criteria. Control group: 20 age and sex matched healthy volunteers were recruited as controls for level of serum PGRN. Informed consent was obtained from all patients and controls for inclusion in the study.

All patients were subjected to full history taking, and clinical examination. Assessment of disease activity by modified DAS-28 score. Progranulin is measured by an ELISA Kit (Elabscience), this kit uses sandwich-ELISA as the method.

The ultrasound examination was performed with GE LOGIQ 7 PRO equipment using a linear transducer with 18 MHz frequency. The patients were examined according to the German US7 score in 7 joint areas.

**Results: Demographic and clinical data of the RA group:** Females represents 90.4% (47 of 52). Age ranged from 21–72 years, mean age was 42.8±10.4 years. Disease duration ranged from 1 to 30 years, median 4 years. Their mean ESR level was 36.4±16 (Range: 5–70). The median of Ultrasound score assessment was 8 while the mean was 8.73±6.9 (Range: 0–33).

**Serum PGRN concentrations in RA patients and healthy controls:** The median of serum PRGN levels in RA patients was 65 ng/ml (mean, 92.54±45.4) which is much higher in comparison to those in normal controls, median 31 ng/ml (mean, 32.74±9.2); the difference showed high statistical significance, p<0.001.

**Correlation analysis:** The relationships between PRGN levels and other continuous variables were analysed using Spearman's rank correlation. There was high statistically significant correlation between PRGN level and USS score (r=0.37, p=0.006). Also, there was high statistically significant correlation between PRGN level and ESR (r=0.67, p<0.000) and between PRGN level and DAS 28 (r=0.74, p<0.000). There was high statistically significant correlation between USS score and ESR level (r=0.54, p<0.000) and between USS score and DAS 28 (r=0.68, p<0.000).

**Conclusions:** The serum Progranulin levels were higher in the serum of RA patients than age and sex matched controls. It is positively correlated with diseases activity measured by DAS 28, ESR and Ultrasound activity measured by

German US7 score. Serum PGRN levels may be a useful biomarker in RA disease. Ultrasound positively correlated with ESR and DAS 28 in our cohort of RA patients.

### REFERENCE:

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**Disclosure of Interest:** None declared

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### AB0109 CHARACTERISATION AND COMPARISON OF SERUM BIOMARKERS IN PATIENTS WITH RHEUMATOID ARTHRITIS VERSUS OSTEOARTHRITIS USING MASS SPECTROMETRY

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**Background:** There is increasing interest in biomarkers in medicine, especially for their use as a diagnostic tool and in disease outcome prognosis. Rheumatoid arthritis (RA) is a chronic autoimmune disease with important debilitating outcome potential, therefore a biomarker panel may improve early diagnosis meaning better therapeutic management and lower social costs. Recently, mass spectrometry has emerged as one of the leading methods to identify new biomarkers for different pathologies as well as being able to determine their potential interactors in their cellular pathway.

**Objectives:** To characterise biomarkers using mass spectrometry, from sera of patients with RA and make a comparison between RA, osteoarthritis (OA) and healthy controls.

**Methods:** Blood was collected from 26 subjects, 12 patients with RA, 12 patients with OA, and 2 HC, centrifuged and sera was collected in dedicated tubes. Sera were separated by SDS-Page electrophoresis and stained with Coomassie staining. The samples were subjected to in gel digestion followed by LC/MS analysis. The obtained spectra were searched with Proteome Discoverer v1.4 using SEQUEST algorithm.

**Results:** A total of 985 proteins were identified, from which 323 were specific to the RA study group and 159 were characteristic to the OA group. Prevalent peptides found in the RA group were EGF-containing fibulin-like extracellular matrix protein 2, isoform DeltaL1 of lactotransferrin, BPI fold-containing family B member 1 and isoform 2 of BPI fold-containing family A member 1. In the OA study group there was a prevalence in homeobox protein TGIF1, major facilitator superfamily domain-containing protein 9, methyltransferase-like protein 23, a fragment of the salivary acidic proline-rich phosphoprotein, serine/threonine-protein phosphatase 4 regulatory subunit 1, zinc finger protein 229.

**Conclusions:** Our results show a prevalence of peptides linked to cell migration, proliferation and activation in the RA sera as compared to peptides related to cell turnover and tissue senescence observed in OA sera. We believe further mass spectrometry studies of biomarkers in larger cohorts to be a promising tool for diagnosis and outcome prognosis in RA.

**Disclosure of Interest:** None declared

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### AB0110 SERUM AND SALIVARY IGA1 AND IGA2 ACPA SUBCLASSES IN ESTABLISHED RHEUMATOID ARTHRITIS AND ASSOCIATIONS TO SMOKING

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**Background:** A prevailing hypothesis regarding the pathogenesis of rheumatoid arthritis (RA) involves an association between mucosal immunity and the development of RA. A pathogenetic role for antibodies against citrullinated peptides (ACPA) is assumed, and there are indications of mucosal immunisation in the lungs, the oral mucosa and the intestinal mucosa preceding overt RA.<sup>1</sup>

IgA antibodies are produced both locally, at mucosal membranes, and systemically. Among the two IgA subtypes, IgA1 dominates in serum IgA2 in mucosal secretions.

We have previously reported the presence of ACPA of IgA isotype in both serum and saliva of RA patients,<sup>2</sup> and that IgA ACPA is associated with cigarette smoking.<sup>3</sup>

**Objectives:** To investigate the presence and levels of mucosal and circulating IgA1 and IgA2 isotypes of ACPA in patients with RA, and to investigate their association to cigarette smoking habits.

**Methods:** Patients with established RA, mean disease duration of 12.2 years (n=196), and healthy controls (n=101), included in the Secretary Antibodies in Rheumatoid Arthritis (SARA) study were analysed by enzyme immunoassays regarding total IgA ACPA and the subclasses IgA1 and IgA2 ACPA in serum and saliva. The results are presented as delta-values of optical density (OD) between each IgA ACPA subclass and the corresponding arginine peptide.

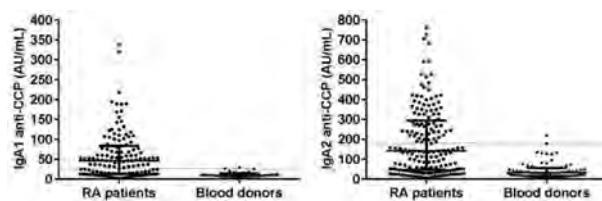
**Results:** Serum IgA1 ACPA was detected in 44% of the RA patients and serum IgA2 in 39%. 10% of the RA patients had detectable salivary IgA1 and/or IgA2 ACPA. Both serum and salivary IgA2 levels were higher among smokers than never-smokers, while this association was not seen for IgA1 class antibodies.

**Abstract AB0110 – Table 1.** Levels of serum and salivary IgA anti-CCP subclasses among RA patients, comparing ever smokers and never smokers.

Antibody level	Smokers (n=85)	Never smokers (n=93)	T-test (p value)
Serum IgA aCCP, AU/mL (SD)	100 (211)	39 (59)	0.013
Serum IgA1 aCCP, AU/mL (SD)	101 (328)	33 (43)	0.061
Serum IgA2 aCCP, AU/mL (SD)	333 (745)	140 (156)	0.022
Salivary IgA aCCP* (SD)	0.31 (0.62)	0.21 (0.65)	0.271
Salivary IgA1 aCCP* (SD)	0.29 (0.55)	0.21 (0.46)	0.283
Salivary IgA2 aCCP* (SD)	0.24 (0.38)	0.14 (0.17)	0.026

aCCP=Antibodies to Cyclic Citrullinated Peptides, SD=Standard Deviation

\*Delta value between Optical Density (OD) value for CCP (Cyclic Citrullinated Peptide) and OD for CAP (Cyclic Arginine Peptide), the corresponding arginine peptide.



**Abstract AB0110 – Figure 1.** Levels of IgA anti-CCP subclasses in RA patients and controls.

**Conclusions:** In this study of patients with established RA, IgA2 ACPA but not IgA1 ACPA was associated to cigarette smoking. As IgA2 predominate over IgA1 in mucosal secretions, this finding strengthens the hypothesis that smoking via mucosal ACPA production is one pathway to develop RA.

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**Disclosure of Interest:** None declared

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#### AB0111 MEMBRANE TNF EXPRESSION ON MONOCYTES AND DIFFERENTIATION OF MONOCYTES INTO M2-M1 MACROPHAGES: 2 NEW BIOMARKERS OF RHEUMATOID ARTHRITIS

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**Background:** Three monocyte subsets have been described based on their CD14 and CD16 expression profiles, the subpopulation CD14<sup>+</sup>CD16<sup>+</sup> being expanded in rheumatoid arthritis (RA) patients. Macrophages contribute *in situ* to the RA pathogenesis. They can display various states of activation or «

polarisation ». Two distinct states of polarisation for macrophages have been recognised: the “classically activated macrophage phenotype” (M1) and the “alternatively activated macrophage phenotype” (M2). To sum-up, M1 are considered to be pro-inflammatory and M2 to be regulatory and anti-inflammatory.

**Objectives:** Here, we have assessed monocytes subsets and their capacity of differentiation into M2 or M1 macrophages in RA patients and controls.

**Methods:** PBMCs were isolated and we first determined monocytes subpopulations and looked at expression of membrane TNF (mTNF). After negative selection of monocytes, Macrophages were Derived from Monocytes(MDM) by 7 days of culture in the presence of M-CSF (M2 differentiation) or GM-CSF (M1 differentiation). Expression of total macrophages markers (CD11b and CD71) and the M2 macrophage polarisation markers (CD163 and CD206) were evaluated.

**Results:** We have confirmed that the CD14<sup>+</sup>CD16<sup>+</sup> monocytes subset was expanded in RA patients. For the first time, we have demonstrated that mTNF expression was significantly increased only in monocytes in RA patients (CD14<sup>+</sup>: Mean 5.6% HD versus 10.6% RA, CD14<sup>+</sup>CD16<sup>+</sup>: Mean 3.3% HD versus 11.1% RA, CD16<sup>+</sup>: Mean 2.4% HD versus 6.3% RA). Moreover, mTNF expression on monocytes correlated with the activity of the disease assessed by DAS28 CRP (Spearman r 0.548 and p=0.0021\*). We have observed a significant decrease of macrophages induction by M-CSF in RA patients as shown by a decreased expression of CD11b-CD71 (Mean 87.2% HD versus 57.1% RA, P value \*\*\*\*). Among MDM, we have found a specific decreased level of M2 markers (CD206 Mean 78.1% HD versus 27% RA and CD163 56.2% HD versus 37.2% RA) suggesting an impaired maturation to M2 stage in RA patients.

**Conclusions:** Monocytes from RA patients have an increased expression of mTNF linked to activity of the diseases. RA patients have an impaired maturation of monocytes to M2 macrophages. This might suggest that RA monocytes have a propensity for preferential maturation towards a pro-inflammatory M1 phenotype thus contributing to synovial inflammation. Deeper characterisation of M1/M2 and effect of the different types of anti-TNF on this differentiation process are on-going and will be presented.

**Disclosure of Interest:** None declared

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#### AB0112 PATHOGENETIC MECHANISMS IN EARLY RHEUMATOID ARTHRITIS: POSSIBLE CORRELATION BETWEEN TH17 AND TREG CELLS AND GUT MICROBIOTA STRUCTURE: A PILOT STUDY

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**Background:** In Rheumatoid Arthritis (RA) pathogenesis T helper17 (Th17) and T regulatory cells (Treg) are largely represented.<sup>1</sup> Recent studies highlighted the role of intestinal mucosa environment in modulation of T cells function. The composition of gut microbiota influences the Th17/Treg cells balance and the host immune response,<sup>2</sup> so the exposure to deranged intestinal microbiota may be crucial in RA.

**Objectives:** The aim of the study was to compare Th17 and Treg cells and gut microbiota composition in patients with early RA (ERA) and in a control group (CG) at baseline and after treatment.

**Methods:** Currently, 10 ERA patients and 10 subjects belonging to the CG have been enrolled. All ERA patients were evaluated before (T0) and after 3 months (T1) of treatment with methotrexate (MTX) and glucocorticosteroids (GCS). Blood and faecal samples were collected. After PBMC isolation, staining with conjugated mAbs targeting specific surface and intracellular antigens (CD4 and CD25, IL-17 and FoxP3 respectively) have been used in order to distinguish Th17 and Treg cells. The composition of the faecal microbiota has been analysed by Next Generation Sequences on Illumina MiSeq platform, through 16S rDNA V3-V4 targeted sequencing.

**Results:** At T0, the percentage of Th17 cells was higher in patients than in the CG (p<0.0001) while Treg cells were higher in the CG (p=0.013). At T1, the total number of CD4<sup>+</sup> and Th17 cells was decreased (p=0.007, p=0.027) while the frequency of Treg cells increased (p=0.028). A normalisation of Treg cells, with frequencies comparable to CG, was present after treatment. Regarding gut microbiota, at phylum level no difference between patients at T0 and the CG were present but we observed a tendency to decrease in the frequency of Actinobacteria after therapy. Furthermore, the relative abundance of Actinobacteria correlated positively with the circulating levels of Th17 (p=0,012, r=0,59) and with the Th17/Treg at T0 (p=0,010, r=0,6), while Nitrospirae correlated positively with Treg (p=0,028, r=0,68) at T1. A significant increase of the relative abundance in the Lachnospiraceae family in patients at T1 compared with T0 (p=0,042) and CG (p=0,043) were noticed.

**Conclusions:** Our results highlight the presence of an imbalance between Th17 and Treg cells in patients with ERA. In agreement with literature,<sup>3</sup> MTX and GCS



influence on Th17 decreasing and Treg cells increasing in patients with ERA, so we can hypothesise that part of the clinical response is own to the improvement in T cells balance. Previous data<sup>4</sup> reported that Actinobacteria are strongly correlated with the production of IL-17 and a reduction of Nitrospirae has been associated to increased inflammatory responses and to gut permeability in mice.<sup>5</sup> Lachnospiraceae family play an important role in the maintenance of intestinal homeostasis.<sup>6</sup> The correlation between gut microbiota composition and Th17/Treg axis observed in our patients may suggest the involvement of some bacteria family in Th17/Treg cells balance in the lamina propria of RA patients treated with MTX, even in the early phases of the disease.

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#### AB0113 EFFICACY OF TREATMENT WITH PROBIOTICS IN THE INFLAMMATORY ACTIVITY OF PATIENTS WITH RHEUMATOID ARTHRITIS. SYSTEMATIC REVIEW OF THE LITERATURE

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**Objectives:** To study the effectiveness of the use of probiotics in the control of inflammatory activity of patients with rheumatoid arthritis and analyse its effect on their metabolic profile.

**Methods:** A bibliographic search was carried out in Medline and Embase. The search strategy included the terms MeSH and the free text of "lactobacillus", "bacillus", "probiotics" and "rheumatoid arthritis." The search strategies were carried out by two authors, which were included according to the type of studies: meta-analysis, systematic reviews and clinical trials, depending on the type of participant: adults with RA who have received probiotics, the main outcome measures: changes in the Disease Activity Score (DAS28), Simplified Disease Activity Index (SDAI) and Clinical Disease Activity Index (CDAI), as well as each of the parameters that constitute them: C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), visual analogue scale of the doctor and the patient (EVA), number of painful joints (NAD) and inflamed (NAI) and functional status by Health Assessment Questionnaire (HAQ) Secondary variables: number of adverse events and parameters of metabolic activity. The quality of the evidence was analysed following the guidelines of the Scottish Network of Intercollegiate Guidelines (SIGN).

**Results:** After the selection of 34 articles, 9 articles were finally included. All were randomised, double-blind, placebo-controlled clinical trials (RCTs) with a level of evidence between 1+ and 1++ and a recommendation grade of A and B. Seven CDs showed improvement in arthritis measurements. In Peltonen et al. observed a high rate of improvement in the experimental group than in the control group (3.1 vs 2, p=0.027). Mandel et al. they described improvement of the EVA in the experimental group (p=0.046). Zamani et al. they described an improvement in DAS28 (-0.3±0.4 versus -0.1±0.4, p=0.01). Vaghef-Mehrabany et al defined this improvement (p<0.01). Pineda et al. showed an improvement in HAQ at 3 months in the experimental group (from 0.97 to 0.80, p=0.02), although not in ACR20 (p=0.33). Allipour et al. found improvements in CRP between the two groups (mean [95% CI]=2.03 [0.54–3.51], p=0.009); NAD: (mean [95% CI]=0.72 [0.25, 1.19], p=0.003); NAI: (mean [95% CI]=0.351 [0.13, 0.58], p=0.003); EVA: (mean [95% CI]=16.71 [8.91, 24.50] p<0.001; DAS-28: (average [CI] 95%)=0.31 [0.02, 0.61], p=0.039) and in cytokine levels, Hatakka et al observed no significant improvement in the experimental group in HAQ, NAD and NAI, and Nenonen et al. Did not observe differences in DAS28. In the last, EC of Vaghef-Mehrabany of 2017 metabolic measures were evaluated without finding significant improvements. If an improvement in insulin resistance was observed as measured by the HOMA B index in the study by Zamani et al.

**Conclusions:** Treatment with probiotics seems to be effective in controlling the inflammatory activity of rheumatoid arthritis.

**Disclosure of Interest:** None declared

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#### AB0114 MODULATION OF ENDOTHELIAL FUNCTION BY PROINFLAMMATORY CYTOKINES INVOLVED IN RHEUMATOID ARTHRITIS. FOCUS ON IL-17A, IL-20, IL-23 AND IL-9

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**Background:** Rheumatoid Arthritis (RA) is the most common inflammatory rheumatic disease, characterised by high circulating of pro-inflammatory cytokines. RA is associated with an increased cardiovascular risk secondary to the accelerated atherogenesis which is the consequence of endothelial dysfunction (ED)<sup>1</sup>. In addition to the well-known cytokines (TNF- $\alpha$ , IL-1 $\beta$  and IL-6), emerging data identified new cytokines such as IL-17A, IL-20, IL-23 and IL-9 as putative key-players of the pathogenesis of RA. To date, whether these cytokines might contribute to RA-associated endothelial dysfunction is not known.

**Objectives:** This study investigated the effect of IL-17A, IL-20, IL-23 and IL-9 on endothelium-dependent relaxation in response to acetylcholine (Ach) in rat aortic rings.

**Methods:** Experiments were conducted on thoracic aortic rings from male Lewis rats (11 week old), incubated for 1 hour or 24 hour at 37°C with 2 concentrations of each cytokine (IL-17A: 250 pg/ml and 10 ng/ml; IL-20: 500 pg/ml and 5 ng/ml; IL-23: 80 pg/ml and 10 ng/ml; and IL-9: 300 pg/ml and 10 ng/ml). Incubation with 10 ng/ml TNF- $\alpha$  was used as a positive control and with vehicle as negative control. At the end of the incubation period, endothelial function was studied by assessing concentration-response curves to Ach (10<sup>-1</sup>–1<sup>-4</sup>–4 mol/L) after phenylephrine (PE, 10–5 mol/L) or KCl (30 mmol/L)-induced contractions.

**Results:** As described in the literature<sup>2</sup>, a 24h- but not 1h-incubation with TNF- $\alpha$  reduced Ach-induced relaxation. The same result was obtained with IL-17A (10 ng/mL). By contrast, IL-20 did not change Ach-induced relaxation whatever the concentration and the incubation time. Impairment in vascular relaxation was observed after exposure to IL-9 (10 ng/mL), both after 1h- and more severely after 24h-incubation. As regards IL-23, an effect was observed only after 1 hour incubation and with high concentration.

**Conclusions:** Our data demonstrated that IL-17A, IL-23 and IL-9 but not IL-20 induced endothelial dysfunction, with different kinetics profiles. Among the cytokines evaluated, IL-9 exhibited the most important effect thus revealing a new putative role of this pleiotropic cytokine in RA-associated cardiovascular risk. Further studies are needed to confirm these data on animal models of diseases.

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#### AB0115 PROPHYLACTIC AND THERAPEUTIC ACTIVITY OF ALKALINE PHOSPHATASE IN ARTHRITIC RATS: SINGLE AGENT ACTIVITY AND IN COMBINATION WITH METHOTREXATE

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**Background:** Alkaline phosphatase (AP) is a gate-keeper of innate immune system responses by detoxifying (dephosphorylating) inflammation triggering moieties (ITMs) released from endogenous and external sources<sup>1</sup> and maintaining physiological barriers.

**Objectives:** We examined whether AP's broad mechanism of action may serve as a safe therapeutic, either as single agent or combined with methotrexate (MTX), in rheumatoid arthritis (RA).

**Methods:** A rat model for RA was used with repeated intra-articular methylated bovine serum albumin (mBSA) injections in one knee ("arthritic" knee), the contralateral knee serving as internal control. Recombinant human AP (200 µg, s.c.) was administered twice (spaced 4 days) before mBSA injections (*prophylactic setting*) or after arthritis induction (4x, 2x/wk, *therapeutic setting*), or combined with MTX (0.3 mg/kg or 1 mg/kg, i.p.) in 4 rats/group. Plasma pharmacokinetics of AP in arthritic and healthy rats was monitored by colorimetric enzymatic assay. As an endpoint of AP/MTX treatment outcome, macrophage infiltration (marking arthritic conditions) in knee sections, liver and spleen was assessed by immunohistochemistry (ED1 and ED2-macrophage specific antibodies), immunofluorescence (macrophage marker; Folate Receptor-β, FRβ), and positron emission tomography (PET) scans and *ex vivo* tissue distribution with the macrophage tracer [<sup>18</sup>F] fluoro-PEG-folate targeting FRβ.

**Results:** After AP administration, both in healthy and arthritic rats, plasma AP levels increased over 1 hour to reach a maximum of 50%–70% above baseline. Increased plasma AP levels in healthy rats were retained for at least 4 hours, whilst in arthritic rats AP plasma levels steadily returned to baseline levels within this time frame, suggesting consumption of available AP by conjugating to its ITM substrates. Prophylactic and therapeutic schedules of AP treatment, either as single agent or in combination with MTX, were well tolerated. Both prophylactic and therapeutic AP markedly reduced synovial macrophage infiltration in arthritic knees (ED1; 3.5–4 fold, ED2; 3.5–6 fold), comparable with MTX treatment effects. AP/MTX combinations slightly improved on single agent effects. PET monitoring and *ex-vivo* tissue distribution studies corroborated the impact of AP, MTX and AP/MTX on reducing synovial macrophage infiltration. Beyond localised articular effects, AP also displayed systemic anti-inflammatory effects by a 2-fold reduction of ED1, ED2 and FRβ-positive macrophages in liver and spleen of arthritic rats.

**Conclusions:** AP as single agent and combined with MTX elicits local and systemic anti-arthritic activity in arthritic rats and appears promising as a new therapeutic compound against arthritic conditions.

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AB0116

#### ADIPOSE DERIVED STEM CELLS SUPPRESSED SYNOVIAL INFLAMMATION IN SKG/JCL MICE IN VIVO AND INFLAMMATORY CYTOKINE IN SYNOVIAL FIBROBLAST IN VITRO

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**Background:** Adipose derived stem cell (ADSC) is one of the stem cells produced by adipose tissue which can be collected easily and in large quantities. It has been reported the anti-inflammatory effect of ADSC in some disease models.<sup>1</sup> However, the effect of ADSC for synovitis such as rheumatoid arthritis (RA) is unknown.

**Objectives:** The aim of this study is to investigate the effects of ADSC for joint synovitis and cartilage degeneration in SKG/Jcl mice *in vivo* and the effects of ADSC for synovial fibroblast *in vitro*.

**Methods:** SKG/Jcl mice which developed auto-immune arthritis by adjuvant stimulation were used as RA animal model.<sup>2</sup> *In vivo*, the intra-articular injections of ADSC (ADSC group; n=10) or PBS (PBS group, n=10) were performed to the bilateral knee of SKG mice with arthritis. The knee joint was histologically assessed with synovitis score and Mankin score at 2 weeks after ADSC injection. *In vitro*, the anti-inflammatory effect of ADSC for stimulated human synovial fibroblast was analysed by real-time RT-PCR.

**Results:** *In vivo*, the synovitis score and Mankin score were statistically lower in ADSC group (synovitis score 2.0±0.7 vs 6.0±1.6, p<0.01 and Mankin score 2.2±0.8 vs 4.9±0.8, p<0.01) (figure 1). *In vitro*, the expression of tumour necrosis factor-stimulated gene-6 (TSG-6), the anti-inflammatory cytokine, was significantly higher in ADSC than in synovial cell (p<0.01). The inflammatory cytokine levels in

stimulated synovial cell were significantly decreased by ADSC treatment (p<0.01) (table 1).

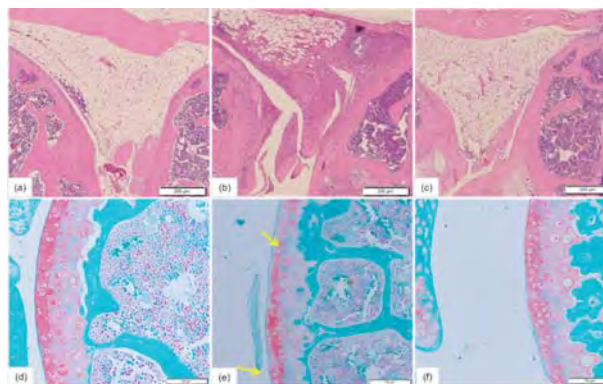
**Abstract AB0116 – Table 1.** Gene expressions in each cell by real-time RT-PCR

	Relative gene expressions referenced GAPDH as 1 (mean ±SD)		
	IL-6	TNF-α	TSG-6
ADSC	0.39±0.03	0.37±0.1	0.77 ±0.06*
Synovial fibroblast	0.21±0.07	0.35±0.1	0.08±0.03
Stimulated synovial fibroblast (non-treatment, 24 hour)	77.8±1.5	38.9±0.1	5.2±0.7
Stimulated synovial fibroblast (non-treatment, 48 hour)	34.9±0.5	39.9±0.1	4.2±0.3
Stimulated synovial fibroblast (ADSC treatment, 48 hour)	5.2 ±0.06**	9.8 ±0.1**	1.9±0.1

ADSC; adipose derived stem cell, IL; interleukin, TNF; tumour necrosis factor, TSG; tumour necrosis factor-stimulated gene.

\*p<0.01 (the comparison to synovial cell by Mann-Whitney U test)

\*\*p<0.01 (the comparison to non-treatment group by Mann-Whitney U test)



**Abstract AB0116 – Figure 1.** The anti-inflammatory effects of intra-articular ADSC injection. The H-E stain of knee joint in SKG/Jcl mice (a) and PBS treated SKG/Jcl mice after induction of synovitis (b). The synovial proliferation was suppressed in ADSC treated SKG/Jcl mice after induction of synovitis (c). The Safranin-O stain in SKG/Jcl mice without synovitis (d), PBS treated SKG/Jcl mice (e) and ADSC treated SKG/Jcl mice (f) after induction of synovitis. The cartilage staining was reduced in SKG/Jcl mice with inflammatory synovitis (yellow arrows).

**Conclusions:** This is the first report to show the anti-inflammatory effect of ADSC for synovitis in RA animal model. ADSC can be collected with a minimally invasive technique more easily than other mesenchymal stem cells. ADSC might have potential to be one of the RA treatment.

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AB0117

#### ASSOCIATION OF VITAMIN D DEFICIENCY WITH CRP/ACPA POSITIVITY IN ALGERIAN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Vitamin D (VD) is a steroid hormone belonging to the class of secosteroids with myriad immune functions and seems to be involved in the development and severity of rheumatoid arthritis (RA).<sup>1–3</sup>

**Objectives:** The aim of this study was to estimate the prevalence of vitamin D deficiency in patients with rheumatoid arthritis as compared to healthy controls and to analyse the association between levels of vitamin D and CRP (C-reactive protein)/ACPA (anti citrullinated protein antibodies) positivity.

**Methods:** Serum 25(OH)D levels were measured in 115 RA patients and 104 age- and gender-matched healthy controls using the chemiluminescent immunoassay method (CLIA).

CRP (mg/dl) was measured by the nephelometric method and ACPA antibodies were evaluated using enzymatic linked immuno-assay (ELISA).

**Results:** There was no statistically significant difference between levels of 25 (OH)D in RA (25.08±9.22 ng/ml) and healthy controls (15.62±5.34 ng/ml).

The vitamin D deficiency (<10 ng/ml) was found in 10% of RA patients, while 60% were insufficient (<20 ng/ml).

Low 25-OHD levels were negatively associated with CRP (23 ng/ml vs 29 ng/ml;  $p=0.023$ ) and ACPA positivity (23 ng/ml vs 28 ng/ml;  $p=0.03$ ).

**Conclusions:** The 25(OH) D levels are inversely related to CRP and ACPA values in Algerian RA patients.

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**Disclosure of Interest:** None declared

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AB0118

#### ORAL CONTRACEPTIVES AND THE RISK OF DEVELOPING RHEUMATOID ARTHRITIS: RESULTS FROM THE MALAYSIAN EPIDEMIOLOGICAL INVESTIGATION OF RHEUMATOID ARTHRITIS CASE-CONTROL STUDY

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**Background:** Hormonal and reproductive factors are implicated in the etiology of rheumatoid arthritis (RA). The association between oral contraceptive (OC) use and the risk of RA has been reported, but the findings are inconsistent across different populations.

**Objectives:** We investigated the association between OC use and risk of RA stratified by anti-citrullinated peptide antibody (ACPA) status in the Malaysian female population.

**Methods:** Data from the Malaysian Epidemiological Investigation of rheumatoid Arthritis (MyEIRA) population-based case control study involving 902 female early RA and 906 age and residential area-matched female controls were analysed. OC use data was assessed through a questionnaire. Never users of OC were compared with ever users of OC to estimate the risk of developing ACPA-positive and ACPA negative RA. The odds ratio (OR) with 95% confidence interval (CI) was calculated.

**Results:** In this study, a total of 28.4% (n=254) RA cases and 34.2% (n=310) controls had reported as ever OC users. Compared with never users, ever OC users had a decreased risk of developing RA in the Malaysian population particularly in ACPA-negative RA (OR 0.68, 95% CI 0.51–0.90,  $p<0.001$ ). No significant

association was observed between ever OC users and ACPA-positive RA (OR 0.80, 95% CI 0.64–1.01). Further stratification analysis by duration of OC use (less than or more than 7 years versus never OC use) demonstrated significant decreased risk of developing ACPA-positive RA (OR 0.66, 95% CI 0.51–0.86,  $p<0.01$ ) and ACPA-negative RA (OR 0.57, 95% CI 0.41–0.80,  $p<0.001$ ), respectively.

**Conclusions:** Oral contraceptives decreased the risk of RA, particularly ACPA-negative RA in the Malaysian population. A long duration of OC use was however decreased the risk in both ACPA-positive and ACPA-negative RA subsets.

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AB0119

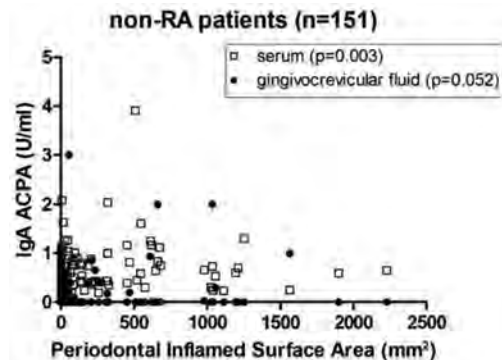
#### RHEUMATOID ARTHRITIS (RA)-ASSOCIATED AUTOANTIBODIES ARE PRESENT IN THE PERIODONTAL EXUDATE OF PATIENTS WITH AND WITHOUT RA

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**Background:** Seropositivity for anti-citrullinated protein antibodies (ACPA) and rheumatoid factor (RF) is a hallmark of RA and can be present years before clinical disease onset. Environmental factors, including smoking and chronic inflamed mucosal tissues of the lungs, gastro-intestinal tract or oral cavity (i.e., the periodontium) are suggested to contribute to initiation of these autoantibodies. While it is known that the inflamed periodontium contains citrullinated proteins and peptides, only Harvey et al. (2013) showed that IgG ACPA is indeed present in periodontal exudate (n=9).

**Objectives:** As the IgA isotype is specific for mucosal immunity, we assessed in patients with and without RA whether IgA RF and IgA ACPA are present gingivocrevicular fluid (GCF), i.e., the periodontal inflammatory exudate.

**Methods:** RA patients fulfilling the ACR<sup>EULAR</sup> 2010 classification criteria were recruited at the Rheumatology department of the Dr. Sardjito General Hospital, Yogyakarta, Indonesia. Patients without RA (non-RA) were recruited from the Oral and Maxillofacial Surgery department of the same hospital. In both groups, patients with diabetes or cardiovascular disease were excluded. Periodontitis was defined as periodontal inflamed surface area (PISA) >130 mm<sup>2</sup> (Leira et al. 2017). RF and ACPA were determined by ELISA in serum (IgM RF, IgA RF, IgG ACPA, IgA ACPA) and GCF (IgA RF, IgA ACPA). Total IgG and IgA were determined in GCF. IgA ACPA seropositivity and IgA RF- and IgA ACPA positivity in GCF were defined as >mean +2 SD of healthy controls (non-RA patients, never smokers, no periodontitis, n=88).



**Abstract AB0119 – Figure 1.** Non-RA patients (n=151)



**Results:** In non-RA patients (n=151), PISA was correlated with total IgG and IgA in GCF ( $p<0.0001$ ). IgA RF and IgA ACPA were present in GCF and correlated with total IgA in GCF ( $p<0.05$  and  $p<0.01$  respectively). In contrast to RA patients (n=72), IgA RF and IgA ACPA in GCF of non-RA patients did not correlate with IgA RF and IgA ACPA in serum. In non-RA patients, IgA ACPA positivity in GCF was more frequent in ever smokers (18%) than in never smokers (9.8%); the same held for presence or absence of periodontitis (18% and 9.3% IgA ACPA positivity, respectively). In non-RA patients PISA was correlated with IgA ACPA in serum ( $p<0.01$ ) and GCF ( $p=0.05$ ) (figure 1).

**Conclusions:** RA-associated autoantibodies are present in GCF of patients with and without RA. In contrast to RA patients, in whom this presence is probably due to leakage from serum, presence of RA-associated autoantibodies in GCF of patients without RA is presumably the result of local formation of these autoantibodies due to periodontitis.

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**Disclosure of Interest:** None declared

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#### AB0120 ADIPONECTIN COULD BE A MEDIATOR OF THE PRESENCE OF P GINGIVALIS IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is a systemic chronic inflammatory disease characterised by joint destruction, deformity, lower functional status and decrease in life expectancy. The *Porphyromonas gingivalis* (*P. gingivalis*) has been reported to be significantly associated with RA. The adipokines are suggested to be a common link between periodontitis and RA

**Objectives:** To determine the association between serum adipokines levels and presence of *P. gingivalis* in patients with early rheumatoid arthritis (eRA) compared to healthy individuals

**Methods:** A cross sectional study was conducted. Patients with the diagnosis of (eRA) according to the ACR/<sup>EULAR</sup> 2010 criteria were studied in Bogota-Colombia. A complete medical history related to RA was obtained. Adiponectin levels measured by Luminex technology (MILLIPLXMAP), IL6 by chemiluminescence (Immulate 1000, Siemens) and leptin quantification by ELISA (Dia-source, ), high-sensitivity CRP (hs-CRP) (Immulate 1000, Siemens) and ESR (Test 1 THL Ali FAX), and the detection of periodontopathic bacteria was carried out by qPCR from subgingival plaque samples. Cancer, autoimmune disease, infection, antibiotic use, diabetes, orthodontics treatment were exclusion criteria. An association analysis was made to evaluate the relationship between adipokines levels and periodontal, rheumatologic conditions using X2 test, Mann Whitney test and logistic regression model was performed to confirm this associations. All the results were performed with a level of significance of 95%

**Results:** A total of 51 patients with eRA and 51 healthy individuals were matched by age and gender. The mean age in RA patients was 48.54±10.93 years, 80.39% were female, between RA patients, 17.64% were in high activity and 27.45% in remission by DAS 28-ESR. 45.1% had APCA>20 UE. 37.25% were overweight and 13.72% were obese. 82.35% of patients had treatment, of which 80.39% received treatment with conventional disease modifying therapy, being methotrexate the most frequent one in 86.8%. In turn, 64.7% and 51% had high leptin and adiponectin levels respectively. An association of high adiponectin levels was found with Body Mass Index-BMI <25 ( $p=0.017$ ). The presence of *P. gingivalis* in RA patients was 78.4% and in healthy individuals was 45.09%  $p=0.001$ . The adiponectin levels>47755 pg/ml were found associated with the absence of *P. gingivalis* (OR=0.078 95% CI 0.01–0.62) adjusted an ever smoking history of cigarette smoking, Body Mass Index>30 and high level of leptin and IL6.

**Conclusions:** The adiponectin plays an anti-inflammatory role in the pathophysiology of several chronic inflammatory diseases and it has been reported to inhibit LPS-induced NFκB nuclear translocation and to affect other LPS-triggered pathways. To promote the weight control in eRA could be to prevent the oral infection

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**Disclosure of Interest:** None declared

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#### AB0121 RESVERATROL-ENHANCED AUTOPHAGIC FLUX REDUCES SEVERITY OF EXPERIMENTAL RHEUMATOID ARTHRITIS

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**Background:** Previously, we have demonstrated that dietary supplementation with resveratrol (RSV) lowers synovial hyperplasia, chemokines and oxidative damage in an acute antigen-induced arthritis (AIA) model developed in rats, and that autophagic cell death and limiting angiogenic response were involved<sup>1</sup>.

**Objectives:** Here, we investigated the autophagic flux induced by RSV and its relation with serum interleukin (IL)-1β levels, since autophagy could regulate IL-1β via inflammasome. Moreover, C-reactive protein (CRP) and prostaglandin E<sub>2</sub> (PGE<sub>2</sub>), which are also closely linked to inflammation and correlated with disease activity, were also evaluated.

**Methods:** Animals were randomly divided into 3 groups: healthy, AIA, and RSV-treated AIA group. RSV (12.5 mg/kg/day) was given orally 8 weeks before AIA induction until sacrifice day (48 hour after intra-articular injection). Healthy and AIA animals were administered 100 μl of water. RSV effects on autophagy were evaluated by the expression of the autophagy proteins, microtubule-associated protein 1 light chain 3 (LC3), and Beclin1 (an autophagic-related protein which up-regulation is associated with increased autophagosome formation), and p62 (an autophagic adaptor protein whose accumulation is associated with autophagic degradation dysfunction), by confocal and immunohistochemistry, respectively. Specific enzyme-linked immunosorbent assay kits and cytokine magnetic milliplex were used to measure CRP and PGE<sub>2</sub> and IL-1β in serum samples, respectively.

**Results:** At the end of the study, RSV significantly reduced the serum levels of IL-1β, CRP and PGE<sub>2</sub> ( $p\leq 0.01$  for IL-1β and PCR, and  $p\leq 0.05$  for PGE<sub>2</sub>). In relation to autophagy proteins, results showed that the expression of LC3 was greater in the AIA synovial membranes than in control synovial samples, in which the presence of vesicles was easily observed. Interestingly, the synovial tissues from the RSV group showed a significantly ( $p<0.001$ ) higher signal for LC3, compared with the AIA samples. As compared with healthy controls, AIA synovial membranes showed increased p62 expression, which was markedly inhibited by RSV treatment ( $p\leq 0.01$ ). The protein level of Beclin 1 was higher in AIA synovial membranes than in healthy samples; however, RSV did not increase the signal of Beclin 1. Moreover, there was a significant correlation between p62 expression and serum IL-1β levels ( $p\leq 0.05$  and  $r=0.617$ ), PGE<sub>2</sub> ( $p\leq 0.01$  and  $r=0.604$ ), and PCR ( $p\leq 0.001$  and  $r=0.692$ ).

**Conclusions:** These data suggest that resveratrol is capable of inducing the non-canonical (Beclin1 independent) autophagy pathway, and in consequence, modulates the cross-talk existence with inflammation in an acute AIA model, which could also ameliorate the severity of rheumatoid arthritis.

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**Disclosure of Interest:** None declared

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AB0122

### RP53 INDUCES ECTODOMAIN SHEDDING OF TNF RECEPTOR 1 AND THEREBY INHIBITS INFLAMMATORY RESPONSES IN RHEUMATOID FIBROBLAST-LIKE SYNOVIOCYTES

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**Background:** Rheumatoid arthritis (RA) is a chronic inflammatory disease by autoimmune disorder that primarily affects joints. Usually RA has been treated with disease modifying anti-rheumatic drugs but biological response modifiers has developed the treatment of RA. Among these anti-tumour necrosis factor (TNF) agents were the first to be successfully used in treating RA. Various anti-TNF- $\alpha$  therapy might be lead to substantial functional improvement in RA patients.

**Objectives:** We studied the isolated two polypeptides (Rp53, Rp54) from *Rubia philippinensis*, traditional medicine plant, about anti-inflammation effects in fibroblast-like synoviocytes (FLS) derived from patients with RA.

**Methods:** The effects of polypeptides on anti-inflammation were measured by cytokine assay kits (TNF- $\alpha$ , IL-6). The underlying for NF- $\kappa$ B signalling pathway was examined by western blot and NF- $\kappa$ B reporter activity. We examined the effect of Rp53 on the formation of the TNFR1 signalling complex, recruitment of TRADD, RIP in response to TNF by immunoprecipitation experiments. To determine whether Rp53 induced TNF receptor 1 shedding were exposed to these compounds for 1 hour, and then culture media and cell lysates were analysed by Western blotting using anti-TNF receptor 1 antibody.

**Results:** Pretreatment with Rp53 resulted in a remarkable decrease of the secretion of TNF-induced proinflammatory cytokines TNF- $\alpha$  and IL-6 in RA-FLS. Rp53 strongly inhibited the nuclear factor  $\kappa$ B (NF- $\kappa$ B) signalling pathway induced by TNF- $\alpha$ , but not that induced by IL-1 $\beta$ . Analysis of the upstream signalling events affected by Rp53 revealed that it strikingly inhibited the TNF-induced recruitment of TNFR1-associated death domain protein (TRADD) and receptor-interacting protein (RIP) to TNFR1. Rp53 reduced the interaction with TNFR1 to TNF cytokines and enhanced the activation of the p38 mitogen-activated protein (MAP) kinase. Rp53, the polypeptides induced the proteolytic cleavage of TNF-R1 and its release into the culture medium by shedding of TNF receptor 1 ectodomain by TNF- $\alpha$ -converting enzyme (TACE). Along with the TACE inhibitor TAPI-2, the p38 kinase inhibitor SB203580 suppressed the ectodomain shedding of TNF receptor 1 induced by Rp53.

**Conclusions:** Rp53 induces the TACE-dependent ectodomain shedding of TNF receptor 1 through the activation of p38 MAP kinase, and thereby inhibits the TNF- $\alpha$  induced NF- $\kappa$ B signalling pathway in RA-FLS cells.

**Disclosure of Interest:** None declared

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AB0123

### EXPLORING THE METABOLOMIC PROFILE OF SYNOVIAL FLUID TO REFLECT THE DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is a chronic, inflammatory disease that mainly affects the synovial joints. Metabolomics, which is defined as the comprehensive analysis of the small-molecule metabolites in a biological system, is a rapidly developing approach in biomarker research.

**Objectives:** This study was to determine whether there is variation in the synovial fluid (SF) metabolome in RA patients according to the degree of disease activity using gas chromatography/time-of-flight-mass spectrometry (GC/TOF-MS), in order to gain more insight into the pathologic metabolic alterations in RA.

**Methods:** SF samples were analysed in 47 patients with active RA, divided into moderately active- (2.8<DAS28 ESR<5.1, n=35, male 28.6%, mean age 55.1 years) and highly active group (DAS28-ESR $\geq$ 5.1, n=12, male 41.7%, mean age 59.1 years). SF metabolite profiles of RA based on DAS28-ESR value were performed using GC/TOF MS, with univariate analysis such as student t-test and correlation analysis followed by multivariate analysis such as partial least-squares regression-discriminant analysis (PLS-DA) and pathway analyses such as metabolite set enrichment analysis.

**Results:** There was no differences in demographic data and medications use between two groups. A total of 123 metabolites were identified from samples. These 123 identified metabolites were classified into various chemical classes, such as amino acids (21% of identified metabolites), organic acids (20%), sugar

and sugar alcohols (19%), fatty acids (15%), amines (11%), and phosphates (6%). The SF metabolite profiles obtained from GC/TOF-MS analysis can distinguish moderately active group from highly active group. The variation values of the PLS-DA model are  $R^2X$  of 0.171,  $R^2Y$  of 0.849, and  $Q^2$  of 0.504, respectively, indicating strong explanation and prediction capabilities of the model. To find potential metabolic biomarkers reflecting the disease activity of RA, variable importance on projection (VIP) values of all the metabolites from the PLS-DA model were determined. Also, other statistical criteria including correlation coefficient and  $P$  value were assessed. Twelve potential metabolites reflecting the disease activity of RA are found (2-hydroxyvalerate, fucose, tryptophan, indole-3-lactate, isothreonate, thymine, phenylalanine, lactose, arabinol, and mannose-6-phosphate, citrate, oxoproline). In pathway analysis, we found six unique pathways, namely, fructose and mannose degradation, phenylalanine and tyrosine metabolism, citric acid cycle, galactose metabolism, tryptophan metabolism and pyrimidine metabolism that were significantly associated with disease activity in RA.

**Conclusions:** Synovial metabolite profiles are robustly altered along the disease activity of RA. Metabolomic approaches based on GC/TOF-MS could provide valuable information on the underlying pathogenic mechanisms of RA activity, and a novel perspective on the search of new biomarkers and drug targets.

**Disclosure of Interest:** None declared

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AB0124

### DETECTION OF PRECURSORS OF RANK-OSTEOCLAST-LIKE CELLS (OLCS) IN PERIPHERAL BLOOD AND OLCS IN BONE TISSUE FROM RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Previously, we reported that novel osteoclast-like cells (OLCs) were induced, both *in vitro* and *in vivo*, from mouse bone marrow-derived macrophages (BMMs) by addition of a combination of TNF $\alpha$  and IL-6<sup>1</sup>. Recently, O'Brien *et al* showed that TNF/IL-6 can drive osteoclastogenesis in BMMs from *RANK*-deficient mice<sup>2</sup>.

**Objectives:** We aimed to examine the differentiation of OLCs, which were induced by a combination of TNF $\alpha$  and IL-6 from human peripheral blood mononuclear cells (PBMCs) and CD14 +monocytes and to identify differences in molecular expression patterns between OLCs and conventional osteoclasts. Furthermore, we identified OLCs and osteoclasts on the bone tissue of the joint in patients with rheumatoid arthritis (RA).

**Methods:** PBMCs and CD14 +monocytes from healthy volunteers and/or RA patients were stimulated with TNF $\alpha$  and IL-6 or RANKL. Quantitative RT-PCR was used to measure mRNA expression levels of *RANK*, *cathepsin K*, *calcitonin receptor*, and *dendritic cell-specific transmembrane protein*. Prepared undecalcified tibial bone from 6 RA or osteoarthritis (OA) patients undergoing joint surgery were stained by tartrate-resistant acid phosphatase (TRAP) staining and immunohistochemistry with anti-RANK antibody, expression of which were analysed. Osteoclasts and OLCs were identified as multinucleated TRAP+/RANK+ cells and TRAP+/RANK- cells, respectively, adherent to the bone surface.

**Results:** The number of OLCs treated with a combination of TNF $\alpha$  and IL-6 from PBMCs or CD14 +monocytes in RA patients was significantly increased compared to that in healthy volunteers. Expression levels of *RANK* mRNA was clearly up-regulated in osteoclasts, and was obviously down-regulated in OLCs compared to that in osteoclast precursors. In cancellous bone, the number of TRAP+/RANK+ osteoclasts was significantly increased in RA patients compared to that in OA patients. Interestingly, numerous TRAP+/RANK- OLCs were present in the cancellous bone of RA patients, while almost none were observed in the cancellous bone of OA patients.

**Conclusions:** The combination of TNF $\alpha$  and IL-6 strongly induced the differentiation of OLCs from PBMCs or CD14 +monocytes in RA patients. OLCs was characterised with TRAP+/RANK- multinucleated cells, which can distinguish conventional TRAP+/RANK+ multinucleated osteoclasts. TRAP+/RANK- OLCs also were present in the bone tissue of RA patients. These results suggest that conventional osteoclasts and novel OLCs could be involved in the pathogenic mechanisms of inflammatory bone destruction such as RA.

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**AB0125 ANTI-DENGUE IGG ANTIBODY POSITIVITY AND RISK OF DEVELOPING RHEUMATOID ARTHRITIS: EVIDENCE FROM THE MALAYSIAN EPIDEMIOLOGICAL INVESTIGATION OF RHEUMATOID ARTHRITIS (MYEIRA) CASE-CONTROL STUDY**

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**Background:** Arthralgia is one of the common symptoms seen in RA and in mosquito-borne viral diseases (dengue and chikungunya infections). Studies have reported that both dengue and chikungunya infections are associated with long-term persistent rheumatic symptoms including joints, muscle and bone pain.

**Objectives:** We investigated the association between anti-dengue IgG antibody positivity and risk of developing anti-citrullinated peptide antibody (ACPA)-positive and ACPA-negative RA in the multi-ethnic Malaysian population.

**Methods:** A total of 1147 early RA cases (515 Malay, 254 Chinese and 378 Indians) and 1519 age, sex and residential area matched population-based controls (1,023 Malay, 208 Chinese, and 288 Indians) were included in this study. Anti-dengue IgG antibody was determined by ELISA method. The presence of anti-dengue IgG antibody and risk of developing ACPA-positive/ACPA-negative RA were estimated by calculating the odds ratio (OR) with 95% confidence interval (95% CI).

**Results:** Our data demonstrated that 79.1% (n=1,003) and 77.1% (n=1,255) RA and control subjects were positive for anti-dengue IgG antibody, respectively. Data analysis revealed that the Chinese RA patients has highest frequency of anti-dengue IgG antibody (86.6%) followed by the Indian (80.4%) and Malay (74.4%) RA patients while 83.7%, 87.5% and 73% Chinese, Indian and Malay healthy controls were positive for this antibody, respectively. The anti-dengue IgG antibody positivity was significantly associated with decreased risk of RA in the Indian population (OR 0.59, 95% CI: 0.38–0.91, p=0.02) and particularly for the ACPA-positive subset of RA (OR 0.60, 95% CI 0.37–0.96, p=0.03). Interestingly, we observed a non-significant increased risk for ACPA-positive RA in the Chinese (OR 1.49, 95% CI 0.81–2.72) and Malay populations (OR 1.06, 95% CI: 0.79–1.41) with anti-dengue IgG antibody. No association was observed between ACPA-negative RA and the antibody positivity.

**Conclusions:** Our study describes the association between anti-dengue IgG antibody occurrence and ACPA-positive RA, but not ACPA-negative RA in an ethnicity-dependent manner. Future research is needed to explore the biological mechanisms behind these findings.

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**AB0126 LOW PREVALENCE OF ANTIBODIES AGAINST MALONDIALDEHYDE-ACETALDEHYDE ADDUCTS IN SPANISH PATIENTS WITH RHEUMATOID ARTHRITIS**

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**Background:** Patients with rheumatoid arthritis (RA) present increased oxidative stress that leads to lipid peroxidation and the formation of malondialdehyde (MDA) and acetaldehyde (AA). These two compounds under oxidative stress form malondialdehyde-acetaldehyde (MAA) adducts with proteins, which are highly immunogenic. Recently, Thiele *et al.*<sup>1</sup> described the presence of antibodies against human albumin MAA adducts in patients with established RA from the Veterans Affairs Rheumatoid Arthritis (VARA) registry. Of particular relevance was the reported presence of IgG anti-MAA antibodies in 92% of the patients, including 88% of the anti-CCP negative patients. These results suggest MAA adducts could contribute to the pathogenesis of RA and the anti-MAA antibodies could drastically reduce the number of patients with seronegative RA.

**Objectives:** To replicate the association of anti-MAA antibodies with RA and explore their value as biomarkers.

**Methods:** Sera from 515 Spanish patients with established RA that fulfilled the 1987 ACR classification criteria and from 274 healthy controls were included. Available information included history of smoking, anti-CCP status, and genotype of HLA-DRB1 and PTPN22 rs2476601. Human serum albumin MAA adducts and hexyl-MAA standard were chemically synthesised. Anti-MAA antibodies against the albumin MAA adducts were determined by indirect ELISA using isotype-specific secondary antibodies for IgG, IgM and IgA.

**Results:** Anti-MAA antibodies were detected in a small fraction of the RA patients, who had slightly increased antibody titers compared to healthy controls, 6.4% were positive for IgG, 15.7% for IgM and 8.0% for IgA. The low prevalence of anti-MAA antibodies persisted in spite of multiple variations in the ELISA protocols including the use of different albumin sources, albumin MAA adducts produced in two different laboratories, and various secondary antibodies. IgM anti-MAA antibody titers were increased in smokers compared to non-smokers. Moreover, the presence of IgM and of IgA anti-MAA antibodies were associated with anti-CCP and RF positivity.

**Conclusions:** Anti-MAA antibodies were detected in a small fraction of the Spanish RA patients, but their low sensitivity questions the value of these antibodies as biomarkers of RA. Due to the contradictory findings, additional studies should be performed that will need to address also the role of MAA adducts on RA pathogenesis.

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**Disclosure of Interest:** None declared

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**AB0127 ANTI-INFLAMMATORY AND PRO-APOPTOSIS EFFECTS OF 18BETA-GLYCYRRHETINIC ACID IN IN VIVO AND IN VITRO MODELS OF RHEUMATOID ARTHRITIS**

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**Background:** Rheumatoid arthritis (RA) is one of the most common autoimmune diseases and it affects 0.5%–2.0% of the human population worldwide.<sup>1</sup> Though disease modifying anti-rheumatic drugs (DMARDs) can improve the clinical condition of patients with RA, toxicities of these drugs will be accumulated with long-term use and the unwanted side effects still cannot be avoided. 18β-glycyrrhetic acid (18β-GA), an active component of licorice, exhibits potential anti-cancer, anti-inflammatory, anti-allergic, and anti-microbial activities.<sup>2</sup> Moreover, 18β-GA has been elucidated to attenuate hepatotoxicity or nephrotoxicity caused by chemical drugs, included methotrexate(MTX).<sup>2</sup> These evidences suggested 18 β-GA may become a candidate for low toxicity RA therapy as the mechanism was revealed.

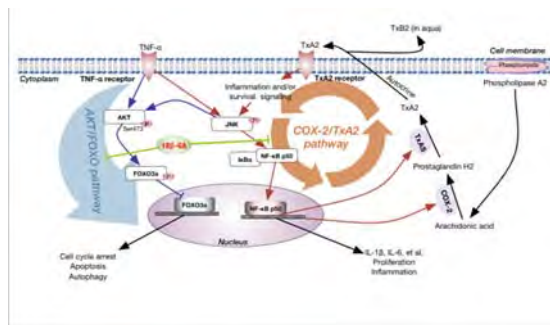
**Objectives:** The aim of this study is to investigate the underline mechanism of 18β-GA on anti-inflammation and anti-proliferation in *in vivo* and *in vitro* models of RA.

**Methods:** CIA rats were treated with 18β-GA, methotrexate, celecoxib and three combination therapies for 30 days. Paw swelling volume, thromboxane synthase (TxAS), proliferating cell nuclear antigenprotein (PCNA), interleukin (IL)–1β, IL-6, and thromboxane B2 (TxB2) were detected to assess the anti-inflammation and



anti-proliferation effects of different treatments. To further study the potential mechanism, TNF- $\alpha$ -induced *in vitro* model was applied. With different treatments, cell proliferation was detected using MTS, meanwhile, cell cycle distribution and apoptosis were examined by flow cytometric analysis. Western blotting and real-time quantitative PCR were conducted to evaluate many molecular targets involved in interested pathways like COX-2/TxA2 pathway and AKT/FOXO3a pathway.

**Results:** The paw swelling volume and histological data indicate that 18 $\beta$ -GA administration attenuates arthritis severity in rats with CIA. Lower level of IL-1 $\beta$ , IL-6, and TxB2 were observed in serum of 18 $\beta$ -GA group as compared with model group. In addition, synovial immunohistochemistry data shows that 18 $\beta$ -GA decreased about half of PCNA intensity induced by collagen. However, *in vivo*, all data exhibited no significant differences among groups with monotherapy and combination therapy. *In vitro*, 18 $\beta$ -GA inhibited the mRNA and protein levels of COX-2 and TxAS that induced by TNF- $\alpha$  in MH7A cell line. Both p-JNK and NF- $\kappa$ B1 (p50) were inhibited by 18 $\beta$ -GA as well as TxAS siRNA transfection. Moreover, 18 $\beta$ -GA inhibited MH7A proliferation in a time- and dose- dependent manner from MTS assay. Flow cytometric analysis revealed that 18 $\beta$ -GA induced cell apoptosis and caused G1-phase cell cycle arrest. Finally, AKT and FOXO3a were predominantly phosphorylated by TNF- $\alpha$ , whereas such effect was blocked by 18 $\beta$ -GA treatment.



Abstract AB0127 – Figure 1

**Conclusions:** This study has for the first time shown that 18 $\beta$ -GA has an inhibitory role in synovial cell inflammation and proliferation, which is, at least in part, dependent on the regulation of COX-2/TxA2 pathway and AKT/FOXO3a pathway. Thus, 18 $\beta$ -GA should be regarded as a new potential drug candidate for RA therapy.

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**Disclosure of Interest:** None declared

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#### AB0128 CXCL1, BUT NOT AUTO-ANTIBODIES OR CD4+CCR6+ MEMORY TH CELLS WITHIN BLOOD, IS A MARKER TO DIFFERENTIATE MICE INTO COLLAGEN INDUCED ARTHRITIS POSITIVE OR NEGATIVE PRIOR TO CLINICALLY MANIFEST DISEASE

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**Background:** There is currently a knowledge gap on early pathogenesis prior to Rheumatoid Arthritis (RA) diagnosis. Additionally, current medication available for RA treatment has not been developed for prevention. Collagen induced arthritis (CIA) could aid in extending knowledge on early RA pathogenesis and testing the preventive effects of medicines.

**Objectives:** In this study we sought a marker that can differentiate mice prior to clinically manifest disease into their future CIA status with the aim to facilitate research into early disease processes and preventive treatment strategies.

**Methods:** Blood was obtained at time points prior (days 12 and 19) and after clinically manifest disease (days 27 and 35) during CIA. Antibodies against bovine and mouse collagen type II (mCII) were measured from plasma by ELISA. CD4<sup>+</sup>CCR6<sup>+</sup> memory Th cells as well as other T cell types were determined in

blood. Cytokines and chemokines were detected in plasma by Luminex. Mice were divided into CIA negative and CIA positive groups based on CIA score reached on day 35.

**Results:** Antibodies against mCII of the IgG2a isotype differed prior to clinically manifest disease but are not suitable as a differentiation marker. CD4<sup>+</sup>CCR6<sup>+</sup> memory Th cells in blood differed only at day 35. The same holds for IL-6, TNF $\alpha$  and CXCL2. In contrast, CXCL1 differed prior to clinically manifest disease with an AUC significantly better (p=0.003) than random.

**Conclusions:** Here we identified CXCL1 as a marker that can differentiate mice prior to clinically manifest disease into CIA positive and CIA negative mice. This might help facilitate research into early disease processes and preventive pre-clinical treatment strategies.

**Disclosure of Interest:** None declared

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#### AB0129 ASSESSMENT OF MORPHOLOGY OF THE EARLY AND LATE STAGE OF JUVENILE RHEUMATOID ARTHRITIS

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**Background:** One of the current problems of modern rheumatology is chronic inflammatory diseases of the knee joint in children. With juvenile rheumatoid arthritis (JRA), an uncontrolled inflammatory process can lead to the formation of contractures and deformities of the limbs

**Objectives:** Our aim is to study morphology of the early and late stage of juvenile rheumatoid arthritis

**Methods:** In total, 81 knee joint surgery was performed on 71 children of the child age in connexion with the JRA. The average age of the patients was 11 years (6–14). To verify the diagnosis during diagnostic arthroscopy, a multifocal biopsy from 7 points was performed. Pathomorphological study of the material was performed according to the conventional histological method of studying soft tissues

**Results:** The results of the pathomorphological examination were analysed for the time frame of the appearance of the JRA. Pathomorphological early and late synovitis criteria were found. Early criteria (typical for the first three months after the JRA debut) – the phenomenon of necrosis in synoviocytes and the subintimal layer, palisade-like cell structures in the sub-synovial layer, synoviocyte proliferation, fibrinoid superimpositions on the surface of the cover layer, productive endovascular endolytic endotheliosis, lymphocyte infiltration and plasmocytes. Late criteria (duration of the disease – more than 3–6 months): marked plasmacytic infiltration with the formation of lymphoid nodules with a hermetic centre, activation of fibrinoid and sclerotic processes with the formation of extensive fibrinoid necrosis with perifocal sclerosis, the formation of rheumatoid nodules, productive synovial hyperplasia, deposition of amyloid masses, formation of pannus granulation tissue with destructively invasive growth articular cartilage and synovium

**Conclusions:** Determining the stage of JRA is of great clinical importance for the early initiation of treatment and prevention of irreversible destructive complications. The proposed new method for determining the prevalence of pathological changes in the synovial membrane of the knee joint in children with JRA using a combined arthroscopic and pathomorphological evaluation of pathological changes in synovium in 7 joints allows to accurately determine the prevalence of the pathological process in the synovium, which has macroscopically only local manifestations

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**Disclosure of Interest:** None declared

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#### AB0130 SERUM LEPTIN AND ADIPONECTIN LEVELS IN RHEUMATOID ARTHRITIS PATIENTS, THEIR ASSOCIATION WITH INFLAMMATORY PROCESS

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**Background:** It is well known that such bioactive substances as leptin and adiponectin are involved in different pathologic process including inflammation. At the same time, in a number of studies it was demonstrated anti-inflammatory properties

of adipokines. Many studies have shown increasing leptin level and reducing adiponectin level in patients with rheumatoid arthritis (RA) compared with healthy ones. On the other hand the roles of adipokines in pathogenesis of autoimmune disorders are still controversial due to their both pro-inflammatory and anti-inflammatory effects.

**Objectives:** The aim of this study was to evaluate adipokine levels in patients with RA and to assess their association with the activity of inflammatory process

**Methods:** The study included 62 patients with RA and 35 practically healthy sex and age matched persons of control group. The diagnosis of RA was established according to the ACR 2010. Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) were used to assess inflammation. Disease activity and functional impairment were evaluated using the Disease Activity Score (DAS28). Serum leptin and adiponectin levels were studied by immunoassay using standard sets (DRG, Germany and "Orgenium", Finland). Results are expressed as mean  $\pm$  standard error of the mean. Spearman's  $r$  was used to calculate correlations between markers of disease activity (ESR, CRP, DAS28) and serum adipokine levels. A  $p$  value  $<0.05$  was considered statistically significant for all tests

**Results:** It was found that the mean value of leptin and adiponectin levels were  $20.7 \pm 12.3$  ng/ml and  $2.47 \pm 1.34$  ng/ml respectively in patients with RA and  $6.47 \pm 3.17$  ng/ml and  $4.21 \pm 1.4$  ng/ml respectively in the control group. Thus, the leptin level in patients with RA was 3.2 times higher, and adiponectin level was 1.7 times lower than in healthy individuals. Levels of adipokines were associated with the activity of the inflammatory process. Thus, serum concentration of leptin level was increased ( $r=0.33$  and  $r=0.35$ ) and adiponectin level was decreased ( $r=-0.25$  and  $r=-0.24$ ) with the increasing of ESR and CRP. Similar patterns were observed for the integral index of RA activity DAS28. In particular, DAS28 was 1.6 times higher in subjects with leptin levels above  $44.7 \pm 9.4$  ng/ml than in the group of patients with leptin levels below  $44.7 \pm 9.4$  ng/ml. The correlation analysis has also confirmed the close association between the leptin and adiponectin levels with DAS28 activity index ( $r=0.37$  and  $r=-0.28$ , respectively).

**Conclusions:** Disadipokineemia in patients with RA is characterised by the increasing of serum leptin level and the decreasing of serum adiponectin level and is closely related to the activity of the inflammatory process.

**Disclosure of Interest:** None declared

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AB0131

#### RHEUMATOID FACTOR IS DETECTED ON CIRCULATING EXTRACELLULAR VESICLES IN A SUBPOPULATION OF RHEUMATOID ARTHRITIS PATIENTS WITH A MORE SEVERE DISEASE PHENOTYPE

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**Background:** Extracellular vesicles (EVs) play a role in cell-cell communication and contain numerous signalling molecules inside and on their cell membrane. Although their function remains to be elucidated, evidence accumulates that EVs play a regulatory role in immunity during health and disease. They contain numerous proteins, lipids, RNA, DNA and sometimes cell organelles such as mitochondria. In a recent study was shown that Immunoglobulin M-Rheumatoid factor (IgM-RF) is present on milk derived exosomes.<sup>1</sup> High IgM-RF levels in Rheumatoid Arthritis (RA) predict a more severe disease and comorbidities, probably due to their involvement in immune complex formation and activation of complement (crucial mediators of the effector phase of inflammation in the pathogenesis of RA).

**Objectives:** In this study we investigate whether RF +EVs are detectable in the circulation of RA patients and if this relates to parameters of disease activity.

**Methods:** EVs were isolated from platelet-free plasma of 38 RA patients and from age and sex-matched 24 healthy controls (HC) by size exclusion chromatography. EV markers (tetraspanins) were detected by Western blot and miRNA content by RT-qPCR. Particle size and concentration were measured by electron microscopy and nanosight tracking analysis. Protein concentration was determined by micro-BCA. RF levels were measured using a commercial ELISA. The percentage of RF +EVs was determined by measuring bound and unbound PHK labelled EVs to Protein L magnetic beads in a fluorometer.

**Results:** Mean EV particle size, concentration and protein content were not different between RA patients and HC. 27 of the 38 RA patients were classified as RF+ ( $>10$  IU/ml) and of the clinical parameters studied only their erythrocyte sedimentation rate (ESR) was higher ( $31$  vs  $14$  mm/hr). In 14 RF +patients, RF was detectable on a small portion of EVs not exceeding 4% of the total number of circulating EVs. Interestingly, RA patients with RF +EVs showed higher disease activity as assessed by patient global health assessment using a visual analogue scale ( $63$  vs  $31$ ), blood C-reactive protein ( $22$  vs  $9$  mg/L) and ESR ( $43$  vs  $19$  mm/hr) levels, than RA patients with undetectable RF +EVs.

**Conclusions:** This study shows for the first time that in a subpopulation of RA patients RF is present on EVs, which might originate from their B-cells. The higher

disease activity in RA patients expressing RF on their EVs suggests that RF +EVs are involved in RA pathogenesis.

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AB0132

#### FRAXINELLONE ATTENUATES RHEUMATOID INFLAMMATION IN MICE

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**Background:** Fraxinellone is isolated from *Dictamnus dasycarpus*, a traditional herbal medicine that attenuates inflammatory conditions.<sup>1,2</sup> Recent studies have suggested that fraxinellone has a potential therapeutic effect in animal models with inflammatory diseases.<sup>3–5</sup>

**Objectives:** We aimed to evaluate the therapeutic effect of fraxinellone on inflammatory arthritis and identify the underlying mechanisms.

**Methods:** Fraxinellone (7.5 mg/kg) or a vehicle control was injected into mice with collagen-induced arthritis (CIA). The severity of arthritis was evaluated clinically and histologically. The differentiation of CD4 +T cells and CD19 +B cells was investigated in the presence of fraxinellone. Osteoclastogenesis after fraxinellone treatment was evaluated by staining with tartrate-resistant acid phosphatase (TRAP) and by measuring the mRNA levels of osteoclastogenesis-related genes.

**Results:** Fraxinellone attenuated the clinical and histologic features of inflammatory arthritis in CIA mice. Fraxinellone suppressed the expression of interleukin-17, and T helper 17 cell-related transcription factors (ROryt and phosphorylated STAT3) in CD4 +T cells. CD19 +B cells showed lower expression of activation-induced cytidine deaminase (AID) and Blimp-1 after treatment with fraxinellone. The formation of TRAP-positive cells and the expression of osteoclastogenesis-related markers were reduced in the presence of fraxinellone. Inhibition of interleukin-17 and osteoclastogenesis was also observed in experiments using human peripheral mononuclear cells.

**Conclusions:** Fraxinellone alleviated synovial inflammation and osteoclastogenesis in mice. The therapeutic effect of fraxinellone was associated with the inhibition of cellular differentiation and activation. The data suggests that fraxinellone could be a novel treatment for inflammatory arthritis, including rheumatoid arthritis.

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**AB0133 EXPRESSION OF PRO-RESOLVING SPECIALISED MEDIATORS' RECEPTORS IN RHEUMATOID ARTHRITIS**

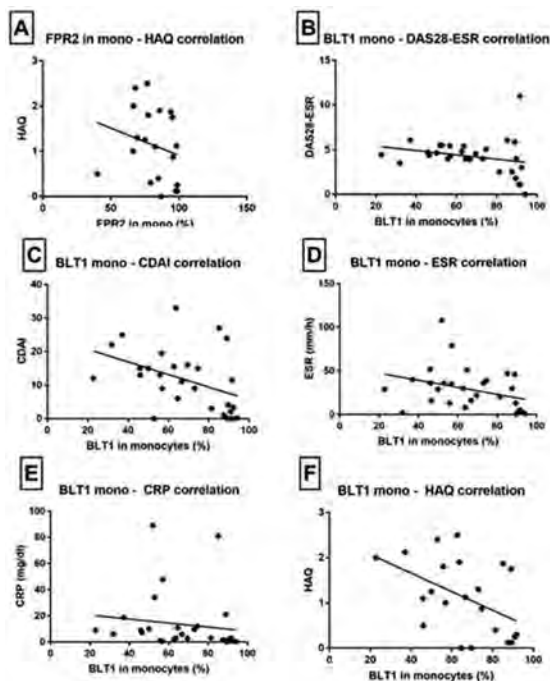
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**Background:** Inflammation is the physiologic response against noxious stimuli to restore homeostasis and tissue repair. At the initial phase, characterised by an increase in pro-inflammatory cytokines aiming to neutralise the tissue injury, the resolution process must follow to down-regulate the inflammation and to promote the tissue repair. That latter phase is driven by the so called Pro-Resolving Specialised Mediators (SPMs), such as Resolvin (RvD and RvE), Protectins, Maresins and Lipoxin A4 (LXA4), bioactive metabolites of omega-3 fatty acids that act by interacting with specific cellular receptors: CMKLR1 and BLT1 for RvE1, FPR2 and GPR32 for RvD1 and FPR2 for LXA4. In rheumatoid arthritis (RA) the reactive inflammation becomes persistent and the innate immune response turns into the adaptive immune activation. Nowadays there is no evidence whether SPMs are involved in RA pathogenesis.

**Objectives:** Purpose of this study was to evaluate the expression of CMKLR1, FPR2 and BLT1 in RA patients and to correlate it to the disease activity.

**Methods:** Patients affected with RA, according to the 2010 EULAR/ACR classification criteria, were enrolled in this study. Exclusion criteria were: minority age, status of pregnancy or breastfeeding, concomitant any other autoimmune disease. At entry, ESR, CRP, DAS28-ESR, CDAI, Health Assessment Questionnaire Disability Index (HAQ) and peripheral venous blood sample were collected. Based on DAS28-ESR, patients were divided into high-moderate (H-Mo/RA if DAS28-ESR  $\geq 3.2$ ) and low-remission (L-Rem/RA if DAS28  $< 3.2$ ) disease activity group. The expression of CMKLR1, FPR2 and BLT1 in peripheral T cells (CD3) and monocytes (CD14) was evaluated by flow-cytometry assay. Differences for continuous variables were evaluated using the Mann-Whitney test, while for categorical data the Fisher's probability test. Correlations were assessed using the Spearman test.

**Results:** Thirty RA patients, 21 H-Mo/RA and 9 L-Rem/RA, were studied. While no difference in the expression of CMKLR1, FPR2 and BLT1 in CD3-T cells between the 2 groups was found, SPMs receptors were differently expressed on CD14-monocytes. BLT1<sup>+</sup>CD14<sup>+</sup> cells were significantly higher in L-Rem/RA (90,96%) than in H-Mo/RA/RA (56,70%) ( $p: 0.0001$ ). Likewise, FPR2<sup>+</sup>CD14<sup>+</sup> cells were significantly higher in L-Rem/RA (92,29%) than in H-Mo/RA/RA (79,94%) ( $p: 0.01$ ). CMKLR1 expression in monocytes was not regulated by disease activity. We also demonstrated an inverse correlation between BLT1 level in monocytes and ESR ( $p: 0.01$ ), CRP levels ( $p: 0.008$ ), DAS28-ESR ( $p: 0.03$ ), CDAI ( $p: 0.0076$ ) and HAQ ( $p: 0.0138$ ) and a weak correlation between FPR2 expression and HAQ ( $p: 0.05$ ) (figure 1).



**Abstract AB0133 – Figure 1.** Statistically significant correlation between the expression of FPR2 or BLT1 in monocytes and different parameters such as ESR ( $p: 0.0166$ ;  $r: -0.434$ ), CRP ( $p: 0.0084$ ;  $r: -0.4726$ ), DAS28-ESR ( $0.0318$ ;  $r: -0.3927$ ), CDAI ( $p: 0.0076$ ;  $r: -0.4936$ ) and HAQ (FPR2:  $p: 0.05$ ;  $r: -0.4438$ ; BLT1:  $p: 0.0138$ ;  $r: -0.5169$ ).

ESR: Erythrocyte Sedimentation Rate; CRP: C-Reactive Protein; DAS28-ESR: Disease Activity Score of 28 joints; CDAI: Clinical Disease Activity Index; HAQ: Health Assessment Questionnaire Disability Index.  $P$ -value  $< 0.05$  was considered statistically significant.

**Conclusions:** In this study, FPR2 and BLT1 expression seem to be regulated by the activity of RA disease. As FPR2 and BLT1 should be involved in down-regulating the inflammation by monocytes, it might be hypothesised that a defective signalling through these SPMs receptors may contribute to sustain chronic inflammation in active RA. However, further studies are needed to explore the intricate mechanisms beyond inflammation and its resolution.

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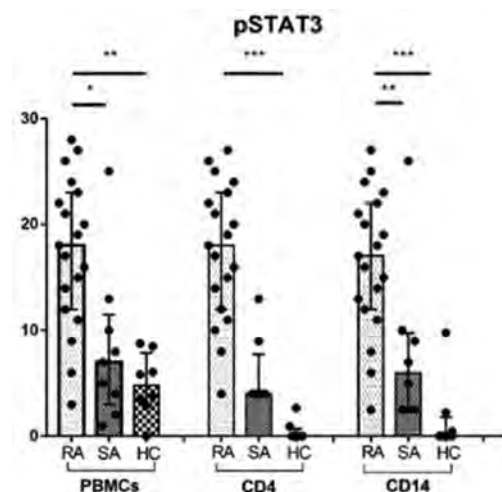
**AB0134 PHOSPHORELATED STAT3 EXPRESSION IN PERIPHERAL BLOOD MONONUCLEAR CELLS IN RHEUMATOID ARTHRITIS**

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**Background:** The JAK-STAT pathway is mainly involved in the regulation of the expression of cytokines and growth factors; so it controls the proliferation, differentiation, migration and death of the cells of the immune system. In patients with RA, studies have shown increased activation of STAT3 with undergoes phosphorylated (pSTAT3), probably due to increased levels of cytokines such as IL-6, IL-11, IL-12.

**Objectives:** This study aims at investigating the level of expression of STAT3 and pSTAT3 in peripheral blood lymphomonocytes cells of patients with Rheumatoid Arthritis (RA), correlating them with disease activity (ESR, CRP, clinimetric tests).

**Methods:** Patients affected with RA, according to the 2010 EULAR/ACR classification criteria, were enrolled in this study. Exclusion criteria were: minority age, status of pregnancy or breastfeeding, concomitant any other autoimmune disease. At entry (new treatment with csDMARDs or biological drugs) ESR, CRP, DAS28-ESR, CDAI and peripheral venous blood sample were collected. The expression of STAT3 and pSTAT3 in lymphomonocytes cells, CD4 and CD14 cells were evaluated by flow-cytometry assay. The level of STAT3 gene was studied by qPCR. Differences for continuous variables were evaluated using the Mann-Whitney test, while for categorical data the Kolmogorov-Smirnov test. Correlations were assessed using the Spearman test.



**Abstract AB0134 – Figure 1**

**Results:** Twenty RA patients were studied, comparing STAT3 and pSTAT3 levels with 9 seronegative arthritis patients (SA) and 8 healthy control (HC). While no difference in the expression of STAT3 levels between the 3 groups (in flow-cytometry and qPCR assays), pSTAT3 was higher in RA (9,5%) than in SA (2,74%) ( $p:$



0.005) or HC (4.81%) ( $p$ : 0.04); between the 3 groups, pSTAT3 was differently expressed in CD4-lymphocytes and CD14-monocytes (figure 1). We also demonstrated a correlation between pSTAT3 level in CD14 +cells and ESR ( $p$ : 0.026;  $r$ : 0.4625). We found no correlation between pSTAT3 expression and Body Mass Index or disease duration.

**Conclusions:** In this study, STAT3 seems to be activated more in RA than SA or HC. Monocytes (as macrophage) and T-cells have important role in RA. Isomaki et al. demonstrated a correlation between IL-6 level and STAT3 activation so it might be suggested a possible role of pSTAT3 as a biomarker of disease activity. However, further studies are needed to explore the important role of JAK-STAT pathway in RA.

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**Disclosure of Interest:** None declared

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#### AB0135 CIRCADIAN RHYTHMS OF IMMUNE CELLS IN HEALTHY INDIVIDUALS AND PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Clinical symptoms of rheumatoid arthritis (RA), such as joint stiffness, swelling and pain, manifest in circadian pattern with the highest intensity occurs at early dawn. This is known to correlate with the circadian expression of IL-6, which peaks before the onset of the symptom. Despite this finding, the circadian behaviour of immune system in cellular and molecular level in RA patients has not yet been extensively investigated.

**Objectives:** Our previous study suggested that immunological circadian rhythms in patients with RA were altered when compared to the healthy individuals. Currently, we are performing 24 hours study involving RA patients and healthy individuals to further monitor the dynamic occurrence of diverse immune cells in the periphery.

**Methods:** Up to this time five eligible RA patients aged 45–75 years and twelve eligible healthy controls were recruited to join the study. On the study day, the blood was drawn in two hours interval throughout 24 hours. The participants were provided with regular meal, allowed to eat snacks ad libitum and carry passive activities. The absolute number of circulating immune cells was determined using TruCount. RNA were isolated from CD14<sup>+</sup> monocytes and analysed by real-time PCR.

**Results:** The major populations of immune cells in the periphery of healthy controls, including CD4 T cells, CD8 T cells, regulatory T cells, B cells and monocytes, displayed circadian rhythm that peaks during the rest phase. The rhythms are in general shifted a few hours later in the RA patients. Noteworthy, CD14 monocyte, which is one of the major sources of IL-6 in RA, showed a more pronounced rhythm with higher amplitude in RA patients compared to healthy individuals. Furthermore, the following clock genes are rhythmically expressed in CD14 monocytes of both groups: *Rorα*, *Per1*, *Per2*, *Per3* and *DBP*. The peak of *Rorα*, *Per1*, *Per3* *DBP* and *CRY1* is shifted a few hours later in RA patients. Interestingly, circadian variation is not observed in the expression of *RevErbα* in healthy individuals, while in the RA patients a rhythm is established.

**Conclusions:** In general, circadian rhythm of immune system in cellular and molecular level in RA patients appears to undergo phase shift and peaks a few hours later in comparison to healthy individuals. New established rhythms were also observed in cellular and molecular level. Another round of study involving seven RA patients is planned this spring to complete the project. Considering our data, we will continue to investigate circadian rhythms in expanded immune cell population using mass cytometry, immunoassay and microarray. Identification of immunological circadian rhythms in patients with RA and healthy individuals will help us to expand our knowledge in autoimmunity and provide an outlook on potential future implications.

**Acknowledgements:** We thank our clinical study team: Dr. Robert Biesen, Dr. Edgar Wiebe, Dr. Kim-Nikola Zeiner, Dr. Desiré Freier, Manuela Jakstadt, Lisa Ehlers, Annemarie Lang, Moritz Pfeiffenberger, Alexandra Damerou, Pierre-Louis Krauß, Gabriela May and Marius Ibach for their help and contribution on the study days.

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#### AB0136 THE EFFECT OF IL-6 RECEPTOR ANTIBODY FOR THE TREATMENT OF MCH-LPR/LPR-RA1 MICE THAT SPONTANEOUSLY DEVELOPED ANKYLOSING ARTHRITIS

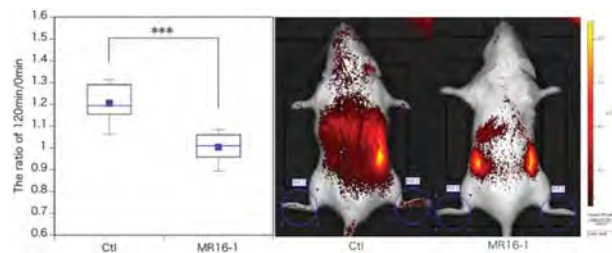
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**Background:** Mch-lpr/lpr-RA1 (RA1) mice are new strain mice which spontaneously developed arthritis in ankle and finally leads to ankylosis. There is no report that drug treatment has been applied to these mice.

**Objectives:** To examine the effect of mouse IL-6 receptor antibody MR16-1 for the treatment of RA-1 mice.

**Methods:** Male RA1 mice were randomly divided into treated and control groups. MR 16-1 was applied from 10 weeks of age for the treatment group. Saline was applied for the control group. The drug was administered every two weeks with the initial dose of 2 mg, then 0.5 mg. The effects were evaluated by histological synovitis score, *in vivo* imaging using ICG-encapsulated liposomes and the expression of serum SAA and IL-6.

**Results:** The tissue evaluation was carried out at 14 weeks, 17 weeks and 20 weeks of age. The histological score of treated groups were significantly improved compared with control group at every age. The interclass correlation coefficient was 0.771. *In vivo* imaging using ICG-encapsulated liposomes showed that significant signal decrease in treated groups at 14 weeks, but no significant difference was observed after 16 weeks. Blood SAA was significantly improved at 17 weeks of age.



**Abstract AB0136 – Figure 1**

**Conclusions:** IL-6 receptor antibody is effective for the treatment of ankylosing arthritis of RA1 mice. IL-6 might be a new potential target of treatment for ankylosing arthritis.

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**Disclosure of Interest:** None declared

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#### AB0137 ARTHRITIS-ASSOCIATED EGGERTHELLA LENTA MODULATE DISEASE VIA METABOLIC AND MICROBIAL ALTERATIONS

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**Background:** Role of environmental factors in predisposition to develop rheumatoid arthritis (RA) has gained interest due, in part, to the studies showing an association of gut microbiota with immune homeostasis. Although the etiology of RA is unknown, recent studies on the role of gut microbiota in inflammatory adaptive immune response have led to the concept that interaction between the host microbiome and genetic factors influences autoimmunity. We have shown an association of rare lineage commensals, *Eggerthella lenta*, with RA.

**Objectives:** In this study, we aimed to determine how human gut commensal *E. lenta* modulates gut epithelial integrity and inflammation via metabolites in humanised mice expressing RA-susceptible HLA-DQ8.

**Methods:** DQ8 mice following immunisation with type II collagen develop arthritis and antigen-specific cellular and humoral response. DQ8 mice orally gavaged

with RA-associated *E. lenta* on alternate days for one week and were induced for arthritis. Gavage with microbes continued for 4 weeks. Mice were monitored for onset and progression of arthritis. Epithelial integrity was done by FITC-Dextran assay and citrulline levels in faecal and plasma samples were measured by liquid chromatography mass spectrometry

**Results:** Mice gavaged with *E. lenta* showed a much higher load of gut microbes compared to controls. Surprisingly, *E. lenta* did not augment gut permeability as it was similar to non-gavaged arthritic mice. *Eggerthella lenta* is involved in ornithine pathway leading to generation of citrulline. To test if gavage with *E. lenta* accumulates citrulline in the gut, we tested citrulline levels in faecal samples by liquid chromatography mass spectrometry. Surprisingly, mice gavaged with *E. lenta* had lower levels of citrulline in faecal samples as compared to mice naïve mice with no gavage or arthritic mice without gavage. One can speculate from these observations that there is an expansion of commensals, like *E. lenta* in RA, leading to production of citrulline. To determine if citrulline could be accumulated outside of gut, we measured citrulline in sera of mice in various groups, gavaged with *E. lenta*, naïve and mice induced for arthritis but no *E. lenta* gavage. Surprisingly, mice gavaged with *E. lenta* and induced for arthritis had lower levels of citrulline as compared to controls induced for arthritis but no gavage,  $p < 0.05$ . Naïve mice gavaged with *E. lenta* also showed significantly much lower levels compared to sera of naïve mice.

**Conclusions:** This data suggests that *E. lenta* may be a major player in determining certain metabolic pathways. If Citrulline is being converted to arginine and used in other pathways is currently under investigation. Our studies suggest that gut commensals influence immune response in and away from the gut. Commensals and their products may provide novel targets for therapeutic strategies in arthritis.

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#### AB0138 THE BONE MARROW OEDEMA IS LINKED TO A OSTEOCLASTIC ENVIRONMENT IN BONE MARROW DURING COLLAGEN INDUCED MICE ARTHRITIS DEVELOPMENT

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**Background:** Bone erosion is a central pathogenic event in Rheumatoid arthritis (RA) and is associated with joint damage and poor functional outcome. The synovitis is traditionally regarded as the primary event of bone erosion in RA and synovial cells are usually thought to play a critical role in this pathologic process. However, the synovitis-centred concept has long been challenged by recent clinical finds. Bone erosion formation also could be found in joints without clinical traits of synovitis, suggesting that synovitis and joint erosion could be uncoupled. Moreover, recent study demonstrated that bone marrow oedema (BME) that identified by magnetic resonance imaging (MRI) is strongly associated with erosive progression, which independent of local synovitis in RA.

**Objectives:** BME is also called osteitis, which represent the replacement of adipose tissue with inflammatory cells in bone marrow. In this study we addressed 2 questions: 1) the course of BME and synovitis in a same joint during CIA development; 2) how BME cause the bone erosion in CIA.

**Methods:** Using collagen induced mice arthritis model, we compared the compared the time course of appearance of BME, synovitis and arthritic symptoms during the development of CIA. The changes RANKL, cytokines, osteoclast and immune cells expression in bone marrow during the development of CIA were analysed by flow cytometric analysis, immunofluorescence staining and RT-qPCR.

**Results:** MRI BME can be identified as early as 25 days after first immunisation, when there is no any histopathological changes and arthritis symptoms. Flow cytometry and immunofluorescence staining indicated that the proportion of pre-OCs were significantly increased in bone marrow after day 25 with the presence of BME. At day 25, accompanied by presence of BME and increased pre-OCs, the number of trabecular bone was significantly diminished as compared with those at day 20 and reached its lowest number at day 35. We then examined the transcription of several pro-inflammatory cytokines and chemokines related to OCs differentiation, migration and activation, such as RANKL, IL-17, TNF $\alpha$ , CCL3, CCL4, CCL12, CCR5 by Real-time PCR. The most prominent RANKL

change was observed at day 35. IL-17 and TNF $\alpha$  mRNA were elevated from day 25, reaching a peak at day 28 and thereafter gradually decreasing. Expression of CCL3 and CCL12 were only higher at day 28 and day 25, respectively, while there was no significant change in CCR5 and CCL4 mRNA in the bone marrow. The proportion of T cells and monocytes in bone marrow were significantly higher from day 25 to day 45. No differences in B cells and plasma cells were detectable at any time points. Bone marrow cells from the presence of BME showed significantly increased ability to formation OCs *in vitro*.

**Conclusions:** BME precede the synovitis and arthritic symptoms during the development of CIA. Accompanied BME appearance, we identified an altered bone microenvironment that favours OCs differentiation and survival in CIA mice. We proposed that BME linked to a unique "osteoclastic environment" in CIA disease progression. These findings provide a new perspective for comprehending the development of erosions in RA.

**Disclosure of Interest:** None declared

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#### AB0139 INVESTIGATION OF PREVOTELLA COPRI FROM RHEUMATOID ARTHRITIS PATIENTS

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**Background:** We have previously reported some of the rheumatoid arthritis (RA) patients had *Prevotella copri* in the intestine. By using germ-free (GF) SKG mice, we also showed that *Prevotella*-dominated gut microbiota contribute to the development of arthritis<sup>1</sup>. However, *P. copri* itself has not been isolated from RA patients and their molecular biology was unknown.

**Objectives:** Firstly, we planned to evaluate the intestinal microbiota in RA patients before and after the treatment. Second, we isolated *P. copri* strains from RA patients and healthy controls (HCs) and analysed whether RA patients-derived *P. copri* expanded in the intestine of GF mice.

**Methods:** We first examined whether RA patients have altered composition of microbiota. All the patients were diagnosed according to the American College of Rheumatology/<sup>European League Against Rheumatism 2010</sup> classification criteria for RA. We collected faecal samples from 55 RA patients (61.5 $\pm$ 9.5 years, mean ages  $\pm$ SD) and 33 HCs (56.2 $\pm$ 8.2 years) to investigate the microbiota by 16S rRNA-based deep sequence technique. We also analysed bacterial counts of *Prevotella* and *Bacteroides fragilis* by qPCR method. Moreover, we isolated *P. copri* from faecal contents of RA patients and HCs. GF mice were inoculated with *P. copri* from RA patients and HCs for further analysis.

**Results:** We found that 34.5% (19/55) of RA patients and 18.1% (6/33) of healthy controls have relatively high abundance of *Prevotella* (>4%) in the intestine. These results were compatible with our previous observations. When we focused on the patients who harboured high abundance of *Prevotella* in the gut, *Prevotella/B. fragilis* ratio was decreased after the treatment. The mean *Prevotella/B. fragilis* ratio were changed from 1.28 to 0.75 ( $p=0.08$ ). Further analyses revealed that RA patients-derived *P. copri* successfully colonised to GF-mice and induced Th17 cells in the large intestine.

**Conclusions:** We found that alternation of microbiota composition was observed after the RA treatment. Moreover, we successfully isolated *P. copri* from RA patients and HCs. RA patients-derived *P. copri* efficiently expanded in the intestine of GF mice.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.5350

#### AB0140 THE ROLE OF RAF KINASE INHIBITORY PROTEIN IN RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is an autoimmune inflammatory disease of the joints and is characterised by immune cell infiltration, synovial hyperplasia, and destruction of cartilage and underlying bone<sup>1</sup>. Raf kinase inhibitory protein

(RKIP), an endogenous inhibitor of the extracellular signal-regulated kinase (ERK) pathway, has been implicated as a suppressor of metastasis and NF- $\kappa$ B pathway in cancers<sup>2</sup>.

**Objectives:** The NF- $\kappa$ B and ERK pathways are considered to be one of the most important pro-inflammatory signalling pathways in RA. Therefore, RKIP might be a potential therapeutic target for RA. However, whether and how RKIP regulates RA is not fully understood. The present study was performed to examine whether and how RKIP are differentially regulated in RA.

**Methods:** The expressions of RKIP were assessed in synovial tissue, fluid and fibroblast-like synoviocytes (FLS) from patients with RA and osteoarthritis (OA) by immunofluorescence staining and western blotting. RA- or OA-FLS were infected with either a recombinant adenoviral RKIP overexpressing vector (Ad-RKIP) or shRNA-expressing vector (Ad-shRKIP). Control cells infected with a GFP-targeted recombinant adenoviral vector (Ad-shGFP) (figure 1C). And then, we investigated the effects of RKIP on the migratory activity and invasion rates of FLS by transwell migration and invasion assay.

**Results:** Here, we show that RKIP expression is inversely correlated with RA. The levels of RKIP were significantly decreased in fibroblast-like synoviocytes (FLS), synovial fluid and synovium of RA patients compare to OA patients. And also find that migration and invasion of RA-FLS were significantly increased by the inhibition of RKIP compare to OA-FLS. Knockdown of RKIP in RA or OA-FLS resulted in a dramatic increase of MMP3 and IL6. We also found osteoclastogenesis of RAW cells were increased by the knockdown of RKIP.

**Conclusions:** Our data identify a role of RKIP in RA and suggest that further studies on the potential involvement of RKIP will be beneficial in better understanding the pathology of and providing a new target for treatment for RA.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.5076

## Spondyloarthritis – etiology, pathogenesis and animal models

### AB0141 CERTOLIZUMAB PEGOL LIKE REDUCES INFLAMMATION AND BONE DAMAGE IN TMTNF TRANSGENIC MICE

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**Background:** Transmembrane (tm)TNF (TgA86) mice is a transgenic line that spontaneously develops peripheral arthritis and spondylitis at 4 weeks of age, mimicking human spondyloarthritis (SpA).

**Objectives:** The aim of this work is to understand the effect of TNF blockade in this SpA-like phenotype mouse strain, focusing on histological inflammation and bone damage.

**Methods:** (tm)TNF (TgA86) mice were treated with a certolizumab pegol like product mice equivalent (Ab501), 100 mg/kg twice a week intraperitoneal, or with vehicle (phosphate buffer saline), for 12 weeks, in a therapeutic (10 weeks of age) and preventive (4 weeks of age) experimental settings. A semi-quantitative score for the severity of histologic inflammation and bone damage, in the paws (infiltration, lining cells, erosions and global), and in the spine (inflammation, intervertebral disc destruction, cartilage damage, bone erosion and ectopic chondrocytes/chondrocyte) was applied to haematoxylin and eosin stained slides.

**Results:** 14 (tm)TNF (TgA86) mice (6M/8F) at 10 weeks of age (therapeutic group), and 15 (tm)TNF (TgA86) mice (10M/5F) at 4 weeks of age (preventive group), were treated with Ab501; and 30 (tm)TNF (TgA86) mice with the respective vehicles, for a period of 12 weeks. A statistically significant reduction of the inflammatory infiltrate ( $p \leq 0.001$ ), lining cells layers ( $p \leq 0.05$ ), erosions ( $p \leq 0.05$ ) and global inflammatory score ( $p \leq 0.05$ ) of the paws, was observed in the Ab501

treated group, when compared to the vehicle group, both in the 10 and 4 weeks of age treatment groups. In the spine, statistically significant reductions of the inflammation ( $p \leq 0.001$ ), intervertebral disc destruction ( $p \leq 0.05$ ), cartilage damage ( $p \leq 0.001$ ), bone erosion ( $p \leq 0.05$ ), and ectopic chondrocytes/chondrocyte scores ( $p \leq 0.001$ ) was also depicted in Ab501 treated group in comparison with vehicle.

**Conclusions:** The certolizumab pegol like product mice equivalent reduced histologic inflammatory infiltrate in paws and spine of (tm)TNF (TgA86) mice. Bone damage, as defined by erosions in the paws and spine and ectopic chondrocytes/chondrocyte formation in the spine, also significantly improved in (tm)TNF (TgA86) mice.

**Acknowledgements:** To Leonie M van Duivenvoorde and Dominique Baeten (Amsterdam Academic Medical Centre) for providing (tm)TNF (TgA86) mice for breeding and colony establishment. George Kollias from Flemming Institute for authorisation for the use this mice line.

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**Disclosure of Interest:** None declared

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### AB0142 A REGULATORY CCR10+ CD8+ T CELL POPULATION DIFFERENTIATES PSORIATIC ARTHRITIS FROM PSORIASIS LIMITED TO CUTANEOUS INVOLVEMENT

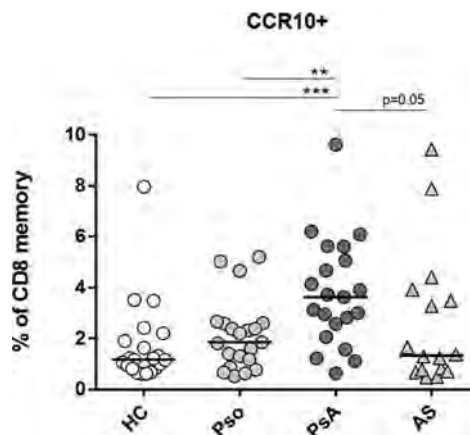
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**Background:** Few studies have compared the immune cell phenotype or function from patients with psoriatic arthritis (PsA) to patients with psoriasis limited to cutaneous involvement (Pso). Head-to-head comparisons of the immune cells in PsA and Pso can provide essential insights into the link between epithelial/cutaneous disease and rheumatic disease.

**Objectives:** Compare the immune cell phenotype and function from patients with PsA compared to Pso.

**Methods:** PBMCs were collected from 23 healthy controls, 21 patients with psoriasis in whom psoriatic arthritis was excluded by a rheumatologist (Pso), 23 patients with psoriatic arthritis (PsA) and 16 patients with ankylosing spondylitis. The Pso and PsA cohorts were free from immunomodulatory therapy and matched for demographics and skin severity. Extracellular and intracellular immunophenotyping using a highly standardised flow-cytometric approach detected over 110 different myeloid and lymphoid cell populations. Lesional and non-lesional skin biopsies and synovial fluid samples were collected from a subset of patients.

**Results:** The circulating immune cell composition showed a remarkable overlap in Pso and PsA, and only one specific cell population was different: CCR10 +CD8 +T cells, being enriched in PsA PBMCs as compared to Pso PBMCs. Further phenotypic and functional evaluation characterised them as effector memory, CXCR3-CCR6-, co-expressing the skin homing markers CCR4 and CLA, but lacking the gut homing marker  $\alpha 4\beta 7$ . Upon re-stimulation, CCR10 +CD8+T cells showed low IFN $\gamma$  production, high IL-10 production and were enriched for FOXP3<sup>high</sup>CD25+ phenotype. Their frequencies in PBMCs were unrelated to joint disease activity and were stable throughout joint disease fluctuations. Synovial fluid displayed low frequencies of CCR10 +CD8+T cells whereas skin contained the most abundant CCR10 +CD8+T cell frequencies. Lesional psoriasis skin displayed relatively fewer CCR10 +CD8+T cells compared to non-lesional skin.



Abstract AB0142 – Figure 1



**Conclusions:** CCR10 +CD8+T cells have regulatory properties and differentiate Pso from PsA. Future studies are needed to uncover if aberrances in regulatory, cutaneous CD8 +T cells precede the transition to joint disease.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.5237

AB0143

#### IMPLICATION OF OSTEONECTIN ON CARDIOVASCULAR RISK IN AXIAL SPONDYLOARTHRITIS: A SEROLOGICAL AND GENETIC STUDY

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**Background:** Cardiovascular (CV) disease and atherosclerosis are common causes of morbidity in axial spondyloarthritis (axSpA),<sup>1</sup> a disease characterised by changes in the osteoproliferative process. A dysregulation in the molecules involved in bone remodelling could also affect the atherosclerotic process, since both processes are linked.<sup>2,3</sup> Osteonectin (ON), a key molecule in bone homeostasis,<sup>4</sup> was associated to obesity, insulin resistance and diabetes.<sup>5</sup>

**Objectives:** Since the exact role of ON on CV risk in axSpA has not been elucidated yet, we evaluated its role in the development of subclinical atherosclerosis and its association with CV risk factors in axSpA patients at the serological and genetic level.

**Methods:** 171 axSpA patients fulfilling the classification criteria for axSpA<sup>6,7</sup> and 84 controls were included in this study. Serum ON levels were measured by multiplex assays. Carotid ultrasound was performed to evaluate the presence of markers of subclinical atherosclerosis. Five ON polymorphisms (rs1054204 [G/C], rs11950384 [G/A], rs13182103 [A/G], rs11745387 [G/A] and rs4958487 [A/G]) were selected by tagging and genotyped using TaqMan assays.

**Results:** No difference was observed in ON levels between axSpA and controls. Serum ON and CRP levels at study positively correlated in axSpA (p=0.008). Higher ON levels were observed in men, smokers and patients with an atherogenic index indicative of dyslipidemia (p=0.008, 0.01 and 0.001, respectively). No association was found between ON and subclinical atherosclerosis in axSpA. Interestingly, we disclosed that the presence of the A allele of rs13182103 and rs11950384 ON polymorphisms led to lower ON serum levels in axSpA (p<0.05). Furthermore, the presence of the A allele of rs13182103 was linked to a later diagnosis of axSpA when compared to those patients bearing the G allele (p=0.002).

**Conclusions:** Our results show that ON is linked to inflammation and CV risk factors in axSpA and suggest that the A allele of rs13182103 and rs11950384 ON polymorphisms may have a protective effect in axSpA, leading to reduced ON serum levels and later diagnosis of the disease. These data support an implication of ON in the development and progression of atherosclerotic disease in axSpA.

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AB0144

#### NMR BASED SERUM AND SYNOVIAL FLUID METABOLOMICS REVEAL SIMILAR METABOLOMIC PROFILE IN PATIENTS WITH REACTIVE ARTHRITIS AND UNDIFFERENTIATED SPONDYLOARTHRITIS

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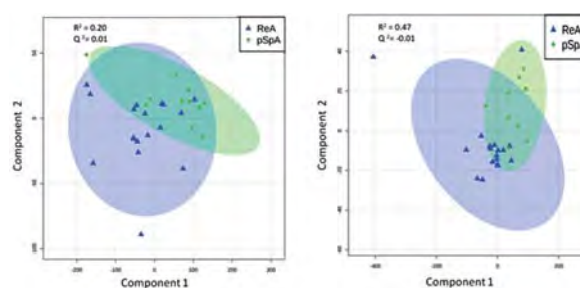
**Background:** Reactive arthritis (ReA) and undifferentiated spondyloarthritis (USpA) have similar clinical picture, the former is preceded by mucosal infections and the latter do not meet criteria of well defined entity of seronegative spondyloarthritis (SSA) We have shown that both ReA and uSpA have similar synovial fluid T cell response to salmonella antigens and cytokine profile.

**Objectives:** To investigate if the metabolic profiles of ReA in sera and synovial fluid are different from those of USpA

**Methods:** Standard definitions were used to classify patients as ReA<sup>2</sup> and uSpA<sup>3</sup> Metabolic profiles in sera and synovial fluid samples were measured using 1D <sup>1</sup>H NMR spectroscopy and analysed using CHENOMX® software. The quantitative profiles between the groups were compared using Partial Least Square-Discriminatory Analysis (PLS-DA) and Q<sup>2</sup> parameter was used to assess the metabolic differences between the groups.

**Results:** The study involved 19 ReA and 13 USpA patients with median age 26 (21–33.75) years. Of 32 patients: 7 (22%) were females, three(12%) had mono-phasic illness, 16 (64%) polyphasic, and six(24%) persistent arthritis (follow-up data was not available for 7). 27% had monoarticular, 59% oligoarticular and 14% polyarticular involvement. Six had inflammatory backpain, three had oral ulcers, one dactylitis, but none had mucocutaneous manifestations. Two had asymptomatic sacroiliitis on radiographs.

Compared to normal controls (n=18, median age=29 years, male:female=17:1), the sera of ReA/USpA patients were characterised by elevated levels of malonate, mannose, N-nitrosodimethylamine, and pyruvate, whereas 3-hydroxyisovalerate was decreased significantly (T-test p-value<0.001). PLS-DA analysis between sera and synovial fluid samples showed clear demarcation with higher pyruvate and acetoacetate and lower aspartate, methanol, ethanol, and methylsuccinate in synovial fluid samples compared to sera (t-test p<0.01). The PLS-DA analysis of sera showed little difference between ReA and USpA (figure 1) while that of synovial fluid showed Q<sup>2</sup> <0 for all models. Further no significant metabolic differences in sera/synovial fluid were found between HLA-B27 positive and negative groups (Q<sup>2</sup> <0 in all models).



**Abstract AB0144 – Figure 1.** (a) PLSDA of sera of HLA B27 positive versus negative patients (b) PLSDA of synovial fluid of HLA B27 positive versus negative patients

**Conclusions:** ReA and USpA have indistinguishable metabolomics profiles in sera and synovial fluid reflecting similar metabolo-inflammatory pathways involved.

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### AB0145 REGULATION OF OSTEOBLASTS BY ALKALINE PHOSPHATASE IN ANKYLOSING SPONDYLITIS

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**Background:** Ankylosing spondylitis (AS) is characterized by excessive spinal ankylosis and bone formation. Alkaline phosphatase (ALP) activity is reported to be high in AS, but little is known about the molecular relationship between ALP and AS.

**Objectives:** The aims of this study were to investigate the relevance of ALP to AS and the role of ALP in the regulation of osteoblast differentiation in AS.

**Methods:** The high-throughput data were downloaded from Gene Expression Omnibus with accession numbers GSE73754 and GSE41038. We retrospectively collected the ALP levels of male patients with AS, to compare with those of gender and age-matched healthy controls (HC) and rheumatoid arthritis (RA) patients. Total ALP and ALP activity in patient's sera were measured in AS and RA groups. ALP gene expression and intracellular ALP activity were analyzed in microarray data of primary bone-derived cells (BdCs) and in In Vitro experiments. Furthermore, the effect of ALP knockdown and inhibitor were performed in primary BdCs and human osteoblasts cells, respectively.

**Results:** ALP level was increased in AS compared with RA and HC. Increased ALP level in AS was associated with radiograph progression. ALP expression was also enriched in bone tissue of AS patients. Furthermore, AS BdCs exhibited elevated ALP activity, leading to accelerating osteoblastic activity and differentiation. Intriguingly, suppression of ALP expression and activity inhibited expression of osteoblastic genes, which are critical for osteogenic differentiation.

**Conclusions:** A multifaceted analysis showed ALP was highly expressed in AS patients. ALP may be involved in the ankylosis of AS and a therapeutic target for preventing ankylosis.

**Disclosure of Interest:** None declared

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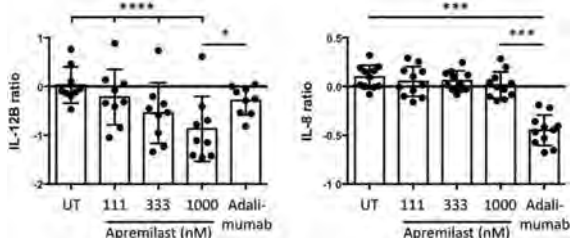
### AB0146 APREMILAST POTENTIALLY INHIBITS IL-12/IL-23P40 PRODUCTION IN HUMAN ARTHRITIC EX VIVO MODELS

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**Background:** Apremilast (Otezla) is a phosphodiesterase 4 (PDE4) inhibitor approved for the treatment of psoriasis and psoriatic arthritis (PsA), but the reason why apremilast shows clinical effect in PsA is not fully understood.

**Objectives:** The objective of this study was to study the downstream effects of apremilast on cells of the inflamed joint in *ex vivo* models of immune mediated inflammatory arthritis. First, we tested the effect of apremilast on the secretion of several cytokines, chemokines and growth factors by synovial fluid mononuclear cells (SFMCs). Then, we tested whether apremilast affect factors involved in structural changes by studying fibroblast-like synovial cells (FLSs), osteoclasts, synovial macrophages, and osteoblasts.

**Methods:** Synovial fluid was obtained from a study population consisting of patients with active rheumatoid arthritis (RA), psoriatic arthritis (PsA) or peripheral spondyloarthritis (SpA) with at least one swollen joint (n=18). Synovial fluid mononuclear cells (SFMCs) cultured for 48 hours were used to study the effect of apremilast on secretion of a large panel of cytokines, chemokines and growth factors using the Olink Proseek Multiplex interferon I panel. These effects were compared with the effects of the tumour necrosis factor alpha (TNF $\alpha$ ) inhibitor adalimumab. Further, fibroblast-like synovial cells (FLSs) were used to study metalloproteinase secretion, SFMCs cultured for 21 days were used to study inflammatory osteoclastogenesis and macrophage differentiation, an osteoclast pit formation assay was used to study osteoclast activity, and a mineralization assay was used to study new bone formation.



Abstract AB0146 – Figure 1

**Results:** In SFMCs cultured for 48 hours apremilast decreased the production of IL-12/IL-23p40 (the shared subunit of IL-12 and IL-23) ( $p < 0.00001$ ), colony stimulating factor 1 ( $p = 0.009$ ), CD6 ( $p = 0.03$ ), CD40 ( $p = 0.04$ ), and MCP-1 ( $p = 0.02$ ), and increased the production of C-X-C motif chemokine 5 ( $p = 0.003$ ) dose-dependently. In sub-analyses, the apremilast induced decrease in cytokine production was greater in cultures with a high lymphocyte count and in cultures from patients with a low C-reactive protein level. Further, apremilast had a very different response signature compared with adalimumab, e.g. with a much greater inhibition of IL-12B ( $p = 0.01$ ) and less inhibition of IL-8 ( $p = 0.0001$ ) (see Figure). In SFMCs cultured for 21 days apremilast increased the secretion of IL-10 ( $p = 0.04$ ) and in FLS cultures apremilast decreased MMP3 production ( $p = 0.005$ ). Apremilast decreased osteoclast pit formation but did not change mineralization by human osteoblasts.

**Conclusions:** This study reveals the downstream effects of apremilast in *ex vivo* models of arthritis with a strong inhibition of IL-12/IL-23p40. Our findings could explain some of the efficacy of apremilast seen in IL-12/IL-23 driven immune mediated inflammatory diseases such as psoriasis and psoriatic arthritis.

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### AB0147 FAECAL MICROBIOTA STUDY IDENTIFIES DYSBIOSIS IN ANKYLOSING SPONDYLITIS PATIENTS

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**Background:** Ankylosing spondylitis (AS), a prototype of spondyloarthritis (SpA), is a chronic inflammatory disorder with diverse clinical phenotypes. It is widely accepted that AS is genetically determined and trigger of environmental factors is common. Accumulating research have indicated that gut microbiota may play a role in the pathogenesis of AS.

**Objectives:** We conduct this study to characterise and investigate differences in the gut microbiome between patients and healthy donors.

**Methods:** 41 patients with AS fulfilled the modified New York criteria for AS and 19 healthy controls (HCs) were recruited in this study. Fresh faecal samples were collected and microbial DNA were extracted by faecal DNA extraction kit according to the manufacture's instruction. V4 hypervariable region of the 16S ribosomal RNA (16S rRNA) was amplified and sequenced on an IlluminaHiSeq2500 platform. The resulting sequencing data were analysed through an in-house bioinformatics pipeline, including removing the barcodes and primers, merging forward and reverse reads, filtering tags, removing chimaeras, clustering and annotation. The mean species diversity for each sample and the differentiation among those samples are captured by alpha and beta diversity, respectively. Principle Coordinate Analysis (PCoA) was performed to get principal coordinates and visualise from complex, multidimensional data.

**Results:** 16S rRNA community profiling of the faecal sample yielded high sequencing depth, with quality-filtered and connexion to generate a mean number of Taxon\_tag being 66398 $\pm$ 5606 versus 63061 $\pm$ 5474 in AS and HCs group respectively. The gut microbial communities were significantly different and more diverse in AS patients when compared with the HCs by calculating metrics (Chao1) of a diversity ( $p < 0.001$ ). PCoA analysis shown that gut microbiota was able to predicted samples to be AS or HCs. At phylum level, the profile of gut microbiota were dominated by *Bacteroidetes* (56.15% vs 53.31%), *Proteobacteria* (11.19% vs 9.97%) and *Firmicutes* (30.10% vs 34.22%) in both AS and HCs groups respectively. However, difference of distribution were appeared between two groups, such that *Bacteroidetes* and *Proteobacteria* were more common in AS group, while *Firmicutes* was more common in HCs group. At genus level, both group were dominated by *Bacteroides* and *Prevotella-9*. Abundance of *Prevotella-9* were great different between AS patients and HCs with relative abundance of 16.07% and 2.86%, respectively.

**Conclusions:** These results suggested that faecal microbiota of patients with AS differed significantly from that of healthy controls. Further analysis and larger cohort replication will be helpful to identified specific microbial marker of AS.

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**Disclosure of Interest:** None declared

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## SLE, Sjögren's and APS – etiology, pathogenesis and animal models

### AB0148 EXTRACELLULAR VESICLE-MEDIATED DELIVERY OF EBV SMALL RNA (EBER1) ACTIVATES LUPUS NEPHRITIS RELATED ANTIVIRAL IMMUNITY IN TUBULAR EPITHELIAL CELLS VIA TLR3

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**Background:** In lupus nephritis (LN), genetic and environmental factors drive the chronic activation of antiviral defenses leading to immune complex-mediated glomerular and tubular damage. Increasing evidence suggests the involvement of extracellular vesicles (EVs) in autoimmune disease. Currently a role for EVs in the pathogenesis of lupus nephritis has not been proposed.

**Objectives:** To investigate the role of EVs in the pathogenesis of LN.

**Methods:** To determine the presence of EVs in kidneys, biopsies from LN patients and IgA-nephropathy and Focal Segmental Glomerulosclerosis control patients were used. Serum samples from SLE patients and from RA patients as controls were used to determine the presence of circulating EVs. Primary renal tubular epithelial cells (TEC) were cultured, and Kidney injury molecule-1 (KIM1) expression was assessed by FACS. Exosomes were analyzed by electron microscopy and western blot. mRNA analysis was performed by qPCR. TLR3 inhibition was performed with TLR3/dsRNA complex inhibitor and with hydroxychloroquine.

**Results:** We show that EVs deliver virus-derived small RNA and activate TEC via toll-like receptor 3 (TLR3). Highly specific stem-loop RT-PCRs revealed Epstein Barr Virus (EBV)-encoded small RNAs in LN biopsies while quantitative EBV-DNA PCR, sensitive to a single copy was negative. In situ hybridization failed to detect nuclear EBV-EBER1 (i.e. EBV-infected cells) in LN biopsies. However, we observed atypical EBER signal in the cytoplasm of TECs in LN but not in disease control biopsies, suggestive of uptake of extra-renal EBER. Consistent with this, we detected EBER1 in circulating EVs of SLE sera. The LN tissues express strongly elevated levels of TLR3, Interferon induced transmembrane-1 and -3, and TNF $\alpha$ . Primary TEC cultured in vitro endocytose EBER1-EVs secreted by EBV-infected B cells via phosphatidylinositol receptors such as KIM-1. Importantly, EV-EBER1 uptake by TEC triggers antiviral immunity and pro-inflammatory cytokine secretion in a Toll-like receptor 3 (TLR3)-dependent manner. Treatment with hydroxychloroquine (HCQ) or a small molecule inhibitor that blocks TLR3-RNA interactions strongly reduced the pro-inflammatory effects of EBER1.

**Conclusions:** We propose that small RNA-loaded EVs exacerbate pre-existing autoimmunity in SLE patients by engaging tubular epithelial TLR3, supporting the rationale for TLR3-blockade as therapeutic strategy in the treatment of lupus nephritis.

**Disclosure of Interest:** None declared

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### AB0149 DECREASED MICRORNA-130A EXPRESSION DRIVES ACTIVATION OF CLASSICAL DENDRITIC CELLS FROM PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME

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**Background:** Primary Sjögren's syndrome (pSS) is a systemic autoimmune disease characterized by lymphocytic infiltration of the exocrine glands and dryness of mouth and eyes. Classical dendritic cells are very potent antigen presenting cells known to induce strong T-cell proliferation and cytokine production.

**Objectives:** Considering the critical role of microRNAs (miRNAs) in regulation of gene expression, we investigated miRNA expression in circulating CD11c<sup>+</sup> dendritic cells (cDCs) of patients with pSS.

**Methods:** Two independent cohorts consisting of pSS patients and healthy controls were established: a discovery cohort (15 pSS, 6 HC) was used to screen the

expression of a large panel of 758 miRNAs. An independent validation cohort (14 pSS, 11 HC) was used to test the reproducibility of the results. cDCs were isolated from peripheral blood using MACS and miRNA profiling of 758 targets was performed using the OpenArray platform in the discovery cohort. A selection of 16 differentially expressed miRNAs was measured in the validation cohort using a custom-made array. Isolated cDCs from HC were stimulated with a panel of Toll-like receptor (TLR) ligands and the expression of miR-130a and miR-708 was measured by qPCR. The effect of transfection with miR-130a on protein synthesis was analysed by using the pulsed stable isotope labelling by amino acids in cell culture (pSILAC) method (quantitative mass spectrometry-based technique) in a HEK-293T cell-line.

**Results:** A total of 24 miRNAs was downregulated in pSS patients versus HC in the discovery cohort ( $p < 0.05$ , with a difference between the groups of  $> \log_2$ ). Of the 16 miRNAs that were selected for replication, the decreased expression of miR-130a and miR-708 in pSS was validated. Activation of cDCs via TLR3 and TLR7/8 induced downregulation of both miRNA-130a and miRNA-708. Transfection with a miR-130a mimic resulted in downregulation of several proteins with a seed match for the miRNA. These proteins are known to be involved in membrane trafficking and cell activation through CREB/NF-kB signalling.

**Conclusions:** miR-130a and miR-708 are significantly downregulated in cDCs of patients with pSS. We show that the expression of these miRNAs is decreased upon cDC activation and that upregulation of miR-130a decreases the expression of proteins involved in the CREB/NF-kB pathway. As such, these miRNAs seem to be involved in cDC activation and reflect enhanced activation of circulating cDCs from pSS patients.

**Disclosure of Interest:** None declared

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### AB0150 DIMINISHED EXPRESSION OF PD-L1 BY ACTIVATED B CELLS IS CHARACTERISTIC OF SLE

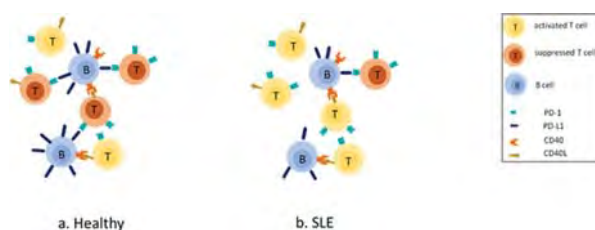
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**Background:** Programmed cell death 1 (PD-1) and its ligands PD-L1 and PD-L2 are known to play an important role in immune response regulation via a co-inhibitory signal during T cell activation. Genome-wide association studies in humans and the fact that PD-1 knock-out mice develop a lupus-like pathology point toward the involvement of the PD-1 pathway in the pathogenesis of systemic lupus erythematosus (SLE).<sup>1,2</sup> However, little is known regarding the role of this pathway in B cells from patients with SLE.

**Objectives:** This study addressed the kinetics of PD-1, PD-L1 and PD-L2 expression on B cells from patients with SLE.

**Methods:** Blood samples were obtained from healthy donors (HD) and SLE patients. PBMCs from HD and SLE patients were stimulated with IL2/IL10, aBCR (IgG/IgM/IgA), CpG oligodeoxynucleotides (CpG) and CD40L alone or in combination. The membrane expression of PD-1, PD-L1 and PD-L2 on CD19<sup>+</sup>CD20<sup>+</sup>B cells was measured by FACS at baseline and after 48 hour stimulation.

**Results:** At baseline, the expression of PD-1, PD-L1 and PD-L2 on B cells between HD and SLE patients was similar. Notably, 48 hour stimulation of B cells with IL2/IL10, aBCR, CpG and CD40L gave rise to twofold reduced expression of PD-L1 by SLE compared to HD B cells. Interestingly, PD-L1 expression by SLE B cells was increased only in presence of CD40L, whereas in HD the mix of CpG, aBCR, and IL2/IL10 led also to a significant increase in PD-L1 expression.



**Abstract AB0150 – Figure 1.** Diminished PD-L1 expression in activated B cells may explain increased activation of T cells in SLE. (A) CD40L activated HD B cells upregulate PD-L1 that suppress activated T cells via PD-1. (B) CD40L activated SLE B cells fail to upregulate PD-L1 leaving activated T cells unchecked



**Conclusions:** The data suggest that activation of B cells from SLE patients require CD40/CD40L interaction to increase PD-L1 expression, which is, however, reduced compared to HD. Diminished PD-L1 expression upon B cell stimulation is consistent with impaired inhibition of T cells in SLE (figure 1).

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**Disclosure of Interest:** None declared

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#### AB0151 CHARACTERIZATION OF THE PLASMATIC GLYCOPROTEIN AND LIPOPROTEIN PROFILES OF SYSTEMIC LUPUS ERYTHEMATOSUS BY NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY

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**Background:** Systemic Lupus Erythematosus (SLE) is an autoimmune disease associated with systemic inflammatory processes. Chronic inflammation alters the number and type of non-cellular elements, including lipoproteins and glycoproteins.

**Objectives:** Here we investigate the plasmatic lipoprotein and glycoprotein profiles associated with SLE.

**Methods:** Plasma samples were obtained from 50 healthy control individuals and 50 SLE patients. All patients fulfilled the ACR criteria for classification of SLE. <sup>1</sup>H-NMR was used to determine the lipoprotein and glycoprotein profiles from cases and controls. For the lipoprotein profiles, VLDL, LDL, IDL and HDL concentration, lipid composition and particle properties were quantified. The glycoprotein profile was decomposed in four reproducible peak regions LMW, Glyc-B, Glyc-A, Glyc-Lipid and baseline, and quantified for concentration, position and aggregation state. Association analysis to disease was performed using logistic regression fitting for age, gender and body mass index. Classifiers were built using recursive-partition algorithm and classification accuracy was evaluated using receiver operating curves.

**Results:** We found a significant perturbation of the lipoprotein profile in SLE patients compared to controls. A statistically significant ( $P < 0.05$ ) reduction of cholesterol-LDL and HDL lipoproteins as well as an increase in triglyceride VLDL was found in SLE. Particle number for LDLs, were found to be reduced compared to controls ( $P < 0.05$ ), and mostly due to lower quantities of large LDL particles ( $P < 0.005$ ). The glycoprotein profile was also significantly altered for several NMR measures. The most significant changes were related to the reduction of the width and area of the Glyc-Lipid peak in SLE patients ( $P < 0.005$  and  $P < 0.05$ ,

respectively). Using the plasma molecular patterns to predict the presence of SLE, we found a significant classifier for the lipoprotein pattern (ROC AUC(95% CI)=0.85(0.78–0.93)), and an optimal classifier for the glycoprotein pattern (ROC AUC(95%CI)=0.90(0.84–0.97))

**Conclusions:** SLE is characterized by perturbations of the plasmatic lipoprotein and glycoprotein profiles. The increase of triglyceride VLDL in patients compared to controls, could explain the increased risk for cardiovascular disease observed in SLE. Our results also show that SLE patients have a significantly different glycoprotein profile compared to controls. In both cases, plasmatic <sup>1</sup>H-NMR profiling could be a valuable source of informative biomarkers for SLE.

**Disclosure of Interest:** None declared

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#### AB0152 MICROARRAYS GENE EXPRESSION PROFILING OF MONOCYTES FROM SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: NOVEL GENES AND PATHWAYS INVOLVED IN THE DISEASE

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**Objectives:** 1. To identify altered genes and pathways in monocytes from Systemic Lupus Erythematosus (SLE) patients involved in the pathogenesis of the disease. 2. To evaluate the contribution of anti-dsDNA antibodies to the regulation of these processes.

**Methods:** Eighty three subjects, including 53 SLE patients and 30 healthy donors (HDs), were recruited. Total RNA was extracted from monocytes isolated of 6 subjects .analyzed as exploratory cohort- and microarray studies were performed in an Agilent G4112F platform (Whole Human Genome Microarray 44k). By using the Ingenuity Pathway Analysis Software (IPA) the altered gene, pathways, and network profiles were identified and functionally categorised. The top differentially expressed genes were validated by RT-PCR in monocytes purified from all the subjects enrolled. The inflammatory profile was evaluated in serum by multiplex assay. The activation of intracellular proteins was analysed by PathScan intracellular signalling protein array. Correlation and association studies were performed with clinical and analytical variables. The effect of anti-ds-DNA antibodies in the altered gene expression signature was evaluated by in vitro studies on monocytes from HD

**Results:** Microarray gene expression profiling identified 553 significantly altered genes in monocytes from SLE patients in relation to HDs ( $p < 0.05$  and fold change  $> 2$ ). IPA analysis showed that the altered genes were mainly related to inflammatory and immunological disease (32,4%), as well as cardiovascular (22,5%), neurological (21,9%), musculoskeletal (10%), renal (6,5%), dermatological (4,5%) and reproductive system disorders (2,2%). The top altered canonical pathway identified was the interferon signalling, and the main altered genes, validated by RT-PCR, were PGC1- $\alpha$  (master regulator of mitochondrial biogenesis and oxidative stress), IFI27, IFI44, IFI44L, IFIT1, IFI6 and RSAD2 (interferon signalling), EDNRB (endothelin receptor involved in the vascular system homeostasis), SERPINE1 (serpine related to haematopoiesis and apoptosis), CDKN1B and CCND2 (proliferation regulators), and IL22RA1 and CMKLR1 (inflammatory mediators). The altered gene signature was associated with the presence of anti-dsDNA antibodies, and clinical features of SLE (early atherosclerosis and nephropathy), and correlated with the disease activity and the levels of inflammatory serum markers (CRP, ESR, C3, C4, IL8, MCP1, IFN $\gamma$ , IP10, PDGFBB). The activation of numerous intracellular signalling proteins was also noticed. *In vitro* studies demonstrated the modulation of several genes by effect of anti-dsDNA.

**Conclusions:** Gene expression profile allowed the identification of relevant genes and pathways altered in monocytes of SLE patients, which were associated with the pathogenesis of the disease and modulated, at least partially, by anti-dsDNA. The identification of relevant genes whose products regulate specific pathological processes might contribute to the development of targeted therapies in SLE

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AB0153

**FUNCTIONAL CHARACTERIZATION OF THE SJÖGREN'S SYNDROME-ASSOCIATED LOCUS DDX6-CXCR5**

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**Background:** Sjögren's syndrome (SS) is a chronic, heterogeneous disease with hallmark features of auto-inflammation and autoantibody production. We previously identified association between the *DDX6-CXCR5* locus and SS surpassing genome-wide significance.

**Objectives:** This study aims to determine the mechanism by which this association contributes to disease.

**Methods:** Fine mapping and imputation allowed enrichment of existing genetic datasets from a total of 1916 SS cases and 3684 controls with 971 testable variants in the *DDX6-CXCR5* interval. Candidate variants were prioritized using statistical and bioinformatics approaches. Electromobility shift assays (EMSAs) and pull-downs (PDs) followed by mass spectrometry (MS) were used to determine allelic-specific differences in binding using lysates from HSB-2 (T), Jurkat (T), Reh (B), Ramos (B), Daudi (B), THP-1 (monocyte), and HEK 293T (epithelial) cells.

**Results:** Bioinformatic analysis of the top associated variants after imputation (rs7125066 and rs7119038) in the *DDX6-CXCR5* region did not yield evidence of regional functionality. However, 46 other candidates that span the region of association were identified through imputation. Chromatin methylation pattern data from the Roadmap database showed several variants in this region were within transcription start sites or enhancer elements depending on the cell type and state. Using RegulomeDB, Haploreg, and other databases, rs4938572, rs12365699, rs57494551, and rs10892294 showed strong evidence affecting binding and/or expression of one or more target genes in the region and were selected for further study. Using EMSAs, statistically significant increase in binding for the risk allele as compared to the non-risk allele was found for rs4938572 ( $p < 0.01$ ) for cell lysates from HSB-2, Reh, THP-1, Ramos, Jurkat, and Daudi but not HEK 293T cells. While decreased binding of risk allele for rs10892294 and rs12365699 were found for Ramos cells only, rs57494551 showed decreased binding for both Ramos and THP-1 cell lysate. The risk allele of rs57494551 also decreases binding using THP-1 cell lysate. Preliminary MS analysis showed several immune related transcription factors likely binding this region, including: IRF8, GTF1, RFX5, IKZF3, PAX5, and IKZF1. Cell type-specific expression of the genes in the region shows the expression of *DDX6* spans many immune cells subsets while the *CXCR5* expression is more restricted.

**Conclusions:** The genetic variants in the *DDX6-CXCR5* locus that were selected based on bioinformatics data resulted in a difference in the direction of binding, with the risk allele all residing on the same risk haplotype. The change in binding of protein to each associated variant likely would alter expression of both protein coding genes in a cell/context specific manner. Ongoing studies will assess the regulatory role of these sequences using luciferase assays and CRISPR/Cas9 based genetic modification of target SNPs in various cell types.

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AB0154

**NOTCH3 IS UPREGULATED IN LUPUS NEPHRITIS AND ITS DEFICIENCY ACCELERATES LUPUS PROGRESSION**

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**Background:** Systemic lupus erythematosus (SLE) is a chronic inflammatory disease that affects the kidneys in about 50% of patients. Lupus nephritis (LN) is a major risk factor for overall morbidity and mortality in SLE patients. Notch signaling constitutes an evolutionarily conserved pathway that determines major decisions in cell proliferation, survival, and differentiation.

**Objectives:** To address the role of Notch-3 signalling in the disease development of SLE and particularly LN.

**Methods:** We measured renal expression of Notch-3 in kidneys of both, LN patients and lupus-prone MRL.lpr mice. Notch-3<sup>-/-</sup> and B6. Fas<sup>lpr/lpr</sup> mice were

crossbred to generate a B6. Fas<sup>lpr/lpr</sup> Notch-3<sup>-/-</sup> genotype and we analyzed the spontaneous disease manifestations in 40 week-old mice. Furthermore, we administered antisense oligodeoxynucleotides (ODNs) targeting Notch-3 or scrambled controls in the more aggressive lupus-prone mice strain (MRL. Fas<sup>lpr/lpr</sup>) mice starting at week 12 for 3 weeks and analyzed these mice at the age of 16 weeks.

**Results:** In 20-week old MRL.lpr mice, receptor Notch-3 and its target gene *Hes2* were significantly up-regulated in kidneys in comparison to 8 and 12 week-old littermates. *De novo* renal Notch-3 expression in lupus mice and SLE patients was especially pronounced in the glomerular compartment. B6. Fas<sup>lpr/lpr</sup> Notch-3<sup>-/-</sup> mice exhibited an aggravated lupus phenotype with earlier mortality, increased lymph nodes/spleen size, enhanced glomerular collagen IV deposition and increased immune cell infiltration in the kidneys. In line with this, application of anti-sense Notch-3 ODNs in MRL.lpr mice at the time of the transition from clinically inapparent to a manifested disease state (starting at week 12), resulted in accelerated disease progression as evidenced by enhanced lymphadenopathy, splenomegaly and an increase of inflammatory markers

**Conclusions:** Overall, these results demonstrate that Notch-3 exerts protective effects in the course of SLE, and its deficiency or inhibition accelerates the development of SLE manifestations.

**Disclosure of Interest:** None declared

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AB0155

**1,25 DIHYDROXYVITAMIN D SUPPLEMENTATION REDUCES HIND PAW EDEMA IN PRISTANE-INDUCED LUPUS MODEL**

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**Background:** Systemic lupus erythematosus (SLE) is a multifactorial, autoimmune inflammatory disease with pleomorphic clinical manifestations involving different organs and tissues. Vitamin D (VITD) deficiency is highly prevalent and evidence is mounting that it contributes to the morbidity and mortality in SLE. VITD is an essential steroid hormone with well-established effects on mineral metabolism, skeletal health, and more recently established profound effects on immune system health.

**Objectives:** To evaluate the development of SLE after VITD supplementation in pristane-induced lupus model.

**Methods:** Female BALB/c mice divided into 3 groups: healthy animals (CO), SLE animals (PIL) and SLE animals + vitamin D supplementation (PIL+VITD). PIL +VITD group received a subcutaneous injection of Calcijex® [2 ug/kg] in PBS-Tween 20 buffer every second day during 180 days. Animals were monitored every 2 months for body weight, free exploratory locomotion, grip strength, endurance exercise performance and edema size. Interleukin 2 (IL-2), IL-4, IL-6, IFN-γ and TNF-α were measured by Luminex technology. The histological and immunofluorescence parameters (IgG, IgM and C3) of the kidney and the joints are under analysis. Data was analyzed with ANOVA Two-Way followed by Bonferroni and independent sample t-test.  $p < 0.05$  was considered significant. All data are represented as Mean±SEM.

**Results:** When compared with CO group (5.12±1.23 g), both PIL (7.53±1.09 g) and PIL+VIT D (8.08±2.28 g) groups exhibited a greater body weight gain by day 180 of the experiment ( $p < 0.05$ ). There was no statistically significant difference in free exploratory locomotion and grip strength between the groups, but both the PIL (29.39±6.75 min) and the PIL+VITD (25.75±12.48 min) groups showed increased fatigue compared to the CO group (42.08±3.47 min). Still, VITD supplementation reduced mean paw swelling to compared PIL group (0.207±0.29 vs 0.24±0.051,  $p < 0.05$ )

**Conclusions:** The supplementation of VITD improves the clinical severity of PIL-manifestations, such as the reduction of hind paw edema. Further analysis of the histology of the joints and the kidney will complement the evaluation of the vitamin D modulating effects on the immune system.

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AB0156

**POLYSACCHARIDES FROM DENDROBIUM OFFICINALE AMELIORATE THE DEVELOPMENT OF MURINE SJÖGREN'S SYNDROME VIA INDUCING IL-10-PRODUCING B CELLS**

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**Background:** Primary Sjögren's syndrome (SS) is a chronic autoimmune disease with salivary gland (SG) hypofunction and inflammation. Currently, effective

therapies for SS patients are still lacking. Polysaccharides derived from *Dendrobium officinale* (DOP) have been shown to possess immunomodulatory functions in various animal models. However, it remains unclear whether DOP can modulate immune responses and have potential therapeutic effects on SS.

**Objectives:** To investigate the immune modulatory and therapeutic effects of DOP on experimental SS (ESS) in mice.

**Methods:** Polysaccharides were extracted from *Dendrobium officinale* with removal of endotoxin. C57BL/6 mice were immunized with SG-derived proteins for ESS induction, followed by daily oral treatment of vehicle and different dosages of DOP. SG functions were assessed by monitoring saliva flow rates whereas lymphocytic infiltration and tissue destruction in SG were examined by histological analysis. Both T and B cell populations in peripheral lymphoid organs were analyzed by flow cytometry. The effects of DOP on IL-10-producing B cell (B10 cell) induction and Th17 cell differentiation were examined in culture. Moreover, TLR4 and TLR9 inhibitors were used to identify the function of TLR4/TLR9 in DOP-mediated effects.

**Results:** ESS mice with DOP treatment displayed significantly higher saliva flow rates than vehicle-treated ESS mice. DOP treatment ameliorated SG tissue destruction accompanied with profoundly reduced lymphocytic infiltration in ESS mice when compared with vehicle-treated counterparts. Moreover, DOP treatment markedly increased the numbers of B10 cells but decreased numbers of Th17 cells in peripheral lymphoid organs of ESS mice. Notably, DOP markedly increased frequencies and numbers of B10 cells but did not affect Th17 cells generation in culture. Moreover, TLR4 inhibitor, but not TLR9 inhibitor, significantly suppressed DOP-induced IL-10 production in B cells.

**Conclusions:** The results show that DOP treatment ameliorates ESS disease development by inducing regulatory B10 cells, suggesting that DOP might be a promising candidate for treating SS.

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#### AB0157 TARGETING T-CELL TRAFFICKING IN A MURINE MODEL OF SJÖGREN'S SYNDROME

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**Background:** Salivary glands of primary Sjögren's syndrome (pSS) are characterised by complex leukocyte infiltration organised into tertiary lymphoid structures (TLS). The mechanisms regulating leukocyte trafficking into inflamed salivary glands are poorly described, but dysregulated T-cell recruitment during inflammation is believed to contribute to disease onset and chronicity. We recently described a homeostatic pathway in which a B cell-derived peptide (PEPITEM), secreted in response to adiponectin, regulates T-cell trafficking during inflammation via sphingosine-1-phosphate activity on endothelial cells<sup>1</sup>. Disruption of this pathway by downregulation of adiponectin receptors on circulating B cells has been demonstrated in type-1 diabetes and rheumatoid arthritis, suggesting a potential role for PEPITEM in the pathogenesis of autoimmune diseases, and indicating a role for adiponectin receptors as biomarkers in these conditions<sup>1</sup>.

**Objectives:** We aimed to investigate the efficacy of PEPITEM as an inhibitor of T-cell trafficking in an inducible animal model of salivary gland inflammation that mimics the histological features of pSS, and to investigate the potential translatability of this pathway in patients with pSS.

**Methods:** Submandibular salivary glands of C57BL/6 mice were intra-ductally cannulated with luciferase-encoding replication-deficient adenovirus to induce TLS formation as previously described<sup>2</sup>. Mice were administered daily either PBS or PEPITEM by intraperitoneal injection from day 0, and their salivary glands dissected at day 5 post cannulation. T-cell infiltration into salivary glands was assessed using a combination of flow cytometry, immunofluorescence, and qRT-PCR for inflammatory chemokines.

**Results:** B cells in sera from cannulated animals express lower levels of both adiponectin receptors 1 and 2 in comparison with non-inflamed control mice. In cannulated animals treated with PEPITEM, histological analysis of salivary glands revealed fewer, as well as less aggregated, infiltrating T cells. Both CD4<sup>+</sup> and CD8<sup>+</sup> numbers were significantly lower in the salivary glands of PEPITEM-treated animals. Furthermore, administration of PEPITEM also decreased mRNA transcripts for lymphotoxin beta, IL-7, lymphoid chemokines (CCL19 and CXCL13)

and T-cell chemokine receptor CCR7, cytokines and chemokines known to regulate ectopic lymphoneogenesis in pSS. Samples from pSS patients are currently being assessed to validate the relevance of this pathway in pSS.

**Conclusions:** These results demonstrate that administration of exogenous PEPITEM can reduce T-cell influx into salivary glands. This may represent a rescue of the homeostatic regulation of leukocyte trafficking which is disrupted in inflammation. Our work suggests that PEPITEM should be considered to address therapeutic needs in chronic inflammatory conditions, and that the detection of decreased levels of adiponectin receptors could serve as a biomarker in pSS.

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#### AB0158 HISTOLOGICAL AND SEROLOGICAL CHARACTERISTICS CONTRIBUTE TO DIVERGENT OUTCOMES FOR INDIGENOUS PATIENTS WITH LUPUS NEPHRITIS

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**Background:** Renal outcomes for Indigenous Australians (IA) with Lupus Nephritis (LN) are worse than for other ethnic groups.

**Objectives:** To investigate whether differences in renal biopsy findings can explain the worse renal outcome in Indigenous patients

**Methods:** A single centre cohort study of 83 SLE patients undergoing a first renal biopsy at our institution for LN evaluation. Histological assessment included review of ISN classification, A/AC/C sub classification, NIH tubulointerstitial activity and chronicity indices, tubulointerstitial index, semiquantitative IF scores for IgG, IgM, IgA, C3 and C1q deposits, localisation of electron dense deposits (EDD) and presence of thrombosis, vasculitis and tubuloreticular inclusions (TRI). Differences in histological and routine clinical findings including autoantibody profiles between IA patients (n=11) and the pooled data from Asian (n=29) and Caucasian (n=43) patients were analysed by non-parametric statistical methods.

**Results:** IA patients were younger at diagnosis (31 vs 38.5 years., p=0.08) and their biopsies contained fewer glomeruli (11 vs 21, p<0.01), more class I/II (28 vs 15%) and no class V lesions (0 vs 21%) (p=0.06 for overall comparison). IA patients were less likely to have cellular crescents (0 vs. 25%, p=0.03), more likely to have fibrous crescents and a low tubulointerstitial index (p=0.08). The overall AI (5.1 vs 4.9) and CI scores (1.1 vs. 1.3) or presence of full house IF deposits (67 vs 71%), renal thrombosis (0 vs 4%) or TRI (55 vs. 39%) was similar across groups (all p>0.3). IA patients had lower eGFR (43 vs 65, p=0.025), more often carried anti-SSA52kd Ab (73 vs 33%, p=0.02) and during a mean follow-up of almost nine years, had a higher proportion of patients developing ESRD (18 vs 3%, p=0.02).

**Conclusions:** IA patients with SLE who develop LN have fewer glomeruli, an increased frequency of mesangial abnormalities with absence of cellular crescents and membranous nephropathy and a high prevalence of anti-SSA 52KD Ab. Although based on small numbers, this suggests that lower nephron mass and immunological pathways involving IFN-inducible anti-SSA expression may contribute to LN development and worse renal outcome in Indigenous patients.

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#### AB0159 CYTOKINE PRODUCTION BY ACTIVATED PLASMACYTOID DENDRITIC CELLS AND NK CELLS IS SUPPRESSED BY AN IRAK4 INHIBITOR

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**Background:** In SLE, immune complexes containing self-derived DNA or RNA (RNA-IC) trigger the synthesis of several pro-inflammatory cytokines by immune cells. Treatment with anti-malarials, such as hydroxychloroquine (HCQ), which



through endosomal TLR inhibition effectively blocks IFN- $\alpha$ , is standard of care. However, few patients experience complete remission.

**Objectives:** We asked how an IL-1 receptor associated kinase 4 (IRAK-4) inhibitor I92 (ND-2158, Nimbus Discovery),<sup>1</sup> acting downstream of TLR 7/9, affects RNA-IC-induced cytokine production compared to hydroxychloroquine (HCQ).

**Methods:** Plasmacytoid dendritic cells (pDCs) and natural killer (NK) cells were isolated from peripheral blood mononuclear cells (PBMCs) of healthy individuals. PBMCs from 15 SLE patients were depleted of monocytes. Cells were stimulated with RNA-IC, consisting of IgG from SLE patient sera and U1snRNP particles, in the presence or absence of I92 or HCQ. Cytokines were measured by immunoassays or flow cytometry. RNA-sequencing was performed on RNA-IC stimulated pDCs from four healthy individuals and the effect of I92 and HCQ was assessed.

**Results:** RNA-IC induced IFN- $\alpha$ , TNF- $\alpha$ , IL-6, IL-8, IFN- $\gamma$ , MIP1- $\alpha$  and MIP1- $\beta$  production in pDC and NK cell co-cultures. I92 reduced the pDC and NK cell derived cytokine production by 74.95%. HCQ interfered with cytokine production in pDCs, but not in NK cells. In monocyte-depleted SLE PBMCs I92 blocked TNF- $\alpha$ , IFN- $\gamma$ , MIP1- $\alpha$  and MIP1- $\beta$  production more efficiently than HCQ. IL-8 production was high in monocyte depleted PBMC from SLE patients, and not blocked by neither drug, despite significant inhibition of IL-8 in pDC-NK co-cultures from healthy individuals. Following RNA-IC activation of pDCs, 975 differentially expressed genes were observed (FDR<0.05), many connected to cytokine pathways, cell regulation and apoptosis. The IRAK4 inhibitor significantly changed more RNA-IC induced genes than HCQ (492 vs. 65 genes). Several top upregulated genes were reversed by both I92 and HCQ, including *IFNA2*, *IFIT2-3*, *OASL*, *CXCL10*, *CD274*, *TNFSF10*, *APOL6*. Genes such as *DKK4*, *LAD1* and *EAF2* were significantly more downregulated by I92 than by HCQ.

**Conclusions:** Whereas both HCQ and the IRAK4 inhibitor block important pro-inflammatory cytokines, the IRAK4i I92 exhibits a broader inhibitory effect than HCQ on pathways triggered by RNA-IC, which suggests that IRAK4 inhibition could be a future therapeutic option in SLE and possibly other systemic autoimmune diseases characterized by the presence of ICs containing nucleic acid.

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#### AB0160 LOSS OF LET-7 MICRORNA UPREGULATES IL-6 IN BONE MARROW-DERIVED MESENCHYMAL STEM CELLS TRIGGERING TREG/TH17 IMBALANCE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Systemic lupus erythematosus (SLE) patients exist an imbalance between CD4+CD25+FoxP3+ T regulatory (Treg) and IL-17-producing cells (Th17). Correction of this Treg/Th17 imbalance may have therapeutic impact for SLE patients. Our previous study demonstrated that bone marrow derived mesenchymal stem cells (BMSCs) from SLE patients are defective in immune modulation, which might be involved in Treg/Th17 imbalance and disease onset, but the mechanisms are not clear yet. The expression imbalance of microRNAs (miRNAs) can cause cell dysfunction, which participates in a variety of diseases development. As an important computer predicted target of let-7, interleukin-6 (IL-6) is an important negative immune regulatory factors secreted by BMSCs. Our previous experiments found that the expressions of let-7 are markedly down-regulated in SLE BMSCs by microRNA array analysis, and the synthesis of IL-6 is significantly higher in SLE BMSCs compared to normal controls.

**Objectives:** To investigate whether loss of let-7 could play its role in SLE BMSCs immune modulation defects by directly up-regulating IL-6 mRNA, which might contribute to Treg/Th17 imbalance in PBMCs from SLE patients, to further understand the pathogenesis of SLE.

**Methods:** BMSCs were isolated, cultured and expanded from iliac crest bone marrow of four healthy donors and four SLE patients. Real-time PCR was used to further determine the let-7 expression and IL-6 mRNA level in BMSCs from healthy controls and SLE patients. The important computer predicted target of let-7, IL-6 was determined using the luciferase reporter assay. Let-7-mimics, let-7-inhibitor, and let-7-negative control were transfected to BMSCs with using Lipofectamine 2000. BMSCs from healthy controls and SLE patients were co-cultured

with PBMCs from SLE patients for 72 hours to detect their effect on the ratio of Treg/Th17.

**Results:** Compared to normal controls, the expression of let-7 was markedly down-regulated in BMSCs from SLE patients by RT-PCR, and the synthesis of IL-6 mRNA and protein levels were significantly higher in BMSCs from SLE patients. Compared to let-7-negative controls, transfection of BMSCs with let-7-mimics markedly lower synthesis of TGF- $\beta$ 1 mRNA, and let-7-inhibitor led to an opposite effect. The mean value of Treg/Th17 was significantly decreased in PBMCs from SLE patients compared to normal controls. Transfection of normal BMSCs with let-7-inhibitor caused significant downregulation of Treg/Th17 compared to let-7-negative controls, while transfection with let-7-mimics led to an opposite effect.

**Conclusions:** SLE patients exist an imbalance between Treg and Th17 cells, which might be associated with up-regulation of IL-6 secretion of BMSCs by loss of let-7.

**Disclosure of Interest:** None declared

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#### AB0161 INTERLEUKIN-37: A THERAPEUTIC FOR LUPUS NEPHRITIS IN MRL-FASLPR MICE

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**Background:** Systemic lupus erythematosus (SLE) is a serious and noticed autoimmune disease, and lupus nephritis (LN) as one of its major complications without effective treatment. IL-37 has been identified as a natural inhibitor of innate immunity. Although increasing evidence shown that serum IL-37 correlated with SLEDAI and nephritis activity, However, it is still unclear that the therapeutic effect of IL-37 on lupus mice *in vivo*.

**Objectives:** This study aims to determine the inhibitory effect of IL-37 in lupus mice and lupus nephritis *in vivo*, and to expose the IL-37 related mechanisms of cell and molecules that inhibits the inflammation in lupus nephritis.

**Methods:** MRL-Fas<sup>lpr</sup> mice with mild and advanced disease were treated with lentiviral vector pLVX-IL-37b. The protein levels of IL-37b in serum and tissue, IL-17, IL-6, IL-10 and TGF $\beta$ -3 produced by cell culture from spleen and kidney of mice were measured by ELISA, the relative mRNA expression of these cytokines in PBMCs was detected by RT-PCR, and the frequency of Th17 and Treg cells in splenocyte were determined by FACS.

**Results:** Our results show that IL-37 was highly effective in prolonging survival, alleviating the pathologic characteristics of lupus nephritis (LN) in MRL-Fas<sup>lpr</sup> mice by reducing the autoimmune complex deposition such as IgM, IgG and C3, decreasing the production of Inflammatory cytokines such as IL-17, IL-6 and promoting the anti-inflammatory cytokines IL-10 and TGF $\beta$ -3. We also found that IL-37 protect lupus mice from LN associated with increasing the frequency of Treg cells and reducing the frequency of Th17 cells.

**Conclusions:** These results indicate the protective action of IL-37 in LN, and strengthen the support for IL-37 as a new target for therapy of SLE.

**Disclosure of Interest:** None declared

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#### AB0162 KLRG1 EXPRESSION IS REDUCED ON NK CELLS FROM SLE PATIENTS AND INVERSELY CORRELATES WITH DISEASE ACTIVITY AND CLINICAL FEATURES

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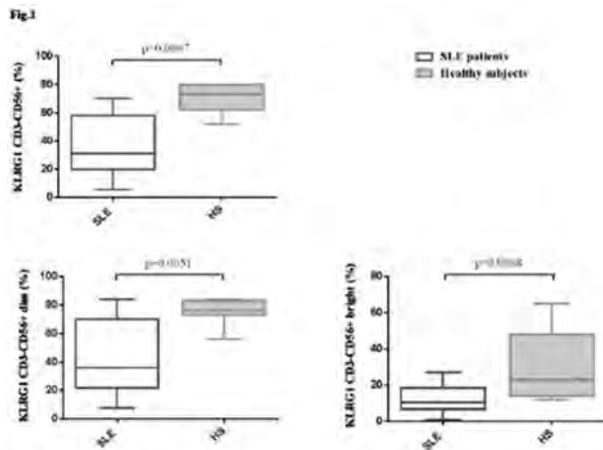
**Background:** Systemic Lupus Erythematosus (SLE) is a multifactorial autoimmune disease, with different immunological alterations and clinical phenotypes. Natural killer (NK) cells participate in the regulation of several immune responses but their function in SLE is not well understood.<sup>1</sup> KLRG1 (killer cell lectin like receptor G1) is a trans-membrane protein expressed in humans especially on NK cells, working as an inhibitory receptor of their cytotoxic activity. Thus, KLRG1-mediated signal might have a role in preventing autoimmunity, increasing the activation threshold of NK cells.<sup>2</sup> KLRG1 gene also, emerged as a disease susceptibility gene for SLE in four different ethnic groups.<sup>3</sup>

**Objectives:** The aim of this study was to characterize KLRG1 expression on NK cells (both CD56<sup>dim</sup> and CD56<sup>bright</sup>) from SLE patients compared to healthy subjects (HS) and to investigate its possible correlations with clinical features, including SLE disease activity.

**Methods:** We enrolled 14 patients (14F, mean age $\pm$ SD 37 $\pm$ 10.7 years, mean disease duration  $\pm$ SD 10.5 $\pm$ 7.9 years) affected by SLE according to the 1997 ACR criteria, and 7 HS (7F, mean age $\pm$ SD 33 $\pm$ 5.5 years). Disease activity was measured by SLEDAI-2K. Peripheral blood mononuclear cells (PBMCs) were purified

and phenotypic characterization was performed. All experiments were conducted by flow cytometry.

**Results:** KLRG1 was expressed in a statistically significant lower amount on total NK cells from SLE patients compared to HS ( $p=0.0007$ ). Analysis of CD56<sup>dim</sup> and CD56<sup>bright</sup> populations showed less amount of KLRG1 in SLE patients compared to HS ( $p=0.0051$  and  $p=0.0068$ ) (figure 1). The low levels of KLRG1 on NK cells inversely correlated with the SLEDAI-2K ( $p=0.029$ ) and were inversely associated with the presence of arthritis ( $p=0.029$ ), arthralgias ( $p=0.0024$ ) and hematological disorders ( $p=0.025$ ). A direct association between KLRG1 expression on NK cells and the use of HCQ was found ( $p=0.001$ ). Analyzing the two main subpopulations of NK cells, we observed an inverse association between KLRG1 on CD56<sup>dim</sup> cells and arthritis ( $p=0.0089$ ), arthralgias ( $p=0.0001$ ), hematological disorders ( $p=0.0329$ ) and SLEDAI-2K ( $p=0.0105$ ). KLRG1 on CD56<sup>dim</sup> was directly associated with the use of HCQ ( $p=0.0010$ ). KLRG1 on CD56<sup>bright</sup> cells was also directly associated with the use of HCQ and MMF ( $p=0.03$  and  $p=0.014$ ).



Abstract AB0162 – Figure 1

**Conclusions:** This study shows for the first time a reduced expression of KLRG1 in SLE patients. The inverse associations between the levels of this receptor on NK cells and the SLEDAI-2K and clinical features, together with the direct association with HCQ and MMF, suggest a possible role of KLRG1 in the pathogenesis of this disease. KLRG1 could be a possible therapeutic target in SLE.

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#### AB0163 INCREASED ERYPTOSIS LEVELS IN ERYTHROCYTES TREATED WITH ANTIBODIES FROM APS PATIENTS: ERYPTOSIS AS NEW ACTOR IN APS PATHOGENESIS

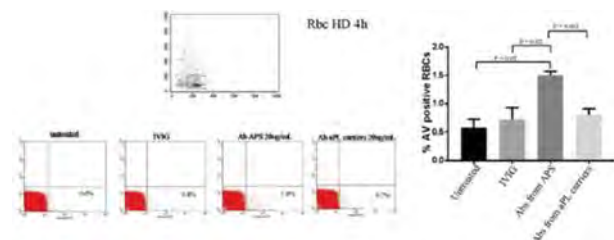
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**Background:** Erythrocytes (RBCs) are highly sensitive cells constantly exposed to several stress stimuli including inflammatory mediators. Despite the absence of nuclei and the lack of crucial elements in the machinery of apoptosis, they have developed a rapid self-destruction process called eryptosis. During this process the externalization of phosphatidylserine (PS) activates the correct elimination of erythrocytes by phagocytes preventing inflammation and intravascular hemolysis. It has been recently demonstrated that PS-exposing erythrocytes are able to adhere to endothelial cells causing an impairment of circulation,<sup>1</sup> suggesting a possible involvement of eryptosis in the increased risk of thrombotic episodes typical of antiphospholipid syndrome (APS).

**Objectives:** Enhanced eryptosis is known to contribute to several pathological conditions but the role of this process in APS has not been investigated yet. For this reason, we evaluated the effect of antibodies (Abs) purified from APS patients and healthy subjects positive for antiphospholipid antibodies without clinical manifestations (aPL carriers) on eryptosis activation. Moreover, spontaneous eryptosis levels in APS, aPL carriers, autoimmune haemolytic anaemia (AIHA) and healthy donors (HD) were analyzed.

**Methods:** 30 patients with primary APS (M/F 7/23, mean age 50.5±8.2 years), 17 aPL carriers (M/F 4/13, mean age 48.6±8.3 years) were recruited after written informed consent. Moreover 13 AIHA patients and 17 HD were also enrolled as positive and negative control group respectively. Ammonium sulfate precipitation is used to purify Abs from sera of APS and aPL carriers subjects. RBCs, isolated from whole blood by centrifugation, were incubated with APS and aPL carriers Abs at concentration of 20ug/mL and after 4 hours the percentage of annexin V-positive cells (PS-exposing cells) was analyzed by flow cytometry. The same technique was used to estimate spontaneous eryptosis levels in all cohorts studied.

**Results:** *In vitro* Abs from APS induced eryptosis in RBCs isolated from HD after 4 hours of culture compared to untreated and RBCs stimulated with Intravenous Immunoglobulins (IVIg), both  $p=0.02$ . On the contrary, Abs from aPL carriers had no effect on the percentage of PS-exposing RBCs (figure 1). *Ex vivo*, APS patients showed higher levels of spontaneous eryptosis compared to HD ( $p=0.001$ ). As expected, eryptosis was upregulated in AIHA patients compared to all populations studied ( $p<0.0001$ ). Interestingly, the percentage of annexin V-positive RBCs was lower in aPL carriers respect to APS patients ( $p=0.001$ ). No significant correlation between eryptosis and clinical parameters was found.



Abstract AB0163 – Figure 1

**Conclusions:** In this study we demonstrated a new aspect of APS pathogenesis based on the capacity of Abs isolated from APS patients, and not those from aPL carriers, to stimulate eryptosis suggesting a possible contribution of this process in APS clinical manifestations.

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**Disclosure of Interest:** None declared

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#### AB0164 NUMBERS OF B-LYMPHOCYTES INCREASE WHEN FORMATION OF LYMPHOEPITHELIAL LESIONS PROGRESSES IN SALIVARY GLANDS OF PRIMARY SJÖGREN'S SYNDROME PATIENTS

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**Background:** The major histopathological finding in salivary glands of primary Sjögren's syndrome (pSS) patients are periductal lymphocytic infiltrates (foci). In association with these infiltrates, lymphoepithelial lesions (LELs) may be formed. LELs are defined by infiltration of lymphocytes within the epithelium with hyperplasia of ductal cells. Although it has been suggested that B-lymphocytes predominate in LELs, the relative role of B- and T-lymphocytes in LEL formation is not known. Since LELs are a characteristic finding in salivary glands of pSS patients, quantification of B- and T-lymphocytes in the different stages of LEL development will give more insight in their formation as well as in the pathogenesis of pSS.

**Objectives:** To quantify the numbers of B- and T-lymphocytes in different stages of LEL development in parotid and labial gland biopsies of pSS patients.

**Methods:** The study population consisted of 15 pSS patients, who fulfilled the ACR-EULAR criteria and underwent salivary gland biopsies of both the parotid and labial gland. Patients were not treated with biologicals and 13 patients were not using other immunosuppressive therapy. Presence and severity of LELs were evaluated on HE stained sections. Severity of lesions was scored from stage 0 to stage 3 (stage 0: lymphocytic ductal infiltration without hyperplasia of the epithelium; stage 1: lymphocytic ductal infiltration and <50% hyperplastic epithelium; stage 2: lymphocytic ductal infiltration and ≥50% hyperplastic epithelium; stage 3: lymphocytic ductal infiltration and fully circumferentially hyperplastic epithelium with occluded lumen). Numbers of B- and T-lymphocytes within LELs were counted (10 ducts per biopsy) by using Image J cell counter on serial CD20 and CD3 stained sections. High molecular weight cytokeratin staining was used to identify ductal borders. Generalized estimating equations (GEE) were used to analyse the numbers of B- and T-lymphocytes and B/T ratio's over the different stages of severity of LELs.

**Results:** B- and T-lymphocytes can both infiltrate within the ductal epithelium forming LELs in salivary glands of pSS patients. T-lymphocytes were present in all LELs, scattered through the whole ductal epithelium. Whereas B-lymphocytes were found in clusters, mostly located in the hyperplastic area of the ductal epithelium. With higher severity of LELs, the numbers of B- and T-lymphocytes increased significantly, in both the parotid and labial gland. The numbers of B-lymphocytes increased relatively more with higher severity of LELs than T-lymphocytes. This has led to an increased intraepithelial B/T ratio in more pronounced LELs. This increased B/T ratio was even more pronounced in parotid than in labial glands. In both glands, there was a predominance of T-lymphocytes in lower LEL stages. In more severe LEL stages, B-lymphocytes outnumbered the T-lymphocytes.

**Conclusions:** Given the relative increase in the number of B-lymphocytes with higher severity of LELs as well as their close association with proliferating ductal epithelial cells, we conclude that B-lymphocytes play a major role in the hyperplasia of the ductal epithelium.

**Disclosure of Interest:** None declared

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#### AB0165 RANK/RANK-LIGAND INTERACTION REGULATES PATHOGENIC T CELL RECRUITMENT IN SJÖGREN'S SYNDROME

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**Background:** The RANKL (ligand)-RANK-OPG triad, members of the TNF(R) superfamily, is implicated in lymphoid organ development and bone homeostasis. It has recently been demonstrated that RANK-activated astrocytes release CCL20 and attract T cells to the central nervous system in a model of Multiple Sclerosis and that transgenic RANK expression in the skin promotes aberrant epithelial cell proliferation and is sufficient to induce ectopic formation of tertiary lymphoid structures (TLS). Ductal epithelial cells (SGEs) have been implicated in Sjögren's Syndrome (SS) pathogenesis where they mediate immune recruitment by expression of pro-inflammatory chemokines and support the formation of pre-malignant myoepithelial lesions.

**Objectives:** A combination of human and mouse studies were used to address the role of RANK-RANKL interaction in primary (p) SS.

**Methods:** Salivary glands (SGs) and saliva samples from patients recruited in the OASIS cohort (University of Birmingham) were studied to evaluate this pathway in human disease. Consecutive stimulated saliva samples (n=69) were analysed using Proseek Multiplex INF<sup>96 × 96</sup>, covering 92 unique inflammation-related protein biomarkers. Taking advantage of a viral induced model of pSS we studied the effect of this pathway with a RANKL blocking antibody and by inducing gain of function with direct cannulation in the salivary glands of recombinant RANKL. Murine SGs were studied by immunofluorescence, flow cytometry and qPCR on total tissue and sorted cells.

**Results:** Fourteen proteins in saliva were significantly separated between pSS and sicca controls, and elevated levels of just two proteins, RANKL and TNFβ, could classify pSS or sicca with 75% accuracy. Levels of salivary RANKL and CCL20 were strongly correlated (r=0.6; p<0.01). We demonstrated that both human and murine inflamed SGEs upregulate both RANK and CCL20, a chemokine known to recruit pathogenic T cells. Upregulation of RANKL was found in human Th2 cells, classically associated with humoral responses and germinal centre (GC) formation. SGs from mice treated with anti-RANKL antibody showed decreased epithelial proliferation, reduced T cell infiltration and defective TLS

establishment. On the contrary, viral infected SGs treated with recombinant RANKL showed increased T cell infiltration, CCL20 expression and enhanced differentiation of GC B cells.

**Conclusions:** *In vivo* RANK/RANKL interaction mediates recruitment of activated T cells that are skewed toward a Th2 phenotype. These, in turn, will favour the establishment of TLS in the SG. Those data were confirmed in human pSS, where expression of RANK is found in inflamed epithelium and RANKL detection in saliva is able to differentiate patients with pSS from sicca controls, thus candidates this pathway both for drug targeting and patient stratification.

**Disclosure of Interest:** None declared

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#### AB0166 TRACKING OF MUCOCUTANEOUS AND MUSCULOSKELETAL FLARES IN SLE USING SERUM FAS, FERRITIN, IGFBP2 AND sTNFR II

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**Background:** SLE is a multisystemic autoimmune disease characterized by unpredictable disease course with periods of flares and remission. The lack of reliable methods which can predict a disease flare hampers the exploration of effective and preventive strategies for disease relapses.

**Objectives:** To study the performance of serum FAS, sTNFR II, Igfbp2 and Ferritin as biomarkers for tracking lupus flares in non-renal SLE patients.

**Methods:** Twenty-nine patients, who met the requirements of American College of Rheumatology (ACR) for classification of SLE, were recruited from Oklahoma Medical Research Foundation (OMRF) for serological testing of all four serum protein markers. None of the patients had lupus nephritis. Serum samples were obtained over 4 consecutive visits. Serum FAS, sTNFR II, Igfbp2 and Ferritin molecules were measured in all patients. Lupus disease activity was assessed by both SLEDAI and BILAG activity indices.

**Results:** In our study, all 4 tested biomarkers (FAS, Ferritin, Igfbp2 and sTNFR II) showed significant correlations with SLEDAI and BILAG. FAS (r= 0.36, p<0.0001 for SLEDAI & r= 0.29, p= 0.0002 for BILAG), Ferritin (r= 0.13, p=0.0494 for SLEDAI & r= 0.22, p= 0.0035 for BILAG), Igfbp2 (r= 0.24, p= 0.0013 for SLEDAI & r= 0.18, p= 0.0106 for BILAG) and sTNFR II (r= 0.30, p<0.0001 for SLEDAI & r= 0.19, p= 0.0112 for BILAG). When serial disease activity changes were examined, different serum markers performed better in different SLE patients, tracking with mucocutaneous or musculoskeletal disease flares. In studying a total of 72 disease intervals, FAS and Ferritin exhibited the highest concordance with concurrent disease activity (58–62%), followed by Igfbp2 (50%) and sTNFR II (46%), all of which were superior to the performance of complement C3, C4 and anti-DNA. Furthermore, adding FAS to other tested molecules increased its ability to track concordant disease activity changes (81% for FAS±Ferritin; 76% for FAS±Igfbp2 and FAS±sTNFR II).

**Conclusions:** Serum FAS and Ferritin emerge as potential serum markers for tracking mucocutaneous or musculoskeletal disease flares in SLE patients.

**Disclosure of Interest:** None declared

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#### AB0167 METFORMIN HAS ANTI-INFLAMMATORY POTENTIAL BY REDUCING P-GP EXPRESSION ON PBMCs OF PATIENTS WITH LUPUS

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**Background:** Metformin causes immunomodulation by activation of AMP-kinase and thereby inhibition of a mTOR pathway. Metformin reduces disease activity in lupus mouse models.<sup>1</sup> A study has shown that its use in lupus patients decreased corticosteroid dose and prevented flares.<sup>2</sup> P-glycoprotein expression is linked to drug resistance and increased cytokine production. Metformin inhibits expression of P-glycoprotein (P-gp) in cancer cells.<sup>3</sup> There is scarce data on effect of metformin on P-gp expression and cytokine secretion on immune cells in autoimmune diseases like lupus.

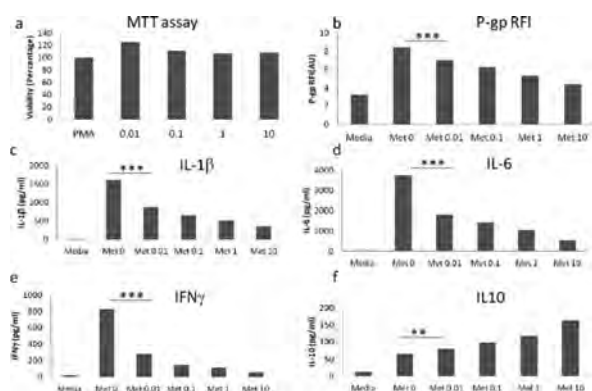
**Objectives:** To study the effect of metformin on P-gp expression in PBMCs of lupus patients and its effect on inflammatory cytokines secretion. To determine optimum concentration required for such an effect.

**Methods:** PBMCs of nine lupus patients (Mean age 30 yrs, all females) were cultured using RPMI medium and then stimulated with PMA/ ionomycin, with or without increasing dose of metformin (0.01, 0.1, 1, 10 mMol/L) for 24 h. Cytokines IL-1b, IL-6, IFN-g and IL-10 were analyzed by ELISA in culture supernatant. Cell



viability was independently assessed by MTT assay. P-gp expression was measured in same samples by flow-cytometry.

**Results:** In MTT assay viability of cells was maintained across all concentrations of metformin used in this study (figure 1a). Metformin decreased expression of P-gp in PBMCs in dose dependent manner ( $p=0.003$ ). (figure 1b). In the PBMC cultures with PMA and increasing concentration of metformin, there was decrease in production of pro-inflammatory cytokines: IL-1 $\beta$  ( $p=0.001$ ), IL-6 ( $p=0.007$ ) and IFN $\gamma$  ( $p<0.001$ ) at even the lowest concentration of metformin. There was increase in production of anti-inflammatory cytokine IL-10 ( $p=0.014$ ). The suppression of IL-1, IL-6, IFN $\gamma$  and increase in IL10 production was dose dependent.



**Abstract AB0167 – Figure 1.** a: MTT assay for cell viability (ns) b: P-gp expression with increasing metformin concentration (shown on X axis in mMOL/L), c,d,e,f: cytokine analyses of IL-1 $\beta$ , IL-6, IFN- $\gamma$  and IL-10 resp. In all experiments, PBMCs were stimulated by PMA and Metformin. \*\*\*= $P<0.01$ , \*\*= $P<0.03$

**Conclusions:** Metformin inhibits P-gp expression which is responsible for resistance to action of various drugs including corticosteroids which are cornerstones of treatment in SLE. Metformin thus may help to reduce corticosteroid dose. Anti-inflammatory activity seen in this study is occurring at concentrations which are therapeutically achievable. Plasma levels of metformin at the therapeutic doses commonly used for diabetes are usually around 0.01–0.04 mM/L.<sup>4</sup> Present study has demonstrated anti-inflammatory effect of metformin at this concentration. Metformin offers dual advantage which has anti-inflammatory activity and also has a potential to reduce drug resistance to other therapeutic agents.

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#### AB0168 ELEVATED SERUM LEVELS OF HMGB1 AND SRAGE IN PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME

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**Background:** Antiphospholipid syndrome (APS) is a systemic autoimmune disease characterised by the presence of at least one clinical event among vascular thrombosis and/or pregnancy morbidity, in the presence of circulating antiphospholipid antibodies (aPL). High-mobility group box-1 (HMGB1) is a non-histonic protein belonging to the family of alarmins. It is associated with chromatin and has

a dual function depending on the cell state: in basal conditions it is located in the nucleus and promotes the interaction of some transcription factors with DNA, in inflammatory conditions it is secreted in the extracellular space and exerts the functions of a pro-inflammatory cytokine. One of the main receptor system responsible for the HMGB1 activity is the "receptor for advanced glycation end products" (RAGE). Increased serum HMGB1 levels have been reported in patients with Systemic Lupus Erythematosus and pre-eclampsia, as other alarmins are increased in patients with early abortions.

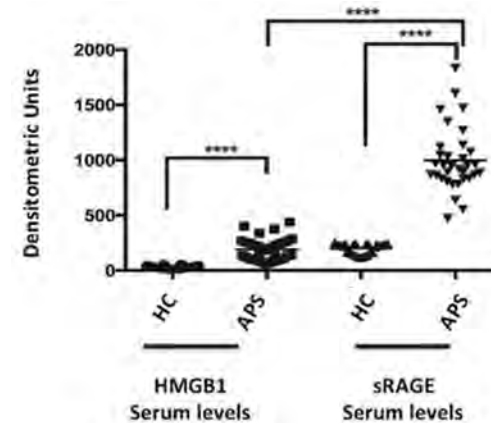
**Objectives:** To evaluate the serum levels of HMGB1 and soluble RAGE (sRAGE) in patients with obstetric and thrombotic APS.

**Methods:** 43 consecutive patients with APS, diagnosed according to the Sapporo criteria, were enrolled. The study cohort included both primary APS (=15) and APS associated with SLE (=28). In addition, 30 healthy subjects (HC) matched for age and sex were studied as controls. Serum levels of HMGB1 and sRAGE were analysed by Western blot.

**Results:** The clinical features of the enrolled patients (40 females and 3 males, mean age 40.98 $\pm$ 13.48 years,) are reported in table 1. HMGB1 and sRAGE serum levels were significantly increased in APS patients in comparison with controls ( $p<0.001$ ) (figure 1). Furthermore, no difference in HMGB1 serum level was detected among patients with thrombotic or obstetric APS and patients with primary or secondary APS. APS patients with thrombosis showed higher levels of HMGB1 than APS patients without thrombosis; in addition, in APS patients there is a correlation between HMGB1 serum levels and thrombosis.

**Abstract AB0168 – Table 1.** Clinical characteristics of APS patients.

Characteristics n (%)	APS (n=43)
Vascular thrombosis	39 (90.7)
Venous thrombosis	26 (60.5)
Arterial thrombosis	18 (41.9)
Recurrent thrombosis	15 (34.9)
Pregnancy morbidity	15/40 (37.5)
Normal fetus deaths	2 (5)
Premature births	1 (2.5)
Spontaneous abortions	13 (32.5)
Vascular thrombosis and Pregnancy morbidity	11 (27.5)
Non-criteria APS features	
Livedo reticularis	16 (37.2)
Thrombocytopenia	11 (25.6)
Migraine	11 (25.6)
Seizures	7 (16.3)



**Abstract AB0168 – Figure 1.** Serum levels of HMGB1 and sRAGE in APS patients and controls.

**Conclusions:** In this study, we investigated for the first time the serum levels of HMGB1 and sRAGE in patients with APS, showing increased levels in both primary and secondary APS compared to controls. Larger studies are needed to assess whether monitoring serum HMGB1/sRAGE levels could be a useful tool for risk stratification in patients with APS.

**Disclosure of Interest:** None declared

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AB0169

### NEURONAL SURFACE P ANTIGEN (NSPA), THE CROSS-REACTING TARGET OF LUPUS ANTI-RIBOSOMAL P AUTOANTIBODIES, IS A POTENTIAL UBIQUITIN-LIGASE THAT REGULATES NMDAR FUNCTION

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**Background:** Anti-ribosomal P protein autoantibodies (anti-P) are found in 10%–15% of all patients with lupus<sup>1</sup> and their pathogenic role is supported by clinical studies showing association with psychosis<sup>2</sup> and cognitive deficit,<sup>3</sup> as well as by experiments in rodents showing depression like behaviour,<sup>4</sup> memory impairment<sup>5</sup> and electrophysiological alterations.<sup>6, 7</sup> The Neuronal Surface P Antigen (NSPA) identified as an anti-P cross-reacting protein<sup>8</sup> very likely mediates anti-P-driven brain diffuse dysfunctions through AMPAR and NMDAR synaptic transmission and plasticity.<sup>6</sup>

**Objectives:** To analyse molecular link between NSPA and NMDAR function involved in synaptic transmission and plasticity associated with memory, as a new approach to understand the neuropathogenic mechanism of anti-P antibodies.

**Methods:** Comparative studies in wild-type and NSPA knock-out mice on water maze performance (spatial memory), electrophysiology of CA3-CA1 glutamatergic transmission by field excitatory postsynaptic potential in hippocampal slices, biochemical analysis of synaptosomes and post-synaptic densities, including the mass and post-translational modifications (tyrosine phosphorylation and ubiquitylation) of relevant proteins.

**Results:** NSPA KO mice displayed the following alterations: 1) Impaired hippocampal-mediated spatial memory; 2) Decreased NMDAR-mediated glutamatergic transmission and long-term potentiation deficit, reflecting synaptic plasticity defects; 3) Selective lowered mass of GluN2A and GluN2B subunits of NMDAR in hippocampal synaptosomes and synaptic densities, accompanied by an enhanced mass and decreased ubiquitylation of the tyrosine phosphatase PTPN4 that interacts with NSPA and dephosphorylates the Tyr1472 of GluN2B of NMDAR. In addition, NSPA contains an APC-10 domain belonging to E3 ubiquitin ligases and a cotransfection assay in HEK293 cells demonstrated NSPA ubiquitylation as expected for these kinds of enzymes.

**Conclusions:** All together, these results suggest that NSPA is an ubiquitin ligase that having PTPN4 as a substrate regulates the tyrosine phosphorylation status and consequently the function of NMDAR at the synaptic region.

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AB0170

### CCR9+ PATHOGENIC T HELPER CELLS FROM PRIMARY SJÖGREN'S SYNDROME PATIENTS ARE CHARACTERISED BY DEREGULATED PATHWAYS ASSOCIATED WITH EFFECTOR T CELL FUNCTION

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**Background:** CCR9 +Th cells produce large amounts of IFN- $\gamma$  and IL-10, lack CXCR5 expression but have features similar to Tfh cells and the recently

described pathogenic PD1 +CXCR5 cells, including expression of ICOS, PD-1, IL-21 and Bcl6, but no CXCR5 expression. CCR9 Th cells and their ligand CCL25 are elevated in salivary glands of primary Sjögren's syndrome (pSS) patients. Since CCR9 Th cells strongly induce antibody production and robustly respond to IL-7, which is indicated to play an essential role in pSS pathogenesis and in formation of ectopic lymphoid structures, these cells may play an important role in pSS immunopathology.

**Objectives:** The goal of this study was to identify the molecular dysregulation of CCR9 Th cells in pSS patients.

**Methods:** CCR9+, CXCR5 +and CCR9-CXCR5- Th cells were sorted from peripheral blood of 7 healthy individuals and 7 pSS patients and RNA sequencing of these sorted cell subsets was performed. Computational analysis identified differentially expressed genes (DEG) and gene expression networks. Pathway enrichment analysis was performed in order to assess differentially regulated pathways. Target genes are technically validated and knockdown experiments will assess the functional role of identified targets.

**Results:** The sorted Th subsets could robustly be distinguished based on their transcriptomes. In the CCR9 +Th cell subset 2777 DEGs (1249 up and 1528 down) were identified between healthy controls and pSS patients, and 1416 and 1077 in the CXCR5 +and CCR9-CXCR5- subsets, respectively. Using network analysis 15 modules were constructed, consisting of genes showing coherent expression patterns. Four modules of interest were selected based on pathway enrichment analysis, revealing pathways involved in e.g. cytokine and chemokine production, proliferation and migration. DEGs of interest within these networks were selected, including upregulated expression of integrin  $\alpha$ E, integrin  $\alpha$ 1 and downregulation of regulatory T cell associated genes FoxP3 and IL2RA. Expression of these markers is being validated using flow cytometry. In addition, knockdown of predicted key transcription factors is studied to reveal their role in the pathogenic potential of CCR9 +Th cells.

**Conclusions:** Transcriptomic analysis of CCR9 +Th cells from pSS patients revealed multiple dysregulated pathways previously shown to be involved in increased effector T cell function. Upregulation of genes associated with pathogenicity and downregulation of regulatory T cell associated genes were found in pSS patients. Targeting predicted key molecules might reveal (novel) therapeutic targets to halt pathogenic processes induced by CCR9 +Th cells.

**Disclosure of Interest:** None declared

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AB0171

### B CELL SUBPOPULATIONS IN LUPUS NEPHRITIS PATIENTS: CORRELATIONS WITH DISEASE ONSET AND OUTCOMES

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**Background:** the relationship between B cells subsets distribution, clinical and laboratory parameters, therapeutic response and prognosis in lupus nephritis (LN) is still underestimated.

**Objectives:** The aim of our study is to establish the value of B cells subsets as biomarkers in patients with active LN than controls, in patients at the onset of renal manifestation than patients with renal flare, and finally in nephritic patients in relation to their clinical and laboratory characteristics at the baseline and during the course of the disease.

**Methods:** 50 patients with a diagnosis of LN have been evaluated every three months. Laboratory, immunological and disease activity data were collected at the baseline and at 6 (T6), 12 (T12), 24 (T24), 36 (T36) months and at the last follow-up (FU). Number of renal flares, time to renal remission and persistent proteinuria at the last FU were evaluated. B cell subsets were obtained through cytofluorimetry and classified using C27/IgD classification. The characterisation of B cells subsets was realised in 50 LN patients and 37 healthy controls.

**Results:** LN patients had a lower percentage of CD19 +cells than controls (9.2% vs 10.6%; p=0.01) as well as a lower percentage of memory unswitched cells CD27 +IgD+ (10.7% vs 15.3%; p<0.001) while patients had an higher percentage of plasmablasts and double negative memory cells CD27-IgD- (respectively 5.9% vs 1%; p<0.001% and 10.9% vs 4.1%; p=0.01).

No significant differences regardless B cells subsets were found between early LN patients and long ones as well as between LN patients at the onset and LN patients during renal flare. We found a correlation between an higher disease activity (assessed with SLEDAI 2K) and lower percentage of memory B cells IgD-CD27+ (p=0.02). Double negative B cells CD27-IgD- tended to be correlated with an higher disease activity. Of interest the correlation between persistent proteinuria detected during the follow-up and a lower percentage of plasmablasts at the baseline (p=0.01).

**Conclusions:** The alteration of B cells subsets is an early event in LN without differences regardless the period of renal involvement (nephritic onset or later LN development). The association between persistent proteinuria and a lower percentage of plasmablasts at the baseline could be a negative prognostic factor considering the correlation between persistent proteinuria and worse renal outcome.

**Disclosure of Interest:** None declared

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#### AB0172 THE RELATIONSHIP BETWEEN THE DIFFERENT TYPES OF CELL DEATH IN SYSTEMIC CONNECTIVE TISSUE DISEASES

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**Objectives:** To study the basic mechanism of cell death (autophagy, apoptosis and necrosis) typical of patients with rheumatoid arthritis (RA), systemic lupus erythematosus (SLE) and systemic scleroderma (SSD). During systemic connective tissue diseases and especially in SLE, a close relationship between various types of cellular death is observed.

**Methods:** 7 SLE-, 10 RA-, 10 SSD patients' and 5 donors' sera were studied. The level of Ca ions was registered by the method of **atomic absorption spectrometry**. Adenosine monophosphate-activated protein kinase (AMPK) was estimated by the Western blotting method. The activity of ATP-ase was measured spectrophotometrically. In order to find out the level of p53 protein, the immune-enzyme "Human p53 Platinum ELISA" method was employed. The quantity of hemoprotein (Cyt c) and the level of 8-hydroxy-2'-deoxyguanosine (8-OH-dG) was measured by employing the immune-enzyme method.

**Results:** Assessing the functional activity of AMPK is an specific marker and a strategic biopower regulator of autophagy, as well as a specific indicator of red-ox cellular potential. In systemic connective tissue diseases, the oxidative stress is matched by urinary calcium and a decrease in the level of calcium in the blood. It reflects the level of seriousness of osteoporosis especially in case of RA. Molecular chaperones (HSP) play a key role in the changing of the way of cellular death. The family of chaperones HSP60 – HSP 100 shows ATPase activity which is most distinct during SLE and RA. The de-energisation of cells during systemic connective tissue diseases and the disappearing of the link between respiration and oxidative phosphorylation lead to proapoptotic protein – Cyt c is being released from mitochondria. High levels of Cyt c reflect cellular mitochondrial apoptosis and show the growing of hypoxia in SLE and RA. The level of protein p53 – a biological marker of apoptosis – is expressed when the DNA is destroyed. It reflects a higher level of the oxidative damage done to the DNA and the extent of the oxidative stress in SLE. This is also evidenced by the data collected by finding out the level of 8-OH-dG which is a biological marker of the free-radical damage of the DNA.

Comparison of markers of autophagy, apoptosis and necrosis in sera in SLE, RA and SSD: AMPK activity (units-mg of protein), the total level of ATP-ase active of HSP-60 – HSP-100 (nmol Pi/min-mg protein), (mM/l), quantity of (ng/ml): Cyt c, p53-protein, 8-OH-dG

**Abstract AB0172 – Table 1**

Groups	AMPK	ATP-ase	Cyt c	p53 protein	8-OH-dG	
SLE	8,7 ±0,3	8,4±0,3	1,99 ±0,12	39,7 ±1,4	1,45±0,03	27,9±3,2
RA	5,7 ±0,2	7,9±0,2	1,87 ±0,24	26,8 ±2,3	1,27±0,04	24,2±2,3
SSD	2,8 ±0,4	5,1±0,2	2,12 ±0,09	14,9 ±2,6	0,98±0,03	18,6±3,4
Donor	1,4 ±0,3	4,0±0,7	2,57 ±0,32	11,7 ±0,3	0,73±0,07	12,56 ±2,4

**Conclusions:** Chaperone-mediated induction of the immune response by autophagy, an evolutionary enshrined only in mammals, perhaps, is the central link in the pathogenesis of systemic connective tissue diseases.

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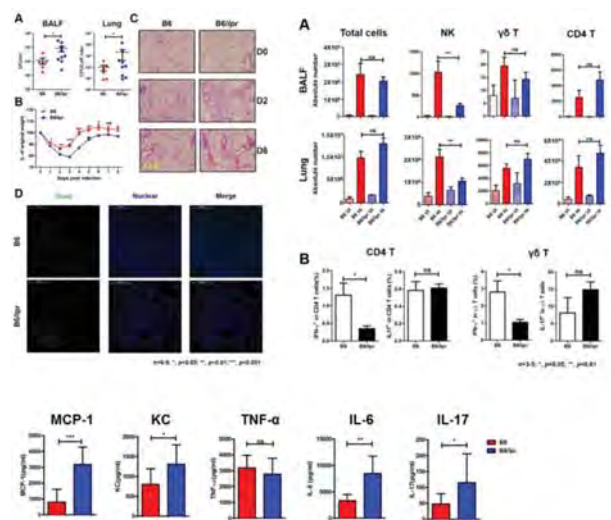
#### AB0173 OVERWHELMING INFLAMMATION INCREASED SUSCEPTIBILITY OF SLE-PRONE MICE TO PULMONARY BACTERIAL INFECTION

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**Background:** Aside from the disease itself, infections represent the major cause of morbidity and mortality in systemic lupus erythematosus (SLE) patients. Inherent defects in immune system play an important role in increasing rates of infection. However, the underlying mechanism of this deficiency remains largely unknown.

**Methods:** Lupus-prone mice B6/lpr were anaesthetized and infected with 1×10<sup>8</sup> CFU of *Haemophilus influenzae* (Hi) intranasally. Then bacterial clearance, body weight change and lung pathology were monitored. Apoptosis of lung cells was analysed by TUNEL assay. Both innate and adaptive immune response in the lung cells determined by flow cytometry. Cytokines in the bronchoalveolar lavage fluid (BALF) were measured by ELISA.

**Results:** Although both wild-type (WT) and B6/lpr mice survived after pulmonary Hi infection, a delay of bacterial clearance and inflammatory resolution was observed in B6/lpr mice. Tissue damage was more severe in the lungs of B6/lpr mice, as more apoptotic cells were detected on Day2 after infection. Cells from lupus-prone lungs produced more pro-inflammatory cytokines IL-6, MCP-1 and KC. TNF-α is comparable between the two groups. NK, γδ T and CD4 T cells are required for control bacterial infection. We that compared with WT controls, in response to infection fewer NK cells were detected in B6/lpr lungs. The numbers of γδ and CD4 T cells were not different, but their ability to secrete IFN-γ was significant lower in B6/lpr mice.



**Abstract AB0173 – Figure 1**

**Conclusions:** The increased susceptibility of SLE-prone mice to pulmonary *Haemophilus influenzae* infection may due to the elevated inflammatory responses and the deficient production of IFN-γ by immune cells.

**Disclosure of Interest:** None declared

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#### AB0174 TNF-A MODULATES MICROGLIA ACTIVATION VIA NF-KB ACTIVITY IN SYSTEMIC LUPUS ERYTHEMATOSUS WITH DEPRESSION

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**Background:** Systemic lupus erythematosus (SLE) is a complex autoimmune disease accompanied by damage to a variety of tissue injuries, such as joints, kidney, and the peripheral and central nervous systems (CNS).<sup>1</sup> The diffuse CNS lupus manifests with a diverse array of neuropsychiatric symptoms that range from headaches, anxiety, depression, to cognitive impairment and, in rare cases, psychosis.<sup>2</sup> Additionally, up to 24% of SLE patients will display



depression.<sup>3</sup> Previous studies have suggested microglia, as critical mediators of depression in SLE.

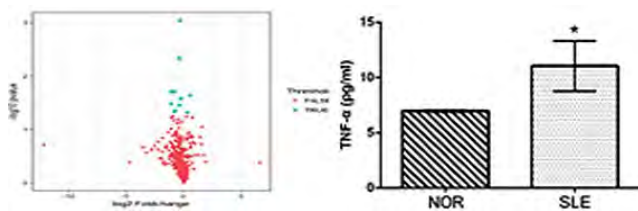
**Objectives:** To date, the pathophysiology of most depression symptoms in SLE has not been well determined. We focused our attention on the potential role of microglia in neuroinflammation in SLE patients.

**Methods:** Cerebrospinal fluid was collected from 3 healthy people and 3 SLE patients. According to the hospital anxiety and depression scale (HADS), we investigate the depression of SLE patients. The cytokines were screened using a RayBio Human Cytokine Antibody Array in cerebrospinal fluid samples by analysing a variety of inflammatory cytokines such as IL-6, Leptin and TNF- $\alpha$ . Cerebrospinal fluid of SLE patients and normal people were tested by ELISA for TNF- $\alpha$ . The depression status of MRL/lpr (C3MRL-Faslpr/J) mice and Balb/c mice was determined by tail suspension test, open-field test and sucrose preference test. Immunofluorescence and Western blot was utilised to detect the activation of microglial cells in brain tissue. Microglia cells were stimulated by TNF- $\alpha$ , Western blot showed the expression of CD68 and activated NF- $\kappa$ B. The concentrations of IL-6 and IL-1 $\beta$  in the cell supernatants were measured by ELISA. After using of NF- $\kappa$ B signalling pathway inhibitor PDTC, the activation of microglia stimulated by TNF- $\alpha$  was determined by immunofluorescence, quantitative PCR, Western blot analysis and ELISA.

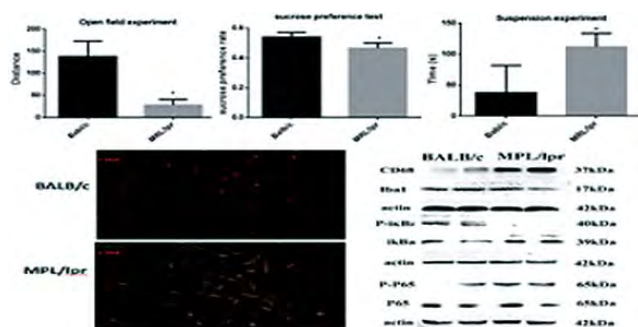
**Results:** The results showed that the level of TNF- $\alpha$  in cerebrospinal fluid of patients with lupus was higher than normal people. At 14 weeks, MRL/lpr mice appear depression by tail suspension test, open-field test and sucrose preference test, MRL/lpr mice had more reactive microglia in the cortex when compared to Balb/c. After microglial cell were stimulated by TNF- $\alpha$ , microglia were active and effectively release IL-6, IL-1 $\beta$  and iNOS. Moreover, the expression of CD68 and activated NF- $\kappa$ B signalling pathway were also higher significantly. However, the use of NF- $\kappa$ B signalling pathway inhibitor PDTC reverse the TNF- $\alpha$  induced microglial activation.

Abstract AB0174 – Table 1. Disease characteristics in SLE patients and control.

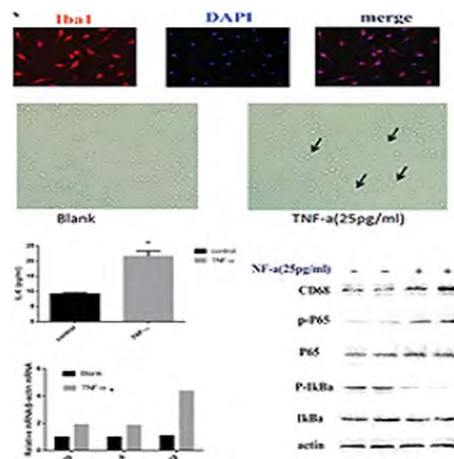
patient	Sex	Age, years	disease	depression	cerebrospinal fluid test results	course of disease, years
1.	female	25.	normal	no	negative	0.
2.	female	31.	normal	no	negative	0.
3.	female	25.	normal	no	negative	0.
4.	male	33.	SLE	yes	Low chloride, protein content increased	6.
5.	female	40.	SLE	yes	negative	5.
6.	female	40.	SLE	yes	Low chloride	2.



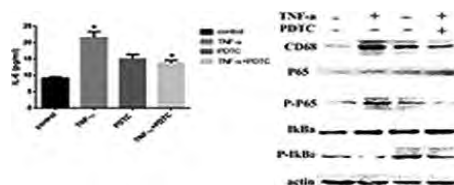
Abstract AB0174 – Figure 1. The level of TNF- $\alpha$  in cerebrospinal fluid of patient with lupus was higher than normal people.



Abstract AB0174 – Figure 2. MRL/lpr mice appear depression by tail suspension test, open-field test and sucrose preference test, MRL/lpr mice had more reactive microglia in the cortex when compared to Balb/c at 14 weeks.



Abstract AB0174 – Figure 3. After microglial cell were stimulated by TNF- $\alpha$  (25 pg/ml), microglia were active and effectively release IL-6, IL-1 $\beta$  and iNOS.



Abstract AB0174 – Figure 4. the use of NF- $\kappa$ B signalling pathway inhibitor PDTC reverse the TNF- $\alpha$  induced microglial activation.

**Conclusions:** The study showed that the different level of inflammatory cytokines of cerebrospinal fluid of SLE patients. Our results highlight the potential role of microglia in neuroinflammation in SLE patients with depression.

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AB0175 **DYSREGULATION OF NF- $\kappa$ B IN GLANDULAR EPITHELIAL CELLS RESULTS IN SJÖGREN'S-LIKE FEATURES**

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**Background:** Hyposalivation and lymphocytic infiltration in salivary glands are common manifestations of primary Sjögren's syndrome<sup>1</sup>. NF-kappa B (NF $\kappa$ B) signalling is one of the most important proinflammatory pathways, and is inhibited by A20 (also known as TNFAIP3)<sup>2</sup>. Although mounting studies are pointing to the central role of epithelial cells in pSS<sup>3-5</sup>, whether pSS-like features can be initiated by immune activation of epitheliums remains to be explored.

**Objectives:** We sought to investigate the hypothesis that epithelial cells are capable of initiating the major pathological salivary gland hallmarks of primary Sjögren's syndrome. In order to achieve this we employ a keratin 14 (KRT14) promoter-driven knockout of the A20 NF $\kappa$ B signalling inhibitor.

**Methods:** A20 gene expression was knocked out in KRT14<sup>+</sup> cells, namely ductal and myoepithelial cells. Whole pilocarpine-stimulated saliva was collected from A20<sup>-/-</sup> mice and wildtype (WT) littermate controls at 10, 20 and 30 weeks of age. Submandibular SGs were harvested at all time points for histological examination and qPCR.

**Results:** In submandibular SGs of A20<sup>-/-</sup> mice at 30 weeks of age, 10% of all cells were CD45<sup>+</sup> leukocytes and 3% were CD3<sup>+</sup> T cells, both significantly more than controls. B cell proportion increased over time in A20<sup>-/-</sup> mice, but was not significantly different to controls. CD45<sup>+</sup> cells formed immune foci (>50 CD45<sup>+</sup> cells together) localised to striated ducts, present at significantly greater frequencies than control mice. CD45<sup>+</sup> cells, T cells and occasional B cells in A20<sup>-/-</sup> mice also invaded striated ducts. Expression of the pro-inflammatory cyto/chemo-kines IFN $\gamma$ , TNF $\alpha$ , IL-6, CXCL10 and CXCL13 was also significantly greater in A20<sup>-/-</sup> mice. Functionally, both volume and mucin 10 content of whole stimulated saliva from A20<sup>-/-</sup> mice was significantly reduced compared to controls.

**Conclusions:** We present a model for epithelial cell involvement in pSS SG pathology development. We confirm that saliva production defects, foci formation and striated duct invasion can be triggered solely by immune activated epithelial cells.

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**Disclosure of Interest:** None declared

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#### AB0176 MORPHOLOGICAL HEART CHANGES IN ANIMALS WITH EXPERIMENTAL SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Heart pathology in systemic lupus erythematosus (SLE) refers to the most common manifestations of the disease and largely determines its prognosis.<sup>1,2</sup> The pathogenetic constructions of myocardium, endocardium and coronary vessel lesions remain insufficiently studied.<sup>3,4</sup> Histological evaluation of separate cardiac structures is performed on native models of SLE in linear mice.

**Objectives:** to study in the experiment on animals (rats) with SLE model the degree of cardiomyocytes, myocardium, endocardium, valves and cardiac vessel damage, comparing the results with thymus and spleen tissues histological data.

**Methods:** The SLE modelling was performed in 53 white non-breeding rats (34 females and 19 males) using full Freund's adjuvant, splenic deoxyribonucleic acid of cattle, cyclophosphamide, azid and sodium deoxyribonucleate. Cadmium sulfate, lithium oxybutyrate and ammonium molybdate were added for feeding animals. Histological heart specimen were stained with hematoxylin and eosin, altsyon blue (pH=2.6), van Gieson. PAS-reaction was applied.

**Results:** Experimental SLE is accompanied by the development of cardiopathy in all animals with cardiomyocytes hypertrophy, dystrophy and necrosis, morphological signs of coronary vessel, myocardial stroma, endocardium and heart valves sclerosis, proliferation of vascular endothelium, which has dispersion and direct correlation relationships with the degree of lymphoma-macrophage infiltration, interstitial tissue, perivascular and valvular histiocytic cell infiltration, and the vessels endothelium damage nature is closely linked to the presence of mast cells in myocardial stroma, it is defined by endocardium necrosis and valves collagenolysis, decrease in spleen lymphoid tissue, and also in the brain layer cells and Gassal cells in the thymus.

**Conclusions:** In the case of experimental lupus cardiopathy, there is determine heart structures lesion, what is more, the immune disorders are involved in their pathogenetic constructions, as indicated by the damage of the immunocompetent organs' (thymus and spleen) corresponding structures.

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**Disclosure of Interest:** None declared

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#### AB0177 TOLL-LIKE RECEPTOR 7(TLR7) IS UPREGULATED ON PERIPHERAL B CELLS AND ASSOCIATED WITH DISEASE ACTIVITY AND DAMAGE IN PRIMARY SJOGREN SYNDROME

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**Objectives:** Primary Sjogren Syndrom(pSS) is characterised by activation of B cells, increased production of RNA-associated antibodies and elevated proportion of transitional B cell. Toll-like receptors 7(TLR7) have been reported promoting the effects above in some murine models of SS. We took up this study to identify if TLR7 expression is associated with disease activity and the role of TLR7 in pSS.

**Methods:** 21 pSS patients and 12 healthy controls(HCs) were selected. The mRNA expression of TLR7 was determined by real-time PCR on peripheral B cells of both pSS patients and HCs. We measured BAFF serum concentrations by ELISA, and the BAFF-R, TACI and BCMA expression was analysed on each B cell subset (CD27<sup>+</sup>CD24<sup>hi</sup>CD38<sup>hi</sup>/transitional B cell; CD27<sup>+</sup>CD24<sup>lo</sup>CD38<sup>lo</sup>/naive B cell;) by flow cytometry. The results were compared among patients with diverse degree of disease activity and damage to HCs.

**Results:** The expression level of TLR7 mRNA were elevated in pSS patients compared with HCs(p=0.004), and correlated with the SSDAI (SS disease activity index) (r=0.803; p=0.009) and the SSDI(SS damage index)(r=0.881;p=0.002). Serum BAFF concentrations increased in pSS patients compared with HCs (p=0.041), but not correlated with TLR7 expression. TACI expression in pSS patients in total B cells and traditional B cells compared to HCs were elevated and are both associated with TLR7 expression (r=0.763,p=0.048,r=0.820,p=0.004, respectively). A lower BAFFR expression was seen in transitional B cell compared with HCs(p=0.018). BCMA expression was of no significance.

**Conclusions:** Increased TLR7 expression on peripheral B cells were associated with disease activity and damage, suggesting that TLR7 may play a role in the development in pSS. Increased serum BAFF concentration and TACI expression were associated with TLR7 expression, indicating that BAFF may regulate TLR7 expression through TACI according to previous studies.TLR7 may be a potential treatment target of pSS and worth of further study.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.1238

#### AB0178 SUPPRESSION OF ENDOPLASMIC RETICULUM STRESS BY 4-PBA IMPROVES THE MANIFESTATIONS OF MURINE LUPUS THROUGH MODULATING REGULATORY T CELLS

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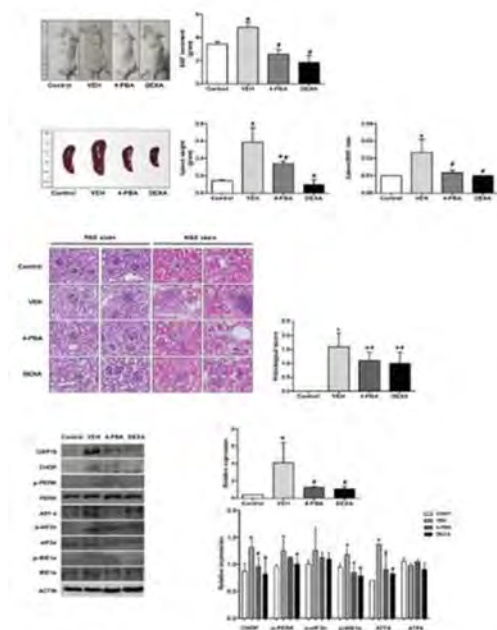
**Background:** Impaired function of regulatory T cells (Treg) contributes to the pathogenesis of systemic lupus erythematosus (SLE). It has been reported that the aberrant responses of T lymphocytes to endoplasmic reticulum (ER) stress in patients with SLE.

**Objectives:** In the present study, we investigated whether ER stress inhibition through 4-phenylbutyric acid (4-PBA) ameliorates lupus manifestation on

experimental lupus model and the effect of ER stress inhibition by 4-PBA on the frequency and function of Treg.

**Methods:** Murine lupus model were induced with female BALB/c mice at 7 or 8 weeks of age through Toll-like receptor (TLR) agonist 7 treatment for 4 weeks. From the 8th week, the mice were treated with phosphate buffered saline (PBS), 4-PBA (500 mg/kg, three times weekly) and dexamethasone (1 mg/kg, once a day) for 4 weeks. The increment of body weight, spleen weight, anti-double-stranded DNA (anti-dsDNA) antibody titer, serum cytokine level and the pathology of glomerulonephritis were analysed at 12 weeks of age. The population of immune cellular subset including activated T, B lymphocyte and Treg and suppressive functions of Treg were measured.

**Results:** 4-PBA significantly decreased the level of anti-dsDNA antibodies, serum TNF- $\alpha$  in murine lupus model, and which were comparable with the efficacy of dexamethasone. A significant decrease in accumulation of immunoglobulin, glomerulonephritis score was also observed in 4-PBA-treated and dexamethasone-treated mice compared with vehicle-treated group. ER stress inhibition decreased the activated T and B lymphocytes population of splenocytes, but the population of Treg was not significantly different between vehicle group and 4-PBA group. However, there was the markedly enhanced suppressive capacity of Treg in 4-PBA-treated group.



Abstract AB0178 – Figure 1

**Conclusions:** The results suggest that ER stress inhibition attenuates disease activity in experimental model, especially in nephritis through improving the suppressive capacity of Treg. Thus, reduction of ER stress could be used as a beneficial therapeutic strategy in SLE.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.2879

#### AB0179 SERUM LEVELS OF INTERLEUKIN-33 ARE ASSOCIATED WITH DEPRESSIVE SYMPTOMS IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME

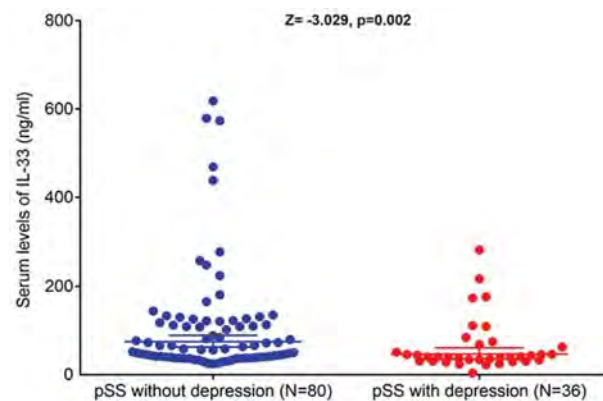
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**Background:** Primary Sjögren's syndrome (pSS) is a systemic autoimmune disease which is more common among women than men. Extraglandular manifestations are commonly reported, including central nervous system (CNS) involvement such as headaches, cognitive deficits and mood disorder. Among mood disorder, depression is one of the most frequent disorders observed in patients with pSS. The pathogenesis of depression in pSS remains unclear.

**Objectives:** The aim of this study was to explore potential relationships between serum interleukin-33 (IL-33) levels and depressive symptoms in primary Sjögren's syndrome (pSS) patients.

**Methods:** We included 116 consecutive pSS patients (36 depression patients), and 71 (18 depression patients) age- and sex-matched healthy controls. The presence of depressive symptoms was determined through the Hospital Depression Scale (HDS). IL-33 levels were measured by enzyme-linked immunosorbent assay (ELISA) using commercial kits.

**Results:** There was no significant difference between pSS patients and controls. But, in pSS patients, the serum IL-33 levels were significantly lower in depression patients as compared to patients without depression [40.18 (IQR, 31.79–66.70) ng/ml vs. 39.95 (IQR, 121.73) ng/ml;  $Z = -3.029$ ,  $p = 0.002$ ]. A direct negative correlation between the score of HDAS-D and sera IL-33 levels ( $r = -0.805$ ,  $p = 0.000$ ) in pSS was also observed. In logistic regression model using depression as the dependent variables, IL-33 is the independent predictors of depression in pSS ( $\beta = 0.004$ ; OR = 1.004; 95% CI: 1.998–0.011;  $p = 0.170$ ). Surprisingly, sera IL-33 levels were lower in depression patients with pSS compared to depression patients without pSS ( $Z = -2.316$ ,  $p = 0.021$ ).



Abstract AB0179 – Figure 1

**Conclusions:** Conclusion: In pSS, IL-33 is the independent predictors of depressive disorders. Serum IL-33 levels are decreased in pSS patients with depressive symptoms, suggesting that IL-33 may play a unique role in depression with pSS.

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**Disclosure of Interest:** None declared

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#### AB0180 IDENTIFICATION OF LNCRNA LNCMKLN1 CONTRIBUTED TO ABNORMAL ACTIVATION OF TYPE I INTERFERON PATHWAY IN SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Dysregulation or dysfunction of some key moleculars in signalling pathway is involved in disease pathogenesis. Type I interferon pathway abnormal activation has been identified as major molecular phenotype of lupus patients. Long non-coding RNA (lncRNA), as a regulator of gene expression, plays great role in signalling pathway.

**Objectives:** We hypothesised that dysregulation of lncRNA may involve in key signalling pathway of SLE.

**Methods:** Deep sequencing of human renal samples to screen differential expression of lncRNAs between LN patients and healthy donors. RNA-FISH was used to identify subcellular location of lncRNA. Stimulation in human renal mesangial cells (HRMC) by all kinds of TLR ligands, IFNs, and TNF $\alpha$ , and transfection in HRMC cells by antisense oligonucleotides (ASOs), and quantitative real-time polymerase chain reaction (RT-qPCR), enzyme linked immunosorbent assay (ELISA) were used to analyse the relative genes expression. LncMKLN1 transcription was activated or inhibited through CRISPR-dCas9 system in Hela cell line. RNA-seq was executed to examine the gene expression profile after changing lncMKLN1 expression, and western blot was applied to determine the key signalling molecules of IFN pathway.



**Results:** lncMKN1, dominantly located in nucleus, was up-regulated in lupus patients compared to healthy donors, and could be induced by IFN $\alpha$  and TLR ligands in HRMC. Silencing lncMKN1 significantly reduced the expression of a group of interferon-inducible genes, including IFIT3, OAS1, CXCL10, etc. We used lose-of-function and gain-of-function strategy through CRISPR system to confirm that lncMKN1 positively regulated type I interferon pathway. Furthermore, it was identified the involvement of lncMKN1 in interferon signalling pathway was through regulating the expression of STAT1, IRF9 and phosphorylation of IRF9 and STAT1 although its mechanism is also needed to investigate.

**Conclusions:** Upregulated lncMKN1 expression contributed to abnormal activation of interferon pathway of SLE.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.6029

#### AB0181 ENHANCED THERAPEUTIC EFFICACY OF APOPTOTIC CELL TREATED MESENCHYMAL STEM CELLS IN LUPUS PRONE MRL/LPR MICE

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**Background:** Mesenchymal stem cells (MSCs) exhibit promising therapeutic potential in systemic lupus erythematosus (SLE). Increased apoptotic cells (ACs) were observed in SLE and our previous study showed MSC transplantation reduced AC levels in patients with SLE. Yet the effects of ACs on MSCs are not clear.

**Objectives:** This study aims to investigate the effects of ACs on MSCs and efficacy of AC treated MSCs (AC-MSCs) in SLE.

**Methods:** Jurkat T cells were irradiated by ultraviolet ray to induce apoptosis and then co-cultured with umbilical cord derived MSCs. Then, ACs were removed and MSCs were further co-cultured with human peripheral blood mononuclear cells (PBMCs). The inhibition of MSCs on PBMC proliferation was detected by flow cytometry. MSCs and AC-MSCs were infused into lupus prone MRL/lpr mice respectively to compare their therapeutic effects.

**Results:** The suppression of MSCs on PBMC proliferation was significantly enhanced after co-culture with ACs. *In vivo* study showed that AC-MSCs significantly increased the survival rate of MRL/lpr mice and decreased urine protein as early as one week after treatment, while MSCs decreased urine protein eight weeks post infusion. Moreover, AC-MSCs remarkably reduced the number of splenic plasma cells and serum anti-dsDNA levels, whereas MSCs only showed decreased tendency.

**Conclusions:** ACs enhanced therapeutic effects of MSC transplantation in lupus mice, which provides new insights into MSC modification in the treatment of SLE.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.3450

## Systemic sclerosis, myositis and related syndromes – etiology, pathogenesis and animal models

#### AB0182 MOLECULAR MECHANISMS MEDIATING ANTIOXIDANT EFFECT OF EPIGALLOCATECHIN-3-GALLATE IN EXPERIMENTAL SCLERODERMA MODEL

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**Background:** Scleroderma (SSc) is an autoimmune multisystemic connective tissue disease characterised by skin and internal organ fibrosis.<sup>1</sup> Underlying mechanism is still unclear for SSc. Besides there is no specific treatment for SSc, various treatments may alleviate symptoms and improve the quality of life. Epigallocatechin-3-gallate (EGCG) is a phenol with antioxidant effects in many disease processes.<sup>2</sup> In this disease, oxidative stress may play a role for pathogenesis.<sup>3-5</sup> Recent studies showed a relationship between oxidative/antioxidative markers and SSc.<sup>5</sup>

**Objectives:** The aim of this study was to investigate the antioxidant effects of epigallocatechin-3-gallate in the scleroderma process in experimental mouse model with bleomycin.

**Methods:** Thirty-two healthy female Balb-c mouse species were used and randomly divided into four groups: control, bleomycin, bleomycin +EGC, EGCG. At the end of the experiment, skin tissues were collected. Sodium dismutase enzyme (SOD) and malondialdehyde (MDA) levels have been analysed for oxidative

stress. High performance liquid chromatography (HPLC) was used for MDA measurements. Colorimetric kit was used for SOD analysis. Furthermore, the ratio of phosphorylated p-38/total p-38 protein, and phosphorylated-Akt/total Akt protein and NF-kappa B were measured by western blotting. Immunohistochemistry ( $\alpha$ -SMA), histochemistry (masson trichrome-hematoxylin and eosin) studies were also performed on FFPE skin samples.

**Results:** When the experimental and control groups were compared, the degree of fibrosis in the connective tissue of the dermis areas stained with masson trichrome decreased in the EGCG groups. SOD activity was increased in the EGCG groups compared to the positive control group, and MDA was significantly decreased in the EGCG groups. According to Western blotting results, pp-38 MAPK and NF- $\kappa$ B were found to decrease significantly in the EGCG groups compared with the controls. Parallel to these findings, phosphorylated Akt protein was found to increase in the EGCG groups compared with the control groups.

**Conclusions:** It has been shown that EGCG can antioxidative effect in scleroderma.

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**Acknowledgements:** This research carried out at Dokuz Eylul University Medicine Faculty of Research Laboratory (R-LAB).

**Disclosure of Interest:** None declared

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#### AB0183 VITAMIN D AND VITAMIN D RECEPTOR IN PATIENTS WITH SCLERODERMA SUBTYPES

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**Background:** The aim of this study was to compare the expression of Vitamin D receptor (VDR) and vitamin D in scleroderma subtypes.

**Objectives:** VDR is a member of the nuclear localised hormone receptor family. 1,25-(OH) 2D, a form of metabolically active Vitamin D3, is the ligand of VDR. When VDR and 1,25-(OH) 2D are linked, many genes initiate molecular interaction reactions that will modulate the transcription.<sup>1</sup> VDR has been shown to be a negative regulator of the TGF- $\beta$ /Smad signalling pathway, which is important in the pathogenesis of scleroderma.<sup>2, 3</sup> Thus, reduced expression of VDR and decreased ligand levels may contribute to hyperactivity of the TGF-beta pathway in SSC and abnormal fibroblast activation. Also, Vitamin D has pleiotropic effects including immunomodulatory and antifibrotic properties in scleroderma pathogenesis.

**Methods:** 19 SSC patients and 6 healthy controls were included in the study and they were classified according to the 2013 ACR/EULAR criteria. They were applied to Dokuz Eylul University, Faculty of Medicine, Department of Rheumatology-Immunology, between 2015–2017. Rodnan scores were calculated of all scleroderma patients. 11 were of the limited type and 8 were of the diffuse type of scleroderma. Informed consent was obtained from all participants. 1 ml of total blood was collected. Vitamin D levels were determined in serum.

VDR gene expression was determined by quantitative PCR in isolated RNAs from the blood. Changes in mRNA levels were analysed according to the  $\Delta\Delta$ CT method and beta-actin was used as the housekeeping gene. Student-t-test was used as a statistic. In addition, Pearson correlation test was used to determine the relationship between Rodnan score and VDR gene expression.

**Results:** VDR gene expressions in diffuse type scleroderma patients were statistically significantly decreased compared to the control (p<0.01).

It was found that VDR gene expression in limited type scleroderma patients did not show any significant difference when compared to control (p: 0.16).

Also, Vitamin D levels and vitamin D expressions were no correlation in scleroderma subtypes (p:0.2)

**Conclusions:** VDR gene expression decreased in patients with diffuse type scleroderma and showed negative correlation with Rodnan score. Further studies are planned to increase the number of samples to obtain more information.

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**Acknowledgements:** This research carried out at Dokuz Eylul University Medicine Faculty of Research Laboratory (R-LAB).

**Disclosure of Interest:** None declared

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AB0184 **DIAGNOSTIC IMPACT IN THE CLINICAL SETTING OF NAILFOLD VIDEOCAPILLAROSCOPY ON CONNECTIVE DISEASES**

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**Background:** Nailfold video-capillaroscopy (NVC) is a non-invasive technique that allows visualisation of structure and distribution of capillaries at the nailfold level<sup>1</sup>, altered somehow in some connective diseases, specially in the Scleroderma (Scl) disease spectrum. The main indication of this technique is the investigation of Raynaud's phenomenon (RF).

**Objectives:** Our objective is to investigate the diagnostic impact of NVC in the daily clinical practice.

**Methods:** The design is an observational, longitudinal, retrospective and descriptive study, which included patients with at least one NVC between June 2012 and December 2016 from our Rheumatology register of patients. We collected demographic data (age, gender, indication, autoantibodies, etc.), number of explorations performed and their result. We also collected in a dichotomist fashion if the NVC contributed in the diagnostic workup, between one consultation and the other after the NVC realisation.

**Results:** 437 patients were included with a total of 637 explorations. Of these 437 patients, 115 (24.1%) had a second NVC, 39 (8.2%) a third one, 9 (1.9%) a fourth and only two with a fifth NVC (both with diagnostic of Scl). We noticed a diagnostic change between the first consultation and the next one in 35 cases (5.49%). In 14/35 (40%) of these cases, the NVC played an important role in the diagnostic change, with changes in the NVC pattern, from normal or unspecific to Scl pattern (table 1). These changes, occurred after the first NVC in 10 patients (71.4%), 3 (21.4%) after the second, and 1 (7.1%) after the third exploration in addition of new disease manifestations, diagnostic tests and other image techniques. Of these 14 patients, 100% had positive ANA, 5 (35.7%) Anticentromere Antibodies (Ab), 1 (7.1%) anti-Ro Ab and 1 (7.1) Antiphospholipid Ab.

Abstract AB0184 – Table 1

Change	n:14 (%)	Pattern
RF to Scl	11 (78.5%)	Early 7/11 (63.6%) Active 2/11 (18.1%) Late 2/11 (18.1%)
UC to Scl	2 (14.2%)	Early 2 (100%)
RF to UC	1 (7.1%)	Early 1 (100%)

Raynaud phenomenon (RF); Scleroderma (Scl); Undifferentiated connective disease (UC); Mixed connective tissue disease (MCTD); Systemic Lupus Erythematosus (SLE); primary Sjögren syndrome (pSS).

Of the 21 patients with a diagnostic change who did not developed a Scl pattern we have:

Normal pattern: 1 RF to possible Scl and 1 RF to UC.

Limit of normality: 1 SLE to MCTD, 4 RF to UC, 1 RF to pSS, 1 RF to MCTD and 1 UC to MCTD.

Unspecific (mild): 3 RF to UC, 2 RF to Scl and 1 UC to overlap syndrome.

Unspecific (moderate): 1 RF to UC, 1 RF to Scl, 1 UC to MCTD and 1 RF to MCTD.

**Conclusions:** The NVC in our centre had a limited but important impact in the diagnostic process of connective diseases. This impact was specially relevant in patients diagnosed with Scleroderma. The probability of having a diagnostic change diminishes with successive explorations.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.6720

AB0185 **ALTERED EXPRESSION OF RELAXIN RECEPTOR RXFP1/LGR7 IN DERMAL FIBROBLASTS CONTRIBUTES TO THE INEFFECTIVITY OF RELAXIN-BASED ANTI-FIBROTIC TREATMENTS IN SYSTEMIC SCLEROSIS**

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**Background:** Systemic Sclerosis (SSc) is an autoimmune disease characterised by progressive fibrosis of the skin and internal organs, coupled to widespread vascular pathology.<sup>1</sup> The pathogenesis is still poorly understood and there is no effective treatment for the fibrotic process.<sup>1</sup> Relaxin is a potent anti-fibrotic hormone that has been tested in the past to ameliorate skin, lung and kidney fibrosis in SSc, but the results remain controversial.<sup>2</sup>

**Objectives:** The aim of the study is to evaluate the presence of mutations in RXFP1 gene (encoding the relaxin receptor RXFP1/LGR7), and to assess mRNA and protein levels of the receptor in dermal fibroblasts of SSc patients, in order to understand the clinical inefficacy of relaxin-based anti-fibrotic treatments in the disease.

**Methods:** Fibroblasts were isolated from unaffected and affected skin samples of (n=20) of limited cutaneous SSc (LcSSc) and from (n=20) affected skin of diffuse cutaneous SSc (DcSSc) patients. Fibroblasts derived from healthy subjects were used as controls. Sequencing of exonic target regions of interest for gene RXFP1 was performed coupled with mRNA transcript variant analysis. RXFP1/LGR7 mRNA and protein levels were assessed by quantitative-real-time-PCR (qPCR) and by immunocytochemistry (ICC) in cultured SSc and healthy fibroblasts. Finally, synthesis of collagen and alpha-smooth-muscle actin (a-SMA) of transforming-growth-factor-beta-1 (TGF- $\beta$ 1) induced fibroblasts were assessed after 24 hours pre-treatment with serelaxin (a recombinant form of human relaxin-2 targeting the relaxin receptor RXFP1/LGR7).

**Results:** Sequencing of RXFP1 gene showed no relevant (single nucleotide polymorphisms) SNPs or small insertions and deletions (InDels) in affected LcSSc/DcSSc fibroblasts. No relevant mutations were found in unaffected LcSSc and healthy fibroblasts as well. However, alternatively spliced transcript variants encoding multiple isoforms were observed for this gene in all the fibroblast populations. The total RXFP1 mRNA levels resulted upregulated (p<0.05) in the affected LcSSc/DcSSc fibroblasts compared to unaffected LcSSc (p<0.05) and to healthy ones (p<0.05). On the contrary, ICC demonstrated the absence of RXFP1/LGR7 receptor in affected LcSSc/DcSSc fibroblasts and the regular expression in unaffected LcSSc and healthy fibroblasts. In fact, serelaxin pre-incubation was unable to counteract the TGF- $\beta$ 1 driven upregulation of collagen and a-SMA in affected LcSSc/DcSSc fibroblasts only, but not in unaffected LcSSc and healthy ones.

**Conclusions:** The absence/altered expression of relaxin receptor RXFP1/LGR7 in the affected fibroblasts of SSc patients could explain the inefficacy of relaxin-based anti-fibrotic treatments in the disease. The exclusion of RXFP1 gene mutations could lead to the hypothesis that the presence of receptor splice variants could exert a dominant negative effect on the wild type isoform in terms of maturation, and subsequent trafficking to the cell surface, resulting in loss of function.

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AB0186

### HIGH-DOSE NARROWBAND ULTRAVIOLET A1 INDUCES THE REGRESSION OF DERMAL FIBROSIS IN ANIMAL MODEL OF SCLERODERMA

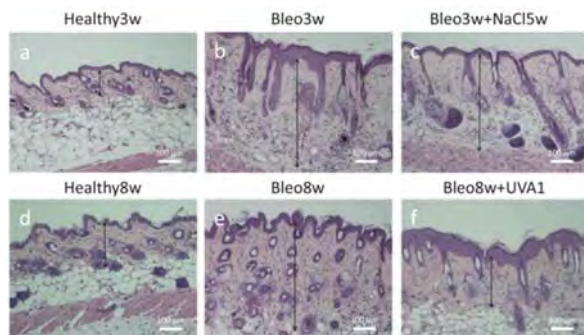
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**Background:** Ultraviolet A1 (UVA1) phototherapy implications for systemic sclerosis still remain area of research. The wide spectral waveband of UVA1 could react with many chromophores in the skin, leading to different effects of the immune system.<sup>1</sup> In accordance with the physical properties of UVA1 and the optical features of the skin, the narrowband UVA1 would influence collagen metabolism with a reduced chance of side effects. None of the previously conducted studies evaluated the effectiveness of narrowband UVA1 on dermal fibrosis.

**Objectives:** The main objective of the present study was to define the impact of high-dose of 365±5 nm UVA1 on the dermal thickness in pre-established, bleomycin-induced mouse model of scleroderma.

**Methods:** Forty two DBA/2 line mice were randomly divided into the following 6 groups (7 animals in each): group I – mice injected with sodium chloride (NaCl) for 3 weeks; group II – mice injected with bleomycin (Bleo) for 3 weeks; group III – mice injected with NaCl for 8 weeks; group IV – mice injected with Bleo for 3 weeks and then with NaCl for 5 weeks; group V – mice injected with Bleo for 8 weeks; group VI – mice injected with Bleo for 8 weeks and parallel treated with average cumulative dose of 1200 J/cm<sup>2</sup> of UVA1 for the last 5 weeks (the treatment group). Light source emitting a narrow band UVA1 of 365±5 nm and 21 mW/cm<sup>2</sup>; power density was used in the study. Histological analysis was performed for the evaluation of dermal thickness. The Mann – Whitney U test was used for statistical analysis.

**Results:** After bleomycin injections that spanned a period of 3 and 8 weeks, the dermal thicknesses were significantly (p=0.002) higher (group II – 433.69 ±54.37 μm and group V – 497.43±57.83 μm, respectively) as compared to that of the healthy controls (group I – 166.04±25.29 μm and group III – 178.18 ±42.35 μm, respectively). The 3 weeks of bleomycin injections and the following 5 weeks of NaCl did not cause any spontaneous regression of dermal fibrosis (group IV – 443.87±41.77 μm; group II – 433.69±54.38 μm; p=0.482). Dermal thickness in mice injected with bleomycin for 8 weeks and irradiated with UVA1 for the last 5 weeks was significantly lower than that in mice challenged only with bleomycin for 8 weeks (group VI – 253.96±31.83 μm and group V – 497.43 ±57.83 μm, respectively; p=0.002). Furthermore, treatment with 1200 J/cm<sup>2</sup> of UVA1 in parallel with profibrotic stimulus of bleomycin resulted in a lower dermal thickness as compared with pre-existing fibrotic changes in the group IV observed after 3 weeks of bleomycin injections (group VI – 253.96±31.83 μm and group IV – 443.87±41.77 μm; p=0.002) (figure 1).



Abstract AB0186 – Figure 1

**Conclusions:** The cumulative dosage of 1200 J/cm<sup>2</sup> of narrowband UVA1 not only prevented the progression of dermal fibrosis, but also induced the regression of pre-existing fibrotic changes in bleomycin-induced mouse model of scleroderma.

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AB0187

### THE ASSOCIATION BETWEEN ACTIVITY OF PURINE AND PYRIMIDINE METABOLISM ENZYMES AND DISEASE ACTIVITY IN SYSTEMIC SCLERODERMA PATIENTS

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**Background:** Recent studies report various metabolic disturbances in systemic sclerosis (SSc) patients. Purine and pyrimidine metabolic pathways are closely interrelated, underlying the central processes of cellular life. Alterations of the enzymes that control these metabolic conversions can disturb proliferation and differentiation of lymphocytes, therefore contributing initiation and progression of the immunopathological phenomena.

**Objectives:** to characterise enzymatic patterns of the major purine and pyrimidine metabolic pathways enzymes in blood plasma and lysed lymphocytes depending on the SSc activity.

**Methods:** 51 SSc patients and 30 healthy controls were enrolled in the study. Mean age of patients (Mean ±SD) was 42,8±1,3 years, mean SSc duration was 7,9±0,7 years. The diagnosis was verified in accordance with the international standards (ACR/<sup>EULAR</sup> 2013). Disease activity was assessed in accordance with the national classification.<sup>1</sup> Adenosine deaminase (ADA; EC 3.5.4.4); adenosine kinase (AK; EC 2.7.1.20); guanylate kinase (GK; EC 2.7.4.8), dihydroorotate dehydrogenase (DODH; EC 1.3.1.14); IMP dehydrogenase (IMPDH; EC 1.1.1.205); purine nucleoside phosphorylase (PNP; EC 2.4.2.1); thymidine kinase (TK; EC 2.7.1.21); thymidine phosphorylase (TP; EC 2.4.2.4); uracil/thymidine dehydrogenase (UDH; EC 1.17.99.4); cytidine deaminase (CDA; EC 3.5.4.5) activities were measured in blood plasma and lysed lymphocytes.

**Results:** We revealed substantial changes in enzymatic activities related to both purine and pyrimidine metabolism in SSc. The increased DODH (p<0,001), IMPDH (p<0,001), PNP (p<0,001), TK (p<0,001), TP (p<0,01), UDH (p<0,001) activities in plasma and AK (p<0,001), IMPDH (p<0,001), TK (p<0,001) activities in lysed lymphocytes; the decreased ADA (p<0,001), GK (p=0,02), PNP (p<0,001) activities in lysed lymphocytes were observed in SSc patients in comparison with healthy controls. Plasma AK, DODH, IMPDH, PNP, TK, UDH activities positively correlated with SSc activity, as well as lymphocytic AK, IMPDH, TK activities did. Negative correlations with SSc activity were revealed for plasma ADA, GK, TP, and also for lymphocytic ADA, GK, DODH, PNP, TP, UDH, CDA. Plasma and lymphocytic adenosine deaminase as well as adenosine kinase activities were the most informative for minimal SSc activity detection, being a promising candidate marker.

**Conclusions:** The changes in enzymatic activity of purine and pyrimidine metabolism participate in pathogenesis of SSc. The enzymatic patterns studied can be used as auxiliary markers of SSc activity. The correction of purine and pyrimidine metabolism changes can be considered as one of the promising ways of increasing the effectiveness of SSc treatment.

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**AB0188** **ACTIVATED PLATELETS ARE INCREASED IN CIRCULATION OF PATIENTS WITH SYSTEMIC SCLEROSIS AND ASSOCIATED WITH CLINICAL CHARACTERISTICS**

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**Background:** Systemic sclerosis (SSc) is a systemic connective tissue disease characterised by excessive fibrosis, microvascular injury and autoantibody production (1), but mechanisms of disease process are still under investigation. Recent studies focused on the role of circulating blood cells in the pathogenesis, especially lymphocytes (2,3) or monocytes (4,5), however other cellular components are not well-examined. Platelets play a significant role in hemostasis physiologically. However, recent studies have revealed that platelets contain various kinds of humoral factors such as cytokines, chemokines and growth factors and can distribute systemically through circulation and contribute to the disease process through activation and release of these factors (6).

**Objectives:** To elucidate the role of platelets in the pathogenesis of SSc, activation status of circulating platelets in patients with SSc and association with clinical characteristics were examined.

**Methods:** Twenty-one patients with SSc who fulfilled 2013 ACR/EULAR classification criteria and 16 healthy controls were involved. Platelets or microparticles (MPs) were defined as vesicles in platelet-rich plasma which is more or less than 1 µm in diameter by forward and side scatter, respectively, and positive staining with anti-CD41 antibody using flow cytometry. Activation status of platelets was examined by the expression of activation markers on platelets such as P-selectin (CD62P) or activated glycoprotein IIb/IIIa (PAC1). Production of microparticles (MPs) is defined as ratio of proportion of MP to that of platelets. Release reaction of platelets was evaluated by release of platelet factor 4 (PF4) in culture supernatant of coculture with skin fibroblasts using enzyme-linked immunosorbent assay (ELISA). Association or correlation between proportion of activated platelets and clinical characteristics or parameters of patients with scleroderma was also examined.

**Results:** As for the characteristics of 21 patients with SSc, male to female ratio was 3: 18, proportion of diffuse cutaneous SSc was 24%, mean age was 63±13 years, and mean disease duration was 16±13 years. In SSc, both proportion of CD62p+or PAC1 +activated platelets (p<0.05, p<0.05, respectively) and production of MP were higher (p<0.05) compared to those in healthy controls. Of these, proportion of CD62p+platelets and MP production were correlated each other (r=0.88, p<0.05). Also, release reaction of platelet was upregulated in platelets from patient with SSc compared to healthy controls (p<0.05). When activation status of platelets was compared to clinical parameters, both proportion of CD62p +activated platelets and MP production were higher in diffuse cutaneous SSc (p<0.05, p<0.05, respectively) and correlated with modified Rodnan skin score (p<0.05, p<0.05, respectively).

**Conclusions:** In SSc, proportion of activated platelets were higher and associated with skin sclerosis, suggesting the involvement in the pathogenesis of SSc.

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**AB0189** **3D SKIN ORGANOID MIMICKING SYSTEMIC SCLEROSIS GENERATED BY PATIENT-DERIVED INDUCED PLURIPOTENT STEM CELLS: 'DISEASE IN A DISH' AND DEVELOPMENT OF ANIMAL MODEL**

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**Background:** Systemic sclerosis (SSc) is a rare autoimmune disease characterised by vasculopathy and fibrosis of various organs including skin. Although SSc has high morbidity and mortality, evidences for disease modifying treatment are

still lacking due to difficulties in performing clinical trials. Patient-specific induced pluripotent stem cells (iPSCs), which can differentiate into various cell types, are used in 3D organoid formation.

**Objectives:** We generated 3D skin organoid model from SSc-derived iPSCs by differentiating them into keratinocytes and fibroblasts. SSc-mimicking 3D skin organoid can be used in studies for disease modelling and drug screening.

**Methods:** Peripheral blood mononuclear cells (PBMCs) from patients with SSc were reprogrammed to iPSCs. SSc-derived iPSCs differentiated into keratinocytes and fibroblasts *in vitro*. Expression of markers for iPSCs, keratinocytes, and fibroblasts were determined by reverse transcription polymerase chain reaction (RT-PCR) analysis and immunofluorescence assay (IFA). 3D skin organoid using iPSC-derived differentiation cell line was generated by 3D culture system. Histologic analysis was performed on 3D skin organoid. SSc-derived 3D skin organoid was applied to SCID skin defect mice. Histologic analysis was also performed on SCID skin graft model.

**Results:** SSc-derived iPSCs formed colonies that resemble embryonic stem cells. Alkaline phosphatase staining showed undifferentiated state of iPSCs. Expression of iPSC markers was increased on SSc-iPSCs. Differentiated keratinocytes and fibroblasts from iPSCs highly expressed their markers for keratinocytes and fibroblasts, respectively. Dermis of SSc-derived 3D skin organoid was thicker and denser than that derived from healthy control. Epidermis and dermis of SCID skin graft model were thickened in those derived from SSc compared to those derived from healthy control.

**Conclusions:** Patient-derived 3D skin organoid and animal model well represented the characteristics of SSc. These models can serve as useful research tools to understand the disease and screen new drugs for SSc.

**Disclosure of Interest:** None declared

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**AB0190** **IMPAIRED ACTIVATION OF ATAXIA-TELANGIECTASIA MUTATED PROTEIN KINASE IN IMMUNE CELLS IS ASSOCIATED WITH CLINICAL FEATURES IN PATIENTS WITH SYSTEMIC SCLEROSIS**

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**Background:** Ataxia-telangiectasia mutated (ATM) is a protein kinase associated with ataxia-telangiectasia (AT), which is an autosomal recessive disorder due to defective functional activity of ATM. Telangiectasia, seen in AT, is also well known as one of the major characteristics of systemic sclerosis (SSc). ATM plays an important role not only in DNA damage repairing system, but also in the process of regulation of oxidative stress.<sup>1</sup> Moreover, it has been reported that oxidative stress may contribute to disease process of SSc<sup>2,3</sup>. Based on these background, we hypothesised that ATM may play a substantial role in the pathogenesis of SSc. However, the possible association between ATM activity and SSc development is not fully understood.

**Objectives:** To clarify the role of ATM in the pathogenesis of SSc, we demonstrated the expression and activation level of ATM in circulating immune cells and analysed the association with clinical characteristics of the patients.

**Methods:** Whole blood samples were collected from twenty-four patients with SSc and 12 healthy controls (HC). Expression levels of total ATM and active phosphorylated ATM (pATM) were examined in each immune cell subset (neutrophil, monocyte, T cell, B cell and NK cell) by mean fluorescence intensity (MFI) using flow cytometer. Each MFI level of ATM and pATM was compared between patients with SSc and HC, and was analysed the correlation with clinical characteristics of SSc patients, retrospectively collected from patients' records.

**Results:** The expression level of pATM was significantly lower in monocytes, neutrophils, and T cells in SSc as compared with HC (<sup>1887</sup>±128 vs 2386±181, p=0.03; <sup>10265</sup>±861 vs 16087±1218, p=0.0004; <sup>1326</sup>±73 vs 1675±103, p=0.009; respectively), whereas no significant difference in total ATM level was observed in each cell subset between two groups. Notably, the expression levels of pATM in monocytes of the patients with interstitial lung disease (ILD) was lower than that of the patients without ILD (<sup>1663</sup>±136 vs 1999±96, p=0.05). Furthermore, there was a tendency of correlation between pATM level in monocyte and parameters of pulmonary function test, such as forced vital capacity. No significant differences and/or correlation between pATM expression level in other cell subsets and clinical parameters of the patients, such as SSc subtype, SSc-specific autoantibodies, presence of pulmonary arterial hypertension, gastrointestinal involvement, digital tip ulcer, pitting scar and modified Rodnan skin score were observed.

**Conclusions:** In SSc, phosphorylated level of ATM in monocytes, neutrophils, and T cells was significantly lower than that of HC. Importantly, we found that ATM activation was impaired in monocyte of the SSc patients with ILD. These results

collectively suggest that the loss of ATM activation in monocytes may contribute to the disease process of SSc, and is possibly due to DNA damage and oxidative stress.

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#### AB0191 ANTI-SSA AND ANTI-JO1 LEVELS IN INTERSTITIAL LUNG DISEASE RELATED TO IDIOPATHIC INFLAMMATORY MYOPATHIES

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**Background:** The lung is the most frequently involved extramuscular organ in idiopathic inflammatory myopathies (IIMs); the most common form of lung involvement is interstitial lung disease (ILD). Some autoantibodies are strongly associated with ILD and with specific phenotypes and prognosis of ILD. Among myositis-specific auto-antibodies (MSAs), antibodies against aminoacyl-tRNA-synthetases (AsAb) are the strongest predictive factors for ILD, and anti-Jo-1 is the most common AsAb. Among myositis-associated auto-antibodies (MAAs), anti-SSA/Ro52 is frequently found in sera of patients with IIM and ILD, often associated with anti-Jo-1. The coexistence of anti-SSA/Ro52 and anti Jo-1 seems to be related to a more severe and extensive pulmonary fibrosis with higher score in HRCT compared with the patients with only anti-Jo-1 antibodies. Furthermore, some reports suggest that presence of anti-Jo-1 could be a biomarker for good prognosis<sup>1</sup>. The significance of antibodies levels for the prognosis of ILD in IIMs was not widely investigated.

**Objectives:** To investigate the relationship between antibody levels and clinical manifestations, laboratory data, pulmonary function tests (PFTs), disease activity indices in ILD associated to IIMs.

**Methods:** Among 130 IIMs admitted to Rheumatology Unit of Bari from January 2010 to January 2018, we retrospectively examined 49 patients (40 F; 22 PM, 25 DM, 1 IBM; mean age at ILD onset 51 years, range: 23–83) because of ILD defined by high resolution computed tomography (HRCT). Clinical manifestations, laboratory data, HRCT pattern, PFTs (FVC, FEV1 and DLCO), therapy, disease activity as Manual Muscle Test (MMT-12), Health Assessment Questionnaire (HAQ), Physician Global Assessment (PGA) at ILD onset, were obtained from medical records. Ferritin levels and autoantibodies were detected in serum samples collected at ILD onset. ANA were tested by IIF on HEp-2 cell substrates, MSAs (JO1, EJO, OJ, PL7, PL12, SRP, HMGCR, Mi2, TIF1 $\gamma$ , MDA5, NXP2, SAE) and MAAs (Ro52, Ku, PM/Sci 75–100, RNP, Sci70) by line-blot method. Anti-SSA and anti-Jo1 were also detected by CLIA method. Correlation analysis were run using parametric and non-parametric test according to data distribution.

**Results:** 45 of 49 (91,8%) patients were positive for MSAs and/or MAAs. 40 of 45 (88%) were positive at least one of MSAs. The double presence of MSAs and anti-Ro52 was observed in 21 of 40 (52,5%), showing anti-Jo1/SSA in most cases (15/21, 71,4%). Among all correlations studied between anti-Jo1 or anti-SSA levels and PGA or PFTs, we found a significantly correlation between anti-Jo1 and PGA ( $p=0,03$ ,  $R=0,46$ ). We didn't find significantly correlation between autoantibodies and ferritin serum levels.

**Conclusions:** These findings confirm that ILD was associated with autoantibodies positivity. Further studies in larger cohort need to investigate if autoantibodies levels have a prognostic role in global outcome. Unlikely some controversial works in literature, serum ferritin does not seem a biomarker of severity of lung involvement in IIMs.

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AB0192

#### DISCOVERY OF POTENTIAL SKIN BIOPSY BIOMARKERS FOR SYSTEMIC SCLEROSIS BY HIGH-THROUGHPUT PROTEOMIC APPROACHES

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**Background:** Systemic Sclerosis (SSc) is an autoimmune connective tissue rheumatic disease characterised by three main hallmarks; vasculopathy, immune system abnormalities and fibrosis. It is considered a multisystemic and heterogeneous disease as many organs of the body may be affected and symptoms vary among patients. Up to date, SSc is untreated and its etiology and pathogenesis remain unclear. Early prognosis and diagnosis of the disease are challenging.

**Objectives:** The aim of this study was to analyse the proteomic profile of SSc patients in order to gain insights into the mechanisms implicated in disease pathogenesis and also discover new biomarkers that would facilitate early prognosis, more accurate diagnosis and therapeutic targeting of SSc.

**Methods:** Human biopsies were obtained from ten affected and three non-affected skin areas of SSc patients and have been classified based on histological criteria. Biopsies were cryo-pulverised and proteins were extracted, purified, reduced, alkylated and digested by trypsin. Purified peptides were analysed on a Waters Synapt G2Si HDMSE instrument operated in ion mobility mode using a UDMS<sup>E</sup> approach. Data were processed by the Progenesis QIP and functional annotation analysis was carried out using multiple bioinformatics resources.

**Results:** Proteomic analysis led to the identification and quantification of approximately 1500 non-redundant proteins per sample. About 400 of these proteins, including interferons and interleukins, are differentially expressed between affected and non-affected samples. Functional annotation analysis of these proteins showed that they are involved in multiple pathways including, antigen processing and presentation, complement, ubiquitin mediated proteolysis and Notch signalling, which are known to be associated with autoimmune diseases and fibrosis.

**Conclusions:** Using a Mass Spectrometry-based proteomic approach for the analysis of SSc human skin biopsies, we identified a number of proteins that might be involved in the development and pathogenesis of SSc. Interestingly, some of these proteins are differentially expressed in specific histological groups and thus could be considered as potential biomarkers for specific SSc stages.

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AB0193

#### SEMAPHORIN4A INDUCES TH17 CYTOKINE PRODUCTION IN SYSTEMIC SCLEROSIS

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**Background:** Systemic sclerosis (SSc) is an autoimmune disease characterised by inflammation, vascular injury and excessive fibrosis in different organs. Different studies have shown that Th17 cells and Th17 cytokines (IL-17, IL-21 and IL-22) play a key role in the pathogenesis of the disease. Semaphorin 4A (Sema4A) is a transmembrane protein that belongs to a large family of proteins initially described as ligands essential for neuronal development. Further studies have shown that they also play a role in other biological processes including the control of immune responses. Importantly, Sema4A has a critical role in the skewing of CD4<sup>+</sup> T cells towards a Th17 phenotype. However, it is unknown if Sema4A contributes to the elevated number of Th17 cells observed in SSc patients.

**Objectives:** The aim of this study was to analyse the potential role of Sema4A as a regulator of Th17-skewing in SScs.

**Methods:** Plasma levels of Sema4A were measured by ELISA. Expression of Sema4A and its receptors PlexinB2, PlexinD1 and neuropilin-1 (NRP-1) was determined by (q)quantitative PCR, western blot and flow cytometry in monocytes and CD4<sup>+</sup> T cells of healthy donors (HD) and SSc patients. Monocytes were stimulated with Poly IC (5  $\mu$ g/ml) or CXCL-4 (5  $\mu$ g/ml) and Sema4A expression

was analysed by qPCR and ELISA. CD4<sup>+</sup> T cells were stimulated with anti-CD3/anti-CD28 beads (ratio 1 bead: 5 cells) alone or in combination with recombinant human Sema4A (200 ng/ml), in the presence or absence of neutralising anti-NRP1 or PlexinD1 antibodies, and the expression of PlexinB2, PlexinD1, NRP-1 and the production of Th17 cytokines was analysed by qPCR, ELISA and flow cytometry.

**Results:** Plasma levels of Sema4A were significantly higher in SSc patients compared to healthy controls (HC) and positively correlated ( $r=0.611$ ) with the skin disease severity. Sema4A and PlexinB2 expression was significantly higher in monocytes and CD4<sup>+</sup> T cells from SSc patients, respectively. Moreover, Poly IC and CXCL-4 significantly up-regulated the expression and secretion of Sema4A in monocytes from SSc patients, and CD4<sup>+</sup> T cells stimulation with anti-CD3/anti-CD28 beads increased the expression of PlexinB2 and NRP-1 in both HC and SSc patients. Finally, functional assays showed that Sema4A significantly enhanced the expression of Th17 cytokines induced by CD3/CD28 in CD4<sup>+</sup> T cells from both HC and SSc patients, and the blocking of the Sema4A signalling using neutralising antibodies anti-PlexinD1 and anti-NRP-1 significantly reduced this expression. Importantly, the Sema4A-induced IL-17 secretion was significantly higher in stimulated CD4<sup>+</sup> T cells from SSc patient compared to HC.

**Conclusions:** Sema4A signalling is deregulated in SSc patients and plays an important role in Th17 skewing. Therefore, Sema4A and its receptors could be promising therapeutic targets for the treatment of SSc.

**Disclosure of Interest:** None declared

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AB0194

#### SPARC IS ELEVATED IN THE AFFECTED SKIN OF SYSTEMIC SCLEROSIS PATIENTS AND INDUCES THE EXPRESSION OF FIBROTIC GENES IN DERMAL FIBROBLASTS AND MACROPHAGES

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**Background:** Systemic sclerosis (SSc) is an autoimmune disease characterised by inflammation, vascular injury and excessive fibrosis in multiple organs. SPARC is a matricellular glycoprotein that can bind to extracellular matrix (ECM) components, as well as cellular receptors and secreted growth factors. In doing so, SPARC regulates biological activities dependent upon cellular interactions with the ECM as well as processes dependent upon cell adhesion, including tissue remodelling, wound healing, angiogenesis and immune responses. Several studies have implicated SPARC in the pathology of SSc but the specific role of SPARC in fibrosis is still unknown.

**Objectives:** The aim of this study was to analyse the potential role of SPARC as a regulator of fibrosis in SSc.

**Methods:** Expression of SPARC in the skin of healthy donors (HD) and SSc patients was measured by immunohistochemistry. Peripheral blood-derived monocytes from HD and SSc patients were differentiated into macrophages with M-CSF (25 ng/ml). Dermal fibroblasts and M-CSF macrophages from both HD and SSc patients were stimulated with SPARC (0.1 and 1 µg/ml) for 6 hour and 24 hour. mRNA and protein expression of SPARC and other fibrosis-related genes were measured by qPCR and western blot.

**Results:** We found increased expression of SPARC in the affected skin of SSc patients compared to HD. We also observed a higher expression of SPARC and ECM components (collagen(Col)-1 and fibronectin-1 (FN1) in dermal fibroblasts derived from SSc patients. SPARC stimulation induced mRNA expression of important fibrosis-related genes such as *TGFβ1*, *PDGFB*, *SERPINE1* and *CTGF*, and ECM components including *COL1A1*, *COL3A1*, *COL4A1* and *FN1* in dermal fibroblasts from SSc patients, but not healthy donors. In M-CSF macrophages from SSc patients, SPARC also up-regulated mRNA expression of *TGFβ1*, *PDGFB*, *STAB1*, *COL1A1* and *FN1*.

**Conclusions:** These results suggest that SPARC is an important pro-fibrotic mediator contributing to the pathology driving SSc. Therefore, SPARC could be a promising therapeutic target for reducing fibrosis in SSc.

**Disclosure of Interest:** S. García Pérez: None declared, B. Malvar Fernández: None declared, M. Bergin Employee of: UCB, T. Johnson Employee of: UCB, W. Marut: None declared, K. A. Reedquist: None declared, T. R. Radstake: None declared

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AB0195

#### PROTEOMIC APPROACH IDENTIFIES DIFFERENTIAL PROTEIN EXPRESSION IN CULTURED FIBROBLASTS UNDER STIMULATION WITH TGF-β1

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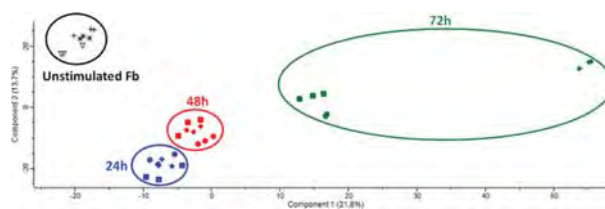
**Background:** Fibroblasts (Fb) are key effectors cells in systemic sclerosis (SSc).<sup>1</sup> Fb stimulation with TGF-β1 is usually considered as the positive control in studies assessing the fibrogenesis in SSc.<sup>2</sup> Yet, the lack of standardisation of TGF-β1 stimulation might be responsible for discrepancies in experiments performed in different conditions. Proteomic approach allows the analysis of differential expression of the whole proteins (proteome) in Fb, and appears an interesting approach to compare different culture conditions.

**Objectives:** We designed this study to compare the whole protein expression in Fb stimulated by TGF-β1 in different conditions.

**Methods:** At fifth passage, primary culture of human Fb from healthy subjects (ATCC; PCS-201-012) were stimulated or not with different concentrations of recombinant human active TGF-β1 (0.04, 1, and 5 ng/mL) (R and D Systems; 240-B-002) during 24, 48 and 72 hours. Proteins were extracted and analysed using an eFASP LC-MS/MS approach on an Orbitrap mass spectrometer (Thermo Scientific; Q Exactive +). Proteins quantitation was performed by Max-quant and statistical analysis by Perseus using ANOVA and principal component analysis (PCA).

**Results:** A total of 3267 proteins were identified, of which 1957 showed differential expression using ANOVA analysis. PCA revealed several clusters of differential proteins expression (figure 1). There were clear clusters of protein expression related to (i) unstimulated and stimulated conditions, (ii) between the three different times of stimulation and (iii) to TGF-β1 concentrations used. Although the expression of proteins in Fb exposed to 0.04 and 1 ng/mL of TGF-β1 during 72 hour were rather close, there was a unique proteins profile related to the condition with 5 ng/mL of TGF-β1 during 72 hour.

Figure 1: PCA representation of differential proteins expression in different conditions. [TGF-β1]=0.04 ng/mL: square; [TGF-β1]=1 ng/mL: circle; [TGF-β1]=5 ng/mL: diamond. The more the points appear distanced, the more different is the protein expression.



**Abstract AB0195 – Figure 1.** PCA representation of differential proteins expression in different conditions.

**Conclusions:** This study highlights a variation of proteins expression depending on both stimulation time and TGF-β1 concentrations in Fb culture. The identification of protein differentially expressed will provide insights in the impact of TGF-β1 on Fb physiology under stimulation conditions. These data underline the need of standardisation of culture conditions to allow inter-data comparisons using in sensitive “omic” approaches.

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### AB0196 ENDOPLASMIC RETICULUM STRESS IN SYSTEMIC SCLEROSIS

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**Background:** Systemic sclerosis is an autoimmune connective tissue disease in which there is inflammation and skin fibrosis. Currently there is no disease modifying treatment due to the limited understanding of the pathogenesis of the disease. Endoplasmic reticulum (ER) stress, characterised by misfolded proteins, can be induced by a variety of stressors such as redox imbalance and calcium depletion. This activation of ER stress by whatever trigger results in activation of an evolutionary conserved cell sensors and a resulting signalling cascade to help restore homeostasis. It is suggested in other fibrotic diseases that ER stress is prominent.

**Objectives:** The aim of this study is to determine the role of ER stress in Systemic Sclerosis.

**Methods:** Healthy dermal fibroblasts where cultured *in vitro* and stimulated with the ER stress inducer thapsigargin and in some experiments with small interfering RNA to X-Box binding protein-1 or scramble controls at the matched concentration. Cells were then lysed and subjected to western blotting of XBP-1, IRE- $\alpha$ , ATF-6, collagen-1 and alpha tubulin for a loading control. In some experiments the dermal fibroblasts were treated with ER stress and 4-phenylbutric acid to inhibit ER stress and markers measured. q-RT-PCR was performed for Fli-1 and 18S using specific primers and subjected to real time with SYBR green and normalised to 18S.

**Results:** ER stress mediated by thapsigargin results in activation of classical ER stress pathways. Inhibition of these pathways through small interfering RNA results in attenuation of collagen expression in dermal fibroblasts. This was also the case with dermal fibroblasts treated with the chemical inhibitor 4-phenylbutric acid. The epigenetic modifier Fli-1 is reduced after ER stress. This is known to act as a brake on collagen regulation.

**Conclusions:** ER stress induced collagen accumulation and could be blocked by chemical and genetic reduction of XBP-1. Mechanistically this could be due to reduced Fli-1 thereby releasing the brake on collagen1 expression. Modulation of ER stress via chemical inhibitors could be a promising new treatment in SS.

**Disclosure of Interest:** None declared

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### AB0197 METALLOPROTEINASE-7 AS AN EARLY MARKER OF LUNG DAMAGE AMONG POLYMYOSITIS AND DERMATOMYOSITIS PATIENTS

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**Background:** Interstitial lung disease (ILD) can complicate the course of polymyositis/dermatomyositis (PM/DM) almost in the half of patients and represents as a high risk factor of mortality among such cohort of patients from chronic pulmonary insufficiency. Lung function monitoring and chest high resolution computer tomography (HRCT) are obligatory methods of investigation among PM/DM patients. However, these methods allow to determine already formed interstitial changes in the lungs. Therefore, there is a need for biomarkers to seek early changes of lung tissue, what allows to prescribe basic treatment in time, encountering its side effects.

Metalloproteinase 7 (MMP-7) reflect lung damage and can also be an early biomarker of ILD which complicates PM/DM. It was early reported that -181A/G (rs11568818) polymorphism in MMP-7 promoter modulates gene expression and plays pivotal role in the MMP-7 upregulation in that way affects ILD progression. Here, we evaluated the impact of -181A/G polymorphism in MMP-7 promoter activity and its association with MMP-7 elevation.

**Objectives:** Our study was aimed to analyse the level of MMP-7 as an early marker of lung damage among PM/DM patients and also probable influence of rs11568818 on the MMP-7 elevation.

**Methods:** 17 patients with PM/DM have been observed in the rheumatology department with primary established diagnosis, 9 patients among them has proved diagnosis of ILD with HRCT. All patients have been examined according to the recommended EULAR standards and paraneoplastic reaction have been excluded. Patients have been divided into 2 groups, 1st group include 9 patients with PM/DM complicated with ILD, 2nd – 8 patients with isolated PM/DM. Control group included 17 healthy volunteers. MMP-7 level was assayed by the enzyme immunoassay system in the blood serum. -181A/G (rs11568818) polymorphism was genotyped by polymerase chain reaction restriction fragment length polymorphism (PCR-RFLP) method. All statistical calculations were done using SPSS software 21.0.

**Results:** Results. Mean age of patients of the 1st group – 48,44±2,74, 2nd – 54,25±2,55, control group – 49,0±2,4 (p=0,33). DM have been established in 7 patients and PM – 10. Mean level of MMP-7 in the 1st group was 4,02±1,58 (CI 95% 2,81–5,24), 2nd – 1,43±0,2(CI 95% 0,93–1,92), control group – 1,3±0,75 (F=30,87, p<0,001). It was determined that the level of MMP-7 was positively correlated with Anti-Jo1 antibodies (r=0,82, p=0,007) and it was higher among PM/DM patients complicated with ILD (p=0,001). Analysis of genotypes frequency AA/AG/GG with regard to rs11568818 polymorphism, shows no significant distribution (p=0,984) and is following in the 1st group – 66,7%/22,2%/11,1% and 62,5%/25%/12,5% – in the 2nd, in the control group – 70,6%/17,6%/11,8% respectively. The analysis of the connexion between studied genetic polymorphism with the level of MMP-7 didn't show any interdependence (p=0,771).

**Conclusions:** The level of MMP-7 is higher among the 1st group, in comparison with 2nd and control groups. Positive correlation connexion between the level of MMP-7 and Anti-Jo1 antibodies among PM/DM patients with ILD was found. The difference between genotypes distribution according to the rs11568818 gen polymorphism depending on existence of ILD and MMP-7 level is absent. Taking into account the results, we can admit that MMP-7 is a perspective marker of lung tissue damage among PM/DM patients.

**Disclosure of Interest:** None declared

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### AB0198 BIOLOGICAL PROPERTIES OF URINE-STEM CELLS AND THERAPEUTIC EFFECT ON SYSTEMIC SCLEROSIS FIBROSIS

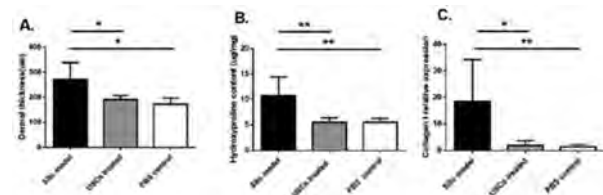
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**Background:** Because of the lack of effective treatment of systemic sclerosis (SSc), cellular therapy is considered as a salvage option.<sup>1-4</sup> Mesenchymal stem cells (MSCs) are gaining attentions in the field of cell therapy of SSc. However, current isolation methods of MSCs are all invasive and challenging.<sup>5</sup> Some studies have reported the isolation from urine recently, and definition of urine-derived stem cells (USCs).<sup>6</sup> The collection of USCs is noninvasive that could be a desired resource of MSC. So far, the information of therapeutic effect on SSc is limited.

**Objectives:** We aimed to explore the biological characterizations of USCs and investigate the therapeutic effect on murine SSc model.

**Methods:** USCs were isolated and cultivated from sterile urine samples of healthy adult individuals. The related cell markers were examined by flow cytometry. The differentiation potentials were observed in adipogenic, osteogenic and chondrogenic medium, respectively. SSc murine models were conducted by daily intradermal injections of bleomycin and were further divided as treated and untreated group. Also, the healthy control group was conducted by daily injection of phosphate buffered saline (PBS). Treated group received an infusion of 2.5 × 10<sup>5</sup> USCs in the tail vein twice in one week after the 3 week modelling. Skin samples were obtained one week after the treatment. Hematoxylin-eosin and Masson staining were accomplished to observe the skin thickness and the hydroxyproline content was detected by hydroxyproline kit. The relative expression of collagen type I alpha 1 chain (Col1- $\alpha$ 1), alpha-smooth muscle actin ( $\alpha$ -SMA), and fibronectin 1 (Fn-1) were detected by real-time quantitative PCR.

**Results:** The morphology of USCs was spindle-shaped. They express CD73, CD90, and CD105 but CD34, CD45, CD19, CD11b, or HLA-DR. USCs possessed the abilities to differentiate into adipocytes, osteoblasts, and chondrocytes. In USCs treated group, the skin thickness (p=0.031) (Figure1A), the deposition of collagen in HE and Masson trichrome-staining (p=0.007) (Figure1B), and Col1- $\alpha$ 1 gene expression (p=0.010) (Figure1C) were significantly reduced in comparison with untreated group and were close to healthy controls.



Abstract AB0198 – Figure 1

**Conclusions:** USCs can be isolated from adult sterile urine. They possess the multipotent differentiation abilities and displays a therapeutic effect on bleomycin-induced skin fibrosis and collagen synthesis.

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**Disclosure of Interest:** None declared

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## Rheumatoid arthritis – prognosis, predictors and outcome

### AB0199 ENDOCAN LEVELS AND SUBCLINICAL ATHEROSCLEROSIS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is an inflammatory autoimmune disease with unknown etiology. Accelerated atherosclerosis (AS) and AS with heart disease are among the major causes of morbidity and/or mortality in RA. Endothelial-specific molecule 1 (endocan) is a potential indicator of vascular events and is expressed in response to inflammatory mediators in endothelial cells. Carotid intima media thickness (cIMT) is used to detect early signs of AS but also progression in cardiovascular diseases related to AS.

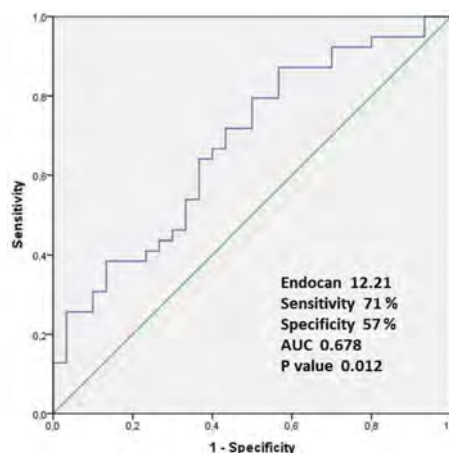
**Objectives:** The aim of the present study is to evaluate the relationship of serum endocan levels with RA and cIMT as a candidate marker of diseases to be used in clinical practice.

**Methods:** The study was conducted between June 2012 and March 2013 at the Rheumatology Clinics of Necmettin Erbakan Meram Medical School, Turkey. Thirty nine<sup>39</sup> RA patients, diagnosed according to the 1987 criteria of the American College of Rheumatology, and 30 age- and sex-matched healthy subjects as the control group were included in this study.

**Abstract AB0199 – Table 1.** The clinical and laboratory parameters in two groups.

	RA patients (n=39) (mean±SD)	Controls (n=30) (mean±SD)	P value
Age (years)	47.7±8.8	43.0±10.8	0.057
Gender (M/F), n (%)	33 (84.6)/6 (15.4)	21 (70)/9 (30)	0.238
BMI (kg/m <sup>2</sup> )	28.0±4.3	27.1±5.1	0.443
ESR (mm/h)	28.56±16.16	18.70±12.27	0.005
CRP (mg/dL)	0.55±0.54	0.42±0.55	0.336
TC (mg/dL)	198.28±48.15	165.43 ±30.59	0.001
TG (mg/dL)	153.58±93.02	132.73 ±55.74	0.252
LDL-c (mg/dL)	123.02±44.88	118.81 ±24.76	0.622
HDL-c (mg/dL)	50.43±10.18	42.12±8.18	<0.001
cIMT (mm)	0.63±0.17	0.51±0.12	0.001
Endocan	14.11±3.27	12.10±2.92	0.009

RA, Rheumatoid arthritis; BMI, body mass index; cIMT, carotid intima media thickness; TC, total cholesterol; TG, triglyceride; LDL-c, low density-lipoprotein cholesterol; HDL-c, high density-lipoprotein cholesterol; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein;



**Abstract AB0199 – Figure 1**

**Results:** No significant difference was detected between groups with respect to age, sex and body mass index. In the patient group the Endocan and cIMT values were found to be 14.11±3.27 ng/mL and 0.63±0.17 mm, while in the control group they were 12.10±2.92 ng/mL and 0.51±0.12 mm, the Endocan and cIMT values were significantly higher in the patient group (p=0.009 and p=0.001, respectively). Positive correlations was found between Endocan, cIMT and Disease Activity Score of 28 joints (p=0.008 and p=0.029, respectively). When assessing the endocan levels of RA patients in the study population, cut off value of 12.21 with sensitivity of 71%, specificity of 57% and p=0.012 (area under curve: 0.678, 95% confidence interval (CI) 0.555–0.805) were observed according to ROC curve analysis.

**Conclusions:** Endocan might be a useful marker to evaluate atherosclerotic lesions in patients with RA and also to assess disease severity.

**Disclosure of Interest:** None declared

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### AB0200 FACTORS ASSOCIATED WITH FUNCTIONAL CAPACITY IN A BRAZILIAN COHORT OF PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS FROM THE "REAL" STUDY

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**Background:** Rheumatoid arthritis (RA) is associated with impairments in functionality, affecting aspects such as physical capacity, independence, mental health, social and professional life. Health Assessment Questionnaire-Disability Index (HAQ-DI) is a validated tool for assessing functional capacity in RA patients. A simple questionnaire with a score of 0 to 3 is applied, with an inverse relationship between grade and functionality. Previous studies have shown worse functional indexes in patients with high disease activity and established joint damage.

**Objectives:** To relate clinical, laboratory and therapeutic aspects with HAQ-DI in a large cohort of Brazilian patients.

**Methods:** A prospective, multicenter cohort study ("REAL" Study) involving 11 Brazilian centres specialised in the treatment of RA patients. All patients were submitted to at least 3 clinical evaluations in a 12 month period. Only patients older than 18 years and classified as RA according to 1987 (ACR) or 2010 (ACR/EULAR) criteria were evaluated. HAQ-DI was applied for assessing functional capacity, and the results were analysed for association with clinical, laboratory and therapeutic elements. Comparison between groups was performed using Mann-Whitney or Kruskal-Wallis tests.

**Results:** Overall, 1116 patients (89.43% females, mean age 58±11 years) took part in the study. Rheumatoid factor (RF) in high levels and bone erosion were both associated with higher HAQ-DI indexes (p: 0.0244 and p<0.0001, respectively). Of all patients, 89.7% were using conventional synthetic disease-modifying antirheumatic drugs (DMARDs) and 36.5% were on biologic DMARDs or

targeted-synthetic DMARDs. The use of any conventional synthetic DMARD was associated with lower HAQ-DI indices ( $p: 0.0243$ ), while the use of any biologic DMARD or targeted-synthetic DMARD was related to greater functional impairment ( $p: 0.0018$ ). By evaluating separately, abatacept ( $p: 0.0046$ ), rituximab ( $p: 0.0001$ ) and tocilizumab ( $p: 0.0441$ ) were associated with higher levels of HAQ-DI. The results are summarised in table 1.

**Abstract AB0200 – Table 1.** Health assessment questionnaire-disability index score position and dispersion measurements and result of comparison between groups

Variable	Category	N	Mean	SD	Median	p-value
Rheumatoid factor	High	612	0.89	0.80	0.88	0.0244*
	Low	247	0.89	0.73	0.75	
	Negative	226	0.82	0.74	0.75	
ACPA	High	202	0.96	0.77	0.88	0.3007*
	Low	96	0.90	0.84	0.83	
	Negative	111	0.88	0.75	0.80	
Bone erosion	No	493	0.77	0.72	0.63	<0.0001*
	Yes	599	1.06	0.80	1.00	
Methotrexate	No	373	0.96	0.60	0.60	0.4020
	Yes	739	0.91	0.76	0.75	
Leflunomide	No	735	0.93	0.77	0.88	0.8030*
	Yes	377	0.93	0.78	0.88	
Hydroxychloroquine	No	993	0.84	0.78	0.88	0.2690*
	Yes	118	0.85	0.75	0.75	
Sulfasalazine	No	1,658	0.93	0.78	0.88	0.6727*
	Yes	54	0.87	0.75	0.81	
Conventional synthetic DMARDs	No	118	1.12	0.88	1.00	0.0242*
	Yes	997	0.91	0.78	0.75	
Adalimumab	No	1,659	0.92	0.77	0.88	0.7728*
	Yes	52	1.06	0.86	0.75	
Infliximab	No	1,064	0.93	0.77	0.88	0.8659*
	Yes	48	0.94	0.78	0.91	
Etanercept	No	1,046	0.94	0.77	0.88	0.1317**
	Yes	66	0.79	0.75	0.69	
Certolizumab pegol	No	1,099	0.93	0.78	0.88	0.3074*
	Yes	17	0.72	0.67	0.50	
Golimumab	No	1,076	0.93	0.78	0.88	0.6372*
	Yes	37	0.85	0.70	1.00	
Tocilizumab	No	1,258	0.92	0.78	0.75	0.6441**
	Yes	54	1.08	0.88	1.00	
Abatacept	No	1,940	0.91	0.77	0.75	0.6046**
	Yes	72	1.18	0.75	1.00	
Rituximab	No	1,063	0.91	0.77	0.75	0.0001**
	Yes	49	1.34	0.77	1.00	
Tocilizumab	No	1,103	0.93	0.77	0.88	0.9211**
	Yes	9	0.93	0.78	0.75	

**Conclusions:** In our prospective cohort, patients with high levels of RF, bone erosion, in use of any biologic DMARD or targeted-synthetic DMARD, abatacept, rituximab or tocilizumab had worse functional capacity indexes. When compared to non-use, the use of any conventional DMARD was associated with better rates of HAQ-DI.

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**Disclosure of Interest:** None declared

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#### AB0201 ASSOCIATION BETWEEN BASELINE CALPROTECTIN SERUM LEVELS AND RESPONSE TO BIOLOGICAL THERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Calprotectin (CLP) is an important proinflammatory factor of innate immunity released from activated granulocytes and macrophages during inflammation, which has also been identified in synovial fluid. It is a potential pro-inflammatory biomarker reflecting joint damage. CLP levels in synovial fluid are well correlated with levels in plasma, which allows measuring it easily in patients with rheumatoid arthritis (RA). However, the additional value of CLP over other biomarkers is unclear

**Objectives:** To study the association of baseline CLP serum levels with the clinical response and serum drug levels in patients under biological therapy at 6 and 12 months after starting treatment.

**Methods:** Prospective observational study including 109 patients with RA who started biological treatment (Infliximab(Ix);Adalimumab(Ada);Etanercept(Etn); Certolizumab(Ctz);Golimumab(Glm); Tocilizumab(Tcz) and Rituximab(Rtx) in a tertiary hospital since 1999 to 2016. Serum CLP levels were measured by ELISA

with the commercial kit CALPROLAB (Lysaker, Norway). Levels of biological drug and ADA were measured by capture and bridging ELISA respectively, except Certolizumab which was measured by Sanquin Diagnostic Service. Clinical response was assessed by  $\Delta$ DAS28. Serological and clinical parameters were evaluated at baseline, 6 and 12 months. For analysis, linear regression models adjusted for confounders (age, sex, BMI, DMARDs, smoking status) and with standardised beta as estimate were employed.

**Results:** Out of 109 studied patients, 22% patients received Ix, 6% Ada, 16% Etn, 18% Ctz, 5% Glm, 25% Tcz and 9% Rtx. Most patients were woman (84%), with a median (IQR) age of 62 (52.3–73.1) and disease duration of 9.5 (4.8–15.3). At baseline, CLP levels directly correlated well with CRP and DAS28( $r=0.411$ ;  $p<0.001$  and  $r=0.308$ ;  $p<0.001$ ). On the other hand, an inverse correlation between baseline CLP levels and the presence of drug at 6 ( $\beta=-0.325$ ;  $p=0.01$ ) and 12 months ( $\beta=-0.397$ ;  $p<0.001$ ) was also found. Moreover, in the adjusted analyses a trend for this correlation at 6 months ( $\beta=-0.199$ ;  $p=0.07$ ) and a significant correlation at 12 months ( $\beta=-0.381$ ;  $p<0.001$ ) was observed. Additionally, in the non-adjusted models, baseline CLP levels significantly directly correlated with the clinical response at 6 months ( $\beta=0.194$ ;  $p=0.04$ ) while the correlation at 12 months was not significant ( $\beta=0.186$ ;  $p=0.06$ ). However, after adjusting for confounders, no significant correlation was found at any study point ( $\beta=0.213$ ;  $p=0.06$  at 6 months and  $\beta=0.206$ ;  $p=0.07$  at 12 months).

**Conclusions:** In patients with RA initiating biological therapy, baseline CLP concentrations are inversely correlated with the circulating drug levels along the treatment. However, the additional value of CLP as a predictor of clinical response remains unclear.

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#### AB0202 GLUCOCORTICOIDS IN THE INITIAL TREAT-TO-TARGET STRATEGY OF EARLY RHEUMATOID ARTHRITIS

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**Background:** As stated in the 2013 update of RA recommendations, glucocorticoids (GCs) should be used as bridging therapy for up to 6 months, ideally tapering them at earlier time points.<sup>1</sup>

**Objectives:** To evaluate whether initial combination therapy with GCs and disease modifying anti-rheumatic drugs (DMARDs) influences clinical and radiological outcome in the real-life practice of a cohort of early rheumatoid arthritis (ERA) patients.

**Methods:** A total of 367 ERA patients with less than 12 months of disease duration were enrolled in the study. ERA patients fulfilled the 2010 ACR criteria for RA and were followed according to the treat-to-target strategy. The mean follow-up (FU) was 38.2±32.8 months. At baseline, and every three months, the ACR/EULAR core data set variables were recorded. At baseline and every year, hand and foot radiographs were examined according to modified Total Sharp score (mTSS). At each visit, clinical improvement and remission were evaluated according to EULAR criteria. The achievement of CDC (28-joint Disease Activity Score using C reactive protein <2.6, Health Assessment Questionnaire <0.5 and change from baseline in mTSS ≤0.5) was assessed every year of follow-up.

**Results:** At baseline 291 (71.9%) ERA patients started GCs at a dosage of 0.2 mg/kg, gradually tapered and withdrawn as rapidly as clinically feasible. As expected, these patients presented higher values of acute phase reactants ( $p=0.001$ ), and higher levels of disease activity scores ( $p<0.001$ ) and disability index ( $p=0.001$ ), compared to the 76 subjects (18.8%) who had not been prescribed GCs. Patients not treated with GCs were in higher percentages anti-citrullinated peptide antibody (ACPA) (75.0%) and IgM-rheumatoid factor (RF) (64.5%) positive, compared to subjects taking GCs (62.9%,  $p=0.05$ ; 49.8%,  $p=0.02$ , respectively). There were no differences regarding age, disease duration, BMI, smoking habit and presence of erosions at onset. The mean duration of GC treatment was 7.5±7.9 months and the mean dosage during FU was <5 mg prednisone per day. During the FU, in the two groups a similar percentage of patients started a combination therapy with biological (b)-DMARDs and no differences were observed regarding radiographic progression.

A higher rate of remission defined according to DAS values, 2011 ACR/EULAR criteria, and CDC criteria, was registered in patients not treated with GCs compared to subjects who required corticosteroid therapy. ERA patients that didn't manage to stop GCs at the sixth month (38.8%) had a higher BMI ( $p=0.04$ ) and a lesser chance of achieving remission defined according to DAS values, 2011 ACR/EULAR criteria, and CDC criteria during follow-up. Moreover, a higher percentage of them required a combination therapy with bDMARDs during FU ( $p<0.0001$ ).

**Conclusions:** In our cohort ERA patients initially treated with GCs had higher disease activity scores at onset compared to subjects without GCs. The lesser chance of achieving remission and the higher rate of bDMARD therapy in ERA



patients not able to stop GCs, reflect a more aggressive disease, refractory to conventional drugs.

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**Disclosure of Interest:** None declared

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AB0203

#### CLINICAL PHENOTYPE AND ULTRASOUND CHARACTERISTICS OF RHEUMATOID ARTHRITIS FLARE AFTER DISCONTINUATION OF CONVENTIONAL SYNTHETIC DMARDS

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**Background:** Current protocols based on early and intensive treatment with csDMARDs in rheumatoid arthritis (RA) have allowed the achievement of remission in a considerable proportion of the patients and opened the perspective, in selected cases, of a drug-free monitoring scheme. Treatment discontinuation can lead, however, to possible recurrence of joint inflammation and clinical flare. Understanding the dynamics acting upstream these events remains a fundamental research task with direct clinical and patho-biologic implications.

**Objectives:** To delineate the clinical, serological and ultrasonographic changes associated to a drug-free flare in patients discontinuing csDMARD after achievement of stable remission. Co-primary objective was to compare, through a retrospective analysis in the same patients, these changes with early features of the pathology at onset, before treatment introduction.

**Methods:** 92 RA patients in stable DAS28 remission following a DAS-steered treatment strategy with MTX were recruited in our Centre and introduced to a drug-free monitoring scheme according to the following inclusion criteria: a) treatment introduced within 12 months from symptoms' onset, b) at least 24 months of continuative treatment, c) DAS28 <2.6 for at least 6 months in the absence of glucocorticoids. After discontinuation, all patients were follow-up at three months intervals across 24 months through complete clinical, ultrasonographic (power Doppler ultrasound –PDUS- in hands-feet and tendons) and serological analyses. Treatment was re-introduced upon occurrence of moderate disease activity (DAS28 ≥3.2) in a single occasion.

**Results:** A total drug-free follow-up of 1398 person-months was analysed with a median (IQR) of 15<sup>6–24</sup> months. Thirty-eight patients (27/38 in ACR/EULAR Boolean remission, 16/38 with PD score=0 at withdrawal visit) required treatment re-introduction after a median (IQR) time from discontinuation of 6<sup>3–9</sup> months (range 3–18). DAS28 variations at re-treatment showed a mean (SD) increase of 2.26 (1.03), reflecting significant differences in all DAS components (p<0.001 for ESR, tender joint count, swollen joint count and GH). Clinical activity in flaring subjects was paralleled by average changes in synovial US, with increased PD scores in hands joints (median [IQR]: 3.5 [0.5–7] vs 1 [0–2], p<0.001), feet (1 [0–4] vs 0 [0–0.5], p=0.002) and tendons (0 [0–2] vs 0 [0–0], p=0.002), determining *ex-novo* PD positivity in 85.7% of PD negative patients (p<0.001). Despite stringent remission achieved at the time of discontinuation, no significant differences were observed between disease onset and drug-free flare in DAS28 (p=0.26), patient global assessment of disease activity (p=0.53) and synovial US scores (p=0.61 for grey scale, p=0.31 for PD) with recurrence of similar patterns of clinical joint involvement.

**Conclusions:** Drug-free clinical flare can occur over a wide temporal window, in the absence of detectable signs of inflammation at the time of treatment discontinuation. It can associate with *ex-novo* recurrence of US pathologic changes at joint and tendon level, reproducing some of the quantitative/qualitative features of disease onset.

**Disclosure of Interest:** None declared

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AB0204

#### RADIOGRAPHIC PROGRESSION OF LARGE JOINT DAMAGE IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH BIOLOGICAL DISEASE-MODIFYING ANTIRHEUMATIC DRUGS (BDMARDS) AND ITS PREDICTIVE FACTORS: RESULTS OF 3 TO 4 YEARS FOLLOW-UP

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**Background:** Although damage to large joints such as the shoulder, elbow, hip, knee, and ankle has a substantially larger impact on functional ability than

damage to the small joints of the hand and foot,<sup>1 2</sup> large joints are not routinely monitored for progressive damage in patients with rheumatoid arthritis (RA). Furthermore, a little information is available regarding long-term follow-up results of radiographic progression of damage (RPD) to the large joints during treatment with biological disease-modifying antirheumatic drugs (bDMARDs).

**Objectives:** We investigated ratios of RPD to the large joints in RA patients treated with bDMARDs for 3 to 4 years and analysed association between RPD and patient backgrounds or Larsen grades of individual large joint.

**Methods:** Sixty-eight patients (naive: 42, switch: 26) receiving bDMARDs (IFX: 5, ETN: 9, ADA: 7, GLM: 3, CZP: 5, TCZ: 28, ABT: 11) for 3 to 4 years or achieving bDMARDs-free status were included in this study. The mean age and disease duration at the start of bDMARDs was 62.7 year-old and 10.7 years, respectively, and baseline DAS28-ESR and HAQ was 4.61 and 1.014, respectively. A total of 311 joints including shoulder, elbow, hip, knee, and ankle were evaluated whether there was RPD during the observation period by comparing radiographs before and after the treatment.

**Results:** RPD was found in 22 patients (31.4%) and 32 joints (10.0%), and it occurred during the former half period in 17 joints and during the latter half period in 15 joints. Joints with Larsen grade (LG) III or more had significantly higher ratios of RPD than those with LG II or less (p<0.01). An ROC analysis was performed to calculate the cut-off value for the progressive damage, which was 2.5 (sensitivity: 50.0%, specificity: 79.6%), suggesting that exceeding LG III would be a risk factor for the RPD to the large joints. A multivariate logistic regression analysis revealed that stage and baseline HAQ were independent risk factors for RPD (cut-off value: 2.5, odds ratio: 8.864 for stage; cut-off value: 1.4375, odds ratio: 6.316 for baseline HAQ).

**Conclusions:** The stage and baseline HAQ were associated with RPD to the large joints, and progressive damage is expected to increase when the stage exceeds III and/or functional disability exceeds an HAQ score of 1.5. Progressive damage also increases when LG exceeds III. Treatment with bDMARDs should be started before stage, HAQ, and LG exceed III, 1.5, and III, respectively.

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AB0205

#### COMPARISON OF THORACIC HRCT AND SELF-REPORTED QUESTIONNAIRES IN THE ASSESSMENT OF PULMONARY INVOLVEMENT IN RHEUMATOID ARTHRITIS PATIENTS: PRELIMINARY RESULTS

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**Background:** Pulmonary involvement in rheumatoid arthritis (RA) is one of the extra-articular manifestations affecting morbidity and mortality during the course of the disease. Pulmonary function tests (PFTs) and thoracic high-resolution computerised tomography (HRCT) are the standard of care in the assessment of pulmonary involvement in RA. In this study, we aimed to compare the findings between self-reported questionnaires and HRCT to detect pulmonary abnormalities in RA patients.

**Methods:** Forty-two RA patients fulfilling ACR/EULAR classification criteria (2010) who had thoracic HRCT within 6 months of any symptom and/or any pathology on radiography of chest were included in the study. The patients were also assessed by modified Borg Scale, SF-36 Quality of Life Scale and Leicester Cough Questionnaire for the evaluation of respiratory symptoms.

**Results:** Demographics and clinical characteristics were summarised in table 1. Warrick score, assessing the severity and extent of alveolitis and fibrosis on thoracic HRCT, was evaluated in 15 patients with ILD (score range:4–28). DLCO values were lower in patients with Warrick score ≥1 (73±22% vs. 88±12%, p=0.019) while FVC were not found to be different. The findings of HRCT and self-reported questionnaires were summarised in table 2. Any relationship between self-reported questionnaires and Warrick scores was not detected. Presence of any parenchymal lesions was found to be associated with SF-36 total score (p=0.048). DLCO levels were found to be negatively correlated with SF-36 total scores (r=-0.470, p=0.006).

**Abstract AB0205 – Table 1.** Demographics and clinical characteristics (n=42)

Age (years)	59±9	DMARDs and Biologics	
Sex (W/M)	32/10	MTX	15 (36%)
Smoking (%)	12 (29%)	LEF	19 (45%)
RF(+)	31 (74%)	ADA	5 (12%)
AntiCCP(+)	27 (64%)	IFX	9 (21%)
DAS28-ESR	3.1±1.0	ETA	10 (24%)
Corticosteroids	28 (67%)	ABA	13 (31%)
		TOC	2 (5%)
		TOF	2 (5%)
		RTX	20 (50%)

**Abstract AB0205 Table 2.** Thoracic HRCT findings and self-reported questionnaires in RA patients

Warrick Score (n=15)	
Alveolitis	2.6±1.2
Fibrosis	12±6.3
Total	15±7
Leicester Cough Questionnaire score (n=42)	
Modified Borg Scale	1.8±2.1
SF-36	53±17

**Conclusions:** In this study, we could not show any relationship between self-reported questionnaires and thoracic HRCT findings, except a weak association of the presence of parenchymal lesions with SF-36 scores. Alveolitis and/or fibrosis on thoracic HRCT were found to be associated with lower DLCO. DLCO was shown to be negatively correlated with SF-36 scores. SF-36 might be included in the detection of pulmonary evaluation in RA patients. The relationship between thoracic HRCT findings and self-reported questionnaires in RA necessitates further studies.

**Disclosure of Interest:** None declared

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#### AB0206 EXPRESSION OF INFLAMMATORY GENES AND THE IL1B GENE ASSOCIATION WITH THE SEVERITY OF RHEUMATOID ARTHRITIS IN TAMIL NADU POPULATION

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**Background:** Rheumatoid Arthritis (RA) is a multifactorial complex and chronic inflammatory disease associated with progressive joint destruction, disabling and systemic complications. The prevalence is about 0.5%–1% worldwide and 0.9% in India. Genetic factors are recognised to have substantial effect on the susceptibility to RA.

**Objectives:** The present study aims to investigate the inflammatory caspase genes (*CASP5* and *CASP8*) as well as proinflammatory cytokine interleukin-1beta (IL-1β) in RA patients. Hence the study was designed to explore the possible association of inflammatory genes in Tamil Nadu population.

**Methods:** We conducted a study involving 55 RA patients and equal number of normal healthy controls and performed gene expression analysis in *CASP5* and *CASP8* genes. We also carried out genotyping of IL-1β gene using PCR-RFLP. For gene expression study, the mRNA levels of inflammatory genes were assessed using qPCR and the inflammatory marker levels (IL-1β) were estimated by ELISA.

**Results:** The gene expression analysis of RA patients showed activation of *CASP5* and *CASP8* compared to the healthy individuals. The inflammatory marker levels in the serum showed significantly higher levels (23.35±2.12 pg/mL) p<0.05) in RA patients compared to the control subjects. The homozygous and heterozygous mutant variants of *IL1B* were observed to be higher in the RA patients (OR=2.1, p<0.01).

**Conclusions:** Thus the results of our study suggests that, the mutant alleles of *IL1B* was associated with RA susceptibility which in turn has direct association with the increased levels of serum IL-1β in RA patients. In addition, the activation of inflammatory genes supports the role of inflammasome in the development of RA in Tamil Nadu population.

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**Disclosure of Interest:** None declared

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#### AB0207 CALPROTECTIN (S100A8/9) PLASMA LEVELS DECREASE AFTER ABATACEPT THERAPY AND CORRELATE WITH DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Calprotectin (S100A8/9) is a damage-associated molecular pattern molecule that is involved in the early phase of tissue injury. It is found mainly in circulating neutrophils, monocytes and macrophages of rheumatoid arthritis (RA) synovial tissue where it acts as a chemoattractant and induces production of proinflammatory cytokines. Several studies have reported its association with clinical disease activity and radiographic damage in patients with RA.

**Objectives:** The aim of our study was to analyse the plasma levels of calprotectin in patients with established RA after the abatacept treatment compared with healthy individuals, and to examine their potential association with disease activity and treatment response.

**Methods:** The plasma levels of calprotectin were determined by ELISA (BÜHL-MANN Laboratories AG) in 40 patients with established RA before and 3 months after initiation of abatacept treatment, and in 30 age-/sex-matched healthy subjects. Disease activity was evaluated by 28-joint Disease Activity Score (DAS28). The CRP levels and erythrocyte sedimentation rate (ESR) were determined by routine laboratory techniques. Data are presented as median ±IQR.

**Results:** Calprotectin levels at baseline were significantly higher in patients with established RA than in healthy individuals (1925 [741; 4093] vs. 506 [302; 754] p<0.0001; ng/ml). After 3 months of therapy, the levels significantly decreased (from 1925 [741; 4093] to 1569 [695; 3115] p=0.045; ng/ml). Calprotectin baseline levels significantly correlated with CRP, ESR and DAS28 at baseline (r=0.57, p=0.0003; r=0.56, p=0.0003; r=0.40, p=0.014, respectively), with change in DAS28 over 3 months (r=-0.54, p=0.001) and with change in CRP over 3, 6, 12 months (r=-0.56, p=0.0006; r=-0.61, p=0.001; r=-0.71, p=0.0001, respectively). Calprotectin levels at month 3 significantly correlated with ESR at month 3 (r=0.43, p=0.013), CRP levels at month 3 and 6 (r=0.39, p=0.27 and r=0.43, p=0.024, respectively) and with change in CRP over 12 months (r=0.45, p=0.023). Change in calprotectin levels over 3 months correlated with the change in DAS28 over 3 months (r=0.39, p=0.028) and with change in CRP over 3, 6 and 12 months (r=0.48, p=0.004; r=0.38, p=0.028; r=0.60, p=0.0009, respectively).

**Conclusions:** We demonstrate here decrease in plasma levels of calprotectin after 3 months of abatacept therapy in patients with established RA, its association with disease activity and disease activity improvement over time.

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**Disclosure of Interest:** None declared

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#### AB0208 UNFAVOURABLE CARDIOVASCULAR RISK PROFILE IN MALE PATIENTS WITH RHEUMATOID ARTHRITIS OF LOW DISEASE ACTIVITY

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**Background:** Rheumatoid arthritis (RA) is associated with the increased cardiovascular (CV) morbidity and mortality, mostly due to accelerating atherosclerosis. Both traditional and non-traditional factors seem to contribute to the excess of CV risk. Data in literature indicate a positive association between RA activity and the extent of CV disease (CVD) risk, suggesting a dominant effect of systemic inflammation. It is reported, that low disease activity is sufficient to achieve a protective effect against CVD and that atherosclerosis is not accelerated in RA of low activity or remission.

**Objectives:** The goal of the study was to assess CV parameters in female and male patients with RA of low disease activity in comparison with healthy controls.

**Methods:** The study was conducted in 70 patients with low RA activity, without known CVD (54 women, 16 men) and 33 healthy volunteers (18 women, 15 men). Patients underwent standard physical examination, assessment of disease activity in 28 joints (DAS28) and laboratory measurements including amino-terminal pro-brain natriuretic peptide (NT-proBNP). The following procedures were performed both in RA patients and controls: blood pressure (BP), carotid intima

media thickness (cIMT), electrocardiography (ECG) and echocardiography with assessment of ejection fraction (EF) and diastolic dysfunction (E/A ratio).

**Results:** The significant differences between male vs female RA patients included: higher mean values of cIMT [0.93 (0.19) vs 0.80 (0.22) mm,  $p=0.04$ ], atherogenic index [4.2 (1.4) vs 3.5 (1.0),  $p=0.03$ ] and SCORE [5.7 (3.7) vs 2.8 (2.7),  $p<0.001$ ]; as well as lower concentration of HDL-cholesterol [(50.2 (12) vs 59<sup>14,6</sup> mg/dl,  $p=0.04$ ) and NT-proBNP [66.6 (61.2) vs 106.8 (61.5) pg/ml,  $p=0.006$ ]. The mean values of age, disease duration, DAS28, C-reactive protein, body mass index, BP, QTc, E/A and EF were not significantly different in male and female patients with RA of low activity.

In the control group no significant differences were observed between male and female subjects, when considering: age, cIMT, BP, QTc, EF, E/A.

All the male RA patients had features of subclinical or advanced atherosclerosis (cIMT  $\geq 0.6$  mm), there were no male patients with normal cIMT ( $<0.6$  mm). In controls normal cIMT was found in 5 (33.3%) and subclinical atherosclerosis in 10 (66.7%), there was no control subject with advanced atherosclerosis ( $p=0.01$ ). The mean age of patients and controls did not differ significantly.

**Conclusions:** The results of the study suggest an unfavourable CV risk profile in male RA patients with low disease activity. The higher CV risk was observed in male RA patients in comparison with both controls of comparable age, as well as with female RA patients of comparable age, disease duration and activity. It seems that the male gender contributes considerably to CV risk in the period of low RA activity.

**Disclosure of Interest:** None declared

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#### AB0209 OPTIMISATION OF ULTRASONOGRAPHIC EXAMINATION FOR THE DIAGNOSIS OF EROSIVE RHEUMATOID ARTHRITIS VERSUS EROSIVE OSTEOARTHRITIS WITH RADIOGRAPHY CONSIDERED AS GOLD STANDARD

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**Background:** Rheumatoid arthritis (RA) is the most prevalent chronic inflammatory joint disease<sup>1,2</sup> responsible for structural damage. Radiography (RX) is considered as the gold standard for visualising and quantifying bone lesions in RA.<sup>3</sup> Musculoskeletal ultrasound (US) is booming in clinical practice for the diagnosis of RA. US can detect more erosions than RX at the joint level, especially at an early stage of the disease.<sup>4</sup>

**Objectives:** To determine thresholds and better scenarios for the diagnosis of erosive RA by US in RA and osteoarthritic (OA) patients.

**Methods:** Patients fulfilling ACR 1987<sup>5</sup> and/or ACR/EULAR 2010<sup>6</sup> criteria for RA or hand OA criteria were prospectively included. A modified Sharp erosion score was assessed by two blinded readers and one adjudicator for discordant cases (number of eroded joints  $\leq$  three). Erosions in US were scored on six bilateral joints (MCP2–3, 5; MTP2–3, 5) with a four-grade scale.

**Results:** A total of 168 patients were included: 122 RA (32 early RA  $<2$  years; 90 late RA  $\geq 2$  years); 46 OA patients. On RX: 42 RA patients (6 early; 36 late) and 5 OA patients were eroded according to ACR/EULAR 2013<sup>6</sup> criteria (sensitivity: 34.4%, specificity: 89.1%). On US, 95 RA patients (21 early; 78 late) and 12 OA patients were eroded. Considering at least two joint facets eroded (threshold 1) or at least one joint facet eroded at grade 2 (threshold 2), sensitivities were good (68%–72.1%) and specificities excellent (89.1%–100%). With only six targeted joint facets examined, 73 and 74 patients were classified as erosive RA with threshold 1 and 2 with good sensitivities (59.8%–60.0%) and excellent specificities (95.6%–100%) respectively. For all scenarios, agreement between RX and US for the diagnosis of erosive RA was excellent (88.1% to 92.8%).

**Conclusions:** US erosion assessment of six targeted joint facets permitted to detect 1.7 times more erosive RA patients than RX in late and early RA.

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#### AB0210 CLINICAL AND MUSCULOSKELETAL ULTRASOUND ASSESSMENT OF THERAPEUTIC RESPONSE TO TOFACITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS: REAL-WORLD CLINICAL EXPERIENCE FROM A SINGLE CENTRE IN HONG KONG

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**Background:** Increasingly, musculoskeletal ultrasound (MSUS) has been demonstrated as an effective method for monitoring disease activity and joint damage in patients with rheumatoid arthritis (RA).

**Objectives:** The objective of this single-centre, 12 week study was to evaluate the effects of tofacitinib therapy in Chinese patients with RA using clinical, laboratory and sonographic assessments, with the view to identifying factors that may predict response to tofacitinib. Furthermore, the study sought to determine whether MSUS would be comparable to conventional techniques for monitoring disease activity in RA.

**Methods:** Patients with RA (n=18) were treated with tofacitinib 5 mg bd for 12 weeks. Clinical, laboratory and ultrasound examinations were conducted at baseline (T0), and weeks 4 (T1), 8 (T2) and 12 (T3). Erythrocyte sedimentation rate, C-reactive protein, physician and patient visual analogue scale for disease activity, number of tender and swollen joints, Clinical Disease Activity Index (CDAI), Simple Disease Activity Index (SDAI) and Disease Activity Score in 28 joints (DAS28) were assessed and compared. MSUS was performed bilaterally in all metacarpophalangeal, interphalangeal, wrist and knee joints. A semi-quantitative score (0–3) was used to indicate the presence of a localised inflammatory process and/or structural damage. The cumulative total was used as an indicator of global change in each joint (single joint score). The sum of the single joint scores was used as an indicator of overall polyarticular involvement in each patient (total joint score).

**Results:** Of the 18 patients recruited into the study, all 18 were examined at T0, T1 and T2, and 17 patients were evaluated at T3. All clinical and laboratory measures, as well as MSUS scores, were significantly reduced during follow-up. There was a significant correlation between MSUS scores and conventional (clinical and laboratory) measures of disease activity. Correlation coefficients between the techniques and factors potentially predicting response to tofacitinib will be reported.

**Conclusions:** A positive response to tofacitinib treatment was shown by both MSUS examination and clinical evaluation, with good correlation between the methods. In a busy, every-day, clinical-practice setting in Hong Kong, MSUS was found to be a useful tool for monitoring and following-up the effects of biologic therapy in RA, for the assessment of both inflammatory and destructive changes.

**Disclosure of Interest:** None declared

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#### AB0211 THE RELATIONSHIP BETWEEN THE ELEVATED SERUM IMMUNOGLOBULIN G4 LEVEL AND DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** High levels of serum immunoglobulin G4 (IgG4) would comprise a useful diagnostic tool in IgG4-related disease, but little information is available about IgG4 in conditions other than IgG4-related disease, including rheumatic diseases. Previous studies indicate that the elevated serum IgG4 in rheumatoid arthritis (RA) is common and disproportional to total IgG.

**Objectives:** The aim of study is to evaluate the level of serum IgG4 and IgG4/total IgG ratio in patients with RA.

**Methods:** Ninety-six patients with RA and one hundred and thirty-five non-RA controls were enrolled between March 2014 and July 2017. All samples were collected before the treatments. The levels of Serum total IgG and IgG4 were determined by nephelometric assay. The cut-off value of serum IgG4 was 135 mg/dL. Data on clinical variables and disease activity markers, such as numbers of tender and swollen joints, levels of acute phase reactants and disease activity score 28 (DAS28) were recorded in RA patients. We compared the levels of serum IgG4 and the ratio of IgG4/total IgG in rheumatoid arthritis with healthy controls and other rheumatic diseases. This study also investigated the difference the relationship between levels of serum IgG4 and disease activity in RA.



**Results:** Among 96 RA patients, the mean of serum IgG4 was 48.0±45.4 mg/dL and 6.3% had elevated serum IgG4. The mean serum IgG4/IgG ratio of RA patients was 3.5%±2.8% (range 0.2%–16.9%). There was no patient with elevated serum IgG4 in ankylosing spondylitis, systemic lupus erythematosus, Sjogren's syndrome, and inflammatory myositis. When the patients were divided according to clinical activity, the percentages of the positive serum IgG4 were 25% in active disease group and 4% in low activity group. However, the serum IgG4 levels of the RA patients with active disease activity were not significantly higher than those of the RA patients with low disease activity (58.3±44.3 mg/dL vs. 39.9±30.1 mg/dL). No significant relationship was observed between the ratio of IgG4/total IgG and disease activity. The IgG4 concentrations and total IgG/IgG4 ratios were similar between RA and the other autoimmune diseases ( $p>0.05$ ).

**Conclusions:** Our results showed that elevated serum IgG4 in RA is relatively common. However the presence of the elevated serum IgG4 was not associated with disease activity of RA. Further investigations are needed to explore the clinical significance in a larger study population.

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#### AB0212 DIAGNOSTIC DELAY FOR RHEUMATOID ARTHRITIS: A SYSTEMATIC REVIEW

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**Background:** Rheumatoid arthritis (RA) is a common inflammatory condition, affecting 1% of the population and causing pain, stiffness and swelling, leading to significant disability and loss of function.<sup>1</sup> Delays in the diagnosis and treatment of RA can lead to worsened joint damage and disability, in addition to a reduced rate of disease-modifying antirheumatic drugs (DMARD)-free remission. <sup>Current (2016)</sup> EULAR guidelines specify that combination DMARD treatment be initiated within 3 months of the onset of persistent RA symptoms.<sup>2</sup> Unfortunately, this target is not always achieved due to delays between symptom onset to treatment initiation.

**Objectives:** The aim of this systematic review, was to determine the extent of delay that occurs at different points in the patient's journey from RA symptom onset to treatment initiation, providing benchmarks of delay.

**Methods:** Embase and Medline were searched for articles examining diagnostic and treatment delay of RA. To be included, articles had to report a time-period of delay in an adult RA population. Papers were screened by three authors (CAH, JAP, IS). The primary outcome was the reported time-period of delay at any point from RA symptom onset to treatment. Due to skewed delay data, medians (with Interquartile range (IQR)) were selected and reported using narrative synthesis. Different time-periods of delay were categorised to facilitate comparison.

**Results:** Of 4925 returned articles, 1501 duplicates were removed. The remaining articles were then screened by title, abstract and full text, leaving 26 from which we extracted data. Delay periods were categorised as 1) symptom onset to initiation of DMARDs (n=9), 2) symptom onset to diagnosis (n=14), 3) symptom onset to 1st healthcare professional (HCP) appointment (n=15), 4) 1st HCP appointment to rheumatology referral (n=4) and 5) 1st HCP appointment to diagnosis (n=4). Time-periods of delay were typically skewed to the right. The total delay from symptom onset to receiving DMARDs has dropped since the 1980's (429 weeks before 1987) and by 2014 data indicates an average delay of 23 (IQR 14, 43) weeks. Within this total delay period, delay from symptom onset to diagnosis is at a minimum 16<sup>(7,55)</sup> weeks and delay from symptom onset to first contact with a HCP predominantly ranges from 2 (1,8) to 10<sup>(4,24)</sup> weeks in data from 2010 onwards. Delay between 1st HCP appointment and Rheumatology referral can be as quick as 2 (1,5) weeks and is within 12<sup>(2,48)</sup> weeks across all data points. Delay acquired between 1st HCP appointment and receiving a diagnosis has decreased overtime, most recently, delay was reported as 21 weeks.

**Conclusions:** Time from RA symptom onset to receiving treatment has reduced considerably in recent decades. However, despite current guidelines and research indicating an optimal treatment window for RA of twelve weeks from symptom onset, this remains unmet, with this delay approximately twice the recommended period. Continued effort is required in reducing delay across all areas of the RA patients' journey to the early treatment needed to improve outcome.

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#### AB0213 CORRELATION BETWEEN COMPONENTS OF THE DAS28 SCORE AND HEALTH ASSESSMENT QUESTIONNAIRE IN EARLY RHEUMATOID ARTHRITIS

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**Background:** The health assessment questionnaire (HAQ) in rheumatoid arthritis (RA) has been widely validated as a patient reported outcome measure (PROM). In the United Kingdom regulatory bodies such as the national institute of health-care and clinical excellence (NICE) have been using improvement in HAQ as a surrogate for efficacy of drugs in RA and has informed their calculation of quality adjusted life year, and calculating health costs using incremental costs effectiveness ratios. Most clinical trials in RA report their primary outcome as improvement in clinical parameters such as swollen and tender joints, inflammatory markers and patient and physician global assessment of disease. What is not clear how the two sets of parameters interact. Some reports<sup>1</sup> indicate that there is a strong correlation in early disease, but this has not been validated.

**Objectives:** We set out to determine the relationship between HAQ scores and clinical parameters of the Disease activity score (DAS28) in addition to physician global.

**Methods:** Patients were recruited from a single centre from the RAMS study in the North west of England. This is a study of patients with early newly diagnosed RA commencing methotrexate A subset of patients filled in the HAQ questionnaire and this as used as an outcome variable using linear regression and the swollen joints, tender joints, patient global assessment of disease as well as physician assessment of disease in addition to inflammatory markers were used as explanatory variables. These were then adjusted for age.

**Results:** 81 patients were included in the analysis. median age was 63.1 years (IQR 52.9,72.5). 50 (61.7%) were female. the median HAQ score at baseline was 1 (IQR 0.5,1.5) the median DAS28 score 5.3 (IQR 4.5,6.3). Tender joints at baseline correlated well with HAQ score Beta=0.058 95% CI, 0.04,0.08 ( $p<0.01$ ). Swollen joints did not correlate with the HAQ beta=0.000 (95%CI -0.3,0.3). Physician global correlated well with disease beta=0.014 (95%CI 0.005,0.022). Patient global assessment also correlated well with HAQ (beta 0.014 95% CI 0.008,0.020). CRP did not correlate with HAQ (beta 0.00261 95% CI -0.002,0.007)

**Conclusions:** In this small study, patient and physician related outcome measures correlate with HAQ scores at baseline more than measures of joint swelling and inflammatory markers. This indicates that using HAQ as an outcome measure underestimates the effect of treatment. When assessing the efficacy of drugs using HAQ this should be taken into account. Validity of the approach needs to be reviewed.

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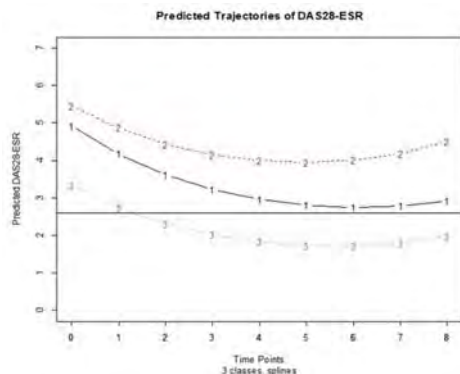
#### AB0214 THE TRAJECTORY OF DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS IN THE FIRST TWO YEARS OF TREATMENT IN AN ASIAN RA COHORT

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**Background:** Response to disease-modifying antirheumatic drugs (DMARDs) is heterogenous. Clinical information and baseline characteristics do not allow reliable prediction of which trajectory patients will follow after DMARD initiation.

**Objectives:** We analysed the change in disease activity over the first two years of treatment in rheumatoid arthritis (RA) to identify different treatment response patterns among RA patients initiating DMARDs. We wanted to establish a predictive model for identifying patients with different treatment response patterns.

**Methods:** We selected patients from our prospective RA disease registry who have been treated for three months or fewer at study entry. We analysed the change of the disease activity, as defined by the DAS28–ESR, over the subsequent two years. A predictive model with parameters from three time points is proposed to stratify patients according to the outcomes.



Abstract AB0214 – Figure 1

**Results:** We analysed the data from 179 patients over 1044 study visits. We discerned three groups of patients according to disease activity trajectories:<sup>1</sup>the first group (53%) has high DAS at study entry and approach remission after 18 months;<sup>2</sup>the second group (22%) has high DAS at entry that remained elevated throughout the study period; and,<sup>3</sup>the third group of patients (25%) started with moderately high DAS and reached remission after 3 months of treatment. Patients at risk of being in the third group can be identified using data from three time points, at initiation of DMARDs, at 3 months and at 6 months.

**Conclusions:** RA patients showed three distinct disease activity trajectories with treatment. Our model can categorise patients into these groups.

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AB0215

#### ASSOCIATION OF RHEUMATOID FACTOR IMMUNOGLOBULIN A SEROPOSITIVITY WITH RISK OF EROSIVE ARTHRITIS IN PATIENTS WITH RHEUMATOID ARTHRITIS: AN OBSERVATIONAL STUDY

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**Background:** In patients with rheumatoid arthritis (RA), erosive arthritis is a major determinant of long-term prognosis. Seropositivity for immunoglobulin (Ig) M rheumatoid factor (RF) or cyclic citrullinated peptide antibodies (anti-CCP) are risk factors for erosive arthritis. However, RA patients can also present IgA RF. The risk for erosive arthritis associated with RF IgA seropositivity is not established.

**Objectives:** To evaluate the risk for erosive arthritis associated with IgA RF seropositivity in RA patients.

**Methods:** Cross-sectional observational study, including RA patients (fulfilling the 2010 ACR/EULAR classification criteria) and consecutively observed in a hospital-based rheumatology outpatient clinic, from April to August 2017. At time of inclusion, patient characteristics were evaluated, including: gender, age, RA duration since time of diagnosis, smoking habits, seropositivity for IgA RF, IgM RF and anti-CCP, erosive arthritis in hand and feet X-rays. Risk association for erosive arthritis was analysed with univariate and multivariable logistic regression models for the putative risk factors and confounders. Odds ratios (OR) and 95% confidence intervals (CI) of IgM RF, IgA RF, and anti-CCP seropositivity for erosive arthritis were estimated. Statistical significance was set at 0.05.

**Results:** 86 patients were included. The univariate logistic regression showed significant positive associations of IgA RF, IgM RF and anti-CCP with erosive arthritis. In the multivariate analyses, adjusting for confounders (gender, age, disease duration and smoking), the OR for erosive arthritis associated with IgA RF, IgM RF and anti-CCP were respectively: OR=2.42 (95% CI 0.72–8.07; p=0.152); OR=3.54 (95% CI 1.16–10.83; p<0.05); OR=4.13 (95% CI 1.33–12.82; p<0.05). The seropositivity for IgM RF, IgA RF and anti-CCP were strongly associated among each other (Chi-square test with p<0.001 for all associations).

**Conclusions:** In this RA cohort, the IgA RF was associated with erosive arthritis in univariate analysis, but did not prove to be an independent risk factor in multivariate regression, due to its strong association with IgM RF and anti-CCP. Determination of IgA RF does not seem to add predictive value for erosive arthritis in RA patients.

**Disclosure of Interest:** None declared

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AB0216

#### LOW MORTALITY RATE IN ITALIAN RHEUMATOID ARTHRITIS PATIENTS FROM A TERTIARY CENTRE. PUTATIVE IMPLICATION OF A LOW ANTICARBAMYLATED PROTEIN ANTIBODIES PREVALENCE

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**Background:** Rheumatoid Arthritis (RA) is a chronic systemic inflammatory disorder associated with increased mortality, in particular from cardiovascular (CV) disease, infections and cancer. We recently demonstrate a incidence mortality rate (IMR) in 654 RA patients enrolled over a 6 year period in a South-Italian tertiary Rheumatology Centre lower than that reported in the Norfolk Arthritis Registry.<sup>1</sup>

**Objectives:** The present study is devoted to investigate differences in IMR between our series and other European tertiary centre cohorts. Furthermore we evaluated the role, if any, of Anticarbamylated protein antibodies (anti-CarP Ab) in modulating the low IMR detected in our patients.

**Methods:** Clinical charts of patients consecutively admitted to our centre, from January 1st, 2008 to December 31st, 2014 were reviewed. IMRs and causes of death as assessed at December 31st 2015, were registered. Sera collected at the time of admission to our centre in 61 patients representative of our RA cohort were investigated for the presence and the level of anti-CarP Ab. Demographic and clinical features, mortality rates and prevalence of anti-CarP Ab detected in our series were compared with those reported in the Better Anti-rheumatic Farmaco-therapy (BARFOT) cohort, the Leiden Early Arthritis Clinic cohort (Leiden EAC) and a Spanish cohort.<sup>2,3</sup>

**Results:** Six hundred and eight patients were observed for a median of 3.51 years. All causes and cause-specific IMRs were significantly lower in our cohort with respect to the BARFOT and the Spanish cohort, while only all causes and CV IMRs were significantly lower in our series with respect to the Leiden EAC. These discrepancies might depend on demographic and clinical differences among the various cohorts. Nevertheless, we failed to find putative differences with respect to each North European cohort, but we detected a significantly lower prevalence of anti-CarP Ab in our series with respect to that reported in the other European cohorts considered (table 1).

**Conclusions:** In conclusion, we confirm that the mortality rate in our South Italian RA cohort is lower than that detected in patients from both North and South European countries.

We detected a very low prevalence of anti-CarP Ab in our sample representative of the entire cohort. Whether this is the aspect underpinning the low mortality rate detected in our series, awaits to be furtherly investigated.

Abstract AB0217 – Table 1

	Factor analysis		Chi-square	df	p	Item-fit statistics			
	Loadings					Outfit mean square	Infit mean square	Outfit t	Infit t
	All <sup>†</sup>	HA							
Item no. 1	0.721	0.460	224.213	183	0.020	1.219	1.111	1.96	1.05
Item no. 2	0.629	0.522	205.899	183	0.118	1.119	1.132	1.17	1.29
Item no. 3	0.750	0.522	142.900	183	0.987	0.777	0.740	-2.18	-2.65
Item no. 4	0.660	0.675	95.060	183	1.000	0.517	0.523	-4.90	-5.34
Item no. 5	0.534	0.807	131.885	183	0.998	0.7171	0.682	-3.05	-3.45
	<b>Factor 1</b>	<b>Factor 2</b>							
Sum of square loadings	2.210	1.869							
Proportion Variance	0.442	0.374							
Cumulative Variance	0.442	0.816							

Abstract AB0216 – Table 1

	NAPLES (n.654)	BARFOT (n.805)	LEIDE N (n.848)	SPAIN (n.331)
Sex F/M ratio	470/184	530/275 (66%) p 0.0137	571/277 (67%) p 0.0392	244/87 p 0.5392
Age in years Mean ±SD	55.7 ±12.4	57.7 ±15.7 p 0.0060	56.8 ±15.8 p 0.1429	68.7 ±8.1 p 0.0001
RF+/RF-	270/162 (62.5%)	452/353 (56%) p 0.0208	489/359 p 0.0091	198/133 p 0.4513
ACPA+/ACPA-	188/172 (52%)	462/343 (57%) p 0.1005	445/403 p 0.9355	215/116 (64.7%) p 0.0007
HAQ-DI Mean ±SD	1.13 ±0.79	1.00 ±0.66 p 0.0006	1.00 ±0.71 p 0.0008	-
IMR	0.79	2.49 p < 0.0001	2.07 p < 0.0001	4.1 p < 0.0001
CV4MR	0.46	1.57 p < 0.0001	0.92 p 0.0354	1.2 p 0.0039
NEQ-IMR	0.17	0.65 p 0.0048	0.39 p 0.1200	0.6 p 0.0137
RESP-IMR	0.13	0.69 p 0.0012	0.36 p 0.0750	1.2 p < 0.0001
antiCCP+ (%) (homemade technique)	3.3% (95% C.I. 0.3-10.3)	3.5% (95% C.I. 3.1-7.38.4) p < 0.0001	4.5% (95% C.I. 4.1-6.48.4) p < 0.0001	32.9% (95% C.I. 27-37.3) p < 0.0001
antiCCP+ (%) (commercial kit)	10% (95% C.I. 3.8-20.4)	3.5% (95% C.I. 3.1-7.38.4) p < 0.0001	4.5% (95% C.I. 4.1-6.48.4) p < 0.0001	32.9% (95% C.I. 27-37.3) p < 0.0001

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**Disclosure of Interest:** None declared

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### AB0217 CONSTRUCT VALIDATION OF THE ITALIAN VERSION OF THE 5-ITEM COMPLIANCE QUESTIONNAIRE FOR RHEUMATOLOGY (I-CQR5)

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**Background:** The 5-item Compliance Questionnaire for Rheumatology (CQR5) allows the identification of patients likely to be high adherers (HA) to anti-rheumatic treatment (i.e. taking ≥80% of their medications correctly), or “low” adherers (LA).<sup>1</sup>

**Objectives:** The objective was to validate the construct of an Italian version of CQR5 in rheumatoid arthritis (RA).

**Methods:** Cross-cultural adaptation comprised: forward translation, synthesis of the translations, back-translation, expert committee assessment and field-testing. Validation was conducted administering the adapted version (I-CQR5) to RA patients (disease duration >1 year, treated with ≥1 self-administered disease-modifying anti-rheumatic drug, capable of completing the questionnaire unaided) on one occasion. Questionnaires were anonymous but contained self-reported data. Construct validity and reliability were assessed with Rasch analysis (Partial Credit model Parametrisation, PCM). Martin-Loef Likelihood ratio test assessed invariance for gender, age, education, social status and disease duration.

**Results:** The adaptation process was closed by the expert committee assessment. I-CQR5 is reported in Figure 1. Among 604 patients, 274 were included in the validation process, 6 questionnaires were incomplete. Median age was 57 years (48–67), females were 201 (77%), disease duration was 13.5 years (8–19.3), most patients lived with partner/family (159,75%) and had a middle/secondary school education (184,69%). HA were 93 (67%) and LA 179 (35%). Factor analysis revealed ordered thresholds in most items, 2 factors were sufficient to explain variability (Chi-square=0.46,p=0.5) (Tab.1). Item-fit statistics showed overall agreement of items with parametrisation (Infit statistics=0.6–1.4; excluding item no.5). Chi-square showed agreement with PCM parametrisation by item (excluding the item no.1). Martin-Loef likelihood ratio test confirmed unidimensionality (Chi-square 65.8, df=53,p=0.11) and Separation Reliability Index confirmed internal consistency (Patient Separation Index 0.91) (Tab.1). I-CQR5 was invariant to age (Chi-square=40.6, df=28,p=0.059), education level (Chi-square=49.9, df=42,p=0.187), social status (Chi-square=10.5, df=15,p=0.79), disease duration (Chi-square=13.6, df=36,p=0.220); Martin-Loef test was significant for gender (Chi-square=25.4, df=14,p=0.031).

Abstract AB0217 – Table 2

### Questionario sulla Compliance in Reumatologia a 5 domande (I-CQR-5)

Di seguito sono riportate delle affermazioni di pazienti affetti da una malattia reumatica. Indichi quanto è d'accordo con ciascuna affermazione cerchiando il numero che riflette maggiormente la Sua opinione.

	Completamente in disaccordo	In disaccordo	D'accordo	Completamente d'accordo
Prendo i farmaci antireumatici perché in questo modo ho meno disturbi.	1	2	3	4
Non mi permette mai di saltare la somministrazione dei farmaci antireumatici.	1	2	3	4
Metto sempre le medicine nella stessa scatola per non dimenticare di prenderle.	1	2	3	4
Prendo i farmaci prescritti perché ho completa fiducia nel mio reumatologo.	1	2	3	4
Seguo sempre le indicazioni del mio medico.	1	2	3	4

**Conclusions:** I-CQR5 was well understood by patients and construct validity, unidimensionality and internal consistency were confirmed by factor analysis and PCM.



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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.4240

**AB0218 HIGH LEVEL OF CARTILAGINOUS OLIGOMERIC MATRIX PROTEIN IS ASSOCIATED WITH THE RADIOGRAPHIC PROGRESSION IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS**

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**Background:** Recent achievements have established that the very first years since the development of the RA are decisive in terms of the progression of the pathological process and the prediction of its remote consequences. This substantiated the need to reflect the heterogeneity and stage of the RA. First of all it concerns the early RA – a time point when the pathological process is in the primary exudative phase and its reversibility is significantly higher, because of not completely formed autoimmune mechanisms and the absence of pannus.

**Objectives:** Our aim was to establish the relationship between the levels of Anti-Citrullinated Peptide Antibody (ACPA), cartilaginous oligomeric matrix protein (COMP) and radiographic progression in patients with early RA

**Methods:** 75 patients with a diagnosis of early RA were examined, the duration of symptoms was less than 1 year (on average –  $4.91 \pm 2.90$  month) that were observed repeatedly on average after 12 months ( $11.8 \pm 1.2$  months). The average age of patients was 46.4 years (from 34 to 62 years), 69.33% of the examined ones were women, the average duration of the disease at the time of the initial study was 107 days (57–194 days). Immune dysregulation in early RA was confirmed with the evaluation of the key proinflammatory cytokines – ACPA and COMP by the enzyme-linked immunosorbent assay (ELISA) according to the instructions for diagnostic kits. For the testing of articular cartilage lesions and injury of flexor's and extensor's tendons, MRI (1.5 T) and ultrasound diagnostics (US) were performed

**Results:** Immunological analysis of serum samples of ACPA, COMP was shown the role of these cytokines as prognostic factors of development and prognosis of early RA. The serological features of the obtained data revealed a correlation between the increased concentration of COMP and the progression of joint lesions without ACPA level increase. According to the baseline US data, the tendons of general flexor muscles and extensor brushes were most commonly observed in the examined patients: in general, 52 patients (69.3%) and 23 (30.7%), respectively. The injury of the tendons of individual fingers (I-V) in the mode of longitudinal and transverse scanning had its own patterns (table 1).

**Conclusions:**

- In patients with seronegative (normal ACPA ranges) early RA and high levels of COMP – the highest frequency of erosive and destructive changes can be observed.
- Injury of the tendons of flexors and extensors determined in major part of the patients with early RA.

**Abstract AB0218 – Table 1.** Injury of the flexor's and extensor's tendons

Fingers	Injury of flexor tendons			Injury of extensor tendons		
	Totally, n (%)	Exudative tenosinovite, n (%)	Exudative – proliferative tenosinovitis, n (%)	Totally, n (%)	Exudative tenosinovite, n (%)	Exudative – proliferative tenosinovitis, n (%)
I	1 (1,3)	1 (1,3)	0 (0,0)	4 (5,2)	3 (3,9)	1 (1,3)
II	58 (77,3)	52 (69,3)	6 (8,0)	26 (34,7)	24 (32,0)	2 (2,6)
III	36 (48,0)	35 (46,7)	1 (1,3)	18 (24,0)	18 (24,0)	0 (0,0)
IV	22 (29,3)	20 (26,7)	2 (2,7)	12 (16,0)	9 (12,0)	3 (3,9)
V	13 (17,3)	13 (17,3)	0 (0,0)	6 (8,0)	6 (8,0)	0 (0,0)

**Abstract AB0218 – Table 2.** Dynamics of radiographic progression after a 12-month follow-up

Value	Group 1	Group 2	Group 3
	1	2	3
ACPA positive, %	31±2,59	18±1,88 $P_{12} < 0,01$	12±1,17 $P_{13} < 0,01$ $P_{23} < 0,01$
COMP, UI	11,8±0,73	15,3±0,82 $P_{12} < 0,01$	8,8±0,94 $P_{13} < 0,01$ $P_{23} < 0,01$
Frequency of erosions detection at baseline / after 12 months, %	48/90 $\chi^2=10,93, p < 0,01$	10/85 $\chi^2=10,67, p < 0,01$	10/32 $\chi^2=0,76, p = 0,383$
Number of erosions at baseline / after 12 months, p	8,04±0,28 18,11±0,71 $P_{12} < 0,01$	2,21±0,23 15,42±0,68 $P_{12} < 0,001$	3,14±0,42 7,08±0,55 p.n.s.
Frequency of synovitis and tendinitis detection at baseline / after 12 months, %	51/81 $\chi^2=4,61, p < 0,03$	32/71 $\chi^2=4,9, p < 0,05$	21/36 $\chi^2=0,18, p = 0,676$

Note:  $P_{12}$  – the level of significance of differences in the pairwise comparison of the corresponding groups.

$P_{12}$  – the level of significance of differences when comparing baseline values (frequencies) and after a 12-month observation period.

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**Disclosure of Interest:** None declared

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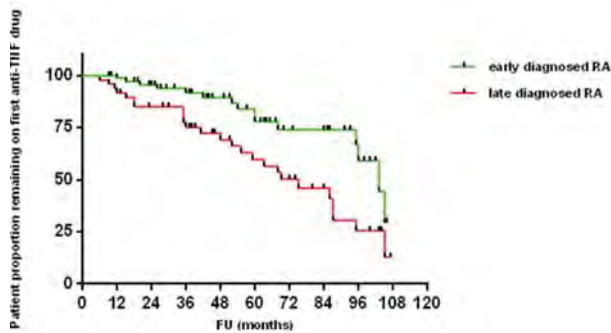
**AB0219 IMPACT OF EARLY DIAGNOSIS ON LONG-TERM EFFECTIVENESS OF FIRST-LINE ANTI-TNF-ALPHA TREATMENT IN RHEUMATOID ARTHRITIS PATIENTS**

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**Objectives:** Aim of this work was to evaluate effectiveness and drug persistence of anti-tumour necrosis factor (TNF)-alpha therapies in early and late diagnosed rheumatoid arthritis (RA) patients naive for biological disease-modifying antirheumatic drug (bDMARD) use.

**Methods:** Baseline and follow-up (FU) charts RA patients with disease onset later than 2002 and access to rheumatology care between January 2007 and December 2016 were reviewed until December 2017. All patients fulfilled 2010 ACR/EULAR classification criteria. At baseline, demographic, anamnestic and serological characteristics were collected. Based on lag time between onset of symptoms and definite diagnosis, RA patients were categorised into two groups: early diagnosed (less than 12 months) and late diagnosed (more than 12 months). Disease activity and treatment response were assessed every three months by Simplified Disease Activity Index (SDAI). Anti-TNF-alpha survival was defined as the length of time from initiation to discontinuation of therapy due to loss of effectiveness over time. It was examined using Kaplan-Meier survival analysis.

**Results:** One hundred and fifteen RA patients (86.1% females, mean age 59.4) were included. The median disease duration between onset of symptoms and diagnosis was 25 months.<sup>20–43</sup> 68 patients (59.1%) were labelled as early diagnosed and 47 (40.9%) as late diagnosed. At baseline, no differences were found in age, gender, smoking habits, body mass index, and rheumatoid factor positivity. The most frequently used first-line anti-TNF drug was etanercept (30.4%), followed by adalimumab (20%), golimumab (18.3%), infliximab (16.5%), and certolizumab (14.8%). All patients received anti-TNF-alpha therapy in combination with csDMARD (methotrexate or leflunomide). Average steroid dosage was 5 mg/day of prednisone (or its equivalent) over time. The median time to initiation of any anti-TNF-alpha treatment after definite diagnosis was 18 months.<sup>6–30</sup> Kaplan-Meier analysis showed a lower anti-TNF-alpha discontinuation rate for early diagnosed RA patients than late diagnosed (9 year retention rate of 29.5% and 12.7%, respectively;  $p = 0.0049$ ) (figure 1).



Abstract AB0219 – Figure 1

**Conclusions:** This small real-world retrospective, observational, cohort study demonstrates that early diagnosis of RA provides higher retention rate of anti-TNF-alpha treatment as first-line bDMARD.

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#### AB0220 SERONEGATIVE RA GROUP HAD Milder SYNOVITIS AND DELAYED PROGRESS OF BONE EROSION THAN SEROPosITIVE RA ON WRISTS AND HANDS IN DMARDs-NaïVE CHINESE COHORT

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**Background:** Contrast to sp-RA, sn-RA was less studied. The report by Nordberg et al mentioned ultrasonic presentations for the first time. They declared early RA patients(with the duration <2 years) without the treatment of DMARDs had more severe synovitis than sp-RA. However, according to the criteria, for the diagnosis of sn-RA, more than 10 swollen joints is necessary. The huge gap of swollen joints counts(SJC)between two groups may influence the sum ultrasound scores and thus cause a prominent selective bias, which was questioned to affect the fact that sn-RA had more synovitis due to more joints involved relative to grouping rules.

**Objectives:** To investigate and compare the disease progress of seronegative Rheumatoid arthritis (sn-RA) and seropositive Rheumatoid arthritis (sp-RA) on typical sites including wrists and hands by means of ultrasound and x-ray in Chinese patients.

**Methods:** All cases were DMARDs-naïve (DMARDs) and conformed to 2010 classification criteria with the characteristics of abnormal swollen or pain in wrists, Proximal Interphalangeal (PIP), Metatarsophalangeal (MCP) joints. 5-joints ultrasound scoring system was improved from Backhaus's US7 scoring system. Erythrocyte sedimentation rate (ESR, mm/h), C reactive protein (CRP, mg/L), Visual analogue scale (VAS) scores (VASs), patient global assessment of disease activity on VASs (PGA), the physician's assessment of disease activity on VASs (PhGA), DAS28(Disease Activity Score-28, DAS28), van der Heijde-modified Sharp scores(vdHSS) were also used to evaluate the disease activity among<sup>1</sup> Group A: sp-RA (positive rheumatoid factor(RF) and/or anticitrullinated peptide antibody(ACPA)) combined with swollen joint counts(SJC)>10;<sup>2</sup> Group B: sp-RA combined with SJC ≤10 and<sup>3</sup> Group C: sn-RA (negative RF and negative ACPA), according to the 2010 criteria with SJC >10.

**Results:** 29 (11.6%) of 249 patients were seronegative. The score of DAS28, CRP, ESR, the sum ultrasound scores, vdHSS, phisican global VAS, Patient global VAS and pain VAS were significantly lower(p<0.05) in Group C than Group A, but no difference between Group B and Group A. The sum ultrasound scores were prominently lower in Group C with the duration over 2 years (p<0.05), and vdHSS were remarkably higher in all groups with the duration over 5 years, but more specifically, for the duration over 2 years(p<0.05), the vdHSS was shown to go up much more earlier in Sp-RA than Sn-RA patients.

**Conclusions:** Seronegative RA group had milder synovitis and delayed progress of bone erosion than seropositive RA on hands and wrists at the same level with SJC >10.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.4053

#### AB0221 THE USE OF ULTRASOUND TO IDENTIFY DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS IN CLINICAL REMISSION OR LOW DISEASE ACTIVITY IN A REAL-LIFE SETTING

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**Background:** The goal of treatment in rheumatoid arthritis (RA) is to achieve remission or low disease activity for as long as possible, in order to prevent joint damage and loss of function. The evaluation and follow-up of disease activity relies on composite indexes with clinical outcomes. However, many studies have shown that a high proportion of patients categorised on remission or low disease activity by clinical methods could have disease activity by ultrasound (US).<sup>1</sup>

**Objectives:** The aim of this study was to evaluate disease activity by US in patients classified as to be in remission or in low disease activity disease activity by clinimetric evaluation.

**Methods:** We performed a cross-sectional study including patients with RA; Clinical follow-up was designed by the authors according to DAS28 as follows: every 3–5 weeks (DAS28 >5.1), every 7–9 weeks (DAS28 ≥3.1 and ≤5.1), and every 11–13 weeks (DAS28 <3.1). Additionally the patient was evaluated by a rheumatologist expert in ultrasound; US studies were carried out with a Esaote MyLab Seven US equipment (Biomedica, Genoa, Italy) equipped with a 10–18 MHz linear transducer; PD was adjusted according to the following parameters: frequency, 8.0, PRF, 0.500, wall filter 3, gain between 50 and 70. The rheumatologist reported erosions, synovitis, osteophytes and power Doppler, we defined as active disease when patients had synovitis or positive power Doppler. We calculated means, and standard deviations for continuous variables and categorical variables were presented as rates. We performed a bivariate analysis using Pearson's Chi<sup>2</sup>

**Results:** We included 243 patients 64% were in remission and 36% in low disease activity, 85% were woman, mean age was 60 years±10. Mean DAS28 was 2.53±0.53. 81% of patients received conventional DMARDs and 19% received biological DMARDs. The most frequent finding was erosions 70% in hands and 7% in feet followed by synovitis in hands 58%. See table 1. We found disease activity in 60% of our patients were 51% had positive Doppler and synovitis, 1% had only positive Doppler and 8% patients only had synovitis. We did not find statistical association between disease activity according to ultrasound and age, sex and type of pharmacological therapy in patients classified as to be in remission or LDA.

**Conclusions:** The evidence found in this real-life setting data, showed that two thirds of RA patients classified according to DAS28 to be in remission or LDA have subclinical disease activity; thus the ultrasound is a very useful tool to evaluate patients with RA in clinical practice. Further research is needed in order to identify the reasons of disease activity in patients were clinical findings point towards remission or LDA.

Abstract AB0221 – Table 1

VARIABLE	PRESENT		ABSENT	
	n	%	n	%
HANDS				
SYNOVITIS	142	58	101	42
POWER	123	51	120	49
DOPPLER				
EROSIONS	170	70	73	30
OSTEOPHYTES	106	43	137	57
FEET				
SYNOVITIS	9	4	234	96
POWER	10	5	233	95
DOPPLER				
EROSIONS	16	7	227	93
OSTEOPHYTES	19	8	224	92

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.6088

AB0222

### DIFFERENCES OF DISEASE IMPRESSION AND TREATMENT EXPECTATION IN RHEUMATOID ARTHRITIS PATIENTS WITH DIFFERENT DISEASE ACTIVITY

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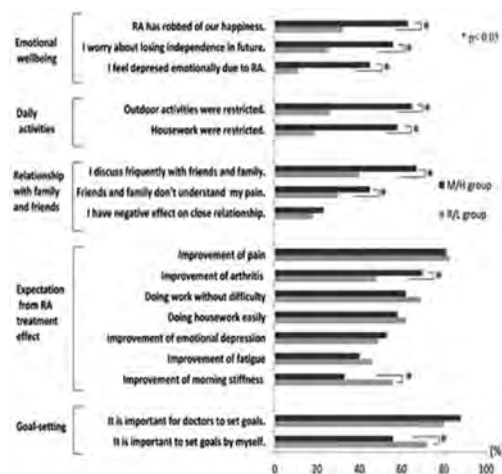
**Background:** Rheumatoid arthritis (RA) is a systemic chronic arthritic inflammatory disease that affects daily life and work. Therefore, the treatment goals include subjective indicators such as activities of daily living disorder and fatigue as well as objective indicators such as disease activity<sup>(1)</sup>. In recent years, the progress of RA therapy has been remarkable, and many patients have achieved low disease activity (LDA) or remission; however, one-third of the patients still have a high disease activity. Is it right to adapt all patients to the same subjective evaluation goal?

**Objectives:** We conducted a questionnaire survey in RA patients to evaluate the following factors: 1) RA influence on emotions, 2) RA influence on daily life or work, 3) patient expectations from RA treatment and 5) a comparison of patients' individual assessment of each disease activity.

**Methods:** We included 289 patients with RA and divided them into two groups based on their disease activity: those achieving LDA or remission (R/L group: n=192) and those with moderate or high disease activity (M/H group: n=97). The mean ages of the R/L and M/H groups were 52.3 (18–81) and 56.7 (25–84) years, respectively. The mean disease duration of the R/L and M/H groups were 4.3 years (2 months – 25 years) and 5.6 years (2 months – 31 years), respectively. The survey comprised 19 questions, which had predefined answers about daily activities, relationship with family and friends, emotional wellbeing, expectation from RA treatment effect, and treatment goal-setting.

**Results:** For questions regarding daily activities and emotional wellbeing, there were more negative responses from the M/H group than from the R/L group. Daily activity which conclude housework and outdoor activities were more restricted in the M/H group than in the R/L group. Regarding emotional wellbeing, 63% patients in the M/H group and 32% in the R/L group felt that RA was depriving their happiness. Furthermore, 56% patients in the M/H group and 25% in the R/L group were worried about their independence in the future. Conversely, patients in the M/H group exchanged views about RA symptoms with family and friends more frequently than those in the R/L group; they were seeking psychological stabilisation. There were also differences in both the groups' expectation of the treatment effect. The most and the second expected treatment effects in both groups were pain improvement and in the early stage, respectively. The third most expected treatment effect was being able to do their work at home and outside in the R/L group and clinical symptoms improvement in the M/H group. Morning stiffness was more important than arthritis in the R/L group because a higher goal was set.

Although it would be desirable for medical professionals to set treatment goals for both groups, this tendency was higher in the M/H group.



Abstract AB0222 – Figure 1. Questionnaire results

**Conclusions:** The subjective goals in RA treatment vary depending on disease activity. High social goal-setting is important for patients whose disease activity is controlled. For patients with high disease activity, emotional support from their family and friends and setting goals regarding clinical symptoms by medical professionals are important.

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- [1] Vibeke Strand, et al. *J Rheumatol* 2015.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.4405

AB0223

### HAS THE PRESENTATION AND SEVERITY OF RHEUMATOID ARTHRITIS CHANGED IN RECENT DECADES?

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**Background:** In recent decades, there have been social, economic and health changes, also in the treatment of rheumatoid arthritis (RA). The development and severity of RA can be affected by these changes. It is discussed if RA is currently less frequent and severe than before<sup>1</sup>.

**Objectives:** To determine the changes in the clinical and demographic variables and the severity of RA that may have occurred over a period of four decades (from 1980 to 2015) and its repercussion in the response to methotrexate (MTX) monotherapy.

**Methods:** We conducted a retrospective study, reviewing the records of patients from a cohort of RA who received MTX monotherapy and compared the results of demographic and clinical variables by natural decades. The statistical analysis was performed using the Chi2 test and the one-way ANOVA test.

**Results:** We included 301 patients (202 women and 99 men) with a mean age at diagnosis of 49.6 (±13.2) years. The table 1 shows the characteristics of the complete sample and distributed by natural decades. The age at diagnosis was higher after 2000 (p<0.01), while the proportion of women, educational level, sedentary lifestyle, habits (tobacco, alcohol) and comorbidities did not change. There was also no variation in the joint pattern of presentation, percentage of RF/ACPA positive or mean value of RF and ACPA. There was a decrease in time from the onset of symptoms to diagnosis (from 21.7 to 15.3 months) (NS), but especially between the diagnosis and the first DMARD (from 34.5 to 1.4 months) and in the number of FAMES before MTX (p<0.01 for both), as well as in the baseline activity of the disease (PCR and DAS28-PCR), early erosions (<2 years) and extra-articular involvement (p<0.01). There were no changes in the dose of prednisone and MTX, nor in the route of administration, while folic acid supplements increased.



The suspension rate due to toxicity decreased ( $p<0.05$ ), while the clinical remission rate improved ( $p<0.01$ ).

Abstract AB0223 – Table 1

	Global	1980–1990	1991–2000	2001–2010	2011–2015	Valour P
<b>Diagnosis age</b> (years), mean (SD)	49,6 (13,2)	39,4 (11,6)	44,0 (11,0)	52,6 (13,5)	51,6 (11,9)	<0,01
<b>Diagnostic delay</b> (months) mean (SD)	17,2 (27,1)	21,7 (29,8)	21,0 (34,6)	15,7 (26,0)	15,3 (19,2)	NS
<b>Diagnostic-treatment interval</b> (months), mean (SD)	24,0 (38,9)	34,5 (66,8)	11,7 (25,2)	2,7 (7,7)	1,4 (3,2)	<0,01
<b>Extra-articular involvement</b> , n(%)	71 <sup>(23,6)</sup>	12 <sup>(52,2)</sup>	25 <sup>(99,1)</sup>	27 <sup>(18,2)</sup>	7 (10,6)	<0,01
<b>Baseline DAS28-RCP</b> , mean (SD)	4,5 (0,8)	5,2 (0,8)	4,6 (0,8)	4,3 (0,8)	4,3 (0,8)	<0,01
<b>Baseline RCP</b> (mg/l), mean (SD)	17,8 (21,3)	27,8 (28,9)	18,4 (17,8)	18,9 (23,3)	10,9 (13,7)	<0,01
<b>Erosions</b> , n(%)	163 <sup>(55,6)</sup>	20 <sup>(80,9)</sup>	48 <sup>(77,4)</sup>	77 <sup>(53,8)</sup>	18 <sup>(27,3)</sup>	<0,01
<b>MTX weekly</b> (mg), mean (SD)	16,5 (3,7)	16,5 (4,2)	16,6 (3,6)	16,5 (3,7)	16,2 (3,6)	NS
<b>MTX SC way</b> , n(%)	177 <sup>(58,8)</sup>	12 <sup>(52,2)</sup>	37 <sup>(27,8)</sup>	87 <sup>(58,8)</sup>	41 <sup>(62,1)</sup>	NS
<b>Withdrawn by AE</b> , n(%)	52 <sup>(17,3)</sup>	6 (27,3)	18 <sup>(27,7)</sup>	20 <sup>(13,5)</sup>	8 (12,1)	<0,05
<b>Remission</b> , n(%)	100 <sup>(33,2)</sup>	2 (8,7)	14 <sup>(21,9)</sup>	56 <sup>(37,8)</sup>	28 <sup>(42,4)</sup>	<0,01

**Conclusions:** In our cohort, the severity of RA has decreased during the last four decades, the time to start MTX has been reduced and better remission rates with MTX monotherapy have been achieved.

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**Disclosure of Interest:** None declared

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#### AB0224 CERVICAL PROPRIOCEPTIVE IMPAIRMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is autoimmune disease that usually involves cervical part of the vertebral column which can cause cervical proprioceptive deficit.

**Objectives:** Assessment of cervical proprioception and its relation with radiographic, clinical and functional characteristics of patients with RA

**Methods:** Rheumatoid arthritis patients who diagnosed according to ACR 2010 criteria and control group with healthy volunteers were recruited in the study. Demographic and clinical parameters were noted. Cervical proprioception was evaluated by Cervical Joint Position Error Test (CJPET). Functional assessment scales that used in this study were Multidimensional Assessment of Fatigue (MAF), Beck Depression Inventory, Health Assessment Questionnaire (HAQ), Euroqol 5D (EQ-5D) and Berg Balance Scale. Cervical subluxations were noted according to cervical radiographic image. The difference in mean scores of CJPET between RA patients and healthy volunteers were analysed with Mann-Whitney U test. Spearman correlation coefficient ( $\rho$ ) was used for correlations between functional parameters. Regression analysis was used for grading factors which had relations with cervical proprioception.

**Results:** One hundred six rheumatoid arthritis patients and one hundred six healthy volunteers were enrolled in this study. Mean age of patients and healthy volunteers were 51,0 (Sd:11,1) and 48,9 (Sd:9,2), respectively. Scores of CJPET are statistically significantly higher in rheumatoid arthritis group than healthy volunteers ( $p=0,001$ ) (table 1). CJPET scores are negatively correlated with Berg Balance Scale results in all directions ( $\rho = -0,421, -0,473, -0,448, -0,515$ ). Scores of CJPET in patients with atlantoaxial subluxations (AAS) were statistically significantly higher than those without AAS ( $p=0,002-0,045$ ). Regression analysis results showed that AAS is related with worse cervical proprioception on right and left rotations. There were no correlation between CJPET scores and functional parameters. Weak correlation were found in scores of CJPET with age and educational status.

**Abstract AB0224 – Table 1.** Comparison of cervical joint position error test scores between rheumatoid arthritis patients and healthy volunteers

	Patients		Healthy Volunteers	P
	Min-Max	Mean±SD	Mean±SD	
<b>CJPET- Right Rotation</b> <sup>1-6</sup>	1,66–6,00	4,55±1,30	3,03±0,81	0001
<b>CJPET- Left Rotation</b> <sup>1-6</sup>	1,50–6,00	4,52±1,37	3,07±0,95	0001
<b>CJPET- Flexion</b> <sup>1-6</sup>	1,00–6,00	4,52±1,36	2,98±0,89	0001
<b>CJPET- Extension</b> <sup>1-6</sup>	1,50–6,00	4,57±1,29	3,00±0,93	0001

CJPET: Cervical Joint Position Error Test, SD: Standard Deviation,  $p<0,05$  is significant

**Conclusions:** Cervical proprioception is impaired in rheumatoid arthritis patients. This impairment is increased with the existence of atlantoaxial subluxations and balance problems.

**Disclosure of Interest:** None declared

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#### AB0225 CLINICAL OUTCOMES OF TREATMENT WITH GOLIMUMAB IN SEROPOSITIVE AND SERONEGATIVE RHEUMATOID ARTHRITIS PATIENTS IN REAL-LIFE SETTINGS. DATA FROM ITALIAN REGISTER GISEA

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**Background:** There is evidence that autoimmunity, namely RF and ACPA antibodies, may influence disease activities and impact the clinical outcomes in RA.

**Objectives:** There is evidence that autoimmunity, namely RF and ACPA antibodies, may influence disease activities and impact the clinical outcomes in RA.

**Methods:** We analysed longitudinal data of consecutive RA patients from the Italian registry GISEA, starting a treatment with golimumab (GOL) and tested for rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA). Demographic and disease related characteristics were collected at baseline, 6 months, 12, and 24 months or at last observation visit. Primary endpoint was the persistence on GOL in RF/ACPA +ve and RF/ACPA -ve patients. Secondary endpoint was the search of baseline predictors of drug survival and clinical outcomes in the two RA subsets. Drug survival was evaluated by Kaplan-Meier life table analysis. Estimates hazard ratios (HRs, 95% confidence intervals (CI)) of drug discontinuation or achievement of low-disease adjusted for patient's demographics, disease characteristics and prior biologic treatments were computed by Cox-regression stepwise backward models.

**Results:** 345 patients had data on RA and ACP testing and were included in this analysis. No significant difference in terms of age, BMI, disease activity, co-therapy with glucocorticoids or methotrexate (MTX) was detected between RF/ACPA+ve and RF/ACPA-ve patients, but the former had significantly higher disease duration (10.6±vs 8.2±6 years) and frequencies of comorbidities (60.6% vs 44.2%). The 2 years global drug retention was 64.5%, and it was almost identical in RF/ACPA+ve 64.2% and in RF/ACPA-ve 65% RA patients. Drug survival was not influenced by the gender or cause of discontinuation (adverse or inefficacy). To note, in 31% of the patients GOL was not associated to MTX.

The only predictor of drug discontinuation was the lack of MTX at baseline (HR 1.62, 95 CI 1.07–2.46,  $p=0.02$ ), and the GOL-naïve status (HR 0.62, 95 CI 0.39–0.99,  $p=0.04$ ). At two years, 44.4% achieved the state of low-disease activity (DAS28 <3.2) with no difference between RF/ACPA+ve (45.4%) and RF/ACPA-ve (42.0%) patients, and none baseline factor correlating with low disease activity. No safety issues were raised during the study.

**Conclusions:** In this study, we demonstrated that RF/ACPA positivity does not negatively impact on drug survival on golimumab. This may aid rheumatologists in their clinical decisions.

**Disclosure of Interest:** None declared

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**AB0226** **DECLINE IN ANTI-CCP AND RHEUMATOID FACTOR LEVELS IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS AFTER 2 YEARS OF TREATMENT WITH INTENSIVE COMBINATION STRATEGIES, INCLUDING PREDNISOLONE: THE COBRA-LIGHT TRIAL**

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**Background:** Previous studies have proven that the COBRA-light strategy has similar effectiveness and safety as the COBRA strategy in treating early rheumatoid arthritis (RA) patients<sup>1,2</sup>. However, the effect of these strategies on anti-cyclic citrullinated peptide (anti-CCP) and rheumatoid factor (RF) levels remains contradictory.

**Objectives:** To investigate whether levels of anti-CCP and RF have changed after 2 years of treatment with COBRA or COBRA-light strategy.

**Methods:** A total of 162 early RA patients were included in a randomised, open-label, multicenter trial and treated with either COBRA or COBRA-light strategy. After 1 year, the treatment protocol ended, and physicians continued treatment according to clinical judgment, aiming at clinical remission. Log-transformation was first performed before running any analyses in case of skewed distribution, and analyses were performed with Generalised Estimated Equations to evaluate the association between the medication strategies and the change of LN anti-CCP and LN RF levels on average over time.

**Results:** Over 2 years' time, median anti-CCP and RF levels decreased significantly in COBRA (6%, and 24% respectively) and COBRA-light (4%, and 13%, respectively; table 1). Of the 102 anti-CCP positive patients at baseline, 10 (10%) became anti-CCP negative during treatment (5 COBRA vs. 5 COBRA-light). No significant difference between the two treatment strategies on the change of anti-CCP and RF levels over 2 years' time was found. Additionally, a significant association between baseline DAS44 and remaining anti-CCP positive over time was found (OR=1.8; 95% CI: 1.2–2.8).

**Abstract AB0226 – Table 1.** Change in anti-CCP and IgM-RF levels over time

	Baseline	Week 52	Absolute median change	Percentage median change	Week 104	Absolute median change	Percentage median change
<b>COBRA</b>							
Anti-CCP	143 (8-1182)	81 (7-710)	-20 (-427-0)	-14	109 (7-507)	-9 (-314-0)	-6
IgM-RF	37 (6-102)	9 (6-40)	-9 (-41-0)	-24	8 (5-48)	-9 (-36-0)	-24
<b>COBRA-light</b>							
Anti-CCP	229 (10-941)	80 (7-499)	-13 (-249-0)	-6	32 (7-402)	-9 (-233-0)	-4
IgM-RF	40 (10-112)	12 (6-50)	-13 (-79-0)	-38	12 (6-84)	-5 (-48-1)	-13

Data are expressed as median (IQR) as well as percentage median change from baseline. Anti-CCP, anti-cyclic citrullinated peptide; IgM-RF, rheumatoid factor type IgM.

**Conclusions:** Both COBRA and COBRA-light strategies lead to substantial decreases in anti-CCP and RF levels over 2 years of treatment. Patients with a higher DAS44 at baseline have higher odds of being anti-CCP positive over 2 years' time.

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**AB0227** **TRANSCRIPTIONAL PROFILING OF SYNOVIAL MACROPHAGES USING MINIMALLY INVASIVE ULTRASOUND-GUIDED SYNOVIAL BIOPSIES IN RHEUMATOID ARTHRITIS**

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**Background:** Despite the many therapies for patients with rheumatoid arthritis (RA), there is little information to guide selection of the most effective treatment for an individual patient. Forty-six percent of patients with RA respond (defined by ACR50 response criteria) to conventional disease modifying anti-rheumatic drugs (cDMARDs) or cDMARDs plus anti-tumour necrosis factor (TNF) therapy. Moreover, 20%–40% of subjects in clinical trials never demonstrate even a minimal response (ACR20 response criteria). Based on a population of over 300 million in the United States, a disease prevalence of 0.6%, and a course of 3–4 months per biologic DMARD therapy, as much as \$2.5 billion is wasted annually on inadequate therapy. There is a clear need to develop precision-based therapy for patients with RA, whereby clinical information such as novel biomarkers will enhance our ability to predict the therapeutic response and thereby limit ineffective therapy.

**Objectives:** Currently, there are no reliable biomarkers for predicting therapeutic response in patients with rheumatoid arthritis (RA). The synovium may unlock critical information for determining efficacy as reduction in numbers of sublining synovial macrophages remains the most reproducible biomarker. Thus, a clinically actionable method for collection of synovial tissue, which can be analysed using high-throughput strategies, must become a reality.

**Methods:** Rheumatologists at six United States academic sites were trained in minimally invasive ultrasound-guided synovial tissue biopsy. Histology, fluorescence-activated cell sorting and RNA-seq were performed on biopsy synovial tissue from patients with RA and compared with osteoarthritis (OA) samples. An optimised protocol for digesting synovial tissue was developed to generate high quality RNA-seq libraries from isolated macrophage populations. Associations were determined between macrophage transcriptional profiles and clinical parameters of RA patients.

**Results:** Patients with RA reported minimal adverse effects in response to synovial biopsy. Comparable RNA quality was observed between synovial tissue and isolated macrophages from patients with RA and OA. Whole tissue samples from patients with RA demonstrated a high degree of transcriptional heterogeneity. In contrast, the transcriptional profile of isolated RA synovial macrophages highlighted a subpopulation of patients and identified six novel transcriptional modules that were associated with disease activity and therapy.

**Conclusions:** Performance of synovial tissue biopsies by rheumatologists in the United States is feasible and generates high-quality samples for research. By utilising cutting-edge technologies on synovial biopsies with corresponding clinical information, a precision-based medicine approach for patients with RA is attainable.

**Disclosure of Interest:** None declared

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**AB0228** **INCREASE IN GLOBAL DNA METHYLATION AT 3 MONTHS OF METHOTREXATE USE IS NOT ASSOCIATED TO RESPONSE IN EARLY RA PATIENTS**

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**Background:** Methotrexate (MTX) is a first-line therapy in early Rheumatoid Arthritis (eRA). Still, up to 40% of treated patients do not adequately respond to MTX. MTX interferes with the folate cycle, where it indirectly inhibits the global DNA methylation donor S-adenosylmethionine (SAM). Thus, we hypothesised that global DNA methylation changes during MTX use are associated with treatment response.

**Objectives:** To examine whether there is a change in global DNA methylation ( $\Delta\%$ Meth) upon MTX use and if this change is associated to MTX response ( $\Delta$ DAS28) in eRA patients.

**Methods:** DNA was isolated from whole blood (n=120) and Peripheral Blood Mononuclear Cells (PBMCs, n=83) of eRA patients, before and 3 months after MTX use. Samples were collected from the Treatment in the Rotterdam Early Arthritis Cohort (tREACH), a multicenter, stratified single-blind clinical trial of eRA patients. Selected patients received triple (MTX +SSZ + HCQ) or monotherapy (MTX) combined with corticosteroids. 7 CpG sites within Long-Interspersed Nuclear Elements (LINE-1), a proxy for global DNA methylation, were quantified by Sequenom Epityper. Paired t-tests or Wilcoxon Signed Rank tests were conducted to assess a change in methylation.  $\Delta$ DAS28 score over 3 months was used as a measure for response. Associations between  $\Delta$ DAS28 and  $\Delta\%$ Meth were corrected for baseline DAS28 in a linear regression model.

**Results:** In leukocytes, %Meth did not significantly change over time. However, in PBMCs %Meth in CpG1 ( $\Delta$ Meth=2.61%,  $p=0.008$ ), CpG2 ( $\Delta$ Meth=0.73%,  $p=0.039$ ) and CpG11.12 ( $\Delta$ Meth=0.56%,  $p=0.016$ ) significantly increased over 3 months of MTX use after Bonferroni correction.  $\Delta$ %Meth in CpG8.9 was significantly associated to the  $\Delta$ DAS28 ( $B=0.29$ ,  $p=0.039$ ), yet this was no longer significant after Bonferroni correction.  $\Delta$ %Meth was not significantly associated to  $\Delta$ DAS28 in any of the other LINE1 CpG sites tested.

**Conclusions:** PBMC global DNA methylation in LINE-1 CpG sites increased upon 3 months of MTX use. However, this change in methylation is not associated to MTX response. Further research is needed to investigate the role of global DNA methylation in these patients.

**Disclosure of Interest:** None declared

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AB0229

#### WHAT WARRANT COMPREHENSIVE DISEASE REMISSION (CDR) AT LONG TERM? – PROBABILITY OF DAS28-CRP REMISSION AT SIX MONTHS –

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**Background:** Comprehensive disease remission (CDR) for rheumatoid arthritis (RA) patient is an ultimate challenge in treatment. Several reports suggested initial treatment is essential for attaining CDR, what means it is necessary to indicate clinical remission in the first treatment year.

**Objectives:** Aim of this study is to clarify how initial treatment until 6 months affect on CDR fulfilment, and whether patient's basic background influences.

**Methods:** We have 441 RA patients who had been treated consecutively for more than four years. These patients were recruited. Parameters such as 28-joints disease activity score with C-reactive protein (DAS28-CRP), modified Health Assessment Questionnaire Disability Index (mHAQ), pain score with visual analogue scale (PS-VAS), were monitored at every visit since first time. Sharp/van der Heijde Score (SHS) was calculated at first visit and every another year period. Average value of DAS28-CRP, mHAQ in fourth treatment year, and average progression of SHS per year (dSHS) were used to make judgment for CDR at fourth year, whether DAS28-CRP less than 2.3, mHAQ less than 0.5, and dSHS less than 0.5. Fulfilment of CDR is evaluated for patient's age, DAS28-CRP, mHAQ, SvdHS, and PS-VAS at first visit and sixth month was evaluated statistically with binary logistic regression analysis (BLR). Patient's background data at first visit were also evaluated in the same manner. For the significant factors, relationship with the background data was also evaluated with multivariate linear regression analysis (MLR). Statistical significance in both analyses was set below 5%. Receiver operating characteristic curve analysis (ROC) was also implicated for the significant factors.

**Results:** Because of lacking data, 310 patients were analysed. 146 (47.1%) of them had fulfilled CDR at fourth treatment year. Statistically significant factor for fulfilling CDR was mHAQ at first visit (odds ratio; 0.032, 95% CI; 0.008–0.139) and DAS28-CRP at sixth months (odds ratio; 0.273, 95% CI; 0.112–0.662). The mHAQ score at first visit correlated significantly with age at onset and first visit, patient's global assessment (PGA), CRP, and PS-VAS at first visit, whereas the DAS28-CRP score at sixth month correlated significantly with being male, tenderness joint count (TJC), physician's global assessment (EGA), CRP, and PS-VAS at first visit, and less reduction of TJC, swollen joint count (SJC), EGA, and CRP. Cut off point for each factor was 0 for mHAQ with 100% in sensitivity and 73.5% in specificity, whereas 1.105 for DAS28-CRP with 100% in sensitivity and 55.2% in specificity, which were used with ROC analysis.

**Conclusions:** These results suggest that treatment with treat-to-target (T2T) strategy, that aims clinical remission in three to six months from starting treatment, is available for attaining CDR. However, T2T is not enough for sustaining CDR in a long term. In order to fulfil and sustain CDR, basic background of the patient, such as age at onset and PGA, CRP, and PS-VAS, and age at first consult, is important factor. Therefore, CDR is not ultimate target at all for every RA patient

**Disclosure of Interest:** None declared

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AB0230

#### AN EFFECT OF DAS28 AND PS-VAS ON HAQ-DI SCORE IN RHEUMATOID ARTHRITIS PATIENT

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**Background:** Pain Score with visual analogue scale (PS-VAS) influences on Health Assessment Questionnaire Disease Index (HAQ-DI) in rheumatoid arthritis (RA) patient, as well as 28-joints disease activity score with C-reactive protein (DAS28-CRP). It is also suggested that these two indices have closely correlated and therefore have overlapping effect on HAQ-DI. However, the relationship of these indices for each other is still unclear.

**Objectives:** Our aim is to clarify what affects most out of the overlap, and what would make influence on when dissociation between the two occurs.

**Methods:** We have treated 549 RA patients consecutively more than four years. Their HAQ-DI, every component of DAS28-CRP, physician's global assessment (EGA), PS-VAS, and Sharp/van der Heijde Score (SHS) were monitored every 3 months. From these patients studies concerning relationship between the parameters were investigated as follows:<sup>1</sup> The relationship between average DAS28-CRP and average PS-VAS after the third year period was calculated using multivariate linear regression analysis (MLR).<sup>2</sup> Then residuals of the each parameter from the approximate equation of MLR were calculated. From these residuals, correlation between residual of DAS28-CRP and disease duration (DD), HAQ-DI, age, SHS, physician's global assessment (EGA), number of comorbidities in throughout treatment (Com) was evaluated with MLR.<sup>3</sup> Correlation between residual of PS-VAS and DD, HAQ-DI, age, SHS, EGA, and Com was evaluated with MLR.<sup>4</sup> Correlation between average HAQ-DI and the residuals, patient's DD, age, SHS, EGA, and Com, was evaluated with MLR. In these analyses, statistical significance between parameters were evaluated statistically. Statistical significance was set lower than 1%.

**Results:** Because of lacking of data, sixty-one cases had discarded, and then 488 cases had been analysed in this study.<sup>1</sup> The approximate equation of the relation between DAS28-CRP and PS-VAS was "DAS28-CRP=1.543+0.1565 \* PS-VAS" (R; 0.5050, Intercept;  $p=0$ , PS-VAS;  $p=0$ ) and "PS-VAS=-0.6528+1.63 \* DAS28-CRP" (R; 0.5050, Intercept;  $p=1.071*10^{-2}$ , PS-VAS;  $p=0$ ).<sup>2</sup> Correlation coefficients of the approximate equation of the correlation between residuals of DAS28-CRP and the other parameters was 0.6398. Parameters that demonstrated within 1% of statistical significance were EGA ( $p=0$ ), SHS ( $p=2.962*10^{-6}$ ), and Com ( $p=1.971*10^{-5}$ ).<sup>3</sup> Correlation coefficients of the approximate equation of the correlation between residuals of PS-VAS and the other parameters was 0.4856. Parameters that demonstrated within 1% of statistical significance were Com ( $p=9.38*10^{-1}$ ), HAQ-DI ( $p=5.738*10^{-9}$ ), and SHS ( $p=1.594*10^{-7}$ ).<sup>4</sup> Correlation coefficients of the approximate equation of the correlation between HAQ-DI and residuals of DAS28-CRP and PS-VAS, and DD, age, SHS, EGA, and Com, was 0.5848. Parameters that demonstrated within 1% of statistical significance were residual of DAS28-CRP ( $p=1.256*10^{-6}$ ), residual of PS-VAS ( $p=3.711*10^{-14}$ ), SHS ( $p=7.73*10^{-4}$ ), and age ( $p=2.389*10^{-10}$ ).

**Conclusions:** These results suggest that the influence of DAS28-CRP and PS-VAS on the HAQ-DI score works in commonly overlapped. However, residual (the independent part) of DAS28-CRP from PS-VAS on HAQ-DI is not statistically evident. Residual of PS-VAS affects on the HAQ-DI score. SHS and Com affect on both of residuals. The HAQ-DI score is influenced by both of common and independent part of DAS28-CRP and PS-VAS, and SHS and age.

**Disclosure of Interest:** None declared

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AB0231

#### HEALTH ASSESSMENT QUESTIONNAIRE DISABILITY INDEX SCORE LESS THAN 0.5 IS NO LONGER TARGET FOR REMISSION IN ELDERLY RHEUMATOID ARTHRITIS PATIENT, BUT IT IS INDEPENDENT FROM COMORBIDITIES

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**Background:** It is well known fact that ageing makes deep influence on Health Assessment Questionnaire (HAQ-DI) score in normalised population. We have suggested that it is also available in rheumatoid arthritis (RA) patient.<sup>1</sup> However, the effect of ageing on the HAQ score is thought to be due to comorbidities.

**Objectives:** The aim of this study is to investigate the impact of ageing on the HAQ score statistically and to evaluate the correlation between the HAQ score and age.

**Methods:** We have been treated 516 RA patient for more than 3 years. Patient's Age, HAQ-DI score, 28-joints disease activity score with C-reactive protein (DAS28), Sharp/van der Heijde Score (SvdHS), pain score measured with visual analogue score (PS) were monitored at every another year since first consult (BL). Relationship between HAQ-DI and the other parameters including number of comorbidities (Com) at BL and last observational year period (FU), and their changes from BL to FU were evaluated statistically with multivariate linear regression analysis (MLR). After correction that aimed to minimise effects on the HAQ score of other parameters but age, relationship between the HAQ score and age was also evaluated with MLR. Relationship between age and Com was also evaluated with MLR statistically. Statistical significant level was set within 5%.

**Results:** After exclusion of cases that lacked data, 441 patients have been analysed for this study. Their average ages at onset, BL, and FU were 60.4, 65.1, and 70.9 years, respectively, and average follow-up term was 5.76 years. Woman's ratio was 75.6%, and their anti-citrullinated cyclic peptide antibodies positive ratio was 77.2%.

At BL, correlation coefficient of the equation (the R-value) in MLR was 0.6251. Factors that demonstrated significant correlation with the HAQ score were PS,



age, and DAS28, and their correlation coefficients (CC) were 0.00004174, 0.01943, and 0.02941, respectively.

At FU, the R-value of the equation in MLR was 0.6309. Factors that demonstrated significant correlation with the HAQ score were age, Com, PS, and SvdHS, and their CCs were 0.00007042, 0.0004365, and 0.002886, 0.02354, respectively.

The R-value of the change of the HAQ score correlation equation demonstrated 0.4755. Factors that demonstrated significant correlation with change of the HAQ score were changes of DAS28-CRP, PS, age, and Com, and their CCs were 0.002703, 0.003750, 0.003480, and 0.009886.

Correlation procedure needed elimination of the case whose average DAS28 exceeded 2.6, SvdHS exceeded 100, and PS exceeded 20 mm. After correction, patients have been limited to 158. However, age demonstrated significant correlation with the HAQ score, and its CC was 0.00004439, and the constant of age was 0.01132. After correction, Com demonstrated no significant correlation with the HAQ score.

Com demonstrated significant correlation with age with 0.01253 for CC. However, the R-value of the equation was 0.1982.

**Conclusions:** These results suggested that age have deep influence on the HAQ score. Com also affects on the HAQ score, however, Com and ageing is independent factor for each other. Therefore effect of ageing on the HAQ score is concluded independent. The HAQ score increases its standard value for approximately 0.01 as age increase one.

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#### AB0232 DISEASE ACTIVITY STATE IN PATIENTS WITH RHEUMATOID ARTHRITIS INCLUDED IN THE BIOBADABRASIL REGISTRY

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**Objectives:** to analyse disease activity of RA patients at the start of treatment with a biologic agent (adalimumab, infliximab, certolizumab, etanercept, golimumab, abatacept, rituximab and tocilizumab -bDMARDs), target (tofacitinib-tsDMARDs) therapy or conventional DMARDs (comparison cohort of RA patients – csDMARDs).

**Methods:** BiobadaBrasil is a prospective observational cohort study, part of an international initiative (biobadaAmerica) in collaboration with BiobadaSeR; established in 2009, is an ongoing study supported by the Brazilian Society of Rheumatology (29 public centres located at academic institutions and 2 in private practice) focused on the study of adverse events in patients on biologic therapy. Additionally, by decision of its investigators, disease activity scores were also recorded at the beginning of each treatment. Sex, age, disease duration, RA -DAS-28, concomitant treatments at baseline were collected. Results expressed in mean  $\pm$ SD, % (n)

**Results:** -Data from 1984 RA patients (67% on tsbDMARDs) were analysed: 86% of the patients were women; mean age=56.6 $\pm$ 14.95 years; disease duration=14.4 $\pm$ 9.42; 87% RF positive. There were 3802 treatment courses, 67% with aTNF (Adalimumab-ADA, Certolizumab-CTZ, Etanercept-ETA, Golimumab-GOL, Infliximab-INFL), 33% non-aTNF (Abatacept-ABA, Rituximab-RIT, Tocilizumab-TCL) including Tofacitinib-TOF. The table 1 below depicted the medications prescribed at the initiation of a new treatment course:

**Abstract AB0232 – Table 1**

n courses	ADA (855)	CTZ (85)	ETA (708)	GOL (113)	INFL (772)	ABA (163)	RIT (184)	TCL (192)	TOF (70)	cDMARDs (660)
DAS28	5.1	4.9	5.1	4.9	5.3	5.3	5.3	5.4	5.3	5.2 $\pm$ 2.8
	$\pm$ 1.6	$\pm$ 1.5	$\pm$ 1.6	$\pm$ 1.7*	$\pm$ 1.6	$\pm$ 1.4	$\pm$ 1.6	$\pm$ 1.4*	$\pm$ 1.3	
CE (%)	58	76	60	61	58	68	74	71	83	78
MTX (%)	55	57	53	56	59	54	51	62	49	83
LFN (%)	27	42	27	31	23	31	25	18	27	45
Chlor (%)	14	15	11	10	15	11	19	17	11	30

Considering the more recent medications patients beginning TCL have more active disease than the ones beginning GOL and CTZ ( $p < 0.006$ ); anti-TNF are prescribed in association with MTX in less than 60% of the treatments. Extensive use of corticosteroids was identified besides consistent use of leflunomide and of hydroxychloroquine. Starting of new treatments was related to moderate/high levels of disease activity.

**Conclusions:** patterns of bDMARDs, csDMARDs and corticosteroid use clearly surfaced. Possibilities of improvement can be addressed.

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#### AB0233 CLINICAL AND FUNCTIONAL EFFICIENCY OF LARGE JOINTS REPLACEMENT IN PATIENTS WITH HIGH ACTIVITY OF RHEUMATOID ARTHRITIS

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**Background:** The synovium in rheumatoid arthritis (RA) produces a variety of cytokines that cause the destruction of articular cartilage, determining, in some cases, the need for replacement of the joint. Inflammatory substrate within the joint can be a source of high activity of RA. At the same time usually patients are taken to surgery only in the period of minimal activity of the disease.

**Objectives:** To evaluate the results of knee and hip joints replacement in patients with high RA activity and the quality of life of patients during the first year after the operation.

**Methods:** Replacement of knee and hip joints was performed in 36 patients (mean age 55.8 $\pm$ 9.4 years) with high RA activity DAS28 (mean 5.53 $\pm$ 0.67). At the time of surgery, the duration of the disease was 11.86 $\pm$ 4.92 years, RF positive in 27 (75%) pts. At baseline, 30 (83.3%) patients were treated with DMARDs (methotrexate-25 (69.4%), leflunomide-3 (8.3%), sulfasalazine 2 (5.6%), steroids (prednisolone in an average dose of 4.2 $\pm$ 4.3 mg per day) – 16 (44.4%) people, of whom, in combination with DMARDs – 8 (22.2%). The volume of therapy did not change after the operation. Biologics (infliximab, adalimumab, rituximab, etanercept) before surgery were given to 7 (19.4%) patients. Before the operation, after it, after 6 and 12 months, pain in the joints (VAS), activity of the disease – DAS28, functional capacity by the HAQ index was estimated.

**Results:** Reduction of VAS was observed already in the first month after surgery (47.3 $\pm$ 18.6 mm), initially it was 72.6 $\pm$ 14.2 mm, after 6 months it decreased 1.5 times to 48.7 $\pm$ 11, 2 mm ( $p < 0.05$ ), after 12 months – up to 29.8 $\pm$ 10.3 mm ( $p < 0.05$ ). After 6 months after surgery, the activity of the disease decreased reliably ( $p < 0.05$ ) with DAS28 from 5.53 $\pm$ 0.67 to 3.84 $\pm$ 0.56; to 12 months DAS28-3.24 $\pm$ 0.61. Positive dynamics of functional ability was recorded according to the HAQ index: 1.74 $\pm$ 0.25 before the operation, 1.64 $\pm$ 0.28 in a month after, and 1.22 $\pm$ 0.28 after 6 months ( $p < 0.05$ ), after 1 year – 1.03 $\pm$ 0.18 ( $p < 0.05$ ).

Complications after operations were not recorded.

**Conclusions:** Joints replacement in patients with high RA activity can be justified and effective in improving the functional ability and pain relief. Removal of pathologically altered joint tissues helps to reduce the activity of RA as a whole.

**Disclosure of Interest:** None declared

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#### AB0234 PATIENT'S EXPECTATIONS ABOUT SURGERY FOR THE RHEUMATOID FOREFOOT DEFORMITY

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**Background:** Forefoot deformity has been a common problem in rheumatoid patients, often demanding surgery. Typical deformities include hallux valgus and deformity of lesser metatarsophalangeal joints (MTPJ) and toes. Patient's satisfaction has not been well dealt in the literature as most studies have focused on radiological and clinical parameters following surgical treatment.

**Objectives:** to assess preoperative patient's expectations and postoperative satisfaction, and also factors (e.g. fulfilment of expectations, radiological parameters, and clinical outcomes) that could affect on postoperative satisfaction following first MTPJ arthrodesis and lesser toe resection arthroplasty in patients with rheumatoid forefoot deformity

**Methods:** 40 patients who underwent first MTPJ arthrodesis on great toe and resection arthroplasty for all less toes were enrolled. Clinical and radiological outcomes were investigated retrospectively. Preoperative primary expectations for surgery were questioned and fulfilment of expectation was assessed by 5-point

ordinal scale. Overall subjective satisfaction, radiological improvements, AOFAS forefoot score, and subjective Foot function index were also assessed. Correlation between overall satisfaction after surgery and above other factors was performed. Statistical analysis was done using SPSS and Spearman's rho rank correlation test was performed to analyse the correlation between factors.

**Results:** Mean follow-up was 38 months (range; 24–54). For preoperative expectations, 30 (75%) patients considered improvement in pain as the most important parameter and improvements in shoe wearable and gross appearance were expected in 7 (17.5%) and 3 (7.5%) patients, respectively. Fulfilment of expectations assessed showed very satisfied in 14 (35%), satisfied in 20 (50%), average in 5 (12.5%) and disappointed in 1 (2.5%) for great toe, and those regarding lesser toe showed very satisfied in 15 (37.5%), satisfied in 18 (45%), average in 6 (15%) and disappointed in 1 (2.5%), respectively. For overall postoperative satisfaction assessment, 16 patients (40%) were excellent while 16 (40%) were good, 6 (15%) fair, and 2 (5%) poor. AOFAS hallux and lesser toe score were 69.7 ±11.71 and 70.7±12.26, respectively. Foot function index was 20.5±12.07 at final follow-up. Preoperative and postoperative hallux valgus angle were 45.6° ±10.55 and 17.4°±5.13, respectively. Those of 1–2 intermetatarsal angle were 14.2°±3.84 and 8.4°±3.72, respectively. Correlation analysis showed that significant factors that affected on overall satisfaction were fulfilment of expectation on the great toe (Spearman's rho=0.842, p<0.001) and that of lesser toe, and AOFAS score. Radiological degree and improvement in HVA and IMA were not significantly associated with patient's satisfaction.

**Conclusions:** Expectations from surgery on rheumatoid forefoot deformity were improvement in pain as the most common parameter, improvements in shoe wearable and gross appearance. Fulfilment of patients' expectations on the great toe as well as on the lesser toe significantly affected on postoperative satisfaction. Careful counselling for patients' expectations and corresponding fulfilment should be performed before performing reconstructive surgery for rheumatoid forefoot deformity.

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AB0235

#### POLYMORPHISMS OF HLA-DRB1 AND TNF-308 G/A ARE ASSOCIATED WITH RADIOGRAPHIC JOINT DESTRUCTION IN PATIENTS WITH VERY EARLY RHEUMATOID ARTHRITIS

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**Objectives:** To clarify the association between HLA-DRB1 and TNF $\alpha$  (–308G>A) genes polymorphism and joint destruction/further progression during 12 months of the follow-up period (FUP) in patients with early (<6 months), active, predominantly ACPA and RF-positive RA treated according to "Treat to target" strategy.

**Methods:** The study included 85 patients with early RA and duration of symptoms <6 months. RA diagnosis was established according to ACR<sup>EULAR 2010</sup> criteria. All patients were initially assigned to subcutaneous methotrexate (MTX) with rapid dose escalation to 20–25 mg/week. Combination MTX+biological therapy, mainly adalimumab, was used when MTX was ineffective. Joint destruction was assessed by Sharp-Van der Heijde modification scoring method at baseline and after 12 months FUP. Real time polymerase chain reaction (PCR-RT) was used for TNF $\alpha$  gene polymorphism (–308G>A) genotyping. Low resolution PCR-RT with subsequent sequence-based typing of \*04 were performed to study HLA-DRB1 gene polymorphism. The HLA-DRB1\*01, \*04:01, \*04:04, \*04:05, \*04:08, \*10 alleles were categorised as SE+ (Shared Epitope) alleles.

**Results:** It was revealed that the number of erosions and joint space narrowings as well as the total Sharpe score were not associated with the presence and the dose of the SE alleles, either at baseline or after 12 months FUP. However, the progression of joint destruction, assessed as the change ( $\Delta$ ) in the number of erosions, joint space narrowings and the total score, was statistically significantly associated with HLA-DRB1\*(SE) genotypes: the carriers of SE (SE+/SE+) double-dose had more advanced progression as compared to (SE+/SE-)/(SE-/SE-) carriers (p<0,028, p<0,019, p<0,035, respectively). As for TNF $\alpha$  gene polymorphism, it was demonstrated that the number of narrowings and total Sharp score values were almost twice as high at baseline in GG genotype carriers as

compared to GA genotype carriers (69,0<sup>49,5; 98,0</sup> and 37,0<sup>29,0; 63,0</sup> respectively, p<0,005) and (72,0<sup>49,5; 98,5</sup> and 37,0, <sup>29,0; 63,0</sup> respectively, p<0,004). Similar association was found after 12mo FUP, however, it should be mentioned that further progression of joint space narrowing and total Sharpe score was minimal (p>0,05).

**Conclusions:** Our data suggest that HLA-DRB1 (SE+) gene polymorphism is associated with the progression of radiographic joint destruction at 12mo FUP in treated pts. Meanwhile TNF $\alpha$  (–308G>A) polymorphism is associated with more pronounced joint destruction at baseline in terms of joint space narrowing and total Sharp score, but without further progression of joint destruction at 12mo in early and active RA pts managed according to "Treat to target" strategy.

**Disclosure of Interest:** None declared

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AB0236

#### DEVELOPMENT AND VALIDATION OF A SENSITIVE LC-MS/MS-BASED METHOD FOR ANALYSIS OF ENZYMIC ACTIVITY OF FOLYLPOLYGLUTAMATE SYNTHETASE AND METHOTREXATE POLYGLUTAMATES IN PERIPHERAL BLOOD MONONUCLEAR CELLS OF RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Methotrexate (MTX) is a widely applied anti-rheumatic and anti-leukemic drug. For its intracellular retention and pharmacologic activity, MTX relies on the enzymatic activity of folypolyglutamate synthetase (FPGS) to convert MTX into its polyglutamate forms (MTX-PG<sub>2-6</sub>). Loss of FPGS activity is associated with reduced MTX activity and although red blood cell (RBC) MTX-PG<sub>n</sub> levels correlate with disease activity in RA patients,<sup>1</sup> it is anticipated to be more relevant to measure MTX-PG<sub>n</sub> in peripheral blood mononuclear cells (PBMCs). Thus, the aim of our study was to develop a LC-MS/MS method to 1) measure FPGS activity replacing laborious radioactive assays, and 2) to measure MTX-PG<sub>n</sub> in PBMCs.<sup>2</sup>

**Objectives:** To validate a rapid, sensitive and non-radioactive assay to measure FPGS activity and MTX-PG<sub>n</sub> in PBMCs based on LC-MS/MS technology.

**Methods:** Protein extracts (n=5) of PBMCs of MTX-treated RA patients were incubated for 2 hours at 37°C in FPGS assay buffer (pH8.8) containing 250  $\mu$ M MTX and 4 mM l-glutamic acid as substrates. Next, MTX-PG<sub>2</sub> formation was analysed with AB Sciex 4000 Q Trap tandem mass spectrometer coupled to an Acquity Ultra Performance LC system. Measurement of PBMC-MTX-PG<sub>n</sub> (n=5) was performed by extraction of MTX-PG<sub>n</sub> from PBMCs by perchloric acid precipitation. Quantification was performed with <sup>13</sup>C<sub>5</sub><sup>15</sup>N-labelled MTX-PG<sub>1-5</sub> internal standards. In FPGS activity and MTX-PG validation studies, human CCRF-CEM leukaemia cells, CEM/R30dm (a FPGS-deficient, MTX-resistant subline of CCRF-CEM), and human acute lymphoblastic leukemia (ALL) cells served as reference.

**Results:** In CCRF-CEM, the FPGS enzymatic assay showed linearity with protein input (10–250  $\mu$ g) and incubation time (0.5–3 hours). Substrate affinity parameters (Km) for MTX (65  $\mu$ M) and l-glutamic acid (2.2 mM) were consistent with earlier reports.<sup>3</sup> FPGS activity in CEM/R30dm was <1% of CCRF-CEM. FPGS activity in ALL blasts was similar to CCRF-CEM while FPGS activity in RA patient PBMCs was 1%–5% of CCRF-CEM, and was non-detectable in RBCs. Average individual fractions of total MTX-PG<sub>n</sub> in RA patient PBMCs were 22,1% (range: 8,2%–36,2%) for MTX-PG<sub>2</sub>, 32,8% (27,1%–43,6%) for MTX-PG<sub>3</sub>, 34,4% (30,4%–41,3%) for MTX-PG<sub>4</sub> and 10,6% (0,0%–28,4%) for MTX-PG<sub>5</sub>. Average total MTX-PG<sub>n</sub> levels per number of RA patient PBMCs were 30–50 fold higher than matched numbers of erythrocytes, and 6–9 fold lower than ALL blasts incubated for 24 hours with 1  $\mu$ M MTX.

**Conclusions:** A sensitive LC-MS/MS based method was developed for the measurement of FPGS activity and MTX-PG<sub>n</sub> levels in PBMCs of RA patients. This method holds promise to guide future MTX-therapy response evaluations.

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**AB0237 ANALYSIS OF THE IMPACT OF CONCOMITANT USE OF CORTICOSTEROIDS ON THE CLINICAL OUTCOMES OF PATIENTS WITH LONG-TERM RHEUMATOID ARTHRITIS IN DIFFERENT TREATMENTS**

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**Objectives:** To analyse the impact of the concomitant use of corticosteroids on the treatment of patients with long-term rheumatoid arthritis in different clinical outcomes.

**Methods:** A cross-sectional study was carried out in a sample of 100 patients with rheumatoid arthritis attended at specialised centres in rheumatology in Florianópolis. Validated instruments were used to evaluate the disease activity (DAS-28 VHS, DAS-28 PCR, SDAI and CDAI), functional ability (HAQ-DI) and quality of life (SF-12 and SF-6D). Statistical analysis was performed using qui-square test (Pearson), Fisher's exact test, Student's t-test, seeking to study the association between the independent variables and the use of corticosteroids.

**Results:** The mean disease duration of the patients was 15.1±8.7 years, which of, 25% used corticosteroids, with an average dose of 6.7±3.9 mg/day. The mean of the physical component summary (PCS) of SF-12 increased significantly by 1.87 points (47.72±3.23 vs 45.85±2.52 p=0.013) in patients who used corticosteroids, on the other hand, in the mental component summary (MCS) we observed a reduction of the mean by 1.5 points (57.91±3.68 vs 56.41±2.98 p=0.046) in these patients. In the association between the use of corticosteroids with ICADs, HAQ and SF-6D no differences were found independent of the synthetic and/or biological DMARD used.

**Conclusions:** Use of corticosteroids in different treatment strategies is not associated with an increase in the frequency of clinical remission in patients with rheumatoid arthritis. In patients using corticosteroids there was a better quality of life evaluated by the PCS, but not by the MCS.

**Disclosure of Interest:** None declared

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**AB0238 PATIENT-CENTRED APPROACH TO MANAGEMENT OF INFLAMMATORY ARTHRITIS WAS ASSOCIATED WITH IMPROVED SATISFACTION OF CARE AND PERCEIVED TREATMENT BENEFIT**

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**Background:** Recently, there has been a paradigm shift from a paternalistic doctor-patient relationship towards more holistic, patient-centred care aimed at promoting patient autonomy. However, the effect of patient-centred care on important clinical outcomes, like patient satisfaction and disability, is unknown.

**Objectives:** To investigate how the various aspects of patients' experiences of the care they received for their inflammatory arthritis was correlated with disease activity and health satisfaction, and use this to guide our clinical practice.

**Methods:** 115 questionnaires (including 51 questions, in addition to HAQ) were randomly given to patients with inflammatory arthritis who attended rheumatology outpatient clinics at University College Hospital, London between November 2014 and January 2015 (104 were returned ~90% response rate). Questions were semi-structured using a Likert scale and focused on diagnosis, symptomatology, treatment history, health status and experiences of clinic attendance. The strength of association between health satisfaction and experience of care was correlated using Spearman's correlation test (p<0.05 was considered statistically significant).

**Results:** We calculated correlations between various aspects of patients' experiences of their care with other components of the questionnaire (table 1).

**Conclusions:** Patients who felt that they experienced a more patient-centred approach (through greater involvement in clinical decisions, emotional support and ease of contact with specialists) reported greater satisfaction and regarded their treatment as more efficacious. This suggests that clinicians who go beyond their role of medically managing inflammatory arthritis to provide more holistic care may improve patient-orientated health outcomes.

Patients in older age groups find it easier to contact the department, perhaps because they have more free time to make and receive calls. As ease of contact is a strong predictor of overall patient satisfaction, employing ideas to increase accessibility for younger age groups, such as improved access beyond working hours may improve satisfaction.

The positive correlation of HAQ with employment status and age is expected, as HAQ is the current gold standard measure of functional status. This reaffirms its accuracy in clinical practice as a measure of a functional ability.

Further research into comparing patients' experience of their care with objective measures of disease activity is needed.

Abstract AB0238 – Table 1

	Systemic disease (years)	Age (years)	Overall satisfaction related to the physical health (1-5) - not considered if not completed at all	How active the disease was to the patient (1-5) - not considered if not completed at all	Treatment efficacy (1-5) - not considered if not completed at all	Treatment tolerability (1-5) - not considered if not completed at all	Being currently employed in a regular full time job (1-5) - not considered if not completed at all
Reached in disease remission (Labour)	R: 0.19179 P: 0.0001	R: -0.14076 P: 0.0076	R: 0.3326 P: 0.0003	R: 0.1972 P: 0.0002	R: 0.2258 P: 0.0014	R: 0.19077 P: 0.0009	R: 0.19096 P: 0.0029
Receiving appropriate emotional support (Labour)	R: 0.19966 P: 0.0012	R: -0.22132 P: 0.023	R: 0.2847 P: 0.00047	R: 0.169191 P: 0.00013	R: 0.274812 P: 0.00003	R: 0.110975 P: 0.02062	R: 0.081764 P: 0.00010
Rate to contact a rheumatology specialist (Labour)	R: 0.22779 P: 0.0017	R: -0.30088 P: 0.00179	R: 0.27638 P: 0.00178	R: 0.196791 P: 0.00179	R: 0.24288 P: 0.00184	R: 0.109176 P: 0.04661	R: 0.027513 P: 0.0001
Great enough information was given about the disease (1-5)	R: 0.34471 P: 0.00002	R: -0.19535 P: 0.2710	R: 0.17718 P: 0.2493	R: 0.200014 P: 0.4227	R: 0.274812 P: 0.00014	R: 0.112307 P: 0.2547	R: -0.137743 P: 0.02998
The questionnaire DASH (1-5) (1-5)	R: 0.19079 P: 0.00007	R: -0.20794 P: 0.00002	R: 0.14268 P: 0.1798	R: 0.103961 P: 0.9127	R: 0.170791 P: 0.0421	R: 0.112307 P: 0.18816	R: 0.081008 P: 0.00042
HAQ	R: 0.00012 P: 0.92077	R: 0.00079 P: 0.92077	R: -0.01626 P: 0.92077	R: 0.00002 P: 0.92077	R: 0.00006 P: 0.92077	R: 0.00001 P: 0.92077	R: 0.00027 P: 0.92077

**Disclosure of Interest:** None declared

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**AB0239 DEVELOPMENT OF A NOVEL „MOLECULAR DISEASE ACTIVITY“ TOOL COMPOSED OF 8 SERUM BIOMARKERS FOR MONITORING RHEUMATOID ARTHRITIS**

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**Background:** Accurate disease activity measurement is a key component of rheumatoid arthritis (RA) management. In 2012, multi-biomarker disease activity (MBDA) test using 12 serum proteins was presented<sup>1</sup>.

**Objectives:** To develop a novel test for measuring inflammatory activity in RA.

**Methods:** Serum samples were obtained from 82 patients with RA (60 females, median disease duration 4.2 years, median age 55.2 years, RF positivity 60.3%, ACPA positivity 69.7%). A detailed stepwise analysis of 20 candidate biomarkers selected from the literature search (IL1β, IL-6, IL-7, IL-8, IL-12p70, IL-17A, IL-22, IL-33, IL-34, IFNγ, VEGF, YKL-40, CXCL-13, MMP-3, resistin, visfatin, leptin, adiponectin, calprotectin and CRP) was performed. Methods of factor analysis (a statistical method used to describe variability among observed, correlated variables in terms of a potentially lower number of unobserved variables called factors) were used in order to develop a tool composed of different serum markers that would optimally reflect disease activity in RA. Spearman correlation index was used to explore associations between newly designed tool and clinical as well ultrasound parameters (German US7 score) of disease activity.

**Results:** We have developed a "Molecular Disease Activity" test covering underlying pathophysiological processes composed of 8 serum markers: calprotectin, CRP, IL-6, MMP-3, VEGF, resistin, IL-22 and IL-7 that optimally reflected inflammatory activity in RA. This model was significantly associated with clinical (DAS28-ESR, DAS29-CRP, CDAI, SDAI) and ultrasound variables (PD syn score, GS syn score) of disease activity in RA, as shown in table 1.

Abstract AB0239 – Table 1. Cross-sectional correlations between "Molecular Disease Activity" tool composed of 8 biomarkers and clinical and ultrasound parameters of disease activity

Parameters	Molecular disease activity (factor score)	p (significance)
DAS28-ESR	0.664**	<0.001
DAS28-CRP	0.666**	<0.001
SDAI	0.731**	<0.001
CDAI	0.669**	<0.001
SJC	0.546**	<0.001
GS syn score	0.657**	<0.001
PD syn score	0.701**	<0.001

\*\* Correlation is significant at ≤0.01

CDAI, Clinical Disease Activity Index; DAS28-CRP, Disease Activity Score with C-reactive protein; DAS28-ESR, Disease Activity Score with erythrocyte sedimentation rate; GS syn, Grey Scale synovitis; PD syn, Power Doppler synovitis; SDAI, Simplified Disease Activity Index; SJC, swollen joint count

**Conclusions:** We believe that this newly designed test based on 8 serum markers may contribute to more accurate measurement of inflammatory activity in



RA and improvement of patients' outcomes. Further evaluation of this tool in a larger cohort is needed.

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#### AB0240 REDUCTION IN FATIGUE AND PAIN ARE ASSOCIATED WITH IMPROVED WORK PRODUCTIVITY IN PATIENTS WITH RA

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**Background:** Despite current treatment options, patients with rheumatoid arthritis (RA) report fatigue and pain, important determinants of quality of life.<sup>1</sup> In prior analyses of a Phase 3 trial of baricitinib (RA-BEAM), baricitinib demonstrated superiority in pain and fatigue reduction over MTX and adalimumab<sup>2</sup> and this pain reduction was associated with improvement in work productivity.<sup>3</sup>

**Objectives:** In this *post hoc* analysis of RA-BEAM, the relationship between fatigue and pain with work productivity was assessed.

**Methods:** Fatigue was measured with the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F, range of 0–52, higher scores represent less fatigue) and pain with the patient's assessment of pain (0–100 mm VAS, higher scores represent greater pain). The Work Productivity and Activity Impairment Questionnaire-RA (WPAI-RA) instrument evaluated the percentages of activity impairment due to RA (impairment in regular daily activities), work-time missed due to RA (absenteeism), impairment while working due to RA (presenteeism), and overall work impairment due to RA (work productivity loss). Analyses were based on pooled data from randomised patients who received  $\geq 1$  dose of study drug. Analyses for impairment in regular daily activities included all patients and for absenteeism, presenteeism, and work productivity loss, patients employed both at baseline and at Weeks 12 or 24 were included. Pain was divided into pain reduction groups (<30%, 30%–<50%,  $\geq 50\%$ ) and actual pain score ( $\leq 10$  mm, >10–<20,  $\geq 20$ –<40,  $\geq 40$  mm); fatigue was divided into fatigue improvement groups (<3.56,  $\geq 3.56$ ) and actual FACIT-F normative value score (<40,  $\geq 40$ ). Pairwise comparisons on improvement in WPAI-RA scores between pain/fatigue reduction groups at Weeks 12 and 24 were assessed by ANCOVA.

**Results:** At baseline across treatment groups, patients reported impairment in all of the WPAI-RA domain scores (absenteeism: 12%–13%, presenteeism: 42%–46%, work productivity loss: 45%–49%, activity impairment: 56%–58%). Reductions in pain and fatigue were associated with improvements in regular daily activities, presenteeism, and work productivity (table 1). Patients who reported lower levels of pain and fatigue tended to experience greater improvement in presenteeism, work productivity, and regular daily activities compared to patients with higher levels of pain or fatigue (table 1). When patients reached a minimal pain level (pain VAS  $\leq 10$  mm), no significant differences were observed in presenteeism and work productivity between patients with different levels of fatigue whereas regular daily activity continued to improve as fatigue improved ( $p \leq 0.001$ ; table 1). No trends were observed with absenteeism. Similar results were observed by treatment group.

**Abstract AB0240 – Table 1.** Improvement in WPAI Domain Scores at Weeks 12 and 24

	Regular Daily Activities		Absenteeism		Presenteeism		Work Productivity	
	FACIT-F <40	FACIT-F $\geq 40$	FACIT-F <40	FACIT-F $\geq 40$	FACIT-F <40	FACIT-F $\geq 40$	FACIT-F <40	FACIT-F $\geq 40$
<b>Pain VAS <math>\leq 10</math> mm</b>								
Week 12	33.8	33.0**	4.1	2.4	32.6	26.1	29.5	26.9
Week 24	38.8	38.5**	4.2	3.1	34.2	28.6	39.5	27.5
<b>16&lt; Pain VAS <math>\leq 20</math> mm</b>								
Week 12	24.8	26.2**	3.2	3.8	13.5	18.1*	19.8	26.8*
Week 24	27.7	29.8**	3.5	4.8	9.5	22.0*	8.7	29.5**
<b>20&lt; Pain VAS <math>\leq 40</math> mm</b>								
Week 12	20.1	22.4**	2.9	1.5*	3.3	11.3*	7.6	11.9*
Week 24	20.2	20.3**	1.2	0.3*	11.5	13.8*	6.1	18.3**
<b>Pain VAS <math>\geq 40</math> mm</b>								
Week 12	7.4	9.2**	2.1	4.6*	0.7	10.3*	1.6	12.1**
Week 24	5.4	11.0**	3.2	3.2*	3.4	7.5**	0.1	7.8**

\* $p < 0.05$ , \*\* $p < 0.001$  for comparisons between FACIT-F groups within each pain group.

**Conclusions:** Reductions in pain and fatigue were associated with improved regular daily activity, presenteeism, and work productivity in RA, with larger reductions related to more improvement. When patients achieved minimal levels of

pain, similar improvements in presenteeism and work productivity were observed regardless of fatigue level.

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#### AB0241 WHAT PROPORTION OF RA PATIENTS ARE TRULY IN REMISSION? A SURVEY OF RHEUMATOLOGISTS OF THE AUVERGNE REGION OF FRANCE

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**Background:** The treatment of rheumatoid arthritis (RA) is aimed to achieve remission.

**Objectives:** To determine the proportion of RA patients in remission among the population treated by rheumatologists in Auvergne, France.

**Methods:** A 3 month survey involving 24 rheumatologists, not practicing at university hospitals, from the Auvergne region of France. The rheumatologists completed records on each RA patient detailing the parameters of RA activity (tender joint count, swollen joint count, pain VAS, patient's assessed activity VAS, physician's assessed activity VAS, ESR and CRP), as well as the RA treatment administered, and if this treatment was modified.

**Results:** Overall, 15 rheumatologists provided 455 records. These comprised 330 women (74%) and 125 men, aged on average 64.8 years old  $\pm 12.6$ . The patients had suffered from RA for 7 years on average, <sup>4-14</sup> 77.3% were positive for rheumatoid factor, and 76.2% for anti-CCP. They underwent the following treatments: NSAIDs (19%), corticoids (24.4%; 5 mg<sup>4-6</sup>), methotrexate (80.4%; 15 mg.<sup>10-15</sup> leflunomide (4.4%), hydroxychloroquine (11%), sulfasalazine (2.4%), anti-TNF (21.9%), other biotherapy (8.8%), no DMARD (3.1%),  $\geq 2$  DMARDs (31.8%). The proportion of patients in remission varied depending on different definitions as follows: DAS28-ESR  $\leq 2.6$ : 61.5% (low activity: 79%); DAS28-CRP  $\leq 2.4$ : 59.5%, DAS 28-CRP  $\leq 2.1$ : 47.2%; SDAI  $\leq 3.3$ : 40.1% (low activity: 80%); CDAI  $\leq 2.8$ : 36.0% (low activity: 81.5%); ACR/EULAR: 31.8%; simplified ACR/EULAR: 39.1%; physician-assessed remission (VAS  $\leq 1$ ): 52.3%; patient-assessed remission (VAS  $\leq 1$ ): 47.3%. There was moderate to good correlation between the ACR/EULAR and SDAI criteria ( $\kappa = 0.70$ ) and CDAI criteria ( $\kappa = 0.72$ ), while there was weak correlation between ACR/EULAR and DAS 28-ESR ( $\kappa = 0.45$ ). The physicians' and patients' assessments did not correlate well with the remission criteria. Compared to those who were not in remission, the patients assessed as being in remission according to DAS28-ESR and ACR/EULAR criteria were younger, had been treated with less corticoids, had more frequently received anti-TNF, and had less frequently had their treatment modified.

**Conclusions:** Our findings were reassuring, with 32% (ACR/EULAR) to 62% (DAS) of RA patients followed up by rheumatologists outside of university hospitals assessed as being in remission, and 80% presenting with low disease activity. A total of 97% received DMARD, 30% received biotherapy, and a quarter corticoids. We found moderate to good correlation between ACR/EULAR and SDAI and CDAI; whereas there was low correlation between ACR/EULAR and DAS 28-ESR. The physicians' and patients' assessments did not correlate well with the remission criteria.

**Disclosure of Interest:** None declared

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**AB0242 DELAY IN DMARD INITIATION IN PATIENTS NEWLY DIAGNOSED WITH RHEUMATOID ARTHRITIS: AN ANALYSIS OF UNITED STATES MILITARY HEALTH SYSTEM BENEFICIARIES**

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**Background:** Prompt initiation of disease-modifying antirheumatic drugs (DMARDs) is recommended for patients diagnosed with rheumatoid arthritis (RA) to improve symptoms and prevent disease progression, but treatment delays may still occur.

**Objectives:** To investigate predictors and temporal trends for delay in DMARD initiation among patients with incident RA in the United States.

**Methods:** We performed a longitudinal cohort study using administrative data from the United States military's TRICARE program (2007–2012). TRICARE beneficiaries, who are demographically similar to the US, include active/retired military members, spouses, and dependents and receive care in military or civilian settings. We identified incident RA cases using billing codes and initial DMARD receipt using prescription fill date. We quantified the time between RA presentation and initial DMARD receipt, temporal changes in time to treatment over the study period, and investigated predictors of treatment delay (>90 days) using logistic regression.

**Results:** We identified 16 680 patients with incident RA that were later prescribed DMARDs. Mean age was 47.2 (SD 13.5) years, 77.6% were female, and 76.5% were spouses/dependents of the military sponsor. The mean time from initial RA presentation to first DMARD prescription was 125.3 days (SD 175.4). Over one-third (35.6%) of incident RA patients experienced treatment delay (>90 days between presentation and DMARD receipt). Time to DMARD initiation was shorter in later years of the study (mean 144.7 days in 2007; 109.7 days in 2012). Patients prescribed opioids between RA presentation and initial DMARD receipt had 4-fold increased risk for delay in initial DMARD (OR 4.07, 95% CI 3.78–4.37). Patients prescribed opioids had mean time to DMARD of 212.8 days (SD 207.4) compared to mean of 77.3 days (SD 132.3) for those who did not use opioids (p<0.0001). Use of prescription NSAIDs between initial RA presentation and DMARD initiation was also associated with delay (OR 3.32, 95% CI 3.09–3.57). Men were less likely than women to experience delay (OR 0.89, 95% CI 0.82–0.98).

**Abstract AB0242 – Table 1.** Odds ratios for delay in DMARD initiation (>90 days) after initial presentation for incident rheumatoid arthritis (n=16,680)

	Unadjusted OR (95% CI)	Multivariable* OR (95% CI)
<b>Sex</b>		
Female	1.00 (Ref)	1.00 (Ref)
Male	<b>0.81 (0.75–0.87)</b>	<b>0.89 (0.82–0.98)</b>
<b>Year of index date</b>		
2007	1.00 (Ref)	1.00 (Ref)
2008	<b>1.29 (1.16–1.44)</b>	<b>1.28 (1.13–1.44)</b>
2009	0.91 (0.81–1.01)	0.90 (0.80–1.02)
2010	<b>0.81 (0.73–0.91)</b>	<b>0.84 (0.74–0.95)</b>
2011	<b>0.77 (0.69–0.86)</b>	<b>0.78 (0.69–0.88)</b>
2012	<b>0.79 (0.71–0.88)</b>	<b>0.78 (0.69–0.89)</b>
<b>NSAID use between index date and DMARD initiation</b>		
No	1.00 (Ref)	1.00 (Ref)
Yes	<b>4.02 (3.76–4.30)</b>	<b>3.32 (3.09–3.57)</b>
<b>Opioid use between index date and DMARD initiation</b>		
No	1.00 (Ref)	1.00 (Ref)
Yes	<b>4.74 (4.42–5.07)</b>	<b>4.07 (3.78–4.37)</b>

\*The multivariable model was also adjusted for age, US region, care setting (military or civilian), military rank of sponsor, number of clinic visits prior to index date, and Charlson Comorbidity Index.

**Conclusions:** In this large US nationwide study, delays in initial DMARD receipt after incident RA were common but time to treatment improved in later years of the study. Avoiding opioid use may decrease delay in initiating DMARDs during this vulnerable period when pain and disease activity are often most pronounced.

**Disclosure of Interest:** None declared

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**AB0243 REAL WORLD CLINICAL TRIAL COMPARING THE PATIENT REPORTED OUTCOMES MEASUREMENT INFORMATION SYSTEM SHORT FORMS AND PROFILES TO CDAI DISEASE CLASSIFICATION IN RHEUMATOID ARTHRITIS PATIENTS**

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**Background:** Pt reported outcomes (PROs) play a role in disease evaluation, therapeutic assessment and care of RA pts. The Pt Reported Outcomes Measurement Information System (PROMIS [P]) questionnaires developed by NIH have been used in RA clinical practice and studies.<sup>Bartlett 2015</sup> AWARE (Comparative and Pragmatic Study of Golimumab Intravenous [IV] Versus Infliximab in RA) is a noninterventional, multi-centre US-based, study of golimumab IV (GLM) vs. infliximab (IFX) in RA and will assess disease activity (DA) and use PROs.

**Objectives:** 1. PRO assessments of Pt response to treatment using PROMIS-29 Profile v2.0 (P29v2), P Pain Interference Short Form-6b (PISF) and P Fatigue Short Form-7a (FSF), and Clinical DA Index (CDAI), and 2. assess relationship between PROMIS T-score and CDAI category.

**Methods:** AWARE is a 1200 adult pt study enrolling pts on initiation of treatment w/GLM or IFX. We report an interim analysis (IA) of 747 pts' baseline PROMIS questionnaire and CDAI scores. PROMIS results are normalised to the US population, reported as a "T-score" (mean=50, SD=10) w/higher scores indicating more of the trait measured. PROMIS T-scores were compared between High DA (HDA) w/Moderate DA (MDA), low DA (LDA) and remission. Data shown are mean ±SD. Statistical testing compared T-scores across CDAI categories using ANOVA for these data (before drug admin). Data from GLM and IFX pts are combined.

**Results:** Mean baseline CDAI score was 32.5±15.4, w/71.7% of pts in HDA, 22.5% in moderate MDA, 5.2% in LDA and 0.7% in remission. PROMIS T-scores were compared to 4 CDAI categories. HDA Pt T-scores were (\*, p<0.05) different from those of MDA, LDA and Remission pts (except between HDA and remission for Anxiety, Depression and Sleep Disturbance domains).

**Abstract AB0243 – Table 1**

	All Patients (n=672-682)	Remission CDAI≤2 (n=5)	LDA 2.8<CDAI≤10 (n=38)	MDA 10<CDAI≤22 (n=165)	HDA CDAI>22 (n=526)
Physical Function	37.9±6.6	47.5±5.7	45.0±7.6	40.0±6.7	36.6±5.9*
Anxiety	53.8±10.4	45.2±6.7*	47.7±8.6	51.3±10.0	55.2±10.4*
Depression	52.5±10.3	42.6±3.6*	45.9±6.3	49.4±9.8	54.0±10.3*
Fatigue	58.8±9.9	42.3±5.4*	49.7±9.7	55.6±9.2	60.8±9.4*
Sleep Disturbance	55.5±8.7	48.2±3.6*	51.5±7.9	51.2±8.4	56.7±8.6*
Ability to participate in Social Roles & Activities	48.2±8.6	57.3±7.6	50.8±8.5	45.9±8.5	41.6±8.0*
Pain interference	63.5±7.7	46.9±7.2*	53.9±8.4	60.1±7.7	65.4±6.5*
Fatigue Short Form 7a	59.3±8.5	46.7±8.8*	51.6±9.0	56.2±7.5	61.0±8.1*
Pain Interference Short Form 6b	62.5±7.6	45.9±7.5*	53.9±9.3	59.3±5.6	64.3±6.4*
Pain intensity (scored 0-10 scale)	6.0±2.2	1.6±2.6	3.5±2.3	5.1±2.2	6.6±1.9*

T-scores >50 indicate worsening, except "Physical Function" & "Ability to participate in Social Roles & Activities", where T-scores <50 indicate worsening. \* = p<0.05 vs respective scores in MDA, LDA & remission categories. † = not different from HDA.

**Conclusions:** Our interim findings demonstrate the feasibility of using PROMIS short forms and profiles to evaluate RA Pts in clinical trials. These results confirm the domain validity of PROMIS measures according to CDAI DA category. PROMIS measures show the range of impact across multiple domains of physical, emotional, and social health experienced by RA Pts.

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AB0244

### DEVELOPMENT OF AN ADJUSTED MULTI-BIOMARKER DISEASE ACTIVITY (MBDA) SCORE FOR RHEUMATOID ARTHRITIS (RA) THAT ACCOUNTS FOR AGE, SEX AND ADIPOSITY, WITH SUBSEQUENT EVALUATION OF ABILITY TO PREDICT RISK FOR RADIOGRAPHIC DAMAGE

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**Background:** The MBDA score, based on 12 serum proteins, is a validated tool for assessing disease activity in RA patients. MBDA biomarkers may be influenced by age, sex and adiposity.

**Objectives:** To develop and validate an adjusted MBDA score that accounted for these three factors, using BMI or serum leptin as proxies for adiposity.

**Methods:** The MBDA score as a continuous variable was adjusted to account for age, sex and a proxy for adiposity (serum leptin) using data from 325,781 RA patients for whom MBDA tests had been ordered as part of routine care. Leptin values came from the MBDA test. As an alternative to using leptin to adjust for adiposity, a cohort of 1411 patients from 5 studies/registries (BRASS, Corrona-CERTAIN, InFoRM, OPERA, RACER) was used to adjust for BMI, which was not available in the larger cohort, adding this BMI adjustment to that for age/sex from the larger cohort. Both types of adjusted MBDA score use the low, moderate, and high disease activity cutpoints of the original MBDA score. The two adjusted MBDA scores and other variables were evaluated for the prediction of radiographic progression (RP) in the 2 cohorts with available data (OPERA, BRASS) using univariate and multivariate linear regression analyses. Rate of RP was assessed as the change in modified total Sharp score ( $\Delta$ mTSS) per year after MBDA testing.

**Results:** The MBDA score increased with age, BMI and leptin concentration. In univariate analysis of the combined OPERA and BRASS cohorts (n=555), the significant variables predicting  $\Delta$ mTSS were leptin-adjusted MBDA score, seropositivity for RF or anti-CCP, BMI-adjusted MBDA score, MBDA score, BMI, CRP, baseline mTSS, disease duration, DAS28-CRP, SDAI, CDAI and DAS28\* (table 1). The leptin- and BMI-adjusted MBDA scores were the first and third most significant univariate predictors of  $\Delta$ mTSS. To compare them directly, DAS28-CRP, MBDA score, BMI-adjusted MBDA score and leptin-adjusted MBDA score were combined in pairs in regression analyses of  $\Delta$ mTSS; the BMI-adjusted (p=0.0027) and leptin-adjusted MBDA score were significant (p=0.00063) after adjusting for DAS28-CRP (p=0.87 and 0.74, respectively) and the leptin-adjusted MBDA score was significant (p=0.024 and 0.020, respectively) after adjusting for either the MBDA (p=0.32) or BMI-adjusted MBDA scores (p=0.094).

**Abstract AB0244 – Table 1.** Univariate Linear Regression Analysis of the Association of Clinical and Laboratory Variables with  $\Delta$ mTSS in the OPERA and BRASS Combined Cohort

Variable	n	F-statistic	p-value
Leptin-adjusted MBDA Score	555	17.1	0.000040
RF or Anti-CCP Status	555	14.8	0.00013
BMI-adjusted MBDA Score	555	14.4	0.00016
MBDA Score	555	12.9	0.00036
BMI	555	10.9	0.001
log <sub>e</sub> (CRP)	555	6.8	0.0093
Baseline mTSS	555	5.3	0.022
log <sub>e</sub> (Disease duration + 1)	401	4.8	0.030
DAS28-CRP	536	4.6	0.032
SDAI	533	4.3	0.040
CDAI	533	3.9	0.049
DAS28*	536	3.1	0.079
Gender	555	1.5	0.23
Smoking Status	478	0.8 (2 df)	0.46
Age	555	0.1	0.76

DAS28\* = DAS28 with no CRP or ESR component, i.e.,  $0.56(\text{TJC28})^{3/2} + 0.28(\text{SJC28})^{3/2} + 0.014(\text{GH})$ .

**Conclusions:** We developed two adjusted MBDA scores that combine molecular and biometric variables to account for age, sex, and adiposity. The leptin-adjusted MBDA score, significantly outperformed DAS28-CRP and the original MBDA score in predicting radiographic progression in RA patients. These results suggest that the leptin-adjusted MBDA score may offer improved clinical utility for the personalised management of patients with RA.

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AB0245

### PERFORMANCE OF THE EULAR DEFINITION OF ARTHRALGIA SUSPICIOUS FOR PROGRESSION TO RHEUMATOID ARTHRITIS IN COMBINATION WITH MUSCULOSKELETAL ECOGRAPHY WITH DOPPLER (USMD) IN CLINICAL PRACTICE

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**Background:** The treatment at an early stage of rheumatoid arthritis (RA), even in the undifferentiated phase, which can prevent the progression and even the reversal of the inflammatory process<sup>1</sup>. Identification in the preclinical phase is complicated. The detection of joint inflammatory activity through the use of UsMD would be useful for diagnosis in arthralgia suspicious for progression to RA (CSA)<sup>2</sup>.

**Objectives:** To assess the usefulness of the EULAR definition of CSA in clinical practice.

To Describe the clinical, serological and ultrasound characteristics and the CSA evolution over time (0, 3, 6 months).

To determine the clinical and ultrasound characteristics that could influence in the RA progression.

**Methods:** A longitudinal prospective study that includes 27 patients referred from primary care (PC) or Rheumatology consultations with CSA according to EULAR criteria of more than 8 weeks and less than 6 months of evolution. All patients were evaluated at 0–3–6 months, including at each visit: serological parameters (RF, ACPA, ESR, CRP), measures of functionality (HAQ) and activity (DAS28); and image (Xray and UsMD). The ultrasound examination included: carpus (palmar and dorsal planes), MCFs 2°–5°, extensor cubital tendons, ankles, posterior tibialis, 5° MTFs and painful IFPs in a comparative and bilateral model. The Us scans were performed by the same researcher without access to the clinical data of the patients, collected by another independent researcher. Proportions were compared using the chi-square test to see which factors were related to RA development.

**Results:** 27 patients with CSA criteria according to EULAR definition have included. 59.3% were derived from PC, 92.6% were women with a mean age of 48.5 years (DS 11.95) and active labour 77.8%. Ten patients (37%) were smokers and dyslipidemics with an atherogenic index of 3.19 (DS1.04). 60.95% presented slight overweight with a BMI of 27.65 Kg/m<sup>2</sup> (DS 5.7). The most frequent form of presentation was polyarticular 12 (50%) followed by oligoarticular. 57.7% of the cases had symmetric involvement and 81.5% a duration of symptoms between 6–16 weeks. 52% patients presented RF + and 4 ACPA and ANA+. During the follow-up: 8 patients (29.6%) were classified as RA (ACR<sup>1</sup>,<sup>EULAR 2010</sup> all of them derived from Rheumatology, 3 (11.1%) microcrystalline arthritis, 1 Sjogren primary syndrome and 15 (55.5%) presented degenerative or tendinosis pathology.



In those patients who progressed to RA, we only found a statistical association with the presence of high RF +and with the presence of doppler at the carpal level ( $p=0.048$ ).

**Conclusions:** The results of our study suggest that the EULAR definition of CSA, although more useful when used by rheumatologists, does not reach sufficient accuracy for the diagnosis of RA, while the presence of subclinical synovitis detected by UsMD could be useful. The highest levels of RF were related to the presence of synovitis in our cohort, unlike ACPA. Further studies would be needed to recommend its introduction into clinical practice and, in our opinion should be considered in future sets of classification criteria.

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**Disclosure of Interest:** None declared

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#### AB0246 GENETIC VARIABILITY WITH TOLL-LIKE RECEPTOR 10 AFFECTS SUSCEPTIBILITY TO RHEUMATOID ARTHRITIS AND MODULATES RESPONSE TO BIOLOGICAL TREATMENT

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**Background:** Genetic variability in Toll-like receptor 10 (TLR10) may change the balance between pro- and anti-inflammatory responses, and hence modulate the susceptibility to infection and to autoimmune disease including rheumatoid arthritis (RA).

**Objectives:** Therefore we aimed to assess the possible associations of the TLR10 genetic variants with RA susceptibility and/or response to treatment

**Methods :** *TLR10* gene (rs 11096957, N241H, A>C) polymorphism was genotyped by LightSNIP assay in 303 RA patients (237F/66M) and in 140 healthy individuals from Polish population.

**Results:** RA patients with the AC genotype showed predisposition to disease development [OR 1.99 (1.32–3.01);  $p=0.001$ ], while the AA homozygosity seemed to play a protective role [OR 0.63 (0.42–0.95);  $p=0.034$ ]. Response to treatment with TNF-alpha inhibitors was more effective after 6 months as compared to 3 months ( $p=0.001$ ), especially in female patients ( $p=0.05$ ). Women carrying the A allele responded better to treatment after 6 months of anti-TNF treatment as compared to those with the CC genotype ( $p=0.053$ ). Response to biological treatment was more effective in patients with low stage of disease ( $p=0.01$ ), with rheumatoid factor (RF) positivity ( $p=0.01$ ) and with double positivity against cytrulinated (CCP) protein and RF ( $p=0.003$ ). RF-positive patients (especially women,  $p=0.001$ ) characterised with a higher degree of the disease as compared to RF-negative cases ( $p=0.01$ ). Men had a higher activity of the disease before anti-TNF treatment ( $p=0.05$ ), therefore the remission of the disease was more common in women ( $p=0.04$ ).

**Conclusions:** These results imply that the TLR10 polymorphism has an important role in RA and may potentially influence risk of the disease and effectiveness of biological treatment.

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#### AB0247 LACK OF AGEING WITH LONG TERM METHOTREXATE: OBJECTIVE MEASUREMENTS OF COGNITION, AUDIOMETRY, AND SLEEP

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**Background:** Methotrexate (MTX) has long been known to improve the cardiovascular system. Myocardial infarction, strokes, and mortality are significantly reduced in patients compliant with long term MTX.<sup>(1)</sup> Hearing loss at middle age is an independent major risk factor for dementia,<sup>(2)</sup> and sleep over 8 hours is associated with better health. MTX use may affect all of these risk factors.

**Objectives:** Our hypothesis is that the cardiovascular benefits of long term MTX treatment would translate into improved cognition, improved hearing, and better sleep patterns.

**Methods:** Cambridge Cognition (CamCog based in Cambridge) developed cognitive objective testing to study brain function. Camcog is widely used to assess cognitive function in atherosclerotic disease, dementia and ageing. The CamCog tests are computer based. Programs used in this trial included "PAL", paired associates learning for new learning memory and "SWM", spatial working memory along with new strategic thinking during the test. These tests provide 22 assessments per patient. In separate testing, each patient was scored on the mini-mental state examination, including serial 7's, WORLD spelled backward, memory retention of 3 items, and drawn forms such as clock faces.<sup>(2)</sup> Sleep patterns were assessed by questionnaire.

**Results:** There were 88 patients with RA between the ages of 80–101 years who had been treated with MTX a minimum of 20 years. The average PALFAM score for the group was 16.3 (sd 2.7) with a maximum score of 20. The SWMBE score for errors for the group was 2.2 (sd 4.4) with the best score 0 errors. In all 22 scoring categories of the CamCog tests, the 88 long term MTX users scored in the top quintile, and better than average for published results for healthy people at age 65. All scores were statistically significant ( $p<0.01$ ) compared to healthy 65 year olds. It was not possible to compare age, sex matched normal individuals because the normative CamCog database only extends to age 90. All 88 subjects scored above 24 on the mini-mental testing (reflecting no cognitive impairment on that test). The audiometry testing was much better than expected for age, in the top tertile. Of the 88 patients on long term MTX, 3 had hearing aides. Sleep duration averaged 8.5 hours/pm which is considered excellent for maintaining cognition.<sup>(3)</sup>

**Conclusions:** This is a subset of people with cardiovascular risk due to age and RA. The CV risk assessment tool\* for our subgroup predicted 10 year risk for MI or CVA at 54%. We did not see MI or CVA over 20 years, despite RA. Expanding on that physiology, we found 88 RA patients on long term MTX had above average cognitive testing, completed mini-mental test, drawings, audiometry close to the scores expected for people 3 decades younger. One reason these preliminary results cannot be generalised to other populations is that only RA patients were studied with long term MTX. Also our group were 80–101 years old and there may be a survival advantage in this subgroup since all were healthy at age 65. A study in a larger general population given MTX for several years would be needed to evaluate the benefit in cognition, hearing, and sleep.

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\* ASCVD algorithm in the ACC/AHA Guidelines on the Cardiovascular Risk

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#### AB0248 EVALUATION OF SUBCUTANEOUSLY (SC) INJECTED Tc 99m TILMANOCEPT LOCALIZATION IN ACTIVE RHEUMATOID ARTHRITIS (RA) SUBJECTS BY PLANAR AND SPECT/CT

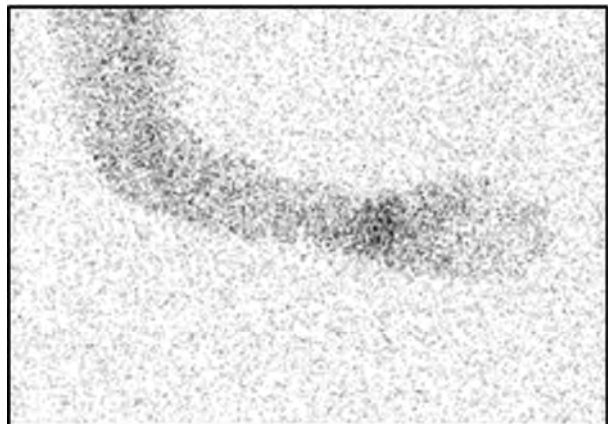
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**Background:** In rheumatoid arthritis (RA), infiltrating macrophages play a critical role in the immunopathogenesis of the disease by generating pro-inflammatory cytokines and chemokines and by contributing directly to joint damage. Current imaging modalities do not directly assess activated macrophage-mediated disease processes in RA. Use of non-invasive imaging to detect macrophage infiltration of synovial joints may allow for more sensitive identification of synovitis and earlier recognition of RA, identify joints at risk for progressive inflammation and destruction, provide a better means of quantifying joint inflammation and disease activity, and measure or even predict response to macrophage-directed therapy. Tc 99 m tilmanocept is a synthetic radiopharmaceutical imaging agent that binds with high affinity to the mannose receptor (CD206) located on the cell surface of synovial macrophages. We investigated whether subcutaneous (SC) administration of tilmanocept labelled with Tc 99 m could specially image macrophage mediated inflammation in RA but not in healthy control (HC) subjects.

**Objectives:** To investigate whether subcutaneous (SC) administration of tilmanocept labelled with Tc 99 m could specially image macrophage mediated inflammation in RA but not in healthy control (HC) subjects.

**Methods:** Subjects received a SC injection of either 50 µg or 200 µg tilmanocept radiolabeled with 2mCi Tc99m in 0.4 mL. 18 subjects were enrolled as follows – Cohort 1: HC: 50 µg/2mCi; n=5; Cohort 2: HC: 200 µg/2mCi; n=4; Cohort 3: RA 50 µg/2mCi; n=4; Cohort 4: RA 200 µg/2mCi; n=5. Subjects were imaged with whole body planar scans at 2–3 hours and 4–6 hours post injection as well as separate 5 min planar images of both hands. If there were areas of increased localization, SPECT images were obtained.

**Results:** Tc 99 m tilmanocept localised most effectively at the 200 µg mass dose 2–3 hours post- administration in RA subjects (cohort 4). Localization was observed in 60% of the subjects in joints of the bilateral wrists, hands, and knees. No localization was observed in HCs receiving the same mass dose (cohort 2).



**Abstract AB0248 – Figure 1.** Contrast of wrist and elbow of SC RA subject

**Conclusions:** Our findings represent a potential advance in the imaging of RA using a novel immunodiagnostic imaging strategy to specifically visualise macrophage-mediated elements of the RA disease process. This study demonstrates the potential for Tc 99 m tilmanocept to be used as an imaging tool for macrophage-mediated synovial inflammation in RA patients. This strategy can be used to identify patients at risk for activated macrophage-mediated joint damage, to quantify synovitis and disease activity, to provide further insight into immune-mediated mechanisms of RA, and to enable future targeted delivery of immunomodulatory therapeutics.

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Russell Engleman Rheumatology Research Centre, University of California San Francisco

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#### AB0249 INFLUENCE OF AUTOANTIBODIES PROFILE ON DISEASE ACTIVITY MEASUREMENT IN A COLOMBIAN COHORT OF RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Traditionally, the role of Rheumatoid Factor (RF) and/or Anti-citrullinated antibodies (ACCP) presence have characterised for diagnosis and prognosis of Rheumatoid Arthritis (RA). However, Anti-nuclear antibodies (ANA) are not routinely measured for the diagnosis of the disease or RA prognosis establishment during first appointment. Recently, evidence showed that positive ANA titles could be considered as poor prognosis factor for RA, and also a higher probability of developing immunogenicity against biologic therapies.

**Abstract AB0249 – Table 1.** Auto-antibodies profile, disease activity by DAS-28 ESR (initial and follow-up to 3, 12, 24 and 36 months) and mean weekly MTX dose in a Colombian cohort of RA patients

PROFILE (FR/ACCP/ANA)	DAS-28 (INITIAL)	DAS-28 (3 MONTHS)	N	DAS-28 (12 MONTHS)	N	DAS-28 (24 MONTHS)	N	DAS-28 (36 MONTHS)	N	MEAN WEEKLY MTX DOSE (mg)
—	3.317	.3072603	73	0.1267188	64	0.9367073*	41	0.8593334*	30	9.26
+-	3.375	-.2905715	7	-.5806667	6	-.2648572	7	0.17	4	10.82
++	3.434	.263663	92	0.6267033*	91	0.7705405*	74	0.6138596*	57	14.01
+-	3.201	.0314815	27	-.2926087	23	0.1705263	19	0.8038461	13	10.2
+-	4.123	.8346712**	73	1.048**	66	1.23**	51	0.53	38	16.19
++	3.542	.3822857	56	0.5656604*	53	0.71325*	40	0.8733333*	33	14.91
++	4.695	1.57*	12	1.77*	14	3.359	6	2.03	2	15.69
+++	4.118	.6474576*	118	0.9343478**	115	1.196**	86	1.25**	66	15.83

\*p<-0.05 \*\*p<0.001

**Objectives:** To compare the disease activity measurement from a Colombian cohort of patients with RA, based on their auto-antibodies profile.

**Methods:** The study used a cohort of Colombian patients with RA. A database was developed using the information from the clinical records. The data included were: RF, ACCP, ANA, and the disease activity measured using DAS-28 ESR. Disease activity results were obtained in the following periods of time: 0, 3, 12, 24 and 36 months. Patients were classified based on the different autoantibody profiles (RF/ACCP/ANA:—, +-, ++, +-, ++, ++, ++, +++). Mean DAS-28 ESR results from each period of time were calculated. Also mean weekly Methotrexate (MTX) dose was calculated for each profile. Mean differences between initial, and the follow-up period were calculated using Kruskal-Wallis test. Statistical analysis was made using STATA 12.0 software.

**Results:** 635 patients with RA were included. 32% of them were men, and 68% were women. Mean age was 54.3 years. The most prevalent profile was +++with 118 patients, and the less frequent was +-. Patients with +++profile had the best response to treatment over time, but also they required more MTX dose. Less response during time was observed with +- profile, however the amount of patients from these group was relatively low. As it was expected,—profile patients required less weekly MTX dose (9.26 mg). It was interesting that patients with —+profile present a worst outcome based on DAS-28 activity, and less response to the treatment.

**Conclusions:** Results from the study suggest the importance of including the measurement of ANA titles in the initial categorization and follow-up of patients with RA. The presence of ANA seems to have a worst prognosis. ANA co-existence with ACCP appear to have a worst outcome, compared to +- or ++-profile. Auto-antibody profile in RA could direct the best therapeutic strategy for each patient. Validation of these results are required based on other cohorts.

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**Disclosure of Interest:** None declared

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#### AB0250 ENDOTYPING OF ARTHRITIC PATIENTS USING NOVEL SEROLOGICAL BIOMARKERS

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**Background:** Accurate patient stratification is critical if medical professionals are to adopt a precision medicine approach when planning clinical trials or prescribing medication. This approach results in a superior level of drug response in the target group, a reduction in adverse effects and reduced costs for payers.

Best practice treatment recommendations and disease activity markers such as DAS28, as opposed to a treat to target approach, guide current treatment of arthritic disease. There is currently a lack of tools to enable patient stratification, in part due to traditional biomarkers reflecting systemic inflammation rather than the target tissue.

**Objectives:** In this paper, we explore the use of a combination of novel tissue specific biomarkers for patient clustering with the objective of identifying different disease profiles.

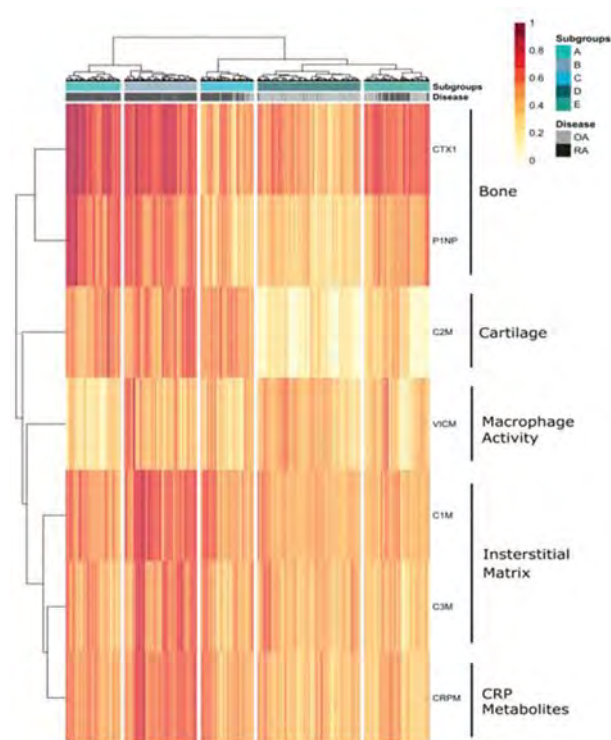
**Methods:** Four biomarker substudy cohorts were pooled for this study, including two RA studies; LITHE (n=574) and OSKIRA-1 (n=131) and two OA studies; SMC1 (n=447) and SMC2 (n=81) all of which have been described in detail before. Whilst the principle focus was to examine RA patient profiles, OA studies were included to enrich the cohort with a non-RA population. OSKIRA and LITHE both had measurements at 24 weeks with additional measurements at 52 week s in LITHE.

Several serological biomarkers were measured in each cohort, selected due to the specific tissue metabolite they represent. These included: C2M (cartilage degradation); CTX-1 and PINP (bone resorption and formation); C1M and C3M (interstitial matrix degradation); CRPM (CRP metabolite) and VICM (macrophage activity).

Each biomarker was log transformed and min-max normalised in order to allow for direct comparison of each of the variables. Patient clustering was performed using Ward hierarchical clustering and the number of clusters determined using the GAP statistic. ANOVA test was used to identify differences in delta change in radiographic scores at 24 and 52 weeks in the RA placebo groups (n=271) only.

**Results:** Clustering analysis resulted in five different clusters (A-E). Cluster A and B were both comprised of >98% RA patients. Cluster D was comprised mainly of OA patients whilst clusters C and E were a mix of OA and RA patients.

Clusters A and B were characterised by high levels of all biomarkers compared to other clusters except for VICM, which is significantly lower in cluster A than in cluster B (Tukey test  $p < 0.001$ ). Biomarker levels in Cluster C were all close to the median. Cluster D was characterised by low levels of all biomarkers compared to other clusters with significantly lower C2M levels, whilst cluster E also had low levels of markers, yet with significantly higher levels of CTX-1 compared to cluster D. When looking at the RA placebo groups there were no difference in change in SHP score at 24 weeks between the groups, (n=271, LITHE, OSKIRA), but a significant difference in SHP change 52 weeks (n=83,  $p < 0.05$ , LITHE).



Abstract AB0250 – Figure 1

**Conclusions:** We have identified putative RA profiles based on novel serological biomarker status. Whether patients in particular clusters may benefit from specific targeted treatments, according to their tissue turnover profile, will be investigated further.

**Disclosure of Interest:** None declared

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#### AB0251 ARE ACPA ASSOCIATED WITH MORE BONE LOSS OVER TIME IN PATIENTS WITH RA?

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**Background:** Anti-citrullinated protein antibodies (ACPA) are one of the most important serological markers for rheumatoid arthritis (RA) and have been suggested to play a pathophysiologic role by directly binding to osteoclasts. However, the effect of ACPA on systemic bone mineral density (BMD) and in particular their effect on changes in BMD over time is currently unknown.

**Objectives:** The aim of this study was to determine whether ACPA associate with changes in BMD over time in patients with RA.

**Methods:** Yearly dual X-ray absorptiometry (DXA) scores were performed during 5 years of follow-up in 412 patients with recent-onset RA participating in the IMPROVED study<sup>1</sup>, a clinical trial in which patients were treated according to a remission- (disease activity score <1.6) steered strategy. The effect of the presence of ACPA on 1) Z-scores of lumbar spine and hip over time, and 2) prevalence of osteopenia/osteoporosis (defined as a T-score  $\leq -1$ ) over time was analysed using generalised estimating equations. Analyses were adjusted for age, gender, BMI, symptom duration, smoking status, disease activity, prednisone intake, usage of bisphosphonates, calcium intake and serum 25-OH vitamin D levels.

**Results:** ACPA-positive patients had a significantly lower lumbar spine ( $p=0.04$ ) and hip ( $p=0.01$ ) Z-score at baseline. There was no difference in prevalence of osteoporosis/osteopenia at baseline between ACPA-positive and ACPA-negative patients (OR (95% CI) 1.02 (0.55 to 1.19)). We hypothesised that ACPA-positive patients would have more BMD loss over time compared to ACPA-negative patients. However, ACPA-positivity did not associate with a stronger decline in Z-score over time at lumbar ( $p=0.43$ ) or femoral sites ( $p=0.67$ ). Additionally, no effect of ACPA-positivity was found on the development of osteoporosis/osteopenia over time ( $p=0.23$ ).

**Conclusions:** ACPA-positive patients have a significantly lower baseline BMD compared to ACPA-negative patients. Surprisingly, ACPA do not associate with a decrease in BMD over time in patients who were treated according to a tight control strategy. These results indicate that ACPA alone do not contribute to bone loss after disease onset in the absence of inflammation/disease activity.

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[1] Wevers-de Boer K, et al. Ann Rheum Dis. 2012 Sep;71(9):1472–7.

**Disclosure of Interest:** None declared

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#### AB0252 LOOSING DAS28-ESR, BUT STAYING IN BOOLEAN REMISSION- IS IT POSSIBLE? DATA FROM THE PROSPECTIVE, RANDOMISED RETRO TRIAL ON RHEUMATOID ARTHRITIS PATIENTS IN STABLE REMISSION

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**Background:** DAS28-ESR is the most widely used instrument to assess remission in rheumatoid arthritis (RA) patients. Nonetheless, substantial residual disease activity can be present in RA patients fulfilling DAS28-ESR remission. Therefore, more stringent criteria for remission have been developed. While it is known that patients can fulfil DAS28-ESR but fail ACR/EULAR Boolean remission criteria, the existence of the reverse is less known.

**Objectives:** To test the possibility to loose DAS28-ESR remission while staying in ACR/EULAR remission in patients with RA

**Methods:** Data were obtained from the prospective randomised RETRO study (EudraCT: 2009–015740–42), which recruits RA patients in stable remission. Remission was assessed by the following instruments every three months: DAS28-ESR, DAS28-CRP, CDAI, SDAI, PAS, and ACR/EULAR criteria. In the group of patients, escaping DAS28-ESR remission, but fulfilling ACR/EULAR Boolean remission, the individual components of DAS28-ESR were analysed that determined their escape from remission.

**Results:** 142 patients analysed, which were all in DAS28-ESR remission at baseline. Of them, 140 (98.59%) were in DAS-CRP-remission, 131 (92.25%) in CDAI-remission, 130 (91.55%) in SDAI-remission, 109 (76.76%) in ACR/EULAR remission and 66 (46.48%) in PAS-remission. We analysed upon the 1 year follow up



those patients losing DAS28-ESR remission over time: 58 patients lost DAS-ESR remission at least once during the 4 follow-up visits. Surprisingly, 24% (3 months), 36% (6 months), 24% (9 months) and 28% (12 months) of the patients still fulfilled the Boolean remission criteria. The only plausible reason for failing DAS28-ESR remission but staying in ACR/EULAR remission is an isolated elevation of the ESR, not accompanied by increased signs and symptoms of disease. Indeed all patients losing DAS28-ESR remission but staying in ACR/EULAR Boolean remission had an elevated ESR equal or higher than 15 mm. However, if DAS28 scores were calculated by C-reactive protein in the same patients, they all fulfilled remission criteria.

**Conclusions:** DAS28-ESR remission can be missed even if a patient fulfils the more stringent ACR/EULAR Boolean remission criteria. The reason for this remarkable constellation is an elevated erythrocyte sedimentation rate without any clinical symptoms. Hence, isolated elevations of erythrocyte sedimentation rate should be seen critical. These data show the limitations of individual instruments to assess remission in RA and show that interpretations of the erythrocyte sedimentation rate need to be done in the clinical context

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AB0253

### RAPID REMISSION DURING THE FIRST YEAR IN EARLY ACTIVE RHEUMATOID ARTHRITIS IS ASSOCIATED WITH BETTER 5 YEARS STRUCTURAL DAMAGE OUTCOMES

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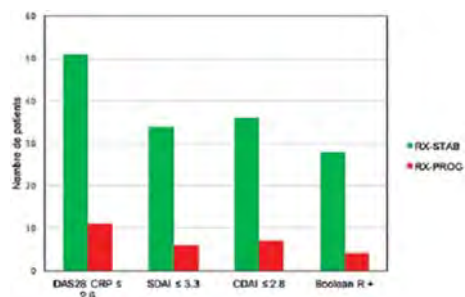
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**Background:** Remission is arguably the best and ultimate therapeutic goal in early rheumatoid arthritis (ERA). ERA patients who reach rapid and sustained remission are likely to retain good radiographic outcomes.

**Objectives:** The aim of this study was to evaluate the radiographic progression and the newly pathological joints in a Belgian ERA cohort during a 5 to 15 years follow-up and to correlate the Sharp score index with different indices of clinical remission observed during the first year.

**Methods:** This was a retrospective analysis of mean (95% CI) change from baseline (BL) to 5 years Sharp/Van der Heijde (SVdH) scoring according to DAS28, SDAI, CDAI and ACR/EULAR Boolean remission scores for patients at Month 3, 6 and 12. Newly pathological joint defined by a SVdH score of 0 at baseline and a score greater than or equal to 1 at follow up were analysed as a secondary objective. 133 ERA patients naïve to DMARDs therapies were analysed (100 women and 33 men) with a mean age  $\pm$ SD (49.9 $\pm$ 13.3), mean DAS 28-CRP (4.89 $\pm$ 1.3), mean HAQ (1.25 $\pm$ 0.67), mean SDAI (28.4 $\pm$ 15.5), mean CDAI (25.8 $\pm$ 14.8) and mean SVdH (6 $\pm$ 14). Differences were statistically tested using t tests.

**Results:** ERA patients were divided in 2 groups: "Xrays Stable" if the delta of SVdH score was <10 (n=90) or "Xrays Progressive" if the delta of SVdH score was >10 (n=43). As expected, presence of ACPA and baseline erosion were significantly higher in the Xrays progressive group. No significant baseline characteristics differences were observed for DAS28-CRP, CDAI, SDAI, HAQ, smoking status, swollen joint count or CRP.% of patients reaching DAS 28CRP, SDAI, CDAI and Boolean remission rates observed at 6 months were statistically significant different between groups (fig). There was no significant difference in clinical responses between subgroups of patients who developed new pathological joints and those who did not.



Abstract AB0253 – Figure 1

**Conclusions:** These results demonstrate that remission is an important therapeutic goal to protect joint damage in ERA. All remission criteria were able to predict the radiological prevention. The identification of a new pathologic joint is not associated with lack of response.

**Disclosure of Interest:** None declared

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AB0254

### THE IMPACT OF THE PATIENT GLOBAL ASSESSMENT VARIATION ON THE DAS 28 VALUE

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**Background:** Rheumatoid arthritis (RA) is the most frequent chronic inflammatory rheumatism. The DAS 28 is a disease activity measure method used to assess RA activity. It is a composite score taking into account 4 items: the number of swollen joints/28, the number of tender joints/28, the erythrocyte sedimentation rate (ESR) or C reactive protein (CRP) rate, the patient global assessment (PGA) indicated on a 0–10 cm visual analogue scale (VAS) with 'not active at all' and 'extremely active' as anchors. The DAS28 determination is very important since it guides the therapeutic decision.

**Objectives:** The aim of this study was to determine the different ways of asking about the PGA and to assess the impact of its value variation on the calculation of the DAS 28.

**Methods:** In order to determine how to evaluate the GPA, a questionnaire including 4 propositions was asked to a cohort of Tunisian rheumatologists:

1. how do you assess your health status this past week?
2. what is the degree of the disease impact in your life this last week?
3. what is the degree of the disease activity this last week?
4. other

Then, a DAS 28 calculation was proceeded according to the different choices of GPA question method for 10 Tunisian patients.

**Results:** The questionnaire was proposed to 37 rheumatologists, 15 working in the private sector and 22 in the public sector. These latter were 9 assistants, 3 professors, 5 specialist doctors and 5 associate professors. The first, second, third and fourth propositions were respectively chosen by 2, 14, 19 and 2 physicians. Subsequently DAS 28 was calculated. In the table 1 below, the variation of the DAS 28 value according to the choice of the PGA method is shown:

Abstract AB0254 – Table 1

Patient	DAS 28 (PGA1)	DAS 28 (PGA2)	DAS 28 (PGA3)	DeltaDAS 28(DAS28 max-min)
1	2.95	2.95	2.81	0.14
2	2.53	2.67	2.67	0.14
3	2.1	1.96	1.96	0.14
4	5.82	5.82	5.54	0.28
5	5.30	5.30	5.16	0.14
6	2.87	2.87	2.87	0.00
7	8.22	8.22	8.22	0.00
8	4.97	5.11	5.11	0.14
9	7.49	7.35	7.63	0.14
10	2.03	2.17	1.89	0.28

**Conclusions:** The GPA question is a subjective item taken into account for the calculation of the DAS 28. Despite the different ways of asking about it, our study showed that this factor have no real impact on the DAS28 value variation since it doesn't exceed 0.6. DAS28 remains a reliable tool in the clinical practice.

**Disclosure of Interest:** None declared

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AB0255

### DOES MENOPAUSE AFFECT DISEASE ACTIVITY OF RHEUMATOID ARTHRITIS(RA)? AN ANALYSIS FROM THE NINJA COHORT IN 2016

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**Background:** Early menopause may be a risk of developing RA<sup>1</sup>. Although there are many reports about menopause and the onset of RA, it is not yet clear how the disease activity of RA differs for each generation including menopause.

**Objectives:** To clarify how disease activity differs for each generation, especially in menopausal period.

**Methods:** Using the Japanese large RA cohort database (NinJa:National database of Rheumatic Diseases in Japan) of 2016, we divided 12257 RA females into three groups of age (under 44 years old=1, 45 to 55 years old=2, defined as a menopausal group, over 56 years old=3) and analysed them cross-sectionally. We conducted a one-way ANOVA on disease activity indexes such as Tender joint count (TJC), Swollen joint count (SJC), DAS28, HAQ-DI.

**Results:** Table 1 shows the number of people per group, the duration of disease, the titer of RF/ACPA, and the proportion of drugs used. The average usage of prednisone and the use of biologics was the most common in group 1. In table 2, TJC was the largest in group 2 ( $p<0.01$ ). Furthermore, the difference between groups seen in TJC tends to be larger than TJC 28. There was no significant difference in SJC (SJC28) between three groups. Other disease activity indicators (ESR, CRP, DAS 28, HAQ-DI) were the largest in group 3 ( $p<0.01$ ) and the percentage of Boolean remission was also lowest in group 3 ( $p=0.02$ ).

**Abstract AB0255 – Table 1.** Characteristics of the three age groups

group	1	2	3	P-value
Number of patients	1071	1699	9487	
Symptom duration, years	8.2	10.5	15.4	$p<0.01$
RF titer, (IU/mL)	186	233	254	$p=0.06$
ACPA titer, (U/mL)	90	102	132	$p<0.01$
On NSAIDs use, n(%)	392 (36%)	710 (41%)	3668 (38%)	$p<0.01$
Daily mean prednisone dose, (mg/day)	4.31	3.95	3.86	$p=0.01$
On DMARDs, n(%)	984 (91%)	1623 (95%)	8835 (93%)	$p<0.01$
On a biologic, n(%)	435 (40%)	550 (32%)	2570 (27%)	

**Abstract AB0255 – Table 2.** Comparisons of values for disease outcomes of the three age groups

	1	2	3	P-value
Tender joint count(TJC), mean	1.65	2.17	1.97	$p<0.01$
Tender joint count(28 joints, TJC28), mean	1.17	1.48	1.44	$p=0.01$
Swollen joint count(SJC), mean	1.35	1.49	1.52	$p=0.23$
Swollen joint count(28 joints, SJC28), mean	1.05	1.19	1.20	$p=0.12$
ESR, mean, (mm/h)	17.3	18.8	29.7	$p<0.01$
CRP, mean, (mg/dl)	0.32	0.37	0.58	$p<0.01$
DAS28, mean	2.51	2.78	3.12	$p<0.01$
HAQDI score, mean	0.25	0.42	0.77	$p<0.01$
Proportion in Boolean remission, n(%)	351 (32%)	485 (28%)	2145 (22%)	$p=0.02$

**Conclusions:** This study shows that TJC may increase during menopause, unlike other disease activity indicators. Especially in group 2, it is possible that the joints which can't be evaluated at TJC 28 are affecting the results because in TJC, compared with TJC 28, there is a larger group difference. Although further studies are needed, an increase in TJC may reflect menopausal joint symptoms.

#### REFERENCE:

[1] Pikwer M, et al. *Ann Rheum Dis.* 2012 Mar;71(3):378–81.

**Disclosure of Interest:** None declared

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AB0256

#### DIFFERENTIAL DIAGNOSIS OF SERONEGATIVE RA: CALCIUM PYROPHOSPHATE DIHYDRATE DEPOSITION DISEASE

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**Background:** Calcium pyrophosphate deposition (CPPD) disease is caused by calcium pyrophosphate (CPP) crystals and seen mainly in elderly. Clinical presentation can be heterogeneous. The arthropathy of CPPD may mimic RA, particularly if involving common joints seen in RA. Diagnosis of CPPD arthritis is based on CPP crystals seen in synovial fluid (SF) analysis, chondrocalcinosis (CC) seen in radiographs and/or on typical clinical presentation for CPPD. Early diagnosis of CPPD can be challenging and a proportion of CPPD patients may be misdiagnosed. We demonstrate 17 cases with CPPD initially diagnosed and treated as seronegative RA.

**Objectives:** To increase awareness that CPPD disease may resemble seronegative RA and to characterise clinical and radiographic phenotypes of these CPPD patients.

**Methods:** Altogether 435 early seronegative early RA patients were clinically diagnosed in a single rheumatology centre and scheduled for 10 year follow-up. All clinical data and radiographs were collected and reviewed. Patients were re-diagnosed as CPPD related arthritis if they had typical radiographic findings and suitable clinical pattern of CPPD or positive CPP crystal finding in SF. These patients are the subjects of this study.

**Results:** 17 patients were identified with a CPPD disease. The mean age at baseline was 71.2 years, and 82% were women. In 7 (41.2%) patients baseline symptoms were polyarticular, and in all these patients' wrist, MCP or PIP joints were affected; other symptomatic joints were hip (1 patient) and ankle (3 patients). The initial symptoms of 6 (35.3%) patients were oligoarticular, including MCP and PIP joint involvement (2 patients) or wrist and MCP, PIP or MTP joint symptoms (4 patients). Four (23.5%) patients were diagnosed as monoarthritis including ankle (1 patient) and wrist (3 patients). Seven patients (41.2%) fulfilled 1987 ACR criteria for RA and the diagnosis of early RA of the other 10 patients (58.8%) was based on clinical judgement. During the follow up period the SF analysis of 4 patients was available, 3 SFs showing positivity for CPP crystals. In 13 patients, SF had not been taken. In retrospect the baseline radiographs of 10 patients showed evidence of CC, either in wrists or knees. During follow up all patients developed typical clinical pattern for CPPD disease: chronic CPP crystal inflammatory arthritis (9 patients), acute CPP crystal arthritis (6 patients) and OA with CPPD (2 patients). All developed similar radiographic findings compatible with CPPD, including CC of triangular fibrocartilage (17 patients), CC of knee (9 patients), CC or narrowing of MCP joints (7 patients), CC of metatarsophalangeal (MTP) joints (4 patients), CC of symphysis pubis (1 patient), CC of glenohumeral joint (1 patient) and SLAC (5 patients). None of these patients developed typical RA-like erosions.

**Conclusions:** The prevalence of CPPD patients in our early seronegative RA patients was 3.9%. CPPD disease can mimic seronegative RA at baseline and is important in the differential diagnosis of seronegative arthritis.

#### REFERENCE:

[1] Zhang W, Doherty M, Bardin T, et al. European league against rheumatism recommendations for calcium pyrophosphate deposition. Part I: Terminology and diagnosis. *Ann Rheum Dis.* 2011;70(4):563–570.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.3244

AB0257

#### PHYSICAL ACTIVITY IN EARLY AND LONG-STANDING RA – RELATIONS TO DISEASE ACTIVITY, CARDIOVASCULAR RISK FACTORS AND ATHEROSCLEROSIS

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**Background:** The excess risk for cardiovascular disease (CVD) in Rheumatoid Arthritis (RA), is partly attributable to traditional cardiovascular risk factors for CVD<sup>1</sup> and systemic inflammation,<sup>1, 2</sup> factors known to be modified by physical activity.<sup>3, 4</sup>

**Objectives:** The aim of this cross-sectional study was to objectively measure and compare the level of physical activity in patients with early and long-standing RA, and to analyse possible associations with disease activity, risk factors for CVD and measures of subclinical atherosclerosis.

**Methods:** This study included 84 patients with early and 37 with long-standing RA (disease duration, mean [SD] 1.4 [0.4] and 16.3 [2.3] years respectively). Physical activity was measured using a combined accelerometer and heart rate monitor and included total physical activity (counts/min), proportion of moderate to vigorous physical activity (MVPA) and sedentary time. Further assessments were; disease activity (ESR, DAS28), functional ability (HAQ), risk factors for CVD (blood lipids, i.e., triglycerides, high density lipoprotein [HDL], low density protein [LDL], blood glucose, blood pressure, waist circumference, body mass index [BMI]), body fat (Dual-energy X-ray), and early signs of atherosclerosis (pulse wave velocity [PWV], augmentation index [AIx] and carotid intima-media thickness [cIMT]).

**Results:** Physical activity variables did not differ between patients with early and long-standing RA. Thirty-seven% of the patients with early and 43% of the patients with long-standing RA did not reach WHO's recommended levels of MVPA. Univariate linear regression analyses with the two groups combined, showed associations between total physical activity and younger age, lower values for HAQ and disease activity (ESR), as well as more beneficial values

for blood glucose, triglycerides, waist circumference, BMI, body fat, sleeping heart rate (SHR), systolic, diastolic and central blood pressure and pulse pressure, Aix, PWV, and cIMT. More time spent in MVPA was associated with younger age and with favourable values of blood glucose, HDL, LDL, waist circumference, SHR and PWV.

**Abstract AB0257 – Table 1.** Physical activity variables in patients with early and long-standing RA, presented as median with inter-quartile range (IQR). P-value refers to Mann-Whitney U-test.

	Early RA (n=84)	Long-standing RA (n=37)	p
<b>Accelerometry</b> (mean counts/ minute)	35.7 (29.9)	38.1 (24.3)	.915
<b>MVPA</b> (% of wear time)	3.2 (6.6)	2.5 (5.5)	.884
<b>Sedentary time</b> (% of wear time)	53.9 (11.0)	52.0 (13.3)	.328

MVPA=Moderate to Vigorous Physical Activity=time $\geq$ 1.75 x resting heart rate. Sedentary time=heart rate data with zero accelerometer counts.

**Conclusions:** Physical activity behaviour was similar in patients with early and long-standing RA. Total physical activity as well as more time spent in moderate to vigorous physical activity were associated with more favourable risk factors for CVD and measures of atherosclerosis. These results stress the importance of promoting physical activity in patients with RA.

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- [3] Stavropoulos-Kalinoglou A, et al. *Annals of the rheumatic diseases* 2013;72(11):1819–25.
- [4] Metsios GS, et al. *Annals of the rheumatic diseases* 2014;73(4):748–51.

**Disclosure of Interest:** None declared

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AB0258

#### IMPACT OF CONTROLLING DISEASE ACTIVITY ON REGAINING NORMAL PHYSICAL FUNCTION, AND ACHIEVING NO OR LIMITED PAIN IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH BARICITINIB

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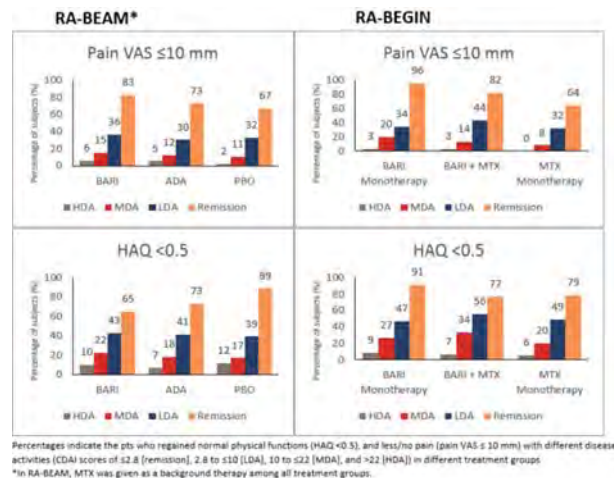
**Background:** Remission or low disease activity (LDA) are the recommended treatment (tx) targets in rheumatoid arthritis (RA).<sup>1</sup> It is still unknown whether achieving remission/LDA is associated with normalisation of physical function, and limiting pain.

**Objectives:** To describe the impact of baricitinib (BARI) tx on regaining normal physical function, and achieving no/limited pain in patients (pts) who achieved remission or LDA, or remained in moderate or high disease activity (MDA, HDA).

**Methods:** This is a post-hoc analysis of RA-BEAM (NCT01710358) and RA-BEGIN (NCT01711359). Mutually exclusive categories were defined as clinical disease activity index (CDAI) scores of  $\leq 2.8$  (remission),  $>2.8$  to  $\leq 10$  (LDA),  $>10$  to  $\leq 22$  (MDA), and  $>22$  (HDA). Last observation carried forward was used for pain visual analogue scale (0–100 mm VAS) and Health Assessment Questionnaire-Disability Index (HAQ-DI) to impute missing values. Descriptive analyses of the pts achieving normalisation of physical function was defined by a HAQ-DI

score of  $<0.5$  (normative value), and limited/no pain by pain VAS of  $\leq 10$  mm at week (wk) 12 and 24 as a function of disease activity.

**Results:** Overall, 1228 pts in RA-BEAM (448, PBO+MTX; 471, BARI+MTX; 309, ADA+MTX) and 543 pts in RA-BEGIN (190, MTX; 156, BARI; 197, BARI+MTX) were included. In RA-BEAM, among pts in remission at wk 12, % pts achieving limited/no pain was numerically higher in BARI (83%; 33/40) group compared with ADA (73%; 16/22) and PBO (67%; 6/9); at wk 24, these percentages were 81% (61/75), 82% (32/39), and 63% (12/19) for BARI, ADA, and PBO, respectively. Among pts who achieved remission on BARI+MTX tx, normal physical function was reported in 65% (26/40) and 73% (55/75) of pts at wk 12 and 24, respectively (Fig 1). For ADA+MTX treated pts, the proportion was 73% (16/22) at wk 12 and 69% (27/39) at wk 24. In RA-BEGIN, among pts in remission, % pts with limited/no pain at wk 12 was numerically higher for BARI (96%; 21/22) compared with BARI+MTX (82%; 32/39) or MTX (64%; 9/14); limited/no pain at wk 24, was reported in 68% (23/34), 87% (40/46), and 77% (17/22) of pts treated with BARI, BARI+MTX, and MTX, respectively. Among pts in remission, % pts achieving normal HAQ-DI at wk 12 and 24 with BARI monotherapy were 91% (20/22) and 82% (28/34); BARI+MTX, 77% (30/39) and 91% (42/46); and MTX monotherapy, 79% (11/14) and 82% (18/22), respectively.



**Abstract AB0258 – Figure 1.** Percentage of pts who achieved pain VAS  $\leq 10$  mm, and HAQ-DI  $<0.5$  scores for the different disease activity states at wk 12

Percentages indicate the pts who regained normal physical functions (HAQ $<0.5$ ), and less/no pain (pain VAS $\leq 10$  mm) with different disease activities (CDAI scores of  $\leq 2.8$  [remission],  $2.8$  to  $\leq 10$  [LDA],  $10$  to  $\leq 22$  [MDA], and  $>22$  [HDA]) in different treatment groups

\*In RA-BEAM, MTX was given as a background therapy among all treatment groups.

**Conclusions:** These data support that controlling the disease activity by achieving remission or LDA increases the chances to regain normal physical function and relieve pain, independent of the tx. The data from RA-BEAM may indicate that achieving limited/no pain at wk 12 may be more likely with BARI vs ADA, when being in remission.

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Celgene, Genentech, GSK, Janssen, Eli Lilly and Company, Pfizer, Sanofi-Aventis, UCB, P. Emery Consultant for: Pfizer, MSD, Abbvie, BMS, UCB, Roche, Novartis, Samsung, Sandoz, Eli Lilly and Company  
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### AB0259 CLINICAL MANAGEMENT OF SERONEGATIVE AND SEROPOSITIVE RHEUMATOID ARTHRITIS: A COMPARATIVE STUDY

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**Background:** Both rheumatoid factor (RF) and anti-cyclic citrullinated peptide antibody (ACPA) are associated with poor radiologic outcomes in patients with rheumatoid arthritis (RA). In general, RA patients positive for RF or ACPA (SPRA) are considered to manifest an aggressive disease course compared with seronegative RA patients (SNRA). However, the relationship between seropositivity and measures of disease severity other than radiologic outcome is disputed.

**Objectives:** In this study, we sought to compare the clinical presentations and treatment outcomes of SNRA and SPRA patients.

**Methods:** A total of 241 patients diagnosed with DMARD-naïve RA under either 1987 American College of Rheumatology (ACR) criteria or 2010 ACR/European League Against Rheumatism (EULAR) criteria were identified (40 with SNRA and 201 with SPRA). We investigated the disease activity measures including ESR, CRP, patient VAS, 28 tender/swollen joint count (28 TJC, 28 SJC) and DAS28 as well as radiologic outcomes at baseline, 1 and 2 years after conventional treatment with DMARD.

**Results:** Age, sex and disease duration were similar between SNRA and SPRA. However, the baseline 28 TJC (4.7±2.9 vs. 3.3±2.7, p=0.004), 28 SJC (4.3±3.0 vs. 2.9±2.3, p=0.001) and DAS28 (5.1±1.0 vs. 4.7±1.0, p=0.043) components were significantly higher in SNRA than in SPRA. Over 2 years of similar treatment with DMARDs, all disease activity measures significantly improved in both groups. Notably, ΔDAS28 from baseline at 1 year was significantly greater in SNRA compared with SPRA (-2.9±1.2 vs. -2.2±1.8, p=0.002). Radiologic outcomes at baseline and at 1- or 2 year follow-up were similar between the 2 groups

**Conclusions:** SNRA patients manifested more active disease at baseline, but showed a better response to treatment compared with SPRA. SNRA does not appear to be a benign subtype of RA

**Disclosure of Interest:** None declared

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### AB0260 ASSOCIATION BETWEEN ANTI-CITRULLINATED PROTEIN ANTIBODY STATUS, EROSIVE DISEASE AND HEALTHCARE RESOURCE UTILISATION IN PATIENTS WITH RA

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**Background:** Anti-citrullinated protein antibody (ACPA) is a highly specific biomarker for RA<sup>1</sup> and ACPA-seropositive patients have a tendency toward severe erosive disease and more rapid disease progression.<sup>2-4</sup> Little is known regarding the impact of poor prognostic factors, such as ACPA and erosive disease, on healthcare resource utilisation (HCRU).

**Objectives:** To characterise the rate of HCRU between anti-cyclic citrullinated peptide (anti-CCP; a surrogate of ACPA) positive (+) patients with or without erosions who initiated biologic (b)DMARD treatment.

**Methods:** This analysis included patients aged ≥18 years, who were enrolled in a large sequential RA registry (October 2001–August 2017) and who had known erosions, as measured by radiography, and anti-CCP +status at or prior to bDMARD initiation visit and a 12 month (±3 months) follow-up visit. Anti-CCP +was defined as ≥20 U/mL. Rates of HCRU, including all-cause hospitalizations, all joint surgeries (total and partial; all sites), radiographic procedures and use of assistive devices, were estimated over 12 months of follow-up from the bDMARD initiation visit in anti-CCP +patients with or without erosions. Rates of HCRU per 100 patient-years and risk ratios, adjusted by baseline age, were estimated with 95% CI using a Poisson regression model.

**Results:** A total of 2047 anti-CCP +patients were included in this analysis, 868 with and 1179 without erosions. At biologic initiation visit, mean (SD) age was 58.9 (12.5) and 55.9 (12.5) years and disease duration was 11.7 (10.1) and 6.4 (7.5) years, respectively, in anti-CCP +patients with and without erosions. Over 12 months of follow-up, the rates of HCRU were higher among anti-CCP +patients with versus those without erosions at baseline bDMARD initiation visit (table 1).

**Conclusions:** ACPA seropositivity with erosive disease predicts high utilisation of healthcare resources, suggesting that early therapeutic intervention may be

warranted in anti-CCP +patients to achieve better disease control and reduce the complications from RA.

**Abstract AB0260 – Table 1.** Age-Adjusted Rates (95%CI) of HCRU and Adjusted Risk Ratios in Anti-CCP+ Patients With RA With and Without Erosions

	Age-adjusted rate (95% CI)*†		Adjusted risk ratio (95% CI)*†
	Anti-CCP+and no erosions (n=1179)	Anti-CCP +and erosions (n=868)	Anti-CCP+/erosions vs anti-CCP+/no erosions‡
<b>Hospitalisation, all cause</b>	9.44 (7.77–11.37)	15.21 (12.72–18.05)	1.47 (1.14–1.90)
<b>Joint surgery visits, all sites</b>	3.74 (2.72–5.02)	5.34 (3.91–7.12)	1.31 (0.86–1.98)
<b>Radiography, all cause</b>	18.12 (15.77–20.72)	22.18 (19.14–25.56)	1.25 (1.03–1.53)
<b>Assistive devices</b>	60.65 (56.28–65.27)	73.03 (67.44–78.97)	1.12 (1.00–1.25)

\*Rates per 100 patient-years with 95% CI based on Poisson distributed counts

†Adjusted for baseline age

‡Reference group: anti-CCP +and erosions

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### AB0261 ONGOING GOOD RESPONSE WITH BIOLOGICS. DATA FROM THE AUSTRIAN BIORG REGISTRY

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**Background:** The goal for the treatment of rheumatoid arthritis (RA) should be remission or at least low disease activity. Using data of the Austrian biologic registry we evaluated disease activity in patients with RA and treated with biologics for more than six years.

**Objectives:** The aim of this evaluation was to elucidate long term disease activity in patients with RA who are treated with a biologic. We checked data at baseline and at control-visits every six months after inclusion in BioReg.

**Methods:** Data were extracted from the Austrian BioReg registry (<http://www.bio-reg.at>) which was initiated in 2009 to document patients treated with one of the biologics approved in Austria. Patients with ongoing biologic therapy as well as biologic-naïve patients starting biologic therapy can be included (baseline, BL). Further documentation is recommended about every 6 months (V2, V2 up to V12). Until September 2017, 2132 patients (1157 RA, 497 SpA, 401 PsA, 77 other diseases) have been documented.

Estimation of disease activity was done using DAS-28, RADAI-5, HAQ as well as ESR and CRP.

**Results:** DAS-28 (median values of BL; V2; V4; V10;V12) of our patients with RA are 3,30; 2,51; 2,33; 2,49; 2,58, the respective RADAI-5 values are 3,20; 2,20; 2,00; 2,00; 2,40 and values of HAQ are 0,75; 0,50; 0,50; 0,50; 0,63. Median values of inflammation's laboratory markers (ESR in mm/1st hour and CRP in mg/l) were always within or close to the normal range (ESR and CRP in RA 15; 12; 11,5; 13,5; 11 and 2,1; 2,0; 2,0; 2,4; 3,0

**Conclusions:** Our data confirm the efficiency of therapy with a biologic. During 6 years of continuous treatment more than half of the patients with RA are continuously in remission or low disease activity with a DAS-28 below 2,6, RADAI-5 equal or below to 2,40 and normal values of ESR and CRP.

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**Disclosure of Interest:** None declared

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**AB0262** **SEARCHING PREDICTORS OF ABATACEPT EFFICACY IN PATIENTS WITH RHEUMATOID ARTHRITIS**

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**Background:** Biologics have revolutionised the treatment of rheumatoid arthritis (RA). Several types of biologics are used in clinical practice, one of them is the blocker of T cells co-stimulation – abatacept (ABA). The search for predictors of biologics efficacy is an important issue in current rheumatology practice.

**Objectives:** To identify predictors of ABA efficacy based on the analysis of various serum biomarkers changes.

**Methods:** 44 RA pts with a history of previous DMARDs and biologics failures and 16 healthy donors as controls were included in the study. The majority of pts were females, RF-positive – 80%, anti-CCP-positive – 79.5%, mean age 49.6 ± 13.9 years, median disease duration 21.4<sup>3</sup> years, with high RA activity (mean DAS28=5.2±0.8). Enzyme-linked immunoassay was used to measure serum concentrations of biomarkers IL-1β, IL-6, IL-17AF, TNF-α, VEGF-A, IP-10, YKL-40, MMP3 at baseline and after 6 months of ABA therapy. Disease activity was assessed every 3 months using DAS28. ABA were administered IV according to standard schedule.

**Results:** RA pts had significantly increased levels of IL-6 (2.4 [1.1–6.4] vs 0.7 [0.62–1.0] pg/ml, p=0.0002), YKL-40 (97<sup>68,4–97,9</sup> vs 64<sup>52,4–107,5</sup> pg/ml, p=0.03), and IP-10 (21<sup>12,9–49,8</sup> vs 14<sup>9,2–15,2</sup> pg/ml, p=0.005) compared to the control group. By the 6-th month ABA significantly reduced the levels of IL-6 up to 1.29 [0.9–2.2] pg/ml, p=0.0006 and IP-10 – to 14<sup>7,5–28</sup> pg/ml, p=0.007, as well as MMP3 and RF from 30.1<sup>13–82</sup> to 10 [7.4–55] pg/ml, p=0.0003 and from 218 [9.6–187] to 159 [9.7–155] pg/ml, p=0.02, respectively. There was a significant correlation between the decrease of IL-6 (r=0.5) and IP-10 (r=0.32) levels and decrease of DAS28 scores (p<0.05). A trend to a more pronounced reduction in disease activity was identified in anti-CCP-positive and anti-MCV-positive pts. By EULAR criteria the percentage of no-responders among anti-CCP-negative and anti-MCV-negative was almost two times higher as compared to antibodies-positive pts, i.e., 27.2% vs 16% and 26.7% vs. 14.8%, respectively, although the difference failed to reach statistical significance. However, by 6 months the percentage of pts with high disease activity among anti-MCV-negative pts were significantly higher than among anti-MCV-positive (20% and 0%, p=0.03, respectively). Higher baseline IL-6 (p=0.03) and YKL-40 (p=0.02) levels were registered among non-responders to ABA therapy.

**Conclusions:** ABA therapy led to a significant reduction in concentrations of pro-inflammatory IL-6 and IP-10 cytokines, as well as of MMP3 and RF. The decrease of IL-6 and IP-10 levels significantly correlated with the decrease of RA activity. There was a trend towards more pronounced reduction of disease activity in anti-CCP-positive and anti-MCV-positive pts. High baseline IL-6 and YKL-40 levels were significantly more frequently registered among non-responders. Therefore, anti-MCV-negativity, high baseline levels of IL-6 and YKL-40 could be used as predictors of insufficient ABA efficacy in this category of pts. A small sample of pts is the major limitation of this study, requiring future studies.

**Disclosure of Interest:** None declared

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**AB0263** **TREND IN TUBERCULOSIS INFECTION INCIDENCE IN RHEUMATOID ARTHRITIS IN SPAIN: AN OBSERVATIONAL COHORT STUDY (1999–2015) (TREND-AR STUDY)**

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**Background:** There have been important changes in the management of rheumatoid arthritis (RA) in the last 20 years, due to the incorporation of new drugs. An increase in the incidence of tuberculosis infection (TB) has been observed

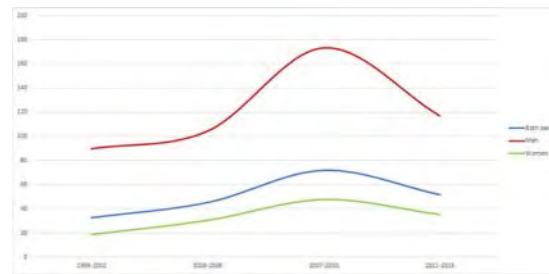
because of reactivation of latent TB with the use of new treatments. Adequate prevention measures have been implemented.

**Objectives:** To analyse the incidence and trend of hospital admissions for TB in patients with RA in Spain during the period between 1999 and 2015.

**Methods:** This is a retrospective population based study. We analysed a national administrative database that includes a Minimum Basic Data Set (MBDS) of hospital admissions of patients with RA. Period: 1999 to 2015. The TB cases were identified by the presence in primary and secondary diagnosis of ICD 9 codes. The population at risk was estimated through the population census of the National Institute of Statistics, with an estimated prevalence of RA of 0.5%. The crude and adjusted rates of TB were calculated. The trend was analysed using Generalised Linear Models (GLM) using the year variable as the analysis variable.

**Results:** Among all the admissions of patients with AR (338.343), 1209 (0.35%) were due to TB, 665 (55%) in women and 544 (44.9%) in men. The mean age was 63.25 (SD 13.7). The mean of the Charlson index was 1.84 (SD 1.45), in women 1.63 (SD 1.3) and in men 2.09 (SD 1.59) (p<0.001).

There were a total of 94 (7.8%) deaths during admission (6.9% in women, 8.8% in men, p=0.231). The TB age-adjusted rate during the study period was 42.78/100.000 inhabitants RA-year (28.2 in women and 100.74 in men). The TB age-adjusted rate in both sexes remains without significant changes between 1999 and 2015 (IRR 0.225; CI95% 0.985–1.025). During the period 1999–2011 an increase of the incidence is observed, while in the period 2011–2015 it is observed a decrease of the same (fig 1).



**Abstract AB0263 – Figure 1**

**Conclusions:** Conclusion: In Spain, in patients with RA, the income rate in relation to tuberculosis increased from 1999 to 2010 and subsequently decreased in the period from 2011 to 2015.

**Disclosure of Interest:** None declared

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**AB0264** **TREND IN HOSPITAL ADMISSIONS IN RHEUMATOID ARTHRITIS IN SPAIN: A NATIONAL OBSERVATIONAL COHORT STUDY (1999–2015) (TREND-AR STUDY)**

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**Background:** There have been significant changes in the management of rheumatoid arthritis (RA) during the past 20 years. The potential impact of these strategies on hospitalisation trend is unknown.

**Objectives:** To analyse the incidence and trend of hospital admissions in patients with RA in Spain from 1999 to 2015.

**Methods:** This is a population based study. We analysed a national administrative database that includes a Minimum Basic Data Set (MBDS) of hospital admissions of patients with RA during the period 1999–2015.

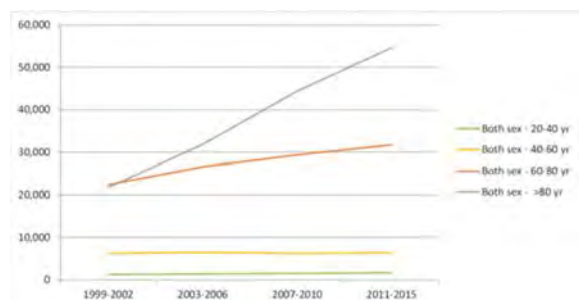
The admission cases in patients with RA were identified by the presence in primary and secondary diagnosis of the ICD9 codes (714.0–714.9). The population at risk was estimated through the population census of the National Institute of Statistics, with an estimated prevalence for RA of 0.5%, with crudes and adjusted admission rates being calculated. The trend was analysed using Generalised Linear Models (GLM).

**Results:** There were a total of 3 38 343 hospital admissions in RA patients during the study period, accounting for a total of 1 76 097 patients (1 17 985 women and 58 112 men). The mean age at admission was 68 years (67.8 in women and 68.5

in men), with a linear increase throughout the study period from 65.3 in 1999 until 70.5 in 2015 ( $p < 0.001$ ).

The main admission code was for Osteoarticular and connective tissue diseases (20%) followed by Circulatory system diseases (16.8%). There were a total of 18 641 in-hospital deaths (5.5% of all the admissions).

The age-adjusted admission rate was 12.03/100 RA patients\*yr (9.12 for women and 1.88 for men). The age-adjusted admission rate increased from 1999 to 2015 (in both genders). An annual increase of admission rate of 3.7% is estimated. When adjusting by age, the largest increase is observed in patients older than 80 years, with an estimated annual increase of 7.5%.



Abstract AB0264 – Figure 1

**Conclusions:** In Spain, despite the improvement in RA management, there is a global tendency to the increase of admissions during the period of 1999–2015, mainly in >60 year, especially in >80 year.

**Disclosure of Interest:** None declared

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#### AB0265 CLINICAL PREDICTOR FACTORS ASSOCIATED WITH SUSTAINED DISEASE ACTIVITY AMONG PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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**Background:** In patients with rheumatoid arthritis (RA), low disease activity (DA) overtime is associated with favourable outcomes. However, the progression of the disease is faster during the first years. Therefore, it is desirable to identify patients with a high probability of sustained DA in an early stage.

**Objectives:** To identify clinical predictor factors at diagnosis associated with sustained DA after 12 months of follow up in patients with early RA.

**Methods:** Baseline (at diagnosis) and 12 months follow-up data from an early arthritis clinic was analysed. At both visits, demographic, clinical, laboratory and treatment data were collected and clinical DA was assessed using DAS28 and SDAI. For this study, patients with RA according to physician's diagnosis were selected. Sustained DA at 12 months was defined as DAS28 >3.2 and SDAI >11. Univariate and multivariable logistic regression models were employed to identify which factors are associated with sustained DA.

**Results:** In total, 566 patients were included. Out of these, 75.8% were women, 74.7% Caucasian, 77.7% RF + and 65.9% ACPA+. Mean (SD) age was 54<sup>17</sup> years and mean symptoms duration was 16<sup>15</sup> weeks. Regarding treatment, 89.8% patients received methotrexate as first line treatment and 81.1% received glucocorticoids. At baseline, 88.8% had moderate-high DA according to DAS28 (>3.2) and 77.6% with SDAI (>11). After one year of follow-up, 34% (DAS28) and 30.9% (SDAI) remained with moderate-high DA. Univariable logistic regression analysis results are shown in table 1. Sustained DA was significantly associated with baseline index and its individual components, HAQ, and GCs used for both indexes definitions, with smoking and MTX use for DAS28 definition and RF + for SDAI definition. In the multivariable analysis, sustained DA at 12 months remained significantly associated only with baseline DAS28 (OR 1.34;  $p < 0.05$ ) for DAS28 definition and with RF (OR 2.6;  $p = 0.02$ ), HAQ (OR 1.06;  $p < 0.01$ ) and use of glucocorticoids (OR 2.1;  $p < 0.05$ ) for SDAI definition.

Abstract AB0265 – Table 1. Univariable logistic regression analysis results

Baseline characteristics	DAS28		SDAI	
	OR	P value	OR	P Value
Age	1.00	0.6	0.03	1.02
Sex (women)	1.64	0.06	0.599	1.14
Tabaco	0.66	0.1	1.12	0.690
Nonsmokers (ref)	0.58	0.05	1.08	0.804
<b>Past smokers</b>				
<b>Smokers</b>				
RF (+)	1.61	0.09	0.444	0.007
ACPA (+)	0.685	0.1	0.691	0.14
DAS28	1.5	<0.001		
SDAI			1.00	0.008
HAQ	1.05	0.001	1.07	<0.001
ESR	1.01	0.001	1.01	<0.001
PCR	1	0.804	1.0	0.91
Pain	1.02	<0.001	1.01	<0.001
Patients Global Assessment	1.01	<0.01	1.01	0.002
Evaluator Global	1.02	<0.001	1.02	<0.001
<b>Assessment</b>				
Swollen Joint count 28	1.07	<0.001	1.07	<0.001
Tender Joint Count 28	1.07	<0.01	1.06	<0.001
Methotrexate use	8,2	<0.05	2,4	0,2
Glucocorticoids use	1.8	<0,05	2,7	<0.001

**Conclusions:** One out of three patients with RA maintains DA 12 months after diagnosis. The predictors for this status depend on the index employed: DAS28 at baseline is the best predictor for sustained disease activity when using DAS28-definition. Conversely, positive RF, impaired functionality and the need of glucocorticoids at baseline are associated with the SDAI-definition.

**Disclosure of Interest:** None declared

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#### AB0266 ESTIMATION OF CEREBROVASCULAR REACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is a chronic autoimmune disease with high cardiovascular risk. Arterial hypertension (AH) is the most common comorbid condition in RA and one of the main risk factors for stroke. Chronic immune inflammation, characteristic of RA, also has a damaging effect on the vascular wall and can lead to a marked decrease in the compensatory possibilities of the cardiovascular system. It has been shown that the violation of cerebrovascular reactivity (CVR) significantly increases the risk of developing acute cerebral ischemia

**Objectives:** The goal is to study the condition of the CVR in RA patients, depending on the level of blood pressure (BP)

**Methods:** the study involved 70 patients with RA at the age of 59,2±7,3 years with the duration of RA 13±8,9 years were examined. The DAS28 index was 3.87 ±1.33. Depending on the level of blood pressure, two groups were isolated: group 1 (n=56) – patients with hypertension and group 2 (n=14) – with normal blood pressure. CVR was assessed by means of transcranial dopplerography of middle cerebral arteries (MCA) using hyperoxic (inhalation of 100% oxygen, phase of vasoconstriction) and hypercapnic (inhalation of 4% of a mixture of carbon dioxide with air, phase of vasodilation) of samples.

**Results:** The result showed that 15 (27%) patients of the I group and 3 (21%) – the II group had an adequate decrease in the linear velocities of the blood flow (LVBF) in the MCA. An insufficient reduction in hypervascular hypertension was found in 28<sup>50%</sup> and 8 (57%) patients, a paradoxical increase in the LVBF (perverse reaction) in 12 (21,4%) and 4 (28,5%) patients, respectively. In a hypercapnia trial, only about a third of patients registered an adequate increase in LVBF for hypercapnia. A decrease in the response occurred in 27 (48%) and 9 (61%) patients, excessive increase in LVBF (hyperergic reaction) – in 15 (26%) and 2 (14%) patients, respectively

**Conclusions:** There was a violation of the CVR on metabolic (hyperoxic and hypercapnic) stimuli based on the results of transcranial dopplerography of most RA patients, regardless of the level of blood pressure

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**AB0267** **BASELINE PREDICTORS OF RESPONSE TO METHOTREXATE IN EARLY RHEUMATOID ARTHRITIS**

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**Background:** The disease activity score (DAS28) is widely used to assess response to treatment in early rheumatoid arthritis. Few studies have looked at the individual components of the DAS at baseline to predict drop in DAS28 in early disease. Specifically at 3, 6 and 12 months. Predicting response early in disease would enable more targeted treatments to be given and patients selected early for more aggressive disease control. Although certain biomarkers have been advocated for use and have shown some promise.<sup>1,2</sup> there is still a place for exploring using more clinically derived indicators.

**Objectives:** To determine whether DAS28 response at 3, 6 and 12 months could be predicted by baseline components of the DAS28

**Methods:** The study used patients from the multicentre UK based RAMS study. All patients with early rheumatoid arthritis starting methotrexate were enrolled. We used data from a single centre in the North west of England for the analysis. DAS28 and its components were recorded at baseline and at 3 6 and 12 months. Baseline components of the DAS28 were used to predict the change in DAS from baseline to 3 6 and 12 months. Linear regression was used with subsequent adjustment for age and gender.

**Results:** 120 patients were enrolled in the study, median age was 62.4 years (IQR42.1, 72.5), 81 (67%) were female. Median das28 at baseline was 5.3 (IQR 4.2,6.2). Duration of symptoms was 9 months (IQR 2,11). There was a drop of DAS28 of 1.49 at 3 months (IQR 0.57,2.45) and at 6 and 12 months it was 1.84 (IQR 0.48,2.91) and 1.63 (IQR 0.72,2.85) respectively. At three months the only baseline predictor of change in DAS28 was the patient global assessment unadjusted and adjusted for age adjusted beta 0.012 95% CI 0.002, 0.023 (p=0.02). At six months the baseline tender joint count adjusted beta 0.08 95% CI 0.015, 0.154 (p=0.01) as well as swollen joint count adjusted beta 0.05 95% CI 0.004,0.095 (p=0.02) also predicted response in addition to the patients global assessment adjusted beta 0.016 95% CI 0.002, 0.03 (p=0.01), but not the ESR or CRP at baseline (p=NS). At 12 months the only predictors of response was the baseline CRP adjusted beta 0.02 95% CI 0.005, 0.04(p=0.02).

**Conclusions:** In this cohort of patients with early disease, response to methotrexate could not be reliably predicted using baseline measures and the ability to predict patients who would improve could not be found in this cohort. Further work on other clinical biomarkers to predict response is needed.

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**AB0268** **HOW DO PATIENTS WITH RHEUMATOID ARTHRITIS EVALUATE THEIR GLOBAL ASSESSMENT?**

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**Background:** The importance of patient-reported outcomes (PRO) has been recently recognised. Patient global assessment (PtGA) is one of the most popular PROs in rheumatology. However, the validity of PtGA as a tool for assessment of disease activity and its relevance compared with other tools is still debated.<sup>1</sup> Patients' perspective is essential to achieve treat-to-target. The significance of measuring PtGA in clinical practice should be verified. We previously found that Japanese rheumatologists changed their strategy to ask patient global assessment (PtGA) according to the patients' understanding ability. It is unknown how patients themselves feel PtGA.

**Objectives:** To investigate how patients with rheumatoid arthritis (RA) evaluate and accept PtGA as assessment tool of RA activity.

**Methods:** During the period of August and September, 2016 a 90 min focus group was held four times. Nine or 10 RA patients participated in each focus group. Totally, 34 women and 4 men, average age 56.1±10.9 years old, and disease history 9.39±9.36 years joined the study. The participants freely discussed how to evaluate their conditions of rheumatism and therapeutic effect. We used the "Steps for Coding and Theorization" (SCAT)<sup>2-3</sup> to analyse the focus group data.

**Results:** Patients determined their PtGA based on pain, swelling, inconvenience of daily life, the mood of the day, comprehensively, although they felt confusing

because the criteria of how to evaluate PtGA was unclear. Most patients set 100 of PtGA as "when most painful after onset", while standard of 0 was varied. Many patients had experienced a discrepancy between PtGA and CRP that their doctors denied. Patients were eager that their doctor would understand the discordance between PtGA and laboratory data and ask the patients "what's wrong with you?"

**Conclusions:** Doctors and patients should discuss how to evaluate PtGA at the start of treatment to avoid patients' confusing. By utilising PtGA as a communication tool, relationship between doctor and patients would be facilitated.

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**AB0269** **ANKLE SYNOVITIS AND TREAT-TO-TARGET STRATEGY IN CLINICALLY AND SEROLOGICALLY DIFFERENT FORMS OF RHEUMATOID ARTHRITIS, A SINGLE-CENTRE EXPERIENCE**

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**Background:** DAS28 based treat-to-target (T2T) strategy<sup>1</sup> was shown to improve outcomes in patients with rheumatoid arthritis (RA). Although previous studies have shown that approximately 1/3 of RA patients have foot symptoms<sup>1,2</sup> ankle and foot joints are not included in DAS28.

**Objectives:** To study the prevalence of ankle synovitis in clinically and serologically different forms of RA, treated according to the updated T2T strategy.

**Methods:** 1109 patients, with RA, treated according to the T2T approach were included in this study. Concurrent tenderness and swelling of the ankle joint were considered as synovitis. Rheumatoid factor (RF) and anti-mutated citrullinated vimentin (anti-MCV) positive and negative patients with different disease activity were evaluated.

**Results:** 8.47% (94) patients had high (DAS28 >5.1); 35.25% (391) moderate (DAS28 ≤5.1;>3.2) and 18.66% (207) low (DAS28 ≤3.2;≥2.6) disease activity. 37.6% (417) of patients were in clinical remission (DAS28 <2.6). 60.71%<sup>17</sup> of anti-MCV and RF positive and 44.8%<sup>13</sup> of anti-MCV and RF negative patients with high disease activity had ankle synovitis (table 1). Regarding patients in remission, 13.7%<sup>18</sup> of anti-MCV and RF positive and 15%<sup>18</sup> of anti-MCV and RF negative patients had ankle synovitis (table 2). Interestingly, ankle synovitis was considerably more common than knee synovitis in all patient groups.

**Abstract AB0269 – Table 1.** Ankle and knee involvement in high disease activity

	DAS28>5.1, 94 patients in total	DAS28>5.1. RF pos., anti-MCV pos: 28 patients	DAS28>5.1. RF neg, anti-MCV neg: 29 patients
Right knee synovitis	21,27%	25%	24,13%
Left knee synovitis	19,14%	25%	10,31%
Both knees synovitis	4,25%	10,71%	0
% of patients with knee involvement	36,17%	39,28%	34,48%
Right ankle synovitis	31,91%	28,57%	34,48%
Left ankle synovitis	37,23%	42,85%	44,82%
Both ankles synovitis	13,82%	10,71%	34,48%
% of patients with ankle involvement	55,31%	60,71%	44,82%

**Abstract AB0269 – Table 2.** Ankle and knee involvement in remission

	DAS28<2.6 417 patients in total	DAS28<2.6, RF pos, anti- MCV pos: 131 patients	DAS28<2.6, RF neg, anti- MCV neg: 120 patients
Right knee synovitis	1,43%	2,29%	0
Left knee synovitis	0,95%	1,52%	0
Both knees synovitis	0	0	0
% of patients with knee involvement	2,39%	3,87%	0
Right ankle synovitis	6,71%	6,87%	6,66%
Left ankle synovitis	7,19%	7,63%	8,33%
Both ankles synovitis	0,23%	0,76%	0
% of patients with ankle involvement	13,66%	13,74%	15%

**Conclusions:** Our present data show that ankle synovitis is rather common in patients with serologically and clinically different forms of RA and highlight the importance of careful medical examination, even in case of clinical remission.

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**Disclosure of Interest:** None declared

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**AB0270**

**TREATMENT RESPONSE TO RITUXIMAB IN COMBINATION WITH LEFLUNOMIDE IS INFLUENCED BY ANTICCP STATUS IN ACTIVE RHEUMATOID ARTHRITIS: RESULTS FROM A MULTICENTER RANDOMISED PLACEBO-CONTROLLED INVESTIGATOR INITIATED CLINICAL TRIAL IN ACTIVE RHEUMATOID ARTHRITIS (AMARA-STUDY)**

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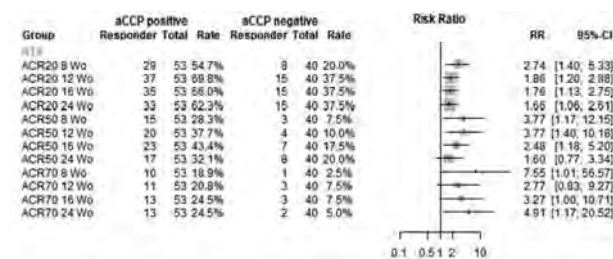
**Background:** Use of biologicals such as Rituximab (RTX) in Rheumatoid Arthritis (RA) is effective and often only licensed in combination with Methotrexate (MTX). In cases of contraindications to or intolerances, other cDMARDs are frequently used in routine care without data from RCTs. Patients with positive antiCCP-status were identified in previous studies to better respond to RTX in combination with MTX.

**Objectives:** Here we present for the first-time data of the impact of antiCCP status on ACR response in the combinational therapy of RTX and Leflunomide (LEF).

**Methods:** A total of 189 patients with active RA (DAS28 >3.2 and at least 3 SJC and 3 TJC) despite stable LEF treatment were screened for a 52 weeks double-blind placebo controlled multicenter RCT. Patients were randomised to receive either two times 1000 mg RTX i.v. or PLA, followed by a second course of RTX of either two times 500 or 1000 mg at week 24. The primary endpoint of the study was superiority of RTX in ACR20 and 50 responses during 24 weeks treatment period. Adult patients who had inadequate response to more than one antiTNF or failed more than three cDMARDs were excluded. Disease activity was measured at each visit and compared according to antiCCP status. For safety evaluation, frequency and severity of adverse events were documented.

**Results:** Of 189 screened patients 148 were randomised. The mean age was 56 years; the mean body weight 76 kg and 74% were female. The disease activity (DAS28) at baseline was 5.57 for RTX and 5.54 for PLA. 57.1% of the patients were antiCCP-positive for RTX compared to 59.6% for PLA. In the RTX group, antiCCP-positive patients' disease duration was 8.8 years compared to 5.6 years in the antiCCP-negative group), DAS28 was 5.73 vs. 5.32 and CRP levels were

11.1 mg/L vs. 5.3 mg/L. RTX demonstrated significant superiority compared to PLA at week 16 in both, ACR 20 and ACR 50 response. AntiCCP-positive patients showed a higher probability to respond to the RTX/LEF treatment than antiCCP-negative patients (figure 1). 43 serious adverse events were reported, 27 of them in the RTX treatment group during the placebo-controlled period.

**Abstract AB0270 – Figure 1**

**Conclusions:** Here we report data of the first RCT investigating the combination of RTX with LEF in RA. The treatment with RTX in combination with LEF demonstrated significant efficacy compared to PLA for ACR20 and 50 responses with highest response level at week 16. AntiCCP-positive patients showed a higher probability for treatment response compared to antiCCP-negative ones. The combination of RTX and LEF demonstrated a reasonable safety profile.

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**AB0271**

**RS12218 POLYMORPHISM IN SAA1 GENE IN THE RUSSIAN POPULATION OF RA PATIENTS IS ASSOCIATED WITH SECONDARY AMYLOIDOSIS. A PILOT STUDY**

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**Background:** Secondary amyloidosis (SA) is a serious complication of rheumatoid arthritis (RA), which is often fatal. Identification of associated risk factors, including genetic ones, is an important task.

**Objectives:** To assess the role of SAA1 gene polymorphism, encoding serum amyloid-A, as a risk factor predisposing to SA in the sample of Russian RA patients.

**Methods:** The study included 60 patients with RA, fulfilled the American College of rheumatology criteria (ACR) 1987. Of these 35 (mean age 49.5±10.8 y, mean disease duration 18.5±8.9) developed SA manifestations, confirmed histologically: group SA (+). 25 patients (mean age 56.7±11.7 y, mean disease duration 16.3±7.5 y) did not have either clinical or histological SA signs: group SA (-). The control group (C) consisted of 65 healthy employees. SAA1 gene polymorphism rs12218 (-13 T/C), mapped in the 5' flanking region of the gene, was studied in 125 subjects by polymerase chain reaction in real time (RT-PCR) with subsequent melting curves analysis.

**Results:** Statistically significant differences in the rates of TT, TC and CC genotypes of rs12218 polymorphism were established between SA(+) group and the controls (17.1%, 64.0%, 48.6% and 38.5%, 46.1%, 15.4%, respectively, p=0.029). High rate (58.6%) of the mutant C allele in SA(+) group compared to the control group (38.5%) predetermines high risk of susceptibility to SA in RA patients [OR 2.26, 95% CI(1.20–4.28), p=0.010]. Significant differences in rs12218 polymorphism rates were found between SA(+) and SA(-) groups [p<0.001]. The frequency of TC +CC genotype was significantly higher in the SA (+) group compared to SA(-) group [82.9% vs 36.0%, p<0.001]. The risk of predisposition to SA development among RA patients was increased when C allele frequencies in the group with SA (58.6%) were compared with the group without SA (22.0%) [OR 5.01, 95% CI (2.07–12.58), p<0.001]. No significant differences were found in the frequencies of genotypes and rs12218 alleles between SA(-) pts and the controls (p>0.05).

**Conclusions:** Our data confirm that genetic polymorphism rs12218 in SAA1 gene, is associated with the development of secondary amyloidosis in RA patients and mutation in this gene is an important risk factor predisposing to the development of this severe complication in the Russian population.

**Disclosure of Interest:** None declared

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AB0272

### MEAN PLATELET VOLUME AS A POTENTIAL BIOLOGICS THERAPY RESPONSE PREDICTOR AND DISEASE ACTIVITY INDICATOR IN PATIENTS WITH RHEUMATOID ARTHRITIS

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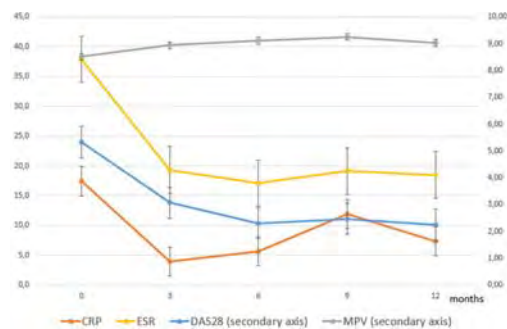
**Background:** Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease that primarily affects joints. Currently, the most widely used markers of acute phase response are C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). However, in recent years it has been suggested that platelet histogram indices, such as mean platelet volume (MPV) could be predictors of disease activity in patients with RA.

**Objectives:** The aim of this study was to assess whether MPV can be used as a disease activity marker by analysing a possible correlation between MPV and DAS-28, serum CRP levels, and ESR in patients starting with or switching between different biological DMARDs (tocilizumab, infliximab). Finally, we investigate whether MPV value at baseline can be a therapy outcome predictor by comparing two groups of patients (remission and active disease) at the 12 month time point based on DAS-28 value.

**Methods:** Fifteen patients (aged 56.5±9.3 years) fulfilling the American College of Rheumatology (ACR) criteria for RA were retrospectively enrolled in the study from the rheumatology outpatient clinic at the University Hospital Centre Zagreb, Croatia. DAS-28 has been used to evaluate disease activity at baseline, 3 months, 6 months, 9 months, and 12 months after starting biological DMARD therapy. Laboratory assessments included a complete blood count (including MPV), ESR, and CRP levels at each visit.

**Results:** We have observed a significant reduction in DAS-28 within the 12 month assessment period (from 5.33±1.24 to 2.25±1.23). MPV varied between 8.5±0.6 at baseline and 9.0±0.8 at the 12 month time point, with its peak being at the 9 month time point (9.3±0.8). Mean MPV had an inverse correlation with mean DAS-28 ( $r=-0.94$ ,  $p=0.02$ ), as well as mean ESR ( $r=-0.91$ ,  $p=0.03$ ). A weaker correlation was observed with mean CRP ( $r=-0.56$ ,  $p=0.3$ ).

When assessing whether MPV could be used as a therapy response predictor, patients were divided into two groups: those in remission at the 12 month time point ( $n=10$ ) and those with significant disease activity ( $n=5$ ), with remission being defined as a DAS-28 value of 2.8 or less. There was no significant difference in MPV values between those groups (8.5±0.56 for those in remission and 8.52±0.545 for those with active disease).



Abstract AB0272 – Figure 1

**Conclusions:** The results of this study provide additional evidence supporting the previously reported correlation between MPV and other disease activity markers (DAS-28, ESR) to treatment response in RA patients. It seems MPV isn't a viable therapy outcome predictor given that there is no significant difference in MPV value in patients in remission and those not in remission.

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AB0273

### ASSESSMENT OF SERUM LEVELS OF 14–3–3H PROTEIN IN RHEUMATOID ARTHRITIS: IS IT A SPECIFIC MARKER FOR THE DISEASE?

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**Background:** 14–3–3η protein was suggested to be significantly higher in serum and synovial fluid of rheumatoid arthritis (RA) patients compared to healthy individuals and other diseases such as osteoarthritis (OA) and ankylosing spondylitis (AS).<sup>1</sup> Accordingly, 14–3–3η is now thought to be a diagnostic marker for early RA. Furthermore, some reports suggest that it correlates well with disease activity.<sup>2</sup>

**Objectives:** To assess the usefulness of serum levels of 14–3–3η protein in the diagnosis of RA in comparison with hands OA patients and healthy controls; furthermore, to correlate its levels with markers of inflammation in RA patients.

**Methods:** This study was carried out as a case control comparative study. Our sample consisted of three groups. Group 1 was made up of 30 RA patients fulfilling 2010 ACR–EULAR classification criteria for RA;<sup>3</sup> Group 2 made up of 30 hands OA patients according to OA ACR criteria<sup>4</sup> and group 3 of 30 healthy volunteers. Patients with other rheumatic and/or systemic diseases or infections were excluded.

Patients were assessed using detailed clinical history and examination. Laboratory investigations included complete blood picture, ESR, CRP, RF, ACPA and serum levels of 14–3–3η protein using manual enzyme-linked immunosorbent assay (ELISA).

**Results:** Mean (SD) age of RA group was 45.5 (9.5) years old; for OA group was 50.3 (8.8) years old, and the control group was 46.2 (6.9) years old. Females represented 96.7% of group 1; 83.3% of group 2, and 86.7% of group 3. RF was positive in 78% of RA group, 6.7% in OA group and 6.3% of control group. Mean (SD) of RF titer was 123 (10.3), 15.3 (5.4) and 14.4 (5.2) IU/ml respectively. ACPA was positive in 96.7% of group 1 and was negative in groups 2 and 3. Mean (SD) ACPA was 64.4 (6.6) U/ml in RA group.

Mean (SD) ESR was 32.5±8.2 in group 1, 22.0 (6.6) in group 2 and 16.1 (7.3) mm/hour in group 3. Mean (SD) CRP was 17.9 (5.04), 5.7 (2.8) in group 2 and 4.9 (2.4) mg/L in group 3.

Mean (SD) levels of 14–3–3η protein were significantly higher among RA compared to OA and control groups (3.63 (1.35), 0.23 (0.14) and 0.28 (0.08) ng/ml, respectively) ( $p<0.0001$ ).

The optimal cutoff point of 14–3–3η protein to diagnose RA was >0.2 with a sensitivity of 80%, specificity of 87%, positive predicted value of 86% and negative predicted value of 81%. The eta protein also had high diagnostic odds ratio (26.1).

No correlation was found between serum levels of 14–3–3 eta and CRP nor ESR ( $p>0.05$ ).

**Conclusions:** 14–3–3η is a specific marker for RA that should be used in conjunction with RF and ACPA for diagnosis of the disease. However, no correlation was found between 14–3–3η and markers of inflammation.

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AB0274

### ASSOCIATION OF SERUM PENTOSIDINE LEVELS WITH INTIMA MEDIA THICKNESS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Advanced glycation end products (AGEs) are formed by a non-enzymatic glycation process. Previously, we showed that pentosidine, as AGEs, was related to the severity of coronary artery disease (Kerkeni et al. 2014). Recently, we showed that AGEs are involved with disease activity in rheumatoid arthritis (RA) (Knani et al. 2017, 2018). No study about the relationship between serum pentosidine levels and intima media thickness (IMT) was evaluated.

**Objectives:** We aim to study the association of serum pentosidine levels with IMT in RA patients.

**Methods:** Our study included 30 control subjects and 40 patients with RA. The carotid IMT was measured using ultrasonography and serum pentosidine levels were determined by ELISA kit.

**Results:** Serum pentosidine levels were increased in RA patients vs control subjects ( $p<0.001$ ) and were increased with disease activity score (DAS28) ( $p<0.001$ ). IMT was increased with disease activity in RA patients ( $p<0.01$ ) and was positively associated with serum pentosidine levels ( $p<0.001$ ).

**Conclusions:** Serum pentosidine levels were increased with DAS28 and were associated with carotid IMT.

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AB0275

### THE MULTI-BIOMARKER DISEASE ACTIVITY SCORE TRACKS RESPONSE TO RITUXIMAB TREATMENT IN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** A multi-biomarker disease activity (MBDA) score was developed to objectively measure disease activity for patients with rheumatoid arthritis (RA).<sup>1</sup> The MBDA score is calculated by an algorithm using concentrations of 12 serum biomarkers. The MBDA score has been shown to track response to treatment with several DMARDs.<sup>2,4</sup>

**Objectives:** To assess the ability of the MBDA score to track response to rituximab treatment in RA patients.

**Methods:** Data were used from 3 cohorts (1 in the United Kingdom, 2 in the Netherlands) of RA patients treated with rituximab 1000 mg and methylprednisolone 100 mg at days 1 and 15. The MBDA score was assessed in serum samples at baseline (BL, n=57) and at 6 months (n=46). Wilcoxon signed-rank test was used to statistically compare the medians at BL and 6 months. Spearman's rank correlation ( $\rho$ ) was used to analyse relationships between BL and 6 month values and change ( $\Delta$ ) from BL to 6 months for MBDA score vs. the following endpoints: DAS28-ESR, DAS28-hsCRP, ESR, hsCRP and Health Assessment

Questionnaire (HAQ). Logistic regression analysis with adjustment for age, sex, smoking, ACPA and RF was used to assess the association between  $\Delta$ MBDA score and non-response, using EULAR response categories at Month 6.  $p<0.05$  was considered statistically significant.

**Results:** At baseline the median MBDA score and DAS28-ESR were 54.5 (range 15.0–84.0) and 6.3 (range 2.5–8.4), respectively. The improvement in both scores after 6 months was statistically significant ( $p=0.003$  and  $p<0.0001$ , respectively). MBDA score correlated with DAS28-ESR, DAS28-hsCRP, ESR and hsCRP at BL and Month 6 (table 1).  $\Delta$ MBDA score from BL to Month 6 correlated with changes in these measures, except for the correlation with  $\Delta$ DAS28-hsCRP ( $\rho=0.419$ ,  $p=0.053$ ). Spearman's correlation for  $\Delta$ MBDA score vs.  $\Delta$ DAS28-ESR was  $\rho=0.548$ ,  $p<0.0001$  (table 1).  $\Delta$ MBDA score also correlated with EULAR non-response (n=39), with adjusted OR=1.115 (95% CI=1.017–1.223,  $p=0.015$ ), which corresponds to an OR of 2.97 for every 10-unit change in MBDA score. Correlations were not observed between MBDA scores or  $\Delta$ MBDA score and the corresponding HAQ measurements (table 1).

**Abstract AB0275 – Table 1.** Correlations (Spearman's  $\rho$ ) between the MBDA score and clinical or biomarker endpoints based on measurements made at baseline (BL) or 6 months (6M), and of change ( $\Delta$ ) from BL to 6 months.

Endpoint	Timepoint or period for comparison with MBDA score	Available samples (N)	Spearman's $\rho$	p-value
DAS28-ESR	BL	46	0.487	0.001
	6M	40	0.478	0.002
	$\Delta$	37	0.548	<0.0001
ESR	BL	44	0.785	<0.0001
	6M	41	0.670	<0.0001
	$\Delta$	41	0.448	0.008
DAS28-hsCRP*	BL	23	0.488	0.015
	6M	23	0.488	0.032
	$\Delta$	23	0.419	0.053
hsCRP*	BL	24	0.801	<0.0001
	6M	23	0.814	<0.0001
	$\Delta$	23	0.676	0.001
HAQ	BL	39	-0.031	0.654
	6M	40	-0.056	0.730
	$\Delta$	33	0.132	0.486

BL: MBDA score and endpoint at baseline; 6M: MBDA score and endpoint at Month 6;  $\Delta$ : changes in MBDA score and endpoint, both from baseline to Month 6; DAS28: disease activity score using 28 joints; ESR: erythrocyte sedimentation rate; HAQ: Health Assessment Questionnaire; hsCRP: high-sensitivity C-reactive protein; MBDA: multi-biomarker disease activity.

\* United Kingdom cohort only

**Conclusions:** We have shown, for the first time, that the MBDA score tracked disease activity in RA patients treated with rituximab and that change in MBDA score reflected the degree of treatment response.

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AB0276

### COMPARISON OF HEALTH ASSESSMENT QUESTIONNAIRE DISABILITY PROGRESSION IN RHEUMATOID ARTHRITIS PATIENTS WITH PROPOSED SDAI, CDAI, AND RAPID3-BASED MINIMAL DISEASE ACTIVITY AND PATIENTS WITH LOW DISEASE ACTIVITY: RESULTS FROM A JAPANESE NATIONAL DATABASE

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**Background:** By OMERACT, a core-set definition of minimal disease activity (MDA) required a tender joint count (TJC) of 0, swollen joint count (SJC) of 0, and erythrocyte sedimentation rate (ESR)  $\leq 10$  mm/hour or the fulfilment of 5 of 7 core criteria, namely, pain  $\leq 2$ , SJC  $\leq 1$ , TJC  $\leq 1$ , health assessment questionnaire (HAQ)  $\leq 0.5$ , physician's global  $\leq 1.5$ , patient's global  $\leq 2$ , and ESR  $\leq 20$ .<sup>1</sup>

In addition to the original Disease Activity Score 28 (DAS28)-based MDA definition (DAS28  $\leq 2.85$ ),<sup>1</sup> we proposed a Simplified Disease Activity Index (SDAI)  $\leq 5.3$ , Clinical Disease Activity Index (CDAI)  $\leq 4.8$ , and Routine Assessment of Patient Index Data 3 (RAPID3)  $\leq 5$ , each value being two points higher than the respective remission criterion, as cut-offs for the MDA index in routine care for rheumatoid arthritis (RA).<sup>2</sup>

**Objectives:** To compare HAQ disability progression in patients with proposed SDAI, CDAI, and RAPID3-based MDA and patients with low disease activity (LDA) for each index.

**Methods:** We evaluated RA patients with functional remission (HAQ  $\leq 0.5$ ) registered with the Japanese National Database. We excluded patients with any missing values for patient SJC, TJC, physician's global, patient's global, pain, CRP, ESR, HAQ, or MDHAQ, which require the MDA to be assessed and the DAS28, SDAI, CDAI, and RAPID3 scores to be determined. HAQ disability progression from 2015 to 2016 was analysed in patients with MDA vs non-MDA and in those with LDA (or remission) vs non-LDA (or remission).

The interclass correlation of the disease activity categories of LDA and MDA in DAS28, CDAI (SDAI), and RAPID3 were also compared.

**Results:** In total 3798 patients were analysed, 76.5% of whom met the core-set definition of MDA and 40.3% of whom were assessed as being in Boolean remission. Patients with a core-set definition of MDA had less HAQ progression over one year (356 $\pm$ 71 days) than those without the core-set definition, at 0.036 (95% CI: 0.026–0.045) and 0.066 (0.050–0.082) (p=0.002), respectively. The progression of HAQ in each disease activity state is summarised in table 1.

Patients in the DAS28, SDAI, CDAI, and RAPID3-based MDA group showed less HAQ progression. The same results were found for LDA. For the MDA categories, the interclass correlation for CDAI (SDAI) vs DAS28, CDAI (SDAI) vs RAPID3, and DAS28 vs RAPID3 was 0.585 (0.617), 0.568 (0.557), and 0.361, respectively, and 0.449 (0.442), 0.411 (0.410), and 0.371 for LDA, respectively.

Abstract AB0276 – Table 1

Index-based MDA	HAQ progression, mean (95% CI)	Index based LDA	HAQ progression, mean (95% CI)
DAS28 $\leq 2.85$	0.032 (0.022–0.041)	DAS28 $\leq 3.2$	0.034 (0.023–0.045)
DAS28 > 2.85	0.064 (0.051–0.077)	DAS28 > 3.2	0.052 (0.041–0.063)
p	<0.001	p	0.011
SDAI $\leq 5.3$	0.036 (0.026–0.045)	SDAI $\leq 11$	0.040 (0.031–0.048)
SDAI > 5.3	0.058 (0.044–0.072)	SDAI > 11	0.074 (0.049–0.099)
p	0.008	p	0.010
CDAI $\leq 4.8$	0.036 (0.027–0.046)	CDAI $\leq 10$	0.039 (0.031–0.048)
CDAI > 4.8	0.056 (0.042–0.070)	SDAI > 10	0.073 (0.049–0.097)
p	0.020	p	0.011
RAPID3 $\leq 5$	0.038 (0.029–0.047)	RAPID3 $\leq 6$	0.037 (0.029–0.046)
RAPID3 > 5	0.058 (0.042–0.074)	RAPID3 > 6	0.068 (0.050–0.086)
p	0.031	p	0.003

**Conclusions:** Among patients with functional remission, both the MDA and LDA categories showed less HAQ progression over one year.

The interclass correlation for MDA was more acceptable than that for LDA. Index-based MDA, which provides more stringent criteria than LDA, may serve as an alternative target for LDA in patients who have difficulty achieving remission.

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AB0277

### LEPTIN AND ADIPONECTIN LEVELS IN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Rheumatoid Arthritis (RA) is a chronic inflammatory autoimmune disorder characterised by systemic inflammation of joints, in particular the synovial membrane, cartilage and bone. Leptin (LEP) and adiponectin (ADIP) belong to a distinct group of biological molecules, adipokines which are secreted by white adipose tissue and have a central role in energy storage and metabolism.

**Objectives:** To compare fasting serum LEP and ADIP in RA to healthy controls and to investigate whether fasting LEP and ADIP serum levels change following a change in RA treatment.

**Methods:** Male and female subjects aged 18 years old or above with RA, fulfilling the 2010 ACR/EULAR classification criteria and having DAS28 score >4.2, were recruited and followed up for 90 days. LEP and ADIP levels were measured using ELISA. Fasting glucose, lipids and insulin levels were also measured as indicating factors for co-morbidities. The associations between RA patients at baseline and controls were assessed by uncorrelated/unrelated t-test analyses while associations between RA patients at baseline, day 30 and day 90 were assessed by one-way correlated/related analysis of variance.

**Results:** We studied 30 RA patients with mean (SD) age of 56.33 (13.84) years, of whom 24 (80%) were female and 15 healthy individuals with mean (SD) age of 53.80 (13.97) years, of whom 12 (80%) were female. LEP and ADIP levels for control subjects were 28.36 (15.08) ng/mL (p=NS vs RA at baseline) and 14.76 (4.42)  $\mu$ g/mL (p<0.05 vs RA at baseline) (table 1). Over 90 days DAS28 and HAQ score improved significantly in RA patients. LEP levels for RA patients were 29.65 (18.17) ng/mL at baseline, 30.81 (17.65) ng/mL at day 30 and 25.90 (15.01) ng/mL at day 90 (p=NS) whilst ADIP levels for RA patients were 16.78 (8.73)  $\mu$ g/mL at baseline, 16.65 (8.70)  $\mu$ g/mL at day 30 and 15.44 (7.24)  $\mu$ g/mL at day 90 (p=NS) (table 2).

Abstract AB0277 – Table 1. Demographics and baseline adipokines for RA patients and control subjects. All values are mean (SD) unless otherwise indicated where we use n (%)\*. (\*\*Levene's test for equality of variances value p<0.05)

Variable	RA Patients	Control subjects	Levene's test for equality of variances (p)
Gender (M/F)	6 (20%)/24 (80%)	3 (20%)/12 (80%)	1.000
Age (years)	56.33 (13.84)	53.80 (13.97)	0.850
LEP (ng/mL)	29.65 (18.17)	28.36 (15.08)	0.421
ADIP ( $\mu$ g/mL)	16.78 (8.73)	14.76 (4.42)	0.023**

Abstract AB0277 – Table 2. Change over time in adipokine levels and RA parameters for RA patients at baseline, day 30 and day 90. All values are mean (SD). (\*\*One Way ANOVA significance value p<0.05)

Variable	LEP (ng/mL)	ADIP ( $\mu$ g/mL)	RA parameters			
			DAS28 score	HAQ score	PAIN score	HEALTH score
RA patients (day 0)	29.65 (18.17)	16.78 (8.73)	5.59 (0.56)	1.20 (0.70)	1.80 (0.73)	1.59 (0.55)
RA patients (day 30)	30.81 (17.65)	16.65 (8.70)	4.39 (0.93)	0.84 (0.66)	1.07 (0.82)	1.11 (0.84)
RA patients (day 90)	25.90 (15.01)	15.44 (7.24)	3.92 (1.08)	0.76 (0.74)	1.07 (0.82)	1.32 (0.81)
One Way ANOVA (p)	0.515	0.791	0.000**	0.045**	0.000**	0.046**

**Conclusions:** ADIP was significantly higher in RA patients at baseline compared to control subjects and there was a trend towards normalisation of levels as inflammation improved. The role of ADIP in active RA remains unclear and further examination of the site of origin of ADIP as well as its role in pro- and anti-inflammatory pathways warrants further study.

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AB0278

### INVESTIGATION OF POOR PROGNOSTIC FACTORS AMONG RHEUMATOID ARTHRITIS PATIENTS IN TURKBIO REGISTRY

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**Background:** TURKBIO is the Turkish version of Danish DANBIO rheumatologic database which has been established in 2011. Patients' data including age, sex, disease type and duration, and previous or current treatment with conventional (cs), targeted synthetic (ts) and biological (b) DMARDs were collected. In 2016, the EULAR RA management guideline recommended assessment of certain prognostic factors while deciding the treatment strategy after the first csDMARD failure.

**Objectives:** We examined the frequency and influence of these poor prognostic factors on treatment response in bDMARD and tsDMARD initiating RA patients enrolled in TURKBIO.

**Methods:** 898 biological and targeted synthetic DMARDs receiving RA patients from 8 participating centres of TURKBIO were studied. Seven investigated poor-prognostic factors were: <sup>1</sup> Moderate to high disease activity (after csDMARD therapy), <sup>2</sup> Elevated acute phase reactants, <sup>3</sup> High swollen joint counts ( $\geq 4$ ), <sup>4</sup> High RF/ACPA titers, <sup>5</sup> Combinations of the above, <sup>6</sup> Erosions, <sup>7</sup> Failure of  $\geq 2$  csDMARDs. The frequencies of these factors at treatment initiation and influence of these on achievement of remission/remission+low disease activity (LDA) according to DAS28-CRP at the 6th month of treatment were evaluated in overall any bDMARD and tsDMARD-receiving patients.

**Results:** Among the prognostic factors; factors 1, 2, 4, 6 and 7 were found in over 60% of patients while factors 3 and 5 were present in about 30%. Factors 1 and 3 were more frequent in patients who were in moderate/high disease activity compared to those in remission +low disease activity (table 1). Same factors 1 and 3 were determined at higher percentage in non-remission than remission group (Factor 1: 93.4% vs. 82.2%,  $p < 0.001$ ; factor 3: 43% vs. 30.7%,  $p = 0.002$ ). These two factors were also significantly more frequent in patients withdrawn from the treatment (Factor 1: 93% vs. 85%,  $p < 0.001$ ; factor 3: 41% vs. 34%,  $p = 0.038$ ). In TNFi group besides factors 1 and 3, factors 5 and 7 were also significantly more frequent in non-remission group whereas, in the RTX group, only factor 1 was significantly more frequent in remission group. For the other bDMARDs and tsDMARD (ABA, TCZ, TOFA), we did not find any difference in poor prognostic factors among patients who did achieve remission and did not.

**Abstract AB0278 – Table 1.** Frequencies of poor prognostic factors in RA patients initiating bDMARDs and tsDMARD by disease activity\* at the 6th month of treatment

Factors	Remission+low disease activity, %	Moderate+high disease activity, %	P value
Factor 1: Moderate to high disease activity (after csDMARD therapy)	95.9	83.6	<0.001
Factor 2: Elevated acute phase reactants	100	99.5	-
Factor 3: High swollen joint counts ( $\geq 4$ )	47.1	31.7	<0.001
Factor 4: High RF/ACPA titers	68.3	71.9	0.465
Factor 5: Combinations of the factors 1, 2, 3, 4	31.3	25.9	0.284
Factor 6: Erosions	56.5	65.6	0.332
Factor 7: Failure of $\geq 2$ csDMARDs	69.4	69	0.918

\* Disease activity was assessed by using DAS28-CRP at the 6<sup>th</sup> month of treatment

**Conclusions:** Five of the seven poor prognostic factors were detected more than half of the RA patients at bDMARD and tsDMARD initiation in TURKBIO. Patients with poor prognostic factors especially factors 1 and 3 achieved remission less frequently. Additionally, there was a relationship between bDMARDs and tsDMARD withdrawal and factors 1 and 3. The influence of these factors was mainly observed in TNFi receiving group.

**Disclosure of Interest:** None declared

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AB0279

### RAPID3 IS NOT LONGITUDINALLY ASSOCIATED WITH DAS28-ESR IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** The Routine Assessment of Patient Index Data 3 (RAPID3) is a patient reported outcome (PRO) proposed to conveniently measure disease activity in rheumatoid arthritis (RA) based on functioning, pain and global health scores. DAS28 (including PRO and objective measures) is the most frequently used score in clinical practice and research for that purpose<sup>[1]</sup>. It has been suggested that composite scores measuring PROs only (e.g. RAPID3) might add to the assessment of disease activity over time but this claim is yet to be formally tested.

**Objectives:** In this study we evaluated a possible longitudinal association between RAPID3 and DAS28-ESR (including individual components) in patients with RA from daily clinical practice.

**Methods:** Adult patients with RA on stable treatment with either conventional synthetic disease modifying drugs (csDMARDs) and/or biologic DMARDs (bDMARDs), followed in one centre, were included. Patients were followed every 3 months up to 3 years and in each visit both clinical and medication data was collected by rheumatologists/research nurses. The longitudinal association between RAPID3 (range: 0–30) with DAS28-ESR and its individual components [tender joint count (TJC; 0–28); swollen joint count (SJC; 0–28); patient global assessment (PGA; 0–10) and ESR (mm/h)] was tested (in separate models) by longitudinal generalised estimating equations (GEE) with auto-regression. Interactions between RAPID3 with gender (male vs female), VAS pain ( $\geq 5$  vs  $< 5$ ), PGA ( $\geq 5$  vs  $< 5$ ) and age ( $\geq 62$  vs  $< 62$ ) at baseline were tested and if significant ( $p < 0.20$ ) and clinically relevant each model (either using DAS28 or its individual components as outcome) was stratified accordingly.

**Results:** In total, 330 patients were included [mean (SD) age: 62<sup>12</sup> years, 68% female, baseline mean (SD) DAS28: 3.3 (1.4) and RAPID3: 11.5 (6)]. The mean (SD) follow-up period was 10.7 (9.7) months. Although, statistically significant, we only found a poor association between RAPID3 and DAS28-ESR over time (table 1). An increase of one unit in RAPID3 (0–30) was associated with an increase of only 0.1 units of DAS28-ESR. Gender, age, PGA and VAS pain were not found to meaningfully modify the association between RAPID3 and DAS28. A far stronger association was found between RAPID3 and the 'subjective components' [TJC:  $\beta = 0.30$  (95%: 0.20; 0.39); and PGA:  $\beta = 0.31$  (95%: 0.28; 0.35)] of DAS28-ESR, as compared to the 'objective components' (i.e., SJC and ESR; the latter only significant in males) (table 1).

**Abstract AB0279 – Table 1.** Longitudinal association between RAPID3 and DAS28 and each individual component

	Main effect $\beta$ (95% CI)	Males $\beta$ (95% CI)	Females $\beta$ (95% CI)
DAS28 ESR	0.10 (0.10; 0.10)	NA	NA
Swollen joint count	0.10 (0.06; 0.14)	NA	NA
ESR	NA	0.12 (0.03; 0.22)	-0.10 (-0.16; 0.14)
Tender joint count	0.30 (0.20; 0.39)	NA	NA
PGA	0.31 (0.28; 0.35)	NA	NA

Each line is a separate model; NA, not applicable.

**Conclusions:** There is no meaningful longitudinal association between RAPID3 and DAS28. DAS28 captures objective signs of disease activity over time in RA while RAPID3 only captures subjective symptoms of RA.

#### REFERENCE:

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**Disclosure of Interest:** None declared

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**AB0280 GENDER-DIFFERENCES IN CARDIO-VASCULAR RISK FACTORS IN PATIENTS WITH INFLAMMATORY RMDs**

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**Background:** Patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) and spondyloarthritis (SpA) have an increased risk of cardiovascular events when compared to the general population. This increase is probably due to both the deleterious effects of inflammation and the traditional cardio-vascular risk factors (CVRF).

**Objectives:** Analyse the differences by gender in the distribution of traditional CVRF in patients with chronic arthritis included in a screening program.

**Methods:** A program for the detection and management of traditional CVRF in patients with chronic arthritis was implemented following EULAR recommendations. Patients with RA, PsA and SpA followed-up at our department were included in this program. Patients underwent a baseline visit in a nurse-clinic where cardiovascular (CV) risk was assessed. Data on smoking status, diet, exercise, diagnosis of hypertension (HT), diabetes mellitus (DM), hypercholesterolemia (HCh) and prior CV events. The height and weight, the abdominal perimeter and the blood pressure of patients were measured. Results of a blood test previously ordered by the managing physician was recorded.

SCORE index was calculated as applied to Spanish population and then modified according to EULAR recommendations. Treatment targets (previously agreed upon by the department of rheumatology) were set; if pharmacological treatment was needed, patients were referred to their rheumatologist or GP.

Data are presented of all patients included in this screening program.

**Results:** The number of patients assessed at the nurse-led clinic for CVRF assessment and with data on gender, is 416. In the table 1 we present the characteristics of these patients grouped by gender

Abstract AB0280 – Table 1

		Women (n=242)	Men (n=174)
Age years, mean (SD)		59.6 (±11.9)	56.7 (±12.8)
Rheumatic disease	RA	179 (73.9%)	62 (35.6%)
	SpA	25 (10.3%)	70 (40.2%)
	PsA	38 (15.7%)	42 (24.2%)
Diabetes mellitus	Prior diagnosis	25 (10.3%)	31 (17.8%)
	New diagnosis	2 (0.9%)	4 (2.8%)
	Poor control	6 (2.4%)	10 (32.2%)
Hypertension	Prior diagnosis	93 (38.4%)	73 (42%)
	New diagnosis	25 (16.7%)	22 (21.7%)
	Poor control	53 (37%)	33 (45.2%)
Hypercholesterolemia	Prior diagnosis	91 (37.6%)	69 (39.6%)
	New diagnosis	28 (18.5%)	23 (21.9%)
	Poor control	33 (36.2%)	16 (23.2%)
Smoker		48 (19.8%)	60 (24.5%)
Obesity		86 (35.5%)	63 (36.2%)
Prior CV event		9 (3.7%)	20 (11.4%)

Data expressed as n (%) except where specified

\* Poor control of hypercholesterolemia is defined as LDL over the target recommended by European guidelines for each risk stratification.

**Conclusions:** In a similar manner as the general population, there is a greater number of CV events in men than in women. However, the gender-distribution of traditional CVRF is similar except for DM, more common in men.

**Disclosure of Interest:** None declared

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**AB0281 REDUCTION RATE OF RHEUMATOID FACTOR REFLECTS DISEASE ACTIVITY OF RHEUMATOID ARTHRITIS**

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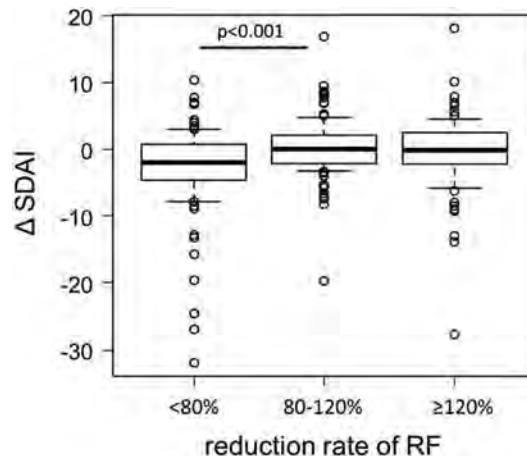
**Background:** Rheumatoid factor (RF) is involved in the pathology of rheumatoid arthritis (RA) and its titer varies during the course of treatment with biological or synthetic DMARD.

**Objectives:** In this study, we examined the relationship between RF change rate and disease activity.

**Methods:** We analysed 287 RA patients (mean age 62.3 years; mean disease duration 13.1 years) in our hospital between 2015 and 2017, who were able to confirm the RF, and 3 groups were classified according to the change rate of RF for 1 year (92 in decreasing less than 80%, 114 in unchanged 80% or more, less

than 120% and 81 in increasing 120% or more). We evaluated disease activity by simplified disease activity index (SDAI).

**Results:** The drugs used are: MTX usage rate 63.1%, mean amount 3.81 mg, PSL usage rate 37.3%, mean amount 1.47 mg, biological drugs usage rate 48.8%. Disease activity change amount in 1 year (delta SDAI) was -0.88 (from 6.90 to 6.02). The median RF titer at baseline was 76 (27.5–178.5), the median RF change rate was 96% (71.5–125) and delta SDAI was significantly improved in the decreasing group (-1.97, 0.005, -0.04, p=0.0011). The swollen joint counts, tender joint counts, global assessment of evaluator and CRP were similarly improved significantly in this group.



**Conclusions:** Although RF dose not decrease in all cases, it suggested that reduction rate of RF reflects disease activity.

**Disclosure of Interest:** None declared

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**AB0282 ADJUSTING THE DOSE OF TOFACITINIB TO ACHIEVE OPTIMAL RESULTS IN THE MANAGEMENT OF PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS (RA) MAY OFFER MORE SUCCESSFUL RESULTS THAN UTILISING A STANDARD FIXED ONE DOSE APPROACH**

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**Background:** We have previously reported results of patients with active RA who had been unresponsive to tofacitinib at 5 mg bid but who had demonstrated significant response after dose escalation to 10 mg bid.<sup>1,2</sup> This extension trial was performed to see if 9 patients who had failed to reach treatment target on 5 mg bid but then responded to 10 mg bid of tofacitinib would maintain their clinical target if the dose was reduced down to 5 mg bid. Furthermore, if the patients could not maintain their clinical response on the lower dose, we explored whether increasing the dose of tofacitinib up to 10 mg bid could again result in a target response.

**Objectives:** The objectives were as follows: to explore the response of patients who achieved a treatment target when taking 10 mg bid of tofacitinib and then reduced the dose down to 5 mg bid; to report the results of the patients who could not maintain the target response at 5 mg bid and then increased the dose back up to 10 mg bid; and to identify if there was any separation between the clinical and structural findings at 5 mg bid vs 10 mg bid.

**Methods:** Nine RA patients who were unresponsive to treatment with tofacitinib at a dose of 5 mg bid plus MTX (10–25 mg weekly) were dose escalated to 10 mg bid and reached low disease activity (LDA) or remission at the increased dose. These patients were maintained on 10 mg bid of tofacitinib for 6 months and sustained a clinical target of LDA or remission. After 6 months, the dose of tofacitinib was reduced back to 5 mg bid which had previously not been an effective dose. The clinical response was measured by the Clinical Disease Activity Index (CDAI) and the structural response was measured by an MRI of the index hand/wrist and blindly read by a musculoskeletal radiologist using a modified OMERACT-RAMRIS score. If the patients could not maintain their positive clinical response for 3 months the dose of tofacitinib was escalated back up to 10 mg bid.

**Results:** Of the 9 enrolled patients, 6 patients maintained LDA or Remission over the next 6 months once the dose of tofacitinib was reduced back down to 5 mg bid. Three<sup>3</sup> patients were unable to maintain their treatment target at the reduced dose and were dose escalated back up to 10 mg bid at which time they achieved the treatment target. (See table 1) The MRI findings showed no difference in structure at either dose and do not appear to demonstrate a relationship to the clinical findings. There were no clinically significant adverse events in either group.

Abstract AB0282 – Table 1

6 Patients who maintain target once reducing dose tofacitinib to 5 mg bid				
Patients	CDAI BSL	CDAI target on 10 mg bid	CDAI 3 months on 5 mg bid	CDAI 6 months on 5 mg bid
003	45.9	2.6	7.2	8.2
004	65.2	4.4	4.7	0.1
005	56.1	3.6	9.4	2.6
007	27.9	2.3	1.7	2.6
012	25.3	5.1	6.4	9.3
014	21.6	1.4	8.5	3.2

3 Patients who could not maintain target at 5 mg bid tofacitinib and were increased to 10 mg bid						
Patients	CDAI BSL	CDAI target on 10 mg bid	CDAI 3 months on 5 mg bid	CDAI 3 months on 10 mg bid	CDAI 6 months on 10 mg bid	CDAI 9 months on 10 mg bid
008	34.3	9.2	19.2 inc dose	2.6	2.5	
018	31.8	2.5	16.2 inc dose	11.9	8.3	
019	27.3	8.9	9.7	11.9 inc dose	1.9	2.7

**Conclusions:** This study confirms the previous findings that 10 mg bid of tofacitinib may be the effective dose needed for some patients with active RA to reach treatment target.<sup>(1)</sup> It also suggests that there is an opportunity to reduce the escalated dose back down to the standard dose once a target response is achieved. This in many ways is similar to the clinical use of other drugs used to treat RA including corticosteroids, MTX and biologics where dose adjustment may well increase the therapeutic benefit of the molecule and allow subsequent dose adjustments to maintain efficacy with a lower adverse event profile. Additional studies will be needed to test the results found in this trial.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.3359

#### AB0283 INDICES OF ANTIBODIES TO FIBRONECTIN ASSOCIATED WITH CLINICAL MANIFESTATIONS OF RHEUMATOID ARTHRITIS

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**Background:** According to available data, fibronectin (FN) is implicated in progressing cartilage destruction in arthritis of varying etiology. It is established that it is not native FN that has the ability to enhance the expression of chondrocyte catabolism gene thus causing. Antibodies enhance both resorption and synthesis of osseocartilaginous tissue; they affect proteoglycan and glycosaminoglycan production in connective tissue, and also block active centres of FN molecule.

**Objectives:** Determining the level of FN antibodies using fibronectin-based magnetocontrollable immobilised adsorbents is an additional criterion of rheumatoid arthritis disease activity. Demonstrating the FN indices and its antibodies in blood serum of healthy individuals, and in that of RA patients depending on the disease activity. Demonstrating that the level of FN antibodies in the blood serum of RA patients reliably differs from that of healthy people.

**Methods:** 117 RA patients receiving hospital treatment at Municipal hospital 25 of Volgograd were examined. The patients' mean age was 49.9±13.9. The mean duration of disease was 9.1±1.57 years. Low (I) disease activity was noted in 14 patients (12%), moderate (II) – in 66 (56.4%), and high (III) – in 37 (31.6%) patients with RA. According to the degree of articular dysfunction the patients were classified in the following way: 11 patients (9.4%) showed articular insufficiency functional class II (intact occupational ability), 87 patients (74.41%)

showed insufficiency functional class III (lost occupational ability), and 19 patients (16.2%) showed insufficiency functional class IV (lost autonomy).

The articular syndrome underlies all clinical presentations of RA. In most patients (102 individuals, 87.2%) RA took the form of polyarthritis; in the remaining 15 people (12.8%) oligoarthritis was noted. 107 patients (91.5%) showed hand joint involvement, 99 (71.8%) – knee joints, 71 (60.7%) – talocrural joints, 61 (52.1%) – elbow joint, 49 (41.9%) – shoulder joints, and 37 patients (31.6%) showed foot joint involvement. Serum from 30 apparently healthy individuals, donors from the regional hemotransfusion centre in Volgograd, was used as control.

The FN antibody titer was determined using an original technique: enzyme immunoassay with FN-based immobilised granulated antibodies with magnetic properties.

**Results:** The mean FN content in the plasma of healthy people was 351.0 ±65.1 mcg/ml. The mean concentration of specific antibodies in donor sera was 0.031±0.0029 optical density units. An elevated concentration of plasma FN was detected in 39 RA patients (33.3%). The mean concentration of serum antibodies to FN in RA patients was 0.095±0.014 optical density units, which exceeded the values in the control group (p<0.05). An elevated content was noted in 49 patients (41.9%).

**Conclusions:** A correlation analysis revealed a positive association between FN antibody concentration, and parameters of ESR (r=0.27, p<0.03), and circulating immune complex (r=0.43, p<0.05), as well as indices indicating the degree of exudative-inflammatory process in the joints, and the extent of pain syndrome (DAS score of 28, articular index, pain score, swelling index) (p<0.05).

**Disclosure of Interest:** None declared

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#### AB0284 RELATIONSHIP OF BIOMARKERS, ULTRASOUND (US) SIGNS OF JOINT DAMAGE AND RADIOGRAPHIC PROGRESSION IN PATIENTS WITH RHEUMATOID ARTHRITIS(RA)

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**Background:** Rheumatoid arthritis (RA) is a chronic inflammatory immune-mediated disease, based on the imbalance of biomarkers, leading to the appearance of inflammatory changes in the joints, the progression of bone and cartilage destruction.

**Objectives:** to identify the relationship between cytokines, their dynamic changes, ultrasound (US) signs and radiologic progression in 12 month prospective study in patients RA.

**Methods:** 35 patients (median age 55.0 [48.0; 64.0] years) with early RA use MTX and/or biologic therapy in accordance with the treat-to-target concept. Serum cytokine concentrations were determined using the xMAP multiplexing technology baseline, 3 and 6 months after the start of therapy. US with grey scale (GS), power Doppler (PD) and destructive changes (erosion), according to the criteria of OMERACT, were performed baseline, 3, 6, 9 and 12 months after the start of therapy. We analysed absolutely levels and their changes(Δ). X-ray examination was conducted baseline and at 12 month of therapy with an assessment of X-ray changes by Sharp van der Heijde scores (ΔSHS).

**Results:** Levels of proinflammatory cytokines (IL1β, IL6, IL12, IL15, TNFα) decreased by 3 month. Significant differences in PD-group at the end of observation were revealed only for IL6 and TNFα, and with X-ray progression – for ΔIL17 level at 6 month.

At baseline a positive correlation was found between PD and levels of IL1β (r=0.34), IL6 (r=0.42). We found correlation between PD at 12 month and ΔIL1β by 6 month, ΔTNFα by 3 month. In the PD-group concentration of IL6 baseline was significantly higher: 75.2 (37.9; 101.7) vs 38.7 (19.2; 59.6); by 6 month level of TNFα in this group also higher: 67.6 (34.3;125.5) vs 38.8 (21.9; 67.2). Radiographic progression was detected in 6 of 35 RA patients; this group was with PD and destructive change by US was significantly higher.

We found correlation between ΔIL17 and ΔFGF levels at 3 month with PD at 3 month: r=0.57 p=0.001 and r=0.52 p=0.004, respectively. Also we found significantly correlation between ΔIL17 and ΔFGF at 3 month and ΔIL17 at 6 month with the X-ray examination: the sum of erosions, the sum of the narrowing of the joints and the total score (for IL17 at 3 month r=0.43 p=0.01, r=0.51 p=0.0018, r=0.52 p=0.001, respectively, for the FGF at the 3 month r=0.37 p=0.03, r=0.41 p=0.014, r=0.41 p=0.014, respectively, for IL17 at 6 month r=0.38 p=0.024, r=0.39 p=0.019, r=0.4 p=0.016, respectively).

**Conclusions:** The revealed relationship of active synovitis by US, X-ray progression and biomarkers of inflammation in RA confirm the role of ultrasound as a method of independent evaluation of the course and outcomes of the disease.

**Disclosure of Interest:** None declared

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**AB0285 DO SPOUSES' ILLNESS PERCEPTIONS AFFECT THE WOMEN WITH RHEUMATOID ARTHRITIS?**

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**Background:** Spouses are often significant source of support and the spouse's views about rheumatoid arthritis (RA) are related to better psychological and physical health in women with RA.

**Objectives:** The aim was to investigate the effect of spouses' illness perceptions on health status of women with RA.

**Methods:** One-hundred and one married women diagnosed with RA and their husbands were enrolled. Husbands' beliefs about RA were assessed by husband-version of the Illness Perception Questionnaire-Revised (IPQ-R). Visual analogue scale-pain (VAS-pain), DAS-28, the Health Assessment Questionnaire-Disability Index (HAQ-DI), and Beck Depression Inventory (BDI) were evaluated in patients. Kolmogorov-Smirnov and Spearman's correlation tests, multiple regression analyses were used for statistical analysis.

**Results:** Median age of patients and husbands were 57<sup>(22-75)</sup> years and 60<sup>(24-77)</sup> years, respectively. There were positive correlations between consequences subscale and VAS-pain, HAQ-DI, and BDI ( $p < 0.001$ ). Positive correlations were detected between emotional subscale and HAQ-DI, BDI ( $p < 0.001$ ) and VAS-pain ( $p = 0.021$ ). Timeline cyclical subscale was positively correlated with HAQ-DI ( $p < 0.001$ ) and BDI ( $p = 0.001$ ). The husband-version of the IPQ-R domains was not correlated with DAS-28. In regression analysis; consequences ( $p < 0.001$ ), emotional representations ( $p < 0.001$ ) and timeline cyclical ( $p < 0.05$ ) subscales were found to be influential variable on HAQ-DI. Significant correlation with VAS-pain was consequences, and BDI was associated with emotional representations ( $p < 0.05$ ).

**Conclusions:** We found that in general having more pessimistic illness perceptions in spouses was related to higher disability, pain and depression levels in women with RA. Having more optimistic perceptions of spouses about RA may result in improved health status in women with RA.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.1140

**AB0286 ASSESSMENT OF TREATMENT ADHERENCE IN RHEUMATOID ARTHRITIS ITALIAN PATIENTS USING A VALIDATED VERSION OF THE 5-ITEM COMPLIANCE QUESTIONNAIRE FOR RHEUMATOLOGY (I-CQR5)**

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**Background:** The 5-item Compliance Questionnaire for Rheumatology (CQR5) allows the identification of patients likely to be high adherers (HA) to anti-rheumatic treatment (i.e. taking  $\geq 80\%$  of their medications correctly), or "low" adherers (LA).<sup>1</sup> We have previously validated an Italian version of the questionnaire (I-CQR5) following standardised guidelines.

**Objectives:** The objective was to investigate what factors are associated with high treatment adherence according to I-CQR5 in RA.

**Methods:** RA patients (disease duration  $> 1$  year, undergoing treatment with  $\geq 1$  self-administered biological or conventional synthetic disease-modifying anti-rheumatic drugs (bDMARDs, csDMARDs), capable of completing the questionnaire unaided) completed I-CQR5 on one occasion. I-CQR5 were anonymous and clinical data were retrieved anonymously from the local database. To investigate what factors were associated with high adherence, we included demographic and social characteristics, clinical and treatment information. Factors achieving a  $p < 0.10$  in univariate analysis were included in the multivariate regression analysis.

**Results:** Among 604 RA patients, 328 patients were enrolled, 18 questionnaires were incomplete.

Median age of the patients was 57 years,<sup>48-67</sup> females were 232 (82%), disease duration was 12 years;<sup>7-19</sup> 193 (64.3%) patients were treated with bDMARDs and 107 (54.6%) with csDMARD only; 270 (90.3%) were in low disease activity or remission (figure 1).

HA were found to be 35.2% (109/310) of the patients. 40.2% (79/193) were on bDMARDs and 22.4% (24/107) on csDMARDs. Older age, lower education level, higher prednisone daily dose, use of a csDMARD (particularly hydroxychloroquine and sulfasalazine) and higher patient-VAS were significantly more frequent in LA compared with HA (figure 1). In the multivariate analysis, bDMARD treatment and employment resulted independently associated with high adherence: OR 2.88 (1.36-6.1),  $p = 0.006$  and OR 2.36 (1.21-4.62),  $p = 0.012$  respectively (table 1).

**Abstract AB0286 – Table 1.** Factors associated with high adherence to anti-rheumatic treatment defined by I-CQR5: a multivariate regression analysis model

	OR (95% C.I.)	p value
Female gender	0.79 (1.58-0.39)	0.501
Employment	2.36 (1.21-4.62)	0.012
bDMARD treatment	2.88 (1.36-6.1)	0.006
Patient-VAS (per 10-unit increase)	0.88 (0.78-1)	0.052
Model constant		<0.001

OR odds ratio, C.I. confidence interval, bDMARD biological DMARD, DMARD disease-modifying anti-rheumatic drug, VAS visual analogic scale.

**Abstract AB0286 – Table 2.** Demographics and clinical variables according to high and low adherence to treatment defined by I-CQR5.

	Total	HA	LA	p value
No.	310	109	201	-
Females (%)	232 (82)	88 (85.4)	144 (80)	0.081 <sup>†</sup>
Age, years, median (IQR)	57 (48-67)	54 (46-64.8)	59 (49-66)	0.011 <sup>†</sup>
BMI, median (IQR)	24 (22-28)	25 (23-28)	24 (21-27.3)	0.094 <sup>†</sup>
Smokers, n (%)	45 (17.2)	13 (16)	32 (17.7)	0.746
Employed, n (%)	127 (44.1)	58 (62.4)	69 (35.4)	$p < 0.001$ <sup>†</sup>
Education level				0.114
Primary school, n (%)	35 (12.1)	10 (9.4)	25 (13.6)	
Middle school, n (%)	115 (39.7)	35 (33)	80 (43.5)	
Secondary school, n (%)	101 (34.8)	45 (42.5)	56 (30.4)	
University, n (%)	39 (13.4)	16 (15.1)	23 (12.5)	
Primary/middle school education, n (%)	150 (51.7)	45 (30)	105 (70)	0.016 <sup>†</sup>
Social status				0.921
Living with parents and family	18 (7)	6 (7.5)	12 (6.8)	
Living alone	34 (13.2)	10 (12.5)	24 (13.6)	
Living with partner and family	167 (72.8)	57 (71.3)	130 (73.4)	
Other	18 (7)	7 (8.9)	11 (6.2)	
Positive RF and/or ACPA, n (%)	129 (53.7)	40 (38.5)	89 (65.6)	0.178
Disease duration, years, median (IQR)	12 (7-19)	12 (7.3-18)	11 (6.8-20)	0.876
Fibromyalgia, n (%)	51 (18)	15 (14.6)	36 (20)	0.252
csDMARD treatment, n (%)	165 (54.5)	44 (40.7)	121 (62.1)	$p < 0.001$ <sup>†</sup>
Methotrexate, n (%)	114 (37.6)	32 (29.6)	82 (42.1)	0.033
Leflunomide, n (%)	31 (10.2)	6 (7.4)	23 (11.8)	0.227
Other csDMARD, n (%)	42 (13.9)	7 (6.5)	35 (17.9)	0.006
bDMARD treatment, n (%)	193 (64.3)	79 (76.7)	114 (57.9)	0.001 <sup>†</sup>
Treatment duration $> 24$ months, n (%)	178 (79.5)	75 (78.1)	103 (80.5)	0.667
PDN daily dose, median (IQR)	1 (0-5)	1 (0-2.5)	1.5 (0-5)	0.011 <sup>†</sup>
NSAIDs, n (%)	185 (65.6)	62 (62.6)	123 (67.2)	0.439
Painkillers, n (%)	76 (28.6)	30 (30.6)	46 (27.4)	0.574
Concomitant chronic treatment, n (%)	156 (53.1)	51 (49)	105 (55.3)	0.307
DAS28, median (IQR)	2.3 (1.8-2.8)	2.1 (1.7-2.7)	2.3 (1.9-2.3)	0.088 <sup>‡</sup>
Remission <sup>§</sup> , n (%)	173 (57.9)	60 (55.6)	113 (59.2)	0.544
Low disease activity <sup>¶</sup> , n (%)	270 (90.3)	101 (93.5)	169 (88.5)	0.158
Patient - VAS, median (IQR)	30 (10-51)	20 (6-54)	40 (20-56.3)	0.003 <sup>†</sup>
Physician - VAS, median (IQR)	10 (5-20)	12.5 (1.3-20)	10 (5-20)	0.984
HAQ, median (IQR)	0.5 (0-1)	0.3 (0-1)	0.5 (0.1-1)	0.114
Disease flares, median (IQR)	44 (31.4)	10 (27)	34 (33)	0.507
No. of assessments per year, median (IQR)	3 (2-4)	3 (2-4)	3 (2-4)	0.49
Distance from clinic, km, median (IQR)	30 (11-45)	30 (20-50)	25 (9-45)	0.037 <sup>†</sup>

<sup>†</sup>defined as DAS28  $< 2.6$ ; <sup>‡</sup>defined as DAS28  $< 3.2$ ; <sup>§</sup>variables included in the multivariate analysis as achieving a  $p$  value  $< 0.10$  in the univariate analysis.

HA high adherers, LA low adherers, IQR interquartile range, BMI body mass index, ACPA anti-citrullinated peptides, RF rheumatoid factor, csDMARD conventional synthetic DMARD, bDMARD biological DMARD, DMARD disease-modifying anti-rheumatic drug, PDN prednisone, NSAIDs non-steroidal anti-inflammatory drugs, HAQ Health Assessment Questionnaire, DAS28 disease activity score in 28 joints, VAS visual analogic scale.

**Conclusions:** Only one third of Italian RA patients were highly adherent to treatment according to I-CQR5. Treatment with bDMARDs and employment status were the major determinants of treatment adherence, increasing by almost 3-fold the likelihood of being highly adherent.

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AB0287

### DECREASE IN 14–3–3ETA PROTEIN LEVELS IS CORRELATED WITH IMPROVEMENT OF CLINICAL DISEASE ACTIVITY IN TOFACITINIB TREATED EARLY RHEUMATOID ARTHRITIS PATIENTS

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**Background:** 14–3–3η protein is a proinflammatory mediator that may represent a novel diagnostic and prognostic biomarker for rheumatoid arthritis (RA).

**Objectives:** To assess the disease activity parameters and 14–3–3η protein concentrations in serum of early RA patients treated with Tofacitinib.

**Methods:** Paired serum samples from 35 previously non-treated early RA patients (disease onset less than 1 year) receiving Tofacitinib were obtained at baseline and 5 months after the initiation of treatment. Levels of 14–3–3η were measured by JOINT stat 14–3–3η ELISA test kits (Augurex Life Sciences Corp.). The cut-off was defined as 0.19 ng/ml. We investigated the correlation between changes in serum 14–3–3η concentrations and changes in clinical disease activity index (CDAI), simplified disease activity index (SDAI), Disease Activity Score (DAS) 4CRP and DAS4ESR.

**Results:** Increased concentrations of 14–3–3η were found in 57% of the patients at baseline and in 37% of the patients after 5 months of treatment. Mean ±SD baseline 14–3–3η concentrations [4.92±8.86 ng/ml] were significantly higher (p=0.005) than those found following treatment [1.97±4.59 ng/ml]. Statistically significant improvement (p<0.001) of CDAI, SDAI, DAS4ESR and DAS4CRP was achieved after the 5 month of treatment. No correlation was found between absolute 14–3–3η concentrations and parameters of clinical disease activity at both time points. Decrease in 14–3–3η protein levels were highly correlated with improvement in DAS4ESR (r=0.50, p<0.01) and moderately correlated with improvement in CDAI (r=0.32), SDAI (r=0.33), and DAS4CRP (r=0.46, p<0.01).

**Conclusions:** The study demonstrates that decrease in 14–3–3η protein concentrations in RA patients treated with Tofacitinib is correlated with improvement of clinical disease activity parameters. 14–3–3η protein is a useful biomarker for monitoring Tofacitinib therapy.

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AB0288

### LEVELS OF METALLOPROTEINASE-3 (MMP-3) CORRELATE BETTER WITH CLINICAL DISEASE ACTIVITY INDEX (CDAI) AND SIMPLIFIED DISEASE ACTIVITY INDEX (SDAI) THAN STANDARD DISEASE ASSESSMENT SCORE (DAS-28)

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**Background:** The MMP-3 is a matrixin calcium-dependent zinc-containing; the major expressed in rheumatoid synovial tissue; with essential role in the degradation of both aggrecan and collagen fibrils.

**Objectives:** The aim was to evaluate the correlation of MMP3 levels with assessment scores of RA activity.

**Methods:** 109 patients with RA as per the 2010 ACR/EULAR criteria were included in the prospective Study ALTRA. Patients were divided into groups of early arthritis active, established arthritis active, and remission with conventional remissive or biological remissive. The levels of MMP3 and activity scores: DAS28-ERS, DAS28-CRP, SDAI and SDAI were on the basis of predefined cut-offs. The correlation was determined with the Pearson Test for parametric variables and the Spearman Test for non-parametric variables.

**Results:** The levels of MMP3 in patients with early RA Vs established were 63.2 and 39.9 U/ml, p<0.021 respectively. MMP3 levels of patients with activity measured by DAS28-ESR were 62.9 in the active and 35.2 U/ml in remission, p<0.000.

The correlation between serum levels of MMP3 and DAS28-ERS was 0.21 (p<0.25), with DAS28-CRP 0.27 (p<0.004); CDAI 0.26 (p<0.06) and with SDAI 0.35 (p<0.002).

**Conclusions:** Elevated MMP3 levels indicate state of disease activity; besides the addition in the expression of the collagen damage. This finding may help in making decisions in clinical practice.

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AB0289

### PARAOXONASA 1 ACTIVITY IS MODULATED BY ANTI-RHEUMATIC TREATMENT AND L55M POLYMORPHISM IN PATIENTS WITH RHEUMATOID ARTHRITIS FROM SOUTHERN MEXICO

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**Background:** Paraoxonase-1 (PON-1) is a high-density lipoprotein (HDL)-associated antioxidant enzyme with anti-atherogenic properties. Although genetic polymorphisms are known to modulate PON-1 activity,<sup>1</sup> other factors as the consumption of disease-modifying anti-rheumatic drugs (DMARDs) and nonsteroidal anti-inflammatory drugs (NSAIDs) can also modulate its function.<sup>2</sup>

**Objectives:** To analyse the association between PON-1 activity according to L55M polymorphism and anti-rheumatic treatment in patients with rheumatoid arthritis (RA) from southern Mexico.

**Methods:** Serum PON1 activity, using 4-chloromethyl phenylacetate (4-CMPA) as substrate<sup>3</sup> was quantified in 246 RA patients (181 treated with DMARDs, NSAIDs and/or corticosteroids, and 65 without treatment). The PON1 rs854560 genotype (L55M) was determined by the PCR-RFLP method.

**Results:** PON-1 activity was decreased in RA patients under treatment anti-rheumatic. In addition, an effect of LM/MM genotype of L55M polymorphism was noted in treated patients who exhibiting the lowest PON-1 activity (10.45 vs 13.91 U/mL, p=0.05). The distribution of L55M genotypes were; 86.8% (LL), 12.8% (LM) and 0.4% (MM). The Leflunamide and diclofenac drugs were associated with the mainly decrease of the PON-1 activity (p<0.05), compared with others DMARDs, NSAIDs and corticosteroids drugs used to RA in pharmacological regimens.

**Conclusions:** PON-1 activity is impaired in association with the anti-rheumatic treatment and L55M polymorphism, so in patients with RA the susceptible background genetic could contribute to increasing the cardiovascular risk linked to PON-1 activity.

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AB0290

### LOWER EDUCATIONAL LEVELS ARE ASSOCIATED WITH A HIGHER RISK OF RHEUMATOID ARTHRITIS IN A SOUTHERN EUROPEAN NESTED CASE-CONTROL STUDY

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**Objectives:** To investigate the association between socioeconomic status (SES) on an individual level and incident RA

**Methods:** EPIC is a multicentre, pan-European prospective cohort study of apparently healthy populations. We undertook a nested case-control study to investigate risk factors for RA, by identifying incident RA cases (pre-RA) and matched controls amongst subjects enrolled in four EPIC cohorts in Italy and Spain. The lifestyle, environmental exposure, anthropometric information and blood samples were collected at baseline. Confirmed pre-RA cases were matched with controls by age, sex, centre, and date, time and fasting status at blood collection. The exposure was SES as measured by level of educational attainment categorised as university (referent), secondary school/technical/professional school, primary school completed, and none. The primary outcome was incident RA. Conditional logistic regression (CLR) analysis was adjusted for ACPA seropositivity, smoking status, and presence of shared epitope (SE). A further model also adjusted for other potential confounders, including body mass index (BMI), waist circumference, physical activity, and alcohol intake.

**Results:** The study sample included 398 individuals of which 99 individuals went on to subsequently develop RA. In this analysis, time to diagnosis (defined as time between date of blood sample and date of diagnosis), was 6.71 years (SD 3.43).

A significant positive association was observed with level of educational attainment and RA incidence (secondary/technical vs university: OR 5.60, 95% CI 1.59–19.7, primary school vs university: OR 5.06, 95% CI 1.45–17.6, no education vs university: 7.11, 95% CI 1.37–36.8; p for trend 0.02) independent of ACPA seropositivity, SE and smoking).

A significant positive association between level of educational attainment and RA incidence was confirmed in the fully adjusted model (secondary/technical vs university: OR 5.52, 95% CI 1.53–19.9, primary school vs university: OR 4.87, 95% CI 1.38–17.1, no education vs university: OR 6.48, 95% CI 1.21–34.6; p for trend 0.02).

**Conclusions:** Lower educational levels were independently associated with higher risk of incident RA in this European Mediterranean population.

**Disclosure of Interest:** None declared

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AB0291

### IDENTIFICATION OF JOINT LOCATIONS THAT ARE POOR PROGNOSTIC INDICATORS AND REQUIRE MORE INTENSIVE THERAPY IN AN EARLY, RAPIDLY PROGRESSING RA COHORT: A POST HOC AGREE ANALYSIS

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**Background:** Patients (pts) with early RA often present with multiple areas of involvement. Limited data exist to identify which specific joints or joint locations may be indicative of poorer prognosis and require more intensive initial therapy.<sup>1</sup>

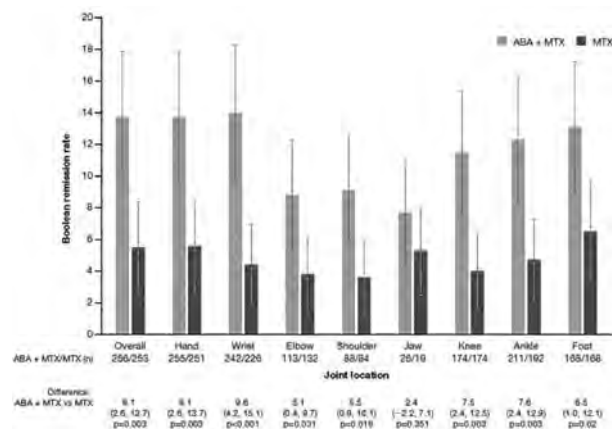
**Objectives:** This analysis investigated which joint locations have the poorest prognosis and compared clinical response rates between abatacept (ABA)+MTX and MTX monotherapy by baseline (BL) swollen joint status for specific joint locations.

**Methods:** Data from AGREE (NCT00122382), a double-blind Phase III study of ABA+MTX (n=256) vs MTX (n=253) in biologic-naïve pts with early (≤2 years [yrs]) erosive RA, were analysed by BL swollen joint status (present, absent) for 8 different joint locations: hands, wrists, elbows, shoulders, jaw, knees, ankles and feet. Overall characteristics and study results were reported previously.<sup>2</sup> Swelling was evaluated at BL and after 6 months (mths) of treatment. Differences between treatment groups in clinical response endpoints (i.e. DAS28 [CRP]<2.6, SDAI≤3.3, CDAI≤2.8, Boolean and HAQ remission ≤0.5 at 6 mths) and swelling resolution at 6 mths were assessed by BL swollen joint status, for each joint location.

**Results:** In an early RA cohort of pts at risk of active, rapidly progressing disease, the proportions of pts (n=509) with a swollen joint at BL were 99% hand, 92%

wrist, 79% ankle, 69% knee, 66% foot, 48% elbow, 34% shoulder and 9% jaw. Pts with a swollen jaw (n=45) had more tender joints (mean [SD] 40.0 [15.1] vs 30.1 [14.1]), more swollen joints (35.9 [13.3] vs 21.1 [9.5]), higher total Sharp score (9.4 [10.1] vs 6.9 [9.1]) and longer disease duration (11.7 [9.2] yrs vs 6.0 [6.9] yrs) than those without jaw swelling (n=464). Higher HAQ-DI was seen in pts with a swollen knee or shoulder (1.8 [0.6] vs 1.5 [0.7] and 1.9 [0.6] vs 1.6 [0.7], respectively). Presence of BL synovitis was not associated with greater BL anti-citrullinated protein antibodies or RF positivity, probably due to the inclusion of mainly seropositive pts.

In general, absence of BL swelling was associated with higher clinical response at 6 mths, both for ABA+MTX and MTX. Independent of BL swollen joint status, ABA+MTX had higher clinical response rates (DAS28, SDAI, CDAI, Boolean and HAQ remission) than MTX, except for the non-swollen wrist. Overall mean Boolean remission rates were 13.7% for ABA+MTX vs 5.5% for MTX with difference in proportions (95% CI) of 8.1% (2.6, 13.7) (p=0.003). The largest difference in Boolean remission rate (95% CI) favouring ABA+MTX was 9.6% (4.2, 15.1) (p<0.001) in pts with a swollen wrist at BL (figure 1). Difference in swollen joint resolution between ABA+MTX and MTX was most pronounced for pts with a swollen hand (mean [95% CI]: 42.7% [36.7, 48.8] vs 27.9% [22.4, 33.4], respectively).



**Abstract AB0291 – Figure 1.** Treatment Group Comparisons of Boolean Remission Rates in Pts with BL Swollen Joint by Joint Location (Proportion [95% CI]).

**Conclusions:** BL swelling in the shoulder, knee and jaw is associated with a more severe RA profile. Remission rates were higher with ABA+MTX than MTX when BL swelling was present, especially in the wrist. Also, swollen joint resolution was more pronounced with ABA+MTX, especially in the hands.

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AB0292

### AUTOANTIBODIES TO A NOVEL PEPTIDE UH-RA.1 ARE ASSOCIATED WITH DISEASE REMISSION IN RHEUMATOID ARTHRITIS

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**Background:** Autoantibodies have been found in the majority of RA patients and are used clinically as diagnostic and prognostic serum biomarkers. Before truly personalised medicine is available for RA patients, markers that can predict a patient's response to different therapeutic regimens have to be found. In this study, we further characterise autoantibodies to the novel University of Hasselt

(UH) peptide UH-RA.1, which have predictive value for an early response to therapy. Antibody reactivity to UH-RA.1 was found in 7%–10% of early RA patients. Presence of anti-UH-RA.1 antibodies in baseline samples from the Leiden Early Arthritis Clinic (EAC) cohort (n=600) appeared to be related to a better outcome as 37% of the antibody-positive group vs 21% of the antibody-negative group reached sustained DMARD-free remission (p=0.016) <sup>1</sup>.

**Objectives:** Our aim is to test the relation between antibody reactivity against UH-RA.1 peptide and early disease remission in baseline RA samples from the CareRA cohort.

**Methods:** Using a custom peptide enzyme-linked immunosorbent assay, the presence of anti-UH-RA.1 antibodies was investigated in the well characterised CareRA cohort <sup>2</sup>. Cut-off for seropositivity was defined by 2 × SD above the mean antibody level of the healthy control group <sup>1</sup>. In the CareRA trial, different treatment regimens consisting of synthetic DMARDs combined with a step down glucocorticoid treatment, were studied. We used 223 baseline RA samples, collected before the start of treatment and early disease remission was defined as a DAS28 (CRP) <2.6 at week 16.

**Results:** Antibodies to UH-RA.1 were found in 5% of the baseline samples from the CareRA cohort. Presence of anti-UH-RA.1 antibodies did not seem to be related to early disease remission in the CareRA cohort. Of the antibody positive group, 9/11 (82%) were in remission at week 16, while 152/212 (72%) of the antibody negative group reached early disease remission (p=0.37). However, in UH-RA.1 seropositive patients from the CareRA cohort, antibody levels were found to be significantly higher in baseline samples of patients that reached remission in week 16 (mean rank 120.51 vs 89.9, p=0.001).

**Conclusions:** In RA patients, presence of antibodies against UH-RA.1 peptide at baseline is related to sustained DMARD-free remission and high levels of antibodies against UH-RA.1 were correlated with early remission after combination therapy consisting of classical synthetic DMARDs with a step down glucocorticoid treatment. In combination with other predictive markers, antibodies against UH-RA.1 peptide might therefore contribute to an improved early patient stratification and prediction of therapy response.

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#### AB0293 FREQUENCY OF JOINT EROSIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS, TREATED WITH BIOLOGICS IN RELATION TO RF AND ACPA SEROLOGY IN REAL LIFE

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**Background:** Rheumatoid arthritis (RA) is a chronic auto-immune disease, characterised by a symmetric polysynovitis and extra-articular manifestations. In 70% to 80% of patients with RA, serologic factors like Rheumatoid Factor (RF) and Anti-Citrullinated Protein Antibodies (ACPA) are present. Early recognition and treatment with disease-modifying antirheumatic drugs (DMARDs) is important in achieving control of disease and prevention of joint destruction. If it is untreated or unresponsive to therapy, inflammation destroys cartilage and bone, resulting in irreversible bone erosions. The 2016 EULAR recommendations for the management of RA stipulate that MTX is recommended as first-line strategy plus short-term GC, aiming at >50% improvement within 3 and target attainment within 6 months. If this fails, stratification is recommended. Without unfavourable prognostic markers, switching to, or adding another csDMARDs (plus short-term GC) is suggested. In the presence of unfavourable prognostic markers (autoantibodies, high disease activity, early erosions, failure of 2 csDMARDs), any bDMARD or Jak-inhibitor should be added to the csDMARD.

**Objectives:** To determine an association between serology status and prevalence of radiographic erosions, the use of biologics and prevalence of erosions, and serology status and use of biologics.

**Methods:** Data were obtained from the electronic patient files of patients who visited the department of Rheumatology at the University Hospital of Ghent (Belgium) between October and December 2016. Patient characteristics with respect to diagnosis, treatment, serology status and erosion status were collected. The

data has been statistically analysed using  $\chi^2$ -, Fisher's exact, Kolmogorov-Smirnov or Kruskal-Wallis tests with  $\alpha=0.05$ .

**Results:** A total of 2001 consultations were analysed, of which 358 patients were identified with RA. 353 patients were included, of which 116 men (32.9%) and 237 women (67.1%). The mean age of the study population was 62 years with a mean age of 52 years at diagnosis. Of these patients, 36.0%, 49.5% and 29.8% were positive for respectively RF, ACPA and RF +ACPA. 38% has ever been treated with a biologic, whereas 26.9% is currently treated with a biologic. 37.4% of the patients showed erosions on a recent radiograph of hands or feet. A positive ACPA serology (p<0.0001. OR=1.87), a positive RF serology (p=0.010. OR=2.26) and a positive RF +ACPA serology (p=0.007. OR=2.74) was more observed in patients with radiographic erosions. A significant difference in erosions was seen between patients treated with or without biologics (p<0.0001. OR=3.45). Biologics were prescribed more in patients with positive ACPA serology (p<0.0001. OR=3.92) and in patients with positive RF serology (p=0.001. OR=2.67).

**Conclusions:** In a consecutive real life cohort of patients with RA, positive ACPA and/or RF status were associated with an increased risk to develop bone erosions in affected joints. Positive serology was also linked to biologic therapies. Patients who received biological treatment were more prone to have erosions.

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#### AB0294 TREATMENT MODES IN RHEUMATOID ARTHRITIS: FACTORS INFLUENCING PATIENT PREFERENCE

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**Background:** Little in-depth qualitative research has been conducted to investigate reasons for rheumatoid arthritis (RA) patient (pt) preferences for different modes of treatment administration. An understanding of pt preference can help physicians personalise therapy recommendations.

**Objectives:** To describe potential RA pt preferences for RA treatment modes and reasons for these preferences.

**Methods:** Pt demographic information was obtained at screening alongside qualitative interviews conducted using a semi-structured interview guide among adult RA pts in the US, UK, France, Germany, Italy, Spain, Switzerland and Brazil who were currently taking a DMARD (biologic or non-biologic). A 100-point allocation task was used to evaluate the strength of preference (0–100; 100=strong) across 4 treatment modes: oral (OR; once daily), self-injection (SI; weekly), clinic-injection (CI; weekly) and infusion (INF; monthly). Transcripts were developed in English; ATLAS.ti software (v7.5) was used for qualitative coding and analysis.

**Results:** 100 interviews (30 US; 10 in each of 7 other countries) were conducted (female: 75.0%; mean age: 53.9 years; mean time since diagnosis: 11.6 years). Current RA medication mode included OR (60.0%), injection (57.0%) and INF (14.0%); 79.0% and 37.0% of pts had experience with injection and INF medications, respectively; 31.0% of pts were taking a combination of biologic and non-biologic DMARDs. Among the 4 treatment modes, OR was allocated the highest mean (standard deviation [SD]) preference points (47.3 [33.1]) and the greatest percentage of pts with a 1st choice rank (57.0%); this was followed by SI (29.7 [27.7]; 29.0%), INF (15.4 [24.6]; 16.0%) and CI (7.5 [14.1]; 2.0%). Preferences by country suggested that the mean points allocated to OR were greater in the US vs other countries. Across all pts and treatment modes, 56.0% of pts had a 'strong' 1st choice preference (ie, a pt allocation  $\geq$  the mean pts across the 1st ranked choices [70]); of these pts, the majority chose OR (62.5%); SI: 23.2%; INF: 10.7%; CI: 3.6%). Speed of administration was among the most common reasons for choosing OR or SI as a 1st choice, together with ease of administration (OR) and frequency of dosing (SI; table 1). Difficulty remembering was the most common reason for not choosing OR and avoidance of pain was the most common reason for not choosing SI as a 1st choice.

**Conclusions:** More pts preferred OR as an RA treatment mode, followed by SI. Rationales for preference included ease of use, concerns about drug interactions, dosing frequency, feelings of control and avoidance of pain and needles. While 56.0% of pts felt strongly about their 1st choice preference, nearly half did not and may be receptive to and benefit from discussions with their healthcare professional and/or pt support groups about RA treatment mode options.



**Abstract AB0294 – Table 1.** Most frequent<sup>a</sup> reasons for choosing or not choosing each treatment mode as 1st choice

Reasons for choosing OR, n (%) (N=57)		Reasons for not choosing OR, n (%) (N=43)	
Speed of administration	30 (52.6)	Difficultly remembering	15 (34.9)
Ease of administration	30 (52.6)	Possible drug-drug interactions	11 (25.6)
Portability	23 (40.4)		
Reasons for choosing SI, n (%) (N=29)		Reasons for not choosing SI, n (%) (N=71)	
Speed of administration	16 (55.2)	Avoidance of pain due to needles	53 (46.5)
Frequency of dosing	12 (41.4)	Avoidance of needles	30 (42.3)
Having a feeling of control	11 (37.9)	Difficulties when traveling	19 (26.8)
		Need to refrigerate	18 (25.4)
Reasons for choosing CI <sup>b</sup> , n (%) (N=10)		Reasons for not choosing CI <sup>b</sup> , n (%) (N=100)	
Feels comfortable with experts administering	4 (40.0)	Need to go to the clinic	38 (38.0)
Prefers someone else to administer	3 (30.0)	Inconvenience	36 (36.0)
Reasons for choosing INF, n (%) (N=16)		Reasons for not choosing INF, n (%) (N=84)	
Frequency of dosing	13 (81.3)	Time-consuming	51 (60.7)
Feelings of safety and care	5 (31.3)	Hassle and inconvenience	28 (33.3)
		Need to go to the clinic	26 (31.0)

<sup>a</sup>Reported by ≥25% of patients. <sup>b</sup>N includes 2 patients who chose CI as clear 1<sup>st</sup> choice and 8 patients who chose CI as clear 2<sup>nd</sup> choice. <sup>c</sup>Based on total sample.

CI, clinic-injection; INF, infusion; OR, oral; SI, self-injection

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## AB0295 RISK FACTORS FOR PROGRESSION AND PROGNOSIS OF RHEUMATOID ARTHRITIS-ASSOCIATED INTERSTITIAL LUNG DISEASE: SINGLE CENTRE STUDY WITH A LARGE SAMPLE OF CHINESE POPULATION

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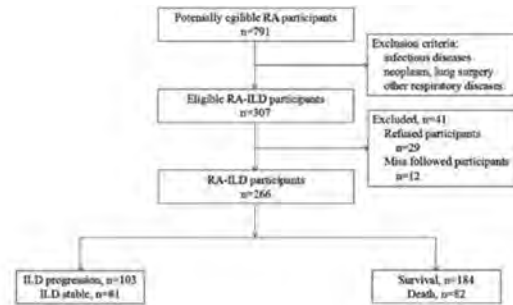
**Background:** Poor prognosis has been shown in rheumatoid arthritis-associated interstitial lung disease (RA-ILD) patients, and the mortality rate was significantly higher than RA patients without ILD. Studies showed that one-third of RA-ILD patients had progressed within two years. However, factors associated with ILD progression and survival in RA-ILD have not been previously described in a large centre China cohort.

**Objectives:** To investigate the risk factors for ILD progression and explore the prognostic factors for survival in RA-ILD patients.

**Methods:** 791 consecutive RA patients who completed lung HRCT were considered as potential participants. 266 RA-ILD patients were finally included in this retrospective cohort study. To identify independent risk factors for ILD progression, multivariate logistic regression analyses were used. Cox hazards analysis was used to determine significant variables associated with survival.

**Results:** 1, The mean age at diagnosis of RA-ILD was 64.80±10.71 years old. 162 (60.90%) were females and 104 (39.09%) were males. 2, UIP and NSIP pattern were the commonly types of RA-ILD, accounting for 37.22% and 25.94% respectively. Extent of lung involvement analysis showed that limited was predominant (130/266, 48.87%), with smaller numbers of moderate (67/266, 25.19%) and extensive (69/266, 25.94%) lung involvement. 3, The 3 year survival rate of RA-ILD patients was 81.24%, and the 5 year survival rate was 69.71%. A total of 82 deaths occurred during follow-up, of which 56 died of respiratory failure due to ILD progression and/or pneumonia, while 14 with malignancies (8 with lung cancer). 4, Logistic regression analysis showed that an increased anti-CCP antibody titer (OR: 4.03, 95% CI: 1.04–15.69, p<0.05) and DLCO%<45% (OR: 8.31, 95% CI: 2.17–31.75, p<0.01) were independent risk factors for the ILD

progression. 5, Cox hazards analysis revealed that advanced age (>60 years old) of RA-ILD diagnosis (HR: 2.32, 95% CI: 1.27–4.25, p<0.05) and extensive lung involvement on HRCT (HR: 2.19, 95% CI: 1.24–3.87, p<0.05) were associated with worse survival. Treatment with cyclophosphamide (HR: 0.43, 95% CI: 0.26–0.69, p<0.01) was associated with better survival.

**Abstract AB0295 – Figure 1.** Study flow diagram

**Conclusions:** In RA-ILD patients, DLCO%<45% is the strongest predictor for ILD progression. Advanced age and extensive lung involvement on HRCT, rather than the baseline UIP pattern, independently predict mortality after controlling for potentially influential variables. Furthermore, cyclophosphamide treatment helps to improve the prognosis in real-world experience.

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## AB0296 14–3–3ETA POSITIVITY IS ASSOCIATED WITH HIGHER RHEUMATOID ARTHRITIS DISEASE ACTIVITY MEASURED BY MULTI-BIOMARKER DISEASE ACTIVITY ASSAY

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**Background:** Early diagnosis of rheumatoid arthritis (RA) is crucial but recognition of its disease activity and prognosis can help tailor treatment for patients in order to avoid debilitating consequences. 14–3–3eta has been described to have diagnostic utility as a biomarker of RA; however its use as prognostic factor is still under investigation.<sup>1</sup> The η (eta) isoform is one of seven from the 14–3–3 family of regulatory proteins and is expressed extracellularly in much higher concentrations in the synovial fluid and serum of patients with RA. A multiple-biomarker disease activity (MBDA) score was recently introduced; 396 candidate cytokines and biomarkers were narrowed to twelve, correlating with disease activity.

**Objectives:** The purpose of our study was to investigate if 14–3–3η can be used as a prognostic factor and if it was associated with higher disease activity in RA patients. We compared the positivity of 14–3–3η in those with low, moderate, and high disease activity based on MBDA scores. In addition, as MBDA scores provide individual biomarker levels, we wanted to determine if there was a correlation between 14–3–3η and specific biomarker patterns.

**Methods:** A retrospective chart review was conducted on 70 RA patients (satisfied the 2010 ACR diagnostic criteria) at an outpatient rheumatology clinic in an inner-city population. Serum 14–3–3η protein was measured by ELISA with a positive threshold range (Quest Diagnostic) of 0.2 ng/mL. The MBDA scoring scale was 1–29 for low disease activity, 30–44 for moderate and 45–100 for high. The t-test was used to analyse for a significant difference in MBDA scores as well as individual biomarker levels in 14–3–3η positive patients.

**Results:** Of the 70 RA patients, 37 were 14–3–3η positive and 33 were negative. Thirty (81%) of 14–3–3η positive patients were on at least one DMARD compared to 16 (48.5%) of negative patients. The mean and median MBDA scores of 14–3–

3η positive patients were 49.4 and 47, while negative patients' scores were 36.9 and 38, respectively ( $p=0.002$ ). Thus, 14–3–3η positive patients had high disease activity while 14–3–3η negative patients had moderate disease activity. Mean levels of matrix metalloproteinase 3 (MMP-3), serum amyloid A (SAA), and CRP in 14–3–3η positive versus negative were 52.3 ng/mL and 28.4 ng/mL ( $p=0.01$ ), 24.3 mg/mL and 6.96 mg/mL ( $p=0.02$ ), and 21.5 mg/L and 9.82 mg/L ( $p=0.02$ ), respectively.

**Conclusions:** 14–3–3η positive RA patients have higher disease activity based on MBDA score and are associated with higher levels of MMP-3, SAA, and CRP. MMP-3 is associated with joint destruction through degradation of the components of extracellular matrix in the synovial joint. SAA and CRP are acute phase reactants but SAA has been linked with increased cardiovascular and renal disease in RA patients. 14–3–3η positive patients should be treated aggressively to decrease disease activity and limit extra-articular manifestations.<sup>2</sup>

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AB0297

#### PREDICTORS OF AN INADEQUATE RESPONSE TO TREATMENT IN LATIN AMERICAN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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**Background:** Inadequate response to treatment in early rheumatoid arthritis (RA) is associated with adverse consequences. We have previously shown high baseline levels of disease activity in Latin American RA patients.<sup>1</sup>

**Objectives:** To identify the baseline predictive factors of inadequate response to treatment in patients with early RA from a GLADAR cohort, at one year from cohort entry.

**Methods:** GLADAR cohort includes 1093 consecutive RA patients with disease <1 year from 46 centres in 14 Latin American countries. For these analyses, patients with complete clinical and laboratory assessments with DAS28-ESR>3.2 at the baseline, and one-year follow up visits were included. Inadequate treatment response was ascertained with the EULAR definition which is based on DAS28-ESR obtained at one-year of follow up [a variation  $\leq 0.6$  in any category of activity (mild, moderate or severe) and a variation  $>0.6$  but  $\leq 1.2$  in the high activity category]. Gender, age at diagnosis, diagnosis delay, socioeconomic status (by the Graffar scale), ethnicity, medical coverage, rural origin, rheumatoid factor (RF) positivity, disability (HAQ-DI), DMARDs use, corticosteroid use, and DMARD treatment delays were examined as potential predictive factors of this outcome. Univariable and multivariable binary logistic regression models, using a stepdown technique were examined in order to determine the predictors of response at 1 year.

**Results:** Four hundred and forty-eight patients were included. Three hundred and eighty-five (85.9%) were female; the mean (SD) age at diagnosis was 46.1 (13.6) years; 78.3% had medical coverage and 347 patients (77.5%) were RF

positive. The mean baseline DAS28-ESR was 6.3 (1.4). EULAR response was met by 347 (77.5%) patients at 1 year. Three hundred patients (67%) have received glucocorticoids, 78.8% at least one DMARD and only 1.1% had received at least one biologic compound. The baseline HAQ-DI was 1.5 (0.0–3.0). Predictors of non-EULAR response at 1 year were: female gender (OR=2.4; CI:1.0–5.6;  $p=0.039$ ), a higher baseline HAQ-DI (OR=1.7; CI:1.2–2.4;  $p=0.003$ ) whereas protective factors were higher DAS28-ESR (OR=0.6; CI:0.4–0.7;  $p<0.001$ ) and having medical coverage (OR=0.5; CI:0.3–0.9;  $p=0.025$ ).

**Conclusions:** We have identified baseline predictors of adverse response to treatment in LA patients with early RA. Absence of medical coverage seems to be an additional adverse factor associated with poor results. Other factors such as early response/remission or adherence to treatment should be taken into account.

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AB0298

#### A LOWER WAIST CIRCUMFERENCE IS ASSOCIATED WITH CLINICAL REMISSION IN PATIENTS WITH ESTABLISHED RHEUMATOID ARTHRITIS

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**Background:** Abdominal Obesity is highly prevalent in patients with RA and this condition is associated with adverse metabolic outcomes, but information about the impact of this condition in clinical activity disease is scarce, specially in our region

**Objectives:** To assess the association between central obesity with baseline clinical activity in a cohort of patients with established rheumatoid arthritis (RA).

**Methods:** Cross-sectional baseline analysis of a single centre RA cohort. This cohort began at 2011 and includes patients with a diagnosis of RA ACR EULAR 2010 criteria), followed by semestral visits. In this analysis, clinical disease activity was measured by SDAI, clinical remission and low disease activity (LDA) was defining according SDAI categories (a value  $<3.3$ , and  $\leq 11$ , respectively), also definition of remission by the ACR-EULAR 2011 was applied (tender and swollen joint counts  $\leq 1$ , CRP  $\leq 1$  mg/dl, and PGA  $\leq 1$  with patient-reported outcomes on a scale of 0–10, or SDAI  $\leq 3.3$ ). Patients with chronic pain disease (fibromyalgia, neuropathic pain and neurologic disorders such as neuropathies) and diagnosis of depression were excluded. Waist circumference (WC) was measured as a continue variable (cm). Potential basal confounders associated with activity disease were analysed: socio demographics variables (age at diagnosis, gender, disease duration, delay of DMARDs treatment, education), anticitrullinated antibody peptide (antiCCP), medication (use and dose of corticosteroid, use of cDMARDs and bDMARDs). Continuous variables were expressed as means and SDs, and categorical variables as percentages and 95% confidence intervals (95% CIs). Univariable and multivariable binary logistic regression models were examined in order to determine the association between abdominal perimeter and remission.

**Results:** Four hundred and twenty-five from 596 subjects of the cohort were include. The mean (SD) age was 58.5 (11.8) years. Disease duration was 15.2 (14.0) years; 90.4% were women and 75.8% were anti CCP positive. Two hundred and fifty-one patients (59.1%) have received glucocorticoids, 50.1% at least one DMARD and only 5.4% had received at least one biologic compound. The mean WC was 98.2 (11.3) cm and central obesity prevalence was 87.8% in men and 96.7% in woman. The baseline SDAI was 29.9 (24.1). Remission was met only by 1.7% patients and remission/LDA by 13.2% subjects. In the univariate analysis, a less WC was associated with remission (OR=0.9; CI:0.8–0.9;  $p=0.042$ ); this association remained significant in the multivariable analysis (OR=0.9; CI:0.8–0.9;  $p=0.022$ ).

**Conclusions:** A lower waist circumference is associated with clinical remission in patients with established RA. This condition should be taken in account in the baseline measure of activity disease.

**Disclosure of Interest:** None declared

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**AB0299 THE INCIDENCE RATE AND THE MANAGEMENT OF EARLY RHEUMATOID ARTHRITIS IN A SINGLE CENTRE INTERVENTIONAL CLINIC**

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**Background:** In patients with rheumatoid arthritis (RA), early diagnosis and adherence to the treat to target recommendations (T2T) limit RA progression and improve patients' quality of life.<sup>1</sup> However, the implementation of T2T has always been a challenge, and real-life data are lacking. Slovenia has 40% less rheumatologists per capita than the European Union average, which makes the implementation of management guidelines even more challenging.

**Objectives:** To determine the incidence of RA and the proportion of patients with incident RA in whom first rheumatology assessment was done within the recommended time frame.

**Methods:** We analysed the prospectively collected data of adult patients diagnosed with RA during years 2014 to 2016 at the Rheumatology Department of the University Medical Centre Ljubljana, Slovenia. The department provides rheumatology services to a well-defined region with a population of 704.000 adult residents. Dates were recorded for inflammatory joint symptom onset, referral to rheumatologist, first rheumatologic assessment and initiation of DMARD therapy. The percentage of patients assessed by a rheumatologist and/or treated with a DMARD within 12 weeks of symptom onset and the median times for delay were then calculated.

**Results:** Between 1 January 2014 and 31 December 2016, 341 incident cases of RA (75% females, median age 61.9 (IQR 52–75.4) years) were identified, resulting in an annual incidence rate of 16/100.000 population (in females: 23.6/100.000; in males 8.3/100.000). Most patients (78.6%) were referred to our early interventional clinic. The median time from symptom onset to consultation was 12.9 (IQR 4.4–26.1) weeks, median time from referral to consultation was 1 (IQR 1–3) day. Median DMARD treatment delay was 16.6 (IQR 8.9–33.3) weeks. Within 12 weeks of symptom onset, 161 (47.2%) new RA patients were examined by a rheumatologist and 123 (36.1%) were started on DMARD therapy.

**Conclusions:** Our prospective data support the recent reports that uncovered a decrease in RA incidence.<sup>2</sup> Moreover, despite the lack of rheumatologists and the heavily protracted nationwide waiting times for first rheumatologist assessment, our early interventional clinic enables us to recognise and manage substantial percentage of RA patients within the recommended time frame.

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**Disclosure of Interest:** None declared

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**AB0300 ULTRASOUND EVALUATION OF ANKLE AND FOOT JOINTS IN RHEUMATOID ARTHRITIS**

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**Background:** The foot and the forefoot particular are often one of the first areas to be affected by rheumatoid arthritis. The joint destruction develops not only as a result of synovitis but also as a result of specific biomechanical stresses leading to deformity

**Objectives:** Evaluate the prevalence of ultrasound signs of rheumatoid arthritis in the joints of the ankle and foot.

**Methods:** This is a cross-sectional study that included 14 consecutive patients (100% female, mean age 55.3 years) with rheumatoid arthritis (median duration of progression of 13.5 years, mean specialised care of 2.1 years). A grey and Doppler ultrasound study was performed by looking for effusions, synovitis, Doppler activity and bone erosions in the joints of the ankle and foot.

**Results:** 28 feet were studied with an ultrasound evaluation of 308 joints. The prevalence of ultrasound signs of RA are shown in table 1 and 2.

**Abstract AB0300 – Table 1.** Prevalence of ultrasound signs of RA in the forefoot (N=28)

Echographic signs	Forefoot				
	MTP1 n=28	MTP2 n=28	MTP3 n=28	MTP4 n=28	MTP5 n=28
Synovitis	57.1	28.6	14.3	21.4	25
Doppler	0	0	3.6	3.6	3.6
Effusion	25	21.4	10.7	10.7	7.1
Erosions	67.9	3.6	10.7	17.9	7.1
Osteophytes	57.1	17.9	14.3	25	25

**Abstract AB0300 – Table 2.** Prevalence of ultrasound signs of RA in the ankle and foot (N=28)

Echographic signs	Ankle		Hindfoot		Midfoot		
	Talocalcaneal N=28	Subtalar N=28	Talo-navicular N=28	Calcaneocuboid N=28	Cubo-metatarsal N=28	Cuneo-metatarsal N=28	
Synovitis	60.7	50	46.4	7.1	7.1	3.6	
Doppler	0	0	0	3.6	0	0	
Effusion	39.3	25	10.7	7.1	0	10.7	
Erosion	10.7	10.7	0	14.3	14.3	3.6	
Osteophyte	28.6	39.3	71.4	39.3	42.9	14.3	

**Conclusions:** This study describes the various ultrasound signs at the joints of the ankle and foot. There is a high prevalence of synovitis in the ankle and hind-foot. Doppler activity has been rarely found.

A large-scale study compared with a control group is necessary to better interpret and complete these preliminary results.

**Disclosure of Interest:** None declared

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**AB0301 SERUM PYRIDINOLINE IS ASSOCIATED WITH RADIOGRAPHIC JOINT EROSIONS IN RHEUMATOID ARTHRITIS**

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**Background:** Pyridinoline (Pyl) is a 3-hydroxypyridinium derivative which is an intermolecular cross-link compound of type I and II collagen.<sup>1</sup> It is a marker of bone resorption based on bone biopsy and radioisotope kinetics studies.<sup>2</sup> In rheumatoid arthritis (RA), destruction of bones may contribute to increased levels of serum Pyl.

**Objectives:** The purpose of this study was to compare the serum pyridinoline (Pyl) levels between RA patients and healthy controls and to determine the correlation of serum Pyl levels with radiographic joint erosions.

**Methods:** This was a monocentric, cross sectional, case-control study which was conducted from June 2016 to February 2017 at the Universiti Kebangsaan Malaysia Medical Centre (UKMMC). Serum samples were obtained from 48 patients with RA and 48 healthy controls. The enzyme-linked immunosorbent assay (ELISA) method was used for quantitative analysis of serum Pyl. Besides, all the RA patients were assessed for joint damage based on Modified Sharp Score (MSS), disease activity based on the disease activity score in 28-joints (DAS 28) and functional capacity based on Health Assessment Questionnaires Disability Index (HAQ-DI).

**Abstract AB0301 – Table 1.** Correlation between serum pyridinoline and other clinical variables

	Serum Pyridinoline		
	r	r <sup>2</sup>	p
DAS 28	- 0.010	7.431	0.945
Joint erosion score	<b>0.285</b>	0.086	<b>0.049</b>
JSN score	- 0.076	7.560	0.605
Total MSS	- 0.009	0.005	0.952
HAQ-DI	- 0.186	0.051	0.205

**Results:** The median serum Pyl levels was much higher among the RA patients (110.20 ng/mL [92.30–120.64]) compared to the controls (98.22 ng/mL [85.54–111.41]); p<0.05. RA patients with erosive disease had significantly higher serum



Pyd levels ( $p=0.024$ ). There was a significant positive correlation between serum Pyd levels and joint erosion score ( $r=0.285$ ,  $p=0.049$ ). The serum Pyd levels had no demonstrable association with disease activity or functional capacity. Neither steroid nor biologic therapy influenced the levels of serum Pyd.

**Conclusions:** RA patients had significantly higher levels of serum Pyd compared to healthy controls. The serum Pyd levels had significant correlation with radiographic joint erosions which reflected disease damage.

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#### AB0302 THE ROLE OF THE BIOMARKER 14-3-3 ETA IN RHEUMATOID ARTHRITIS: A REVIEW

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**Background:** Biomarkers are of much interest in rheumatoid arthritis (RA). Valid, reliable and convenient biomarkers, to detect early disease, predict severity and monitor treatment response are essential to achieving optimal outcomes. Several biomarkers have been suggested but are largely not validated. Validated measures of rheumatoid factor (RF), citrullination antibodies (ACPA), C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) do not provide a complete picture. 14-3-3 $\eta$ , a protein from a family of highly conserved regulatory molecules, has promising data as a novel RA biomarker and is the focus of this review.

**Objectives:** This review aimed to identify the literature characterising 14-3-3 $\eta$  and its utility in RA.

**Methods:** Search terms 14-3-3 $\eta$ , biomarker and rheumatoid arthritis were used in Pubmed, Web of Science and Embase databases and reference lists of relevant papers were scanned. Inclusion criteria were confirmed RA, 14-3-3 $\eta$  and English language.

**Results:** Seven key papers were identified on 14-3-3 $\eta$  proteins<sup>1-6</sup> and one on 14-3-3 $\eta$  antibodies (14-3-3 $\eta$ -Ab)<sup>7</sup>. **Detecting RA:** 14-3-3 $\eta$  was elevated in patients with RA compared to healthy controls<sup>2,4</sup> and patients with other diseases ( $p<0.001$ )<sup>4</sup>. Being positive for 14-3-3 $\eta$  ( $>0.19$  ng/mL) showed sensitivity and specificity of 63.3% and 92.6%<sup>4</sup> to detect RA, increasing to 91.7% and 99.6%, respectively when an ROC-determined optimal cut-off of 0.879 ng/mL was used<sup>2</sup>. When combined with current markers RF  $\pm$  ACPA the detection capacity for early RA increased to 78% and for established RA to 96%, compared to 72% and 88%<sup>4</sup>, respectively for RF  $\pm$  ACPA alone. Including the 14-3-3 $\eta$ -Ab further increased detection<sup>7</sup>. The 14-3-3 $\eta$ -Ab appeared at higher levels in early, treatment naïve RA, while no difference was seen in established RA compared to controls<sup>7</sup>. The 14-3-3 $\eta$ -Ab was not associated with inflammatory markers ESR or CRP<sup>7</sup>. Although higher levels of the 14-3-3 $\eta$  protein were detected in early RA ( $p<0.05$ ), rate of detection was higher in established RA<sup>2</sup>. **Predicting disease severity:** Baseline 14-3-3 $\eta$  status was associated with increased disease severity<sup>1,2,3,4,5</sup>, higher median DAS (6.3 vs 5.7,  $p=0.026$ ) and HAQ scores (1.9 vs 1.0,  $p=0.001$ )<sup>4</sup>. Significant associations with baseline DAS28-ESR, CDAI and SDAI ( $p<0.045$  –  $p<0.001$ ) were also reported<sup>3</sup>. Physical symptoms are closely related to 14-3-3 $\eta$  levels<sup>2</sup>; patients achieving DAS28-ESR-defined remission had significantly lower levels than non-remitters<sup>3</sup>. Radiographic progression was significantly associated with higher 14-3-3 $\eta$ <sup>1,5</sup>, OR=6.2 (95%CI 1.3 to 30.2) in early RA and 2.5 (95%CI 1.0 to 1.4) in established RA<sup>5</sup>. Conflicting results on associations with existing markers ESR, CRP, RF, and ACPA have been reported<sup>1,2,3,4,5,6</sup>. **Treatment response:** 14-3-3 $\eta$  levels are dynamic with changing disease activity<sup>1,3</sup>. Also, pre-treatment 14-3-3 $\eta$  levels were an independent predictor of response to some therapies<sup>3</sup>.

**Conclusions:** 14-3-3 $\eta$  protein and Ab are promising biomarkers in RA diagnosis, disease severity and response to treatment. Future research characterising the protein in RA and its relationship with validated biomarkers and composite measures, and expanding on the 14-3-3 $\eta$ -Ab would be well directed.

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#### AB0303 ULTRASOUND ASPECT OF POSTERIOR TIBIAL TENDON IN RHEUMATOID ARTHRITIS

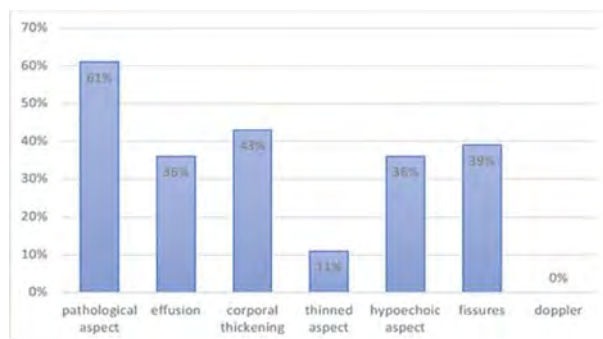
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**Background:** Posterior tibial tendon involvement is common in rheumatoid arthritis. Ultrasound has an important place in the examination of this tendon.

**Objectives:** Evaluate the prevalence of ultrasound signs of posterior tibial tendon involvement in rheumatoid arthritis.

**Methods:** This is a cross-sectional study that included fourteen consecutive patients (100% female, mean age 55.3 years) with rheumatoid arthritis (median duration of progression of 13.5 years, mean specialised care of 2.1 years). A grey and Doppler ultrasound study was performed on affected feet, looking for effusion, thickening or corporal thinning, hypoechoic aspect, fissures, and Doppler activity in the posterior tibial tendon.

**Results:** 28 feet were studied with ultrasound evaluation of the posterior tibial tendon. Figure 1 illustrates the prevalence of the pathological aspects of the posterior tibial found on ultrasound examination.



**Abstract AB0303 – Figure 1.** Ultrasound aspects of the posterior tibial tendon in patients RA

**Conclusions:** This study illustrates the different pathological aspects of the posterior tibial tendon. It highlights the high prevalence of this tendinopathy in the rheumatoid foot. Ultrasound allows accurate assessment of this tendon in RA patients.

A large-scale study compared with a control group is necessary to better interpret and complete these preliminary results.

**Disclosure of Interest:** None declared

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#### AB0304 THE DELAY IN THE MANAGEMENT OF RHEUMATOID ARTHRITIS BY A RHEUMATOLOGIST IS ASSOCIATED WITH AN ALTERATION OF THE FUNCTION OF THE FOOT

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**Background:** Impairment of foot function is known in rheumatoid arthritis.

**Objectives:** Evaluate the functional status of the foot in patients with RA and look for factors associated with impaired foot function.

**Methods:** This is a cross-sectional study that consecutively included 14 patients (100% female, mean age 55.3 years) with RA (median duration of evolution of 13.5 years, mean specialised care of 2.1 years). The functional status of RA was assessed by the HAQ (Health Assessment Questionnaire). RA activity was evaluated by DAS28 and DAS44. The FFI score (Foot Function Index) was used to determine the functional status of the foot. A correlation analysis was made between the FFI score and DAS28, DAS44 and HAQ as well as with the duration of progression of the RA and the delay of specialised management.

**Results:** The median score of the HAQ (Health Assessment Questionnaire) was 1.6. The median score for the Foot Function Index (FFI) was 53.6. The medians of DAS 28 and DAS 44 were 5.3 and 3.8. The median of the different FFI score items was:

Pain Sub-scale: How severe is your foot pain ?

Q1: Foot pain at its worst ? 7 (6; 9,25), Q2: Foot pain in morning ? 5,5 (2; 7), Q3: Pain walking barefoot ? 4 (1,75; 8,15), Q4: Pain standing barefoot ? 5 (3,25; 8,25), Q5: Pain walking with shoes ? 4 (1,75; 5,75), Q6: Pain standing with shoes ? 4,5 (3; 5,5), Q7: Pain walking with orthotics ? 3 (3; 3), Q8: Pain standing with orthotics ? 3 (3; 3), Q9: Foot pain at end of day ? 5 (2,75; 7)

Disability sub-scale: How much difficulty did you have ?

Q10: Difficulty walking in house ? 2 (0; 3,25), Q11: Difficulty walking outside ? 5,5 (3; 8), Q12: Difficulty walking 4 blocks ? 5 (4; 9), Q13: Difficulty climbing stairs ? 6,5 (4; 8,25), Q14: Difficulty descending stairs ? 6 (3,5; 8,25), Q15: Difficulty standing tip toe ? 8,5 (5,25; 10), Q16: Difficulty getting up from chair ? 5 (1,5; 8), Q17: Difficulty climbing curbs ? 4,5 (2; 7,25), Q18: Difficulty walking fast ? 8,5 (4,75; 10)

Activity Limitation sub-scale: How much of the time do you ?

Q19: Stay inside all day because of feet ? 7 (2; 8,25), Q20: Stay in bed all day because of feet ? 5 (2; 3,25), Q21: Limit activities because of feet ? 5,5 (1; 8), Q22: Use assistive device (cane, walker, crutches, etc) indoors ? 0 (0; 3,25), Q23: Use assistiw device (cane, walker, crutches, etc) outdoors ? 0 (0; 0,75).

No correlation was found between the FFI and the HAQ. DAS 28 and DAS44 did not correlate with the FFI either.

Alteration of foot function as indicated by a high FFI score was associated with a delay in specialist management by a rheumatologist ( $r=0.535$ ,  $p=0.04$ ).

**Conclusions:** This study provides insight into the impact of RA on foot function. The HAQ, DAS28 and DAS44 would not reflect the functional deterioration of the foot in RA. In addition, an alteration of foot function would be associated with a delay in specialist management by a Rheumatologist.

A large-scale study is underway to validate and complete these preliminary results.

**Disclosure of Interest:** None declared

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#### AB0305 REMAINING FOOT SYNOVITIS MAY PREDICT RELAPSE IN RHEUMATOID ARTHRITIS PATIENTS IN DAS28 REMISSION (DAS28-CRP<2.3)

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**Background:** DAS28 (Disease Activity Score based on 28 joints) is widely used to determine remission in rheumatoid arthritis (RA). The problems with DAS28 due to omission of the lower extremity joints have long been discussed. There are reports demonstrating that some patients meeting DAS28 remission criteria still have synovitis in their feet.<sup>1</sup> It is suggested that patients with remaining foot synovitis can experience up to a 2-fold increase in relapse rates.<sup>2</sup> Evidence supporting this hypothesis is still scarce.

**Objectives:** We hypothesised that RA patients in remission according to the DAS28 remission criterion with remaining foot synovitis are less likely to stay in remission. We aimed to test this hypothesis among Japanese patients with RA.

**Methods:** In 2015, 15,071 RA patients were registered in a large nationwide database in Japan (NinJa). Among those patients, those who were in remission based on DAS28-CRP were included. We used DAS28-CRP<2.3 as the remission criteria. The study population was then divided into groups with or without tender/swollen joints in the feet. These patients were followed for one year and the remission rate was then calculated for each group. Comparison was performed with Chi-square test.

**Results:** We included 706 RA patients in remission based on DAS28-CRP with foot synovitis in 2015 and 5182 without foot synovitis. Among patients with foot

synovitis in 2015, 225 (31.9%) were not in remission in 2016 while among those without foot synovitis, 985 (19.0%) were not in remission. ( $X\text{-squared}=62.953$ ,  $df=1$ ,  $p=2.117 \times 10^{-15}$ )

**Conclusions:** In our study, RA patients in remission according to the DAS28 remission criterion with remaining foot synovitis had more relapses than those without it. Remission defined by DAS28-CRP does not take remaining foot synovitis into account. But a thorough foot examination may still be useful in RA patients with DAS28-CRP remission as they may be more at risk for relapse.

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**Disclosure of Interest:** None declared

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#### AB0306 PREDICTORS OF MEDICATION ADHERENCE IN SERBIAN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Adherence to pharmacologic therapy is a significant problem in patients with rheumatoid arthritis (RA). Nonadherence in patients with RA using disease modifying antirheumatic drugs (DMARD) may result in unnecessarily high levels of disease activity and function loss.

**Objectives:** The aim of this study was to evaluate the predictive ability of demographic (age, sex, marital status, employment status, education) and clinical factors (duration of disease, patients assessment of pain, concomitant use of biological therapy and presence of comorbidity) for medication adherence.

**Methods:** In the period between March 1 and May 30, 2017, 195 consecutive RA patients who were treated in one of three randomly chosen Serbian clinics were enrolled in cross-sectional study. The inclusion criteria were: age  $\geq 18$  years, current diagnosis of RA per the 1987. ACR Diagnostic Criteria, completing the questionnaire self-reported medication adherence and written informed consent. Demographic and clinical characteristics of adherent and non-adherent participants were compared using independent samples t-tests for continuous variables and Chi square analyses for categorical variables. The associations between investigated demographic and clinical characteristics of the patients and non-adherence to DMARDs were assessed applying logistic regression analysis.

**Results:** Study population was predominantly female (88%), and the average current age was  $57.4 \pm 11.2$  years. The median duration of RA was 9 years. Only one quarter (25%) of participants were employed, those unemployed 26% or retired (48%) comprised the majority of the sample. In terms of education approximately 60% participants finished secondary school. The participants in this study were primarily married (77%). The majority of the patients were prescribed methotrexate (77%), other common DMARDs prescribed for these patients included hydroxychloroquine (13%) and prednisone (18%). Approximately 20% of patients were receiving a biological drug. Half of the patients estimated that they had severe pain on visual analogue scale (VAS >5). The majority of the RA patients had some comorbidity (80%). The most of these RA patients (89.7%) were considered adherent to medication prescriptions and the remainder (11.3%) were non-adherent. There were no significant difference in clinical or demographic factors between groups except for employment and concomitant use of biological therapy. One third (33.3%) of the non-adherent participants were using biologic drug, while only 19% of the adherent patients were using biologics. There were significantly more employees (29%) among the non-adherent patients. According to the results of univariate regression analysis the following factors are significantly associated with non-adherence to DMARDs: employment (OR=2.277;  $p=0.049$ ), and concomitant use of biological therapy (OR=2.312;  $p=0.002$ ). Finally, in the multivariate regression model concomitant use of biological therapy (OR=2.067;  $p=0.017$ ) remained statistically significant and was identified as independent predictor of non-adherence to DMARDs.

**Conclusions:** The results of our study have shown that about 10% of RA patients met the criteria for non-adherence to DMARDs. Concomitant use biologics and employment are independent predictors of non-adherent.

**Disclosure of Interest:** None declared

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AB0307

### PREDICTIVE VALUE OF THE BASELINE CLINICAL, LABORATORY AND ECHOSONOGRAPHIC PARAMETERS OF RA ACTIVITY IN PROGRESSION OF STRUCTURAL DAMAGE IN DMARDS NAÏVE EARLY RA PATIENTS – 6 MONTHS FOLLOW-UP-

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**Background:** The structural damage of RA usually develops within the first two years of disease and the risk of joint destruction is still difficult to predict<sup>1</sup>

**Objectives:** To assess predictive value of the clinical, laboratory and echosonographic parameters activity of early RA in progression of structural damage in DMARDs/gluocorticoid naïve patients in the first 6 months.

**Methods:** Sixty-five pts. (56 females, mean age 53±14.1 years) with early RA (EULAR/ACR 2010 criteria) and symptoms duration of ≤1 years. (mean duration of 3.6 months) were included during the 2012–14 years. and followed up 6 months. Patients were DMARDs/gluocorticoid naïve and had no X-ray visible structural damage. The ESR, CRP, RF, ACPA and MMP3 were measured. DAS28 index was calculated. US assessment was performed blindly to patient's medical history, on the same day when early RA diagnosis was established and repeated after 6 months, using 18MHz linear probe by ESAOTE My Lab 70 machine. Presence of bone erosions and Power Doppler (PD) signal, were recorded at each hand's joint, as well as at MTP1–5 joints of both side, according to OMERACT US group definition. The semi quantitative method (0–3) was applied for assessing US synovitis and total Power Doppler joint score (TPDJs)/pts. was calculated.

**Results:** Fifty-nine pts. had finding of US bone erosions at baseline visit and 62 pts had it after 6 months. The significant increase of bone erosions and significant decrease of TPDJs/pts were found after follow-up (2.2. vs. 3.1 respectively; 10. vs. 4.5 respectively; Wilcoxon test: p<0.001). There was no statistical significant difference between the groups of pts. with (42 pts.) and without (23 pts.) new (≥1) US bone erosion after 6 months regarding value of ESR (41. vs. 39; p=0.973), CRP (18. vs. 11; p=0.255), RF (82. vs. 114; p=0.652), ACPA (184. vs. 319; p=0.784) MMP3 (110. vs. 83; p=0.245), DAS28 (5.7. vs. 5.3; p=0.269), total number of bone erosions (2. vs. 2; p=0.06) and TPDJs/pts (10. vs. 12; p=0.831). Uni-variant logistic regression analysis showed significant predictive value for US bone erosions finding at baseline visit OR 0.68 (0.48–0.98), p=0.04 for progression of structural damage after 6 months of follow up but not for value of: ESR: OR 1.28 (0.45–3.61), p=0.635; CRP: OR 2.75 (0.95–7.93), p=0.06; RF: OR 0.83 (0.30–2.30), p=0.726; ACPA: OR 0.96 (0.33–2.78), p=0.904; MMP3: OR 1.28 (0.42–3.88), p=0.656; DAS28: OR 1.23 (0.82–1.86), p=0.311 and TPDJs/pts OR 0.98 (0.93–1.02), p=0.344.

**Conclusions:** Initial finding of US bone erosion is the most important risk factor for progression of structural damage with our DMARDs/gluocorticoid naïve early RA patients in the first 6 months of disease duration.

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AB0308

### IMPORTANCE OF PATIENT EDUCATION FOR MANAGEMENT OF RHEUMATOID ARTHRITIS PATIENTS

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**Background:** People living with chronic diseases such as rheumatoid arthritis (RA) are extremely in need to Patient education (PE) which enables them to cope and adapt with their disease and treatments. PE comprises all educational activities provided for patients, including aspects of health and therapeutic education and promotion. Evolutions have been seen at the last five decades of the patient/clinicians relationship, where the patients can share in decision-making (*Mwidimi Ndosí and Ade Adebajo, 2015*).

**Objectives:** To evaluate the effect of PE program following the eight evidence-based EULAR-2015 recommendations in the management of RA patients.

**Methods:** Comparative study with randomised parallel two arms with ratio (1:1) conducted on 100 rheumatoid arthritis (RA) patients (both sexes), aged 19–71 years patients were carried out at the Department of Rheumatology and Rehabilitation -faculty of medicine of Fayoum University, Egypt. Patients are excluded if they had evidence of mental disorder or psychiatric diseases. Patients can leave

the study at any time for any reason. Two main comparable groups; group I received health education through designed Health education program, Group II were not prone to health education program. Disease activity and disability of patients were assessed prior to the commencement of the program, (visit I pre-intervention), 3 months later (Visit II post-intervention) and 6 months after the first visit (Visit III post-intervention). **Intervention:** A PE program designed by authors addressed EULAR 2015 recommendation of patient education and tailored according to each patient condition. Groups of 8–10 participants randomised to intervention arm attended 1 session each week for 6 consecutive weeks, with each one hour in duration, and then one session every two weeks until the second assessment visit (Visit II) and then every month until the second assessment visit (Visit III).

**Results:** While 50 patients of group I continued at the end of the study, out of 50 patients of group II, 36 patients were available at 2nd visit, and only 24 patients were available to be assessed at the 3rd visit. By comparing lab investigation and outcome scores at follow up visits; although no significant difference between the two study groups regarding lab investigations, DAS28 and HAQ scores at start of study, difference was reported in follow up visits that a significant decrease of these labs and scores were reported in Group I, while no difference reported in Group II.

**Abstract AB0308 – Table 1.** Lab and measuring scores comparison between GI and GII at 3rd Visit

Lab investigation	G I		G II		P value	
	N (=50)	%	N (=24)	%		
ESR	Positive	20	40.0	23.0	95.8.	<b>0.00</b>
	Negative	30	60.0	1		
CRP	Positive	19.0	38.0	19.0	79.2.	<b>0.001</b>
	Negative	31	62.0	5	20.8	
RF	Positive	50.0	100.0	19	79.2	<b>0.003</b>
	Negative	0	0.0	5	10.8	
DAS28	Mean±SD, range	1.6±0.4		3. 6±1.5		<b>0.00</b>
		1.2: 2.3		1.3:5.1		
HAQ	Mean±SD, range	29.0±7.6		59. 8±23.13		<b>0.00</b>
		15:75		23: 88		

**Conclusions:** Patient education (PE) interventions in patients with (RA) documented significant improvements in behaviour, pain, disability of those patients.

#### REFERENCE:

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AB0309

### NEED TO A WALK TO THE COMPLETE REMISSION; FOOT AND/OR ANKLE ARTHRITIS IMPEDE COMPLETE REMISSION IN RHEUMATOID ARTHRITIS –PART 1, CROSS-SECTIONAL STUDY FROM KOREAN COLLEGE OF RHEUMATOLOGY BIOLOGICS (KOBIO) REGISTRY

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**Objectives:** To determine the prevalence of foot synovitis, and the most stringent disease activity index reflecting complete remission among patients with rheumatoid arthritis in Korea.

**Methods:** We conducted a cross-sectional study using data from the Korean College of Rheumatology BIOlogics (KOBIO) registry. Foot arthritis defined as having one or more tender or swollen joints in ankle and/or 1st to 5th metatarsal joints. Functional status and disease activity evaluated by the routine assessment of patient index data3 (RAPID3), the disease activity score 28 ESR (DAS28), the simplified disease activity index (SDAI), the clinical disease activity index (CDAI), and the ACR/EULAR Boolean criteria.

**Results:** Baseline data of 2046 patients were analysed. Patients with foot arthritis showed significantly younger age at the diagnosis, longer disease, duration,



higher DAS-28/SDAI/CDAI/RAPID-3, lower rate of ACR/EULAR Boolean criteria remission, use of higher dose of glucocorticoid, and higher rate of bone erosion not only on foot but also hand X-rays. Among those patients, 174 patients (8.5%) were in DAS 28 clinical remission. Twenty-one of 174 patients (12.1%) had foot arthritis, who showed higher swollen and tender joint count, RAPID-3 score, and patients' global assessment but not physicians' global assessment than those without foot arthritis. Among patients with foot arthritis, rate of complete remission was the highest in patients with CDAI (66.7%).

**Conclusions:** In patients with rheumatoid arthritis, foot and/or ankle arthritis is associated with high disease activity, not achieving complete remission despite of various clinical remission criteria and discordance between patients' and physicians' global assessment.

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AB0310

#### USING TREAT-TO-TARGET STRATEGY BY DETERMINING PHYSICAL DISABILITY AND GLUCOCORTICOID REDUCTION STRONGLY INFLUENCE FUNCTIONAL REMISSION IN RHEUMATOID ARTHRITIS

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**Background:** The initial target in the treatment of rheumatoid arthritis (RA) is to achieve clinical remission (CR) through Boolean definition and/or index-based criteria and sustain CR, and the final target is to maximise long-term health-related quality of life (HRQoL) through arthritis control, joint damage prevention, function normalisation and social participation.<sup>1</sup>

**Objectives:** We aimed to determine the factors that inhibit the achievement of functional remission (FcR) in terms of HRQoL.

**Methods:** A total of 227 patients with RA who had underwent first treatment between October 2014 and December 2017 and had not changed/added another disease-modifying anti-rheumatic drugs (DMARDs) for 12 weeks before the observation day were examined. We used daily-life function and social activity participation to evaluate HRQoL. We adopted the Health Assessment Questionnaire Disability Index (HAQDI) as daily-life functional assessment and EuroQoL 5 dimensions–5 levels (EQ5D) for health status with considerable potential assessment. FcR was defined in this study as HAQDI  $\leq 0.5$  and EQ5D  $\geq 0.867$  "0.867 is the lowest QoL score when only one category permits  $\leq 2$  of the 5 levels, but others need 1 in all five categories". We investigated their age at RA onset, sex, Steinbrocker stage and functional class, HAQDI, disease activity level, rheumatoid factor, anti-cyclic citrullinated peptide antibody at the first consultation, age, disease activity level, HAQDI, EQ5D, and status of methotrexate (MTX), glucocorticoids (GCs) and biologic/target synthetic DMARD (b/ts-DMARD) use at the last observational day. First, the assumed remissions were analysed using the FcR as a purpose variable for these factors. Subsequently, the odds ratio and 95% confidence interval (95% CI) were examined using multiple logistic regression analysis for the statistically significantly different factors and risk factors.

**Results:** The CR achievement rate at the last observational day by Boolean definition and Simple Disease Activity Index were 40.5% and 50.2%, respectively. The achievement ratio of HAQ-DI  $\leq 0.5$ , EQ5D  $\geq 0.867$  and FcR was 73.1%, 48.5%, and 46.7%, respectively. The differences in disease duration, stage, class and HAQDI at the time of the first interview; state of MTX, GCs and b/ts-DMARD use; and age at the last observational day for the achievement of FcR were statistically significant. The odds ratios, as determined by multiple logistic regression analysis of the above-mentioned results, were 1.034 (95% CI 0.982–1.088,  $p=0.202$ ) for disease duration (per 1 year), 1.576 (95% CI 1.257–1.977,  $p<0.001$ ) for HAQDI at first interview (per 0.5), 0.615 (95% CI 0.277–1.365,  $p=0.232$ ) and 4.943 (95% CI 1.683–14.524,  $p<0.01$ ) for GCs state (non-use vs temporal use and non-use vs continuous use, respectively), and 1.164 (95% CI 1.037–1.307,  $p<0.05$ ) for age at last observational day.

**Conclusions:** HRQoL is important as they will influence future treatment strategy. Our results indicated the importance of functional assessment at first interview and demonstrated how to use GCs for the treatment of RA. Ageing always contributes to patients' frailty, and it is unavoidable it. To achieve FcR, functional assessment should be performed during the first interview and short-term use of GC is useful for prompt functional recovery, in consideration of ageing.

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**Disclosure of Interest:** None declared

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AB0311

#### DETERMINANTS OF NON-NOCICEPTIVE PAIN IN RHEUMATOID ARTHRITIS

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**Background:** A neuropathic component (NP) of Rheumatoid Arthritis (RA) pain was described in nearly a third of the patients. Radiographic damage is a reflection of cumulative disease activity and other pathophysiological processes. Some clinical predictors of RA NP were recently identified by our group, but association and adjustment for radiographic damage were not studied.

**Objectives:** To estimate the clinical predictors of NP in RA patients adjusting for their radiographic damage.

**Methods:** Cross-sectional study was performed with RA patients followed at our Rheumatology department. Patients with diagnosed neuropathy or non-RA risk factors for NP were excluded. Selected patients were evaluated in a medical visit. Demographic and clinical data were collected and two questionnaires were applied to assess NP: the Leeds Assessment of Neuropathic Symptoms (LANSS) and the painDETECT (PDQ). Wrists, hands and feet radiographic studies from the previous 12 months were classified according to the modified van der Heijde Sharp's method by one trained reader, blinded for patient clinical variables and treatment allocation. Univariate and multivariate logistic regression were performed adjusting for global radiographic score (GS). Significance level was set as  $<0.05$ .

**Results:** Ninety one RA patients were included. Seventy (77%) were women, with a mean (SD) age of 55.6 (10.8) years and median disease duration of 12 years;<sup>2–41</sup> 84% patients were seropositive for Rheumatoid Factor and/or ACPA; 85 (93%) were treated with DMARDs and 41% with a biological DMARD (bDMARDs). The mean (SD) DAS28 4V CRP was 3.15 (0.77). The median joint erosion score was 28 (range: 3–143) and the median joint space narrowing (JN) was 46 (range: 10–133). Forty-two (46%) patients had LANSS NP ( $\geq 12$ ) and 29% had a possible/likely NP in the PDQ ( $>12$ ). JN was a significant negative predictor of LANSS NP (OR: 0.98,  $p=0.02$ ). After adjusting for GS, gender was not associated with NP. Pain VAS, patient global activity and the tender joint count were positive predictors of NP by both tests. Swollen joint count, ESR or CRP levels were not significantly associated with NP. DAS28 CRP was a significant positive predictor of NP by both tests (OR 1.89 for LANSS and OR: 2.06 for PDQ,  $p<0.05$ ); as well as the HAQ score (OR: 2.68 and OR: 4.85, respectively,  $p<0.05$ ). Positivity for ACPA was a negative predictor of LANSS NP (OR: 0.31,  $p=0.048$ ), as previously described. Current methotrexate treatment had lower odds of LANSS NP (OR: 0.35,  $p=0.04$ ) but did not remained significant after adjustment for DAS28 CRP. Previous/current Hydroxychloroquine (HCQ) treatment was once more a negative predictor for PDQ NP (OR: 0.11,  $p=0.04$ ) and remained significant after adjustment for DAS28 CRP. Previous/current leflunomide (LFN) was newly a positive predictor of NP in both tests (OR: 3.41 for LANSS and OR: 2.95 for PDQ,  $p<0.05$ ), persisting after disease activity adjustment for LANSS NP. No other associations were found.

**Conclusions:** Consistently with our previous data, this study supports an association between NP and disease activity/functional scores but not with objective inflammatory measures. Possible increased risk of NP in LFN treated patients was newly pointed and protective role of ACPA positivity and HCQ was reinforced.

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- [2] Martins-Rocha T, et al. *Ann Rheum Dis*, 2017;76(suppl 2):1177.

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AB0312

#### INFLAMMATORY ACTIVITY APPEARS WELL CONTROLLED IN MOST PATIENTS WITH RHEUMATOID ARTHRITIS (RA) IN CONTEMPORARY RHEUMATOLOGY CARE, BUT JOINT DAMAGE AND DISTRESS REMAIN AS PROBLEMS OF GREATER MAGNITUDE THAN INFLAMMATION

T. Pincus, I. Castrejón, J.A. Block. *Rheumatology, Rush University Medical Center, Chicago, USA*

**Background:** Rheumatologists traditionally use quantitative measures such as swollen and tender joint counts and laboratory tests to assess inflammatory activity. However, structural damage to joints, as well patient distress seen as fibromyalgia, depression, etc., may be important clinical problems for many RA patients, but are described narratively in the medical record rather than estimated

by the physician as quantitative data. Quantitation only of inflammation, while damage and distress are recorded only as narrative descriptions, may limit the capacity to document optimally both clinical status and the rationale for clinical decisions, such as non-intensification of therapy according to "treat-to-target" in patients who may have moderate or high scores on an RA index<sup>1</sup>. We have used 0–10 visual analogue scales (VAS) to score not only physician global assessment (DOCGL), but also levels of inflammation, damage, and distress.

**Objectives:** To analyse 0–10 VAS for DOCGL, as well as for levels of inflammation, damage, and distress in patients with rheumatoid arthritis (RA).

**Methods:** At one academic site, rheumatologists complete four 0–10 VAS for overall physician global assessment (DOCGL), as well as for inflammation or reversible findings (DOCINF), joint and other organ damage or irreversible findings (DOCDAM), and patient distress such as fibromyalgia, depression, etc. (DOCSTR). In a cross-sectional study, mean values of 4 physician VAS were computed in RA patients, and 3 subgroups were compared according to whether scores for inflammation were 2/10 units higher than for damage, similar for inflammation and damage (within 2/10 units), or 2/10 units higher for damage than for inflammation. Mean levels of the 4 VAS in the 3 groups were compared, using analysis of variance (ANOVA).

**Results:** In 50 unselected RA patients, mean 0–10 DOCGL VAS was 4.2, inflammation VAS 2.2, damage VAS 3.5, and distress VAS 2.2 (table 1). Only 9/50 patients had an inflammation VAS more than 2/10 units greater than damage VAS; in these patients, mean VAS for DOCGL=4.6, inflammation=4.9, damage=2.1, and distress=1.1. In 21 patients in whom inflammation=damage, mean VAS for DOCGL=3.9, inflammation=1.8, damage=2.1, and distress=3.2. In 20 patients with damage >inflammation, mean VAS for DOCGL=4.4, inflammation=1.4, damage=5.7, and distress=1.7.

**Abstract AB0312 – Table 1**

	DOC/INF> DOCDAM	DOC/INF= DOCDAM	DOC/ DAM> DOCINF	TOTAL
<b>N</b>	9	21	20	50
<b>VAS DOCGL</b>	4.6	3.9	4.4	4.2
<b>Mean subscale VAS Scores:</b>				
<b>VAS DOCINF</b>	4.9	1.8	1.4	2.2
<b>VAS DOCDAM</b>	2.1	2.1	5.7	3.5
<b>VAS DOCSTR</b>	1.1	3.2	1.7	2.2

**Conclusions:** Physician VAS scores indicated that a damage VAS was 50% higher than an inflammation VAS in all 50 RA patients (3.5 vs 2.2), and identical (2.1) in the 9 with an inflammation VAS 2 units higher than a damage VAS or 21 with an inflammation VAS within 2 units of a damage VAS. A mean distress VAS was identical to an inflammation VAS (2.2) in the 50 patients. Control of inflammation remains a primary concern for rheumatologists, but has improved considerably in recent years, as damage and distress may have become more prominent in routine patient care. Systematic quantitative VAS assessment of damage and distress, in addition to inflammation, appears of value to document patient status and support clinical decisions.

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[1] Tymms K, et al. *Arthritis Care Res (Hoboken)* 2014;66:190–6.

**Disclosure of Interest:** T. Pincus Shareholder of: Dr. Pincus holds a copyright and trademark for MDHAQ and RAPID3 for which he receives royalties and license fees. All revenue is used to support further development of quantitative questionnaire measures for patients and doctors in clinical rheumatology care., I. Castrejon: None declared, J. A. Block: None declared  
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#### AB0313

**PHYSICIAN GLOBAL ASSESSMENT OF THE STATUS OF PATIENTS WITH RHEUMATOID ARTHRITIS (RA) AT THEIR FIRST VISIT TO AN ACADEMIC ROUTINE CARE SETTING ARE EXPLAINED AS MUCH BY DAMAGE AND DISTRESS AS BY INFLAMMATION, ACCORDING TO PHYSICIAN RATINGS: SHOULD THE STRUCTURE OF RHEUMATOLOGY CARE BE MODIFIED?**

T. Pincus, I. Castrejon, J.A. Block. *Rheumatology, Rush University Medical Center, Chicago, USA*

**Background:** A physician global assessment (DOCGL) on a 0–10 visual analogue scale (VAS) reflects inflammatory activity in patients who meet criteria for RA clinical trials, in which DOCGL is more efficient than laboratory tests or joint counts to distinguish active from control treatments.<sup>1</sup> However, in routine clinical

care, patients are not selected for inflammatory activity, and may have joint damage and/or distress (fibromyalgia, depression, etc.) as important clinical problems. Some rheumatologists consider damage and distress in assigning a 0–10 DOCGL; others consider only inflammation. One approach to resolve this matter is for physicians to estimate the proportion of DOCGL attributed to inflammation, damage, or distress (total=100%).

**Objectives:** To analyse a physician 0–10 VAS overall global assessment for estimates of the proportions attributed to inflammation, damage, or distress (total=100%).

**Methods:** Rheumatologists at one academic setting complete a 0–10 VAS for DOCGL, and estimates of the proportion of DOCGL attributed to inflammation, damage, and/or distress (total=100%). These scales were analysed in 38 new patients with RA seen between April and November 2017, using cross-tabulations to compare patients whose DOCGL was 0–4 vs 4.1–10 vs the proportion of inflammation, damage, or distress (total=100%) as 0%–40% or 41%–100%.

**Results:** Physician global assessment was 4–10 in 23/38 patients (61%) at first visit, and 0–4 in 15/38 (39%) (table 1). In all 38 patients, inflammation was rated as explaining 41%–100% of DOCGL in 11/38 (29%), compared to damage in 18/38 (47%), and distress in 6/38 patients (16%). Among the 23/38 patients with DOCGL 4–10, inflammation was rated as explaining 41%–10% of DOCGL in 6/23 (29%), versus 10/23 (43%) for damage, and 5/23 (22%) distress. Therefore, inflammation appear to account for >40% of DOCGL only in a minority of new RA patients, which were explained more by either damage or distress (or both).

**Abstract AB0313 – Table 1.** Number of patients in whom a 0–10 physician global assessment VAS was attributed by the physician to inflammation, damage, or distress (total=100%) at the initial visit of 38 patients with RA

Physician global assessment	All		0–		4.1–		All		0–		4.1–	
	All	0–	4.0	10	4.0	10	All	0–	4.0	10		
% attributed by rheumatologist	Inflammation			Damage			Distress			to...		
0%–40%	27	10	17	20	7	13	32	18	14			
41%–100%	11	5	6	18	8	10	6	5	1			
Total	38	15	23	38	15	23	38	15	23			

**Conclusions:** At one academic rheumatology site, a physician global assessment VAS at the initial visit of patients with RA was explained as much by damage and/or distress as by inflammatory activity. One important limitation of the study is that some patients had already received treatment at other rheumatology sites. Nonetheless, the data indicate that damage and distress appear as prominent as inflammation in contemporary management of RA, reflecting a well-known delay in diagnosis and patient management. The findings suggest a possible need to restructure rheumatology practice to see patients more urgently, including education of primary care physicians, in order to improve outcomes for patients with RA. The data also support the possible value of physician estimates of the proportion of DOCGL attributed to inflammation, damage, or distress.

**Disclosure of Interest:** T. Pincus Shareholder of: Dr. Pincus holds a copyright and trademark on MDHAQ and RAPID3 for which he receives royalties and license fees. All revenue is used to support further development of quantitative questionnaire measures for patients and doctors in clinical rheumatology care., I. Castrejon: None declared, J. Block: None declared  
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#### AB0314

**SETTING TREATMENT TARGET FOR JOINT SURGERY IN LOWER LIMBS IN PATIENTS WITH LONG-STANDING RHEUMATOID ARTHRITIS BASED ON MULTICENTER PROSPECTIVE COHORT STUDY; VALIDATION AND RELIABILITY OF OBJECTIVE INDEX OF ACTIVITY SPEED, TIMED UP AND GO TEST, FOR MEASURING PHYSICAL FUNCTION**

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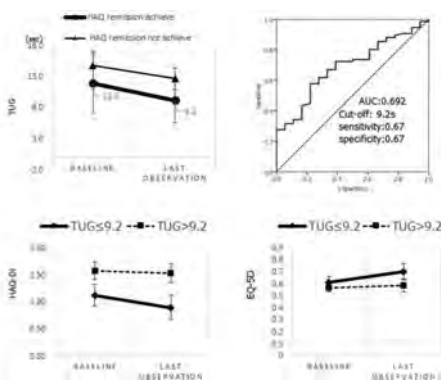
**Background:** Total management including reconstructive joint surgery and rehabilitation should be needed for further improvements of physical function for long-

standing RA patients. It is very important to set treatment goal for those management.

**Objectives:** The purpose of this study is to set treatment target using Timed Up and Go test (TUG) in relation to achievement of HAQ-DI remission (HAQ-DI <0.5) with joint surgery in lower limbs.

**Methods:** Multicenter prospective observational cohort study was conducted among patients who underwent elective joint surgery for RA from April 2012 to March 2016 (Study registration: UMIN000012649). In this study, we collected data including age, sex, disease duration, drug therapies, and disease activity (DAS), TUG, and patient-reported outcome [HAQ-DI, EQ-5D (QOL), patient's global assessment (PtGA) and BDI-II (depression)] at baseline and at 6 or 12 months after the surgery. Association between TUG and achievement of HAQ remission and cut-off values for HAQ remission were also determined using logistic regression analysis with adjustment of age and sex and ROC curve, respectively.

**Results:** Totally, 139 patients with elective joint surgery in lower limbs were analysed. Mean age, disease duration, HAQ-DI and TUG were 65.4 years, 17.5 years, 1.022, and 12.7 s, respectively. Performed joint surgeries were total hip arthroplasty; 10.1%, total knee arthroplasty; 33.8%, total ankle arthroplasty or ankle fixation; 10.1%, and forefoot arthroplasty; 46.0%. The surgeries can significantly improve the outcome measures, including TUG, DAS, PtGA, pain, EQ-5D and BDI-II other than HAQ-DI. In this study, 45 of 139 patients (32.4%) had HAQ remission status at baseline. 18 of 94 patients (19.1%) who had HAQ-DI >0.5 can achieve HAQ remission with the surgery. Notably, TUG at last observation was significantly associated with achievement of HAQ remission even after adjustment for age, sex, and DAS (1 s increasing of TUG. OR:0.72, 95% CI: 0.53–0.97). The adjusted-TUG at last observation of patients with achievement of HAQ remission was 9.2 s (95% CI: 5.6–12.8) (figure 1). Cut-off of TUG at observation for achievement of HAQ remission was 9.2 s based on ROC analysis (figure 2). Importantly, We confirmed significant more improving of EQ-5D, HAQ-DI and TUG in patients who achieved TUG 9.2 s at last observation than in patients who did not (figure 3).



Abstract AB0314 – Figure 1

**Conclusions:** TUG was significantly associated with PRO; HAQ-DI and EQ-5D. The cut-off values of TUG (9.2 s) should be important to achieve good QOL and physical function for patients with joint surgery in lower limbs and could be suitable target for surgical procedure.

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**Disclosure of Interest:** None declared

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AB0315

**HIGH DISEASE ACTIVITY AT BASELINE, NOT RF NOR ACPA STATUS, PREDICTS INADEQUATE RESPONSE TO METHOTREXATE (MTX) IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS IN REAL WORLD: A SINGLE CENTRE COHORT IN JAPAN**

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**Background:** In 2016 update of the EULAR recommendations for management of rheumatoid arthritis (RA), the poor prognostic factors include moderate to high disease activity according to composite measures and presence of Rheumatoid

factor (RF) and/or anti-citrullinated peptide antibodies (ACPA), especially at high levels.

**Objectives:** In this retrospective study, we investigated the association between baseline clinical prognostic factors and inadequate response to methotrexate for early RA in clinical practice.

**Methods:** Patients aged 18 years or over whose date of clinical onset of RA was within the previous 12 months to the first visit to our hospital from 2009 to 2016, who had at least 6 months of follow-up data and composite measure score (DAS-SER, DAS-CRP, SDAI, CDAI) recorded at 12 months from MTX treatment were included. Data collected included baseline demographics, rheumatoid factor (RF), ACPA status and the level of its titer, time from symptom onset to treatment and disease activity at baseline. In this study, we define that it was inadequate response to MTX (MTX-IR) when the patient didn't achieve low disease activity in at least three of four composite measures at 12 months after treatment, or was stopped to treat due to any reason or added biologic DMARDs (bDMARDs) in the observation period. Univariate and multivariate logistic regression of Inadequate response to MTX at 12 months after were performed.

**Results:** Data from 486 patients treated with MTX of 571 started to treat as early RA were analysed: 72.0% female; mean age 59.6 years (SD: 14.4); time from symptom onset to treatment is 7.3 months (SD 10.5); 66.1% RF-positive, 66.9% ACPA-positive. The number of patients is 138 (45.8% of ACPA positive) whose ACPA is in the higher level, over 150IU/ml. 411 patients were initially treated with MTX, and 75 were initially treated with other csDMARDs but added or changed to MTX within 1 years after treatment. Concomitant rate of corticosteroid at the start of MTX was 41.5% and mean dose of prednisolone was 5.7 mg/day. 270 (55.6%) patients were MTX-IR in 12 months after treatment. There is no significant difference between the dose of MTX at start in MTX-IR patients and that in others (6.70 versus 6.69 mg/week, respectively) but the dose at 12 months after treatment was 8.29 mg/w in MTX responders and significantly lower than that of MTX-IR, 8.68 mg/dl (p<0.05). The strongest baseline predictor of Inadequate response were Low disease activity at baseline, but there was no statistically significant association with sex, age at onset, RF or ACPA status additionally the level of its titers.

**Conclusions:** In this observational study, patients with early RA at risk of inadequate response to MTX include only with high disease activity at baseline, and the level of ACPA titers or other baseline characteristics don't predict it.

**Disclosure of Interest:** None declared

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AB0316

**IS THERE A NEED TO RELOOK AT THE CUT OFFS OF RHEUMATOID FACTOR IN INDIAN POPULATION ?**

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**Background:** Population specific cut offs of titers of Rheumatoid Factor (RF) in diagnosis of Rheumatoid arthritis (RA) and the role of anti citrullinated peptide antibodies (ACPA) remains unknown.

**Objectives:** To define cut offs for RF titres in diagnosis of RA in Indian population  
**Methods:** RF titers of consecutive adult RA patients fulfilling ACR 1987 as well as ACR/EULAR 2010 criteria were compared with healthy normal and diseased non RA controls encountered in the rheumatology OPD of a tertiary care Armed forces Hospital using ROC-AUC analysis. Reclassification of disease phenotype as seropositive and seronegative RA using various the cutoffs was looked into and corresponding Anti-CCP titers in the subset of patients with RA was analysed.

**Results:** Overall 589 cases of RA (range: 18–69 years; 29.9% Females) were compared with age and sex matched 192 non RA and 51 controls. Mean (+SE) RF titers in RA cases was 107.7 IU/L (+ 6.17) while that in non RA disease cases was 29.3 IU/L (+ 6.08) and normal healthy controls 14.7 IU/L(0.43). ROC analysis revealed a cutoff titer of 20.3 IU/L (AUC 0.705 (95% CI:0.66–0.74)) with the best combination of sensitivity and specificity for a diagnosis of RA from non RA and healthy controls. With the currently used cut offs of 60 IU/L in our centre as well as high titre RF as per ACR/EULAR 2010 criteria, subjects were seropositive in 286/589 (48.5%) cases. Cutoffs of 40 IU/L and 20 IU/L led to a label of seropositivity in 322 (54.7%) and 396 (67.2%) cases respectively. Simultaneous Anti-CCP was done in 480 (81.4%) cases: 363 (75.6%) of these were positive. Using a cutoff of 60 IU/L as seropositive RA, anti CCP positivity was noted in 246/286 (86%) cases while with a cutoff of 40 IU/L and 20 IU/L it was 278/322 (86.3%) and 334/396 (84.3%) respectively. The RF titers in 117 anti-CCP negative cases was >20, >40 and >60 IU/L in 62 (52.9%), 44 (37.6%) and 40 (34.1%) cases respectively.

**Conclusions:** For this cohort of Indian population, a cut off of 20 IU/L of RF titers has the best performance for a diagnosis of RA with an additional 18.7% cases labelled as seropositive as against the current ACR cutoffs. Anti CCP positivity also no substantially changed by using this lower cutoff. There is a need to reevaluate the population specific RF titers in conjunction with anti-CCP in Indian population.

**Disclosure of Interest:** None declared

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AB0317

### DO MECHANICAL AND INFLAMMATORY RHEUMATOLOGIC DISEASES LEAD TO THE SAME SLEEP DISORDERS?

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**Background:** Sleep disorders are frequent feature of chronic rheumatologic diseases. They are reported in inflammatory diseases as well as in mechanical disorders but they are not systematically assessed by clinicians. It is necessary to identify the frequency and factors associated to sleep problems in order to reduce their impact on patient's quality of life.

**Objectives:** We aim to describe the sleep pattern in inflammatory and mechanical chronic rheumatologic diseases and to assess factors associated with sleep disorders.

**Methods:** We conducted a cross-sectional study during 1 year including Tunisian patients with chronic inflammatory rheumatism (rheumatoid arthritis: RA according to the criteria ACR 1987 and axial spondyloarthritis: AS according to modified NEW YORK criteria) and patients with mechanical disorders (chronic low back pain and primitive knee osteoarthritis). Sleep has been evaluated by the MOS-SS questionnaire. For each group specific disease parameters were assessed at the same time of the administration of the questionnaire.

**Results:** We collected 120 patients with chronic inflammatory rheumatism (group 1) and 80 patients with mechanical disorder (group2). Group 1 was composed of 70 RA and 50 SPA including 65 women and 55 men. The average age was 46.95 [18.75]. Group 2 was composed of 40 chronic low back pain and 40 primitive knee osteoarthritis including 48 women and 32 men. The average age was 51.95 [18.82]. Sleep disorders were frequent in both groups, but they were more noticeable in Group 1 patients than Group 2 patients 53.68% vs 26.38% ( $p=0.00$ ). Risk factors for sleep disorders in rheumatoid arthritis were disease activity ( $p=0.00$ ) and functional impairment ( $p=0.00$ ). In patients with spondyloarthritis, risk factors for sleep impairment were disease activity (BASDAI ( $p=0.00$ ), ASDAS vs ( $p=0.00$ ) et ASDAS CRP ( $p=0.00$ )) and impaired quality of life ( $p=0.00$ ). The factors involved in sleep disorders in chronic low back pain was the reduced lumbar spine mobility assessed by the finger-to-ground distance ( $p=0.00$ ) and the schober index ( $p=0.01$ ) and functional impairment assessed by Eiffel questionnaire ( $p=0.00$ ). In patients with knee osteoarthritis the Lequesne index ( $p=0.008$ ), the knee extension limitation ( $p=0.00$ ) and the radiological damage ( $p=0.004$ ) were associated to sleep impairment.

**Conclusions:** Our results illustrate the frequency of sleep disorders in chronic rheumatic diseases. They should not be under estimated in patients with mechanical disorders. A better control of the factors associated to sleep impairment for each disease should help promoting a better sleep quality in patients with chronic rheumatologic diseases.

**Disclosure of Interest:** None declared

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AB0318

### ARE PATIENTS EXPERIENCING DIFFERENT SORT OF FATIGUE DEPENDING ON THE TYPE OF CHRONIC RHEUMATISM?

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**Background:** Fatigue is frequently reported by patients with inflammatory chronic diseases as well as in mechanical rheumatologic disorders. But it's not recognised and treated as priority by clinicians. It is necessary to identify the frequency of this symptom and to determinate it's impact on the quality of life of patient.

**Objectives:** We aimed to assess and to compare the frequency and the intensity of fatigue between inflammatory and degenerative chronic rheumatologic diseases, and to identify the factors correlated with fatigue in these diseases.

**Methods:** We conducted a cross-sectional study during 1 year including Tunisian patients with chronic inflammatory rheumatism (rheumatoid arthritis: RA according to the criteria ACR 1987 and axial spondyloarthritis: AS according to modified NEW YORK criteria) and patients with mechanical disorders (chronic low back pain and primitive knee osteoarthritis). Fatigue was assessed by the Chalder questionnaire including physical and mental fatigue.

**Results:** We collected 120 patients with chronic inflammatory rheumatism (group 1) and 80 patients with mechanical disease (group2). Group 1 was composed of 70 RA and 50 AS including 65 women and 55 men. The average age was 46.95 [18.75]. Group 2 was composed of 40 chronic low back pain and 40 knee osteoarthritis including 48 women and 32 men. The average age was 51.95 [18.82]. Fatigue was more significantly observed in group 1 than in group 2: 8.40% vs 5.54% ( $p=0.000$ ). Mental and physical fatigue was noted in 2.1% and 6.25% in group 1 and 1.0% and 4.49% in group 2, respectively. The risk factors for fatigue were in the RA the tender and swollen joint count, the DAS 28

and the HAQ. In AS, factors associated to fatigue were the visual scale of pain, BASFI, BASDAI, ASDAS<sub>ESR</sub> and CRP. In the chronic low back pain fatigue was associated by the functional impairment assessed by the Eiffel questionnaire. Finally knee in osteoarthritis fatigue was associated to Lequesne index and radiological stage.

**Conclusions:** Fatigue seems to be a frequent symptom in rheumatic diseases and mostly associated to severity and activity of the disease.

**Disclosure of Interest:** None declared

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AB0319

### MOOD DISORDERS AND CHRONIC RHEUMATOLOGIC DISEASES: ABOUT 200 CASES

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**Background:** Mood disorders are frequently associated to chronic diseases. They are reported in inflammatory diseases as well as in mechanical rheumatologic disorders but they are not systematically recognised and assessed by clinicians. It is necessary to identify the frequency of mood disorders in order to reduce their impact on patient's compliance to treatment.

**Objectives:** The aim of this study was to assess the impact of chronic rheumatologic diseases on the mood of patients by comparing inflammatory and mechanical diseases and to identify factors correlated with anxiety and depression.

**Methods:** We conducted a cross-sectional study during 1 year including Tunisian patients with chronic inflammatory rheumatism (rheumatoid arthritis: RA according to the criteria ACR 1987 and axial spondyloarthritis: AS according to modified NEW YORK criteria) and patients with mechanical disorders (chronic low back pain and primitive knee osteoarthritis). Anxiety and depression were assessed by the BAI (Beck anxiety index) and the BDI (Beck depression index), respectively.

**Results:** We included 120 patients with chronic inflammatory rheumatism (group 1) and 80 patients with mechanical disease (group2). Group 1 was composed of 70 patients with RA and 50 patients with AS including 65 women and 55 men. Their average age was 46.95 [18.75]. Group 2 was composed of 40 patients with chronic low back pain and 40 patients with knee osteoarthritis including 48 women and 32 men. Their average age was 51.95 [18.82]. Anxiety was significantly more frequent in group 1 than group 2: 15.52% vs 9.37% ( $p=0.000$ ). Depression was significantly more noted in group 1 than group 2: 16.29% vs 7.16% ( $p=0.009$ ). The risk factors for anxiety and depression were respectively in the rheumatoid arthritis: tender and swollen joint count, DAS 28, the HAQ and the sharp erosion score. In AS, factors associated to mood disorders were the visual scale of pain, BASFI, BASDAI, ASDAS<sub>ESR</sub> and CRP. In the chronic low back pain mood disorders are associated to functional impairment assessed by the Eiffel questionnaire and the reduced mobility of the lumbar spine assessed by the distance finger-soil. Finally knee in osteoarthritis mood disorders were associated to Lequesne index and the reduction of knee extension.

**Conclusions:** Patients with chronic rheumatologic diseases suffer very often from anxiety and depression which was related in majority of cases to functional impairment, hence the need for multidisciplinary management.

**Disclosure of Interest:** None declared

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AB0320

### IMPACT OF RHEUMATOID ARTHRITIS ON LIFE QUALITY: BEFORE AND AFTER TREATMENT

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**Background:** Life quality issues in rheumatoid arthritis (RA) are often spontaneously mentioned by patients or identified by rheumatologists. Besides classic follow up parameters like DAS28, we have to consider those issues to improve our patients life quality.

**Objectives:** Explore and quantify the impact of RA on life quality via everyday's life and psychological items and the effect of treatment on them.

**Methods:** RA cases were collected by a group of 20 private practice rheumatologists in the Paris area. Basic informations about the patient and his disease were provided by his rheumatologist. Questionnaire including 12 themes and 41 items was filled in by the patient.

**Results:** 167 cases collected: 82% women, mean age 57 years, 56% moderate and 14% severe disease, 76% ACPA positive, 73% structural damage. Initial DAS28 4,7. Post treatment DAS28 2,7. Drugs: classic DMARDs 95%, corticosteroids 73%, biological DMARDs 22%, combination therapy 76%.

Life quality issues are spontaneously mentioned by 55% of the patients.

Before treatment, psychological well-being and housework ability are altered in more than 50% of the patients. Impact on economy, food and social life occurs in less than 25% of the cases.

Life quality is mostly altered by pain (85%), then fatigue (75%) and handicap (58%).

We find a correlation between the severity of RA and the importance of the impact on psychological well-being, sexual life and hobbies.

After treatment, psychological well-being improves in 53% of the patients, and social life, work, getting about and sexual life in 45%–32%.

Items improved around 50% of the patients are in order: sleep, relation to other people, feeling excluded, social life, depression, sick leave, concentration problems, anxiety and shopping.

We find and improvement in a third of cases in house-keeping, going out, sports and libido.

72% of the patients feel a lack of listening by their families, even under treatment.

**Conclusions:** Treatment of RA, including drugs and associated measures, reduces the frequency of negative impact on life quality.

We observe that, when DAS28 drops by 43%, the frequency of RA related repercussions diminishes by 31% (14%–50%) on the chosen items. All the items are impacted by RA before treatment and stay impacted after treatment, but less frequently, except family relations. More than one patient of 2 gains correct sleep and almost half of them aren't depressed or anxious anymore. Impact on social activity and house-keeping activity are less frequently improved.

Regarding these facts, the rheumatologist has to accomplish a tight follow-up and suggest, besides drug treatment, associated measures like physiotherapy, professional activity and environment adaptation and rest among others.

A qualitative evaluation of the improvement will be the subject of a further study.

**Disclosure of Interest:** None declared

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AB0321

**NEGATIVE CORRELATION OF THE ABSOLUTE NUMBER OF CD4 +CD25+FOXP3+REGULATORY T CELLS TO THE LEVELS OF RHEUMATOID FACTOR IN PERIPHERAL BLOOD OF NEW ONSET PATIENTS WITH RHEUMATOID ARTHRITIS**

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**Background:** Rheumatoid arthritis (RA) is a progressive immune-mediated disease that can culminate in joint destruction and early mortality. High levels of serum RF are associated with a worse prognosis in RA. The role of is not fully understood. Recently, Our studies have found that the absolute number of peripheral CD4<sup>+</sup> CD25<sup>+</sup> Fxp3<sup>+</sup> regulatory T (CD4<sup>+</sup>Treg) cells decreased in RA patients. Interestingly, regulatory T cell epitopes (Tregitopes) in IgG have been reported as the main component of intravenous immunoglobulin therapy (IVIg) and provide one explanation for the expansion and activation of Treg cells following IVIg treatment. We hypothesise that RF joins with IgG to form large molecular complexes, which interrupts the production of Tregitopes in antigen presenting cells as a cause of reduction of CD4<sup>+</sup>Treg cells.

**Objectives:** The aim of this study is to investigate whether the absolute number of CD4<sup>+</sup>Treg cells is associated with the titers of auto-antibodies in blood of new-onset diagnosed patients with RA.

**Methods:** A total of 57 new-onset diagnosed patients with RA were enrolled and healthy donors as control. The absolute number of peripheral CD4<sup>+</sup>Tregs cells was detected by multicolor flow cytometry combined with an internal microsphere counting standard. 46 of new-onset cases were tested the levels of RF and anti-CCP with ELISA method. IIF method was used to detect APF and AKA. Low titers group and high titers group around with the value 1:80. All data was analysed by SPSS 22.0.

**Results:** The absolute number of CD4<sup>+</sup>Treg cells in peripheral blood of new-onset patients with RA was significantly lower than in healthy controls [25.1 (16.01, 40.75) vs 33.0567 (22.9, 43.18), p<0.05]. Interestingly, the reduction of peripheral CD4<sup>+</sup>Treg cells was negatively correlated to RF titers (correlation coefficient -0.488, p<0.01) but not to other auto-antibodies against CCP, APF and AKA. The absolute number of CD4<sup>+</sup>Tregs in high titers RF group was lower than in low titers RF group [20.5 (14.0,40.0 vs 34.0 (29.7,44.6),p<0.05]. There was statistically significant difference in two titers groups.

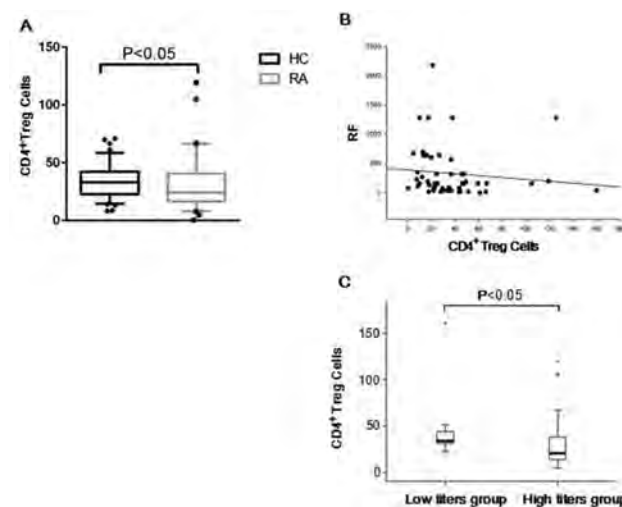
**Abstract AB0321 – Table 1.** Spearman correlation analysis of absolute number of CD4<sup>+</sup> Treg cells and autoantibodies titers in 46 new-onset RA patients

	RF	AKA	APF	a-CCP
CD4 <sup>+</sup> Treg	-0.488**	-0.126	-0.328	0.104

\*\*p<0.01

**Abstract AB0321 – Table 2.** The absolute number of CD4<sup>+</sup>Treg cells Contrast with different titers group

RF	n	M (P <sub>25</sub> , P <sub>75</sub> )	Z	P
Low titer group	13	34.0 (29.7,44.6)	-2.127	0.033
High titer group	33	20.5 (14.0,40.0)		



**Abstract AB0321 – Figure 1.** The absolute number of CD4<sup>+</sup> Treg cells were reduced in peripheral blood of the all enrolled new-onset RA patients (n=57) (A). The reduction of peripheral CD4<sup>+</sup> Treg cells from new-onset patients were negatively correlated with the levels of RF tested in these subjects (B). There was statistically significant difference in two titers groups of RF (C).

**Conclusions:** The absolute number of CD4<sup>+</sup>Treg cells in peripheral blood of new-onset patients with RA was significantly decreased compared with that in healthy controls. Furthermore, the reduction of peripheral CD4<sup>+</sup>Treg cells was negatively correlated to the titers of RF, suggesting that RF contributes to the reduction of CD4<sup>+</sup>Tregs cells. The correlation of decreased CD4<sup>+</sup>Treg and RF may be involved in the pathogenesis of poor prognosis in RA.

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**Disclosure of Interest:** None declared

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AB0322

### DEVELOP AN MASTER ALGORITHM FOR DRUG WITHDRAW STRATEGY IN REDUCTION OF ADVERSE EVENTS WITH COMBINATION THERAPY- A MACHINE LEARNING MODEL FROM THE SMART SYSTEM OF DISEASE MANAGEMENT (SSDM)

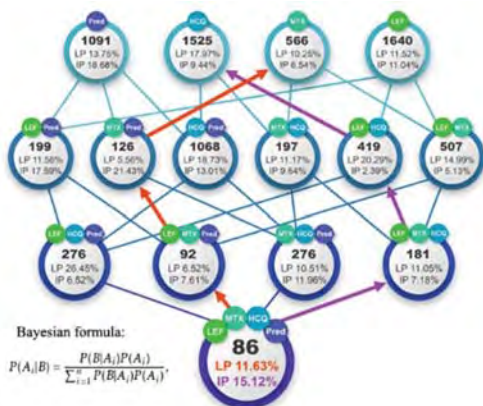
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**Background:** Combination therapy with DMARDs for treating RA is considered as standard of care. However, certain rates of adverse events (AEs) are unavoidable. The stigma is which drug should be stopped first once AEs emerge. The decisions made by clinicians are always empirically.

**Objectives:** To develop an algorithm for decision making on drug withdraw sequence in face of adverse events with combination therapy based on data mining and machine learning from the SSDM.

**Methods:** SSDM is an interactive mobile disease management tool, including the doctors' and patients' application system (App). The patients can input medical records and perform self-evaluation via App. The data synchronises to the mobiles of authorised rheumatologists through cloud and advices could be delivered. In order to develop the master algorithm, abnormal white blood cell (WBC) counts in blood were first targeted. WBC and medication data was collected, extracted, validated, and then based on Bayesian networks, data mining, modelling, calculating, analysing were performed. WBC under 4,000/ml is defined as leukocytopenia (LP), and over 10,000/ml as infection predisposing (IP).

**Results:** From Jun 2014 to Jan 2018, 24,731 RA patients from 486 centres registered in SSDM. 6099 are male and 18 632 are female with mean age of 49.28 ±16.08 (18 to 99) years. 19 different drugs and 126 types of combination therapies are identified. Lab test results showed LP happened in 87 and IP in 123 treatment regiments. Among them we selected prednisone (Pred), leflunomide (LEF), methotrexate (MTX) and hydroxychloroquine (HCQ) as an example to develop a master algorithm based on Bayesian networks and learning model. Figure 1 shows Bayesian network and data processing, in which, quartet are correlating with 15 different regiments. Based on Bayesian method and network data, the calculation for LP and IP probabilities is generated through 32 modelling, and the algorithm for drug withdraw strategies are generated. Drug withdraw sequence for LP is HCQ, then LEF and then Pred, and the risks of LP are reduced by 64%, 52% and 26%, respectively. For IP, withdraw sequence is Pred, then MTX and then LEF, and the risks of IP are reduced by 57%, 63%, and 14%, respectively.



**Abstract AB0322 – Figure 1.** Bayesian network and data processing: patients' number (black bold as blow showed) and the rate of either LP or IP in 15 regiments.

Pred: prednisone; HCQ: hydroxychloroquine; MTX: methotrexate; LEF: leflunomide; LP: leukocytopenia; IP: infection predisposing

**Conclusions:** Big data system can be built using SSDM via empowering patient. Through data mining, networking, modelling, and Bayesian calculation, a master algorithm for drug withdraw strategy in reduction of adverse events with combination therapy is developed, which can be applied on the other AEs in SSDM and may replicated in other diseases. Following the continuing data inputs and machine learning, an artificial intelligent system in assisting clinical decision making may be achieved.

**Limitations:** This study only focus on rate of AE without considering the efficacy, without stratifying dosing.

**Disclosure of Interest:** None declared

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AB0323

### RELATIONSHIP BETWEEN SERUM LEVELS OF LEPTIN & HOMOCYSTEIN IN RHEUMATOID ARTHRITIS PATIENTS WITH OR WITHOUT EXTRA ARTICULAR MANIFESTATIONS

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**Background:** Rheumatoid arthritis (RA) is a chronic, systemic disorder with unknown etiology, which is characterised by involvement of hand joints and deformation. Rheumatoid arthritis is characterised by synovial inflammation and hyperplasia. chronic inflammatory process of the joints that progresses through different stages of increasing severity characterises rheumatoid arthritis.

**Objectives:** In this study we aimed to determine the relationship and correlation between serum homocystein and leptin levels in (patients with rheumatoid arthritis (RA) without extra articular manifestation (non Ex RA)(GROUP-A) and RA patients with extra articular manifestation (ExRA) (GROUP B) and disease progression.

**Methods:** 80 patients diagnosed as rheumatoid arthritis (according to ACR/EULAR 2010 classification criteria) (according to ACR/EULAR 2010 classification criteria) and selected as follow:

(Group A)

40 patients without extra articular manifestation (nonExRA) and

(Group B)

40 patients with variable extra articular manifestation (ExRA),

CONTROL GROUP (C)

Another 40 apparently healthy persons as controls.

RA patients were divided into three groups based on Disease Activity Scores in 28 joints (DAS28) as low disease activity, moderate disease activity, and high disease activity groups.

Of the patients (non Ex RA), 11 (27.5%) had low disease activity (DAS28=2.6–3.2), 15 (37.5%) had moderate disease activity (DAS28=3.2–5.1), and 14 (35.0%) had high disease activity (DAS28 ≥5.1). Laboratory investigations were performed for all patients, including determination of haemoglobin concentration (Hb), erythrocyte sedimentation rate (ESR), and C-reactive protein. Serum concentrations of tumour necrosis factor-alpha (TNF-α), IL-6, Homocystein and Leptin were measured.

**Results:** Significant differences were found between RA patients (group A+group B) and controls healthy group (group C) with regard to the mean levels of Hb, ESR, TNF-α and IL-6 (p<0.05).

As regards to serum leptin, non significant level differences between healthy control group (20.43±8.73 ng/ml) and patient groups (group II and III) (22.43 ±7.73 ng/ml).

while A statistically significant higher mean level serum Homocystein concentration (p<0.05) was found in patients (group A and B) (11.79+8.72 μmol/L) than in control (group C) (8.8+1.58 μmol/L).

Significant differences were found between non ExRA (group A) and ExRA (group B) with regard to the mean levels of Hb, ESR, TNF-α and IL-6 (p<0.05).

A statistically non significant differences in mean level of serum Leptin concentration (p>0.05) was found in group A (22.43±5.73 ng/ml) than in group B (24.43 ±5.73 ng/ml).

While a significant mean level of serum Homocystein concentration (P value<0.05) was found in Group B patients (19.43±1.08 μmol/L) than in group A (11.79±13.05 μmol/L) (p<0.05).

Positive significant correlations were detected between serum Homocystein and ESR, TNF-α, IL-6, and DAS-28 (p<0.05) in group B

Multiple linear regression analysis showed that DAS- 28 and ESR were the main variables associated with serum Homocystein in RA patients (p<0.05).

**Conclusions:** Serum leptin can't be considered of value as an inflammation marker in monitoring RA patients.

Seum homocystein can be used as a marker for probability of extra articular complication of RA.

**Disclosure of Interest:** None declared

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**AB0324** **DISTRIBUTION AND CLINICAL SIGNIFICANCE OF ANTI-HETEROGENEOUS NUCLEAR RIBONUCLEOPROTEIN A2 ANTIBODY IN CONNECTIVE TISSUE DISEASES**

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**Background:** The anti-heterogeneous nuclear ribonucleoprotein A2 (hnRNP-A2) antibody is specific for rheumatoid arthritis (RA). But, it is also reported that there is no significant difference between RA and systemic lupus erythematosus (SLE) in terms of the antibody.

**Objectives:** To investigate the distribution and clinical significance of anti-hnRNP-A2 antibody in connective tissue diseases.

**Methods:** Serum anti-hnRNP A2 antibody level was measured by solid-phase enzyme linked immunosorbent assay (ELISA) in 1464 patients with RA, 209 patients with SLE, 204 patients with ankylosing spondylitis (AS), 63 patients with mixed connective tissue disease (MCTD), 133 patients with undifferentiated connective tissue disease (UCTD), 60 patients with Sjogren syndrome (SS), 47 patients with polymyositis/dermatomyositis (PM/DM), and 45 patients with systemic sclerosis (SSc). The positivity rate of anti-hnRNP-A2 antibody was compared among various patient groups, and its correlation to clinical and laboratory parameters and its diagnostic significance were analysed.

**Results:** The positivity rate of anti-hnRNP-A2 antibody was 38.0% (556/1464), 36.8% (77/209), 3.9% (8/204), 52.4% (33/63), 17.3% (23/133), 5.0% (3/60), 4.3% (2/47), and 8.9% (4/45) in RA, SLE, AS, MCTD, UCTD, SS, PM/DM and SSc, respectively. The rate differed insignificantly between the RA, SLE and MCTD groups ( $p>0.05$ ), but was significantly higher than in other disease groups ( $p<0.01$ ). The titers of anti-hnRNP-A2 antibody were significantly higher in the RA, SLE, MCTD groups than in other disease groups ( $p<0.01$ ), but differed insignificantly between the RA, SLE, MCTD groups ( $p>0.05$ ). In RA patients, anti-hnRNP-A2 antibody weakly correlated negatively to anti-Cyclic citrullinated peptide (CCP) antibody ( $r=-0.135$ ,  $p<0.01$ ), but correlated insignificantly to age, course of disease, time of morning stiffness, erythrocyte sedimentation rate, C reactive protein, rheumatoid factor (RF), anti-keratin antibody (AKA) and glucose phosphate isomerase (GPI) ( $p>0.05$ ).

**Conclusions:** Anti-hnRNP-A2 antibody can be found in various connective tissue diseases, and its positivity rate is relatively high in RA, SLE and MCTD. It is not a RA-specific antibody. In RA, anti-hnRNP-A2 antibody does not coincide with other RA-related serological indicators; hence, it may serve as an adjunctive indicator for RA diagnosis.

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**Disclosure of Interest:** None declared

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**AB0325** **CLINICAL OUTCOME OF 2 YEARS TREATMENT OF THE EARLY PHASE RHEUMATOID ARTHRITIS**

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**Background:** Few studies have reported long term clinical outcome of patients with early phase rheumatoid arthritis (RA).

**Objectives:** The objectives of this study were to investigate outcome of 2 years treatment for RA which was started less than 12 months after RA symptoms first appeared and to evaluate prediction factors of poorly controlled patients at 2 years.

**Methods:** From a total of 1663 RA patients registered in the Akita Orthopaedic Group on Rheumatoid Arthritis (AORA), 66 patients were treated within the first year of RA appearance, and enrolled in this study. Sex, age, RA disease duration, Steinbrocker's stage, Steinbrocker's class, medications and DAS28-CRP at

the baseline and 2 years post-treatment were evaluated. Furthermore, we compared the group of remission (REM) or low disease activity (LDA) with the group of medium disease activity (MDA) or high disease activity (HDA) at 2 years.

**Results:** At the baseline, the patients included 13 males and 53 females. Mean age and RA disease duration were 59<sup>21–85</sup> years and 7<sup>1–11</sup> months, respectively. Fifty-four, 8, 4 and 0 patients were classified into Steinbrocker's stage I, II, III, and IV, respectively. Thirty-nine, 25, 2 and 0 patients were classified into Steinbrocker's class I, II, III, and IV, respectively. Thirty-seven (56%), 24 (36%), and 16 (24%) patients were treated with MTX, DMARDs, and PSL, respectively. In DAS28-CRP, 19 (29%), 13 (20%), 32 (48%), and 2 (3%) patients showed REM, LDA, MDA, and HDA, respectively. Forty-four patients were followed-up for 2 years. At 2 years, 30, 7, 5, and 2 patients were classified into Steinbrocker's stage I, II, III, and IV, respectively. Thirty-one, 12, 1, and 0 patients are classified into Steinbrocker's class I, II, III, and IV, respectively. In DAS28-CRP, 33 (75%), 4 (9%), 7 (16%), and 0 (0%) patients showed REM, LDA, MDA, and HDA, respectively. Compared with the group of REM or LDA, the group of MDA or HDA had significantly older age ( $p=0.018$ ), higher Steinbrocker's stage ( $p=0.012$ ) and higher DAS28-CRP ( $p=0.049$ ) at the baseline.

**Conclusions:** At 2 years, 75% of patients with early phase RA achieved REM. Older age, higher Steinbrocker's stage and higher DAS28-CRP at the baseline could be prediction factors of poorly controlled patients at 2 years.

**Disclosure of Interest:** None declared

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**AB0326** **MATRIX METALLOPROTEINASE-3 IS A GOOD PREDICTOR FOR JOINT DESTRUCTION ONLY IN MALE PATIENTS WITH RHEUMATOID ARTHRITIS**

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**Background:** Serum level of matrix metalloproteinase-3 (MMP-3) is elevated by synovial inflammation. It destroys articular cartilage such as proteoglycans so that it has been used as a clinical biomarker of joint destruction in patients with rheumatoid arthritis (RA).

**Objectives:** The purpose of this study is to investigate a relation between radiographic progression, MMP-3 and other factors such as ultrasonography (US) findings.

**Methods:** 259 patients (213 women) with RA were enrolled in this study. Their baseline data such as age, sex, disease duration, use of glucocorticoid (GC) or DMARDs, disease activity (DAS28), laboratory data (MMP-3, CRP, RF and ACPA), and the Power Doppler (PD) score at digits and wrists by US were collected. The modified total Sharp score (mTSS), erosion score (ERN) and joint space narrowing (JSN) were examined at baseline and 1 year. Their changes from baseline to 1 year ( $\Delta$ ) were calculated. Relationship between baseline MMP-3 and other variables was examined. Predictors for joint destruction was investigated by multiple regression. Statistical analysis was separated by sex because upper limit of MMP-3 is different between men and women.

**Results:** MMP-3 showed no correlations with GC use, DAS28, CRP or mTSS. MMP-3 was correlated with  $\Delta$ mTSS and  $\Delta$ JSN only in men, but PD score only in women (table 1). Multiple regression analysis revealed that MMP-3 was correlated independently with  $\Delta$ mTSS only in men, whereas PD score was correlated independently with  $\Delta$ mTSS in women. PD score, but not MMP-3, could predict joint destruction at 1 year in women (table 2).

**Abstract AB0326 – Table 1.** Correlation with baseline MMP-3; univariate analysis

variables	Male		Female	
	correlation coefficient	P value	correlation coefficient	P value
DAS28-ESR	-0.004	0.980	0.043	0.191
duration	-0.225	0.133	0.088	0.189
RF	-0.083	0.687	-0.192	0.024
ACPA	-0.050	0.797	0.051	0.538
CRP	-0.003	0.986	0.060	0.370
GC use	0.042	0.781	0.109	0.104
mTSS	0.029	0.850	0.100	0.138
$\Delta$ mTSS	0.375	0.010	0.074	0.267
$\Delta$ ERN	0.223	0.137	0.101	0.133
$\Delta$ JSN	0.412	0.004	-0.009	0.891
PD score	0.224	0.143	0.181	0.010

$\Delta$ : difference in values from baseline to 1 year

**Abstract AB0326 – Table 2.** Predictor for joint destruction; multivariate linear regression analysis

	variables	coefficient	P value
Male	MMP3	0.013	0.001
	ACPA	0.010	0.002
	GC use	0.378	0.197
Female	PD score	0.267	<0.001
	ACPA	0.007	0.101
	GC use	-0.449	0.062

**Conclusions:** The baseline MMP-3 was a good predictor for joint destruction at 1 year only in male patients with RA. On the other hand, the baseline PD score was a useful predictor for joint destruction only in female patients with RA.

**Disclosure of Interest:** None declared

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## Rheumatoid arthritis – comorbidity and clinical aspects

### AB0327 CLINICAL SIGNIFICANCE OF HORMONE-RELATED (ISOLATED) AMYLOIDOSIS OF THE ISLETS OF LANGERHANS – A POSTMORTEM CLINICOPATHOLOGIC STATISTICAL STUDY OF 234 RHEUMATOID ARTHRITIS PATIENTS

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**Background:** “All forms of amyloidosis related to the circulation of blood are systemic, and all forms of amyloidosis not connected to the circulation are isolated (localised)”.<sup>1</sup>

Systemic AA amyloidosis (AAa) – characterised by amyloid A deposition – is one of the major chronic complication of rheumatoid arthritis (RA), in most of the cases leading to renal and less frequently to cardiac insufficiency and death.<sup>2</sup>

Islet amyloidosis (IA) (islet amyloid polypeptide – IAPP – prohormone fragment deposition localised to islets of Langerhans) is an isolated (localised) form of amyloidosis of clinical (diagnostic) significance in adult type II diabetes mellitus (DM).

**Objectives:** The aim of this study was to determine the prevalence of AAa and IA in RA, to analyse the relationship between them, furthermore to evaluate the possible role of IA in DM in RA patients.

**Methods:** At the National Institute of Rheumatology 11 558 patients died between 1969 and 1998; among them 234 with RA, and all of them were autopsied. RA was confirmed clinically according to the criteria of the ACR.<sup>3</sup>

The diagnosis of DM based on clinical data. Tissue samples of pancreas were available for histologic evaluation in 150 of 234 patients. AAa and IA was diagnosed histologically, amyloid A and IAPP deposits were confirmed histochemically.<sup>4</sup> The relationships between AAa and IA further more between IA and DM were analysed by Pearson's chi-squared ( $\chi^2$ ) test.

**Results:** AAa complicated RA in 32 (21.33%) of 150 patients. Hormone-related IA localised to the islets of Langerhans was observed in 15 (10.0%) of 150 pancreases: Clinically diagnosed DM was associated with RA in 31 (20.66%) of 150 patients. AAa was associated with IA in 2 (6.45%) of 31 cases. The relationship between AAa and IA was not significant, even the association's coefficient was negative:  $-0.2381$ ,  $\chi^2=0.0785$ ,  $p<0.77$ ). IA associated with clinically diagnosed DM in 8 (53.3%) of 15 patients. There was a positive and significant correlation between clinically diagnosed IA and DM (association's coefficient:  $0.6953$ ,  $\chi^2=10.8475$ ,  $p<0.0009$ ). IA was present without the clinical diagnosis of DM in 7 (46.7%) of 15 patients. The relationship between IA and clinically not diagnosed DM was also positive and significant (association's coefficient:  $0.6037$ ,  $\chi^2=6.8717$ ,  $p<0.008$ ).

**Conclusions:** Systemic or localised types of amyloidosis may exist simultaneously side by side or may be present independently from each other. AAa and IA are independent phenomena based on the negative association's coefficient and not significant relationship between them, and may coexist in RA. According to our interpretation the early stage of IA (involving only a few islets with minimal IAPP deposits) represents a clinically latent DM and the advanced stage of it is clinically manifest DM. The strong positive and significant correlation between IA and clinically manifest DM suggest close relationship between them. Based on the positive and significant correlation between IA and clinically not diagnosed DM, the IA may be a good indicator of potential DM in the latent stage of disease. This correlation may help recognise DM in its early stage. For this reason we recommend that all biopsy material and surgical specimens of pancreas to be tested for IA or IAPP deposition.

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### AB0328 CARDIOVASCULAR RISK EVALUATION IN LONG STANDING RHEUMATOID ARTHRITIS: REAL CLINICAL DATA

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**Background:** According to recent national and EULAR recommendation cardiovascular risk (CVR) in pts with RA should be evaluated using modified SCORE system. But a lot of investigations and real clinical data demonstrate that this system commonly down-estimates CVR in RA pts.

**Objectives:** Aim of our study was to compare standard CVR assessment and additional CVR evaluation on the basis of specific disease-associated risk factors (RF) and CV system investigations in long standing RA.

**Methods:** 118 pts (96 female, 22 male) aged from 34 to 74 years old (mean age  $55.91\pm 5.21$ ) with long standing RA (duration >5 years) were observed. In all pts CVR was stratified according to modified SCORE. We have analysed pts medical cards and standard examination data to determine clinical features of RA and associated conditions to verify severity of CVR. In term to reveal asymptomatic CV disease pts had undergone additional investigations (echocardiography, Dopplerography of carotid arteries, ECG-monitoring).

**Results:** Conventional CVRF were registered in 110 (93.22%) pts. Age>45 (male), >50 (female) was in 85 (72.03%) pts, BMI>25 kg/m<sup>2</sup>; in 10.17%, elevated cholesterol level and/or dyslipidemia in 41.52%, AH with target organ damage was detected in 45.76%, T2DM in 11.8%, CKD 3 stage in 10.17%, history of MI was in 2 (1.69%) pts. According to modified SCORE for RA very high, high, moderate and low CVR was detected in 17.80%, 47.46%, 18.64%, 16.10% cases respectively. High activity of RA was diagnosed in 61.02%, and erosive arthritis in 84.75% pts. Inadequate disease-modifying treatment was qualified in 15.26% cases. Majority of pts (59.32%) received systemic glucocorticoids (GC) in daily doses from 2 to 12 mg of methylprednisolon, among these pts 14 (11.86%) have been taken GC in moderate and high dose for a long period. On the basis of instrumental data asymptomatic atherosclerosis of aorta and/or aortic valve and/or carotid arteries was detected in 44 pts (37.29%). Silent ischemia was revealed in 3 pts (2.54%). High disease activity and long term systemic GC treatment were associated with significantly high CV events in observed pts ( $p<0.05$ ). Using obtained results we reassessed CVR in studied cohort. Revised data of CVR stratification suggest that 49 (41.53%) pts were in VH-CVR, 41 (34.75%) – in H-CVR, 16 (13.56%) in M-CVR and only 12 (10.17%) in L-CVR. The difference in pt ratio for CVR stratification was significant in accordance with  $\chi^2$ ; criterion.

**Conclusions:** Obtained data suggest that modified SCORE is not absolutely reliable tool for precise CVR stratification in long standing RA. Additional investigations to define asymptomatic atherosclerosis and coronary artery disease are required in term to prevent CV complications especially in pts with high active erosive RA treated with systemic GC.

**Disclosure of Interest:** None declared

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### AB0329 THE METHOD OF EVALUATION OF CARDIORESPIRATORY SYSTEM NEUROVEGETATIVE REGULATION IN RHEUMATOLOGIC PATIENTS

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**Objectives:** To study the characteristics of cardiorespiratory system (CRS) neurovegetative regulation disorders and to define the correlation with disease activity.

**Methods:** 40 rheumatoid arthritis (RA) patients (14 m:30 f; median age  $45\pm 2,32$ ), 18 ankylosing spondylitis (AS) patients (13 m:5 f; m.a.  $39.6\pm 2,44$ ), 17 osteoporosis (OP) patients (3 m:14 f; m.a.  $55.5\pm 1,47$ ), 50 healthy persons (HP, 25 m:25 f; m.a.  $23,8\pm 0,84$ ) were studied. The diagnosis<sup>1</sup> of RA, AS, OP were established by the current diagnostic and classification criteria. The cardiorespiratory system neurovegetative regulation was studied with the use of

Spiroarteriocardiorhythmograph, that was able to synchronously analyse the variability of heart rate (HR), respiration (R), systolic (S) and diastolic (D) arterial pressure, respiratory phase structure, baroreceptor sensitivity and some other cariohemodynamics parameters. Following parameters were calculated: spectrum of fluctuations total power (TP), the activity of suprasedgmental (VLF), sympathetic (LF), parasympathetic (HF), cortical (IC) and subcortical (SNCA) contours and sympatho-vagus balance parameters (LF/Hf) in regulation HR, R, S, D, baroreceptor sensitivity (BR), inhale (Ti) and exhale (Te) time (V. Marchenko, 2004).

**Results:** Different severity dysregulation of CRS at all levels is typical for the AS patients, which expresses in decrease of the variability of the basic contours of regulation of heart rate, respiration, systolic and diastolic blood pressure with a shift of sympatho-vagal balance in favour of parasympathicotonia, reduction baroreceptor sensitivity. The heterogeneity of the analysed groups according to the parameter LF/HF<sub>HR</sub> is shown. The ratio of patients with parasympathotony, normotony, sympathotony in groups made up, respectively, in HP (34:48:18), RA (23:54:23), AS (55:28:17), OP (29:53:18). It is established that a significant number of AS patients had parasympathetic type of regulation, and the rest of the groups were dominated by patients with normotonic type of regulation. It is shown that in groups of patients neurovegetative regulation system was more stringent, as evidenced by the increase in their number of reliable correlations compared with the group of healthy individuals. The features of dysregulation in each analysed group were established, the nature of which requires further analysis. Significant correlations ( $\tau > \pm 0,45$ ;  $p = 0,029$ ) between the parameters of the neurovegetative regulation of cardiorespiratory system on the one hand and the clinical and laboratory parameters of inflammatory activity (in the first place, DAS28, CRP, ESR) on the other hand in patients with RA; with parameters BAS-DAl, the activity of the inflammatory process (ESR, CRP) in patients with AS; densitometric parameters in patients with OP were identified. The close connexion between vascular component and the activity of the inflammatory process is shown, which may be a manifestation of endothelial dysfunction.

**Conclusions:** Thus, the method of variability of cardiorespiratory allows to detect the neurovegetative dysregulation of the cardiorespiratory system in rheumatologic patients and can be recommended for the evaluation of the system of regulation in general, the possible role of its disorders in the pathogenesis of clinical manifestations of diseases, and assessing the dynamics of regulatory processes in the treatment of patients.

**Disclosure of Interest:** None declared

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AB0330

#### OSTEOPOROSIS, SARCOPENIA AND OSTEOSARCOPENIA IN WOMEN WITH RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is a systemic inflammatory disease associated with polyarthritis, progressive joint damage, and physical impairment that can lead to osteoporosis and sarcopenia, increasing the risk of fractures and leading to a greater loss of autonomy in RA patients.

**Objectives:** To assess frequency of osteoporosis, sarcopenia and osteosarcopenia in women with RA.

**Methods:** 40 female patients with RA (mean age 63±7 years) and 40 female controls without RA (mean age 64±9 years) were enrolled in this study. Body composition and bone mineral density (BMD) in lumbar spine and proximal hip were assessed by using dual X-ray absorptiometry (DXA, Hologic Discovery A). Sarcopenia in women was defined as a skeletal muscle index (SMI)  $\leq 5.67 \text{ kg/m}^2$  and osteosarcopenia – if sarcopenia and low BMD were present together.<sup>2</sup> The participants performed Short Physical Performance Battery (SPPB) and handgrip strength was measured. Body mass index (BMI) and Disease Activity Score (DAS28) were calculated.

**Results:** Low BMD at least in one of measured area was found out in 19 (48%) RA persons and in 18 (45%) controls. Sarcopenia occurred in 10 (25%) RA patients and in 5 (12,5%) people without RA ( $p > 0,05$ ). Among them osteosarcopenia was found in 6 (15%) RA women and 2 (5%) controls. Skeletal muscle index (SMI) was lower in patients with RA ( $6.43 \pm 0.978$ ) than in controls ( $7.01 \pm 1.064$ ,  $p < 0,05$ ). In RA patients SMI had a positive correlation with BMI ( $r = 0,58$ ,  $p < 0,05$ ) and handgrip strength ( $r = 0,34$  for right,  $r = 0,30$  for left,  $p < 0,05$  for both). Sarcopenia was more common in RA patients who were normal or underweight than in those who were overweight or obese according to their BMI ( $p < 0,01$ ). There was no correlation between SMI and DAS28, drug use, frequency of falls during the last year, SPPB in the RA group

**Conclusions:** In RA patients 48% had osteoporosis and 25% – sarcopenia, among them 15% women – osteosarcopenia. The risk of sarcopenia and osteosarcopenia was higher in nonobese patients.

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**Disclosure of Interest:** None declared

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AB0331

#### INCIDENCE OF MALIGNANCY IN PSORIATIC AND RHEUMATOID ARTHRITIS PATIENTS LIVING IN NEWFOUNDLAND AND LABRADOR

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**Background:** Rheumatoid Arthritis (RA) and Psoriatic Arthritis (PsA) are reported to be associated with an increased risk of malignancy. Newfoundland and Labrador (NL) has one of the highest cancer rates in Canada. There is a paucity of literature on the prevalence of malignancy in NL patients with PsA and RA.

**Objectives:** Evaluate the incidence of malignancy in a cohort of PsA and RA patients and compare rates with the general population. Evaluate the impact of therapy of these two diseases.

**Methods:** Data was extracted from the charts of 200 PsA and 500 RA patients seen at a rheumatology clinic in St. John's between 2011 and 2014. Statistical analyses were performed using SPSS version 21.0 for Windows (IBM Inc.). Person-time Rate (PYs) per 100,000, stratified by age and gender, were used to estimate overall cancer risk and proportions between the two cohorts. Observed rates were compared with Statistics Canada reported general NL rates.

**Results:** We identified 37 (5.3%) malignancies: 34 (91.8%) solid and 3 (8.1%) hematologic. Mean (SD) age was 58.4 (12.28) and age at diagnoses of disease was 46.8 (12.88). Four hundred and eighty (68.6%) were females. No difference was observed in rates between the study population and the NL general population ( $p < 0.3217$ ). The most common solid tumours were breast 8 (21.6%) and skin 8 (21.6%), followed by five bowel and lung cancers in equal proportions (13.5%). Distribution of cancers between the two cohorts were similar.

**Conclusions:** The results suggests there is no difference in the cancer rate between our cohorts and the NL general population. We acknowledge study limitations related to shorter duration of follow-up and lower sample size.

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AB0332

### COMORBIDITIES PREVALENCE AND CHARLSON INDEX IN A COHORT OF PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** The Charlson comorbidity index (CCI) is a prognostic scale, which gives a numerical value that indicates the burden of comorbidities in a patient. This index is obtained from the sum of 19 medical conditions that have been related to mortality and has been validated in several studies. Patients with rheumatoid arthritis (RA) are more at risk than the general population of developing comorbidities. However, these often go unnoticed despite the impact on the disease activity and to treatment response, as shown by different studies such as COMORA.

**Objectives:** To determine the prevalence of comorbidities in a cohort of patients with RA and estimate CCI.

**Methods:** Cross-sectional descriptive study, patients diagnosed with RA according to the EULAR<sup>ACR 2010</sup> classification criteria were included. All patients were followed up in a rheumatology service in a tertiary hospital. Comorbidities were obtained from the medical records. To measure comorbidities, CCI was calculated, the diagnosis of RA was not included in the index. We defined three categories of comorbidity according to CCI: 0 (no comorbidity, applied to patients with no previous record of conditions included in the CCI), 1 to 2 (moderate) and 3 or more (severe). Others comorbidities not included in CCI, such as hypertension (HTN), dyslipidemias (DLP), thyroid disease (TD), osteoporosis (OP) were collected.

**Results:** 130 patients (103 women) were analysed; mean age was 58.6±12.9 years and disease duration of 6.0±4.4 years. 82.8% were seropositive for rheumatoid factor (n: 83) and/or anti-CCP (n: 97). 44.6% had previous smoking history, 22 were current smokers. The most observed comorbidities in our cohort were: overweight and obesity (BMI ≥25; 63%), DLP (38.8%), HTN (31.5%), chronic kidney disease (32.3%; 6.9% ≥Stage III) and chronic lung disease (23.8%). Other diseases included TD (18.5%), OP (17.7%), diabetes mellitus (9.2%) and liver disease (9.2%). Five patients with a history of tumour (2 metastases) and 2 lymphomas in the last 5 years. Four patients had a heart disease, in 3 as an ischaemic event.

According to CCI, 20.8% of the patients had a Charlson 0, 43.8% Charlson 1–2, and 35.4% Charlson ≥3.

**Conclusions:** In our cohort, despite being a relatively young population, the presence of comorbidities and cardiovascular risk factors is relatively high, in agreement with what has been observed in other studies. 1 out of 3 patients has a severe comorbidity burden.

**Disclosure of Interest:** None declared

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AB0333

### ANALYSIS OF THE ASSOCIATION OF COMPOUND INDICATES OF DISEASE ACTIVITY AND QUALIFICATIONS OF FUNCTIONAL CAPACITY AND QUALITY OF LIFE RELATED TO HEALTH IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** The correlation analysis of ICADs with questionnaires of functional evaluation and quality of life is essential, since it is the outcomes that matter to the patients.

**Objectives:** To evaluate the correlations between ICADs with questionnaires of functional capacity (HAQ) and health-related life quality (SF12).

**Methods:** Cross-sectional study with 100 out-patients of Santa Catarina, participants of a multicenter cohort, followed between August 2015/January 2016. Evaluated ICADs were: DAS-28 VHS, DAS-28 PCR, SDAI, CDAI, RADAI. The questionnaires were: HAQ and SF12. Tests Qui Square, test t Student, prevalence ratio and Pearson's correlation were used, with reliability interval 95%. Approved by Ethics Committee in Research of UNISUL.

**Results:** Moderate correlation between ICADs and HAQ (variation r 0,52–0,65). Weak correlation between ICADs and SF12 (Physical: variation r 0,15–0,24 and Mental: variation r 0,40–0,45).

**Abstract AB0333 – Tabel 1.** Correlation between Laboratory Parameters and Functional Capacity (HAQ) in patients with Rheumatoid Arthritis of Santa Catarina.

Variables	HAQ*
	r
ESR† (mm/1 <sup>h</sup> )	0,238
CRP‡ (mg/dl)	0,287
DAS-28§ ESR	0,580
DAS-28 CRP	0,551
SDAI	0,524
CDAI ¶	0,524
RADAI**	0,655

\*Health Assessment Questionnaire † Erythrocyte Sedimentation Rate ‡ C-Reactive Protein § Disease Activity Score-28 || Simplified disease activity index ¶ Clinical disease activity index \*\*Rheumatoid arthritis disease activity.

Source: Elaboration of the author, 2017.

**Conclusions:** ICADs correlate poorly with quality of life, assessed by SF12, but moderately with functional limitation, assessed by HAQ.

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AB0334

### NEOPLASM RISK IN A RHEUMATOID ARTHRITIS COHORT: A RETROSPECTIVE STUDY

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**Background:** It is well known that the risk of neoplasms is increased in rheumatic patients, especially in Rheumatoid Arthritis (RA), SLE and inflammatory myopathies. Although the relationship between neoplasms and some factors involving the pathophysiology and immunomodulatory therapy of this diseases is well known, we still don't know all the mechanisms underlying this process. Thereby, this theme has been of ongoing interest and research.

**Objectives:** To determine whether the incidence of neoplasm is increased in patients with RA compared to a matched comparison cohort and to identify risk for any individual malignancy in RA.

**Methods:** A cohort of 243 RA patients, who fulfilled 1987 ACR criteria for RA and a comparison cohort, sex and age matched without RA (non-RA) were evaluated retrospectively for cancer occurrence. Demographic, epidemiological, clinical, laboratorial and imaging data were collected through medical record review. All paraneoplastic cases were excluded. Descriptive statistics were used to summarise data of the RA and comparator group.

**Results:** 243 RA patients (mean age 62,9 y, 68,7% female, mean disease duration 10,6 y) were enrolled. 148 RA patients had rheumatoid factor (RF) present

and 120 had anti-citrullinated peptide (anti-ccp) positive. Erosions were present in 106 RA patients. The prevalence of neoplasms was similar in RA and non-RA groups ( $n=24$  vs  $23$ ,  $p=0,8$ ) and 5 of the deaths occurred in the RA-neoplasm group were due to the cancer. Of the 24 neoplasms in RA group, 9 appeared after the RA diagnosis was established (mean 10 years) and 17 before (mean 9,65 years). In RA patients correlation was found between male sex and neoplasm ( $p=0,04$ ) as well as absence of RF rheumatoid factor and neoplasm ( $p=0,049$ ). No correlation was found between the presence of neoplasm and anti ccp presence or erosions ( $p=0,3$  and  $p=0,51$  respectively). In this study, the overall risk of neoplasms in patients with RA was not associated with conventional or biological DMARD's. No differences were found between the type of tumour in RA patients vs non-RA, except for colon cancer, more prevalent in RA patients ( $p=0,03$ ). Only 21 non-RA patients vs 19 RA patients were smokers and for so, it wasn't possible to establish any correlations.

**Conclusions:** In this study we found a prevalence of colon cancer in RA patients, as was found in other studies whoever, the increased risk for lung cancer and lymphoma often reported, was not found. It seems that male sex and the absence of rheumatoid factor are responsible for an increased risk. However we have several limitations: a very small sample, the population of the study was predominately Caucasian. Further studies examining specific aspects such as treatments, smoking or other lifestyle factors are needed to investigate the underlying mechanisms for the increased or decreased risk of specific cancers observed in patients with RA compared with the general population.

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AB0335

#### ARE EULAR RHEUMATOID ARTHRITIS (RA) MANAGEMENT RECOMMENDATIONS APPLICABLE AT THE COUNTRY LEVEL? SIMILARITIES AND DIFFERENCES WITH THE RECENT FRENCH RA MANAGEMENT RECOMMENDATIONS

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**Background:** Recently, EULAR updated the rheumatoid arthritis (RA) management recommendations.<sup>1,2</sup> In 2018, the French Society of Rheumatology (SFR) updated their recommendations regarding the management of RA.<sup>3</sup> This gave us the opportunity to compare the recommendations.

**Objectives:** To update the 2014 French recommendations for the management of RA and to compare them to the EULAR recommendations.

**Methods:** The SFR approach was based on the literature and on expert opinion. A systematic literature review (SLR) was performed by 2 fellows, collecting data to answer 11 questions. The previous (2014) recommendations were updated by a committee including 11 rheumatologists, 2 patients and 1 healthcare professional, during a 1 day meeting in January 2018. The recommendations were compared to the recently issued EULAR recommendations.<sup>1,2</sup>

**Results:** The SLR included 137 papers. The consensus process led to 4 overarching principles and 15 recommendations. The overarching principles emphasise the need for shared decisions between the rheumatologists and the patient and the importance of a global approach of RA including pharmaceutical and non-pharmacological management. The recommendations address the diagnostic phase of RA, early initiation of disease-modifying antirheumatic drugs (DMARDs) and the usefulness of regular disease activity assessments through validated composite indices with a target of clinical remission or low disease activity. As first strategy, the expert committee recommends methotrexate (MTX). In case of intolerance or inadequate response to MTX, treatment must be optimised. If unfavourable prognostic markers are present, adding a targeted treatment (either biologic or synthetic) can be proposed, at best in combination with MTX; if not, switching to another conventional synthetic DMARD (csDMARD) or combined csDMARDs therapy can be proposed. While waiting for csDMARDs efficacy, short term (less than 6 months) glucocorticoids (GC) can be proposed. Second-line and further treatments and management of remission are also addressed, as well as the importance of managing comorbidities and of non-pharmacological measures.

**Conclusions:** These recommendations are designed to improve the management of RA and are concordant with the recent EULAR recommendations on several items. Main differences concern the place of GC and of combined csDMARD therapy, as well as additional points on diagnosis, non-pharmacological measures, comorbidities and the importance of a global approach.

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AB0336

#### HEPATITIS B VIRUS REACTIVATION IN RHEUMATOID ARTHRITIS PATIENTS WITH HBSAG-NEGATIVE/ANTI-HBC-POSITIVE STATUS

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**Background:** Hepatitis B virus (HBV) reactivation in rheumatoid arthritis (RA) patients with positive hepatitis B surface antigen (HBsAg+) is one of the treatment-related complications. The risk of reactivation in patients with negative hepatitis B surface antigen but positive anti-hepatitis B core antibody (HBsAg-/anti-HBc-) is less well defined compared to their HBsAg +counterparts.

**Objectives:** This retrospective, single centre study aimed to study the prevalence of HBV reactivation (defined as HBV DNA becoming detectable) among RA patients with HBsAg+/anti-HBc +status, and to investigate any factors predicting reactivation.

**Methods:** RA patients attending the rheumatology specialist clinic in a local tertiary hospital between 1st January 2011 and 31st December 2016 were included if they had of<sup>1</sup> HBsAg-/anti-HBc +status and<sup>2</sup> undetectable HBV DNA at baseline. Demographic data, clinical parameters including treatments for RA and any use of antiviral prophylaxis, and laboratory results including anti-hepatitis B surface antibody (anti-HBs) and serial HBV DNA levels were obtained. Chi-square (or Fisher exact test if number was less than 5) was used for analysis of categorical variables. Student's t-test and Mann Whitney test were used for analysis of parametric and non-parametric continuous variables respectively.

**Results:** Majority (80%) of the 107 included patients included were female and the mean age was 62.5-year-old (SD 12.09). All the patients were receiving disease modifying anti-rheumatic drugs (DMARDs), 43% of which (n=46) were on biological therapy (with or without concomitant synthetic DMARDs) and the remaining (n=61) were only on conventional synthetic DMARDs (8 on monotherapy, 53 on combination therapy). As antiviral prophylaxis was not mandatory in HBsAg-/anti-HBc +patients according to local guideline, only 13 patients (12.1%) were on antiviral cover (12 on entecavir and 1 on lamivudine).

Ten patients (9.3%) experienced HBV reactivation during their disease course. Three of them were on antiviral prophylaxis and four had positive anti-HBs. All of these reactivations were only transient low-grade viraemia with HBV DNA level <20 IU/ml. Spontaneous resolution of viraemia in less than 12 months' time were observed in all of these patients. None of the reactivation resulted in any adverse clinical event including acute hepatitis, hepatic failure or mortality.

Among all synthetic and biological DMARDs, only the use of methotrexate was found to be a significant predictor of HBV reactivation ( $p<0.05$ ). Other parameters including age, the lack of antiviral prophylaxis, negative anti-HBs status and anti-HBs titre did not predict HBV reactivation.

**Conclusions:** HBV reactivation among RA patients with HBsAg-/anti-HBc +status and undetectable HBV DNA at baseline was infrequent. Reactivation may occur in patients with positive anti-HBs or on antiviral prophylaxis, but was unlikely to be associated with adverse clinical outcome. The use of methotrexate was a predictor of HBV reactivation in these patients.

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AB0337

### ASSESSMENT OF NUTRITIONAL STATUS IN WOMEN WITH RHEUMATOID ARTHRITIS MEASURED BY DUAL ENERGY X-RAY ABSORPTIOMETRY

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**Background:** As many other chronic diseases, rheumatoid arthritis (RA) has been related to an impairment of the nutritional status of multifactorial etiology. Even if Body Mass Index (BMI) has traditionally been used, it is not always a valid method, and there are still lots of questions without answer in how to evaluate ideally the nutritional status in these patients. Only very few studies had evaluated it by Dual Energy X Ray Absorptiometry (DXA).

**Objectives:** 1) To evaluate the nutritional status in women with RA and to compare with a population of same age women without RA using DXA for the analysis of whole body composition, 2) differences between the prevalence of alterations of the nutritional status measured by DXA and by the classical methods used in clinical care, 3) relation of RA time of evolution, inflammatory activity, physical function and dietary intake on altered nutritional status evaluated by DXA.

**Methods:** Case-control study including 89 patients that were diagnosed with RA and a control group (100) composed by patients affected by other non-inflammatory rheumatic diseases as soft tissue diseases. All the clinical charts were revised in order to record the following data: age, BMI, RA duration, history, activity and disability, serum albumin, Dietary intake, Whole body DXA assessment and Skeletal muscle index (SMI).

**Results:** Mean age of patients was 62±8 years. Mean duration of RA was 13.7±9.3 years. Mean DAS28 was 3.7±1.4 and mean Health Assessment Questionnaire was 0.88±0.77. BMI of the patients was 27.43±5.16 and 27.78±3.98 in controls (p: ns). Albumin was within normal range in all patients.

RA patients presented a statistically significant lower lean mass than controls in all locations and lower fat mass in limbs, along with a higher fat trunk.

RA duration was found to be inversely correlated to BMI and lean mass and directly correlated with fat mass.

Neither BMI nor albumin correlated with DXA parameters.

RA patients fulfilled criteria of sarcopenia in 44% of de cases vs 19% of controls (p<0,001). In RA patients, regarding SMI, BMI showed a high specificity to detect sarcopenia (94% of the patients with low BMI had sarcopenia) but low sensitivity (47% of the patients with normal or overweight BMI had sarcopenia).

**Conclusions:** RA patients have an impairment of nutritional status associated to time of evolution that resembles sarcopenia and that is not predicted by BMI.

**Disclosure of Interest:** None declared

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AB0338

### CLINICAL CHARACTERISTICS OF PATIENTS WITH RHEUMATOID ARTHRITIS WHO USED COMPUTER TERMINALS FOR SELF-ASSESSMENT OF DISEASE ACTIVITY AND QUALITY OF LIFE

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**Objectives:** To present the clinical features, pharmacotherapy, activity and quality of life in pts with rheumatoid arthritis (RA) who used computer terminals for self-assessment of pts with rheumatic diseases.

**Methods:** The study included 976 RA patients from the cohort of "TERMINAL" multicenter study, envisaging pts' self-assessment of disease activity and quality of life using a designated computer system ("Computer terminals for self-assessment of pts with rheumatic diseases) before the visit to the rheumatologist. Mean age 52,3±13,3 years, mean disease duration 10,2±8,5 years, 85% female. Baseline clinical parameters and pharmacotherapy were assessed, as well as disease activity (using DAS 28 and RAPID-3), and quality of life (using HAQ and EQ-5D).

**Results:** 83% of pts were RF positive, and 60% ACCP positive. Almost all (91,2%) pts received conventional DMARDs. 70,2% of them received methotrexate: 56,7% 15 mg/week and 13,5% >15 mg/week (from 17,5 to 40 mg/week). 20,5% pts were treated earlier with low doses of glucocorticoids. 6,6% pts received Infliximab, 16,4% – Rituximab and 9,8% pts were treated with more than 1 biological agent in anamnesis. 46,2% of pts had high disease activity, 40,9% moderate, 4,5% low and 1,5% pts achieved clinical remission (mean DAS28 score 4,2±1,8, RAPID 13,6±3,6). Only 14,3% pts achieved general population HAQ values. The remaining showed significant reduction in the quality of life (mean HAQ 1,7±0,9, EQ-5D 0,6±0,2). 7,4% of the pts had prosthetic joints.

**Conclusions:** In the studied population almost all patients were treated with DMARDs (mostly methotrexate), and about 30% received biological agents. High to moderate disease activity and reduction in quality of life were typical for this population. Persistence of disease activity and functional insufficiency in pts who received DMARD therapy may be explained by poor monitoring in real clinical practice. The introduction of computer system for self-assessment of disease activity and quality of life in the out-patient facilities will improve the interaction

between doctors, nurses and patients, providing better control of therapy efficacy in RA patients.

**Disclosure of Interest:** None declared

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AB0339

### SARCOPENIA AND EARLY FRAILITY SYNDROME IN RHEUMATOID ARTHRITIS

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**Background:** Sarcopenia and frailty are common in older persons and pose particular challenges for health and social care systems.

Sarcopenia, the loss of skeletal muscle mass, is a core component of physical frailty that together impact negatively on an individual's capability to live independently.

Frailty is defined as a syndrome of physiological decline in late life, characterised by marked vulnerability to adverse health outcomes. Frail adults are less able to adapt to stressors such as acute illness or trauma than non-frail adults. This increased vulnerability contributes to increased risk for multiple adverse outcomes, including procedural complications, falls, institutionalisation, disability, and death.

Rheumatoid arthritis (RA) is a chronic disabling disease, which leads to functional limitations and diminishes health-related quality of life. The presence of comorbidity and polypharmacy are both related to RA severity.

**Objectives:** The aim of this study was to assess the prevalence of sarcopenia and frailty syndrome in patients with RA.

**Methods:** Cross-sectional, observational and descriptive study in patients with RA (ACR criteria) older than 50 years.

Sarcopenia was defined as per the European Working Group on Sarcopenia in Older People definition as Skeletal muscle mass index (SMI) ≤8.87 kg/m<sup>2</sup> in men and ≤6.42 kg/m<sup>2</sup> in women. Body composition analysis was performed using bioelectrical impedance analysis (BIA).

Fragility was measured according to the 5 criteria proposed by Fried, using the Frail scale, and it was considered fragile to the patient who met at least 3 and pre-fragiles to those who met at least 2.

Frail scale: Based on five items, reflecting performance, self-reports and common co-morbidities (Morley JE et al. *J Nutr Health Ageing* 2012;16(7):601–8).

**FRAIL SCALE**

Did you feel worn out? or Did you feel tired?

Ability to climb one flight of stairs

Ability to walk 100 m

Self-report of >5% wt loss

≤5 of: dementia; heart Disease; depression; arthritis; asthma; bronchitis/emphysema; diabetes; hypertension; osteoporosis; stroke.

**Results:** 283 consecutive RA patients were included, 83.4% were female. Mean age was 63.3 years and mean disease duration was 10.4 years.

Mean number of comorbidities was 1.48, with systemic hypertension and obesity as the most frequent ones (33.8% and 26.4%, respectively). Polypharmacy was found in 96.8% and 64.7% received more than five drugs simultaneously.

31% presented some degree of sarcopenia. 21.5% met frailty criteria (42% in ≥65 years old patients).

**Conclusions:** Prevalence of sarcopenia and frailty syndrome in this study was high. Rheumatologists should make an early detection of signs of frailty.

The screening and early detection of frailty can spur reforms to make routine care less hazardous, can focus on outcomes most relevant to patients and can aid in understanding effectiveness of health care interventions, including at the population level.

**Disclosure of Interest:** None declared

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AB0340

### ASSOCIATION BETWEEN MICROALBUMINURIA AND METABOLIC SYNDROME IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is an autoimmune, symmetrical polyarticular disease characterised by chronic inflammation of the synovial joints. Microalbuminuria (MA) occurs as a leakage of small amounts of albumin into the urine. Metabolic syndrome (MetS) describes risk factors for cardiovascular diseases such as dyslipidaemia, obesity, hypertension and diabetes.



**Objectives:** The aim of this study is to detect the prevalence of MA in patients with RA and study its correlation with disease activity and severity. Our aim extends to identify the association of MA with MetS in rheumatoid arthritis

**Methods:** This study was carried out on 30 adult RA patients, 30% male patients and 70% female patients (mean  $\pm$ SD 42.27 $\pm$ 10.99 years). Their mean disease duration was 12.8 $\pm$ 7.06 years. Twenty apparently healthy adults of matched age and sex served as a control group. All the patients were subjected to full history taking, full clinical examination, laboratory investigations and assessment of disease activity using DAS 28 Score. Urinary microalbumin level was measured in all subjects in early morning samples by the immunoturbidometry method. MetS was assessed in all subjects according to Grundy's criteria.

**Results:** The RA patients' group had highly significantly ( $p < 0.001$ ) elevated mean values of urinary microalbumin and urinary albumin to creatinine ratio compared to the control group (63.9 $\pm$ 2.57 mg/dl vs 21.95 $\pm$ 13.88 mg/dl, 46.6 $\pm$ 35.28 ug/mg vs 14.9 $\pm$ 11.45 ug/mg respectively).

The frequency of the metabolic syndrome according to Grundy's criteria was 60% in the RA patients' group. This frequency was highly statistically significant ( $p < 0.001$ ) compared to the control group (10%). The MetS was prevalent in 13/15 (87%) of RA patients with microalbuminuria (MA), while 5 normo-albuminuric RA patients (33%) had the MetS. A statistically significant difference was observed among these groups ( $p < 0.05$ ). On the other hand, 13/18 (72%) of RA patients with MetS had MA.

Although RA patients with MA had and increased mean values of disease duration, body mass index, waist circumference, fasting blood sugar, triglycerides, high density lipoprotein, DAS 28 and Larsen's score, they had no statistically significant differences compared to normo-albuminuric patients.

RA patients with the MA had a statistically significantly higher mean disease duration ( $p = 0.004$ ) than patients without the MetS. There were highly statistically significant positive correlations ( $p < 0.001$ ) of urinary microalbumin levels with disease duration, duration of morning stiffness, number of tender joints, number of swollen joints, ESR 1st hour, C-reactive protein, Larsen's score, DAS 28, and A/CR.

**Conclusions:** MA and MetS are frequent in RA, particularly in those with long standing disease. Early detection of albuminuria allows early intervention with the goal of reducing inflammation development in RA, CV risk. MetS is frequent in RA patients with MA.

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**Disclosure of Interest:** None declared

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#### AB0341 METATARSOPHALANGEAL JOINTS HAVE MORE EROSIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is a chronic inflammatory disease characterised by destruction of synovial joints, especially in the hand and feet, leading to severe disability and premature mortality. The erosions seen in RA differentiate it from other rheumatological diseases.

**Objectives:** The aim of the study was to evaluate the relationship between attack frequency and erosions seen in RA.

**Methods:** Forty-four patients according to 2010 ACR/EULAR Classification Criteria for RA were included into the study. Involved joints and number of attacks were recorded. The X-rays of the involved joints were assessed on admission and after 3 months in terms of joint erosion as a blinded manner. Comparison of erosions were calculated by chi-square.

**Results:** Kappa value of intra-observer agreement of reading of x-ray films was 0.68. Erosions were detected in 16 of 44 patients with RA. The Ratios of erosion in joints with more than 10 attacks were different according to involved joints. The ratios of erosions were 10% for metacarpophalangeal (MCP), 8% for proximal interphalangeal (PIP), 0% for knee, 5% for ankle and 69% for metatarsophalangeal (MTP) joints. When compared MTP joints with MCP, PIP and wrist joints, it was seen that the erosion rate was higher in MTP joints than the other joints ( $p < 0.01$ ). Knee and ankle joints were combined as a single group and compared with MTP joints in terms of erosion. It was seen that the erosions in the MTP joints were significantly higher than the erosions in the knee and ankle joints ( $p < 0.01$ ).

**Conclusions:** In RA, the erosion ratio of MTP joints was significantly higher than seen in MCP, PIP and wrist joints. On the other hand the erosion rate in knee and

ankle joints was rare. These results show us the erosion in MTP joints may not related to mechanical overload. Therefore foot imaging with x-ray may be important in the following of patients with RA. In addition existence of false positive erosions in MTP joints of healthy people should be studied.

**Disclosure of Interest:** None declared

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#### AB0342

#### THE CHRONIC HAND PAIN IN RHEUMATOID ARTHRITIS, OSTEOARTHRITIS, AND FIBROMYALGIA: THE ROLE OF CENTRAL SENSITISATION

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**Background:** Modern pain medicine divided chronic pain as nociceptive, neuro-pathic, central sensitisation (CS) and mixed pain. CS syndromes are a group of disorders characterised by chronic non-neuropathic and non-nociceptive pain.<sup>1</sup> Central sensitisation inventory (CSI) suggest the tool generates reliable and valid data that quantify the severity of several symptoms of CS.<sup>2</sup>

**Objectives:** Hand pain in RA, OA, and FMS have different features. The aim of this study was to show the role of CS pain in these patients.

**Methods:** Totally 151 patients with chronic hand pain (56 RA, 45 OA, and 50 FMS) were included. CSI was used for evaluation of CS.<sup>2,3</sup> CSI consists of 2 parts: CSI-A scoring 0–100 and CSI-B including 10-CS related syndromes (restless leg, chronic fatigue, fibromyalgia, temporomandibular disorders, migraine/tension type headache, irritable bowel, multiple chemical sensitivity, whiplash, anxiety/panic attack, and depression).

**Results:** Sixteen patients (28.57%) had active (DAS28  $\geq$  2.6) RA. Disease activity was not related with CSI-A and CSI-B scores. Rheumatoid hands was less painful compared with them of OA and FMS ( $p < 0.001$ ). The CS pain was detected in most of the patients with FMS, compared with OA and RA patients ( $p < 0.001$ ). Similarly, CSI-A score was the highest in patients with FMS group ( $p < 0.001$ ) and similar in both OA and RA groups ( $p > 0.05$ ). CS-related syndromes were also detected in both RA and OA groups, but less than FMS group ( $p < 0.005$ ). The numbers of CS syndromes were similar in both RA and FMS ( $p = 0.084$ ) and higher than OA group ( $p = 0.036$ ). Table 1 shows the demographic and pain parameters in all groups. CSI-A score was correlated with VAS-pain score ( $r = 0.364$ ,  $p < 0.001$ ).

Abstract AB0342 – Table 1. The comparisons of groups

	1.RA	2.OA	3.FMS	P1–3	P2–3
Age(mean $\pm$ SD)	54.52 $\pm$ 10.33	61.2 $\pm$ 9.67	45.22 $\pm$ 8.6	0000	0000
Female%	%83.92	%88.88	% 94	0.564	0370
DAS28	2.21 $\pm$ 0.66				
VAS	4.09 $\pm$ 2.27	6.78 $\pm$ 1.70	8.00 $\pm$ 1.8	0000	0001
CSI-A (+)%	%41.07	%62.22	%94	0000	0000
CSI-A	38.43 $\pm$ 16.2	43.6 $\pm$ 13.1	58.92 $\pm$ 14.78	0000	0000
CSI-B (+)%	%60	%28.88	%100	0000	0000
CSI-B	1.30 $\pm$ 1.6	0.51 $\pm$ 1.05	1.98 $\pm$ 1.2	0000	0000
Restless leg	%19.64	%4.44	%8	0101	0477
Chronic fatigue	%16.07	%2.22	%6	0131	0360
Fibromyalgia	%14.28	%2.22	%100	0000	0000
TMD	%23.21	%17.77	%0	0000	0132
Migraine/TTH	%12.5	%2.22	%30	0032	0231
Irritable bowel	%5.3	%2.22	%4	0742	0621
Multi-chemical s.	%3,57	%0	%4	0908	0175
Whiplash injury	%7.14	%0	%2	0212	0340
Anxiety/panic	%10.71	%2.22	%18	0403	0030
Depression	%16.07	%15.55	%28	0161	0215

**Conclusions:** Central sensitisation should be considered in patients with chronic persistent pain, not only having FMS, but also half of the patients having RA and OA. It is not a rare phenomenon and if it exists, effective pain management strategies could be needed in addition to the specific pharmacologic treatment.

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**Disclosure of Interest:** None declared

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AB0343

#### MYOCARDIAL INVOLVEMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS EVALUATED BY TWO-DIMENSIONAL SPECKLE TRACKING ECHOCARDIOGRAPHY BEFORE AND AFTER 18 MONTHS OF TREATMENT WITH ANTI-TNF DRUGS

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**Background:** Cardiovascular (CV) mortality and morbidity is increased in rheumatoid arthritis (RA). Studies found a more than two- three-fold higher prevalence of ischaemic heart disease in RA patients compared to controls. However, a number of studies indicate that RA is also associated with various non-atherosclerotic CV manifestations. The inflammatory processes in RA may affect different structures of the heart: the most characteristic lesions are conduction defects, but other less frequent manifestations are pericarditis, cardiomyopathy and valve disease.

**Objectives:** The aim of this study was to evaluate left ventricular myocardial function with two-dimensional speckle tracking echocardiography (STE), in addition to conventional Doppler and tissue Doppler echocardiography, in order to detect subclinical left ventricular myocardial dysfunction in patients with RA.

**Methods:** The study involved 30 outpatients who fulfilled the 2010 ACR/EULAR criteria for RA (11 males and 19 females; mean age 54.63±9.36 years, median disease duration 2 years), at baseline and after 18 months of treatment with anti-TNF drugs and 30 healthy controls matched in terms of age, gender and other anthropometric characteristics. All patients underwent a complete physical examination and routine laboratory analysis. CV risk profiles were assessed by means of standard ECG, conventional and stress trans-thoracic echocardiography with the measurement of CFR, carotid ultrasonography and pulse wave velocity (PWV). Two-dimensional echocardiographic images were obtained using the apical 4-chamber view at a high frame rate of 70–80 frames/s, and three cardiac cycles were stored in cine-loop format for off-line analysis using commercially available QLAB 9 software (Philips Medical System, USA) in order to assess global longitudinal strain (GLS).

**Results:** None of the patients showed any signs or symptoms of CV disease, pulmonary involvement, or any other complication. The results of the speckle tracking analysis were significantly different between the two groups, with GLS being significantly lower in the RA patients compared to healthy controls (GLS%: 18.51±9.63 vs 20.23±2.71; p<0.05). Right and left PWV (PWV right, m/sec: 7.52±1.64 vs 6.85±2.02; p=0.06 and PWV left, m/sec: 7.56±1.60 vs 6.88±2.11; p=0.07) and right and left coronary intima media thickness (cIMT) (cIMT right mm: 0.90±0.22 vs 0.75±0.13; p<0.05 and cIMT left, mm: median 0.89±0.18 vs 0.75±0.09; p<0.05) values were all higher in the RA patients and the differences of cIMT were statistically significant. Furthermore, a significant improvement in GLS in RA patients at 18 months of anti-TNF treatment was observed (GLS%: 18.51±9.63 vs 19.09±9.72 p<0.01).

**Conclusions:** GLS measured by means of speckle tracking echocardiography was impaired in RA patients in the absence of any clinical evidence of CV disease and echocardiographic evaluations negative. This data suggests an early myocardial alteration.

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**Disclosure of Interest:** None declared

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AB0344

#### DOES THE PRESENCE OF ILD INFLUENCE THE CHOICE OF DMARD AND BIOLOGIC THERAPY IN RHEUMATOID ARTHRITIS?

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**Background:** Interstitial lung disease (ILD) is a progressive fibrotic disease of the lung parenchyma. It is the only complication of rheumatoid arthritis (RA) reported to be increasing, accounting for around 7% of all RA deaths.<sup>1</sup> Prognosis of patients with RA-ILD is reported to be poor, with usual interstitial pneumonia (UIP) being the predominant pattern associated with poor survival.<sup>2</sup> It is a challenge to determine specific pattern of ILD and formulate an appropriate treatment plan to achieve stabilisation. Early use of Methotrexate (MTX) and biologics in RA has improved outcomes and quality of life. However, this causes difficulty when RA patients develop ILD. There are reports of ILD with biologics and DMARDs, although it is difficult to establish a causal relationship or if an exacerbation of pre-existing ILD. There are no evidence based guidelines regarding introducing biologics in such patients and clinicians face a dilemma as to whether they should be denied.

**Objectives:** The aim of this retrospective study is to:

- Check the overall management of RA and ILD.
- Examine whether ILD diagnosis influences treatment of RA.

**Methods:** We reviewed 37 patients with RA-ILD from 3 hospitals (2001–2017). We collected data on demographics, clinical, Pulmonary function tests, imaging, time from diagnosis to treatment and outcomes.

**Results:** The majority developed ILD after RA except for 3 patients. Mean age of onset of RA was 67 years, 22 (60%) were female. 32 (87%) were RF or ACPA positive, 25 (68%) patients smoked. 29 (78%) patients had baseline PFTs. HRCT showed 13 had NSIP, 20 UIP and 4 were unclassified. Following the diagnosis of ILD, MTX was stopped in 16 patients, reduced in 3 and unchanged in 2. Leflunomide was stopped in 4 and SLZ stopped in 4, of which 1 had definite alveolitis. Infliximab was stopped in 2 patients.

**Specific Treatment for ILD:** 12 patients received Rituximab, of those 8 were for ILD and 4 for RA. 4 Patients continued Anti-TNF. 26 patients received steroids, 4 received MMF and 2 Cyclophosphamide. 2 received Abatacept for ILD with active RA and one received Etanercept. 3 were on Carbocysteine, 2 on NAC and 3 on oxygen.

**Outcomes:** 20 ILD patients were stable and 8 (21%) progressed and died despite treatment. RA disease activity was low to moderate in 23 patients. RA progressed in 8 patients and 1 who received Etanercept was in remission. MTX was stopped in the majority of patients. Steroids were the commonest treatment for RA in the presence of ILD. Rituximab was the drug of choice for RA with severe ILD, followed by MMF and Cyclophosphamide. DMARDs such as HCQ, Leflunomide and SLZ were used for RA in milder ILD and biologics were generally avoided.

**Conclusions:** There appears to be significant variation in the treatment of RA in the presence of ILD. However Rituximab seems to be the preferred option for severe ILD. There is a need for stratified and standardised guidance for management of RA-ILD.

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**Disclosure of Interest:** None declared

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AB0345

#### DOES IRON DEFICIENCY CONTRIBUTE TO FATIGUE OF PATIENTS WITH RHEUMATOID ARTHRITIS WITHOUT ANAEMIA?

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**Background:** Iron deficiency (ID) without anaemia is a cause of fatigue, which is itself a recurring complaint of patients with rheumatoid arthritis (RA).

**Objectives:** The objective of the study was to determine the prevalence of ID in patients with RA without anaemia and to analyse the relationship between ID with fatigue, disease activity and depression.

**Methods:** This study included patients with RA according to the ACR/<sup>EULAR</sup> 2010 classification criteria (American College of Rheumatology/European League Against Rheumatism) followed up in the Rheumatology Department of Rouen University Hospital and who had a haemoglobin >12.5 g/dl. Patients were either from the single-centre monocentric longitudinal cohort or from the seventh visit of the VERA (Very Early Arthritis) High-Norman regional cohort. For each patient of the longitudinal cohort, DAS 28 ESR (Disease Activity Score – erythrocyte sedimentation rate) the FACIT – version 4 fatigue score (Functional Assessment of Chronic Illness Therapy) and a depression score (Hospital Anxiety and Depression Scale) were collected. Serum ferritin, transferrin, serum iron and saturation coefficient of transferrin were measured for each patient. ID was defined as serum ferritin <50 µg/L.

**Results:** One hundred and forty-one patients were included in the longitudinal cohort (78.7% women, mean age 13.50±9.51 years, positive rheumatoid factor and anti-citrullinated peptide antibodies in 83.6% and 86.5% of patients) and 74 RA patients from the VERA cohort (70.3% women, mean disease duration 2.74 ±0.24 years). The prevalence of ID was 15.6% in the longitudinal cohort (n=22/141) and 14.9% in the VERA cohort (n=11/74). In the longitudinal cohort, there were no significant differences between ID patients and non-deficient patients in fatigue (mean FACIT of 27.80±12.4 vs. 32.3±12.0; p=0.14), disease activity (mean DAS 28 VS 2.85±1.38 vs. 2.96±1.48; p=0.74) and depression (mean HAD score 5.86±4.12 vs. 5.80±3.84; p not calculated).

**Conclusions:** The prevalence of ID without anaemia was similar between early and old RA and was similar to that of the general French adult population (15.5%).<sup>1</sup> ID does not appear to be a major cause of fatigue in RA and does not affect the activity of the disease. The search for an ID is of limited value in exploring fatigue of RA patients.

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**Disclosure of Interest:** None declared

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#### AB0346 INVESTIGATION OF ALEXITHYMIA IN PATIENTS AFFECTED BY RHEUMATOID AND PSORIATIC ARTHRITIS: CROSS-SECTIONAL OBSERVATION

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**Background:** Rheumatoid arthritis (RA) and Psoriatic arthritis (PsA) are chronic inflammatory diseases that lead to an overthrow of articular structure, functional limitation and disability. Alexithymia is a personality trait characterised by deficits in cognitive processing and regulation of emotions. A broad association between alexithymia and symptoms as depression, inflammation and pain has been demonstrated.

**Objectives:** to evaluate the prevalence of alexithymia in patients affected by Rheumatoid and Psoriatic arthritis.

**Methods:** We prospectively enrolled, from January to December 2017, patients affected by RA diagnosed according to the ACR revised criteria and PsA diagnosed according to the CASPAR criteria referred to the out-patients clinic of the Rheumatology Unit of Policlinico Tor Vergata, Rome. The 20-item Toronto Alexithymia Scale (TAS-20) was used to assess alexithymia. Disease activity, function and quality of life, clinimetric tests as well as ESR and CRP were assessed.

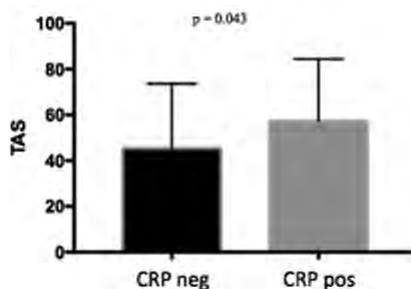
Statistical comparisons were performed using Pearson's Coefficient of Skewness, the unpaired t-Test and Mann-Whitney test.

**Results:** A total of 50 RA patients and 51 PsA patients were enrolled (table 1). The TAS-20 score showed that 38.6% (39/101) of patients had alexithymia, 26.7% (27/101) patients were in the borderline of alexithymia and 34.7% (35/101) patients had not alexithymia. A statistical significant association was observed between alexithymia and inflammatory indexes (ESR: p=0.029, CRP: p=0.043, figure 1 and 2) and also between alexithymia and clinimetric parameters (ptVAS, pVAS, GH, p<0.0001 for all comparisons). No correlations were observed between alexithymia and disease duration, gender, therapies with bDMARDs. A significant trend has been demonstrated between alexithymia and corticosteroidal therapy

**Abstract AB0346 – Table 1.** Characteristics, therapies and clinimetric evaluation of the study population

	RA	APs	Total
Female Sex - No. (%)	41 (40.6%)	31 (30.7%)	72 (71.3%)
Male Sex- No. (%)	20 (19.8%)	9 (8.9%)	29 (28.7%)
Age (years) (in mean ± (DS))	59.5 ± (11.46)	52.6 ± (12.84)	56 ± (12.66)
Mean Disease Duration ± (DS)	6.19 ± (3.82)	6.29 ± (3.96)	6.24 ± (3.89)
Patients on csDMARDs - No. (%)	10 (9.9%)	34 (33.6%)	44 (43.5%)
Patients on bDMARDs - No. (%)	12 (11.8%)	38 (37.6%)	50 (49.5%)
Patients on steroids - No. (%)	37 (36.6%)	12 (11.9%)	49 (48.5%)
patient VAS (0-100)	42.6 ± (20.95)	58.23 ± (26.52)	50.49 ± (25.17)
pain VAS (0-100)	38.1 ± (20.87)	56.9 ± (26.59)	47.59 ± (25.71)
GH (0-100)	44 ± (23.08)	49.7 ± (22.58)	46.88 ± (23.01)

Data are expressed as Mean ± Standard Deviation; csDMARDs: conventional synthetic disease-modifying antirheumatic drugs; bDMARDs: biological disease-modifying antirheumatic drugs; VAS: Visual Analogic Scale; GH: Global Health; percentages calculated for total population.



**Abstract AB0346 – Figure 1**

**Conclusions:** This study suggests that alexithymia assessment should be a part of the comprehensive care of patients with RA and PsA. We are in the process of extending this investigation on a larger sample population to improve our investigation field and to consolidate our dates.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.4919

#### AB0347 BODY COMPOSITION IN PATIENTS WITH RHEUMATOID ARTHRITIS KAZAKH NATIONALITY

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**Background:** Chronic inflammation in rheumatoid arthritis (RA) leads to a decrease in fat and muscle mass [Baker J.F., Von Feldt J. Mostoufi-Moab S. et al., 2014 Low muscle mass in RA is considered as the main criterion of sarcopenia.

Recently, much attention has been paid to various phenotypes of sarcopenia, among which osteopenic sarcopenia, sarcopenic obesity and osteosarcopenic obesity (most unfavourable in terms of functional disorders) are distinguished.

In the modern literature there are works devoted to changes in the composition of the body in the aspect of abdominal obesity and its influence on cardiovascular risk in RA [Crowson C.S., Myasoedova E., Davis J.M., 2011]. Studies with the evaluation of muscle mass and sarcopenia in RA are few. In Kazakhstan, the composition of the human body was not studied.

**Objectives:** The purpose of the study was to study the body composition (muscle and fat mass) of patients with RA of Kazakh nationality using bioelectrical impedance analysis.

**Methods:** In our study we used Bioimpedance analyzer 101 (BIA 101, Italy).

Bioimpedansometry was performed in 585 participants, including 295 patients with RA and 290 of their siblings.

**Results:** In patients with RA, in contrast to the comparison group (sibs), BMI (pro-bands – 25.34±5.1, siblings – 24.86±4.45), the girth of the waist and hips were slightly higher than those of the siblings. The ratio of RT/OB in both groups was virtually the same. At the same time, a decrease in the lean mass was found



(probands – 45.37±12.2, siblings – 48.67±11.01), which, in all probability, is due to sarcopenia. The presence of sarcopenia is also confirmed by a decrease in the sarcopenia index (probands 0.6884±0.1, sibs 0.6947±0.1). On the contrary, the fat content of RA patients is higher than that of siblings.

**Conclusions:** Thus, in our patients cachexia is formed in RA, which is characterised by loss of muscle mass with the preservation or even growth of fat mass, which stabilises body mass indexes, and in some cases even leads to its increase (so-called cachexial obesity).

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**Disclosure of Interest:** None declared

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#### AB0348 GRIP POWER AND INDEPENDENT DAILY LIVING IN THE PATIENTS WITH RHEUMATOID ARTHRITIS

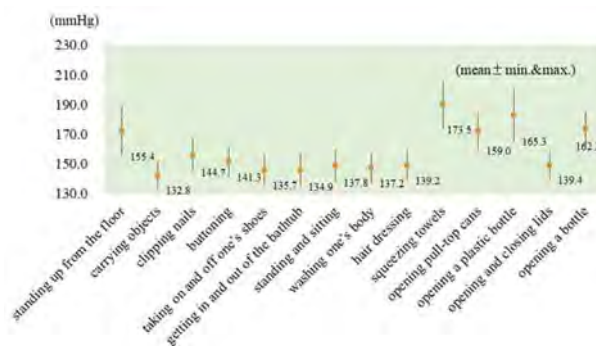
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**Background:** Grip power is known to be a simple and useful objective index that can be used in the self-assessment of disease activity in patients with rheumatoid arthritis (RA)<sup>1</sup>. However, the clinical significance of this physical function is unknown.

**Objectives:** The objective of this study was to clarify the relationship between the grip power and the level of activities of daily living (ADL).

**Methods:** The grip power was measured in 221 inpatients of our hospital with RA using a mercury dynamometer. The independence level (0: impossible, 1: incomplete and not practical, 2: practical but the means thereof are unusual, 3: normal) for 44 ADL items, including most daily activities was investigated. For each item, the site with the problem (shoulder, elbow, forearm, wrist, thumb, fingers, lower extremity and trunk) and cause of disability (pain, loss of power, decreased range of motion, abnormal prehensile pattern and fatigue) were investigated by interviewing the patient. There were 33 male and 188 female patients. The average age of the patients was 64.6 years, and the average duration of the disease was 13.3 years. Biological therapy had been given to 23% of the patients. The average grip power of the right and left hands was used.

**Results:** There were 14 items requiring others' assistance (level 0 or 1) in more than 10% of patients. For these 14 items of ADL, the grip power increased with the increase in the independence level ( $p < 0.001$ )<sup>2</sup>. The site with a problem was, in order of frequency, the fingers (26.1%), wrist (14.8%) and lower extremity (14.0%). The cause of disability was, in order of frequency, pain (38.8%), loss of power (32.8%) and a decreased range of motion. Based on the results of a stepwise regression analysis, the first factor, consisting mainly of "reaching function", including "hair dressing", "washing one's body", "taking on and off one's shoes", "clipping nails", "buttoning", etc., was most strongly related to a loss of grip power and problems at the elbow, the shoulder and the wrist. The second factor, consisting mainly of the "prehensile function", including "opening a plastic bottle", "opening lids", "squeezing towels", etc., was most strongly related to a loss of grip power and problems at the wrist and the thumb. The third factor, consisting mainly of "activities involving changing body position and transfer", including "getting in and out of the bathtub", "standing and sitting", etc., was most strongly related to ageing and problems with the lower extremities and at the elbow and the wrist. In the receiver operating characteristic (ROC) curve, the grip power with the maximum Youden index was 136.5 mmHg (11.8 kg) in females and 152.5 mmHg (13.5 kg) in males. Most activities were performed independently with the grip power more than 136.5 mmHg in females (figure 1). The explanatory variables for the grip power in the female patients were ageing; a long disease duration; a high disease activity score (DAS) 28; problems at the fingers, the thumb and the elbow; decreased flexion at the shoulder and a decreased range of forearm rotation.



**Abstract AB0348 – Figure 1.** Minimally required grip power to perform daily activities independently in females with level 3 after age adjustment

**Conclusions:** The grip power was a determinant of independent daily living in patients with RA in our study.

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#### AB0349 OTO-RHINO-LARYNGOLOGICAL MANIFESTATIONS OF RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is a chronic inflammatory disorder that can damage a wide variety of body systems. Ear, nose and throat (ENT) involvement is frequent but not often reported. The purposes of our work are to determine the prevalence of ENT involvement during RA and to evaluate its correlation with RA disease activity.

**Objectives:** The purposes of our work are to determine the prevalence of ENT involvement during RA and to evaluate its correlation with RA disease activity.

**Methods:** This is a cross-sectional study of 90 consecutive RA, followed at the Rheumatology department of Monastir Teaching Hospital in Tunisia, during 06 months (November 2016 to April 2017) and 46 matched volunteers. ENT clinical examination with tonal audiometry and thyroid tests (TSH, T4, anti-Thyroperoxidase Ab (Anti TPO Ab) and Anti-Thyroglobulin Ab (Ab anti Tg) were performed.

**Results:** ENT involvement prevalence was 78%. The most frequent functional signs were intermittent dysphonia in 50% and dysphagia in 42% of cases. The neck examination revealed painful larynx mobilisation in 58% cases and cervical lymph nodes in 7% of cases. Indirect laryngoscopy, performed in the 67% of symptomatic patients, noted inflammatory mucosa in 38% of cases and decrease in vocal cord mobility in 8% of cases. Seventy percent patients had temporomandibular Joint (TMJ) involvement. Tonal audiometry revealed 42% of cases of deafness: 27% sensorineural deafness, 13% conductive deafness and 2% cases mixed hearing loss. The ENT manifestations significantly associated to RA compared to the witness group ( $p < 0.01$ ) were intermittent dysphonia, dysphagia, painful larynx mobilisation, inflammatory nasal mucosa, painful TMJ and deafness. Active disease (DAS 28>3.2) is statistically associated with deafness ( $p < 0.048$ ) and TMJ involvement ( $p < 0.009$ ). Logistic regression study shows that RA duration over 10 years was associated to laryngeal dyspnea (OR=4.4,  $p < 0.012$ , IC (95%) [1.377, 14.134]) and deafness (OR=3.8,  $p < 0.03$ , IC(95%) [1.142, 12.882]). In the other hand, RA moderate functional handicap is a protective factor (OR=0.123,  $p < 0.016$ , IC (95%) [0.076, 0.772]) of ENT involvement and biotherapy use was associated to thyroid involvement (OR=7.8,  $p < 0.017$ , IC(95%) [1.431, 43.175]).

**Conclusions:** ENT involvement is a very common, usually asymptomatic extra-articular manifestation during RA. It is, mainly, TMJ involvement, deafness and dysphonia. The main relevant determinants are RA disease activity and duration.

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### AB0350 TEMPORO-MANDIBULAR JOINT INVOLVEMENT IN RHEUMATOID ARTHRITIS

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**Background:** Temporomandibular joint (TMJ) disorder in rheumatoid arthritis (RA) may be associated with significant osteoarticular destruction and may be responsible of significant functional impairment.

**Objectives:** We aimed in this study to determine the prevalence of TMJ involvement and its correlations with RA parameters.

**Methods:** We report a descriptive monocentric cross-sectional study of 90 consecutive RA, followed at the Rheumatology department of Monastir Teaching Hospital in Tunisia, during 06 months (November 2016 to April 2017) and 46 matched volunteers. Clinical assessment and stomatological examination were performed in all cases.

**Results:** Sixty-three RA patients out of 90 (70%) had TMJ involvement. TMJ painful mobilisation, mastication difficulties, swollen TMJ, dental malocclusion and limitation of mouth opening were noted in 55 (81%), 49 (74%), 20 (30.3%), 19 (29%) and 8 (12%) of cases, respectively. Compared with the control group, painful palpation of TMJ ( $p < 0.000$ ) was significantly associated with RA.

In RA, TMJ disorder is more common in adults between 40 and 60 years of age, patients with HAQ>0.5 and a high total Vander Heijde Sharp radiographic score (SS). TMJ painful mobilisation is significantly associated with increased body mass index (BMI). Swollen TMJ is significantly associated with age (more frequent in elderly subjects), increased BMI, high RA disease activity (high DAS 28 ESR and/or DAS 28 CRP) and HAQ>0.5. Limitation of mouth opening is significantly associated with age (more common in elderly subjects), overweight, high methotrexate dose (20 mg/day), leflunomide and biotherapy use. Dental malocclusion was significantly associated with high doses corticosteroids (more than 5 mg/day). Mastication difficulties are significantly associated with more than 10 year RA duration, HAQ>0.5 and radiological impairment.

**Conclusions:** Temporomandibular disorder is frequent in RA (70%). TMJ disorder is observed especially in active (high DAS 28), serious (radiological impairment, HAQ>0.5) and advanced (more than 10 year duration) RA. Physicians must be careful to assess systematically TMJ in RA patients.

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**Disclosure of Interest:** None declared

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### AB0351 DIFFERENTIAL PERCEPTION ABOUT THE CSDMARDs ON DRUG-INDUCED INTERSTITIAL LUNG DISEASE BETWEEN RHEUMATOLOGISTS AND NON-RHEUMATOLOGISTS

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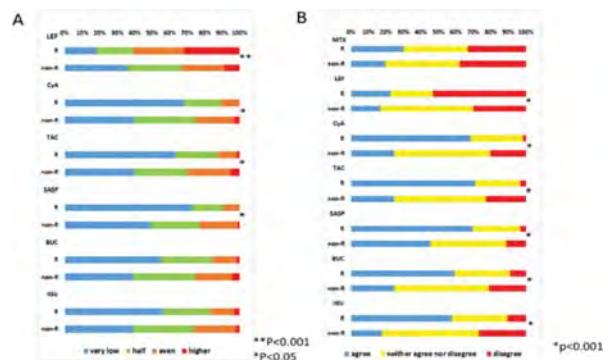
**Background:** As disease modified anti-rheumatic-drugs (DMARDs) were the mainstay in the treatment of rheumatoid arthritis (RA), the opportunity for general physicians to also prescribe DMARDs has recently increased in Japan. After DMARDs were initiated by specialists, subsequent drug prescription by general physicians during remission should be expected<sup>1</sup>. However, general physicians

are more likely than rheumatologists to feel it difficult to accept patients taking even conventional synthetics (cs) DMARDs but not biologics and such discomforts may be potential barriers to cooperative management between specialists and general physicians<sup>2</sup>. One of the reasons is because some csDMARDs such as methotrexate and leflunomide may induce pneumonitis or worsen RA-related pre-existing interstitial lung disease (ILD) as a rare but severe adverse event<sup>3</sup>. To minimise the risk, rheumatologists may choose low-risk csDMARDs smartly when the patients are concomitant with risk factors on ILD.

**Objectives:** To measure the physicians' perspective toward the risk of each csDMARDs on drug-induced ILD and their attitude in prescribing the csDMARDs to a pre-existing ILD case.

**Methods:** A questionnaire was given in an internet survey to registered physicians who take care of more than ten patients with RA in Japan. Topics covered were i) how is the risk of each csDMARD for drug-induced lung injury compared to methotrexate, ii) which csDMARDs should be applied to a case with mild pneumonitis on the chest CT. Cross tabulation analysis and  $\chi^2$  test as a statistical analysis was performed.

**Results:** A total 184 physicians consisting of 66 rheumatologists (36%) and 118 non-rheumatologists (64%) responded. The physicians' mean age was 45 years old. The rheumatologists tended to belong to rheumatology and take care of more than 200 RA patients per month in university hospitals. On the other hand, the non-rheumatologists tended to belong to general medicine and manage less than 50 patients per month in their clinics. The csDMARDs except for methotrexate were more significantly prescribed by the rheumatologists. All rheumatologists but 24% of non-rheumatologists had managed RA patients with exacerbated ILD. On physicians' perspective toward the risk of each csDMARD, the rheumatologists considered that LEF was equal to or higher than MTX and that cyclosporine A (CyA), tacrolimus (TAC), salazosulfapyridine (SASP) was relatively safer (Figure A.). In cases with pre-existing ILD, more rheumatologists agreed to use the csDMARDs except for methotrexate and leflunomide. (Figure B.)



**Abstract AB0351 – Figure 1.** A) Physician's opinion about how is the risk of the following csDMARDs for drug-induced ILD compared to methotrexate. B) Physician's opinion about if the following csDMARDs should be applied to a case with mild ILD on the chest CT.

R: rheumatologists, non-R: non-rheumatologists, MTX: methotrexate, LEF: leflunomide, CyA: cyclosporine A, TAC: tacrolimus, SASP: salazosulfapyridine, BUC: bucillamine, IGU: iguratimod

**Conclusions:** We can find the gap of risk perception about each csDMARDs between rheumatologists and non-rheumatologist and the difference of attitude in prescribing to patients concomitant with risk factors. Considerable consensus and additional enlightenment to general physicians should be necessary.

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**Disclosure of Interest:** None declared

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AB0352

### SIGNIFICANCE OF OCCULT INFECTIONS IN INFLAMMATORY ARTHRITIS PATIENTS RECEIVING BIOLOGIC THERAPIES IN EAST LONDON

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**Background:** Chronic hepatitis B virus (HBV) infection remains a significant global health problem. In high endemic areas like African and Asian countries, most infections occur from vertical transmission, whilst in western countries HBV is primarily acquired in adulthood. Either way, HBV can persist in infected hepatocytes lifelong, even if undetectable in the serum, allowing reactivation during immunosuppression. HBsAg carriers, those with detectable HBV viral load, or receiving concomitant corticosteroids are at greater risk. Most guidelines recommend screening for occult infections prior to starting biologic treatment including testing for HBV, HCV, HIV and TB infection.

**Objectives:** This study was carried out to estimate the prevalence of occult infections, particularly chronic HBV, in an East London rheumatology population receiving biologic therapies, and to evaluate the rate of HBV reactivation after starting treatment.

**Methods:** Inflammatory arthritis patients starting biologic therapies in Barts Health NHS Trust between August 2014 and August 2017 were identified from databases of Whipps Cross and Mile End Hospitals. Health records were reviewed focusing on HBV core antibody (HBcAb), HBV surface antigen (HBsAg), HBV DNA, HCV and HIV antibody status. Latent TB tests included IGRA and ELI-Spot assays.

**Results:** 757 patients were included in the study. Of those, 51 (6.7%) were HBcAb positive, 6 patients (0.8%) were HBsAg positive and two patients had low level HBV viraemia with detectable DNA antibody at baseline. 61% (n=31) of HBcAb positive patients were female, whilst 39% (n=20) were male, with median age of 58 years (IQR, 43–65). The ethnic distribution was the following: 43% asian (n=22; Bangladeshi or Pakistani), 29% african or afro-Caribbean black (n=15), and 18% white caucasian (n=9). The underlying rheumatological conditions included rheumatoid arthritis (59%), ankylosing spondylitis (33%) and psoriatic arthritis (8%). Fifteen patients (29%) received concomitant prophylactic anti-viral therapies (lamivudine, entecavir or tenofovir). After commencing biologic therapies, no HBV reactivation was noted in the HBcAb positive cohort. Intermittent mild transaminitis were detected on monitoring blood tests in 22% (n=11). The rate of latent TB infection was 11.5%; HCV IgG was detected in three patients, whilst HIV infection was absent in our cohort.

**Conclusions:** Approximately 50% of the patient population of Barts Health NHS Trust is coming from minority ethnic groups. Likely because of the diversity of the population, the prevalence of chronic HBV infection (HBsAg and HBcAb positives) in our East London rheumatology population receiving biologic therapies was higher than the national average (0.8% vs. 0.3%, respectively). No HBV reactivation was observed in the follow up period indicating that the risk of reactivation is relatively low. Nevertheless, for patients with evidence of previous infection (HBcAb positive) careful surveillance continues to be recommended.

**Disclosure of Interest:** None declared

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AB0353

### GENETICALLY PREDISPOSITION AND PRO-INFLAMMATORY DYSREGULATIONS – CONNECTING RHEUMATOID ARTHRITIS AND MENTAL DISORDERS

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**Background:** Depressive and anxiety disorders are reported as the more prevalent psychiatric comorbidities in chronic inflammatory diseases and their occurrence has been correlated with higher serum levels of cytokines and chemokines (IL-6, IL-1, IL-12, IL-18, TNF- $\alpha$ , and even TNF-RI and TNF-RII). Some single nucleotide polymorphisms (SNPs) in TNF- $\alpha$  gene have been found to play a common part in pro-inflammatory alterations in patient with rheumatoid arthritis (RA) and depressive symptoms.

**Objectives:** To investigate the possible influence of four single-nucleotide polymorphism in the tumour necrosis factor receptor II (TNFR2) genes and development of psychiatric disorders in patients with active RA. The second aim was to evaluate some correlation between these SNPs, the level of four chemokines and the incidence of mental disorders.

**Methods:** We included 89 Caucasian patients with active RA treated in a tertiary Department of Rheumatology from Cluj-Napoca. All demographic, clinical, and biological data and RA comorbidities were completed. The presence of

depressions or anxiety was confirmed at the baseline by psychiatrist. Four potentially functional SNPs within TNFR2 (rs1061622, rs1062624, rs1061631, rs3397) were selected to be genotyped in all patients using PCR (KASPar) asASys (KBiosciences, Hoddesdon, Hertfordshire, UK) at the Centre for Genomics and Oncological Research (GENYO), Granada, Spain. Plasmatic levels of soluble tumour necrosis factor receptor II (sTNFR2), interleukin (IL)-6, monocyte chemoattractant protein (MCP)-1 and vascular endothelial growth factor (VEGF) was quantified using cytofluorometry-based ELIAS technique in accordance with manufacturer's instructions using FlowCytomix kit (eBioscience, UAS) at Instituto Maimonides de Investigacion Biomedica de Cordoba – Reina Sofia Hospital, Spain.

**Results:** According to DAS28 (CRP) all the patient have active arthritis (5.87  $\pm$  0.6) with median disease duration of 9 (4–14) years. Most of the patients were diagnosed with depression (n=33), 84.8% were female. Anxiety was present at 21 subjects (80.9% female). In 3 cases these two mental disorders coexist.

In a subgroup with depression the polymorphism rs1061631 (GG) was significantly associated with increased level of VEGF (p=0.007). A significant correlation was also found between the polymorphism rs3397 (CC/TT) and MCP-1 level (p=0.01).

In a subgroup with anxiety the significant association was found between the polymorphism rs1061631 (GG) and the level of MCP-1 (p=0.04).

**Conclusions:** Pro-inflammatory dysregulation might be particularly relevant in some patients with RA and psychiatric illness. Amongst genetic factors that influence the susceptibility to the development of RA and psychiatric disorders some single nucleotide polymorphisms (SNPs) in TNF- $\alpha$  gene have been considered with increasing interest. Further investigation in a larger cohort is needed.

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AB0354

### FACTORS OF THE POSITIVE OR NEGATIVE ANSWER ON THERAPY WITH DENOSUMAB IN WOMEN WITH RHEUMATOID ARTHRITIS AND OSTEOPOROSIS

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**Objectives:** To define a contribution of factors: anamnesis, clinical/laboratory markers, glucocorticoids (GC) intake, etc. on the response to therapy with denosumab in women with rheumatoid arthritis (RA) and osteoporosis (OP).

**Methods:** 66 postmenopausal women (mean age 59.6 $\pm$ 7.4) with RA (mean duration 17.7 $\pm$ 10.4 years) and OP received s/c denosumab 60 mg every 6 months pro 1 year. RF- positive were 72%, ACCP – 74% of patients. 34 (49%) continued GC. At baseline and after 12 months it was carried out the dual energy x-ray absorptiometry at 3 sites: lumbar spine (L1-L4), hip neck (HN) and distal forearm (DF) and x-ray of hands and feet (Sharp/van der Heijde (SVH) score). After therapy it was noted the increase of BMD in L1-L4 and HN, a tendency to increase (p=0.0529) in DF. Positive dynamics (increase or stabilisation of BMD) was noted in 89% patients at L1-L4, 67% – at HN and 60% – at DF. The erosion score was increased in 12% (n=8) patients, the joint space narrowing score (JSN) – in 9% (n=6) (p=0.0117 and p=0.027, respectively). The Statistica 6.0 was used.

**Results:** Results of analysis of influence of statistically significant factors on the response to therapy in BMD showed that the negative response in L1–L4 is associated with GC intake (>3 months in anamnesis) (p=0,034) and the beginning of GC intake after menopause onset (p=0,023). In HN positive response is associated with higher concentration of the RF (initially and in dynamics) (p<0,05) and the beginning of menopause later than RA onset (p=0,024), the negative response – with GC intake (>3 months in anamnesis) (p=0,024). In DF positive response on therapy is associated with RF-positivity (p=0,02), the negative response back correlates with increase in erosion score and total SVH score: r=–0360 (p<0,05).

In table 1 it is shown the most significant factors, which influence on SVH score dynamics (increase) after 12 months of denosumab therapy.

**Abstract AB0354 – Table 1.** The factors which influence on SVH score increase (n=66), p<0.05.

SVH score	The score increase is associated with
Erosion score	- lower BMD in L1-L4 (at baseline and after treatment) - higher cumulative GC dose - back correlates with BMD increase in DF - back correlates with bone alkaline phosphatase (BAP) base level - correlates with increase in JSN
Joint space narrowing score (JSN)	- presence at patients in anamnesis a surgical menopause - lower value of BMD dynamics (%) in DF - correlates with increase in erosion score and total SVH score.



**Conclusions:** There was established that positive response on therapy with denosumab in BMD in NH and DF is associated with RF-positivity. The particular contribution to the negative response in L1-L4 and HN is associated with GC intake (previous intake more than 3 months in the anamnesis), purpose of the GC after menopause onset. There was note that the increase of erosion score is associated with either lower BMD in L1-L4 (at baseline and after treatment) or back correlation with BMD increase in DF. Also the higher cumulative GC dose and back correlation with BAP base level were observed at patients with increased erosion score. The only factors that we could reveal in patients with increased JSN score were surgical menopause in anamnesis and lower value of BMD dynamics (%) in DF after treatment. In general it was a direct correlation between erosion score and JSN score.

**Disclosure of Interest:** None declared

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AB0355

#### THE RELATIONSHIP BETWEEN HAND PREHENSILE STRENGTH, CLINICAL ACTIVITY AND FUNCTIONAL CAPACITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** The hand is an anatomical structure with a large number of joints; its prehensile grasp capability constitutes a highly specialised biomechanical function. In rheumatoid arthritis (RA), the structures of the joint are damaged by the characteristic inflammatory process<sup>1</sup>. The *Disease Activity Score* (DAS28) considers twenty hand joints in the evaluation of rheumatoid arthritis (RA). While the *Health Assessment Questionnaire* (HAQ) *disability index* (DI) (HAQ-DI) is the most frequently used instrument for measuring self-reported physical function in rheumatoid arthritis and considers the ability to dress and groom, get up, eat, hygiene, reach, grasp, situations in which the functional capability of the hand is crucial.

**Objectives:** To assess the relationship between hand prehensile strength, the DAS28 index and HAQ-DI score in patients with diagnosis of RA.

**Methods:** The prehensile strength was obtained by the dynamometry method from 105 AR patients, the maximum strength levels in the dominant and non-dominant hand were considered. The Disease Activity Score in 28 joints using the erythrocyte sedimentation rate (DAS28-ESR) and HAQ-DI were recorded.

**Results:** The maximum prehensile strength, on average, was 14 kg, and the weak force category was more prevalent. The prehensile strength of both hands was negatively correlated with the HAQ-DI score and DAS28 index. In an adjusted logistic regression model, the "weak" strength category of the non-dominant hand was associated with "moderate clinical activity" in the DAS28 score (OR=8.59, p=0.02), while the category of "weak" strength of the dominant hand was associated with the presence of "some difficulty" of HAQ-DI score (OR=4.75, p=0.10).

**Conclusions:** The decrease in prehensile strength represents a marker associated with the DAS28 index and HAQ-DI score in the patient with RA, regardless of age, muscle mass, total fat or body mass. The measurement of the prehensile strength can be a useful and inexpensive tool to be considered in the clinical evaluation of the RA.

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AB0356

#### BUILDING A PATIENT-CENTRED CARDIOVASCULAR RISK REDUCTION PROGRAM FOR PATIENTS WITH INFLAMMATORY ARTHRITIS

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**Background:** Cardiovascular disease (CVD) is the most common cause of death among patients with inflammatory arthritis (IA) such as rheumatoid arthritis (RA), psoriatic arthritis (PsA) or ankylosing spondylitis (AS).

**Objectives:** This study is the formative work to help design a patient-centred intervention for a CVD risk reduction program for patients with IA.

**Methods:** We conducted a qualitative study guided by Bandura's Social Cognitive Theory, placing special focus on knowledge about the relationship between arthritis and CVD as well as barriers and facilitators to receiving healthcare related to CVD risk such as screening and management for hyperlipidemia. Participants had to have either RA, PsA or AS and were recruited from a single academic centre. Data were analysed thematically.

**Results:** We conducted three focus groups with a total of 17 participants. Mean age of participants was 56 (SD ±7.7) years; 15 were women; 3 were on a statin; and 1 previously had a stroke. The majority of the participants were Five themes emerged: 1) Need for more information about IA and medications; 2) Lack of education about CVD risk and IA; 3) CVD risk reduction as an integrated lifestyle modification; 4) Uses for peer support around relevant CVD risk factor mitigation approaches; and 5) Improving doctor-patient communication about RA. The themes that emerged in our study showed that the majority of these IA patients were not aware of the relationship between CVD and IA, and were very interested in learning about IA, medication side effects, and prognosis of IA. These participants wanted to learn first about IA and, as a secondary goal, learn about their CVD risk in the context of their IA rather than as a new condition.

**Conclusions:** Providing a clear understanding about systemic effects of IA and how to treat it will be needed before focusing on CVD risk reduction. By doing so, there will be better opportunity for the CVD risk reduction program to succeed.

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AB0357

#### THE SUPPORT OF MEDICAL CLERKS IN RHEUMATIC DISEASE CLINIC AIDS T2T PRACTICE FOR RHEUMATOLOGISTS AND IMPROVES DISEASE ACTIVITIES OF PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** With treat-to-target (T2T), the physician always has to evaluate disease activity and joint damage of rheumatoid arthritis (RA) patients exactly to maintain the activities of daily living of the patient for the long term. However, the amount of work required by physicians to complete T2T can be onerous, so the cooperation of medical staff is necessary to practice T2T.

**Objectives:** The purpose of this study is to clarify the role and effectiveness of medical clerks (MCs) in a rheumatic disease clinic.

**Methods:** In our rheumatic disease clinic, MCs have supported rheumatologists since April 2011. We individually evaluated 50 RA patients in May 2010 (before MC support: "preceding period"), April 2011 (1 year after the start of MC support: "early period"), April 2013 (3 years after the start of MC support: "middle period"), April 2015 (5 years after the start of MC support: "late period") and April 2017 (7 years after the start of MC support: "last period"). We assessed the prevalence of T2T practice, disease activity, and drug use. When all components of the Simplified Disease Activity Index (SDAI) of patients had been listed in the medical record and radiography of hand and foot joints had been undertaken more than once a year, the medical examination was defined as "T2T practice". Disease activity was assessed using the SDAI and Clinical Disease Activity Index (CDAI).

**Results:** Prevalence of T2T practice was 50%, 86%, 94%, 100% and 100% at preceding, early, middle, late and last periods, respectively. Prevalence of T2T practice increased after the start of MC support. Accordingly, disease activities improved gradually. SDAI remission was 30.8% in the preceding period, 28.5% in the early period, 30% in the middle period, 58% in the late period and 56% in the last period, respectively. CDAI remission improved towards the last phase, similar to that seen with the SDAI. The mean dose of methotrexate (MTX) increased gradually towards the last phase, but the prevalence of MTX use did not show a remarkable change. Prevalence of use of biological disease-modifying anti-rheumatic drugs did not increase during the study period.

**Conclusions:** MC support in rheumatic disease clinics aids T2T practice for rheumatologists. The disease activities of RA patients can be improved by MC support.

**Disclosure of Interest:** None declared

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**AB0358 PHENOTYPES OF SECONDARY SARCOPENIA IN PATIENTS WITH RHEUMATOID ARTHRITIS**

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**Background:** Secondary sarcopenia may be caused by low physical activity, eating disorders, chronic inflammation. In patients with rheumatoid arthritis (RA), sarcopenia co-occurs with osteoporosis as well as obesity and, in most cases, both osteoporosis and obesity co-occur with sarcopenia. Therefore, 3 phenotypes of sarcopenia can be identified: sarco-osteoporosis, sarcopenic obesity, osteosarcopenic obesity.

**Objectives:** The aim of the research was to study the features of sarcopenia and her phenotypes in patients with RA. There were examined 40 women with stage II-III RA, Rtg stage II-III, functional limitation stage II. The patients average age was 40.7±2.25 years.

**Methods:** The algorithm for diagnosing phenotypes of sarcopenia recommended by the European Working Group on Sarcopenia in Older People (2009) was used. Body mass index was determined. Dynamometry (the measurement of hand-grip strength using handgrip dynamometer) was performed and the evaluation of physical fitness. Serum levels of leptin and creatine phosphokinase MM (CPK MM) fraction were determined. The dual-energy X-ray absorptiometry DEXA (to calculate a T-score) was performed

**Results:** According to the results of laboratory tests and methods of evaluating functional muscle disorders, 87.5% of patients were diagnosed with sarcopenia. The mean values of dynamometry were within 18.3±0.7 kg being significantly lower as compared to healthy individuals – 28.3±0.5 kg. After the evaluation of physical fitness, the average score was 7.9±0.7, while in healthy individuals, it was 11.3±0.4. The mean CPK MM concentration was 175±2.34 U/L, while in healthy individuals, it was 144±3.5 U/L. The average T-score were within the limits (–1.83±0.17) SD and was significantly lower than in healthy (–0.56±0.10) SD. After conducting studies in 17 patients were diagnosed with osteosarcopenic obesity in 11 – sarco-osteoporosis, 7 – sarcopenic obesity, 5 patients sarcopenia has not been diagnosed.

**Conclusions:** RA leads to muscle metabolism disorders which result in the development of secondary sarcopenia. Therefore, a high-protein diet, physical exercise, namely aerobic exercise (swimming, cycling) and medical preparations that improve muscle metabolism should be included in therapeutic measures and preparations of calcium.

**Disclosure of Interest:** None declared

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**AB0359 CLINIC PROFILE OF PATIENTS WITH RHEUMATOID ARTHRITIS AND PULMONARY AFFECTON IN A COHORT FROM A UNIVERSITY HOSPITAL**

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**Background:** Pulmonary affection is a serious complication in Rheumatoid Arthritis (RA) with an important impact on mortality and morbidity.

**Objectives:** To describe the clinical and radiographic characteristics of patients with RA in our centre, and specifically from those with interstitial lung disease (ILD).

**Methods:** Retrospective analysis of patients with RA and pulmonary affection from a University Hospital with a referral area of 85.000 inhabitants. Clinical, laboratory, imaging and pulmonary function test (PFT) data was recorded.

**Results:** Data from 85 patients, 37 (43.5%) male and 48 (56.5%) female, were recorded. The mean time from RA diagnosis to pulmonary disease was 9.2 years, with mainly erosive (58.8%) and seropositive (84.7% were positive rheumatoid factor (RF) and 84.2% anti-citrullinated protein antibodies (ACPA)) disease. The 56.5% of the patients were smokers or ex-smokers. PFT results were documented in 75.3% of the patients: diffusing capacity for carbon monoxide (DLCO) baseline values were over 60% in a 38.8% of cases and forced vital capacity (FVC) baseline values were over 50% in a 69.4% of patients. The most frequent High Resolution CT scan pattern was the presence of bronchiectasis (64.7%), followed by ILD (31.8%) and, specifically, the Usual Interstitial Pneumonia pattern (UIP, 66.6%); lung infections (25.8%), rheumatoid lung nodules (22.4%), pleural effusion (15.3%), lung tumours (9.4%) and bronchiolitis (5.8%). The presence of extra articular manifestations as rheumatoid nodules (27%), episcleritis (2.3%) and vasculitis (9.4%) was registered. The coexistence of Chronic Obstructive Pulmonary Disease (COPD) was recorded too (24.7%). Related to treatment, 84.7% of patients had received Methotrexate and in a 40% of cases, at least one

biological disease-modifying antirheumatic drug had been administrated. Though the causes were not registered, a 25.9% of deaths were documented. In parallel we did a subanalysis of ILD related to RA cases, summarised in table 1 (n=27):

**Conclusions:** Bronchiectasis is the most common pulmonary manifestation of RA patients in our area. The most frequent clinical profile is a non-smoker woman with seropositive disease.

ILD affects approximately one third of RA patients in our area and is an underdiagnosed entity. We consider that it is necessary to establish a screening program to diagnose and treat it early.

**Abstract AB0359 – Table 1**

Gender, male (%)	44.4%	
RA – pulmonary affection time of evolution (years), mean ±SD	7.5±7.7	
ACPA positive (%)	Yes (88.9%)	No (7.4%)
RF positive (%)	Yes (92.6%)	No (7.4%)
Erosive disease (%)	Yes (59.3%)	No (40.7%)
Smoker or ex – smoker (%)	Yes (48.1%)	No (51.9%)
Baseline FVC (%)	<50% (3.7%)	≥50% (66.7%)
Baseline DLCO (%):<40%	7.4%	
41%–59%	18.5%	
≥50%	40.7%	

**Disclosure of Interest:** None declared

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**AB0360 LEFT ATRIAL DILATION IS INCREASED IN PATIENTS WITH RHEUMATOID ARTHRITIS: A CASE-CONTROL STUDY**

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**Background:** Rheumatoid arthritis (RA) is a chronic, systemic inflammatory disease, which mainly affects synovial joints.<sup>1</sup> Heart structural abnormalities are more prevalent in RA-patients than in general population, such as pericarditis, increased left ventricle mass and valvular disease.<sup>2</sup> Left atrial (LA) dilation predicts atrial fibrillation and congestive heart failure. It also increases the risk of developing thromboembolic events.<sup>3</sup>

**Objectives:** The aim of this study was to determine the prevalence of LA dilation in RA-patients and compare it with matched controls.

**Methods:** An observational, cross-section, case-control study was designed. Patients who fulfilled 1987 ACR and/or 2010 ACR/EULAR classification criteria for RA, 40–75 years old, with no overlap syndromes or atherosclerotic cardiovascular disease were included. The control group was matched by age, gender and comorbidities. A standard transthoracic echocardiogram was performed by a board-certified cardiologist. LA structure alterations were evaluated according to the American Society of Echocardiography guidelines.

**Results:** A total of 63 RA-patients and 41 control subjects were included. Demographic characteristics are shown in table 1. LA dilation, defined as a LA indexed volume (LAIIV) >34 mL/m<sup>2</sup>, was found in 9 (14.3%) patients of the RA-group, whereas no control subjects presented that condition (p=0.011). Mitral regurgitation was detected in 39 (62%) RA-patients and 7 (17%) control subjects (p<0.001).

**Abstract AB0360 – Table 1. Demographic characteristics**

	RA (n=63)	Control (n=41)	P
Age, mean±SD	55.26±8.32	53.71±6.16	0.277
Disease duration (years), mean±SD	10.84±8.95	-	-
DAS-28 CRP, mean±SD	11.21±9.36	-	-
Women, n (%)	61 (96.8)	36 (87.8)	0.109
Hypertension	24 (38)	8 (19.5)	0.052
Body Mass Index, mean±SD	28.63±5.04	28.58±4.71	0.964
Active smoking, n (%)	6 (9.5)	3 (7.3)	>0.999
Type 2 Diabetes mellitus, n (%)	6 (9.5)	6 (14.6)	0.533
DAS-28 CRP – Disease activity score 28 using C-reactive protein.			

**Abstract AB0360 – Table 2.** Echocardiographic findings

	RA (n=63)	Control (n=41)	p
Left atrial dilation, n (%)	9 (14.3)	0 (0)	<b>0.011</b>
Mitral regurgitation, n (%)	39 (61.9)	7 (17)	<b>&lt;0.001</b>
LVMI (gm/m <sup>2</sup> ), mean±SD	70.96±18	70.29±16.3	0.854
Diastolic dysfunction, n (%)	34 (53.9)	14 (34.1)	0.07
LVCR, n (%)	21 (36.8)	6 (15)	<b>0.022</b>
LVCR or LVCH, n (%)	27 (42.8)	7 (17)	<b>0.01</b>

LVCR – Left ventricular concentric remodelling, LVCH – Left ventricular concentric hypertrophy, LVMI – Left ventricular mass index

**Conclusions:** LA dilation is more prevalent in RA-patients when compared to matched controls. Prospective studies are needed to evaluate the influence of this condition in cardiovascular outcomes.

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#### AB0361 THE IMPACT OF OBESITY IN CLINICAL AND ULTRASONIC ACTIVITY OF TUNISIAN RHEUMATOID ARTHRITIS

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**Background:** Obesity is one of the most frequent comorbidities among patients with rheumatoid arthritis (RA). It has been proposed as a risk factor of poorer response to treatment and lower likely chance of achieving RA disease remission.<sup>1</sup>

**Objectives:** The objective of this study was to evaluate the effect of obesity on clinical and musculoskeletal ultrasound (MSUS) disease activity.

**Methods:** Cross-sectional clinical and laboratory data were collected on 44 RA patients. MSUS assessment of power Doppler (PDUS) and grey scale (GSUS) hypertrophy and effusion was performed on 11 joints of dominant hand (wrist, metacarpal-phalangeal 1–5 and proximal interphalangeal 1–5). PDUS and GSUS were scored semi-quantitatively on a scale of 0–3. The max score of the views obtained for each joint was computed and then was these maximums were summed across all 11 joints to obtain total PDUS (range 0–33) and GSUS (range 0–33) scores. DAS28/ESR was calculated. Patients were categorised by BMI (kg/m<sup>2</sup>): <25 (group 1), 25–30 (group 2), and >30 (group 3). Demographic, clinical and ultrasonographic characteristics were compared across BMI groups. P values < 0.05 were considered statistically significant.

**Results:** The overall cohort was 88.6% female, 43.2% ACPA positive and 63.6% RF seropositive with a mean age of 53.8 and disease duration of 12.9 years. The mean BMI was 28.6. Eighty two percent of patients were on sDMARD, 18.2% were on Biologics, and 68.2% of patients were on prednisone. There were no significant differences in these characteristics across the BMI categories. The overall median and interquartile ranges (IQR): 4.1 (1.3) for DAS28/ESR, 3.9 (4.1) for GSUS scores and 4 (5.1) for PDUS scores. The disease activity as measure was not significantly different across the BMI groups (p=0.61). Both GSUS and PDUS scores were not significantly different across BMI groups. Concerning GSUS score: the median (IQR) scores was 5.3 (5.4) for group1, 4.4 (4.3) for group2 and 2.6 (2.7) for group3 (p=0.41). For the PDUS scores the median (IQR) scores was 6 (8.6) for group1, 4.3 (4.1) for group2 and 2.3 (2.7) for group3 (p=0.37). There was no statistically significant correlation of BMI with ultrasound scores (r = -0.19, p=0.2 for GSUS score and r = -0.22, p=0.14 for PDUS score).

**Conclusions:** Our study didn't proved differences in clinical or ultrasonic disease activity of RA among BMI. This finding doesn't exclude the hypothesis suggesting that obesity is risk factor of refractory RA which requires a larger number of patients to confirm.

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#### AB0362 FACTORS ASSOCIATED WITH THE DEVELOPMENT OF ARTHRITIS IN PATIENTS WITH ARTHRALGIAS CLINICALLY SUSPECTED OF EVOLVING INTO ARTHRITIS: EXPERIENCE OF A PRE-ARTHRITIS CLINICS

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**Background:** Despite the fact that genetic and serological risk factors have been studied in rheumatoid arthritis (RA), the symptoms phase of preclinical RA is poorly characterised. Taking into account the importance of early diagnosis and effective treatment for the prevention of structural damage and long-term disability in RA, it is important to find clinical or image variables that identify patients with clinically suspected arthralgias at risk of developing a chronic arthritis (CSA).

**Objectives:** To identify baseline clinical, immunological and ultrasound variables in patients with arthralgias clinically suspected of progression to chronic arthritis.

**Methods:** Longitudinal prospective study of patients with CSA and follow-up from November 2015 in pre-arthritis clinics. Patients were assessed at baseline and every 6 months until 2 years, with clinical, laboratory and ultrasound data using standardised protocols. The criteria for eligible patients for inclusion in the study were: ≤12 months of symptoms onset, inflammatory arthralgias (predominance in nights or mornings, improvement during the day or with movement, and morning stiffness of ≥30 min), and the involvement of small joints of hands or feet. Patients with clinical synovitis at baseline visit, patients with fibromyalgia or osteoarthritis were excluded.

**Results:** Twenty-six patients were recruited in 26 months of the study (1 male, 25 female), with an average baseline age of 44.7±12.6 years, an average delay time of symptoms to first visit of 8.7±3.3 months, a mean follow-up time of 7.7±8.1 months an average body mass index (BMI) of 27.7±7.2. Five patients had familial background of autoimmune diseases in first degree relatives (RA, psoriasis, inflammatory bowel disease), 6 (23.1%) were seropositive (RF and/or ACPA), 7 (26.9%) had increased baseline acute-phase reactants (PAR), and 11 (47.8%) were smokers or former smokers. Most of the patients reported a progression of the arthralgias (55%) and a subjective joint swelling at some point (70%). Of 24 patients, 8 (33.3%) developed clinical arthritis (7 RA, 1 undifferentiated arthritis), with a longer follow-up (15.7±7.4 vs. 7.5±7.2 months, p=0.016), greater baseline HAQ (11.8±8.3 vs. 3.9±4.8, p=0.033) and higher percentage of moderate inflammatory activity in the baseline ultrasound (83.3% vs. 8.3%, p=0.004), compared to patients that didn't develop arthritis. There was a trend towards a higher seropositivity, (37.7% vs. 18.8%), a higher patient global disease assessment (45±29 vs. 30±27 on a 100 mm scale), higher patient pain scores (using a visual analogue pain 100 mm scale) (58±41 vs. 34±23) among patients who eventually developed arthritis, although not statistically significant. No differences were found with PAR, BMI, age, smoking habit or painful joint count at baseline visit.

**Conclusions:** In our pre-arthritis clinics of patients with clinically suspicious arthralgias, 33% progressed to arthritis, underlying the importance of these clinics. Functional disability and ultrasound at baseline visit are especially useful in predicting future progression to arthritis. It is necessary to recruit more patients in order to obtain more robust conclusions.

**Disclosure of Interest:** None declared

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#### AB0363 RHEUMATOID ARTHRITIS AND SICKLE CELL DISEASE: CLINICAL, BIOLOGICAL, RADIOLOGICAL AND THERAPEUTICS SPECIFIC ASPECTS. A RETROSPECTIVE OBSERVATIONAL STUDY

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**Background:** Thanks to medical advances in sickle cell disease (SCD) treatments, practitioners have to be aware of new comorbidities, as rheumatoid arthritis (RA).

**Methods:** We conducted a retrospective, observational and monocentric study about clinical, biological and radiological specific aspects of RA in SCD patients and studied the impact of anti-rheumatic drugs, comparing the number of SCD



flares occurring six months before/after their introduction, using medical files and phone inquiry.

**Results:** Twenty-three patients were included in this study. Data about RA treatments and SCD flares could be collected for 15 patients. Middle age at RA diagnosis was 32.9 years-old, sex ratio was 4.75F/1M. 74% of the patients were RF positive, 65% were ACPA positive. 74% of the patients had articular damages. Among them, 100% had severe carpite which appears to be the major radiological expression of RA in SCD patients, occurring sometimes without finger bone erosion. 100% received at least one specific drug for RA, 35% a biotherapy. There was no significant difference in the number of crisis before and after methotrexate introduction ( $p=1$ ) or anti TNF alpha drugs ( $p=0.35$  IC95% [-1.26;0.51]). Methotrexate had to be stopped for 3 patients because of acute chest syndrome, which did not occur with anti TNF. No infection was noticed.

**Conclusions:** In conclusion, in SCD, RA occurs sooner in life course and to be more severe with a particular pattern: carpite and tarsite without finger bone erosion. The use of biotherapy appears to be safe, with a close monitoring.

**Disclosure of Interest:** None declared

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### AB0364 REMARKABLE INTERNATIONAL VARIABILITY IN REASONS FOR NON-PARTICIPATION IN THE GLORIA TRIAL

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**Background:** GLORIA is an ongoing large pragmatic trial that examines harm, benefit and costs of low-dose glucocorticoids added to the standard treatment of RA patients of 65 years or older. The eligibility criteria are non-restrictive: RA, age  $\geq 65$  years, disease activity score (DAS28) of  $\geq 2.6$ , and no current glucocorticoid treatment. Patients with comorbidity are expressly included, and the impact of trial procedures on normal care is minimal. Nevertheless, inclusion proves to be challenging. We have prospectively sampled all the reasons for ineligibility across a number of centres in different countries participating in the GLORIA trial.

**Methods:** Rheumatologists from 8 centres in Germany, Hungary, The Netherlands, Portugal and Romania screened the patient list of at least two full clinic days. For each patient, the eligibility and all possible reasons of exclusion were recorded.

**Abstract AB0364 – Table 1.** Percentage of patients ineligible for the GLORIA trial, per reason (patients can have more than one reason)

Center	n	Percent ineligible for:				
		Age	Disease Activity	Current GC	Temporary	Other
<b>Total</b>	<b>370</b>	<b>58</b>	<b>58</b>	<b>28</b>	<b>5</b>	<b>11</b>
<b>The Netherlands</b>						
Amsterdam	156	54	70	22	5	11
Rotterdam	43	63	58	12	2	9
Leeuwarden	46	51	70	11	4	19
<b>Germany, Berlin</b>						
	23	52	52	65	0	17
<b>Portugal</b>						
Coimbra	21	58	21	8	4	17
Lisbon	10	60	60	80	80	10
<b>Hungary, Debrecen</b>						
	46	75	43	55	0	2
<b>Romania, Bucharest</b>						
	18	56	22	44	0	6

**Results:** In total, 385 patients were screened. Of these patients, 15 (4%) were eligible to participate in the GLORIA trial. In Germany, Romania and Portugal (Lisbon) none of the screened patients proved eligible.

The most common reasons for ineligibility were inactive disease and age (both 58%) (table 1). Current glucocorticoid use was reported in 28%, 5% had a temporary reason (i.e. recent switch of therapy or glucocorticoid use), and 51% had more than one reason for ineligibility. We found remarkable differences between the sites in the distribution of the main reasons for ineligibility (table 1).

Of the eligible patients, 1 was already participating, 3 were included after this screening, and 2 were currently considering participation; 9 declined participation (most common reasons: fear of glucocorticoids, not interested to participate, preference for GC injections or declining additional therapy).

**Conclusions:** In this prospective study, we found remarkable differences between countries in reasons for non-participation in our ongoing GLORIA trial. The willingness of eligible patients to participate was low in this elderly population, despite the pragmatic design. Earlier studies also showed that it is challenging to include elderly patients in a clinical trial.<sup>1,2</sup> Pre-screening of patients in potential sites can provide important information on the potential to recruit patients in a trial, but the actual willingness of patients to participate remains hard to predict.

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### AB0365 THE INSULIN RESISTANCE, METABOLIC SYNDROME AND TYPE 2 DIABETES MELLITUS DEVELOPMENT RISK ASSESSMENT IN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** The insulin resistance (IR) is the known risk factor of type 2 diabetes mellitus (DM) and potential cardiovascular complications. But it's not feasible in routine practice to calculate special indices to determine IR, as insulin levels monitoring is not a standard procedure in RA pts. Metabolic syndrome (MS) criteria and questionnaires designed to assess the risk of DM development can help to differentiate a subgroup of pts, requiring more accurate evaluation of their IR status.

**Objectives:** To determine how IR relates with MS and DM development risk assessment in RA patients.

**Methods:** A total of 46 RA pts (39 women, 7 men, 57 [39; 64] years old) without established DM were enrolled in the study, including 14 pts with IR and 32 pts without IR, matched by age and sex. IR was defined as Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) index  $>2.77$ . National Cholesterol Education Program/Adult Treatment Panel III (NCEP/ATPIII) and International Diabetes Federation (IDF) criteria were used to confirm MS. The abdominal obesity was determined as waist circumference (WC)  $\geq 80$  cm for women and  $\geq 94$  cm for men (by IDF), and WC  $\geq 88$  cm for women and  $\geq 102$  cm for men (by NCEP/ATPIII). If the total score of questionnaire Finnish Type 2 Diabetes Risk Assessment Form (FINDRISK) was  $\geq 12$ , the DM development risk was considered as moderate or high.

**Results:** The body mass index was higher in pts with IR than in those without IR (28,5 [24,8; 32,5 kg/m<sup>2</sup> vs 22,4 [20,1; 25,4 kg/m<sup>2</sup>,  $p<0.001$ ). Abdominal obesity was documented in 100% pts with IR and in 41% pts without IR by IDF criteria ( $p=0.002$ ), in 64% and 22% pts, respectively, by NCEP/ATPIII criteria ( $p=0.01$ ). There were no differences in DAS28, CRP and ESR values and glucocorticoids users proportions. MS by IDF criteria was diagnosed in 57% pts with IR and 19% pts without IR ( $p=0.02$ ), and MS prevalence by NCEP/ATP III criteria was similar in both groups (36% vs 16%, respectively,  $p=0.2$ ). Higher rates of moderate and high risk for DM development were found in pts with IR compared to pts without IR (71,4% vs 31,2%,  $p=0.03$ ).

**Conclusions:** The FINDRISK and IDF questionnaires, but not the NCEP/ATP III criteria of MS, can be helpful in selecting RA pts with potential IR. Abdominal obesity was the key factor indicative of IR in RA pts. On the other hand, IR may not be there even in the presence of several traditional DM risk factors. Therefore further clarification of potential contribution of RA-related risks is needed.

**Disclosure of Interest:** None declared

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AB0366

### CLINICAL, EPIDEMIOLOGICAL CHARACTERISTICS AND COMORBIDITIES IN A COHORT OF PARAGUAYAN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is a chronic rheumatic inflammatory disease with a higher risk of developing some cardiovascular pathology compared to the general population. The presence of comorbidities in patients with RA represents an increase in the cost of care, work disability and hospital admissions.

**Objectives:** To describe clinical, epidemiological characteristics, frequency of comorbidities and their association with clinical and analytical characteristics in Paraguayan patients with rheumatoid arthritis.

**Methods:** Descriptive, cross-sectional study of a cohort of patients with established rheumatoid arthritis, followed in the Department of Rheumatology of the Hospital de Clínicas. epidemiological (i.e. sex, age, origin), clinical (i.e., comorbidities (i.e. HBP was defined as BP  $\geq$ 140/90), obesity BMI  $\geq$ 30, dyslipidemia according to lipid profile levels), time of evolution of the disease, DAS28, etc.), laboratorial (i.e. RF, anti-CCP) and radiographic variables were recorded. Qualitative variables were expressed in frequencies and percentages and quantitative variables were characterised by their means and standard deviations. The comparison of clinical, epidemiological, serological variables was performed using the chi-squared test and the student test respectively for qualitative and quantitative variables. The statistical analysis was performed with the statistical program SPSS V.23.0.

**Results:** 177 patients with RA were included, 82.5% were women, with a mean of age at onset of 44.8 $\pm$ 13.8 years, mean disease duration of 8.64 $\pm$ 8.3 years. 68.3% came from Asunción and Gran Asunción, 44.6% of the patients were married, the average number of children per patient was 3.55 $\pm$ 2.2. Most of the patients (43.6%) were from social stratum 1–2, according to the GRAFFAR questionnaire. Family income with minimum salary or less was found at 55, 7% of patients with an average household income of 2.350.515 $\pm$ 1.6220.409 Guaranes. Most patients work at home, 54. 5% were housewife, and only 11.9% had a university degree. Only 15.3% had extra-articular manifestations, mainly rheumatoid nodules. The average body mass index was 29.6 $\pm$ 12.7. 75.9% were RF positive, with a mean of level of 436.7 $\pm$ 301 UI/L and 85% were anti-CCP positive, with a mean of level of 224,7 $\pm$ 201 UI/L. Methotrexate was the most frequent treatment (87%), 57.7% were using prednisone, with a median dose of 7.9 $\pm$ 4.8 mg. 40.9% had erosions. In this cohort median disease activity was 3.5% $\pm$ 1.2. 30.7% of patients were in remission by DAS 28 (<2.6). Regarding comorbidities, 38% presented hypertension, 11.9% had dyslipidemia, 5.3% type-2 Diabetes Mellitus, 39.4% were obese and 35% were overweight. Only 5% were smoker, and 16.5% had osteoporosis. When comparing the presence or absence of comorbidities with the clinical, epidemiological, serological and radiological characteristics, we did not find significant differences between them.

**Conclusions:** In this cohort of patients with established RA a little more than half receive a monthly income less than or equal to the minimum salary, and only the minority had university studies. The most frequent comorbidities were obesity, hypertension and dyslipidemia. One third of patients were in clinical remission, only with DMARDs.

**Disclosure of Interest:** None declared

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AB0367

### "THE STRUCTURAL INDEX SCORE – SIS" FOR RHEUMATOID FOOT AND ITS RELATION TO FOOT FUNCTION, DISABILITY AND PHYSICAL PERFORMANCE TESTS

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**Background:** Feet are involved in 90% of Rheumatoid arthritis (RA) patients. The Structural Index Score (SIS) is a score that evaluates forefoot and rearfoot aspects. Although it has been used as a clinical tool to quantify foot deformities in RA, its relevance in clinical practice is uncertain.

**Objectives:** The aim of this study was to evaluate the relation of SIS with foot function, disability and physical performance tests in RA.

**Methods:** 104 RA patients of the outpatient clinic of Rheumatology/Unicamp were evaluated for SIS total, forefoot, rearfoot and its items (hallux valgus, metatarsophalangeal (MTP) subluxation, 5th MTP exostosis, claw/hammer toe deformities, calcaneus varus/valgus angle, ankle range of motion (ARM) and planus/cavus foot deformity). Subjects also performed Foot Function Index-FFI, Health Assessment Questionnaire Disability Index-HAQ-DI, lower limb HAQ-LL-HAQ and physical tests: Berg Balance Scale-BBS, the Timed Up and Go-TUG and the 5-time sit down-to-stand up-SST5 tests. SIS items were compared with HAQ, LL-HAQ, FFI and physical tests through Kruskal-Wallis test and Spearman correlation coefficient with a 5% level of significance.

**Results:** SIS-Forefoot score did not correlate with any variables. Among the SIS-forefoot items, hallux valgus was associated with FFI-pain ( $p=0.007$ ), FFI-disability ( $p=0.005$ ) and FFI-total ( $p=0.016$ ); MTP subluxation was weakly correlated with FFI-disability ( $r_s=0.196$ ) and 5th MTP exostosis was associated with FFI-pain ( $p=0.018$ ). SIS-Total, SIS-Rearfoot and its associated and correlated items are shown in table 1.

Abstract AB0367 – Table 1

Variables	SIS-Rearfoot items			SIS-Rearfoot total score	SIS-Total
	Planus/Cavus foot deformity	Calcaneus valgus/varus angle	Ankle range of motion		
	p-value <sup>a</sup>	$r_s$ #/p-value	$r_s$ #/p-value	$r_s$ #/p-value	$r_s$ #/p-value
LL-HAQ	0.016	0.103/0.294	0.338/0.000**	0.392/0.0001**	0.195/0.046**
HAQ-DI	0.023	0.073/0.457	0.306/0.001**	0.346/0.000**	0.144/0.142
FFI-Pain	0.038	0.213/0.029**	0.257/0.008**	0.257/0.008**	0.256/0.008**
FFI-Disability	0.052	0.228/0.019**	0.293/0.002**	0.293/0.002**	0.233/0.017**
FFI-Activity Limitation	0.307	0.060/0.542	0.259/0.007**	0.259/0.007**	0.087/0.375
FFI-Total	0.094	0.203/0.038**	0.307/0.001**	0.307/0.001**	0.231/0.0178**
TUG	0.642	0.052/0.599	0.248/0.011**	0.248/0.011**	0.016/0.868
SST5	0.716	0.047/0.630	0.306/0.001**	0.306/0.001**	0.024/0.808
BBS	0.063	-0.107/0.276	-0.360/0.000**	-0.360/0.000**	-0.055/0.574

<sup>a</sup> Mann-Whitney's test; # Spearman's rank correlation coefficient; \*\* significant p-value

**Conclusions:** It is not clear if the use of SIS may be related to function and disability in RA. Forefoot SIS did not show correlation although hallux valgus, MTP subluxation and 5th MTP exostosis may be related to foot function. Rearfoot SIS and its items seem to be most correlated with function and disability in RA.

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AB0368

### THE OCCURRENCE OF ANTIBODIES DEPENDING ON THE DURATION OF RHEUMATOID ARTHRITIS

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**Background:** Recently heterogeneous nuclear ribonucleoproteins (hnRNPs) were identified as antigenic targets for autoantibodies in RA. Autoantibodies to RNP B1, B2 and heterogeneous complex A2/b are the most studied and are referred to as "antigen RA33". Clinical value of anti-RA33 in RA continues to be studied, so the question is about the diagnostic and pathogenic significance of these autoantibodies in patients with RA remains open.

**Objectives:** The aim of this study was to investigate the frequency of occurrence of anti – RA33y patients with RA and compare them with clinical manifestations and immunological parameters of disease.

**Methods:** The study included 139 patients with RA. The diagnosis was verified according to the classification criteria of ACR/EULAR 2010 Autoantibodies to RNP B1 IgG was assessed in samples of blood serum by enzyme immunoassay (ELISA; Medipan AG, Germany). A recombinant human RNP antigen B1 was used as the antigen, which was synthesised in the E. coli. system of the protein production. Anti-CCP, RF and antibodies to Sa-antigen (anti-Sa) was evaluated by ELISA according to the manufacturer's instructions (Euroimmun AG company, Germany). The results were expressed in relative units (U/ml). Statistical data processing was carried out using the software Statistica 7.0 (StatSoft, USA) and

Medcalc 12.5.0.0 (USA), including standard methods of parametric and nonparametric analysis. Differences were considered significant at  $p < 0.05$ .

**Results:** Levels and frequency of occurrence of anti-RA33, anti-CCP, RF IgM and anti-Sa were analysed for the examined patients depending on disease duration. Patients were divided into two groups: patients with early RA (disease duration less than 12 months) and patients with established RA (disease duration over 12 months). In the analysis it was found that the incidence of anti-Sa in established RA are much higher in comparison with the early RA (77.98% vs. 52.00% respectively,  $p < 0.05$ ). The levels of anti-Sa autoantibodies were lower in early RA than in established RA 21,57 U/L; 95% CI 12,10–27,42 vs. 33,10 U/L; 95% CI 27,58–37,71 respectively,  $p < 0.05$ ). Frequency of occurrence of anti-CCP and RF IgM is no different in the early and developed stage of RA. The frequency of occurrence of anti-RA33 in early RA was higher than in established RA (52.00% vs. 32.45% respectively,  $p < 0.05$ ).

**Conclusions:** Thus, anti-RA33 is a perspective independent biomarker of RA, which has its own potential. Further study of the anti-RA33 as a diagnostic biomarker of early stage RA is promising. Based on preliminary studies the anti-RA33 could have diagnostic and prognostic value in diagnosis and evaluation of patients with early RA, and its differentiation from other small joint disorders, particularly when the other serologic tests are negative.

To clarify the diagnostic and pathogenic value of anti-RA33 further research with a large sample size, comparison of immunological data with genetic factors, the results of other laboratory and instrumental studies, clinical manifestations of the disease are required. The obtained data will allow us to more thoroughly study the pathogenesis of RA and contribute to the search for new therapeutic options.

**Disclosure of Interest:** None declared

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#### AB0369 ADULT-ONSET STILL'S DISEASE TREATMENT PREDICTORS AT 1-YEAR FOLLOW-UP IN A SINGLE RHEUMATOLOGIC CENTRE EXPERIENCE

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**Background:** Adult-onset Still's disease (AOSD) is a rare systemic inflammatory disorder mainly characterised by persistent high spiking fevers, evanescent rash, and joint involvement. Data on the efficacy of biologic therapy in the management of AOSD<sup>1</sup> is increasing and represents a breakthrough in the management of patients with AOSD refractory to corticosteroids (CS) or conventional (c) DMARDs.

**Objectives:** We aimed to evaluate possible predictor on the need to use a biologic agent in the management of AOSD patients.

**Methods:** In this retrospective monocentric study we evaluated AOSD patients followed in our outpatient's clinic since 2010 with at least 1 year follow-up. Clinical manifestations, joint involvement, CS and c- or bDMARD use were main outcome measures. T-test or ANOVA and Chi-squared were used to compare continuous or categorical data, when appropriate, and the odds ratio (OR) for which condition had an influence on clinical outcome was calculated.

**Results:** We evaluated 28 AOSD patients (mean age  $43 \pm 14$  years; median disease duration 3 (95%CI 2.5–17.3) months). All patients at baseline were treated with a median CS of 18.7 (95%CI 14.3–24.8) mg/die prednisone equivalent dose, and median methotrexate (MTX) dose of 15 (95%CI 13.4–16.28) mg/week. After 1 year follow-up, in the 8 patients (28.6%) that needed to start a bDMARD (4 anti-IL1; 3 anti-IL6 and 1 anti-TNF), we observed that baseline joint involvement was the more prevalent manifestation of the disease with higher DAS28 compared to those patients still on CS +MTX (DAS28  $3.8 \pm 1.2$  vs  $2.8 \pm 1.1$ , respectively  $p = 0.03$ ). Moreover, we showed that clinical manifestations of systemic involvement (i.e. fever, rash, organomegaly and anaemia) were associated with a protective risk to start a bDMARD at 1 year (OR 0.4 95% CI 0.2–0.76). Consistently, in those patients with concomitant elevated ESR ( $> 20$  mm/h), CRP ( $> 15$  mg/L) and ferritin ( $> 250$  ng/ml) levels at baseline, we observed a low risk to start a bDMARD at 1 year follow-up (OR 0.4 95% CI 0.18–0.87).

**Conclusions:** In our cohort about one third of AOSD patients required to be treated with a bDMARD at 1 year follow-up, mainly if joint involvement was the predominant clinical manifestation at disease onset. Systemic manifestations of the disease seem to benefit from high dose CS+MTX combination therapy. Further studies with more extensive cases are necessary.

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#### AB0370 LOW SERUM IGF1 IS ASSOCIATED WITH HIGHER CARDIOVASCULAR RISK IN THE MIDDLE-AGED WOMEN WITH RHEUMATOID ARTHRITIS INDEPENDENTLY OF THE DISEASE RELATED PARAMETERS

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**Objectives:** To analyse the relation between serum levels of IGF1 and cardiovascular risk (CVR) in women with rheumatoid arthritis (RA).

**Methods:** The risk of dying of CV disease within 5 years was calculated using the strategy proposed by Pocock et al. *BMJ* 2001 in 185 women with RA (mean age 51.7 years) with no previous history of CV events. The CVR and characteristics related to it were analysed with respect to serum IGF1. IGF1 levels below the median of the total cohort were considered low.

**Results:** The RA women with low IGF1 ( $n = 91$ , mean 104 pg/ml) had significantly higher CVR compared to those with normal IGF1 ( $n = 94$ , mean 194 pg/ml) with the predicted risk of 0.51% and 0.17%, respectively ( $p > 10^{-5}$ ). Among the traditional CVR factors, the low IGF1 group was 10 years older (mean 56.8 vs. 46.9 y,  $p = 10^{-5}$ ), lower in height (165 vs. 168 cm,  $p = 0.013$ , 21% of the patients being  $< 160$  cm) and had high prevalence of hypertension (24% vs. 8.5%,  $p = 0.004$ ), while current smoking was similar between the groups (15% vs. 14%).

The low IGF1 group displayed the unfavourable metabolic profile with higher BMI ( $p = 0.002$ ) and obesity in 22%, higher predicted body fat content (mean 39.5 vs. 35%,  $p = 10^{-5}$ ), and higher total and LDL cholesterol ( $p = 0.0014$  and  $p = 0.0053$ , respectively). The levels of adiponectin ( $p = 0.032$ ) and HDL-cholesterol ( $p = 0.25$ ) tended to be higher in the low IGF1 group, which resulted in the comparable total cholesterol to HDL ratio between the groups. This could also explain that the prevalence of diabetes mellitus and metabolic syndrome were low.

With exception of the disease duration, the groups displayed no significant difference in the RA-related CVR factors such as the disease activity measured by DAS28 (3.29 vs 2.99), systemic inflammation measured by serum IL6 (mean 8.46 vs. 5.99 pg/ml) and IL1 $\beta$  (mean 19.47 vs. 23.1 ng/ml), and the prevalence of seropositivity (91% vs. 92%). The prevalence of treatment with MTX monotherapy was higher in the low IGF1 group (56% vs. 39%,  $p = 0.024$ ), while the use of TNF-inhibitors and other biologic and synthetic anti-rheumatic drugs was similar within the groups.

**Conclusions:** Serum IGF1 levels in the normal low range are associated with higher CVR in RA female patients. This increase in CVR seems to be independent of the RA-related characteristics. The combination of low height and hypertension argues for the important role of congenital factors in defining serum IGF1 levels in the studied RA women.

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#### AB0371 THE EFFECT OF CUMULATIVE EXPOSURE TO CIGARETTE SMOKING ON VASCULAR DAMAGE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Smoking is described as a classic cardiovascular (CV) risk factor and we also know the beneficial effect on the CV system of smoking cessation. However, there is contradictory data about its effect in patients with rheumatoid arthritis (RA). It is possible that the measure of cumulative exposure to tobacco expressed in pack-year gives us more information than the smoking status.

**Objectives:** To explore the relation between smoking exposure, measured in pack-year, and subclinical vascular damage, mortality and vascular events in patients with RA.

**Methods:** Observational ambispective study. We included, consecutively, RA patients controlled in a tertiary hospital. We gathered demographic (sex, age, body mass index [BMI]), clinical (characteristics of RA, classic CV risk factors and history of vascular events) and analytical variables (CRP, ESR). We estimated the modified SCORE. We explored the extracranial branches of the carotid artery



with an Esaote MyLab70XVG ultrasound device with a linear probe (7–12mHz) and an automated program measuring intima media thickness (IMT) by radiofrequency ("Quality intima media thickness in real-time, QIMT"), and registered the presence of atheroma plaques (per Mannheim consensus). We determined pulse wave velocity (PWV) by a validated MobilOGraph device. We considered as pathological an IMT >900  $\mu$  and a PWV  $\geq$ 10 m/s and the presence of plaque and/or pathological IMT. We prospectively collected mortality and the development of new vascular events over four years and the current smoking status and exposure calculated in pack-year. Statistical analysis was performed using SPSS 17.0 software.

**Results:** We included 198 patients, excluding 15 because of previous CV events. The mean age was 66.5 years (SD 13.44) 76% were women and the mean BMI was 27.35 (SD 4.82). 31.1% were smokers, 43.2% hypertensive, 47.5% dyslipemic and 10.4% were diabetic. The mean duration of RA was 19.95 years (SD 11.88). 76.5% of patients were seropositive and 75.4% had erosions. The mean CRP and ESR were 9.51 mg/L (SD: 32.29) and 13.83 mm/h (SD:14.26), respectively. The mean modified SCORE was 1.81 (SD: 1.81). Regarding the vascular study, 48.1% had atheroma plaques, 32.2% a pathologic PWV [mean value of 9.13 (SD 2.12)], and 16.7% had a pathologic IMT [mean value of 748  $\mu$ (DE 168.73)].

31.1% of the patients (57) were smokers or former smokers. The average pack-year was 24.17 (SD: 21.37). No relation was found between current or previous use of tobacco and any of the outcome measures described. However, when considering cumulative exposure to tobacco, there was a trend to correlate with higher values of PWV ( $p=0.07$ ) and a higher plaque presence ( $p=0.089$ ) was detected. After 4 years of follow-up, 3 deaths were recorded among smoking patients, but a higher incidence of CV events was not detected in relation to cumulative exposure to tobacco ( $p=0.99$ ).

**Conclusions:** The quantification of the exposure by pack-year of cigarette smoked could give us more information about vascular damage in patients with RA. The limitation of our study is the small number of smokers in the time they were followed.

**Disclosure of Interest:** None declared

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AB0372

#### LEFT ATRIAL FUNCTION IN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Rheumatoid arthritis (RA) is a common autoimmune systemic inflammatory disease affecting approximately 1% of the worldwide population. The interaction of genetic and environmental factors results in a cascade of immune reactions, which ultimately lead to the development of synovitis, joint damage, and structural bone damage.<sup>1</sup>

The importance of the left atrium in cardiovascular performance has long been acknowledged. Quantitative assessment of left atrial (LA) function is laborious, requiring invasive pressure-volume loops and thus precluding its routine clinical use. In recent years, novel postprocessing imaging methodologies have emerged, providing a complementary approach for the assessment of the left atrium. Atrial strain and strain rate obtained using either Doppler tissue imaging or two-dimensional speckle-tracking echocardiography have proved to be feasible and reproducible techniques to evaluate LA mechanics.<sup>2</sup>

#### Objectives:

1. To screen cardiac affection in rheumatoid arthritis patients
2. To assess subclinical echocardiography affection in RA patients

**Methods:** 30 healthy control, and 45 RA patient subjected to full clinical assessment, DAS 28 ESR score, full laboratory evaluation, conventional and tissue Doppler imaging (TDI) and strain (S) and strain rate (SR) analysis by two-dimensional speckle tracking of the left atrium.

**Results:** we found statistically significant difference in 2 Left atrial PEF, 2 Left atrial EI, 2 Left atrial TEF, TDI mitral lateral annulus e', TDI mitral lateral annulus S, Average SR E 1/s between patients and controls, and negative correlation between TDI lateral e, TDI lateral s, and Strain rate e and rheumatoid factor, There was negative correlation between 2LA PEF, 2LA EI, and 2LA TEF. Rheumatoid factor is correlated to strain rate e, and negatively correlated with left atrial passive emptying

**Conclusions:** RA had alteration in left LV longitudinal myocardial function, left atrial expansion volume can be a predictor of AF in RA. RA patient had more left atrial stiffness. Our study concluded cardiac affection is more in seropositive RA patients.

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AB0373

#### SARCOPENIA COULD NOT PREDICT FALLS IN PATIENTS WITH RHEUMATOID ARTHRITIS FROM THE CHIKARA STUDY

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**Background:** The falls ratio is higher among patients with sarcopenia than among healthy individuals. We reported that the prevalence of sarcopenia was 28% and locomotive syndrome (locomo) was 52% in patients with rheumatoid arthritis (RA)<sup>1</sup>. Whether patients with RA complicated by sarcopenia show a higher ratio of falls compared to those without sarcopenia remains unclear.

**Objectives:** We investigated events of falls and fractures, and predictors of those events in patients with RA.

**Methods:** We used data from a prospective observational study (CHIKARA study, UMIN000023744) started in 2016. Sarcopenia was diagnosed using the criteria of the Asia Working Group on Sarcopenia<sup>2</sup>. We counted the number of patients and events of falls and fractures they had per year[A1], and investigated correlations between those events and disease activity, body composition and sarcopenia. Predictors at baseline influencing those events were analysed by uni- and multivariate analysis.

**Results:** Participants comprised 100 patients with RA (females, 78%; mean age, 66.1 years). Falls occurred in 21 patients (19 women), as 33 events (mean, 2 times/patient). Fractures occurred in 4 patients (4 women), as 5 events. Table 1 shows predictors for falls, with positive correlations for bone mass index, obesity level, fat percentage, and locomo, and negative correlations for height, trunk muscle mass, and grip strength. No relationships were seen between falls and CRP, DAS28ESR, skeletal muscle mass, and sarcopenia. Height (odds ratio, 0.912;  $p=0.003$ ) and obesity level (odds ratio, 1.04;  $p=0.006$ ) were independent predictors by multivariate analysis (table 1). In terms of fracture events, falls was the only predictor ( $r=0.469$ ,  $p=0.001$ ).

**Abstract AB0373 – Table 1.** Predictors of falls in patients with RA

	Univariate		Multivariate		
	R	P	Odds ratio	95% CI	P
Body mass index	0.195	0.040			
Obesity level	0.194	0.040	1.040	1.011–1.069	0.006
Fat percentage	0.211	0.025			
Locomotive syndrome	0.237	0.012			
Height	–0.263	0.005	0.912	0.858–0.968	0.003
Trunk muscle mass	–0.188	0.048			
Grip strength	–0.198	0.036			
CRP	0.063	0.512			
DAS28ESR	–0.008	0.932			
Skeletal muscle mass	0.091	0.337			
Sarcopenia	–0.093	0.327			

**Conclusions:** Falls have been reported as significantly more frequent with sarcopenia. However, no relationship was seen between fall events and sarcopenia in this study. We may need to evaluate not only skeletal muscle mass, but also muscle function to predict falls.

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AB0374

**NONTUBERCULOUS MYCOBACTERIUM INFECTIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS: A SINGLE-CENTRE EXPERIENCE IN JAPAN**

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**Background:**

**Objectives:** Nontuberculous mycobacteria (NTM) infection has been increasing in both general population and immunocompromised patients in Japan. This study aimed to identify the incidence and clinical characteristics of NTM infections in patients with rheumatoid arthritis (RA).

**Methods:** We performed a cross-sectional analysis and assessed 11 RA patients, who were all female, complicated with NTM (mean age, 66.6 years) at our institute. We examined Steinbrocker Stage and Class, disease duration, positivity of anti-CCP antibody and rheumatoid factor, HAQ-DI, DAS28-ESR, NTM species, radiological features, methotrexate use and dosage, prednisolone use and dosage, biological agent use, and anti-NTM therapy.

**Results:** Average values obtained with SD were as follows: age (years), 66.6 ±8.0; Steinbrocker Stage I, 1; II, 0; III, 1; and IV, 9; Class 1, 2; 2, 5; 3, 4; and 4, 0; disease duration (months), 274.9±126.9; positivity of anti-CCP antibody, 80.0%; positivity of rheumatoid factor, 100%; HAQ-DI, 1.35±0.72; DAS28-ESR, 3.61 ±0.90; detection by sputum culture, 81.8%; NTM species, *M. avium*, 8 cases and *M. intracellulare*, 3 cases; bronchiectasis, 90.9%; interstitial pneumonia, 0%; methotrexate use and dosage (mg/week); 63.6% and 7.4±3.4; prednisolone use and dosage (mg/day); 81.8% and 4.3±2.0; biological agent use, 45.5%; and anti-NTM therapy, 36.4%.

**Conclusions:** At our institute, RA patients complicated with NTM were long-standing, had high disease activities and worse HAQ-DI. In all five patients (45.5%) who were treated with biologics, 3 who had preceding episodes of NTM infection were treated with anti-NTM therapy before treatment with biologics, and the other 2 who had asymptomatic NTM infection after treatment with biologics were not treated with anti-NTM therapy thereafter. In RA patients who are treated with biologics, it is necessary to perform sputum cultures constantly to detect possible NTM infections. This finding is important in the management of RA complicated with NTM.

**Disclosure of Interest:** None declared

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AB0375

**A SYSTEMATIC LITERATURE REVIEW OF OMEGA 3 IN THE TREATMENT OF RHEUMATOID ARTHRITIS**

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**Background:** Many different elements and variations of diet in the management of rheumatoid arthritis (RA) have been studied over the years such as vegan or Mediterranean diets.

**Objectives:** This systematic literature review covers one food stuff, omega-3 polyunsaturated fats efficacy in the management of RA alongside or independent of conventional DMARD therapy.

**Methods:** A systematic review of the literature between 1966–2017 was conducted using MEDLINE, CINAHL and EMBASE databases, with key words "RA" and "omega-3" for English-language articles producing 209 hits. We then refined to publications within the last 10 years, giving 96 results. Only including clinical trials gave 12 hits pertaining to 8 trials.

**Results:** The table above shows a summary of the evidence found. In total, 751 were exposed to omega-3 versus 1733 controls with the smallest study being an

RCT involving 13 people and the largest a case-control study with 1569 participants. A notable difference between these studies was the use of DMARD therapy as part of the inclusion or exclusion criteria. Another difference noted was the RA stage eligible for a trial. Some studies required a diagnosis of RA of <12 months whereas most required stable RA ongoing for >12 months.

**Conclusions:** This review concludes that omega-3 leads to clinical and statistically significant improvements in RA. There was a significant heterogeneity in the trials published with different inclusion criteria especially regarding disease duration and concomitant DMARD therapy. It would seem prudent to include dietary advice in our advice to patients when treating RA. Possible reasons for this evidence would include altering the microbiome.

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AB0376

**RAPAMYCIN INDUCES REMISSION IN PATIENTS WITH NEWLY DIAGNOSED RHEUMATOID ARTHRITIS**

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**Background:** Rheumatoid arthritis (RA) is an autoimmune disease characterised by chronic inflammation of the joints. We found that there was an imbalance between Th17 and Treg cells in the patients with active refractory RA, reduced absolute number of Treg cells was found in these patients.

**Objectives:** To observe the medium-term curative effect of rapamycin in the treatment of 25 cases newly diagnosed rheumatoid arthritis.

**Methods:** Collecting 25 patients of newly diagnosed rheumatoid arthritis, which accorded with RA diagnosis standard of ACR in 1987. The patients were treated with rapamycin at a dose of 0.5 mg every 2 days for 24 weeks, then we observed the change of clinical improvement and immunological assessments after 24 weeks.

**Results:** There was 25 patients enrolled. After rapamycin treatment for 24 weeks, the mean DAS28 of them was decreased from 5.36 [1.42] to 3.45 [1.29](p=0.001). The absolute number of Treg<sup>CD4+CD25+Foxp3+</sup> cells significantly higher than baseline (30.24 [14.44],46.64 [27.54],p=0.025). The absolute number of Th17 cells was not significantly different (6.40 [4.46],7.03 [5.60],p>0.05), and the same as the ratio of Th17/Treg cells (0.25 [0.18],0.19 [0.16]),p>0.05). Meanwhile, the mean dose of prednisone was decreased from 11.25 mg/d to 9.6 mg/d.

**Conclusions:** Rapamycin could induce the balance of Th17 cells and Treg cells, especially up-regulate the absolute number of Treg cells, thus induce remission in patients with newly diagnosed RA.

**Disclosure of Interest:** None declared

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Abstract AB0375 – Table 1

Reference:	Study type	Participants in intervention group	Participants in control group	Omega-3 dose	Duration	Did it show efficacy?	How did they assess response?
Proudman et al <sup>1</sup>	RCT	86	53	3.7 g/day	1 year	Yes	Success/failure of DMARDs
Shapiro et al <sup>2</sup>	Case-control	324	1245	>2 servings boiled/baked fish per week	Diet from a 1 year period	Yes	RA risk
Lee et al <sup>3</sup>	Meta-analysis	183	187	>2.7 g/day	>3 months	Clinical not statistical significance	NSAID consumption, tender/swollen joint count, physical function
Bahadori et al <sup>4</sup>	RCT	8	5	0.2 g/kg– fish oil emulsion	22 weeks	Yes	Decrease in swollen and tender joint counts
Rajaei et al <sup>5</sup>	RCT	30	30	3.9 g/day	12 weeks	Yes	DAS28
Tedeschi et al <sup>6</sup>	Cross sectional analysis	31	145	Eat fish>2 x per week (<5.5 g/day)	Diet from past yr	Yes	DAS28
Galarraga et al <sup>7</sup>	RCT	49	48	2.2 g/day	9 months	Yes in reducing NSAID intake but not in DAS28	Daily NSAID requirement
Veselinovic et al <sup>8</sup>	RCT	40	20	600 mg/day	12 weeks	Yes	DAS28

**AB0377** **ARE CO-MORBIDITIES DURING RHEUMATOID ARTHRITIS DIFFERENT FROM THOSE IN ANKYLOSING SPONDYLOARTHRITIS ?**

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**Background:** Patients with inflammatory rheumatic diseases are certainly not unscathed from a lot of comorbidities which may be due to the systemic inflammatory activity of rheumatic diseases themselves, immune dysfunction, or iatrogenic, they may also occur independently.

Cardiovascular morbidity remains one of the most important to detect and is increased during these diseases.

So are there significant differences between co-morbidities associated with rheumatoid arthritis (RA) and those with ankylosing spondyloarthritis (AS)?

**Objectives:** To highlight the difference between comorbidities in RA and AS.

**Methods:** This is a retrospective study of 111 patients followed for RA ACR 1987 criteria, and 60 patients followed for AS, compiled between January 2005 and December 2016.

**Results:** The mean age of patients with RA was 51.04 years [18–80 years] with a sex ratio (M/F) of 0.18. The average duration of disease progression was 6.54 years [0–29 years]. The mean age of patients with AS was 40.4 years [18–61] with a sex ratio (M/F) of 19. The average duration of disease progression was 16.8 years [1–45 years].

About cardiovascular comorbidities, 16.2% of patients with RA and 5.1% with AS were diagnosed with high blood pressure. Dyslipidemia was found in 2.7% of patients with RA and in 0% with AS.

31.5% with RA and 21.7% of AS have overweight and obesity was illustrated in 22.5% of RA and 11.7% of AS.

Heart and coronary failure were documented in 5.4% of RA and 1.7% of AS. Likewise renal failure in 3.6% of RA and 3.4% of AS. Diabetes was found in 18% of RA and 10% of AS. Hypothyroidism in 5.4% of RA and 1.7% of AS. Gout attack in 0.9% of RA and 0% with AS and osteoporosis in 21.3% of RA and 40% of AS.

**Conclusions:** Our study concluded at the frequency of comorbidities and mostly cardiovascular in rheumatoid arthritis compared with AS. Osteoporosis is also more common in our studied population with RA, although not rare with our patients with AS. This can be explained by the prescription of corticosteroid therapy in RA.

**Disclosure of Interest:** None declared

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**AB0378** **PULMONARY AFFECTION IN EGYPTIAN PATIENTS WITH RHEUMATOID ARTHRITIS**

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**Background:** Rheumatoid arthritis(RA) is a disabling autoimmune systemic inflammatory disease. It manifests as peripheral symmetric inflammatory polyarthritis and produces a wide range of extra-articular manifestations. Interstitial lung disease (ILD), a diffuse progressive disease of the lung parenchyma, is the most serious manifestation of RA lung affection, it remains as a significant source of morbidity and mortality.

**Objectives:** To evaluate the frequency and pattern of pulmonary affection in a cohort of Egyptian rheumatoid arthritis (RA) patients and the relation to disease activity and severity.

**Methods:** Seventy RA patients who fulfilled 2010 (ACR/EULAR) classification criteria underwent full clinical assessment, plain X ray chest, chest high-resolution computed tomography (HRCT) with assessment of the extent and severity of pulmonary affection by Warrick score. Pulmonary function tests (PFTs) including diffusion lung capacity for carbon monoxide (DLCO) were done. Transthoracic echocardiography to screen for pulmonary hypertension (PH). Assessment of disease activity by DAS28 score and of radiographic joint damage by modified Larsen score.

**Results:** The mean age of the patients was 44±10.8 years; females(87.1%) and males (12.9%), mean disease duration 7.3±6 years. PFTs were abnormal in (45.7%) with restrictive pattern in (24.3%) of patients followed by small airway affection in (10%), mixed pattern in (8.6%), the least is the obstructive pattern in (2.8%) of patients. DLCO was abnormal in (72.86%) with mild affection in (48.57%), moderate in (15.7%) and severe affection in (8.6%) of patients. HRCT abnormalities were found in 30 patients (42.85%). Interstitial abnormalities were detected in (35.7%). Septal or reticular lines, ground glass appearance, pleural irregularities and bronchiectasis were the most common findings. Most common HRCT pattern was nonspecific interstitial pneumonia (NSIP) in 12.8% (9/70), usual interstitial pneumonia (UIP) in 7% (5/70), organising pneumonia (OP) in 1.4% (1/70) and indeterminate subtype in 14% (10/70). HRCT total score (Warrick score) was correlated with age, disease activity (DAS ESR 28), ESR, modified Larsen score, FVC, FEV1 and DLCO. Age, dyspnea and DLCO impairment were

significant predictors for development of HRCT chest abnormalities. Pulmonary hypertension(sPAP >30 mmHg) was detected in (14%) of patients.

**Conclusions:** Pulmonary abnormalities are common in Egyptian RA patients. HRCT and PFTs including DLCO can be used effectively for early diagnosis and monitoring of pulmonary affection in RA patients. DLCO can detect pulmonary abnormalities early in clinically asymptomatic patients. Age, disease activity and severity, PFTs and ESR are correlated with the pulmonary affection in RA. Age, dyspnea and DLCO impairment are significant predictors of pulmonary affection in RA patients. Echocardiography can be used as a screening tool for detection of pulmonary hypertension.

**Disclosure of Interest:** None declared

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**AB0379** **MUSCULOSKELETAL INVOLVEMENTS IN GIANT CELL ARTERITIS**

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**Background:** Joint involvement is frequent in Giant cell arteritis (GCA), mostly polymyalgia rheumatica (PMR). The aim of this study was to describe clinical features of joint involvement in GCA.

**Objectives:** To compare patients according to the presence or not of PMR.

**Methods:** A retrospective and descriptive study of 96 patients with GCA diagnosed between 2000 and 2015. ACR 1990 criteria were used for the diagnosis of GCA. Clinical, biological and histological features were recorded and analysed.

**Results:** Joint involvements were noted in 67 patients with GCA (69.8%); 34 women and 33 men. Mean age at diagnosis was 72.4±6.36 years. PMR was diagnosed in 45 patients (46.8%) and revealed the disease in two patients. Neck pain was noted in 48 patients. Twenty one patients (21.8%) complained of peripheral arthralgias which revealed GCA in five cases. Joint manifestations were associated to cardinal symptoms of GCA: headache (97%), jaw claudication (62%), scalp tenderness (49.3%) and ophthalmologic manifestations (36.9%). Erythrocyte sediment rate and C-reactive protein were high in 89.2% and 82.7% of cases respectively.

Constitutional symptoms (60% vs 39.2%; p=0.042), jaw claudication (68.2% vs 47.1%; p=0.038) and neck pain (62.2% vs 39.2%; p=0.024) were significantly more frequent in patients with PMR. Peripheral arthralgias (28.9% vs 15.7%) were more frequent in patients with PMR without significant differences. Giant cell vasculitis on temporal arterial biopsy was more frequent in patients with PMR (57% vs 30%; p=0.037).

Corticosteroids were given in 97% of patients while methotrexate was used in 20.9%.

**Conclusions:** PMR in patients with GCA seem to be associated to different joint manifestations.

**Disclosure of Interest:** None declared

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**AB0380** **DELAY IN TIME TO DIAGNOSIS INCREASES THE RISK OF SUFFERING CLASSIC CARDIOVASCULAR RISK FACTORS IN PATIENTS WITH RHEUMATOID ARTHRITIS**

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**Background:** Rheumatoid arthritis (RA) is a chronic inflammatory disease that constitutes an independent cardiovascular risk factor (CVRF). In addition, patients with RA have a higher prevalence of CVRF than the general population.

**Objectives:** To assess whether delay in time to diagnosis of the disease may increase the risk of CVRF in patients with RA.

**Methods:** Patients diagnosed with RA, according to the EULAR/ACR 2010 classification criteria, were consecutively selected and recruited for a period of 12 months. Delay in time to diagnosis was calculated as the interval between the beginning of first joint symptoms and the diagnosis of RA with start of specific treatment. Furthermore, the presence or absence of arterial hypertension (AHT), dyslipidemia (DL) and diabetes mellitus (DM) were recorded. Whether its diagnosis was prior or subsequent to the diagnosis of the inflammatory disease was also recorded. SPSS version 17.0 software was used for statistical analysis, considering statistical significance for p<0.05.

**Results:** A total of 244 patients were studied, 73.8% (180) of whom were women and 26.2% (64) men. The mean age was 60.42 years (SD 13.24). Mean Delay in time to diagnosis was 2.1 years (SD 5.5). Mean age at diagnosis was 48.9 years (SD 15.7). Regarding classic CVRF, the percentage of patients with AHT, DL and DM before RA diagnosis were 17.6% (43), 6.1% (15) and 6.1% (15), respectively.



After RA diagnosis, 22.5% (55), 43.4% (106) and 3.3% (8) of patients were diagnosed with AHT, DL and DM. Delay in time to diagnosis was significantly associated with AHT, DL and DM diagnosis after RA diagnosis.

**Conclusions:** A higher inflammatory load, such as that accumulated in RA patients who have delayed the start of treatment, is associated with a higher probability of developing CVRF, which are associated with the appearance of vascular structural damage in the long term. These results are consistent with the effect of inflammatory cytokines on peripheral tissues (increased lipolysis in adipose tissue, increased insulin resistance, increased arterial stiffness).

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#### AB0381 CLINICAL AND RADIOGRAPHIC CHARACTERISTICS OF AIRWAY DISEASE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Airway disease (AD) has drawn attention both clinically and etiologically in rheumatoid arthritis (RA), but is still poorly understood.

**Objectives:** We aimed to elucidate the clinical and radiographic characteristics of AD in patients with RA.

**Methods:** We retrospectively reviewed high-resolution computed tomography (HRCT) images and clinical data of 131 consecutive RA patients in whom HRCT were scanned for clinical purposes and screening. Overlap patients with other collagen tissue diseases and patients complicated with active infection or lung cancer were excluded. Patients who had a history of drug-induced lung disease, thoracic radiation, or exposure to dust were also excluded. HRCT images were reviewed independently by a pulmonologist and a radiologist in blind fashions, and cases of disagreement were discussed to reach a final consensus. AD was radiographically sub-categorised into 3 sub-groups: central AD, small AD, and middle lobe and lingular bronchiectasis. The associations between AD and interstitial lung disease (ILD) and each pair of the subtypes of AD were analysed by Fisher's exact test. The risk factors for AD and subtypes of AD were identified by multivariate logistic regression analyses.

**Results:** The mean age of the patients was 65 years old, the mean disease duration of the patients was 123 months, 69% of the patients were women, and 42% of the patients had past/current histories of smoking. The mean Disease Activity Score 28 (DAS28)-erythrocyte sedimentation rate (ESR) value was 2.87. AD and ILD were observed in 53 (40%) and 36 (27%) patients, respectively, and both in 19 (15%) patients. AD and ILD were not significantly associated ( $p=0.11$ ). By multivariate logistic regression analyses, rheumatoid factor (RF) was identified as risk factors for whole AD (odds ratio [OR] 2.7; 95% confidence interval [CI], 1.0 to 6.9;  $p=0.04$ ). Central AD, small AD, and middle lobe and lingular bronchiectasis were observed in 45 (34%), 31 (24%), and 17 (13%) patients, respectively. Each pair of these 3 subtypes were significantly associated with each other ( $p<0.001$  in all comparisons). By multivariate logistic regression analyses without considering the overlaps with multiple subtypes of AD in the same patients, age and RF were identified as risk factors for central AD: the OR for age was 1.04 (95% CI, 1.00 to 1.08;  $p=0.04$ ); the OR for RF was 3.0 (95% CI, 1.1 to 8.5;  $p=0.034$ ). In contrast, DAS28-ESR values was identified as a risk factor for small AD: the OR for DAS28-ESR values was 1.5 (95% CI, 1.0 to 2.4;  $p=0.0498$ ). Lastly, no significant risk factor was identified for middle lobe and lingular bronchiectasis by the multivariate logistic regression analysis, although disease duration tended to be longer in the patients with middle lobe and lingular bronchiectasis than in those without ( $p=0.12$ ). In contrast, smoking histories was not significantly associated with whole AD or any subtypes of AD.

**Conclusions:** Radiologically defined AD was frequent comorbidity in RA patients, and multiple subtypes of AD were observed and coexisted. Furthermore, AD may be related to the pathology of RA, and different AD subtypes may have

distinct risk factors. Prospective studies with early RA patients were warranted to further clarify these findings and clinical impact of AD.

**Disclosure of Interest:** None declared

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#### AB0382 RAPAMYCIN SELECTIVELY INCREASES CIRCULATING TREG CELLS AND MAINTAIN REMISSION OF PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** It is thought that Rheumatoid arthritis (RA) arises from a breakdown in immunological self-tolerance. We have given a direct evidence for this conception that absolute number of peripheral CD4<sup>+</sup>Regulatory T-cells (Tregs) decreased in RA patients<sup>[1]</sup>. Furthermore, rapamycin can significantly induce immune tolerance through up-regulate Tregs and down-regulate Th17 cells<sup>[2]</sup>.

**Objectives:** To investigate the effect of rapamycin on the absolute numbers of Th17 and Treg cells and on maintenance of disease remission in RA patients instead of DMARDs.

**Methods:** Thirty-two patients, who achieved remission (DAS28  $\leq 2.6$ ) by the treatment with two kinds of DMARDs for more than half a year, received rapamycin at a dose of 0.5 mg every other day for 12 weeks. Before and after treatment with rapamycin, the disease activity and immunological assessments of them were performed. In this study, BD Trucount tubes with the lyophilized pellet of a known number of internal counting beads were used for determining absolute counts of total CD4<sup>+</sup> T cells in peripheral blood and then calculating the absolute number of Th17 cells and CD4<sup>+</sup>Tregs.

**Results:** At week 12, 65.6% of the patients maintained remission (DAS28  $\leq 2.6$ ). The DAS28 was increased from a median of 2.03 (at week 0) to 2.15 (at week 12) ( $p>0.05$ ). The absolute number of Treg cells was increased significantly from a median of 22.16 (at week 0) to 32.19 (at week 12) ( $P=0.039$ ). The absolute number of Th17 cells was decreased from a median of 5.98 (at week 0) to 5.56 (at week 12) ( $p>0.05$ ). The ratio of Th17/Treg cells was also decreased from a median of 0.245 (at week 0) to 0.19 (at week 12) ( $p>0.05$ ). At the same time, the mean dosage of prednisone decreased from 6.29 mg/d to 5.35 mg/d and that of DMARDs were also reduced from 93.75% to 56.25%.

**Conclusions:** Rapamycin was effective in the maintenance of remission (DAS28  $\leq 2.6$ ) by increase of Treg cells and correcting the imbalance of Th17/Treg cells. Meantime, the mean dosage of conventional drugs such as glucocorticoid and DMARDs gradually decreased. In the future, rapamycin may replace current immunosuppressant for treatment of RA.

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#### AB0383 CHANGES OF METABOLIC BIOMARKER LEVELS UPON ANTI-TNF THERAPY IN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Rheumatoid arthritis (RA) has been associated with cardiovascular disease and metabolic syndrome. Numerous pro-inflammatory cytokines (e.g. TNF- $\alpha$ , IL-1, IL-6) are released, which cytokines cause increased reactive oxygen species (ROS) production and thereby contribute to the increased lipid peroxidation and reduction of many antioxidants. These processes not only lead to the deterioration of joints and other tissues but may also contribute to comorbidities, such as atherosclerosis.

**Objectives:** The aim of this study was to assess the effects of anti-TNF therapy on different metabolic markers, such as PON1 (paraoxonase 1), arylesterase, chemoerin and adiponectin. We also investigated whether these biomarkers correlated with various demographic, clinical and laboratory markers.

**Methods:** We treated 37 RA patients with either etanercept (ETN) or certolizumab pegol (CZP) in a 12 month follow-up study. Assessments were performed at baseline, and 3, 6 and 12 months after treatment initiation. Serum chemerin and adiponectin concentrations were measured by commercially available ELISA kits (R and D System, MN and USA). PON1 and arylesterase activities were measured by spectrophotometry. In addition, age, disease duration, disease activity (DAS28), CRP, anti-CCP, IgM rheumatoid factor and plasma lipid levels were also assessed. Arterial flow-mediated vasodilation (FMD), carotid intima-media thickness (cIMT) and arterial pulse-wave velocity (PWV) were assessed by ultrasound.

**Results:** Anti-TNF treatment resulted in a significant decrease in the levels of chemerin ( $p<0.001$ ) and adiponectin ( $p<0.007$ ) after 12 months. There were no significant changes in the levels of other metabolic biomarkers. We found the following correlations between the baseline values: the PON1 levels correlated with the age of patients ( $R=0.466$ ,  $p=0.004$ ). The adiponectin correlated with the disease activity ( $R=0.385$ ,  $p=0.030$ ), HDL-C ( $R=0.417$ ,  $p=0.012$ ) and the triglyceride levels ( $R=0.481$ ,  $p=0.003$ ). The total cholesterol correlated with the PWV ( $R=0.449$ ,  $p=0.021$ ) and the levels of the LDL-C ( $R=0.911$ ,  $p<0.001$ ). The baseline triglyceride correlated with the IgM rheumatoid factor ( $R=0.343$ ,  $p=0.021$ ); and the levels of LDL-C correlated with the PWV values ( $R=0.444$ ,  $p=0.023$ ).

**Conclusions:** Metabolic factors, such as certain adipokines, PON1 and arylesterase may play a role in oxidative stress and atherosclerosis associated with RA. Anti-TNF treatment may affect adipokine levels.

**Disclosure of Interest:** None declared

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#### AB0384 RHEUMATIC ARTHRITIS PATIENTS WITH VERY HIGH CARDIOVASCULAR RISK: POOR RESULTS IN CHANGES IN LIFESTYLE DURING FOLLOW-UP

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**Background:** Rheumatoid arthritis (RA) is associated with accelerated atherosclerosis, which results in high cardiovascular morbidity and mortality. The European Atherosclerosis Society recommends a strict control of cardiovascular (CV) risk factors, focusing in a healthy lifestyle, for the prevention of future CV events.

**Objectives:** Our aim was to assess the characteristics of healthy lifestyle in patients with RA and very high risk of CV events.

**Methods:** Prospective study that included a group of 113 patients, of whom 65 presented carotid plaques on carotid ultrasound study and, due to this, were categorised as having very CV high risk at the baseline visit. At this time, patients were informed about the risks associated to their disease and the high risk of having CV events. They were even warned of the need of healthy lifestyle habits.

Data on lifestyle, smoking, obesity and diabetes mellitus were collected at baseline and last visit (with an interval of more than 5 years)

**Abstract AB0384 – Table 1.** Clinic characteristics of 65 patients with RA and very high CV risk.

CLINIC CHARACTERISTICS	LAST VISIT (n = 65)
Age (years): Mean (SD)	67 (8.7)
Sex: Women (%)	44 (68%)
Duration of RA (years): Mean (SD)	17 (7.7)
Baseline Visit- Final Visit (years): Mean (SD)	5.5 (0.95)
Dyslipidemia: Yes (%)	47 (72%)
High blood pressure: Yes (%)	40 (62%)
Diabetes Mellitus: Yes (%)	12 (18%)
Smoking: Yes (%)	17 (26%)
Obesity: Yes (%)	26 (40%)
Total Cholesterol (mg/dl): Mean (SD)	186 (42.4)
Waist circumference: Yes (%) ( $\geq 102$ cm, $\geq 88$ cm)	42 (65%)
LDL- Cholesterol (mg/dl): Mean (SD)	104 (34.6)
Atherogenic index: Mean (SD)	3.37 (0.88)
Systolic blood pressure (mmHg): Mean (SD)	136 (14.2)
Diastolic blood pressure (mmHg): Mean (SD)	80 (8.2)

**Results:** The results of the 65 patients at the last visit are shown in table 1. The average age was of 67 years, with a disease duration of 17 years and high prevalence of dyslipidemia (72%), HTA (62%) and obesity (40%).

Data obtained at the basal and last visit (with an average difference of 5.5 years) were compared in table 2. At last follow-up none of the smokers at baseline had discontinued smoking. There were no significant differences in the body mass index (BMI) average. Nevertheless, there was increase in the number of patients

with a BMI  $<30$  (36% vs 31%). Only a few patients claimed to go on any type of diet (20%), although the majority (88%) had classic CV risk factors (DM, HTA, obesity or dyslipidemia) at baseline that required adequate diet regime. Yet, more than half of the patients (62%) made regular exercise ( $>3$  times/week) and did not have a sedentary lifestyle (50%), despite having a mean age of 67 years and long disease duration at baseline. Poor control of diabetes mellitus (DM), was found in more than half of the patients.

**Abstract AB0384 – Table 2.** Variables assessed at baseline visit and last visit of 65 patients with RA and very high CV risk.

Variables	BASILINE VISIT (n = 65)	LAST VISIT (n = 65)
Smoking: Yes (%)	17 (26%)	17 (26%)
Discontinued smoking: Yes (%)	-	0
Obesity: Yes (%)	24 (37)	26 (40%)
BMI: Mean (SD)	28.2 (5)	28.6 (5.5)
BMI $> 30$ : Yes (%)	22 (36%)	19 (31%)
Diet: Yes (%)	-	12 (20%)
Exercise: Yes (%)	-	38 (62%)
Sedentariam: Yes (%)	-	30 (50%)
Diabetes Mellitus (DM): Yes (%)	6 (9%)	12 (18%)
DM. Treatment: Yes (%)	4 (67%)	6 (50%)
DM. Higher Glycosylated Hemoglobin: Yes (%)	-	7 (58%)

**Conclusions:** Despite having been informed on the high risk of CV events, patients with RA included in the category of very high CV risk performed poor long-term control of factors that include a healthy lifestyle.

**Disclosure of Interest:** None declared

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#### AB0385 COMPARATIVE ASSESSMENT OF BMD IN PRE-, POSTMENOPAUSAL WOMEN AND MAN WITH RHEUMATOID ARTHRITIS (RA)

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**Background:** RA doubles the risk of hip and vertebral fractures, regardless of the use of GCs, and disease activity is consistently associated with low BMD. But now, it is not clearly identified predictors of the individual risk of bone loss depends on sex and menopausal status patients with RA

**Objectives:** To compare BMD in man, pre- and postmenopausal women with RA

**Methods:** The study was performed on 145 patients: 117 women (mean age 45.4  $\pm$  13.0 years, mean disease duration 9.7  $\pm$  7.7 years, 41% (n=48) postmenopausal) and 28 man (mean age 46.4  $\pm$  16.9 years, mean disease duration 4.2  $\pm$  4.1 years) with RA. 91.6% have moderate/high disease activities by DAS 28. 68.4% women and 64.3% men received prednisolon  $\leq 10$  mg/day more than 3 month, 87% of patients received MTX. BMD was measured in 3 part of the skeleton: hip, lumbar spine, distal part of forearm. Female patients were divided in two groups by menopause: premenopausal (PreM) in mean age 36.9  $\pm$  9.3 years and postmenopausal (PM) in the mean age 57.6  $\pm$  5.9 years.

**Results:** BMD was decreased in 44.5% of women and 42.9% of man. BMD of hip, lumbar spine, distal part of forearm were respectively decreased in 26.1%, 26.1%, 18.8% PreM women and 66.7%, 70.8%, 79.2% PM women. 39.3% of man had decrease BMD in the hip and 42.8% – in the lumbar spine. In women the age was strong associated with BMD decrease, in man no association with age was found. In PreM women was not found association between BMD, disease duration, DAS28 and X-ray changes in hands and feet, only cortical index was correlated with BMD in all part of the skeleton. In PM women the disease duration was negatively correlated with BMD in total hip and forearm, in men – with BMD in lumbar spine and hip neck ( $p<0.01$ ). It was found association between BMD and X-ray stage by Steinbrocker in PM women and man. DAS28 was strong associated with low hip and forearm BMD in PM women and low spine BMD in men. According to dispersion analysis PM women with III-IV X-ray stages has significantly lower BMD in the hip (total:  $Z=2.16$ ,  $p=0.04$ ; neck:  $Z=2.61$ ,  $p=0.01$ ) and medium part of forearm ( $Z=2.92$ ,  $p=0.001$ ). Man had significantly lower BMD in all part of the skeleton since II X-ray stage ( $p<0.001$ ) and negative correlation between BMD and presence of erosion.

**Conclusions:** A sexual differences in BMD loss was observed in different parts of the skeleton. In man the most affected part of the skeleton was spine and BMD changes were more likely to PreM women, had high association with disease activity by DAS28 and presence of erosion, and no association with age. In PreM women only cortical index had high predictive value for decrease BMD in all parts of the skeleton. Age, disease deration, duration of menopause, DAS28 and x-ray changes in hand and feet was strong associated with decreased BMD in the hip and forearm in PM women.

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**AB0386** RELATIONSHIP BETWEEN EXTRA-ARTICULAR MANIFESTATIONS AND JOINT SURGERY IN RHEUMATOID ARTHRITIS

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**Background:** Extra-articular organ involvement is a serious condition in rheumatoid arthritis (RA) associated with increased mortality. These manifestations may affect the course of the disease, but could they accelerate the joint destruction and shorten the pre- joint surgical period?

**Objectives:** Our objective was to study the impact of extra-articular manifestations (EAM) on joint surgery during RA management.

**Methods:** It is a retrospective comparative study involving 500 RA patients (according to 1987 ACR or 2010 ACR/EULAR criteria) in rheumatology department between 2000 and 2014. The assessment of EAM was systematically done in RA diagnosis and during management. We compared 2 groups of RA patients according to the presence or not of EAM.

**Results:** We enrolled 422 women and 78 men with mean age of 53.3 years (21–83) and mean disease duration of 12 years [2–40]. RA was Rheumatoid Factor positive and erosive in 71.4% and 90% cases respectively. A surgical procedure was considered necessary in 59 cases (11.8%). An EAM was diagnosed in more than a half of patients (62.4%) with a predominance of ocular and bone manifestation, mainly xerophthalmia (173 cases, 34.6%) and osteoporosis (120 cases, 24%). Secondary Sjögren's syndrome was confirmed in 70 cases. Pulmonary manifestations related to RA were noted in 70 patients (14%), especially diffuse interstitial pulmonary in 48 cases (9.6%). Renal involvement was present in 45 patients, of which interstitial renal disease was the most common manifestation (29 patients, 64.4%). Rheumatoid nodules (4.6%) and small vessel vasculitis (0.6%) were the most frequent skin manifestations. A significantly higher incidence of joint surgery was noted in osteoporotic RA patients (OR=1.91; p=0.029). There was no significant correlation between joint surgery resort and other EAM (table 1).

**Abstract AB0386 – Table 1.** Correlation between EAM and joint surgery during RA

EAM (N)	Joint surgery (+)	Joint surgery (-)	p
Xerophthalmia	22	151	0875
Secondary Sjögren's syndrome	9	61	0633
Osteoporosis	31	89	0029
Pulmonary manifestation	3	67	0601
Renal manifestation	3	42	0257
Skin manifestation	1	25	0502

**Conclusions:** Our study concluded to a higher incidence of EAM during RA management. Osteoporosis was the only EAM associated to greater frequency of joint surgery.

**Disclosure of Interest:** None declared

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**AB0387** IS RHEUMATOID ARTHRITIS A RISK FACTOR FOR DEMENTIA ?

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**Background:** A direct link between chronic inflammation and dementia was well established by different epidemiological studies. Nevertheless, data on impaired cognitive function during rheumatoid arthritis (RA) are still controversial and doubtful.

**Objectives:** To assess the association of RA and impaired cognitive function.

**Methods:** This is a case-control study involving patients with RA according to ACR/EULAR criteria 2010 and randomly-chosen controls by matching on age and gender during 4 months. The Mini Mental State Examination (MMSE) was used to evaluate cognitive functions. Cognitive impairment was defined by a MMSE score

lower than 24 (or 26 in patients with primary education). The activity of RA was evaluated using Disease activity score (DAS28).

**Results:** A total of 20 RA patients (12 women and 8 men) with a mean age of 52.6 years [31–72] and 20 healthy controls (15 women and 5 men) with a mean age of 55.8 years [50–77] were included. No significant differences for age or gender between RA patients and controls were observed. Rheumatoid factor was positive in 95% of cases. Mean disease duration was 3.2 years [2–6]. Thirteen RA patients had active disease with mean DAS28 of 4.73. Three-quarters of RA patients had been treated with methotrexate and only 8 patients received biotherapy: 5 anti TNF alpha and 3 Rituximab. Forty percent of RA group were illiterate versus 49% in control group. Eleven RA patients (55%) had a normal cognitive function versus 15 (75%) in control group. A moderate cognitive impairment (mean MMSE of 18.62) was found in 8 RA patients (40%) and 2 controls (10%) primarily affecting constructional apraxia. No severe cognitive impairment was found in the 2 groups. Significant positive association was found between cognitive impairment and RA (p=0.001). Patients with RA using methotrexate had higher risk for cognitive impairment comparing to patients using biotherapy (p=0.02).

**Conclusions:** Our study highlighted a serious psychological expression of RA which was early onset of cognitive impairment and dementia. This is a possible effect of inflammation and vascular disease caused by RA.

**Disclosure of Interest:** None declared

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**AB0388** SLEEP DISTURBANCES IN INFLAMMATORY RHEUMATIC DISEASES

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**Background:** Inflammatory rheumatic joint diseases such as Ankylosing Spondylitis (AS) and Rheumatoid Arthritis (RA) have recently been found to be associated with sleep disturbances especially obstructive sleep apnoea.<sup>1,2</sup>

**Objectives:** The aim of our study was to evaluate the occurrence of sleep disturbances, especially REM Sleep Behaviour Disorder (RBD), in inflammatory rheumatic diseases, (rheumatoid arthritis -RA and Spondyloarthritis -SpA).

**Methods:** We enrolled 103 consecutive patients affected by inflammatory rheumatic diseases [RA (64, 62.1%) or SpA (39, 37.9%)]. Patients underwent a neurologic and psychopathological assessment, including identification of sleep disorders by means of the Pittsburgh Sleep Quality Index (PSQI), the Berlin and the REM sleep behaviour disorder (RBD) questionnaires, a structured interview on sleep terrors and sleep paralysis, Beck Depression Inventory (BDI-II) and the Spielberger State-Trait Anxiety Inventory (STAI). Statistical analysis was performed utilising SPSS software.

**Results:** No significant differences were found between RA and SpA patients in age at diagnosis, disease duration, smoke habit, alcohol consumption, anamnestic comorbidities (especially metabolic diseases, anxiety or depression), disease activity/remission and biologic Disease Modifying Antirheumatic Drugs use. No differences demonstrated in BDI-II, STAI, PSQI and RBD questionnaires; only the Berlin Questionnaire showed significant differences (17.2% in RA vs 35.9% in SpA, p=0.036). No differences in sleep paralysis (10.9% in RA vs 7.7% in SpA, p=0.74) and sleep terrors (37.5% in RA vs 20.5% in SpA, p=0.0826) which were found to be increased if compared with general population (2.6%).

**Conclusions:** Our data show an increased prevalence of sleep terrors in rheumatic patients when compared to the general population although no differences were highlighted between RA and SpA; also increased risk of sleep apnoea (Berlin Questionnaire) has been demonstrated in patients with SpA compared with RA.

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**Disclosure of Interest:** None declared

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**AB0389 HIPERTRIGLYCERIDEMIC-WAIST PHENOTYPE: A MARKER OF CARDIOVASCULAR RISK IN RHEUMATOID ARTHRITIS PATIENTS**

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**Background:** The risk of cardiovascular disease (CVD) is increased in rheumatoid arthritis (RA); about 50% of associated deaths in rheumatoid arthritis (RA) are attributed to CVD.<sup>1</sup> Both traditional cardiovascular risk (CVR) factors and inflammation contribute to this risk. The hyperuricemia (HUC) and metabolic syndrome (MetS) are considered parameters of CVR, both closely related,<sup>2</sup> and recently the hypertriglyceridemic-waist (HTGW) phenotype has been defined as well a marker to identify HUC in the general population.<sup>3</sup>

**Objectives:** To determine the prevalence of HTGW phenotype and to evaluate its association with CVR parameters among RA patients.

**Methods:** HTGW phenotype was defined as waist girth  $\geq 102$  cm in male and  $\geq 88$  cm in female and TG  $> 150$  mg/dl in 250 patients diagnosed with RA according to the ACR/EULAR 2010 criteria. The levels of uric acid  $> 5.5$  mg/dL defined HUC. The MetS and its individual components (NCEP-ATPIII) were evaluated as parameters of CV risk.

**Results:** We identified 51 AR patients (20.4%) with HTGW phenotype. Adjusting for covariates in a logistic regression model, it was observed that the HTGW phenotype is associated with the presence of HUC (OR=6.14,  $p < 0.001$ ), and MetS (OR=5.7, IC95%, 2.7–12.2,  $p < 0.001$ ).

**Conclusions:** HTGW is prevalent in RA patients from southern Mexico. The HTGW phenotype can be considered at low cost marker, used as a tool screening to predict high metabolic risk during the clinical course of the rheumatic disease.

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**AB0390 RELATIONSHIP BETWEEN BODY MASS INDEX AND PERSONALITY IN AN EARLY ARTHRITIS COHORT OF PATIENTS**

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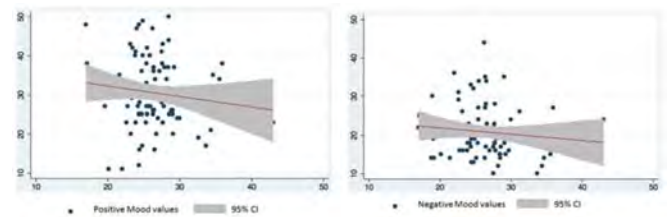
**Background:** According to previously reported data from our early arthritis registry (PEARL, Princess Early Arthritis Register Longitudinal), patients with a higher BMI have higher scores in pain and disability scales. We also described some years ago that, in the same population, the structure of personality explored with the PANAS questionnaire (Positive and Negative Affect Scale) affects some outcomes in arthritis measures. Specifically, higher scores on the negative affect subscale associate higher scores in pain and disability scales.

**Objectives:** To analyse the relationship between BMI and the structure of the affect in the PEARL cohort.

**Methods:** PEARL registry includes patients with early arthritis (less than one year of duration), in whom, sociodemographic, disease related and treatment data are recorded in five protocolised visits. We analysed data from those patients in which the PANAS questionnaire data were available and whose classification, after 2 years of follow-up, were rheumatoid arthritis -according to the 1987 ACR classification criteria – or undifferentiated arthritis. The structure of the affect was evaluated with the PANAS questionnaire administered in one single occasion. This questionnaire is used to evaluate the components of positive (PA) and negative affect (NA). It consists of 20 questions and the score obtained from its administration ranges between 10 and 50 points for each affect. The WHO definition was used for low weight, normal weight, overweight and obesity (BMI  $< 18.5$ , 18.5–25, 25–30 or  $\geq 30$  kg/m<sup>2</sup> respectively). The statistical analysis were performed with

ANOVA and Pearson's correlation tests, as well as multivariate linear regression (including as independent variables sex, age and study level) using the Stata 12.1 software.

**Results:** We analysed the data of the 71 patients for whom PA values were available and of the 65 patients with NA values available. There was not a statistically significant relationship observed between PA and NA and BMI when analysed as a continuous variable ( $R = -0.12$ ,  $p = 0.25$  and  $R = -0.1$ ,  $p = 0.36$ , respectively) or as a categorical variable. However, there was a non-significant trend to lower scores for both PA and NA in patients with a higher BMI (figure 1). The multivariate analyses, adjusted for sex, age and study level, also showed no statistically significant relationship between the BMI (analysed as continuous or categorical variable) and the PA and NA; but there was also a non-significant trend that sets a relationship between lower scores of both PA and NA and higher BMI values.



**Abstract AB0390 – Figure 1**

**Conclusions:** In our early arthritis registry there is no relationship between the BMI and the structure of the affect evaluated through the PANAS questionnaire. However, it is necessary to evaluate this relationship in a greater number of patients and in different populations before discarding this relationship definitely.

**Disclosure of Interest:** None declared

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**AB0391 CLINICAL, SEROLOGICAL AND TREATMENT ANALYSIS OF RHUPUS SYNDROME: A RETROSPECTIVE MONOCENTRIC STUDY**

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**Background:** Rhupus syndrome is a rare condition in which rheumatoid arthritis (RA) features overlap with systemic lupus erythematosus (SLE) manifestations. Disease characterisation tends to improve, but some uncertainties remain, and therapeutic management has still to be defined.

**Objectives:** We aimed to perform a study of the patients followed at the Rouen University Hospital with rhupus diagnosis using both recent criteria and expert diagnosis, in order to perform an analysis of the clinical, radiological and biological characteristics, and to report the therapeutic procedures carried out.

**Methods:** We performed a retrospective research work covering a period of 10 years, using diagnosis code extraction for both RA and SLE from database of the medical information department, as well as biological data extraction concerning ACPA testing, anti-dsDNA and anti-RNP antibodies. Patients satisfying both ACR/EULAR 2010 and SLICC 2012 classification criteria for RA and SLE respectively, or with an expert diagnosis of rhupus were included. A screening of medical records was performed to collect clinical, biological and treatment data for each patient.

**Results:** Sixteen patients were identified and 12 fulfilled both classification criteria. RA most often preceded rhupus, and clinical analysis found a predominant articular pattern at initial and established disease, with erosive arthropathy ( $n = 11$ ). Skin involvement was the most frequent associated manifestation ( $n = 12$ ). Among other associated manifestations, serious events were reported, including active glomerulonephritis ( $n = 2$ ), ischaemic stroke ( $n = 1$ ) and myocardial infarction ( $n = 1$ ). Immunological profiles showed positivity for ( $n = 14$ ), anti-dsDNA ( $n = 9$ ) and ACPA ( $n = 9$ ). Ten patients required biological DMARD, in addition to conventional treatment. All types of RA approved bDMARD were used. Rituximab was the most prescribed ( $n = 9$ ) and the most effective, with sustained response in 5 patients.

**Conclusions:** Rhupus is a rare condition, with predominant articular pattern, but serious SLE-related manifestations can occur. In rhupus refractory to conventional treatment, biologics, and particularly rituximab, are a promising therapeutic approach.

**Disclosure of Interest:** None declared

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### AB0392 RHEUMATOID ARTHRITIS AND RISK OF INCIDENT CHRONIC KIDNEY DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS OF COHORT STUDIES

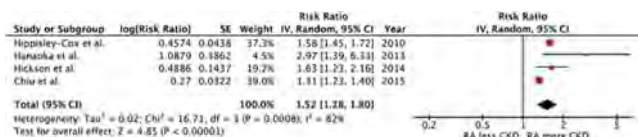
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**Background:** Patients with rheumatoid arthritis (RA) may have a higher risk of developing chronic kidney disease (CKD) compared with general population. However, the data on this risk are limited and not well-characterised.

**Objectives:** This systematic review and meta-analysis aimed to comprehensively investigate the risk of incident CKD among patients with RA by reviewing all available studies.

**Methods:** A systematic review was performed using MEDLINE and EMBASE database from inception to December 2017 to identify all cohort studies (either retrospective or prospective) that compared the risk of incident CKD in patients with RA versus individuals without RA. Adjusted point estimates were extracted from individual studies and the pooled risk ratio and 95% confidence interval (CI) were calculated using random-effect, generic inverse-variance method of DerSimonian and Laird. Visualisation of funnel plot was used for evaluation for publication bias.

**Results:** A total of 4 retrospective cohort studies with 1,627,981 participants were included. The risk of incident CKD was significantly increased among patients with RA with the pooled risk ratio of 1.52 (95% CI, 1.28–1.80). The statistical heterogeneity of this study was high with an  $I^2$  of 82%. The forest plot of this systematic review and meta-analysis is shown as figure 1. The funnel plot was relatively symmetric and, thus, did not suggest the presence of publication bias in favour of positive studies.



**Abstract AB0392 – Figure 1.** Forest plot of the meta-analysis on the risk of CKD among patients with RA

Abbreviation: SE, standard error; IV, inverse variance; CI, confidence interval, RA, rheumatoid arthritis; CKD, chronic kidney disease

**Disclosure of Interest:** None declared

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### AB0393 ELECTROCARDIOGRAPHIC DISTURBANCES IN PATIENTS WITH RHEUMATOID ARTHRITIS USING ANTIMALARIAL DRUGS

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**Background:** Cardiac involvement is present in 7% to 35% of patients with rheumatoid arthritis (RA). Anecdotal case series have associated the use of antimalarial drugs with the presence of electrocardiographic disturbances in patients with RA

**Objectives:** To assess whether the use of antimalarial drugs is associated with the presence of electrocardiographic abnormalities in RA patients. The main clinical associations were also evaluated

**Methods:** A single-centre, case-control (1:1 proportion) medical chart review study was performed. A total of 144 patients with RA (ACR/EULAR 2010 criteria) were studied, and grouped as follows: 72 with a history of antimalarial drug use (case) and 72 who never used antimalarial drugs (control). We excluded individuals with a history of ischaemic heart disease or an already diagnosed disturbance of the cardiac rhythm/conduction.

**Results:** A total of 37 cases of electrocardiographic disturbances were found in patients receiving antimalarials (51%), but only 18 cases (25%) in the control group ( $p=0.001$ ), giving an odds ratio (OR) of 3.17 (95% CI, 1.57 to 6.42).

Rhythm disturbances observed in the antimalarial group were: left anterior branch hemiblock ( $n=12$ , 32.4%), right branch block ( $n=10$ ; 27.02%), 1st degree AV block ( $n=5$ ; 13.5%), bifascicular block ( $n=4$ ; 10.8%), posterior hemiblock of the left branch ( $n=3$ ; 8.1%), incomplete left bundle branch block ( $n=2$ , 5.4%), and left bundle branch block ( $n=1$ , 2.7%). Right bundle branch block was the only statistically significant conduction disorder (27.02% vs 5.5% with  $p$  value of 0.004 [OR 11.45 1.43–92]).

The average dose of hydroxychloroquine was  $3.02 \pm 0.41$  mg/kg, while the dose of chloroquine was  $2.23 \pm 0.13$  mg/kg. A history of prednisone consumption also was associated with an increased risk to present an electrical cardiac disturbance ( $p=0.005$ ; OR 9.73, from 2.00 to 47.32).

#### Abstract AB0393 – Table 1

Outcomes	Antimalarial (n=72)	No Antimalarial (n=72)	p	OR (IC 95%)
Cardiac conduction electrocardiographic abnormalities	37	18	<b>0.001</b>	3.17 (1.57–6.42)
1st Degree AV Blocking	5	1	0.095	5.3 (0.6–46.54)
Left Branch Block	1	5	0.095	0.19 (0.02–1.66)
Right Branch Block	10	1	<b>0.004</b>	11.45 (1.43–92)
IBRB	0	1	0.315	-
IBLB	2	1	0.559	2.03 (0.18–22.88)
AHLB	12	5	0.070	2.68 (0.89–8.05)
PHLB	3	0	0.080	-
Bifascicular block	4	4	1.000	1 (0.24–4.16)

**Conclusions:** In this study, the use of antimalarial drugs was associated with an increased risk to present disturbances of the cardiac rhythm/conduction in patients with established RA.

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**Disclosure of Interest:** None declared

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### AB0394 OBSERVATIONAL STUDY OF THE INCIDENCE OF CARDIOVASCULAR EVENTS AND ASSOCIATED COMORBIDITIES IN A COHORT OF PATIENTS WITH RECENT ONSET RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is a systemic autoimmune disease whose main characteristic is persistent joint inflammation that results in joint damage and loss of function. and can involve other tissues and organs (extra-articular manifestations).<sup>1, 2</sup> RA is associated with a high risk of morbidity and premature death secondary to the earlier development of cardiovascular, lung diseases and malignancy, being cardiovascular disease secondary to accelerated atherosclerosis the main cause of morbidity and mortality in these patients.<sup>3, 4</sup>

**Objectives:** Main objective: To calculate the incidence of comorbidities and CV events in patients with recent onset RA. Secondary objectives: -To determine the clinical disease features according to baseline RA profile. To analyse the relationship between CV event and the different variables. To describe classic CV risk factors evolution throughout the follow-up.

**Methods:** We conducted a retrospective longitudinal observational study of 70 patients with recent onset RA according to ACR/EULAR 2010 or ACR 1987 criteria, at 5 years of follow-up. A descriptive study of the variables was carried out. For the bivariate analysis, the Chi-square test was used for the qualitative variables and the Mann Whitney U test for the independent quantitative ones. For the paired data, the McNemar test was used for the qualitative variables and T Student for the quantitative ones. A logistic regression model was used to associate the main variable with the rest of the variables. Finally, the analysis of survival and regression of COX was carried out. All the contrasts were bilateral and were considered significant when  $p < 0.05$ . The statistical analysis was performed using SPSSV17.

**Results:** The incidence of CV event was 18.57% (31% acute myocardial infarction). During follow-up, an improvement in inflammatory and quality of life

parameters (DAS28, ESR, CRP and HAQ) was observed ( $p < 0.05$ ). Likewise, the % of hypertensive and dyslipidemic patients increased during follow up ( $p < 0.05$ ), while the levels of cholesterol, triglycerides, glucose and diabetic patients remained similar. The presence of CV event was related to high levels of ESR, male sex and hypertension, ( $p < 0.05$ ).

#### Conclusions:

- The incidence of cardiovascular event in our recent onset RA cohort resembles that previously described in the literature, with the majority occurring during the first 5 years of follow-up.
- The development of hypertension and dyslipidemia occurs mainly during the first 5 years of follow-up.
- The presence of a cardiovascular event was related to male sex, high blood pressure and high ESR levels.

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#### AB0395 CORRELATION BETWEEN CARDIOVASCULAR RISK CALCULATORS IN A COHORT OF PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** EULAR recommends for patients with rheumatoid arthritis (RA) a cardiovascular (CV) risk assessment at least once every five years. Several risk calculators are available but most of them are based on data from general population, so they may underestimate the risk of RA patients. To obtain a more accurate estimation they should be adapted for RA by a 1.5 multiplication factor, unless the instrument includes RA as a variable. To date, there are no studies analysing the concordance and correlation between different CV risk calculators in Spanish population.

**Objectives:** To analyse concordance and correlation of CV risk calculated using different tools and to determine the proportion of CV risk factors in a cohort of patients with RA.

**Methods:** We performed a cross-sectional study including patients with RA according to ACR/EULAR 2010 criteria, treated in a tertiary hospital. Individuals with previous CV events, diabetes and chronic kidney disease were excluded.

Ten-year CV risk was obtained with the following calculators: Framingham-body mass index (FRS-BMI), Framingham-lipids (FRS-L), SCORE CV risk calculator (SCORE) and the Expanded CV Risk Prediction Score for RA (ERS-RA). A 1.5 multiplying factor was used to adapt the results for RA patients in those which didn't include it in their models. CV risk was categorised as low or high using 10% as a cut-off for FRS-BMI and FRS-L and 5% for SCORE y ERS-RA. Correlation was evaluated using Spearman correlation coefficient (Rho) and concordance with weighted kappa.

**Results:** We included 88 patients (18 male), 87.5% Caucasian, mean age 56.9  $\pm$  10.6 years, mean disease duration 5.8  $\pm$  3.3 years. 67% and 76% had positive RF and ACPA respectively and 15% presented extra-articular manifestations (rheumatoid nodules, interstitial lung disease, pleuropericarditis). Regarding CV risk factors: 14.8% were active smokers, 60.2% were overweight or obese, 25% had hypertension, 47.8% had dyslipidemia.

The median CV risk predicted at 10 years was 15% (1.5–70.20) for FRS-IMC, 11.8% (1.2–54.0) for FRS-L, 1.5% (1.1–16.5) for SCORE and 6% (0.6–27.8) for ERS-AR. 64 patients were categorised as low risk and 22 as high risk for ERS-AR. No significant differences were observed in the means of risk obtained by the different calculators or in the risk categories according to ERS-RA when stratified by disease duration (more or less than 5 years).

For the correlation between ERS-RA and FRS-BMI, FRS-L and SCORE, Spearman's Rho coefficients were 0.84, 0.79 and 0.80. ( $p < 0.005$ ).

For the concordance between ERS-RA vs FRS-BMI a weighted  $\kappa = 0.29$  ( $CI_{95\%}$ : 0.15–0.42) was obtained. For ERS-AR vs FRS-L,  $\kappa = 0.34$  ( $CI_{95\%}$ : 0.19–0.50) and for ERS-AR vs SCORE,  $\kappa = 0.70$  ( $CI_{95\%}$ : 0.52–0.87).

**Conclusions:** A strong correlation was observed between the CV risk calculators evaluated and good agreement only between ERS-AR and SCORE. Additionally, overweight, obesity and dyslipidemia were the most prevalent comorbidities.

**Disclosure of Interest:** None declared

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#### AB0396 RELATIONSHIP BETWEEN PATIENT GLOBAL ASSESSMENT AND PAIN ASSESSMENT IN THE DISEASE ACTIVITY INDEXES IN RHEUMATOID ARTHRITIS, AND ITS CORRESPONDENCE WITH SONOGRAPHIC ALTERATIONS

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**Background:** Disease activity indexes in rheumatoid arthritis (RA) provide information of different parameters in a single value. It is very useful in the evaluation of the disease activity and its progression. The subjective component of these indexes can modify the index final value.

**Objectives:** The aim of our study was to describe the relation between the patient global assessment (PGA) and pain assessment (PA) with the sonographic alterations in AR.

**Methods:** Transversal study describing the ultrasonographic changes and disease activity indexes in AR. We included patients with RA according to ACR/EULAR classification criteria. They were sent by their usual clinician, in random selection. They were reviewed in the same day by a rheumatologist and blind sonographer. PGA, PA, HAQ, tender and swollen joint count, CDAI, SDAI and DAS28 were evaluated. The ultrasound were realized by grey scale and doppler in 12 joints (wrists, second to fifth MCF and fifth bilateral MTF).

**Results:** A total of 48 patients had PGA  $< 50$  and 37 PGA  $\geq 50$ . The mean age was 53.2  $\pm$  11.7 for group 1 and 56.5  $\pm$  10.2 for group 2, women 64.6% and 83.8% respectively. The positive rheumatoid factor resulted in 72.9% vs 73%. The evolution of the disease in months presented a median of 96 (47.2–132.7) vs 108 [48–138],  $p = 0.564$ . The Body Mass Index in the groups was 26.6 (23.5–29.7) and 26.0 (22.8–30.0),  $p = 0.647$ , and the tobacco consumption of 11 patients group 1 and 12 in group 2 ( $p = 0.397$ ). No significant difference was found in the treatment at the time of the evaluation with methotrexate, median of 10 (0–15) vs 7.5 (0–15),  $p = 0.350$ , or corticosteroids 1.4 (0–2.3) vs 2.5 (0–4.5),  $p = 0.05$ . 23 patients in the group 1 and 19 in the group 2 were in biological therapy. The results referring to the patient's assessment of their disease, acute-phase reactants, clinical examination, ultrasound and disease activity indexes are presented in table 1.

**Abstract AB0396 – Table 1**

	Group 1 (PGA<50)	Group 2 (PGA>50)	P value
ESR: median (p25-p75)	9 (4,2–17)	8 (4,5–16)	0578
CRP: median (p25-p75)	2,4 (1,02–4,7)	5 (1–5,7)	0996
DAS 28 (CRP)	2,1 $\pm$ 0,97	3,37 $\pm$ 1,19	0000
DAS 28 (ESR)	2,6 $\pm$ 0,72	3,25 $\pm$ 0,92	0000
Pain assessment, 100 mm VAS: median (p25-p75)	20 (0–40)	70 (50–80)	0000
HAQ: average $\pm$ DE	0,8 $\pm$ 0,14	2,27 $\pm$ 0,18	0000
Tender joint count: median (p25-p75)	0 (0–2)	2 (0–3)	0001
Swollen joint count: median (p25-p75)	0 (0–1)	1 (0–3)	0090
CDAI: median (p25–75)	5 (1–8,8)	13 (9,4–17,4)	0000
SDAI: average $\pm$ DE	8,69 $\pm$ 5,82	17,67 $\pm$ 6,49	0000
Synovitis in grey scale: median (p25-p75)	1 (0–3)	2 (0–4)	0159
Synovitis in doppler: median (p25-p75)	0 (0–1)	1 (0–2,7)	0231

**Conclusions:** Disease activity indexes in AR have been established as a very useful measure, both in the homogenization of the results obtained in the research and in the daily clinical practice. In our study, we observed the modification in the values of disease activity indexes due to PGA and PA, even those in which its contribution is less decisive than other parameters, as it happens in the DAS 28.

Those variables no related in their value with the patient assessment of his disease status did not show statistical significance between the groups. The patients' valuation about activity of their AR and the modification of the indexes in which it participates in our study were not concordant with the echographic alterations found in grey scale and doppler echo.

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AB0397

### PREVALENCE AND FACTORS ASSOCIATED WITH DEPRESSION AMONG PATIENTS AFFECTED BY CHRONIC INFLAMMATORY ARTHRITIS: PRELIMINARY RESULTS OF A SINGLE-CENTRE EXPERIENCE IN ITALY

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**Background:** Depression and anxiety disorders are more common in chronic inflammatory arthritides (CIA) than in the general population.<sup>1</sup> In rheumatoid arthritis (RA), depressive and anxiety symptoms have been associated with disease activity and pain perception,<sup>1</sup> physical disability,<sup>2</sup> health care costs,<sup>3</sup> and mortality.<sup>4</sup> To our knowledge, data on the prevalence of depression in Italian patients with RA are scarce.

**Objectives:** To estimate the prevalence and factors associated with depression among patients affected by RA.

**Methods:** During an one year period, patients affected by RA have been consecutively enrolled. For each patient demographics and disease characteristics were recorded; the Hospital Anxiety and Depression Scale (HADS) was administered. HADS is a validate questionnaire to assess depressive and anxiety symptoms in patients affected by somatic disorders admitted to general hospital. An HADS  $\geq 11$  was considered diagnostic for depression.

**Results:** The table summarises the main results. We recruited 231 patients affected by RA, finding a prevalence of depression of 13.9% (95% CI 9.4%–18.3%). Overall, patients with depression, when compared with patients without, were older, more frequently females, with a lower education, higher physician global assessment and patient global assessment, more comorbidities. In particular, they had any cardiovascular, neurologic or musculoskeletal issue ( $p=0.018$ ,  $p=0.032$ ,  $p=0.014$ , respectively) and more often used glucocorticoids or NSAIDs. Conversely, no association was found between depressive symptoms and the use of biologic therapies or the presence of inflammatory markers. Interestingly, a positive history of depression was present only in few patients with an HADS  $\geq 11$ .

Abstract AB0397 – Table 1

	Non-depressed (n=199)	Depressed (n=32)	P value
Age, years	57.5 (12.3)	63.5 (11)	0.008
Female sex	152 (76)	29 (91)	0.049
Employed	86 (43)	5 (16)	0.002
Higher education	89 (45)	8 (25)	0.036
Disease duration, years	12 (9.2)	14.2 (8.3)	0.202
Erosive disease	72 (36)	12 (38)	0.516
TJC 0–28	1.9 (3.4)	2.3 (2.6)	0.500
SJC 0–28	0.9 (2.2)	1.1 (2.0)	0.688
PhGA 0–10	3.9 (2.7)	5.6 (2.4)	0.001
PGA 0–10	4.9 (2.4)	6.8 (2.0)	<0.001
ESR, mm/h	19.2 (16.1)	22.2 (13.5)	0.326
CRP, mg/L	6.4 (14)	4.4 (3.8)	0.425
Comorbidities	176 (88)	32 (100)	0.027
csDMARD	136 (68)	18 (56)	0.127
bDMARD	129 (65)	24 (75)	0.177
Glucocorticoid	87 (44)	20 (63)	0.037
NSAID	32 (16)	12 (38)	0.007
Antidepressant	18 (9)	11 (34)	<0.001

**Conclusions:** These preliminary results suggest that more than one every seven patients with RA could suffer from depression, thus depression might be undiagnosed in a significant number of patients. Comorbidities, anti-inflammatory medications and both physician- and patient- driven evaluation of disease burden were the most striking factors associated with depression in this cohort of patients with RA.

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**Disclosure of Interest:** None declared

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AB0398

### INVESTIGATION OF PREOPERATIVE INTRANASAL COLONISATION IN ORTHOPAEDIC SURGERY FOR PATIENT WITH RHEUMATOID ARTHRITIS

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**Objectives:** Coagulase-negative staphylococci (CoNS) is listed as the major SSI causative organism in the field of orthopaedic surgery, but detailed report on the presence or absence of methicillin-resistant CoNS of intranasal colonisation is not found.

**Methods:** In 13 months from July 2016 to the end of July 2017, 1000 cases of consecutive cases in which nasal cavity culture was performed within one month prior to hospitalisation for patients scheduled for our orthopaedic surgery. 223 men, 777 women, average age 66.4 years old, 197 cases of RA patients, 803 cases except RA patients.

The method of intranasal culture is as follows. After culturing for 18 hours at 35 °C using blood agar medium (daily water) and CHROMager MRSA selective medium (Kanto Kagaku), identification of bacterial species of the genus *Staphylococcus* grown and cultivation of drug susceptibility tests It was carried out by BD Phoenix according to the method of the Association (CLSI).

**Results:** The results of intranasal culture showed that *S. aureus*, *S. epidermidis*, CoNS (excluding *S. Epidermidis*) and culture negative were 18.2%, 27.8%, 7.8%, and 23.9%, respectively. MRSA, MRSE and MRCoNS (excluding MRSE) with methicillin resistance were 3.2%, 22.1% and 1.7%, respectively, and 27.0% of methicillin resistant bacteria were found to exist.

Especially in patients with RA, the methicillin-resistant bacterial colonisation rate was significantly higher ( $p<0.05$ ) than 38.6% compared with 24.2% other than RA patients.

**Conclusions:** Methicillin-resistant *Staphylococcus* was found to be 27.0% intranasal colonisation of patients in orthopaedic surgery. Especially in RA patient, it was high rate of 38.6%. In the future, we need to consider the selection of perioperative preventive antibacterial drugs.

**Disclosure of Interest:** None declared

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AB0399

### AUDIT OF INFLUENZA AND PNEUMOCOCCAL VACCINATIONS IN A COHORT OF RHEUMATOID ARTHRITIS PATIENTS ON BIOLOGICS

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**Background:** Rheumatoid arthritis (RA) patients are at increased risk of pneumococcal and influenza disease secondary to a deficient immune system and immunosuppressive medications.<sup>1</sup> Despite the possible reduction in vaccine efficacy in RA, prophylactic vaccination for preventing pneumococcal pneumonia and influenza in RA patients should be routinely advised and practised.<sup>2</sup> EULAR guidelines recommend that influenza and pneumococcal vaccinations should be strongly considered for all patients with RA.<sup>3</sup>

**Objectives:** To study pneumococcal and influenza vaccination rates in a cohort of RA patients on biologic medications.

**Methods:** We undertook a prospective audit of RA patients on biologics attending routine rheumatology clinics in a DGH over a 6 week period. A proforma was given to patients, and data was collected on medications, comorbidities, Disease Activity Score (DAS) and vaccination status for influenza and pneumococcus.

**Results:** Of the 25 patients audited, 17 (68%) were female and 8 (32%) were male. The average age of patients included was 59 years (range 37–75). 18 (72%) patients were seropositive, and 7 (28%) were seronegative. The patients included had the following comorbidities; 14 (56%) none, 6 (24%) thyroid disease, 1 (4%) osteoporosis, 1 (4%) hypertension, 1 (4%) type 2 diabetes, 1 (4%) interstitial lung disease.

On reviewing their medications, 7 (28%) patients were on an Etanercept biosimilar (Benpali), 2 (8%) on Tocilizumab, 2 (8%) on Rituximab, 9 (36%) on Adalimumab, 2 (8%) on an Infliximab biosimilar (Remsima), 2 (8%) on Etanercept, and 1 (4%) on Certolizumab. In addition to their biologic agent, all 25 patients were on Methotrexate. 2 patients (8%) were also on Sulphasalazine, and 2 (8%) were on Hydroxychloroquine additionally. The average DAS CRP score was 2.7.

8 (32%) patients had received both influenza and pneumococcal vaccinations, and 9 (36%) patients had neither. On analysing the vaccination rates individually, 16 (64%) patients were up to date with influenza and 7 (28%) were up to date with pneumococcal. Of the 9 patients that had neither vaccination, 5 (20%) patients were unaware of their requirement, and 3 (12%) felt they were too unwell to receive them. 1 (4%) patient was unsure whether they could have the vaccinations as they had been recruited into a research trial.

**Conclusions:** Only 32% patients had received both influenza and pneumococcal vaccinations. The uptake rate for influenza vaccination was reasonable at 64%, however the rate for pneumococcal vaccination was only 28%. Vaccination assessment should be performed routinely for all RA patients in clinic, and in particular those on biologic medications to reduce the risk of developing these infections in this high risk cohort.

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#### AB0400 HIGH PREVALENCE OF COMORBIDITIES IN PATIENTS WITH RHEUMATOID ARTHRITIS IN SOUTH AFRICA

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**Background:** Patients with rheumatoid arthritis (RA) are at increased risk to develop comorbidities. Data on the prevalence of comorbidities in RA patients in South-Africa is lacking.<sup>1</sup> Poorly controlled joint inflammation, common use of glucocorticosteroids and nonsteroidal anti-inflammatory drugs, a high prevalence of smoking and obesity, together with a high burden of infectious diseases may be important risk factors for comorbidities in this population.

**Objectives:** To assess the prevalence of comorbidities in RA patients in Cape Town, South-Africa and the association with disease activity and DMARD use using the METEOR (Measurement of Efficacy of Treatment in the 'Era of Outcome' in Rheumatology) database.

**Methods:** This is an ongoing cross-sectional study. Data from 109 RA patients from regular clinic visits at Groote Schuur Hospital in Cape Town, South Africa have been entered in the Meteor database (from December 2016). The Meteor database is a free online tool that was developed to improve the management of RA patients by helping rheumatologists to register, monitor and tightly control disease activity. The tool is currently widely used in other countries, but has it has not yet been described in any African countries. Information on the following parameters were reported: demographics, disease duration, disease activity (CDAI), current DMARDs used and comorbidities.

**Results:** The mean age (SD) was 57.6 (14.7) years, disease duration (SD) 14.1 (14.6) years, female gender 86.7%, RF positive 85.1% and ACPA positive 80.4%. The average (SD) CDAI was 13.1 (9.8) and 49.3% were smokers. Current DMARDs used was Methotrexate (72%), Sulphasalazine (29%), Chloroquine (67%), Low dose corticosteroids (47%), Leflunomide (11%), Etancept (1%), but no other biological agents (0%). At least one comorbidity was present in 69% of the patients, two in 40%, three in 26%, four in 13% and five in 2% of the patients. The most frequently observed comorbid diseases were hypertension (45.5%), tuberculosis (TB) (11.1%), Diabetes Mellitus Type 2 (10.9%) and osteoarthritis (10.9%). Other diseases included hypercholesterolemia (7.1%), gastro-oesophageal reflux disease/peptic ulcer (6.1%), COPD/emphysema (6.1%), HIV (4.0%), hypothyroidism (4.0%), ischaemic heart disease (3.0%), liver disease (3.0%), DVT/pulmonary embolism (3.0%), malignancies (3.0%), asthma (2.0%), discoid lupus erythematosus (2.0%), interstitial lung disease (1.0%), anaemia (1.0%), rheumatic heart disease (1.0%), cerebrovascular accident (1.0%) and depression (1.0%).

**Conclusions:** This study shows a high prevalence of comorbidities among indigent patients with RA in South Africa. In particular, hypertension, TB and osteoarthritis were very common. More patients will be included in this study in the next few months. Furthermore, we will assess the association between comorbidities, disease activity and DMARD use. The METEOR tool offers the unique opportunity to study daily practice care as well as research questions in real life setting in a South African clinic. This study will provide information that is necessary to address the burden of comorbidities in patients with RA in South Africa.

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#### AB0401 ECHO-CARDIOGRAPHIC ABNORMALITIES IN RHEUMATOID ARTHRITIS PATIENTS COMPARED TO AGE AND SEX-MATCHED CONTROLS

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**Background:** Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease of the joints with several extra-articular features. Cardiovascular disease (CVD) mortality accounts for 40%–50% of all deaths in RA. Apart from atherosclerotic heart disease other cardiac abnormalities had been found to be prevalent in RA; including, pericarditis, heart failure, coronary vasculitis and valve disease.

**Objectives:** Due to scarcity of data regarding cardiac disease in the Middle East population, we studied echocardiographic features in RA patients compared to their age, sex, and traditional CVD risk factors matched controls.

**Methods:** In a cross-sectional study, we recruited 39 RA patients meeting the 1987 revised criteria of RA and 37 age, sex and traditional CVD risk factors matched controls. Standard trans-thoracic echocardiography examination was carried out by a specialties cardio-sonographer who was blinded to the status of the participants. Left ventricular dimensions, wall geometry, ejection fraction, diastolic parameters, right ventricular size and function, valve structure and function, pericardium, pulmonary pressures and aortic root dimensions were assessed by echocardiography. t-test and chi-2 test were used to compare the echocardiographic findings between the two groups. P value of <0.05 was considered significant.

**Results:** Thirty-nine RA patients (34 F, 4 M) and 37 controls (32 F, 5 M) were studied. Among RA, 27 (69%) were RF positive. The two groups were similar in terms of age (p=0.86), gender (p=0.71), and traditional cardiovascular risk factors. No significant difference was found between RA and the controls in term of left ventricular ejection fraction, wall geometry, diastolic parameters, right ventricular size and function, valve disease, pulmonary pressures, pericardium and aortic root dimensions. However, left ventricular end-diastolic diameter (43.11±1.14 vs. 39.35±0.84 mm respectively, p=0.01), end-systolic diameter (24.39±0.70 mm vs. 26.96±0.96, respectively, p=0.03) and Left ventricular mass index (79.83±5.11 vs. 63.64±3.15, respectively, p=0.01) were significantly higher in RA patients than in the controls.

**Conclusions:** Patients with rheumatoid arthritis have higher left ventricular end-diastolic and end-systolic dimensions, and greater left ventricular mass index compared to their age, sex and traditional CVD risk factors-matched controls. As the increase in the left ventricular mass index is a predictor of cardiac sudden death, echocardiography might be a simple non-invasive tool for cardiac risk screening in RA.

**Disclosure of Interest:** None declared

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#### AB0402 RECENT ONSET RHEUMATOID ARTHRITIS HAVE AND INCREASED LEFT ANTERIOR DESCENDING CORONARY ARTERY WALL THICKNESS: EVIDENCE OF SUBCLINICAL CORONARY ARTERY DISEASE

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**Background:** Rheumatoid arthritis (RA) is associated with increased cardiovascular disease (CVD). Using different methods, presence of sub-clinical atherosclerosis changes have been reported in RA. As no previous study has measured left anterior descending (LAD) coronary artery thickness in RA

**Objectives:** this study aimed to investigate atherosclerotic changes of coronary artery in early RA of 12 months of symptom onset.

**Methods:** 15 RA patients and 20 control subjects who matched 10 RA participants were included in the study. Demographic details, RA characteristics, and laboratory values of 15 RA patients at first presentation. None of the patients or the control participants had previous CVD/cerebrovascular events or diabetes and matched 10 of the RA group for age and sex. LAD coronary artery wall thickness compared between RA and their matched control. Among early RA patients, Correlation was assessed between LAD coronary artery wall thickness and the demographic features, RA activity features, and cardiovascular risk factors.

**Results:** Within early RA, LAD coronary artery wall thickness was related to Disease Activity Score (p=0.025,  $\beta$ -coefficient 0.066, CI:0.010–0.122) and to the patient global assessment of disease activity at RA onset (p=0.006,  $\beta$ -coefficient 0.003, CI:0.001–0.005), in a positive linear relationship. LAD wall thickness was

thicker among RA patients with rheumatoid factor (RF) positive ( $p=0.015$ , CI:0.53–0.66). LAD coronary artery wall thickness was increased in early RA compare to controls ( $0.61\pm 0.04$  mm (CI:0.52–0.70); and  $0.48\pm 0.08$  mm (CI:0.44–0.51) respectively,  $p=0.001$ .

**Conclusions:** Early RA patients have increased coronary arteries atherosclerotic burden compared to controls matched for age, and sex. Rheumatoid factor positivity, high Disease Activity Score and Patient Global Assessment of disease activity were associated with coronary wall thickness.

**Disclosure of Interest:** None declared

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#### AB0403 FACTORS CONTRIBUTE TO THE LEVEL URIC ACID IN RHEUMATOID ARTHRITIS

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**Background:** Uric acid (UA) is a strong correlate of renal dysfunction in rheumatoid arthritis (RA), even in the absence of crystal deposition, by causing endothelial dysfunction, intrarenal vascular disease and renal impairment. In hyper or normo-uricaemia RA, UA was the strongest independent predictor of GFR, even after adjustments for most of the potential confounding factors. Additionally, in RA patients UA had been found to be an independent predictor of hypertension and cardiovascular disease (CVD).

**Objectives:** this study aimed to investigate what could be the determinants of the UA level in RA patients.

**Methods:** RA patients with no clinically evident gout, CVD, thyroid disease, liver or renal disease were studied. Serum UA was obtained for all the patients. Renal function parameters, RA disease characteristics, inflammatory markers, and traditional CVD risk factors relation to uric acid level was examined using simple linear regression analysis. To test for the independence association between uric acid and the variables of interest, multiple model was built for the same dependent and independent variables. Statistical significance was accepted at  $p$ -value<0.05.

**Results:** The study recruited 86 consecutive patients meeting the 1987 RA revised ACR criteria, attending routine outpatient clinics at the Department of Rheumatology. Basic demographics and clinical characteristics of were obtained. Of the total 86 patients, 10 (11%) were men and 77 (89%) were women. The mean age of the participants was  $47\pm 14$  years, with mean RA duration of  $68\pm 87$  months. 64 out of 86 participants (74%) had rheumatoid factor positive.

The mean UA value was  $255\pm 86$   $\mu\text{mol/L}$  (NR: 180–340). The mean GFR, calculated using modified MDRD (Modification of Diet in Renal Disease) formula was  $133\pm 52$  ml/min/1.73m<sup>2</sup>.

Using univariate analysis revealed a positive linear relationship between uric acid level and each of the age of the participants ( $p<0.016$ , CI: 0.31, 2.92), age at RA symptoms onset ( $p<0.04$ , CI: 0.025, 0.039), age at RA diagnosis ( $p<0.03$ , CI: 0.101, 2.565), systolic blood pressure ( $p=0.04$ , CI: 0.054, 2.167), diastolic blood pressure (DBP) ( $p=0.02$ , CI: 0.322, 3.777), monocytes absolute count ( $p=0.014$ , CI: 2.510, 4.801), monocytes percentage ( $p=0.005$ , CI: 34.599, 193.595), cholesterol level ( $p=0.008$ , CI: -39.934, -6.286), Triglyceride level ( $p=0.04$ , CI: 0.064, 56.546), urea level ( $p<0.001$ , CI: 9.356, 28.743), creatinine ( $p\leq 0.001$ , CI: 2.345, 3.960), urinary microalbumin ( $p=0.024$ , CI: 0.0296, 0.399), urinary microalbumin/creatinine ratio ( $p=0.006$ , CI: 0.791, 4.616), and ferritin level ( $p=0.025$ , CI: 0.044, 0.633).

As well, univariate analysis revealed a negative linear relationship between UA level and GFR ( $p<0.001$ , CI: -1.127, -0.486)

Building a multiple model, including the entire variable with significant association with the UA in the univariate analysis showed that the UA level in RA is determined by GFR, microalbumin creatinine ratio, cholesterol level, monocytes count and DAS score. The adjusted R2 of the model was 54

**Conclusions:** Whether serum uric acid is merely a marker that reflects the integration of co-morbidities and subclinical renal impairment or a true risk-causative factor for CVD outcome remains as an important question, therefore it is important to know the determinant of UA level and control it.

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#### AB0404 APELIN CONCENTRATIONS ARE ASSOCIATED WITH A REDUCED LEFT ATRIAL VOLUME INDEX AND IMPROVED SYSTOLIC FUNCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** We recently reported that apelin concentrations are associated with reduced atherosclerosis and plaque vulnerability as well as improved aortic function in rheumatoid arthritis (RA)<sup>1,2</sup>. These relations were influenced by RA characteristics<sup>1,2</sup>. Besides protecting against atherosclerosis, apelin is also a vasoactive peptide that improves cardiac contractility. In this regard, patients with RA experience a 2-fold increased risk of developing heart failure<sup>3</sup>. RA patients often demonstrate diastolic dysfunction and heart failure with a preserved ejection fraction (HFpEF). Traditional cardiovascular risk factors do not fully explain the increased heart failure incidence in this population. Metabolic risk factor driven inflammation is highly implicated in HFpEF.

**Objectives:** This study aimed to determine whether apelin can impact left ventricular function in RA and whether disease characteristics can modify this potential effect.

**Methods:** Relationships of apelin concentrations with echocardiographically determined markers of systolic and diastolic function including stroke volume, endocardial fractional shortening, midwall fractional shortening, ejection fraction, relative wall thickness, left ventricular mass, mitral inflow (E/A), filling pressure (E/e') and left atrial volume index (LAVI) were determined in multivariable regression models among 169 patients without established cardiovascular disease.

**Results:** In demographic characteristic adjusted analysis, rheumatoid factor (RF) positivity, joint deformity counts, and CRP were associated with increased apelin concentrations ( $p=0.01$ , 0.02 and 0.05, respectively). Apelin was associated with a reduced LAVI [ $\beta$ (SE)=-4.6 (2.2);  $p=0.04$ ] but not with E/A, lateral e' or E/e' ( $p>0.05$  for all). RA characteristics including disease duration, CRP, erythrocyte sedimentation rate (ESR), RF positivity, and joint deformity counts did not impact apelin concentration-diastolic function marker relationships (interaction  $p$  values>0.05). Apelin levels were associated with increased endocardial fractional shortening [ $\beta$ (SE)=5.99 (2.97);  $p=0.04$ ] and midwall fractional shortening [ $\beta$ (SE)=6.92 (3.0);  $p=0.03$ ]. The ESR and anti-citrullinated peptide antibody (ACPA) status impacted the apelin level-endocardial fractional shortening relationships (interaction  $p=0.05$  and 0.01, respectively). In stratified analysis, apelin concentrations were associated with improved endocardial fractional shortening in those with [ $\beta$ (SE)=14.1 (3.9);  $p=0.001$ ] but not without an ESR >12 mm/hr (median value), and in those with [ $\beta$ (SE)=8.2 (3.7);  $p=0.03$ ] but not without ACPA positivity.

**Conclusions:** In RA, apelin concentrations are associated with a reduced LAVI irrespective of RA activity and severity characteristics. Apelin concentrations are also associated with improved endocardial fractional shortening in patients with RA, particularly in those with high-grade inflammation and ACPA positivity. Whether apelin can improve left ventricular systolic and diastolic function in RA merits further exploration in longitudinal studies.

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#### AB0405 CLINICAL FEATURES AND PROBLEMS OF ELDERLY ONSET RHEUMATOID ARTHRITIS IN ULTRA-AGEING SOCIETY –SINGLE CENTRE RETROSPECTIVE COHORT STUDY-

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**Background:** Japan is the ultra-ageing society ahead of any other country in the world, which ageing rate (the ratio of the population aged 65 and older to the total population) was reported to be 27.3% on October 1, 2016. The rate of aged patients, who followed up at the division of rheumatology in Saitama medical centre, had exceeded 40%.

**Objectives:** The aim of our study is to reveal recent clinical features and problems of elderly onset rheumatoid arthritis (EORA) patients for better management.

**Methods:** Patients had a diagnosis by 1987 classification criteria or 2010 ACR/EULAR criteria. We firstly listed up RA patients who were followed up our hospital from April 1 to September 30, and above aged 65 years old as of September 30. Then we retrospectively collected clinical information of EORA patients who onset



above 60 years old, diagnosed and made starts of treatment in our hospital, and observed more than 6 months, from medical records.

**Results:** One hundred eighty eight EORA patients were enrolled in this study. Female were 116 (62.0%). Mean observation period from first visit until September 30, was 68 months. Rheumatoid factor positive rate was 67.0%. Anti-CCP antibody-positive was 68.2% (107/157), and most of them (65.5%, 70/107) had high antibody titer over 100 U/mL. At the time of diagnosis, average CRP was 3.1 mg/dL. Respiratory complications were seen in 26.1% (49 cases), including 28 interstitial lung disease, 10 COPD/emphysema, 7 non-tuberculous mycobacteriosis/obsolete tuberculosis, and 6 bronchiectasis. Other complications were diabetes 16.5% (past 25 cases, new 6), hypertension 38.3% (past 66, new 6), and hyperlipidemia 23.9% (past 33, new 12). Histories of cerebrovascular or cardiovascular events were seen in 10.6% (20 cases), and history of malignancy was seen in 6.9% (13 cases). During observation period, newly developed malignancy was seen in 14 cases (14.1/1000 person-years) including 4 MTX related lymphoproliferative disorders (MTX-LPD), 3 gastrointestinal cancer, 3 gynaecological cancer, 2 lung cancer, and so on. Infectious adverse event were occurred in 35 patients (35.3/1000 person-years). From the point of treatment, corticosteroids were prescribed in 32%, csDMARDs 88%, and biological DMARDs (BIO) 47%. Of 89 EORA patient treated with BIO, average DAS28-ESR was 5.77, and HAQ-DI 1.48 at the baseline. Twenty-nine cases were started to treat with BIO as monotherapy, 13 cases as switching to BIO from csDMARDs, and 47 as addition BIO to csDMARDs. During observation period, reasons of cessation of the first BIO were remission in 21, adverse events in 19 (7 infections, 6 injection-site/infusion reaction, 3 malignancies, and so on), insufficient response in 16, and patient's hope in 2.

**Conclusions:** RF/anti-CCP antibody positive rate was lower than general RA population, but slightly higher than previous reports on EORA.<sup>1)</sup> BIO could be discontinued in 24% of 89 patients who received BIO because of remission. On the other hand, the frequency of infection and malignancy was still higher in EORA patients. So it is necessary to adjust anti-rheumatic therapy for poor prognostic cases, and we should be careful to follow up EORA patients.

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#### AB0406 SIGNIFICANT ASSOCIATION BETWEEN RENAL FUNCTION AND AREA OF AMYLOID DEPOSITION IN KIDNEY BIOPSY SPECIMENS IN BOTH AA AMYLOIDOSIS ASSOCIATED WITH RHEUMATOID ARTHRITIS AND AL AMYLOIDOSIS

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**Background:** The kidney is a major target organ for systemic amyloidosis, which results in proteinuria and an elevated serum creatinine level. The clinical manifestations and precursor proteins of amyloid A (AA) and light-chain (AL) amyloidosis are different, and the renal damage due to amyloid deposition also seems to differ.

**Objectives:** The purpose of this study was to clarify how the difference in clinical features between AA and AL amyloidosis are explained by the difference in the amount and distribution of amyloid deposition in the renal tissues.

**Methods:** A total of 119 patients participated: 58 patients with an established diagnosis of AA amyloidosis (AA group) and 61 with AL amyloidosis (AL group). We retrospectively investigated the correlation between clinical data, pathological manifestations, and the area occupied by amyloid in renal biopsy specimens. In most of the renal specimens the percentage area occupied by amyloid was less than 10%. For statistical analyses, the percentage area of amyloid deposition was transformed to a common logarithmic value (Log10%amyloid).

**Results:** The results of sex-, age-, and Log10%amyloid-adjusted analyses showed that systolic blood pressure (SBP) was higher in the AA group. In terms of

renal function parameters, serum creatinine, creatinine clearance (Ccr) and estimated glomerular filtration rate (eGFR) indicated significant renal impairment in the AA group, whereas urinary protein indicated significant renal impairment in the AL group. Pathological examinations revealed amyloid was predominantly deposited at glomerular basement membrane (GBM) and easily transferred to the mesangial area in the AA group, and it was predominantly deposited at in the AL group. The degree of amyloid deposition in the glomerular capillary was significantly more severe in AL group. The frequency of amyloid deposits in extraglomerular mesangium was not significantly different between the two groups, but in AA group, the degree amyloid deposition was significantly more severe, and the deposition pattern in the glomerulus was nodular. Nodular deposition in extraglomerular mesangium leads to renal impairment in AA group. There are significant differences between AA and AL amyloidosis with regard to the renal function, especially in terms of Ccr, eGFR and urinary protein, even after Log10%amyloid was adjusted; showing that these inter-group differences in renal function would not be depend on the amount of renal amyloid deposits.

**Conclusions:** These differences could be explained by the difference in distribution and morphological pattern of amyloid deposition in the renal tissue.

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#### AB0407 THE IMPACT OF DEPRESSION ON SOCIAL CONTACTS OF PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) affects the psychological and emotional state of the patient, leading to a significant reduction in the quality of life and social contacts.

**Objectives:** Assess the occurrence and degree of depression in RA patients and their impact on quality of life and social contacts.

**Methods:** The study involved 110 patients, 78.4% women and 22.6% men, with RA of median age 58.7. The average disease duration was 13.6 years. 68% of patients were treated with methotrexate monotherapy (MTX), 32% by combination of MTX and other DMARD. The disease activity in patients was determined by the ideax DAS28, the functional status -HAQ-DI questionnaire. The intensity of the pain was determined using a visual analogue scale for VAS pain (0–100 mm). The degree of radiological changes was determined based on the classification by Steinbrocker. Patients completed a questionnaire related to the quality of social relationships. The degree of depression was determined using Bäck scale for depression.

**Results:** The incidence of depression had 65.4% of the patients. A mild degree of depression was observed in 26.4%, moderate 24%, expressed 13% while 2% of the patients had a more severe degree. There was a significant statistic correlation between the degree of depression with age, the duration of the disease, the high degree of DAS28, HAQ-DI, VAS pain and the degree of radiological changes. By analysing the quality of life and social contact, patients in 62% were supported by a close family and a spouse, 28% of their close relatives, 7% of the wider family, while 3% of the patients lived alone.

**Conclusions:** Depression is the most common and most important psychological state that occurs in patients with RA. It is important to recognise and start treatment on time, which should be based on a multidisciplinary approach. In addition to family support, overall social support also takes a significant place.

**Disclosure of Interest:** None declared

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AB0408

### ANALYSIS OF THE CORRELATION OF COMPOSITE INDICATORS OF ACTIVITY OF THE DISEASE AND THE CONCORDANCE BETWEEN THE DIFFERENT STATES OF ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is an inflammatory joint disease of systemic involvement and varied evolution, which uses different disease evaluation scores. It is essential that these instruments be evaluated according to the disease, so that the treatment algorithms can be applied independently.

**Objectives:** To analyse a correlation of disease activity indexes (ICADs) and a concordance between different states of activity in patients with Rheumatoid Arthritis.

**Methods:** Cross-sectional study based on 100 patients of outpatient care from a multicenter prospective cohort study. Approved by CEP UNISUL. Statistical analysis by the SPSS 18.0 program, using the Pearson Correlation Coefficient and McNemar-Bowker Concordance, considering significance level  $p < 0,05$ .

**Results:** Majority female patients (86%), with an average age of 54 years, who were active in their jobs (53%) and had a positive rheumatoid factor in 65%. The average values of the ICADs were DAS-28 (3.6), DAS-28 PCR (3.0), SDAI (13.4), CDAI (12.5) and RADAI (3.5), respectively. Many were classified with moderate disease activity of the disease. The degree of correlation was very strong ( $>0.8$ ) and strong (between 0.8 and 0.6) in most ICADs and a concordance of remission DAS-28PCR ranged from 41.3% to 54.3% with the other ICADs.

**Conclusions:** The ICADs presented a strong correlation with each other, as well as a level of similarities in the classification of the different degrees of activity. These results confirm that in different patients with RA, the ICADs serve to define active disease and to aid in the treatment strategy, so it is not imperative to use only a single evaluation score.

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AB0409

### MISSING THE BIG PICTURE? AN AUDIT OF HAND X-RAYS IN BIOLOGIC TREATED RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Rheumatoid arthritis (RA) treatment is target driven. The aim is to prevent joint damage and relieve pain and functional loss. X-ray (XR) erosions are an unambiguous sign of disease activity and progression.

**Objectives:** We aimed to review our practice in looking for erosions in our biologic treated patients. We chose this group as they were likely to have the most severe and clearly defined RA.

**Methods:** 100 random biologic treated patients from our biologics database were selected for analysis. We used patient letters and our digital imaging system (PACS) for further information. Our PACS has records running back to 2004.

**Results:** Mean age was 58 years. 77% were female. Mean duration of RA was 10.6 years (range 0.9–44 years). 46 were currently receiving etanercept; 17 tocilizumab; 15 adalimumab; 14 certolizumab; 5 rituximab and 3 abatacept. 61 patients were current prednisolone users. The mean duration of biologic treatment was 4.8 years. 44 patients had received more than one biologic drug; 17 more than two. Mean DAS was 3.4. 72 patients had had previous documented hand XRs; 25 (34%) of these had erosions. The mean duration since the last hand XR was 37 months. 27 patients had had 2 previous hand XRs; 11 had had 3, 4 had had 4 and 2 had had 6 previous XRs. In 19 cases hand erosions appeared to have progressed in the patients who had had more than one XR. 44 patients had had

previous foot XRs; 15 (34%) had erosions. 26 patients had had more than one foot XR. 36 patients had had previous joint ultrasound (US); in 17 (47%) US suggested active synovitis. The mean duration since the last US was 17 months.

**Conclusions:** Our patients had relatively high disease activity despite biologic treatment, over half were also on steroids and significant numbers had had several biologic switches. Despite this only around two thirds of patients had had previous hand XRs documented over an average of 10 years RA duration, and there was a long average time since the last imaging. US rates were lower, but scans were more recent, perhaps suggesting a more modern trend to US over XR. Less than half of patients had had foot XRs. Although there was a lower rate of foot XRs the rate of erosions was similar in hand and foot XRs, suggesting similar patterns of joint damage. Interestingly, despite erosions being a hard end point in most treatment trials, NICE guidance only suggests XR early in RA in 'people with persistent synovitis'<sup>1</sup> and EULAR guidance suggests assessing for 'structural damage' without specifying time intervals.<sup>2</sup> Although newer imaging techniques may be more sensitive, XRs remain cheap, quickly accessible and allow objective assessment, particularly in long term patients being assessed for biologic switches. Our audit suggests that this well established and useful measure of disease burden may currently be relatively neglected.

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AB0410

### DIAGNOSIS OF LUNG DISEASE ASSOCIATED WITH RHEUMATOID ARTHRITIS, A PROSPECTIVE MONOCENTRIC STUDY

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**Background:** Respiratory involvement in rheumatoid arthritis (RA) is the most common extra-articular localisation, affecting 50% of patients, even though only 5% become symptomatic. Lung pathology as RA related interstitial lung disease is associated with significant morbidity and mortality. Involvement of the respiratory system seems frequent but remains underestimated because of the absence of guidelines about its detection in patients with RA.

**Objectives:** This study aimed at determining the prevalence of respiratory involvement among symptomatic and asymptomatic patients with rheumatoid arthritis managed in a university hospital.

**Methods:** We conducted a prospective observational study from May 2017 to January 2018 at the Strasbourg University Hospital. The patients included were over 18 years of age, had rheumatoid arthritis according to the ACR/EULAR 2010 criteria and signed informed consent. They responded to a self-administered questionnaire about their medical history, cardiorespiratory symptoms and lifestyle. Epidemiological, clinical and radiological data were assessed. All of the patients had a chest computed tomography (CT) and respiratory function tests (RFT). A collection of salivary flow and a test of Shimer were carried out, to investigate the presence of a sicca syndrome. Chest CTs were interpreted by a radiologist specialised in lung area.

**Results:** We included 102 successive patients, 73 women and 29 men. The average disease duration was 34 years. 60 patients were seropositive for rheumatoid factor and 68 for anti-CCP. 59 patients had bone erosions. The average disease activity score (DAS28-CRP) at inclusion was 3.5. 49 patients had associated Sjogren's syndrome. 22 were active smoker. 43 patients were taking long-term corticosteroid therapy. 96 patients were treated with conventional DMARD treatment, 28 with anti-TNF alpha therapy, 16 with Tocilizumab, 12 with Abatacept, 2 with JAK selective inhibitor, and 16 patients were under Rituximab.

Of the 87 RFT performed, 39 were abnormal: 14 reported an obstructive syndrome, 8 a restrictive syndrome, 32 peripheral expiratory braking, suggestive sign of bronchiolitis, and 24 a decrease in the DLCO.

Of the 91 chest CTs, 42 revealed lung nodules (42%), 15 of which were more than 6 mm; 29 interstitial syndrome (29%), among which 5 were non-specific interstitial pneumonitis (PINS), 3 common interstitial pneumonitis (PIC), and the other were non specific interstitial syndrome. 2 chest CT showed pleural effusion and 1 pericarditis. 44 patients had coronary calcifications, among whom 32 had no lipid-lowering therapy.

**Conclusions:** Pulmonary systemic assessment of RA patients show high prevalence of respiratory involvement: 42% of patients had lung nodules and 29% had an interstitial syndrome. Detection of interstitial lung disease may raise questions about RA treatment such as anti-TNF alpha therapy. Rheumatologist should be more aware of respiratory involvement in RA patients and RFT, a non-invasive test, might be useful at diagnosis and follow-up.

**Disclosure of Interest:** None declared

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**AB0411 RISK OF REACTIVATION OF HEPATITIS B VIRUS IN RHEUMATOID ARTHRITIS PATIENTS WHO RECEIVED LONG-TERM LOW DOSE CORTICOSTEROID THERAPY**

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**Background:** It is well known that the use of corticosteroids results in increased viral replication and elevated ALT in patients with hepatitis B virus. The use of high dose corticosteroids for more than 4 weeks usually results in hepatitis worsening after cessation of steroids. However, few studies have investigated the effect of low dose corticosteroids on hepatitis B virus (HBV) reactivation.

**Objectives:** The aim of this study is to investigate the reactivity of HBV in rheumatoid arthritis (RA) patients treated with long term low dose corticosteroids and its risk factor.

**Methods:** Patients with HBsAg positive who were diagnosed with RA and who received prednisolone of less than 10 mg/day over four weeks and immunosuppressive agent were selected at four university hospitals in South Korea between June 1996 and March 2017. Medical records and laboratory data were retrospectively analysed and multivariate analysis was performed.

**Results:** One hundred forty five patients were included in the study and 26 (17.9%) patients were reactivated with HBV. Mean age at diagnosis of RA was 50.7 years and 41 (28.3%) patients were male. Baseline characteristics including sex, age and laboratory findings at diagnosis of rheumatoid arthritis were not significantly different in patients with HBV reactivation compared to those without HBV reactivation. The average daily dose of prednisolone was 3.65±2.77 mg and the mean duration of prednisolone was 5.11±5.05 years and the average cumulative dose of prednisolone was 5821.6±7021.3 mg. Eleven (42.3%) of 26 HBV reactivated patients were reactivated within one year after prednisolone administration and the period from the start of prednisolone administration to the reactivation was 4.08±5.77 years on average. The duration of prednisolone administration, mean daily dose of prednisolone, and cumulative prednisolone dose and administration of methotrexate, tacrolimus, tumour necrosis factor inhibitor and hydroxychloroquine did not significantly affect HBV reactivation in both univariate and multivariate analyses. However, the administration of leflunomide showed a significant difference in the reactivation of HBV (adjusted odd ratio 3.76; p=0.04)

**Conclusions:** The hepatitis B virus can be exacerbated by spontaneous viral reactivation, so it is difficult to conclude that hepatitis is caused by the administration of steroids. In this study, the administration of low-dose steroids did not affect the reactivation of HBV. However, leflunomide increased the risk of HBV reactivation when the effects of other disease modifying antirheumatic drug (DMARD) were corrected. Therefore, a prospective study is needed to evaluate the effect of DMARDs on HBV reactivation in the long – term administration of low – dose corticosteroids in RA patients.

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**AB0412 DYNAMICS OF QUANTITATIVE BODY COMPOSITION INDICES BY THE METHOD OF DUAL-ENERGY X-RAY ABSORPTIOMETRY (DRA) IN PATIENTS WITH EARLY RA DEPENDING ON THE ACHIEVED ACTIVITY OF THE DISEASE**

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**Background:** Adipose tissue an active endocrine organ. In pts with RA the redistribution of body fat mass. Using BMI and WC do not allow to distinguish between

fat and lean (muscle) mass. Performing dual-energy X-ray absorptiometry allows to specify the quantitative composition of the body(mass of adipose tissue and muscle) in pts with early RA.

**Objectives:** to compare the indicators of the quantitative composition of the body in groups of RApts with different disease activity before and after the appointment of therapy.

**Methods:** included 37pts with early RA(ACR/EULAR2010), 57 [46.5, 62] yrs, duration of disease 6 [5.5,15.5]mths, IgMRF seropositive antiCCP, with high RA activity(DAS285.5 [5.1,6], SDAI 32.4 [22.4, 42], CDAI 29 [19.7, 39.5]). After inclusion in the study, all pts started receiving MTX 10 [10–15 mg/week], after 12 weeks, with ineffective MTX, ADA 40 mg/2 weeks was prescribed. The quantitative composition of the body was determined initially and after 6mths by means of DXA using the apparatus HOLOGIC,analysing the following parameters:the total, of fat and lean mass.

**Results:** By the 24th week of therapy, 13 (35%)pts with earlyRA received combined therapy(ADA, MTX), 24 (65%) pts with RA monotherapy MTX. Depending on the activity of RA(DAS28)by the 24th week of therapy, pts are divided into 2groups: I(n=18) pts with remission/low activity, II(n=19)with moderate/high RA activity (table 1). Initially, the groups differed in fat mass:this index was higher in the group of pts with moderate/high activity persisting, compared with the group of pts with remission/low activity of RA:30.2 kg versus 19.4 kg. In the I group of pts before the treatment and after 6mths of therapy,a statistically significant decrease in muscle mass was observed:from 45.2 kg to 41.6 kg. A decrease in the mass of adipose tissue after 24 weeks of therapy was noted in the IIgroup of pts with RA: from 30.2 kg to 28.2 kg. The difference in the indices between the groups by the 6 month of therapy was noted for the mass of adipose tissue. This composition of the body score was also higher in pts with moderate and high RA activity, compared to the group of pts with remission/low RA activity: 28.2 kg versus 18.9 kg (p<0.05 in all cases).

**Abstract AB0412 – Table 1**

	Group I(n=18)Remission/low activity			GroupII(n=19)Medium/high activity		
	0	24 weeks	Δ, %	0	24 weeks	Δ, %
Fat mass, kg	19,4	18,9	-3	30,2	28,2	-7
	[15,8;25,9]**	[16,4;24,3]***		[20,7;37,6]	[22,7;40,2]*	
Lean mass, kg	45,2	41,6	-8	42,9	44,2	+3
	[38,9;54,4]	[38,6;48,4]*		[38,9;54]	[40,1;55,4]	
Total weight, kg	70	64,9	-7	72,8	74,7	+3
	[58;80,8]	[59,5;81]		[60,;102]	[64;97,9]	
BMI, kg/m <sup>2</sup>	23,4 [21,5;27,5]	23,8	+1	26,8	26,0	-2
	**	[20,2;26,5]		[22,8;34,6]	[23,3;34,3]	

\*p<0,05 reliability of differences in factors before treatment and after 6mth(Wilcoxon);

\*\*p<0,05 differences in baseline values in Groups I and II(Mann-Whitney test);

\*\*\*p<0,05 difference in the indices between the groups by the 6mth of therapy; Δ,% the difference between the indices between the groups by the 6mth of therapy.

**Conclusions:** pts with RA who achieved Igroup after 6 mths of therapy initially had a smaller volume of adipose tissue, compared with pts with moderate and high RA activity. Despite the achievement of remission after 6mths of therapy,a loss of lean mass(probably the development of rheumatoid cachexia) continued in some pts, but these data need confirmation in studies with a large number of pts and a longer period of follow-up.

**Disclosure of Interest:** None declared

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**AB0413 NODULAR POLYARTERITIS AS AN UNFORESEEABLE ADVERSE REACTION IN RA PATIENT TREATED WITH TOFACITINIB**

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**Background:** Tofacitinib basic prescribing information and guidelines for medical use do not provide any description of such adverse drug reaction (ADR) as vasculitis, in particular polyarteritis nodosa. We present a clinical case of vasculitis emerging during tofacitinib therapy.

**Objectives:** demonstration of an unexpected reaction to tofacitinib

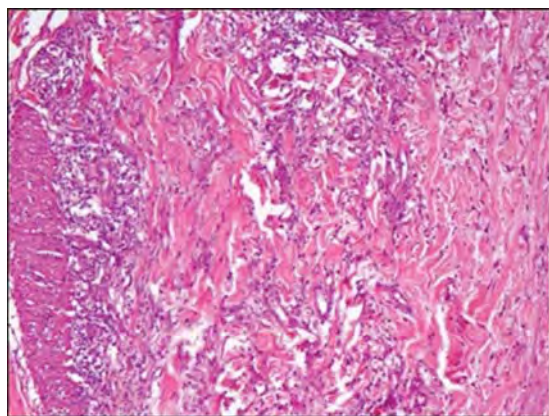
Demonstration of an unexpected reaction to tofacitinib

**Methods:** A 59 y.o. RA female patient was hospitalised in December 2016 due to eruption of indurated nodules on her hips and legs producing sharp pain, ulceration of nodules on the legs, painful hip and ankle joints, and morning stiffness lasting for about one hour.

**Results:** Seropositive RA was diagnosed in this patient in April 2004 with subsequent DMARD with methotrexate (MT) at 7,5 mg/week. The remission achieved



lasted until November 2005. Gradual dose escalation up to 20 mg/week was required during 2006 in view of RA exacerbations, nevertheless, clinical and lab RA activity persisted. Therefore tofacitinib (Jakvinius) was administered in November 2015 at 10 mg/day, with rapid achievement of minimum RA activity (DAS28=3.0). By the end of May 2016 clinical manifestations of vasculitis emerged, and in June 2016 tofacitinib was discontinued due to increasing lab activity of the disease. Clinical examination: patient's condition is moderately grave. The thinned skin looks dry, showing multiple regenerating ulcers on the anterior leg surface and sharply painful ulcerated indurations on the right inner thigh producing serosanguinous fluid. The RA activity is equal to DAS28=5.72, Hb 125 g/L, WBC  $6.0 \times 10^9/L$ , platelets  $40 \times 10^9/L$ , ESR 22 mm/h, CRP 42 mg/L, RF 413 IU/ml, *antibody to cyclic citrullinated peptide* (ACPA) is 195 U/ml, TNF – 13.9 pg/ml. Wrist and distal foot radiographs show moderate extended osteoporosis, narrowing of some joint spaces, rare bone and articular surface erosions, subluxation of some joints. Histopathology of skin and subcutaneous fat biopsy samples is presented on figure 1a, 1b. Histopathology data suggests the presence of cutaneous and subcutaneous fat productive and destructive vasculitis and acute, predominantly lobular, panniculitis; such structural changes are usually present in cutaneous polyarteritis nodosa and other systemic vasculitis. The casual relationship between this ADR and tofacitinib therapy was assessed as probable using Naranjo scale.



Abstract AB0413 – Figure 1

**Conclusions:** development of vasculitis (polyarteritis nodosa) in RA patient can be caused by tofacitinib.

**Disclosure of Interest:** None declared

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#### AB0414 RELATIONSHIP BETWEEN SERUM OXYTOCIN LEVELS AND DEPRESSION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Oxytocin (OXT), also referred to as a happy hormone, has been associated with various psychiatric disorders, including depression. However, the relationship between depression and rheumatoid arthritis (RA) has not yet been clarified.

**Objectives:** The objective of this study was to investigate the relationship between serum oxytocin levels and disease activity, depressive state, activity of daily life (ADL), and quality of life (QOL) in RA.

**Methods:** This study included 119 RA patients. We measured the following variables: baseline characteristics including age, sex, disease duration, smoking history, body mass index, prednisolone dose, and methotrexate (MTX) dose, serum levels of rheumatoid factor, matrix metalloproteinase-3, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) level. The disease activity of RA was assessed using the Simplified Disease Activity Index (SDAI); depression was assessed using the Hamilton Depression Rating Scale (HAM-D); ADL were assessed using the Health Assessment Questionnaire; and QOL was assessed using the 36-Item Short Form Health Survey (SF-36). Serum OXT levels were determined by enzyme-linked immunosorbent assay. The subjects were divided into two groups according to the higher or lower of the serum OXT levels, and a retrospective study was performed.

**Results:** The serum OXT levels were correlated with the disease duration ( $r=0.443$ ,  $p=0.000$ ). Weak correlations of MTX dose ( $r=0.208$ ,  $p=0.030$ ), swollen

joint count (SJC) ( $r=-0.306$ ,  $p=0.001$ ), ESR ( $r=-0.245$ ,  $p=0.010$ ), CRP ( $r=-0.283$ ,  $p=0.003$ ) and the mental component summary (MCS) score ( $r=-0.196$ ,  $p=0.041$ ) of SF-36. The binominal logistic analyses findings were as follows: younger age ( $p=0.0209$ , odd ratio: 0.96, 95% CI: 0.94–0.99) and longer disease duration ( $p=0.0053$ , odd ratio: 1.08, 95% CI: 1.02–1.13). Other items did not correlate to the serum OXT levels included with the HAM-D score.

**Conclusions:** The serum oxytocin levels were correlated with longer disease duration and younger age.

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## Rheumatoid arthritis – biological DMARDs

### AB0415 DISEASE FLARES AMONG EARLY RHEUMATOID ARTHRITIS PATIENTS TREATED WITH CONTINUED METHOTREXATE EITHER ALONE OR IN COMBINATION WITH ADALIMUMAB

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**Background:** Some rheumatoid arthritis (RA) patients (pts) may experience flares in their disease even after reaching stable low disease activity (sLDA), but the consequences of even temporary elevations in disease activity are poorly understood.

**Objectives:** The purpose of this analysis was to explore the rates of flares after reaching sLDA in pts treated to target with either methotrexate (MTX) monotherapy or adalimumab combination therapy (ADA+MTX).

**Methods:** This post hoc analysis included pts from the randomised, double-blind, double-period OPTIMA<sup>1</sup> trial achieving sLDA [DAS28(CRP) <3.2 at weeks (wks) 22 and 26] at the end of period 1 (P1). In P1, pts were randomised to receive ADA +MTX or placebo (PBO) +MTX for 26 wks. Pts on ADA +MTX achieving sLDA were randomised to receive PBO +MTX (ADA Withdrawal) or continue on ADA +MTX (ADA Continuation) for an additional 52 wks in period 2 (P2). Pts who achieved sLDA on PBO +MTX in P1 continued their treatment in P2 (MTX Continuation). Pts achieving sLDA in each treatment group were categorised based on whether they experienced a flare [change in DAS28(CRP)  $\geq 0.6$  at consecutive visits and DAS28(CRP)  $\geq 3.2$ ]; the proportion of pts experiencing flares and time to flare were assessed. For each group, mean change from wk 26 to wk 78 in disease activity [DAS28(CRP)], functional (HAQ-DI) and structural (mTSS) measures were analysed.

**Results:** In pts achieving sLDA at the end of P1, flare rates in P2 differed based on initial treatment assignment (ADA Continuation: 11.7% [11/94]; MTX Continuation: 22.4% [22/98]). Interestingly, flare rates in pts randomised to withdraw ADA in P2 (ADA Withdrawal: 25% [22/88]) were numerically similar to the MTX Continuation group. The mean time to flare was 193, 191, and 177 days in the ADA Withdrawal, ADA Continuation, and MTX Continuation groups, respectively. During P2, the mean DAS28(CRP) scores were predictably higher in pts who flared compared with those who did not across treatment groups. In pts experiencing flares in P2, disease activity and functional measures worsened from wk 26 to wk 78 as compared with pts without flares (table 1). Of the individual DAS28(CRP) components, pt global assessment of disease activity (PtGA) showed the greatest worsening. There were small differences in radiographic progression between pts experiencing flares compared with pts without flares.

**Abstract AB0415 – Table 1.** Change from Week 26 in Disease Activity, Functional and Structural Measures Based on Flare Status in Patients Achieving Stable LDA\*

Outcome measure Mean (SD)		Visit Mean at Week 26		Mean Change ( $\Delta$ ) from Week 26 to Week 78	
		Flare	No Flare	Flare	No Flare
DAS28(CRP)	ADA Withdrawal	2.2	2.0	1.0 (1.2)	-0.1 (0.6)
	ADA Continuation	2.1	2.0	0.6 (1.1)	-0.2 (0.7)
	MTX Continuation	2.2	2.1	1.0 (1.2)	-0.1 (0.6)
HAQ-DI	ADA Withdrawal	0.4	0.2	0.3 (0.6)	0.0 (0.3)
	ADA Continuation	0.5	0.3	0.2 (0.5)	-0.1 (0.3)
	MTX Continuation	0.4	0.3	0.2 (0.5)	0.0 (0.4)
mTSS	ADA Withdrawal	8.4	11.5	0.3 (0.7)	0.2 (1.1)
	ADA Continuation	6.9	12.7	0.1 (0.5)	-0.1 (0.7)
	MTX Continuation	10.5	9.2	0.1 (0.6)	0.1 (1.0)

\*Flare was defined as change in DAS28(CRP)  $\geq 0.6$  at consecutive visits and DAS28(CRP)  $\geq 3.2$ .

LDA=low disease activity; DAS28(CRP)=28 joint disease activity score based on C-reactive protein; ADA=adalimumab; MTX=methotrexate; HAQ-DI=health assessment questionnaire disability index; mTSS=modified total Sharp score.

**Conclusions:** In early RA pts achieving sLDA, flares were generally infrequent; however, they were more prevalent in pts receiving PBO+MTX compared with ADA+MTX. Flares were numerically associated with higher disease activity, functional deterioration, and higher PtGA, underscoring its impact on health-related quality of life and the importance of preventing flares as a therapeutic outcome.

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#### AB0416 ESTIMATING THE SHORT-TERM COSTS ASSOCIATED WITH NON-MEDICAL SWITCHING IN RHEUMATIC DISEASES

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**Background:** As biosimilars are approved and commercialised for rheumatic diseases, patients may be switched from originator biologic treatment to biosimilars due to perceived cost savings between the two biologic products. However, in the short term, non-medical switching (NMS) may require additional patient education, office visits, lab/imaging tests, and administrative support which could lead to substantial costs.

**Objectives:** To estimate the short-term costs associated with NMS from originator biologics to biosimilars among stable patients with rheumatic conditions (e.g., rheumatoid arthritis, RA; ankylosing spondylitis, AS; psoriatic arthritis – PsA) from the perspective of a rheumatology medical centre in the United Kingdom.

**Methods:** An economic model was constructed including two components: the administrative burden for NMS program set-up and support, and the provider burden for initiating and managing NMS. Administrative burden was modelled at the center-level and considered staff time for program set-up, patient education, scheduling, documentation, and departmental meetings from pre-NMS planning

to post NMS implementation (<1 year). The provider burden was modelled at the patient-level and considered the expected additional provider time needed and extra laboratory/imaging tests when managing NMS from the time of switching until 3 month post NMS implementation. Model inputs for the administrative burden came from the literature<sup>1</sup> and for provider burden from survey of physicians. Literature was used to inform both the total number of rheumatology patients that underwent NMS, and the unit cost associated with provider/staff time and laboratory/imaging tests.

**Results:** From a rheumatology centre perspective, setting up an NMS program and the subsequent administrative support was estimated to cost £19 617 per centre, attributed to general overhead (40%), pharmacist time (26%), consultant time (21%), and nurse time (13%). After the set-up, provider burden for initiating and managing NMS was estimated to be £113 per switched patient. Assuming 5000 patients with relevant rheumatoid conditions in a centre, 572 stable patients with RA, PsA or AS were estimated to switch to biosimilars. The overall short-term cost associated with NMS was estimated to be £84 174 for the entire centre, with 23% attributed to the NMS program set-up and support, and 77% attributed to extra provider time and monitoring (on average £147 cost per switched patient).

**Conclusions:** Switching stable patients with a rheumatic condition from originator biologics to biosimilars could have considerable short-term costs for a centre. Additional real world studies are needed to better weigh the potential saving vs. cost associated with NMS.

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#### AB0417 BIOLOGICAL DRUGS IN THE TREATMENT OF RHEUMATOID ARTHRITIS: REAL LIFE DATA IN A BRAZILIAN MULTICENTRIC STUDY

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**Background:** Rheumatoid arthritis (RA) is a chronic disease, characterised by inflammatory involvement of the synovial joints. The “treat to target” concept is well established in the rheumatologic community, however, in many patients, especially in developing countries, its implementation is not feasible. Considering the high costs of treatment com of RA and the limited national epidemiological data available on this disease, we sought to describe the profile of use of biological drugs in Brazilian patients with RA to help the decision-making process by public health managers.

**Objectives:** To describe the frequency and time of use of biological drugs in Brazilian patients with rheumatoid arthritis.

**Methods:** The REAL – RA in real life in Brazil – is a multicenter prospective cohort study, with twelve-month follow-up period. To be included in this study, consecutive patients from 11 tertiary rheumatology centres had to meet the 1987 ACR or the 2010 ACR/European League Against Rheumatism (EULAR) criteria. Data were collected during routine clinical care and previous medical records were used as secondary sources. The present study present data taken from the participants’ initial assessment. This research was approved by the Ethics Committees of each centre.

**Results:** A total of 1125 patients were analysed. 89% were women with a mean age of 56.6 years. The main clinic data were: DAS 28 (median)=3.52, HAQ (median)=0.87 and CDAI (median)=9. 1022 (90.84%) used synthetic DMARDs



and 406 (36.09%) biologic therapy. The frequency of use of the biologic therapy was: abatacept (73 patients/6.49%), etanercept (66/5.87%), tocilizumab (60/5.33%), adalimumab (54/4.8%), infliximab (50/4.44%), rituximab (49/4.36%), golimumab (37/3.29%), certolizumab (17, 1.51%). The time of use of the biological drugs is presented in table 1.

**Abstract AB0417 – Table 1.** Time (in years) of use of biological drugs in patients with rheumatoid arthritis

DRUG	MEAN	MAXIMUM
ABATACEPT	1.95	8
ADALIMUMAB	1.70	12
CERTOLIZUMAB	0.63	2.0
ETANERCEPT	1.49	9.0
GOLIMUMAB	0.65	2.0
INFLIXIMAB	1.56	9.0
RITUXIMAB	1.27	6.0
TOCILIZUMABE	2.0	6.0

**Conclusions:** The therapeutic profile of this cohort of Brazilian RA patients shows some interesting results. The relatively high number of patients on biologics, compared to other studies, may be related to fact that the centres involved were reference centres, probably dealing with more difficult cases.

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#### AB0418 THE EFFECT OF CONCOMITANT METHOTREXATE ON SERUM TNF INHIBITORS LEVELS AND CLINICAL RESPONSE IN PATIENTS WITH RHEUMATOID ARTHRITIS IS DOSE DEPENDENT AND GREATER THAN OTHER DMARDS

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**Background:** Several factors influence on the pharmacokinetics(PK) of TNF inhibitors(TNFi). One of the most relevant influencing factors is the development of antidrug- antibodies(ADA), which is associated with low circulating drug levels and loss of clinical efficacy. Previous studies, mostly about Adalimumab (Ada), have demonstrated a beneficial effect of concomitant use of methotrexate(MTX) in patients(pts) under TNFi therapy by reduction of immunogenicity. There are other csDMARDs(OD) as leflunomide, hydroxychloroquine or sulfasalazine which may have also an effect on PK.

**Objectives:** To investigate the effect of csDMARDs on the presence of serum TNFi levels and on the clinical response during the first year of Ada or Infliximab (Ifx) treatment in RA pts. Secondly, to evaluate if MTX has a dose-dependent effect on these outcomes.

**Methods:** This is an inception cohort including pts with RA starting Ifx or Ada in a tertiary hospital since 1999. At baseline, 6 and 12 months clinical(DAS28, EULAR response and  $\Delta$ DAS28) and serological(drug and ADA levels) parameters were measured. Patients were clustered according to the use of concomitant csDMARDs at baseline in three groups: i)TNFi monotherapy;ii)TNFi +MTX;iii) TNFi +OD. Pts within the TNFi +MTX group were also classified according to the MTX dose:MTX <15 mg/week(TNFi +MTX <15) and MTX  $\geq$ 15 mg/week(TNFi +MTX  $\geq$ 15).

**Results:** A total of 92 RA pts[Ada(n=25) or Ifx(n=67)] under TNFi were included. The number and percentage of pts in each group were as follows:TNFi monotherapy,12 pts(13%);TNFi +MTX, 59 pts(64%);TNFi +OD 21 pts(23%). According to MTX dose, the distribution was:TNFi +MTX <15,18 pts(20%);TNFi +MTX  $\geq$ 15, 41 pts(45%). Considering the overall of pts receiving any dose of MTX, the percentage of them with drug levels after 12 months(71%) was numerically higher than in the other groups(20% in TNFi +OD and 9% in TNFi monotherapy,p=0.1). However, after stratifying pts by MTX dose, we observed that circulating drug levels at 12 months were more frequent in higher dose of MTX(54% of the pts with TNFi +MTX  $\geq$ 15) compared to patients with TNFi +MTX <15 (17%), with TNFi +OD (20%) and with TNFi monotherapy (9%);p=0.002). According to EULAR

response, pts treated with TNFi +MTX(81%) achieved more frequently a good response compared with the other groups (11% on TNFi +OD and 8% on TNFi monotherapy, p=0.6). Moreover, differences on clinical response were observed depending on MTX dose. While 58% with TNFi +MTX  $\geq$ 15 were good EULAR responders, 23% with TNFi +MTX <15 achieved this. Overall, the best effect on clinical response was observed in the group of MTX; p=0.4. Finally, the TNFi median survival time(mst) was significantly higher in pts with TNFi +MTX than in pts with TNFi +OD or on TNFi monotherapy(5 years vs 2 years vs 2.15 years, respectively;p=0.03). Analysing by MTX dose, drug survival was superior for high ( $\geq$ 15) and low MTX doses(<15) (mst 5.2 and 3.3, respectively)compared to OD and/or TNFi monotherapy although the difference was not statistically significant p=0.09.

**Conclusions:** In RA pts under Ifx or Ada treatment, the presence of TNFi in serum, the clinical response and the TNFi survival are influenced by MTX but not by OD. Moreover, a MTX dose-dependent effect is closely associated with these outcomes.

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#### AB0419 FREQUENCY OF DISEASE FLARE AND STUDY OF THE CD4+CD25+HIGHCD127LOW/- CELL POPULATIONS AFTER DISCONTINUATION OF ANTI-TNFA THERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS IN PERSISTENT REMISSION

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**Background:** Rheumatoid arthritis (RA) patients in a prolonged remission status represent a population whose future management has yet to be established. Treg cell function in patients with active RA is assumed to be impaired, a trend that seems to be reversed by TNFalpha antagonist therapy (aTNF). Theoretically a deeper remission may be represented by an immunological resetting of immune system, a condition which could enable to consider the possibility of a drug-free remission.

**Objectives:** To evaluate the incidence of disease flare after cessation of aTNF in pts in remission together with reconstitution of the CD4 +CD25highCD127low/- Tcell subset respect to those patients in the same remission status with persistent low CD4 +CD25highCD127low/-Tcell population, assuming the Treg populations as a markers of deep remission allowing a better selection of those patients at low-risk of flare after aTNF withdrawal.

**Methods:** inclusion criteria: patients with RA (>18 years) fulfilling the 1987 ACR classification criteria treated with aTNF and synthetic DMARDs for at least 12 months, in remission (DAS28 <2.6/DAS44 <1.6)>6 months, without glucocorticosteroid. Exclusion criteria:<18 years, glucocorticosteroids within the three months before; another inflammatory disease other than RA; ongoing infections. Intervention: aTNF drug withdrawal with continuation of DMARDs previously associated (MTX or LFN); a 24 months of follow up was performed. Serial clinical and instrumental evaluation, blood sampling and radiographs have been performed according to the scheduled protocol. Treg population and several cytokines/chemokines/growth factors were analysed (Human Cytokine/Chemokine Panel I, Millipore).

**Results:** 23 patients were included, mean age 53 years (SD 12.3), 68% RF +, 52% ACPA +, DAS28 medium 1.41 (SD 0.48); average duration of illness 9.62 years (SD  $\pm$ 5.73). During the 24 month post-suspension follow-up, for a total of 267 person-months, 11 patients presented a flare, for a flare rate of 3.74/100 person-months (CI95% 1.79–6.88). The average observed exacerbation time from aTNF withdrawal was 14.6 months (SD  $\pm$ 9.32). None statistical predictive value of Treg levels regarding disease outcome after aTNF withdrawal was observed IIR (95% CI) 1.38 (0.82–2.30). None significant correlation among cytokines concentrations and disease status/Treg levels was observed. A correlation was observed between the presence of a synovitis with PD1+\* at the baseline and the loss of remission [HR 7.062 (1.64–30.41, p 0.009);\*higher values were exclusion criteria]. All 3 patients with positive US (PD1) who had flare-up were asymptomatic at baseline.

**Conclusions:** 47.8% of pts maintained aTNF-induced remission at 24 months continuing only sDMARDs therapy (MTX). Only in 1 case reintroduction of Adalimumab did not allow to regain clinical remission, which was obtained using another therapeutic target (anti-CTL4). The presence of a residual synovitis, although mild (PD1), was correlated with the risk of exacerbation. Further results will be discussed.



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AB0420

#### DRUG SURVIVAL ON CERTOLIZUMAB AND PREDICTORS THEREOF IN PATIENTS WITH RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS, AND AXIAL-SPONDYLOARTHRITIS FROM THE APULIAN BIOPURE REGISTRY

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**Background:** In BIO.PU.RE. Registry are collected data from patients being treated with Biologics from rheumatologic centres in Apulia (Southern Italy).

**Methods:** We analysed longitudinal data of consecutive patients, affected with RA, PsA or axial-SpA starting a treatment with certolizumab (CTZ) in the time frame from 1st January 2011 to 30th June 2017. Demographic and disease related characteristics were collected at baseline and at last observation visit. Primary endpoint was the persistence on CTZ, and secondary endpoint was the search of baseline predictors of drug survival and clinical outcomes. Drug survival was evaluated by Kaplan-Meier life table analysis. Estimates hazard ratios (HRs, 95% confidence intervals (CI)) of drug discontinuation or achievement of low-disease/remission in RA, and minimal disease activity (MDA) in PsA at last visit, adjusted for patient's demographics, disease characteristics and prior biologic treatments were computed by Cox-regression stepwise backward models.

**Results:** 345 patients were included in this analysis (table 1). Global median survival time (95% CI) was 30 [23–36] months. Drug survival rate was significantly higher in SpA (63.9%, p=0.009) than in RA (54.0%) or PsA (54.5%). Within each disease, naïve-CTZ patients showed higher survival rates than biologic-experienced patients in RA (63.4% vs 45.7%, p=0.0001), but not in PsA (59.1% vs 52.3%, p=0.60), or SpA (62.5% vs 64.4%, p=0.94). In the whole cohort, the only negative predictor of drug discontinuation was the CTZ-naïve status (HR 0.62, 95 CI 0.40–0.96, p=0.03). This association was even stronger for RA (HR 0.45, 95 CI 0.26–0.77, p=0.004). In SpA, patient's age at baseline was weakly correlated to CTZ stopping (HR 0.96, 95 CI 0.93–0.99, p=0.02), but no predictor of CTZ discontinuation was detected in PsA. No factor did correlate to the achievement of low disease/remission in RA, while co-medication with MTX was significantly associated to the achievement of MDA (HR 3.82, 95 CI 1.26–11.54, p=0.01) in PsA. Globally, the causes of discontinuation were: ineffectiveness (nr 94, 27.2%), adverse event (nr. 40, 11.6%), pregnancy (nr.1, 0.3%), remission (nr. 3, 0.9%), others (nr.13, 3.8%).

Abstract AB0420 – Table 1

	All (nr. 345)	RA (nr. 172)	PsA (nr.88)	Ax- SpA (nr.83)
Age (mean)	46.9±11	48.8±12	44.4 ±10	45.7 ±11
Female	72.9%	86.2%	71.6%	43.3%
BMI (mean)	27.3±5	26.4±4	29.4±5	26.7±5
Dis Durat (mean)	8.8±8	8.7±8	8.6±7	9.2±9
Naive	37.1%	47.1%	25.0%	28.9%
Prior biologics	62.9%	52.9%	75.0%	71.1%
Glucocorticoids	64.6%	79.3%	50.0%	41.0%
Methotrexate	60.3%	73.0%	45.5%	27.3%
Comorbidities	62.3%	58.0%	68.2%	65.1%
DAPSA (mean)			22.8 ±12	
DAS28 (mean)		4.8±1		5.4±2
Extra-articular				21.7%
HLA-B27 (nr.44)				64.8%
RF/ACPA +		72.4%		

**Conclusions:** In our real-life experience CTZ seems to have better drug survival in PsA rather in RA and SpA; in all these polyarthritis was observed CTZ-naïve status as negative predictor of drug discontinuation.

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AB0421

#### LOW RATES OF RETENTION OF BIOLOGIC DMARD MONOTHERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS IN REAL LIFE SETTINGS

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**Background:** A number of cross-sectional studies have shown that approximately one quarter of rheumatoid arthritis (RA) patients are being treated with biologic disease modifying anti-rheumatic drugs (bDMARDs) as monotherapy. Data regarding the retention of bDMARD monotherapy in real-life settings are limited.

**Objectives:** To study the survival rate of bDMARD monotherapy in RA patients in daily clinical practice.

**Methods:** Multicenter (11 hospital, 3 private office practices), prospective, RA epidemiological study in Greece. At baseline and after one year of follow-up, demographics, disease characteristics, treatments, co-morbidities and serious events (serious infections, cardiovascular events, neoplasms, osteoporotic fractures) were collected via a web-based platform.

**Results:** 1.323 RA patients with paired evaluations one year apart (mean interval: 13.2±3.7 months) were included. Among 611 bDMARD treated patients, 155 patients (25%) were on bDMARD monotherapy (women: 87%, mean age: 60.4 years, mean disease duration: 15 years, RF and/or anti-CCP positive: 66%, TNFi therapy: 57%). The majority had been previously on and had discontinued their csDMARDs (90%). During follow-up, 15% (n=24) discontinued their bDMARD; most of them stayed off any type of therapy (83%) while the rest continued with synthetic DMARD (csDMARD) monotherapy (17%). From the remaining 131 patients, 96 (73%) remained on bDMARD monotherapy (85%, n=82 on the same biologic) while in 27% (n=35) a csDMARD was added. Serious events occurred in 7.7% of patients (n=12). Overall, at the end of 1st year, approximately half of patients (53%, n=82) remained on their initial bDMARD monotherapy. Factors associated with continuation of the same bDMARD by multivariate analysis were a low HAQ score (OR=0.48, 95% C.I.=0.23–0.99, p=0.047) and corticosteroid use (OR=2.2, 95% C.I.=1.02–5.1, p=0.044) at baseline as well as the absence of a serious event during the 1st year of follow-up (OR=0.14, 95% C.I.=0.016–1.3, p=0.094).

**Conclusions:** In real life settings, only half of patients who are on bDMARD monotherapy continue the same agent one year later. Low HAQ score, corticosteroid use and absence of a serious event during therapy predicted bDMARD monotherapy survival.

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AB0422

#### COST EFFECTIVENESS ANALYSIS OF MODIFIED DOSING REGIMEN OF BIOLOGICAL THERAPY IN CHRONIC INFLAMMATORY DISORDER: AN OBSERVATIONAL STUDY

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**Background:** Cost of biologics in rheumatology is a prime concern in India. Due to lack of reimbursement system, a majority of the patients need to pay from their pocket for the therapy.

**Objectives:** Our objective was to estimate the cost-effectiveness in patients with the chronic inflammatory disorder on biological therapy with modified dosing regimen in patients of a tertiary care clinic.

**Methods:** In this retrospective observational study, data were captured from patients' record in a tertiary care centre located in North India who received biological therapy in rheumatology care practice between 1 January 2013 and 31 December 2017. Modification in the dosing pattern was carried out in the patients and cost of therapy were estimated. These patients, who carried out the therapy, were monitored for any safety outcomes for up to 72 weeks.

**Results:** During the study period, 342 patients received modified dosing of biologicals indicated for rheumatoid arthritis and spondyloarthritis. The cost comparison of biologicals is shown in table 1. Among all, 44 (12.86%) patients got reimbursement/claims from central and state government agencies. There were 73 (21.34%) patients who were followed up to 72 weeks (minimum possible) of the period for safety assessment. These patients achieved remission or low disease activity and after six months, mean DAS28 (mean  $\pm$ SD) was 2.26 $\pm$ 0.83, BASDAI (mean  $\pm$ SD) was 2.32 $\pm$ 0.98 and DAPSA (mean  $\pm$ SD) was 3.11 $\pm$ 1.05. A total 11 (3.21%) cases of known adverse events including hematuria (1.05% patient with etanercept), pneumonia (4.34% patient with tocilizumab), sinusitis (3.63% patient with infliximab), mild fungal infection (1.81% patient with infliximab) and urinary tract infection (5.26% patient with adalimumab) were reported. One patient (1.05% patient with rituximab) diagnosed with tuberculosis and diabetes after 37 months of initiation of rituximab and one case of hospitalisation was seen due to community-acquired pneumonia in the patient receiving infliximab. Two cases of mortality were reported in patients receiving etanercept after 18 months (due to clinical parkinsonism with aspirational pneumonia) and adalimumab after one month (reason unknown). After modified dosing, the patients tend to remain longer on therapy with no new safety signal.

**Abstract AB0422 – Table 1.** Cost Comparison of biologicals in protocolled vs modified dosing

Biologics	Number of Patients (%) n=342	Monthly Cost of Protocol Driven Dosing (euro/month)	Monthly Cost of Modified Dosing (euro/month)	Cost Benefit for the Patient (euro/month)
Etanercept	112 (32.7%)	303.12 €	151.56 €	151.56 €
Rituximab	95 (27.7%)	118.09 €	58.98 €	59.11 €
Adalimumab	57 (16.6%)	290.49 €	145.25 €	145.25 €
Infliximab (3 mg/kg body weight)	55 (16%)	252.60 €	151.56 €	101.04 €
Tocilizumab (8 mg/kg body weight)	23 (6.7%)	353.64 €	176.82 €	176.82 €

**Conclusions:** In developing countries, out of pocket biological cost can be brought down with a lower dose than suggested. In this study, our data show comparable safety and efficacy of biologicals achieved till 72 weeks with modified dosing regimen.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrhumdis-2018-eular.6119

**AB0423 SEVERE INFECTIONS IN RHEUMATOID ARTHRITIS (RA) ARE RELATED TO THE USE OF BIOLOGIC DMARDS. ASSESSMENT OF REAL-LIFE PATIENTS**

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**Background:** Current strategies for treatment of RA promotes early use of synthetic (s-)DMARDs, their combination, or biologic (b-)DMARDs to achieve remission or low-disease activity. However, such strategies are related to a wide variety of adverse effects, from mild to life threatening. Infections could be detected more frequently among patients with b-DMARDs, although comorbidities, steroid use, chronic accumulated damage, or disease activity could bias such conclusions.

**Objectives:** To investigate the frequency and severity of infections comparing RA patients users of s-DMARDs or b-DMARDs in a long-term period.

**Methods:** Patients were selected from our RA Clinic. Those with at least 5 years using b-DMARD were compared with patients on s-DMARD, each one matched by disease duration, age, and comorbidities in a 1:1 ratio. Demographic features, disease characteristics, number and nature of infections during the follow-up, as well as disease activity, and treatment were recorded. Infections were considered as severe when it required hospitalisation or intravenous antibiotics. Comparison between groups was made with X<sup>2</sup> or t-test as required.

**Results:** A total of 200 patients were prospectively assessed, 100 per group, mean age was 63.5 $\pm$ 12.03 year-old, 91% were female, 78% were RF or ACPA positive, 20% had diabetes mellitus, and 3% other relevant comorbidities. When patients starting the use of b-DMARD, they had more active disease than those in the s-DMARD group (DAS28=4.99 $\pm$ 1.5 vs. 3.91 $\pm$ 1.2; p=0.01). Throughout 5 years of follow-up, there were 18 episodes of severe infections in the b-DMARDs group, and 2 episodes in the s-DMARD group (p=0.01); number of non-severe infections was 569 vs. 577 in such period, respectively (p=NS). No association was observed between severe infections and presence of diabetes mellitus, cumulative annual dose of prednisone, or DAS28, which did not differ in any other measure between groups. Sixteen patients in b-DMARD had severe infections: 6 acute pyelonephritis, 4 pneumonia, 4 acute bronchitis, 1 infectious diarrhoea, 1 emphysematous cystitis, 1 septic arthritis, and 1 haemorrhagic dengue compared with two severe infections in the s-DMARDs group: 1 pneumonia and 1 infectious diarrhoea. Median of hospitalisation days was 4.5, and no deaths were recorded. Infectious agents isolated were *E. coli*, *C. albicans*, *Salmonella* sp., and *P. aeruginosa*. The most frequent non-severe infections were upper respiratory disease, urinary tract infection, herpes zoster, acute diarrhoea, and bacterial vaginosis. Notoriously, 11 episodes of severe infection occurred in the first 2 years of b-DMARD use (7 in first, and 4 in second year), the other 7 in remaining 3 years. b-DMARDs more frequently used were etanercept, rituximab, adalimumab, certolizumab pegol, and tocilizumab, without association between severe infections and any biologic agent.

Item	b-DMARD group	s-DMARD group	p value
Gender MF (n%)	6/94 (6%/94%)	12/88 (12%/88%)	NS
Age years (mean $\pm$ SD)	62.64 $\pm$ 10.14	64.43 $\pm$ 13.63	NS
BMI Kg/m <sup>2</sup> (mean $\pm$ SD)	27.23 $\pm$ 4.61	26.95 $\pm$ 4.81	NS
Disease duration months (median)	156	156	NS
Initial DAS28 (mean $\pm$ SD)	5.14 $\pm$ 1.37	3.99 $\pm$ 1.26	0.001
Average cumulative annual prednisone dose	386.12	378.77	NS
Diabetes mellitus yes/no (n%)	22	21	NS
Other comorbidities yes no (n%)	5	2	NS
Severe infections yes/no (n%)	18	2	.003
Average patient's annual non-severe infections	1.154	1.138	NS

**Abstract AB0423 – Figure 1**

**Conclusions:** b-DMARDs use in our setting, combined with low dose methotrexate, reach higher frequency of severe infections than s-DMARDs, irrespective of comorbidities, steroid use or disease characteristics including disease activity.

**Disclosure of Interest:** None declared

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**AB0424 IL-6 RECEPTOR BLOCKADE INDUCED A DIFFERENT IMMUNE RESPONSE IN RHEUMATOID ARTHRITIS PATIENTS WITH AND WITHOUT REMISSION**

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**Background:** Tocilizumab (TCZ) is a humanised antibody that blocks IL-6 receptor. Despite its effectiveness in rheumatoid arthritis (RA), there are patients that do not respond to the IL-6R blockade. The immune characteristics that would explain this lack of response are not known.

**Objectives:** Our aim was to determine the tocilizumab-induced changes in CD4 +T cells of patients that achieve, or not, remission at 12 m.

**Methods:** Prospective, multicenter study in 47 RA patients treated with TCZ during one year following standard clinical practice. Demographic, disease and treatment characteristics were collected at each visit. Ultrasound (US) grey scale and power doppler were assessed for joints and tendons using a semiquantitative scale from 0–3 points. Phenotyping of T lymphocytes was determined by flow cytometry and the plasma cytokine concentration was quantified by ELISA.

**Results:** Forty seven patients were treated with a mean age of 54 $\pm$ 11 y and 85% were women. Years of disease were 13 $\pm$ 8. We segregated patients according to the DAS28-remission. 44% achieved remission at month 12. We observed that absolute counts of neutrophils and CD4 +T lymphocytes decreased significantly in the remission group but not in the other one. Both memory and naïve CD4 +T

cells decreased in the remission group. The analysis of T cells classified according to chemokine receptors showed that memory ( $29.1 \pm 4.0$  vs  $22.7 \pm 2.7 \times 10^4$  cells/mL;  $p=0.06$ ) and naïve ( $22.6 \pm 4.1$  vs  $17.2 \pm 2.8$ ;  $p=0.04$ ) CD4 +with CXCR3 +and with CCR4 +were the subsets that decreased significantly in the remission group but not in the non-remission group. Since the expression of chemokine receptors defines the different Th subpopulations, we analysed them in the two groups of patients. Th1 tended to decrease in the remission group ( $3.5 \pm 0.7$  vs  $2.5 \pm 0.4$ ;  $p=0.06$ ) and Th9 decreased significantly in both groups ( $R: 5.0 \pm 0.8$  vs  $2.5 \pm 0.3$ ;  $p=0.006$  and Non R  $5.5 \pm 0.8$  vs  $3.1 \pm 0.4$ ;  $p=0.001$ ). In regard to the cytokines produced by CD4 +T lymphocytes, IL-17 ( $2.1 \pm 1.1$  vs  $1.2 \pm 0.5$  ng/ml;  $p=0.04$ ) and VEGF ( $0.5 \pm 0.2$  vs  $0.3 \pm 0.1$  ng/ml;  $p=0.05$ ) but not IL-6 and IL-22 changed significantly in the remission group. Interestingly, IL-17 and VEGF correlated with US findings before the initiation of the treatment (grey scale  $R=0.378$ ,  $p=0.01$  and  $R=0.322$ ,  $p=0.03$ ; power Doppler  $R=0.415$ ,  $p=0.004$  and  $R=0.320$ ,  $p=0.03$  respectively).

**Conclusions:** Tocilizumab induced changes in specific subsets of CD4 +T cells and their inflammatory associated cytokines in the remission group.

**Disclosure of Interest:** None declared

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**AB0425 PREVALENCE AND RISK FACTORS OF SERIOUS INFECTIONS IN RHEUMATOID ARTHRITIS PATIENTS RECEIVING THE BIOLOGIC/TARGETED SYNTHETIC DMARDs: A PROPENSITY SCORE ANALYSIS FROM THE HONG KONG BIOLOGICS REGISTRY**

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**Objectives:** To study the prevalence and risk factors for serious infections in rheumatoid arthritis (RA) patients receiving the biologic/target synthetic (b/ts) DMARDs.

**Methods:** Patients who fulfilled the EULAR/ACR criteria for RA and were ever treated with b/tsDMARDs were included. Withdrawal of b/tsDMARDs due to serious adverse events (SAEs) and serious infections (SIs) was analysed. Demographic data, medical comorbidities and concomitant use of glucocorticoids and csDMARDs were retrieved and their contribution to SIs was evaluated by logistic regression. The propensity score for SIs was calculated and patients were stratified into 5 quintiles. The hazard ratios (HRs) of SIs with respect to individual b/tsDMARDs in each quintile were studied by Cox regression.

**Results:** Up to December 2017, 2355 courses of b/tsDMARDs were used in 1355 RA patients (83% women; age  $54.0 \pm 12.7$  years). The usage of various b/tsDMARDs was: adalimumab(12%), etanercept(24%), infliximab(17%), golimumab(9.4%), certolizumab(0.9%), tocilizumab(19%), rituximab(6.6%), abatacept(7.7%) and tofacitinib(2.7%). After a follow-up of 5056 patient-years, 1433 courses of b/tsDMARDs were discontinued, with major reasons being inefficacy (50%), SAEs (22.4%) and cost (8.4%). Among those b/tsDMARD courses terminated because of SAEs, 32% were due to SIs (103 episodes). The rate of SIs was 1.17/100 patient-years. The commonest causes of SIs were pulmonary tuberculosis (TB) (41%), severe pneumonia (33%), soft tissue infection (6.8%), atypical TB (2.9%), urogenital sepsis (2.9%), septic arthritis (2.9%), hepatobiliary/gastrointestinal sepsis (2.9%), central nervous infection (1%), severe viral infections including herpes zoster (5.8%), and opportunistic infections (2.9%). A logistic regression model showed that increasing age (OR1.02 [1.001–1.04 per year]), male sex (OR1.88 [1.08–3.26]) and concomitant chronic obstructive pulmonary disease/asthma (OR2.55 [1.05–6.23]) were risk factors significantly associated with SIs. The rate of TB infection was highest in users of infliximab (2.32/100 patient-years), followed by tofacitinib (1.47), adalimumab (1.27), etanercept (0.62) and tocilizumab (0.36). Non-TB SIs occurred most frequently with infliximab (2.32/100 patient-years), tofacitinib (1.47) and abatacept (1.15). In the quintile of patients with the highest propensity score for SIs, infliximab had the highest withdrawal rate due to SIs (18%), followed by tofacitinib (10%), etanercept (8%), adalimumab (6%), abatacept (2.8%) and tocilizumab (2.6%). Cox regression revealed the following HRs for SIs with reference to adalimumab: infliximab (2.81 [0.80–9.88]), tofacitinib (HR 2.12 [0.19–23.4]), etanercept (HR 0.82 [0.22–3.11]), abatacept (HR 0.41 [0.04–3.98]) and tocilizumab (HR 0.38 [0.06–2.26]). Concomitant low-dose glucocorticoid was associated with an insignificantly increased risk of SIs only in the three quintiles of patients with lower propensity to SIs.

**Conclusions:** SIs causing withdrawal of b/tsDMARDs in patients with RA account for one-third of all SAEs. Increasing age, male sex and concomitant chronic chest conditions were independent risk factors for SIs. Infliximab was associated with the highest rates of serious TB and non-TB infection, and this observation was consistent in all quintiles of patients with different propensity to SIs.

**Disclosure of Interest:** None declared

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**AB0426 EFFICACY OF MONOTHERAPY OF THE BIOLOGIC DMARDs IN PATIENTS WITH RHEUMATOID ARTHRITIS: REAL LIFE DATA FROM THE HONG KONG BIOLOGICS REGISTRY**

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**Objectives:** To report the prevalence and efficacy of biologic DMARD (bDMARD) monotherapy in real life treatment of rheumatoid arthritis (RA).

**Methods:** RA patients registered in the Hong Kong Biologics Registry who were receiving bDMARD monotherapy (without concomitant conventional synthetic DMARDs [csDMARDs] except low dose prednisolone) were identified. The efficacy (clinical response and drug retention rate) of bDMARD monotherapy was compared with bDMARD combination therapy (with csDMARDs) using statistical tests.

**Results:** From December 2007 to April 2017, 2123 courses of bDMARDs/tsDMARDs were used in 1250 RA patients (83% women, mean age at therapy  $53.8 \pm 12.7$  years). Among 1881 courses of therapies with complete data, 164 (8.7%) was monotherapy at baseline. Low dose prednisolone (<10 mg/day) was used in 56% of these courses. In the combination group, the commonest csDMARDs used in combination with bDMARDs were methotrexate (79%), sulphasalazine (27%), hydroxychloroquine (25%) and leflunomide (21%). The bDMARDs/tsDMARDs most frequently used as monotherapy were tofacitinib (14.3%), tocilizumab (11.6%) and abatacept (11.2%). Overall, the non-TNF was more commonly used as monotherapy (11.2%) than the anti-TNF bDMARDs (7.4%). At 6 months of bDMARD/tsDMARD therapy, the DAS remission rate was non-significantly higher in the combination than monotherapy group (11% vs 5%;  $p=0.42$ ). The change in DAS28 score was also non-significantly greater in the combination group ( $-1.95 \pm 1.26$  vs  $-1.68 \pm 1.56$ ;  $p=0.30$ ). The difference in 6 month efficacy between the combination and monotherapy groups was greater in anti-TNF users. The overall cumulative withdrawal rate of the bDMARDs/tsDMARDs due to either inefficacy or serious adverse events (SAEs) was 0.55 at 3 years and 0.47 at 5 years. The anti-TNF biologics had a significantly higher withdrawal rate than the non-TNF biologics (hazard ratio [HR] 1.83 [1.56–3.14];  $p<0.001$ ). In Cox regression models, monotherapy of the bDMARDs was not significantly associated with drug withdrawal due to inefficacy (HR 0.95 [0.53–1.71];  $p=0.87$ ) or SAEs (HR 1.27 [0.51–3.19];  $p=0.61$ ) after adjustment for age, sex, anti-TNF (vs non-TNF) biologic use, previous use of bDMARDs (vs first time use) and DAS28 at baseline. Separate analyses of the anti-TNF and non-TNF biologics again did not reveal a significant relationship between monotherapy of the biologics with the drug withdrawal due to inefficacy or SAEs after adjustment for age, sex, previous use of bDMARDs and disease activity at baseline (HR 1.002 [0.56–1.80];  $p=0.99$  for anti-TNF and HR 1.20 [0.47–3.08];  $p=0.70$  for non-TNF biologics, respectively).

**Conclusions:** Monotherapy of bDMARD/tsDMARD was used in 8.7% of our RA patients in real life practice, probably due to intolerance, inefficacy or non-compliance to the csDMARDs. Short-term efficacy tended to be better with bDMARDs/csDMARDs combination, especially in the anti-TNF biologics, but the long-term drug retention rate was similar between bDMARD monotherapy and combination therapy with the csDMARDs.

**Disclosure of Interest:** None declared

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**AB0427 COMPARATIVE SAFETY OF ABATACEPT VS TOFACITINIB IN ADULTS WITH MODERATE-TO-SEVERE RA: A SYSTEMATIC LITERATURE REVIEW AND NETWORK META-ANALYSIS**

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**Background:** While targeted (biologic or synthetic) DMARDs are overall highly effective in improving symptoms and function in RA patients (pts), their comparative safety relative to each other remains inconclusive.

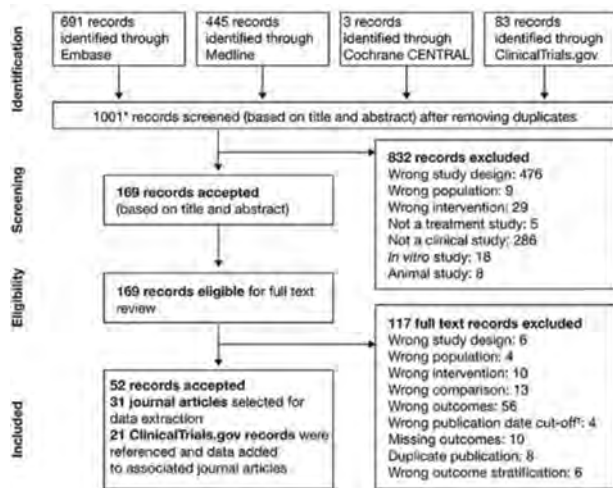
**Objectives:** Compare the safety of abatacept (ABA) and tofacitinib (TOF) through a systematic literature review (SLR) and network meta-analyses (NMA).

**Methods:** A comprehensive search of randomised and non-randomised clinical trials was conducted across MEDLINE, Embase and Cochrane CENTRAL databases from inception to June 2017. The PICO framework (population=moderate to severe RA pts; intervention=ABA and TOF; comparison=placebo and other RA therapies; outcome=AEs, treatment-related AEs [TrAEs], serious infections and treatment-related deaths) was used to design searches and define the eligibility of studies for inclusion. Additional searches were performed on relevant conference proceedings and the US clinical trials registry from the past 2 years (figure 1). Data configuration was performed by expert methodologists using DOC Data 2.0 (Doctor Evidence, Santa Monica, CA). NMAs using the random-effects model were used to examine the risk of AEs, TrAEs and serious infections in



conventional DMARD-experienced ABA- and TOF-treated pts. Treatment-related death was not analysed in an NMA due to insufficient data.

**Results:** Thirty-one randomised controlled trials (n=13,978) were included for data extraction. Of these, ABA and TOF were examined in 16 and 15 trials, respectively. There were no head-to-head comparisons of ABA vs TOF. Most of the trial population were Caucasian (48%–98% across trials), had an average age ranging from 40 to 60 years and were predominantly female (60%–90%). Of the trials, 26 included a US population and 5 a non-US population. Out of 11 studies reporting treatment-related mortality, one study reported four deaths for pts on TOF 5 mg (n=321) within a 1 year follow-up. No such deaths were reported for ABA pts. The NMAs showed no significant differences in the risk of TrAEs for pts on TOF 5 or 10 mg compared with ABA with/without MTX (TOF 5 mg +MTX vs ABA+MTX: risk ratio [RR] 1.1, 95% CI: 0.77, 1.5; TOF 10 mg vs ABA: RR 1.1, 95% CI: 0.78, 1.6). These findings remained consistent for the risk of total AEs and serious infections.



Abstract AB0427 – Figure 1. PRISMA Diagram Showing Study Selection

\*One reference identified manually from a ClinicalTrials.gov record

<sup>†</sup>Wrong publication date cut-off: meeting abstract published before 2015

**Conclusions:** Without head-to-head trials, the data available to make comparisons between abatacept and TOF are limited. Even after conducting an SLR and NMAs, precision is lacking in estimating differences. Additional studies, such as real-world observational analyses with larger patient samples and higher incidence of measured outcomes, are needed to further examine the safety differences of abatacept vs TOF.

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#### AB0428 PREFERENCES IN THE USE OF BIOLOGIC DRUGS AND ADVERSE EVENTS IN PATIENTS WITH RHEUMATIC DISEASE FROM A NATIONAL BIOLOGICS REGISTRY IN MÉXICO

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**Background:** National registries of biologic drugs have proven to be valuable tools in following patients with rheumatic disease and some outcomes in real-life situations.

**Objectives:** The objective of this study was to describe Mexican Rheumatologists' preferences when treating patients with biologic drugs and to analyse factors associated to the use of this therapy.

**Methods:** Data from patients undergoing biologic treatment in México is gathered into the BIOBADAMEX online database, which is part of the BIOBADAMERICA

initiative and based on the BIOBADASER Phase 3 platform. Phase 3 in México started gathering patient data in April 2016 and to date has information on 216 patients. The database collects information such as gender, age, diagnosis, disease duration, biologic treatment, DMARD treatment, concomitant therapy, motives for discontinuation of biologics, comorbidities, adverse event (AE) severity, infection site and germ involved. Descriptive statistics were applied on the data collected from April 2016 to January 2018.

**Results:** We analysed data on the use of 267 biologic treatments in 216 patients. Most of them receive biologic therapy through socialised medical insurance programs which may have led to bias. 89.1% of patients were female, mean age 49 ±15.2 (4–85) years, 42.5% belonging to the <50 group. 69.9% of patients in the registry have RA, 12.5% AS and 5.5% PsA. Mean disease duration is 11±8.9 (0–58) years. The most commonly used biologic overall is Abatacept (15.3%), followed by Adalimumab (13.8%), Tocilizumab (11.2%), Certolizumab (10.1%), Golimumab (8.6%), Rituximab (8.2%), Etanercept biosimilar (7.4%), Etanercept (6.3%), Infliximab (4.1%) and Benlystia (1.1%). All others, including JAK inhibitors, are used in <1% of patients. The preference for first biologic drug was Etanercept (32.4%), followed by Adalimumab (12%), Infliximab (8.3%), Rituximab and Tocilizumab (5.5% each) and Abatacept (2.7%). Most treatments were stopped due to lack of efficacy (60.4%), disease remission (7.4%), other causes (20.1%), AE (4.4%), with the rest of the causes each affecting <5% of patients. The most commonly used DMARD were Methotrexate (49.8%), steroids (33.3%) and leflunomide (23.2%). Comorbidities were present in 87 patients (40%), the most common being Hypertension (13.4%), Diabetes (7.8%) and Dyslipidemia (6.9%). Non-lymphoma neoplasms were reported in 1.3%. 25% of AE were considered serious but most (70%) were mild. Only 6 patients reported infections with the most common sites being the skin (33.3%), urinary tract (16.6%) and middle-ear (16.6%). The causal germ was often undetermined (60%).

**Conclusions:** When using biologic drugs, TNF inhibitors are the most commonly used initial mechanism of action for the treatment of rheumatic diseases in the BIOBADAMEX registry. Upon treatment failure, patients undergo a switch to another mechanism of action, mainly using Abatacept. Adverse events and infections related to the use of biologics are infrequent, but 40% of patients present chronic comorbidities.

**Disclosure of Interest:** D. Xibillé Speakers bureau: Abbvie, Pfizer, BMS, S. Carrillo Speakers bureau: Abbvie, Pfizer, BMS, Roche, S. Sicsik Speakers bureau: Roche, Pfizer, BMS, F. Irazoqui Speakers bureau: Abbvie, Pfizer, BMS, Roche, A. Ramos: None declared, S. Durán: None declared, M. Saavedra: None declared, L. Barile Speakers bureau: Abbvie, Pfizer, BMS, Roche, G. Olvera: None declared

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#### AB0429 NO DIFFERENCE IN EFFECTIVENESS WITH EITHER ETANERCEPT ORIGINATOR OR BIOSIMILAR AS FIRST LINE BIOLOGIC TREATMENT FOR RHEUMATOID ARTHRITIS

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**Background:** Biosimilars and their reference agents have been shown to be equivalent in clinical trials. In the United Kingdom, etanercept biosimilars (ETA-B) are, since 2016, a first-line treatment option for the management of severe rheumatoid arthritis (RA) defined as no response to 2 or more csDMARDs. However, real world data, including how it compares to the etanercept originator (ETA-O) are lacking.

**Objectives:** This study aims to compare the short-term effectiveness of etanercept originator with its biosimilar in patients with RA when used as a first biologic following csDMARDs.

**Methods:** This study included patients with RA registered with the British Society for Rheumatology Biologics Registers for RA (BSRBR-RA) at the point of starting either ETA-O or an ETA-B since 2011 as their first biologic. Baseline information is collected at drug start and includes demographic and clinical data. Follow-up (FU) data are captured every 6 months and include details on therapy changes, current disease activity, and development of any adverse events. The primary outcome of this study is effectiveness as calculated by change in the 28 joint count disease activity score (DAS28). Only patients with a complete DAS28 at baseline and their 1st FU were included in the final analysis of this study. Hazard ratios (HR) comparing drug survival and risk of first serious adverse event (SAE) between ETA-O and ETA-B patients were calculated using Cox regression.

**Results:** Between January 2010 and 11 December 2017, 1217 and 412 patients starting ETA-O or ETA-B respectively were recruited and had ≥1 FU available. Complete DAS28 data at baseline and 1st FU were available for 740 ETA-O patients and 177 ETA-B patients. Patient characteristics were similar between the 2 cohorts (Table). After adjusting for baseline differences, no difference between groups was seen in DAS28 (p=0.1) or remission status (p=0.1) at 1st FU.

Nine (5%) and 48 (6%) of ETA-B and ETA-O patients had stopped their respective treatments by the 1st FU. The adjusted hazard ratio for stopping ETA-O versus ETA-B over this time period was similar (HR=0.8 (0.4-1.6); p=0.5). Risk of SAEs over the first 6 months was also similar between groups (HR (ETA-B versus ETA-O)=0.6 (0.3-1.1); p=0.1), with 10 (6%) and 73 (10%) SAEs reported in ETA-B and ETA-O patients respectively until 1st FU.

Abstract AB0429 – Table 1

Patients who are	Biological naive	Switched from a non-originator	Switched from originator
<b>Number</b>	36	17	5
<b>Biosimilar</b>			
Infliximab biosimilar	28 (77%)	17 (100%)	3 (60%)
etanercept biosimilar	8 (22%)	0 (0%)	2 (40%)
<b>ILAR class</b>			
Persistent Oligoarthritis	4 (11%)	4 (24%)	0 (0%)
Extended Oligoarthritis	8 (22%)	5 (29%)	1 (20%)
RF Negative Polyarthritis	13 (36%)	4 (24%)	1 (20%)
RF Positive Polyarthritis	0 (0%)	0 (0%)	0 (0%)
Psoriatic Arthritis	2 (6%)	3 (18%)	3 (60%)
Enthesitis Related Arthritis	8 (22%)	1 (6%)	0 (0%)
Unknown	1 (3%)	0 (0%)	0 (0%)
<b>Active uveitis at start of therapy</b>	4 (11%)	7 (41%)	2 (40%)
<b>Female</b>	22 (61%)	12 (71%)	2 (40%)
<b>Age (years)</b>	13 (9-15)	14 (11-15)	13 (12-16)
<b>Disease duration (years)</b>	2 (1-5)	6 (3-10)	7 (6-13)
<b>Active Joints (71 joints)</b>	2 (1-4)	0 (0-2)	0 (0-0)
<b>Limited Joints (71 joints)</b>	2 (1-4)	2 (0-4)	0 (0-1)
<b>Physician Global (0-10cm)</b>	2 (2-4)	1 (0-2)	0 (0-0)
<b>Patient Global (0-10cm)</b>	5 (1-7)	2 (0-4)	2 (0-4)
<b>Pain VAS (0-10cm)</b>	4 (1-7)	4 (2-5)	1 (0-1)
<b>CHAQ (0-3)</b>	1 (0-3)	0 (0-2)	0 (0-1)

All data presented are number (percentages) or median (interquartile range). International League of Associations for Rheumatology (ILAR), Rheumatoid Factor (RF), Visual Analog Scale (VAS), Childhood Health Assessment Questionnaire (CHAQ).

**Conclusions:** In the UK, etanercept biosimilars are now frequently used as first-line biologics in RA patients. These short-term follow-up data demonstrate in routine clinical care that ETA-B appears to be equivalent to ETA-O in terms of short term effectiveness, drug survival and safety.

**Disclosure of Interest:** None declared

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#### AB0430 SUBJECTIVE ASSESSMENTS OF PATIENTS WITH RHEUMATOID ARTHRITIS REPORTED THAT BIO-HOLIDAY THERAPY BROUGHT THEM FINANCIAL AND PSYCHOLOGICAL IMPROVEMENTS

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**Background:** At EULAR 2016 and 2017 we reported that it is possible to maintain disease activity, radiographic progression, physical function, and bone metabolism status in rheumatoid arthritis (RA) patients with clinical disease activity index (CDAI) remission using the biologic agents (Bio)-holiday therapy. Currently, in RA therapy, subjective assessment of patients as well as objective assessment of doctors is becoming more important<sup>(1)</sup>. How does the patient think about Bio-holiday therapy?

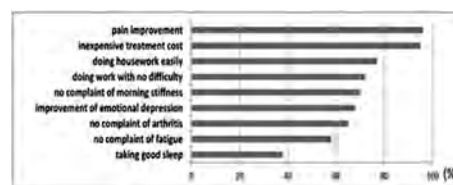
**Objectives:** We conducted questionnaire survey in RA patients with CDAI remission who underwent Bio-holiday therapy or Bio-continue therapy to evaluate the benefits of their therapies and to clarify the number of patients concerned about flare-up.

**Methods:** The first and second survey comprised 9 and 11 questions, respectively; each provided predefined answers. In the first survey, we questioned 85 RA patients in CDAI remission: those treated with any DMARDs. We asked them about the expected elements of RA treatment. In the second survey, we questioned two groups of patients with CDAI remission; those treated with Bio-continue after achieved CDAI remission (BC group: n=26) and those treated with Bio-holiday therapy after achieved CDAI remission (BH group: n=28). We asked them by a questionnaire what was expected from the treatment effect and how much they felt anxiety about the activity of daily life (ADL) deterioration, RA flare-up and treatment costs.

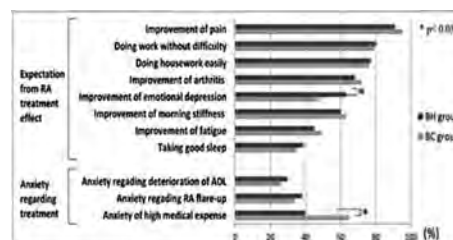
For Bio-holiday therapy, patients with CDAI remission were treated with golimumab or tocilizumab. Bio was discontinued if they achieved CDAI remission. Patients were treated with Bio within 3 months after falling out of CDAI remission. They could be taken off Bio again when they reached CDAI remission.

**Results:** In the first survey (figure 1), pain improvement and inexpensive treatment were the most and the second expected treatment effect, respectively. In the second survey (Figure 2), for questions regarding expectation from RA treatment effect, the patients reported that the most beneficial points was pain improvement and the second one was the active daily living without difficulty. Patients in both groups equally recognised reduction in pain and recovery of activities of daily

living, which are important for patients with CDAI remission. Interestingly, improvement of emotional depression is the higher in BH group than in BC group. For question regarding anxiety, the high medical expense was the most anxious point. Anxiety regarding high medical expenses in BH group was lower than that in BC group. Anxiety regarding flare-up was equal to that in BC group as patients were assured of retreatment with Bio in case of a flare-up.



Abstract AB0430 – Figure 1. Questionnaire results of all RA patients with CDAI remission



Abstract AB0430 – Figure 2. Questionnaire results of RA patients with CDAI remission who underwent Bio-holiday therapy or Bio-continue therapy

**Conclusions:** Patients in both groups were equally satisfied with the improvement of their disease activity and progression of ADL. Reduction of the anxiety regarding treatment costs and flare-up in Bio-holiday therapy also helped to improve psychological aspects. Therefore, we recommended Bio-holiday therapy for RA patients with CDAI remission.

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**Disclosure of Interest:** None declared

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#### AB0431 EARLIER AGE AT THERAPY INITIATION IS ASSOCIATED WITH BETTER RESPONSE TO TOCILIZUMAB THERAPY IN PATIENTS WITH JUVENILE IDIOPATHIC POLYARTHRITIS

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**Background:** The use of therapy with anti-cytokine biologics in routine practice has significantly increased the percentage of children showing good response to therapy and reduced the time to achieve pharmacological remission. Nevertheless, the problem related to selecting the optimal drug for a certain patient still remains to be solved.

**Objectives:** This study was aimed at identifying clinical and laboratory parameters associated with response to tocilizumab (TOC) treatment in patients with RF-negative polyarticular JIA.

**Methods:** The prospective study to assess TOC efficacy involved 55 patients with RF-negative polyarticular JIA aged 9.42 years (IQR 5.96–13.42), with females (85.5%) predominating was conducted at the National Medical Research Centre of Children's Health (Moscow). Treatment efficacy was evaluated using the ACRPed criteria; Wallace's criteria were used to assess whether a patient had reached inactive disease or remission. The potential baseline characteristics associated with treatment response were identified using univariate and multivariate logistic regression analyses. Baseline factors included the clinical, laboratory, and anamnestic data.

**Results:** TOC therapy showed high efficacy in children with RF-negative polyarticular JIA: 81.8/67.3/47.3/23.6% of patients reached the ACR30/50/70/90 criteria for the end of follow-up, respectively. The median time of achieving at least 30% improvement from baseline (ACR30) was 1 month (IQR 1:3).

Univariate analysis showed that earlier age at initiation of Tocilizumab therapy, higher physician's global assessment score using the 100-point Visual Analogue Scale, and longer morning stiffness were the factors associated with reaching ACR90. Younger age at therapy initiation, greater number of swollen joints and joints with limited range of motion, and history of using fewer biologicals are the factors associated with reaching inactive disease and remission. However, multi-factorial analysis showed that only earlier age at initiation of TOC therapy was a statistically significant factor associated with reaching the best response to therapy in all the models.

**Conclusions:** Earlier initiation of TOC therapy is associated with higher chances for reaching ACR90 and pharmacological remission in patients with RF-negative polyarticular JIA. Further studies in larger cohorts are needed to identify the optimal age at therapy initiation.

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#### AB0432 BIOLOGIC DMARDS TREATMENT RETENTION IN PATIENTS WITH RHEUMATOID ARTHRITIS ACCORDING TO THE MOSCOW ARTHRITIS REGISTRY (MERA)

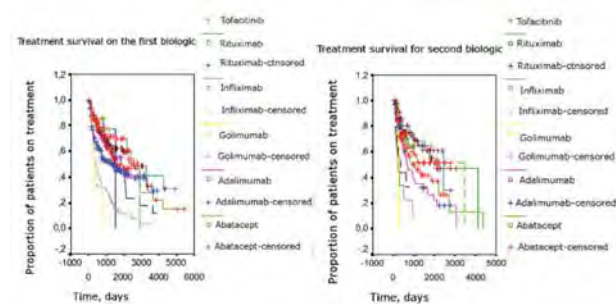
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**Background:** Retention on treatment is a good index of efficacy and safety of treatment used in the real clinical practice. These data may be useful to planning the treatment among some years.<sup>1,2</sup>

**Objectives:** To compare the drug survival of biological therapies.

**Methods:** We followed rheumatoid arthritis patients treated with biologics DMARD and registered in MERA 2012–January 2018. All patients had more than one visit in the registry.

**Results:** We analysed 799 patients (mean age 57.3±13, mean diseases duration 15.6±10.3 years). The average time until a change of treatment for infliximab was 399 days – the shortest treatment duration. Abatacept (median survival – 2922 days) demonstrated significant superiority over adalimumab (1339 days) ( $p<0.001$ ), infliximab (399 days) ( $p<0.001$ ), rituximab (2557 days) ( $p=0.004$ ) and etanercept (1492 days) ( $p=0.035$ ) when they were used as the first biologic drug. Among second-line therapy, the longest treatment survival has etanercept (3435 days), the shortest – infliximab (212 days).



Abstract AB0432 – Figure 1

**Conclusions:** The results of the trial show the differences in treatment survival of some biologics. It can be reasonable to take these significant differences into consideration by the long-term planning of the biologic treatment of rheumatoid arthritis patients.

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**Disclosure of Interest:** None declared

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#### AB0433 TNF-INHIBITORS AND ANTI-B-CELL TREATMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS. REAL-WORLD DATA FROM THE RUSSIAN NORTH-WESTERN BIOLOGICAL TREATMENT COHORT

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North-Western State Medical University named after I.I. Mechnikov, Sankt-Peterburg, Russian Federation

**Background:** Biologics are drugs that improved the status of rheumatoid arthritis (RA). At the same time real-world data (RWD) from large cohorts can give some additional information about efficacy and safety of the biological agents.

**Objectives:** The aim of the study was to analyse the efficacy and safety of biological treatment in large prospective cohort during 102 weeks of treatment.

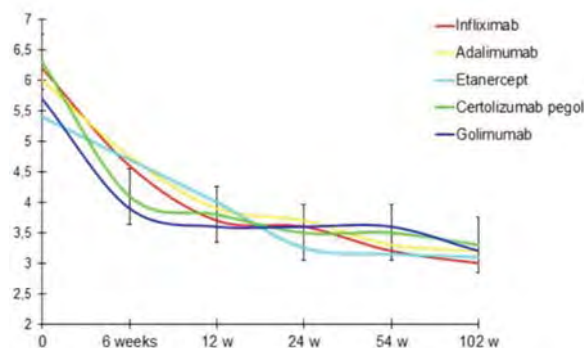
**Methods:** The data from 1 400 patients on biological treatment from North-Western State Medical University Biological Treatment Cohort Study (St. Petersburg, Russia) were analysed. In final analysis data from 758 patients with RA/EULAR 2010 criteria, were included. Following drugs were used: adalimumab (n=22), certolizumab pegol (n=62), etanercept (n=64), golimumab (n=21) and infliximab (n=69), rituximab (n=520). The disease activity index (DAS28) and high-sensitive C-reactive protein (C-RP) were evaluated as markers of RA activity. Side effects were registered during the study.

**Results:** RA activity, demographic characteristics, and concomitant treatment (including methotrexate, glucocorticoids, NSAIDs, analgesics) at baseline were similar in all the treatment groups ( $p\geq 0.05$  for all the parameters). The faster response was found in golimumab and certolizumab pegol patients ( $p$  and  $It$ ; 0.01 for difference of DAS28 in golimumab, certolizumab pegol treatment and other treatment groups at week 6), figure 1. After week 12 the similar efficacy of all the TNF $\alpha$ -blockers (figure 1).

RA activity, demographic characteristics, and concomitant treatment (including methotrexate, glucocorticoids, NSAIDs, analgesics) at baseline were similar in all the treatment groups ( $p\geq 0.05$  for all the parameters). The faster response was found in golimumab and certolizumab pegol patients ( $p<0.01$  for difference of DAS28 in golimumab, certolizumab pegol treatment and other treatment groups at week 6), figure 1. After week 12 the similar efficacy of all the TNF $\alpha$ -blockers (figure 1). C-RP levels were similar in all the treatment groups in all time-points ( $p\geq 0.05$ ). DAS28 (mean  $\pm$ SD) in RA patients, treated with rituximab, at baseline, and at weeks 24, 54, and 102 was 6.6 $\pm$ 2.4, 3.7 $\pm$ 1.7, 3.62 $\pm$ 2.1 and 3.2 $\pm$ 2.05, respectively;  $p\geq 0.05$  for the differences with all another treatment groups at the same time-points.

The most frequent side-effects were opportunistic infections, OR=1.8 [95% CI 1.4–2.1]. Risk of infections was higher in patients, receiving monoclonal antibodies to TNF $\alpha$ , as compared to other TNF $\alpha$  inhibitors ( $p<0.01$  for differences between infliximab/adalimumab/golimumab and etanercept, and  $p<0.05$  for differences between infliximab/adalimumab/golimumab and certolizumab pegol).

The risk of cancer in RA patients on biological treatment and in total Russian population (including lymphomas and skin cancer) was comparable: for all the tumours OR=0.98 [95% CI 0.76–1.26], for lymphomas OR=1.23 [95% CI 0.92–1.41], for skin cancer OR=1.11 [0.88–0.36].



Abstract AB0433 – Figure 1. The dynamics of the disease activity index DAS28 in patients with RA receiving different TNF $\alpha$  blockers

**Conclusions:** According to the RWD from the North-Western Biological Treatment Cohort, the efficacy of all the TNF $\alpha$ -inhibitors and rituximab in RA treatment



after week 12 is the same. Infections, but not tumours, are the most frequent side-effects of biological treatment in RA patients.

**Disclosure of Interest:** None declared

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AB0434

#### THE INFLUENCE OF BODY MASS INDEX ON THE EFFICACY OF TUMOUR NECROSIS FACTOR BLOCKING THERAPY AND DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** The impact of Body Mass Index (BMI) on efficacy of TNF blocking therapy in Rheumatoid Arthritis (RA) patients and therefore on control of the disease is an important question.

**Objectives:** The aim of this study is to determine the influence of BMI on the efficacy of TNF blocking therapy in terms of disease activity in patients with RA.

**Methods:** A retrospective, observational study of 168 consecutive RA patients who received subcutaneously (SC) TNF blocking treatment (adalimumab, etanercept, golimumab and certolizumab pegol). Their follow-up data, for at least 26 weeks, and their baseline BMIs were available. The WHO definition for normal weight, overweight and obesity was applied, whereas clinical response was compared by BMI subgroups.

**Results:** The average BMI was 26.83±4.34 kg/m<sup>2</sup> and the baseline Disease Activity Score in 28 joints (DAS28 [ESR]) was high at 5.72±0.84. Mean age was 63.47±12.58 years and 135 (80.36%) were female. The median disease duration was 13.01±8.57 years. Overall, patients with normal weight responded better to treatment regimen, followed by overweight and obese subgroups. After a follow-up period of 26 weeks, the obese group had significantly higher DAS28 (ESR) and Health Assessment Questionnaire (HAQ) than either normal or overweight subgroups (3.26±0.84 vs 2.72±0.78 vs 2.81±0.82, p<0.001, 0.423±0.002 vs 0.076±0.01 vs 0.178±0.01, p<0.001 respectively). Furthermore, obesity was significantly associated with a decreased tendency of achieving week 26 remission, based on DAS28 (<2.6) p:0.002 and normal HAQ (≤0.5) p: 0.003.

**Abstract AB0434 – Table 1.** Summary of responses to TNF-blocking therapy (SC) by BMI category at week 26 in subjects with RA

Variable		% (n/N)			p value [95% CI]
		BMI <25 kg/m <sup>2</sup>	BMI 25-30 kg/m <sup>2</sup>	BMI >30 kg/m <sup>2</sup>	
DAS28 HAQ	Remission (<2.6)	58.18 (22/55)	35.8 (29/81)	0 (0/32)	0.002 [15–16.5]
	LDA (>2.6 – <3.2)	9.09 (5/55)	40.74 (33/81)	37.5 (12/32)	0.001 [16.6–16.7]
	MDA (>3.2 – <5.1)	30.91 (17/55)	23.46 (19/81)	62.5 (20/32)	0.001 [15.2–16.9]
	HDA (>5.1)	1.82 (1/55)	0 (0/81)	0 (0/32)	ns
	<0.5	61.81 (34/55)	58.02 (47/81)	46.88 (15/32)	0.003 [8.9–16.6]

LDA: low disease activity, MDA: moderate disease activity, HDA: high disease activity

**Conclusions:** Patients with RA and higher BMIs demonstrated a diminished clinical response after 26 weeks of SC-administered TNF-blocking treatment compared with their counterparts with lower BMIs.

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**Disclosure of Interest:** None declared

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AB0435

#### THE TREATMENT PATTERN OF TOCILIZUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS IN CHINA: A MULTICENTER OBSERVATIONAL STUDY

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**Background:** Tocilizumab (TCZ) is a humanised monoclonal antibody targeting interleukin-6 receptor. Since TCZ Label for RA has been issued in many countries, administration patterns and dose modifications for managing adverse events (AEs) seems differ depending on clinical opinion. Few data are available from real world practice in China.

**Objectives:** To observe in routine clinical practice the treatment patterns of TCZ in RA patients with regard to persistence on drug and adherence to the licensed label recommendations.

**Methods:** This a 6 month non-interventional, multi-centre study enrolled patients with moderate to severe RA diagnosed per revised 1987 ACR criteria (age ≥18 years) and being treated with TCZ. Data was recorded during routine visit. The primary variable was the proportion of patients on TCZ treatment after 6 months.

**Results:** Of 407 patients from 23 centres in China, 396 were eligible, including 330 (83.3%) women. The mean age was 49.1±13.44 years. The mean RA diagnosis course was 5.4±6.24 years. Among 396 patients, 250 (63.1%) were RF positive, 235 (59.3%) were anti-CCP positive and 123 (31.1%) had anaemia (Hb <90 g/L). Of eligible patients, 293 (74.0%) completed the study. The primary reason of premature termination was treatment costs (n=49, 12.4%). There were 37 (9.3%) patients received anti-TNF biologics previously and 330 (83.3%) received concomitant DMARDs, of which 84 (21.2%), 149 (37.7%) and 97 (24.5%) received single, 2 or ≥3 types of DMARDs, respectively. Methotrexate (n=255, 64.4%) and Leflunomide (n=184, 46.5%) were the most commonly used DMARDs. A total of 126 and 197 patients received corticosteroids or nonsteroidal anti-inflammatory drugs (NSAIDs), respectively. During 6 months observation, 21.0% and 67.7% had TCZ dose modification or discontinuation, respectively. At month 3 and month 6, 161 (40.7%) and 102 (25.8%) kept TCZ treatment, respectively. The mean frequency of TCZ usage was 3.7±1.62. Effectiveness of TCZ was analysed in patients who were still using TCZ at month 6. The mean score of total TJC (28-joint count) at baseline and at month 6 was 11.2±8.0 (n=63) and 2.3±4.12 (n=77), respectively; mean change from baseline was -9.5±8.02 (n=53). The mean score of total SJC (28-joint count) at baseline and at month 6 was 8.0±6.81 (n=63) and 1.7±2.35 (n=77), respectively; mean change from baseline was -6.5±7.2 (n=53). The mean score of DAS28 at baseline and at month 6 was 6.13±1.33 (n=56) and 2.79±1.39 (n=66); mean change from baseline was -3.45±1.48 (n=46). Patients in low disease activity (DAS28 <3.2) or remission (DAS28 <2.6) in those who still using TCZ at month 6 was 63.6% and 51.5%. The mean change from baseline in SDAI and CDAI was -28.03±16.75 (n=41) and -24.25±16.94 (n=51), respectively. Of 396 patients, 90 (22.7%) and 8 (2.0%) experienced at least one treatment-emergent AE and SAE, respectively. One patient died of severe pneumonia.

**Conclusions:** This was the first real-world study in RA patients treated with TCZ in China. The results show that Chinese RA patients have long disease history. TCZ was frequently used in combination with DMARDs, especially with ≥2 types of DMARDs. Compared with the dose recommendations, shorter treatment duration and longer dose interval of TCZ were found in China. TCZ demonstrated effectiveness in treatment of Chinese RA patients in real-life clinical practice with manageable safety profile.

**Acknowledgements:** This study was sponsored by Shanghai Roche Pharmaceuticals Limited.

**Disclosure of Interest:** None declared

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AB0436

#### CONSOLIDATED LONG-TERM SAFETY OF INFlixIMAB IN INFLAMMATORY ARTHRITIS FROM A PROSPECTIVE, OBSERVATIONAL REGISTRY

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**Background:** The Biologic Trial Registry Across Canada (BioTRAC) was a multi-centre, prospective, longitudinal, observational program that gathered and analysed data on inflammatory arthritis patients treated with infliximab (IFX), golimumab and ustekinumab. Patients specifically treated with IFX were recruited from July 2002 to June 2015 and followed up to June 2017.

**Objectives:** The objective of this abstract is to document the final consolidated safety data from the BioTRAC IFX cohort.

**Methods:** Treatment was prescribed by the physician per actual clinical practice or standard of care for rheumatoid arthritis (RA), ankylosing spondylitis (AS) and psoriatic arthritis (PsA); there was no randomised assignments to treatment. There were no restrictions on the use of concomitant medications. At enrolment (baseline) and approximately every 6 months thereafter, information was collected to assess safety, clinical outcomes, quality of life, comorbidities, pharmacoeconomics and treatment regimens.

**Results:** A total of 1390 patients were enrolled and used for this analysis. The proportion of patients by indication was 59.2% for RA (n=890), 25.9% for AS (n=389) and 7.4% for PsA (n=111). The mean (SD) exposure was 3.10 (3.26) years for a sum of 4290.25 patient-years. Treatment with IFX was generally safe, with AEs and SAEs being reported for 64.3% and 19.5% of patients, respectively. The incidence rate of AEs and SAEs was 116.0 and 11.2 events per 100 pt-years, respectively. More specifically, 338 SAEs were reported by 189 (21.2%) RA patients [SAEs/100 pt-yrs: 11.7], 130 SAEs were reported by 60 (15.4%) AS patients [SAEs/100 pt-yrs: 10.5] and 28 SAEs were reported by 22 (19.8%) PsA patients [SAEs/100 pt-yrs: 8.82]. The most commonly reported AE identified was arthralgia, viral upper respiratory tract infection, upper respiratory tract infection and nausea. For SAEs, the most commonly reported SOC ( $\geq 3\%$  of patients) was "Infections and infestations" [5.3% (n=73); 2.16 SAEs/100 pt-yrs] and "Neoplasms benign, malignant and unspecified" [3.5% (n=49); 1.24 SAEs/100 pt-yrs] which occurred at similar rates to the general RA patient population<sup>1</sup> and included two lymphomas [0.1%; 0.05/100 pt-yrs]. Across 3 closely monitored categories of AEs, a total of 302 closely monitored AEs were reported by 293 (21.1%) patients, including cancer (3.7%), lack of efficacy (17.1%) and tuberculosis (0.2%). A total of 21 deaths were reported during the study in 18 RA, 1 AS and 2 PsA patients. Cause of death included MACE (x5), lung cancer (x2), pulmonary fibrosis (x2), pneumonia (x2), respiratory failure, bronchitis, intestinal cancer, throat cancer, intestinal gangrene, disseminated TB, septic shock, procedural complication and drowning. The cause of death was not known for one patient.

**Conclusions:** The results of this longitudinal observational study showed that treatment with IFX was well tolerated in people living with AS, PsA and RA over a 15 year period in a real-world setting.

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**Disclosure of Interest:** D. Choquette Grant/research support from: Janssen Inc., P. Rahman Grant/research support from: Janssen Inc., Consultant for: Janssen Inc., Speakers bureau: Janssen Inc., A. Chow: None declared, R. Faraawi Consultant for: Janssen Inc., Speakers bureau: Janssen Inc., W. Olszynski Consultant for: Janssen Inc., E. Rampakakis: None declared, O. Asin-Milan Employee of: Janssen Inc., B. Osborne Employee of: Janssen Inc., A. Lehman Employee of: Janssen Inc., F. Nantel Shareholder of: Johnson and Johnson, Employee of: Janssen Inc.

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#### AB0437 ADALIMUMAB THERAPY RESULTS IN SUSTAINED RESPONSE IN RHEUMATOID ARTHRITIS PATIENTS OVER 5 YEARS: THE GERMAN NONINTERVENTIONAL AGIL STUDY

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**Background:** Observational studies provide important insights into therapeutic response during daily clinical practice, including data on the effects of long-term treatment.

**Objectives:** To evaluate treatment responses in rheumatoid arthritis (RA) patients during 5 years of adalimumab (ADA) therapy.

**Methods:** We analysed data from a large German multicenter observational study of patients with active RA who initiated ADA therapy during routine clinical care (the AGIL study). Outcomes of interest included Disease Activity Score-28 joints (DAS28), DAS28 therapeutic response as assessed by the statistical critical difference (dcrit.),<sup>1</sup> Health Assessment Questionnaire-Disability Index (HAQ-DI), and patient-reported global health and pain.

**Results:** A total of 4283 patients had data available for analysis at baseline. The mean age was 55.2 years, 74% of patients were female, the mean disease duration was 9.3 years, and 26% had received previous treatment with one or more biologic drugs. At month 60, 726 patients (17%) of patients remained in the study. During the 5 year study, 41.3% of patients were lost to follow-up, 22.3% discontinued due to lack of effectiveness (about half within the first 6 months), and 4.0% discontinued due to

adverse events. Mean values in patients treated with ADA showed a rapid response to treatment by both objective and patient-reported measures. Responses were maintained over 5 years in patients remaining on therapy (table 1). ADA was well tolerated and no unexpected safety signals were observed.

**Abstract AB0437 – Table 1.** Therapeutic response to ADA in the AGIL study. Values are presented as mean (standard deviation) unless otherwise indicated

	Month							
	0	2	6	12	24	36	48	60
<b>DAS28 outcomes</b>								
n	4283	3595	3106	2532	1761	1222	906	644
DAS28	5.15 (1.15)	3.82 (1.38)	3.56 (1.36)	3.39 (1.35)	3.21 (1.32)	3.10 (1.28)	3.01 (1.21)	2.94 (1.22)
Therapeutic response (dcrit), %	—	38.7	42.7	45.9	48.7	53.7	55.3	59.5
DAS28 remission, %	0	20.3	25.9	30.1	36.8	39.2	42.7	45.2
<b>HAQ-DI outcomes</b>								
n	4269	3973	3409	2778	1957	1368	988	722
HAQ-DI	1.3 (0.70)	1.08 (0.73)	1.02 (0.74)	0.98 (0.74)	0.95 (0.74)	0.94 (0.73)	0.90 (0.72)	0.92 (0.71)
HAQ-DI remission, %	19.9	28.1	32.1	34.6	35.6	35.8	37.2	35.2
<b>Patient-reported disease activity</b>								
n	4293	3599	3442	2799	1975	1381	999	726
Patient global health <sup>1</sup>	6.05 (2.25)	4.49 (2.34)	4.24 (2.37)	4.03 (2.38)	3.78 (2.35)	3.60 (2.38)	3.46 (2.32)	3.45 (2.35)
<b>Patient-reported pain</b>								
n	4272	4006	3443	2796	1975	1380	998	724
Pain <sup>2</sup>	6.04 (2.27)	4.34 (2.47)	4.15 (2.46)	3.93 (2.46)	3.66 (2.41)	3.48 (2.38)	3.29 (2.39)	3.28 (2.44)

<sup>1</sup>Measured on a scale ranging from 0 (best) to 10 (worst)

**Conclusions:** The AGIL study is one of the largest observational cohorts to provide long-term data on ADA therapy. Both objective and subjective measures support the effectiveness and safety of ADA in patients with RA during 5 years of therapy. Approximately 43% of patients experienced a therapeutic response to treatment at 6 months as assessed by statistical methods (DAS28-dcrit),<sup>1</sup> and this level of response increased to 60% at 5 years in patients remaining on therapy. About one-third of patients recovered full functional ability (HAQ-DI remission) at the 6 month and subsequent visits. Our data indicate that ADA is an effective and safe long-term therapy in RA patients who continue on treatment.

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#### AB0438 SAFETY OF TNF BLOCKERS IN CASE OF NON-ALCOHOLIC FATTY LIVER DISEASE AND CIRRHOSIS SYSTEMATIC REVIEW

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**Background:** The management of inflammatory rheumatism and psoriasis has largely evolved over the last 15 years with the emergence of biotherapies whose main adverse effect is the increased infection risk. The prevalence of metabolic syndrome is increasing and has been estimated at 30% in patients with rheumatoid arthritis with an excess of 45% compared to healthy subjects. One of the major complications of the metabolic syndrome is the Non Alcoholic Fatty Liver Disease (NAFLD), which prevalence is 25% in the global population, and 30% in a cohort of patients with rheumatoid arthritis. The main complication of NAFLD is

the development of cirrhosis, known to increase infectious risk. Surprisingly, there are no data on the safety of TNF antagonists in patients with chronic inflammatory disease and NAFLD or cirrhosis.

**Objectives:** To assess infectious and liver safety of the main TNF blockers used in chronic inflammatory diseases in patients with cirrhosis or NAFLD.

**Methods:** A systematic review of the literature, following the Prisma recommendations, was conducted on the Pubmed and Embase databases with the following keywords: "adalimumab", "infliximab", "etanercept", "certolizumab", "golimumab" "TNF -blockers "AND" liver cirrhosis "," non alcoholic fatty liver disease ". We selected only studies including patients treated with TNF blockers and with cirrhosis or ultrasonically characterised NAFLD. We excluded animal models and non-English articles.

**Results:** We identified 39 articles and only 11 fulfilled the inclusion criteria. 9 Case Reports have reported the tolerance of TNF-blockers in patients with cirrhosis and one controlled study (44 patients) assessed the safety of etanercept in case of NAFLD. One study (7 patients) investigated the impact of infliximab in refractory autoimmune hepatitis. The cause of cirrhosis was primary biliary cholangitis (5 cases), alpha1 antitrypsin deficiency (4 cases) and post hepatitis B cirrhosis (2 cases). All cirrhosis were compensated. Inflammatory diseases requiring the introduction of TNF blocker were rheumatoid arthritis (n=5), psoriatic arthritis (n=4), ulcerative colitis (n=2) and psoriasis (n=44). The TNF-blockers prescribed were adalimumab in 2 patients, infliximab in 11 patients and etanercept in 49 patients. The duration of treatment ranged from 6 to 24 months. For the 9 cirrhotic patients with an inflammatory disorder, no infection was reported and two of them (2 cases of primary biliary cholangitis) even had an improvement in liver function secondary to the introduction of biotherapy. For the 7 patients receiving infliximab to treat auto-immune hepatitis, 5 patients presented recurrent infections. For patients with NAFLD, no infectious event was reported and an improvement of the hepatic biological parameters was observed, suggesting an improvement in liver function.

**Conclusions:** The results of this review suggest that in case of compensated cirrhosis, TNF-blockers were not deleterious for the liver and did not increase the infectious risk. In case of auto-immune cirrhosis, TNF-blockers increased the infectious risk. In case of NAFLD, TNF-blockers might improve liver function and prevent fibrosis.

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AB0439

#### TRAVELLING WITH ARTHRITIS: A CROSS-SECTIONAL ANALYSIS OF DANISH ARTHRITIS PATIENTS TREATED WITH BIOLOGICS

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**Background:** The development and introduction of biologics has rapidly revolutionised the therapeutic approach of chronic inflammatory diseases. Well-treated patients have high physical activity levels and long life expectancy. They travel widely for holiday, business or family visits. Biological drugs are administered either intravenously or subcutaneous and have to be kept cool.

**Objectives:** To describe the travel patterns, the extent of pre-travel advice, travel insurance, vaccinations, adherence to biological treatment, and self-reported health related problems encountered by rheumatology patients in biologic treatment during their travel.

**Methods:** A cross-sectional study was conducted in an out-patient clinic at the Department of Rheumatology, North Denmark Regional Hospital. During 2017 a questionnaire with focus on travel history was distributed to 300 consecutive arthritis patients treated with biologics.

**Results:** A total of 273 (91%) completed the questionnaire. Median age was 67 years, and 53% were females. Overall 64% of them were receiving subcutaneous (sc) and 28% intravenous (iv) treatment, while in 8% administration route were not stated. Overall 15% of patients reported reduced travel activity after having started biologics and 21% reported that biological treatment or disease have directly influenced their decision about travelling. A total of 74% of patients have travelled outside of Denmark and 45% of these have travelled outside of Europe while treated with biologics. Pre-travel advice was sought by 26% and travel insurance was taken out by 86% of the travellers. However, 59% did not inform the insurance company about their disease or biologics. Only 6% of the travellers have experienced minor health problems which were not related to arthritis, while three patients were hospitalised. Overall 10% of patients were given additional travel vaccination. Patients, receiving sc biologics travelled significantly more than those, receiving iv treatment: 68% versus 21% (p<0.05). Overall 42% of the travellers in sc treatment group continued to take biologics during their travel, 21% had stopped the treatment before and 5% during the travel. A large proportion (72%) of travellers, who discontinued

sc treatment prior to travelling, stopped the medication due to concerns about carrying biologics in general.

**Conclusions:** Biological treated patients with rheumatic diseases travel frequently. Neither health-related problems nor treatments were reported to be major problems. The main problems were failure to seek pre-travel advice, worry for carrying biologics and the lack of disclosure regarding biologic treatment while seeking travel insurance. Patients receiving subcutaneous biological treatment travelled significantly more often than patients treated with intravenous biologics.

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AB0440

#### ETHNIC MINORITIES EXPERIENCE INFREQUENT BIOLOGIC SWITCH DESPITE ACTIVE RHEUMATOID ARTHRITIS DISEASE

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**Background:** The expanded therapeutic modalities in rheumatoid arthritis (RA) provide options to achieve low disease activity or remission. Yet, in routine care, the frequency and choice of switching of biologic DMARD (bDMARD) amongst ethnic subsets when there is inefficacy, is unknown.

**Objectives:** To evaluate frequency and choice of biologic switch in ethnic RA subsets

**Methods:** Patients enrolled in the Ethnic Minority RA Consortium (EMRAC), with at least one followup visit were analysed. Data included clinical outcomes as assessed by RAPID3 tender/swollen joint counts; medication use (prednisone, methotrexate, other DMARD), and bDMARD (Tumour Necrosis factor inhibitors (TNFi) and non-TNFi). Minimally clinical improvement (MCI) in RAPID3 was defined as a decrease of  $\geq 3.2$  points during followup. Differences between medication usage, biologic switch, and RAPID3 improvement between race and ethnicity groups while on biologics, was investigated.

**Abstract AB0440 – Table 1.** Demographic and clinical features of EMRAC cohort by race group

	White	African-American	Hispanic	Other	Total
<b>N</b>	366	252	158	264	1040
<b>Age (years)</b>	55.4 (15.8)	56.5 (14.5)	54.4 (13.5)	53.9 (16.3)	55.1 (15.3)
<b>Education (years)</b>	15.1 (3.2)	13.4 (3.2)	12.6 (4.5)	15.2 (3.5)	14.2 (3.6)
<b>Female [N(%)]</b>	286 (78%)	208 (83%)	126 (80%)	218 (86%)	838 (81%)
<b>Followup (weeks)</b>	57.0 (53.0)	92.8 (87.6)	48.7 (45.0)	52.2 (50.5)	63.2 (63.9)
<b>RAPID3 [0–30]</b>	11.3 (7.2)	12.9 (7.1)	12.6 (7.7)	10.8 (7.5)	11.9 (7.3)
<b>Tender Joints [0–28]</b>	1.0 (3.6)	2.5 (5.0)	2.4 (4.9)	0.5 (2.4)	1.5 (4.1)
<b>Swollen Joints [0–28]</b>	0.5 (2.0)	2.0 (3.8)	1.7 (3.9)	0.3 (1.8)	1.0 (2.9)
<b>Prednisone Use [N(%)]</b>	130 (36%)	89 (35%)	66 (42%)	78 (30%)	363 (35%)
<b>Methotrexate Use [N (%)]</b>	207 (57%)	130 (52%)	92 (58%)	160 (61%)	589 (57%)
<b>Other DMARD Use [N (%)]</b>	102 (28%)	74 (29%)	60 (38%)	101 (38%)	337 (32%)
<b>Any Biologic Use [N (%)]</b>	198 (54%)	84 (33%)	56 (35%)	105 (40%)	443 (43%)
<b>TNF Use [N(%)]</b>	160 (44%)	71 (28%)	41 (26%)	90 (34%)	362 (35%)
<b>Non-TNF Use [N(%)]</b>	54 (15%)	16 (6%)	16 (10%)	25 (9%)	111 (11%)

**TNF:** adalimumab, certolizumab, etanercept, golimumab, infliximab

**Non-TNF:** abatacept, anakinra, tocilizumab, tofacitinib, rituximab



**Results:** 1040 subjects with 3719 follow-up visits spanning an average of 63.2 weeks were analysed. African Americans and Hispanics comprised 24% and 15%, respectively. Compared to Whites, African Americans and Hispanics had significantly less education ( $p < 0.001$  for both), significantly less biologic use ( $p < 0.001$  for both) and significantly less TNF use ( $p < 0.001$  for both). African Americans had significantly higher RAPID3 scores at enrollment than Whites as well ( $p = 0.018$ ).

Switching between TNFi and non-TNFi was recorded in only 9 subjects, with 7 subjects switching from TNFi to non-TNFi. There was no statistical difference between race/ethnic groups in frequency of bDMARD switching, nor within bDMARD class (TNFi class,  $p = cc$ ; non-TNFi class,  $p = bb$ ). bDMARD treatment led to MCI in RAPID3 in 101 (38%) subjects and in more African Americans (29 [48%]) and Hispanics (12 [41%]) than in Whites (49 [37%]) (but not statistically significant).

**Conclusions:** In our cohort, disparity was seen in bDMARD use between race and ethnic groups but had similar and infrequent biologic switch. Based upon these data, efforts to eliminate biologic use disparity remains paramount and supersedes concerns regarding disparity in biologic switching.

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AB0441

#### DRUG SURVIVAL AND REASON FOR DROP-OUT IN RHEUMATOID ARTHRITIS PATIENTS WITH A NON-MEDICAL SWITCH FROM ORIGINATOR TO BIOSIMILAR ETANERCEPT – PRELIMINARY DATA FROM A NORWEGIAN MULTICENTER STUDY

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**Background:** Norwegian rheumatologists are encouraged to prescribe the lowest-priced biologic DMARDs according to the national tender system. Thus, non-medical switch from the originator drug to its biosimilar is extensively performed. There is a need for more real life data to clarify the clinical outcomes, dropout rates and reasons for these dropouts after a non-medical switch from the originator to biosimilar ETN.

**Objectives:** To explore drug survival and clinical outcomes in rheumatoid arthritis (RA) patients after a non-medical switch from the originator to biosimilar ETN (SB4) in ordinary outpatient clinics across Norway.

**Methods:** Herein we present preliminary data collected at one participating centre. Patients were monitored and data were collected by the use of a hospital clinical computer system GoTreatIT Rheuma. The computer system is also used for data collection for the Norwegian national arthritis registry, NorArtritt. Demographic, clinical and treatment data were retrieved (21st of January 2018) from the computer system for the time point of non-medical switch of ETN and the last follow up. Wilcoxon matched-pair signed rank test was used for comparison between the two-time points.

**Results:** Since April 2016 191 RA patients (mean age 60.8 years, 67% females) underwent a non-medical switch from originator to biosimilar ETN. Mean (SD) observation time for the 163 patients (85.3%) still on biosimilar ETN was 1.23 (0.46) yrs. 28 patients (14.7%) stopped treatment. Among them mean (SD) observation time for the 7 patients (3.7%) in remission was 0.53 (0.33) yrs, for the 10 patients (5.2%) reporting adverse events 0.44 (0.32) yrs and for the 11 patients (5.8%) reporting lack or loss of efficacy 0.44 (0.35) yrs. The adverse events reported was: 1 chest pain, 1 neuropathy, 1 GI reaction, 1 visual impairment, 1 infection, 2 joint stiffness (1 patient went back on ETN SB4) and 3 skin reactions. For all 191 patients no significant change (median [IQR]) from baseline to last observation was seen for DAS28 (2.1 [1.5–2.8] vs 1.9 [1.5–2.5],  $p = 0.33$ ), MHAQ (0.3 [0.0–0.7] vs 0.4 [0.1–0.6],  $p = 0.62$ ) and patient VAS global (20.0 [10.0–43.0] vs 25.0 [10.0–43.3] mm,  $p = 0.73$ ), whereas CRP improved significantly during follow up (2.0 [1.0–5.0] vs 1.0 [1.0–5.5] mg/dl,  $p = 0.02$ ). For the subgroup of RA patients who stopped treatment because of lack of efficacy a minor non-significant impairment was observed for DAS28 (2.0 [1.4–2.5] vs 2.6 [1.2–4.0],  $p = 0.32$ ), CRP (0.0 [0.0–6.0] vs 3.5 [0.8–13.3] mg/dl,  $p = 0.66$ ), MHAQ (0.1 [0.0–0.1] vs 0.5 [0.3–0.5],  $p = 0.66$ ) and patient VAS global (20.0 [10.0–30.0] vs 29.0 [17.0–58.5] mm,  $p = 0.66$ ).

**Conclusions:** Our preliminary data indicate that for the majority of patients, a non-medical switch from originator to biosimilar ETN (SB4) was well tolerated with no impairment in disease measures. Whether the reported adverse events were associated to the switch needs to be further studied. In patients who stopped the biosimilar because of lack of effect only a minor numerically increase in disease

measures was seen. Our promising preliminary results need to be confirmed in a large scale study.

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AB0442

#### LONG-TERM SAFETY AND EFFICACY OF BIOSIMILAR INFLIXIMAB (CT-P13) AFTER SWITCHING FROM ORIGINATOR INFLIXIMAB: RESULTS FROM THE 26-WEEK OPEN LABEL EXTENSION OF A NORWEGIAN RANDOMISED TRIAL

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**Background:** The NOR-SWITCH study was funded by the Norwegian government to investigate if switching from originator infliximab (INX) to biosimilar CT-P13 is safe in rheumatoid arthritis (RA), spondyloarthritis (SpA), psoriatic arthritis (PsA), Crohn's disease (CD), ulcerative colitis (UC), and chronic plaque psoriasis (Ps).

**Objectives:** Assessing efficacy, safety, immunogenicity at week 78 in patients on CT-P13 for 78 weeks (maintenance group) vs CT-P13 for 26 weeks (switch group).

**Methods:** 481 adult patients on stable originator infliximab were randomised 1:1 to continued INX or switch to CT-P13 treatment in the main study<sup>1</sup>. All extension participants received CT-P13. The primary endpoint was disease worsening, analysed with logistic regression, adjusted for diagnosis and treatment duration.

Abstract AB0442 – Table 1

Demographic and baseline characteristics (52 w) Number of patients (FAS)	Maintenance group 197	Switch group 183	Data are n (%) or mean (SD)
Age (years)	48.8 (14.9)	48 (14.3)	
Duration of ongoing infliximab treatment (years)	7.7 (3.8)	7.4 (3.5)	
Concomitant immunosuppressive therapy	97 (49%)	75 (41%)	
Rheumatoid arthritis	27 (14%)	28 (15%)	
Spondyloarthritis	38 (19%)	29 (16%)	
Psoriatic arthritis	9 (5%)	11 (6%)	
Crohn's disease	65 (33%)	62 (34%)	
Ulcerative colitis	42 (21%)	38 (21%)	
Psoriasis	16 (8%)	15 (8%)	
<b>Disease characteristics</b>			
DAS 28 RA	2.4 (0.9)	2.8 (0.9)	
DAS 28 PsA	2.1 (1.1)	2.9 (1.8)	
ASDAS (SpA)	1.9 (0.8)	1.7 (0.7)	
<b>Disease worsening</b>			
<b>Number of patients (PPS)</b>	<b>190</b>	<b>173</b>	<b>Risk difference (95% CI)</b>
All	32 (16.8%)	20 (11.6%)	-5.9% (-12.9–1.1)
Rheumatoid arthritis	9 (34.6%)	6 (22.2%)	-10.5% (-34.6–13.6)
Spondyloarthritis	3 (7.9%)	2 (7.1%)	-0.6% (-13.5–12.2)
Psoriatic arthritis	1 (12.5%)	3 (33.3%)	20.8% (-17.6–59.1)

ASDAS, Ankylosing Spondylitis Disease Activity Score. DAS28, Disease Activity Score in 28 joints.

**Results:** 380 patients entered the extension trial. Demographic and baseline (52 w) characteristics of the extension study population are shown (table 1). Disease worsening in the study arms (Per Protocol Set, PPS) and in each diagnosis (explorative analyses) are shown (table 1). Generic disease variables, disease specific composite measures, trough drug levels, anti-drug antibodies and reported adverse events were comparable between groups (data not shown).

**Conclusions:** We found no difference between patients switched from INX to CT-P13 vs those on maintained CT-P13

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#### AB0443 THE EFFECTS OF DENOSUMAB FOR RHEUMATOID ARTHRITIS PATIENT

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**Background:** Denosumab (dMAB), an anti-receptor activator of nuclear factor kappa-B ligand (RANKL) monoclonal antibody, is now popular anti bone absorption suppressant for osteoporosis. Recently, this drug has indicated for rheumatoid arthritis (RA) treatment, for expectance for suppressant in joint destruction. However, except of the effect on joint deformation, anti inflammation effect is not evident in randomised control trial (RCT), although rich case series for OP in RA patient is already collected in clinical practice.

**Objectives:** Aim of this study is to investigate effects of dMAB on RA, and evaluate other effects but joint destruction suppression.

**Methods:** In 352 patients who have been treated with dMAB, RA patients who have been treated with dMAB consecutively for more than 1 year, were picked up for this study. Patient who have had experience of biologic disease modifying anti rheumatic drug (bdMARD) or targeted synthetic DMARD, had been eliminated. In whom bone mineral density (BMD) in lumbar spine (LS), femoral neck (FN), and greater trochanter (GT), and tartrate-resistant acid phosphatase 5b (TRACP5b), 28-joints disease activity score with C-reactive protein (DAS28-CRP), Health Assessment Questionnaire Disease Index (HAQ-DI), yearly progression of Sharp/van der Heijde score (dSHS), joint space narrowing score (dJSN) and bone erosion score (dBE), and pain score with visual analogue scale (PS-VAS) were measured, and their mean values were compared between 6 months before start (BEF) and 6 months after start (AFT) statistically with paired T-test. Statistically significant level was set less than 1%.

**Results:** One hundred and three patients, in whom 100 were female and three were male, were donated in this study. All of them had been supplemented with Denotas Chewable Combination Tablets (Daiichi Sankyo Co., Ltd; Tokyo, Japan), which is medical compound with calcium and natural vitamin D<sub>3</sub>. Average age at start was 71.17 years old, and disease duration of RA at start was 7.42 years. Glucocorticoid was administered in 45 patients (44.7%), and methotrexate was administered in 72 patients (69.9%). BMD demonstrated from 74.03 (%YAM) to 77.32 in LS, whereas from 69.79 to 69.63 in FN, and from 71.99 to 74.27 in GT, from BEF to AFT, respectively. BMD of LS and GT at AFT demonstrated significant increase, while FN demonstrated no significant difference. TRACP5b demonstrated significant less value than at BEF. Disease activity, namely DAS28-CRP, tenderness joint count (TJC), swollen joint count (SJC), patient's global assessment (PGA), evaluator's global assessment (EGA), CRP, pain score with visual analogue scale (PS-VAS), HAQ-DI, SHS, JSN, and BE from BEF to AFT demonstrated 2.12 to 1.86, 1.32 to 0.89, 2.13 to 0.97, 2.23 to 2.01, 1.27 to 0.68, 0.80 to 0.70, 0.537 to 0.590, 81.76 to 80.98, 36.16 to 37.08, 46.96 to 44.27, respectively. DAS28-CRP, and all of its components, and EGA demonstrated significant decrease, although PS-VAS showed decrease yet demonstrated no significance, while HAQ-DI showed increase with no statistical significance. dSHS and dBE demonstrated significant less at AFT than at BEF, while no significance for dJSN yet slightly increased in the AFT, even no significant difference demonstrated for absolute values (table 1).

**Abstract AB0443 – Table 1.** Change of each parameters and statistical significance. BMD, bone mineral density; % YAM, percentage of young adult mean value; BEF, before administration of denosumab; AFT, first value after denosumab was administered; S.S., statistical significance; LS, average value of lumbar spine from L1 to L4; FN, femoral neck; GT, greater trochanter; DAS28-CRP, 28-joints disease activity score with C-reactive protein; TJC, tenderness joint count; SJC, swollen joint count; PGA, patient's global assessment; CRP, C-reactive protein; EGA, evaluator's global assessment; PS-VAS, pain score with visual analogue scale; HAQ-DI, Health Assessment Questionnaire Disability Index; SHS, Sharp/van der Heijde Score; JSN, joint space narrowing score; BE, bone erosion score; n. s., not significant; \*, AFT is statistically significantly smaller than BEF within 1%; §, BEF is statistically significantly larger than AFT within 1%.

BMD (%YAM)	BEF	AFT	S.S.
LS	74.03±15.74	77.32±15.79	*
FN	69.79±11.65	69.63±11.93	n.s.
GT	71.99±13.82	74.27±13.28	*
TRACP-5b	489.3±214.4	255.3±133.6	§
DAS28-CRP	2.12±0.91	1.86±0.72	*
TJC	1.32±2.20	0.89±1.99	*
SJC	2.13±3.54	0.97±1.85	*
PGA	2.23±2.30	2.01±1.88	*
CRP	0.80±1.55	0.70±1.36	n.s.
EGA	1.27±1.64	0.68±1.07	*
PS-VAS	28.34±23.32	27.07±21.65	n.s.
HAQ-DI	0.537±0.611	0.590±0.648	§
SHS	81.76±89.36	80.98±89.65	n.s.
JSN	36.16±37.76	37.08±38.57	§
BE	45.96±53.08	44.27±52.18	*

**Conclusions:** The effect of dMAB on RA is suggested suppression of dBE, BMD increase in LS and GT, improvement of DAS28-CRP, and may have decrease of PS-VAS.

**Disclosure of Interest:** None declared

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#### AB0444 DESCRIPTION IN REAL-WORLD OF THE EFFICACY AFTER SWITCHING FROM INTRAVENOUS TO SUBCUTANEOUS ADMINISTRATION OF TOCILIZUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS. THE ROSWITCH STUDY

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**Background:** It has been proven, in a pivotal RCT, that SC tocilizumab (TCZ) was non-inferior to IV TCZ.<sup>1</sup> However the switch from IV to SC TCZ has not been evaluated to date in a large real-world study.

**Objectives:** The main objective was to assess the maintenance of efficacy of SC TCZ 6 months (M6) after switching from IV to SC formulation in patients (pts) with rheumatoid arthritis (RA) in real-world. Secondary objectives were: characteristics of pts and RA, efficacy of TCZ at M12, TCZ retention rates at M6 and M12 for Switch (IV-SC) and No-Switch pts (IV-IV), predictive factors of switching.

**Methods:** We analysed all RA pts of the shared medical file "RIC Nord de France" with ≥1 DAS 3 months before inclusion, treated with TCZ, switching or not from IV to SC TCZ, between April 30 2015 and January 15 2016. The primary efficacy endpoint was the % of pts remaining in their DAS28-ESR category remission/LDA or moving to an inferior DAS category at M6. Various sensibility analyses were realised on the primary criterion of which a propensity score (IPTW).

**Results:** From the 314 included pts, 30% switched from IV to SC TCZ. At baseline, 77.7% were females, mean BMI was 27.5±6.4, mean RA duration was 14.9 ±9.2 years. Mean IV TCZ duration before inclusion was 35.0±23.1 months in Switch and 26.8±22.1 months in No-Switch pts. Mean DAS28 were 2.1±1.1 in Switch and 2.9±1.6 in No-Switch pts. 81.9% and 59.5% of the pts were in DAS28 remission/LDA, 18.1% and 28.6% in MDA, 0% and 11.8% in HAD in Switch and

No-Switch pts respectively. The improvement of initial DAS28-ESR category or maintenance in remission/LDA was comparable in both groups at M6 and M12 (table 1).

**Abstract AB0444 – Table 1.** DAS28-ESR improvement or maintenance in remission/LDA category

% of pts*, 95% CI	Switch, n=94	No Switch, n=220
M6, n/N	66/90	137/195
	73.3% [63.0–82.1]	70.3% [63.3–76.6]
M12, n/N	63/91	118/204
	69.2% [58.7–78.5]	57.8% [50.8–64.7]

\* Permanent discontinuation of TCZ considered as failure.

Using the IPTW for balancing on baseline characteristics between groups, similar proportions were observed at both M6 and M12. TCZ retention rates at M12 were 78% (95% CI<sup>68–85</sup>) and 80% (95% CI: 74–85 p=0.555 for Switch and No-Switch groups respectively. In the 208 pts with a DAS28 ≤3.2 at inclusion, multivariate analysis showed no parameters associated to the switch. Conversely in the 106 pts with a DAS28 >3.2 at inclusion, rheumatoid nodules (OR=4.78, 95% CI [1.23–18.55], p=0.024) and duration of IV TCZ before inclusion (OR=1.37, 95% CI [1.08–1.73], p=0.009) were significantly associated to the switch.

**Conclusions:** The RoSwitch study showed the maintenance of efficacy at 6 and 12 months in RA pts switching from IV to SC TCZ. Similar efficacy and therapeutic retention rates were observed for No-Switch pts. No factor was associated with the switch in pts in remission/LDA at inclusion suggesting that patient's personal appreciation was preponderant in the choice of the switch.

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#### AB0445 THERAPEUTIC MAINTENANCE OF ABATACEPT IN RHEUMATOID ARTHRITIS: RESULTS OF THE RIC-ABA STUDY (517 PATIENTS)

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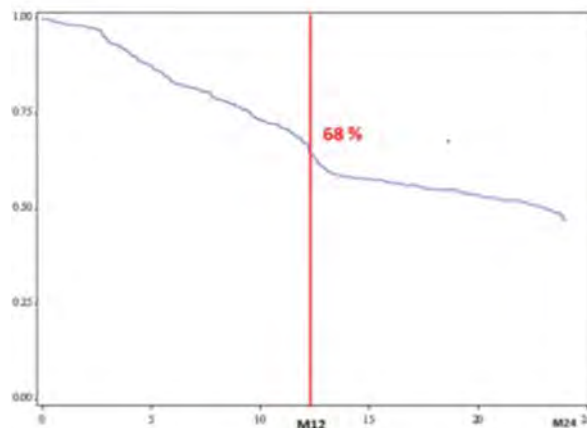
**Objectives:** Study the therapeutic maintenance, associated factor with maintenance at 12 months and reasons for abatacept (ABA) stop in daily practice.

**Methods:** Retrospective multicentric study, from the RIC Nord de France network, of patients treated for rheumatoid arthritis who received at least one ABA treatment between January 2008 and July 2016. We studied the therapeutic maintenance at 12 months, according to the number of previous bDMARDs and according to the date of initiation (group 1: from 2008 until 31/07/2010 (ABA authorised in anti-TNFfailure) and group 2 from 01/08/2010 (ABA authorised in the first line)). Therapeutic maintenance was evaluated using the Kaplan-Meier method.

**Results:** Of the 517 patients (74% women) who were included, the mean age was 61.4±13.3 years. There were 76% positive anti-CCP. ABA was used as monotherapy in 176 patients (34%) and 22% of patients were naïve to bDMARDs. The mean DAS 28-VS at initiation of ABA was 4.7±1.3.

Therapeutic maintenance at 12 months was 68%. Among the 166 patients (32%) stopped ABA, the reason for discontinuation was primary ineffectiveness (n=54, 32.5%), loss of efficacy (n=40, 24%), adverse events (n=43, 26%) and other (n=29, 17.5%). On multivariate analysis CRP <10 mg/L was associated with better maintenance at 12 months.

No significant difference in therapeutic maintenance was found at 12 months according to the date of initiation and according to the number of previous bDMARDs.



**Abstract AB0445 – Figure 1.** Therapeutic maintenance of Abatacept at 12 months

**Conclusions:** Therapeutic maintenance at 12 months was 68%, this rate is similar to Pan-European Registry. The rate of CRP at initiation seems to have an impact on the maintenance of ABA at 12 months.

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#### AB0446 PHYSICIAN-REPORTED BEHAVIOURS AND TREATMENT TRENDS OF TUMOUR NECROSIS FACTOR INHIBITOR USE: CYCLING VERSUS SWITCHING IN FIVE EUROPEAN COUNTRIES: FRANCE, GERMANY, ITALY, SPAIN AND THE UK

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**Background:** Previously, most biologics prescribed for treating rheumatoid arthritis (RA) were tumour necrosis factor inhibitors (TNFi) and it was common practice to prescribe a second TNFi after failure of the first. Biologics with different mechanisms of action (MOA) have become available and 2016 European League Against Rheumatism guidelines recommend cycling to another TNFi or switching to a biologic with a new MOA following failure of the first TNFi.

**Objectives:** Describe the proportion of patients in 5 EU countries who, after failure of a first TNFi, cycle to a second TNFi ('TNFi cycling') vs switch to a treatment with a different MOA ('Switch'), and identify patient characteristics and physician attitudes associated with TNFi cycling vs switching.

**Methods:** Data were from the Adelphi Disease Specific Programme (DSP), a cross-sectional survey conducted in 2017 in France, Germany, Italy, Spain and the UK. Rheumatologists prospectively completed records about the next 10 patients with RA who consulted them during the study period; records captured treatment history and clinical details. Patients were included in the analysis if they had been prescribed at least 2 different biologics, their first was a TNFi and their second was known. Patients were assigned to 2 cohorts: 'TNFi cycling' patients received a TNFi at first- and a different TNFi at second-line; 'Switch' patients received a TNFi at first-line and a non-TNFi at second-line. Bi-variate comparisons of groups were conducted using nonparametric tests as appropriate.

**Results:** All physicians in the DSP sample (n=301) were questioned on their beliefs around TNFis; 86.4% believed that there is a class effect with TNFis regarding efficacy and/or safety (table 1). Data from 359 patients were included in the analysis (75.8% female; mean [SD] age 56.5 [12.7]), of whom 167 (46.5%) were TNFi cycling, and 192 (53.5%) were Switch patients (female: 70.7% vs 80.2%, respectively; p=0.04; age: 55.8 [13.1] vs 57.1 [12.4], respectively; p=0.42). The most common reasons for discontinuing first-line therapy among the TNFi cycling and Switch cohorts were worsening condition (36.3% vs 45.3%,



respectively;  $p=0.13$ ) and loss of efficacy (48.9% vs 48.3%, respectively;  $p=1.0$ ). Prior to the second biologic, patients in the TNFi cycling cohort spent a numerically longer amount of time on first-line therapy vs the Switch cohort (2.0 [2.2] years vs 1.7 [1.9] years;  $p=0.35$ ), and had a longer disease duration at the time of initiation of second-line non-TNFi (7.3 [6.6] years vs 6.6 [7.8] years;  $p=0.15$ ).

**Abstract AB0446 – Table 1.** Physician beliefs around tumour necrosis factor inhibitors

	n, %
<b>Do you believe that there is a class effect with the TNFis?</b>	
Yes, with regards to efficacy	81 (26.9)
Yes, with regards to safety	30 (10.0)
Yes, with regards to both efficacy and safety	149 (49.5)
No	41 (13.6)
<b>When do you believe there is a benefit in prescribing another TNFi?</b>	
After primary lack of efficacy (non-response) to a first TNFi	127 (42.2)
After secondary lack of efficacy (response decreasing over time) to a first TNFi	160 (53.2)
After poor tolerability with a first TNFi	127 (42.2)
After primary lack of efficacy (non-response) to a second TNFi	28 (9.3)
After secondary lack of efficacy (response decreasing over time) to a second TNFi	47 (15.6)
After poor tolerability with a second TNFi	31 (10.3)
None of the above	25 (8.3)
<b>How do you believe the practice of TNFi cycling is changing?</b>	
Decreasing	188 (62.5)
Not changing	93 (30.9)
Increasing	20 (6.6)
<b>Assuming no restrictions, which biologics would you prefer to use first for RA?</b>	
Non-TNFi	50 (16.6)
TNFi	251 (83.4)
<b>Assuming no restrictions, which biologics would you prefer to use second for RA?</b>	
Non-TNFi	123 (40.9)
TNFi	178 (59.1)
<b>Assuming no restrictions, which biologics would you prefer to use third for RA?</b>	
Non-TNFi	190 (63.1)
TNFi	111 (36.9)

**Conclusions:** Despite evidence from literature suggesting that RA patients have a better treatment response switching to a non-TNFi after initial TNFi inadequate response<sup>1</sup> and despite the majority of physicians in our study believing that there is a class effect with TNFis, regarding efficacy and safety, 46.5% of patients still cycled to a second TNFi rather than switched to a non-TNFi as second-line therapy.

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#### AB0447 AUDIT OF THE CLINICAL EFFICACY AND SAFETY OF ETANERCEPT BIOSIMILAR TO ITS REFERENCE PRODUCT IN PATIENTS WITH INFLAMMATORY ARTHRITIS: EXPERIENCE FROM A DISTRICT GENERAL HOSPITAL IN THE UNITED KINGDOM

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**Background:** Etanercept has been widely used in rheumatology practice since NICE approval in 2000. Biologics have been pivotal treatments for inflammatory arthritis but are associated with a considerable economic burden. The expiry of patent protection has led to the introduction of biosimilar drugs at competitive prices. SB4 was the first biosimilar of etanercept approved by the European Medicine Agency. SB4 was launched in February 2016 in the UK for use in all adult indications for which reference etanercept is approved. The rheumatology team at the Dudley Group of Hospitals (DGH) negotiated with commissioners to share the cost savings of switching the cohort of patients who were on reference etanercept to SB4.

**Objectives:** This audit aimed to compare the clinical efficacy and safety profile of etanercept biosimilar SB4i (post switch) with its reference etanercept (pre switch).

**Methods:** The first 50 patients switched were sampled and followed up for 6 months. Data was collected from hospital databases and patient records (demographic; disease activity scores 6 months pre and post switch; adverse events (AE)). Inclusion criteria: all patients established on reference etanercept for more than 12 months. Exclusion criteria: patients attempting to conceive, pregnant or breast feeding women, patients on 25mg of reference etanercept or with JIA.

**Results:** Of the 194 patients on reference etanercept in the Dudley area, 160 (83%) were successfully switched at the time of audit. Of the first 50 patients who switched, 32 (64%) patients had rheumatoid arthritis (RA), 15 (30%) ankylosing spondylitis (AS), and 3 (6%) psoriatic arthritis (PsA). The mean age was 60 years (range 29-83 years) with equal gender distribution. Mean years on reference etanercept was 6 years (range 1-13 years). In the RA cohort: 23(72%) patients were female with mean change of DAS28: +0.1(SD:0.87). In the AS cohort, 14(93%) patients were male with mean change of BASDAI: -0.6 (SD:1.34). PsA: 2 patients' symptoms were unchanged, 1 patient's tender and swollen joint count decreased. At 6 months post switch, 84% patients continued etanercept biosimilar SB4. Reasons for discontinuation included: AE (n=4), inefficacy (n=3) and new contraindication (cancer n=1).

**Conclusions:** Following switching to etanercept biosimilar SB4, no clinically significant change in DAS28 or BASDAI were observed during the audit period. Switching from reference etanercept to SB4 has resulted in a potential yearly saving of £660,000, from which the rheumatology department has secured funding to employ an additional clinical nurse specialist and secretary. Our audit found SB4 to be as safe and effective as its reference etanercept and has demonstrated a positive experience with biosimilar switching. This is relevant given the expiry of their biologic drugs' patent protections and further biosimilar drugs becoming available.

**Disclosure of Interest:** None declared

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#### AB0448 PATIENT-REPORTED OUTCOMES FOLLOWING DISCONTINUATION OF METHOTREXATE IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH SUBCUTANEOUS TOCILIZUMAB: RESULTS FROM A RANDOMISED CONTROLLED TRIAL

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**Background:** Patients with rheumatoid arthritis (RA) often receive methotrexate (MTX) in combination with biologics; however, MTX may be discontinued due to intolerance or to reduce the medication burden once disease control is achieved. Whereas previous studies have established the efficacy of tocilizumab (TCZ) initiated as monotherapy (MONO) for the treatment of RA,<sup>1,2</sup> patient-reported outcomes (PROs) after MTX withdrawal in patients achieving good clinical response to TCZ +MTX have not been evaluated. PROs are important measures when determining response to therapy in patients with RA with respect to health-related quality of life (HRQOL).<sup>3,4</sup>

**Objectives:** This study evaluated PROs between patients with RA who achieved low disease activity with TCZ +MTX and then continued or discontinued MTX in the COMP-ACT trial (NCT01855789).

**Methods:** US patients with RA who were inadequate responders to MTX were enrolled; initial combination therapy included MTX ( $\geq 15$  mg/week orally) plus TCZ 162 mg subcutaneous either weekly (qw) or every 2 weeks (q2w). Patients who achieved DAS28-ESR $\leq 3.2$  at Week 24 were randomised 1:1 to receive TCZ-MONO or continue TCZ +MTX until week 52 (double-blind). Changes in PRO scores were measured between Week 24 and Weeks 40 and 52, and included patient global assessment of disease activity (PtGA; visual analogue score [VAS], 0–100 mm), pain (VAS), Health Assessment Questionnaire Disability Index (HAQ-DI, 0–3) and Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue.

**Results:** Of the 296 randomised patients (TCZ +MTX, n=148; TCZ-MONO, n=148), 74.8% were women, mean age was 55.5 years, mean RA duration was 6.8 years and mean DAS28-ESR was 6.3 at baseline. At Week 24 (randomization), PRO scores were similar between the randomised treatment groups. The mean changes in PtGA, pain, HAQ-DI and FACIT-fatigue scores from Week 24 to Weeks 40 were similar between the TCZ +MTX and TCZ-MONO groups (table 1). The proportion of patients with HAQ-DI  $< 0.5$  was similar between the groups at Week 24 (randomization), and remained similar at Weeks 40 and 52.

**Abstract AB0448 – Table 1.** Changes in Patient-Reported Outcomes from Week 24 (Randomization) to Week 40 and Week 52

PRO Measure*	TCZ + MTX n = 147	TCZ-MONO n = 147	Difference (95% CI) (TCZ-MONO minus TCZ + MTX)†
<b>Δ PtGA, mean (SEM)</b>			
Week 24 to week 40	1.72 (1.79)	5.95 (1.75)	4.78 (-0.00, 9.56)
Week 24 to week 52	-0.33 (1.77)	3.58 (1.83)	4.14 (-0.56, 8.84)
<b>Δ Pain, mean (SEM)</b>			
Week 24 to week 40	1.64 (1.74)	5.32 (1.61)	4.19 (-0.23, 8.61)
Week 24 to week 52	-0.05 (1.84)	4.26 (1.69)	4.69 (0.14, 9.24)
<b>Δ HAQ-DI, mean (SEM)</b>			
Week 24 to week 40	0.01 (0.030)	0.04 (0.034)	0.03 (-0.05, 0.12)
Week 24 to week 52	0.01 (0.028)	0.02 (0.038)	0.01 (-0.08, 0.10)
<b>Δ FACIT-Fatigue, mean (SEM)</b>			
Week 24 to week 40	1.57 (0.67)	-0.68 (0.64)	-1.68 (-3.39, 0.02)
Week 24 to week 52	1.30 (0.67)	-1.12 (0.75)	-1.82 (-3.69, 0.06)
<b>HAQ-DI &lt; 0.5, n (%)</b>			
Week 24	64 (43.5)	56 (38.1)	-5.4 (-16.7, 5.8)
Week 40	60 (43.8)	54 (40.6)	-3.2 (-15.9, 8.6)
Week 52	60 (46.9)	53 (41.7)	-5.1 (-17.3, 7.0)

FACIT, Functional Assessment of Chronic Illness Therapy; HAQ-DI, Health Assessment Questionnaire Disability Index; MONO, monotherapy; MTX, methotrexate; PtGA, patient global assessment; SEM, standard error of the mean; TCZ, tocilizumab.

\* A negative change in score represents an improvement in the respective PRO except for Fatigue.

† Estimated means from ANCOVA model includes Week 24 value as a covariate, treatment group, and the randomization stratification factors: DAS28 remission status at Week 24 (<2.6, ≥2.6 to <3.2), baseline weight-by-dosing group (<80 kg every 2 weeks [q2w], <80 kg weekly [qw], 80 to <100 kg q2w, 80 to <100 kg qw, ≥100 kg qw), patient anti-TNF exposure (Yes or No).

**Conclusions:** Patients receiving TCZ who discontinue MTX appear to have similar PROs across multiple measures compared with patients continuing TCZ +MTX. Differences observed in clinical parameters between TCZ-MONO and TCZ +MTX did not appear to achieve a threshold that would be considered clinically meaningful. Similarities in PROs on both treatments were consistent with the clinical efficacy measures previously reported from COMP-ACT.

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#### AB0449 SDAI REDUCTION AT WEEK 2 PREDICT THE SDAI REMISSION AT WEEK 24 WHEN CERTOLIZUMAB PEGOL (CZP) WAS ADMINISTERED TO PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Certolizumab pegol (CZP) is approved for treatment of rheumatoid arthritis.

**Objectives:** To explore the predictor of efficacy of certolizumab pegol (CZP) for MTX-IR patients with rheumatoid arthritis in our retrospective study.

**Methods:** 50 patients who received CZP for rheumatoid arthritis of MTX-IR after 2013 were examined by logistic regression analysis using Age, sex, duration of disease, HAQ, TJC, SJC, gVAS, eVAS, CRP, SDAI, DAS 28-CRP, previous use of biologics, prednisolone use, ACPA, RF, the reduction rate of SDAI at week 2 to assess the predicting factor for SDAI remission at week 24.

**Results:** As a factor capable of achieving SDAI remission at 24 weeks after CZP administration, SDAI reduction rate of 50% or more (n=28, p<0.001), females (p=0.01), the number of swollen joints (p=0.02) were extracted as significant factors. The odds ratio at which SDAI remission can be obtained at 24 weeks point is 15.4 (95% CI: 3.1–109.6) when the SDAI reduction rate at 2 weeks after the start of administration is 50% or more. SDAI remission rate at week 24 were 67% in

SDAI reduction ≥50% at week 2 group and 22% in another. The continuation rate at week 24 in SDAI reduction ≥50% at week 2 is 93%.

**Conclusions:** When SDAI decreased by 50% or more at 2 weeks after initiation of CZP administration SDAI remission was easy to obtain after 24 weeks, and continuation rate was also good.

**Disclosure of Interest:** None declared

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#### AB0450 IMPACT OF THERAPEUTIC PATIENT EDUCATION ON SAFETY SKILLS AND INFECTIOUS EVENTS OF PATIENTS TREATED BY BIOLOGICAL DMARDs IN RHEUMATOLOGY: A BI-CENTRIC STUDY

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**Background:** Patients treated with biologic DMARDs have to be aware of the specific adverse events and have to be able to manage their treatments in case of infectious disease. Therapeutic Patient Education aims to enable patient to acquire these safety skills.

**Objectives:** To assess the impact of Therapeutic Patient Education on safety skills and management of infectious events in patients treated with biologic DMARDs in rheumatology.

**Methods:** Bi-centric analytical study comparing safety skills and infectious events between two cohorts of patients (TPE and TPE-naïve). Safety skills were assessed by an auto-assessment called "Biosecure", rated on a scale from 0 to 100. This assessment explores several dimensions of treatment management and was validated for assessment of safety skills in patients treated with biologic DMARDs in rheumatology in a preliminary study. Infectious events and their management were self-reported by patients. A cluster analysis aimed to separate patients into working group based on their shortcomings (on the basis of their answers to the Biosecure Assessment).

**Results:** 414 patients answered the assessment. The median Biosecure Score was 70.98/100 (Q1Q3: 60.97–84.63)

47% attended Therapeutic Patient Education. The median Biosecure Score was significantly higher in the TPE group than in the TPE-naïve group (74.88 versus 67.20/100; p<0.05). Regarding the observance to treatment, activity scores, vaccination rates on incidence of infectious events, there were no significant difference between the groups TPE and TPE-naïve. Nevertheless, there were more treatment interruption for infectious events in the TPE group, suggesting that TPE could lead to better management of treatment during infectious events.

Cluster analysis based on Biosecure assessment separated patients into 3 level groups but failed to identify specific patient profiles.

**Conclusions:** Therapeutic Patient Education could provide better safety skills and better treatment management in patients treated with biologic DMARDs in rheumatology. Prospective studies may confirm the impact of TPE on treatment management during infectious events. Further studies may assess the impact of TPE on incidence of serious infectious events.

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#### AB0451 INCIDENCE OF OPPORTUNISTIC INFECTIONS DURING RITUXIMAB, ABATACEPT OR TOCILIZUMAB TREATMENTS FOR RHEUMATOID ARTHRITIS IN CLINICAL PRACTICE

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**Background:** With the expanding use of biologic disease-modifying anti-rheumatic drugs (bDMARDs), opportunistic infections (OI) are a major concern in Rheumatology.

**Objectives:** Our purposes were to describe and compare the incidence of OI in RA treated by non-TNF-targeted biologics.

**Methods:** We performed a retrospective longitudinal observational study from 2007 to 2017. We included subjects followed in our outpatient clinic, diagnosed with RA according to ACR criteria, whom started treatment with a bDMARD [rituximab (RTX), abatacept (ABA), or tocilizumab (TCZ)]. According to the microbiologist criteria, we consider OI when there was a positive culture (for Virus, Fungus, bacterial or parasitary) or compatible symptoms that responded to specific treatment. Severe IO was considered if required hospitalisation. We also collected secondary variables: sociodemographic, clinical and other treatments. We used survival techniques to estimate the incidence of OI, expressed per 1000 patient-year [CI 95%]. Exposure time was defined from the start date of each bDMARDs until the development of an OI, discontinuation, loss of follow up or end of study (01/02/2017).

**Results:** We analysed a total of 164 patients with 219 different courses of bDMARDs treatment. Of these, 76% were women with a mean age at first bDMARD of 61.4±15 years. Rheumatoid factor was positive in 73.6%. Main comorbidities were: Hypercholesterolemia (53.3%), Hypertension (53.2%), Depression (25%), Diabetes (15%), and Ischaemic Heart Disease (9.8%). VSG mean was 38±28, and the mean WBC count was 7.8±2.7. The median time from onset of RA until onset of bDMARD was 2.8 years [0.8–6.2]. Of these, 132 were on RTX, 47 were on ABA and 40 were on TCZ. There were 12 OI (9 with RTX, 2 with ABA and 1 with TCZ). RTX have 2 Fungus (*Candida krusei* and *Klebsiella*), and 7 Virus (4 Herpes Zoster, 1 virus B reactivation, 1 virus C reactivation). OI for ABA was 2 Virus (1 Herpes Zoster, 1 virus B reactivation), while we found one virus OI with TCZ Fungus (*Herpes Zoster*). There were no bacterial or parasitary OI. Global incidence rate of OI was 30.49 [17.3–53.6]. The incidence of OI was 38.92 [20.2–74.8] for RTX, followed by ABA with 21.61 [5.4–86.4], and TCZ with 14.3 [2–101.6]. We found 3 severe OI (2 fungus infections, 1 virus B reactivation). The incidence of severe OI was 7.62 [2.4–23.6], all of them requiring hospitalisation with no deaths. Severe OI have a higher incidence for men 21.1 [5.2–84.2] than women 3.3 [0.4–23.7]. All patients with severe OI were taking corticosteroids, and at least one synthetic DMARD. TCZ did not have any severe OI, and the incidence of severe OI was 10.8 [1.5–76.7] for ABA, followed by RTX with 8.6 [2.1–34.5].

**Conclusions:** The incidence of OI in three non-TNF-targeted biologics in real life conditions is described. Incidence found was near 31 cases per 1000 patients - year. Virus and fungus are the OI more frequent in these bDMARDs. Doctors using bDMARDs should be concerned about this problem and be aware for the detection and management of OI.

**Disclosure of Interest:** None declared

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#### AB0452 BIOLOGICAL THERAPY ADVERSE EVENTS IN BIOBADAGUAY REGISTRY

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**Background:** BIOBADAGUAY is the Paraguayan/Uruguayan registry of adverse events (AE) in patients with inflammatory rheumatic conditions under biologic therapy (BT)

**Objectives:** To determine the frequency and severity of AE in patients under BT from the BIOBADAGUAY registry

**Methods:** Prospective, observational study of undetermined length to verify the efficacy, safety and survival of the BT. The methodology applied is available at <https://biobadaguay.ser.es>. For the present study epidemiological and clinical variables, BT, type and severity of AE were analysed. The incidence rate (IR) was calculated as the total number of adverse events per 1000 patients/year and the incidence rate ratio (IRR) was analysed using the Poisson regression model.

**Results:** 778 BT were analysed (56.6% adalimumab, 23.7% etanercept, 9.6% tocilizumab, 5.7% rituximab, 3.5% infliximab, 0.5% golimumab, 0.38% infliximab biosimilar, 0.13% abatacept). In these, 330 AE were observed, 256 (77.6%) mild and 74 (24.4%) severe. The global IR of AE was 143.9 (95% CI, 128.8–160.8) and 32.6 (95% CI, 25.3–40.5), 111.6 (95% CI, 98.4–126.2) for severe and mild respectively. Infection was the most frequent AE in 175 (53.0%) and 39 (22.3%) of them were severe. Infection's IR was 76.3 (95% CI, 65.4–88.5), 59.3 (95% CI, 49.76–70.2) and 17.0 (95% CI, 12.1–23.3) for global, severe and mild respectively. Out of the 39 severe AE, respiratory infections were the most frequent in 43.6% of the cases. 5 tuberculosis, 6 malignancies and 6 deaths were observed.

When analysing the IR according to diagnosis, Idiopathic Juvenile Arthritis (JIA) was associated with a higher IR of global AE when comparing to the other diagnosis (IRR=2.3 [95% CI, 1.6–3.4] p=4.27 × 10<sup>-6</sup>). RA diagnosis was significantly associated with a higher risk of severe AE (IRR=2.20 [95% CI, 1.2–4.1] p=1.17 × 10<sup>-2</sup>). tocilizumab was significantly associated with a higher incidence of global AE, (IRR=2.69 [95% CI, 1.90–3.82] p=3.13 × 10<sup>-8</sup>) and severe ones (IRR=3.34 [95% CI, 1.81–6.1] p=1.10 × 10<sup>-4</sup>). Adalimumab was significantly associated with a lower rate of global AE (IRR=0.6 [95% CI, 0.4–0.8] p=1.86 × 10<sup>-4</sup>).

**Abstract AB0452 – Table 1.** Incidence rate and incidence rate ratio of adverse events according to diagnosis and biological therapy

Variable	IR	IRR	P value
Psoriatic Arthritis	88 [52,2–139,1]	0,59 [0,33–1,04]	7,03e-02
Ankylosis Spondylitis	102,3 [68,0–147,8]	0,68 [0,40–1,17]	1,63e-01
Rheumatoid Arthritis	134,2 [115,6–155,0]	0,85 [0,62–1,15]	2,81e-01
Idiopathic Juvenile Arthritis	286,4 [229,4–353,2]	2,34 [1,63–3,37]	4,27e-06
Adalimumab	113,5 [96,9–132,1]	0,57 [0,43–0,77]	1,86e-04
Etanercept	190,4 [152,7–234,6]	1,44 [1,03–2,02]	3,30e-02
Rituximab	66,9 [26,9–137,8]	0,45 [0,18–1,13]	8,93e-02
Infliximab	75,0 [24,3–175,0]	0,51 [0,21–1,23]	1,35e-01
Tocilizumab	340,0 [261,8–434,2]	2,69 [1,90–3,82]	3,13e-08

IR: incidence, IRR: incidence ratio (per 1000 patients year)

**Conclusions:** AE were mild in general and infections were the most frequent. In the present study, it was found that JIA and treatment with tocilizumab presented a higher IRR of AE while RA presented a higher rate of severe AE.

**Disclosure of Interest:** None declared

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#### AB0453 BIOLOGICAL THERAPIES RETENTION RATE IN TWO SUDAMERICAN COUNTRIES. DATA FROM BIOBADAGUAY REGISTRY

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**Background:** The retention rates (RR) of biological therapies (BT) have been extensively studied in European countries and the United States, but there is a lack of information about them in emerging populations.

**Objectives:** To analyse BT retention rates and variables associated to them at the BIOBADAGUAY registry

**Methods:** Patients with a chronic inflammatory arthritis enrolled in the Paraguayan-Uruguayan biological register (BIOBADAGUAY) between 2015 and 2017 where included in the study. Phase I of the study was focused in the global RR analysis and association with clinical and epidemiological variables. In phase II we analysed BT retention rate according to different discontinuation motives and association with clinical and epidemiological variables. Survival analysis was performed using Kaplan-Meier estimators and proportional hazard regression models

**Results:** A total of 778 BTs were included in the study (etanercept n=184, adalimumab n=440, rituximab n=44, infliximab n=27, tocilizumab n=75, and others n=8). The underlying diagnosis associated to these BTs were rheumatoid arthritis (RA; 58.2%), juvenile arthritis (JIA; 14.2%), ankylosing spondylitis (SA; 12.5%) and psoriatic arthritis (PA; 8.0%).

In phase I we found that mean survival times were 322 (±17.9), 315 (±22.32), 289 (±8.52) and 233 (±16.69) weeks for AS, PA, RA and JIA respectively. The survival association analysis has shown that JIA diagnosis (p=2.26 × 10<sup>-4</sup>, HR=1.80 [95%CI, 1.32–2.46]), corticosteroids (p=1.54 × 10<sup>-2</sup>, HR=1.38 [95% CI, 1.06–1.79]), and previous BT (p=3.32 × 10<sup>-2</sup>, HR=1.43 [95% CI, 1.03–1.98]) were variables significantly associated with a lower BT retention.

In phase II, we stratified the survival analysis by cause of discontinuation. We found that corticoids (p=9.48 × 10<sup>-4</sup> HR=2.02 [95% CI, 1.33–3.06]), female gender (p=4.36 × 10<sup>-2</sup>, HR=1.66 [95% CI, 1.01–2.72]) and previous BT (p=2.56 × 10<sup>-2</sup>, HR=1.72 [95% CI, 1.07–2.78]) were associated with lower BT retention due to inefficacy. When we analysed withdrawn according to adverse events, we found that RA (p=02.80 × 10<sup>-2</sup>, HR=1.83 [95% CI, 1.07–3.15]), previous BT (p=4.83 × 10<sup>-2</sup>, HR=1.76 [95% CI, 1.00–3.09]) and age (p=7.14 × 10<sup>-5</sup>, HR=1.05 [95% CI, 1.02–1.05]) were significantly associated with therapy discontinuation. In the group of treatments with discontinuation due to remission, we found that JIA diagnosis (p=7.93 × 10<sup>-8</sup>, HR=30.58 [95% CI, 8.77–106.71]), age (p=7.83 × 10<sup>-6</sup>,



HR 0,83[IC 95% 0,76–0,90]) and gender ( $p=4,36 \times 10^{-2}$ , HR 1,66[IC 95% 1,01–2,72]) were associated to discontinuation due to remission.

**Conclusions:** Our results show that different sets of clinical and demographical variables are significantly associated to biological therapy survival depending on the discontinuation cause.

**Disclosure of Interest:** None declared

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#### AB0454 BIOLOGICAL THERAPIES SURVIVAL IN ADULTS AND JUVENILE ONSET ARTHRITIS. DATA FROM BIOBADAGUAY REGISTRY

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**Background:** Survival of biological therapies (BT) may be considered as an indicator of efficacy and safety of the drug. BT survival have been studied mainly in adult's patients, whereas only few studies have been focused on paediatric population to date.

**Objectives:** To analyse and compare BT survival in adults and juvenile onset arthritis patients from BIOBADAGUAY registry.

**Methods:** Patients with a chronic inflammatory arthritis enrolled in the Paraguayan-Uruguayan biological register (BIOBADAGUAY) between 2015 and 2017 where included. For this study, patients were divided in two groups: 1. Adults with an chronic inflammatory arthritis and 2. Patients with juvenile idiopathic arthritis (JIA). To compare the groups according to BT, only the first bioterapy was considered.

Survival analysis was performed using Kaplan-Meier estimators and proportional hazard regression model. First we analysed global BT survival in both groups; secondly we compare BT survival between groups.

**Results:** From 778 BTs(etanercept n=184, adalimumab n=440, rituximab n=44, infliximab n=27, tocilizumab n=75, and others n=8), 556 where identify as first line BTs. Of these, only adalimumab and etanercept were included in the study due to sufficient number prescriptions in both groups for the analysis.

We found a mean survival times for adults of 289 ( $\pm 20.7$  SD) weeks for etanercept and 287 ( $\pm 8.6$  SD) weeks for adalimumab. In JIA patients the mean survival were 243 ( $\pm 26.0$  SD) and 216 ( $\pm 24.0$  SD) weeks for etanercept and adalimumab respectively

When comparing survival between groups, we found that JIA presented more discontinuation of BT when compare with adult patients ( $p=4.4 \times 10^{-4}$ , HR=0.51 [95%CI, 0.35–0.73]). Similar results were observed when analysing only etanercept ( $p=3.92 \times 10^{-2}$ ; HR=0.50 [95% CI, 0.26–0.97]) or adalimumab ( $p=1.20 \times 10^{-3}$ ; HR=0.48 [95% CI, 0.30–0.75]) treatments. Then we analysed withdrawn motive in JIA patients, and found that remission was the principal reason of discontinuation in this group of patients.

Finally, we stratified survival analysis by discontinuation according to adverse events, and found that JIA group presented a lower risk of discontinuation due to adverse events than adults ( $p=1.96 \times 10^{-1}$ ; HR=2.18 [95% CI, 0.67–7.07]).

**Conclusions:** In our study we have analysed mean BT survival between adults and JIA at the BIOBADAGUAY registry. When we compared both groups of patients it was observed that JIA patients presented more BT discontinuation but due to remission.

**Disclosure of Interest:** None declared

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#### AB0455 IMPACT OF ONE-YEAR TREATMENT WITH BIOTECHNOLOGIC DRUGS ON WORK DISABILITY AND ACTIVITY IMPAIRMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Disease activity significantly impacts on work ability of patients with Rheumatoid Arthritis (RA). Biologic agents can control disease activity, but their effects on productivity outcomes were not adequately investigated in Italian population.

**Objectives:** Aim of the study was to evaluate the impact of biologic therapy on work productivity outcomes in a cohort of biologic-naïve patients with active RA from northern Italy.

**Methods:** This is a multicentre prospective study on patients with active RA in working age (18–65 years), scheduled to undergo their first biologic treatment. Demographics and clinical data were collected at baseline and at 6 and 12 months, together with productivity outcomes assessed with the RA-specific work productivity survey (WPS-RA)<sup>1</sup> and the Health and Labour Questionnaire (HLQ)<sup>2</sup>. Primary outcome was the productivity loss or gain after 1 year of treatment.

**Results:** We included 100 patients from 7 rheumatology centres in northern Italy with active RA [mean DAS28: 5,1 (SD 0,9), median SDAI: 25,2 (IQR 18,7–33,2)]. Most of them were females (85%), with a mean age of 49,1 (SD: 10,3) years and a median disease duration of 7 (IQR: 3–14) years. Patients were treated with TNF-inhibitors (68%), Abatacept (24%) or Tocilizumab (8%). At baseline 39 patients were unemployed. After 1 year of treatment, 85 patients were still on follow-up, with an improvement in all indexes of disease activity [mean DAS28: 2,8 (SD 1,3), median SDAI: 5,1 (IQR 1,9–12,9)]. A significant reduction in number of days of work missed (absenteeism) and of reduced productivity (presenteeism) was observed in employed subjects, as well as a significant decrease in number of days missed of household work and social activities in all the study population (table 1).

Abstract AB0455 – Table 1

	Baseline [mean (SD)]	12 months [mean (SD)]	p (t-test for paired data)
Number of days of work missed (absenteeism)	2.5 (3.6)	0.5 (1.3)	0.003
Number of days of reduced productivity (presenteeism)	6.7 (7.9)	0.7 (1.6)	0.000
Rate of arthritis interference with work productivity (0–10 points scale)	3.8 (3.6)	1.3 (2.1)	0.014
Number of days of household work missed	7.5 (8.9)	3.2 (6.2)	0.000
Number of days of reduced productivity in household work	8.9 (9.6)	2.9 (5.3)	0.000
Number of days with social activities missed	6.8 (9.3)	1.9 (4.8)	0.000
Number of days with need for outside help	5.5 (8.2)	1.5 (4.6)	0.000
Rate of arthritis interference with household work productivity (0–10 points scale)	6.1 (2.8)	3.1 (3)	0.000

**Conclusions:** One year of treatment with biological drugs was associated with a significant improvement in outcomes related to productivity both within and outside home in a cohort of patients with RA.

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#### AB0456 EFFICACY AND SAFETY OF SWITCHING FROM ETANERCEPT REFERENCE PRODUCT TO LBEC0101 (ETANERCEPT BIOSIMILAR) COMPARED WITH CONTINUING LBEC0101 IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** LBEC0101 is a newly developed biosimilar of etanercept (ETN). As rheumatoid arthritis (RA) treatment is a long-standing process in the clinical practice, the long-term safety and efficacy of anti-TNF inhibitors have been studied and reported.<sup>1</sup> Clinical studies have been conducted to evaluate the efficacy and safety of biosimilar after switching from their originator drug.<sup>2</sup>

**Objectives:** To evaluate the long-term efficacy, safety, and immunogenicity of switching from the ETN reference product (RP) to LBEC0101 or continuing LBEC0101 in patients with RA.

**Methods:** This multicenter, single-arm, open-label extension study enrolled patients with RA who had completed the 52 week treatment period of the

randomised, double-blind, parallel-group, Phase III study for LBEC0101 (NCT02357069). Patients who were deemed requiring continuous treatment for RA upon the investigator's discretion and agreed to participate in this study were allowed for participation. All patients received LBEC0101 50 mg/ml once a week for 48 weeks with the stable dose of methotrexate regardless of the randomization group in the Phase III study. Efficacy, safety and immunogenicity were assessed up to Week 100. Data were analysed for patients who continued to receive LBEC0101 for 100 weeks (maintenance group) and for those who had received ETN-RP for 52 weeks and then switched to LBEC0101 for 48 weeks (switch group).

**Results:** A total of 148 patients were enrolled in this study; 70 patients continued to receive LBEC0101 and 78 patients switched to receive LBEC0101 from ETN-RP. DAS28-ESR score in the full analysis set were maintained in both groups from week 52 through week 100 (from 3.068 to 3.103 in maintenance group vs. from 3.161 to 3.079 in switch group). Response rates at week 100 for maintenance and switch groups, respectively, were 79.7% vs. 83.3% for ACR20, 65.2% vs. 66.7% for ACR50% and 44.9% vs. 42.3% for ACR70. The incidences of adverse events were comparable between the groups (70.0% for maintenance group and 70.5% for switch group, respectively). The proportion of patients who newly developed antidrug antibodies was similar between the groups (1.4% for maintenance group and 1.3% for switch group, respectively).

**Conclusions:** The efficacy and safety of LBEC0101 were comparable in both maintenance and switch groups. The efficacy of LBEC0101 was well sustained over 100 weeks.

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AB0457

#### CLINICAL EQUIVALENCE IN EFFICACY BETWEEN ABP 501 AND ADALIMUMAB IN PATIENTS WITH MODERATE TO SEVERE RHEUMATOID ARTHRITIS: A TIPPING POINT SENSITIVITY ANALYSIS

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**Background:** ABP 501 is the first approved biosimilar to adalimumab. Patient withdrawals from clinical trials can result in missing data, which may lead to loss of statistical power and bias of the treatment difference estimate. Therefore, it is critical to examine the potential effects of missing data and analyse the sensitivity of the results under various assumptions on the mechanism of missing data.

**Objectives:** To examine and confirm the robustness of the clinical similarity conclusion between ABP 501 and adalimumab reference product (RP) through tipping point sensitivity analyses on ACR20 at week 24, the primary endpoint of the phase 3 study in patients with rheumatoid arthritis.

**Methods:** The primary analysis for this trial has been previously published. The proportions of patients achieving ACR20/50/70 responses with last observation carried forward imputation at weeks 2, 4, 8, 12, 18 and 24, were similar between ABP 501 and the RP over time. Tipping point sensitivity analyses were used to estimate the difference between ABP 501 and the RP with varying assumptions on the outcomes in patients who withdrew from the study early and those who completed the study.

**Results:** The table 1 displays the results of tipping point analyses on the primary endpoint of ACR20 at week 24. There were no scenarios in which the 90% confidence interval (CI) failed to rule out a 12% loss/increase in the ACR20 response.

**Abstract AB0457 – Table 1.** Tipping point analysis results for RD (90% CI) of ACR20 at week 24

Shift between dropouts and completers in ABP 501	Shift between dropouts and completers in adalimumab RP				
	-0.700	-0.525	-0.350	-0.175	0.000
-0.700	0.002	-0.005	-0.014	-0.019	-0.023
	(-0.063, 0.067)	(-0.072, 0.061)	(-0.080, 0.052)	(-0.085, 0.047)	(-0.088, 0.042)
-0.525	0.013	0.005	-0.003	-0.008	-0.012
	(-0.052, 0.078)	(-0.060, 0.071)	(-0.068, 0.063)	(-0.073, 0.057)	(-0.077, 0.053)
-0.350	0.024	0.016	0.008	0.003	-0.001
	(-0.041, 0.088)	(-0.049, 0.081)	(-0.057, 0.072)	(-0.062, 0.067)	(-0.066, 0.063)
-0.175	0.035	0.027	0.019	0.014	0.010
	(-0.030, 0.100)	(-0.038, 0.093)	(-0.046, 0.084)	(-0.051, 0.079)	(-0.055, 0.075)
0.000	0.048	0.040	0.032	0.026	0.023
	(-0.016, 0.111)	(-0.025, 0.105)	(-0.033, 0.096)	(-0.038, 0.090)	(-0.041, 0.086)

The shift represents the assumed difference in week 24 ACR20 response between patients who dropped out prior to week 24 and those who completed week 24. Among completers, the ACR20 response rate was 77.0% and 74.7% for the ABP 501 and adalimumab groups, respectively.

**Conclusions:** The tipping point sensitivity analyses support the findings of the key efficacy analyses in the phase 3 RA study and confirm that the effects of missing data would not change the conclusion of clinical similarity between ABP 501 and the RP.

**Disclosure of Interest:** N. Zhang Shareholder of: Amgen Inc., Employee of: Amgen Inc., H. Wang Shareholder of: Amgen Inc., Employee of: Amgen Inc., E. Krishnan Shareholder of: Amgen Inc., Employee of: Amgen Inc.

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AB0458

#### EFFICACY AND B-CELL DEPLETION WITH VERY LOW DOSE RITUXIMAB (BIOSIMILAR) IN SERO-POSITIVE DMARD RESISTANT RHEUMATOID ARTHRITIS: A 24 WEEK STUDY

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**Background:** Very Low dose Rituximab (RTX) (100 mg) has been variously used in autoimmune diseases like ITP and rheumatoid arthritis (RA). As cost of treatment is an important issue in resource poor setups, we decided to study efficacy of very low dose RTX in patients with RA.

**Objectives:** 1) To study clinical efficacy of very low dose RTX in DMARD refractory RA. 2) To study B cell depletion with very low dose RTX

**Abstract AB0458 – Table 1.** Demographic profile and response to very low dose Rituximab

Demographic Profile	100 mg × 4 doses				100 mg single dose			
	Baseline	Week 12	Week 24	p	Baseline	Week 12	Week 24	p
Total number of patients	14	14	14	-	13	11	11	-
Male:Female		1:6		-		1:3		-
Mean Age		47±12 years		-		49±10 years		-
Mean duration of illness		6.7±4 years (median 5 years)		-		7.1±3 years (median 4.5 yrs)		-
<b>Disease Activity measures</b>								
DAS28(ESR)	5.5±1.1	3.3±1	3.4 ±0.9	<0.001	5.7±0.7	3.3 ±0.4	3.4 ±0.6	<0.001
RAPID3	5±0.8	2.6 ±1.3	3.3 ±1.5	<0.001	5.1±1.1	2.9 ±1.4	2.8 ±1.6	<0.001
CDAI	26.3±8.5	10±8	8.6±6	<0.001	28.2±7.8	12±6	11±6	<0.001
HAQ	1.7±0.3	0.7 ±0.5	0.5 ±0.4	<0.001	1.9±0.4	0.8 ±0.5	0.7 ±0.5	<0.001
Mean ΔDAS28 (24 weeks)		2.2±1.5		-		2.3±1		-
Mean CD19	152	28	-	-	78	18	-	-
<b>EULAR Response</b>								
EULAR remission	0	3	4	-	0	1	3	-
EULAR low disease activity	0	4	4	-	0	3	4	-
EULAR good response	0	11	11	-	0	9	9	-

**Methods:** Prospective open labelled study. Biologic naïve, conventional DMARD refractory, sero-positive RA patients (ACR 2010 criteria) with high disease activity (DAS 28 ESR) were included after informed consent.

Arm 1: Total 4, weekly 100 mg doses (total dose 400 mg) of a RTX biosimilar were infused.

Arm 2: Single 100 mg RTX infusion.

Efficacy was assessed using standard outcome measures for RA (including RAPID3) at week 24. B cell depletion (CD19 levels in peripheral blood by flow cytometry) was studied at baseline, week 1 and week 12.

**Results:** Total number of patients in Arm 1=14 and in Arm 2=13.

In Arm 1: 28% (4/14) achieved EULAR remission while 78% (11/14) had EULAR good response. In Arm 2: 70% (9/13) had EULAR good response. All patients achieved complete B-cell depletion (defined as <0.01%) at week 1 after just single dose of 100 mg RTX remained so at 6 weeks only to start rising again at week 12. There were no adverse events noted. Steroid doses were reduced in most patients at follow up visits with delta change in steroid dose- 2.2 mg/day. Results comparable with other studies using both low dose and conventional dose of RTX. Limitations of the study includes small sample size and short follow-up.

**Conclusions:** Very Low dose RTX is efficacious in conventional DMARD refractory RA patients. Single dose (100 mg) is as good as 400 mg upto week 24. Complete B cell depletion can be achieved even with 100 mg RTX as early as week 1.

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#### AB0459 REMISSION RATE OF TOCILIZUMAB IN CONTROLLED TRIALS AND OBSERVATIONAL STUDIES: SYSTEMATIC REVIEW OF RHEUMATOID ARTHRITIS

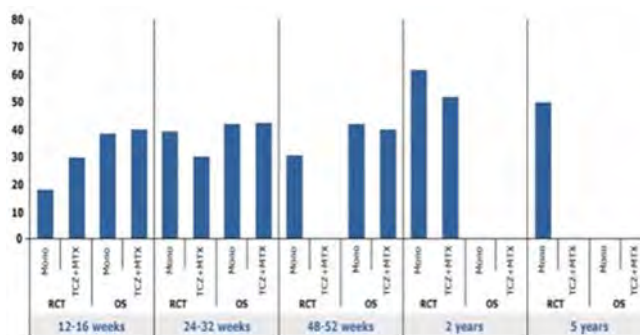
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**Background:** In concept, the state of remission constitutes a clinical condition in which no active disease is present. Target of rheumatoid arthritis (RA) is achieve to remission. Tocilizumab (TOC) is a humanised monoclonal antibody that binds to the interleukin-6 receptor

**Objectives:** The aim of this study was to assess the remission rate of TOC for the treatment of RA patients in randomised controlled trials (RCTs) and longitudinal observational studies (LOS).

**Methods:** In January 2017, a systematic Review (SR) was performed in PUBMED MEDLINE. Publications were identified using the MeSH terms: ("rheumatoid arthritis and Tocilizumab") with a limitation to "humans", "all adults: 19 +years", "English" and "clinical trials". All available studies describing the retention rate of TOC were recruited to SR. Retention rate of TOC were calculated according to route (SC or IV), dosage (4 mg/kg vs 8 mg/kg), monotherapy or combination with methotrexate. Of the 662 publications identified by the literature search, 42 were recruited in the analysis. Retention rates of TOC at 12–16 weeks, 24–32 weeks, 48–52 weeks, 2. Years, 3. Years and 5. years were analysed. Open label extension period of RCTs included to LOS. The causes of withdraw of TOC were recorded as inefficacy, adverse event, and others.

**Results:** Of the 34 studies, 13 (38%) were RCTs and 21 (62%) were LOSs. Totally 12 043 patients (9834 (81%) female) were pooled to analysis that 6190 patients (51%) were from RCTs. The mean age was 53 years and mean disease duration was 9 years. Seropositivity was 73.6% for rheumatoid factor and 72.2% for ACPA. Overall, 5493 (54.6%) of patients were biologic-naïve. TOC was used as monotherapy (2469/6077, 35.4%), or concomitant with methotrexate (8037/11429, 70.3%). Available baseline DAS-28 score, CDAI, SDAI, and HAQ-DI score were 6.2, 32.1, 33.3, and 1.49 respectively. Remission rate of TOC according to study type were shown in table 1.



Abstract AB0459 – Figure 1

**Conclusions:** These systematic literature results show that treatment with of TOC has a high likelihood of inducing a clinically important benefit in terms of different remission criteria. Remission achieved both RCTs and real life results. Moreover, remission rate of TOC in LOSs was comparable with other biologic DMARDs, as well.

**Disclosure of Interest:** None declared

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#### AB0460 LONG-TERM DRUG SURVIVAL OF ETANERCEPT VS OTHER TNF INHIBITOR THERAPIES IN PATIENTS WITH RHEUMATOID ARTHRITIS

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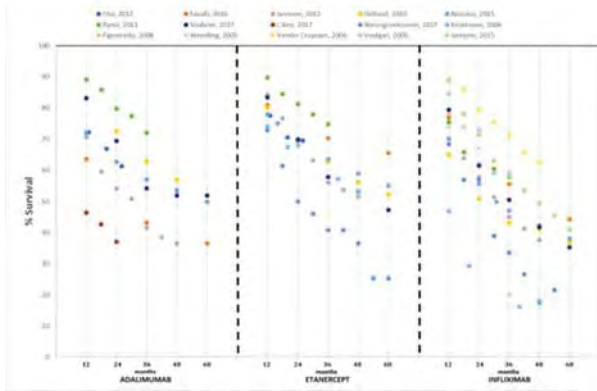
**Background:** TNF $\alpha$  inhibitors have profoundly altered outcomes for patients with rheumatoid arthritis (RA) since they were introduced >15 years ago, by reducing disease activity and radiographic progression and improving quality of life. As a chronic disease, RA often requires life-long treatment, understanding drug survival in real-world settings can be beneficial in optimising disease management.

**Objectives:** To compare the long-term drug survival of adalimumab (ADA), certolizumab pegol (CZP), etanercept (ETN), golimumab (GLM), and infliximab (IFX) in patients with RA based on systematic literature review (SLR).

**Methods:** In this SLR, the goal was to identify full-text articles containing registry data or systematic reviews on TNF $\alpha$  inhibitors, following Cochrane dual-reviewer methodology. Searches were conducted in November 2017 with no date restriction, using Embase<sup>®</sup>, MEDLINE<sup>®</sup>, the Cochrane Central Trials Register and Database of Systematic Reviews, other Cochrane Library databases, and PubMed. Outcomes extracted included drug survival data that were analysed and reported using Kaplan-Meier or Cox regression methods.

**Results:** Of 3688 non-duplicated publications initially identified, 3299 were excluded based on titles or abstracts and 344 based on full-text screening, leaving 26 publications published between 2005 and 2017 included in the analysis. The number of studies (range of sample size) for each drug were ADA: 15 (25–2349), ETN: 17 (20–3892), IFX: 21 (26–2898), GLM: 4 (2–88) and CZP: 1 (N/A). Among the analysed studies, the mean disease duration in years (range) was ADA: 10.7 (8.2–15.1); ETN: 15.9 (5.0–18.5); IFX: 14.2 (8.5–19.3); CZP: 10.3 (N/A); GLM: 8.9 (8.1–11.5) and mean baseline DAS28 (range) was ADA: 5.0 (4.2–5.9), ETN: 5.2 (4.3–6.3), IFX: 5.3 (4.1–6.4); CZP: 4.7 (N/A) and GLM: 4.7 (4.1–5.1). Trends for survival rates of first-line ETN were slightly higher than ADA at time points  $\geq$ 36 months; ADA and ETN had higher survival rates than IFX at >48 months (figure 1).





**Abstract AB0460 – Figure 1.** Survival of First-Line Anti-TNF Therapies in Patients with Rheumatoid Arthritis

**Conclusions:** Long-term survival rates for ADA, ETN, and IFX were similar and relatively high for treatment periods up to 36 months. After 36 months, there was a noticeable decline in drug survival for all three TNF $\alpha$  inhibitors. Heterogeneity in study size and design may contribute to the range of survival data for each agent.

**Disclosure of Interest:** P. Emery Consultant for: Pfizer, MSD, Abbvie, BMS, UCB, Roche, Novartis, Samsung, Sandoz and Lilly, B. Vlahos Shareholder of: Pfizer, Employee of: Pfizer, P. Szczypa Shareholder of: Pfizer, Employee of: Pfizer, M. Thakur Shareholder of: Pfizer, Employee of: Pfizer, H. Jones Shareholder of: Pfizer, Employee of: Pfizer, J. Woolcott Shareholder of: Pfizer, Employee of: Pfizer, P. Santos Estrella: None declared, A. Gibofsky Shareholder of: AbbVie, Angen, Celgene, Pfizer, GSK, J and J, Regeneron, Consultant for: AbbVie, Celgene, MSD, Pfizer, Iroko, Horizon, Samumed, Relburn, Sandoz, Speakers bureau: Amgen, AbbVie, Pfizer, Celgene, Iroko, Horizon, MSD, Novartis, C. Rolland Employee of: Envision Pharma Group, G. Citera Consultant for: Pfizer, AbbVie, Bristol Myers Squibb, Novartis, Roche, L. Marshall Shareholder of: Pfizer, Employee of: Pfizer

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AB0461

**EXPERIENCE WITH SUBCUTANEOUS ABATACEPT IN ROUTINE CLINICAL PRACTICE: 6-MONTH INTERIM ANALYSIS OF A 2-YEAR, PROSPECTIVE, NON-INTERVENTIONAL, MULTICENTRE STUDY IN PATIENTS WITH RA**

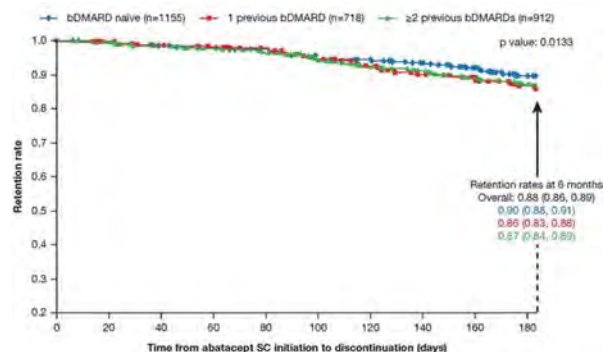
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**Background:** ASCORE (Abatacept SubCutaneOus in Routine clinical practicE; NCT02090556) is an ongoing, prospective, non-interventional, multicentre study of patients (pts) with RA receiving SC abatacept (ABA). In a similar real-world setting, IV ABA retention was >88% at 6 months (M).<sup>1</sup>

**Objectives:** To present baseline (BL) pt characteristics and 6M interim retention rates and clinical outcomes for SC ABA by biologic (b)DMARD treatment line.

**Methods:** Pts ( $\geq 18$  years) with active, moderate-to-severe RA, naïve to ABA and who initiated SC ABA 125 mg weekly were enrolled across 10 countries (March 2013–January 2017) in 2 cohorts: biologic-naïve pts and pts who had failed  $\geq 1$  prior bDMARD. In some countries, an IV loading dose was administered according to local practice. Pt demographics and disease characteristics at SC ABA initiation were recorded. The retention rate (95% CI) of SC ABA over 6M was estimated by Kaplan–Meier analysis. Good/moderate EULAR response rates based on DAS28 (ESR, otherwise CRP), low disease activity (LDA) or remission according to DAS28 (ESR), CDAI, SDAI and Boolean criteria were assessed at 6M.

**Results:** Of 2943 pts enrolled, 2785 (94.6%) were evaluable: 1155 (41.5%) biologic naïve; 718 (25.8%) had failed 1; and 912 (32.7%) had failed  $\geq 2$  prior biologics. At BL, there was a higher proportion of females and pts with longer disease duration among those who had failed  $\geq 2$  vs 1 or no prior bDMARDs; disease activity was similar across treatment lines; CRP was higher in biologic-naïve vs -failure pts; 402 (48.4%) biologic-naïve pts had erosive disease vs 261 (53.7%) or 390 (63.8%) who had received 1 or  $\geq 2$  prior bDMARDs, respectively. Probability of overall SC ABA retention at 6M was 0.88 (95% CI 0.86, 0.89); retention was higher in pts receiving ABA as a first or second vs later bDMARD (figure 1). At 6M, 335 pts had discontinued ABA, 172 (51.3%) of whom due to inefficacy and 140 (41.8%) due to safety. At 6M, among pts continuing ABA, good/moderate EULAR response rates were 83.5%, 75.1% and 72.0% for biologic-naïve pts and pts with 1 and  $\geq 2$  prior bDMARD failures, respectively. DAS28 (ESR), CDAI or SDAI LDA/remission, or Boolean remission rates were higher with earlier vs later treatment lines. The safety profile was consistent with IV ABA studies.<sup>1,2</sup>



**Abstract AB0461 – Figure 1.** Abatacept Retention (Time to Discontinuation of SC Abatacept) Over 6 Months by Treatment Line

**Conclusions:** In this first observation of SC abatacept in a real-world setting, overall retention of SC abatacept at 6M was high and similar to that observed with IV abatacept.<sup>1</sup> Better retention and response rates were achieved with abatacept as an earlier bDMARD treatment line. Good/moderate EULAR response rates at 6M were consistently >70%, irrespective of treatment line and higher BL radiographic erosion in biologic-failure pts.

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AB0462

### UP TO 5-YEAR RETENTION OF ABATACEPT IN BELGIAN PATIENTS WITH MODERATE-TO-SEVERE RA: PROSPECTIVE DATA FROM THE REAL-WORLD ACTION STUDY

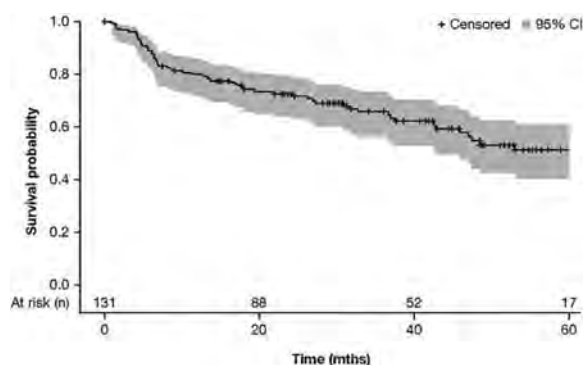
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**Background:** With its specific mechanism of action, abatacept (ABA) has shown good efficacy, acceptable safety and is well tolerated in patients (pts) with RA in randomised clinical studies.<sup>1,2</sup> In a chronic disease such as RA, the long-term efficacy and safety of treatment are crucial and require validation in a real-world setting.

**Objectives:** To explore long-term safety and retention in pts with RA treated with IV ABA in routine clinical practice in the Belgian cohort of the AbataCepT In rOuTiNe clinical practice (ACTION) study.

**Methods:** ACTION is a noninterventional, multicentre, prospective, longitudinal study of pts (aged >18 years) with established active moderate-to-severe RA, who initiated IV ABA in routine care.<sup>3</sup> In Belgium, reimbursement criteria require failure with 2 conventional synthetic DMARDs and DAS28 (CRP) >3.7. The primary study objective was retention rate estimated using the Kaplan–Meier method.

**Results:** Overall, 135 Belgian pts from 16 sites (6 [4.4%] first-line biological and 129 [95.6%] second or further line) were enrolled between October 2010 and December 2012. Of these, 131 were evaluable for effectiveness analysis. Pts had a mean (SD) disease duration of 10.5 (9.7) yrs and were at high risk of disease progression: 25.4% of the evaluable pts had erosions (n/n=33/130), 71.6% were anti-cyclic citrullinated peptide positive (n/n=63/88) and 76.7% were RF positive (n/n=79/103). Overall, pts showed high disease activity at baseline according to mean (SD) DAS28 (ESR) 5.21 (1.02), DAS28 (CRP) 4.72 (1.09), CDAI 28.5 (11.1), SDAI 29.9 (11.9) and HAQ-DI score 1.23 (0.65). Patient and Physician Global Assessment of disease were mean (SD) 65.3 (20.95) and 58.02 (21.77), respectively. The overall retention rate (95% CI) was 76% (68.8, 82.5), 64% (54.8, 71.5) and 34% (22.6, 45.4) at 12, 24 and 60 mths, respectively. When temporary discontinuations (>84 days, n=24) were not included in the number of events, retention rates were 80% (72.0, 85.9), 73% (64.0, 79.4) and 51% (40.1, 61.0) at 12, 24 and 60 mths, respectively (Fig). Average DAS28 (CRP) before discontinuation and at restart was stable (3.37 [1.30] vs 3.73 [1.78], respectively [n=12]), suggesting that a temporary discontinuation of >2 consecutive ABA infusions does not seem to have a major clinical consequence. Pts who discontinued ABA due to lack of efficacy (n=37) had significantly shorter disease duration, higher CRP, higher number of prior DMARDs at baseline, mean DAS28 (CRP) of 3.61 (1.17) and DAS28 (ESR) of 4.66 (1.35) at discontinuation. Overall, ABA was generally well tolerated and no new safety signals were identified.



**Abstract AB0462 – Figure 1.** Treatment Retention Rate Over Time (Mths) in Study Population Evaluable for Effectiveness.

**Conclusions:** These real-world data demonstrate an acceptable safety profile for abatacept in Belgian pts with a stable retention rate of up to 5 years in a difficult-to-treat population. A temporary discontinuation also seems feasible.

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AB0463

### A REVIEW OF THE OUTCOMES OF WOMEN WITH RHEUMATOID ARTHRITIS (RA) TREATED WITH BIOLOGIC AGENTS ATTENDING THE SHEFFIELD COMBINED OBSTETRICS AND RHEUMATOLOGY CLINIC 2002 TO 2013

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**Background:** Women with RA have increased risk of complications including preeclampsia, low birth weight babies and Caesarean sections compared with unaffected women.<sup>1</sup> Higher levels of disease activity have a negative influence on birth weight.<sup>2</sup> More women are being treated with biologic agents, and there is growing evidence for their safe use in pregnancy.<sup>3</sup>

**Objectives:** To assess disease activity during pregnancy, and to review foetal and maternal outcomes.

**Methods:** Retrospective review of case notes.

**Results:** Between 2002 and 2013, 17 women with RA treated with biologic agents attended the combined clinic. 13 were treated with Etanercept, 2 Adalimumab, 1 Tocilizumab and 1 Rituximab. 13 were in combination with disease modifying anti-rheumatic agents (DMARDs). There were 17 pregnancies. 2 women stopped their biologic prior to conception; 14 stopped on confirmation of pregnancy. 12 women had active disease during pregnancy. All had some form of steroid treatment, 3 had a DMARD introduced, and 1 restarted Etanercept at 20 weeks.

There were 14 live births and 2 first trimester miscarriages. There was 1 elective Caesarean section, 7 spontaneous deliveries, and 5 inductions, 3 of which proceeded to Caesarean. Data is missing for 2 women. 10 babies were born at term, 3 were pre-term and data is missing for 2. 2 babies weighed less than 2500 g and 2 more than 4500 g. Data is missing for 3 babies. The low birth weight babies were also pre-term, had cardiac abnormalities and required admission to the neonatal unit. Both mothers had stopped Etanercept at confirmation of pregnancy. Both flared during pregnancy.

6 women developed complications: hypertension, diabetes, proteinuria, cervical incompetence, and hypothyroidism. 4 of these had active disease during their pregnancies. 2 babies had intrauterine growth restriction, 2 cardiac abnormalities and 1 macrosomia. All had mothers who flared during pregnancy.

**Conclusions:** Our group of patients is small, but the outcomes are comparable to those of women with RA. There is no discernible increase in adverse events due to biologic use. In 2014 product recommendations were to stop biologics prior to conception.<sup>4</sup> Since 2016 the British Society for Rheumatology has advised that Etanercept and Adalimumab are compatible with use in the first and second trimesters. Tocilizumab and Rituximab should still be stopped prior to conception.<sup>3</sup> Local practice has changed to reflect this guidance, and the next step in this project is to review the data from more recent pregnancies to determine whether more prolonged use of biologics improves disease control and in turn foetal and maternal outcomes.

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**Disclosure of Interest:** None declared

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**AB0464** 'REAL LIFE' BIOLOGIC DRUG TAPERING RESULTS IN FEW FLARES OF DISEASE AND SIGNIFICANT COST SAVINGS

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**Background:** The treatment of rheumatic diseases has been revolutionised in the biologic era. Remission and low disease activity are realistic targets. Several trials have suggested that dose reduction is achievable without loss of clinical effect. However, 'real life' response data is still lacking.

**Objectives:**

- To increase interval dose of biologic drugs in a standard rheumatology clinic setting
- To assess the clinical response and determine potential cost savings

**Methods:** Patients were identified by database interrogation and hospital prescription record, from a regional population of 4 00 000 over a 2 year period. All rheumatic conditions treated with anti-TNF and IL-6 blockers were potentially accepted for tapering. Those with low disease activity scores (RA and PsA DAS <2.1, AS BASDAI <4.1) for >1 year were screened and invited to consider dose reduction following discussion in a clinic.

**Results:** 154 biologic patients were screened and 97 contacted to consider dose tapering. Of these, 40 patients agreed to participate in biologic dose reduction. Demographics: Mean age 51 years, 18 male patients and 22 females, concomitant MTX use in 49%. Diagnosis: RA-24, PsA -9, AS- 7. Drugs tapered included Adalimumab (28), Etanercept (5), Golimumab (5) and Tocilizumab (2). 8 patients flared during the programme and response was recaptured in 2 patients after increasing dose. 32 patients were successfully maintained on reduced dose with no requirement to date to increase dosing frequency. Biologic drug was completely withdrawn in 1 patient and 2 patients were commenced on reduced dose of DMARD. Prior to dose reduction mean DAS was 1.91 and mean BASDAI was 2.45. Low disease activity scores were recorded (mean DAS 2.1, mean BASDAI 2.6) post dose reduction (although incomplete data capture). Estimated cost savings are between 170,000 EUR and 340000 EUR for the 2 years.

**Conclusions:** Successful tapering of biologic drugs can be achieved and sustained in non-trial settings for patients with low disease activity. Significant cost savings have been confirmed with likelihood of recurrent savings over future years.

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**Acknowledgements:** Ms Vandana Raghuvir

Medical student at Glasgow University

**Disclosure of Interest:** None declared

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**AB0465** SAFETY AND DURATION OF BIOLOGIC TREATMENT IN ELDERLY PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Several differences may be expected between young and elderly patients with rheumatoid arthritis (RA), safety and efficacy results are variable in the different previous studies.<sup>1,2</sup>

**Objectives:** To compare the duration and safety of biological treatment in patients with RA depending on the age of onset of therapy, in a Spanish tertiary centre.

**Methods:** We conducted a retrospective observational study of patients with a diagnosis of RA who were receiving biologic treatment. They were diagnosed between February 1980 and February 2017, on the basis of criteria ACR/EULAR 2010 or 1987 ACR criteria. The information was obtained from review of medical records. We divided the patients in two groups according to age of the onset of treatment: elderly group ( $\geq 65$  years) and young group (<65 years).

**Results:** 140 patients were included. At the beginning of the treatment 89 were under 65 years and 51 older (65–74 years: 28 patients, >75 years: 23). The average duration of the disease from diagnosis until the beginning of the biological treatment was 103 $\pm$ 91 months in young patients and 142,86 $\pm$ 109,5 months in elderly patients (p: 0,023). We detected no differences between both groups at baseline characteristics, except for comorbidities and sex. DAS28PCR prior to biologic therapy was 5.20 $\pm$ 1.44 in young patients and 5.14 $\pm$ 0.813 in elderly (p: 0,37).

Duration of the treatment was similar in both groups. Suspension of biologic treatment occurred in 50 young patients (56%) and 30 elderly patients (58%) (table 1). The causes are detailed in table 2. Adverse effects were more frequent in the elderly but without statistical significance. There were 9 cases of cancer in elderly patients (17.3%) and 4 cases in young patients (4.6%) p: 0.013. The average diagnosis of cancer prior to the introduction of biologic treatment was 5.8 $\pm$ 7.1 years.

**Abstract AB0465 – Table 1**

	Young patients (<65 years) n=89	Elderly patients ( $\geq 65$ years) n=51	p
Age diagnostic AR (years)	42,87 ( $\pm 11.34$ )	62 ( $\pm 10.65$ )	0.42
Age biological treatment (years)	51,39 ( $\pm 10.32$ )	73,8 ( $\pm 5.30$ )	<0.001*
Sex: female	74 (83.1%)	35 (68,65%)	0.04 *
Comorbidities	0	4 (8.3%)	0.006 *
Heart failure	2 (2.2%)	5 (9.8%)	0,048*
Renal failure			
Type biological	16 (18%)	11 (21%)	0,013*
Infliximab	31 (34.8%)	10 (19.6%)	
Adalimumab	27 (30.3%)	10 (19.6%)	
Etanercept	3 (3.4%)	2 (3.9%)	
Certolizumab	4 (4.5%)	2 (3.9%)	
Abatacept	7 (7.9%)	8 (15.7%)	
Tocilizumab	0	6 (11.8%)	
Rituximab			
Duration treatment(months)	39,98 ( $\pm 41,04$ )	46,31 ( $\pm 33,28$ )	0,095
Adverse events	13 (14.6%)	12 (21.56%)	0.7
Serious/recurrentinfection	6 (46%)	6 (54%)	
Active tumour	0	1 (9.1%)	
Cytopenias	1 (7.1%)	1 (9.1%)	
Skin lesions	3 (23%)	0	
Gastrointestinal symptoms	2 (15%)	1 (9.1%)	

**Abstract AB0465 – Table 2**

	Young patients	Elderly patients	p
Lack of efficacy (<6 months)	10 (20%)	0	0.015*
Lack of efficacy (>6 months)	22 (44%)	10 (33%)	0.55
Adverse event	8 (16%)	8 (26.6%)	0.16
Remission	4 (8%)	4 (13.3%)	0.350

**Conclusions:** Our study corroborate that biologic treatment has similar duration and safety in elderly and young patient.<sup>1,2</sup>

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**Disclosure of Interest:** None declared

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**AB0466** SAFETY OF RITUXIMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS. ELEVEN-YEAR FOLLOW-UP OBSERVATIONAL STUDY

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**Background:** Rituximab (RTX) is a chimeric monoclonal antibody approved for the treatment of active rheumatoid arthritis (RA) in patients who failed to respond to tumour necrosis factor inhibitors (TNFi). Due to its effect on induction of B cell depletion, the administration of multiple cycles can lead to a decrease in immunoglobulins (Ig) which may increase the risk of infection.

**Objectives:** To assess the long-term safety of RTX in patients with RA and to evaluate factors associated with the presence of infections.



**Methods:** A retrospective observational study was conducted including patients with RA treated in a tertiary hospital between June 2006 and May 2017 who had received at least one RTX cycle. At RTX initiation we analysed: age, sex, comorbidities and Charlson score, disease duration, presence of rheumatoid factor (RF)/anti-citrullinated protein antibodies (ACPA), disease activity (DAS28), acute phase reactants (CRP, ESR), previous biological treatments; concomitant treatment (csDMARD/glucocorticoids (GC)). Serum Ig levels before every RTX cycle, the number of RTX cycles and adverse events (AE), including serious and opportunistic infections were also analysed.

**Results:** We included 53 patients (86.8% women, mean age 55.5±13.5 years), 58% with a Charlson score ≥3. Mean disease duration was 16±9.1 years; 84.9% and 92.5% were RF and ACPA positive, respectively.

Before starting RTX, 81% of patients had received other biologic drugs (58.5% ≥ 2), 88% received concomitant csDMARD, (52% methotrexate and 32% leflunomide) and 81% were treated with GC (median dose 10 mg, P<sub>25-75</sub> 5–10 mg). The median number of RTX cycles received per patient was 5 (P<sub>25-75</sub> 2–6).

80 AE were reported: 12 infusion reactions, 8 cases of neutropenia, 51 infections (18 respiratory, 8 urinary, 4 skin and soft tissues, 8 gastrointestinal, 4 cases of non-disseminated *herpes zoster*, 1 bacteremia, 2 septic shock and 6 other) of which 19 were serious, and 5 malignancies (2 melanomas, 2 cervix, and 1 bladder) were also notified. No opportunistic infections were reported.

Ig levels were obtained for 41 subjects: 7, 5 and 1 patients had low levels of IgG, IgM and IgA, respectively.

Patients who developed infections received a greater number of RTX cycles (p<0.0002) and had more frequently low levels of serum IgG during follow-up (p<0.044) than those who did not have infections.

**Conclusions:** Long-term exposure to RTX showed a good safety profile with a low incidence of serious infectious and no opportunistic infections.

Factors associated with the development of infections were the number of cycles received and low serum levels of IgG at any point during follow-up.

**Acknowledgements:** The authors would like to thank Dr. García de Yébenes who provided statistical support

**Disclosure of Interest:** None declared

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#### AB0467 SUSTAINED CLINICAL RESPONSE IN REFRACTORY RHEUMATOID ARTHRITIS PATIENTS WITH A LOW-DOSE RITUXIMAB RETREATMENT REGIMEN

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**Background:** The standard dose of rituximab (RTX) in rheumatoid arthritis (RA) is two intravenous (iv) 1 g infusions, separated by two weeks. Recently, the efficacy of a low-dose of RTX for retreatment in RA patients has been reported.<sup>1</sup>

**Objectives:** Our aim was to assess the long-term sustained effectiveness of a low-dose of RTX in daily clinical practice.

**Methods:** Observational retrospective study including all RA patients treated on a tertiary hospital who had received at least one cycle of RTX, at the standard dose, between June 2006 and May 2017. We selected those patients who achieved a good or moderate EULAR response and thereafter were down-titrated to a low-dose regimen (1 g). Variables analysed: age, sex, disease duration, presence of ACPA (antiCCP2) and rheumatoid factor (RF), glucocorticoid (GC) and conventional synthetic DMARD (csDMARD) use and dosage before and after RTX treatment, number of biologic DMARD (bDMARD) used prior to initiating RTX. Disease activity was measured using DAS28 index (prior to first RTX infusion, at low-dose regimen initiation and at last follow-up visit).

**Results:** 53 patients received, at least, one cycle of 2 g RTX, 70% achieved a good or moderate EULAR response and were stepped-down to a low dose retreatment regimen. Baseline characteristics of patients receiving low-dose RTX were: mean age 56.4±10.9 years; 13.5% male, mean disease duration 12.7±9.8 years, 91.9% RF + and 97.3% ACPA +; mean DAS28 prior to RTX initiation 5,79 ±1,17.

73% of patients had received other bDMARD before RTX, 48% 2 or more. 92% were on cs-DMARDs, 51.4% methotrexate (MTX) and 37.8% leflunomide (LEF) and 86.5% were receiving concomitant GC (median dose 10 mg, P<sub>25-75</sub> 5–10 mg). 73% of subjects received only one standard cycle before RTX dose reduction.

Mean DAS28 decreased significantly between the first visit on 1 g RTX vs the last follow-up visit (4.08 vs 3.04; p<0.0001). Additionally, 11 patients (8 MTX, 3 LEF) were able to reduce csDMARD dosage, 56.3% of patients receiving GC at the initiation of low-dose retreatment were able to reduce the dose (median 10 mg vs 5 mg; p<0.0001), and 28% discontinued GC therapy.

After a mean follow-up of 3±1.8 years, RTX was withdrawn in 10 patients: 8 due to adverse events (recurrent infections in 4) and 2 cases due to loss of efficacy.

**Conclusions:** A sustained clinical response was observed with the 1 gr retreatment of RTX after a long-term follow-up period.

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**Disclosure of Interest:** None declared

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#### AB0468 CLINICAL AND ULTRASONOGRAPHIC EFFECTIVENESS IN TWO COHORTS OF RHEUMATOID ARTHRITIS PATIENTS TREATED WITH ABATACEPT: A REAL LIFE STUDY

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**Background:** Synovitis in Rheumatoid Arthritis (RA) is a phenomenon related to the development of erosions and progressive structural damage; early synovitis improvements are successfully associated with long-term clinical and structural outcomes.

**Objectives:** The aim of this study was to evaluate the efficacy of abatacept in two cohort of patients treated with Abatacept as the first and second or third line of treatment.

**Methods:** We evaluated patients affected by RA (according to ACR 2010 criteria) and were divided into two groups:

**Group A:** patients with moderate or severe active RA, non-responders to Methotrexate (MTX), bDMARDs naïve, treated with Abatacept 125 mg/wk;

**Group B:** patients with moderate or severe active RA, non-MTX and anti-TNF responders, treated with Abatacept 125 mg/wk;

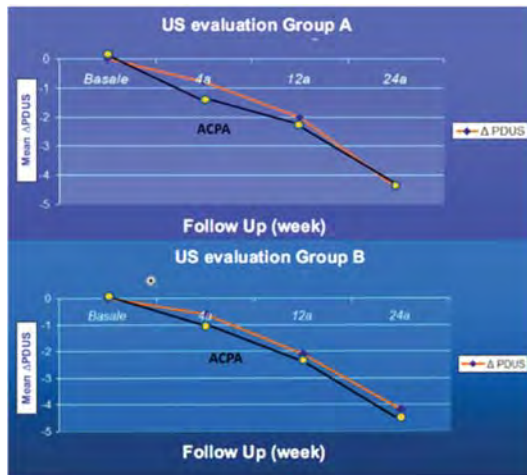
The concomitant treatment with MTX was maintained unchanged in those patients who were taking it at stable doses before the start of the study (10–15 mg/week for ≥28 days); concomitant therapies such as low-dose systemic CS (prednisone ≤7.5 mg/day) and NSAIDs have been maintained for at least 4 weeks if stable. The activity of RA was calculated with the DAS28-CRP according to the clinical practice protocol (week 0,4,12,24). The Ultrasound (US) evaluation of the synovitis was done according to the Omeract criteria (Grey Scale and PDUS score: 0 to 3).

**Results:** We recruited consecutively 34 patients with RA, 16 pts (male n=4; 25,00%) took Abatacept as the first line (Group A), and 18 pts (males n=5; 27,70%) took Abatacept as followed by another anti-TNF drugs (Group B). The mean age was 57.2±10.7 years (median 60, range 45–72); mean of DAS28 at baseline was 4.8±0.9 (median 4.7; range 3.9–5.6); mean duration of the disease was 15.3±5.7 years (median 10; range 3–22). Tab.1

A constant improvement of the DAS28 score is shown in both groups examined until the end of the follow up, resulting respectively -Δ 2.0 for Group A (p<0.05) and -Δ 2.1 (p<0.05) for Group B. The total PDUS score decreased in both groups from week 4, with a mean change (95% CI) compared to baseline of -0.8 (range -1.4/-0.2) and progressive mean significant improvement until follow-up (Gr.A p<0.05; Gr.B p<0.05). No serious adverse events or infections were observed. Patients with ACPA positive showed a greater improvement trend compared to other patients in both groups (p: 0,068). Figure 1.

**Abstract AB0468 – Table 1.** Cohort of patients at baseline

Characteristics	Group A (Abatacept 1 <sup>st</sup> line)	Group B (Abatacept 2 <sup>nd</sup> or 3 <sup>rd</sup> line)
Patients (n <sup>o</sup> )	16	18
Age (mean±SD), yy	44,20 (±8,7)	56,10 (±10,6)
Female (%)	76,00%	77,00%
Disease Duration (mean±SD), yy	7,80 (±5,3)	12,70 (±5,6)
DAS28-CRP (mean±SD)	5,10 (±0,9)	4,90 (±1,1)
PDUS score (mean±SD)	12,30 (±2,5)	12,60 (±3,1)



Abstract AB0468 – Figure 1. PDUS evaluation of two cohorts with ACPA positive

**Conclusions:** The treatment with Abatacept, administered in the first or second or third line, has shown significant efficacy in reducing the synovial inflammation in patients with RA, monitored with clinical and ultrasonographic outcome. Moreover, we have not demonstrate statistically significant differences between two groups into the timing of improvement.

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**Disclosure of Interest:** None declared

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#### AB0469 EFFICACY AND SAFETY OF INTERLEUKIN 6 INHIBITORS IN RHEUMATOID ARTHRITIS: A SYSTEMATIC LITERATURE REVIEW

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**Background:** Interleukin 6 (IL-6) inhibitors constitute a therapeutic option for patients with rheumatoid arthritis (RA). Currently, apart from Tocilizumab (TCZ), we have data from other drugs targeting the IL-6 pathway.

**Objectives:** To review published evidence on safety and efficacy of IL-6 inhibitors in RA.

**Methods:** We performed sensitive systematic literature searches in Medline and Cochrane (up to October 2017), screened EULAR and American College of Rheumatology meeting-abstracts. An expert librarian designed the strategies that included Mesh and text word terms. The search was limited to human RA, adults and the English and Spanish language. The inclusion criteria were as follow: 1) RA patients on IL-6 Inhibitors including TCZ, sarilumab (SAR), olokizumab, sirukumab and clazakizumab; 2) Placebo and an active comparator were accepted as comparators; 3) Articles including typical efficacy and safety variables such as DAS-28, radiographic progression or the infections rate; 4) Only meta-analyses, systematic reviews and clinical trials were selected. Two reviewers screened the titles and abstracts of the retrieved articles independently. They also collected the data from the studies included by using ad hoc standard forms. All collection was double by article and independent. Subsequently, a secondary manual search of the bibliography of the articles that were finally included was performed. Evidence tables were produced. The quality was evaluated with the Oxford 2009 scale.

**Results:** We included 64 articles of moderate-high quality, variable duration, between 12 and 108 weeks. These articles analysed more than 8000 patients with RA, most of them with established RA (although there are data on early RA), with high disease activity and severity criteria. More than a half of the studies are of TCZ. IL-6 inhibitors were effective both in the short and long term in terms of clinical remission, RA activity, radiographic progression, function, fatigue, bone metabolism, morning stiffness, pain, quality of life, or anaemia. They also decreased and even normalised CRP values in a rapid and sustained manner. The efficacy of blocking IL-6 has been seen in RA refractory to DMARD or anti-

TNF $\alpha$  and in MTX-naïve patients, as well as in the intravenous and subcutaneous formulations (TCZ). TCZ and SAR are more effective than adalimumab in monotherapy. In general, no statistically significant differences were found between combined therapy and monotherapy. In terms of safety, the rate of adverse events increased over time and with the concomitant use of DMARDs. Infections and hypersensitivity reactions were the most frequent adverse events and infections the most frequent serious adverse events. IL-6 inhibitors were associated with a rapid and subsequently sustainable increase in serum lipid parameters, although this was not associated with a higher prevalence of cardiovascular events and related mortality, nor was it associated with neoplasms. Transaminase elevations were generally mild and without serious disorders. The incidence of gastrointestinal perforations was very low, and it was associated with a previous history of diverticulitis.

**Conclusions:** IL-6 inhibitors are effective to control RA activity and symptoms and to prevent radiographic damage in different disease profiles, with an acceptable safety profile.

**Disclosure of Interest:** None declared

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#### AB0470 INFLUENCE OF USING ADALIMUMAB IN COMPLEX TREATMENT ON FREQUENCY OF EYES INVOLVEMENT IN PATIENTS WITH JIA

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**Background:** Extra-articular organs involvement in JIA is frequent and mostly includes rheumatoid uveitis in ANA-positive oligoarthritis. In Ukraine almost 10% of children with JIA during systematic ophthalmologic examination have signs of ocular involvement. Early treatment with biological agents can influence inflammation progression in eyes of the JIA patients

**Objectives:** Objective of the study was to investigate the frequency of recurrences of uveitis in patients with JIA and eyes involvement on methotrexate alone and methotrexate with adalimumab.

**Methods:** There were 23 patients with JIA and rheumatoid uveitis involved into the study. Mean age was 9,6 (4–16) years. Among them there were 14 (61%) girls and 9 (39%) boys. Serological characteristic included 17 (74%) patients with positive ANA, and 3 (13%) children with positive HLA-B27. All patients received 15 mg/m<sup>2</sup>/week of SC methotrexate. During onset and recurrence of uveitis all children received glucocorticoids with slowly tapering dosage (from 1 mg/kg/day to 0.2–0.1 mg/kg/day) until uveitis remission. Of 23 patients 11 (47,8%) received adalimumab in standard doses. Study were hold for 5 years during which every child were investigated by ophthalmologist every 3 months irrespectively of clinical status.

**Results:** During 5 year follow up in "methotrexate" group (n=12) there were 15 episodes of uveitis recurrence (0,25 episodes per patient/year). Of them 10 (66,6%) were revealed only by ophthalmological assessment and had no obvious clinical signs (subclinical uveitis). Same time only 2 episodes of uveitis recurrence were registered in "methotrexate +adalimumab" group (0,04 episodes per patient/year) (p<0.05).

**Conclusions:** Adding adalimumab to methotrexate in complex treatment of patients with JIA and eyes involvement allows decreasing frequency of both clinically evident and subclinical recurrences of rheumatoid uveitis.

**Disclosure of Interest:** None declared

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#### AB0471 BIOSIMILAR MEDICINE IS ACCEPTABLE TO PATIENTS IF RECOMMENDED BY A RHEUMATOLOGIST IN AN AUSTRALIAN TERTIARY RA COHORT

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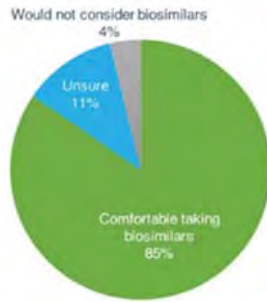
**Background:** Advancement in biological disease-modifying antirheumatic drugs (bDMARDs) has greatly improved the prognosis of patients with rheumatoid arthritis. Their high costs, however, pose a significant health-economic challenge. Biosimilars are being adopted in Australia and worldwide to improve affordability and access to treatment. While the predominant focus of current literature has been on physicians' awareness and confidence of biosimilars, an effective introduction of biosimilars requires an understanding of patient acceptance of these products.

**Objectives:** To investigate patient awareness and attitudes to biosimilar medicine in a tertiary hospital RA clinic.

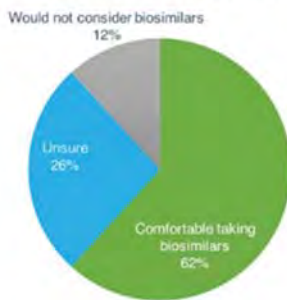
**Methods:** A cross-sectional study of 127 patients with rheumatoid arthritis was performed in Melbourne, Australia. A brief education on biosimilars was provided. Patients rated concerns regarding biosimilar efficacy, side-effect profile, operation

of the medication, and general attitude towards the new medication on a ten-point scale.

**Patients willing to take generic medicines**



**Patients unhappy to take generic medicines**



Abstract AB0471 – Figure 1

**Results:** 45.2% of our cohort have received biological DMARDs. Although only 5.6% have some knowledge of biosimilars, 75.4% would accept biosimilars if their rheumatologist recommends it, with only 5.6% refusing to switch. 19% of patients were unsure. Of those refusing biosimilars, the main concerns related to efficacy and general concerns about change. In our RA cohort, 61.9% took generic medicines regularly and 84.6% of these they would also be comfortable taking biosimilars. In those refusing generic medicines (27%), 61.8% would be still comfortable taking biosimilars. 15.9% and 12.7% of patients had great concerns about the efficacy and safety profile of biosimilars, respectively. 26.2% were significantly worried that their physician may be unaware if they were receiving the biosimilar or reference product.

**Conclusions:** Despite being unfamiliar with biosimilars, most patients in our cohort would be comfortable taking biosimilars if recommended by their rheumatologist, highlighting the role of trust in doctor-patient relationships. Of patients usually refusing generic medicines, nearly two-thirds would still accept biosimilars. Almost a quarter of the patients were unsure about the use of biosimilars and many patients indicated that they would like more information regarding these products. This patient group offered the opportunities to improve the uptake rate of biosimilars by allaying their concerns through information-education strategies. The current legislation in Australia allows pharmacists to substitute biological DMARDs in consultation with the patient without informing the prescriber. This concerns nearly all (89%) prescribers in Australia. The majority of patients in our study were not concerned, whilst approximately one quarter were worried about unrecognised switching. A successful introduction of biological DMARDs is likely to improve patient access to effective biological therapy and to ensure sustainability of the healthcare budgets.

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**Disclosure of Interest:** None declared

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AB0472

**PHARMACODYNAMIC EFFECT AND SAFETY OF SINGLE-DOSE SARILUMAB SC OR TOCILIZUMAB IV OR SC IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA)**

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**Background:** Two studies (PDY14191 [NCT02404558]: randomised, open-label, Japanese patients; 6R88-RA-1309 [NCT02097524]: randomised, open-label, non-Japanese patients) assessed the pharmacodynamic profiles of two monoclonal antibody blockers of IL-6Rα, sarilumab and tocilizumab.

**Objectives:** To evaluate the pharmacodynamics of absolute neutrophil count (ANC), C-reactive protein (CRP), IL-6, soluble IL-6R (sIL-6R), and safety after a single dose of subcutaneous (SC) sarilumab, or intravenous (IV) or SC tocilizumab in patients with RA.

**Methods:** 30 Japanese patients (PDY14191) were randomised 1:1 and received a single injection with SC sarilumab 150 mg or SC tocilizumab 162 mg without background medication. 101 non-Japanese patients (6R88-RA-1309) were randomised 1:1:1:1 and received a single dose of SC sarilumab (150 or 200 mg) +methotrexate (MTX), or IV tocilizumab (4 or 8 mg/kg)+MTX. Pharmacodynamic and safety outcomes were assessed through Week 6.

**Results:** Baseline demographics were comparable between studies except for higher mean body weight in non-Japanese patients (mean 83 vs 57 kg). Although there were numeric differences in baseline pharmacodynamic parameters in the two studies, onset of effects on ANC, CRP, IL-6, and sIL-6R during the first week after a single drug dose were similar regardless of drug, dose, or route of administration in both studies. Within both studies, maximal effects on ANC and CRP nadir and on IL-6 and total sIL6-R peaks were comparable for sarilumab and tocilizumab (table 1). The pharmacodynamic response was more prolonged with IV tocilizumab. Time for pharmacodynamic effects to return to baseline was consistent with the dosing intervals for SC sarilumab (q2w), and IV (q4w) and SC (q2w) tocilizumab. The safety profiles of sarilumab and tocilizumab were generally similar and both drugs were associated with laboratory effects consistent with their mechanism of action (ie, decrease in neutrophil count). There was a dose-dependent effect on ANC<1.0 Giga/L in study 6R88-RA-1309 and numeric differences in ANC<1.0 Giga/L between sarilumab and tocilizumab in PDY14191. The decrease in ANC was not associated with increased risk of infections.

Abstract AB0472 – Table 1. Baseline and change in pharmacodynamic parameters, and safety in studies 6R88-RA-1309 and PDY14191

	6R88-RA-1309 (non-Japanese patients)*				PDY14191 (Japanese patients)	
	SC Sarilumab 150 mg + MTX (N=24)	SC Sarilumab 200 mg + MTX (N=26)	IV Tocilizumab 4 mg/kg + MTX (N=25)	IV Tocilizumab 8 mg/kg + MTX (N=24)	SC Sarilumab 150 mg (N=15)	SC Tocilizumab 162 mg (N=15)
<b>Neutrophils</b>						
Baseline, mean±SD, Giga/L	4.32±1.53	4.72±1.96	4.04±1.36	4.52±2.45	3.45±1.11	3.81±0.99
Nadir, mean±SD (min-max), Giga/L	1.55±0.36 (0.63-3.07)	1.76±1.04 (0.71-3.97)	1.78±0.60 (0.96-2.92)	1.64±0.89 (0.69-4.51)	1.11±0.51 (0.3-1.9)	1.78±0.56 (0.9-2.5)
Time to nadir, median, days	3.5	4.0	5.0	3.0	2.0	4.0
<b>CRP</b>						
Baseline, median, mg/L	5.50	6.05	4.28	5.87	0.85	0.89
Nadir, median* (min-max), mg/L	0.67 (0.10-4.82)	0.49 (0.10-5.33)	0.44 (0.10-1.73)	0.31 (0.10-1.35)	0.06 (0.0-0.2)	0.35 (0.0-0.6)
Time to nadir, median, days	7.0	7.0	15.0	25.0	10.0	10.0
<b>IL-6</b>						
Baseline, mean±SD, pg/ml	23.9±58.4	9.86±10.5	7.33±11.1	22.1±49.4	4.97±5.42	5.79±15.5
Peak, mean±SD (min-max), pg/L	399±356 (23-3844)	277±231 (17-3078)	383±168 (3-644)	288±246 (25-1095)	44.0±41.7 (11-469)	48.4±67.3 (7-311)
Time to peak, median, days	5.0	4.5	6.0	6.5	5.0	7.0
<b>sIL-6R</b>						
Baseline, mean±SD, ng/ml	42.9±11.9	42.9±11.7	43.3±14.4	43.8±15.7	86.0±7.9	86.6±11.6
Peak, mean±SD (min-max), ng/ml	274±22.7 (125-406)	344±22.5 (259-442)	415±109 (230-603)	401±120 (180-704)	345±54.6 (155-348)	291±83.6 (206-469)
Time to peak, median, days	11.0	11.0	19.0	22.0	14.0	14.0
<b>AEs</b>						
Patients with TEAEs, N (%)	10 (38.5)	13 (46.2)	8 (32.0)	12 (50.0)	7 (46.7)	4 (26.7)
SAE, n (%)	0	0	0	1 (4.2)	1 (6.7)	0
Patients with AEs <1.0 Giga/L, n (%)	4 (15.4)	7 (26.9)	3 (12.0)	6 (25.0)	5 (33.3)	3 (19.7)
<b>ANC grade</b>						
ANC maximum grade: Grade 3+0.5 to 0.0 Giga/L, n (%)	4 (15.4)	6 (23.1)	3 (12.0)	6 (25.0)	2 (13.3)	1 (6.7)
ANC maximum grade: Grade 4 +0.5 Giga/L, n (%)	0	1 (3.8)	0	0	1 (6.7)	0

**Conclusions:** The pharmacodynamic and safety profiles observed after a single-dose of sarilumab SC or IV/SC tocilizumab are consistent with results anticipated in patients with RA administered an IL-6R inhibitor.

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Employee of: Regeneron, A. Boyapati Shareholder of: Regeneron Pharmaceuticals, Employee of: Regeneron Pharmaceuticals, C. Xu Shareholder of: Sanofi, Employee of: Sanofi

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AB0473

### IMMUNOGENICITY OF BIOSIMILARS FOR RHEUMATIC DISEASES: AN UPDATED REVIEW FROM REGULATORY DOCUMENTS AND CONFIRMATORY CLINICAL TRIALS

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**Background:** Several biosimilars have been approved for the treatment of rheumatic diseases by the European Medicines Agency (EMA) or the US Food and Drug Administration (FDA).

**Objectives:** To summarise immunogenicity data from regulatory documents or confirmatory trials of biosimilars approved by the EMA or FDA for the treatment of rheumatic diseases.

**Methods:** EMA Public Assessment Reports (EPARs), FDA Clinical Summaries, PubMed records, and EULAR and ACR abstracts were searched for immunogenicity data from confirmatory trials of approved TNF $\alpha$  or CD20 inhibitor biosimilars in patients with rheumatic diseases. Data collected included the proportion (%) of patients positive for anti-drug antibodies (ADABs) among all patients and the proportion (%) of patients with neutralising antibodies (nAbs) among ADAB-positive patients.

**Results:** We identified 10 biosimilars approved by the EMA or FDA: three each for adalimumab (BI 695501, SB5, and ABP 501) and infliximab (SB2, CT-P13, and infliximab-qbtx) and two each for etanercept (GP2015 and SB4) and rituximab (CT-P10 and GP2013). The duration of treatment periods in the 16 identified trials (which varied in design and methodology of ADAB/nAb detection) ranged from 12 weeks to 102 weeks. Across treatment groups in all trials, 0% to 62% of patients were ADAB-positive, of whom 0% to 100% were also nAb-positive. The lowest proportions of ADAB-positive (0%–13%) and nAb-positive patients (0%–3%) were observed in the trials of etanercept and its biosimilars, and the highest in the trials of infliximab and its biosimilars (ADABs: 20%–62%; nAbs: 88%–100%). Consistent with the biosimilar designation, the proportions of ADAB- and nAb-positive patients in individual trials were similar between the originator and biosimilar products. Of note, in a 52 week trial of etanercept and its biosimilar SB4, the incidence of ADAs by Week 52 was significantly lower with SB4 than with etanercept (1% [3/299] vs 13% [39/296],  $p < 0.001$ ). However, as noted in the SB4 EPAR, this difference, which was not reflected in the incidence of nAbs and efficacy or safety of etanercept, may have been due to an ADAB assay bias in samples collected at Weeks 4 and 8, when 37/39 ADABs in the etanercept group and 2/3 in the SB4 group were detected.

**Conclusions:** Immunogenicity of the approved biosimilars is generally similar to that of originator products. For ETN, which has been associated with relatively low

ADAB levels, there was a discrepancy in ADAB incidence compared with its biosimilar SB4, but those differences were transient and did not affect clinical activity or safety.

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**Disclosure of Interest:** V. Strand Consultant for: AbbVie, Amgen, AstraZeneca, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Celltrion, Corrona, Crescendo, EMD Serono, Genentech/Roche, GSK, Janssen, Eli Lilly, Merck, Novartis, Pfizer, Regeneron, Samsung, Sandoz, Sanofi, and UCB, J. Goncalves: None declared, T. Hickling Shareholder of: Pfizer, Employee of: Pfizer, H. Jones Shareholder of: Pfizer, Employee of: Pfizer, L. Marshall Shareholder of: Pfizer, Employee of: Pfizer, J. Isaacs Grant/research support from: Pfizer, Roche, Consultant for: Pfizer, Abbvie, Janssen, Roche, Speakers bureau: Pfizer, Abbvie, Roche

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AB0474

### THE CLINICAL EFFECTIVENESS AND COST SAVINGS OF TAPERING BIOLOGIC DMARDs IN PATIENTS WITH INFLAMMATORY ARTHRITIS AT A UK DISTRICT GENERAL HOSPITAL

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**Background:** Biologic DMARDs (bDMARDs) have led to substantial improvement in clinical outcomes for treatment of rheumatoid arthritis (RA), psoriatic arthritis (PsA) and axial/peripheral spondyloarthritis (SpA), making remission a realistic target. Current guidelines suggest clinicians should consider tapering after achieving remission in RA.<sup>1</sup> Nevertheless, the optimal approach for tapering bDMARDs remains unknown and un-standardised across conditions.<sup>2</sup>

**Objectives:** To evaluate the tapering strategies on 3 major rheumatological disease entities (RA, PsA, SpA), the number of patients successfully tapered and the total cost saving from successful tapering.

**Methods:** The study was conducted at North Devon District Hospital in Barnstaple, UK and includes all bDMARDs users up until 31st December 2017. The tapering strategy was identified from hospital notes. Patients who are deceased, lost to follow-up or discontinued bDMARDs due to contraindication or adverse effects were excluded. Successful tapering is defined as patient on tapered dose or had their biologics withdrawn and remains at target treatment level (RA: DAS-28 <2.6; PsA: <3 tender joints and <3 swollen joints; SpA: BASDAI <4).

**Results:** There are a total of 298 patients: 174 RA; 59 PsA; 57 SpA; 8 other diagnoses. 94 patients (31.5%) had attempted tapering: 52 RA, 18 PsA, 22 SpA. 60 (20.1%) successfully tapered their bDMARDs: 34 RA (56.7%); 13 PsA (21.7%); 13 SpA (21.7%). Out of 34 RA, 30 seropositive; 4 seronegative; 24 co-prescribed with synthetic DMARDs, 10 on monotherapy. Out of 13 PsA, 8 co-prescribed with synthetic DMARDs; 5 on monotherapy.

59 tapered by increasing interval of subcutaneous treatment. Only 1 RA patient tapered its IV dose of tocilizumab. This patient is excluded from the final analysis. Tapering of subcut bDMARDs therapy by disease and price (table 1). Number rounded to 2 decimal points.

Abstract AB0474 – Table 1

Disease	bDMARDs	No. of patients	Usual dose of interval (days)	Mean tapered dose interval (days)	Mean period of tapering (months)	% saving per unit biologic	Cost per unit biologic (£)	Cost Saving per patient (£)	Total cost saving (£)
RA	ADA	12	14	7.00	27.75	50.00	352.14	9771.89	117262.68
	CZP	13	14	6.85	22.92	48.92	357.50	8016.92	10421.96
	ETN	5	7	8.20	34.40	117.14	134.06	21608.41	108042.05
	TOC	3	14	3.00	14.75	42.86	179.20	4531.50	13594.50
<b>Total</b>		<b>33</b>						<b>249321.19</b>	
PsA	ADA	7	14	3.14	14.86	22.43	352.14	2347.43	16432.01
	GOL	4	28	10.50	18.25	28.57	701.93	4803.83	19215.32
	ETN	2	7	2.00	11.50	28.57	134.06	1761.84	3523.68
<b>Total</b>		<b>13</b>						<b>39171.01</b>	
SpA	ADA	9	14	4.89	20.30	34.93	352.14	4993.90	44945.10
	GOL	2	28	10.50	5.63	37.50	701.93	7121.81	14243.62
	CZP	1	14	10.00	10.00	71.43	357.50	5107.25	5107.25
	ETN	1	7	3.00	31.00	42.86	134.06	7124.81	7124.81
<b>Total</b>		<b>13</b>						<b>71420.78</b>	
<b>Grand Total</b>		<b>59</b>							<b>359912.98</b>

ADA – adalimumab; TOC – tocilizumab; ETN – etanercept; GOL – golimumab; CZP – certolizumab pegol

**Conclusions:** In our study, 20% of bDMARDs users successfully tapered their dose. The total cost saving is significant at £359,912.98 over the tapered period, of which £249,321.19 (69%) in RA; £39,171.01 (11%) in PsA; £71,420.78 (20%) in SpA.

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AB0475

#### THE INFLUENCE OF SWITCHING FROM ETANERCEPT ORIGINATOR TO ITS BIOSIMILAR ON EFFECTIVENESS AND THE IMPACT OF SHARED DECISION MAKING ON RETENTION AND WITHDRAWAL RATES

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**Background:** With biological patents expiring, biosimilars are becoming a realistic, less costly alternative to their originator. The data from numerous randomised clinical trials support that it is safe, effective and cost saving to switch to a biosimilar. However, real world data about efficacy, safety, and cost-effectiveness of such a switch are lacking.

Since shared decision making (SDM) is a key factor in the treatment of rheumatic diseases, a non-mandatory open label transitioning from Etanercept originator to its biosimilar was performed at the rheumatology department of Bernhoven.

**Objectives:** The first goal of this study was to investigate the effect of switching from Etanercept originator to its biosimilar on the effectiveness of treatment. The second aim was to analyse the effect of SDM on the 1 year retention rates and reasons for withdrawal in daily clinical practice.

**Methods:** All patients with rheumatoid arthritis (RA), axial spondyloarthritis (SpA) and psoriatic arthritis (PsA) that were using Etanercept originator between 01–06–2016 and 23–10–2017 were informed by letter of the possibility to switch to its biosimilar. During the next outpatient visit with their rheumatologist the possibility to switch was discussed. Patients had the opportunity to ask questions regarding biosimilars and the switch to a biosimilar. If patients agreed the switch was made, with the reservation that they could switch back to the originator if they encountered difficulties with the biosimilar.

Using the registry of the rheumatology department at Bernhoven data were collected on disease activity (DA), medication use and adverse events from the moment of switch till 23–10–2017. As measure for DA the DAS28 was used for RA and PsA, the ASDAS was used for SpA. Stop reasons for biosimilars were verified using the health record system of the hospital. Reasons for change in disease activity and discontinuation of biosimilar treatment were assessed.

**Results:** Between 01–06–2016 and 23–10–2017 80% (69 patients) of the Etanercept originator users switched to its biosimilar. These patients switched to biosimilar after a median time of 5.1 (IQR 2.8–8.3) years. By 23–10–2017, median follow-up of 307 (IQR 196–357) days, the mean DA did not significantly differ from the DA at baseline, 3.1 (95%>CI 2.5–3.7) vs. 2.8 (95%>CI 2.5–3.1). At end of follow-up 25% of the patients had discontinued their treatment and either switched back to originator (18%), switched to another biological (3%) or stopped treatment with biologics (4%).

Reasons for switching back to originator were adverse events (58%), lack of effect (17%) and “adverse event and lack of effect” (25%). Only one serious adverse event was reported. This was a drug hypersensitivity reaction. After the patient was recovered, the originator was restarted without any difficulties.

**Conclusions:** An open label non-mandatory switch from Etanercept originator to its biosimilar showed that around 80% of the patients is willing to perform this switch. Switching did not affect effectiveness of treatment during one year follow-up. 75% of the patients were able to continue biosimilar therapy. In the 69 patients that switched only one serious adverse effect occurred.

**Disclosure of Interest:** None declared

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AB0476

#### THE EFFICACY OF IMMUNOADSORPTION WITH INFlixIMAB THERAPY ON THE MODULATION OF DISEASE ACTIVITY IN PATIENTS WITH SEVERE RHEUMATOID ARTHRITIS

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**Background:** Active refractory rheumatoid arthritis (RA) is common in real-world. Patients with active refractory RA usually have poor prognosis. And they respond poorly to a variety of therapies. The arrival of remission or low disease activity

(LDA) as soon as possible is an important way to improve their prognosis. We investigated the effectiveness of immunoadsorption therapy, a novel blood purification treatment, as a rapid and sustained disease-modifying therapy for active refractory RA.

**Objectives:** To evaluate the efficacy of additional immunoadsorption therapy (2 times) besides infliximab (IFX) on disease remission in patients with active refractory RA.

**Methods:** 90 patients with severe RA were included in this study. 43 patients were treated with basic IFX 3 mg/kg+methotrexate (MTX) therapy, and other different 47 patients, besides of basic therapy, were previous given 2 times additional immunoadsorption therapy. IFX 3 mg/kg was infused at weeks 0, 2, 6, 14, 22 and 30. Age, sex ration, mean disease duration and core index of disease activity in two treatment groups were collected at weeks 0, 2, 6 and 30 weeks to compare the efficacy and safety of combined immunosorbent therapy in the treatment of severe RA.

**Results:** The baseline age, sex ration and core indexes of disease activity were comparable between the two treatment groups ( $p > 0.05$ ). After treatment, the core indexes of disease activity of all patients decreased significantly compared with their baseline levels ( $p < 0.05$ ). The degree of reduction in the combined therapy group was significantly better than that in the basic treatment group ( $p < 0.05$ ), and the proportion of ACR remission patients in the combined treatment group was higher than that in the basic treatment group at different stages after treatment.

**Conclusions:** Additional immunoadsorption therapy can rapid relive the disease activity of severe RA patients, and the remission rate of 30 W was significantly higher than only IFX treatment. However, due to the limited sample size of this study, the efficacy of additional immunoadsorption needs further observations.

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AB0477

#### INHIBITION OF LARGE JOINT DESTRUCTION IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH TOCILIZUMAB

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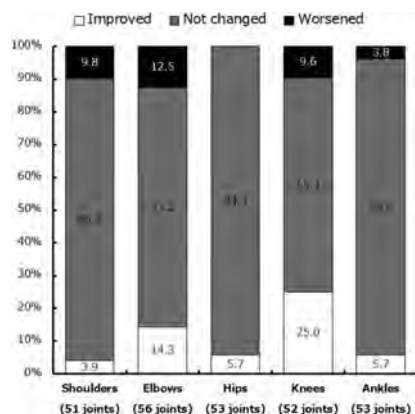
**Background:** Rheumatoid arthritis (RA) causes not only inflammation of small joints, such as hands and feet, but also inflammation of large joints. Destruction of large joints is correlated with impairments of physical activity in RA patients more than destruction of small joints is<sup>(1)</sup>. We experience strong inhibitory effect of inflammation in synovial joints, not only small joints but also large joints, by treatment with tocilizumab (TCZ), an antibody to IL-6 receptor in RA patients in daily clinical practice. Although inhibitory effects of small joint destruction by TCZ is well known, inhibitory effects of large joint destruction is unknown.

**Objectives:** This retrospective study investigated inhibitory effect of large joint destruction by TCZ treatment in RA patients.

**Methods:** Toyohashi RA database (TRAD) was used. TCZ was initiated in 65 RA patients in our institute. 31 cases (23 female and 8 male) who continued TCZ over 2 years were utilised in this study. Baseline characteristics and time course of disease activity were investigated. Delta-modified Sharp score ( $\Delta$ mTSS) per year was used to evaluate small joint destruction. ARASHI score<sup>(2)</sup> was used to evaluate large joints destruction. Shoulders, elbows, hips, knees and ankles were evaluated using ARASHI score.

**Results:** Treatment continuation rate of TCZ was 86.3% at one year and 77.7% at two years in whole 65 cases (Kaplan-Meier methods). Baseline characteristics of 31 cases was as followed. Average age: 56 years old. Average RA duration: 6.6 years. Concomitant rate of MTX: 74.2%. Concomitant rate of prednisolone:

64.5%. Order of TCZ: 1st biologics in 9 cases, 2nd biologics in 9 cases, 3rd biologics in 13 cases. Rates of symptomatic joints (pain or swelling): 45.1% in shoulders, 44.6% in elbows, 0.0% in hips, 51.9% in knees and 37.7% in ankles. Average CDAI was 23.3 at baseline, 6.8 at one year and 5.0 at two years. Average  $\Delta$ mTSS was 8.1 at baseline, 2.7 from baseline to one year and 1.1 from one year to two years. Evaluation using ARASHI change score from baseline to two years was as followed [worsened, not changed, improved (%)]. Shoulders (51 joints) [9.8, 86.3, 3.9]. Elbows (56 joints) [12.5, 73.2, 14.3]. Hips (53 joints) [0, 94.3, 5.7]. Knees (52 joints) [9.6, 65.4, 25.0]. Ankles (53 joints) [3.8, 91.6, 5.7]. Joint surgery was not performed in evaluated joints during study periods. Influence of symptoms at baseline on large joint destruction: There was a significant difference between ARASHI change score in symptomatic knee joints and that in non-symptomatic joints (-0.5 vs. 0.1,  $p < 0.01$ ).



**Abstract AB0477 – Figure 1.** Evaluation of large joint destruction using ARASHI score during two-year tocilizumab treatment

**Conclusions:** Over 90% of large joints was not destructed during two-year TCZ treatment. Improvement was frequently observed in knees and elbows. Major reasons of improvement of joint destruction were stabilisation of joints by osteophyte formation and repair of bone erosions.

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## Rheumatoid arthritis – non biologic treatment and small molecules

### AB0478 MILD AND MODERATE HEPATIC IMPAIRMENT HAVE NO CLINICALLY RELEVANT IMPACT ON UPADACITINIB PHARMACOKINETICS: RESULTS FROM A DEDICATED PHASE 1 STUDY

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**Background:** Upadacitinib is a selective Janus kinase 1 (JAK1) inhibitor being developed for the treatment of several inflammatory diseases, including rheumatoid arthritis (RA). Upadacitinib efficacy was demonstrated in Phase 2 studies in RA, Crohn's disease, atopic dermatitis, in addition to three completed Phase 3 trials in RA. Upadacitinib is a non-sensitive substrate for hepatic metabolism by cytochrome P450 3A; however, 38% and 24% of upadacitinib immediate-release dose are eliminated unchanged in faeces and urine, respectively. Since, there is a potential for upadacitinib use in some patients with hepatic impairment, evaluation of impact of hepatic impairment on upadacitinib exposure is of key clinical relevance. Doses of 15 mg and 30 mg once daily (QD) using upadacitinib extended-release formulation have been evaluated in Phase 3 trials in RA.

**Objectives:** To evaluate the effect of mild and moderate hepatic impairment on the pharmacokinetics of upadacitinib.

**Methods:** This was a Phase 1, open-label study in subjects with mild (n=6) or moderate (n=6) hepatic impairment, according to the Child-Pugh classification, and demographically-matched healthy subjects (n=6). Subjects received a single 15 mg dose of upadacitinib extended-release formulation under fasting conditions. Blood samples for upadacitinib assay were collected over 120 hours after administration. Upadacitinib maximum observed plasma concentration ( $C_{max}$ ), area under the plasma concentration curve (AUC), and terminal phase elimination half-life ( $t_{1/2}$ ) were calculated using non-compartmental analyses. Analyses of covariance were conducted to estimate upadacitinib exposure in subjects with hepatic impairment relative to subjects with normal hepatic function.

**Results:** There was no statistically significant difference in upadacitinib  $C_{max}$  or AUC in subjects with mild and moderate hepatic impairment compared to subjects with normal hepatic function. One subject with moderate hepatic impairment showed significantly lower upadacitinib exposures than subjects with normal hepatic functions and was excluded as an outlier to ensure a conservative estimate for effect of hepatic impairment on exposure. Upadacitinib exposure ratio central values [and 90% confidence intervals] in subjects with mild and moderate hepatic impairment were 1.28 [0.91–1.79] and 1.24 [0.87–1.76] for AUC and 1.04 [0.77–1.39] and 1.43 [1.05–1.95] for  $C_{max}$ , respectively, compared to subjects with normal hepatic function. Upadacitinib terminal elimination half-life (harmonic mean  $\pm$  pseudo standard deviation) was 7.99 $\pm$ 4.60 and 4.14 $\pm$ 1.46 in subjects with mild and moderate hepatic impairment relative to 8.93 $\pm$ 4.87 in subjects with normal hepatic function. Upadacitinib was generally well tolerated by the subjects in the study.

**Conclusions:** Mild and moderate hepatic impairment result in only a very limited effect on upadacitinib plasma exposures (<30% increase in upadacitinib AUC). Therefore, in clinical trials, dose adjustments in subjects with mild or moderate hepatic impairment are not warranted.

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### AB0479 CHARACTERISATION OF THE EFFECT OF RENAL IMPAIRMENT ON UPADACITINIB PHARMACOKINETICS

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**Background:** Upadacitinib is a selective inhibitor of Janus kinase 1 (JAK1) which is currently being evaluated for the treatment of several autoimmune disorders, including rheumatoid arthritis (RA). Although renal elimination plays a minor role in upadacitinib clearance (<20% of upadacitinib dose is eliminated unchanged in urine), a considerable number of RA patients have renal dysfunction. As such, characterisation of the effect of different degrees of renal impairment on upadacitinib plasma exposures is important for this patient population.

**Objectives:** The objective of this study was to assess the pharmacokinetics of upadacitinib in subjects with mild, moderate, and severe renal impairment compared to subjects with normal renal function.

**Methods:** This Phase 1 study was conducted in 24 adult subjects, who were assigned to one of four groups (six subjects per group) according to the estimated glomerular filtration rate (eGFR) as calculated by the Modification of Diet in Renal Disease (MDRD) equation: normal renal function (eGFR of  $\geq 90$  mL/min/1.73 m<sup>2</sup>), mild renal impairment (60–89 mL/min/1.73 m<sup>2</sup>), moderate renal impairment (30–59 mL/min/1.73 m<sup>2</sup>), and severe renal impairment (15–29 mL/min/1.73 m<sup>2</sup>). Subjects received a single 15 mg dose of upadacitinib extended-release formulation under fasting conditions. Blood samples for pharmacokinetic assessments were collected for 120 hours after dosing. The effect of renal impairment on upadacitinib plasma exposures was assessed through regression analysis as well as analysis of covariance across the renal impairment categories.

**Results:** The point estimates for upadacitinib plasma exposure ratios [90% confidence interval] in subjects with mild, moderate, and severe renal impairment were 1.18 [1.06–1.32], 1.33 [1.11–1.59], and 1.44 [1.14–1.82] for AUC and 1.06 [0.92–1.23], 1.11 [0.88–1.40], and 1.14 [0.84–1.56] for  $C_{max}$ , respectively, relative to subjects with normal renal function. In this analysis, one subject with moderate renal function showed exposures significantly lower than subjects with normal



renal function. This subject was excluded to ensure a conservative estimate of the impact of renal impairment on upadacitinib exposure. Results from the categorical analysis were consistent with the results from the primary regression analysis.

**Conclusions:** Renal impairment has only a limited effect on upadacitinib pharmacokinetics. Upadacitinib mean plasma exposures (AUC) in subjects with severe renal impairment are within 44% of mean exposures in subjects with normal renal function. This is in agreement with the known limited role of urinary excretion in upadacitinib elimination.

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#### AB0480 FOLIC ACID SUPPLEMENTATION DELAYS CLINICAL IMPROVEMENT IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH METHOTREXATE

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**Background:** Methotrexate (MTX) is the disease-modifying anti-rheumatic drug (DMARD) most commonly used in the treatment of rheumatoid arthritis (RA), and folic acid (FA) supplementation is usually employed to prevent MTX-related adverse effects.<sup>1</sup> However, the need of FA supplementation remains controversial, as it might influence the efficacy of MTX therapy.<sup>2</sup>

**Objectives:** The aim of this retrospective study was to evaluate the effects of FA supplementation on both efficacy and safety of low-dose MTX in the treatment of RA patients.

**Methods:** 120 RA patients (mean disease duration 11±30 months, mean age 61±13 SD years), according to ACR criteria,<sup>3</sup> who started low-dose MTX treatment were retrospectively evaluated. Patients were not complaining of serious diseases other than RA. Two groups of patients were selected: patients supplemented with FA (#58) and patients not-supplemented with FA (#62). MTX dose, prednisone dose, disease activity (DAS28), and adverse event (AE) were recorded at 3, 6, 9, 12, 24, 36, and 48 months. At baseline, MTX mean dose was 8.3±1.9 and 8.1±1.4 mg/weekly, prednisone mean dose was 7.4±3.1 and 5.3±3.2 mg/daily, and mean DAS28 was 5.1±1.2 and 4.8±1.1, respectively for both groups. The patients were followed-up until MTX discontinuation, new DMARD/BiologicDMARD addition, need for FA supplementation, or after 48 months of therapy (mean follow-up 40±20 months). The maximum MTX dose administered during the follow-up was 15 mg/weekly. Statistical analysis was performed by non parametric tests.

**Results:** DAS28 decreased in both groups during the study. However, DAS28 was found significantly lower (p<0.04) in patients without FA supplementation, when compared with patients taking FA supplementation, at months 3, 6, 9, and 12. Patients without FA supplementation required significantly lower (p<0.01) doses of both prednisone and MTX during the follow-up. AEs were observed in 26% of patients with FA supplementation, as well as in 43% of patients without FA supplementation. The difference was statistically significant (p=0.049). No difference in AE type was observed between the groups (mainly, transaminase or mean red blood cell volume elevation, oral mucositis, urinary tract infections). AEs have been successfully managed in the majority of cases by either discontinuing MTX for two weeks or adding FA if required.

**Conclusions:** In RA patients taking low-dose MTX, FA supplementation decreases the efficacy of the treatment, delaying the clinical responsiveness. The lack of administration of FA increases the risk of AEs; however, by considering the benign type of AEs usually observed in this subset of patients, the treatment with low doses of MTX might be started without FA supplementation, and the FA administration deferred until AE appearance.

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**Disclosure of Interest:** None declared

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#### AB0481 TRANSCUTANEOUS VAGUS NERVE STIMULATION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid Arthritis is a prevalent, autoimmune disease causing joint destruction and severe physical disability. In various studies the vagal nerve has been postulated to play a role in modulation of systemic inflammation.

**Objectives:** Our aim was to investigate the effect of transcutaneous stimulation of the vagal nerve (t-VNS) in patients with rheumatoid arthritis. We hypothesised that stimulation of the vagal nerve and thereby enhanced parasympathetic tone would increase the activity of the vagal nerve and improve experienced clinical pain.

**Methods:** Sixteen patients with rheumatoid arthritis and flare (DAS28-CRP>3.2) and twenty without flare were recruited. Three bilateral electrical stimulations of the vagal nerve were done with a handheld device for 4 days. Cardiac vagal tone (CVT) was assessed with linear vagal scale (LVS) and DAS28-CRP were collected on the 1st, 2nd and 5th day.

**Results:** Cardiac vagal tone was significantly lower in patients with flare in comparison to patients without flare (3.2 vs. 4.9 LVS, p=0.03). t-VNS did not alter CVT in patients with flare, however decreased CVT in patients without flare (baseline: 4.9, 2nd day: 3.8 LVS, p=0.03). A decrease in DAS28-CRP in patients with flare was seen in response to t-VNS (baseline: 4.2, 5th day: 3.9, p=0.03), due to decrease in CRP (baseline: 8.2, 5th day: 6.0 mg/L, p=0.02) and number of swollen joints (baseline: 5.4, 5th day: 4.4, p=0.01) and tender joints (baseline: 3.7, 5th day: 2.8, p=0.02) in RA patients with flare. A negative association between baseline CVT and baseline DAS28-CRP was found in all RA patients, showing that lower CVT was associated to higher disease activity.

**Conclusions:** Baseline CVT was lower in RA patients with flare, possibly due to higher level of inflammation, and the observed decrease in DAS28-CRP was not associated to CVT modulation.

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**Disclosure of Interest:** None declared

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#### AB0482 SIMILAR EFFICACY OF TOFACITINIB ON DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS PATIENTS WITH AND WITHOUT PREVIOUS BIOLOGICALS; RESULTS FROM THE TURKBIO REGISTRY

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**Background:** The aim of this study was to investigate the drug survival, its efficacy and safety in patients with RA based on the database from the Turkish TURKBIO registry

**Methods:** A total of 180 patients were treated with TOFA for RA. Drug survival was assessed. In 118 patients with available data, treatment response was evaluated using the number of sensitive and swollen joints, VAS values, DAS28, HAQ and CRP at weeks 12, 24, 48 and 60

**Results:** At baseline, RA patients had a median(Q1-Q3) disease duration of 14 years. 75 patients had used ≥1 biologics previously. The other demographic and clinical features of the patients were shown in table 1. Median(Q1-Q3) followup period was 137 weeks. After 48 and 137 weeks, 75% and 48% of the patients respectively, maintained TOFA (figure 1). The most common reason for drug discontinuation was ineffectiveness of treatment (63%), followed by adverse events (23%). After 12 weeks, all disease activity parameters were reduced significantly compared to the baseline and most of them continued to be reduced until week 60. No difference was observed in disease activity parameters between the groups

Abstract AB0482 – Table 1

	Week 0	Week 12	Week 24	Week 36	Week 48	Week 60	*p	**P	***p
Patients with response data, (n)	118	39	41	31	32	28			
Disease activity level, n (%)									
Remission		7 (6)	17 (47)	10 (32)	16 (59)	12 (43)		17 (63)	
Moderate		64 (59)	14 (39)	12 (39)	7 (26)	10 (36)		8 (30)	
High		29 (27)	1 (3)	1 (3)	1 (4)	2 (7)		2 (7)	
DAS28, Median (Q1-Q3)	4.4 (3.7–5.1)	2.8 (2–3.5)	3 (2.4–3.6)	2.2 (1.9–3.3)	3.1 (1.9–4.2)	2.1 (1.9–4.1)	<0.001	<0.001	<0.001
Swollen joint (0–28); Median(Q1-Q3)	2 (0–4.3)	0	0	0	0	0	<0.001	<0.001	<0.001
Tender joint (0–28); Median (Q1-Q3)	4 (2–10)	0 (0–1.3)	0 (0–2)	0 (0–0)	0 (0–2)	0 (0–0)	<0.001	<0.001	<0.001
CRP (mg/L); Median (Q1-Q3)	13 (4.7–29)	4.8 (3–12.8)	4.3 (3–10.3)	4 (3–9)	6 (3–12)	9 (3–17.5)	0.005	0.015	0.110
Patient global score (0–100); Median	62.5 (42–80)	44 (12–60)	30 (20–50)	27(12–31)	30.5 (15–69)	27.5 (13–46)	<0.001	0.001	<0.001
HAQ score; Median	1 (0.8–1.5)	0.5 (0–1.3)	0.6 (0.1–1.3)	0.5 (0.3–0.8)	0.6 (0.2–1.2)	0.6 (0–1)	0.003	0.008	0.001

Abstract AB0482 – Table 2. Disease activity parameters baseline and weeks 12,24,36,48 and 60

	Response data:n	58	18	15
First biological tofacitinib n:105	DAS28, Median	4.5 (3.7–5.2)	2.4 (1.6 3.6)	3 (2.4–3.6)
	(Das 28<3.1) n	11 (19%)	11 (61%)	8 (53%)
Using other biological drugs before TOFA n:75	response data, n	50	18	16
	DAS28, Median	4.4 (3.7–5)	2.9 (2.4 3.5)	3 (2.3–3.7)
	Das28<3.1 n (%)	4 (8%)	10 (56%)	10 (63%)
	#p	0.577	0.516	0.921
	##p	0.173	1.000	0.879

\*p for week 0 vs 12; \*\*p for week 0 vs 48,\*\*\*p for week 0 vs 60 #p das28median for TOFA versus other biological ##p das28 <3.1for TOFAversus other biological

with and without previous  $\geq 1$ biologics at weeks 0,12 and 24 (table 2) Remission rate was(43%)at week 60(observed data) (table 2) A total of 9 adverse events (3infection,3allergic rx,2 rash)were observed during the followup period

**Conclusions:** Treatment with TOFA may provide good response rates in RA patients refractory previous biologics

**Disclosure of Interest:** None declared

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#### AB0483 PHYSICIANS' AWARENESS ON THE USE OF METHOTREXATE BY RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Methotrexate (MTX) is an anchor drug used in the treatment of rheumatoid arthritis (RA). It is notable that although MTX has severe potential side effects, most of these side effects could be prevented. Patients should be informed very well regarding MTX and prescriptions should be prepared carefully.

**Objectives:** In this research, we sought to investigate patients with RA and also physicians, awareness regarding use of MTX, which is under-researched.

**Methods:** Following Fayet et al., the data were collected from rheumatoid arthritis patients (n=98) and physicians (n=82) through a questionnaire that included questions regarding the effects of MTX, MTX administration, drug interaction, side effects, the frequency of patient follow-up and changes regarding daily life. The questionnaire was filled by the patients in the hospital and physicians filled the on-line questionnaire.

**Results:** 23% patients responded correctly about that MTX is drug modifying anti-rheumatic drugs (DMARD). 88% of the patients stated that they used MTX weekly, only 16% of the patients were able to explain the reason why they used folic acid was reducing the toxicity of MTX and only 5% reported that folic acid did not increase the efficacy of MTX. 95% did not know that trimethoprim should not be combined with MTX. 11% were familiar with haematologic risks. 7% were aware of hypersensitivity pneumonitis. 42% had information regarding laboratory tests. 20% were conscious concerning the need for contraception. 33% noted that alcohol consumption must be limited. The striking findings physicians responded wrongly was that according to 51% physicians, MTX leads to cancer. Surprisingly, approximately 30% physicians responded wrongly concerning surgery protocol.

Abstract AB0483 – Table 1

	Right answer (%)		Wrong answer (%)		Unknown (%)	
	Patient	Physician	Patient	Physician	Patient	Physician
<b>Mechanism of action</b>						
Methotrexate is a disease-modifying drug	23	93	17	7	60	0
Time when MTX becomes effective	12	83	20	12	68	5
Should not be stopped on the disappearance of symptoms	13	98	16	0	71	2
Dosage should not be adjusted to the pain	40	76	15	19	45	5
Maximum dosage allowed	12	82	7	13	81	5
Once weekly administration	88	100	4	0	8	0
Folic acid reduces toxicity of MTX	16	94	5	5	79	1
Decreases efficacy at high doses	3	61	11	28	86	11
Does not increase efficacy of MTX	5	93	10	6	85	1
Should not be combined with trimethoprim	5	71	4	11	91	18
Nonapplicable interactions with analgesics	23	94	16	5	61	1
NSAIDs	22	93	13	3	65	4
Corticosteroids	23	98	13	2	64	0
DMARDs	23	94	12	6	65	0
Nonapplicable interactions with antibiotics	11	88	11	5	78	7

**Conclusions:** The findings showed that patients with RA, who used MTX frequently, had insufficient information regarding MTX. Notably, patients are lack of information about the side effects of MTX, drug interactions and the need for contraception. Hence, we recommend that patients' knowledge should be increased regarding MTX. Physicians should be provided with training to raise awareness proper use of MTX.

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AB0484

### MONOTHERAPY WITH FILGOTINIB, A JAK1-SELECTIVE INHIBITOR, REDUCES DISEASE SEVERITY AND ALTERS IMMUNE CELL SUBSETS IN THE NZB/W F1 MURINE MODEL OF LUPUS

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**Background:** Systemic lupus erythematosus (SLE) is a heterogeneous autoimmune disease characterised by immune system hyperactivation leading to the production of autoantibodies and immune attack on multiple organs including the skin and kidneys. High levels of type I interferons (IFN $\alpha$ /b) alter the activation state of immune cell populations and have been identified as a risk factor for SLE. Antibody blockade of the interferon alpha receptor (IFNAR) has demonstrated clinical efficacy in a Phase 2b study in SLE, and validates targeting this pathway in SLE<sup>1</sup>. Janus kinase 1 (JAK1) is critical for mediating downstream signalling of type I IFNs. Inhibition of JAK1, therefore, is anticipated to reduce IFN signalling, activation of immune cell subsets, and SLE disease activity. The JAK1 selective inhibitor filgotinib (FIL) is currently being evaluated in three proof-of-concept Phase 2 studies in SLE-like diseases.

**Objectives:** To characterise the efficacy and mechanism-of-action of FIL in the NZB/W F1 spontaneous mouse model of lupus in a therapeutic setting.

**Methods:** FIL was tested in the NZB/W F1 model of lupus at two concentrations (0.05% and 0.1%) formulated in chow and administered *ad libitum* from weeks 28–40. Cyclophosphamide (CP) was used as a positive control at 5 mg/kg, once daily, i.p. Efficacy was determined by changes in proteinuria, renal histopathology, and survival. Splenic cell populations were analysed by flow cytometry at study termination at week 40 to measure changes in immune cell subsets in diseased versus non-diseased mice and following FIL treatment. An *in vitro* murine whole blood pSTAT1 assay and PK exposure data were used to assess target coverage in the model.

**Results:** In the NZB/W model, FIL showed a dose-dependent decrease in proteinuria with a concomitant reduction in BUN levels, renal inflammation, improved glomerular morphology, and increased survival (table 1). Diseased mouse spleens had decreased frequencies of naive T cells, increased frequencies of CD11<sup>+</sup>dendritic cells (DCs), and an increased ratio of memory:naive T cells versus non-diseased mice. FIL treatment showed a dose-responsive reversal of these populations toward non-diseased levels. FIL inhibited *in vitro* IFN $\alpha$ -stimulated pSTAT1 signalling in T cells. Calculated JAK target coverage of pSTAT1 inhibition was similar to that observed in human studies at clinical doses.

**Abstract AB0484 – Table 1.** Efficacy scores in the NZB/W F1 model

	Placebo	FIL (0.05%)	FIL (0.1%)	CP (5 mg/kg)
Proteinuria <sup>a</sup>	30.72	29.03 (-5%)	23.40 (-24%)*	17.47* (-43%)
Survival	55%	73%	93%*	100%*
Glomerular diameter	3.66	2.10 (-43%)	0.83 (-77%)*	0.75*
Summed renal histology <sup>b</sup>	14.71	6.81 (-54%)	3.20 (-78%)*	0.37 (-90%)*
Glomerular myeloperoxidase	3%	2% (-52%)	1.1% (-101%)*	1.6% (-73%)*

<sup>a</sup>Urine score AUC (week 28–40)

<sup>b</sup>Includes: glomerular diameter, protein casts, interstitial inflammation, and vasculitis p-values comparing % changes between treatment and placebo groups: \*p<0.05

**Conclusions:** FIL demonstrated efficacy in the NZB/W F1 murine model of lupus with an alteration of splenic immune cell subsets affected by type I IFNs toward non-diseased levels. This data provides the basis for the evaluation of FIL as monotherapy in the currently ongoing Phase 2 studies in lupus-related diseases.

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**Disclosure of Interest:** C. Pohlmeier Shareholder of: Gilead Sciences, Inc, Employee of: Gilead Sciences, Inc, Z.-H. Cui Shareholder of: Gilead Sciences, Inc, Employee of: Gilead Sciences, Inc, P. Han Shareholder of: Gilead Sciences, Inc, Employee of: Gilead Sciences, Inc, A. Clarke Shareholder of: Gilead Sciences, Inc, Employee of: Gilead Sciences, Inc, R. Jones Shareholder of: Gilead Sciences, Inc, Employee of: Gilead Sciences, Inc, N. Mollova Shareholder of: Gilead Sciences, Inc, Employee of: Gilead Sciences, Inc, I. Mikaelian Shareholder of: Gilead Sciences, Inc, Employee of: Gilead Sciences, Inc, S. Zaboli Shareholder of: Gilead Sciences, Inc, Employee of: Gilead Sciences, Inc, A. Shauf Shareholder of: Gilead Sciences, Inc, Employee of: Gilead Sciences, Inc, J. Di Paolo Shareholder of: Gilead Sciences, Inc, Employee of: Gilead Sciences, Inc  
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AB0485

### COMPARATIVE EFFICACY OF TOFACITINIB AND BIOLOGIC DMARDS IN PATIENTS WITH RHEUMATOID ARTHRITIS WITH INSUFFICIENT RESPONSE TO SUBCUTANEOUS METHOTREXATE IN CLINICAL PRACTICE

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**Background:** Tofacitinib (TOFA) – the first registered member of the group of Janus-kinase inhibitors – actively entered into practice. Some clinical trials show efficacy similar to biological DMARDs, but we still do not have enough data from the practice of post-marketing use.

**Objectives:** To evaluate the comparative effectiveness of TOFA and biological DMARDs in clinical practice.

**Methods:** Patients with RA (according to the ACR/EULAR 2010 criteria) having active disease despite treatment by subcutaneous (SC) methotrexate (MTX) were included in post-marketing observational study (REMARCA trial). The patients received a combination of MTX and biologics or TOFA. The follow-up period was 12 months. Patients received biologics in clinical practice according to national standards of care. We used SDAI as a main parameter of disease activity.

**Results:** In total 163 patients were included (81,6% females, 80,4% anti-CCP positive, 79,8 RF-positive, 74,9% with erosive disease, mean age 50,65±12,54, disease duration 30,45±41,9, BMI 27,1±5,78). All patients received SC MTX in the mean dose 22,17±3,92 mg per week, but the most of them had high activity at baseline (SDAI=32,42±14,59). After switching to a combination treatment regimen 88 patients received TNF inhibitors (70 patients – adalimumab, 18 patients – certolizumab pegol), 34 patients – abatacept (ABA), 41 patients – TOFA. Patients in the groups were comparable according to age and the main characteristics of disease severity. We found significant decrease of disease activity in every group (see table 1). In the group receiving TOFA results at 12 months were comparable with patients on anti-TNFs and significantly better than in patients on ABA. Remission (SDAI <3,3) has been achieved in 35,7% of patients on TOFA, in 28,4% – on anti-TNFs and in 14,7% on ABA (p=0055 in comparison with TOFA). No significant differences in safety parameters were found.

**Abstract AB0485 – Table 1.** Changes in disease activity in RA patients during follow-up period.

Group	SDAI at baseline	SDAI at 12 months
Biologics (total), n=122	33,22±15,18	11,05±9,94
Anti-TNFs, n=88	33,98±14,49	9,79±9,22
Abatacept, n=34	31,11±17,05	14,32±11,09*
Tofacitinib, n=41	30,20±12,24	7,59±8,37*

\*) p<0,05 between the groups

**Conclusions:** Tofacitinib demonstrated similar efficacy in comparison to TNF inhibitors and was slightly better than abatacept in clinical practice in RA patients who did not respond to SC methotrexate.

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**AB0486** SUBCUTANEOUS METHOTREXATE DISCONTINUATION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Safety of methotrexate (MT) therapy remains the most important issue of early rheumatoid arthritis (RA) therapy.

**Objectives:** A prospective evaluation of most common causes of MT discontinuation in RA patients with disease duration <3 years.

**Methods:** An open 1 year study included 106 patients with active RA meeting ACR/EULAR 2010 or ACR 1987 (DAS28 >3.2) criteria, naïve to subcutaneous (SC) MT. All pts were administered SC MT, starting with 10–15 mg/week dose, and following 5 mg up-titration each 1–2 weeks (to max 30 mg/week) until achieving the target (remission or minimum disease activity) or emergence of adverse reactions (AR). Pts' monthly monitoring procedures included physical examination, blood analysis and biochemistry panel. T. Woodworth et al. inventory was used to assess the severity of ARs, and Naranjo scale was used to assess casual relationship of MT with an AR.

**Results:** Totally 12 (11%) MT discontinuations for the period of >3 weeks were analysed. Permanent discontinuation occurred in 9 pts (8%), and temporary (from 4 weeks to 4 months)—in 3 (3%). 83% of all cases of withdrawal took place during the first 3 months. In 3 patients MT was discontinued because of an AR and inefficiency. Combination of drug failure with AR was the reason for permanent SC MT discontinuation in 3 pts.

The causes led to SC MT discontinuation were: skin reactions in 3 pts (25%), "after-dose reactions"—in 2 (17%), allergic rash—in 2 (17%), diarrhoea—in 2 (17%), elevated liver enzymes—in 3 (25%), leukopenia—in 1 (8%), breast abscess—in 1 (8%). Some patients manifested multiple ARs. Two ARs (17%) were serious (grade 4 severity). Grade 3 ARs were documented in 4 cases (30%), Grade 2 ARs—in 4, and Grade 1 (mild) ARs—in 2 (17%) pts.

Skin lesions became the underlying cause for SC MT discontinuation, such as active dermatitis (n=1) and lichenoid skin reaction (n=1).

Totally 12 (11%) MT discontinuations for the period of >3 weeks were analysed. Permanent discontinuation occurred in 9 pts (8%), and temporary (from 4 weeks to 4 months)—in 3 (3%). 83% of all cases of withdrawal took place during the first 3 months. In 3 patients MT was discontinued because of an AR and inefficiency. Combination of drug failure with AR was the reason for permanent SC MT discontinuation in 3 pts. The causes led to SC MT discontinuation were: skin reactions in 3 pts (25%), "after-dose reactions"—in 2 (17%), allergic rash—in 2 (17%), diarrhoea—in 2 (17%), elevated liver enzymes—in 3 (25%), leukopenia—in 1 (8%), breast abscess—in 1 (8%). Some patients manifested multiple ARs. Two ARs (17%) were serious (grade 4 severity). Grade 3 ARs were documented in 4 cases (30%), Grade 2 ARs—in 4, and Grade 1 (mild) ARs—in 2 (17%) pts. Skin lesions became the underlying cause for SC MT discontinuation, such as active dermatitis (n=1) and lichenoid skin reaction (n=1).

**Conclusions:** Skin reactions were the most common cause for SC MT discontinuation. Therapeutic failure as the leading cause for drug discontinuation was not documented in a single patient.

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**AB0487** MULTICENTER 24-WEEK STUDY TO ASSESS THE EFFICACY AND SAFETY OF TACROLIMUS IN ACTIVE RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Rheumatoid arthritis (RA) is characterised by persistent synovitis and structural joint damage with T cell-driven inflammation. Tacrolimus suppress activation of T cells through the inhibition of calcineurin.

**Objectives:** We evaluated the efficacy and safety of tacrolimus in Korean active RA patient who had inadequate response to disease-modifying anti-rheumatic drugs (DMARDs) including Methotrexate (MTX).

**Methods:** During the study period from Aug. 2012 to Jan. 2016 in this open labelled, multicenter study, 115 patients were enrolled with DAS28 ≥3.2. Patients received tacrolimus during 24 weeks. The initial dose was 1 mg once daily and was increased to 3 mg by every 4 weeks. The disease activity and safety was assessed.

**Results:** Data from 97 patients were evaluated in full set analysis. At week-24, EULAR response rate were 83.5% (81 of 97) with improvements from week-16 in 74.2% (72 of 97). Mean DAS28-ESR was continuously decreased of 5.64 at baseline, 4.14 (±1.22, p<0.001) at week-16 and 3.66 (±1.39, p<0.001) at week-24. Efficacy rates according to SDAI were 89.7% (87 of 97) and KHAQ-20 score decreased -2.42 (±4.37, p<0.001) from baseline 7.27 (±4.59) at week-24. Mean ESR was decreased -10.97 (±24.16, p<0.001) at week-16, -14.77 (±24.57, p<0.001) at week-24 from baseline 46.05 (±23.22). Mean CRP was decreased from 2.86 (±7.85, p=0.0578) at baseline to 1.34 (±3.02, p=0.0367) at week-24. In serious adverse events (6 of 108, 5.56%), two cases (pneumonia, high glucose level) were related with tacrolimus and recovered with treatment.

**Conclusions:** This study demonstrated the efficacy of add on tacrolimus therapy to MTX in patients with active RA patients.

**Disclosure of Interest:** None declared

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**AB0488** DISEASE ACTIVITY AT ONE YEAR AFTER ADDITION OF IGRATIMOD OR SULFASALAZINE TO METHOTREXATE IN JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS: PROPENSITY SCORE ANALYSIS

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**Background:** Igratimod (IGU) is a small-molecule disease-modifying anti-rheumatic drug (DMARD) that has been shown to suppress inflammation via the inhibition of nuclear factor-kappa B activation *in vitro*. The efficacy of combination therapy with IGU and methotrexate (MTX) has been demonstrated in comparison with that of placebo in rheumatoid arthritis (RA). However, its efficacy in comparison with other DMARDs such as sulfasalazine (SSZ) has not been elucidated.

**Objectives:** To assess the disease activity at one year after addition of IGU in comparison with SSZ to MTX in typical clinical practice.

**Methods:** We analysed data from 16,988 RA patients registered in a large database (NinJa: National Database of Rheumatic Diseases by iR-net in Japan) from April 2012 to March 2017.<sup>1</sup> In this study, we compared the two groups who received IGU or SSZ in addition to methotrexate in the earlier year. We excluded patients who started receiving biologic DMARDs, and IGU or SSZ the year prior to the study period, and those whose regimens were changed to other DMARDs such as tacrolimus and bucillamine.

Baseline characteristics were compared using the *t* test, Wilcoxon test, or chi-square test. Fisher analysis was conducted for both outcomes. The predicted probability of IGU treatment was calculated by fitting a logistic regression model using all clinically relevant variables as presented in table 1. Moreover, to reduce the effect of treatment-selection bias and potential confounding in this observational study, we performed rigorous adjustment for significant differences in the baseline characteristics of patients with propensity-score matching using the following algorithm: 1:1 optimal match with a ±0.2 calliper and no replacement. We used the standardised difference to measure covariate balance, whereby a standardised mean difference of >0.1 represents meaningful imbalance. The outcome was remission rate with disease activity score 28 CRP (DAS28-CRP) in the year after initiation of IGU or SSZ therapy.

**Results:** The group that received IGU in addition to MTX included 113 patients; the other group that received SSZ in addition to MTX included 244 patients. Table 1 shows the results of the pre- and post-propensity score matching of patients' characteristics.

One hundred and nine patients were compared in each group after score matching. The remission rates of DAS28-CRP in the following year was 45.0% (49/109 patients) and 54.1% (59/109 patients; p=0.22), and drug retention rate was 79.8% (87/109 patients) and 78.9% (86/109 patients; p=1.00), in the IGU and SSZ groups, respectively.

**Abstract AB0488 – Table 1.** Patients' Characteristics in Full and Propensity Score-Matched Cohorts according to Initiation of Igaratimod or Sulfasalazine

Characteristic	Full Cohort			Propensity Score-Matched Cohort		
	IGU (n=113)	SSZ (n=244)	SMD	IGU (n=109)	SSZ (n=109)	SMD
Sex, male (%)	17 (15.0)	45 (18.4)	0.091	17 (15.6)	18 (16.5)	0.025
Age (mean [SD])	60.23 (12.07)	60.16 (13.13)	0.004	60.48 (11.98)	60.39 (13.31)	0.007
CRP mg/dl (mean [SD])	0.64 (0.92)	0.74 (1.26)	0.082	0.66 (0.93)	0.74 (1.05)	0.087
MTX mg/wk (mean [SD])	9.00 (3.00)	9.12 (3.14)	0.037	8.93 (2.96)	8.70 (3.35)	0.074
PSL mg/d (mean [SD])	1.91 (2.88)	1.47 (2.53)	0.170	1.78 (2.56)	2.02 (3.01)	0.065
SJC (mean [SD])	3.04 (4.02)	2.15 (2.94)	0.253	2.76 (3.46)	3.04 (3.32)	0.081
TJCS (mean [SD])	3.42 (6.59)	2.66 (4.27)	0.136	3.13 (6.52)	3.29 (5.00)	0.011
Disease duration yr (mean [SD])	11.10 (9.18)	9.41 (9.85)	0.180	11.11 (9.24)	10.40 (10.33)	0.073
PGA 0-10 (mean [SD])	3.11 (2.31)	2.91 (2.33)	0.085	3.02 (2.23)	2.99 (2.47)	0.016
mHAQ (mean [SD])	0.38 (0.51)	0.26 (0.41)	0.266	0.37 (0.51)	0.38 (0.49)	0.032

CRP: C reactive protein; IGU: iguratimod; mHAQ: The modified Health assessment questionnaire; MTX: methotrexate; PGA: patient's global assessment; PSL: prednisolone; SD: standard deviation; SJC: swollen joint count; SSZ: sulfasalazine; TJC tender joint count

**Conclusions:** Combination therapy with IGU or SSZ and methotrexate for rheumatoid arthritis did not show a significant difference in disease activity. Further studies are needed.

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#### AB0489 TOFACITINIB IMPROVES LEFT VENTRICULAR MASS AND CARDIAC OUTPUT IN RHEUMATOID ARTHRITIS PATIENTS WITH CHRONIC HEART FAILURE

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**Background:** Rheumatologists need to develop primary and secondary prevention strategies for cardiovascular disease (CVD) in rheumatoid arthritis (RA) patients. We reported tofacitinib (Tofa) improved left ventricular mass index (LVMI) in patients with rheumatoid arthritis<sup>1</sup>. We have experienced RA patient with chronic heart failure (CHF). We couldn't use some TNF blockers in RA patients with CHF<sup>2</sup>. There is no evidence that Tofa effects on left ventricular (LV) morphology and function in RA patients with CHF.

**Objectives:** To study the effect of Tofa on LV morphology and function in conventional synthetic (cs) DMARDs resistant active RA patients with CHF, in a cohort study design.

**Methods:** RA patients with CHF were eligible if they had active disease despite treatment with cs DMARDs. Consecutive 24 patients with moderate to severe active RA patients (DAS28 >3.2) despite cs DMARDs were received Tofa plus cs DMARDs. LV morphology and function was assessed with cardio-MRI at baseline and 24 weeks follow-up. Cardiovascular risk factors and clinical data were collected at regular visits.

**Results:** 21 patients completed 24 weeks. New York heart association functional classification (NYHA) class 1 is 12 cases, class 2 is 7 cases, and class 3 is 2 cases respectively. Left ventricular mass index (LVMI) was attenuated significantly by Tofa (week 0 week24,  $-9.02 \pm 5.8$  g/m<sup>2</sup>; p=0.02). Cardiac output (CO) was attenuated significantly by Tofa (week 0 week24,  $-0.42 \pm 1.2$  l/min). DAS28 and CRP improved significantly by Tofa (week 0 week24; DAS28:  $-2.16 \pm 0.95$ ; CRP:  $15.1 \pm 5.7$  mg/L) (p<0.05). Surprisingly, the change of disease activity (DAS

28 and CRP) is no correlation with the change of LVMI or CO in this study. Observationally, 2 cases significantly improved right ventricular mass as well as left ventricular mass (10% improved right ventricular mass index from baseline).

**Conclusions:** Tofa improved LVMI and CO in active RA despite cs DMARDs with CHF. Tofa improves LVMI and CO independently of its effects on disease activity. Tofa might be improved right ventricular mass. JAK-STAT pathway might be an important role of LV hypertrophy. Tofa, JAK-STAT pathway blocking, may prevent cardiovascular morbidity and mortality in RA with CHF.

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#### AB0490 EVALUATION OF INHIBITORY FACTOR OF RADIOGRAPHIC PROGRESSION BY IGURATIMOD ADD-ON THERAPY IN RHEUMATOID ARTHRITIS PATIENTS WITH INADEQUATE RESPONSES TO DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS

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**Background:** Igaratimod (IGU) is one of csDMARDs (Conventional synthetic Disease modified anti-rheumatoid arthritis drug) for RA patients in Japan. It was reported to suppress the production of inflammatory cytokines by inhibiting NFκB pass-way. IGU add-on therapy was efficient in patients with RA who were previously designated MTX-monotherapy inadequate responders (MTX-IR). The efficacy of IGU add-on therapy in bDMARDs (Biological DMARD)-IR patients was also reported. In this study, we showed disease activity and safety, and showed also radiographic evaluation for the first time by adding IGU.

**Objectives:** To obtain DAS28-ESR and adverse event data about adding IGU on RA patients with poor response to csDMARDs and/or bDMARDs in single-centre, open label and retrospective study. Furthermore, to show the radiological evaluation after one year.

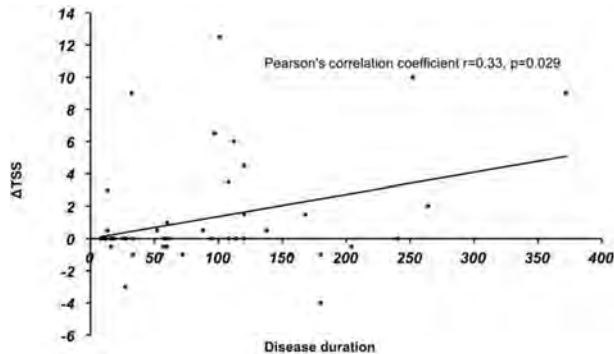
**Methods:** Clinical and radiographic efficacy was assessed by disease activity score of 28 joints (DAS28) ESR (n=68) and the modified total Sharp score (mTSS) (n=44), respectively. We evaluated which factors are important in determining a prognosis of clinical response and mTSS. For safety, adverse events (AE) were investigated on all patients (n=89).

**Abstract AB0490 – Table 1**

	Non Response		p		Non Response		p
	Response	Response			Response	Response	
SEX	76%	74%	ns	CRP	0.92±0.20	2.38±0.59	<0.05*
AGE	60.19±1.64	61.58±2.44	ns	ESR	24.48±2.96	35.61±3.98	<0.05*
DUR	86.67±10.11	101.03 ±15.76	ns	TJC	3.52±0.54	5.03±0.62	ns
a-CCP-Ab	180.11 ±50.79	153.25 ±40.11	ns	SJC	3.67±0.42	5.32±0.60	<0.05*
RF	133.10 ±28.67	161.39 ±47.20	ns	VAS	32.74±3.34	47.19±4.43	<0.05*
DAS28-CRP	3.85±0.15	4.83 ±0.15	<0.05*	MMP-3	149.33 ±27.60		
CDAI	13.63±0.94	20.06±1.28	<0.05*	PreTSS	5.72±1.07	5.26±0.82	ns
mHAQ	0.34±0.07	0.54±0.11	ns				

**Results:** 89 RA patients were recruited, and male was 28% (n=25). Mean age was 61.5 years old and mean of disease duration was 87 months. Main csDMARDs were MTX (72%). The mean dose of MTX was 7 mg/week (The average dose in Japan). Observational period was 13 months (range, 1 to 30). DAS28-ESR changed from 4.3±1.1 to 3.6±1.2 after adding IGU for 6 months (p<0.0001). The relation with the predictive factors before treatment and the response by using Igaratimod. CRP, ESR, swelling joint, DAS28-ESR, CDAI and

VAS at the baseline were all significantly high in Response (good response+ moderate response) group than No-response group (table 1). Yearly mTSS was 0.60 and rate of structural remission (mTSS  $\leq 0.5$ ) was 87%. Rapid radiological progression was not seen even if yearly mTSS at the baseline was 5.52. The relation between yearly mTSS and disease duration was shown in Figure ( $r=0.33$ ,  $p=0.029$ ). Adverse AE were observed such as transaminase elevation, stomatitis and dizziness. All AE was not serious. DAS28-ESR, CRP, ESR and swelling joint were prognostic factors of the group of good and moderate response against no response group.



Abstract AB0490 – Figure 1

**Conclusions:** Adding IGU to csDMARDs with poor response in RA patients is effective, but AE should be considered. Radiographic progression by Igaratimod might be inhibited in early phase of RA.

**Disclosure of Interest:** None declared

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**AB0491 POSSIBLE LINKAGE BETWEEN INTESTINAL BACTERIA COMPOSITION CHANGES AND DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH NATURAL MILK ANTIBODIES AGAINST ENTERIC BACTERIA AND THEIR TOXINS**

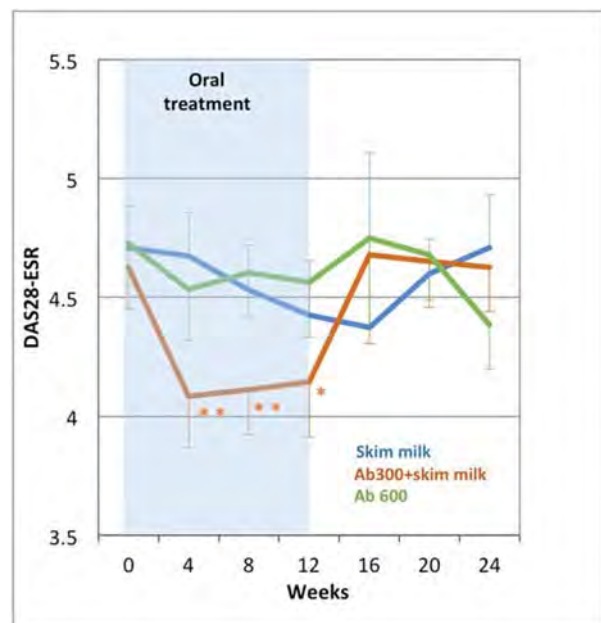
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**Background:** A growing body of research has indicated potential association between dysbiosis or imbalance of intestinal bacterial flora and RA. Previously, we demonstrated the natural milk antibody preparation containing high levels antibodies against pathogenic enteromicrobes and their toxins seems to be effective in a certain RA subset in an open labelled pilot study.<sup>1</sup>

**Objectives:** To investigate the effects of natural milk antibodies (Ab) on intestinal bacteria composition, and consequent therapeutic effect on disease activity of RA by multicenter randomised double blind clinical trial (UMIN CTR: 000009492).

**Methods:** Eighty-seven patients with RA with disease activity score of 28 joints with ESR (DAS 28-ESR) values above 3.2 were divided into 3 groups (29 patients each), and treated with 600 mg of Ab, 300 mg of Ab plus 10 g of skim milk (prebiotics), and 20 g of skim milk alone, respectively, for 12 weeks. The therapeutic effects of milk antibody treatment were determined by DAS28-ESR, swollen joint count (SJC), tender joint count (TJC), and visual analogue score (VAS). The biological effects of milk antibodies were examined by serum and faecal LPS concentration, and faecal bacterial composition changes before and after the treatment. Bacteria composition changes was determined by quantitative PCR of bacterial 16S rRNA.

**Results:** A significant reduction in DAS28-ESR values from 4.6 to 4.1 was observed at 4th week in Ab 300 mg plus skim milk group (figure 1). Importantly, this effect was lasted through until 12th week ( $p<0.01$ ), but DAS28-ESR values gradually returned to original levels after discontinuation of the treatment. On the other hand, neither high dose of milk antibody (600 mg) nor 20 g of skim milk had little effect on DAS28-ESR. Characteristic effect of milk antibody treatment observed in the Ab 300 mg plus skim milk group was the improvement of SJC, TJC, and Pain VAS. No severe adverse events have been observed. Enteric microbe analysis before the treatment indicated lower *Bacteroides fragilis* (less than 1/100 compared to healthy adults) and higher *Staphylococcus aureus* population (1000x higher) in patients with RA, indicating a dysbiosis in RA. The DAS28-ESR value reduction in the Ab 300 mg group was associated with an increase in the *Lactobacillus* population. In contrast, the improvement of Pain VAS was associated with an increase in the *B. fragilis* population. Possible improvement in the intestinal barrier function was assumed by the reduction of serum and faecal LPS concentration ratio in the Ab 300 mg groups.



\* :  $p<0.05$ , \*\* :  $p<0.01$  (Paired t-test), Data: mean  $\pm$  SE

Abstract AB0491 – Figure 1. Therapeutic effect of natural milk antibodies on rheumatoid arthritis

**Conclusions:** Natural milk antibody treatment modulates the intestinal bacterial composition, and consequently may contribute to improving disease activity of RA.

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**Disclosure of Interest:** None declared

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**AB0492 JAK-INHIBITION WITH PEFICITINIB AND FILGOTINIB IN FIBROBLAST-LIKE SYNOVIOCYTES IN RHEUMATOID ARTHRITIS**

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**Background:** With the approval of the Janus kinase inhibitors (JAKi) Tofacitinib and Baricitinib for the treatment of rheumatoid arthritis (RA) in the European Union (EU), the opportunities for a successful therapy were extended by a new substance class. Other JAKi like Peficitinib and Filgotinib are currently examined in clinical trials. Peficitinib is a pan-JAKi, whereas the other substances differ clearly in the capability to block the four members of the Janus kinase family. It is unclear, if the new substances offer an additional benefit in RA treatment in comparison to the approved JAKi.

**Objectives:** This study characterised the effect of the different JAKi on inflammatory response of activated fibroblast-like synoviocytes from patients with RA (RA-FLS).

**Methods:** RA-FLS were isolated from synovial tissue of patients with RA undergoing joint replacement surgery. The cells were pretreated for 2 hour with different concentrations of JAKi or vehicle control and then stimulated with IL-1 $\beta$  (10 or 20 ng/ml) or Oncostatin M (OSM, 100 ng/ml). After the indicated time (17–24 hour), the supernatants were collected and the concentrations of IL-6 and MMP-3 were measured by ELISA. An assay combining the measurement of cell viability, cytotoxicity and apoptosis was performed to exclude effects of JAKi caused by cell toxicity.



**Results:** To detect the most effective JAKi in blocking the inflammatory response induced by IL1- $\beta$ , RA-FLS were first pretreated with different JAKi for 2 hour with concentrations of 1  $\mu$ M and 10  $\mu$ M and then additionally stimulated with IL1- $\beta$  (20 ng/ml) for 18 hour. Even at the highest concentration of 10  $\mu$ M Tofacitinib and Baricitinib did not change the IL-6 levels, whereas Peficitinib and Filgotinib reduced the IL-6 release at 10  $\mu$ M. Tofacitinib and Baricitinib reduced the cytokine release if the RA-FLS were stimulated with OSM, a factor directly inducing the JAK-dependent IL-6-pathway (n=3).

To obtain a dose-response curve for the clinically relevant range of concentrations between 0.01  $\mu$ M and 5  $\mu$ M, RA-FLS were pretreated with Filgotinib and Peficitinib for 2 hour and then stimulated with IL1- $\beta$  (10 ng/ml) for 17 hour. In contrast to Filgotinib, Peficitinib at 5  $\mu$ M caused a reduction of IL-6 levels of 66% compared to control with IL1- $\beta$  (p<0.01, n=5). The MMP-3 release was decreased by both substances at 5  $\mu$ M: In comparison to the control with IL1- $\beta$ , Peficitinib caused a reduction of 92% (p<0.0001, n=5) whereas Filgotinib only reduced the levels by 43% (p<0.05, n=3). Furthermore, Peficitinib at 1  $\mu$ M decreased the MMP-3 release by 46% (p<0.01).

The treatment with Peficitinib did not affect the viability, cytotoxicity or apoptosis of RA-FLS (n=3). Therefore, the effects of Peficitinib on the inflammatory response were not caused by cell death.

**Conclusions:** Peficitinib reduced the release of proinflammatory cytokines and of matrix metalloproteinases after activation of RA-FLS with IL1- $\beta$  and appeared to be superior to Tofacitinib and Baricitinib in targeting the pro-inflammatory and matrix destructive properties of RA-FLS.

**Disclosure of Interest:** None declared

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#### AB0493 EFFECTIVENESS OF SUBCUTANEOUS PRESENTATION OF METHOTREXATE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Methotrexate (MTX) is one of the most used drugs for the treatment of rheumatoid arthritis (RA) and has become the gold standard of therapy. It can be given via oral, intramuscular or subcutaneous (SC). MTX is a highly effective therapy for patients with RA; however, oral MTX has been associated with gastrointestinal intolerance diminishing the adherence of patients to treatment and increasing the switching to biological therapy. Thus, the use of SC methotrexate can improve its efficacy compared to oral MTX.

**Objectives:** The aim was to determine the effectiveness and safety of SC MTX in patients with rheumatoid arthritis.

**Methods:** We performed a retrospective descriptive analysis; our main goal was to provide real-life data regarding effectiveness of SC MTX in patients with RA. We excluded patients who were in remission. Clinical follow-up was designed by the authors according to DAS28 as follows: every 3–5 weeks (DAS28 >5.1), every 7–9 weeks (DAS28  $\geq$ 3.1 and  $\leq$ 5.1), and every 11–13 weeks (DAS28 <3.1). Tender joint count (TJC), swollen joint count (SJC) and DAS28 were measured on each visit. Therapy had to be adjusted with DAS28 >3.2 unless patient's conditions don't permit it; regarding the effectiveness of SC MTX we calculated means, and standard deviations for continuous variables and categorical variables were presented as rates. We performed a bivariate analysis using Pearson's  $\chi^2$

**Abstract AB0493 – Table 1.** DAS28 and CDAI in patients with RA receiving SC MTX

DAS 28	BASELINE		12 MONTHS	
	n	%	n	%
Remission			44	33
LDA	36	28	29	22
MDA	84	63	50	38
SDA	12	9	9	7
CDAI	n	%	n	%
Remission			38	29
Low	87	66	62	47
Moderate	34	26	25	19
High	11	8	7	5

**Results:** A total of 132 patients meet our inclusion criteria, 88% were female and 12% male. Mean age was 61 years $\pm$ 9. Mean DAS28 at baseline was 3.8 $\pm$ 0.83, while at 12 months mean DAS28 was 3.28 $\pm$ 1.12. Clinical disease activity CDAI at baseline had a mean of 9.6 $\pm$ 7.2 and at 12 months 7.8 $\pm$ 7.5. We achieved

remission in 33% of patients according to DAS28 and 29% according to CDAI, also it was a significant decrease in patients with moderate disease activity see table 1. Finally, there was a statistical significance between disease activity at baseline compared to disease activity at 12 months (p<0.005). It was not observed major complaints with SC MTX, only 5% of the patients reported some mild and transient discomfort at the local application site.

**Conclusions:** Subcutaneous MXT is an effective and safe alternative for the treatment in patients with RA and intolerance to oral MTX, and could be a good option to prevent a premature switching to biological therapy.

**Disclosure of Interest:** None declared

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#### AB0494 USABILITY OF A PRE-FILLED PEN FOR SELF-ADMINISTRATION OF SUBCUTANEOUS METHOTREXATE

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**Background:** Methotrexate (MTX) is the first-line DMARD for the treatment of rheumatoid arthritis (RA).<sup>1</sup> It is also of high significance in the treatment of psoriasis arthritis (PsA) and psoriasis vulgaris (PsV).<sup>2,3</sup> Studies in RA patients found that there are advantages in terms of bioavailability and efficacy when MTX is administered subcutaneously (SC) as compared to orally.<sup>4,5</sup>

Since the introduction of MTX pre-filled syringes, patients are principally enabled to self-administer methotrexate subcutaneously, however not all patients are able to use syringes easily. Auto-injection using a pre-filled pen can facilitate administration by the patient. Results of a comparative crossover study showed that SC self-injection with a pre-filled pen is mainly preferred to a pre-filled syringe with regard to use, acceptability, and satisfaction<sup>6</sup>. Usability of the pre-filled pen was proven in an actual-use study<sup>7</sup>, however no comprehensive data from routine clinical use is available so far.

**Objectives:** The aim of this practice documentation was the evaluation of the usability of a MTX pre-filled pen under everyday clinical conditions.

**Methods:** This multicentric non-interventional practice documentation, which took place from 2013 to 2015 in Germany, was open to naïve patients and to those who had already been treated with the pre-filled pen in accordance with the approved indications. Usability was evaluated by the patient and the physician through assessment of the individual steps of two self-injections in an interval of approximately 12 weeks (V1, V2) and through a final overall assessment using ordinal scales. Data analysis was carried out descriptively by means of standard statistical methods. Calculation of a total usability score allowed for comparison of V1 and V2.

**Results:** The 478 participating patients had a mean age of 56.2 $\pm$ 13.7 years, 57.1% were female; 39.3% suffered from RA, 34.7% from PsV, 23.4% had PsA, and 12.6% were diagnosed with other conditions. 87.7% received treatment with the pre-filled pen for the first time, and 61.5% had previously received MTX. The individual steps of self-injection, removing of a protective cap, placing the device onto the skin, pressing the injection button, removing the pen, and ergonomics of the pen, were rated as "very good" and "good" by more than 90% of patients as well as of physicians in both visits. Comparing V1 and V2, usability was assessed to be even better at the second visit (p<0.0001 in the total score). Injections were carried out accurately by more than 93% of the patients.

**Conclusions:** Autoinjection with a pre-filled pen enables patients to self-administer subcutaneous MTX easily and comfortably in routine clinical practice.

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**Disclosure of Interest:** M. Hattesoeh Employee of: medac GmbH, M. Tribanek Employee of: medac GmbH, K. Gescher Employee of: medac GmbH

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AB0495

**POST-MARKETING SURVEILLANCE OF TOFACITINIB IN JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS: AN INTERIM REPORT OF SAFETY DATA**

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**Background:** Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA). Efficacy and safety of tofacitinib have been shown in patients (pts) with RA in global Phase (P)2, P3 and a long-term extension (LTE) study and in 2 P2 and 1 LTE study in Japanese pts.

**Objectives:** To evaluate safety of tofacitinib following drug approval in Japanese pts with RA using all-case post-marketing surveillance (PMS) data.

**Methods:** An interim analysis (IA) of safety data from an ongoing 3 year PMS study was conducted (5 Nov 2017 data-cut). All Japanese RA pts receiving tofacitinib were prospectively registered in the PMS study. All adverse events (AEs) were collected during tofacitinib treatment. Follow-up surveillance after discontinuation was conducted for serious infection events (SIEs; 1 year), malignancy and death (3 years). For all AEs and serious AEs, 6 month IA data was used. For AEs of special interest, all-period data (up to 36 months) was used to calculate cumulative incidence rates (IRs: pts with events/100 pt-years [yrs]) over time for herpes zoster (HZ) and SIEs during treatment +28 days and for malignancies during the full observation period.

**Results:** Overall, 3929 tofacitinib-treated pts with 1704.1 pt-yrs of exposure were included in the 6 month IA of safety: 80.5% were female, mean age was 62.7 years, with 32.6% of pts ≥70 years. Of these, 892 pts (22.7%) discontinued treatment, mainly due to AEs (351 pts; 8.9%) or lack of effectiveness (335 pts; 8.5%). At least one AE was observed in 1313 pts (33.4%); infections were observed in 493 pts (12.5%). The most frequent AEs were HZ (145 pts; 3.7%) and abnormal hepatic function (72 pts; 1.8%). SAEs occurred in 287 pts (7.3%); the most frequent SAEs were HZ (24 pts; 0.6%) and pneumonia/bacterial pneumonia (33 pts; 0.8%). SIEs occurred in 130 pts (3.3%). Malignancy (all causality) was reported in 25 pts (0.6%); lymphoma/lymphoproliferative disorder occurred in 5 pts (0.1%) and breast cancer in 3 pts (0.08%). There were 21 deaths (0.5%) during the 6 month period. The most common causes of death (including pts with multiple causes listed) were infection (6 cases) and malignancy (5 cases). For AEs of special interest from all-period data the IR of HZ (serious and non-serious) was 6.81 (264 pts; 3876 pt-yrs), the IR of SIEs was 5.38 (212 pts; 3941 pt-yrs) and the IR of malignancy was 1.25 (61 pts; 4874 pt-yrs).

**Conclusions:** This IA of tofacitinib PMS in Japan did not reveal any new or unexpected safety signals vs the tofacitinib RA clinical trials. IRs for HZ and malignancy were similar to IRs in clinical trials of tofacitinib in Japanese RA pts and the SIE IR was within the range reported in PMS of biologic treatments. Continuous monitoring of SAEs is required until the final PMS results.

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AB0496

**T2T WITH SUBCUTANEOUS METHOTREXATE IN VERY EARLY RHEUMATOID ARTHRITIS (RA)**

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**Objectives:** Adherence to foundations T2T and education of patients (pts) according to T2T Connect program increase possibility of favourable outcome of RA

**Methods:** In open prospective 36 months study of efficacy and safety of subcutaneous methotrexate (MT) 74 pts with definite very early RA (ACR/EULAR 2010) were included: mean age was 45.2±15.9, mean duration of RA – 5.2±3.48 months, mean DAS28 – 5.66±1.99 (max 7.06, min 4.44), RF positivity 73% and ACCP positivity 77% of pts. 3 pts had joint erosions. FK II had 43% and III- 53% of pts. Education conducted by program T2T Connect. Initial dose of MT was 15 mg/week, all pts used 5–10 mg/week folic acid and NSAIDs in therapeutically dose according to comorbidities, systemic glucocorticoids (GK) were not prescribed. 72 pts completed 12 months of treatment, 54–24 months, 29–36 months.

**Results:** In 88% of pts improvement was observed in first 4–5 weeks. After 3 months low disease activity (LDA) was registered in 18 pts, in over pts therapy wasn't corrected in view with clear tendency to decrease of RA activity, intraarticular injection of GK was performed in 3pts. Changes of DAS28 are in the table 1. After 6 months moderate disease activity was in 49% of pts, LDA – in 51%. After 12 months of study in all pts target of treatment was achieved: LDA in 81% of pts and remission (ACR/EULAR 2010) in 19%; after 24 months 57% and 43% respectively, after 36 months – 36% and 64% respectively (18 pts without treatment). The minimal radiographic progression was observed in 18 pts (24%, mean erosion's score 1.63±1.02), that wasn't cause of firm decrease of functional ability in pts. 3 women with remission after 18 and 20 months of treatment with MT became pregnant and gave birth to normal newborns. Withdraw MT because of AE was in 2 pts (flu-syndrome).

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Abstract AB0496 – Table 1

Months	0	3	6	12	24	36
Mean DAS28±SD	5.66±1.77	4.41±2.09	3.25±1.63	2.72±1.10	2.81±1.75	2.69±1.14

**Conclusions:** Peculiarity of our group of pts was the beginning of the treatment by MT, in most cases, at the first 6 months of RA onset. It is possible in this case to achieve remission more, than in half of pts without GK treatment. Thus, the subcutaneous form of MT is effective as regards activity and progression in early RA, safety for the long time in case of the using principles of controlled treatment allows achieve target after 6–12 month of therapy in most of pts with RA.

**Disclosure of Interest:** None declared

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AB0497

### EFFECTIVENESS, TOLERABILITY, AND SAFETY OF TOFACITINIB IN RHEUMATOID ARTHRITIS: A RETROSPECTIVE ANALYSIS OF REAL-WORLD DATA FROM THE ST. GALLEN AND AARAU COHORT

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**Background:** Tofacitinib is an oral JAK inhibitor indicated for the treatment of RA. Efficacy and safety of tofacitinib have been shown in several randomised clinical studies.

**Objectives:** The study presented here aimed to assess the clinical tolerability and effectiveness of tofacitinib among patients with RA in real life.

**Methods:** Consecutive patients between June 2013 and April 2017 with RA who fulfilled the American College of Rheumatology/EULAR 2010 criteria were analysed in a prospectively designed analysis of retrospective data. Patients were initiated on tofacitinib 5 mg bid. The primary objective was to analyse safety of tofacitinib in a real life cohort. Safety was assessed by the reasons to stop tofacitinib during follow up and changes of liver enzymes, haemoglobin, and creatinine. The secondary outcome was to analyse the frequency of and time to achieve low disease activity (LDA) and remission as defined by DAS28.

**Results:** Overall, 144 patients were treated with tofacitinib. 84.9% of the patients were pre-exposed to at least one biological agent. The average DAS 28 at initiation of tofacitinib was 4.43. 50.0% were rheumatoid factor and 49.0% ACPA positive. The mean follow up was 1.22 years (range 10d – 3.7a) after initiation of tofacitinib treatment. 94 (64.4%) patients remained on tofacitinib during follow up. The average time to stop tofacitinib was 190.0 days. Reasons to stop tofacitinib were: insufficient response (n=23), gastrointestinal symptoms (n=18), infection (n=5), myalgia (n=2), remission (n=2), headache,<sup>2</sup> cough, blue toe syndrome, intolerance, heart burn, psoriasis, and increased liver enzymes (all n=1). Increased ALAT or ASAT >2 x ULN were detected in 3.3% and 4.4%, respectively. These elevated transaminase levels were transient in 50% and 60% of the cases, respectively. Haemoglobin decrease of >10% was detected in 15.1% of the patients and decreased lymphocytes<500/ $\mu$ l in 3.4%. An increase of creatinine >20% was detected in 9.4%.

62.9% and 50.0% of the patients achieved LDA or remission after a median 260 and 616 days, respectively. These rates were significantly higher in patients naïve to biologic agents as compared to patients pre-exposed to biologics (LDA: naïve 100% after median 100d, pre-exposed 57.0% after 359d; remission: naïve 86.7% after 132d, pre-exposed 44.1% after 720)

**Conclusions:** Tofacitinib is a safe and effective treatment option for patients with RA. Tofacitinib may induce high rates of LDA and remission in patients with active disease, even after use of one or more biologics, though the rate is significantly higher in patients naïve to biologics. Tofacitinib may be a valuable option in a treat to target approach. Our data justify an early use of tofacitinib in the therapeutic strategy.

**Disclosure of Interest:** None declared

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AB0498

### OPTIMISATION OF METHOTREXATE DOSE INDUCED SUCCESSFUL REDUCTION OF GLUCOCORTICOID WITHOUT IMPAIRED DISEASE CONTROL IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Use of short-term glucocorticoids (GCs) along with methotrexate (MTX) have been recommended for newly onset patients with rheumatoid arthritis (RA) in EULAR recommendation 2016. However, it is not always easy to reduce or withdraw GCs due to patients' fear of relapsed pain or fatigue. As well, some patients are negative to increase MTX dose for fear of adverse events.

**Objectives:** To clarify whether GCs could be reduced without impaired disease control by optimising MTX dose in RA patients with stable medication in real-world clinical practice setting.

**Methods:** 70 patients with RA who regularly visit our outpatient clinic for  $\geq 1$  year were enrolled. Clinical characters, disease activity, and medications at present and 1 year before were retrospectively collected. Therapeutic strategy was to increase MTX with reducing prednisolone (PSL) based on patient's consent. Initiating bDMARDs was allowed in case of uncontrollable disease. Wilcoxon test and chi-square test were used for statistics.

**Results:** Clinical characters (median [IQR]) were; age 62<sup>51, 68</sup> yrs; female 69%; disease duration 6.8 [3.4, 13.7] yrs. Rate of MTX was elevated from 57% to 62%,

and dose (mean  $\pm$ SD) was increased from 9.8 $\pm$ 3.2 to 11.6 $\pm$ 3.7 mg/w ( $p < 0.0001$ ) for uses only, whereas PSL was suppressed from 56% to 26%, and decreased from 2.0 $\pm$ 3.1 to 0.8 $\pm$ 1.8 mg/d ( $p = 0.0004$ ) for all patients. bDMARDs were used for 16 patients, and newly initiated for 2 patients. Although not significant, median CDAI, SDAI, and DAS28 were suppressed from 5.7 to 3.8, 6.2 to 3.9, and 2.92 to 2.77, and remission rate were increased from 24% to 39%, 27% to 41%, and 36% to 41%, respectively.

Abstract AB0498 – Table 1

	Baseline	1 Year	p-value
%MTX	57%	67%	0.2226
MTX[mg/w] for users	9.8 $\pm$ 3.2	11.6 $\pm$ 3.7	<0.0001
%PSL	56%	26%	0.0003
PSL[mg/d] for all patients	2.0 $\pm$ 3.1	0.8 $\pm$ 1.8	0.0004
CDAI remission	24%	39%	0.0687
SDAI remission	27%	41%	0.075
DAS28 remission	36%	41%	0.4874

**Conclusions:** GCs could be reduced or withdrawn without deterioration with appropriately increased MTX. Moreover, disease control rather showed improved tendency.

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AB0499

### EVALUATION OF THE EFFECTIVENESS OF METAXODINE IN THE HEPATIC TOXICITY DUE TO METHOTREXATE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Methotrexate inhibits the metabolism of purines resulting in the accumulation of adenosine; it also inhibits the activation of T cells and suppresses the expression of intercellular adhesion molecules for T cells. Side effects may show up during the treatment and among them there is hepatic toxicity, characterised by an increase of AST and ALT; such increase is usually asymptomatic but it may lead to a suspension of the treatment. Metadoxine (MTDX) is a drug which is used in order to treat both acute and chronic alcohol intoxication; it also prevents the inactivation of ATP from acetaldehyde and pyroglutamic acid. MTDX also showed to improve hepatic function markers and to decrease oxidative stress leading to a protective effect against radicals.

**Objectives:** The aim of this preliminary study was to evaluate the possible effect of MTDX on hepatic function in patients affected by RA in therapy with MTX.

**Methods:** The study involved the recruitment of patients affected by RA in treatment with MTX; a following random selection of a subgroup of patients who took MTDX (500 mg twice a day for 28 days, from the 5th to the 8th week of therapy with MTX) was performed. All the patients underwent a 12-week-follow up in which these parameters were evaluated: demographics, blood tests required for MTX in accordance with datasheets (especially AST and ALT), CRP, ESR, ACPA, numbers of swollen and tender joints, concomitant medications (NSAIDs and steroids) and the degree of disability (HAQ, table 1).

**Results:** 24 patients affected by RA (20 women), with a mean age of 51.3 years ( $\pm 14.1$ ) and mean MTX dose of 12.3 $\pm$ 2.6, were recruited. 70.3% took GC with a medium dosage (3.72 $\pm$ 2.71). Among these 24, 13 patients were under MTDX 500 mg twice a day from the 5th to the 8th week. Patients treated with MTDX+MTX showed a significant decrease of hepatic markers (AST  $\Delta$  -18.38  $p = 0.004$  – ALT  $\Delta$  -19.23  $p = 0.004$ ) compare with patients with MTX only (AST  $\Delta$  -4.27  $p = 0.110$  – ALT  $\Delta$  -6.09  $p = 0.045$ ) after a 12-week-monitoring, with no statistically significant difference concerning disease activity (table 2).



**Abstract AB0499 – Table 1.** Variables at baseline

VARIABLES	MTX	MTX+MTDX	p-value
Disease duration (yy), m±SD	4.91±1.70	4.69±1.80	ns
AST (U/l), m±SD	13.18±3.19	18.46±7.15	ns
ALT (U/l), m±SD	17.09±6.35	20.23±7.96	ns
VAS Pain, m±SD	23.64±19.76	27.31±20.17	ns
DAS28, m±SD	3.6±0.91	3.72±0.87	ns
HAQ, m±SD	0.61±0.47	0.68±0.37	ns
MTX (mg), m±SD	12.27±2.61	12.69±2.59	ns
GC (mg), m±SD	3.41±2.80	4.04±2.61	ns

SD: standard deviation; ns: not significant; AST: aspartate amino transaminase; ALT: alanine amino transaminase; MTX: methotrexate; MTDX: Metadoxine; GC: glucocorticoids

**Abstract AB0499 – Table 2.** Comparison of Hepatic Functions between two groups

LIVER ENZYMES	MTX			MTX+MTDX		
	4a wk	12a wk	Δ	4a wk	12a wk	Δ
AST(U/l), m±SD	39,09	34,82	4,27	42,46	24,08	18,38
ALT(U/l), m±SD	46,82	40,73	6,09	43,92	24,69	19,23

AST: aspartate amino transferase; ALT: alanine amino transferase; MTX: Methotrexate; MTDX: Metadoxine;

**Conclusions:** This study showed the possible effect of MTDX in increasing the tolerance to the MTX without affecting its effectiveness. Its role may indeed have useful implications in patients who start the therapy with MTX or in those who develop hepatic toxicity during the treatment.

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**Disclosure of Interest:** None declared

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### AB0500 EFFICACY AND SAFETY OF TOFACITINIB (TOF) IN PATIENTS WITH RHEUMATOID ARTHRITIS AT 52 WEEKS IN CLINICAL PRACTICE

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**Objectives:** There are few long-term experience of TOF for Rheumatoid arthritis (RA) patients in clinical use. We evaluated 52 and 104 weeks efficacy and safety of TOF in patients with rheumatoid arthritis in clinical practice.

**Methods:** We enrolled 77 RA patients started to treat with TOF between December 2013 and November 2016 in our hospital. All patients received 5 mg of TOF twice daily. We evaluated clinical disease activity in composite measures (including Disease Activity Score 28(DAS28) -Erythrocyte (-ESR), -C-reactive protein (-CRP), Simple Disease activity Index (SDAI) and Clinical Disease Activity Index (CDAI)) every three months and adverse events (AEs) during 52 and 104 weeks after treatment with TOF. We estimated the drug survival rate with Kaplan-Meier survival analysis.

**Results:** The mean age of patients was 66.3 years and the duration of disease was 15.4 years. Fifty-four (74.0%) patients have positive rheumatoid factor (RF) and 59 (78.7%) patients have positive anti-citrullinated protein antibodies (ACPA). Twenty-three patients were biologic-naïve and fifty-four patients have ever been treated with biologic DMARDs of whose mean number is 2.6 prior to TOF. Regarding the last biologic DMARDs: 14 patients have treat with TNF inhibitor (Infliximab, etanercept, adalimumab, golimumab, certolizumab-pegol), 30 patients with tocilizumab and 10 patients with abatacept. Twenty-three (29.9%) patients were treated with TOF without methotrexate (MTX). Disease activity at TOF start with measured with DAS28-ESR, DAS28-CRP, SDAI and CDAI were 5.15, 4.07, 23.3 and 21.5 respectively. The Drug survival rate at 24 weeks is 84.4% and that at 52 weeks is 73.8%. Twenty-seven patients have been treated with tofacitinib over 104 weeks. Twelve patients was stopped to treat within initial 24 week, including due to adverse events (n=5) and lack of efficacy (n=7). Analysed by last observation continued forward (LOCF) method, the mean of DAS-ESR decreased to 3.52 at 24 week and 3.59 at 52 week. CDAI decreased from 21.5 to 7.94 at 24 week and

7.93 at 52 week. Sixteen (20.8%) patients were remission as which defined less than 2.6 in DAS-ESR and 13 (16.9%) were low disease activity (LDA) as which defined less than 3.2 in DAS-ESR. In 23 patients without MTX, 6 (26.0%) and 5 (21.7%) have achieved remission and LDA at 52 W respectively. The adverse events due to which the patients had to be stopped to treat with TOF occurred in 20.6% of patients in initial 52 weeks. Infection was the most frequent AE to TOF, especially herpes zoster (7 patients). Six patients experienced herpes zoster within 6 month after treat with TOF. All of them could restart to treatment of TOF. Two solid tumours were discovered within 6 months after treatment, both of them had been removed by surgery and has not recurred.

**Conclusions:** Our study shows that TOF can be much effective clinically and have longer-lasting effectiveness. In our patients, herpes zoster was almost as frequent as reported in the phase III trials in Japan and we could retreat almost of them with TOF.

**Disclosure of Interest:** None declared

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### AB0501 ADVERSE EVENTS WITH TREATMENT REGIMENS OF RHEUMATOID ARTHRITIS (RA) REPORTED BY PATIENTS APPLYING SMART SYSTEM OF DISEASE MANAGEMENT (SSDM) MOBILE TOOLS: A COHORT STUDY OF RA PATIENTS IN CHINA

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**Background:** Hepatic, hematologic and other adverse events (AE) during treatment in RA patients are unavoidable. And monitoring AE in long-term treatment is quite necessary as a part of chronic disease management. SSDM is a smart mobile tool to help patients upload their therapeutic regimens, lab test records and report AEs. Our previous study showed that patients in China can master the application of SSDM after training.

**Objectives:** To determine and compare the incidence of adverse events during treatment of RA with different therapeutic regimens, focusing on mono and combination therapy.

**Methods:** The SSDM includes interfaces of both physicians' and patients' application. Patients were educated to enter the data of lab test records and treatment regimens once a month, all data can be synchronised automatically to the authorised physicians' mobile tool, which formed a large patient reported database. The rheumatologists can also adjust treatment regimens base on patients' profile.

**Results:** From Aug 2014 to Jan 2018, a total of 7048 RA patients from 480 centres in China were entered in the cohort study. These patients contributed more than 12 600 patient-years (PY) of total followup. The mean age was 48.98 ±16.08 (18 to 99) years and the median disease duration was 23.27 months. The treatment regimens include mono or combination of leflunomide(LEF), MTX, hydroxychloroquine (HCQ), sulfasalazine(SSZ), glucocorticoid(GC), biologic DMARD, Tripterygium wilfordii, meloxicam, celecoxib, iguratimod, etc. In this database the five most common treatment regimens is LEF monotherapy (3801 PY), MTX monotherapy (1321 PY), LEF +MTX (1086 PY), HCQ monotherapy (715 PY), LEF +HCQ (576 PY). The incidence rate of hepatic events was lower for LEF monotherapy (35 events/1000 PY) than MTX (52 events/1000 PY) and LEF +MTX combination therapy (115 events/1000 PY) (p<0.01). The incidence rate of leukopenia was lower for LEF monotherapy (42 events/1000 PY) and MTX monotherapy (39 events/1000 PY) than LEF +MTX combination therapy (84 events/1000 PY) (p<0.01).

**Conclusions:** The findings show that mono or combination of csDMARDs are the most commonly used drugs in Chinese RA patients. And AEs may be well described in this patient report database because of the large sample sizes and empowering patient themselves. RA patients can get better safety in the long-term treatment via SSDM.

**Disclosure of Interest:** None declared

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**AB0502 DRUG SURVIVAL ANALYSIS OF TOFACITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS**

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**Background:** The drug survival rate of tofacitinib in patients with Rheumatoid Arthritis (RA) has not been reported so far.

**Objectives:** To determine the tofacitinib drug survival rate and the factors that may affect it in patients with RA from a single rheumatology clinic.

**Methods:** We have retrospectively analysed the track records of RA patients to whom tofacitinib was prescribed between June 2014 to December 2017. Descriptive analysis includes sex, duration of disease, autoantibody association, smoking, major trauma exposure, initiation in DMARD/Anti-TNF resistant patients, monotherapy/use in combination with DMARD. According to the duration of the disease, the patients were grouped as early (0–4 year), established (5–10 year), and late RA (>10 year).

Drug survival was estimated using Kaplan-Meier survival analysis, and the independent variables that may affect the discontinuation were investigated by log-rank test and modelled by Backward Stepwise Cox regression analysis.

Tofacitinib was prescribed to patients who were resistant to at least three different types of csDMARDs. Low-dose Steroid (below 10 mg) and NSAID drugs were used as needed.

**Results:** During the study period, 192 (163 F, 85%) patients were prescribed tofacitinib in our clinic. Median age was 56<sup>21–81</sup> years, the median age at onset was 45<sup>6–72</sup> years, and median disease duration was 10<sup>1–40</sup> years. In this study, the ratio of RF and anti-CCP positivity were 63% and 60%, respectively. 33% of patients were seronegative. The patients with a smoking history were 26%, and exposure to major trauma was 16%. 15% of patients were early, 31% established, and 54% late Ra.

Tofacitinib was prescribed in 92 (48%) bio-naïve and 100 (52%) bio-experienced patients. It was used as monotherapy in 112 (58%) and in combination with csDMARDs 80 (42%).

The drug survival rates in Kaplan Meier analysis were 77% at 3rd, 69% at 6th, 62% at 12th, 54% at 18th and 49% at 24th, 49% at 30th months. Tofacitinib was discontinued in 51 (27%) patients due to no response and in 22 (11%) patients due to side effects. None of the independent variables in regression analysis showed a relationship to tofacitinib discontinuation ( $p > 0.05$ ). During the follow-up period, one patient had breast cancer, and one had recurrent pneumonia. There were no tuberculosis or shingles cases reported. Two patients died from pulmonary thromboembolism.

**Conclusions:** We found that drug survival rates of tofacitinib in RA patients were 77% at 3rd month, 69% at 6th month, 62% at 12th month, 54% at 18th month and 49% at 24th month, 49% at 30th months. The main cause of discontinuation of the drug was inefficiency and the loss of efficiency. We could not find any link between the predetermined independent variables and the drug discontinuation. This result raises questions about why the drug loses its efficacy in some patients in time, and how this could be preventable.

**Acknowledgements:** One of the theories of autoimmunity is that Damage-Associated Molecular Patterns (DAMPs) may give rise to autoimmune inflammation. We were curious about how many of patients suffered from major trauma, which was defined as accidents terminated with fractures and dislocations or falls from a height of at least three metres.

**Disclosure of Interest:** None declared

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**SLE, Sjögren's and APS – treatment**
**AB0503 THERAPEUTIC STRATEGY AND SHORT-TERM OUTCOME IN NEUROPSYCHIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS**

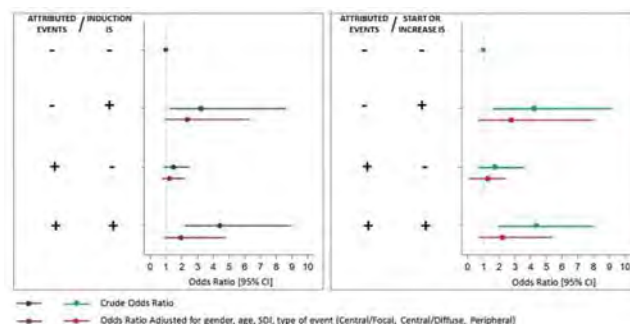
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**Background:** The treatment of neuropsychiatric systemic lupus erythematosus (NPSLE) is extremely challenging and only a few clinical trials have been performed to establish optimal management.

**Objectives:** To describe the therapeutic approach and the short-term outcome of a multi-centre cohort of patients with NPSLE, enrolled at the time of the first NP event.

**Methods:** This is a retrospective cohort study. All NP events were defined according to American College of Rheumatology (ACR) case definition and divided into 3 clusters: central/diffuse (C/D), central/focal (C/F) and peripheral (P). A validated attribution algorithm was used to determine the attribution of all NP events. Demographic variables, global SLE disease activity<sup>Index 2000</sup> (SLEDAI-2K), cumulative organ damage (SLICC/ACR Damage Index (SDI)) and treatment adopted for NP manifestations were collected. The clinical outcome of all NP events was determined by a physician-completed seven-point Likert scale (1=patient demise, 2=much worse, 3=worse, 4=no change, 5=improved, 6=much improved, 7=resolved). The relationship between the variables of interest and the outcome was analysed by crude and adjusted logistic models and reported as Odds Ratio (OR) and 95% confidence intervals (95% CI).

**Results:** 461 SLE patients with at least one NP event were included. 91.8% of patients were female, mean (SD) age 35.4 (13.6) years. 19.7% (91) of events were observed at diagnosis of SLE, 13.4% (62) before and 66.8% (308) after the diagnosis. 111 events (24.1%) were C/F, 286 (62%) C/D and 64 (13.9%) P. 198 (42.95%) of all NP events were attributed to SLE. The overall probability of immunosuppressive therapy was 28.4% (95% CI 24.3–32.8), 38.7% (95% CI 29.6–48.5) in C/F, 21.3% (95% CI 16.7–26.5) in C/D and 42.2% (95% CI 16.7–26.5) in P manifestations. The probability of immunosuppressive therapy was 47.9% (95% CI 40.8–55.2) in attributed events. The one-year outcome was available in 355 patients. Physician assessment indicated resolution (76 patients) or improvement (150 patients) in 49% (226/461) of cases. The crude and adjusted OR of attributed NP events and immunosuppressants on a favourable outcome is illustrated in Figure 1. The multivariable logistic regression analysis was done adjusting for age at diagnosis of SLE [OR 0.96, 0.94–0.98]  $p = 0.001$ , female gender [OR 0.97, 0.33–2.7]  $p = 0.959$ , SDI [0.85, 0.68–1.08]  $p = 0.202$ , SLEDAI-2K [1.06, 1.01–1.11]  $p = 0.008$  and type of event [F/C [REF], C/D [0.37, 0.16–0.83]  $p = 0.016$ , P [0.54, 0.21–1.42]  $p = 0.215$ ].



**Abstract AB0503 – Figure 1.** Crude and adjusted OR of attributed NP events and induction immunosuppression (IS, Figure 1A) or start/increase IS (Figure 1B) on a favourable outcome

**Conclusions:** In our study, the therapeutic immunosuppressive approach was mostly used in attributed, C/F and P manifestations. In patients treated with immunosuppressants, the favourable outcome was lower in C/D phenotype.

**Disclosure of Interest:** None declared

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**AB0504 EFFICACY OF PROLONGED MAINTENANCE MONOTHERAPY WITH RITUXIMAB IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME: THREE-YEAR FOLLOW-UP**

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**Background:** There are currently no effective systemic therapies of primary Sjögren's syndrome (pSS); however, open label series have suggested that rituximab may be beneficial for systemic and glandular manifestations.

**Objectives:** To estimate clinical efficacy and safety of prolonged maintenance B-cell targeted monotherapy for pSS.

**Methods:** 25 with pSS ACR-EULAR criteria, 2016 were included in this research. Indications for treatment were significant immunological activity (high titres of rheumatoid factor (RF) and anti-nuclear antibodies) and/or hypergammaglobulinemia in 20 patients, parotid enlargement (lymphoma was excluded) – 5, arthritis – 3, lymphadenopathy – 3, severe keratoconjunctivitis sicca in 7, of them corneal

ulceration – 3, leukopenia – 4 patients. Patients were treated initially with 2 infusions of rituximab (1000 mg) given once every two weeks with premedication (methylprednisolone (250 mg) and chlorpyramine). Then all patients received maintenance therapy with rituximab 500 mg every 6 months. Duration of treatment and follow-up was at least 3 years. Median follow-up was 45 months (36–90). Patients were evaluated, using immunologic, subjective parameters, salivary/lacrimal function at baseline and in 24 weeks and then every year during the follow-up. Patients were not concomitantly treated with another immunosuppressant agent or glucocorticoids daily.

**Results:** All patients were women with a mean age at diagnosis of 49 years [29–70] and median duration of disease was 6 years (1–20). The average cumulative dose of rituximab was 10000 mg (7000–12000 mg). The median European Sjögren's Syndrome disease activity index (ESSDAI) decreased from 2.5 (2–3) to 0 (0–1) ( $p=0.01$ ) by the end of the study. The increase in salivation and lacrimation according to Schirmer test and tear film break-up time was insufficient, however, in all patients the size of the salivary glands normalised and the recurrent parotitis stopped. Furthermore, 7 patients with severe keratoconjunctivitis sicca improved the course of the disease. The healing of corneal ulceration in all patients was observed one year after the initiation of therapy. A significant decrease in the RF level (from 198 IU/ml (51–442) to 71 IU/ml,<sup>30–73</sup>  $p=0,002$ ) and gammaglobulins (from 28%±5% to 19,3%±3,5%,  $p=0,001$ ) was observed one year after this study beginning. Unreliable decrease of immunoglobulins was noted in 23% of patients by the end of the follow-up, that did not increase the risk of secondary infections. We observed good tolerability of therapy, only 4 patients had mild infusion reactions.

**Conclusions:** Rituximab therapy is highly effective, well tolerated and helps to avoid long-term use of glucocorticoids/cytotoxic agents in pSS.

**Disclosure of Interest:** None declared

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AB0505

**EARLY AND SUSTAINED REMISSION IN SLE CAN BE ACHIEVED BY USING PULSE METHYL-PREDNISOLONE, HYDROXYCHLOROQUINE AND LOW-MEDIUM DOSE-PREDNISONE**

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**Objectives:** To compare the different therapeutic schemes used in two longitudinal cohorts of patients with Systemic Lupus Erythematosus (SLE): the Systemic Autoimmune Diseases Unit of Cruces University Hospital, Barakaldo, Spain (cohort C), using a low-medium dose prednisone scheme; and the Internal Medicine Department of Bordeaux, France (cohort B) which follows the standard treatment guidelines.

**Methods:** We included patients from both cohorts diagnosed with (SLE from year 2000), with a follow-up from the time of diagnosis (inception cohorts) and for at least 5 years. We analysed the different use of glucocorticoids (prednisone and pulse methylprednisolone), hydroxychloroquine (HCQ) and immunosuppressive drugs in both cohorts. To compare the efficacy of both therapeutic schemes, we analysed the rate of clinical remission and clinical remission on treatment, according to the DORIS definitions, during the 5 years of follow-up

**Results:** 173 patients were studied: Bordeaux (B): 81 and Cruces (C): 92. Baseline clinical variables were similar between both groups, including demographics, autoimmunity and organ involvement. The baseline SLEDAI was: 8 (B) vs. 7 (C),  $p=0.06$ . The proportion of patients in treatment with prednisone was similar from year 1: 79% (B) vs. 72% (C),  $p=0.269$ , to year 5: 63% (B) vs. 55% (C),  $p=0.315$ . However, patients in cohort B received higher doses of prednisone: mean maximum dose at year 1: 38 mg/d (B) vs. 14 mg/d (C),  $p<0.05$ ; at year 5: 8 mg/d (B) vs. 3 mg/d (C),  $p<0.05$ ; average dose of prednisone at year 1: 15.8 mg/d (B) vs. 4.4 mg/d (C),  $p<0.05$ ; at year 5: 6.6 mg/d (B) vs. 3.2 mg/d (C),  $p<0.05$ . Methyl-prednisolone pulses were ever used in 26% (B) vs. 42% (C),  $p<0.05$ ; the mean total pulses per patient was 3 (B) vs. 7 (C),  $p<0.05$ ; however, the mean total dose of methyl-prednisolone per patient was similar 1725 mg (B) vs. 1635 mg (C),  $p=0.835$ , revealing a lower dose per pulse in patients from cohort C. The proportion of patients in treatment with HCQ was lower in cohort B at year 1: 80% (B) vs. 97% (C),  $p<0.05$  and at year 5: 73% (B) vs. 99% (C),  $p<0.05$ . Methotrexate was used more frequently in cohort C ( $p<0.05$ ) with no differences in cyclophosphamide, azathioprine and mycophenolate use.

Clinical remission in both cohorts was as follows: year 1: 25% (B) vs. 40% (C),  $p<0.05$ ; year 2: 29% (B) vs. 42% (C),  $p=0.07$ ; year 3: 37% (B) vs. 42% (C),  $p=0.54$ ; year 4: 37% (B) vs. 48% (C),  $p=0.15$ ; year 5: 36% (B) vs. 49% (C),  $p=0.08$ .

Clinical remission on treatment: year 1: 43% (B) vs. 84% (C),  $p<0.05$ ; year 2: 70% (B) vs. 87% (C),  $p<0.05$ ; year 3: 73% (B) vs. 88% (C),  $p<0.05$ ; year 4: 73% (B) vs. 93% (C),  $p<0.05$ ; year 5: 73% (B) vs. 93% (C),  $p<0.05$ .

**Conclusions:**

- The more frequent use of hydroxychloroquine, pulse methylprednisolone and methotrexate in the Cruces cohort resulted in reduced doses of oral prednisone.
- Patients from the Cruces cohort achieved clinical remission earlier and in a more sustained way during the follow-up.

**Disclosure of Interest:** None declared

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AB0506

**HYDROXYCHLOROQUINE HAS NO PROTECTIVE EFFECT ON THE DEVELOPMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS IN 7004 PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME: A NATIONWIDE POPULATION-BASED STUDY**

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**Background:** Hydroxychloroquine (HCQ) has been proposed to be associated with later onset of systemic lupus erythematosus (SLE)<sup>1</sup> and is widely used in patients with primary Sjögren's syndrome (pSS) which may evolve to SLE.<sup>2</sup> We want to explore the potentially protective role of HCQ in the development of SLE among patients with pSS.

**Objectives:** This study was conducted to assess whether exposure to HCQ in pSS patients is associated with a reduction in the development of SLE.

**Methods:** This retrospective cohort used claims data from the National Health Insurance Registry Database (NHIRD) in Taiwan. Patients with incident Sjögren's syndrome (SS) from 2000 to 2010 in the Registry of Catastrophic Illness Database (RCIPD) of the NHIRD, which was certified by two rheumatologists, were identified. The date when SS was diagnosed in the RCIPD was defined as the index date. Those who were diagnosed as having SLE, rheumatoid arthritis, polymyositis, dermatomyositis, or systemic sclerosis in the RCIPD before the index date were excluded. Other exclusion criteria included<sup>1</sup> patients who were diagnosed as having SLE in the RCIPD within one year after the index date,<sup>2</sup> patients who withdrew from the NHIRD within one year after the index date, and<sup>3</sup> patients who used oral, intramuscular, or intravenous corticosteroids, methotrexate, azathioprine, leflunomide, sulfasalazine, cyclosporine, tacrolimus, mycophenolate, mercaptopurine, or cyclophosphamide for more than or equal to 90 days within one year before or after the index date. The included SS patients who used HCQ for more than or equal to 90 days within one year after the index date were eligible to HCQ group. The study endpoint was defined as newly-diagnosed SLE in RCIPD or withdraw from NHIRD during the 14 year follow-up period (January 1st, 2000 to December 31st, 2013).

**Results:** A total of 7004 pSS patients were identified. The mean follow-up time was 6.9 years in the HCQ group ( $n=4282$ ) and 7.0 years in the non-HCQ group ( $n=2722$ ). There were 22 newly-diagnosed SLE (0.5%) in the HCQ group and 16 (0.6%) in the non-HCQ group. The overall event rate of SLE was 8.78/10,000 person-years in the HCQ group and 9.83/10,000 person-years in the non-HCQ group (adjusted hazard ratio 0.97, 95% confidence interval 0.50–1.88, in a Cox proportional hazard model).

**Conclusions:** There is no protective effect of HCQ on the development of SLE in patients with pSS.

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AB0507

**BELIMUMAB IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: OUTCOMES IN ROUTINE CLINICAL PRACTICE**

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**Background:** Systemic lupus erythematosus (SLE) is a systemic autoimmune disease with a wide range of clinical manifestations. The persistence of activity of the disease and the prolonged use of corticosteroids are amongst the main predictors of accumulated organ damage in patients with SLE. Therefore, we need new strategies to induce long-lasting remission and minimise the adverse effects of standard medications.

**Objectives:** to assess the effectiveness and safety of Belimumab in actual clinical practice during the first year of treatment in patients with SLE.

**Methods:** retrospective observational study of patients treated with Belimumab. This study involves 6 hospitals in Castilla y León (Spain). It collects clinical and analytical data before the start of Belimumab, and 6 and 12 months after the initiation of the therapy. The data collected include the daily dose of prednisone received at different time points and the activity of the disease was classified as mild, moderate and severe based on SELENA-SLEDAI index. A reduction from baseline of 3 points on the SELENA-SLEDAI indicates meaningful symptomatic improvement.

**Results:** Among the twenty-five patients were included, with a mean age of 43.7 +12.2 years, 72% were female and 96% caucasian. The average time from diagnosis of SLE to Belimumab infusion was 9.5+7.1 years; 32% were diagnosed with SLE <5 years ago. Up to 56% of the patients had moderate disease activity and only 8% patients had very high activity of the disease. All but one of the patients had previously received an immunosuppressant (azathioprine in 50% of the cases) and 16% of the sample had not responded to rituximab. The most frequent reasons for initiating Belimumab were an ineffective previous treatment regimen (60%), the intend to decrease steroid use (56%), and worsening patient condition (52%); whereas the most frequent manifestation of SLE in these patients were arthritis (44%), followed by mucocutaneous (20%) and immunologic findings (20%). As for immunologic markers of activity, DNA was elevated by 40% and 68% of the patients showed hypocomplementemia, that dropped to 24% in both cases at 12 months. The mean score of the SELENA-SLEDAI index decreased from 9.5 to 6 in the first 6 months and to 5.2 in the 12 months of follow-up. A reduction in the initial mean steroid dose was also observed from 20 mg/day to 8.9 mg/day and 6.4 mg/day at 6 and 12 months respectively. Hence, the dose of steroid was reduced by 68% during the first year (p=0,06). This reduction was clinically significant, but it did not reach statistical significance in our study. Two patients (8%) had discontinued Belimumab within the first 6 months of therapy (1 pregnancy and 1 worsening proteinuria); 34.7% had discontinued it within the first 12 months, mostly due to ineffectiveness (62.5%). Two patients with severe renal involvement (>1 gr proteinuria/24 hour) were treated with Belimumab, allowing to reduce the steroids to a low dosis (<7.5 mg/day) at 12 months.

**Conclusions:** Belimumab appears to be effective, reducing disease activity as measured by the SELENA-SLEDAI Index and, also, the mean dose of steroids needed, mainly after 12 months of treatment. No significant adverse effects were reported as previous studies have shown.

**Disclosure of Interest:** None declared

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AB0508

**FIXED, LOW-DOSE HYDROXYCHLOROQUINE VERSUS WEIGHT-ADJUSTED DOSE IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS WITH LOW ACTIVITY**

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**Background:** Optimal hydroxychloroquine (HCQ) dose to reduce ocular toxicity risk is 5 mg/kg or actual weight daily, according to new recommendations. In systemic lupus erythematosus patients (SLE) with low or no disease activity, fixed low-dose HCQ might be equally effective in relapse prevention weight-adjusted doses, thus resulting in lower cumulative dose.

**Objectives:** Our aim was to compare a fixed dose of HCQ 200 mg daily with a weight-adjusted dose (5 mg/kg of actual weight daily) in SLE patients with low activity.

**Methods:** SLE activity was assessed using the SLE Disease Activity Index (SLEDAI-2K), the Safety of Oestrogen in Lupus Erythematosus National Assessment (SELENA)-SLEDAI and the Physician Global Assessment (PGA, 0–3 scale) in each visit. Low-activity SLE (LLDAS) was defined according to Franklyn et al: 1) a SLEDAI-2K score ≤4, 2) no new SLE-related activity events compared with the previous visit, 3) a PGA score ≤1, 4) prednisone dose ≤7.5 mg daily and 5) stable

doses of maintenance immunosuppressant therapy. LLDAS was evaluated at baseline and months 3 and 6. In order to adjust doses to weight, and given the impossibility of fractionating HCQ tablets, the adjusted dose was calculated for every week. For example, for 62 kg patient, the calculated dose would be 5 mgx52 kg=260 mg daily, which would mean 1820 mg weekly. Therefore, the patient would receive 400 mg daily for 2 days and 200 mg daily for 5 days every week. A relapse was defined as an increase of SLEDAI scores ≥3, according to current recommendations

**Results:** A total of 50 LLDAS patients were compared, 25 with a fixed dose and 25 with a weight-adjusted dose. No significant differences regarding body weight between groups were observed: 52 kg (41–58.5 kg) vs. 51 kg (44–55 kg). Baseline activity scale scores were not significantly different. No patient relapsed on follow-up in either of both groups. Finally, the mean HCQ cumulative dose at 6 months was reduced by approximately 9.6 grams.

**Conclusions:** In LLDAS patients, a fixed HCQ dose of 200 mg daily may be as effective as the weight-adjusted dose in preventing disease relapses, thus resulting in a decrease in the HCQ cumulative dose and, therefore, a reduction of the risk of ocular toxicity.

**REFERENCE:**

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**Disclosure of Interest:** None declared

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AB0509

**KZR-616, A SELECTIVE INHIBITOR OF THE IMMUNOPROTEASOME, SHOWS A PROMISING SAFETY AND TARGET INHIBITION PROFILE IN A PHASE I, DOUBLE-BLIND, SINGLE (SAD) AND MULTIPLE ASCENDING DOSE (MAD) STUDY IN HEALTHY VOLUNTEERS**

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**Background:** Proteasome inhibition is a standard of care for plasma cell malignancies. Bortezomib targets the constitutive proteasome and immunoproteasome, and is effective in the treatment of Systemic Lupus Erythematosus (SLE) and lupus nephritis (LN), but is associated with hematologic (e.g. thrombocytopenia) and constitutional (e.g. peripheral neuropathy) adverse events (AEs).

**Objectives:** We report the safety, pharmacokinetics (PK), pharmacodynamics (PD) and immunomodulatory effects of KZR-616, a first-in-class selective inhibitor of the immunoproteasome, in healthy volunteers (HV) following single and repeat subcutaneous (SC) administration.

**Methods:** Cohorts (6 drug:2 placebo) received single or 4 weekly SC doses. Safety assessments, PK and PD were measured to Day 7 (SAD) or Day 28 (MAD). SAD cohorts included 7.5, 15, 30 and 60 mg (SC). MAD cohorts included 30, 45, 60 mg, and 2 intrasubject escalation cohorts with 1 dose at 30 mg and 3 doses at 45 mg. PK was measured by LC/MS<sup>2</sup>. PD was measured using enzymatic and active site binding assays. Inflammatory cytokine release was measured following *ex vivo* stimulation of whole blood in HV receiving placebo or 45 mg KZR-616.

**Results:** 32 HV (24:8) were enrolled in 4 SAD cohorts. The most common AEs were injection site reactions (ISRs), which were generally mild and transient. No clinically-significant (CS) laboratory or ECG abnormalities and no dose limiting toxicities were observed in the SAD subjects. Following SC administration, drug exposure increased dose proportionally and was characterised by rapid absorption (T<sub>max</sub>15–30 min) and clearance (T<sub>1/2</sub> ~2 hours). Inhibition of the immunoproteasome exceeded 80% at ≥30 mg with significant recovery noted over 7 days. Constitutive proteasome inhibition was <37% in all cohorts.

40 HV (30:10) were enrolled in 5 SC MAD cohorts. In the initial cohort of 60 mg, a systemic drug reaction (chills, elevated heart rate, nausea) occurred ~8 hours after the first dose in 4 subjects. Dosing for this cohort was stopped. Subsequent cohorts (initiated at 30 mg) received prophylactic treatment with antihistamines ±prednisone 1 hour prior to the first and second dose. No similar AEs occurred with repeat dosing of 45 mg. No CS laboratory or ECG abnormalities were seen in the remaining MAD cohorts. ISRs did not appear to increase in severity or frequency with repeat dosing. There were no AEs of peripheral neuropathy, and 45 mg was well tolerated across 3 cohorts.

Consistent PK was noted following repeat administration and no drug accumulation was observed. At 45 mg, inhibition of 2 key subunits of the immunoproteasome, LMP7 and LMP2, was ~95% and ~70%, respectively. Reduced *ex vivo* stimulated production of multiple cytokines (IL-23, IL-6, TNF-α, IL-17) was noted in subjects receiving repeat administration of 45 mg KZR-616.

**Conclusions:** KZR-616 up to 45 mg was well tolerated in HV and demonstrated consistent PK and PD. Selective immunoproteasome inhibition did not induce hematologic or constitutional toxicities associated with bortezomib. Candidate dose levels were identified to explore safety, tolerability and efficacy in patients with SLE and LN in an ongoing Phase 1b/2 study.

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AB0510

#### IMPROVING KNOWLEDGE OF SLE DISEASE FLARES AND TREATMENT OPTIONS AMONG RHEUMATOLOGISTS AND PRIMARY CARE PROVIDERS: EFFECT OF AN ONLINE EDUCATIONAL INTERVENTION

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**Background:** With a significantly higher mortality in patients affected by systemic lupus erythematosus (SLE) developing chronic damage, prevention is a major goal in management.<sup>1</sup> Flares are a common feature throughout the course of SLE and can result in organ damage.<sup>2</sup> As a result, clinician knowledge on how to prevent, recognise, and treat flares is crucial.

**Objectives:** Determine whether an online educational intervention could effectively address a knowledge gap and an underlying educational need in the areas of SLE disease management among rheumatologists and primary care providers (PCPs).

**Methods:** An online educational intervention focusing on SLE disease management was made available online, intended for rheumatologists and PCPs who treat patients with SLE. The intervention consisted of a 30 min video presentation by a recognised expert in the treatment of SLE. Synchronised slides supported the presentation. The educational impact was assessed by comparing participants' responses to 3 repeated-pair, multiple-choice pre- and post-intervention questions. The impact on self-reported confidence was also assessed through a separate, 5-point Likert-scale question. Data were collected from 9/28/2017 through 11/29/2017. Statistical analysis included a paired 2-tailed t-test comparing mean pre-intervention and post-intervention scores, McNemar's  $\chi^2$  statistic for measuring changes in responses to individual questions, and Cramer's *V* to determine the overall impact of the intervention.

**Results:** Analysis of pre- versus post-intervention responses demonstrated a significant ( $p < 0.05$ ) improvement in overall knowledge in both rheumatologists (79% to 87%,  $n = 118$ ) and PCPs (61% to 73%,  $n = 253$ ). The overall impact of the intervention was similar in both groups ( $V = 0.106$  for rheumatologists and  $V = 0.123$  for PCPs). This intervention resulted in increased knowledge surrounding several specific areas of SLE, such as pathophysiology, relationship between disease activity and organ damage, and selection of SLE therapies (see table 1).

Abstract AB0510 – Table 1

Topic area	Rheumatologists (n=118)	PCPs (n=253)
Pathophysiology	9% (75% to 84%, $p = 0.106$ )	23% (40% to 63%, $p < 0.05$ )
Relationship between disease activity and organ damage	8% (84% to 92%, $p < 0.05$ )	5% (70% to 75%, $p = 0.197$ )
Treatment selection	7% (79% to 86%, $p = 0.173$ )	6% (74% to 80%, $p = 0.093$ )

The intervention resulted in a +4% shift in self-reported confidence in addressing flare symptoms among rheumatologists, and a +26% shift among PCPs.

**Conclusions:** Participation in an online video educational intervention with synchronised slides was associated with significant overall improvement in knowledge levels of rheumatologists and PCPs in several important aspects of SLE management. Based on assessment of residual gaps, future directions for education should be tailored to specific learner groups including case-based reinforcement of knowledge and competence among rheumatologists, and additional foundational education for PCPs in the areas of pathophysiology and disease progression.

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AB0511

#### THE EFFECT OF MILNACIPRAN ON FATIGUE IN A CLINICALLY STABLE LUPUS COHORT

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**Background:** Systemic lupus erythematosus (SLE) is a chronic multi-system autoimmune disease impacting the physical wellbeing and health related quality of life (HRQOL) of patients<sup>1</sup>. Fatigue occurs in up to 90% of SLE patients and affects their HRQOL<sup>2</sup>. The purpose of this pilot study is to determine the effect of milnacipran, a norepinephrine and serotonin reuptake inhibitor used to treat fibromyalgia, on fatigue in clinically stable SLE patients with widespread pain (WSP). To date, no clinical trials have demonstrated efficacy for the primary treatment of fatigue and WSP in adult SLE patients.

**Objectives:** The objective is to determine the effect of milnacipran on fatigue in a clinically stable lupus cohort.

**Methods:** SLE patients, 18 years and older, with fatigue, WSP and on more than 4 weeks of stable therapy were recruited for a 15 week prospective, double-blind, placebo-controlled study. Patients were randomised at a 1:1 ratio to receive 14 weeks of milnacipran 50–100 mg twice a day or placebo. Disease activity was measured by the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI). Measurements of fatigue, pain and a patient's general impression of change from baseline were assessed at baseline and week 14 using the Fatigue Severity Scale (FSS), the Short-Form McGill Pain Questionnaire (SF-MPQ)<sup>3</sup>, and the Patient's Global Impression of Change (PGIC) respectively.

**Results:** A total of 14 patients were included in the final analysis with seven patients in each group. Upon entry and throughout this study, both groups had low disease activity (mean SLEDAI  $< 3.5$  at week 0 and week 14). Fatigue as measured by FSS in the intervention group improved from 5.70 at week 0 to 5.14 at week 14 and improved in the placebo group from 5.90 to 5.59 respectively ( $\Delta = 0.56$ , 0.31 for the intervention and placebo group, respectively,  $p = 0.70$ ). Pain as measured by the SF-MPQ changed in the treatment group from 20.80 at week 0 to 18.80 at week 14, and in the placebo group from 15.40 to 13.2 respectively ( $\Delta = 2.00$ , 2.20 for the intervention and placebo group, respectively,  $p = 0.97$ ). The patient's Global impression of change was greater in the intervention group than the placebo group (0.67, 0.49,  $p = 0.21$ ).

**Conclusions:** Although results were not significantly different in this pilot study, improvement in fatigue and the patient's impression of global change appeared to be greater in the intervention group than the placebo group even though lupus activity remained low in both groups and the difference in pain between the two groups were nearly identical. Therefore, milnacipran may improve fatigue independently of disease activity and pain in lupus patients. Future randomised controlled trials of the drug's effect with larger cohorts are needed to confirm these findings.

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AB0512

#### OCCURRENCE AND CONSEQUENCES OF ANTI-DRUG ANTIBODIES TO RITUXIMAB IN SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Anti-drug antibodies (ADA) to rituximab (RTX) have been reported to a limited extent in rheumatoid arthritis (RA, 4%–11%) and in multiple sclerosis (MS, 26%–37%), in the latter being associated with incomplete B-cell depletion.<sup>1</sup> In SLE, data on the clinical significance of ADA are lacking.

**Objectives:** To define the frequency and consequences of ADA to RTX in a SLE population by setting a disease specific threshold using a sensitive ADA method.

**Methods:** SLE patients fulfilling the 1982 ACR classification criteria who received RTX treatment at the Karolinska University Hospital during the years 2001–2015 were included. Stored serum samples obtained prior to and after six months from initiation of treatment were analysed for the detection of ADA using a GSK-developed and validated electrochemiluminescence assay. Disease specific screening and confirmation cut-point for SLE samples (1.44 AU and 29% respectively) were used. Clinical and laboratory data were retrieved from electronic medical charts. SLE activity was measured using SLE disease activity index 2000 (SLEDAI-2K). We defined treatment response according to the SLE responder index (SRI).<sup>2</sup>

**Results:** Thirty-eight patients (89.5% females, median age 35.0 years; IQR: 27.7–55.0) were included in this retrospective analysis. The median disease duration was 6.2 years (IQR: 2.1–11.6) and the baseline median SLEDAI-2K was 6.9 (IQR: 7.0–16.5). The indications for RTX were active lupus nephritis (65.8%), CNS involvement (10.5%), arthritis (13.2%), haematological manifestations (7.9%), or mucocutaneous involvement (2.6%). Twenty-six patients (68.4%) received RTX according to the lymphoma regimen (375 mg/m<sup>2</sup> at day 1, 7, 14, 28) while 12 (31.6%) according to the arthritis regimen (2 infusions at a dose of 1 g, 14 days apart). Intravenous corticosteroids and cyclophosphamide were given in 65.8% and 63.2% of the patients, respectively.

ADA were detected in 18 patient samples (47.4%) at follow-up and stratified into reactive samples (confirmed positive but with a titer <2 AU/mL; n=3), low positive (2–10 AU/mL; n=6), medium positive (11–50 AU/mL; n=4), and high positive (>51 AU/mL; n=5).

We found no association between the occurrence of ADA and either SRI response (p=0.26, Fisher exact test) nor the concomitant use of high dose IV 6-methylprednisolone (p=0.56,  $\chi^2$  test) or IV cyclophosphamide (p=0.11,  $\chi^2$  test). At follow-up, patients positive for ADA had higher levels of CD19 +B cells (median:  $0.03 \times 10^9$  cells/L; IQR: 0.01–0.13) compared to negative patients (median:  $0.01 \times 10^9$  cells/L; IQR: 0.005–0.01; p=0.007, Mann-Whitney test).

**Conclusions:** ADA to RTX in SLE are more frequent than in RA and MS and occur irrespective of treatment response and cotreatments, but are associated with higher counts of CD19 +B cells at follow-up. Such finding could reflect either incomplete B-cell depletion in ADA positive patients, or earlier repopulation. Further studies should address the relation between ADA titers and clinical outcomes as well as immunological consequences.

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### AB0513 B AND T LYMPHOCYTES MODIFICATIONS AFTER BELIMUMAB TREATMENT IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** B- and T-cell hyper-activation is one of the pathogenic mechanisms of systemic lupus erythematosus (SLE). SLE patients have a severe defect in the B cell tolerance check, resulting in high numbers of autoreactive mature naïve B-cells (CD19 +CD27-IgD+) and of peripheral transitional B-cells (CD19 +38high24high). On the other hand, in patients with active SLE a reduced thymic output with a decreased number of recent thymic emigrants T-cells (RTE; CD4 +CD31+) was demonstrated, whereas repeated antigenic stimulation drives modifications in T-cells subpopulations, with enhanced differentiation into effector memory cells (CCR7-CD45RA-).<sup>1</sup>

Belimumab is a monoclonal antibody against soluble BLYS used in the treatment of severe SLE. Although B cells are the main target of this treatment, a BLYS-dependent T-cell activation pathway has also been demonstrated.<sup>2</sup> However, few data are available on the effects of belimumab on circulating B- and T-cell subsets.

**Objectives:** The aim of this study was to characterise B and T-cell phenotype in a cohort of patients with SLE, and to analyse their modifications during belimumab therapy.

**Methods:** Phenotypic analysis of peripheral blood B and T lymphocyte subsets was made by flow-cytometry in 14 SLE patients before the first infusion of belimumab, and after 12 months of treatment. SLEDAI 2K-score was used to determine disease activity: a score  $\geq 6$  indicated high disease activity. Sex and age-matched healthy controls were enrolled for the comparisons.

**Results:** At baseline, SLE patients had lower numbers of B- (82 vs 153 cell/ $\mu$ l; p=0.05), T- CD4+ (365 vs 1131 cell/ $\mu$ l; p<0.01), T- CD8+ (340 vs 516 cell/ $\mu$ l; p=0.01), and RTE (95 vs 240 cell/ $\mu$ l; p=0.03) than healthy donors.

After treatment there was a decrease of total B lymphocytes (82 vs 19 cell/ $\mu$ l; p<0.01), and particularly of naïve (45 vs 19% of CD19+; p<0.01) and transitional cells (1 vs 0.2 cell/ $\mu$ l; p=0.03). The absolute number of unswitched memory B cells decreased (2.2 vs 1.4 cell/ $\mu$ l; p=0.05), whereas the percentage of switched memory B cells increased (16 vs 44% of CD19+; p<0.01). The absolute number of CD8 +effector memory cells was also reduced (61 vs 53 cell/ $\mu$ l; p=0.05), as well as percentages of RTE (20 vs 10% of CD4+; p=0.01).

After 1 year therapy in the only 2 patients with persistent high disease activity the percentages of transitional B cells and unswitched memory cells were higher than in 7 patients in which an initially high disease activity decreased below SLEDAI=6 (9% vs 1%; p=0.03; and 29% vs 6%; p=0.04, respectively).

**Conclusions:** The effects of belimumab on B cell subpopulations are likely to be directly explained by the blockage of soluble BLYS. On the other hand, the effects on the phenotype of T cells are modest and it cannot be excluded that they are indirectly explained by the reduction of disease activity obtained through the therapy. The number of certain circulating B cell subsets might be a marker of response to treatment.

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**Disclosure of Interest:** None declared

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### AB0514 THE EFFECT OF HYDROXYCHLOROQUINE ON REDUCING PROTEINURIA IN STABLE SLE PATIENTS

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**Background:** It is thought that hydroxychloroquine (HCQ) reduces proteinuria by preventing endothelial dysfunction in mouse models, but the effects in systemic lupus erythematosus (SLE) patients are not known.

**Objectives:** To investigate the effects of HCQ on proteinuria in stable SLE patients.

**Methods:** This was a single-centre, retrospective cohort study. We included stable SLE patients who met the updated or revised American College of Rheumatology 1997 criteria for SLE or the 2012 Systemic Lupus International Collaborating Clinics criteria, and had no active organ dysfunction that needed an increase in immunosuppressive therapy. The subjects (HCQ group) were SLE patients with proteinuria >0.2 g/gCr who started HCQ between 11/1/2015 and 8/1/2017. The controls (non-HCQ group) were SLE patients with proteinuria >0.2 g/gCr seen between 5/1/2016 and 10/31/2016. The reduction in proteinuria over 6 months in the HCQ and non-HCQ groups was compared. The following patients were excluded from the analysis: those who had proteinuria of other aetiologies (diabetic nephropathy, etc.), those who increased the prednisolone (PSL) dose or started immunosuppressive agents, angiotensin converting enzyme inhibitors, or angiotensin II receptor blockers beginning 1 month before the observation period started until its end. Improvement was defined as a reduction in proteinuria  $\geq 0.1$  g/gCr. The statistical analysis was performed with the *t*-test and chi-square test.

**Results:** There were no significant differences in disease duration, sex, Systemic Lupus Erythematosus Disease Activity Index, or the use of immunosuppressants at baseline between the HCQ (n=16) and non-HCQ (n=14) groups. The respective mean PSL dose at baseline was  $5.9 \pm 2.8$  and  $3.3 \pm 3.8$  mg in the HCQ and non-HCQ groups (p=0.042). Patients in the HCQ group were younger (mean  $47 \pm 12$  vs.  $63 \pm 14$  years, p=0.005). The kidney pathology of the HCQ group was 6.25, 25, 6.25, 6.25, and 6.25% class I to V, respectively, compared with 7.14% class IV, 14.2% class V, and 14.2% class IV+V in the non-HCQ group. The other patients were diagnosed with lupus nephritis clinically.

Proteinuria was significantly lower in the HCQ group than in the non-HCQ group ( $-0.170 \pm 0.343$  g/gCr vs.  $+0.129 \pm 0.401$  g/gCr, p=0.036). The mean proteinuria at baseline and 6 months later was  $0.501 \pm 0.276$  and  $0.331 \pm 0.274$  g/gCr, respectively, in the HCQ group, and  $0.587 \pm 0.409$  and  $0.717 \pm 0.720$  g/gCr in the non-HCQ group. The proportion of patients who improved in the HCQ and non-HCQ groups was 68.7% (11/16) and 28.5% (4/14), respectively (p=0.028).

**Conclusions:** HCQ may reduce proteinuria in SLE patients. This suggests that HCQ administration protects the kidneys of SLE patients.

**Disclosure of Interest:** None declared

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AB0515

**SPANISH SOCIETY OF RHEUMATOLOGY (SER) RECOMMENDATIONS ON PRIMARY ANTIPHOSPHOLIPID SYNDROME (APS). IN A PATIENT WITH OBSTETRIC APS, WHICH TREATMENTS ARE MORE EFFECTIVE? SYSTEMATIC REVIEW**

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**Background:** Pregnancy complications and poor obstetric prognosis are part of the manifestations of APS. The obstetric APS (O-APS) includes 3 or more early miscarriages, 1 or more intrauterine foetal deaths, prematurity secondary to preeclampsia or placental insufficiency, intrauterine growth retardation and HELLP syndrome among others. There is disagreement among different published studies regarding the need of preconceptual or primary thromboprophylaxis (treating with anticoagulant/antiaggregant drugs in the presence of specific autoantibodies but without previous clinical events) and the most effective and safest drug to use, as well as which treatment should be chosen in the case of secondary thromboprophylaxis (treating in the presence of autoantibodies and recurrent miscarriages or previous obstetric complications).

**Objectives:** To evaluate the available scientific evidence on which treatments are the most effective and safest in O-APS.

**Methods:** A systematic review (SR) was performed to evaluate the efficacy and safety of different interventions (Aspirin (ASA), Heparin, Antimalarials, Immunglobulin IV (IVIg), others) in pregnant women with O-APS. We included SR, randomised clinical trials (RCTs) and comparative cohort studies. Result measures on morbidity (prematurity, low birth weight, need for intensive care, impaired cognitive development, preeclampsia, eclampsia, HELLP, abruptio placentae) and mortality included both the newborn and the pregnant woman. A peer review selection and analysis of the studies was carried out (SP,H; NA, MB).

**Results:** 788 citations were identified (Medline, EMBASE, CENTRAL, May 2017). We included 17 studies: 5 SR, 5 RCTs and 7 cohort studies. Results are shown on the table 1 below:

Abstract AB0515 – Table 1

Drugs	Efficacy	Level of evidence
ASA vs placebo	Inconclusive	1+
ASA + Heparin	The combination is more effective than ASA on its own in order to achieve better obstetric results in women with O-APS One SR and one RCT did not found added benefits with the combination compared to ASA monotherapy	1+, 1+, 1-,2+ 1+, 2+
IVIg	Inconclusive, but: Comparing IVIg with ASA+heparin is favourable to this combination: it is easier to use and has a lower cost IVIg compared with prednisone could be a better option to decrease maternal complications in patients with O-APS	1+, 1-,2+ 2-
Corticoids	There is not enough evidence available.	1+, 2-
Statins	There is not enough evidence available.	2+

**Conclusions:** In women with O-APS:

- **Secondary thromboprophylaxis:** The combination of ASA +Heparin is more effective than ASA monotherapy.

With regards to the use of IVIg, corticosteroids and statins: NO representative conclusions can be drawn from published studies

- **Pre-conceptual thromboprophylaxis, primary thromboprophylaxis:** NO representative conclusions can be drawn from published studies.

**Acknowledgements:** This review is part of the preparation of SER Recommendations on Primary APS treatment.

**Disclosure of Interest:** None declared

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AB0516

**THERAPEUTIC STRATEGIES AND PROGNOSIS IN CHINESE PATIENTS WITH SEROLOGICALLY ACTIVE CLINICALLY QUIESCENT SYSTEMIC LUPUS ERYTHEMATOSUS**

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**Background:** SACQ patients with SLE appears to account for 6%–12% of all patients with SLE, but there is disagreement about whether such patients are indeed clinically stable, especially in Chinese patients. And there is no conclusion as to what kind of treatment should be taken for such patients.

**Objectives:** The aim of our study was to identify the frequency and outcome of SACQ patients with SLE. And we tried to find out potential predictors of flare.

**Methods:** 682 patients with systemic lupus erythematosus who were followed up for more than 6 months at Peking University First Hospital from January 2007 to December 2015 were summarised. SACQ was defined as an at least a 6 month period with persistent serologic activity and without clinical activity and could be taking a daily dose of prednisone or equivalent less than 7.5 mg. Serologically quiescent clinically quiescent (SQCQ) patients and serologically active clinically active (SACA) patients served as control groups. Data including demographics, initial symptoms, duration to SACQ, treatments before and after SACQ, and characteristics of the flare group were analysed.

**Results:** Of the 682 patients, 170 were SACQ patients (24.9%), 187 were SQCQ patients, and 325 were SACA patients (47.7%). SQCQ patients (38.61±15.08 years old) were older at study start than did SACQ patients (38.61±15.08 years vs. 32.09±14.35 years, p=0.000), but there was no significant difference between that of SACQ and SACA patients. 56 of the 170 SACQ patients (32.9%) experienced flare. Corticosteroids (OR 1.323, 95% CI 1.135 to 1.542; p=0.000) was an independent risk factor for flare, while antimalarials (OR 0.040, 95% CI 0.004 to 0.418; p=0.007) and immunosuppressants (OR 0.321, 95% CI 0.153 to 0.673; p=0.003) were protective factors.

**Conclusions:** SLE patients with SACQ remained relatively stable, with 32.9% of patients relapsed. The group of flare patients took greater use of corticosteroids than non-flare ones, whereas antimalarials and immunosuppressants agents were protective factors.

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AB0517

**INVASIVE ASPERGILLOSIS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A RETROSPECTIVE STUDY FOCUS ON CLINICAL CHARACTERISTICS AND RISK FACTORS OF IN-HOSPITAL MORTALITY**

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**Objectives:** To analyse the clinical features and outcomes of patients with invasive aspergillosis (IA), the mortality risk factors and all-cause mortality in patients with systemic lupus erythematosus (SLE) in single centre of Taiwan.

**Methods:** A retrospective study was performed to identify the mortality risk factors associated with IA in patients with systemic lupus erythematosus (SLE). We reviewed the medical records of patients with SLE who were diagnosed with invasive aspergillosis between Jan. 2006 and Jun. 2017 from Taipei Veterans General Hospital in Taiwan. Clinical and laboratory parameters as well as treatment outcomes were analysed.

**Results:** Twenty-one patients diagnosed with proven (n=4; 19.04%) and probable (n=17; 80.95%) invasive aspergillosis according to revised definition by European Organisation for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses Study Group (EORTC/MSG) Consensus Group were enrolled in the study and separated into survivors (n=7; 33.33%) and non-survivors (n=14;

66.67%) groups. All patients in invasive aspergillosis demonstrated significantly high incidence of pneumonia (n=19; 90.47%), concurrent infections (n=17; 80.95%), and high mortality (n=14; 66.67%). The coinfections with bacteremia (n=8; 38.10%), cytomegalovirus (n=9; 42.86%), and candida (n=6; 28.57%) were common in patients with invasive aspergillosis. Gram-negative bacilli (38 isolates; 69.09%), of which the most common isolates were carbapenem-resistant *Acinetobacter baumannii* (8 isolates; 21.05%). The most common Gram-positive isolates were methicillin-resistant *Staphylococcus aureus* (6 isolates; 35.29%), followed by Vancomycin-resistant *Enterococcus* (4 isolates; 23.52%). The daily glucocorticoid dose  $\geq 20$  mg (p=0.007, HR 2.000, 95% CI 1.185–3.377), rates of recent pulse glucocorticoid therapy (p=0.022, HR 2.800, 95% CI 1.387–5.654), rates of azathioprine use (p=0.022, HR 2.000, 95% CI 1.185–3.377), rates of rituximab within six months (p=0.022, HR 2.000, 95% CI 1.185–3.377), plasmapheresis during hospital course (p=0.022, HR 2.000, 95% CI 1.185–3.377), and acute respiratory distress syndrome (p=0.022, HR 2.000, 95% CI 1.185–3.377) among non-survivor group were statistically higher than the survivor group. Non-survivors had significantly higher rate of concurrent infections (p=0.002, HR 5.667, 95% CI 2.029–15.824) and cytomegalovirus (CMV) viremia (p=0.040, HR 1.750, 95% CI 1.112–2.775) than survivors. The sensitivity of Galactomannan assay was not good to exclude the diagnosis of invasive aspergillosis. Septic shock (n=7, 50% of non-survivor group) is the most common cause of in-hospital mortality in patients with invasive aspergillosis.

**Conclusions:** The daily glucocorticoid dose  $\geq 20$  mg, recent pulse glucocorticoid therapy, azathioprine, rituximab within six months, concurrent infections, and CMV viremia are risk factors of in-hospital mortality in invasive aspergillosis patients with Systemic Lupus Erythematosus.

within six months, concurrent infections, and CMV viremia are risk factors of in-hospital mortality in invasive aspergillosis patients with Systemic Lupus Erythematosus. within six months, concurrent infections, and CMV viremia are risk factors of in-hospital mortality in invasive aspergillosis patients with Systemic Lupus Erythematosus.

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**Disclosure of Interest:** None declared

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#### AB0518 EFFICACY OF BELIMUMAB FOR PRIMARY SJÖGREN SYNDROME: RESULTS OF A SYSTEMATIC REVIEW OF THE LITERATURE

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**Background:** Belimumab is a human monoclonal antibody that inhibits B-cell activating factor shown to be efficacious in systemic lupus erythematosus. In other B cell mediated autoimmune disease such as primary Sjögren's syndrome (pSS) the efficacy is unclear.

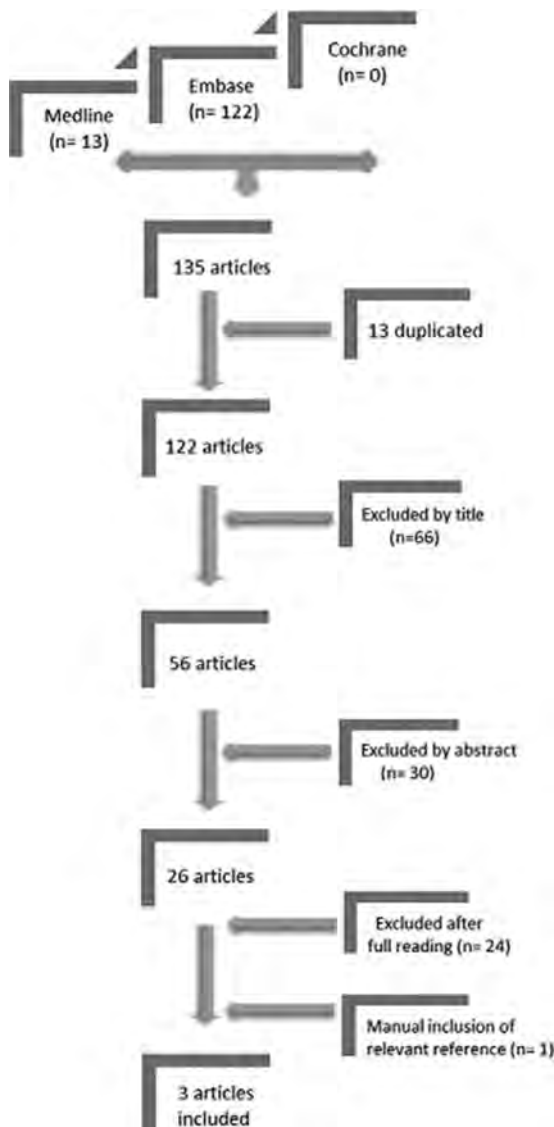
**Objectives:** To evaluate the efficacy of belimumab in patients with pSS.

**Methods:** A systematic literature review was performed (EMBASE, MEDLINE and Cochrane) as part of the Spanish Rheumatology Society's Recommendations for the Use of Biological Therapies in Primary Sjögren's Syndrome. Inclusion criteria was defined as: Population: patients with pSS according to American-European Consensus Criteria 2002 Intervention: belimumab; Control: synthetic or biologic DMARDs, corticosteroids, ursodesoxicolic acid or placebo; Outcome: efficacy in dryness, glandular and extraglandular manifestations. Studies with <10 patients or <3 months of follow up were excluded. Two reviewers independently selected the articles and evaluated the quality of the evidence following SIGN guidelines.

**Results:** 3 articles were included out of 135. All of them published results from the same study<sup>1</sup> at different timepoints. The study design was experimental but with a small sample size and no control group or randomization.

The article of Mariette et al 2015<sup>1</sup> evaluated the efficacy and safety of belimumab in 30 patients with systemic activity or early disease until week 28 (W28). There was a significant decrease in mean ESSDAI (8.8 to 6.3 p=0.02), ESSPRI (6.4 to 5.6 p=0.02) and VAS for dryness (7.8 to 6.2 p=0.02). Physician's VAS for disease systemic activity also decreased in 43% as well as parotid inflammation in 76.9% of patients. Also, B cell biomarkers decreased: IgG (21.2 to 18.2 g/L, p=0.02), IgA (3.7 to 3.3 g/L, p=0.04), IgM (1.6 to 1.3 g/L, p<0.001), RF (146.2 to 106.7 UI p<0.001) and number of B cells (187.2 a 65.1/mm, p<0.001).

The study of De Vita et al 2015<sup>2</sup> compared results at week 52 (W52) and W28 in 19 patients, of whom 15 had previously responded to treatment. Of these 15 patients 13 maintained response and 3 out of the 4 patients that did not respond achieved primary outcome. The improvement at W52 continued for ESSDAI, glandular inflammation, lymphadenopathy and joints. B cell biomarkers remained stable. Overall items contributing to ESSDAI decreased but only physician's VAS for disease systemic activity was statistically significant (3.2 W28 vs 2.5 W52; p=0.04).



**Abstract AB0518 – Figure 1**

The study of Quartuccio et al.<sup>3</sup> compared clinical and lab variables of W52 with 12 months of follow up after interrupting belimumab. A significant decrease in ESSDAI in 9 out of 13 patients (3.5±3.7 vs 7.0±5.7; p<0.01) was observed as well as in RF (52 vs 69UI; p<0.01), IgM (131.9 vs 165 mg/dl; p=0.04) and BLYS (1304 vs 2882 pg/ml; p=0.01).

**Conclusions:** Published evidence to determine the efficacy of belimumab in primary Sjögren is limited and poor. Belimumab seems to be effective to reduce systemic activity, parotid enlargement, dryness, lymphadenopathies, articular manifestation, fatigue and B cell biomarkers.

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**AB0519** **IMPACT OF HIGHER BODY MASS INDEX (BMI) IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS**

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**Background:** Systemic lupus erythematosus (SLE) patients may have nutritional changes triggered by disease itself or by treatment with possible implication for patients prognosis.

**Objectives:** The main focus of the study was to evaluate nutritional status and its impact in a SLE cohort with disease duration of at least 1 year.

**Methods:** 105 SLE patients admitted in Sf. Maria Clinical Hospital in 2017 were enrolled. Inclusion criteria were represented by disease evolution of at least 1 year. All patients agreed to participate in this observational study. Data about demographic, clinical or serological characteristics, but also activity (SLEDAI), damage accrual (SLICC damage index SDI) and treatment or complications (osteoporosis, cataract, glaucoma, etc) were collected. Nutritional status was evaluated by calculating Body Mass Index (BMI) for each patient. A descriptive and analytical statistics was performed with SPSS.

**Results:** 99 females and 6 males were enrolled. Mean age at SLE diagnosis was 34.39, SD 11.34. BMI was calculated as ratio of body weight to squared height (kg/m<sup>2</sup>). According to BMI, 5% of patients were underweight (BMI <18.5), 56% had normal weight (BMI 18.5–25), 25% were overweight (BMI 25–30) and 14% were obese (BMI >30). Increased BMI was correlated with longer disease duration (p 0.0001, r 0.30) and older age (p 0.0001, r 0.35), but these correlation loose the strength for patients older than 40 years (p 0.04, r 0.15), suggesting a more pronounced weight gain at the beginning of the disease. Quality of sleep was significantly altered in patients with abnormal BMI (p 0.005, r 0.35). As expected, overweight and obese patients had a sedentary life style (p<0.01). Higher BMI was correlated also with higher SDI score (p 0.026, r 0.35) and higher number of complications related to chorticotherapy per patient (p 0.0001, r 0.45).

**Conclusions:** SLE patients have an increased risk for higher BMI, especially patients younger than 40 years, in the first years after diagnosis. Optimising weight in our SLE patients should be in our focus in order to limit number of complications, damage accrual and lifestyle patterns that negatively impact their life.

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**AB0520** **ASSESSMENT OF ANTI-MÜLLERIAN HORMONE LEVELS IN SYSTEMIC LUPUS ERYTHEMATOSUS TREATED WITH IMMUNOSUPPRESSOR**

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**Background:** Systemic lupus erythematosus (SLE) is a chronic immune-mediated inflammatory disease that affects predominantly females during childbearing age. Fertility in SLE patients is considered to be normal but several factors, such as disease activity, renal involvement and treatment with immunosuppressor may negatively influence fertility.

**Objectives:** To investigate the ovarian reserve of patients with SLE by measuring anti-müllerian hormone (AMH) levels, and compare the AMH levels before and after treatment with immunosuppressor.

**Methods:** This was a self-control study performed on newly diagnosed premenopausal female SLE patients fulfilled the 1997 American College of Rheumatology (ACR) criteria. Serum concentrations of AMH in peripheral venous blood were measured using a human AMH ELISA kit (MSKIBIO, Wuhan, China) before and after treatment with 6 month immunosuppressor.

**Results:** 45 patients were recruited. AMH serum levels reduced after treatment in the cyclophosphamide (CTX) group (n=6) and leflunomide (LEF) group (n=7), P<0.05. AMH serum levels did not differ before and after treatment in the mycophenolate (MMF) group (n=11), tacrolimus group (n=8) and methotrexate (MTX) combined with cyclosporin A (CsA) group (n=13), p≥0.05.

**Conclusions:** In this self-control study, the AMH serum levels reduced after 6 month treatment of CTX or LEF, indicating CTX and LEF might negatively influence ovarian reserve function. AMH serum levels did not differ after 6 month treatment of MMF, tacrolimus or combined use of MTX and CsA, indicating these immunosuppressor might be relatively safe for ovarian reserve function.

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**AB0521** **SAFETY, PHARMACOKINETICS, AND PHARMACODYNAMICS OF SINGLE DOSES OF A BISPECIFIC ICOSL AND BAFF INHIBITOR, AMG 570, IN HEALTHY SUBJECTS**

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**Background:** Autoimmune diseases, including systemic lupus erythematosus (SLE), are associated with dysregulation in both T cell and B cell responses. Targeting the activity of both cell types simultaneously holds promise as a treatment for autoimmune disease. AMG 570 is a bispecific molecule targeting both T cell and B cell activity through neutralisation of the inducible costimulator ligand (ICOSL) and the B cell activating factor (BAFF).

**Objectives:** To investigate the safety, tolerability, pharmacokinetics, and pharmacodynamics of AMG 570 in healthy subjects after single subcutaneous doses.

**Methods:** This ongoing, double-blind, randomised, placebo-controlled trial has enrolled healthy subjects (age ≥18 years) into escalating single-dose cohorts. Eight participants were enrolled into each cohort and were randomised 3:1 to receive either AMG 570 or placebo across six cohorts of increased dose level. The primary endpoint of the study was treatment-emergent adverse events (AEs). Secondary endpoints included pharmacokinetics and pharmacodynamics (eg, receptor occupancy of ICOSL, changes in B cell subpopulations, and serum immunoglobulin levels).

**Results:** As of an ad hoc interim analysis on October 5, 2017, 48 participants were enrolled and received one dose of investigational product (either AMG 570 or placebo). 73 AEs were reported; all were mild (n=56) to moderate (n=14) in severity (3 injury AEs had no grade reported). Upper respiratory tract infection and injection site erythema were the most commonly reported AEs. No drug-related serious adverse events were reported. No severe, life-threatening, or fatal AEs were reported. AMG 570 demonstrated nonlinear pharmacokinetics consistent with cell surface target (ICOSL) interaction. In the highest dose tested, AMG 570 achieved greater than 90% mean ICOSL receptor occupancy on circulating B cells 8 days after dosing, and high levels (>85% mean ICOSL receptor occupancy) were observed 29 days after dosing. AMG 570 led to a reduction in circulating naïve B cells and an increase in circulating memory B cells. No apparent changes were observed in serum IgM or IgG.

**Conclusions:** Overall, AMG 570 was safe and well tolerated by healthy subjects. AMG 570 demonstrated pharmacodynamic activity consistent with ICOSL and BAFF neutralisation.

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AB0522

### TACROLIMUS IN REFRACTORY LUPUS NEPHRITIS: A PROSPECTIVE MULTICENTRIC STUDY CARRIED OUT IN CLINICAL PRACTICE SETTING

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**Background:** The efficacy of tacrolimus (TAC) in lupus nephritis (LN) has been recently demonstrated in several randomised controlled trials in asian cohorts.<sup>1</sup> Nevertheless, data on real-life experience and long-term safety of TAC are still lacking.

**Objectives:** To assess efficacy and safety of TAC in SLE patients with refractory LN in a multi-centric prospective cohort.

**Methods:** Adult SLE patients with refractory LN from 4 Italian centres were prospectively followed for at least 12 months. Clinical and serological variables and previous/concomitant medications were collected at baseline, 3, 6, 12 months after starting TAC. Renal response was assessed by using EULAR/ERA-EDTA definitions.<sup>2</sup> Adverse events (AEs) included non-infectious and infectious AEs; they were defined severe (SAE) when hospitalisation and/or death and/or life-threatening manifestations occurred. Data were analysed using SPSS (v.24.0).

**Results:** Thirteen SLE patients (8 females, 5 males, mean age 33.7±10.2, mean disease duration 11.9±5.9) were enrolled (table 1). Concomitant medications included: prednisone (100%), mycophenolate mofetil (92.3%), hydroxychloroquine (53.8%), azathioprine (7.7%), belimumab (7.7%) and cyclosporine (7.7%). The average number of previous immunosuppressants taken by each patient was 3.15±1.90. Six-months renal response was achieved by 5/13 patients (38.5%): complete renal response (CRR) in 3 (60.0%) and partial renal response (PRR) in 2 patients (40.0%). Twelve-months renal response occurred in 4/13 patients (30.8%): CRR in 2/13 (50.0%) and PRR in 2/13 (50.0%). One patient achieved CRR at 6 and 12 months; one patient achieved PRR at 6 months and CRR at 12 months. Six patients (46.1%) discontinued TAC after an average follow up period of 10.2±7.8 months. Causes of discontinuation were: 3 non-infectious non-SAEs, 1 flare, 1 non-infectious SAE, and 1 non-response. Concerning AEs, no severe infections or deaths occurred.

**Abstract AB0522 – Table 1.** Demographic, clinical and serological features at baseline, 3, 6, 12 months after starting TAC (mean±SD)

	Baseline	3 months	6 months	12 months
Prednisone daily dosage (mg/day)	17.1 ±11.3	12.7±9.5	12.8±13.1	9.6±5.6
Tacrolimus daily dosage (mg/day)	4.1±1.3	3.5±1.9	4.2±1.8	4.0±0.8
Creatinine (mg/dL)	0.8±0.5	0.8±0.3	0.7±0.3	0.9±0.5
24 hour proteinuria (g/day)	3.8±2.2	1.4±1.2	1.5±1.6	2.0±1.6
SLEDAI-2k	8.8±2.4	7.2±4.5	7.5±4.3	7.4±4.4
SLICC-DI	1.3±1.4	/	1.6±1.5	1.4±1.1

SLEDAI-2k: Systemic Lupus Erythematosus Disease Activity Index 2000; SLICC-DI: Systemic Lupus International Collaborating Clinics Damage Index.

**Conclusions:** Our preliminary data from clinical practice setting suggest that TAC could be a therapeutic rescue strategy for refractory LN. Further studies are needed to prove TAC efficacy in the long term.

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AB0523

### METFORMIN COMBINED WITH CONVENTIONAL THERAPY INCREASES ABSOLUTE NUMBER OF REGULATORY T CELLS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

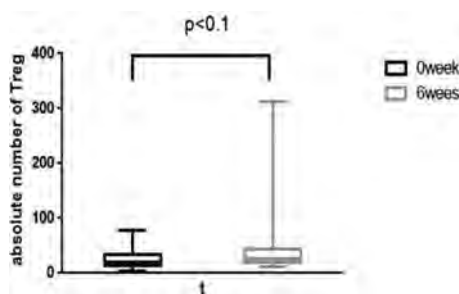
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**Background:** Systemic lupus erythematosus (SLE) is multisystem and multiorgan autoimmune diseases and the main treatment is hormone combined with immunosuppressant and biological agents. Since the conventional treatment regimens have not achieved expected effects, it is of great practical value to search for good efficacy, lower side-effects, and low-cost drugs. Recently, we have found that the absolute number of CD4<sup>+</sup>CD25<sup>+</sup>FOXP3<sup>+</sup> regulatory T (CD4<sup>+</sup> Treg) cells reduced in SLE. Metformin, a basic hypoglycemic drug, has been shown to increase the number of Treg cells and decrease the number of Th17 cells.<sup>1,2,3</sup>

**Objectives:** To observe the clinical efficacy of metformin on the treatment of SLE and levels of CD4<sup>+</sup>Treg and Th17 cells.

**Methods:** Twenty-three patients with SLE were enrolled in this study. They fulfilled the ACR<sup>1997</sup> standard, their average age was 32.22±8.18 years, and duration was 51.41±15.52 months. These patients were administered metformin (250 mg Bid) combined with conventional therapy for 6 weeks. At week 0 and week 6, the absolute numbers of Th17 cells and Treg, the symptoms, and laboratory indicators were collected.

**Results:** After metformin treatment combined with conventional therapy, average absolute number of Treg cells in 23 patients increased significantly from 20.2 (20.28) (week 0) to 25.76 (25.1) (week 6) (p=0.073) while that of Th17 cells increased slightly from 5.29 (6.43) (week 0) to 5.57 (6.05) (week 6) (p=0.956), which led to reduce average ratio of Th17/Treg from 0.25 (0.31) (0 week) to 0.19 (0.23) (6 weeks) (p=0.147). The treatment attenuated the symptoms of the patients and meantime, the dose of prednisone was decreased. At week 6, metformin combined with interleukin-2, the dosage of prednisone in SLE patients were decreased from 23.70±19.41 mg/d(0 week) to 20.44±17.03 mg/d(6 weeks) (p=0.548).



**Abstract AB0523 – Figure 1**

**Conclusions:** Our findings suggest metformin can effectively up-regulate Treg cells as well as increase Th17 to a certain extent, which restores the balance of Th17/Treg cells in SLE, metformin combined with conventional therapy can reduce the dosage of glucocorticoid, but the long-term effect needs further investigation.

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AB0524

### HOW DO WE TREAT DRYNESS IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME? A NATIONWIDE STUDY IN SPAIN FROM THE SJÖGRENSER REGISTRY

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**Background:** Primary Sjögren syndrome (pSS) is a systemic autoimmune disease whose main characteristic is the involvement of the exocrine glandular system. Thus, its most common clinical manifestation is eye and mouth dryness. No therapy has been demonstrated to significantly modify disease course and, currently, evidence-based therapy for pSS is mainly limited to symptomatic drugs for dryness.

**Objectives:** To describe the dryness treatment in a cohort of primary Sjögren Syndrome patients.

**Methods:** SJÖGRENSER registry is a multicentre descriptive cross-sectional study of pSS patients, fulfilling European/American criteria, from 33 Spanish rheumatology departments. Data were collected by reviewing clinical records and interviewing the patients. Informed consent was obtained and local ethics committees approved the study. Variables were analysed by descriptive statistics using means, medians and ranges. Chi square test was used to compare categorical variables. A  $p < 0.05$  was considered significant.

**Results:** Four hundred and thirty seven patients were included (female 95%; median age 58 years). Ninety four per cent of the patients complained of daily, persistent, troublesome dry eyes for more than 3 months, 92% had sensation of sand in the eyes, 16% developed corneal ulcer. Ninety four per cent of the patients complained of dry mouth for more than 3 months and 27% had dental loss. The most frequent ocular dryness treatments were tear substitutes (96%), followed by lubricating ophthalmological ointments (46%), autologous sera solutions (14%), topical corticosteroids (13%), topical cyclosporine (6%). Comparing patients with and without ocular dryness, only pilocarpine and lubricating eye ointment were used significantly with more frequency in symptomatic patients ( $p < 0.05$ ); tear substitutes was used significantly with more frequency in symptomatic patients only in the subgroup of patients that used tear substitutes more than 3 times a day. The most frequent oral dryness treatments were chewing gums or candies without sugar (65%), followed by pilocarpine (56%), special toothpaste (22%), mucolytic agents (20%), saliva substitutes (19%), lubricating oral gel (13%) xylitol (11%) and fluoride (11%). Comparing patients with and without oral dryness, chewing gums or candies without sugar, xylitol and fluoride were not used significantly more frequently in symptomatic patients. In contrast, saliva substitutes, lubricating oral gel, pilocarpine, mucolytic agents and specific toothpaste were used significantly more frequently in symptomatic patients ( $p < 0.05$ ). The median in ESSPRI (Eular Sjögren's Syndrome Patient Reported Index) in SJÖGRENSER cohort was 5.3 (p25-p75, 3.67-7). Only topical corticosteroids and pilocarpine were used significantly more frequently in patients with a dryness VAS<sub>≥5</sub> in ESSPRI index.

**Conclusions:** Despite the high number of symptomatic patients, the use of dryness treatments is limited in pSS patients. Chewing gums or candies without sugar, xylitol and fluoride remain underutilised in this cohort. Despite the dryness VAS score, patients do not seem to use all the symptomatic therapeutic options available.

**Disclosure of Interest:** None declared

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AB0525

### IDENTIFICATION OF EFFECTIVE PARAMETERS INFORMING THE SELECTION OF INTRAVENOUS CYCLOPHOSPHAMIDE VERSUS MYCOPHENOLATE MOFETIL FOR INDUCTION THERAPY FOR LUPUS NEPHRITIS

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**Background:** The 2012 EULAR recommendations gave equal weight to intravenous cyclophosphamide (IVCY) and mycophenolate mofetil (MMF) as the induction therapy for class III/IV lupus nephritis (LN). However, there are no effective parameters that could inform the choice the induction therapy (IVCY or MMF) in individual cases.

**Objectives:** This study examined the patient characteristics that determine the most appropriate treatment for LN: IVCY or MMF.

**Methods:** We retrospectively examined 29 patients with LN who received induction therapy with IVCY (n=16) or MMF (n=13) between January 1994 and December 2015. Their baseline characteristics and the complete response (CR) rate at

week 24 were analysed. CR was defined as a urine protein:creatinine ratio  $< 0.5$  g/gCr with normal urine sediment.

**Results:** At baseline, the time since diagnosis of systemic lupus erythematosus (SLE) was longer in the IVCY group than the MMF group (4.8±6.4 vs. 1.3±2.5 years,  $p=0.06$ ) and the IVCY group had more frequent flares (1.9±2.4 vs. 0.7±1.1 times,  $p=0.08$ ); however, the differences were not significant. Moreover, there was no difference in age, sex, complement levels, anti-dsDNA antibody titers, anti-Sm/RNP antibody positivity rates, proteinuria, or rate of abnormality in urine sediment at baseline between the two groups. CR was achieved at week 24 in 11/16 patients (69%) in the IVCY group and 9/13 patients (69%) in the MMF group. Considering the 20 patients who achieved CR at week 24, univariate analyses revealed that in addition to a longer time since diagnosis of SLE (4.5±6.6 vs. 1.0±1.7 years,  $p=0.12$ ) and more frequent flares (1.9±2.8 vs. 0.6±1.0 times,  $p=0.16$ ), the anti-RNP antibody positivity rate was higher (OR 8.15;  $p=0.07$ ) in the IVCY group. Furthermore, the positivity rate of anti-RNP antibody differed significantly (OR 12.9;  $p=0.03$ ) in the multivariate analysis.

**Abstract AB0525 – Table 1.** Univariate analyses of patients with CR at week 24

	IVCY (n=11)	MMF (n=9)	p value
age (years)	31.2±10.9	39.6±18.8	0.23
sex (male,%)	9.1	22.2	0.57, OR=2.11
time since diagnosis of SLE (years)	4.5±6.6	1.0±1.7	0.12
flares (times)	1.9±2.8	0.6±1.0	0.16
complement C3 level (mg/dL)	48.3±29.3	47.6±21.5	0.95
anti-dsDNA antibody (IU/mL)	161.2±187.4	128.8±154.2	0.68
anti-Sm antibody (%)	63.6	33.3	0.37, OR=3.27
anti-RNP antibody (%)	72.7	22.2	0.07, OR=8.15

**Abstract AB0525 – Table 2.** Multivariate analyses of patients with CR at week 24

	Model 1		Model 2	
	OR (95% CI)	p value	OR (95% CI)	p value
age	–	–	0.9 (0.8–1.0)	0.15
sex (female)	–	–	1.2 (0.04–38.8)	0.92
time since diagnosis of SLE	1.1 (0.7–1.7)	0.77	1.0 (0.6–1.6)	0.91
flares	1.5 (0.5–4.2)	0.44	1.7 (0.6–4.4)	0.30
anti-RNP antibody	12.9 (1.3–132.3)	0.03*	31.8 (1.1–892.9)	0.04*

Model 1 was adjusted by all of the characteristics which showed  $p < 0.20$  in the univariate analysis; model 2 was adjusted by age and sex in addition to model 1.

dsDNA, double strand DNA; anti-Sm antibody, anti-smith antibody; anti-RNP antibody, anti-ribonucleoprotein antibody; OR, odds ratio; CI, confidence interval. (\* $p < 0.05$ )

**Conclusions:** Although IVCY and MMF are equivalent treatment options for LN, IVCY might be more effective for patients with anti-RNP antibody.

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AB0526

### IMBALANCE IN ELASTIN-ELASTASE SYTEM LEADING TO CLINICAL MANIFESTATIONS OF SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** It is believed that in systemic lupus erythematosus antibodies induce a disturbance in the elastin-elastase metabolism, which yields altered soluble isoforms followed by triggering of autoimmunity mechanisms, which damage the elastin-containing tissues.

**Objectives:** Studying antibody formation in the elastin-elastase system in patients with systemic lupus erythematosus (SLE) using magnetocontrollable adsorbents with an immobilised form of corresponding antigen.

**Methods:** Sera from 30 donors and 65 SLE patients were studied. Antibodies to elastin and elastase were determined using ELISA test and magnetocontrollable adsorbents with an immobilised form of corresponding antigen.

**Results:** We analysed changes in the content of antibodies to elastin and elastase in patients with SLE of varying severity assessed using SLAM, SLEDAI scale, and criteria by V.A. Nasonova.

The greatest elastin antibody titer was noted in patients with SLE grade III (57.1%, 4 people), with grade II – in 42.5% (17 people), and with grade I – in 33.3% (6 people).

The elastin antibody titer in SLE patients being admitted to hospital was reliably higher than in donors ( $p < 0.001$ ).

An analysis of the findings showed that patients with vascular lesions demonstrated a significant elevation of elastin antibodies ( $p < 0.05$ ).

Besides studying elastin antibodies, we analysed elastase antibodies. Elevated elastase antibodies were revealed in 72.2% of SLE patients with grade I of the condition; in 80.0% with grade II, and in 85.7% of patients with grade III. The titer of elastase antibodies in SLE patients admitted to hospital was reliably higher than in the control group ( $p < 0.01$ ). The highest elastase antibody titer was noted when the skin and joints are affected, and vasculopathy is present.

**Conclusions:** The regularities revealed by pathogenetic method can be accounted for by considerable B-clonal expansion in SLE patients as the condition progresses. From the point of view of immunology, hyperproduction of elastin and elastase autoantibodies is noted, which results in autoimmune lesion of the ligamentous apparatus, joints, skin and vessels where this protein is naturally present.

**Disclosure of Interest:** None declared

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AB0527

### S100A8 AND S100A9 PROTEINS ARE NOVEL BIOMARKERS FOR THE EFFICACY OF HCQ TREATMENT TO SKIN LESION IN SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Systemic lupus erythematosus (SLE) is deeply associated with not only acquired immunity but also innate immunity throughout toll like receptors (TLRs) signalling. Among many TLRs, TLR7 and TLR9 were reported to be closely associated with IFN- $\alpha$  production which contributed the pathogenesis of SLE. On the other hand, several reports demonstrated that S100A8 and S100A9 proteins which was known as one of damage-associated molecular patterns (DAMPs), were associated with disease activity of lupus nephritis. These proteins were also shown to reflect the treatment response by immunosuppressive therapy for SLE.<sup>1,2</sup> However, there is no report about the effect of hydroxychloroquine (HCQ) on S100A8 and S100A9 proteins expression.

**Objectives:** To find a new biomarker of treatment with HCQ, we focused on expression of S100A8 and S100A9 proteins in SLE.

**Methods:** We enrolled all SLE patients treated with HCQ in the absence of additional immunosuppressive therapy more than 3 months in our institute from Jan 2016 to Dec 2017. Serum levels of S100A8 and S100A9 proteins were measured by ELISA (CircuLex ELISA Kit, MBL) at the screening, 3 months and 6 months after HCQ administration. Disease activity of SLE was measured using the SLENA-SLEDAI 2011. Cutaneous disease activity was evaluated by Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI). Immunological activity was examined by the levels of complement (C3, C4, CH50), anti-dsDNA anti-body and counting blood cell.

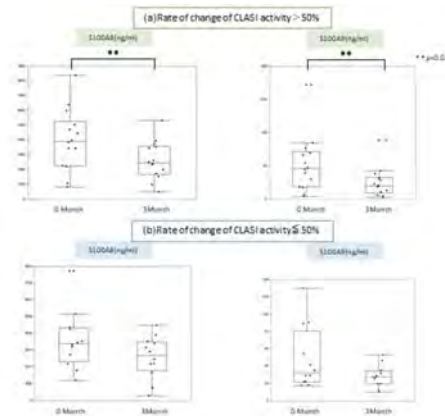
**Results:** 61 patients were enrolled in this study. HCQ was administered 48 cases with usual dose (based on ideal weight), 15 cases with low dose than usual dose (table 1).

Abstract AB0527 – Table 1

HCQ dose	Usual dose (n=46)	Low dose (n=15)	P
Age, years, mean $\pm$ SD	40 $\pm$ 12	46 $\pm$ 9	0.07
Female, no. (%)	43 (93)	13 (87)	0.40
Disease duration, years	13 $\pm$ 10	11 $\pm$ 8	0.61
skin lesion	40 (87)	14 (93)	0.48
renal lesion	19 (41)	0 (0)	<0.001
SLEDAI score	3.9 $\pm$ 2.2	2.7 $\pm$ 1.8	0.06
anti-dsDNA, IU/ml	15 $\pm$ 17	9.9 $\pm$ 3.1	0.91
C3, mg/dl	79 $\pm$ 24	87 $\pm$ 26	0.32
C4, mg/dl	16.1 $\pm$ 7.6	19.2 $\pm$ 9.2	0.30
CH50, U/ml	33.6 $\pm$ 9.6	37.3 $\pm$ 7.4	0.30
CLASI activity	3.6 $\pm$ 3.2	2.6 $\pm$ 2.8	0.11
Prednisone	41 (89)	15 (100)	0.11
Dose, mg/day	5.6 $\pm$ 3.1	8.1 $\pm$ 5.1	

CLASI was improved by the treatment with HCQ independent of HCQ dose. However, the effect of HCQ on SLENA-SLEDAI and immunological biomarker was shown in the patients treated with usual dose HCQ, not shown in those treated

with low dose HCQ. On the other hand, serum levels of S100A8 and S100A9 proteins were significantly elevated in SLE patients with renal lesion ( $p = 0.02$ ). These proteins were significantly decreased by the treatment with HCQ regardless of the HCQ dose ( $p < 0.0001$ ). The changes of serum S100A8 and S100A9 proteins during HCQ treatment (for 3 months) were significantly associated with changes of CLASI (figure 1).



**Abstract AB0527 – Figure 1.** S100A8 and S100A9 proteins associated with CLASI score. Compared with SLE patients of 50% and less rate of change of CLASI activity, those of more than 50% rate of change of CLASI activity significantly decreased serum levels of S100A8 and S100A9 proteins after administration of HCQ. There were no SLE patients whose skin lesion got worse during HCQ treatment in this study.

**Conclusions:** HCQ reduced the expression of serum S100A8 and S100A9 proteins, which reflected SLE disease activity especially in skin lesion. The measurement of S100A8 and S100A9 proteins is novel predictive biomarker for the efficacy of HCQ treatment on skin lesion in SLE patients.

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**Disclosure of Interest:** None declared

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AB0528

### CONCOMITANT MEDICATION IN SYSTEMIC LUPUS ERYTHEMATOUS (SLE) PATIENTS TREATED WITH BELIMUMAB IN CLINICAL PRACTICE SETTINGS: RESULTS FROM THE OBSERVE STUDY IN SWITZERLAND

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**Background:** Systemic lupus erythematosus (SLE) is a complex and potentially severe autoimmune disease. Belimumab is the latest drug, and the first biologic compound, that was registered for treatment of SLE. There is limited information on safety and effectiveness of belimumab and its effects on the use of concomitant medication outside of randomised controlled trials.

**Objectives:** To describe the overall patterns of SLE care, outcomes and concomitant medication among belimumab users in Switzerland.

**Methods:** OBSERVE Switzerland (GSK 201232) was a retrospective, multi-centre observational cohort study collecting data on the use of belimumab therapy in routine care of SLE Patients in Switzerland. SLE patients were included who had started therapy with 10 mg/kg belimumab/4 weeks at least six months before documentation. All patients were included regardless of treatment discontinuation during the study period. All statistical analyses were descriptive for both categorical and quantitative data.

**Results:** 53 SLE patients with belimumab as part of their routine treatment were analysed for this study. 81% of the patients were female, the mean age was 46.7 years and the mean BMI was 25.4 kg/m<sup>2</sup>. The reasons to initiate belimumab were ineffective previous treatment (66.0%), worsening of patient condition (28.3%), and/or the intent to decrease glucocorticosteroid (GC) dose (47.2%).



During treatment, 58% of patients (n=53) showed an improvement of  $\geq 20\%$  and 23% of  $\geq 50\%$ , based on physicians' evaluation of disease activity. This was consistent with an improvement of SELENA-SLEDAI (mean) from 8.0 at therapy start to 3.6 after six months on the basis of all available data (n=27).

Similar outcomes were observed for arthritis, fatigue, rash, dsDNA antibody and complement levels.

Among the 42 patients treated with GC at time of belimumab initiation, GC dose was reduced by 5.7 mg/day (mean) during treatment with belimumab ( $11.6 \geq 5.9$  mg/day at six months). During the six months before initiation of belimumab, GC dose was stable or had to be increased in the majority of patients; however, during the six months therapy with belimumab, GC dose could be reduced in the majority of patients and GCs was discontinued in two patients. The percentages of patients receiving SLE co-medication other than GC were stable over the first six months of belimumab therapy. Within the first six months of treatment, no included patient had discontinued therapy with belimumab.

**Conclusions:** Treatment with belimumab over six months after initiation led to clinical improvement in a significant number of patients in real life settings and had an overall steroid-sparing effect. Belimumab was well-tolerated; no included patient discontinued the treatment within the first six months.

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#### AB0529 AN AUDIT FOR SCREENING OF OSTEOPOROSIS AND ITS MANAGEMENT IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

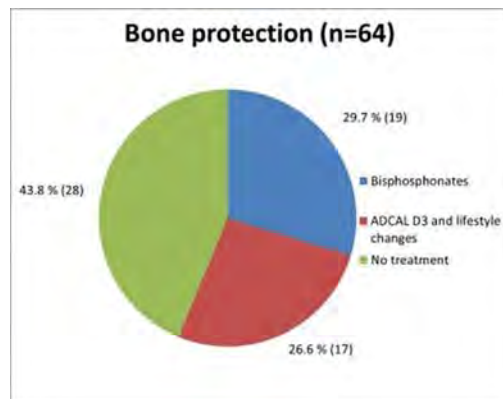
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**Background:** Systemic lupus erythematosus (SLE) is an autoimmune, multi-system, chronic inflammatory condition. It is managed with long-term immunosuppressive therapy which includes steroid use. SLE is therefore considered an independent risk factor for osteoporosis.

**Objectives:** This clinical audit was undertaken to evaluate the screening of osteoporosis in patients diagnosed with SLE and assess adherence to national guidelines for the management of patients with low bone mineral density (BMD) on prolonged steroid therapy.

**Methods:** We studied 64 SLE patients seen at the Leicester Royal Infirmary. Demographic and clinical data was collected from the clinic letters. Steroid use for a cumulative period of over 4 weeks per year was considered significant and use of bisphosphonates or calcium and vitamin D supplements alone were taken into account for bone protection. BMD measurements by dual X-ray absorptiometry were performed. Osteoporosis was defined as a T score less than  $-2.5$  SD in at least 1 region of measurement.

**Results:** Of the 64 patients studied, 54 (84.4%) were female and 10 (15.6%) male with an age range of 23 to 86 years and mean age of 47.45 years. Steroids were used in 46 (71.9%) patients while 18 (28.1%) patients did not receive any steroids. Twenty-one (32.8%) patients had DEXA scans and whilst 43 (67.2%) had not. Of those who had received steroids, 20 (43.4%) patients underwent DEXA scans and 26 (56.5%) did not. Osteoporosis was diagnosed in 3 (14.3%) patients out of the 21 scanned. The therapies used are summarised in figure 1.



Abstract AB0529 – Figure 1. Bone protection (n=64)

**Conclusions:** Studies have shown that SLE is an independent risk factor for low BMD and use of corticosteroids is already a well-recognised risk for osteoporosis. Our study has shown that a large section of patients (43.8%) did not receive any form of bone protection although, a significant proportion (71.9%) were on oral steroids. Although a small section of those scanned demonstrated osteoporosis (14.3%), many patients were already initiated on bisphosphonates without a DEXA. There was also no exclusion criteria set for young patients (age <45 years) or those who were newly diagnosed. Despite this, our study demonstrates the need for robust guidelines for the screening and management of bone health in patients with SLE in order to improve morbidity and mortality rates in this patient cohort.

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**Acknowledgements:** We acknowledge the contribution of the clinical audit team at the University hospitals of Leicester NHS trust for their help in analysing the data.

**Disclosure of Interest:** None declared

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#### AB0530 TREATMENT OUTCOME IN LUPUS NEPHRITIS PATIENTS TREATED WITH MYCOPHENOLATE MOFETIL: FROM REAL-WORLD CLINICAL PRACTICE

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**Background:** Systemic lupus erythematosus (SLE) is a systemic autoimmune disease often characterised by the development of glomerulonephritis.<sup>1</sup> There is a growing interest in the use of mycophenolate mofetil (MMF) as induction therapy and maintenance therapy for lupus nephritis.<sup>2,3</sup>

**Objectives:** This study aimed to evaluate the therapeutic outcome of MMF in lupus nephritis from real-world clinical practice, and identify the predictors for failure of remission after MMF treatment.

**Methods:** Korean patients with pathologically proven lupus nephritis class III, IV, and V were recruited from rheumatology clinic in Severance Hospital, Yonsei University College of Medicine between Nov 2011 and Aug 2017 Patients who treated with MMF for at least 3 months were included in the analysis. The probability of remission after MMF therapy, and the difference between patients who achieved remission or failed to achieve remission were analysed using Kaplan-Meier analysis and Cox proportional hazards model.

**Results:** Of 153 patients with lupus nephritis, 116 patients were included in this study. Seventy two patients continued MMF until the last follow-up. The mean age of patients was 34.2 years, and the median duration of SLE was 5.7 months. Anti-dsDNA antibody was positive in 82.8% of patients, and 9.5% of patients showed a histological class with pure V pathology. Mean protein/creatinine ratio in spot urine was 4.6, and active urinary sediment was found in 82.8% of patients. During median follow-up period of 5 years, 80% of patients achieved clinical remission of lupus nephritis. Median time to remission was 4.2 months (IQR 0.9–9.1). Risk factors for failure of remission were nephrotic-range proteinuria and seronegativity of anti-dsDNA antibodies.

**Conclusions:** This study shows the real-world data on MMF treatment in patients with lupus nephritis. Patients with risk factors for failure to remission may require more intensive treatment and management.

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**Acknowledgements:** None

**Disclosure of Interest:** None declared

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#### AB0531 DECISION TO INITIATE IMMUNOSUPPRESSION IN PATIENTS WITH PRIMARY SJOGREN'S SYNDROME

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**Background:** There is limited data available (case series, small clinical trials and expert opinion) regarding the need to initiate immunosuppressive therapy in patients with primary Sjogren syndrome (pSS).

**Objectives:** The aim of this study is to determine the factors that correlate with physician's decision to start immunosuppressive therapy in pSS patients.

**Methods:** Subjects with pSS diagnosed according to the classification criteria in use at the time of their first presentation, were included in a monocentric cohort. A retrospective analysis was performed. The EULAR Sjogren's Syndrome Disease Activity Index (ESSDAI) at onset and Sjogren Syndrome Damage Index (SSDI) at the last evaluation were calculated. Treatment was given according to the physician's decision. Laboratory tests and Ultrasonography (US) of major salivary glands were performed in all cases. The data was analysed using Windows Excel/SPSS20.0.

**Results:** Corticotherapy was prescribed in 26/30 cases (86.6%), mean duration 50.65 months. Immunomodulatory treatment with hydroxychloroquine was given in 26/30 cases (86.6%). Immunosuppressive treatment was required in 10/30 patients (33.3%) - azathioprine 7 (23.3%) cases, methotrexate 3 (10%) cases. The mean ESSDAI score was 6.83±SD 1.8. In 19 (63.3%) cases disease activity was moderate or high (ESSDAI >5). The mean damage score value (SSDI) was 3.1±SD 1.2. There was a moderate correlation between the activity score ESSDAI and the damage score SSDI ( $r=0.41$ ,  $p<0.05$ ). The physician's decision to start immunosuppression correlated significantly with the presence of hypergammaglobulinemia ( $r=0.4$ ,  $p<0.05$ ). The duration of immunosuppressive treatment correlated moderately with specific Sjogren's US pattern of salivary glands ( $r=0.40$ ,  $p<0.05$ ). In contrast, immunosuppressive treatment duration did not correlate with the activity and damage scores (ESSDAI and SSDI).

**Conclusions:** An important number of patients received corticotherapy, immunomodulatory agents and immunosuppressive therapy. The decision to initiate and maintain immunosuppressive therapy correlated with hypergammaglobulinemia and specific Sjogren's US changes. The damage score (SSDI) does not correlate with immunosuppressive therapy duration.

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**Disclosure of Interest:** None declared

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#### AB0532 THE EFFECTIVENESS OF EXERCISE THERAPY IN PATIENTS WITH SYSTEMIC SCLEROSIS: A SYSTEMATIC REVIEW

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**Background:** Exercise therapy is an important and relatively often used nonpharmacological intervention<sup>1</sup>, yet its effectiveness based on studies where exercise therapy is evaluated as single intervention (and not part of a comprehensive program<sup>2</sup>) has not been determined.

**Objectives:** To evaluate the effectiveness of exercise therapy in SSc patients by means of a systematic review of the literature.

**Methods:** A systematic literature search was performed in February 2017 in ten databases including Pubmed and Embase from 1990 to February 2017. We included clinical studies with an observational or experimental design as long as the study population concerned  $\geq 3$  SSc patients, the intervention consisted only of exercise therapy (categorised into hand exercises, mouth opening exercises, and aerobic exercises either or not combined with other exercises) and its clinical outcome according to at least one assessment of effectiveness done before and after the intervention was reported. Studies where exercise therapy was part of a multidisciplinary intervention were excluded. The selection of studies, data extraction and assessment of methodological quality was done by two of the researchers independently.

**Results:** The search strategy yielded 636 titles and abstracts, with eventually six studies being included (2 randomised controlled trials (RCTs), 3 observational designs (ODs) and 1 single subject experimental design (SSED)). The total number of patients included per study ranged from 4 to 48, patients' mean age from 44.0 to 66.5 years and mean disease duration from 3.5 to 12.6 years. One study concerned hand exercises (an RCT comparing strengthening and mobility exercises using a telemedicine intervention consisting of a portable device guiding patients during workout and sending data to health professionals to no-telemedicine), two studies on mouth stretching and oral-augmentation exercises (an OD and a RCT), and three studies on aerobic exercise (two ODs and one SSED; one program with only aerobic training and two programs combining aerobic and resistance training, lasting 30–60 min, 2–3 days/week for 8–12 weeks). The study on hand exercises reported a greater improvement of hand function using the telemedicine intervention. The RCT on mouth exercises showed a statistically significant effect on maximum mouth opening in the exercise group compared to no exercise at 3 months but not at 6 months follow-up, whereas the OD showed improvement of mouth opening directly after the mouth exercise program. The three studies on aerobic exercise indicate effectiveness and no dropouts were observed. The program of solely aerobic exercise on a treadmill improved patient's exercise tolerance and aerobic capacity. The two programs combining aerobic and resistance exercise showed improvements of strength and muscle function in the OD and improvements of muscular endurance and aerobic capacity in the SSED.

**Conclusions:** The literature on the effect of exercise therapy in SSc patients is scanty. Collaborative efforts to conduct methodologically sound intervention studies with adequate reporting is needed.<sup>3</sup>

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#### AB0533 PATTERN OF DRUG USE IN SYSTEMIC LUPUS ERYTHEMATOSUS IN REAL WORLD CLINICAL PRACTICE

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**Background:** Pharmacological treatment for systemic lupus erythematosus (SLE) is aimed at reducing disease activity, preventing flares and minimising the damage. The use of medication varies widely and therapeutic strategies are well defined only for certain organ manifestations. Hydroxychloroquine is the standard treatment for most SLE patients during the entire disease course, while immunosuppressants are recommended for those with severe organ involvement. Belimumab is the only biological currently licensed for SLE, although others are used off-label in clinical practice.

**Objectives:** To describe the real-world patterns of drug use in SLE patients, and their relationship with disease phenotype.

**Methods:** Observational study of adult SLE patients registered in the Rheumatic Diseases Portuguese Registry, who have clinical diagnosis of SLE, followed for at least 1 year and with available data on medication, which was retrieved. Sociodemographic and clinical characteristics were compared among treatment groups defined as: group 1 antimalarials and/or glucocorticoids; group 2 immunosuppressants (azathioprine (AZA)/mycophenolate mofetil (MM)/methotrexate (MTX)) ±antimalarials and/or glucocorticoids; group 3 biologics±immunosuppressants and/or antimalarials and/or glucocorticoids. To assess possible differences

between the groups, univariate regression analyses were made. In all analyses significance level was set at 0.05.

**Abstract AB0533 – Table 1.** Sociodemographic and clinical characteristics according to treatment groups

Characteristic	Group 1 (N=498)	Group 2 (N=272)	Group 3 (N=52)	Global p-value
Female, N (%)	377 (92.2%)	249 (91.5%)	49 (92.3%)	<0.001
Caucasians, N (%)	579 (99.8%)	335 (93.1%)	42 (87.5%)	<0.001
Age, years (mean±SD)	48.7±14.4	44.9±12.1	40.8±14.2	<0.001
Duration of disease, years (mean±SD)	12.8±8.4	13.2±8.0	11.7±8.0	<0.001
Non-smokers, N (%)	145 (70.2%)	94 (86.2%)	22 (88.7%)	<0.001
Physician global VAS (0-10) (mean±SD)	6.2±2.2	6.4±2.5	6.4±2.5	<0.001
SLEDAI (mean±SD)	1.8±1.7 (min=0, max=8)	2.9±2.3 (min=0, max=10)	3.5±4.2 (min=0, max=18)	<0.001
Renal disease (≥4) (N (%))	189 (48.2%)	152 (44.5%)	22 (79.6%)	<0.001
Mucocutaneous disease (≥1) (N (%))	28 (9.7%)	48 (13.1%)	5 (11.9%)	<0.001
Salivary gland disease (≥1) (N (%))	10 (3.4%)	7 (3.4%)	1 (3.9%)	<0.001
Organ damage (SLICC) (mean±SD)	0.5±1.1	0.7±1.5	1.0±1.4	<0.001
SLICC, 0-10 (N (%))	119 (30.7%)	180 (78.1%)	24 (88.9%)	<0.001
Acute cutaneous lupus, N (%)	107 (37.9%)	154 (60.9%)	25 (74.5%)	<0.001
Chronic cutaneous lupus, N (%)	73 (23.5%)	89 (32.9%)	10 (32.7%)	<0.001
Low or stable vitreous, N (%)	91 (23.5%)	80 (30.7%)	25 (52.1%)	<0.001
Non-erosive arthritis, N (%)	59 (15.9%)	87 (32.8%)	10 (20.0%)	<0.001
Arthritis, N (%)	115 (38.4%)	143 (57.8%)	45 (90.0%)	<0.001
Serositis, N (%)	77 (24.8%)	62 (25.7%)	12 (28.1%)	<0.001
Renal involvement, N (%)	76 (20.4%)	134 (53.0%)	19 (63.2%)	<0.001
Neurologic involvement, N (%)	11 (3.7%)	24 (9.4%)	8 (28.2%)	<0.001
Hematologic involvement, N (%)	149 (45.4%)	194 (74.9%)	39 (81.2%)	<0.001
Immunologic anemia, N (%)	29 (9.4%)	41 (15.7%)	7 (18.9%)	<0.001
Thrombopenia, N (%)	179 (57.9%)	142 (58.9%)	43 (79.2%)	<0.001
Leukocytopenia, N (%)	79 (24.9%)	71 (28.4%)	13 (28.9%)	<0.001
Glucocorticoids, N (%)	145 (65.9%)	213 (77.9%)	45 (81.2%)	<0.001
Antimalarials, N (%)	409 (100%)	252 (77.2%)	57 (89.4%)	<0.001
Immunosuppressants, N (%)	117 (50.4%)	117 (50.4%)	11 (20.0%)	<0.001
Anti-Ro/SSA antibodies, N (%)	142 (38.1%)	117 (50.4%)	11 (20.0%)	<0.001

**Results:** A total of 824 SLE patients were included, mean age of 47.3±14.4 years, 92.3% female. The mean age at first symptoms was 31.6±14.1 and at SLE diagnosis of 34.1±14.3 years. On their last assessment, 678 (82.3%) were being treated with antimalarials, 463 (56.2%) glucocorticoids, 343 (41.6%) immunosuppressants (149 AZA, 99 MM, 67 MTX, 14 cyclosporine, 11 cyclophosphamide, 3 leflunomide), 53 (6.4%) biologics (32 rituximab, 21 belimumab) and 26 (3.2%) were off medication. The sociodemographic and clinical characteristics according to treatment groups are shown in table 1. Gender distribution was similar across groups. A high prevalence of women, Caucasians, non-smokers, acute cutaneous lupus and arthritis was found in all groups. Patients in group 1 had lower disease activity measured by SLEDAI, less organ damage measured by SLICC and lower physician's global assessment. In group 2 patients were younger and had higher prevalence of renal involvement. Patients in group 3 had higher SLEDAI score and damage, higher prevalence of mucocutaneous, articular, neurologic and hematologic involvement and more use of glucocorticoids.

**Conclusions:** Almost all SLE patient with established disease were chronically medicated, most with antimalarials and/or glucocorticoids. As expected, group 1 had less severe disease. Patients under immunosuppressants had a higher frequency of renal involvement, which denotes a targeted therapeutic strategy. In routine clinical settings biologics are rarely used, being restricted to patients with very active SLE and multiple clinical manifestations.

**Disclosure of Interest:** None declared

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**AB0534** PROPORTION OF SJÖGREN'S SYNDROME PATIENTS REFERRED TO ORAL SPECIALISTS AT A RHEUMATOLOGY TERTIARY CENTRE AND FACTORS ASSOCIATED WITH THEIR REFERRAL

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**Background:** Ideally all patients with Sjögren's Syndrome (SS) and symptoms of mouth dryness should be assessed by an oral specialist (OS) team at 3–6 monthly intervals for optimisation of their treatment for xerostomia and minimisation of the risk of dental loss<sup>1</sup>. However, in reality specialist input is not always offered.

**Objectives:** To determine the proportion of SS patients at a rheumatology tertiary centre who were referred to OS and evaluate if any factors were associated with referral.

**Methods:** We retrospectively collected data about 105 patients with primary or secondary SS who attended outpatient clinics in October – November 2016, including duration of symptoms and years since diagnosis, presence of SS associated symptoms, medications trialled to date, and serological, imaging and histological patient features. We have also assessed proportion of patients referred to OS, as well as the medication recommended by the OS. p<0.05 was considered significant.

**Results:** In our cohort, 58.1% of SS patients were referred to an OS. We compared patient demographics and various disease features (table 1) in SS patients who were referred to OS and those who were not.

**Abstract AB0534 – Table 1**

	SS patients seen by oral specialists n=61	SS patients never referred to oral specialists n=44	P value
Gender F (%)	93	98	0.17
Age (years) mean±SD	60.1±16.7	50.1±15.3	<b>0.023</b>
Disease duration (years) mean±SD	9.7±7.9	7.4±5/2	0.57
Symptoms duration (years) mean±SD	11.0±8.47	10.0±5.80	0.2
<i>Medication</i>			
Oral prednisolone N (%)	13.1	27.3	0.069
Hydroxychloroquine/Chloroquine N (%)	65.6	68.2	0.78
Azathioprine N (%)	12.5	15.4	0.75
Methotrexate N (%)	8.82	24	0.12
Saliva substitutes N (%)	59.5	32	<b>0.034</b>
<i>Associated Symptoms</i>			
Oral dryness (VAS>5/10) N (%)	95.1	72.7	<b>0.0012</b>
Glandular enlargement N (%)	27.9	13.6	0.082
Maximum ESSDAI score (Median (interquartile range))	7 (4–12)	6 (4–10.75)	0.36
<i>Serology, Histology and Imaging</i>			
Anti Ro antibodies N (%)	79.2	78.4	0.92
Anti La antibodies N (%)	61.4	58.1	0.77
Positive salivary gland biopsy N (%)	100	83.3	0.20
Ultrasound scan of salivary glands showing definite features of SS N (%)	86.4	66.7	0.38

The parameters that correlated with the referral to OS were oral dryness (VAS>5/10) (p=0.0012) and the use of saliva substitutes (p=0.034).

The most common OS treatment recommendations were for use of Duraphat 5000 ppm (50.8%), Salivix pastilles (44.3%), mouth wash (41%) and Glandosane (36%), apart from frequent sips of water recommended in all patients.

**Conclusions:** 58.1% of SS patients at a tertiary rheumatology centre were referred to OS. The factors that correlated with onward referral to the OS from the Rheumatologist in SS patients were oral dryness and treatment with saliva substitutes. This suggests that Rheumatologists adequately treat xerostomia and refer to OS appropriately when patients remain symptomatic. Further research is needed to assess whether there is a difference in outcome for patients referred to an OS versus those who are not.

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AB0535

**EFFECT OF METFORMIN ON THE ABSOLUTE NUMBER OF CD4+ T CELL SUBSETS IN PATIENTS WITH PRIMARY SJOGREN'S SYNDROME**

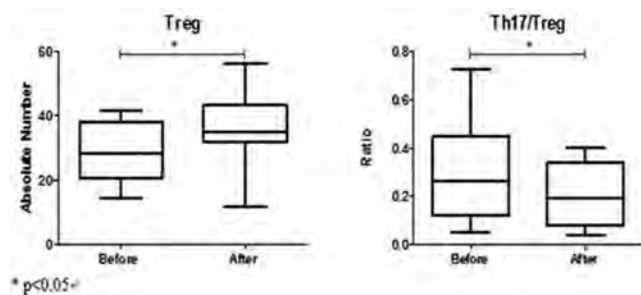
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**Background:** Primary Sjogren's syndrome is a chronic inflammatory autoimmune disease characterised by the infiltration of lymphocytes into exocrine glands such as the salivary gland and lacrimal gland. Although its etiology and pathogenesis is unclear at present, we consider immune dysfunction plays a significant role in the process. A lot of studies have confirmed that the formation of Treg and Th17 cells interact between each other, and their balance can affect the immune response results, notably reflected in various autoimmune and inflammatory diseases, including primary Sjogren's syndrome. However, there are few studies on the absolute number of CD4 +T cells in peripheral blood of patients with primary Sjogren's syndrome. In addition, metformin can affect the balance of Th17/Treg cells through the AMPK-mTOR pathway.

**Objectives:** To explore whether metformin can affect the balance of Th17/Treg cells in peripheral blood of patients with primary Sjogren's syndrome, and then be applied in the treatment of pSS patients.

**Methods:** The number of Treg cells(28.74 (21.22,38.68) vs 34.05 (30.14,42.31), P=0.023)significantly increased after the treatment. At the same time, there was a significantly decrease in the ratio of h17/Treg cells(0.25 (0.08,0.44) vs 0.18 (0.04,0.32),P=0.014). Besides, after the treatment the absolute number of Th17 cells were increased, but it was not statistically significant(4.5 (3.64,14.23) vs 7.87 (2.37,19.89),P=0.835). In addition, the clinical symptoms of the metformin group were obviously improved, while the dosage of prednisone, leflunomide or hydroxychloroquine reduced significantly.

**Results:** The number of Treg cells(28.74 (21.22,38.68) vs 34.05 (30.14,42.31), P=0.023)significantly increased after the treatment. At the same time, there was a significantly decrease in the ratio of h17/Treg cells(0.25 (0.08,0.44) vs 0.18 (0.04,0.32),P=0.014). Besides, after the treatment the absolute number of Th17 cells were increased, but it was not statistically significant(4.5 (3.64,14.23) vs 7.87 (2.37,19.89),P=0.835). In addition, the clinical symptoms of the metformin group were obviously improved, while the dosage of prednisone, leflunomide or hydroxychloroquine reduced significantly.



Abstract AB0535 – Figure 1

**Conclusions:** Metformin can increase the absolute number of Treg cells and decrease the ratio of Th17/Treg cells in the peripheral blood of patients with pSS, while reducing the use of hormones and DMARDs drugs. And it may be one of the mechanisms adopted in the treatment for pSS.

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AB0536

**RAPAMYCIN ATTENUATES SYMPTOM AND RESTORES THE BALANCE OF TH17/TREG IN REFRACTORY PRIMARY SJOGREN'S SYNDROME**

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**Background:** Primary Sjögren's syndrome (pSS) is one of the more common rheumatological diseases. Despite continued advances, the use of conventional drugs or biologic agents in patients with pSS did not provide expected efficacy and a targeted treatment of pSS is not available at present. We have shown that absolute number of peripheral CD4<sup>+</sup>CD25<sup>+</sup>FOP3<sup>+</sup>regulatory T cells (Tregs) decreased in pSS patients. And rapamycin is an inhibitor of mTOR that can decrease Th17 cells but increase regulatory T cells (Treg cells).

**Objectives:** To observe the effect of rapamycin on Th17/Treg cell balance in patients with refractory pSS.

**Methods:** Twenty-eight refractory SS patients (26 women and 2 men) and 93 health controls were enrolled, with a mean duration of 76.64±49.66 months and mean age of 52.39±10.62 years. They fulfilled the 2002 PSS international classification criteria and were treated with glucocorticoid and immunosuppressant for more than one year, but had not yet reached the disease relief. After the eligible patients are given rapamycin in combination with conventional therapy at 0, 12, 24 weeks, we respectively collect the clinical symptoms, blood routine, urine routine, ESR, the absolute number of Th17 and Treg cells, the ratio of Th17/Treg, and the dosage of corticosteroids and immunosuppressant. Alleviation criteria: no clinical symptoms, inflammation normal range, no organ damage.

**Results:** The absolute number of Treg cells decreased significantly in peripheral blood of pSS patients compared with that of healthy controls. By rapamycin combined with conventional therapy, flow cytometry showed the absolute number of Treg cells in refractory SS patients was increased from 25.51 cells/μl (at week 0) to 27.88 cells/μl (at 12 weeks) and 29.6 cells/μl (at 24 weeks) (P>0.05) respectively. The ratio of Th17/Treg decreased from 0.38 (at week 0) to 0.21 (at 12 weeks) and 0.22 (at 24 weeks) (P>0.05). There was no significant difference in the usage of prednisone, whereas 5 patients gradually stopped using CTX at 24 weeks. Also, the dose of hydroxychloroquine and leflunomide were markedly diminished.

**Conclusions:** Our results suggest that rapamycin combined with the conventional treatment greatly alleviated symptoms of patients with pSS, and gradually reduced the use of DMARDs. The absolute number of peripheral Tregs decreased in pSS patients and restored by this combined therapy. It still needs to be further confirmed by large sample studies.

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**SLE, Sjögren's and APS – clinical aspects (other than treatment)**

AB0538

**INCREASED BODY MASS INDEX MAY NOT BE A RISK FACTOR FOR THE DEVELOPMENT OF LUPUS NEPHRITIS**

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**Background:** Studies have indicated that elevated body mass index (BMI) increases risk of Chronic Kidney Disease (CKD). Obesity is a low grade inflammatory state which leads to CKD by glomerulosclerosis. Systemic Lupus Erythematosus (SLE) is associated with high leptin levels and dyslipidemia. We hypothesised that obese SLE patients may be at increased risk of nephritis.

**Objectives:** We studied BMI as possible predictor for development of lupus nephritis (LN) in SLE.

**Methods:** We performed a retrospective cross sectional study on a longitudinal lupus cohort. Patients were enrolled from year 1987 to 2015. We compared demographics, clinical information, labs between patients with and without LN (table 1) and between patients with SLE with and without obesity. Mean and standard

deviations were reported for continuous variables. Number and percentages were shown for categorical variables and chi-square test was utilised for comparison. T-test was used to compare patients between the groups.

**Results:** Total of 1362 patients with SLE fulfilling revised ACR criteria were included; 60.9% were Caucasian and 32.8% African American. 596 had biopsy-proven LN however 524 patients were excluded because they had proteinuria before or at cohort entry. Only first available BMI were analysed: 32.7% were obese (BMI >30 kg/m<sup>2</sup>), 27.2% overweight (BMI: 25–29.9 kg/m<sup>2</sup>), 37.5% normal (BMI: 18.5–24.9 kg/m<sup>2</sup>) and 2.6% underweight (BMI <18.5 kg/m<sup>2</sup>). 39.4% (537) patients were on steroids at first BMI measurement. Results are described in table 1. BMI measured as continuous (p=0.51) and categorical variables (overweight p=0.64, obese p=0.67) were not associated with LN after adjusting for age, sex and ethnicity. SLE patients with obesity were found to have lower disease activity (SLEDAI), proteinuria, dsDNA titers and higher complement levels.

**Abstract AB0538 – Table 1.** SLE Patients with vs without Lupus Nephritis (P<0.05 in bold)

	Lupus Nephritis (n=72) Mean (SD) /N (%)	SLE without Lupus Nephritis (n=1290) Mean (SD) /N (%)	P Value
Age when BMI are measured	32.07 (8.4)	42.53 (13.48)	<0.0001
Kidney Biopsy Age	35.14 (10.9)	–	
Ethnicity	20 (27.78%)	811 (62.87%)	<0.0001
Caucasian			
Asian	5 (6.94%)	36 (2.79%)	
African American	42 (58.33%)	404 (31.32%)	
Others	5 (6.94%)	39 (3.02%)	
Male	6 (8.33%)	76 (5.89%)	0.4387
Age when SLE was diagnosed	27.39 (8.47)	35.46 (12.85)	<0.0001
BMI (continuous)	26.93 (6.72)	28.02 (7.32)	0.1855
BMI (Categorical)	32 (44.44%)	475 (36.82%)	0.6242
Underweight			
Normal Weight	2 (2.78%)	38 (2.95%)	
Overweight	19 (26.39%)	372 (28.84%)	
Obesity	19 (26.39%)	405 (31.4%)	
SLEDAI (continuous score)	5.04 (4.03)	2.13 (2.8)	<0.0001
SLEDAI (≥2)	65 (90.28%)	690 (53.61%)	<0.0001
Anti dsDNA (≥10)	40 (59.7%)	252 (20.31%)	<0.0001
Low C3 (<79)	37 (53.62%)	178 (14.19%)	<0.0001
Low C4 (<12)	27 (39.13%)	146 (11.67%)	<0.0001
ESR (>20)	47 (70.15%)	576 (47.56%)	0.0004

**Conclusions:** Obesity was not associated with the development of lupus nephritis. Obese patients with SLE had lower disease activity as measured by SLEDAI, dsDNA titers and complement levels.

**Disclosure of Interest:** None declared

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#### AB0539 CORRELATION BETWEEN MORPHOLOGICAL AND FUNCTIONAL MICROVASCULAR DAMAGE IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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**Background:** Numerous articles have investigated peripheral microcirculation in primary Raynaud's phenomenon (PRP).<sup>1–3</sup> However, reports that analyse peripheral microcirculation in systemic lupus erythematosus (SLE) are scanty.<sup>4,5</sup>

**Objectives:** The aim of this study was to investigate possible correlations between morphological and functional aspects of microcirculation in different skin areas of the hands and face in SLE patients and to compare the results with PRP patients and healthy subjects (HS).

**Methods:** A total of 14 SLE patients without RP (ACR criteria)<sup>6</sup> (mean age 53 ±14 SD years, mean disease duration 7±4 years), 14 PRP patients (LeRoy and ACR/EULAR 2013 criteria)<sup>7,8</sup> (mean age 53±17 years, mean RP duration 6±5 years) and 14 HS (mean age 50±17 years) were enrolled during the winter period. Nailfold videocapillaroscopy (NVC) and laser speckle contrast analysis (LASCA) were performed in the three groups of patients. The absolute nailfold capillary number (CN) per linear millimetre at first distal row was assessed by NVC. Blood perfusion (BP) was detected by LASCA at the level of fingertips, periungual areas, dorsum and palm of both hands and face. The average BP was calculated as perfusion units (PU).<sup>2</sup> Patients were not taking vasodilator drugs since at least one month. Statistical analysis was performed by non parametric tests.

**Results:** SLE patients showed a positive correlation between BP and nailfold CN in all areas of hands (p<0.0001), but no statistically significant correlation was observed between BP and nailfold CN at the level of face (p=0.10). In both PRP and HS no statistically significant correlation was observed between BP and nailfold CN in all examined areas (p=0.70 and p=0.20, respectively). SLE patients showed a statistically significant lower nailfold CN than both PRP and HS (median 9.1 vs 10.3 vs 11.0, respectively, p<0.0005). Conversely, no statistically significant difference of nailfold CN was observed between PRP and HS. PRP patients showed a statistically significant lower BP than both SLE and HS at the level of fingertip (median 90, 114, 187 PU, respectively; p<0.0001), periungual (median 74, 100, 141 PU, respectively, p<0.0001), dorsal (median 61, 72, 128 PU, respectively, p<0.0001), and palm areas (median 76, 96, 124 PU, respectively, p<0.0001). Conversely, PRP, SLE and HS patients showed similar BP values at the level of face (median 141, 139, 137 PU, respectively, p=0.30).

**Conclusions:** This study demonstrates a correlation between morphological and functional microvascular features in SLE patients. SLE patients without RP have a subclinical microangiopathy, showing lower nailfold CN and BP than HS. Conversely, PRP patients show only a functional dysfunction, having a lower peripheral skin BP than both SLE patients and HS. The clinical value of this new finding is undergoing further analysis.

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**Disclosure of Interest:** None declared

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#### AB0540 USEFULNESS OF CARDIAC SCREENING IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND ANTI-RO POSITIVE ANTIBODIES

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**Background:** Cardiac block in neonatal lupus is associated with placental transfer of anti-Ro antibodies. The effect of these antibodies on cardiac conduction disorders in adult patients is controversial. The association between anti-Ro antibodies and heart rhythm disorders have been described in isolated cases. However, there are just a few studies that analyse the relationship between auto-immune diseases and electrocardiographic disturbances.

**Objectives:** To determine if there are differences in cardiac conduction of SLE patients in presence of anti-Ro antibodies.

**Methods:** All patients included fulfilled the SLE criteria, SLICC 2012 and they were followed up in a single centre. The inclusion was consecutive and voluntary. Patients who took drugs that altered the conduction (except antimalarial drugs), and those who had heart or thyroid disease were discarded. All patients were assessed blindly by a cardiologist who performed an interrogation and physical examination, an electrocardiogram, an echocardiogram and a 24 hour Holter study. Besides, a rheumatologist performed a clinical and analytical assessment including a qualitative analysis by immunoblotting of anti-Ro Ab and a quantification by chemiluminescence of the anti-Ro52 and Ro60 Ab. The presence of other SLE specific Ab (ANA, DNA, antiphospholipids), was also analysed. Clinical, analytical and, activity and damage indexes, were collected (SLEDAI and SLICC). The data were compared by Student's t test, Fisher's test and Chi square using 21 SPSS version. The level of significance was established at 5%.

**Results:** 145 patients were included: 91.7% women, average age 45±12, average disease duration 11 years. The patients were undergoing the following treatments: antimalarial 91%, mycophenolate 20%, azathioprine 12%, biological treatment 5% and glucocorticoids 70%. The clinical characteristics are summarised in table 1.

There were no significant differences between the group of positive and negative anti-Ro Ab in terms of gender, age, clinical characteristics or cardiovascular risk factors. None of the patients was affected by an atrio-ventricular block and the rest of the electrocardiographic alterations had no clinical significance and did not predominate in the positive Ro Ab group. Additionally, no differences in heart rate, ventricular extrasystoles or PR, QT or QRS intervals were detected between both groups. The echocardiogram's findings were not relevant and there were no differences between groups.

Since the majority of patients with SLE are double positive, differences between the two subspecificities of Ro (52 and 60) could not be analysed. On the other hand, no differences were found in cardiac conduction regarding the treatments received, the activity or damage indexes, or the analytical or clinical characteristics of the patients.

Cumulative clinical manifestations (%)	
Articular	80
Cutaneous	63
Leuco-lymphopenia	42
Renal	24
Serositis	30
Neurologic	9
Secondary antiphospholipid syndrome	10
Secondary Sjögren syndrome	10
Activity and damage indexes	
SLICC	0,32 ± 0,7
SLEDAI in diagnosis	7,97 ± 4,2
SLEDAI in inclusion	1,82 ± 2,48
Analytical parameters	
Increased DNA	51 %
Average DNA	207,86 ± 357 (UI/L)
Hypocomplementemia	39 %
Anti-Ro positive antibodies	31 %

Abstract AB0540 – Figure 1

**Conclusions:** The study results show that there are no differences in cardiac conduction according to the presence of anti-Ro antibodies in SLE patients. Thus, the cardiac screening in SLE patients with anti-Ro positive antibodies seems not helpful in clinical practice.

**Disclosure of Interest:** None declared

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#### AB0541 HEPICIDIN AND INTERFERON-A IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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**Background:** Systemic lupus erythematosus (SLE) is a chronic autoimmune disease where interferon (IFN)  $\alpha$ , is considered to play a central role in its pathogenesis. Anaemia of chronic disease (ACD) in SLE is common. Hepcidin may contribute to anaemia by limiting iron availability for erythropoiesis.

**Objectives:** The aim of the study was to evaluate INF- $\alpha$  and hepcidin levels in sera of anaemic and non-anaemic SLE patients.

**Methods:** This was a pilot study of SLE patients with established disease. Patients were divided as anaemic and non-anaemic according to the haemoglobin (Hb) levels: Hb value <13.5 gm% for men and <11.5 gm% for females. ACD was defined according the levels of iron and ferritin. Serum hepcidin (the active 25 amino acid form) was measured using ELISA (Peninsula Laboratories International). IFN alpha was also measured using ELISA (eBioscience, affymetric). The inter-assay coefficient of variation was <20% for both assays. All analyses were performed with IBMSPSS Statistics for Windows (version 21). Data are expressed as the mean  $\pm$  standard deviation (SD). Statistical analysis was performed using

Student's t-test for independent samples. The relationships between hepcidin level and all variables were analysed using two-tailed Pearson's correlation test. P values less than 0.05 were considered significant.

**Results:** Forty SLE patients (36 women and 4 men) were studied. Demographic parameters were as follows: age 46.78 $\pm$ 16.04 years, disease duration 10.55 $\pm$ 6.58 years. Levels of Hb were 12.49 $\pm$ 1.28 g/dl. Levels of INF- $\alpha$  were 0.16 $\pm$ 0.47 pgr/ml while hepcidin levels were 2.54 $\pm$ 2.63 ngr/ml. When the patients were divided into anaemic (20 patients) and non-anaemic (20 patients) groups (Hb:11.41 $\pm$ 0.56 vs. 13.57 $\pm$ 0.77 g/dl,  $p<0.001$ ), patients with anaemia had lower disease duration (9.75 $\pm$ 6.16 vs. 11.35 $\pm$ 7.03 years,  $p=0.45$ ), lower levels of INF- $\alpha$  (0.13 $\pm$ 0.035 vs. 0.19 $\pm$ 0.036 pgr/ml  $p<0.001$ ) and higher hepcidin levels (2.92 $\pm$ 2.9 vs. 2.17 $\pm$ 2.35 ngr/ml,  $p=0.37$ ) than the patients without anaemia. No correlation was observed between levels of hepcidin with all variables. There was also no correlation between hepcidin and INF- $\alpha$  levels.

**Conclusions:** INF- $\alpha$  does not seem to contribute in ACD pathogenesis in SLE patients and does not correlate with hepcidin levels in SLE patients. Further studies will clarify the role of INF- $\alpha$  in anaemia in SLE.

**Disclosure of Interest:** None declared

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#### AB0542 MULTIPLE SCLEROSIS IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME

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**Background:** Imaging and histopathologic studies in patients with primary Sjögren's Syndrome (pSS) have demonstrated white matter lesions which are indistinguishable from those observed in multiple sclerosis (MS).

**Objectives:** The purpose of this study was to evaluate the frequency of MS in a cohort of patients with pSS.

**Methods:** One hundred and twenty-one patients with pSS had been evaluated and followed up in the outpatient Rheumatology Clinic at predefined times since 1994. All patients were classified according to the 2016 ACR-EULAR criteria for SS. During follow-up the clinical, laboratory and imaging findings were all recorded. In addition, Magnetic Resonance Imaging and electrophysiological studies as well as spinal fluid analysis were performed when indicated. The diagnosis of MS was based on the 2010 revised McDonald criteria.

**Results:** Seven patients were diagnosed as having MS. All patients with MS were female. Mean age at the time of MS diagnosis was 65.5 $\pm$ 3.6 years, while pSS has been diagnosed at the mean age of 54.4 $\pm$ 3.2 years. Mean time of MS development was approximately 10 years after the pSS diagnosis. pSS patients who developed MS had severe sicca symptoms without other extraglandular manifestations and had positive Ro (SSA) antibodies and a positive minor salivary gland biopsy. pSS patients with MS development were treated appropriately in the Neurology department with biological medications with some improvement of the sicca symptoms.

**Conclusions:** We found that 5.8% of pSS patients as having MS. This percentage of patients clearly indicates the possibility for the coexistence of a second autoimmune disease with similar if not common pathogenetic mechanisms. Thus patients with pSS should be evaluated carefully and screened appropriately for MS when indicated.

**Disclosure of Interest:** None declared

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#### AB0543 CORRELATION BETWEEN SYSTEMIC LUPUS ERYTHEMATOSUS DISEASE ACTIVITY AND OCULAR SIGNS IN OPHTHALMOLOGICALLY ASYMPTOMATIC PATIENTS

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**Background:** Systemic lupus erythematosus (SLE) is an autoimmune disease involving different organs and systems. Ocular manifestations of lupus may manifest as a presenting feature of the disease or as a complication that can be sight threatening. Almost any part of the eye and visual pathway can be affected by inflammatory or thrombotic processes yet ophthalmological assessment in those patients may be delayed.

**Objectives:** Detection of various ocular pathologies in ophthalmologically asymptomatic SLE patients using Optical Coherence Tomography (OCT), Fundus Fluorescein angiography (FFA), and fundus examination, in addition to studying the



relation of between detected ocular changes and SLE disease activity assessed by SLEDAI score.

**Methods:** 26 ophthalmologically asymptomatic SLE patients recruited from Kasr Alainy hospital, Cairo University, and were subjected to comprehensive ocular assessment in the form of the measurement of visual acuity, fundus examination, FFA, and OCT. Hypertensive, diabetic and renal impairment patients were excluded.

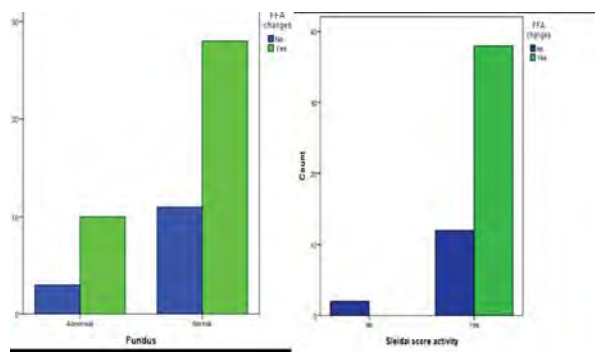
**Results:** SLE patients were 25 females and 1 male, age mean of 25.15 ( $\pm 8.6$ ) years, SLEDAI mean 14 ( $\pm 8.3$ ), duration of illness mean 27 ( $\pm 42.3$ ) months. FFA showed that 38 out of 52 eyes (73%) had signs of pathological changes in the form of splinter haemorrhages, venular occlusion, diffuse mottling and optic nerve leakage and also degenerative changes which indicate chronicity, in the form of hyperfluorescence areas outside the arcades and pre-papillary areas and capillary dropouts. Besides; OCT detected changes in 67.3% of the examined eyes with 26.9% revealing degenerative thinning. There was significant correlation between disease activity and changes detected by FFA (p value 0.017), but neither the fundus findings nor the OCT pathological changes had correlation with disease activity. On the other hand, there was significant correlation between OCT changes and prolonged use of hydroxychloroquine more than 5 years (p value 0.032) and steroid intake for more than 3 month (p value 0.039). There was no correlation between FFA or OCT changes and proteinuria or anti-phospholipid antibodies.

**Abstract AB0543 – Table 1.** Relation between disease activity and FFA changes

SLEDAI	Negative FFA changes	Positive FFA changes	p-value
Inactive	2 (0.03%)	0	0.017
Active	12 (23%)	38 (73%)	

**Abstract AB0543 – Table 2.** Relation between Hydroxychloroquine (HXQ) and OCT changes

	Negative OCT changes	Positive OCT changes	p-value
HXQ<5 years	17 (32.6%)	27 (51.9%)	0.032
HXQ≥5 years	0.0%	8 (15.3%)	



**Abstract AB0543 – Figure 1.** Revealing discrepancy between fundus and FFA changes (left), Correlation between SLEDAI score and FFA changes (right)

**Conclusions:** FFA is can detect early retinopathy changes in patients of SLE which cannot be detected by fundus examination. FFA changes are correlating with disease activity. On the other hand, there was no correlation between OCT changes and disease activity. OCT is more sensitive to detect changes from hydroxychloroquine and steroids intake.

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#### AB0544 ROLE OF ANTI-NEURONAL ANTIBODIES (A-NA) IN EPILEPSY LUPUS PATIENTS

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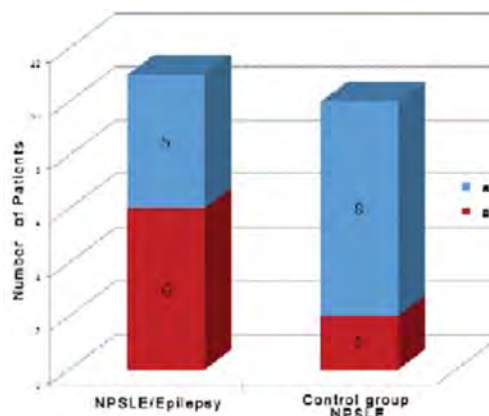
**Background:** Epilepsy may occur before, during or after SLE diagnosis, with a prevalence of 6.7%–14%. Recent works showed that a significant proportion of patients with not responding to antiepileptic drugs (AED)-resistant epilepsy harbour neural-specific autoantibodies. The detection of these antibodies may predict a favourable response to immunotherapy (75% of patients).<sup>1</sup> A small number of recent studies have described the existence of antibodies directed against a-NA in neuropsychiatric SLE (NPSLE), and data are contrasting.<sup>2</sup>

**Objectives:** Evaluate the clinical features of epilepsy in patients with SLE. Evaluate any clinical-instrumental differences in epilepsy in patients diagnosed with epilepsy prior to many years of SLE. Evaluate antibodies associated with neurological phenotypes.

**Methods:** We retrospectively evaluated a SLE cohort for epileptic seizures. We single out 11 epileptic SLE patients (about 10%). A control group of 10 SLE patients with no NPSLE was matched for sex and age. Sera patients were tested for: ANA, a-ds-DNA, a-ENA, LAC, anticardiolipin IgG and IgM, anti- $\beta 2$ -glycoprotein IgG and IgM, a-nucleosomes, a-ribosomal.

All sera were evaluated for the presence of autoantibodies directed to neural antigens by indirect immunofluorescence on frozen sections of mouse brain, cell-based assays (a-NA, a-NMDA).

**Results:** In our cohort of SLE patients with epilepsy we confirm the association between SLE and epilepsy of the mesial temporal lobe (MTLE). Six patients had epilepsy at least 5 years prior to SLE diagnosis (average 11.6 years), the presence of minor symptoms suggestive of SLE (eg arthralgia, rash,) was reported many years before immunological diagnosis. Moreover seizure frequency was achieved when they started immunosuppressive drugs. Anti-NA antibodies were present in 6/11 (54%) of patients with SLE/epilepsy compared with 2/10 (20%) of the control group (p=0.05). We obtained specificity 0.80 (95% CI 0.44–0.97), and sensitivity 0.54 (95% CI 0.23–0.82). Among the other antibodies studied, we have not found any statistically significant difference between the two groups.



**Abstract AB0544 – Figure 1**

**Conclusions:** Anti-NA antibodies could be a useful biomarker of NPSLE, allowing a more precocious diagnosis and therefore a more early therapeutic intervention with improvement of long-term prognosis and quality of life.

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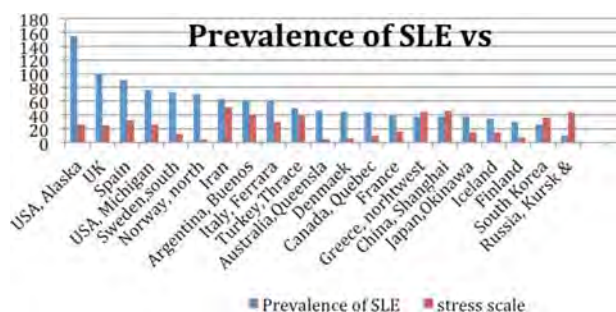
### AB0545 IS LUPUS MORE PREVALENT IN WORLD'S MOST STRESSED COUNTRIES?

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**Background:** A number of studies have implicated psychological stress as a trigger for autoimmune diseases. In a questionnaire study involving 120 lupus patients emotional stress was selected in over 75% cases as a trigger for their disease<sup>1</sup>. The role of stress as a trigger in lupus however is controversial. Here we study whether there is an association between the prevalence of lupus in various countries and their reported stress measures.

**Methods:** We undertook a literature review of the reported prevalence of lupus in various countries across the world. We then recorded the reported stress index in those countries from Bloomberg's study<sup>2</sup>, which utilised seven equally weighted variables: homicide rates, GDP per capita income inequality, corruption perception, unemployment, urban air pollution and life expectancy to rank 74 countries according to stress levels. Pearson's correlation was used to measure association between national stress indices and lupus prevalence

**Results:** Results are presented in graph 1. Prevalence data was only available in the literature for limited countries. Of the countries studied no correlation was found between national stress indices and lupus prevalence ( $r = -0.028$  (p-value 0.449))



Abstract AB0545 – Figure 1

**Conclusions:** We found no association between a country's prevalence of lupus and the measured stressfulness of its living environment.

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**Disclosure of Interest:** None declared

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### AB0546 CRYOGLOBULINEMIA IN SYSTEMIC LUPUS ERYTHEMATOSUS: CLINICAL AND IMMUNOLOGICAL FEATURES

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**Background:** Systemic lupus erythematosus (SLE), as the prototype of systemic autoimmune diseases, has a wide array of clinical manifestations. An association between cryoglobulinemia and certain clinical and immunological features of SLE has been proposed, and there are various physiopathologic pathways that could be involved in this relationship. Although the presence of cryoglobulinemia in SLE patients may be related to specific disease features and could even have prognostic value, this association has not been addressed thoroughly.

**Objectives:** To describe clinical and immunological characteristics in SLE patients with cryoglobulinemia.

**Methods:** We performed a retrospective, case-control study, in which we included all patients with a cryoglobulin determination between January 2005 and December 2016 in a third level referral centre in Mexico City. Patients with SLE and a positive cryoglobulin test (cryocrit  $\geq 1\%$ ) were included in the case group, whereas SLE patients with a negative cryoglobulin determination were considered controls. We studied demographic, clinical and immunological

characteristics at the time of the positive cryoglobulin result, as well as three months earlier, and 6 and 12 months later.

**Results:** Thirty-six SLE patients had a cryoglobulin determination throughout the study period. Ten patients had cryoglobulin levels  $\geq 1\%$  and were included in the case group, whereas 26 patients with a negative determination were included as controls. Mean age was  $37.7 \pm 18.3$  in cases and  $41.7 \pm 19.3$  in controls. 70% of cases and 88.5% of controls were women.

Among subjects with cryoglobulinemia, the cryocrit was 1% in 9 patients, and 3% in one. Regarding clinical and immunological characteristics, a positive lupus anticoagulant and a history of vasculitis were more frequent in patients with serum cryoglobulins ( $p=0.004$  and  $0.04$ , respectively).

At the time of the cryoglobulin measurement, patients in the case group had lower levels of C3 and C4 ( $p=0.026$  and  $p=0.003$ , respectively), and serum albumin ( $p=0.028$ ). They also had a higher prevalence of serositis ( $p=0.021$ ) and peripheral oedema ( $p=0.034$ ), as well as a higher SLICC Damage Index score ( $p=0.014$ ) than controls.

Regarding follow-up, patients in the case group had a higher SLEDAI score after six and twelve months ( $p=0.009$  and  $0.034$ , respectively). Also, after 12 months they had a higher prevalence of renal activity ( $p=0.004$ ) and lower C4 levels ( $p=0.001$ ). Among patients with renal activity, 20% of cases and 55% of controls had achieved complete remission after 12 months.

**Conclusions:** Serum cryoglobulins in SLE patients were associated with positive lupus anticoagulant and hypocomplementemia. Cryoglobulinemia was also associated with specific disease manifestations, such as serositis and vasculitis, and with damage accrual. At follow-up, patients with cryoglobulinemia had a higher prevalence of renal activity, as well as an increased disease activity overall. Whether cryoglobulins could be used as a biomarker for renal activity or worse renal prognosis remains to be determined, and larger prospective studies will be needed to address this possibility.

**Disclosure of Interest:** None declared

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### AB0547 LYMPHADENOPATHY IN SYSTEMIC LUPUS ERYTHEMATOSUS: CLINICAL RELEVANCE AND HISTOLOGICAL SUBTYPES

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**Background:** Some patients with Systemic Lupus Erythematosus (SLE) have lymphadenopathy (LAP) at diagnosis or at follow-up. The prevalence of LAP in SLE was 59% in the oldest series,<sup>1</sup> 12% in the 1993 EUROLUPUS series<sup>2</sup> and in the last two decades its prevalence was not mentioned. However, the presence of LAP and their histological type may have clinical relevance.<sup>3</sup>

**Objectives:** To study the prevalence and histologic characteristics of LAP in a cohort of patients with definite SLE and evaluate its relationship with clinical manifestations.

**Methods:** All patients diagnosed with SLE according to the 1997-ACR criteria at the Autoimmunity Units of three different hospitals since 2005 were followed looking for lymph node enlargement at every consult. The moment when LAP was detected, the concomitant clinical symptoms, SLE manifestations and laboratory variables were recorded. The group of patients with and without LAP were compared. A tissue sample was obtained when indicated. All patients agree to participate in the study.

**Results:** 103 patients with definite SLE were included in the study. Valuable LAP ( $>10$  mm) was found in 28 patients (27%). The gender and age of SLE patients with and without LAP was similar (80% vs 78% females, and  $34 \pm 15$  vs.  $40 \pm 28$  years respectively). LAP was detected at the time of SLE diagnosis in 54% of patients. Fever was significantly more frequent in patients with LAP (60% vs 5%,  $p < 0.01$ ) like dermatopathy (86% vs. 60%;  $p < 0.05$ ) and serositis (45% vs 16%  $p < 0.01$ ). High titers of anti-dsDNA antibodies (71% vs. 42%;  $p < 0.05$ ) and hypocomplementemia (89% vs. 60%;  $p < 0.05$ ) were also more frequent in patients with LAP. A total of 28 tissue samples were obtained in 17 patients (FNA 6, Ultrasound-guided biopsy 6 and surgical excision in 17). The histopathological study showed: Reactive lymphadenitis 20, histiocytic necrotizing lymphadenitis in 6 and Non-Hodgkin Lymphoma in 2 (B-cell lymphoma on methotrexate treatment, and a Burkitt lymphoma). All 6 patients with SLE and histiocytic necrotizing lymphadenitis have cutaneous involvement but none of them developed lupus nephritis.

**Conclusions:** Patients con SLE and lymphadenopathy had significantly more fever, cutaneous lesions and serositis. High levels of anti-dsDNA antibodies and hypocomplementemia were more frequent in these patients. In some occasions malignancy could be the cause of lymphadenopathy.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.4125

AB0548

**ANTIBODY TO PURINNUCLEOSOID PHOSPHILASE CAN BE USED AS AN ADDITIONAL MARKER OF INFECTIOUS COMPLICATIONS WITH SYSTEMIC LUPUS ERYTHROMATOSIS**

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**Background:** Purine nucleoside phosphorylase (PNP, EC 2.4.2.1) plays a leading role in the assimilation of nucleosides and nucleotides by the cell, as well as in maintaining the immune status of the organism. Patients with PNP deficiency are highly susceptible to various infections, in view of the fact that the decreased activity of PNP is closely related to the insufficiency of cellular immunity.

**Objectives:** Study of the possibility of using the level antibodies to purine nucleoside phosphorylase as an additional marker of infectious complications in patients with systemic lupus erythematosus (SLE).

**Methods:** The study included 60 patients with SLE (women – 91.7%, mean age 36.32±15.27 years, average duration of the disease 7.96±7.35 years) with different clinical manifestations (SLEDAI activity 8.93±5.74, ECLAM activity 5.30±2.79, damage index SLICC/ACR 1.95±1.71). Antibodies to PNP (anti-PNP) were determined in our indirect ELISA test using the immobilised form of the enzyme as an antigenic matrix.

The presence of infectious complications in SLE patients was assessed by characteristic clinical manifestations and was considered to be confirmed when the causative agent was recognised and/or the serological analyses are positive. Infections were diagnosed in 38.3% of patients, the most frequent localization was the urinary system (n=12; 52.2%) and female genitalia (n=5; 21.7%).

**Results:** In the presence anti-PNP in the blood serum of patients with SLE we have often noted infectious complications ( $p=0.025$ , criterion  $\chi^2$ ) and less often lung damage ( $p=0.17$ ) (when compared with a group of patients with SLE seronegative for the presence of anti-PNP).

Statistically significant differences (Mann-Whitney U-criterion) were detected only for pyuria ( $p<0.0005$ ), C-reactive protein level ( $p=0.048$ ) and the number of ceruloplasmin ( $p=0.008$ ), while comparing the groups of SLE patients with the presence of infectious complications and without it; differences in the level of antibodies to CP ( $p=0.052$ ) did not reach statistical significance. Other clinical and laboratory parameters do not have statistically significant differences between the two sessions. This fact complicates the recognition and differential diagnosis of infectious complications in SLE significantly.

The analysis of the characteristic curve of antibodies to PNP in the diagnosis of infectious pathology in SLE shows limited possibilities for using this parameter. The square under the curve was 0.687 (95% confidence interval 0.523–0.804,  $p=0.008$ ), the separation point was 0.386 U/ml with a sensitivity of 55% and a specificity of 83%.

Taking into account that the typical clinical manifestations of infection with SLE can be erased as a result of the actual activity of SLE, and due to the use of immunosuppressive drugs, timely diagnosis and treatment become especially relevant. This study indicates the possibility of using the level of antibodies to PNP as an additional marker of infection, but the balance between specificity and sensitivity of this test does not allow to recommend it as a single study.

**Conclusions:** A high level of anti-PNP in the serum, especially combined with the C-reactive protein increase and in the absence of other markers of SLE activation allows to suspect the presence of infection and points to the need for in-depth research directed to identify the pathogen.

**Disclosure of Interest:** None declared

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AB0549

**CAN THE OVERALL THROMBOTIC RISK IN SYSTEMIC LUPUS ERYTHEMATOSUS BE DETERMINED? THE COMBINED ROLE OF CLASSIC CARDIOVASCULAR FACTORS AND ANTIPHOSPHOLIPID ANTIBODIES**

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**Background:** Systemic Lupus Erythematosus (SLE) is a chronic inflammatory disorder. Antiphospholipid syndrome (APS) is a thrombotic disorder associated with the presence of antiphospholipid antibodies (APA) and increased cardiovascular risk (CVR). Framingham (FRM) and SCORE (Systematic Coronary Risk Evaluation) scales are available CVR assessment systems. aGAPSS (adjusted Global Antiphospholipid Syndrome Score) combine positive APA and CVR factors, which was suggested to determine the thrombotic risk in persistently positive APA (PPAPA) patients.

**Objectives:** To determine the role of the thrombotic factors in SLE patients, considering CVR factors and APA. To assess the application of different thrombotic risk scales.

**Methods:** A retrospective cohort study of 84 patients with SLE followed in an out-patient setting of a Portuguese central hospital was performed. The study evaluated patient gender, current age, age at diagnosis, duration of illness, presence of another autoimmune disease (AID), CVR factors [obesity (OB), diabetes (DB), arterial hypertension (AH), dyslipidaemia (DL), smoking (SM)], presence of APA, treatment, dose and duration of steroids. The FRM, SCORE and aGAPSS scores were calculated. The data was analysed using SPSS and considered significant if  $p<0.05$ .

**Results:** Table 1 characterises the study population. Male patients had a higher prevalence of AH ( $p=0.022$ ), DL ( $p=0.047$ ), and SM ( $p=0.001$ ), with a risk of 11%–20% in the FRM scale and a risk of 5%–14% in the SCORE ( $p=0.000$ ). Female patients had a higher presence of another AID ( $p=0.014$ ) and treatment with disease-modifying antirheumatic drugs ( $p=0.014$ ). FRM scale reveals a risk of 11%–20% in the presence of AH and >20% in SM ( $p=0.001$ ). The SCORE scale reveals a risk of 5%–9% in the presence of AH ( $p=0.003$ ) and 10%–14% in DL ( $p=0.024$ ). When the risk is 6%–20% in the FRM scale, the risk is lower in SCORE ( $p=0.000$ ). APA does not correlate with an increased CVR. All APA are associated with another AID, APS and PPAPA. The aGAPSS associates a score of 7–12 if another AID is present ( $p=0.000$ ); 4–9 with APS; >7 with PPAPA ( $p=0.000$ ); 4–6 with DB ( $p=0.039$ ), DL ( $p=0.002$ ) and AH ( $p=0.000$ ); >7 with lupus anticoagulant (LA), >7 with anticardiolipin antibodies (aCL) and >12 with anti- $\beta$ -2glycoprotein-I antibody (anti $\beta$ 2GPI) ( $p=0.000$ ).

**Abstract AB0549 – Table 1**

Women	74%
Current age	52.3±16.2 years
Age of diagnosis	44.9±17.4 years
Duration of disease	7.2±7.5 years
Another AID	30% (APS 60%, Sjögren syndrome 36%)
PPAPA	12%
CVR	AH 42.8%, DL 21.4%, OB 11.9%, DB 10.7%, SM 9.5%
APA	LA 19%, aCL 15.5%, anti $\beta$ 2GPI 7.1%
Steroid use	61%
DMARDs	89%

**Conclusions:** This study highlights the existence of thrombotic factors in SLE. Their risk is even more elevated when another AID is present. The FRM and SCORE scales reflects the CVR. In SLE patients both the CVR factors and the presence of APA must be evaluated. Therefore, not only should the FRM scale be calculated, but also the global thrombotic risk, using the aGAPSS, must be accessed.

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AB0550

### CLINICAL-EPIDEMIOLOGICAL FEATURES OF PATIENTS WITH A LATE-ONSET LUPUS IN A TERTIARY CARE HOSPITAL

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**Background:** Different frequency of clinical and serological manifestations has been detected according to the age of onset of the patients with Systemic lupus erythematosus (SLE). According to the literature, senile SLE manifests between 6% and 18% of the patients with lupus.

#### Objectives:

1. To identify and analyse the clinical-serological and epidemiological features of senile SLE in our environment.
2. To determine the average survival time and mortality in these patients, identifying its main cause.

**Methods:** Observational retrospective study of 319 patients diagnosed with SLE (according to ACR 1992 and SLICC 2012 criteria) at the Hospital of León between 1997–2017 and with an age of onset  $\geq 65$  years, obtaining a total of 68 patients with senile SLE.

**Results:** The mean age at diagnosis was  $75.4 \pm 12.1$  years, with a female/male ratio of 2.4. The most frequent manifestations were as joint (63.2%) and haematological manifestations in the form of leuco-lymphopenia (55.9%). The hemolytic anaemia only appeared in 2.9% of the cases and the thrombocytopenia in 25%. 36.8% of patients showed photosensitivity and 29% had other cutaneous manifestations, being the malar erythema the most prevalent type (60%), followed by the discoid lupus erythematosus (20%) and the subacute lupus (15%). Alopecia was only observed in 4.4%. Lupus nephritis was detected in the form of proteinuria in 4.4% of the patients, and only one patient had microscopic haematuria. Lung involvement was uncommon (8.8%), taking precedence the UIP (33.3%) over the rest of the pulmonary manifestations. Only 11.1% of the patients with senile SLE had serositis, being in the form of pleuritis in 75% of the cases, pericarditis in the 37.5% and ascites in the 12.5%. Regarding the neurological involvement, 5 patients showed polyneuropathy and 1 had chorea. Likewise, the frequency of Sjögren, Raynaud and secondary antiphospholipid syndrome was of 16.7%, respectively.

The most important serological findings were: 97.3% ANA; 44.1% DNA and 20.6% hypocomplementemia, with 54.4% of the patients having serological activity. Only 5.9% had anti-Sm. Antiphospholipid antibodies were positive in 41.2% of the cases, with 4.4% of them showing triple positivity.

The average survival time was of 13.7 years (SD: 10.9–16.5). Out of the total patients, 14 died (20.59%), mostly due to infectious etiology (35.7%) and 14.28% due to disease activity. Other less common causes were neoplasia or ischaemic heart disease (7.14% respectively).

#### Conclusions:

- The late-onset SLE prevails in our environment, one of every 5 patients diagnosed with SLE in our consulting room is older than 65 years.
- It is found most often in women and it is confirmed a lower male/female ratio than expected.
- Joint and haematology manifestations and cutaneous involvement in the form of malar erythema define the clinical profile of our patients with senile SLE, with the renal involvement or the presence of serositis being uncommon.
- Half of the patients had serological activity at the onset, having hypocomplementemia only in 1 out of 5 cases.
- Infections were the first cause of mortality in our sample with an average survival time of around 13 years.

**Disclosure of Interest:** None declared

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AB0551

### OBSTETRICAL MORBIDITY RELATED TO ANTI-SSA ANTIBODIES: DATA FROM A FRENCH MONOCENTRIC RETROSPECTIVE STUDY

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**Background:** Obstetrical morbidity is an issue among autoimmune diseases patients. Anti-SSA positivity is well known for its effect on fetus and risk of

congenital heart block but no evidence has been yet found for its effect on obstetrical morbidity

**Objectives:** To investigate anti-SSA positivity effect among a large monocentric cohort of obstetrical morbidity patients and to evaluate the efficacy of different treatment regimens

**Methods:** All women who were seen from January 2010 to January 2015 in Jean-Verdier University Hospital for obstetrical morbidities were retrospectively included. All patients had been tested for anti-nuclear antibodies and anti-SSA/Ro and anti-SSB/La antibodies.

**Results:** We included 244 women (median age 34 years [interquartile range 21–53]) with 869 pregnancies overall. In 27 (11%) patients with anti-SSA antibodies, the median age at the time of pregnancy was 29.5 (17–40) years, with mean number of 3.66 pregnancies per woman. For these 27 patients, 83/99 pregnancies (84%) had an adverse obstetrical outcome: fetal loss (n=65; at a median of 20 (4–38) weeks' gestation), preeclampsia (n=15), intrauterine growth restriction (n=7), prematurity (n=7), and congenital heart block (n=2). In comparing women with obstetrical antiphospholipid syndrome and unexplained adverse complications, there was no major difference in frequency of recurrent miscarriages, preterm deliveries, preeclampsia or fetal loss. Among factors associated with obstetrical outcome and fetal loss, aspirin and hydroxychloroquine treatments were significantly associated with a favourable obstetrical outcome: odds ratio 0.05 [95% confidence interval 0.01; 0.37] (p=0.003) and 0.15 [0.02; 0.98] (p=0.04).

**Conclusions:** Women with unexplained recurrent obstetrical complications should be screened for anti-SSA antibodies. The benefit of aspirin and hydroxychloroquine treatment to improve the obstetrical outcome should be confirmed in prospective studies.

**Disclosure of Interest:** None declared

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AB0552

### THE CLINICAL AND LABORATORY FEATURES OF ANTIPHOSPHOLIPID ANTIBODY POSITIVE PATIENTS WITH OR WITHOUT SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** A multicenter antiphospholipid antibody (aPL) clinical database was created in 2016 with the participation of six rheumatology centres around the country. The purpose has been to better define aPL-related clinical manifestations and management strategies; and also to establish a resource for future clinical studies.

**Objectives:** In this first analysis, we compared the clinical and laboratory features of aPL-positive patients with and without systemic lupus erythematosus (SLE).

**Methods:** The demographic, clinical, laboratory, treatment characteristics of the aPL-positive patients with/without other systemic autoimmune diseases (SAID) are recorded at enrollment according to a predefined protocol. The inclusion criteria are positive aPL (lupus anticoagulant test [LA], anticardiolipin antibody [aCL], and/or anti  $\beta_2$ -glycoprotein-1 antibody [ $\beta_2$ GPI]) based on the Updated Sapporo Antiphospholipid Syndrome (APS) Classification Criteria at least twice within one year prior to enrolment.<sup>1,2</sup> For the purpose of this analysis, we only included aPL-positive patients without other autoimmune diseases (primary aPL/APS) and aPL-positive SLE patients (SLE aPL/APS).

**Results:** As of January 2018, 105 aPL-positive patients were recruited (mean age:  $42.6 \pm 10.1$  [min-max: 19–70]; 83 [79%] female; and 67 [64%] with another SAID). Ten patients were excluded from the analysis due to their SAID history other than SLE. Of the remaining 95 patients, 38 (40%) had primary aPL/APS; 57 (60%) fulfilled the ACR SLE Classification Criteria; 42 (44%) had thrombotic APS (TAPS) (8 arterial, 24 venous, and 8 both); 21 (22%) had obstetric APS (OAPS); 22 (23%) had both TAPS and OAPS (7 arterial, 14 venous, and 1 both); and 10 (11%) had no TAPS/OAPS. Fifty percent of the patients had history of at least one non-criteria aPL-manifestation. Demographics, clinical and laboratory manifestations, and medications were similar between primary aPL/APS and SLE aPL/APS patients except increased frequency of autoimmune hemolytic anaemia, aCL IgG, and hydroxychloroquine use in SLE aPL/APS patients (table 1).

Abstract AB0552 – Table 1

n (%)	Primary aPL/APS n=38	SLE aPL/APS n=57	p
Mean Age (min-max)	41.7±10.5 (24-65)	42.9±10.0 (19-70)	0.57
Female	28 (74)	47 (83)	0.3
Thrombosis	18 (47)	24 (42)	0.61
Arterial	4 (10)	4 (7)	0.55
Venous	9 (24)	15 (26)	0.77
Arterial and venous	4 (10)	4 (7)	0.55
Transient Ischemic Attack	3 (8)	7 (12)	0.49
Pregnancy Morbidity*	10 (26)	11 (29)	0.42
Non-criteria aPL Manifestations	18 (47)	30 (53)	0.12
Livedo Reticularis	6 (16)	6 (11)	0.45
Thrombocytopenia	7 (18)	12 (21)	0.75
Hemolytic Anemia	0	11 (19)	0.004*
Valvular Heart Disease	8/32 (25)	13/55 (24)	0.43
Chronic Skin Ulcer	2 (5)	3 (5)	1.0
Biopsy proven aPL nephropathy	2 (5)	2 (4)	0.68
White Matter Changes	3/25 (12)	11/46 (24)	0.23
Positive Lupus Anticoagulant	22/35 (63)	33/57 (58)	0.79
Positive aCL (≥40 GPL/MPL)	25/37 (68)	44/57 (77)	0.30
IgG	15/25 (60)	35/44 (80)	0.08
IgM	11/25 (44)	20/44 (46)	0.77
Positive β <sub>2</sub> GPI (≥40 GPL/MPL)	7/23 (18)	10/37 (18)	0.77
IgG	6/7 (86)	7/10 (70)	0.45
IgM	3/7 (49)	6/10 (60)	0.48
Medications at Database Entry			
Aspirin	19 (50)	37 (65)	0.15
Warfarin	20 (53)	29 (51)	0.87
Hydroxychloroquine	14 (37)	55 (97)	0.000*

\*Defined based on the Updated Sappora APS Classification Criteria

**Conclusions:** The analysis of our multicenter aPL database demonstrates that the frequencies of thrombosis and pregnancy morbidity are similar between aPL-positive patients with or without SLE. Half of the patients in both groups had history of at least one "non-criteria" aPL-manifestation; only autoimmune hemolytic anaemia was more frequent in aPL-positive patients with SLE.

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#### AB0553 CHARACTERISTICS OF SYSTEMIC LUPUS ERYTHEMATOSUS AMONG VARIOUS AGE GROUPS: COMPARISON BETWEEN JUVENILE ONSET, ADULT ONSET, AND LATE ONSET SYSTEMIC LUPUS PATIENTS FROM A SINGLE TERTIARY CENTRE IN EGYPT

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**Background:** Systemic lupus erythematosus (SLE) is a complex autoimmune disease with several factors affecting the characteristics of the disease, including age of onset which is one of these major factors.<sup>1</sup>

**Objectives:** To highlight the differences in disease characteristics among various age groups in an Egyptian cohort from a single tertiary centre.

**Methods:** Information in this study was derived from medical records of patients admitted to the Rheumatology department in Cairo University from December 2015 to June 2017. All patients fulfilled the SLICC classification criteria of 2012.<sup>2</sup> Demographic, clinical and serologic characteristics of all patients were recorded. Age of onset was defined as the age at the time of development of manifestations; upon which patients were divided into 3 groups: juvenile onset (JSLE: onset ≤16 years), adult onset (ASLE: onset 17–50), and late onset lupus (LSLE: onset >50) patients.

**Results:** The study included 369 patients, of which 44 (11.96%) were males and 324 (88.04%) were females. The mean age of onset of the cohort was 24.04 ±10.15 (7–63) years, while the mean disease duration was 65.6±58.4 (0.5–408) months. The study included 75/369 (20.3%) JSLE, 283/369 (76.6%) ASLE, and 10/369 (2.7%) LSLE patients. The median age of onset of JSLE patients was 13 (11–15), 23 (20–30) in ASLE patients, and 54 (52–58) years in the LSLE group. The median disease duration in JSLE patients was 78 (36–125), 36 (24–84) in ASLE patients, and 12 (9–38) months in LSLE patients. Apart from arthritis, malar

rash, and nephritis, there were no differences between the three groups. The prevalence of arthritis was highest among ASLE patients and lowest in JSLE (p=0.004) patients, with LSLE patients showing a comparable prevalence of arthritis to ASLE (p=0.5) and JSLE (p=0.3) patients. On the other hand, JSLE patients showed the highest prevalence of malar rash (p=0.006), as opposed to both ASLE (p=0.04) and LSLE (p=0.004) patients; yet ASLE patients showed a substantially high prevalence of malar rash when compared to LSLE patients (p=0.03). Nephritis was most common in JSLE patients (p=0.007) and least common in LSLE patients. Although there was no statistical difference in the prevalence of nephritis between JSLE and ASLE patients (p=0.1), both groups showed a higher prevalence of nephritis than LSLE patients (p=0.002 and p=0.01 respectively).

**Conclusions:** Adult onset SLE patients showed the highest prevalence of arthritis. On the other hand, JSLE patients showed the highest prevalence of nephritis as opposed to LSLE patients with the lowest prevalence, indicating a predilection towards a more severe disease in the former group.

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#### AB0554 FACTORS AFFECTING QUALITY OF LIFE IN INDIAN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** SLE has a profound impact on Quality of Life (QoL). In addition to disease activity and damage, other factors such as fatigue, fibromyalgia and psychiatric comorbidities also influence QoL.<sup>1</sup> However, there is lack of data in the form of comprehensive assessment of all these factors in the same cohort.

**Objectives:** To assess the quality of life and its correlates among patients with SLE.

**Methods:** Using a cross-sectional study design, 144 patients with SLE were assessed for disease activity and damage by using SELENA –SLEDAI and SLICC/ACR damage Index (SDI)), depression (by using Patient Health Questionnaire-9 (PHQ9)), anxiety (by using Generalised Anxiety Disorder 7 (GAD7)), fatigue (by using Fatigue severity scale (FSS)) and fibromyalgia (as per using ACR 2010 criteria). QoL was assessed using a generic QoL scale – Short Form 36 (SF-36).<sup>2</sup> Statistical analysis was done using STATA version 14.

**Results:** The study sample included 140 females and 4 males. Mean age of the participants was 32.48 (SD-7.26) years and the mean duration of illness was 3.92 (SD-3.76) years. The mean SELENA SLEDAI and SDI was 3.42±4.04 and 0.26 ±0.65 respectively. Prevalence of depression (PHQ9 ≥10) and anxiety (GAD7 ≥10) was 25% and 22.9% respectively. Fatigue (FSS ≥4) was present in 51.4%. Physical domains of SF36 were affected more often than the mental domains, 71.5% of the respondents had scores less than 50 in Physical component Summary (PCS) and 61.1% in Mental Component Summary (MCS) of SF36. No correlation was found between disease activity and damage and various domains of SF36. Depression, anxiety and fatigue had a significant negative correlation with all the domains of SF36 (table 1). On multivariate regression only fatigue was an independent predictor of PCS of QoL.

**Abstract AB0554 – Table 1.** Spearman Correlation between various domains of SF36 and other variables

	SELENA SLEDAI	SDI	Fatigue (FSS)	Depression (PHQ9)	Anxiety (GAD7)
Physical Function	-0.1264	-0.0415	-0.3166**	-0.3307**	-0.2987**
Role Physical	-0.0996	-0.1082	-0.3004 **	-0.2304*	-0.2286*
Bodily pain	-0.0913	-0.1086	-0.3902**	-0.34**	-0.3549**
General health	-0.1681*	-0.1356	-0.3145**	-0.2486*	-0.3115**
Vitality	-0.1589	-0.0582	-0.4135**	-0.3595**	-0.3795**
Social function	-0.1645*	-0.096	-0.2619*	-0.3853**	-0.3732**
Role Emotional	0.0471	-0.0783	-0.1905*	-0.2389*	-0.2089*
Mental Health	-0.0025	-0.0123	-0.2811**	-0.4545**	-0.4873**
PCS	-0.2062*	-0.1136	-0.3875**	-0.2868**	-0.285**
MCS	-0.0139	-0.0265	-0.2673*	-0.4174**	-0.4253**

\*p<0.05 \*\*p<0.001

**Conclusions:** Fatigue, depression and anxiety have a greater influence on QoL in SLE than disease activity and damage. Of these, fatigue appears to be the most important variable which influences QoL.

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**AB0555 IS HIGHER FITNESS ASSOCIATED WITH BETTER HEALTH-RELATED QUALITY OF LIFE IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS?**

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**Background:** Patients with systemic lupus erythematosus (SLE) present reduced health-related quality of life (HRQoL).<sup>1</sup> As an adjunct to traditional medical therapy, higher levels of physical fitness seem to be associated with better symptomatology and HRQoL.<sup>2</sup> However, a comprehensive characterisation of the association of different components of physical fitness with the different dimensions of HRQoL in this population is lacking and would provide valuable information for the design of prospective studies.

**Objectives:** The aim of this study was to investigate the association of different physical fitness components (flexibility, muscle strength and cardiorespiratory fitness (CRF) with the dimensions of HRQoL.

**Methods:** This cross-sectional study included a total of 70 women with SLE (age 42.5; SD 13.9). The back scratch test, 30 s chair stand test and 6 min walk test (n=49) (from the Senior Fitness Test battery) as well as the handgrip strength test were used to assess physical fitness. The median value of each fitness test [flexibility (0.125 cm), upper muscle strength (24.2 kg), lower muscle strength (15 repetitions) and CRF (575 metres)] was used to consider high ( $\geq$ median value) or low ( $<$ median value) fitness. HRQoL was assessed through the 36-item Short-Form Health Survey (SF-36). Partial correlation was used to examine the association of physical fitness components with all dimensions of the SF-36. For those dimensions significantly associated with fitness, analyses of covariance compared the differences in HRQoL between patients with low and high fitness level. All analyses were controlled for age, body mass index, depression and fatigue.

**Results:** Flexibility was correlated with physical function, social functioning and physical component ( $r_{\text{partial}}$  between  $-0.26$  and  $0.28$ ; all,  $p < 0.05$ ). Patients with a high level of flexibility only presented better physical function than those with a low level ( $p = 0.03$ ). Upper and lower muscle strength were correlated with physical function, physical role, bodily pain and physical component ( $r_{\text{partial}}$  between  $0.28$  and  $0.50$ ; all,  $p < 0.05$ ) with differences between groups of low and high muscle strength (upper and lower body) in all those dimensions ( $p < 0.05$ ). CRF was correlated with physical function, bodily pain and physical component ( $r_{\text{partial}}$  between  $0.39$  and  $0.65$ ; all  $p < 0.01$ ), with differences in physical function and physical component between groups of low and high CRF ( $p < 0.05$ ).

**Conclusions:** The main findings of the present study suggest that flexibility, muscular strength and cardiorespiratory fitness are associated with different dimensions of HRQoL, particularly with those related to self-reported physical health, in women with systemic lupus erythematosus. Future prospective research should assess the predictive role of fitness regarding disease activity and function.

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**AB0556 THE DIAGNOSTIC AND PREDICTIVE SIGNIFICANCE OF NAILFOLD VIDEO CAPILLAROSCOPY IN CTD PATIENTS WITH PULMONARY ARTERIAL HYPERTENSION**

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**Background:** Pulmonary arterial hypertension (PAH) is a serious complication of connective tissue diseases (CTD), defined as an elevation in mean pulmonary artery pressure 25 mmHg at rest. The 1 year, 3 year survival rates of CTD-PAH are only 69% and 30% respectively. Therefore, to early prediction and diagnosis of PAH is very critical for prolonging survival of CTD patients. Nailfold video capillaroscopy (NVC), is an imaging technique for the study of microcirculation. Until now, capillary abnormalities in systemic sclerosis (SSc) are well documented, but rare study focus on the association between the abnormality of capillary with PAH in CTD patients.

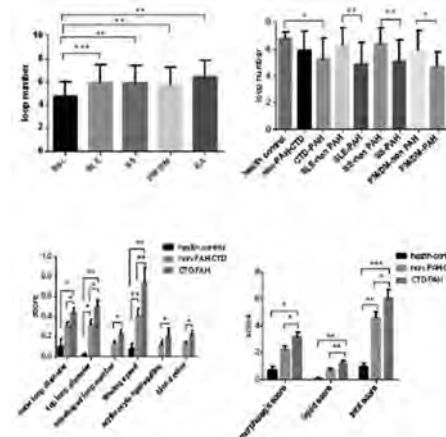
**Objectives:** Through estimating the correlation of the abnormality of nailfold capillary with pulmonary arterial hypertension (PAH) and other organs injury to find out its importance on early diagnosis and prediction for PAH in the patients with connective tissue disease (CTD).

**Methods:** Nailfold video capillaroscopy (NVC) was performed using a videocapillaroscope to test the fingers capillaries of 123 hospitalised CTD patients with and without PAH. The parameters of NVC were estimated including: the inter, outer and top loop diameter, loop number, misshaped or giant capillaries, flowing speed, haemorrhage, erythrocyte aggregation, et al. The organ involvement like interstitial lung disease (ILD) and cardiovascular complications were also considered. Mann-Whitney test was used to estimate the difference.

**Results:** 1) The number of capillary loops in patients with SSc was much lower, but morphologic score, liquid score, and total score were all higher than other CTD patients (Tab). 2) The loop number was significantly decreased but abnormal scores of morphology, liquid, diameter, misshaped loop number, flowing speed, erythrocyte aggregation were increased in CTD-PAH patients especially in SLE-PAH compared with non-PAH patients (Fig). 3) ILD relates the abnormality of peripheral circulation such like capillary malformation, decreased loop number, diameter and blood flow, increased haemorrhage, but the influence of PAP may be larger than ILD. 4) Down-regulated loop number, increased morphology, liquid and total score, and abnormal diameter, malformation, erythrocyte aggregation were found in CTD patients with cardiovascular complications, especially in CTD-PAH patients and SLE patients. 5) Age doesn't directly influence the capillaries of CTD patients, but in young and middle age patients, the difference between PAH and non-PAH groups were more evident.

**Abstract AB0556 – Table 1.** Comparison of number of nail fold capillaries in patients with various CTD

disease	SSc	SLE	SS	PM/DM	RA
loop number	4.688 $\pm 1.301$	5.915 $\pm 1.512^{***}$	5.875 $\pm 1.495^{**}$	5.717 $\pm 1.49^{**}$	6.417 $\pm 1.429^{**}$
morphologic score	4.117 $\pm 0.293$	2.389 $\pm 0.342^{**}$	2.378 $\pm 0.376^{***}$	2.293 $\pm 0.346^{***}$	2.5 $\pm 1.253^*$
liquid score	1.942 $\pm 0.402$	0.5277 $\pm 0.101^{***}$	0.6541 $\pm 0.111^{***}$	0.7367 $\pm 0.125^{**}$	0.5333 $\pm 0.217^*$
total score	8.321 $\pm 0.874$	4.628 $\pm 0.612^{***}$	4.297 $\pm 0.569^{***}$	4.54 $\pm 0.572^{***}$	4.633 $\pm 1.972^{***}$



**Abstract AB0556 – Figure 1.** Loop number and other indexes of nail fold capillaries in patients with various CTD and CTD-PAH with non-PAH CTD



**Conclusions:** In all CTD, the capillaries in SSc patients are most severely damaged. The disease of capillaries in CTD patients correlates with PAH, ILD and cardiovascular complications. So, NVC could be a predictive detection method for PAH and cardiopulmonary disease in CTD patients.

**Disclosure of Interest:** None declared

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AB0557

#### HAEMATOLOGICAL INVOLVEMENT (CYTOPENIA) AT THE TIME OF THE DIAGNOSIS IS ASSOCIATED WITH LESS SEVERE OCULAR INVOLVEMENT IN PATIENTS WITH PRIMARY SJOGREN SYNDROME

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**Background:** In patients with primary Sjogren Syndrome (pSS), haematological involvement – autoimmune cytopenia, might be present at the time of the diagnosis or can develop in time after the characteristic glandular involvement. <sup>(1,2)</sup>

**Objectives:** The objective of the study is to evaluate the correlation between glandular involvement (ocular) and presence of cytopenia in patients diagnosed with pSS.

**Methods:** A retrospective analysis was performed on a cohort of patients diagnosed with primary Sjogren Syndrome under surveillance in one Rheumatology Centre between 2009 and 2016. The documented cases have been diagnosed according to the 2002 American-European Consensus group classification criteria, the 2012 ACR criteria or 2016 ACR/EULAR Classification Criteria for pSS. The EULAR Sjogren's Syndrome Disease Activity Index (ESSDAI) was calculated for all patients. Ocular assessment and follow-up were performed in collaboration with the same ophthalmologist. The data was analysed using Windows Excel/SPSS20.0.

**Results:** 30 female patients diagnosed with pSS were included in the study. The mean age at the time of diagnosis was 52.1 years±SD 9.1. The ESSDAI was calculated for all patients at baseline: 5 (17%) patients presented high disease activity (ESSDAI >14), 14 (46%) patients moderate disease activity (5≤ESSDAI≤13) and 11 (37%) patients low disease activity (ESSDAI <5). The domain weight for glandular involvement when calculating ESSDAI is fairly low (2),<sup>1</sup> so in the studied group there wasn't obtained a statistically significant correlation between ocular involvement and disease activity as evaluated by ESSDAI.

In the clinical case series, Spearman's rank correlation coefficient between haematological (autoimmune cytopenia), and biological markers (hypocomplementemia) and ocular involvement were calculated. A strong negative correlation was found between autoimmune cytopenia and glandular manifestations (ocular involvement-xerophthalmia) ( $r=-0,60$ ;  $p<0,05$ ). Another strong negative correlation was obtained between hypocomplementemia and severe ocular involvement (corneal ulceration) ( $r=-0,59$ ,  $p<0,05$ ), respectively.

**Conclusions:** Patients diagnosed with primary Sjogren Syndrome that presented at disease's onset cytopenia and hypocomplementemia had a less severe ocular involvement.

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AB0558

#### ARE REGULATORY T CELL LEVELS DIFFERENT IN ACTIVE AND INACTIVE SLE PATIENTS?

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**Background:** The subgroups of T helper cells and regulatory T cells (T-reg) are involved in the pathogenesis of systemic lupus erythematosus (SLE). T-reg cells

suppress immune response to autoantigens and prevent autoimmune diseases (AID). Although there are studies suggesting that Treg cells are reduced during the active period of SLE, there are also studies claiming reversal.

**Objectives:** To determine whether there is a difference between T-reg and Th-17 cell levels in active and inactive SLE patients and to demonstrate the effects of these cells on disease course.

**Methods:** 21 SLE patients without active infection were included. Erythrocyte sedimentation rate, CRP, C3, C4, anti-ds-DNA levels, SLEDAI values were recorded in terms of organ and system involvement, hemogram results, disease activation. SLEDAI ≥6 were considered active disease. Concurrent peripheral blood Th17 and T-reg levels were studied. 15 healthy control subjects were included in the study.

**Results:** 19 of the patients were women, the mean age was 37.3±12.9 years and mean duration of the disease was 7.9±1.29 years. Hematologic involvement was present in 15 (71.4%) of the patients, renal involvement in 17 (81%) and joint involvement in 7 (42.9%). Both Treg cells and CD4 +IL17+ cell levels were significantly higher in SLE group than HC group in terms of CD4 +CD25+, CD4 +FOXP3+T reg, CD4 +CD25+FOXP3+T reg ( $p=0.011$ ,  $p=0.001$ ,  $p=0.001$  and  $p=0.040$ , respectively). There was no significant difference between active ( $n=12$ ) and inactive ( $n=9$ ) SLE patients in terms of Th17 and T-reg levels. However, in the inactive period, the levels of CD4 +FOXP3+T reg and CD4 +CD25+FOXP3+Treg cells tended to increase compared to the active period.

**Conclusions:** This study showed the tendency of increasing in Treg cells in the inactive period. This may be related to the modification of immunosuppressive drugs. It may be more appropriate to perform similar studies before and after treatment.

**Disclosure of Interest:** None declared

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AB0559

#### THE PREVALENCE OF NON-CRITERIA ANTI-PHOSPHOLIPID ANTIBODIES IN ANTI-PHOSPHOLIPID SYNDROME

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**Background:** Antiphospholipid syndrome (APS) is an autoimmune disease characterised mainly by arterial and/or venous thrombosis, recurrent pregnancy morbidity, with the presence of a variety of heterogeneous circulating antiphospholipid antibodies. However, there are a group of APS patients with persistently negative antiphospholipid antibodies. It is necessary to validate new specific antibodies to better recognition of these APS patients.

**Objectives:** To explore the clinical significance of non-criteria anti-phospholipid antibodies in a large cohort of Chinese patients with anti-phospholipid syndrome (APS).

**Methods:** Serum samples were obtained from 214 APS patients, 122 disease control including systemic lupus erythematosus, sjogren syndrome, ankylosing spondylitis, rheumatoid arthritis, osteoarthritis and 50 healthy control. Antiphosphatidylserine(IgA/IgG/IgM) (aPS), anti-phosphatidylethanolamine (IgA/IgG/IgM) (aPE), anti-prothrombin-antibodies (IgA/IgG/IgM) (aPT), anti-annexin V-antibodies (IgA/IgG/IgM) (aAnxV), anti-phospholipid-antibody(IgG/IgM)(aPL), anti-oxLDL antibody(IgG/IgM)(aoxLDL) were tested by ELISA kits(HUMAN Diagnostics Products, Germany) and IgG/IgM APL were tested by ELISA(Louisville APL Diagnostic, USA). The Chi-square ( $\chi^2$ ) test was used to examine the difference of frequencies of antibodies in APS patients and patients with other diseases. Spearman correlation analysis was performed to investigate the relationship between aPS/PT and other clinical/laboratory parameters.

**Results:** The prevalence of aPS IgG, aPS IgM, aPT, aPE, aAnxV, aPL, aoxLDL and IgG APL, IgM APL were 44.8%, 22.4%, 46.3%, 9.8%, 17.8%, 44.4%, 22.4%, 45.3% and 22.9%. The specificity of the antibodies were 82.6%, 95.3%, 96.0%, 99.4%, 95.3%, 92.4%, 87.2%, 95.3% and 94.8%. The highest positive predictive values of these antibodies were aPE, aPE, aPS IgM and APL IgM were associated with thrombotic events and oxLDL, aPE, aPL, aPS IgG, aPS IgM, aPT, aoxLDL, APL IgG and APL IgM were correlated with anti-cardiolipin antibody (ACL). aPL, aPS IgG, aPS IgM, aPT, APL IgG and APL IgM were associated with  $\beta$ 2-GP1 antibody. APL IgG, APL IgM and PS IgG were the highest prevalence in both ACL and lupus anticoagulant (LAC) negative patients. aPT has the highest prevalence in ACL and  $\beta$ 2-GP1 negative patients and APL IgG and aPS IgG were the highest two antibodies in LAC and  $\beta$ 2-GP1 negative patients and aPT has the highest prevalence in seronegative APS patients.

**Conclusions:** Non-criteria aPLs have a good diagnostic value in APS and were associated with thrombotic events.

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### AB0560 PATIENTS WITH RHEUMATOID ARTHRITIS AND LUPUS HAVE SIMILAR PREVALENCE OF PERIODONTITIS – A CROSS-SECTIONAL SURVEY

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**Background:** Periodontitis (PD) is a chronic inflammatory disease of the gingival tissues triggered by a dysbiotic microflora and causing the loss of soft and hard tissues surrounding the dentition. Over the last two decades, PD has been linked to a systemic inflammatory response and an increased risk of other comorbidities including cardiovascular diseases and diabetes. Numerous observational studies have confirmed an association between PD and rheumatic diseases. Some evidence suggests an association with rheumatoid arthritis (RA) and a beneficial effect of periodontal treatment on RA outcomes. Scarce evidence instead exists on the association between PD and Systemic Lupus Erythematosus (SLE). The main aim of this study was to evaluate the prevalence of PD in RA and SLE.

**Methods:** We conducted a cross-sectional survey of consecutive eligible outpatients with RA and SLE attending the Rheumatology Department at UCLH. PD diagnosis was estimated administering a validated self-reported questionnaire. Medical histories, cardiometabolic risk factors and assessment of standard biomarkers of inflammation and RA activity were collected as part of the outpatients' visit.

**Results:** 86 patients affected by RA and 122 by SLE and 5 presenting both diseases were recruited and agreed to complete the questionnaire. PD was detected in 100 patients of the overall survey (47%). 38 (44%) patients with RA and 59 (48%) patients with SLE had prevalent PD. There was no statistically significant difference in the prevalence of PD between the two patients' groups ( $p=0.575$ ). PD was associated with diagnosis of diabetes ( $p=0.023$ ), hypertension ( $p=0.004$ ) and hypercholesterolemia ( $p<0.0001$ ). Diagnosis of PD was associated with increased levels of C-reactive protein (CRP) ( $2.8\pm 3.3$  vs  $4.0\pm 4.4$ ,  $p=0.03$ ) in the whole population. In RA patients PD was associated with increased CRP ( $3.2\pm 3.2$  vs  $5.2\pm 4.4$ ,  $p=0.014$ ) and ESR ( $9.8\pm 10.0$  vs  $18.3\pm 16.6$ ,  $p=0.008$ ).

**Conclusions:** Prevalence of PD is similar in both RA and SLE (approximately 45%) and to the UK national estimates (Adult Dental Survey 2009). PD could contribute to an increased inflammatory profile in patients with RA and SLE. Our data highlight the need of assessing oral health needs of patients with rheumatic diseases.

**Disclosure of Interest:** None declared

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### AB0561 INFECTIONS IN NEWLY DIAGNOSED SPANISH PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: DATA FROM THE RELES COHORT

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**Background:** Infections continue to be an important source of morbidity and mortality in systemic lupus erythematosus (SLE).<sup>1</sup> Susceptibility to infections is thought to be due to a combination of disease related factors and immunosuppression, however differential contributions during disease course has not been yet studied.

**Objectives:** Using data of patients from the longitudinal inception cohort Registro Español de Lupus Eritematoso Sistémico (RELES), we aimed to analyse how predictors of infection change during the course of the disease.<sup>2</sup>

**Methods:** Two hundred and eighty-two patients from the RELES cohort were included. Markers of lupus activity, average prednisone doses and use of immunosuppressive drugs were compared between patients with and without infections within the first and second year of disease. For the analysis, drugs given during

the first month of follow-up were considered for infections during the first year and medications given during the first year were considered for infections during the second.<sup>3</sup>

**Results:** Nineteen patients (6.4%) had a documented episode of infection during the first year of follow-up and 16 patients (8 (5.67%) during the second. The following variables were associated with infections during the first year: hypocomplementemia at diagnosis ( $p=0.01$ ), nephritis at diagnosis ( $p=0.03$ ), SLEDAI score ( $p<0.01$ ), average dose of prednisone higher than 30 mg/day ( $p=0.01$ ), methylprednisolone pulses ( $p=0.05$ ) and mycophenolate use ( $p=0.02$ ). The independent variables in the final model were hypocomplementemia (OR 4.41, 95% CI 0.96–20.2) and average dose of prednisone higher than 30 mg/day (OR 6.60, 95% CI 1.3–32.4). The following variables were predictors of infections during the second year in the univariate analysis: average dose of prednisone higher than 7.5 mg/day ( $p=0.05$ ), methylprednisolone pulses ( $p=0.07$ ), duration of therapy with anti-malarials ( $p=0.09$ ), mycophenolate use ( $p=0.01$ ) and cyclophosphamide use ( $p=0.05$ ). The independent variables in the final model were average dose of prednisone higher than 7.5 mg/day (OR 4.5, 95% CI 0.99–21) and duration of therapy with anti-malarials as a protective factor (OR 0.99, 95% CI 0.99–1.00).

**Conclusions:** Patients with high baseline activity are at a higher risk of infection during the first months but intensive lupus therapy, specifically with medium-high doses of prednisone, is the strongest predictor of infectious events. Continued use of anti-malarials protects from infections.

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### AB0562 EXTRAGLANDULAR MANIFESTATIONS IN PATIENTS WITH PRIMARY SJÖGREN SYNDROME IN A TERTIARY HOSPITAL IN MADRID

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**Background:** Primary Sjögren syndrome (pSS) is a chronic autoimmune disorder characterised by generalised dryness. In a variable percentage of cases (up to 50%) patients can present extraglandular disease, which frequently determines the prognosis.

**Objectives:** To determine the frequency of both glandular and extraglandular disease in patients with pSS seen in a tertiary hospital in Madrid and to compare them with the frequency observed in the large cohorts (SER and EULAR).

**Methods:** A descriptive, observational cross-sectional study was conducted. We included patients with diagnosis of pSS according to the ACR/EULAR Classification criteria (2016) attended in our Rheumatology Unit from 2012 to 2017. A database was created, including clinical and epidemiological data and a descriptive analysis was carried out comparing the results with those obtained in the Sjögren-SER project and EULAR group.

**Results:** 106 patients with pSS were included. 92.5% were female (98), with a mean age at diagnosis of 45 years (range: 32–58). Frequency of exocrine gland disease is shown in table 1. Dry eye was the most frequent symptom (91%), with nearly half of them presenting ocular complications. 69.8% complained of dry mouth and 18.9% associated complications such as dysphagia and oral candidiasis. 16 patients (15%) suffered from recurrent parotiditis and 13 (12.3%) from salivary gland enlargement. Glandular disease also included xerosis (25%), dyspareunia (11.3%), upper respiratory tract dryness (12.3%) and atrophic chronic gastritis (14%). Frequency of extraglandular disease is shown in table 2. Chronic fatigue was the most frequent symptom, similar to the observed in both cohorts (50.9%), followed by arthralgia which was less frequent than in the Spanish cohort (40.6% vs 34.5%). 35 patients suffered from inflammatory arthritis and 3 cases associated fibromyalgia, less than the expected (2.8% vs 14.6% and 22%–33%). Sixteen patients suffered from interstitial lung disease, this being higher than the observed in both cohorts (15.1% vs 6.64% and 5%). Fewer patients suffered from depression compared with the EULAR group (24.5% vs 40%). Both peripheral neuropathy and renal disease were diagnosed in a percentage of patients similar to the expected (11.3% vs 8.92% y 1.88% vs 1.83% respectively). 7 patients had autoimmune thyroid disease. Finally, 5 patients (4.7%) developed lymphoma, 3 of them being MALT lymphoma of the parotid gland

which is higher than the observed in the Spanish cohort but it is within the EULAR range. The frequency of Raynaud's phenomenon, cutaneous vasculitis, lymphadenopathy, splenomegaly and pericarditis were similar to those observed both in the Spanish national group and EULAR cohort.

Abstract AB0562 – Table 1. Exocrine Gland Disease

EXOCRINE GLAND DISEASE	NO PATIENTS AFFECTED	PERCENTAGE (%)	SJÖGREN-SER PERCENTAGE (%)
Dry eye	96	91	94.51
Keratoconjunctivitis sicca	43	40.6	91.99
Dry mouth	74	69.8	94.05
Recurrent parotiditis	16	15	85.24
Salivary gland enlargement	13	12.3	4.35
Xerosis	27	25	72.31
Atrophic chronic gastritis	15	14	4.81
Upper respiratory tract dryness	14	13.3	15.13
Vaginal dryness / dyspareunia	12	11.3	48.97

Abstract AB0562 – Table 2. Extraglandular Disease

EXTRAGLANDULAR DISEASE	NO PATIENTS AFFECTED	PERCENTAGE (%)	SJÖGREN-SER PERCENTAGE (%)	EULAR PERCENTAGE (%)
Chronic fatigue	54	50.9	43.16	50.75
Asthma	43	40.6	34.56	33
Inflammatory arthritis	35	33	4.97	15.90
Fibromyalgia	3	2.8	14.65	22.98
Depression	26	24.5	-	40
Raynaud's phenomenon	22	20.8	21.05	18.37
Interstitial lung disease (ILD)	16	15.1	6.64	5
Cutaneous vasculitis	15	14.2	9.13	10.15
Peripheral neuropathy	12	11.3	8.92	5.40
Lymphoma	5	4.7	1.18	5.10
Renal disease	2	1.8	1.83	<5

**Conclusions:** Extraglandular disease in SS, although less frequent than sicca symptoms, have a special relevance when it comes to patient management. In our study the frequency of both glandular and extraglandular disease was similar to the observed in Sjögren-SER and EULAR groups although there were some differences. Fibromyalgia was less frequent in our group, whereas interstitial lung disease and peripheral neuropathy were more prevalent.

**Disclosure of Interest:** None declared

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#### AB0563 METABOLIC SYNDROME PREDICTS NEW DAMAGE IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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**Background:** The metabolic syndrome (MetS) is a complex of interrelated risk factors for the occurrence of cardiovascular disease and diabetes, and it is now both a public health and a clinical problem.<sup>1</sup> The MetS has also been reported to be associated with new organ damage, vascular events and mortality in Systemic Lupus Erythematosus (SLE) patients.<sup>2</sup>

**Objectives:** To determine whether the MetS predicts damage accrual in SLE patients.

**Methods:** This prospective study was conducted in a cohort of consecutive SLE patients seen since 2012 at one single institution. Patients had a baseline visit and follow-up visits every 6 months. Patients with  $\geq 2$  visits were included. Evaluations included interview, medical records review, physical examination and laboratory tests. Damage accrual was ascertained with the SLICC/ACR damage index (SDI) and disease activity with the SLEDAI. The MetS was defined if the patient fulfilled 3 of 5 criteria according to Alberti et al.<sup>1</sup> Survival univariable and multivariable Cox-regression models were carried out to determine the risk of developing new damage. The multivariable model was adjusted for age at diagnosis, disease duration, socioeconomic status, SLEDAI, baseline SDI, the Charlson Comorbidity Index, baseline use of prednisone (PDN), antimalarials and immunosuppressive drugs.

**Results:** Two hundred and forty-nine patients were evaluated; 232 were females and 17 males. Their mean (SD) age at diagnosis was 35.8 (13.1) years; nearly all patients were mestizo. Disease duration was 7.4 (6.6) years. The SLEDAI was 5.2 (4.3) and the SDI 0.9 (1.3). The average daily dose of PDN was 7.3 (6.4) mg/d and the time of exposure to PDN was 6.9 (6.2) years. One hundred and eight patients (43.4%) had MetS at baseline. During follow-up, 116 (46.6%) patients accrued at least one new point in the SDI damage index. In multivariable analyses, the presence of MetS was a predictor of development of new damage; with a Hazard Ratio (HR) 1.54 (1.05–2.26);  $p < 0.029$ .

**Conclusions:** The presence of MetS predicts the development of new damage in SLE patients, despite of other well-known risk factors for such occurrence.

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**Disclosure of Interest:** None declared

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#### AB0564 DRY SYNDROME IN RA PATIENTS. COMPARISON WITH SJÖGREN'S SYNDROME PATIENTS

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**Objectives:** The aim of the study is to analyse the clinical characteristics of Rheumatoid Arthritis (RA) patients and dry syndrome, and to compare with primary Sjögren's syndrome (PSS) patients.

**Methods:** Patients with RA and dry syndrome derived from Rheumatology Clinic to Cornea Unit were evaluated. According to symptoms and ophthalmological examination, patients were classified as high or low probability of Sjögren Syndrome (SS). Clinical and laboratory assessments included sex, age and smoking habit, DAS28, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), rheumatoid factor (RF), anti-citrullinated peptide antibodies (ACPA), antinuclear antibodies (ANA), anti Ro, anti La and presence of other extraarticular symptoms. In addition, the ophthalmological examination data (Ocular Staining Score [OSS] and Schirmer test), salivary gland scintigraphy (SGS) and salivary gland biopsy (biopsy) were analysed. The percentage of patients who would be classified according to the criteria of the Revised American-European Consensus Group (AECG) 2002, NIH-funded Sjögren's International Collaborative Clinical Alliance (SICCA) 2012 criteria and ACR/EULAR 2016 criteria is evaluated. RA patients with high probability of SS are compared with SSP patients. Statistics analysis was made by mean  $\pm$ SD, and comparison was made by t-Student test (quantitative parameters) and non parametric test (qualitative) ( $p < 0.05$ ).

**Results:** 24 RA with dry syndrome were included. 71% were women and the mean age was 64 $\pm$ 14 years. The disease duration was 17 $\pm$ 12 years. All patients had ocular manifestations, 2/3 oral manifestations, and 17% other extra-articular manifestations. According to DAS28, 33% of the patients were in clinical remission, 33% in high activity, and the others in low-moderate activity. 17 patients (71%), 19 (86%) and 5 (21%) were positive (+) for RF, ACPA and ANA, respectively. One patient had Anti Ro + and another anti La +. The mean OSS was 4.2 ( $\pm 3.1$ ) and the average of Schirmer was 10 ( $\pm 11$ ). In relation to other tests: 7 patients had a biopsy performed (2 positive [29%]), 5 patients had GGS (2 positive [40%]).

17 of the 24 RA patients (71%) were considered "high probability Sjögren's Syndrome" (SS and AR). These patients were compared with the PSS group (see table 1), showing differences in immunological parameters, sex, age and in the% that fulfilled the classification criteria. No significant differences were found in the ophthalmological examinations or the acute phase reactants.

Abstract AB0564 – Table 1

	SS and RA (n 17)	PSS (n 16)
OSS (mean $\pm$ sd)	6 $\pm$ 2	6.4 $\pm$ 2.6
SCHIRMER (mean $\pm$ sd)	6.8 $\pm$ 8.3	4 $\pm$ 4
ANA	4 (23%)	16 (100%)**
Anti RO/ANTI LA	1 (6%)/1 (6%)	15 (94%)/13 (81%)**
ACPA (media $\pm$ DS)	667 $\pm$ 866	0.1 $\pm$ 0.3 **
Gender (♂/♀)	6/11	0/16*
AECG 2002 criteria	4 (23%)	15 (94%) **
N (%)		
ACR 2012 criteria	2 (12%)	15 (94%) **
N (%)		
ACR/EULAR 2016 criteria	3 (18%)	16 (100%) **
N (%)		
Age	66.7 $\pm$ 11.6	56 $\pm$ 17.2*

\* $p < 0.05$ ; \*\* $p < 0.01$



**Conclusions:** Most of this RA patients cohort with dry syndrome were considered as "high probability SS", however only a small percentage (12%–23%) fulfilled the classification criteria. This can be explained by the low rate of specific antibodies (6%), and by the poor performance of some tests included in the criteria.

**Disclosure of Interest:** None declared

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### AB0565 CHANGES IN HEALTH RELATED QUALITY OF LIFE IN RENAISSANCE COHORT OF RUSSIAN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** The Lupus Quality of Life (LupusQoL) is recommended to assess health related quality of life (HRQOL) in systemic lupus erythematosus (SLE).

**Objectives:** The aim of the current study was to assess HRQOL in the first year observation in cohort of patients with systemic lupus erythematosus in Russian Federation (RENAISSANCE).

**Methods:** The LupusQoL-Russian was administered to a cohort of 128 Russian patients affected with SLE at baseline and follow up visit (in 12 months). Disease activity was evaluated by the SLE disease activity Index-2000 (SLEDAI-2K), and chronic damage by the Systemic Lupus International Collaborating Clinics Damage Index score (SDI) at baseline and follow up visit.

**Results:** 128 patients (118 (92%) women; aged 33,02±11,04 years, mean disease duration 100,0±84,3 months) were included. At baseline mean SLEDAI 2K was 11,2±8,5; mean SDI – 1,3±1,6, mean daily prednisolone 16,8±10,9 mg/day). For 12 months all patients received standard therapy according SLEDAI 2K and their clinical manifestations (prednisolone 100%, Hydroxychloroquine 72,4%, Mycophenolate mofetil 25%, Cyclophosphamide 17%, Azathioprine 12,5%, Rituximab 27,3%, belimumab 12,5% pts). At follow up visit SLEDAI 2K score significantly improved up to 6,94±6,93 (p<0,000029), SDI significantly worse up to 1,7±1,9 (p<0,04), mean daily prednisolone significantly reduced up to 12,2±7,3 mg/day (p<0,04). All 8 subscales LupusQoL showed improvement in the 12 months versus baseline (table 1). Spearman's correlation with SLEDAI 2K was obtained for Physical health (r=-0,13), Pain (r=-0,16), Planning (r=-0,21), Intimate relationship (r=-0,17) Burden to others (r=-0,16), emotional health (r=-0,13), Body image (r=-0,21).

**Abstract AB0565 – Table 1.** Changes in LupusQoL domains in the first year observation in cohort of patients with systemic lupus erythematosus in Russian Federation (RENAISSANCE)

LupusQoL domains	Baseline, mean ±SD	12 month, mean ±SD	p
Physical health	63,54±24,03	66,77±23,09	0004
Pain	67,42±25,10	73,62±24,27	0002
Planning	61,28±28,70	67,35±27,11	0008
Intimate relationship	64,96±35,60	72,53±29,58	0,01
Burden to others	53,03±27,78	57,35±29,62	0,04
Emotional health	63,16±22,02	67,65±19,99	0,01
Body image	58,32±29,45	69,49±23,01	0,0003
Fatigue	59,88±24,6	65,68±22,95	0006

**Conclusions:** The LupusQoL-Russian is sensitive to change in SLE patients with active SLE. The HRQOL correlated with disease activity, daily prednisolone and biologic.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.1663

### AB0566 ANTI-PHOSPHOLIPID ANTIBODIES SERONEGATIVIZATION IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS TREATED WITH BELIMUMAB

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**Background:** Belimumab is a monoclonal antibody that blocks the B lymphocyte stimulator, preventing it to bind its receptor on B-lymphocyte's surface, thus avoiding B cell activation. Despite some benefits showed in murine models of anti phospholipid syndrome (APS),<sup>1</sup> the use of belimumab in this condition needs further investigation.

**Objectives:** To investigate changes in the antiphospholipid antibodies (aPL) profile in Systemic Lupus Erythematosus (SLE) patients treated with belimumab.

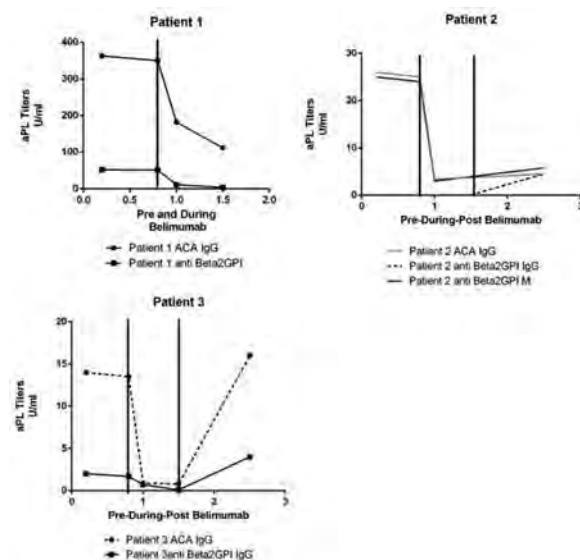
**Methods:** We retrospectively collected data from patients who attended the S. Giovanni Bosco Hospital, Turin, Italy. Inclusion criteria comprised: a) fulfilled ACR criteria for SLE, b) persistent aPL positivity (confirmed ≥3 occasions over a time >24 months before belimumab treatment), c) previous or ongoing belimumab therapy.

**Results:** This retrospective study included 3 patients with diagnosis of SLE [median age 39(range 33–51), male:female 2:1]. Table 1 resumes the characteristics of patients. All 3 patients received belimumab because of SLE flares. Before the treatment, Patient#1, classified as SAPS,<sup>2</sup> presented a persistent triple positivity for lupus anticoagulant (LA), high-titer aCL IgG isotype (>200 GPL) and anti-β2glycoprotein I antibodies (>50 GPL) (anti-β2GPI) IgG isotype. Patient#2 was persistently positive for IgG aCL and IgM anti-β2GPI (both 20–30 GPL and MPL, respectively; cut-off >7U), and had a history of pregnancy morbidity. Patient#3, classified as SAPS, presented positivity of LA and IgG aCL (10–20 GPL).

After 12 months since belimumab was started, a marked reduction of aPL was noticed, as follows. Patient#1 became negative for antiβ2GPI, while his aCL titre significantly decreased. Anti-β2GPI and aCL both turned negative in Patient#2. After being on belimumab for one year, she planned a pregnancy and she stopped the treatment; after 8 months since suspension, IgG antiβ2GPI antibodies were detectable (cut-off >3.5 U). Patient#3 was persistently negative for aCL while being on belimumab. When he discontinued the therapy, IgG aCL antibodies returned positive. Figure 1 illustrates aPL titres of the 3 patients in relationship with belimumab therapy.

**Abstract AB0566 – Table 1.** Characteristics of the patients included in the study

	Sex	Age	Diagnosis	Associated Autoimmune Disease	aPL positivity	Clinical Events
Patient#1	M	51	SAPS	SLE	LA, aCL IgG, anti-β2GPI IgG	Sub-popliteal arteriopathy
Patient#2	F	33	aPL carrier	SLE	aCL IgG, anti-β2GPI IgM	2 miscarriages <10 th week of gestation
Patient#3	M	39	SAPS	SLE	LA, anti-β2GPI IgG	3 episodes of TVP, severe thrombocytopenia



**Abstract AB0566 – Figure 1.** aPL titres of the three patients in relationship with belimumab therapy.

**Conclusions:** Despite its limitations, this pilot study is the first report of aPL negativization after starting therapy with belimumab. The clinical relevance of these findings should be investigated in prospective multicenter studies.

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**Disclosure of Interest:** None declared  
**DOI:** 10.1136/annrheumdis-2018-eular.6269

**AB0567** **CLINICAL SIGNIFICANCE OF THE DETECTION OF HLA-DRB1 ALLELES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS**

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**Background:** Associations between clinical manifestations of systemic lupus erythematosus (SLE), presence of antiphospholipid antibodies (aPL) and HLA-DRB1 alleles have been established, these associations however need clarification.

**Objectives:** Clarify the associations between clinical features of APS in patients with SLE and the presence of aPL and the HLA-DRB1 alleles.

**Methods:** 79 SLE patients were enrolled in the study (M/F 7/72; mean age 11.0 years, range (18,0;78,0). The main group consisted of 41 aPL carriers (28 of them with antiphospholipid syndrome (APS), a comparison group consisted of 38 aPL-negative SLE patients. The groups were comparable in age, duration and SLE activity.

ELISA was used to test for aPL. Lupus anticoagulant (LA) was evaluated using the DRVV test method. The HLA-DRB1 alleles were identified using HLA-typing.

**Results:** While comparing both groups, HLA-DRB1\*03 allele was found significantly less frequently in aPL-carriers group ( $p=0.04$ ). In APS group HLA-DRB1\*08 allele was present significantly more often ( $p=0.002$ ), both HLA-DRB1\*03 and \*15 alleles were found significantly less often ( $p=0.008$ ) in comparison with the aPL-negative group.

SLE patients with HLA-DRB1\*16 allele were more likely to develop an early pregnancy loss (OR=19,  $p=0.04$ ), patient with HLA-DRB1\*11 allele – more likely to develop a fetal loss (OR=4.9,  $p=0.04$ ) in comparison with other alleles; in patients with HLA-DRB1\*01 allele both early pregnancy loss and fetal loss occurred less often (OR=0.18,  $p=0.04$ ; OR=0.29,  $p=0.04$ ) compared with other alleles. The highest level of anti-double-stranded DNA was found in patients with HLA-DRB1\*13 allele (Me=54, [17.0, 290.0 IU/ml],  $p=0.005$ ), and lowest level – in patients with HLA-DRB1\*04 (Me=0.15, [0.0; 14.2 IU/ml],  $p=0.005$ ).

In the group of aPL carriers significant correlations between the HLA-DRB1\*08 allele and elevated level of anticardiolipin antibodies (aCL) IgM ( $r=-0.42$ ,  $p=0.005$ ) and anti-annexin V antibodies IgG ( $r=0.3$ ,  $p=0.01$ ), between HLA-DRB1\*04 allele and elevated level of aCL IgG ( $r=0.31$ ,  $p=0.008$ ), between the HLA-DRB1\*12 allele and an elevated level of anti-annexin V antibodies IgM ( $r=0.31$ ,  $p=0.01$ ) were found.

Correlations between HLA-DRB1\*16 allele and early pregnancy loss ( $r=0.37$ ,  $p<0.001$ ), between HLA-DRB1\*11 allele and fetal loss ( $r=0.30$ ,  $p<0.001$ ) were observed.

**Conclusions:**

1. HLA-DRB1\*08 allele is a risk factor for the development of APS in SLE patients.
2. HLA-DRB1\*03 and \*15 alleles were more often detected in aPL-negative SLE patients.
3. The presence of HLA-DRB1\*16 and \*11 alleles in SLE patients is a risk factor for the development of obstetric complications.
4. In the group of aPL carriers significant correlations between HLA-DRB1 alleles and elevated levels of aPL were found.
5. SLE patients with HLA-DRB1\*01 were less likely to develop any obstetric complications.

**Disclosure of Interest:** None declared  
**DOI:** 10.1136/annrheumdis-2018-eular.4737

**AB0568** **KNOW YOUR VACCINES – A CLINICAL AUDIT ON THE UPTAKE OF VACCINATIONS IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS**

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**Background:** Systemic Lupus erythematosus (SLE) is a multi-system autoimmune disease with an increased mortality and morbidity rate compared to the controlled population. One of the commonest causes of mortality and morbidity in SLE is infection. This is a result of not only the immunosuppressive effect of the disease process itself but also treatment involving disease modifying anti-rheumatic drugs (DMARDs). In fact, corticosteroids and immunosuppressants increase the risk of opportunistic infection, in addition to the more common pathogens.

Vaccines provide long lasting protective immunity against microbial pathogens and prevent clinically relevant infections. Recommended vaccinations in SLE patients include H. Influenza, Pneumococcal, Hepatitis A and B, and Human Papilloma Virus (HPV). Influenza vaccines are given annually and a Pneumococcal booster dose is given at 5 years following the initial vaccine.

**Objectives:** To assess whether, in routine clinical practise, patients with SLE are immunised against preventable disease according to EULAR recommendations and to assess the level of patient awareness.

**Methods:** A questionnaire was designed to assess the degree of compliance with current recommendations adapted from the EULAR-recommended vaccinations in patients with autoimmune inflammatory rheumatic diseases on DMARD therapy. The questionnaire enquired into the awareness and uptake of the influenza B, pneumococcal and hepatitis B vaccines. They were sent out by postal mail, with an enclosed stamped address envelope, to all SLE patients within the university hospitals of Leicester (UHL) NHS trust identified via the rheumatology patient database. Questions included awareness of the need to have vaccinations whilst on DMARDs. The audit was conducted over a three month period and the results were compiled in Microsoft excel.

**Results:** Of the 396 SLE patients within UHL, 86 responded. Among the patients studied 38% were on DMARD therapy, an equal proportion claimed they were not and 23% were unclear if they were on DMARD therapy. Approximately 60% were unaware of the need for vaccinations and only 27.9% acknowledged awareness for the need of the 3 vaccines mentioned above. Fifty-six (60%) patients had the influenza vaccine yet only 26 (28%) and 15 (21.8%) had the Pneumococcal and Hepatitis vaccines respectively.

**Conclusions:** The increased infection rate in SLE can be reduced through vaccination. This highlights the importance of increasing both physician and patient awareness. Although the sample size was small, the above audit has revealed that current local practice, with regards to ensuring that all SLE patients are appropriately vaccinated, requires improvement. This can be achieved through patient and healthcare worker education, and also creating a checklist that can be added to the clinic notes. Working together with our primary care colleagues will also help bridge the divide between compliance and non-compliance. Such measures will aim to improve mortality and morbidity in SLE patients.

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**Disclosure of Interest:** None declared  
**DOI:** 10.1136/annrheumdis-2018-eular.7536

**AB0569** **RELATIONSHIP BETWEEN THE LEVELS OF VITAMIN D AND THE ACTIVITY IN SYSTEMIC LUPUS ERYTHEMATOSUS IN DOMINICAN REPUBLIC**

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**Background:** 25 (OH) D is a steroid prohormone that participates in calcium homeostasis and bone health.<sup>1</sup> Nonclassical functions of this vitamin have been described in a variety of cells of the innate and adaptive immune system. Currently, the immunomodulatory role of 25 (OH) D in Systemic Lupus Erythematosus (SLE) continues in debate. In addition, a correlation between non-optimal levels of 25 (OH) D and disease activity has been observed.<sup>2</sup> In the SLE, there is a high prevalence of non-optimal levels of vitamin D. A prevalence of 25 (OH) D insufficiency of 15% to 75% is reported.<sup>3</sup>

**Objectives:** To determine the relationship between vitamin D levels and disease activity in SLE.

**Methods:** It is a prospective, cross-sectional study, in all patients who attended the rheumatology clinic of the Hospital Docente Padre Billini in the period August – October 2017, where the levels of vitamin D and activity of the disease were measured with SELENA-SLEDAI ( $\leq 3$  without activity, 3–12 moderate activity,  $\geq 12$  high activity). Vitamin D deficiency is defined as serum levels of 25 (OH) D  $<10$  ng/ml, insufficiency levels serum levels of 25 (OH) D of  $<30$  ng/ml.<sup>3</sup> Inclusion criteria: all patients with at least 18 years of age who met the SLE SLICC 2012 classification criteria were included with determination of vitamin D and calcium.

**Results:** 45 patients who met criteria SLE SLICC 2012 were included. 97.7% (44) were women. The most frequent age range was 31–45 years. 24.4% (11) had decreased calcium values. The vitamin D values were insufficient in 77.7% (35) of the patients and deficient in 4.4% (2) According to SELENA-SLEDAI, 77.7% (35) had no activity of the disease, 20% (9) had moderate activity and 2.2% (1) had

high activity. Of the patients who reported disease activity, only 13.3%<sup>6</sup> had insufficient vitamin D. There is no significant difference between patients who have vitamin D values greater than or less than 20 ng/ml. In both groups, the majority had SLENA-SLEDAI in low activity.

**Conclusions:** The vitamin D levels were not associated with an increase in disease activity in our study patients. Although our country is an island, the use of sunscreen and avoid sunbathing is something common, it causes to find low levels of vitamin D, not only in patients with SLE, where avoiding sunbathing is a recommendation, but also in other pathologies that come to our service. We believe that vitamin D levels should be measured in the general population, to have a reference range and study their influence on health.

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**Disclosure of Interest:** None declared

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#### AB0570 ASSOCIATION BETWEEN SLEDAI-2K DOMAINS AND ORGAN DAMAGE ACCRUAL

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**Background:** Prevention of permanent organ damage is a key goal of SLE management<sup>1</sup>. Overall disease activity measured by SLE Disease Activity Index (SLEDAI-2k) is a risk factor for damage<sup>2</sup>, but the contribution of organ-specific activity to damage risk has not been enumerated.

**Objectives:** We sought to determine the degree to which organ domains of SLEDAI-2k are associated with damage accrual.

**Methods:** A dataset of SLE patients (2007 – 2017) at the Australian Lupus Registry was studied. Variables collected at each visit included all domains of SLEDAI-2k, Physician Global Assessment, and medications. Systemic Lupus International Collaborating Clinics/ACR Damage Index (SDI) was recorded annually and each visit was labelled “damage transition” or “non-damage transition” based on whether SDI increased at the subsequent annual measure. The association of risk of SDI increase with SLEDAI-2k domains was assessed using multivariable logistic regression analysis adjusted for confounding by medication use.

**Results:** 5538 visits from 266 patients (86.5% female, 47.4% Caucasian, 66% dsDNA positive) were analysed; at enrolment median (range) SLEDAI-2k was 4 (0–26) and SDI was 0 (0–4). Upon multivariable regression analysis, domains found to be significant were: low complement, proteinuria, haematuria, leukopenia, pyuria, pericarditis, alopecia, rash and arthritis. Upon further adjustment for prednisolone exposure, the effects of some domains were attenuated, but pericarditis (odds ratio (OR)=4.06, 95%CI=1.68–9.83), pyuria (OR=1.94, 1.47–2.56), arthritis (OR=1.71, 1.35–2.16), and rash (OR=1.43, 1.20–1.70), alopecia (OR=1.43, 1.10–1.86) and leukopenia (OR=1.36, 1.03–1.78) remained significant. No other SLEDAI-2k domains showed a significant association, in part due to infrequent occurrence. SLEDAI-2k domains weightings were not congruent with the respective risk of damage accrual.

**Conclusions:** In study, only some SLEDAI-2k domains were significantly associated with organ damage accrual. Re-appraisal of weightings in SLE disease activity scores based on their association with outcome is potentially warranted.

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**Disclosure of Interest:** None declared

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#### AB0571 FACTORS RELATED TO ALEXITHYMIA IN SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Alexithymia describes the difficulties of people in identifying, differentiating and articulating emotions of others and themselves and in discriminating those from bodily sensations, with a limited fantasy and a concrete, externally oriented cognitive style.<sup>1</sup> A high prevalence of alexithymia has been found in patients with a variety of health conditions, including SLE.<sup>2</sup> Previous authors identified mood states<sup>2</sup> and quality of life<sup>3</sup> as the main factors related to alexithymia in Systemic Lupus Erythematosus (SLE).

**Objectives:** Aim of our study was to assess the impact of clinical, immunological, psycho-social factors on the presence of alexithymia in Systemic Lupus Erythematosus (SLE).

**Methods:** We consecutively enrolled 104 patients in a cross-sectional study. Alexithymia was assessed using the Toronto Alexithymia scale (TAS-20). We also evaluated symptoms of mood disorders using BDI and HAM-H, quality of life using MOS-SF36, sleep disorders with PSQI and physical activity using IPAQ.

**Results:** The mean (standard deviation) TAS-20 score was 49.5 (15.6). The prevalence of alexithymia (TAS-20 ≥61) was 28%. Alexithymic patients (TAS-20 ≥61) were significantly older (p 0.0005), presented more severe depressive and anxiety symptoms (p<0.0001), a higher score of sleep disorders (p<0.0001), a reduced Facit-Fatigue score (p 0.0007), reduced SF-36 mental and physical component summary scores (p 0.0001 and 0.004) and increased daily sedentary time (p 0.002). In the multiple logistic regression analysis the variables associated to the presence of alexithymia were age (OR 1.07, p 0.02) and the score of depressive symptoms (OR 1.15, p 0.02).

**Conclusions:** About a third of SLE patients presented a dysfunctional processing of emotion. It is necessary to carefully consider the symptoms of mood disorders to optimise SLE patient management.

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**Disclosure of Interest:** None declared

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#### AB0572 CORRELATION OF 24 HOURS URINARY PROTEIN QUANTIFICATION WITH RANDOM SPOT URINE PROTEIN/CREATININE RATIO IN PATIENTS WITH ACTIVE LUPUS NEPHRITIS

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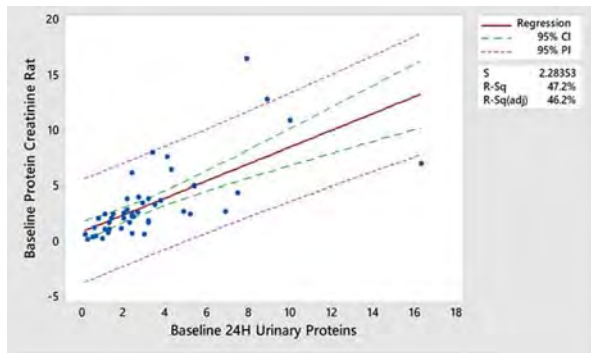
**Background:** Proteinuria is an important signal of Lupus nephritis. The standard method of proteinuria quantification is 24 hours urine collection. The ongoing practice of using spot urine sample to determine the ratio between protein and creatinine excretion as a convenient, alternative method of proteinuria estimation is not without limitation and criticism questioning its accuracy.

**Objectives:** Given the cumbersome expressed by some patients on collecting 24 hours urine for protein quantification, our aim was to determine the correlation between spot urine protein-to-creatinine ratio (PCR) and 24 hour urinary protein (UP) in patients with active Lupus nephritis.

**Methods:** The active patients included in the analysis was 53 attending Dubai Hospital shared Rheumatology/Nephrology clinic during the period of June 2016 till Dec 2017. All diagnosed to have systemic lupus erythematosus who either had flare with proteinuria or newly diagnosed as Lupus nephritis. Suspicion of active Lupus nephritis was evidenced by active urine sediment and 24 hours UP quantification of more than 0.5 gm or more than 1.0 gm regardless to urine sediment. Paired baseline urine samples were obtained and results included in the final analysis. Most of the patients underwent ultrasound guided kidney biopsy to classify the nephritis according to ISN/RPS 2003 classification, unless contra-indicated or patient refused to give consent. We used Minitab 18.1 software to determine the Spearman’s correlation coefficient (r), and its significance. P-Value <0.05 was considered statistically significant



**Results:** Total of 54 patients evaluated, one patient excluded from the analysis as the patient nephritis was not related to lupus. 93% of the patients were females (49/53) while 7% were males (4/53). 42 patients underwent ultrasound guided kidney biopsy (79%) while 21% of the patients the histopathology class was not defined as no biopsy obtained either due to contra-indication to the procedure (i. e.: single kidney, flared during pregnancy) or the patient refusal to go for biopsy. 15 patients out of 53 (28%) had nephrotic range proteinuria (defined as urinary proteinuria level of more than 3.5 gm per 24 hours), on the other hand 72% (38/53) had sub nephrotic range. Linear regression Analysis revealed positive correlation between the two methods of estimation mainly at lower levels of proteinuria (less than 3.5 gm). We found a positive correlation between PCR and 24 hours UP quantification. The overall corrected correlation coefficient was  $r=0.46$ , with P value  $<0.0001$ .



Abstract AB0572 – Figure 1

**Conclusions:** PCR in spot urine specimens is an accurate and convenient method to estimate the protein excretion in urine only when proteinuria is at sub nephrotic range. Prospective study is required to explore the effect of disease activity, disease duration and co-morbidities on the correlation and predictive power of the model.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.3785

AB0573

#### INFLUENCE OF SMOKING AND OBESITY ON THE RISK OF DEVELOPING PRIMARY SJÖGREN'S SYNDROME: A POPULATION-BASED COHORT STUDY

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**Objectives:** Cigarette smoking and obesity have been identified as risk factors for developing several autoimmune diseases, and may be protective for others. This study explored the role of these risk factors in primary Sjögren's syndrome (pSS).

**Methods:** A cohort of Olmsted County, Minnesota residents diagnosed with pSS between January 1, 2000 and December 31, 2015 was identified based on individual medical record review. Each of the cases was matched to 3 age- and sex-matched comparators without pSS randomly selected from Olmsted County residents, indexed to the date of pSS diagnosis. Smoking status was divided into three categories of current smoker, ex-smoker and never smoker. The body weight and height closest to date of diagnosis/index date ( $\pm 1$  year) were used. Obesity was defined as a body mass index (BMI)  $\geq 30$ /kg/m<sup>2</sup>.

**Results:** 106 incident cases of pSS and 318 controls were identified. The odds ratio (OR) of pSS comparing current smokers with never smokers was 0.34 (95% confidence interval (CI): 0.14, 0.85;  $p<0.05$ ), while the OR for former smokers compared to never smokers was 1.27 (95% CI, 0.80, 2.03). Smoking status was

not associated with antinuclear antibody, anti-SSA, anti-SSB or rheumatoid factor positivity ( $p>0.05$ ). The OR of pSS comparing obese subjects with non-obese subjects was 0.79 (95% CI, 0.48, 1.30), while the OR of pSS for BMI analysed as a continuous variable was 0.97 (95% CI, 0.94, 1.01).

**Conclusions:** In this population-based study, current smokers have a lower risk of developing pSS while BMI does not affect this risk.

**Disclosure of Interest:** None declared

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AB0574

#### RENAL ACTIVITY PATTERNS AND THERAPEUTICS IN LUPUS NEPHRITIS OBSERVATIONS IN 5 MEXICAN RHEUMATOLOGY CENTRES

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**Background:** Lupus nephritis (LN) develops in 40%–60% of Systemic Erythematosus (SLE) patients; 45% don't achieve complete response or eventually relapse and 10%–20% progress to end stage renal disease.

**Objectives:** Describe renal activity patterns and therapeutic schemes employed in 5 Mexican Rheumatology Centres.

**Methods:** Retrospective analysis of renal activity in 193 patients with LN with  $\geq 6$  months follow-up. If follow-up was  $\leq 1$  year, response was classified as complete (CR), partial (PR) or no response (NR). If follow up was  $>1$  year, response was classified as one of the following patterns: persistent inactive (PI), relapsing-remitting (RR), chronic active (CA) and mixed.

**Results:** Biopsy was available in 166 subjects (86.01%): class IV (42.77%), III (23.49%), V(10.24%), II(9.03%). The most prevalent schemes were CYC+MMF 46.6%, only CYC 18.13%, only MMF 12.4%, CYC+MMF+ TAC 9.84%. Thirty eight patients had follow-up  $\leq 1$  year with the following response: CR 16 (42.1%), NR 13 (34.21%) y PR 9 (25.7%). One hundred and fifty five patients had  $>1$  year follow-up with the following activity patterns: PI 55 (35.48%), RR 38 (24.51%), CA 31 (20%), mixed 31 (20%).

We then compared patients whose therapeutic schemes were classified as the National Institutes of Health regime (n=109) (as considered by the treating physician) to those with different therapeutic schemes. We observed a higher final GFR ( $100\pm 39.2$  SD VS  $87.1\pm 37.9$  SD,  $p=0.029$ ) and more frequent CYC use ( $106\pm 100$  SD VS  $37\pm 49.3$  SD,  $p<0.0001$ ) in the NIH group. There weren't statistically significant concerning renal response or activity patterns. Although treating physicians stated they had used the NIH regime in 57.9%, 64.03% actually received CYC+MMF and 11.4% CYC+MMF+ TAC. We then compared the group that received CYC monotherapy to the groups that received CYC+MMF and CYC+MMF+ TAC and did not observe any statistically significant differences.

**Conclusions:** The most prevalent renal activity patterns were those that translated intermittent of continuous activity (64.51%). Strict adherence to the original NIH regime is questionable, most subjects actually received CYC+MMF at some point. We did not observe any statistically significant superiority of renal outcomes of combination therapy over CFM monotherapy. Limitations: preliminary initial analysis, heterogeneous information and missing data.

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AB0575

#### CLINICAL ANALYSIS OF 22 CASES OF SYSTEMIC LUPUS ERYTHEMATOSUS COMPLICATED WITH HEMOPHAGOCYTIC LYMPHOHISCYTIOSIS

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**Objectives:** To investigate the clinical features of hemophagocytic lymphohiscytosis (HLH) in systemic lupus erythematosus(SLE).

**Methods:** Twenty – two cases of systemic lupus erythematosus complicated with hemophagocytic syndrome were retrospectively analysed. The clinical manifestations, laboratory tests and prognosis were collected.

**Results:** Twenty-two patients with systemic lupus erythematosus complicated with hemophagocytic syndrome developed fever in 22 patients, including 18 with hyperpyrexia, 20 with hyperferritin, 20 with cytopenia, 10 with splenomegaly, 6 with hyperglycemia, 5 cases of hypofibrinogenemia, 14 cases of bone hemoptysis occurred in the bone wear, nk cell activity decreased or absent in 7 cases, 15 cases of lymphadenopathy, mostly bilateral armpit lymph nodes and neck bilateral lymph nodes, liver function Abnormalities/hepatic insufficiency in 11 cases, ultrasound showed 10 cases of cardiac involvement, MRI showed 5 cases of cumulative brain. 22 patients were diagnosed with high-dose glucocorticoid, 9 cases of hormonal impact, 17 cases of human immunoglobulin immunosuppression in 9 cases, 4 cases of ganciclovir, 1 cases of acyclovir, 1 case of relying on Park Glycosides. 21 cases improved, 1 case to persuade invalid to abandon treatment and discharge.

**Conclusions:** SLE and hemophagocytic syndrome have some similarities. The clinical diagnosis is easy to miss. When patients with SLE continue to have high fever, splenomegaly, blood cells decrease, phagocytosis occurs in bone wears, coagulation dysfunction should be combined with vigilance HLH, Improve the relevant inspection. High-dose glucocorticoid combined with immunosuppressive agents, human immunoglobulin therapy can effectively improve the prognosis.

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**Disclosure of Interest:** None declared

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#### AB0576 FEATURES OF NEUROLOGICAL MANIFESTATIONS OF SYSTEMIC LUPUS ERYTHEMATOSUS IN THE KYRGYZ COHORT OF PATIENS

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**Background:** The development of a variety of neuropsychiatric symptoms in SLE patients starts with the dysregulation of the immune system. Involvement of the CNS in the pathological process during the onset of the disease can significantly worsen the patient's condition and complicate the prognosis.

**Objectives:** To study the features of neurological manifestations of SLE in the Kyrgyz cohort of patients.

**Methods:** The basis of the study were the results of an initial examination of 460 patients with prospective observation, with a reliable diagnosis of SLE. Out of them, 112 patients were neurological, at the age of 30 (median) [26, 41], predominantly of Kyrgyz nationality (87), with duration of the disease from 6 months to 7 years (median – 2.0) treated in the National Cardiology and Therapy Centre named after M. Mirrahimov (NCTC) from January 2012 to December 2017.

Neurologic manifestations of SLE were diagnosed by clinical examination by a neurologist using some instrumental methods of investigation.

To assess the neuropsychiatric state of patients, the classification criteria by the American College of Rheumatology (1999) were used. Neuropsychiatric disorders were diagnosed through a clinical examination by the psychotherapist using the classification of mental disorders and behavioural disorders according to ICD (International Classification of Diseases) – 10.

**Results:** The damage of the nervous system was observed in 112 (24.305%) Kyrgyz patients from 460, mainly of the central nervous system – in 77 (68.75%), to a lesser extent – the peripheral nervous system (PNS) – in 35 (31.25%) out of 112. In half of the observed patients with CNS lesions, various neuropsychiatric disorders were registered – in 39 (50.65%) out of 77, with psychosis prevalence with visual and auditory hallucinatory syndrome – in 34 (87.18%) out of 39 patients. There were 14 patients with cerebrovascular infection (18.18%) out of 77, mainly with ischaemic stroke in the SMA basin. There was one patient with aseptic meningoencephalitis with manifestations of mild hemiparesis and with the disruption of the function of the pelvic organs in the form of mandatory urges. Symptoms of myelopathy with malfunction of the pelvic organs were registered in 9 (11.69%) patients out of 77.

Five patients had symptoms of combined CNS and PNS lesions. In one of them cases the patient had encephalopolyneuradiculopathy of the Guillain-Barre type with the phenomena of coarse tetraparesis and with disruption of the function of pelvic organs in the form of delay, with a single epicrism.

**Conclusions:** Neurological manifestations of SLE in the majority of Kyrgyz patients were mainly caused by CNS lesions (68.75%), mostly in the form of neuropsychiatric disorders (50.65%), with a predominance of psychosis with visual and auditory hallucinatory syndrome (87.18%).

**Disclosure of Interest:** None declared

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#### AB0577 CHARACTERISTICS OF VALVULAR HEART DISEASE IN A MONOCENTRIC MALAYSIAN LUPUS COHORT

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**Background:** Valvular heart disease (VHD) is one of the commonest cardiovascular manifestations of autoimmune disease, including systemic lupus erythematosus<sup>1</sup>. Its prevalence ranges from 18% to 74%, with predominantly regurgitant lesions and valvular thickening. The cause of such abnormalities is yet unclear. There have been very few such studies performed in Asian patients, and only one in Malaysian patients to date.

**Objectives:** We sought to evaluate the valvular abnormalities of a multiracial cohort of lupus patients and also examine the association of these abnormalities with potentially related factors.

**Methods:** The medical records of all patients with SLE who had attended the Rheumatology Clinic of Kuala Lumpur Hospital between January 2008 and December 2016 were reviewed. All patients fulfilled the 1997 updated ACR criteria for SLE. Transthoracic echocardiographic examinations as part of their standard of care were performed by trained technicians using a standardised protocol. Multivariable logistic regressions were conducted to determine factors associated with valvular abnormalities in these patients.

**Results:** There were 207 patients in this study. VHD was found in 67.1% of patients: they were asymptomatic and did not have murmurs. The main abnormalities were tricuspid regurgitation (TR) (45.4%), mitral regurgitation (MR) (40.6%) and valvular thickening (19.2%). The majority of cases comprised mild TR (37.2%), mild MR (25.1%) and mitral valve thickening (10.6%). There were more patients with moderate to severe MR compared to TR (15.5% vs 8.2%). Median pulmonary artery systolic pressure was 23.0 mmHg (IQR 13.2). Risk of VHD was higher in patients with lower C3 levels (<0.83 g/L) (OR 3.36, 95% CI 1.74–6.66). MR (83.3%) and mitral valve (MV) thickening (58.3%) were the commonest abnormalities in patients with APS. Having APS greatly increased the risk of MR (OR 8.10, 95% CI 1.65–77.95) and mitral valve thickening (OR 16.30, 95% CI 3.93–73.84). Risk of mitral valve thickening was increased by presence of lupus anticoagulant (OR 20.82, 95% CI 3.64–223.08), anticardiolipin antibody (OR 5.24, 95% CI 1.42–17.76), anti-β2GPI antibody (OR 6.35, 95% CI 1.18–37.14) and diabetes (OR 7.85, 95% CI 1.43–40.24). Risk for MR was increased by presence of lupus anticoagulant (OR 3.55, 95% CI 1.10–12.43). Hypertension was associated with an increased risk for developing aortic regurgitation (OR 4.70, 95% CI 1.67–13.44). Anti-histone antibody positivity appeared to protect against development of MR (OR 0.46, 95% CI 0.213–0.968).

**Conclusions:** More than half of our patients had VHD, with regurgitant lesions and valvular thickening being the commonest abnormalities. Our finding of the association of MR and mitral valve thickening with APS and individual antiphospholipid autoantibodies concurs with earlier studies. However, what were unusual about our cohort were that TR was the prevalent abnormality and the association of VHD with low C3. We suggest that all patients with SLE have at least one echocardiogram, especially the patients with APS or antiphospholipid antibodies.

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#### AB0578 ANALYSIS OF CLINICAL FEATURES AND RISK FACTORS OF IN-HOSPITAL MORTALITY IN CYTOMEGALOVIRUS (CMV) DISEASES WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Cytomegalovirus (CMV) is known as a major cause for life-threatening complications in immunocompromised hosts, including status post allogeneic bone marrow transplantation, solid organ transplantations, and acquired

immunodeficiency syndrome (AIDS). The reactivation of CMV depends on the immune status of host. Systemic lupus Erythematosus (SLE) often requires steroid and immunosuppressive agents to induce remission and lower disease activity. This study presents the clinical presentations, laboratory characteristics, medical profile (including steroid, immunosuppressive agents, and biological agents) and clinical outcomes in SLE patients with diagnosis of CMV diseases. Further, we attempted to investigate the mortality risk factor in these patients.

**Objectives:** To analyse the clinical features, the mortality risk factors and all-cause mortality of Cytomegalovirus (CMV) diseases in patients with systemic lupus erythematosus (SLE) in single centre of Taiwan.

**Methods:** A retrospective study was performed to investigate the clinical features and identify the mortality risk factors associated with CMV diseases in patients with systemic lupus erythematosus (SLE). We reviewed the medical records in patients with SLE who were diagnosed with CMV diseases between Jan. 2006 and Dec. 2016 from Taipei Veterans General Hospital in Taiwan. Clinical and laboratory parameters as well as treatment outcomes were analysed.

**Results:** Fifty-six patients diagnosed with CMV diseases were enrolled in the study and separated into survivors (n=24) and non-survivors (n=32) groups. All patients in CMV disease demonstrated significantly high incidence of CMV pneumonitis (71.43%). The higher SLEDAI-2000 score (p=0.009, HR1.154, 95% CI 1.037–1.285), percentage of recent pulse therapy (p=0.013, HR 4.569, 95% CI 1.313–15.902), and plasmapheresis during hospital course (p=0.005, HR6.905, 95% CI 1.637–29.122) was more common characteristics in non-survivor group than in survivor group. Non-survivors had significantly higher percentage of pancytopenia (p=0.001, HR9.667, 95% CI 2.307–40.511), CMV-positive PCR of blood and bronchoalveolar (BAL) lavage fluid (Blood: p<0.001, HR 15.000, 95% CI 3.932–57.223, BAL fluid: p=0.021, HR 6.176, 95% CI 1.151–33.151), and presence of concurrent infections (bacteremia: p=0.026, HR 4.833, 95% CI 1.122–20.824, other fungal infections: p<0.001, HR 11.424, 95% CI 2.722–47.952) than survivors. Septic shock (n=10, 41.2% of non-survivor group) is the most common cause of in-hospital mortality in CMV diseases.

**Conclusions:** The recent pulse therapy, pancytopenia, and concurrent infections are risk factors of in-hospital mortality in CMV diseases of patients with Systemic Lupus Erythematosus. The serological data of non-survivor groups showed negative findings of CMV immunoglobulin M (IgM) with detection of CMV DNA by polymerase chain reaction (PCR) was observed in CMV diseases. The pulmonary haemorrhage and acute respiratory distress syndromes (ARDS) were the factors of in-hospital mortality in CMV pneumonitis.

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AB0579

## IMMUNOLOGICAL RESULTS OF SALIVARY GLAND BIOPSY AND THEIR RELATIONSHIP WITH CLINICAL AND SEROLOGICAL PARAMETERS IN PRIMARY SJÖGREN'S SYNDROME

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**Background:** Positive minor salivary gland biopsy (MSGB) is a major criteria for the diagnosis of primary Sjögren's Syndrome (PSS). In our centre the MSGB analysis is carried out by Immunology and Pathology Department in parallel. The immunological analysis identifies the lymphocytic composition of the inflammatory infiltrate. Their results show: the number of T and B cells, the ratio between CD4 and CD8 T lymphocytes and other non infiltrating lymphocytes.

**Objectives:** The goal of our study was to evaluate whether there is an association between the lymphocytic composition of the MSGB with the clinical and serological findings of PSS patients.

**Methods:** Patients diagnosed of PSS according American-European criteria (2002) underwent . MSGB between February and November of 2017

Demographic (sex and age), clinical (disease duration, xerostomia, keratoconjunctivitis sicca, Schirmer test, systemic disease) data were collected. Present or previous treatment with steroids and/or immunosuppressive therapy, serological studies such as ANA, RF, anti Ro and anti La were also included. MSGB data with the number of infiltrates, quantitative composition of T and B lymphocytes, CD4/CD8 ratio and presence of other non infiltrating lymphocytes were registered. Pathology data concerning Chisholm-Mason scale, presence of fibrosis, atrophy and size of infiltrate (small, moderate and severe) were also registered. A multiple logistic regression for each item of the immunological analysis adjusted for sex and age was made. We also measured the odds ratio and performed correlation test for all variables included.

**Results:** Table 1 and 2 summarise our cohort characteristics. The presence of T lymphocyte was associated with B lymphocyte, OR 99.21 (IC95% 5.12–1921, p=0.002) and with higher CD4/CD8 ratio, OR 17.34 (IC95% 1.45–206.15, p=0.024). CD4/CD8 ratio was also associated with the presence of T lymphocytes OR 10.54 (IC95% 2.16–51.50, p=0.004) and B lymphocytes were associated with the presence of T lymphocytes as well OR 5.38 (CI95% 1.63–17.72, p=0.006). Other non infiltrating lymphocytes were composed of CD8 T cells and were associated with a positive Schirmer test OR 17.47 (IC95% 1.62–188.13, p=0.018) but inversely associated with Chisholm-Mason grade  $\geq 3$  OR 0.09 (IC95% 0.014–0.58, p=0.011). There was no other association observed with clinical or analytical parameters. Colinearity test between pathological and immunological analysis was negative.

**Abstract AB0579 – Table 1.** Immunology, serological and treatment characteristics of patients with PSS

Variable	Absolute number (percent)	Proportion %
Men	26	45.2%
Systemic disease	34	35.2%
ANA titration		
<1/80	15	25.9%
1/80	10	17.2%
1/160	19	32.4%
1/320	10	17.2%
1/640	7	12.1%
1/1280	3	5.2%
ANA pattern	64	
Speckled	34	53.1%
Homogeneous	13	20.2%
Speck B Homocent	12	18.8%
Others	5	7.8%
Ac. Anti Rn	3	5.2%
Ac. Anti La	0	0
Rheumatoid factor	11	19.0%
Other		
Antiphospholipid Ab	5	8.0%
Choglobulins	2	3.4%
Immunosuppressant	5	8.0%
<4mc	14	24.2%
Immunosuppressant		
>4mc	14	24.2%
Corticosteroids <4mc	8	12.6%
Corticosteroids >4mc	15	25.9%

**Abstract AB0579 – Table 2.** Immunological analysis

Variable	Absolute number (patient)	Proportion %
Number of Infiltrates		
0	3	5.2%
1	32	55.2%
2	6	10.3%
3	16	27.6%
Number of T cells		
<50	11	19.0%
50-90	17	29.3%
90-100	11	19.0%
100-120	2	3.4%
120-150	9	15.6%
>150	8	13.8%
CD4/CD8 Ratio		
0	11	19.0%
1/2	2	3.4%
1/1	3	5.2%
2/1	15	25.9%
3/1	19	32.4%
>3/1	4	6.9%
Number of B cells		
<50	17	29.3%
50-90	11	19.0%
90-100	6	10.3%
100-120	4	6.9%
120-150	9	15.6%
>150	7	12.1%
Other infiltrates		
None	38	65.5%
CD8 cells	19	32.8%
CD4+CD8 cells	3	5.2%
Inadequate sample	1	1.7%

**Conclusions:** MSGB in our PSS patients demonstrated an association between T lymphocytes, B lymphocytes and CD4/CD8 ratio. The infiltrate is mostly based on CD4 more than CD8 T cells. Other significant findings were the association between CD8 T lymphocytes and Chisholm-Mason scale grade  $\geq 3$ , regardless of the number of infiltrates. No correlation or colinearity was observed with the number of infiltrates by immunological analysis and the Chisholm-Mason grade reported by the pathology analysis.

**Disclosure of Interest:** None declared

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AB0580

### CONGENITAL HEART BLOCK AND MATERNAL POSITIVE ANTI-RO AND ANTI-LA AUTOANTIBODIES: A SINGLE CENTRE-STUDY

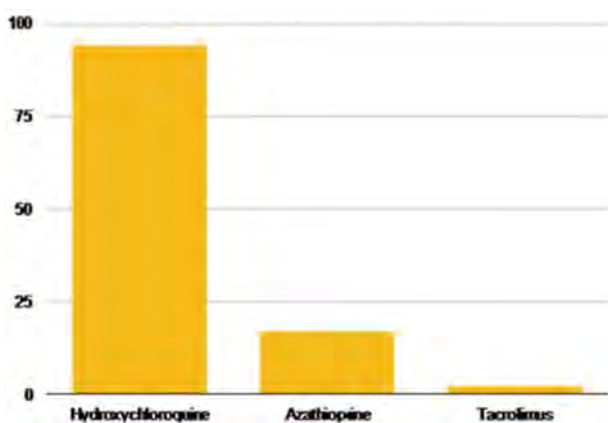
I. Añón Oñate, M.Á. Ferrer González, I. Notario Ferreira, L. Pérez Albaladejo, M. Ramírez de la Torre, S. Quirosa Flores, A. García Sánchez, M.C. Ramírez Barberena, J.M. Andreu Ubero, R. Cáliz Cáliz. *Rheumatology, Hospital Universitario Virgen de las Nieves de Granada, Granada, Spain*

**Background:** The fetal Congenital Heart Block (CHB) is thankfully a rare occurrence. It can develop during pregnancy in women with Rheumatic Diseases who have positive autoantibodies anti-Ro/La.

**Objectives:** To evaluate the efficacy of hydroxychloroquine (HCQ) treatment and the monthly control in a multidisciplinary unit of Rheumatic Diseases and pregnancy on the pregnancy outcomes in women with positive anti-Ro/La.

**Methods:** Descriptive, prospective, longitudinal and open study of 28 pregnant patients with positive anti-Ro/La. They were attended in a specialised multidisciplinary unit of Rheumatic Diseases and pregnancy and 46 pregnancies were developed with no complications. The following variables were collected: age, maternal pathology, presence of anti-Ro52, anti-Ro60 y anti-La, prior abortions, prior babies born with CHB, result of fetal echocardiograms, treatment during pregnancy, obstetric outcomes births/abortion, pregnancy length and maternal/fetal complications.

**Results:** 28 pregnant women were included in the study. 64.3% were diagnosed with Systemic Lupus Erythematosus, 21.4% with Sjögren's syndrome, 10.7% with undifferentiated connective tissue and 3.6% with rheumatoid arthritis. Our patients were an average of  $32.24 \pm 5.34$  years old and the 35% were elder than 35 years. 46 pregnancies were developed during the monitoring with an average of  $1.61 \pm 0.74$  pregnancies per patient. Before the inclusion in our unit, the following fetal history was collected: 1 baby with CHB and 11 abortions. Nevertheless, during the multidisciplinary evaluation and treatment there was no baby developing CHB and only 2 abortions occurred during the first trimester. The positivity of anti-Ro52, anti-Ro60 y anti-La was 89.3%, 32% and 29% respectively. Besides, 2 patients had triple positive autoantibodies and 6 patients double positive autoantibodies. 18% of our patients were diagnosed with lupus nephritis and 29% were diagnosed with secondary antiphospholipid syndrome and/or thrombophilia. The immunosuppressive therapy received during the 46 pregnancies is specified in figure 1. Also, 50% pregnant women received treatment with acetylsalicylic acid, 24% with low-molecular-weight heparin and 41% with corticoid. The mean gestational age was 38 weeks and 11% births were caesarean. 11% babies were preterm with an average birth weight of  $2871.6 \pm 494.8$  grams. 87% of our patients did not have complications in the puerperium. All of our patients were monitored with periodic fetal echocardiograms from the 16th week of gestation and none had a baby with CHB or neonatal lupus (100% of the babies were born healthy).



Abstract AB0580 – Figure 1. Immunosuppressive therapy received during the 46 pregnancies (%)

**Conclusions:** Our results demonstrate that both treatment with hydroxychloroquine and close control in a multidisciplinary unit are effective in the prevention of congenital heart block development, in the decrease in the number of abortions and in a reduction of maternal and fetal morbidity and mortality. The multidisciplinary evaluation is essential in women diagnosed with rheumatic diseases with high obstetric risk.

**Disclosure of Interest:** None declared

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AB0581

### PREGNANCY OUTCOMES IN WOMEN WITH ANTIPHOSPHOLIPID SYNDROME AND THROMBOPHILIA TREATED IN A MULTIDISCIPLINARY UNIT

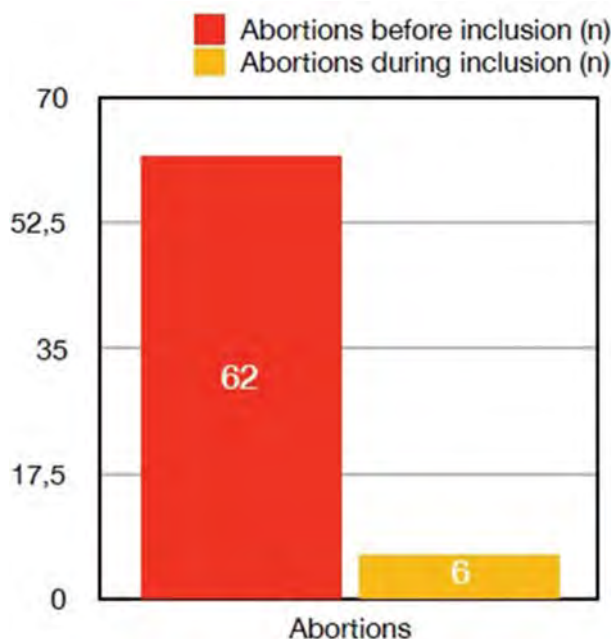
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**Background:** The Antiphospholipid Syndrome (APS) and Thrombophilia predominantly affect women of fertile age, so their pregnancies should be considered high obstetric risk. These pregnant women need close monitoring in a multidisciplinary unit.

**Objectives:** To evaluate the efficacy of the treatment on the pregnancy outcomes of women with APS and thrombophilia from a Spanish cohort.

**Methods:** Descriptive, prospective, longitudinal and open study of 88 pregnant patients with primary and/or secondary APS and thrombophilia assisted in a specialised multidisciplinary unit of Rheumatic Diseases and pregnancy (integrated by Gynaecologists, Haematologists and Rheumatologists). The following variables were collected: age, maternal pathology, presence of antiphospholipid antibodies, thrombotic episodes and prior abortions, number of childbirths, treatment during pregnancy, obstetric outcomes births/abortion and pregnancy length and maternal/fetal complications.

**Results:** 88 pregnant women were included in the study. 44 patients were diagnosed with thrombophilia (mostly, Heterozygotes for MTHFR gene), 33 with primary or secondary APS and 11 patients were diagnosed with both APS and thrombophilia. 140 pregnancies were developed during the monitoring: 61% of women had a single birth, 30% had two births and 5% had three births. Abortions registered before and during inclusion in our unit are specified in figure 1. Before the inclusion in our unit, 52% patients had 1 or 2 abortions, 25% had 3 abortions and 23% had 4 or more abortions. 10% patients had presented a previous thrombosis. Our patients were an average of  $33.6 \pm 5.5$  years old and the 44.3% were elder than 35 years. Among the 44 patients with APS: 50% presented positivity to Lupus Anticoagulant (LA), 25% had triple positive antiphospholipid antibodies (LA, anticardiolipin antibodies and anti-β2-glycoprotein) and 27% had double positive autoantibodies. As for the treatment received during the 140 pregnancies: 50% pregnant women received treatment with prophylactic doses of low-molecular-weight heparin (LMWH) together with acetylsalicylic acid (ASA), 26% were treated in monotherapy with LMWH and 9% in monotherapy with ASA. 10 patients diagnosed with thrombophilia, with an average of  $5.3 \pm 1.5$  abortions per patient, received treatment with LMWH, ASA and intravenous gammaglobulin. All patients who received LMWH during pregnancy also received LMWH after birth for 6 weeks. The mean gestational age was 38 weeks with an average birth weight of  $3058.5 \pm 595.6$  grams. 13% babies were preterm and 32% births were caesarean. 87% of our patients did not have complications in the puerperium.



Abstract AB0581 – Figure 1

**Conclusions:** The treatment is effective in the prevention of abortions. Our results demonstrate a decrease in the number of abortions and a larger number of term pregnancies since the inclusion of patients with high risk pregnancies in our unit. The multidisciplinary evaluation is essential to prevent complications in women diagnosed with APS and thrombophilia in order to reduce adverse pregnancy outcomes and exacerbations of the mother's pathology.

**Disclosure of Interest:** None declared

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**AB0582 SOLUBLE TRIGGERING RECEPTOR EXPRESSED ON MYELOID CELLS-1 (STREM-1) AND ADRENOMEDULIN ARE ELEVATED IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS**

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**Background:** Adrenomedulin is a peptide firstly isolated from human pheochromocytoma with vasodilatory effects. Secretion of adrenomedulin is modified by inflammatory cytokines and it may be important as a suppressor of lupus nephritis activity. Triggering receptor expressed on myeloid cells-1 (TREM) is a member of immunoglobulin superfamily clearly elevated in inflammatory conditions. Some subgroups of patients with systemic lupus erythematosus-SLE may have especially elevated levels of s-TREM.

**Objectives:** The aim of this study was to examine adrenomedulin and s-TREM levels in patients with SLE and healthy controls and to assess their relation with SLE disease activity index-SLEDAI

**Methods:** Serum samples from 50 SEL patients and 40 healthy blood donors were analysed. Serum levels of adrenomedulin, s-TREM, complement components C3 and C3, and anti-dsDNA antibodies were measured

**Results:** Patients with SLE had higher adrenomedulin (9.8±4.5 vs. 15.3±7.2 pg/mL, p<0.05) and s-TREM (11.7±4.1 vs. 20.3±13.1 pg/mL) (p<0.05) levels. s-TREM showed correlation with anti-dsDNA antibodies ( $\rho=0.405$ , p<0.05) and SLEDAI score ( $\rho=0.386$ , p<0.001). In multivariate analysis s-TREM did not appear as an independent predictor of SLEDAI score, while only anti-dsDNA antibodies were significant in multivariate analysis.

**Conclusions:** Increased adrenomedulin and s-TREM are found in lupus sera. Despite of correlation with SLEDAI score, s-TREM is not better than anti-dsDNA antibodies as a predictor of SLE disease activity.

**Disclosure of Interest:** None declared

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**AB0583 NEOPLASIA PREVALENCE IN PRIMARY SJÖGREN'S SYNDROME IN HISPANIC PATIENTS**

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**Background:** A rheumatic disease may be a casual factor in the pathogenesis of a neoplastic disease, as in other cases, cancer may lead to the development of paraneoplastic rheumatic manifestations that may be the only initial symptoms<sup>1</sup>. Lazarus *et al.* demonstrated in its cohort study with 112 patients that of the 22% of patients who developed some neoplasm during the study, the most prevalent was lymphoma with 44%. according to the same study, patients with pss present a risk 37.5 times more than that of the general population. of generating lymphoma, with another risk 2.6 times of developing another type of cancer<sup>2</sup>. it was also shown that in patients with pss there is an incidence of 320 cases per 100 000 a year of presenting non-hodgkin's lymphoma<sup>3</sup>. In our country there are no epidemiological studies to know the prevalence of cancer in patients with pss, so these numbers are difficult to estimate

**Objectives:** Determine the prevalence of cancer in patients with ss in the mexican population.

**Methods:** Cross-sectional, observational study was conducted in which 393 patients were included, of which 221 (52%) came from the national institute of medical sciences and nutrition "salvador zubiran", 92 (23.4%) from the university hospital "José E González" and 80 (20.6%) of the Juárez Mexico hospital/ABC medical centre whom fulfilled the diagnosis of ssp according to the 2002/2012 criteria of the american college of rheumatology/european league against

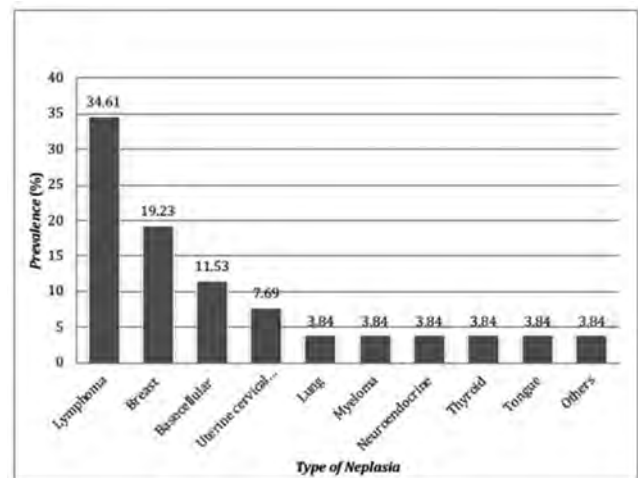
rheumatism. Bivariate analysis was performed, normality was demonstrated using the K.S test, the student's T test was used for the numerical variables and the chi2 test for the categorical ones, and no difference was found between the characteristics of patients with or without cancer.

**Results:** We include 393 patients, the majority were women (n=377, 95.9%) with an average age of 56.4 (±13.60), of these 23 (5.85%) had some type of neoplasm regardless of their malignancy. the most prevalent was lymphoma with 9 cases (34.6%), followed by breast cancer with 5 (19.2%), 3 (11.5%) of basal cell cancer and 2 (7.7%) cases of cervical uterine cancer

**Abstract AB0583 – Table 1.** Demographic characteristics in Patients with Primary Sjögren Syndrome (n:393)

	Neoplasia	No neoplasia	P
Age years, mean(SD)	61.57 (15.40)	56.10 (13.44)	0.519
Female gender, n(%)	23 (100%)	354 (95.7%)	0.309
Positive Anti-Ro/SSA, n(%)	15 (71.4%)	238 (64.7%)	0.528
Positive Anti-La/SSB, n(%)	9 (42.9%)	168 (46.3%)	0.760
Positive Schirmer test, n(%)	15 (78.9%)	245 (83.9%)	0.572
Abnormal NSWSF, n(%)	12 (63.2%)	215 (77.1%)	0.169
Positive GSM biopsy, n(%)	18 (81.8%)	276 (77.1%)	0.607
Use of glucocorticoids, n(%)	9 (45%)	131 (36.2%)	0.426
Use of hydroxychloroquine, n(%)	6 (28.6%)	167 (46.1%)	0.116
Use of methotrexate, n(%)	3 (15%)	74 (20.4%)	0.555
Another immunosuppressive agent, n(%)	5 (21.7%)	76 (20.5%)	0.890

NSWSF: non-stimulated whole salivary flow, MSG: Minor salivary gland



**Abstract AB0583 – Figure 1.** Neoplasia prevalence in primary sjögren syndrome in Mexican-Mexitzo patients

**Conclusions:** We confirmed lymphoma as the most prevalent neoplasia in a cohort of non-Caucasian pSS patients. We observed the presence of non-hematological malignancy 60.86% of our patients, whether it risk is increased in pSS population still needs to be addressed.

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AB0584

**PAEDIATRIC VS ADULT ONSET SYSTEMIC LUPUS ERYTHEMATOSUS: THE SIMILARITIES AND DIFFERENCES; A STUDY FROM A TERTIARY CARE CENTRE FROM NORTHERN INDIA** \*;+

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**Background:** Systemic lupus erythematosus (SLE) is a chronic autoimmune disease with myriad of systemic features. While the disease manifestations and therapy remain same for both paediatric onset(cSLE) and adult onset SLE (aSLE), disease manifestation and burden of disease differs in the two populations.

**Objectives:** To study disease profile within 6 months of disease onset and burden of disease by SLEDAI of aSLE and cSLE to understand the similarities and differences and to compare with those from around the world

**Methods:** Retrospective review done of 100 aSLE and cSLE patients, from June 2015 to June 2016, fulfilling SLICC criteria. Demographic data, clinical profile and ds burden at onset(highest of 1st 6 mths of ds onset) by SLEDAI 2K were recorded on a predesigned proforma

**Results:** The incidence of skin involvement (acute and chronic cutaneous lupus, alopecia) serositis more in aSLE. Oral mucositis, neuropsychiatric SLE(NPSLE) and lupus nephritis(LN) more common in cSLE.LN was also higher in cSLE from other centres around the world as compared to aSLE. Of statistical significance were non SLICC features like fatigue, Raynaud phenomenon and fatigue in aSLE. cSLE significantly differed in higher incidence of non SLICC features like fever, vasculitic rash and in laboratory features like leucopenia, low complements, dsDNA positivity and antiphospholipid antibody(APLA) positivity. Although APLA antibodies were frequent in cSLE, thrombotic events were rare. On the other hand, thrombotic events were significantly associated with aSLE. Median SLEDAI at onset was higher in cSLE than aSLE. The higher incidence of LN in CSLE than aSLE was similar from the inception cohort from Toronto.<sup>1</sup>The mean SLEDAI at onset was also similarly higher in cSLE. The spanish SLE registry also reported similar findings.<sup>2</sup>

Abstract AB0584 – Table 1

Data at onset	aSLE(n=100)	cSLE(n=100)	P value	SLICC FEATURES	aSLE(%)	cSLE(%)	p value
Male/ Female	15/85	24/76	0.15	Acute cutaneous lupus	67	55	0.11
Median Age at onset	34 (β - 71)	9.5 (3.4 - 17.4)	-	Chronic cutaneous lupus	07	05	0.77
Median Age at diagnosis(years)	35 (β - 71)	10.25 (3.5 - 19.0)	-	Mouth ulcer	46	55	0.26
Median delay to diagnosis(years)	1 (0 - 15)	0.75 (0 - 5.33)	-	Alopecia	63	57	0.47
Fever	57	82	0.0002 *	Arthritis	47	65	0.015 *
Fatigue	88	57	0.0001 *	Serositis	23	13	0.097
Weight loss	47	33	0.06	Pleural effusion/pericardial effusion	20	11	0.12
RP	39	09	0.0001 *	Lupus nephritis	26	36	0.17
Myalgia	42	52	0.20	NPSLE	13	24	0.068
Vasculitic rash	04	29	0.0001 *	Leukopenia	07	29	0.0008 *
Lymphadenopathy	27	48	0.0034 *	Thrombocytopenia	32	21	0.11
SLEDAI (mean)	12.9	16.59	-	ANA positivity	100	99	1.0
Thrombosis	18	01	0.0001 *	Anti-dsDNA positivity by IF	47	77	0.0001 *
				Anti-5M	24	13	0.068
				Anti-cardiolipin antibody	09	21	0.028 *
				LAC	09	22	0.018 *
				Low complements	41	82	0.0001 *
				DAT positivity	31	33	0.88

**Conclusions:** This study showed significant difference in initial systemic involvement and onset of presentation in aSLE and cSLE.cSLE present with more subtle features and seldom have a classic presentation with malar rash, oral mucositis and alopecia which oft herald aSLE. cSLE and aSLE though being the same disease often have a varied spectrum of presentation and the generalist and the treating teams need to be aware of these for prompt recognition of the disease and optimum therapy

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AB0585

**A LUPUS LOW DISEASE ACTIVITY STATE IS ASSOCIATED WITH REDUCED FLARE, LOWER ORGAN DAMAGE ACCRUAL, AND BETTER QUALITY OF LIFE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS**

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**Objectives:** To identify the potential predictors of a lupus low disease activity state (LLDAS), and the relationship between LLDAS and disease flare, organ damage, and quality of life in Korean patients with systemic lupus erythematosus (SLE).

**Methods:** The study followed 181 SLE patients from a single centre for three years. LLDAS was defined as follows:<sup>1</sup> SLE Disease Activity Index (SLEDAI)–2K≤4, with no activity in major organ systems;<sup>2</sup> no new lupus disease activity compared with the previous assessment;<sup>3</sup> SLEDAI Physician Global Assessment≤1;<sup>4</sup> a current prednisolone (or equivalent) dose ≤7.5 mg daily; and<sup>5</sup> well-tolerated standard maintenance doses of immunosuppressive drugs. We assessed data annually and divided 4 groups according to the number of LLDAS; LLDAS=0, 1, 2, and 3. Univariate and multivariate analyses were performed to identify predictors of LLDAS.

**Results:** Of the 181 patients, 16.0% attained LLDAS on three consecutive years. Each group shows as follows; no LLDAS (n=30), LLDAS=1 (n=60), LLDAS=2 (n=62), and LLDAS=3 (n=29). The patients who had higher number of LLDAS had shorter duration of symptoms, lower anti-histone antibody positivity, lower cumulative prescribed dose of prednisolone at baseline, lower mean PGA, lower mean SLEDAI, lower mean Mental Component Summary in SF-36, lower change in SLICC/ACR damage index, and a lower frequency of flare. In the multivariate analysis, LLDAS was significantly associated with lower mean PGA (OR=0.671, 95% CI: 0.112–0.989, p=0.019) and a reduced risk of flare after adjusting for confounders (OR=0.012, 95% CI: 0.001–0.448, p=0.017).

**Conclusions:** Attaining LLDAS was associated with an improved outcome, as represented by a decreased rate of disease flare, lower organ damage accrual, and better quality of life in Korean patients with SLE.

**Disclosure of Interest:** None declared  
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AB0586

**CURRENT IMPACT OF ETHNICITY ON RENAL HISTOLOGY AND OUTCOME OF LUPUS NEPHRITIS**

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**Background:** Lupus Nephritis (LN) remains a serious complication of Systemic Lupus Erythematosus (SLE) and continuous worldwide demographic changes as well as new mechanistic insights and treatment options necessitate regular updating of our knowledge of LN.

**Objectives:** To investigate the current relevance of demographic, clinical and histological characteristics as outcome predictors in patients with Lupus Nephritis.

**Methods:** A retrospective single centre cohort study of all SLE patients undergoing a first renal biopsy for LN evaluation between 1997–2017 in a metropolitan hospital in Western Australia with a 750,000 catchment area. Demographic, laboratory and treatment data were collected at baseline and at last follow-up using a predefined form and histological findings (ISN class) were re-evaluated. Kaplan Meier survival estimates for patient and renal survival were tested by log-rank test.

**Results:** The final study cohort included 90 SLE patients (age 31.5 years, 88% female, time since SLE diagnosis 0.3 years.) of Caucasian (n=42), Asian (n=30), Aboriginal (n=11) and other ethnicity (n=7, mainly SubSaharan Africans). The annual LN incidence estimate was 0.6/100,000. There were no significant differences across subgroups regarding renal (overall median 14) and nonrenal SLEDAI (median 4) scores, proteinuria (median PCR 300 mg/mmol), presentation with raised serum creatinine (31% overall), anti-dsDNA Ab (89%) or hypocomplementemia (88%) or presence of proliferative (Class III/IV: 66%) or membranous (Class V:19%) LN. Corticosteroid (86%), immunosuppressive (87% overall) and



antihypertensive drug (69%) use were similar across ethnic subgroups (all  $p > 0.2$ ). After a mean follow-up of 95 months, eight patients (9%) had died, six (7%) received renal replacement therapy and five (6%) had developed CKD. Five and ten years patient survival was similar for Asian and Caucasian patients (95%) and poorest in Aborigines (81% and 70%) ( $p = 0.016$ ) with no impact of gender, ISN class, full house IF findings or PCR  $> 300$ . Renal 5 and 10 year survival (endpoint RRT) was 100% for Asian, 100% and 96% for Caucasian vs 86% and 64% for Aborigines ( $p = 0.02$ ). PCR  $> 350$  predicted worse renal survival ( $p = 0.03$ ), which was not influenced by gender, increased baseline creatinine, ISN class, A/AC/C subclass or presence of full house IF deposits.

**Conclusions:** Asian patients have similar clinical and histological LN findings and experience equally good renal and patient outcomes as Caucasian patients in Western Australia, where the incidence rate of LN is comparable with Europe. Whether the grim outlook for Aboriginal patients relates to intrinsic differences in LN pathophysiology and/or socioeconomic circumstances deserves further study.

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AB0587

#### HAEMATOLOGICAL ALTERATIONS IN COLOMBIAN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Systemic Lupus Erythematosus (SLE) is an autoimmune disease, with multiple organs and system involvement. The most usual haematological findings are anaemia, leukopenia, and thrombocytopenia. The prevalence of SLE in Colombia was 8.77 per 10 000 persons between 2012 and 2016<sup>1</sup>.

**Objectives:** To evaluate the haematological alterations in a cohort of patients with SLE in Bucaramanga, Colombia.

**Methods:** A retrospective cohort study of 149 patients diagnosed with SLE according to the Systemic Lupus International Collaborating Clinics (SLICC) criteria. Descriptive analysis with frequencies, measures of central tendency and dispersion was done using Stata 12.0 software. The primary outcome was the presence of cytopenia, the secondary outcomes were anaemia, leukopenia, and thrombocytopenia. In the group comparison analysis, a chi-square test was used for qualitative variables and Wilcoxon or T student test for quantitative variables according to their distribution. Bivariate analysis using logistic regression with OR measurement,  $p$ -value, and confidence intervals was performed.

**Results:** 82.5% were women, average age was 36.8 years. The primary outcome was found in the 79.8%, anaemia in the 76.5%, thrombocytopenia in the 22.1% and leukopenia in the 18.7%. In group comparison analysis (cytopenia vs no cytopenia) a statistical difference was found in the variables sex ( $p = 0.023$ ), skin involvement ( $p = 0.003$ ), acute pneumopathy ( $p = 0.050$ ), activity of the disease measured by the ECLAM scale ( $p = 0.037$ ) and anti-DNA antibody titers ( $p = 0.032$ ). In the bivariate analysis, there was an increased risk of cytopenias with statistical significance in male patients (OR: 3.82), ECLAM score greater than 5 (OR: 4.75) and strongly positive anti-DNA antibodies (OR: 3.97). Regarding leukopenia, there was an association with antiphospholipid syndrome (OR: 2.75), ECLAM greater than 5 (OR: 2.51), SLEDAI MEX greater than 10 (OR: 2.35) and strongly positive anti-DNA antibodies (OR: 2.36). Likewise, an increased risk of mortality was found in patients with leukopenia (OR: 3.92). In the case of thrombocytopenia, an association was found with a pericardial alteration (OR: 2.46), ECLAM greater than 5 points (OR: 3.65), SLEDAI MEX greater than 10 points (OR: 2.42). An association with mortality was also observed (OR: 2.97). The risk of presenting anaemia was increased with the variables man (OR: 4.4), ECLAM greater than 5 points (OR: 3.14) and strongly positive anti-DNA antibodies (OR: 3.25).

**Conclusions:** This is the first Colombian study that evaluates haematological alterations in patients with SLE. The most frequent cytopenia was anaemia. It is possible to identify variables that can predict the appearance of cytopenia, such as the increase in the activity of the disease, which is susceptible to intervention. It is noteworthy that both leukopenia and thrombocytopenia are markers of mortality in patients with SLE.

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AB0588

#### IDENTIFICATION OF RISK FACTORS FOR HERPES VIRUS INFECTIONS WITH IMMUNOPHENOTYPING DURING INDUCTION THERAPY IN PATIENTS WITH ACTIVE LUPUS NEPHRITIS

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**Background:** Herpes virus infections (HVIs) including cytomegalovirus infections (CMVs) and herpes zoster (HZ) remains as major complications during treatments with immunosuppressant (IS) in patients with autoimmune diseases.<sup>1, 2</sup> Previous reports have suggested the associations between virus infections and characteristics of T cells.<sup>3, 4</sup>

**Objectives:** To elucidate the characteristics of peripheral immune cells associated with risk factors of HVIs during induction therapies in patients with active lupus nephritis (LN).

**Methods:** Standardised peripheral immunophenotyping was performed using flow cytometry in active LN and ANCA-associated vasculitis (AAV) patients starting induction therapy and also with inactive LN patients with maintenance therapy between April 2015 to April 2017. The definition of HVIs was the infection necessary to administer anti-viral agents.

**Results:** Sixty-two LN patients and 11 AAV patients were enrolled. Among 30 active LN patients, 27 were analysed except for 3 patients (2 died and 1 withdrawn consent). Mean age was 41.7 years, 9 patients (33%) had newly-onset, and mean SLE disease activity index (SLEDAI) was 19.3. All active LN patients were treated with prednisolone (PSL) (mean 51.7 mg/day) and 25 were treated with an additional IS (cyclophosphamide [CYC];13, mycophenolate mofetil;8, tacrolimus;3, rituximab [RTX];1). Six (22.2%) patients developed HVIs (5 CMVs and 1 HZ) within 3 months following induction therapy. None of the 32 LN patients in maintenance phase (mean age, 54.8; SLEDAI, 2.5; PSL 2.5 mg/day) developed HVIs during the mean 2.8 years-observational period. Two (18.2%) AAV patients developed HVIs within 3 months following induction therapy. All AAV patients (mean age, 64.3) were treated with PSL (mean 41.8 mg/day) and 10 with IS (CYC;5, RTX;3, azathioprine;1, methotrexate;1).

Among active LN patients, univariate analysis revealed that older age, lower proportions of naïve CD8 +T cells, higher proportions of effector CD8 +T cells and HLA-DR +regulatory T cells (Tregs) at baseline and lower naïve CD8 +T cells at month 3 associated with HVIs ( $p = 0.011$ ,  $p < 0.001$ ,  $p = 0.009$ ,  $p = 0.024$ ,  $p < 0.001$  respectively). Unexpectedly, lymphocyte count, IgG titer, usage of CYC at baseline, renal response and change in SLEDAI at month 3 did not associate with HVIs. Multivariate analysis revealed that low proportions of naïve CD8 +T cells and high proportions of HLA-DR +Tregs at baseline were the only detectable independent risk factor for HVIs ( $p = 0.014$ ).

Among AAV patients, univariate analysis showed that older age, lower proportions of naïve CD8 +T cells, higher proportions of Tregs at baseline associated with HVIs. However, multivariate analysis showed no independent risk factor for HVIs among them.

**Conclusions:** Our results suggest that active LN patients with low proportion of naïve CD8 +T cells and high HLA-DR +Tregs at the time of induction therapy should be closely monitored for HVIs. The different results between LN and AAV implicated the different risks of HVIs by immunophenotyping. Larger prospective study is desired to confirm our results.

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AB0589

### RELEVANCE OF B AND T CELL SUBSETS TO LUPUS FLARE IN KOREAN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Systemic lupus erythematosus (SLE) is a systemic autoimmune disease with heterogeneous clinical manifestations and is characterised with autoreactive T cells and autoantibody overproduction by activated B cells.

**Objectives:** The aims of this study were to characterised T-cell and B-cell subpopulation phenotype in Korean patients with SLE, and to elucidate the association between lymphocyte subpopulation and lupus activity.

**Methods:** We used multicolor flow cytometry to analyse subsets of peripheral blood B-cells (defined by CD19, IgD, CD27, and CD38) and T-cells (CD3, CD4, CD8, CD45RA, CCR7) in 26 patients with SLE and 22 age- and sex-matched healthy subjects. Baseline and 6 month follow-up SLE disease activity index (SLEDAI) was recorded, and SLEDAI score  $\geq 6$  was considered as lupus flare-up. Lymphocyte phenotype was also compared between stable disease and lupus flare-up.

**Results:** The number of B cells and CD8 +T cells were not different between SLE patients and healthy subjects; however, non-switched memory (NSwM) B cells was decreased in SLE patients. Double negative (DN) T cells, CD4 +T cells and its subset [naïve, central memory (CM), effector memory (EM) and terminally differentiated effector memory (TEMRA) cells] were decreased in SLE patients compared to healthy controls. Patients with lupus flare-up showed significantly decreased CD4 +and DN T cells, whereas CD4 +EM T cells were increased in patients with lupus flare up, compared to stable SLE. SLEDAI was correlated with DN T cells ( $\rho = -0.728$ ,  $p < 0.001$ ), CD4 +CM T cells ( $\rho = -0.544$ ,  $p = 0.004$ ), CD4 +EM T cells ( $\rho = -0.697$ ,  $p < 0.001$ ) and CD8 +EM T cells ( $\rho = -0.408$ ,  $p = 0.039$ ). Six (23%) patients experienced lupus flare and a patient presented still high disease activity at 6 month follow-up visit. Interestingly, these patients showed the low number of DN T cells, CD4 +EM and TEMRA cells at baseline when they were stable.

**Conclusions:** Biased differentiation of T-cells was associated with lupus flare and aggravation of SLE 6 months later. Understanding T cell subset enables accurate stratification of lupus flare-up and personalised approach.

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AB0590

### A VALIDATION STUDY OF THE PREGNANCY MORBIDITY QUESTIONNAIRE(PMQ) IN WOMEN WITH ANTIPHOSPHOLIPID ANTIBODIES AND PREGNANCY MORBIDITY

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**Background:** The presence of antiphospholipid antibodies (aPL) are associated with pregnancy complications. There is a lack of validated pregnancy

questionnaires to assess previous pregnancy morbidity reliably in aPL positive patients. We therefore designed the pregnancy morbidity questionnaire (PMQ).

**Objectives:** To validate the pregnancy morbidity questionnaire (PMQ) in the prospective Vienna Lupus Anticoagulant and Thrombosis Study (LATS) cohort.

**Methods:** The Vienna Lupus Anticoagulant and Thrombosis Study (LATS) is an ongoing, single-centre, biobank-based, prospective observational cohort study enrolling patients (age >18 years) who are persistently positive for lupus anticoagulant (LA) (two positive tests at least 12 weeks apart) with or without a history of thrombosis or pregnancy complications<sup>1</sup>. The cohort currently consists of 150 patients (mean age: 41.3 years, female gender: n = 122 (81.3%), history of thrombosis or pregnancy complications: n = 111 (74.0%)). Of these 150 women, 15 were approached at their follow up visit and invited to fill out the PMQ. The PMQ consists eight questions outlined in table 2.

**Results:** Twelve women agreed to participate, of whom nine had a previous history of pregnancy and/or pregnancy complications. Patient characteristics are shown in table 2. PMQ results are outlined in table 2.

Abstract AB0590 – Table 1

Patient Characteristics (N=9)	
Age at the time of questionnaire, mean (SD, range)	58 (+/-13.6, 25-86)
Years since last pregnancy, mean (SD, range)	35 (+/- 10, 20-58)
Lupus anticoagulant positive only	5 (25%)
Antiphospholipid syndrome	2 (10%)
Pregnancies (N=20)	
Maternal age at pregnancy, mean (SD, range)	24.5 (+/- 4.3, 18-33)
Live-birth rate	17/20 (85%)
Gestational age, weeks (SD, range)	34.8 (+/- 11, <10-24)
Birthweight, kg (SD, range)	3.2 (+/- 0.5, 2.2-4)
aPL related early pregnancy loss (<10 weeks)	2 (10%)
aPL related preterm delivery (<34 weeks)	1 (5%)
aPL related preterm delivery due to placental insufficiency	1 (5%)
Aspirin taken during pregnancy	0 (0%)
Heparin taken during pregnancy	0 (0%)

Key: SD, standard deviation

Abstract AB0590 – Table 2. Pregnancy questionnaire results

	Correct answer, validated against cohort info	Detailed answer, but not captured on cohort entry	Incorrect answer
Q1: Pregnancy date	20 (100%)	0%	0%
Q2: Live birth	20 (100%)	0%	0%
Q3: Gestational age at delivery	9 (45%)	11 (55%)	0%
Q4: Weight at delivery	1 (5%)	19 (95%)	0%
Q5: aPL related pregnancy complications	18 (90%)	0%	2 (10%)
Q6: Aspirin during pregnancy	20 (100%)	0%	0%
Q7: Heparin during pregnancy	20 (100%)	0%	0%
Q8: Other medications during pregnancy	20 (100%)	0%	0%

**Conclusions:** Our aim was to validate the PMQ in the prospective Vienna Lupus Anticoagulant and Thrombosis Study (LATS) cohort. Patients were able to recall their pregnancy history in great detail over a period of more than three decades. Our PMQ may provide a tool to assess previous pregnancy morbidity in patients with antiphospholipid antibodies.

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**AB0591 SLE RES PONDER INDEX (SRI) UNDERESTIMATES CLINICAL RESPONSE IN MUSCULOSKELETAL SYSTEMIC LUPUS ERYTHEMATOSUS**

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**Background:** Musculoskeletal (MSK) manifestations are common in SLE. Many recent clinical trials were negative or had small benefits vs. placebo. SRI is a common primary endpoint but has not been independently validated. Ultrasound is an objective measure of synovitis validated in inflammatory arthritis.

**Objectives:** To compare the responsiveness of clinical outcome measures with ultrasound in MSK-SLE.

**Methods:** 20 SLE patients meeting SLICC 2012 criteria with inflammatory MSK symptoms were studied with clinical assessment (BILAG2004, SLEDAI-2K over 30 days, patient and physician VAS, symptomatic, tender and swollen joint counts in 28 joints) and MSK ultrasound (grey scale and power Doppler scores, number of abnormal joints) at 0, 2, and 4 weeks after 120 mg IM depomedrone. Change in each variable was measured using Wilcoxon matched pairs and effect sizes ( $r=Z/\sqrt{2N}$ ) compared using Cohen (1988) criteria. Changes were compared for SRI-4 responders and non-responders.

**Results:** All patients were ANA positive, CCP negative and female. At baseline, 15/20 had clinical synovitis. The others had either ultrasound synovitis (GS in 18/20, PD in 17/20) or >60 min EMS. 19/20 patients scored 4 points on SLEDAI for musculoskeletal involvement, BILAG scores were A in 7/20, B in 8/20, and C in 5/20. MSK-SLEDAI score improved in 9/20 at 4 weeks, MSK-BILAG improved in 16/20. For changes, see table 1.

**Abstract AB0591 – Table 1**

		No. pairs	P	Z	Effect Size r	Cohen Criteria	
<b>Week 0 – Week 2</b>	PhysVAS	16	0.001	-3.409	-0.603	Large	
	GS Score	16	0.002	-3.13	-0.571	Large	
	US Joints	16	0.011	-3.160	-0.559	Large	
	PD Score	16	0.002	-3.099	-0.548	Large	
	SymJC	10	0.047	-1.988	-0.445	Medium	
	Pt VAS	16	0.016	-2.409	-0.426	Medium	
	SJC	16	0.059	-1.889	-0.334	Medium	
	TJC	15	0.274	-1.093	-0.200	Small	
	<b>Week 0 – Week 4</b>	PhysVAS	20	<0.001	-3.388	-0.593	Large
		MSK BILAG	20	0.008	-3.643	-0.576	Large
PD Score		20	<0.001	-3.627	-0.573	Large	
US Joints		20	0.001	-3.627	-0.573	Large	
GS Score		20	<0.001	-3.503	-0.554	Large	
MSK-SLEDAI		20	0.003	-3.000	-0.474	Medium	
TJC		20	0.007	-2.683	-0.424	Medium	
SymJC		14	0.010	-2.576	-0.487	Medium	
SJC		20	0.007	-2.425	-0.383	Medium	
PtVAS		20	0.020	-2.331	-0.369	Medium	

19 patients with MSK-SLEDAI=4 at baseline were grouped into SRI-4 responders (n=9) and non-responders (n=10). There were large effect sizes for improvement in TJC and SJC in responders ( $r=-0.505$  and  $-0.492$  respectively) and medium effect sizes in non-responders ( $-0.365$  and  $-0.331$ ). For ultrasound, large effect sizes for improvements in both grey scale and power Doppler were observed in both responders ( $r=-0.517$  and  $-0.564$ ) and non-responders ( $r=-0.629$  and  $-0.596$ ).

**Conclusions:** In MSK-SLE, ultrasound was the variable most consistently sensitive to change. All commonly used clinical variables significantly improved by week 4 but there was variation in responsiveness between them. BILAG-2004 and physician VAS had similar responsiveness to ultrasound. SRI-4 underestimated response, with substantial objective improvements in synovitis in SRI-4 non-responders. Developing organ-specific outcome measures may improve the ability to measure treatment effects in SLE clinical trials.

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**AB0592 IMPAIRMENT IN HAND STRENGTH, DEXTERITY AND ACTIVITIES OF DAILY LIVING PERFORMANCE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: RESULTS OF A CROSS-SECTIONAL STUDY**

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**Background:** Systemic lupus erythematosus (SLE) is a prototypic autoimmune disease affecting multiple systems. To date a small number of studies have assessed the hand function and performance of daily activities in SLE<sup>1</sup>.

**Objectives:** To examine the grip and pinch hand strength, the dexterity, and the performance of Activities of Daily Living (ADL) in SLE patients compared with healthy controls.

**Methods:** 197 SLE patients (48,03±12,76, 88,3% female) and 100 healthy controls (47,87±12,77, 86% female), matched by age and gender, were enrolled in the study. Both groups were assessed by hand grip and pinch grip strength, dexterity and ADL performance tests. Hand grip strength was measured by Jamar dynamometer, and pinch grip strength by pinch gauge, in both hands. Dexterity was measured by purdue pegboard test. Disabilities of the Arm, Shoulder and Hand (DASH) questionnaire and Health Assessment Questionnaire (HAQ) were used in order to determine the difficulties in ADLs.

**Results:** Hand grip strength, both lateral and jaws pinch grip strength, and dexterity, were significantly impaired ( $p<0,001$ ) in both hands of SLE patients compared to healthy subjects (table 1). DASH questionnaire (19.78±20.93 vs 2.43±2.9,  $p<0,001$ ) and Health Assessment Questionnaire score (HAQ) (0.41±0.52 vs 0.03±0.52,  $p<0,001$ ) were also significantly different between SLE patients and healthy controls.

**Abstract AB0592 – Table 1**

	Right Hand			Left Hand		
	Patient group	Control group	P value	Patient group	Control group	P value
Grip Strength	25.59 ±9.12	30.89 ±9.00	<0.001	24.54 ±9.80	29.56 ±9.21	<0.001
Tip to tip Pinch Strength	3.94±2.03	4.25±1.66	0.194	3.45±1.73	4.11±1.55	0.002
Lateral Pinch Strength	6.03±2.12	7.24±1.85	<0.001	5.52±1.98	6.66±1.93	<0.001
Jaws Pinch Strength	4.68±1.99	5.86±1.93	<0.001	4.37±1.94	5.62±1.80	<0.001
Purdue Score	13.09 ±2.58	14.28 ±2.58	<0.001	12.42 ±2.16	13.10 ±2.30	<0.001

All values are presented as mean ±SD

**Conclusions:** These findings demonstrate that SLE patients have lower grip, pinch strength and dexterity and more difficulties in ADL performance. These findings underline the need to develop specific hand therapy programs for SLE patients.

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AB0593

### PREDICTORS OF FATIGUE AND SEVERE FATIGUE IN A LARGE MULTICENTER INTERNATIONAL COHORT OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: THE FATILUP STUDY

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**Background:** Fatigue is an important issue in systemic lupus and has a major impact on quality of life of the patients. Data are controversial about the factors associated with this complex symptom.<sup>1</sup>

**Objectives:** To identify the factors associated with fatigue and severe fatigue in patients with systemic lupus erythematosus (SLE) in a large cohort using a multivariate model to precise the importance of each parameter in this multidimensional symptom.

**Methods:** We used the LBBR data base, a German French data base of SLE patients. All patients fulfilled the 1997 ACR criteria for SLE. The Fatigue Scale for Motor and Cognitive Functions (FSMC) was used to assess fatigue and severe fatigue. The depression and anxiety were measured with Hospital Anxiety and Depression Scale (HADS). Tests were performed at sampling.

**Results:** A total of 570 patients were included (89.1% female). The median age was 42 years (QR25–75: 34–52). The median value of the SELENA-SLEDAI was 2 (QR25–75: 0–4) and 136 patients had a SELENA-SLEDAI score >6. Fatigue was reported by 386 patients (67.7%) including severe fatigue by 209 (36.7%). In univariate analysis among the individual components of the SLEDAI arthritis (p=0.003) and oral ulcers (p=0.002) were associated with severe fatigue.

In multivariate analysis fatigue was strongly associated with anxiety (OR: 4.49 [95%CI: 2.60–7.77], p<0.0001) and depression (OR: 4.72 [95%CI: 1.39–16.05, p=0.01]. It was also associated with age at sampling (OR: 1.01 [95%CI: 1.00–1.03, p=0.03] per 1 year increase), SLEDAI (OR: 1.05 [95%CI: 1.00–1.12, p=0.043] per 1 SLEDAI point increase) and glucocorticoids treatment (OR: 1.54 [95%CI: 1.00–2.38, p=0.04]). It was not associated with physical activity.

Severe fatigue was strongly associated with depression (OR:6.87 [95%CI: 3.12–15.11], p<0.0001) and anxiety (OR: 3.80 [95%CI: 2.46–5.87], p<0.0001) but not with SLEDAI or physical activity.

**Conclusions:** Fatigue is a common symptom in SLE patients and is strongly associated with anxiety and depression. While remission remains an important therapeutic target, these manifestations should also be taken care of with psychological counselling and pharmacological intervention, when needed.

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AB0594

### PREVALENCE OF FRAGILITY FRACTURES IN WOMEN WITH SLE, THEIR CONNEXION WITH THE COURSE OF THE DISEASE AND THE NATURE OF PHARMACOTHERAPY

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**Background:** Patients with rheumatic diseases are known to have the risk of osteoporosis and fragility fractures, which is significantly higher than in the healthy population. Recent studies demonstrate that age, sex, postmenopausal status, inactivity, glucocorticoid use, nutrition etc. play an important role in the reduction of bone mineral density (BMD) in systemic lupus erythematosus (SLE) patients. The role of the disease severity and the activity of the inflammatory process in the reduction BMD and the incidence of fractures in SLE patients is discursive.

**Objectives:** The aim of the study was to determine the frequency of osteoporosis and fragility fractures in the Ukrainian SLE patients and to establish their connexion with the course of the disease.

**Methods:** The main study group involved 91 women with a diagnosis of SLE according to the American College of Rheumatology criteria. The disease activity was determined using the SLE Disease Activity Index (SLEDAI), and organ damage was measured using the Systemic Lupus International Collaborating Clinics American College of Rheumatology (SLICC/ACR) Damage Index. In all patients the cumulative dose of glucocorticoids was calculated. Serum CRP and IL-6 levels were determined by immunoassay. BMD at the lumbar spine (L1–L4) and femoral neck were measured using dual-energy X-ray absorptiometry. For premenopausal SLE patients BMD by Z-score <−2.0 SD was defined as «below expected range for age». For postmenopausal women osteoporosis was defined by T-score ≤ −2.5 SD, and osteopenia – between −1.0 and −2.5 SD. To determine fractures female SLE patients were examined with x-ray.

**Results:** In premenopausal SLE patients the abnormal BMD of the lumbar spine was found in 9.8%, at the level of the femoral neck it was in 11.1%, in postmenopausal SLE patients – 18.4 and 13.6%, respectively. In the control group there was any premenopausal woman with low bone mass at both sites, whereas among postmenopausal individuals, these were 12.5 and 6.2%, respectively. Osteoporotic fractures were detected in 13 (14.2%) SLE patients, of which 30.7% had hip fractures and 69.3% had vertebral fractures. The reduction of bone strength and fractures were associated with a high damage index. In particular, in persons with fractures it equaled to 4.85±0.65 points, and in persons without fractures – 3.09±0.22 points. A similar tendency was detected by the disease activity SLEDAI. Glucocorticoid use also had a negative effect on the bone strength in patients with SLE. Thus, in women with fractures, the cumulative dose of glucocorticoids defined 60.9±6.63 g, and was by 37.1% higher than in patients without fractures.

**Conclusions:** In patients with SLE the prevalence of low BMD and fragility fractures is high. Progressive loss of the BMD and the occurrence of osteoporotic fractures are closely associated with the severity of organ damage and glucocorticoid use.

**Disclosure of Interest:** None declared

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AB0595

### ANTIPHOSPHOLIPID SYNDROME (HUGHES SYNDROME) IS A DISEASE WITH PROTEAN FACES: MULTIDISCIPLINARY APPROACHES ON SERBIAN COHORT OF APS PATIENTS

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**Background:** Antiphospholipid syndrome (APS) is a systemic autoimmune disease characterised by thrombophilic state and circulating antiphospholipid antibodies (aPL) including anti beta2-GPI.

**Objectives:** Since than it became one of the most systemic conditions. In the last three and half decades, a variety of clinical manifestations involving almost all organs and tissues (cardiac, pulmonary, neurological, renal, cutaneous, hematologic, gastrointestinal, ocular, skeletal and endocrinology), have been described associated with antiphospholipid antibodies (aPL).

**Methods:** Our study comprises a total of 608 patients: 420 primary APS (PAPS) patients and 188 SLE patients with secondary APS (SAPS). aPL analysis included detection of aCL, aβ2GPI, and LA.

**Results:** Thrombosis was diagnosed in 46.5% patients, with higher prevalence in PAPS compared to SAPS patients: 51.2% and 38.3%, respectively, p=0.045. Pseudo-infective endocarditis was observed in 12.8% secondary APS patients and 3.1% in primary APS patients (p=0.004). 30% of the patients with high levels of aCL IgG antibodies had valve thickening and dysfunction, as compared to 4.1% without valve abnormalities (p=0.002). Presence of β2GPI IgG was significantly related to stroke, and overall β2GPI (IgG and IgM) positivity was significantly related to TIA in SAPS patients. Valvular manifestations were significantly related to TIA in both groups of patients and were independent risk factors for TIA in PAPS (OR 3.790 CI 1.597–8.998 p=0.003: table 2). In PAPS, epilepsy correlated with β2GPI-IgM, migraine with aCL-IgM, thrombocytopenia with aCL-IgM, aCL-IgG, anti β2GPI-IgG and LA. Livedo reticularis was more prominent in PAPS with high levels of aCL-IgG. Skin ulcerations were more prevalent in aCL-IgM positive SAPS patients and epilepsy more frequently had high levels of anti β2GPI-IgG in SAPS.

**Conclusions:** In this cross-section analysis of a large cohort of APS patients we analysed that APS patients can be presented with a wide variety of thrombotic

and nonthrombotic manifestations. The key the success is multidisciplinary approach in all time of patient's life. Antiphospholipid syndrome is really a disease with protean faces.

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#### AB0596 THE IMMUNE COMPLEXES OF IGG/IGM BOUND TO B-2-GLYCOPROTEIN I ARE ASSOCIATED WITH LIVEDO RETICULARIS, THROMBOCYTOPENIA AND SICCA IN APS PATIENTS

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**Background:** Several manifestations strongly associated with APS have been excluded as classification criteria.<sup>1,2</sup>

**Objectives:** The aim of this study was to investigate correlation between circulating immune-complexes of IgG or IgM antibodies bound to B2GPI (B2G-CIC and B2M-CIC) and clinical manifestations in Serbian cohort of APS patients.

**Methods:** A total of 57 patients with APS were evaluated: 35 with PAPS and 22 patients with SAPS. Mean age was 47.6±1.6 years; 36 (63.2%) were women. All patients have met the 2006 revised Sydney criteria for APS. Quantification of B2G-CIC and B2M-CIC levels was performed as previously, for detect B2G-CIC was used anti-human IgG HRP-conjugate and for B2M-CIC human IgM HRP-conjugate, both from INOVA (INOVA Diagnostics Inc., San Diego, CA, USA).

**Results:** In our cohort Serbian APS patients the prevalence of CIC was 19.29% (11/57); 8 patients with B2M-CIC and the remain 3 patients with B2G-CIC. Livedo reticularis was diagnosed with higher prevalence in patients with CIC compared with patients without CIC; 63.6% and 23.9%, respectively (OR: 5.57, p=0.01). In patients with CIC, thrombocytopenia and leukopenia were more prominent; 54.4% vs 17.4% (OR: 5.70, p=0.01) and 45.5% vs 13.0% (OR: 5.56, p=0.01), respectively. Ophthalmic sicca was more prevalent in patients with CIC; 54.4% vs 8.7% (OR: 12.6, p<0.001). Although complement consumption was more frequent in patients with CIC (figure 1).

Figure 1. Mean levels of C3 (A) and C4 (B) complement in groups. Mean levels of C3 (115.6±9.2 mg/dL and 140.9±4.3 mg/dL, group-1 and group-2 respectively) and mean levels of C4 (140.9±4.3 mg/dL and 30.8±1.6 mg/dL, group-1 and group-2, respectively).

**Conclusions:** B2G-CIC and B2M-CIC are strongly associated with clinical manifestations related to APS. Widening the APS spectrum is indispensable to better understand this syndrome.

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AB0597

#### CHANGES IN THE THYROID HORMONES IN PATIENTS WITH SJOGREN'S SYNDROME IN DOMINICAN REPUBLIC

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**Background:** Sjogren's syndrome (SS) is an autoimmune chronic where there is a B-cell activation and lymphocytic infiltration of exocrine glands, this can be primary or secondary and characterised by xerostomia, xerophthalmia and extraglandular manifestations<sup>1</sup>. Thyroid involvement is frequent in patients with SS sharing histological and antigenic characteristics<sup>2</sup>. 10–24% of patients with SS have thyroid involvement, the most common are Hashimoto's thyroiditis or Grave's disease are the most frequent autoimmune syndromes. Some reports indicated that Hashimoto's Thyroiditis and Grave's disease has an incidence of 4.2% and 3.4% in the patients with SS respectively. A study showed that in patients with SS 45% had changes in the values of thyroid hormones and 24% autoimmune thyroiditis.<sup>3-5</sup>

**Objectives:** Determine the changes in the thyroid hormones in patients with Sjogren's syndrome.

**Methods:** A cross-sectional study. The information was collected from the digital records of Hospital Docente Padre Billini Rheumatology department during the period October 2017-January 2018. Inclusion criteria: age ≥18 years old, patients with Sjogren's syndrome according to ACR/EULAR 2016 criteria. Excluded patients who did not thyroid test during the study and patients who have a thyroid disorder under treatment. The data was analysed using SPSS V23 Windows 10.

**Results:** 79 cases were reviewed, of which 51 met the inclusion criteria. 98% were women, average age of 45 years, 9.8% had hypothyroidism and 3.9% hyperthyroidism by laboratory tests. 82.3% were euthyroid. 82.3% had anti Ro and anti La, 96% Schirmer test + and 37.2% positive biopsy report for SS.

**Conclusions:** In our study, we found that 9.8% of patients with Sjogren's syndrome could be associated with subclinical hypothyroidism and 3.9% with hyperthyroidism what can mask the clinical manifestations at the time of diagnosis. The screening in high-risk patients such as patients with autoimmune disorders remains important.

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AB0598

#### SIGNIFICANCE OF NON CRITERIA ANTI-PHOSPHOLIPID ANTIBODIES IN THE PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS ASSOCIATED WITH ANTIPHOSPHOLIPID SYNDROME

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**Background:** Systemic Lupus Erythematosus (SLE) is a chronic inflammatory autoimmune disease in which the uncontrolled activation of the immune system leads to overproduction of autoantibodies (Ab) with different mechanisms of action. Coexistence of anti-phospholipid antibodies (aPL) significantly increases the risk of thromboembolic complications and worsens the clinical course and prognosis of SLE.

**Objectives:** The aim of study was to determine the relationship between the presence of non-criteria aPLs in SLE patients with criteria and non-criteria clinical symptoms of APS.

**Methods:** The study involved 70 (52-female and 18-male) patients treated in the Department of Rheumatology and Connective Tissue Diseases. All patients fulfilled the SLICC classification criteria of SLE. 46/70 pts fulfilled clinical and laboratory criteria of Antiphospholipid Syndrome (I group SLE/APS-46pts) and 24/70 pts (II group SLE/aPL (+) -24) -they had criteria antibodies but did not display clinical criteria symptoms of APS. In the whole study group the mean age was: 38,5±12,9 years (range 18–71), the duration of the disease was 8,3±6,5 years (range 0–37). The presence of Ab was detected in patients' serum using the commercially available tests: aPL-immunodot assay Anti-Phospholipid 10 Dot, for the qualitative detection of IgG or IgM antibodies. Statistical data analysis was performed using Statistica v13.0

**Results:** In the study group of 70 patients we detected the presence of the following aPLs: a-cardiolipin IgM -33,7%, IgG -50%; a-phosphatidic acid IgM -17,5%, IgG -11,2%; a-phosphatidylcholine IgM and IgG -0; a-phosphatidylethanolamine IgM and IgG -0; a-phosphatidylglycerol IgM -4,4%, IgG -10%; a-phosphatidylinositol IgM-11,2%, IgG-10%; a-phosphatidylserine IgM-31,2%, IgG-48,7%; a-annexin V IgM -20%, IgG -10%; a-b2-GP I IgM-33,7%, IgG-30%; a-prothrombin IgM -51,4%, IgG-30%.

The following non-criteria clinical symptoms of APS were present: nephropathy in 27,1%, hypertension-41,1%, livedo reticularis 11,4%, convulsions/chorea-5,7%, thrombocytopenia- 20% of the study group.

No statistically significant differences in the frequency of occurrence of individual non-criteria aPLs, as well as non-criteria clinical symptoms of APS have been found in the examined subgroups of SLE/SAPS and SLE/aPL (+) patients.

**Conclusions:** The prevalence of non-criteria aPLs in SLE and APS pts is similar to pts with SLE with criteria- aPL. Non-criteria clinical symptoms of APS occurred with the same frequency in pts with SLE and APS and in SLE with criteria aPL.

**Disclosure of Interest:** None declared

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#### AB0599 RELATION BETWEEN THE DEFICIT/DEFICIENCY OF VITAMIN D AND THE DEPRESSION/ANXIETY IN PATIENTS WITH LUPUS IN THE DEPARTMENT OF RHEUMATOLOGY OF THE HOSPITAL OF CLINICS

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**Background:** It has been postulated that low concentrations of 25-hydroxivitamin D serum [25 (OH) D] is associated with a greater prevalence of depression. People with deficient levels of vitamin D are more likely to experience mood disorders such as depression and anxiety. The vitamin D plays a role in the release of neurotransmitters such as serotonin and dopamine which is why is interesting the study of this in patients with systemic lupus erythematosus, who are discouraged from sun exposure.

**Objectives:** Determine the association between the deficit/insufficiency of vitamin D and the anxiety/depression in patients with SLE of the Department of Rheumatology of the Hospital de Clínicas

**Methods:** Observational study of longitudinal court based in a questionnaire according to the scale HADS (*Hospital anxiety and Depression Scale*) and the dosages of vitamin D performed on patients who entered the LUPUS PY cohort with prior informed consent. The dosage of vitamin D realised by chemiluminescence. Data and samples were taken in week 0 and week 24 and the prevalence of depression and anxiety and its association with vitamin D deficiency and insufficiency were identified. Patients with vitamin D deficiency or insufficiency were supplemented with vitamin D. For the descriptive analysis of the quantitative variables, average and SD were used, for the qualitative frequencies and percentages. For the analysis of association the test  $\chi^2$  was used. The value of the p considered statistically significant was less than 0,05.

**Results:** In relation to the characteristics of the studied cohort, we can see that 90.5% were female, with an average age of 33±10.2 years. At week 0 the average value of vitamin D concentration was 31.8±10.2 ng/ml. It is found that 4,48% of patients had depression and 33,69% of patients have anxiety. In the week 24 the value of the average of vitamin D was of 31,1±13,6 ng/ml. It was observed in this week that 6% of patients presented depression and 12% of patients anxiety. In the analysis of association there was no association between vitamin D deficits and the presence of depression or anxiety of these patients both at the week 0 as a week 24 post vitamin D supplementation such, and as seen in table 1.

**Abstract AB0599 – Table 1.** Deficit and insufficiency of vitamin D associated with the depression and anxiety in patients with SLE.

	Deficit/insufficiency of Vit D	Depression	P value
Week 0	35(47,29%)	3 (4,48%)	0,287
Week 24	33(44,59%)	4 (6%)	0,092
	Deficit/insufficiency of Vit D	Anxiety	P value
Week 0	35(47,29%)	14 (33,69%)	0,287
Week 24	33(44,59%)	8(12%)	0,092

**Conclusions:** A significant percentage of patients with deficient or insufficient vitamin D were found, as well as a considerable percentage had depression or anxiety, although no association was found between the state of this vitamin and the alterations of the studied mood. More studies are required that include more patients in order to obtain more conclusive results.

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**Disclosure of Interest:** None declared

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#### AB0600 RELEVANCE OF OPHTHALMOSCOPIC EVALUATION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: UNDERESTIMATION OF INTRAOCULAR PRESSURE VALUES

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**Background:** The evaluation of the size of the optic nerve papilla in ophthalmoscopy is an important tool for the diagnosis of glaucoma in individuals who do not present elevated intraocular pressure (IOP) levels. The calibration of the IOP is performed through Goldmann's tonometry, which consists of flattening the central cornea with a tonometer. Patients with Systemic Lupus Erythematosus (SLE) have circulating autoantibodies and immunocomplexes that alter corneal biomechanics, resulting in underestimated IOP values.

**Objectives:** To evaluate the IOP values and the presence of increased excavation in patients with SLE, reinforcing the importance of ophthalmoscopy in this population.

**Methods:** Descriptive study. Analysis of IOP measurement and papillary excavation of 50 SLE patients.

**Results:** All patients had IOP values within the normal range (8–21 mmHg). In a total of 100 eyes evaluated, four (4%) had increased papillary excavation.

**Conclusions:** Type I collagen is essential for the maintenance of biomechanical parameters and resistance of the cornea. At the corneal level, the activation of the complement system results in the lysis of type I collagen fibres, reducing corneal thickness and resistance. Therefore, IOP values for tonometry will be reduced and underestimated. Comparing the IOP values of SLE patients and healthy volunteers, there are lower results ( $p < 0.001$ ) in lupus patients. In the present study, no patient had IOP changes. However, 4% of the eyes revealed increased excavation. These findings reflect the results of Yazici et al, and reinforce the importance of ophthalmoscopy in the screening of glaucoma in SLE patients.

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**AB0601**    **ENTHESES ULTRASONOGRAPHY IN TUNISIAN PRIMARY SJÖGREN'S SYNDROME PATIENTS**

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**Background:** Primary Sjögren's Syndrome is an auto-immune disease characterised by dryness of the eyes and the oral cavity. Musculoskeletal manifestations are common. However, the underlying mechanism remains often unknown.

**Objectives:** The aim of the current study was to describe subclinical enthesal involvement in patients with Primary Sjögren's Syndrome via ultrasound, to calculate a modified Madrid sonography enthesitis index and to compare it with a group of healthy controls.

**Methods:** The study was conducted in the rheumatology department of Mongi Slim hospital in Tunisia, between June 2015 and December 2017, including 25 patients with Primary Sjögren's Syndrome and 25 healthy sex- and age-matched controls. Cases were defined according to the American-European Consensus Criteria for Sjögren's Syndrome. All the included subjects underwent an enthesal ultrasound exploration (EsaoteMyLab 60 machine and a 13–18 MHz linear array transducer) by a rheumatologist experienced in ultrasound. Five enthesal locations bilaterally (distal Achilles tendon, distal and proximal patellar ligaments, distal quadriceps, and brachial triceps tendons) in each patient were explored. The following elemental lesions of enthesal were evaluated: thickening, presence of calcifications, erosions, enthesophyte, loss of fibrillar pattern and power Doppler signal. The calculated index was compared by Mann-Whitney U test between cases and controls. The significance level was set at 5%.

**Results:** In our study population, the median age was 53.2±11.3 years and the median body mass index was 29.±6.4 kg/m<sup>2</sup>. All included subjects were female. The ultrasound abnormalities in the Primary Sjögren's Syndrome were as follows: erosions in 19.2% of cases, enthesophytes in 16.4% of cases, calcifications in 6% of cases, hypoechogenicity in 2.8% of cases, thickening in 2.4% of cases, power Doppler signal in 1.6% of cases and loss of fibrillar pattern in 1.2% of cases. The total enthesitis index was 4,96±2,59 among cases and 5,72±2,92 among healthy control subjects with no statistically significant difference. Considering each affected enthesal, cases had no significantly higher scores than controls.

**Conclusions:** Our study did not find a significant enthesal involvement among patients with Primary Sjögren's Syndrome that could explain the chronic indefinable pain. The diagnosis of an associated fibromyalgia should be kept in mind.

**Disclosure of Interest:** None declared

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**AB0602**    **ANTIPHOSPHOLIPID SYNDROME COMPONENTS IN PATIENTS WITH CORONARY HEART DISEASE**

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**Background:** Antiphospholipid antibodies (aPL), such as anticardiolipin antibodies (aCL), are the immunological markers of the antiphospholipid syndrome (APS).<sup>1</sup> The aPL are found in association with venous and/or arterial thrombosis. Myocardial infarction (MI) is usually related to atherosclerosis and thrombosis of coronary arteries.<sup>2</sup> The clinical significance of aPL in MI, however, has not yet been well established.

**Objectives:** To evaluate the presence and levels of aPL in patients with history MI.

**Methods:** 50 patients (100% male) with average age 49.5±6.09 (M±SD) years with history of MI were examined. Serum IgG aPL (anti-cardiolipin, -phosphatidylserine, phosphatidylinositol, -phosphatidylacetate) were determined by enzyme-linked immunosorbent assay (ELSSA).

**Results:** IgG isotype aPL were detected in 26 (52%) patients with the history of MI and 24 patients were negative.

The average age (M±SD) of aPL positive patients was 44.1±5.00 years and of aPL negative patients was 47.7±4.83 years (p<0.01). The difference comprises more than 3,5 years.

Patients with recurrent MI (two and more) had higher level of IgG aPL, then patients with one MI (18,0±7,53 v.s. 11,5±4,21 GPL-U/ml). The difference is significant (p<0.05).

**Conclusions:** Determined younger age of the first MI in aPL positive patients and higher level of IgG aPL in patients with recurrent MI indicate the possible involvement of the autoimmune factor in the pathogenesis of MI. This proves the necessity for further research in this direction.

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**AB0603**    **FRAGMENTED QRS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: RELATION TO THE DISEASE ACTIVITY: A CROSS-SECTIONAL STUDY**

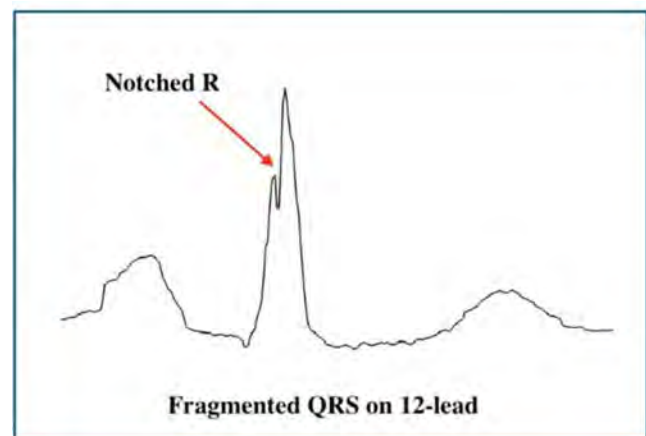
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**Background:** Cardiovascular disease is an important contributor to mortality in Systemic Lupus Erythematosus (SLE)<sup>1</sup>. Fragmented QRS (fQRS) is an easily evaluated non-invasive electrocardiographic parameter defined as additional spikes within the QRS complex<sup>2</sup>. fQRS can represent conduction disturbance and a predictor of cardiac events<sup>3</sup>. Even in a patient with SLE, it has reported that the prevalence of fQRS appears to be higher than in controls<sup>4</sup>. However, no clinical studies have investigated the prevalence at the time of diagnosis. In addition, there is no report that examined the association of disease activity of SLE and fQRS.

**Objectives:** This study aimed to assess the relationship between disease activity of SLE and fQRS in Japanese SLE patients at the time of diagnosis. We hypothesised that the frequency of fQRS on ECGs would be greater in SLE patients with high disease activity.

**Methods:** The study design was a cross-sectional study. The participants were SLE patients who diagnosed at Showa University Hospital and Showa University Koto Toyosu Hospital from January 2010 to December 2017. The participants who satisfied American College of Rheumatology (ACR) criteria were included. The patients with already treatment at the time of an ECG measurement, cardiovascular disease, history of arrhythmia, cardiomyopathy, rheumatoid arthritis, systemic sclerosis were excluded. The exposure was the appearance of fQRS. The primary outcome was Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K). The secondary outcomes were the complement level, the ds-DNA antibody level and the organ involvement. In the main analysis, a multiple regression analysis was conducted to assess the association between fQRS and SLE activity adjusted for age, sex and period from the estimated date of onset to the date of diagnosis. In the secondary analysis, a multiple regression analysis was conducted to analysis the association between fQRS and the serological activity of SLE (the complement level, the ds-DNA antibody level) and the organ involvement under the same conditions as above.

**Results:** In total, 45 participants were enrolled. The mean age was 42.3 years, and 37 (82%) were female. The median SLEDAI-2K was 14 [IQR, 10 to 20]. The median period from the estimated date of onset to the date of diagnosis was 3 months [IQR, 2 to 14.5]. 25 patients (56%) had fQRS. In the main analysis, the regression coefficients [95% CI] of fQRS for SLEDAI were 2.99 [ 1.15 to 4.84, p=0.002 ] with reference to non-fQRS. In the secondary analysis, there were no significant associations between fQRS and the blood test or the organ involvement.



**Abstract AB0603 – Figure 1**

**Conclusions:** Our results demonstrated that the frequency of fQRS on ECGs would be greater in SLE patients with high disease activity.

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AB0604

#### INITIAL CLINICAL AND IMMUNOLOGICAL FACTORS ASSOCIATED WITH MANIFESTATIONS IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME: A SINGLE CENTRE RETROSPECTIVE STUDY

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**Background:** Primary Sjögren's syndrome (pSS) is a prototypical systemic autoimmune disease that manifests various signs and symptoms. Although a few studies have focused on these manifestations over the long term,<sup>1,2</sup> the association of initial clinical and immunological factors with subsequent longer-term manifestations has not been fully elucidated.

**Objectives:** To identify initial clinical and immunological factors associated with manifestations in patients with pSS.

**Methods:** A retrospective review was performed on pSS patients followed over a 10 year period at our department. Clinical and immunological data, including levels of serum immunoglobulin (Ig) and autoantibodies, were collected and statistically analysed.

**Results:** A total of 224 patients diagnosed with pSS who had met the classification criteria<sup>3</sup> were enrolled. Among them, 201 patients were diagnosed with pSS at our hospital. Of these, we followed the 91 patients who continued to visit our hospital over 10 years. Of the other 110 patients, 69 suddenly interrupted treatment, 20 visited different hospitals, and 13 interrupted treatment at our department and visited dentistry or ophthalmology departments. During observation, 7 patients were newly diagnosed with rheumatoid arthritis in addition to SS and one patient died.

We then analysed the 91 patients who continued to visit. Of these, 88 were female and 3 were males. Average age was 52 years. 72 and 33 patients had anti-SS-A antibody and rheumatoid factor (RF). 82, 68 and 7 patients had neutropenia, anaemia and thrombocytopenia, respectively. 15% of patients used corticosteroid and/or immunosuppressant treatment. 10% of patients took traditional Chinese medicine. On follow-up for 10 years, titers of IgG, A and M were significantly decreased, whereas complement levels were elevated. The proportion of patients with extraglandular involvement decreased from 90% to 73%, whereas 14% of patients had new extraglandular organ involvement. The frequency of extraglandular involvement at 10 years was high in patients with hyper IgG at the initial test (39% vs 85%,  $p < 0.01$ ). The frequency of extraglandular organ involvement at 10 years was high in patients who were RF-positive at diagnosis (3% vs 15%,  $p < 0.05$ ). 9% of patients developed malignancies. 29% of patients without RF at the initial test had RF during the 10 years observation. The presence of dry eyes or mouth findings did not change during follow-up in pSS patients.

We then created a multivariate model of predictors for malignancies, extraglandular involvement and extraglandular organ involvement with possible variables at diagnosis. Age, anti-centromere antibody, hyper IgG and anaemia were identified to be significant variables associated with malignancies. Extraglandular involvement was associated with the presence of hyper IgG ( $p < 0.01$ ), and extraglandular organ involvement was associated with RF positivity ( $p < 0.05$ ).

**Conclusions:** Our study newly identified initial clinical and immunological factors associated with manifestations in patients with pSS over a long period. pSS patients with RF and hyper IgG at diagnosis were candidates for the development of extraglandular involvements in the future.

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AB0605

#### PROCALCITONIN MIGHT BE USED FOR DISCRIMINATING INFECTIONS FROM INCREASED DISEASE ACTIVITY IN PRIMARY SJÖGREN SYNDROME

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**Background:** Procalcitonin is a polypeptide which is secreted as a response to bacterial stimulus and accepted as an early and sensitive marker of infection. In healthy subjects procalcitonin should be  $< 0.1$  ng/mL. In case of infection it may rise over 0.5 ng/mL. Its level in inflammatory diseases usually does not reach to such high levels as in infections. Differentiating infection and disease activation may be confusing in autoimmune diseases. For this purpose, there were several studies that evaluated the role of procalcitonin for excluding infection on suspicion of increased autoimmune disease activity.<sup>2</sup>

**Objectives:** As far as we know, there is no study in literature that evaluated procalcitonin levels in patients with primary Sjögren's syndrome (pSS). Our aim is to evaluate procalcitonin levels in pSS and determine whether we can use it as a marker to differentiate infection from disease activation.

**Methods:** The following two groups of patients were included in the study: Forty-eight patients with pSS, who met ACR<sup>2012</sup> Classification Criteria for Sjögren's Syndrome; and fifty-three subjects as control group who have no chronic diseases. Patients with possible infection were excluded according to their clinical evaluation and laboratory data. Then, serum procalcitonin levels were compared between the groups. Finally, we evaluated the correlation between disease activity, measured by Sjögren's syndrome disease activity index (SSDAI) and procalcitonin levels.

**Results:** Procalcitonin levels in pSS group were found statistically higher than control group, whereas it was still in normal ranges ( $p < 0.01$ ). Furthermore, no correlation was found between disease activation and the procalcitonin levels ( $p = 0.63$ ).

**Abstract AB0605 – Table 1.** Demographic properties and Laboratory results of the subjects

	Sjögren (n=48)	Control (n=53)	p
Gender(M/F)	3/45	2/51	0.66
Age	53,50 (48,50–58,75)	50,00 (43,50–55,00)	0.04
Sedimentation (mm)	22,00 (12,00–31,75)	18,00 (11,00–27,00)	0.13
CRP (mg/dl)	3,27 (3,27–3,27)	3,27 (3,16–3,27)	0,16
SSDAI score	1,00 (1,00–2,00)	N/A	
Procalcitonin(ng/ml)	0,036 (0,031–0,044)	0,020 (0,020–0,020)	<b>&lt;0,01</b>
Haemoglobin (gr/dl)	12,50 (11,65–13,50)	12,80 (11,95–13,50)	0,82
Thrombocyte( $10^3$ / $uL$ )	231,00 (189,50–278,00)	265,00 (226,5–304,50)	<b>0,02</b>
WBC (/uL)	6000,00 (5400,00–7200,00)	6700,00 (5450,00–8000,00)	0,15
Creatinine (mg/dl)	0,66 (0,59–0,76)	0,57 (0,52–0,62)	<b>&lt;0,01</b>
ALT (U/L)	18,5 (13,25–25,00)	18,00 (13,50–25,00)	0,74
AST(U/L)	22,50 (19,00–25,00)	21,00 (17,50–25,50)	0,30

Statistically significant P values were shown bold. Numerical variables were summarised by median [interquartile range]

**Conclusions:** Procalcitonin levels were found higher in pSS patients. But, none of the patients had clinically significant increase in procalcitonin. We thought that with careful clinical evaluation, procalcitonin would be an indicator for differentiating infection from disease activation in pSS patients.

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**AB0606 NEUROPSYCHIATRIC LUPUS IN A SAMPLE OF EGYPTIAN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: PREVALENCE AND CLINICAL CHARACTERISTICS**

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**Background:** Neuropsychiatric (NP) lupus is common among patient with systemic lupus erythematosus (SLE). It occurs in about 30%–56% of all SLE patients. However, the diagnosis of neuropsychiatric SLE (NPSLE) remains difficult. Neuropsychiatric lupus (NPL) can present with a wide variety of clinical manifestations.

**Objectives:** The aim is to determine prevalence of NPSLE among a sample of Egyptian SLE patients from a single centre and to describe its features and characteristics.

**Methods:** The study included 301 adult SLE patients from Cairo University Hospital. The patients are classified according to the Systemic Lupus International Collaborative Clinics (SLICC) criteria for SLE. Neuropsychiatric manifestations were recorded using the ACR NPSLE nomenclature and case definitions (1999) Global disease activity was quantified by the SLE Disease Activity Index 2000 (SLEDAI-2K) at first and at last visit of the patient. Systemic Lupus International Collaborative Clinics/ACR Damage Index (SLICC/ACR-DI) was used to measure damage. The period of data collection took 4 months. The collected data included demographic, clinical, serologic data and medications.

**Results:** 301 SLE patients (87.4%) females and (12.6%) males with mean age 30.7±9.2 years and disease duration 72 months (2–288) were included. 101 (33.5%) were diagnosed as having NPSLE. The highest NP manifestation in frequency is headache (55.4%) followed by psychosis (33.7%) then seizures (21.8%). NP manifestation is the onset of the disease in 42.6% of all NPSLE patients. Compared to non-NPSLE group, NPSLE group is significantly older at onset of disease and have longer disease duration ( $p<0.05$ ). They are significantly more active at the onset of the disease than non-NPSLE and have significantly more disease damage ( $p<0.05$ ). Regarding clinical manifestations of lupus; NPSLE are significantly higher in frequency of discoid rash, cutaneous vasculitis, serositis, secondary anti-phospholipid syndrome (APS), associated avascular necrosis of the joints and osteoporosis ( $p<0.05$ ). Anti-cardiolipin IgM antibodies are significantly more frequent in NPSLE group ( $p<0.05$ ). Notably, frequency of psychosis, superior sagittal thrombosis and cerebrovascular disease were significantly higher in NPSLE with positive APS than those with negative APS ( $p<0.05$ ).

**Conclusions:** NPL is common in SLE, its prevalence is about 30% in Egyptian SLE patients. NPSLE patients may present diverse clinical manifestations most commonly headache, psychosis and seizures. NPL is different from non-NPL and presence of APS has an impact on clinical presentation of NP involvement in the patients.

**Disclosure of Interest:** None declared

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**AB0607 CLINICAL PROFILE OF FILIPINO PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS**

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**Objectives:** To determine the clinical profile of Filipino SLE patients as determined using the 2012 Systemic Lupus Collaborating Clinics (SLICC) criteria.

**Methods:** We checked which among the SLICC criteria were fulfilled by Filipino SLE patient when we examined them and their case records, as part of a nationwide genetic study on SLE conducted from October 2015 to March 2017.

**Results:** Two hundred twenty-five patients who were diagnosed to have SLE after 18 years of age were evaluated. The mean age of the population at the time of evaluation was 37.76 years.

Females comprised 98% of our population. Mean age of onset was 30.68-year-old, while the mean age at diagnosis was 31.52-year-old. Acute cutaneous rash was found in 82%; arthritis

80%; non-scarring alopecia 65%; oral ulcers 52%; renal disorder 41%; chronic cutaneous rash in

28%; leukopenia 23%; hemolytic anaemia 17%; thrombocytopenia 16%; serositis 13%; and neurologic disorder 6%. Anti-nuclear antibody was present in 88%; low complement 33%; antidsDNA in 29%; direct Coombs' 4%; antiphospholipid antibody 2%; and anti-Smith antibody in

2%. Kidney biopsy was performed in only 6% (15/225) of patients, 33% of whom had Class IV histopathologic results.

**Conclusions:** Filipino SLE patients typically present with acute cutaneous rash, arthritis, non-scarring alopecia and oral sores. Renal disorder, hematologic and

neurologic manifestations are found to be less common among them. Finally, it was noted that renal biopsy is not commonly performed among these patients.

**Disclosure of Interest:** None declared

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**AB0608 CLINICAL PROFILE OF FILIPINO PAEDIATRIC PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS**

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**Background:** The clinical profile of paediatric SLE patients may present differently from that of adults.

**Objectives:** To determine the clinical profile of Filipino paediatric SLE patients as determined using the 2012 Systemic Lupus Collaborating Clinics (SLICC) criteria.

**Methods:** We checked which among the SLICC criteria were fulfilled by Filipino paediatric SLE patient when we examined them and their case records, as part of a nationwide genetic study on SLE conducted from October 2015 to March 2017.

**Results:** Ninety-eight who were diagnosed to have SLE before 18 years of age were evaluated.

The mean age of the population at the time of evaluation was 19.77 years. Females comprised

94% of our population. Mean age of onset was 14.42-year-old, while the mean age of diagnosis was at 14.58-year-old. Acute cutaneous rash was found in 87%; oral ulcers 65%; renal disorder

65%; non-scarring alopecia 61%; arthritis 58%; chronic cutaneous rash in 37%; leukopenia 36%; hemolytic anaemia 34%; serositis 24%; thrombocytopenia 22% and neurologic disorder 8%.

Anti-nuclear antibody was present in 88%; low complement 33%; anti-dsDNA in 28%; direct

Coombs' 16%; antiphospholipid antibody 3%; and anti-Smith antibody in 1%. Kidney biopsy was performed in only 14% (15/104) of patients, of whom 27% had class III histopathologic characteristic.

**Conclusions:** Filipino paediatric SLE patients typically present with cutaneous, mucocutaneous renal and musculoskeletal involvement. Hematologic and neurologic manifestations are found to be less common among them. Finally, it was noted that renal biopsy is not commonly performed among these patients.

**Disclosure of Interest:** None declared

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**AB0609 CORRELATION BETWEEN PLASMA LIPOPROTEIN PHOSPHOLIPASE A2 (LP-PLA2) AND ANTI PHOSPHOLIPID ANTIBODY (APL-AB) IN PATIENTS WITH CONNECTIVE TISSUE DISEASES**

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**Background:** Plasma Lp-PLA2 has both anti-inflammatory and pro-inflammatory activity in vascular-related pathologies and is an independent risk predictor for coronary heart disease and stroke because of its important role in atherosclerosis and thrombosis. However, vasculitis is a common pathological feature of connective tissue disease.

**Objectives:** Therefore, the aim of this study was to investigate the association of plasma Lp-PLA2 level with antinuclear antibody (ANA) titer, karyotype, anti-cardiolipid antibody (ACA) and anti-β2GP1 antibody and lupus anticoagulant (LA, including PT-IgG and PT-IgM).

**Methods:** Outpatient and inpatient with connective tissue diseases from Department of Rheumatology of the Third Affiliated Hospital of Sun Yat-sen University from 2015 to 2016 were randomly selected. Venous blood was collected, plasma Lp-PLA2 level was measured by Elisa method. ANA titer and karyotype were detected by indirect immunofluorescence assay. ACA, anti-β2GP1 antibody, PT-IgG and PT-IgM were detected by Elisa method. SPSS23.0 statistical software was used for statistical analysis.

**Results:** A total of 176 patients with connective tissue disease including 38 males (21.59%) and 138 females (78.41%) were enrolled in this study, and the average age was 42.22±17.31 years. The mean plasma level of Lp-PLA2 was (363.96±203.19 ng/ml). There was no significant difference in Lp-PLA2 level between different genders ( $p=0.072$ ), and LP-PLA2 level have no correlation with age ( $p=0.098$ ). The ANA titers were classified as negative (35.80%), weakly positive 1: 100 (11.93%), positive 1: 100 (18.75%), positive 1: 320 (12.50%), positive 1: 1000 and positive 1: 3200 (9.66%). There was no significant difference in plasma Lp-PLA2 level between different titers of ANA ( $p=0.088$ ). ANA karyotypes



included nucleolus type (0.88%), centromere type (3.54%), cytoplasm type (7.96%), homogeneity (29.20%) and granularity (58.41%). Also, there was no significant difference in plasma Lp-PLA2 level between different karyotypes ( $p=0.153$ ). The average level of ACA was  $12.88\pm 23.87$  RU/ml and there was no significant correlation between plasma Lp-PLA2 level and ACA level ( $p=0.839$ ). Anti- $\beta$ 2GP1 antibodies were classified as negative ( $<20$  U/ml, 91.48%) and positive ( $\geq 20$  U/ml, 8.52%). Plasma Lp-PLA2 level did not differ significantly between anti- $\beta$ 2GP1 antibody negative and positive patients ( $p=0.449$ ). Lupus anticoagulant PT-IgG and PT-IgM were classified as negative ( $<18$  U/ml) and positive ( $>18$  U/ml). PT-IgM were all negative and there was no significant difference in plasma Lp-PLA2 level between PT-IgG negative (96.59%) and positive (3.41%) patients ( $p=0.279$ ).

**Conclusions:** Plasma Lp-PLA2 level in patients with connective tissue disease have no significant correlation with age, gender, ANA titer, karyotype, ACA, anti- $\beta$ 2GP1 antibody and LA. The role of plasma Lp-PLA2 in connective tissue disease may be different from APL-Ab.

**Disclosure of Interest:** None declared

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AB0610

#### CORRELATION BETWEEN TRADITIONAL CARDIOVASCULAR RISK INDEXES AND ARTERIAL STIFFNESS IN PATIENTS WITH GENERALISED LUPUS ERYTHEMATOSUS

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**Background:** Cardiovascular disease (CVD) is the leading cause of late death in patients with systemic lupus erythematosus (SLE). SLE is related with up to 50 fold risk of CVD. SLE is recognised as an independent cardiovascular risk factor (CVR). However, traditional scales underestimates the CVR in SLE.

**Objectives:** Determine the correlation between traditional CVR scores (Framingham, systematic coronary risk evaluation (SCORE), arteriosclerotic cardiovascular disease (ASCVD) and arterial stiffness (AS) in an open population of SLE, assessing AS by pulse wave velocity (PWV), vascular damage through cardio-ankle vascular index (CAVI), ankle-brachial index (ABI), quality intima media thickness (qIMT) and SLE disease activity using the systemic lupus erythematosus disease activity index (SLEDAI) and systemic lupus international collaborating clinics (SLICC).

**Methods:** Patients with SLE of 18 years old and older, diagnosed according to SLICC 2012 criteria. Informed written consent. AS was determined by PWV, CAVI, ABI, and qIMT. Disease activity was recorded by SLEDAI and SLICC. Comparison between qualitative variables will be done through the X2 test or the Fisher exact test. For comparison of the quantitative variables with normal distribution Student's T and ANOVA tests were done. The correlation coefficient (r) of Pearson was calculated. Variables with a  $p\leq 0.2$  value were included in a multiple linear regression model to evaluate the influence of the disease variables on CVR. SPSS v.22 software (IBM, inc) and the Graphpad V software were used.

**Results:** The total of SLE patient were 44 (100%), with a mean age of  $34\pm 12$  years old. Thirty six women (82%). The mean evolution time was  $6\pm 5$  years. Smoke was registered in 16% (7 cases). Systolic blood pressure  $110\pm 14$ , diastolic blood pressure  $73\pm 11$  mmHg. Body mass index  $28.4\pm 9.1$ , total cholesterol  $186\pm 47$ , triglycerides  $143\pm 67$ , cHDL  $42.9\pm 5.1$ , cLDL  $57\pm 27$  mg/dL. Erythrocyte sedimentation rate of  $17\pm 14$  mm/hr, cReactive protein  $7.1\pm 4.8$  mg/L. Anti-dsDNA antibodies were present in 47.7% of the cases.<sup>21</sup> Secondary antiphospholipid syndrome in 13.6%.<sup>6</sup> Mean SLEDAI 8 (range 0–32), mean SLICC 1 (range 0–6). C3 levels  $83.6\pm 21.4$ , C4  $19.5\pm 18.8$  mg/dL. The most important correlations found were with qIMT and age 0.651 ( $<0.001$ ), BMI 0.513 ( $p 0.001$ ), cRp 0.351 (0.033), cLDL 0.400 (0.01). Framingham score was able to predict CVR up to 44.8% the measurement of PWV, ASCVD in 30% and SCORE up to 22%.

**Conclusions:** Traditional scores (Framingham, SCORE, ASCVD) underestimate cardiovascular risk in patients with SLE. The most important finding is that qIMT was able to correlate more than age, to BMI and cLDL in SLE patients.

**Disclosure of Interest:** None declared

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AB0611

#### DISEASE ACTIVITY AND ORGAN DAMAGE IN PATIENT WITH CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS, FROM CHILDHOOD TO ADULTHOOD: A RETROSPECTIVE STUDY OVER THE LAST 25 YEARS

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**Background:** Although clinical symptoms and immunological findings are common in both children and adults with systemic lupus erythematosus (SLE), children generally have a more severe clinical presentation at the time of diagnosis with a larger number of affected organs, a much more aggressive clinical course and greater chance of developing organ damage over time.

**Objectives:** To compare the SLEDAI-2K disease activity index in patients with SLE at the time of diagnosis with SLEDAI-2K in the same patients in adulthood and to compare of the SLICC/ACR damage index (SDI) in patients with cSLE at the last follow up in childhood with SLICC/ACR of the same patients in adulthood.

**Methods:** This retrospective study included children who were diagnosed with cSLE, according to the ACR 1997 and SLICC 2012 criteria, in the period from 1991–2016 at the Referral Centre for Paediatric and Adolescent Rheumatology Republic of Croatia, Department of Paediatrics, University Hospital Centre Zagreb and who by the end of March 2017 reached the age of majority at 18 and continued their treatment at the Department of Internal Medicine, University Hospital Centre Zagreb.

**Results:** Out of 95 children with cSLE, 48 patients (42 females and 6 males) who attained the age of majority, were included in the study. Mean age at the time of diagnosis was 13.5 years (range 6–18), and the mean disease duration was 11 years. Mean SLEDAI-2K was 19,25 (range 0–42) in childhood and 7125 (range 0–30) in adulthood. In adulthood, thirty-two patients (66.67%) showed improvement, three (6.25%) disease progression, six (12.5%) had the same disease activity and seven patients (14.58%) were in remission. 13 children (27%) had organ damage at the last follow up with mean SDI 0.43 (0–6) and 20 patients in adulthood (41.67%) had organ damage with SDI 0.75 (0–6). Cataract, erosive arthritis and avascular necrosis were the most common organ damage in both groups. The most common presenting symptoms in childhood were musculoskeletal (predominantly arthritis) occurring in 34 children (70.83%), mucocutaneous (rash) noted in 31 (64.58%) and fever in 21 patients (43.75%). Of different laboratory tests the most common were positive antinuclear antibodies (ANA) screen (95.83%) and hypocomplementaemia (75%). Proteinuria was noticed in 26 children (54.17%). Similarly, in adulthood the most common symptoms were arthritis in 10 (20.83%) and rash in 8 patients (16.67%). Alopecia, headaches and visual disturbances were represented with 12.5% each. ANA screen was positive in 27 patients (56.25%) and hypocomplementaemia present in 22 patients (45.83%).

**Conclusions:** At the time of diagnosis in childhood, disease activity is very high while in adulthood there is a significant decrease in disease activity. Higher disease activity in childhood is related to the development of the organ damage in adulthood.

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AB0612

### INFRINGEMENT OF THE BLOOD LIPID SPECTRUM IN CHILDREN AND ADOLESCENTS WITH SLE AND THEIR PREDICTIVE VALUE FOR THE FURTHER COURSE OF THE DISEASE

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**Background:** Infringements of the lipid blood spectrum, or so-called dyslipidemia, are common in adults suffering from SLE and ranges from 36% to 60%.<sup>1</sup> Many researchers confirmed the accelerated development of atherosclerosis among patients and high risk of epy cardiovascular complications with deterioration of life expectancy. However, the role of prolonged storage of dyslipidemia and subclinical signs of hypercoagulability on the course of the disease is unspecified.

**Objectives:** The aim of the study was to clarify the prognostic importance of the role of storage of metabolic shifts in children with SLE on the background of treatment for the course of the disease.

**Methods:** A total of 35 people aged 7–18 years with SLE who were ill for more than one year and received complex therapy with glucocorticoids and immunosuppressive drugs were examined. The average age of the patients was 173.56 ± 4.17 months; the total duration of the disease was 48.45 ± 3.18 months. General clinical trials included the complex included autoantibodies, disease activity, drugs. Total cholesterol (TCh), triglycerides (TG), high density lipoprotein cholesterol, low-density lipoprotein cholesterol, apolipoprotein B, ApoA-I and lipoprotein- $\alpha$  were evaluated. The state of the blood coagulation system was also studied: fibrinogen of the blood, prothrombin index, thrombin time, active partial thrombin time, d-dimer, international normalised ratio.

**Results:** The presence of atherogenic dislipoproteinemia in 60.0% of ill children and adolescents on SLE in children and adolescents, disorders in the system of hemostasis in 25.0% was established.

The data on the presence of interconnection of blood triglycerides with glomerular filtration rate ( $r = -0.892$ ;  $p < 0.05$ ) and activity of transaminases (alanine transaminase) ( $r = 0.848$ ;  $p < 0.05$ ).

As a result of multiple regression analysis with step-by-step exclusion of minor variables, serum creatinine serum levels in patients with SLE depend on the level of TG of blood with high predictive accuracy: blood creatinine = 0.0672684 + 0.0127034 \* TG;  $R = 69.79\%$ ;  $R^2 = 62.34\%$ ;  $p < 0.05$ .

A multivariable regression analysis also proved that the level of circulating immune complexes in patients with SFV significantly depends on the level of total cholesterol, complement and TG by the formula:  $CIC = 1.44278 + 0.188976 * TCh - 1.51503 * complement + 0.35538 * TG$ ;  $R = 94.25\%$ ;  $R^2 = 90.02\%$ ;  $p < 0.01$ .

The mean indices of state of the blood coagulation system indices for children and adolescents with SLE and signs of dyslipidemia were within the norm except for fibrinogen (2.76 ± 0.29 g/L in the presence of dyslipidemia against 3.72 ± 0.46 g/L in patients with dyslipidemia,  $p < 0.05$ ). Its increase persisted in 27.78% of patients.

**Conclusions:** Thus, violations in the lipid spectrum of blood are often formed in children and adolescents on the background of SLE with the duration of the disease for more than one year. They are not only a risk factor for atherosclerotic lesions; they are also a factor in maintaining the activity of the disease and the development of sustained kidney damage.

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**Disclosure of Interest:** None declared

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AB0613

### CLINICAL AND SEROLOGICAL CHARACTERISTICS OF LUPUS ENTERITIS AND ITS PROGNOSTIC FACTORS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Lupus enteritis, known as mesenteric vasculitis including multiple ulcers or ischaemic colitis, and protein-losing enteropathy, is a potentially life-threatening complication of systemic lupus erythematosus (SLE). Although glucocorticoid therapy is usually effective, some patients experience recurrences or severe complications in that surgical treatment or intensive immunosuppressive therapy is required. Little evidence, however, is available with characteristics and prognostic factors of lupus enteritis.

**Objectives:** The aim of this study is to clarify clinical characteristics and associated factors for the prognosis with lupus enteritis.

**Methods:** Consecutive SLE patients in our hospital between 2009 and 2017 were retrospectively reviewed. Patients who developed lupus enteritis which were associated with mesenteric vasculitis or protein losing enteropathy were enrolled. The diagnosis was made by physical examination, contrast enhanced computed tomography and <sup>99m</sup>Tc Albumin scintigraphy. Poor prognosis was defined as any surgical treatment or recurrence.

**Results:** Among 591 SLE patients who fulfilled the 1997 American College of Rheumatology classification criteria, 23 (3.9%) were identified as developing lupus enteritis, and enrolled. Eighteen (78%) were mesenteric vasculitis and 5 (22%) were protein-losing enteropathy. Eighteen (78%) were female, the mean age at SLE onset was 31.5 years, and the mean duration between the onset of SLE and lupus enteritis was 10.6 years. The mean SLE disease activity index at the onset of lupus enteritis was 9.6. All patients were treated with glucocorticoid (mean initial prednisolone dose was 40.4 mg/day), and 4 patients (17%) were in combination with cyclophosphamide. Among the mesenteric vasculitis patients, 4 patients required surgical treatment and 4 patients experienced recurrence. Comparison between patients with poor prognosis and those without revealed that patients in the poor prognosis group had a higher ratio of multiple ulcer type than ischaemic colitis type (43% vs. 0%,  $p = 0.043$ ), colon lesions (71% vs. 9.1%,  $p = 0.012$ ), higher serum IgA (391 mg/dl vs. 247 mg/dl,  $p = 0.008$ ), and lower serum total cholesterol (152 mg/dl vs. 191 mg/dl,  $p = 0.012$ ). No difference was found in abdominal symptoms, SLE disease activity index score at lupus enteritis onset, anti-dsDNA antibodies and complement levels, initial prednisolone dose, and the concomitant cyclophosphamide use between the two groups. No recurrence was seen in patients with protein-losing enteropathy.

**Conclusions:** The higher level of serum IgA and lower level of serum total cholesterol are associated with surgical treatment or recurrence and are potential predictive biomarkers for poor prognosis.

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AB0614

### THE LUPUS STUDIES: THE EUROPEAN AND SPANISH POINT OF VIEW

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**Background:** Improving systemic lupus erythematosus patient care comes from the advances performed first in basic science that improved our understanding of the mechanism underlying the pathogenesis and finding effective and safe medications that led to treatment improvement. Furthermore, clinical trials play a key role in advancing both our medical knowledge of the disease and novel treatments.

**Objectives:** This work aims to offer an overview of the type and characteristics of lupus studies and to analyse the contribution that Europe and Spain have made in supporting those investigations.

**Methods:** A systematic review of the public registry database of publicly and privately supported clinical studies (CS), ClinicalTrials.gov, was done considering “lupus” as a search criteria (database generated with all CS registered on the 19th September 2017). Data collected included: CT code, title, sponsor, countries participating, study phase, condition and intervention.

**Results:** *Study distribution.* By 19th September 2017 there were a total of 256127 CS registered in the world, from which 611 (0.24%) are associated with lupus studies. From those, 27.2% are carried out in Europe. Spain is the third country in Europe in number of lupus CS after France and Germany.

*Type and distribution of the studies.* In the generated clinicaltrials.gov data base, the studies are associated to a type of study. The distribution varies depending on the geographical area. In general, the main type of lupus studies conducted in the world are related to the discovery and development of new treatments (n=406) but there are also behavioural, devices investigation, diagnostic test, dietary supplementation, genetic and radiation studies. In Spain, 94.6% of the studies registered are related to new treatment development.

The distribution of the lupus studies are as follows:

*Financial support.* 58.6% of all studies are funded by sources other than industry and 34.8% are supported by it. In a detailed analysis, 12.5% of the studies are under the economic support of the National Institutes of Health (NIH) or the partnership of NIH+other partners. The scenario is different in Europe where industry supported 54.8% of the studies and in Spain where industry supported 87.3% of the studies.

Moreover, the funding profile in Spain showed that 92.3% of the studies associated with new treatments are supported by industry and 7.7% of them are supported by other sources. On the other hand, 100% of the studies not related with

new treatments development are supported by funding source other than industry.

Abstract AB0614 – Table 1

Phase	Worldwide (n)	%	EU (n)	%	Spain (n)	%
Early Phase 1	7	1.1	2	1.2	0	0.0
Phase 1	76	12.4	17	10.2	3	5.5
Phase 1/2	24	3.9	4	2.4	0	0.0
Phase 2	143	23.4	57	34.3	23	41.8
Phase 2/3	15	2.5	5	3.0	1	1.8
Phase 3	76	12.4	34	20.5	21	38.2
Phase 4	47	7.7	7	4.2	3	5.5
No data	223	36.5	40	24.1	4	7.3

\* The percentages have been rounding

**Conclusions:** Europe participate in more than a quarter of Lupus clinical studies and Spain is the third European country participating in those clinical studies.

New treatment development studies are the main CT performed worldwide and the percentage is even higher in Spain. Regarding the study phase, the distribution of CT in Europe and Spain are similar although phase I studies in Spain are less frequent.

From all studies registered, the majority are non-industry sponsored studies. In Europe and in Spain the situation is the opposite, as 87.3% of the studies are pharma-sponsored studies.

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#### AB0615 CHANGES IN SOMATOSENSORY EVOKED POTENTIALS IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME

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**Background:** Primary Sjogren's syndrome (pSS) is a chronic autoimmune disease, which, in addition to impaired function of exocrine glands, can affect other organs including nervous system.

**Objectives:** The aim of the study was to establish whether in patients with pSS without central nervous system (CNS) involvement, the function of the central portion of the sensory pathway can be challenged.

**Methods:** In 33 patients diagnosed with pSS without clinical features of CNS damage and normal head CT scan, somatosensory evoked potentials (SEP) were studied. The results were compared to other clinical parameters of the disease, particularly to immunological status. The control group consisted of 20 healthy volunteers selected with respect to age and sex.

**Results:** Mean latency of all components of SEP were considerably prolonged in patients compared to the control group. Mean interpeak latency N20-N13 (duration of central conduction TT) did not differ significantly between the groups. However, in the study group, mean amplitude of N20P22 and N13P16 was significantly higher compared to healthy individuals. In patients with PSS, significant differences in SEP parameters depending on duration of the disease, duration of arthralgia and presence of SSA and SSB antibodies were noted. No significant differences in mean SEP parameters were observed with respect to skin lesions, xerophthalmia, current joint pain and swelling, focus score, levels of C3 and C4 complement components, ESR, CRP and presence of Ro52 antibodies.

**Conclusions:** The authors confirmed central nervous system involvement often observed in patients with pSS. They also showed dysfunction of the central sensory neuron as a difference in amplitude of cortical response, which indicates sub-clinical damage to the CNS.

**Disclosure of Interest:** None declared

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#### AB0616 THE CORRELATION BETWEEN FOCUS SCORE AND ULTRASONOGRAPHY OF MAJOR SALIVARY GLANDS IN PRIMARY SJÖGREN SYNDROME

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**Background:** Currently, the role of salivary gland ultrasonography (SGUS) in the diagnosis of primary Sjogren's syndrome (pSS) is being determined. So far, in none of the proposed classification criteria for pSS SGUS is taken into consideration. The most recent analyses of patients show that SGUS can prove to be useful in the identification of even early forms of pSS.

**Objectives:** We analyzed the SGUS changes in patients with pSS and its correlations with focus score (FS) of minor salivary glands and immunological and laboratory profile.

**Methods:** We included 68 patients with pSS in the mean age of 51, based on the classification criteria from 2002.

**Results:** In 33 (48%) patients were abnormal findings in major salivary glands detected (table 1). Scattered hypoechoic changes of different size were the most common observed changes in SGUS, mainly in parotid glands.

Abstract AB0616 – Table 1. Abnormal images in salivary and mandibular glands in patients with pSS.

Number of patients – 33	Parotid and submandibular glands
Changes in SGUS	Parotid glands 23 patients (70% of changes) Submandibular glands 10 patients (30% of changes)
SGUS changes:	
- gland enlargement	48% of changes
- scattered hypoechoic changes of different size	85% of changes
- fibrosis	6% of changes
- lymph glands	15% of changes
- gland atrophy	12% of changes
- ducts enlargement	3% of changes

The FS was significantly higher in patients with changes in SGUS compare to the patients with normal images of major salivary glands (2.6 SD 1.3 vs 1.8 SD 1.2; p=0.02).

In patients with SGUS abnormalities the hypergammaglobulinemia was most often observed (1.7 g/dl vs 1.2 g/dl; p=0.02). There was not the correlation between changes in major salivary glands and age (p=0.5), CRP value (p=0.1), ESR value (p=0.1), with blood cell count (p=0.1), rheumatoid factor (p=0.1), dry eye (p=0.1), oral dryness (p=0.2), anti-SSA antibodies (p=0.5), anti-SSB antibodies (p=0.2), anti-Ro52 antibodies (p=0.4) observed.

**Conclusions:** SGUS is a useful tool in patients with pSS. The abnormal images in SGUS of major salivary glands correlated with focus score of minor salivary glands and hypergammaglobulinemia but not with specific antibodies.

**Disclosure of Interest:** None declared

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#### AB0617 ACROSS-SECTIONAL STUDY OF NAILFOLD MICROVASCULAR CHANGES IN INDIAN PATIENTS WITH RNP+ LUPUS AND MCTD USING NAILFOLD VIDEOCAPILLAROSCOPY

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**Background:** Nailfold Capillary (NFC) changes represent degree of microvascular involvement in autoimmune connective tissue diseases. Anti U1-RNP is associated with specific internal organ involvement in SLE. Nailfold capillaroscopy may objectively predict the systemic microvascular abnormalities in SLE patients with positive Anti U1-RNP antibody.

**Objectives:** To study nailfold microvascular changes (NFVC) in SLE patients with RNP +and compare them with NFVC changes observed in patients with RNP negative SLE and Mixed connective tissue disease (MCTD).

**Methods:** Nailfold videocapillaroscopic (NFVC) examination (Optilamediscope, 200X) was performed in consecutive patients satisfying classification criteria of



SLE with or without Anti-U1 RNP positivity. Patients satisfying criteria for MCTD were recruited as disease controls. Individual NFC parameters were analysed by a blinded assessor. Changes in three groups were compared using non-parametric tests. Ordinal logistic or linear regression were used wherever applicable to assess any independent association of NFC changes with disease groups.

**Results:** Total of 81 patients were studied, of which 28 had SLE with RNP+ (age 30.0±10.37; 26 females), 26 had SLE without RNP positivity (age 29.42±9.20; 25 females) and 26 had MCTD (age 37.0±9.86; 25 females). Capillary density was significantly reduced in MCTD as compared to RNP+SLE patients (5.11±1.69/mm vs 7.25±1.38/mm, p=0.0001), as well as in RNP+SLE as compared to RNP negative SLE patients (7.25±1.38/mm vs 8.92±1.13/mm, p=0.0001). Conversely, patients with RNP+SLE had more frequent giant capillaries, enlarged capillaries and ramified/branched capillaries as compared to RNP negative SLE patients (p=0.047, 0.001 and 0.029 respectively). However, there was no statistical difference in number of haemorrhages among these groups. These changes were more severe in patients with MCTD as compared to RNP+SLE. Ordinal logistic regression showed more severe reduction in capillary density in patients with RNP+SLE as compared to RNP negative SLE (OR=9.5, p=0.007) independent of the presence of Raynaud's, ILD and disease duration.

**Conclusions:** Presence of anti-U1RNP antibody is associated with micro-vascular abnormalities in SLE as detected by NFVC. Patients with MCTD have more profound abnormalities as compared to RNP+SLE patients.

**Disclosure of Interest:** None declared

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AB0618

**PREVALENCE OF HYPOVITAMINOSIS D IN ADULTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND THE RELATIONSHIP WITH SLEDAI 2K IN PATIENTS TREATED IN TWO RHEUMATOLOGY SERVICES, BOGOTA 2017**

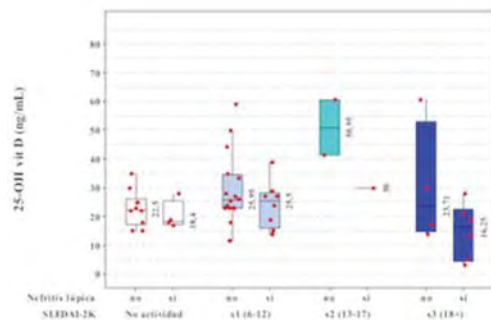
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**Background:** Vitamin D is a steroid hormone with pleiotropic effects on physiological processes. Among others, immune system regulation and their analogues prevent symptom development of autoimmune diseases such as SLE. A previous research in a colombian clinic found a prevalence of hypovitaminosis D of 87% in healthy population, but hypovitaminosis D is higher in SLE patients than healthy controls.

**Objectives:** To establish the prevalence of hypovitaminosis D in patients with SLE and relationship with SLEDAI-2K.

**Methods:** A cross sectional study was carried out. 80 medical records with a diagnosis of SLE o CIE-10 M30-M36 were identified and we included patients >18 years of age who meet at least 4 of the 11 criteria to diagnoses of SLE for medical record. The analysis included means, DS and Kruskal Wallis with p-value < 0.05.

**Results:** The majority of patients are women (94%), with an average age of 39.9 years, married (41%), with secondary education (56.7%) and different occupations. It was found that the patients with higher activity, had lower vitamin D levels. Additionally, if the patient had lupus nephritis, vitamin D levels decreased even more.



Abstract AB0618 – Figure 1

**Conclusions:** Patients with active systemic lupus Erythematosus, (SLE) have hypovitaminosis D more frequently and we noticed that patients with renal involvement have the lowest levels of vitamin D, which justifies a later analysis.

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AB0619

**MANY PERIPHERAL FRACTURES DESPITE NORMAL BONE MINERAL DENSITY IN CAUCASIAN SLE PATIENTS**

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**Background:** Clinical outcome has improved in systemic lupus erythematosus (SLE) and thus, early management of comorbidities like cardiovascular disease and osteoporosis has become highly important. In this disease, osteoporotic risk factors such as female gender, early onset of disease leading to long disease duration, high degree of systemic inflammation, high frequencies of glucocorticoid usage often at higher doses, and chronic fatigue or pain compromising physical activities are often present in combination.<sup>1</sup> Rh-GIOP (NCT02719314) is an ongoing prospective study monitoring glucocorticoid (GC)-induced osteoporosis of rheumatic patients, established in 2015 at the Charité University Hospital. To date, the database comprises clinical data and bone mineral density data measured by dual x-ray absorptiometry (DXA) of 592 patients with inflammatory rheumatic diseases.

**Objectives:** To quantify bone mineral density and fractures in SLE patients.

**Methods:** Bone mineral density (BMD) data of SLE patients as measured by dual x-ray absorptiometry (DXA) were analysed with regard to their relation to detailed clinical data.

**Results:** 43 female and 6 male SLE patients aged between 20 and 77 years (mean: 46.31 years) were assessed by DXA (all of Caucasian ethnicity, mean disease duration: 15.49 years; 61% denied any physical activity). SLE medication included glucocorticoids (93.9%; mean cumulative dose: 25.5 g), antimalarials (67.3%), azathioprine (30.6%), mycophenolate-mofetil acid (22.4%), belimumab (16.3%), cyclophosphamide (10.2%) and methotrexate (8.1%).

In 26 (60.5%) of all studied SLE patients, 36 (92.3%) peripheral and 3 (7.7%) vertebral fractures were recorded. Notably, 6 of these patients with fractures were younger than 30 and only 4 older than 60 years. 10 of all 39 fractures (25.6%) were low-trauma fractures. Of note, 11/26 patients (42.3%) with fractures had a normal BMD, 9/26 (34.6%) osteopenia and 6/26 (23.7%) osteoporosis, while only 4 (15.4%) of them initially received anti-osteoporotic medication.

**Conclusions:** There is a high occurrence of peripheral fractures in SLE. Moreover, 4 out of 10 SLE patients developed fractures despite a normal BMD, stressing that this parameter is of limited value for correctly identifying the fracture risk in SLE. The analysis of a larger number of patients and in-depth analyses are necessary to improve management of osteoporosis and to better prevent fractures in SLE patients.

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AB0620

### HIGH RISK OF MISTAKEN CLASSIFICATION OF PRIMARY ANTIPHOSPHOLIPID SYNDROME AS SYSTEMIC LUPUS ERYTHEMATOSUS ACCORDING TO THE SLICC CRITERIA: ANALYSIS OF A COHORT OF 214 ANTIPHOSPHOLIPID PATIENTS

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**Background:** The diagnosis of systemic lupus erythematosus (SLE) is based on the association of clinical and biological manifestations and on clinical experience. In 2012, a major revision by the Systemic Lupus International Collaborating Clinics (SLICC) group sought to improve their sensitivity and specificity. In replications, the SLICC classification produced fewer errors than the previous version; its higher sensitivity but lower specificity meant that some patients could be classified with SLE although they had another disease. In fact, the distinction between PAPS, APS associated with SLE, and isolated SLE may be difficult in some cases because the two diseases share some clinical and biological manifestations.

**Objectives:** To assess the limitations of the SLICC (Systemic Lupus International Collaborating Clinics) classification criteria for systemic lupus erythematosus (SLE), in patients with primary antiphospholipid syndrome (PAPS).

**Methods:** Retrospective study of a cohort of APS patients (Sydney criteria). We successively excluded patients with<sup>1</sup> at least one "SLE-specific" manifestation (biopsy-proven SLE nephropathy, arthritis, cutaneous, or neurologic SLE manifestations, pericarditis, autoimmune haemolytic anaemia, oral and nasal ulcers, non-scarring alopecia, anti-dsDNA, and anti-Sm antibodies),<sup>2</sup> any other autoimmune connective tissue disease, and/or<sup>3</sup> antinuclear antibodies >1/320. Careful file review confirmed PAPS among the remaining patients. We then assessed the number of SLICC criteria each patient met.

**Results:** Among these 214 APS patients, we excluded 85 with at least one SLE-specific manifestation, 8 with another connective tissue disease, and 21 with antinuclear antibodies >1/320, leaving 100 patients with primary APS. Among them, 28% met at least 4 SLICC classification criteria including one clinical and one immunological criterion (antiphospholipid antibodies, aPL, by definition) and could thus theoretically be classified with SLE. Fourteen had an arterial phenotype (50%), 9 a history of catastrophic APS (32%), and 18 a triple-positive profile for aPL (64%). None had developed SLE during a median follow-up of 12 [6.5–17] years.

**Conclusions:** Because 28% of our patients with longstanding and strictly defined PAPS could be mistakenly classified as SLE, they were at risk of deleterious therapeutic management. We therefore suggest that any future classification for SLE should specifically require at least one SLE-specific criterion for patients with aPL.

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AB0621

### EPIDEMIOLOGY, CLINICAL CHARACTERISTICS AND THERAPY APPROACHES OF A RETROSPECTIVE COHORT OF PAEDIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS IN A TERTIARY CENTRE

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**Background:** Systemic lupus erythematosus (SLE) is a chronic autoimmune disease, potentially severe, with broad clinical spectrum, which can affect multiple organs and systems.

**Objectives:** To analyse the initial manifestations, laboratory examinations and therapeutic approaches of patients diagnosed with childhood onset systemic lupus erythematosus (c-SLE) followed in a tertiary hospital in the last 14 years.

**Methods:** Retrospective chart review. Inclusion criteria were: children under 18 years diagnosed with c-SLE between January 2003 and January 2017.

**Results:** During the study period, 38 patients were identified (ratio female/male: 3/1). The mean age at the onset of disease was 11.5 years (range 6–17). All had caucasian origin, except 5 coming from South America, 2 from India and 1 from Africa. Onset of the disease took place in spring in 22 (58%) patients, while in 10 (26%) patients onset was in summer, 5 (13%) in autumn and only one (3%) in winter season.

The most frequently clinical manifestations found at the debut were cutaneous involvement (66%, predominantly in the form of a malar rash), renal (65%) and joint (60%, 48% arthralgia and 52% polyarthritis). Other manifestations were fever (50%), cytopenias (39%), asthenia (36%), serositis and neurological clinic (both 26%) and oral aphthosis (23%). Among the neurological manifestations, 4 patients showed bradypsychia, 3 headache, 2 seizures and 1 manifested a paralysis of the sixth cranial nerve. Only 1 patient presented macrophage activation syndrome after primoinfection by *Ebstein Barr Virus*. During the study period, no deaths occurred.

Ten patients also had some other associated autoimmune disease: 6 hypothyroidisms, 2 IgA deficiency, 1 vitiligo and 1 celiac disease. No case of diabetes mellitus was identified.

Regarding immunology, in all cases, positive antinuclear antibodies (ANA) were detected, although with variable titers (1/80 – 1/5120). Of the 25 patients who presented renal disease at the onset, 19 associated Anti-dsDNA antibodies positive at the initial time of the determination. Although antibodies related to antiphospholipid syndrome (APS) (anticardiolipin, anti-2glycoprotein and lupus anticoagulant) were detected in 12 patients (32%), only two developed associated clinical manifestations (both deep vein thrombosis in the lower limbs).

Regarding treatment, all patients required corticosteroids. Therapy with acetylsalicylic acid was indicated in all patients with APS-associated immunology. Only 6 patients received treatment with corticosteroids and hydroxychloroquine exclusively. Nineteen (50%) patients initially received azathioprine therapy, being necessary to switch to mycophenolate mofetil for lack of response in eleven, receiving the last treatment 20 patients finally (52%). Eighteen patients (47%) received cyclophosphamide therapy, 16 of them as a consequence of their renal involvement. In addition, biologic therapy (rituximab and belimumab, respectively) was used in two multirefractory patients.

**Conclusions:** As widely already reported, SLE is a disease that affects predominantly women. Moreover, as it has been previously described in the literature the most frequently initial manifestations found in c-SLE are cutaneous, renal and articular. However, a large variability of onset symptoms exists, thus c-SLE should be ruled out in patients with multisystemic involvement

**Disclosure of Interest:** None declared

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AB0622

### CHARACTERISTICS OF SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS IN MALTA; A POPULATION BASED CROSS-SECTIONAL COHORT STUDY

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**Background:** Systemic Lupus Erythematosus (SLE) is an autoimmune disorder that involves multiple systems including the skin, musculoskeletal, renal, neurological, haematologic, cardiovascular and respiratory systems.

**Objectives:** The aim of this study was to characterise the patients with systemic lupus erythematosus living in Malta, in terms of age of disease onset, BMI, comorbidities, drug history, disease activity, damage and other factors including fatigue, sleep quality, depression, anxiety and vitamin D level.

**Methods:** The study consisted of a cross-sectional cohort study of all known SLE patients, over the age of 18, living in Malta. 92 patients who fulfilled the SLICC classification criteria for SLE, gave informed consent and an interview was carried out. Fatigue, anxiety, depression, sleep quality and disability were assessed respectively by filling in the following questionnaires: Fatigue Severity Scale (FSS), Hospital Anxiety and Depression Scale (HADS), Pittsburgh Sleep Quality Index (PSQI) and modified Health Assessment Questionnaire (mHAQ).

**Results:** 92.4% of SLE patients studied were female. Table 1 summarises the characteristics of the SLE patients.

23.9% of SLE patients were in remission (SLEDAI-2K 0), while 52.2% had a low disease activity (SLEDAI-2K 1–5) at the time of the interview. 20.7% and 3.3% had a moderate (SLEDAI-2K 6–10) and high (SLEDAI-2K 11–19) disease activity respectively. A significant positive correlation was noted between function measured by mHAQ and SLEDAI (R=0.417, p=0.000). 56.5% were noted to have an abnormally high level of fatigue (FSS >3.7). 6.5% were noted to have depression (HADS D>10) and 35.9% had anxiety (HADS A>10). 55.4% were noted to have poor sleep quality (PSQI >5) and 26.1% had an abnormal level of function (mHAQ >0.3). 15.2% were found to have vitamin D deficiency and 27.2% were vitamin D insufficient.

**Abstract AB0622 – Table 1.** Clinical characteristics of the cohort

Characteristics	Values
Age, mean (S.D.) years	46.9 (13.9)
Caucasian race, n/N (%)	90/92 (97.8)
Disease duration, median (range) years	13 (0–35)
Age of SLE onset, mean (S.D.) years	33.8 (12.8)
BMI, median (range) kg/m <sup>2</sup>	26.5 (17.7–53.5)
Current smoker, n/N (%)	14/92 (15.2)
Family history of SLE in first degree relative, n/N (%)	3/92 (3.3)
Osteopaenia/osteoporosis, n/N (%)	30/92 (32.6)
Hypertension, n/N (%)	22/92 (23.9)
Diabetes mellitus, n/N (%)	7/92 (7.6)
Fibromyalgia, n/N (%)	9/92 (9.8)
Anti-phospholipid syndrome, n/N (%)	7/92 (7.6)
Sjogren's syndrome, n/N (%)	4/92 (4.3)
Rheumatoid arthritis, n/N (%)	3/92 (3.3)
Current prednisolone, n/N (%)	41/92 (44.6)
Current hydroxychloroquine, n/N (%)	55/92 (59.8)
Current azathioprine, n/N (%)	20/92 (21.7)
Current methotrexate, n/N (%)	10/92 (10.9)
Current mycophenolate, n/N (%)	6/92 (6.5)

**Conclusions:** This is the first population based study on SLE to be carried out in Malta. The prevalence of SLE in Malta is estimated to be 25.5 patients per 1 00 000 and the estimated incidence is 1.05 patients per 1 00 000 per year. A high frequency of obesity and vitamin D deficiency and insufficiency were noted in SLE patients. Other unmet needs include an uncontrolled disease activity, fatigue, poor sleep quality and anxiety.

**Disclosure of Interest:** None declared

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#### AB0623 PREGNANCY OUTCOME IN SYSTEMIC LUPUS ERYTHEMATOSUS: A RETROSPECTIVE STUDY

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**Background:** Pregnancy represents a challenge for patients with systemic lupus erythematosus. One of the major risk is the occurrence of a flare during pregnancy. The influences are mutual, and the risk of complications depend mostly on the disease activity in the last 6–12 months before pregnancy. Therefore, these patients need a multidisciplinary approach, the obstetrician should collaborate with the rheumatologist and nephrologist.

**Objectives:** To determinate the associations between disease activity and pregnancy outcomes, and the risk factors that predict pregnancy complications and flare.

**Methods:** We present a retrospective study conducted between January 2010 and December 2015. We enrolled 35 pregnant patients, diagnosed with SLE with ages between 21 and 46 years old. All patients were followed up since the beginning of the pregnancy until delivery. We tested the correlations between different biomarkers and clinical manifestations of disease activity and pregnancy outcomes.

**Results:** Maternal complications occurred in 71.24% of the cases. The most common complications were: miscarriages, hematologic abnormalities (anemias, thrombocytopenia), premature birth and preeclampsia. The prematurity rate was 11% and most common delivery mode was the caesarian section. Also, the planning of the pregnancy was a predictor of a good fetal outcome ( $p=0.01$ ). The presence of the lupus anticoagulant was associated with prematurity ( $p=0.046$ ) at univariate analysis. Antiphospholipid syndrome was associated in 12% of the cases. Univariate analysis did not show a correlation between the presence of the syndrome and any pregnancy outcome.

**Abstract AB0623 – Table 1.** Risk Estimate preeclampsia in patients with APS

	Value	95% Confidence Interval	
		Lower	Upper
Odds Ratio for Preeclampsia	6667	.607	73 195
For cohort APS=yes	2417	1104	5292
For cohort APS=no	.363	.065	2014
N of Valid Cases	33		

**Conclusions:** Pregnancy should be planned when the disease is in remission. Lupus nephritis, is an important risk factor for preeclampsia. Also, the presence of lupus anticoagulant is a risk factor for preeclampsia, and hematologic determinations during pregnancy. The risk factors for pregnancy complications were; secondary antiphospholipid syndrome, presence of lupus nephropathy,

thrombocytopenia. our study shows that the exacerbations depend on the disease activity in the moment of conception.

**Disclosure of Interest:** None declared

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#### AB0624 DYSLIPIDEMIA IN SYSTEMIC LUPUS ERYTHEMATOSUS: CORRELATION WITH DISEASE SEVERITY AND CYTOKINES

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**Objectives:** The patients with systemic lupus erythematosus (SLE) are obviously at high risk of cardiovascular disease (CVD) and the relationships between disturbed lipid metabolism and lupus activity remain to be elucidated. We evaluated dyslipidemia in association with disease severity, organ involvement and cytokines in patients with SLE.

**Methods:** Outpatients with SLE (n=105) and healthy controls (n=75) were recruited in this study. The concentrations of plasma tumour necrosis factor receptors A (sTNFR1), tumour necrosis factor receptors B (sTNFR2) and adipokine angiopoietin-like 4 (ANGPTL4) were measured by ELISA. The clinic and laboratory data were collected from patient records using electronic data processing. The data collected included serum lipid (TG, TC, HDL, LDL, ApoA1, ApoB), renal function (proteinuria, albuminuria, creatinine, blood urea nitrogen, uric acid), liver function (Alanine transaminase [ALT], glutamic oxalacetic transaminase [AST], total protein, albumin, globulin), blood system (lymphocyte, white blood cell [WBC], platelet [PLT], haemoglobin [HB]).

**Results:** Compared with the healthy controls, the level of serum TG, TC, LDL, ApoB were significantly increased, while HDL and ApoA1 were decreased. The serum levels of LDL and ApoB were positively correlated to SLEDAI, while HDL and ApoA1 were negatively correlated to SLEDAI. The patients with lupus nephritis had more severe dyslipidemia. The blood TG, TC, LDL, ApoB levels were positively correlated to 24 hour proteinuria and serum creatinine, urea nitrogen, uric acid. The blood levels of TG, TC, LDL, ApoB were positively correlated to serum total protein, albumin, globulin. The serum level of ANGPTL4 was positively correlated to HDL and ApoA1 as well as sTNFR1 and sTNFR2 with TG

**Conclusions:** Dyslipidemia in SLE was significantly correlated with SLEDAI and kidney involvement. The circulated levels of sTNFR1, sTNFR2 and ANGPTL4 were associated with dyslipidemia in SLE.

**Disclosure of Interest:** None declared

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#### AB0625 SYSTEMIC LUPUS ERYTHEMATOSUS IN EGYPTIAN COHORT OF PATIENTS: A MULTICENTER STUDY

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**Background:** Systemic lupus erythematosus (SLE) is a chronic systemic autoimmune disease that mainly affects females in the reproductive age.<sup>1</sup> The disease presents with a diverse spectrum of clinical and immunological manifestations which has been studied in many countries and ethnic groups. Data from North Africa especially Egypt are minimal.

**Objectives:** To study the clinical and immunological characteristics of an Egyptian cohort with SLE and compare it with data from MENA region and international data.

**Methods:** In this retrospective study, data of 569 SLE patients who fulfilled the modified American College of Rheumatology (ACR) criteria for the diagnosis of SLE<sup>2</sup> were collected from three tertiary care centres in Cairo and Alexandria from the period of January 2014 to December 2017. Disease activity was assessed by using the SLE disease activity index (SLEDAI).<sup>3</sup>

**Results:** Of 569 patients 92.6% were females and 4.7% males with mean age at presentation 26.3±8.8 years and median disease duration four years (min 0.08-max 30 years). The main presenting symptom was musculoskeletal (arthritis/arthralgia) in 44.1% followed by fever in 39.4% and nephritis in 14.2%. Renal affection was present in 374 patients (65.7%) and renal biopsy was done in 268 patients with the most common is class III and IV lupus nephritis (18.3% and 14.1% respectively) (table 1). Antinuclear antibodies (ANA) was positive in all patients and immunofluorescence pattern was done in 256 patients; homogenous



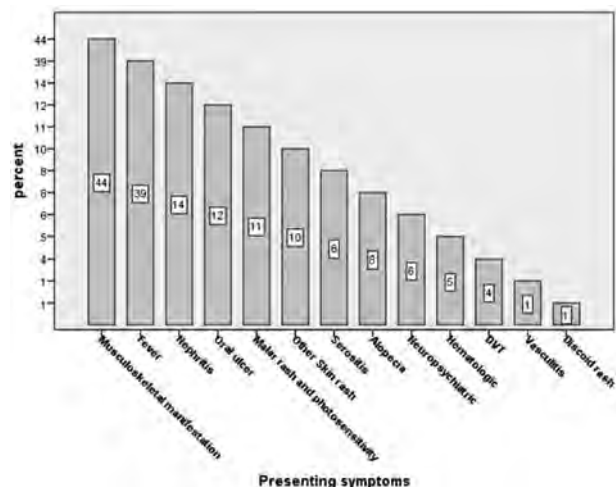
pattern was the most common followed by speckled (29.9% and 13.4% respectively). Anticardiolipin antibodies was positive in 71.2% while lupus anticoagulant was detected in 50.8% (table 2). Mean SLEDAI was 13.38±9.75 with proteinuria in 58.9%, increased binding to DNA in 54.9% and low complement in 45.5%.

**Abstract AB0625 – Table 1.** Renal biopsy of 268 Egyptian SLE patients

Renal Biopsy	Frequency	Percent
Not done	301	52.9
Class I LN	23	4.0
Class II LN	34	6.0
Class III LN	104	18.3
Class IV LN	80	14.1
Class V LN	20	3.5
Class VI LN	7	1.2

**Abstract AB0625 – Table 2.** Immunological pattern of 569 Egyptian SLE patients

	Number	Percent
ANA pattern	313	55
- Not done	170	29.9
- Homogenous	76	13.4
- Speckled	10	1.8
- Rim		
Anti.ds DNA	488	85.8
Anticardiolipin antibodies	405	71.2
Lupus anticoagulant	289	50.8
Anti-Ro antibodies	16	2.8
Anti-La antibodies	12	2.1



**Abstract AB0625 – Figure 1**

**Conclusions:** These data are similar to that reported from MENA region; however, with little difference from international data as regard presenting symptom and immunological pattern. Differences observed among ethnic groups probably reflect the genetic component of ethnicity.

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**Disclosure of Interest:** None declared

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#### AB0626 CLINICAL FEATURES OF SYSTEMIC LUPUS ERYTHEMATOSUS IN MALES

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**Background:** Systemic lupus erythematosus (SLE) is an autoimmune disease that primarily affects the adult woman. Male involvement is rare.

We report a series of men with systemic lupus in order to specify the particularities of the different manifestations of SLE in men.

**Objectives:** we aim to describe the clinical feature of male tunisien patients presenting SLE

**Methods:** This is a retrospective study of male lupus patients hospitalised in internal medicine for a period of 9 years. All patients are Tunisian and meet the lupus criteria established by the ACR.

**Results:** Twenty-one patients with male lupus were enrolled in a total of 97 systemic lupus (gender-to-sex ratio 3.6). The mean age at diagnosis was 34 years (range: 14 to 84 years). A family 1 lupus in one case. The clinical manifestations are dominated by joint damage (95%) with non-erosive arthritis in 9 cases and arthralgia in 12 cases, followed by cutaneous manifestations (erythema vespertilio=71%, photosensitivity=41%), Raynaud (25%). Pericarditis was found in 37.5% and pleurisy in 23%. Venous thrombosis was only observed in 4 cases associated with anti-cardiolipin antibodies in one case, and complicated by pulmonary embolism in one case. Sixteen patients had progressive nephropathy (permanent proteinuria >0.5 g/24 hours with mean proteinuria of 3.2 g/24 hours and extremes of 0.7 and 8 g/24 hours) of which 9 underwent kidney biopsy puncture. Membranoproliferative glomerulonephritis was observed in 4 cases, segmental and focal in 3 cases, mesangial and extramembranous, each in one case. Two patients had progressed to end-stage renal disease requiring hemodialysis. Concerning haematological involvement, anaemia, observed in 50% of cases, was haemolytic in 12.5% of cases. Leukopenia and lymphopenia were each scored in 46% of cases. Sixteen patients 16 were put on chloroquine, all patients were placed on high dose corticosteroids for an average of 25 months with boli in 7 cases, combined with cyclophosphamide (700 mg/month IV) in 4 patients cases in patients with proliferative glomerulonephritis. The evolution was enlabeled with flares in 11 cases, 2 of which had progressed to end-stage renal failure. Aseptic osteonecrosis of the femoral head was observed in one patient after 1 year of corticosteroid therapy. Complete remission was observed in 3 patients with a follow-up of 14, 24, and 144 months and one patient died as a result of peritonitis.

**Conclusions:** Systemic lupus is a disease essentially of adult women and rarely affects humans. The prevalence of the disease in the female gender suggests the intervention of a hormonal factor. In favour of the deleterious role of estrogens, lupus relapses are triggered by pregnancy, the peri and postpartum, as well as the oostroprogestative pill. The most common manifestations in humans in our study were renal impairment including membranoproliferative glomerulonephritis and segmental and focal glomerulonephritis complicated by renal failure in two patients. These data join those of the literature. The same is true for hemolytic anaemia.

LES is rare in men, nevertheless it correlates with a higher mortality in front of the association most frequent with the renal involvement which imposes a better knowledge of these clinical and laboratory particularities.

**Disclosure of Interest:** None declared

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#### AB0627 PHYSICAL ACTIVITY BY SELF-REPORTED PHYSICAL ACTIVITY AND LUPUS NEPHRITIS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Physical activity is found to be associated with clinical status such as disease activity, organ damage, disability, fatigue, and quality of life in systemic lupus erythematosus (SLE).

**Objectives:** The aim of this study was to identify the association between physical activity and disease activity and organ damage in patients with SLE.

**Methods:** A total of 415 patients with SLE were consecutively enrolled from KOREan lupus Network (KORNET) registry. This registry assessed clinical features, disease activity Systemic Lupus Erythematosus Disease Activity Index 2000 [SLEDAI-2K]), and disease damage (Systemic Lupus International Collaborating Clinics/American College of Rheumatology [SLICC/ACR] damage index [SDI]) at the enrollment of study. Self-reported physical activity was measured by International Physical Activity Questionnaire (IPAQ). Statistical analyses were used by Mann-Whitney U test and multivariate logistic regression analysis.

**Results:** There is significant difference of vigour activity between patients with lupus nephritis (n=93) and without lupus nephritis (n=322) (p=0.012), but not moderate and walking activities. In contrast, the differences of each physical activity,

walking, moderate, and vigorous intensity, according to SLEDAI-2K and SDI were not found. In addition to high PCS of SF-36 ( $p=0.006$ ) and SLEDAI-2K ( $p=0.038$ ), less vigorous physical activity were related with lupus nephritis ( $p=0.033$ ). However, the risk of CVD was not associated with physical activity of SLE.

**Conclusions:** This study showed that patients with lupus nephritis had less vigorous physical activity. It implicates that SLE-related organ damage might be associated with levels of physical activity.

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**Disclosure of Interest:** None declared

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AB0628

#### INFECTIONS IN HOSPITALISED PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS- A PROSPECTIVE OBSERVATIONAL STUDY FROM A TERTIARY CARE CENTRE IN SOUTHERN INDIA

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**Background:** Infections are one of the main causes of morbidity and mortality in SLE.<sup>1</sup> The high prevalence of infection is attributed to use of immunosuppressive agents and disease activity. There is paucity of literature from India on infections, types of infections, predictors and outcome.

**Objectives:** To determine the frequency, types and determinants of major infections in hospitalised patients with SLE.

**Methods:** Patients with SLE (2012 SLICC-ACR criteria) aged  $\geq 13$  years, admitted to Clinical Immunology and Medicine wards were included. Clinical evaluation for major organ involvement of SLE, disease activity was assessed by SLEDAI-2K. Whenever there was a suspicion of infection appropriate work up to find the etiology of infections was done. Major infection was defined as presence of either one of the following a) sepsis b) pneumonia, or pyelonephritis, or endocarditis, or meningitis. c) skin or soft tissue infection requiring hospital admission for treatment d) Infection requiring IV antibiotic therapy. The diagnosis of infection was made by compatible clinical, microbiological and imaging criteria.

**Results:** From December 2016 till January 2018, 63 (55 women and 8 men) were included; Mean age was  $28.8 \pm 9.8$  years; mean SLEDAI-2K was  $14.6 \pm 7.03$ . Median duration of hospital stay was 14 days; range 2–64 days. Disease manifestation (including present and ever present) were arthralgia/arthritis in 51 (81%), oral ulcers 56 (88.9%), myositis 10 (15.9%), lupus nephritis 35 (55.6%), CNS lupus 14 (22.2%), serositis 14 (22.2%), cardiac involvement 13 (20.6%), APS 3 (4.8%). At the time of enrollment thrombocytopenia was present in 13 (20.6%), and leukopenia 11 (17.5%).

Twenty-three of 63 (36.5%) had infections (table 1), 14/23 (60.8) were microbiologically proven, remaining (39.2%) were confirmed by compatible clinical features and imaging.

Seven of 63 (11.1%) died; 5 (21.7%) in the infection group versus 2 (5%) in no infection group,  $p=0.08$  OR 5.58 [CI 0.98–31.7]. Thirty-four of 63 (54%) had fever on admission; 17/23 (74%) patients with infection had fever compared to 17/40 (42.5%) in no infection group,  $p=0.02$  [OR=3.8, CI 1.2–11.7]. There was no association of lupus nephritis, CNS lupus, leukopenia, receipt of cyclophosphamide, rituximab, methylprednisolone pulse therapy with occurrence of infection.

**Abstract AB0628 – Table 1.** Infections in SLE patients

Type of Infections	n=23 (%)
Bacterial Pneumonia	3 (13.7)
Fungal Pneumonia	2 (8.7)
(Invasive Aspergillosis)	
Pulmonary tuberculosis	2 (8.7)
Disseminated tuberculosis	2 (8.7)
Urinary tract infection	4 (17.4)
Skin and soft tissue infection	4 (17.4)
Blood stream infections	3 (13)
Suspected brain abscess	1 (4.3)
Pyogenic meningitis	1 (4.3)
Disseminated Varicella	1 (4.3)
Viral bronchiolitis	1 (4.3)

**Conclusions:** Almost 36% of SLE patients in hospital have infections. There appeared to be an increase in number of deaths among patients with infections. There was no association of infections with the dose of prednisolone or previous immunosuppression with cyclophosphamide.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.1383

AB0629

#### PREVALENCE OF ASYMPTOMATIC VERTEBRAL FRACTURES IN POSTMENOPAUSAL WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Objectives:** To investigate the prevalence of vertebral fractures and to identify risk factors associated with vertebral fractures in postmenopausal women with systemic lupus erythematosus (SLE).

**Methods:** 86 consecutive postmenopausal women with SLE were included in this study. Bone mineral density (BMD) measurements of the hip and spine were performed using the dual energy X-ray absorptiometry (DEXA). Vertebral fracture assessment (VFA) was done for detection vertebral fractures using a method described by Genant. Accumulated damage was scored using the SLICC/ACR damage index (SDI).

**Results:** Vertebral fractures were defined in 42 (48.8%) postmenopausal women with SLE. Half of all patients with SLE ( $n=22$ , 25.6%) had asymptomatic vertebral fractures which were diagnosed only in this study. Every patient had 1.7 vertebral fractures on average (from 0 to 4). Distribution of vertebral fractures along the spine showed one peak at Th7. Univariate analyses of variables associated with fractures were longer duration of postmenopausal status in women with SLE, longer glucocorticoids intake, higher cumulative dose of glucocorticoids, higher SDI, lower BMD of the spine. Multivariate analysis showed longer duration of postmenopausal status in women with SLE (odds ratio 4.05,  $p=0.007$ ), cumulative dose of glucocorticoids  $\geq 60000$  mg of prednisone (odds ratio 3.68,  $p=0.009$ ),  $SDI \geq 7$  (odds ratio 2.94,  $p=0.028$ ) and low BMD ( $T \leq -2.0$ ) of the spine (odds ratio 2.48,  $p=0.015$ ) were significantly associated with vertebral fractures in the thoracic and/or lumbar spine.

**Conclusions:** Vertebral fractures were occurred in 48.8% of postmenopausal women with SLE and half of them were asymptomatic. The current method using DEXA to predict the presence of vertebral fracture has limited value and there is a need for assessment of bone quality. Vertebral morphometry in patients with SLE is recommended and early therapeutic intervention is necessary to prevent vertebral fractures in postmenopausal women with SLE.

**Disclosure of Interest:** None declared

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AB0630

#### EXPRESSION OF TNF-A AND IL-6 IN SYSTEMIC LUPUS ERYTHEMATOSUS: RELATIONSHIP WITH DISEASE ACTIVITY

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**Background:** Cytokines play an important role in the pathogenesis of SLE. TNF- $\alpha$ , IL-6 are the cytokines with suggested proinflammatory and immunoregulatory actions in the pathogenesis of SLE with differential effects on B or T cells, as well as on programmed cell death. Fas/APO-1 and Fas ligand (FasL) are involved in the apoptosis. FasL is a marker of apoptosis, it induces cell apoptosis when binds to Fas/APO-1. Both are expressed in membrane-associated and soluble forms (sFas/APO-1 and sFasL). sFas/APO-1 is known to inhibit the apoptosis via blocking the binding of Fas/APO-1 to FasL/sFasL.

**Objectives:** We evaluated the levels of IL-6 and TNF- $\alpha$  and their possible association with disease activity, apoptosis markers.

**Methods:** The study included 52pts (89% female, age 30,0 [26,5–44,5 years] (median [interquartile range 25% >75%])) with SLE ACR, 1997 and 20 controls (100% female without any rheumatic and infectious diseases, age 30,0 [25,0–39,5 years]). SLE-related factors, including disease duration, clinical features, SLE Disease Activity Index (SLEDAI 2K) and Systemic Lupus International Collaborating Clinics (SLICC) damage index were evaluated in parallel with relevant laboratory findings, autoantibodies. Serum levels of IL-6 and TNF- $\alpha$  (pg/ml), sFas/

APO-1 (pg/ml) and sFasL (ng/ml) were measured by ELISA (Bender MedSystem GmbH, Austria).

**Results:** Median SLE duration was 5 [1–11] years, SLEDAI 2K–9.5 [4.0–16.0], SLICC-0 [0–1], current prednisone dose–5.0 [0–11.9] mg/day, 44% of pts received hydroxychloroquine, 17% >cyclophosphamide, 10% >azathioprine, 4% >mycophenolate mofetil, 8% >biologics. SLEpts had higher level of IL-6 vs control (2.9 [1.5–9.7] vs 1.4 [0.7–2.1] pg/ml,  $p<0.01$ ) and lower level of TNF- $\alpha$  (1.9 [0.5–3.2] vs 4.5 [3.5–6.4] pg/ml,  $p<0.0001$ ), lower levels of sFas/APO-1 vs control (657.5 [483.2–791.4] vs 1456.9 [426.5–2060.8] pg/ml,  $p>0.05$ ) and lower levels of sFasL vs control (0.01 [0.01–0.03] vs 0.07 [0.05–0.10] ng/ml,  $p<0.0001$ ). In SLE pts serum level IL-6 correlated with IgM ( $r=0.69$ ,  $p<0.01$ ), K<sup>+</sup> ( $r=0.43$ ,  $p<0.01$ ), TNF- $\alpha$  ( $r=0.50$ ,  $p<0.001$ ), APRIL ( $r=0.39$ ,  $p<0.01$ ) and sFas/APO-1 levels ( $r=0.29$ ,  $p<0.05$ ); TNF- $\alpha$  level correlated with SLICC ( $r=0.32$ ,  $p<0.05$ ), APRIL ( $r=0.42$ ,  $p<0.01$ ), IL-6 ( $r=0.50$ ,  $p<0.001$ ), haemoglobin concentration ( $r=0.39$ ,  $p<0.01$ ), sFasL ( $r=0.44$ ,  $p<0.01$ ) and total cyclophosphamide dose ( $r=0.28$ ,  $p<0.05$ ). We divided SLEpts on two groups: the 1st-pts ( $n=31$ ) with high activity (SLEDAI 2K $\geq$ 8), the 2nd-pts ( $n=21$ ) with low (SLEDAI 2K $<$ 8). The pts in the 1st group had lower level of TNF- $\alpha$  compared to 2nd (1.6 [0.3–2.2] vs 2.8 [1.3–4.5] pg/ml,  $p<0.05$ ), with no difference in IL-6 level.

**Conclusions:** SLEpts demonstrated higher IL-6 and lower TNF- $\alpha$  levels as compared to healthy controls. Pts with high activity of SLE had decreased level of TNF- $\alpha$ . There is no correlation between disease activity and IL-6 level, as well as between elevated IL-6 and acute phase indicators. We suggest an immunoregulatory not proinflammatory role of IL-6 in SLE and probable protective role of TNF- $\alpha$  in SLE pathogenesis (it's deficiency can lead to the development and high activity of SLE). There was no correlation between IL-6, TNF- $\alpha$  levels and any SLE features. The correlation of IL-6 with sFas/APO-1 level (apoptosis inhibitor that blocks binding of sFas/APO-1 to sFasL) and TNF- $\alpha$  with sFasL concentration (a marker of apoptosis) suggests their different roles in the mechanisms of apoptosis.

**Disclosure of Interest:** None declared

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AB0631

#### IS HYPERHOMOCYSTEINEMIA (HHC) ADDITIONAL RISK FACTORS OF THROMBOSES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND ANTIPHOSPHOLIPID SYNDROME

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**Background:** HHC may be additional factor of thrombosis in SLE patients

**Objectives:** To assess the role of HHC as additional risk factors in development of vascular complications in SLE and antiphospholipid syndrome (APS).

**Methods:** A total of 125 patients (24 M and 101 F, mean age 38 $\pm$ 13 years and the disease duration 14 $\pm$ 11 years) were divided into three groups: group 1 – SLE patients ( $n=51$ ); group 2 – SLE +APS patients ( $n=49$ ); group 3 – primary APS patients ( $n=25$ ). Homocystein (HC) was assayed by high performance liquid chromatography. DNA diagnostics by the method of polymerase chain reaction was used to determine gene mutation C677T methylenetetrahydrofolate (MTHFR) reductase in 93 out of 125 patients.

**Results:** HHC (HC >15 mcg/L) was diagnosed in 82 of 125 (66%) patients: in 59% patients of group 1, 67% – of group 2 and 76% – of group 3. There was a relationship between HHC and digital necrosis (DN): 80% of patients with DN had HHC while HHC was in 57% patients without DN ( $\chi^2=4.76$ ,  $p=0.03$ ). Elevated level of HC was registered in 43 of 55 (78%) APS patients with thromboses vs. 9 of 19 (47%) aPL-positive SLE patients without thromboses ( $p=0.03$ ). HHC occurred significantly more frequently in patients with arterial thromboses (in all 14 patients) than in patients with venous thromboses – in 16 of 23 (69.9%) pts ( $p=0.03$ ) and in the absence of thromboses ( $p=0.04$ ). HHC was associated with thromboses of cerebral (in 90%), peripheral arteries (in 84%) and myocardial infarction (in 79%) vs. 47% of patients without thromboses ( $p=0.005$ ;  $p=0.04$ ,  $p=0.04$  respectively), (79 vs. 47%). Mutation of C677T MTHFR was revealed in 33.3% of SLE patients, in 57.7% – of SLE +APS and in 63.2% – PAPS. Mutation C677T in the gene MTHFR was detected in 57% of examined patients, 20% of them had homozygous variant and 80% are heterozygous. Patients with a homozygous C677T MTHFR gene was observed the tendency to develop arterial thrombosis

**Conclusions:** More than 50% APS pts had elevated level of HC as additional thromboses factors. Correlation between HHC and thromboses, primarily arterial, in APS patients gives grounds for the role of HHC in development of vascular complications in SLE and APS pts.

**Disclosure of Interest:** None declared

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AB0632

#### ESSDAI DOMAIN EVALUATION OF PRIMARY SJÖGREN'S SYNDROME (PSS) PATIENTS ENROLLED IN TWO INDEPENDENT POC STUDIES INDICATES DIFFERENTIAL UTILITY OF DOMAINS FOR TRIAL INCLUSION AND COMPOSITE ENDPOINTS IN PSS TRIALS

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**Background:** According to international consensus, disease activity in primary Sjögren's syndrome (pSS) patients shall be scored across 12 different domains according to the European Sjögren Syndrome Disease Activity Index (ESSDAI<sup>1</sup>). Two separate phase 2 proof-of-concept (PoC) studies using either BAFF receptor inhibitor (VAY736; ionalumab) or CD40 inhibitor (CFZ533) have recently been completed in comparable pSS cohorts with ESSDAI as the primary endpoint.

**Objectives:** To evaluate contribution of individual domains to composite ESSDAI scores at baseline and after interventional treatment with either VAY736 or CFZ533, or placebo. Aggregate efficacy and safety results were presented at previous meetings.<sup>2,3</sup>

**Methods:** Key inclusion criteria for both studies were fulfilling revised European US consensus criteria for pSS,<sup>4</sup> autoantibody positivity, exclusion of secondary SS and ESSDAI  $\geq$ 6. Permitted background medications in both trials included stable doses of hydroxychloroquine, methotrexate and prednisone  $\leq$ 10 mg/d and also azathioprine in the CFZ533 trial. The primary endpoint was change in ESSDAI at week 12. Descriptive and principal component analysis were done with the goal to identify distinct subgroups of patients based on ESSDAI involvement at baseline (BL), and the relative importance of single domain contribution to overall ESSDAI responses were explored.

**Results:** 27 patients received single i.v. dose VAY736 10 mg/kg ( $n=12$ ) or 3 mg/kg ( $n=6$ ) or placebo, and 44 patients received multiple doses of CFZ533 10 mg/kg i.v. ( $n=21$ ) or 3 mg/kg s.c. ( $n=8$ ) or placebo. ESSDAI breakdown at BL showed a predominance of the articular, glandular, biological, constitutional and lymphadenopathy domains in both trials. Activity in more than 3 domains was recorded for 12/27 (44%) and 12/44 (27%) of patients in the VAY736 and CFZ533 studies, respectively. Principal component analysis identified the articular domain as the key component describing the difference between patients in their ESSDAI domains at BL. Two other domains that explained the variability between patients were the biological and glandular domains. Treatment effects in domains with low BL scores were more difficult to assess using ESSDAI. The majority of ESSDAI domains were not amenable to quantitative analysis, due to absence or low incidence at baseline.

**Conclusions:** The most frequently observed ESSDAI domain was articular involvement. Our results provide insights into ESSDAI domain frequency and distribution in the randomised controlled trial setting that may have implication for future trial design in pSS.

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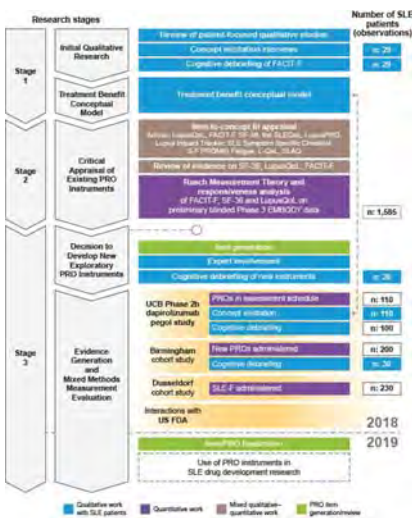
**AB0633 MEASURING WHAT MATTERS TO LUPUS PATIENTS: TRANSLATING PATIENT VIEWS INTO NOVEL PATIENT-REPORTED OUTCOMES**

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**Background:** The 2010 U.S. FDA guidance<sup>1</sup> on systemic lupus erythematosus (SLE) acknowledged that ‘improvements in clinical outcome measures in patients with SLE may not always translate to improvements in how patients feel or function’ and encourages the use of patient-reported outcome instruments (PROs) to assess changes in outcomes that matter most to patients. Fatigue, identified by patients as their chief complaint during the Lupus Patient-Focused Drug Development (PFDD) meeting<sup>2</sup>, is not optimally measured by existing PROs<sup>1</sup>. There is a need for new patient-centred outcome measures as they are pivotal to PFDD. To address this, UCB has been conducting a multi-faceted, patient-centric, mixed methods research programme including evidence generated from >2100 SLE patients.

**Objectives:** There were three main objectives of the programme: 1) identify what concepts are most important to measure for SLE patients when evaluating treatment benefit; 2) critically evaluate the extent to which these concepts are captured by existing PROs; and 3) explore the opportunity to develop and evaluate new conceptually-based PROs in SLE.

**Methods:** There were three stages: 1) development of a preliminary treatment benefit conceptual model related to SLE including disease symptoms and impacts (generated from literature review, and patient and clinician input); 2) formal comparison of i) the conceptual model and the content validity (qualitative review) of existing SLE PROs and ii) psychometric properties (ie. SF-36, FACIT-F, and LupusQoL in the discontinued EMBODY Phase 3 studies for epratuzumab); 3) development of new conceptually-based PROs in SLE (figure 1).



Abstract AB0633 – Figure 1

**Results:** A preliminary treatment benefit conceptual model in SLE was developed. Among the many symptoms and disease impacts reported by SLE patients, physical fatigue, mental fatigue (‘brain fog’), sudden fatigability, joint/muscle stiffness and pain, skin symptoms and mobility difficulties featured as most troublesome. The content validity of 10 widely used PROs was found to be limited when compared to this conceptual model. Psychometric analysis (based on Rasch Measurement Theory) confirmed the limitations of the SLE PROs used in the EMBODY studies and suggested post-hoc reconceptualisation would improve the ability of the scales to detect clinical change. This led to the development of five new conceptually-based SLE PROs (ie. fatigue, pain, mobility, symptom severity, and emotional state), which are currently being explored in >500 SLE patients in a Phase 2b dapirolizumab pegol study (NCT02804763) and two cross-sectional, non-interventional, observational studies. Data on the new PROs are currently being assessed at several sites in the USA, Latin America, UK and Germany and will be available in the coming months.

**Conclusions:** New, well-defined and reliable PROs to better capture the patient perceptions of the symptoms and impact of SLE are needed. UCB has developed

five new PROs which offer the promise of improved patient-centred outcome measurements in SLE and other autoimmune diseases.

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**AB0634 CHARACTERISATION OF SLE PATIENTS WHO UNDERWENT CARDIOVASCULAR SURGERY**

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**Background:** SLE is characterised by alternate occurrences of flares and remissions throughout its course. During these flares, immune complexes are excessively produced and deposited in affected tissues. Previous reports suggest that immune complexes deposited in the blood vessels, atrioventricular valves, and other associated components of the heart cause disorders in these tissues. Although, the characteristics of patients in whom tissue injuries progress and ultimately require surgery have not been clarified.<sup>1</sup>

**Objectives:** Heart diseases are categorised into valvular disease, ischaemic heart disease, and aortic aneurysm. This study was conducted to determine whether there was a correlation between the activity of SLE and the progress and aggravation of heart disease in each category.

**Methods:** Of the 2707 patients who were diagnosed with SLE at Juntendo University Hospital from 2012–2017, 35 underwent cardiac surgery. Six patients met the exclusion criteria, and thus, 29 patients were included. Patients with infectious endocarditis and those in whom SLE had not been diagnosed prior to surgery were excluded. Indices for SLE activity were anti-DNA Ab and CH50. Peak and bottom values of these indices before surgery were recorded, and the values obtained during the pre-surgery 180 day period were compared with those that had been determined prior to this period.

**Results:** The mean disease duration at the time of cardiac surgery was 24.2 years. The cardiac diseases were heart valve disease (V) in 10, ischaemic heart disease (I) in 7, and aortic aneurysm (A) in 12 patients. The integrated values obtained by the activity indices, anti-DNA Ab, and disease duration were 14 020 for V, 32 966 for I, and 29 444 for A. Thus, there was a tendency for values to be slightly lower in the heart valve disease category. The peak/bottom values for CH50 and anti-DNA Ab in the pre-surgery 180 day period were no different from those obtained prior to this period. Investigation of anti-phospholipid antibodies indicated that the rates of positive result for either CLβ<sub>2</sub>GPI, anti-CL antibodies, or LA were 60% for V, 28% for I, and 33% for A, and thus, higher in the heart valve disease category. All patients were treated with steroids, and five patients (17.2%) of the 29 used immunosuppressants. This rate tended to be lower than the previous frequency of the combined use of immunosuppressive drugs at our hospital (onset:18.4%, first flare 33.3%).<sup>2</sup>

**Conclusions:** There is a possibility that the long-term duration of SLE may lead to cardiac disease requiring surgery. The integrated value for DNA Ab was lower in the heart valve disease category; therefore, the presence of anti-phospholipid antibodies may be a risk factor for valvular disease. The low frequency of combined use of immunosuppressants in SLE patients with cardiovascular manifestations requiring surgery, suggest the possibility that treatment with a single steroid may require heart surgery.

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AB0635

### ANTI-PHOSPHOLIPID ANTIBODIES IN LUPUS MYOCARDITIS

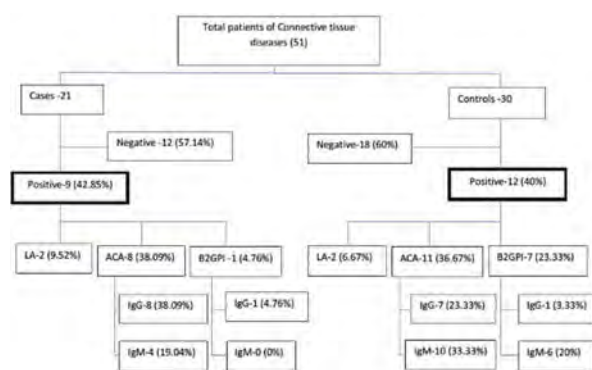
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**Background:** Myocarditis in lupus is an uncommon clinical manifestation, with unknown pathogenesis.<sup>(1)</sup> Suggested etiologies includes Immune-complexes, cell mediated damage and anti-phospholipid antibodies. The latter may affect the myocardial function microthrombi in cardiac vessels or direct cytotoxicity.<sup>(2)</sup> Previously, small studies have suggested an association between antiphospholipid tests as myocarditis.

**Objectives:** To evaluate whether myocarditis in SLE is associated with antiphospholipid positivity.

**Methods:** This was a cross-sectional study in which patients fulfilling SLICC criteria 2012 for SLE or Alarcon Segovia criteria for MCTD were included after consent. Patients were recruited as 'Cases' if they had myocarditis/cardiomyopathy defined by poor generalised contractility and/or dilation of all chambers nad/or reduced ejection fraction on echocardiography without any obvious cause. Those with regional wall motion abnormalities or pulmonary artery hypertension (moderate or severe) were excluded. Controls were age ( $\pm 2.5$  years) and disease duration ( $\pm 25\%$ ) matched patients of SLE without any abnormality on echocardiography. Serum titers of anticardiolipin antibodies and b2 GP1 (both IgG and IgM) were measured by commercial ELISA kit. Lupus anticoagulant was detected by Dilute Russell Viper Venom Test (dRVVT) with both screening (prolonged) and confirmation steps (shortening on higher phospholipid content, ratio  $>1.2$ ) on doubly centrifuged, platelet poor plasma. Proportions were compared using chi-square test (or Fischers exact test) and continuous variables by Mann-Whitney U test.

**Results:** A total of 51 patients were recruited in this study that included 21 cases and 30 controls. All had SLE, except 1 case was of MCTD (among cases). There was no difference in mean ( $\pm$ SD) age ( $33.3 \pm 14.7$ ,  $32.8 \pm 12.4$  years,  $p=0.9$ ) or median (interquartile range) disease duration ( $30^{8-38}$  25 (13.5–45) months,  $p=0.6$ ) between groups. Mean ejection fraction of Cases was 31.7% ( $\pm 9.3\%$ ) while that of Controls was 55.7% ( $\pm 1.7\%$ ) ( $p<0.001$ ). There were no significant differences between proportion of Cases (42.9%) and Controls (40%) with positive antiphospholipid tests ( $p=0.7$ ). The majority had positive anticardiolipin antibodies, followed by b2 GP1, and lupus anticoagulant was positive in only two in each group (figure 1). Among 9 Cases positive at baseline, 6 patients could be re-tested (2 expired and 1 was lost), out of which 3 had persistent positivity. Out of 12 Controls positive once, 8 could be retested (1 expired and 3 were lost), with 1 being persistently positive. There was no significant difference in persistent positivity between groups. ( $p=0.3$ ).



Abstract AB0635 – Figure 1

**Conclusions:** This study did not find any significant association between antiphospholipid antibodies (single time or persistent) with cases of lupus myocarditis.

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AB0636

### DAMAGE ACCRUAL IN SYSTEMIC LUPUS ERYTHEMATOSUS NOT RELATED TO SUSTAINED HYPOCOMPLEMENTEMIA

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**Background:** Hypocomplementemia (HC) represents a significant clinical finding in Systemic Lupus Erythematosus (SLE) as it suggests complement activation by immune-complexes, which can initiate inflammation. As disease activity contributes to damage accrual in SLE patients, we investigated the role of HC as a predictor of subsequent organ damage.

**Objectives:** Investigate the relationship between HC, disease flares and organ damage accrual in SLE patients.

**Methods:** Longitudinal cohort study of 102 SLE patients with HC defined as a C3 and/or C4 levels below cut-off during median follow-up of 13.8 years (IQR 7.0, 23.1). Disease activity was scored by time averaged SLEDAI-2K without the serological components (cWAS), flares by SELENA-SLEDAI and damage accrual by SLICC-DI. Analysis included comparisons between normocomplementemic (NC) and hypocomplementemic (HC) patients, and multivariate logistic and Cox regression modelling determined the predictive value of HC on organ damage.

**Results:** HC occurred in 2/3 of patients overall and was more often due to low C3 (97%) than low C4 (54%). HC patients had a higher prevalence of anti-dsDNA Ab (72% vs 36%,  $p<0.01$ ) and aPL (74% vs 40%,  $p<0.01$ ), but HC concurred with anti-dsDNA presence in only 36% of cases. HC patients had higher maximum cSLEDAI scores, but the time adjusted cWAS scores (1.9 vs 1.2,  $p=0.9$ ) and the frequency and risk of overall damage accrual ( $SDI>0$ ,  $n=60$ ) associated with HC was similar as for NC patients (OR 1.08,  $p>0.20$ ).

**Conclusions:** Low complement levels occur in 2/3 of SLE patients but have negligible impact on time averaged disease activity and damage accrual in SLE. Discrepancies between low C3, low C4 and anti-dsDNA Ab occurrence indicate that in SLE alternative complement activation occurs frequently and requires further translational study.

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**Disclosure of Interest:** None declared

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AB0637

### HAEMATOLOGICAL INVOLVEMENT OF PRIMARY SJOGREN'S SYNDROME PATIENTS IN A SINGLE CENTRE STUDY OF 232 CHINESE CASES

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**Background:** Primary Sjögren's syndrome (pSS) is a common systemic autoimmune disease, characterised by lymphocytic infiltration of the secretory glands and different extraglandular manifestations. Besides haematological disorders are prevalent but not well recognised in patients with pSS.

**Objectives:** Our aim is to determine the existence of cytopenia at diagnosis or during follow-up of our pSS patients as well as the associated factors.

**Methods:** A cohort of pSS patients that had been followed-up in the Department of Rheumatology, Tongji hospital of Tongji University, from 2011 to 2017 was retrospectively assessed. Clinical and laboratory findings about the patients were recorded.

**Results:** Out of 232 pSS patients composing the cohort, cytopenia was already present in 55.60% ( $n=129$ ) at the time of diagnosis. Anaemia was detected in 30.17% ( $n=70$ ), leukopenia in 37.5% ( $n=87$ ), neutropenia in 22.41% ( $n=52$ ), and thrombocytopenia in 26.72% ( $n=62$ ) of patients. The proportion of patients with cumulative cytopenia was 6.47% ( $n=15$ ). Cumulative cytopenia was disease-related in 5.60% ( $n=13$ ) and medication-related in 0.86% ( $n=2$ ) of the patients. In patients with cytopenia at the time of diagnosis, erythrocyte sedimentation rates (ESR) were higher ( $p<0.001$ ), C3 and C4 hypocomplementemia was more prevalent ( $p<0.001$ ,  $p=0.060$ ), and they were positive for anti-SSB at a greater proportion ( $p=0.058$ ). Hyperglobulinemia, C3 hypocomplementemia, positive anti-SSA and anti-SSB might increase the incidence of anaemia in pSS, with OR of 2.700, 2.042, 1.537 and 1.901, respectively. In addition, logistic regression analysis suggest C3 hypocomplementemia might be associated with different types Leukopenia ( $p<0.01$ ), while abnormal Transaminase and C4 hypocomplementemia are independent risk factors for thrombocytopenia with a OR of 4.171 (1.516–11.480) and 5.697 (1.662–19.523). Cytopenia in pSS patients not either at diagnosis or during follow-up, was always easy to be ameliorated, but several cases led to unfavourable outcome.

**Conclusions:** The most common haematological disorders in pSS patients are leukopenia, and cytopenia in pSS patients might be related to disease activity.

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#### AB0638 CLINICAL SIGNIFICANCE OF ESR IN CHINESE PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

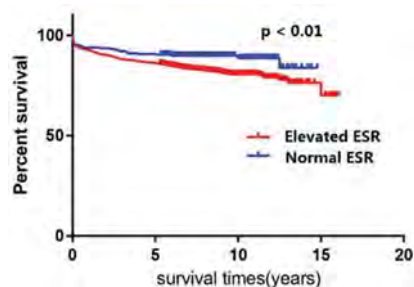
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**Background:** During the process of systemic lupus erythematosus (SLE), disease flare and infection are often accompanied by each other and always pose a major challenge to clinical treatments. Although erythrocyte sedimentation rate (ESR) has been tested in SLE patients for many years, there is still a lack of consensus on its value.

**Objectives:** To validate the value of ESR in Chinese SLE patients at the time of their first admission and to determine whether it is related to a poor outcome.

**Methods:** Clinical data of patients with ESR tested on their first admission were extracted from our SLE database; (Feng et al. *PLoS ONE* 2016;11(12): e0168619) and analysed for the relation with disease activity (SLEDAI), infection status, organ involvements and survival situation. To determine the risk of ESR for long-term mortality, cumulative survival was illustrated with the Kaplan-Meier plot and factors were compared using the Log-rank test.

**Results:** Totally 1225 patients were included in this study, of which 92.2% were female and the median age at admission was 34.3 years. The most often seen organ involvements were mucocutaneous (66.4%), musculoskeletal (55.0%), renal (51.7%) and hematologic (45.2%) respectively. ESR levels were correlated with SLEDAI scores ( $r=0.145$ ,  $p=0.000$ ), but not elevated in patients with infections. Patients with cardiopulmonary, renal or hematologic impairments had higher ESR levels (all  $p<0.05$ ). Subgroup analysis showed that serositis, renal insufficiency and anaemia might be responsible for the respective organ involvement. The ten year survival rates for patients with elevated ESR was 80.57%, lower than that of 88.62% for patients with normal ESR ( $p<0.01$ ) (figure 1).



**Abstract AB0638 – Figure 1.** Cumulative survival rates for patients with elevated or normal ESR at first admission

**Conclusions:** High ESR levels in SLE patients are associated with active disease and specific organ involvements, and may predict a poor prognosis. It should be checked routinely for the monitoring of SLE patients.

**Disclosure of Interest:** None declared

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#### AB0639 RISK OF MORTALITY IN SJOGREN'S SYNDROME AFTER 1ST ADMISSION

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**Background:** The long-term prognosis of patients with SS is unclear. Population-based studies have shown conflicting evidence regarding relative mortality in SS.

**Objectives:** There is conflicting evidence regarding prognosis in patients with SS (pSS). The aim of this study was to estimate the risk factors of mortality in patients with SS through a in hospital review.

**Methods:** Through a review of databases through October 2002 till 2016, we identified cohort studies reporting relative risk (compared with standardised population), risk factors and causes of mortality in patients with SS.

**Results:** We identified 695 (83.2% females) with SS, of whom 88 patients died over a median average follow-up of 13 years. Leading causes of mortality were infections; Risk factors associated with increased mortality were advanced age at diagnosis [HR 1.045 (95% CI 1.024, 1.067)], male sex [RR 2.18 (95% CI 1.45, 3.27)], associated with SLE [HR 2.448 (95% CI 1.108, 5.406)], diabetes [HR 1.986 (95% CI 1.125, 3.505)]

#### Abstract AB0639 – Table 1

	Regression coefficient	P value	HR	95.0% CI for HR	
				Lower	Upper
Gender	0.173	0.568	1.189	0.657	2.152
Age	0.044	0.000	1.045	1.024	1.067
BMI	-0.051	0.075	0.950	0.898	1.005
RA	0.245	0.576	1.277	0.541	3.017
SLE	0.895	0.027	2.448	1.108	5.406
Diabetes	0.686	0.018	1.986	1.125	3.505

**Conclusions:** After first admission, the risk factor for mortality include old age, associated with SLE and diabetes. These require close follow-up.

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#### AB0640 IMPLAUSIBLE ANTI-SMITH ANTIBODY IS NOT IMPLAUSIBLE TO AUTOIMMUNE DISEASE IN CHINESE POPULATION USING THE EUROIMMUN LINE IMMUNOASSAYS

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**Background:** Anti-Sm antibody is important test for lupus. In China, many labs detected anti-Sm using Euroimmun line immunoassays (LIA) kit, which mixture with purified Sm and RNP antigens as target antigens in Sm/RNP band and purified Sm antigens in Sm band. On the instruction, anti-Sm results should be determined according to the 2 bands. That is divided as true anti-Sm positive cases (having positive Sm and Sm/RNP bands) and implausible cases (having Sm band without Sm/RNP band), the value of implausible anti-Sm is not very clear now.

**Objectives:** We aimed at investigating the clinical value of the implausible anti-Sm in Chinese population.



**Methods:** Total of 39 766 patients were analysed for anti-Sm antibody using the EURO lineimmuno assay skit, of which 1208 cases are positive for anti-Sm. All cases with positive anti-Sm were divided into true anti-Sm group and implausible group according to the result of Sm/RNP band. The proportion of clinical diagnosis including autoimmune diseases (AIDs) and non-immune diseases (NAIDs) and the level of some clinical serum indexes were retrospectively analysed for the implausible anti-Sm cases.

**Results:** Implausible anti-Sm were evidenced in 271/1208 (22.42) of all positive anti-Sm cases. Among patients with positive anti-Sm, 177 cases have definitive diagnoses (65.31%, 177/271), with autoimmune diseases accounting for 68.36% (121/177), of whom 96 had systemic lupus erythematosus (SLE) (79.34%). In addition, there are 5 implausible cases with rheumatoid arthritis (RA), 3 with Sjogren syndrome (SS) and 10 with mixed connective tissue diseases (MCTDs). The titer of antinuclear antibodies (ANA) in patients with implausible anti-Sm is lower than ones with true anti-Sm. Impausible group have the same gender ratio, mean onset age and frequency of autoantibodies with true group. The prevalence of one of NAIDs, kidney disease, was significantly lower in implausible group than in true group ( $X^2=3.841$ ,  $p=0.05$ ).

**Conclusions:** Implausible anti-Sm have great diagnostic value in AIDs just as true anti-Sm. Patients with implausible anti-Sm have less incidence of evolving to autoimmune injury and kidney injury. Patients with implausible anti-Sm but without autoimmune diseases may be potential autoimmune disease victims.

**Acknowledgements:** This work was supported by fund of Department of Science and Technology of Sichuan Province, Grant No. 2016 JY0035 and the fund of Health and Family Planning Commission of Sichuan Province, Great. No.16pg326.

**Disclosure of Interest:** None declared

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#### AB0641 CORRELATION BETWEEN PHYSICIANS AND PATIENTS IN THE ASSESSMENT OF DISEASE ACTIVITY IN SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** In the assessment of systemic lupus erythematosus (SLE), laboratory data and clinical findings have been more focused than patient-reported outcomes which reflect quality of Life. Previous studies showed discrepancy between patients and physicians in assessments of disease activity in SLE.<sup>1</sup> The Systemic Lupus Activity Questionnaire (SLAQ), a lupus disease activity index which consisted of only patient reported outcomes, and SLE Disease Activity Index 2000 (SLEDAI-2K) were poorly correlated.<sup>2</sup>

**Objectives:** We aimed to investigate the correlation between SLAQ and SLEDAI-2K scores in those who had discordance between patients' VAS and physicians' VAS or not.

**Methods:** Both SLEDAI-2K and SLAQ were routinely measured at every outpatient visit in all SLE patients. We analysed the data between 9/12/2017 and 12/31/2017. Patients were divided into concordance (|patients' VAS-physicians' VAS| <25) or discordance group (|patients' VAS-physicians' VAS| ≥25).<sup>3</sup> We measured correlation between SLAQ score vs SLEDAI-2K or SLEDAI-2K-nolab scores by Spearman's correlation in the concordance group and the discordance group. Comparison between the concordance group and the discordance group were performed using chi-squared test for categorical variables and Student t-test, Welch's t-test or Mann-Whitney U test for continuous variables.

**Results:** Total 130 patients were analysed; 91% of female, a mean age (SD) of 44<sup>15</sup> years, steroid use of 91%, immunosuppressant use of 54%, HCQ use of 70%. Median SLAQ, SLEDAI-2K and SLEDAI-2K-nolab scores were 4 [IQR: 2–7], 4 [IQR: 2–4] and 0 [IQR: 0–2], respectively. Among them, 86 (66%) were classified in the concordance group. The SLAQ scores were weakly correlated with the SLEDAI-2K scores ( $\rho=0.228$ ,  $p=0.009$ ), and with SLEDAI-2K-nolab scores ( $\rho=0.352$ ,  $p<0.001$ ). In the concordance group, the SLAQ scores correlated with SLEDAI-2K scores ( $\rho=0.327$ ,  $p=0.002$ ) and SLEDAI-2K-nolab scores ( $\rho=0.523$ ,  $p<0.001$ ). The pain VAS and RAPID3 in the discordance group were significantly higher than those in the concordance group (30.77±26.54 vs 10.71±14.31,  $p<0.001$ , 8.11±5.87 vs 2.97±3.23,  $p<0.001$ , respectively). In the discordance group, the SLAQ scores were not correlated with SLEDAI-2K scores ( $\rho=-0.029$ ,  $p=0.849$ ) and with SLEDAI-2K-nolab scores ( $\rho=-0.083$ ,  $p=0.957$ ).

**Abstract AB0641 – Table 1.** LLDAS: Lupus low Disease Activity State \*Student t-test \*\*Welch's t-test †Mann-Whitney U test

	concordance group(n=85)	discordance group(n=44)	p value
Age (mean, SD)	41.74 (14.74)	49.00 (15.83)	0.010*
Sex (female) (%)	76 (90.7)	40 (90.9)	1.000
Disease duration (year, mean, SD)	10.78 (9.47)	12.18 (10.75)	0.447*
Antimalarial (%)	81 (70.9)	30 (68.2)	0.903
Immunosuppressant (%)	47 (54.7)	23 (52.3)	0.943
PSL doses (mean, SD) (mg)	5.13 (4.48)	5.59 (5.95)	0.929†
LLDAS (%)	48 (55.9)	22 (50.0)	0.858
MDHAQ (mean, SD)	0.20 (0.55)	0.33 (0.46)	0.015†
Pain (100mm VAS) (mean, SD)	10.71 (14.31)	30.77 (26.54)	<0.001**
Patient's global (100mm VAS) (mean, SD)	14.43 (15.72)	29.57 (23.25)	<0.001**
Physician's global assessment (100mm VAS) (mean, SD)	15.94 (13.64)	15.07 (15.38)	0.829†
RAPID3 (mean, SD)	2.97 (3.23)	8.11 (5.87)	<0.001**
SLAQ score (mean, SD)	4.83 (3.83)	8.16 (4.88)	0.056*
SLEDAI-2K (mean, SD)	3.50 (3.14)	3.82 (2.90)	0.575*
SLEDAI-2K-nolab (mean, SD)	0.92 (2.22)	1.73 (2.68)	0.030†

LLDAS: Lupus low Disease Activity State \*Student t-test \*\*Welch's t-test †Mann-Whitney U test

**Conclusions:** The correlation between SLAQ vs SLEDAI-2K or SLEDAI-2K-nolab scores was exhibited in the concordance group. Musculoskeletal pain may be associated with the discordance between patients' and physicians' assessment.

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#### AB0642 GLUCOCORTICOID INTAKE, HYPERGLYCEMIA AND OSTEOPOROSIS IN PATIENTS WITH AUTOIMMUNE DISEASES

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**Background:** Autoimmune diseases (AID) are often treated with glucocorticoids. Glucocorticoids have a number of substantial side effects in human body, including hyperglycemia and osteoporosis.

**Objectives:** Our study was to investigate the use of glucocorticoid in patients with autoimmune diseases and its negative influence on blood glucose and osteoporosis in the patients who receiving glucocorticoid treatment.

**Methods:** Patients with autoimmune diseases were enrolled from July to December in 2017 in rheumatology department of the Third Affiliated Hospital of Sun Yat-sen University. Demographic information, family history, past medical history, and clinical information were collected by two rheumatologists, including years of having glucocorticoids for treatment, largest dose of methylprednisolone, current dose of glucocorticoids. Blood glucose, glycosylated haemoglobin, and bone mineral density was required. The Statistical Package for Social Sciences (SPSS) software version 21 was used for all data management and analysis.

**Results:** Of all the 75 patients, 15 (20%) were male patients. 14.7% had primary education, while 26.6% received education in university. Numbers of the patients were stated as follows. Lupus, 29; rheumatoid arthritis, 4; Sjogren's syndrome, 10; systemic sclerosis, 10; myositis, 4; mixed connective tissue disease, 1; autoimmune hepatitis, 1; vasculitis, 5; other diseases, 11. Mean age was 40.29±14.64 years. Mean disease duration was 4.74±6.62 years. 3 (4%) patients had family history of diabetes. 3 (4%) patients had past medical history of diabetes. Mean duration of taking glucocorticoids was 3.30±4.40 years. 13 (17.3%) of the patients underwent high dose of glucocorticoid intravenous pulse (120 mg to 1000 mg of methylprednisolone). Current dose of glucocorticoids was 5.30±3.96 tablets of methylprednisolone. Mean blood glucose was 4.61±0.92 mmol/L. Mean glycosylated haemoglobin was 5.46±0.84. 2 patients were found to have diabetes in this study. 5 other patients were found to have higher blood sugar than normal range (3.9–6.1 mmol/L, according to our laboratory). 14 (18.7%) of the patients had osteoporosis according to BMD scores. In 17 patients who had receiving glucocorticoids for more than five years, 3 (17.6%) patients were found to have higher

blood sugar than normal range and 5 (29.4%) patients were found to have osteoporosis.

**Conclusions:** Glucocorticoids have substantial side effects in hyperglycemia and osteoporosis in the patient receiving glucocorticoid treatment. More years of taking glucocorticoids could lead to more hyperglycemia and osteoporosis. We should evaluate side effects of glucocorticoids in the patients with AIDs.

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AB0643

### FT3 STRONGLY CORRELATES WITH LIPID PROFILES AND DISEASE ACTIVITY IN SLE PATIENTS

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**Background:** Dyslipidemia is prevalent in Systemic Lupus Erythematosus (SLE) patients and associated with lupus nephritis. Non-thyroidal illness syndrome (NTIS) frequently occurs in some autoimmune diseases. The incidence of dyslipidemia and NTIS in SLE patients vary in different studies and the association of NTIS and dyslipidemia in SLE patients has not yet elucidated.

**Objectives:** To investigate the frequency of dyslipidemia and NTIS in SLE patients and their association with laboratory parameters and SLE disease activity index (SLEDAI). To further explore the association between FT3 and blood lipid profiles in SLE patients.

**Methods:** This cross-sectional and prospective study included 271 patients fulfilled the ACR criteria for SLE. Forty-one patients who had a history of thyroid disease and/or familial hyperlipidemia and/or other rheumatologic diseases, and those took lipid-lowering agents or thyroid medications are excluded. Detailed laboratory parameters were collected and SLEDAI were assessed by qualified specialists of Rheumatology.

**Results:** Frequencies of dyslipidemia and NTIS in SLE patients are 61.8% and 57.2%, respectively. Laboratory indexes such as BUN ( $p<0.05$ ), urine acid ( $p<0.01$ ), CRP ( $p<0.001$ ), ESR ( $p<0.001$ ) and SLEDAI ( $p<0.05$ ) are significantly increased in SLE patients with dyslipidemia than non-dyslipidemia. Compared to euthyroid SLE patients, SLE patients with NTIS showed substantially elevated 24 hour urine protein ( $p<0.001$ ), fasting blood glucose ( $p<0.001$ ), BUN ( $p<0.001$ ), serum creatinine ( $p<0.01$ ), uric acid ( $p<0.05$ ), CRP ( $p<0.05$ ), ESR ( $p<0.001$ ) and SLEDAI ( $p<0.01$ ). Moreover, triglyceride ( $p<0.01$ ), total cholesterol ( $p<0.01$ ), LDL ( $p<0.01$ ) and ApoB ( $p<0.001$ ) levels are markedly higher in SLE patients with NTIS than euthyroid ones, while HDL levels obviously decreased in the former group ( $p<0.01$ ). More notably, the lower FT3 patients showed more severe lipid profiles and significantly higher 24 hour urine protein ( $p<0.001$ ), BUN ( $p<0.001$ ), serum creatinine ( $p<0.001$ ), uric acid ( $p<0.05$ ), and SLEDAI ( $p<0.05$ ) than patients with normal FT3. FT3 levels are negatively correlated with triglyceride ( $r=-0.263$ ,  $p<0.0001$ ), total cholesterol ( $r=-0.295$ ,  $p<0.0001$ ), LDL ( $r=-0.273$ ,  $p<0.0001$ ) and positively correlated with HDL ( $r=0.180$ ,  $p<0.01$ ).

**Conclusions:** Dyslipidemia and NTIS are prevalent in SLE patients and strongly correlates with disease activity. SLE patients with NTIS are more likely to combine with dyslipidemia, FT3 levels significantly correlates with lipid profiles and FT3 may plays a protective role in dyslipidemia.

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AB0644

### PREGNANCY OUTCOMES OF PLANNED PREGNANCY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A RETROSPECTIVE MULTICENTER STUDY

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**Background:** Compared with the general population, patients with SLE are still at high risk of adverse pregnancy outcomes (APOs). A number of studies have shown that patients with SLE are more likely to develop fetal complications, including fetal loss, preterm birth and IUGR, compared to healthy women.

**Objectives:** To investigate the fetal and maternal outcomes, as well as predictors for APOs in women with SLE who conceived when disease was stable, the so called "planned pregnancy".

**Methods:** A retrospective multicenter study of 243 patients with SLE who underwent planned pregnancy was performed. APOs in fetus and mothers were recorded.

**Results:** The average age at conception was 28.9±3.9 years. Duration of SLE prior to pregnancy was 4.4±4.3 years. Fetal APOs occurred in 86 (86/243, 35.4%) patients. Preterm births, intrauterine growth retardation (IUGR), fetal distress, and fetal loss accounted for 22.2%, 14.8%, 11.1%, and 4.9%, respectively. Forty-two preterm infants (42/54, 77.8%) were delivered after the 34th week of gestation. All the preterm infants were viable. Fifty-two patients (52/243, 21.4%) had disease flares, among which 45 (45/52, 86.5%) cases were mild, 6 (6/52, 11.5%) were moderate and 1 (1/52, 1.9%) was severe. Fifty-two disease flares (21.4%) occurred, among which 8 disease flares occurred during the first-trimester, 15 during the second-trimester, and 29 during the third-trimester. Disease activity was mild in 45 (45/52, 86.5%) patients, moderate in 6 (6/52, 11.5%), and high in 1 (1/52, 1.9%). Disease flares were mainly presented as active lupus nephritis (41/52, 78.8%), thrombocytopenia (10/52, 19.2%), and skin/mucosa lesions (9/52, 17.3%). Pregnancy-induced hypertension (PIH) occurred in 29 patients, among which 3 were gestational hypertension and 26 were preeclampsia. Multiple analysis showed that disease flares (OR 8.1, 95% CI 3.8–17.2,  $p<0.001$ ) and anticardiolipin antibodies positivity (OR 7.4, 95% CI 2.5–21.8,  $p<0.001$ ) were associated with composite fetal APOs.

**Conclusions:** Planned pregnancy improved fetal and maternal outcomes, presenting as lower rate of fetal loss, more favourable outcomes for preterm infants as well as less severe disease flares during pregnancy. Our research reinforced the importance of planned pregnancy, which allowed women with SLE to conceive in a proper time monitored by multidisciplinary experts.

**Disclosure of Interest:** None declared

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## Vasculitis

AB0645

### ANCA VASCULITIS: THE EXPERIENCE AND TRENDS IN PATIENT CARE FROM A SINGLE CENTRE

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**Background:** ANCA-associated vasculitis [AAV] is a small-medium vessel vasculitis that presents in a multi-systemic fashion, and is associated with significant mortality. Outcomes have improved with the introduction of immunosuppressive medications [ISM], the evidence supporting the initial choice ISM is limited, and may be influenced by health disparities related to social factors.

**Objectives:** The objective of this study was to compare various factors known to influence management and outcomes in AAV. Factors including, patient demographics, socioeconomic, clinical presentations, and medication choices were reviewed in relation to outcomes within the cohort.

**Methods:** This was a retrospective, single centre, hospital-affiliated cohort study. A list of all patients seen by the Rheumatology service between 2011 and 2016 with a diagnosis of AAV was generated. A review of the 3000 charts confirmed 77 patients that met the 1990 American College of Rheumatology criteria for AAV. General demographic data including age, gender, zip code, and median household income as well as disease related data including serology, disease manifestation, and treatment were obtained through a chart review and recorded in the database. Supplemental socioeconomic information for each patient zip code was obtained from the United States Government Census website.

**Results:** In our cohort the anti-proteinase 3 [PR3] antibody was the most common positive antibody. There was a relationship between PR3 antibody positivity rate

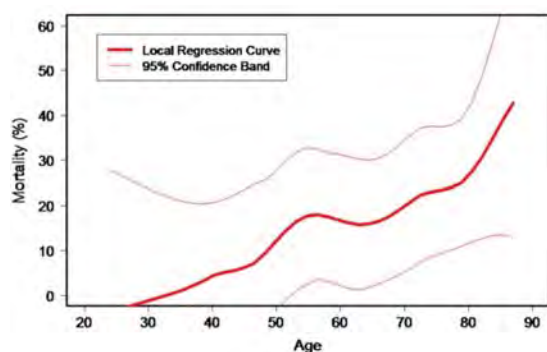
and body mass index [table 1]. Given the low number of non-Caucasians we were unable to comment on the relationship between antibody and race. Medication choice and mortality were independent of mean household income. Rituximab was the most commonly prescribed ISM [44%]. The median age of rituximab exposure patients was 65 years and 60 years for unexposed patients. There was no significant relationship between age and medication choice. Rituximab was prescribed 60% of the time in renal AAV [ $p < 0.01$ ] and 53% of the time in pulmonary AAV [ $p < 0.01$ ]. Other commonly prescribed medications in the cohort included Mycophenolate [20%], Methotrexate [24%] and Cyclophosphamide [28%].

The overall mortality rate was 17% [13/75] [figure 1]. There was no significant difference in the mortality rate of patients 65 years and older [23%, 9/39] compared to patients 64 and younger [11%, 4/36;  $p = 0.17$ ]. The mortality rate was also independent of median household income.

Abstract AB0645 – Table 1

	PR3 antibody		MPO antibody	
	Negative	Positive	Negative	Positive
BMI<29.9	69%	31%	71%	29%
BMI 30–39.9	35%	65%	75%	25%
BMI>40	20%	80%	100%	N/A
p-value	<0.01		0.38	

BMI: body mass index, PR3: proteinase 3, MPO: Myeloperoxidase



Abstract AB0645 – Figure 1

**Conclusions:** There was no relationship between age, sex, income, immunosuppressive therapy, and mortality in our AAV cohort. The mortality rate was higher in more severe disease and rituximab was more commonly used in such cases as well as in older patients. The limitations of the study include this being a hospital based cohort, where social demographics may have less of an impact. There was a lack of racial diversity, though the cohort did reflect the general demographics in southwest Virginia.

**Disclosure of Interest:** None declared

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#### AB0646 IDENTIFICATION OF RISK FACTORS FOR RECURRENCE IN POLYMYALGIA RHEUMATICA

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**Background:** Glucocorticoids (GCs) are effective for polymyalgia rheumatica (PMR); however, some patients relapse during GC tapering and develop adverse events of GCs.

**Objectives:** To identify risk factors for recurrence in patients with polymyalgia Rheumatica (PMR).

**Methods:** Cox proportional hazards regression analyses was performed 78 patients with PMR who had been treated by 2015 EULAR/ACR recommendations between January 2015 and December 2017 in our centre. The following data at baseline were collected retrospectively: age, sex, time of diagnosis, location of arthralgia/myalgia, maximum dose of prednisolone, US findings of shoulder, laboratory data before the initial treatment.

**Results:** Seventy-eight patients had been diagnosed with the 2012 EULAR/ACR provisional classification criteria for PMR, and had been treated first with GCs. They were at the age of  $71.7 \pm 9.5$ , including 34 males and 44 females. Duration of symptoms before therapy was  $2.0 \pm 2.0$  months and the PMR duration was  $21.2 \pm 15.5$  months. Twenty-seven patients had arthralgia/myalgia other than shoulders and hips. The maximum dose of prednisolone was  $15.9 \pm 4.4$  mg/day. US findings

of shoulder were positive in 65 patients. Relapses occurred in 37 patients (47%), when the dose of prednisolone was reduced to  $5.6 \pm 5.5$  mg/day at  $8.9 \pm 6.4$  months. MTX ( $8.6 \pm 3.1$  mg/wk) was added in 29 patients or the dose of prednisolone was increased in 8 patients, similarly to the 2015 EULAR/ACR recommendations for the management of PMR. Additional MTX was ineffective in 16 patients, followed by adding tocilizumab in 8 patients. Forty patients discontinued GCs at  $17.6 \pm 10.6$  months.

On univariate analysis, 4 variables were identified as significant risk factors affecting PMR recurrence: increased platelets ( $p = 0.00192$ ), low IgA ( $p = 0.00149$ ), arthralgia/myalgia limited to shoulders and hips ( $p = 0.02$ ), and the maximum dose of prednisolone used ( $p = 0.0062$ ). These 4 variables were introduced into the multivariate analysis, and the following 3 variables were retained as independent significant risk factors: the maximum dose of prednisolone ( $p < 0.005$ ), limitation of arthralgia/myalgia to shoulders and hips ( $p < 0.05$ ) and low IgA ( $p < 0.005$ ).

**Conclusions:** These results indicate that the maximum dose of prednisolone, the absence of peripheral joint pains and low IgA may be associated with the recurrence in PMR patients

**Disclosure of Interest:** None declared

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#### AB0647 TAKAYASU'S ARTERITIS IN ITALY: CLINICAL PRESENTATION, DIAGNOSTIC DELAY AND VASCULAR PATTERN

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**Background:** Takayasu arteritis (TA) is a large vessel vasculitis<sup>1</sup>. At disease presentation TA patients may present with inflammatory symptoms, sometimes associated with vascular pain. As arterial lesions ensue, more characteristic features may be found, such as limb claudication, decreased or absent pulses, vascular bruits, discrepancies in blood pressure<sup>2</sup>. Since initial symptoms are often non-specific, early detection of TA is challenging and patients at diagnosis frequently have established damage<sup>3</sup>

**Objectives:** To describe symptoms presentation and vascular involvement in a large cohort of Italian TA patients. To assess the diagnostic delay associated with symptoms and arteries involved at presentation

**Methods:** Data from 114 TA patients diagnosed according to ACR classification criteria at our tertiary centre were retrospectively collected. Signs and symptoms subsequently attributed to TA, age at first symptom onset, and age at diagnosis were analysed. The diagnostic delay was calculated. Arteries involved before the diagnosis were identified. Non-parametric statistic tests were used

**Results:** The cohort included mostly female patients (104;91.2%). Mean age at first symptom subsequently attributed to TA was 30.5 years ( $\pm 13.1$ ). Age at presentation of first TA related symptom was 18–40 years in 68 (59.6%), <18 years in 20 (17.5%), >40 years in 26 (22.8%) patients. Mean age at diagnosis was 36 years ( $\pm 12.7$ ). Mean diagnostic delay was 65.6 months ( $\pm 85.3$ ). Diagnostic delay was >1 year in 75 patients (65.8%). The most frequent finding before diagnosis was raised inflammatory markers (82.4%), the least common pulmonary hypertension (2.8%). The features significantly associated with a diagnostic delay >1 year were arthralgias, hypertension, previous vascular surgery. The mean diagnostic delay (in months) was significantly higher in patients with raised inflammatory markers ( $8.4 \pm 4.9$  vs  $100.5 \pm 121.8$ ,  $p = 0.005$ ), carotidynia ( $5.8 \pm 5.7$  vs  $34.2 \pm 32.9$ ,  $p = 0.034$ ) and in patients who had upper limb claudication ( $11.0 \pm 13.2$  vs  $65.44 \pm 77.01$ ,  $p = 0.002$ ). Data about arteries involved before diagnosis were available for 86 patients (75.4%). They were: subclavian in 43 (50%), carotid in 38 (44.2%), renal in 19 (22.1%), abdominal aorta in 18 (20.9%), ascending aorta in 15 (17.4%), axillary in 12 (14%), vertebral in 11 (12.8%), superior mesenteric in 10 (11.6%), thoracic aorta in 10 (11.6%), aortic arch in 9 (10.5%), celiac tripod in 9 (10.5%), brachiocephalic in 8 (9.3%), iliac in 8 (9.3%), coronary in 6 (7%), femoral in 6 (7%), pulmonary in 5 (5.8%), brachial in 3 (3.5%), popliteal in 2 (2.3%) patients. There was no significant difference in the arteries involved between patients diagnosed <1 year and >1 year from symptoms onset. Mean diagnostic delay was not significantly different according to the arteries involved

**Conclusions:** In Italy TA diagnosis is burdened with an important diagnostic delay. In our cohort it seems that the presence of both specific and non-specific symptoms is associated with delayed recognition of TA. Moreover, the need for vascular surgery in young women should rise the concern about TA

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#### AB0648 CORRELATES OF FATIGUE IN ANCA-ASSOCIATED VASCULITIS

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**Background:** Fatigue is a common symptom among patients with ANCA-associated vasculitis (AAV) identified as the greatest burden of their disease.<sup>1,2</sup> Research revealed associations between fatigue and bio-psychosocial factors but not with clinical factors.

**Objectives:** To assess fatigue and its correlates among patients with granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA).

**Methods:** 37 patients (44% women; mean age 52.3 years; range 18–85) with GPA (27 patients) and MPA (10 patients) hospitalised in 3 clinical centres completed Multidimensional Fatigue Inventory-20 (MFI-20).<sup>3</sup> Anxiety and depression were assessed by the Hospital Anxiety and Depression Scale (HADS). Socio-demographic data including age, sex, education, marital and occupational status were recorded. Disease characteristics included its' duration, severity, activity, organ involvement and laboratory data.

**Results:** The mean age was 52.3 years (range 18–85 years), and the mean disease duration was 43.1 months (range 1–248). 4 patients had limited type of the disease, 13 – early systemic, 16 – systemic and 4 – severe type of the disease. 75% of patients had active disease as defined by Birmingham Vasculitis Activity Score, BVASv3 (mean BVASv3 in active patients 12.2). 8% of patients were not taking steroids. 40.5% of patients had CRP >5 mg/l, 43% had anaemia, 10% – thrombocytosis and 43% had renal insufficiency. Mean score of MFI-20 was 57 points (range 31–100). There were no differences in MFI-20 overall score between groups according to sex, education, marital and occupational status. No significant associations between fatigue and disease-related factors as well as steroid dose were observed. Depression ( $r=0.79$ ,  $p<0.00000$ ) and anxiety ( $r=0.63$ ,  $p<0.00002$ ) were strongly correlated with MFI-20 overall score.

**Abstract AB0648 – Table 1.** Socio-demographic characteristics of the study sample.

Variable	n (%)
<b>Education</b>	
primary	6 (16)
occupational	3 (8)
secondary	12 (32)
higher	16 (43)
<b>Marital status</b>	
married	29 (78)
divorced	3 (8)
free state	4 (11)
widower	1 (3)
<b>Occupational status</b>	
employed	18 (49)
unemployed	3 (8)
pensioner	8 (22)
annuitant	5 (13)
student	3 (8)

**Conclusions:** Since fatigue was not related to clinical characteristics, tiredness declared by the patient should not be interpreted as a symptom of active disease. There were no connexions between fatigue and socio-demographic variables. The strong association between fatigue and depression and anxiety levels indicates the necessity to supplement the standard drug therapy and/or cognitive-behavioural therapy aimed at reducing anxiety and improving mood.

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#### AB0649 USE OF BIOLOGICAL DMARDS IN PATIENTS WITH PRIMARY VASCULITIS; RESULTS FROM TURKBIO REGISTRY

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**Background:** Untreated, The systemic vasculitides can be devastating, with high rates of morbidity and mortality. Recently, most of biological agents have evaluated in clinical trials, and management of systemic vasculitis has been revolutionised over the last decade.<sup>1,2</sup>

**Objectives:** Here, we report the frequency of using and switching rate of biological agents in different types of primary vasculitis patients.

**Methods:** TURKBIO registry is the Turkish version of Danish DANBIO rheumatological database which has been established in 2011. All patients with primary vasculitis who received biological agents registered in TURKBIO registry between dates of October 2011 and January 2018 were included in this study. The demographic data, the date of starting to use of biological drug, frequency of using and switching biological agents were collected.

**Results:** As of January 2018, 108 primary vasculitis patients were recruited (mean age: 38.4±10.9 [min-max: 19–67]; female 48%); 48 patients (44%) of them had Behçet's disease (BH), 35 (32%) had Takayasu arteritis (TA), 24 (22%) had granulomatosis polyangiitis, and one of them had microscopic polyangiitis. The most commonly used biological agents in current treatment were as follows: 75% of patients received infliximab (INF) and 15% received adalimumab (ADA) in BD patients; 48.6% received tocilizumab (TCZ), 23% received INF and 20% received ADA in TA patients; all patients with granulomatosis with polyangiitis (GPA) were treated with rituximab. The switching rate was 54% in TA patients, 27% in BD patients, and 4% in GPA patients. The most frequent switching was found at INF (28/78) and ADA (9/23) which was the most commonly used agent in TA and BD. The lowest switching rate was TCZ (2/17) in TA patients (table 1).

**Abstract AB0649 – Table 1.** Demographical features and managements of patients with primary vasculitis

n (%)	All Patients n:108	BD n=48	TA n=35	GPA n=24
<b>Mean Age year mean±sd (min-ma)</b>	<b>38.4±10.9 (19–67)</b>	<b>37±8.3 (19–54)</b>	<b>35.7±11.1 (20–59)</b>	<b>47.7±11.1 (23–67)</b>
<b>Gender (F)</b>	<b>52(48)</b>	<b>11 (23)</b>	<b>32 (91)</b>	<b>9 (37.5)</b>
<b>Current Treatment</b>	19 (18)	2 (4)	17 (49)	0
Tocilizumab	25 (23)	0	0	24 (100)
Rituximab	2 (2)	0	2 (6)	0
Certolizumab	44 (41)	36 (75)	8 (23)	0
Infliximab	14 (13)	7 (15)	7 (20)	0
Adalimumab	3 (3)	2 (4)	1 (3)	0
Etanercept	1 (1)	1 (2)	0	0
Golimumab				
<b>Last Drug Survival mean±sd (min-max) (month)</b>	<b>25.2±17.9 (2–88)</b>	<b>26.8±16.2 (3–77)</b>	<b>28±21.7 (2–88)</b>	<b>22.3±15.9 (2–60)</b>
<b>Switching Rate</b>	<b>33 (31)</b>	<b>13 (27)</b>	<b>19 (54)</b>	<b>1 (4)</b>
Tocilizumab	3	0	2	1
Infliximab	28	10	18	0
Adalimumab	9	4	5	0
Etanercept	4	3	1	0

**Conclusions:** This is the first evaluation of primary vasculitis patients who used biological agents from TURKBIO registry. According our data, there was high switching rate with anti-TNF agents in TA patients. The limitation of this study was the low number of the patients with primary vasculitis who used biological agents.

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**AB0650 THROMBOTIC MICROANGIOPATHY ASSOCIATED TO ANCA-POSITIVES VASCULITIS: A FRENCH RETROSPECTIVE CASE CONTROL STUDY AND LITERATURE REVIEW**

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**Objectives:** In this large nationwide French case-control study, we describe the features of TTP and ANCA-positive vasculitis; compare to vasculitis without associated TTP; describe the outcome and treatments.

**Methods:** We collected all cases with TTP and associated vasculitis. We conducted a literature review using PubMed, Web of Science, congress posters from January 2005 to August 2017 of PTT and ANCA-positive vasculitis.

A control group of MPA without TTP during all the disease follow-up was extracted from the Saint Antoine and Montfermeil Hospital patients with vasculitis. Firstly we compared our PTT cases and the literature review cases and secondary with a control group ANCA vasculitis without MAT.

**Results:** 8 patients with MAT secondary to ANCA associated vasculitides were included in our French series 75% of Women with a median age 45 years, 21–76 positive ANCA in 50% and 37.5% is MPO, BVSA score at 16, FFS at 1. In 10 literature cases 90% Women, a median age 60 years [17–77], positive ANCA in 100% and 30% is MPO, BVSA score at 39, FFS at 1.

The clinical features at the diagnosis of vasculitis were fever (n=5; 62%), ENT involvement (25%), kidney crescent glomerular involvement (n=6; 75%) with kidney failure in joint involvement (n=2; 25%) polyarthralgia type, with gastrointestinal involvement type mesenteric ischemia and pericarditis and lung involvement (nodules and alveolar haemorrhage) (n=1; 12.5%), in one case each Median C-reactive protein levels were at 49 mg/L [1–204], with creatinemia at 170 mg/dl [80–588]. ANCA were present in 4 patients (50%), MPO in 3 cases (37.5%). The time between the diagnosis of vasculitis and TTP was 9 months [0–51].

TTP features were: Hb at 7.8 g/dl [4.8–10], LDH 1658 [777–3110], platelets 33000 [3000–1 25 000], haptoglobin at 0 [0–0.05], creatinine at 205 [80–757]. ADAMTS 13 levels were at 10 [1–138], and x patients have normal ADAMTS13 levels, with anti ADAMTS 13 antibodies in 1 case. Plasma exchanges were done in all patients with median of 10 exchanges [4–23], 37.5% are dialyzed.

**Conclusions:** In comparison to our cases, the literature patients have similar organs involvement, but median creatinemia levels and BVAS levels were higher in the literature cases. Considering TTP features, our cases have less frequent active vasculitis, less important creatinine levels and thus less recurs to kidney dialysis.

In vasculitis associated with TTP, there was no significant differences in organ involvements, BVAS and FFS scales values, laboratory data and ANCA levels. Only creatinemia as expected was higher in vasculitis associated with TTP (225 Mmol vs 150 Mmol, p=0.0044).

**Disclosure of Interest:** None declared

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**AB0651 FREQUENCY OF PULMONARY HYPERTENSION IN BEHÇET'S DISEASE**

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**Background:** Behçet's disease (BD) is a systemic vasculitis that involvement of pulmonary arteries can be seen.

**Objectives:** The aim of this study was to determine the frequency and the causes of pulmonary hypertension (PH) in patients with BD.

**Methods:** We studied consecutively 154 BD patients who were fulfilled the International Study Group criteria for diagnosis of BD. All patients were evaluated with transthoracic echocardiography (TTE) for the presence of PH. BD patients were categorised according to the involved organs in 5 groups: group 1 mucocutaneous and articular, group 2 ocular, group 3 vascular, group 4 gastrointestinal and group 5 neurologic involvements. The presence of PH was defined as estimated sPAB  $\geq 40$  mmHg, by TTE. Every subject evaluated by a detailed medical history and

physical examination was performed. Additional laboratory results were obtained from hospital file records.

**Results:** The mean age (SD) and the median (min-max) months disease duration of the patients were 41.8 $\pm$ 12.6 years and 126 (6–540) months respectively. PH was detected in 17 (11%) BD patients. Only 9 (52%) patients were symptomatic (NYHA FC >1). Left sided heart disease (Group II: 9 (52%) patients) was the leading cause of PH. Four (23%) patients had group IV PH and 75% (3/4) were symptomatic. Diastolic dysfunction (DD) was found in 32 (20.8%) patients and only 1 patient had systolic dysfunction. The number of patients with DD was significantly higher in patients with PH as compare to patients without PH (8 (47.1%) vs 24 (17.6%), p=0.005). There were no difference in demographic and clinical features of patients with and without PH. Only acneiform lesion was more frequently in patients without PH as compare to patients with PH, p=0.047 (table 1). There were no differences in frequency of PH in BD groups (table 2).

**Abstract AB0651 – Table 1.** Demographic and clinical characteristics features of Behçet disease

	All	sPAP $\geq 40$ mm HG	sPAP <40 mm HG
Female, n (%)	62 (40.3)	6 (35.3)	56 (40.9)
Age, mean, SD	41.8 $\pm$ 12.6	48.1 $\pm$ 14.6	41.0 $\pm$ 12.1
Disease duration (month), median (min-max)	126 (6–540)	168 (12–540)	120 (6–480)
Smoking, n (%)	76 (49.4)	7 (41.2)	69 (50.4)
Never smoker	47 (30.5)	5 (29.4)	42 (30.7)
Current smoker	31 (20.1)	5 (29.4)	26 (19.0)
Ex-smoker			
Oral ulcer, n (%)	154 (100)	17 (100)	137 (100)
Genital ulcer, n (%)	104 (67.5)	11 (64.7)	93 (67.9)
EN, n (%)	64 (41.6)	7 (41.2)	57 (41.6)
Papulo-pustular lesion, n (%)	35 (22.7)	3 (22.7)	32 (23.4)
Acneiform lesion*, n (%)	105 (68.2)	8 (47.1)*	97 (70.3)*
Articular, n (%)	33 (22.7)	4 (23.5)	31 (22.6)
Uveitis, n (%)	75 (48.7)	9 (52.9)	66 (48.2)
Pathergy, n (%)	40 (26)	6 (35.3)	34 (24.8)
Vascular, n (%)	48 (31.2)	9 (52.9)	23 (31.1)
Neurologic, n (%)	18 (11.7)	2 (11.8)	16 (11.7)
Gastrointestinal, n (%)	12 (7.8)	1 (5.9)	11 (8.0)

sPAP: Systolic pulmonary artery pressure, EN: Erythema nodosum

**Abstract AB0651 – Table 2.** Behçet disease group distribution in the pulmonary hypertension patients

Behçet disease (n)	Mucocutaneous and articular (39)	Ocular (75)	Vascular (48)	Gastrointestinal (12)	Neurologic (18)	p
sPAP $\geq 40$ , n (%)	2 (5.1)	9 (12)	9 (18.8)	1 (8.3)	2 (11.1)	0.413

sPAP: Systolic pulmonary artery pressure

**Conclusions:** The most frequent cause of PH in BD patients was group II PH. There were also significant number of patients with group IV PH. Pulmonary endarterectomy may be an option of treatment in inactive patients with group IV PH.

**Disclosure of Interest:** None declared

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**AB0652 PET/MR IN LARGE-VESSEL VASCULITIS: CLINICAL VALUE FOR THE DIAGNOSIS AND ASSESSMENT OF DISEASE ACTIVITY**

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**Background:** The diagnosis and the activity determination could be challenging in large-vessel vasculitis (LVV).

**Objectives:** The aim of this study was to analyze the value of hybrid PET/MR in LVV.

**Methods:** All consecutive patients with LVV who underwent PET/MR were included. PET/MR patterns were defined as inflammatory in the case of positive PET (grade=3) and abnormal MR (stenosis and/or wall thickening) and fibrous in the case of negative PET (grade 1 or 2) and abnormal MR.

**Results:** Thirteen patients with median age at 67 years (23–87 years) and 10 (77%) females were included, and underwent 18 PET/MR scans. Eleven PET/MR performed at diagnosis (n=4) or relapse (n=7) and 7 in patients in remission. 8/18 (44%) had PET/MR inflammatory pattern and 3/18 (17%) had fibrous pattern. PET/MR were normal in 2/10 (20%) cases of TA versus 5/8 (62%) cases of GCA

( $p=0.3$ ). The median SUVmax was 3.0 [1.8–8.6] without significant difference between GCA and TA: 3.4 (2.1–8.6) versus 2.6 (1.8–7.1) ( $p=0.4$ ), respectively. Eleven PET (61%) were performed under treatment, which consisted of steroids with a median dose at 30 mg/day [3–240]. Among 11 patients with active disease, 8 had inflammatory patterns and 3 had normal PET/MR, i.e. a sensibility of 73%, and the sensibility increased to 100% in patients with active TA disease. Median SUVmax were 4.7 [2.1–8.6] in patients with active disease versus 2 [1.8–2.6] in patients with remission ( $p=0.003$ ).

**Conclusions:** PET/MR is a new hybrid modality of imaging which is interesting for the diagnosis and the follow-up of large-vessel vasculitis.

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#### AB0653 PREDICTION OF RELAPSES IN AUTOIMMUNE LARGE-VESSEL VASCULITIS – TOWARDS PERSONALISED IMMUNOSUPPRESSIVE TREATMENT STEWARDSHIP

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**Background:** Giant cell arteritis (GCA) is an autoimmune disease of the large arteries. Treatment consists in long-term immunosuppression with glucocorticoids (GC). About half of the patients have disease flares ('relapses') despite standard therapy. Tocilizumab (TCZ) – an anti-IL6 receptor antibody – is highly effective in reducing relapses, but has high costs.

**Objectives:** Here, we tested whether the initial clinical presentation and/or immunological findings might predict a GCA patient subset with poor response to GC. These might benefit from early TCZ therapy.

**Methods:** We performed a chart review on 113 patients from our prospective GCA cohort over the first two years after diagnosis. All had a follow-up of at least three months (median follow-up 24 months, IQR 12.6–24). Clinical findings at diagnosis, routine labs (at 0, 1, 3, 6, and 12 months) and therapy information (drug and dose) were extracted from the electronic database.

Relapses were defined as the presence of GCA-related symptoms (ischaemic pain, polymyalgia (PMR)) and/or elevated systemic inflammation parameters (CRP, ESR) that responded to an increase in GC-dose. GC receptor (GCR) expression levels in T cells were assessed using flow cytometry. Patients were genotyped for two polymorphisms in the Glucocorticoid receptor gene (NR3C1) that have been associated with steroid-responsiveness in other autoimmune disease (Systemic lupus, Pemphigus...).

**Results:** Over the first 12 months, 50,6% experienced at least one relapse. The majority of relapses occurred after three months of treatment (median time to relapse 102 days, range 19–312). This is when the GC dose is tapered below 20 mg/d. 'Relapsers' had an average of 1.66 (range 1–4) relapses in the first year. Patients with fever at initial presentation had a 2.2-fold (CI 1.1–5.05) higher risk to experience relapses ( $p=0.02$ ). Other clinical findings were not associated with subsequent relapses. Low lymphocytes after the first month of therapy was the only lab value associated with relapse free follow up (698/ul vs 1021/ul,  $p=0.02$ ). This was independent of the cumulative GC dose that 'non-relapsers' and

'relapsers' received in this period (1747 mg vs. 1710 mg mg,  $p=0.4$ ). Relapsers had lower GCR expression levels, as assessed by flow cytometry.

**Conclusions:** Fever, lack of lymphocytopenia after one month of therapy and low GCR expression are risk factors for relapses in GCA. Low GCR expression combined with absence of lymphocytopenia during high dose GC therapy points at a constitutional steroid-resistance in relapsers. Whether patient stratification based on these parameters allows to safely adapt ('personalise') the intensity and/or duration of GCA treatment needs to be tested in a prospective clinical trial.

**Disclosure of Interest:** None declared

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#### AB0654 CLINICAL PROFILE AND RISK FACTORS OF INFECTIONS IN PATIENTS WITH ANCA-ASSOCIATED VASCULITIS (AAV) – 18-YEAR DATA FROM A SINGLE TERTIARY CENTRE

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**Background:** Despite advances in the treatment of AAV, there are still considerable morbidities related to treatment-related complications. Infection is one of the most commonly encountered problems in patients on immunosuppressive therapy.

**Objectives:** This single centre, retrospective study reviewed the clinical features and investigated the risk factors for infections among patients with AAV.

**Methods:** 104 patients with AAV diagnosed between January 2000 and December 2017 in a tertiary hospital were included. Demographic data and clinical parameters were reviewed. Logistic regression was performed to identify factors predicting infections.

**Results:** Around two-thirds of the 104 patients included were female (63.5%  $n=66$ ). Mean age at diagnosis was 64.4-year-old. The majority (65.4%,  $n=68$ ) had microscopic polyangiitis (MPA), 19.2% ( $n=20$ ) had granulomatosis with polyangiitis (GPA) and 15.4% ( $n=16$ ) had eosinophilic granulomatosis with polyangiitis (EGPA).

More than half of the patients (58%,  $n=61$ ) experienced at least one episode of infection and 22% ( $n=23$ ) had recurrent sepsis during their disease course. Infection was the leading cause of mortality of the 56 deceased patients in this series. Infections were less frequent in EGPA patients compared to their counterparts with MPA and GPA (37.5% vs 61.8%–65%).

Most infections were bacterial and multiple-drug resistant organisms were the causative agents in 8 patients. Two had neutropenic sepsis. Three had M. tuberculosis and five had herpes zoster. One had concomitant VZV and pneumocystis jiroveci pneumonitis.

Abstract AB0654 – Table 1.

Factors predicting infection	Odds Ratio ( $p<0.05$ )
– · Age	1.034
– · Renal insufficiency (serum creatinine $\geq 140$ umol/L) at diagnosis	5.452
– · Disease-related organ failure	3.006
– · Dialysis support	6.504
– · Use of cyclophosphamide as induction agent	2.956

**Conclusions:** Infections were common and often led to significant morbidities and mortalities among AAV patients. Risk factors included age, renal insufficiency (serum creatinine  $>140$  umol/L) on presentation, disease-related organ failure, need for renal supportive therapy, and the use of cyclophosphamide as induction agent.

**Disclosure of Interest:** None declared

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#### AB0655 AGREEMENT BETWEEN 18-FDG PET/CT AND CLINIMETRIC TAKAYASU ACTIVITY SCORES

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**Background:** The 18-FDG PET/CT is an objective tool employed for the diagnosis of Takayasu arteritis and also is used for the assessment of disease activity of this vasculitis.<sup>1</sup> There are few clinimetric scores developed for Takayasu clinical activity assessment such as the Indian Takayasu Clinical Activity Score (ITAS2010/ITAS.A),<sup>2</sup> the National Institutes of Health criteria (NIH score) from USA<sup>3</sup> and the Mexican effort by Dabague-Reyes (DR score).<sup>4</sup> The validity and



utility of 18-FDG PET/CT to measure the disease activity by studying wall enhancement compared to the clinimetric assessment has been slightly studied.

**Objectives:** To explore the agreement between 18-FDG PET/CT and the clinimetric tools for the estimation of Takayasu activity in one national reference centre.

**Methods:** The clinical records of patients that had performed an 18-FDG PET/CT were consecutively included. The required information to fulfil the ITAS2010, ITAS.A, NIH and DR were gathered from clinical charts. The cut-off points we used are the following: SUVmax  $\geq 2.1$  for 18-FDG PET/CT, for ITAS2010  $\geq 2$  points, for ITAS.A  $\geq 4$  points, for NIH  $\geq 2$  points and for DR  $\geq 5$  points. Kappa index was calculated, comparing SUVmax with all the clinimetric measures. As an exploratory exercise, ROC curves were performed. A p value less than 0.05 was considered statistically significant.

**Results:** Thirty six clinical records were reviewed. There was enough information to score ITAS2010 in 31 patients, ITAS.A in 28 patients, NIH and DR in 35 patients each. In our patients, moderate agreement was observed between 18-FDG PET/CT and DR score (Kappa=0.542, p=0.001). A tendency of weak agreement was observed with the NIH score (Kappa=0.215, p=0.086) and ITAS.A (kappa=0.351, p=0.063). There was no agreement with ITAS2010 (Kappa=0.107, p=0.519). Significant AUC were observed with DR (AUC=0.817, p=0.005) and NIH (AUC=0.756, p=0.025); however, this results were not obtained with ITAS2010 (AUC=0.675, p=0.124) and ITAS.A (AUC=0.697, p=0.083).

**Conclusions:** There was no strong agreement between 18-FDG PET/CT and any of these activity indices. On the other hand, these data suggest that the best disease activity tool in Mexican patients were DR and the NIH scores. Comparative studies in other populations are warranted.

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#### AB0656 CRYOGLOBULIN EVALUATION: ANALYSIS OF INTRA-LABORATORY AND INTER-LABORATORY VARIABILITY

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**Background:** Cryoglobulins (CRG) are immunoglobulins that precipitate in serum at temperatures below 37°C and resolubilize upon warming. The main reasons of interest of a clinical pathologist in the study of cryoglobulinemia are: 1) lack of standardisation in the preanalytical, analytical and postanalytical phases of the process (classification and reporting); 2) peculiarities of physiopathological mechanism 3) important clinical consequences. Vermeersch et al. studied these issues in 2008. To assess current practice in the detection, analysis, and reporting of cryoglobulins, a questionnaire was sent to 140 laboratories. They showed that only 36% of laboratories used standard procedures of analysis. Consequently, they concluded that standardisation was needed for cryoglobulin detection to avoid missed diagnoses and improve the comparability of results. Sargur et al. in 2010 reviewed the classification and clinical features of cryoglobulins and suggested “best practice” guidelines for laboratory detection and identification of cryoglobulins. They particularly highlighted the relevance of preanalytical and analytical phases: maintenance of the sample at a stable temperature of 37°C, especially throughout the initial steps (collection and transportation); centrifugation and separation methods; cryoprecipitate quantification; cryoprecipitate washing techniques; immunocharacterization of cryoprecipitates especially through immunofixation techniques (considered the “gold standard”).

**Objectives:** To verify and assess the variability of laboratory processes of CRG. **Methods:** We checked laboratory databases of Hospital and University (Lab A and B) of Modena with long tradition in the cryoglobulin analysis (more than 6000 tests from 2002 to 2017). Concerning CRG testing, 734 patient samples were studied in both laboratories. We compared our results according to Brouet classification into subgroups: type I, II and III. Therefore, we evaluated intra-laboratory variability, compared to previous or more frequent results. Finally, we studied inter-laboratory variability based on non-concordant laboratory reports.

**Results:** In the following table, we have represented the comparison between labs about the same patient cohort in 734 patient samples:

**Abstract AB0656 – Table 1.**

	I type (n)	II type (n)	III type (n)
Lab A	21	242	108
Lab B	42	270	108
Chi-quadro	p=0.0016	p=0.0004	Ns

Intra-laboratory variability: 14% Lab A, 16% Lab B (ns). Inter-laboratory variability: non-concordance in 25% of cases, considering 133 patients studied in both laboratories (Chi-square test).

**Conclusions:** No data about variability in CRG analysis are reported in literature. National and international guidelines are not explicative enough. Furthermore, many doubts about classifications are established. Our experience is unique but limited in two laboratories. Given the variability of testing conditions used in different laboratories and the lack of test standards and reference values, we confirm the need of further investigations into standardisation of CRG testing. New guidelines are fundamental, in order to optimise all phases of CRG research (pre and post analysis) and to ensure correct diagnosis and adequate treatments of the associated diseases.

**Disclosure of Interest:** None declared

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#### AB0657 CYCLOPHOSPHAMIDE-SPARING ROLE OF AN INTENSIFIED B-CELL DEPLETION PROTOCOL IN ANCA-ASSOCIATED VASCULITIS: A CASE-CONTROL STUDY

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**Background:** The management of ANCA-associated-vasculitis (AAV) requires the use of immunosuppressive drugs with potential toxicity. Recently, two trials demonstrated the efficacy of Rituximab (RTX) for the therapy of AAV.

**Objectives:** this case-control study aims to evaluate the immunosuppressive-sparing effect of a RTX-based protocol compared to the standard CYC treatment.

**Methods:** 26 patients with AAV and extracapillary glomerulonephritis were prospectively enrolled. Thirteen patients received an intensified protocol of B-cell depletion therapy (IBCDT) consisting of 4-weekly infusions of 375 mg/sm RTX followed by 2 infusions after 1 and 2 months, 3 pulses of methylprednisolone followed by prednisone tapered to 5 mg/day in three months and 2 pulses of 10 mg/kg CYC, without further maintenance therapy. Thirteen patients treated with 2 mg/kg/day CYC followed by azathioprine as a maintenance therapy served as controls.

**Results:** A significant improvement (p<0.05) of B-VAS, ESR, CRP and ANCA was observed in the IBCDT-group at 3, 6 and 12 months, with decrease of mean creatinine values from 4.81±6.4 mg/dl to 2.21±3.8 mg/dl.

When compared to controls, no difference was observed in terms of complete and partial response. However, the IBCDT regimen achieved a 1 g/month reduction of CYC cumulative dose (p<0.001).

**Conclusions:** in the treatment of this sample of severe AAV patients, the IBCDT protocol appeared to be noninferior to CYC-based regimen. Notably, the IBCDT regimen allowed a significant reduction of CYC cumulative dose.

**Disclosure of Interest:** None declared

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#### AB0658 DIFFERENT ORBITAL MANIFESTATIONS OF GRANULOMATOSIS WITH POLYANGIITIS. COMPARATIVE STUDY

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**Background:** Ophthalmic manifestations are typical for granulomatosis with polyangiitis (GPA), and occur in 28.6%–60% of patients. In 8% of cases they lead to permanent visual loss. According to different studies orbital lesion develops in 5%–30.6% of GPA patients and is considered to be the second most prevalent ophthalmic manifestation after conjunctivitis/episcleritis.

**Objectives:** to study clinical features of different orbital manifestations of GPA.

**Methods:** 74 GPA patients with orbital involvement were studied and compared. 3 types of orbital involvement were proposed: orbital mass (45 patients),

dacryoadenitis (26 patients) and myositis (3 patients). Patients with orbital mass (group 1) and dacryoadenitis (group 2) were included into further investigation.

**Results:** Patients in group 1 had systemic disease in 51,1% compared to 7,7% in group 2. Patients with orbital mass presented with more severe clinical manifestations, including significant exophthalmos (82,2%), periorbital oedema (95,5%) and hyperemia (46,7%), strabismus (31,1%), globe movement restriction (71,1%), chemosis (8,9%). Orbital mass was accompanied by necrotizing scleritis in 7 and PUK in 6 patients. Symptoms included orbital pain (88,9%) and binocular diplopia (73,3%). BCVA in this group was 0.67. Clinical outcome was relatively unfavourable: in 24,4% BCVA was less than 0.3, in 5 patients enucleation was performed, in 24,4% strabismus developed and in 73,3% globe movement restriction occurred. Clinical course and outcome were significantly more favourable in patients with dacryoadenitis. Periorbital oedema, exophthalmos and chemosis did not show significant difference in groups, though orbital pain, binocular diplopia, globe movement restriction, strabismus, optic neuropathy, necrotizing scleritis, PUK were observed in group1 significantly more often. Clinical outcome in group 2 was much more favourable with no cases of enucleation and persistent visual loss. They only had moderate exophthalmos 1–3 mm (65,4%), strabismus (7,7%) and mild globe movement restriction (19,2%).

**Conclusions:** Three types of orbital involvement in GPA were proposed: orbital mass, dacryoadenitis and myositis. Patients with orbital mass are characterised more often with systemic disease, more severe clinical course not uncommon associated with other ocular manifestations (necrotizing scleritis, PUK, orbital walls destruction), relatively unfavourable outcome with high level of morbidity (optic nerve atrophy, anophthalmos, strabismus) and higher rate of recurrences.

**Disclosure of Interest:** None declared

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#### AB0659 PREVALENCE AND CLINICAL FEATURES OF CRANIAL AND EXTRACRANIAL GIANT CELL ARTERITIS

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**Background:** Giant cell arteritis (GCA) is the most common systemic vasculitis in adults. Although it typically affects the cranial branches derived from the aortic arch, there is increasing evidence of the damage occurring to large vessel extracranial arteries, which is usually misdiagnosed. This subset of large vessel extracranial GCA may have specific clinical features that could hinder the diagnosis, which highlights the need for a different treatment and follow up.

**Objectives:** To analyse the frequency and clinical and analytical features in cranial and extra-cranial GCA.

**Methods:** An observational retrospective descriptive study analysing data from patients with GCA was performed in our hospital. Colour duplex sonography (CDS) studies carried out in the last 29 months were revised. Standardised CDS images from the frontal and parietal branches of the temporal superficial artery (TA) and axillary artery (AXE) with GCA compatible image with intra or extra-cranial involvement (hypochoic, homogeneous and circumferential thickening of the artery wall  $\geq 0.34$  mm in TA, and  $\geq 1$  mm in AXE, respectively). SPSS version 23 were used to analyse a total of 29 variables.

**Results:** Out of the 119 patients that were tested in our fast track GCA clinic, with standardised CDS of TA and AXE, 22 had GCA. All GCA patients was halo sign in CDS. From them, 7 had large vessel involvement (31.8%), from whom 6 were mixed and 1 had exclusively extra-cranial involvement. Mean age at diagnosis was 76 $\pm$ 9.7 SD in the extracranial GCA arteritis and 79 $\pm$ 5.7 SD in the cranial GCA. The extracranial subset had a greater number of men than the cranial (28.6% and 26.6%, respectively) and suffered usually more fever (28.5%>6.6%, respectively), constitutional syndrome (85.7%>40%, respectively) or polymyalgia rheumatica (42.8%>40%, respectively). However, they suffered with more frequency from headache (85.7% vs 93.3%) and jaw claudication (28.5% vs 33.3%). None of them suffered from visual impairment or central nervous system involvement; both do appeared in the cranial GCA group in 13.3% and 6.6%. In the blood tests, mean  $\pm$ standard deviation was: ESR 87.6 $\pm$ 36 mm/h in cranial GCA and 89.5 $\pm$ 19.5 SD mm/h in extracranial GCA, CRP 65 $\pm$ 57.6 and 82.6 $\pm$ 48.4 mg/L and Hb 11.4 $\pm$ 1.3 and 12.1 $\pm$ 1.3 g/dl, respectively. Patients with large vessel involvement met ACR criteria in 80% opposite 92.8% from these with solely cranial GCA. AT biopsy was performed in 7 patients in the cranial subset and 2 in the extra-cranial, testing positive for GCA in 5 (71.4%) in the first group, and none in the second one. CT-PET was performed in 2 patients with cranial GCA with negative results, and in 4 with large vessel involvement, testing positive in 50%. Despite the large differences, the statistical analysis didn't reach statistical significance due to the small sample size.

**Conclusions:** One third of the patients in our study had large vessel involvement, making axillary vessel CDS an important tool for the clinical exam of this disease. These patients tend to be younger and start more often with fever or general

syndrome and less with GCA typical symptoms like headache, jaw claudication or visual loss.

**Disclosure of Interest:** None declared

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#### AB0660 THE ROLE OF ANTI-NEUTROPHIL CYTOPLASMIC AUTOANTIBODY SPECIFICITY FOR MPO OR PR3 IN PHENOTYPE OF ANCA ASSOCIATED VASCULITIS: KNOWING THE AUTOIMMUNITY IN LATIN AMERICA

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**Background:** Antineutrophil cytoplasmic antibodies (ANCA) are present in up to 90% granulomatosis with polyangiitis, 80% microscopic polyangiitis and 70% eosinophilic granulomatosis with polyangiitis. MPO-ANCA has been associated with vasculitis limited to the kidney, chronic renal damage and less frequent gastrointestinal or respiratory tract involvement. PR3-ANCA are characterised by destructive lesions of the ears, nose and throat, alveolar haemorrhage, combination of upper and/or lower respiratory tract involvement with renal compromise and increased number of relapses. The frequency of pulmonary involvement is similar in both serotypes, and most ANCA associated vasculitis (AAV) patients are diagnosed between ages 50 and 70 years.

**Objectives:** To describe differences in clinical profiles of patients with AAV regarding ANCA specificity against MPO or PR3 in a Colombian based adult population

**Methods:** All medical records of patients with a diagnosis of AAV in two high complexity hospitals in Medellín, Colombia from January 1, 2014 to December 31, 2016 were reviewed. The clinical and demographic characteristics were abstracted and analysed with descriptive and inferential statistics in SPSS.22

**Results:** Of 59 cases of AAV, 44 were positive for MPO or PR3-ANCA with male predominance (65.5% men vs 34.5% women) and similar age at diagnosis (47 years in MPO-ANCA vs 50 in PR3-ANCA). MPO-ANCA group had more fever and weight loss (34.8% vs 20%), arterial hypertension (34.5% vs 26.7%), hematuria (34.5% vs 26.7%), proteinuria (31% vs 26.7%), creatinin higher than 5.6 mg/dL (20.7 vs 13.3%), myalgias (13.8 vs 0%) pachymeningitis (7% vs 0%) and skin compromise. PR3-ANCA patients had more arthralgias/arthritis (40% vs 31%), escleritis (33% vs 13.8%), episcleritis (13.3% vs 0%) and uveitis (10% vs 7%).

**Conclusions:** In this Latin American population ANCA specificity affected the phenotype of clinical disease. MPO-ANCA patients had more constitutional symptoms, renal and central nervous system compromise while PR3-ANCA patients showed more articular and ocular involvement.

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#### AB0661 ASSESSMENT OF DAMAGE AND PROGNOSIS IN PATIENTS WITH ADULT IGA VASCULITIS: RETROSPECTIVE MULTICENTERED COHORT STUDY

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**Objectives:** IgA Vasculitis is a leukocytoclastic vasculitis involving small vessels with depositions of immune complexes containing IgA. IgA Vasculitis is a predominantly paediatric vasculitis. There is limited data for the prognosis of adult IgA Vasculitis, with also no damage assessment. In this study, we aimed to evaluate

the clinical characteristics, treatment, outcome and damage of patients with adult IgA Vasculitis.

**Methods:** We assembled a retrospective cohort of patients with adult IgA Vasculitis from tertiary Rheumatology Centres in Turkey. The demographics, clinical characteristics, treatment and outcomes of patients were abstracted from medical records. Birmingham Vasculitis Activity Score (BVAS), prognostic Five Factor Score (FFS) and vasculitis damage index (VDI) were calculated.

**Results:** The study included 103 (male/female: 67/36) patients with adult IgA Vasculitis. The mean age was 42.6±17 years. Infection history within 6 weeks before presentation was present in 40 (38.8%) patients (32 upper respiratory tract, 3 urinary tract, 2 gastrointestinal, 3 others). Cutaneous manifestations and arthritis/arthralgia were the most common clinical manifestations (table 1). 92 (89.3%) patients were treated with oral glucocorticoids (GC). Pulse GC treatment was also given to 29 (28.1%) patients. As additional immunosuppressive agents, azathioprine was given to 36 (34.9%) and pulse cyclophosphamide to 13 (12.6%) patients. Fifty-nine patients (58.2%) had follow-up of mean 35.6 months. Eleven (18.6%) patients relapsed during follow-up. While 5 relapses were major, six of them were minor relapses. At the last visit, disease status was evaluated as active or treatment failure by the treating physician in 7 (11.8%) patients. The rate of chronic renal failure was 8.3%(n=5). Mortality was 1.6% (n=1) during follow-up, due to pneumonia. The mean VDI score was 0.3 in the last visit. Twelve (20.3%) patients had at least one damage item at the end of follow-up period.

**Abstract AB0661 – Table 1.** Baseline clinical characteristics of patients with adult Henoch Schönlein Purpura

	Adult Henoch Schönlein Purpura (n=103)
<b>Laboratory parameters</b>	
Anemia (<12 mg/d for female, <13 mg/d for male) (n, %)	36 (35%)
Erythrocyte Sedimentation Rate (mm/hour) *	34.7 ± 22
C-reactive protein (mg/l) †	18.11 (207)
Proteinuria (>100mg/24 hours)	87 (84.5%)
Creatinine (mg/dl) †	0.8±0.3
Hepatitis B positivity (n)	8/92 (8.7%)
Hepatitis C positivity (n)	0/97
ANA positivity	23/97 (23.7%)
RF positivity	5/88 (5.7%)
c-ANCA positivity	2/87 (2.3%)
p-ANCA positivity	1/89 (1.1%)
<b>Clinical Manifestations, n/SOI (%)</b>	
Fever	24 (23.3%)
Weight loss	28 (25.2%)
Myalgia/Weakness/Leg tenderness	44 (42.7%)
Arthritis and/or arthralgia	87 (84.5%)
Neurologic manifestations	3 (0.9%)
Testicular pain or tenderness	4 (3.9%)
Recent onset or severe hypertension	2 (1.9%)
<b>Cutaneous Manifestations</b>	
Peripheral limb edema	14 (13.6%)
Gastrointestinal manifestations	71 (68.9%)
Cardiac manifestations	5 (4.8%)
Ocular manifestations	3 (2.9%)
Pulmonary manifestations	2 (2.9%)
FFS=0	71 (68.9%)
FFS=1	24 (23.3%)
FFS=2	5 (4.8%)
FFS=3	3 (2.9%)
BVAS score at diagnosis*	56.7

ANA: Anti nuclear antibody, FR: Rheumatoid factor, ANCA: Antineutrophilic cytoplasmic antibody, FFS: Five Factor Score, BVAS: Birmingham Vasculitis Activity score. \*Mean ±SD †Median (Minimum-maximum)

**Conclusions:** Our results showed that approximately one fifth of patients with adult IgA Vasculitis had relapses during follow-up and had at least one damage item at the end of follow-up. Although, 31% of patients had FFS≥1, the mortality rate was observed to be very low in the present study.

**Disclosure of Interest:** None declared

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### AB0662 SUBGLOTTIC STENOSIS IN GRANULOMATOSIS WITH POLIANGIITIS

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**Background:** The characteristic lesion of laryngotracheal involvement in granulomatosis with polyangiitis (GPA) is subglottic stenosis (SGS), due to active disease or from chronic recurrent inflammation, 8% to 23% during the course of GPA and as initial manifestation in 1% to 6% of cases.

**Objectives:** Describe clinical features and treatment of patients with SGS

**Methods:** We retrospectively reviewed the medical records of 46 patients with SGS due to GPA diagnosed at a Rheumatology department (2000–2017).

We retrospectively reviewed the medical records of 46 patients with SGS due to GPA diagnosed at a Rheumatology department (2000–2017).

**Results:** 6/46 patients with GPA diagnosis presented SGS (13%). 83% women, mean age of 37.8 years (DS ±14.8). Mean time between the presentation of the GPA and the diagnosis of SGS:18 months. Most frequent clinical manifestations of SGS: dyspnea (83%), stridor (83%), dysphonia (50%), cough (33%), bronchospasm (16%). One patient presented SGS as initial manifestation of the disease. Mean BVAS:14. Two patients presented such complication with evidence of systemic manifestations. Re stenosis was observed in one patient.

**Treatment:** IV CYC 83%, oral CYC 16%, methylprednisolone (MP) 83%, oral steroids, plasma exchange (16%) in each one. Endoscopic intervention and balloon dilatation 33%, and intralesional Mitomycin 16%.

**Conclusions:** 13% patients with GPA presented SGS, being in the majority of cases associated with other manifestations of the disease. However, 67% had no signs of systemic involvement (localised disease). Local treatment was necessary in only 33% because there was a good response to IS in 67% of the cases.

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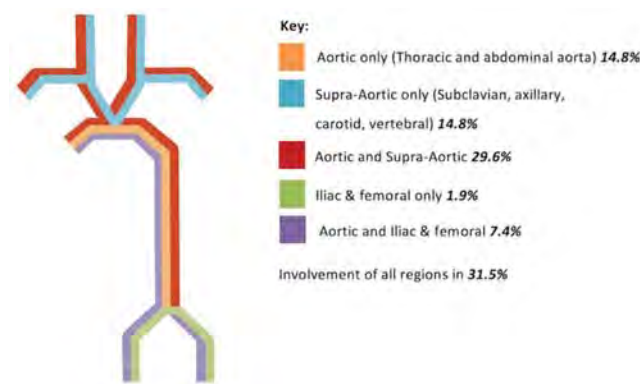
### AB0663 18F-FDG-PET/CT DISEASE DISTRIBUTION IN A LARGE VESSEL VASCULITIS COHORT – SUPPORTS VASCULAR ULTRASOUND AS A SCREENING AND DIAGNOSTIC TOOL

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**Background:** Subsets of GCA have extensive vascular involvement, termed Large Vessel GCA (LV-GCA), seen in 12%–37% depending on imaging used. These patients have higher relapse rates and are more often refractory to glucocorticoids (GC), requiring steroid-sparing treatment to minimise GC toxicity and vascular complications. Diagnosis is reliant upon imaging, given the relative inaccessibility of tissue for histological analysis beyond temporal artery biopsy (TAB). If axillary and subclavian arteries are often affected, vascular ultrasound could be an effective screening tool.

**Objectives:** To determine disease distribution in the Southend Large Vessel Vasculitis (LVV) cohort, particularly levels of axillary and subclavian involvement.

**Methods:** The cohort has sixty-five patients (2010–2017), from which sixty <sup>18</sup>F-FDG-PET/CT scans were performed. They were retrospectively examined by two nuclear radiologists. Vascular involvement was determined by consensus opinion at six territories (thoracic-aorta, abdominal-aorta, subclavian, axillary, carotid, vertebral, and iliac and femoral). Six negative scans were excluded from analysis, with LVV confirmed from other evidence (ultrasound, computed tomography). Of these, four were on concurrent GC (7–12 mg prednisolone), raising the possibility of “false negatives”. Nineteen scans were positive despite GC (1–60 mg prednisolone). Higher doses tended to be of short duration, being unable to postpone due to clinical necessity, but exceeded the 3 day limit at which FDG signal starts to attenuate.



**Abstract AB0663 – Figure 1.** Disease distribution via <sup>18</sup>F-FDG-PET/CT

**Results:** 14.8% (n=8) had isolated supra-aortic disease, 14.8% (n=8) had isolated aortic disease, and 29.6% (n=16) had involvement in both (Fig 1). 72.2% of



Abstract AB0662 – Table 1

Case	Sex/Age at diagnosis of SGS	Time from diagnosis (months)	Manifestations of SGS	Manifestations of vasculitis/BVAS	ANCA	Treatment Induction (I) Maintenance (M)	Evolution
1	W/20	12	Stridor Dysphonia Bronchospasm	No systemic manifestations BVAS: 6	MPO	I: IV CYC+IV steroids M: MTX+oral steroids	Resolution
2	M/42	3	Dyspnoea Dysphonia Dyspnoea	Glomerulonephritis Interstitial lung disease Pulmonary nodules Otitis Rhinosinusitis Saddle nose Mononeuritis BVAS: 33	PR3	I:IV CYC+MP M: AZA	Infectious complications Gammaglobulin Treatment
3	W/35	6	Dyspnoea Stridor	Pulmonary nodules Rhinosinusitis Saddle nose Crusting BVAS: 9	PR3	I: oral CYC+oral steroids M: MTX + Oral steroids	Resolution
4	W/67	24	Stridor Dysphonia Cough	Crusting Rhinosinusitis Otitis Mononeuritis BVAS: 17	PR3	I: IV CYC+MP M: AZA Local treatment: dilatation with balloon	Restenosis with immunosuppression. Resolution with local treatment
5	W/27	24	Dyspnoea Stridor	Sensorineural hearing loss Arthritis Rhinosinusitis Crusting Pulmonary nodules BVAS: 10	PR3	I: MP+IV CYC Plasma exchange Balloon dilatation and intralesional Mitomycin C	Re stenosis with immunosuppression. Resolution with local local treatment
6	W/36	24	Cough Dyspnoea Stridor	Pulmonary nodules BVAS: 9	C (IFI)	I: IV CYC+MP M: oral steroids local dilatation with balloon	Resolution

scans had involvement at either or both of the axillary and subclavian territories. Femoral and iliac involvement alone was seen in 1.9% (n=1), and in addition to aortic involvement in 7.4% (n=4). In this latter group, it was limited to the abdominal aorta in half, and included 1 case of Retroperitoneal Fibrosis. 31.5% (n=17) had involvement in all 3 regions. 24.1% (n=13) had no supra-aortic involvement.

**Conclusions:** This cohort demonstrates LVV has a predilection for aortic and supra-aortic regions. High axillary and subclavian involvement supports the use of vascular ultrasound as an effective imaging tool. Further imaging would still be warranted if suspicion remained high despite negative ultrasound, or to assess for vascular complications and alternate pathology. <sup>18</sup>F-FDG-PET/CT is not without limitations. Atherosclerosis and vascular remodelling display increased FDG uptake, so requires cautious interpretation. Further research on GC influence is also needed. As such it has a role in monitoring flaring or non-responsive patients, rather than routine interval scanning. For the latter, ultrasound may be an alternative, especially if there is previously documented intimal-medial thickening at ultrasound accessible sites.

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AB0664

#### LIFE EXPECTANCY IN PATIENT WITH GIANT CELL ARTERITIS (GCA): IMPACT OF VISION LOSS

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**Background and purpose:** Several epidemiologic studies reported increased mortality in patients with GCA, while others found that the overall survival was essentially identical to that of the general population. Those studies used different methods to calculate the mortality rates.

**Objectives:** In this retrospective study we evaluated longevity in a group of GCA patients using specific gender and age-matched life expectancy tables.

**Methods:** Medical records of patients diagnosed with GCA in one Medical Centre between 1980–1999 were reviewed for clinical parameters at the time of diagnosis and during the first year of treatment, and for time of death and cause of death. All patients diagnosed as GCA during that time period have already passed away. For each patient the observed survival was compared with the specific age and gender-matched life expectancy in the general population, based on life expectancy tables of the Israel Central Bureau of Statistics.

**Results:** 87 patients (51 females, 36 males) were included, their mean age at the time of GCA diagnosis was 73.9±8.4 and 75±8.1 years, respectively. The calculated mean life expectancy for this group of patients, from the time of diagnosis, was 14.1±6 years for females and 12±5.2 for males. However, the actual survival was significantly shorter, 7.5±6.2 years (p<0.001) in females, and 7.7±7.3 years (p=0.005) in males. Survival was not significantly affected by the intensity of inflammation at the time of diagnosis (based on the presence of fever, anaemia, sedimentation rate above 100 mm/h, thrombocytosis and leukocytosis), by the daily dose of prednisone at 1 year, or by the use of low-dose aspirin during the first year. However, vision loss at the time of presentation (n=13), was associated with further decrease in survival, 4.1±4.4 years compared to 8.3±6.8 years in GCA patients with no vision loss (p=0.035). Causes of death were defined in 54 patients. The leading causes of death were cardiovascular/cerebrovascular diseases, in 43% of the patients, slightly exceeding the respective rate in the age-matched general population (40%, p=0.8), and infectious diseases, in 37% of the patients, significantly exceeding the respective rate in the age-matched general population (22%, p=0.015).

**Conclusion:** Infectious diseases were often the cause of mortality in this group of GCA patients, relative to the background population. Survival following GCA diagnosis was significantly shorter than expected, especially in patients presenting with vision loss.

**Disclosure of Interest:** None declared

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AB0665

#### INTERSTITIAL LUNG DISEASE AMONG PATIENTS WITH GIANT CELL ARTERITIS

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**Background:** Lately interstitial lung disease (ILD) has been recognised more and more as a manifestation of primary systemic vasculitis, particularly among patients with microscopic polyangiitis (MPA), which is predominantly a disease of the elderly in Japan. Another primary systemic vasculitis that occurs frequently in

the elderly is Giant Cell Arteritis (GCA) and one of the unusual manifestations of GCA includes non-productive cough that can occur in about 10% of patients. It is speculated that vasculitis in the area of cough receptors results in this manifestation. There have been only anecdotes about the association of GCA with ILD and it is unknown whether ILD is truly prevalent in patients with GCA.

**Objectives:** Here we systematically reviewed chest images of patients with GCA and investigated the prevalence of CT scan abnormality consistent with ILD among patients with GCA.

**Methods:** Single centre retrospective chart review was conducted at St. Luke's International Hospital in Tokyo. The charts of patients with the diagnosis of GCA who were seen from March 2004 till August 2017 were extracted. The clinical data were obtained. Pulmonary images were reviewed by one of the authors, who is a pulmonologist and characteristics of the pulmonary lesions based on computed tomography (CT) of the lung were recorded.

**Results:** Forty-six patients had a diagnosis of Giant Cell Arteritis. Thirty-nine of them had a chest CT scan. The mean age of the patients was 69±17 years and 27 patients (58%) were female. Ten patients (26%) had abnormality in the CT scan. The abnormality included linear infiltrates beneath the posterior aspect of the pleura in the lung bases (n=9), ground glass opacities (n=3), honeycombing (n=3), and reticulonodular infiltrates (n=2). Two patients received prednisolone for ILD, ILD of whom were stable. No patients died during the median follow up of 14.5 months.

**Conclusions:** Chest CT abnormality consistent with mild ILD was prevalent among patients with GCA. The prognosis of these patients appears to be favourable and these patients responded to prednisolone.

**Disclosure of Interest:** None declared

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AB0666

#### CLINICAL AND SEROLOGICAL OUTCOMES OF PATIENTS WITH GIANT CELL ARTERITIS TREATED WITH TOCILIZUMAB OR ABACEPT AS STEROID-SPARING AGENTS

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**Background:** Giant cell arteritis (GCA) is a common form of systemic vasculitis. The current mainstay of GCA management is glucocorticoid (GC) therapy. Recently, at least 2 biological therapies [tocilizumab (TCZ) and abatacept (ABA)] have been proven to be effective in the management of CGA in randomised controlled trials. Nevertheless, their use as steroid sparing agents might need further investigation.

**Objectives:** We aimed to investigate the steroid-sparing effect of biological therapies, namely TCZ and ABA, in a cohort of GCA patients when compared to standard GC treatment.

**Methods:** We retrospectively collected data from GCA patients who attended the S.G. Bosco Hospital, Turin, Italy, who were treated with TCZ, both intravenous (IV) and subcutaneous (SC), and/or ABA SC (8 mg/kg/month, 162 mg/week, and 125 mg/week respectively). These therapies were prescribed as first line agents or as second line when patients were refractory/intolerant/contraindicated to standard immunosuppressive therapies. Complete response to the treatment was defined as a clinical and serological remission after 12 months of therapy; partial response was defined as clinical or serological remission after 12 months of therapy.

**Results:** This retrospective study included 33 GCA patients [mean age 74 (range 85–57), females 63%, mean follow-up from GCA diagnosis 44.4±33.5 months]. *Table 1* resumes the characteristics of the GCA patients included in the study. Twenty-eight patients out of 33 (85%) received one biologic agent. Five patients (15%) needed a therapeutic switch (one patient from TCZ to ABA, and 4 patients from ABA to TCZ). Patients were treated as follow: 9 with TCZ IV, 11 with TCZ SC, and 18 with ABA.

Among the TCZ IV group, all patients experienced a response (57% complete response, and 43% partial response). Among the TCZ SC group, 83% experienced a response (67% complete response, and 16% partial response). Among the ABA group, 86% experienced a response (36% complete response and 50% partial response). After 12 months of therapy, 100% of patients in TCZ groups, both IV and SC, and 64.2% of ABA group were treated with low doses of oral prednisone (≤7.5 mg/day) as maintenance. We noticed a significant reduction of inflammatory parameters [C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR)] after 12 months of therapy with TCZ [TCZ IV group: mean baseline CRP (mg/dl) 1.9±2.3, mean CRP after 12 months of therapy 0.3±0.2; mean baseline ESR (mm/h) 58.1±25.6, mean ESR after 12 months 9.5±4.2; TCZ SC group: mean baseline CRP 4.5±3.8, mean CRP after 12 months 0.2±0.2; mean baseline ESR 51.9±27, mean ESR after 12 months 6.5±6]. When compared to standard GC regimen,<sup>1</sup> in patients treated with TCZ, both IV and SC, we estimated a median steroid-sparing effect quantifiable in 30 mg/daily in the first month and an overall steroid-sparing effect of 15 mg/daily when assessed in 12 months.

**Abstract AB0666 – Table 1.** Characteristics of GCA patients included in the study

	Total number of patients (33)	%
<b>Demographic characteristics</b>		
Female/Male	21/12	
Age (years) (mean, SD)	73.6 ±8.7	
<b>Clinical characteristics at the onset of GCA</b>		
Fever (n)	12	36.4
Fatigue (n)	18	54.5
Headache (n)	28	84.8
Scalp tenderness (n)	8	24.2
Jaw claudication (n)	15	45.4
Vision loss (n)	16	48.5
PMR (n)	11	33.3
<b>Diagnosis</b>		
Biopsy proven	27/32	84.4
PET positivity	12/29	41.4
Eco-color-doppler positivity	30/31	97
<b>GC therapy</b>		
Previous methylprednisolone pulses (n)	7	21.2
Oral prednisolone (n)	33	100
Dose of oral prednisolone (mg/day) (mean, SD)	49.7 ±15.1	
<b>Previous immunosuppressive therapies</b>		
Methotrexate (n)	11	33.3
Mean dose (mg/week) (mean, SD)	15.6 ±1.7	
Mycophenolate (n)	6	18.1
Mean dose (g/day) (mean, SD)	2.2 ±0.4	

**Conclusions:** This retrospective study confirms the efficacy of biological therapies in the management of CGA. Besides, in our experience TCZ allowed a significant reduction of GCs use, especially in the first month of therapy, when compared to standard GCs-based regimens.

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AB0667

#### PREGNANCY OUTCOMES IN A TERTIARY TAKAYASU ARTERITIS CARE CENTRE

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**Background:** Fertility and pregnancy are concerning issues in women of child-bearing age with Takayasu arteritis (TA). Available data on the management and expected events in TA during pregnancy are sparse and inconsistent among study populations<sup>2,3</sup>. Conflicting reports exist on both favourable pregnancy outcomes as well as increased fetal or maternal complications<sup>1,4</sup>.

**Objectives:** To assess the obstetric and maternal outcomes in a tertiary centre TA cohort.

**Methods:** 15 female patients fulfilling the American College of Rheumatology 1990 criteria for the classification of TA were included in this retrospective study. Data regarding number of pregnancies, disease characteristics and pregnancy related events were gathered from medical records. Disease extent was classified according to Numano classification criteria for TA: type I (4 patients, 26.66%), type III (4 patients, 26.66%), type V (3 patients, 20%), type IV (2 patients, 13.33%), type IIa (1 patient, 6.66%), type IIb (1 patient, 6.66%). The prevalence of obstetric and maternal complications was evaluated in women before or after TA diagnosis. 6 patients were further excluded due to the paucity of information concerning pregnancy outcomes.

**Results:** A total of 15 pregnancies were identified in 9 patients, with 9 (60%) occurring before TA diagnosis – group 1, and 6 (40%) occurring concomitant with or after TA diagnosis – group 2. In the first group the extent of arterial involvement was mostly consistent with type I TA (6 pregnancies, 66.66%). No fetal or maternal complications were observed in this group. Type III TA was most commonly encountered (4 pregnancies, 66.66%) in group 2. Only one patient from the second group had more than 1 pregnancy after TA diagnosis. Active disease (National Institutes of Health/NIH score >1) was reported in 2 (33.33%) pregnancies in the second group. Cardiovascular events occurred exclusively during 2 (33.33%) pregnancies exhibiting active disease. One patient suffered severe aortic regurgitation and gestational hypertension during pregnancy, while the second patient experienced worsening of preexisting hypertension. These required steroid dose increase and addition of antihypertensive drugs. There were no obstetric events in group 2.

**Conclusions:** Most TA pregnancies are uneventful, bearing favourable fetal-maternal outcomes. However, pregnant TA patients with active disease, have higher risk of developing maternal complications, especially cardiovascular events. In this setting, close monitoring and disease remission should be maintained during pregnancy.

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### AB0668 TREATMENT OF THROMBOTIC EVENTS IN BEHÇET DISEASE: A SYSTEMATIC LITERATURE REVIEW

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**Background:** Behçet's disease (BD) is a systemic disease which etiopathogenesis is largely unknown. It is characterised by a wide variety of clinical manifestations. Venous disorder is a serious manifestation being potentially life-threatening. There is little evidence on the management of the venous complications in BD.

**Objectives:** To perform a systematic literature review on the treatment used in venous thrombotic events in BD.

**Methods:** The objective was reformulated according to the PICO approach. Several synonyms for the main components (i.e. Behçet, thrombosis, treatment) were used. Search limits were applied for humans. The literature search was performed in Medline and Embase from databases inception to 1st November 2017. Only articles in English and Latin languages were retained. We excluded abstracts, reviews and letters. From the selected studies, data about the venous involvement and treatments were retired using a predefined data collection form.

**Abstract AB0668 – Table 1**

Treatment	Nº articles (%)
Anticoagulant	22 (78.6)
Antiplatelet	9 (33.3)
Corticosteroids	22 (78.6)
Immunosuppressive	25 (89.3)
Cyclophosphamide	16 (57.1)
Azathioprine	16 (57.1)
Cyclosporine A	5 (17.9)
Mycophenolate mofetil	2 (7.1)
Interferon alpha	2 (7.1)
Methorexate	4 (14.3)
Hydroxychloroquine	1 (3.6)
Anti-TNF alpha	4 (14.3)
Colchicine	11 (39.3)
Thalidomide	1 (3.6)
Dapsona	1 (3.6)
Fibrinolytic	3 (10.7)
Surgery	7 (25.9)

**Results:** The literature search resulted in 1552 articles, of which 632 were captured in Medline and 920 in Embase. Figure 1 shows the study flow-chart for article selection. The main reasons for article exclusion after full-text review were the lack venous involvement and the lack of explanation of venous involvement treatment. 28 articles reporting 1904 patients were included in qualitative analysis. The mean (range; SD) duration time between the disease onset and the vascular onset was evaluated in 15 articles and was 4.9 (1.2–9.3; 2.7) years. Superficial thrombosis was evaluated in 6 (21.4%) articles, profound thrombosis in 19 (67.9%) articles, cerebral in 7 (25%), inferior or superior cava vein in 15 (53.6%) and Budd-Chiari syndrome in 8 (28.6%) articles. Table 1 shows the treatments described in the selected articles. Treatment response was evaluated in 20 (71.4%) articles; in 7 of these treatments response was evaluated in a subjective way. In total, 52 (2.7%) deaths were reported in relation to BD. In 319 (16.7%) patients, partial efficacy or recurrence of thrombosis was reported. Considering the heterogeneity of the reported data and the variability in the measures of treatment response, predictors of mortality risk cannot be analysed. However, in the reviewed articles, a higher mortality rate was observed in patients with hepatic involvement due to Budd-Chiari syndrome. We have also observed a higher risk for the development of venous thrombosis in patients with patergia phenomenon and male sex. Two studies suggested that immunosuppressive treatment

concomitant with anticoagulant treatment is associated with a lower risk of thrombosis relapse compared with anticoagulant treatment alone.



**Abstract AB0668 – Figure 1**

**Conclusions:** There is a great variability in the treatment of venous thrombosis related to Behçet's disease. Budd-Chiari syndrome seems to be related to a worse prognosis of the disease.

**Disclosure of Interest:** None declared

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### AB0669 MAINTENANCE TREATMENT WITH ADALIMUMAB IN REFRACTORY UVEITIS DUE TO BEHÇET'S DISEASE: OPTIMISED VS NON-OPTIMISED GROUP

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**Background:** Uveitis is the most common ocular manifestation in Behçet's Disease (BD), which can cause irreversible blindness.<sup>1–2</sup>

**Objectives:** To assess efficacy, safety and cost-effectiveness of adalimumab (ADA) therapy optimisation in a series of patients with uveitis due to BD.

**Methods:** Multicenter study of 74 ADA-treated patients with BD uveitis refractory to conventional immunosuppressants. Following remission, optimisation was performed by increasing the ADA dosing interval. Comparison between optimised and non-optimised group was performed.

**Results:** Ocular remission was achieved in 65 (86.6%) patients after a median ADA duration of 6<sup>3–12</sup> months. ADA was optimised in 23 cases. In the remaining 42 ADA was maintained at 40 mg/sc/2 weeks. No baseline differences were found at ADA onset between the optimised and non-optimised groups. Ocular outcomes were similar after a mean  $\pm$ S.D. follow-up of 34.7 $\pm$ 13.3 and 26 $\pm$ 21.3 months in the both groups (table 1). Adverse effects were seen in non-optimised group (lymphoma, pneumonia, local reaction and bacteremia). Mean ADA treatment costs were lower in the optimised vs non-optimised group (6101.25 €/patient/year vs 12339.48).



Abstract AB0669 – Table 1

	Optimized Group N=23	Non-Optimized Group N=42	P
<b>Demographic features</b>			
Age (years) (mean±S.D.)	37.2±13.4	39.1±9.3	0.8
Sex (n, %)	15/8	19/23	0.13
Positive HLA-B51 (%)	61	74	0.26
Duration of uveitis (months) prior to ADA (median [IQR])	43 [23-74.5]	24 [6-56]	0.1
Previous immunosuppressants (n) (mean±S.D.)	2±1.1	1.7±1.1	0.3
<b>Ocular pattern at ADA onset</b>			
BCVA (mean±S.D.)	0.61±0.36	0.56±0.33	0.46
AC cells (median [IQR])	0 [0-2]	1 [0-2]	0.85
Vitritis (median [IQR])	1 [0-2]	1 [0-2]	0.66
OCT (mean±S.D.)	306.7±122.9	332.8±129.1	0.51
<b>Ocular pattern at last visit</b>			
BCVA (mean±S.D.)	0.89±0.19	0.77±0.25	<0.01
AC cells (median [IQR])	0 [0-0]	0 [0-0]	0.7
Vitritis (median [IQR])	0 [0-0]	0 [0-0]	0.3
OCT (mean±S.D.)	250.5±17.9	249±26.1	0.87
<b>Follow-up on ADA therapy, months, (mean±S.D.)</b>			
Relapses, n (per 100 patients/year)	2 (3.0)	4 (9.4)	0.66
Severe side-effects, n (per 100 patients/year)	0 (0)	4 (4.4)	0.18
Cost (mean, euros per year)	9101.25	12399.48	<0.01

**Conclusions:** ADA optimisation in BD uveitis refractory to conventional therapy is effective, safe and cost-effective.

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**AB0670 SHORT AND LONG-TERM TREATMENT WITH INFILIXIMAB IN RETINAL VASCULITIS OF BEHÇET'S DISEASE. MULTICENTER STUDY OF 72 PATIENTS**

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**Background:** Retinal vasculitis (RV) is a serious complication of uveitis due to Behçet's disease (BD).<sup>1-2</sup>

**Objectives:** We assess the short/long-term efficacy of Infliximab (IFX) in refractory RV of BD.

**Methods:** Multicenter study of patients with RV of BD refractory to corticosteroids and at least 1 conventional immunosuppressant (IS). We compared efficacy of IFX between baseline, 1st week, 1–6 months and 1–6 years.

**Results:** 72 patients/129 affected eyes (40♂/32♀) with mean age of 39.6±9.7 years. HLA-B51 was (+) in 63%. Before IFX onset, patients had received: oral/e.v. glucocorticoids (n=98), CyA (n=56), AZA (n=43), MTX (n=34) and other IS (n=22). IFX was used as monotherapy in 17 patients and combined with conventional IS in the remaining 55.

IFX dose was as follows: 3 mg/kg/4–8 w (n=5), 4 mg/kg/4 w (n=1), 5–5.5 mg/kg/4–8 w (n=66).

Following IFX onset, an improvement in RV was seen, as well as in the other ocular outcomes. This enhancement was maintained (table 1).

After a mean follow-up of 26.5±22.1 months, IFX was discontinued in 44: remission (n=15), primary failure (n=16), preference of another route of administration (n=8), pregnancy (n=1) and adverse effects (n=4).

Abstract AB0670 – Table 1

	Basal	1 <sup>st</sup> week	1 <sup>st</sup> month	3 <sup>rd</sup> month	6 <sup>th</sup> month	1 <sup>st</sup> year	2 <sup>nd</sup> year	3 <sup>rd</sup> year	4 <sup>th</sup> year	5 <sup>th</sup> year	6 <sup>th</sup> year
Retinal Vasculitis (n, affected eyes, %)	117 (100%)	51 (79.7%)	45 (76.3%)	21 (67.7%)	13 (51.5%)	4 (5.7%)	4 (5.7%)	3 (6.4%)	1 (6.9%)	0 (0%)	0 (0%)
BCVA (mean±SD)	0.43±0.31	0.44±0.31	0.53±0.32	0.53±0.34	0.53±0.34	0.63±0.35	0.63±0.35	0.67±0.32	0.63±0.32	0.66±0.32	0.66±0.32
Tyndall (median [IQR])	1 [0-2]	0 [0-2]	0 [0-2]	0 [0-2]	0 [0-2]	0 [0-2]	0 [0-2]	0 [0-2]	0 [0-2]	0 [0-2]	0 [0-2]
Vitritis (median [IQR])	1 [0-2]	0 [0-2]	0 [0-2]	0 [0-2]	0 [0-2]	0 [0-2]	0 [0-2]	0 [0-2]	0 [0-2]	0 [0-2]	0 [0-2]
OCT (mean±SD)	346.9±140.7	338.6±125.4	333.3±111.4	325.4±113.7	308.7±107.3	288.6±102.7	285.2±103.7	275.8±101.9	278.6±101.8	278.9±101.8	284.7±101.8

\*p<0.05

**Conclusions:** IFX seems an effective short/long-term treatment in RV of BD.

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**AB0671 FIRST DOCUMENTATION OF RS3PE AFFECTING THE HANDS ON 18F-FDG WHOLE BODY PET/CT IN POLYMYALGIA RHEUMATICA**

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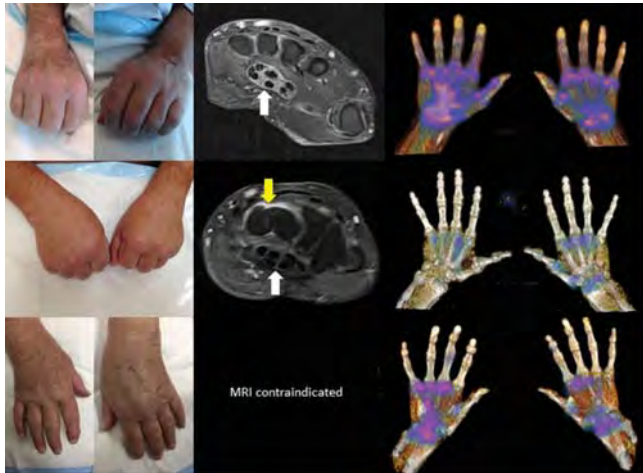
**Background:** Remitting seronegative symmetrical synovitis with pitting oedema (RS3PE) syndrome describes a clinical entity characterised by distal synovitis with pitting oedema, the absence of rheumatoid factor (Rf) and an excellent response to glucocorticoid therapy.<sup>[1]</sup> Most frequently associated with polymyalgia rheumatica (PMR), tenosynovial sheath inflammation represents the magnetic resonance imaging (MRI) hallmark of this condition, with concomitant joint synovitis also present in some cases.<sup>[1]</sup> More recently, diffusely increased <sup>18</sup>F-fluorodeoxyglucose (<sup>18</sup>F-FDG) uptake in the soft tissues around the ankles and feet has been described as the correlate of RS3PE on whole body positron emission tomography/computed tomography (PET/CT).<sup>[2]</sup>

**Objectives:** To document the clinical and radiologic appearance of RS3PE syndrome affecting the hands on MRI and whole body PET/CT in PMR patients.

**Methods:** Patients with newly diagnosed PMR were prospectively recruited as part of the Melbourne Predictors of Relapse in PMR (MPR-PMR) study. A standard physical examination was carried out with specific focus upon the presence of peripheral synovitis and pitting oedema. In patients with findings suggestive of RS3PE, clinical photography was undertaken. All study participants underwent a whole body PET/CT scan including dedicated views of the hands using the Philips T/F machine prior to prednisolone commencement. To precisely identify anatomic correlates of abnormal <sup>18</sup>F-FDG uptake in patients with RS3PE, MRI of the wrist and hand was performed using a 1.5 Tesla magnet.

**Results:** 3/35 patients (0.86%) were noted to have distal synovitis and pitting oedema of the hands at enrolment. Mean age was 70.9±10.1 years, two patients were male, and all were Caucasian. Rf and anti-citrullinated peptide autoantibodies were negative in all cases. On whole body PET/CT, intense <sup>18</sup>F-FDG uptake was visualised at the wrist joint and hand in a distinctive volar distribution. MRI of the wrist and hand in two participants (contraindicated in the third)

confirmed flexor tenosynovitis (white arrows) and intercarpal synovitis (yellow arrow) in keeping with RS3PE syndrome.



Abstract AB0671 – Figure 1

**Conclusions:** On whole body PET/CT, RS3PE syndrome is associated with a distinctive volar pattern of abnormal  $^{18}\text{F}$ -FDG uptake at the wrist and hand, which correlates with flexor tenosynovitis and intercarpal synovitis as previously described on MRI.

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**Disclosure of Interest:** None declared

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#### AB0672 18F-FDG WHOLE BODY PET/CT AS A DIAGNOSTIC TEST FOR POLYMYALGIA RHEUMATICA IN PATIENTS WITH NORMAL INFLAMMATORY MARKERS

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**Background:** Despite abnormal C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) being required in the 2012 EULAR/ACR classification criteria, 7%–20% of polymyalgia rheumatica (PMR) patients possess normal inflammatory markers at diagnosis.<sup>1</sup> A characteristic pattern of  $^{18}\text{F}$ -fluorodeoxyglucose ( $^{18}\text{F}$ -FDG) uptake is seen on whole body positron emission tomography/computed tomography (PET/CT) in PMR, hence this imaging modality may be a useful diagnostic test in this clinical scenario.

**Objectives:** To report the utility of whole body PET/CT for diagnosing PMR in patients with normal inflammatory markers and compare the clinical and radiologic characteristics of this subgroup with patients from the Melbourne Predictors of Relapse in PMR (MPR-PMR) study.

**Methods:** Patients presenting with clinical features of PMR according to the 2012 EULAR/ACR classification criteria but normal CRP and ESR underwent  $^{18}\text{F}$ -FDG PET/CT as part of their diagnostic work-up. A whole body scan from skull vertex to feet (including dedicated hand views) was performed using the Phillips T/F machine prior to prednisolone commencement. Qualitative and semi-quantitative (standardised uptake value maximum [SUV<sub>max</sub>]) scoring of abnormal  $^{18}\text{F}$ -FDG uptake was undertaken. Newly diagnosed and untreated PMR patients who underwent the same  $^{18}\text{F}$ -FDG PET/CT protocol as part of the MPR-PMR study were used as the comparator group. Statistical analysis was conducted using Stata 13.1 (StataCorp, College Station, TX, USA).

**Results:** Three patients with normal inflammatory markers (Median CRP 1 [0.9–2], median ESR 6<sup>1–7</sup>) underwent  $^{18}\text{F}$ -FDG PET/CT. Mean age was 60.15±7.55

years, two patients (66.67%) were male and all were Caucasian. Shoulder and hip pain was present in all cases, but only one patient reported peripheral joint involvement. Median early morning stiffness (EMS) was 30 min.<sup>15–60</sup> On whole body PET/CT, characteristic  $^{18}\text{F}$ -FDG uptake was visualised in each patient at the shoulder capsule, trochanteric bursae and adjacent to the ischial tuberosities, with hip capsule involvement similarly present in 2/3. When compared with 35 patients from the MPR-PMR study, there were no statistically significant differences in the clinical characteristics nor the distribution or intensity of abnormal  $^{18}\text{F}$ -FDG uptake between the two populations.

**Conclusions:** In patients with suggestive clinical features but normal inflammatory markers, whole body PET/CT may be utilised to confirm a diagnosis of PMR.

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#### AB0673 ANCA-ASSOCIATED VASCULITIS AND INFECTIONS: RETROSPECTIVE ANALYSIS IN A REFERRAL CENTRE

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**Background:** The antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) are rare multisystem autoimmune diseases of unknown cause, characterised by inflammatory cell infiltration causing necrosis of blood vessels. The AAV comprise granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) and eosinophilic granulomatosis with polyangiitis (EGPA). The AAV are autoimmune diseases with potentially severe systemic involvement that require prolonged immunosuppressive therapy. Infection is a frequent complication in AAV and is associated with increased morbidity and mortality.

**Objectives:** The aim of this study was to define epidemiology, ANCA patterns, treatments, infections and outcomes of a series of 39 patients with AAV.

**Methods:** We retrospectively analysed 39 patients diagnosed with AAV between 1995 and 2017 from the Internal Medicine Department of a Spanish referral centre.

**Results:** A total of 39 patients were reviewed. 23 female (58.9%). Mean age at diagnosis was 55.6 years. Median time delay to diagnosis was 7.6 weeks. Median follow-up was 91.3 months. Most frequent AAV was MPA with 18 patients (46.2%), followed by GPA with 11 (28.2%) and EGPA with 10 (25.6%). 6 patients (15.4%) had a concomitant autoimmune disease: Systemic sclerosis,<sup>2</sup> Antiphospholipid syndrome,<sup>2</sup> Lupus<sup>1</sup> and Sjögren.<sup>1</sup> Only 2 patients (5.1%) had previous infection with hepatitis C virus. Regarding the treatments, all patients received corticoids (bolus 24 patients, 61.5%), 29 (74.4%) cyclophosphamide, 10 (25.6%) rituximab, 19 (48.7%) azathioprine, 4 (10.3%) mycophenolate and 1 (2.6%) methotrexate. 16 patients presented post-treatment lymphopenia, 5 pancytopenia, and 15 hypogammaglobulinemia. 21 patients (53.8%) presented any infection after the diagnosis. The most frequent were bacterial infections (15 patients), presenting 9 patients with sepsis criteria (7 due to gram-negative organisms). 9 opportunistic infections were described: 3 infections by cytomegalovirus, 5 by tuberculosis and 1 by *Mycobacterium avium*. There were no cases of *Pneumocystis jirovecii* despite the fact that only 16 patients (41%) performed primary prophylaxis. The factors associated with increased risk of infections were: lymphopenia, pancytopenia and increased BVAS ( $p < 0.05$ ). 6 patients had died at the time of the study (3 associated with infections, 2 with neoplasms and 1 directly with AAV). The Charlson index performed at the time of the study was the best predictor of mortality ( $p < 0.01$ ).

**Conclusions:** Infections were a frequent complication in patients with AAV and one of the main causes of mortality. Risk factors were lymphopenia, pancytopenia and increased BVAS. Bacterial infections were the most frequent but opportunistic infections must be taken into account.

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**Disclosure of Interest:** None declared

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**AB0674 RISK FACTORS OF ATHEROSCLEROSIS IN PATIENTS WITH TAKAYASU'S ARTERITIS**

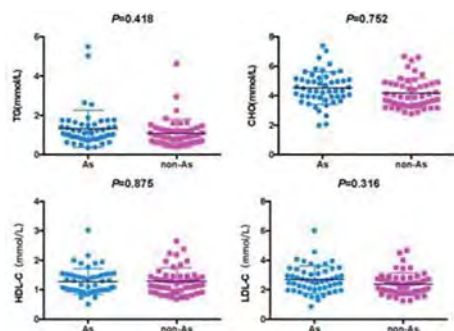
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**Background:** The incidence of atherosclerosis (As) in Takayasu's arteritis (TAK) was significantly higher than that of other people of the same age and gender. The incidence of carotid artery plaque in TAK patients was 27%, while only 2% of the age and sex matched controls were in the control group<sup>1</sup>. Autopsy confirmed that atherosclerotic lesions were found in arterial wall in TAK<sup>2</sup>. Inflammation of the vascular wall may promote As in TAK, which may be related to the disorder of lipid metabolism disorder, which accelerates the development of As. The ratio of low-density lipoprotein cholesterol (LDL-C)/high-density lipoprotein cholesterol (HDL-C) predicted As progression better than LDL-C or HDL-C alone<sup>3</sup>. Higher triglyceride (TG)/HDL-C ratio was found to be associated with presence of endothelial dysfunction and As<sup>4</sup>.

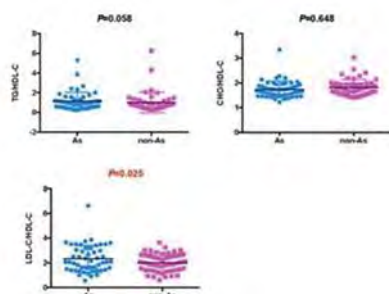
**Objectives:** The aim of this study is to investigate the clinical manifestations, serological and imaging features in TAK with As and non-As, to find the risk factors of As in those patients.

**Methods:** A retrospectively study of 105 patients in TAK were divided into 2 groups according to with or without As. We compared the difference of general information, traditional risk factors, disease activities and imaging features between 2 groups. Logistic model were used to determine the risk factors of As in TAK patients.

**Results:** In this study, 53 patients (50.48%) with TAK were had As. The duration of disease in TAK patients with As significantly longer than non-As group ( $p=0.011$ ). LDL-C/HDL-C ratio in TAK with As significantly higher than non-As ( $p=0.025$ ). Serum level of CRP in TAK with As patients lower than non-As patients. In disease activities, there were no differences in Kerr score and ITAS between 2 groups. The traditional risk factors of As in two groups were compared, hypertension ( $p=0.001$ ) and family history of As ( $p=0.012$ ) were all higher in As group than non-As group. In As group, most common angiographic type was Numano type V, which was higher than that in non-As patients (58.49% vs 38.46%,  $p=0.040$ ). Logistic regression showed the age above 40 years old is 5.196 times higher than the patients who are under 40 ( $p=0.002$ , 95%CI: 1.843–14.648) to develop to As. The incidence of As increased by 2.945 times every 5 years ( $p=0.003$ , 95%CI: 1.431–6.062). History of hypertension has more risk to As ( $p=0.029$ , OR=4.088, 95%CI: 1.153–14.494). More important, the LDL-C/HDL-C ratio was above the predicted cut-off value 3.038, the incidence of As increased by 8.515 times ( $p=0.023$ , 95%CI: 1.343–53.976), the TG/HDL-C ratio was above predicted 0.909 cut-off value, the incidence of As increased by 3.725 times ( $p=0.024$ , 95%CI: 1.185–11.711).



**Abstract AB0674 – Figure 1.** Levels of serum lipids in 2 groups of TA patients. There were no differences in TG, CHO, HDL-C and LDL-C between TA patients with atherosclerosis (As) and non-atherosclerosis (non-As)



**Abstract AB0674 – Figure 2.** Ratios of serum lipids in 2 groups of TA patients. There were no differences in TG/HDL-C ratio and CHO/HDL-C ratio between 2 group. LDL-C/HDL-C

ratio in patients with atherosclerosis (As) were higher than that of non-atherosclerosis (non-As) group ( $2.33\pm 1.09$  vs  $2.00\pm 0.74$ ) ( $p=0.025$ ).

**Conclusions:** Our study showed the duration of disease and LDL-C/HDL-C more higher in TAK patients with As than without As. Age  $\geq 40$  years old, the duration of disease, hypertension, TG/HDL-C and HDL-C/HDL-C ratios were the risk factors of As in TAK patients.

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**Disclosure of Interest:** None declared

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**AB0675 RHEUMATOID FACTOR POSITIVITY IS RELATED TO CLINICAL AND IMMUNOLOGICAL CHARACTERISTICS IN PATIENTS WITH EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS**

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**Background:** Eosinophilic granulomatosis with polyangiitis (EGPA) is a rare anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV), which is characterised by vasculitis with allergic features such as asthma and eosinophilia. Although rheumatoid factor (RF) positivity is known to be as high as 37%–50% in AAV patients<sup>1</sup> the clinical significance of RF-positivity remains unknown.

**Objectives:** To investigate clinical features in patients with RF in EGPA.

**Methods:** Consecutive patients who were diagnosed with EGPA between January 2008 and January 2018 in Keio University Hospital were enrolled. Clinical information were collected from medical records retrospectively. We divided patients into 2 groups according to RF positivity, and compared clinical features.

**Results:** Seventeen patients were enrolled in the study. The mean age was 57.4 years old, and 82% were female. Among them, 11 patients were RF positive (RF positive group) and 6 patients were negative (RF negative group). The female rate tended to be higher in the RF positive group than the negative group (82% vs 50%,  $p=0.087$ ). While the Birmingham Vasculitis Activity Score was comparable between the two groups (21.5 vs 17.3,  $p=0.329$ ), general symptoms (fever and weight loss) and gastrointestinal lesions were more frequent in the RF positive group (55% vs 17%,  $p=0.072$ ; 45% vs 17%,  $p=0.137$ ) and central nervous involvement was less frequent (18% vs 67%,  $p=0.024$ ). No patient with negative RF presented with arthralgia/arthritis. The count of eosinophil and IgA levels at diagnosis were significantly higher in the RF positive group than the RF negative group (15704/ $\mu$ l vs 4751/ $\mu$ l,  $p=0.009$ ; 238 mg/dL vs 162 mg/dL,  $p=0.048$ ). Interestingly, ANCA positivity was negatively correlated with RF positivity. MPO-ANCA was positive in 27% of the RF positive group and in 66% of the RF negative group, and PR3-ANCA was positive in none of the RF positive group and 17% of the RF negative group. Double negative was more frequent in RF positive group (73% vs 33%,  $p=0.060$ ).

**Conclusions:** RF positivity was associated with clinical and serological characteristics in patients with EGPA, suggesting different pathogenesis or immunological disturbances is related.

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**Disclosure of Interest:** None declared

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AB0676

### EFFICACY OF RITUXIMAB THERAPY AGAINST ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODY-RELATED HYPERTROPHIC PACHYMEINGITIS: A CASE SERIES

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**Background:** Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis presents with various symptoms. ANCA-associated hypertrophic pachymeningitis (HP) is a very rare pathology.

**Objectives:** This study aimed to investigate the efficacy of rituximab (RTX) against patients with ANCA-related HP.

**Methods:** Seven patients were identified by retrospective chart review from local registries at four Hospitals in Japan. All patients met Chapel Hill 2012 Consensus Conference definitions of ANCA-associated vasculitis and were complicated with HP. We assessed the dose of prednisolone, CRP, and MRI findings of HP before and after RTX administration.

**Results:** Three female and 4 male were evaluated. Median age was 66 years-old. Four cases had HP at the onset of vasculitis. Relapse of HP before RTX administration was found in 2 cases. RTX was used as an initial treatment in one patient. Daily dose of prednisolone and CRP were significantly decreased from baseline levels 24 weeks after RTX treatment. Evaluation of HP by contrast MRI showed improvement in six of seven cases. No relapse after RTX treatment was observed during the follow-up period of 24 weeks. Severe adverse effects were not found in any patients.

**Conclusions:** Our case series highlight the efficacy of RTX against patients with difficult-to-treat ANCA-related HP. Future studies in this context in a prospective manner are definitely required to establish the B-cell depletion therapy by RTX as a treatment option for ANCA-related HP.

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**Disclosure of Interest:** None declared

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AB0677

### BONE MINERAL DENSITY AND GLUCOCORTICOID TREATMENT IN PATIENTS WITH GIANT CELL ARTERITIS AND/OR POLYMYALGIA RHEUMATICA

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**Background:** Glucocorticoids (GC) are widely used in treating giant cell arteritis (GCA) and polymyalgia rheumatica (PMR) because of their strong anti-inflammatory and immunomodulatory effects. However, considerable adverse effects like osteoporosis can occur, especially when GC are used as a long-term treatment and disease relapses are frequent. While additional treatment options with conventional immunosuppressive drugs such MTX showed modest effects, the most recent and promising evidence points towards use of biologic agents like the IL-6-receptor antagonist Tocilizumab (TCZ) as an efficient novel treatment option in GCA.

**Objectives:** Rh-GIOP is an ongoing prospective study monitoring GC induced osteoporosis in patients with inflammatory rheumatic diseases, established in 2015 at the Charité University Hospital (ClinicalTrials.gov Identifier NCT02719314). To date, our database comprises clinical data and bone mineral density (BMD) data measured by dual x-ray absorptiometry (DXA) collected from 592 patients with inflammatory rheumatic diseases. The objective of this cross-sectional analysis was to describe GCA and PMR patients in terms of their clinical characteristics, immunosuppressive therapies and BMD.

**Methods:** We evaluated data from the initial visit of 61 patients (37 female, 24 male), 43 (70.5%) with PMR, and 18 (29.5%) with GCA (with or without PMR symptoms). Statistical analyses were performed for the overall cohort (GCA +PMR) and separately for the subgroups GCA and PMR. For subgroup analyses non-parametric tests were used.

**Results:** The whole group showed a mean age of 70.4 years ( $\pm 9.0$ ), BMI of 27.7 kg/m<sup>2</sup> ( $\pm 4.8$ ), disease duration of 2.9 years ( $\pm 4.0$ ), daily GC dose of 12.5 mg ( $\pm 19.6$ ) and cumulative GC dose (CGCD) of 6.1 g ( $\pm 6.5$ ). While 40 (93%) PMR patients and all 18 GCA patients received GC on a daily base, GCA patients took significantly higher median doses (8.75 mg, interquartile range (IR) 5/27.5 mg) than PMR patients did (5 mg, IR 3.5/10 mg,  $p=0.03$ ). However, no significant difference was seen in the CGCD. Overall, 34 (55.7%) patients demonstrated osteopenia and 5 (8.2%) patients osteoporosis. 27 (44.3%) patients suffered from at least one fracture, while 10 (16.4%) of these cases were confirmed fragility fractures. Methotrexate (MTX) was the most common conventional immunosuppressive drug being used in 12 (27.9%) PMR and in 6 (33.3%) GCA patients. 2 (11.2%) GCA patients and 1 (1.6%) PMR patient were treated with TCZ.

**Conclusions:** No increased prevalence of osteoporosis or fractures was found in our patient cohort compared to a normal German population over 50 years.<sup>1</sup> This might be due to therapeutic approaches, which include optimal disease control, the use of lowest possible GC doses and GC-sparing co-medications, and a rigorous osteoporosis prevention and treatment strategy. Alternatively, the number of patients may be still too small to identify significant differences when comparing with a non-diseased population.

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AB0678

### PERIPHERAL ULCERATIVE KERATITIS ASSOCIATED TO AUTOIMMUNE SYSTEMIC DISEASES: VISUAL PROGNOSIS AND OCCURRENCE WHILE SYSTEMIC DISEASE IN REMISSION

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**Background:** Background: Peripheral ulcerative keratitis (PUK) is a corneal crescent-shaped inflammatory damage with/without concomitant scleritis. PUK can occur isolated or as part of an underlying systemic disease (SD).

**Objectives:** Objective: To characterise a cohort of PUK patients with a long-term follow-up and to evaluate clinical (ocular and systemic) parameters as predictors of ocular prognosis, in terms of relapses and visual outcomes.

**Methods:** Methods: Retrospective review (1996–2017) of patients with PUK from a multidisciplinary Uveitis Unit (Ophthalmology/Autoimmune Diseases). Data recorded included ophthalmological features, clinical assessment and laboratory markers at disease onset, and therapeutic interventions, ocular relapses and visual outcomes during follow-up.

**Results:** Results: Among 18 PUK patients evaluated, 3 were idiopathic, 3 infectious and 12 (67%) associated with systemic diseases (SD-PUK): 8 rheumatoid arthritis (RA), 2 ANCA-vasculitis, 1 SLE and 1 Takayasu's arteritis. Among SD-PUK patients, sex ratio favoured women (rate 9:3) with a median age of 72 (range 33–85) years. Unilateral/bilateral involvement occurred in 7/5 patients and associated scleritis in 50% (11 eyes). All patients presented with eye pain/redness and visual impairment. Four (33%) patients (5 eyes) suffered ocular perforation and required surgery. All patients received topical glucocorticoids (GC), 75% systemic GC, 33% additional immunosuppressant, and 42% biologic therapy. Mean follow-up were 7.3 (range 0.5–12) years. The annual relapse rate was 0.3. Final visual acuity worsened in 42% (8 eyes). In 10 (83%) patients PUK onset occurred previous to SD diagnosis or with SD in remission, and only 3 (25%) were receiving

treatment for SD. No prognostic factors were found to correlate with PUK relapses and final visual acuity/ocular perforation.

**Conclusions:** RA and ANCA-vasculitis are the SD more frequently associated with PUK. Visual outcomes are poor in less than 50% of patients despite of topical and systemic GC/biologic therapy. SD-PUK may emerge previous to the SD diagnosis or with the associate SD in remission.

**Disclosure of Interest:** None declared

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#### AB0679 LEVEL OF SERUM 25(OH)D WITH DISEASE ACTIVITY OF A COHORT STUDY

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**Background:** Takayasu's arteritis (TAK) is a chronic large vessel vasculitis primarily involving the aorta and its major branches. TAK has been considered a rare disease that affected mostly young Asian women<sup>[1]</sup>. Its pathogenesis is still under investigation. However, some studies have demonstrated that immune disorder results in TAK. Especially cellular immunity plays a vital role in TAK. Recently, some studies shown that Vitamin D can regulate immune system in rheumatological diseases, such as SLE, RA and so on<sup>[2]</sup>. The relationship between Vitamin D and disease activity of TAK has not been reported yet. This study focuses on identifying the role of Vitamin D in pathogenesis of TAK through studying the correlation of serum 25(OH)D level and the disease activity of TAK

**Objectives:** To evaluate the level of serum 25-hydroxyvitamin D in patients with Takayasu's Arteritis (TAK)

**Methods:** Totally 57 untreated TA patients (TA group) and 51 healthy people (control group) were enrolled. The level of serum 25(OH)D were measured and compared between groups. The correlations of 25(OH)D level with related indicators were analysed.

**Results:** Lower concentrations of serum 25(OH)D were detected in TAK patients compared with healthy subjects [(11.91±5.26) ng/ml versus (17.64±8.85) ng/ml] (p<0.01). In all patients with TAK, serum 25(OH)D correlated negatively with erythrocyte sedimentation rate (ESR), interleukin (IL)-6 (r=-0.321, p=0.022; r=-0.322, p=0.031). There was no correlation between serum 25(OH)D level and NIH score, ITAS2010 score, ITAS.A score, anti-tumour necrosis factor (TNF)-α antibody. TAK Patients with therapy showed a significantly higher serum level of 25(OH)D compared with that before therapy [(10.74±3.49) ng/ml versus (18.66±8.03) ng/ml] (p<0.01). After therapy, the changes of 25(OH)D level present a positive correlation with the changes of NIH score, ITAS2010 score AND ITAS.A score.

**Conclusions:** We observed a high prevalence of vitamin D deficiency in patients with TAK. The 25(OH)D levels in serum was negatively correlated with ESR and IL-6. Levels of 25(OH)D were improved after therapy. The changes of 25OHD level correlation to Disease Activity of Index.

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**Disclosure of Interest:** None declared

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#### AB0680 NON OPHTHALMOLOGICAL NEUROLOGIC ISCHAEMIC MANIFESTATIONS OF GIANT CELL ARTERITIS

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**Background:** Giant cell arteritis (GCA) is a very infrequent cause of stroke. It is diagnosed in 0.15% of brain infarctions. On the other hand, in scientific literature there are very little patients with ischaemic brain infarctions that describes stroke as the clinical presentation of GCA. It might suggest that it is a underdiagnosed condition.

**Objectives:** To check the frequency of stroke as presentation symptom of GCA and other findings related with it.

**Methods:** Retrospective observational study of 123 consecutive patients diagnosed of GCA in our hospital. We reviewed the past medical history to obtain sings, symptoms and ultrasound parameters of the first medical evaluation. We searched for: age, sex, hypertension, diabetes, dyslipidemia, anterior ischaemic

optic neuropathy (AION), headache, visual disturbances, Polymyalgia Rheumatica (PMR), jaw claudication, general symptoms, non oftalmological brain ischaemic symptoms, disease outbreak and laboratory test: erythrocyte sedimentation rate (ESR), C reactive protein (CRP), Haemoglobin (Hb). For the analysis we divided the sample into two groups: a). Neurological symptoms b). Other presentations.

For statistical comparisons, we used SPSS version 17.0. Descriptive analysis and comparison was performed of the two groups. X<sup>2</sup> was used for qualitative values and means comparisons for quantitative.

Abstract AB0680 – Table 1

	Non ophthalmic neurologic symptoms	Non neurologic symptoms	p value
Age *	79±5.42	77.86±8.86	0.62
Sex ** (Women)	7 (58,33%)	67 (60,36%)	0.56
ESR* (mm/h)	66,63±32.24	68,18±30,41	0.89
CRP* (mg/L)	53,73±79,43	42,55±45,35	0.60
Hb* (g/dL)	12,56±2.12	13,34±4,71	0.64
Outbreak**	5 (41,66%)	57 (51,35%)	0.52
Headache**	6 (50%)	68 (61,26%)	0.22
Visual disturbances**	1 (8,33%)	24 (21,62%)	0.27
PMR**	0 (0%)	25 (22,52%)	0.06
Jaw claudication**	0 (0%)	14 (12,61%)	0.19
General symptoms**	1 (8,33%)	20 (18,01%)	0.61
<b>Total patients</b>	<b>12</b>	<b>111</b>	

\*Mean ±SD. \*\* n (%).

**Results:** Of our 123 patient's cohort: 37 patients (30.08%) suffered from ischaemic events of the internal carotid artery, 25 patients (20.32%) of AION and 12 patients (9.8%) presented with neurological symptoms different from AION.

Out of the 12 patients with non ocular ischaemic symptoms of the central nervous system: 5 (44.66%) were diagnosed of transitory ischaemic accident (TIA), 4 (33.33%) of stroke, 2 (16.66%) of VI cranial nerve paresis, one the patients that presented with III and VI par paresis suffered also from TIA, at last, one patient presented ischaemic phenomena related with small-vessels vasculitis and one patient with dizziness due to cerebellum affection.

Clinical and analytical data are presented in the table:

No patient was presented with PMR or jaw claudication.

3 (25%) patients died during the follow up in the neurologic symptoms group in comparison with 11 (9.90%) of the non neurological (p 0.11).

**Conclusions:** Stroke is not a rare form of presentation of GCA and should be suspected in all ischaemic brain events that are associated with high acute phase reactants in elderly patients. It is important to identify these patients due to the severity of the disease and the possibility of specific treatment that may avoid new events.

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#### AB0681 BIOPSY RESULTS FROM PATIENTS WITH SUSPECTED GRANULOMATOSIS WITH POLYANGIITIS A DECADE (2005–2015). ALEATORISED SAMPLE ANALYSIS OF CLINICOPATHOLOGICAL CORRELATION

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**Background:** The diagnostic yield of airway biopsies in granulomatosis with polyangiitis (GPA) is usually less than 50%.

**Objectives:** To review the histologic diagnostic yield of airway biopsies sent with a suspected GPA diagnosis in a single-centre devoted to respiratory diseases by use of previously published criteria. Also, to know the interobserver variability among in-house pathologists, correlate signs and symptoms with GPA positive histologic findings, and with additional paraclinical data, apply the algorithm proposed by the European Medical Agencies (EMA) to know if a higher number of biopsies confidently supported a GPA diagnosis.

**Methods:** From 137 airways biopsies during a decade (2005–2015), fifty were randomly selected for the second review by an expert pathologist. Thereafter, with the incorporation of antineutrophil cytoplasm autoantibodies (ANCA) the EMA algorithm was applied. Demographic data were descriptively analysed, and

results expressed according to their distribution. Categorical data, expressed in percentages, were analysed with  $\chi^2$  test and variance analysis. The associations of independent variables were analysed with one-tail exact Fisher test. Simple logistic regression was used for variable associations. The interobserver correlation was tested with calculation of the kappa coefficient.

**Results:** A poor interobserver correlation was found among pathologists (kappa = 0.19), and no airway sign or symptom was predictive of a positive GPA biopsy. Several pitfalls were noticed: lack of adequate clinical information on files (including endoscopic); incomplete relevant information sent to pathologists and inadequate tissue sampling. Nevertheless, in patients with generalised disease, a 2.6 probability to obtain a diagnostic GPA airway biopsy was found. After expert pathologist's review, and applying Devaney et al and Travis et al proposed criteria, from 16 initial GPA diagnoses, the number increased to 25. It further raised to 35/50 randomised biopsies when ANCA results were incorporated, and the EMA algorithm was applied.

**Conclusions:** Carefully retrieved clinical, endoscopic and serological data, coupled with systematic histopathologic sample review in patients with a GPA suspicion shall be incorporated in an orderly fashion in order to increase the diagnostic yield of this malady, especially in patients with the limited form of the disease.

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#### AB0682 RISK FACTORS ASSOCIATED WITH RELAPSE OF ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODY-ASSOCIATED VASCULITIS

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**Background:** Several factors increasing the risk of anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis have been reported. These include pulmonary and cardiovascular lesions, PR3-ANCA-positivity in patients with granulomatosis with polyangiitis, and persistent ANCA-positivity or an increase in the titer of such antibodies.

**Objectives:** We aimed to identify potentially novel factors predicting relapse in patients with ANCA-associated vasculitis.

**Methods:** We reviewed data on 73 patients (61 with microscopic polyangiitis [MPA], 12 with granulomatosis with polyangiitis [GPA]; 46 females) treated in our centre from 1998 to 2017 for whom medical histories were available. All achieved at least one remission after induction therapy. Relapse was defined as novel organ involvement or a need for therapy intensification. Follow-up continued to the first relapse or for as long as possible if no relapse was noted.

**Results:** The median age at disease onset (interquartile range) was 74 years (range: 67–80 years). The relapse rate was 42.5% (MPA 41%, GPA 50%), thus not significantly different between the two groups ( $p=0.75$ ). The median follow-up duration was 23 months (range: 11–65 months) and the median time to relapse was 18 months (range: 10.5–54 months). Although pulmonary and cardiac lesions reportedly increase the relapse rate, neither contributed significantly to the rate in this study. Furthermore, ANCA-positivity after remission and increases in ANCA levels prior to relapse did not significantly increase the relapse risk. In terms of medical histories recorded at the time of first onset of disease, the frequency of diabetes, dyslipidemia, coronary artery disease, and cerebral infarction did not differ significantly between patients who did and did not relapse. However, in MPA patients, a history of hypertension was significantly less in those who relapsed ( $p=0.01$ ). In a multiple logistic regression analysis adjusted for sex and age, history of hypertension was a significant predictor of fewer relapse (odds ratio: 0.23; 95% confidence interval 0.07–0.69,  $p=0.009$ ).

**Abstract AB0682 – Table 1.** The clinical characteristics of two groups

	Relapse, n=31	Non-relapse, n=42	p	OR (95% CI)
Age, years	70.8±10.8	74.6±9.2	0.10	-
Mean±SD	73 (65–79)	76 (68–82)		
Median (interquartile range)	18 (11–54)	30 (13–67)	-	-
Median follow up, month	*Time to 1st relapse			
Male/female	10/21	17/25	0.62	0.7 (0.23–2.05)
ANCA phenotype, n (%)	4 (13.0%)	7 (16.7%)	0.75	0.74 (0.14–3.29)
	27 (87.1%)	36 (85.7%)	>0.99	1.12 (0.24–5.97)
PR3-ANCA				
MPO-ANCA				
Disease type, n (%)	6 (19.4%)	6 (14.3%)	0.75	0.70 (0.17–2.94)
GPA	25 (80.6%)	36 (85.7%)		
MPA				
Organ involvement	24	33	>0.99	0.94 (0.27–3.41)
Pulmonary	1	2	>0.99	0.67 (0.01–13.44)
Cardiovascular				
Medical histories	7	3	0.09	3.70 (0.76–18.44)
Diabetes mellitus	9	7	0.26	24.44
Dyslipidemia	10	28	0.005	2.02 (0.58–7.43)
Hypertension				0.24 (0.08–0.71)

ANCA: antineutrophil cytoplasmic antibody; PR3: proteinase 3; MPO: myeloperoxidase; GPA: granulomatosis with polyangiitis; MPA: microscopic polyangiitis; OR: odds ratio; 95% CI: 95% confidence interval

**Conclusions:** In addition to known factors, a history of hypertension recorded at the time of disease onset may predict fewer MPA relapse.

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**Disclosure of Interest:** None declared

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#### AB0683 TREATMENT WITH STATINS IN PATIENTS STUDIED BY FDG-PET/CT FOR POSSIBLE LARGE VESSEL VASCULITIS IS ASSOCIATED WITH A LOW VASCULAR SCORE

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**Background:** Polymyalgia rheumatica (PMR), giant cell arteritis (GCA), and fever of unknown origin (FUO) may show large vessel vasculitis (LVV) when studied with FDG-PET/CT. Statins, widely used to lower cholesterol concentrations, have shown anti-inflammatory activity in both the atherosclerotic plaque and in rheumatoid arthritis.

**Objectives:** To test the hypothesis that the concomitant treatment with statins induces a low uptake of the vessels in patients with PMR, FUO and GCA.

**Methods:** Consecutive patients with a diagnosis of PMR, GCA or FUO underwent a thorough clinical examination, including drug history, and a PET/CT scan. Arterial uptake of FDG was scored relative to liver uptake as 0=no uptake present, 1=lower than liver uptake, 2=similar to liver uptake, 3=higher than liver uptake. The values of each district were summed to obtain a total vascular score (TVS). A further semi-quantitative analysis of FDG uptake was carried out, drawing regions of interest (ROIs) on the theoretical arterial wall and within the left ventricular chamber (blood-pool, BP). Arterial FDG uptake was quantified by calculating the mean standardised uptake value (SUV) within each ROI and the results expressed as the ratio between mean SUV value of each ROI and BP ROI (SUV/BP).

**Results:** 129 patients were included, 87 women, with median age of 74 years (range 50–92). 95 patients were diagnosed with PMR, 13 with GCA, 16 with both PMR and GCA and 5 patients presented with FUO. 37/129 patients (28.7%) were assuming glucocorticoids (GC) at the time of examination. The mean interval between onset of symptoms and PET/CT was 85 days (range 4–1957 days). LVV was present in 75 patients (58.2%) when a cut-off  $\geq 2$  was used and 32 patients (24.8%) had a score of 3.

Twenty/129 patients (15.5%) were treated with statins for hypercholesterolemia. The median TVS was significantly lower in these patients when compared with those not treated with statins (8 [range 1–27] vs. 12 [range 0–42],  $p=0.02$ ). This difference was present at the ascending aorta ( $p=0.017$ ), the aortic arch ( $p=0.023$ ), and the femoral arteries ( $p=0.025$ ). The analysis of SUV was not



significant ( $p=0.45$ ). As expected, the arterial calcium load, corresponding to the extent of vessel calcification, was higher in patients treated with statins (14 [range 2–35] vs. 8 [range 0–35];  $p=0.012$ ). However, calcium load did not correlate with the TVS, whereas it inversely correlated with SUVs ( $p=0.03$ ). At multiple regression, assumption of statins was not predicted by sex, type of diagnosis, GC treatment or presence of LVV at PET/CT. Only age predicted statin therapy ( $p=0.04$ ), but age was not associated with LVV ( $p=0.23$ ). Among clinical features, only fever was significantly less frequent in patients treated with statins ( $p=0.03$ ).

**Conclusions:** With the limits of an observational retrospective study, our data suggest that treatment with statins may lower arterial uptake in patients studied for LVV. This finding was seen using the theoretically more subjective TVS but not with SUV analysis. We feel that the latter is more easily influenced by the presence of calcific plaques, as suggested by its inverse correlation with arterial calcium load. The role of statins in tempering arterial inflammation deserves further studies.

**Disclosure of Interest:** None declared

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#### AB0684 A REVIEW OF TEMPORAL ARTERY BIOPSIES AT A DISTRICT GENERAL HOSPITAL

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**Background:** Giant cell arteritis is the most common vasculitis in the western world in the over 50 population. The morbidity associated with its natural progression and treatment is significant. No single investigation has been identified to accurately confirm or reject its diagnosis, though for some years biopsy of the superficial temporal artery has been carried out to support the diagnostic process. More recently, doppler ultrasound of the artery has gained prominence, though its widespread use is limited.

Temporal artery biopsy (TAB) is a significant use of resources, involving a surgeon and their team, as well as a histopathologist. It is an invasive procedure with the risks that this entails. It behoves the referring doctor to ensure that the probability of a positive result is as high as practicable.

**Objectives:** To determine the factors providing the highest likelihood of a positive TAB result.

**Methods:** The notes of all patients undergoing a TAB during a 3 year period 2013–2016 were requested from the Medical Records department at a district general hospital. The first 100 of these were reviewed by the authors. Each set of notes was examined for the following:

- Demographics (sex, age)
- The first department the patient was referred to (Rheumatology/Ophthalmology/Neurology/direct from the General Practitioner to Vascular Surgery)
- Period of time from symptom onset to biopsy
- Period of time on steroids to biopsy
- Initial dose of steroids prescribed
- Pre-treatment ESR
- Pre-treatment CRP
- Presence of symptoms (headache/jaw claudication/polymyalgia rheumatica)
- Other causes for a raised ESR
- The pre-test probability of a positive TAB result as assessed by the reviewer
- TAB result as reported by local histopathologist
- Evidence of the biopsy result impacting treatment

**Results:** Of the 100 TAB's reviewed, 16 yielded positive results (16%). A breakdown of the notes review for these patients is included in the following table:

**Abstract AB0684 – Table 1**

Positive TAB	16/100	Visual symptoms	6/16
Age (years)	58–88, Mean 73	Jaw claudication	5/16
Female:Male	13:3	Headache	11/16
GP referral direct to Vascular Surgery	5/16	PMR	1/16
Initial referral to Rheumatology	4/16	Other causes of raised ESR	3/16
Initial referral to Ophthalmology	4/16	Pre-test probability of positive result	9/16
Initial referral to Neurology	3/16	Biopsy influencing treatment	6/7
Symptom onset to TAB (days)	14–90, Mean 52		
Steroid duration before TAB	1–28 days		
Steroid starting dose range	30–500 mg		

**Conclusions:** This study has shown that less than a fifth of TAB's conducted during this period at our district general hospital yielded a positive result. There is scope to improve this yield significantly if we identify candidates for TAB better.

There was no positive result for any of the 16 patients less than 58 years of age. The majority had a raised CRP and ESR, though one patient had a CRP of 2. This reflects the need for vigilance before discounting GCA as a diagnosis.

One patient had a positive TAB even after 28 days of prednisolone 40 mg daily. The majority (14/16) had their biopsy within 3 weeks of steroid initiation, indicating that a short delay in biopsy does not rule out a positive result.

This study will help us develop a local pathway including Ophthalmology, Neurology, Vascular Surgery and Primary Care to improve the yield of positive TAB. This will improve patient experience as well as ensure appropriate use of resources.

**Disclosure of Interest:** None declared

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#### AB0685 THE INCIDENCE OF GIANT CELL ARTERITIS IN SLOVENIA – PROSPECTIVE STUDY

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**Background:** Giant cell arteritis (GCA) represents the most common vasculitis in adults over age of 50 years in Europe. Recently the diagnostic options greatly improved with the implementation of imaging techniques such as colour Doppler ultrasonography (CDS) and positron emission tomography-computed tomography (PET/CT).

**Objectives:** The aim of our single centre prospective study was to determine the incidence of GCA in well-defined Slovenian region, based on the temporal artery (TA) biopsy (TAB) and/or the result of CDS and/or PET/CT.

**Methods:** The study was conducted at University medical centre Ljubljana (UMC Ljubljana), that represents the only secondary/tertiary centre in a region, serving a population of 3 23 297 residents aged 50 years or more (1 76 104 females and 1 47 193 males). Patients with suspected GCA are referred either to the Department of Rheumatology, or in case of severe visual disturbances, to the Department of Ophthalmology. In the analysis we included all GCA cases diagnosed between 1 January 2012 and 31 December 2017. The diagnosis of cranial GCA (c-GCA) was established with the help of American College of Rheumatology (ACR) 1990 classification criteria, positive TAB and/or TA CDS. Cases of extracranial large vessel vasculitis (lv-GCA) were diagnosed using CDS of branches of the aortic arch and/or PET-CT.

**Results:** During the six-year observation we identified 169 new GCA cases (66.3% females), with a median (IQR) age of 75.1 (68.6–80.0) years. Forty-two (24.8%) patients had lv-GCA, and the others had c-GCA. One-hundred and thirty-nine patients (24 lv-GCA and 115 c-GCA) fulfilled ACR 1990 classification criteria. The other patients had positive arterial CDS or PET-CT (18 CDS, 9 CDS and PET-CT, 3 PET-CT). TAB was performed in 119 patients and was positive in 88.2%. Clinical characteristics of our GCA cases are presented in table 1. The estimated annual incidence rate of GCA was 8.7 per 1 00 000 adults aged  $\geq 50$  years (95% CI 7.5–10.1), in c-GCA 6.5 per 100.000 adults aged  $\geq 50$  years (95% CI 5.5–7.8) and in lv-GCA 2.2 per 100.000 aged  $\geq 50$  years (95% CI 1.6–2.9).

**Abstract AB0685 – Table 1.** Characteristics of GCA cohort

Characteristics	all GCA	lv-GCA	c-GCA
No. of cases	169	42	127
Female gender (%)	66.3	76.2	63.0
Age (years) <sup>#</sup>	75.1 (68.6-80.0)	69.5 (64.4-78.1)	75.7 (72.2-81.6)
Disease duration (day) <sup>#</sup>	30 (14-60)	60 (30-97.5)	28 (14-45)
Constitutional symptoms (%)	69.2	71.4	68.5
Headache (%)	71.6	45.2	80.3
PMR (%)	14.2	11.9	15.0
Jaw claudication (%)	45.0	26.2	51.2
Vision disturbances (%)	33.1	19.0	37.8
Clinically abnormal TA <sup>†</sup>	62.1	38.0	69.3
TAB (%)	88.2(105/119)	79.2 (19/24)	85.6 (89/104)
TA CDS (%)	76.9 (130/160)	54.8 (23/42)	92.4 (109/118)
ESR $\geq 50$ (mm/h) (%)	82.8	81.0	85.0
ACR criteria (%)	82.2	57.1	90.5

Legend: GCA giant cell arteritis; lv-GCA extracranial large vessel GCA; c-GCA cranial GCA; PMR polymyalgia rheumatica; TA temporal artery; <sup>‡</sup> TA tenderness or decreased pulse; TAB temporal artery biopsy; CDS colour Doppler sonography; ESR erythrocyte sedimentation rate; ACR American Colleague of Rheumatology; <sup>#</sup> median (interquartile range);

**Conclusions:** GCA is the most common vasculitis in adults aged 50 years or above, with an annual incidence rate of 8.7 per 100.000. c-GCA is nearly 3 times more common than lv-GCA.

**Disclosure of Interest:** None declared

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**AB0686** **ARTERIAL ANEURYSMS IN BEHÇET'S DISEASE: A RETROSPECTIVE DESCRIPTIVE ANALYSIS AND LONG-TERM OUTCOME**

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**Background:** Behçet's Disease (BD) was described in 1937 after Hulusi Behçet; as a triad of recurrent aphthous and genital ulcers together with iridocyclitis.<sup>1,2</sup> Arterial disease is seen in 3%–5% of the patients.<sup>3,4</sup> Thrombosis and/or aneurysmal formation are common sequelae mainly false aneurysms.<sup>5</sup> In spite of the fact that BD is not uncommon in the clinical practice in Egypt; the paucity of data that looked specifically to the arterial aneurysms in the Egyptian patients with BD had prompted the present study.

**Objectives:** Arterial aneurysm in Behçet's disease is a rare manifestation of Behçet's disease. The presence of Arterial aneurysm in Behçet's disease change the course of disease and it is management remains a challenge for rheumatologists

**Methods:** A retrospective revision of files of 160 patients admitted and followed up in the rheumatology department, Cairo University Hospitals between 2004–2017 was done. We looked specifically for the prevalence of arterial aneurysms. Demographic characteristics of patients with aneurysms, clinical presentation, and associated clinical features.

**Results:** Twenty-seven (16.8%) patients had arterial aneurysms. All of them were males and the onset of development of the aneurysm is usually under the age of 40 years, 74% of the patients developed aneurysm 3.2±3.0 years after their disease onset. Apart from the oro-genital ulcerations; deep venous thrombosis was the most common associated manifestation. Pulmonary artery was the most common artery involved in 12 (44.4%) of patients, followed by the abdominal aorta in 4 (14.8%). Surgical intervention was done for 11 (40.7%) patients; all of them received cyclophosphamide pulses before surgery except one. Four (14.8%) patients in this study died.

**Conclusions:** Arterial aneurysms are common in Egyptian patients with BD. The profile of Egyptian BD patient that is susceptible for development of arterial aneurysm is a male patient, under the age of 40 years, smoker with relatively short disease duration.

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**AB0687** **DOES ANTI-GLOMERULAR BASEMENT MEMBRANE (ANTI-GBM) ANTIBODY POSITIVITY CORRELATE WITH RELAPSE IN PATIENTS WITH ANTI-GBM DISEASE?**

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**Background:** Anti-GBM disease is characterised by rapidly progressive glomerular nephritis with or without pulmonary haemorrhage. It is usually monophasic in nature and disease severity correlates with antibody titer. The disease is mediated by pathogenic antibodies directed against the non-collagenous region of the  $\alpha 3$  chain of type IV collagen.

Despite the known pathogenicity of anti-GBM antibodies, and the correlation of disease severity with their titers, there is conflicting reports on whether anti-GBM antibody positivity correlates with disease relapse on long term follow up.

**Objectives:** To assess for correlation of anti-GBM antibody positivity and disease relapse in patients with anti-GBM disease.

**Methods:** Patients seen in one single academic centre between 1997 and 2017 were initially screened for the presence of anti-GBM disease by ICD 9/10 code for anti-GBM disease or Goodpasture's syndrome. 435 patients were identified. Patients were then included in the study if the diagnosis was confirmed by a board certified rheumatologist or nephrologist at our institution and had positive anti-GBM antibodies and/or biopsy results consistent with a diagnosis of anti-GBM

disease. The primary endpoint of this study was anti-GBM antibody positivity at the time of relapse. All charts were reviewed for baseline demographics, clinical manifestations, anti-GBM antibody and anti-neutrophil cytoplasmic antibody (ANCA) positivity at the time of initial presentation; these were compared between those with relapsing and non-relapsing disease. Results were analysed using a two tailed standard t-test. These same characteristics were also examined the relapsing cohort at the time of relapse.

**Results:** 40 patients were confirmed as having anti-GBM disease at our institution. Mean follow up from disease onset to the date of last follow up was 56.2 months. 8 patients had relapsing disease and 32 patients had non-relapsing disease. Baseline characteristics and clinical manifestations were similar between groups (table 1). Patients with relapsing disease had a statistically higher incidence of ANCA co-positivity as compared to non-relapsing patients (62.5% vs. 21.7% respectively p value- 0.03).

In patients with relapsing disease, only 14.7% (1/7 tested patients) had positive anti-GBM antibodies at the time of their relapse.

**Abstract AB0687 – Table 1.** Clinical features and laboratory values at baseline and at the time of relapse of Anti-GBM disease

	Non-relapsing Anti-GBM Disease (n=32)	Relapsing Anti-GBM Disease (n=8)	p-Value
<b>Baseline characteristics</b>			
Length of follow up, mos (range)	62.79 (2-228)	26.29 (3-78)	0.16
Time to diagnosis, days (range)	30 (1-182)	62 (5-243)	0.33
Age, Yr (range)	46.06 (17-78)	41 (14-62)	0.52
Male Gender (%)	53.1	37.5	0.44
Non-Smoking Status (%)	43.8	50.0	0.61
Renal involvement (%)	93.8	100	0.48
Peak creatinine mg/dL (range)	7.24 (0.9-17.6)	5.37 (1.6-13.7)	0.33
Pulmonary hemorrhage (%)	30.0	37.5	0.69
Positive Anti-GBM antibodies (%)	73.9 (17/23)*	37.5 (3/8)	0.07
Positive ANCA (%)	21.7(5/23)*	62.5 (5/8)	<b>0.03</b>
<b>Characteristics at time of relapse</b>			
Time to relapse, weeks (range)		77.14 (6-480)	
Positive Anti-GBM antibodies (%)		14.3 (1/7)*	
Positive ANCA (%)		75 (3/4)*	
Renal involvement (%)		93.3	
Peak creatinine mg/dL (range)		3.42 (2.7-4.85)	
Pulmonary hemorrhage (%)		71.4	

Values are expressed as mean (range) or percent

\*Incomplete data available. Number of positive patients out of total tested represented in parentheses

**Conclusions:** In this study, anti-GBM positivity did not correlate with disease relapse in patients with anti-GBM disease. Patients with relapsing disease had a higher incidence of ANCA positivity, consistent with previous investigations. In patients with newly diagnosed anti-GBM disease, ANCAs should be obtained to assess for the risk of relapse. Larger studies are needed to validate our results.

**Disclosure of Interest:** None declared

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**AB0688** **PULMONARY AND THORACIC VASCULAR FINDINGS OF BEHÇET'S DISEASE AT COMPUTED TOMOGRAPHY**

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**Background:** Behçet disease is a multisystemic and chronic inflammatory disorder with unknown etiology. Pulmonary involvement is relatively infrequent.

**Objectives:** To investigate the pulmonary parenchymal changes and thoracic vascular abnormalities due to Behçet's disease at computed tomography.

**Methods:** 21 patients diagnosed with a diagnosis of Behçet's disease between 2004–2017 were evaluated. Clinical, laboratory, and thoracic computed tomography findings were retrospectively evaluated. Also, the immunosuppressive treatments of the patients were documented.

**Results:** 18 of the patients (85.7%) were male. The mean age of the patients was 44.42±11.7 years, onset age of the disease was 32.4±6.4 years, length of follow-up was 8.1±2.3 years. 13 of the patients (61.9%) had hemoptysis at the time of initial diagnosis of Behçet's disease. 14 of the patients (66.6%) showed vascular involvement except pulmonary system. Pulmonary artery aneurysm was observed in 9 patients (42.8%). Pulmonary artery thromboembolism was observed in 15 patients (71.4%). Thoracic computed tomography demonstrated that 5 patients (23.8%) with pulmonary infarct, 4 patients (19%) with pulmonary consolidation, 5 patients (23.8%) with ground-glass opacity in the lung representing pulmonary haemorrhage, 2 patients (9.5%) with pleural effusion, 7 patients (33.3%) with non-specific parenchymal changes, and one patient with focal atelectasis. Also, one of the patients had intracardiac thrombus. Five of the patients were smokers.

**Conclusions:** Aneurysm of the pulmonary artery with or without thrombosis is the most common manifestation of Behçet's disease. Pulmonary vasculitis and thrombosis of pulmonary vessels result in infarction, hemorrhage, focal

atelectasis. Thoracic computed tomography can clearly demonstrate the pulmonary and vascular abnormalities of Behçet's disease.

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**Disclosure of Interest:** None declared

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#### AB0689 EXTRAVASCULAR MANIFESTATIONS OF TAKAYASU ARTERITIS: HISTORICAL COHORT STUDY IN KOREA

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**Background:** Takayasu arteritis (TAK) is systemic disease characterised by large vessel involvement. Although the vascular characteristics of TAK are well characterised, there is no well-organised study demonstrating the extravascular manifestations of TAK.

**Objectives:** To evaluate the characteristics of extravascular manifestations of TAK, and to identify the association between vascular and extravascular manifestations of TAK.

**Methods:** TAK patients from two independent cohorts who fulfilled the 1990 ACR classification and encoded M314 according to ICD-10 code between January 2012 and October 2017 were included in the study. Characteristics of the patients were retrospectively collected from the electronic dataset. A radiologist reviewed CT scans of all included patients to evaluate the pattern of vascular involvement and presence of sacroiliitis. Clinical findings including uveitis, skin lesion, oral ulcer, arthritis, and inflammatory bowel disease (IBD) were reviewed. Logistic regression analysis was performed to evaluate the association between vascular and extravascular manifestation.

**Results:** A total of 268 TAK patients were included. Mean age at diagnosis was 41.2±14.2 years and 236 (88.1%) were female. The most commonly involved vessel was common carotid artery (176 [65.7%]), and the most common type of vascular involvement was type V (120 [44.8%]). Extravascular manifestation of TAK was observed in 51 (19.0%) patients (table 1). The most common extravascular manifestation was arthritis (axial arthritis [sacroiliitis] [7.1%] and/or peripheral arthritis [6.0%]) (11.9%) followed by recurrent aphthous stomatitis (8.6%) and IBD (2.6%). In multivariable logistic regression analysis, the following factors were significantly associated with presence of arthritis (axial and/or peripheral arthritis): type IIB vascular involvement (adjusted OR 2.956, 95% CI 1.337–6.537, p=0.007) and erythrocyte sedimentation rate (ESR) (adjusted OR 1.014 95% CI 1.003–1.025, p=0.012).

**Abstract AB0689 – Table 1.** Extravascular manifestations of Takayasu arteritis

	n=268
Any extravascular manifestation	51 (19.0%)
Arthritis (axial arthritis [sacroiliitis] and/or peripheral arthritis)	32 (11.9%)
Recurrent aphthous stomatitis	23 (8.6%)
Inflammatory bowel disease	7 (2.6%)
Erythema nodosum	4 (1.5%)
Uveitis	2 (0.7%)

**Conclusions:** Extravascular manifestations of TAK are not rare and observed in up to one-fifth of patients. The most common extravascular manifestation was arthritis including sacroiliitis (11.9%). Type IIB vascular involvement pattern and high ESR were significantly associated with arthritis in TAK.

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#### AB0690 DIAGNOSTIC VALUES OF ENDOTHELIN-1 IN PATIENTS WITH SYSTEMIC NECROTIZING VASCULITIS

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**Background:** Systemic necrotizing vasculitis (SNV) is characterised by destructive and inflammatory changes in the vessels. Binding of autoantibodies and immune complexes on the surface of endothelial cells stimulates the synthesis of endothelin-1 (ET-1), which leads to activation of macrophages and adhesion of neutrophils, remodelling of the vascular wall and its damage.

**Objectives:** To evaluate the serum level of ET-1 in patients with SNV and the possibility of its using for the diagnosis of SNV and involvement of individual organs.

**Methods:** The study included 36 patients with SNV (polyarthritis nodosa – 8, ANCA – associated vasculitis – 28) and healthy controls (n=26). Clinical activities of patients were calculated according to the Birmingham Vasculitis Activity Score (BVAS). All patients had active disease (BVAS >11). The serum levels of ET-1 (pmol/L) were determined by immunoassay analysis using the kits of Biomedica. The outcomes of this study were the differences in marker levels between patients with active SNV and healthy controls, patients with different forms of vasculitis, with varying degrees of BVAS activity, with involvement different organs and systems estimated by analysis of the absolute changes in marker levels and the areas under receiver operating characteristic (ROC) curves (AUC).

**Results:** The level of ET-1 (M±σ) in the general group of patients with SNV was 0.31±0.24 and did not differ significantly from the control group (0.27±0.10, p>0.05). At the same time, in patients who did not receive at screening glucocorticoids and cytotoxic agents (n=9), it was significantly elevated (0.62±0.58, p=0.03). However, ROC analysis indicated the moderate sensitivity (67%) and the low specificity (48%) of ET-1 for diagnosis of SNV. There were no significant differences in the levels of ET-1 between patients with different forms of vasculitis and with varying degrees of BVAS activity. In the analysis of the values of the ET-1 depending on the involvement of different organs and systems, it was found that only in patients with kidney involvement (n=15) its level (0.40±0.33) was significantly higher compared with patients without kidney involvement (0.28±0.22, p=0.04) and control group (p<0.01). ROC analysis showed that the AUC for ET-1 is 0.75±0.10 (p=0.004), which indicates acceptable capacity for ET-1 differentiate groups of patients with kidney involvement and patients without kidney involvement (sensitivity – 80.0%, specificity – 78.3%).

**Conclusions:** The serum levels of ET-1 were elevated in patients with SNV with kidney involvement (48% compared to healthy controls and 43% compared with patients without kidney involvement), which can be used for diagnostic purposes.

**Disclosure of Interest:** None declared

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#### AB0691 INTERSTITIAL LUNG DISEASE AND MICROSCOPIC POLYANGIITIS IN CHILEAN PATIENTS

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**Background:** Microscopic Polyangiitis (MPA) is an ANCA associated vasculitis (AAV), associated with p-ANCA (perinuclear) fluorescence pattern and anti-myeloperoxidase (MPO) specificity. Most frequently involved organs are kidney (80%–100%), peripheral nervous system and skin (30%). There is Pulmonary involvement in 25%–35% of patients, being alveolar haemorrhage frequently described. Interstitial lung disease (ILD) has also been recognised.

**Objectives:** The aim of our study is to report the characteristics of MPA Chilean patients with ILD and to compare it with other series.

**Methods:** Retrospective study. Patient diagnosed between 2007 and 2016 at the Hospital Clínico Universidad de Chile, with ILD, defined as interstitial lung disease on CT scan with Usual Interstitial Pneumonia (UIP) or Non Specific Interstitial Pneumonia (NSIP) pattern, and MPA were included. Demographic, clinical, laboratory and mortality data were plotted. Data from other series were compared with our results. Other causes that could explain the pulmonary involvement were excluded.

**Results:** From 94 patients with AVV, 36,1% were MPA, being 16 patients with ILD. All were Hispanic, median age 65.3 years, <sup>32–84</sup> female 62.5% (table 1). Common manifestations were constitutional symptoms (100%), weight loss (68,7%) and fever (68,7%). All patients had anaemia, high ESR (mean 84 mm/hr. range 33–120) and CRP (8–22 times above upper normal limit). All patients were ANCA-p and MPO positive. In 10 cases ILD was diagnosed concomitantly with MPA and in 6 was 0.5 to 15 years before. 4 patients developed pulmonary haemorrhage. Images patterns were 10 UIP and 5 NSIP. All patients received corticosteroid as induction therapy, 15 also received cyclophosphamide. One patient plasmapheresis, and one received Rituximab after a relapsed. Azathioprine was used as



Maintenance therapy. Four patients died during follow-up. table 2 shows data from other worldwide region compared with our data.

**Abstract AB0691 – Table 1.** Characteristic of Chilean patient with ILD an MPA

Age	Sex	CT	Oral (months)	RENAL	MUCOCUTANEOUS	NEUROLOGIC	MPO	TREATMENT	MORTALITY
55	M	UIP	C	NO	NO	MM	MP/50	CS/CY/AZA	NO
68	F	UIP	B (30)	NO	LR	PNP	MP/50	CS/CY/AZA	NO
79	M	UIP	B (5)	NO	LR	PNP	MP/50	CS/CY/AZA	NO
69	F	UIP	C	NO	LR	PNP	SI	CS/CY/AZA	NO
77	F	UIP	C	GN	LR / CV	MM/NSIP	SI	CS/CY/AZA	YES
64	F	UIP	C	GN	NO	NO	MP/50	CS/CY/AZA	NO
81	M	UIP	C	GN	NO	NO	NO	CS/CY/AZA	NO
84	F	UIP/DAH	C	RFON	Oral Ulcers	NO	NO	CS/CY/AZA	YES
63	F	UIP	B (16)	GN	NO	CKD/NSIP	NO	CS/CY/AZA	NO
83	M	NSIP	B (24)	NO	NO	MM	SI	CS/CY/AZA	NO
53	F	NSIP	C	GN	LR	NO	SI	CS/CY/RTX/AZA	YES
68	F	NSIP/DAH	B (30)	NO	NO	PNP	MP	CS/CY/PLX/AZA	YES
57	M	NSIP/DAH	C	RFON	NO	PNP	NO	CS/CY/AZA	NO
78	M	NSIP/DAH	C	NO	NO	NRHL	MP/50	CS/CY/AZA	NO
54	F	NSIP	C	NO	LR	PNP	SI	CS/CY/AZA	?
32	F	UIP/DAH	B (8)	NO	CV	NO	NO	CS/CY/AZA	NO

**Abstract AB0692 – Table 1.** Baseline disease characteristics

n (%)	BEL (n=53)	PBO (n=52)
GPA	42 (79)	41 (79)
MPA	11 (21)	11 (21)
ANCA type (historical diagnosis)		
Anti-PR3	41 (77)	40 (77)
Anti-MPO	12 (23)	12 (23)
ANCA positive	24 (49)	22 (44)
IR		
IV CYC	21 (40)	24 (46)
Oral CYC	18 (34)	15 (29)
Rituximab	14 (26)	13 (25)

ANCA, anti-neutrophil cytoplasm antibodies; BEL, belimumab; CYC, cyclophosphamide; GPA, granulomatosis with polyangiitis; IR, induction regimen; IV, intravenous; MPA, microscopic polyangiitis; MPO, myeloperoxidase; PBO, placebo; PR3, proteinase 3; RTX, rituximab  
\*n=49 (BEL); n=50 (PBO)

**Abstract AB0691 – Table 2.** Characteristic of patient with lid and MPA worldwide

Country	CHN	IND	USA	UK	GER	ITA	USA	USA	USA
Number of Patients	18	9	19	19	19	9	6	10	40
Age (years)	65.3	58.4	54.2	63.6	66.2	72.3	69.8	70	68
Sex (% Female)	61.1	55.6	47.1	58	58	76.7	50	20	59
Oral (months)	57.5/42.4/0	55.5/54.5/0	82.1/71.7/0	88.1/11.5/0	52.4/42.1/0	33.5/28.7/0	102/11/1/0	50/10/20	61/19/22
% of patients with oral	62.5/71.25/6/23	88.8/9/11.2	100/0/0	100/0/0	100/0/0	0/0/100	100/0/0	60/10/30	NA
Mortality (%)	23	44.4	43.2	31	47	58.3	83.3	50	36

**Conclusions:** Among Chilean patients there are more females, have a more NSIP pattern, and less mortality than other worldwide series.

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**AB0692 BELIMUMAB IN COMBINATION WITH AZATHIOPRINE FOR REMISSION MAINTENANCE IN GRANULOMATOSIS WITH POLYANGIITIS AND MICROSCOPIC POLYANGIITIS: EFFECT ON BIOMARKERS**

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**Background:** GPA and MPA (related types of ANCA-associated vasculitis [AAV]) are organ-/life-threatening systemic vasculitides. B cells and increased circulating BLYS (a B cell survival factor) are implicated in AAV pathogenesis, suggesting a role for BLYS in these vasculitides. BEL is an anti-BLYS human immunoglobulin (Ig) G1 $\lambda$  monoclonal antibody.

**Objectives:** Examine the effects of BEL plus azathioprine (AZA), on biomarkers in patients with AAV for remission maintenance following standard induction (IND) with glucocorticoids (GC) and CYC or RTX.

**Methods:** This double-blind, placebo-controlled, multicentre study (BEL115466/NCT01663623) randomised (1:1) patients ( $\geq 18$  years) with new/relapsing AAV following IND (oral or IV CYC or RTX), to AZA 2 mg/kg/day and oral GC, plus IV BEL 10 mg/kg or PBO (Days 0, 14, 28 and every 28 days until completion). Remission was defined as Birmingham Vasculitis Activity Score=0, plus GC  $\leq 10$  mg/day. The study was truncated after initiation (n~300 to~100) due to revised AAV standard of care (SoC) affecting recruitment. Biomarker endpoints (serum Igs, B cells and ANCA [anti-MPO/PR3]) were measured at baseline (BL) and thereafter. Summaries by IR were post hoc; no analyses were performed.

**Results:** At BL, RTX patients had B cell counts  $\leq$  LLQ. CYC patients had notably low BL B cell counts: the lowest were in oral-CYC patients. Circulating memory B cells (CD20+/CD27+) increased rapidly with BEL, then gradually returned to BL (CYC); no major changes occurred with PBO. BEL had no impact on the proportion of naive CD20 +CD27 – B cells vs PBO, post CYC IND. The number of RTX patients with quantifiable data was low; partial reconstitution occurred in a minority of patients (PBO 2/13; BEL 4/14) and did not translate into vasculitis relapses. Overall Ig levels declined more noticeably with BEL vs PBO; suggesting BEL affects antibody-secreting cells. ANCA+patients were similar between groups (PBO 32/50; BEL 30/49). No trends in change in ANCA status over time occurred, regardless of IR. Individual patient data showed no apparent trends between ANCA titres and AAV activity.

**Conclusions:** Choice of IR for active AAV affects B cell dynamics. BEL pharmacodynamic effects occurred in patients with AAV receiving SoC. Given the small sample size and high variability, data must be interpreted with caution.

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**AB0693 DEMOGRAPHIC, CLINICAL, LABORATORY AND IMAGING CHARACTERISTICS OF AN INCIDENCE COHORT OF 93 PATIENTS WITH LARGE VESSEL GCA**

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**Background:** Few study have evaluated the clinical and imaging data of patients with large vessel GCA (LVGCA)

**Objectives:** To evaluate clinical, demographical and imaging data of an inception cohort of 93 patients with LVGCA recruited in Reggio Emilia (Northern Italy)

**Methods:** All patients with incident large vessel GCA diagnosed between 1 January 2005 and 31 December 2016 and living in the Reggio Emilia area, were identified by capture and re-capture checking of computerised discharge diagnosis codes (ICD10) and using outpatients databases from rheumatology, internal medicine, surgery, pathology, imaging departments of Reggio Emilia Hospital as well

as by examining the Reggio Emilia district database for rare diseases. To be included in the study, patients must satisfy the following 2 criteria: Age at disease onset  $\geq 50$  years; evidence of large-vessel vasculitis by clinical criteria, angiography, MRA, CTA, PET/CT and/or ultrasonography. Demographic, clinical, laboratory and imaging data collected at first visit were retrieved from patients records.

**Results:** There were 93 incident cases of LV GCA (66 women, 71%) during the 12 year study period; Mean  $\pm$ SD age at diagnosis was 72 $\pm$ 9 years. The three most prevalent signs an symptoms were: systemic in 49 pts (52.7%), GCA cranial symptoms in 39 pts (41.9%) and PMR in 35 pts (37.6%). Peripheral ischaemic symptoms were observed only in 8 pts (8.6%). Forty four pts had temporal artery biopsy and 70.5% resulted positive. At US examination the three most common involved arteries were: common carotid artery (59.2% pts), subclavian artery (53.3% pts) and axillary artery (49.3 pts). At PET/CT scan examination the most common involved arteries were: thoracic aorta (72.1% pts), subclavian artery (61.8% pts) and abdominal aorta (58.8% pts). Celiac trunk and mesenteric artery were involved in 18.4% of pts and renal artery in 10.2% of pts.

**Conclusions:** In an inception cohort of LVGCA systemic manifestations had the highest prevalence among presenting symptoms. Imaging studies demonstrated an high prevalence of aortic and subclavian involvement.

**Disclosure of Interest:** None declared

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#### AB0694 GIANT CELL ARTERITIS EPIDEMIOLOGY IN LA REUNION: A RETROSPECTIVE CASES SERIES

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**Background:** Giant Cell Arteritis (GCA) is the most common vasculitis in people over 50 years, with incidence varying according to geographic location. In Europe, the average incidence is 10–30 per 1 00 000 inhabitants over 50 years, whereas in Africa and Asia it is approximately 1.5 per 1 00 000.

**Objectives:** To define GCA epidemiology in La Réunion, a French oversea territory in South West Indian Ocean characterised by several ethnic groups and genetic admixture.

**Methods:** Retrospective study between January 2005 and August 2017 in the 4 main hospitals of La Réunion. Patients were identified through hospital informatics databases and practitioner records. A definite diagnosis of GCA was considered for patients fulfilling ACR criteria and/or by assessment by a trained rheumatologist. Incidence and prevalence calculation was based on French national census data.

**Results:** Sixty patients were included, of which 60% were women. Mean age at diagnosis was 73.7 years, with a mean delay to diagnosis of 6.8 months. Cases met an average of 3.78/5 ACR criteria, and 78% had >2 criteria. The mean annual incidence was 2.33 per 1 00 000 inhabitants older than 50 years (203,000), with 95% confidence interval (IC) of 1.74–2.92. The prevalence at the end of period study was 24 cases per 100,00 (IC: 18–30). There was no seasonal variation regarding disease onset. Clinically, patients complained of asthenia and headache in 75%, fever in 33% and ophthalmologic damage for 32% of the cases, of which 5 had anterior ischaemic optic neuropathy. Polymyalgia rheumatica was associated in 42% of all cases. Total blood cells counts were usually within normal values, whereas mean CRP was 111 mg/L. Anicteric cholestasis was a common finding: mean GGT=78 IU/L (n<42) and alkaline phosphatase=107 IU/L (n<104). Radiological examinations contributed to diagnosis in only 9/31 cases. Temporal artery biopsy was performed in 91% of patients and showed specific histological features of GCA in 55%. Corticosteroid regimen was introduced in 59 patients (1 died the day after the biopsy) and mean treatment duration was 26 months, for a total dose of 10.6 g. Antiplatelet therapy was given in 47% of patients. One patient in three experienced one or more relapses.

**Conclusions:** This is the first study to describe GCA in La Réunion, and more generally in Indian Ocean. It shows an incidence 4–12 times lower than in most European countries with white ancestry background. This discrepancy could be explained by the contribution of the various ethnic groups of La Reunion, especially those coming from parts of the world characterised by a lower GCA incidence (Africa, India, South East Asia). A shorter life expectancy may also account for this observation, assuming that GCA incidence increases with age. Sex ratio and age at diagnosis were similar to European studies, as well as clinico-biological features, response to treatment and side effects. Some limitations of our study should be taken in consideration: inclusions of hospitalised patients only, informatics record limits and retrospective design that did not afford for ethnic background determination.

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#### AB0695 PREDICTIVE FACTORS OF LONG-TERM CLINICAL OUTCOME IN BEHCET'S SYNDROME PATIENTS WITH OCULAR INVOLVEMENT: DOES ACTUALLY THE DISEASE TEND TO GROW DIM OVER TIME?

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**Background:** Behçet's syndrome (BS) is a multisystemic, chronic relapsing inflammatory disease classified among the vasculitis. Eye involvement represent one of the most serious manifestation of BS and occurs in half of all patients. It seems more frequent and severe among young males and, unluckily, it still represents a significant cause of morbidity.

**Objectives:** The aims of the study were: to study the relapse rate of BS patients with ocular involvement and to identify factors able to predict long-term outcome

**Methods:** Among a cohort of 138 patients with a diagnosis of BS according the ISG criteria, 62 patients (37 males and 25 females; mean age at the onset 38 $\pm$ 5 years) with ocular involvement were prospectively studied. The probability of clinical relapse after remission of the first ocular attack was calculated using the Kaplan-Meier method. Predictors of long-term outcome were identified by univariate analysis using the log-rank test and by multivariate analysis using Cox proportional hazards regression models.

**Results:** The mean time between the first initial symptoms of BS and the onset of eye lesions was 2 $\pm$ 2 years. The number of ocular attacks were the following: 43 posterior uveitis, 27 anterior uveitis, 26 retinal vasculitis, while panuveitis developed in 18 subjects. The cumulative relapse rates at 1 year, 3 years, and 5 years after remission of the first ocular attack were 41%, 31%, and 28%, respectively. On multivariate analysis, a younger age (<30 years) at the onset of ocular involvement, male sex and medical treatments other than biological agents represent independent predictive factors for more early relapses in BS patients with ocular involvement.

**Conclusions:** The relapse rate seems to be more frequent in the first years of diseases, and probably it could be related to the fact the disease tend to grow dim over time. As literature data suggest, younger age and male sex still represent predictive factors of poor long-term clinical outcome.

**Disclosure of Interest:** None declared

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#### AB0696 CLINICAL CHARACTERISTICS AND OUTCOME OF PATIENTS WITH GRANULOMATOSIS WITH POLYANGIITIS (GPA) ACCORDING TO ANCA POSITIVITY AND SPECIFICITY

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**Background:** GPA is a necrotizing granulomatous vasculitis associated with ANCA that usually involves ENT, lung and kidneys. ANCA are mostly directed against proteinase 3 (PR3), although in few cases are directed against myeloperoxidase (MPO) or negative.

**Objectives:** To analyse the phenotype, clinical course and outcome of patients with GPA according to ANCA positivity and specificity

**Methods:** multicenter retrospective-longitudinal study that included patients diagnosed with AAV between Jan 1995 and Jan 2016 in 21 Hospitals from Spain (REVAS-Study). We analysed the clinical characteristics, treatment and outcome, depending on the ANCA positivity and specificity. Statistical analysis was performed using SPSSv20

**Results:** 221 patients with GPA were included:162 with PR3-ANCA, 36 with MPO-ANCA, and 23 with negative-ANCA. The mean-age at disease onset was higher in patients with MPO-ANCA (59.9 $\square$ 16.5 years) than in patients with PR3-ANCA (50.5 $\square$ 16.5) and negative ANCA (48 $\square$ 14.5), p=0.006. Compared to

patients with PR3-ANCA, patients with MPO-ANCA presented a lower prevalence of toxic syndrome (42.9% vs. 55.6%,  $p=0.021$ ), arthralgias (34.3% vs. 59.9%,  $p=0.008$ ), arthritis (8.6% vs. 26.5%,  $p=0.026$ ), pulmonary involvement (cavitated/infiltrated nodules,  $p=0.007$  and  $p=0.05$ ), and anaemia (57.1% vs. 77.8%,  $p=0.05$ ). Renal disease was less severe in patients with MPO-ANCA (creatinine  $\geq 1.58$  mg/dL 14.3% vs. 30.4%,  $p=0.04$ ). Subglottic stenosis and sensoryneural deafness were more frequent in patients with MPO-ANCA (20% vs. 6.8%,  $p=0.05$  and 34.3% vs. 18%,  $p=0.03$ ). The mean BVAS at baseline was lower in patients with MPO-ANCA (16.3 $\square$ 8.8) and negative ANCA (12.5 $\square$ 6.7) than in patients with PR3-ANCA (19.6 $\square$ 8.9),  $p=0.029$ . Patients with negative ANCA had less frequently toxic syndrome, fever, arthritis, subglottic stenosis, kidney disease, and peripheral neuropathy, and more frequently orbital masses. Disease relapses were less frequent in patients with MPO-ANCA than in patients with PR3-ANCA (37.1% vs. 48.8%,  $p=0.04$ ), but more frequent than in patients with negative ANCA (20.8%),  $p=0.002$ . Patients with MPO-ANCA and negative ANCA received less frequently oral cyclophosphamide. No significant differences were found related to death in patients with MPO-ANCA and PR3-ANCA. Patients with negative ANCA had the lower mortality

**Conclusions:** A small percentage of patients with GPA present MPO-ANCA or negative ANCA. In our series, patients with MPO-ANCA were older at the disease onset, presented limited or less severe organic disease than patients with PR3-ANCA, lower percentage of relapses and lower requirement of aggressive therapies. Patients with negative ANCA had the best prognosis. Our findings are similar to those recently published,<sup>1</sup> although our patients with MPO-ANCA were older. Classification of GPA patients considering ANCA specificity can improve the treatment stratification and reduce adverse events.

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AB0697

#### GIANT CELL ARTERITIS WITH NORMAL INFLAMMATORY MARKERS AT DIAGNOSIS

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**Background:** GCA is an inflammatory vasculitis affecting medium and large-sized arteries, that can result in arteritic anterior ischaemic optic neuropathy. C-reactive protein (CRP) level and erythrocyte sedimentation rate (ESR) are usually elevated at GCA diagnosis, but inflammatory-marker negative disease does occur.

**Objectives:** To analyse the clinical and histological findings of patients with biopsy-proven GCA and negative inflammatory-markers at diagnosis.

**Methods:** multicenter-longitudinal retrospective study that included patients with biopsy-proven GCA recruited at 10 Hospitals from Spain (REVAS Study). Statistical analysis was performed using SPSS vs. 21.

**Results:** 418 patients: 290 (69.4%) females (ratio F/M: 2.3/1) were included. The mean age at diagnosis was 75.5 $\pm$ 7 (53–92). The most frequent symptoms at diagnosis were recent onset headache (81%), toxic syndrome (47%) and rheumatic polymyalgia (44.5%). Jaw claudication, cranial hyperesthesia and amaurosis fugax were reported by 44.5%, 31.8% and 16.5% of patients, respectively. A total of 84 patients suffered permanent vision loss. Fourteen patients (3.3%) had normal ESR (<40 mm/h) and CRP (<5 mg/L) at diagnosis. No significant differences were found related to age at disease onset in these patients. Most patients (85%) reported headache; 42.9% jaw claudication, 28.6% cranial hyperesthesia and 42% rheumatic polymyalgia. Fever was less frequent in patients with negative inflammatory-markers (7.7% vs. 40.4%,  $p=0.020$ ), as well as toxic syndrome (21.4% vs. 51.5%,  $p=0.031$ ). In contrast, patients with negative inflammatory-markers had more frequently amaurosis fugax (35.7% vs. 16.8%,  $p=0.03$ ) and optic ischaemic neuropathy (50% vs. 18.7%,  $p=0.009$ ). Temporal arteries were abnormal (thickened and/or pulse less) in 78.6% of patients with negative inflammatory-markers vs. 37% of patients with elevated ESR and/or CRP. Anaemia was less common in patients with negative inflammatory-markers (28.6% vs. 81.5%,  $p<0.001$ , mean haemoglobin 12.9 $\pm$ 1.1 g/dL). No significant differences were found related to temporal artery biopsy findings, although patients with normal ESR and CRP showed giant cells in 74.3% of cases vs. 62%.

**Conclusions:** typically patients with GCA present with elevated inflammatory-markers (ESR and CRP) at disease onset. However, a few percentages of patients (4%–5%) have normal ESR and CRP at diagnosis.<sup>1</sup> In our series, 3.3% of patients had negative inflammatory-markers at diagnosis. These patients had fewer constitutional symptoms and more visual symptoms (amaurosis fugax and permanent visual loss) than patients with elevated ESR and/or CRP. Our result are similar to those published in the literature. Abnormal temporal arteries on physical examination may help to diagnosis

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AB0698

#### A COMPARISON OF THE EFFECTIVENESS OF MYCOPHENOLATE MOFETIL OR METHOTREXATE IN COMBINATION WITH PREDNISOLONE VERSUS PREDNISOLONE ALONE IN THE TREATMENT OF LARGE VESSEL VASCULITIS

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**Background:** The mainstay of treatment for large vessel vasculitis is glucocorticoids. Immuno-suppressants, including mycophenolate mofetil (MMF) and methotrexate (MTX) are used as steroid-sparing agents.<sup>1</sup> A previous study at our centre showed MMF to have a steroid sparing effect in 97% of patients and to reduce C-reactive protein (CRP) in 80%.<sup>2</sup>

**Objectives:** This study was undertaken to compare the efficacy of MMF or MTX combined with prednisolone or prednisolone alone in the treatment of large vessel vasculitis.

**Methods:** Patients with large vessel vasculitis (LVV) confirmed on positron emission tomography (PET) scan and those meeting ACR criteria for a diagnosis of giant cell arteritis (GCA), treated with prednisolone alone, prednisolone with MMF or prednisolone with MTX started within 3 months of prednisolone being commenced and with a minimum follow up of 24 months were included in a retrospective single centre study. CRP and prednisolone doses were recorded at baseline, after 3, 6, 9, 12, 18 and 24 months of treatment and area under the curve (AOC) calculated for CRP and prednisolone doses. Median AOC prednisolone dose for patients treated with MMF or MTX was then compared with that of patients treated with prednisolone alone. A quantile regression model was also constructed to compare prednisolone dose between the 3 treatment groups, adjusted for CRP. StataCorp. 2013. *Stata Statistical Software: Release 13*. College Station, TX: StataCorp LP was used for all statistical calculations.

**Results:** 65 patients were included in the study, 41 with GCA and 24 LVV. 49 were female and 16 male. Mean age at diagnosis was 68; range 21 to 87. 37 patients were treated with prednisolone alone; 35 had GCA and 2 LVV. 20 were treated with MMF and prednisolone; 4 with GCA and 16 LVV. 8 were treated with MTX and prednisolone; 2 had GCA and 6 LVV. The AOC for prednisolone and CRP were not normally distributed across the cohort, and non-parametric methods were therefore used for comparisons. Median AOC prednisolone dose for the prednisolone only group was 68.0, (interquartile range (IQR) 17.7,  $n=37$ ), for the MMF treated group 70.8 (IQR 28.7,  $n=20$ ) and for the MTX treated group 67.8 (IQR 20.4  $n=8$ ). Median AOC CRP was highest in the group treated with prednisolone alone (58.9, IQR 34.5) compared to MMF (43.8, IQR 26.5) and MTX (49.3 IQR 67.5) but there were no statistical differences between median AOC prednisolone dose or CRP in either the unadjusted or regression models.

**Conclusions:** No significant difference was shown between the groups. MMF is as effective as MTX and prednisolone alone in the treatment of LVV. However, there are limitations to the study. The patient group was small. There was no randomisation to treatment group; treatment choice was based on clinician preference. There was potential bias in that patients perceived to be more difficult to treat may have been given MMF or MTX in addition to prednisolone, and there was a higher proportion of patients with LVV compared to GCA in the MMF and MTX treated groups.

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**AB0699 BENZATHINE PENICILLIN IN TREATMENT OF ULCERS OF BEHCET'S DISEASE**

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**Background:** Prednisone therapy, Thalidomide, azathioprine, anti-TNF-alpha inhibitors are presently used in resistant mucocutaneous lesions of Behçet's Disease (BD). In this study, we used only ambulatory Benzathine Penicillin (BP), without being preceded by high doses of penicillin infusion. This Study confirm the value of BP in the treatment of refractory ulcers of BD and point out a probable role of Streptococcus on the pathogenesis of BD

**Objectives:** This open Study confirm the value of BP in refractory oral, genital and skin ulcers of BD. We propose to use BP when ulcers of BD are resistant to colchicine 1.5 mg/day and to add BP in the recommendations of EULAR for the treatment of resistant cases of mucocutaneous involvement.

**Methods:** 15 patients with BD (12 patients fulfilled all criteria for BD) had Giant (mean size of ulcer superior to 1 cm), or Multiple oral, genital, skin ulcers received BP at the dose of 2.4 million units in intramuscular injection; 3 intramuscular injections with an interval of 3 weeks between injection. Colchicine at the dose of 1 mg/day was maintained. Serology of syphilis was negative. Patients had seen 15 days, 3 months and 1 year after the starting treatment.

**Results:** This study started in 2012, in a private office and comprised 15 patients:9 males; 6 females. Arthritis was observed in 11 patients, uveitis in 6 cases. BP was used in 8 patients with oral ulcers(4 Giants and 4 multiples), Genital ulcers in 3 patients (2 multiple and 1 Giant), oral and genital ulcers(2 Multiples) and cutaneous aphthosis in 2 patients 0.2 weeks after the first injection of BP, recovery from ulcers was achieved. BP was administrated a second time with success, in 9 patients who have developed resistant ulcers, after 1 to 3 years of recovery. One patient with panuveitis treated with azathioprine in 2013 and interferon alpha in 2015 and 2017, developed refractory ulcers: Excellent efficacy of BP was observed in this patient.

**Conclusions:** In this study, we confirm the recovery from refractory oral, genital and cutaneous ulcers (Giant, Multiple) in these 15 patients with BP. We recommend using more frequently BP and we propose to add BP in the recommendations of EULAR for the treatment of resistant cases of mucocutaneous involvement because treatment with BP is rather easy in outpatients, it is efficient, it has a low cost and have few side-effects

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**Disclosure of Interest:** None declared

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**AB0700 IS IT FEASIBLE TO WITHDRAW IMMUNOSUPPRESSIVE TREATMENT IN REAL-LIFE PATIENTS WITH ANCA-ASSOCIATED VASCULITIS?**

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**Background:** The optimal duration of remission-maintenance treatment in ANCA-associated vasculitis (AAV) is still unknown,<sup>1</sup> with International recommendations suggesting to maintain it for at least 24 months. Data supporting the correct balance between relapse risk, treatment-related adverse events and damage are highly needed.

**Objectives:** To analyse the frequency and predictors of withdrawal of remission-maintenance immunosuppressive drugs (IS) in a large real-life cohort of AAV patients.

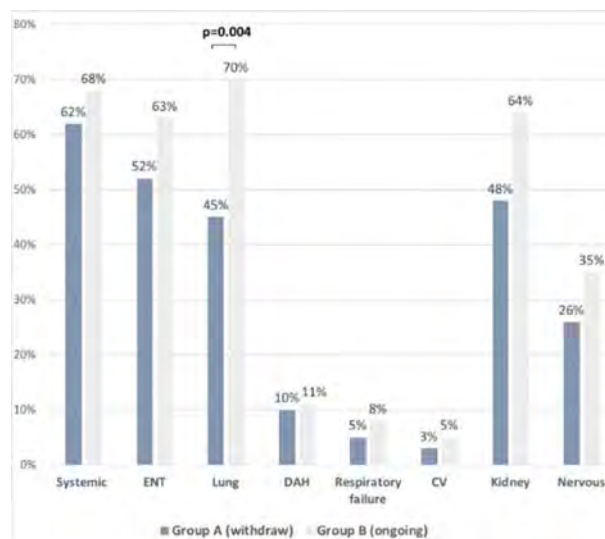
**Methods:** Clinical records of patients with granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA) were retrospectively analysed from a multicentric cohort. We divided the cohort into group A (withdrawal) and group B (ongoing).

**Results:** We included 185 patients. Forty-one patients (22%) had withdrawn IS at the end of follow-up (median 73.5 months, IQR 54–115). Concomitant glucocorticoids were stopped in 33%. There were no significant differences in AAV subtype,

ANCA pattern, age at diagnosis, diagnostic delay or comorbidities rates between group A and group B (table 1). Disease onset with pulmonary involvement was significantly more frequent in patients in whom IS was maintained (69.7% vs 45%; p=0.004). Figure 1. Disease activity at onset, but not during follow-up, was significantly higher in patients from group B (ongoing): median BVAS 18 (12–24) vs 15; (8–20) p=0.02. The type of IS used for remission induction did not differ between the two groups. Maintenance treatment with Rituximab (RTX) was associated with higher probability of discontinuing IS by the end of follow-up (21% vs 7.6%; p=0.02). There was no difference in the number of major relapses between the two groups. Safety profile was equally good in both groups, except for a higher number of infections over the course of disease in patients who withdrew IS (5% vs 0). Vasculitis damage index (VDI) was comparable between the two groups.

**Abstract AB0700 – Table 1.** Clinical characteristics and outcome: comparison between IS withdrawal group (A) and ongoing group (B).

	Group A (withdrawal) n=41	Group B (ongoing) n=144	p
Sex:	18 (43.9%)	67 (46.5%)	0.769
Male, N (%)			
Diagnostic delay, months, median (IQR)	4 (2–11.75)	3.5 (1–8)	0.551
Age at diagnosis (mean±SD)	53.85±16.30	54.41±15.39	0.847
Mean follow up duration months, median (IQR)	73.5 (54–115)	66 (36.5–109.5)	0.315
AAV subtypes N(%)			
GPA	32/41 (78%)	112/144 (77.8%)	0.976
MPA	9/41 (21.9%)	29/144 (20.1%)	0.801
p-ANCA (MPO) N(%)	10/41 (24.4%)	47/143 (32.9%)	0.302
c-ANCA (PR3) N(%)	19/41 (46.3%)	78/143 (54.5%)	0.355
Number of major flares, median (IQR)	0 (0–1)	0 (0–1.25)	0.695
Safety: cancer	6/41 (14.6%)	11/135 (8.1%)	0.220
Safety: infections: >3, N(%)	2/40 (5%)	0/134 (0%)	0.009
Number of hospitalisations, median (IQR)	0 (0–1)	0 (0.1)	0.454
VDI last follow-up	3 (2–4.75)	3 (2–4)	0.773



**Abstract AB0700 – Figure 1**

**Conclusions:** IS withdrawal was observed in a minority of real-life patients with AAV. Drug-free remission was negatively associated with pulmonary involvement and higher BVAS at disease onset. Remission maintenance with RTX was associated with a higher frequency of drug withdrawal at the end of follow-up.

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**Disclosure of Interest:** None declared

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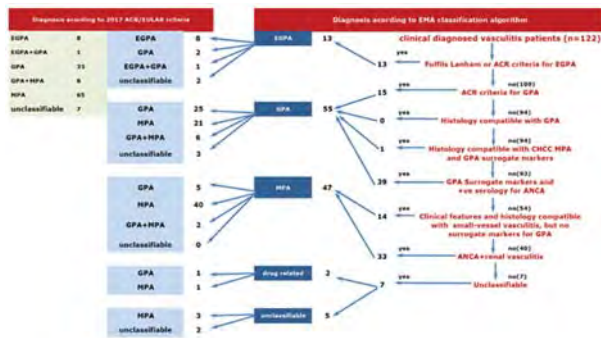
**AB0701** **COMPARISON OF THE NEW ACR/EULAR CLASSIFICATION CRITERIA OF ANCA-ASSOCIATED VASCULITIS WITH THE EMA ALGORITHM IN CLASSIFICATION OF VASCULITIS**

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**Objectives:** A new set of classification criteria for ANCA-associated vasculitis (AAV) was presented in 2017's ACR annual scientific meeting. In order to evaluate this new set of classification, we conducted the current study to compare it with the EMA's consensus algorithm for classification of systemic vasculitis proposed by Watt et al. in our centre.

**Methods:** One hundred and twenty-two Chinese patients with clinically diagnosed as AAV in our centre during the past 15 years were retrospectively studied. We compared the new set of ACR/EULAR's classification criteria for AAV, with the EMA's consensus algorithm with surrogate parameters, in the same cohort of patients with primary systemic vasculitis.

**Results:** Applying the EMA's consensus algorithm with surrogate parameters, the diagnoses were EGPA (n.3), GPA (n.55), microscopic polyangiitis (MPA) (n.47), drug related AAV (n.2), and unclassified (n.5). Using the new ACR/EULAR's classification criteria for AAV, the diagnoses were EGPA (n.8), GPA (n.33), MPA (n.65), overlap with EGPA and GPA (n.2), overlap with GPA and MPA (n.8), and unclassified (n.7) (See the below picture).



Abstract AB0701 – Figure 1

**Conclusions:** The new 2017 ACR/EULAR classification criteria for AAV and Watts' algorithm were all useful methods to classify patients with systemic vasculitis. The Watts' algorithm can classify all patients into a single category, with more GPA patients, less unclassified patients and without overlapping diagnosis, in comparison, the new 2017 ACR/EULAR classification criteria classified more MPA patients, more unclassified and more overlapping patients.

**Disclosure of Interest:** None declared

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**AB0702** **ALKALINE PHOSPHATASE AS A PREDICTOR OF GIANT CELL ARTERITIS – A RETROSPECTIVE ANALYSIS OF CLINICAL FEATURES AND TEMPORAL ARTERY BIOPSY FINDINGS**

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**Background:** Giant cell arteritis (GCA) is the most common large vessel vasculitis in the United Kingdom and Northern Europe. Inadequate treatment and delay in diagnosis can lead to a number of devastating consequences.

**Objectives:** This study looks at whether the presence of a raised alkaline phosphatase (ALP) may aid the diagnosis of GCA, improve the sensitivity of TAB, including in the presence of other proven serum markers and whether it has any correlation with severity of clinical presentation.

**Methods:** Retrospective multicenter cohort study. Information was retrospectively gathered on patients who underwent TABs following a clinical working diagnosis of GCA. Only patients who fulfilled the American College of Rheumatology (ACR) classification criteria and had ALP measured within 4 weeks of undergoing TAB were included in the study. Once patients were identified, further information was extrapolated including the values of other serum markers taken, and presenting clinical features.

**Results:** Our 223 patients sample population who fulfilled the inclusion criteria reflected typical GCA patients: 147 (65.9%) were female and mean age was 73.1 years (SD 10.5). TAB was positive in 54 patients (24.2%). Two patients (3.7%) who had a positive TAB had completely normal serum markers. We were unable

to comment on variables, which could have contributed to this but they likely represented already administered aggressive glucocorticoid treatment at time of serum measurement or atypical presentation of GCA. Raised ALP sensitivity at the current cut off value was very low (14.8%) but with high specificity (90.5%), which was reinforced following ROC curve analysis. Pearson coefficient analysis suggested that there was a weakly associative relationship between raised ALP and degree of clinical suspicion (Correlation 0.346, Sig 0.01)

**Conclusions:** Patients with a higher level of clinical suspicion and TAB positivity were more likely to have a raised ALP. However, the association strength was weak. ALP is suggested to be highly specific for TAB positivity. The association of raised ALP to degree of clinical features and suspicion of GCA is weak and of low significance, likely a reflection of the limitations of this study. Further robust research may further evaluate this observed relationship.

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**AB0703** **LONG TERM FOLLOW-UP OF BEHÇET'S SYNDROME PATIENTS TREATED WITH CYCLOPHOSPHAMIDE**

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**Background:** Cyclophosphamide (CYC) remains an important treatment option for Behçet's syndrome (BS) patients with life-threatening conditions such as arterial aneurysms. However, several adverse events may occur with CYC and this has led to increased use of biologic agents such as rituximab in other vasculitides.

**Objectives:** The aim of this study is to delineate the outcome and short and long-term adverse events with CYC use among BS patients.

**Methods:** We conducted a retrospective chart review of all BS patients treated with oral or intravenous CYC between 1976 and 2006. Patients were called and a standard form was used for collecting demographic characteristics, CYC indication, cumulative dose of CYC and short-term serious adverse events necessitating the cessation of therapy and/or requiring hospitalisation and long-term adverse events (malignancy and infertility), and outcome.

**Results:** We identified 198 (M/W: 184/14) BS patients who had received CYC. After a median follow up of 17 (IQR: 9–26) years after the initiation of CYC therapy, 52 (26%) patients had died within a median duration of 4<sup>1–12</sup> years, 33 (17%) were lost after a median follow-up of 9 (3.5–14) years, and 113 (57%) were contacted. CYC was prescribed for vascular involvement in 132 (67%) patients, eye involvement in 52 (26%), central nervous system involvement in 5, both vascular and eye involvement in 7 and both vascular and central nervous system involvement in 2 patients. The median duration of CYC use was 12 (IQR:4–24) months and median cumulative dose was 13.5 (IQR:6–49) gr. Among the 52 patients who died, reasons for death were vascular involvement in 26, malignancies in 7, infections in 5 (5 bacterial infections, 1 additional tuberculosis), neurologic involvement in 2, ischaemic stroke in 1, traffic accident in 1, and secondary amyloidosis in 1, esophageal variceal bleeding in 1, and unknown in 5 patients. Sixteen (8%) patients experienced serious adverse events associated with short-term CYC use and 1 of them died due to infection. Among these adverse events, haemorrhagic cystitis occurred in 7 patients, infections in 4 (1/4 died), leukopenia, acute myocardial

infarction, anaphylactic reaction, azoospermia, liver toxicity, and severe nausea in 1 patient each. Overall, 16 malignancies were observed in 14 (7%) patients after a median follow up of 25 (IQR:15–26) years. The malignancies were bladder carcinoma (n=4), lung adenocarcinoma (n=3), prostate adenocarcinoma (n=2), carcinoma of unknown primary origin, pancreas adenocarcinoma, t-MDS-AML, lymphoma, colon adenocarcinoma, squamous cell carcinoma and thyroid papillary carcinoma. Among the 113 patients, we were able to question regarding infertility, 67 patients (59%) had children, 22 (19.5%) did not wish to have a child and 24 (21.5%) tried to have a child, but was not able to.

**Conclusions:** Short term serious adverse events occurred in 8% of the patients during CYC treatment. During long term follow-up malignancies occurred in 7% and infertility in 21.5% of the patients. These results underline the need for safer and effective alternatives to CYC for serious organ involvement in BS, similar to that in other vasculitides.

**Disclosure of Interest:** None declared

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AB0704

#### CLINICAL-ANALYTICAL CHARACTERISATION OF 52 DIAGNOSED PATIENTS OF BEHÇET DISEASE WITH INCLUSION OF PAEDIATRIC CASES IN A SPANISH TERTIARY HOSPITAL

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**Background:** Behçet's disease (BD) is a chronic and recurrent inflammatory disease of unknown etiology, classified into polygenic autoinflammatory diseases or variable vessel vasculitis. It has a wide spectrum of symptoms with a very variable range of severity, from mucocutaneous involvement to neurological manifestations, systemic vascular or severe ocular manifestations. About 5.4%–7.6% of Behçet's cases have a paediatric debut.

**Objectives:** To evaluate and compare the clinical and laboratory manifestations of a series of 52 patients, adults and children, diagnosed with BD according to the classification criteria of the International Study Group of BD (ISGBD-1990).

**Methods:** Retrospective cross-sectional observational study, which included 43 adult patients and 9 paediatric patients diagnosed with EB in the Rheumatology Department of a Madrid tertiary hospital. The clinical-analytical characteristics of both groups were evaluated, as well as the correlation of HLA-B51 with the described symptomatology.

**Results:** The mean age at diagnosis of BD was 36.9±11.8 years in adults and 11.4±5.1 years in children. 27.3% of adults and 11.1% of children with BD were male, with oral ulcers close to 90% in both groups. Contrary to what was reported in other series, genital ulcers were more frequent in children (77.8% versus 65.9% of adults), as was the presence of uveitis (44.4% in children compared to 22.7% in adults) and neurological manifestations (22.2% in children versus 6.8% in adults). Joint involvement was also more frequent in children (88.9% versus 52.3% in adults), as well as fever (44% in children versus 14% in adults); being these two manifestations the only parameters that were associated in a statistically significant way with their presentation in the paediatric age in BD. In contrast, skin involvement and vascular manifestations were more frequent in adults. The positivity of HLA-B51 did not correlate statistically with any clinical manifestation, but those who had it had a mean age at diagnosis of 26.5 years compared to a mean of 39 years in those who did not present this genetic marker.

**Conclusions:** Behçet's disease presents with a wide spectrum of clinical manifestations, potentially serious, ranging from skin lesions to neurological or vascular manifestations. In our series, patients diagnosed at paediatric age most frequently had systemic manifestations (fever), arthritis or severe clinical manifestations such as neurological involvement or uveitis. **Limitations:** a small number of paediatric cases included in our study.

**Disclosure of Interest:** None declared

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AB0705

#### LONG-TERM OUTCOMES AND PROGNOSTIC FACTORS ASSOCIATED WITH AORTIC VALVE SURGERY IN PATIENTS WITH TAKAYASU ARTERITIS AND AORTIC VALVEREGURGITATION

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**Background:** Some patients with Takayasu arteritis (TA) have aortic valve (AV) involvement, which can lead to aortic regurgitation (AR). However, data on the long-term outcomes, including survival of TA patients with AR, are lacking. Moreover, previous studies were limited to patients who underwent AV surgery.

**Objectives:** This study aimed to characterise the long-term outcomes and clinical characteristics of TA patients with AR regardless of whether they underwent surgical intervention.

**Methods:** Medical records of patients with TA between January 1995 and December 2015 were retrospectively reviewed. AR was diagnosed using transthoracic echocardiography. Poor outcomes were defined as all-cause death and major adverse cardiac and cerebrovascular events (MACCE). Multivariate analysis was performed to determine the factors affecting poor prognosis in the surgical group.

**Results:** Of the total 105 patients with TA and AR, 41 (39.0%) underwent AV surgery. Among patients who underwent AV surgery, inflammation values (Erythrocyte sedimentation rate, 62.07±31.8 mm/hr vs. 39.16±28.4 mm/hr; C-reactive protein, 3.66±4.1 mg/dL vs. 0.92±1.7 mg/dL), AR degree (3.56±0.7 grade vs. 2.08±1.0 grade), and sinus diameter (37.24±5.7 mm vs. 33.22±4.5 mm) were significantly higher than in those who did not undergo AV surgery. Long-term survival and freedom from MACCE were not significantly different between the groups (10 year survival, 84.3% vs. 79.4%; p=0.827; 10 year event-free survival, 51.8% vs. 71.2%; p=0.29). Twelve of the 41 patients who underwent AV surgery had a poor outcome during follow-up (median, 92.5 months; IQR, 54.5–183.5), and eight of them had a recurrence of AR requiring reoperation. Multivariate Cox analysis revealed that coronary disease [hazard ratio (HR), 4.234; 95% confidence interval (CI), 1.381–12.979; p=0.012], LV dysfunction (HR, 3.387; 95% CI, 1.143–10.042; p=0.028), and impaired renal function (HR, 19.983; 95% CI, 3.480–114.731; p=0.001) were significant risk factors associated with poor outcomes at follow-up (table 1).

**Abstract AB0705 – Table 1.** Multivariate analysis of predictive factors of poor outcomes in patients with Takayasu arteritis who underwent aortic valve surgery.

Variables	HR	95% CI	p-value
Coronary disease*	4.234	1.381–12.979	0.012
LV dysfunction**	3.387	1.143–10.042	0.028
Impaired renal function	19.983	3.480–114.731	0.001

\*coronary disease: severity is more than moderate stenosis

\*\*LV dysfunction: EF <50%

**Conclusions:** In patients with TA with AV involvement, there were no significant differences between long-term survival rate and event-free survival (MACCE) among those who had or had not undergone AV surgery. In the surgical group, the prognosis was poor when coronary artery disease, LV dysfunction, and renal impairment were present at the time of surgery.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.3042

AB0706

#### OCULAR PRESENTATION IN GRANULOMATOSIS WITH POLYANGIITIS (GPA) PATIENTS: RELATION TO AUTOANTIBODIES AND DISEASE ACTIVITY

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**Objectives:** To study the disease characteristics, autoantibodies and activity in granulomatosis with polyangiitis (GPA) patients with ocular manifestations.

**Methods:** 46 GPA patients visiting the ophthalmology clinic were included. Ocular manifestations, clinical and slit lamp examination were performed. The Birmingham Vasculitis Activity Score (BVAS) was recorded. Laboratory investigations were recorded and the antineutrophil cytoplasmic antibody (ANCA) performed.

**Results:** The median age of the patients was 44.5 (32–63) years, 22 males:24 females and disease duration 6.5 (1–16) years. Ocular manifestations were present in all patients; 12 (26.1%) had proptosis, 40 (87%) scleritis/episcleritis with perforation in 3 (6.5%), keratoconjunctivitis in 33 (71.7%) – acute infiltrative stromal keratitis in 11, peripheral ulcerative keratitis in 15 and sclerosing keratitis in 11 patients. Uveitis was present in 11 (23.9%) and retinal changes included vasculitis, exudates and haemorrhage was present in 7 (15.2%). 43 (93.5%) of the patients had blurring of vision and vision loss was present in 2 (4.3%). Glaucoma was present in 4 (8.7%) and hypotony in 2 (4.3%). Involvement was bilateral in 32 (69.6%) patients. Rheumatoid factor was positive in 56.5% and significantly associated with uveitis (p=0.04) while ANA was positive in 45.7% and significantly associated with keratoconjunctivitis (p=0.04). BVAS tended to be higher in those with uveitis (p=0.05).

**Conclusions:** Ocular involvement must be considered in all GPA patients and referral to an experienced ophthalmologist is mandatory for proper management and improved outcome of such a rare systemic disease. ANA and RF positivity may raise suspicion for KC or uveitis respectively. There was a remarkable association between uveitis and disease activity.



**Disclosure of Interest:** None declared  
**DOI:** 10.1136/annrheumdis-2018-eular.5230

**AB0707** **FOUR DISTINCT CLINICAL PHENOTYPES OF VASCULITIS AFFECTING MEDIUM-SIZED ARTERIES**

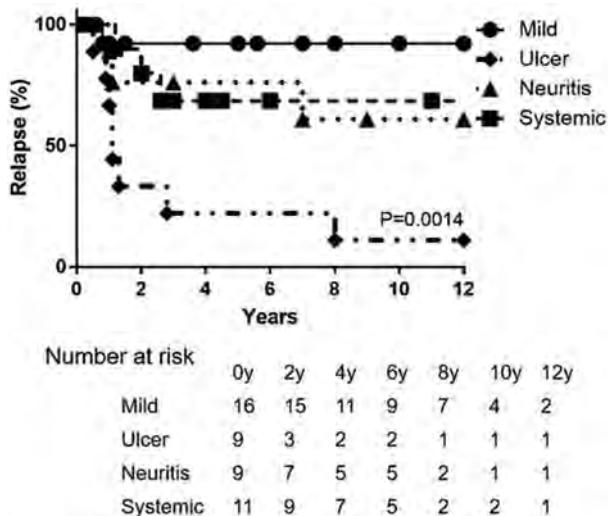
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**Background:** Polyarteritis nodosa (PAN) is a necrotizing arteritis of medium-sized arteries. PAN is divided into systemic and cutaneous PAN (cPAN). cPAN is further classified into mild cPAN or severe cPAN, which presents with ulcer, necrosis, or neuritis. However, it is sometimes difficult to distinguish between severe cPAN and systemic PAN, and their optimal managements are still unclear. The aim of this study is to evaluate clinical characteristics of patients with necrotizing arteritis of medium and small artery.

**Objectives:** To evaluate the clinical characteristics of patients with necrotizing arteritis of medium-sized arteries in order to further clarify the subtypes of PAN.

**Methods:** Forty-nine patients diagnosed with necrotizing arteritis of medium-sized arteries between 2008 and 2017 at our institution were enrolled to this study. Patients with evidence of glomerulonephritis or vasculitis in arterioles, capillaries, or venules, which are hallmarks of small-vessel vasculitis, were excluded. Clinical backgrounds, laboratory findings including inflammatory markers and antineutrophil cytoplasmic antibodies (ANCA), affected organs, treatments, and rates of relapse and death were evaluated.

**Results:** Among 49 patients, 11 patients (22%) presented with systemic vasculitis. Organ involvement was diverse and ranged from central nervous system to cutaneous manifestations. The remaining 38 patients were diagnosed as cPAN and further classified as mild cPAN (16 patients) or severe cPAN (22 patients: ulcer type, 9; neuritis type, 9; both, 4). There was one case of cPAN which resulted in renal damage. The clinical characteristics of mild cPAN included female predominance (87.5%) and younger age (median, 32), and patients tend to have normal inflammatory markers and laboratory findings. Those of systemic PAN included older age (median, 69), higher levels of inflammatory markers, lower levels of serum proteins, and organ damage. Nonspecific elevation of autoantibodies is frequently observed. Particularly, 54.5% of systemic type possessed MPO-ANCA though the titers were significantly lower than those of microscopic polyangiitis, suggesting non-specific elevation of MPO-ANCA in Japanese population. Severe cPAN manifested with intermediate phenotypes, and inflammatory activities were significantly correlated with age ( $p < 0.001$ ). Although the mortality rates were indistinguishable, the relapse rates of cPAN (ulcer type) were significantly higher than those of other types (88.9%, Figure). The mean doses of prednisolone (PSL) used to treat mild cPAN, severe cPAN, and systemic type were 18.5, 38.6, and 39.1 mg/day, respectively. Immunosuppressants were used in 20% of mild cPAN, 90.9% of severe cPAN, and 72.7% of systemic PAN patients. Most patients with cPAN (ulcer type) were initially treated by corticosteroid monotherapy, and immunosuppressive agents were added when they relapsed. Considering its high relapse rate, it might be reasonable to select combination therapy with cyclophosphamide for severe cPAN (ulcer type) as is proposed in nonsystemic vasculitic neuropathy.



Abstract AB0707 – Figure 1

**Conclusions:** The clinical characteristics of mild cPAN, severe cPAN (ulcer type), severe cPAN (neuritis type), and systemic PAN were distinct from each other. Particularly, patients with severe cPAN (ulcer type) had higher relapse rates, thus indicating the importance of combination therapy in this patient cohort.

**Disclosure of Interest:** None declared  
**DOI:** 10.1136/annrheumdis-2018-eular.2247

**AB0708** **THE USE OF TEMPORAL ARTERY BIOPSIES (TAB) IN DIAGNOSIS AND MANAGEMENT OF PATIENTS WITH GIANT CELL ARTERITIS (GCA)- A RE-AUDIT IN RHEUMATOLOGY IN THE BELFAST HEALTH AND SOCIAL CARE TRUST (BHSC)**

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**Background:** Patients should meet at least 3/5 American College of Rheumatology (ACR) criteria for a diagnosis of GCA. British Society of Rheumatology (BSR) guidelines on the management of GCA from 2010 emphasise the importance of early referral for specialist management. TAB should be considered depending on local experience and availability of other imaging modalities. Biopsy should be at least 10 mm in length and ideally done within 14 days of presentation. TABs performed in BHSC over a three-year period were audited in 2014.

**Objectives:** We re-audited the Rheumatology TAB referrals in the BHSC from August 2016 to August 2017 to assess how biopsies influenced the management of patients with GCA in comparison to the previous audit.

**Methods:** Histopathology based LabCentre search detected 36 TABs within the given period. A retrospective audit was carried out with the use of Electronic Care Record and 16 of these patients were Rheumatology based TAB referrals. A proforma was used to aid data collection.

**Results:** Female:Male ratio was 2.2:1, age range was 61–91 with a mean age of 76. 94% of patients presented with headache. Of those patients referred for biopsy, 100% already fulfilled 2 of ACR criteria, compared with only 80% in previous audit. TAB was positive in 25%. In those with a positive biopsy, 75% had an ESR >50. All patients were on steroid treatment at the time of biopsy. In 42% of patients with a negative biopsy, steroids were rapidly reduced. 100% of patients with a positive biopsy continued on steroids. 68% of biopsies were greater than 10 mm compared with 38% in the previous audit. 68% of patients had a TAB within 14 days of commencing on steroids, with 31% having biopsy within 7 days of commencing steroids. 63% of patients developed steroid related complications. In 56% of patients the biopsy result changed patient management.

**Conclusions:** The percentage of appropriate referrals for biopsy (based on the ACR criteria) has improved compared with the previous audit. The length of biopsy improved. 32% of patients were waiting longer than 2 weeks for biopsy but some of these patients presented late to the rheumatology team. Biopsy results changed management in 56% of patients. Areas for consideration include improvement in time to biopsy and biopsy length.

**REFERENCE:**

- [1] BSR and BHPR guidelines for management of giant cell arteritis. Bhaskar Dasgupta, et al. *Rheumatology*, Volume 49, Issue 8, 1 August 2010, Pages 1594–1597. Published: 05 April 2010

**Disclosure of Interest:** None declared  
**DOI:** 10.1136/annrheumdis-2018-eular.7339

**AB0709** **SWITCHING FROM ORIGINATOR INFILIXIMAB TO BIOSIMILAR INFILIXIMAB: EFFICACY AND SAFETY IN A COHORT OF PATIENTS WITH ESTABLISHED BEHÇET'S DISEASE**

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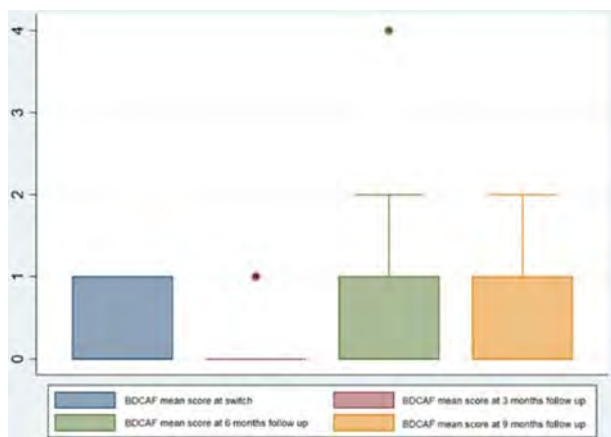
**Background:** Infliximab (IFX) has been proved to be effective in several organ involvement of Behçet's Disease (BD). A recent report<sup>1</sup> describing rapid loss of efficacy of biosimilar IFX after switching from originator IFX suggests the necessity to exercise caution regarding the automatic substitution of originator IFX with biosimilar IFX in patients achieving remission with originator IFX.

**Objectives:** The purpose of the present study was to describe our experience with biosimilar IFX CT-P13 in patients affected with BD, who were switched from originator IFX.

**Methods:** Retrieved data including demographic characteristics, clinical manifestations and previous treatments were collected. All patients met the ISG and/or ICBD classification criteria for Behçet's Disease. In order to evaluate disease activity, the BD Current Activity Form (BDCAF) has been evaluated before starting biosimilar, at three, six and nine months after switching to CT-P13. The occurrence of adverse events was also recorded. Wilcoxon matched-pairs signed-ranks test was carried out to evaluate differences between BDCAF distributions pre-switch and either at three, at six and at nine months after switching.

**Results:** Thirteen caucasian adult BD patients (mean age 39.77±7.46 years) with a mean disease duration of 12.54±4.21 years, underwent IFX treatment at licensed dosage for a period of 117.66±48.01 months. After 106.92±46.37 months of treatment with originator IFX, all of them were switched to CT-P13 biosimilar IFX. At 3 months after switching, none of them had discontinued CT-P13 biosimilar IFX treatment. No significant difference was noticed between BDCAF mean score assessed at switch and 3 months after switching ( $p=0.15$ ). At 6 months follow up, 2/13 patients (15.38%) discontinued CT-P13 biosimilar IFX treatment, both for recurrence of mucocutaneous involvement. One out of 2 patients who discontinued CT-P13 IFX had previously experienced a disease flare under originator IFX therapy, requiring a modification of ongoing therapy. BDCAF mean score assessed before and 6 months after switching were not significantly different ( $p=0.81$ ). Nine months after switching 2 out of the remaining 11 patients were lost at follow up. Once more, no difference was shown between BDCAF mean score assessed at switch and at 9 months follow up ( $p=0.85$ ). No adverse events occurred during the observed period.

Female n(%)	3 (23.08%)
Age at Onset (mean±SD)	27.15±10.02
Clinical Manifestations n(%)	
Uveitis	10 (76.92)
Oral Aphthosis	9 (69.23)
Genital Aphthosis	7 (53.85)
Cutaneous Involvement	7 (53.85)
Concomitant Treatment n(%)*	
Colchicine	5 (38.46)
csDMARDs	4 (30.77)
Corticosteroids	1 (7.69)



Abstract AB0709 – Figure 1

**Conclusions:** Despite the short follow up period, these data suggest that switching BD patients from originator IFX to CT-P13 seems to be effective and safe; only a small percentage of patients experienced relapse of symptoms, whereas a significant modification of BDCAF pre-switch and post-switch was not noticed. Although encouraging, these results need to be confirmed over a longer follow up period and on larger cohorts of patients.

#### REFERENCE:

- [1] Cantini F, et al. (2017) Rapid loss of efficacy of biosimilar infliximab in three patients with Behçet's disease after switching from infliximab originator. *Eur J Rheumatol* 4 (4):288–290

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.3093

#### AB0710 INTERFERON A2A FOR THE TREATMENT OF REFRACTORY BEHÇET'S DISEASE UVEITIS

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**Background:** Behçet's Disease uveitis(BDU) mostly involved bilateral panuveitis and retinal vasculitis, which are very challenging to treat. Interferon alfa-2a (IFN $\alpha$  2a) has been shown to have comparable effectiveness and tolerance profiles for BDU as tumour necrosis factor (TNF) inhibitors in a number of studies with a much lower cost. IFN $\alpha$ -2a treatment combined with corticosteroids without immunosuppressants was common in previous studies. We herein report a cohort of highly refractory BDU patients who experienced recurrence despite aggressive treatment with multiple immunosuppressants at their therapeutic doses.

**Objectives:** To investigate the efficacy and safety of IFN $\alpha$ 2a treatment in combination with corticosteroids and immunosuppressants in patients with refractory BDU.

**Methods:** Clinical records of refractory BDU patients who underwent IFN $\alpha$ 2a treatment in our centre between 2015 and 2017 were retrospectively reviewed. IFN $\alpha$ 2a was initially given 3.0 million IU (MIU) subcutaneously daily for 4 weeks, on the basis of conventional corticosteroid and immunosuppressive therapy. The dosage was gradually tapered down to 3.0 MIU three times or even once per week for maintenance. Primary outcome measure was success rate and changes in ocular relapse rates before and after initiation of IFN- $\alpha$ 2a treatment. Disease activity, corticosteroid- and immunosuppressive agent-sparing effects and potential side effects were considered to be secondary outcomes.

**Results:** A total of 26 patients (23 males and 3 females) were included, with a median disease course of 41 months (range 5–168) before IFN $\alpha$  2a treatment. No major organ involvement except for ocular inflammation was noted. Concomitant medical conditions include chronic hepatitis B virus infection in 2 patients, pulmonary tuberculosis in 1 patient who was treated with antitubercular agents in the meanwhile. Prior to IFN $\alpha$ 2a therapy, the median minimum dosage of corticosteroids was 20 (range 15–45) mg/day prednisone or equivalent, and 17 patients (65.4%) were treated with at least two immunosuppressive agents. Four received short terms of TNF $\alpha$  inhibitor therapy but stopped due to economic burden. Severe side effects related to previous therapies including femoral head necrosis and secondary hypertension were observed in some patients. Treatment success of IFN $\alpha$ 2a was achieved in the majority of the patients (24/26, 92.3%). During a mean follow-up of IFN $\alpha$ 2a therapy for 13.6±6.0 months, the median rate of uveitis relapse decreased notably from 8 per patient-year (range 2–12) to 0 per patient-year (range 0–6) ( $p=0.000008$ ). Oral corticosteroids were successfully decreased in 20 cases (76.9%) and completely discontinued in 2 patients (7.7%), with the median minimum dosage reduced from 20 mg/day (range 15–45) to 15 mg/day (range 0–50) ( $p=0.006221$ ). Moreover, immunosuppressive agents were cut down on types and dosage in 15 (57.7%) and 23 patients (88.5%), respectively, and were totally quitted in 5 cases (19.2%). Slight elevated liver and renal function parameters were detected in one and two patients, respectively. No other severe adverse events occurred. The serum autoantibodies were all negative during treatment with IFN $\alpha$ 2a.

**Conclusions:** IFN $\alpha$ 2a, in combination with corticosteroids and immunosuppressants, was effective and relatively safe in refractory BDU, with a potential steroid- and immunosuppressive agent-sparing effect.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.3453

#### AB0711 TOCILIZUMAB FOR SEVERE/REFRACTORY VASCULAR BEHÇET'S DISEASE

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**Background:** Vascular Behçet's Disease (BD) is a common yet severe complication of BD. Despite aggressive conventional therapy, vascular BD remains as one of the leading causes of morbidity of BD. Tocilizumab (TCZ), an IL-6 receptor antagonist, is an emerging biological agents for neurologic BD or ocular BD, however, the efficacy of TCZ for vascular BD is unknown.

**Objectives:** To elucidate the efficacy and safety of TCZ for severe/refractory vascular BD.

**Methods:** We retrospectively analysed the clinical data of vascular BD patients treated with TCZ in our centre between 2014 and 2017.

**Results:** Seven patients (6 males and 1 female) were enrolled, with a mean age and median course of 32.9±9.1 years old and 72 months (range 54 to 138), respectively. Multiple arterial lesions were documented in all patients, including arterial aneurysm (n=5), stenosis (n=4), occlusion (n=3), and multiple venous thrombosis were documented in two patients. Recurrent aneurysms together with

graft occlusion or endoleak occurred in two out of 3 aneurysms patients who underwent endovascular stent placements. As for concomitant medical conditions, one patient complicated with hepatitis B infection, and three complicated with latent tuberculosis infection and received anti-tuberculosis prophylaxis. Prior to TCZ therapy, all patients experienced disease progression despite high-dose glucocorticosteroid in combination with multiple immunosuppressants. All patients received TCZ, 8 mg/kg iv every 4 weeks for a median of 7 (range 3 to 15) doses, and baseline medium-to-low dose corticosteroid and immunosuppressants. After a median follow-up of 16 months (range 4 to 29), all patients achieved both clinical and serological improvements. Radiologic improvement of artery stenosis was demonstrated in one patient. The condition of one patient with endoleak after the stent placement remained stable without surgical intervention. No newly-onset arterial lesions or venous thrombosis were observed. The median ESR (18 vs 7 mm/h,  $p < 0.05$ ) and hsCRP level (30.6 vs 2.0 mg/L,  $p < 0.05$ ) were also significantly decreased. Furthermore, corticosteroids dose was tapered from 27.1  $\pm$  6.3 mg to 8.9  $\pm$  1.2 mg ( $p < 0.05$ ), and immunosuppressants were tapered in number and dosage in 3 (42.9%) and 3 patients (42.9%), respectively. No serious adverse event or TB reactivation was observed.

**Conclusions:** TCZ, in combination with corticosteroids and immunosuppressants, was effective and well tolerated in severe/refractory vascular BD, with a favourable steroid- and immunosuppressant-sparing effect.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.4152

AB0712

#### ELIGIBILITY OF PATIENTS WITH GIANT CELL ARTERITIS FOR ENTRY INTO A PROSPECTIVE RANDOMISED CONTROLLED TRIAL: A SINGLE-CENTRE EXPERIENCE

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**Background:** The interest in pharmaceutical trials in giant cell arteritis (GCA) is increasing. Trial recruitment may be more challenging in GCA than in other rheumatic diseases because of a higher proportion of elderly patients who are additionally faced with a new diagnosis when being considered for trial participation.

**Objectives:** To analyse the eligibility of newly diagnosed and flaring GCA patients in one centre for randomization in the SIRRESTA trial (ClinicalTrials.gov Identifier, NCT02531633; sirukumab versus placebo), to list reasons for non-randomization, and to compare eligible with non-eligible patients.

**Methods:** All patients with newly diagnosed or relapsing GCA considered for trial participation between August 2016 until trial termination in October 2017 were included. The trial was prematurely terminated by the sponsor based on the decision to discontinue development of sirukumab in autoimmune diseases. Analysis of variance, two-sided Fisher's exact and Pearson's chi-squared tests were applied for calculating statistical significance.

**Abstract AB0712 – Table 1.** Comparison of eligible and non-eligible GCA patients for trial participation

	Total	Eligible for trial	Not eligible for trial	Significance
N	95	12 (13%)	83 (87%)	
Age (SD)	71.1 (8.3) years	65.3 (8.0) years	71.8 (8.5) years	0.008*
Females	61%	75%	59%	0.356
New diagnosis	81%	58%	84%	0.047*
Cranial GCA only	46%	58%	45%	0.537
Cranial and extracranial GCA	35%	25%	36%	0.533
Extracranial GCA only	19%	17%	19%	1.0
Ischaemic events	14%	0%	16%	0.208
Headache	59%	58%	59%	1.0
Jaw claudication	34%	33%	34%	1.0
PMR	62%	83%	59%	0.125
ESR (SD)	71 (33) mm/h	85 (31) mm/h	69 (34) mm/h	0.125
CRP (SD)	90 (69) mg/l	121 (83) mg/l	85 (65) mg/l	0.095

\* $p < 0.05$ , significant; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; GCA, giant cell arteritis; PMR, polymyalgia rheumatica; SD, standard deviation

**Results:** Ninety-five patients were pre-screened. Fifteen of these patients were screened and only 12 of the 95 (13%) pre-screened GCA patients were eligible for randomization based on inclusion and exclusion criteria. The other 83 patients were not eligible for one or more of the following reasons: Concomitant diseases (42%) including second autoimmune disease (11%), malignancy (6%), history of diverticulitis (5%), hepatopathy (2%), renal insufficiency (1%) frailty (6%) and dementia (2%), ischaemic disease (2%); 1 myocardial infarction and 1 severe tongue necrosis), abnormal or inconclusive tests for tuberculosis (5%) and

hepatitis (1%); failure to meet inclusion criteria (41%), including symptoms (12%), histology/imaging (1%), exceedance of maximum glucocorticoid dose (7%), too low ESR and CRP (10%), too long treatment duration (11%); declined consent (29%), before (11%) and after receiving the consent form (18%); too long distance to study centre (5%).

Patients eligible for the trial were younger. They had no ischaemic complications (see table 1). A higher proportion of relapsing GCA patients were included. This subgroup of a larger trial represents only data from one centre. It may not be representative for the findings in other centres or the whole study.

**Conclusions:** Many newly diagnosed or relapsing GCA patients were not eligible for a trial due to concomitant diseases, failing inclusion criteria or declined consent. Eligible patients were younger; and more had relapsing disease.

**Disclosure of Interest:** W. Schmidt Grant/research support from: Roche, GSK (principle investigator), Consultant for: Roche, GSK, Sanofi, Speakers bureau: Roche, K. Hofheinz: None declared, S. Burger Grant/research support from: GSK (sub-investigator), V. Schäfer Grant/research support from: GSK (sub-investigator), A. Juche Grant/research support from: GSK (sub-investigator)

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AB0713

#### INTERFERON-ALPHA FOR THE MANAGEMENT OF LOWER EXTREMITY DEEP VEIN THROMBOSIS IN BEHCET'S SYNDROME: A CASE SERIES

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**Background:** Lower extremity deep vein thrombosis (LEDVT) is a disabling complication of Behçet's syndrome (BS). Relapses are frequent and cause permanent disability due to post-thrombotic syndrome.<sup>1</sup> The management of LEDVT in Behçet's syndrome (BS) constitutes mainly of azathioprine (AZA) and corticosteroids (CS) as first-line agents.<sup>2</sup> Interferon- $\alpha$  (IFN) has been used with good results in the management of eye involvement of BS. However data regarding its efficacy for vascular involvement has been scarce.<sup>3</sup>

**Objectives:** We aimed to evaluate the efficacy and safety of IFN for LEDVT in BS.

**Methods:** All BS pts who had a first episode of acute LEDVT since March 2010 are being prospectively followed with a standard protocol in our dedicated BS centre. Acute LEDVT is confirmed by Doppler ultrasonography (DUS) at initial diagnosis and serial DUS assessment is performed and also repeated in case of clinical suspicion of relapse. Our standard treatment strategy consists of AZA and CSs as first-line treatment in pts with LEDVT. IFN has been used in pts who were refractory or intolerant to this regimen, or who had co-existing eye involvement. Our endpoints for assessing efficacy of IFN have been recanalisation of the index thrombus and prevention of relapses. Presence of recanalisation of thrombosed vein and extension of thrombosis have been assessed at each visit. Recanalisation has been assessed in the transverse plane and defined as the ratio of the vein area at maximum compressibility to the non-compressed vein area. Good recanalisation was defined as a ratio of at least 50%. Adverse events during IFN use were recorded.

**Results:** 33 pts with LEDVT (26 M/7 F) were prospectively followed for a mean of 40.7  $\pm$  13.4 mo. Among these IFN was started in 18/33. In 2 pts IFN was started at the first episode of LEDVT due to co-existing uveitis. Seven pts were treated with IFN due to LEDVT relapses under AZA. In the remaining 9 pts, the reasons for switching from AZA to IFN were adverse events with AZA (n=2), relapse of superficial thrombophlebitis (n=4), leg ulcers due to severe post-thrombotic syndrome (n=2) and eye involvement (n=1). Among 17 pts treated with IFN mainly for vascular involvement during a mean follow-up of 29  $\pm$  20 mo, 3 pts already had good recanalisation when starting IFN. In the remaining 14 pts, 13 (93%) had good recanalisation under IFN. Two pts (11%) experienced relapses. One of the 2 pts who had a relapse had had poor recanalisation despite IFN. In contrast, among the 29 pts treated with AZA, only 13 (45%) had good recanalisation and 13 (45%) pts experienced relapses. Nine of the 13 pts who had relapses under AZA had poor recanalisation. Overall we observed 23 LEDVT relapses in 15 pts. Relapse rates were 29%, 37% and 45% at 6, 12 and 24 months respectively. The only adverse event with interferon-alpha causing drug withdrawal was thyroiditis in 1 patient.

**Conclusions:** Relapse rate for LEDVT in BS is high despite AZA treatment. IFN seems to be a promising agent for preventing LEDVT relapses and achieving good recanalisation, an important predictor of relapse. The small number of pts and the lack of a parallel control group are the limitations of this prospective study.

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AB0714

### MONOCYTES TO LYMPHOCYTES RATIO IS CORRELATED WITH DISEASE ACTIVITY IN BEHÇET'S DISEASE

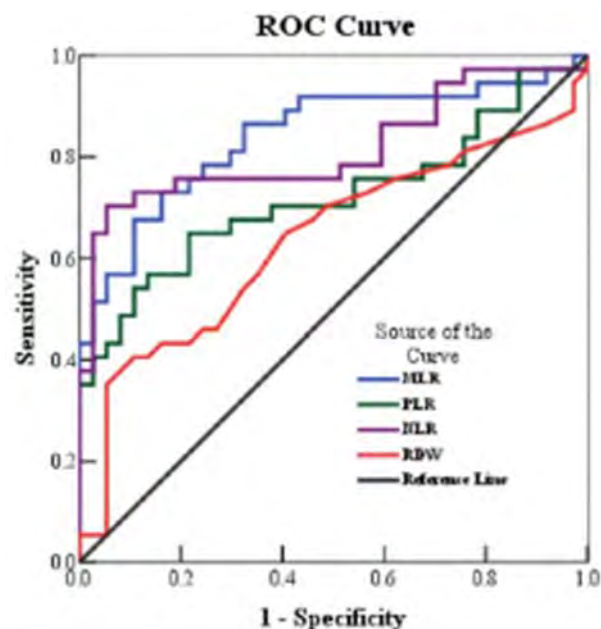
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**Background:** Behçet's disease (BD) is a complex, inflammatory multisystem disorder. Since the lack of universally recognised pathognomonic laboratory test, the diagnosis relies heavily on clinical findings. Currently, the Monocytes to lymphocytes ratio (MLR), Neutrophils to Lymphocytes ratio (NLR), Platelets to Lymphocytes ratio (PLR) and Red blood cell Distribution Width(RDW) have been demonstrated as a assessment of disease severity in many rheumatism diseases. Nevertheless, to our knowledge, only a few studies have investigated NLR, PLR, RDW in patients with BD.

**Objectives:** The aim of this study is to determine MLR, NLR, PLR and RDW in BD and to investigate their relationships with disease activity.

**Methods:** A total of 37 patients with BD fulfilling the criteria of the International Study Group for BD and 37 age and gender-matched healthy controls were enrolled in the study retrospectively. MLR, NLR, PLR, RDW, C-reactive protein (CRP) level and Erythrocyte Sedimentation Rate(ESR) level were evaluated. The correlation between the variables were tested with Pearson correlation. Area Under Curve(AUC) value, sensitivity, specificity, and the optimal cut-off values were determined using Receiver Operating characteristic Curves (ROC). According to the optimal cut off value, BD patients were divided into low-value group (<the optimal cut off value) and high value group ( $\geq$ the optimal cut off value). The patient's clinical characteristics between the two group were compared.

**Results:** The MLR, NLR, PLR and RDW were (0.37 $\pm$ 0.24), (2.91 $\pm$ 1.95), (155.09 $\pm$ 55.08) and (13.83 $\pm$ 1.77) in BD group, while (0.18 $\pm$ 0.04), (1.45 $\pm$ 0.46), (115.66 $\pm$ 28.01) and (13.07 $\pm$ 1.19) in control group, the difference was significant (P all<0.05). MLR, NLR and PLR were all correlated positively with ESR(r=0.363, P<0.05; r=0.611, P<0.05; r=0.496, P<0.05) and CRP(r=0.713, P<0.05; r=0.785, P<0.05; r=0.394, P<0.05). RDW was not correlated with ESR and CRP. ROC curve results showed that the AUC of MLR, NLR, PLR and RDW for BD were 0.841(CI95%: 0.748–0.935), 0.815(CI95%: 0.712–0.918), 0.720(CI95%: 0.699–0.840), 0.635(CI95%: 0.505–0.765), MLR yielded a highest AUC. In addition, the optimal cut off value of MLR for BD was 0.23, with the specificity of 73.0% and sensitivity of 83.8%. In 37 BD patients, 14 belong to low MLR group, 23 belong to high MLR value group. The comparison results show that high MLR value group have higher CRP level and higher incidence of genital ulceration(P<0.05).



Abstract AB0714 – Figure 1

**Conclusions:** MLR was elevated in BD patients as compared to control group, having a close relationship with disease activity.

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AB0715

### GIANT CELL ARTERITIS IS COMORBID WITH TUBERCULOSIS

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**Background:** Giant cell arteritis (GCA) is a medium- and large-vessel vasculitis with an onset age after 50 years, whereas Takayasu arteritis (TA) is a rare large-vessel vasculitis with an onset age younger than 40 years. The association between TA and tuberculosis (TB) was suggested. However, the association between GCA and TB was rarely reported.

**Objectives:** To understand the association between TA and TB

**Methods:** Clinical data between November 1998 and October 2017 at PUMCH, Beijing, China, were retrospectively reviewed. Ninety-one patients diagnosed with GCA were included in the study. Precise clinical data were collected and analysed.

**Results:** A total of 20 patients (22.0%) had a history of active tuberculosis and received anti-tuberculosis therapy. On comparing the clinical features of the patients with TB and those without TB, obvious weight loss (p=0.011), lower percentage of dyslipidemia (p=0.042), higher percentage of anti-phospholipid (p=0.010), and lower white blood cells (p=0.006) were noted in the TB group.

Abstract AB0715 – Table 1. Clinical features and comorbid diseases of the patients with TB and without TB

	GCA with TB n=20 (%)	GCA without TB n=71 (%)	P value
Age (year, diagnosis)	65.10 $\pm$ 8.39	65.38 $\pm$ 7.51	0.886
Scalp tenderness or pain	2 (10)	22 (31.0)	0.060
Tenderness and abnormal pulsation of temporal artery	6 (30)	13 (18.3)	0.256
Visual loss	8 (40)	25 (35.2)	0.694
Hearing loss	3 (15)	20 (28.2)	0.231
Jaw claudication	6 (30)	20 (28.2)	0.873
Arthralgia	11 (55)	36 (50.7)	0.734
GI symptoms	1 (5)	11 (15.5)	0.221
Weight loss	16 (80)	34 (47.9)	<b>0.011</b>

**Conclusions:** This study demonstrated that the percentage of TB history in patients with GCA was higher than that in the general population. The definite association between TB and GCA remains unknown. Hence, further studies are required to elucidate the mechanisms underlying TB in the pathogenesis of GCA. Clinicians should recognise the possibility of comorbid TB in patients with obvious weight loss and relatively lower white blood cell count.

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## Scleroderma, myositis and related syndromes

### AB0716 AN AUTOPSY CASE OF SYSTEMIC SCLEROSIS WITH SEVERE INTESTINAL INVOLVEMENT AND LITERATURE REVIEW

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**Background:** The gastrointestinal tract (GIT) is the second most common internal organ affected by systemic sclerosis (SSc). The rate of SSc patients who develop severe GIT symptoms is lower than 10%, although various degrees of chronic intestinal pseudo-obstruction (CIPO) may occur in as many as 40% of cases (1,2).

**Objectives:** To report an autopsy case of SSc with severe intestinal involvement and review the associated literature.

**Methods:** We will present the clinical features and autopsy findings of a SSc patient and literature concerning Japanese SSc autopsy cases associated with severe intestinal involvement, found *Igaku-chuo* and *Pub-med* on Internet.

**Results:** A 69-year-old Japanese woman was diagnosed with diffuse cutaneous SSc from skin sclerosis, Raynaud's phenomenon, and mild interstitial pneumonia in January 2013. The antinuclear antibody was positive (1:160, speckled pattern), but the specific antibodies, including the anti-RNP, topoisomerase I, and centromere antibodies, were negative. In August 2015, at the age of 71, she was hospitalised for vomiting and abdominal pain. Plain abdominal radiograph showed dilation of the small bowel with air-fluid levels. Abdominal CT revealed large dilation of the small bowel in the absence of any mechanical obstruction. These findings were consistent with CIPO. Her symptoms soon improved by decompression with a long intestinal tube. But she experienced frequent relapse of CIPO. During the third hospitalisation in May 2016, an abdominal CT showed pneumatosis cystoides intestinalis (PCI) and free air in the peritoneal cavity. Medical management failed to control the CIPO. Her general conditions had gradually worsened with weight loss of 10 kg in 3 years. Home parental nutrition was initiated in January 2017. On May 2017, she developed severe pneumonia after vomiting, and her condition gradually deteriorated. She finally succumbed to her illness and an autopsy was performed. The whole alimentary tract except for the duodenum showed a thinning of the lamina propria and atrophy of the smooth muscular layers. Intimal proliferation and narrowing of arterioles were also noted. There was non-specific interstitial pneumonitis in the both lower lobes and diffuse alveolar damage in the both of upper lobes of the lungs. Vasculopathy was also seen in the lungs and heart.

The cases in the literature are summarised in table 1. Vascular damage and/or smooth muscle atrophy were presented in all cases.

**Abstract AB0716 – Table 1.** Autopsy cases of systemic sclerosis associated with severe gastrointestinal symptoms in Japan

Case No.	Publication year	Age of death (yr) / Sex	Time from onset of 1 <sup>st</sup> to death		Cause of death	Comorbidity / Past history	GIT symptoms	Pathological findings of intestine		
			*Raynaud phenomenon	*GIT symptoms				Vascular damage <sup>1)</sup>	Muscle atrophy	Pneumonia
1	1973	49/M	1 yr 6mo	5mo	respiratory failure	Silicosis, IP	Malnutrition	○	○	
2	1976	32/F	12 yr	1y 3mo	general prostration	IP	Severe constipation	○	○	○
3	2000	60/F	5 yr 4mo	4y 5mo	Sepsis	Polymyositis	CIPO, PCI	○	○	○
4	2001	72/F	1 yr	2 weeks	GIT bleeding	Hypertension, Renal failure	Bleeding	○		
5	2002	58/F	3 yr 7mo	2 weeks	Pneumonia	Dermatomyositis, IP	CIPO, PCI	○	○	○
6	2007	71/F	6 mo	2 mo	Septic shock	Renal failure/gastric and lung cancer	CIPO	○		
7	this report	72/F	4 yr	1y 10mo	Pneumonia	IP / breast cancer	CIPO, PCI	○	○	○

M, male; F, female; yr, years; mo, months; GIT, gastrointestinal tract; IP, interstitial pneumonia; CIPO, chronic intestinal pseudo-obstruction; PCI, pneumatosis cystoides intestinalis;

1) Intimal proliferation and narrowing of the small arteries

**Conclusions:** Vasculopathy in SSc involves small vessels, and it precedes fibrosis.<sup>3</sup> The triggering event of vasculopathy is unknown, but the narrowing of intestinal arterioles causing hypoxia might be responsible for dysmotility of GIT.

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### AB0717 RISK ASSOCIATION BETWEEN SCLERODERMA DISEASE CHARACTERISTICS, PERIODONTITIS AND TOOTH LOSS

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**Background:** Systemic Sclerosis (SSc) is a multi-system disorder that can have significant adverse effects upon the health of the mouth.

**Objectives:** The aim of this study was to investigate the associations between the disease characteristics of SSc, periodontal disease (PD) and tooth loss.

**Methods:** Fifty-four patients affected by SSc and 55 non-diseased controls were matched for age and gender. SSc was characterised in subtypes and with the mean duration of disease and the Modified Rodnan Skin Score [mRSS]. Patients were surveyed and examined through the evaluation of the periodontal parameters and the number of teeth.

**Results:** A logistic regression analysis showed that patients with SSc presented a higher number of missing teeth (p=0.001) and a significant median increased odds 2.95 (95% CI 1.26 to 6.84) of PD (defined as clinical attachment loss, CAL) compared to non-diseased controls (6.83, 95% CI 1.94 to 24.36). Moreover, the less values of PD was correlated with mRSS in the total SSc group and with the mean duration of disease in patients with limited SSc (p=0.007), even after adjusting this correlation with the presence of the major organs involvement.

**Conclusions:** This study showed that patients with SSc presented an increased odds of PD and tooth loss compared to non-diseased controls. In SSc patients, the magnitude of PD was strongly associated with the mRSS and with the mean duration of the disease. The clinicians should be aware of the potential systemic health problems related to PD.

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### AB0718 AUTOLOGOUS HEMATOPOIETIC STEM-CELL TRANSPLANTATION IN SEVERE AND REFRACTORY DIFFUSED SYSTEMIC SCLEROSIS. LONG-TERM STUDY IN A SINGLE REFERENCE CENTRE

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**Background:** Pharmacological therapy does not reverse the natural course of systemic sclerosis (SS). Autologous hematopoietic stem-cell transplantation (AH SCT) has been used in refractory autoimmune diseases, including SS. The autologous hematopoietic stem-cell transplantation is based on the ablation of the immunoreactive system with high doses of chemotherapy and a subsequent regeneration of the immune system.

**Objectives:** Study of the efficacy of autologous hematopoietic stem-cell transplantation in a cohort of patients with SS from a referral centre.

**Methods:** Descriptive study of patients with SS (ACR/EULAR<sup>2013</sup> criteria) treated with autologous hematopoietic stem-cell transplantation in a single reference centre between 2002 and 2017. These clinical variables were reviewed

(Raynaud's phenomenon, pulmonary interstitial involvement, digital ulcers, digestive alterations, presence of sclerodermic renal crisis) and activity index variables (modified Rodnan score, HAQ-DI, SHAQ-VAS).

**Results:** Four patients were included (75% women). The median age at the time of the AHSCT was 36.5 years (range 27–51). In all cases, the initial diagnosis was diffuse cutaneous ES, refractory to corticosteroids and at least one DMARD. Prior to autologous hematopoietic stem-cells transplantation, the clinical manifestations presented were a) severe Raynaud's phenomenon (100%) with significant joint and cutaneous involvement; b) digital ulcers (50%); c) interstitial lung disease (50%) and d) sclerodermal renal crisis (25%). In 3 of the cases (75%) the antitopoisomerase antibodies were positive. The conditioning treatment for the autologous hematopoietic stem-cells transplantation was cyclophosphamide at high doses (50 mg/kg x4 days) and anti-thymocyte globulin. In 3 patients (75%) there were slight post-transplant complications (febrile neutropenia, diarrhoea) after a median follow-up of 6.5 years (range 1–15).

The response to AHSCT is summarised in table 1. All patients showed values <1 in the Health Assessment Questionnaire on the Disability Index (HAQ-DI), in 75% with a modified Rodnan skin score (mRSS) lower than 7.

Abstract AB0718 – Table 1

PATIENT	FOLLOW-UP	MODIFIED RODNAN SKIN SCORE PRE-TRASPLANT	MODIFIED RODNAN SKIN SCORE POST TRASPLANT	HAQ-DI POST TRASPLANT	SHAQ-VAS POST TRASPLANT
Patient 1	15 years	Unknown	1/51	0,25	4/13
Patient 2	8 years	Unknown	7/51	0	3/13
Patient 3	5 years	28/51	6/51	0	0/13
Patient 4	1 year	33/51	20/51	0,50	7/13

**Conclusions:** Autologous hematopoietic stem-cells transplantation can be a therapeutic option in refractory and severe SS. These hopeful data must be ratified in larger studies.

**Disclosure of Interest:** None declared

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#### AB0719 CLOSE TEMPORAL ASSOCIATION BETWEEN SILICONE COSMETIC SURGERY AND SYSTEMIC SCLEROSIS ONSET

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**Background:** The pathogenesis of systemic sclerosis (SSc) still remains unclear, however it is increasingly thought to result from interactions between environmental factors and epigenetic features leading to the onset and progression of SSc in genetically susceptible patients.<sup>1</sup> Case reports of women with silicone breast implants who developed SSc have been published, but several case-control series and prospective studies in connective tissue diseases (including SSc) failed to find an increased risk of SSc associated with silicone cosmetic surgery.<sup>2</sup> However, several biases may be recognised in these studies, i.e. heterogeneous cohorts of enrolled patients not selective for SSc, non homogeneous either disease duration or disease stage at study entry. For these reasons the possible effect of silicone implants as immune adjuvants is not clear.<sup>3</sup>

**Objectives:** Retrospective study to find out patients who developed SSc after cosmetic surgery.

**Methods:** The clinical files of 110 female patients with systemic sclerosis were retrospectively evaluated. Among these, four patients showing a history of silicone cosmetic surgery (3.6%) were identified, and clinical data collected.

**Results:** The clinical data of the four patients are below reported. 1. LS 28 year old female who underwent cosmetic breast prosthesis: two years later she complained of Raynaud's phenomenon (RP), and one more year later aggressive diffuse cutaneous SSc, along with anticentromere antibodies (ACA) positivity. 2. PJ 38 year old female who underwent cosmetic breast prosthesis: one year later she experienced RP and one more year later aggressive diffuse cutaneous SSc; antinuclear antibodies were positive with a speckled pattern, but specific SSc-related autoantibodies negative. 3. BS 33 year old female who underwent cosmetic breast prosthesis: two years later she complained of RP and one more year later limited cutaneous SSc with ACA positivity; SSc clinical condition partially improved and its progression stopped after breast prosthesis removal. 4. CM 58 year old female who underwent cosmetic lip silicone application: one year later she complained simultaneous onset of RP and aggressive diffuse cutaneous SSc with anti-Topoisomerase positivity; she died during follow-up.

**Conclusions:** This study reports a prevalence of 3.6% of silicone cosmetic surgery before SSc onset. The close temporal association between silicone implant

and disease development suggests a possible role of silicone in SSc pathogenesis. Specifically addressed clinical studies or big-data studies need to rule out this matter.

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#### AB0720 SYSTEMIC SCLEROSIS AND CANCER DEVELOPMENT. A SINGLE-CENTRE EXPERIENCE

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**Background:** Systemic Sclerosis (SSc) is an autoimmune connective tissue disease with multisystem involvement, and sometimes devastating results. In bibliography there are reports that scleroderma patients present a higher incidence of risk for cancer when compared with the general population. However, different estimates have been reported.

**Objectives:** The purpose of the present study was to evaluate the frequency of cancer development (CD) in a cohort of patients with SSc.

**Methods:** Patients that fulfilled the 2013 American College of Rheumatology/European League Against Rheumatism criteria for SSc and were followed up since 1999, were included. Date of disease onset, disease duration, autoantibodies, age, pulmonary hypertension, comorbidities and the type of CD have all been taken into account, during the period 1991–2016.

**Results:** Seventy-nine SSc patients have been included. 46 with limited (lcSSc) and 33 with diffuse cutaneous Systemic Sclerosis (dcSSc). Six of them, (7.6%) developed different types of cancer. Most of them were adenocarcinomas. More specifically, 2 developed pulmonary adenocarcinoma (1 with lcSSc and 1 with dcSSc), 1 follicular carcinoma of the thyroid gland (lcSSc), 1 colorectal adenocarcinoma (lcSSc), 1 B-cell lymphoma (MALT lymphoma), and 1 prostate adenocarcinoma (dcSSc). Five out of six were female patients. Mean age at the time of cancer diagnosis was 66.8-years-old, while SSc has been diagnosed at the mean age of 49.4 years. Mean time of developing any type of cancer was 15.8 years after SSc diagnosis. The diagnosis of cancer was done the last 20 months. All patients were non-smokers, had gastro-oesophageal reflux disease and pulmonary fibrosis, while 4/6 had also pulmonary hypertension and were under treatment with phosphodiesterase 5 inhibitors and bosentan. Scleroderma patients with CD have been referred to the corresponding oncology clinic for further treatment.

**Conclusions:** The present study on SSc and CDE provides data showing a potential association between the two entities. We found a high frequency of cancer development in patients with SSc (7.6%). Thus, a careful monitoring and screening is required when physicians follow-up scleroderma patients.

**Disclosure of Interest:** None declared

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#### AB0721 TRANSFER OF SYSTEMIC SCLEROSIS AFTER ALLOGENEIC BONE MARROW TRANSPLANTATION

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**Background:** It is accepted that donor-derived immunity is transferred with allogeneic bone marrow transplantation (BMT)<sup>1</sup>.

**Objectives:** To show evidence of the transfer of systemic sclerosis by allogeneic BMT.

**Methods:** In this report we describe a patient with T acute lymphoblastic leukaemia who underwent BMT and developed systemic sclerosis.

**Results:** 34-year-old man in complete remission from a T acute lymphoblastic leukaemia treated with allogeneic BMT from his mother in February of 2012.

First seen in November 2017 for digital ulcers that appeared one year before.

He presented two necrotic ulcers: one on the second finger of the left hand and other on the third finger of the right hand (IMAGE 1). He was admitted to receive intravenous prostaglandins and complete the study.

After the BMT he developed Raynaud's phenomenon and in the examination he only presented facial and corporal telangiectasia, attributed before to chronic graft versus host disease (cGVHD).



The analysis showed ANA 1/640 centromere pattern, anticentromere antibodies, rheumatoid factor (RF) (652 UI/mL) and C3 of 86.4 mg/dL. Previously to the BMT he had negative ANA, but we do not know the rest of the previous autoimmunity. On the videocapillaroscopy we observe an active scleroderma pattern (IMAGE 2–3).

He was diagnosed with systemic sclerosis based on Raynaud’s phenomenon, digital ulcers, anticentromere antibodies and abnormal nailfold capillaries.

He had not familiar background of connective tissue diseases, but his mother presented Raynaud’s phenomenon since she was thirty. So we studied her.

She presented facial telangiectasia, puffy fingers and fingertip pitting scars and the same autoantibodies: ANA 1/320 centromere pattern, anticentromere antibodies, RF (159 UI/mL) and consumption of C3 (74.3 mg/dL) and C4 (7.6). We do not have previous autoimmune studies of her. On the videocapillaroscopy we observed a late scleroderma pattern (IMAGE 4–5).

She was also diagnosed with systemic sclerosis, based on Raynaud’s phenomenon, puffy fingers, fingertip pitting scars and facial telangiectasia, anticentromere antibodies and abnormal nailfold capillaries.

**Conclusions:** Experimental animal studies and human clinical reports have described the transfer of immune-mediated diseases from affected donors to unaffected recipients, because of that the importance of screening these diseases in the donor before a BMT<sup>2</sup>.

To our knowledge, this will be the first described case of transmission of systemic sclerosis by this mechanism. However, other explanations should also be taken into consideration. This include recipient’s own persistent intrathymic lymphocyte population that may produce autoantibodies and autoimmunity in the context of cGVHD. However, this last hypothesis is not supported since there is a familiar background and presence of anticentromere antibodies.

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**AB0722 CAPILLAROSCOPY AND PULMONARY ARTERIAL HYPERTENSION IN SYSTEMIC SCLEROSIS: A SYSTEMATIC REVIEW**

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**Background:** At this very moment, no systematic review evaluating the role of nailfold videocapillaroscopy (NVC), with standardised definitions, in pulmonary arterial hypertension (PAH) has been published.

**Objectives:** To systematically identify and review all available literature evaluating the role of capillaroscopy in PAH in SSc, according to the definitions of the EULAR study group on microcirculation in Rheumatic diseases.

**Methods:** A systematic literature search was performed in Pubmed, EMBASE and Web of Science. All retrieved articles were screened on title, abstract and full-text level. Reference lists and google scholar were additionally searched. Original research papers that documented an association between NVC and PAH (confirmed on right heart catheterization [RHC]) in SSc were included. Subsequently, NVC parameters were subdivided in quantitative (density, dimension, morphology and haemorrhages), semi-quantitative (NVC score) and qualitative assessment (presence of scleroderma pattern, severity of scleroderma pattern and worsening of scleroderma pattern) according to the definitions of the EULAR study group on microcirculation in Rheumatic diseases.

**Results:** The systematic search identified 215 unique search results, of which 171 references were withheld after title screening. Abstract screening resulted in 51 references, only 19 were eligible for full-text review. Finally, 9 references were included in the final analysis after full-text screening (n=7) and bibliographic and google scholar search (n=2) (see table 1).

Regarding cross-sectional studies, density has been evaluated in 5 studies, with no unequivocal results for mean density; avascular score has been unequivocally associated with PAH. Dimension has been evaluated in 4 studies, with no unequivocal results. Morphology has been evaluated in 1 study and has been unequivocally associated with PAH. Haemorrhages and scleroderma pattern has been evaluated in 1 and 2 studies respectively, with no association. Severity of

scleroderma pattern has been evaluated in 3 studies and has been unequivocally associated with PAH.

Regarding longitudinal studies, density (i.e. capillary loss) has been evaluated in 2 studies and has been unequivocally associated with incident PAH. Dimension and haemorrhages have been evaluated in 1 study both, with no association. Morphology has been evaluated in 2 studies, with no unequivocal results. Worsening of scleroderma pattern has been evaluated in 2 studies and has been unequivocally associated with incident PAH.

Capillaroscopic parameter	Significant association	Non-significant association	CONCLUSION
Density	Mean density Numerically correlated with PAH (p<0.0017) (p<0.00022) (p<0.00036) +PAH (p<0.00022)	PAH (p<0.0016)	Regarding cross-sectional studies *Avascular score unequivocally associated with PAH
	Capillary loss Incident PAH (p=0.03) (p=0.00022) (p=0.00022) Worsening PAH (p<0.00022)	N/A	No unequivocal results regarding mean density and PAH
	Avascular score Mean (p<0.0017) +PAH (p=0.00022)	N/A	Regarding longitudinal studies *Capillary loss unequivocally associated with incident PAH
Dimension	Width Mean (p<0.0013)	PAH (p=0.0022), CSR, HA+	Regarding cross-sectional studies *No unequivocal results
	Mean Mean (p<0.0013)	Incident PAH (p=0.03) (p=0.00022) (p=0.00022)	Regarding longitudinal studies *No association
	Morphology Normal N/A	N/A	Regarding cross-sectional studies *Morphology unequivocally associated with PAH
Haemorrhages	Abnormal PAH (p<0.0013) Incident PAH (p<0.00022)	Incident PAH (p=0.03) (p=0.00022) (p=0.00022)	Regarding longitudinal studies *No unequivocal results
	N/A	PAH (p=0.0022) Incident PAH (p=0.03) (p=0.00022) (p=0.00022)	Regarding cross-sectional studies *No association
	N/A	N/A	Regarding longitudinal studies *No association
NVC score	PAH (p<0.0017) +PAH (p=0.00022)	N/A	NVC score unequivocally associated with PAH in cross-sectional studies
	N/A	N/A	NVC score unequivocally associated with PAH in cross-sectional studies
Qualitative assessment	Scleroderma pattern in non-scleroderma patients N/A	PAH (p=0.0022)	No association in cross-sectional studies
	Severity of scleroderma pattern (with/without/none) PAH (p<0.0013) Mean (p<0.0017)	N/A	Severity of scleroderma pattern unequivocally associated with PAH in cross-sectional studies
	Worsening of scleroderma pattern Incident PAH (p<0.03) (p=0.00022) (p=0.00022) Worsening PAH (p=0.03) (p=0.00022) (p=0.00022)	N/A	Worsening of scleroderma pattern unequivocally associated with incident PAH in longitudinal studies

Abstract AB0722 – Figure 1

**Conclusions:** This systematic literature review, on behalf of the EULAR study group on microcirculation in Rheumatic diseases, is the first to investigate unequivocal associations between (incident) PAH and capillaroscopic alterations in a standardised way. Unequivocal associations were found in cross-sectional studies between avascular score, morphology, NVC score and severity of scleroderma pattern and PAH and in longitudinal studies between capillary loss and worsening of scleroderma pattern and incident PAH.

**Disclosure of Interest:** None declared  
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**AB0723 SEROPREVALENCE OF EPSTEIN-BARR VIRUS AND CYTOMEGALOVIRUS IN SYSTEMIC SCLEROSIS PATIENTS: PRELIMINARY RESULTS**

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**Background:** Epstein-Barr Virus (EBV) and cytomegalovirus (CMV) are among the most diffused virus in humans, with prevalence of 90% and 80% respectively in adult immunocompetent population<sup>1,2</sup>. Hypothesis for a role of EBV and CMV in systemic sclerosis pathogenesis was reported<sup>3</sup>.

**Objectives:** To evaluate the prevalence of EBV and CMV in a population of patients affected by SSc. As an exploratory aim, correlations with available clinical variables were evaluated.

**Methods:** A total of 49 patients (44 females and 5 males, age 65.6±9 years, 34 with limited cutaneous involvement and 14 with diffused cutaneous involvement) diagnosed according to the 2013 ACR/EULAR criteria<sup>4</sup> were randomly enrolled at their follow-up visit for a further more detailed analysis. After consent, all participants undergone serological testing for VCA-IgM, VCA-IgG and EBNA-IgG and CMV IgM and IgG, to determine prior or actual EBV and/or CMV infection. All SSc patients undergone also to clinical examination and instrumental evaluations according to SSc clinical standard follow up.

**Results:** Results for EBV seroprevalence were: VCA-IgM negative=43 (87%), positive=4 (8,2%), borderline=2 (4,1%) in all SSc patients. VCA-IgG resulted positive in 48 patients (98%) and EBNA-IgG resulted positive in 40 (81,6%) patients, borderline in 4 (8,2%) and negative in 5 (10,2%) patients. Forty-six (93,9%) patients resulted positive for CMV-IgG and 22 (44,9%) showed detectable CMV IgM. Consequently, EBV and CMV seroprevalence was significantly higher (p=0.01 and p=0.032 respectively) than that calculated in general population (90% and 80% respectively). Interestingly, the presence of higher CMV-IgM correlated linearly with higher pulmonary arterial pressure values (p=0.036) and was different in patients with or without sicca syndrome (p=0.012) and arthralgias

( $p=0.04$ ). Finally, higher CMV-IgG correlated with diffused cutaneous SSc form ( $p=0.023$ ) and nephropathy ( $p=0.036$ ).

**Conclusions:** The seroprevalence of EBV and CMV positivity was found significantly higher in the sample of SSc patients. EBV seropositivity (VCA-IgG) was present nearly in the totality of patients (98%). Of relevance, the high presence of CMV-IgG (93%) and CMV-IgM (44.9%) in SSc patients: the last correlated linearly with higher pulmonary arterial pressure values. EBV and CMV infections, among the supposed triggers in several autoimmune diseases, might also play a role in SSc patients, at least with progressive disease.

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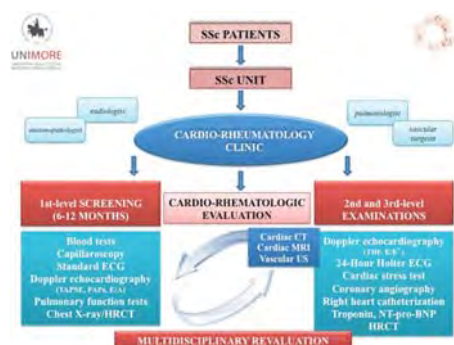
### AB0724 CARDIO-PULMONARY DISEASE MANAGEMENT IN PATIENTS WITH SYSTEMIC SCLEROSIS: CARDIO-RHEUMATOLOGY CLINIC AND PATIENT CARE STANDARDISATION PROPOSAL

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**Background:** Systemic sclerosis (SSc) is a chronic connective tissue disease characterised by endothelial dysfunction, dysregulation of fibroblasts with excessive fibrosis of the skin and internal organs and autoimmune abnormalities. Cardio-pulmonary manifestations are common in SSc and their detection in the early stage of the disease as well as their careful follow-up are mandatory in order to counteract their impact on the overall disease outcome. Despite the need of establishing a proper methodology, literature provides few reports about this issue.

**Objectives:** To evaluate the activity of our Cardio-Rheumatology Clinic in order to optimise diagnostic management of cardio-pulmonary disease in SSc patients.

**Methods:** We retrospectively analysed data from 350 consecutive SSc patients referred to our University-based Rheumatology Centre and SSc Unit (F/M 308/42; lc/dcSSc 45/305; mean age 50.8±14.7 years; mean disease duration 10.9±7.0 years). All patients underwent general and cardio-pulmonary assessment, in particular they were evaluated in the Cardio-Rheumatology Clinic. The following parameters were considered: physical examination; past and current drugs; blood tests, in particular Erythrocyte sedimentation rate-ESR, C-reactive protein-CRP, CPK enzymes, troponin, NT-pro-BNP, d-dimer, serum autoantibodies, 25-OH-vitamin D; capillaroscopy; pulmonary function tests; high resolution scan of the lungs (HRCT); standard electrocardiogram (ECG) and 24 hour Holter ECG monitoring; Doppler echocardiography; cardiac stress test; coronary angiography and right heart catheterization (RHC); cardiac MRI and CT; vascular ultrasound (intima-media-thickness, carotid-femoral and brachial-ankle pulse-wave-velocity). The clinicians decided to perform these examinations according to clinical picture and current methodologies.



Abstract AB0724 – Figure 1

**Results:** In the last 12 months we assessed 300 patients with 1st-level screening (cardio-rheumatologic evaluation, standard ECG, Doppler echocardiography, pulmonary function tests, thoracic imaging). Among 2nd-level, 30 procedures of 24 hour Holter ECG and 15 RHC tests were performed. Cardiac MRI, coronary CT angiography and vascular ultrasound were assessed, when requested, as 3rd-level examinations (30 procedures). After 1 year we observed a mean time of 10±5 days between request and clinical cardio-rheumatologic evaluation, 20±12 days to perform 1st-level screening, 25±15 days to execute the 2nd-level examinations. Figure-1 shows Cardio-Rheumatology algorithm for the management of SSc cardio-pulmonary disease.

**Conclusions:** The activity of our Cardio-Rheumatology Clinic optimises the cardio-pulmonary SSc assessment, determining an early detection of these harmful complications with reduced waiting times which are critical issues. Screening algorithms are useful to stratify the risk and to establish the most appropriate diagnostic-therapeutic protocols, improving outcome of scleroderma patients. The development of a cardio-pulmonary risk score and the standardisation of a patient care approach, according to international quality indexes, could represent further tools to optimise SSc management.

**Disclosure of Interest:** None declared

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### AB0725 SEVERE DYSPHAGIA “POOR PROGNOSTIC MARKER” IN IDIOPATHIC INFLAMMATORY MYOPATHIES

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**Background:** In Idiopathic Inflammatory Myopathies (MII), 18%–20% of patients have dysphagia.

**Objectives:** To evaluate the frequency of dysphagia in patients with MII, association with other manifestations of the disease, treatment and evolution.

To evaluate clinical characteristics and evolution of severe dysphagia.

To compare clinical characteristics and evolution of mild-moderate versus severe dysphagia.

**Methods:** Retrospective, observational study. Patients with a diagnosis of MII were included according to modified classification criteria of Bohan and Peter. Demographic, clinical and complementary studies were recorded. Serious dysphagia was considered: contraindication of oral feeding. Descriptive statistics were performed. Chi2 test, Student's test or Mann Whitney as appropriate.

**Results:** We included 91 of 106 patients evaluated from 1992 to 2017: 76% female, mean age at diagnosis 48±14 years. 53% presented dysphagia: mild/moderate 62.5% (30/48 pts), severe 37.5% (18/48). Idiopathic dermatomyositis was the most frequent MII in these patients (71%). In patients with dysphagia, proximal muscle weakness was 90%, weakness of neck muscles 45%, weakness of respiratory muscles 27%.

A significant association was found between dysphagia and weakness of respiratory muscles, weak neck muscles, glucocorticoid pulses, gammaglobulin, grave infections and death. (Data not shown in the summary).

In patients with **severe dysphagia**, we observed a significant association with the requirement for mechanical ventilation, hospitalisation in an intensive care unit, serious infections and death (table 1).

When comparing mild-moderate dysphagia vs severe dysphagia, a statistically significant association was found with neck muscles weakness, respiratory muscle weakness, glucocorticoid pulses, gamma globulin use, requirement for mechanical ventilation, hospitalisation in an intensive care unit, severe infections and mortality (table 2).

Abstract AB0725 – Table 1

	Severe dysphagia (SI) 18/91	Severe dysphagia (NO) 72/91	p	OR	IC 95%
Weakness of respiratory muscles	8/18	6/63	0 00 054	7,6	2,1–26,6
Weak neck muscles	8/16	6/63	0 00 129	8	2,5–26
Glucocorticoid pulses	12/18	8/69	<0,0001	15	4,4–51,9
Gammaglobulin	10/18	7/72	<0,0008	11,60	0,8–10
Intensive therapy unit	7/18	8/72	0,0046	5	1,5–16,8
Mechanical respiratory assistance	6/18	5/72	0002	6,70	1,7–25
Grave Infections	10/17	11/66	0,0003	7	2,2–22,8
Death	12/18	9/72	<0,0001	14	4,2–46,6

Abstract AB0725 – Table 2

	Dysphagia (mild-moderate) 30/48	Dysphagia (severe) 18/48	p	OR	IC 95%
Weakness of respiratory muscles	4/30	9/18	0.005	6,5	1,6–26
Weak neck muscles	9/30	13/18	0.004	6	1,6–22
Glucocorticoid pulses	5/28	13/18	0,0002	12	2,9–49
Gammaglobulin	3/30	10/18	0,0005	10	2,4–51
Intensive therapy unit	1/30	7/18	0,0013	18	2–167
Mechanical respiratory assistance	1/30	6/18	0.004	14,50	1,5–133
Grave Infections	5/27	10/18	0.009	5,50	1,4–21
Death	3/30	13/18	<0.001	23,5	4,8–113

**Conclusions:** Fifty-three percent of patients with MII had dysphagia at some point during their evolution. Severe dysphagia was associated with parameters of disease severity, poor prognosis and increased mortality.

**Disclosure of Interest:** None declared

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#### AB0726 INTERSTITIAL LUNG DISEASE IN SCLERODERMA PATIENTS – A PORTUGUESE PORTRAIT

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**Background:** Systemic sclerosis (SSc) is characterised by inflammation and fibrosis of skin and internal organs. Lung involvement, particularly interstitial lung disease (ILD), is a major cause of morbidity and a leading cause of SSc-related mortality.

**Objectives:** To characterise SSc patients (pts) with ILD and identify possible predictors for its development.

**Methods:** A multicenter prospective cohort study using the Rheumatic Diseases Portuguese Register/Scleroderma database was performed. All patients fulfilled ACR/EULAR<sup>2013</sup> classification criteria for SSc. Demographic and clinical data until 15th January 2018 were collected as well as pulmonary function tests (PFTs), including diffusing capacity of carbon monoxide (DLCO). ILD was defined by fibrosis in chest x-ray and/or high-resolution computed tomography (HRCT) scan. Disease progression was defined by an increase from baseline in the area of involved parenchyma and/or development of honeycombing in pts with previous ground glass imaging and/or reduction of more than 15% in DLCO or 10% in forced vital capacity in pts with established ILD. We performed a descriptive analysis of SSc cohort. Logistic regression analysis was used to identify variables independently associated with ILD.

**Results:** A total of 146 pts were included, 88.4% female, with a mean age of 61.5 ± 14.4 years (yrs) and mean disease duration of 14.3 ± 11.3 years. Limited cutaneous SSc (lSSc) was present in 66.4%, diffuse cutaneous SSc (dSSc) in 24%, overlap syndrome in 6.8% and very early diagnosis SSc in 1.4% (information missing in 2pts).

In our cohort, 42 pts (28.8%) presented ILD after 17.5 ± 14.1 years of disease duration, 83.5% of them were female; 45.2% had dSSc and 42.9% lSSc. Anti-Scl70 antibody occurred in 23 pts, anticomere antibody (ACA) in 8, anti-Pm/Scl in 2, anti-RNA polymerase I in 2, anti-RNA polymerase III in 1 and anti-U3RNP in 1. Ten pts had current/previous smoking habits. Nailfold capillaroscopy (NCP) was available in 23 out of 42 pts and 21 had a SSc pattern (5 early, 6 active and 10 late). Table 1 shows differences between pts with and without ILD.

In multivariate analysis, anti-Scl70 (OR:3.7 95% CI 1.3–10.5) and current/previous digital ulcers (OR:2.2 95% CI 1.9–5.3) were associated with ILD development. ACA had a protective effect (OR:0.3 95% CI 0.1–0.8).

Mycophenolate mofetil was used in 11pts, with 5 of them having previous treatment with cyclophosphamide (CYC; 4 as induction drug). Four pts received azathioprine, half of them as maintenance therapy after induction with CYC. Two pts received rituximab and 1 nintedanib.

During follow-up, disease progression occurred in 17 pts (40.1%), 3 of them under immunosuppression.

Death occurred in 7 pts with ILD, 5 of them with direct relation to lung disease, 14.4 years after the diagnosis.

Table 1 Differences between patients with and without ILD (total=146)

**Conclusions:** This was the first multicentre Portuguese study about ILD in SSc. In our cohort, ILD occurred in about 30% of the pts and was associated with a mortality rate of 3.4%.

Our results confirm that some variables are associated with pulmonary disease development, and thus its identification may help the clinician to detect pts with a higher risk of early ILD.

**Disclosure of Interest:** None declared

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#### AB0727 ANTIBODY PROFILE AND SYSTEMIC SCLEROSIS CLINICAL FEATURES – MYTH OR REALITY?

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**Background:** Antinuclear antibodies(ANA) occur in 80%–98% of systemic sclerosis(SSc) patients (pts), with different specificities. Anticentromere antibody (ACA), antitopoisomerase I(anti-Scl70) and anti-RNA polymerase III are the commonest and are included in the new SSc ACR/EULAR classification criteria. According to literature, ANA specificities are associated with clinical features of the disease.

**Objectives:** Evaluate the relationship between antibody profile and clinical manifestations in a cohort of SSc pts.

**Methods:** We conducted a retrospective analysis of SSc pts followed in our department. Demographic data, disease duration, ANA specificities and clinical manifestations were collected. Mann-Whitney U test and Chi-square were used for comparisons between pts who tested positive or negative for different ANA specificities.

**Results:** In total, 117 pts were included, 91.5% female with mean age of 60.7 ± 15.2 years and mean disease duration of 11.9 ± 10.7 years. Seventy-five pts (64.1%) had limited cutaneous SSc(lcSSc), 26 (22.2%) diffuse cutaneous SSc (dcSSc), 8 (6.8%) very early diagnosis SSc, 7 (6%) overlap syndromes and 1 (0.9%) SSc sine scleroderma. Most (92.3%) were ANA positive, with 53.8% having ACA, 26.5% anti-Scl70, 3.4% anti-U3 RNP, 2.6% anti-U1 RNP, 1.7% anti-PM/Scl and 0.9% anti-RNA polymerase III and 0.9% anti-Th/To.

Positivity for ACA was significantly associated with female gender (OR: 1.18 95% CI 1.04–1.34) and lcSSc phenotype (OR: 9.43 95% CI 3.86–23.03). ACA was also associated with older age at disease onset (p=0.008). Vascular involvement, defined by current/previous digital ulcers and/or telangiectasias, was also more prevalent in this group (OR: 5.59 95% CI 2.47–12.66). Pulmonary arterial hypertension (group 1 ERS/<sup>ECS 2013</sup> classification) was present in 6.3% of pts with ACA. Oesophageal involvement was the second commonest manifestation and occurred in 57.1% of pts with ACA, although this association was not statistically significant. ACA seemed to have a protective effect for interstitial lung disease (ILD) (OR: 0.027 95% CI 0.004–0.213).

Anti-Scl70 positivity was associated with dcSSc phenotype (OR: 9.29 95% CI 3.26–26.5) and ILD (OR: 10.39 95% CI 3.86–27.92).

From the 4 pts with anti-U3 RNP, 3 had dcSSc subtype. The only patient with renal manifestations was anti-U3 RNP positive and had rapidly progressive cutaneous involvement.

Abstract AB0727 – Table 1. Clinical features according to auto-antibody positivity

Antibody	ACA (n=63)	Anti-Scl70 (n=31)	AntiU3-RNP (n=4)	AntiU1-RNP (n=3)	Anti-PM/Scl (n=2)	Anti-RNA pol 3 (n=1)	Anti-Th/To (n=1)
Onset age mean±SD (years)	57.1±12.9	52±20.3	49.4±9.2	48.7±10.4	42.5±14.8	46	26
Female	98.4%	50.3%	75%	66.7%	50%	0%	100%
lcSSc	95.7%	38.7%	25%	0%	50%	100%	100%
dcSSc	0%	54.8%	75%	33.3%	0%	0%	0%
Overlap	1.6%	6.4%	0%	66.7%	50%	0%	0%
Vascular involvement	79.4%	51.6%	25%	33.3%	0%	0%	100%
PAH	6.3%	3.2%	0%	0%	0%	0%	0%
Lung involvement	1.6%	45.2%	25%	0%	50%	0%	0%
Cardiac involvement	0%	3.2%	0%	0%	0%	0%	0%
Oesophageal involvement	57.1%	45.2%	0%	0%	0%	100%	0
Faecal incontinence	4.8%	0%	25%	0%	0%	0%	0%
Renal involvement	0%	0%	25%	0%	0%	0%	0%
MS involvement	12.7%	12.9%	25%	66.7%	50%	0%	0%

Legend: ACA – anticentromere antibody; anti-Scl70 – antitopoisomerase I; lcSSc – limited cutaneous systemic sclerosis; dcSSc – diffuse cutaneous systemic sclerosis; PAH – pulmonary arterial hypertension; GI – gastro-intestinal; MS – muscle-skeletal



Anti-U1RNP was associated with muscle-skeletal manifestations (OR: 10.7 95% CI 0.92–20.44) and with overlap syndromes (OR: 15.2 95% CI 4.7–29.1). Pts with anti-Th/To and anti-RNA-polymerase III had lcSSc subtype. Vascular manifestations, oesophageal involvement and calcinosis cutis were the main manifestations, respectively. Table 1 shows detailed clinical manifestations and antibody profile.

**Conclusions:** In our cohort, ACA and anti-Scl70 were the commonest antibodies and were associated with lcSSc and dsSSc phenotype, respectively. ACA positivity conferred a higher risk of vascular disease and had a protective effect for ILD, while anti-Scl70 was associated with ILD.

Pts with anti-U1 RNP and anti-PM/ScI had mainly muscle-skeletal manifestations. This study confirms an association between immunological profile and clinical manifestations, reinforcing the importance of antibody profile and raising awareness for possible disease complications. Larger national studies would be desirable, specially for a better understanding of major organ involvement associated with least common antibodies.

**Disclosure of Interest:** None declared

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**AB0728 NAILFOLD CAPILLAROSCOPY IN SYSTEMIC SCLEROSIS – SIX YEARS IN REVIEW**

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**Background:** Microvascular dysfunction is a dynamic process that is crucial in systemic sclerosis (SSc) pathogenesis. Nailfold capillaroscopy (NCP) is a rapid, non-invasive exam that illustrates the early capillary changes in SSc and monitor their evolution. It is extremely useful in clinical practice and has been recognised in 2013 ACR/EULAR classification criteria for SSc.

**Objectives:** Evaluate the prevalence and evolution of NCP scleroderma pattern in SSc patients and analyse possible associations with disease-phenotype.

**Methods:** NCP of SSc patients followed in our centre were reviewed; clinical and demographic features were collected. A descriptive analysis was performed and nonparametric tests compared patients with and without SSc pattern.

**Results:** In total, 70 out of 117 SSc patients had at least 1 NCP available during the last 6 years. Most of these patients (62.9%) had limited cutaneous SSc, 21.4% diffuse cutaneous SSc, 11.4% very early diagnosis SSc and 4.3% overlap syndromes; mean disease duration was 10.7±9.6 years.

At the moment of the first NCP, 46 patients (39.4%) had a scleroderma pattern, 12 (10.3%) had non-specific(NS) NCP abnormalities and 12 had a normal NCP. During the 6 years follow-up, NCP changed in 5 patients as illustrated in figure 1. However, none had concomitant development/worsening of other clinical manifestations.

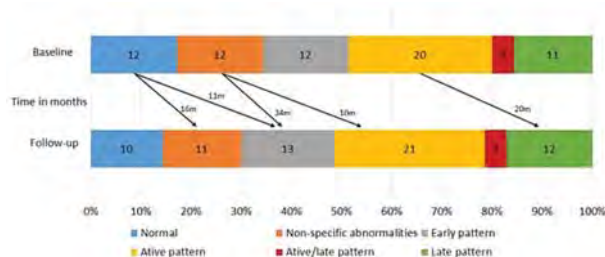
At the end of the follow-up, 49 (70%) patients had a NCP scleroderma pattern. Early pattern was present in 13 (26.5%) patients, active pattern in 21 (42.9%), active/late pattern in 3 (6.1%) and late pattern in 12 (24.5%).

When comparing patients with and without scleroderma specific patterns (table 1), the presence of scleroderma pattern was associated with the presence of current/previous digital ulcers (OR 1.49 95% CI 1.17–1.92). However, this difference was not confirmed between the different scleroderma patterns.

Regarding, major organ involvement, although there were no statistical differences between both groups, patients with scleroderma pattern had a higher prevalence of oesophageal involvement.

**Abstract AB0728 – Table 1.** Comparison between patients with and without scleroderma pattern

NCP pattern	Non-scleroderma		Scleroderma				p
	Normal (n=10)	Non-specific abnormalities (n=11)	Early (n=13)	Active (n=21)	Active/Late (n=3)	Late (n=12)	
Female	100%	72.7%	100%	85.7%	66.7%	91.7%	0.623
Age	55.3 ±16.2	66.7±5.7	58.2 ±20.7	53.8 ±15.8	44.9 ±18.2	64.9 ±9.3	0.219
Disease duration (years)	9.4±6.6	8.3±4.4	7.6±6	10.2 ±7.1	4.2 ±0.6	19.6 ±16.6	0.947
Diffuse cutaneous disease	10%	27.3%	7.7%	14.3%	33.3%	33.3%	0.689
Digital ulcers	10%	0%	30.8%	28.6%	33.3%	33.3%	<b>0.021</b>
Pulmonary arterial hypertension	0%	0%	0%	0%	0%	0%	NA
Interstitial lung disease	10%	18.2%	7.7%	9.5%	33.3%	25%	0.948
Oesophageal involvement	40%	45.4%	46.2%	71.4%	66.7%	50%	0.148
Anticentromere +	50%	45.4%	69.2%	57.1%	0%	58.3%	0.557
Antitopoisomerase I +	20%	27.3%	15.4%	19%	33.3%	33.3%	0.971



**Abstract AB0728 – Figure 1.** Progression of nailfold capillaroscopy alterations during follow-up

**Conclusions:** This study demonstrates how NCP can illustrate the dynamic vascular damage in SSc. In our data, a NCP scleroderma pattern was significantly associated with a higher number of digital ulcers and these patients had a higher percentage of oesophageal involvement.

In daily clinical practice, NCP is useful not only for corroborating SSc diagnosis, but also for monitoring endothelial injury and potential macrovascular/systemic damage. Although our sample is too small to demonstrate possible associations between specific NCP alterations and internal organ involvement, some studies have already identify NCP patterns as predictive factors for organ damage.

**Disclosure of Interest:** None declared

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**AB0729 QUALITY OF LIFE ASSESSMENT IN SYSTEMIC SCLEROSIS PATIENTS TREATED WITH AUTOLOGOUS STEM CELL TRANSPLANTATION: A LONGITUDINAL STUDY**

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**Background:** Autologous Hematopoietic Stem Cell Transplantation (AHSCT) has been explored as a therapeutic option for patients with systemic sclerosis (SSc) that do not respond to conventional treatment.

**Objectives:** To investigate changes in quality of life of severe and rapidly progressive SSc patients treated with AHSCT.

**Methods:** This is a longitudinal and comparative study. Patients were evaluated before (n=27), and at 6 (n=27) and 12 months (n=21) after AHSCT. The Generic Questionnaire for Evaluation of Quality of Life Medical Outcomes Study 36 Item Short-Form Health Survey (SF-36) was applied individually, face-to-face, under patient written consent. This questionnaire evaluates eight domains: physical functioning (PF), role-physical (RP), bodily pain (BP), general health (GH), social functioning (SF), vitality (VT), role-emotional (RE) and mental health (MH). Results were transformed into a 0–100 scale, where zero corresponds to a worse health condition and 100 to the best possible score, and submitted to statistical analysis. Significance was defined as p<0.05.

**Results:** Most participants were females (n=24), with mean age of 33 years (standard deviation, SD=10.33) and mean time from diagnosis of 34.4 months (SD=34.89). Before AHSCT, the mostly impaired aspects were: PF (mean=8.33, SD=18.34), and RP (mean=38.52, SD=21.56), while MH (mean=61.63, SD=15.46) and SF (mean=56.87, SD=27.17) were mostly preserved. At 6 and 12 months post-AHSCT, there was significant improvement of the SF-36 scores in the following domains: PF (6 months, p<0.01, 12 months, p<0.01); RP (6 months, p<0.01, 12 months, p<0.01); BP (6 months, p<0.01, 12 months, p<0.01); GH (6 months, p<0.01, 12 months, p=0.02); VT (6 months, p<0.01, 12 months, p<0.01); MH (6 months, p<0.01, 12 months, p<0.01). The SF domain showed significant increase only at 12 months (p=0.02). The only domain in which there was no significant change was RE.

**Conclusions:** Increases in the physical components of quality of life are more evident in the initial periods that follow AHSCT, while improvements in mental state, which are also associated with social aspects, are detected on longer follow-up. These data reinforce the relevance of AHSCT upon patient quality of life, signalling the importance of psychotherapeutic evaluations and follow-up.

**Disclosure of Interest:** None declared

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**AB0730** **COMPARISON OF A SINGLE-CENTRE IDIOPATHIC INFLAMMATORY MYOPATHY COHORT FROM ARGENTINA WITH THE EUROMYOSITIS INTERNATIONAL REGISTRY**

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**Background:** The idiopathic inflammatory myopathies (IIM) are rare systemic autoimmune diseases that affect the muscle and other organs. Traditionally, IIM encompasses polymyositis (PM) and dermatomyositis (DM), but progressively inclusion body myositis (IBM), Immune-mediated necrotising myopathy (IMNM), the antisynthetase syndrome (ASS) and connective tissue diseases-over myositis (CTD-OM) have been recognised within the IIM spectrum

**Objectives:** To compare the clinical characteristics and treatment in a IIM cohort from an Argentinian university hospital with the international IIM cohort EUROMYOSITIS

**Methods:** Descriptive, retrospective study. IIM patients defined by expert opinion followed in our centre between October 2007 and October 2017 were included. ASS was defined by the presence of arthritis, raynaud's phenomenon, mechanic hands, elevated CK, muscle weakness, interstitial lung disease and/or presence of antisynthetase antibodies and, as in EUROMYOSITIS, patients with IIM with positive antisynthetase antibodies were reclassified as ASS. CTD-OM was defined as patients with IIM fulfilling classification criteria for other CTD. Demographic data, accumulated clinical features, time interval between disease onset and diagnosis, IIM subtype, treatment and presence of neoplasm were evaluated.

Ethnicity was defined using the same classification as in EUROMYOSITIS

**Results:** 58 patients were included: DM 24, PM 4, ASS 10, CTD-OM 20. 89.6% Hispanic, mean age 48.4±15.2 years, median time interval between disease onset and diagnosis 5 months (IQR 2–11 months), been higher in AAS (8.5 months, IQR 1.5–18.2 months). 6.89% (4/58) patients presented associated neoplasm, 3 with DM and 1 with CTD-OM. Table 1 shows the demographic and clinical features of our IIM cohort and EUROMYOSITIS. Table 2 shows treatments received in our cohort and EUROMYOSITIS.

**Abstract AB0730 – Table 1.** Demographic and clinical features

	DM		PM		ASS		CTD-OM	
	HCJSM (n=24)	EUROMYO (n=949)	HCJSM (n=4)	EUROMYO (n=13)	HCJSM (n=10)	EUROMYO (n=512)	HCJSM (n=20)	EUROMYO (n=358)
Gender % (M/F)	20 (71)/20 (29)	36 (38)/56 (59)	2 (50)/2 (50)	4 (31)/7 (54)	4 (40)/6 (60)	20 (39)/31 (61)	10 (50)/10 (50)	21 (59)/15 (41)
Mean Age at Onset, years (SD)	48.7 (15.20)	49 (16)	41 (13.36)	49 (15)	48.5 (13.80)	48 (19)	45.8 (15.90)	49 (19)
Mean Age at Diagnosis, years (SD)	46.7 (15.10)	47 (16)	44 (15.20)	52 (19)	43.3 (13.34)	48 (19)	42.3 (15.53)	48 (19)
Median interval between onset and diagnosis, months (IQR)	4 (1-8)	5 (2-11)	5.5 (2-6.5)	9 (3-19)	5.5 (1.5-18.2)	7 (3-17)	6 (2-25)	11 (4-20)
Muscle weakness (%)	79 (33)	72	100	100	100	90	100	84
Raynoud's phenomenon (%)	58 (24)	19	0	0	50	44	40	52
Raynaud's phenomenon (%)	33.3	26	0	25	50	53	60	60
Pericardial effusion (%)	20 (8)	62	0	0	10	19	10	33
Arthritis (%)	25 (10)	28	100	25	60	50	60	43
Antisynthetase (%)	0	0	0	0	20	36	0	16
Calcinosis (%)	20 (8)	7	0	0	0	3	0	13
Interstitial Lung Disease (%)	12.5	13	0	0	10	3	0	18
Cardiac involvement (%)	16.6	21	0	0	20	11	10	22

**Conclusions:** DM was the most frequent IIM subtype in both cohorts. In our group, CTD-OM was second and ASS was third.

Muscle weakness was found less frequently in our DM and AAS than reported in EUROMYOSITIS. However, calcinosis was more frequent. This could be explained by our mostly Hispanic population and/or by frequent Systemic Sclerosis overlap in our patients. It's important to remark that the ethnic variety defined as Hispanic in EUROMYOSITIS has a complex composition in Latin America, due to interbreeding.

No difference was found in terms of most frequent treatments between both cohorts. However, use of IVIg was more frequent in our patients.

To our knowledge, this is the first comparative report of an argentinian single-centre IIM cohort and an international multi-centre cohort

**Disclosure of Interest:** None declared

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**Abstract AB0730 – Table 2.** Treatment

	DM		PM		ASS		CTD-OM	
	HCJSM (n=24)	EUROMYO (n=949)	HCJSM (n=4)	EUROMYO (n=813)	HCJSM (n=10)	EUROMYO (n=512)	HCJSM (n=20)	EUROMYO (n=358)
Steroids	95	98	50	100	90	98	85	96
Hydroxichloroquine	50	37	25	11	40	16	40	29
Methotrexate	37.5	69	50	76	20	60	25	72
Leflunomide	0	0	0	3	20	3	5	4
Azathioprine	33.3	44	25	52	60	60	35	51
Mycophenolate	0	20	25	20	30	31	10	29
Cyclophosphamide	8.33	15	0	14	20	39	10	18
IVIg	29.16	11	0	13	20	7	5	7

**AB0731** **TREATMENT ALGORITHMS FOR SYSTEMIC SCLEROSIS ACCORDING TO EXPERTS**

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**Background:** Treatment for many aspects of systemic sclerosis (SSc) lacks agreement.

**Objectives:** To generate SSc treatment algorithms endorsed by high percentage of SSc experts.

**Methods:** Experts from the Scleroderma Clinical Trials Consortium and the Canadian Scleroderma Research group (n=170) were asked whether they agreed with SSc algorithms (from 2012<sup>1</sup>). A further 2 consensus rounds refined agreement; 62 (36%), 54 and 48 experts completed surveys.

**Results:** For scleroderma renal crisis (SRC), 82% of the experts agreed (1st line ACEi, 2nd and 3rd adding: CCB or ARB). Pulmonary arterial hypertension (PAH) had 81% agreement. For mild PAH, PDE5i, then endothelin receptor antagonists plus PDE5i, then prostanoids; while for severe PAH prostanoids were first-line. Raynaud's phenomenon (RP) had 78% of agreement [mild (1st CCB, 2nd adding PDE5i, 3rd ARB or switching to another CCB, 4th prostanoids), severe (1st CCB, 2nd adding PDE5i, 3rd ERA, 4th prostanoids)]. Digital ulcer (DU) treatment had 69% agreement (1st CCB, 2nd PDE5i). Interstitial lung disease (ILD) had 65% agreement including induction (Mycophenolate mofetil (MMF) then intravenous cyclophosphamide then rituximab) and maintenance (1st line MMF). Skin involvement had 71% agreement. For a modified Rodnan skin score (mRSS) of 24 1st MTX, 2nd MMF; and for mRSS 32 1st MMF, 2nd MTX, 3rd intravenous cyclophosphamide (CYP), 4th hematopoietic stem cell transplantation. For inflammatory arthritis 79% agreed with 1st MTX, 2nd low dose glucocorticoids, 3rd hydroxychloroquine, 4th rituximab or tocilizumab. Cardiac and gastrointestinal algorithms had ≥75% agreement. The evolution of the agreement rates is shown in table 1:

**Abstract AB0731 – Table 1**

Algorithms for SSc treatment	Agreement 2012 <sup>1</sup> (%)	Agreement 2017 (%)
Scleroderma renal crisis	69	82
Pulmonary arterial hypertension	45	81
Raynaud's phenomenon	66	78
Digital ulcers	58	69
Interstitial lung disease	64	65
Gastrointestinal involvement	NA	77
Skin involvement	56, 40, 36 <sup>†</sup>	71
Inflammatory arthritis	45	79
Cardiac involvement	NA	75

Agreement is the% who agreed to the algorithm.

SSc: Systemic Sclerosis; NA: Not applicable; <sup>†</sup>For modified Rodnan skin scores 10, 24 and 32, respectively

**Conclusions:** Total agreement for SSc algorithms was considerable. These SSc algorithms may guide treatment.

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**AB0732 EFFICACY AND SAFETY OF RITUXIMAB IN SYSTEMIC SCLEROSIS: FRENCH RETROSPECTIVE STUDY AND LITERATURE REVIEW**

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**Background:** Interstitial lung disease occurs in 42% of diffuse SSc patients and have a major impact on the overall survival.<sup>1</sup> Cyclophosphamide and mycophenolate mofetil can allow the lung disease stabilisation.<sup>2,3</sup> Recently several case-reports and little series reported the efficacy of rituximab in SSc, showing a possible improvement of pulmonary involvements.<sup>4,5,6</sup> Large studies are lacking to determine the factors associated with rituximab response, the maintenance regimen and the long term efficacy of rituximab in SSc.

**Objectives:** To describe safety and efficacy of rituximab in patients with systemic sclerosis.

**Methods:** We included 13 patients with systemic sclerosis treated with rituximab and pooled with 40 additional patients from the literature. SSc rituximab untreated patients were matched to rituximab treated ones.

**Results:** Thirteen patients who received rituximab and 26 rituximab-untreated patients were included. In comparison to 26 patients who did not received rituximab, FVC changes were not significantly different, whereas DLCO improved in 13 patients who received rituximab (0 [-4; 4] vs loss of -7 [-19; 0]; p=0.05). Considering 7 rituximab treated and 14 untreated diffuse SSc, FVC was improved during the 24<sup>12</sup>; 46 months of follow up in dSSc who received rituximab (gain of 12 [7.5;14]%) vs loss of 1.5 [-16.8; 2.5]; (p=0.003). Pooled analysis of 53 patients (40 literature patients and 13 from personal series) showed significant improvement of median mRSS from 18<sup>8</sup>; 32 at baseline to 9<sup>4</sup>; 19 at M6 (p=0.007), 13<sup>8</sup>; 18 at M12 (p=0.008) and 10<sup>4</sup>; 16 at the last follow-up (p=0.0002). FVC increased from 71%<sup>66</sup>; 80 at baseline to 84%<sup>75</sup>; 90 at M12 (p=0.001). DLCO increased from 58%<sup>39</sup>; 65 at M0% to 63%<sup>53</sup>; 78 at M12 (p=0.04).

**Conclusions:** Our personal data and pooled literature analysis suggest the efficacy of rituximab in the subset of diffuse SSc in particular in skin and interstitial disease involvements. The safety of rituximab seems to be reasonable and similar to previous data in other autoimmune diseases.

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**Disclosure of Interest:** None declared

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**AB0733 ASSOCIATION OF HAEMATOLOGICAL PARAMETERS WITH DISEASE MANIFESTATIONS, ACTIVITY, AND SEVERITY IN PATIENTS WITH SYSTEMIC SCLEROSIS**

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**Background:** Neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), eosinophil-to-lymphocyte ratio (ELR), basophil-to-lymphocyte ratio (BLR), and mean platelet volume (MPV) may potentially reflect inflammatory status in systemic autoimmune diseases.

**Objectives:** The aim of this study is to investigate the association of NLR, MLR, ELR, BLR and MPV with disease manifestations, activity and severity in patients with systemic sclerosis (SSc).

**Methods:** 59 patients with SSc and 50 healthy controls were included in the study. All patients were diagnosed according to the 2013 ACR/EULAR systemic sclerosis classification criteria. Adult patients with SSc and healthy controls were compared in terms of NLR, MLR, ELR, BLR and MPV.

**Results:** SSc and control groups had similar ages and genders. Lymphocyte number was lower in SSc group compared to controls (p<0.001). SSc group also have higher NLR and MLR (table 1). There were no significant differences in ELR and BLR ratios between SSc patients and controls. Patients with active disease (2.9 [IQR 2.13], p=0.042), pulmonary hypertension (PHT), digital ulcers, and tendon friction rubs (TFR) had higher NLRs (table 2). MLR was also higher in dcSSc patients (0.28 [IQR 0.73]) compared to lcSSc (0.2 [IQR 0.48] (p=0.045), and there were also significant associations with disease manifestations like digital ulcers, tendon friction rubs (table 2). MLR was positively correlated with mRSS (rho=0.35 p=0.009), Valentini (rho=0.453 p=0.001) and Medsger (rho=0.283 p=0.036) scores. According to capillaroscopy images, patients with late stage findings had higher MLRs compared to patients with normal findings (0.27 [IQR 0.3] vs 0.15 [IQR 0.04], p<0.001). Patients with digital ulcers (p=0.02) and arthritis (p=0.013) had higher ELRs and patients with tendon friction rubs has higher ELRs (p=0.014) and BLRs (0.036) compared to those without. There was no significant relation between MPV and disease manifestations (table 2). There were no relationships between dysmotility and haematological parameters.

**Abstract AB0733 – Table 1.** Comparison of laboratory features of disease and control groups

	SSc n=59	Control n=50	p value
Neutrophil*	4.13 (11.88)	3.57 (5.19)	0.150
Lymphocyte*	1.67 (3.04)	2.08 (2.75)	<0.001
Monocyte*	0.34 (1.21)	0.35 (0.73)	0.959
CRP, mg/L	2.3 (29.9)	1.2 (8.1)	0.031
ESR, mm/hour	19 (58)	13 (30)	0.092
MPV, fl	9 (4.8)	8.7 (5.3)	0.557
NLR	2.47 (7.82)	1.73 (2.29)	<0.001
MLR	0.20 (0.79)	0.16 (0.34)	<0.001

\* x10<sup>9</sup>/L (IQR)

**Abstract AB0733 – Table 2.** Association of disease manifestations with NLR, MLR and MPV

	n=59*	MPV	NLR	MLR
ILD	+(n=17)	8.9 (2.8)	2.71 (7.82)	0.21 (0.77)
	-(n=42)	9 (4.8)	2.43 (3.92)	0.2 (0.32)
	P	0.412	0.431	0.738
PHT	+(n=3)	9.2 (1.3)	3.2 (1.78)	0.26 (0.11)
	-(n=56)	9 (4.8)	2.43 (7.82)	0.2 (0.82)
	P	0.856	0.044	0.276
Digital Ulcer	+(n=12)	9.1 (3.4)	2.75 (3.05)	0.27 (0.74)
	-(n=47)	8.9 (4.8)	2.43 (4.31)	0.19 (0.48)
	P	0.971	0.049	0.009
TFR	+(n=5)	9.1 (1.6)	3.62 (1.26)	0.28 (0.27)
	-(n=54) p	9 (4.8)	2.41 (4.31)	0.2 (0.48)
	P	0.911	0.003	0.030

MPV, NLR and MLR are given as medians (interquartile ranges).+and – denote presence and absence, respectively.

**Conclusions:** According to our study, as NLR and MLR are simple, practical, cost-effective markers, they can used for evaluation of disease manifestations, activity and severity in SSc.

**Disclosure of Interest:** None declared

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**AB0734 SERUM IL-35 LEVELS IN SYSTEMIC SCLEROSIS AND RELATIONSHIP WITH CLINICAL FEATURES**

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**Background:** Interleukin (IL)-35 is a member of the IL-12 family. Studies show that IL-35 is an important anti-inflammatory cytokine and suppresses effector T cell activity. Systemic sclerosis (SSc) is a chronic disease characterised by vascular damage, autoimmunity and fibrosis.

**Objectives:** In this study, we aimed to evaluate serum IL-35 level in SSc patients and its potential relation with disease findings.

**Methods:** Fifty-five SSc patients and 25 healthy controls were included in the study. All patients were diagnosed according to 2013 ACR/EULAR systemic sclerosis classification criteria. Serum IL-35 was measured using a commercial ELISA kit (Cloud-Clone Corp, Wuhan, China).

**Results:** SSc patients and healthy controls had similar ages and genders. The mean of serum IL-35 level was significantly higher in SSc patients (8.2±1.3 pg/ml) than in healthy controls (6.9±0.7 pg/ml) ( $p < 0.001$ ). Serum IL-35 levels were similar in lcSSc (n=44) and dcSSc (n=11) groups (8.3±1.2 and 8±0.1, 6 pg/ml, respectively). There were no significant relationships between serum IL-35 level and digital ulcer, interstitial lung disease, pulmonary hypertension, tendon friction rub, gastrointestinal motility disorder, cardiac involvement and Anti-SCL70, anti-CENP-B positivities (table 1). There was not any correlation between IL-35 level and disease duration, modified Rodnan skin score, Valentini disease activity score, Medsger disease severity score, erythrocyte sedimentation rate and C-reactive protein (CRP) levels. Serum IL-35 levels between patients treated with or not vasodilating agents such as calcium channel blockers, endothelin receptor antagonists and prostaglandin analogues, and also immunosuppressive drugs did not differ significantly.

**Abstract AB0734 – Table 1.** Relationship between clinical and laboratory features and IL-35

		IL-35 (pg/ml)	P
		*	
Digital ulcer	- (n=32) + (n=23)	8.3±1.4 8.1±1	0.5
Gastrointestinal involvement	- (n=43) + (n=12)	8.3±1.2 8±1.5	0.512
Cardiac involvement	- (n=52) + (n=3)	8.1±1.3 9.5±0.8	0.073
Interstitial pulmonary disease	- (n=34) + (n=21)	8.3±1.3 8.1±1.3	0.593
Pulmonary arterial hypertension	- (n=51) + (n=4)	8.2±1.3 7.9±1.2	0.617
Arthritis	- (n=36) + (n=19)	8.4±1.3 7.9±1.2	0.160
Tendon friction rub	- (n=47) + (n=8)	8.2±1.3 8.3±1	0.798
Anti-Scl 70	- (n=34) + (n=20)	8.3±1.3 8.2±1.2	0.793
Anti-CENP B	- (n=33) + (n=21)	8.1±1.3 8.4±1.3	0.442

\*mean ±std, + and – denote presence and absence, respectively.

**Conclusions:** It has been reported that serum IL-35 level is higher SSc patients than healthy volunteers and is associated with interstitial lung disease. In our study, the level of IL-35 was higher SSc patients than healthy controls. There is no relationship between clinical parameters and IL-35 levels, this may be due to small sample size. Our results suggest that IL-35 may have a role on the pathogenesis of SSc. Further investigations are needed in large sample size of SSc patients.

**Disclosure of Interest:** None declared

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**AB0735 NAILFOLD CAPILLARY COUNTS CORRELATE MOST WITH COMPLICATIONS OF SYSTEMIC SCLERODEMA IN JAPANESE PATIENTS**

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**Background:** Connective tissue diseases (CTD) patients have various clinical manifestation including pulmonary hypertension (PH) and digital ulcer (DU). Especially, Raynaud's phenomenon (RP) is one of the common symptoms. On the other hand, "abnormal nailfold capillaries" are important as the findings that suggest RP associated with CTD. They are included in one of the items of classification criteria for Scleroderma (SSc) in 2013 Classification Criteria for Systemic Sclerosis (ACR/EULAR) <sup>1</sup>. Recently, some reports presented the usefulness of nailfold capillaroscopy (NFC) in SSc <sup>2</sup>. NFC findings showed enlarged/giant capillaries, fresh or old haemorrhages, avascular areas, ramified/bushy capillaries. These findings are known as "scleroderma pattern" features. Additionally, there are some reports that nailfold capillary density in SSc related with DU, PH and interstitial pneumonia (IP).

In this study, we clarify the association between nailfold capillary density and clinical manifestation by analysis of the case in our institution.

**Objectives:** To clarify the association between nailfold capillary density and clinical manifestation.

**Methods:** We enrolled Japanese SSc patients from May 2016 to May 2017 in our institution.

We measured total nailfold capillary count per 1 μm from second to fifth finger by NFC "OptiPIX Capillaroscopy Clinic 1.7.x". In addition, we investigated relationship with NFC findings and clinical manifestation such as current and previous DU, PH and IP.

**Results:** We enrolled 42 SSc patients. Total nailfold capillary counts significantly decreased, especially in SSc patients with, previous DU ( $\rho = -0.4122$ ,  $p = 0.0054$ ), and PH ( $\rho = -0.3226$ ,  $p = 0.0023$ ). In addition, there is significant difference between DU and existence of giant capillaries ( $\rho = 0.3019$ ,  $p = 0.0464$ ), existence of avascular areas ( $\rho = 0.4057$ ,  $p = 0.0063$ ). On the other hand, there is no significant difference between IP, PH and other "scleroderma pattern" features.

**Conclusions:** Our study revealed that total nailfold capillary counts were associated with PH and DU in SSc patients. We suggest that nailfold capillary density may most predict complications with SSc patients.

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**AB0736 SYSTEMIC SCLEROSIS SINE SCLERODERMA: CHARACTERISTICS OF A SOUTH INDIAN COHORT FROM A TERTIARY CARE CENTRE**

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**Background:** Systemic Sclerosis is a complex disorder characterised by autoimmunity, vasculopathy and fibrosis. The hallmark of Systemic Sclerosis is skin thickening. Systemic Sclerosis sine scleroderma is a variant of Systemic sclerosis which shares visceral, serological and vascular manifestations but lacks skin thickening. Systemic Sclerosis sine scleroderma still remains a rarely reported subtype of Systemic Sclerosis unlike commonly reported limited cutaneous and diffuse cutaneous types.

**Objectives:** Aim of this study was to analyse the characteristics of patients with Systemic Sclerosis sine scleroderma from a cohort of Systemic Sclerosis patients.

**Methods:** This study was done at Institute of Rheumatology, Madras Medical College, Chennai, India. It was a retrospective observational study (January 2006 to November 2016). Patients satisfying ACR/<sup>EULAR</sup> 2013 Classification criteria for Systemic Sclerosis were included in this study. Patients with Overlap syndrome, MCTD, UCTD, children and pregnant women were excluded. Poormoghim criteria was used for diagnosis of Systemic Sclerosis sine scleroderma: Absent skin

thickening +Raynaud's Phenomenon or peripheral vascular involvement +Positive ANAs+One visceral organ involvement typical of SSc +Absence of another defined connective tissue disease. Demographic, clinical and laboratory profile of all patients were analysed.

**Results:** Among the 249 patients included in this study, patients with limited cutaneous systemic sclerosis were 59.4% (n=148) and diffuse cutaneous systemic sclerosis were 31.3% (n=78). 9.2% (n=23) of patients satisfied poormoghim criteria for Systemic Sclerosis sine scleroderma. The following characteristics of Systemic Sclerosis sine scleroderma were observed in our cohort. Dyspnoea (82.6%) was the most common presenting complaint and Raynauds (100%) the most common sign observed. Most common internal organ involvement was oesophageal dysfunction (78%) followed by lung involvement in the form of interstitial lung disease (52.1%) and pulmonary hypertension (47.8%). Renal involvement was not observed in any of the patients. Most common autoantibody detected among patients with Systemic Sclerosis sine scleroderma was anti-centromere antibody (78.2%) followed by anti-scl70 antibody (21.8%). Nine patients (39.1%) received pulse cyclophosphamide therapy and 3 patients received rituximab therapy in view of interstitial lung disease.



Abstract AB0736 – Figure 1

**Conclusions:** The most common pattern of Systemic Sclerosis sine scleroderma observed in our cohort was Oesophageal dysfunction +Raynauds Phenomenon +Anti centromere antibody positivity +Interstitial lung disease with or without pulmonary hypertension which are usually the characteristics of limited cutaneous type of Systemic Sclerosis. Hence Systemic Sclerosis sine scleroderma could be a subset of limited cutaneous type without the phenotypic skin involvement.

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AB0737

#### AMINAPHTONE INCREASES SKIN BLOOD PERFUSION AND IMPROVES CLINICAL SYMPTOMS IN PATIENTS WITH RAYNAUD'S PHENOMENON INDEPENDENTLY FROM DIFFERENT TREATMENT BACKGROUNDS

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**Background:** Aminaphtone is a vasoactive drug that was recently demonstrated to improve both peripheral blood perfusion (BP) and clinical symptoms of Raynaud's phenomenon (RP) in patients with either primary or secondary RP to systemic sclerosis (SSc).<sup>1-2</sup>

**Objectives:** The aim of this study was to evaluate possible interferences of different treatment backgrounds on both skin BP and RP-related clinical symptoms in patients treated with aminaphtone, during a six-month follow-up.

**Methods:** Forty-six patients with active RP were enrolled during routine clinical assessment after informed consent (11 primary RP, mean age 49±19 SD years, mean RP duration 6±3 years; and 35 secondary RP to systemic sclerosis, mean age 61±17 years, mean RP duration 11±9 years). Aminaphtone was orally administered 75 mg twice daily in addition to current treatments, and all patients were on a stable drug regimen for at least two months, which remained unmodified during the follow-up. All patients were taking cardioaspirin. Six groups of treatment backgrounds were identified: 1) no further treatments (12 patients); 2) hydroxychloroquine (2 patients); 3) colchicine (5 patients); 4) methotrexate (3 patients); 5) cyclosporine A (6 patients); 6) mycophenolate (6 patients); 7) proton-pump inhibitors (12 patients). Blood perfusion was measured by Laser Speckle Contrast Analysis (LASCA)<sup>3</sup> at the level of fingertip, periungual areas, dorsum and palm of hands, and face at baseline (T0), after one (T1), four (T4), twelve (T12) and twenty-four (T24) weeks of treatment. Raynaud's condition score (RCS) and both frequency and duration of Raynaud's attacks were assessed at the same time. Statistical analysis was performed by non-parametric tests.

**Results:** During aminaphtone treatment, a progressive statistically significant increase of blood perfusion, as well as an improvement of RP clinical symptoms (decrease of RCS, frequency and duration of RP attacks/day), were observed in all above reported seven groups of RP patients with different treatments backgrounds from T0 to T12 in all skin areas (p<0.01). There were no statistically significant difference between the seven groups of patients concerning skin BP at different times (p=0.60). The results were similar in both primary and secondary (SSc) RP patients (p=0.40). Aminaphtone administration had to be stopped in 2 patients due to headache, and one patient was lost during follow-up.

**Conclusions:** This study demonstrates that the increase of skin blood perfusion and the improvement of RP clinical symptoms is not influenced by different treatment backgrounds in RP patients treated with aminaphtone. These preliminary results should be further confirmed by a randomised blind clinical trial.

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AB0738

#### IMPROVEMENT OF DERMAL THICKNESS IN SYSTEMIC SCLEROSIS PATIENTS TREATED WITH ENDOTHELIN RECEPTOR ANTAGONIST: LONG TERM STUDY BY HIGH FREQUENCY ULTRASOUND

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**Background:** Systemic sclerosis (SSc) is a connective tissue disorder characterised by skin involvement, which may be evaluated by both modified Rodnan skin score (mRSS) and skin high frequency ultrasound (US).<sup>1-4</sup> Endothelin-1 (ET-1) seems implicated in the development of dermal fibrosis in SSc.<sup>5</sup> Bosentan, a dual ET-1 receptor antagonist seems effective in reducing skin fibrosis in SSc patients.<sup>6,7</sup>

**Objectives:** The aim of this study was to evaluate by US the long-term effects of bosentan on dermal thickness (DT) in SSc patients, in combination with long-term cyclic intravenous iloprost versus iloprost monotherapy.

**Methods:** Thirty-eight SSc patients were enrolled during their standard treatment for digital ischemia. At baseline (T0), 19 patients already receiving cyclic intravenous infusion of iloprost (5 continuous days, average 80 mcg/day, every two

months), continued the treatment for further 4 years (T4) (ILO group). Other 19 patients, although they continued the same cyclic intravenous iloprost treatment as the previous group, also received bosentan 125 mg twice a day for 4 years (ILO +BOS group), due to digital ulcers. DT was yearly evaluated by both US (18 MHz probe, MyLab 25, Esaote, Italy) and mRSS at the level of the usual seventeen skin areas (zygoma, fingers, dorsum of hands, forearms, upper-arms, chest, abdomen, thighs, legs, and feet).<sup>1-4</sup> Non-parametric tests were used for the statistical analysis.

**Results:** A statistically significant decrease of DT, measured by US, was observed in the ILO+BOS group from T0 (median DT 1.135 mm) to T4 (median DT 1.088 mm) ( $p=0.01$ ). No statistical significant variation of mRSS was observed during the follow-up in this group of patients (median mRSS at T0 12/51 and at T4 11/51,  $p=0.70$ ). Conversely, in ILO group, a statistically significant increase of DT was observed after four years, as measured by US (median DT at T0 1.070 and at T4 1.258,  $p<0.0001$ ), as assessed by mRSS (median mRSS at T0 4/51 and at T4 8/51,  $p<0.0001$ ). Transient increase of transaminases was managed by temporary bosentan discontinuation.

**Conclusions:** In this open study, the long-term treatment with ET-1 receptor antagonist in combination with iloprost seems to be associated with a decrease of DT in SSc patients, in contrast to the treatment with iloprost alone. DT evaluated by US over long term seems to be more susceptible to change than by mRSS.

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AB0739

#### LONGITUDINAL ASSESSMENT OF NAILFOLD CAPILLARY NUMBER, PERIPHERAL BLOOD PERFUSION AND DERMAL THICKNESS IN SYSTEMIC SCLEROSIS PATIENTS OVER A PERIOD OF 5 YEARS

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**Background:** Several studies demonstrated the relationship between blood perfusion (BP), dermal thickness (DT) and nailfold microangiopathy (“Early”, “Active” and “Late” videocapillaroscopic patterns) in patients with systemic sclerosis (SSc).<sup>1-3</sup>

**Objectives:** The aim of this study was to evaluate the changes of BP and DT, during a follow-up of 5 years, in SSc patients with persistent “Late” NVC pattern at baseline, as well as to confirm the correlations among microvascular damage extent, absolute nailfold capillary number (CN), BP and DT, during the follow-up.

**Methods:** Twenty-three female patients affected by SSc according to the LeRoy criteria<sup>4</sup> (mean age 63±4 SD years, mean disease duration 6±4 years), displaying the most advanced “Late” NVC pattern of microangiopathy at baseline (T0), were enrolled and followed for five years (T5), after informed consent. Laser speckled contrast analysis (LASCA), skin high frequency ultrasound (US), modified Rodnan skin score (mRSS), and nailfold videocapillaroscopy (NVC) were yearly performed. Blood perfusion (BP), assessed by LASCA at the level of fingertips, periungual areas, dorsum and palm of both hands, was calculated as perfusion units (PU).<sup>1-3</sup> Dermal thickness (DT) was assessed by both US and mRSS in the same above reported areas.<sup>5</sup> The microangiopathy evolution score (MES) and the CN per linear millimetre at first distal row were evaluated by NVC.<sup>6,7</sup> Patients were receiving a wide range of drugs, including vasodilators, immunosuppressive agents and endothelin receptor antagonists. Statistical analysis was performed by non parametric tests.

**Results:** A progressive statistically significant decrease of both BP ( $p<0.0001$ ) and nailfold CN ( $p<0.0001$ ) values was observed from T0 to T5 at the level of all areas, as well as a progressive statistically significant increase of DT ( $p<0.0001$ ), mRSS ( $p<0.0001$ ) and MES ( $p=0.01$ ) values. The progressive decrease of BP positively correlated over time with the worsening of nailfold CN ( $p=0.03$ ,  $r=0.62$ ), MES ( $p=0.05$ ,  $r=0.62$ ), mRSS ( $p=0.002$ ,  $r=0.72$ ) and DT ( $p=0.002$ ,  $r=0.64$ ).

**Conclusions:** Microvascular damage with progressive reduction of nailfold capillary number was found, in a five-year follow-up, associated with progressive

functional microvascular damage and DT worsening in the present cohort of SSc patients showing a persistent “Late” NVC pattern.

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AB0740

#### EVALUATION OF HAND DERMAL THICKNESS AND PERIPHERAL BLOOD PERFUSION IN SYSTEMIC SCLEROSIS PATIENTS

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**Background:** Systemic sclerosis (SSc) is characterised by progressive skin involvement. The modified Rodnan Skin Score (mRSS) is the gold standard to assess skin damage, but it has significant limitations. Recently, several studies demonstrated the utility of skin high frequency ultrasound (US) as an alternative.

**Objectives:** The aim of this study was to identify possible correlations between peripheral blood perfusion (BP) and ultrasound dermal thickness (US-DT) at level of hand and finger in SSc patients.

**Methods:** Sixty-seven patients, satisfying the 2013 ACR/EULAR SSc criteria (mean age 64±9 SD years, mean disease duration 6±4 SD years) were enrolled. BP was measured as perfusion units (PU) by laser speckle contrast analysis (LASCA) at the level of dorsal region of hands. In a second time, different regions of interest (ROIs) were created at level of dorsum of the middle phalanx of 3rd finger and dorsum of hand bilaterally and the average BP was scored as perfusion units (PU), as previously reported.<sup>1,2</sup> Both skin high frequency US and mRSS were used to evaluate DT at the above mentioned skin sites.<sup>2</sup> The same examinations were performed in 65 healthy subjects.

**Results:** BP was negatively correlated with both US-DT ( $p=0.0005$ ) and mRSS ( $p=0.007$ ) in SSc patients at the finger sites, but not at the level of dorsum of the hands. In healthy subjects, there was no statistically significant correlation between BP and DT as evaluated by both US and mRSS at either skin sites. SSc patients showed a statistically significant lower BP at the finger sites than healthy subjects ( $p<0.0001$ ). No statistically significant difference in BP values was observed between SSc and healthy subjects at the dorsum of hand.

**Conclusions:** This study demonstrates a negative correlation between BP, as evaluated by LASCA and DT, as evaluated by both US and mRSS, in the 3rd finger of SSc patients. Additionally, the results confirm a reduced finger BP in SSc patients when compared to healthy subjects.

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AB0741

#### T-REG AND TH17 LEVELS IN PATIENTS WITH SYSTEMIC SCLERODERMA

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**Background:** Regulatory T-cells (T-reg) may play an inhibitory role in the development of autoimmune diseases (AID) by suppressing the immune response to autoantigens. Impaired or decreased T-reg and/or increased Th17 cells may be responsible for the development of AID. However, studies about the association of T-reg and systemic scleroderma (SSc) are limited and conflicting.

**Objectives:** Our aim is to determine whether there is a relationship between T-reg and Th-17 levels and disease activation in patients with SSc.



**Methods:** 17 patients with <sup>SSc who met 2013</sup> ACR/EULAR SSc criteria were included in the study. Clinical and laboratory parameters, Rodnan skin scores, Valentini disease activity index, were evaluated in detail. Concurrent peripheral blood T-regs (CD4 +CD25+, CD4 +FOXP3+T reg, CD4 +CD25+FOXP3+T reg) and Th17 (IL-17 producing T cells) were studied. Age and sex matched 11 subjects were included as healthy control (HC) in this study.

**Results:** Fifteen of seventeen patients were female, median age was 52.8±9.36 years, median disease duration was 5.41±4.51 years. While skin involvement and Raynaud's phenomenon were determined in all of the patients, esophageal involvement was determined in 13 of the patients (76.5%), digital ulcer in 2 patients (11.7%), and lung involvement in 14 (94.1%) patients. Median ESR level was 31.29±12.7 mm/hour, median CRP level was 0.573±0.474 mg/dl, median Valentini disease activity index was 3.23±1.53. The medications of the patients during the follow up period were as; nifedipine n=15 (88.2%), hydroxychloroquine n=14 (82.4%), corticosteroids n=14 (82.4%), azathioprine n=10 (58.6%), mycophenolate mofetil n=1 (5.9%), cyclophosphamide n=7 (41.2%). In comparison of SSc and HC, all the T-reg cell levels were significantly higher in SSc group than HC (p≤0.0001, p≤0.0001 and p≤0.0001, respectively). Although the levels of CD4 +IL-17 cells in SSc group were high compared to HC, it was not significant (p=0.100). A positive correlation between CD4 +IL-17-cell levels and CRP (r=0.613, p=0.009), a negative correlation between CD4 +CD25+T reg cell levels and dosage of corticosteroid (r=-0.513, p=0.035), a negative correlation between CD4 +CD25+T reg cell levels and platelet levels (r=-0.560, p=0.019) and a negative correlation between CD4 +CD25+FOXP3+T reg cell levels and platelet levels (r=-0.500, p=0.041) were determined.

**Conclusions:** In a cross-sectional study, it is rather difficult to explain the meaning of increased T-reg cell in SSc patients. These results may be due to modification of the cells by immunosuppressive treatment. It might be more meaningful to evaluate T-reg cell before and after the treatment.

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AB0742

#### HAND X-RAY LESIONS ARE FREQUENT IN ANTISYNTHEASE SYNDROME PATIENTS WITH ARTHRALGIA AND INCREASE WITH THE RADIOGRAPHIC FOLLOW-UP, WHATEVER THE EXTRA-ARTICULAR FEATURES AND THE SEROTYPE OF ANTISYNTHEASE SYNDROME

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**Background:** Arthritis is frequent in antisynthetase syndrome (ASS) but the prevalence, the characteristics and the risk factors of radiographic lesions have been poorly assessed.

**Objectives:** To report prevalence, characteristics and risk factors of radiographic abnormalities in ASS patients with arthralgia.

**Methods:** A mono-centric cohort of 101 patients with ASS and arthralgia was screened for hand X-ray availability. Patients with osteoarthritic lesions were excluded from the analysis. ASS patients with radiographic lesions were compared to ASS patients with normal X-ray.

**Results:** Thirty one patients were included. Thirteen patients (41.9%) had radiographic lesions on hand X-ray, including periarticular calcifications (53.8%), joint pinching (46.1%), erosions (23%), and subluxations (15.3%). Age (54.15±4.5 vs 49.17±3.3 years old, p=0.17) and sex ratio were similar in both groups.

Duration of ASS was two-fold longer at first hand X-ray with radiographic lesion compared to the ASS patient without radiographic lesion at last radiographic

follow-up (10,08±2,4 years vs. 4,83±1,6, p=0,06). However, the cumulative number of immunomodulatory drugs at first hand X-ray with radiographic lesion or last hand X-ray if normal tended to be lower in patients with radiographic lesions (0,818 vs 1,28, p=0,55).

History of extra-articular involvements (including myositis, interstitial lung disease, skin lesions and Raynaud phenomenon) were not different in both groups, although mechanic's hand tended to be less frequent in patients with radiographic lesions (23.1% vs 61.1%, p=0.07).

Patients with radiographic lesions had more frequently anti-EJ (31% vs. 0%, p<0.05). Other anti-tRNA synthetase antibodies were not significantly associated with abnormal hand x-ray which were found in 50% of anti-PL-7 positive patients (2/4), 33,3% of anti-PL-12 positive patients (1/3), 30% of anti-Jo1 positive patients (6/20), and 0/1 anti-OJ positive patient (one patient was positive for anti-Jo1 and anti-PL7). ACPA (27.3% vs 7.1%, p=0.29) and rheumatoid factor (50% vs 14.2%, p=0.09) were more frequently positive in case of radiological abnormality.

**Conclusions:** Hand X-ray lesions are frequent in ASS patients with arthralgia, whatever the extra-articular features and the ASS serotype and was associated is a longer duration of ASS.

**Disclosure of Interest:** None declared

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AB0743

#### THE CLINICAL MANIFESTATIONS IN ANTI-RO52 ANTIBODY- POSITIVE PATIENTS WITH SYSTEMIC SCLEROSIS; A RETROSPECTIVE CASE CONTROL STUDY

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**Background:** Autoantibodies (abs) directed against Ro52/TRIM21 are common in systemic sclerosis (SSc) but their clinical significance remains uncertain. Some reports suggested that anti-Ro52/TRIM21 abs-positive SSc patients present interstitial lung disorders (SSc-ILD). However, it is not clear whether positive for anti-Ro52/TRIM21 related to other clinical manifestations in patients with SSc.

**Objectives:** The aim of this study is to clarify the prevalence of anti-Ro52/TRIM21 abs in patients with SSc. Then, we investigated the clinical manifestations between anti-Ro52/TRIM21 abs-positive and negative patients with SSc.

**Methods:** This study is a retrospective case control study. The medical records of 42 patients who were diagnosed as having SSc admitted to our hospital were reviewed. We evaluated the clinical manifestations at the first-onset of SSc such as Rodnan skin score, digital ulcer, abnormal subcutaneous calcification, esophageal reflux, pulmonary hypertension, myositis and arthralgia. Co-existing rheumatic diseases were also reviewed such as Sjogren syndrome (SjS), rheumatoid arthritis (RA), and polymyositis. All subjects underwent SSc-associated abs testing using EUROLINE immunoblot assay. The autoantibodies include anti-Scl-70, anti-centromere A and B (CENP-A, CENP-B), anti-RNA polymerase III (RP-11, RP-155), anti-fibrillarin (U3RNP), anti-90-kd nucleolar protein (NOR-90), anti-Th/To, anti-PM/Scl-100, anti-PM/Scl-75, anti-Ku, anti-platelet-derived growth factor receptor (PDGFR), and tripartite motif-containing protein 21 (Ro-52). The association between clinical features and autoantibody profile was evaluated. Diagnosis of ILD was evaluated by chest high-resolution CT (HRCT).

**Results:** Thirty-five patients with SSc are female (87%). Twenty-one and nine patients with SSc are positive and negative for anti-Ro52/TRIM21 abs, respectively (47 v.s 52%). There is no difference in population of diffuse type of SSc between anti-Ro52/TRIM21 abs-positive and negative SSc patients. In addition, the prevalence of ILD is not different between two groups (57 v.s 52%, p=0.76). The prevalence of SjS is tended to be higher in anti-Ro52/TRIM21 abs-positive SSc patients than in negative SSc patients (68 v.s 33%, p=0.05). Unexpectedly, 57% of anti-Ro52/TRIM21 abs-negative SSc patients present polyarthralgia at the onset of SSc. In addition, there were not any complications such as osteoarthritis and RA in anti-Ro52/TRIM21 abs-negative SSc patients. The prevalence of arthralgia was higher in anti-Ro52/TRIM21 abs-negative SSc patients than in positive SSc patients (p=0.02).

**Conclusions:** The prevalence of anti-Ro52/TRIM21 abs in SSc patients of this study seems to be high compared to other reports. In addition, there seems to be no difference in the prevalence of ILD regardless of existence of anti-Ro52/TRIM21 abs in SSc patients. Anti-Ro52/TRIM21 abs-negative SSc patients were tended to present polyarthralgia. This musculoskeletal disorder of anti-Ro52/TRIM21 abs-negative SSc patients may be not associated with other rheumatic diseases such as SjS and RA in this study. It is necessary the large number study to clarify whether anti-Ro52/TRIM21 abs involve in the pathogenesis of musculoskeletal disorders in patients with SSc.

**Disclosure of Interest:** None declared

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**AB0744** A "LOST-TO-FOLLOW-UP" AUTOANTIBODY FOR THE DIAGNOSIS OF AUTOIMMUNE DISEASE: PREVALENCE AND CLINICAL CHARACTERISTICS OF ANTI-NOR90/HUBF POSITIVE PATIENTS

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**Background:** Anti-nuclear antibody (ANA) patterns in indirect immunofluorescence testing (IIF) have been valuable in the diagnosis of autoimmune diseases. A pattern of speckling with fluorescent mitotic dots is considered to represent autoantibodies against nucleolar organising regions (NORs). Anti-NOR90 antibodies target the human upstream binding factor (hUBF) which activates RNA polymerase I-activated ribosomal RNA transcription. They have been anecdotally associated with systemic sclerosis (SSc), Sjögren's Syndrome (pSS) and rheumatoid arthritis (RA).

**Objectives:** To analyse the prevalence and clinical characteristics of patients found to be anti-NOR90 positive by immunology at The Dudley Group NHS FT (DGH) which also serves Worcestershire Acute Hospitals NHS Trust (WAH).

**Methods:** Clinical letters and electronic patient records of anti-NOR90 positive patients identified in the DGH immunology laboratory between July 2016 and October 2017 were reviewed. Advice was sought regarding ethical approval and consent; this was deemed unnecessary for this clinical survey. Anonymized patient data was collected on Excel. Anti-NOR90 was tested for when the characteristic ANA pattern was observed and as part of an extended SSc blot (EUROLINE SSc (Nucleoli) profile (IgG) – EUROIMMUN).

**Results:** We identified 11 anti-NOR90 positive patients among 8000 positive ANA results (estimated prevalence 0.0137%). Patient demographics, diagnoses and immunology are illustrated in table 1. Patients were in their vast majority female (10/11, 91%) and had a median age of 63 (IQR:53–74) years. The median anti-NOR90 titer was 111 (IQR:14–139) intensity units. 6/11 (54.5%) had a confirmed diagnosis of rheumatic disease. The most common clinical features were Raynaud's phenomenon (63.6%), sicca symptomatology (36.4%) and polyarthritis (36.4%). Interstitial lung disease (ILD) and oesophageal dysmotility (OD) were predominant clinical features in two cases (SSc, pSS). In general, patients lacked skin involvement (scleroderma, telangiectasias, calcinosis).

**Abstract AB0744 – Table 1.** Demographic, clinical and immunological characteristics of anti-NOR90 positive patients

Patient	Age/ Sex	Diagnosis	Rheumatoid Factor	ANA titre	ANA pattern	anti- NOR90 titre
1	82/F	SSc	-	weak positive	mitotic dots	positive
2	80/ M	pSS	-	1:320	speckled mitotic dots	11
3	35/F	UCTD	-	1:2560	nucleolar with mitotic dots	140
4	63/F	RA	+	weak positive	mitotic dots	positive
5	81/F	Bronchiectasis	-	1:1280	speckled mitotic dots	107
6	18/F	Raynaud's	-	1:1280	mitotic dots	139
7	68/F	Raynaud's	-	1:320	nucleolar with mitotic dots	130
8	56/F	UCTD	+	1:320	mitotic dots	11
9	66/F	Raynaud's	-	negative	negative	14
10	53/F	Raynaud's/ Crohn's disease	-	1:1280	nucleolar +homogenous with mitosis dots	151
11	52/F	Polyarthritis	-	weak positive	mitotic dots	111

**Conclusions:** Literature regarding anti-NOR90 auto-antibodies has been scarce and in the age of automated IIF ANA testing, it is plausible that their specific nucleolar pattern is frequently missed. In our survey, they were observed in the context of several rheumatic diseases and linked to Raynaud's, sicca symptoms and polyarthritis. Studies in larger relevant patient cohorts are needed to further clarify their clinical value.

**Disclosure of Interest:** None declared

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**AB0745** MECHANICS OF EARLY VENTRICULAR IMPAIRMENT IN SYSTEMIC SCLEROSIS AND THE EFFECTS OF PERIPHERAL VASCULOPATHY

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**Background:** Multiple mechanisms commonly lead to severe cardiac involvement in systemic sclerosis (SSc), an autoimmune disease characterised by microvascular lesions, systemic inflammation and fibrosis.

**Objectives:** To examine the mechanics of right and left ventricles (RV, LV) at the early stage of possible impairment and test the hypothesis that peripheral arterial hemodynamics are associated with an early LV compromise.

**Methods:** Ninety-five asymptomatic SSc patients free of cardiovascular disease (88% women, 53±14 years) and 54 apparently healthy controls matched for age, gender, arterial hypertension, dyslipidaemia, and diabetes mellitus underwent echocardiography, including multilayer speckle-tracking, and tonometry-based pulse wave analysis of the peripheral arteries; 66 SSc patients were prospectively assessed after 32±7 months. Indices of ventricular and arterial structure and function, as well as LV-arterial coupling, were calculated.

**Results:** At baseline, patients presented RV diastolic/systolic impairment, as well as LV remodelling and diastolic/systolic impairment in terms of reduced deformation parameters versus controls. No association was evident between RV and LV strain within individual patients, whereas by multivariate analysis including age, gender and SSc characteristics we found that the global longitudinal strain of RV free wall was associated only with the presence of diffuse skin involvement (b=2.63, p=0.042) and both global longitudinal and circumferential strain of LV were correlated only with disease duration (b=0.14, p=0.001 and b=0.17, p=0.032, respectively). Both RV and LV abnormalities progressed independently during follow-up. Moreover, in the absence of differences in aortic stiffening and LV-arterial coupling between patients and controls, arterial pressure wave reflections assessing small vessel function and/or microcirculation were abnormal in SSc patients and strongly correlated with impaired indices of LV diastolic function and remodelling.

**Conclusions:** These novel findings show the mechanics of RV early impairment in SSc that develops and progresses independently from the concomitant LV impairment, which, in turn, may be influenced by peripheral microvascular abnormalities in the absence of macrovascular damage.

**Disclosure of Interest:** None declared

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**AB0746** FREQUENCY AND CLINICAL ASSOCIATION OF RARE ANTIBODIES IN A LARGE CONNECTIVE TISSUE DISEASE COHORT

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**Background:** Connective tissue diseases (CTDs) are characterised by the presence of specific antibodies (Abs). These are useful in diagnosis and prognostic stratification. Rare Abs have been reported but their clinical significance is currently not as clear.

**Objectives:** to assess the diagnosis, and frequency of clinical features within each rare antibody subgroup in our CTD cohort

**Methods:** The immunology results for 5828 patients obtained over the past 17 years and patients positive for 1 of the rare Abs (Jo-1, PCNA, XR, PL-4, PL-7, PL-12, SRP, Ku, Mi-2, EJ, SL, PmScl, rRNP, Th/To, NuMA-1, OJ and hnRNP) were identified. Diagnosis and frequency of major organ involvement were reported.

**Results:** 758 patients (12.5%) were positive for at >1 rare Abs. Clinical information confirming a diagnosis of a CTD was available for 514 patients. The most frequent rare Ab in our cohort was PmScl (3.10%). The majority of patients had clinical features of overlap syndromes (33.8%), the 2nd most common diagnosis was systemic sclerosis (SSc) (31.10%). Interstitial lung disease (ILD) was more commonly seen in patients with PL-7+ (82.4%), PL-12+ (75%), Jo-1+ (70.8%) and SRP+ (66.7%). ILD was not reported in PCNA+, PL-4+, NuMA-1+ and hnRNP+. Pulmonary arterial hypertension (PAH) was most frequently seen in patients with XR+ (31.8%). Inflammatory myositis (IM) was found in all Jo-1+ and SRP+ patients, and in the majority of PL-7+ (88.2%) patients. Inflammatory arthritis was commonly reported in patients with PCNA+ (57.1%), NuMA-1+ (50.0%) and rRNP+ (40%). Renal involvement was classified as either glomerulonephritis (GMN) or scleroderma renal crisis (SRC). GMN was more common in patients with rRNP+ (60%), PL-4+ (45.4%) and PCNA+ (42.9%) patients. SRC was diagnosed in patients with SL+ (3.2%), PM/Scl+ (5.5%) and Th/To+ (2.5%) (table 1).

**Conclusions:** Our data from a large CTD cohort suggest that rare Abs associate with distinct features in particular ILD and inflammatory myositis. A majority of these patients fulfil the criteria for overlap syndrome and SSc.

**Disclosure of Interest:** None declared

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### AB0747 INTERSTITIAL LUNG DISEASE IS INDEPENDENTLY ASSOCIATED WITH INCREASED FAECAL CALPROTECTIN LEVELS IN SYSTEMIC SCLEROSIS

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**Background:** Interstitial lung disease (ILD) is one of the leading cause of death in systemic sclerosis (SSc).

**Objectives:** The aim of this paper was to evaluate the relationship between faecal calprotectin (FC) and ILD.

**Methods:** 129 outpatients with SSc were enrolled. Data about disease characteristics, in particular lung involvement, were collected and FC was measured.

**Results:** Eighty-seven patients (67.4%) had a limited subset with a mean disease duration of 13.3 (7.1) years. Anti-Scl70 antibodies were found in 35 (27.1%) patients. GI tract involvement was severe/end stage in 3 cases (2.4%). ILD affected 35 patients (27.1%). Median levels of FC were 80 µg/g (157 µg/g). FC was found to be higher in patients with a moderate/severe/end stage score for gastrointestinal tract (p=0.046) and on steroids (p=0.015). In addition, it positively correlated with age (p<0.001).

Other than well-known risk factors such as higher mRSS or diffuse subset, patients with ILD had higher values of FC (p<0.001). In multivariate analysis correcting also for factors affecting FC levels (i.e. disease duration, mRSS, Valentini activity score, total Medsger severity score, proton pump inhibitor, anti-Scl-70 antibody, diverticulosis, limited cutaneous subset, faecal calprotectin levels, steroid treatment), diffuse disease subset (p=0.001), higher mRSS (0.04), longer disease duration (0.046), higher severity scores (0.026), higher FC levels (p=0.003) and steroid treatment (0.014) were associated with increased risk of ILD, while diverticulosis was protective. In addition, we ran a second multivariate analysis considering the 110 cases with FC level <275 µg/g, in order to correct for a possible small intestine bacterial overgrowth. Increased FC levels (p=0.019), steroid treatment (p=0.03), higher severity scores (p=0.016) and diffuse disease subset (p=0.002) were confirmed to be associated with ILD.

**Conclusions:** in this paper we have found a possible link between gut inflammation and ILD. Many hypothesis may be done but it is intriguing that these data further support what previously found by other authors (Andreasson et al. 2016), that is a correlation between gut inflammation and dysbiosis and non-gastrointestinal disease manifestation. Our study may support the hypothesis of a role of gut

dysbiosis in triggering a pathologic immune response leading to ILD. It may also be that increased FC simply reflects a more severe disease but this still doesn't explain why only ILD was found to be linked with FC. Is it because lung is a filter of molecule (i.e. antigens, cytokines, metabolites, etc.) produced in the gut? Further studies with longitudinal evaluation are warranted.

**Disclosure of Interest:** None declared

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### AB0748 POLIAUTOIMMUNITY IN SCLERODERMA: DATA FROM DE SPANISH SCLERODERMA REGISTRY

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**Background:** Systemic sclerosis (SSc) is a disorder with a well-known autoimmune base. There is evidence suggesting a common background with other connective tissue diseases, thus predisposing to the development of other autoimmune disorders in these patients, that is, poliautoimmunity (PAI).

**Objectives:** To assess PAI in a cohort of SSc patients.

**Methods:** A nationwide, cross-sectional study was performed including the 1928 patients enrolled in the Spanish SSc Registry (RESCLE). Ethics Committee approval was obtained by all participating centres.

**Results:** Prevalence of PAI was 45%, with 32% having more than one association. Most of these patients were women (93%, p<0.001), with older age at diagnosis (53.7±14.7 years, p=0.027). Regarding subtypes, PAI was significantly more frequent in limited cutaneous SSc (48%, p=0.004) and pre-SSc (47%, p<0.001). Sjögren's syndrome was by far the most common association (55%), followed by global autoimmune thyroid disorders (31%), autoimmune liver disorders (17%) and inflammatory myopathies (12%). Clinical features are shown on table 1.

**Abstract AB0746 – Table 1.** Diagnosis and clinical features in patients positive for rare antibodies

Antibody(n, %)	Diagnosis					Clinical features					
	SSc	SLE	SS	IM	Overlap	UCTD	ILD	PAH	IM	Arthritis	Renal
Jo1(72)	0	0	0	51 (70.8)	21 (29.2)	0	51 (70.8)	11 (15.3)	72(100)	21 (29.2)	0
PCNA <sup>(7)</sup>	1 (14.3)	6 (85.7)	0	0	0	0	0	1 (14.3)	0	4 (57.1)	3 (42.9)
XR <sup>(22)</sup>	9 (40.9)	6 (27.3)	0	0	7 (31.8)	0	9 (40.9)	7 (31.8)	3 (13.6)	6 (27.3)	1 (4.5)
PL-4(11)	0	11(100)	0	0	0	0	0	0	0	0	5 (45.5)
PL-7(17)	2 (11.8)	0	0	9 (52.9)	6 (35.3)	0	14 (82.4)	0	15 (88.2)	5 (29.4)	0
PL-12 <sup>(12)</sup>	2 (16.7)	2 (16.7)	1 (8.3)	5 (41.7)	2 (16.6)	0	9 (75.0)	0	6 (50.0)	4 (33.3)	1 (8.3)
SRP <sup>(9)</sup>	0	0	0	5 (55.6)	4 (44.4)	0	6 (66.7)	2 (22.2)	9 (100.0)	1 (11.1)	0
Ku <sup>(47)</sup>	14 (29.8)	5 (10.6)	0	2 (4.3)	21 (44.7)	5 (10.6)	21 (44.7)	2 (4.3)	8 (17.0)	16 (34.0)	4 (8.5)
Mi-2(7)	0	0	0	6 (85.7)	1 (14.3)	0	4 (57.1)	0	1 (14.7)	0	0
EJ <sup>(2)</sup>	1 (50.0)	0	0	0	1 (50.0)	0	1 (50.0)	0	0	0	0
SL(94)	33 (35.1)	34 (36.1)	10 (10.6)	1 (1.1)	10 (10.7)	6 (6.4)	16 (17.0)	9 (9.6)	12 (12.7)	36 (38.3)	14 (14.9)
Pm/ScI(182)	70 (38.7)	2 (1.1)	1 (0.6)	6 (3.3)	99 (54.7)	3 (1.7)	75 (41.4)	11 (6.1)	94 (51.9)	35 (19.3)	10 (5.5)
rRNP <sup>(5)</sup>	0	5 (100)	0	0	0	0	1 (20.0)	0	0	2 (40.0)	3 (60.0)
Th/To <sup>(40)</sup>	34 (85.0)	0	0	1 (2.5)	4 (10.0)	1 (2.5)	16 (40.0)	10 (25.0)	5 (25.0)	2 (5.0)	1 (2.5)
NuMA-1(2)	2 (100.0)	0	0	0	0	0	0	0	0	1 (50.0)	0
OJ <sup>(1)</sup>	0	0	0	1 (100.0)	0	0	1 (100.0)	0	1 (100.0)	1 (100.0)	0
hnRNP <sup>(3)</sup>	0 (0.0)	2 (66.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	3 (100.0)	0 (0.0)



Abstract AB0748 – Table 1

	TOTAL	ISOLATED SSC	PAI	p
Raynaud's Phenomenon	1826	1005 (55%)	821 (45%)	1.000
Digital ulcers	745	408 (55%)	337 (45%)	0.888
Calcinosis	322	142 (44%)	180 (56%)	<0.001
Arthritis	270	128 (47%)	142 (53%)	0.064
Myositis	172	37 (22%)	135 (78%)	<0.001
Gastrointestinal involvement	1222	632 (52%)	590 (48%)	<0.001
ILD	795	399 (50.2%)	396 (49.8%)	<0.001
PH confirmed by right heart catheterisation	148	66 (45%)	82 (55%)	0.438
Heart involvement	409	196 (48%)	213 (52%)	0.001
Scleroderma renal crisis	43	27 (63%)	16 (37%)	0.353

We found no significant differences concerning capillaroscopy patterns, or causes of death, neither SSc-related nor non-SSc-related.

Finally, a multivariate analysis with logistic regression was performed to evaluate the risk factors for PAI, which are shown on the table 2.

Abstract AB0748 – Table 2

Variables	Multivariate analysis OR (95% I.C.)	p value
Gender	2,72 <sup>1,87-3,98</sup>	<0001
Age at dianosis	1,01 <sup>1,00-1,02</sup>	0012
Calcinosis	1,63 <sup>1,23-2,16</sup>	<0001
ILD	1,37 <sup>1,08-1,73</sup>	<0001
Gastrointestinal involvement	1,32 <sup>1,05-1,66</sup>	0019
Centomere Ab	1,41 <sup>1,12-1,77</sup>	<0001
Ro Ab	1,61 <sup>1,18-2,18</sup>	<0001

**Conclusions:** PAI in SSc is a frequent condition that special attention in these patients. We found a rather higher prevalence compared with those published in the literature, even though the distribution of those associated disorders was similar. In our cohort, there were no remarkable differences between both groups concerning clinical manifestations (although not always statistically significant). Finally, certain circumstances should make us aware of a possible associated condition to SSc.

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#### AB0749 DON'T FORGET THE CAREGIVERS OF PATIENTS WITH SYSTEMIC SCLEROSIS

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**Background:** Systemic sclerosis (SSc) is a disease with considerable physical and psychosocial impact. Previous studies among partners of patients with other chronic diseases, such as Parkinson's and stroke, showed that 6%–25% of caregivers experience high levels of stress related to caregiving. To our knowledge, the burden experienced by caregivers of patients with SSc has not been determined so far.

**Objectives:** To evaluate perceived strain, quality of life and health care needs among SSc caregivers.

**Methods:** During a patient information meeting, companions of SSc patients were invited to complete 3 questionnaires: 1. The Caregiver Strain Index questionnaire (CSI), in which a score  $\geq 7$  indicates high care burden, 2. Short Form-36 (SF-36): a measure of self-reported Quality of Life (QoL) and 3. a self-designed questionnaire on the needs and preferences for caregiving support. Caregivers with and without high care burden were compared regarding their general characteristics and QoL.

**Results:** Thirty-six SSc caregiver filled out questionnaires (n=31 completed the CSI questionnaire). Respondents were mostly men (64%), on average 62 years old (SD 14), 35% (n=11) had a paid job, and 50% (n=18) suffered from chronic disease. The majority was in a spousal relationship (75%) with the SSc patient and 56% of patients had been diagnosed with SSc more than 5 years ago. Nineteen percent of patients (n=7) needed daily personal caregiving and 25% (n=9) was

transport-dependent. Median CSI was 2 (range 0 to 5), and 6/31 (19%) perceived high care burden (CSI  $\geq 7$ ). Caregivers with high care burden were significantly more often involved in daily personal caregiving of the patients (3/6 vs. 2/25). Although not statistically significant, all caregivers perceiving a high burden were spouses, while the remaining caregivers had varying relationships with SSc patients. SF-36 summary scale scores were similar in both groups (table 1). Regarding needs and preferences of caregivers, 15% (n=5) reported a need for additional individual information, and 21% (n=7) a need for contact with fellow caregivers of patients, preferably during information meetings.

Abstract AB0749 – Table 1. Characteristics of caregivers of SSc patients with and without high care burden (CSI  $\geq 7$ ).

	Total (n=36)	CSI<7 (n=25)	CSI $\geq 7$ (n=6)	p-value
CSI, median (IQR)	2.0 (0.0–5.0)**	2.0 (0.0–4.0)	8.0 (7.0–8.0)	n.a.
Gender, n (% female)	13 (36)	10 (40)	1 (17)	0.383 <sup>1</sup>
Age (years, median (IQR))	65.5 (53.8–72.0)	66.0 (51.0–73.0)	63.5 (56.8–66.0)	0.448 <sup>2</sup>
Relationship (%)				
Partner	27 (75)	18 (72)	6 (100)	0.293 <sup>1</sup>
Father/mother	2 (6)	2 (8)	0 (0)	
Friend	2 (6)	1 (4)	0 (0)	
Son/daughter	4 (11)	4 (16)	0 (0)	
Involved in daily personal caregiving patient SSc (%)	7 (19)*	2 (8)	3 (50)	0.038 <sup>1</sup>
Transport dependency patient SSc (%)	9 (25)*	5 (20)	2 (33)	0.596 <sup>1</sup>
SF –36 (mean $\pm$ SD)				
Physical component score	50.9 $\pm$ 7.2***	51.2 $\pm$ 7.0****	53.6 $\pm$ 3.4	
Mental component score	43.7 $\pm$ 6.8***	43.4 $\pm$ 7.8****	42.9 $\pm$ 3.8	

<sup>1</sup> Fisher's exact <sup>2</sup> Mann-Whitney U \*n=35, \*\*n=31, \*\*\*n=28, \*\*\*\*n=19

**Conclusions:** Within a small group of SSc caregivers, 19% experienced high care burden. In particular caregivers involved in personal caregiving seem to be at risk for increased strain related to caregiving. The results of the current study can direct clinical practice aiming at support of the caregivers.

**Disclosure of Interest:** None declared

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#### AB0750 RHEUMATIC DISEASES WITH LUNG INVOLVMENT AND PSYCHOLOGICAL STATUS

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**Objectives:** assess the impact of psychological status indicators on lung function in patients with rheumatic diseases with lung lesions

**Methods:** A study of 30 patients with diagnoses of systemic sclerosis (SSD) – 14 patients, systemic vasculitis (CB) – 10, rheumatoid arthritis (RA) – 6 patients.

The average age of the patients was 56.55 $\pm$ 10.59 (from 22 to 77 years). All patients had high activity of the underlying disease and received pathogenetic therapy in the form of pulse therapy for HA – 19 patients, high doses of HA (1 mg/kg) per os – 11 patients; were hospitalised in connexion with the first detected lung lesions or signs of progression of the existing lung injury (increased dyspnea, reduced exercise tolerance). Patients are consulted by a cardiologist to exclude the cardiac genesis of symptoms.

All patients underwent a standard clinical examination, in addition they performed: high-resolution RCT of lung (64-slice CT system Philips Diamond Select Brilliance), a 6 min walk test.

Evaluation of lung function was carried out using spirometry, bodiplotzomography, diffusion "single breath".

The following scales were used to assess the psychological status: State-Trait Anxiety Inventory (STAI) personal and situational anxiety assessment, symptomatic questionnaire SCL-90-R (English Symptom Check List-90-Revised), anxiety and depression, the Toronto Alexitimic Scale (TAS)

**Results:** All patients according to RKT data had manifestations of IZL in the form of nonspecific interstitial pneumonia. Among the patients examined, the group with DV 1st. was 11 patients, DN 2 tbsp. – 14 patients, DN 3 tbsp. – 5 patients. A high level of situational anxiety was present in 11 patients (36.7%), personal – in 13 patients (43.3%). At the same time, the DLCO relationship to the alveolar volume was identified with the level of personal anxiety ( $r=-0.526$ ,  $p<0.05$ ) and situational ( $r=-0.423$ ,  $p<0.05$ ). In addition, the DV index has an average correlation with the level of anxiety ( $r=0.513$ ,  $p<0.05$ ). The symptomatic questionnaire revealed a significant degree of somatization in patients with IBD – in 14 patients

(46.7%), which is the somatic equivalent of depression and anxiety. TAS data indicate the presence of apparent alexithymia in 10 patients (33.3%), the "risk group" for alexithymia is 26.7%.

In addition, saturation after a 6 min walk was correlated with alexithymia ( $r = -0.526$ ,  $p < 0.05$ ).

**Conclusions:** The psychological status of patients with rheumatic diseases with lung involvement in the form of nonspecific interstitial pneumonia is characterised by depression, anxiety, alexithymia.

**Disclosure of Interest:** None declared

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#### AB0751 THE EPSTEIN-BARR VIRUS INFECTION IN SYSTEMIC SCLEROSIS

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**Background:** Epstein-Barr virus (EBV) infection has been considered trigger of various autoimmune diseases, including systemic sclerosis (SSc), mainly due to studies investigating cross-reactive responses amongst EBV and disease-specific antigens. Meticulous assessment of antibody reactivities to the most immunodominant EBV antigens in SSc has not been performed.

**Objectives:** To assess ab reactivity against EBV viral capsid antigens (VCA), early antigens (EA) and EBNA-1 in SSc, and investigate their clinical relevance.

**Methods:** Sera from 59 SSc patients, including 31 diffuse SSc (dcSSc) and 28 limited SSc (lcSSc), 43 matched multiple sclerosis (MS) as controls and 32 matched healthy controls (HC) were tested for IgG anti-EBV VCA, EA and EBNA-1 abs by immunoblotting, using EBV whole SDS extract as antigen substrate.

**Results:** Percentages of EA and EBNA-1 reactivities were significantly higher in SSc patients compared to HC (EA: 33.9% vs 3.1%,  $p = 0.001$ ; EBNA-1: 89.8% vs 68.8%,  $p = 0.012$ ), but were comparable between SSc and MS. These differences remained when SSc was divided in dcSSc and lcSSc (EA: 32.3% in dcSSc and 35.7% in lcSSc,  $p_{dcSSc vs HC} = 0.002$ ,  $p_{lcSSc vs HC} = 0.001$ ; EBNA: 92.9% in lcSSc,  $p_{lcSSc vs HC} = 0.020$ ). VCA positivity was comparable between SSc or its two subgroups and MS or HCs. Also, triple positivity for all three antigen categories was observed more frequently in SSc, dcSSc and lcSSc compared to HCs (32.2% in SSc, 29% in dcSSc and 35.7% in lcSSc vs 3.1% in HC,  $p = 0.001$ ,  $p = 0.004$  and  $p = 0.001$ , respectively). Anti- EA was present more frequently in SSc patients with calcinosis compared to those without (75% vs 27.5%,  $p = 0.014$ ) and tended to be more frequent in patients with pulmonary fibrosis compared to those without (47.8% vs 25%,  $p = 0.071$ ).

**Conclusions:** Antibodies against EBV appear to be more frequent in SSc than in healthy controls, and equally prevalent with MS, a disease known to be associated with anti-EBV antibody responses and a known risk factor for MS. Whether an EBV-specific response is also an initiating trigger of SSc remains to be investigated.

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#### AB0752 CLINICAL FEATURES OF SYSTEMIC SCLEROSIS ASSOCIATED TO ANTI RNA POLYMERASE III ANTIBODIES IN VALLD'HEBRON HOSPITAL

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**Objectives:** Systemic sclerosis (SSc) is an autoimmune disease whose clinical features are related closely with the specific autoantibody that is expressed. The main objective was to analyse the clinical characteristics of patients with positive anti-RNA polymerase III antibody (anti-RNAP III) and compare them with patients who were negative.

**Methods:** We analysed 221 patients with SSc who visited Vall d'Hebron Hospital from 1980 to 2016. 26 patients who were positive were compared with 195 who were negative. Different epidemiological, clinical, capillaroscopic and immunological variables were analysed.

Data from the Vall d'Hebron Hospital cohort were collected from patients diagnosed with ES since 1980. 24 patients with positive anti-RNAP III antibodies were

selected using the technique of immunoblot on paper or enzyme immunoassay and were compared with 151 who were negatives. Different epidemiological, clinical, capillaroscopic and immunological variables were analysed. Statistical analysis was performed using SPSS 20.0. Statistical significance was considered  $p < 0.05$ .

**Results:** 24 patients (13.7%) showed anti-RNAP III reactivity. Female sex (151, 86.3%) was the most frequent. There were no differences in the age at onset of the disease ( $40.3 \pm 15.9$ ) or in the age at diagnosis ( $46.6 \pm 15.7$ ). Diffuse cutaneous (Dc) subtype was more frequent in the anti-RNAP III group (70% vs 16.6%  $p < 0.001$ ). Patients with positive anti-RNAP III met the ACR/EULAR 2013 diagnostic criteria more frequently (24, 100% vs. 118, 78.1%  $p < 0.01$ ). Regarding the first manifestation, Raynaud's phenomenon was less frequent in the anti-RNAP III group (13, 54.2% vs. 121, 80.1%  $p < 0.01$ ). Regarding to vascular features, there were no differences in digital ulcers (15, 62.5% vs. 66, 43.7%,  $p = 0.08$ ), in the presence of Raynaud's phenomenon (24, 100% vs. 145, 96.7%) or telangiectasias (18, 75% vs. 102, 67.5%). There were no differences with respect to the overall digestive involvement (21, 87.5 vs. 124, 82.1%) No differences were found in cardiac involvement in both groups (9, 37.5% vs. 51, 47%). Scleroderma renal crisis (SRC) was significantly more frequent in patients with anti-RNAP III (3, 12.5% vs. 3, 1.9%  $p = 0.03$ ). There were no differences in prevalence of cancer (4, 16.7% vs. 12, 7.9%  $p = 0.24$ ). There were no differences in mortality (2, 8.3% vs. 16, 10.6%). The slow-type capillary pattern of Maricq was the most frequent in both groups (20, 83.3% vs. 132, 87.4%). Regarding the expression of other auto-antibodies, anti-Ro52 positivity was less frequent in patients with anti-RNAP III (2, 8.2% vs. 14, 9.3%  $p = 0.03$ ).

**Conclusions:** Patients with ES who presented positivity for anti-RNA polymerase III antibodies had more frequent onset manifestations different from the Raynaud's phenomenon, more DcSSc subtype and higher frequency of SRC. Regarding positivity against other antibodies, they expressed less reactivity to anti-Ro 52 than patients without anti-RNA pol III antibodies.

**Disclosure of Interest:** None declared

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#### AB0753 COMPARATIVE STUDY OF SYSTEMIC SCLEROSIS WITH OTHER AUTOIMMUNE DISEASES FOR HEALTH-RELATED QUALITY OF LIFE

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**Background:** Systemic sclerosis (SSc) is a rare autoimmune disease characterised by fibrosis of the skin and multiple internal organ involvement. Previous studies reported a poorer health-related quality of life (HRQoL) in patients with SSc compared to the general population. However, very little is known about HRQoL of SSc as compared with other systemic autoimmune diseases, including rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and Sjogren's syndrome (SJS)

**Objectives:** To compare the HRQoL of patients with SSc and other systemic autoimmune disease and general population.

**Methods:** HRQoL was captured by the Korean short form-36 health survey version 2 (SF-36), short form-6D (SF-6D) and 3 level version of EuroQol five-dimensional (EQ-5D) descriptive system (EQ-5D-3L). Between March and July 2017, consecutive patients with SSc, and randomly chosen patients with RA, SLE and SJS were recruited from the outpatient rheumatology clinics of Seoul National University Hospital, and were asked to answer SF-36 and EQ-5D. Disease activity of RA was evaluated by Disease Activity Score 28-ESR (DAS 28-ESR), SLE by Systemic Lupus Erythematosus Disease Activity Index-2k (SLEDAI-2k), and SJS by EULAR Sjogren's syndrome disease activity index (ESSDAI). For patients with SSc, Korean version of Health Assessment Questionnaire Disability Index (HAQ-DI) and Systemic sclerosis HAQ-DI (SSc HAQ-DI) were also evaluated. Demographic, clinical, laboratory information were obtained through a medical chart review. Data on representative Korean healthy controls were obtained from a study of psychometric properties of the Korean SF-36 v2 for assessing the general population, which was performed on six hundred healthy Koreans.

**Results:** A total of 480 patients with SSc (n=120), RA (n=120), SLE (n=120) and SJS (n=120) and 600 healthy controls were included. The demographic features of patients were similar to the known features of each rheumatic disease group. Patients with rheumatic diseases had significantly lower SF-36 scores ( $p < 0.001$  in all domains), SF-6D scores ( $p < 0.001$ ), EQ-5D-3L index scores and EQ-VAS ( $p < 0.001$ ) than the healthy controls; adjustments for age and sex did not change those results. Patients with SSc showed significantly lower scores in the mental component summary scores compared with patients with RA (age and sex-adjusted scores,  $43.0 \pm 0.9$  vs  $48.9 \pm 0.9$ ;  $p < 0.001$ ). Specifically, domain of mental health was lower in SSc patients than RA patients (age and sex-adjusted scores,  $61.3 \pm 1.8$  vs  $71.7 \pm 1.8$ ,  $p < 0.001$ ). Among the physical domains scores, SSc

patients showed lower score in general health domain than RA patients (age and sex-adjusted scores,  $41.4 \pm 1.8$  vs  $51.3 \pm 1.8$ ,  $p < 0.001$ ). Moreover, SSc patients reported remarkably lower scores of EQ-5D-3L index scores than all comparative rheumatic disease groups (RA, SLE, SJS) ( $p < 0.001$ ). HRQoL of patients with SSc was associated with HAQ-DI and SSc HAQ-DI.

**Abstract AB0753 – Table 1.** Comparisons of the SF-36, SF-6D and EQ-5D-3L, adjusted by age and sex in study subjects.

	Group					Anova <sup>1</sup>
	SSc (N=128)	RA (N=120)	SLE (N=128)	SJS (N=120)	Control (N=600)	
Physical function	70.5 (2.2)	70.3 (2.2)	68.2 (2.2)	73.9 (2.2)	82.4 (1.0)	<0.001
Role-physical	67.8 (2.3)	70.5 (2.3)	65.8 (2.3)	68.6 (2.4)	86.3 (1.1)	<0.001
Bodily pain	61.3 (2.2)	61.4 (2.2)	66.1 (2.2)	63.1 (2.3)	81.4 (1.0)	<0.001
General health	41.4 (1.1) <sup>2</sup>	51.3 (1.1)	44.2 (1.1)	45.8 (1.1)	61.9 (0.8)	<0.001
Vitality	53.2 (1.0)	51.8 (1.0)	49.7 (1.0)	45.8 (1.0)	64.4 (0.9)	<0.001
Social function	72.4 (2.1)	77.8 (2.1)	74.6 (2.1)	71.3 (2.1)	87.1 (1.0)	<0.001
Role-emotional	68.4 (2.3)	77.2 (2.3)	72.7 (2.3)	69.6 (2.4)	87.7 (1.1)	<0.001
Mental health	61.3 (1.1) <sup>2</sup>	71.7 (1.1)	67.2 (1.0)	63.7 (1.1)	75.2 (0.8)	<0.001
Physical component score	44.6 (0.3)	45.3 (0.3)	44.3 (0.3)	46.9 (0.3)	51.9 (0.4)	<0.001
Mental component score	43.0 (0.9) <sup>2</sup>	48.9 (0.9)	46.6 (0.9)	44.2 (0.9)	59.1 (0.5)	<0.001
SF-6D	0.70 (0.01)	0.73 (0.01)	0.72 (0.01)	0.71 (0.01)	0.79 (0.00)	<0.001
EQ-5D-3L index score	0.75 (0.01) <sup>2</sup>	0.81 (0.01)	0.82 (0.01)	0.83 (0.01)	0.90 (0.01)	<0.001
EQ VAS	63.98 (1.55)	69.95 (1.56)	67.49 (1.55)	64.84 (1.56)	77.88 (0.72)	<0.001



**Conclusions:** HRQoL of patients with systemic autoimmune diseases is significantly worse and affects all health domains in comparison to healthy controls. Patients with SSc have poorer HRQoL than patients with other rheumatic diseases. Specifically, SSc patients have more impaired mental health than RA patients, and the perception of an individual's general health is also poor compared to RA.

**Disclosure of Interest:** None declared

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#### AB0754 LONG-TERM FOLLOW-UP OF 214 PRIMARY RAYNAUD'S PHENOMENON PATIENTS

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**Background:** Raynaud's phenomenon (RP) is frequently associated with the presence of scleroderma or other connective tissue diseases (CTD). Identify the presence of secondary RP is important to perform an adequate therapeutic management and to achieve the early control of these patients. Nailfold capillaroscopy is safe, economic, and relatively easy to perform and has proven to be useful in identifying patients with secondary RP.

**Objectives:** To assess a long-term follow-up primary RP patient's series.

**Methods:** Retrospective observational study of a wide and unselected series of patients diagnosed as primary RP from a single university hospital from January 2012 to August 2017. Patients were classified as primary RP after the presence of CTD at the onset was excluded.

**Results:** We studied 214 patients (85.98% were female), with a mean age of  $47.6 \pm 16.7$  years (range 15–88). After a mean follow-up period of  $46.4 \pm 23.3$  months, 8 patients were diagnosed of a CTD (2 Scleroderma/Systemic sclerosis, 3 Systemic Lupus Erythematosus, 1 Rheumatoid arthritis and 2 Sjogren's syndrome). The remaining 206 patients continued classified as primary RP.

The main capillaroscopic patterns observed were: Normal ( $n=157$ ), unspecific ( $n=49$ ), scleroderma pattern ( $n=2$ ) and suggestive of other rheumatic diseases pattern ( $n=6$ ).

All patients who developed a CTD during the follow-up, showed changes in successive nailfold capillaroscopic examinations. 20 of 206 patients who remained primary RP showed minor changes at successive nailfold capillaroscopy. The main capillaroscopic changes detected on this group were: presence of capillary tortuosity ( $n=4$ ), presence of a decreased capillary density<sup>2</sup> and the presence of capillary bleeding ( $n=16$ ).

Antinuclear antibodies (ANA) were positive at the onset in 34 patients and after follow-up in 39 patients.

**Conclusions:** After a mean follow-up period next to four years, most of our primary RP patients remained free of CTD. A minority of our patients showed changes at nailfold capillaroscopy exam or positivity of ANA.

**Disclosure of Interest:** None declared

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#### AB0755 SKIN SCORE PROGRESSION AFTER DISCONTINUATION OF MYCOPHENOLATE TREATMENT IN SYSTEMIC SCLEROSIS PATIENTS

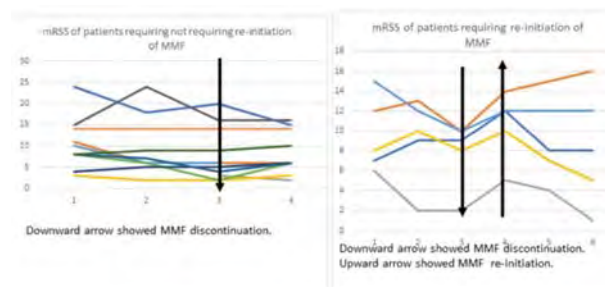
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**Background:** Rapid progressive skin involvement in diffuse Systemic Sclerosis (rp-dcSSc) is associated with higher mortality and internal organ involvement. Treatment with Mycophenolate Mofetil (MMF) has been shown to halt the progression of the disease. However, the optimal duration of therapy is unknown and has not been studied. We follow up a known cohort of rp-dcSSc patients treated with MMF after discontinuation of therapy.

**Objectives:** To describe the progression of skin involvement in rp-dcSSc patients after discontinuation of MMF

**Methods:** Twenty-five previously untreated consecutive patients with recent-onset (<24 mo) rp-dcSSc received MMF as the only disease-modifying therapy. Their Modified Rodnan skin score (mRSS) and Pulmonary function tests were followed after discontinuation of MMF after 2 years of treatment. Patients were followed up every 3–6 months. Therapy was re-initiated if their mRSS increased more than 20% or worsening respiratory symptoms with progression of restrictive lung disease were reported.

**Results:** Six patients lost follow up after terminating the open label trial with MMF. From the 19 patients followed up after MMF discontinuation, 26.3%<sup>5</sup> required to resume MMF. All these patients required to resume MMF within 6 months after discontinuation. All of them presented increase in mRSS. Two of them (10.5%) presented respiratory symptoms associated with restriction pattern at PFTs. Skin score returned to baseline in 80% of the patients after resuming therapy.



**Abstract AB0755 – Figure 1.** mRSS after MMF discontinuation.

**Conclusions:** Recurrent skin progression occurs in up to 26.3% of patients with rp-dcSSc after discontinuation of 2 years of MMF, requiring longer term immunosuppression. In this group, all patients presented active skin disease recurrence within 6 months of treatment discontinuation. Ergo, slow decrease of MMF dose over time and very close follow up is recommended in patients with rp-dcSSc discontinuing MMF even after a prolonged period of time. In addition, these findings support the therapeutic effect of MMF in rp-dcSSc.



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**AB0756** **MDA 5 DERMATOMYOSITIS AND RESPONSE TO RITUXIMAB IN A SMALL COHORT AT OUR INSTITUTION**

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**Background:** Treatment for anti-melanoma differentiation-associated gene 5 antibody (MDA 5) Dermatomyositis is posing challenging to clinician and there is currently no consensus on therapy. The MDA5 was recently classified as a myositis-specific antibody (MSA), and has been associated with rapidly progressive interstitial lung disease (ILD), amyopathic dermatomyositis (ADM), mechanic's hands, ulcerations, inflammatory arthritis, and increased mortality.

**Objectives:** This study sought to characterised response to Rituximab in a small cohort of patients with MDA 5 DM at our institution.

**Methods:** A retrospective chart review was done to identify all MDA5 positive patients who were evaluated at our centre from 2015 to 2017 with suspected myositis and had myositis-associated autoantibodies tested using a commercial panel (MyoMarker Panel 3). For all patients who were positive for MDA5, we collected clinical information on the presence of myopathy, skin involvement and ILD, data on the autoantibody profile, PFTs and high resolution CT pattern along with therapy response.

**Results:** 11 were positive for MDA5. 7 were females and 4 were males, with mean age 56.6 years. Eight patients were treated with Rituximab from which seven had ILD at presentation: 4 NSIP, 2 with organising pneumonia, one had UIP and one had fatal acute interstitial pneumonitis 2 months after onset of mechanics' hands and inflammatory arthritis. Three patients without ILD were treated with other DMARDs.

All had responded well to Rituximab with improvement in skin ulceration, inflammatory arthritis and mechanics' hands and most patients had stable ILD except for one patient with fulminant interstitial pneumonitis for with Cytoxan was added without any additional benefit.

**Conclusions:** Rituximab is a good management option for all manifestation of MDA 5 DM. Further studies are needed to elucidate the association of MSA and the clinical manifestations and response to treatment response of patients with inflammatory myopathies.

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**AB0757** **PERSISTENT CRP ELEVATION IS ASSOCIATED WITH HIGH MORBIDITY IN SYSTEMIC SCLEROSIS**

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**Background:** Elevated levels of C-reactive protein (CRP) in systemic sclerosis (SSc) have been linked to early inflammatory stages of the disease.

**Objectives:** This study has been set to investigate CRP levels in a longitudinal cohort of SSc patients and to correlate these findings to comorbidities and disease characteristics.

**Methods:** In this retrospective study patients with SSc were recruited from the outpatient clinic of the Department of Rheumatology and Clinical Immunology, University Medical Centre Freiburg. Only patients with at least three consecutive visits at our centre over at least one year were included in this study. CRP serum levels were measured at every visit and categorised as positive if CRP concentrations were  $\geq 5$  mg/L. Subjects with elevated CRP levels at more than 80% of visits

were defined as being persistently positive. The longitudinal CRP profile was correlated to comorbidities and disease characteristics.

**Results:** A total of 1852 consecutive visits of 131 SSc patients were analysed. Over the observed time span (91<sup>136–56</sup> months) 19% (n=25) of patients had continuously elevated CRP levels, whereas in 29% (n=38) CRP levels were always in the normal range. There was no association between disease duration and CRP levels at first visit ( $p>0.5$ ). Persistent CRP elevation was associated ( $p<0.05$ ) with anti-topoisomerase I-antibodies, diffuse cutaneous SSc (dcSSc), modified Rodnan skin score (mRSS), pulmonary fibrosis, and cardiac arrhythmia, whereas no associations with arthritis or malignancy were found ( $p>0.1$ ). In a patient with dcSSc and persistent elevated CRP even cyclophosphamide and autologous stem cell transplantation did not alter CRP levels.

**Conclusions:** Persistently elevated CRP levels characterise a more severe fibrotic phenotype and a higher prevalence of cardiac arrhythmias.

**Disclosure of Interest:** None declared

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**AB0758** **EVALUATION OF NAILFOLD VIDEO CAPILLAROSCOPY IN 296 PATIENTS WITH CONNECTIVE TISSUE DISEASES**

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**Background:** The influence of the presence of Raynaud's phenomenon (RP) on microangiopathy is not well characterised in connective tissue diseases (CTDs).

**Objectives:** To characterise capillary density and capillary morphology by nailfold video capillaroscopy (NVC) in different CTDs with a special focus on the presence/absence of Raynaud's phenomenon (RP) and overlap syndromes.

**Methods:** 296 patients with systemic sclerosis (SSc), systemic lupus erythematosus (SLE), idiopathic inflammatory myopathies (IIM), Sjogren's syndrome (SS), antiphospholipid syndrome (APS), rheumatoid arthritis (RA), systemic vasculitis and undifferentiated connective tissue disease (UCTD) were investigated by NVC. Control groups consisted of 25 healthy controls (HC) and 22 primary RP (PRP) cases.

**Results:** The mean capillary density was significantly decreased in SSc, SLE, SS, IIM and APS either compared to HC or PRP cases. Mean microangiopathy evolution score (MES) was higher in SSc, SLE, SS, IIM and APS compared to both HC and PRP cases. SSc, SLE, SS patients had a significantly higher giant capillary number compared to either HC or primary RP control cases. Average haemorrhage score was significantly higher in SSc and SS but not in SLE, RA, IIM and APS compared to HC. Average dilatation point was higher in all investigated CTDs compared to HC. Except RA, all investigated CTDs showed significantly higher capillary loss score compared to either PRP controls or HC. RA cases showed such a difference only compared to HC. Average disorganisation score was significantly higher in all CTDs compared to HC but not compared to PRP cases. Ramification score was significantly elevated in SSc and IIM compared to PRP and HC, but no difference was observed in SLE, SS, APS and RA. The mean capillary density was decreased, and MES was higher in RP associated cases compared to patients without RP in cases with SLE, IIM, and RA. Conversely, the presence of RP did not influence these particular parameters in cases with APS and SS. Except SSc, the impact of overlap features was not remarkable on major capillaroscopic findings. SSc capillary pattern was present in 75.3% of all SSc cases, most commonly SSc late pattern was observed (58.43%). SSc pattern was present in other CTD cases too (15.4%–40.7%). SSc patients with a DLCO<70% had significantly more giant capillaries, avascularity, late SSc pattern, increased MES, and lower capillary density compared to cases with DLCO>70%, but in the other CTDs decreased DLCO was not associated with similar pronounced capillary damage.

**Conclusions:** Microangiopathy with decreased capillary density and increased MES were present in all CTDs compared to controls. RP caused most pronounced impairment in SLE, IIM and RA compared to non-RP patients, but had no major effect on SS, and APS. Except SSc, the presence of overlap syndrome did not show a remarkable influence on the microvascular abnormalities compared to pure idiopathic cases. SSc late pattern was most frequently observed in CTDs other than SSc, and it may appear even in patients without RP. Previous associations shown by other authors of decreased DLCO and capillary damage in SSc was confirmed. Capillaroscopy is useful not only in IIM and SSc patients but also in all SLE cases and RP associated SS and RA patients. Capillary density and MES are the most valuable parameters.

**Disclosure of Interest:** None declared

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AB0759

### THE ASSESSMENT OF GASTROINTESTINAL TRACT INVOLVEMENT THROUGH UCLA SCTC GIT 2.0 QUESTIONNAIRE IDENTIFIES SCLERODERMA PATIENTS WITH REDUCED BONE MINERAL DENSITY

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**Background:** Gastrointestinal (GI) symptoms are seen in majority of patients with Systemic Sclerosis (SSc) and are a common presenting feature of disease. Severe GI involvement may lead to malabsorption which represents a poor prognostic factor. Accordingly, a regular monitoring of gastrointestinal tract involvement and nutritional status appears crucial in SSc patients. Previous studies reported low values of bone mass density (BMD) in SSc patients<sup>1</sup>. While no specific relationship has emerged between the two conditions, it's likely that disease related GI involvement may contribute to the alterations in BMD.

**Objectives:** To determine if GI-related clinical status was associated to low bone density in our cohort of SSc patients.

**Methods:** Two-hundred-ten unselected SSc patients have been enrolled. The 7-items UCLA SCTC GIT 2.0 questionnaire and Malnutrition Universal Screening Tool (MUST) were administered to each patient. A comprehensive medical history was collected. A blood panel for nutritional status was also performed. T-scores and Z-scores at lumbar spine, femoral neck, Ward's and total hip measured by dual-energy X-ray absorptiometry (GE Lunar Prodigy) were measured.

**Results:** In our cohort, 86.7% of patients reported some GI symptoms. The mean UCLA GIT total score was 0.345±0.34 and 51 patients (24.3%) were at risk of malnutrition according to MUST (score ≥1). 53.7% patients had BMD values <1, and 12.5% had BMD values ≤-2.5 at any of the considered sections. Patients with reduced BMD (<-1) showed similar levels of selected nutritional blood markers compared to subjects with normal BMD, including vitamin D and albumin. Patients with spine T-score <-1 had lower BMI (23.2±3.9 vs 25.2±4.8; p=0.011) and reported higher UCLA GIT reflux (0.66±0.63 vs 0.42±0.48; p=0.016), distention (0.80±0.72 vs 0.53±0.56; p=0.15) and total score (0.42±0.37 vs 0.27±0.30; p=0.006) compared to patients with normal BMD. Similar significant differences were observed in the same domains for patients with total hip T-score values <-1. Femoral neck T-score <-2.5 was associated with higher UCLA GIT reflux (0.88±0.78 vs 0.48±0.50; p=0.022), soilage (0.50±0.78 vs 0.14±0.52; p=0.041) and total score (0.50±0.37 vs 0.31±0.33; p=0.012).

On the other hand, the comparison of patients with severe, moderate and mild symptoms according to UCLA GIT total score<sup>2</sup> showed an association between progressively lower values of spine and total hip T-score and increasing severity of GI symptoms (ANOVA for spine T-score: p=0.015; for total hip T-score: p=0.048).

Patients at risk of malnutrition (MUST score ≥1) presented significant lower T-score for all the considered sections (spine and hip) and significant lower total hip Z-score.

**Conclusions:** In our SSc cohort gastrointestinal symptoms were frequent and were associated with low BMD. Considering the heterogeneity of GI involvement, UCLA SCTC GIT 2.0 emerged as a useful and feasible tool to assess GI involvement and other associated comorbidities. In particular, SSc patients who report remarkable GI symptoms and are at risk of malnutrition according to MUST may benefit from a stricter control of BMD to promptly detect osteopenia and osteoporosis.

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AB0760

### ADVANCED OXIDATION PROTEIN PRODUCTS IN SERUM OF PATIENTS WITH SYSTEMIC SCLEROSIS: A POSSIBLE INDICATOR OF CLINICAL EVOLUTION

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**Background:** Systemic sclerosis (SSc) is a chronic, multisystem connective tissue disease characterised by immune dys-regulation, obliterative microvasculopathy and fibrosis. Endothelial dysfunction, immune system imbalance and fibroblast activation constitute the three major factors of the pathogenetic process. In this context, oxidative stress could play a significant role through direct damage of endothelial cells and the persistent activation of the immune system.<sup>1,2</sup>

**Objectives:** This study investigated the presence of advanced protein oxidation products (AOPP) in serum of patients with SSc and its correlation with disease's features.

**Methods:** 50 patients with SSc (M:F 1:7, mean age 57.3±11.2 SD, mean duration of disease 10±9.1 SD years), were screened for AOPP in the serum, using the AOPP OxiSelect Kit of CELL BIOLABS (San Diego, Ca, USA). Among 50 SSc patients, 39 had limited cutaneous subset, while 11 had the diffuse one. Anamnestic and clinical data were collected for all SSc patients. As a control group 50 consecutive healthy subjects, sex and age matched, were recruited.

**Results:** We found serum levels of AOPP increased in the SSc group compared with the controls (p<0.0001) with mean values of 336.9±167.8 mmol/L and 167.5±59.2 mmol/L, respectively. In addition, higher levels of AOPP directly correlated with the diffuse cutaneous subset (p=0.0242), presence of digital ulcers (p=0.005), esophagopathy (p=0.006) and pulmonary fibrosis (p=0.0128).

**Conclusions:** Serum AOPP levels are significantly higher in patients with SSc than in controls. In addition, the correlations of AOPP with SSc diffuse cutaneous subset, digital ulcers, and pulmonary involvement (indicative of progressive disease and worse prognosis) suggest a possible role of this marker in the identification of the cases with worse clinical evolution. The data of this preliminary study should be confirmed on larger case series and analysed in prospective studies, in order to understand its eventual usefulness during the follow-up of SSc patients.

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AB0761

### FOLLOW-UP OF NAILFOLD MICROVASCULAR DAMAGE IN MIXED CONNECTIVE TISSUE DISEASE VERSUS SYSTEMIC SCLEROSIS PATIENTS

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**Background:** Nailfold videocapillaroscopy (NVC) is a non invasive diagnostic technique useful for evaluating microvascular status in patients with connective tissue diseases.<sup>1</sup> In systemic sclerosis (SSc) capillary abnormalities, when evaluated by NVC, evolve in a clearly defined sequence called the "scleroderma patterns" (Early, Active, Late).<sup>2</sup> On the contrary, mixed connective tissue disease (MCTD) doesn't show characteristic either nailfold capillary abnormalities or typical sequence.<sup>1,2</sup> Until today, few studies described the main NVC changes in MCTD.<sup>3</sup>

**Objectives:** To retrospectively study nailfold microangiopathy by NVC in MCTD patients with a follow-up of three years and to compare capillaries abnormalities between patients affected by MCTD and SSc.

**Methods:** Ten patients (mean age 50±19 years) affected by MCTD with Raynaud phenomenon (Kasukawa's criteria)<sup>4</sup> who performed their first NVC were enrolled. Among these, complete capillaroscopic and clinical data at three years were available for 7 patients (disease duration 6.4±4.2 years). Main NVC parameters (absolute number of normal and total capillaries and scores of capillary ramifications, enlarged capillaries, giant capillaries, microhemorrhages, number of capillaries) were evaluated by NVC at baseline (T0, first NVC), and after one (T1) and three years (T3). Possible variations of capillary findings were analysed, along with correlations among capillaroscopic and clinical parameters. Furthermore, we compared main NVC parameters at T0 of ten above-mentioned MCTD patients versus ten random SSc patients with the same disease duration (6.4±4.2 years) and similar age (51±17 years). Statistical analysis was performed by non parametric tests. The patients were receiving different immunosuppressive treatments.

**Results:** No statistically significant variation of the scores as well as of the absolute value of the above reported capillary parameters was observed during the 3 years of follow-up. No statistically significant correlation was observed between capillary parameters and MCTD clinical aspects (Raynaud phenomenon, dysphagia, dyspnoea, sclerodactyly, sicca syndrome, telangiectasies and arthralgia) at first visit and during follow-up. The scores of enlarged capillaries and giant capillaries were found significantly higher (p<0.05) in patients with SSc versus MCTD patients at T0. Moreover, the absolute number of total capillaries and normal capillaries were found significantly lower (p<0.05) in SSc patients versus MCTD patients. On the contrary, no statistically significant difference was observed for

the other capillary parameters (capillary ramification, microhemorrhages) between the two groups of patients.

**Conclusions:** In a limited cohort of MCTD patients with an average disease duration of 6.4 years and a follow-up of three years, the nailfold microangiopathy does not seem to be significantly progressive. Patients with MCTD seem to show less enlarged/giant capillaries, and larger absolute number of total and normal capillaries than SSc patients. Still difficult to identify a defined NVC pattern in MCTD patients.

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#### AB0762 RELATIONSHIP OF THE SIX MINUTE WALKING TEST AND QUALITY OF LIFE IN PATIENTS WITH SYSTEMIC SCLEROSIS

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**Background:** The six minute walking test (6MWT) is a standardised measure of submaximal exercise capacity. It is a surrogate measure of heart and lung involvement. There are no studies on relationship between 6MWT and quality of life evaluated by Short form 36.

**Objectives:** To evaluate the relationships between of the 6 min walking distance (6MWD) and each items of SF36

**Methods:** Fifty consecutive SSc patients were investigated. They underwent 6MWT and complete the SF-36 (assessed the 8 domains of the questionnaire as well as the physical component score-PCS and mental component score-MCS).

**Results:** 6MWD ranged from 253 to 582 (median 420); we listed the correlations from 6MWT and only the statistically significant features of SSc and the items of SF36

Age: median 48 (range 20–72); Rho  $-0.51$ ;  $p < 0.00001$

EScSG Activity Index: median 0.5 (range 0–5); Rho  $-0.33$ ;  $p 0.009$

HAQ-DI: median 0.375 (range 0–2.275); Rho  $-0.26$ ;  $p 0.048$

mRSS: median 2 (range 0–17); Rho  $-0.35$ ;  $p 0.007$

Pulmonary hypertension (echocardiography): median 30 (range 13–80); Rho  $-0.26$ ;  $p 0.048$

SF36: PCS: median 43 (range 20–65); Rho  $0.41$ ;  $p 0.0016$

PF: median 75 (Range 0–100); Rho  $0.40$ ;  $p 0.002$

GH: median 50 (range 10–92); Rho  $0.43$ ;  $p 0.0007$

**Conclusions:** Our study first demonstrates that 6MWT is correlated to some aspects of quality of life as measured by SF36 in the SSc patients. This results must be considered when assessing 6MWT in SSc.

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#### AB0763 BIOELECTRICAL IMPEDANCE ANALYSIS FOR THE ASSESSMENT OF BODY COMPOSITION IN PATIENTS WITH SYSTEMIC SCLEROSIS

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**Objectives:** The aim of the present study was to evaluate the body composition by bioelectrical impedance analysis (BIA) and to assess the nutritional status by BMI and possible correlations with epidemiological and clinical characteristics in patients with SSc

**Methods:** Malnutrition was defined as BMI  $< 18.5$  kg/m<sup>2</sup> or unintentional weight loss  $> 10\%$  in combination with a fat-free mass index (FFMI)  $< 15$  kg/m<sup>2</sup> for women or  $< 17$  kg/m<sup>2</sup> for men or BMI  $< 20.0$  kg/m<sup>2</sup> (age  $< 70$  years) or  $< 22$  kg/m<sup>2</sup> (age  $> 70$  years). Body composition was assessed in 40 patients (female) (age mean  $\pm$ sd:  $45.2 \pm 12.2$ ) and 20 healthy controls (age mean  $\pm$ sd  $41.5 \pm 5.3$ ) with BIA

(Akern, Italy) and BMI. The manufacturer's equation and the Geneva equation were used to estimate fat mass (FFM).

In addition, correlations with disease activity, gastrointestinal severity, disease subset, autoantibody profile, skin score were evaluated.

**Results:** Malnutrition was found in 10% of patients vs 8% of healthy controls; and low FFMI in 30% of patients vs 10.5% of HC. Bioimpedentiometry showed a Fat Free Mass (FFM) (metabolically active component of fat free mass) reduced in patients compared to controls ( $46.8 \pm 7.6$  vs  $53.6 \pm 6.3$  respectively;  $p = 0.01$ ). Furthermore, with the same instrument a lower basal metabolic rate was found in patients compared to controls:  $1462 \pm 145$  vs  $1720 \pm 169$  calories ( $p = 0.001$ ). The correlations between FFM and basal metabolism with the clinical features of the patients were not statistically significant

**Conclusions:** This study confirms the study of Spanjer MJ et al<sup>1</sup> and shows a relatively low prevalence of malnutrition in comparison with other studies, but a high prevalence of low FFMI, underlining the necessity of measuring body composition in SSc patients with a standardised and validated method. Furthermore, Caporali et al,<sup>2</sup> have shown an alteration of the nutritional status of patients of SSc probably related to a gastro-intestinal commitment. In our patients despite the presence of an apparent good nutritional status the use of bioimpedanceometry revealed a different body composition, a lower share of muscle mass, in patients compared to controls, related, in part, to musculoskeletal involvement by systemic sclerosis (increase in muscle catabolism and/or poor nutrient supply due to malabsorption phenomena). The early detection of such alterations could be useful to insert subjects at risk in physical rehabilitation programs.

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#### AB0764 COMPARISON OF DISEASE CHARACTERISTICS IN PATIENTS WITH JUVENILE-ONSET AND ADULT-ONSET PROGRESSIVE SYSTEMIC SCLEROSIS

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**Background:** Progressive systemic sclerosis (PSSc) has been known to affect mainly adults of 30–50 years of age. Juvenile-onset has been reported to be rare and studies comparing clinical differences between juvenile-onset and adult onset form have been limited.<sup>1</sup> These studies were coming from European and North American countries.<sup>1–2</sup> As there would be also effects of ethnic differences, we aimed to assess clinical differences between the two forms of pSSc of paediatric and adult rheumatology centres of a tertiary centre, in Turkey.

**Methods:** Adult onset patients were defined as those who were registered and followed as 'scleroderma' at the departments of adult and paediatric rheumatology at Cerrahpasa Medical Faculty, Istanbul, between 2005 and 2017. Only those with at least 2 follow-up visits were included. Patients's charts were re-evaluated retrospectively.

Abstract AB0764 – Table 1

	Adult onset, n=137	Juvenile onset, n=26	P
Age at disease onset, mean $\pm$ SD	38.6 $\pm$ 13.4	10.1 $\pm$ 4.3	-
Age at diagnosis, mean $\pm$ SD	43.6 $\pm$ 14.0	11.4 $\pm$ 3.2	-
Follow-up duration, med. [IQR], years	5 [2.0–7.0]	4 [2.5–6.0]	NS
Male/Female	20/117	2/24	NS
Familial history of chronic inflammatory diseases, n (%)	20 (14.6)	4 (15.4)	NS
Sclerodactyly, n (%)	128 (93.4)	25 (96.2)	NS
Raynaud phenomenon, n (%)	135 (98.5)	24 (92.3)	NS
Digital ulcers, n (%)	55 (41.4)	14 (54.0)	0.001
Interstitial lung disease, n (%)	71 (52.2)	6 (24.0)	0.009
PAH, n (%)	20 (14.9)	0	0.045
Arrhythmia/heart failure, n (%)	14 (10.4)	1 (4.0)	NS
Joint involvement, n (%)	20 (14.9)	13 (50.0)	<0.001
Skeletal muscle involvement/myopathy n (%)	10 (7.5)	7 (28.0)	0.002
Gastrointestinal system involvement, n (%)	42 (31.8)	8 (32.0)	NS
Arterial hypertension, n (%)	24 (18.2)	0	0.015
ANA positivity, n (%)	119 (93.0)	18 (75.0)	0.007
DMARD use, n (%)	90 (65.7)	25 (96.2)	0.002
Vasodilators, n (%)	113 (82.5)	13 (50.0)	<0.001

**Results:** There were 140 patients with scleroderma in the adult outpatient clinic records and 51 in the paediatric clinic records. Of these patients, 3 (2%) adults



and 25 (49%) paediatric patients had localised scleroderma ( $p < 0.001$ ). We studied the remaining patients (adults:  $n = 137$ , juvenile:  $n = 26$ ) who had systemic pattern. Male/female ratio, median follow-up duration, familial history of chronic inflammatory diseases and the frequency of sclerodactyly, digital ulcers, Raynaud phenomenon, arrhythmia/heart failure and gastrointestinal involvement were similar between two groups (table 1). The frequency of interstitial lung disease, pulmonary artery hypertension, and serum ANA positivity were significantly more common in the adult onset group. Whereas joint and muscle involvements were significantly more common among juvenile onset patients. DMARD use was significantly more common in the juvenile group while the use of vasodilators was more frequent among adults<sup>1</sup>

**Conclusions:** Our results are online with previous reports: juvenile onset patients seem to have a milder form of disease. Major organ involvement as defined interstitial lung disease and pulmonary artery hypertension was more common among adult onset patients. On the other hand, as expected, joint involvement and myopathy were major causes of morbidity in the juvenile group. Contrary to that previously reported, cardiac involvement was not common in the juvenile group.

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#### AB0765 DEVELOPMENT AND ASSESSMENT OF A STRUCTURED TRAINING PROGRAM FOR PATIENTS WITH SYSTEMIC SCLEROSIS

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**Background:** Structured patient education programs are a key element of patient care in many chronic diseases. They are often based on the Stanford University chronic disease self-management program and aim to empower patients and to improve compliance and coping abilities. However, not in every condition self-management education programs yield the expected benefit.<sup>1</sup>

**Objectives:** To develop a structured patient education program for SSc patients and to prove training-specific effects on patients' quality of life and disability.

**Methods:** We developed a structured patient education program. The content of the program was created by a team of rheumatologists and dermatologists. The program consists of three modules focusing on general knowledge about the disease, gastrointestinal involvement, digital ulcers (DU), skin and wound care and a patient diary on disease symptoms. Patients were either included in the intervention or in the control group. Disease symptoms and severity as well as clinical parameters were assessed at baseline (intervention and control), at the follow-up visit at month 3 (intervention only) and at the final follow-up visit at month 6. In the intervention group satisfaction with the education program was analysed.

Primary outcome measures were SHAQ, SF-12, BFI, SHAQ\_DU. Secondary outcome measure was the satisfaction survey. For comparisons between different times analysis of variance for repeated measures was used. For description of cohorts Mann-Whitney Wilcoxon test was used.

**Results:** 58 SSc patients were included, 27 received the educational program (intervention group) and 31 patients served as a control group. Both groups were matched regarding demographics and disease subtype. Incidence of DUs was significantly higher in patients from intervention group resulting in a more frequent administration of vasoactive therapies. SHAQ, SF-12, BFI, SHAQ\_DU were comparable between control and intervention group. However, patients in the intervention group rated the training program as helpful and reported an increase in knowledge about their disease afterwards. A positive impact of the training program on SHAQ, SF-12, BFI, SHAQ\_DU was observed in individual patients.

**Conclusions:** Patients who participated in the training were overall satisfied with the program. However, no significant effects on quality of life after the intervention were observed. One reason for this finding might be the disease duration (mean 11.5 years). This needs to be further analysed in a consecutive study considering patients with shorter disease duration.

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**Disclosure of Interest:** None declared

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#### AB0766 INITIAL CHARACTERISATION OF WOMEN WITH BREAST IMPLANTS IN A GROUP OF PATIENTS WITH SYSTEMIC SCLEROSIS REFERRED FOR AUTOLOGOUS HSCT

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**Background:** The causal relationship between breast implants (BI) and systemic sclerosis (SSc) is still strongly contested.

**Objectives:** To add further input to this medical controversy, we studied the initial clinical characteristics of patients with breast implants and systemic sclerosis that are referred to our centre for autologous hematopoietic stem cell transplant.

**Methods:** From 163 patients, with the diagnosis of systemic sclerosis (SSc), limited SSc, CREST, Morphea or scleroderma sine scleroderma, referred to our centre for autologous hematopoietic stem cell transplantation, 132 were found to be females. To identify those with breast implants (BI) or have a history of breast implants, we performed a systemic chart review for all patients. Once the patients with actual breast implant devices or have history of breast implants were identified, alive patients were contacted to check the type of their breast implants (silicone vs saline), the year of insertion, the local complications, whether they were removed or replaced and the year of removal and replacement, and the type of replacement if applicable. Clinical and biological data were collected for all patients and were compared between those who have breast implants or history of breast implants and those who do not have.

**Results:** From 132 patients with SSc or SSc variants, thirteen had history of BI (9.8%). In 12, the breast augmentation therapy preceded the development of SSc, with median time between BI insertion and the emergence of initial symptoms of SSc of 12 years (range 7–29). The remaining patient showed acceleration of her disease after BI surgery. Surprisingly, in all 12 patients for whom we could know the type of initial implants, the prostheses were saline. When we compared the clinical characteristics of those with BI and those without. Patients with BI appeared to have higher age (mean 49.95 vs 44.42 years,  $p = 0.012$ , shorter time from initial symptoms to diagnosis (mean 4.76 vs 12.24 months,  $p = 0.0001$ ), more frequently positive ANA (13/13 vs 89/114,  $p = 0.06$ ) and more frequently positive anti RNA polymerase III (7/10 vs 20/78,  $p = 0.004$ ).

**Conclusions:** Our data may support the hypothesis of a possible association between BI and SSc. Furthermore, these results raise questions regarding the safety of saline breast prosthesis. Finally, our finding may indicate a possible difference in the initial characteristics of SSc patients with BI and those without.

**Disclosure of Interest:** None declared

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#### AB0767 EFFICACY OF SUBCUTANEOUS TOCILIZUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS AND SYSTEMIC SCLEROSIS OVERLAP SYNDROME

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**Background:** Systemic sclerosis (SSc) is a connective tissue disease that develops sclerotic changes in the skin and visceral organs. SSc is a disease of uncertain etiology, and is characterised by fibrotic changes. Pulmonary, cardiac, gastrointestinal, and renal complications contribute to patient morbidity and decreased survival<sup>1</sup>. And patients present with stiffness of the limbs because of sclerosis and joint swelling in the skin and periarticular connective tissues. Interleukin-6 (IL-6) is a pleiotropic factor that plays a major role in inflammation; furthermore, IL-6 overexpression and pathogenicity in SSc have been demonstrated<sup>2</sup>. IL-6 expression is reportedly high in both the skin and serum of SSc patients<sup>3</sup>, and its elevation depends on the skin score<sup>4</sup>. And it is a candidate factor that can reproduce the pathological conditions of SSc as well as RA.

**Objectives:** We report the cases of rheumatoid arthritis (RA) patients with SSc who was administered anti-interleukin-6 receptor antibody tocilizumab (TCZ).

**Methods:** Two RA with refractory SSc patients were administered tocilizumab at 162 mg/kg twice a month for 12 months. RA disease activity is evaluated by DAS28-ESR and CDAI. Skin condition of SSc is evaluated by pinching the skin according to the modified Rodnan total skin score (mRTSS).

**Results:** They were both female, and age at the time of SSc diagnosis was 74 (patient 1) and 51 (patient 2) years old. The time lapse since SSc diagnosis was at first visit and 14 years, respectively. And it since RA diagnosis was 14 years and 6 years, respectively. Tocilizumab was administered at 162 mg every 2 weeks, which is equal to the dosage used for RA. Administration of prednisolone at 5 mg/day and DMARDs were continued. Overall, TCZ was well tolerated, and both patients experienced a general improvement in coping with normal daily activities. During the 12 month tocilizumab therapy, both RA disease activity and mRTSS decreased. The patient global assessment improved by 70 (75 to 5) and 44 (68 to 24) in patients 1 and 2 in 12 months, respectively. In RA disease activity, DAS28 decreased from 5.66 to 1.73 in 12 months in patient 1 and 7.14 to 4.43 in

patient 2. CDAl decreased from 31.8 to 7.4 in 12 months in patient 1 and 34.6 to 10.7 in patient 2. Skin thickness evaluated with the 17 site modified Rodnan skin score improved in patient 1 (from 23 to 2) and patient 2 (from 15 to 8) in 12 months.

Adverse reactions were observed cellulitis in right foot planter at 6 week treatment in patient 2. She did withdrawal tocilizumab for 4 week. After cure cellulitis, she continued tocilizumab treatment.

**Conclusions:** In the two cases of RA with SSc that we report here, softening of the skin was observed during the treatment with tocilizumab. Tocilizumab may be effective against RA and SSc for which conventional treatment is inadequate.

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#### AB0768 OSTEOMYELITIS COMPLICATING DIGITAL ULCERS IN SYSTEMIC SCLEROSIS

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**Background:** Skin ulcers are a frequent manifestation of systemic sclerosis (SSc). Skin ulcers are painful, represent a cause of disability and heavily affect patients' quality of life. The presence of local infection may be responsible for osteomyelitis (OM) of the underlying bone. If gangrene develops, surgical amputation may be required. At the moment is not clear if there are predisposing factors to osteomyelitis development.

**Objectives:** To describe a population of SSc patients affected by cutaneous ulcers and osteomyelitis

**Methods:** We collected data of SSc patients satisfying the 2013 ACR criteria for SSc referring to our outpatient clinic from January 1st 2016 to December 31st 2017. The patient's data were evaluated on the basis of individual clinical records, including demographic, clinical and serological findings. Cutaneous ulcers were defined as epithelial loss and loss of dermis; post-traumatic skin lesions were excluded. In cases suspected of infection, microbiological investigations were carried out. We have diagnosed OM by clinical, radiological and laboratory means, in particular the presence of pain, swelling, fever, erythema, purulent secretions, blood chemistry alterations and typical radiological characteristics at either plain X ray and/or MRI. Statistical analysis was performed using STATA software for descriptive analysis and groups comparisons. Given the low number of events only univariate analysis was conducted.

**Results:** A total of 189 patients were enrolled in the study. Of them, 21 (11.1%) were males, mean age was 64.39±12.5 years and median disease duration 11.59 (5.6–19.3) years. A diffuse cutaneous (dcSSc) involvement was present in 50 (26.5%), limited cutaneous (lcSSc) in 131 (69.3%) and a limited disease in 8 patients (lSSc) (4.2%). Digital ulcers (DU) were present in 29 patients (15.3%) and in 5 cases (2.6%) were complicated by the occurrence of OM. The pathogens responsible of the infections were isolated in 3/5 (60%) cases and were represented by: Methicillin-sensitive Staphylococcus Aereus (2 cases) and P. Aeruginosa, also multisensitive. OM affected the third finger of right hand in 2 (40%) patients, the second finger of right hand in 1 (20%) patient and the third finger of left hand in 2 patients (40%). In 2 cases (40%) surgical amputation had to be performed. Patients with OM were significantly younger (54.9±16.07 vs 64.65 ±12.34, p 0.0432) and had higher CRP levels than the rest of the patients (1.27 ±0.59 vs 0.42±0.74, p 0.0061) In patients with DU, the only predictive factor for the development of OM was the total number of ulcers in the single patient (OR 2.27, 1.39–3.71, p<0.001) while no significant influence was found for other demographic or disease specific parameter.

**Conclusions:** OM is a severe complication of DU in SSc. In most cases the aetiological agents are community-acquired pathogens. SSc patients with OM were younger but did not show any other obvious distinguishing feature. The number of ulcers in the single patients were predictive of OM development. Further and larger studies are needed to address this aspect of the microvascular involvement of SSc.

**Disclosure of Interest:** None declared

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#### AB0769 SCLERODERMA MIMICS IN COHORT FROM AN EUSTAR CENTRE

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**Background:** The differential diagnosis of systemic sclerosis (SSc) can be sometimes challenging, especially when you have symmetrical skin thickening, Raynaud's phenomenon (RP) or acroosteolysis. When symptoms and signs are unclear, patients should be referred to a specialist centre for assessment to differentiate between scleroderma and its mimics.

**Objectives:** Assessing the types of scleroderma mimics presenting in a tertiary care centre and underlining the diagnosis difficulties.

**Methods:** We evaluated a cohort of 140 patient admitted in our clinic with the suspicion of SSc from January 2007 until December 2017. 130 of them are with SSc and 10 patients with scleroderma mimics. The patients were evaluated for quality and distribution of skin involvement, the presence of systemic complications, the presence of scleroderma specific antibodies and the capillaroscopic pattern. If they haven't met any criteria for SSc, they underwent further specific investigations.

**Results:** From the 140 patients evaluated, 10 (7,14%) were with scleroderma mimics. All these 10 patients were admitted in our clinic with the suspicion of SSc. 3 of them had severe RP, one had acroosteolysis and 6 had symmetric skin thickening. There were 4 males and 6 females. All the patients had no organ involvement (pulmonary arterial hypertension or pulmonary fibrosis), normal capillaroscopic pattern and negative antinuclear antibodies and negativespecific scleroderma antibodies. The patients with RP had no skin sclerosis or other clinical or laboratory changes and the diagnostic was primary RP. The patient with acroosteolysis had no skin sclerosis or RP and after genetic testing a diagnosis of Hajdu-Cheney syndrome was made. The 6 patients with skin thickening had no RP. There were 2 patient with solvent induced scleroderma, 2 with scleroedema adutorum, 1 with scleromixedema, 1 with eosinophilic fasciitis. The 2 patients with solvent induced scleroderma had sclerodactily and one of them the "prayer sign" and they had a complete resolution of skin sclerosis after eliminating the solvent exposure after a few years of follow up. The 2 patients with scleroedema adutorum had no underlying gammopathy or infections. The patient with eosinophilic fasciitis had extended skin thickening with eosinophilia ant typical aspect on MRI, with partial clinical resolution after immunosupresion. The patient with scleromixedema had associated hypothyroidism. The period from first symptoms to diagnosis was variable from months to years.

**Conclusions:** Even though are rare, scleroderma mimics can be a challenging diagnostic even in tertiary care centre and sometimes diagnostic can be delayed. A correct diagnostic is necessary to avoid unnecessary immunosupresion.

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#### AB0770 18 FDG PET/CT PREDICTS DECLINE IN FUNCTIONAL RESPIRATORY TESTS IN SYSTEMIC SCLEROSIS PATIENTS BUT NOT IN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Interstitial lung diseases (ILD) it's a frequent complication in connective tissue diseases (CTD) such as rheumatoid arthritis (RA) or systemic sclerosis (SS), but the lung is the only affected organ in the idiopathic pulmonary fibrosis (IPF). Nonspecific interstitial pneumonia (NSIP) is the more frequent form in SS while usual interstitial pneumonia (UIP) predominates in RA patients and in the IPF form. Some studies suggested that 18-FDG-PET/CT could help to detect zones of activity in lung tissue in IPF and this in turn could predict the disease

progress, but results are inconclusive. Moreover, little is known about the value of 18-FDG PET uptake in ILD associated to RA or SS.

**Objectives:** The purpose of this study is to evaluate the predictive value of 18 FDG-PET/CT scan images in functional pulmonary progression of ILD associated to RA or SS.

**Methods:** We conducted a 12 month prospective observational study on patients diagnosed with ILD associated to SS or RA between January 2015 and May 2017. ILD diagnosis was based on clinical assessment, pulmonary function tests (PFTs) and expert HRCT evaluation. We performed three visits: basal, 6 month and 12 month. On all visits a general exploration, forced vital capacity (FVC) and diffusing capacity of the lungs for carbon monoxide (DLCO) were carried out. On basal and 6 month visit a 18-FDG-PET/TC was performed within a period of three months from the PFTs. Patients continued with their treatment (corticosteroids, DMARDs or immunosuppressants). The nuclear medicine physician identified the maximum and mean standardised uptake value (SUVmax and SUVmean) in the three areas with the most FDG uptake, and adenopathies uptake. PET/CT images were reviewed by 2 combined radiologist/nuclear medicine physicians in consensus.

**Results:** We included 17 patients, 10 had UIP associated with RA and 7 NSIP related to SS. It appeared that RA patients had longer lung illness evolution and worse FVC than SS patients (table 1), in spite of not having found statistical differences. We detected significant statistical relation between the highest SUVmax and FVC ( $p=0.009$ ) or DLCO progression ( $p=0.006$ ) in SS patients, independently of the basal FVC and DLCO, and duration of lung illness in a multivariable linear mixed model. We didn't find any relation between SUVmax and FVC or DLCO progression in RA patients.

**Conclusions:** In our cohort of patients with SS, 18 FDG PET/TAC can aid in predicting the progression of ILD associated disease, which does not occur in RA patients.

**Disclosure of Interest:** None declared

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AB0771

#### ABNORMAL CAPILLAROSCOPY AND PULMONARY HYPERTENSION IN PATIENTS WITH SYSTEMIC SCLEROSIS

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**Background:** Systemic sclerosis (Ss) is an autoimmune disease characterised by microvascular damage with clinical manifestations such as Raynaud Phenomenon, digital ulcers, abnormal capillaroscopy and pulmonary hypertension. Systemic sclerosis is a major risk factor for the development of pulmonary arterial hypertension. Positive capillaroscopy has been associated with involvement of pulmonary vasculature.

**Objectives:** To determine if there is association between abnormal capillaroscopy and pulmonary hypertension in patients with systemic sclerosis.

**Methods:** Cross-sectional study with a study group of 48 patients with Ss according to ACR/EULAR 2013 criteria; we included a control group with Rheumatoid arthritis patients (RA) and healthy subjects. The peripheral microangiopathy was studied by nailfold capillaroscopy and pulmonary involvement with transthoracic echocardiography. Descriptive statistics with mean and standard deviation were done. We did a chi-square test of homogeneity for groups comparison. Pearson's test was done for correlation analysis. We used SPSS software for statistics.

**Results:** 48 patients with Ss were included, 24 with RA and 24 subjects. 96% were women mean age 48 ( $\pm 13.6$ ). More frequent co-morbidities were systemic hypertension 17% in Ss vs 25% in RA. The most frequent clinical finding was Raynaud phenomenon in 81% and dysphagia in 67%. 64% of the patients with Ss were positive to anti-centromere antibody. Abnormal capillaroscopy was found in 77% of the Ss patients with the following patterns: early 42%, active 33% and late 23%, also we found abnormal capillaroscopy in 8% of the AR and healthy controls. We found 6% of pulmonary hypertension in Ss 4% was mild and 2% severe. Positive Correlations were Abnormal capillaroscopy and Lung interstitial disease  $r=0.36$  ( $p=0.009$ ), active pattern  $r=0.385$  ( $p=0.006$ ), dilated capillaries  $r=0.457$

( $p=0.001$ ). The Modified Rodnan score was correlated with: active pattern  $r=0.525$  ( $p=0.000$ ), dilated capillaries  $r=0.444$  ( $p=0.001$ ) and avascular areas  $r=0.495$  ( $p=0.000$ ). We did not find association between abnormal capillaroscopy and pulmonary hypertension  $r=0.106$  ( $p=0.300$ )

**Conclusions:** We found positive association between abnormal capillaroscopy and interstitial lung disease and no correlation with pulmonary hypertension

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AB0772

#### PROSPECTIVE STUDY OF CARDIOVASCULAR RISK ASSESSMENT IN SYSTEMIC SCLEROSIS

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**Objectives:** Evaluate evolution of cardiovascular risk (CVR) in a cohort of systemic sclerosis (SSc) in one year of follow-up.

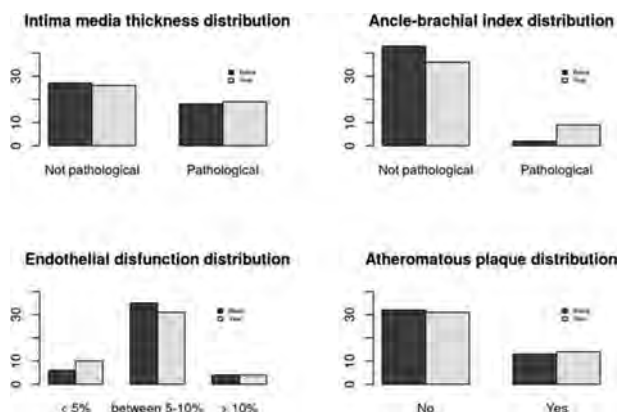
**Methods:** Prospective longitudinal study of a cohort of 45 patients with SSc during a period of one year. Sociodemographic and analytical variables were analysed at the time of inclusion in the study (baseline) and after 12 months of follow-up. The vascular protocol with carotid ultrasound was performed, including the determination of carotid intima-media thickness (IMT) and the evaluation of atheromatous plaques; in addition to the performance of the ankle-brachial index (ABI) and the determination of endothelial dysfunction (ED) through the measurement of flow-mediated vasodilation (FMVD), all at baseline and at one year.

**Results:** 45 patients were included, 94% of them female, with a mean age of  $52.2 \pm 11.5$  years and mean evolution time of  $4.6 \pm 5.1$  years. The distribution by subgroups was 44.4% limited SSc, 35.5% diffuse SSc, 4.4% pre-scleroderma, 4.4% sine scleroderma SSc, 6.6% MTCD, and 4.4% overlap syndrome. Classical CVR variables were collected as smoking habit, DM, HTN, obesity, DLP, hyperhomocysteinemia, and clinical variables of the SSc were added such as modified Rodnan Skin Score (mRSS), pulmonary arterial hypertension (PAH), interstitial lung disease (ILD), capillaroscopic pattern, SSc specific antibodies and previous treatments.

A bivariate analysis was performed using binomial logistic regression, both at baseline and at one year. Pathological IMT ( $>0.9$  mm) was significantly associated with hyperhomocysteinemia ( $p=0.024$ , OR=3.03, CI 1.33–9.58). The presence of atheromatous plaque was associated with corticosteroid treatment ( $p=0.048$ , OR=0.58, CI 0.28–0.97). Pathological ITB ( $<0.9$ ) was significantly associated with the 25-OH-vitamin D deficit ( $p=0.031$ , OR=0.25, CI 0.06–0.77). ED did not show a statistically significant association with the parameters studied.

To evaluate the effect of time, a binomial model was adjusted by linear regression of mixed effects for the variables of CV affection considered (see table 1). Time proved to be a risk factor to present pathological ITB values, since it was evidenced at baseline in 4.4% of the sample compared to 20% in the one-year study. Consequently, a multivariate analysis was performed showing pathological ABI was significantly associated to time ( $p<0.001$ , OR=59.7, CI 59.64–59.75) and mRSS, although with little effect ( $p<0.001$ , OR=0.042, IC 0.036–0.047). Time was not a risk factor for the appearance of pathological IMT, ED or plaques.





Abstract AB0772 – Figure 1

**Conclusions:** In our study, we observed the significant variation in ABI in one year, this may be due to the fact that this measurement has a high sensitivity for the detection of early peripheral arterial disease, in those patients who have not manifested signs and symptoms of arterial disease due to more evolved time of evolution.

**Acknowledgements:** Thank you Casandra Jimenez for her help with the vascular database compilation

**Disclosure of Interest:** None declared

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**AB0773 INTERVENTIONS FOR MORPHEA: A COCHRANE SYSTEMATIC REVIEW**

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**Background:** Morphea is a chronic inflammatory and fibrosing disorder usually limited to the skin and underlying tissues. It is an immune-mediated disease in which excess synthesis and deposition of collagen in the skin and connective tissues results in hardened cutaneous areas.

**Objectives:** To assess the effectiveness and safety of treatments for individuals with any form of morphea.

**Methods:** We searched the following databases up to March 2017: the Cochrane Skin Specialised Register, CENTRAL, MEDLINE, Embase, LILACS, and five trials registry databases. We checked the reference lists of included studies for further references to relevant randomised controlled trials.

We included randomised controlled trials assessing the effects of topical, intralesional, or systemic treatments for morphea (isolated or combined).

Two authors independently assessed study eligibility, extracted data, assessed risk of bias and performed analyses. A third author settled any disagreements.

**Results:** We included 13 trials, totalling 426 participants. There were both juvenile and adult participants (mostly women). The majority had limited morphea, followed by linear morphea.

The studies evaluated heterogenous therapies for morphea, covering a wide range of comparisons. Thus, we could not pool data from the studies in a meta-analysis. Six studies investigated topical medications, two evaluated intralesional medications, and five investigated systemic medications.

Regarding our primary outcome global improvement of disease activity or damage:

- The number of juvenile participants with a significant clinical response was higher with oral methotrexate plus oral prednisone than with placebo plus oral prednisone (RR 2.31, 95% CI 1.20 to 4.45, after the 12 month treatment; NNT 3; low-certainty evidence);

- We are uncertain whether fractional carbon dioxide laser and the combination of acupuncture, hot herbal compress and moxibustion plus Centella triterpenes tablets and vitamin E may reduce this outcome, as the certainty of the evidence was very low;

- We found no differences in the MSS score between the following comparisons (very low-certainty evidence): oral hydroxychloroquine plus topical corticosteroid versus oral methotrexate plus folic acid and topical corticosteroid; and medium-

dose ultraviolet A-1 (50 J/cm<sup>2</sup>) versus low-dose ultraviolet A-1 (20 J/cm<sup>2</sup>) phototherapy versus narrowband UVB.

We are uncertain regarding adverse effects of interventions as the certainty of the evidence was very low. However, participants reported marked pain and pruritus during fractional carbon dioxide laser therapy, and had mild tanning after ultraviolet A-1 phototherapy.

**Conclusions:** There is a lack of high-certainty evidence for the treatment of morphea, and the effectiveness and safety of the interventions are unclear. Low-certainty evidence supports the effectiveness of oral methotrexate plus oral prednisone for treating juvenile morphea. More studies are necessary to assess the effectiveness and safety of interventions for morphea.

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**AB0774 IMPACT OF STANDARDISED EDUCATION PROGRAM ON THE ACCURACY OF MODIFIED RODNAN SKIN SCORING IN PATIENTS WITH SYSTEMIC SCLEROSIS**

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**Background:** Modified Rodnan skin score (mRSS) has been used as not only a primary outcome in many clinical trials, but also as an important surrogate marker of disease activity in patients with systemic sclerosis (SSc). Therefore, establishment of well-organised training program of mRSS is essential for the proper management of patients. Recently, Scleroderma Clinical Trials Consortium and the World Scleroderma Foundation published the recommendation for 2-phase mRSS training and emphasised assessing scoring accuracy after the training.

**Objectives:** To investigate the effect of modified Rodnan skin scoring (mRSS) education on improving its accuracy

**Methods:** Ten rheumatologists (6 professors and 4 fellows) received an education program composed of video education and live demonstration by master instructor (Marco Matucci-Cerinic) at (Seoul in June, 2017). Physicians measured mRSS of 8 patients with SSc 1) before the education, 2) after the video education and 3) after live demonstration without any clinical information of the patients. Accuracy of skin scoring was estimated by the difference from the pre-defined gold-standard score measured by master instructor. Change in accuracy of mRSS during the education course was analysed using linear mixed model. Intra-observer reliability of the mRSS and its change was assessed by intraclass correlation coefficient (ICC).

**Abstract AB0774 – Table 1.** Multivariable analysis indicating effect of the education program on the accuracy of modified Rodnan skin scoring

Education	Regression coefficient*	95% CI	P-value
Before education	Reference	NA	NA
After video education (vs. before education)	-0.95	-2.13 to 0.23	0.002
After live demonstration (vs. before education)	-0.44	-0.83 to -0.05	0.000
Education & live demonstration (vs. before education)	-1.59	-2.97 to -0.21	<0.001
Professor vs. before video education	1.79	0.33 to 3.25	0.000
Professor vs. before live demonstration	0.66	0.04 to 1.28	0.000
Professor vs. before education (vs. fellow type vs. limited type)	-0.07	-0.43 to 0.29	0.150
Fellow vs. limited after video education	1.00	-0.00 to 2.00	0.230
Fellow vs. limited after live demonstration	0.05	-0.10 to 0.20	0.500
Doctor/limited	0.52	-0.11 to 1.15	0.140
Gold-standard skin score†	-0.00	-0.00 to -0.00	0.990
Physician's accuracy‡ (vs. no. correct)	-0.47	-0.84 to -0.10	0.010

\*. Dependent variable = (Examiner's skin score – gold-standard skin score). Regression coefficient indicates the difference in dependent variable as compared with reference.

†. This clinical factor consistently influence the dependent variable irrespective of education course.

‡. indicates P value for type 3 fixed effect

§. (Physician's skin score – gold-standard skin score) (95% CI) was estimated as 7.66 (6.03 to 9.29) before the education.

**Results:** The number of SSc patients ever experienced by each physician was significantly higher in the professors than fellows but the number of mRSS ever performed was comparable between the two groups. Median (IQR) skin score

measured by master instructor was 10.5 (9.0). Mean (SD) difference between skin scores by physicians and master instructor was 7.7 (9.5) units. In the univariable analysis, video education significantly reduced the difference from the gold-standard score ( $\beta = -1.96$ , 95% CI  $-3.83$  to  $-0.10$ ) whereas live demonstration did not show additional enhancement in scoring skill. Effect of education program was significantly different according to the physician's status and patient's disease type (diffuse vs. limited). In addition, male patient, shorter disease duration and higher gold-standard skin score was associated with more accurate skin scoring irrespective of the education. In the multivariable analysis where above clinical factors were adjusted, video education also led to significantly accurate skin scoring (table 1). When the educational effect was stratified by individual site of examination, face and distal extremities showed greater enhancement of scoring accuracy whereas difference from gold-standard score in proximal extremities was rather increased. ICC of physicians' skin scores was acceptable over all scoring times (0.63 to 0.88) but was not significantly changed after the education.

**Conclusions:** The mRSS education program can significantly enhance the accuracy of mRSS, which is mainly achieved by video education.

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#### AB0775 CHARACTERISTICS OF PATIENTS WITH SCLERODERMA (SSC) TREATED WITH VARIOUS DRUGS IN THE CLINICAL ASSESSMENT AND TGF B AND IL13 CONCENTRATION IN COMPARISON TO THE HEALTHY GROUP

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**Background:** Scleroderma (SSc) is a rare multisystem chronic disease the treatment of which is still challenging. Until now, there is no effective therapy that can modify the overall disease course. However, the main aim of SSc treatment is directed toward managing organs involvement and providing symptomatic relief. Effective drug therapy should inhibit three components of the disease: tissue fibrosis, vascular abnormalities and autoimmunity. Moreover, potential drug needs to be considered in the context of specific four subsets of the disease: fibroproliferative, inflammatory, limited, and normal-like. It was shown that various subsets could have different profile of specific cytokines: TGF $\beta$  – associated with fibroproliferative and inflammatory type of disease and IL13 – mediator of fibrotic and vascular pathology.

**Objectives:** The aim of the study was to assess the level of TGF $\beta$  and IL-13 in SSc pts with various treatment regimen comparing to healthy control.

**Methods:** 55 patients (71% were women) with SSc diagnosed according to EULAR/ACR 2013 criteria were divided into 5 treatment groups: 1st group – 8 pts treated with methotrexate (MTX), 2–13 pts with mycophenolate mofetil (MMF), 3–5 pts with cyclophosphamide (CYC), 4th group- 7 pts with azathioprine (AZA), 5th group- 22 pts without immunosuppressive treatment. All patients have been treated based on a scheme required for organs involvement in accordance with the update of EULAR recommendations from 2016. Mean age of patients was 54.56  $\pm$  13.97. The blood and serum samples have been collected for basic examination. TGF $\beta$  and IL13 concentration in serum was quantitated by ELISA. Differences in cytokine concentration were determined using non-parametric Kruskal-Wallis test. The level of statistical significance was set at  $p < 0.05$ . The modified Rodnan Skin Score (mRSS) examination were taken by one assessor at the beginning of the study and six months later. There were measured DLCO, HRCT, echocardiography and capillaroscopy.

**Results:** In 82% pts positive antinuclear antibodies have been revealed: in 16% positive results for CENPB were obtained and in 44% for Scl70. Capillaroscopy shown in 23% of pts early pattern, in 38% – active pattern, and in 27% – late pattern. 32% of SSc pts had confirmed pulmonary fibrosis, while 90% – Raynaud's syndrome. The median of mRSS in CENPB (+) pts was 5,4<sup>-24</sup> in Scl70 (+) pts – 12,2<sup>-30</sup>. Statistically significant differences were found between IL13 and TGF $\beta$  levels in patients treated with immunosuppressants and healthy subjects. There was no correlation between IL13 or TGF $\beta$  with lung fibrosis progression or skin involvement.

**Abstract AB0775 – Table 1.** Comparison of serum level of IL 13 and TGF $\beta$  in SSc pts

	MTX (n=8)	MMF (n=13)	CYC (n=5)	AZA (n=7)	patients without immunosuppressive treatment (n=22)	healthy control (n=6)	p value
<b>TGF<math>\beta</math></b>							$<0.001$
Minimum	170.8	175.4	203.0	96.15	104.4	44	
Maximum	226.6	272.3	273.2	272.3	202.0	150	
Average	414.0	385.3	306.5	306.6	309.9	323	
<b>IL13</b>							$<0.001$
Minimum	0	0	0	0	0	150	
Maximum	88	175.2	0	172.4	178.0	250	
Average	185	191	197	197.3	224.4	309	
<b>IL13</b>							$<0.001$
Minimum	90.14	123.8	75.29	163.7	115	228.7	
Maximum	95.42	85.96	150.3	95.81	96.7	31.53	
Average	34.09	33.89	44.96	38.59	31.13	0.572	
ICC (95% CI)	0.73	0.85	0.89	0.89	0.73	0.972	

**Conclusions:** In conclusion, our findings indicate that IL 13 and TGF $\beta$  are characteristic cytokines in scleroderma, but these parameters did not correlate with severely progressive course of SSc.

**Disclosure of Interest:** None declared

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#### AB0776 MUSCLE ULTRASONOGRAPHY: A POTENTIAL NEW DIAGNOSTIC TOOL FOR INFLAMMATORY MYOPATHIES

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**Background:** Quantitative muscle ultrasound (QMUS) imaging has proven to be a useful, non-invasive technique to visualise normal and pathological skeletal muscle tissue. <sup>1</sup>Electromyography (EMG) findings are not always disease specific in patients suspected of idiopathic inflammatory myopathies (IIM).

**Objectives:** To assess diagnostic value of QMUS in patients suspected for an IIM and to compare results with EMG.

**Methods:** In 57 patients, suspected for IIM, panel diagnosis blinded for QMUS was used as reference standard. QMUS results were used to classify patients according an ultrasound neuromuscular disorder (NMD) algorithm (normal/borderline/abnormal). The predictive value of QMUS and EMG was assessed in a two by two table and a multivariate logistic regression model.

**Results:** Twenty-two patients (39%) were diagnosed with IIM; 8 polymyositis, 4 dermatomyositis, 4 necrotizing myopathy, 3 inclusion body myositis and 3 non-specific myositis. Sixteen patients were classified with other NMD. We found an increased echointensity of the sternocleidomastoid, biceps, forearm flexor and tibialis anterior in the IIM group. Sensitivity, specificity, positive and negative predictive values (PPV/NPV) were 82%, 51%, 51%, 82% for ultrasound NMD algorithm and 63%, 64%, 50%, 75% for EMG. Multivariate analyses showed area under the curve (AUC) (0.81) (0.69–0.92) for ultrasound NMD algorithm, EMG (0.79) (0.67–0.92) and ultrasound NMD algorithm plus EMG (0.82) (0.70–0.93).

Predictor	Model A	Model B	Model C
Age $\geq$ 50 year	2.97 (0.65–13.59)	2.88 (0.62–13.28)	2.98 (0.62–14.21)
Serum CK $\geq$ 2 x upper limit	7.52 (1.57–36)	8.76 (1.55–49.55)	7.35 (1.22–44.21)
<i>Muscle ultrasound</i>			
Total echointensity of proximal muscles/ measured muscle			
Total number of affected proximal muscles			
Distal muscles affected (yes/no)			
NMD algorithm:			
- No NMD	Reference:		Reference:
- Borderline presence of NMD (yes/no)	1.61 (0.13–18.87)		1.62 (0.13–19.57)
- Presence of NMD (yes/no)	3.01 (0.44–20.55)		3.01 (0.43–21.09)
<i>EMG qualitative report:</i>			
Negative myopathic results		Reference:	Reference:
Borderline myopathic results		1.00 (0.08–11.67)	0.94 (0.07–12.09)
Positive myopathic results		1.28 (0.23–7.13)	1.03 (0.17–6.04)
Cox and Snell R square	0.28	0.26	0.28
Nagelkerke R square	0.38	0.35	0.38
Hosmer Lemeshow Test	0.91	0.94	0.69
AUC (95% CI)	0.81 (0.69–0.92)	0.79 (0.67–0.92)	0.82 (0.70–0.93)

**Conclusions:** QMUS with NMD algorithm provides a fair diagnostic value for patients suspected for an IIM and is similar to EMG results. A sizeable NPV indicates a low rate of false negative QMUS results. In addition to the relevant PPV for the presence for NMD, QMUS could serve as a potential screening tool for clinicians to detect possible myopathies and to rule out the presence of IIM.

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AB0777

#### INFLAMMATORY MYOSITIS ASSOCIATED WITH MYASTHENIA GRAVIS WITH AND WITHOUT THYMIC PATHOLOGY: CASE SERIES AND LITERATURE REVIEW

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**Background:** Inflammatory myopathies (IM) and Myasthenia gravis (MG) are two well-recognised and distinctive neuromuscular diseases. The association of myasthenia gravis (MG) and inflammatory myositis (IM) is rare and often only one of the diseases is diagnosed. The coexistence of MG and IM might be associated with thymoma. Even less common is the association of IM (polymyositis or dermatomyositis) and myasthenia gravis in the absence of thymoma.

**Objectives:** Here, we report a case series of 6 patients with concurrent MG and IM who were followed at the Neuromuscular Disease Unit (NMDU) at a tertiary referral centre in Vancouver, British Columbia. We also conducted literature review on clinical characteristics, diagnostic challenge and management of this condition.

**Methods:** In this study, we retrospectively examined patients seen at NMDU from 2004 to 2017 who had diagnosis of concurrent MG and IM. We reviewed medical records to assess their clinical presentations, laboratory findings, imaging studies and electrophysiological features. The data is presented descriptively.

**Results:** We identified 6 patients with MG-IM overlap. Three patients had simultaneous onset of MG and IM, 2 of whom presented with myasthenia crisis and fulminant myositis. In the other 3 patients, MG was the initial presentation and IM occurred 3–11 years after MG.

Diagnosis of MG was confirmed with clinical features, electromyography and/or serology. All had symptoms of MG with predominant ocular or bulbar weakness. Among these 6 patients, 3 had underlying thymic pathology including two benign thymoma and one stage IV thymoma; all 3 patients had Acetylcholine Receptor (AChR) Antibody. Of the 3 patients with no thymic pathology by computed tomography (CT) or thymectomy, 1 had high positive AChR antibody and 2 were negative.

Four patients had biopsies confirming the diagnosis of dermatomyositis or polymyositis. The other 2 patients declined biopsy; however, their MRI and EMG findings were consistent with IM. Only one patient had typical dermatomyositis rash.

Among the 3 patients with underlying thymic pathology, thymoma were resected; all 3 were treated with high dose glucocorticoid, IVIG, and methotrexate with complete remission after 2 years. Of the 3 patients with no thymic pathology identified, one patient (AChR+) was in remission on mycophenolate and passed away from pancreatic cancer; two patients (AChR-) had refractory MG and IM, and both responded to rituximab.

**Conclusions:** In summary, this is one of the largest case series with MG-IM overlap with or without thymic pathology. It is very important to recognise such association and the different pattern of muscle involvement because therapies may be adjusted to treat both conditions. In patients with thymic pathology, conventional disease modifying agents, IVIG and glucocorticoid in addition to thymoma resection appear to be effective. In patients with refractory MG and myositis who were AChR negative, rituximab may be effective.

**Disclosure of Interest:** None declared

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AB0778

#### CLINICAL CHARACTERISTICS AND PROGNOSIS OF POLYMYOSITIS AND DERMATOMYOSITIS ASSOCIATED WITH MALIGNANCY: A 25-YEAR RETROSPECTIVE STUDY

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**Background:** Previous studies indicate that malignancies in polymyositis (PM) or dermatomyositis (DM) patients are associated with high mortality. Hence, it becomes important clinically to identify patients who are at high risk of developing

malignancy. However, previous studies to characterise such risk factors for malignancy in patients with PM and DM were small size or the findings were not conclusive.

**Objectives:** This study investigated factors predictive of malignancy and prognosis in patients with PM and DM.

**Methods:** We conducted a retrospective study of PM and DM patients who were inpatients at our hospital between January 1992 and September 2016. The diagnosis of PM or DM was made according to Bohan and Peter criteria. The collected data included gender, age at onset, laboratory test results at presentation, clinical features and complications in all progress. Past history of hypertension or diabetes mellitus was determined upon diagnosis of myositis. All patients in this study were followed from the baseline visit until loss of follow-up or death or otherwise until censor date 1 September 2017. Fisher exact test and Mann-Whitney U test were used for group comparisons. Univariate and multivariate analysis of the predictors of malignancy associated with PM or DM were performed by logistic regression to identify independent risk factors. Patient survival was analysed by using Kaplan-Meier curve and log-rank test.

**Results:** Among 134 patients, 29 had cancer diagnosed between 2 years prior and 3 years following identification of PM or DM. Esophageal cancer (n=5, 14.7%) and lung cancer (n=5, 14.7%) were the most frequent. Univariate analysis showed that male sex (55.2% vs 23.8%, p=0.003), older age (64.6±11.3 vs 53.4±16.5, p<0.001), past history of diabetes mellitus (28.6% vs 2.9%, p<0.001), dysphagia (41.4% vs 17.3%, p=0.01) and absence of interstitial lung disease (37.9% vs 64.8%, p=0.01), arthralgia (17.2% vs 47.1%, p=0.005) and the Raynaud phenomenon (3.4% vs 23.1%, p=0.02) were associated with increased malignancy. Multivariate analysis showed that independent factors included male sex (OR=3.65, p=0.03), older age (OR=1.05, p=0.02), past history of diabetes mellitus (OR=10.4, p=0.005) and absence of interstitial lung disease (OR=0.25, p=0.03) (table 1). Survival was significantly lower in patients with malignancy than in patients without malignancy (p<0.001).

**Abstract AB0778 – Table 1.** Multivariate analysis of PM/DM with and without cancer

Variables	Adjusted OR	95% CI	P value
Male, n(%)	3.65	1.17–11.30	0.03
Onset age, years, mean±SD	1.05	1.01–1.10	0.02
Interstitial lung disease, n(%)	0.25	0.08–0.84	0.03
Diabetes mellitus	10.4	2.00–54.3	0.005
Arthralgia, n(%)	0.55	0.15–2.04	0.37
Dysphagia, n(%)	2.82	0.82–9.71	0.10
Raynaud phenomenon, n(%)	0.25	0.03–2.29	0.22

Abbreviation: OR, odds ratio; CI, confidence intervals.

**Conclusions:** This study is the first to associate a past history of diabetes mellitus with malignancy; 28.6% of PM or DM patients with malignancy had diabetes mellitus whereas 7.3 percent of cancer patients had diabetes mellitus.

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AB0779

#### LONG TERM FOLLOW-UP OF A SYSTEMIC SCLEROSIS GROUP TREATED WITH BOSENTAN

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**Background:** Prospective studies with Bosentan have shown short term efficacy, while it is not clear whether long-term treatment may be effective or whether ulcers may recur once treatment is discontinued.

**Objectives:** Our objective was to evaluate the long term efficacy and tolerability of bosentan in patients with systemic sclerosis (SSc) who develop digital ulcers (DU).

**Methods:** In the present prospective, observational, non-controlled study, we followed 26 SSc patients treated with Bosentan from Sept 2014 to Dec 2017 Number of DU, semiquantitative capillaroscopic scoring, VAS (visual analogue scale) for Raynaud, VAS for DU and HAQ were evaluated every 6 month. Results are presented as mean(sd). The difference between efficacy measures at follow-up visits was tested with the Wilcoxon's signed-rank test.

**Results:** The group included 26 patients, 16 females, 11 diffuse subsets, age was 48.08 (9.8) years, disease duration was 84.35 (76.04) months, number of DU was 4.27 (3.71), most of them had a late scleroderma pattern pattern (16/26).



Microangiopathy evolution score was 5.19 (2.04), VAS for DU was 75.52 (16.17), VAS for Raynaud was 67.43 (14.16), HAQ was 1.62 (0.55). 5 patients received Bosentan less than 6 months, so they were excluded from the statistical analysis. 6 month evaluation revealed significant decrease in the number of DU ( $p<0.01$ ), the VAS for DU ( $p<0.01$ ), the VAS for Raynaud ( $p=0.03$ ) and the HAQ ( $p=0.04$ ), but not of the microangiopathy evolution score. No significant difference was noticed of the above mentioned parameters at the next follow-up evaluations.

Regarding Bosentan safety: 6 patients died during the follow up (3 cases of severe pulmonary arterial hypertension, 1 scleroderma renal crisis, 1 heart failure, 1 post vascular surgery). Bosentan was stopped due to lack of efficacy in 2 cases and due to side effects in 3 cases: 2 elevated liver enzymes, 1 severe thrombocytopenia and 1 dyspnea aggravation.

12 patients had a follow up after 6 months Bosentan stop. We did not notice any significant increase in the number of DU, the VAS for DU or Raynaud, the capillaroscopic semiquantitative scoring or the HAQ.

**Conclusions:** We noted a significant decrease in the number of DU, patients perception of Raynaud and of DU after 6 months of treatment and the effect was maintained in the 3 years follow-up, even 6 months after Bosentan was stopped. In this long-term follow-up no new unidentified adverse reactions were found, except for the unexpected severe thrombocytopenia. The present study is limited due to the small sample size, to the observational nature and should be viewed as descriptive. Questions rise about drug costs (6 months or long term treatment), but it also has to be emphasised that most of these lesions were chronic and non-responsive to previous treatments.

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#### AB0780 PROLONGED PROTON PUMP INHIBITOR EXPOSURE IS ASSOCIATED WITH DEVELOPMENT OF CALCINOSIS IN SYSTEMIC SCLEROSIS

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**Background:** Long-term use of proton pump inhibitors (PPI) has been associated with some safety concerns, including potential vascular calcification. In a previous retrospective analysis, we noted a possible association between PPI use and calcinosis in scleroderma (SSc).

**Objectives:** To investigate the association between PPI use and the presence and extent of calcinosis in SSc patients.

**Methods:** Data from prospectively recruited patients were collected by patient survey, physician assessment and medical records. Calcinosis was graded; size ( $=<1$  cm,  $+=1-3$  cm,  $++>=>3$  cm) and number of sites involved (NSI) ( $I=1$  body site,  $II=2-3$ ,  $III\geq 3$ ). A total daily PPI equivalent dose (TDED) was calculated for each patient. We calculated PPI exposure score (PPE) by multiplying the total duration of use by TDED. For analysis, PPE was categorised into four groups; 0=no exposure, 1=up to 5 years, 2=6–10 years, 3> $\geq 10$  years. Fisher's exact test was used to assess categorical variables. Logistic regression assessed association between calcinosis and independent variables.

**Results:** 216 patients were recruited, 81.5% females, mean age 57.46 (SD 13.5) years. 56.5% had limited, 31.5% diffuse SSc, 9.7% had overlap features and 2.3% other CTD. Mean disease duration was 10 years (SD 9). ANA subtypes were defined: ACA positive (31.5%), ATA (25.5%), ARA (12.0%), ANA +ENA- (11.6%), U3RNP (5.1%), ANA- (4.2%), PmSCL (3.7%) and 6.5% other antibodies. Gastroesophageal reflux symptoms occurred in 83.3% of patients, most were on PPI (81%) and 14.8% had previously been on PPI. Current calcinosis (CC) was present in 30.1% patients, 9.7% reported past calcinosis. 39.8% had calcinosis at any time (CAT). 60.2% of patients never had calcinosis. Of those with CC, 47.7% had  $>1$  site involved. The most frequent sites affected were; finger (70.8%), elbow (35.4%) and knee (18.5%).

Univariable analysis found an association between disease duration and calcinosis, with odds of CAT increased by 7% per year (OR 1.07, CI 1.04–1.11,  $p<0.001$ ). Similarly, every year of PPE increased odds of CAT by 3% (OR 1.03, CI 1.01–1.05,  $p=0.003$ ). Increasing age associated with CAT (odds increasing by 2% per annum,  $p=0.043$ ). Exposure to a standard dose of PPI for over 10 years increased the odds of calcinosis by 4 times (OR 4.07, CI 1.68–9.85,  $p=0.002$ ) compared to no exposure. PPE category associated with NSI ( $p=0.04$ ). 73.3% of patients with

large volume calcinosis ( $>3$  cm) had a PPE for  $>10$  years and all with calcinosis  $>3$  cm had exposure to PPI.

Multivariable logistic regression found that disease duration (OR 1.07, CI 1.03–1.11,  $p=0.001$ ) and antibody specificity strongly associated with calcinosis. Presence of ATA (OR 0.32, CI 0.14–0.75  $p=0.008$ ), ANA- (OR 0.13, CI 0.02–0.79,  $p=0.026$ ), and ANA +ENA- (OR 0.17, CI 0.05–0.52,  $p=0.002$ ) reduced odds of calcinosis. Although the effect of PPIs on calcinosis was attenuated after adjusting for disease duration and antibodies, higher exposure to PPIs remained a significant predictor of calcinosis, with PPE category ( $>10$ ) increasing risk of CAT (OR 3.34, CI 1.16–9.17,  $p=0.025$ ).

**Conclusions:** Our data support a novel association of PPI exposure with calcinosis and confirm association of disease duration and antibody profile. Given the clinical impact of calcinosis, a potentially modifiable risk factor of PPI exposure warrants further study.

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#### AB0781 GLUCOCORTICOID DOSE AND CARDIAC INVOLVEMENT MIGHT BE POTENTIAL RISK FACTORS FOR SCLERODERMA RENAL CRISIS

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**Background:** Scleroderma renal crisis (SRC) is a rare but life-threatening complication of systemic sclerosis (SSc). SRC remains a major risk factor for mortality in SSc. It is important to identify potential risk factors for SRC, and avoid developing overt SRC.

**Objectives:** To perform a retrospective case series analysis of the characteristics, management and outcomes of SRC in Chinese SSc patients.

**Methods:** SSc patients hospitalised at Sun Yat-Sen Memorial Hospital from January 1992 to December 2017 were recruited. Clinical data were collected. SRC was defined as new onset, with blood pressure (BP)  $>140/90$  mmHg or  $\geq 30$  mmHg rise in BP from baseline, rising serum creatinine (Scr) levels and/or oliguria. Data were showed as mean  $\pm$  standard deviation.

**Results:** (<sup>1</sup> There were 749 SSc patients recruited and 16 patients (2.1%) of them were hospitalised for SRC. Among these 16 patients, 56% were females, age was  $54.6\pm 13.6$  years, mean duration from SSc onset to SRC occurred was 4 years.

(<sup>2</sup> SRC developed in 14 patients (87.5%) with diffuse cutaneous SSc (dcSSc), and in 2 patients (12.5%) with limited cutaneous SSc (lcSSc). Eleven patients (68.8%) were under glucocorticoid treatment before SRC onset: 4 patients received  $\geq 30$  mg/d of prednisone, 6 patients received  $\geq 7.5$  mg/d prednisone and 1 patient received  $<7.5$  mg/d prednisone. No patient was treated with angiotensin-converting enzyme (ACE) inhibitors before SRC.

(<sup>3</sup> All 16 patients manifested progressive renal failure, with Scr levels increase to  $420\pm 256$   $\mu\text{mol/L}$ . Ten patients manifested new onset hypertension, with systolic BP  $175\pm 21$  mmHg and diastolic BP  $108\pm 13$  mmHg. Five patients who had a history of well-controlled hypertension manifested accelerated increase in BP  $178\pm 17/108\pm 7$  mmHg. One patient was normotensive, but manifested rapidly progressive oliguric renal failure with Scr increase to 969  $\mu\text{mol/L}$ , massive proteinuria and hemolytic anaemia.

(<sup>4</sup> Twelve patients (75%) had pulmonary fibrosis, 11 patients (68.8%) had cardiac involvement, 6 patients had pulmonary arterial hypertension (PAH) and 6 patients had gastrointestinal dysfunction. Cardiac involvement was common, manifested pericarditis, myocardial damage and heart failure ( $n=7$ , 43.8%, respectively). All 5 dead patients were accompanied by cardiac involvement.

(<sup>5</sup> Eleven patients had Raynaud's phenomenon, 8 patients had digital ulcers, 5 patients had arthritis and 2 patients had oliguria. Thirteen patients (81%) manifested anaemia, 8 patients (50%) manifested thrombocytopenia, and 8 patients (50%) manifested microangiopathic haemolytic anaemia (MAHA).

Eleven patients (68.8%) received ACE inhibitor treatment. Fifteen patients were treated with glucocorticoid and 12 patients with immunosuppressant (Cyclophosphamide  $n=10$ , Azathioprine  $n=2$ ). After treatment, renal recovered in 4 patients (25%), kidney function improved and developed to chronic kidney disease (CKD) without dialysis in 5 patients (31%), 2 patients required permanent dialysis (13%). Five patients (31%) died.

**Abstract AB0781 – Table 1.** Characteristics of 16 patients with Scleroderma renal crisis

Pt.No	Age(y)	Sex	SRC diagnosis	Prednisone before SRC	Ssc form	Pulmonary fibrosis	Cardiac involvement	PAH	MAHA	BP (mmHg)	Ser (mmol/L)	ACE inhibitor	Outcome
1	62	F	0.25	10mg/d	dcSSc	-	-	-	-	170/100	206	None	Recovered
2	20	F	10	None	dcSSc	-	-	-	-	168/120	209	Ibuprofen	died
3	61	F	1	30mg/d	dcSSc	-	-	-	-	170/100	153	Losartan	Recovered
4	60	M	1	30mg/d	dcSSc	-	-	-	-	173/128	511	Captopril	CKD
5	63	M	5	None	dcSSc	-	-	-	-	198/97	174	Captopril	Recovered
6	64	M	5	5mg qod	dcSSc	-	-	-	-	190/90	504	Captopril	CKD
7	62	F	1	10mg/d	dcSSc	-	-	-	-	130/102	429	Captopril	died
8	64	F	10	None	dcSSc	-	-	-	-	160/110	259	None	CKD
9	58	M	2	15mg/d	dcSSc	-	-	-	-	189/122	349	Captopril	Recovered
10	24	M	0.5	30mg/d	dcSSc	-	-	-	-	200/120	986	Captopril	Dialysis
11	64	M	8	None	lcSSc	-	-	-	-	194/102	400	Captopril	CKD
12	45	F	15	10mg/d	dcSSc	-	-	-	-	200/120	248	Captopril	died
13	61	M	2	15mg/d	dcSSc	-	-	-	-	110/70	986	Captopril	Dialysis
14	61	F	1	15mg/d	lcSSc	-	-	-	-	193/110	587	None	CKD
15	58	F	1	None	dcSSc	-	-	-	-	150/86	473	None	died
16	46	F	1	35mg/d	dcSSc	-	-	-	-	180/100	392	Captopril	died

SRC: Scleroderma renal crisis, SSc: systemic sclerosis, dcSSc: diffuse cutaneous SSc, lcSSc: limited cutaneous SSc, PAH: pulmonary arterial hypertension, MAHA: microangiopathic haemolytic anaemia, CKD: chronic kidney disease

**Conclusions:** Medium-to-high doses of glucocorticoids (prednisone  $\geq 7.5$  mg/d) were associated with an increased risk of SRC. Cardiac involvement was common and associated with high mortality in SRC patients.

**Disclosure of Interest:** None declared

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### AB0782 SYSTEMIC SCLEROSIS PATIENTS WITH CONCOMITANT PSORIASIS: A PROOF-OF-CONCEPT PILOT STUDY

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**Background:** Psoriasis and Systemic Sclerosis (SSc) are chronic inflammatory diseases characterised by a systemic immunological response which is mainly driven by activated T helper (Th) Th1/Th17 lymphocytes.<sup>1,2</sup> Further, genome-wide association studies (GWAS) in SSc have demonstrated an association at PSORS1C1, the same gene linked to psoriasis susceptibility<sup>3</sup>

**Objectives:** Evaluate the statistical significance of a clinical correlation between Scleroderma and Psoriasis

**Methods:** From April 2014 to April 2017, we enrolled 180 consecutive patients with a diagnosis of SSc fulfilling 2013 ACR/EULAR classification criteria. Patients with Localised Scleroderma (Morphea) had to have a diagnostic skin biopsy before being included. Patients satisfying VEDOSS criteria<sup>4</sup> were also included. Patients with psoriasis had a dermatologist-proven diagnosis.

**Results:** 11/180 (6.1%, 95% IC:0.03–2.9) with scleroderma had a dermatologist-proven diagnosis of Psoriasis, and 23 patients (12.7%) had a family history of Psoriasis in a first-degree relative. For all the psoriatic patients except one, BMI was calculated; 50% had a BMI of >20 (average: 23.7). A metabolic syndrome was present in 3 out of 11 (27.2%), and in ten patients there were data available to calculate the presence of average moderate cardiovascular (CV) risk (11.5%). Finally, 3/11 patients (27.2%) had Psoriatic Arthritis (CASPAR classification criteria). In all 11 patients, Psoriasis was defined as mild (PASI  $\leq 10$ ).<sup>5</sup> The average value of modified Rodnan Skin Score (mRSS) was curiously low (0.5), [limited cutaneous (lcSSc) 5 patients, Morphea 3 patients, Very Early Systemic Sclerosis (VEDOSS) 2 patients, and diffuse cutaneous disease (dcSSc) 1 patient. Anticentromere antibodies (ACA) were detected in 5/11 patients; antinuclear antibodies, with negative extractable nuclear antigens in 4/11; Anti-topoisomerase I were found in two cases.

**Conclusions:** Psoriasis was significantly associated with SSc ( $p=0.014$ ), with a 2-fold higher frequency than that observed in general population (3%). Psoriasis +SSc, represent a further increased risk of CV disease. Th17 seems to play a crucial role in the pathogenesis of both diseases.

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### AB0783 CLINICAL CHARACTERISTICS OF A COHORT OF PATIENTS WITH ANTI-JO1 ANTIBODIES

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**Background:** Anti-synthetase syndrome (ASSD) is characterised by myositis associated with anti-synthetase antibodies, fever, arthritis, Raynaud's phenomenon, "mechanic's hands" and diffuse interstitial lung disease (ILD); 80% of patients present incomplete forms. The most frequently detected anti-synthetase antibody is anti-Jo1 (anti-histidyl-tRNA synthetase), which usually leads to a greater lung involvement. In some cases of myositis, the simultaneous presence of anti-Jo1 and anti-Ro52 antibodies has been described, and it is debated whether the presence of both antibodies is accompanied by more severe pulmonary involvement.

**Objectives:** To compare the clinical manifestations of the positive anti-Jo1 patients, with and without associated anti-Ro52 antibodies.

**Methods:** This is a retrospective observational study of anti-Jo1 positive patients confirmed in the Immunology Laboratory, between 2009 and 2018. Two techniques were used to identify the anti-Jo1 and anti-Ro52 antibodies: Western blot (EUROLINE Myositis Profile 3 (IgG)) and Fluoroenzimoinmunoassay (EliA, Thermofisher).

**Results:** In this study, 22 patients with anti-Jo1 antibodies were included, 16 (72.7%) women and 6 (27.2%) males. There was no association with FR or ACPA. The mean age was 57.3 years (SD:14.6) and the mean time of follow-up was 4.01 years (SD: 2.1). Of all patients, 5 had ASSD, the rest expressed the clinical picture of incomplete form. The most frequently clinical manifestations associated with anti-Jo1 were: muscular involvement (n=18, 81.8%), ILD (n=13, 59.1%), arthritis (n=9,40.9%), Raynaud's phenomenon (n=4, 18.2%). No patient developed lesions of mechanic's hands. The majority of patients with muscular involvement (83.3%), had histological confirmation of inflammatory idiopathic myopathy (Dermato or Polymyositis). The most frequently found X-ray pattern (HRCT) in patients with ILD was Non-specific interstitial pneumonia (NSIP) (n=9, 69.2%), followed by 2 Respiratory bronchiolitis interstitial lung disease (RB-ILD) and 2 Idiopathic interstitial pneumonia (IIP). Nine patients presented ILD and Myositis concomitantly (40.9%), more than half had fibrosing pulmonary involvement. 50% (n=11) also had criteria for other autoimmune diseases (2 rheumatoid arthritis, 4 polymyositis, 4 dermatomyositis, and 1 overlap). Half of the patients with anti-Jo1 presented also anti-Ro52, which 27.3% exclusively developed myopathy, 18.2% ILD and both entities 54.5%. Half of the ILD presented a radiological fibrosing radiological pattern. During follow-up, 7 patients (31.8%) died, 2 of metastatic cancer (one renal and one ovarian) and 5 of complications of the ILD, of which 80% were anti-Jo1/anti-Ro52 "doublet" positives.

**Abstract AB0783 – Table 1**

	Age years (SD)	Follow-up years (SD)	Arthritis n(%)	Raynaud n(%)	Myositis n(%)	ILD n (%)	ILD/Myositis n(%)	Exitus n(%)
Anti-Jo1 (n=22)	57,3 (14,6)	4,0 (2,1)	9 (40,9)	4 (18,2)	18 <sup>(81,8)</sup>	13 <sup>(59,1)</sup>	9 (40,9)	7 (31,8)
"Doublet"	59,2 (15,3)	3,8 (2,0)	6 (54,5)	3 (27,3)	9 (81,8)	8 (72,7)	6 (54,5)	4 (36,4)
Anti-Jo1/ Anti-Ro52 (n=11)								

**Conclusions:** The ILD is a frequent manifestation and the main cause of death in the patients with anti-Jo1 of our cohort. The presence of anti-Jo1/anti-Ro52 "doublet" seems to lead to a worse prognosis in these patients.

**Disclosure of Interest:** None declared

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**AB0784 MYOCARDIAL FIBROSIS DETECTED BY MAGNETIC RESONANCE IMAGING IN SYSTEMIC SCLEROSIS—PATHOPHYSIOLOGICAL SIGNIFICANCE**

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**Background:** Systemic sclerosis (SSc) is characterised by chronic fibrosis in various organs such as skin, lung and heart leading to poor prognosis. Myocardial fibrosis is one of factors of pulmonary hypertension (PH) as well as pulmonary arterial hypertension or interstitial lung disease (ILD). Detection of cardiac lesions has progressed much using imaging techniques such as echocardiography (UCG) in combination with measurement of various biomarkers such as BNP. Recently, cardiac magnetic resonance imaging (CMR) has been shown to be sensitive to detect even subclinical cardiac lesions. However, it is unclear what subtype of SSc is prone to myocardial fibrosis, when it manifests in the clinical course, or whether fibrosis occurs simultaneously in various organs.

**Objectives:** To clarify the pathophysiological significance of myocardial fibrosis in SSc, CMR was performed in the patients with limited (lc) and diffuse (dc) cutaneous SSc with or without PH.

**Methods:** Twelve patients (male 2, female 10) who fulfilled ACR/EULAR criteria (2013) for SSc were enrolled. Eight patients were diagnosed as having lcSSc and 4 dcSSc. In addition to CMR, chest CT scan, UCG and laboratory tests including serum autoantibodies specific for SSc, blood brain natriuretic peptide (BNP) and pulmonary function test (%FVC,%DLCO) were performed in all patients. Right heart catheterization was performed in patients whose systolic right ventricular pressure estimated by UCG was higher than 30 mmHg. Positivity of late gadolinium enhancement (LGE) was compared with clinical findings and these parameters. Difference between the patient groups were tested using Student's t-test.

**Results:** LGE was positive in 6 out of 12 patients. Patient composition of dc/lc in LGE (+) and LGE (-) group was 1/5 and 3/3, respectively. Complication of ILD was present in 3 among LGE (-) patients, while esophageal involvement in 3 among LGE (+) patients. The mean age of LGE (+) group tended to be higher than that of LGE (-) group (73.8±5.8 vs 68±6.4), duration of disease (year) tended to be shorter in LGE (+) group than those of LGE (-) group (1.8±3.0 vs 7.7±5.5), and BNP level (170.6±150.1 vs 90.1±69.0 pg/ml) and RVP (33.5±8.1 vs 29.7±8.1 mmHg) tended to be higher in LGE (+) than in LGE (-) group, although difference was not statistically significant. There was no tendency of positivity of autoantibodies and pulmonary function test, while patients with low%DLCO (<70) and without ILD were positive for LGE. LGE tended to be positive in the patients whose E/e' ratio determined by UCG or pulmonary capillary wedge pressure by RHC was elevated.

**Conclusions:** Since myocardial fibrosis was found rather in the cases without ILD, there might be difference in the progression of fibrosis depending on the organ, although it accelerates by ageing. If LGE is seen, PH, especially that associated with left heart disease, might occur in future. This study suggests that CMR might be useful to detect cardiac lesions from early period of clinical course, as well as in the cases with some abnormalities in biomarkers such as BNP or DLCO regardless of existence of ILD, although further study is needed to clarify the indication of CMR using more cases of SSc.

**Disclosure of Interest:** None declared

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**AB0785 RED CELL DISTRIBUTION WIDTH IS A PROMISING MARKER OF PULMONARY ARTERIAL HYPERTENSION IN SCLERODERMA-RELATED DISORDERS**

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**Background:** The early identification of those Systemic Sclerosis (SSc) patients harbouring Pulmonary Arterial Hypertension (PAH) is a mainstay in the management of SSc. Novel biomarkers might improve the specificity of screening algorithms currently available.

**Objectives:** In this study we aimed to test the potential diagnostic value of Red cell distribution width (RDW), which has been previously described as a potential prognostic marker in thromboembolic and idiopathic PAH.

**Methods:** We prospectively recruited 118 patients affected by Scleroderma related disorders (Mixed connective tissue disease N. 7, 5.9%; SSc N. 93, 78.8%; Scleroderma overlap syndromes N. 11, 9.3%, undifferentiated connective tissue

diseases N. 7, 5.9%) in a PAH outpatient clinic of a University Hospital. All patients underwent an extensive clinical and laboratory evaluation and an echocardiographic examination; a right heart catheterization was performed in 13 patients according to clinical indication.

**Results:** According to echocardiography and right heart catheterization, 14/118 patients were diagnosed with PAH. Patients affected by PAH had a higher RDW (15 [13.4–18.9] vs. 13.9 [12.1–19.1]; p=0.005), despite similar haemoglobin levels between groups. Patients affected by PAH also showed a higher BNP plasma concentration (245.6 [81.6–494.3] vs. 60.3 [50.3–77.4]; p=0.0001) and lower platelets count [206 188–243 × 10<sup>3</sup>/μl vs 240 [198–299] × 10<sup>3</sup>/μ; p=0.04]. RDW was also directly related to ultrasound-assessed Pulmonary Artery Pressure (PAPs) (ρ=0.20; p=0.03) and DLCO corrected for haemoglobin (ρ=-0.30; p=0.001); finally, RDW was related to the mean PAP measured by right heart catheterization (ρ=0.65; p=0.015).

**Conclusions:** RDW is an inexpensive, potentially useful marker in the detection of SSc-related PAH; its inclusion in screening algorithms could be considered to further improve their diagnostic performance.

**Disclosure of Interest:** None declared

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**AB0786 ROLE OF CALCIUM ANTAGONISTS IN THE CANCER OF SYSTEMIC SCLEROSIS, AN ASSOCIATION UNDER DISCUSSION**

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**Background:** The use of calcium channel blockers (CCB) is widespread in systemic sclerosis (SSc) for the treatment of Raynaud's phenomenon, present in 95% of patients. CCB can alter apoptosis, a mechanism for the destruction of cancer cells. In SSc the risk of cancer is increased, but the role that CCB can play is not clear, with contradictory data obtained so far.<sup>1,2</sup>

**Objectives:** To analyse the role of CCB in the appearance of cancer in a cohort of patients with systemic sclerosis.

**Methods:** Encoded patients under the diagnosis of SSc in our hospital from 1985 until December of 2017 were collected. Medical records were reviewed, recording clinico-epidemiological data and treatments used.

**Results:** 120 patients have been diagnosed of SSc (103 females, 17 males), 22 of whom (18,3%) have developed cancer. The type of cancer were (in order of frequency): breast (12 patients, 57%), gastrointestinal (4 patients, 33%), one hypernephroma, one endometrial carcinoma, one lymphoma, one skin cancer and one epidermoid of tongue. Adenocarcinoma was the most frequently histologic pattern found (16 patients, 76%). Interestingly, the diagnosis of SSc was made at an older age in those patients diagnosed of cancer (66,4±11,7 vs 54,8±17,3 years old, p=0,019); An age older than 55 years old conferred a relative risk (RR) of cancer of 1,69<sup>1,26-2,25</sup> in the global cohort and a RR of 3,26<sup>1,18-8,99</sup> in the female cohort. Although the association cancer and CCB did not reach statistical significance, the association CCB and female patients older than 55 years elevate de RR of cancer to 4,16 (0.96–17,95). All other characteristics (epidemiological, clinical, analytical and another treatments) analyzed did not reach statistical significant differences.

**Conclusions:** CCB increase in our series the risk of cancer in women over 55 years old. CCB could be implicated in the pathogenesis of cancer in SSc. Due to the broad use of this in the SSc population, it may be require to study in a large number of patients in order to explore this association.

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AB0787

### THE EULAR SYSTEMIC SCLEROSIS IMPACT OF DISEASE (SCLEROID) SCORE – A NEW PATIENT-REPORTED OUTCOME MEASURE FOR PATIENTS WITH SYSTEMIC SCLEROSIS

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**Background:** Patient reported outcome measures (PROs) are increasingly important for clinical practice and research. Given the unmet need for a comprehensive PRO for systemic sclerosis (SSc), the ScleroID questionnaire was developed by a joint team of patients with SSc and medical experts in the field. This approach was designed as a brief, specific, patient-derived, disease impact score for research and clinical use in SSc. A preliminary analysis was previously reported. Here, we present the first computation of the ScleroID score and an extended pre-final analysis from the ongoing ScleroID validation study.

**Methods:** This EULAR-endorsed project involves 11 European expert SSc centres. Patients fulfilling the ACR/EULAR 2013 criteria were prospectively included since 05/16 in the ongoing observational cohort study. Patients completed the ScleroID questionnaire (figure 1), as well as the selected comparators mSHAQ, EQ5D, and SF36. Additionally, they weighted the 10 dimensions of the ScleroID by distributing 100 points according to the perceived impact on their health. The final score calculation was based on the ranking of the weights. The study included a reliability arm (follow-up questionnaire 7–10 days from baseline), as well as a longitudinal arm, looking at sensitivity to change at follow-up visits after 6 and 12 months from baseline.

How much have the different aspects of systemic sclerosis affected you during the last week? Please mark your responses on the scale by choosing the appropriate number for each of the following dimensions:

Reynaud's phenomenon:  
Circle the number that best describes the severity of your Reynaud's phenomenon during the last week:  
None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Hand function:  
Circle the number that best describes your hand function limitations due to your systemic sclerosis during the last week:  
No limitation 0 1 2 3 4 5 6 7 8 9 10 Extreme limitation

Upper gastrointestinal tract symptoms (e.g. swallowing difficulties, reflux, vomiting):  
Circle the number that best describes the severity of your upper gastrointestinal tract symptoms due to your systemic sclerosis during the last week:  
None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Pain:  
Circle the number that best describes the pain you felt due to your systemic sclerosis during the last week:  
None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Fatigue:  
Circle the number that best describes the impact of overall fatigue due to your systemic sclerosis during the last week:  
None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Lower gastrointestinal tract symptoms (e.g. bloating, diarrhea, constipation, anal incontinence):  
Circle the number that best describes the severity of lower gastrointestinal tract symptoms during the last week:  
None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Limitations of life choices and activities (e.g. social life, personal care, work):  
Circle the number that best describes how severe the limitations of life choices and activities due to your systemic sclerosis were during the last week:  
None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Body mobility:  
Circle the number that best describes how much your body mobility was affected due to your systemic sclerosis during the last week:  
Not affected 0 1 2 3 4 5 6 7 8 9 10 Extremely affected

Breathlessness:  
Circle the number that best describes how severe your breathlessness due to systemic sclerosis was during the last week:  
None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Digital ulcers:  
Circle the number that best describes how much your digital ulcers affected you overall during the last week:  
None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Abstract AB0787 – Figure 1. The EULAR Scleroderma Impact of Disease Score (ScleroID)

**Results:** As of January 2018, the study cohort included 417 patients with valid baseline data, 80 patients also had a reliability visit and 42 patients a follow-up

visit. 84% of patients were female, 62% had limited cutaneous SSc, mean age was 56 years, and median disease duration 10 years. 19% of patients were not able to work. The highest weights by the patients were assigned to Raynaud's phenomenon, fatigue, hand function and pain, in accordance with our previous results. The total ScleroID score showed good Spearman correlation coefficients with the comparators (mSHAQ, 0.59; EQ5D –0.62; Patient's global assessment, VAS 0.75; SF36 physical score –0.62; each p<0.001). The internal consistency was good with a high Cronbach's alpha by 0.86.

**Conclusions:** The EULAR ScleroID score is a promising, novel PRO tool designed for use in clinical practice and clinical trials to display the disease impact of SSc, showing good performance in this pre-final analysis. Importantly, Raynaud's phenomenon, impaired hand function, pain and fatigue were the main patient reported drivers of disease impact. To date the recruitment has reached more than 80% of the targeted number, the study is ongoing.

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AB0788

### OSTEOARTICULAR INVOLVEMENTS IN PATIENTS WITH SYSTEMIC SCLEROSIS

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**Background:** Osteoarticular involvements are common in systemic sclerosis (SS) and are considered as an important cause of disability.

**Objectives:** The aim of this study was to assess clinical, radiological and immunological characteristics of patients with systemic sclerosis and who present with osteoarticular involvements at any time of the disease course. Patients with arthralgia and/or arthritis and/or imaging abnormalities were included.

**Methods:** A retrospective descriptive and comparative study was performed in an internal medicine department. One hundred thirty one patients who fulfilled 2013 ACR/EULAR criteria for SS were studied.

**Results:** We identified 101 patients with osteoarticular involvements (77.1%); 92 women and 9 men. Mean age at SS diagnosis was 47.6±12.4 years. Disease was revealed by joint manifestations in 10.7% of cases. Arthralgia and arthritis were observed in 61.8% and 21.4% of cases respectively. Flexion deformities with disability were noted in 26 cases. X-Ray investigations revealed distal phalanges resorption (n=24), dystrophic calcifications (n=10) and joint space narrowing (n=9). Tendinitis was observed in one patient. Patients with osteoarticular manifestations developed more frequently digital ulcers (100% vs 78.3%; p<0.001). Osteoarticular involvements was associated to diffuse cutaneous sclerosis (37.7% vs 12.5%; p=0.002) and to telangiectasis (91.3% vs 70%; p=0.027), gastrointestinal manifestations (90.1% vs 54.5%; p=0.001) and interstitial lung disease (92.7% vs 67.9%; p=0.001). SS was associated to sjögren syndrome (n=20), to systemic lupus erythematosus (n=15) and to rheumatoid arthritis (n=2). Patients received non-steroidal anti-inflammatory drug (n=26), corticosteroids (n=8) and methotrexate (n=8).

**Conclusions:** Osteoarticular involvement in systemic sclerosis has heterogeneous aspects. Its frequency ranges from 40% to more than 85% of cases in some studies. Early screening and treatment associated with physiotherapy session are essential to avoid complication and loss of function.

**Disclosure of Interest:** None declared

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**AB0789** HOW DOES THE DURATION OF THE DISEASE INFLUENCE THE QUALITY OF LIFE?

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**Background:** It is noticed that over the last decades the prognostic in patients with Idiopathic Inflammatory Myopathies (IIM) – a group of autoimmune disease characterised by muscle involvement, has improved along with increase of disease duration and thus affects the quality of life.

**Objectives:** To assess the patient's quality of life related to the duration of the disease.

**Methods:** We performed a cross-sectional study from December 2015 to December 2017, the patients included fulfilled the Bohan and Peter<sup>1</sup> criteria for IIM. Demographic and clinical data were collected using a special questionnaire. Consistent with the objective the study group was divided in two subgroups by disease duration 1-less than 24 months and second subgroup more than 2 years. In order to estimate the quality of life (QoL) was applied Short Form-8 with 8 items for 8 domains and two components: mental and physical. Statistical data was analysed using MedCalc software version 12.

**Results:** There were 67 patients enrolled in the study, including 51 females and 16 males with a F:M ratio of 3.2:1, mean age 53.1±12.5 (range 25–78). The disease mean duration was 8.3±5.3 (range 0.5–12) years, there were 16 patients in the subgroup with the disease duration less than 2 years. The mean physical component was 36.48±9.05 and the mental component – 41.69±9.62 points, determined as reduced quality of life. Regarding the QoL of patients from subgroup 1, we found the physical component – 38.15±8.83 and the mental was 40.95±9.22 points. In the second subgroup we appreciated the physical and the mental component – 35.77±9.14 and 42.01±9.86 points, respectively. It was identified moderate correlation ( $r=0.49$   $p<0.005$ ) between the both domains of the QoL and disease duration till 2 years, for the duration of more than 2 years we found moderate correlation ( $r=0.51$   $p<0.005$ ) with mental component and a weak one for physical domain ( $r=0.24$   $p<0.005$ ).

**Conclusions:** Patients with idiopathic inflammatory myopathies had reduced quality of life by both domains. Disease duration in patients with early idiopathic inflammatory myopathies – less than 2 years, has a greater impact on patient's quality of life.

**REFERENCE:**

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**AB0790** FREQUENCY OF OSTEOPOROSIS IN POSTMENOPAUSAL WOMEN WITH SYSTEMIC SCLEROSIS

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**Background:** The prevalence of low bone mass or osteoporosis in patients with systemic sclerosis (SSc) varies significantly between studies performed in different countries and vary from 3% to 51% (Omair MA et al. 2013).

**Objectives:** To determine the frequency of osteoporosis (OP) in postmenopausal women with SSc in comparison with healthy control.

**Methods:** 163 postmenopausal women were enrolled in the study: 83 with SSc (mean age 58.5±8.1 years, mean disease duration 9.7±6.8 years) and 80 healthy control (mean age 59.2±6.6 years). Demographic characteristics and risk factors for OP in study groups are summarised in table 1. BMD was measured at lumbar spine, femoral neck and total hip by dual energy X-ray absorptiometry (DXA, Hologic 4500A). BMD decreasing grade was determined in according to WHO criteria.

**Results:** BMD in women with SSc was significantly lower than in control group at any site: lumbar spine – 0.832±0.119 vs 0.867±0.098 g/cm<sup>2</sup> ( $p=0.031$ ); femoral neck – 0.633±0.098 vs 0.739±0.114 g/cm<sup>2</sup> ( $p<0.0001$ ), and total hip – 0.752±0.116 vs 0.839±0.119 g/cm<sup>2</sup> ( $p<0.0001$ ). Frequency of OP in SSc group was 32%, in control group – 13% ( $p<0.002$ ). Mean age at menopause was less in SSc women than in control ( $p<0.05$ ).

OP was significantly more often in SSc patients taking oral glucocorticoids compared to those without glucocorticoid therapy (39% and 20%, respectively,  $p<0.05$ ). Low BMD was associated with age and interstitial lung disease in SSc women ( $p<0.05$ ). At the same time no associations were found out among low BMD and disease duration, daily and cumulative doses of glucocorticoids. 23 (28%) of patients had osteoporotic fracture, among them 8 (10%) of women had two or more fractures in the anamnesis. The most frequent localizations of the fractures were distal forearm and vertebrae: 7 (32%) and 5 (23%) patients, respectively.

**Abstract AB0790 – Table 1.** Demographic characteristics of the study groups and risk factors of osteoporosis

Factor affecting BMD	SSc (n=83) Mean±SD or%	Control (n=80) Mean±SD or%
Age (years)	58.5±8.1	59.2±6.6
Body height (m)	1.61±0.06	1.59±0.06
Body weight (kg)	67.7±14.3	66.5±11.7
Body mass index (kg/m <sup>2</sup> )	26.1±5.2	25.7±5.7
Age at menopause (years)	46.4±5.4*	49.7±3.0
Postmenopause duration (years)	12.2±7.2*	9.5±7.0
Smoking et presence time	3 (3.6%)	5 (6.3%)
Low energy fracture	23 (28%)	16 (20%)

\* $p<0.05$  compared vs control group

**Conclusions:** OP in postmenopausal women with SSc were detected among 1/3 of cases, significantly exceeded its frequency in healthy control. Risk factors for OP were age, oral glucocorticoids and interstitial lung disease.

**REFERENCE:**

- [1] Omair MA, Pagnoux C, McDonald-Blumer H, Johnson SR. Low bone density in systemic sclerosis. A systematic review. *J Rheumatol*.2013;40(11):1881–90. doi:10.3899/jrheum.130032

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**AB0791** SPECIFIC FEATURES OF SKIN INVOLVEMENT IN PATIENTS WITH SYSTEMIC SCLEROSIS AND ASSOCIATED PULMONARY ARTERIAL HYPERTENSION

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**Background:** Pulmonary arterial hypertension, associated with systemic sclerosis (SSc-PAH), is a severe irreversible manifestation of the disease, potentially fatal in its' late stage. It was shown that survival in SSc-PAH pts is much worse than in pts with idiopathic pulmonary arterial hypertension (IPAH). Unfavourable outcomes due to late recognition can be explained by predominance of subtle, clinically poor manifest SSc types, especially in terms of cutaneous and vascular syndromes.

**Objectives:** To assess the clinical features and survival rates in pts with systemic sclerosis sine scleroderma (ssSSc), associated with PAH.

**Methods:** 14 pts with ssSSc-PAH were analysed in comparison with 54 pts with clinically manifest skin involvement SSc-PAH (3 pts with diffuse (dcSSc-PAH) and 51 pts with limited cutaneous involvement (lcSSc-PAH)), and 48 pts with IPAH.

**Results:** Pts with IPAH were younger than both type SSc-PAH – 37 (28; 44), 48 (37; 56) and 54 (48; 62) y, respectively. In SSc-PAH pts with skin involvement and the diagnosis of PAH was established earlier (within 18 (10; 44) mo) than in pts with ssSSc (23 [15; 47] mo), although differences are not statistically significant. The PAH functional class was slightly higher in ssSSc-PAH, than in IPAH and SSc-PAH, the differences are not significant. Raynaud's phenomenon (RP) was present in all SSc-PAH pts, although in cutaneous SSc pts digital ischaemic lesions were more frequent (51% vs 14%,  $p=0.03$ ), as well as contractures (53% vs 7%,  $p=0.006$ ). There were no other differences in clinical features between the groups. Anticentromere antibodies (ACA) were present in 7 (50%) pts with ssSSc-PAH and in 36 (65%) pts with cutaneous SSc. Anti-topoisomerase-I antibodies (anti-Scl-70) were found only in 2 pts with lcSSc. More than 1 type of autoantibodies was detected in the majority of SSc pts. A wide range of antinuclear ABs was found in pts with ssSSc-PAH with prevailing ACA (in 7 pts), as well as anti-Sm, anti-La ABs, anti-nucleosome ABs (in one case), anti-Ro ABs (in 5 pts), anti-RNP-70 ABs – in 4 pts, anti-dsDNA ABs – in 2 pts, RF – in 3pts. SSc diagnosis was established according to ACR-EULAR 2013 classification criteria. The following diagnostic criteria were present in ssSSc-PAH pts: RP (in all pts), ulcers (3), scars (2), telangiectasia (10), PAH (14), SSc-associated ABs (7), capillaroscopic lesions (12). The mean total score was 11 (9;12) while  $\geq 9$  scores are required for SSc diagnosis, 100% pts with ssSSc-PAH met ACR-EULAR 2013 criteria, thus, justifying the SSc confirmation in this group of pts. There were significant differences in survival rates between IPAH pts and pts with various types of SSc-PAH (log-rank test,  $p=0.06$ ). 5 year survival in ssSSc-PAH was somewhat lower, than in SSc-PAH – 50.6% vs 64.9%, respectively; IPAH pts had the best survival rates of 82.5%, and these differences are close to significant.

**Conclusions:** Clinical features and survival ssSSc-PAH are very similar to those in pts with cutaneous SSc-PAH with the exception of skin involvement and associated symptoms (digital ischaemic lesions and contractures). Rheumatologists

should be aware of such specific features as similar survival rates in cutaneous and ssSSc pts, and late recognition of PAH in pts with ssSSc, as well as its similarity with IPAH.

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AB0792

### AUTOIMMUNE AND INFLAMMATORY DISTURBANCES IN PATIENTS WITH PULMONARY ARTERIAL HYPERTENSION ASSOCIATED WITH SYSTEMIC SCLEROSIS

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**Background:** The prognosis of patients with pulmonary arterial hypertension associated with systemic sclerosis (SSc-PAH) is significantly worse, than other forms of PAH, and mechanisms of this phenomenon are unknown. Therefore, the isolation of autoimmune disorders is of great importance for early diagnosis and differential diagnosis, as well as the search for new therapeutic targets.

**Objectives:** To identify the autoimmune disorders in patients with SSc-PAH.

**Methods:** The study includes 52 pts with idiopathic pulmonary arterial hypertension (IPAH), 51 pts with SSc-PAH, 65 pts with SSc without PAH. Serum concentrations of the C-reactive protein (CRP), anticentromere antibodies (ACA) and antibodies to topoisomerase-I (anti-Scl-70) were routinely measured. The control group consists of 146 volunteers. Statistical analysis includes univariable logistic regression, ROC analysis and Kaplan-Mayer method.

**Results:** The average age of patients with IPAH was 37.9±10.5 years, SSc-PAH – 52.3±12.7 years, SSc without PAH – 51.2±13.2. Patients did not differ in functional class (FC), which was the main criterion of comparability. Mean values of FC in groups with SSc-PAH and IPAH also did not differ (2.7±0.8 and 2.6±0.7, respectively). ACA was associated with a 15.2-fold increased odds of developing PAH in SSc (OR 15.2, 95% CI 5.4–43.0), on the contrary, presence of anti-Scl-70 associated with low risk of PAH (OR 0.5, 95% CI 0.01 to 0.21). The level of CRP in the serum was significantly higher in patients with PAH than in the control group: 4.1 (1.9, 10.0) and 0.61 (0.25, 1.9), p<0.000001, and also in comparison with patients without PAH (1.9 (0.8, 6.4), p=0.02). In pts with PAH, the level of CRP correlated with FC and right atrium pressure and 6 min walk test distance. The level of CRP was significantly higher in patients with FC III-IV compared with FC I-II and in non-surviving patients. The Kaplan-Mayer analysis showed that pts with CRP level more than 4.75 mg/L at the time of diagnosis of PAH had a significantly lower survival rate (median 48 months) than pts with normal values (median 91 months) (p<0.005), with 67% sensitivity and 61% specificity.

**Conclusions:** SSc-PAH is a unique phenotype combining the manifestations of SSc and PAH, the pathogenetic mechanisms of which modify the course of these states. It is based on a feature of autoimmunity with the predominance of ACA and a low occurrence of anti-Scl-70. An increase in the concentration of CRP, as well as the effect of its baseline level on survival, attests to the significant role of autoimmunity and inflammation in the pathogenesis of this fatal SSc complication.

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AB0793

### DESCRIPTIVE ANALYSIS OF A COHORT OF PATIENTS DIAGNOSED WITH INFLAMMATORY MYOSITIS IN A TERTIARY HOSPITAL

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**Background:** Inflammatory myopathies are a group of rare systemic diseases characterised by muscle weakness and inflammation. Clinical manifestations, course and prognosis of these pathologies are very heterogeneous.

**Objectives:** The aim is to describe the main characteristics of patients diagnosed with inflammatory myositis fulfilling Bohan and Peter criteria.

**Methods:** Descriptive analysis of a cohort of 34 patients from the same hospital with follow-up between January 2010 and December 2017. We recorded demographic characteristics, clinical manifestations, treatment, comorbidity and mortality.

**Results:** 34 patients (73% female) were recruited with an average age at diagnosis of 56.3 years<sup>27–83</sup> among adults and 10 years<sup>4–15</sup> among children. Most of them were Caucasian (94%). 18% were smokers and 15% previous smokers. The most frequent type was dermatomyositis (DM) (40%) followed by antisynthetase syndrome (ASS) (15%), necrotizing myopathy (12%), inclusion body myopathy (12%), overlap myositis (9%) and polymyositis (9%). 2 patients (out of 4) with necrotizing myopathy were treated with statins.

Clinical manifestation included muscle weakness (84%) and skin manifestations (48%) mainly among DM patients. 8 patients (24%) showed interstitial lung disease (4 non-specific interstitial pneumonia, 3 usual interstitial pneumonia and 1 cryptogenic organising pneumonia), especially among patients with overlap syndrome (n=3), DM (n=2) and ASS (n=2). Pulmonary hypertension occurred in 7 patients (21%), 30% among patients with overlap myositis associated to systemic sclerosis. The rest of extramuscular manifestations are expressed in the table 1. Muscle biopsy was performed in 57% of patients (77% compatible with myopathy). MRI was carried out in 45% (100% with active myositis). EMG was performed in 94% of patients with myopathic findings in 67% of them. 20 patients (60%) presented positive antinuclear antibodies, being the most frequent antiPML-SCL (18%), antiJo1 (18%), antiRo (12%) and anti-MDA5 (9%).

All patients were treated with corticosteroids. Only 2 responded to corticosteroids in monotherapy. More than 90% needed additional immunosuppressive treatment and 65% received 2 or more immunosuppressants. The most commonly used drugs were methotrexate (72%), rituximab (28%), azathioprine (25%), immunoglobulins (21%) and cyclophosphamide (21%). Only in 12% treatment could be stopped because of sustained remission.

3 cases of cancer (9%) were reported: myelodysplastic syndrome, lung neoplasm (in the case of paraneoplastic myositis) and lymphoma.

During the follow-up period 4 deaths were registered (12%) due to infections and cancer.

38% of patients required a multidisciplinary approach.

	n	%	Dermatomyositis	Polymyositis	Inclusion Body Myopathy	Necrotizing Myopathy	Antisynthetase syndrome	Overlap syndrome
Raynaud	7	21.2%	3	0	0	1	2	2
Cardiac Manifestations	7	21.2%	1	2	1	2	1	0
Arrhythmia	4	12.2%	1	1	1	0	1	0
Cardiomegaly	1	3%	0	0	0	1	0	0
Heart block	1	3%	0	1	0	0	0	0
Aortic stenosis	1	3%	0	0	0	1	0	0
Gastrointestinal Manifestations	6	18.1%	1	1	2	1	1	0
Dysphagia	3	9.1%	1	1	0	0	1	0
Chronic gastritis	2	6%	0	0	1	1	0	0
Constipation	1	3%	0	0	1	0	0	0
Severe Infections	5	15.1%	3	1	0	0	1	0
Hematologic Manifestations	5	15.1%	0	0	2	1	1	1
Anemia	4	12.1%	0	0	2	1	1	0
Anemia + Thrombocytopenia	1	3%	0	0	0	0	0	1
Antibodies	4	12.1%	1	0	0	0	1	2

**Conclusions:** Inflammatory myopathies have frequent multiorganic involvement and represent a heterogeneous group of systemic diseases as shown in our registry and in the literature. Most patients need chronically combined immunosuppressive treatment and few achieve sustained remission. In consequence the collaboration of several specialties is necessary for the diagnosis and management of these pathologies.

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AB0794

### MYOSITIS DAMAGE INDEX IN A MYOSITIS POPULATION COHORT

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**Background:** Idiopathic inflammatory myopathies (IIM) are a heterogeneous and uncommon group of diseases characterised by muscular involvement and many systemic manifestations. They usually have a chronic course, and despite treatment they often develop functional impairment. MDI-MYODAM a score to assess damage has been recently developed. Few publications in this regard have reported a prevalence of 92%. There are no studies in Mexican-mestizo population describing the extent of damage and its main determinants.

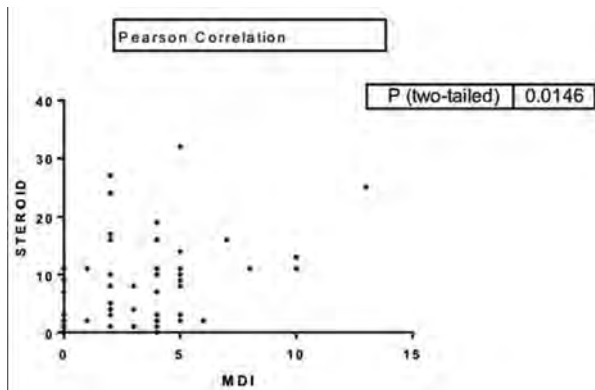
**Objectives:** To investigate the prevalence of damage measured with the MDI-MYODAM tool in patients with IIM and its relationship with characteristics of the disease and treatment

**Methods:** A cross-sectional study was conducted in an IIM cohort from a national reference hospital. MDI questionnaire was applied to all patients. Demographic, disease characteristics, IIM subgroup (dermatomyositis, polymyositis and overlap), comorbidities (Charlson index), medical treatment were collected. Descriptive statistics were applied. Bivariate Pearson correlation test was conducted to



analyse associations between MDI score and clinical characteristics. P value<0.05 was considered as a statistically significant.

**Results:** Fifty subjects participated, 75% were women, mean age at diagnosis was 40.7 years (SD±) and mean duration of the disease was 11.8±8.3 years. Thirty-one percent of patients had polymyositis, 31% dermatomyositis, 12% juvenile dermatomyositis, 10% overlap myositis (mainly systemic lupus erythematosus, scleroderma and rheumatoid arthritis). The mean Charlson index was 2.7±2.4. Eighty-one percent had a score greater than 0 for at least one category; majority within the endocrinological systems (55%), skeletal (51%), gastrointestinal (35%). The mean total damage score (MDI) was 3.6±2.9. The mean score for the total damage according to the MYODAM score was 6.9±5.1. A moderate correlation between the MDI score and the use of glucocorticoids ( $r$  0.3, CI 95% 0.1–0.6,  $p$ <0.01). No associations between damage and activity of the disease or IIM subgroup were observed.



Abstract AB0794 – Figure 1

**Conclusions:** Most patients with IIM develop some kind of damage, with greater impact on the endocrinological, skeletal and gastrointestinal systems. There increases with the time of evolution and the use of steroids in a non-linear way. Therefore, these results should be taken into account in the decision-making process in long-term treatment.

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AB0795

#### LONG-TERM EFFICACY AND SAFETY OF RITUXIMAB IN SYSTEMIC SCLEROSIS REFRACTORY TO CONVENTIONAL IMMUNOSUPPRESSANTS

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**Background:** Recent studies<sup>1 2</sup> have shown that B-cells are involved in the pathogenesis of systemic sclerosis (SSc) suggesting that B-cell depletion might have a role in the treatment of the disease<sup>3</sup>.

**Objectives:** To describe the long-term efficacy and safety profile of Rituximab (RTX) in SSc patients who failed previous conventional immunosuppressive drugs.

**Methods:** We retrospectively analysed medical records of all SSc patients treated with Rituximab in our Rheumatology Unit from July 2011 to December 2017. Disease manifestations, particularly skin, pulmonary and articular involvement, were evaluated at baseline (T0), at 8±2 months (T1) and at the last follow-up visit (T2).

**Results:** Thirteen patients, 11 females and 2 males, were treated with 32 RTX cycles (median per patient 2.5, range 1–4). Eleven patients had diffuse and 2 limited cutaneous form; all had positive ANA, 9 anti-TopoI, 2 anti-RNA polIII, and 1 anti-SSA.

The mean age at first RTX infusion was 49.3±13.6 years and the mean disease duration was 6.5±3.3 years. The main indications to RTX were: interstitial lung disease (11/13), worsening of skin involvement (6/13) and arthritis (5/13), refractory to at least one previous immunosuppressive drug (median 2, range 1–3). Twelve patients were treated with mycophenolate mofetil, 5 with cyclophosphamide, 4 with methotrexate and 2 with azathioprine.

All patients were treated with RTX (1000 mg twice, two weeks apart). Twelve patients received more than one cycle; the interval between cycles was 12.7±5.4 months. The mean follow-up period was 41.4±21.9 months.

Five patients had arthritis and we observed complete remission of arthritis in all of them. 8 months after the first RTX administration arthritis relapsed in 4 patients who were successfully retreated.

We did not observe a significant decrease in modified Rodnan Skin Score over time (T0: 15.6±6.9, T1: 14.6±7.8, and T2: 13.1±8.3;  $p$ =ns).

Lung involvement, detected in 11/13 patients, remained radiologically stable in 8 patients and worsened in 3. No significant changes in the pulmonary function tests was observed from T0 to T2.

Five patients had a follow-up longer than 33 months after the last RTX cycle: 3 patients had a stable disease, 1 developed severe PAH and 1 lung neoplasia.

CD19 cell depletion (<2%) was observed after each RTX cycle, without significant changes in immunoglobulin levels. No infusion reactions were observed. We registered only one severe side effect: hand cellulitis in a patient with digital ulcer, requiring hospitalisation.

**Conclusions:** Our experience suggests that RTX is well tolerated and could be effective in the management of severe and refractory SSc manifestations.

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AB0796

#### SHORT TERM TREATMENT RESPONSE TO INTRAVENOUS PULSE CYCLOPHOSPHAMIDE TREATMENT IN CONNECTIVE TISSUE RELATED INTERSTITIAL LUNG DISEASE

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**Background:** Interstitial lung disease (ILD) is a major cause for morbidity and mortality in patients suffering from connective tissue diseases. Early detection and prompt recognition of symptoms with appropriate treatment is necessary for effective control of the disease and for better prognosis and long-term survival. Various treatments have been approved based on observational studies. We have very few studies as regards ILD treatment from the Indian subcontinent. In a resource constrained country like India, we mainly rely on cheap drugs like cyclophosphamide. We have done a study to assess the short-term treatment response of connective tissue related interstitial lung disease to cyclophosphamide in a tertiary centre in India.

**Objectives:** 1. To assess short treatment outcome for Connective tissue disease related interstitial lung disease treated with intravenous pulses of cyclophosphamide (CYP) based on improvement in-

Lung function 1) Forced vital capacity (FVC)% predicted, forced expiratory volume in first second (FEV1)% predicted 2) Dyspnoea Borg scale 3) Cough visual analogue score

2. To determine the factors affecting treatment outcome like age, sex, duration of the connective tissue disease, type of connective tissue disease, HRCT type and presence of PAH.

**Methods:** A cohort study was conducted in the Department of General Medicine, Rheumatology and Pulmonology in Amala Institute of Medical Sciences, Thrissur, Kerala from November 2015 to June 2017, that evaluated 74 patients who were having connective tissue disease related ILD. Detailed history and a thorough clinical examination was done. Treatment with 6 intravenous pulses of cyclophosphamide was done and response was assessed after 6 months. Response to treatment and associations were analysed using SPSS software (version 15). Method used for statistical analysis was Chi-Square test and paired t test.

**Results:**

Abstract AB0796 – Table 1

Count of FEV1	Column Labels				
Row Labels	31–50	51–70	71–90	91–110	Grand Total
31–50	4	4			8
51–70		25	23	4	52
71–90			14		14
<b>Grand Total</b>	<b>4</b>	<b>29</b>	<b>37</b>	<b>4</b>	<b>74</b>

There was no association between treatment response and age, sex or type of connective tissue disease. Following treatment there was a definite improvement in the clinical aspects of the patient which was assessed by dyspnoea Borg score and cough visual analogue score. Following treatment there was a definite improvement in PFT (FVC, FEV1) as well as 6 min walk test which was also statistically significant. CT pattern of Non specific interstitial pneumonitis also had a better outcome.

**Conclusions:** Our study proves that there is definite clinical and FVC improvement in CTD-ILD patients after giving treatment with cyclophosphamide. Determinants that can predict treatment outcome are duration of disease, HRCT type, (NSIP), presence of Pulmonary artery hypertension(PAH). Poor treatment response should be anticipated in those with longer duration of disease and UIP type in HRCT, presence of PAH.

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AB0797

#### A RANDOMISED DOUBLE BLIND PLACEBO CONTROLLED TRIAL TO COMPARE THE EFFICACY OF INITIAL COMBINATION THERAPY VS MONOTHERAPY FOR PULMONARY ARTERIAL HYPERTENSION IN SYSTEMIC SCLEROSIS

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**Background:** Pulmonary Arterial Hypertension(PAH) is one of the leading cause of death in Systemic Sclerosis(SSc) population. Trials that have studied the efficacy of initial oral combination therapy versus monotherapy for the treatment of PAH in SSc are limited.

**Objectives:** To study the efficacy and safety of monotherapy (sildenafil) versus initial combination therapy (sildenafil and bosentan) for treatment of SSc related PAH.

**Methods:** In a single centre, double blind, prospective, randomised, placebo controlled trial, 34 patients of SSc related PAH defined as Pulmonary Artery Systolic Pressures(PASP)>35 mmHg as measured by echocardiography, New York heart Association(NYHA) functional class II and III with forced vital capacity >60% were randomised in 1:1 ratio to sildenafil (20 mg thrice a day) and matched placebo or bosentan to one study arm or to the combination of sildenafil(20 mg thrice a day) and bosentan (62.5 mg twice daily for 4 weeks maximum up to 125 mg twice daily) to the other arm for 24 weeks. The primary end point of the study was to assess the change in pulmonary artery pressures measured by echocardiography at 24 weeks from baseline. The secondary efficacy end points was to compare the change in 6 min Walk Distance (6MWD), Time To Clinical Worsening(TTCW) and adverse events at 24 weeks. Intention to treat analysis was carried for the primary and secondary outcomes. p<0.05 was considered significant. Kaplan Meier survival analysis was done to estimate the time to PAH worsening and hazard ratio was calculated.

**Results:** The mean change in Pulmonary Artery Systolic Pressures in the monotherapy arm was -1.0 mmHg versus +2.1 mmHg in the combination arm (p=0.56). TTCW is prolonged in the combination arm. The mean survival time in the initial combination arm was 23.76±0.59 weeks and 23.28±0.23 weeks in the monotherapy arm. The hazard ratio was 0.73[95% C.I 0.04–11.7] (p=0.87). The mean change in the 6 min walk distance in the monotherapy arm was 15.88 ±31.83 m and 25.88±38.25 m in the combination arm (p=0.38). The satisfactory clinical response in the combination arm was 82.3% versus 70% in the

monotherapy arm (O.R=1.9[C.I 0.38–9.88] p=0.44). The upfront combination of sildenafil and bosentan was well tolerated with similar rates of adverse events in both group.

**Conclusions:** In this study we could not demonstrate any significant difference in the efficacy of initial combination therapy of sildenafil and bosentan over sildenafil monotherapy. The patients of systemic sclerosis tolerated the initial combination of sildenafil and bosentan well and the treatment prevented further deterioration. Larger studies with more number of subjects may be required to confirm the results.

Trial Registration- Clinical Trials.gov:NCT03053739

**Disclosure of Interest:** None declared

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AB0798

#### CLINICAL ASSOCIATIONS OF VASCULAR ENDOTHELIAL GROWTH FACTOR AND ITS RECEPTOR 2 TYPE IN SYSTEMIC SCLEROSIS

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**Background:** Systemic sclerosis (SSc) is characterised by impaired angiogenesis and peripheral microvasculopathy. A major role in the regulation of angiogenesis attributed to vascular endothelial growth factor, which performs its functions through interaction with its receptor 2 type (VEGFR2).

**Objectives:** The aim of our study was to assess the levels of VEGF in serum and its associations with clinical manifestations in patients with SSc.

**Methods:** We studied 46 patients with SSc who underwent clinical examination, pulmonary function tests and echocardiography. Serum VEGF-A and VEGFR2 levels were determined by ELISA in 46 SSc patients and 20 healthy controls

**Results:** Mean VEGF levels were increased in SSc patients compared to controls (212,35±253,93 and 97,74±71,46 pg/ml, respectively; p=0,032). Patients with limited cutaneous SSc (n=23) had higher levels of serum VEGF than those with diffuse cutaneous SSc (n=23) (267,11±268,74 vs 120,40±141,09 pg/ml; p=0,012). Patients with fingertip ulcers (n=19) were found to have higher levels of VEGF than pts without fingertip ulcers.(n=27) (214,25±265,93 vs 162,88±188,97) but this difference wasn't significant. Serum VEGF levels were higher in SSc patients with sPAP >30 mmHg than in those with sPAP ≤30 mmHg (286,51 ±287,42 vs 92,88±108,06 pg/ml; p=0,0042) and correlated with DLCO values (R=0,40; p=0,007). Mean VEGF levels in patients with DLCO <50% (n=14) were significantly higher than those with DLCO ≥50% (n=30): 364,20±381,95 vs 128,55±142,70 pg/ml, respectively (p=0,034). There weren't significant differences in VEGF levels between patients with FVC <80% (n=11) and those with FVC ≥80% (219,15±252,57 vs 154,26±208,91 pg/ml, respectively).

Mean VEGFR2 levels were also increased in SSc pts compared to controls (5784,6±4773,8 and 1552,6±272,8 pg/ml, respectively; p<0,0001). There weren't any differences between pts with diffuse or limited SSc. In pts with digital ulcers, or normal levels of sPAP, or DLco ≥50% mean VEGFR2 levels didn't differ from those without digital ulcers, or sPAP >30 mm Hg, or DLco <50%, respectively. Serum VEGF levels directly correlated with sPAP (R=0,40; p=0,007).

**Conclusions:** Our findings show significantly higher circulating levels of VEGF and VEGFR2 in SSc patients. Associations of VEGF with some clinical signs indicate its role in pathology of SSc.

**Disclosure of Interest:** None declared

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AB0799

#### ALTERATIONS OF BODY COMPOSITION IN SCLERODERMA PATIENTS ARE ASSOCIATED WITH DISEASE ACTIVITY AND PHYSICAL ACTIVITY BUT NOT WITH LUNG INVOLVEMENT

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**Background:** Systemic sclerosis (SSc) is characterised by fibrosis of the skin and visceral organs, especially digestive tract, and musculoskeletal and lung involvement, which limit mobility/self-sufficiency of patients and can have a negative impact on body composition and physical activity.

**Objectives:** To assess body composition and physical activity of SSc patients and healthy controls (HC).

**Methods:** 59 patients with SSc [50 females; mean age 52.5; disease duration 6.7 years; limited cutaneous (lcSSc, 34)/diffuse cutaneous (dcSSc, 25)] and 59 age-/sex-matched HC (50 females, mean age 52.5) without rheumatic diseases were

included. SSc patients fulfilled ACR/EULAR 2013 criteria. Anthropometric parameters and body composition were assessed (by densitometry: iDXA Lunar, and by bioelectric impedance: BIA-2000-M), and physical activity was evaluated using Human Activity Profile (HAP) questionnaire. Routine biochemistry analysis was performed after 8 hours of fasting. Pulmonary function and diffusing capacity of lung were examined, disease activity was evaluated by ESSG activity index. Data are presented as mean  $\pm$ SD.

**Results:** Compared to HC, patients with SSc had significantly lower body-mass index (BMI: 27.9 $\pm$ 8.3 vs. 22.4 $\pm$ 4.3 kg/m<sup>2</sup>,  $p < 0.0001$ ) and body fat% assessed by both iDXA (BF%: 38.0 $\pm$ 7.6 vs. 32.6 $\pm$ 8.2%,  $p < 0.0001$ ) and BIA (BF%: 31.3 $\pm$ 7.6 vs. 24.3 $\pm$ 7.9%,  $p < 0.0001$ ), and decreased visceral fat weight (1.0 $\pm$ 0.8 vs. 0.5 $\pm$ 0.5 kg,  $p = 0.001$ ). Compared to HC, SSc patients also demonstrated significantly decreased lean body mass assessed by both iDXA (LBM: 51.9 $\pm$ 8.4 vs. 47.8 $\pm$ 7.0 kg,  $p = 0.005$ ) and BIA (LBM: 45.4 $\pm$ 7.3 vs. 40.9 $\pm$ 6.8 kg,  $p = 0.005$ ), significantly lower bone mineral density (BMD: 1.2 $\pm$ 0.1 vs. 1.0 $\pm$ 0.1 g/cm<sup>2</sup>,  $p < 0.0001$ ), and had increased extracellular mass/body cell mass (ECM/BCM) ratio (1.03 $\pm$ 0.1 vs. 1.28 $\pm$ 0.4,  $p < 0.0001$ ), which reflects deteriorated nutritional status and worse muscle predispositions for physical exercise, aerobic fitness/performance. Increased ECM/BCM in SSc patients positively correlated with disease activity (ESSG:  $r = 0.273$ ,  $p = 0.0439$ ), skin score (mRSS:  $r = 0.371$ ,  $p = 0.0045$ ) and inflammation (CRP:  $r = 0.292$ ,  $p = 0.0278$ ; ESR:  $r = 0.302$ ,  $p = 0.0226$ ). Increased ECM/BCM was also associated with worse quality of life (HAQ:  $r = 0.438$ ,  $p = 0.0007$ ; SHAQ:  $r = 0.268$ ,  $p = 0.0436$ ), fatigue (FSS:  $r = 0.366$ ,  $p = 0.0040$ ), and worse ability to perform physical activity (HAP:  $r = -0.644$ ,  $p < 0.0001$ ). Disease activity (ESSG) negatively correlated with BF% by iDXA ( $r = -0.324$ ,  $p = 0.0138$ ). Physical activity (HAP) positively correlated with BMD ( $r = 0.280$ ,  $p = 0.032$ ). There was no significant correlation of lung involvement with alterations of body composition.

**Conclusions:** Compared to healthy age-/sex-matched individuals we found significant negative changes in body composition of our SSc patients, which are associated with their disease activity and physical activity, and could reflect their nutritional status, and gastrointestinal and musculoskeletal involvement. We found no significant association between lung involvement and changes of body composition.

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AB0800

#### CHANGES OF BODY COMPOSITION IN MYOSITIS PATIENTS ARE ASSOCIATED WITH DISEASE DURATION, INFLAMMATORY STATUS, SKELETAL MUSCLE INVOLVEMENT AND PHYSICAL ACTIVITY

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**Background:** Idiopathic inflammatory myopathies (IIM) are characterised by inflammation and atrophy of skeletal muscles, pulmonary and articular involvement, which limit the mobility/self-sufficiency of patients, and can have a negative impact on body composition.

**Objectives:** To assess body composition and physical activity of IIM patients and healthy controls (HC).

**Methods:** 54 patients with IIM (45 females/9 males; mean age 57.7; disease duration 5.8 years; polymyositis (PM, 22)/dermatomyositis (DM, 25)/necrotizing myopathy (IMNM, 7)) and 54 age-/sex-matched HC (45 females/9 males, mean age 57.7) without rheumatic diseases were included. PM/DM patients fulfilled Bohan/Peter criteria for PM/DM. Anthropometric parameters and body composition were assessed (by densitometry: iDXA Lunar, and by bioelectric impedance: BIA2000-M), and physical activity was evaluated using Human Activity Profile (HAP) questionnaire. Routine biochemistry analysis was performed after 8 hours of fasting. Muscle involvement was evaluated by manual muscle test (MMT-8) and functional index 2 (FI2). Data are presented as mean  $\pm$ SD.

**Results:** Compared to HC, patients with IIM had a trend towards significantly increased body fat% as assessed by iDXA (BF%: 39.9 $\pm$ 7.1 vs. 42.4 $\pm$ 7.1%,  $p = 0.077$ ), but significantly decreased lean body mass as assessed both by iDXA (LBM: 45.6 $\pm$ 8.1 vs. 40.6 $\pm$ 7.2 kg,  $p = 0.001$ ) and BIA (LBM: 52.6 $\pm$ 8.8 vs. 48.7 $\pm$ 9.0 kg,  $p = 0.023$ ), and increased extracellular mass/body cell mass (ECM/BCM) ratio (1.06 $\pm$ 0.15 vs. 1.44 $\pm$ 0.42,  $p < 0.0001$ ), which reflects worse muscle predispositions for physical exercise, aerobic fitness/performance, and also deteriorating nutritional status. Compared to HC, IIM patients had significantly lower bone mineral density (BMD: 1.2 $\pm$ 0.1 vs. 1.1 $\pm$ 0.1 g/cm<sup>2</sup>,  $p < 0.001$ ). Disease duration negatively correlated with BMD ( $r = -0.392$ ,  $p = 0.004$ ) and LBM-BIA ( $r = -0.272$ ,  $p = 0.047$ ). CRP was positively associated with BF% assessed both by DEXA ( $r = 0.276$ ,  $p = 0.035$ ) and BIA ( $r = 0.306$ ,  $p = 0.025$ ). Higher BF% $>$ DEXA was associated with worse physical endurance (FI2:  $r = -0.311$ ,  $p = 0.026$ ) and worse ability to

perform physical activity (HAP:  $r = -0.292$ ,  $p = 0.032$ ). MMT-8 score negatively correlated with ECM/BCM ratio ( $r = -0.385$ ,  $p = 0.006$ ).

**Conclusions:** Compared to healthy age-/sex-matched individuals we found significant negative changes in body composition of our IIM patients, which are associated with their disease duration, inflammatory status, skeletal muscle involvement, and physical activity, and could reflect their impaired nutritional status and predispositions for physical exercise, aerobic fitness and performance.

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AB0801

#### SARCOPENIA AND MICROCIRCULATION IN SYSTEMIC SCLEROSIS PATIENTS: A PILOT ASSAY

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**Background:** Systemic sclerosis (SSc) patients may present muscle involvement in the form of myositis or non-inflammatory myopathy with different degree of weakness and muscle atrophy.<sup>1</sup> Sarcopenia is described as a multifactorial syndrome with muscle mass loss associated to functional impairment; according to the anthropometric equation by Baumgartner et al. sarcopenia was defined as relative skeletal muscle mass index (RSMI)  $< 5.5$  Kg/m<sup>2</sup> for women and  $< 7.26$  Kg/m<sup>2</sup> for men. The relationships between sarcopenia and other clinical aspects in SSc are poorly investigated.

**Objectives:** The aim of the study was to evaluate the associations between sarcopenia and other clinical factors in SSc patients.

**Methods:** 20 female patients fulfilling the ACR 2013 criteria for SSc (mean age 61.7 $\pm$ 13.6 years, disease duration 86.2 $\pm$ 67.1 months) were enrolled. The RSMI (Kg/m<sup>2</sup>) was evaluated by dual-energy X-ray absorptiometry scan (Lunar Prodigy). Nail fold videocapillaroscopic (NVC) patterns (early, active, late) were analysed. Serum 25(OH)<sub>2</sub>D concentration was tested by immunofluorescence. Non parametric statistical tests were used.

**Results:** Patients showed a modified Rodnan skin score (mRSS) 12.2 $\pm$ 7.7, RSMI 6.01 $\pm$ 0.97 Kg/m<sup>2</sup>, serum vitamin D (25(OH)<sub>2</sub>D) 22.01 $\pm$ 13.1 ng/dL and CPK 70.16 $\pm$ 31.8 U/L. In this cohort 23% of SSc patients were found affected by sarcopenia, and almost 42% showed the most advanced level of microvascular damage, as characterised by the NVC late pattern. However, no statistically relevant correlations were observed between RSMI, BMI, age, disease duration, CPK, mRSS, 25(OH)<sub>2</sub>D and active or late NVC patterns. Comparing age, disease duration, CPK and mRSS in both sarcopenic and non sarcopenic SSc patients there was no difference between the groups, however sarcopenic patients showed statistically significant lower BMI ( $p = 0.02$ ), lower RSMI ( $p = 0.0008$ ) and higher 25(OH)<sub>2</sub>D serum concentrations ( $p = 0.01$ ). Particularly, RSMI showed a strong negative correlation with age ( $p = 0.01$ ). No statistical differences were found when grouping the patients according to the positivity for serum anti-topoisomerase I Ab or according to cutaneous diffuse (dcSSc) or limited (lcSSc) systemic sclerosis.

**Conclusions:** This pilot study suggests that sarcopenia seems present in almost 25% of the SSc patients, particularly in a condition of advanced microcirculation failure (late NVC pattern), however does not seem to correlate with skin fibrosis or disease duration. The study had some limitations due to absence of control group and to the small patient sample analysed. Further larger studies would be necessary to better investigate the role of sarcopenia in SSc.

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**Disclosure of Interest:** None declared

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AB0802

#### OSTEOPOROSIS IN SYSTEMIC SCLEROSIS: CASE-CONTROL STUDY WITH A FRENCH OFELY COHORT AND RISK FACTORS

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**Background:** Systemic sclerosis (SSc) is a rare autoimmune disorder characterised by a vascular and fibrosing involvement of the skin and internal organs. Data



about the association between systemic sclerosis (SSc) and osteoporosis (OP) are controversial and scarce about the risk factors of OP in SSc.<sup>1,2</sup>

**Objectives:** The aim of the study was to determine the OP frequency in SSc and assess its risk factors.

**Methods:** In a prospective cohort of SSc patients, usual risk factors of OP were assessed, as well as SSc organ involvements: pulmonary, cardiac, skin and renal involvements and SSc treatments. All patients underwent dual energy X-ray absorptiometry: bone mineral density (BMD) was measured at the lumbar spine (LS), femoral neck (FN) and total hip (TH). Osteoporosis was defined as having a T-score inferior to -2.5.

**Results:** Forty-eight patients were included with a median age of 60 years,<sup>27-81</sup> 41 women (85.4%), with a diffuse cutaneous subtype in 13 cases (27.1%) and illness duration of 12.6 years (0.3-41.1). Average BMD was 0.98±0.21 in LS, 0.84±0.13 in FN and 0.86±0.15 in TH. OP was found in 19 patients (40%). Among patients with OP, an associated auto-immune disorder was found in 13 patients (68.4%) versus 10 (34.5%) in the non-OP group (p=0.04), digestive sub-occlusion in 4 patients (21% versus 0 patients, p=0.02), and chronic liver disease in 6 patients (31.6%) versus 2 (6.9%, p=0.04). Respiratory explorations found a DLCO of 12.7 (6.8-17.2) versus 15.6 (9.6-32.2) (p=0.007), a CVF of 2.47 (1.1-4) versus 3 (1.7-5.9) (p=0.03). DAS28-CRP was significantly higher (2.29 (1.53-4.46) in the OP group versus 1.86 (0-3.8) in the non-OP group, p=0.02); with a higher frequency of hand X-ray erosions (6 OP patients (31.6%) versus 2 (6.9%), p=0.04). No difference was found in Rodnan score, SSc subtype, illness duration, malnutrition, treatments (proton pump inhibitors, cyclophosphamide, steroids), autoantibodies profile; nor with the usual OP risk factors: age, smoking, personal or family history of OP fractures, alcohol consumption, weight, BMI, long term steroid treatment, early menopause and thyroid disease. No difference in serum vitamin D, calcium, thyroid hormones and C-reactive protein levels was found between OP and non-OP groups.

**Conclusions:** Osteoporosis was associated with SSc-related factors such as: articular, digestive and respiratory involvements, and associated auto-immune diseases. Usual OP risk factors were not significantly different between osteoporotic SSc patients and non-osteoporotic patients.

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**Disclosure of Interest:** None declared

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**AB0803 A REAL LIFE EXPERIENCE ON THE EFFICACY AND SAFETY OF MYCOPHENOLATE MOFETIL IN CONNECTIVE TISSUE DISORDER ASSOCIATED INTERSTITIAL LUNG DISEASE – A RETROSPECTIVE STUDY**

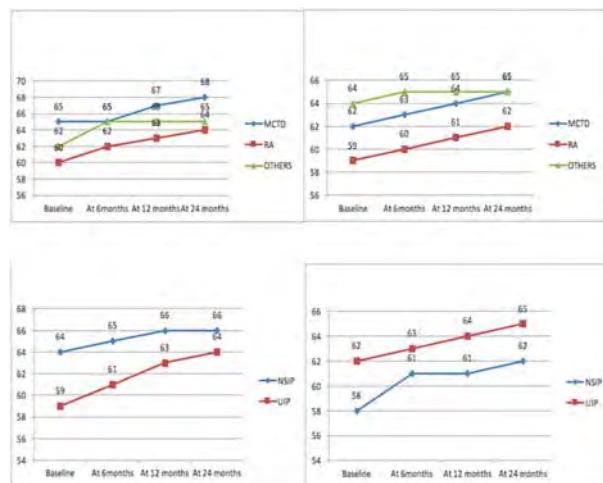
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**Background:** Interstitial lung disease(ILD) is one of the common extra articular manifestations of various connective tissue disorders(CTD). We don't have enough evidence on the drugs used, except for ILD in systemic sclerosis and the results of the same has been extrapolated to other diseases. Mycophenolate mofetil(MMF) has antiproliferative and anti fibrotic action in addition to anti inflammatory property and hence we wanted to study the efficacy and safety of MMF in our diverse cohort of CTD-ILD.

**Objectives:** To study the efficacy and safety of mycophenolate mofetil (MMF) in a diverse cohort of patients with connective tissue disease(CTD) associated interstitial lung disease(ILD).

**Methods:** This is a retrospective observational study with records of outpatients with CTD associated ILD were screened from Oct 2014 to Dec 2017. Among them, patients with imaging (HRCT chest) documented ILD were included. All patients underwent detailed clinical assessment, serological investigations (baseline blood test, erythrocyte sedimentation rate, C-reactive protein, rheumatoid factor, ACPA Ab, antinuclear antibody, ANA profile, complements), urine routine, pulmonary function test(PFT), HRCT chest and echocardiogram. The response of ILD to treatment(follow up of 2 years) was assessed clinically, radiologically and by PFT.

**Results:** 54 patients were identified with CTD-ILD of which 33 patients were on MMF. 13 patients were diagnosed with MCTD, 12 with RA, 3 with diffuse cutaneous systemic sclerosis, 2 with SSc/myositis overlap, 1 with primary sjogren's syndrome, 1 with SLE/Sjogren's overlap and 1 with lung dominant CTD(Scl 70+ve). The cohort was divided in to 3 groups – MCTD, RA and others (SSc predominant). Among patients with MCTD, 10 had NSIP pattern of ILD, 3 UIP. In RA, 7 had NSIP and 5 UIP and among others 7 NSIP and 1 UIP. The mean FEV1 and FVC values over 2 years and the treatment response has been discussed in table 1 and Figure 1. FEV1 and FVC had high positive correlations (Pearson correlation, p<0.05) with treatment for all groups of diseases. The values go together in the positive direction with treatment. Among the groups, all patients who improved had NSIP pattern and all who worsened had UIP. Though there were numerical differences in the mean values of FEV1 and FVC between two groups (NSIP and UIP), it was not statistically significant (paired 't' test, p>0.05). There was no significant difference in FEV1 and FVC values with treatment between the three groups (one way ANOVA test).



Abstract AB0803 – Figure 1

**Conclusions:** Treatment with MMF over a median duration of 24 months stabilised the ILD in majority. MMF appears to be efficacious, safe and well tolerated in our diverse cohort of CTD-ILD and needs to be evaluated further in prospective studies with a bigger sample size.

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Abstract AB0803 – Table 1

Variables	Mean FEV1 (%)				Baseline	Mean FVC (%)			ILD after treatment (PFT and Radiological)		
	Baseline	At 6 months	At 12 months	At 24 months		Baseline	At 6 months	At 12 months	At 24 months	Improved	Stable
MCTD	65	65	67	68	62	63	64	65	4	8	1
RA	60	62	63	64	59	60	61	62	4	7	1
OTHERS	62	65	65	65	64	65	65	65	0	7	1

AB0804 **THE RELATIONSHIP BETWEEN AUTOANTIBODIES AND CLINICAL SYMPTOMS IN PATIENTS WITH INFLAMMATORY MYOPATHY**

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**Background:** Myositis-specific autoantibody (MSA) and myositis-associated autoantibody (MAA) are often detected in dermatomyositis (DM) and polymyositis (PM), and are useful diagnostic markers. In addition, autoantibodies are reportedly related to clinical symptoms, including skin findings, muscle symptoms, and interstitial lung disease, and provide information useful for medical treatment. However, the clinical significance of the presence of multiple MSA/MAA and anti-Ro52 autoantibodies has not been determined.

**Objectives:** The purpose of our study was to clarify the clinical significance of multiple MSA/MAA and anti-Ro52 autoantibodies.

**Methods:** We enrolled 58 patients diagnosed with DM and PM at Kagawa University Hospital. PM and DM were diagnosed according to the Bohan and Peter criteria.<sup>1</sup> The patients were analysed for MSA (anti-Mi-2, anti-Jo-1, anti-SRP, anti-PL-7, anti-MDA5, anti-TIF1 $\gamma$ , anti-PL-12, anti-EJ, and anti-OJ) and MAA (anti-RNP, anti-Ku, and anti-PM-Scl) by ELISA (MESACUP anti-ARS, MDA5 and TIF1 $\gamma$  test, MBL, Nagoya, Japan) and Line blot (EUROLINE Myositis Profile 3, EUROIMMUN, Lübeck, Germany). We extracted MSA/MAA(+) and anti-Ro52(+) patients and analysed the association between the presence of multiple MSA/MAA or anti-Ro52 autoantibodies and patients' clinical features (skin findings such as Gottron papule, heliotrope rash and mechanic's hand, interstitial lung disease, malignancy, and arthritis).

**Results:** 53/58 patients were positive for MSA/MAA, followed by anti-Ro52 (n=27), anti-PL7 (n=12), anti-Jo1 (n=8), anti-PM-Scl75 (n=7), anti-Ku (n=6), anti-SRP (n=4), anti-EJ (n=4), anti-TIF1 $\gamma$  (n=4), anti-MDA5 (n=4), anti-Mi2 (n=3), anti-PL12 (n=1), anti-PM-Scl100 (n=1), and five cases were MSA/MAA(-). Five patients had multiple MSA/MAA (anti-PL-7+anti-Jo-1, anti-PL-7+anti-PL-12, anti-PL-7+anti Ku, anti-Ro52 +anti-Jo1+anti-PM-Scl75, and anti-Ro52 +anti-Jo1+anti Ku). In patients with DM/PM, anti-Ro52(+) patients were complicated by interstitial lung disease (ILD) and had a higher KL-6 value at onset (p<0.05). Notably, 17/27 patients with anti-Ro52 autoantibodies were also anti-ARS(+) and all patients with anti-ARS autoantibodies had ILD. In contrast, among the anti-ARS(-) patients (n=35), there was no significant correlation between anti-Ro52(+) and ILD. Therefore, anti-ARS may be a greater risk factor for ILD than anti-Ro52. Furthermore, patients with multiple MSA/MAA had a higher incidence of rapidly progressive ILD (p<0.05). There was no correlation between multiple MSA/MAA or anti-Ro52 autoantibodies and CK or muscle symptoms.

**Conclusions:** We hypothesise that the presence of multiple MSA/MAA may be useful for predicting ILD. However, in this study, anti-Ro52 autoantibodies did not correlate with ILD and myositis.

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**Disclosure of Interest:** None declared

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AB0805 **CLINICAL FEATURES AND OUTCOME IN SCLERODERMA RENAL CRISIS**

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**Background:** Systemic sclerosis (SSc) is a chronic, autoimmune disease of the connective tissue that involves skin, subcutaneous tissue, muscles and joints, as well as the internal organs: kidneys, lungs, heart. Depending on the extent it can occur as limited (lcSSc) or diffuse (dcSSc) clinical variant. About half of the patients with renal involvement the clinical manifestation is limited to a moderate increase in serum creatinine, mild proteinuria, and moderate hypertension. The most serious complication remains scleroderma renal crisis (SRC). There was significant heterogeneity in definitions. As a rule for SRC was characterised by new-onset severe hypertension, hypertensive encephalopathy and seizures, acute kidney injury with oliguria, proteinuria and erythrocyturia, and microangiopathic hemolytic anaemia with thrombocytopenia.

**Objectives:** The aim of our study was to analyse the clinical features and outcome of patients with scleroderma renal crisis.

**Methods:** We retrospectively reviewed the medical records of patients with scleroderma renal crisis between January 2002 and December 2016. Conditional logistic regression and multivariate analysis was performed to determine factors independently associated with outcome in patients with SRC.

**Results:** 18 (14 females and 4 males, median age 47.3±14.6 years) patients diagnosed with SRC were included in the study. The mean duration from first symptom of systemic sclerosis (Raynaud's phenomenon, cutaneous sclerosis, arthralgia/arthritis, puffy hands, interstitial lung disease, pulmonary arterial hypertension, digestive hypomotility and etc.) to SRC attack was 4.47±2.9 years. 13 SRC patients belonged to dcSSc, and 5 patients – to lcSSc. Among SRC patients, 9 were negative of anti-centromere antibodies (ACAs). All these 18 patients had hypertension and renal insufficiency, including 4 dialysis dependent after the onset of SRC and 6 with thrombotic microangiopathy. There were 6 patients receiving renal biopsy (the pathological findings were mainly summarised as intimal thickening and stenosis of renal arterioles). Among 16 patients with long-term followed-up, 15 patients received angiotensin converting enzyme inhibitors (ACEI), 8 patients died, 1 patient was dialysis dependent. Survival from first symptom in those patients with Raynaud's phenomenon mode of onset was higher at 5 years and at 10 years than those with onset as non-Raynaud's phenomenon (p < 0,05). In multivariate analysis, factors related to mortality in SRC were older age at onset, male gender, treatment with corticosteroids, dcSSc subset, interstitial lung disease, pulmonary arterial hypertension, heart involvement, and the mode of onset with non-Raynaud's phenomenon, especially in the form of pulmonary involvement. The mode of onset should be considered an independent prognostic factor in SRS. The treatment of SRC relies on aggressive blood pressure control with an ACEI, combined with other antihypertensive drugs if needed.

**Conclusions:** SRC usually occurred at the early course of SSc. dcSSc was more frequent than lcSSc. ACAs were found in 50% of SRC patients. The use of ACEIs was still the cornerstone of SRC treatment.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.1693

AB0806 **THE IMPACT OF DYSPHAGIA IN IDIOPATHIC INFLAMMATORY MYOSITIS: AN ONLINE SURVEY OF HIGHLY-SPECIALISED CENTRES**

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**Background:** Dysphagia represents a frequent and disabling symptom in patients with idiopathic inflammatory myopathies (IIM). Despite this, there are not widely accepted diagnostic and therapeutic guidelines for dysphagia in IIM.

**Objectives:** This study is aimed at surveying the approach to dysphagia in IIM patients in European and worldwide referral centres.

**Methods:** An anonym on-line survey was designed and clinicians from European Union (EU) countries, and countries from North and Central America and South Korea were invited via email to participate. The questionnaire included 11 items about the characteristics of the hospital of the responder, the evaluation of the impact of dysphagia on disease severity assessed on a visual analogue scale (10 VAS), the techniques used for the assessment of dysphagia, the use of validated patients reported outcome (PRO) and the therapeutic approach of dysphagia.

**Results:** Between December 2017 and January 2018, 52 clinicians from different centres working in 21 different countries (18 EU countries, 3 non-EU countries) completed the survey. The total numbers of patients followed in the participating centres were 3817 with an average number of patients followed in each centre of 75 (±83). The majority of centres followed only adult patients,<sup>45</sup> 2 only paediatric patients (<18 years) and 5 both. The impact of dysphagia on disease severity was considered severe by all the participants with a mean VAS score of 7.3. All but one centre routinely ask the patients for the presence of dysphagia during the clinical examination. The assessment of dysphagia is performed using validated PRO questionnaires in only 7 centres (SWAL-QOL 2 centres, EAT-10 2 centres, MDADI 2 centres, UCLA-GIT 1 centre); 2 centres evaluate dysphagia using a graduate dysphagia scale by means a 10 cm VAS, and 2 routinely screen patients by a functional test (time necessary to drink a glass of water).

In all the centres an instrumental evaluation of esophageal motility is performed: esophageal manometry in 24 centres, videofluoroscopic swallowing exam in 17, esophageal barium x-rays in 16, and pHmetry and functional endoscopy in 14 each. Esophageal scintigraphy and esophagogastrosopy were respectively performed in 5 and 3 centres. The presence of dysphagia greatly influences the therapeutic approach to IIM in 49 centres leading to an increase of the corticosteroids dosage (11 centres), a change of the immunosuppressive treatment<sup>12</sup> or the initiation of intravenous immunoglobulins (IVlg).<sup>26</sup>

**Conclusions:** This study suggests that the approach to dysphagia is variable, but dysphagia has an impact on IIM patients and influences the therapeutic

decisions of the treating physician. Different therapeutic strategies are adopted regarding the treatment, and in many cases highly expensive drugs as Ivlg are prescribed. Further studies and recommendations are certainly needed for homogenising the patient management for this severe aspect of the disease.

**Disclosure of Interest:** None declared

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#### AB0807 PLATELET INDICES AS MARKERS OF INFLAMMATION IN SYSTEMIC SCLEROSIS

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**Background:** Systemic sclerosis (SSc) is a connective tissue disease involving multiple organs with an unknown etiology. Platelet function may be associated with endothelial dysfunction and immune regulatory mechanisms. Recently, an increased tendency to platelet aggregation and enhanced platelet activation have been described in SSc patients, suggesting a role for platelets in the disease itself.<sup>1,2</sup>

**Objectives:** To evaluate platelet indices in systemic sclerosis (SSc) patients and identify their clinical significance as novel inflammatory biomarkers in correlation to markers of endothelial dysfunction: vascular endothelial growth factor (VEGF) and flow mediated dilatation (FMD).

**Methods:** Thirty-five SSc patients were enrolled in addition to thirty-five age and sex matched healthy volunteers as controls. All patients and controls underwent full medical history taking, thorough clinical examination, assessment of severity extent of skin sclerosis using the modified Rodnan skin score, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), complete blood count with special consideration to mean platelet volume (MPV), platelet distribution width and platelets count, assay for serum VEGF concentration, and brachial FMD assessment by colour duplex sonography.

**Results:** There was a highly significant decrease in the mean MPV in SSc patients compared to the controls (8.65±0.6 fl vs. 9.55±0.52 fl). There was a significant increase in the mean platelet count in SSc patients compared to controls (331.63±64.66 × 10<sup>3</sup>/ml vs. 297.80±44.48 × 10<sup>3</sup>/ml). In SSc patients, a significant negative correlation was found between the mean MPV and each of ESR, CRP and VEGF (r=-0.42, -0.368 and -0.55 respectively, p<0.05); and a significant positive correlation was found between the mean MPV and mean FMD (r=0.378, p<0.05). Linear regression test, showed an association between mean MPV and each of ESR and CRP (t=-3.312, -2.92 respectively, p<0.05).

**Conclusions:** MPV levels could be an easily measurable parameter to reflect the inflammatory condition and disease activity in systemic sclerosis patients.

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**Disclosure of Interest:** None declared

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#### AB0808 MULTICENTRIC STUDY OF SYSTEMIC SCLERODERMA IN TUNISIA

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**Background:** Scleroderma is an autoimmune connective tissue disorder which is characterised by fibrosis of visceral organs, skin and blood vessels. This condition can be localised or systemic. Its estimated prevalence is 250 cases in a million and it is more common in women than in men.

**Objectives:** The aim of this retrospective multicenter study was to analyse demographic, clinical, laboratory features and outcome of SSc in Tunisia throughout 8 Departments of Internal Medicine and to compare them with those of other geographic groups.

**Methods:** One hundred and eight cases of SSc were recorded (American College of Rheumatology criteria) during a 15 years period. They were 93 women and 15 men with an average age at SSc onset of approximately 46.9 years.<sup>17-75</sup>

**Results:** Only 18 patients had limited cutaneous SSc, 11 patients had a CREST syndrome. Our Tunisian patients were characterised by a high frequency of cutaneous signs: sclerodactyly (80.6%), proximal sclerosis (81%), telangiectasia (34.3%), Raynaud's syndrome (91%), pigmentation disorders (36%), ulceration (24%) and subcutaneous calcification (4.6%). The other clinical manifestations were dysphagia in 54% (n=59), pulmonary involvement in 55.6% (n=60), cardiac

manifestation in 27% (n=29), arthritis in 19.4% (n=21), renal involvement in 13.8% (n=15), and neurological involvement in 12 cas. 78.7% were antinuclear antibody (ANA) positive, 25% were Antitopoisomerase-I antibodies (anti-Scl-70 antibody) positive and 10% with anti-centromere antibodies.

SSc was associated to Sjögren's syndrome n=27, systemic lupus erythematosus (n=8), Polymyositis (n=5) and Rheumatoid arthritis (n=1)

Treatment regimen included, calcium channel blockers (65.7%), steroids (47%), Colchicine (47.2%), D penicillamine (21%), immunosuppressive therapy was added in patient with partial control (n=13). Median follow-up period was 3.7 years. With the above treatment protocol, (29.6%) patients achieved disease control on treatment, (43.3%) had partial control while (26.8%) showed no response or progressive disease, Six patients died, three of them with scleroderma renal crisis.

**Conclusions:** The findings of this study documents The high frequency of extensive cutaneous sclerosis, Potential limitations and biases in our study need discussion. Specific recruitment of patients in tertiary referral centres may be the source of selection bias. Patients were evaluated by different doctors. The therapeutic management and outcome monitoring were heterogeneous. This study remains the most representative of Tunisian Scleroderma patients recruited from all parts of Tunisia

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#### AB0809 A NEW SCORE TO PREDICT DIGITAL ULCERS COMBINING CLINICAL DATA, IMAGING AND PATIENT HISTORY IN SYSTEMIC SCLEROSIS

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**Background:** Ischaemic complications such as digital ulcers (DU) are a common complication in systemic sclerosis (SSc) patients.

**Objectives:** The aim of this study was to combine clinical characteristics and imaging methods to a composite predictive score.

**Methods:** Seventy-nine SSc patients received clinical examination and their patient history was taken. Furthermore, we performed nailfold capillaroscopy (NC), colour Doppler ultrasonography (CDUS) and fluorescence optical imaging (FOI) of the hands at baseline. Newly developed digital ulcers over a period of approximately 12 months were registered. We used criteria with significant (p<0.5) OR values above 3.5 in regard to the development of these new DU to create the score (CIP-DUS, clinical features, imaging, patient history – digital ulcer score)

**Results:** Twenty-nine percent of the patients developed new DU during follow-up (48.1% diffuse SSc, 18.4% limited SSc). The following criteria were used: SSc diffuse subtype (OR 4.127, p=0.0087), modified Rodnan skin score >8 (OR 9.429 [95%CI: 3.0–29.2], p<0.0001), pulmonary arterial hypertension (OR 6.854 [95%CI: 1.6–9.7], p=0.0088), present digital ulcers or pitting scars at baseline (OR 15.71 [95%CI: 3.3–74.3], p<0.0001), history of digital ulcer or pitting scars (OR 36.15 [95%CI: 2.1–626.9], p<0.0001), NC pattern (OR 18.6 [95%CI: 1.1–326.4], p=0.0035), reduced capillary density (n<7/mm) in digit III of the right hand in NC (OR 9.0 [95%CI: 1.1–73.6], p=0.0266), missing initial enhancement in FOI in digit III of the right hand (OR 3.857 [95%CI: 1.2–12.8], p=0.0323), percentage of pathologic (i. e. narrowed or occluded) vessels>35% in CDUS (OR 4.286 [95%CI: 1.5–12.4], p=0.0099). Criteria with greater OR should impact the score to a higher degree so we appointed three points to dichotomous criteria with OR >10, two points for criteria with OR between 5–10, and one point for criteria with OR <5. Regarding the NC pattern, 3 points were given to patients with late pattern, 2 points for active and 1 point for early pattern.

Best results were found for a cut-off of >10 points with obtained sensitivity levels of 95% and specificity levels of 74% in regard to new DU (AUC=0.8687, p<0.0001). In the absence of CDUS and FOI data, specificity levels dropped slightly to 72% with unchanged sensitivity values of 95%.



**Conclusions:** A new score was introduced with the aim to predict digital ulcers. If applied correctly and with the new imaging techniques proposed, 95% of patients at risk of digital ulcers throughout 12 months could be identified.

**Disclosure of Interest:** None declared

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AB0810

#### A COMPARISON OF CLINICAL PRESENTATION AND INCIDENCE RATE OF CARDIOPULMONARY INVOLVEMENT BETWEEN MALE AND FEMALE PATIENTS WITH EARLY SYSTEMIC SCLEROSIS

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**Background:** Data regarding the incidence rate (IR) of cardiopulmonary involvement in comparison between male and female patients with early systemic sclerosis (SSc) are limited.

**Objectives:** To compare the prevalence of clinical manifestations and the IR of cardiopulmonary involvement comparing between male and female patients with early SSc.

**Methods:** An inception cohort of early SSc patients (disease duration  $\leq 3$  years from the first non-Raynaud's phenomenon) seen at the Rheumatology clinic, Maharaj Nakorn Chiang Mai Hospital, Thailand, between January 2010 and June 2016, was used. All patients were assessed for clinical manifestations and underwent ECG, echocardiography, and HRCT at the study entry and every 12 months thereafter. In the last visit, the cumulative clinical manifestations were recorded. Patients who continue to follow up at least 12 months were included for analysis.

**Results:** One hundred and fifteen patients (89 dcSSc) with a mean (SD) disease duration of 11.6 (8.8) months at cohort entry were enrolled during a mean (SD) observation period of 3.8 (1.6) years. There were 46 male patients (40%). Tests for anti-topoisomerase I and anti-centromere antibodies were positive in 91 (79.1%) and 7 (6.1%) patients, respectively. The male group had higher prevalence of dcSSc subtype (91.3% vs. 69.5%,  $p=0.006$ ) and positive test for anti-topoisomerase I antibody (89.1% vs. 72.5%,  $p=0.031$ ) compared with the female group. At enrollment, the male group had higher prevalence of hypo-hyperpigmentation (84.8% vs. 65.2%,  $p=0.021$ ), suspected myositis (26.1% vs. 10.1%,  $p=0.024$ ), and right ventricular dysfunction (8.7% vs. 0%,  $p=0.024$ ) compared with the female group. In the last visit, the male group had higher cumulative prevalence of digital ulcer (47.8% vs. 27.5%,  $p=0.026$ ), telangiectasia (93.5% vs. 69.6%,  $p=0.002$ ), joint contracture (69.6% vs. 43.5%,  $p=0.006$ ), tendon friction rub (39.1% vs. 20.3%,  $p=0.027$ ), LVEF  $<50\%$  (21.7% vs. 8.7%,  $p=0.048$ ) and right ventricular dysfunction (34.8% vs. 7.2%,  $p<0.001$ ) compared with the female group. The male group had significant higher IR of right ventricular dysfunction (8.21 vs. 1.99 per 100 person-years,  $p=0.006$ ) and interstitial lung disease (ILD) determined by HRCT (63.66 vs. 39.19 per 100 person-years,  $p=0.022$ ) compared to the female group. However, no significant IR of LVEF  $<50\%$  (5.63 vs. 2.10 per 100 person-years,  $p=0.078$ ), and elevated systolic pulmonary artery pressure  $\geq 50$  mmHg determined by echocardiography (2.81 vs. 1.55 per 100 person-years,  $p=0.339$ ) were observed among the two groups.

**Conclusions:** Our study cohort found that male gender had higher proportion of dcSSc subtype and had more severe clinical manifestations compared with female. In addition, during the follow-up period, the IR of right ventricular dysfunction and ILD were higher in male than that in female patients in the early stage of SSc.

**Disclosure of Interest:** None declared

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AB0811

#### INCREASED LEVELS OF SERUM WISTERIA FLORIBUNDA AGGLUTININ-POSITIVE MAC-2 BINDING PROTEIN IN SYSTEMIC SCLEROSIS

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**Background:** Mac-2 binding protein is a cell-adhesive glycoprotein of the extracellular matrix secreted as a ligand of galectin-3 (Mac-2). Recently, a Wisteria floribunda agglutinin positive-M2BP (M2BP) assay developed using a lectin-antibody sandwich immunoassay has shown promise as a new fibrotic marker in liver fibrosis and interstitial lung disease (ILD) to detect unique fibrosis-related glycoalteration. Systemic sclerosis (SSc) is an intractable connective tissue disease that causes skin and organ fibrosis. Progressive fibrosis is now recognised to be one of the major causes of morbidity and mortality in SSc.

**Objectives:** The aim of this study is to evaluate the utility of serum M2BP levels in patients with SSc.

**Methods:** We retrospectively measured serum M2BP levels in 76 patients with SSc and 16 healthy controls (HC). We excluded patients of viral hepatitis and cirrhosis. Serum levels of M2BP were measured using HISCL<sup>®</sup> M2BP glycosylation isomer Assay Kit. IHC was performed on 5 samples of normal skin, 7 stored samples of SSc skin and 2 samples of SSc-ILD lung tissue. We examined the relationship between serum M2BP levels and clinical parameters in patients with SSc.

**Results:** The mean age was 62.7 years in SSc patients and 54.6 years in HC. There were 57 limited cutaneous SSc patients and 19 diffuse cutaneous SSc patients. The mean duration of SSc patients was 9.8 years. Serum M2BP levels were significantly higher in patients with SSc than in HC (0.853 $\pm$ 0.701 cutoff index [COI], 0.325 $\pm$ 0.111 COI, respectively;  $p<0.00001$ ). Receiver operating characteristic (ROC) curve analysis indicated that serum M2BP correctly differentiated between SSc patients and HC with a sensitivity of 81.6% and specificity of 87.5%. In patients with SSc, a significant correlation was not found between serum M2BP levels and age, sex, mRSS, ILD, pulmonary artery hypertension (PAH), SSc-types, dermatoscopy findings. In multivariate analysis, disease duration was a only independent factor for higher serum M2BP levels more than 0.64 COI, serum M2BP median (odds ratio 0.935, 95% CI 0.878–0.996,  $p=0.0385$ ). We detected the protein level of M2BP in SSc patient's fibroblast of skin and SSc Patient's proliferating type II alveolar cells adjacent to fibrotic lesions of lung tissue.

**Conclusions:** In this study, for the first we demonstrated that M2BP is expressed in skin and lung tissue in SSc patients in IHC and more over the serum M2BP level tends to be higher in patients with short disease duration. It is reveal that M2BP play an important role of fibrosis in early stage of SSc. The serum level of M2BP may be a novel biomarker of SSc.

**Disclosure of Interest:** None declared

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AB0812

#### ULTRASONOGRAPHY FOR THE ASSESSMENT OF SKIN IN SYSTEMIC SCLEROSIS: A SYSTEMATIC REVIEW

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**Background:** Skin involvement is the clinical hallmark of systemic sclerosis (SSc). A palpation-based semi-quantitative tool, the modified Rodnan skin score, is the current gold standard for the assessment of skin involvement. However, this method has significant limitations, with emphasis on low sensitivity to change and a high inter-observer variability. Ultrasound has been explored, in the past decades, as a basis for more objective, sensitivity and reproducible measure of skin involvement.

**Objectives:** To identify and synthesise the best available evidence on the use of ultrasound as a source of skin outcome measures in patients with SSc.

**Methods:** Two independent reviewers systematically searched Pubmed MEDLINE and Embase (up to December 2017). A study was eligible if it included at least one defined group of patients with SSc, and reported a structured evaluation of the skin with ultrasound and/or ultrasound elastography. This search was augmented by review of bibliographic references from the included studies. The same two reviewers independently extracted the data and classified the quality of evidence of the included studies by the Effective Public Health Practice Project system.

**Results:** A total of 30 studies (21 observational cross-sectional and 9 longitudinal) were included. They enrolled a total of 1171 SSc patients, mostly middle-aged, female and with a limited form of SSc (59.0%). The most common ultrasound outcome measure used was skin thickness (in 28 studies), although the definition of this parameter was a highly heterogeneous. Other outcome measures were echogenicity (in 7), and/or stiffness (in 6) and/or vascularity (in 1). There was a substantial discordance in the number and exact location of skin sites examined. The main comparator was global and site specific mRSS.

There was a lack of construct and criterion validity (only 1 study assessed the correspondence between ultrasound measures and histological findings). Few studies reported information about inter- and intra-rater reproducibility, but when reported, it showed excellent results. Data regarding evidence for responsiveness to change and feasibility were also scarce.

**Conclusions:** This systematic review highlights a remarkable literature heterogeneity and limited quality of most reported studies. This hinders the evidence currently supporting the use of skin ultrasound evaluation in clinical practice, but the very promising data (e.g good reliability and early detection of skin involvement) support its use in clinical research. Further well-designed and dimensioned studies are needed to support the role of skin ultrasound assessment in the early diagnosis and monitoring SSc patients. These may be crucial to improve our

understanding the disease process and to foster the development of much-needed new intervention strategies.

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#### AB0813 SEVENTEEN MYOSITIS AUTOANTIBODIES: SEROLOGICAL PROFILE OF HISPANIC PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES

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**Background:** The idiopathic inflammatory myopathies (IIM) are a heterogeneous group of subacute, chronic, or acute acquired diseases of skeletal muscle, they can be classified into the following clinical pathologic groups: dermatomyositis (DM), polymyositis (PM), and inclusion body myositis (IBM) which differ in clinical presentation, season of onset, genetics, and prognosis.<sup>(1)</sup> Furthermore, the seropositivity of antibodies in these diseases can help to predict the evolution of the disease, and influence therapeutic strategies.<sup>(2)</sup> Anti-Mi-2 is a classic marker for DM and its associated with good response for steroid treatment and good prognosis. Anti-SRP is specific for PM and its associated with treatment-resistant myopathy, histologically characterised as necrotizing myopathy. Several new myositis specific antibodies (MSA), autoantibodies with strong clinical significance have been described in IIM manifestations.<sup>(3)</sup> The literature about this topic is limited in Hispanic population. This study represents an effort for a better understanding of this group of diseases.

**Objectives:** To determine the prevalence of myositis specific and myositis associated autoantibodies in a cohort of patients with idiopathic inflammatory myopathies, who were treated from January 2016 to January 2018 in a Rheumatology Service from a University (Hospital Jose E. Gonzalez) from UANL and a centre for arthritis at north of Mexico.

**Methods:** Cross-sectional, retrospective descriptive study cohort of 95 patients who attended the rheumatological clinic in the period from January 2016 to January 2018 who met Bohan and Peter's classification criteria. The determination of antibodies was performed by the Immunoblot technique with Euroimmun kit. The following serotypes were included: OJ, Ro 52, Mi2  $\alpha$ , MDA-5, TIF 1 gamma, PM/Sc1 75, Mi 2B, SRP, PL12, PL 7, PM/Sc1 100, Ku, Jo1, EJ, cN1A, NXP2, SAE 1. Statistical analysis was performed with univariate, for the categorical variables, absolute frequencies and percentages were analysed and for the numerical means and standard deviation with the SPSS V22 (Armonk, NY: IBM Corp.)

**Results:** From a cohort of 95 patients, 68.42% were women and 31.75% were men. The average age was 47 $\pm$ 15.42. A prevalence of seropositive antibodies were observed for Mi2  $\alpha$  of 29 (30.52%), 14 (14.73%) in *Tif 1 gamma* and 12 (12.63%) has positive *Mda 5*.

**Abstract AB0813 – Table 1.** Positive Antibodies.

Antibody	IIM n= 95	
	mean $\pm$ SD	n (%)
Mi2 $\alpha$	21.79 $\pm$ 14.85	29 (30.52)
Mi2 $\beta$	19.60 $\pm$ 12.81	10 (10.52)
Tif1 $\gamma$	42.42 $\pm$ 24.36	14 (14.73)
Mda5	28.83 $\pm$ 25.84	12 (12.63)
Nxp2	66 $\pm$ 54.11	3 (3.15)
Sae1	48.50 $\pm$ 58.68	2 (2.10)
Ku	9.75 $\pm$ 2.87	4 (4.21)
PM-Sc1100	45 $\pm$ 29.10	7 (7.36)
PM-Sc175	37.63 $\pm$ 27.72	9 (9.47)
Jo1	44.08 $\pm$ 24.40	5 (5.26)
Srp	20.20 $\pm$ 8.13	5 (5.26)
Pl-12	9.85 $\pm$ 4.81	7 (7.36)
Ej	–	1 (1.05)
Oj	25 $\pm$ 26.81	6 (6.31)
Ro-52	42.70 $\pm$ 27.67	24 (25.26)
Cn-1 $\alpha$	1.14 $\pm$ 0.05	5 (5.26)
Pl7	23.50 $\pm$ 11.79	8 (8.42)
CpK	525.11 $\pm$ 110.49	54 (56.84)

\*SD: Standard Deviation

**Conclusions:** The systematic and standardised evaluation of the determination of antibodies in patients with inflammatory myopathies play an important role in the predictive evaluation. Knowledge of the prevalence and clinical scenarios in various cohorts increase the standardisation and prompt use of antibodies in the classification of inflammatory myopathies

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#### AB0814 SODIUM THIOSULFATE 10% INTRALESIONAL TO TREAT CALCINOSIS IN PATIENTS WITH SYSTEMIC SCLEROSIS AND DERMATOMYOSITIS: CASE SERIES

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**Background:** Calcinosis is a frequent complication of systemic sclerosis and dermatomyositis, causing local pain, joint mobility reduction, ulcerations, secondary infections and disability. Currently, there is no effective treatment to calcinosis, but the use of topical dressing or intralesional sodium thiosulfate (STS) has showed promising results.

**Objectives:** To evaluate efficacy of intralesional STS 10% in calcinosis of patients with dermatomyositis and systemic sclerosis.

**Methods:** Prospective and open-labelled study including dermatomyositis and systemic sclerosis patients with calcinosis. The primary endpoints were: pain relief evaluated through visual analogue scale (VAS) and reduction of major diameters of calcinosis in x-ray. The secondary endpoints were: improvement in the quality of life and function evaluated by SF12 and HAQ respectively.

**Results:** A total of 10 calcinosis from 7 patients, one with dermatomyositis and 6 with systemic sclerosis were treated. The average dosage of STS per application was 9.27 mg at intervals ranging between 15 and 30 days (mean=17.85) between each injection. The number of injections per each calcinosis ranged between 3 and 8 (mean 3.3). All patients reported improvements in pain, however the results were not statistically significant (table 1). There were no reductions in calcinosis diameters, nor improvement of quality of life and function.

**Conclusions:** Low doses of sodium thiosulfate applied through intralesional injections, in a restrict number of applications and long intervals were not effective to treat calcinosis.

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**Abstract AB0814 – Table 1.** Descriptive data of 7 patients treated with STS

Diagnosis	Age/ gender	Localization	Number of injections	Interval (days)	Dosis (mg)	VAS pre- treatment (mm)	VAS after treatment (mm)	Size pre treatment (mm)	Size after treatment (mm)
DM	33, F	Left leg (medial)	3	15	2	10	0	1.1	1.1
		Left leg (posterior)	3		2			0.8	0.6
Limited SSc	67, F	Hand dystal phalanx	2	15	5	80	60	1.6	1.4
		Elbow	2		12			1.2	1.2
Limited SSc	55, F	Elbow	3	15	10	0	0	2.5	2.5
		Leg	3		20			2.3	2.3
Limited SSc	67, F	Hand dystal phalanx	8	15	9.1	50	20	1.6	1.7
Diffuse SSc	52, F	Ear	2	23	7.6	70	20	0.5	0.5
Diffuse SSc	56, F	Hand dystal phalanx	4	12	7.5	60	60	2.5	2.3
Diffuse SSc	62, M	Elbow	3	30	17.5	0	0	13.	13.21
Mean±Sd	56±10.14	-	3.3±1.67	17.85±5.86	9.27±5.66	38,75±31.81	22,85±24.90	2.73±3.55	2.70±3.62

\*DM=dermatomyositis and SSc=systemic sclerosis; Sd=standart deviation

### AB0815 HEALTH RELATED QUALITY OF LIFE IN PATIENTS WITH SYSTEMIC SCLEROSIS TREATED WITH TWO DIFFERENT INTRAVENOUS ILOPROST REGIMENS

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**Background:** In systemic sclerosis (SSc), Raynaud's phenomenon (RP) and digital ulcers (DU) can decrease health related quality of life (HRQoL). Intravenous (IV) iloprost (ILO) is administered for RP, after oral therapy failure, and DU healing. HRQoL is considered fundamental to assess the impact of the disease and therapy on patients: EQ-5D-5L has been satisfactory used to assess the general HRQoL in SSc.

**Objectives:** Aim of our study was to estimate HRQoL in SSc patients treated with two different IV ILO regimens and in patients not requiring IV ILO.

**Methods:** This was a monocentric, prospective, pragmatic and non-randomised study. Enrolled SSc patients were divided into 3 groups: no IV ILO (group A), IV ILO once monthly (B) or IV ILO for 5 consecutive days every 3 months (C). HRQoL was assessed using EQ-5D-5L through a telephone interview. Group A patients were evaluated at baseline and after 3 months; group B 2 days before each infusion and 2 weeks after each infusion; group C 2 days before each therapy cycle, and after 2 and 6 weeks after the first cycle of therapy. The EQ-5D-5L describes HRQoL, measures the overall health state with a 0–100 visual analogue scale (VAS) and values health with a utility index. Multiple regression analyses was performed to calculate VAS and mean utility index in each group (confounders: age, sex, treatment group, baseline utility or VAS score, average outdoor temperature the week before the evaluation at patient's place of residence, RP VAS, disease duration and modified Rodnan skin score).

**Results:** 96 patients were enrolled: 52 in group A, 24 in B, and 20 in C. Of these 35, 21 and 16 completed the study respectively. Utility and VAS score at the end

of the three months, as adjusted for the possible confounders, were not statistically different in the three groups.

**Conclusions:** Utility and VAS, at 3 months follow-up, were not different in the 3 groups as if IV ILO was able to make patients requiring IV ILO as similar as patients not requiring IV ILO. Moreover, in this model there was no difference between the two ILO regimens (1 days monthly vs 5 every 3 months). These results suggest that our therapeutic approach, based on various criteria such as demographic, clinical characteristics, logistic aspects and patients' preferences, allows to reach or to maintain HRQoL at comparable levels between the three groups considered.

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### AB0817 PROMINENT NAILFOLD CAPILLARY AVASCULAR AREA PREDICTS MALIGNANCY IN PROGRESSIVE SYSTEMIC SCLEROSIS

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**Background:** Systemic sclerosis (SSc) is an autoimmune disease characterised with proximal scleroderma and internal organ involvement. Observational studies demonstrated increased incidences of cancer in SSc patients<sup>1</sup>. Nailfold capillaroscopy is useful for the diagnosis and disease activity assessment of SSc.

**Abstract AB0815 – Table 1**

Independent variable description	Utility				VAS			
	Coefficient	P	95% CI	P	Coefficient	P	95% CI	
Age (years)	-0,001	0149	-0,002	0000	-0,332	0026	-0,623	-0,041
<b>Sex</b>								
Female (reference)	-	-	-	-	-	-	-	-
Male	0028	0148	-0,010	0067	3637	0521	-7,618	14 891
<b>Treatment group</b>								
ILO monthly (reference)	-	-	-	-	-	-	-	-
ILO for 5 days every 3 months	0001	0975	-0,037	0038	7252	0182	-3,486	17 990
No ILO	-0,005	0771	-0,037	0028	9160	0005	-0,185	18 505
Utility at baseline	0731	0000	0526	0936	0270	0012	0061	0478
Average temperature	0003	0155	-0,001	0007	0219	0714	-0,971	1409
RP VAS	-0,005	0054	-0,010	0000	-1,114	0131	-2,569	0341
Disease duration	0001	0534	-0,001	0002	0172	0510	-0,348	0693
Skin score (mRSS)	-0,003	0021	-0,006	-0,001	-0,161	0695	-0,977	0655
Constant	0241	0025	0032	0451	68 969	0000	37 504	100,43



However, whether the nailfold capillaroscopy pattern is distinct in SSc patients with malignancy remained unknown.

**Objectives:** The aim of this study was to investigate the incidence rate of malignancy in SSc patients. Nailfold capillaroscopy morphology patterns in SSc patients with cancer were also compared to those without cancer.

**Methods:** During 2004 to 2014, consecutive 310 SSc patients who visited outpatient clinics at Taichung Veterans General Hospital, Taiwan were enrolled. Nailfold capillaroscopy was performed at a magnification of 200x. Abnormal morphology description were analysed and categorised by the scoring system proposed by Dr. Cutolo<sup>2</sup>. SSc with malignancy was defined if the subject had a cancer diagnosis during the follow-up period.

**Results:** Among 310 SSc patients, 28 (10.9%, 13 males, 25 females) patients had cancer. The mean age of SSc with malignancy is 62±10.9 years. Sixty-four percent SSc patients with cancer is diffuse type, but only 42% of them were tested positive for anti-Scl-70 antibodies. The most common cancer were genitourinary tract and gastrointestinal tract, accounting for almost two-thirds patients. Cancer and SSc were frequently diagnosed at the same year. In SSc patients with cancer, 19 patients received nailfold capillary microscope exams when SSc was diagnosed. The assessment of nailfold capillaroscopy morphology patterns in SSc patients with cancer demonstrated neither enlarged loop, giant loop, microhemorrhage nor angiogenesis. However, prominent avascular areas could be observed universally in SSc patients with malignancy.

**Conclusions:** Rheumatologists should be aware of malignancy in SSc patients, especially those with diffuse type and within the 1st year of symptoms onset. SSc patients with malignancy tend to present atypical capillaroscopic pattern of prominent avascular area without loop dilatation, microhemorrhage and angiogenesis.

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#### AB0818 THE COMPARATIVE STUDY OF SYSTEMIC SCLEROSIS AND SYSTEMIC LUPUS ERYTHEMATOSUS-ASSOCIATED PULMONARY ARTERIAL HYPERTENSION

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**Background:** Systemic Sclerosis(SSc) is the main cause of Connective Tissue Disease-associated pulmonary arterial hypertension (CTD-PAH) in western countries, while Systemic Lupus Erythematosus(SLE) is the first cause in Asian.

Systemic Sclerosis(SSc) is the main cause of Connective Tissue Disease-associated pulmonary arterial hypertension (CTD-PAH) in western countries, while Systemic Lupus Erythematosus(SLE) is the first cause in Asian.

**Objectives:** This study aimed to identify the clinical difference between SSc-PAH and SLE-PAH.

This study aimed to identify the clinical difference between SSc-PAH and SLE-PAH.

**Methods:** SSc and SLE patients with pulmonary arterial hypertension who visited Guangdong General Hospital in China from 2009 to 2017 were recruited. PAH was diagnosed by transthoracic echocardiography or right heart catheterization and clinical data of patients was collected. Comparative study between SSc-PAH and SLE-PAH was conducted to identify the difference.

SSc and SLE patients with pulmonary arterial hypertension who visited Guangdong General Hospital in China from 2009 to 2017 were recruited. PAH was diagnosed by transthoracic echocardiography or right heart catheterization and clinical data of patients was collected. Comparative study between SSc-PAH and SLE-PAH was conducted to identify the difference.

**Results:** Twenty-nine SSc-PAH and 55 SLE-PAH patients were enrolled. The baseline characteristics of two groups was shown in table 1. In comparative study: the gender( $p=0.018$ ), the age of PAH diagnosis( $p=0.001$ ), Raynaud's phenomenon( $p<0.001$ ), WHO function state( $p=0.019$ ), PASP ( $p=0.013$ ), the diameter of RA( $p=0.045$ ) and RV( $p=0.029$ ) showed significant difference between SSc and SLE-PAH.

**Abstract AB0818 – Table 1.** Baseline Characteristics of SSc-PAH and SLE-PAH Patients

	SSc-PAH(29)	SLE-PAH(55)	<i>p</i>
Female	23(79.3%)	53(96.4%)	<b>0.018</b>
Age	46.0±14.3	34.2±10.3	<b>0.001</b>
Course <sup>a</sup> (year)	3.0[0.5, 6.4]	0.8[0.0, 9.5]	0.833
Raynaud's phenomenon	28(96.6%)	22(40.0%)	<b>&lt;0.001</b>
Anti-U1RNP antibody	11(37.9%)	27(49.1%)	0.329
WHO Fc(III/IV)	18(62.1%)	45(84.9%)	<b>0.019</b>
NT-proBNP(pg/ml)	2051[489, 5227]	1392[113, 3632]	0.176
<b>TTE</b>			
PASP(mmHg)	67.1±25.9	81.1±24.0	<b>0.013</b>
Diameter of RA(mm)	48.9±7.7	53.0±8.5	<b>0.045</b>
Diameter of RV(mm)	52.9±6.6	55.9±6.7	<b>0.029</b>
LVEF(%)	63.0±10.5	67.4±7.6	0.081
Pericardial effusion	11(37.9%)	22(41.5)	0.752
<b>RHC<sup>b</sup></b>			
SPAP(mmHg)	88.3±17.5	75.9±22.2	0.109
DPAP(mmHg)	28.0±9.2	29.5±11.6	0.764
mPAP(mmHg)	48.3±11.7	47.5±14.8	0.773
PVR(WU)	13.1±7.2	11.4±6.1	0.363
CI(L·min <sup>-1</sup> ·m <sup>-2</sup> )	2.9±0.8	3.2±1.1	0.687

TTE: transthoracic echocardiography; PASP: pulmonary arterial systolic pressure; RA: right atrium; RV: right ventricle; LVEF: left ventricle ejection fraction; RHC: right heart catheterization; PAP: pulmonary arterial pressure; PVR: pulmonary vascular resistance; CI: cardiac index.

<sup>a</sup> the time between the onset of CTD and PAH;

<sup>b</sup> 6 SSc patients and all SLE patients received RHC;

n=number at risk, SpA=Spondyloarthritis; PsA=Psoriatic arthritis

**Conclusions:** The SSc-PAH patients tend to be older, have more angiopathic characteristics and more silent clinical course than SLE patients, which might bring some insight into the different pathophysiological process between SSc and SLE-PAH.

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**Disclosure of Interest:** None declared

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#### AB0819 Tfh CELLS CONTRIBUTE TO ABNORMAL B CELL PROFILES IN DERMATOMYOSITIS

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**Background:** CD4 +CXCR5+PD-1+T follicular helper (Tfh) cells assist B cells in their proliferation, differentiation and antibody class switch.<sup>1</sup> Several studies indicate that Tfh cells play important roles in autoimmune diseases such as SLE, RA and pSS, which are characterised by the production of multiple antibodies.<sup>2-4</sup> The frequency of Tfh cells in the peripheral blood from patients with dermatomyositis(DM) and whether they participate in the development of DM remain to be elucidated.

**Objectives:** To investigate the frequencies of Tfh cells and B cell profiles in DM patients. To further determine the association of Tfh cells and B cells in DM patients and clarify the possible mechanism.

**Methods:** Peripheral blood mononuclear cells (PBMCs) were isolated from DM patients and age, gender-matched healthy controls (HCs), respectively. The frequency of Tfh (CD4 +CXCR5+PD-1+) cells, total B (CD19+) cells naïve B (CD19 +CD27-) cells, memory B(CD19 +CD27+) cells and plasmablasts (CD19 +CD38+) were examined by flow cytometry. The serum levels of IL-21, IgG, IgM, IgE and IgA were tested by enzyme linked immunosorbent assay (ELISA).

**Results:** The percentages of circulating Tfh cells are significantly higher in DM patients than HCs ( $p < 0.0001$ ). Compared to HCs, the absolute numbers of circulating Tfh cells also upregulate markedly in DM patients ( $p < 0.05$ ). The mRNA expression levels of Bcl-6, a typical transcription factor of Tfh cells, increase apparently in PBMC from DM patients ( $p < 0.05$ ). Serum levels of IL-21, a Tfh-specific cytokine, are obviously higher in DM patients ( $p < 0.01$ ). The percentages of total B cells ( $p < 0.01$ ) and Naïve B cells ( $p < 0.01$ ) upregulate significantly in DM patients while Memory B cells ( $p < 0.05$ ) downregulate markedly when compared with HCs. The absolute numbers of plasmablasts ( $p < 0.05$ ) and Naïve B cells ( $p < 0.05$ ) increase notably while memory B cells decreased obviously ( $p < 0.01$ ). Serum levels of IgG ( $p < 0.01$ ), IgM ( $p < 0.0001$ ), IgE ( $p < 0.01$ ) and IgA ( $p < 0.05$ ) are obviously higher in DM patients ( $p < 0.05$ ). The frequencies of Tfh cells are positively correlated with total B cells ( $r = 0.633$ ,  $p < 0.001$ ) and Naïve B cells ( $r = 0.643$ ,  $p < 0.01$ ).

**Conclusions:** Tfh cells may contribute to abnormal B cell profiles and antibodies production in DM and participate in the pathogenesis of DM. Tfh cell-targeted therapy might be a potential strategy for DM.

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#### AB0820 ANTI-KS AUTOANTIBODY IS ASSOCIATED WITH SICCA SYNDROME AND INTERSTITIAL LUNG DISEASE

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**Background:** Anti-aminoacyl-tRNA synthetase (anti-ARS) autoantibodies have been found in patients with polymyositis/dermatomyositis (PM/DM). Anti-KS, an anti-ARS antibody, often presents with interstitial lung disease (ILD) without other clinical symptoms of connective tissue disease (CTD). However, the clinical manifestations of anti-KS-positive patients are not well-studied.

**Objectives:** To clarify the clinical and laboratory characteristics of Japanese patients with antibodies against anti-KS antibody.

**Methods:** Sera from 326 patients with CTD (including PM/DM) or ILD at Tokai University were screened for anti-KS antibody using RNA and protein immunoprecipitation assays. Demographic data, clinical symptoms, laboratory findings and chest computed tomography (CT) scan results were retrospectively reviewed from medical charts.

**Results:** Five patients with anti-KS autoantibody were identified. All five patients were female with a mean age ( $\pm$ SD) of 59.4 ( $\pm$ 13.9) years at onset, presenting with respiratory symptoms without any sign of myositis. In all patients, ILD was chronic and chest CT scan revealed a non-specific interstitial pneumonia pattern in three patients and the remaining two showed a usual interstitial pneumonia pattern. Three patients (60%) had arthritis, mechanic's hand, while one (20%) had Gottron's sign and was diagnosed as amyopathic DM with ILD. Interestingly, three patients (60%) showed symptoms of the Sicca syndrome with presence of anti-SSA antibody and two of those were diagnosed as Sjögren's syndrome. The frequency of Sicca syndrome in anti-KS-positive patients was significantly higher compared with other anti-ARS antibody-positive patients (60% vs. 14%, respectively,  $p = 0.031$ )

**Conclusions:** These results highlight that the presence of anti-KS antibody is associated with the Sicca syndrome as well as ILD without muscle symptoms.

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#### AB0821 EARLY DETECTION OF THE CHANGES IN PULMONARY ARTERIAL PRESSURE AND VASCULAR FUNCTIONS IN SYSTEMIC SCLEROSIS: EXPLORING NON-INVASIVE CLINICAL TEST METHODS AND UNDERLYING GENE EXPRESSIONS

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**Background:** Pulmonary arterial hypertension (PAH) is prominent as a vascular involvement in systemic sclerosis (SSc), which remains a leading cause of death in spite of current best treatments. Although recent studies focused on early diagnosis of established PAH, it is known that more than a half of the pulmonary circulation is impaired before early PAH is detected. However, there is little study about the changes of vascular functions or the underlying gene expressions during its subclinical stage.

**Objectives:** I. To detect the pathological changes in pulmonary arterial pressure (PAP) and vascular functions before PAH is manifested. II. To explore the changes in its underlying gene expressions of peripheral blood.

**Methods:** Total of 103 cases without PAH symptoms (NYHA I) with either Raynaud phenomenon (RP: n=87), skin sclerosis (n=65) or SSc-related autoantibody (n=68) were enrolled. To detect the pathological change of PAP, exercise Doppler echocardiography was carried out, and exercise induced pulmonary hypertension (exPH) group was segregated from normal response group (exN) with using the definition described in R. Naeije *et al.*<sup>1)</sup> Vascular function was evaluated with thermography after 0°C-stress and determination of ankle-brachial index (ABI) and cardio-ankle vascular index (CAVI). Furthermore, reactive hyperemic index (RHI), augmentation index (AI) and second derivative of photoplethysmogram ageing index (SDPTGAI) were assessed with using EndoPAT. Micro-vascular changes were also recorded with nailfold videocapillaroscopy. Meanwhile, genome-wide gene expression analysis was performed with using whole peripheral blood. The genes correlated with each vascular function tests were analysed by weighted gene co-expression network analysis (WGCNA) and pathway enrichment analysis (PathVisio).

**Results:** There were significant differences between exPH and exN group in the result of thermography after 0°C-stress test, CAVI and AI normalised to heart rate of 75bpm (AI@75bpm). As the CAVI and AI are known to correlate positively with age, careful interpretation was necessary because the mean age of exPH group was higher as compare with exN group (69.05 $\pm$ 11.04 vs. 60.23 $\pm$ 14.73). However, the fact that recovery of blood-flow from RP was significantly delayed in exPH group suggested the additional pathological changes of vascular and endothelial functions. Gene expression analysis revealed that several mutual pathways such as "type2 interferon signalling", "oxidative damage" and "fatty acid omega oxidation" seemed to underlie some vascular changes.

**Conclusions:** The results of vascular function tests including thermography after 0°C-stress, CAVI and AI@75bpm were significantly different between exPH and exN group. On the other hand, gene expression analysis showed that many factors such as ageing, arteriosclerotic and immunological mechanisms were involved in the changes of these vascular functions. Although further prospective study is required to select appropriate set of the tests, it is possible that evaluation of these vascular functions may be useful as a non-invasive test to assess the pulmonary vascular disease before PAH is manifested.

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#### AB0822 A MEASUREMENT OF ANTI-ARS ANTIBODIES, ANTI-MI-2 ANTIBODY, ANTI-TIF1 GAMMA ANTIBODY AND ANTI-MDA5 ANTIBODY BY ENZYME-LINKED IMMUNOSORBENT ASSAY AS A DIAGNOSTIC TOOL OF IDIOPATHIC INFLAMMATORY MYOPATHY AT RHEUMATOLOGY DAILY PRACTICE

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**Background:** Enzyme-linked immunosorbent assay (ELISA) tests of anti-ARS antibodies, anti-Mi-2 antibody, anti-TIF1 $\gamma$  antibody and anti-MDA5 antibody

became available at daily clinical practice on Oct. 2016 in Japan. Diagnostic accuracy study of myositis-specific autoantibodies (MSAs) except for anti-Jo-1 antibody in daily clinical practice is scarce.<sup>1</sup>

**Objectives:** This study investigated the diagnostic utility of newly available myositis-specific autoantibodies (ELISA) in idiopathic inflammatory myopathy (IIM) suspected patients at a rheumatology clinic with muscle and skin biopsy as a reference standard.

**Methods:** This study is a retrospective, cross-sectional study. The electrical medical records of patients who visited the department of rheumatic diseases at Tokyo Metropolitan Tama Medical Centre between Nov. 2016 and Aug. 2017 were retrospectively searched for clinical variables and laboratory data. Patients with serum creatine phosphokinase (CK) greater than two-fold of normal upper limit (over 300 IU/ml) or suspected dermatomyositis skin rash were included. Anti-ARS antibodies, anti-Mi-2 antibody, anti-TIF1 $\gamma$  antibody and anti-MDA5 antibody were measured by ELISA.<sup>2-4</sup> Two muscle pathologists interpreted muscle biopsy. The skin biopsies with interface-dermatitis were considered positive. The biopsy results of patients who did not have biopsy procedure but whose symptoms and signs improved without immunosuppressive therapy were assumed negative. IIM diagnosis was based on 2017 EULAR/ACR classification criteria.<sup>5</sup> We calculated likelihood ratio of MSAs for biopsy results and IIM diagnosis.

**Results:** Eight hundred and eighty-six new patients visited an outpatient clinic of rheumatic disease department and 38 patients met inclusion criteria. 14 patients were excluded because of apparent causes (1 each for sepsis, rhabdomyolysis, macro CK, serotonin syndrome, motor neuron disease, statin myopathy, SSC, idiopathic IP, seborrheic dermatitis, 3 for symptoms not compatible with IIMs.) and no biopsy results (2 patients). 17 (71%) of 24 patients analyses were female. The median age was 56.5 (IQR 41–65) years, median CK 658 (IQR 105–1866) IU/ml. 11 (46%) patients had the positive biopsy result (6 muscle biopsy and 5 skin biopsy) and IIM diagnosis. 10 (42%) patients were positive for MSAs (anti-ARS antibodies in 3, anti-Mi-2 antibody in 1, anti-TIF1 $\gamma$  antibody in 2, anti-MDA5 antibody in 3 and double positive for anti-ARS and anti-MDA5 antibody in 1). The positive likelihood ratio of MSAs for the biopsy result and IIM diagnosis was  $\infty$  (95% CI cannot be calculated). The negative likelihood ratio was 0.091 (95% CI 0.086–0.097).

**Conclusions:** Our analysis demonstrated that MSAs measured by ELISA efficiently differentiated biopsy-proven IIMs from other medical conditions at rheumatology daily practice.

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#### AB0823 PATIENTS WITH CONNECTIVE TISSUE DISEASE HAVE MORE ANXIETY IN COMPARISON WITH PATIENTS WITH OTHER RHEUMATIC DISEASES

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**Background:** Rheumatic diseases often coexists with psychological disorders. Psychological symptoms not only have a substantial negative impact on the quality of life, but also on the course and outcome of the chronic disorders.<sup>1</sup>

**Objectives:** Our study was to investigate psychological disorders in Chinese patients with rheumatic diseases and to compare the differences of psychological disorders among different diseases.

**Methods:** Patients with rheumatic diseases were enrolled from July to December in 2017 in rheumatology department of the Third Affiliated Hospital of Sun Yat-sen University. Participants were required to complete a set of questionnaires and examinations, including demographic and clinical information, Zung self-rating anxiety scale (SAS), and Zung self-rating depression scale (SDS). The Statistical Package for Social Sciences (SPSS) software version 21 was used for all data management and analysis. The Mann-Whitney U test and Student's t test were used to compare patients with different rheumatic diseases and psychological disorders. Stepwise linear multiple regression was used to determine the contributors to SAS and SDS.

**Results:** Of all the 153 patients, 49 (32%) were male patients. 14.4% had only primary education, while 32% received education in university. Numbers of the patients were stated as follows. Lupus, 44; rheumatoid arthritis, 11; Sjogren's syndrome, 11; systemic sclerosis, 9; myositis, 7; vasculitis, 6; spondyloarthritis, 9; gout, 10; other diseases 46. Mean age was 37.64±15.23 years. Mean disease

duration was 3.78±5.07 years. Mean SAS scores were 43.44±8.51, and mean SDS scores were 46.66±12.43. 35 (22%) of the patients had anxiety, while 6 (3.9%) had moderate anxiety. 50 (32.7%) patients suffered from depression, of which 5 (3.3%) had severe depression, and 13 (8.5%) had moderate depression. Patients with connective tissue diseases had more anxiety (30.5%) than average score ( $p<0.05$ ), especially in patients with lupus. SDS ( $B=1.073$ ,  $p<0.001$ ), educational scale ( $B=-2.147$ ,  $p<0.05$ ) contributed to SAS scores.

**Conclusions:** Psychological disorders could occur with rheumatic diseases, especially in connective tissue diseases. Physicians should be aware of psychological status in these patients.

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#### AB0824 EVALUATION OF THE DETECTION OF MYOSITIS-SPECIFIC ANTIBODIES BY LINEBLOT AS A TOOL FOR THE CHARACTERISATION OF A PROSPECTIVE MULTICENTER COHORT

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**Background:** Traditionally, the diagnosis of idiopathic inflammatory myopathies (IIM) is based on clinical findings, muscle enzyme levels, electromyography and biopsy. Newer approaches include the detection of myositis-specific autoantibodies (MSA), with MSA identified in about 50% of patients.

Today, several commercial platforms for MSA detection have become commercially available. In the context of the start-up of a prospective multicentre cohort, we evaluated the usefulness of a multiparameter line blot for the serological characterisation of patients with clinical suspicion of IIM.

**Objectives:** To evaluate the usefulness of a multiparameter line blot for the serological characterisation of patients with clinical suspicion of IIM.

**Methods:** A total of 225 samples (118 consecutive routine samples for which MSA were requested and 107 controls [50 systemic sclerosis (SSc), 29 systemic lupus erythematosus (SLE) and 28 rheumatoid arthritis patients (RA)]) was analysed on indirect immunofluorescence (HEp-2000, Immunoconcepts) and lineblot (MYO12 blot, D-Tek). All consecutive samples were retrospectively categorised by the treating medical specialist as definite IIM (n=16), probable IIM (n=10), immune mediated inflammatory disease (IMID) – myositis overlap not excluded (n=28), myopathic features without IIM (n=1), IIM excluded (n=44), and lost from follow-up/no data available (n=19). Data to calculate the EULAR/ACR probability score were also collected.

**Results:** MSA were detected in 12% of the 225 samples, showing no multiple reactivities. A sensitivity of 50% in the IIM patients (definite and probable n=13/26 – based on judgement of the clinician) was observed, with the highest frequencies observed for anti-HMGCR (15%, n=4), anti-Mi2 (12%, n=3) and anti-Jo1 (12%, n=3). Less frequent antibodies were anti-EJ (n=1), anti-MDA5 (n=1) and anti-NXP2 (n=1). All these patients had a MSA-compatible clinical IIM subtype. The median minimal EULAR/ACR probability score was 97% (range 6%–100%, no biopsy data entry), with the lowest score observed in the anti-EJ patient. In contrast, MSA were also observed in 8 patients with no convincing clinical diagnosis of IIM or myositis overlap syndrome (anti-TIF1 $\gamma$  in 4 [3 SSc and 1 SLE]; anti-SRP in 1 [1 RA]; anti-SAE in 3 [1 SSc, 1 RA and 1 IIM excluded], mostly showing low antibody titres (n=6/8) and no compatible immunofluorescence pattern on HEp-2000 (n=7/8). For 2 other positive samples the results were not conclusive (anti-PL7 in patient with myopathic features and anti-SRP in an unspecified IMID patient).

**Conclusions:** The detection of MSA by lineblot will be useful for the prospective serological characterisation of patients with clinical suspicion of IIM. Nevertheless, careful interpretation in correlation with the clinical findings and other technical examinations is necessary in case of low titres and absence of a compatible immunofluorescence pattern.

**Disclosure of Interest:** None declared

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**AB0825** **MANAGING SYSTEMIC SCLEROSIS: ASSESSING THE EDUCATIONAL NEEDS OF RHEUMATOLOGISTS**

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**Background:** Systemic sclerosis (SSc) is an uncommon, complex and heterogeneous condition, making it challenging to manage. Individual rheumatologists see relatively few cases and patient surveys identify numerous gaps in clinical care. There are no published data on the educational needs of rheumatologists caring for patients with SSc. We aimed to determine rheumatologists' self-rated knowledge and learning needs.

**Methods:** Survey questions were adapted from the EULAR Recommendations for the Treatment of SSc with reference to patient-identified care gaps. The survey was conducted on paper and on SurveyMonkey (a cloud-based online survey development software program). The target audience was Ontario rheumatologists, serving a population of 13.6 million. We sought to explore self-reported knowledge, experience, attitudes and perceived barriers in caring for SSc patients. Physician demographics and preferred educational methods were also collected. Gaps between perceived and desired knowledge were calculated to identify the greatest unmet learning needs.

**Results:** One hundred and eighteen responses were received with a response rate of 54%. The greatest unmet learning needs were seen in the management of sexual dysfunction (average gap of 1.4 on a 5-point scale), pulmonary hypertension (1.1), interstitial lung disease (1.0) and gastrointestinal manifestations of the disease (1.0). The smallest learning gap concerned screening recommendations (0.7). 19% of rheumatologists agreed with the statement "Scleroderma is an untreatable disease." Agreement with this statement was highest (33%) among rheumatologists who treat relatively small numbers<sup>1-10</sup> of scleroderma patients.

**Conclusions:** We have identified several unmet learning needs regarding the management of SSc among rheumatologists. These can be used to inform future educational resources and programs for rheumatologists regarding SSc and to direct further research into their needs.

**Disclosure of Interest:** None declared

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**AB0826** **PROFILE OF MYOSITIS-SPECIFIC ANTIBODIES IN PATIENTS WITH POLYMYOSITIS/DERMATOMYOSITIS AND ASSOCIATION WITH CLINICAL MANIFESTATIONS AND OUTCOME: EXPERIENCE FROM A TERTIARY REFERRAL CENTRE**

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**Background:** Myositis-specific antibodies (MSAs) have been found to be associated with distinct clinical phenotype and prognosis in patients with Idiopathic Inflammatory Myopathies.

**Objectives:** To assess the profile of MSAs in Chinese patients with polymyositis (PM)/dermatomyositis (DM) and explore association of antibody profile with clinical characteristics, laboratory findings and prognosis.

**Methods:** 90 patients with PM/DM were enrolled. 12 MSAs (mi-2 $\alpha$ , mi-2 $\beta$ , TIF1 $\gamma$ , MDA5, NXP2, SAE1, Jo-1, SRP, PL-7, PL-12, EJ, OJ) were measured by immunoblotting. Associations between antibody profile and clinical manifestations, laboratory data and outcome were determined.

**Results:** The study population comprised 20 patients with PM and 70 patients with DM, in which 17 DM patients were identified as clinically amyopathic dermatomyositis (CADM). Overall, the most common MSA was anti-ARS (Jo-1/PL-7/PL-12/OJ/EJ) (41.1%), followed by anti-MDA5 (33.3%), anti-SRP (15.6%), anti-NXP2/anti-SAE1 (13.3%), anti-TIF1 $\gamma$  (12.2%) and anti-mi-2 $\alpha$ /mi-2 $\beta$  (5.6%). Anti-MDA5 antibody was exclusively seen in DM and CADM patients and the prevalence was higher in CADM than in conventional DM (82.4% vs 30.2%,  $p < 0.001$ ). Compared with those who were anti-MDA5 negative, patients with positive anti-MDA5 had more rapidly progressive interstitial lung disease (ILD) and Gottron sign (93.3% vs 61.7%,  $p < 0.05$ ; 93.3% vs 38.3%,  $p < 0.001$ ) as well as lower creatine kinase concentrations (70.0 vs 992.5 IU/L,  $p < 0.001$ ). Anti-Jo-1 antibody was more prevalent in PM (55.0% vs 20.8%,  $p < 0.05$ ) and patients with positive anti-Jo-1 demonstrated higher prevalence of mechanic's hands (18.2% vs 1.5%,  $p < 0.05$ ). Anti-SRP positive patients had higher creatine kinase levels than those with negative, although there is no statistical significance (1649.5 vs 199.0 IU/L,  $p = 0.056$ ). Moreover, anti-TIF1 $\gamma$  antibody was associated with more frequent tumour (18.2% vs 0.0%,  $p < 0.01$ ). In logistic regression analysis, anti-MDA5 [OR=9.601, 95% CI (1.940, 47.515),  $p < 0.01$ ] was an independent risk factor for ILD. During the follow-up period (median 8 months), 13 patients died, among

which 9 were anti-MDA5 positive. The survival time of anti-MDA5 positive patients was significantly less than those who were negative (3.0 vs 11.0 months,  $p < 0.01$ ). **Conclusions:** Anti-ARS antibodies are the most common MSAs in Chinese PM/DM patients. Anti-MDA5 is predominantly seen in patients with CADM and closely associated with rapidly progressive ILD and high mortality thus serve as a marker of poor prognosis. Anti-TIF1 $\gamma$  positive patients routinely screened for tumours will be of clinical significance.

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**Spondyloarthritis – treatment**

**AB0827** **HIP ARTHRITIS REMAIN FREE FROM RADIOGRAPHIC PROGRESSION FOR 24 MONTHS FOLLOWING TREATMENT OF ANKYLOSING SPONDYLOARTHRITIS WITH TNF-A INHIBITORS: A PROSPECTIVE STUDY**

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**Background:** Hip involvement is the most frequent extra-spinal arthritic manifestation of ankylosing spondyloarthritis (AS). It can be severe and may worsen outcomes for patients. There is a large body of high quality evidence for clinical efficacy of TNF- $\alpha$  inhibitors at treating this condition. However, their structural hip benefit remains unknown.

**Objectives:** In this prospective study undertaken in Algeria, we aimed to evaluate clinical and structural efficacy of TNF- $\alpha$  inhibitor therapies on non-synostose hip involvement in AS, for a 24 months period.

**Methods:** This study pursued a follow-up of patients SA using modified New York criteria or ASSAS criteria. Patients were TNF- $\alpha$  inhibitors naïf diagnosed with SA, with hip involvement (identified using clinical and/or radiological findings). Patients were treated with one of the following: adalimumab, infliximab or etanercept. Exclusion criteria were: history of tuberculosis, serious infections, hepatitis, neoplasms, other inflammatory conditions, and hip involvement due to any other causes. The following data were collected: clinical rating of hip involvement using the Harris Hip scoring system, biological characteristics (CRP), and radiological characteristics of hip lesions using Bath Ankylosing Spondylitis Radiology Index of the hip (BASRI hip). Specific disease indexes such as BASDAI and BASFI were also collected. Follow up was undertaken at the following time periods in months: 0, 3, 6, 12 and 24. Statistical analysis of findings was performed using SPSS 11.0 software

**Results:** The study recruited a total of 30 patients, 22 males and 8 females. Mean age was (24, 1 $\pm$ 3, 1 years). Bilateral and unilateral hip involvements were identified in 67% and 33% of patients, respectively. Mean time for appearance of hip lesions was (3, 9 $\pm$ 2, 1 years). HLAB 27 was present in 30% of this study population. Baseline characteristics of hips examined have shown an altered function (Harris Hip mean score of 56, 1 $\pm$ 5, 1) and a relatively advanced structural score (BASRI hip mean score 2, 4 $\pm$ 1, 1). These scores correlated with high disease activity (BASDAI mean score 5, 5 $\pm$ 1, 2) and a poor mean BASFI score (5, 4 $\pm$ 2, 0). This was accompanied by a mean CRP score of 22, 1 $\pm$ 8, 1. Non-steroidal anti-inflammatory drugs were ineffective. During the 24 months treatment period using TNF- $\alpha$  inhibitors, there was a statistically significant improvement in hip scores from the third month onwards with mean Harris Hip scores of 70, 3 $\pm$ 21, 5 ( $p < 0,001$ ), and 81, 3 $\pm$ 11, 5 ( $p < 0,001$ ) at months 3 and 6, respectively. This was maintained until the end of the study period at 94, 2 $\pm$ 10, 5 ( $p < 0,001$ ). There have also been statistically significant improvements in BASDAI and BASFI scores as well as CRP (all  $p < 0,001$ ). Mean BASRI score, however, remained unchanged after 24 months. Treatment was well tolerated, and no significant complications (e.g. serious infections or tuberculosis) were observed. No prosthesis was indicated for any patient

**Conclusions:** Hip involvement is associated with severe and rapidly evolving AS. In this study, we have demonstrated improved outcomes and stability of radiographic lesions of hip arthritis for a period of 24 months, when SA was treated with TNF- $\alpha$  inhibitors.

**Disclosure of Interest:** None declared

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**AB0829 PERSISTENCE ON GOLIMUMAB AS SECOND LINE BIOLOGICAL THERAPY IN PATIENTS WITH SPONDYLOARTHRITIS (AXIAL SPONDYLOARTHRITIS AND PSORIATIC ARTHRITIS). GO-BEYOND, A RETROSPECTIVE STUDY**

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**Objectives:** In this retrospective study we assess the 1 to 3 year probability of persistence on golimumab in patients with spondyloarthritis (SpA), axial SpA or psoriatic arthritis (PsA) who started treatment with golimumab as second biological (after withdrawal of a first anti TNF-alpha drug)

**Methods:** GO-BEYOND was a retrospective study undergone in 20 Spanish rheumatology clinics. Information was collected on all axial SpA and PsA patients who initiated golimumab between January 2013 and December 2015 as second anti TNF-alpha (i.e. after discontinuation of a first anti TNF-alpha drug). Centres in which all the patients could not be included were excluded from the analysis. The probability of persistence was calculated with a Kaplan-Meier test and comparisons were done with the log-rank test.

**Results:** 210 patients were included (131 with axial SpA and 79 with PsA, mean age 49 years [SD=12], 40% women, median duration of disease at the initiation of golimumab 80.5 months). Reasons for discontinuation of the first anti TNF-alpha were loss of efficacy (71.4%), poor tolerability or adverse event (11.0%) and patient or physician preference (17.6%). During a median follow-up of 29.3 months, 72 of 210 patients (34.3%) discontinued golimumab, due to primary failure (n=21), disease reactivation or secondary failure (n=29), poor tolerability (n=4), adverse events (n=10), inactive disease or patient-physician agreement (n=8). The probability of persistence on golimumab since treatment initiation was 80% at year 1 (95% CI 75–86), 70% at year 2<sup>64–77</sup> and 65% at year 3 [59–72]. The figures were similar in patients with axial SpA or PsA, and in patients who discontinued the first anti TNF-alpha due to loss of efficacy or to other reasons (p=0.121 and p=0.835, table 1).

Abstract AB0829 – Table 1

	All SpA patients			Baseline disease			Reason for discontinuation of the first anti TNF-alpha		
	n	Probability of persistence	p	Axial SpA patients	PsA patients	Probability of persistence	Loss of efficacy	Other	p
Baseline	210			131	79		150	60	
Year 1	166	80%		102	65	81%	119	49	81%
Year 2	132	70%	0.121	83	49	67%	94	38	71%
Year 3	82	65%		52	30	59%	60	22	66%
Year 4	43	65%		30	13	59%	30	13	66%

n=number at risk, SpA=Spondyloarthritis; PsA=Psoriatic arthritis  
**Conclusions:** After discontinuation of a first anti TNF-alpha, patients with spondyloarthritis showed a high probability of persistence on golimumab. The probability of persistence was similarly high in patients with axial SpA or PsA, and in

patients who discontinued the first anti TNF-alpha due to loss of efficacy vs other reasons. Real life effectiveness of golimumab as second anti TNF-alpha is high and durable in SpA patients.

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**AB0830 MRI EVALUATION OF THE EFFECT OF ANKYLOSING SPONDYLITIS TREATMENT ON HIP JOINTINVOLVEMENT**

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**Background:** Coxitis is one of the leading causes of early disability in ankylosing spondylitis (AS) patients. There's no mild course of the disease as soon as hip joints (HJ) are involved, but epidemiological surveys in Russia show that only 7% of AS associated hip damage require total hip replacement.

**Objectives:** To evaluate case follow-up data in treated AS patients with hip involvement using hip MRI and radiography for dynamic assessment.

**Methods:** 30 AS patients (mean age of 27.7±17 y.) meeting modified 1984 N-Y criteria with MRI signs of HJ inflammation were followed up for 2 years. Patients' mean age at the onset of the disease was 22.3±18,3 years, 77% of the population were HLA-B27 positive. Median AS duration was 47 (12–144) months, and median BASDAI score was 5.9±3,1. The median duration of clinically manifest coxitis by the time of the study was 45 months. [25%<sup>c</sup>; 75%<sup>c</sup>], and pain intensity by numeric ranking scale (NRS) was 6 (2; 8). HJ MRI using T1 and STIR modes was performed in all participants in addition to clinical and radiological examinations. All patients were grouped into three arms based on therapeutic regimens: Group I was administered non-steroidal anti-inflammatory drugs (NSAIDs), Group II – genetically engineered biological agents (GEBAs) +NSAIDs, and Group III was treated with a combination of NSAIDs+DMARD (methotrexate or sulfasalazine). In case of baseline regimen failure patients from Group III were switched to NSAIDs+DMARD+ GEBAs combination at Mo 6 after initiation of treatment.

**Results:**

Abstract AB0830 – Table 1

Parameters	Group (I) n=5		Group (II) n=17		Group (III) n=8	
	Baseline	2 years FUP	Baseline	2 years FUP	Baseline	2 years FUP
AS duration, mo, Me [25% <sup>c</sup> , 75% <sup>c</sup> ]	27 [12;32]	51 [36;56]	32 [18;40]	56 [42;64]	38 [18;42]	62 [42;66]
BASDAI, Me [25% <sup>c</sup> , 75% <sup>c</sup> ]	2,5 [2,0;3,7]	2,4 [1,8;3,5]	5,6 [4,1;8,2]	1,8 [0,4;2,6]	4,1 [3,6;5,2]	3,2 [2,4;4,6]
BASFI, Me [25% <sup>c</sup> , 75% <sup>c</sup> ]	1,7 [0,8;3,2]	2,8 [1,8;4,2]	3,2 [2,6;4,7]	2,8 [1,8;3,6]	3,6 [2,2;5,0]	3,2 [1,9;4,8]
HLA-B27, n (%)	95%	95%	93%	93%	75%	75%
ASDAS (CRP) Me [25% <sup>c</sup> , 75% <sup>c</sup> ]	2,0 [1,8;3,0]	2,3 [1,9;3,4]	4,3 [3,8;5,6]	2,6 [1,3;3,7]	3,9 [2,6;4,2]	2,3 [1,8;3,6]
ESR, mm/h, Me [25% <sup>c</sup> , 75% <sup>c</sup> ]	10 [3;15]	12 [5;15]	30 [15;60]	10 [0,8;4,5]	18 [12;28]	12 [6;18]
CRP, mg/mL, Me [25% <sup>c</sup> , 75% <sup>c</sup> ]	7,0 [4,3;10,7]	6,8 [4,2;11,0]	36 [15;47]	10,8 [0,8;34]	15,8 [8,4;28,9]	6,9 [4,7;17,8]
NRS, Me [25% <sup>c</sup> , 75% <sup>c</sup> ]	4 [2;6]	4 [2;6]	6 [4;8]	5 [2;6]	4 [2;7]	2 [0;4]
MRI Synovitis n (%)	5 (100%)	5 (100%)	17 (100%)	4 (24%)	8 (100%)	1 (12,5%)
Osteitis n(%)	0	0	6 (35%)	2 (12%)	2 (25%)	0 (0%)
BASRI (0-I) n(%)	4 (80%)	1 (20%)	12 (70%)	9 (53%)	7 (88%)	7 (88%)
BASRI (II-IV)	1 (20%)	4 (80%)	5 (30%)	8 (47%)	1 (12%)	1 (12%)

- Conclusions:** 1. Long-standing MRI symptoms of HJ synovitis should be viewed as the factor predisposing to radiographic progression of coxitis in AS patients.
- 2. NSAIDs therapy does not modify the radiographic progression of coxitis.
- 3. GEBAs+NSAIDs in combination with DMARDs reduce the risk of further radiographic progression.
- 4. Future studies are warranted to better understand potential factors contributing to radiographic progression of coxitis.

**Disclosure of Interest:** None declared  
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**AB0831 THE INFLUENCE OF REMISIVE AND ANTI-INFLAMMATORY TREATMENT ON AXIAL MOBILITY IN PATIENTS WITH ANKYLOSING SPONDYLOARTRITIS**

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**Background:** In advanced ankylosing spondyloarthritis (AS), bone ankylosis or ossification of the involved joints can make the chest practically immobile, decrease its compliance, or even lead to intercostal muscle atrophy.

**Objectives:** The purpose of the study was to evaluate chest involvement in AS by measuring toracoabdominal movements during quiet breathing, by dividing the chest and abdominal contribution to the current volume, by inductive plethysmography methods.

**Methods:** 60 consecutive patients were recruited from the Rheumatology Department of the Republican Clinical Hospital. They were selected based on AS diagnosis, with no existing cardiovascular or neuromuscular diseases that would alter respiratory mechanisms and the absence of severe obesity.

**Results:** Monotherapy with DMARD was 27 out of 60 patients (45%) (Sulfasalazine 3 g/day) for a period of 1–48 months (mean value=19.4 (15.5) months). There were no differences in the angle of the Ct-Abd curve between patients with DMARD and DMARD-naive treatment (38.2 (14.5)° and 34.7 (19.5)° for sitting position, 49.3 (18.1)° and 47.2 (23.1)° in orthostatism, and 19.1 (15.6)° and 16.1 (14.6)° for clinostatism,  $p < 0.05$ ). In the baseline study, the Ct-Abd patient angle was lower than the control group in sitting position (36.3 (17.3)° and 51.5 (8.9)°,  $p = 0.0002$ ) in orthostatism (48.1 (20.8)° and 62.4 (12.5)°,  $p < 0.01$ ) or orthostatism (17.4 (15.0)° and 24.5 (9.8)°  $p < 0.05$ ). In the entire patient group, the Ct-Abd angle correlated negatively with BASFI in all three body positions ( $r = -0.50$ ,  $p < 0.0001$  in the sitting position,  $r = -0.36$ ,  $p < 0.01$  in orthostatism,  $r = -0.47$ ,  $p < 0.0001$  in clinostatism); did not correlate with BASDAI, BASMI, or the modified Schoeber test in either of the three body positions.

In 15 AS patients who underwent repeated measurements of toracoabdominal movements while receiving their associated DMARD treatment (Methotrexate 15 mg/week and Sulfasalazine 3 g/day) 3 months after treatment, the angle of the Ct-Abd slope was significantly higher than that of the fundamental study, in all bodily positions.

The Ct-Abd angle continued to increase, with increments less pronounced and reached significant value only between measurements of 3 months and 12 months. Improvements in standardised clinical signs following associated DMARD treatment followed a similar pattern, with scores at each interval significantly different from those measured in the baseline study, improvements continuing at a faster pace slowly after the third month.

In the control group, the angle of the slope of the Ct-Abd curve was not different in the two measurements in any of the body positions (51.4 (8.9)° and 50.7 (9.3)° in the sitting position, 62.4 (12.4)° and 61.6 (11.8)° in orthostatism, and 24.6 (9.8)° and 24.8 (10.4)° in clinostatism,  $p < 0.05$ ). In orthostatism, the difference between the measurements was 0.8° (confidence interval 95%–0.9 to 2.52, upper and lower boundaries of 6.6° and 8.2°).

**Conclusions:** The slope of the Ct – Abd curve during quiet breathing correlates negatively with BASFI and responds significantly to associated DMARD treatment and NSAIDs. Our data suggest that this measure can be targeted for further evaluation of its usefulness in monitoring chest involvement and its response to treatment in AS patients.

**Disclosure of Interest:** None declared

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**AB0832 THE EFFECTS OF ANTI-TNF BIOLOGICAL AGENTS IN PATIENTS WITH SPONDYLOARTRITIS: A COMPARATIVE STUDY**

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**Objectives:** The aim of the present study was to compare the efficacy of three anti-TNF agents (adalimumab, infliximab and etanercept) in patients with spondyloarthritis (SpA) at 24 weeks.

**Methods:** We achieved a retrospective descriptive and comparative monocentric study, on 49 patients, with SpA including ankylosing spondylitis (AS), psoriatic arthritis (PsA), enteropathic arthritis (EA), reactive arthritis (ReA) and undifferentiated spondyloarthritis (uSpA) (according to Amor criteria, <sup>ASAS 2009</sup> and CASPAR criteria), during 12 years (2004–2015). The patients were treated with at least one anti-TNF, during at least 6 months. Disease activity was assessed by the BASDAI, ASDAS, ESR and CRP. To compare mean differences between time points (week 0 versus week 24), a Wilcoxon test was applied. To compare efficacy between the 3 anti-TNF, a Mann-Whitney test was applied.

**Results:** Twenty three patients (47%) had AS, 13 patients (27%) had PsA and 11 patients (22%) had EA. One patient had an uSpA, and 1 patient had a ReA. The mean age was 42,81 years±11,77. The median age at disease onset was 29,41

years±11,29. The mean disease duration was 10,16 years. Nineteen patients received etanercept (ETN), 18 infliximab (IFX) and 12 adalimumab (ADA). At six Months, the 3 anti-TNF showed improvement in the disease activity scores: BASDAI ( $p < 0,0001$ ), ASDAS CRP ( $p < 0,0001$ ), ESR ( $p < 0,0001$ ) and CRP ( $p < 0,0001$ ). Sixty two percent of the patients have reached BASDAI 50 response at 6 months.

**Abstract AB0832 – Table 1.** Summary of median change from baseline to week 24 in clinical outcomes

	Week 0	Week 24	p
BASDAI	6,04±2,28	2,5±2,32	<0,0001
ASDAS	4,27±1,13	2,17±1,3	<0,0001
CRP			
CRP (mg/l)	44,68	14,03	<0,0001
	±33,45	±10,09	
ESR (mm)	62,24	25,65	<0,0001
	±39,16	±24,97	

BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, ASDAS: Ankylosing Spondylitis Disease Activity Score, C-Reactive protein, ESR: Erythrocyte Sedimentation Rate

At week 24, patients on ETN achieved more frequently a significant reduction of BASDAI (–5,13 vs –2,53;  $p = 0,004$ ), ESR (–52,69 vs –16,64;  $p = 0,006$ ) and CRP (–36,7 vs –21,34;  $p = 0,009$ ) than IFX. The efficacy comparison between ETN and ADA showed ETN superiority concerning BASDAI (–5,13 vs –2,04;  $p = 0,004$ ) and ASDAS CRP (–3,03 vs –1,4;  $p = 0,006$ ). The comparison ADA vs IFX had shown no significant efficacy differences.

**Conclusions:** Our results showed a BASDAI 50 response in 62% of patients. The comparison between the three biologics was consistent with a better efficacy of the ETN.

**Disclosure of Interest:** None declared

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**AB0833 REAL-WORLD EFFICACY AND SAFETY OF SECUKINUMAB: DATA FROM VERONA'S COHORT**

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**Background:** Secukinumab has been approved for the treatment of active ankylosing spondylitis (AS) and psoriatic arthritis (PsA). Its efficacy has been demonstrated in phase III trials where eligibility criteria ensured a homogeneous population. Although this strategy reduces confounding factors, it does not guarantee the same results in the real world, where clinicians deal with advanced disease, comorbidities, adherence and persistence challenges.

**Objectives:** Aim of this study was to assess efficacy and safety of Secukinumab in real-world clinical practice.

**Methods:** Patients received Secukinumab (150 or 300 mg) at weeks 0,1,2,3 and 4 as induction therapy and then every 4 weeks as maintenance therapy. Assessment of disease activity was done at months 0,6 and 12 using DAPSA, ASDAS, BASDAI, BASFI, pain VAS.

**Results:** 61 patients affected by PsA (65% females, 35% males) and 29 affected by AS (70% males, 30% females) were included. 64% of patients reached 12 months follow up. Baseline characteristics of both groups are shown in the tables below.

In the PsA cohort, the median DAPSA at baseline was 19.5 (IQR 9.6), at 6 months 9.09 (IQR 6.5,  $p < 0.001$ ), at 12 months 8.53 (IQR 6.9,  $p < 0.001$ ). Median pain VAS showed a downward trend as well, from 6 at baseline (2 IQR) to 4.5 at 6 months (2 IQR) and 4 at 12 months (IQR 1.4). No differences emerged among PsA patterns. Clinical trials did not assess efficacy of Secukinumab in patients previously treated with biologic agents other than anti-TNF agents, due to exclusion criteria. We performed subgroup analysis to evaluate its efficacy in patients previously treated with Ustekinumab, finding a reduction in median DAPSA from 19.4 (IQR 9.8,  $p < 0.001$ ) at baseline to 8.7 (IQR 8.3,  $p < 0.001$ ) at 1 year.

In the AS cohort, the median BASDAI at baseline was 5.5 (IQR 2.2), at 6 months 3.6 (IQR 1.2,  $p < 0.001$ ), at 12 months 3.1 (IQR 1,  $p < 0.001$ ). Median BASFI decreased from 4.8 (IQR 2.7) to 3.8 (IQR 2.4,  $p < 0.001$ ) and 3 (IQR 2.4,  $p < 0.001$ ) at 6 and 12 months respectively. ASDAS recuded from 3.02 (IQR 1.65), to 1.21 (IQR 1.92,  $p < 0.001$ ) at 6 months and to 1.05 (IQR 0.7,  $p < 0.001$ ) at 1 years follow up. Median pain VAS dropped off from 7 at baseline (IQR 2) to 4 (IQR,  $p < 0.001$ ) at 6 months and 3 (IQR,  $p < 0.001$ ) at 12 months. Of note, patients with advanced disease (ankylosis of the spine) reported a decrease in pain and morning stiffness, thus improving their quality of life.

4 patients switched therapy at 6 months due to partial response, 1 patient experienced an expected adverse event (Candida infection). Overall, no serious side effects were observed and none resulted in Secukinumab discontinuation.



Abstract AB0833 – Table 1

Psoriatic Arthritis Cohort		Ankylosing Spondylitis Cohort	
Mean age (years)	54.3 ± 8.5	Mean age (years)	47 ± 13.4
Disease duration (years)	9.7 ± 7.9	Disease duration (years)	12 ± 9.5
Symmetrical polyarthritis	32 (52.4%)	Presence of syndesmophytes	2 (6.9%)
Asymmetric oligoarthritis	12 (19.7%)	hDMARDs Naive	17 (58.6%)
Spondyloarthritis	12 (19.7%)	Previous anti-TNF therapy	12 (41.4%)
Digital arthritis	4 (6.5%)		
Arthritis mutilans	1 (1%)		
hDMARDs Naive	15 (24.6%)		
Previous anti-TNF therapy	43 (70.5%)		
Previous anti-IL1/2/3 therapy	12 (19.7%)		

**Conclusions:** In this first real-world cohorts of patients with PsA and AS Secukinumab has proven to be effective, regardless of PsA subtype, radiographic progression in AS and previous exposure to biologic therapy. The safety profile was favourable and similar to previous studies.

**REFERENCE:**

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.1799

**AB0834 BETTER IMPROVEMENT OF ASDAS WERE ACHIEVED IN 841 AS PATIENTS AMONG 6 MONTHS OF ANTI-TNF USERS COMPARED TO NON-ANTI-TNF USERS: RESULTS FROM A REAL WORLD PROSPECTIVE COHORT MANAGED BY SMART PHONE SYSTEM**

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**Background:** Ankylosing spondylitis (AS) is a chronic and progressive condition of the spine, which is the most common form of spondyloarthritis (SpA). Although anti-TNF agents are the most effective therapy for AS or SpA, it is recommended as the second-line treatment for individuals who have persistently high disease activity despite treatment with at least 2 non-steroidal anti-inflammatory drugs (NSAIDs), intolerance or contraindication to NSAIDs. Changes in ankylosing spondylitis disease activity score (ASDAS) are often measured to reflect outcomes in AS trials. However, anti-TNF does not always maintain long-term remission. There is limited evidence about remission rate of 6 months treatment from real-world AS cohorts.

**Objectives:** The purpose of this study is to compare the remission rate of AS patients among biologics users or non-biologics users from China Ankylosing Spondylitis/Spondyloarthritis Prospective Imaging Cohort (CASPIC).

**Methods:** CASPIC is an ongoing prospective cohort established by a smart management system [Smart Management System for Spondyloarthritis (SMSP)]. Clinic visits were scheduled based on visits reminder set by rheumatologists (1~6 months). Anti-TNF users were defined as patients who used biological agents during the follow-up period and the baseline was defined as the start time to use the biological agents. Non-biologics users were served as control groups. ASDAS was calculated to assess disease activity in AS. Generalise additive mixed model and curve fitting were used to show the difference between two groups.

**Results:** There were 841 AS patients in this cohort, 83.4% were male, with mean (±SD) age 30.8 (±8.8) years, mean time since diagnosis 8.3 (±6.1) years (table 1). Mean duration of anti-TNF treatment was 4.1 (±3.5) months. Significant improvements were observed in ASDAS (table 2). Anti-TNF users had more serious disease activity, and better clinical improvement (figure 1). If the duration of anti-TNF treatment was less than 6 months, relapsed rates were higher than those with longer than 6 months of anti-TNF (figure 1).

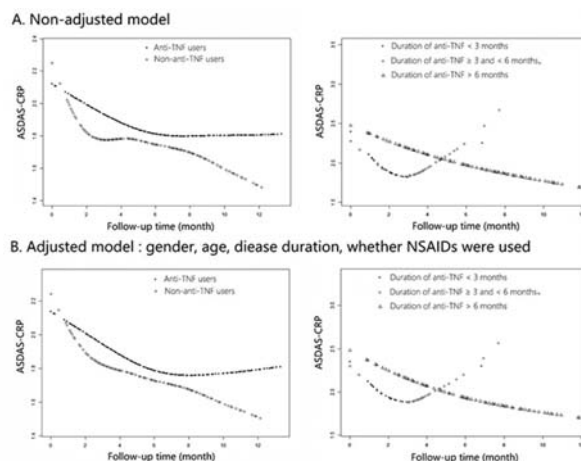
Abstract AB0834 – Table 1. Baseline characteristics

mean(SD)/N(%)	Anti-TNF users (n=633)	Non-anti-TNF users (n=208)	P
Age	31.2 (9.0)	29.7 (8.1)	0.040
Disease duration	8.3 (6.2)	8.4 (5.7)	0.869
ASDAS-CRP	2.1 (1.0)	2.6 (1.1)	<0.001
Male	535 (84.5%)	166 (79.8%)	0.114
HLA-B27 positivity	495 (87.3%)	176 (89.3%)	0.451
With NSAIDs	526 (99.1%)	162 (98.2%)	0.356

Abstract AB0834 – Table 2. Change in ASDAS per month

	Anti-TNF users	Non-anti-TNF users	P
Non-adjusted	-0.027 (-0.043,-0.011)	-0.065 (-0.094,-0.036)	<0.01
Adjusted	-0.032 (-0.048,-0.015)	-0.063 (-0.092,-0.033)	<0.01

Adjusted model: gender, age, disease duration, whether NSAIDs were used



Abstract AB0834 – Figure 1. Curve Fitting of Change in ASDAS

**Conclusions:** Anti-TNF therapy had superior improvement than NSAIDs therapy. Anti-TNF should be used for more than 6 months to achieve better and sustained remission and prevent recurrence.

**Disclosure of Interest:** None declared

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**AB0835 COMPARISON OF LONG TERM ANTI-TNF SURVIVAL IN PATIENTS WITH ANKYLOSING SPONDYLITIS AND NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS; DATA FROM TURKBIO REGISTRY**

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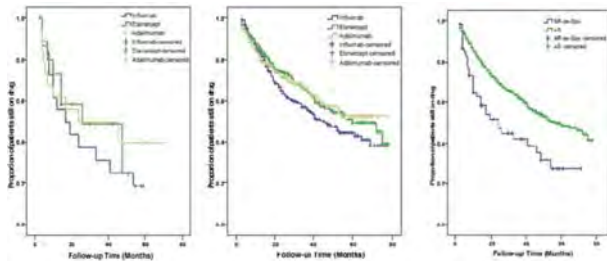
**Background:** Limited data are available on anti-TNF survival in non-radiographic axial spondyloarthritis (nr-axSpA) patients and their long-term survival in ankylosing spondylitis (AS).

**Objectives:** The aim of the study was to evaluate long term survival of the first anti-TNF drug treatment among patients with AS and nr-axSpA enrolled in the TURKBIO database and to compare the discontinuation rates for infliximab (INF), etanercept (ETN), and adalimumab (ADA) in each of the two groups.

**Methods:** All AS and nr-axSpA patients receiving biological therapies registered in the TURKBIO database between the dates of October 2011 and April 2017 were included in the study. AS diagnosis was made according to modified New York classification criteria and nr-axSpA according to ASAS AxSpA classification criteria. Demographic and clinical data, the date of starting to use biological drug, using frequency and dose of biological drugs, BASFI, BASDAI, BASMI, ASDAS scores, date and reason for discontinuing to use drug were collected. Baseline characteristics and drug survival rates were compared between AS and nr-axSpA patients. Drug survival was calculated by the Kaplan-Meier method and risk for discontinuation among treatment groups compared by Long Rank test.

**Results:** A total of 924 patients were included in the study (AS, n=871 and nr-axSpA, n=53). More than half of the patients with AS were male (60.7% in AS vs 34.0% in nr-axSpA group, p<0.001). AS patients had longer symptom duration (104.90±79.06 vs 75.11±45.29 months, p<0.036) compared to nr-axSpA. Median levels of CRP and ESR were similar for nr-axSpA (CRP: 27.03±34.71, ESR: 30.50±25.77) and AS (CRP: 22.32±29.95, ESR: 35.40±22.91). The scores of

BASFI, BASMI and ASDAS were found to be similar in both groups. Median BASDAI scores at first TNFi initiation were higher in patients with nr-axSpA than in patients with AS ( $58.65 \pm 18.21$ ,  $51.06 \pm 18.91$ ,  $p=0.030$ ). Cumulative drug survival rates did not show significant difference among INF (at 59. months:18,5%), ADA (at 71. months: 39,5%) and ETN (at 51. months: 24,2%) in nr-axSpA group ( $p=0,699$ ) (figure 1). Similarly, drug survival rates at 78, 77, 78. months for 3 anti-TNF drugs had shown no difference in AS patients (INF (at 78. months: 38,1%), ADA (at 77. months: 52,4%), ETN (at 78. months: 39,0%)) ( $p=0,151$ ) (Figure 2). Cumulative survival rates in AS patients (at 78. months:42,2%) were found to be significantly higher than that (at 71. months:28,2%) in nr-axSpA patients ( $p<0,001$ ) (Figure 3).



**Abstract AB0835 – Figure 1.** Drug survival rates anti-TNF in nr-axSpA. **Abstract AB0835 – Figure 2.** Drug survival rate by anti-TNF in AS. **Abstract AB0835 – Figure 3.** Overall drug survival on first anti-TNF in nr-axSpA and AS patients.

**Conclusions:** In contrast to the literature that revealed similar short term survival rates for anti-TNF drugs in patients with AS and nr-axSpA, we found higher survival rates in patients with AS compared to patients with nr-axSpA in this long-term observational study. A limitation of the study may be the low number of nr-axSpA patients using anti-TNF, related to the requirements of social insurance system.

**Disclosure of Interest:** None declared

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AB0836

#### DRUG RETENTION RATE OF THE FIRST TNF INHIBITOR IN RADIOGRAPHIC AND NON RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: DATA FROM A MULTICENTER STUDY

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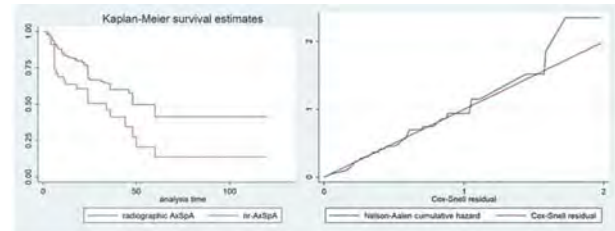
**Background:** Good survival rates of TNF inhibitors (TNFi) have been shown in patients affected with axial Spondyloarthritis (axSpA) treated in a real-life setting, irrespective of administered anti-TNF agent.<sup>1</sup> Although the use of these drugs in patients with non radiographic axSpA (nr-axSpA) remains topic of debate,<sup>2</sup> several RCTs support their employment in these patients.<sup>3</sup>

**Objectives:** To assess the retention rate of the first TNF inhibitor between axSpA and nr-axSpA patients. Additional aims: i) to evaluate any difference in persistence rates between anti-TNF monoclonal antibodies and etanercept (ETN) ii) to assess any impact of clinical, therapeutic and demographic features as well as radiographic findings on drug survival.

**Methods:** We retrospectively assessed 221 patients with axSpA, all fulfilling the ASAS criteria, who underwent first line therapy with TNFi from January 1st 2012 to September 30th 2016. Clinical, therapeutic and demographic features as well as radiographic findings were recorded at baseline and at the moment of therapy discontinuation. 126/221 patients (57.01%) were treated with Adalimumab, 45/221 with ETN, 22/221 with Infliximab, 20/221 (9.05%) with Golimumab, whereas 8/221 (3.62%) with Certolizumab Pegol. Drug retention rates were analysed using Kaplan-Meier curves; log-rank test was performed to demonstrate differences in the survival function. Cox regression models were used to estimate the inference of several clinical and disease characteristics on drug discontinuation. Goodness of fit of the final model was assessed comparing Cox-Snell residuals to Nelson-Aalen cumulative hazard function.

**Results:** Drug survival in first line therapy was significantly lower in patients who had nr-axSpA than in those with radiographic sacroiliitis ( $p=0.005$ , figure 1) whereas survival rate did not differ significantly between patients treated with ETN and anti-TNF $\alpha$  monoclonal antibodies ( $p=0.057$ ). Multivariate Cox model shown that nr-axSpA (HR 1.90), higher BMI (HR 1.18), higher HAQ, (HR 1.82) and higher

BASDAI (HR 1.25), were predictors of drug discontinuation, Nelson-Aalen hazard function following very closely Cox-Snell residuals for drug persistence in first line therapy showed that the final model fitted well the data, except for large values of time (figure 2).



**Abstract AB0836 – Figure 1.** Kaplan-Meier curves. **Abstract AB0836 – Figure 2.** Cox-Snell residuals vs Nelson-Aalen cumulative Hazard function

**Conclusions:** Effectiveness of TNFi, estimated by drug survival, seems to be lower in patients with nr-AxSpA than those affected with axSpA. The reason of these findings remain to be elucidated. However, a possible explanation may be found in the limit of the classification criteria for nr-axSpA. In addition overweight and high disease activity negatively impact the persistence on first line anti-TNF $\alpha$  treatment in axSpA patients in real life setting.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.3069

AB0837

#### THE EFFECT OF ANTI-TNF ON RENAL FUNCTION IN PATIENTS WITH ANKYLOSING SPONDYLITIS: A PROSPECTIVE COHORT STUDY

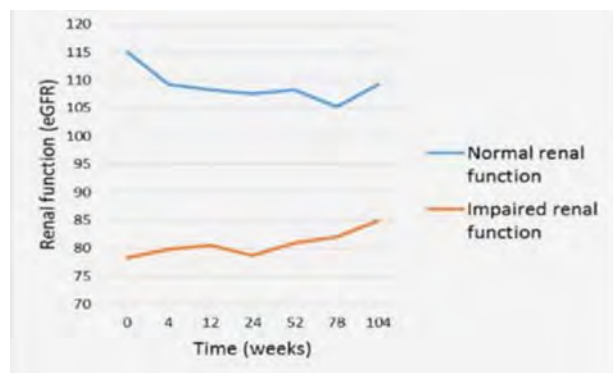
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**Background:** Impaired renal function is common in patients with ankylosing spondylitis (AS) and patients also have an increased risk of cardiovascular disease (CVD). Previous studies showed that biologicals, such as anti-Tumour Necrosis Factor (anti-TNF) reduce CVD in patients with inflammatory rheumatic disease. Impaired renal function is a known predictor of CVD (also elevated in AS). We postulated that the favourable cardiovascular effect of anti-TNF might be mediated by improving renal function. However, data about the effect of biologicals on renal function in patients with AS are lacking.

**Objectives:** To assess the effect of anti-TNF on renal function in patients with AS.

**Methods:** Biological-naïve consecutive AS patients treated with etanercept or adalimumab were prospectively followed from 2005 to 2014. Renal function was determined by calculation of the estimated Glomerular Filtration Rate (eGFR), which was estimated with the abbreviated Modification of Diet in Renal Disease (MDRD) formula. Patients were divided into two groups: patients with normal renal function at baseline and patients with impaired renal function at baseline, to investigate whether the effect is different for these groups. Normal renal function was defined by  $eGFR \geq 90$  mL/min/1.73 m<sup>2</sup> at baseline and impaired renal function was defined by  $eGFR < 90$  mL/min/1.73 m<sup>2</sup> at baseline. The effect of anti-TNF on eGFR was analysed using mixed model analysis.

**Results:** 211 AS patients were followed for a median of 156 (36 – 286) weeks. 153 patients had normal renal function and 58 had impaired renal function at baseline. In patients with normal renal function at baseline eGFR decreased significantly over time ( $\beta = -0.041$ ,  $p=0.001$ ), although this association did not remain significant after adjustment for disease activity ( $\beta = -0.015$ ,  $p=0.212$ ). Patients with impaired renal function at baseline did not have a significant change in eGFR over time ( $\beta = 0.022$ ,  $p=0.087$ ) and this association remained not significant after adjustment for alcohol consumption, BMI, disease duration and disease activity ( $\beta = 0.008$ ,  $p=0.593$ ). The change in eGFR on average over time after starting anti-TNF in AS patients with normal and impaired kidney function are presented in figure 1.



Abstract AB0837 – Figure 1

**Conclusions:** This study demonstrates that anti-TNF is not associated with renal function in AS patients, which means that use of anti-TNF is safe concerning renal function in patients with AS. From our results it seems that the effect of anti-TNF on CVD in AS patients is not mediated by an effect on renal function.

**Disclosure of Interest:** None declared

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#### AB0838 THE EFFICACY OF ADALIMUMAB AND SULFASALAZINE IN ALLEVIATING AXIAL AND AORTIC INFLAMMATION DETECTED IN PET/CT IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

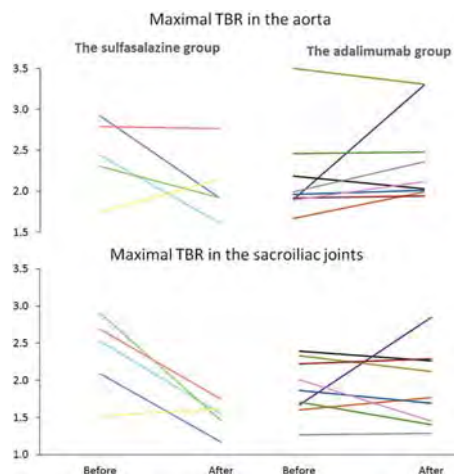
J.-P. Kaijasilta<sup>1</sup>, A. Kerola<sup>1</sup>, R. Tuompo<sup>2</sup>, M. Kauppi<sup>3</sup>, H. Relas<sup>2</sup>, A. Loimaala<sup>4</sup>, H. Koivu<sup>5</sup>, J. Schildt<sup>4</sup>, T. Kerola<sup>1</sup>, K. Eklund<sup>2</sup>, T. Nieminen<sup>6</sup>. <sup>1</sup>Internal Medicine, Päijät-Häme Central Hospital, Lahti; <sup>2</sup>Inflammation Center, Helsinki University Hospital, Helsinki; <sup>3</sup>Rheumatology, University of Tampere School of Medicine, Tampere; <sup>4</sup>Medical Imaging Center, Helsinki University Hospital, Helsinki; <sup>5</sup>Department of Nuclear Medicine, Päijät-Häme Central Hospital, Lahti; <sup>6</sup>Heart and Lung Center, Helsinki University Hospital, Helsinki, Finland

**Background:** Inflammatory pathways are likely the central link from axial spondyloarthritis to the known increased risk of cardiovascular morbidity. Literature on positron emission tomography imaging together with computed tomography (PET/CT) in the context of spondyloarthritis is limited.

**Objectives:** The aim was to grade the inflammatory signals in the sacroiliac joints and aorta in the PET/CT imaging before and after antirheumatic treatment of clinically active axial spondyloarthritis with either sulfasalazine (SSZ), the firstline antirheumatic drug in Finland for axial spondyloarthritis, or adalimumab (ADA).

**Methods:** Fourteen patients aged 18–75 years with axial spondyloarthritis and radiologic sacroiliitis as detected either by MRI or X-ray and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and visual analogue scale (VAS)  $\geq 4$  have been recruited to the pilot study. DMARD-naïve patients started SSZ for 12 weeks. Those who failed to reach remission (BASDAI and VAS  $\geq 4$ ) with SSZ or were known to be resistant to conventional DMARDs before inclusion, adalimumab was started for 16 weeks. The patients were scanned with 18F-fluorodeoxyglucose (FDG) PET/CT after inclusion and after treatment with SSZ and/or ADA. Target-to-background ratio (TBR) was assessed from the aortic root to abdominal aorta as well as for the sacroiliac joints. For statistical comparisons before and after antirheumatic treatment, paired t-test was used. Mean  $\pm$ SD are shown.

**Results:** Our pilot study comprised of nine patients with ADA and five with SSZ. In the SSZ patients (three men, age 36.0 $\pm$ 13.4 years), mean BASDAI was 4.7  $\pm$ 1.6 before and 3.4 $\pm$ 1.8 after the treatment ( $p=0.091$ ). In the ADA patients (six men, age 35.1 $\pm$ 9.8 years), BASDAI decreased from 4.9 $\pm$ 1.2 to 2.3 $\pm$ 1.8 ( $p=0.004$ ). Among the SSZ patients, maximal TBR in sacroiliac joints declined from 2.35 $\pm$ 0.55 to 1.51 $\pm$ 0.22 (-35.8%,  $p=0.03$ ) (figure 1). Aortic maximal TBR declined from 2.44 $\pm$ 0.46 to 2.07 $\pm$ 0.43 (-15.0%,  $p=0.23$ ). In the ADA patients, maximal TBR in sacroiliac joints was 1.89 $\pm$ 0.37 before and 1.90 $\pm$ 0.51 after treatment (+0.3%,  $p=0.97$ ), and in aorta 2.15 $\pm$ 0.54 before and 2.37 $\pm$ 0.53 after treatment (+10.4%,  $p=0.19$ ).



Abstract AB0838 – Figure 1. Maximal TBR in PET/CT in sacroiliac joints and aorta are shown before and after treatment with either sulfasalazine (five patients) or adalimumab (nine patients). Each colour depicts one unique patient.

**Conclusions:** As detected by reduced 18F-FDG uptake, SSZ reduced inflammation in sacroiliac joints. There was also clear trend towards reduction of inflammation in aorta. ADA and SSZ both reduced clinical symptoms, but only ADA reached statistical significance. PET/CT could not show any reduction in FDG uptake in the ADA group. This may be due to the fact that ADA was used as the second line treatment, when the inflammation had already been reduced to the limit detectable by the method.

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**Disclosure of Interest:** J.-P. Kaijasilta: None declared, A. Kerola: None declared, R. Tuompo: None declared, M. Kauppi: None declared, H. Relas: None declared, A. Loimaala: None declared, H. Koivu: None declared, J. Schildt: None declared, T. Kerola: None declared, K. Eklund: None declared, T. Nieminen Grant/research support from: Abbvie Inc

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#### AB0839 RADIOLOGIC PARAMETERS OF ANKYLOSING SPONDYLITIS PATIENTS TREATED WITH ANTI-TNF- $\alpha$ VERSUS NON-STEROIDAL ANTI-INFLAMMATORY DRUGS AND SULFASALAZINE

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**Background:** The introduction of anti-tumour necrosis factor- $\alpha$  (anti-TNF- $\alpha$ ) has significantly altered the treatment landscape of inflammatory arthritis. It has proven to be an excellent treatment option for reducing Ankylosing spondylitis(AS) symptoms. The impact of anti-TNF- $\alpha$  on the radiographic progression of AS has been difficult to characterise, in part because of the relatively slow rate of radiographic change in AS and the hurdles it imposes on longer-term placebo-controlled trials. Despite symptomatic improvement, conclusions concerning effect of anti-TNF- $\alpha$  treatment on radiographic progression in patients with AS remain inconsistent. Furthermore, while many studies have reported the impact of anti-TNF- $\alpha$  on radiographic progression, limited data are available on the relationship between treatment agents and sagittal balance in AS.

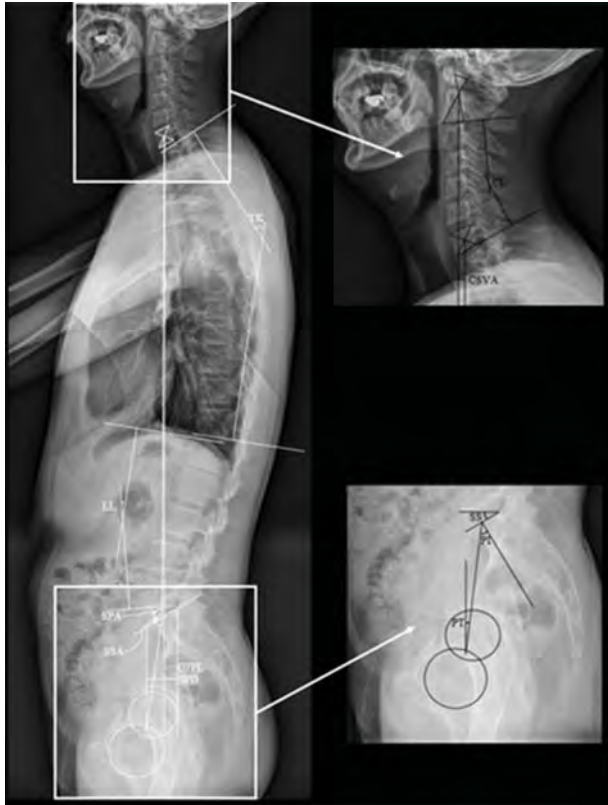
**Objectives:** Limited data are available on the relationship between treatment agents and sagittal balance in AS. We investigated radiological features related to treatment agents and compared sagittal balance between patients treated with anti-tumour necrosis factor- $\alpha$  (anti-TNF- $\alpha$ ) or non-steroidal anti-inflammatory drugs (NSAIDs) and sulfasalazine.

**Methods:** We prospectively enrolled 133 consecutive AS patients. Patients were eligible for the trial if they were under medical treatment with the same treatment agents for at least 1 year. All patients were treated initially with NSAIDs and



sulfasalazine. Sixty-nine patients were achieved an excellent pain control outcome with these agents (Group A). Sixty-four patients who complained of intractable low back pain were switched to anti-TNF- $\alpha$  treatment (Group B). Twelve radiographic parameters were measured. Clinical outcome was assessed with the Bath AS Disease Activity Index (BASDAI), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP). All parameters were measured at enrolment, upon changing treatment agents, and every 6 months during follow-up.

**Results:** Mean ESR, CRP, BASDAI, and thoracic kyphosis at baseline were significantly higher in group B. After treatment, group B had significantly higher lumbar lordosis and significantly better clinical outcomes. Correlation analysis revealed significant relationships between radiologic parameters and BASDAI. On multiple regression analysis, lumbar lordosis was a significant predictor of BASDAI.



Abstract AB0839 – Figure 1

**Conclusions:** This study demonstrated a clear association between treatment agents and radiologic parameters in AS. Anti-TNF- $\alpha$  treatment improved lumbar lordosis and slowed thoracic kyphotic progression with improvement of clinical outcomes. Lumbar lordosis was a significant predictor of clinical outcome in AS patients treated with anti-TNF- $\alpha$ .

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.3590

AB0840

**DETERMINATION OF SERUM LEVELS OF AND ANTI-DRUG ANTIBODY PRODUCTION AGAINST TNF INHIBITORS IN ANKYLOSING SPONDYLITIS: TESTING MAY BE USEFUL FOR THE ASSESSMENT OF COMPLIANCE BUT NOT THAT OF TREATMENT EFFECTIVENESS**

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**Background:** Targeted therapies, such as TNF-alpha inhibitors revolutionised the treatment of spondyloarthritis including ankylosing spondylitis (AS).

**Objectives:** To determine the correlation between serum TNF-alpha inhibitor levels of patients receiving biological therapy and concentration of anti-drug antibodies, disease activity (treatment effectiveness), age of patients and elapsed time since the onset of the diagnosis and from the initiation of the therapy.

**Methods:** Serum levels of TNF-alpha inhibitors (mg/ml) and concentration of anti-drug antibodies (AU/ml) were measured in 37 AS patients. Altogether 12 patients were treated with infliximab (IFX), 15 received adalimumab (ADA) and 10 received etanercept (ETN). Demographic data and parameters measuring disease activity (BASDAI) were also included in the analysis.

**Results:** A strong negative correlation was found between the concentration of anti-drug antibodies and drug serum levels (IFX:  $R^2=0.833$ ; ADA:  $R^2=0.426$ ; ETN:  $R^2=0.587$ ). On the other hand, similar correlation could not be demonstrated between serum concentrations of IFX, ADA or ETN and other factors, such as age of the patient (IFX:  $R^2=0.050$ ; ADA:  $R^2=0.090$ ; ETN:  $R^2=0.016$ ), BASDAI (IFX:  $R^2=0.099$ ; ADA:  $R^2=0.071$ ; ETN:  $R^2=0.015$ ), disease duration (IFX:  $R^2=0.024$ ; ADA:  $R^2 < 0.001$ ; ETN:  $R^2=0.182$ ) and time since the initiation of therapy (IFX:  $R^2=0.008$ ; ADA:  $R^2=0.052$ ; ETN:  $R^2=0.062$ ).

**Conclusions:** As anti-TNF-alpha antibodies decrease the serum concentration of TNF inhibitors. In our study, drug serum levels and anti-drug antibody concentrations significantly correlated with each other. However, similarly to some other reports, drug levels did not correlate with treatment efficacy. Therefore, routine assessment of serum drug and anti-drug antibody levels should not be recommended in the everyday practice in order to determine treatment effectiveness. However, the parallel evaluation of drug and anti-drug antibody levels may be effectively used in order to determine patient compliance in the case of subcutaneously administered drugs.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.4446

AB0841

**ASSESSMENT OF RELATIONSHIP BETWEEN LONELINESS, PERCEIVED SOCIAL SUPPORT, DEPRESSION AND MEDICATION ADHERENCE IN ANKYLOSING SPONDYLITIS PATIENTS**

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**Background:** Ankylosing spondylitis (AS) is a chronic, progressive, inflammatory disease which can cause labour loss and deformities and requiring long-term treatment. Loneliness, perceived social support, depression, patients' beliefs about medicines and treatment may affect their medication adherence and treatment success.

**Objectives:** In this study, we aimed to investigate the relationship between loneliness, perceived social support, depression and medication adherence in AS patients.

**Methods:** This cross-sectional study was conducted in a tertiary rheumatology outpatient clinic. One hundred and nineteen AS patients were enrolled to the study. The socio-demographic and clinical features of the patients agreeing to participate were recorded to the "Patient Assessment Form". The patients' disease activity and functional status were determined with the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), and the Bath Ankylosing Spondylitis Functional Index (BASFI), respectively. The pain and global assessment of the patients' were assessed with a numerical visual analogue scale (nVAS; 0–10 cm). The medication adherence of the patients was assessed with the Morisky Green Levine Scale (MGLS). The UCLA Loneliness Scale, the Multidimensional Scale of Perceived Social Support (MSPSS) and the Beck Depression Inventory (BDI) were used to determine loneliness, perceived social support, and depression of the patients.

**Results:** One hundred five patients (88.2%) were male, the mean age was 35.80  $\pm$  9.08 years, and the mean disease duration was 9.88  $\pm$  6.34 years. The mean BASDAI, BASFI and patient global assessment scores were; 4.57  $\pm$  2.63, 3.23  $\pm$  2.76, and 4.13  $\pm$  3.23, respectively. According to the MGLS medication adherence groups, patients with low medication adherence had higher BASDAI, spinal pain, spinal pain at night, fatigue and patient global assessment scores and had lower mean ages ( $p < 0.05$ ). Among the MGLS medication adherence groups, patients with low medication adherence had lower MSPSS scores, and had higher UCLA Loneliness Scale and Beck Depression Inventory scores ( $p = 0.037$ ,  $p < 0.001$ ,  $p = 0.022$ , respectively) (table 1).

**Abstract AB0841 – Table 1.** Comparison of the perceived social support, depression and loneliness scores with the Morisky Green Levine Scale subgroups.

Characteristics	Morisky Green Levine medication adherence groups				F	p
	Overall	High (n=43) <sup>a</sup>	Medium (n=66) <sup>b</sup>	Low (n=10) <sup>c</sup>		
Multidimensional Scale of Perceived Social Support total score <sup>12-84</sup>	63.52 ±17.13	65.09 ±16.85	64.65 ±16.59	49.30 ±17.01	3.958	0.022
Beck Depression Inventory (0-63)*	13.65 ±10.41	13.07 ±11.29	12.15 ±8.51	26.10 ±10.73	8.952	<0.001
UCLA Loneliness Scale <sup>20-80</sup>	37.34 ±11.22	35.19 ±11.26	37.56 ±10.90	45.20 ±10.56	3.388	0.037

F: Oneway ANOVA, Statistically significant between a and c, and b and c (p<0.05). \* It shows the lowest-highest scores that can be taken from the scale and its sub-dimensions.

**Conclusions:** In this study, it was shown that as the average age and social support scores of patients decreased, and as the BASDAI, spinal pain, spinal pain at night, fatigue, patient global assessment, loneliness and depression scores increased, adherence to treatment were decreased. It is thought that patients should be handled holistically in terms of biopsychosocial aspect in order to improve adherence to medical treatment.

**Disclosure of Interest:** None declared

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#### AB0842 DRUG SURVIVAL AND EFFECTIVENESS OF THE FIRST TNF INHIBITORS IN PATIENT WITH LATE ONSET SPONDYLARTHRTIS: TREASURE REAL-LIFE RESULTS

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**Background:** Spondylarthritis (SpA) are usually observed in young patients and a clinical onset after 45 years is rare. The average life expectancy is getting longer and the proportion of late onset of SpA in rheumatology practice may become more common. SpA patients with late onset may have a distinctive clinical pattern in terms of functional impairment, extra-articular disease, co-morbidities and treatment status.

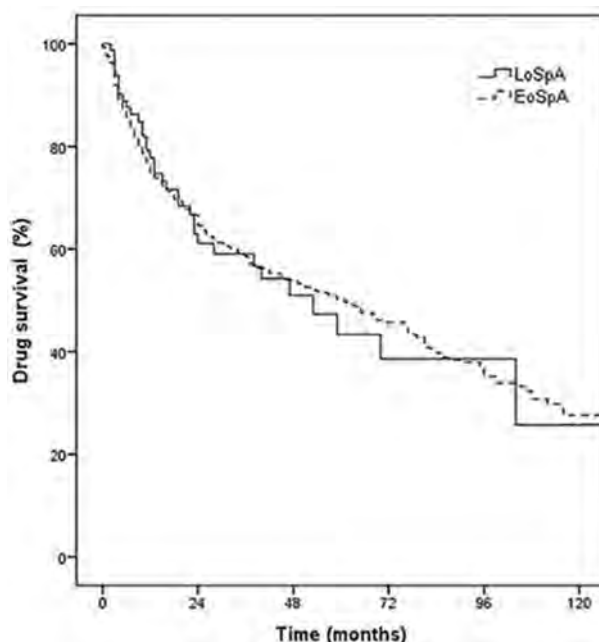
**Objectives:** The aim of this study was to compare the drug survival and effectiveness of tumour necrosis factor (TNF) inhibitors in patients with late onset SpA (LoSpA) compared with early onset SpA (EoSpA).

**Methods:** TReasure is a prospective, multicenter biological treatments registry from Turkey since 2016. It includes 15 different rheumatology centres. Patients with SpA fulfilling the ASAS criteria from TReasure database were divided into two groups as LoSpA (symptom onset >45 years of age) and EoSpA (symptom onset ≤45 years of age). Drug retention rates of first TNF inhibitors were calculated using the time until drug discontinuation independent of the reason that drug interruption. Specific reasons for discontinuing drugs were also assessed.

**Results:** Of 1382 SpA patients treated with TNF inhibitors, 9.4% (n=130) were included in the LoSpA and 90.6% (n=1252) were included in the EoSpA group. LoSpA had more female, enthesitis and psoriasis. The median treatment duration was 53 months in LoSpA and 61 months in EoSpA. The baseline disease activity measures were similar except from ASDAS-ESH which is higher in LoSpA (table 1). The rate of major treatment response (BASDAI50) was lower in LoSpA than EoSpA at the last visit (26.1% vs 46.2%; p=0.009). Regarding the survival rates of TNF inhibitors, there was no significant difference between the patient groups (figure 1). The major cause of discontinuation in both of the groups was drug ineffectiveness (68.6% in LoSpA and 60% in EoSpA, p>0.05).

**Abstract AB0842 – Table 1**

	LoSpA n: 130	EoSpA n:1252	p values
Age [median (min-max)]	56,5 (45-75)	35 (0-76)	<0.001*
Female n (%)	90 (69)	494 (40)	<0.001*
Disease duration [median (min-max)]	61 (1-334)	108 (0-686)	<0.001*
BASDAI [median (min-max)]	6.1 (0-10)	6 (0-10)	0.748
BASFI [median (min-max)]	5.3 (0-10)	4.5 (0-10)	0.098
ASDAS-ESH [median (min-max)]	3.29 (1.23-4.92)	2.91 (0-5.7)	0.001*
ASDAS-CRP [median (min-max)]	3.55 (1.49-5.92)	3.35 (0.7-8)	0.251

**Abstract AB0842 – Figure 1**

**Conclusions:** LoSpA patients were almost 10% of all biological registry. LoSpA patients were predominantly female, and they had relatively higher baseline disease activity and lower biological treatment response. On the other hand the drug survival rate and discontinuation reasons of TNF inhibitors in the LoSpA group was comparable to that in the younger group.

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#### AB0843 EFFECT OF TNF INHIBITORS ON BONE MICROARCHITECTURE IN PATIENTS WITH ANKYLOSING SPONDYLITIS: A LONGITUDINAL STUDY BASED ON HIGH-RESOLUTION PERIPHERAL QUANTITATIVE BASED (HRPQCT)

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**Background:** Ankylosing spondylitis (AS) is associated with high risk of fractures. BMD, bone microarchitecture and strength are negatively affected in AS. TNF inhibitors such as etanercept, adalimumab, golimumab and infliximab are the mainstay of treatment in AS. However no data is available on the effect of TNF inhibitors on bone microarchitecture and strength.

**Objectives:** This study aimed to assess the effect of TNF inhibitors on bone microarchitecture in patients with AS.

**Methods:** AS was defined by Modified New York criteria. Areal BMD was measured by DXA. Volumetric BMD (vBMD) and bone microarchitecture were measured using high-resolution peripheral quantitative CT (HRpQCT) at the radius and tibia at baseline and after one year of treatment with TNF inhibitors. Intake of calcium and vitamin D were optimised.

**Results:** There were 31 subjects (58% men). Mean (+SD) age and BASDAI were 40+14 years and 4.1+2.1 respectively. Median duration of disease was 14 (IQ: 6.5-25.5) years. Mean duration of follow-up was 15 months. Areal BMD (n=22) at lumbar spine (1.053+0.235 vs. 1.049+0.202, p=0.89), total hip (0.944+0.152 vs. 0.912+0.164, p=0.5), and femoral neck (0.955+0.151 vs. 0.954+0.191, p=0.2) did not change significantly. HRpQCT (n=31) on follow-up demonstrated that total, trabecular and cortical volumetric BMD were unchanged at both radius and tibia (table 1). Also, HRpQCT based trabecular parameters such as trabecular number, thickness and separation, BV/TV and cortical parameters such as cortical porosity and thickness remained stable (table 1). FEA estimates of bone stiffness and

stress tended to be lower at the radius on follow-up however these parameters were not significantly different at the tibia (table 1).

Abstract AB0843 – Table 1

	RADIUS			TIBIA		
	Baseline	Follow-up	p	Baseline	Follow-up	p
Total volumetric BMD (mg/cm <sup>3</sup> )	318.93 ±311.80	317.37 ±378.61	0.49	301.89 ±48.99	302.06 ±50.71	0.70
Cortical volumetric BMD (mg/cm <sup>3</sup> )	857.22 ±51.43	851.48 ±52.96	0.08	869.69 ±38.21	866.62 ±39.91	0.11
Trabecular volumetric BMD (mg/cm <sup>3</sup> )	158.33 ±42.34	156.81 ±41.88	0.21	155.200 ±44.34	154.26 ±45.25	0.35
BV/TV (%)	0.132 ±0.035	0.131 ±0.035	0.19	0.129 ±0.037	0.129±0.04	0.37
Trabecular number (per mm <sup>3</sup> )	1.985 ±0.302	2.017 ±0.319	0.32	1.793 ±0.36	1.809±0.37	0.56
Trabecular thickness (mm)	0.067 ±0.013	0.065 ±0.013	0.12	0.072 ±0.01	0.071±0.01	0.17
Trabecular separation (mm)	0.435 ±0.104	0.429 ±0.106	0.46	0.483 ±0.13	0.478±0.13	0.06
Cortical thickness (mm)	0.765 (0.72–0.85)	0.760 (0.71–0.82)	0.80	0.751 (0.58–0.84)	0.745 (0.55–0.83)	0.78
Cortical porosity (%)	0.019 (0.71–0.82)	0.017 (0.016–0.024)	0.81	0.049 (0.02–0.06)	0.048 (0.017–0.065)	0.80
Stiffness (N/mm)	1.37±0.42	1.33±0.34	0.03	1.57±0.31	1.58±0.31	0.72
Stress (MPa)	27.23 ±10.52	26.30±9.83	0.03	32.78±7.8	32.70±7.71	0.71

**Conclusions:** This is the first study to document the changes in bone strength in AS patients with the use of TNF inhibitors. Treatment with TNF inhibitors might maintain bone microarchitecture at cortical and trabecular sites in patients with AS.

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AB0844

#### EFFECTIVENESS AND RETENTION RATE OF CERTOLIZUMAB PEGOL IN SPONDYLOARTHRITIS. REAL LIFE DATA

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**Background:** Certolizumab pegol (CZP) is available for patients with axial spondyloarthritis (axSpA), including ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-axSpA). The efficacy and the safety of CZP are well established from clinical trials. However, evidence of its effectiveness in regular clinical practice is limited.

**Objectives:** To evaluate the effectiveness and safety of CZP in a real word setting in axSpA patients.

**Methods:** Multicentric cohort of SpA patients treated with CZP according to routine clinical practice. The study was approved by the local Ethics Committee. Maximum follow-up was 12 months. Clinical response was evaluated through BASDAI, ASDAS, BASFI and MASES scores. Safety variables: discontinuation rate.

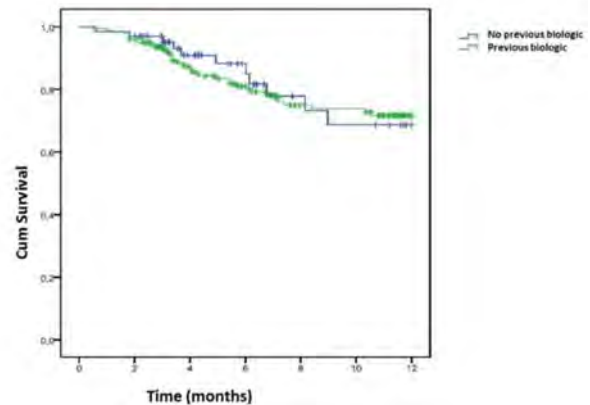
**Results:** 336 patients with axSpA were included: 56.5% male, mean age 45.8 (±12.1) years, median disease time 4.3 (0, 49.5) years, 68.5% of patients were HLAB27 positive, and never smokers 64.7%. Prior bDMARD received (27.2% none; 37.9% 1, 35%≥2). At baseline 36.8% had concomitant DMARDs and 82.8% NSAIDs. 31.8% of patients had peripheral arthritis and 42.7% entesitis at baseline. CZP retention time 10.3 months. Statistically significant differences in BASDAI, BASFI, ASDAS y MASES were observed at the last visit comparing to baseline (table 1). In the last observation, 41.0% of the patients achieved BASDAI50, 34% were in ASDAS remission (ASDAS <1.3) and 49% presented a minimal clinical improvement (ASDAS at least 1.1). 46.3% of patients had resolution of the entesitis (MASES=0). According to Kaplan-Meier analysis, the drug survival of CZP was 83.3%, and no differences were observed in retention rates

when CZP were used as first option (83.3%) or after failure to other biologicals (79.1%) (figure 1). 56/336 (16.7%) withdrawn CZP treatment: 34/336 (10.1%) due to lack of effectiveness, 16/336 (4.8%) due to adverse event and 6/336 (1.8%) for other reason. Serious adverse event was found in 23/336 (6.8%) patients.

Abstract AB0844 – Table 1. Evolution of clinical variables of activity

	Baseline	Last visit
BASDAI evolution	6,2±1.6(n=263)	3,9±2.2(n=260)*
BASFI evolution	5,6±2.1(n=225)	3,7±2.3 (n=241)*
ASDAS evolution	3,7±2.7(n=322)	2,4±2.2 (n=321)*
MASES score	3,9±2.7(n=78)	1,2±1.8(n=51)*

\*p<0,001, Wilcoxon's test



Abstract AB0844 – Figure 1. CZP Retention rate in axSpA patients without and with previous biological experience.

**Conclusions:** Real life experience from this nationwide rheumatology study, demonstrated the effectiveness and safety of CZP in patients with axSpA, with a significant reduction of BASDAI, BASFI, ASDAS and MASES scores. No differences were observed in the retention rate regardless previous biological treatment.

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AB0845

#### THE EFFECT OF BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS PATIENT REPORTED OUTCOMES IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS; A SYSTEMATIC LITERATURE REVIEW AND A CALL FOR ACTION

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**Background:** Patient reported outcomes (PROs) have gained relevance in the evaluation of several diseases such as axial spondyloarthritis (axSpA). They allow the clinician to have a quantitative measurement of several aspects of the disease, according to the patient perspective.

**Objectives:** In this review we intended to evaluate the efficacy of different biologic disease-modifying anti-rheumatic drugs (bDMARD) in achieving the minimum clinically important difference (MCID) in several PROs's. Data from randomised controlled trials (RCT) conducted in radiographic axSpA (r-axSpA) and non-radiographic axSpA (nr-AxSpA) patients were included.

**Methods:** A systematic literature review (SLR) was performed using the MEDLINE database (August 17 2017) with the filters "published in the last 10 years" and "humans". Abstracts from the EULAR 2017 were also considered. The PICO (P,



population; I, intervention; C, comparison; O, outcome) concept was used to perform the analysis according to: Patients: adults (>18 years old) with r-axSpA or nr-axSpA; Intervention: any bDMARD regardless of formulation or duration; Comparison: placebo and/or any different drug; Outcomes: The Bath Ankylosing Spondylitis Functional Index (BASFI), the Ankylosing Spondylitis Quality of Life (ASQoL), the EuroQoL-5D (EQ-5D), the Short Form 36 Health Survey physical component summary (SF36-PCS), the Short Form 36 Health Survey mental component summary (SF36-MCS), and the Functional Assessment of Chronic Illness Therapy – Facit (FACIT-F). For each outcome we assessed whether the treatment group was superior, equal or inferior to the placebo (PBO) group regarding the achievement of the MCID of the assessed PRO over time.

**Results:** After screening 557 references (after de-duplication), 16 RCTs were included, studying interleukin 17 inhibitors (IL17i) and tumour necrosis factor inhibitors (TNFi). In r-axSpA, the treatment group (for both TNFi and IL17i) reached the MCID for all the assessed PROs, except for a single study in which both the treatment and PBO groups reached the MCID for the SF36-PCS. For nr-axSpA the results were more heterogeneous (table 1).

Abstract AB0845 – Table 1

Phenotype	PRO and MCID cut-off for improvement	Difference between MCID from baseline to RCT end in favour of treatment arm (against PBO)	Drug (reference)
r-AxSpA	BASFI (0-10) (≥7mm)	YES	ADA (Maksy 2008); SEC (Deodhar 2017); ADA (van der Heijde 2009)
	ASQoL (0-18) (≥1.8)	YES	SEC (Deodhar 2017); GOL (Deodhar 2017)
	EQ-5D (≥10.0)	YES	SEC (Deodhar 2017; Marzo-Ortega 2017); GOL (Reveille 2017)
	SF36-PCS (≥2.5)	YES	SEC (Deodhar 2017; Marzo-Ortega 2017)
	SF36-PCS (≥2.5)	YES#	GOL (van Heijde 2014; Reveille 2017)
	SF36-MCS (≥2.5)	YES	SEC (Deodhar 2017); GOL (van der Heijde 2004; Reveille 2017)
	FACIT-F (≥4)	YES	SEC (Kvien 2017; Kvien 2017)
nr-axSpA	BASFI (0-10) (≥7mm)	YES	ETN (Maksymowich 2016)
	BASFI (0-10) (≥7mm)	YES#	ADA (Haibel 2008); IFX (Sieper 2014)
	ASQoL (0-18) (≥1.8)	YES	CZP (Sieper 2015)
	EQ-5D (≥10.0)	YES#	ADA (Haibel 2008); IFX (Sieper 2014)
	EQ-5D (≥10.0)	NO	ETN (Dougados 2015)
	SF36-PCS (≥2.5)	YES	ADA (Sieper 2013)
	SF36-PCS (≥2.5)	YES#	ADA (Haibel 2008); ETN (Dougados 2015)
	SF36-MCS (≥2.5)	YES	ADA (Haibel 2008)
	SF36-MCS (≥2.5)	NO	ETN (Dougados 2015)

PRO: Patient reported outcome; RCT: Randomised control trial; PBO: Placebo; r-axSpA: radiographic axial spondyloarthritis; nr-axSpA: non-radiographic axial spondyloarthritis; BASFI: The Bath Ankylosing Spondylitis Functional Index; ASQoL: Ankylosing Spondylitis Quality of Life Questionnaire; EQ-5D; the EuroQoL-5D; SF36-PCS: Short Form 36 Health Survey physical component summary; SF-36-MCS: the Short Form 36 Health Survey mental component summary; FACIT-F: the Functional Assessment of Chronic Illness Therapy – Facit; ADA: Adalimumab; SEK: Secukinumab; GOL: Golimumab; ETN: Etanercept; IFX: Infliximab; CZP: Certolizumab pegol; YES: There was an improvement on treatment but not on PBO groups; YES# There was a MCID improvement in both treatment and PBO groups; NO: there was no improvement in neither treatment nor PBO group.

**Conclusions:** The assessment of PROs in RCT is scarce. The profile of PROs response seems to be different between r-axSpA and nr-axSpA patients; these differences must be further validated in future trials.

This study launches a call for action in PROs reporting standardisation.

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## AB0846 PERSONALISING CARE: USING INFLIXIMAB DRUG TROUGH AND ANTI-DRUG ANTIBODY LEVELS IMPROVES CLINICAL TREATMENT DECISIONS AND IS A COST EFFECTIVE STRATEGY IN SPONDYLOARTHRITIS

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**Background:** Personalised medicine tailors treatment to the individual's needs. The advent of biosimilars has led to therapy re-appraisals driven by healthcare commissioning bodies' demand for cost-effective interventions. Yet, biologic drug dosing is standardised and little is known about the rationale and efficacy of dose adjustment.

**Objectives:** As part of a service evaluation exercise, we measured serum drug trough levels (DLs) and anti-drug antibodies (ADABs) in our cohort of patients with axial spondyloarthritis (axSpA) and Psoriatic arthritis (PsA) receiving bio-originate infliximab with the aims of a) informing our decision making upon switching to a biosimilar and b) assessing the impact of this approach to our clinical practice.

**Methods:** Eligible subjects identified, were counselled and consented by an experienced specialist nurse on DLs and ADAB testing and possible associated outcomes including change in drug class, dose, infusion time interval and switching from bio-originate infliximab to the biosimilar infliximab CT-P13. A treatment algorithm was developed to guide the treating physician. Clinical and outcome data were recorded as per routine practice including disease status, DLs and ADAB titre, and clinical outcome.

**Results:** We identified 53 subjects. Based upon disease activity, DL and ADAB level, bio-originate infliximab was discontinued in 3 (6%) subjects, the infusion interval was extended in 8 (15%), shortened in 3 (6%), and the dose reduced in 3 (6%) subjects. Four patients (8%) changed to an alternative biologic due to persistent high disease activity on infliximab. ADABs were absent in 20/28 (71%) subjects on concomitant methotrexate (MTX). Very high titre ADABs were identified in 8 (15%) subjects with corresponding very low (n=2) or undetectable (n=6) DLs suggesting likely drug-neutralisation. The total estimated cost-savings from drug discontinuation and interval extension or dose reduction were £28,689 per annum in addition to the biosimilar switch saving of £41,184 per annum.

Abstract AB0846 – Table 1

	axSpA (n=32, 60%)	PsA (n=21, 40%)
M:F	30:1	7:14
Bio-originate infliximab duration (years), (median, IQR)	11 (8–15)	9 (6–14)
Concomitant csDMARD, n (%)	12 (36%)	17 (81%)
MTX, n (%), (median dose)	12 (100%, 15 mg/week)	16 (94%, 10 mg/week)
Previous biologic (bDMARD)	5 (16%)	5 (24%)
Positive ADABs (median, IQR) AU/mL	12 (37%), 46.5 (18–74)	8 (38%), 86.5 (29–212)
Therapeutic range DL	14 (44%)	10 (48%)
High ADAB/very low or undetectable drug (likely drug-neutralising)	4 (13%)	4 (27%)
Drug discontinued (no alternative bDMARD required)	1 (3%)	2 (10%)
Dose reduced or interval extended	8 (25%)	3 (14%)
Alternative bDMARD (either TNFi or different mode of action)	1 (3%)	3 (14%)
Switched to biosimilar	14 (44%)	10 (48%)

**Conclusions:** These data from a small cohort suggest that measuring ADABs and DLs to characterise treatment response, tailor treatment regime and inform biosimilar switching is a clinically efficacious and cost-effective strategy in infliximab-treated SpA patients. We anticipate further significant savings with our

cohort receiving subcutaneous therapies. This approach unlocks the potential of "personalised medicine" which supports individualised treatment and brings significant savings to the healthcare provider.

**Disclosure of Interest:** None declared

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#### AB0847 IMPACT OF SPONDYLOARTHRITIS ON LIFE QUALITY: BEFORE AND AFTER TREATMENT

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**Background:** Life quality issues in spondyloarthritis (SPA) are often spontaneously mentioned by patients or identified by rheumatologists. Besides classic follow up parameters, we have to consider those issues to improve our patients life quality.

**Objectives:** Explore and quantify the impact of SPA on life quality via everyday's life and psychological items and the effect of treatment on them.

**Methods:** SPA cases were collected by a group of 14 private practice rheumatologists (Rh) in the Paris area. Basic informations about the patient and his disease were provided by his rheumatologist. Questionnaire including 12 themes and 41 items was filled in by the patient.

**Results:** 50 cases collected, 59.5% men, mean age 45 years, 82% working Axial SPA 42%, peripheral 4%, mixt 52%. Mean duration before study: 14 years. Moderate disease 57%, severe 26.5%. HLA B27 positive 84%

Drugs: NSAIDS 96%, classic DMARDS 31%, biological DMARDS 84%, corticosteroids 36%, combination therapy 42%.

Associated measures were suggested by the Rh: Physical activity (62%), rest (56%), psychological support, physiotherapy, yoga, adapting professional activity and environment...

Life quality issues are spontaneously mentioned by 40% of the patients.

Before treatment, 72% of the patients report consequences on their hobbies, 68% on their psychological well-being, 54% on their getting about, 50% on their family relations. The less impacted items are food (26%) and economy (24%).

Life quality is mostly altered by pain (71%), then fatigue (17%), handicap (7%) and other people's attitude (5%).

After treatment, social repercussions diminish by 47%, then getting about, house-work, family relations, holidays, sexual life, psychological well-being, hobbies and work (between -21% and -44%).

Drug intolerance: 36%.

The items improving by more than 50% after treatment are in this order: cultural life, transports, house-keeping, do-it-yourself, sleep, going out, work (53% less sick leave).

The treatment is less efficient (<22%) on economy, dependance, disillusion, depression and sexual life.

Family circle lacks empathy in 66% of the cases, family relations stay difficult after treatment.

**Conclusions:** SPA diminishes quality of life in 75% of our patients, but only 40% mention it spontaneously. All the parameters impacted by SPA were significantly improved after treatment. The best improvement concerned hobbies, including culture, do-it-yourself and going out. One patient of two found correct sleep and felt psychologically better. Sick leave was reduced by half, but, unfortunately, family relations didn't improve.

The rheumatologist has to track, in a trusting patient-physician relation, the daily situation impacted by the SPA.

**Disclosure of Interest:** None declared

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## Spondyloarthritis – clinical aspects (other than treatment)

#### AB0848 FOUR YEARS OF DELAY IN THE DIAGNOSIS OF SAPHO SYNDROME: SINGLE TERTIARY CENTRE EXPERIENCE

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**Background:** SAPHO syndrome is a chronic disease with bone, joint and skin involvement characterised by synovitis, acne, pustulosis, hyperostosis and osteitis. It is a rare disease and its diagnosis may depend on detailed clinical examination as well as radiological evaluation

**Objectives:** In this study, we aim to present clinical features and diagnostic course of patients with SAPHO syndrome who are followed in our tertiary referral clinic.

**Methods:** All patients with SAPHO syndrome diagnosed since February 2014 have been registered with a standard form. Patients are prospectively monitored since then. Diagnosis was based on the criteria by Benhamou et al.<sup>1</sup> In the questionnaire, demographic data (age, sex, duration of illness), clinical features (skin and joint involvement), laboratory characteristics (acute phase reactants, HLA-B27), radiological imaging (bone scintigraphy (increased activity in the sternum, bilateral sternoclavicular joints and clavicles), MRI) disease activity parameters (BASDAI, BASFI) were questioned. There were 24 patients with SAPHO syndrome. The data of 21 patients were presented because the clinical findings of 3 patients were insufficient.

**Results:** Data of 21 patients with SAPHO syndrome were available and 11 (52.4%) patients were female. Mean age at diagnosis was 39.9±12.9, mean age of symptom onset was 35.2±12.9, mean follow-up duration was 18.1±25.1 months. The mean delay time of diagnosis SAPHO syndrome was calculated as 49.0±82.5 months. Thirteen patients (61.9%) were followed up with another clinical diagnosis before SAPHO diagnosis. The clinical characteristics of the patients are shown in Figure 1. HLA-B27 was positive in 3 of 13 patients. Mean activity scores of our patients at initial visit were; BASDAI: 4.8±2.8, BASFI: 4.6±2.2, CRP2.3±4.2 mg/dL and erythrocyte sedimentation rate 23.8±22.6 mm/h. Scintigraphy findings were positive in 16 (94.1%) of 17 patients. The diagnosis of 2 patients was supported by MRI. The remaining 2 patients were diagnosed with X-ray and clinic findings.

Involvement pattern	n (%)
Spinal involvement	14 (66.7)
Peripheral joint involvement	8 (38.1)
Skin involvement	16 (76.2)
- PPP	10 (47.6)
- Serious acne	5 (23.8)
- Psoriasis vulgaris	5 (23.8)
- Hidradenitis suppurativa	1 (4.8)
Skin involvement time	
- Before muscle skeletal symptoms	7 (43.8)
- Muscle skeletal symptoms at the same time	1 (6.3)
- After musculoskeletal symptoms	8 (50)
Osteoarticular symptoms	19 (90.5)
- Cervical pain	10 (47.6)
- Thoracic pain	15 (71.4)
- Lumbosacral pain	15 (71.4)
Anterior chest wall pain	20 (95.2)
IBP	12 (57.1)
Morning stiffness (more than 1 hour)	10 (47.6)
Sternocostal joint involvement	7 (33.3)
Sternoclavicular joint involvement	18 (85.7)
Manubrium sternal involvement	11 (52.4)
Costochondral joint involvement	6 (28.6)
Hip joint involvement	10 (47.6)
Sacroiliitis	10 (47.6)
Osteitis	10 (47.6)
Entesis	4 (19)
Ulcers	3 (14.3)

**Abstract AB0848 – Figure 1.** Clinical characteristics of patients at diagnosis

PPP: palmoplantar pustulosis, IBP: Inflammatory Back pain

**Conclusions:** There is a certain diagnostic problem in the SAPHO syndrome. Delay of SAPHO diagnosis was almost 4 years and 62% of patients had wrong diagnosis before SAPHO syndrome. Anterior chest wall involvement with dermatological findings should be alerting to the physicians. Bone scintigraphy can be helpful to diagnose SAPHO syndrome. It is important to distinguish SAPHO syndrome from other spondyloarthritis and/or psoriatic arthritis because of the potential different treatment strategies.

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**AB0849 CORRELATION BETWEEN RAPID3 AND PROMIS10 IN PATIENTS WITH ANKYLOSING SPONDYLITIS**

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**Background:** Patient-reported outcome (PRO) measures are important in managing and improving the quality of care in patients with chronic rheumatic conditions including ankylosing spondylitis (AS). The RAPID3 was developed for use in patients with rheumatoid arthritis, but it has shown good correlation with the BASDAI and ASDAS in patients with AS.<sup>1</sup> The PROMIS10 is a universal (non-disease specific) PRO measure that quantifies physical and mental health;<sup>2</sup> validity of PROMIS10 has not been examined in patients with AS.

**Objectives:** To evaluate the relationship between RAPID3 and PROMIS10 in patients with AS.

**Methods:** US patients aged ≥18 years with a self-reported diagnosis of AS were recruited through CreakyJoints (www.CreakyJoints.org), an online patient support community comprising patients with arthritis and arthritis-related diseases and their caregivers and via outreach on social media. Respondents completed a web-based survey designed to collect data on socio-demographics and clinical symptoms, RAPID3, and PROMIS10. The RAPID3 score consists of three patient self-reported scores (0–10): functional impairment, pain, and patient global assessment; total scores ≤3.0=near remission, 3.1 to 6.0=low disease severity, 6.1 to 12.0=moderate disease severity, and ≥12.1 = high disease severity. PROMIS10 is a 10-item questionnaire measuring physical, mental, and social domains; physical and mental health domain scores are transformed to T-score distributions normalised to the general population (mean score=50). PROMIS10 individual scores and global physical and mental health T-scores were stratified by RAPID3 disease severity and compared across RAPID3 severity levels using Kruskal-Wallis or ANOVA or tests, respectively. Spearman's correlation coefficient was calculated between the RAPID3 total score and the PROMIS10 physical health and mental health T-scores, respectively.

**Results:** Among 235 respondents, 174 (74%) were female, with a mean (SD) age of 49.8 (10.7) years. The mean (SD) RAPID3 cumulative score was 15.4 (5.4) The mean (SD) PROMIS10 global physical and mental health T-scores were 35.60 (7.39) and 39.89 (8.76), respectively, with individual domain scores and global T-scores decreasing with worsening RAPID3 disease activity (table 1; p<0.0001 for all). PROMIS10 physical and mental health T-scores showed a strong correlation with RAPID3 (r<sub>s</sub>=−0.84 and −0.63, respectively).

**Abstract AB0849 – Table 1.** PROMIS10 Scores by RAPID3 Disease Activity in Patients with AS

PROMIS10 domain, mean (SD)	RAPID3 Disease Activity*				P value
	Near Remission (n = 5)	Low Severity (n = 9)	Moderate Severity (n = 52)	High Severity (n = 169)	
Overall health	4.20 (0.45)	3.89 (0.60)	2.77 (0.70)	2.09 (0.77)	< 0.0001
Quality-of-life	4.80 (0.45)	3.67 (0.71)	3.10 (0.63)	2.28 (0.88)	< 0.0001
Physical health	4.40 (0.55)	3.44 (0.53)	2.65 (0.65)	1.97 (0.78)	< 0.0001
Mental health	4.80 (0.45)	3.44 (0.53)	3.06 (0.78)	2.56 (0.96)	< 0.0001
Satisfaction with social activities/relationships	5.00 (0.00)	3.00 (0.71)	2.94 (1.00)	2.15 (1.01)	< 0.0001
Ability to carry out every day physical activities	4.80 (0.89)	3.67 (0.71)	2.98 (1.11)	2.09 (0.85)	< 0.0001
Emotional distress	4.40 (0.89)	3.22 (0.83)	2.75 (0.78)	2.20 (0.78)	< 0.0001
Fatigue	4.40 (0.89)	3.22 (0.83)	2.75 (0.78)	2.20 (0.78)	< 0.0001
Pain	4.20 (0.45)	4.00 (0.00)	3.25 (0.44)	2.38 (0.54)	< 0.0001
Global physical health T-score	57.84 (3.90)	47.62 (4.24)	40.92 (4.40)	32.66 (5.37)	< 0.0001
Global mental health T-score	63.56 (5.63)	46.72 (4.05)	44.26 (6.27)	37.48 (7.90)	< 0.0001

AS, ankylosing spondylitis; PROMIS10, Patient-Reported Outcome Management Information System Global Health short form; RAPID3, Routine Assessment of Patient Index Data 3.

\* Disease severity classified by RAPID3 scores: ≤3.0=near remission; 3.1 to 6=low severity; 6.1 to 12.0=moderate severity; ≥12.1= high severity.

**Conclusions:** RAPID3 and PROMIS10 are relatively short questionnaires that can be used in the real world to track and monitor disease symptoms and health-related quality of life in patients with AS. RAPID3 and PROMIS10 were strongly correlated in patients with AS; although, the PROMIS mental health T-score likely measures a slightly different construct than RAPID3.

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**AB0850 DO SYMPTOMS OF DEPRESSION AND ANXIETY INFLUENCE TREATMENT RESPONSE AND LONG-TERM PHYSICAL HEALTH OUTCOMES IN ANKYLOSING SPONDYLITIS?**

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**Background:** Psychological disturbances, frequently observed in inflammatory rheumatic diseases, seem to negatively influence patient's clinical status and treatment response.

**Objectives:** The aim of this study was to examine the longitudinal impact of depression (D)/anxiety (A) in treatment response, disease activity, physical disability and quality of life in patients with Ankylosing Spondylitis (AS).

**Methods:** Data from patients who fulfilled the modified New York criteria for AS were collected at baseline, weeks 2 and 14 post-treatment with Adalimumab. The Hospital Anxiety and Depression Scale (HADS) was used to evaluate D/A symptoms severity. The primary outcomes were AS disease activity score – C reactive protein (ASDAS-CRP), Bath AS Disease Activity Index (BASDAI), Bath AS Functional Index (BASFI) and AS Quality of Life (ASQoL) Scale. Secondary outcomes were patient and physician global assessment by Visual Analogue Scale (VAS), erythrocyte sedimentation rate (ESR), CRP and BASDAI question 1 (fatigue). Difference-in-differences estimation took into account the covariates gender, age at baseline and disease duration.

**Results:** Data from 54 patients were included. At baseline, D/A symptoms significantly influenced the mean value of BASFI (p=0.006; p=0.003) and ASQoL (p<0.001; p=0.004). On the other hand, BASDAI (p=0.009), CRP (p=0.017), patient's VAS (p=0.003) and fatigue (p=0.015) were only influenced in the individuals with A symptoms, while the physician's VAS (p=0.005) was only influenced in patients with D symptoms. After 14 weeks of treatment, significant differences in ASQoL mean values were found in patients with both D/A symptoms at baseline (p=0.005; p=0.022) and in BASFI (p=0.044) and patient VAS (p=0.006) for the population showing only A symptoms at the baseline. Apart from the physician VAS (p=0.023), D/A baseline symptoms did not affect the treatment's response.

**Abstract AB0850 – Table 1.** Difference-in differences estimation results. †p-value<0.05.

Difference-in-differences	Baseline Mean Difference (95% CI)	3 Months Mean Difference (95% CI)	Global Mean Difference (95% CI)	
				†p-value
Anxiety symptoms (HADS-A)	ASDAS-CRP	2.27 (0.39)	3.26 (0.37)	0.03 (0.12)
	BASFI	1.40 (0.089)	1.58 (0.090)	-0.15 (0.041)
	BASDAI	2.48 (0.089)	1.82 (0.084)	-0.62 (0.088)
	CRP	1.22 (0.009)	0.51 (0.009)	-0.70 (0.088)
	ESR	-2.24 (0.20)	-0.97 (0.044)	1.27 (0.122)
	CRP	-0.07 (0.17)	-0.90 (0.016)	0.74 (0.126)
	Physician's VAS	21.41 (0.007)	23.52 (0.007)	2.11 (0.007)
	Patient's VAS	0.75 (0.09)	0.54 (0.01)	-0.19 (0.09)
	Fatigue	1.80 (0.04)	1.69 (0.04)	-0.11 (0.12)
	ASQoL-CRP	0.47 (0.10)	0.33 (0.09)	-0.17 (0.10)
Depression symptoms (HADS-D)	ASDAS-CRP	0.88 (0.20)	0.50 (0.27)	-0.37 (0.19)
	BASFI	2.19 (0.009)	1.88 (0.009)	-0.30 (0.078)
	BASDAI	1.84 (0.009)	1.28 (0.027)	-0.56 (0.08)
	CRP	0.87 (0.00)	-0.48 (0.00)	-1.13 (0.00)
	ESR	0.48 (0.00)	1.38 (0.00)	0.90 (0.02)
	Physician's VAS	11.28 (0.02)	7.70 (0.03)	-3.58 (0.00)
	Patient's VAS	0.78 (0.00)	0.68 (0.02)	-0.10 (0.02)
	Fatigue	0.69 (0.00)	0.27 (0.00)	-0.42 (0.00)

**Conclusions:** Psychological status does not seem to affect response to treatment with Adalimumab, even if the overall characteristics of the population are different at baseline between patients with/without D/A symptoms.

**Disclosure of Interest:** None declared

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**AB0851** **CLINICAL ASSOCIATIONS OF UVEITIS IN ASAS DEFINED AXIAL SPONDYLOARTHRITIS GROUP AND MODIFIED NEW YORK CRITERIA DEFINED ANKYLOSING SPONDYLITIS GROUP**

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**Objectives:** To identify and compare the associated factors for uveitis in Chinese patients with axial spondyloarthritis (SpA) and ankylosing spondylitis (AS).

**Methods:** Patients fulfilling the Assessment of SpondyloArthritis (ASAS) axial SpA criteria were recruited consecutively from three rheumatology centres in Hong Kong. Clinical and biochemical parameters were collected. History of uveitis was enquired from both history and medical records. All patients received lumbosacral spine x-rays, and whole spine and sacroiliac (SI) joint magnetic resonance imaging (MRI). MRIs were scored according to the Spondyloarthritis Research Consortium of Canada (SPARCC) scores. Patients were defined as axial SpA if they fulfilled the ASAS criteria, and AS if they fulfilled the modified New York (mNY) criteria. Clinical and radiological findings were compared between patients with and without uveitis in the two groups. Factors associated with uveitis were identified with univariate analyses and multivariate logistic regression analyses.

**Results:** Among 253 patients, 67 (26.5%) patients had a history of uveitis. The male to female ratio was 55.7 to 44.3. Disease duration was 12.3±11.7 years. In the axial SpA group, univariate analyses showed that the following factors were associated with uveitis: back pain duration, age, HLA-B27 positivity, history of inflammatory bowel disease (IBD), tender joint count, Ankylosing Spondylitis Disease Activity Index (ASDAS) and SPARCC score of spine. Multivariate regression showed that older age (OR 1.05; p=0.01), HLA-B27 positivity (OR 11.79; p=0.01) and history of IBD (OR 9.74; p=0.04) were positively associated with uveitis. In the AS group, univariate analyses showed that the following were associated with uveitis: back pain duration, age, male sex, HLA-B27 positivity, tender joint count, ASDAS, SPARCC score of spine and SPARCC score of SI joints. Multivariate regression showed that back pain duration (OR 1.05; p=0.01) and male sex (OR 3.46; p=0.03) were associated with uveitis.

**Conclusions:** Clinical factors associated with uveitis are similar in the axial SpA and AS groups. The former group is associated more with IBD, and the latter with male sex.

**Disclosure of Interest:** None declared

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**AB0852** **GENDER DIFFERENCES IN AXIAL AND PERIPHERAL SPONDYLOARTHRITIS: RESULTS FROM THE ESPERANZA COHORT**

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**Background:** In patients with spondyloarthritis (SpA), published data indicate different manifestations and outcomes between genders. Nevertheless, the evidence in patients with early and peripheral disease is lacking.

**Objectives:** To evaluate differences in the presentation of the disease between genders in patients with early axial and peripheral SpA (axSpA, pSpA).

**Methods:** This study was carried out within the framework of the ESPERANZA program, which was a Spanish multicenter initiative aiming to facilitate early diagnosis and follow-up of patients with SpA between 2008–11. Out of 775 patients referred, 377 patients fulfilled the ASAS classification criteria for SpA:291(77%) axSpA and 86 (23%) pSpA. Demographic and disease characteristics were compared between genders using Chi-square (for categorical variables) and Student t (for continuous variables) tests.

**Results:** In total, 241 (64%) patients were males (191 axSpA and 50 pSpA). In the axSpA group, males had more frequently radiographic sacroiliac damage, elevated CRP, HLA-B27 positive and morning stiffness, while females had higher values of ESR and more frequency of peripheral arthritis (table 1). Within the pSpA group, male gender was significantly associated with higher diagnostic delay, psoriasis and elevated CRP while women had higher rates of functional limitation and ESR values.

Characteristic	Axial Spondylarthritis (n: 291)			Periferical Spondylarthritis (n:86)		
	Males (n: 191)	Females (n:100)	P value	Males (n: 50)	Females (n: 36)	P value
Age (yrs)	31.6 ± 7.1	32.8 ± 6.8	0.2	33.1 ± 8.4	32.4 ± 6.9	0.7
Family history	67 (35.1)	34 (34.0)	0.9	15 (30.0)	16 (44.4)	0.2
Symptoms dur (m)	13.1 ± 6.9	12.7 ± 6.4	0.6	10.4 ± 6.4	7.7 ± 5.5	0.04
Morning stiffness	138 (72.3)	60 (60.0)	0.03	3 (6.0)	3 (8.3)	0.7
IBP (ASAS criteria)	74 (38.7)	38 (38.0)	0.9			
Arthritis	42 (22.0)	11 (11.0)	0.02	48 (96.0)	35 (97.2)	0.8
Enthesitis	38 (19.9)	19 (19.0)	0.9	28 (56.0)	15 (41.7)	0.2
Dactylitis	13 (6.8)	3 (3.0)	0.2	17 (34.0)	11 (30.6)	0.7
Psoriasis	23 (12.0)	10 (10.0)	0.6	21 (42.0)	7 (19.4)	0.03
IBD	8 (4.2)	1 (1.0)	0.1	6 (12.0)	4 (11.1)	0.9
Uveitis	11 (5.8)	12 (12.0)	0.06	1 (2.0)	0 (0)	0.4
HLA-B27+	151 (79.1)	68 (68.0)	0.03	16 (32.0)	12 (33.3)	1.0
CRP (mg/L)	12.4 ± 16.6	7.8 ± 11.7	0.01	17.4 ± 39.5	8.6 ± 11.5	0.1
ESR (mmHg)	12.3 ± 13.9	16.0 ± 12.5	0.04	11.9 ± 14.1	17.4 ± 11.6	0.09
SIC (0-68)	0.3 ± 1.6	0.2 ± 0.6	0.2	1.4 ± 2.4	1.3 ± 2.3	0.8
VAS (0-100) physician	30 ± 22	28 ± 22	0.5	22 ± 19	27 ± 25	0.4
VAS (0-100) patient	40 ± 26	45 ± 29	0.2	29 ± 22	35 ± 29	0.4
BASDAI (0-10)	3.7 ± 2.2	4.0 ± 2.3	0.3	3.2 ± 2.1	3.8 ± 2.4	0.2
BASFI (0-10)	2.2 ± 2.3	2.6 ± 2.4	0.2	1.3 ± 1.4	2.3 ± 2.3	0.04
BAMI (0-10)	1.4 ± 1.3	1.5 ± 1.1	0.4	1.2 ± 1.1	1.4 ± 1.0	0.5
MASES (0-13)	0.5 ± 1.2	0.5 ± 1.5	0.9	0.2 ± 0.6	0.2 ± 0.4	0.6
Sacroiliitis-xRay (mNY)	81 (42.4)	28 (28.0)	0.02			
Sacroiliitis-MRI (ASAS)	72 (37.7)	53 (53.0)	0.3			
Disability to work (%)	24 (12.5)	7 (7.0)	0.2	13 (26.0)	6 (16.7)	0.5
ASQoL (0-18)	5.5 ± 4.9	6.6 ± 4.5	0.08	4.1 ± 4.7	4.9 ± 5.3	0.5

**Conclusions:** In patients with SpA, different disease manifestations between genders are observed already from the first stages of the disease. In patients with axSpA, males have worst prognostic factors compared with females. However, in pSpA, females report poorer functionality despite being diagnosed earlier than male patients. This difference in phenotypes may be relevant when therapeutic decision-making.

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**AB0853** **THE ASSOCIATION OF VITAMIN D RECEPTOR LEVELS WITH DISEASE ACTIVITY PARAMETERS IN PATIENTS WITH ANKYLOSING SPONDYLITIS**

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**Background:** Ankylosing Spondylitis (AS) is a chronic, systemic, inflammatory disease that involves sacroiliac, axial and peripheral joints with an unknown etiology. The role of vitamin D receptor (VDR) in the regulation of multiple pathophysiological processes, like inflammation, infection and malignancies and systemic disease is not fully understood.

**Objectives:** The aim of this study, was to investigate the relationship between serum VDR levels and disease activity parameters in patients with AS.

**Methods:** Sixty-two patients with AS and 32 healthy volunteers were included into the study. Demographic features like age, duration of illness, medication, history of uveitis and peripheral involvement of the patients were recorded. Erythrocyte sedimentation rate (ESR), serum C-reactive protein (CRP) levels were recorded. The Bath AS Disease Activity Index (BASDAI) scores were calculated to determine disease activity. Serum Vitamin D receptor (VDR) level was measured by ELISA.

**Results:** There was no difference in Serum VDR levels between the patient and the control group (p=0.658). In patients with active AS (BASDAI score ≥4) serum VDR level was significantly high (p=0,000). Also serum VDR levels were statistically significantly high in patients with peripheral joint involvement and enthesitis (p=0,000, non-steroidal anti inflammatory drugs (NSAID) compared to patients treated with biological agents (p=0.00). Serum VDR levels were also significantly correlated with BASDAI, CRP and ESR in the patient group (p=0.00, r=0,751, p=0.00, r=0751 p=0.00, r=0806 respectively).

**Conclusions:** In our study, serum VDR levels are related with disease activity, clinical parameters, peripheral joint involvement and enthesitis in patients with AS. Our results suggest that serum VDR level may be used to predict disease activity and prognosis. Further studies in large cohorts are needed to determine the role of Serum VDR level in the pathophysiology of AS.

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### AB0854 DYSFUNCTIONAL PAIN COMPONENT IN ANKYLOSING SPONDYLITIS PATIENTS

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**Background:** As a result of chronic inflammation, repetitive activation of primary afferent fibres changes the functional state and activity of Central nervous pathways. On this patients when describing their complaints use neuropathic pain descriptors include numbness, burning, tingling, increased pain response to a stimulus nabulivou etc.

**Objectives:** The study of chronic pain syndrome in patients with ankylosing spondylitis (AS) to identify dysfunctional component of pain (DCP).

**Methods:** Was studied 150 patients as 127 men and 23 women. The average age of 35, and 52±10,55, mean disease duration of 7.19±0.631. All the patients were performed clinical and rheumatological examination (indices BASDAI, BASFI), the assessment of pain intensity on visual analogue scale (VAS), to identify DCP were investigated neurological status with the use of questionnaires neuropathic pain DN4 and PainDETECT, and identifying the emotional-affective disorders (HADS questionnaire).

**Results:** 22 patients (14.7%) on the DN4 questionnaire revealed 4 or more points, but lesions of the somatosensory nervous system in these patients was not detected, hence 14,7% of patients were identified DCP. When comparing patients with the presence of TCS group I (22 people) and no DCP group II (128) it has been found that statistically significantly in patients in group I had higher pain intensity on VAS (6,09±1,85 vs 4,55±2,06, p=0.001, respectively); active disease BASDAI index (of 7.05±vs 1,58 4,87±2,16, p=0.001, respectively); the expression of functional impairment index BASFI (6,46±2,24 vs 4,05±2,81, p=0.001); the indicators of the questionnaire HADS in group I, consistent with the presence of clinically significant anxiety and lack of it in group II (10,09±2,86 vs 6,17±3,35, p=0.0001). However, duration of disease distinguish authentic in the groups was not (9,41±6,89 6,81 vs ±6,13 p=0,07). Correlation analysis revealed a significant relationship between DCP and the intensity of the pain in VAS back, as well as with the severity of anxiety, disease activity, functional disorders (p=0.05)

**Conclusions:** The study identified 22 patients, the presence of neuropathic pain descriptors in combination with anxiety disorders, resulting in the conclusion that, along with nociceptive component of pain in 14.7% of cases detected by the DCT. So the pain of some AS patients should be considered as a multicomponent syndrome, providing a comprehensive approach with the use of antidepressants (TCA and SSRI's).

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### AB0855 IDENTIFYING PATIENTS WITH AXIAL SPONDYLOARTHRITIS BY DATA MINING MRI RADIOLOGY REPORTS

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**Background:** Axial Spondyloarthritis (axSpA) encompasses ankylosing spondylitis (AS) and non radiographic axSpA (nr-axSpA) as part of the ASAS classification criteria<sup>1, 2</sup>. The role of MRI is now central in identifying patients early in the disease course<sup>3</sup>, but our use of this needs to be standardised to ensure appropriate requesting and correct interpretation of MRI axSpA features.

**Objectives:** (1) To identify the MRI protocols used to investigate patients with back pain

(2) To describe the prevalence of axSpA associated spinal lesions in patients with known axSpA

(3) To describe the prevalence of axSpA associated spinal lesions in patients with back pain and their relevance in subsequently diagnosed axSpA

**Methods:** MRI reports between 4th January 2015 and 25th February 2017 containing the key words 'ankylosing spondylitis' (AS), 'bone marrow oedema' (BMO), 'spondyloarthritis' and 'sacroiliitis' were identified using a computerised word finding programme, in a tertiary referral hospital for Rheumatology.

**Results:** 194 patients had MRI features of axSpA. 60.8% were female; mean age 39.3 years (SD 13.3). 96.4% (n=187) contained the term 'sacroiliitis', with 'AS', 'BMO' and 'spondyloarthritis' in 2.6%, 0.5% and 0.5% respectively. 63.4% were referred by a rheumatologist, and 19.1% from primary care. Musculoskeletal radiologists reported 16.0%, general radiologists 37.1%, and external radiology services 46.4%. The most common MRI protocol was the inflammatory spinal protocol (ISP-MRI, 57.2%), with sacroiliac (SIJ) MRI in 17%. 87.4% ISP-MRI and 48.5% MRI SIJ were requested by Rheumatology. GPs requested more ISP-MRI than other sequences (29.7% of their total MRIs). 144 cases had a diagnosis stated on the MRI request; 100 (69.4%) had an existing diagnosis of axSpA, and 20 (13.9%) of a peripheral arthritis. In patients with known AxSpA, the most frequent findings were BMO (70.3%), and erosions (67%). Ankylosis was only seen in 4 patients. Features of axSpA were identified in 26 MRIs requested for mechanical back pain, and 11 for unrelated medical reasons. 33 cases of BMO and 29 of SIJ erosions were identified in patients who did not have a pre existing diagnosis of AxSpA, and one showed ankylosis. 16 patients went on to have a diagnosis of axSpA.

**Abstract AB0855 – Table 1.** Radiological features seen on MRI imaging, and by diagnosis

MRI finding	Frequency n (%)	Pre existing axSpA diagnosis, n (%)	Without pre existing axSpA diagnosis, Total n=44		
			peripheral arthritis, n (%)	back pain as yet undiagnosed, n (%)	alternative diagnosis, n (%)
<b>Total n</b>	194	100	20	13	11
<b>Oedema</b>	150 (77.3)	78 (70.3)	15 (13.5)	8 (7.2)	10 (9.0)
<b>Irregularity or erosions</b>	111 (57.2)	59 (67.0)	16 (18.2)	6 (6.8)	7 (8.0)
<b>Sub-articular sclerosis</b>	81 (41.8)	39 (63.9)	13 (21.3)	4 (6.6)	5 (8.2)
<b>Fatty infiltration</b>	29 (14.9)	18 (75.0)	5 (20.8)	0	1 (4.2)
<b>Corner inflammatory spinal lesions</b>	30 (15.5)	18 (69.2)	4 (15.4)	2 (7.7)	2 (7.7)
<b>Ankylosis</b>	5 (2.6)	4 (80.0)	0	1 (20.0)	0
<b>Fracture</b>	4 (2.1)	4 (100)	0	0	0
<b>Post MRI diagnosis:</b>		<b>axSpA, n (%)</b>	16 (36.4)		
		<b>Mechanical, n (%)</b>	8 (18.2)		
		<b>Seronegative arthritis, n (%)</b>	8 (18.2)		
		<b>Isolated sacroiliitis (without full criteria for axSpA), n (%)</b>	7 (15.9)		

**Conclusions:** Through data mining of MRI reports, we have found that appropriate MRI sequences are being requested when features of AxSpA are suspected. The rate of chronic features of AxSpA such as ankylosis was low, suggesting this cohort may have short disease durations. Multiple features of AxSpA were identified in patients without an existing diagnosis prior to imaging. 16 new cases of AxSpA were identified.

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**AB0856 THE IMPACT OF SYSTEMIC INFLAMMATION AND RADIOLOGICAL CHANGES ON MOBILITY IN ANCHYLOSING SPONDYLITIS**

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**Objectives:** The purpose of the study was to investigate the relationship between disease activity, structural lesions and physical function by testing the hypothesis that the level of structural lesions contributes independently to physical impairment.

**Methods:** For this analysis, the database of Rheumatology Department was used and included 78 consecutive SA patients who have been observed for many years, implying that they have used NSAID's and DMARD for progression disease, no one has used TNF blocking agents.

**Results:** BASFI and DFI correlated significantly ( $r = 0.88$ ). The correlation coefficient for mSASSS and BASFI was 0.508 and for mSASSS and DFI equal to 0.464, suggesting a moderate correlation relationship. The correlation coefficient for the relationship between BASDAI and BASFI was equal to 0.79 and for BASDAI and DFI equal to 0.69 suggesting a moderate to significant correlation. The correlation between mSASSS and BASFI or DFI was dependent on the BASDAI level.

To further investigate the relationship between mSASSS and BASFI/DFI, concurrently adjusting for BASDAI and other covariates, a multivariate analysis was performed using GEE with BASFI or DFI as dependent variables, and mSASSS and BASDAI as covariates, concurrently adjusting for age, sex, duration of illness, HLA-B27 status and hip involvement.

Both BASDAI and mSASSS contributed independently to the BASFI and DFI explanations with significant parameter estimates. Regression coefficients describe the independent relationship between the explanatory variables and the dependent variable: in the environment, compared to a patient with mSASSS 40, a patient with the mSASSS score 50 has a BASFI of 0.57 times greater, independent of BASDAI.

All mSASSS subscripts contributed independently to the explanation of BASFI variations ( $p < 0.001$ ). Compared to the mSASSS model, which had the best result, the model with the total score of the syndesmofite, the number of the affected vertebral units, the number of vertebral vertebral units, and the model with the non-syndesmofite summary score, it was deduced that the syndesmofites are in much but not exclusively responsible for explaining variations in BASFI. A model with the syndesmofites summary score ( $p < 0.001$ ) and the non-syndesmofite ( $p = 0.002$ ) shows that both components contribute significantly to the explanation of BASFI variations. Results with DFI were similar.

Using mSASSS, the syndesmofite subservices, the affected vertebral units or vertebral vertebral units, we showed that lumbar and cervical spine involvement contributed independently and almost similarly to explaining variations in BASFI and DFI.

**Conclusions:** The study conducted by us demonstrates that the patient's physical function is not only dependent on signs and symptoms reported by the patient (activity of the disease), but also on the degree of structural lesions. Optimal AS treatment should not only include strategies aimed at removing pain, redness and fatigue, but also strategies aimed at preventing the formation and growth of syndesmofite.

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**AB0857 THE BURDEN OF DISEASE IN PATIENTS WITH NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS IS NOT INFERIOR TO THAT OF ANKYLOSING SPONDYLITIS. THE PROOF STUDY**

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**Background:** According to the 2009 ASAS classification criteria, a patient with chronic low back pain (CLBP) may be classified as axial spondyloarthritis (ax-SpA), with or without radiographic evidence of sacroiliitis, if at least one other SpA feature is present in the first case and positive HLA-B27 and at least two SpA features in the second one. There is concern about whether the classification "axial non-radiographic spondyloarthritis" (ax-SpA-nr) includes patients with a mild disease that do not require treatment or special care by rheumatology.

**Objectives:** To compare disease burden between patients fulfilling criteria for AS and ax-SpA-nr.

**Methods:** Sub-analysis of Spanish patients from the PROOF study, an international prospective observational longitudinal study conducted in rheumatology clinics. All patients who attended rheumatology clinics due to CLBP ( $\geq 3$  months, start  $< 45$  years of age) from <sup>Jan 2015</sup> to <sup>Feb 2017</sup> not previously diagnosed were consecutively included. The ASAS criteria were applied to all, with centralised image reading. Patients with AS and ax-SpA-nr were compared.

**Results:** 192 patients with CLBP were included, of whom 151 (79%) met criteria of SpA-axe, 56 (43%) of AS and 74 (57%) of ax-SpA-nr (21 patients had X-ray missing or no central reading had been done so far). The table shows the description of patients with AS and ax-SpA-nr and their comparison.

**Abstract AB0857 – Table 1**

Characteristic	AS (n=56)	ax-SpA-nr (n=74)	p
Age, m (SD)	33.8 (8.0)	36.2 (8.6)	0.117
Men, n (%)	41 (73.2)	39 (52.7)	0.019
HLA-B27 positive, n (%)	37 (66.1)	44 (61.1)	0.585
BASDAI, m (SD)	3.9 (2.4)	4.3 (2.3)	0.397
ASDAS-CRP, m (SD)	2.8 (1.2)	2.6 (1.1)	0.224
C-reactive Protein (mg/L), m (SD)	13.9 (15.0)	10.3 (19.9)	0.264
Erythrocyte sedimentation rate (mm/h), m (SD)	18.0 (19.1)	13.6 (17.5)	0.208
BASFI, m (SD)	3.0 (2.5)	3.1 (2.4)	0.828
SF-12 (physical component), m (SD)	44.1 (10.7)	42.2 (9.2)	0.283
SF-12 (mental component), m (SD)	46.9 (10.0)	43.1 (10.5)	0.040
Items from WPAI-SHP			
Active (employed), n (%)	39 (69.6)	54 (74.0)	0.693
Presentism, m (SD)*	26.2 (25.6)	33.9 (29.8)	0.206
Absenteeism, m (SD)*	2.4 (6.9)	11.2 (28.2)	0.041
Impact of work productivity, m (SD)*	27.0 (27.5)	34.0 (29.6)	0.280
Total impact on work activity, m (SD)*	34.2 (29.8)	41.0 (30.2)	0.209
Smokers, n (%)	24 (43.6)	19 (26.0)	0.040
Time in months from pain onset until 1 <sup>st</sup> study visit, m (SD)	37.5 (42.9)	43.3 (56.1)	0.509
Treatments used in the study visit, n (%)			
Non-steroidal anti-inflammatory drugs	24 (42.9)	24 (32.4)	0.223
Methotrexate	1 (1.8)	1 (1.4)	1.000
Sulfasalazine	1 (1.8)	3 (4.1)	0.634
Glucocorticoids	8 (14.3)	8 (10.8)	0.550
Analgesics	7 (12.5)	13 (17.6)	0.428
TNF inhibitors	0	1 (1.4)	-

\*Only among actively employed.

Abbreviations: m, mean; SD, standard deviation; BASDAI, Bath Ankylosing Spondylitis Disease Activity Score; ASDAS-CRP, Ankylosing Spondylitis Disease Activity Score calculated with C-reactive protein; BASFI, Bath Ankylosing Spondylitis Functional Index; SF-12, Short Form questionnaire, 12 items version; WPAI-SHP, Work Productivity and Activity Impairment Questionnaire related to disease; TNF, tumour necrosis factor.

**Conclusions:** Patients referred by CLBP to rheumatology clinics meeting ASAS criteria for AS or ax-SpA-nr differ little in terms of impact and disease activity; therefore, non-radiographic forms of ax-SpA require as much attention as classic AS.

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**AB0858 IMPACT OF APPLICATION OF ASAS CRITERIA FOR AXIAL SPONDYLOARTHRITIS ON THE DIAGNOSTIC DELAY IN EGYPTIAN PATIENTS**

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**Background:** Diagnostic delay is a major challenge in axial spondyloarthritis (SpA). The 2009 Assessment of SpondyloArthritis international Society



classification (ASAS) criteria for axial SpA formally recognised the utility of MRI in diagnosis.<sup>1</sup> There are conflicting reports whether there had been any recent improvement in the period of diagnostic delay after application of ASAS criteria.<sup>2</sup>

**Objectives:** To evaluate the period from symptoms onset to diagnosis in Egyptian patients with axial SpA before and after application of ASAS criteria for axial SpA and to examine possible reasons for delayed diagnosis.

**Methods:** The study included all axial SpA patients attending a university tertiary referral centre for regular follow up in the period between May 2016 to November 2017. The patients were divided into 2 groups; group 1 included patients with a diagnosis of axial SpA before the beginning of 2010 (when ASAS criteria became widely available and in use) and group 2 included patients with a diagnosis of axial SpA after the beginning of 2010. A face-to-face interview was applied for both groups to take medical history, and a questionnaire that contains some clinical aspects of disease was used. Diagnosis delay was described as the gap between first SpA symptom and correct diagnosis of axial SpA. Clinical and functional assessment of axial SpA measured by Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI), Bath Ankylosing Spondylitis Metrology Index (BASMI). The direct medical cost during years of delay (including costs of medical consultations, medications, investigations, physiotherapy and surgical treatment) had been estimated.

**Results:** As presented in table 1; more axial SpA cases were in group 2 (diagnosed after the beginning of 2010) with significantly narrower gap of delay, younger age at diagnosis, lesser number of doctor visits, lesser number of unnecessary spinal surgeries, lower total direct estimated costs and better BASDI, BASFI and BASMI.

**Abstract AB0858 – Table 1.** comparison between axial SpA patients diagnosed before and after 2010

Variable	Group 1 (n=56)(44.4%)	Group 2 (n=70) (55.6%)	p-value
<b>Delay in years:</b> <i>Mean±SD</i>	11.3±3.9	4.6±2.8	<b>0.02**</b>
<b>Sex:</b>			<b>0.3*</b>
Male:	49 (83.3)	56 (7.9)	
Female:	7 (16.7)	14 (92.1)	
<b>Age at diagnosis (years):</b> <i>Mean±SD</i>	34.9±6.4	25.8±4.5	<b>0.03**</b>
<b>Cost of delay period by \$:</b> <i>Mean±SD</i>	9879.3 ±3827.2	2373.9±881.8	<b>&lt;0.001**</b>
<b>Doctor Visits during years of delay:</b> <i>Mean±SD</i>	14.3±6	5.6±3.4	<b>&lt;0.001**</b>
<b>Spinal Surgery:</b>	34 (65.4%)	18 (34.6%)	<b>&lt;0.001*</b>
<b>Loss of work at time of diagnosis:</b>	36	7	<b>&lt;0.001*</b>
<b>BASDAI:</b> <i>Mean±SD</i>	9.1±1.4	4.3±2.2	<b>&lt;0.001**</b>
<b>BASFI:</b> <i>Mean±SD</i>	9.1±1.4	3.9±2.2	<b>&lt;0.001**</b>
<b>BASMI:</b> <i>Mean±SD</i>	8.9±1.2	2.2±2	<b>&lt;0.001**</b>

\*: Chi-square test. SD: Standard Deviation. \*\*: Independent sample t test. Significance p value<0.05.

**Conclusions:** Application of ASAS criteria for axial SpA has resulted in a significant decrease in the diagnostic gap which is reflected in a significant decrease in age at diagnosis and in the costs of unnecessary medications. On the other side, the gap is still large and more sensitive criteria are still needed.

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AB0859

#### SIMILARITIES AND DIFFERENCES BETWEEN NON-RADIOGRAPHIC AND RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS IN PROOF CHINA COHORT

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**Background:** National observational studies, mostly from Europe, have reported some differences between radiographic axial spondyloarthritis (axSpA) and non-radiographic axSpA (nr-axSpA).

**Objectives:** To compare demographic and clinical characteristics of patients (pts) with nr-axSpA and radiographic axSpA (ankylosing spondylitis, AS) in a Chinese subpopulation in the PROOF study.

**Methods:** PROOF is a prospective observational study evaluating clinical and radiographic outcomes in axSpA pts in rheumatology clinical practice in 29 countries over 5 years. Pts diagnosed ≤1 year before study enrollment with axSpA fulfilling ASAS classification criteria were eligible. Investigator confidence with the axSpA diagnosis was ascertained on a numeric rating scale (0–10) at enrollment and end of follow-up. Baseline characteristics are reported, including demographics and clinical characteristics (table 1). Classification as nr-axSpA or AS was according to the radiologic criterion of the modified New York criteria. If there was a disagreement in classification (nr-axSpA or AS) between a local and central reader, the radiograph was evaluated by a second central reader, who was blinded to previous assessments; the final classification was based on the decision of 2 of 3 readers.

**Results:** 464 (21.8%) pts in PROOF were enrolled in China; 307 (66.2%) were classified as AS and 157 (33.8%) as nr-axSpA according to the investigators. Confidence with the axSpA diagnosis was 9.0±1.5. The final classification based on central assessment of sacroiliac radiographs was confirmed in 372 (80%) pts included in further analyses; 301 pts (80.9%) were classified as AS and 71 (19.1%) as nr-axSpA. AS pts had longer time since diagnosis, more frequent and higher CRP elevations, and were more often male and treated with TNF inhibitors (table 1). HLA-B27 positivity and prevalence of other SpA features were comparable between the 2 groups. Most disease burden assessments were comparable, but ASDAS-CRP, BASFI, and SF-12v2 physical component score were higher in AS pts (table 1).

**Abstract AB0859 – Table 1.** Baseline Demographics and Clinical Characteristic of the Chinese PROOF Subpopulation

Characteristic	nr-axSpA (n=71)	AS (n=301)	P Value*
Age, y, mean ± SD	30.1±8.9	29.4±8.7	0.517
Time since back pain onset, mo, mean ± SD	28.9±47.1	36.8±50	0.216
Time since diagnosis, mo, mean ± SD	1.7±2.1	2.8±3.5	<b>0.005*</b>
Male sex, n (%)	40 (56.3)	239 (79.4)	<b>&lt;0.001**</b>
Number of positive SpA parameters, mean ± SD	3.5±1.1	3.6±1.3	0.508
SpA parameters, n (%)			
HLA-B27+	54 (77.1)	237 (81.2)	0.503
Inflammatory back pain	68 (95.8)	291 (96.7)	0.720
Peripheral arthritis	21 (29.6)	97 (32.2)	0.777
Enthesitis (heel)	22 (31.0)	62 (20.6)	0.082
Dactylitis	3 (4.2)	10 (3.3)	0.720
Uveitis	4 (5.6)	18 (6.0)	1.000
Psoriasis	0	2 (0.7)	1.000
IBD	0	0	—
Good response to NSAIDs	44 (62.0)	175 (58.1)	0.556
Family history of SpA	13 (18.3)	45 (15.0)	0.471
Elevated CRP, n (%)	22 (31.0)	157 (52.2)	<b>0.002*</b>
Disease activity			
CRP, mg/L	10.2±20.4	15.5±21.4	<b>0.033*</b>
ASDAS-CRP	2.2±1.0	2.6±1.0	<b>0.013*</b>
PRO measures, mean ± SD			
BASDAI, NRS (0–10)	3.3±1.9	4.3±1.9	0.946
Patient global, NRS (0–10)	3.7±2.4	3.9±2.3	0.828
BASFI, NRS (0–10)	1.3±1.4	1.8±1.8	<b>0.002*</b>
SF-12v2 PCS	45.2±6.5	42.1±8.2	<b>0.001*</b>
SF-12v2 MCS	44.3±9.7	45.4±9.4	0.358
WPAI-SHP TAI	31.7±20.6	34.7±23.8	0.289
Current treatment, n (%)			
NSAID	55 (77.5)	213 (70.8)	0.304
Methotrexate	3 (4.2)	19 (6.3)	0.779
Sulfasalazine	27 (38.0)	88 (28.2)	0.156
Steroids	1 (1.4)	4 (1.3)	1.000
Analgesics	1 (1.4)	4 (1.3)	1.000
TNF-α inhibitors	8 (11.3)	79 (26.3)	<b>0.008**</b>

AS=ankylosing spondylitis; ASDAS-CRP=AS Disease Activity Score containing C-reactive protein; BASDAI=Bath Ankylosing Spondylitis Disease Activity Index; BASFI=Bath Ankylosing Spondylitis Functional Index; CRP=C reactive protein; HLA-B27=human leukocyte antigen B27; MCS=Mental Component Summary; nr-axSpA=non radiographic axial spondyloarthritis; NSAID=non steroidal anti-inflammatory drug; PCS=Physical Component Summary; SF-12v2=Short Form 12-item Health Survey version 2; TNF=tumour necrosis factor; WPAI-SHP TAI=Work Productivity and Activity Impairment Questionnaire–Specific Health

Problem Total Activity Impairment. <sup>a</sup>P values from 2-sided t test for scale variables and Fisher exact test for categorical variables; statistical comparison between nr-axSpA and AS; \*p<0.05, \*\*p<0.001.

**Conclusions:** Clinical features and disease burden were generally similar between nr-axSpA and AS pts in the Chinese PROOF subpopulation. AS pts were more frequently men, had higher inflammatory burden (CRP and ASDAS-CRP), more functional impairment, and were more frequently treated with TNF inhibitors.

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### AB0860 ACUTE PHASE REACTANT CHANGE IN ANKYLOSING SPONDYLITIS PATIENTS

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**Background:** The aim of this study is to investigate the levels of acute phase reactants (APRs) in patients with ankylosing spondylitis (AS) at the time of diagnosis and during follow-up. We also evaluated the associations between APR levels and disease activity.

**Methods:** The study included 948 patients with AS who were followed-up at Dokuz Eylul University School of Medicine Rheumatology outpatient clinic. The patients' erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels across all visits were retrospectively reviewed through the Turkbio registry and the hospital's database. Disease activity and follow-up parameters as BASDAI, ASDAS, BASFI and BASMI were taken from Turkbio visit charts. The correlation between APR and follow-up parameters were evaluated with Spearman correlation coefficient analysis.

**Results:** There were 948 AS patients (69% male, mean age 46.6±12.1 years) who fulfilled the 1984 modified New York criteria. At first visit, high levels of CRP and ESR were observed in 626 (68.5%) and 578 (64.6%) patients respectively. During follow-up 84.6% of patients had high CRP and 69.5% patients had high ESR at any visit (figure 1). However in 10% of AS patients APRs did not increase at any visits.

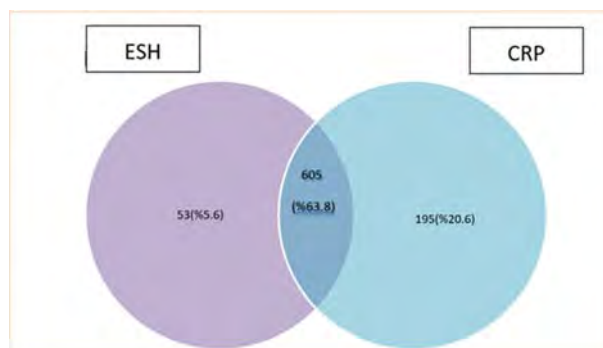
There was good correlation between ESR and CRP ( $r=0.666$ ,  $p<0.001$ ). A better correlation was observed at first visit between CRP and BASDAI ( $r=0.81$ ,  $p=0.23$ ) or ASDAS ( $r=0.468$ ,  $p<0.001$ ) compared to ESR and BASDAI ( $r=0.111$ ,  $p=0.02$ ) or ASDAS ( $r=0.334$ ,  $p<0.001$ ) (table 2). Compared to BASDAI, ASDAS with either ESR ( $p<0.001$ ) or CRP (*very high disease activity*- $p<0.001$ , *inactive disease*- $p=0.001$ ) had better performance in evaluating the activity of the patient in inactive and very high levels of severe disease (table 2).

**Abstract AB0860 – Table 1.** Demographic and clinical features

Age; Mean±SD (yrs)	46,6±12,1
Age at onset of illness; Mean±SD (yrs)	27,3±10,5
Age of diagnosis; Mean±SD (yrs)	34,5±12,0
Females/Males sex, n (%)	293 (%30,9)/655 (%69,1)
HLA-B27 Positive/Negative/Unknown	237 (%25)/100 (%10,5)/611 (%64,5)

**Abstract AB0860 – Table 2.** Correlation between first visit ESR/CRP and disease activity parameters

	ESR		CRP	
	r	p	r	p
BASDAI	0111	0,02	0,81	0023
BASMI	0123	0003	0205	0,00
BASFI	0219	0,00	0224	0,00
ASDAS	0334	0,00	0468	0,00



**Abstract AB0860 – Figure 1**

**Abstract AB0860 – Figure 1.** Ven diagram of patients that elevation only ESR/CRP or with both elevation together at any visit

**Conclusions:** In over 80% patients with AS had elevated levels of CRP, the most frequently used laboratory parameter, during follow-up. CRP is well correlated with ESR, and disease activity parameters as BASDAI, ASDAS, BASFI and BASMI. Compared to BASDAI; ASDAS had better agreement between activity and APRs. Interestingly, in 10% of AS patients APRs did not increase in follow-up.

**Disclosure of Interest:** None declared

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### AB0861 HEALTH STATUS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS (AXSPA) AS DETERMINED BY THE ASSESSMENT OF SPONDYLOARTHRITIS INTERNATIONAL SOCIETY HEALTH INDEX (ASAS-HI)

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**Background:** The ASAS-HI is a new instrument based in the International Classification of Functioning, Disability and Health to assess the impact of axSpA; ASAS-HI has been validated in Mexican patients.

**Objectives:** To investigate the status of health in Mexican patients with axSpA using the ASAS-HI

**Methods:** This is multicenter, cross-sectional study of 377/423 patients with axSpA (ASAS criteria) referred by 64 rheumatologists with private or institutional practice across the country in a period of six months. Sociodemographic and clinical data were collected at each site and analysed centrally.

**Results:** The ASAS imaging arm were fulfilled 87.5% and the clinical by 61.8%; HLA-B27 was positive in 80.1%; 71.6% were males; 51.9% received bDMARDs. Mean ages at onset and diagnoses were 25.8 (9.9) and 32.8 (11.7) years; median age was 41.6 (13.7) years. The correlation between ASAS-HI and BASDAI, BASFI, and EQ-5D was significant. ASAS-HI mean score was 6.4 (4.2); the cut off was six; values below six meant good health, which corresponded to 203 (53.84%) patients. Univariate analysis disclosed significant differences between groups in variables that were significant in the regression models (see below) and in health care coverage, enthesitis, joint counting, glucocorticoids, HLA-B27, sacroiliitis, BASMI, and ASDAS. In the multivariate analysis, two models were associated ASAS-HI: 1) sex, education, comorbidities, joint surgery, and physician global assessment; 2) BASDAI, BASFI, and EQ-5D

**Conclusions:** ASAS-HI cut off of six identified good health in 46.15% of patients with axSpA. ASAS-HI correlated with other measures of disease activity, functioning, and quality of life. In multivariate analysis, ASAS-HI associated with those measures as we all as with demographic and clinical variables.

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**AB0862 ANTERIOR THORACIC FATTY CORNER LESIONS ARE USEFUL IN AXIAL SPONDYLOARTHRITIS (SPA) DIAGNOSIS—DATA FROM A MULTICENTER BACK PAIN-MRI COHORT IN HONG KONG**

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**Background:** A fatty corner lesion (FCL), as defined by fat infiltration at the vertebral corner in T1 Magnetic Resonance Imaging (MRI) sequence, has been reported to be useful in Spondyloarthritis (SpA) diagnosis.

**Objectives:** Our objective is to systematically evaluate the diagnostic utility of FCLs in a large, multicenter back pain-MRI cohort in Hong Kong.

**Methods:** Three hundred and one patients with back pain were recruited from 3 rheumatology centres. Clinical, biochemical and radiological parameters were collected and all patients underwent a whole spine and sacroiliac (SI) joints MRI. FCLs from C4 to L5 levels were scored. Results were compared to expert-diagnosed axial SpA to determine the usefulness of FCLs in disease diagnosis.

**Results:** Anterior FCLs of whole or thoracic spine were found to be useful in axial SpA diagnosis. (AUC 0.622; p=0.003, AUC 0.640; p=0.001 respectively) Applying FCLs to the Modified New York (MNY) criteria and Assessment of SpondyloArthritis international Society (ASAS) axial SpA criteria, a minimum of 5 FCLs at whole spine level had a sensitivity of 66.4% and 91.6%, specificity of 98.4% and 91.9% respectively. Applying a minimum of 3 FCLs at thoracic spine level to the MNY criteria and ASAS axial SpA criteria yielded a sensitivity of 68.5% and 92.0%, specificity of 95.2% and 93.5% respectively. Three FCLs improves both classification criteria.

**Conclusions:** FCLs are useful in axial SpA diagnosis. A minimum of 3FCLs at the thoracic level is useful for the disease diagnosis.

**Disclosure of Interest:** None declared

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**AB0863 ANALYSIS OF THE FREQUENCY OF UVEITIS IN SPONDYLOARTHRITIS PATIENTS AND ASSOCIATIONS WITH CLINICAL PARAMETERS OF THE DISEASE**

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**Background:** Acute anterior uveitis is the most common extra-articular manifestation of spondyloarthritis (SpA). The ocular inflammation in SpA is restricted to the uvea, usually unilateral and in some cases may precede the clinical characteristics of SpA.

**Objectives:** The aim of this study is to analyse if the presence of uveitis is associated with a different clinical manifestation, laboratorial, radiological and therapeutic among spondyloarthritis patients.

**Methods:** This was an observational retrospective study with 153 patients with spondyloarthritis attended in the period from 1997 to 2017 in Florianópolis, Brazil. It was analysed demographical, laboratorial, clinical and therapeutic data in spondyloarthritis patients with or without uveitis.

**Results:** 26,8% of the patients with spondyloarthritis presented uveitis. The presence of complications was rare, with cataract occurring in only four patients and glaucoma in two of them. A higher frequency of acute anterior uveitis in males (p=0.06) was observed in patients with a family history (p=0.19) and HLA-B27 positive (p=0.14). Patients with spondyloarthritis and uveitis more frequently used anti-TNF (p=0.04) and presented sacroiliitis on imaging tests (p=0.02). There was no association between uveitis and cardiovascular (p=0.44), cutaneous (p=0.13) or gastrointestinal involvement (p=0.10).

**Conclusions:** Uveitis in patients with spondyloarthritis is common, predominantly in males and more frequently, in HLA-B27 positive patients. Ocular manifestation in spondyloarthritis has a low degree of complication when compared to uveitis from other etiologies. The use of immunobiological agents such as anti-TNF is common in patients with uveitis.

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**AB0864 THE IMPACT OF DISEASE ACTIVITY, STRUCTURAL DAMAGE, AND FATIGUE ON PHYSICAL FUNCTION IN PATIENTS WITH ANKYLOSING SPONDYLITIS: DIFFERENCES IN EARLY AND LATE DISEASE**

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**Background:** In patients with ankylosing spondylitis (AS), the physical function impairment caused by the disease is among the biggest concerns for both patients and clinicians. Previous studies have shown that disease activity and structural damage are the main underlying causes for physical function impairment. There is accumulating evidence that suggests fatigue as well contributes to functional limitations. However, the differential impact of these factors on physical function at early and late stage of disease remains unclear.

**Objectives:** Study the strength of association in AS patients with varying disease duration, between physical function and the three potential determinants of interest: disease activity, structural damage, and fatigue.

**Methods:** AS patients satisfying the modified New York criteria were followed from 2003 to 2017. Patients completed a standardised annual protocol including demographic and clinical factors, with radiographic data collected biennially. Baseline physical function (BASFI) was analysed for association with factors including disease activity (BASDAI), radiographic changes (mSASSS), and fatigue (FSS). The same analysis was conducted again with patients sub grouped with respect to disease duration (<5 years, 5–9 years, 10–20 years, >20 years), and again with respect to change in BASFI between the first and last patient visit. Multivariable regression analysis was performed to identify independent predictors of physical function at baseline and the change with time.

**Results:** A total of 611 patients were followed and completed the standard protocol (mean age at initial visit 38.2 years; 74% male; 76.5% HLA-B27+). At baseline BASFI was independently associated (table 1) with BASDAI (p<0.0001), CRP (p<0.0001), mSASSS (p<0.0001), and FSS (p<0.0001). In the disease duration subgroup analysis, BASFI was independently associated with BASDAI (p<0.05) and mSASSS (p<0.05) in all disease durations, and with FSS in subgroups with disease duration of 5 years or greater (p<0.05). In the longitudinal analysis, change in BASFI was independently associated with changes in BASDAI (p<0.0001) and FSS (p<0.05), but not with change in mSASSS (p=0.283).

**Abstract AB0864 – Table 1**

	Univariable analysis		Multivariable analysis	
	$\beta$ (95% CI)	P	$\beta$ (95% CI)	P
Sex	0.001 (–0.063–0.066)	0.975	–0.01 (–0.07–0.05)	0.776
CRP	0.282 (0.200–0.364)	<0.0001	0.15 (0.09–0.21)	<0.0001
BASDAI	0.728 (0.672–0.783)	<0.0001	0.62 (0.51–0.73)	<0.0001
mSASSS	0.294 (0.204–0.378)	<0.0001	0.24 (0.18–0.31)	<0.0001
BASDAI	0.61 (0.54–0.67)	<0.0001	0.06 (–0.6–0.17)	0.313
Q1				



**Conclusions:** The study demonstrated that disease activity and structural changes consistently contributes to physical function impairment in both early and late stages of disease. Fatigue does not associate with physical function at early stages of the disease, but it increases in contribution to functional impairment as disease duration increases.

**Disclosure of Interest:** None declared

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#### AB0865 DO ASAS, ASDAS AND BASDAI THERAPY RESPONSE EVALUATION TRANSLATE THE SAME INFORMATION?

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**Background:** The ASAS-EULAR recommendations for the continuation of biological Disease-Modifying Anti-rheumatic Drugs (DMARD) suggest the evaluation of patients after at least 12 weeks of treatment by either the Ankylosing Spondylitis (AS) Disease Activity Score – C reactive protein (ASDAS-CRP) or by the Bath AS Disease Activity Index (BASDAI). For ASDAS-CRP, a Minimal Clinical Important Difference (MCID)  $\geq 1.1$  is necessary, while for the total BASDAI score a 50% reduction or a change of  $\geq 2.0$  points is considered clinically relevant. In clinical trials, the Assessment in Ankylosing Spondyloarthritis (ASAS) response criteria – ASAS 20, ASAS 40 and ASAS 70 – are still the most frequent primary outcome measures to evaluate improvement in treatment response. However, in clinical practice the BASDAI is still routinely used.

**Objectives:** The aim of this work was to assess the concordance/agreement between different therapeutic outcome measures, such as the ASAS response criteria,  $\Delta$ ASDAS-CRP and BASDAI 50.

**Methods:** Data from 54 patients who fulfilled the modified New York criteria for AS were collected at baseline, weeks 2 and 14 post-treatment with Adalimumab. Pearson's correlation (PCCs) and the Cohen's Kappa coefficients were calculated for the three scores.

**Results:** A strong correlation was found between the three scores throughout the visits:  $\rho = -0.676$  for ASDAS/ASAS,  $\rho = -0.807$  for ASAS/BASDAI, and  $\rho = 0.786$  for BASDAI/ASDAS (all PCCs with  $p < 0.001$ ). Additionally, when the categorization in different disease activity states and response levels was performed, PCCs revealed significant concordance/agreement between the three scores' cut-offs (see table 1).

The individuals categorised as responders, by either BASDAI50 or  $\Delta$ ASDAS  $\geq 1.1$ , have shown similar clinical characteristics (Erythrocyte Sedimentation Rate, CRP, AS Quality of Life Scale and Bath AS Functional Index).

Importantly, when more stringent measures of ASAS response criteria and ASDAS were used (i.e. ASAS 70 and ASDAS  $\geq 2.1$ ) the agreement with BASDAI values decreased.

**Abstract AB0865 – Table 1.** Summary information of the Agreement and Cohen's kappa.

Concordance/agreement	n	Agreement	Cohen's $\kappa$	p-value
$\Delta$ ASDAS $\geq 1.1$ and ASAS $\geq 0$	130	76.92%	0.496	<0.001†
$\Delta$ ASDAS $\geq 1.1$ and ASAS $\geq 40$	130	74.62%	0.492	<0.001†
$\Delta$ ASDAS $\geq 1.1$ and ASAS $\geq 70$	133	57.14%	0.259	<0.001†
$\Delta$ ASDAS $\geq 2.1$ and ASAS $\geq 0$	130	61.54%	0.310	<0.001†
$\Delta$ ASDAS $\geq 2.1$ and ASAS $\geq 40$	130	73.08%	0.462	<0.001†
$\Delta$ ASDAS $\geq 2.1$ and ASAS $\geq 70$	133	75.19%	0.365	<0.001†
BASDAI50 and ASAS $\geq 0$	150	82.67%	0.638	<0.001†
BASDAI50 and ASAS $\geq 40$	152	84.21%	0.687	<0.001†
BASDAI50 and ASAS $\geq 70$	156	61.54%	0.301	<0.001†
BASDAI50 and $\Delta$ ASDAS $\geq 1.1$	134	79.85%	0.571	<0.001†
BASDAI50 and $\Delta$ ASDAS $\geq 2.1$	134	64.93%	0.351	<0.001†

†p-value < 0.05, n: number of visits

**Conclusions:** Our results suggest that the ASAS response criteria,  $\Delta$ ASDAS-CRP and BASDAI 50 report the same clinical information. Hence, the clinician's decision should still be consistent independently of the score adopted. However, this study also highlights the importance of establishing a new and more stringent BASDAI cut-off, in alignment with ASDAS-CRP  $\geq 2.1$  and ASAS 70.

**Disclosure of Interest:** None declared

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#### AB0866 ADVANCED METROLOGY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: LUMBAR OR THORACIC +LUMBAR MEASUREMENTS FOR SPINAL MOBILITY ASSESSMENT?

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**Background:** Advanced technologies for measuring human mobility have recently emerged: motion capture, inertial measurement units (IMU) and wearable devices. Some of them are used for mobility assessment of rheumatic patients.<sup>1</sup> Certain devices analyse only lumbar mobility of the patients. Axial Spondyloarthritis (axSpA) reduces spinal mobility at all levels and not only at the lumbar level.

**Objectives:** To analyse what is the contribution of the thoracic spine to spinal mobility, and if this contribution should be taken into account in the metrological assessment of patients with axSpA.

**Methods:** 20 patients with axSpA and 20 age, BMI and sex-matched healthy subjects were recruited. An IMU sensor-based system (ViMove©) was used to measure spinal mobility. This system uses two IMU sensors and the angle between both is obtained in real time. Two tests were recorded: one with the recommended anatomical location (pelvis and L1) and another one aimed at combining lumbar +thoracic movement (pelvis and T3). Conventional metrology, radiographic structural damage (axSpA patients) and PROs were also collected.

**Results:** The table shows the results obtained for measuring only lumbar or lumbar +thoracic mobility, in both groups. The contribution of the thoracic spine is expressed in% of the total movement. Pearson correlation coefficients (only for patients) with conventional metrology (BASMI), PRO questionnaires (BASDAI, BASFI and ASQoL) and structural damage (mSASSS) scores are also presented.

**Abstract AB0866 – Table 1**

	Anterior Flexion	Extension	Lateral Left Flexion	Lateral Right Flexion	Rotation Left	Rotation Right
<i>AxSpA (n=20)</i>						
Lumbar	40.8 (17.2)	8.9 (7.4)	22.4 (9.3)	19.4 (8.8)	12.9 (4.9)	8.2 (4.9)
Lumbar +Thoracic	49.2 (19.9)	18.2 (12.9)	30.1 (12.6)	28.2 (11.7)	41.6 (11.5)	35.5 (12.4)
Contribution of T spine	17%	50%	26%	33%	68%	76%
<i>Control (n=20)</i>						
Lumbar	54.4 (8.6)	11.1 (5.7)	29.4 (6.1)	25.6 (5.2)	15.4 (5.2)	10.5 (2.6)
Lumbar +Thoracic	62.6 (11.9)	22.2 (9.6)	40.4 (4.6)	37.9 (4.4)	45.5 (7.9)	37.3 (8.2)
Contribution of T spine	13%	50%	27%	32%	66%	72%
<i>Correlations (Lumbar/Lumbar+Thoracic)</i>						
BASMI	-0.82***/ -0.76***	0.50†/ 0.71***	0.89***/ 0.94***	-0.87***/ -0.89***	0.46†/ 0.69***	-0.67**/ -0.60**
BASDAI	-0.14/- 0.21	0.44/ 0.58**	0.30/0.40	-0.35/- 0.45*	0.26/ 0.38	-0.49†/ -0.71***
BASFI	-0.46†/ -0.48*	0.4/0.64**	0.54†/ 0.71***	-0.59**/ -0.65**	0.39/ 0.47*	-0.67**/ -0.50*
ASQoL	-0.19/- 0.30	0.43/0.53*	0.39/0.50*	-0.36/-0.41	0.26/ 0.33	-0.44/- 0.58**
mSASSS	-0.74**/ -0.76**	0.49/0.59	0.74**/0.56	-0.69†/ -0.78**	0.07/ 0.64*	-0.28/- 0.47

\*\*\*p < 0.001; \*\*p < 0.01; \*p < 0.05.

**Conclusions:** Thoracic +Lumbar results reflect better the spinal mobility impairment of axSpA patients compared to lumbar spine assessments only. Compared to isolated lumbar spine assessment, the combined assessment showed better correlations with conventional metrology, disease activity, physical function, health-related quality of life and spinal structural damage. Despite this, the magnitude of the differences is not enough to reject the use of a system that only considers assessment of lumbar spinal mobility.

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**AB0867 AXIAL SPONDYLOARTHRITIS POSTURE ASSESSMENT USING INERTIAL SENSORS**

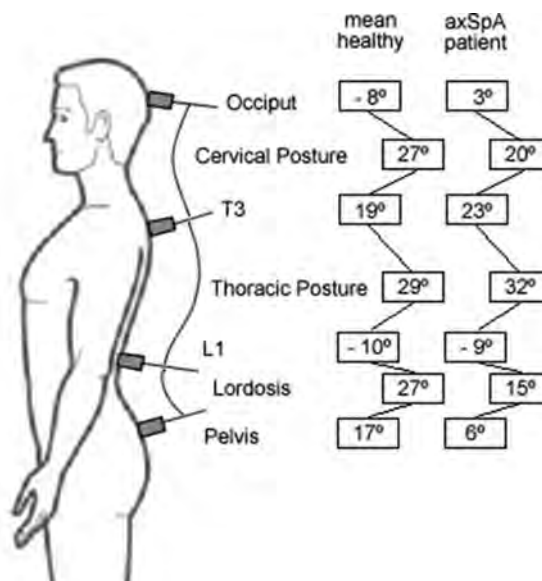
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**Background:** Axial Spondyloarthritis (axSpA) often causes spinal deformity in patients, most commonly a flexed kyphotic posture. In the early stages a flattening of the lumbar spine or reduced lordosis may become apparent. Kyphosis of the thoracic and cervical spine is also common in severe cases, resulting in an increased 'tragus to wall distance' as clinically assessed in the BASMI score. No other measurement related to posture is routinely recorded in clinical practice. Inertial Measurement Units (IMU) is a new technology that can measure angles of anatomical regions where the sensor is located.

**Objectives:** To compare the spinal curvature of axSpA and healthy individuals to analyse if there are any significant differences between them and to correlate these with conventional assessment variables.

**Methods:** 20 axSpa patients and 20 healthy age, BMI and sex matched controls, were recruited. An IMUs system (ViMove©) was used to obtain angles at key points along the spine. Sensors were located at Pelvis, L1, T3 and occiput (figure 1). Calibrated angles for all the participants were obtained with the subject in quiet standing position looking to a point in front of her/him. PRO questionnaires (only patients) and metrology for axSpA (both groups) were also assessed. ROM for cervical and lumbar spine was also measured using IMUs.

Posture. Lordosis angle shown a good correlation with mobility measured by Schöber and by IMU system, especially for flexion movements. Pelvis angle correlates better than L1 angle with all mobility variables. For cervical angles, occiput angle appears to be the best indicator for functional assessment. Thoracic angle is very similar between patients and healthy subjects. Figure represents the location of sensors with mean angles obtained by healthy group and the worst patient of axSpA group.



Abstract AB0867 – Figure 1

Abstract AB0867 – Table 1

	Pelvis	Lordosis	L1	Thor. Posture	T3	Cerv. Posture	Occiput
axSpA	13.9 (8.5)	23.4 (8.8)	-9.5 (4.0)	29.1 (5.1)	19.6 (3.8)	26.1 (3.2)	-6.5 (3.8)
Control	16.7 (7.8)	27.2 (8.0)	-10.5 (4.5)	29.8 (9.7)	19.4 (7.5)	27.3 (8.6)	-7.9 (8.2)
Age	-0.14	0.05	-0.24	0.33	0.19	0.44*	0.57***
Flex. Lat	0.09	-0.24	-0.29	0	-0.31	-0.22	-0.47**
Tragus	-0.37*	0.48**	0.26	0.15	0.47**	0.34	0.74***
Wall							
Schöber	0.50**	-0.62***	-0.28	0.1	-0.16	-0.42*	-0.52**
BASMI	-0.38*	0.51**	0.29	0.09	0.42*	0.25	0.60***
BASDAI	0.06	-0.13	-0.2	0.22	0.09	0.31	0.41*
Lumb.	0.52***	-0.56***	-0.1	-0.03	-0.11	-0.09	-0.18
Flexion							
Lumb.	0.30*	-0.39**	-0.2	-0.10	-0.28*	-0.21	-0.47***
Lateral							
Lumb.	0.23	-0.34*	-0.27	-0.12	-0.35**	-0.09	-0.41**
Rotation							
Cerv.	0.44***	-0.46***	-0.07	-0.22	-0.34*	-0.02	-0.32*
Frontal							
Cerv.	0.24	-0.24	-0.03	-0.08	-0.13	-0.16	-0.28*
Lateral							
Cerv.	0.30*	-0.30*	-0.02	-0.10	-0.15	-0.2	-0.33*
Rotation							

Results in degrees(standard deviation). Pearson correlations: \*p<0.05; \*\*p<0.01; \*\*\*p<0.001

**Results:** Greater values of posture angles were obtained in healthy controls. Despite this, differences where significant (p<0.05) only for Lordosis and Cervical

**Conclusions:** IMU based sensors are a useful new tool for the assessment of axSpA patients. This is the first formal evaluation of posture in axSpA and seems to be a promising tool in the functional evaluation of axSpA patients. More studies (reliability, feasibility, sensitivity to change, etc.) are needed for validating these measures.

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**Disclosure of Interest:** None declared

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**AB0868 LUMBAR MUSCLES STIFFNESS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS IS ALTERED IN COMPARISON WITH HEALTHY SUBJECTS**

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**Background:** Axial Spondyloarthritis (axSpA) patients have inflammation and/or structural damage in the lumbar spine that reduces their mobility and quality of life. The biomechanical features of axSpA have not been investigated in detail, but could prove to be a very important factor contributing to pain, stiffness and

Abstract AB0868 – Table 1

	Measures		p – values	Age	BASMI	Pearson correlations (axSpA/Control)				
	AxSpa	Controls				mSASSS	LumbarFlex	LumbarExt	Lateral	Rotation
Tone (Hz)	18.81 (4.43)	15.91 (2.40)	p<0.001	0.60**/0.69**	0.65**	0.82**	-0.39/-0.65**	0.12/0.24	0.02/-0.71***	0.11/-0.49*
Stiffness (N/m)	416.12 (141.36)	323.31 (77.88)	p<0.001	0.54*/0.63*	0.63**	0.77**	-0.32/-0.67**	0.1/0.19	-0.01/-0.70***	0.08/-0.48*
Decrement	1.45 (0.37)	1.48 (0.31)	N.S.	0.3/0.34	-0.11	-0.39	0.03/0.21	0.14/0.02	0.15/0.41	0.31/0.25
Relaxation (ms)	13.73 (3.55)	16.98 (3.35)	p<0.001	-0.43/-0.54*	-0.57**	-0.53	0.28/0.62**	-0.02/-0.08	-0.12/0.60**	-0.06/0.54*
Creep	0.87 (0.20)	1.05 (0.18)	p<0.001	-0.39/-0.53	-0.57**	-0.55	0.28/0.62**	0.03/-0.06	-0.15/0.63**	-0.03/0.56*

\*p<0.05, \*\*p<0.01, \*\*\*p<0.001

loss function. Myotonometry is being used to quantify stiffness muscles in a valid and reliable way.

**Objectives:** To measure and compare the stiffness in the erector spinae muscles of axSpA patients and healthy subjects to analyse if there are any significant differences between them.

**Methods:** 20 axSpA patients and 20 healthy subjects matched in age, BMI and sex, were recruited. The stiffness of the lumbar erector spinae (ES) muscles was assessed at L4–5 using myotonometry (MyotonPRO®) (figure 1). Measures were obtained twice in the left and right muscles, in a first test and five minutes later. PRO questionnaires, radiographic structural damage and metrology for axSpA were also assessed. Lumbar spinal mobility was also measured using an inertial sensor system (ViMove®).

**Results:** No statistical differences were found between left and right muscles neither after five minutes, so the mean values were used for analyses. All muscular measures, except Decrement showed statistically significant differences between groups. The table shows results of muscular stiffness parameters analysed, statistical differences in all parameters between groups and correlations of these parameters with conventional metrology, patient reported questionnaires (only patients) and structural damage. For control subjects, the only significant correlation was between stiffness and age. However in the axSpA patients, the myoton readings correlated with mobility measures, especially with BASMI, frontal flexion (not extension), lateral flexion and rotation, measured with the inertial sensors system. Some correlations ( $p < 0.05$ ) were also found for BASFI and BAS-G but not for BASDAI or ASQoL.



Abstract AB0868 – Figure 1

**Conclusions:** axSpA increases lumbar muscle stiffness with respect to healthy individuals. Muscle stiffness, as measured by myotonometry, was related to loss of movement and this could be contributing to a loss of function independently of structural damage and inflammation in axSpA. These new outcome measures could be helpful for understanding the evolution of the disease and for the functional assessment.

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**Disclosure of Interest:** None declared

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#### AB0869 PREVALENCE OF SPONDYLOARTHRITIS IN PATIENTS WITH ANTERIOR UVEITIS

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**Background:** Anterior uveitis (AU) is a common extraarticular manifestation in spondyloarthritis (SpA). The disease can precede the typical axial and peripheral features. Additionally, some studies had described the imaging signs of sacroiliac involvement in patients with AU lacking chronic back pain.

**Objectives:** The aim of this study was to examine patients with AU, to determine whether the patients already fulfil criteria for axial and/or peripheral SpA and to stratify risk factors for SpA development.

**Methods:** We recruited 27 patients without prior rheumatologic diagnosis who developed at least one episode of AU. The clinical data were collected and

rheumatology examinations were performed by trained rheumatologists. Magnetic resonance imaging (MRI) of sacroiliac joints (SIJ) was read by trained rheumatologist who was blinded to the patient data. Patients were further divided into SpA subsets (axial: imaging and clinical arm and peripheral SpA) fulfilling The Assessment of SpondyloArthritis international Society (ASAS) classification criteria<sup>1</sup> and non-SpA subset. The ASAS modified Berlin algorithm for diagnosis of axial SpA<sup>2</sup> (axSpA) was also applied.

**Results:** Bone marrow oedema (BME) was found in 63.0% (n=17) of all patients with AU, however 40.7% (n=11) had highly suggestive BME<sup>3</sup> corresponding to typical findings in sacroiliitis. Altogether, 22.2% (n=6) referred inflammatory back pain, 48.1% (n=13) referred non-inflammatory back pain and 29.6% (n=8) did not refer back pain. The diagnosis of SpA was confirmed in 44.4% (n=12) of all patients with AU, 33.3% (n=9) patients fulfil the imaging arm and 7.4% (n=2) fulfil the clinical arm of ASAS classification criteria for axSpA, 7.4% (n=2) patients fulfil ASAS classification criteria for peripheral SpA (one patient fulfil both axial and peripheral criteria). The diagnosis of axSpA according to the ASAS modified Berlin algorithm was confirmed in 37.0% (n=10) patients. Analysis of clinical characteristics showed significant difference between Ankylosing Spondylitis Disease Activity Score (ASDAS) in SpA vs. non-SpA (1.5±0.7 vs 0.7±0.6,  $p=0.01$ , respectively), and remained significant in axSpA and also in those fulfilling only imaging arm of axial SpA (i-axSpA) (1.4±0.7, 1.3±0.7 vs. 0.7±0.6,  $p=0.01$ ,  $p=0.04$ , respectively). The levels of CRP were significantly higher in SpA and axSpA compared to non-SpA subsets (8.3±10.5, 7.1±10.1 vs. 1.8±1.6 mg/L,  $p=0.02$ ,  $p=0.05$ , respectively). Presence of back pain was increased in SpA and similarly in axSpA as well as i-axSpA compared to non-SpA subsets (91.7%, 100%, as well as 100% vs. 53.3%,  $p=0.04$ ,  $p=0.01$ ,  $p=0.02$ , respectively). Furthermore inflammatory back pain was more frequently described in axSpA and i-axSpA compared to non-SpA subsets (45.5%, 44.4% vs. 6.7%,  $p=0.05$ ,  $p=0.01$ , respectively).

**Conclusions:** More than one third of patients with anterior uveitis fulfilled the criteria for axial or peripheral SpA. Furthermore, these patients had significantly higher presence of back pain, ASDAS and serum CRP levels. Inflammatory back pain was significantly increased in patients classified as axSpA.

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**Disclosure of Interest:** None declared

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#### AB0870

#### THIRTEEN-YEAR CLINICAL FOLLOW-UP OF SPONDYLOARTHRITIS PATIENTS: DATA FROM THE REGISPONSER DATABASE

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**Objectives:** To describe the clinical characteristics of the SpA patients included in the REGISPONSER database during 13 years of follow-up, regarding the evolution of the clinical manifestations and the treatment used.

**Methods:** An observational and analytical study of a retrospective cohort was carried out, in which 78 patients were analysed at the Reina Sofía University Hospital of Córdoba for the first time in the year 2004/05. The last visit registered was reviewed during the years 2016/17. Data about his clinical condition, including extra-axial manifestations, and treatment was collected.

**Results:** Seventeen out of 78 SpA patients included in the registry were lost. The characteristics of this cohort are shown in table 1. Recurrence of uveitis was observed in 10 out of 14 (71.4%) patients ( $p < 0.001$ ), with a low recurrence at the end of the follow-up (5%). At the time of inclusion, uveitis was not present in 45 SpA patients, however was present in 8 of them (17.8%) during follow-up. Three out of the 15 patients who had history of lower limbs peripheral arthritis in the first registry, presented new flares at the end of the study, showing a low level of recurrence (3%). During follow-up, enthesitis was present in 8 out of 45 SpA patients (17.8%) who didn't have a previous history of enthesitis. In addition, only one episode of dactylitis was detected from the 55 SpA patients who didn't have a previous history of dactylitis. The last CRP value was mean of 5.90 (8.13) mg/dl. Besides, three patients required placement of a hip prosthesis during follow-up. At last visit, we found a response to NSAIDs in 54 patients (88.5%), 33 of them (61.1%) with daily treatment. Biological therapy was present in 25% of the patients,<sup>15</sup> showing a mean time of 18.8 (7.4) years from the appearance of the first symptoms until their indication. A good response was achieved in 50% of



patients with the first biologic indicated. Loss of efficacy was the most frequent cause (62%) of therapy change. Currently golimumab and etanercept are the most commonly used, prescribed in 5 (33%) and 4 (26%) patients respectively.

**Abstract AB0870 – Table 1.** Baseline characteristics of the cohort (first recorded visit) (N=78)

Type of SpA N(%)	AS 78 (100%)	Inflammatory back pain (%)	75 (96.2%)
HLA-B27 + N(%)	70 (89.6%)	Sacroiliitis (NY criteria) N (%)	Mild: 8 (10.3%) Moderate: 25 (32.1%) Severe: 45 (57.7%)
Sex N (%)	Male 67 (85.9%) Female 11 (14.1%)	CRP Mean(DS) mg/dL	12.2 (13.4)
Age Moment of registration	48 (9.7)	Extra-axial manifestations	19 24.7% 19 (24.4%) 34 (43.6%)
Start of symptoms	25.9 (10.2)	Uveitis	6 (7.7%)
Moment of the diagnosis	35.01 (10.3)	Lower limbs peripheral arthritis	
Mean (DS) years		Enthesitis	
		Dactylitis N(%)	
Time of evolution	13 (9.2)	Hip prosthesis N (%)	5 (6%)
Diagnosis-inclusion in the registry			

**Conclusions:** The results obtained suggest that the follow-up of a cohort of patients with spondyloarthritis in a specialised monographic medical centre allows a control of the symptoms, with a low recurrence of extra-axial manifestations. We can conclude from this study that most patients with spondyloarthritis (75%) could have good control of their disease with NSAIDs in the long term.

**Disclosure of Interest:** None declared

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**AB0871 PREDICTIVE VALUES OF INFLAMMATORY LOW BACK PAIN, POSITIVE HLA B 27 ANTIGEN, INCREASED C REACTIVE PROTEIN, POSITIVE MAGNETIC RESONANCE AND OTHER FEATURES IN AXIAL SPONDILOARTHRITIS (SPA). A PROSPECTIVE 2 YEARS FOLLOW UP**

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**Background:** Diagnosis of Spondyloarthritis remains challenging in the daily practise. Inflammatory back pain might be a good tool for early diagnosis.

**Objectives:** To analyse sensitivity, specificity and predictive values of inflammatory back pain (IBP), positive HLA B27 antigen, increased C-reactive protein (CRP), positive sacroiliac joints (SI) magnetic resonance (MRI) imaging, additional features (AF) such as peripheral arthritis, dactylitis, psoriasis, uveitis, inflammatory bowel disease (IBD) and familiar history (FH) and assess probabilities to develop SPA.

**Methods:** We prospectively collected and follow up 82 patients referred to our department with suspicion of SPA from September 2014 to December 2016. Data such as IBP, HLA B27, additional features, familiar history of SPA, increased CRP, sacroiliac x-Rays and sacroiliac MRI imaging was performed for each patient. Each MRI image was separately and independently evaluated by rheumatologist and radiologist.

**Results:** The average age in our study was 39.8 years with male/female ratio 0.4/1. 37 (45.1%) patients were diagnosed with axial SPA. Radiographic sacroiliitis had only 5 (6.1%) patients. AF had 21 (25.6%) patients. IBP was found in 36 (43.9%) patients, positive HLA B 27 antigen in 24 (29.3%) and increased CRP in 22 (26.8%). Sacroiliac joints (SI) MRI images were assessed as clearly positive if patients had more than 2 highly specific for SPA bone marrow oedema (BME) lesions, at least 3 fatty lesions and more than 1 erosion, positive MRI image if patients had at least 2 highly specific BME lesions, and clearly negative MRI images if patients had not got any of those features. We found 83.78% sensitivity and 88.89% specificity for IBP, 37.84% sensitivity and 80.95% specificity for positive HLA B27 antigen, 43.24% sensitivity and 88.1% specificity for increased CRP. AF such as such as peripheral arthritis, dactylitis, psoriasis, uveitis and IBD, evaluated together reached sensitivity 37.84% and specificity 84.44%. Positive FH only contributed to the diagnosis with 13.51% sensitivity, but showed higher specificity (84.44%). Sensitivity for positive SIJ MRI imaging were poor (51.35%) but reached excellent specificity (100%). Predictive values in our study were as follows: 86.11% predictive positive values (PPV) and 86.96% predictive negative value (PNV) for IBP, 63.64% PPV and 59.65% PNV for HLA B27, 76.19% PPV and 63.79% PNV for increased CRP, 66.67% PPV and 62.30% PNV for AF.

Positive FH contributed to the diagnosis with 66.67% PPV and 62.30% PNV. Positive MRI reached 100% PPV and showed high PNV –71.43. Multivariate analysis displayed 81.8% likelihood to be diagnosed for SPA if only IBP without AF at the onset of the diagnosis and 94.8% if both IBP and AF were presented.

**Conclusions:** At the onset, IBP may be a good indicator for SPA with high sensitivity and acceptable specificity. Additional feature such as peripheral arthritis, dactylitis, psoriasis, uveitis and IBD might increase the possibility of SPA. HLA B27 antigen, increased CRP and FH brings low sensitivity for SPA nevertheless, specificity is better. Positive SI MRI imaging is highly specific but lacks sensibility. Normal SI radiography at the onset does not rule out diagnosis of SPA.

**Disclosure of Interest:** None declared

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**AB0872 QUANTIFERON TB GOLD TEST IN DIAGNOSIS OF LATENT TUBERCULOSIS INFECTION AMONG A MOROCCAN POPULATION WITH SPONDILOARTHRITIS**

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**Background:** Patients treated with anti-tumour necrosis factor-alpha (anti-TNF- $\alpha$ ) are at increased risk for latent tuberculosis reactivation. However, the best method for latent tuberculosis infection (LTBI) detection before initiation of anti-TNF therapy remains to be determined.

**Objectives:** The aim of this study is to investigate the role of QuantiFERON-TB Gold test as one of the interferon-gamma release assays (IGRAs) in detecting LTBI before initiation of biotherapy in a population of Moroccan patients suffering from spondyloarthritis (SpA).

**Methods:** We have conducted a cross-sectional study over two months in our department of rheumatology. All SpA patients fulfilled ASAS 2009 criteria.

Tuberculin skin test (TST), QuantiFERON-TB Gold in Tube (QFT-GIT) assay and chest radiographs were performed before starting anti-TNF-alpha. Computed tomography was performed in patients with abnormal chest radiographs.

**Results:** We included ninety two patients with SpA. Among them, 35 (38%) received anti-TNF- $\alpha$  therapy. A history of tuberculosis disease was noted in 6 patients (6.6%) (3 Pulmonary TB and 3 extrapulmonary TB). Two patients (2.2%) had contagious tuberculosis. The positive QFT-GIT rate was 15.2% (14/35). The TST was negative in 16.3% of cases (15/35). The results of QFT-GIT and TST performed in the same patients were discordant in 5 cases (5.4%). Sputum smears were negative. Chest CT performed in 29 patients had shown bronchiectasis in 3 cases (3.7%), interstitial syndrome in 2 cases (2.5%) and was normal in 24 cases (29.6%).

The chemoprophylaxis was prescribed in 14 persons with a positive QFT-GIT. It was based on Isoniazid (INH) alone in 12 cases (13%), a triple therapy (RHZ) in one case (1.1%) and a quadritherapy (RHZE) in another case with active tuberculosis. The duration of chemoprophylaxis varied between 6 and 9 months in the case of monotherapy, 2 months in the case of triple therapy because of biologic hepatotoxicity and 6 months in the case of quadritherapy because of active TB occurring during anti-TNF alpha therapy. The delay in initiating biotherapy varied between 1 and 6 months. At the time of blood sampling for QFT-GIT, patients were receiving: steroids in one case (1.1%), Methotrexate (MTX) and steroids in 3 cases (3.3%), Sulfasalazine (SZP) in 3 cases (3.3%), MTX in 4 cases (4.3%) and MTX and SZP in 2 cases (2.2%).

**Conclusions:** QTB-G may be a more sensitive screening tool for LTBI before initiating anti-TNF therapy in immunocompromised patients, especially in a TB endemic country.

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**AB0873** **US RHEUMATOLOGISTS HAVE MIXED PERCEPTIONS ABOUT MANAGING PATIENTS WITH NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS AND ANKYLOSING SPONDYLITIS**

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**Background:** Non-radiographic axial spondyloarthropathy (nrAxSpA) is a relatively new term used to describe patients who clinically appear to have ankylosing spondylitis (AS) but do not exhibit radiographic sacroiliitis. Though several biologics are currently FDA approved for the treatment of AS, there are no agents approved for patients in which there is not radiographic evidence of sacroiliitis. With several agents under investigation with the hopes of gaining a line-extension label for nr-axSpA, it is important to understand how the current treating rheumatologists view these two diseases and their current and future plans for spondyloarthropathy management.

**Objectives:** The study sought to (a) evaluate the differences between AS and nr-axSpA diagnosis and treatment patterns (b) highlight the challenges clinicians face in managing patients with nr-AxSpa and (c) understand rheumatologists' willingness to use biologic agents to treat nr-AxSpa.

**Methods:** An independent market analytics firm collaborated with US rheumatologists (n=98) to learn about current and anticipated changes to the management of Ankylosing Spondylitis and Non-radiographic Axial Spondylitis. Participants were administered an online survey, lasting approximately 30 min in length and respondents were compensated for their professional time. Following the fieldwork, data were analysed in SPSS, a statistical software, to determine significant differences.

**Results:** 87% of the surveyed rheumatologists agree that AS and nr-AxSpA are part of a spectrum, and 37% report that they often find it challenging to differentiate between the two conditions. The majority of the respondents report that they treat these conditions in a very similar manner. In fact, 40% agree that distinguishing between the two has no relevance to their treatment decisions. Use of biologics is significantly more pronounced in AS (56% vs. 39%, respectively), largely because there is currently no FDA indicated biologic for nr-AxSpA and because many rheumatologists view nr-AxSpA simply as a less severe precursor to AS, where aggressive treatment with a biologic is not warranted. In order to gain reimbursement for a biologic in patients with nr-AxSpA, rheumatologists frequently classify patients as having AS (as opposed to nr-AxSpA). Although adalimumab is the most frequently prescribed biologic in both conditions, rapid adoption of an IL-17 inhibitor (secukinumab) is occurring in the US market.

**Conclusions:** There is a need to educate both primary care physicians and rheumatologists about the differences between AS and nr-AxSpA. The official FDA approval of biologic agents in nr-AxSpA is anticipated to lead to more aggressive treatment of these patients earlier in the spectrum.

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**AB0874** **MENTAL HEALTH DISORDERS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: INCREASING OUR UNDERSTANDING OF THE DISEASE. RESULTS FROM THE ATLAS-2017**

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**Background:** Depression and other mental disorders are among the most prevalent comorbidities in patients with axial spondyloarthritis (axSpA).

**Objectives:** To assess the association between sociodemographic characteristics, disease progression, and mental health comorbidity with risk of mental disorders (RMD).

**Methods:** In 2016 a sample of 680 axSpA patients was interviewed as part of the Spanish Atlas. To quantify the RMD, GHQ-12 scale was employed. Possible RMD predictors taken into account in the analysis were: sociodemographic characteristics (age, gender, being part of a couple, patient association membership, job status); disease characteristics (BASDAI, spinal stiffness, functional limitation in 18 daily activities; and mental health comorbidities. All clinical variables showed a Cronbach's alpha coefficient guaranteeing the reliability of the scales used. First, a descriptive analysis was employed to describe the sample and study

variables. Second, univariate correlation and homogeneity analyses between each predictor (independent variable) and RMD (GHQ-12) were performed.

**Results:** All variables except educational level and thoracic stiffness showed significant univariate correlation with RMD. BASDAI, functional limitation and age showed higher coefficient ( $r=0.543$ ,  $p<0.001$ ;  $r=0.378$ ,  $p<0.001$ ;  $r=-0.174$ ,  $p<0.001$ , respectively).

Multiple hierarchical regression analysis showed as sociodemographic variables explained in great detail the RMD ( $R^2=83.2\%$ ). By contrast, having established sociodemographic as a control variable, the inclusion of depression and anxiety to the model increased the  $R^2$  value to just 0.6% ( $p<0.001$ ), while the inclusion of variables related to the disease characteristics add 5.5% ( $p<0.001$ ) to the GHQ-12 punctuation variability. The only variables presenting a significant coefficient different from 0 were BASDAI (0.52,  $p<0.001$ ) and functional limitation (0.14,  $p<0.01$ ). This suggests that once the sociodemographic and mental comorbidity variables are established, a change in BASDAI levels or functional limitation impacts the GHQ-12 score.

In the stepwise regression analysis, four variables (BASDAI, functional limitation, association membership, cervical stiffness) showed a significant relation to GHQ-12 and explained the majority of RMD variability. BASDAI displayed the highest explanatory degree ( $R^2=0.875$ ,  $p<0.001$ ).

**Abstract AB0874 – Table 1.** Sample characteristics (n=474, unless other specified)

Variables	Values (means $\pm$ SD or percentage)
Age, mean $\pm$ SD	45.43 $\pm$ 10.78
Sex, No. of men	233 (49.2%)
Having a couple, No. of participants (N=444)	386 (86.9%)
Education level, No. of university studies	185 (39.3%)
Job status, No. of unemployed	68 (14.4%)
Association Membership	227 (47.9%)
BASDAI (0-10) mean $\pm$ SD (N=442)	5.49 $\pm$ 2.17
Cervical stiffness, No. (N=447)	201 (45.0%)
Thoracic stiffness No. (N=435)	186 (42.8%)
Lumbar stiffness No. (N=458)	288 (62.9%)
Functional Limitation, (0-54) mean $\pm$ SD (N=473)	27.54 $\pm$ 12.78
Depression, No. (%) (N=474)	99 (20.9)
Anxiety, No. (%) (N=474)	134 (28.3)
GHQ-12, (0-36) mean $\pm$ SD	18.30 $\pm$ 8.01

**Conclusions:** In axSpA, patients at certain sociodemographic levels are more prone to present a higher BASDAI. Taking these conditions for granted, the degree of disease progression measured by BASDAI is a good indicator of RMD. Therefore, in those patients with higher disease activity, psychiatric evaluation and intervention should be considered within the medical treatment.

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**Disclosure of Interest:** None declared

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**AB0875** **QUALITY OF LIFE IMPROVEMENT IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS TREATED WITH NSAIDS AND BIOLOGICAL THERAPY FROM THE PATIENT'S PERSPECTIVE: RESULTS FROM THE ATLAS-2017**

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**Background:** In patients with axial spondyloarthritis (axSpA), the main long-term outcome is quality of life. Clinical trials and observational studies have shown the efficacy of biological therapy (BT) on improving the signs and symptoms of the disease. However, data assessing the impact of BT on quality of life is scarce and mainly comes from clinical trials.

**Objectives:** To assess in clinical practice the improvement in quality of life from the patient's perception as a result of pharmacological treatments in axSpA.

**Methods:** A sample of 680 patients diagnosed with axSpA was interviewed through an online survey as part of the Spanish Atlas-2017, which aimed to promote early referral, improve healthcare, and the use of effective treatments in patients with axSpA. For this study, self-reported data from patients who had received both NSAIDs and BT were analysed. Patients were asked about the improvement they had experienced on 7 different aspects of quality of life after starting treatment with NSAIDs or BT: independence, leisure and free time, social relations, sport and physical activity, and mood and sexual relations. Improvements were measured on a 0 to 10 Likert Scale and classified as low ( $\leq 5$ ) and high ( $\geq 6$ ). Non-parametric (Wilcoxon) tests were used to compare the degree of improvement between patients with biological therapy and those with NSAIDs.

**Results:** A total of 189 patients who had received both types of drugs were included. The mean (SD) age was 44.03 ( $\pm 10.11$ ) years, 50.3% were females, 70.9% married and 47.1% belong to a patients' association. The mean (SD) disease duration was 21.3 $\pm$ 10.7 years and 67.7% were HLA-B27+. A higher percentage of patients perceived a high level of improvement after receiving a BT than after receiving an NSAID, for both overall quality of life assessment (57% vs 22%, respectively) and the different quality of life-related aspects. Additionally, the mean degree of improvement for overall quality of life assessment and the different aspects related to this were reported to be significantly higher after receiving BT than after NSAIDs (overall improvement: 5.46 $\pm$ 2.59 vs 3.19 $\pm$ 2.45;  $p < 0.001$ , respectively).

**Abstract AB0875 – Table 1.** Mean improvement degree and percentage of patients who reported high improvement ( $\geq 6$  in 0–10) in different aspects related to quality of life after receiving biological therapy and NSAIDs

	NSAID		Biological Therapy		p value Wilcoxon
	High improvement (%)	Degree of improvement, Mean (SD)	High improvement (%)	Degree of improvement, Mean (SD)	
Independence	22.6	3.40 (2.79)	53.0	5.83 (3.01)	<0.001
Leisure & Spare Time	22.9	3.41 (2.73)	58.2	5.81 (2.80)	<0.001
Employment	20.7	3.01 (2.84)	53.6	5.48 (3.36)	<0.001
Social Relations	19.4	3.05 (2.50)	52.1	5.45 (2.95)	<0.001
Sport & Physical Activity	14.4	2.62 (2.71)	41.3	4.88 (3.05)	<0.001
Emotional Wellbeing	17.4	2.70 (2.83)	53.9	5.78 (2.88)	<0.001
Sexual Activity	16.0	2.52 (2.66)	53.4	4.65 (3.28)	<0.001
Global	22.2	3.19 (2.45)	57.0	5.46 (2.59)	<0.001

**Conclusions:** In clinical practice, patients' self-reported satisfaction overall and related to different aspects of quality of life is substantially greater after being treated with BT than with NSAIDs. However, these results need to be confirmed in a longitudinal study

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#### AB0876 CORRELATION BETWEEN FAECAL CALPROTECTIN LEVELS AND TOBACCO USE IN PATIENTS WITH SPONDYLOARTHRITIS AND WITHOUT PREVIOUS DIAGNOSIS OF INFLAMMATORY BOWEL DISEASE

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**Background:** It is estimated that between 5% and 10% of patients with spondyloarthritis (SpA) are associated with inflammatory bowel disease (IBD). It has also been proven through endoscopic and histological studies that up to 60% of patients with SpA have microscopic inflammatory intestinal lesions, with a subclinical character and of which the true clinical relevance is unknown, although a greater percentage of these are those that will evolve to IBD.

**Objectives:** To assess whether tobacco use may be associated with higher faecal calprotectin (FC) levels in patients with diagnosis of SpA and without clinical suspicion or previous diagnosis of IBD.

**Methods:** This is a single centre, cross-sectional, observational study with prospective collecting data. Data were included for consecutive patients from Rheumatology consultation who had been previously diagnosed of SpA, fulfilled ASAS criteria and without digestive symptoms suggestive of IBD (chronic diarrhoea, rectal bleeding, perianal disease, chronic abdominal pain – persistent or recurrent). Details about demographic characteristics, clinical and laboratory variables related with SpA (BASDAI, HLA B27, acute phase reactants), treatments and FC were collected. A pathological cut-off point of FC > 50 mg/kg was determined. Patients on NSAIDs treatment were advised to discontinue its use 2 weeks before collecting stool samples. This study was approved by the Clinical Research Ethics Committee.

**Results:** 99 patients were included: 53.5% women, with a mean age of 46 $\pm$ 11 years. nonspecific digestive disorders (dyspeptic symptoms, H. pylori y gastroesophageal reflux) were observed in 9% of the patients. Among all, 18% were smokers. Mean BASDAI was 3.7 $\pm$ 2.5; 39% of patients were being treated with any concomitant DMARD and 67% were on NSAIDs. 49.5% of the patients<sup>49</sup> showed elevated FC determinations, with an mean level of 276 mg/kg (range 52–3,038). The percentage of patients with high levels of FC was significantly increased in smokers (72.2% vs. 44.4%,  $p = 0.033$ ), with higher levels of FC in smokers than non-smokers (262 mg/L vs. 121 mg/L.  $p = 0.126$ ). The remaining analysed variables did not show any significant differences in terms of FC levels.

**Conclusions:** Microscopic bowel inflammation is described in approximately 50% of patients with SpA and it is related with more severe disease. Tobacco use has been associated with worse prognosis and response to treatment in SpA. A relationship between elevated FC levels (inflammatory activity biomarker) and tobacco use in patients with SpA without previous diagnosis or clinical suspicion of IBD is established in this study.

**Disclosure of Interest:** None declared

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#### AB0877 ANALYSIS OF THE ASSOCIATION OF THE PERIPHERAL INVOLVEMENT OF THE SPONDYLOARTHRITIS WITH THE EXTRA-ARTICULAR MANIFESTATIONS

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**Objectives:** Patients with SpA present peripheral involvement, such as arthritis and enthesitis, or only axial involvement, such as sacroiliitis and spondylophytes. The differentiation of the peripheral and axial presentation is important, being able to guide different therapeutic strategies.

**Methods:** This is a retrospective observational study, conducted in two clinics in Florianópolis. The population was composed of patients with AS and non-radiographic and peripheral axial SpA, according to the criteria of modified New York and ASAS group, respectively, served from 1997 to 2017.

**Results:** 153 patients were analysed, 82 were male (53.59%), 71.29% were HLA B27 positive (77/108 tested), 87.3% had sacroiliitis detected on x-ray, CT or MRI, 104 presented peripheral involvement (67.97%) and 49 (32.02%) purely axial involvement. Arthritis occurred in 86 (56.2%) and enthesitis in 57 (37.3%) patients. The use of synthetic DMARD occurred in 78.4% of the patients, more frequently in the group with peripheral involvement, with methotrexate being used in 74% versus 56.3% of those with purely axial involvement ( $p < 0.05$ ). The use of biological DMARD occurred in 104 (68%), in the majority of the anti-TNF class (96.1%), with the highest frequency of use in patients with axial involvement (77.1% versus 64.4%), but not statistically significant ( $p > 0.05$ ). Extra-articular manifestations were found in 72 (47.1%) of the patients, with uveitis being the most frequent (26.8%). The presence of uveitis occurred in 68.3% of patients with isolated axial involvement versus 31.7% of patients with peripheral involvement ( $p = 0.179$ ). The cutaneous involvement occurred in 18.3% of the patients with peripheral involvement compared to 8.3% of those with an isolated axial condition. Regarding bowel involvement and cardiovascular impairment, there was no significant difference in prevalence between the two groups.

**Conclusions:** Extra-articular manifestations are frequent in SpA, but are not more frequent in patients with peripheral involvement versus patients with pure axial involvement. Peripheral involvement is associated with greater use of synthetic DMARDs when compared to pure axial involvement.

**Disclosure of Interest:** None declared

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**AB0878** **COMPARISON OF CLINICAL FEATURES IN PATIENTS WITH PSORIATIC ARTHRITIS AND PATIENTS WITH SPONDYLOARTHRITIS WITH INFLAMMATORY BOWEL DISEASE**

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**Background:** Spondyloarthritis (SpA) is one of the representative comorbidity in patients with psoriasis (PsO) and inflammatory bowel disease (IBD) disease. However, the difference of clinical features between SpA due to PsO (PsA) and SpA due to IBD (IBD-SpA) are unclear.

**Objectives:** The purpose of this study is to compare the clinical features between patients with PsA and IBD-SpA.

**Methods:** Overall, 192 patients with PsO and 37 patients with IBD were included in this cross-sectional study. Clinical classification of PsA and IBD-SpA were performed according to the CASPAR<sup>1</sup> criteria and ASAS criteria.<sup>2</sup> Disease activity (DAS28-CRP), C-reactive protein (CRP), matrix metalloproteinase-3 (MMP-3), anti-cyclic citrullinated peptide antibody (ACPA), rheumatoid factor (RF), biologic disease modifying anti-rheumatic drugs (bDMARDs) use, and proportion of peripheral and axial disease were evaluated in patients with PsA and IBD-SpA.

**Results:** In this analysis, 74 patients were classified as PsA, 65 patients as PsO, 17 patients as IBD-SpA and 20 patients as IBD. The mean age was 56.0±14.7 years in PsA, 44.7±10.9 years in IBD-SpA (p=0.003). The mean BMI was 24.2±4.5 kg/m<sup>2</sup> in PsA, 23.3±7.2 kg/m<sup>2</sup> in IBD-SpA (p=0.18). DAS28-CRP was 3.26±1.26 in PsA, 4.02±1.5 in IBD-SpA (p=0.12). Axial SpA was observed in 4 (5.4%) in PsA, 5 (29.4%) in IBD-SpA (p=0.01). Biologics were used in 29 (39.2%) patients in PsA, 13 (76.5%) patients in IBD-SpA (p=0.007). Proportion of seropositive ratio was not significant in this two groups.

**Abstract AB0878 – Table 1.** Characteristics in patients with PsO, PsA, IBD and IBD-SpA.

	PsA (n=74)	PsO (n=65)	IBD-SpA (n=17)	IBD (n=20)	P value*
Age, years	56.0±14.7	60.2±14.0	44.7±10.9	45.0±12.8	0.003
Female, n (%)	36 (48.6)	29 (44.6)	8 (47.0)	16 (80.0)	1.0
Height, m	1.63±0.09	1.61±0.09	1.65±0.07	1.59±0.06	0.43
Body weight, kg	65.3±16.8	61.7±13.1	64.7±24.8	51.8±12.2	0.34
BMI, kg/m <sup>2</sup>	24.2±4.5	23.7±3.9	23.3±7.2	20.4±3.9	0.18
DAS28-CRP	3.26±1.26	1.91±0.9	4.02±1.5	2.53±0.8	0.12
CRP, mg/dl	1.32±3.3	0.32±0.6	1.0±1.1	0.78±2.4	0.12
MMP-3, ng/ml	99.9±95.3		92.1±59.0		0.90
ACPA positive, n (%)	6 (8.1)		0 (0)		0.59
RF positive, n (%)	7 (9.5)		1 (5.9)		1

\*Mann-Whitney U-test and Fisher's exact test were performed in comparison with PsA and IBD-SpA.

**Abstract AB0878 – Table 2.** Prevalence of axial SpA and peripheral SpA in patients with PsA and IBD-SpA.

	PsA (n=74)	IBD-SpA (n=17)	P value
Axial SpA, n (%)	4 (5.4)	5 (29.4)	0.01
Peripheral SpA, n (%)	70 (94.6)	12 (70.6)	

**Conclusions:** The clinical features between patients with PsA and IBD-SpA were compared. The patient with IBD-SpA was younger than patient with PsA and the prevalence of axial disease was more frequent in IBD-SpA.

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**AB0879** **FIBROMYALGIA IN PATIENTS WITH ANKYLOSING SPONDYLITIS: PREVALENCE AND RELATIONSHIP WITH DISEASE ACTIVITY**

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**Background:** Spondyloarthritis (SpA) is an inflammatory rheumatic disease, characterised by spinal involvement, peripheral arthritis, or enthesitis with marked pain, stiffness, and fatigue. Fibromyalgia (FM) may be associated with SpA, and shares some common symptoms.

**Objectives:** We aimed to estimate the prevalence of FM in SpA and its influence on the assessment of SpA disease activity.

**Methods:** This single-centre cross-sectional study included consecutive patients with SpA according to the Assessment of SpondyloArthritis International Society criteria. FM was diagnosed according to the 2010 American College of Rheumatology criteria. All patients underwent clinical evaluation of disease activity using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), the Bath Ankylosing Spondylitis Functional Index (BASFI) and the Ankylosing Spondylitis Disease Activity Score (ASDAS) and then compared in patients with and without FM.

**Results:** The study included 100 patients with SpA, 67 males and 33 females with a median age of 44.65 years. The prevalence of fibromyalgia was 20%. Patients fulfilling the criteria of FM presented a higher total BASDAI (5.86 (±1.97) vs. 3.15 (±1.99), p<0.01), higher ASDAS-CRP (3.43 (±1.13) vs. 2.41 (±1), p<0.01), higher ASDAS-VS (3.5 (±1.12) vs. 2.53 (±1.02), p<0.01) and poorer function scores (BASFI) (6.76 (±1.97) vs. 3.8 (±2.59), p<0.01).

**Conclusions:** FM is a frequent comorbidity in patients with SpA. In patients with SpA-FM, disease activity may be overestimated and this overestimation could lead to inappropriate treatment escalation.

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**AB0880** **THE OBJECTIVE AUTOMATED MEASUREMENT OF FLUORESCENCE-SIGNAL INTENSITIES IN FLUORESCENCE-OPTICAL IMAGING TECHNIQUE DISCRIMINATES BETWEEN DISEASE ACTIVITY AND ITS RESPONSE IN ANTITNF TREATED PSORIATIC ARTHRITIS PATIENTS – AN INTERIMS ANALYSIS OF THE XPLORE-STUDY**

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**Background:** Psoriatic arthritis (PsA) is a chronic inflammatory disorder combining joint and musculoskeletal inflammation. AntiTNF-therapy is induced after failure of NSAID and DMARD treatment. Up to 30%–40% of the patients are primary not responding adequately to the induced biological therapy. In daily practice response is calculated by improvement of disease activity measured by clinical examination and calculated using composite indices. Feasible and robust biomarkers for prediction of response are missing.

**Methods:** Fluorescence optical imaging (FOI) is used as method for detection of changes in microvascularisation of the hands as potential marker for inflammation. ICG is injected as fluorescence agent, that is than stimulated by light and recorded by a specific camera system. An automated computer-based reading of the disease activity (DACT) is used as an objective method to display overall fluorescence-signals and their intensities. In a prospective multicentre study, the value of FOI in measurement of disease activity and its predictive value to discriminate responders in newly treated PsA patients is currently investigated in the XPLORE-study. This interim analysis investigates the value of baseline (BL) DACT to discriminate between responders (at least low disease activity (LDA) with DAS28 ≤3.2) and non-responders compared to standard clinical disease measurements (SJC, TJC, DAS28) over the 52 weeks observational period.

**Results:** Data from 23 patients were analysed during the 52 weeks observational period. Mean age was 54.7 years, 60% of the patients were female. Mean DAS28 at baseline was 4.26, mean BSA 9%, whereas mean values for SJC were 5.9 and TJC 11.4 using 66/68 joint count. All patients were negative for ACPA and rheumatoid factor.

ROC analysis revealed that a DACT cut-off of 4.55 at baseline, indicating moderate expression of fluorescence intensities in context of disease activity, shows a predictive quality to LDA achievement at W52 with 80% specificity, 78% sensitivity and likelihood ratios of 3.89 (LQ+) and 0.28 (LQ-). The corresponding AUC value is 0.717 (95%CI=[0.393, 1]; p=0.146). Compared to clinical disease measurements such as baseline DAS28, TJC or SJC, the DACT at BL is more discriminative to identify patients who attain LDA at W52.

**Conclusions:** This interim analysis of the XPLORE study shows promising data for the use of FOI as possible imaging biomarker for disease activity measure and prediction of response in PsA-patients newly treated with antiTNF-therapy: Baseline values evaluated using the automated computer-based reading of the fluorescence intensities with a cut-off of 4.55 are predictive for later achievement of DAS28 low-disease activity or remission within the treatment course. Data will be verified in a larger cohort of the XPLORE study.

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**AB0881 ASSOCIATION OF RS12218 POLYMORPHISM IN SAA1 GENE WITH LUMBAR SPINE SYNDESMOPHYTES IN THE RUSSIAN ANKYLOSING SPONDYLITIS POPULATION. A PILOT STUDY**

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**Background:** Ankylosing spondylitis (AS) is a chronic inflammatory disease from the group of spondyloarthritis (SpA). Earlier studies showed a correlation between SAA1 gene polymorphism, encoding serum amyloid A, and the development of secondary AA-amyloidosis in familial Mediterranean fever and rheumatoid arthritis in Caucasian and Asian populations. The Moriguchi et al (2005) study showed that the -13 T/C polymorphism in the gene 5'-flanking region (rs12218) is a better marker of AA-amyloidosis than mapping of polymorphisms in SAA1 exon 3 (SAA1.1 and SAA1.1.3). Data on rs12218 polymorphism contribution into predisposition to AS and its clinical phenotypes are very scarce. One of the clinical phenotypes, determining the severity of spine damage, is associated with presence of syndesmofytes (SM) in the lumbar (SMl), thoracic (SMt) and cervical (SMc) spine, confirmed by x-ray data.

**Objectives:** To study potential associations of rs12218 polymorphism in SAA1 gene with AS and phenotypes of radiographic progression, with the presence of SMl, SMt and SMc, and correlation with BASDAI, BASFI and ASAS indices.

**Methods:** rs12218 polymorphism was studied in 112 subjects: 47 AS patients (37 males and 10 females, mean age 40y, mean disease duration 213 weeks, mean age at onset 22y, positive for HLA-B27), and 65 healthy volunteers (controls). Genotyping was performed using allele-specific polymerase chain reaction in real time (PCR-RT).

**Results:** The Pearson Correlation analysis showed negative correlation between rs12218 polymorphism and presence of SMl, as well as BASDAI, BASFI scores ( $r=-0.39$ ,  $r=-0.35$  and  $r=-0.36$ ,  $p=0.006$ ,  $p=0.017$ ,  $p=0.014$ , respectively). There were no correlations between rs12218 and pts' age, AS duration and pts' age at AS onset. There were similar rs12218 allele distribution rates between AS patients and the controls. rs12218C allele rates were significantly higher in SMl group (n=23) compared to subjects without SMl (n=24) [50.0% vs. 15.2%,  $p=0.001$ ]. No association was established between C allele and presence of SM in other parts of the spine. A correlation between BASDAI and BASFI scores and SAA1 gene rs12218 polymorphism was established. Mean BASDAI score was significantly higher in carriers of TC and CC genotypes compared to carriers of TT genotype ( $5.6\pm 1.3$  vs.  $3.9\pm 2.3$ ,  $p=0.004$ ). The mean BASFI scores in carriers of the respective genotypes were ( $6.1\pm 2.3$  vs  $4.1\pm 2.8$ ,  $p=0.012$ ). No significant correlation was found between rs12218 genotypes and mean ASDAS score values.

**Conclusions:** Therefore, this pilot study is the first to show the possible participation of rs12218 polymorphism in SAA1 gene in AS pathogenesis in Russian population. We suggest that C allele may be a risk factor predisposing to SMl [OR 5.14 95% CI(1.75–16.17),  $p=0.001$ ]. The data obtained on a limited sample of patients require further validation on larger samples of patients involving different population groups.

**Disclosure of Interest:** None declared

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**AB0882 ACHILLES ENTHESITIS IN THE PATIENTS WITH SPONDYLOARTHRITIS: RELATIONSHIP WITH MUSCLE STRENGTH, ACTIVITIES OF DAILY LIVING AND QUALITY OF LIFE**

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**Background:** Enthesitis is a central feature of spondyloarthritis (SpA). In SpA, the entheses of the lower extremities are more commonly involved than those of the upper limbs, and the heel is the most frequent site. Investigation of peripheral enthesitis in SpA is based on clinical findings and/or imaging findings. The involvement of Achilles tendon may lead to pain, movement restrictions, decrease in muscle strength, and eventually a diminished quality of life (QoL).

**Objectives:** In the present study, we aimed to evaluate clinical enthesopathy and relation with ankle muscle strength, activities of daily living (ADLs) and foot and ankle related QoL in the patients with SpA.

**Methods:** Sixty SpA patients fulfilling the Assessment of SpondyloArthritis International Society (ASAS) classification criteria for SpA (M/F=39/21) ( $35.61\pm 9.85$  years) and 50 healthy controls (M/F=32/18) ( $35.40\pm 10.62$  years) were enrolled in the study. Clinical enthesopathy was defined by the presence of at least one of the spontaneous pain, tenderness elicited by pressure, mobilisation and contraction against resistance of the corresponding tendons and local swelling of the enthesis. Pain by visual analogue scale (VAS), disease activity by Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), functional capacity by Bath Ankylosing Spondylitis Functional Index (BASFI), enthesitis severity by SPARCC index was assessed in the patients. Isokinetic measurements of ankle dorsiflexion and plantarflexion were performed by the isokinetic dynamometer. The participants were tested at 30° and 120°/sec angular velocities. Pain, other symptoms (stiffness, swelling, range of motion), ADLs, sport and recreational activities, and foot and ankle-related QoL were evaluated by the Foot and Ankle Outcome Score (FAOS) in which higher scores indicate lesser problems and/or functional limitations.

**Results:** There was no significant difference between the patients and controls regarding age, sex, and body mass index. Clinical enthesopathy was detected in 36.7% of the SpA patients. Although ankle plantarflexion and dorsiflexion muscle strength in all angular velocities were lower in the SpA patients, the difference did not reach statistical significance ( $p>0.05$ ). All of the FAOS subscales were found to be significantly lower in the patients with SpA than in the controls ( $p<0.001$ ). When the SpA patients were divided into two groups as with clinical enthesopathy (n=22) and without clinical enthesopathy (n=38), there were significant differences between the groups regarding VAS pain, BASDAI, BASFI and SPARCC scores whereas there was no significant difference in muscle strength. Also, all FAOS subscale scores were significantly lower in the patients with clinical enthesopathy. Additionally, in the patients with SpA, while there were negative correlations between VAS pain, BASDAI, BASFI, SPARCC and FAOS subscale scores, there was a positive correlation between ankle muscle strength and FAOS scores ( $p<0.05$ ).

**Conclusions:** We found that all the FAOS subscale scores were lower in the SpA patients and they were correlated with clinical findings. The results of our study indicate that even though there was not a significant decrease in the muscle strength, ADLs, sport and recreation activities, foot-related QoL are poorly affected in the SpA patients with Achill enthesitis.

**Disclosure of Interest:** None declared

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**AB0883 ASSESSMENT OF EARLY MYOCARDIAL DYSFUNCTION USING SPECKLE TRACKING ECHOCARDIOGRAPHY IN PATIENTS WITH RADIOGRAPHIC AND NONRADIOGRAPHIC AXIAL SPONDYLOARTHRITIS**

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**Background:** Axial spondyloarthritis (axSpA) is a chronic inflammatory disease that mainly affects axial skeleton. Although some differences like sex and objective signs of inflammation were described between these two subgroups, overall disease burden was found to be similar in radiographic (r-) and non-radiographic (nr-) axSpA patients. The association of chronic inflammation with cardiac dysfunction was well documented in many inflammatory rheumatic diseases. However it was not assessed in the subgroups of axSpA patients. Advanced two-dimensional (2D) speckle tracking echocardiographic analysis is more sensitive and accurate method of early detection of myocardial dysfunction than the conventional 2D transthoracic echocardiography (TTE).

**Objectives:** To evaluate the left ventricular function by using speckle tracking echocardiography in patients with both r- and nr-axSpA.

**Methods:** In total 64 patients with r-axSpA (70% male) and age- and sex-matched 27 patients with nr-axSpA (63% male) and 30 healthy control subjects

(63% male) were included in the analysis. Patients with hypertension, diabetes and known cardiac disease were excluded. All patients underwent detailed echocardiographic examination including M-mode, pulsed-wave Doppler imaging, pulsed-wave tissue Doppler imaging and 2D speckle tracking.

**Results:** Age and sex distribution were not different between groups. Some demographic and disease related characteristics were shown in the table. BASDAI, BASFI, global assessment of disease activity and ASAS-HI scores were found to be similar between r- and nr-axSpA patient groups. Although ejection fraction (EF) ( $p=0.112$ ) and the other echocardiographic variables were similar between groups, global longitudinal strain (GLS) ( $p=0.045$ ) were found to be different among groups (table 1). Post-hoc analysis showed that GLS was similar between nr-axSpA and control groups however GLS was significantly low in r-axSpA patients. In univariate analysis GLS was correlated with age ( $p=0.025$ ), EF ( $p<0.001$ ), peripheral arthritis ( $p=0.047$ ), and smoking ( $p=0.019$ ). However in regression only peripheral arthritis ( $p=0.032$ ) and EF ( $p=0.015$ ) were found as the independent predictors of GLS.

**Abstract AB0883 – Table 1.** The demographic and disease related characteristics of study groups.

	Radiographic axSpA patients (n=64)	Non-radiographic axSpA patients (n=27)	Control subjects (n=30)	P
Age, years (mean±SD)	40.9±10.2	37.6±9.4	42.3±4.3	0.056
Duration of disease, years (mean±SD)	14.1±7.8	10.6±8.1	N/A	N/A
BASDAI, (mean±SD)	2.7±2.1	3.0±1.8	N/A	N/A
BASFI, (mean±SD)	2.5±2.3	2.6±2.0	N/A	N/A
Ejection fraction, (mean ±SD)	58.9±5.2	60.1±4.7	61.2±4.9	0.112
<b>Global Longitudinal Strain, (mean±SD)</b>	<b>20.4±3.3</b>	<b>21.3±3.8</b>	<b>22.3±2.5</b>	<b>0.045</b>

**Conclusions:** The results of the present study showed that left ventricular function had impaired in r-axSpA patients and speckle tracking echocardiography may be a useful tool for early demonstration of left ventricular dysfunction.

**Disclosure of Interest:** None declared

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#### AB0884 SERUM FIBROBLAST GROWTH FACTOR-23 LEVELS WERE HIGHER IN PATIENTS WITH AXIAL SPONDYLOARTRHRITIS AND MAY BE ASSOCIATED WITH DISEASE ACTIVITY

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**Background:** Axial spondyloarthritis (axSpA) is a chronic inflammatory disease that mainly affects axial skeleton. The disease is characterised by new bone formation; it usually starts with the bony fusion of sacroiliac joints (SIJs) and also causes syndesmophyte formation in the intervertebral space, enthesophytes in the tendon and ligament insertion sites. Underlying mechanisms of new bone formation in axSpA patients is not completely understood and low levels of sclerostin may be associated with the development of syndesmophyte in patients with ankylosing spondylitis (AS). Beside sclerostin another osteocyte factor is fibroblast growth factor-23 (FGF-23) and it has been first described as a phosphaturic hormone. It was also shown that FGF-23 may inhibit osteoblast differentiation and matrix mineralization.

**Objectives:** To evaluate serum FGF-23 and sclerostin levels in patients with axSpA and to compare them with those of healthy control subjects. We also assessed relationship between the serum FGF-23, sclerostin levels and disease related variables in particular the presence of structural changes.

**Methods:** In total 109 axSpA patients according to ASAS classification criteria and age- and sex-matched 57 healthy control subjects were included in the analysis. Subjects with renal failure and significant comorbid conditions and axial SpA patients who were using anti-TNF agents were excluded. Demographic and disease related characteristics were collected by using a standard questionnaire. Serum levels of FGF-23 and sclerostin were measured using commercially available enzyme-linked immunosorbent assay (ELISA) kits in accordance with the supplier's instructions.

**Results:** In the present study there were 55 patients with non-radiographic axSpA and 54 patients with AS. Serum levels of FGF-23 levels were significantly higher in axSpA patients than healthy subjects. Although there was a trend towards a lower sclerostin levels in axSpA patients this difference did not show statistical significance (table 1). In axSpA patients serum FGF-23 levels were found to be correlated with erythrocyte sedimentation rate (ESR) ( $p=0.006$  and  $r=0.265$ ), C-

reactive protein (CRP) ( $p=0.017$  and  $r=0.229$ ) and patients' height ( $p=0.027$  and  $r=-0.221$ ). There was no relationship between FGF-23 and mSASSS score or the presence of syndesmophyte. Subgroup analysis revealed that the duration of disease ( $p=0.005$ ), ESR ( $p=0.007$ ), CRP ( $p<0.001$ ) and mSASSS ( $p=0.008$ ) scores were significantly higher in AS patients than nr-axSpA patients. However serum sclerostin levels were significantly higher in nr-axSpA patients ( $1464.4±728.1$  vs  $1150.8±754.3$  pg/mL and  $p=0.029$ ).

**Abstract AB0884 – Table 1.** Demographic characteristics and serum FGF-23 and sclerostin levels in study groups

	Axial spondyloarthritis (n=109)	Healthy controls (n=57)	P
Mean age (years)	39.8±10.3	37.0±8.2	0.055
Male (%)	51	44	0.513
Mean fibroblast growth factor-23 (pg/mL)	188.5±160.7	130.8±100.3	0.005
Mean sclerostin (pg/mL)	1309.0±754.4	1365±676.7	0.633

**Conclusions:** Our results suggested that serum FGF-23 is increased in axSpA patients. And also disease activity may contribute to an up-regulation in serum FGF-23 levels.

**Disclosure of Interest:** None declared

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#### AB0885 CHARACTERISTICS OF JUVENILE ONSET HIP ARTHRITIS IN PATIENTS WITH SPONDYLOARTRHRITIS

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**Background:** Axial spondyloarthritis (AS) is a chronic inflammatory rheumatic disease that affects the axial skeleton. It typically occurs in the late teens or early twenties and rarely in childhood, defining the juvenile onset (JoAS).

The adult-onset AS (AoAS) and Juvenile-onset (JoAS) may share many common features including hip involvement. But their impact on function and quality of life may differ.

**Objectives:** To compare demographic, clinic and functional outcome of patients with hip involvement in JoAS, with that of patients with AoAS

**Methods:** Cross-sectional study including patients with AS according to the <sup>ASAS</sup> criteria of 2009 with hip involvement. The juvenile onset of coxitis was defined by an onset before 16 years of age. An analysis of demographic and clinical comparisons between the two groups was performed including HLA B27 status. Mobility spine outcomes were assessed by the Bath AS Metrology Index (BASMI) and radiographic disease severity by the Bath AS Radiology Index (BASRI).

**Results:** There were 100 AS aged on average  $36.4±12.2$  years old.<sup>16-69</sup> The sex ratio was 4.6. The mean duration of progression of AS was  $10.93±9.89$  years [0.5–24]. It was a JoAS in 15 cases. All patients had a hip involvement. The juvenile onset of hip arthritis was associated with male gender ( $p=0.042$ ), younger age of patient with AS at the time of recruitment ( $p=0.007$ ), less severe clinical spinal involvement assessed by schober index ( $p=0.029$ ) and more frequent and severe enthesitis assessed by MASES ( $p=0.024$ ). Extra-articular manifestations were significantly more frequent in patients with juvenile onset of hip arthritis ( $p=0.008$ ). Otherwise the comparison of the two groups showed no difference in the presence of uveitis ( $p=0.407$ ) and pulmonary involvement ( $p=0.097$ ). HLAB27 antigen was significantly more common in JoAS ( $p=0.037$ ). BASRI and BASMI as well as ESR and CRP, were comparable between the two groups ( $p=0.976$ ,  $p=0.626$ ,  $p=1.000$ , respectively)

**Conclusions:** Hip involvement is common in the AS, particularly in JoAS. Our study showed that juvenile onset hip arthritis was associated with male gender, less severe spine involvement, enthesitis and the presence of HLA B27. This would help physicians to identify patients at higher risk of developing hip involvement, to enable early diagnosis.

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AB0886

### DOES RADIO-ANATOMIC FEATURE OF HIP ARTHRITIS IN SPONDYLOARTHRITIS PREDICT FUNCTIONAL IMPAIRMENT?

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**Background:** Axial spondyloarthritis (AS) is a chronic inflammatory disease that primarily affects the axial skeleton. Hip involvement is common in AS patient. The reported prevalence of clinical hip involvement in AS ranges from 24% to 36% and prevalence of radiographic hip arthritis ranges from 9% to 22%.<sup>1, 2</sup> Several radio-anatomic features are described with often significant clinical impact.

**Objectives:** To assess for an association between the radio-anatomic feature of hip arthritis and its clinical impact in patients with AS.

**Methods:** Cross-sectional study including patients with AS according to the <sup>ASAS</sup> criteria of 2009 with hip arthritis. All patients had pelvic X-rays. This one allowed to distribute the patients according to five radio-anatomic features of the hip arthritis: destructive, protrusive, ankylosing, mimicking osteoarthritis and early hip arthritis. To evaluate the functional impairment, two clinical indices were calculated: Lequesne index and Intermalleolar distance between the two medial malleoli in centimetre. The comparison of qualitative variables was performed with the Chi square test and the comparison of quantitative variables was performed with the Student's test. The significance level was set at 0.05.

**Results:** One hundred patients were included with 176 hips arthritis. The delay between onset of AS and hip arthritis was on average 5.6 years [0–34]. The distribution of coxitis according to the radio-anatomic feature was as following: destructive (110 cases), protrusive (10 cases), mimicking osteoarthritis (29 cases), ankylosing (7 cases) and early hip arthritis (20 cases). According to the Larsen classification for destructive hip arthritis: a grade 4 was found in 41 cases, a grade 2 in 33 cases, a grade 3 in 33 cases and a grade 1 in 3 cases.

The destructive form had the most important functional impairment with the highest Lequesne index in comparison with other forms (13,05 vs 9,7, p=0,000) and the smallest intermalleolar distance (74,40 vs 87,29, p=0,010).

The early hip arthritis and protrusive forms had the least important functional impact in with the following scores: Lequesne index (8,83 vs 12,29, p=0,015) and (10,78 vs 11, 96, p=0,000) and the intermalleolar distance (76,36 vs 65,00 p=0,015) and (105,56 vs 70,22, p=0,002) respectively.

Scores were comparable for osteoarthritis and ankylosing forms.

**Conclusions:** Our study showed that radio-anatomic feature of hip arthritis could influence functional impairment. Distinguishing these forms may allow the rheumatologist to select the hip arthritis that deserves more attention because of the highest risk of functional impairment.

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AB0887

### JIA PATIENTS WITH HIGH DISEASE ACTIVITY HAVE INCREASED ACTIVITY OF BOTH THE IDO AND GTP-CH1 PATHWAY, BUT DECREASED BH4 EFFICACY: CONSEQUENCES FOR FATIGUE AND WELL-BEING

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**Background:** Juvenile idiopathic arthritis (JIA) patients suffer from an inflammatory condition, resulting in painful joints. In addition, JIA patients often report symptoms of sickness behaviour, including depressive symptoms and fatigue. Recent animal studies suggest that proinflammatory cytokines produce sickness behaviour by increasing the activity of indoleamine-2,3-dioxygenase (IDO) and guanosinetriphosphate-cyclohydrolase-1 (GTP-CH1). Here it is hypothesised that inflammation in JIA patients affects the enzymatic activity of IDO and GTP-CH1

and the co-factor BH4. These compounds play a crucial role in the metabolism of the neurotransmitters serotonin and dopamine.

**Objectives:** The aim of our study was to reveal whether inflammation affects BH4, IDO and GTP-CH1 (enzymatic) activity in JIA patients.

**Methods:** Serum samples were collected of twenty-four JIA patients. In these samples, the concentrations of tryptophan, kynurenine, tyrosine, neopterin and phenylalanine were measured. An HPLC method with electrochemical detection was developed to quantify tryptophan, kynurenine and tyrosine. Neopterin and phenylalanine were quantified by ELISA. Kyn/trp ratio was measured as an index of IDO activity, while Phen/Tyr ratio was measured as an index of BH4 activity. Neopterin concentrations were used as an indirect measure of GTP-CH1 activity.

**Results:** JIA patients with high disease activity showed higher levels of both neopterin and kynurenine, and a higher ratio of both Kyn/Trp and Phen/Tyr and lower tryptophan levels than clinically inactive patients.

**Conclusions:** Altogether, these data support our hypothesis that inflammation increases the enzymatic activity of both IDO and GTP-CH1 and decreases the efficacy of the co-factor BH4. Further animal studies are needed to investigate whether inflammation-induced changes in these enzymatic pathways and co-factor lower the levels of the brain neurotransmitters dopamine and serotonin, and consequently produce sickness behaviour and fatigue.

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AB0888

### PLATELET COUNT IN ANKYLOSING SPONDYLITIS: CAN IT SHOW THE DISEASE ACTIVITY ?

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**Background:** C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are the main inflammatory biomarkers used in assessment of disease activity in numerous inflammatory diseases such as ankylosing spondylitis (SA). In recent years, it has been shown that Platelet count (PC) provided additional information on inflammatory status.

**Objectives:** The present study aimed to investigate the correlation between PC and clinical activity indices assessed by Bath ankylosing spondylitis disease activity index (BASDAI)

**Methods:** The study included 68 patients who fulfilled Assessment of Spondyloarthritis International Society Criteria. A cell blood count, including platelet count, ESR (mm/h), CRP (mg/L) and albumin (g/L), was obtained for each patient.

Disease activity measures at the time of blood sampling were obtained using the BASDAI. Statistical Package for Social Sciences (SPSS) was used for analysis.

**Results:** Of the 68 patients, 73.5% were male (Sex Ratio: 2.7). The mean age was 36±12.9 years. The mean disease duration was 40 months [0–192]. The average age of the onset of the disease was 36.6±11.9 years. No patient had ongoing infection at time of study. The mean BASDAI score was 5.1 [1.55–9.2]. Forty-one% of our patients (n=28) had active AS (BASDAI >4)

The mean ESR, CRP, albumin and PC were 39.4 (mm/h), 34.1 (mg/dL), 39.32 g/L and 311 (10<sup>3</sup>/mL), respectively.

There was a positive correlation between platelet count and following biomarkers: ESR (r: -0.481; p: 0.000), CRP (r: 0.417; p: 0.000) and albumin levels (r: -0.556; p: 0.000). A negative correlation between and Haemoglobin (Hb) was noted (r: -0.643; p: 0.000).

There was no significant difference in laboratory parameters (ESR, CRP, albumin, PC, Hb) between patients with active AS (BASDAI >4) and those with inactive AS (BASDAI <4) patients.

**Conclusions:** Although acute phase reactant such as ESR, CRP and PC mirror disease activity in AS,<sup>1</sup> their values were not associated with disease activity assessed by BASDAI in our study. However, new prospective studies including larger study groups are required to verify the findings of the present study.

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**Disclosure of Interest:** None declared

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**AB0889 CLINICAL CHARACTERISTICS OF 88 PATIENTS WITH PUSTULOTIC ARTHRO-OSTEITIS (PAO) IN JAPAN**

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**Background:** The prevalence rate of PPP in Japan is somewhat as 0.13%<sup>1)</sup>, accounting for 61% of cutaneous manifestations diseases associated with SAPHO syndrome<sup>2)</sup>. SAPHO syndrome<sup>3)</sup> is not a new disease concept in which the cause of the disease has been clarified but is a name that classified diseased groups by collecting known diseases. On the other hand, PAO is a concept of disease that is a "proper subset" of SAPHO syndrome and is the smallest unit disease concept. Therefore, detailed information on PAO was sought.

**Objectives:** To examine the clinical features and treatment of PAO

**Methods:** We conducted a multicenter, non-intervention retrospective study of 88 PAO patients who were able to visit directly in 4 hospitals in Japan from January to June 2017. the criteria of "Sonozaki et al. 1981 4)" was used for PAO diagnosis. Evaluation items were clinical features, image/blood biochemical examination, treatment methods.

**Results:** The average age at the time of visit was 55.4 years old, palmoplantar pustulosis/PAO onset age was 44.4 years old, 49.3 years old, the onset pattern was skin leading type/simultaneous onset/joint advanced type (66.7/25.6/7.7%). The clinical features were pain joints of 33.0% of the thoracic joints, 22.7% of the shoulder joints and 10.2% of the joints of the ankle joints, and the adhesion flame was the most abundant in the Achilles tendon at 21.4%. ASDAS-CRP was 1.4 ± 0.8 on average, breakdown was inactive disease 52.3%, moderate 22.7%, severe 22.7%, very high disease activity 2.3%, and insufficient disease activity remained in 25% of cases. Radiographic change showed in 81.8% of the sternum/the sternocostoclavicular joint, 33.0% of the spine, 31.0% of the sacroiliac joint (NY Ilor more), and 9.8% of the peripheral joint. MRI findings showed changes in intraosseous luminance in 76.9% around the sternum, 52.2% in the spine and 65.2% in the sacroiliac joint. Bone scintigraphy showed abnormal findings in the anterior chest 96.4%, spine 23.6% and sacrum 30.9%. Blood biochemical examination showed CRP 0.35±0.52 mg/dl, RF positive rate 9.4%, ACPA positive rate 5.1%. First-line drugs (NSAIDs, biotin, anti-bacterial drugs) and second-line drugs (Iguratomod sulfasalazine MTX) were selected as therapeutic agents. For other treatments, 64.8% of topical therapy, 12.5% of phototherapy and 18.6% of tonsillectomy were performed.

**Conclusions:** In this study, we reported the clinical features, radiological findings and treatments in 88 Japanese patients with PAO in Japan. The treatment outcome for PAO in Japan is not sufficient, and it is necessary to try to elucidate further disease condition.

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**AB0890 EFFICIENCY OF 8-YEAR EDUCATIONAL PROGRAMS FOR PRIMARY CONTACT PHYSICIANS IN DIAGNOSIS AND TREATMENT OF AXIAL SPONDYLOARTHRITIS IN KAZAN**

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**Background:** In recent years, there have been cardinal changes in terminology, understanding of pathogenesis of axial spondylitis (AxsSpA) and ankylosing spondylitis (AS), early diagnosis has improved. An important role is played by the level of awareness of primary care physicians in the early diagnosis of AxsSpA and AS.

**Objectives:** To evaluate the effectiveness of educational activities for primary contact physicians in AxsSpA (including AS) diagnostics for a long time.

**Methods:** From 2010 to the present time, educational activities are conducted for primary care physicians in diagnostics and tactics of managing patients with AS with discussion of the criteria for inflammatory back pain, options for onset and the algorithm for diagnosis and examination of patients with AxsSpA for primary contact physicians in Kazan. Since 2014, educational modules have been integrated into the system of continuing education of doctors. Assessment of the results of educational schools was carried out according to the analysis of reports of outpatient admission to rheumatologist of the City Rheumatological Centre in Kazan (Clinical Hospital # 7) and the analysis of medical records of patients sent to a rheumatologist in 2009 (base year) in comparison with 2010–2017 in the process of schools.

**Results:** In the process of conducting schools (2010–2017) the number of patients with AxsSpA and AS significantly increased for the first time this year. In 2010–2011, the number of patients almost doubled (575 pts in 2010, 683 pts in 2011) compared to 2009 (378 pts). The second sharp increase in the number of patients was observed in 2016 (1178 pts) and in 2017 (1298 pts).

The same dynamics was observed for AxsSpA patients (including AS) who applied for the first time to rheumatologist with a significant increase in patients in 2010–2011 (2009–118 pts, 2010–190 pts, 2011–204 pts) and in 2016–506 pts, 2017 year – 711 patients

"Peak" increase in the number of patients in 2010–2011 can be explained by the beginning of educational activities for doctors; in 2016–2017 – an increase in the number of activities (including remote ones), the amount of information, increased availability of MRI examinations for patients with AxsSpA.

Primary care physicians were more likely to refer patients with suspected AxsSpA or diagnosed AS, the percentage of discrepancies between diagnoses (referral and rheumatology) decreased from 78% in 2009 to 18.1% in 2011, 8.9% in 2013, 2.1% in 2015 and 3.3% in 2017.

The number of patients coming from the primary contact physician to rheumatologist with the required volume of examination (description of back pain, laboratory tests, HLAB27 determination, radiographs and/or MRI) increased significantly from 23.7% in 2009 to 87% in 2017, which allows to verify diagnosis without repeated consultations.

**Conclusions:** Educational programs for primary care physicians (lectures, schools, remote programs) have great importance for the timely diagnosis of AxsSpA, reducing the number of consultations before the diagnosis and with the subsequent appointment of adequate therapy.

**Disclosure of Interest:** None declared

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**AB0891 DISEASE ACTIVITY PREDICTS FUNCTIONAL IMPAIRMENT AND SPINAL MOBILITY IN AXIAL SPONDYLOARTHRITIS**

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**Background:** Axial Spondyloarthritis (axSpA) is a chronic inflammatory disease, mainly affecting the spine and sacroiliac joints. This results in progressive spinal immobility and can result in a level of disability comparable to Rheumatoid Arthritis<sup>1</sup>. The natural history of axSpA and relationships between active inflammation,

structural damage and functional impairment remain poorly understood. Previous studies have hypothesised that functional impairment and spinal mobility in axSpA are independently influenced by disease activity and radiographic damage<sup>1,2,3</sup>.

**Objectives:** To define the relationship between disease activity, spinal mobility and radiographic damage with other patient-reported outcome measures in axSpA.

**Methods:** We performed a cross-sectional analysis of axSpA patients attending the Royal National Hospital for Rheumatic Diseases, Bath. The most recent outcome measures for each patient were compared. Spinal mobility was assessed using the BASMI; structural radiographic damage by the mSASSS; disease activity by the BASDAI; functional impairment by the BASFI; fatigue by the FACIT score; work disability by the WPAI-overall; quality of life by the ASQoL; overall health by the EQ5D. We analysed the correlation between these variables, separately for patients with Ankylosing Spondylitis (AS) and non-radiographic axSpA (nr-axSpA).

**Results:** 721 axSpA patients were included for analysis (548 AS; 42 nrAxSpA; 39 inflammatory bowel disease-related SpA; 47 juvenile-onset SpA; 24 psoriatic SpA; 3 reactive SpA; 18 undifferentiated SpA). Results are summarised in table 1:

Abstract AB0891 – Table 1

AS (n=185–655)	BASMI	BASDAI	mSASSS
BASFI	.52**	.67**	.10
ASQoL	.26**	.69**	–0.14
FACIT	–0.14**	–0.61**	.18*
WPAI-overall	.18**	.54**	–0.07
EQ5D	–0.34**	–0.65**	.11
mSASSS	.63**	–0.13	
BASDAI	.18**		
nr-axSpA (n=15–41)	BASMI	BASDAI	
BASFI	.67**	.71**	
ASQoL	.38*	.64*	
FACIT	–0.34	–0.55**	
WPAI-overall	.10	.56**	
EQ5D	–0.24	–0.58	
BASDAI	.68**		

\*\*Correlation is significant at the 0.01 level (2-tailed); \*Correlation is significant at the 0.05 level (2-tailed)

**Conclusions:** Spinal mobility and disease activity are both correlated with functional impairment, along with other measures of disability and poor health in axSpA, with BASDAI the strongest predictor of BASFI. Consistent with other studies, BASDAI was more predictive of spinal mobility in nrAxSpA than AS patients ( $p=0.002$ , 1-tailed). Structural radiographic damage is the strongest predictor of spinal mobility in AS. BASMI scores merit further investigation to ascertain their potential as a surrogate for radiographic disease burden in axSpA.

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**Disclosure of Interest:** None declared

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#### AB0892 PREDICTING SYNDESMOPHYTE FORMATION IN AXIAL SPONDYLOARTHROPATHY

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**Background:** Axial spondyloarthropathy (axSpA) is a chronic inflammatory arthritis affecting the sacroiliac joints and spine. The consequence of inflammation in axSpA is new bone formation, or syndesmophytes, which can result in complete ankylosis of the spine. The pathogenesis of syndesmophyte formation is incompletely understood. It is agreed that presence of baseline syndesmophytes predicts further syndesmophytes, but other predictive factors have been difficult to define. In particular, the impact of extra-articular manifestations (EAMs) on syndesmophyte formation is unclear.

**Objectives:** 1. To assess the burden of radiographic disease in a well-characterised axSpA cohort.

2. To investigate demographic and disease-related variables associated with syndesmophytes (specifically EAMs).

**Methods:** A cross-sectional study of AxSpA patients was performed, comprising standardised clinical assessment and structured interviews. Validated measures of disease severity were used: BASDAI and ASDAS-CRP (disease activity), BASMI (spinal mobility), HAQ (disability), BASFI (function). Lateral x-rays of the lumbar and cervical spine were performed to quantify syndesmophytes using a validated score (mSASSS) ranging from 0–72, with higher numbers indicating a higher burden. BASRI-hip was used to determine hip involvement, assessed on x-ray of pelvis.

**Results:** One hundred and four patients with axSpA were included: 78.8% (n=82) male, 98.1% (n=102) Caucasian, average (SD) age 50.8 (12) years and average disease duration 25<sup>13</sup> years. Modified New York (mNY) criteria were fulfilled by 84.6% (n=88) of the cohort. An EAM was present in 29.1% (n=30) of patients. Uveitis was the most prevalent EAM (29%), followed by inflammatory bowel disease (IBD) (18.4%) and psoriasis (17.5%). Average (SD) BASDAI was 3.9 (2.2), ASDAS-CRP 2.3 (1), BASMI 4.2 (1.9), indicating a mild to moderate disease burden in the cohort.

Median (IQR) mSASSS was 9.5 (33.8), 10.6% (n=11) of patients had an mSASSS of 0% and 7.7% (n=8) had a bamboo spine. There was no significant difference in the median cervical and lumbar spine mSASSS scores (4 v 6,  $p>0.05$ ). The distribution of mSASSS was similar in males and females. HLA-B27 status had no effect on mSASSS scores.

Increasing mSASSS correlated significantly ( $p<0.05$ ) with increasing age ( $\rho=0.6$ ), longer disease duration ( $\rho=0.5$ ), rising BASMI ( $\rho=0.8$ ), higher BASFI ( $\rho=0.4$ ) and higher HAQ ( $\rho=0.3$ ). Worsening hip disease, as measured by BASRI, also correlated with an increasing mSASSS ( $\rho=0.4$ ,  $p<0.01$ ). There was also a statistically significant difference between patients who met mNY criteria compared to those that didn't (median 14.4 v 2.5,  $p<0.01$ ).

Patients with hypertension had a significantly higher median mSASSS score than patients without (25.4 v 7,  $p<0.01$ ). Smoking status, hypercholesterolaemia, ischaemic heart disease and diabetes had no impact on mSASSS.

The presence or absence of uveitis, psoriasis or IBD had no effect on syndesmophyte formation. Equally, peripheral arthritis had no effect. Patients with moderate or severe hip disease were more likely to have a higher mSASSS score (OR 3.8, 95% CI 1.5–9.3).

**Conclusions:** In keeping with previous literature, higher mSASSS was associated with more severe disease. However, in contrast to other published studies, gender had no effect on the severity of mSASSS in our cohort. EAMs did not affect the mSASSS score, but worse hip disease did. It remains a challenge to predict which patients will develop syndesmophytes.

**Disclosure of Interest:** None declared

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#### AB0893 INFLUENCE OF INFLAMMATION AND STRUCTURAL DAMAGE ON GLOBAL FUNCTIONING IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS – USING THE ASAS HEALTH INDEX IN ROUTINE CARE

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**Background:** Global functioning of patients with spondyloarthritis (SpA) can be influenced by many different factors. ASAS Health Index (ASAS HI) has aims to measure global functioning in patients with SpA. So far, its association with inflammatory spinal changes and structural damage has not been examined.

**Objectives:** To investigate the relationship between spinal mobility and self-report global functioning as assessed by the ASAS HI, and to study the influence of structural and inflammatory spinal changes on global functioning.

**Methods:** Patients from the outpatient clinic of our hospital suffering from axial or peripheral SpA completed questionnaires assessing disease activity and functioning (ASAS HI, pain, BASDAI, ASDAS, BASFI). Axial inflammation as detected by magnetic resonance imaging (MRI) was assessed by the Berlin score, structural damage by the modified Stokes ankylosing spondylitis (AS) Spine Score (mSASSS) and spinal mobility by the Bath AS Metrology Index (BASMI). Imaging were scored by two independent readers. Correlations between the ASAS HI and other health outcomes were analysed by Spearman's test. Logistic regression analyses were performed to investigate the association between functioning and other clinical characteristics.

**Results:** A total of 203 patients (76 non-radiographic (nr)-axSpA, 115 AS patients, and 12 with peripheral SpA (pSpA) were included: 63.5% male, mean (SD) age 46.6 (14.1), symptom duration 18.8 (12.8) years, and 76.4% HLA-B27 positive. The mean values of clinical assessments were ASAS HI 7.9 (4.0), BASDAI 5.0 (2.2), ASDAS 2.8 (1.1), BASMI 3.3 (1.8), pain 6.0 (2.6), and BASFI 5.0 (2.6). Elevated CRP levels were found in 37.4% of the patients, while 59.1% of the AS patients had syndesmophytes and 11.3% a bamboo spine. The median (IQR)



mSASSS value was 3.8 (IQR 1.0–22.1) in AS and 0.0 (IQR 0.0–1.4) in nr-axSpA patients. The mean Berlin AS Spine Score for patients with axSpA was 5.3 (SD 7.1). Patients received a treatment with NSAIDs (62.7%), DMARDs (20.9%) and/or biologics (49.4%). A significant correlation of the ASAS HI was found for BASMI ( $r=0.5$ ), BASDAI ( $r=0.7$ ), ASDAS ( $r=0.5$ ), BASFI ( $r=0.8$ ), BMI (0.3) and Berlin Score (0.3). ASAS HI did not correlate with radiographic damage (mSASSS  $r=0.2$ , presence of bamboo spine  $r=0.2$ ) and CRP ( $r=0.07$ ). Stratifying patients by symptom duration (cut-off 3 years) did not affect these results. Logistic regression showed influence of obesity but not of inflammation or structural damage on global functioning (table 1).

Abstract AB0893 – Table 1

	Univariable		Multivariable	
	OR (CI)	p	OR (CI)	p
Age	1.04 (1.02–1.06)	<b>0.001</b>	-	NS
Male sex	0.47 (0.24–0.93)	0.003	0.09 (0.01–0.71)	<b>0.022</b>
BMI	1.10 (1.03–1.18)	0.006	1.24 (1.05–1.48)	<b>0.013</b>
BASDAI, 0–10	1.35 (1.17–1.57)	<b>&lt;0.001</b>	-	NS
ASDAS	2.51 (1.76–3.57)	<b>&lt;0.001</b>	-	NS
BASFI, 0–10	2.03 (1.66–2.48)	<b>&lt;0.001</b>	1.85 (1.19–2.87)	<b>0.006</b>
BASMI, 0–10	2.0 (1.56–2.54)	<b>&lt;0.001</b>	-	NS
mSASSS, 0–72	1.02 (1.00–1.05)	0.089	-	NS
Berlin Score, 0–72	0.98 (0.91–1.04)	0.490	-	NS

**Conclusions:** The influence of obesity on functioning is remarkable in patients with SpA. In contrast, the influence of structural damage and spinal inflammation on functioning was limited in this study, probably due to the relatively low mSASSS and MRI scores. Further studies with inclusion of more severely affected patients are needed to study the association of functioning, spinal mobility, obesity and radiographic damage over a broader range of affected patients.

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AB0894

#### A COMPARISON OF CLINICAL FEATURES IN PATIENTS WITH SPONDYLOARTHRITIS AND UNILATERAL OR BILATERAL HIP ARTHRITIS

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**Background:** Axial spondyloarthritis (AS) is a frequent chronic and progressive disease that affects mainly young adults and is characterised by inflammation of the axial skeleton, but peripheral joints such as hips may also be involved. The incidence of hip involvement in AS is around 30%.<sup>1</sup> Nevertheless, data concerning clinical features in patients with spondyloarthritis comparing unilateral and bilateral hip arthritis are lacking.

**Objectives:** To compare clinical, functional and radiologic outcomes in patients with AS with unilateral or bilateral hip arthritis.

**Methods:** Cross-sectional study on 100 patients with AS according to the ASAS criteria of 2009<sup>2</sup> who had unilateral and bilateral hip joint lesions defined by hip pain, limited joint motion and radiographic hip abnormalities. Demographic and clinical outcomes were performed including HLA B27 status. Spinal mobility outcomes were assessed by Schöber index and Bath Ankylosing Spondylitis Metrology Index (BASMI). Radiographic measurements were performed and included Bath Ankylosing Spondylitis Radiology Index (BASRI) and modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS).

**Results:** Bilateral hip joint lesion was reported in 76% of patients which 14 were women and mean age was 37.14 years. Bilateral hip involvement was associated with less height ( $p=0.002$ ), more long disease duration ( $p=0.015$ ), more several clinical spinal involvements with more spinal stiffness ( $p=0.000$ ) and less spinal mobility ( $p=0.004$ ). Extra-articular manifestations were comparable in patients with unilateral and bilateral hip arthritis ( $p=0.55$ ), however HLA B27 antigen was significantly more common ( $p=0.003$ ) in patients with bilateral hip arthritis. BASRI hip ( $p=0.042$ ) and mSASSS ( $p=0.009$ ) scores were used to assess structural damage on plain radiographs and were significantly more important in bilateral involvement. Nevertheless, protrusive form was more frequent in patient with unilateral hip involvement ( $p=0.05$ ).

**Conclusions:** Bilateral hip arthritis seems to be more frequent and more severe than unilateral involvement in patients with AS.

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**Disclosure of Interest:** None declared

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AB0895

#### ARE LATERAL SPINE BONE MINERAL DENSITY MEASUREMENTS USEFUL IN AXIAL SPONDYLOARTHRITIS?

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**Background:** Bone loss leading to osteoporosis (OP) is a well-known feature of axial spondyloarthritis (AS) although this disease is characterised by calcification in extra osseous tissues and new bone formation. In fact, dual-energy X-ray absorptiometry (DEXA) is the most common imaging method used to measure the bone mineral density (BMD). However, many studies have shown an inferiority of the postero-anterior (PA) spine measurements in reflecting the bone loss compared to lateral spine measurements because of the bridging syndesmophytes which may overestimate the BMD.

**Objectives:** Our aim is to evaluate the Lateral spine BMD (L-BMD) in AS and to assess its association with the disease features.

**Methods:** Seventy-five patients who met the Modified New York Classification criteria for AS were enrolled in this cross-sectional study. BMD was measured using DEXA at PA lumbar, lateral lumbar and hip regions.

**Results:** Sixty-two men and 13 women were enrolled with an average age of 36.8 ± 11.8 years. Bone loss (osteopenia or OP) was noted in 65% of the patients ( $n=46$ ) in PA lumbar and in 63% in lateral lumbar ( $n=45$ ). In L-BMD, BMD was correlated with early menopause and vitamin D level ( $p=0.01$  and  $p=0.04$  respectively). T-score in lateral spine was correlated with coffee consumption ( $p=0.02$ ), physical inactivity ( $p=0.037$ ), sexual hormones disorders ( $p=0.02$ ), hip arthritis ( $p=0.017$ ), BASMI ( $p=0.001$ ), BASFI ( $p=0.03$ ) and ASDAS<sub>vs</sub> ( $p=0.03$ ) scores, ESR ( $p=0.003$ ) and CRP ( $p=0.03$ ) levels, and hip ( $p=0.004$ ), spine ( $p=0.007$ ) and total ( $p=0.001$ ) BASRI.

**Conclusions:** L-BMD seems to be a reliable measurement in AS, and may avoid the overestimation of the BMD values and allows consequently to detect spinal osteoporosis and prevent fractures in AS.

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AB0896

#### ASSOCIATION OF IGA ANTIBODIES AGAINST CD74 WITH PRODUCTION OF IL17A BUT NOT OF TNFALPHA IN PATIENTS WITH ACTIVE AXIAL SPONDYLOARTHRITIS

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**Background:** Axial spondyloarthritis (axSpA) is strongly associated with HLA-B27. Recently, IgA antibodies (Abs) against CD74 (IgA-anti-CD74) and T-cells carrying CD-74-specific T-cell receptors were also found to be associated with axSpA, especially in patients with ankylosing spondylitis, the radiographic form of axSpA. Tumour necrosis alpha (TNF $\alpha$ ) inhibitors and IL-17 antagonists are efficacious in patients with active axSpA.

**Objectives:** To investigate whether IgA-anti-CD74 Abs are associated with pro-inflammatory cytokines in the sera of patients with HLA-B27-positive and -negative patients with active axSpA.

**Methods:** Blood samples of 62 HLA-B27-positive and 58 HLA-B27-negative patients with axSpA (44% AS) prior to starting a biologic therapy were collected. A cytometric bead-array (CBA Flex Set) was used to measure serum levels of interleukin (IL)-17A, IL-6, IL-1 $\alpha$ , TNF $\alpha$ , and interferon (INF)- $\gamma$ . IgA-anti-CD74 Abs were measured by ELISA, using the predefined cut-off of 15 U/ml. Their mean concentrations were compared between groups using T-tests. The patients who were positive or negative for IgA-anti-CD74 Abs were compared using chi-square test.

**Results:** IgA-anti-CD74 Abs were detected in 54/120 axSpA patients (45%). There were no differences in the baseline demographics and clinical assessments in patients with or without IgA-anti-CD74 Abs. The presence of IgA-anti-CD74 Abs

was associated with higher serum concentrations of IL-17A ( $p=0.01$ ), irrespective of the presence of HLA-B27, CRP and IL-6 (both  $p<0.05$ ) but not TNF $\alpha$  ( $p=0.2$ ).

**Conclusions:** In a cross-sectional study, the presence of IgA Abs against CD74 was associated with serum levels of pro-inflammatory biomarkers such as CRP (and IL-6) and IL-17 but not TNF $\alpha$  irrespective of HLA-B27 status. Longitudinal prospective studies are needed to show that the measurement of IgA anti-CD74 Abs and/or serum cytokines can help to guide treatment decisions.

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#### AB0897 THE RELATIONSHIP BETWEEN DISEASE-SPECIFIC INDICES AND BALANCE IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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**Background:** Axial and periferal joint stiffness, impaired joint mobility and postural deformities may affect balance in AS. However factors affecting balance in AS patients are still unclear. There is limited literature investigating balance-related factors in patients with AS and the results are contradictory.

**Objectives:** The aim of the study was to investigate relationship between disease-specific indices and balance in patients with AS.

**Methods:** 72 patients (46 male, 26 female) with AS were included in the study. The demographic and anthropometric features (age, weight, height, body mass index (BMI)) of patients were recorded. Disease-specific indices used in the study were Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI) and Bath Ankylosing Spondylitis Mobility Index (BASMI). BASDAI for disease activity, BASFI for functional capacity, BASMI for spinal mobility were used. Static and dynamic balance was evaluated with Biodex Balance System SD. Limits of stability and bilateral stance (stable and unstable platform), single leg stance (stable platform) postural stability test results were recorded. Overall stability (OA) indices were used. A high score in the OA index indicates poor balance. Spearman correlation test used for statistical analysing. Correlation analyses were performed between BASDAI, BASFI, BASMI scores and Biodex test results

**Results:** The mean age of patients was 39,95±8,84 years and mean BMI was 26,55±3,82 kg/m<sup>2</sup>. BASDAI, BASFI and BASMI scores of patients are shown in table 1.

**Abstract AB0897 – Table 1.** BASDAI, BASMI and BASFI scores

	AS patients (n=72) Median (IQR 25–75)
BASDAI	2,10 (1,02–3,78)
BASFI	1,10 (0,30–2,74)
BASMI	2,20 (1,00–3,40)

Only positive weak correlation was found between BASFI score and right leg stance overall postural stability index ( $r=0,25$ ,  $p=0,034$ ). No other correlation was detected between BASDAI, BASFI, BASMI scores and Biodex balance test results.

**Conclusions:** The results of our study indicated that there is no relationship between BASDAI, BASFI, BASMI scores and balance except BASFI score and right leg stance postural stability. Our results contradict some previous studies while supporting some studies. This may be due to in our study BASDAI, BASFI and BASMI scores are lower than previous studies or the usage of different methods from previous studies for evaluating balance and postural stability in AS. Further studies are required to establish the actual status of relationship between balance and clinic measurements in AS patients.

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#### AB0898 COURSE OF ANKYLOSING SPONDYLITIS IN PREGNANCY

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**Objectives:** To study the effect of pregnancy on ankylosing spondylitis (AS) course.

**Methods:** 86 AS patients having pregnancy in the course of the disease were included into questionnaire survey. Patients' mean age was 34 [30:37] years, mean disease duration was 120 [72:180] month. The questionnaire items were designed to elucidate modifications in AS course during the last pregnancy with live birth outcome. The study is based on patient's self-reported health (SRH) status (improvement, worsening, no change).

**Results:** All responders reported delivery of full-term babies at mean 39 weeks [38:40] of gestation, vaginal delivery was documented by 46 (53,5%) responders, Caesarean section – by 40 (46,5%). AS worsening or improvement during all three trimesters is shown in the table 1.

**Abstract AB0898 – Table 1**

Trimester	Improvement n=42/ 48,8%	Worsening n=58/ 67,4%
I	30/34,8%	15/17,4%
II	21/24,4%	26/30,2%
III	18/20,9%	36/41,8%

Comparison of improvement rates in I and III trimesters,  $p=0,05$ .

Worsening of underlying disease (as compared to the condition 3 months prior to pregnancy) during whole pregnancy was reported by 3 (3,5%) women, absence of noticeable changes was reported by 13 (15,1%) patients, and AS improvement – by 9 (10,4%) participants.

61 (71%) of responders reported fluctuating AS activity during pregnancy. AS worsening was associated with exacerbation of back pain in 44 (51%), emergence and/or recurrence of arthritis – in 15 (17,4%), or uveitis – in 9 (10,4%), and other symptoms – in 11 (12,8%) patients.

**Conclusions:** Therefore, the majority of participants reported the diverse fluctuations in AS course during pregnancy, although 50% of responders reported the improvement in the course of the disease at least during one trimester (more often in the first). Nevertheless, almost 70% of responders reported AS worsening with exacerbations rates increasing in parallel with increasing gestation age. 50% of participants noticed worsening back pain, although special attention should be given to correct evaluation of AS activity in these patients keeping in mind the increased physiological load on the backbone during the second half of pregnancy.

**Disclosure of Interest:** None declared

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#### AB0899 ANKYLOSING SPONDYLITIS AND PREGNANCY: DATA FROM THE QUESTIONNAIRE SURVEY-BASED PILOT STUDY

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**Objectives:** To study parity and pregnancy outcomes, as well as causes for not getting pregnant in women with ankylosing spondylitis (AS).

**Methods:** 326 AS female patients were covered by questionnaire survey during the period from November 2016 until October 2017. Mean age of the participants was 32 [28:36] years, mean AS duration – 102 [48:168] months. The questionnaire items covered such issues as prior pregnancies, maternal and neonatal outcomes and potential reasons for not getting pregnant.

**Results:** 194 (59%) (mean age 34,1±5,4 y) females out of 326 surveyed had from 1 to 8 pregnancies, totally 396. Pregnancy outcomes are presented in the table 1.

Abstract AB0899 – Table 1

Pregnancy outcomes	Number of pregnancies (n=396)		p
	before AS onset n=185	after AS onset n=211	
Childbirth: n/%	100/54%	143/67.8%	0.004
-vaginal delivery n	76 (76% of deliveries)	78 (54.5% of deliveries)	0.0005
- Caesarean section n	24 (24% of deliveries)	65 (45.5% of deliveries)	0.0008
Woman's choice abortion	61/33%	30/14.2%	0.0000
Unfavourable maternal outcome *	24/13%	38/18%	0.17
Neonate's birth weight [Me±IQR] (g)	3240 [3050:3600]	3.260 [2950:3600]	0.3
Neonate's birth length [Me±IQR] (cm)	52 [51:53]	51 [50:52]	0.02
Apgar score at 1 min after birth [Me±IQR]	8 [7:8]	8 [7:8]	0.8

\* – non-developing pregnancies, spontaneous abortions, medical abortions and preterm births.

There were no pregnancies in 132 (41%) surveyed females (mean age 29,1 ±5,4 y).

Reasons and causes for not getting pregnant in 132 AS females:

- 48% cases – social, household/domestic and familial, including spouses' unwillingness to have children;

- 44% – presence of AS (fear of teratogenic effect of pharmacotherapeutic agents – 18%, fear of AS inheriting by the baby – 3%, physician's forewarnings – 8%, a combination of abovementioned causes – 15%);

- 8% – infertility.

**Conclusions:** Therefore, data from questionnaire survey of females with AS demonstrates that presence of AS does not increase the incidence of unfavourable maternal outcomes of pregnancies, or negatively affects anthropometric parameters of neonates. Of notice is the fact, that women's choice abortions become more rare after AS diagnosis is established. The rate of Caesarean sections is higher in AS patients. Fear of potentially harmful effects of the disease and it's therapy on the fetus and the baby underlies 30% of all not getting pregnant cases among AS female patients of child-bearing age.

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## Psoriatic arthritis

### AB0900 DESCRIPTIVE STUDY OF PSORIATIC ARTHRITIS IN A HISTORICAL COHORT OF 383 PATIENTS AT A UNIVERSITY HOSPITAL

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**Background:** There are few recent large cohort epidemiological studies that analyse the clinical profile of patients with psoriatic arthritis (PsA) who require biological treatment, as well as pharmacological survival and reasons for the suspension of these treatments.

Abstract AB0900 – Table 1

N	383	Basal radiological involvement	
Age at PsA (years), mean (SD)	45.9 (14.5)	Erosive arthritis (%)	33.1
Male sex, n (%)	203 (53)	Mutilating arthritis (%)	1.9
History of psoriasis (%)	84.8	Sacroiliitis (%)	21.2
Nail involvement (%)	46.3	Syndesmophytes (%)	5
Dactylitis (%)	32.9	<b>Immunity</b>	
Enthesitis (%)	36.9	RF positive (%)	6.3
DAS-28 (ESR), mean (SD)	3.5 (1.46)	ANA positive (%)	14.5
CRP mg/L, mean (SD)	8.11 (15.9)	HLA B27 positive (%)	14.1
ESR mm/h, mean (SD)	20.3 (19.2)	<b>Treatment</b>	
<b>Comorbidities</b>		NSAID (%)	96.7
Dyslipidemia (%)	34.2	csDMARDs (%)	84.8
AH (%)	20.9	bDMARDs (%)	32.3
Obesity (%)	28.2		

CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; AH: arterial hypertension; RF: rheumatoid factor; ANA: anti-nucleotide antibodies; NSAID: non-

steroidal anti-inflammatory drugs; csDMARDs: conventional synthetic disease-modifying antirheumatic drugs; bDMARDs: biological disease-modifying antirheumatic drugs.

**Objectives:** To describe the clinical, demographic, epidemiological and radiographic characteristics of patients with PsA in our centre, as well as pharmacological survival and reasons for the suspension of different biological treatments.

**Methods:** Retrospective analysis of patients with PsA treated between 1985 and 2015 at a University Hospital with a referral area of 8 50 000 inhabitants. Demographic, clinical, laboratory and imaging data, as well as patients' clinical and medical treatment records.

**Results:** The main characteristics of the cohort are summarised in table 1:

Approximately one third of patients with PsA (32.3%) required treatment with a biological drug during the course of their disease. The most frequently prescribed first-line drugs (89.5%) were tumour necrosis factor- $\alpha$  inhibitors (TNFi).

During the course of their disease, 27 (21.9%) patients who started biological treatment received a biological drug other than TNFi. Of the 124 patients who started treatment with a biological DMARD, more than half (65, 52.8%) required a change to a second drug, and of these, 27 (41.5%) changed to a third, with up to 7 different biological drugs required in one case. The mean survival time for the first bDMARD was 42.8±42.3 months, with secondary failure the most frequent cause of treatment change (37.8%), followed by adverse effects (27.1%) and primary failure (18.9%). The adverse effects registered were: 20% infections, 20% appearance of neoplasms, 5% allergic reactions and 55% other causes.

**Conclusions:** PsA presents a similar distribution by sex and is usually diagnosed at around the age of 50, having been preceded by cutaneous involvement. PsA is an entity of considerable severity and up to a third of patients will require biological treatments during its evolution. More than half of them will receive a second biological treatment. The retention rate of each drug varies but tends to decrease with each drug change.

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### AB0901 VASPIN AND LIPOCALIN2 LEVELS IN PSORIATIC ARTHRITIS

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**Background:** Psoriatic arthritis (PsA) is a type of spondyloarthropathies which is affiliated with psoriasis. Metabolic syndrome, diabetes mellitus and cardiovascular diseases are comorbid conditions associated with psoriatic arthritis. Adipokines are suggested to be playing proinflammatory or antiinflammatory roles in the proceeding of inflammatory situations.

**Objectives:** The aim of this study is to investigate the recently interested adipokines vaspin and lipocalin2 levels and their association with disease activity of patients diagnosed with psoriatic arthritis.

**Methods:** The study was conducted between October 2017 and January 2018 at the Rheumatology Clinic of Ankara Numune Training and Research Hospital, Turkey. The vaspin and lipocalin2 levels of 50 PsA patients, diagnosed according to the Classification Criteria for Psoriatic Arthritis (CASPAR), and 36 age- and sex-matched healthy subjects were analysed in current study. The disease activity was assessed by using Psoriasis Area Severity Index, Bath Ankylosing Spondylitis Functional Index, Bath Ankylosing Spondylitis Disease Activity Index and Disease Activity Index for Psoriatic Arthritis. Indexes were applied to the patients in order to evaluate the disease activity.

**Results:** No significant difference was found between groups with respect to age, sex and body mass index. There was significant difference between vaspin (p=0.001) and lipocalin2 (p=0.014) levels among the PsA patients and control groups. There was no significant difference between the groups in terms of disease activity (p>0.05).

Abstract AB0901 – Table 1. The clinical and laboratory parameters in two groups.

	PsA patients (n=50)	Healthy subjects (n=36)	P value
	Mean(±SD)	Mean(±SD)	
Males/Females	15/35	11/25	0.956
Age (years)	44.58 (13.88)	43.08 (11.03)	0.57
Vaspin (ng/L)	391.63 (436.4)	176.67 (122.75)	0.001
Lipocalin2 (ng/L)	5.2 (2.67)	1.94 (2.09)	0.014

PsA: Psoriatic Arthritis, SD:Standard deviation

**Conclusions:** The results of this study points out the possible role of vaspin and lipocalin2 in PsA. In our knowledge, this is the first study comparing the vaspin and lipocalin2 levels of patients with PsA to healthy subjects and these findings



may pioneer further studies investigating the usage of adipokines such as vaspin and lipocalin2 levels as biomarkers in the diagnose and disease course of PsA.

**Disclosure of Interest:** None declared

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**AB0902 EFFICACY OF TOFACITINIB BY BACKGROUND METHOTREXATE DOSE IN PATIENTS WITH PSORIATIC ARTHRITIS: A POST-HOC ANALYSIS OF POOLED DATA FROM 2 PHASE 3 TRIALS**

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**Background:** Tofacitinib is an oral Janus kinase inhibitor for the treatment of psoriatic arthritis (PsA). The efficacy of tofacitinib has been evaluated in 2 Phase 3 studies in patients (pts) with PsA.

**Objectives:** To describe the efficacy of tofacitinib by background methotrexate (MTX) dose in pts with PsA.

**Methods:** This post-hoc analysis utilised efficacy data pooled from 2 Phase 3, randomised, double-blind, placebo-controlled studies (OPAL Broaden [12 months; NCT01877668] and OPAL Beyond [6 months; NCT01882439]) in pts with a diagnosis (≥6 months) of active PsA (≥3 swollen and ≥3 tender joints). Pts in OPAL Broaden were tumour necrosis factor inhibitor (TNFi)-naïve and had an inadequate response (IR) to ≥1 conventional synthetic disease-modifying antirheumatic drug (csDMARD). Pts in OPAL Beyond had an IR to ≥1 TNFi. Pts were randomised to tofacitinib 5 or 10 mg twice daily (BID), placebo or adalimumab 40 mg subcutaneous every 2 weeks (OPAL Broaden; adalimumab data not shown). All pts received a stable dose of 1 csDMARD (eg MTX, leflunomide or sulfasalazine) as background therapy. The maximum dose of MTX allowed per protocol was 20 mg/week. Efficacy outcomes for tofacitinib at Month 3 were evaluated by background MTX dose (≤15 vs >15 mg/week) and included: ACR20/50/70 response rates (≥20/50/70% improvement from baseline, respectively), Health Assessment Questionnaire-Disability Index (HAQ-DI) response rate (reduction from baseline ≥0.35 points) and mean change from baseline in HAQ-DI score. Analyses were based on the full analysis set for pts receiving MTX on Day 1; pts with missing data were considered as having a non-response for binary endpoints. No statistical testing was performed.

**Results:** In total, data from 556 pts who received tofacitinib plus MTX only or placebo plus MTX only (tofacitinib 5 mg BID, n=186; tofacitinib 10 mg BID, n=178; placebo, n=192) were included in this analysis. Most pts were treated with background MTX at doses ≤15 mg/week (n=371, 66.7%; mean [SD] dose, 12.6 [3.1] mg/week) vs >15 mg/week (n=185, 33.3%; mean [SD] dose, 19.8 [0.8] mg/week). Baseline demographics and disease characteristics were generally similar between arms in MTX dose groups (table 1). At Month 3, tofacitinib 5 and 10 mg BID were generally associated with numerically greater ACR and HAQ-DI response rates and greater changes from baseline in HAQ-DI score compared with placebo. The magnitude of tofacitinib effects on efficacy outcomes appeared broadly similar between background MTX dose groups (table 1).

**Abstract AB0902 – Table 1.** Patient demographics and disease characteristics at baseline, and efficacy outcomes at Month 3 by MTX dose

	MTX dose ≤15 mg/week			MTX dose >15 mg/week		
	Tofacitinib 5 mg BID (N=186)	Tofacitinib 10 mg BID (N=178)	Placebo (N=192)	Tofacitinib 5 mg BID (N=186)	Tofacitinib 10 mg BID (N=178)	Placebo (N=192)
<b>Patient demographics and disease characteristics</b>						
Female, n (%)	99 (53.2)	79 (44.3)	76 (39.6)	43 (23.1)	31 (17.4)	33 (17.2)
Age, years (SD)	46.9 (12.4)	46.7 (12.4)	46.8 (12.4)	46.8 (12.4)	47.4 (12.4)	46.9 (12.5)
Duration of disease, years (SD)	8.8 (7.4)	7.9 (6.3)	8.8 (8.3)	9.1 (8.7)	7.4 (6.9)	8.1 (8.1)
Number of swollen joints (range)	9.2 (3-49)	9.2 (3-49)	9.2 (3-49)	9.2 (3-49)	9.2 (3-49)	9.2 (3-49)
Number of tender joints (range)	10.8 (4-49)	10.8 (4-49)	10.8 (4-49)	10.8 (4-49)	10.8 (4-49)	10.8 (4-49)
CRP, mg/L (range)	1.1 (0.1)	1.2 (0.6)	1.2 (0.7)	1.2 (0.6)	1.2 (0.6)	1.1 (0.6)
ESR, mm/h (range)	22.2 (22.1)	19.3 (21.3)	17.7 (21.2)	19.9 (22.0)	18.4 (22.4)	18.1 (22.4)
MTX dose, mg/week (range)	12.6 (3.1)	12.6 (3.1)	12.6 (3.1)	19.8 (0.8)	19.8 (0.8)	19.8 (0.8)
<b>Efficacy outcomes at Month 3</b>						
ACR20 response rate, % (95% CI)	47.4 (35.1-59.8)	54.8 (41.5-68.1)	58.3 (45.0-71.6)	51.4 (38.1-64.7)	51.8 (38.5-65.1)	58.8 (45.5-72.1)
ACR50 response rate, % (95% CI)	37.4 (25.1-49.7)	39.3 (26.0-52.6)	41.5 (28.2-54.8)	37.7 (24.4-51.0)	37.6 (24.3-50.9)	41.5 (28.2-54.8)
ACR70 response rate, % (95% CI)	37.4 (25.1-49.7)	39.3 (26.0-52.6)	41.5 (28.2-54.8)	37.7 (24.4-51.0)	37.6 (24.3-50.9)	41.5 (28.2-54.8)
HAQ-DI response rate (reduction from baseline ≥0.35 points), % (95% CI)	47.4 (35.1-59.8)	54.8 (41.5-68.1)	58.3 (45.0-71.6)	51.4 (38.1-64.7)	51.8 (38.5-65.1)	58.8 (45.5-72.1)
Change from baseline in HAQ-DI score (95% CI)	-0.21 (0.01)	-0.20 (0.04)	-0.27 (0.01)	-0.29 (0.04)	-0.28 (0.04)	-0.21 (0.01)

\*Among pts with baseline HAQ-DI score ≥0.35  
Missing values for ACR20/50/70 response rates and HAQ-DI response rate were considered as non-response to treatment  
LSM were calculated based on a mixed model for repeated measures without imputation for missing values

The maximum permitted dose of MTX was 20 mg/week  
The analyses included all pts who received MTX as background therapy only on Day 1 in the FAS

ACR, American College of Rheumatology; BID, twice daily; CRP, C-reactive protein; FAS, full analysis set; HAQ-DI, Health Assessment Questionnaire-Disability Index; LSM, least squares mean; MTX, methotrexate; n, number of pts with response; N, number of pts included in the analysis; N1, number of pts included in the HAQ-DI response analysis; N2, number of pts evaluable for change from baseline in HAQ-DI at Month 3; pts, patients; SD, standard deviation; SE, standard error

**Conclusions:** The results of this pooled analysis suggest that the efficacy of tofacitinib in pts with PsA was greater than placebo and does not differ when evaluated by background MTX dose (≤15 vs >15 mg/week), although small pt numbers in some groups may limit the conclusions that can be made. These results are consistent with findings from similar analyses of tofacitinib in pts with rheumatoid arthritis.

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**AB0903 EFFICACY OF TILDRAKIZUMAB IN ETANERCEPT PARTIAL OR NONRESPONDERS**

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**Background:** Etanercept (ETN) is an anti-tumour necrosis factor (TNF) medication that was among the first biologics approved for psoriasis. Additional medications have been developed or are in development for psoriasis, and patients who do not adequately respond to ETN may benefit from these more recent biologics.

**Objectives:** Here we report the efficacy of tildrakizumab (TIL), a humanised anti-IL-23p19 monoclonal antibody, as evaluated in patients with moderate to severe chronic plaque psoriasis who were partial (Psoriasis Area and Severity Index [PASI] ≥50 <75) or nonresponders (PASI <50) to ETN and subsequently rerandomized to TIL in the phase 3 reSURFACE 2 trial (NCT01729754).

**Methods:** Patients with psoriasis (≥10% body surface area, Physician's Global Assessment [PGA], and PASI ≥12) participated in reSURFACE 2, a 3-part, 52 week, randomised controlled trial. In Part 1 (Weeks 0–12), patients were randomised to subcutaneous TIL 200 mg, TIL 100 mg, or placebo (PBO) administered at Weeks 0 and 4, or ETN 50 mg administered twice weekly. In Part 2 (Weeks 12–28), TIL and ETN patients remained on the same treatment (TIL administered at Week 16; ETN once weekly), whereas PBO patients were rerandomized to TIL 100 or 200 mg. In Part 3 (Weeks 28–52), ETN responders (PASI ≥75) were discontinued, and partial and nonresponders were switched to TIL 200 mg (administered at Weeks 32, 36, and 48). For this post hoc analysis, the proportion of patients (±SD) with PASI response and PGA response (score of 0 [clear] or 1 [minimal]) with at least a 2-grade score reduction from baseline) were determined at Week 52. Primary results from the trial have been previously reported.<sup>1</sup>

**Results:** In total, 1090 patients were randomised. Of the 313 patients randomised to ETN, by Week 28 there were 83 partial responders and 39 nonresponders. At Week 52 (after 20 weeks of TIL treatment) for ETN partial responders, 75%±5%, 34%±5%, 15%±4%, and 58%±5% had achieved PASI 75, 90, 100, and PGA response of 0/1, respectively, with TIL 200 mg treatment. At Week 52 for ETN nonresponders, 54%±6%, 31%±5%, 10%±3%, and 56%±5% had achieved PASI 75, 90, 100, and PGA response of 0/1, respectively, with TIL 200 mg treatment. Adverse events were similar in patients switched from ETN to TIL at Week 28, compared with the patients who were maintained on TIL through Week 52.

**Conclusions:** A substantial portion of patients with moderate to severe chronic plaque psoriasis who were partial or nonresponders to ETN may respond after switching to treatment with TIL 200 mg. TIL may be a reasonable option for those who do not achieve adequate response to ETN.

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#### AB0904 CORRELATION OF RAPID3 AND PROMIS10 IN PATIENTS WITH PSORIATIC ARTHRITIS

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**Background:** In addition to clinician assessment and laboratory tests, patient-reported outcomes (PROs) are important for managing and improving the quality of care in patients with psoriatic arthritis (PsA). The RAPID3 was originally developed for use in patients with rheumatoid arthritis, but it may be used in clinical practice to assess disease activity in patients with PsA.<sup>1</sup> The PROMIS10 is a general (nondisease-specific) PRO instrument that measures physical, mental, and social health.<sup>2</sup> Developed for the general population, PROMIS10 has not yet been specifically validated in PsA.

**Objectives:** To evaluate the relationship between RAPID3 and PROMIS10 in patients with PsA.

**Methods:** US adults with a self-reported diagnosis of PsA were recruited through CreakyJoints (www.CreakyJoints.org), an online patient support community comprising patients with arthritis and arthritis-related diseases and their caregivers. Respondents completed an online survey that was designed to collect data on socio-demographics and clinical symptoms and included the RAPID3 and PROMIS10 to evaluate disease activity and health-related quality of life (HRQoL), respectively. The RAPID3 consists of three patient self-reported scores (0–10): functional impairment, pain, and patient global assessment; total score  $\leq 3.0$  = near remission, 3.1 to 6.0 = low disease severity, 6.1 to 12.0 = moderate disease severity, and  $\geq 12.1$  = high disease severity. PROMIS10 is a 10-item survey measuring physical and mental domains; individual scores are transformed to T-score distributions normalised to the general population. PROMIS10 individual scores and global physical and mental health T-scores were stratified by RAPID3 disease severity and compared across RAPID3 severity levels using Kruskal-Wallis or ANOVA tests, respectively. Spearman's correlation coefficient was calculated between RAPID3 total score and the PROMIS10 physical health and mental health T-scores, respectively.

**Results:** Among 203 respondents, the mean (SD) age was 51.6 (10.8) years and 172 (84.7%) were female. The mean (SD) cumulative RAPID3 score was 14.7 (5.8) with mean (SD) functional impairment, pain tolerance, and patient's global estimate scores of 3.3 (1.8), 6.0 (2.3), and 5.4 (2.5), respectively. Patients' mean (SD) PROMIS10 global physical and mental health T-scores were 36.4 (7.3) and

40.2 (9.3), respectively. The mean individual domain scores and global T-scores worsened with increasing RAPID3 disease severity levels (all  $p < 0.001$ ) (table 1). PROMIS10 physical and mental health T-scores showed a strong ( $r_s = -0.84$ ) and moderate correlation ( $r_s = -0.57$ ) with RAPID3, respectively.

**Abstract AB0904 – Table 1.** PROMIS10 Scores and Impact of PsA on Work by RAPID3 Disease Activity in Patients with PsA

	RAPID3 Disease Activity*				P value
	Near Remission	Low Severity	Moderate Severity	High Severity	
PROMIS10 domain, mean (SD)	n = 5	n = 14	n = 45	n = 139	
Overall health	3.60 (0.55)	2.93 (0.73)	2.87 (0.69)	2.10 (0.73)	< 0.0001
Quality-of-life	4.20 (0.84)	3.07 (0.83)	3.16 (0.74)	2.29 (0.89)	< 0.0001
Physical health	3.60 (0.55)	2.79 (0.89)	2.73 (0.62)	1.97 (0.73)	< 0.0001
Mental health	4.40 (0.55)	3.14 (1.10)	3.11 (1.05)	2.63 (1.10)	0.0004
Satisfaction with social activities/relationships	4.20 (0.45)	3.00 (0.96)	3.09 (1.06)	2.06 (1.09)	< 0.0001
Ability to carry out every day physical activities	4.80 (0.45)	4.36 (0.63)	3.80 (0.73)	2.68 (0.76)	< 0.0001
Emotional distress	4.80 (0.45)	3.43 (1.16)	3.16 (0.80)	2.65 (1.00)	< 0.0001
Fatigue	4.00 (1.00)	3.50 (0.65)	3.04 (0.71)	2.25 (0.76)	< 0.0001
Pain	4.20 (0.45)	3.93 (0.27)	3.38 (0.49)	2.40 (0.56)	< 0.0001
Global physical health T-score	52.84 (3.07)	46.66 (3.69)	42.35 (4.54)	32.91 (5.06)	< 0.0001
Global mental health T-score	58.44 (5.86)	45.17 (7.60)	44.84 (7.53)	37.50 (8.56)	< 0.0001

PROMIS10, Patient-Reported Outcome Management Information System Global Health short form; RAPID3, Routine Assessment of Patient Index Data 3.

\* Disease severity classified by RAPID3 scores:  $\leq 3.0$  = near remission; 3.1 to 6.0 = low severity; 6.1 to 12.0 = moderate severity;  $\geq 12.1$  = high severity.

**Conclusions:** RAPID3 and PROMIS10 physical health T-scores were strongly correlated in patients with PsA. PROMIS10 mental health scores moderately correlated with RAPID3, suggesting the mental health questions add a different construct. PROMIS10 and RAPID3 are relatively short questionnaires that can be used in the real world to track and monitor disease symptoms and HRQoL in patients with PsA.

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#### AB0905 LONG-TERM (5-YEAR) EFFICACY AND SAFETY OF APREMILAST MONOTHERAPY IN DMARD-NAÏVE SUBJECTS WITH ACTIVE PSORIATIC ARTHRITIS

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**Background:** Apremilast (APR) is an oral phosphodiesterase 4 inhibitor that helps regulate the immune responses that cause joint inflammation and other manifestations of psoriatic arthritis (PsA), including skin disease.

**Objectives:** To describe the long-term (5 year) efficacy and safety of APR monotherapy in DMARD-naïve subjects with active PsA from the phase 3 PALACE 4 study.

**Methods:** Subjects were randomised (1:1:1) to receive placebo, APR 30 mg BID (APR30), or APR 20 mg BID (APR20). At Week 16, subjects were eligible for early escape; placebo subjects were re-randomised to APR treatment, and APR subjects remained on their assigned dose. At Week 24, all subjects remaining on placebo were re-randomised to APR. Double-blind treatment continued to Week 52, with open-label APR treatment for up to 4 additional years.

**Results:** A total of 527 subjects were randomised and received  $\geq 1$  dose of placebo (n=176), APR30 (n=176), or APR20 (n=175). Among subjects randomised to APR30 at baseline, 45.5% (80/176) completed the Week 260 visit. At Week 52, modified ACR20, ACR50, and ACR70 responses were achieved by 58.0%, 29.8%, and 15.5% of subjects receiving APR30, respectively, regardless of when APR was started (baseline, Week 16, or Week 24). Rates of improvement in PsA signs and symptoms and physical function were sustained up to Week 260 with continued APR30 treatment, including reduction rates in SJC of 84.8% and in TJC of 76.4% (table 1). At Week 260, 65.8%, 39.0%, and 20.3% of subjects achieved a modified ACR20, ACR50, and ACR70 response, respectively, and 71.2% of APR30 subjects with baseline enthesitis achieved a MASES of 0; 95.1% with baseline dactylitis achieved a dactylitis count of 0. At Week 260, 52.9% of subjects achieved a HAQ-DI MCID  $\geq 0.35$ , 60.3% achieved a PASI-50 response, and 47.6% achieved a PASI-75 response (table 1). No new safety concerns were identified with APR up to 260 weeks. During Weeks>208 to $\leq$ 260, the most common adverse event (AEs) among APR30-exposed subjects was nasopharyngitis (6.9%). Serious AEs occurred in 5 APR30 subjects; serious infections were reported in 2 APR30 subjects (pelvic abscess and bacterial urinary tract infection), and no opportunistic infections were reported during Weeks>208 to $\leq$ 260.

#### Abstract AB0905 – Table 1

	Outcomes at Week 260	
	APR30 n=119 <sup>a</sup>	
ACR20, n/m (%)	77/117 (65.8)	
ACR50, n/m (%)	46/118 (39.0)	
ACR70, n/m (%)	24/118 (20.3)	
SJC, mean % change	-84.8	
TJC, mean % change	-76.4	
MASES of 0, n/m (%) <sup>b</sup>	47/66 (71.2)	
Dactylitis count of 0, n/m (%) <sup>c</sup>	58/61 (95.1)	
HAQ-DI (0-3), mean change	-0.38	
HAQ-DI MCID $\geq 0.35^d$ , n/m (%)	63/119 (52.9)	
PASI-50, n/m (%) <sup>e</sup>	38/63 (60.3)	
PASI-75, n/m (%) <sup>f</sup>	30/63 (47.6)	

**Conclusions:** APR monotherapy demonstrated sustained response or improvements in PsA signs and symptoms, including SJC and TJC, enthesitis, dactylitis, physical function, and psoriasis in the population of subjects continuing treatment over 260 weeks. APR continued to demonstrate a favourable safety profile and was generally well tolerated.

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#### AB0906 IXEKIZUMAB IMPROVES FATIGUE IN A SUBSET OF PATIENTS WITH PSORIATIC ARTHRITIS

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**Background:** Psoriatic arthritis (PsA) is a chronic, systemic, inflammatory disease with both articular and extra-articular symptoms including joint pain, enthesitis, dactylitis, and fatigue. Fatigue is increasingly recognised as a priority symptom to patients and has been added to the PsA core set of outcomes for clinical trials.<sup>1</sup> The best instrument to assess fatigue has not yet been defined.

**Objectives:** To assess fatigue improvement following treatment with ixekizumab (IXE), an anti-interleukin (IL)-17A monoclonal antibody, relative to placebo (PBO) in PsA patients.

**Methods:** In two phase 3 randomised controlled trials, patients naïve to and experienced with biologic disease-modifying antirheumatic drugs (SPIRIT-P1, SPIRIT-P2, respectively) received subcutaneous PBO, ADA 40 mg every 2 weeks (SPIRIT-P1 only; reference arm), or IXE 80 mg every 2 weeks (Q2W) or every 4 weeks (Q4W) after a 160 mg starting dose for up to 24 weeks. At Week 16, all patients considered inadequate responders (IR) received rescue therapy. PBO and ADA patients were re-randomised (1:1) to Q2W or Q4W at Week 16 (IR) or Week 24; ADA patients underwent a washout prior to IXE treatment. Patients rated their worst level of fatigue during the past 24 hours at baseline, Week 4, 12, 16, 24, 32, and 52 on the 11-point Fatigue Severity Numeric Rating Scale (Fatigue NRS; not yet validated) where 0=no fatigue and 10=as bad as you can imagine. The minimal clinically important difference (MCID) was defined as an improvement  $\geq 3$  on the Fatigue NRS.

**Results:** At Week 24 significantly more patients in both studies achieved fatigue improvements  $\geq 3$  on the Fatigue NRS with both IXE doses versus PBO (table 1; NRI). When evaluating group level changes, statistically significant improvements on the Fatigue NRS were observed with both IXE doses versus PBO prior to Week 24 in both studies. At Week 24, significance was observed in the SPIRIT-P2 study only (table 1; MMRM). For patients who continued IXE treatment beyond Week 24, mean improvements on the Fatigue NRS persisted through Week 52 (table 1; MI).

Table 1

	SPIRIT-P1				SPIRIT-P2		
	PBO n=106	ADA n=101	Q4W n=107	Q2W n=103	PBO n=118	Q4W n=122	Q2W n=123
Baseline fatigue mean (SD)	5.37 (2.22)	5.45 (2.34)	5.76 (2.29)	5.52 (2.44)	5.9 (2.28)	5.9 (2.48)	6.0 (2.49)
Change from baseline at Week 24 <sup>a</sup>	-1.3 (0.25)	-1.5 (0.24)	-1.6 (0.24)	-1.9 (0.24)	-0.7 (0.37)	-2.0 (0.35)	-2.1 (0.34)
LS mean (SE)					**	**	**
Number (%) of patients achieving MCID at Week 24 <sup>b,c</sup>	19 (20.4)	28 (32.9)	35 (36.8)*	34 (40.5)*	6 (5.6)	33 (30.8)	36 (33.6)
Change from baseline at Week 52 <sup>d</sup> mean (SE)			-2.2 (0.28)	-2.3 (0.28)	-2.2 (0.24)	-2.2 (0.27)	

<sup>a</sup>Mixed models repeated measures (MMRM) analysis was used to calculate change from baseline.

<sup>b</sup>Analysis of patients with Fatigue NRS  $\geq 3$  at baseline. SPIRIT-P1: PBO, n=93; ADA, n=85; Q4W, n=95; Q2W, n=84. SPIRIT-P2: PBO, n=108; Q4W, n=107; Q2W, n=107.

<sup>c</sup>Nonresponder imputation (NRI) was used to impute missing data based on logistic model.

<sup>d</sup>Multiple imputation (MI) was used to impute missing data.

\*p<0.05 vs PBO; \*\*p<0.001 vs PBO.

**Conclusions:** In a subset of PsA patients, clinically meaningful improvements in fatigue level were observed following IXE treatment. Fatigue improvement persisted with up to 1 year of IXE treatment.

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**AB0907 TREATMENT PATTERNS IN PSORIATIC ARTHRITIS IN US AND EUROPE: RESULTS FROM A REAL-WORLD INTERNATIONAL SURVEY**

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**Background:** With the availability of a greater range of Psoriatic Arthritis (PsA) treatment options, it is increasingly necessary to understand their use and impact on disease control in real-world practice.

**Objectives:** To assess treatment patterns and their impact on clinical outcomes among PsA patients currently receiving conventional/targeted synthetic disease-modifying anti-rheumatic drugs (cs/tsDMARD) or biologic DMARD (bDMARD).

**Methods:** A point in time survey was conducted in 2015 across the US, France, Germany, Italy, Spain and UK. Patients had physician-confirmed PsA and had to have been receiving their current cs/tsDMARD (bio naïve) or bDMARD (1st or 2nd line) for ≥6 months. Physicians provided information on demographics, treatment history, disease severity, clinical measures included body surface area (BSA), joint count, flare/remission status. Student t-tests, Pearson's chi-squared and Fisher's exact tests were used to compare physician-reported patient profile variables, clinical status and treatment outcomes.

**Results:** 519 physicians (331 rheum, 188 derms) provided data for 2467 PsA patients, 1463 of whom met the inclusion criteria (1136 EU, 327 US). No significant differences were observed between EU and US patients in demographics (male 52.6%, mean age 49.0 years), disease duration 6.3 years; disease severity 29.1% moderate to severe). In the EU, 32.3% patients were on cs/tsDMARDs, 55.4% 1st-line bDMARD, 12.3% 2nd-line bDMARD vs 21.7%, 58.4%, 19.9% respectively in the US.

Time in months (mo) from diagnosis to first cs/tsDMARD was similar in the EU and US (EU mean 4.7 mo; US 8.1 mo, p=0.24), from 1st cs/tsDMARD to 1st bio (EU 37.4 mo; US 29.4 mo, p=0.15). Patients in the EU received more cs/tsDMARDs prior to bDMARD initiation than US patients (mean 1.4 v 0.8; p<0.001). US patients were more likely to have bDMARD without combination cs/tsDMARDs (US 65.1% vs EU 52.3%; p=0.004).

Patients receiving cs/tsDMARDs had a worse clinical profile than those on 1st-line bDMARD in all areas other than joint count. Patients on 2nd-line bDMARD had more symptoms, more affected joints and more likely to flare vs 1st-line bDMARD. They had more affected joints but were less likely to flare vs cs/tsDMARD. These findings were directionally similar in the EU and US (table 1). BSA was higher for cs/tsDMARD patients than for any bDMARD patients.

Table 1

	Current cs/tsDMARD (n=438)	Current ±Line bDMARD (n=820)	P value (cs/tsDMARD v 1st Line bDMARD)	Current 2nd Line bDMARD (n=205)	P value (2nd Line bDMARD v cs/tsDMARD)	P value (2nd v 1st Line bDMARD)
Mean No. of PsA Symptoms	1.7	1.4	<0.001	1.9	0.378	<0.001
Mean No. of Joints Affected	3.2	3.3	0.531	4.0	<0.001	<0.001
Patients currently flaring	6.7%	3.4%	0.032	5.4%	<0.001	<0.001
Currently not in Remission	60.5%	39.5%	<0.001	45.9%	<0.001	0.112
Mean BSA	11.4%	7.8%	<0.001	8.6%	0.001	0.583

**Conclusions:** Only 39%–60% of patients were considered by physicians as in remission, revealing a considerable unmet need in both the EU and US in patients treated with cs/tsDMARDs and bDMARDs. Further research is needed to identify patients on cs/tsDMARDs who may be a candidate for advanced therapy and to recognise patients who might fail on bDMARD who therefore may benefit from a different therapeutic alternative.

**Disclosure of Interest:** A.-M. Orbai Grant/research support from: AbbVie, Celgene, Eli Lilly, Horizon, Janssen, Novartis, Pfizer, Consultant for: Eli Lilly, Janssen, Novartis, Pfizer, UCB, L. Gossec Grant/research support from: UCB, Lilly,

Pfizer, BMS, Consultant for: AbbVie, BMS, Celgene, Janssen, Novartis, Pfizer, Roche UCB, S. Lobosco Employee of: Adelphi Real World, R. Moon Employee of: Adelphi Real World, O. Massey Employee of: Adelphi Real World, J. Piercy Employee of: Adelphi Real World, J. Cappelleri Shareholder of: Pfizer, Employee of: Pfizer, L. Fallon Shareholder of: Pfizer, Employee of: Pfizer, P. Young Employee of: Pfizer, A. Romero Employee of: Pfizer, M.-A. Hsu Shareholder of: Pfizer, Employee of: Pfizer

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**AB0908 ABILITY OF THE REDUCTIVE X-RAY SCORE FOR PSORIATIC ARTHRITIS (REXSPA) TO DETECT CHANGE IN AN OBSERVATIONAL COHORT OF PATIENTS WITH PSA**

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**Background:** The measurement of radiographic joint damage is important in characterising disease severity, progression, and prognosis in psoriatic arthritis (PsA). Existing radiographic measures are time-consuming to perform, leading to limited data collection from existing longitudinal observational studies.

**Objectives:** We have previously proposed a Reductive X-ray Score for Psoriatic Arthritis (ReXSPA)<sup>1</sup> as more feasible method, and in this study set out to examine the sensitivity of ReXSPA in a new cohort of patients.

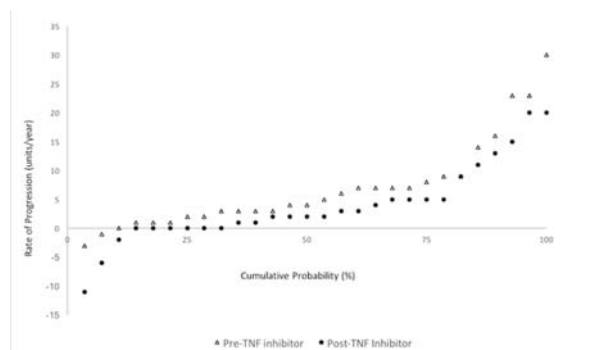
**Methods:** A retrospective sample of 28 patients who had hand and feet radiographs at 3 time points (5 years before [T<sup>0</sup>], at the time of [T<sup>1</sup>], and 5 years post [T<sup>2</sup>] commencement of anti-TNF treatment) were taken from the Bath longitudinal PsA cohort. Radiographs were scored for erosion, joint space narrowing and proliferation to calculate the Sharp-van der Heijde modified method (VDH) and ReXSPA scores. A sample of 9 radiographs were scored by all assessors (WT, AA and AA) to determine inter- and intra-rater reliability using intra-class correlation coefficients (ICC). Sensitivity to change was determined from timepoint T<sup>0</sup> to T<sup>2</sup> using the Standardised Response Mean (SRM) and Smallest Detectable Change (SDC).

**Results:** The patients' mean age (SD) at T<sup>0</sup> was 61 years (13.4), the mean disease duration was 11.2 years (11.14). Patients were followed up for a mean (SD) of 10.2 years (2.76). Overall inter- and intra-rater reliability for ReXSPA and VDH were 0.80 and >0.92 and 0.91 and >0.90 respectively. The median (IQR) of ReXSPA score was 8.5 (1–14), 12.5 (5–20) and 14.5 (8–36) at T<sup>0</sup>, T<sup>1</sup>, and T<sup>2</sup> respectively. The percentage SDC was 0.91 for the ReXSPA method and 0.77 for the VDH method, and the SRMs were 0.92 and 0.87 respectively (table 1), demonstrating the sensitivity of both methods in detecting change. There was a trend towards slowing in radiographic progression following the initiation of TNF-inhibitors, but ReXSPA was less sensitive compared to the VDH and was not able to detect a significant change in the rate of progression post-TNF inhibition (p 0.08) (Graphic 1).

Abstract AB0908 – Table 1. Sensitivity to change of each scoring method

Method	Mean Change	SD of change	SEM	SRM	SDC	SDC as% of total score
VDH	22.11	19.14	3.62	0.87	4.09	0.77
Erosion	7.29	10.62	2.01	1.46	2.27	0.71
JSN	16.96	15.17	2.87	0.89	3.24	1.56
ReXPSA	10.9	10.0	1.89	0.92	2.14	0.91
Erosion	3.21	5.31	1.00	1.65	1.13	1.03
JSN	6.36	5.11	0.97	0.80	1.09	1.24
Proliferation	0.96	2.32	0.44	2.40	0.50	1.39

Sharp-van der Heijde modified method (VDH), Standard deviation (SD), Standard error of mean (SEM), Standardised response mean (SRM), Smallest detectable change (SDC).



**Abstract AB0908 – Figure 1.** Cumulative probability plot demonstrating ReXSPA progression pre- and post- TNF inhibition

**Conclusions:** The RexSPA is a reliable and sensitive alternate scoring method for the detection of radiographic progression in an observational cohort of patients with PsA, but not as sensitive to change as the VDH method.

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- [1] Tillett W, et al. (2016) Novel Composite Radiographic Score for Longitudinal Observational Studies of Psoriatic Arthritis: A Proof-of-concept Study. *J Rheum*; 43(2):367–370

**Disclosure of Interest:** None declared

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AB0909

#### CERTOLIZUMAB PEGOL'S EFFECTIVENESS, RETENTION RATE AND SAFETY IN PSORIATIC ARTHRITIS. ROUTINE CLINICAL PRACTICE DATA

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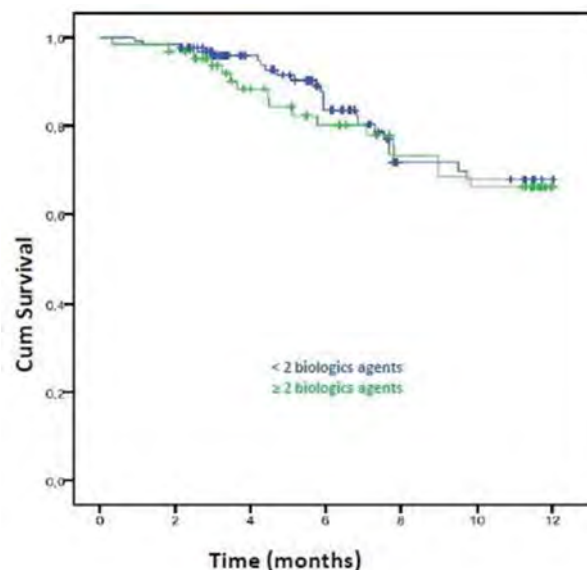
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**Background:** Certolizumab pegol (CZP) is the only antiTNF pegylated without Fc available for patients with psoriatic arthritis (PsA). The efficacy and safety of CZP in clinical trials is known, but there are few published data on the effectiveness of CZP in a setting of usual clinical practice.

**Objectives:** To evaluate the effectiveness and safety of Certolizumab Pegol (CZP) in a real in PsA patients.

**Methods:** Multicentric cohort of PsA patients treated with CZP according routine clinical practice. Study approved by local Ethics Committee. Maximum time of observation was 12 months. Effectiveness variables: SJC, TJC, PtGA (Patient Global Assessment) and DAS28-CRP. Safety variables: discontinuation rate.

**Results:** 262 patients with PsA were included: 43.5% male, mean (SD) age 49.9 (11.9) years, mean (Q1-Q3) disease duration 6.9 (1.9–9.3) years, 14.9% of patients HLAB27 positive, mean (SD) IMC (kg/m<sup>2</sup>) 26.9 (4.7), never smokers 70.3%. Extra-articular manifestations ever: Psoriasis (90%; PASI<sub>10</sub> ≥10 40.9%), enthesitis (44.4%), dactylitis (41.9%), nail disease (32%), inflammatory bowel diseases (4.9%), 37.3% of the PsA patients had bone erosions and 3% arthritis mutilans. 48.9 patients received 1 prior csDMARD and 52.1% at least 2 csDMARD. Prior bDMARD: 28.4% none; 38.1% 1, 33.5% ≥2. 29.6% of PsA patients received CZP in monotherapy. Mean time on treatment with CZP 10 months.



**Abstract AB0909 – Figure 1.** CZP retention rate and biologics exposure (n° of previous biologics)

Statistically significant differences in SJC, TJC and DAS28-CRP were observed at the last visit comparing with baseline (table 1). Percentage of patients with enthesitis at baseline (25.4%) decrease to 9.5% at the last visit; 73.2% of the patients had a resolution of the enthesitis (MASES=0). The percentage of patients with dactylitis at baseline (29.1%) decrease to 8.6% in the last visit; 82.5% of these patients had a resolution of the dactylitis. Statistically significant reduction of patients with nail disease was observed from 30.6% to 16.4%.

According to Kaplan-Meier analysis, the drug survival of CZP was 78.2%, and no differences were observed in patients who received CZP as first/second biologic or after more than 1 failure to other biologicals agents (Figure1).

262 patients were included in the safety analysis, 21.8% withdrawn treatment: 12.6% due to lack of effectiveness, 5.3% due to intolerance and 3.8% other reasons.

**Abstract AB0909 – Table 1.** Effectiveness

	Baseline	Last visit
DAS28; mean (SD)	4.6 (0.9)	3.8 (1.0)*
TJC; mean (SD)	7.2 (5.1)	4.0 (4.0)*
SJC; mean (SD)	5.0 (3.7)	2.8 (2.8)*
PtGA; mean (SD)	6.9 (1.7)	4.3 (2.5)

\*p<0,001, Wilcoxon's test

**Conclusions:** In this study of routine clinical practice CZP was effective in patients with PsA, with a significant decrease in DAS28-CRP and the percentage of patients with enthesitis and dactylitis. The retention rate of certolizumab pegol was not affected by the number of previous biological treatments.

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**AB0910 LONG-TERM GOLIMUMAB RETENTION RATE IN PATIENTS WITH PSORIATIC ARTHRITIS. IS CONCOMITANT DMARD IMPORTANT?**

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**Background:** The efficacy of Golimumab treatment in psoriatic arthritis (PsA) patients has been widely documented.

**Objectives:** The aim of this study was to analyse the long-term retention rate of golimumab and to identify independent predictors of drug retention in patients with PsA including concomitant synthetic disease-modifying antirheumatic drugs (sDMARD)

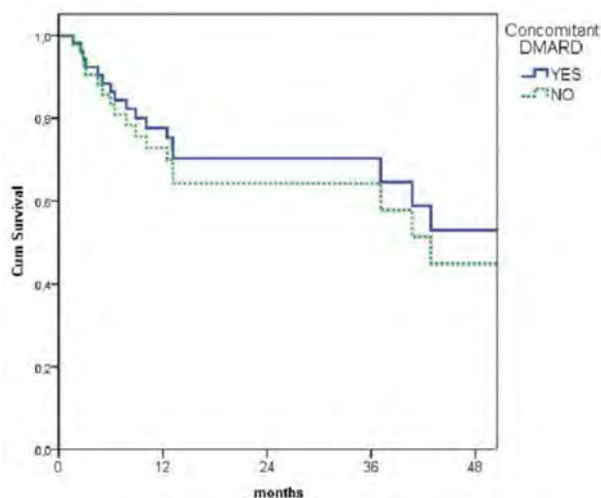
**Methods:** Prospective monocentric cohort of PsA patients treated with golimumab according to clinical practice. Study was approved by local Ethics Committee. Demographic and clinical variables were analysed with Cox proportional hazard regression model.

**Results:** 48 patients were included, 20/48 (41.7%) oligoarticular, 19/48 (39.6%) polyarticular and 9/48 (18.7%) with peripheral and axial PsA. The baseline characteristics of the patients are shown in table 1.

**Abstract AB0910 – Table 1.** Baseline demographic and clinical characteristics of the patients.

Age –mean (SD)-years	48.3 (11.1)
Female gender (%)	25 (52.1%)
Mean evolution time- (SD)- years	8.4 (7.9)
TJC –mean (SD)	4.1 (4.1)
SJC – mean (SD)	2.9 (2.7)
CRP mg/dl – mean (SD)	0.6 (0.7)
DAS 28- CRP – mean (SD)	3.7 (1.5)
Concomitant DMARD (%)	24 (50%)
Biological Therapy naïve (%)	25 (52.1%)

Follow-up time was 89.25 patients-year. Mean survival time was 40.3 months (95% CI: 32.0–48.5). Age, mean evolution time and previous biological use were significant in the univariate analysis. Concomitant sDMARD had no influence on golimumab retention rate (HR: 1.3; 95% CI: 0.5–3.2; p: 0.6). Figure 1. When golimumab was used as first or second biologic treatment, it had a better retention rate than when it was used as third or fourth, but did not reach statistical significance (HR: 2.3; IC 95%: 0.8–6.2; p=0.1). 18/48 patients (37.5%) withdrew golimumab treatment. 13/18 (72.2%) due to lack of efficacy, 1/18 (0.6%) due to adverse events and 4/18 (22.2%) due to other reasons.



**Abstract AB0910 – Figure 1.** Golimumab retention rate and concomitant DMARD

**Conclusions:** Real-world Golimumab retention rate in patients with PsA was good and did not depend on concomitant treatment with sDMARD. When used as first or second biologic, Golimumab retention rate tended to be better.

**Disclosure of Interest:** None declared

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**AB0911 THE RELATIONSHIP BETWEEN NEUROPATHIC PAIN AND DISEASE ACTIVITY, SLEEP, FATIGUE, QUALITY OF LIFE IN PATIENTS WITH PSORIATIC ARTHRITIS**

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**Background:** Neuropathic pain (NP) is composed of several abnormal sensations, including burning, prickling hyperalgesia and allodynia. NP is a common problem in rheumatic diseases such as rheumatoid arthritis and ankylosing spondylitis due to inflammatory processes. Previous studies showed that NP in other rheumatic diseases had a negative influence on sleep and quality of life.<sup>1,2</sup>

**Objectives:** To examine the relation of neuropathic pain symptoms in Psoriatic Arthritis (PsA) with demographic, clinical and functional parameters.

**Methods:** PsA patients according to CASPAR criteria were recruited into the study. Demographic and clinical parameters were noted. PainDETECT measurement tool was used for evaluation of NP. Physical examination such as manual muscle testing and sensory examination for hyperalgesia and allodynia was performed (pinprick and light touch test). Disease Activity Score-28 (DAS-28) was noted for disease activity. Associations of NP with quality of life, sleep and fatigue were analysed by filling out Psoriatic Quality of Life (PsAQoL), Pittsburgh Sleep Quality Index (PSQI), Multidimensional Assessment of Fatigue (MAF). PainDETECT scores were categorised as no NP (<12 points), ambiguous NP (13–18 points), probable NP (≥19 points). Group analysis was performed with Independent-Samples Kruskal-Wallis test. Spearman correlation coefficient (rho) was used for correlations between functional parameters. p<0.05 was accepted as significant.

**Results:** Forty eight PsA patients (31 female, 17 male) with a mean age 50.4 years (SD:10.0) and mean disease duration 92.2 months (SD: 90.2) were recruited into the study. The number of patients with ambiguous NP was 6 patients (4 female, 2 male) and probable NP was 12 patients (10 female, 2 male). The mean scores of PSQI, PsAQoL and MAF were significantly higher in patients with NP (p<0.05). There was no difference in mean scores of DAS-28 and disease duration among groups. The correlations between PainDETECT and other functional parameters were found moderate-strong as PSQI (rho=0.43, p=0.002), MAF (rho=0.44, p=0.002), PsAQoL (rho=0.66, p=0.0005). Also, the probability of NP existence increased with the age (rho=0.40, p=0.01). There was no significant correlation between and clinical parameters such as disease duration and DAS-28 (p>0.05).

**Conclusions:** These findings suggest that a substantial number of PsA patients suffering from NP. The neuropathic pain symptoms are found to be associated with worse self-reported quality of life and sleep disturbances. It is important to consider the existence of NP in the assessment and treatment process of PsA.

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**Disclosure of Interest:** None declared

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**AB0912 TWO-YEAR EFFICACY AND SAFETY OF GUSELKUMAB FOR TREATMENT OF MODERATE-TO-SEVERE PSORIASIS: PHASE 3 VOYAGE 1 TRIAL**

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**Background:** Guselkumab (GUS) is an interleukin-23 inhibitor recently approved in the US for treatment of moderate-to-severe psoriasis.

**Objectives:** Efficacy and safety data for up to 100 wks of GUS treatment are reported.

**Methods:** In the VOYAGE 1 Phase 3, randomised, double-blind, placebo/active comparator-controlled trial, 837 patients were randomised at baseline to placebo (PBO) at wks0/4/12 then GUS 100 mg at wks16/20 and q8w (n=174); GUS at wks0/4/12, and q8w (n=329); or adalimumab (ADA) 80 mg at wk 0, 40 mg at wk1, and q2w through wk47 then GUS at wk52 and q8w (n=334). Efficacy was assessed using nonresponder imputation through wk48 and treatment failure rules from wks52–100.

**Results:** Among patients randomised to GUS, or PBO→GUS at wk16, efficacy (PASI, Psoriasis Area and Severity Index; IGA, Investigator's Global Assessment) was maintained from wks52–100 with continuous GUS treatment. Among those



randomised to ADA (→GUS at wk52), efficacy improved from wks52–100. Similar findings were observed for patient-reported outcomes (PSSD, Psoriasis Symptoms and Signs Diary; DLQI, Dermatology Life Quality Index; table 1). Through wk100, there were no disproportionate increases in rates of Adverse Events (AEs) compared with rates through wk48. Serious AE rates were low and remained stable; no TB, opportunistic infections, or serious hypersensitivity reactions were reported.

**Abstract AB0912 – Table 1.** Efficacy assessments in VOYAGE 1 (wks48/52–100); n%

	PBO→GUS		GUS		ADA→GUS	
	wk52	wk100	wk52	wk100	wk52	wk100
<b>n</b>	161	158	307	290	279	275
<b>PASI90</b>	127 (78.9)	130 (82.3)	246 (80.1)	238 (82.1)	141 (50.5)	223 (81.1)
<b>PASI100</b>	75 (46.6)	87 (55.1)	155 (50.5)	142 (49.0)	67 (24.0)	142 (51.6)
<b>Mean%PASI improvement(SD)</b>	94.6 (9.1)	95.5 (7.8)	92.3 (17.3)	93.1 (16.6)	77.6 (31.9)	94.2 (12.6)
<b>IGA0/1</b>	142 (88.2)	134 (84.8)	254 (82.7)	239 (82.4)	168 (60.4)	231 (84.0)
<b>IGA0</b>	86 (53.4)	93 (58.9)	165 (53.7)	156 (53.8)	76 (27.3)	153 (55.6)
					<b>ADA</b>	<b>ADA→GUS</b>
	<b>wk48</b>	<b>wk100</b>	<b>wk48</b>	<b>wk100</b>	<b>wk48</b>	<b>wk100</b>
<b>PSSD symptom score=0<sup>ab</sup></b>	46/129 (35.7)	49/118 (41.5)	104/248 (41.9)	89/225 (39.6)	63/273 (23.1)	94/225 (41.8)
<b>PSSD sign score=0<sup>ab</sup></b>	37/129 (28.7)	44/118 (37.3)	89/248 (35.9)	69/225 (30.7)	51/274 (18.6)	66/226 (29.2)
<b>DLQI0/1<sup>ac</sup></b>	111/159 (69.8)	126/152 (82.9)	200/320 (62.5)	202/284 (71.1)	124/319 (38.9)	194/262 (74.0)

PASI90/100, 90.100% improvement in PASI score, IGA0/1=minimal or cleared(0) psoriasis, <sup>a</sup>Data not collected at wk52, <sup>b</sup>Pts with baseline PSSD scores>0, <sup>c</sup>Pts with baseline DLQI scores>1

**Conclusions:** Efficacy among GUS patients was maintained through 2 years of continuous treatment. Efficacy among ADA→GUS patients improved from wks52–100. GUS was well-tolerated, with a similar safety profile as previously reported.

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#### AB0913 TO DETERMINE THE ASSOCIATION BETWEEN PLAQUE AND NON PLAQUE PSORIASIS WITH THEIR JOINT MANIFESTATION IN PSORIATIC ARTHRITIS PATIENT – A SINGLE CENTRE EXPERIENCE IN MALAYSIA

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**Background:** Psoriatic arthritis (PsA) which is a member of the spondyloarthritides includes spinal and peripheral joint involvement. It affects women and men equally. The clinical patterns of PsA were classified into 5 groups according to Moll and Wright.<sup>1</sup> Psoriasis is a common chronic inflammatory skin disease and chronic plaque psoriasis is the commonest form.

**Objectives:** To study the relationship between plaque and non-plaque psoriasis with their joint manifestation and to describe the demographic characteristics of PsA patients.

**Methods:** This was a retrospective study. The electronic medical records of all PsA patients under rheumatology clinic Hospital Sultan Ismail followed up from 1/1/2009 to 31/12/2017 were reviewed. Data on demography, type of skin disease, joint manifestation, past medical history, fasting serum lipid and body mass index were obtained and analysed.

**Results:** We identified 163 patients, 84 were male patients with male to female ratio of 1.06. The Malays (84/163) were the majority being affected, followed by the Chinese (46/163), Indians (30/163) and others (3/163). The patients were divided into plaque psoriasis (140/163) and non-plaque psoriasis (23/163). The commonest joint involvement in the study was peripheral joint involvement (121/163), axial involvement (22/163) and both axial and peripheral joint involvement (20/

163). The peripheral joint involvement was categorised as polyarthritis (67/121), followed by oligoarthritis (47/121), distal interphalangeal arthritis (4/121) and arthritis mutilans (3/121). In the study, we divided the patients into plaque psoriasis [peripheral joint involvement (102/140); axial involvement (16/140); both (18/140)] and non-plaque psoriasis [peripheral joint involvement (15/23); axial involvement (6/23); both (2/23)] and analysed the results by using the SPSS logistic regression. It showed no significant association between type of skin psoriasis with its joint manifestation. (p>0.05).

Amongst the 163 patients, 68/163 (42%) had hypertension, 50/163 (31%) had diabetes mellitus, 32/163 (20%) had hypercholesterolemia, 12/163 have ischaemic heart disease, 1 patient had congestive heart disease, 3 had breast cancer, 1 had hepatocellular carcinoma and 2 have chronic kidney disease and cerebral vascular disease respectively.

The fasting serum lipid (FSL) was taken for 140 of them (23 patients no data available) and it was noted in 64/140 (without background history of hypercholesterolemia was noted to have FSL≥5.18 mmol/L). 37/64 have borderline high total cholesterol (5.18 mmol/L –<6.2 mmol/L) and 27/64 have high total cholesterol (≥6.2 mmol/L) according to ATP iii cholesterol classification.<sup>2</sup> 43% (61/142 patients) had body mass index in the overweight group, 29% (41/142 patients) in the obese group and 25% (36/142 patients) in normal group according to WHO classification.<sup>3</sup>

**Conclusions:** There was no association between types of skin psoriasis with their joint manifestation. There was a significant number of patients who had deranged fasting serum lipid and majority of them have BMI in the overweight and obese group.

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**Disclosure of Interest:** None declared

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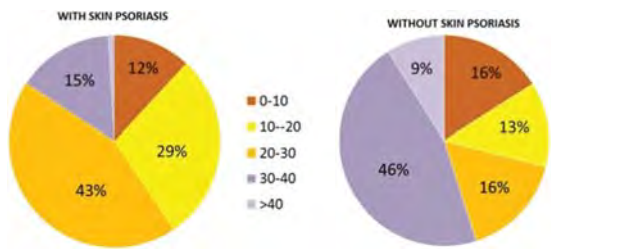
#### AB0914 COMPARISON OF 25-HYDROXYVITAMIN D3 SERUM LEVELS IN PATIENTS WITH PSORIATIC ARTHRITIS WITH OR WITHOUT PSORIASIS SKIN INVOLVEMENT

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**Objectives:** To determine 25-hydroxyvitamin D3 (25OH-D3) serum levels in patients with psoriatic arthritis (PA) and to assess differences according to the presence or absence of psoriasis skin involvement. To evaluate the response to vitamin D oral supplements in case of deficiency in both groups.

**Methods:** We conducted an observational retrospective study including patients with diagnosis of PA according to the CASPAR classification criteria who had at least one serum determination of 25OH-D3 in the last 36 months. Clinical and epidemiological data were collected, including arthritis distribution, age of diagnosis, presence of psoriasis skin involvement, treatment received and serum 25OH-D3 levels at baseline and within the subsequent 3 months if treatment with oral supplements had been initiated. Patients already receiving oral vitamin D supplements at baseline were excluded.

**Results:** Sixty patients met the inclusion criteria and were analysed. 42 were female (70%), with a mean age of 47.6 years (range: 30–82). Psoriasis skin involvement was present in 40 patients and preceded onset of arthritis in 80% of them (20% with psoriatic nail dystrophy). Regarding 25OH-D3 levels, mean value was 17.99±13.23 ng/dL. In the global analysis, 7 patients (11.6%) had levels between 0–10 ng/dL, 22 patients (36.6%) between 10–20 ng/dL, 23 patients (38.3%) between 20–30 ng/dL, 6 patients (10%) between 30–40 ng/dL and 2 patients had ≥40 ng/dL. In our sample, 58.53% of patients with psoriasis skin involvement had 25OH-D3 levels higher than 20 ng/dL, in contrast to the group without skin involvement, who reached sufficiency levels only in 37.5% of the cases. In the comparative analysis, patients with psoriasis skin involvement had a mean 25OH-D3 serum level of 20.88 ng/dL whereas patients without skin involvement had lower levels (mean value 19.42 ng/dL). Similarly, patients with skin psoriasis had more frequently 25OH-D3 levels between 20–30 ng/dL (insufficiency) compared to those without this manifestation, who presented lower levels (44% vs 16%) but without statistically significant difference. Results are shown in Figure 1. Finally, all patients presenting 25OH-D3 deficiency at baseline (<20 ng/dL) were treated with oral supplements (calcifediol 0.266 mg every two weeks). Of them, 23 patients had a second determination of 25OH-D3 within the subsequent 3 months, with only 13 patients reaching sufficient levels (56%), whereas the rest did not respond to the dose administered. No statistically significant differences were found in the response depending on the presence or absence of cutaneous psoriasis.



**Abstract AB0914 – Figure 1.** 25-Hydroxyvitamin D3 levels in patients with Psoriatic arthritis with and without psoriasis skin involvement (ng/dL)

**Conclusions:** In patients with PA, the presence of psoriasis skin involvement correlates with higher 25OH-D3 serum levels. This finding could be explained by the treatment received in these patients for moderate-severe skin involvement, which includes topical vitamin D analogues and phototherapy that could increase 25OH-D3 serum levels. After oral supplements, there was no statistically significant difference in the percentage of patients that reached sufficiency levels in both groups.

**Disclosure of Interest:** None declared

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#### AB0915 BONE MINERAL DENSITY AND FRACTURE FREQUENCIES IN PATIENTS WITH PSORIASIS OR PSORIASIS ARTHRITIS

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**Background:** Reports on the prevalence of osteoporosis, osteoporotic fractures and risk factors for osteoporosis in patients with Psoriasis or Psoriasisarthritis are scarce, and the published results on this are, at least in part, contradictory. Additionally, there is no firm understanding of the impact of potential risk factors such as smoking and low Vitamin D (Vit D) levels have on the occurrence of osteoporotic fractures in this patient group.

**Objectives:** Rh-GIOP is an ongoing prospective study monitoring glucocorticoid (GC)-induced osteoporosis of rheumatic patients, established in 2015 at the Charité University Hospital. To date, the database comprises clinical data and bone mineral density data measured by dual x-ray absorptiometry (DXA) of 592 patients with inflammatory rheumatic diseases. (ClinicalTrials.gov Identifier NCT02719314) The objective of this cross-sectional analysis was to evaluate the prevalence of osteoporosis and frequency of fractures in patients with Psoriasis (PSO) or Psoriasisarthritis (PSOA). Additionally, smoking and Vit D status were investigated as possible risk factors for low BMD.

**Methods:** We evaluated the initial visit of 55 patients with PSO (80% female) or PSOA (60% female). Descriptive analyses were performed, and values are displayed as means and standard deviations. For subgroup analyses non-parametric tests were used.

**Results:** Overall mean age was 60 years ( $\pm 12$  years), and 69% of the patients were female. The mean disease duration was 16 $\pm$ 13 years and patients generally showed a good functional status as quantified by the Health Assessment Questionnaire (HAQ mean: 1.0 $\pm$ 0.8). While osteoporosis and osteopenia were present in 16% and 38%, respectively, osteoporotic fractures were found in 33% of all patients. However, the family history for osteoporosis was positive in 20% of the patients. The prevalence of osteopenia and osteoporosis was higher in PSO compared to PSOA patients (70% vs. 45%) without reaching statistical significance. 27% of all patients were treated with glucocorticoids: mean daily dose 3 $\pm$ 8 mg, mean cumulative dose (GCCD) 10.9 g $\pm$ 20.3 g. No significant difference was seen comparing medians of BMD in patients with a GCCD >10 g versus a GCCD <10 g. In terms of risk factors, 27% were smokers and 32% former smokers. 60%

of all patients showed Vit D levels <75 nmol/L. Yet, in subgroup analyses neither smoking nor Vit D deficiency could be identified to have a measurable effect on the BMD. The mean body mass index (BMI) was 28.9 ( $\pm 5.9$ ), and a higher BMI correlated positively with BMD ( $p=0.01$ ).

**Conclusions:** In our patient cohort, the GCCD does not have a measurable impact on the BMD. Additionally, according to current literature the prevalence of osteoporosis seems to be in the same range as in the normal population.<sup>1</sup> Keeping in mind the (still) small number of patients, neither smoking nor Vit D deficiency could be identified as possible risk factors for low BMD, but further investigations are necessary to corroborate these observations.

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**Disclosure of Interest:** D. Freier Grant/research support from: Amgen, BMS, Celgene, Generic Assays GSK, Horizon, medac, Mundipharma, Pfizer and Roche, K. Zeiner Grant/research support from: Amgen, BMS, Celgene, Generic Assays GSK, Horizon, medac, Mundipharma, Pfizer and Roche, R. Biesen Grant/research support from: Amgen, BMS, Celgene, Generic Assays GSK, Horizon, medac, Mundipharma, Pfizer and Roche, E. Wiebe Grant/research support from: Amgen, BMS, Celgene, Generic Assays GSK, Horizon, medac, Mundipharma, Pfizer and Roche, T. Buttgerit Grant/research support from: Amgen, BMS, Celgene, Generic Assays GSK, Horizon, medac, Mundipharma, Pfizer and Roche, S. Hermann Grant/research support from: Amgen, BMS, Celgene, Generic Assays GSK, Horizon, medac, Mundipharma, Pfizer and Roche, F. Buttgerit Grant/research support from: Amgen, BMS, Celgene, Generic Assays GSK, Horizon, medac, Mundipharma, Pfizer and Roche

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#### AB0916 EFFICACY AND PREDICTIVE FACTORS OF CLINICAL RESPONSE TO TNF INHIBITORS IN PATIENTS WITH AXIAL AND PERIPHERAL PSORIASIS ARTHRITIS

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**Background:** Patients with psoriatic arthritis (PsA) may have predominant axial (axPsA) or peripheral (pPsA) manifestations. The development of TNF inhibitors (TNFi) has changed the course of PsA. However, most published data is focused on pPsA but almost no data is available for TNFi response in axPsA.

**Objectives:** to analyse the efficacy and the predictive factors of clinical response in patients with axPsA and pPsA starting treatment with TNFi in clinical practice.

**Methods:** An observational study analysing data from a prospective cohort including 93 patients (pts) with axPsA or pPsA treated with TNFi from 2002–2018 was conducted. Demographic information, disease activity indexes (ASDAS for axPsA and DAS28 for pPsA) and laboratory tests were collected before starting TNFi (baseline visit) and 6 months later (6 m visit). At 6 m, the percentage of pts achieving inactive disease (ASDAS <1.3) for axPsA or remission (DAS28 <2.6) for pPsA as well as the percentage of pts achieving clinical improvement (defined as ASDAS-clinically important improvement= $\Delta$ ASDAS>1.1 or  $\Delta$ DAS28 >1.2) were determined. Baseline predictor factors of inactive disease/remission and clinical improvement at 6 m were identified using a univariable and multivariable binary regression models adjusted for confounder factors.

**Results:** Out of 93 included pts, 45 pts had predominant axPsA and 48 pPsA. Administered TNFi was etanercept for most pts (42%), infliximab in 29%, adalimumab in 22% and golimumab in 7%. Baseline characteristics are shown in table 1. Male sex was more frequent in axPsA vs pPsA (62% vs 42%;  $p=0.04$ , respectively). In axPsA, 55% clinically improved and 32% pts achieved inactive disease. After multivariable analysis, male gender (OR 25.8,  $p=0.01$ ) and higher baseline ASDAS (OR 6.3,  $p=0.01$ ) were associated as independent predictors of clinical improvement at 6 m. Also, male gender (OR 15.7,  $p=0.03$ ) and lower BMI (OR

0.7,  $p=0.03$ ) were associated as independent predictor factors for achieving inactive disease. In pPsA, 48% pts clinically improved and 33% pts were on remission at 6 m. The percentage of pts on remission tended to be higher in males than females (47% vs 20%;  $p=0.08$ , respectively). However, after running the regression analyses, none of the baseline predictor factors was significantly associated neither with clinical improvement nor with remission in patients with pPsA.

Abstract AB0916 – Table 1

	Total n=93		p-value
	axPsA n=45	pPsA n=48	
Male, n (%)	28 (62%)	20 (42%)	0.04
BMI, Mean (SD)	27.4 (5.5)	26.4 (5.5)	0.3
Age (years), mean (SD)	56 (12.9)	60 (14.2)	0.2
Smokers, n (%)	18 (41.9%)	15 (31.9%)	0.3
Disease duration (years), mean (SD)	19 (10.8)	18 (8.4)	0.6
HLA B27, n/N (%)	8/22 (36%)	-	
RF, n/N (%)	-	3/44 (6.8%)	
ACPA, n/N (%)	-	0/45	
csDMARDs, n (%)	25 (68%)	24 (68%)	0.9
bASDAS, mean (SD)	3.1 (1.2)	-	
bDAS28, mean (SD)	-	4.7 (1.3)	
bCRP mg/L, mean (SD)	13.2 (14.7)	10.5 (15.3)	0.3
bESR, mean (SD)	26.3 (20.9)	27.8 (19.8)	0.5

**Conclusions:** In clinical practice, 1 out of 3 pts with PsA is on remission 6 m after initiating a TNFi, and 1 out of 2 clinically improve; both proportions are similar for axPsA and pPsA. Male gender, higher baseline disease activity and lower BMI are associated with more probability to achieve inactive disease or an important clinical improvement in axPsA.

**Disclosure of Interest:** None declared

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#### AB0917 CLINICAL AND RADIOLOGICAL CHARACTERISATION OF AXIAL PSORIATIC ARTHRITIS

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**Background:** Defining axial involvement in psoriatic arthritis (PsA) is a challenge; thus, according to which criteria used, the differences in prevalence of axial PsA range from 20% to 70%. Two different phenotypes have been suggested in axial PsA. One of them remind us typical Ankylosing Spondylitis (AS) with bilateral sacroiliitis according to the New York modified criteria (mNY) and a strong association with HLA-B27 and another phenotype with more indolent course, with unilateral and asymmetric sacroiliitis and a lower association to HLA B27

**Objectives:** To define clinical and radiological characteristics of a cohort of patients with axial PsA with associated sacroiliitis in a third level hospital in southern Spain.

**Methods:** Cross-sectional study of an axial PsA cohort with sacroiliitis from a third level hospital. Demographic, clinical and radiological variables were collected. Sacroiliitis was defined as: sacroiliitis according to mNY, or unilateral sacroiliitis grade II in X-ray, and/or according to ASAS criteria of positive MRI. We excluded those patients with axial PsA without sacroiliitis according to definition. The statistical package SPSS v21 was used. The qualitative variables were analysed by the Chi2 and Fisher tests, as required. The quantitative variables were analysed by Student's T Test/Mann-Whitney U Test. Statistical significance was considered, values of  $p<0.05$

**Results:** Of 209 patients with axial SpA with sacroiliitis according to the definition found, 39 patients with diagnosis of PsA were analysed. The main characteristics of the patients are shown in image 1. Of the 39 patients, 62% did not meet mNY criteria. Regarding the patients who met mNY criteria, those who did not comply them had the following differences (specifying the significance). The initial diagnosis was different from PsA more frequently (40% Vs. 17%,  $p=0.124$ ). They presented a lower evolution of the disease (7 Vs. 13 years,  $p=0.052$ ). They presented as initial symptomatology a greater frequency of peripheral arthritis (71% Vs 27%,  $p=0.03$ ); and consequently, a greater presence of mixed forms (92% Vs 53%,  $p=0.015$ ). They presented a lower frequency of positive HLAB27 (21 V. 60,  $p=0.042$ ).

No significant differences were found in reference to the presence of extra-articular involvement (dactylitis, uveitis, psoriasis, onychopathy), nor in reference to the presence of related family history (spondyloarthritis, psoriasis, uveitis).

Abstract AB0917 – Table 1. MAIN CHARACTERISTICS

VARIABLES		
MEN n(%)		27 (69)
AGE median (IQR)		51 (40-57)
AGE AT DIAGNOSIS median (IQR)		41 (29-52)
YEARS OF DISEASE EVOLUTION median (IQR)		6 (2-13)
INITIAL DIAGNOSIS n(%)		
- AS		4 (10)
- PsA		29 (74)
- Indiferenciada SpA		4 (10)
- SAPHO		2 (5)
FINAL DIAGNOSIS n(%)		
- PsA		39 (100)
SAME DIAGNOSIS AS INITIAL n(%)		29 (74)
INITIAL SYMPTOM n(%)		
- Low back pain		17 (43)
- Oligoarthritis		9 (23)
- Poliarthritis		12 (31)
- Dactylitis		1 (3)
INITIAL JOINT PATTERN n(%)		
- Axial		9 (23)
- Peripheral		12 (31)
- Mixed		18 (46)
FINAL JOINT PATTERN n(%)		
- Axial		9 (23)
- Mixed		30 (77)
POSITIVE HLA B27 n(%)		14 (36)
BIOLOGICAL THERAPY n (%)		13 (33)
FAMILY HISTORY n (%)		9 (23)
EXTRAARTICULAR MANIFESTATION n(%)		
- Psoriasis		30 (77)
- Uveitis		3 (8)
- Dactylitis		2 (5)
- Onychopathy		8 (20)

**Conclusions:** Patients with axial PsA with sacroiliitis according to ASAS criteria of positive MRI/unilateral grade II X-ray sacroiliitis presented more peripheral joint involvement, and less association with HLA B27 compared to patients who did not meet mNY criteria. A smaller proportion of patients with axial PsA that meet the mNY criteria suggests a less aggressive structural sacroiliac involvement.

**Disclosure of Interest:** None declared

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#### AB0918 PATIENT-REPORTED OUTCOMES IMPROVEMENT IN THE RUSSIAN COHORT OF EARLY PERIPHERAL PSORIATIC ARTHRITIS PATIENTS TREATED ACCORDING TO TREAT-TO-TARGET STRATEGY (OPEN-LABEL REMARCA STUDY)

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**Background:** Psoriatic arthritis (PsA) has a significant impact on patients' (pts) mood and quality of life. Patient reported outcome (PRO) measures are an important component to assessing disease impact and therapy response in PsA pts. There is limited data concerning the influence of T2T strategy on PROs.

**Objectives:** To assess the effect of tight control T2T strategy on the PROs dynamics over 1 year (yr) period.

**Methods:** 78 pts (M/F=39/39) with early PsA according to CASPAR criteria were included; mean age  $36.5\pm 10.7$  years, disease duration  $12.2\pm 10.3$  mo. Disease activity indexes (DAS)= $4.0\pm 1.4$ , DAS28= $4.2\pm 1.1$ . Pts underwent standard clinical examination of PsA activity. At baseline all pts were treated with MTX (s/c). The dose of MTX was escalated by 5 mg eow from 10 mg/wk to 20–25 mg/wk. If the patient did not achieve minimal disease activity (MDA) or remission after 3 mo of



MTX mono-therapy, combination therapy with MT +adalimumab 40 mg s/c eow was started. At baseline and after 1 year. of therapy the following PROs were analysed: trends in fatigue (according to FACIT) and in RAPID3 were studied in 64 pts, trends in patient's global disease activity (PGA) and in patient's pain VAS were studied in 78 pts, trends in levels of anxiety and depression (HADS) were studied in 49 pts. The data acquired was analysed with the use of Spearman's correlation.

**Results:** After 1 year of therapy, there was a significant improvement in the following scores: anxiety changed from  $5.7\pm 3.1$  to  $4.3\pm 3.2$ , ( $p=0.003$ ), fatigue from  $35.3\pm 9.6$  to  $41.3\pm 9.9$  ( $p<0.001$ ), RAPID3 from  $13.4\pm 5.1$  to  $6.2\pm 5.2$  ( $p<0.001$ ), PGA from  $56.0\pm 17.8$  to  $18.9\pm 17.1$  ( $p<0.001$ ), pain from  $53.7\pm 18.6$  to  $16.9\pm 16.6$  ( $p<0.001$ ). Depression scores had also changed though not significantly: from  $3.8\pm 3.0$  to  $3.2\pm 3.1$  ( $p=0.235$ ). The dynamics of anxiety and depression indexes correlated with the dynamics of fatigue ( $r=0.64$  and  $r=0.39$ , accordingly), as well as dynamics of FACIT and RAPID3 indexes ( $r=0.36$ ). Correlation of the dynamics of RAPID3 indexes with DAS ( $r=0.45$ ) and DAS28 ( $r=0.41$ ) activity reduction was found. Association of RAPID3 dynamics with the achievement of remission according to DAS ( $p<0.001$ ) and DAS28 ( $p<0.001$ ) was detected. Interrelation between RAPID3 dynamics and the achievement of MDA ( $p<0.001$ ) was found. Correlation between dynamics of anxiety and depression indexes and the reduction of tender joint count (TJC) ( $r=0.38$  and  $r=0.36$ , accordingly) was found. There is correlation between the dynamics of fatigue indexes and TJC, swollen joint count (SJC) and PGA ( $r=0.30$ ,  $r=0.25$  and  $r=0.35$ , accordingly). Dynamics of RAPID3 correlated with TJC and SJC dynamics ( $r=0.33$ ,  $r=0.25$ ), as well as with PGA and pain dynamics ( $r=0.49$  and  $r=0.58$ ). PGA and pain dynamics correlated with TJC and SJC dynamics ( $r=0.34$  and  $r=0.26$ ;  $r=0.43$  and  $r=0.39$ , accordingly).

**Conclusions:** The T2T strategy in the Russian cohort of peripheral early PsA pts demonstrated the improvement of PROs indexes and decrease in PsA activity. Interrelation between the improvement of psychological status according to PROs (anxiety, depression and fatigue) and improvement in joint status (TJC and SJC) was found. RAPID3 is a reliable tool for evaluating patient's status: RAPID3 indexes correlate with the achievement of MDA and DAS/DAS28 remission.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.2413

#### AB0919 VALIDATION OF PROTEOMIC BIOMARKERS OBSERVED IN MONOZYGOTIC TWINS CONFIRMS TWO PROTEINS ASSOCIATED WITH PSORIATIC DISEASE

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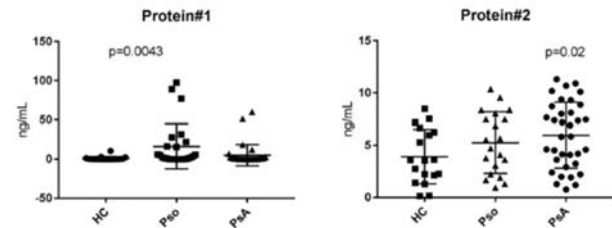
**Background:** Skin psoriasis affects 3% of the general population and as much as 20%–40% of patients will develop psoriatic arthritis (PsA), with the two conditions representing a clinical and immunological continuum within a prototype for chronic inflammation. Different from most rheumatic diseases, no serum autoantibody is associated with PsA, and there are currently no biomarkers for an early diagnosis and prediction of PsA onset in psoriasis, frequently causing a delayed diagnosis. Monozygotic twins discordant for psoriasis/PsA represent a unique setting to investigate the influence of environmental and stochastic factors on disease phenotype. Through a high-throughput proteomic analysis (SomaLogic) we have previously identified a set of 13 proteins differentially expressed in the serum of monozygotic twins discordant for psoriatic disease.

**Objectives:** To validate serum proteomic biomarkers of psoriatic disease using commercially available ELISA in monozygotic twins and in unrelated patients with psoriasis or PsA.

**Methods:** Our study included sera from our cohort of monozygotic twins previously described and from 70 unrelated patients with psoriatic disease (psoriasis without PsA 34%–49%, PsA with/without psoriasis 36%–51%; women 46%, median age 52 years, interquartile range 41–59) followed at Humanitas Research Hospital, and 25 healthy subjects (52% women, median age 52 years, IQR 44–62). Candidate serum proteomic biomarkers obtained by SomaLogic analysis were validated using commercially available ELISA kits and proteins are herein anonymized due to a pending patent request.

**Results:** We found a significant correlation between SomaLogic results in monozygotic twins and ELISA results in unrelated psoriatic cases in the serum levels of 2 proteins (figure 1), which are involved in inflammatory and immune response, and one has been previously reported in psoriatic plaques. Four proteins showed

a significantly different expression between psoriasis and PsA versus controls, in particular two proteins have a potential role in disease pathogenesis, as protein #1 acts as cell-surface receptor and regulates differentiation, proliferation and survival of dendritic cells, while protein #2 is involved in regulation of UV radiation-induced apoptosis and protein folding.



**Abstract AB0919 – Figure 1**

**Conclusions:** Two serum proteomic biomarkers, previously identified in a cohort of monozygotic twins discordant for psoriatic disease, can discriminate psoriatic disease, thus representing potential biomarkers of disease and possibly playing a pathogenetic role in disease.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.6250

#### AB0920 TUMOUR NECROSIS FACTOR INHIBITORS PERSISTENCE IN PSORIATIC ARTHRITIS PATIENTS

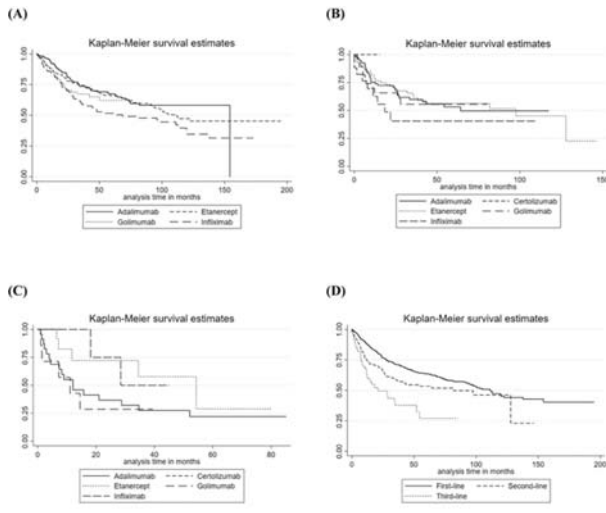
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**Background:** Tumour necrosis factor inhibitors (TNFi) lead to a dramatic improvement in the management of psoriatic arthritis (PsA). Nevertheless, a significant proportion of patients still do not respond and/or are intolerant to TNFis, requiring treatment switch for an adequate control of disease activity.

**Objectives:** To assess TNFis drug retention and the main reasons for TNFi discontinuation in PsA patients.

**Methods:** This was a non-interventive study of PsA patients registered at the Rheumatic Diseases Portuguese Registry (Reuma.pt), with at least one TNFi prescription. Drug retention for a first, second and third line TNFi was assessed by Kaplan-Meier survival analysis. The reasons for discontinuation were described as frequencies.

**Results:** 750 PsA patients were included, with a mean age of 47.6 years ( $\pm 11.6$ ); 50.3% (n=377) female. 200 patients (26.7%) treated with adalimumab, 335 (44.7%) with etanercept, 114 (12.2%) with golimumab and 101 (13.5%) with infliximab, as first line TNFi. The majority (67.6%) were receiving concomitantly conventional synthetic disease modifying anti-rheumatic drugs (62.3% MTX) and 33.9% corticosteroids. The mean duration of TNFi retention was of  $48.5\pm 40.1$  months, when treated with a 1st TNFi, decreasing to  $35.5\pm 33$  months for the 2nd TNFi, and to  $22.7\pm 22.9$  months for the 3rd TNFi (figure 1). After being treated with a 1st TNFi, the majority of discontinuers (35.8% of the total population), withdraw due to lack or loss of effectiveness (53.5%) and due to adverse events (24.4%). The rates of discontinuation for the 2nd and 3rd TNFi were of 39% and 54%, respectively. Lack or loss of effectiveness and adverse events were maintained the two main reasons of withdrawal for the 2nd (62.3%; 21.6%) and 3rd TNFi (63%; 22.2%).



**Abstract AB0920 – Figure 1.** Drug retention of psoriatic arthritis patients registered at Rheumatic Diseases Portuguese Registry (Reuma.pt), treated with a first (A) second (B) and third (C) tumour necrosis factor inhibitor (TNFi) and overall (D) TNFi drug retention.

**Conclusions:** PsA patients registered at Reuma.pt treated with a 1st TNFi had an overall drug retention of 49 months. We observed a decrease in the average retention of TNFi therapy of 13.0 months in PsA patients who switched to a 2nd TNFi or a 3rd TNFi. Lack or loss of response were the main reason for TNFi discontinuation, independently of TNFi position, responsible for more than half of the discontinuations. The observed short survival of TNFis in PsA, and the inability to regain drug expectancy when switching to another TNFi, highlights the limitations from recycling between TNFi when aiming at long-term disease remission.

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**Disclosure of Interest:** None declared

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**AB0921** **IMPACT OF BASELINE DEMOGRAPHICS, DISEASE ACTIVITY AND CONCOMITANT MEDICATION ON AMERICAN COLLEGE OF RHEUMATOLOGY 20 RESPONSE RATE AND HEALTH ASSESSMENT QUESTIONNAIRE-DISABILITY INDEX SCORE WITH TOFACITINIB IN ACTIVE PSORIATIC ARTHRITIS: A POOLED SUBGROUP ANALYSIS OF 2 PHASE 3 STUDIES**

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**Background:** Tofacitinib is an oral Janus kinase inhibitor for the treatment of psoriatic arthritis (PsA). In a pooled analysis of data from 2 Phase 3 trials in patients (pts) with active PsA, tofacitinib 5 and 10 mg twice daily (BID) significantly improved American College of Rheumatology (ACR) 20 response rates vs placebo (PBO) (50.0, 53.0 vs 28.0%, respectively; p<0.001) and least squares mean (LSM) change from baseline (BL) in Health Assessment Questionnaire-Disability Index (HAQ-DI) score vs PBO (0.38, -0.38 vs -0.16, respectively; p<0.001) at Month 3.<sup>1</sup>

**Objectives:** To compare the efficacy of tofacitinib 5 and 10 mg BID vs PBO in predefined pt subgroups based on differences in BL demographics, disease activity and concomitant medication.

**Methods:** This was an analysis of pooled efficacy data from 2 Phase 3, randomised, double-blind, PBO-controlled studies (OPAL Broaden [12 months; NCT01877668] and OPAL Beyond [6 months; NCT01882439]) in pts with active

PsA (defined as ≥3 swollen and ≥3 tender joints). Pts in OPAL Broaden were tumour necrosis factor inhibitor (TNFi)-naïve with an inadequate response (IR) to ≥1 conventional synthetic disease-modifying antirheumatic drug (csDMARD). Pts in OPAL Beyond had an IR to ≥1 TNFi. Pts were randomised to receive tofacitinib 5 or 10 mg BID, subcutaneous adalimumab 40 mg every 2 weeks (OPAL Broaden; data not included) or PBO. Pts continued to receive a stable dose of a single csDMARD. ACR20 response rates and LSM change from BL in HAQ-DI at Month 3 (primary endpoint data) were evaluated by subgroup category (demographic and disease characteristics at BL or at screening). Analyses were based on the full analysis set (table 1).

**Results:** In total, 238, 236 and 236 pts received tofacitinib 5 mg BID, 10 mg BID, or PBO, respectively. Across all subgroups analysed, tofacitinib 5 and 10 mg BID were generally associated with greater improvements at Month 3 in ACR20 and change from BL in HAQ-DI score than PBO (table 1). In pts classified as current smokers, slightly lower ACR20 response rates and similar changes from BL in HAQ-DI score to corresponding PBO at Month 3 were observed relative to never- or ex-smokers; however, the sample size was small.

**Abstract AB0921 – Table 1.** Pooled efficacy at Month 3 by subgroup

Subgroup	Baseline category	ACR20 response rate (% [n/N1])			LSM change from baseline in HAQ-DI (N2)		
		Tofacitinib 5 mg BID (N=238)	Tofacitinib 10 mg BID (N=236)	Placebo (N=236)	Tofacitinib 5 mg BID (N=238)	Tofacitinib 10 mg BID (N=236)	Placebo (N=236)
<b>Race</b>	White	48.7 (110/226)	51.4 (114/221)	28.4 (69/222)	-0.37 (220)	-0.37 (213)	-0.18 (211)
	Other	70.0 (9/13)	70.0 (13/13)	24.0 (3/13)	-0.01 (12)	-0.13 (12)	-0.18 (12)
<b>Ethnicity</b>	Hispanic/Latino	45.7 (23/50)	52.3 (23/50)	28.0 (23/50)	-0.48 (23)	-0.41 (23)	-0.38 (23)
	Non-Hispanic/Latino	47.3 (96/203)	50.9 (111/205)	28.4 (110/206)	-0.33 (207)	-0.33 (203)	-0.13 (206)
<b>Gender</b>	Male	53.8 (113/171)	53.3 (113/169)	27.8 (107/169)	-0.31 (168)	-0.31 (165)	-0.14 (169)
	Female	46.3 (24/52)	52.9 (27/51)	28.7 (28/51)	-0.37 (52)	-0.37 (51)	-0.18 (51)
<b>Geographic region</b>	US/Canada	50.0 (28/56)	48.3 (27/56)	28.9 (33/45)	-0.38 (56)	-0.38 (56)	-0.19 (49)
	Rest of World (ROW)	36.2 (22/60)	46.1 (26/56)	22.3 (21/60)	-0.22 (60)	-0.22 (56)	-0.09 (60)
<b>PsA duration, years</b>	≤2	53.7 (22/41)	49.1 (27/55)	34.1 (31/46)	-0.34 (41)	-0.38 (41)	-0.18 (41)
	>2	46.0 (27/59)	54.0 (30/55)	28.0 (28/55)	-0.38 (59)	-0.38 (55)	-0.13 (55)
<b>Age, years</b>	≤65	47.7 (20/42)	54.0 (31/57)	27.0 (27/51)	-0.38 (42)	-0.39 (42)	-0.20 (42)
	>65	70.0 (7/10)	42.9 (21)	34.0 (23/67)	-0.39 (10)	-0.27 (21)	-0.17 (23)
<b>Baseline body weight, kg</b>	≤80	55.0 (26/48)	56.0 (26)	34.0 (26/76)	-0.33 (48)	-0.33 (48)	-0.20 (48)
	>80	43.0 (17/39)	56.7 (30/53)	28.0 (28/53)	-0.38 (39)	-0.40 (39)	-0.18 (39)
<b>BMI, kg/m<sup>2</sup></b>	≤25	45.2 (20/45)	55.1 (27/49)	27.0 (27/45)	-0.30 (45)	-0.30 (45)	-0.20 (45)
	>25	46.3 (16/35)	53.1 (26/49)	28.0 (27/45)	-0.31 (35)	-0.31 (35)	-0.20 (35)
<b>CRP, mg/L</b>	≤10	51.8 (18/35)	50.8 (18/35)	27.4 (26/35)	-0.38 (35)	-0.37 (35)	-0.19 (35)
	>10	44.1 (17/39)	47.1 (18/39)	23.0 (18/39)	-0.34 (39)	-0.34 (39)	-0.20 (39)
<b>PsA entheses, number of joints</b>	≤1	61.0 (2)	66.0 (0/0)	42.0 (0/0)	NC <sup>a</sup>	NC <sup>a</sup>	NC <sup>a</sup>
	>1	50.4 (18/36)	52.0 (21/38)	27.0 (23/38)	-0.38 (36)	-0.38 (36)	-0.18 (36)
<b>Disease interdigital joint involvement<sup>b</sup></b>	Yes	46.4 (71/139)	50.3 (76/131)	28.1 (33/136)	NC	NC	NC
	No	56.1 (16/29)	57.1 (16/29)	30.0 (16/29)	NC	NC	NC
<b>Arthritis medication<sup>c</sup></b>	Yes	37.3 (16/43)	33.3 (18)	24.1 (16/43)	NC	NC	NC
	No	46.9 (13/28)	54.0 (13/28)	28.3 (10/28)	NC	NC	NC
<b>Spondylitis<sup>d</sup></b>	Yes	46.9 (20/43)	42.0 (20/47)	22.7 (16/44)	NC	NC	NC
	No	51.1 (10/19)	53.6 (10/19)	29.2 (10/19)	NC	NC	NC
<b>Smoking status<sup>e</sup></b>	Never smoked	51.1 (71/139)	54.3 (76/140)	24.7 (31/138)	-0.37 (137)	-0.39 (140)	-0.13 (137)
	Smoker	33.1 (13/37)	44.0 (20/45)	40.3 (18/39)	-0.34 (37)	-0.34 (45)	-0.18 (39)
	Ex-smoker	36.1 (13/36)	50.0 (20/40)	23.0 (19/39)	-0.40 (36)	-0.40 (40)	-0.13 (39)
<b>Baseline CRP, mg/L</b>	≤10	53.8 (18/34)	50.8 (18/34)	27.0 (26/34)	-0.38 (34)	-0.40 (34)	-0.14 (34)
	>10	42.1 (17/41)	49.0 (20/41)	29.0 (21/41)	-0.37 (41)	-0.39 (41)	-0.19 (41)
<b>PASDAQ</b>	≤2	61.0 (2)	100 (0/1)	33.0 (0/1)	NC <sup>a</sup>	NC <sup>a</sup>	NC <sup>a</sup>
	>2	50.8 (18/35)	51.0 (18/35)	29.0 (20/47)	-0.38 (35)	-0.38 (35)	-0.17 (35)
<b>PASI score<sup>f</sup></b>	≤5	51.0 (16/31)	53.0 (16/31)	27.0 (16/31)	-0.42 (31)	-0.40 (31)	-0.14 (31)
	>5	40.0 (17/42)	34.0 (17/42)	26.0 (17/42)	-0.37 (42)	-0.39 (42)	-0.17 (42)
<b>DSS-0</b>	Yes	47.2 (16/34)	52.0 (16/32)	27.0 (16/32)	-0.35 (34)	-0.35 (32)	-0.10 (32)
	No	51.7 (18/35)	51.7 (18/35)	29.0 (18/35)	-0.40 (35)	-0.39 (35)	-0.20 (35)
<b>SPARCC -0 vs LEI -0</b>	Yes	49.7 (10/18)	53.0 (10/18)	29.0 (10/18)	-0.38 (18)	-0.38 (18)	-0.12 (18)
	No	50.0 (20/40)	50.0 (20/40)	45.0 (21/46)	-0.40 (40)	-0.40 (40)	-0.13 (40)
<b>Concomitant csDMARD</b>	MTX only	48.9 (15/31)	51.0 (16/30)	28.0 (16/30)	-0.37 (31)	-0.41 (31)	-0.11 (31)
	Other	53.0 (27/51)	47.0 (27/58)	23.0 (18/42)	-0.41 (51)	-0.35 (51)	-0.13 (41)
<b>Concomitant use (yes)</b>	Yes	46.3 (15/33)	51.4 (19/37)	29.0 (19/37)	-0.33 (33)	-0.41 (37)	-0.18 (33)
	No	51.0 (18/35)	53.0 (18/34)	27.0 (11/37)	-0.40 (35)	-0.38 (34)	-0.18 (34)

<sup>a</sup>Analysis was not conducted due to small sample size; <sup>b</sup>At screening; <sup>c</sup>In pts with baseline PASI >0 and baseline BSA ≥3%

Statistical methods: ACR20 response was defined as achieving a ≥20% improvement in ACR criteria components Missing ACR20 response was considered a non-response to treatment

LSMs were calculated based on a mixed model for repeated measures without imputation for missing values

ACR, American College of Rheumatology; BID, twice daily; BMI, body mass index; BSA, body surface area; CRP, C-reactive protein; csDMARD, conventional synthetic disease-modifying antirheumatic drug; DSS, Dactylitis Severity Score; HAQ-DI, Health Assessment Questionnaire-Disability Index; LEI, Leeds Enthesitis Index; LSM, least squares mean; MTX, methotrexate; n, number of patients in full analysis set (randomised and received ≥1 treatment dose); n, number of responders; N1, number of patients in the full analysis set by category of subgroup and treatment; N2, number of patients included in the repeated measures model by category of subgroup and treatment; NC, analysis not conducted; PASDAQ, Psoriatic Arthritis Disease Activity Score; PASI, Psoriasis Area and Severity Index; PsA, psoriatic arthritis; pts, patients; ROW, rest of world (Brazil, Mexico and Taiwan); SPARCC, Spondyloarthritis Research Consortium of Canada (enthesitis index)

**Conclusions:** In this analysis of pooled data from 2 Phase 3 studies in pts with active PsA, tofacitinib 5 and 10 mg BID consistently improved efficacy at Month 3 compared with PBO across all predefined subgroups evaluated, with the exception of current smoking; however, as this was not a pre-specified analysis and some subgroups (including smoking status) were small, interpretation should be made with caution.





decrease in PsA patients, and also to the arousal of central heart rhythm regulation mechanisms combined disorders.

**Disclosure of Interest:** None declared

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**AB0924 EFFICACY OF SUBCUTANEOUS USTEKINUMAB THERAPY IN PATIENTS WITH PSORIATIC ARTHRITIS: A SINGLE CENTRE-STUDY**

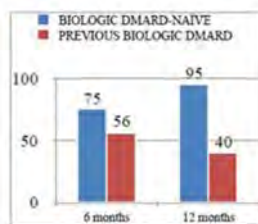
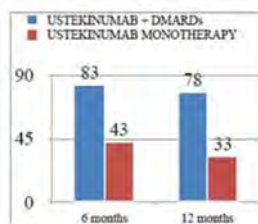
I. Añón Oñate, I. Notario Ferreira, L. Pérez Albaladejo, M. Á. Ferrer González, M. Ramírez de la Torre, S. Quirosa Flores, A. García Sánchez, M.C. Ramírez Barberena, J.M. Andreu Ubero, R. Cáliz Cáliz. *Rheumatology, Hospital Universitario Virgen de las Nieves de Granada, Granada, Spain*

**Background:** Ustekinumab is a monoclonal antibody that inhibits IL-12 and 23 that has demonstrated efficacy and safety for the treatment of patients with psoriatic arthritis, plaque psoriasis and Crohn's disease.

**Objectives:** To evaluate the efficacy of subcutaneous Ustekinumab (USTE) in patients with psoriatic arthritis in a real-world clinical setting in Spain.

**Methods:** Descriptive, prospective, longitudinal and open study of 66 patients diagnosed with psoriatic arthritis: 63 patients received subcutaneous USTE 45 mg and 3 patients received USTE 90 mg every 12 weeks, both groups received a first dose of induction according to technical specifications. The following variables were collected: age, sex, years of evolution, previous treatment with Synthetic Disease Modifying Anti-Rheumatic Drugs (DMARDs) and/or biologic DMARD, counting of painful and swollen joints, determination of C-reactive protein, presence of dactylitis, onychopathy and cutaneous psoriasis. Clinical efficacy was evaluated by EULAR response criteria and Disease Activity Score (DAS28) according to low activity criteria (DAS28 >2.6–3.2) and remission clinical (DAS28 <2.6) at 6 and 12 months of treatment. Efficacy was compared between 2 subgroups; one group was: patients with USTE monotherapy vs USTE in combination therapy with DMARDs and the other group was: naïve patients vs patients who received previous treatment with biologic DMARD. Entthesis affectation was evaluated with the MASES index.

**Results:** 66 patients were included, 51.5% were female. The mean age was 47.2 ±11.3 years and the mean disease duration was 6±7.76 years. USTE was prescribed in 44% as a first line therapy and was administered in combination with DMARDs in 51.5% of the patients (mostly, methotrexate). In our cohort, 74.2% of patients had exclusively peripheral involvement, 10.6% had axial involvement and 15.2% had mixed involvement. 21% of our patients had dactylitis and 36% enthesitis, as well as cutaneous psoriasis (74%) and onicopathy (42%). At 6 and 12 months of treatment, we observed a statistically significant decrease in the count of painful and swollen joints, in the DAS28 index and in the MASES index. DAS28 low disease activity rates were 38% at 6 months and 21% at 12 months of treatment. DAS28 remission rates were 21% and 14% at 6 and 12 months respectively. When comparing efficacy by subgroups, we observed higher EULAR response rates in patients with USTE in combination therapy with DMARDs (figure 1) and biologic DMARD-naïve patients (Figure 2) at 6 and 12 months of treatment.



**Abstract AB0924 – Figure 1.** EULAR response rates (%) at 6 (p=0.027) and 12 months

**Conclusions:** Ustekinumab is effective for the treatment of psoriatic arthritis and constitutes an alternative to treatment with anti-TNFα. The dose of Ustekinumab

90 mg may improve the response to treatment in some patients, but we would need a greater number of studies in clinical practice.

**Disclosure of Interest:** None declared

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**AB0925 COMPARISON OF PSORIATIC ARTHRITIS THERAPEUTIC TARGETS – PSA-MDA AND DAPSA REMISSION/LOW DISEASE ACTIVITY IN PATIENTS TREATED IN THE INSTITUTE OF RHEUMATOLOGY PRAGUE**

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**Background:** According to the Czech Society of Rheumatology guidelines for therapy and monitoring of psoriatic arthritis from 2016<sup>(1)</sup> which are based on the EULAR recommendations 2015<sup>(2)</sup> the target of the therapy is to attain either minimal disease activity (MDA)<sup>(3)</sup> or remission/low disease activity according to DAPSA<sup>(4)</sup>. In fact, the majority of our patients have only mild skin disease and that's why DAPSA, which is more feasible to use could be sufficient as a target of therapy, even though these two indices assess the disease from different points of view (MDA being more comprehensive, including also entheses, skin and function and DAPSA only joint disease).

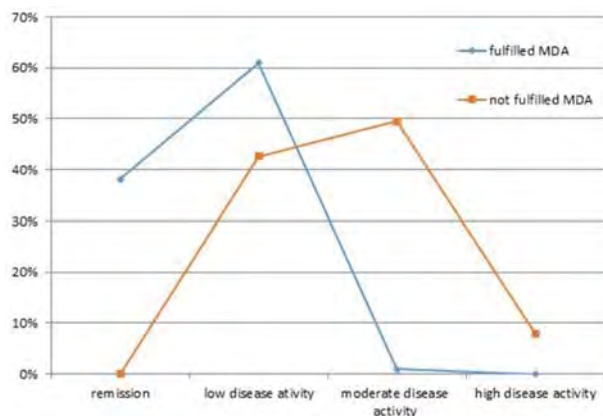
**Objectives:** To compare the ability of these two indices in the evaluation of the response to treatment.

**Methods:** We compared both indices from 206 visits in 32 patients with PsA from our database of 247 patients. At first we took the patients who complied with MDA criteria and looked at what percentage of them were in remission/low disease activity, moderate, or high activity respectively at the same time. Then, we took the patients, who did not comply with MDA criteria and again looked at the level of activity according to DAPSA.

**Results:** In the group of patients who fulfilled the MDA criteria (5/7), 99,5% were also in the state of remission or low disease activity according to DAPSA. In only 1 case the activity was assessed as moderate and no patient was in high disease activity state. In the group of patients who did not comply with MDA criteria, 42,6% of pats. were in mild disease activity state and only 57,4% of patients were in moderate, or high activity according to DAPSA – Tab. 1

**Abstract AB0925 – Table 1**

Pats. total. (n):	206	100%	Total:			
Fulfilled MDA	105	50,97%				
				Of total in remission (DAPSA):	40	38,10% 99,05% p<0,01
				Of total in mild activity (DAPSA):	64	60,95%
				Of total in moderate activity (DAPSA):	1	0,95%
				Of total in high activity (DAPSA):	0	0,00%
Not fulfilled MDA	101	49,03%				
				Of total in remission (DAPSA):	0	0,00%
				Of total in mild activity (DAPSA):	43	42,57%
				Of total in moderate activity (DAPSA):	50	49,50% 57,43% p<0,05
				Of total in high activity (DAPSA):	8	7,92%



Abstract AB0925 – Figure 1

**Conclusions:** DAPSA correlates well with MDA in patients with mild skin disease and can be used in these patients instead of MDA. In patients who fail to respond to therapy according to MDA there can be a substantial proportion of patients with mild joint disease, due to more severe skin disease and/or presence of enthesitides, which are nevertheless vaguely defined.

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AB0926

#### EFFECTIVENESS OF CERTOLIZUMAB PEGOL IN PSORIATIC ARTHRITIS. RELATIONSHIP WITH SMOKING STATUS AND BMI

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**Background:** Previous literature have investigated that tobacco and weight in patients with psoriatic arthritis (PsA) is associated with a poorer response to antiTNF.

**Objectives:** To investigate the response and survival of Certolizumab pegol (CZP) in PsA patient in daily clinical practice according to their baseline smoking status and Body Mass Index (BMI).

**Methods:** Multicentric cohort of PsA patients treated with CZP according to routine clinical practice. This study was approved by local Ethics Committee. Maximum observation time was 12 months. Effectiveness variables: DAS28 (CRP). Survival rate: Kaplan-Meier.

**Results:** 262 patients with PsA were included: 43.5% male, mean (SD) age 49.9 (11.9) years, mean (Q1-Q3) disease duration 6.9 (1.9–9.3) years, and 14.9% of patients were HLAB27 positive. Among these, 229 (87.4%) had known smoking status (29.7% smokers and 70.3% never smokers) and 85 (32%) had known BMI

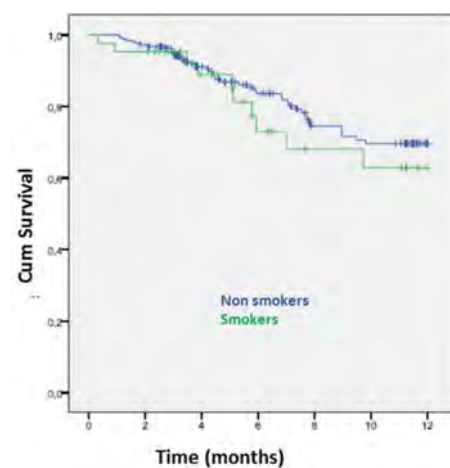
(median 26.9 kg/m<sup>2</sup>, SD 4.7). Statistically significant differences in DAS28 were observed at last visit comparing to baseline in both groups according to BMI and smoking status (table 1).

CZP retention rate was 78.5% in non-smokers and 76.7% in smokers. In patients with BMI <25 kg/m<sup>2</sup> CZP retention rate was 78.6% compared to 78.9% in patients with BMI ≥25 kg/m<sup>2</sup> (figure 1). No statistical differences were observed in both sub-groups.

Abstract AB0926 – Table 1

		DAS28
Baseline	BMI <25 kg/m <sup>2</sup>	4.6 (0.9)
	BMI ≥25 kg/m <sup>2</sup>	4.5 (0.8)
	Never smokers	4.6 (0.9)
Last visit	Smokers	4.6 (0.9)
	BMI <25 kg/m <sup>2</sup>	3.6 (1.1)*
	BMI ≥25 kg/m <sup>2</sup>	3.9 (1.0)*
	Never smokers	3.9 (1.0)
	Smokers	# 3.3 (0.8)

\*p<0,05, Wilcoxon test; #p<0.001 T-Student's test (last visit vs basal).



Abstract AB0926 – Figure 1. CZP Retention Rate according to BMI and smoking status in PsA patients.

**Conclusions:** In this daily clinical practice study of patients with PsA treated with certolizumab pegol there was a significant decrease in DAS28-CRP independent of smoking status and BMI. No differences were found in the retention rate of certolizumab pegol based on these two variables.

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AB0927

#### PROBABILITY AND IMPACT OF ACHIEVING LOW DISEASE ACTIVITY OR REMISSION IN PATIENTS WITH PSORIATIC ARTHRITIS TREATED WITH APREMILAST: POOLED ANALYSIS OF THE PALACE 1–3 PHASE 3 TRIALS

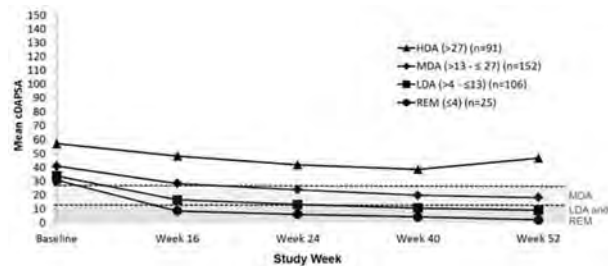
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**Background:** Baseline (BL) disease characteristics and short-term response status and its implications for long-term achievement of low disease activity (LDA) or remission (REM) in pts with active psoriatic arthritis (PsA) treated with apremilast (APR) are unknown.

**Objectives:** 1) To assess BL clinical Disease Activity for Psoriatic Arthritis (cDAPSA) levels associated with achieving cDAPSA LDA or REM at Week 52 (Wk52); 2) predict cDAPSA response categories at Wk52 based on BL or Wk16 cDAPSA; 3) assess disease activity in different PsA domains associated with cDAPSA categories at Wk52.

**Methods:** Pooled analyses (PALACE 1–3) were performed of pts assigned to receive APR 30 mg BID (APR30) at BL who completed Wk52 and had cDAPSA components available to calculate responses. Pts were grouped according to the cDAPSA categories reached at Wk52 (REM ≤4; LDA>4–≤13; MDA>13–≤27; HDA >27). Shifts of cDAPSA response categories from BL, Wk16 to Wk52 were reported and provided the predictability of BL status or early response to the achievement of cDAPSA categories at Wk52. Mean disease activity in core PsA domains, including swollen (0–76)/tender joint (0–78) (SJ/TJ), enthesitis (MASES), dactylitis count, Patient Global Assessment of Disease Activity (PtGA), Patient Assessment of Pain (PAP), Psoriasis Activity Severity Index (PASI), and Physical Function (HAQ) were reported longitudinally, allocated by cDAPSA category at Wk52. To better describe predictors associated with pts potentially being considered for APR in routine clinical practice, analyses were repeated removing pts in HDA at BL.

**Results:** 374 APR30 pts were included in the analyses. Pts who achieved MDA, LDA or REM at Wk52 indicated sustained improvements in cDAPSA over time; Means of BL cDAPSA scores ≤41 were associated with achievement of MDA, LDA and REM at Wk52 (figure 1). At BL, pts in HDA had 42%, 24% and 5% chances of achieving MDA, LDA or REM at Wk52, respectively. Pts in MDA at BL had 41% and 12% chances of achieving LDA or REM. Pts in LDA had 20% chances of achieving REM. At Wk16, pts in HDA had 43%, 8% and 1% chances of achieving MDA, LDA or REM. Pts in MDA had 38% and 2% chances of achieving LDA or REM. Pts in LDA at BL had a 20% chance of achieving REM and pts in REM a 67% chance of staying in REM. Achieving cDAPSA LDA or REM with APR at Wk52 was associated with residual disease activity as follows: SJ (1.2 vs. 0.24); TJ (2.6 vs. 0.52); MASES (1.2 vs. 0.43); dactylitis (0.47 vs. 0); PtGA (28.0 vs. 7.7); PAP (25.1 vs 7.2); PASI (4.0 vs. 2.7); HAQ (0.62 vs. 0.14). Removing pts with HDA at BL suggested that a mean cDAPSA 21 was associated with achieving LDA or REM at Wk52, corresponding to 5.5 in mean SJC and 9 in mean TJC at BL.



Abstract AB0927 – Figure 1

**Conclusions:** Chances of achieving LDA or REM were greater for pts in MDA at BL or Wk16 vs. HDA. Achieving LDA or REM at Wk52 with APR was associated with good outcomes across core PsA domains. Results suggest that pts with BL moderate cDAPSA disease activity may be particularly suitable for APR therapy.

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AB0928

**USTEKINUMAB AND TNF INHIBITORS IN PSORIATIC ARTHRITIS: FIRST FOLLOW-UP DATA FROM A ROUTINE CARE STUDY IN 8 EUROPEAN COUNTRIES (PSABIO)**

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**Background:** The purpose of PsABio (ClinicalTrials.gov Id: NCT02627768) is to evaluate the efficacy, tolerability and persistence of TNF inhibitors (TNFi) and ustekinumab (UST) for patients with psoriatic arthritis (PsA) starting 1st, 2nd or 3rd line biologic disease-modifying antirheumatic drugs (bDMARDs) in real-world routine care.

**Objectives:** Here we present the first interim follow-up data on joint-related outcomes.

**Methods:** Of 278 UST- and 285 TNFi-treated patients consecutively enrolled between Dec 2015 and Aug 2017 152 and 151, respectively, had data available at 6 months for their initial line of treatment. Joint-related outcomes, as observed data, were compared between baseline and 6 months within the treatment cohorts.

**Results:** Among all enrolled patients, 7.6% of UST- and 10.2% of TNFi-treated patients stopped or switched to another bDMARD before the 6 month timepoint. For those with 6 month data for their initial bDMARD, UST was used as the first-line bDMARD in 40.1%, as 2nd in 35.5%, and as 3rd in 24.3% of patients; these numbers were 64.2%, 28.5%, and 7.3%, respectively, for TNFi. DAS28 scores improved significantly at 6 months from mean baseline values of 4.3 (SD 1.2) and 4.3 (SD 1.2) for UST and TNFi, respectively, by means of -1.3 (95% CI: -1.6, -1.0) and -1.3 (95% CI: -1.6, -1.1). Significant improvements were seen in both cohorts across all treatment lines (table 1) and subtypes of PsA (data not shown). Minimal disease activity (MDA) was achieved at 6 months for 28.8% of UST- and 29.7% of TNFi-treated patients. CDAI results similarly and significantly improved. For the DAPSA, equally, statistically significant improvements were seen: mean -18.4 (95% CI: -22.2, -14.5) and -19.5 (95% CI: -22.5, -16.5) for UST and TNFi, respectively, with 12.2% and 15.7% reaching DAPSA remission and 37.8% and 37.1% reaching low disease activity. cDAPSA showed similar improvement. For details on components of the DAS28 and of the DAPSA, see table 1. Axial joint involvement was significantly improved with reductions in BASDAI and ASDAS.

**Abstract AB0928 – Table 1.** Baseline and follow-up data for joint-related outcomes for patients having reached 6 months on their initial bDMARD. Values are mean (SD) or mean (95% CI) if not otherwise indicated. na, not applicable.

	Baseline UST (n=152)	Change UST 6 months	Baseline TNFi (n=151)	Change TNF 6 months
Age, yrs	49.9 (12.2)	na	48.8 (12.6)	na
Disease duration since diagnosis, yrs	7.7 (7.6)	na	6.7 (7.4)	na
Sex (male), %	47.8	na	51.2	na
Smoking, % ever	47.1	na	47.4	na
current	26.1		26.1	
never	52.9		52.2	
Weight (kg)	82.3 (18.9)	-0.6 (-1.2, 0.1)	80.4 (15.2)	0.7 (0.2, 1.2)
BMI (kg/m <sup>2</sup> )	28.2 (5.5)	-0.2 (-0.4, 0.03)	27.9 (5.0)	0.2 (0.1, 0.4)
DAS28	4.3 (1.2)	-1.3 (-1.6, -1.0)	4.3 (1.2)	-1.3 (-1.6, -1.1)
1st line	(n=81) 4.1 (1.1)	-1.0 (-1.3, -0.6)	(n=97) 4.1 (1.3)	-1.3 (-1.6, -1.1)
≥2nd line	(n=91) 4.5 (1.3)	-1.5 (-1.9, -1.1)	(n=54) 4.5 (1.2)	-1.4 (-1.7, -1.0)
CDAI	22.8 (12.2)	-10.9 (-13.1, -8.6)	21.8 (12.2)	-10.8 (-12.6, -9.0)
1st line	(n=48) 21.6 (11.3)	-10.2 (-13.2, -7.1)	(n=76) 20.4 (11.7)	-10.0 (-12.2, -7.8)
≥2nd line	(n=73) 25.6 (12.7)	-11.3 (-14.4, -8.2)	(n=40) 24.4 (12.9)	-12.2 (-15.4, -9.1)
DAPSA	24.7 (21.2)	-18.4 (-22.2, -14.5)	35.4 (19.1)	-18.5 (-22.5, -16.5)
1st line	(n=32) 32.2 (15.3)	-16.2 (-21.3, -11.1)	(n=56) 32.7 (18.2)	-17.8 (-21.8, -13.9)
≥2nd line	(n=50) 36.2 (24.3)	-19.7 (-25.3, -14.2)	(n=33) 40.0 (20.1)	-22.5 (-27.3, -17.7)
cDAPSA	31.6 (19.9)	-15.6 (-18.6, -12.5)	32.2 (19.1)	-16.9 (-19.4, -14.4)
Swollen Joint Count (28)	3.9 (5.1)	-2.7 (-3.4, -1.9)	4.0 (4.5)	-2.5 (-3.1, -1.9)
Swollen Joint Count (66)	6.4 (8.4)	-4.3 (-4.4, -3.2)	7.0 (7.1)	-4.5 (-4.4, -3.6)
Tender Joint Count (28)	7.5 (6.8)	-3.6 (-4.3, -2.4)	6.3 (6.1)	-3.1 (-4.0, -2.3)
Tender Joint Count (68)	13.0 (12.7)	-4.1 (-4.4, -4.4)	12.8 (10.9)	-6.7 (-6.1, -5.3)
Patient pain VAS	55.9 (25.1)	-21.2 (-26.0, -16.4)	61.5 (23.7)	-27.8 (-32.3, -23.3)
Patient global VAS	60.5 (23.2)	-23.1 (-27.7, -18.4)	60.2 (23.7)	-27.8 (-32.3, -23.2)
Physician global VAS	56.3 (18.4)	-25.1 (-29.0, -21.2)	55.0 (20.5)	-25.1 (-28.5, -21.7)
CRP (mg/dl) median (IQR)	0.7 (0.3, 1.3)	-0.2 (-0.6, 0.0)	0.7 (0.3, 1.9)	-0.4 (-1.2, -0.04)
BASDAI*	5.8 (2.2)	-1.9 (-2.4, -1.5)	5.7 (2.1)	-2.1 (-2.5, -1.7)
ASDAS*	3.2 (1.1)	-1.0 (-1.2, -0.7)	3.4 (1.0)	-1.3 (-1.5, -1.1)

<sup>a</sup>Among all patients with available data at baseline and month 6 (UST, n=128; TNFi, n=114).

<sup>b</sup>Among all patients with available data at baseline and month 6 (UST, n=82; TNFi, n=87).

**Conclusions:** Both UST- and TNFi-treated patients showed statistically significant and considerable improvements in joint-related measures after 6 months in a real-world setting, irrespective of whether first or further line of treatment.



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**AB0929** **BURDEN OF SKIN AND JOINT SYMPTOMS OF PSORIATIC DISEASE: RESULTS OF A MULTI-NATIONAL PATIENT SURVEY**

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**Background:** Psoriatic Arthritis (PsA) and Psoriasis (PsO), have a significant impact on health-related quality of life and work productivity loss. In patients with both PsA and PsO, the full extent of the physical and emotional burden due to either joint related or skin related symptoms is not well understood from the perspective of the patient.

**Objectives:** To evaluate the patients' perspective on the overall burden of skin and joint related symptoms of PsA in a cross-sectional online survey.

**Methods:** A 20 min web based survey was developed based on analysis of 1-on-1 interviews with 30 PsA patients from the US, France and Germany. The final survey contained validated instruments including the PSA Quality of Life (PSAQoL) and Work Productivity and Activity Impairment (WPAI) questionnaires as well as custom questions designed to capture emotional burden of PsA and its impact on daily activities/situations. Additional data collected included demographics, severity of PsO by patient-reported body surface area involvement (BSA), severity of PsA by RAPID3, impact of PsO and PsA by a Patient Global Assessment scale with focus on skin or joint symptoms. In total, 439 psoriatic arthritis (PsA) patients from the US (68%), Germany (20%) and France (12%) were recruited to complete the survey.

**Results:** Among all participants, 30% had mild and 70% had mod-severe PsA based on RAPID-3 cutoffs, while 51% had mild and 48% had mod-severe PsO based on BSA cutoffs. According to multiple regression analyses, severity of joint symptoms and skin symptoms were significantly associated with lower PSAQoL ( $p < 0.0001$ ) as was age ( $p < 0.0001$ ). In patients with mild joint severity, impact of skin symptoms was significantly associated with PSAQoL ( $p < 0.0001$ ) as well as age and gender ( $p < 0.05$ ). Joint severity and impact of joint symptoms were the strongest contributors to the WPAI scores ( $p < 0.05$ ). When asked to select the 2 emotions most associated with the impact of their joint symptoms, patients most often chose fatigue (36%), worry/concern (19%) and depression (17%), and with respect to their skin symptoms, patients most often chose embarrassment (24%), fatigue (23%), worry/concern (14%) and depression (12%). When asked to rate the impact of their disease in certain scenarios or situations, more than 25% of patients reported that their joint symptoms had a severe impact (a choice of 8, 9 or 10 on a 10-point scale with 0=no impact and 10=severe) on fatigue (32%) "leisure activities" (26%), "how they think of themselves" (25%) and "how others felt about them" (26%). More than 25% of patients reported that their skin symptoms had a severe impact on fatigue (28%) "how they think of themselves" (27%), "how others thought of them" (27%) and "making a first impression" (28%).

**Conclusions:** In this survey of patients with PsA, we evaluated the patient's perspective on the burden of both skin-related and joint-related symptoms with the PsAQoL and WPAI as well as with a set of novel questions. Both skin and joint symptoms have a broad and meaningful impact on patient QoL, work productivity and patients reported a range of emotions as well as a variety of impacts on their daily activities with respect to skin and joint symptoms. This data highlights that there is a unique impact of PsA for each patient.

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**AB0930** **REAL-WORLD EFFECTIVENESS AND SAFETY OF APREMILAST IN GERMAN PATIENTS WITH PSORIATIC ARTHRITIS: ANALYSIS OF AN ONGOING MULTICENTRE, PROSPECTIVE, NON-INTERVENTIONAL STUDY**

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**Background:** Apremilast (APR) has been studied extensively in phase III randomised, controlled trials. However, there is a lack of real-world evidence of effectiveness and safety in a broad population of pts with psoriatic arthritis (PsA).

**Objectives:** To assess effectiveness and safety of APR in pts with active PsA from routine clinical practice settings in Germany.

**Methods:** In this multicentre, prospective, non-interventional study, the primary endpoint was the proportion of pts reaching  $\geq 1$  point ( $\geq 20\%$ ) improvement from baseline (BL) in the Physician's Global Assessment of Disease Activity (PhGA) score. Other endpoints included effects on tender and swollen joint counts, psoriasis-affected body surface area (BSA), enthesitis, dactylitis, Patient's Global Assessment of Disease Activity score (PtGA), Psoriatic Arthritis Impact of Disease tool (PsAID), pain and pruritus. The current analysis is based on observed data.

**Results:** The first 202 of a planned 500 German pts receiving APR for  $\geq 4$  month ( $\geq 1$  month [V1],  $\geq 4$  month [V2]) and 127 pts receiving APR for  $\geq 7$  months (V3) were evaluated. Mean age was 54 years, mean BMI was 29 kg/m<sup>2</sup> and 61% were female. The mean duration of psoriasis was 25 years and of PsA was 18 years;  $\approx 30\%$  of pts were biologic-experienced. The mean (SD) PhGA was 2.5 (0.56) at BL. After V1, 60% of pts achieved  $\geq 1$  point improvement in PhGA, which increased to 76% (V2) and 87% (V3). Mean (SD) PhGA decreased to 1.7 (0.69), 1.4 (0.73) and 1.1 (0.74) at V1, V2, and V3 respectively. Achievement of a PhGA of 0-1 increased from 0% of pts at BL to 36.8% (V1), 65.0% (V2) and 77.2% (V3). Median improvements in tender and swollen joint counts from BL to V3 were 57.1% and 60.0%, respectively. BSA improved from 11.4% at BL to 8.3%, 5.1% and 3.5% at V1, V2 and V3, respectively. At BL, 48.4% of pts had enthesitis based on Leeds Enthesitis Index; 46% reached a score of 0 by V1, 57% by V2% and 60% by V3. At BL, 27.3% of pts had dactylitis; a score of 0 was achieved by 40.0%, 66.7% and 71.9% of pts by V1, V2, and V3, respectively. BL mean PsAID score (5.33; max=10.00) decreased to 4.40 (V1), 3.85 (V2) and 3.36 (V3). Improvements were also seen in PtGA, overall pain and pruritus. A sub-analysis suggests that APR was associated with greater benefits in biologic-naive pts compared with pts who previously received biologic therapies. The observed safety and tolerability after V3 was consistent with the known overall safety profile of APR. Common AEs in clinical trials were similar, with a lower incidence: diarrhoea (10.4%), nausea (5.6%), headache (4.0%), and respiratory tract infection (1.2%).

**Conclusions:** The first results from this real-world PsA study reinforce findings from previous clinical trials of APR. In pts with  $\geq 4$  and  $\geq 7$  months of follow-up, APR was associated with improvements in both physician-assessed and patient-reported outcomes, with possibly a greater benefit in biologic-naive compared with biologic-experienced pts. Safety and tolerability were similar to the known profile of APR.

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AB0931

### PERSISTENCE WITH SUBCUTANEOUSLY ADMINISTERED BIOLOGICS AMONG PATIENTS WITH PSORIATIC ARTHRITIS: ANALYSES FROM A US CLAIMS DATABASE

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**Background:** Persistence with biologic therapies among patients with psoriatic arthritis (PsA) provides insight into the real-world effectiveness of biologics in routine clinical practice. With different dosing schedules and durations of action of currently available biologics, measuring persistence using varying treatment gap cutoffs may better guide physicians in their treatment decisions.

**Objectives:** To evaluate the persistence of subcutaneously (SC) administered biologics in patients with PsA.

**Methods:** Patients with  $\geq 1$  pharmacy claim for an FDA-approved SC biologic (adalimumab, certolizumab pegol, etanercept, golimumab, and secukinumab) for the treatment of PsA between 01/15/2016 and 07/31/2017 were identified in the Truven Health Analytics MarketScan Commercial and Medicare Supplemental Databases. Eligible patients were aged  $\geq 18$  years at the time of biologic initiation (index date) and continuously enrolled with medical and pharmacy claims  $\geq 12$  months prior to (baseline period) and  $\geq 12$  months after the index date. Patients had  $\geq 1$  PsA diagnosis (ICD-9-CM 696.0 or ICD-10-CM L40.5x) and no pharmacy claims for the index biologic during the baseline period. Persistence over 12 months was measured as the discontinuation rate and number of days persistent on the biologic therapy from the index date to reported treatment gaps of  $\geq 45$ ,  $\geq 90$ , and  $\geq 180$  days based on clinical expert opinion, or the end of follow-up if no gap was observed. The median time to discontinuation of the index biologic over 12 months was assessed by Kaplan-Meier analysis for each treatment gap cutoff.

**Results:** A total of 1558 patients with PsA enrolled in the analysis initiated SC biologics, including adalimumab (n=720), certolizumab pegol (n=93), etanercept (n=426), golimumab (n=64), and secukinumab (n=255). Overall, 680 patients (43.6%) discontinued their index biologic therapy during 12 month follow-up. The 12 month discontinuation rate for each treatment gap cutoff was lowest with secukinumab compared with other SC biologics (51.8%, 36.5%, and 21.6% for patients with treatment gaps  $\geq 45$  days,  $\geq 90$  days, and  $\geq 180$  days, respectively). Mean days persistent on the index biologic was the highest with secukinumab for each treatment gap cutoff (254.5 days, 282.8 days, and 307.5 days for patients with treatment gaps  $\geq 45$  days,  $\geq 90$  days, and  $\geq 180$  days, respectively) and the lowest with certolizumab pegol (218.1 days and 240.7 days for patients with treatment gaps  $\geq 45$  days and  $\geq 90$  days, respectively) and etanercept (270.7 days for patients with a treatment gap  $\geq 180$  days; table 1). The median (95% CI) time to discontinuation for patients with a treatment gap  $\geq 45$  days was the highest with secukinumab (308 [238 to >365] days) and lowest with certolizumab pegol (216 [155 to 274] days). Median time to discontinuation could not be calculated for patients with treatment gaps  $\geq 90$  days or  $\geq 180$  days due to low event rates and limited follow-up.

**Abstract AB0931 – Table 1.** Persistence With Index Biologic Therapies Over 12 Months of Follow-Up in Patients With Psoriatic Arthritis (N = 1558)

	Adalimumab (n = 720)	Certolizumab Pegol (n = 93)	Etanercept (n = 426)	Golimumab (n = 64)	Secukinumab (n = 255)
<b>Discontinuation of index drug, n (%)</b>					
Treatment gap $\geq 45$ days	395 (54.9)	61 (65.6)	255 (59.9)	38 (59.4)	132 (51.8)
Treatment gap $\geq 90$ days	307 (42.6)	48 (51.6)	203 (47.7)	29 (45.3)	93 (36.5)
Treatment gap $\geq 180$ days	208 (28.9)	32 (34.4)	148 (34.7)	21 (32.8)	55 (21.6)
<b>Days persistent on index drug, mean (SD)</b>					
Prior to gap of $\geq 45$ days	253.2 (120.5)	218.1 (127.1)	236.5 (125.8)	233.5 (128.4)	254.5 (123.8)
Prior to gap of $\geq 90$ days	206.0 (123.8)	240.7 (131.9)	249.5 (130.4)	253.7 (132.4)	282.8 (117.5)
Prior to gap of $\geq 180$ days	288.7 (122.7)	272.1 (131.8)	270.7 (132.5)	273.0 (135.7)	307.5 (112.2)

<?>Days persistent (ie, time to discontinuation) was defined as the time from the index prescription fill to the last day the drug was on hand to give a gap of  $\geq 45$ , 90, or 180 days without the index drug, or the end of follow-up if no gap was observed.

**Conclusions:** Patients who initiated secukinumab showed higher persistence over 12 months of follow-up compared with the other SC biologics assessed, regardless of the treatment gap.

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AB0932

### HELICOBACTER PYLORI ANTIGEN SPECIFIC ANTIBODIES IN PSORIATIC ARTHRITIS

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**Background:** The role of *Helicobacter pylori* (Hp) infection in the aetiopathogenesis of psoriatic arthritis (PsA) and psoriasis (Ps) is currently inconclusive, as studies reported increased, decreased or comparable to controls frequency of anti-Hp antibodies.

**Objectives:** To test antigen-specific Hp antibodies in a well-defined cohort of PsA patients and demographically matched Ps patients and healthy controls (HCs).

**Methods:** A total of 140 serum samples (48 PsA, 37 Ps and 55 HCs) were tested for anti-Hp antibodies by a western blot immunoassay using whole Hp extract as antigenic source.

**Results:** Overall, anti-Hp seropositivity was similar in PsA (19/48, 39.6%) and Ps (16/37 43.2%, p>0.05) but significantly lower compared to HCs (33/55, 60%, PsA vs HC, p=0.039). Overall, IgG anti-CagA and VacA, the most diagnostically relevant anti-Hp antibodies, were present in 26/48 (54.2%) and 5/48 (10.4%) PsA patients, respectively, compared to 15/37 (40.5%) (p=ns) and 1/37 (2.7%) (p=ns) Ps respectively, as well as in 39/55 (70.9%), (p=0.079) and 4/55/97.2%) (p=ns) HCs, respectively. Compared to HCs, patients with PsA had higher reactivity to p29 (UreA) (31/48, 64.6% vs 24/55, 43.5%, p=0.033) and to p54 (24/48, 50% vs 15/55, 27.2%, p=0.017) and tended to have higher positivity against p75 antigen (9/48, 18.9% vs 3/55, 5.4%, p=0.062). Reactivity to p50 (15/48, 31.3% vs 50.9, p=0.042) and p33 antigen (3/48, 6.3% vs 10/55, 18.2%, p=0.061) was lower in PsA than in HCs. No differences on anti-Hp antigen specific antibodies was found between PsA and Ps.

**Conclusions:** Although overall reactivity to Hp in PsA and Ps is lower than HCs, Hp infection cannot safely be considered a protecting microbial agent for these diseases, as reactivities to some Hp antigens are more frequently recognised to these diseases than in HCs.

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AB0933

### SURVIVAL AT 6 AND 12 MONTHS OF USTEKINUMAB IN PATIENTS WITH PSORIATIC ARTHRITIS IN CONDITIONS OF CLINICAL PRACTICE

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**Introduction:** Psoriatic arthritis (PsA) is a chronic inflammatory disease associated with skin psoriasis. Ustekinumab is a monoclonal antibody which inhibits IL12/23 and has proven efficacy and safety in the treatment of patients with PsA.

**Objectives:** To determine the survival rate and the reasons for Ustekinumab discontinuation in a patient cohort with PsA in conditions of clinical practice.

**Methods:** Descriptive, prospective, longitudinal and open study including 66 patients diagnosed with PsA and treated with Ustekinumab at dosis according to the data sheet (45 mg in the 0, 4 and every 12 weeks), except for 3 patients who were administered a 90 mg dose with the aforementioned regimen. The patients were monitored at 6 and 12 months. The following variables were collected: age, sex, years of evolution, previous treatment with Synthetic Disease Modifying Anti-Rheumatic Drugs (DMARDs) and/or biologic DMARD. All the adverse events (AE) which caused the discontinuation of the drug in patients who had received at least one dose of Ustekinumab were also collected. The Kaplan-Meier method was used to analyse the survival rate. The survival rate in naïve patients with biologic DMARD was compared with those who had received at least one biologic DMARD treatment before; and patients treated with Ustekinumab in monotherapy with those who were in a combined therapy with DMARDs. The Log-Rank Test was used for the comparative analysis of both subgroups

**Results:** Out of the 66 patients of our cohort, 34 (51.5%) were women, whose mean age was 47.2 $\pm$ 11.3 years. 49 presented only peripheral affection (74.2%), mainly in polyarticular form, and 10 had mixed affection. The rest presented axial affection exclusively. Our patients had been suffering from this disease for



an average of 6±7.7 years, and had received an average of 1.26±1.45 previous biologic DMARD. 51.5% were receiving Ustekinumab in a combined therapy with DMARD (most of them Methotrexate) and 48.5% were in monotherapy. The survival rates at 6 and 12 months were 85% and 74.6% respectively. Comparing the subgroups, the naïve patients with biologic DMARDs presented higher survival rates at 6 (91.6% vs 80.7%) and at 12 months (85.1% vs 66.7%), a statistically significant difference with the group that received previous biologic DMARD ( $p=0.036$ ). The patients in combined therapy with DMARDs presented higher rates of survival than the patients in monotherapy with Ustekinumab (90% vs 80%; 78% vs 71.1% at 6 and 12 months respectively), although the differences were not statistically significant. The main reason for discontinuation was the decrease of efficacy (14 patients; 21.2%), mostly in patients who had received previous treatment with biologic DMARD. 5 patients (7.6%) did not continue due to AE (2 due to relapsing herpes zoster; 1 patient deceased, with a personal history of neoplasms and a previous treatment with anti-TNF; and 2 had reactions at the injection site).

**Conclusions:** Ustekinumab is a safe drug, presenting high rates of drug retention, especially in patients who have not received any previous biologic therapy.

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AB0934

### OBESITY IN PATIENTS WITH PSORIATIC ARTHRITIS IN OUR AREA

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**Background:** Obesity is a comorbid condition in patients with psoriasis which tends to be less common in patients with psoriatic arthritis (PsA). In the general population, obesity is associated with increased inflammatory load and vascular risk, and with hypovitaminosis D.

**Objectives:** To explore the relationship between obesity and disease activity, vascular damage, serum concentrations of vitamin D (25OHD) and bone mineral density (BMD) in patients with PsA.

**Methods:** Descriptive cross-sectional study. Patients with PsA patients and peripheral joint involvement were consecutively included. Demographic (age, sex), clinical [duration of the disease, BMI (body mass index), DAS28] and analytical (25OHD, CRP, ESR) variables were collected. Patients with a BMI  $\geq 30$  kg/m<sup>2</sup>; were considered obese, and we considered vitamin D deficiency when 25OHD  $< 20$  ng/ml and vitamin D insufficiency when 25OHD 20–30 ng/ml. Within a period of 3 months, atheroma plaque and intima media thickness (IMT) measurement was performed by ultrasonography of the carotid arterial tree using an Esaote MyLab70XVG with a 7–12 MHz linear transducer and an automated program measuring IMT through radiofrequency (Quality intima media Thickness in real time, QIMT). Pulse wave velocity (PWV) was obtained by analysis of brachial pulse waves with an automated and validated system (Mobil O Graph). IMT  $> 900$   $\mu$  and PWV  $\geq 10$  m/s were considered pathological. Measurement of BMD was performed using an HOLOGIC densitometer. Statistical analysis was performed with the SPSS 17.0 program.

**Results:** We included 108 patients, 60% women, with a mean age of 55.6 (SD 12.6) years and a mean duration of PsA of 19.5 (SD 28) years. The mean BMI was 27 (DE 5.4) kg/m<sup>2</sup>; 35% of the patients being obese. The mean CRP, ESR and DAS28 were 6.6 (DE 4.5) mg/l, 10.7 (DE 11) mm/h and 2.32 (DE 0.8), respectively. 28% of patients had 25OHD deficiency and 32% had 25OHD insufficiency. The mean values of the IMT and PWV were 715 (SD 149)  $\mu$  and PWV 8 (SD 1.8) m/s, respectively. 12% of patients had osteoporosis, and up to 39% had osteopenia. Obesity was associated with a higher PsA activity measured by CRP (8.5 vs 5.7 mg/L,  $p=0.001$ ) and ESR (38.6 vs 8.7 mm/h,  $p=0.04$ ), although DAS28 was not different between groups. We also observed differences between obese and non-obese regarding the mean values of IMT (770 vs 709  $\mu$ ,  $p=0.046$ ) and PWV (8.9 vs 8 m/s,  $p=0.021$ ), the presence of atheroma plaque nearly reaching statistical significance (39% vs 30%,  $p=0.07$ ). No association was observed between obesity and 25OHD levels, BMD and DAS28.

**Conclusions:** obesity is linked to an increased inflammatory load and more vascular damage in our PsA patients. A strategy of tight control of obesity and other vascular risk factors should be implemented when monitoring PsA patients.

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AB0935

### CANADIAN ADALIMUMAB POST-MARKETING OBSERVATIONAL EPIDEMIOLOGICAL STUDY ASSESSING THE EFFECTIVENESS OF ADALIMUMAB VS NON-BIOLOGIC DMARDs IN PSORIATIC ARTHRITIS (COMPLETE-PSA): 12-MONTH EFFECTIVENESS DATA

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**Background:** To date, observational studies comparing the effectiveness of adalimumab (ADA) to non-biologic DMARDs (nbDMARD) in psoriatic arthritis (PsA) patients failing prior treatment are scarce. COMPLETE-PSA is a Canadian post-marketing observational study which assessed real-life effectiveness of ADA and non-biological therapies (NSAIDs and DMARDs) in PsA management following initial treatment failure.

**Objectives:** This analysis aimed to describe the baseline demographic and disease parameters of patients initiating nbDMARD or ADA and compare the 12 month real-life effectiveness of both treatments.

**Methods:** Patients eligible for COMPLETE PsA are anti-TNF $\alpha$  naïve adults, with active PsA who require change in their treatment regimen, per the judgment of the treating physician. In the current analysis patients enrolled during Jul/2011–Jun/2016 were included. Outcome measures analysed were: DAS28, SF-12, DLQI, presence of extra-articular manifestations (EAMs; enthesitis and dactylitis), psoriasis BSA, achievement of modified MDA (defined as achievement of [i] 4 of 6 (MDA 1) and [ii] 5 of the following 6 criteria (MDA 2): TJC  $\leq 1$ , SJC  $\leq 1$ , BSA  $\leq 3\%$ , pain VAS  $\leq 15$  mm, PtGA  $\leq 20$  and HAQ  $\leq 0.5$ ), modified remission (defined as SJC=0, TJC=0, absence of enthesitis and dactylitis, BSA  $\leq 3\%$  and HAQ  $\leq 0.5$ ), DAPSA LDA ( $\leq 14$ ), and DAPSA remission (REM;  $\leq 4$ ). Analyses were conducted by initial group assignment (intent-to-treat approach).

**Results:** 406 patients were included (nbDMARD n=146, ADA n=260). Baseline demographics were comparable between treatment groups. However, patients initiating ADA were more likely to be unemployed (47.3% ADA vs 34.9% nbDMARD,  $p=0.015$ ), had higher DAS28 (4.8 vs 4.4,  $p=0.002$ ) and total DLQI score (6.1 vs 4.3,  $p=0.007$ ), and were more likely to have BSA  $\geq 3\%$  (44.6% vs 35.0%,  $p=0.063$ ) and high DAPSA disease activity (50.8% vs 32.3%,  $p=0.015$ ). A higher proportion of nbDMARD patients had dactylitis (36.1% vs 25.3%,  $p=0.023$ ). No differences were observed between groups in enthesitis, overall EAMs, or QoL at baseline.

Upon 12 months of treatment, mean adjusted DAS28 (2.6 vs 3.4,  $p<0.001$ ) and DLQI (2.2 vs 2.9,  $p=0.530$ ) scores, but not SF-12, were lower in the ADA group. Furthermore, although statistical significance was not always met, patients treated with ADA had lower DAPSA score ( $p=0.025$ ) (LDA/REM: 64.9% vs 58.6%; REM: 37.7% vs 17.1%), were more likely to be in modified remission (14.7% vs 9.7%,  $p=0.311$ ), and to have mMDA (mMDA 1: 15.6% vs 12.6%,  $p=0.529$ ; mMDA 2: 17% vs 11.5%,  $p=0.253$ ) and BSA  $< 3\%$  (89.3% vs 83.9%,  $p=0.207$ ). Also, EAM prevalence decreased in both groups but was significantly lower in the ADA group (17.4% vs 35.8%,  $p<0.001$ ).

Over time, 9.6% of ADA patients initiated another biologic and 32.2% of patients in the nbDMARD group initiated biologic treatment ( $p<0.001$ ).

**Conclusions:** PsA patients initiating ADA in Canadian routine clinical care have significantly greater baseline disease severity compared with those initiating nbDMARDs. However, 12 month ADA treatment improved disease control and EAMs. DAPSA-REM evaluation seems more sensitive than mMDA in differentiating both populations.

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AB0936

**GOLIMUMAB IMPROVES DISEASE SIGNS AND SYMPTOMS, CONCOMITANT DISEASES AND CONCOMITANT DRUG USE IN PATIENTS WITH PSORIASIS ARTHRITIS IN A REAL-LIFE SETTING IN GERMANY**

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**Background:** Golimumab (GLM) has demonstrated efficacy and safety in several randomised clinical trials in Psoriatic Arthritis (PsA) patients. Data on disease signs and symptoms, concomitant diseases and concomitant drug in daily clinical practice are rare

**Objectives:** The aim of this subanalysis was to assess the effectiveness of GLM in patients with established PsA in a real-world setting in Germany

**Methods:** Descriptive post-hoc analysis of the non-interventional, prospective, 24 month study GO-NICE. Patients with established PsA starting with GLM 50 mg SC once monthly under routine clinical care conditions. Endpoint measures were: Physician's Global Assessment (PhGA) of patient's health status (visual analogue scale VAS: 0 no discomfort – 10 strong discomfort), change in concomitant diseases, concomitant drug use, inflammatory markers (CRP/ESR), improvement of the skin (PhGA-score: 0=none – 3=severe).

**Results:** A total of 501 patients with PsA were included at 121 sites and 231 (46.1%) completed the 24 month observation period. At baseline (BL) mean age 50.3 (±12.1) years, 271 (54.1%) females, mean time since first diagnosis 13.0 ±11.5 years, BMI 28.1 (±5.4) kg/m<sup>2</sup>. 169 (73.8%) patients received basic therapeutics, 286 (57.1%) had none previous biologics use, 136 (27.1%) one, and 79 (15.8%) at least two biologics.

439 (87.8%) had extra-articular diseases manifestations at BL. The most common were psoriasis (n=394, 78.8%), nail involvement (n=197, 39.4%), dactylitis (n=106, 21.2%), and enthesitis (70, 14.0%) at BL. The three most concomitant diseases were cardiovascular disease (n=151, 30.1%), depressive disorder (n=60, 12.0%), and diabetes mellitus (n=52, 10.4%). On GLM treatment, remarkable improvements were seen (table 1):

Abstract AB0936 – Table 1

Measures	visit 1/ BL	visit 5/ month 12	visit 9/ month 24
Number of evaluable patients n (%)	501 (100)	283 (56.5)	231 (46.1)
Physician's Global Assessment (PGA) of patient's health status (0–10)±SD	5.5 (±2.2)	2.4 (±2.0)	2.1 (±2.0)
<b>Concomitant diseases</b>			
· cardiovascular disease: n (%)	151 (30.1)	90 (18.0)	74 (14.8)
· depressive disorder: n (%)	60 (12.0)	33 (6.6)	32 (6.4)
· diabetes mellitus: n (%)	52 (10.4)	32 (6.4)	33 (6.6)
<b>Concomitant drug use</b>			
· MTX: n (%)	333 (66.5)	135 (47.7)	127 (55.0)
· sys. glucocorticoids: n (%)	206 (41.1)	74 (26.1)	48 (20.8)
· NSAIDs/Coxibs: n (%)	333 (66.5)	173 (61.1)	127 (55.0)
<b>Inflammatory markers</b>			
· CRP [mg/l] (% outside n.r.)	19.8 (45.8)	8.7 (16.3)	8.4 (15.1)
· ESR [mm/h] (% outside n.r.)	24.9 (36.5)	13.7 (13.0)	13.6 (15.1)

Additionally, the percentage of patients with severe psoriatic symptoms decreased from 11.8% (BL) to 1.8% (M12) to 0.4% (M24), and the percentage of patient without any symptom increased from 8.8% (BL) to 31.8% (M12) to 36.2% (M24). An increase in any of the prespecified concomitant diseases was not observed. No new safety signals were detected.

**Conclusions:** GLM SC once-monthly, administered to PsA patients according to routine clinical practice in Germany, showed remarkable improvements in Physician's Global Assessment of patient's health status, decrease in the number of concomitant diseases and concomitant glucocorticoids use, inflammatory markers (CRP/ESR) and skin symptoms over 24 months of treatment.

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AB0937

**EFFICACY OF NEW TREATMENTS ON DACTYLITIS OF PSORIASIS ARTHRITIS: UPDATE OF SYSTEMATIC LITERATURE REVIEW**

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**Background:** Dactylitis is a frequent disabling feature of psoriatic arthritis (PsA). Therapeutic strategy on dactylitis is not really codified.

**Objectives:** The objective of the study was to evaluate efficacy on dactylitis of different treatments actually available in PsA.

**Methods:** We performed a literature review from June 2014 to October 2017 based on Pubmed, using the search terms "psoriatic arthritis" and "treatment" with only clinical trials. 89 articles were identified (English-language reports only). Thus, we selected only randomised, double-blind placebo-controlled trials in which analysis of dactylitis was exposed: 11 articles were selected for full review.

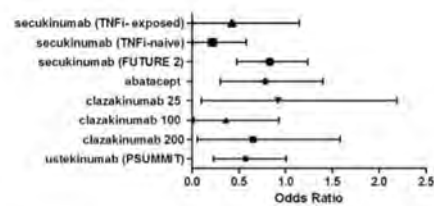
**Results:** Significant improvement of dactylitis (p<0.05) compared to placebo was observed with the use of golimumab in GO-VIBRANT, ustekinumab in PSUMMIT-1/PSUMMIT-2 trial, with apremilast 30 mg only in PALACE 3, with ixekizumab and adalimumab in SPIRIT-P1 (post hoc analysis).

For secukinumab, results are different: McInnes *et al.* (FUTURE 2) found no significant efficacy with 47% of dactylitis resolution at 24 weeks for secukinumab vs 11% for placebo (p=0.9195). At the opposite, Kavanaugh *et al.* (FUTURE 2) demonstrated secukinumab efficacy on anti-TNF-naïve (300 mg and 150 mg dosages) and anti-TNF-exposed patients (only 300 mg).

For Mc Innes *et al.*, clazakizumab permitted great decreases in the mean number of dactylitis from baseline to weeks 16 and 24 but no statistical data are available in the report. Similarly, in a recent publication, promising results were found for tofacitinib and abatacept, but no statistical data are available.

At the opposite, no significant efficacy was demonstrated in a randomised controlled trial with brodalumab.

Calculating of effect size was possible and available only in one study: secukinumab's effect size was 4.35 in McInnes study (FUTURE 2). Calculation of Odds Ratio (with of residual dactylitis between treatment and placebo groups was possible on part of studies with significant results for clazakizumab (200 mg dosing) and secukinumab in patients TNF exposed (figure 1).



Treatment	Ustekinumab (PSUMMIT 1-2)	Clazakizumab 200 (McInnes)	Clazakizumab 100 (McInnes)	Clazakizumab 25 (McInnes)	Abatacept (McInnes)	Secukinumab (FUTURE 2, McInnes)	Secukinumab (TNFi-naïve) (FUTURE 2, Kavanaugh)	Secukinumab (TNFi-exposed) (FUTURE 2, Kavanaugh)
Lower range	0.21	0.06	0.02	0.10	0.30	0.48	0.01	0.01
Mean	0.48	0.21	0.14	0.47	0.65	0.77	0.07	0.13
Upper range	1.01	1.58	0.93	2.19	1.40	1.24	0.58	1.15

Abstract AB0937 – Figure 1. Odds Ratio for residual dactylitis in treatment/placebo groups

**Conclusions:** Dactylitis was always used as secondary outcome criteria with heterogeneous results. So conclusions need to be cautious. This invalidating clinical manifestation need to be evaluated as a primary outcome in the future.

**Disclosure of Interest:** None declared

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**AB0938 TREATMENT PATTERNS IN EARLY PSORIATIC ARTHRITIS ACCORDING TO THE AGE OF ONSET**

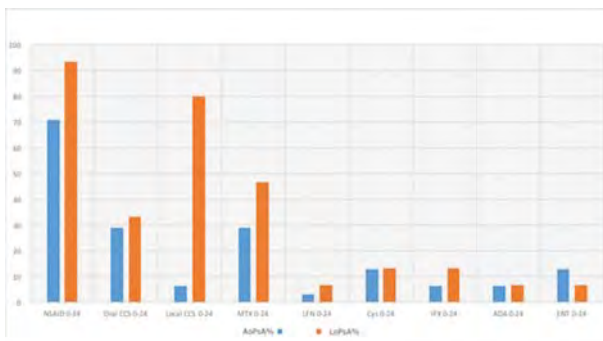
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**Background:** The initial treatment of Psoriatic Arthritis (PsA) is largely based on the extent of musculoskeletal involvement and disease severity according to the stepwise approach of EULAR and GRAPPA recommendations for PsA management, but without regard to the age of onset.

**Objectives:** This prospective observational study aimed<sup>1</sup> to describe treatment prescribing patterns in PsA over the first 2 years of follow-up and<sup>2</sup> to determine if the treatment patterns are conditioned by the age of onset.

**Methods:** Patients with at least 2 years of follow-up within the PsArT (Psoriatic arthritis Age-related Treatment patterns) study were included. Patients with a diagnosis of early (symptom duration <52 weeks) PsA, made by rheumatologists with long-standing expertise in PsA, were consecutively recruited and divided into Adult-Onset (AOPsA) (age <60 years) and Late-Onset (LOPsA) (onset age ≥60 years) PsA according to the age at the onset of musculoskeletal manifestations. For the aim of this study, patient's data were collected at the enrolment (baseline) (T0), at 12 months (T12) and at 24 months (T24). Clinical, laboratory features and treatment patterns, over 2 years were described according to the age stratification.

**Results:** 46 PsA patients (22 M, 24 F; age 49±16, range 16–90 years) with a disease duration of 20±15 weeks (range 1–52) were enrolled. Compared to the 31 patients with AOPsA, the 15 patients with LOPsA had a significant shorter disease duration (17±15 vs. 21±15 weeks, p<0.05) and showed more frequently increased levels of ESR (75% vs. 43%, p<0.05) and CRP (87% vs. 52%, p<0.01). In addition, patients with LOPsA developed more frequently inflammatory extremity swelling with pitting oedema (IESPE) over the dorsum of hands and/or of the feet (56% vs. 13%, p<0.01). There were no other significant differences between the 2 groups even though more males were observed in the LOPsA group (56% vs. 42%, p>0.05). The sensitivity of the CASPAR criteria was similar in AOPsA (78%) and LOPsA (75%). Of 46 patients during the first year 80.4% received non steroidal anti-inflammatory drugs, 32.6% received oral corticosteroids, 13.0% received local corticosteroids, 19.5% received synthetic disease-modifying anti-rheumatic drugs (sDMARDs) and 6.5% received biologics (bDMARDs: IFX, ADA, GOL, ETN). During the second year of follow up 73.9% received non steroidal anti-inflammatory drugs, 30.4% received oral corticosteroids, 50% received synthetic disease-modifying anti-rheumatic drugs (sDMARD), 15.2% received biologics (IFX, ADA, GOL, ETN) and received 30.4% local corticosteroids. (see figure) About the drug intake the only statistical significant difference between the two groups was the rate of patients using NSAIDs in LoPsA group during the first year (100% vs. 70.9%, p value 0.02). There were no other significant differences in drug intake, therapy changes, discontinuation, add-on therapy according to the age of PsA onset.



Abstract AB0938 – Figure 1

**Conclusions:** During the two years of follow up period a high proportion of patient received NSAIDs in LoPsA group during the first year. The main limit of our study is the low number of patients, therefore a greater number could help to understand whether the age of onset may affect the use of specific type of drugs.

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**Disclosure of Interest:** None declared

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**AB0939 OFF-LABEL SECUKINUMAB DOSE ESCALATION IN THE TREATMENT OF MODERATE-TO-SEVERE PSORIASIS: A MULTICENTER, RETROSPECTIVE STUDY**

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**Background:** There have been significant advancements in the development of biologics over the past decade that revolutionised treatment for psoriasis and psoriatic arthritis. Interleukin (IL)-17A is a pro-inflammatory cytokine that plays a pivotal role in the pathogenesis of psoriatic disease, and is therefore a target for biologic drug development. Secukinumab is an IL-17A antagonist approved in 2015 for the treatment of psoriatic arthritis and moderate-to-severe psoriasis in adults. Its current approved dosing schedule for psoriasis patients is 300 mg subcutaneous weekly for 5 weeks, followed by monthly maintenance dosing.<sup>1</sup>

Some psoriasis patients in clinical practice exhibit a suboptimal response to secukinumab or experience relapse with the approved dosing schedule. In these cases, clinicians may use off-label secukinumab dose escalation regimens, which involve increasing the maintenance dosing frequency to every 2 or 3 weeks, or increasing the monthly dose to 450 mg. No guidelines currently exist for high dose secukinumab regimens.

**Objectives:** The objective of this study was to assess the efficacy and safety of off-label high dose secukinumab regimens in adults with moderate-to-severe psoriasis.

**Methods:** We performed a retrospective chart review for adult patients diagnosed with moderate-to-severe psoriasis treated with an off-label secukinumab up-dose regimen. Efficacy was measured using Psoriasis Area and Severity Index (PASI)-75 or a Physician Global Assessment (PGA) score of 0 or 1 after dose escalation. To assess safety, adverse events (AEs) were recorded.

**Results:** Twenty-five patients were included in this study, 13 (52%) of which also had psoriatic arthritis. The mean treatment time with secukinumab prior to dose escalation was 44.5 weeks. Twelve patients had PASI recorded prior to dose escalation, with a mean score of 5.7. Of the remaining 13 patients, 1 had no documentation of disease severity and 12 had PGA scores of 0 (n=2), 1 (n=1), 2 (n=5), 3 (n=2), and 4 (n=2). These patients then increased their dose to 300 mg secukinumab every 3 weeks (n=10), 300 mg every 2 weeks (n=9), or 450 mg monthly (n=6). Mean follow-up time was 15.9 weeks after dose escalation, where 4 patients achieved PASI-75 and 10 achieved PGA 0 or 1. Therefore, 14 out of 25 (56%) patients had effective outcomes from secukinumab dose escalation based on our study endpoints. AEs included one case of the common cold and an upper respiratory tract infection after dose escalation.

**Conclusions:** This study provides evidence of safety and moderate efficacy for high dose secukinumab regimens in psoriasis patients who display an inadequate response to the approved regimen. Increased dosing did not result in more AEs compared to secukinumab phase 3 clinical trials that used the approved regimen.<sup>2</sup> As such, there may be a role for increased dosing in psoriatic arthritis patients.

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**Disclosure of Interest:** None declared

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**AB0940 HEALTH SERVICES RESEARCH PROJECT FOR THE EARLY DIAGNOSIS OF PSORIATIC ARTHRITIS: MONOCENTRIC QUESTIONNAIRE-BASED STUDY TO IDENTIFY PATIENTS WITH ARTHRITIS AND DETECT SIGNS OF DEPRESSION IN 150 PATIENTS**

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**Background:** Psoriatic arthritis (PsA) is an inflammatory rheumatic disease affecting approximately 30% of psoriasis (PsO) patients. Despite increased awareness there is still a considerable delay in diagnosis. Untreated PsA may lead to irreversible joint destruction associated with a high rate of disability and depression. A timely diagnosis and initiation of treatment are therefore essential.

**Objectives:** In order to minimise diagnostic delay and improve patient care, we have implemented a questionnaire-based screening procedure in the dermatology outpatient clinic to identify patients with suspected PsA.

**Methods:** A questionnaire-based screening (PEST, FFbH, WHOQOL-BREF, Phq9, GHQ-12) was used to assess PsO patients for PsA, depression, comorbidities, and quality of life (QOL).

**Results:** So far we have assessed 150 PsO patients. 79% reported joint affection with a mean number of 4.58 involved joint regions, predominantly at the lower extremities. 34% described axial involvement. 42% had a score of  $\geq 3$  in the PEST tool, being suspicious for PsA. 4% had a clinically relevant functional impairment in daily life assessed by FFbH questionnaire (score  $< 60\%$ ). In WHOQOL-BREF PsO patients scored lower on the physical health as well as the psychological wellbeing scale when compared to reference values for healthy controls, while results in the social relationship and environment domains were comparable. When comparing patients with suspected PsA to PsO without arthritis the former group reached significantly lower scores in the physical health domain ( $p=0.0001$ ), in the psychological wellbeing ( $p=0.0434$ ), and environment domains ( $p=0.0384$ ), especially regarding items assessing body image/appearance and negative feelings for psychological wellbeing as well as physical security and mobility/transport in the environment domain. For the social domain there were no differences. In the Phq9 questionnaire patients reached a mean of 6.5 points equalling mild depressive symptoms. 16% of PsO patients had moderate depressive symptoms, while 9% had severe depressive symptoms. In patients with suspected PsA 44% had moderate (26%) or severe (18%) depression compared to 7% and 2% respectively in PsO patients without arthritis.

**Conclusions:** Screening questionnaires are valuable tools for dermatologists as well as general practitioners and help to identify PsO patients with musculoskeletal involvement pointing towards psoriatic arthritis. Thus, screening questionnaires can add to ensure timely referral of patients with inflammatory joint involvement and depression to the corresponding specialists and help to avoid a delay of treatment. Our data confirm an association of psoriasis, depressive symptoms and reduced quality of life, which was even stronger in patients with psoriatic arthritis.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.5834

AB0941

#### PATIENT AND PHYSICIAN GLOBAL ASSESSMENTS REFLECT STRONGLY DIVERGING ATTITUDES BETWEEN PATIENTS WITH PSORIATIC ARTHRITIS AND THEIR RHEUMATOLOGISTS TO SEVERITY OF DISEASE AND TO THE RELATIVE IMPORTANCE OF DIFFERENT OUTCOME MEASURES

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**Background:** Assessment of disease activity is important in the evaluation and monitoring of patients with psoriatic arthritis (PsA) in clinical care and research. As there is no single 'gold standard' variable for assessment of disease activity several markers of disease activity are used, among these "global assessment" by the patient (PaGI) and by the physician (PhGI). The agreement and interplay between PaGI and PhGI are not well clarified in patients with PsA, however.

**Objectives:** The study aimed to examine associations on the group level and agreements on the individual patient level between PaGI and PhGI as scored on visual analogue scales (VAS) in the daily clinic by patients with active PsA and by their rheumatologists.

**Methods:** Traditional disease activity data on 76 PsA patients with active disease planned to initiate biological treatment were extracted from the Danish DANBIO registry for biological treatment in rheumatology. Data comprised PaGI, PhGI and pain (0–100 VAS), 28 swollen joint count (SJC), 28 tender joint count (TJC), CRP, HAQ-DI and DAS28-CRP(4 v). Analyses were performed using parametric statistics. The association between PaGI and PhGI was examined by simple linear regression analysis. The predictability of PaGI and PhGI, respectively, by all other disease markers mentioned and by age and sex was examined using stepwise multiple regression analysis. Agreement between the VAS scores was expressed as the bias (mean difference between intra-individual scores) and the 95% lower and upper limits of agreement (LLoA; ULoA) according to the Bland-Altman method.

**Results:** Mean age was  $52.2 \pm 11.1$  years and mean DAS28-CRP  $4.7\% \pm 1.1$ . 59.2% of the patients were women. Mean PaGI was  $63.7 \pm 23.2$  and mean PhGI  $39.9 \pm 19.8$  ( $p < 0.0001$ ). Thus the difference between PaGI and PhGI was substantial on the group level. Differences between PaGI and PhGI were even more

pronounced on the individual level, however. The average difference was 23.8 (bias) but differences on the individual level ranged from  $-21.9$  (LLoA) to  $+69.5$  (ULoA). The corresponding results for PaGI vs. pain was 4.9 (bias),  $-17.1$  (LLoA) and 22.0 (ULoA), and for pain vs. PhGI 18.9 (bias),  $-23.0$  (LLoA) and 60.8 (ULoA). PaGI was significantly but weakly correlated with PhGI ( $R=0.42$ ,  $p < 0.0001$ ) with a high standard error of estimation (SEE)=21.2. PaGI was independently predicted by pain ( $\beta=0.76$ ,  $p < 0.0001$ ) and HAQ-DI ( $\beta=0.19$ ,  $p < 0.01$ ) and was not predicted by PhGI ( $p=0.61$ ) ( $R=0.78$ ,  $SEE=10.5$ ,  $p < 0.0001$ ). PhGI was independently predicted by SJC ( $\beta=0.43$ ,  $p < 0.0001$ ) followed by pain ( $\beta=0.41$ ,  $p < 0.0001$ ) and CRP ( $\beta=0.20$ ,  $p < 0.05$ ) ( $R=0.70$ ,  $SEE=14.4$ ,  $p < 0.0001$ ) with no significant contribution by PaGI ( $p=0.49$ ).

**Conclusions:** In patients with active PsA initiating biological treatment, PaGI was in general scored considerably higher than PhGI. On the individual patient level, differences between PaGI and PhGI varied substantially. PaGI was best explained by pain, and PhGI by SJC. The findings reflect strongly diverging attitudes between PsA patients and their rheumatologists to severity of disease and to the relative importance of different outcome measures.

**Disclosure of Interest:** None declared

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AB0942

#### CONCORDANCE BETWEEN FATIGUE, PAIN AND PATIENT GLOBAL ASSESSMENT IN INDIVIDUAL PATIENTS WITH PSORIATIC ARTHRITIS

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**Background:** Associations between fatigue (FTG), pain and patient global assessment (PaGI) have been examined on the group level in patients with psoriatic arthritis (PsA), but studies focusing on the concordance between these patient-reported outcome measures (PROMs) in individual patients are missing. A better understanding of how tight the measures are bounded in individuals may improve our ability to deal with them in the daily clinic.

**Objectives:** To examine associations on the group level and concordance on the individual patient level between FTG, pain and PaGI as scored on 0–100 visual analogue scales (VAS) in the daily clinic by patients with PsA. The influence of other clinical disease activity measures on these measures was also examined.

**Methods:** Data on 132 outclinic PSA patients treated with biological agents were extracted from the Danish registry for biological treatment in rheumatology (DANBIO). Data comprised VAS FTG, pain, PaGI and physician global assessment (PhGI), and HAQ-DI, swollen and tender joint counts (66/68), CRP, DAS28-CRP and age. Simple linear regression analyses were used to assess the association between FTG, pain and PaGI. Independent predictors of FTG, pain and PaGI were identified using stepwise multiple regression analysis. Degrees of association were expressed by coefficients of correlation, beta-values and standard errors of estimation (SEE). Concordance between FTG, pain and PaGI on the individual patient level was examined using the Bland-Altman method yielding 95% lower and upper limits of agreement (LLoA and ULoA) and corresponding biases (mean of intra-individual differences).

**Results:** Mean age was  $54 \pm 13$  years, mean DAS28  $3.7 \pm 1.5$  and mean PaGI  $56 \pm 28$ . FTG, pain and PaGI were strongly inter-associated but errors of estimation were substantial ( $r$ -range 0.80–0.94,  $p < 0.0001$ ,  $SEE$ -range 11.5–16.9). FTG, pain and PaGI were only poorly correlated with objective measures of disease activity (for example,  $r$ -range for swollen joint count 0.19–0.25,  $p < 0.05$ ). FTG was independently predicted ( $\beta$ ,  $p$ -value) by PaGI (0.51,  $< 0.001$ ) and pain (0.31,  $< 0.05$ ) ( $R^2=0.66$ ,  $p < 0.05$ ,  $SEE=16.7$ ), pain by PaGI (0.82,  $< 0.0001$ ) and HAQ-DI (0.15,  $< 0.005$ ) ( $R^2=0.88$ ,  $p < 0.005$ ,  $SEE=10.5$ ) and PaGI by pain (0.80,  $< 0.0001$ ) and fatigue (0.17,  $< 0.001$ ) ( $R^2=0.89$ ,  $p < 0.001$ ,  $SEE=12.4$ ). Swollen and tender joint count, CRP and PhGI did not add to the explanation of the patient-reported VAS scores. The bias [LLoA; ULoA] for FTG versus pain was  $8.5 \pm 19.1$  ( $p < 0.0001$ ) [ $-29.1$ ; 45.9], for FTG versus PaGI  $4.1 \pm 19.4$  ( $p < 0.05$ ) [ $-34.0$ ; 42.2] and for PaGI versus pain  $4.4 \pm 11.5$  ( $p < 0.0001$ ) [ $-18.1$ ; 26.9]. Thus biases were small but limits of agreement were pronounced.

**Conclusions:** In patients with PsA, VAS FTG, pain and PaGI were nearly identical and were strongly inter-associated on the group level with no explanatory influence of more objective measures. However, on the individual patient level substantial discrepancies between the VAS scores were observed. The findings emphasise the complexity of understanding and dealing with PROMs in the daily clinic.

**Disclosure of Interest:** None declared

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AB0943

**SUSTAINED IMPROVEMENTS WITH UP TO 104 WEEKS OF APREMLAST MONOTHERAPY IN BIOLOGIC-NAÏVE SUBJECTS WITH ACTIVE PSORIATIC ARTHRITIS: RESULTS FROM A PHASE 3B, RANDOMISED, CONTROLLED TRIAL**

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**Background:** ACTIVE is the first apremilast (APR) study to demonstrate onset of response to APR starting at Week 2 in biologic-naïve subjects with psoriatic arthritis (PsA) who may have had exposure to 1 prior conventional disease-modifying anti-rheumatic drug.

**Objectives:** To determine the efficacy and safety of APR through Week 104 in the ACTIVE study.

**Methods:** Subjects were randomised (1:1) to receive APR 30 mg BID or placebo (PBO) for 24 weeks; thereafter, all subjects received active treatment with APR. The long-term durability of APR treatment on various PsA manifestations was evaluated. Along with safety data, adverse events (AEs) of diarrhoea were further characterised.

**Results:** A total of 219 subjects were randomised (APR: n=110; PBO: n=109); 89% (142/160) of subjects entering year 2 of the study completed the Week 104 visit, and 64.8% (142/219) of randomised subjects completed the Week 104 visit, including 60.9% (67/110) of subjects randomised to APR at baseline. Early onset of response to APR was observed for ACR20 response and improvements in DAS-28 (CRP), HAQ-DI, enthesitis (in subjects with enthesitis at baseline), and morning stiffness severity. With continued APR exposure, the Week 104 ACR20 response rate was 62.9%; ACR50 and ACR70 response rates were 33.3% and 20.1%, respectively. Mean percent change in swollen joint count was -75.9%, and mean percent change in tender joint count was -68.3%. In all, 65.7% of APR subjects with baseline enthesitis reached a Gladman Enthesitis Index score of 0 (table 1). More than half of the APR subjects had improvements in morning stiffness severity. Sustained improvements in physical function were also observed, with a mean change of 5.9 in the SF-36v2 Physical Functioning score and a mean change in HAQ-DI score of -0.37 at Week 104. Safety findings for the APR-exposure period were consistent with previous reports. The most commonly reported AEs ( $\geq 5\%$  of subjects) during the APR-exposure period were bronchitis (5.3%), headache (6.3%), hypertension (6.3%), nasopharyngitis (8.3%), upper respiratory tract infection (8.3%), nausea (8.7%), and diarrhoea (16.5%). New incidences of protocol-defined diarrhoea ( $\geq 2$  watery/liquid stools/day) decreased during long-term APR exposure. Over the APR-exposure period, serious AEs occurred in 7.3% of subjects; 8.3% of subjects discontinued treatment due to an AE. No serious opportunistic infections, including tuberculosis reactivation, or cases of serious depression were seen.

	Week 52 APR 30 mg BID n=171	Week 104 APR 30 mg BID n=144
ACR20, n/m (%)	107/169 (63.3)	90/143 (62.9)
ACR50, n/m (%)	55/170 (32.4)	48/144 (33.3)
ACR70, n/m (%)	24/171 (14.0)	29/144 (20.1)
DAS-28 (CRP), mean change	-1.59	-1.66
Swollen joint count (0-76), mean % change	-74.5	-75.9
Tender joint count (0-78), mean % change	-65.6	-68.3
Gladman Enthesitis Index score (0-6)*, mean change	-1.5	-1.5
Gladman Enthesitis Index score=0*, n/m (%)	54/86 (62.8)	46/70 (65.7)
Improvement in morning stiffness severity, n/m (%)	98/171 (57.3)	79/144 (54.9)
SF-36v2 Physical Functioning score, mean change	5.5	5.9
HAQ-DI score (0-3), mean change	-0.36	-0.37
HAQ-DI MCID $\geq 0.30$ , n/m (%)	78/171 (45.6)	68/144 (47.2)

Abstract AB0943 – Figure 1

Week 52 and Week 104 analyses were data as observed among all subjects who received APR, regardless of when APR treatment started (baseline, Week 16 or Week 24); actual number of subjects may vary for each end point depending on availability of data.

\*Evaluated in subjects with enthesitis at baseline (Gladman Enthesitis Index score  $>0$ ).

ACR20/50/70= $\geq 20\%/ \geq 50\%/ \geq 70\%$  improvement in modified American College of Rheumatology response criteria; n/m=number of responders/number of subjects with sufficient data for evaluation; DAS-28=28 joint count Disease Activity Score; CRP=C reactive protein; SF-36v2=36 item Short-Form Health Survey version 2; HAQ-DI=Health Assessment Questionnaire-Disability index; MCID=minimal clinically important differences.

**Conclusions:** In biologic-naïve subjects treated with APR, early onset of effect was observed across PsA manifestations, including morning stiffness severity and enthesitis, with sustained improvements through Week 104 in the subjects continuing APR therapy. AEs were consistent with those reported for other APR phase 3 PsA and psoriasis studies.

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AB0944

**EFFICACY AND SAFETY OF IXEKIZUMAB WHEN USED ALONE OR IN COMBINATION WITH CONVENTIONAL DISEASE-MODIFYING ANTIRHEUMATIC DRUGS (CDMARDs) IN TNF-EXPERIENCED PATIENTS WITH PSORIATIC ARTHRITIS**

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**Background:** Registry studies<sup>1,2</sup> suggest that cDMARDs do not improve TNFi efficacy in the treatment of psoriatic arthritis (PsA), but studies of novel biologics are warranted. In SPIRIT-P2, TNFi-experienced patients with active PsA were treated with ixekizumab (IXE), a high-affinity monoclonal antibody that selectively targets IL-17A.

**Objectives:** We conducted post-hoc analyses of SPIRIT-P2 data to investigate the efficacy and safety of IXE relative to placebo (PBO) when used alone or in combination with background MTX or cDMARDs in patients with PsA.

**Methods:** SPIRIT-P2 (NCT02349295) is a phase 3, multi-centre, randomised, double-blind, placebo-controlled trial of IXE in adults with active PsA and prior TNFi-inadequate response or intolerance. Patients were randomised 1:1:1 to receive PBO, 80 mg IXE either every 4 weeks (Q4W) or every 2 weeks (Q2W), after receiving a 160 mg initial IXE dose. Eligible established background cDMARD therapy was allowed in the double-blind treatment period (Week 0–24), but no changes were allowed unless for safety reasons or due to inadequate response at week 16. Efficacy and safety were assessed at week 24. Efficacy outcome measurements included ACR 20/50 responses, achievement of minimal disease activity (MDA), 28-joint disease activity score using CRP (DAS28-CRP), disease activity in psoriatic arthritis (DAPSA), and HAQ-DI. All comparisons were made relative to PBO by Fisher's exact test for categorical end points and analysis of covariance models for continuous end points.

**Results:** At baseline, 185 (51%) patients received background cDMARDs. Of these patients, 149 received background MTX. ACR20, ACR50, and MDA response rates were significantly higher in patients treated with IXE versus PBO regardless of background cDMARD use (table 1). Disease activity improved significantly with IXE versus PBO in each subgroup, as measured by DAS28-CRP and DAPSA. Likewise, physical function improved with IXE versus PBO as indicated by significantly more profound decreases in HAQ-DI with IXEQ4W with or without background cDMARDs, and with IXEQ2W monotherapy. HAQ-DI improvements were significantly more profound versus PBO in patients treated with IXEQ4W with or without background cDMARDs, and with IXEQ2W monotherapy. Among IXE treated patients, higher proportions of patients achieved HAQ-DI MCID in all subgroups versus PBO, but these were only significantly higher in patients treated with IXEQ4W or IXEQ2W monotherapy. Regardless of background cDMARD use, efficacy outcomes were significantly improved with both IXE groups versus PBO, except for HAQ-DI for IXEQ2W in combination with cDMARDs and HAQ-DI MCID in all background cDMARD subgroups. The proportions of patients who experienced  $\geq 1$  treatment emergent adverse events (AE), serious AEs (including serious infections), or discontinuations due to AEs were comparable to the overall trial population.<sup>3</sup>

**Abstract AB0944 – Table 1.** SPIRIT-P2 outcomes and safety results at 24 weeks according to cDMARD use at baseline.

Outcomes	Background cDMARD			Background MTX			Monotherapy		
	PBO n=52	IXEQ4W n=60	IXEQ2W n=73	PBO n=40	IXEQ4W n=48	IXEQ2W n=61	PBO n=66	IXEQ4W n=62	IXEQ2W n=50
ACR20, n (%)	12 (23.1)	30 (50.0)*	34 (46.6)*	7 (17.5)	24 (50.0)*	31 (50.8)*	11 (16.7)	35 (56.5)*	25 (50.0)*
ACR50, n (%)	4 (7.7)	17 (28.3)*	22 (30.1)*	3 (7.5)	15 (31.3)*	20 (32.8)*	2 (3.0)	28 (45.2)*	19 (38.0)*
MDA <sup>†</sup> , n (%)	1 (1.9)	18 (30.0)*	14 (19.2)*	0	15 (31.3)*	13 (21.3)*	3 (4.5)	16 (25.8)*	15 (30.0)*
DAS28-CRP, LSM (SE)	-0.6 (0.17)	-1.8 (0.16)*	-1.2 (0.14)*	-0.5 (0.21)	-1.9 (0.19)*	-1.2 (0.16)*	-0.4 (0.17)	-1.7 (0.17)*	-1.8 (0.15)*
DAPSA, LSM (SE)	-11.5 (2.8)	-25.4 (2.7)*	-19.0 (2.4)*	-9.2 (3.4)	-24.7 (3.1)*	-18.2 (2.7)*	-6.4 (2.8)	-26.0 (2.8)*	-26.9 (3.2)*
HAQ-DI, LSM (SE)	0.0 (0.07)	-0.3 (0.06)*	-0.2 (0.06)	0 (0.1)	-0.3 (0.1)*	-0.2 (0.1)	0.0 (0.06)	-0.5 (0.06)*	-0.4 (0.07)*
HAQ-DI MCID <sup>‡</sup> , n (%)	9 (17.3)	17 (28.3)	20 (27.4)	7 (19.4)	14 (35.9)*	17 (32.1)*	9 (13.6)	28 (45.2)*	23 (46.0)*
Safety									
TEAE (≥1), n (%)	33 (63.5)	43 (71.7)	51 (69.9)	25 (62.5)	35 (72.9)	40 (65.6)	43 (65.2)	40 (64.5)	39 (78.0)
Serious AEs, n (%)	2 (3.8)	1 (1.7)	4 (5.5)	2 (5.0)	1 (2.1)	3 (4.9)	2 (3.0)	2 (3.2)	4 (8.0)
Serious Infections <sup>§</sup> , n (%)	0	0	2 (2.7)	0	0	2 (3.3)	0	0	1 (2.0)
Discontinuation due to AE, n (%)	4 (7.7)	3 (5.0)	3 (4.1)	4 (10.0)	1 (2.1)	3 (4.9)	2 (3.0)	2 (3.2)	5 (10.0)

<sup>†</sup>Patients classified as achieving MDA if they fulfilled 5 of 7 MDA criteria.  
<sup>‡</sup>HAQ-DI (Health Assessment Questionnaire-Disability Index) minimal clinically important difference (MCID) defined as improvement  $\geq 0.35$  in patients with a baseline HAQ-DI  $\geq 0.35$   
<sup>§</sup>None of the reported serious infections were related to *Candida* or *Tuberculosis*  
<sup>¶</sup>p<0.05, <sup>††</sup>p<0.01, <sup>†††</sup>p<0.001, all versus placebo; ACR, American College of Rheumatology; LSM, least squares mean; n, number of patients; SE, standard error  
**Conclusions:** The efficacy of IXE versus PBO in PsA was similar in patients with or without background cDMARD use in this post hoc analysis with safety profiles comparable to the overall trial population.<sup>3</sup>

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**Disclosure of Interest:** P. Nash Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Hospira, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi, UCB, Consultant for: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Hospira, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi, UCB, Speakers bureau: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Hospira, Janssen, MSD, Novartis, Pfizer, Roche, Chugai, Prophylix, Novartis, Iron4U, Consultant for: Abbvie, Pfizer, Roche, Chugai, UCB, BMS, Celgene, MSD, Novartis, Biotest, Janssen, Genzyme, Sanofi, Lilly, Sandoz, Speakers bureau: Abbvie, Pfizer, Roche, Chugai, UCB, BMS, Celgene, MSD, Novartis, Biotest, Janssen, Genzyme, Sanofi, Lilly, Sandoz, A.-M. Orbai Grant/research support from: Abbvie, Celgene, Eli Lilly and Company, Horizon, Janssen, Novartis, Pfizer, Consultant for: Eli Lilly and Company, Janssen, Novartis, Pfizer, UCB, S. Rathmann Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, D. Adams Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, O. Benichou Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, A. Deodhar Grant/research support from: Pfizer, Consultant for: Pfizer  
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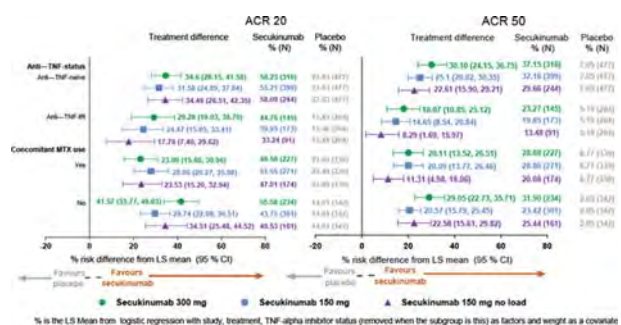
**AB0945 SECUKINUMAB EFFICACY IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS: POOLED ANALYSIS OF FOUR PHASE 3 TRIALS BY PRIOR ANTI-TNF THERAPY AND CONCOMITANT METHOTREXATE USE**

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**Background:** Secukinumab has demonstrated rapid, significant and sustained improvement in the signs and symptoms of psoriatic arthritis (PsA) in multiple Phase 3 studies.<sup>1-3</sup>  
**Objectives:** To report pooled efficacy results for secukinumab versus placebo at Week (Wk) 16 in PsA patients (pts) by previous anti-TNF therapy and with or without concomitant methotrexate (MTX) use from four Phase 3 studies: FUTURE 2, FUTURE 3, FUTURE 4 and FUTURE 5.  
**Methods:** Overall, 397, 414, 341, and 996 pts with active PsA were randomised in FUTURE 2, FUTURE 3, FUTURE 4 and FUTURE 5, respectively. Secukinumab doses included subcutaneous (s.c.) 300 mg and 150 mg administered at

baseline (BL) with loading doses at Wks 1, 2, and 3, followed by maintenance dose every 4 wks (q4w) starting at Wk 4 and s.c. secukinumab 150 mg administered at BL without loading dose, followed by q4w starting at Wk 4. Data collected up to Wk 16 were pooled. Assessments included ACR20/50/74, DAS-28 CRP, PASI 75/90, SF-36 PCS, HAQ-DI, and resolution of dactylitis, and enthesitis. Pooled analyses examined the effect of prior anti-TNF use (naïve/inadequate response or intolerance to these agents, -IR) and with/without MTX use on clinical endpoints and are reported after application of non-responder imputation for binary variables and a mixed-effects model for repeated measures for continuous variables.

**Results:** A total of 2049 pts were included in the analysis, of which 461, 572, 335, and 681 pts received secukinumab 300 mg, 150 mg, 150 mg without load and placebo, respectively. Improvements were observed with secukinumab vs placebo for all endpoints at Wk 16 in both anti-TNF-naïve and anti-TNF-IR pts and in pts with and without concomitant MTX use. Higher ACR and PASI responses and greater improvement of disease activity were observed in anti-TNF-naïve pts compared to anti-TNF-IR pts. Secukinumab 300 mg provided numerically higher ACR and PASI responses compared to the 150 mg dose particularly for anti-TNF-IR pts and in pts with no concomitant MTX use. Earlier responses were observed with secukinumab with load compared to without load primarily across ACR, DAS28-CRP and PASI endpoints.



**Abstract AB0945 – Figure 1**

**Conclusions:** Secukinumab provided improvements in the signs and symptoms of active PsA regardless of previous anti-TNF therapy or concomitant MTX use. Higher response rates were generally observed in anti-TNF-naïve pts compared to anti-TNF-IR pts. Secukinumab 300 mg was associated with higher responses compared to 150 mg particularly in anti-TNF-IR pts and in pts with no concomitant MTX use.

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**AB0946 IMPROVEMENTS IN WORK PRODUCTIVITY WITH UP TO 104 WEEKS OF APREMILAST MONOTHERAPY: RESULTS FROM A PHASE 3B, RANDOMISED, CONTROLLED STUDY IN BIOLOGIC-NAÏVE SUBJECTS WITH ACTIVE PSORIATIC ARTHRITIS**

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**Background:** Psoriatic arthritis (PsA) patients may experience disease manifestations across multiple domains and impaired functioning in daily activities at home and work. The phase 3b ACTIVE study is evaluating the efficacy of apremilast (APR) monotherapy in biologic-naïve subjects with active PsA who may have had exposure to 1 prior conventional DMARD.

**Objectives:** To assess work productivity through Week 104.

**Methods:** Subjects were randomised (1:1) to receive APR 30 mg BID or placebo (PBO). Subjects who did not improve by  $\geq 10\%$  in swollen and tender joint counts at Week 16 were eligible for early escape. At Week 24, all remaining PBO subjects were switched to APR. Work productivity and activity impairment were assessed at baseline (BL) and Week 16 using the 6-item, self-administered Work Productivity and Activity Impairment Questionnaire: Psoriatic Arthritis (WPAI:PsA). WPAI:PsA includes 4 subscale scores (Absenteeism, Presenteeism, Work Productivity Loss, and Activity Impairment), each ranging from 0% to 100%; higher scores indicate greater impairment. Work-related subscales were evaluated only among employed subjects, while activity impairment was evaluated among all subjects, regardless of employment. Correlations were examined at Week 16 between WPAI:PsA subscale scores and the SF-36v2 domain scores for Physical Functioning (PF), Bodily Pain (Pain), and Vitality (VIT), as well as associations with ACR20 response. Improvement in work productivity was assessed through Week 104.

**Results:** BL characteristics were similar between APR and PBO subjects with WPAI:PsA scores included in this analysis. At Week 16, APR significantly improved work productivity and the ability to carry out daily activities vs PBO, with significantly greater mean improvements observed in the overall Work Productivity Loss ( $p=0.001$ ) and Activity Impairment ( $p<0.001$ ) scores (table 1). Estimated mean change in the Absenteeism score was similar with APR vs PBO ( $p=0.679$ ). By contrast, the Presenteeism score showed significant improvement with APR vs worsening with PBO ( $-10.8\%$  vs  $4.1\%$ ;  $p=0.002$ ). At Week 16, statistically significant correlations were observed between WPAI:PsA subscale scores (except Absenteeism) and the SF-36v2 domain scores for PF, Pain, and VIT, as were associations with ACR20 response. Among subjects randomised to APR at BL, improvements in Week 16 WPAI:PsA subscale score were generally maintained through Week 104 in those continuing APR.

Improvements in WPAI:PsA Subscale Scores (% Point) at Week 16				
WPAI:PsA Subscale	APR 30 mg BID LS Mean (95% CI)	PBO LS Mean (95% CI)	Treatment Difference (95% CI)	P Value
Presenteeism	n=39 -10.8 (-17.8, -3.8)	n=56 4.1 (-1.7, 9.9)	-14.9 (-24.1, -5.8)	0.002
Work Productivity Loss	n=40 -11.9 (-18.8, -5.0)	n=55 3.5 (-2.4, 9.4)	-15.4 (-24.5, -6.2)	0.001
Activity Impairment	n=87 -11.8 (-16.4, -7.1)	n=103 -0.5 (-4.7, 3.8)	-11.3 (-17.6, -5.0)	<0.001
Absenteeism	n=40 -3.6 (-5.9, -1.3)	n=55 -3.0 (-4.9, -1.0)	-0.6 (-3.7, 2.4)	0.679

Abstract AB0946 – Figure 1

Results are from an analysis of covariance model, adjusted with BL WPAI:PsA subscale score, BL prednisone use (yes/no), and previous DMARD use (yes/no). LS mean is estimated using the observed margins of the covariates. WPAI:PsA scores were evaluated for subjects with values at both BL and Week 16. Absenteeism, Presenteeism, and Work Productivity Loss were evaluated only among employed subjects. Activity Impairment scores were evaluated among all randomised subjects with scores at BL and Week 16, regardless of employment status. CI=confidence interval; LS=least square.

**Conclusions:** In biologic-naïve subjects with PsA, APR monotherapy contributed to an overall improvement in work productivity at Week 16, which correlated with SF-36v2 PF, Pain, and VIT scores and was associated with ACR20 response; improvements in WPAI:PsA subscale scores were generally maintained to Week 104.

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**AB0947 IMPACT OF CLINICAL SPECIALTY SETTING ON DISEASE MANAGEMENT IN PATIENTS WITH PSORIATIC ARTHRITIS: RESULTS FROM A CROSS-SECTIONAL OBSERVATIONAL STUDY IN THE UNITED STATES**

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**Background:** Early diagnosis and effective treatment has been shown to decrease functional disability and structural progression in patients (pts) with psoriatic arthritis (PsA).<sup>1</sup> However, factors that influence treatment management decisions are poorly understood.

**Objectives:** To evaluate the impact of clinical specialty setting on the management of US pts with PsA.

**Methods:** LOOP was a multi-centre, cross-sectional observational study conducted across 44 sites in US. Adult pts who was suspected or an established diagnosis of PsA who were routinely visiting a rheumatologist (rheum) or a dermatologist (derm) were eligible to participate in this study. Each enrolled pt was assessed by both rheum and derm. The association between enrolling or diagnosing clinical specialty setting and time from symptom onset to PsA diagnosis and to different disease management steps were examined.

Abstract AB0947 – Table 1. Current Disease Activity and Disease Burden by Clinical Specialty in US Patients with PsA from LOOP Study

Measure*	Rheum (N=366)	Derm (N=147)	P-value*
TJC68	8.2 (10.8)	9.9 (10.3)	.095
SJC66	3.4 (6.4)	4.3 (6.0)	.154
DAS28 (CRP)	3.2 (1.5) <sup>b</sup>	4.2 (2.0) <sup>c</sup>	.095
DAS28 (ESR)	3.1 (1.6) <sup>d</sup>	3.8 (2.1) <sup>e</sup>	.192
Enthesitis based on LEI	1.0 (1.6)	1.5 (1.8)	.005
Dactylitis count	0.6 (1.5)	0.8 (1.7)	.241
BASDAI (axial involvement)	4.6 (3.2) <sup>f</sup>	4.3 (3.3) <sup>g</sup>	.248
BSA (%)	5.0 (10.9)	8.1 (14.5)	.024
Psoriatic nail count	1.9 (3.1) <sup>h</sup>	2.0 (3.1)	.734
PASI	3.0 (5.1)	5.5 (7.9)	<.001
PtGA at the time of diagnosis	6.7 (2.7) <sup>i</sup>	5.9 (3.1)	.003
PtGA during last visit	4.7 (2.9) <sup>m</sup>	4.7 (3.0) <sup>n</sup>	.976
HAQ-DI	0.9 (0.7)	0.7 (0.7)	.057
SF1v2 PCS	40.6 (10.5) <sup>m</sup>	41.8 (10.3)	.244
SF12v2 MCS	46.9 (11.1) <sup>m</sup>	47.9 (11.9)	.361
DLQI	5.4 (5.9) <sup>o</sup>	7.8 (7.4)	.001

\*P-value from two sample t-test: Rheumatologist vs Dermatologist.

<sup>a</sup>All data are presented as mean (SD) unless otherwise specified.

<sup>b</sup>N=40; <sup>c</sup>N=8; <sup>d</sup>N=67; <sup>e</sup>N=13; <sup>f</sup>N=361; <sup>g</sup>N=144; <sup>h</sup>N=321; <sup>i</sup>N=314; <sup>j</sup>N=145; <sup>k</sup>N=365; <sup>l</sup>N=138; <sup>m</sup>N=341; <sup>n</sup>N=65; <sup>o</sup>N=361.

BSA=body surface area with psoriasis; DAS28 (CRP)=28 joint disease activity score based on C-reactive protein; DAS28 (ESR)=DAS28 based on erythrocyte sedimentation rate; Derm=dermatologist; DLQI=Dermatology life quality index; HAQ-DI=health assessment questionnaire – disability index; LEI=Leeds enthesitis index; MCS=mental component score; PASI=psoriasis area and severity index; PCS=physical component score; PGA=physician global assessment; PsA=psoriatic arthritis; PtGA=patient's global assessment of disease; Rheum=rheumatologist; SF12v2=Short form 12-item health survey version 2.0; SD=standard deviation; SJC66=swollen joint count, 66 joints; TJC68=tender joint count, 68 joints.



**Results:** Of 681 pts enrolled, 513 pts with a confirmed diagnosis of PsA were included in this analysis. PsA diagnosis was established prior to study entry in 404 pts (established pts), while diagnosis was confirmed during the study in 109 pts (suspected pts). In established pts, PsA was first diagnosed in 352 (87.1%) pts by a rheum and 40 (9.9%) pts by a dermatologist. Among suspected pts, 87 (79.8%) and 15 (13.8%) pts were being managed by dermatologist and rheumatologist setting, respectively. Patient demographics and disease characteristics were comparable between PsA pts enrolled by rheumatologist and dermatologist setting. Current disease activity and disease burden were also mostly similar between rheumatologist and dermatologist setting (table 1); though pts enrolled in dermatologist setting had higher scores on skin measures and enthesitis. The median (95% CI) time from symptom onset to PsA diagnosis was 1.0 (0.5, 1.1) and 2.6 (1.7, 4.1) years (y) in pts enrolled in rheumatologist and dermatologist setting, respectively ( $p < 0.001$ ). However, the median time to PsA diagnosis was 0.9 (0.5, 1.0) and 1.0 (0.0, 2.0) y in pts diagnosed by rheumatologists and dermatologists, respectively. After PsA diagnosis, the median time to first csDMARD and to first bDMARD was 1.0 and 2.4 y, respectively. Overall, 282 (55.0%) and 354 (69.0%) pts received csDMARDs and bDMARDs, respectively. Treatment with first csDMARD occurred in 106 (20.7%) pts before PsA diagnosis and 176 (34.3%) pts after diagnosis; for first bDMARD, it was 121 (23.6%) and 233 (45.4%) pts, respectively.

**Conclusions:** The duration from symptom onset to PsA diagnosis was longer in pts enrolled by dermatologists and was similar in pts diagnosed by both rheumatologists and dermatologists. The median time was longer for treatment with first bDMARD compared with first csDMARD. Current disease activity and disease burden highlight the delay in PsA diagnosis and the need for appropriate management of PsA pts, irrespective of clinical specialty setting.

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AB0948

#### TUMOUR NECROSIS FACTOR INHIBITORS AND THEIR IMPACT ON DIABETES MELLITUS AMONG PATIENTS WITH PSORIATIC ARTHRITIS

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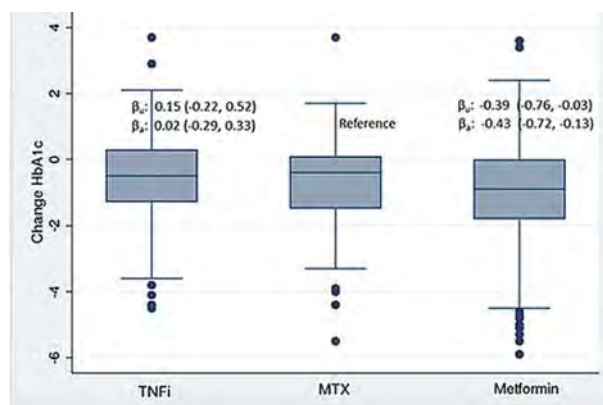
**Background:** Tumour necrosis factor is a key inflammatory cytokine in the pathogenesis of psoriatic arthritis (PsA) and diabetes mellitus (DM). <sup>1,2</sup>Tumour necrosis factor inhibitors (TNFi) have been shown to be associated with a decreased incidence of DM, but it is unknown whether treatment of PsA with TNFi has off-target therapy benefits for patients with DM. <sup>3</sup>

**Objectives:** To determine whether initiation of a TNFi, compared to initiation of methotrexate (MTX) or metformin, results in a decrease in Haemoglobin A1c (HbA1c) in patients with PsA, DM, and elevated HbA1c.

**Methods:** A retrospective cohort study was conducted in OptumInsight, a de-identified administrative claims database that includes laboratory values for approximately 10% of patients. Data from 2000–2014 was included. We identified patients with PsA and DM (defined by ICD-9CM codes), with an HbA1c  $\geq 7$  and examined change in HbA1c among new initiators of a TNFi (etanercept, adalimumab, certolizumab, or golimumab), MTX, and metformin (positive control). A baseline period of 12 months prior to the index date was required to capture potential confounders. All patients were required to have one HbA1c in the six months prior to and one HbA1c in the 6 months after drug initiation. We evaluated median

HbA1c change in each group and then assessed statistical differences using the Wilcoxon Rank Sum test (unadjusted). We then used linear regression models to determine the relative differences in HbA1c change using MTX as the reference and adjusted for age, sex, baseline A1c, DM medications, and comorbidities in the baseline period, with clustering to account for multiple new drug initiations per patient.

**Results:** Among 914 drug initiations in 756 patients with PsA and available HbA1c values, HbA1c was  $\geq 7$  before 125 (44%) of TNFi initiations, 90 (43%) of MTX initiations, and 233 (55%) of metformin initiations. The average time between baseline and follow-up HbA1c values was 231 days. Median HbA1c change was  $-0.50$  (IQR  $-1.30, 0.30$ ) after TNFi initiation,  $-0.40$  (IQR  $-1.50, 0.10$ ) after MTX initiation, and  $-0.90$  (IQR  $-1.80, 0$ ) after metformin initiation (figure 1). In adjusted analyses, TNFi initiators had a similar decrease in HbA1c compared to MTX initiators,  $\beta$  0.02 (95%CI:  $-0.29, 0.33$ ). Metformin initiators had a significantly greater change in HbA1c than MTX patients,  $\beta$   $-0.43$  (95%CI:  $-0.72, -0.13$ ).



Abstract AB0948 – Figure 1

**Conclusions:** TNFi and MTX initiation lead to a decline in HbA1c by half as much as metformin. Changes in HbA1c were not different among patients initiating TNFi versus MTX.

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AB0949

#### SERUM 25-HYDROXYVITAMIN D STATUS IN PATIENT WITH PSORIATIC ARTHRITIS

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**Background:** Vitamin D has been recognised not only in calcium metabolism and bone metabolism but also in the physiological activities of a wide variety of cells, and its deficiency is caused by fractures/falls, osteoporosis and other various disease risks have been reported.

**Objectives:** To clarify vitamin D satisfaction status of patients with PsA, which is one of spondyloarthritis, by measuring serum 25OHD concentration.

**Methods:** 180 patients with PsA satisfying CASPAR criteria during the visit to our hospital between August 2016 and June 2017, 125 males, averaging age 54.1 y.o., BMI average 24.2, mean disease duration of PsA and psoriasis were 8.1 years, 19.3 years, respectively. The type of psoriatic arthritis was 79 spondylitis type and 101 peripheral type. MTX was 51.7% as an agent for treating PsA, and the average dose was 8.3  $\pm$  3.1 mg/week. The number of biologics use was 37.2%. There were 9 cases of osteoporosis and 21 cases of osteopenia, 20 patients who were undergoing treatment for osteoporosis, and all patients were treated with activated VD3. 110 patients (61.1%) had active type VD3 paint applied to psoriasis eruption. The ACPA positive rate was 7.4%, the rheumatoid factor positive was 17.7%, and

average CRP was  $0.25 \pm 0.36$  mg/dl. The test method for the serum 25OHD concentration was measured with the CLIA antibody method (SRL, Inc.). Regarding the judgment criteria of deficiency, although various discussions are in progress, "the index of serum 25OHD deficiency less than 20 ng/ml" prepared by the institute of medicine (IOM) in 2011 was used. As a study item, firstly, the degree of satisfaction of vitamin D using serum 25OHD concentration was determined. Second, it divided into VD deficient group and non-deficient group age, sex, disease duration, psoriatic arthritis type, blood biochemical test, presence of active VD administration, presence or absence of active type VD coating for skin, presence or absence of MTX · BIO, Osteoporosis · Percentage of osteopenia · The presence or absence of vulnerability fracture history was compared between both groups.

**Results:** Mean serum 25OHD concentration in patients with PsA was  $16.4 \pm 6.3$  ng/ml and serum 25OHD deficiency was observed in 134 cases (74.4%).

Factors that showed significant differences between the two groups (VD deficient group/normal group) were age ( $54.4/59.0$  y.o.  $p=0.032$ ), gender (female rate) 35.0%/11.9%:  $p=0.040$ , ACPA negative rate 97.0%/85.2%:  $p=0.010$ , serum MMP-3 ( $69.0/98.4$  ng/ml  $p=0.030$ ), active vitamin D top coating use rate for skin 54.0%/88.9%:  $p=0.001$ , Biologics treatment rate 49.3%/11.1%:  $p<0.001$ .

**Conclusions:** 74.4% of patients with PsA had vitamin D deficiency.

In the vitamin d-deficient group, low age, high female rate, ACPA negative, low serum MMP-3, VD coating low use rate for skin, biological product high usage rate were significant.

**Disclosure of Interest:** None declared

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### AB0950 MINIMAL DISEASE ACTIVITY IN REAL LIFE IN PSORIATIC ARTHRITIS

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**Background:** Minimal disease activity (MDA) is an important target in patients with psoriatic arthritis (PsA), however it is also criticised for having low threshold for patient reported outcomes (PRO).

**Objectives:** The aim of the study was to assess the prevalence of MDA components in patients with PsA and to evaluate disease characteristics and patterns in patients with or without MDA.

**Methods:** PsArt-ID (Psoriatic Arthritis- International Database) is a prospective, multicentre web-based registry ([www.trials-network.org](http://www.trials-network.org)). PsA patients who had at least 1 year of disease duration were included for this analysis. Patients were considered in MDA when they met at least 5/7 of the MDA criteria (figure 1).

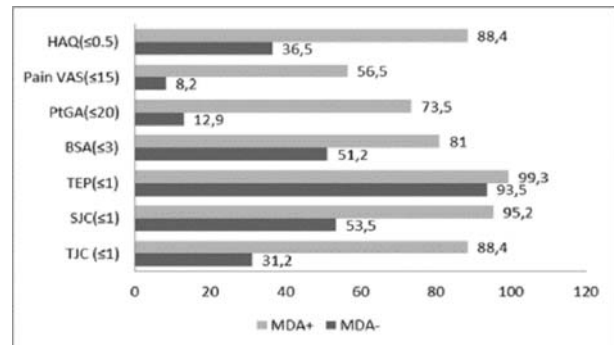
**Abstract AB0950 – Table 1.** The demographics and disease characteristics according to MDA

	no MDA 170/317 (53.9)	MDA 147/317 (46.0)	p value
Female	109/188 (58)	79/188 <sup>42</sup>	0.061
Age (years)*	50 (40–59)	51.5 (37–60.5)	0.924
Education years*	11 (5–15)	11 (5–14)	0.738
Disease duration (months)*	95 (66–155)	88 (59–155)	0.843
Nail involvement	92/171 (53.8)	73/146 <sup>50</sup>	0.500
Dactylitis	65/170 (38.2)	55/147 (37.4)	0.881
Enthesitis	35/170 (20.6)	16/147 (10.9)	<b>0.022</b>
<b>PsA clinical pattern</b>			
Polyarthritis	78/170 (45.9)	70/146 (47.9)	0.714
Oligoarthritis	66/170 (38.8)	50/146 (34.2)	0.415
Monoarthritis	1/170 (0.6)	9/146 (6.2)	<b>0.007</b>
DIP joint involvement	42/170 (24.7)	23/146 (15.8)	<b>0.050</b>
Axial involvement	79/170 (46.5)	56/146 (38.4)	0.171
Arthritis mutilans	0/170 (0)	1/146 (0.7)	0.462

**Results:** In January 2018, 1283 patients from Turkey and 119 patients from Canada were recruited, 317 of whom had full data for MDA and were included in this analysis. The demographics, disease characteristics and patterns in patients with MDA achieved vs not are summarised in the table. There were no differences regarding demographics in both groups. The monoarthritis subtype (RR: 2.01, 95% CI: 1.579–2.559), the absence of enthesitis (RR: 1.570, 95% CI: 1.027–2.398) and the absence of distal interphalangeal joint disease (RR: 1.1, 95% CI: 1.001–1.25) were associated with higher probability of achieving MDA. Across different domains included in MDA, pain VAS $\leq 15$  and PtGA  $\leq 20$  could less frequently be achieved even when MDA is fulfilled as 44.5% and 26.5% of patients

respectively still did not fulfil these domains (figure 1). On the other hand, for patients that did not achieve MDA, the body surface area (51.2%) and swollen joint count (53.5%) domains could be achieved in the majority of the patients and 93.5% of them had no enthesitis using the Leeds enthesitis index. Physician global assessment ( $>21$  vs  $\leq 20$ ) and BASDAI ( $>41$  vs  $\leq 40$ , only for axial disease) had only moderate agreement with MDA (achieved or not) ( $\kappa=0.47$ ,  $p=0.05$  and  $\kappa=0.469$ ,  $p=0.072$ ; respectively).

All data were given n/total n (percentage (%)) or median (first-third percentiles)\*. MDA: minimal disease activity; PsA: Psoriatic Arthritis; DIP: distal interphalangeal.



**Abstract AB0950 – Figure 1.** The distribution of all MDA domains in patients achieving MDA and patients not achieving MDA. TJC: tender joint counts; SJC: swollen joint counts; TEP: tender enthesal points; BSA: body surface area; PtGA: patient global activity; VAS: visual analogue scale; HAQ: Health Assessment Questionnaire.

**Conclusions:** The MDA criteria provide an objective target for treatment in trials and clinical practice; however in real life PROs are the most significant barriers to achieve MDA within all domains. Leeds enthesitis index was not able differentiate MDA, for being negative in the vast majority of the patients. Monoarthritis subtype is a good prognostic factor whereas DIP joint disease and history of enthesitis are poor prognostic factors to achieve MDA.

**Disclosure of Interest:** None declared

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### AB0951 ULTRASONOGRAPHIC ASSESSMENT OF NAIL IN PSORIATIC DISEASE FOUND A LINK BETWEEN NAIL DISORDER AND SOFT TISSUE SWELLING AROUND THE NAIL

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**Background:** Although skin lesion is the most typical findings in patients with psoriasis (PsO), nail psoriasis is also one of the clinical manifestation. Moreover, nail disorders in PsO are known as a risk factor for psoriatic arthritis (PsA). However, pathological feature and the relationship with inflammation of the soft tissue around the nail is unknown.<sup>1–2</sup>

**Objectives:** The aim of this study was to compare the soft tissue thickness around the nail in patients with PsO, PsA and other rheumatic diseases by using ultrasonography.

**Methods:** Twenty-five PsO · 35 PsA · 23 rheumatoid arthritis (RA) · 28 ulcerative colitis (UC) and 13 Crohn's disease (CD) patients performed ultrasonographic assessment in nail were included in this analysis. Ultrasonographic examination was performed by using HI VISION Ascendus (Hitachi Medical Corporation, Japan) with a multifrequency linear transducer (18–6 MHz) and the grey scale (GS) and power Doppler (PD) findings were assessed. The distance between the proximal nail fold on the dorsal side of the nail matrix and the nail bed on the volar side of the nail matrix was measured by electric calliper

**Results:** The distance between the proximal nail fold and the nail bed was  $2.58 \pm 0.56$  mm in PsA and  $2.55 \pm 0.58$  mm in PsO patients ( $p=0.603$ ). Among the 60 patients who combined PsO and PsA patients, 41 patients with nail psoriasis and 19 patients without nail psoriasis was compared. The distance was  $2.68 \pm 0.62$  mm in patients with nail psoriasis and  $2.30 \pm 0.41$  mm in without nail psoriasis ( $p<0.001$ ), which was also swelling compared with the RA, UC and CD group.

**Abstract AB0951 – Table 1.** The thickness of proximal nail fold, nail bed and proximal nail fold + nail bed in patients with psoriasis, psoriatic arthritis and other rheumatic disease

	proximal nail fold (mm)	nail bed (mm)	proximal nail fold +nail bed (mm)
Psoriasis (n=25)	1.23±0.27	1.33 ±0.47	2.55±0.58
Psoriatic arthritis (n=35)	1.33±0.35	1.25 ±0.38	2.58±0.56
Psoriasis or psoriatic arthritis with nail psoriasis (n=41)	1.34±0.34	1.36 ±0.45	2.68±0.62
Psoriasis or psoriatic arthritis without nail psoriasis (n=19)	1.18±0.27	1.11 ±0.29	2.30±0.41
Rheumatoid arthritis (n=23)	1.14±0.27	1.14 ±0.33	2.27±0.46
Ulcerative colitis (n=28)	1.21±0.28	1.22 ±0.33	2.43±0.49
Crohn's disease (n=13)	1.11±0.25	1.14 ±0.37	2.25±0.49

**Conclusions:** Soft tissue thickness around the nail in patients with PsO and PsA was compared with other rheumatic diseases by ultrasonographic assessment. In patients with PsO and PsA with nail psoriasis, soft tissue swelling around nail was observed.

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AB0952

#### HIGH PREVALENCE OF INFLAMMATORY AND NON-INFLAMMATORY LIVER AND GASTROINTESTINAL DISEASES IN YOUNG PATIENTS WITH PSORIATIC ARTHRITIS: A HOSPITAL-BASED STUDY

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**Background:** Psoriatic arthritis (PsA) is associated with numerous comorbidities, including gastrointestinal (GI) and liver diseases (LD). But there is limited data about the prevalence of these disorders among patients (pts) with PsA and severe psoriasis (PsO) in Russian population.

**Objectives:** to evaluate the prevalence of LD and GIT comorbidity in a hospital-based cohort of PsA pts.

**Methods:** 417 (304 Male (M.)/113 Female (F.)) PsA pts, according the CASPAR criteria, mean age 38.5±11.3/36.1±11.0 years (yrs) accordingly, PASI 49.4±0.56, PsA duration 6.6±7.4 years were included. PsA pts with all GIT and LD, including Diseases of oesophagus, stomach and duodenum (K20–K31), Disorders of gallbladder, biliary tract and pancreas (K80–K87), Alcoholic and toxic liver disease (K70–K77) (LD), Viral hepatitis (B15–B19) (VH), non-infectious enteritis and colitis (K55–K63) NEC were identify in the hospital Database and coding by International Statistical Classification of Disease and Related Health Problems (ICD-10) between 2010–2015 years. M±m, t-test, (%) were calculated. All p<0.05 were considered to indicate statistical significance.

**Results:** 229 (159 – M./70 – F.) out of 417 pts (54.9%) had LD and GIT disorders. Gallbladder, biliary tract and pancreas disease coding as K80–K87 were found in significantly more cases in F. compare to M. pts – in 26 out of 70 pts (37.4%) and in 31 out of 159 pts (19.4%) accordingly (p<0.05). NEC coding as K55–K63 was found in M. only – in 1 out of 159 (0.62%) pts. Diseases of oesophagus, stomach and duodenum coding as K20–K31 were found in 96 out of 229 pts (42%). All of the alcoholic, toxic and viral liver disease were found in 75 out of 229 pts (32.75%). LD coding as K70–K77 were found in 33 out of 75 pts (44%). VH coding

as B15–B19 were found in 42 out of 75 pts (56%). No significantly gender differences were found in those group of pts.

**Conclusions:** GIT and LD were found in more than half of young pts with PsA and severe PsO. That information should be taken in account during the choice of safety therapy in this group of pts.

**Disclosure of Interest:** None declared

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AB0953

#### PSAID-12 CAN BE USED TO DETERMINE THE ANTI-TNF TREATMENT DECISION IN THE PSORIATIC ARTHRITIS REGISTRY

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**Background:** Psoriatic Arthritis Impact of Disease (PsAID-12) score has 12 questions and each question has its own weight. PsAID-12 is developed to be used in daily practice. However, in the daily practice, there has been no information on the utilisation of determining the response of the biological DMARD treatment.

**Objectives:** The assessment of utilisation of PsAID-12 for PsA patients on determination of the efficiency and inefficiency of anti-TNF treatment in a biological registry.

**Methods:** In this study patients were taken from Hacettepe University biological database (HUR-BIO). Since January 2013 PsAID-12 score was built in HUR-BIO database. PsAID-12 score was known for 116 patients before starting off the first anti-TNF treatment and 88 patients whose PsAID-12 score was 4 and above were included in the enquiry. Overall, 70 PsA patients included to analysis. Demographic data before anti-TNF treatment of PsA patients were noted. The decision of continuation, stopping or switching to another anti-TNF drugs were performed by both clinicians and the patients agreement. According to baseline evaluation, decrease of 20 mm and above on pain-VAS score and PGA, improvement of 0.22 unit and above on HAQ-DI score, or decrease of 1.2 unit and above on DAS-28 score were considered favourable to the anti-TNF treatment. Stopping or switching the anti-TNF treatments due to inefficiency was definitely a negative response. Pain-VAS score being under 15 mm or below, global-VAS score being 20 mm and below, HAQ-DI score being 0.5 and below, DAS-28 score being 2.6 and below were determined as targeted goals. Changes were analysed comparing to baseline level in PsAID-12 score, in compliance with the favourable and unfavourable responses to Anti-TNF treatments. In determining the response of the treatment, standardised response mean (SRM) was used.

**Results:** Seventy (78.6% female) patients were analysed, mean age was 45.5 (12.0). Mean follow-up duration was 18.3 (12.6) months, and total of 213 clinical visits were performed, median 3<sup>1-3</sup> control visits were done. At baseline, the mean (SD) DAS-28 4.07 (1.22), HAQ-DI 0.86 (0.53), pain-VAS 6.9 (2.1), PGA-VAS 6.4 (1.7), and PsAID-12 6.6 (1.5) were as follows. Anti-TNF treatments were stopped due to inefficacy in 43/210 (20.5%) outpatient visit during the follow-up period. The results of anti-TNF stopped and continuing patients; Δ PsAID-12 were 0.38 (1.71), and 3.12 (2.14), respectively and PsAID-12 baseline/control visits 0.96 (0.29) vs 0.50 (0.33), respectively. Level of favourable response and achieving to goal according to ΔPsAID-12 and PsAID-12 Baseline/control visit were shown table 1. On the follow up visits, among measured parameters one of the highest SRM was detected in PsAID-12; PsAID-12 (1.10), DAS-28 (1.14), PGA (0.88), Pain (0.85), and HAQ-DI (0.51), respectively.

**Abstract AB0953 – Table 1.** Goals and responses of Anti-TNF treatment

			ΔPsAID-12	PsAID-12 Baseline/control
Level of favorable response to anti-TNF treatments	Δ Pain ≥ 20 mm	Yes n=136	3.4 (1.9)	0.47 (0.33)
		No n=77	1.1 (1.9)	0.81 (0.34)
	Δ PGA ≥ 20 mm	Yes n=133	3.4 (2.1)	0.45 (0.33)
		No n=80	1.2 (2.0)	0.84 (0.31)
	Δ HAQ-DI ≥ 0.22	Yes n=110	3.5 (2.0)	0.44 (0.29)
		No n=103	1.6 (2.1)	0.74 (0.38)
Δ DAS-28 ≥ 1.2	Yes n=122	3.5 (2.1)	0.44 (0.31)	
	No n=70	1.2 (1.8)	0.80 (0.32)	
Level of achieving the goal of PsA treatment	Pain ≤ 15 mm	Yes n=57	4.3 (2.1)	0.28 (0.32)
		No n=156	1.9 (2.1)	0.71 (0.32)
	PGA ≤ 20 mm	Yes n=68	4.2 (2.1)	0.28 (0.29)
		No n=145	1.8 (2.0)	0.74 (0.32)
	HAQ-DI ≤ 0.5	Yes n=136	3.5 (2.1)	0.43 (0.32)
		No n=77	0.9 (1.7)	0.89 (0.28)
DAS-28 < 2.6	Yes n=118	3.1 (2.3)	0.48 (0.35)	
	No n=85	1.7 (2.2)	0.75 (0.36)	

**Conclusions:** Having 3.5 unit or 50% decrease in the PsAID-12 score indicates a favourable response to anti-TNF treatment, 4 unit or 70% decrease indicates level



of targeted response. PsAID-12 appears to be an effective composite index for retaining the response of the treatment in biological registry.

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AB0954

**A RANDOMISED, DOUBLE-BLIND TRIAL COMPARING THE EFFICACY, SAFETY AND IMMUNOGENICITY OF MSB11022, A PROPOSED BIOSIMILAR OF ADALIMUMAB, VERSUS ADALIMUMAB ORIGINATOR IN PATIENTS WITH MODERATE-TO-SEVERE PLAQUE PSORIASIS**

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**Background:** Adalimumab is a fully human anti-TNF mAb, indicated for the treatment of multiple inflammatory disorders. MSB11022 is a proposed adalimumab biosimilar that has shown analytical similarity [1] and bioequivalence to US-licensed and EU-approved adalimumab originator, as well as comparable safety, tolerability and immunogenicity in a phase I trial [2].

**Objectives:** The aims of this multicentre, double-blind, parallel-group, 52-week phase III study (AURIEL-PsO, NCT02660580) were to demonstrate equivalence in efficacy (Psoriasis Area and Severity Index [PASI] 75) and to compare the safety and immunogenicity of MSB11022 vs. adalimumab originator in patients with moderate-to-severe chronic plaque psoriasis. This study was designed in-line with the biosimilar regulatory framework as part of the totality of evidence to confirm similarity and rationale for extrapolation.

**Methods:** A total of 443 eligible patients (391 evaluable, including 43 with psoriatic arthritis) from 69 sites in 12 countries were randomised 1:1 and treated with MSB11022 (n=202) or adalimumab originator (n=189) (80 mg subcutaneously [SC] on day 1; 40 mg SC every other week from weeks 2–14). The primary endpoint was PASI 75 at week 16; equivalence was established if the 95% confidence interval (CI) for the treatment difference was within ±18%. Secondary endpoints included % change from baseline in PASI (equivalence confirmed if 95% CI within ±15%), Physician Global Assessment (PGA), quality of life (QoL), immunogenicity and safety. Interim results at week 16 are presented.

**Results:** Patient baseline characteristics were comparable between MSB11022 and adalimumab originator groups: mean age 44.8 vs. 42.4 years, male 66.8% vs. 68.3%, mean PASI score 20.7 vs. 21.2, respectively. PASI 75 scores were 89.6% for MSB11022 and 91.5% for adalimumab originator (difference -1.9% [95% CI -7.82-4.16]). Mean % change from baseline in PASI was -90.6% for MSB11022 and -91.7% for adalimumab originator (difference -1.0% [95% CI -1.23-2.98]). PGA and QoL scores were comparable between treatment groups. The incidence of treatment-emergent adverse events (TEAEs)/serious TEAEs was 51.1/3.6% for MSB11022 and 53.2/2.7% for adalimumab originator. Immunogenicity profiles of MSB11022 and adalimumab originator were also similar and consistent.

**Conclusions:** Week 16 results of this phase III confirmatory study demonstrated equivalent efficacy and similar safety and immunogenicity profiles for MSB11022 vs. adalimumab originator at 16 weeks in patients with moderate-to-severe chronic psoriasis.

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AB0955

**TILDRAKIZUMAB EFFICACY OVER TIME BY WEEK 28 RESPONSE LEVELS IN TWO PHASE 3 CLINICAL TRIALS IN PATIENTS WITH CHRONIC PLAQUE PSORIASIS**

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**Background:** Tildrakizumab (TIL), a high affinity, humanised, IgG1/κ monoclonal antibody for IL-23p19, recently demonstrated efficacy in patients with chronic plaque psoriasis in two, phase 3 clinical trials.

**Objectives:** To examine efficacy from baseline to week 52 among TIL patients achieving various Psoriasis Area and Severity Index (PASI) responses at week 28.

**Methods:** ReSURFACE 1 (NCT01722331) and reSURFACE 2 (NCT01729754) were double-blind, randomised controlled trials in subjects with moderate-to-severe chronic plaque psoriasis<sup>1</sup>. Part 1 (0–12 weeks) was placebo controlled; Part 2 (12–28 weeks) re-randomised placebo patients to TIL; Part 3 (28–64 weeks, reSURFACE 1; 28–52 weeks, reSURFACE 2) patients with ≥PASI 50 were re-randomised to continue or increase TIL dose or to placebo based on response at week 28. In this post-hoc pooled analysis, patients on TIL 100 mg and 200 mg from baseline to week 52 were classified in 5 mutually exclusive groups based on their week-28 PASI response: PASI <50, PASI 50–74, PASI 75–89, PASI 90–99, and PASI 100. Baseline characteristics and % PASI improvement from baseline up to week 52 (observed data) were examined for each group.

**Results:** This analysis included 575 (TIL 100 mg) and 581 (TIL 200 mg) patients; the overall pooled Week 28 PASI 75/90/100 responses were 77%/54%/23% (TIL 100 mg) and 78%/58%/29% (TIL 200 mg). At week 28, 133 (23.1%), 175 (30.4%), 137 (23.8%), 82 (14.3%), and 48 (8.3%) TIL 100 mg patients and 170 (29.3%), 169 (29.1%), 114 (19.6%), 105 (18.1%), and 23 (4.0%) TIL 200 mg achieved PASI 100, PASI 90–99, PASI 75–89, PASI 50–74, and PASI <50, respectively. On average, PASI 100 patients were younger, lighter, and had shorter disease duration at baseline compared to other response groups. For TIL 100 mg, % PASI improvement was highest for PASI 100 and least for PASI <50 patients for all visits up to week 28 (week 4: 53%, 46%, 38%, 30%, and 16%; week 28: 100%, 95%, 83%, 64%, and 33% for PASI 100, PASI 90–99, PASI 75–89, PASI 50–74, and PASI <50 categories, respectively). Among patients achieving PASI >50 at week 28 and continued up to 52 weeks, % PASI improvement remained consistent or improved from week 28 to week 52. Similar results were observed for TIL 200 mg as well as subgroup analysis with bio-naïve and bio-experienced patients, respectively.

**Conclusions:** The majority of TIL 100 and 200 mg patients achieved PASI>50 response at week 28, and PASI improvement was maintained from week 28 to week 52. Among patients achieving ≥PASI 90 at week 28, TIL 100 and 200 mg were associated with rapid improvement by week 4.

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**AB0956** **LEUCINE-RICH ALPHA-2 GLYCOPROTEIN IS A PREDICTABLE BIOMARKER FOR THERAPEUTIC RESPONSE AND CLINICAL RELAPSE TO BIOLOGICS, BUT NOT TO APREMILAST IN PATIENTS WITH PSORIASIS**

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**Background:** Leucine-rich alpha-2 glycoprotein (LRG) is a 50 kDa protein produced by hepatocytes, endothelial cells, neutrophils and macrophages, and it was identified as an inflammatory biomarker that correlates with the disease activity of autoimmune diseases such as inflammatory bowel disease and rheumatoid arthritis. We recently reported that LRG could also be a biomarker of psoriasis, which correlated with the clinical severity scores such as Psoriasis Area and Severity Index (PASI), Disease Activity Score 28 (DAS-28) and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) more closely than common inflammation markers like C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). The biologics are innovative therapies for psoriasis, however they can cause side effects and increase medical cost. Recently, apremilast, a small molecule inhibitor of phosphodiesterase 4, was approved for treatment of psoriasis in Japan, yet the precise mechanism remains unknown.

**Objectives:** To explore the eligibility of serum LRG for a biomarker to monitor the responses to biologics and apremilast in psoriasis.

**Methods:** Antibodies to TNF-alpha, IL-12/IL-23p40, IL-17A and IL-17 receptor A and apremilast were administered in patients with psoriasis vulgaris and psoriatic arthritis (n=15, 6, 14, 4 and 8 respectively). Serum LRG levels were measured by enzyme-linked immunosorbent assay. Serum CRP and ESR, and PASI, DAS-28 and BASDAI were also recorded.

**Results:** Serum LRG decreased along with the improvement of clinical scores after the administration of biologics, and reflected the change of scores more accurately than CRP and ESR. Furthermore, the LRG levels preceded the changes of clinical symptoms and predicted both primary and secondary treatment failure at the early time point, allowing us to determine if we should increase the doses, discontinue or switch to another drug. In some patients with PASI clear, complete regression of eruption, after biologics, serum LRG rose from the baseline while their PASI scores remained stable; however, they later relapsed. On the other hand, LRG did not reflect the therapeutic effectiveness of apremilast.

**Conclusions:** Serum LRG in psoriasis patients would be a sensitive biomarker for predicting the effectiveness and treatment failure of biologics, but not of apremilast. Monitoring LRG levels may enable us to decide the timing of bio-attenuation and to detect the relapse after discontinuation of biologics.

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**AB0957** **SEVERITY OF SKIN SYMPTOMS IS NOT ASSOCIATED WITH MUSCULOSKELETAL MANIFESTATIONS IN PATIENTS WITH PSORIASIS**

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**Background:** Among patients with psoriasis, risk factors for developing musculoskeletal manifestations, known as psoriatic arthritis (PsA), are not recognised well.

**Objectives:** The aim of this study is to clarify the relationship between severity of skin disease and arthritis.

**Methods:** Psoriasis patients referred from dermatologists for assessment of musculoskeletal manifestations between June 2015 and July 2017 were enrolled. Their age, comorbidity, disease duration and treatment were collected. Presence of inflammatory back pain, sacroiliac joint tenderness or enthesitis were examined. Severity of skin symptoms were evaluated by dermatologists in Psoriasis area and severity index (PASI). Psoriatic arthritis screening and evaluation (PASE) and disease activity score (DAS28 ESR) were also evaluated. PsA was diagnosed by The Classification for Psoriatic Arthritis (CASPAR) criteria assisted with musculoskeletal ultrasound examination.

**Results:** Among 107 patients with psoriasis referred from dermatologists during designated period, 63 patients were diagnosed as PsA. These PsA patients were compared with 44 patients who had no arthritis (PsO). Multiple logistic regression analysis showed neither of age, sex, PASI, disease duration, rheumatoid factor (RF), CRP or Matrix Metalloproteinase-3 (MMP3) had no association with presence of PsA (table 1). Among 63 patients with PsA, those using NSAIDs (p=0.028), those with inflammatory back pain (p=0.002) and male patients (p=0.017) had significantly high PASI. PASI significantly correlated with age (Spearman's correlation coefficient R=-0.303; p=0.016), body height (R=0.301; p=0.019) and weight (R=0.383; p=0.002), but not with DAS28 ESR, MMP3 or disease duration (table 2).

Table 1 multiple logistic regression analysis for presence of PsA

variables	OR	95% CI	P value
age	0.99	0.95-1.03	0.538
sex	2.13	0.66-6.90	0.207
PASI	0.96	0.89-1.03	0.258
disease duration	0.99	0.96-1.04	0.847
RF	0.99	0.99-1.01	0.408
CRP	2.76	0.76-10.10	0.125
MMP3	1	1.00-1.01	0.271

Abstract AB0957 – Table 2. Correlations with PASI in patients with PsA (Spearman's correlation)

variables	R	P value
age	-0.303	0.016
body height	0.301	0.019
body weight	0.383	0.002
disease duration	0.134	0.311
PASE	0.088	0.504
DAS28 ESR	-0.268	0.110
RF	0.152	0.273
CRP	0.211	0.105
MMP3	0.133	0.310

**Conclusions:** PASI did not associate with presence of arthritis. Furthermore, even DAS28 ESR, reflecting musculoskeletal manifestations, or disease duration did not correlated with PASI among patients with PsA. These indicates severity of skin symptoms is not associated with musculoskeletal manifestations in patients with psoriasis.

**Disclosure of Interest:** None declared

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## Osteoarthritis

### AB0958 KNEE PAIN IN OSTEOARTHRITIS: CORRELATION WITH SONOGRAPHIC FINDINGS

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**Background:** Osteoarthritis (OA) is a common joint disorder, with the knee being one of the most frequently involved sites. Knee OA causes pain and stiffness and can lead to considerable disability and consequently to a reduced quality of life (Wideman et al. 2014). The level of radiographic knee OA is, at most, moderately associated with the level of pain. Therefore, it is unlikely that pain is predominantly caused by only bone and cartilage pathology. Mechanical, structural, inflammatory, bone-related, neurological and psychological factors play a role in the process that results in painful knee OA (Wenger et al. 2013).

As OA is a disease of the entire joint that is characterised by cartilage breakdown, subchondral bone alterations and formation of osteophytes, as well as soft tissue abnormalities including meniscal degeneration, bursitis, tendonitis, Baker's cyst and synovial inflammation; information about these soft tissue structures might provide more insight into their potential role in the complex process of pain in knee OA (Cook 2016).

Musculoskeletal ultrasonography (US) is a relatively new imaging tool that is non-invasive, safe and relatively inexpensive and is able to create static as well as dynamic images. In addition, it has been shown to be more sensitive than clinical examination in picking up peri- and intra-articular soft tissue lesions (Beyers et al. 2014).

**Objectives:** To investigate the cause of pain in Knee OA by comparing sonographic and clinical findings in painful and non-painful osteoarthritic knee.

**Methods:** A cross-sectional case-control study carried out on fifty patients attending to Sohag University Hospitals rheumatology and rehabilitation outpatient clinic with Knee OA fulfilling ACR clinical criteria. They were divided into two groups. Group A (53) patients with knee pain (VAS 33 mm) during physical activity once at least in the previous 3 days prior to inclusion. Another (42) patients without knee pain for at least 1 month prior to inclusion (VAS 0 mm). All of the participants were subjected to the following:

- Full history (demographic data and personal history, detailed history of general health condition and chronic or current diseases).
- Knee clinical examination (including varus deformity angle assessment)
- Sonographic evaluation: of Effusion, Synovial hypertrophy, Baker's cyst, Enthesitis, Power Doppler by SOLAR score, menisci protrusion, bursitis, sonographic signs of Gout or CPPD and scoring of the osteophytes and cartilage

**Results:** Our study showed that the painful OA group are more obese, more varus deformities, effusion, synovial hypertrophy, cartilage changes, and higher grading of osteophytes than the control group. On the other hand, Baker cyst and meniscal protrusion echogenic foci, double contour, erosions, meniscal and cartilage calcification showed a non-significant difference between the two groups. We included all of the demographic, clinical and sonographic factors in a univariate regression analysis, and this analysis showed that synovial hypertrophy, effusion, the degree of cartilage changes, the degree of osteophytes, bursitis, and weight may be possible risk factors for pain among OA patients.

**Abstract AB0958 – Table 1.** Multivariate logistic regression analysis of the possible independent risk factors for pain among painful OA group compared to the non painful OA group.

Item	Odd's ratio	CI of Odd's	P value	Rank as a possible risk for pain
Weight	1.078	0.726-1.602	0.710	6
Effusion	4.312	2.172-24.422	0.013	3
Synovial hypertrophy	7.230	0.741-70.526	0.089	4
Degree of cartilage changes	9.523	2.354-38.532	0.002	1
Grade of osteophytes	12.268	2.112-71.283	0.005	2
Bursitis	5.151	0.239-0.296	0.296	5

Abstract AB0958 – Figure 1

**Conclusions:** Cartilage degeneration, osteophytes, effusion, synovial hypertrophy, bursitis, and overweight respectively, are the leading causes of pain in knee OA.

**Disclosure of Interest:** None declared

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### AB0959 CONSUMPTION OF DAIRY PRODUCTS IN RELATION TO PRESENCE OF CLINICAL KNEE OSTEOARTHRITIS: THE MAASTRICHT STUDY

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**Background:** Observational studies showed inverse associations between milk consumption and knee osteoarthritis (knee OA).<sup>1, 2</sup> There is lack of information on the role of specific other dairy product categories.

**Objectives:** To explore the association between dairy consumption and presence of clinical knee OA in individuals aged 40–75 year participating in the Maastricht Study.

**Methods:** Presence of clinical knee OA was defined according to a slightly modified version of the American College of Rheumatology (ACR) clinical classification criteria.<sup>3</sup> Data on dairy consumption was appraised by a 253-item Food Frequency Questionnaire covering 47 dairy products with categorization on fat content, fermentation or dairy type. Multivariable logistic regression analyses were performed to estimate odd ratios (ORs) and 95% confidence intervals (95% CI), while correcting for relevant factors.

**Results:** Of the 3010 participants included in this study, 427 individuals (14%) were classified as having clinical knee OA. Significant inverse associations were observed between presence of clinical knee OA and intake of full-fat dairy and Dutch, primarily semi-hard, cheese, with OR for the highest compared to the lowest tertile of intake of 0.68 (95%CI 0.50–0.92) for full-fat dairy, and 0.75 (95%CI 0.56–0.99) for Dutch cheese. No significant associations were found for other dairy product categories.

**Conclusions:** In this Dutch population, higher intake of full-fat dairy and Dutch cheese, but not milk, was cross-sectionally associated with lower presence of clinical knee OA. Prospective studies need to assess the relationship between dairy consumption, and in particular semi-hard cheeses, with incident knee OA.

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### AB0960 POLYORBIDITY AND COGNITION IN AMBULATORY POSTMENOPAUSAL HIP AND KNEE OSTEOARTHRITIS PATIENTS

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**Background:** Osteoarthritis (OA) has been reported to be a risk factor of morbidity, disability and premature cardiovascular mortality.

**Objectives:** to assess the impact of polyorbidity on cognitive function in postmenopausal women with primary OA.



**Methods:** cross-sectional study included ambulatory 682 postmenopausal women aged 48 to 62 (median 56; 25%–75%: 52.0 / 60.0). Inclusion criteria were: confirmed postmenopausal status and Kellgren stage 2 or 3 OA of the knee and/or hip joints fulfilling ARA criteria. Cognitive impairment (CI) was verified by MMSE scale (Mini Mental State Examination). For all patients expected individual risk of premature death and Charlson index were calculated.

**Results:** Median Charlson comorbidity index in women with OA was 4 (3 / 4). None of the patient had a comorbidity index of 0. The most frequent comorbidities were chronic heart failure (364 women (53.4%) and type 2 diabetes mellitus (180 women, 26.4%).

Charlson index increase was associated with decline of cognitive function (see table 1) with incline of quantity and severity of CI cases.

Abstract AB0960 – Table 1

Charlson Index	n	Age (Me, 25%–75%)	MMSE value	
			(Me, 25%–75%)	Lower limit
1	11	48 (45–49)	28 (28–29)	28
2	102	59 (47–55)	28 (27–29)	24
3	202	54 (51–57)	27 (26–29)	22
4	200	57 (53–60)	26 (25–28)	20
5	119	60 (57–65)	26 (24–27)	21

#### Conclusions:

- Hip and knee joints OA in postmenopausal women is associated with polymorbidity.
- Polymorbidity in OA patients is associated with cognitive impairment.

**Disclosure of Interest:** None declared

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#### AB0961 CARDIORESPIRATORY RESPONSE ACCORDING TO BODY WEIGHT SUPPORT AND GAIT VELOCITY VIA ANTI-GRAVITY TREADMILL AFTER BILATERAL TOTAL KNEE ARTHROPLASTY

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**Background:** Patients undergoing total knee arthroplasty (TKA) may benefit from early focused postoperative rehabilitation, and progressive weight-bearing activities, such as walking, are routinely recommended during rehabilitation to facilitate return to normal gait function. Not all patients are capable of full weight-bearing activity in the early postoperative period and assistive devices such as walkers, crutches, and canes, are routinely employed. The anti-gravity treadmill, consisting of a treadmill enclosed within an airtight chamber, applies air pressure to a patient's lower body to alter body weight support and can reduce the forces at the knee during weight bearing exercise. The anti-gravity treadmill could be a useful device for early postoperative rehabilitation of TKA, especially for those patients with reduced physical strength and cardiovascular fitness. However, so far, there have been no reported investigations of the physiologic cardiorespiratory responses via anti-gravity treadmill in patients following TKA.

**Objectives:** This study was conducted to investigate cardiorespiratory response according to body weight support and gait velocity elicited using an anti-gravity treadmill during walking and to find specific gait velocity and body weight support combinations early after bilateral TKA.

**Methods:** Twenty five patients who underwent a primary TKA were enrolled in this study. Subjects walked with 2.5 km/h and 3.5 km/h on an anti-gravity treadmill at 3 levels (50%, 75%, 100%) of body weight (BW). Each trial was performed for 2 min with at least 1 min rest between trials. For cardiorespiratory responses, oxygen consumption ( $VO_2$ ), Heart rate, systolic (SBP) and diastolic blood pressure (DBP), respiratory exchange ratio (RER) and rate pulse product (RPP) were measured continuously with average values. The  $VO_2$ , heart rate and RER were measured by using the K4b2 (Cosmed, Rome, Italy), which is a wireless cardiopulmonary diagnostic device, and the values of these exercise variables were defined as the averages of values recorded during the last 30 s of exercise. The RPP was calculated ((heart rate x SBP)/100). In addition, Borg's rating of perceived exertion scale (RPE) and visual analogue scale (VAS) of knee pain were recorded immediately after each condition.

**Results:** There were 20 females and 32 men, with the average age being 71.3 ±5.4 years. In the two-way repeated measures ANOVA,  $VO_2$  levels ( $p<0.01$ ), HR ( $p<0.01$ ), RPP ( $p<0.01$ ), RPE ( $p<0.01$ ), RER ( $p<0.01$ ) and VAS ( $p<0.01$ ) were significantly increased in proportion to 3 levels (50%, 75%, 100%) of BW. In the post-hoc analysis, all other conditions except comparison of RER values between 50% level of BW and 75% level of BW under a speed of 2.5 km/h and a speed of 3.5 km/h were statistically significant. Meanwhile, SBP ( $p=0.65$ ) and DBP ( $p=0.39$ ) were not influenced by difference of BW levels.

While walking with a speed of 3.5 km/h at same fraction of BW level,  $VO_2$  ( $p=0.03$ ), RPE ( $p<0.01$ ) and RER ( $p=0.01$ ) values were statistically greater than 2.5 km/h. In the post-hoc analysis, all other conditions except comparison of RER values between a speed of 2.5 km/h and a speed of 3.5 km/h under 100% level of BW was statistically significant.

In addition, multiple linear regression analysis was performed to defining  $VO_2$  as functions of gait speed and fraction of BW under each condition. Based on BW and gait velocity settings of the LBPP treadmill, the equations were  $VO_2=1.46 v +0.08 BW+3.13$  (adjusted  $F^2=0.34$ )

**Conclusions:** This study demonstrated that cardiorespiratory responses were variably computed by combination of weight support and gait velocity during anti-gravity treadmill walking, and these cardiorespiratory responses and knee pain were more significantly influenced by body weight support than gait velocity. These findings suggest that body weight support and gait speed should be considered for gait training program for cardiovascular fitness early after bilateral total knee arthroplasty.

**Disclosure of Interest:** None declared

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#### AB0962 IRISIN LEVELS ARE ASSOCIATED WITH EXERCISE, PAIN AND FUNCTION IN PATIENTS WITH KNEE OSTEOARTHRITIS

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**Background:** Muscle strengthening and aerobic exercise have been shown to improve joint pain and function in patients with knee osteoarthritis (OA). Irisin is a hormone-like myokine synthesized by skeletal muscle and its secretion appears to be related to physical activity in healthy people.

**Objectives:** To determine the levels of irisin synovial fluid and plasma and evaluate their association with exercise level and pain and function in patients with symptomatic knee OA.

**Methods:** Cross-sectional study with systematic inclusion of 108 symptomatic primary knee osteoarthritis patients (VAS>4) with ultrasound-confirmed joint effusion. Age, physical exercise, knee osteoarthritis symptoms duration and different anthropometric measurements were collected. Radiographic severity was evaluated according to Kellgren-Lawrence scale. Physical exercise was categorised as never, occasional (less than 150 min per week) or regular (more than 150 min per week). Pain and disability were assessed by the Lequesne algo-functional questionnaire. Irisin was measured by ELISA in synovial fluid and plasma. Summary of clinical data and laboratory parameters and their association with Lequesne scale were performed using non-parametric methods. Medians and Spearman correlation ( $r$ ) were used for continuous measures, and Mann-Whitney test was applied to categorical variables. This study was approved by the local ethics committee.

**Results:** Plasma and synovial irisin levels were strongly related ( $r=0.7$ ). Plasma and joint irisin levels showed an inversely significant association with the level of exercise in patients with symptomatic knee OA: no exercise 763.3 ng/mL, occasional exercise 631.8 ng/mL and regular exercise 523 ng/mL ( $p<0.01$ ). Patients with severe pain and disability (Lequesne algo-functional score >11) had higher plasma (791.5 vs 680.4 ng/mL,  $p<0.05$ ) and synovial (711.4 vs 468.7 ng/mL,  $p<0.05$ ) irisin levels compared to patients with less disability and pain. No relationship was found between irisin concentration in plasma or synovial fluid and radiographic severity.

**Conclusions:** Irisin levels were associated with pain and function in patients with knee osteoarthritis. Irisin levels were negatively associated with exercise level in this population.

**Disclosure of Interest:** None declared

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#### AB0963 CALPROTECTIN AS A USEFUL MARKER OF INFLAMMATION IN KNEE OSTEOARTHRITIS

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**Background:** Low-grade synovial inflammation is known to be present in many patients with knee osteoarthritis and appears to have clinical and prognostic implications. Calprotectin seems to be more sensitive than CRP to detect minimal inflammatory activity in many inflammatory rheumatic diseases and could be a biomarker in osteoarthritis with inflammatory features.

**Objectives:** To determine the levels of synovial calprotectin in patients with knee osteoarthritis showing inflammatory traits and their relationship with clinical and ultrasonographic features and other proinflammatory markers.

**Methods:** Cross-sectional study with systematic inclusion of 108 symptomatic primary knee osteoarthritis patients (VAS>4) with ultrasound-confirmed joint

effusion. Age, physical exercise, knee osteoarthritis symptoms duration and different anthropometric measurements were collected. Radiographic severity was evaluated according to Kellgren-Lawrence scale. Pain and disability were assessed by WOMAC-pain and WOMAN-function. Calprotectin, TNF- $\alpha$ , IL-6 and high-sensitivity C-reactive protein (hs-CRP) were measured by ELISA in synovial fluid. Summary of clinical data and laboratory parameters and their association with WOMAC scales were performed using non-parametric methods. Medians and Spearman correlation ( $r$ ) were used for continuous measures, and Mann-Whitney test was applied to categorical variables. This study was approved by the local ethics committee.

**Results:** Median higher synovial calprotectin levels were associated with worse WOMAC pain (671.5 vs 431.8 ng/mL,  $p < 0.05$ .) and function (713.4 vs 400.1 ng/mL,  $p < 0.05$ .) scores than patients with inferior levels. Patients with moderate to severe synovial effusion ( $> 8$  mm on midline suprapatellar line) had higher calprotectin levels compared with those with mild effusion (626.1 vs 417.5 ng/mL,  $p < 0.05$ ). Synovial calprotectin levels showed moderate correlations with intra-articular TNF- $\alpha$  levels ( $r = 0.26$ ), hs-CRP ( $r = 0.27$ ) and a high correlation with synovial IL-6 levels ( $r = 0.53$ ).

**Conclusions:** Calprotectin showed association with inflammatory features as measured by ultrasound and inflammatory markers such as hs-CRP, TNF- $\alpha$  and IL-6, and was related to pain and function in patients with knee osteoarthritis with inflammatory features. Calprotectin appears to be a useful marker of inflammation and could be a useful marker for assessing response to treatments targeting inflammation.

**Disclosure of Interest:** None declared

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AB0964

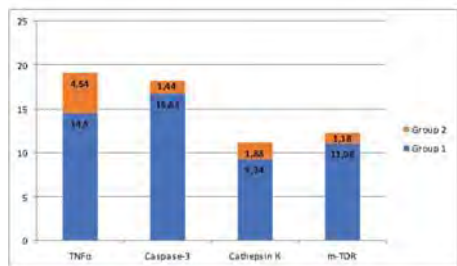
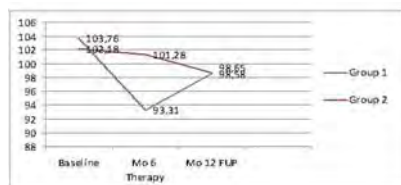
#### THE ROLE OF MTOR GENE EXPRESSION, APOPTOSIS AND INFLAMMATION IN OBESE PATIENTS WITH KNEE OSTEOARTHRITIS

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**Background:** Metabolic osteoarthritis (OA) has been identified in rheumatology as a specific phenotype due to the growing rates of obesity and other comorbidities, with meta-inflammation as the key factor in its pathogenesis. On the other hand, OA progression is associated with altered regulation of chondrocytes' metabolism, namely, with up-regulated expression of genes encoding m-TOR, apoptosis, cartilage degeneration and inflammation.

**Objectives:** To measure the expression levels of genes encoding mTOR, apoptosis (caspase-3), cartilage destruction (cathepsin K), and inflammation (TNF- $\alpha$ ) in patients with knee OA (KOA) and obesity.

**Methods:** 50 female patients (45–65 y.o.) with Kellgren-Lawrence stage II-III KOA and obesity (BMI  $> 30$  kg/m<sup>2</sup>;) were randomised into 2 groups. Pts in Group 1 ( $n = 25$ ) were administered orlistat as a specific therapy for obesity for the period of 6 months, and life-style modifications including low caloric diet and physical exercises for 12 months, pts in Group 2 were recommended to observe the diet and physical exercises during 12 months. Peripheral blood samples were obtained at Mo12 for PCR evaluation of gene expression.



**Abstract AB0964 – Figure 1.** Body mass dynamics. **Abstract AB0964 – Figure 2.** Gene expression in obese pts with knee OA

**Results:** Following orlistat therapy pts from Group 1 managed to reduce their body weight by 10,07% at Mo 6 ( $p < 0,05$ ), while pts from Group 2 lost only 0,88% ( $p = 0,8$ ) of their body weight versus the baseline values. During the following 6 months pts from Group 2 on life-modifying regimen continued to lose their body weight, achieving 3,5% ( $p > 0,05$ ) weight reduction versus baseline values, while pts from Group 1 gained weight by 5,6% as compared to the values at Mo 6 during the study (figure 1). Expression of genes encoding inflammation, apoptosis and cell proliferation was assessed at Mo12 to evaluate possible correlation with the dynamics of body weight. Up-regulated expression ( $p < 0,05$ ) of genes encoding inflammation (TNF- $\alpha$ ), cartilage destruction (cathepsin K), apoptosis (caspase-3) and cell proliferation (m-TOR) was documented in KOA obese pts from Group 1, gaining body weight during the second stage of the study, as compared to the expression values in pts from Group 2 (figure 1). The analysis demonstrated direct positive correlation ( $p < 0,05$ ) between expression of genes encoding inflammation, cartilage destruction and apoptosis and pain intensity in knee joints assessed by VAS and WOMAC scales.

**Conclusions:** Therefore up-regulation of m-TOR, caspase-3, TNF- $\alpha$  and cathepsin K gene expression is observed in obese pts with KOA following weight gain and worsening of clinical parameters, which is suggestive of aggravated apoptosis, inflammation and cartilage destruction, providing further KOA progression.

**Disclosure of Interest:** None declared

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AB0965

#### MEDICAMENTAL AND NON-MEDICAMENTAL THERAPY PREGNANT WOMEN WITH HIP OSTEOARTHRITIS

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**Objectives:** The management of patients with severe pain caused by primary or secondary osteoarthritis (OA) of the hip joint (TBS) has not been developed. The aim of the present work was to evaluate the impact of NSAIDs, glucocorticoids (GCS), analgesics and non-drug treatment methods on pregnancy outcomes in patients with primary and secondary OA TBS

**Methods:** The study included 99 pregnant women aged 35 to 49 with an intensive pain ( $\geq 4.0$  points for VAS) due to primary or secondary OA TBS. Depending on the form of OA, the severity of the pain and the patient's opinion, the therapy was prescribed – ibuprofen up to 800 mg per day orally ( $n = 31$ ) or paracetamol up to 1000 mg per day orally ( $n = 20$ ) or methylprednisolone up to 12 mg per day orally ( $n = 27$ ) or non-pharmacological methods ( $n = 21$ ). The efficacy of the treatment was evaluated within a month from the start of the therapy, pregnancy outcomes for the mother and fetus and pathology of the child after 12 months after the birth. The factors, associated with low efficacy of treatment, were evaluated.

**Results:** In 50 (51%) women was established primary OA TBS, in 49 (49%) – secondary OA TBS. A decrease of pain in TBS in patients of all treatment groups ( $p < 0.05$  for comparison with baseline) was registered. Patients with secondary OA, who received Methylprednisolone, showed a statistically significant ( $p < 0.05$ ) improvement in pain compared to patients in other clinical groups. A correlation was found between the intensity of pain syndrome (VAS) and BMI.

85 (85%) patients had urgent deliveries, 14 (14%) had premature, natural delivery in 82 (82%) women, and a caesarean section was performed in 29 (29%) cases. The cases of ante- and perinatal fetal death were not recorded.

Pathological conditions were absent in 28 (84.85%) of newborns, whose mothers refused medical treatment, in 28 (90.32%) newborns, who received ibuprofen, in 15 (75%) – paracetamol, and in 23 (85.19%), who were on methylprednisolone therapy (differences between groups are unreliable,  $p \geq 0.05$ ). In 12 months after birth in the group of newborns receiving antenatal ibuprofen, pathological conditions were observed in 3 children, paracetamol – in 5, metiprednisolone – in 4 children who were "without therapy" – in 5 children.

**Conclusions:**

- The use of non-medicamental and medicamental (non-selective NSAIDs or GCS in small doses or analgesics) treatment in pregnant woman with hip osteoarthritis has equal efficiency and safety for the health of the mother and fetus.
- Children, born to mothers with primary or secondary hip osteoarthritis, treated with NSAIDs or analgesics or GCS by medical treatment in age of 12th month do not differ from children, born to mothers with osteoarthritis of hip joints, receiving non-medicamental therapy.
- An increase of the body mass index of a pregnant woman with osteoarthritis of the hip joints is a predictor of refractoriness to any form of drug and non-drug therapy.

**Disclosure of Interest:** None declared

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AB0966

### CROSS-CULTURAL ADAPTATION AND VALIDATION OF THE KOREAN VERSION OF THE FUNCTIONAL INDEX FOR HAND OSTEOARTHRITIS (FIHOA)

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**Background:** Osteoarthritis (OA) is one of the most common type of arthritis and it most frequently involves joints of the hands. Measuring functional ability of hand OA patients is important in terms of assessment of treatment response, patient management and improvement of quality of life. The functional index for hand osteoarthritis (FIHOA) is one of the most frequently utilised questionnaire to assess the physical function of hand OA patients. The FIHOA has been translated into 17 languages, however, no Korean version of FIHOA is yet available.

**Objectives:** To translate the FIHOA into Korean, and establish the reliability and validity of the cross-culturally adapted Korean version of FIHOA (K-FIHOA) in patients with hand OA.

**Methods:** The FIHOA was translated into Korean following cross-cultural adaptation guidelines. The K-FIHOA was pretested in 40 hand OA patients (defined by ACR classification criteria). The adapted K-FIHOA was then administered to 100 consecutive hand OA patients together with the modified Health Assessment Questionnaire (mHAQ) and visual analogue scale (VAS) for hand pain. The test-retest reliability of each item and total scores were assessed using Spearman's correlation coefficient and intraclass correlation coefficient (ICC). The internal consistency reliability was evaluated as the Cronbach's alpha. The external construct validity was assessed using correlation between K-FIHOA and mHAQ and hand pain VAS.

**Results:**

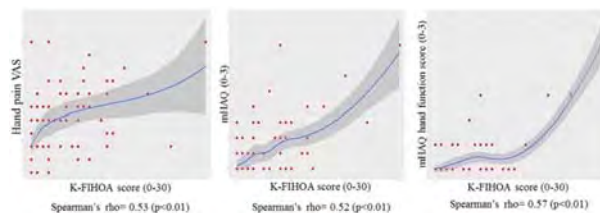
Abstract AB0966 – Table 1

K-FIHOA items	Test-retest reliability			Internal consistency			
	Test	Retest	Spearman's correlation coefficient	ICC	Adjusted item-total Correlation	Item-item correlation	Cronbach's alpha if item is deleted
Item 1	0.19 ±0.54	0.20 ±0.55	0.63	0.58	0.37	0.20–0.36	0.88
Item 2	0.25 ±0.59	0.25 ±0.59	0.58	0.54	0.51	0.26–0.48	0.88
Item 3	0.22 ±0.60	0.25 ±0.61	0.73	0.74	0.52	0.31–0.60	0.87
Item 4	0.35 ±0.66	0.30 ±0.59	0.62	0.58	0.59	0.33–0.52	0.87
Item 5	0.83 ±1.06	0.74 ±1.04	0.76	0.74	0.70	0.33–0.62	0.87
Item 6	0.40 ±0.85	0.40 ±0.88	0.66	0.75	0.63	0.22–0.73	0.86
Item 7	0.43 ±0.88	0.32 ±0.74	0.70	0.71	0.70	0.32–0.73	0.86
Item 8	0.19 ±0.53	0.13 ±0.37	0.62	0.56	0.47	0.25–0.60	0.87
Item 9	1.10 ±1.16	1.07 ±1.16	0.81	0.79	0.74	0.28–0.62	0.88
Item 10	0.43 ±0.79	0.39 ±0.69	0.85	0.80	0.44	0.20–0.52	0.88

Values are given as mean ±standard deviation.

Abbreviations: K-FIHOA, the Korean version of functional index of hand osteoarthritis; ICC, intra-class correlation coefficient.

The mean total score of the K-FIHOA was 4.39 [Standard deviation (SD)=5.56] in the first assessment and 4.04 (SD=5.22) in the second assessment. The test-retest reliability for the total score was strong ( $r=0.87$  and  $ICC=0.75$ ). Spearman's rho for single item correlation ranged from 0.58 to 0.85 and ICC between single items were good or excellent (0.54–0.80). Cronbach's alpha was high (0.88) suggesting a strong internal coherence in the items of the questionnaire. We identified significant correlations between K-FIHOA and hand pain VAS ( $r=0.53$ ,  $p<0.01$ ), mHAQ ( $r=0.52$ ,  $p<0.01$ ), and mHAQ hand function score ( $r=0.57$ ,  $p<0.01$ ).



Abstract AB0966 – Figure 1. External construct validity of K-FIHOA with hand pain VAS, mHAQ, mHAQ hand function.

**Conclusions:** The K-FIHOA is a reliable and valid instrument for evaluating functional disability in Korean hand OA patients.

**Disclosure of Interest:** None declared

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AB0967

### IS THE ICOAP A VALID TOOL FOR MEASURING PAIN AND FUNCTION IN PATIENTS WITH KNEE OA AND RA IN CLINICAL PRACTICE?

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**Background:** Osteoarthritis (OA) is primarily managed in general practice however, care is provided on an ad hoc basis, and a structured approach to continuing care is not offered. Studies have demonstrated the high prevalence of secondary OA of the knee in patients with RA, however, about 52% of these cases are under-reported or under graded by general radiological reports. With its increasing prevalence, it is important to use valid and responsive instruments to evaluate the effectiveness of interventions and to understand the pathology's impact on functioning and general health status.

**Objectives:** We hypothesised that the ICOAP can accurately measure the severity of pain in patients with OA in the clinical setting and can equally detect secondary OA in patients with pre-existing RA.

**Methods:** Patients with longstanding knee OA or RA from outpatient rheumatology clinics alongside GP surgeries were recruited. The ICOAP's formatting was modified and brief abstract was added to the top of the questionnaire to aid patient comprehension. After its modification, it was tested for internal consistency, reliability and construct validity by correlating its yield with other disease activity parameters including the WOMAC and DAS. To examine the test-retest reliability patients were asked to fill out the ICOAP questionnaire again after two weeks.

**Results:** The study included 57 patients with OA and 45 with RA. Total ICOAP-C was 42 with patients with OA compared to 56 in patients with RA while ICOAP-I was 49 in patients with OA compared to 53 in patients with RA. Subgroup analysis of ICOAP-C and ICOAP-I identified that while intermittent pain had a greater impact on QOL in patients with OA, constant pain had a greater impact on OA patient QOL. Patients with RA for more than 10 years had more similar results to patients with OA.

**Conclusions:** The ICOAP questionnaire is easy to use clinically, with the majority of patients approached willing to participate. Respondents with both OA and RA also commented on the lack of complication and ease of understanding of questions. It was responsive to changes in management, proving to be a useful tool in general practice to follow disease progression. The findings demonstrate that the ICOAP has a potentially wider clinical utility in measuring pain in patients with both OA and RA. The similarities in responses of the majority of respondents with knee OA and long-standing RA also strongly suggest that ICOAP might be likely detecting under-reported secondary OA. Future research will examine the effects of variables like pain catastrophizing on pain perception and response.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.7356



**AB0968 EVALUATION OF OSTEOARTHRITIS OF TEMPOROMANDIBULAR JOINT BY COMPUTED TOMOGRAPHY, CLINICAL FEATURES AND CORRELATIONS**

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**Background:** Osteoarthritis (OA) of the temporomandibular joint is a unilateral, degenerative disease of the jaw joint. It is characterised by breakdown of the articular cartilage, architectural changes in bone, and degeneration of the synovial tissues causing pain and/or dysfunction in functional movements of the jaw

**Objectives:** To determine the prevalence and relationship between clinical signs, symptoms and computed tomography (CT) manifestations of temporomandibular joint (TMJ) osteoarthritis

**Methods:** The study included 56 patients with osteoarthritis of the TMJ, included 25 unilateral and 31 bilateral lesions, a total of 87 joints with degenerative changes. Clinically, there was a significant restriction of the movement of the lower jaw and chewing efficiency and a significant increase in articular sounds and general complaints of pain

**Results:** CT data of the most frequent bone changes were erosions of the joint surfaces of the condyles (70 joints, 81%), osteophytes (73 joints, 87%), then their smoothing (67 joints, 77%), hypoplasia (24 joints, 27.6%), sclerosis (6 joints, 6.8%) and subchondral cysts (4 joints, 4.6%). Smoothing of the joint elevation and pneumatization were observed in five joints. Thirty-one patients had bilateral degeneration. In 25-one-sided degeneration. Hypermobility is found in 37 degenerative joints. Chewing efficiency was negatively correlated both with the degree of smoothing of condyles. Sclerosis and the general complaints of pain positively correlated with the smoothing of condyles

**Conclusions:** Conjunctural erosion, flattening, osteophytes, revealed with CT, along with pain, noise in the joint, restriction of the jaw movement and deterioration of the chewing movement were characteristic signs of the TMJ. A correlation was found between bone changes and the severity of the clinical signs and symptoms of the TMJ. CT is a powerful diagnostic tool for the diagnosis of TMJ osteoarthritis

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**Disclosure of Interest:** None declared  
**DOI:** 10.1136/annrheumdis-2018-eular.2174

**AB0969 CONVENTIONAL AND BIOLOGIC DISEASE MODIFYING ANTI-RHEUMATIC DRUGS FOR OSTEOARTHRITIS: A META-ANALYSIS OF RANDOMISED CONTROLLED TRIALS**

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**Background:** The role of inflammation in osteoarthritis (OA) is controversial. Some perceive OA as a reparative process where modest inflammation is secondary to largely biomechanical insult.<sup>1</sup> In contrast, others believe synovial inflammation to be a central driver of OA pain and progression.<sup>2</sup> This has encouraged randomised controlled trials (RCTs) of conventional and biologic disease modifying anti-rheumatic drugs (DMARDs) in OA. However, it is unknown whether these treatments that are primarily used for rheumatoid arthritis are effective for OA.

**Objectives:** To examine the efficacy of DMARDs, including biologics, in people with symptomatic OA.

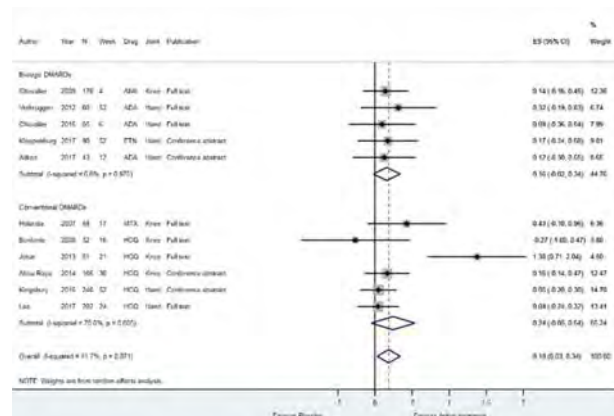
**Methods:** A systematic literature search was conducted (to November 2017) for placebo-controlled RCTs of DMARDs in OA. Data extraction and Cochrane's risk of bias assessments were conducted independently by two reviewers (MP, AS). Pain relief at treatment peak time-point was combined using a random-effects meta-analysis. All DMARDs were pooled and sensitivity analysis was undertaken for high-quality trials and subgroup analyses for DMARD type, biologic target, joint site, OA subtype, and publication type.

**Abstract AB0969 – Table 1.** Subgroup analysis

	ES	95% CI
<b>Sensitivity analysis</b>		
High-quality trials	0.11	–0.06 to 0.28
<b>Subgroup analysis</b>		
Joint		

Knee	0.34	–0.05 to 0.73
Hand	0.09	–0.05 to 0.24
<b>OA type (hand OA)</b>		
Erosive	0.19	–0.06 to 0.45
Non-erosive	0.05	–0.12 to 0.22
<b>Biologic target</b>		
IL1-inhibitor	0.14	–0.16 to 0.45
TNF-inhibitor	0.17	–0.05 to 0.39
<b>Publication type</b>		
Full text	0.27	–0.01 to 0.55
Conference abstract	0.11	–0.05 to 0.27

ES, effect size; CI, confidence interval



**Abstract AB0969 – Figure 1.** Meta-analysis of DMARDs. ADA: adalimumab; ANK: anakinra; ETN: etanercept; HCQ: hydroxychloroquine; MTX: methotrexate; N: number of participants

**Results:** Eleven RCTs (n=1205), including six (n=757) for conventional and five (n=448) for biologic DMARDs, were included in the meta-analysis (7 full texts, 4 abstracts). Overall, conventional and biologic DMARDs were marginally superior to placebo. However, statistical superiority was not observed in high-quality studies (table 1) or subgroup analysis for conventional or biologic DMARDs separately (figure 1). Furthermore, no differences were observed between erosive versus non-erosive hand OA, hand versus knee OA, anti-IL1 versus anti-TNF biologics, or full text versus abstract-only publications (table 1).

**Conclusions:** No significant pain relief was observed from either conventional or biologic DMARDs compared to placebo. Combining all DMARDs gave statistical separation from placebo, but this was below the minimal clinically important difference threshold (0.5 SD) used in the UK.<sup>3</sup> Furthermore, the analysis is based on peak time point for the intervention, so even at their most effective timepoints these treatments do very little over placebo. Lack of efficacy of DMARDs supports the perspective that inflammation is not an important driver for OA pain and differs fundamentally from that in rheumatoid arthritis.

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AB0970

### INVESTIGATION OF THE EFFECTS OF BALANCE TRAINING ON BALANCE AND FUNCTIONAL STATUS IN PATIENTS WITH TOTAL HIP ARTHROPLASTY DUE TO OSTEOARTHRITIS: A RANDOMISED CONTROLLED PILOT STUDY

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**Background:** Osteoarthritis (OA) of the hip is one of the most common disorders in musculoskeletal system. The hip osteoarthritis is painful and this pain causes disability of various degrees, postural and gait disorders.<sup>1</sup> Total hip arthroplasty (THA) has been to one of the most frequent elective surgical procedures that can effectively reduce pain and improve the function in patient with hip OA.<sup>2</sup> It was reported that patients with coxarthrosis and THA have decreased proprioception with motor control and balance disorders, compared to healthy subjects.<sup>3</sup>

The purpose of current study was to investigate the effects of balance exercises on balance and functional level with objective assessment methods until the 26th week of surgery in patients with THA.

**Objectives:** The purpose of our study is investigating of the effects of balance training on balance and functional status in patients with THA.

**Methods:** Sixteen patients with unilateral elective THA were randomised to 2 groups: conventional rehabilitation (CR, n=8) or conventional rehabilitation plus balance training (CR + BT, n=8) groups. The CR group completed typical surgery-specific joint range-of-motion and muscle strengthening exercises, while the CR + BT group completed the CR plus balance exercises during 6 weeks. The patients were evaluated by single leg stance test, Tetrax balance system, Harris hip scoring, lower extremity function scale, 5 times sit to stand test and 50-foot timed walk test preoperatively and 8, 14, and 26 weeks after THA.

**Results:** While there was significant improvement, in terms of on the right extremity eyes closed single leg stance test in the CR group ( $p<0.05$ ), there was no significant difference in terms of other assessment parameters between CR and CR +BT groups ( $p>0.05$ ). There were significant improvement after THA surgery in both groups ( $p<0.05$ ).

**Conclusions:** The results of our study indicate that there were similar improvements in the balance and functional parameters in the CR and CR +BT groups. There was no additional benefit of the balance exercises in balance in the 14 and 26 weeks after THP. Significant differences could be found between groups by continuing balance training with more patients for 1–2 years following THA.

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AB0971

### COMBINATION OF HYALURONATE AND SODIUM SUCCINATE IN TREATMENT OF KNEE OSTEOARTHRITIS

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**Background:** At present hyaluronic acid (HA) is rather widely used in treatment of patients with osteoarthritis (OA). HA normalises the properties of the synovial fluid; has a protective effects; promotes the cartilage nutrition and so improves the signs of OA and function of the joints. To the contrary the effects of sodium succinate (the salt of the succinic acid) are not investigated but can be promising in OA treatment due to its known anti hypoxic and energetic properties.

**Objectives:** To investigate the clinical efficacy of combination of hyaluronate and sodium succinate in OA treatment in early stages.

**Methods:** The study included 126 patients with knee OA (stages I-II, Kelgren and Lawrence), mean age (54.3±2.7) years, among them – 75 women(60%) and 51 men(40%). All enrolled patients had OA exacerbation (without clinically evident synovitis) and received standard OA treatment (NSAIDs, exercises, orthopaedic devices) for 15 days; Gr.1 patients (58) also got 5 intra-articular injections of 1.1% hyaluronic acid, stabilised with sodium succinate (2 ml, once a week); patients of Gr.2 (68) in addition to standard treatment received 5 intra-articular injections of 1,1% solution of non-stabilised HA (2 ml, once a week). Clinical observation and

evaluation of the results were performed at the beginning of the treatment, at 6th, 12th and 24th week after the study beginning

**Results:** During the treatment period, patients in both groups showed the positive changes in clinical signs and symptoms of OA. The VAS score in both groups indicated a significant pain reduction, but the stability and duration of the clinical effect in the groups was different. In patients of Gr.1, the pain syndrome continued to decrease after 12 weeks till 24th week, whereas in Gr.2 after the treatment course there was no significant changes in further pain regression after 6th week point. The general WOMAC index was decreased from (78.3±4.1) in Gr. 1 and (75.4±3.8) in Gr. 2 at the beginning of the study to (27.9±2.6) and (29.8±1.9) accordingly at week 12,  $p<0.05$ . The changes in Lisholm score were also significantly better in Gr.1 than in Gr. 2 (before treatment (21.7±4.6) and (22.6±5.3), at week 6 – (86.4±5.7) and (71.3±4.8), at week 12 – (87.6±6.2) and (63.8±5.3), respectively,  $p<0.05$ ).

**Conclusions:** Combination of the hyaluronic acid and sodium succinate in early stages of knee OA (as intra-articular injections) allows to increase the treatment efficacy. Add of sodium succinate to hyaluronic acid achieve better pain control and longer remission.

**Disclosure of Interest:** None declared

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AB0972

### THE EFFECTIVENESS OF PHYSICAL ACTIVITY INTERVENTIONS FOR PEOPLE WITH OSTEOARTHRITIS AND OBESITY: A META-ANALYSIS

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**Background:** Osteoarthritis (OA) is one of the diseases with the highest prevalence of comorbidity. Clinical guidelines recommend physical activity (PA) for people with OA irrespective of comorbidity. Research investigating the effectiveness of PA interventions in OA and comorbidity is needed.

**Objectives:** To synthesise existing evidence investigating the effectiveness of PA interventions in adults with OA and obesity.

**Methods:** A systematic review with meta-analysis was conducted (PROSPERO Registration: CRD42017055582). Six electronic databases; MEDLINE, EMBASE, AMED, CINAHL, SportDiscus and CENTRAL were searched for studies from their inception to 29.03.17. Inclusion criteria were: randomised controlled trials (RCTs) comparing the effectiveness of any PA intervention to non-PA control group; including adults aged 45 years old and over with clinical or radiographic OA at any site; at least one of the comorbidities of interest (COPD, depression, diabetes, hypertension, obesity, T2DM); and measuring pain, physical function, quality of life, global health post intervention and adverse events. Included study risk of bias (ROB) was assessed using the Cochrane risk of bias tool. Two reviewers screened titles, abstracts and full text articles, checked data extraction, and carried out ROB assessment. Random-effects model meta-analysis pooled outcomes from sufficiently homogeneous studies to calculate effect sizes (Standardised Mean Difference (SMD) with 95% confidence interval (CI)). Meta-analysis findings of the OA and obesity subgroup are reported.

**Results:** The literature search retrieved 8171 citations of which 14 studies (n=4224 participants) were included in the full review, with 9 (n=1382 participants) analysed in the OA and obesity subgroup. PA interventions included: aquatic, aerobic, strengthening and functional activity; of 1–18 months in duration.

Four studies of OA and obesity measuring either Western Ontario Osteoarthritis Index (WOMAC) pain, WOMAC function or Six Minute Walking Test (6MWT) and were included in three meta-analyses. Best estimates showed PA to improve WOMAC pain (n=3 studies; n=547 participants; SMD=–0.09 (95% CI) –0.65, 0.47), improve WOMAC function (n=3 studies, n=415 participants; SMD=–0.35 (95% CI) –0.89, 0.18) and the 6MWT (n=4 studies, n=573 participants; SMD=–0.93 (95% CI) –0.49, 2.35). However, results were not statistically significant. There was substantial between-trial outcome heterogeneity ( $I^2=89.4%$  ( $p=0.000$ ); 77.5% ( $p=0.012$ ); 97.8% ( $p=0.000$ ); respectively); results should be interpreted with caution.

ROB domain judgements were generally either low or unclear. A small minority of judgements were at high risk of bias.

**Conclusions:** Best estimates suggest small beneficial effects of physical activity on WOMAC pain, WOMAC function and the 6MWT. Mixed effectiveness among individual RCTs was likely due to heterogeneous intervention types, intensity and duration.

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AB0973

### THE EFFICACY OF ELECTROMYOGRAPHIC BIOFEEDBACK ON PAIN, FUNCTION AND MAXIMAL THICKNESS OF VASTUS MEDIALIS OBLIQUE MUSCLE IN PATIENTS WITH KNEE OA; A RANDOMISED CLINICAL TRIAL

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**Background:** Isometric exercises play important role in treatment of Knee OA and are easy to do by the growing elderly population. Electromyographic (EMG) biofeedback devices are designed to enhance patient's participation in these exercises by giving them feedback signals of visual or auditory nature, so that it can affect the subject's voluntary activity.

**Objectives:** The aim of this survey was to study the effect of EMG biofeedback on pain, function, thickness of the vastus medialis oblique muscle and maximal electrical activity of this muscle in isometric contraction, in patients with knee OA.

**Methods:** In this single-blinded clinical trial, 46 patients aged between 45 to 70, referring to Shohadaye Tajrish and Shahid Modarres hospitals with diagnosis of knee OA, were recruited. Patients were randomly assigned to two groups of case (23 patients), with EMG biofeedback associated exercise, and control (23 patients), with sham biofeedback associated exercise. The exercise program includes 12 sessions of 15 min isometric quadriceps exercise. Data were gathered via VAS score, the Persian version of WOMAC and Lequesne questionnaires, ultrasonography of VMO muscle and surface electromyography of this muscle at baseline and at the end of 2 months period of this study. Variables compared before and after exercises program in each group and between the two groups.

**Results:** At the end of the study, there were no significant differences between the two groups regarding VAS score, VMO muscle electrical activity, maximal VMO muscle thickness, WOMAC and Lequesne questionnaires scores including overall scores and scores in each subcategories. Although all assessed parameters, except for VMO muscle thickness, were found to be improved significantly in each group, the changes were not more significant in case group except for the VAS score. VMO muscle thickness didn't change significantly after 12 sessions of exercise in either of the groups.

**Conclusions:** Isometric exercises accompanied by EMGBF and the same exercises with sham biofeedback for 2 months both lead to significant improvements in pain, and function of patients with knee OA. Real EMG biofeedback was not superior to sham biofeedback. The only parameter found to be improved to a greater extent in the EMGBF group was the subjective measure of VAS score.

**Disclosure of Interest:** None declared

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AB0974

### THE EFFICACY AND SAFETY OF INTRA-ARTICULAR BOTULINUM TOXIN INJECTION IN KNEE OSTEOARTHRITIS

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**Background:** Osteoarthritis (OA) is a common disease that has a great burden through pain and decreased functional capacity. Botulinum toxin-A (BTA) injection has been recently proposed for knee OA patients to reduce pain and disability.

**Objectives:** In this study we evaluate BTA injection efficacy and safety among non-advance knee OA participants in a before-after trial.

**Methods:** This trial was conducted on knee OA patients presented to our PM and R clinic. Thirty participants aged 40–75 years who had radiographic OA grades of II and III KLS were included. Single intra articular injection of half of a 500<sup>U</sup> vial BTA was applied for all participants. Patients were prospectively evaluated at baseline and then at 8 and 24 weeks after injection using the visual analogue scale (VAS) for pain and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) in three subscales: pain, stiffness and function.

**Results:** Both main outcome measures of this trial (VAS and WOMAC) significantly improved after 24 weeks follow up. About two third of final VAS improvement was achieved in the first week after injection (from 7.2 to 4.5, MD%=36%, p value=0.008); then at 8 and 24 weeks post injection VAS reached 3.8 and 3.3, respectively. Almost 81%–77% of patients had more than 30% decline in their baseline VAS at 8th and 24th week visits, respectively. Also a similar pattern was observed for WOMAC index of sixth month (from 56.7 to 31.0, Mean Difference=-25.7 [MD%=45%], p value=0.005), with more remarkable changes in function subscale (MD%=46%). In this study no major adverse events were noted.

Measure	Before	After	Mean Diff (SD)	P value
WOMAC	10.62 (3.31)	6.00 (1.78)	4.62 (2.35)	0.000
<b>Pain</b>				
WOMAC	5.08 (1.41)	2.85 (1.19)	2.23 (0.90)	0.000
<b>Stiffness</b>				
WOMAC	41.08 (9.52)	22.15 (4.83)	18.92 (7.88)	0.000
<b>Function</b>				
WOMAC	56.77 (13.03)	31.00 (6.96)	25.7 (10.22)	0.000
<b>Total</b>				

Abstract AB0974 – Figure 1

**Conclusions:** BTA showed promising effects in improving knee pain, ROM and functional status. Therefore this single session method could be considered as an alternative to other intra articular injections in knee OA patients who did not response to preliminary conservative treatments. Further data is necessary to assess long-term effects and cost-benefit analysis of BTA against other similar choices.

**Disclosure of Interest:** None declared

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AB0975

### DOES PLATELET RICH PLASMA CHANGE THE VOLUMETRIC FINDINGS OF MRI IMAGING? (A RANDOMISED CLINICAL TRIAL)

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**Background:** Several studies have shown the effect of platelet rich plasma (PRP) on knee osteoarthritis. Most of these studies have focused on subjective and clinical symptoms effect of PRP and fewer papers have studied its objective effect on cartilage. MRI is the gold standard imaging for cartilage lesion.

**Objectives:** In this study, we investigated the effect of PRP on cartilage characteristics by special MRI sequencing.

**Methods:** In the double blind randomised clinical trial, patients with grade 1, 2 and 3 of osteoarthritis were included in this study. All of the knees divided to groups randomly and exercise was prescribed for all of knees. Beside, PRP was injected 2 courses with 4 weeks interval in PRP group. For all of patients before and 6 months after treatment VAS (visual analogue scale) and WOMAC (Western Ontario and McMaster Universities Arthritis Index) were fulfilled and MRI was performed. Sequencings of MRI were PD fat saturated (coronal and sagittal) and transverse TRUFISP 3D. Imaging was scored according to 4 cartilage's characteristics including, Patellofemoral cartilage volume, Subarticular bone marrow abnormality, Medial and lateral meniscal disintegrity and Synovitis.

**Results:** 23 knees in case group and 23 knees in control group were studied. All of patients were female with mean age 57.57±5.9 years old and mean BMI 28.49 ±3.24 (Kg/m<sup>2</sup>). 52% of knees had grade 2 of osteoarthritis. Mean total WOMAC and VAS changes before and after treatment in control group were 11.61±1.3 and 8.5±1.1 respectively. In PRP group, mean total of WOMAC and VAS changes showed better improvement with 20±3.2 and 12.3±1.6 respectively (P-Value<0.05). In PRP group all of the radiologic variables except subarticular bone marrow abnormality had significantly improvement (P-Value<0.05). In comparison between 2 groups, Patellofemoral cartilage volume and synovitis had significantly changes in PRP group (P-Value<0.05).

**Conclusions:** In this study, in addition to the effect of PRP on VAS and WOMAC, there is effect on radiologic characteristics (Patellofemoral cartilage volume and synovitis) significantly. For more evaluation, Study with more sample size is recommended.

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**AB0976 EFFICACY OF INTRA-ARTICULAR INJECTION OF PRP-DRIVEN GROWTH FACTOR (PRP WITHOUT PLATELET AND WBC) VERSUS HYALURONIC ACID ON PAIN AND FUNCTION OF PATIENTS WITH KNEE OSTEOARTHRITIS: A SINGLE-BLINDED RANDOMISED CLINICAL TRIAL**

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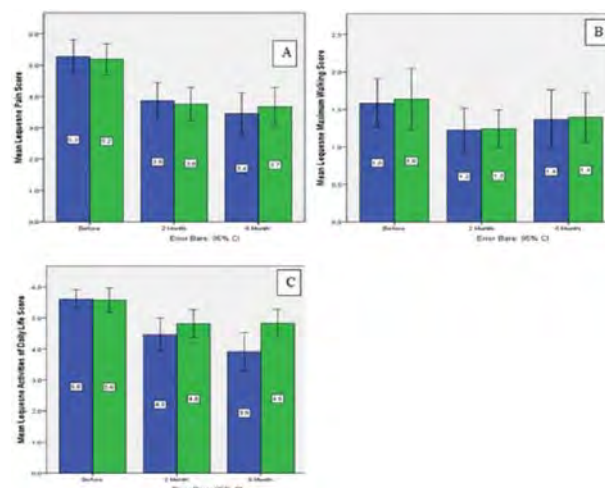
**Background:** Knee osteoarthritis is the most common joint disease.  
**Objectives:** We aimed to compare the efficacy and safety of intra-articular injection of PRP-driven growth factor versus hyaluronic acid (HA) on pain and function of patients with knee osteoarthritis.  
**Methods:** In this single-blinded randomised clinical trial, patients with symptomatic osteoarthritis of knee were assigned to receive 2 intra-articular injections of PRP-driven growth factor in 3 weeks or 3 weekly injections of HA. Our primary outcome was the mean change from baseline until 2 and 6 months post intervention in scores of visual analogue scale, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), and Lequesne index.  
**Results:** A total of 69 patients entered final analysis. The mean age of patients was  $58.2 \pm 7.41$  years and 81.2% were women. Total WOMAC index decreased from  $42.9 \pm 13.51$  to  $26.8 \pm 13.45$  and  $24.4 \pm 16.54$  at 2 and 6 months in the PRGF group (within subjects  $p = 0.001$ ), and from  $38.8 \pm 12.62$  to  $27.8 \pm 11.01$  and  $27.4 \pm 11.38$  at 2 and 6 months in the HA group (within subjects  $p = 0.001$ ), respectively (between subjects  $p = 0.631$ ). There was no significant difference between PRP-driven growth factor and HA groups in patients' satisfaction and minor complications of injection, whereas patients in HA group reported significantly lower injection-induced pain.

**Abstract AB0976 – Table 1**

WOMAC scores		VAS				
		Pain	Function	Stiffness	Total	
PRGF	Baseline	9.2±2.97	30.6 ±10.09	3.0±2.01	42.9 ±13.51	7.8±1.78
	At 2 month	5.8±2.96	19.5±9.79	1.6±1.66	26.8 ±13.45	4.9±2.21
	At 6 month	5.3±3.60	17.6 ±11.70	1.5±1.84	24.4 ±16.54	4.6±2.78
<i>P value within groups</i>		0.0001	0.0001	0.0001	0.0001	0.0001
Hyalgan	Baseline	8.7±3.01	27.8 ±9.62	2.3±1.64	38.8 ±12.62	
	At 2 month	5.9±2.65	20.6±8.04	1.2±1.39	27.8±11.01	
	At 6 month	5.9±2.79	20.1±7.77	1.3±1.48	27.4±11.38	
<i>P value within groups</i>		0.0001				

7.4±1.48  
 At 2 month  
 5.9±2.65  
 20.6±8.04  
 1.2±1.39  
 27.8±11.01  
 4.8±1.80  
 At 6 month  
 5.9±2.79  
 20.1±7.77  
 1.3±1.48  
 27.4±11.38  
 4.8±2.39  
 P value within groups  
 0.0001

0.0001  
 0.0001  
 0.0001  
 0.0001  
 P value Between Groups  
 0.847  
 0.894  
 0.189  
 0.985  
 0.648



**Abstract AB0976 – Figure 1**

**Conclusions:** In 6 months follow up, PRP-driven growth factor and HA, both are effective options to decrease pain and improvement of function in patients with mild to moderate knee osteoarthritis.

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**AB0977 CORRELATION OF THE LEVEL OF C-REACTIVE PROTEIN AND BONE MINERAL DENSITY IN PATIENTS WITH GONARTHROSIS**

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**Background:** The results of recent studies also indicate a link between loss of bone mineral density (BMD) and progressive loss of articular cartilage in patients with knee joint osteoarthritis (OA). The presence of correlation of changes in bone tissue and degradation of cartilage in OA is due to the possible presence of common pathogenesis chains, including activation of proinflammatory mediators.  
**Objectives:** Determine the relationship between the level of C-reactive protein (CRP) and the level of BMD in patients with gonarthrosis.  
**Methods:** We conducted a cross sectional study including confirmed radiographic knee osteoarthritis according to Kellgren-Lawrence scale, with normal and reduced BMD according to the classification of Report of a WHO Study Group. The structural and functional status of bone tissue in patients was

evaluated using the method of ultrasonic densitometry and DEXA at the beginning of treatment and 12 months. The CRP level was determined at the beginning of the observation and after 1, 3, 6, 9 and 12 months. The two groups were compared on the level of BMD, radiological grade, the level of CRP and WOMAC function after adjusting for significant covariates. Multiple regression analysis was used to identify the independent effects to each specific component for level of CRP on knee osteoarthritis parameters.

**Results:** One hundred forty women were included. The mean age was 55.28  $\pm$  0.80<sup>37-75</sup> years. Overweight had 86.42% of patients. The body mass index averaged 30.18  $\pm$  0.43<sup>23-37</sup> kg/m<sup>2</sup>. According to Kellgren-Lawrence classification, 55% of patients had II and 45% of patients – III radiological stage of gonarthrosis. 55.7% of knee OA patients had reduced bone mineral density. Multiple regression analysis showed, after adjusting for significant covariates, that the CRP level was significantly higher ( $p < 0.0001$ ) in patients with reduced BMD compared to normal (6.32  $\pm$  1.67 mg/L and 4.74  $\pm$  0.75 mg/L respectively), an average of 33, 3%.

**Conclusions:** It was found that in patients with gonarthrosis with reduced BMD, a higher level of CRP was observed at 33.3%, which was associated with a more severe course of the disease.

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- [1] It is recommended to study the severity of the progression and progression of OA to study the level of CRP and mineral density of bone tissue.

**Disclosure of Interest:** None declared

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AB0978

#### DECREASED PAIN AND IMPROVED DYNAMIC KNEE INSTABILITY MEDIATE THE BENEFICIAL EFFECT OF WEARING A SOFT KNEE BRACE ON ACTIVITY LIMITATIONS IN PERSONS WITH KNEE OSTEOARTHRITIS

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**Background:** We have previously shown that wearing a soft knee brace reduced activity limitations in persons with knee osteoarthritis (OA).<sup>1</sup> Several underlying mechanisms have been proposed via which a soft knee brace reduces activity limitations in persons with knee OA.<sup>2</sup> However, to our knowledge, no study has identified mechanisms explaining this effect.

**Objectives:** The aim of the study was to identify mechanisms explaining the beneficial effect of wearing a soft knee brace on activity limitations in persons with knee OA.

**Methods:** This was an exploratory analysis of data from 44 participants with knee OA from Amsterdam Osteoarthritis cohort, who enrolled in a single-session within-subject cross-over design study, comparing a soft brace with no soft brace, and comparing a non-tight soft brace with a tight soft brace (GENUTEX A2, Human I). A mediation analysis was performed and the mediation effect was calculated based on the product of coefficients approach. Confidence intervals were calculated with a bootstrap procedure. The outcome measures were activity limitations assessed with the 10-metre walk test and the Get up and Go test. The studied mediators were the changes in: knee joint proprioception, pain, pressure pain threshold (PPT) and objective dynamic knee instability. Knee joint proprioception was assessed by the active movement extent discrimination assessment; pain with the Numeric Rating Scale (NRS); PPT with a hand-held pressure algometer, and dynamic knee instability with the Perturbation Response i.e. a measure reflecting deviation in the mean knee varus-valgus angle after a controlled mechanical perturbation on the treadmill, in respect to level walking.

**Results:** Both a decrease in pain during walking and a decrease in dynamic knee instability mediated the association between wearing a soft knee brace and reduction in time to complete both 10 m walk test and the GUG test ( $p < 0.05$ ). Changes in proprioception and PPT did not mediate these associations ( $p > 0.05$ ). Magnitudes of the mediation effects were similar for a non-tight and a tight soft knee brace.

**Conclusions:** The decrease in activity limitations in persons with knee OA who wear a soft knee brace might be explained by a decrease in self-reported pain and a reduction in dynamic knee instability.

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AB0979

#### ULTRASOUND-MEASURED RADIAL DISPLACEMENT OF THE MEDIAL MENISCUS AS AN INDIRECT SIGN OF MRI-DETECTED CARTILAGE DAMAGE IN PATIENTS WITH MEDIAL TIBIOFEMORAL OSTEOARTHRITIS

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**Background:** Extrusion of the medial meniscus is a consequence of the complex interactions among joint structures and altered tissue mechanics involved in the osteoarthritis (OA) process.<sup>1</sup> Potential contributing factors are cartilage loss, meniscal tears, obesity and knee malalignment<sup>2-4</sup> – features strongly associated with knee OA. Ultrasound (US) measurement of medial meniscus radial displacement (MRD) is an easy to implement procedure that may serve as a starting point for assessment of the cartilage loss in patients with knee osteoarthritis.

**Objectives:** The aim of the study was to investigate the correlation between ultrasound-measured MRD and magnetic resonance imaging (MRI)-detected cartilage damage, as a referent method, in patients with medial femorotibial knee OA

**Methods:** 60 osteoarthritic knees of 48 patients (83% female) aged 40 to 80 years, meeting the ACR criteria for knee osteoarthritis, were included in the study. Patients with severe malalignment (varus or valgus deformity  $\geq 20$  degrees) were excluded. Radiographic stage was assessed according to the Kellgren-Lawrence (KL) grading system, as only KL I-III knees were included. MRD was measured in millimetres using diagnostic US with patients in the supine (non-weight-bearing) position. Magnetic resonance images were acquired by using 1.5 T MRI and were evaluated by a trained radiologist using Whole-Organ Magnetic Resonance Imaging Score (WORMS) for cartilage abnormalities of the medial femorotibial joint (MFTJ) and medial meniscal tears.

**Results:** There was a significant difference in values of MRD among studied radiographic groups ( $p < 0.001$ ). The mean (SD) levels of MRD were 2.70 (1.43) mm, 3.97 (1.25) mm and 6.03 (1.30) mm for KLI, KLII, and KLIII, respectively. All knees that were KLII/KLIII ( $n=41$ ) had MRD higher than 1.8 mm (range 1.8–8.7 mm). MRD correlated significantly and positively with WORMS grades for cartilage abnormalities of MFTJ ( $p < 0.001$ ,  $r=0.758$ ), WORMS grades for medial meniscal tears ( $p < 0.001$ ,  $r=0.576$ ), and body mass index (BMI) ( $p=0.011$ ,  $r=0.315$ ). Correlation between MRD and MRI-detected cartilage damage remained significant after adjustment for age, BMI and medial meniscal tears score.

**Conclusions:** Joint space narrowing (KL  $> 2$ ) on radiography is associated with higher level of meniscal extrusion. Higher values of measured MRD by ultrasound may be indicative of greater cartilage damage of MFTJ.

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AB0980

**FACTORS ASSOCIATED WITH LOSS OF CARTILAGE IN KNEE OSTEOARTHRITIS**

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**Background:** Osteoarthritis (OA) is one of the leading causes of pain and disability worldwide. The structural changes in knee OA are characterised mainly by the progressive loss of cartilage, which is associated with additional structural changes such as subchondral bone lesions and alterations in the menisci. Unfortunately, these changes cannot be effectively treated conservatively. Further determination of modifiable risk factors of cartilage loss is extremely important for improvement of OA management.

**Objectives:** The main objective of the study was the determination of factors associated with loss of cartilage in knee OA.

**Methods:** 294 patients (277 female, 17 male, mean age 55, 09±8,56 years) with newly diagnosed mild to moderate primary knee osteoarthritis were investigated. X-ray and ultrasound examinations of knee joints were performed. The thickness of cartilage and synovial layer, as well as presence of synovitis, tendinitis, osteophytes, Baker's cysts, tear of meniscus were determined. For determination of factors associated with loss of cartilage both univariate and multivariate analyses were performed. The data is introduced as odds ratios (OR) with 95% confidence interval (CI). The results were considered significant when  $p < 0.05$ .

**Results:** Expressed thinning of cartilage ( $\leq 2$  mm) was observed in 216 (73,5%) patients, abnormal thickening of synovial layer ( $\geq 3$  mm) – in 76 (25,9%), synovitis – in 88 (29,9%), tendinitis – in 38 (12,9%), osteophytes – in 273 (92,9%), Baker's cysts – in 93 (31,6%), tears of meniscus – in 93 (31,6%) patients.

Univariate analysis had shown that loss of cartilage ( $\leq 2$  mm) was significantly ( $p < 0,05$ ) associated with age  $> 55$  (OR/95% CI= $2,0/1,3-3,4/$ ,  $p < 0,05$ ), thickening of synovial layer (OR/95% CI= $2,9/1,5-6,2/$ ,  $p < 0,01$ ), synovitis (OR/95% CI= $2,6/1,3-5,0/$ ,  $p < 0,01$ ) and osteophytes (OR/95% CI= $14,8/4,8-45,5/$ ,  $p < 0,01$ ). Following factors were then stepwise included in the model of multivariate logistic regression: age  $> 55$ , thickening of synovial layer and osteophytosis. According to results of analysis, age  $> 55$  had lost its significance, was evaluated as confounding factor (OR/95% CI= $1,2/0,7-2,2/$ ,  $p = 0,4$ ) and excluded from the model. Finally, loss of cartilage (thickness  $\leq 2$  mm) was found to be significantly and independently associated with abnormal thickening of synovial layer (OR/95% CI= $2,8/1,3-6,0/$ ,  $p < 0,05$ ) and osteophytosis (OR/95% CI= $12,8/3,9-41,6/$ ,  $p < 0,01$ ).

**Conclusions:** A positive association of cartilage loss with abnormal thickening of synovial layer (with further development of synovitis) and presence of osteophytes was determined. While cartilage loss and meniscal damage are not yet clearly treatable, treatments targeting inflammation within the joint are available. Thereby, forehanded treatment of secondary inflammatory conditions of joint, as well as strategies, directed toward dissection of osteophytes, can decrease cartilage loss and structural damage in OA.

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AB0981

**PRIORITIES FOR OSTEOARTHRITIS RESEARCH SHOULD BE DONE IN CHINA**

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**Background:** Osteoarthritis(OA) exacts a tremendous toll on patients and society due to limited treatment options and unclear pathological mechanism. Furthermore, rising rates of obese and senior population are predicted to increase the prevalence of OA in the coming years in China. With the development of economy, Chinese government increasingly encourage researches for prevention and treatment of chronic diseases including OA. However, the studies of OA in China remain inadequate.

**Objectives:** This study was designed, in collaboration with Chinese rheumatologists, to investigate key priorities for OA in the next five years to make use of limited funding and resource in China. In addition, it will also help researchers, especially Chinese rheumatologists, to get more support from the government, which will push OA studies faster towards elusive breakthroughs. Therefore, it will improve prognosis and health and quality of life for OA patients.

**Methods:** The study comprised 4 stages, including 1) Identify research priorities for the next five years that match the strengths and expertise of Chinese OA

researchers at the OA potential priority-setting summit. 2) Initial ranking of suggested research priorities using 1000Minds software prior to the summit. 3) Discussion and selection of top five thematic priorities from the original list of 10 priorities at the final OA priority-setting summit. 4) Final ranking of five research priorities by all attendees at the summit and design experimental aims and approaches for the priorities. Finally, the top three priorities from five prioritised topics were selected.

**Results:** 39 Chinese rheumatologists attended stage one and identified 10 priorities in the next five years. There were 313 Chinese rheumatologists invited to participate in stage two, among them, 104 rheumatologists finished the process and identified the initial prioritised rankings of the research topics. 29 Chinese rheumatologists attended the final OA priority-setting summit. Through these multistage processes, three key topics about OA were identified as essential and were prioritised. These three priorities include targeting inflammation should be a focus of research in osteoarthritis, seeking biomarkers for osteoarthritis diagnosis and monitoring, research into early OA would be expected to understand OA across disease development and translate to better therapy. Experimental aims included to detect inflammatory in OA pathology, to identify well-established criteria for early OA, to protect and repair chondrocytes and cartilage, and the approaches included longitudinal study, placebo-controlled randomised controlled trial, animal experiments.

**Conclusions:** Chinese rheumatologists identified OA priorities for the first time, and these key topics would have guiding effect significantly on Chinese OA research in the future.

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AB0982

**PREVALENCE OF OSTEOARTHRITIS IN HIGH ALTITUDE AREA OF TIBET**

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**Background:** Osteoarthritis is a degenerative joint disease; the specific etiology and pathogenesis are unclear. The prevalence of osteoarthritis of subtypes of joints is different, whereas the most common osteoarthritis occurs in knees. In China, the prevalence of osteoarthritis is about 15%, the prevalence of the patients over 40 years old is 10%~17%, and 50% over the age of 60, while over 75 years old was as high as 80%. Few data exist regarding the prevalence of OA in plateau in China.

**Objectives:** To investigate the prevalence of osteoarthritis(OA) in Jiuhue village, which is located about 3.5 kilometres high of Qonggyai County of Tibet and the associated factors in order to provide the guidance for the prevention and treatment of OA.

**Methods:** The participants in this analysis were all the resident people aged 50 years and above in Jiuhue village, Qonggyai County of Tibet. All subjects were invited to completed a questionnaire, physical examination and radiographic examination. The questionnaire included sex, age, body mass index(BMI) and dietary habit.

**Results:** A total of 136 participants aged 50–86 years were enrolled, including 47 males with mean age of 62.00±9.11 years, and 89 females with mean age of 61.30±9.52 years. Altogether 102 knee OA can be diagnosed, the total prevalence of knee OA was 75.00%. Knee OA occurred in 78.72% of male and 73.03% of female. The prevalence of knee OA combined with hand OA was 19.12%, and 21.28% for male and 17.98% for female. The prevalence of knee OA combined with hand OA increased with age in the female, no such trend was observed in male or in only knee OA patients. No significant difference was found about sex, BMI, drinking between the OA patients and the controls.

**Conclusions:** The prevalence of osteoarthritis in Jiuhue village, plateau of Tibet was significantly high. The prevalence in male is higher than that in female. The prevalence of knee OA combined with hand OA increased with age in the female.

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AB0983

### HYALURONAN DERIVATIVE HYMOVIS® INCREASES CARTILAGE VOLUME AND TYPE II COLLAGEN TURNOVER IN OSTEOARHRITIC KNEE: DATA FROM MOKHA STUDY

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**Background:** Intra-articular injections of hyaluronan represent one of the well-accepted standard of care for treating symptomatic knee osteoarthritis (OA). Until now, not much is known about the structural-modifying effect of this treatment justifying this pilot study.

**Objectives:** This exploratory non-controlled study aims to study effects of HYMOVIS on imaging, biological and clinical variables.

**Methods:** Forty six patients with symptomatic knee OA (mean age 61.4 years [min.35-max.80; 67.4% female; Kellgren and Lawrence grade II and III (63% and 37%, respectively); mean BMI 30.6 kg/m<sup>2</sup>] were enrolled in this open-label, prospective, multicenter, pilot study. Patients received two treatment cycles of intra-articular injections (3 mL) of Hymovis (8 mg/mL of the 500–730 kDa hyaluronic acid hexadecylamide) at 6 months interval. Each treatment cycle corresponded to two intra-articular injections one week apart. All patients had MRI of the target knee at baseline and 1 year, and blood samples (D30, D90, D180, D210 and D360) to assess joint biomarkers. The primary outcome was the change in type II collagen-specific biomarkers (Coll2–1, Coll2–1NO2 and CTX-II) after Hymovis treatment versus baseline. Secondary endpoints included levels changes in AGG, COMP, PIINP, MMP-3, MPO and IL-6 serum biomarkers, the ratio Coll2–1/PIINP, CTX-II/PIINP, MRI cartilage volume and KOOS index.

**Results:** Coll2–1 serum levels significantly increased overtime (0.05<P<0.001) while Coll2–1NO2 levels was only increased at D360 (p<0.05). Serum PIINP levels also progressively and significantly enhanced with time (p<0.001). In contrast, other serum biomarker levels including CTX-II, AGG, COMP, MMP-3, MPO or IL-6 did not change significantly overtime. Interestingly, the ratios Coll2–1/PIINP and CTX-II/PIINP decreased (p<0.005), indicating a decrease of cartilage catabolism. Compared to baseline value, MRI cartilage volume increased in lateral femoral and lateral trochlea compartments (p<0.05) and not in medial compartment. Interestingly, WOMBS effusion score, an indicator of synovitis, significantly decreased (p<0.016). Finally, global KOOS score and subscales significantly increased overtime (p<0.001) while pain at rest, walking pain and patients or investigators global assessment of disease activity decreased (p<0.001). The safety profile was favourable with a low incidence of injection-site pain.

**Conclusions:** Hymovis, a well-tolerated intra-articular treatment, significantly enhanced type II collagen turnover as suggested by the increase in Coll2–1 and PIINP levels and cartilage volume observed by MRI in lateral knee compartment. Importantly, this study highlighted the potential symptomatic benefit of Hymovis on pain and function and provides critical information for the design of a larger phase III clinical trial.

**Disclosure of Interest:** None declared

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AB0984

### CADMIUM TOXICITY AS A PROBABLE CAUSE OF SMOKING INDUCED BONE LOSS

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**Background:** Cigarette smoking supposed to be a risk factor for osteoporosis. There is an inverse relationship between smoking and both bone mass and fracture risk. Tobacco smoking is the most important single source of cadmium exposure in the general population. The absorption of cadmium from the lungs is much more effective than that from the gut.

**Objectives:** This study was designed to evaluate the effect of cigarette smoking on bone mineral density, due to cadmium toxicity.

**Methods:** This study was carried on 100 persons, selected from AL-Azhar university hospital and divided into three groups: group I: included 40 persons with active smokers; group II: included 40 persons with passive smokers and group III included 20 nonsmokers. All persons were subjected to full history taking,

thorough clinical examination, routine lab tests, serum and urinary cadmium and lead, and bone mineral density was measured by DEXA.

**Results:** Serum and urinary cadmium and lead were statistically significantly higher in group I in comparison to groups II or III and in group II in comparison to group III. Also, there was statistically significant decrease of BMD in group I in comparison to either group II or group III and in group II in comparison to group III. There was an inverse statistically significant correlation between serum and urinary cadmium and bone mineral density.

**Abstract AB0984 – Table 1.** Comparison between studied groups as regard serum and urinary cadmium levels

		Mean	S. D	Minimum	Maximum	F	P
Serum cadmium (µg/l)	Group I	0.449	0.287	0.18	1.80	27.92	<0.001(S)
	Group II	0.232*	0.040	0.16	0.32		
	Group III	0.094*	0.047	0.01	0.16		
Urinary cadmium (µg/l)	Group I	0.555	0.304	0.30	2.00	27.16	<0.001(S)
	Group II	0.335*	0.042	0.26	0.42		
	Group III	0.181*	0.052	0.11	0.26		

\*=statistically significant decrease in comparison to group I or group II

#=statistically significant decrease in comparison to group I

**Conclusions:** Results of the present study revealed that: there are harmful effects of smoking on the bone mineral density and it may be occurred by direct (increased blood and urinary levels of both cadmium and lead) or indirect effects (effects of both renal and liver functions) of cadmium and lead.

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AB0985

### PERSISTENCE AND ADVERSE EVENTS IN PATIENTS TREATED WITH DENOSUMAB

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**Background:** Denosumab (DNS) is a human monoclonal antibody directed against RANKL, which blocks the maturation of the osteoclast, inhibiting bone resorption. The binding of DNS to RANKL suppresses bone resorption mediated by osteoclasts and decreases bone turnover.

**Objectives:** To evaluate the survival rate of DNS, adverse events and reasons for the DNS discontinuation.

**Methods:** This was a prospective observation study in patients with OP which initiated treatment with DNS between January 2013 and December 2017. Patients included were followed up in the Rheumatology Nurse Clinic every six months. Demographics data, disease features, concomitant disease and treatments, adverse events and reasons for discontinuation were collected.

**Results:** We included 220 patients (80.5% women) with a mean age (range, SD) of 67.19 (30–89, 11.2) years. In average (range, SD), patients received 3.85 (1–11, 2.2) doses of DNS, with a mean duration of treatment (range, SD) of 23.03 (6–66, 13.3) months. 191 (86.8%) patients received also treatment with calcium and vitamin D supplements. Before the start of the treatment with DNS, 123 (55.9%) patients had received another specific treatment for OP with mean previous treatment duration of 51.6 months. Previous fragility fractures were reported in 150 (68.1%) patients, of whom 91 (41.3%) patients had two or more fractures before starting treatment with DNS.

Of all included the patients, 108 (49%) patients had an inflammatory autoimmune disease (IAD) diagnosed. In addition, 100 (45.4%) patients had concomitant biological and/or synthetic treatment and 77 (35%) patients received concomitant treatment with corticosteroids.

During the treatment with DNS, 30 (13.6%) patients had new fractures, 5 (2.3%) patients had 2 fractures. Eleven fractures were vertebral, 3 of femur, one of radius and 21 other locations. There were no differences between patients with or without glucocorticoid treatment (0.234).

The most frequent adverse events (AE) were infections in 88 (40%) patients, muscle pain in 15 (0.6%) patients, fatigue in 7 (0.31%) patients, itching, heat and fever in 2 (0.9%) patients and osteonecrosis of the jaw in 2 (0.9%) patients. The 2 patients with osteonecrosis of the jaw had previous treatment with bisphosphonates for more than 24 months.

At 60 months, 185 (84.1%) patients continued with DNS. In 37 (1.6%) patients, DNS was discontinued; in 4 patients DNS was restarted. The reasons for suspension were hypercalcaemia 1 (0.04%), hypocalcaemia 1 (0.04%), local hypersensitivity reactions 4 (0.18%), normalisation of BMD 5 (0.2%), dental problems 11 (0.4%) and others 17 (0.7%). The mean (SD, 95% CI) of DNS survival was 51.2 (1.9; 47.3–55.1) months. There are no differences in the survival rates of DNS between patients with and without concomitant biologic therapy ( $p=0.995$ ).

**Conclusions:** The majority of patients who started treatment with DNS continue the treatment with good tolerance. The most frequent adverse effects were infections but they have not led to suspension of treatment.

**Disclosure of Interest:** None declared

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AB0986

#### MANAGEMENT OF OSTEOPOROSIS AFTER MAJOR FRACTURE IN A COHORT OF WOMEN AGED OVER 50 IN A REAL LIFE SETTING

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**Background:** Osteoporosis is the most common metabolic bone disease. Fractures constitute a major health concern because prior fractures are associated with an increased risk of subsequent fracture. Moreover, osteoporotic fractures have been associated with increased mortality risk.<sup>1</sup> Hence secondary fracture prevention is recommended. Anti-osteoporotic drugs are available, but in the last decade an alarming decrease of anti-osteoporotic therapy use was observed.<sup>2</sup>

**Objectives:** The objective of this study was to analyse the management of osteoporosis after major fracture (hip, vertebral and humerus fractures) in women aged over 50 in a real life setting.

**Methods:** We conducted an observational study on all women over 50 years of age who experienced a major fracture at Nîmes University Hospital in 2015 identified by informatic codes. Only fragility fractures were included. Data collected prospectively in the computerised medical files were extracted: prescription of a postmenopausal osteoporosis therapy; therapy initiation; prescription and completion of generalised bone mineral density testing; and prescription and completion of blood sample tests to look for secondary osteoporosis. We also recorded the department in which the hospitalizations occurred and the fracture localization.

**Results:** Of 375 women over 50 with a registered fracture in 2015, 264 were included. The exclusion criteria were women with traumatic fracture or minor

osteoporotic fracture. The median age was 84 years old. The most common major fractures were hip (52.3%), humerus (20.8%) and spine (18.9%).

Forty-five (17.0%) patients had experienced a fracture prior to the 2015 fracture.

Only 12 patients (4.5%; IC95%[2.4–7.8]) had an anti-osteoporotic drug prescription at the end of the hospitalisation and only 45 women (17%) had anti-osteoporotic drug prescription planned later. The median period until anticipated prescription was 9 days and the median period until prescription in practice was 18 days.

Assessment of bone mineral density was planned later in only 23 patients (8.7%; IC95% [5.6–12.8]). Blood sample tests were realised in 49 women (18.6%; IC95% [14.1–23.8]).

In surgical department, anti-osteoporotic drug prescription was planned in only 3 women (1.5%) compared with 40 women (56.3%) in medical departments.

**Conclusions:** A large majority of women with osteoporotic major fracture are not receiving appropriate therapy and recommended management in 2015 in Nîmes University Hospital. The rate is dependent on the department in which patients are hospitalised.

The results of our study highlight the urgent need for optimisation of osteoporotic fracture management, especially in the surgical department.

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AB0987

#### FREQUENCY OF UTILISATION OF THE CENTRAL DXA BONE DENSITOMETRY IN PATIENTS WITH MULTIPLE SCLEROSIS

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**Background:** Multiple sclerosis patients can have a higher risk from occurrence of osteoporosis. Reduced bone mass density can be related to a cumulative effect of different factors, most common ones being physical inactivity, reduced intake of vitamin D and use of medications such as glucocorticoids.

**Objectives:** The aim of this research was to explore the level of awareness in patients and physicians on the significance of the utilisation of DXA bone densitometry in patients with multiple sclerosis.

**Methods:** The observational analytical cross-section study included 366 multiple sclerosis patients on stationary treatment at the Special rehabilitation hospital "Banja Kanjiža" in Kanjiža in the period between 2013 and 2017. The following parameters were observed in patients: sex, age, duration and form of basic disease, the level on the Kurtzke Expanded Disability Status Scale, utilisation of glucocorticoids, occurrence of pathological fractures and intake of vitamin D, i.e. of medication for the treatment of osteoporosis in order to determine their impact on the frequency of the low bone mineral density (BMD). Statistical data processing and analysis was conducted in the SPSS ver 20.0 program by IBM corporation.

**Results:** In the period in question, an average of 128 multiple sclerosis patients were treated, out of those 62.3% (n=228) with relapsing-remitting type of disease, and n=366 first time patients. Within the given period, 36% more women than men were rehabilitated (f=249 vs. m=117). During the five-year long period of observation of said patients, only 8.5% (n=31) of patients with different levels of bone metabolic disorders established underwent central DXA bone densitometry. Pathological fracture on a small trauma was suffered in 6.8% (n=25) patients. Of the abovementioned parameters, only the female sex ( $X^2=84.492$ ;  $p<0.001$ ) and age ( $t=2.100$ ;  $p=0.036$ ) statistically significantly influenced the occurrence of low bone mineral density.

**Conclusions:** It is necessary to increase the level of health education of multiple sclerosis patients on the consequences of low bone mineral density. The highest risk of osteoporotic fracture is in older women suffering from multiple sclerosis.

**Disclosure of Interest:** None declared

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**AB0988** **BONE QUALITY EVALUATION USING THE NEW TRABECULAR BONE SCORE (TBS) TOOL IN RHEUMATOID ARTHRITIS PATIENTS SUPPLEMENTED WITH VITAMIN D**

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**Background:** Patients affected by Rheumatoid Arthritis (RA) show an increased risk of low bone mass, as a result of multi-systemic disorders including toxic drug, low vitamin D levels, use of glucocorticoids and physical inactivity. Trabecular Bone Score (TBS), is an index extracted from the dual-energy X-ray absorptiometry (DXA) images, that provides an indirect measurement (Score) of bone axial microarchitecture and allows to get information about bone quality.<sup>1,2</sup>

**Objectives:** The aim of this investigation was to evaluate by TBS the bone quality in RA patients (high risk population) receiving vitamin D supplementation from at least 3 months (1000 IU/die).

**Methods:** 108 female patients (mean age 61±8 years) affected by RA and 60 age- matched controls (CNT) (mean age 64±11 years) were analysed in winter time. Bone Mineral Density (BMD, g/cm<sup>2</sup>) of the lumbar spine (L1-L4) was analysed using a DXA scan (GE, Lunar Prodigy). Lumbar spine TBS (TBS iNsite Medimaps) was derived for each spine DXA examination. All patients were evaluated for serum 25 hydroxyvitamin D (25(OH)D) serum concentrations.

**Results:** RA patients showed lower 25(OH)D concentrations (18.4±1.3 ng/ml) than CNT (26.2±0.9 ng/ml; p<0.04) possibly due to low dosage and short treatment. Seventy-eight RA patients (80% of study population) presented a bone loss that was significant when compared to the control group (p<0.001). In particular, BMD was found significantly lower in RA patients compared with matched control group (respectively, Lumbar spine: 0.862±0.194 g/cm<sup>2</sup> vs 1.240±0.932 g/cm<sup>2</sup>; Femoral neck: 0.668±0.141 g/cm<sup>2</sup> vs 0.845±0.164 g/cm<sup>2</sup>; Ward: 0.486±0.221 g/cm<sup>2</sup> vs 0.657±0.106 g/cm<sup>2</sup>; Trochanter: 0.598±0.231 g/cm<sup>2</sup> vs 0.725±0.143 g/cm<sup>2</sup>; Total hip: 0.764±0.244 g/cm<sup>2</sup> vs 1.033±0.161 g/cm<sup>2</sup>, all p<0.001). Likewise, lumbar spine TBS score was found significantly lower in RA patients when compared with CNT (0.904±0.148 vs 1.361±0.126, both p<0.001)

**Conclusions:** This study shows in RA patients a reduction of TBS values that seem placed side by side with reduced BMD values and in presence of serum 25 (OH)D insufficiency. A more careful analysis of the clinical status/treatments should let to better identify RA patients at higher risk of bone loss.

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**AB0989** **THE IMPACT OF A LOW-COST DIGITAL AND PRINT AWARENESS CAMPAIGN ON PATIENT BEHAVIOUR IN RELATION TO PERSONAL RISK OF OSTEOPOROSIS AND FRAGILITY FRACTURE**

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**Background:** The National Osteoporosis Society (NOS) 'Stop at One' campaign aims to encourage people who are over 50 and have broken a bone to find out, by taking an online quiz, if they are at risk of osteoporosis and to take action to reduce their risk of further fractures. A low-cost marketing intervention was trialled making printed campaign materials available direct to patients at the point of care (fracture clinic).

**Objectives:** The analysis sought to establish whether the marketing intervention increased take up of the online quiz, and to what extent taking the quiz influenced people's behaviour with regard to their bone health.

**Methods:** Between May and October 2017, the NOS placed Stop at One printed campaign materials encouraging people to take the online bone health quiz at 8 sites across the UK covering 13% (16/124) of UK postcode areas. 7 sites had no enhanced provision for secondary fracture prevention such as a fracture liaison service, 1 had a partial service. People who took the online quiz were sent a follow-up survey one month later.

**Results:** Up to 1st, <sup>January 2018</sup> 1909 people took the quiz:

- 89% (1699) of these were over 50
- 95% (1814) were female.
- 21% (443) of these lived in postcode areas of the pilot sites.
- 1359 people were sent a follow up survey one month after taking the online quiz, and 10% (142) completed it. 27%<sup>39</sup> of these were individuals living in the postcode areas of the pilot sites.
- When surveyed, of the 142 respondents:
  - 50% (71) of respondents had broken a bone in the previous ten years.
  - 73% (104) thought they were at risk of osteoporosis after taking the test.
  - 24%<sup>34</sup> had either booked or attended an appointment with their GP to discuss their possible risk of osteoporosis.
  - A further 10%<sup>14</sup> planned to book a GP appointment to discuss their risk.
  - 31%<sup>43</sup> had made changes to their exercise habits.
  - 33%<sup>45</sup> had made changes to their diet.

**Conclusions:** Digital activity (patients accessing website) and the electronic patient survey show meaningful changes in patient behaviour to reduce their fracture risk. Visibility of the awareness campaign at the point of care increased uptake of the quiz and subsequent survey.

**Disclosure of Interest:** None declared

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**AB0990** **THREE YEARS IMPROVEMENT IN OSTEOPOROSIS TREATMENT ADHERENCE FOLLOWING A THERAPEUTIC PATIENT EDUCATION (TPE) PROGRAM**

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**Background:** The management of osteoporosis requires a restrictive drug treatment over several years and lifestyle changes: maintaining a suitable physical activity, a sufficient calcium intake and maintenance of ground balance. Unfortunately, treatment adherence at one year doesn't exceed 50%. The education of the patient allows to take care of himself in his therapeutic approach but requires a relay to continue the follow-up over several years.

**Objectives:** To improve the follow-up of the patient, we created a cooperation between the doctor and the pharmacist.

**Methods:** We suggested to patients treated for osteoporosis by diphosphonate, denosumab or teriparatide to participate at two half-day TPE sessions, one year apart. It's taught that osteoporosis requires at least 5 years of treatment, and must be associated with the absorption of three daily dairy products, maintaining physical activity and preventing falls.

A follow-up notebook that contains 6 doctor and 6 pharmacist questionnaires is given to each patient participating in a TPE session. The patient sends his book to the doctor, and then to the pharmacist twice a year for three years. The pharmacist questionnaire explains the drug intake. The doctor questionnaire evokes lifestyle changes. This one is completed by the patient in the waiting room and is discussed with the doctor during the consultation. Each completed questionnaire provides a financial compensation to the health professional.

The program is funded by the Regional Health Agency of Lorraine and by the Regional Union of Health Professionals (doctors and pharmacists). Inclusions started in January 2013. We studied the results of the 3 year questionnaires for 94 patients included in 2013 and 2014.

**Results:** Among the 94 patients, only 49 continue their treatment at 3 years. Patients who stopped treatment, 4 died, 1 presented an atypical fracture of the femoral shaft, 6 stopped due to dental treatment, 4 had a contraindication to any anti-osteoporosis treatment, 1 stopped treatment due to multiple sclerosis 11 left the program, 2 had poorly tolerated the infusion and 1 discontinued treatment because of improved bone mineral density (BMD). Among the 49 patients who continue their treatment, 13 returned a doctor and pharmacist questionnaire at 3 years. There are 4 doctors and 2 pharmacists who refused to fill out the questionnaire, 20 patients didn't agree to respond to our request for news about their health condition and 4 patients lost to follow-up.

The study of 13 questionnaires received shows that at 3 years, 38% of patients continue to consume 3 daily dairy products against 56% at 6 months. Nearly 70% of patients maintained their physical activity, 8% improved and 8% decreased it. It also shows that 46% of patients walk more than 30 min per day. The ground balance is satisfactory for 62% of patients compared to 71% at 6 months. Regarding compliance, at 6 months and 3 years, only 69% of patients never forget their treatment and 15% wanted to stop it. During the 3 years of follow-up, all patients were re-contacted at least once.

**Conclusions:** 52% of patients included continue the treatment at 3 years. 21% refuse to participate in the program. The doctor/pharmacist collaboration around the patient requires time and understanding. Patients recall and their participation in a research program improves their adherence to treatment and lifestyle changes.

**Disclosure of Interest:** None declared



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AB0991

**OSTEOPOROSIS AND FRACTURES IN PATIENTS WITH CIRRHOSIS. CAN FRAX BE USEFUL FOR SCREENING?**

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**Background:** Osteoporotic fractures are a serious complication in patients with cirrhosis. In addition to the high morbidity and mortality of the patients who suffer them, fragility fractures represent a high cost for Healthcare systems.

However, there are very few studies that evaluate the prevalence of osteoporosis and fractures in patients with liver cirrhosis different than primary biliary cirrhosis (non-PBC cirrhosis). There are also no clinical guidelines with recommendations for osteoporosis screening in these patients.

**Objectives:** To assess the prevalence of osteoporosis and fragility fractures in patients with non-PBC cirrhosis in our environment, and the associated risk factors.

To analyse if the FRAX tool can be useful in the diagnostic screening of these patients.

**Methods:** From November 2015 to September 2017, outpatients older than 40 years diagnosed with non-PBC cirrhosis (any Child stage) were randomly included.

Demographic, clinical and analytical data (calcium, phosphorus, 25-hydroxyvitamin D and PTH) were collected from all patients. A bone densitometry, GE, Lunar Prodigy (DXA) and vertebral fracture assessment (VFA) were also performed, for the diagnosis of osteoporosis (T-score  $\leq -2.5$ ), and vertebral fracture. The 10 year absolute fracture risk was calculated using FRAX (<https://www.sheffield.ac.uk/FRAX/tool.aspx?country=4>).

A descriptive statistic of the main variables was carried out, with univariate and multivariate analysis to assess which predictive factors could be related to the presence of osteoporosis and/or fragility fractures.

**Results:** Ninety-two patients were included (71% male and 29% female). Age 63  $\pm 11$  years. The etiology of cirrhosis was: alcohol (52%), hepatitis C virus (27%) and alcohol +hepatitis C virus (9%). Stage: Child A (80.4%), B (17.4%) and C (2.2%). Mean 25-hydroxyvitamin D was 18.5 $\pm$ 9.8 ng/ml and PTH 51.8 $\pm$ 23.0 pg/ml.

16 patients (17%) had osteoporosis by DXA, 54 patients (59%) osteopenia and 22 (24%) had a normal bone mineral density (BMD). 8 patients (9%) had suffered some fragility fracture (vertebral fracture in 6 cases).

The 10 year absolute risk for major fracture (vertebra, humerus, femur or radius) by FRAX without BMD was 5.7 $\pm$ 4.5; and with BMD 4.7 $\pm$ 4.9.

Age and female sex were associated with the presence of osteoporosis, and a BMI higher than 30 was found to be a protective factor. A BMD in the range of osteoporosis was the only factor associated with fracture.

FRAX for major fracture without BMD higher than 6.6% in this population had a high sensitivity (69%) and specificity (85%) for the diagnosis of osteoporosis, which implies a negative predictive value of 93%. Using this FRAX cut-off for indicating DXA in cirrhotic patients could expect a saving of 76% of DXA scans.

**Conclusions:** The prevalence of osteoporosis and fractures in patients with non-PBC cirrhosis, even in mild stages, is higher than in the healthy population, being more frequent in women and older patients.

The FRAX tool can be useful in the selection of patients with cirrhosis to be assessed by a bone densitometry.

**Disclosure of Interest:** None declared

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AB0992

**BONE REMODELLING BIOMARKERS IN HIV INFECTED PATIENTS**

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**Background:** Bone metabolism is an equilibrium of resorption and growth, maintained by many regulating factors. Several molecules have been identified that estimate bone turnover, being P1NP and b-CTX the most commonly used. Many studies have shown a relationship between their levels and metabolic bone disease, and possibly with risk of fracture.

Human Immunodeficiency Virus (HIV) infected patients have lower bone mineral density (BMD), as documented on many studies. An increased incidence of

fractures has been noted as well, probably due to predisposing factors related to HIV infection, apart from the traditional risk factors.

**Objectives:** To assess the relationship between mean values of bone biomarkers P1NP and b-CTX and incidence of vertebral fractures (VF) in a HIV infected population; and compare such values with those of a Spanish healthy population of reference.

**Methods:** We performed a cross-sectional study with HIV infected patients followed up in the Infectious Diseases Department of our centre from 2014 to 2016. P1NP and b-CTX values were determined and lumbar and thoracic spine radiographs made to assess presence of VF (Genant grading scale). Other clinical and demographic data were collected retrospectively. P1NP and b-CTX values in the presence (VF group) and absence of fractures (non-FV group) were compared. Mean values were also compared with the Camargo cohort, comprised of 1080 healthy postmenopausal Spanish women, used as reference. Statistical analysis were made with STATA. All patients signed and informed consent, previously approved by the Hospital's Ethics Committee.

**Results:** A total of 144 patients were included, 38 were women with a mean age of 56,4 years old<sup>45-77</sup> and 106 men with mean age of 56,5 years old.<sup>45-86</sup> 27 of the patients had at least one VF. No statistically significant differences were found between P1NP mean levels in the FV and the non FV groups, with values of 45,30 ng/ml ( $\pm 17,59$  ng/ml) and 49,48 ng/ml ( $\pm 32,92$  ng/ml) respectively, ( $p=0,52$ ). Mean levels of b-CTX were 0,38 ng/ml ( $\pm 0,18$  ng/ml) in the VF group and 0,43 ng/ml ( $\pm 0,22$  ng/ml) in the non-FV group, again without significant differences ( $p=0,35$ ).

Mean general b-CTX values in our population were 0,41 ng/ml ( $\pm 0,21$ ); 0,46 ng/ml ( $\pm 0,20$ ) in women and 0,39 ng/ml ( $\pm 0,20$ ) in men. Higher levels were found in HIV infected women than in the Camargo cohort (0,38 $\pm$ 0,19 ng/ml), with statistical significance ( $p=0,03$ ). Mean general P1NP values were 48,34 ng/ml ( $\pm 29,47$ ), 58,63 ng/ml ( $\pm 32,9$ ) in women and 44,95 ng/ml ( $\pm 27,56$ ) in men, with no statistically significant differences found when HIV infected women were compared with those of the Camargo cohort, (47,7 $\pm$ 19,9 ng/ml) ( $p=0,06$ ), although a trend towards higher levels in HIV infected women was observed.

**Conclusions:** In the present study no correlation between P1NP and b-CTX levels in HIV infected patients and incidence of vertebral fracture was found.

P1NP and b-CTX mean values in HIV infected women in our study are higher than those of healthy postmenopausal Spanish women, which means a higher bone turnover in this population. More studies are needed to clarify the extent and clinical impact of this finding.

**Disclosure of Interest:** None declared

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AB0993

**PAIN RELIEF MANAGEMENT OF ACUTE OSTEOPOROTIC VERTEBRAL FRACTURE IN A REAL LIFE STUDY**

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**Background:** Among all osteoporotic fractures the painful vertebral fractures (PVF) are the minority and their management is challenging for the clinician because the evidences about the best approach are conflicting and of low quality. Moreover there are no guidelines or consensus of experts. A real life picture of the management of the PVF is lacking in the literature.

**Objectives:** The primary end point of the study is to describe the pharmacological and non-pharmacological management of PVF through the record of use of individual classes, associations and sequences of drugs or procedures. Secondary end point is the outcome of treatment in term of pain, disabilities and quality of life.

**Methods:** We present the interim analysis results of a multicentric cross-sectional observational study. 400 interviews will be collected consecutively about pain, disability, pharmacological, spinal orthoses and orthopaedic surgery after the diagnosis of PVF in postmenopausal women treated by orthopaedics, endocrinologists, geriatricians, physiatrists, neurosurgeons and E.R. physicians. Pain and disability were quantified by NRS scale and by QUALEFFO-41. Data collected from the first 100 patients have been analysed.

**Results:** One hundred postmenopausal women aged 73.1 $\pm$ 7.49 y.o (age of menopause 48.6 $\pm$ 3.9 years, L1-L4 T-score  $-2.75\pm 0.92$ , Total hip T-score  $-2.35\pm 0.98$ ) with a new or first PVF were recorded. About 49% of them had a previous vertebral fracture and 22% a previous non-vertebral fragility fracture, 27% was not on osteoporosis treatment. The interviews were collected 135 $\pm$ 114 days from diagnosis of PVF, 174 $\pm$ 141 days from onset of pain. 92.3 $\pm$ 12% of subjects were treated for pain relief for a mean time of 98 $\pm$ 12 days. Only 1.6% of cohort

underwent to percutaneous vertebroplasty while 84.6%±17.1% had spinal orthoses. Pharmacological treatment for pain was prescribed to 98.2±7.1% of subjects: acetaminophen (42%), tapentadol (24%), opioids (24%), NSAID (6%) and codeine with acetaminophen (4%). In 95% of patients with spinal orthoses drugs for pain were assumed. In about 40% of cases NSAID was switched to acetaminophen, in 18% opioid and tapentadol switched to NSAID or acetaminophen. Only a few titration of opioids/tapentadol were reported. Not adequate pain relief (NRS scale 6.2±3.1; QUALEFFO-41 pain score 70±14.2) and impairment quality of life (mean total QUALEFFO-41 score 65.1±20.1) were reported.

**Conclusions:** With the limits of the study design and low number of cases, preliminary data seem to confirm an inadequate pain relief in PVF. The emerging critical issues crossing all categories of physicians are the lag of diagnosis, the inappropriate use of acetaminophen, the missing titration of opioids or tapentadol. A definition of optimal management of acute vertebral fracture is missing due to conflicting and scarce evidences in this field predisposing to chronic pain and disability.

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**AB0994** **IMPACT ON THE ADHERENCE AND PERSISTENCE OF DENOSUMAB VS WEEKLY BISPHOSPHONATE IN HEALTH-RELATED QUALITY OF LIFE IN POSTMENOPAUSAL OSTEOPOROSIS**

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**Background:** Long term adherence and persistence in patients undergoing treatment for postmenopausal osteoporosis remains poor despite the proven efficacy of the therapy.

**Objectives:** In this study, we evaluated whether greater adherence and persistence in treatment can lead to an improvement in the quality of life.

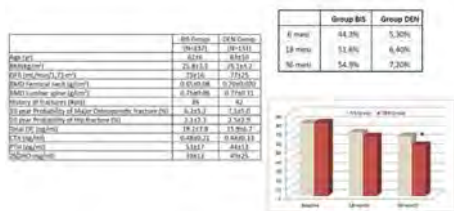
**Methods:** A cohort of 268 patients, all women, in postmenopausal osteoporosis divided into two groups was evaluated: "DEN Group" (DEN) in treatment with denosumab (n=131) and "BIS Group" (BIS) in treatment with bisphosphonates (n=137). Table 1 shows demographic and clinical data. Patients were followed for 3 years with baseline, 6 month, 18 month, and 36 month evaluation. The evaluation criteria were the persistence in therapy and the self-related treatment compliance, as well as the quality of life assessed with the 41-item Quality of Life questionnaire for osteoporosis (QUALEFFO-41) performed at baseline, at 18 and at 36 months.

**Results:** Table 2 shows the percentage of patients who abandoned treatment at different times with a statistical significance towards both 18 and 36 months. In the BIS the main reason for abandonment were the adverse events (gastrointestinal, dental interventions, etc.), in the DEN the abandonment was due to drop-out. [In BIS, the most frequent reason for non-compliance with therapy was oversight, and most patients who continued treatment always used the drugs regularly on the recommended days and dosages.] In the period of time considered the majority of patients both BIS and DEN said they were satisfied with the treatment and wanted to continue it. The QUALEFFO scores (Fig 1) of patients from the baseline visit were significantly improved in the 36 month visit (BIS 79.6±25.4 vs 65.4±14.6; DEN 80.2±18.5 vs 55.6±16.4 (\*p<0.001); the difference was not significant between BIS and DEN groups at both baseline visit and 36 month visit, but in the DEN group there was significance between baseline and 36 month visit.

**Abstract AB0994 – Table 1.** Baseline characteristics (Mean±SD)

OC=Osteocalcin, CTX=C terminal telopeptide, PTH=parathyroid hormone, 25OHD=25 hydroxyvitamin D;

**Abstract AB0994 – Table 2.** Percentage of patients who abandoned.



**Abstract AB0994 – Figure 1.** Qualeffo-41 Score (\* see text)

**Conclusions:** In conclusion, the observation, although numerically limited, notes that the use of denosumab in patients with postmenopausal osteoporosis leads to a greater persistence in treatment and a statistically significant adherence to therapy, which allows to obtain the maximum therapeutic effect of the therapy, also determining in 36 months of treatment an improvement in the quality of life, which is not achieved in subjects treated with bisphosphonates.

**Disclosure of Interest:** None declared

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**AB0995** **VERTEBRAL FRACTURES CASCADE: POTENTIAL ETIOLOGIES AND RISK FACTORS**

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**Background:** Vertebral fracture (VF) is the most common osteoporotic fracture, and a strong risk factor of subsequent vertebral fracture. Prospective studies have shown that a recent VF increases an imminent risk of a subsequent one, and attention has been paid recently to a possible cascade phenomenon i.e. the occurrence of multiples VFs in less than one year.

**Objectives:** This cascade could have severe consequences, and we prompted a study to identify potential causes of osteoporosis and risk factors.

**Methods:** Vertebral fractures cascade (VFC) observations were collected retrospectively between January 2016 and April 2017. VFC was defined as the occurrence of at least 3 vertebral fractures within one year. Patients with other etiologies than osteoporosis (i.e. malignant or traumatic VFs) were excluded. The cause of osteoporosis associated with VFC was the one retained by the physician at the time of diagnosis.

**Results:** Ninety-five observations of VFC (80% of women, mean age of 71 years) were collected in 10 centres (9 tertiary centres and 1 outpatient centre). The median number of incident VFs over 1 year was 4.3-11. Forty-five patients (45.9%) had a previous major fracture before the VFC and 65 (70.7%) had densitometric osteoporosis (T-Score ≤ -2.5 SD either at lumbar or femoral site). Eighteen (19%) patients currently received oral glucocorticoids treatment at the time of VFC, with a mean daily dose of 20 mg. Thirty-three (35.1%) patients received systemic glucocorticoids in the past. The main comorbidities were history of cancer (n=19) and chronic inflammatory diseases (n=21) including asthma (n=7), chronic obstructive pulmonary disease (n=7) and rheumatoid arthritis (n=7).

A secondary osteoporosis associated with the cascade was diagnosed in 54 patients (54.5%) with the following causes: glucocorticoid-induced osteoporosis (n=22, 23.7%), benign hemopathies (mastocytosis, MGUS) (n=7, 7.1%), use of aromatase inhibitors (n=3, 3.1%), anorexia nervosa (n=3, 3.1%), alcoholism (n=3, 3.1%), pregnancy and lactation-associated osteoporosis (n=2, 2.1%), primary hyperparathyroidism (n=2, 2.1%) and hypercorticism (n=1, 1.1%). In addition, 11 cases (11.3%) were reported following a vertebroplasty procedure.

Primary either postmenopausal or idiopathic osteoporosis was diagnosed in 48 patients (51.6%). A total of 29 (29.6%) patients previously received an anti-osteoporotic treatment. In six patients (6.3%), VFC occurred early (in the year) following discontinuation of an anti-osteoporotic treatment: 5 after denosumab and one 12 months after an infusion of zoledronic acid.

**Conclusions:** The results of this retrospective study show that almost half of VFC occurred in patients with secondary osteoporosis. While they suggest that a careful management has to be given to these patients in order to prevent VFC in these circumstances, prospective studies are needed to further explore the determinants of such a severe complication of osteoporosis.

**Disclosure of Interest:** None declared

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**AB0996** **BONE MINERAL DENSITY AT DIFFERENT SITES AS A PREDICTOR OF RIB FRACTURES: A CASE-CONTROL STUDY**

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**Background:** Rib fractures commonly occur as a result of direct trauma, though pathological causes have also been identified. Literature on the specific risk factors of rib fractures is scarce. There was an American prospective cohort study

which highlighted the relationship between risk factors of osteoporosis and rib fractures in older men aged 65 or above.<sup>1</sup> It was observed that the incidence of rib fractures was 3.5/1000 years. Only 3% of rib fractures occurred with absence of trauma. Bone mineral density (BMD) is an important measure for predicting various bone fractures.<sup>2</sup> However, prediction of rib fractures using BMD measurement in different body sites is not reported.

**Objectives:** To determine if reduction in femoral neck and lumbar spine BMD are predictive of rib fractures.

**Methods:** Patients referred from primary care to a DEXA scanner in the north west of England between January 2006 and December 2016 were used in this study. Patients with a history of rib fractures at first scan were matched with controls who did not have any indication for scanning. Cases and controls were matched for age and gender. Differences in BMD at L1-L4 spine and the femoral neck were analysed using two-sample t test. Logistic regression models were fitted to analyse the association between lumbar spine and femoral neck BMD and rib fracture occurrence. The fit of each model was compared using receiver operating characteristic (ROC) curves.

**Results:** A total of 1554 patients were included in the study (777 cases of rib fractures and 777 controls). Mean age for both cases and controls were 62.5 years (SD 12.0). 605 patients (77.9%) were female in both the case cohort and the controls. The mean T score in the lumbar spine is 1.00 in cases versus 1.10 in controls (diff 0.100 95% CI 0.0488, 0.142 p<0.001). The mean T score in the femoral neck is 0.812 in cases versus 0.935 in controls (diff 0.123 95% CI 0.108, 0.137 p<0.001). The odds of lumbar spine BMD and femoral neck BMD were 0.111 (95% CI 0.0640, 0.194, p<0.001) and 0.00209 (95% CI 0.000903, 0.00485, p<0.001) respectively. The areas under ROC curve (AUC) for lumbar spine BMD and femoral neck BMD were 0.623 and 0.733.

**Conclusions:** This study demonstrated that reduction in BMD at the lumbar spine and femoral neck positively correlated to the risk of rib fractures. Reduction in femoral neck BMD is a stronger predictor of the two. Prediction of rib fractures could be affected by other factors influencing lumbar spine and femoral neck BMD. Further work in different demographic groups should be done for comparison and analysis.

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**DOI:** 10.1136/annrheumdis-2018-eular.1360

AB0997

### CLINICAL CHARACTERISTICS OF NON-RESPONDER TO DENOSUMAB TREATMENT FOR POSTMENOPAUSAL OSTEOPOROSIS IN JAPANESE WOMAN

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**Background:** Denosumab (d-mab), an anti-receptor activator of nuclear factor kappa-B ligand (RANKL) monoclonal antibody, is now widely used in postmenopausal osteoporosis (OP) treatment. It can attain reliable increase of bone mineral density (BMD) despite any OP drugs previous used, and that can be predicted in a long period. However, sometimes we observe BMP decrease. Factor that suppresses BMD gain is still unclear.

**Objectives:** This study investigates non-responder to d-mab, and attempted to evaluate factors that concerns non-responder in clinical practice retrospectively.

**Methods:** 212 postmenopausal OP patients have been treated with d-mab continuously for more than two years under vitamin D supplement and calcium since June 2013. These patients were enrolled, and their clinical background (CBs) such as age at start of d-mab, past history of bone fragility fracture, alcohol habitat, current smoking, being treated for rheumatoid arthritis (RA), glucocorticoid steroid thrown, OP drug naive, length of administration (LA), concurrence of lifestyle disease (LSD) such as diabetes mellitus, hypertension, and chronic obstructive lung disease, and number of comorbidity (N.Com), were investigated (table 1a). BMD of lumbar spine (LS), femoral neck (FN), greater trochanter (GT), and whole femur (WF) at the start and every six months thereafter were measured. Tartrate-resistant Acid Phosphatase 5b (TRACP5b) and total dose of type-one pro-collagen -N-pro-peptide (P1NP) at the same time of BMD measurement, and reduction ratio (RR) of them compared to the first shot were calculated. Patients were divided into two groups whether BMD increased. BMD in each part at final measurement relative to that at start was compared statistically with paired T-test. CBs were statistically evaluated between the two BMD groups (Res and n-Res; Responder and non-Responder) with Mann-Whitney U-test (MWT), and then correlation between the BMD groups and factors of CB that had demonstrated significantly difference,

and TRACP5b and P1NP was also evaluated statistically with Binary Logistic Analysis (BLR). Statistical significance was set less than 5%.

**Results:** For all patients, BMD in LS, WF, and GT demonstrated significant increase at final measurement than at start (p<0.001), while FN demonstrated no significant increase. However, n-Res counted 30, 89, 46, and 44 for LS, FN, WF, and GT, respectively. LA demonstrated negative significant correlation for being n-Res in all part, while LSD, N.Com, TRACP5b at start, and RR of TRACP5b at second shot and last shot, demonstrated significant positive correlation in LS with MWT. However, with BLR, only RR of TRACP5b at second shot demonstrated significant negative correlation with n-Res in LS (OR:0.0702, 95% CI:0.0051–0.9655) with 0.39 cut-off index (COI), while no other factors but LA demonstrated significant negative correlation with n-Res in WF (OR:0.9669, 95% CI:0.9433–0.9911) and GT (OR:0.9632, 95% CI:0.9391–0.9878) with 26 and 24 months COI, respectively (table 1b).

Table 1a Patient's background. Age at Start, Length Administered, Number of Chronic Comorbidities, and Bone Mineral Density, show average value and standard deviation. The other parameters show numbers.%YAM:% of young adult mean value. LS: lumbar spine, FN: femoral neck, WF: whole femur, GT: greater trochanter, SERM: selective oestrogen receptor modulator.

Table 1b Parameters that demonstrated significant difference between responder and non-responder to denosumab, and their p-values, and results of these parameters with binary logistic regression analysis. LS: lumbar spine, FN: femoral neck, WF: whole femur, GT: greater trochanter, LSD: concurrence of lifestyle disease, LA: length of administration, N.Com: number of concurrent comorbidities, TRACP5b at start; tartrate-resistant acid phosphatase 5b (TRACP5b) at start of administration, rTRACP5b@1stP: reduction ratio of TRACP5b of second shot compared to the first, rTRACP5b@LT: reduction ratio to TRACP5b of last shot compared to the first, Drug Naive: initial drug as osteoporosis treatment, PINP: total dose of type-one pro-collagen -N- pro-peptide.

Patient's Background		In Mann-Whitney U-test		In Binary Regression Analysis	
Part	Parameters	p-value	Odds Ratio	95% CI	
Age at Start (year-old)	79.66, 9.47				
Alcohol Habitat	LS	LSD	0.021700	7.228	0.5880-8.886
	LA	LA	0.001700	1.026	0.9708-1.084
	N.Com	N.Com	0.000117	0.9291	0.7201-1.199
Operation Experienced	TRACP5b at start	0.002894	0.995	0.9897-1.0000	
	rTRACP5b@1stP	0.001247	0.97015	0.905096-0.9665	
Rheumatoid Arthritis	rTRACP5b@LT	0.004489	2.913	0.3290-2.580	
	LA	0.026510	0.9969	0.9465-1.050	
Lifestyle Disease	Drug Naive	0.016500	1.026	0.2346-4.572	
	P1NP at start	0.000030	1.031	0.9546-1.037	
Glucocorticosteroid	P1NP at second shot	0.000006	0.9872	0.9877-1.007	
	P1NP at last shot	0.000045	1.014	0.9857-1.043	
Vitamin-D3 Supplemental	210				
Length Administered (year)	TRACP5b at start	0.000013	1.002	0.9985-1.006	
	LA	0.007389	0.9669	0.9433-0.9911	
Number of Chronic Comorbidities	WF	0.003872	0.9632	0.9391-0.9878	
	LA	0.003872	0.9632	0.9391-0.9878	
Bone Mineral Density (NYAM) at start in LS	66.95, 15.81				
Bone Mineral Density (NYAM) at start in FN	60.96, 11.47				
Bone Mineral Density (NYAM) at start in WF	62.56, 11.94				
Bone Mineral Density (NYAM) at start in GT	63.43, 14.44				
Drug Naive	95				
Previous Drug					
Biphosphonate	54				
SERM	22				
Tartrate	19				

**Conclusions:** These results suggest that non-responder to d-mab exists. Length of administration works for BMD to increase in femur, and concurrence of LSD, and N.Com are suggested to be risk factors in LS. Less reduction ratio of TRACP5b at second shot is referred for prediction of non-responder. However, there is no parameter that predicts non-responder before administration.

**Disclosure of Interest:** None declared

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AB0998

### OSTEOPOROSIS PREVALENCE IN POST-MENOPAUSAL PATIENTS TREATED WITH AROMATASE INHIBITORS USING BONE MINERAL DENSITY VALUES FROM A SPANISH POPULATION

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**Background:** The majority of cases of breast cancer (BC) are hormone receptor positive and are sensitive to antiestrogen therapy. For postmenopausal women, adjuvant hormonal therapy with an aromatase inhibitor (AI) is the standard of care, and is associated with greater prevalence of osteoporosis (OP)<sup>1</sup>. Definition of osteoporosis is made depending on the T-Score value, which is calculated according to the bone mass peak obtained from a reference population; in our country, BMD reference values in clinical practice are obtained from the National Health and Nutrition Examination Survey cohort (NHANES III) for femoral neck (FN) and those proportionated by the commercial brand Hologic for lumbar spine (LS), which may not be representative of our population and could be distorting the assessment of OP in our patients.



**Objectives:** To assess the prevalence of OP in Spanish postmenopausal patients diagnosed with BC and treated with AI using BMD values obtained from a local cohort for T-Score calculation.

**Methods:** We performed a cross-sectional study with postmenopausal women diagnosed with BC and treated with AI attended in our hospital between August 2011 and December 2014. We estimated BMD for LS and FN using dual X-Ray absorptiometry. The prevalence of OP in our cohort was assessed using BMD reference values from the Spanish cohort of Diaz-Curiel<sup>2</sup>, which included a group of 2442 healthy patients from both genres stratified by age, and compared it with OP prevalence obtained using clinical practice reference values applied in our country (NHANES III/Hologic).

**Results:** A total of 54 patients were included. The mean age at diagnosis was 61.50±6.50 years. The AI used in both groups was letrozole. For LS we didn't find statistically significant differences between both groups. For FN we found 13 patients (24%) with OP according to NHANES/Hologic, and 8 patients (14.8%) according to Diaz-Curiel values. These values are summarised in the table.

Abstract AB0998 – Table 1

	(NHANES/ Hologic)	Number of patients (%)	(Diaz Curiel cohort)	Number of patients (%)	p- value
<b>Lumbar spine (L2-L4)</b>	Normal	10 (18.6%)	Normal	10 (18.6%)	0.110
	Osteopenia	16 (29.6%)	Osteopenia	15 (27.7%)	
	<b>Osteoporosis</b>	<b>28 (51.8%)</b>	<b>Osteoporosis</b>	<b>29 (53.7%)</b>	
	Mean T-score=-2.16		Mean T-score=-2.28		
<b>Femoral neck</b>	Normal	17 (32%)	Normal	15 (27.8%)	0.018*
	Osteopenia	24 (44%)	Osteopenia	31 (57.4%)	
	<b>Osteoporosis</b>	<b>13 (24%)</b>	<b>Osteoporosis</b>	<b>8 (14.8%)</b>	
	Mean T-score: -1.77		Mean T-score: -1.57		

**Conclusions:** In our study, we observe statistically significant differences in osteoporosis prevalence for FN, and around 10% of patients could be reclassified using our local BMD values, which highlights the relevance of the use of BMD values obtained from local population for T-score calculation.

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**Disclosure of Interest:** None declared

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#### AB0999 OPPORTUNISTIC SCREENING FOR OSTEOPOROSIS USING THORACO-ABDOMINO-PELVIC COMPUTED TOMOGRAPHY FOR ASSESSMENT OF VERTEBRAL DENSITY IN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Screening for osteoporosis is crucial in rheumatoid arthritis (RA) patients. Computed tomography (CT) attenuation assessment has been proved to be of interest in general population for detection of osteoporosis.

**Objectives:** To assess the value of thoraco-abdomino-pelvic CT-derived bone mineral density (BMD) in L1, compared with dual energy X-ray absorptiometry (DXA) for osteoporosis screening in rheumatoid arthritis patients.

**Methods:** Consecutive RA patients who underwent a CT-scan and a DXA within a two-year period are retrospectively included. CT sagittal images are evaluated from T4 to L5 for vertebral fractures according to Genant classification. CT attenuation values (in Hounsfield units [HU]) of trabecular bone in L1 are measured on axial images and compared to DXA results.

**Results:** One hundred and five patients (mean age 61.1 years (±9.5), 78.1% women) were included. Twenty-eight patients (26.7%) have DXA-defined osteoporosis and 32 (30%) have osteoporotic fractures (vertebral and/or non-vertebral). According to CT assessment, mean (SD) vertebral L1 attenuation is 142.2 HU (±18.5). The diagnostic performance for vertebral CT-attenuation measurement was good, with an AUC of 0.67 for predicting osteoporotic fractures and of 0.69 for predicting vertebral fractures. Among 31 patients with osteoporotic fractures, 23

(74%) patients are categorised as osteoporotic with L1 CT-attenuation of 135 HU or less, whereas only 13 patients (42%) with DXA.

**Conclusions:** This technique offers a combined opportunistic screening for osteoporosis by assessing both vertebral fractures and bone density on routine CT-scans. This seems of particular interest in RA patients who are at high risk for osteoporosis.

**Disclosure of Interest:** None declared

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#### AB1000 ASSOCIATION OF SERUM URIC ACID LEVEL WITH BONE MINERAL DENSITY AND OSTEOPOROSIS IN POSTMENOPAUSAL WOMEN WITH RHEUMATOID ARTHRITIS

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**Background:** Previous studies have reported that higher serum uric acid (SUA) levels are associated with higher bone mineral density (BMD) in men and postmenopausal women, and lower risk of fragility fracture in men. However, whether this association is also present in patients with rheumatoid arthritis (RA) has not yet been investigated.

**Objectives:** To examine the association of SUA levels with BMD and osteoporosis in postmenopausal women with RA.

**Methods:** We retrospectively evaluated 447 postmenopausal female RA patients (mean age 61.1 years) who underwent measurement of L1–4, femoral neck, and total hip BMD using dual energy X-ray absorptiometry, in addition to SUA levels at a university rheumatology centre in South Korea between 2004 and 2017. Osteoporosis was defined as a T-score of ≤-2.5 according to the World Health Organization classification.

**Results:** The median (interquartile range) SUA level was 4 (3.3–4.8) mg/dL. The mean (±SD) L1–4, femoral neck, and total hip BMD were 0.93±0.16 g/cm<sup>2</sup>, 0.75±0.12 g/cm<sup>2</sup>, and 0.81±0.12 g/cm<sup>2</sup>, respectively, and the frequencies of osteoporosis in the spine, hip, and either site were 25.6%, 15.9%, and 32.5%, respectively. SUA levels were positively correlated with L1–4 ( $\rho=0.102$ ,  $p=0.032$ ), femoral neck ( $\rho=0.123$ ,  $p=0.01$ ), and total hip BMD values ( $\rho=0.146$ ,  $p=0.002$ ) and body mass index ( $\rho=0.231$ ,  $p<0.001$ ), and negatively correlated with glomerular filtration rate ( $\rho=-0.363$ ,  $p<0.001$ ) in Spearman correlation analysis. In multivariable linear regression models adjusted for confounding factors, SUA levels showed a significant positive association with femoral neck BMD ( $\beta=0.0099$ ,  $p=0.015$ ) and total hip BMD ( $\beta=0.0118$ ,  $p=0.01$ ) but not with L1–4 BMD ( $\beta=0.0086$ ,  $p=0.159$ ) as shown in table 1. In addition, multivariable logistic analysis revealed that the third (OR=0.44,  $p=0.038$ ) and fourth SUA quartiles (OR=0.37,  $p=0.021$ ) were associated with lower risk of hip osteoporosis, as compared with the first SUA quartile. However, this association was not observed in lumbar spine osteoporosis.

Abstract AB1000 – Table 1. Linear regression models evaluating the association between serum uric acid levels and bone mineral density in postmenopausal women with rheumatoid arthritis

Independent variables	Dependent variables	Univariable model		Multivariable model	
		Unstandardized $\beta$ (SE)	p-value	*Unstandardized $\beta$ (SE)	p-value
Serum uric acid, mg/dL	Femoral neck BMD	0.0125 (0.0045)	0.006	0.0099 (0.004)	0.015
Serum uric acid, mg/dL	Total hip BMD	0.0138 (0.0048)	0.004	0.0118 (0.0045)	0.01
Serum uric acid, mg/dL	L1–4 BMD	0.0127 (0.0063)	0.044	0.0086 (0.0061)	0.159

\*Estimated using stepwise multivariable linear regression models adjusting for age, BMI, DAS28-ESR, cumulative GCs dose, disease duration and eGFR

**Conclusions:** Higher SUA levels were associated with a reduced risk of low BMD and osteoporosis at hip in postmenopausal women with RA, but no significant association between SUA levels and lumbar spine BMD was found. Our data suggests that uric acid may act as a protective factor against hip bone loss in RA patients.

**Disclosure of Interest:** None declared

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AB1001

### MANAGEMENT OF GLUCOCORTICOID-INDUCED OSTEOPOROSIS IN RHEUMATOID ARTHRITIS: THE EXAMPLE OF THE "RIC NORD DE FRANCE" COHORT

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**Background:** Glucocorticoid-induced osteoporosis (GIOP) is the most common cause of secondary osteoporosis. Patients followed for Rheumatoid Arthritis (RA) are particularly exposed to OP and have a greater risk of fracture, which must be prevented. The newest French guidelines for GIOP management were published in 2014 and it is not known yet how they are applied in real life.

**Objectives:** The objective of our study was to investigate the treatment of glucocorticoid-induced osteoporosis in the Rhumatismes Inflammatoires Chroniques – Nord de France (formerly known as RIC-NPC) network in 2016 for patients with rheumatoid arthritis (RA).

**Methods:** In this observational study, the patients studied were followed in the RIC network for RA from 2004 until June 2016, had at least one bone mineral density (BMD) assessment and glucocorticoid therapy during follow-up. Demographic characteristics of patients, BMD results, fractures and treatments implemented were collected from network data completed during consultations by practitioners.

**Results:** 647 patients were enrolled, including 511 women (79%). The average age of patients was 65.5 years (SD=12) with a mean DAS28 of 3.91 (SD=1.44), mean dose of steroid of 7.6 mg (SD=6.6) and a mean duration of treatment of 49 months (SD=53.7). The average T-score at the first BMD assessment was -0.99 at the spine and -1.03 at the total hip. 298 patients received an anti-osteoporotic treatment (46%). Treated patients were older ( $p<0.0001$ ), with lower weight ( $p=0.001$ ) and had a lower T-score at both the spine and the total hip ( $p<0.0001$  for both sites). They most often underwent a prior fracture ( $p<0.0001$ ), and an initial T-score less than -1.5 SD ( $p<0.0001$ ).

**Conclusions:** Our study has the advantage of reflecting the management of GIOP in a "real life" cohort. Almost half of our patients followed for RA who received corticosteroids had received treatment. According to French guidelines the number of patients requiring an anti-osteoporotic treatment should be higher.

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AB1002

### DIFFERENCES IN BONE METABOLISM BETWEEN INTERMITTENT AND CONTINUOUS TREATMENT WITH LHRH AGONISTS IN PROSTATE CANCER PATIENTS

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**Background:** Prostate cancer is an hormone dependent neoplasia, therefore androgenic inhibition by LHRH agonists is the mainstay of treatment. There are different treatment regimen options: continuous or intermittent in order to decrease side effects. As for the bone effects, therapy with LHRH agonists increases bone resorption and decreases bone mineral density (BMD) all together increasing the risk of fracture. The influence of the different treatment regimen in bone metabolism has not been studied enough.

**Objectives:** To evaluate the effect of the LHRH agonists therapy different regimens on bone metabolism in prostate cancer patients, and whether antiresorptive treatment influences the evolution of BMD according to LHRH agonists treatment regimen.

**Methods:** We recruited patients from the Prostate Cancer Protocol of Osteoporotic Risk Assessment in our institution. The patients were evaluated in a basal visit (month 0) and 6–12–18–24 months after basal evaluation. Data of bone metabolism biomarkers, BMD values, LHRH agonists regimen and antiresorptive treatment was collected. Biostatistical analysis with software R was performed.

**Results:** We reviewed 69 patients and 52 prostate cancer patients without bone metastasis with 12 months follow up were selected. The mean age at cancer diagnosis was 68.92 (8.44) years old, with a mean Gleason score of 7.<sup>1</sup>

81% of patients had LHRH agonists active treatment, 81% of them were under continuous treatment scheme. 39% of patients initiated antiresorptive therapy, 24% with intermittent LHRH agonists and 76% with continuous LHRH agonists. At the basal evaluation 12% of patients had osteoporosis and the 32% had osteopenia. 43% of patients displayed vitD values under 20 ng/mL.

Antiresorptive treatment influenced lumbar spine, femoral neck and hip BMD values ( $p<0.001$ ). In patients with antiresorptive treatment, LHRH agonists intermittent scheme did not have an independent effect in any locations of BMD. In patients without antiresorptive therapy, intermittent LHRH agonists regimen have a positive effect on BMD in total hip and lumbar spine increasing their values compared to those on continuous LHRH agonists regimen. The effect in lumbar spine depends on the time of the intermittency. LHRH agonist intermittent therapy showed no significant influence on T score values of femoral neck, this effect was independent of antiresorptive therapy. In patients without antiresorptive treatment elevated beta-CTX levels were related to a decrease of BMD values ( $p=0.017$ ). No fractures were reported during the follow up period.

**Conclusions:** In our patients there is a high prevalence of vitD deficiency. Antiresorptive therapy had a positive effect in the BMD on both LHRH agonists treatment schemes. Patients without antiresorptive treatment under an intermittent LHRH agonists scheme display a better evolution in BMD values compared to those under a continuous scheme. In patients without antiresorptive treatment the evolution of BMD values was related to beta-CTX levels during follow up.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.6948

AB1003

### USEFULNESS OF DOPPLER ULTRASOUND EXAMINATIONS FOR DETECTING DEEP VENOUS THROMBOSIS DURING THE PERIOPERATIVE PERIOD IN PATIENTS WITH OSTEOPOROTIC FRACTURES OF THE PROXIMAL FEMUR

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**Background:** Deep venous thrombosis (DVT) can lead to a venous thromboembolism and increase the risk of a pulmonary thromboembolism (PE). PE is one of the most common causes of death in hospitalised surgical patients.

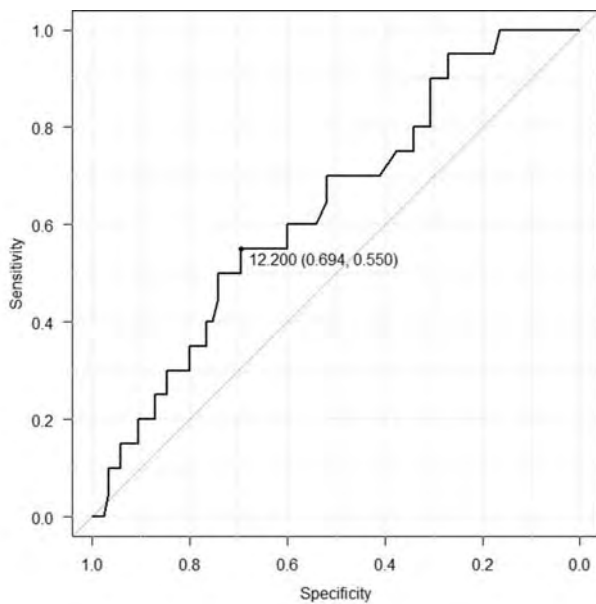
Although there have been some prospective studies regarding the prevalence of DVT on Doppler ultrasound examinations of the lower extremities, there have not been any prospective studies in which three consecutive Doppler ultrasound examinations were performed to detect DVT during the perioperative period.

The purpose of the present study was to prospectively evaluate the occurrence of DVT in patients with osteoporotic fractures of the proximal femur, based on the results of examinations involving three consecutive ultrasound scans. In addition, the usefulness of the d-dimer level as a predictor of DVT was investigated.

**Objectives:** This study was a single-centre prospective study. One hundred-five patients (18 males and 87 females) between the ages of 46 and 97 years with osteoporotic fractures of the proximal femur were enrolled. All patients were asymptomatic in terms of their clinical DVT findings.

**Methods:** Three Doppler ultrasound examinations of the lower extremities were conducted in each case: on admission, one day before surgery, and one week after surgery. The period from admission to surgery ranged from 2 to 8 days (mean: 5.4 days). The d-dimer level was measured at one week after surgery and its relationship with the presence/absence of DVT was evaluated by calculating sensitivity, specificity, positive predictive, and negative predictive values.

**Results:** DVT was detected in 20 patients (2 patients on admission, 9 patients one day before surgery, and 9 patients one week after surgery). The overall prevalence of DVT in the perioperative period was 19.0% (20/105). As for the characteristics of the patients that did and did not develop DVT, there were no significant differences between the two groups. When the d-dimer cut-off level was set at 4.3 µg/ml, the sensitivity and negative predictive value reached 100%, while the specificity was 16.5%, and the positive predictive value was 22.0%. A receiver operating characteristic (ROC) curve was drawn, and the optimal d-dimer cut-off level was examined. The ROC curve was closest to the upper left corner when the d-dimer cut-off level was 12.2 µg/ml. At that point, the sensitivity, specificity, positive predictive value, and negative predictive value were 55.0%, 69.4%, 28.9%, and 86.8%, respectively.



Abstract AB1003 – Figure 1

**Conclusions:** In this prospective study, DVT was detected in 2 patients on admission, 9 patients one day before surgery, and 9 patients one week after surgery. As DVT can occur at any moment, performing repeated Doppler ultrasound examinations in the perioperative period is useful for quickly detecting DVT, which can cause PE. As for the d-dimer level, its sensitivity and negative predictive value reached 100% at a cut-off level of 4.3  $\mu\text{g/ml}$ . Therefore, d-dimer assays could be a useful screening tool for DVT and might be a suitable substitute for Doppler ultrasound examinations.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.1314

#### AB1004 OSTEOPOROSIS SCREENING IN A TERTIARY RHEUMATOID ARTHRITIS CLINIC. WHO'S SCREENING NOW?

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**Background:** Osteoporosis is a complication of rheumatoid arthritis (RA) due to inflammatory disease and treatment with glucocorticoids<sup>1</sup>. Screening and management of osteoporosis (OP) is shared amongst General Practitioners (GP) together with subspecialists including rheumatologists<sup>2</sup>.

**Objectives:** To assess the adequacy of osteoporosis screening in a tertiary RA clinic in Melbourne, and to determine where most screening is occurring.

**Methods:** A cross-sectional study of patients at a tertiary RA clinic was undertaken. Osteoporosis screening, therapy and related factors were evaluated. This was compared to best practice screening ACR/GIOP guidelines.

**Results:** 116 RA patients, 66% female (median age 58 years) were included. OP screening occurred in 61.2% of patients with 40.5% and 20.7% performed by their rheumatologist and by the GPs respectively. The remainder 38.8% of patients recalled no recent screening.

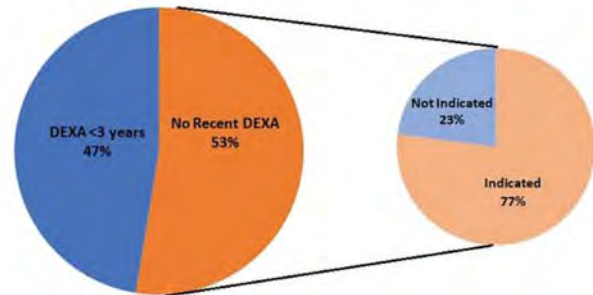
36.2% of patients were taking prednisolone, while 74% reported prior exposure. 58.6% of patients had prednisolone for over 3 months. Calcium or vitamin D supplementation was noted in 62% of the population. 21.6% reported a history of minimal trauma fracture and alarmingly only 10% reported currently taking anti-resorptive therapy.

47% of patients had a DEXA scan performed within the last 3 years. Of the 53% that did not have a recent DEXA scan, three quarters had indications for osteoporosis screening based on the 2010 ACR/GIOP guidelines. 35 patients had indications based on age, 11 patients based on glucocorticoid exposure and 1 patient based on history of minimal trauma fracture.

#### Osteoporosis Screening



#### DEXA Scans



Abstract AB1004 – Figure 1

**Conclusions:** One third of at-risk patients in this sub-cohort are not screened for osteoporosis. More patients are currently screened for osteoporosis by their rheumatologist than their GPs. Underscreening and treatment of osteoporosis in this clinic could be addressed by clearer GP-rheumatologist shared treatment model.

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**Disclosure of Interest:** None declared

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#### AB1005 RELATIONSHIP BETWEEN AUTOIMMUNITY AND OSTEOPOROSIS IN

#### RHEUMATOID ARTHRITIS

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**Background:** Osteoporosis (OP) is more prevalent in patients with rheumatoid arthritis (RA) than in the general population. Positive anti citrullinated peptide antibody (ACPA) has been related with juxta-articular OP, but their relationship with systemic OP in RA is controversial.

**Objectives:** To determine if RA autoantibodies (RF and ACPA) are associated with bone mineral density (BMD) in a cohort of patients with established RA diagnosed following the <sup>ACR</sup> 1987 criteria.

**Methods:** Observational study. We analysed the relationship between RF and/or ACPA with the DXA BMD values of the femoral neck (FN) and lumbar spine (LS) (GE LUNAR Prodigy). We perform the analysis using logistic regression, bi and multivariate models, and correlation models. The control variables were sex, body mass, age, duration of RA, prednisone and vitamin D.

**Results:** We included 294 patients with RA who had all the tests, with a mean age of 63.4 ( $\pm 10.9$ ) years and duration of RA of 9.8 ( $\pm 7.9$ ) years. There were 229 (77.9%) women, 229 (77.9%) positive-RF, 196 (66.7%) positive-ACPA, 109 (37.1%) deficient in 25-OH cholecalciferol ( $< 20$  ng/ml) and 59 (20.1) smoker patients. They received corticosteroids at low doses 207 (70.4%) and suffered some bone fracture 42 (14.3%) patients. In the BMD, 226 (76.9%) patients had a T-score  $< -1$ , of who 86 (27.6%) reached a T-score  $< -2.5$  in LS and/or in FN.



Lumbar OP was associated with the female sex (OR=3.6). The FN T-score (and, to a lesser extent, lumbar T-score), showed a correlation with age ( $r=-0.515$ ,  $p<0.01$ ). No differences were found in the mean values of BMD, T-score y Z-score of FN and LS between positive or negative patients for FR or ACPA (t-student), neither between their possible combinations (one-way ANOVA). Association between positivity of RF, ACPA or their combinations and T-score  $<-1$  (osteopenia) or T-score  $<-2.5$  (OP) in LS or FN were not found. A negative weak correlation was found between the RF and lumbar BMD values ( $-0.121$ ,  $p=0.04$ ) and a positive weak correlation between ACPA and FN (0.136 with BMD, 0.131 with T-score and 0.138 with Z-score;  $p<0.05$  for all).

	Patients n (%)	BMD FN g/cm <sup>2</sup> mean(SD)	BMD LS g/cm <sup>2</sup> mean(SD)	T-score <-1 n (%)	T-score <-2,5 n (%)
Total	291	0805 (0,16)	1063 (0,21)	226 <sup>(76,9)</sup>	81 <sup>(27,6)</sup>
FR+	229	0806 (0,15)	1061 (0,21)	175 <sup>(76,4)</sup>	62 <sup>(27,1)</sup>
ACPA+	194	0808 (0,15)	1065 (0,21)	151 <sup>(77,0)</sup>	49 <sup>(25,0)</sup>
FR+y ACPA+	185	0813 (0,14)	1065 (0,22)	143 <sup>(76,5)</sup>	48 <sup>(25,7)</sup>
FR+ ó ACPA+	51	0767 (0,21)	1049 (0,20)	40 <sup>(78,4)</sup>	15 <sup>(29,4)</sup>
FR- y ACPA-	56	0815 (0,16)	1074 (0,18)	43 <sup>(76,8)</sup>	18 <sup>(32,1)</sup>

**Conclusions:** OP was very common in our RA population, especially in women and elderly. Any association was demonstrated between OP and the presence/titer of autoantibodies (RF and ACPA) and low dose of corticosteroids treatment.

**Disclosure of Interest:** None declared

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#### AB1006 BONE STATUS OF PATIENTS TREATED WITH ANTI-AROMATASE: RESULTS AT ONE YEAR

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**Background:** First cancer in Algeria, first cause of cancer mortality in women. One in 10 women will develop breast cancer in her lifetime. Its incidence is increasing with 55.8/100000 inhabitants. The majority of these cancers are hormone-dependent. The bone loss induced by anti-aromatase (AA) leads to an increase in bone resorption with bone loss 2 to 4 times greater than the physiological loss. Randomised controlled trials (RCTs) including women under AA for 5 years have suggested an increased risk of fracture of 18% to 20% ie 1 in 5 women will experience this risk.

**Objectives:** The aim of our work is to describe the initial bone status and after one year of follow-up in patients starting an anti-aromatase.

**Methods:** Three hundred and twenty seven (327) patients were recruited from the oncology department of Tizi Ouzou University Hospital, 292 patients were analysed in the initial phase of the study and only 250 patients were evaluated at one year. Of these patients, 157 non-osteoporosis patients received calcium and vitamin d-related health care and 93 patients were osteoporotic and treated with calcium and vitamin D bisphosphonates. - Inclusion criteria: Women with oestrogen receptor breast cancer Treatment with anti-aromatase indicated: a- Immediately after conventional breast treatment b- Tamoxifen relay- Criteria for non-inclusion: Bone metastases

**Methods:** Clinical evaluation: screener risk factors for osteoporosis and fractures. Biological Evaluation: Calcium, Phosphoremia, 25 Hydroxy Vitamin D. Radiological assessment: chest radiograph (profile) or IVA (vertebral fracture assessment) looking for vertebral fractures Lumbar and femoral bone densitometry (HOLOGIC QDR)

**Results:** The mean age of the patients is 56.8±7.3 years, mean body mass index is 27.4±2.8 kg/m<sup>2</sup>. 48% of patients received chemotherapy. The anti-aromatases were given as follows: Anastrozole in 64%, Letrozole in 14% and Exemestane in 11%. At baseline assessment n=292, 31.6% of patients had densitometric osteoporosis (T score  $<-2$ ) in the lumbar spine and 9.5% in the femoral neck. 37 patients have a history of peripheral fracture. Six patients have at least one vertebral fracture. The average level of vitamin D is 15.2±3.5 ng/L. 6 - 29 283 patients or 97% have a deficiency in vit D ( $<30$  ng/L). After one year of follow-up, patients without osteoporosis (n=157), annual bone loss is 1.5% at the lumbar spine and 1.24% at the hip. 16 patients became osteoporotic. Four patients developed a new vertebral fracture. The one-year follow-up result in osteoporotic patients treated with bisphosphonates with calcium and vitamin D (n=93) had stable bone mineral density (0.3% non-significant bone loss). 57% of patients still have vitamin D insufficiency and two patients had a new vertebral fracture.

**Conclusions:** Antiaromatases lead to an increased risk of osteoporosis. It is important to evaluate the fracture risk of breast cancer patients through a rheumatology consultation to find all the risk factors, to detect frequent calcium and vitamin D deficiencies and to treat osteoporosis.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.5557

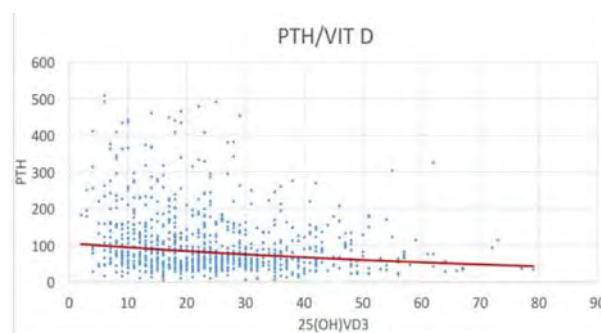
#### AB1007 SEASONAL VARIATIONS OF 25-HYDROXYVITAMIN D3 LEVELS AND ITS RELATION TO PARATHYROID HORMONE LEVELS

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**Objectives:** To analyse the relationship between 25-hydroxyvitamin-D3 and parathyroid hormone levels and to determine its variation between the different seasons of the year.

**Methods:** An observational descriptive study was carried out, collecting and analysing 25-hydroxyvitamin-D3 (25OH-D3) and parathyroid hormone (PTH) serum levels of patients from January to December of 2017. The frequencies distribution analysis of both variables was compared and Pearson's correlation coefficient (PCC) was used to analyse linear relationship between them. The results were classified by date in four seasons: winter, spring, summer, and autumn, assessing the mean seasonal oscillations of each variable and calculating correlation in each case. Different levels of 25OH-D3 were evaluated in order to identify differences in the grade of correlation.

**Results:** Serum samples from 6265 patients were recollected. 59% of the patients had 25OH-D3 levels lower than 25 ng/ml. Pearson's correlation coefficient between both variables was  $-0.159$  ( $p<0.01$ ). The mean values of 25OH-D3 were calculated for each seasonal period, establishing a mean level of 23 ng/ml for winter, 25 ng/ml for spring, 31 ng/ml for summer and 29 ng/ml for autumn. Regarding PTH levels, the mean values for each season were 108 pg/ml, 101 pg/ml, 86 pg/ml and 84 pg/ml from winter to autumn respectively. PTH/Vitamin D correlation was also assessed for each period: Pearson's correlation coefficient during winter was  $-0.08$  ( $p<0.01$ ), for spring  $-0.249$  ( $p<0.01$ ), for summer  $-0,21$  ( $p<0.01$ ) and for autumn  $-0,19$  ( $p<0.01$ ). At last, correlation calculated with deficiency levels of 25OH-D3 ( $<30$  ng/ml) was  $-0.18$  ( $p<0.01$ ), and with levels inferior than 10 ng/ml was  $-0.12$  ( $p<0.01$ ).



Abstract AB1007 – Figure 1

**Conclusions:** Linear correlation between levels of 25OH-D3 and PTH could not be established in our study, not even using levels classified as vitamin D deficiency. 25OH-D3 levels tended to increase from winter to summer whereas PTH levels decreased inversely during these seasons, without any linear correlation.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.3908

#### AB1008 COMPARISON OF BONE MINERAL DENSITY BETWEEN RHEUMATOID ARTHRITIS PATIENTS AND HEALTHY INDIVIDUALS OVER SEVEN YEARS FROM THE TOMORROW STUDY

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**Background:** Despite advances in treatment, rheumatoid arthritis (RA) remains a key cause of secondary osteoporosis and is also a risk factor for fragility fracture. We have previously reported that bone mineral density (BMD) was lower in patients with RA than in healthy individuals (HI) and examined changes in BMD over 3 years<sup>1</sup>.

**Objectives:** To observe BMD changes over 7 years and identify factors that affect BMD changes in patients with RA.

**Methods:** We analysed data from the TOMORROW study (UMIN000003876), a prospective cohort for patients with RA and age- and sex-matched HI. BMD was measured at three parts (whole body, lower limb, lumbar spine) using dual-energy X-ray absorptiometry (DXA). We compared the percentage change in BMD (%Δ BMD) at the three parts in RA and HI from 2010 to 2017. Factors affecting %Δ BMD in RA were analysed.

**Results:** Participants comprised 172 HI and 119 RA, after excluding those who dropped out (HI, n=21; RA, n=19) or underwent implant surgery (HI, n=12; RA, n=60). Height and weight reduced significantly over 7 years ( $p<0.001$  each) in both groups (table 1). The  $\Delta$ BMDs of RA were  $-2.6\%$  (whole body),  $-3.6\%$  (lower limb), and  $1.8\%$  (lumbar spine), compared to  $-2.0\%$ ,  $-2.7\%$ , and  $0.6\%$ , respectively, for HI. No significant differences in BMD for the whole body or lower limb were seen during 7 years, while BMD of the lumbar spine was significantly increased in both groups ( $p<0.0001$ ). No significant differences between groups were identified. In patients with RA, DAS28ESR improved significantly over 7 years ( $p=0.008$ ; table 1) and  $\Delta$ BMD of the lumbar spine correlated significantly with cumulative period of treatment for osteoporosis ( $r=0.341$ ,  $p<0.001$ ). The cumulative period of osteoporosis treatment was identified as a regulatory factor for increasing BMD of the lumbar spine (odds ratio: 1.36;  $p=0.003$ ) adjusted by age and sex (table 2). However, cumulative period of biologics, change of glucocorticoid and DAS28ESR were not detected as factors affecting BMD by logistic regression analysis.

**Abstract AB1008 – Table 1.** Changes in characteristics over 7 years

Parameter	Total population (n=291)	Healthy individuals (n=172)	Patients with RA (n=119)	P value
Age 2010	56.6±12.7	57.1±12.3	55.9±13.3	0.431
Height 2010 (cm)	157.3±7.8	157.9±7.1	156.4±8.7	0.107
Height 2017 (cm)	156.1±8.1	156.8±7.3	155.2±9.1	0.107
Body weight 2010 (kg)	56.1±10.0	56.5±10.3	55.6±9.7	0.418
Body weight 2017 (kg)	55.1±10.4	55.8±10.7	54.0±9.9	0.145
DAS28 ESR 2010	-	-	3.17±1.27	-
DAS28 ESR 2017	-	-	2.86±1.24	-

**Abstract AB1008 – Table 2.** Factors associated with increased BMD of the lumbar spine in patients with RA

Factor	Odds ratio	95% CI	P value
Period of osteoporosis treatment	1.36	1.11–1.66	0.003
Period of biologics	1.02	0.92–1.13	0.683
Change of glucocorticoid	1.01	0.83–1.23	0.933
Change of DAS28ESR	1.04	0.76–1.44	0.798

**Conclusions:** BMD of the whole body and lower limb tended to decrease slightly over 7 years in both groups. However, BMD of the lumbar spine increased significantly. Continued osteoporosis treatment is important for increasing BMD at the lumbar spine in patients with RA.

#### REFERENCE:

- [1] Use of bisphosphonate might be important to improve bone mineral density in patients with rheumatoid arthritis even under tight control: the TOMORROW study. *Rheumatol Int* 2017;37:999–1005.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.2298

#### AB1009 CONCORDANCE BETWEEN VERTEBRAL FRACTURE ASSESSMENT AND CONVENTIONAL RADIOGRAPHY IN DETECTION OF VERTEBRAL FRACTURE

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**Background:** Vertebral fractures (VFs) are considered as severe fractures, but often asymptomatic. The VFA (Vertebral Fracture Assessment) performed at the same time as the bone mineral density (BMD) measure, allows the detection of these fractures. Nevertheless, standard radiography remains the reference technique in the diagnosis of VFs.

**Objectives:** Our objective is to compare the contribution of VFA and the standard thoraco-lumbar spine X-ray in the diagnosis of VFs in patients at risk.

**Methods:** This is a cross sectional study, including women referred in rheumatology department for measure of bone mineral density (BMD). During the same exam, we practiced a vertebral fracture assessment (VFA) image. An X-Ray of dorsal and lumbar spine was done. The interpretation of the two methods was to diagnose asymptomatic vertebral fractures (VFs) which are defined according to Genant's semi-quantitative classification.

**Results:** The mean age of our patients (31 patients) was  $61.3\pm 11.3$  years<sup>38–82</sup> with an average body mass index (BMI) of  $27.65\pm 4.8$  Kg/m<sup>2</sup>; [17.8–40.1]. According to the WHO classification, 17 women (54.8%) had osteoporosis, 10 (32.3%) had osteopenia and 4 (12.9%) had normal BMD. The indications for VFA practice were: age over 60 years with T score  $\leq -2$  SD, historical height loss  $\geq 4$  cm, a

history of VF, a long-term corticosteroid therapy, and aromatase inhibitors therapy in 25.8%, 12.9%, 6.5%, 45.2% and 9.7% respectively.

VFA objectified 15 VFs in 6 women (19.4%) which were grade 1, 2 and 3 in respectively 2, 5 and 8 vertebrae. However plain X ray showed 21 VFs in 10 women (32.2%) which were grade 1, 2 and 3 in respectively 5, 7 and 9 vertebrae. The concordance between the two methods was found in 87.1% of cases, with a coefficient of Cohen (kappa) at 0.76 (strong agreement). A significant correlation ( $p=0.000$ ) was found between the two methods concerning the detection of VFs grade II and III.

**Conclusions:** Our study proved the good agreement between the VFA and the standard X-ray in the detection of VFs. This shows the sensitivity of this technique which has the advantages of low cost and less irradiation.

**Disclosure of Interest:** None declared

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#### AB1010 RISK OF INFECTION IN PATIENTS WITH RHEUMATOID ARTHRITIS TAKING DENOSUMAB CONCURRENT WITH BIOLOGIC THERAPY

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**Background:** Apart from Denosumab effects on bone, there are some promising data on its inhibitory effect on structural damages in patients with Rheumatoid Arthritis (RA).<sup>1</sup> Despite some clinical concerns on its potential harm for increasing risk of infections, Denosumab is officially approved for the treatment of postmenopausal osteoporosis. Still there are even greater debates on its use and predisposing patients to infection in cases receiving immunosuppressive therapy.<sup>2</sup> Considering the importance of infection in such cases, lack of sufficient convincing safety data has prevented, at least in part, the current guidelines to recommend Denosumab in treatment of osteoporosis in patients on immunosuppressive agents.<sup>3</sup>

**Objectives:** We aimed to compare the infection risk in patients with RA taking biologic Disease Modifying Anti Rheumatic Drugs (bDMARDs) alone or concurrent with Denosumab.

**Methods:** Using records from the files covering January 2013 to May 2016, a retrospective comparative study was performed on two groups of postmenopausal RA patients, group A including 40 patients receiving Denosumab+bDMARDs (Etanercept, Rituximab, Adalimumab), and group B consisting of 44 patients receiving bDMARDs alone. Patients were included if the current therapeutic regimen was used for at least one year. All patients were also on a daily dose of prednisolone (2.5–7.5 mg) and folic acid, and a weekly dose of Methotrexate. Occurrence of serious bacterial or viral infections was extracted from recorded files of the patients' routine visits.

**Results:** The mean age of the patients was  $63.1\pm 12$  years and  $62.6\pm 11.7$  years in group A and B, respectively ( $p=0.42$ ). The mean disease duration was  $7.2\pm 1.9$  years and  $7.1\pm 1.6$  years in group A and B, respectively ( $p=0.39$ ). The mean duration of biologic use was  $15.4\pm 3.2$  months and  $15.8\pm 4.6$  months in group A and B, respectively ( $p=0.28$ ). Type 2 diabetes mellitus was present in four and five patients of group A and group B, respectively ( $p=0.35$ ). In total, four infections occurred in our study groups, two in each group ( $p=0.94$ ). In group A, the first one was an osteomyelitis of the first metatarsal bone in a diabetic patient receiving Etanercept+Denosumab. The second one was a herpes zoster infection in a patient receiving Adalimumab+Denosumab. In group B two cases of herpes zoster were recorded in two patients receiving Adalimumab.

**Conclusions:** This study showed that the potential infection risk of concurrent use of Denosumab and bDMARDs was not significantly different from using bDMARDs alone. Based on this finding, Denosumab seems safe in the treatment of osteoporosis in RA patients receiving bDMARDs.

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AB1011

### CLINICAL TRIAL OF INTRAVENOUS INFUSION OF FUCOSYLATED BONE MARROW MESENCHYMAL STEM CELLS IN PATIENTS WITH OSTEOPOROSIS

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**Background:** Osteoporosis (OP) is a systemic bone disease characterised by decreased bone mass and deterioration of bone microarchitecture with increased brittleness and fracture risk. It associates high morbidity and mortality for patients and has a high impact on health expenditure. Bone marrow stromal mesenchymal stem cells (BM-MSC) give rise to osteoprogenitor cells and osteoblasts and influence bone homeostasis. However after their intravenous (i/v) infusion their osteotropism is limited. Our group has demonstrated that the exofucosylation of the CD44 membrane antigen in MSC improves their homing to bone tissue and that the infusion of these cells is safe in a murine model.

**Objectives:** To evaluate the safety of i/v infusion of fucosylated BM-MSC in patients with OP, and secondarily assess their ability to improve the course of the disease

**Methods:** 10 women between 50 and 75 years old diagnosed with osteoporosis with a low impact fracture will be included and treated i/v with autologous fucosylated BM-MSC. The first 4 patients were treated with a dose of  $2 \times 10^6$  cells/kg body weight and the other 6 with  $5 \times 10^6$  cells/kg body weight. A 24 month follow-up will be conducted to evaluate the rate of severe and non-serious adverse events and secondary endpoints (decreased fracture rate, pain scores, functional status and quality of life, biochemical indexes of bone metabolism, quantitative computed tomography for morphometric and mechanical analysis of bone quality, densitometry, and histomorphometry)

**Results:** Seven patients have been recruited to date. Two left the study for lack of cell proliferation and appearance of a complex form in karyotype during the cell culture, respectively. The first 4 patients were successfully infused, and after a median follow-up of 3 months no related adverse effects have been observed, no new osteoporotic fractures have appeared, and the analogue pain scale score (EVA) shows a tendency to decrease of pain in 3 of the 4 patients.

**Conclusions:** Our preliminary data indicate that clinical and GMP-grade production of BM-MSC is feasible. We have not observed any short-term adverse effects associated with treatment in infused patients.

**Disclosure of Interest:** None declared

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AB1012

### BONE MASS CHANGES CORRELATE WITH DISEASE ACTIVITY IN NON-ARTHRITIC PSORIATIC PATIENTS

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**Background:** Psoriasis is a chronic inflammatory skin disease, and as all inflammatory processes, it could induce osteoclast activation<sup>1</sup> ending up with osteoporosis. It is well known that a recognised contributing factor to bone strength, independent from bone mass, is micro-architectural damage; therefore, evaluation of microarchitecture seems to be necessary to get adequate information about bone quality health. Trabecular bone score (TBS) is a new tool to assess bone quality.<sup>2</sup> To date, studies on TBS assessment in psoriasis are lacking, even if it was suggested to be correlated with inflammation and metabolic parameters.<sup>3</sup>

**Objectives:** The aim of the study was to investigate bone quality and bone quantity in psoriatic patients without arthropathic involvement and its relationship with dermal disease activity (PASI).

**Methods:** Thirty-five psoriatic patients and thirty-four healthy controls were enrolled. We first assessed Body Mass Index (BMI), Bone Mineral Density (BMD)

and Trabecular Bone Score (TBS) in both patients and healthy control. The Bone Mineral Density (BMD) (g/cm<sup>2</sup>) was analysed by dual-energy X-ray absorptiometry scan (Lunar Prodigy) and, using same machine, anteroposterior spine analysis was performed to evaluate TBS for L1-L4 using TBS insight Medimaps software. TBS >1.350 units was considered normal. Psoriatic patients were also divided in two subgroups according to skin lesion presentation (plaque psoriasis and guttate psoriasis) and dermal disease activity was measured by Psoriasis Area and Severity Index (PASI).

**Results:** In the psoriatic cohort (mean age 62.8±12.6 years, BMI 27.8±3.4 g/m<sup>2</sup>, disease duration 18.6±11.9 years, PASI 8.3±7.6) 36% of patients showed low bone mass, particularly, 33.3% showed osteopenia and 2.7% osteoporosis. There was not significantly statistical difference between mean BMD and TBS in psoriatic patients when compared to the healthy control group. However, in psoriatic patients a negative correlation between neck-BMD and PASI (p=0.003) was detected independently of sex and age. Conversely, TBS was not statistically correlated with PASI or with BMI. It was interesting to verify that the plaque psoriasis group showed a positive correlation between PASI and age (p=0.01). Conversely, PASI was negatively correlated with lumbar spine T-score (p=0.01) and both lumbar spine and femoral neck BMD (p=0.04 and p=0.02 respectively).

**Conclusions:** This pilot study suggests that in psoriasis, particularly in the plaque subgroup, the severity of skin involvement might correlate with bone mass but not with bone quality (TBS). Despite previous evidences, we can't assess any correlation between TBS and metabolic parameters. Further studies with larger cohorts are needed on this topic.

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AB1013

### PREDICTION OF BONE MINERAL DENSITY CHANGES IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Osteoporosis and its related fractures is one of the most dominant, troublesome complications in rheumatoid arthritis (RA). Newly-introduced drugs such as methotrexate and biological and targeted synthetic disease modifying anti-rheumatic drugs have decreased disease activity drastically, but the improvement of osteoporosis remains to be investigated.

**Objectives:** To find useful factors for bone mineral density (BMD) management of RA patients under the current treatment.

**Methods:** We consecutively recruited 370 RA patients treated at Kyoto University Hospital in 2012. We prospectively collected the BMD values of the lumbar spine and the distal forearm measured by dual-energy X-ray absorptiometry (DXA), blood sampling test, urinalysis including bone metabolic biomarkers and clinical parameters of the RA patients in 2012 and 2014. Multivariate regression analysis was performed after adjustment by age, sex, body mass index (BMI), steroid use, anti-osteoporosis medication. We set the annualised BMD change as an outcome variable and allotted the other parameters as explanatory variables by a stepwise procedure.

**Results:** The average values (minimum-maximum value) of age and BMI were 63.3 (32–85) years and 22.1 (12.3–30.0), respectively. Female patients and steroid users accounted for 91.1%, and 41.0%, respectively. Coincidentally, anti-osteoporosis drug-user also reached 41.0%. User of biological accounted for 30.8%. The averages of disease activity score (DAS) 28-erythrocyte sedimentation rate, Health Assessment Questionnaire was 2.6 (0.1–5.9) and 0.8 (0–2.9), respectively. The average of total Sharp score was 122.6 (0–443). Laboratory data showed serum tartrate-resistant acid phosphatase (TRACP)–5b, serum homocysteine, serum undercarboxylated osteocalcin, bone specific alkaline phosphatase, and urinary pentosidine were 320.0 (68–877) mU/dl, 9.7 (3.2–28) nmol/ml, 4.8 (0–23) ng/mL, 15.6 (5.8–43.6) µg/L, and 50.0 (11.5–561) pg/ml, respectively. Next, we describe by the result of multiple regression analysis. The levels of serum homocysteine ( $\beta=-0.19$ ; 95%CI: 0.24 to 1.75; p=0.01) and anti-osteoporosis drug ( $\beta=-0.19$ ; 95%CI: -0.26 to -0.04; p=0.009) were consistently significant predictive variables of annualised BMD change of the lumbar-spine. On the other hand, serum TRACP-5b ( $\beta=-0.28$ ; 95%CI: -0.005 to -0.001; p=0.002) was significant predictive one for the distal forearm.

**Conclusions:** Anti-osteoporosis medication may be particularly important for lumbar spine BMD for RA patients, regardless of steroid-use. Specific biomarkers would be useful such as homocysteine as lumbar spine BMD and TRACP-5b as



the forearm BMD. These findings would be helpful for osteoporosis management in RA patients.

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AB1014

#### EPIDEMIOLOGICAL FEATURES OF PERIPHERAL FRAGILITY FRACTURES IN WOMEN IN REPUBLIC OF MOLDOVA

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**Background:** Osteoporosis is a disease which is frequently asymptomatic until fragility fractures occur. The study of risk factors in osteoporosis is continuously developing, considering that there is a tremendous geographic variety in osteoporosis occurrence. We present the results of an epidemiological study of fragility fracture cases in Republic of Moldova, trying to underlie differences in fragility fracture epidemiology, based on residence region, and possibly lifestyle factors, in a female population.

**Objectives:** The purpose of the study was to determine the incidence and prevalence of fragility fractures in women, with comparison of epidemiological indexes between urban and rural areas in Republic of Moldova.

**Methods:** Approximately 6% of the state population was included in the study. Data regarding peripheral fragility fracture cases was collected from all specialised and primary medical institutions from the defined area. Fragility fractures of proximal humerus, distal forearm, proximal femur and distal calf, in women aged over 40 years old were collected. Using population statistics provided by the National Bureau of Statistics, epidemiological indexes regarding fracture incidence and prevalence were derived, with further comparison of derived epidemiological indexes for urban and rural areas, as well as separate epidemiological indexes for the four fracture regions.

**Results:** A general incidence of 1033.4 peripheral fragility fractures per 1 00 000 female population >40 years was determined, with a significantly higher incidence in urban areas (1216.7 vs 980.1,  $p<0.05$ ). The incidence of proximal humerus fracture was 149 per 1 00 000 female population >40 years, with a small, but significantly higher incidence in urban areas (159.5 vs 145.9,  $p<0.05$ ). The incidence of distal forearm fractures was 393.4 per 1 00 000 population >40 years, significantly higher in urban areas (528.5 vs 354.1,  $p<0.05$ ). The incidence of proximal femur fracture was 208.5 per 1 00 000 population >40 years, significantly higher in urban areas (227.9 vs 202.9,  $p<0.05$ ). The incidence of distal calf fractures was 282.5 per 1 00 000 population >40 years, with a small, but significantly higher incidence in urban areas (300.7 vs 277.2,  $p<0.05$ ).

**Conclusions:** There was an overall higher incidence of fragility fractures in the urban female population compared to the rural one, with a similar relationship in all four fracture groups. The association between urban residence and increased incidence of fragility fractures in women, could be attributed to a less active physical lifestyle (known risk factor in osteoporosis) in urban areas. Distal forearm fractures showed a greater prevalence both in urban and in rural areas, compared to other fracture types. Moreover, the incidence difference between urban and rural areas was most prevalent in the distal forearm fracture group. The latter observation was not determined in a similar study in men, in the same population and period of time.

**Disclosure of Interest:** None declared

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AB1015

#### BONE MINERAL DENSITY IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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**Background:** Chronic kidney disease (CKD) is commonly associated with disorders of mineral and bone metabolism.<sup>1</sup> However, the relationship between renal function and bone mineral density (BMD) is controversial.<sup>2-3</sup>

**Objectives:** We aimed the relationship between markers of renal function and BMD in patients with CKD.

**Methods:** 95 patients both sexes with CKD aged 55.49±10.07 years were studied. Control group included 84 healthy subjects the same age. Standard laboratory analyses were performed in all patients. Renal function was assessed by the estimated glomerular filtration rate (eGFR), which was calculated using an equation based on creatinine (eGFRcr) and cystatin C (eGFRcys\_c). Osteoporosis was defined as a femoral neck BMD T-score below -2.5.

**Results:** The serum cystatin C level was negatively correlated with BMD and T-score right and left femoral neck ( $p<0.05$ ), but not with BMD T-score lumbar spine. The level of creatinine was negatively correlated only with BMD and T-score right femoral neck ( $r=-0.653$ ,  $p<0.05$ ). Higher cystatin C levels were associated with a higher prevalence of osteoporosis in CKD patients (OR 3.54; 95% CI 1.63-7.85;  $p=0.002$ ). In logistic regression analysis, after adjusting for age, body mass index, calcium, only cystatin C showed a negative correlation with femoral BMD. In addition, the eGFRcys\_c showed a stronger positive correlation with femoral BMD than the eGFRcr.

**Conclusions:** Our findings suggest that serum cystatin C level could be a marker for femoral BMD and might help identify patients with osteoporosis who are susceptible to fractures.

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AB1016

#### OSSEOINTEGRATED IMPLANTS FOR LOWER LIMB AMPUTEES: EVALUATION OF BONE MINERAL DENSITY

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**Background:** The use of dual-energy X-ray absorptiometry (DXA) is a standard clinical procedure for the evaluation of bone mineral density (BMD). Amputee patients are known to have decreased BMD and an increased risk of osteoporosis in the affected proximal femur and hip region. The major cause of these issues in these patients is the absence adequate loading leading to bone resorption in accordance to Wolff's law.

**Objectives:** In this paper, we present a prospective study reporting changes in BMD among amputees who received osseointegrated implants to determine if the loading through the Osseointegrated implant can overcome the bone resorption issues.

**Methods:** This is a prospective study of 33 patients, consisting of 24 males and 9 females, aged 22-77 (mean=51.0±2.0) years with one and two-year follow-up. Selection criteria included age over 18 years, unilateral amputees with socket-related problems. All patients received osseointegrated implants press-fitted into the amputated limb. BMD was assessed using DXA in the femoral neck (operative and contralateral) and lumbar spine (L2-L4) regions, and corresponding Z-scores were generated. DXA scans were taken preoperatively as well as one-year and two-years following osseointegration surgery.

**Results:** Mean BMD and Z-scores of spine, and operative and contralateral sides were generated for all patients. Dependent t-tests were used to test for significant differences ( $p<0.05$ ) preoperative, one-year, and two-years for mean changes in BMD and Z-Scores following surgery. Analysis of the BMD and Z-scores indicated that patients showed improvements at one-year post-surgery.

**Conclusions:** These results suggest that osseointegrated implants are effective at encouraging bone growth and restoring BMD levels for amputees within a short period of time post-surgery. Osseointegrated implants therefore have the potential to address stress distribution issues associated with socket prostheses and restore the normal bone loading regime in lower limb amputees.

**Disclosure of Interest:** None declared

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**AB1017 VERTEBRAL FRACTURES ARE LIKELY TO OCCUR IN LUMBAR VERTEBRA IN PATIENTS WITH OSTEOPOROSIS AND EVEN IN OSTEOPENIA**

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**Background:** Osteoporosis is a common disease, which can lead to fracture. New diagnosis includes fracture of the vertebral bodies and hips, T-scores of bone mineral density (BMD) less than 2.5 or osteopenia together with humeral, forearm or the pelvis fracture. Vertebral assessment should be considered in some conditions.<sup>1</sup>

**Objectives:** Our study was to investigate the condition of osteoporosis in patients who underwent bone mineral density in our hospital and fracture status according to lateral X-ray of cervical, thoracic and lumbar vertebra.

**Methods:** Patients were enrolled from September to December in 2017 in the Third Affiliated Hospital of Sun Yat-sen University. Demographic information, past medical history, and clinical information were collected by two rheumatologists. Bone mineral density measured by Dual Energy X-ray Absorptiometry was performed based on clinical needs. Patients with osteoporosis or osteopenia were asked to have X-ray scan of cervical, thoracic and lumbar vertebra. The Statistical Package for Social Sciences (SPSS) software version 21 was used for all data management and analysis.

**Results:** Of all the 210 patients, 60 (28.6%) were male patients. 59.5% of female patients were in post-menopause stage. Mean age was 57.60±13.17 years. 124 patients were asked to perform BMD by the rheumatologists. 20 patients did the test after they saw an endocrinologist. 40 patients did the test after they saw an orthopedist. 102 patients had T-scores less than 2.5. 61 patients had osteopenia according to BMD. 22 patients had fracture according to past history or X-ray scans' findings. 10 patients had multiple fractures. The most frequent fractures were located in L1 (nine patients) and L2 (four patients). The other parts included L3, L5, C7, T12, T6, T8, and T9. Two patients had ankle or humeral fractures before because of injury. Vertebral fractures were founded in 5 (8.2%) of the patients with T-scores of -2.5 to -1 during this study.

**Conclusions:** Lateral X-ray scans of the vertebra can detect vertebral fractures in patients with osteopenia according to BMD scores, even in patients less than 50-year-old. Osteoporosis could be underestimated without measurement of the vertebra. The most frequent vertebra fracture happens in L1.

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crystal diseases, metabolic bone diseases and bone diseases other than osteoporosis

**AB1018 INTRAVENOUS NERIDRONATE IN THE TREATMENT OF BONE MARROW OEDEMA SYNDROME: EFFICACY AND SAFETY OF TWO DIFFERENT TREATMENT SCHEDULES**

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**Background:** Bone Marrow Oedema Syndrome (BMES) is a severely disabling pain syndrome without a definite treatment well established.

**Objectives:** The aim of this monocentric prospective trial was to test the efficacy and the safety of the amino-bisphosphonate neridronate in patients with BMES administered in two different schedules.

**Methods:** one hundred seventy-three patients with BMES at various joints were consecutively assigned to I.V. infusion of 100 mg neridronate given four times over 10 days (Group A) or alternatively to I.V. infusion of 100 mg every 21 days over 63 days (Group B). At baseline (T0) and after 90 days from the first infusion we performed a MRI (T2). We assessed a 0–100 mm pain VAS in each patient at T0, at the day of the last infusion (T1: day 10 for group A and day 63 for group B)

and at T2. Primary outcome was to evaluate the MRI changes, secondary endpoint was the VAS change.

**Results:** we observed a significant improvement in MRI with the resolution of bone marrow oedema present at T0 ( $p < 0.01$ ), without a significant difference between Group A and Group B. Visual analogue scale (VAS) score decreased significantly during the study in both groups ( $p < 0.05$ ) without a significant difference between the two treatment groups ( $p > 0.1$ ).

**Conclusions:** In patients with BMES, the infusions of neridronate 100 mg every 21 days over 3 months or alternately every 3 days over 10 days are associated with clinically relevant and persistent benefits without significant differences between the two treatment-schedules. These results provide conclusive evidence that the use of bisphosphonates, at appropriate doses, is the treatment of choice BMES

**Disclosure of Interest:** None declared

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**AB1019 PATIENTS COMPLIANCE TO CHRONIC GOUT THERAPY WHEN ADMINISTERED BY DIFFERENT MEDICAL PROFESSIONALS**

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**Background:** in everyday practice chronic gout patients are frequently consulted by general practitioners, surgeons, cardiologists and other specialists. In general, chronic gout patients have been reported to be quite incompliant, but it remains unclear whether low compliance depends on the speciality of the prescribing physician.<sup>1</sup>

**Objectives:** to compare the clinical course of gout in patients consulted by different specialists and to identify factors of low patients' compliance in Russia.

**Methods:** cross-sectional study included 56 chronic gout patients aged 31 to 82 (median 54 years). Average gout symptoms duration was 6.8 years, average attacks frequency was 6.4 per year. Tofi were present in 21.4% of patients. All subjects were divided into three groups: Group 1 consisted of treatment naive patients at primary rheumatologist visit, Group 2 and Group 3 included patients who had previously been treated. Group 2 subjects were visiting both non-rheumatologists and rheumatologists. Group 3 were managed by rheumatologists strictly according to the EULAR evidence-based recommendations.<sup>2</sup>

**Results:** Group 1 primary consulted rheumatologists at the age of 47.3±14.5, Group 2 patients were assessed at the age of 58.4±15.2, and Group 3 were aged 51.2±13.5. Disease symptoms duration was maximal in Group 2 (10.6±10.6 years) while 5 years in Groups 1 and Group 3. Flares frequency was the lowest in Group 3 (2.2±1.8 per year), while in Group 2 it was extremely high – (10.58±10.56 per year). The incidence of tofi and urolithiasis was lowest in the Group 3 whereas every third treatment naive patient had tophi or/and urolithiasis. To relieve gouty arthritis vast majority of patients used NSAIDs, though at 50% strength of the recommended dose. Only 9%–14% of flares were controlled by colchicine in Groups 2 and 3. Colchicine prevention of flares was prescribed only in 45% of cases by rheumatologists. The most frequent urate-lowering therapy (ULT) was allopurinol, it was taken only by 63% of patients of the third group and 35.7% in the second group. While patients in the third group took the drug daily, the other patients did not follow the administration scheme. Serum creatinine level was the lowest (87.5 ±16.8 μmol/L) in Group 3, being the highest in treatment of naïve patients (102.7 ±30.0 μmol/L). Serum uric acid target level was achieved only in the compliant Group 3 patients (343 μmol/L), while Group 2 levels varied between 462–546 μmol/L, being the highest (625 μmol/L) in treatment naïve Group 1.

Low compliance risk factors were: age under 45, absence of comorbidity and long term multiple drugs consumption.

**Conclusions:** chronic gout patients' compliance and quality of patient management can be assessed as alarmingly low. Rheumatologists adhering to EULAR evidence-based approach to gout management can actually achieve recommended treatment targets. Both general practitioners and other specialists are in need of consistent educational program on gout management. Younger and comorbidity-free gout patients should be encouraged to follow attending physician's recommendations.

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**Disclosure of Interest:** None declared

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**AB1020** **PILOT ASSESSMENT OF CURRENT CHRONIC GOUT TREATMENT IN RUSSIA**

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**Background:** In 2016 EULAR evidence based clinical guidelines on Gout treatment have been updated.<sup>1</sup>

**Objectives:** to assess current daily practice physicians' approach to management of chronic gout patients

**Methods:** a cross-sectional anonymous survey had been offered to hospital and outpatient departments physicians dealing with gout patients resulting in 97 backfeed replies yielded. This publication deals with chronic gout treatment practice.

**Results:** all survey participants were divided into 3 groups. Group 1 consisted of 18 rheumatologists (professional experience median 19.6 years, range 1 to 43), group 2 included 60 general practitioners (GP, professional experience 27; 4–47), group 3 included other specialists (cardiologists, surgeons etc.) who reported frequent contacts with gout patients (professional experience 16.5; 1–44). Rheumatologists reported to contact median 15 (range 2–40) gouty subjects per month, while group 2 reported to see 3<sup>1–10</sup> and group 3 consults 4<sup>1–12</sup> patients per month. All rheumatologists and 45 GPs reported initiation of allopurinol or febuxostat after gouty arthritis resolution, while 11 general practitioners did not start antihyperuricemic drugs in subjects with kidney and/or cardiovascular comorbidities. In Group 3 only 6 responders had experience of antihyperuricemic drugs administration, but 3 of them reported allopurinol initiation during gout flare. Only 2 rheumatologists and 2 GPs were aware of gout flare low dose colchicin prophylaxis during allopurinol dose adjustment. Administration of maximal allopurinol daily maintenance doses over 300 mg was reported only by 7 rheumatologists and 7 GPs. Other specialists did not have any personal experience of allopurinol dose adjustment. By responders' assessment every 2–3 patient continues to experience gout flares in spite of prescribed treatment

**Conclusions:** intensive educational intervention is urgently required to change current practice of chronic gout treatment in Russia.

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**AB1021** **ANEURYSMAL BONE CYSTS OF THE SPINE: 4 CASE REPORTS AND REVIEW OF LITERATURE**

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**Background:** Aneurysmal bone cysts (ABC) are rare, benign, highly vascular pseudotumors of unknown cause. It most often affects individuals during their second decade of life.

**Objectives:** Our goal was to document the clinical characteristics, diagnostic modalities and treatment results of ABCs.

**Methods:** We reviewed our institution's database over a period of 15 years to identify patients diagnosed with aneurysmal bone cysts of the spine. Four patients underwent surgery in our department (2 men and 2 women). For those four patients, we tabulated the clinical characteristics, location, diagnostic modalities and treatment.

**Results:** The clinical manifestations were gait disturbance in 2 patients and leg-pain in the other two. The tumour occurred in the dorsal spine in 2 cases and in the lumbar spine in the other two. All patients underwent surgical resection with total removal in only 2 patients. Postoperatively, clinical signs improved in all patients. Only one case presented tumour recurrence requiring second intervention and instrumentation.

ABCs constitute approximately 1.5% of spinal bone tumours. They usually affect the posterior elements of the spine. MRI is the most useful modality for preoperative planning. It also helps to evaluate the fluidfluid level, which is characteristic for ABC on MRI. The differential diagnosis is mainly with giant cell tumours and osteoblastomas. The primary option for treatment is surgery. Instrumentation is sometimes necessary because of the increased risk of postoperative instability, especially in cervical spine surgery. The recurrence rate is 20% to 30% in case of incomplete resection.

**Conclusions:** ABCs are benign lesions. Surgical resection en bloc has the lowest recurrence rate. Instrumentation is sometimes necessary because of the increased risk of postoperative instability.

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**AB1022** **EFFICACY AND TOLERANCE OF SODIUM THIOSULFATE INJECTION IN CALCIFIC TENDINOPATHY OF THE ROTATOR CUFF**

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**Background:** Calcific tendinitis of the rotator cuff is one of the most common causes of shoulder pain. Ultrasound guided percutaneous lavage of calcific tendinopathy (UGPL) is indicated when conservative treatments have failed. It has been shown that dense calcifications are associated with a higher risk of treatment failure. Sodium thiosulfate (STS) has recently been used with success in the treatment of tumoral calcinosis. We hypothesised that STS lavage could be of interest in the treatment of dense calcification of the rotator cuff.

**Objectives:** To evaluate the tolerance and efficacy of sodium thiosulfate lavage in the treatment of calcific tendinitis

**Methods:** This was a prospective phase II open label study. We included only patients with a type A calcification according to the Molé classification. Patients were treated with a US-guided single needle technic. When backflow of calcific material could be identified in the syringe, lavage of the deposit was performed using STS 25% until the backflow becomes clear followed by the injection of 1 mL (250 mg) of STS inside the calcific deposit. Finally, 1.5 mL of cortivazol was injected in the subacromial bursa. All patients had follow-up visits at 1 week, 1 month and 3 months after intervention. At each time point, VAS pain at rest and during activities was recorded and US and X-ray were performed. Our primary outcome was the percentage of patients with more than 50% of decrease of the calcification size at 1 month. Based on our experience and on the literature, we expected that more than 60% of the patients should have more than 50% of decrease in their calcification for the results to be significant.

**Results:** A total of 17 patients were included. Mean age was 50±11 years. There were 9 female (52.9%). Baseline VAS at rest and during daily activities was a mean 40.2±25.9 and 65.5±21.6 (27–91) respectively. Calcification involved the supraspinatus in 12 cases (70.6%) and the infraspinatus in 5 cases (29.4%). Mean surface on radiography was 80.7 mm<sup>2</sup> ±52.4 and the calcification longest size was 18.8±7.1 mm. All patients underwent the entire procedure with no adverse event apart of a mild and transient vasovagal reaction. Calcium backflow could be obtained in 15 patients (88.2%) with a small amount of calcium in 8 cases (53.3%) and a large quantity in 7 cases (46.7%). We found that 5 patients (30%) had more than 50% decrease of their calcific deposit at 1 month and 8 (47%) patients at 3 months. VAS pain during activities and at rest decreased significantly from 65±22 and 40.2±26 at baseline to 37.8±31 and 24.1±24 at 3 month respectively (p=0.0004; p=0.001)

**Conclusions:** Overall, our study is the first to evaluate the tolerance and efficacy of sodium thiosulfate for the treatment of the calcifications of the rotator cuff. We could not demonstrate a significant effect of one STS lavage and injection in patients with dense calcification. This treatment was well tolerated with no side effect occurring during the procedure and the follow-up. New studies using larger volume and repeated injections of STS will be needed to definitely conclude on the interest of this molecule in the treatment of calcific tendinopathies.

**Disclosure of Interest:** None declared

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**AB1023** **ENHANCED RENAL TRANSPORTER ACTIVITIES OF OAT1 AND OAT3 BY KEISHIBUKURYOGAN (K-06) AND IN VIVO URIC ACID MODULATING EFFECT AT POTASSIUM OXONATE-INDUCED MOUSE SETTING**

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**Background:** Studies on renal solute carrier transporters have made the renal pathophysiology be in progress towards more mechanistic and the knowledge on renal drugs including drug-drug interaction be more evidentiary. Among the evidence, uricosuric phenomenon has been known that rodent experimental model is also useful for predicting human uricosuria.

**Objectives:** The aim of this study was to assess the substrate uptake at the over-expression of renal transporters, OAT1, OAT3 and URAT1 at kidney proximal tubular cell lines with or without a commercial herbal medicine, Keishibukuryogan (K-06) and to further measure serum and urinary uric acid concentrations in the setting of potassium oxonate (PO)-induced ICR mouse model with or without K-06.

**Methods:** The transporter-expressed HEK293-OAT1 and HEK293-OAT3 cells were seeded on BD poly-d-lysine microplates to uptake the [<sup>3</sup>H] estrone sulfate for 5 min in absence or presence of K-06. URAT1 was overexpressed using Xenopus oocytes being injected with *in vitro*-copied RNA of URAT1, and then to measure the uptake of [<sup>14</sup>C] uric acid with/without K-06. Total radioactivity was measured using a liquid scintillation counter. Serum and urinary uric acid was measured in PO ICR mice after three-day intake of K-06. They were assigned by 4 per each group; 1) control group, 2) PO-induced group, 3) PO-induced with allopurinol 50 mg/kg/day intake group and 4) PO-induced with allopurinol plus K-06 300 mg/kg/day intake group.

**Results:** To determine the kinetic parameters of concentration-dependent uptake of overexpressed OAT1 and OAT3 transporters in HEK293 cells, the K-06 inhibitory parameters on OAT1 and OAT3 were presented with the IC<sub>50</sub> values of 49.3 and 31.5 µg/mL, respectively. The K-06 inhibited URAT1 with IC<sub>50</sub> of 59.3 µg/mL. The K-06 (300 mg/kg) reduced serum levels of uric acid approximately 30% compared to that of PO-control group (p=0.039) and K-06 showed the slight elevation of urinary uric acid by 12% compared to that of PO-control group with no statistical significance.

**Conclusions:** The present findings demonstrated that the K-06 modulated basolateral and apical renal transporters and the K-06 showed the slight increased uric acid excretion and the uric acid lowering effect in experimental mouse setting.

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**Disclosure of Interest:** None declared

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**AB1024** **RISK OF DRUG INDUCED LIVER INJURY FROM NSAIDS IN PATIENTS WITH GOUT**

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**Background:** Drug Induced Liver Injury (DILI) in patients under nonsteroidal anti-inflammatory drugs (NSAIDs) is more frequently presented by hepatocellular damage when serum alanine aminotransferase (ALT) level exceeds 2 times (or more) the upper limits of norms.<sup>1</sup> The value of minimal hypertransaminasemia (MHTE) (when serum ALT exceeds the upper limit of normal up to twice) is still not clear today.

**Objectives:** To define the terms of DILI development and the value of MHTE in patients with gouty arthritis (GA) under NSAIDs.

**Methods:** 189 patients (25.6%) of 738 with GA<sup>ACR, 1977</sup> were included in our retrospective study. At the onset of gout attack, all patients had normal basal serum ALT, which elevated after starting NSAIDs therapy. Pre-existing liver impairment was not registered. Patients were divided into 2 groups according to the changes in serum ALT after NSAIDs treatment: patients with MHTE (n=101) and those with

DILI (n=88). The mean age of 55<sup>49–60</sup> years and 54<sup>44–59.5</sup> years as well as the sex distribution (men 90,1% and 93,3%, respectively) were compatible in both the groups (p<0,05). In DILI group, elevated serum ALT exceeded 2–3 times the upper norms in 81,8% (n=72) of patients; 3–5 times in 14,8% (n=5); more than 5 times in 3,4% (n=3) with the mean serum ALT being of 89<sup>75–108.5</sup> U/L. In MHTE group, serum ALT exceeded the upper norms by more than 50% in 50,5% (n=51) of cases. After NSAIDs therapy, the mean serum ALT of 51<sup>(47–57)</sup>U/L was revealed.

**Results:** The mean duration of NSAIDs therapy in the groups made 8<sup>5–10</sup> days in MHTE group and 10<sup>6–14</sup> days in DILI group. Statistically significant difference (U=3236, p<0,001) was revealed between the groups when comparing the duration of NSAIDs treatment. In addition, in DILI group, 97,7% of patients received NSAIDs in high doses (χ<sup>2</sup>=19,4; p<0,001) during all period of treatment. ROC analysis showed that the probability of DILI development decreased in patients with GA taking NSAIDs in high doses during less than 11 days (AUC=0,64±0,04, p=0,010, S=47,7%, Sp=82,2%, OR=4,21, 95% CI – 3,38–5,24).

**Conclusions:** 25,6% of patients with GA have demonstrated elevated serum ALT after NSAIDs therapy: MHTE developed in 13,7% of cases, DILI in 11,9%. Our study showed that MHTE developed in the period less than 11 days of high dose NSAIDs treatment with DILI being likely to occur during more prolonged treatment. MHTE group may be considered as a risk group for DILI development.

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**AB1025** **MONOSODIUM URATE CRYSTAL FORMATIONS FROM TOPHI IN SYNOVIAL FLUID**

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**Background:** At the joints MSU crystals form primarily at the cartilage surface; on occasions also tophi form at joint margins. Most often monosodium urate (MSU) crystals at the synovial fluid (SF) are found isolated. In tophi MSU crystals often show as spherulitic formations, fanning away from a central point<sup>1</sup> (Figure 1, 200x, polarised light). We have detected in synovial fluid formations of MSU crystals with an organisation indicative that they formed in tophi, draining later to the fluid. The formations also help to understand how crystals formed in tophi.

**Methods:** Our photographic archive of SF has been reviewed.

**Results:** Two types of formations are found. A) A spherulitic formation where the crystals fan radially as in the segment of a sphere (Figure, middle, 600x, polarised light). B) Paired crystals bound longitudinally to each other (Figure, right, 600x, phase contrast).



**Abstract AB1025 – Figure 1**

**Conclusions:** At tophi spherulitic crystal formations are usual (figure 1) in which MSU crystals radiate as in a fan. A) Pieces of these same formations, seen as the segment of a sphere, are occasionally seen in SF (Figure 2), usually containing a large number of crystals and suggesting that they have drained from a tophus. Likely to build these formations, the initial crystals served as a template on which successive crystals formed by epitaxia, – the crystal formation method of least energy requirement –, explaining the rapid growth that tophi can present. Their unimpeded migration to the joint cavity suggest that they formed freely and unconnected to any organic structure within the tophus. B) In SF containing large numbers of crystals, paired crystals – two crystals lying side by side and usually of similar length and width – are also found. Their paired position likely indicates that one served as template to the other, or that they grew together sharing a crystal net – twin crystals. In all, these MSU crystal formations appear to indicate that besides the crystals formed in the surface of joint cartilages, the content of tophi can drain into the joint fluid, also contributing to the presence of crystals in it; the

periarticular tophi frequently seen in ultrasound appear as the likely source for these formations.

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**Disclosure of Interest:** None declared

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AB1026

#### CLINICAL CHARACTERISTICS AND RISK FACTORS FOR GOUT ATTACK DURING THE POSTSURGICAL PERIOD

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**Objectives:** To evaluate the clinical features and risk factors for gout attack during the postsurgical period in patients with gout.

**Methods:** Seventy patients who had histories of gout and had been consulted to rheumatologic clinic before surgery under general anaesthesia at a single tertiary hospital were included. Clinical characteristics of patients who developed postsurgical gout attack were compared with patients who did not developed gout attack.

**Results:** Among 70 patients, 31 (44.3%) patients developed gout attack during postsurgical period. Mean time of gout attack after surgery was 3.7±4.9 days. Most of attacks involved lower extremity joints (83.9%) and tended to monoarticular involvement (61.3%). Knee joint (26%) and foot except 1st metatarsophalangeal (MTP) joint (26%) were more frequently involved than 1st MTP joint (13%). Uric acid levels before surgery (OR 1.46, 95% CI 1.13–1.88, p=0.004) and amount of uric acid changes between before and after surgery (OR 1.62, 95% CI 1.21–2.18, p=0.001) were risk factors for postsurgical gout attack. Taking medications for gout including uric acid lowering agents and/or colchicine reduced the risk of postsurgical gout attack (OR 0.11, 95% CI 0.04–0.32, p<0.001). Operation time, amount of blood loss during surgery, amount of fluid administration during surgery, and surgery site were not significantly associated with postsurgical gout attack.

**Conclusions:** Adequate uric acid control and taking medications for gout could prevent the postsurgical gout attack.

**Disclosure of Interest:** None declared

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AB1027

#### THE PREDICTIVE VALUE OF CYSTATIN C FOR GOUTY NEPHROPATHY

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**Background:** Gout is the most common cause of an inflammatory arthritis in men elder than 30 years, varies up to 1,7% of the total morbidity. One of the most common complication of chronic gout is gouty nephropathy with the morphological signs of kidney damage, even in the early stages.<sup>1</sup>

It's well known, that urine albumin and glomerular filtration rate (GFR) are the generally accepted markers of nephropathy. But, recent data has shown, that the informative and obtainable new biomarkers of the kidney function are still needed. Thus, evaluation of the pathogenic role in the renal failure of cystatin C could be a "clue". The dozen trials have shown that an increasing of ranges cystatin C in serum could be tested at the stage of subclinical reduction of GFR with normal level of creatinine.<sup>2;3</sup>

**Objectives:** To determine the serum ranges of cystatin C and creatinine as the markers of nephropathy in patients with gout.

**Methods:** The main group was the 80 males with primary gout (average age – 53,4±8,2 years), with the disease duration from 3 up to 25 years. The second group – 20 healthy men (49,5±4,5). We determined the concentration of serum uric acid, serum cystatin C, creatinine, calculate the GFR using CKD-epi formula. For urine albumin evaluation we used the albumin/creatinine ratio in the morning urine portion.

**Results:** e determined that the main group identified by more significant violations of renal function. In the main group was found the statistically significant increase of the serum creatinine (97±18 μmol/l) and decrease of GFR (73<sup>64; 94</sup> ml/min<sup>2</sup>.

The serum cystatin C concentration in the main group was (1,7<sup>1,4; 1,9</sup> mg/l which was the significantly larger than in the comparison group (0,8 [0,7; 0,92] mg/l, p<0,001).

The albumin/creatinine ratio was statistically higher in the main group (26<sup>14; 56</sup> mg/g than in comparison (0,8 [0,7; 0,92] mg/l, p<0001). Also the patients with gout are characterised by the larger concentration of uric acid in the serum (530±74) μmol/l than healthy men (347±75) μmol/l and negative correlation between uric

acid level and GFR (r=-0,4, p<0,05) which explain the increase of uric acid concentration in the serum.

We determined the correlation between level of urine albumin and creatinine concentration (r=+0,5, p<0,05) in the main group, but concentration between albuminuria and cystatin C was stronger (r=+0,6, p<0,05). We detected that cystatin C level had a greater accuracy for the diagnosis of albuminuria than creatinine according to the ROC-analysis. These facts show that serum concentration of cystatin C more closely connected with the renal function than creatinine.

**Conclusions:** 1. The increase of serum cystatin C level can be identified before the clinical manifestation of renal dysfunction while the serum creatinine remain relatively normal.

2. Serum ranges of cystatin C more closely correlate with elevation of urine albumin than creatinine.

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AB1028

#### ACTH VS BETAMETHASONE FOR THE TREATMENT OF ACUTE GOUT IN HOSPITALISED PATIENTS

#### AN OPEN LABEL, COMPARATIVE STUDY

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**Background:** The management of gout can be problematic in the hospital setting; hospitalised patients usually have significant comorbidities and receive multiple medications which leads to a high frequency of contraindications to established gout therapies. We have previously shown the ACTH is a safe and fast acting therapeutic option for acute gout in hospitalised patients in a large scale retrospective study.<sup>1</sup>

**Objectives:** To directly compare the efficacy of ACTH vs betamethasone for the treatment of acute gout in hospitalised patients in a prospective manner.

**Methods:** Hospitalised patients with acute gout, fulfilling the ACR criteria, were treated with an IM injection of either 100 IU of ACTH (Synachten Depot) or 6 mg of betamethasone (Celestone Chronodose-the most widely use IM steroid formulation in our country) on an alternate 1/1 basis. Clinical efficacy was assessed at 24, 48, 72 hour and 5 days as follows: a) Intensity of pain using a Visual Analogue Scale (VAS 0–10), b) physician global assessment (0–10) and c) swelling, redness and warmth (0–3 scale). Pain VAS was also self reported by the patient at 6 and 12 hour. Comorbidities representing contraindications to established gout therapies were recorded. Primary outcome of the study was the change in pain VAS at 24 and 48 hour. Secondary outcomes were changes in physician global assessment and changes in objective signs of inflammation.

**Results:** This is a 6 month interim analysis of an ongoing investigator initiated clinical study. Twelve patients (8 male) with a mean ±SD of 66.9±12.3 years were recruited and treated with ACTH or betamethasone on an alternate basis (6 in each treatment group). In most cases (n=11) the attack was monoarticular. The majority of patients had multiple comorbidities with the commonest being hypertension (9/12). Both treatments were effective. ACTH led to a significant decline in pain VAS at 24 hour compared to baseline (mean ±SEM: 2.33±1.21 vs 7.66 ±0.81 respectively, p=0.0002) and at 48 hour (1.40±1.14, p=0.0011 compared to baseline). Betamethasone was also effective with an improvement in pain VAS at 24 hour compared to baseline (mean ±SEM: 1.83±0.98 vs 5.33±2.16 respectively, p=0.0024) and at 48 hour (0.75±0.95, p=0.02 compared to baseline). However, direct comparison between treatment arms showed that ACTH treated patients exhibited a higher change in pain VAS at 24 hour compared to betamethasone treated patients (mean ±SEM: 5.5±0.5 vs 3.5±0.61 respectively, p=0.03). At the 48 hour time point ACTH treated patients still showed a higher change in pain VAS (mean ±SEM: 6.4±0.6 vs 4±0.91 respectively, p=0.056). A trend favouring ACTH was already evident at the 12 hour time point; the change in pain VAS was 4±1.54 vs 3.1±1.47 for ACTH vs betamethasone, respectively, p=ns). No changes in physician global assessment and objective signs of

inflammation was found at 24 and 48 hour between treatment groups. Treatment was well tolerated in both groups.

**Conclusions:** Both steroids and ACTH are effective in the treatment of gout in hospitalised patients but ACTH is faster acting. ACTH may be an attractive therapeutic choice in patients with multiple comorbidities that cannot receive standard treatment.

#### REFERENCES:

- [1] Daoussis et al, Joint Bone Spine, 2013

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AB1029

#### ALLOPURINOL AND CARDIOVASCULAR OUTCOMES IN PATIENTS WITH ISCHAEMIC HEART DISEASE (ALL-HEART) STUDY: BASELINE CHARACTERISTICS OF THE RANDOMISED PATIENT POPULATION

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**Background:** Allopurinol is licensed for the prevention of gout. In recent years, several studies have suggested that allopurinol may have beneficial effects on cardiovascular parameters. The ALL-HEART study is a large outcome trial designed to investigate whether allopurinol improves cardiovascular outcomes in patients with ischaemic heart disease<sup>1</sup>. It is a multicentre, controlled, prospective, randomised, open-label, blinded endpoint trial of allopurinol (up to 600 mg daily) versus no treatment added to usual care in patients aged 60 and over with ischaemic heart disease. Patients are followed up by electronic record-linkage and annual questionnaires. Patient recruitment to the trial started in 2014 and completed in 2017 and follow-up is ongoing.

**Objectives:** To describe the baseline characteristics of the patients randomised into the ALL-HEART study.

**Methods:** The primary endpoint of the ALL-HEART study is the composite of non-fatal myocardial infarction, non-fatal stroke or cardiovascular death. Secondary outcomes include all-cause mortality, quality of life and cost-effectiveness of allopurinol. The study will end when 631 adjudicated primary outcomes have occurred.

**Results:** 5938 patients from the UK have been randomised into the ALL-HEART study. The mean age at randomisation was 72.1±6.8 (SD) years. 75.2% of participants are male. 56.5% are former smokers and 9.4% current smokers. Mean systolic blood pressure was 133±18 mmHg and mean diastolic blood pressure 72±11 mmHg. Mean body mass index was 28.9±5.3 kg/m<sup>2</sup>. The average duration of ischaemic heart disease was 11.5±7.9 years. 47.4% of participants had a history of previous myocardial infarction, 64.2% a history of angina, 56.4% a history of coronary revascularisation and 69.3% had other evidence of ischaemic heart disease. 57.6% had a history of hypertension. 3.9% had a history of previous cerebrovascular accident, 7.6% of peripheral arterial disease, 21.8% of diabetes mellitus, 8.9% of chronic obstructive pulmonary disease and 5.2% of heart failure.

**Conclusions:** This large ongoing trial will determine whether allopurinol improves major cardiovascular outcomes in patients with ischaemic heart disease.

#### REFERENCE:

- [1] Mackenzie IS, Ford I, Walker A, et al. Multicentre, prospective, randomised, open-label, blinded endpoint trial of the efficacy of allopurinol therapy in improving cardiovascular outcomes in patients with ischaemic heart disease: protocol of the ALL-HEART study. *BMJ Open* 2016;6:e13774. doi:10.1136/bmjopen-2016-013774.

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AB1030

#### FEBUXOSTAT VERSUS ALLOPURINOL STREAMLINED TRIAL (FAST): BASELINE CHARACTERISTICS OF THE RANDOMISED PATIENT POPULATION

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**Background:** The Febuxostat versus Allopurinol Streamlined Trial (FAST) is a prospective, randomised, open-label, blinded endpoint trial comparing the cardiovascular safety of allopurinol and febuxostat in patients with symptomatic hyperuricaemia.<sup>1</sup> The trial includes patients aged over 60 years who are taking chronic allopurinol therapy at baseline and have at least one additional cardiovascular risk factor. After up-titration on allopurinol to reach EULAR urate targets, patients are randomised to febuxostat or allopurinol then followed up for events. Patient recruitment to the trial completed in late 2017 and follow-up is ongoing.

**Objectives:** To describe the baseline characteristics of the patients randomised into the FAST study.

**Methods:** The primary endpoint of the FAST study is the composite of non-fatal myocardial infarction, non-fatal stroke or cardiovascular death. The primary analysis is a non-inferiority analysis with a non-inferiority upper limit for the hazard ratio for the primary outcome of 1.3.

**Results:** 6142 patients from UK, Denmark and Sweden have been randomised into the FAST study. The mean age at randomisation was 71.0±6.4 (SD) years. 85.3% of participants are male. 57.3% are former smokers and 7.9% current smokers. Mean systolic blood pressure was 138±18 mmHg and mean diastolic blood pressure 75±12 mmHg. Mean body mass index was 31.1±5.2 kg/m<sup>2</sup>. 10.7% of participants had a history of previous myocardial infarction, 5.0% a history of previous cerebrovascular accident and 4.8% a history of peripheral arterial disease. 22.5% had a history of diabetes mellitus and 4.6% a history of heart failure. 78.0% had a history of high blood pressure. 33.3% had a history of any cardiovascular disease (defined as history of myocardial infarction, cerebrovascular accident, transient ischaemic attack, acute coronary syndrome, coronary revascularisation, angina pectoris or heart failure). The mean baseline urate at study entry (screening) was 297±47 umol/L. The mean allopurinol dose being taken at study entry (screening) was 225±106 mg daily. 2206 patients (35.9%) had at least one up-titration of allopurinol dose prior to randomisation.

**Conclusions:** This ongoing European trial will report on the cardiovascular safety of febuxostat versus allopurinol in patients with symptomatic hyperuricaemia.

#### REFERENCE:

- [1] MacDonald TM, Ford I, Nuki G, Mackenzie IS, et al. Protocol of the Febuxostat versus Allopurinol Streamlined Trial (FAST): a large, prospective, randomised, open, blinded-endpoint study comparing the cardiovascular safety of allopurinol and febuxostat in the management of symptomatic hyperuricaemia. *BMJ Open* 2014;4:e005354. doi:10.1136/bmjopen-2014-005354

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AB1031

#### ANALYSIS OF MECHANISM OF TRANSIENT INCREASE IN PLASMA URATE LEVELS INDUCED BY FRUCTOSE IN RATS

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**Background:** Hyperuricemia induces gout and kidney stones and accelerates the progression of renal diseases. Hyperuricemia is a common multifactorial disorder having several environmental factors such as sex, diet, alcohol consumption, and obesity. The increasing prevalence of hyperuricemia in recent years is thought to be due to environmental factors, particularly diet. Based on the reported association between sugar-sweetened beverages and hyperuricemia in epidemiological studies, it has been hypothesised that fructose, the primary sweetener in sugar-sweetened beverages, directly increase plasma urate levels.

**Objectives:** The aim of this study was to investigate whether and how fructose induces an increase in plasma urate levels.



**Methods:** Urate in plasma and urine were measured after fructose, glucose, or water was administered to Sprague-Dawley rats at doses of 2.5 or 7.5 g/kg at a time. Intestinal closed loops were made using approximately 10 cm of ileum. Phosphate buffered saline was injected into each intestinal loop. After 4 hours, urate levels in the loops were measured.

**Results:** Plasma urate level was significantly increased within 15–30 min by oral administration of fructose, without an increase in urinary and intestinal urate excretion, and a decreasing tendency of urate clearance was observed. These actions were evident at a dose of 7.5 g/kg body weight. The absence of an increase in urinary and intestinal urate excretion indicated that an increase in urate production did not result in the increase in plasma urate level. In the meantime, a decrease in urate clearance was suggested to cause the increase in plasma urate level.

**Conclusions:** The present study demonstrated that oral intake of fructose induces an increase in plasma urate level within a short time and that a decrease in renal urate clearance could mainly work for that.

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AB1032

### HIGHER BODY FAT IS AN INDEPENDENT RISK FACTOR FOR METABOLIC SYNDROME IN GOUT

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**Background:** The development of gout is associated with obesity and metabolic syndrome (MS). Obesity is defined by body mass index (BMI). However, BMI has been challenged for the limitation of not distinguishing different comprising tissues of the body. Body composition (BC) has been frequently recommended to assess metabolic status and will eventually replace BMI as a more reliable measure.

**Objectives:** To investigate the characteristics of BC in gout patients and their significance with disease characteristics.

**Methods:** BC was assessed in 180 consecutive gout patients and 1,860 control subjects (white-collar employees in Zhangjiang Innopark of Shanghai) by bioelectric impedance analysis. Overfat was defined by body fat percentage (BF%) as  $\geq 25\%$  for men and  $\geq 35\%$  for women. Demographic and clinical data as well as comorbid diseases were collected simultaneously. For the significant differences in the proportion of gender and age between two groups, the age- and gender-matched control subjects were randomly selected with the ratio of 1:1 for further statistics.

**Results:** (1) Among 180 gout patients recruited, the mean age was  $42.5 \pm 15.5$  years, mean serum uric acid (sUA) was  $9.0 \pm 2.4$  mg/dl and 17.2% of patients presented tophi. The mean BMI was  $25.4 \pm 3.5$  kg/m<sup>2</sup> with 44.4% overweight and 25.6% obesity. The mean BF was  $26.2 \pm 6.6\%$  with 50.5% overfat. (2) Compared with control subjects, gout patients were characterized by higher BMI ( $25.4 \pm 3.5$  kg/m<sup>2</sup> vs.  $24.3 \pm 3.3$  kg/m<sup>2</sup>), fat mass ( $19.3 \pm 6.9$  kg vs.  $16.5 \pm 6.2$  kg), trunk fat mass ( $10.2 \pm 5.4$  kg vs.  $8.4 \pm 3.4$  kg), BF ( $26.2 \pm 6.6\%$  vs.  $22.4 \pm 6.2\%$ ), proportion of overfat ( $50.5\%$  vs.  $27.2\%$ ), but lower lean mass ( $53.0 \pm 7.7$  kg vs.  $55.6 \pm 7.7$  kg, all  $p < 0.05$ ). (3) Compared with normal fat patients ( $n=89$ ), gout patients with overfat ( $n=91$ ) presented higher duration of gout, the count of affected joints, flare times in the past year, family history and presence of tophi (all  $p < 0.05$ , table 1). Overfat gout patients also exhibited higher BMI, more obesity, hyper-low density lipoproteinemia, MS and fatty liver (all  $p < 0.05$ ). (4) There were 9 (17.3%) overfat gout patients in 53 normal weight patients who presented more hypercholesterolemia ( $55.6\%$  vs.  $13.3\%$ ), hyper-low density lipoproteinemia ( $55.6\%$  vs.  $17.8\%$ ) and fatty liver ( $77.8\%$  vs.  $35.6\%$ ) and less skeletal muscle mass index (SMMI,  $8.3 \pm 0.5$  kg/m<sup>2</sup> vs.  $9.7 \pm 0.7$  kg/m<sup>2</sup>) than those patients with normal fat and weight (all  $p < 0.05$ ). Meanwhile, there were 44 (34.9%) gout patients with normal fat among 126 overweight and obesity patients who had less MS ( $40.9\%$  vs.  $63.4\%$ ) and more SMMI ( $11.1 \pm 0.9$  kg/m<sup>2</sup> vs.  $10.6 \pm 1.1$  kg/m<sup>2</sup>) than overfat patients (both  $p < 0.05$ ). (5) Overfat was a risk factor for MS [OR 3.4 (1.8, 6.4),  $p < 0.001$ ] after adjusted by age and gender.

**Abstract AB1032 – Table 1.** Comparison of disease characteristics between gout patients in BF subgroups

Clinical characteristic	all gout patients (n=180)	over fat group (n=91)	normal fat group (n=89)	p
Male, n (%)	168 (93.3)	85 (93.4)	83 (93.3)	1.0
Age, years	42.5±15.5	42.8±15.5	42.3±15.6	0.804
Duration of gout, years	3.0 (1.0,8.0)	5.0 (2.0,9.0)	3.0 (1.0,5.0)	0.005
Count of affecting joints	3.0 (2.0, 6.0)	4.0 (2.0, 8.0)	2.0 (1.0, 4.0)	<0.001
Frequency of flare in the last year	4.0 (2.0,10.0)	5.0 (2.0,12.0)	3.0 (2.0,6.0)	0.002
Tophi, n (%)	31 (17.2)	21 (23.1)	10 (11.2)	0.035
Family history, n (%)	63 (35.0)	39 (42.9)	24 (27.0)	0.025
Serum uric acid, mg/dl	9.0±2.4	9.2±2.2	9.0±2.2	0.616
Hypertension, n (%)	58 (32.2)	33 (36.3)	25 (28.1)	0.267
Diabetes mellitus, n (%)	26 (14.4)	17 (18.7)	9 (10.1)	0.137
Dyslipidemia, n (%)	117 (65.0)	63 (69.2)	54 (60.7)	0.274
Hypercholesterolemia, n (%)	45 (25.0)	28 (30.8)	17 (19.1)	0.086
Hyper-low density lipoproteinemia, n (%)	53 (29.4)	34 (37.4)	19 (21.3)	0.022
BMI, kg/m <sup>2</sup>	25.4±3.5	27.2±3.4	23.6±2.4	<0.001
Obesity, n (%)	46 (25.6)	42 (46.2)	4 (4.5)	<0.001
Body fat, %	26.2±6.6	31.1±4.3	21.1±4.3	<0.001
SMMI, kg/m <sup>2</sup>	10.4±1.2	10.4±1.2	10.4±1.1	0.981
Metabolic syndrome, n (%)	82 (45.6)	54 (59.3)	28 (31.5)	<0.001
Fatty liver, n (%)	99 (55.0)	60 (65.9)	39 (43.8)	0.004

BMI: body mass index; SMMI: skeletal muscle mass index

**Conclusions:** Our results indicated higher body fat in gout patients which is an independent risk factor for MS.

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**Disclosure of Interest:** None declared

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AB1033

### COMORBIDITIES AND METABOLISM INDEXES IN PATIENTS WITH HUA COMPARED WITH NORMAL URIC ACID: A DATA FROM 33319 PATIENTS BETWEEN 2014 AND 2015

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**Objectives:** To investigate and compare the differences in Comorbidities and metabolism indexes between peoples with high and normal uric acid.

**Methods:** All the outpatients were enrolled in this cross-sectional study from September 2014 to September 2015 in Peking University People's Hospital. The patients were divided into high uric acid (HUA) and normal uric acid according to the international definition of HUA. The distribution characteristics of UA level and correlations between UA level and prevalence rate of comorbidities and metabolism indexes, including glutamic-pyruvic transaminase, glutamic-oxalacetic transaminase, serum total cholesterol (TC), triglyceride (TG), low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), blood glucose, creatinine (CRE), carbonyldiamide, estimated glomerular filtration rate (eGFR) were analysed.

**Results:** (1) Among 33 319 outpatients, with an average age of 56.4, 44.4% were men with a higher uric acid level than women ( $368 \pm 113.1$  umol/L vs  $300 \pm 95.5$  umol/L,  $p < 0.001$ ). In all patients, 25.6% had HUA and the sex ratio was about 1:1, while 50–59 age were most common in men and women with 60–69 age were the most. (2) Both the levels of uric acid in males and females had a significant relationship with the metabolism indexes above-mentioned. However, the levels of uric acid in females had a positive correlation with age and blood glucose, the levels of uric acid in males were negative correlated with age and blood glucose. And the uric acid levels in females displayed a higher relationship with carbonyldiamide and eGFR. (3) The prevalences of common chronic metabolic disorders, were significantly increased in HUA patients than those with normal uric acid, such as hypertension, hypertensive renal disease, hyperlipidemia, diabetes mellitus (DM), diabetic nephropathy (DN), chronic renal failure. And male patients with HUA had higher prevalence of gout than females (10.76% VS 2.58%,  $p < 0.001$ ). In patients with normal uric acid, the prevalence of DM and DN in males was higher than females. In contrast, the prevalence of DM and DN in males was lower than females in the patients with HUA (25.7% VS 57.1%,  $p < 0.05$ ; 6.52% VS 41.76%,  $p < 0.001$ ).

**Conclusions:** The prevalence of HUA in females was showing an increasing trend and the uric acid level in females had more influence in blood glucose and renal function than males.

**Disclosure of Interest:** None declared

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**AB1034 THE URATE-LOWERING EFFECT OF FEBUXOSTAT 80 MG AND 40 MG (80 MG FILM-COATED TABLETS SPLIT IN HALF) IN GOUT PATIENTS IN DAILY CLINICAL PRACTICE**

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**Background:** In Europe, the urate-lowering drug febuxostat for gout is registered in two strengths, 80 mg and 120 mg, but not 40 mg. Starting 40 mg can sometimes be considered desirable, for instance for safety reasons. Splitting an 80 mg film-coated tablet in half is an option, but is off-label and might violate coating function and influence effectiveness and safety.

**Objectives:** To investigate the urate-lowering effect and safety of starting febuxostat at 40 mg once daily (80 mg film-coated tablet split in half) in gout patients compared to 80 mg once daily.

**Methods:** Single-centre retrospective study on all gout patients starting febuxostat 80 mg or 40 mg (80 mg film-coated tablets split in half). Patients characteristics were collected, as well as starting dose and starting date of febuxostat, follow-up time, adverse events (AEs), stop date and reason, serum urate (sU) and creatinine (sCreat) over time and relevant comorbidity.

Patient characteristics were compared by Chi-square or T-test. Mean sU, percentage change from baseline and percentage of patients reaching targets (sU <0.36 or 0.30 mmol/L) were tested using the appropriate t-test.

**Results:** 36 gout patients started febuxostat between April 1st 2012 and July 1st 2017. Twenty-three started on 80 mg and 13 on 40 mg once daily. Patient characteristics are shown in table 1. Table 2 shows mean sU at baseline and after start, percentage change in sU and percentage of patients reaching targets.

Median follow-up time was 1.6 years (range 0–6.7); 1.4 y (0–6.7) resp. 1.9 (0.4–5.5) for 80 mg resp. 40 mg group. Figure 3 shows mean sU per group in the first year.

5 of 36 (14%) stopped during follow-up, all within 8 weeks after start and all because of AEs: diarrhoea (n=2, 40 mg and 80 mg), coronary syndrome (n=1, 80 mg), erectile dysfunction (n=1, 40 mg) and gout attacks (n=1, 40 mg). Other possible related AEs were dry mouth (n=1, 80 mg), elevated liver enzymes (n=1, 40 mg) and flushing (n=1, 40 mg).

**Abstract AB1034 – Table 1.** Patient characteristics

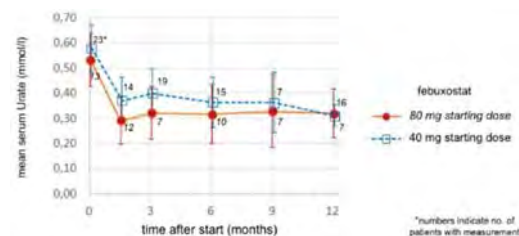
	Total group, n=36	80 mg group, n=23	40 mg group, n=13	p-value
Age, y, median (range)	60 (33–90)	60 (34–90)	64 (33–87)	ns
male gender, n(%)	29 (81%)	21 (91%)	8 (62%)	<0.05
time since diagnosis, y, median (range)	1.7 (–0.1–13.0)	0.8 (–0.1–12.3)	2.9 (0.9–13.0)	ns
crystal prove, n(%)	22 (61%)	15 (65%)	7 (54%)	ns
tophi*, n(%)	15 (44%)	8 (23%)	7 (54%)	ns
renal impairment (GFR 30–59 ml/min/1.73 m <sup>2</sup> ), n(%) <sup>§</sup>	16 (44%)	7 (30%)	9 (69%)	<0.05
other relevant comorbidity <sup>#</sup> , n(%)	30 (81%)	19 (83%)	11 (85%)	ns

\*tophi information missing in 2. <sup>§</sup>Lowest GFR was 30 ml/min/1.73 m<sup>2</sup>. <sup>#</sup>DM, obesitas, hypertension, hyperlipidemia, cardiovascular disease

**Abstract AB1034 – Table 2.** Febuxostat effect on sU within 12 weeks

	Total group, n=36	80 mg starting dose, n=23	40 mg starting dose, n=13	p-value
sU at start, mean (SD)	0.55 (0.11)	0.53 (0.10)	0.59 (0.10)	ns
sU within 12 weeks*, mean (SD)	0.35 (0.12)**	0.31 (0.10)**	0.39 (0.10)**	<0.01
% on target<0.36 mmol/L	68%	76%	57%	ns
% on target<0.30 mmol/L	36%	50%	8%	<0.01
% change in sU, mean (SD)	35 (18)	40 (18)	32 (17)	ns

\*available in resp. 33, 21 and 12. \*\*p-value within groups<0.001 compared to baseline



**Abstract AB1034 – Figure 1.** mean serum Urate over time after start of febuxostat

**Conclusions:** Both daily dosages febuxostat of 80 and 40 mg (80 mg film-coated tablets split in half) result in significant decline in sU levels within 12 weeks. A starting dose of 80 mg febuxostat appears more effective in reducing sU levels. Selection bias may be a problem.

**Disclosure of Interest:** None declared

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**AB1035 ULTRA-LOW DOSE ANTI-INTERLEUKIN1 IN CHRONIC GOUT: A SAFE AND SUCCESSFUL COMBINATION THERAPY WITH LOW DOSE COLCHICINE AND URATE LOWERING AGENTS**

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**Background:** Gout is the most common inflammatory arthritis in humans; is caused by deposition of monosodium urate (MSU) crystals within and around joints. Left untreated, a more chronic course may develop, characterised by persistent inflammation and visible MSU deposits (tophi), bone erosion, irreversible joint damage, and significant disability.<sup>(1)</sup> Management is based on two strategies: treating pain and inflammation with NSAIDs, steroids and colchicine and preventing flares and urate deposition with urate-lowering therapy.<sup>(2)</sup> For many patients, standard treatments are ineffective or contraindicated, mainly due to comorbidities.<sup>(3)</sup> The main mechanism of crystal-induced inflammation is interleukin 1 $\beta$  (IL-1 $\beta$ ),<sup>(4)</sup> which strengthens the relevance of targeting IL-1 $\beta$  in patients with crystal-induced arthritis. Selective blockade of IL-1 $\beta$  has shown to drastically reduce pain, inflammation and risk of flares. Three biologic therapies inhibit IL-1 $\beta$  and have been studied for difficult to treat acute gouty arthritis flares: anakinra, rilonacept and canakinumab.<sup>(5–6)</sup>

**Objectives:** Evaluate the efficacy of low dose anti-IL1 inhibitors administered by sublingual route in gout arthritis with remitting course that cannot be completely controlled with standard therapy regimens

**Methods:** Inclusion criteria was diagnosis of chronic gouty arthritis with remitting course (acute flares in patients with chronic gout and no inter-critical period), high CRP levels and need of chronic assumptions of NSAIDs or steroids, with flare at suspension. 20 patients fulfilled the criteria (exclusion criteria: intolerance to the study drug, poor compliance to therapies or diet, hyperuricemia, end stage renal disease) The study consist of two consecutive parts. An observational part were patients are treated for 6 months with 0.5–1 mg/daily of colchicine and 300 mg/daily of allopurinol. They performed visits at baseline, 3 and 6 months and we collected data about blood tests, VAS score, number of flares, compliance to therapy and adverse events. An experimental part were we added GUNA anti-IL1 (an infinitesimal dilution of anakinra that has a concentration of 10 fg/mL) 20 drops administered SL. Again patients performed visits at baseline (which coincides with the last visit of the observational phase), 3 and 6 months and we collected the same kind of data.

**Results:** At 6 months after introduction of GUNA anti-IL1 all patients, except 1, experienced no flares of disease, levels of CRP became negative and VAS pain scale was significantly reduce (CRP level p<0.0001; VAS p<0.0001). NSAIDs and steroid consumption was significantly reduced. No adverse events happened

**Conclusions:** Ultra-low dose of anti-IL1 agents added to standard therapy is an effective and safe way to achieve disease remission

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AB1036

### FEATURES OF KIDNEY FUNCTION AND URODYNAMICS AT PATIENTS WITH CHRONIC GOUT BASED ON COMPLEX RENAL SCINTIGRAPHY DATA

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**Background:** One of the frequent manifestations of gout is the gout nephropathy. For assessment of the urinary system functional reserves and the risk of renal failure routine analyses of urine in combination with a sonography are often not enough. Modern technology of the systemic examination of nephrourological status based on complex renal scintigraphy (SENS-CRS) was developed in the laboratory of radioisotope diagnosis in «N.N. Blokhin National Medical Research Centre» and realised as an automated workplace. SENS-CRS technology is designed for assessment of the urinary system functional reserves and the risk of renal failure at all macrostructural levels, and allows lowest radiation doses (0.6 mSv for one patient).

**Objectives:** To define features of kidney function and urodynamics at patients with chronic gout based on the complex renal scintigraphy (CRS) data.

**Methods:** 59 medical records of patients with gout (2007–2011) were analysed retrospectively. Most of the patients (95%) were men, average age was 54.4±9.5 years. Duration of the disease was 8<sup>4–11</sup> years. All patients had chronic gouty arthritis, 28% of patients had tophuses. The CRS tests was carried out on a two-detector gamma camera with simultaneous 2 projections recording. <sup>99m</sup>Tc-technephore was used, a Russian radiopharmaceutical (RP) from the group of bisphosphonates that has hemodynamics of a glomerulotropic product, concentrating mainly in the nephrons via filtration, with partial (10%–15%) involvement of secretion. Working protocol consisted of a base 21 min (1 min angiophase) study with administration of RP and a delayed 21 min study without administration of RP, but after taking 200–300 ml of water and/or an antispasmodic or diuretic drug to identify persistent urodynamic dysfunction. The interpretation of CRS data is based on a concentrational-hydrodynamic model of urinary excretion and SENS-CRS software. The Statistica 10.0 software was used too.

**Results:** According to CRS tests patients with gout had, on average, the level of blood cleansing from RP reduced slightly with a trend to a moderate level, and buffer retention of RP labelled blood in extrarenal structures increased. The signs of a relative hemostasis were found against the background of fast excretion accelerated by taking hypotensive drugs. Quantitative analysis of CRS data allows to estimate sustainability of relative urine delays in the pyelocaliceal system (PCS): in 70% of patients residual urostatics in the renal parenchyma and groups of calyx remained relatively stable, and the urostatics signs in the renal pelvis were disappearing. This result means that there could be a latent increased residence time of substances such as uric acid as well as nephrotoxic drugs in the kidney parenchyma. This requires control of correct drugs dosage and when prescribing repeated therapy courses.

**Conclusions:** The SENS-CRS technology provides the quantitative assessment of kidney blood cleansing from RP and concentrational function of parenchyma as well as unique quantitative indicators of urodynamic delays in all parts of urinary tract. This kind of functional diagnostics allows to monitor parenchyma and urinary tract condition promptly and with lowest radiation doses, apply therapeutic measures to prevent more severe kidney dysfunction and refer patients to a specialist consultation.

**Disclosure of Interest:** None declared

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AB1037

### RELATIONSHIP BETWEEN CALCIUM PYROPHOSPHATE DIHYDRATE CRYSTAL AND OPERATED KNEE OSTEOARTHRITIS-GENDER SPECIFIC ANALYSES-

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**Background:** Calcium pyrophosphate dihydrate (CPPD) crystal deposition disease is a common arthritic disorder in mainly elderly patients. CPPD crystals are found in multiple joints in association with severe cartilage degeneration in osteoarthritis (OA). The knee is a key target site for both CPPD crystals and OA. CPPD crystals are also one of the common types of crystals causing crystal-induced inflammatory arthritis. There is a need to elucidate factors that can cause progression of knee OA. To address this question, we investigated the relationship between CPPD crystals and operated knee OA.

**Objectives:** We investigated the relationship between CPPD crystal and operated knee OA separated by gender.

**Methods:** Three hundred sixty-six unicompartmental knee arthroplasty (UKA), total knee arthroplasty (TKA) and high tibial osteotomy (HTO) (average age 73.3: male 59: female 307) were performed for over grade III knee OA classified by Kellgren-Lawrence grading scale from 2010 to 2017. At the operation, joint fluids

were collected and elucidated the CPPD crystal using polarising microscope. We evaluated the relationship between CPPD crystals, and age, body mass index (BMI), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), matrix metalloproteinase-3 (MMP-3) at the operation. We defined the osteophyte formation degree (OFD) as grade 0–3<sup>1</sup>. We also defined the lower extremity alignment as varus (femorotibial angle: FTA ≥180°), neutral (170°≤FTA<180°) and valgus (FTA <170°). The relationship between CPPD crystals, and osteophyte formation and lower extremity were also evaluated.

**Results:** CPPD crystals were detected from 101 Knee OA (27.6%). CPPD(+) rate in female (30.0%: 92/307) was significantly higher than that in male (15.3%: 9/59). There was a significant difference between CPPD(+) and (-) in male about only FTA (186.9°/182.0°). There were significant differences between CPPD(+) and (-) in female about age (76.3/72.4), FTA (182.7°/183.2°), BMI (24.9/26.6). The more severe OFD became, the higher CPPD(+) rate was in female, significantly. CPPD (+) rate in valgus knees (60.9%) was higher than that in varus knees (29.6%) in female significantly.

**Conclusions:** The European League Against Rheumatism (EULAR) reported that female gender was not a risk factor associated with CPPD crystals<sup>2</sup>. In contrast, a recent study using a relatively large sample size of Japanese cadaveric knees showed a significant correlation for CPPD crystals and female gender<sup>3</sup>. Our data also showed a significantly high CPPD(+) rate in females. Because our data were based on Japanese patients only, Japanese ethnicity may influence the gender difference in the CPPD(+) population. In addition, the significantly different items in male and female were different. These results may suggest that the mechanism of CPPD deposition may be different by gender.

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AB1038

### PHARMACOKINETICS, PHARMACODYNAMICS AND SAFETY OF NC-2500, A NOVEL XANTHINE OXIDOREDUCTASE INHIBITOR, IN HEALTHY JAPANESE MALE SUBJECTS

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**Background:** Gout flare due to rapid urate reduction after initiating urate-lowering therapy (ULT) is one of the major issues in the therapy, which impairs patients' quality of life and adherence. For the prevention of it, the guidelines in the ACR, the EULAR and Japan recommend initiating ULT with a low starting dose followed by adequate titrations, however it is rare in clinical settings. NC-2500 is a novel orally active xanthine oxidoreductase (XOR) inhibitor in development for the treatment of gout/hyperuricemia. Preclinical studies showed that multiple doses increase the plasma concentration and enhance the urate-lowering effect of NC-2500, suggesting that NC-2500 may decrease the risk of gout flare when initiating the treatment.

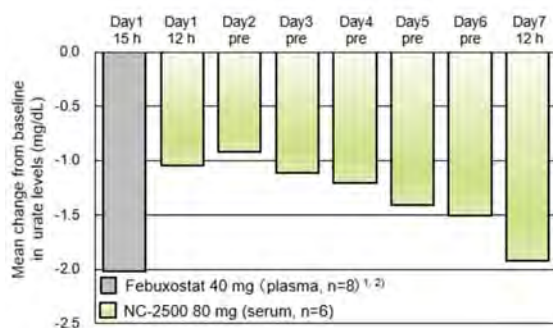
**Objectives:** The aim of this study was to evaluate the pharmacokinetics, pharmacodynamics and safety of NC-2500 in healthy Japanese male subjects.

**Methods:** A Phase 1, randomised, single-blind, placebo-controlled, single and multiple ascending dose study was conducted. Each cohort consisted of 8 subjects, with 6 receiving NC-2500 and 2 receiving placebo orally. A total of 5 cohorts were studied in the single-dose study (10 mg to 160 mg, fasted conditions) and 4 cohorts were studied in the multiple-dose study (10 mg to 80 mg, fed conditions). The levels of NC-2500 and urate in plasma/serum and urine were assayed at pre-determined time points. Safety and tolerability were assessed by physical examination, vital signs, electrocardiography, clinical laboratory tests and adverse events (AEs).

**Results:** Following single oral doses of NC-2500, maximum plasma concentration (C<sub>max</sub>) and area under the plasma concentration-time curve (AUC) increased approximately in a dose-proportional manner except that the increase in the C<sub>max</sub> at 160 mg was less than dose proportional. The time to reach the C<sub>max</sub> (T<sub>max</sub>, median) was at 2.0–3.5 hours post dose and food intake delayed the T<sub>max</sub> by 1 hour. In the presence of food, NC-2500 absorption appeared to decrease slightly or not be affected. Plasma NC-2500 concentration increased



with multiple doses and the Cmax and AUC on Day 7 at 80 mg were 1.4–1.5 times higher than those on Day 1. NC-2500 was hardly excreted into the urine. Effects of NC-2500 on serum urate (sUA) levels were approximately dose-dependent. The sUA level in the single 160 mg dose cohort decreased by 1.03 mg/dL. Moreover, in the subjects receiving multiple doses of 80 mg, the sUA level decreased gradually over the 7 days with a decrease from baseline of 1.93 mg/dL. The incidence of AEs was similar between NC-2500 and placebo treatments and all AEs were mild in severity.



Abstract AB1038 – Figure 1

**Conclusions:** From the results, NC-2500 is expected to have potential to resolve the issues of current ULT by its unique urate-lowering property to decrease acute flare, with no or minimal titrations. As for safety, NC-2500 was considered safe and well-tolerated. Furthermore, NC-2500 was hardly excreted through the kidneys, which can be a favourable profile for patients with renal impairment, frequently observed in gout.

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### AB1039 DIET MAY PLAY ESSENTIAL ROLE FOR THE SUCCESS OF THE URATE LOWERING THERAPY IN GOUT

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**Background:** Chronic deposition of monosodium urate crystals, in case of hyperuricemia, is the main cause of the gout.<sup>1</sup> Furthermore, lowering uric acid to the targeted levels is the main therapeutic objective in chronic gout treatment. Uric acid lowering treatment (ULT) has three main arms: Practicing lifestyle modifications, pharmacologic ULT and targeting co-morbid illnesses.<sup>2</sup> Thus, patients' medical and therapeutic properties may have a role in successful ULT.

**Objectives:** We evaluated the demographic and therapeutic properties; co-illnesses and disease features of the patients that would relate with the success of ULT. Then, we compared these parameters between the gout patients with successful ULT and inadequate ULT.

**Methods:** 66 gout patients on pharmacologic ULT were enrolled to the study. Non-adherence to pharmacologic ULT was accepted an exclusion criteria. Demographic and therapeutic features; co-illnesses and disease features of the patients were obtained during the study. Then, we compared these parameters between the patients with successful ULT and inadequate ULT.

**Results:** Adherence to diet was found different between groups (OR, 7.00; CL% 95 2.27–21.56). All other features including maximum allopurinol dosage were similar. Only one patient from successful ULT group and none of the patients in inadequate group had an drinking habit.

Abstract AB1039 – Table 1. Demographic properties, therapeutic features and laboratory values of the patients

	Successful ULT n=32	Inadequate ULT n=34	p
Gender (M/F)	29/3	28/6	0.47
Age	60.3±13.1	55.8±11.8	0.14
Body mass index	27.2±9.8	27.8±8.9	0.32
Diabetes mellitus n(%)	7 (21.9)	11 (32.4)	0.24
Hypertension n(%)	19 (59.4)	18 (52.8)	0.39
Chronic cardiac disease* n(%)	9 (28.1)	6 (17.6)	0.23
Hyperlipidemia n(%)	1 (3.1)	2 (5.9)	0.52
Chronic kidney disease n(%)	6 (18.8)	3 (8.8)	0.20
ACE inhibitors/AT II blockers n (%)	18 (56.3)	13 (38.2)	0.14
Beta-blockers n(%)	5 (15.6)	4 (11.8)	0.72
Diuretics n(%)	5 (15.6)	5 (14.7)	0.91
Acetylsalicylic acid n(%)	5 (15.6)	3 (8.8)	0.46

Abstract AB1039 – Table 2. Disease and treatment features of the patients

	Successful ULT n=32	Inadequate ULT n=34	p
Pretreatment SUA (mg/dL)	9.47±1.6	8.8±1.6	0.18
Maximum allopurinol dosage (mg)	290.6±92.8	313.8±134.8	0.75
Adherence to diet n(%)	26 (81.2)	13 (38.2)	<0001
Chronic gout arthritis n(%)	8 (25.0)	11 (32.3)	0.56
Tophus n(%)	5 (15.6)	2 (5.8)	0.25
Erosion n(%)	7 (21.8)	7 (20.5)	1.00

**Conclusions:** We found that diet was the only factor that relate with success of ULT while patients were on pharmacologic ULT. So, clinicians should emphasise the importance of all part of ULT including diet with informing patients about the nature of disease and benefits of ULT during visits.

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**Disclosure of Interest:** None declared

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### AB1040 IS GOUT A CHRONIC INFLAMMATORY DISEASE OF A LOW LEVEL OF ACTIVITY?

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**Objectives:** To determine the presence of physical, laboratory and ultrasound (US) signs of inflammation on the affected joints, but also on the joints that in the clinical sense never showed an inflammatory reaction in the intercritical gout period.

**Methods:** This prospective study included 43 patients (pts.) with diagnosis primary gout (20 with and 23 without acute gout attacks). The research included: demography; medical history; laboratory analyses: sedimentation of erythrocytes (ESR), C reactive protein (CRP), and serology; physical: detect tender and swollen joint; and US examination detect synovial fluid and hypertrophy, Power Doppler (PD) signal and "double contour" sign on the wrist, first metatarsal joint (MTP1), tibiotalar (TT) joint and knee.

**Results:** A physical examination showed presence of 78% tender and 43% swollen joints in the group pts. with acute gout attack, but also 23% pts. had painful and 10% swollen joints in the group without acute gout attack (p<0.001). In the group with acute gout attacks the mean ESR was 32.80 mm/L, value CRP was 8.20 mg/L and leukocytes (Le) (9.09 × 10<sup>9</sup>/L), and in the group without acute gout attacks SE was 21.60 mm/L median CRP was 6.40 mg/L and also a higher average Le (8.39 × 10<sup>9</sup>/L). So we found that there was no statistical difference (p>0.5) in the laboratory parameters (ESR, CRP and Le) between the groups. There was also no statistically significant difference in the findings of US signs of "double contour" (p>0.5), synovial fluid and hypertrophy (p>0.05), per group, but the presence of PD signal statistics was more often observed in a group of patients in an acute gout attack (p<0.05), table 1.

**Abstract AB1040 – Table 1.** US signs in groups; Group I- pts.with acute gout attacks; II- pts.without acute gout attacks

Joint	"Double contour",N (%)		Synovial fluid, N (%)		Synovial hypertroph,N(%)		PD signal,N(%)	
	Group		Group		Group		Group	
	I	II	I	II	I	II	I	II
Wrist	14 (35%)	11 (25%)	8 (21%)	6 (14%)	5 (13%)	5 (11%)	4 (10%)	1 (2%)
MTP1	31 (78%)	30 (65%)	34 (85%)	28 (61%)	23 (58%)	22 (49%)	22 (55%)	10 (20%)
TT	18 (46%)	15 (32%)	10 (25%)	8 (18%)	6 (16%)	5 (12%)	5 (14%)	1 (2%)
Knee	27 (68%)	24 (53%)	17 (43%)	17 (37%)	11 (28%)	9 (20%)	3 (8%)	0 (0%)
<b>P</b>	<b>&gt;0.5</b>		<b>&gt;0.05</b>		<b>&gt;0.05</b>		<b>&lt;0.05</b>	

**Conclusions:** Our results show the presence of laboratory and ultrasound indicators of joint inflammation in gouty patients at the interclinical stage as well as in patients with acute gout attack. The results of this study show that gout is a chronic inflammatory disease of low activity.

**Disclosure of Interest:** None declared

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### AB1041 OCCURRENCE OF MAJOR CARDIOVASCULAR EVENTS IN PATIENTS WITH GOUT TREATED WITH FEBUXOSTAT

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**Background:** Controversy persists regarding the use of febuxostat (FBX) in patients with gout and the development of cardiovascular (CV) events. In both APEX<sup>1</sup> and FACT<sup>2</sup> trials a higher risk was identified in those on the FBX arm compared to those on allopurinol, but this was later not confirmed in CONFIRMS trial<sup>3</sup> and the extension phases. Recently, the FDA has published a warning on the risk of CV death in relation to FBX, based on preliminary data of a safety study enrolling 6000 participants.<sup>4</sup>

**Objectives:** To assess the occurrence of CV events in patients with gout after been prescribed with FBX in clinical practice.

**Methods:** Retrospective review of patients with crystal-proven gout enrolled in an inception cohort since January 2014. Epidemiological (age, gender), clinical (CV risk factors, CV disease background), and laboratory variables (serum urate – SU –, glomerular filtration rate – GFR) were registered. The primary endpoint was the occurrence of CV events (death, coronary heart disease (CHD), congestive heart failure (CHF), stroke, peripheral artery disease (PAP)) developed during treatment with FBX. A comparison on secondary study variables regarding the development of CV events was performed by Mann-Whitney's U, chi-square and Fisher's exact tests.

**Results:** In the cohort, 43 patients were treated with FBX, but three were excluded (two early stopped FBX because of rash, and one was lost of follow-up), so finally 40 patients were analysed. Their median age was 76 years (p25-p75 70–79), being 24 of them men (60%). CV risk factors were prevalent, especially hypertension (87.5%), and 20 of them (50%) had established CV disease. Median time since first gout attack was 1.5 years (p25–75 0.0–9.5) and 14 patients (35.0%) were tophaceous. After initiating FBX, 7 cases (17.5%, 95% CI 5%–30%) of CV events were identified: three of CHF (7.5%), two of CHD (5.0%) and one stroke (2.5%), with no PAP events. Five CV-related deaths (12.5%) were noted. The occurrence of CV events significantly associated with an older age and background of established CV disease (table 1).

**Abstract AB1041 – Table 1**

	No CV events	CV events	<b>p</b>
<b>AGE*</b>	74 (67–79)	80 (78.2–81.0)	<b>0.049</b>
<b>HT*</b>	28 (84.8%)	7 (100%)	0.565
<b>DM*</b>	14 (42.4%)	3 (42.9%)	1.000
<b>DLP*</b>	21 (63.6%)	4 (57.1%)	1.000
<b>SMOKING*</b>	12 (38.7%)	3 (42.9%)	0.711
<b>PRIOR CV DISEASE*</b>	13 (39.4%)	7 (100%)	<b>0.008</b>
<b>BASELINE GFR*</b>	37.4 (20.7–53.1)	28.0 (22.5–37.3)	0.530
<b>BASELINE SU*</b>	8.9 (7.7–10.7)	10.7 (8.4–14.6)	0.147
<b>GOUT DURATION*</b>	2.5 (0–10)	1 (0–8)	0.147
<b>TOPHI*</b>	12 (38.7%)	2 (40.0%)	1.000

\*median (p25–75);+n(%)

**Conclusions:** In our cohort, about one on six patients treated with FBX suffered from a CV event, some being fatal. The development associated with older age and CV disease background, so it merits a cautious use in this setting, although whether these CV events are directly related to FBX needs further clarification.

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**Disclosure of Interest:** None declared

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### AB1042 PATHOLOGIC MUSCULOSKELETAL ULTRASOUND FINDINGS IN PATIENTS WITH CHRONIC KIDNEY DISEASE ON DIALYSIS- A PILOT CONTROLLED STUDY

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**Background:** There are numerous studies about the musculoskeletal abnormalities associated with dialysis, but most of them target osteoporosis and the bone metabolism. While this is, in fact, of great importance, we consider that the abarticular anomalies should also be taken into account. Because of the pain they cause and the quality of life impairment in patients already affected in this domain, suffering from depression or at its' edge.

**Objectives:** We aimed to detect the dialysis associated soft tissue abnormalities, using musculoskeletal ultrasound(MSUS) scanning of patients diagnosed with late-stage chronic kidney disease(CKD) on dialysis. In order to achieve this, we compared the data obtained from this group, to a control group of pre-dialysis late-stage CKD.

**Methods:** Over the last 8 months, we ran a prospective study including 102 patients. The study group included 52 patients with stage G5D (GFR <15 ml/min/1.73 m<sup>2</sup>, on dialysis – hemodialysis (HD)/peritoneal dialysis (PD)), while the control group included 50 patients with stage G5 (GFR <15 ml/min/1.73 m<sup>2</sup>, pre-dialysis). Each patient had 68 joints scanned with a Samsung HM70A machine, by the same ultrasonographer, in order to avoid the inter-observer variability. Also, each patient completed a visual analogue scale (VAS) for evaluating pain.

Sex study group: M: 30 (57.69%) F: 22 (42.3%)

Sex control group: M: 28 (56%) F: 22 (44%)

Age (years) study group: 62,52<sup>30–82</sup>

Age (years) control group:64,1 (33–84)

HD/PD study group: HD: 46 (88.46%) DP: 6 (11.53%)

Time on dialysis (years) study group: 6,41 (0,5–22)

**Results:** The findings included median nerve entrapment (71.1% – study group, 18% – control group), tendon calcifications (61.5% – study group, 38% – control group), degenerative abnormalities (57.6% – study group, 50% – control group), synovitis (32.6% – study group, 22% – control group) and tenosynovitis (13.4% – study group, 8% – control group). There were no particular abnormalities found only in the study group, but the percentages of the common findings were significantly higher.

The VAS results were split in three groups: low, moderate and high. Among the patients on dialysis, 46.1% declared a low VAS, 36.5% moderate and 17.3% a high VAS, while in the control group the distribution according to VAS was 46% in the low lot, 34% in the moderate and 20% in the high lot.

**Conclusions:** We detected soft tissue abnormalities in an important percentage of patients on dialysis, but the results were disproportionate to the algo-functional symptoms. We found a higher percentage of low VAS then we were expecting. Considering the results, we plan to continue our study, aiming to create a rehabilitation programme adapted to the needs of the dialysed patient.

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**AB1043 THE CLINICAL PROFILE OF GOUT SIGNIFICANTLY DIFFERS BETWEEN MALE AND FEMALE**

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**Background:** Gout, the most common type of inflammatory arthritis, is considered as a predominant male disease. Notwithstanding, there is an increased risk of gout in female after the menopause.

**Objectives:** Our objective was to assess differences in the clinical features between female and male patients.

**Methods:** Data of newly diagnosed gout patients attending the rheumatology out-patient clinics of one secondary and one tertiary i.e. university centre in the south of the Netherlands were used. We compared baseline characteristics of males and females regarding to demographics, BMI, presence of tophi, medication use (diuretics, prophylaxis of gout and uric acid lowering drugs), serum and urine concentration of uric acid and creatinine, and comorbidities. Additional, fractional excretion of uric acid (FEUa), calculated as (urinary uric acid x serum creatinine)/(serum uric acid x urinary creatinine), was compared. FEUa gives the percentage of uric acid renally filtered and thus excreted in the urine (normal range 7%–12%). Independent t-tests and chi square were used to assess differences between females and males statistically.

**Results:** 66 female (16.6%) and 331 male (83.4%) patients with gout (MSU crystals 60.6 vs 68.6%, respectively) were included. At baseline, females compared to males had a significantly higher age (73±12 vs 63±13 years, p<0.001), BMI (30.1±5.2 vs 28.7±4.7 kg/m<sup>2</sup>, p=0.034) and diuretic use (63.6 vs 27.8%, p<0.001). Females had also a significantly higher percentage of comorbidities, including hypertension (77.3 vs 59.5%, p=0.003), diabetes (48.5 vs 22.7%, p<0.001) and chronic kidney disease (eGFR of 46.4±24.2 vs 62.5±22.9, p<0.001). There was no significantly difference in serum and urine uric acid concentration, current urate lowering and prophylactic medication, presence of tophi and nephrolithiasis. Also, the FEUa was similar in females vs males (5.1±3.0 vs 4.4%±1.7%, p=0.201).

**Conclusions:** The clinical profile of gout in females significantly differs compared with males: significantly older, more advanced decrease in renal function and higher prevalence of hypertension in the females. As Dutch guidelines recommend starting with a diuretic for the treatment of hypertension in patients aged 70 +; this may have a role in explaining the higher numbers of females using diuretics. The start of diuretics has previously been associated with hyperuricemia and increases the risk of gout in the female population. Although diuretic use has proven to be a safe and effective first-line treatment for hypertension, our results suggest that diuretic use in combination with a decreased renal function is associated with an increased risk at developing gout in females, and possibly needs reconsideration. Furthermore, despite the fact that the FEUa was similar distributed between genders, females did seem to have a lower urinary uric acid excretion. However, the number of patients with tophi and nephrolithiasis and the serum uric acid level are comparable between the genders. This suggests that the urate burden is similar but that the clinical profile for the development of gout differs due to the uric acid production vs excretion. In depth analysis of our population underlines the differences in female and male gout patients which highlight the need for more research into pathophysiology and management of gout between sexes.

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**AB1044 THE EDUCATION OF PATIENTS WITH GOUT IMPROVES THE EFFECTS OF TREATMENT**

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**Background:** The recent studies about gout demonstrated the correlation between gout and cardiovascular disease (CVD). The urate lowering therapy (ULT) ameliorates the outcomes of CVD. The poor adherence with ULT in patients with gout is the main obstacle. It is induced mainly due to a lack of adequate information about the efficacy of ULT.

**Objectives:** This study was performed to analyse the effects of the education for patients with gout.

**Methods:** 116 patients with gout were enrolled and categorised by two groups, education and non-education. The face to face education was conducted by the specially educated nurse. And all participants in two groups received an leaflet about general information of gout including lifestyle advice, nutrition and drugs of ULT. The patients in non-education group were also educated by nurse on their

second visit (after two or three month from first visit). The score of patients' satisfaction using the visual analogue scale (from 0 to 100 mm) and questionnaire about satisfaction and questionnaire of patients' knowledge about disease (gout) were assessed. And we analysed patients' serum uric acid level and drug compliance.

**Results:** A total of 116 patients were randomised to education or non-education group equally. Patients' satisfaction in visual analogue scale was significantly higher in education group (education group: 82.7±21.0 mm, vs. non-education group: 72.8±20.7 mm, p<0.001).

Patients' satisfaction questionnaire was significantly higher in education group (education group: 3.89±0.5, vs. non-education group: 3.69±0.4, p=0.017). The level of knowledge about gout was higher in education group (education group: 7.4±2.0, vs. non-education group: 6.2±2.3, p=0.004). The serum uric acid level on second visit is decreased after education (baseline: 5.97±1.93 mg/dL, vs. second visit: 5.32±1.35 mg/dL, p=0.001). Besides drug compliance on second visit is improved after education (baseline: 89.6%±16.4%, vs. second visit: 94.3%±9.9%, p=0.018).

**Conclusions:** The face to face education for gout improved the patients' satisfaction, drug adherence and serum uric acid level. The education is very important part in treatment of gout.

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**AB1045 MICROPROTEINURIA AS A MARKER OF SUBCLINICAL GOUTY NEPHROPATHY**

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**Background:** The prevalence of kidney damage in patients with gout ranges from 30% to 70%. Currently the concept of "gouty nephropathy" (GN) comprises all renal pathologies due to gout. There is no clear opinion whether hyperuricemia is a marker of renal dysfunction or risk factor. It is important to identify the early stages of GN as its course is subclinical for a long period of time. Microproteinuria is the first harbinger of kidney damage. However, predictors of GN have not been established for today.

**Objectives:** To establish predictors of GN.

**Methods:** A total of 103 patients with chronic gouty arthritis were examined in rheumatology department of Ternopil University Hospital. All patients had no history of any kidney disease. ELISA method was used to determine microproteins in urine. Subsequently, patients were divided into 2 groups: I (n=58) – patients with subclinical gouty nephropathy, abnormal microproteins level (56.3%), II (n=45) – control group, patients without kidney damage, normal microproteins level (43.7%). Statistical analysis was performed with STATISTICA software.

**Results:** Patients with subclinical gouty nephropathy had a higher prevalence of arterial hypertension and metabolic syndrome. The prevalence of osteoarthritis, diabetes mellitus and dyslipidemia was the same in both groups. Also, group I patients showed longer duration of the disease, greater radiologic changes, higher levels of hyperuricemia, tophi, work incapacity, greater number of affected joints and more frequent changes in urinalysis than the control group.

**Conclusions:** Formation of GN is asymptomatic, causing delays in early diagnosis, but can be suspended timely. Gouty nephropathy develops in 56.3% of patients with chronic gout arthritis, and manifestes by microproteinuria in the early subclinical stages. Duration of the disease, obesity, presence of tophi, arterial hypertension, hyperuricemia, increased triglycerols and low-density lipoproteins levels were found to be predictors of gouty nephropathy.

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**AB1046 ALLOPURINOL USE IN CHRONIC KIDNEY DISEASE- IS THERE A DIFFERENCE IN ACHIEVING TARGET URIC ACID?- A RETROSPECTIVE STUDY**

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**Background:** Patients with gout are recommended to treat to target uric acid level of 6 mg/dL in absence of tophi, and <5 mg/dL if tophi present. A case-controlled retrospective analysis by Stamp et al of allopurinol hypersensitivity reaction confirmed that the highest risk of severe hypersensitivity reaction is in the first few months of therapy and thus a low starting dose is recommended (as low as 50 mg in stage 4 chronic kidney disease and worse). Due to concerns related to adverse effects from Allopurinol, we hypothesised that allopurinol use would be less aggressive in terms of achieving target uric acid.

**Objectives:** We aim to compare the frequency of achieving target uric acid level in patients with glomerular filtration rate (GFR) of less than 60 and more than 60.

**Methods:** We reviewed charts of patients in a large private practice who were prescribed Allopurinol. Patients who had at least two office visits and had been on Allopurinol at least six months were included in the study. Charts were reviewed of patients for uric acid level, Allopurinol dose, GFR and any major adverse events. Major allopurinol related adverse event was defined as any adverse event leading to hospitalisation or cessation of medication.

**Results:** Mean Allopurinol dose for patients with GFR of more than 60 was 244. There were no major adverse events and 52 out of total 103 patients (50.5%) had achieved goal uric acid.

Mean Allopurinol dose for patients with GFR of less than 60 was 238. There were no major adverse events and 19 out of total 38 patients (50%) had achieved goal uric acid.

**Conclusions:** There was no difference noted in patient with GFR less than 60 or more than 60 in terms of achieving goal uric acid level. No major adverse events were noted in either group.

**Disclosure of Interest:** None declared

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## Infection-related rheumatic diseases

**AB1047 CERVICAL POTT'S DISEASE: 5 CASE REPORTS AND REVIEW OF LITERATURE**

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**Background:** Spinal tuberculosis (Pott's disease) is the most common as well as one of the most dangerous forms of skeletal tuberculosis and accounts for 50% of all cases of skeletal tuberculosis. Pott's disease is still common in developing countries. Although the thoracolumbar junction seems to be the most common site of the spinal column involvement, cervical localization is scarce and accounts for 2% to 5% of spinal tuberculosis. Furthermore, the incidence of neurologic complications in spinal tuberculosis varies from 10% to 43%.

**Objectives:** The purpose of this study was to perform an updated review and present our experience with 5 cases of tuberculosis of cervical spine, including clinical characteristics, diagnostic modalities and management of spinal tuberculosis.

**Methods:** A review of 5 cases of cervical Pott's disease collected at the Department of Neurosurgery of National Institute of Neurology of Tunis over a period of 2 years, between 2011 and 2012 and an updated literature review.

**Results:** The average age of our patients was 35 years old with extremes ranging from 16 to 63 years old. There is a slight male predominance. The diagnostic delay is on average 6 months. The clinical manifestations were dominated by cervical pain (4 cases) and progressive spinal cord compression syndrome (3 cases). The biological inflammatory syndrome is found in only one patient. The intra-dermal reaction to tuberculin is positive in 4 patients. X-ray of the cervical spine, CT scan and magnetic resonance imaging were performed in all patients. All patients underwent a surgical resection. The medical treatment was administered to all our patients. The evolution was favourable, clinically and biologically, under anti tubercular treatment.

Tuberculous spondylodiscitis remains a major global public health problem in endemic countries that affects mostly young adults in their most productive years. Thoracolumbar junction seems to be the most common site of the spinal column involvement in spinal tuberculosis (95%) and cervical spine is concerned in only 5% of cases. The delayed diagnosis, between 3 and 20 months, explains the frequency of neurological deficits which are found in proportions of 20% to 40%. For the diagnosis of spinal tuberculosis, magnetic resonance imaging is more sensitive imaging technique than x-ray and more specific than computed tomography. Antituberculous treatment remains the cornerstone of treatment. Surgery may be required in selected cases. With early diagnosis and early treatment, prognosis is generally good.

**Conclusions:** Cervical Pott's disease is a rare localization. The diagnosis is easy in front of the cervical signs. The conservative management of cervical spine immobilisation and antitubercular chemotherapy remains a sufficient attitude to healing. Surgery is reserved in case of neurological aggravation or spinal instability.

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**AB1048 EVOLUTION OF INFECTIOUS SACROILIITIS ACCORDING TO THE GERM**

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**Background:** infectious sacroiliitis is a rather rare rheumatological emergency that has a misleading semiology because of the deep condition of the joint, the germ responsible plays an important role in this semiology and in its evolution

**Methods:** This is a retrospective study of 42 patients who have been hospitalised in the LA Rabta for Infectious Sacroiliitis from 1999 to 2017. the epidemiological data (age/sex) were recorded as well as the clinical radiological and biological data (symptoms, inflammatory assessment, x-rays, CT scan and/or IRM, biopsy).

**Results:** forty two patients were included in this study. the average age is 36,7 years old, sex distribution is: 19 women 23 men.

banal sprouts are responsible in 48.15% of cases: *Staphylococcus aureus* 28.7% *Escherichia coli* 17.07% and 2.38% streptococcus. the progression was favourable in 87.4% of the cases under appropriate antibiotic therapy for the rest: 2.38% deaths, 2.38% state of septic shock, 7.84% of complication inherent to the treatments. tuberculosis is responsible for 37.2% of infectious sacroiliitis with a favourable evolution in 77.6%, a complication related to treatment is noted in 17.64%, a subcutaneous abscess 2.34%, multifocal bone tuberculosis 2.38%. brucellosis sacroiliitis is diagnosed in 14.65% of cases, the evolution is favourable in 7.51%, in 4.76% a rapid progression towards ankylosis was noted despite appropriate antibiotic therapy, 2.38% a progression towards brucellosis chronic

**Conclusions:** common germs are most responsible during infectious sacroiliitis and seem to have the best prognosis, tuberculosis is responsible for various complication and its treatment is at high risk of iatrogenic which limits the therapeutic choice of the clinician. chronicity is the most feared development during *Brucella sacroiliitis* as antibiotic therapy is no longer effective

**Disclosure of Interest:** None declared

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**AB1049 RHEUMATOLOGICAL MANIFESTATIONS DURING CHRONIC HEPATITIS C**

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**Background:** Chronic hepatitis C (CHC) is assimilated to a systemic disease because of his multiple extrahepatic manifestations notably rheumatological.

**Objectives:** The aim of this study was to determinate the prevalence and the characteristics of rheumatological manifestations (RM) associated with CHC.

**Methods:** A retrospective study including all patients suffering from CHC followed over a period of 11 years (2002–2012). Were excluded all patients co-infected by hepatitis B virus or by human immunodeficiency virus and those having decompensated cirrhosis. Different RM were collected and analysed according to the epidemiological, clinico-biological, immunological, virological and histological data of the CHC.

**Results:** Two hundred and four patients affected by CHC were included, mainly aged by 52 years [22–66 years]. The sex-ratio was 0,46. MR were noted in 76 patients (37,25%) dominated by inflammatory polyarthralgia of big joints (88,25%). Non erosive arthritis was observed in a woman and was localised to the proximal interphalangeal articulation of the index. Myalgia were noted in 11 cases (14,47%) among them, 2 appeared under antiviral treatment. Sicca Syndrome was observed in 17 cases (22,36%). RM were associated to other extrahepatic manifestations of CHC in 69,7% of cases, notably to mixed cryoglobulinemia (MC) (60%) and to antinuclear antibodies (21,6%). Anti DNA, anti SSA, anti SSB, rheumatoid factor and anti CCP were absent in all cases. A partial to total amelioration of RM was noted in almost patients under antiviral treatment and sometimes associated to symptomatic measures. In univariate analyse, only femal sex and presence of MC were significantly correlated to the presence of MR.

**Conclusions:** During CHC, MR are frequent, dominated by arthralgia, myalgia and sicca syndrome. Authentic arthritis are rare and constitute a diagnostic problem essentially when they inaugurate the disease. MC is the immunological factor the most associated with RM. Treatment of MR still antiviral.

**Disclosure of Interest:** None declared

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#### AB1050 REACTIVE ARTHRITIS DUE TO PARVOVIRUS B19 MAY BE OVERLOOKED IN ADULT RHEUMATOLOGY

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**Background:** In 1991 parvovirus B19 analyses, for the 5th disease of childhood, were established in Denmark, revealing the first epidemic. Prior to this, erythema infectiosum, "slapped cheek appearance" and reactive arthritis were only clinical diagnoses. A project in the PhD thesis Human Parvovirus B19 Erythrovirus – Methods established for *Virological and Diagnostic Aspects 2006* APMIS 120;114:1–121, revealed that 35.4% of 3.628 pregnant women were susceptible to parvovirus B19 infection.

**Objectives:** To present manifestations of parvovirus B19 in a susceptible adult population

**Methods:** During the years 2011 2014 and 2017 the following patients were admitted.

**Case 1:** A 61-year-old woman with rash and thrombocytopenic purpura in April 2011. Routine blood tests, RF, anti-CCP, tuberculosis, ANA and anti-ds DNA, serological tests for viral and autoimmune hepatitis were performed. Also ECG and finally, parvovirus B19 IgM and IgG, PCR for Parvovirus B19 was performed, June 2011

**Case 2:** A 52-year-old woman with rash, swollen joints and pericarditis in May 2011

**Case 3:** A 45-year-old woman with swollen joints, March 2011

**Case 4:** A 45-year-old woman with swollen joints and rash, November 2014

**Case 5:** A 68-year-old man admitted to the Department of Dermatology and diagnosed with Sweet's Syndrome, severe anaemia and swollen joints, September 2014

**Case 6:** A 62-year-old woman transferred due to parvovirus B19 positive IgM and IgG antibodies with reactive arthritis and itching skin rash, June 2017

All six patients were tested as mentioned above in Case 1.

**Results:** In all 6 patients, routine tests were normal. HBV, STD, ANA, anti-dsDNA, TB, RF and anti-CCP were negative. Parvovirus DNA by PCR, IgM and IgG antibodies were positive except for the last patient, who did not have PCR but a punch biopsy of her maculo-papular rash performed. Ultrasound revealed oedema and synovitis in the patients.

The 1st patient contracted parvovirus B19 from her 4-year-old grandchild, the 2nd during work in a daycare. They both had self-limiting infections and pericarditis resolved without treatment. The 3rd patient was also infected from daycare and her persistent synovitis, required DMARDs and biologic treatment.

The 4th patient was treated with DMARDs for one year. The 5th patient had severe anaemia for ½ year, almost overlooked due to Sweet's syndrome but his anaemia (due to replication of the parvovirus in erythroblasts) was finally diagnosed. The patient continues treatment for Sweet's Syndrome at the Department of Dermatology.

The 6th patient slowly recovered from her skin rash and reactive arthritis.

**Conclusions:** The 5th disease of childhood was almost overlooked in 6 patients probably due to their ages. Therefore, clinicians must be aware of the need for parvovirus B19 analyses in seronegative RA patients. Parvovirus B19 occurs as epidemics approximately every 3rd year as an occupational risk, jeopardising

patients' female family members who may be pregnant and develop foetal hydrops and anaemia necessitating intrauterine blood transfusion at a Foetal Medical Centre.

**Disclosure of Interest:** None declared

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#### AB1051 BRUCELLOSIS IN RHEUMATOLOGY: A STUDY OF 27 CASES IN TUNISIA

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**Background:** Brucellosis is an endemic zoonosis in the Mediterranean basin. The osteo articular localization, although rare, remains redoubtable.

**Objectives:** The aim of our work is to study the characteristics of osteoarticular brucellosis in Tunisia.

**Methods:** This is a descriptive retrospective study including 27 cases of osteoarticular brucellosis, collected in a rheumatology department over a period of 12 years (2006–2017)

**Results:** The Sex Ratio Female/male was 1.07 with an average age of 50.9 years.<sup>15–76</sup> Diagnosis delay was 5.9 months [0.3–13]. The diagnosis of spondylo-discitis was retained in 23 patients (85.2%) and sacroiliitis in 4 cases (14.8%). Spinal or sacroiliac pain was found in all patients. Fever was present in 22 patients, sweat in 11 patients, loss of weight or appetite were respectively found in 16 and 12 patients. Eleven patient reported fatigue.

Laboratory examination found high erythrocyte sedimentation rate in 23 patients with an average of 69.4 mm.<sup>10–120</sup> CRP was elevated in 26 patients with an average of 59.6 mg/L [3.3–237], the WBC average was 9451 elements/ml [5550–14 000]. Wright serology was positive in all cases, Rose Bengal was positive in 15 cases, and IFI was positive in 3 cases. *Brucella melitensis* was isolated in blood cultures in 3 cases.

Standard X Rays showed disk involvement in 21 patients, vertebral lesions in 20 cases and sacroiliitis in 4 patients. Sectional imaging (MRI or CT) was performed for all patients confirming standard X rays data and showing abscess in 13 patients and epiduritis in 7 patients.

The most affected spinal segment was the lumbar one (13 cases), cervical localization was found in 5 cases and thoracic in only 1 case. The spondylitis was multifocal in 2 cases.

Spinal disc biopsy was performed in only 4 cases, neither anatomopathologic nor bacteriological examination were conclusive.

The treatment was based on the cycline and rifampicin combination for an average duration of 4.5 months.<sup>3–9</sup>

The evolution was favourable in the majority of the cases with a relapse in only 2 cases.

**Conclusions:** Osteoarticular brucellosis is a focal form of brucellosis, the most frequent location is spinal and whose adequate treatment allows a favourable evolution.

**Disclosure of Interest:** None declared

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#### AB1052 COMPARISON OF SEVERAL BIOMARKERS (MMP-2, MMP-9 AND ITS INHIBITOR TIMP-1, CTX-II, CALPROTECTIN AND COMP) IN THE SYNOVIAL FLUID AND SERUM OF PATIENTS WITH AND WITHOUT SEPTIC ARTHRITIS

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**Background:** Diagnosing septic arthritis (SA) is an emergency, and for a diagnosis to be made a microorganism must be found in the synovial fluid or blood culture. Besides direct bacteriological examination, which is positive in only 25% to 50% of cases, no laboratory examination can differentiate SA from other forms of arthritis.

**Objectives:** To assessed the performances of several serum and synovial biomarkers (matrix metalloproteinase [MMP]–2, MMP-9, the metalloproteinase inhibitor [TIMP]–1, cartilage oligomeric matrix protein [COMP], C-terminal telopeptide of type II collagen [CTX-II], and calprotectin [CALP]) for discriminating between septic and non-SA in a population of patients with suspected SA.

**Methods:** Using the ELISA technique, a number of potential biomarkers (MMP-2, MMP-9, TIMP-1, COMP, CTX-II, and CALP) were measured in the synovial fluid and serum of 39 patients with suspected SA (of whom 21 had SA and 18 non-SA). The levels of the various markers were compared on univariate and then multivariate analysis using logistic regression.

**Results:** The two groups were similar in terms of age, gender, history of diabetes and type of joint affected. SA patients had higher whole blood white blood cell counts ( $p=0.03$ ) but similar C-reactive protein levels. Synovial fluid was more frequently turbid in septic cases than in non-septic ones.

Serum TIMP-1 ( $p=0.003$ ), synovial MMP-9 ( $p=0.002$ ), serum ( $p=0.03$ ) and synovial CTX-II ( $p=0.004$ ), and serum ( $p=0.04$ ) and synovial CALP ( $p=0.03$ ) were significantly higher in the septic group than in the non-septic group. The AUCs for diagnosing SA of synovial MMP-9, serum TIMP-1, synovial CTX-II, and serum and synovial CALP were, respectively, 0.84, 0.79, 0.81, 0.7 and 0.72.

A combination of serum TIMP-1 and synovial CTX-II led to 75% sensitivity and 94% specificity for diagnosing SA (AUC 0.89) and correctly classified patients in 86% of cases.

Serum TIMP-1 and synovial CTX-II did not correlate with each other ( $r=0.1$ ) and did not correlate with C-reactive protein ( $r=0.4$  and  $r=0.25$ , respectively) or synovial white blood count ( $r=-0.04$  and  $r=0.27$ , respectively).

**Conclusions:** The combination of two laboratory measurements, serum TIMP-1 and synovial CTX-II, may make it possible to differentiate SA from other forms of arthritis in 86% of cases. These results need to be confirmed in larger samples of patients.

**Disclosure of Interest:** None declared

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AB1053

#### ADVERSE EFFECTS AND THEIR CONSEQUENCES IN PATIENTS WITH CHRONIC INFLAMMATORY ARTHROPATHIES IN TREATMENT WITH BIOLOGICAL THERAPY

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**Background:** The introduction of biological therapies (BT) for the treatment of chronic inflammatory arthropathies (CIA) has improved the prognosis of these diseases and the quality of life of patients. However, the safety of these drugs in the long term continues to be an aspect of interest.

**Objectives:** This study aims to review the safety of BT in patients with CIA and the consequences of these adverse effects for patients and the health system under daily clinical practice conditions.

**Methods:** A descriptive, observational and retrospective study was performed. All patients with CIA: rheumatoid arthritis (RA), ankylosing spondylitis (AS) and psoriatic arthritis (PsA) who started BT (abatacept, adalimumab, certolizumab, etanercept, golimumab, infliximab, tocilizumab and ustekinumab) from January 2009 to January 2017 in the Rheumatology Department of the Sanitary Area of Vigo (Spain) were included. Demographic variables (age, sex), variables related to CIA and their comorbidities: clinical and analytical data (CRP, ESR, haemoglobin, DAS and BASDAI) and years of disease evolution and variables about BT: concomitant treatment (glucocorticoids, methotrexate and leflunomide), persistence, adherence and number of lines were collected. Variables about the adverse effects (AEs) of BT: type and clinical consequence, requirement for additional visits to the Rheumatology clinic, visits to the Emergency Department or need for hospital admission was also collected.

**Results:** Three hundred sixty-two patients and 478 BT lines (250 lines in patients with RA, 119 with AS and 109 with PsA) were analysed (mean  $\pm$ SD of BT lines:  $1.7 \pm 1.1$  per patient). In 301 (63.0%) BT lines, some AEs occurred. In total, 683 AEs were detected (0.57 AEs per patient and year of treatment). The most frequent types of AEs were: bacterial infection (0.39 events per year of BT), viral infections (0.04 events per year of BT), fungal infections (0.04 events per year of BT), reactions related to the administration of BT (0.03 events per year of BT) and cardiovascular alterations (0.02 events per year of BT). Certolizumab and abatacept were the drugs that were more associated with bacterial infections: 0.82 and 0.69 per year of BT, respectively. Infliximab was the BT that was less associated with bacterial infections: 0.24 per year of BT. There were 7 deaths in probable relation with the AEs (4 bacterial infections, 1 cardiovascular event and 2 solid tumours). The AEs caused 71 hospital admissions (668 days of hospital stay), 113 hospital emergency room visits and 42 urgent visits to the Rheumatology Department. Sixty percent of the AE were managed from Primary Care without having to go to the hospital. The AEs caused a definitive interruption of BT in 51 episodes and a switch to a different BT in 52 episodes.

**Conclusions:** In our setting, patients with CIA on BT have an incidence of 0.57 AE per patient and year of BT. Infection (particularly bacterial) is the most frequent AE. Although more than 50% of these AEs are managed from Primary Care, they imply a high consumption of hospital resources.

**Disclosure of Interest:** None declared

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AB1054

#### FACTORS ASSOCIATED WITH TUBERCULOSIS IN RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is associated with infections that are favoured by the disease itself or by its treatments. Tuberculosis (TB) is a severe infection that can occur in patients with RA, especially with the use of anti TNF.

**Objectives:** We aimed to estimate the incidence of TB in RA patients and identify factors associated with TB during RA.

**Methods:** This is a retrospective study of RA patients according to ACR/<sup>EULAR</sup> criteria<sup>2010</sup> collected in rheumatology department during the period from April 2010 to April 2015. Diagnosis of latent or patent TB was made as part of the pretreatment screening (biotherapy) or if signs of infection occurred.

**Results:** During the study period, 150 RA patients (124 women and 26 men) were enrolled. The mean age was 57.09 years.<sup>25-85</sup> Mean disease duration was 7.52 years.<sup>1-26</sup> Rheumatoid Factor was positive in 79% of cases. Eighty eight per cent of patients received corticosteroids with a mean dose of 10 mg/day.<sup>5-20</sup> All patients were treated with at least one conventional synthetic disease-modifying antirheumatic drug (methotrexate, sulfasalazine and leflunomide in respectively 87%, 37% and 7% cases) and only 36 (24%) patients received biotherapy. A history of patent TB treated appropriately and prior to RA, was found in 5 patients (3%): 3 pulmonary TB and 2 lymph node forms. The pretreatment test showed 11 cases of latent TB (30%). No relapsed TB was reported on RA treatment. Nine cases (25%) of new active TB were noted during biotherapy: 5 pulmonary TB (under infliximab, adalimumab and tocilizumab), 2 lymph nodes TB (under infliximab) and 2 urogenital TB (under infliximab). In our study, factors associated to TB infection were an advanced age, high level of C-reactive protein, a history of diabetes, dose of steroids  $\geq 7.5$  mg/day and dose of Infliximab  $> 3$  mg/kg (table 1).

**Abstract AB1054 – Table 1.** Factors associated to TB in RA patients

Factors	Odds ratio	P
Age	1.7	0.02
Sex: male/female	0.3	0.5
Diabetes	1.6	0.04
Erythrocyte sedimentation rate (mm)	0.6	0.7
C reactive protein(mg/l)	1.5	0.03
RA duration	0.95	0.31
Corticosteroid duration	0.9	0.45
Dose of steroid $\geq 7.5$ mg/day	11	0.01
Dose of methotrexate	0.5	0.64
Dose of Infliximab $> 3$ mg/kg	1.7	0.04
Infliximab	0.95	0.34
Adalimumab	0.9	0.72
Tocilizumab	0.8	0.25

**Conclusions:** Our study showed that RA patients were exposed to a higher risk of TB, especially when using anti TNF therapy with increased incidence of extra pulmonary TB. Understanding associated factors with TB may lead to establish a continuous monitoring in order to improve the quality of care.

**Disclosure of Interest:** None declared

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AB1055

#### BRUCCELLAR SPONDYLODISCITIS: DO MRI SIGNS OF SEVERITY INFLUENCE THE DURATION OF THE TREATMENT

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**Background:** Brucellar spondylodiscitis is rarely associated with neurological involvement. Magnetic resonance imaging has high sensitivity for detecting the paravertebral and epidural extension

**Objectives:** The purpose of this study was to determine the influence of the MRI severity signs on the treatment duration

**Methods:** A retrospective study of 27 patients with Brucellar spondylodiscitis during a period of 17 years [2000–2016] was performed. Diagnosis was made on clinical presentation, laboratory findings, radiographic evidence and Brucellar seroagglutination tests. Three patients underwent CT scans and a spinal MRI was carried out for 24 patients. All of them received antibiotic treatment based on a combination of Rifampicin and Doxycycline of varying duration

**Results:** Ten women and 17 men were included. The mean age was 54 years. Twenty-six patients suffered from spinal pain (96.3%) and 12 patients had radiculargia (44.4%). The lumbar spine was the most frequently involved region (59.3%), followed by the dorsal spine (18.5%) and the cervical spine (11.1%). The



neurological examination showed no abnormalities. Spinal MRI showed paravertebral abscess in 56.5% of cases. Seventeen patients (73,9%) had epiduritis and 9 patients (39,9%) had spinal cord compression on the MRI. An abnormal signal of the spinal cord was observed in 2 cases (8,7%). All patients received a combination of Rifampicin and Doxycycline. The mean duration of the antimicrobial treatment was 8 months. There was no statistically significant association between the occurrence of abscesses, epiduritis, spinal cord compression, abnormal signal of the spinal cord on the MRI and the duration of treatment ( $p=0.935$ ,  $p=0.929$ ,  $p=0.379$ ,  $p=0.889$  respectively).

**Conclusions:** MRI of the spine frequently revealed signs of severity in brucellar spondylodiscitis patients, although without clinical expression. Despite their severity these signs did not result in a longer period of antibiotic therapy

**Disclosure of Interest:** None declared

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AB1056

#### DIAGNOSIS VALUE OF PERCUTANEOUS SPINAL NEEDLE BIOPSY IN BRUCELLAR SPONDYLODISCITIS

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**Background:** spondylodiscitis is a serious condition with a large variety of infectious etiology. Vertebral biopsy is needed to perform the microbiologic diagnosis when no causative organism is identified. CT-guided percutaneous spinal biopsy (CTSB) may reduce the risk of contamination and complications.

**Objectives:** The aim of this study is to determine the contribution of CTSB to the diagnosis of Brucellar spondylodiscitis.

**Methods:** we conducted a retrospective study on 27 patients admitted for Brucellar spondylodiscitis over a 17 years period [2000 to 2016]. The etiological diagnosis was based on Brucella agglutination test which was positive for all patients. Twelve patients had a CTSB with cyto-bacteriological and histological tests.

**Results:** twenty seven patients (17 men and 10 women) with a mean age of 54 years were included. Twenty six patients (96,3%) reported a spinal pain. This pain involved the lumbar spine (59,3%), the dorsal spine (18,5%) and less frequently the cervical spine (11,1%). Eight patients reported lombosciatica (29,6%). An etiological doubt subsisted in 12 cases and a CTSB was performed. Culture results were negative for 11 biopsy samples and one culture was positive to Staphylococcus in a case of a co-infection. The results of the histological examination showed chronic non-specific inflammation in 92,3% of cases. An infectious etiology was suspected histologically in 53,8% of cases and particularly of a pyogenic germ (23,1%). The biopsy was not contributive in one case

**Conclusions:** Our results suggest that CT-guided spinal biopsy is not useful to diagnose Brucellar spondylodiscitis. However, the absence of tubercloid granuloma and caseous necrosis helped ruling out the tubercular origin

**Disclosure of Interest:** None declared

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AB1057

#### BRUCELLAR SPONDYLODISCITIS: THE IMAGING FINDINGS

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**Background:** Brucellar spondylodiscitis is an important complication of brucellosis that can cause neurologic involvement and spinal deformities if not appropriately treated. Imaging examination is a major key in diagnosis

**Objectives:** The aim of this study was to report the imaging findings in brucellar spondylodiscitis

**Methods:** We performed a retrospective study including 27 patients with Brucellar spondylodiscitis over a period of 17 years from 2000 to 2016. Diagnosis was made on clinical presentation, laboratory findings, radiographic evidence and Brucellar seroagglutination tests. All patients underwent X-rays of the involved spine levels. Spinal computed tomography (CT) was carried out in 13 cases and spinal MRI in 24 cases

**Results:** seventeen men and 10 women aged from 33 to 75 years were included. Plain radiographs showed a disc space narrowing for 26 patients (96,3%) and an irregularity of the vertebral end plate in 16 cases (59,3%). A paravertebral abscess formation was detected for 3 patients. No obvious abnormalities were found in one case. CT scans of most patients revealed signs of spondylodiscitis (92,3%). This examination showed an erosion of the vertebral end plates (69,2%), intervertebral disc space narrowing (61,5%) and bone destruction (38,5%). The severity signs detected on the CTs were the soft tissue thickening (46,2%), abscesses formations (7,4%), epiduritis (30,8%) and one patient had a spinal cord compression. The 24 MRIs realised exhibited a signal abnormality of the vertebral body (95,7%) and the intervertebral disc (47,8%) in addition to disc space narrowing (73,9%) with erosions of the vertebral end plates (56,0%). The contrast enhanced T1-

weighted images showed marked enhancement of affected vertebrae and disc (78,3%). Thirteen patients had abscesses formations (56,5%), 17 had epiduritis (73,9%) and 9 patients (31,9%) presented a spinal cord compression on MRI. Brucellar spondylodiscitis involved one spinal level in 23 cases whereas multilevel involvement was found in the 4 others

**Conclusions:** plain radiographs and spinal CT scans lack sensitivity in diagnosing brucellar spondylodiscitis and spinal MRI remains the referential imaging modality to recognise early bone infection, allowing complete lesion topography and identifying the complications.

**Disclosure of Interest:** None declared

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AB1058

#### IS HEPATITIS B SURFACE ANTIGEN (HB S AG) ENOUGH ALONE AS A SCREENING TEST FOR HBV INFECTION IN RHEUMATIC DISEASE PATIENTS BEFORE STARTING IMMUNOSUPPRESSIVE THERAPIES?

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**Background:** Prevalence of hepatitis B virus in patients with rheumatic diseases has been reported differently among studies. The loss of immune control in these patients may result in the reactivation of HBV replication within hepatocytes. Considering the lifelong use of multiple anti-rheumatic drugs, screening for HBV is recommended before starting immunosuppressive or immunomodulatory therapy.

**Objectives:** The aim of this study was to select the best and simplest test for screening of HBV in rheumatic patients in Egypt.

**Methods:** This cross sectional study was carried out on 102 patients with different rheumatic diseases. Screening to all patients by hepatitis B surface antigen (HBsAg), hepatitis C virus (HCV) and human immune deficiency virus antibodies (HIV) were done. HBV core antibodies and real time PCR to detect HBV DNA were done.

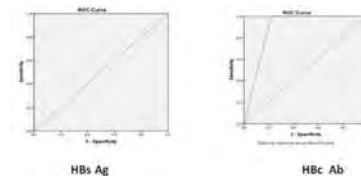
**Results:** The mean age of the patients was  $37.18\pm 12.37$ . 3.9% of them were males and 96.1% were females. We found that HBsAg was positive in two patients (2%) and negative in 100 patients (98%). HbCAb was positive in 24 patients (23.5%) and negative in 78 patients. however PCR for hepatitis B DNA was positive in 2 patients (2.0%) only who were positive for both HBsAg and HbC Ab. HBsAg had 100% Sensitivity, 100% Specificity, 100% PPV, 100% NPV and 99.0% accuracy. While antiHbC had 100% Sensitivity, 78% Specificity, 8% PPV, 100% NPV and 78% accuracy in screening of HBV.

**Abstract AB1058 – Table 1.** Serological diagnosis of HBV in rheumatic disease patients

	Negative No%	Positive No%	Total (n=102) No%
Anti-HBc:	78 76.5	24 23.5	102 100.0
HBs Ag	100 98.0	2 2.0	102 100.0
PCR	100 98.0	2 2.0	102 100.0

**Abstract AB1058 – Table 2.** The validity of HBsAg and HbCAb in relation to HBV DNA by PCR

validity of HBs-Ag in relation to PCR in diagnosis of HBV				
Sensitivity	Specificity	PPV	NPV	Accuracy
100.0%	100.0%	100.0%	100.0%	99.0%
validity of AntiHbC Ab in relation to PCR in diagnosis of HBV				
Sensitivity	Specificity	PPV	NPV	Accuracy
100.0%	78.0%	8.0%	100.0%	78.0%



**Abstract AB1058 – Figure 1.** Receiver operating characteristic (ROC) plot for "HBs Ag in relation to PCR in diagnosing HBV" on the left side & "HBc Ab in relation to PCR" on the right side.

**Conclusions:** We can conclude that screening for hepatitis B virus is essential for all patients with rheumatic diseases before starting therapies either steroids, immunosuppressive therapies or biologics. For financial issues especially in developing countries screening by HBsAg may be enough as an initial test especially if non biological therapies are used as it is superior to anti HBc for screening for HBV infection.

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AB1059

#### CONTRIBUTION OF CT-GUIDED DISCOVERTEBRAL BIOPSY DURING INFECTIOUS SPONDYLODISCITIS

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**Background:** Infectious spondylodiscitis is an infection involving the vertebral endplates and the intervertebral discs. The diagnosis is based on a combination of clinical symptoms, biological and radiological findings. Identifying the causative germ is sometimes difficult and a CT-guided discovertebral biopsy (DVB) might be of help, with varying success rates.

**Objectives:** The aim of this study was to assess the contribution of CT-guided DVB in the diagnosis of infectious spondylodiscitis in a rheumatological environment in Tunisia.

**Methods:** A retrospective study including patients diagnosed with infectious spondylodiscitis in the rheumatology department of Farhat Hached hospital, Sousse, Tunisia, between 1998 and 2017. Only patients who underwent a DVB for etiologic diagnosis of infectious spondylodiscitis were included in this study.

**Results:** Thirty five patients, with 12 (34.3%) women, were included. The mean age was 57.31±19.14 years [15–83 years]. All patients presented with back pain for 83.06±73.32 days [10–330 days], seven (20%) patients had fever and six (17.1%) patients had abnormal neurological signs on examination. The mean WBC, CRP and ESR levels were respectively 8170.83±3476.94 elements/mm<sup>3</sup>, 50.22±59.22 mg/L and 86.85±50.74 mmh1. The affected levels were the lumbar in 23 (65.7%) cases and dorsal spine in 9 (25.7%) cases. Three patients (8.6%) had both dorsal and lumbar spondylodiscitis.

First DVB was contributive in 11 (31.4%) cases. Isolated germs were staphylococcus aureus in 4 (36.4%) cases, tuberculosis in 3 (27.3%) cases, and brucellosis, coagulase negative staphylococcus, enterobacter cloacae, streptococcus oralis in one case each. Only one patient underwent a second DVB attempt, which was contributive, isolating a staphylococcus aureus. The rest of patients were treated based on late bacteriological findings (2 cases of brucellosis, 2 cases associated with Escherichia coli urinary infection and 1 case with pulmonary tuberculosis), or presumption arguments (6 cases treated as pyogenic infection and 12 cases as tuberculosis).

**Conclusions:** DVB remains essential for the positive diagnosis of infectious spondylodiscitis. Nevertheless, its bacteriological insufficient contribution should not delay therapeutic management based on presumption arguments.

**Disclosure of Interest:** None declared

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AB1060

#### WHIPPLE DISEASE WITH INITIAL PRESENTATION AS NON-EROSIVE SERONEGATIVE POLYARTHRITIS: A CASE REPORT FROM A SINGLE CENTRE

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**Background:** Whipple disease (WD) is a rare disease caused by the bacterium *Tropheryma whippelii* (TW), which manifestations may range from joint and GI-tract involvement to severe neurological complications.

**Objectives:** To present a clinical case of WD with non-erosive seronegative polyarthritis, sacroiliitis, abdominal and CNS involvement, and immune reconstitution inflammatory syndrome after antibiotic therapy.

**Methods:** Case report. Prospective follow-up of the patient E. with WD, who was diagnosed HLA-B27-negative nonerosive seronegative rheumatoid arthritis in 2013. The disease was partially responsive to glucocorticoids with temporary effect to different DMARDs (MTX, leflunomid, etanercept, abatacept, tocilizumab either as monotherapy or in combination).

**Results:** A 54 y.o. male patient E. was admitted to the Rheumatological department with complaints of joint swelling, low back pain, weight loss, diarrhoea, headache and low grade fever. Peripheral joint arthritis appeared about 4 years ago with progressive worsening of general condition and development of additional complaints during the past year. From 2013 to 2017 the patient received in-hospital and outpatient treatment because of active seronegative polyarthritis without sufficient effect. On admission: clinical examination and joint ultrasound (US) investigation revealed the signs of polyarthritis. Neurological evaluation showed organic psychiatric disorder with signs of pseudodementia, bradykinesia without focal neurological deficits.

Because of both incomplete responsiveness to DMARD-therapy and suspicion of chronic infection or malignant neoplasm, abdominal US and transthoracic echocardiography, gastroscopy, colonoscopy, immunofixation, bone marrow biopsy, chest X-ray and bone scintigraphy, tests for viral hepatitis (B,C), HIV, Lues and QFT-Tb were performed, however without objective evidence of the cause. PET-CT was performed as well, but showed no signs of malignancy or infection. MRI revealed bifrontal brain atrophy, low-grade bilateral sacroiliitis and degenerative changes of the cervical spine.

For differential diagnosis PCR stool investigation for TW was performed and was positive. Upon the suspicion of WD duodenoscopy with duodenal biopsy were done. Histological examination showed PAS-positive macrophages, typical for WD. Immunohistochemical analysis also supported the diagnosis. PCR investigation of liquor and synovial fluid from ankle joint for TWi were also positive. Antibiotic treatment using a 2 week course of parenteral Ceftriaxon 2 g/day was initiated. On the third day of the treatment the patient developed immune reconstitution inflammatory syndrome with febrile temperature and increased inflammatory markers. The symptoms regressed after additional prednisolon 20 mg/day prescription. Because of organic brain syndrome, administration of Co-trimoxazole was recommended. Under the antibacterial therapy the patient had rapid positive response. PCR stool test in October 2017 didn't detect TW.

**Conclusions:** This presentation emphasises the importance of excluding a rare infection as a cause of atypical inflammatory arthropathy. In patients with seronegative rheumatoid arthritis or axial and peripheral spondyloarthritis, who don't adequately respond to immunosuppression, Whipple disease should be taken into account.

**Disclosure of Interest:** None declared

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AB1061

#### MULTIFOCAL SPONDYLODISCITIS IN IMMUNOCOMPETENT PATIENTS

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**Background:** The prevalence of Infectious spondylodiscitis (SPD) has decreased recently with the development of effective means of prevention. Multifocal forms are more common in immunocompromised persons, but may be seen in immunocompetent ones. They are severe, and fortunately remain rare.

**Objectives:** The aim of our study was to report the clinical, biological, radiological and therapeutic features of multifocal SPD in immunocompetent patients.

**Methods:** A retrospective study was performed including patients hospitalised in the department of rheumatology between January 2007 and December 2017. Clinical data, laboratory findings and radiologic features were evaluated.

**Results:** Six patients were included. Their mean age was 53 years.<sup>34-81</sup> No comorbidities were found in all patients. The interval between the beginning of the symptomatology and the diagnosis was 3 to 6 months. Fever was noticed in 4 cases. All the patients had inflammatory spinal pain. Two patients had neurologic deficiency: one spinal compression and one root compression. The localization of the infection was lumbar and thoracic in 3 cases, cervical in 1 case and lumbar in 2 cases. MRI showed epiduritis in 3 cases and paravertebral abscess in 1 case. The infectious agent was identified by blood cultures in 1 case (*Staphylococcus Aureus*), by disco vertebral biopsy in 3 cases (tuberculosis) and by brucella serology in 2 cases. All patients underwent antibiotic therapy and immobilisation with a good outcome, only one patient needed surgery aiming to decompress the spinal cord. Investigation for immunodeficiency was negative in all patients.

**Conclusions:** Multifocal SPD in immunocompetent patients remains rare. Its etiology is dominated by tuberculosis. The most frequent localizations are lumbar and thoracic spine.

**Disclosure of Interest:** None declared

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**AB1062 RISK FACTORS FOR MORTALITY AFTER TUBERCULOUS ARTHRITIS**

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**Background:** Tuberculosis arthritis is an emerging international problem despite advances in the methods of diagnosis and treatment; it is still prevalent in developing countries and on the increase in developed ones.

**Objectives:** Patients with tuberculous (TB) arthritis increase mortality This study investigated to search for the risk factors of mortality in TB arthritis.

**Methods:** We retrospectively reviewed patients with TB arthritis who admit to Kaohsiung Chang Gung Memorial Hospital January 2001 to December 2015. The long-term outcomes of the patients were analysed.

**Results:** A total of 281 patients (124 females and 17 males; mean age: 64.86 ±14.51 years) were enrolled. At the end of the study, 229 patients were alive and 52 had died. The mean follow up period were 8.31±4.52 years. The patients who were old age (p=0.004, HR=1.038, 95% CI 1.012–1.065), liver disease (p=0.036, HR=2.571, 95% CI 1.062–6.224) and underlying cancer (p=0.001, HR=3.640, 95% CI 1.725–7.679) had a significantly higher mortality rate than others.

Abstract AB1062 – Table 1

	Regression coefficient	SE	P value	HR	95.0% CI for HR	
					Lower	Upper
Age	0.037	0.013	0.004	1.038	1.012	1.065
Gender	-0.057	0.320	0.859	0.945	0.505	1.769
BMI	-0.025	0.044	0.573	0.976	0.896	1.063
cancer	1.292	0.381	0.001	3.640	1.725	7.679
Steroid use	-0.173	0.398	0.664	0.841	0.385	1.836

**Conclusions:** When we treat TB arthritis, old age and underlying liver and cancer history should paid more attention to decrease the risk of mortality.

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**Fibromyalgia**
**AB1063 SWALLOWING DIFFICULTY IN FIBROMYALGIA: REAL OR MYTH?**

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**Background:** Fibromyalgia Syndrome (FMS) is a chronic disease that the most common disease in medical practice. This syndrome is including some general symptoms such as chronic pain, fatigue, tenderness and sleep disturbance, that can be seen in many disorders. Other than these, there are symptoms such as dysphagia, which are reported less frequently but have serious consequences such as aspiration. Studies in literature have been reported that this may not be a real swallowing difficulty and may be a symptom of somatization or may be due to adverse events such as drug side effects.

**Objectives:** This study was aimed to reveal the presence of dysphagia with objective diagnostic tests in FMS patients.

**Methods:** This study was conducted on 165 subjects. Patients (n=83) with FMS regardless of whether the complaint is difficulty swallowing as well as had ages between 18–65 were included in the study. Healthy volunteers (n=82) consisting of hospital staff and relatives of patients and sex, age and body mass index-matched with patients were included as control group.

Demographic and disease characteristics were recorded. Fibromyalgia Impact Questionnaire (FIQ) was used to assess severity of disease, functional disability and specific quality of life of patients. Also, the general quality of life of patients was evaluated with Short Form-36 (SF-36). All subject were evaluated with clinical screen test (10-item eating assessment tool=Eat-10) flexible fiberoptic endoscopic evaluation of swallowing (FEES) and electrophysiologic evaluation (EE) as well as ultrasonography (US).

The patients were divided into two groups according to the presence of complaints of difficulty in swallowing, which was taken with eat-10 as group 1 (with dysphagia) and group 2 (with normal swallowing). Patients ve healthy volunteers (group 3) were compared in terms of swallowing evaluation methods.

**Results:** Twenty-one (25.3%) of the 83 patients were defined with dysphagia (group 1) as well as 62 (74.7%) patients with normal swallowing (group 2) according to the eat-10 scale. The groups were similar in terms of demographic characteristics (p>0.05).

The mean disease severity of the all patients was between moderate and severe levels as well as there was a mild impact on quality of life. Disease severity and quality of life by using FIQ and SF-36 were significantly worse in patients with dysphagia (group 1) compared with normal swallowing patients (group 2) (p<0.05).

None of the subjects had dysphagia with endoscopic evaluation. All subjects could drink 20 ml of water which normal dysphagia limit.

Swallowing intervals in patients groups were significantly prolonged compared to healthy volunteers (p<0.05). There was no significant difference between the patient groups in swallowing intervals (p>0.05).

Ultrasonographic measurement results in healthy subjects were higher than patient groups (p<0.05). But ultrasonographic values of patients groups were similar (p>0.05).

**Conclusions:** Swallowing functions and structures are affected in patients with FMS, even though there are no symptoms of swallowing difficulty. Hence, while the main symptoms such as pain, fatigue and sleep disturbance are being questioned, a detailed evaluation including swallowing should be performed.

**Disclosure of Interest:** None declared

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**AB1064 EXPLORING CEREBROSPINAL FLUID PROTEOME IN FIBROMYALGIA**

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**Background:** Fibromyalgia (FM) is a heterogeneous disease of unknown etiology characterised by chronic widespread pain that affects up to 4% of population. Overlapping and heterogeneous symptoms of various chronic pain conditions complicate their diagnosis, emphasising the need for more specific biomarkers to improve the diagnosis and understand the disease mechanisms. Cerebrospinal fluid (CSF) flows in the ventricles within the brain and diffuses over the brain and spinal cord. Due to direct contact of CSF with CNS, content of CSF reflects biochemical changes in CNS making it an excellent source for biomarker discovery.

**Objectives:** In current study we aim to explore CSF proteome of FM patients utilising quantitative proteomics method based on stable isotope labelling of CSF peptides combined with multivariate data analysis (MVDA) in order to monitor the dynamics of the proteome while comparing to the CSF proteomes in patients with rheumatoid arthritis (RA) and other neurological diseases (OND) and define the potential biomarker candidates in FM. We also investigate, which protein products have been found in human CSF with respect to known "pain" genes,<sup>1</sup> human CSF proteome explored if these proteins represent any clear subgrouping of "pain proteins".

**Methods:** CSF samples from patients with FM, RA and control OND group were collected by lumbar puncture and equal aliquots were subsequently reduced, alkylated and digested by trypsin. Obtained peptides were labelled by stable isotopes and mixed prior sample fractionation. The degree of sample complexity was reduced by off-line peptide separation using HPLC instrumentation. Obtained 80 peptide fractions were combined into 10 fractions across the gradient area. Fractions were analysed by LC-MS/MS, proteins in acquired data were identified and quantified, and data was analysed using MVDA.

**Results:** Out of the 1422 proteins identified, 855 proteins were included in the quantitative data analysis. Comparing FM, RA and OND groups to each other using univariate testing we found 53 statistical significant proteins (q-value <0.05). Six out of these have been reported as "pain proteins" (Complement C4-A, Prostaglandin-H2 d-isomerase, Apolipoprotein D, Granulins, Pro-cathepsin H, and BMP and activin membrane-bound inhibitor homolog).

**Conclusions:** We have employed quantitative proteomics methods combined with extensive bioinformatics data analysis to investigate differences in proteome profiles in CSFs obtained from patients with FM, and identified six differentially expressed pain proteins of various functions in CSF of FM patients. The involvement of these proteins in the disease pathogenesis as well use of the identified proteins as potential biomarkers should be investigated.

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AB1065

**PRELIMINARY FINDINGS OF A 2-MONTHS ACUPUNCTURE INTERVENTION ON SYMPTOMATOLOGY AND QUALITY OF LIFE IN PATIENTS WITH FIBROMYALGIA**

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**Background:** Acupuncture is frequently used in the treatment of different chronic pain conditions. In Fibromyalgia (FM) the evidences available are somewhat conflicting, and the correct positioning of such kind of therapy has not yet precisely defined.

**Objectives:** To assess the response to a single course of acupuncture in patients with FM non-responsive to the usual pharmacological treatment.

**Methods:** Consecutive FM patients with unsatisfactory response or intolerance to the pharmacological treatment (duloxetine and/or pregabalin) were involved in this study. Unsatisfactory response was defined by the presence of a revised Fibromyalgia Impact Questionnaire (FIQ-R) total score  $\geq 40$  and of a Patient Health Questionnaire 15 (PHQ15)  $\geq 5$  after 3 months of stable pharmacological treatment. Acupuncture treatment consisted in 8 weekly sessions. The acupuncture formula, according to the Traditional Chinese Medicine indications, included the following points: LV3 +LI4 (to move Qi), ST36 +CV6+CV12 (to tonify Qi and Blood), GV20 (to raise Qi), and Ex-HN-3 (Yintang) (to calm the Shen), with acupuncture needle 0.25 x 25 mm with guide tube (Huanqiu). For each session needles were retained for 30 min. At baseline (before the first session) and at the end of the treatment course (after the eighth session) were collected the number of tender points (TP) and patient-reported outcomes (PROs). Differences between baseline and end of the acupuncture treatment were evaluated through the Wilcoxon test, results expressed in median values with 95% confidence interval (CI).

**Results:** Thirty-four subjects were enrolled in the study. Thirty-two patients (29 women, 3 men, mean age 49 years, range 18–72 years) completed the acupuncture treatment. In two patients (one woman and one man) the acupuncture therapy was stopped at the second session for poor tolerance to the needles. Eleven patients were in pharmacological therapy with pregabalin, nine with duloxetine, while 12 resulted intolerant both to pregabalin and duloxetine. From baseline, after the 2 months of acupuncture treatment, different parameters showed a significant improvement. Particularly, it has been observed a significant reduction in the TP number (17 [95% CI 16–18] to 10 [95% CI 8–12];  $p < 0.0001$ ), in the somatic symptoms assessed with the PHQ15 (13.5 [10.0–17.0] to 7.0 [6.0–10.0];  $p < 0.0001$ ), but also in the FIQ-R total score (61.5 [39.8–70.3] to [30.2–66.5];  $p = 0.0029$ ), in the Fibromyalgia Activity Score (FAS) (6.7 [4.8–7.7] to 4.6 [CI 3.2–6.1];  $p = 0.0017$ ), and in the Self-Assessment Pain Scale (SAPS) (4.5 [3.8–5.6] to 3.2 [2.9–4.2];  $p = 0.0192$ ). Interestingly, acupuncture revealed a good effect even in the neuropathic-like features of pain, measured by the painDETECT questionnaire (19.0 [15.0–25.0] to 14.5 [10.9–17.0]).

**Conclusions:** A 2 months acupuncture treatment provides an important global improvement in the health status in FM patients refractory/intolerant to the pharmacologic therapy. The strongest ameliorations are represented by the reduction in the TP number and in the somatic symptoms.

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AB1066

**DIABETES MELLITUS TYPE 2 RISK ASSESSMENT IN FIBROMYALGIA WOMEN**

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**Background:** Fibromyalgia (FM) female are less physically active than sedentary healthy women.<sup>1</sup> Low physical activity (PA) is among the leading causes of the major noncommunicable diseases, including diabetes mellitus type 2 (DM2).<sup>2–3</sup> An increased prevalence rate of FM in DM2 patients was revealed.<sup>4–5</sup> Risk of the development of DM2 in FM is unknown.

**Objectives:** The purpose of this study was to assess the risk of DM2 development in FM women.

**Methods:** The study involved 67 FM women<sup>ACR 1990 and 2010</sup> criteria) aged 42.6  $\pm$  7.8 (M $\pm$ SD) yrs without known diabetes, and 51 healthy controls (HCs) (all women) aged 44.8 $\pm$ 7.3 years. All participants were asked to complete a modified version of the Finnish Diabetes Risk Score (FINDRISC), which evaluates age, body mass index, waist circumference, current antihypertensive medication, frequency of fruit and vegetable consumption, physical activity, personal history of high blood glucose, and family history of DM2.<sup>6</sup> Fasting plasma glucose (FPG), oral glucose tolerance test (OGTT) and/or glycated haemoglobin (HbA1C) values were collected from all subjects to determine their glucometabolic state. Prediabetes was diagnosed by the presence of impaired FPG ( $\geq 100$  mg/dL to  $< 126$  mg/dL), impaired OGTT ( $\geq 140$  mg/dL to  $< 200$  mg/dL) and/or impaired HbA1c ( $\geq 5.7\%$  to  $\leq 6.4\%$ ).<sup>7</sup>

**Results:** According to the FINDRISC questionnaire low risk of DM2 in the next 10 years was found in 14.92% of FM women, intermediate risk—in 22.39%, moderate risk—in 29.85%, high risk—in 23.88%, a very high risk—in 8.96% of patients. In the group of HCs low risk of DM2 was found in 19.61% of women, intermediate risk—in 39.22%, moderate risk—in 21.57%, high risk—in 15.68%, a very high risk—in 3.92% of subjects. Therefore, in most of FM female (53,73%) risk of DM2 was detected as moderate-to-high, while in the majority of HCs (60.79%) it was detected as intermediate-to-moderate. Prediabetes was diagnosed in 11.94% of FM female compared to 5.88% among healthy women.

**Conclusions:** FM women are found to have increased risk of DM2 development compared to healthy women.

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AB1067

**PREVALENCE OF FIBROMYALGIA IN PATIENTS WITH PAINFUL KNEE OA**

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**Background:** Fibromyalgia (FM) has been conceptualised as a central nervous system (CNS) disorder, characterised by augmented sensory processing and inability to modulate pain effectively.<sup>1</sup> Global mean prevalence of FM is 2.7% with female/male ratio of 4:1. Several studies highlight the importance of central sensitisation (CS) as a significant manifestation of neuropathic pain symptoms in knee osteoarthritis (OA).<sup>2–3</sup> Possible similar mechanisms of chronic pain maintenance in OA – structural pathology, and FM – central sensitivity syndrome, provoke

further interest in investigation of any links between these conditions. Therefore, prevalence of FM in patients with painful knee OA is of considerable interest.

**Objectives:** The purpose of this study was to evaluate the prevalence of fibromyalgia (FM) in patients with painful knee OA.

**Methods:** The study involved 92 patients (63 females and 29 males) with painful knee OA<sup>ACR 1986 Osteoarthritis Knee Criteria</sup> with non-surgical management aged 59.4±14.3 (M±SD) yrs.<sup>4</sup> Radiographic findings for OA were classified according to Kellgren-Lawrence scale grading.<sup>5</sup> FM was diagnosed in these subjects if both <sup>ACR 1990</sup> and <sup>2010</sup> criteria were met.<sup>5-6</sup>

**Results:** FM was diagnosed in 21 painful knee OA patients (22.83%). Among female patients FM was confirmed in 19 from 63 subjects (30.16%) compared to 2 from 29 male patients (6.90%). No relationship was found between the radiologic stage of the knee OA and FM prevalence in the investigated subjects.

**Conclusions:** FM prevalence is relatively high in painful knee OA patients, mostly female. Further studies investigating possible FM impact on pain modulation, functional disability and quality of life in painful knee OA are needed.

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AB1068

#### PAIN, FATIGUE AND FUNCTIONAL IMPAIRMENT IN FIBROMYALGIA PATIENTS MAY BE REDUCED BY ADDING A CYCLE OF HYPERBARIC OXYGEN THERAPY (HBOT) TREATMENT

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**Background:** Fibromyalgia Syndrome (FM) is a persistent and debilitating disorder estimated to impair the quality of life of 2%–4% of the population. FM is an important representative example of central nervous system sensitisation and is associated with abnormal brain activity. The syndrome is still elusive and refractory. Hyperbaric oxygen therapy (HBOT) can rectify abnormal brain function underlying the symptoms of FM patients. Increasing oxygen concentration by HBOT may change the brain metabolism and glial function to rectify the FM-associated brain abnormal activity.<sup>1</sup>

**Objectives:** To evaluate the effect of HBOT on clinical symptoms in FM resistant to the usual pharmacological treatment

**Methods:** Thirty female patients, aged 21–67 years and diagnosed with FM at least 2 years earlier, and resistant to any pharmacological treatment were assigned to be added on with HBOT. The treated group patients were evaluated at baseline and after 10 and 20 HBOT sessions. Evaluations consisted of physical examination, including tender point count, extensive evaluation of quality of life. Study endpoints included assessments of pain (VAS), the FACIT Fatigue Scale which is a short, 13-item, that measures an individual's level of fatigue during their usual daily activities over the past week. A validated Italian version of the Fibromyalgia Impact Questionnaire (FIQ-R) was used to evaluate the level of functional impairment as well as the FAS index which is a short and easy to complete self-administered index combining a set of questions relating to non-articular pain, fatigue and the quality of sleep that provides a single composite measure of

disease activity ranging from 0 to 10. The HBOT protocol comprised 20 sessions, 3 days/week, 90 min, 100% oxygen at 2.5 ATA.

**Results:** The effect of the hyperbaric oxygen treatment on the clinical symptoms are summarised in table 1. HBOT treatments of treated group led to statistically significant improvements in the mean scores of pain and fatigue (FACIT) after 10 and 20 HBOT sessions (mean change of pain after 20 sessions  $-1.76 \pm 2.5$ ,  $p < 0.001$ ) (mean change of fatigue after 20 sessions  $5.93 \pm 2.10$ ,  $p < 0.001$ ) The FIQ-R score significantly improved following HBOT in the treated group (mean change after 20 sessions  $-12.89 \pm 17.04$ ,  $p = 0.001$ ). The FAS score showed a positive trend after 10 sessions and a significant improvement after 20 sessions (mean change  $-2.02 \pm 3.14$ ,  $p = 0.006$ ).

**Abstract AB1068 – Table 1.** Clinical data at baseline and after HBOT treatment

	Baseline	Follow up (10 sessions)	Paired samples t-test	Follow up (20 sessions)	Paired samples t-test
VAS PAIN	8.11±1.81	6.84±2.07	p=0.0062	6.32±2.58	p=0.0023
FACIT	20.42 ±7.06	23.76±6.82	p=0.0836	26.36±8.25	p=0.0069
FIQ-R total	68.04 ±3.90	59.83±4.41	p=0.0090	55.56±5.19	p=0.0019
FAS total score	8.14±0.47	7.07±0.50	p=0.0928	5.99±0.49	p=0.0065

**Conclusions:** These preliminary data show that HBOT may determine a significant clinical improvement in patients affected by FM and resistant to the common pharmacological treatment. However, further studies of large numbers of patients are required in order to confirm this preliminary finding and modify treatment strategies accordingly.

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AB1069

#### CHRONIC WIDESPREAD PAIN, SLEEP PROBLEMS AND PRESSURE PAIN THRESHOLDS IN A POPULATION SAMPLE

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**Background:** Chronic musculoskeletal pain is common in the general population and 11% report chronic widespread pain (CWP). A sensitisation of the nociceptive system has been proposed to be one possible mechanism behind CWP, a prerequisite for fibromyalgia (FM). A reduced pressure pain threshold (PPT) has been reported in subjects with FM, but also as an effect of bad sleep.

**Objectives:** The aim was to study pain thresholds in people with CWP in comparison with those having no chronic pain (NCP) or chronic regional pain (CRP), but also in relation to self-reported sleep problems.

**Methods:** From a 21 year follow-up of the Swedish population based Epipain cohort (n 1321), 146 subjects, with and without a report of chronic pain, were invited to a clinical assessment including measurement of PPT. Subjects were classified as having NCP, CRP or CWP, according to the definition of CWP in the <sup>ACR 1990</sup> criteria for FM, based on a pain mannequin presenting 0–18 body regions. Sleep problems (initiating sleep, frequent awakenings, not feeling rested, early awakening) were reported by Uppsala Sleep Inventory (four items scored from 1–5, best to worst). PPTs were measured in kPa at eight different anatomical sites representing upper, lower, left and right side of the body using the AlgoMed Computerised Pressure Algometer FPIX (Medoc Ltd. Advanced Medical Systems, Israel). A mean was calculated from all eight points to create a global pressure pain threshold (PPTg), where a lower PPTg indicated a higher sensitivity to pain. ANCOVA regression analysis was performed to study associations between PPTg and reports of chronic pain and sleep problems, controlled for age and gender.

**Results:** Out of 146 subjects, 89 (61%) were women. Mean age was 64.6 (SD 12.7) years. This sub-population from the Epipain cohort reported a high prevalence of CWP without significant difference between men and women (33.9% vs 44.9%;  $p = 0.411$ ). Women had lower PPTg than men (345.0 kPa vs. 563.9 kPa;  $p < 0.001$ ). Subjects classified as CWP had lower PPTg than those classified as NCP (362.0 kPa vs. 479.9 kPa;  $p = 0.003$ ). A report of CRP did not affect PPTg in

comparison with those reporting NCP (471.8 kPa vs. 479.9 kPa;  $p=0.855$ ). The number of reported pain regions correlated negatively with PPTg in women ( $r=-0.384$ ;  $p<0.001$ ) but not in men ( $r=-0.195$ ;  $p=0.149$ ). Subjects having a score of  $\geq 4$  for the sleep problem "frequent awakenings" had lower PPTg than those with a lower score (332.9 vs. 464.7;  $p<0.001$ ). This was also true, but with less difference, for the sleep problems "not feeling rested" (335.7 vs. 449.1;  $p=0.023$ ), and "early awakening" (353.0 vs. 452.6;  $p=0.020$ ), but not for "initiating sleep" (361.5 vs. 436.8;  $p=0.199$ ). In the ANCOVA analysis both a higher number of painful regions ( $B=-9.2$ ;  $p=0.016$ ) and more problems with frequent awakenings ( $B=-40.1$ ;  $p=0.003$ ) were associated to a lower PPTg, controlled for age and gender.

**Conclusions:** Subjects with CWP according to self-reported pain distribution were more sensitive to pain pressure than those with CRP and NCP, and so were also subjects reporting problems with sleep. In the clinic, self-report of CWP can be used as an indicator of pain sensitivity, but it is also important to assess sleep problems, and especially frequent awakenings and reports of not feeling rested.

**Disclosure of Interest:** None declared

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## Back pain, mechanical musculoskeletal problems, local soft tissue disorders

AB1070

### VARIATIONS IN THE LENGTH OF MUSCULOSKELETAL TEMPORARY WORK DISABILITIES IN PATIENTS INCLUDED IN AN EARLY INTERVENTION PROGRAM

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**Background:** Musculoskeletal disorders cause in Spain 23% of temporary work disability (TD) and they are the first cause of permanent work disability (PD). A study of early intervention (early assessment and immediate treatment by a rheumatologist) reduced TD days (39%) and evolution to PD (50%)<sup>1</sup>. Using the "Fit for Work" European coalition led by AbbVie, the program is implemented nationwide.

**Objectives:** The aim of this study is to analyse the variation in the number of days of sick leave in the patients included in an early intervention program comparing to usual average.

**Methods:** Observational cross-sectional study of a hospital cohort of outpatients referred during 18 consecutive months. The patients were referred for the first time to the Rheumatology Early Intervention consultation program because of temporary work disabilities due to musculoskeletal disorders. All of them received medical treatment; and underwent joints ultrasound, joint injections and learned exercises when needed. Patients whose disabilities were due to trauma or surgery were not included in the study.

**Results:** We evaluated 270 patients with a mean age of 48.9 years. 64% were women. The most frequently reported diseases were lumbar/sciatic pain (28.5%), shoulder pain (20%), neck pain (8%), knee pain (5.6%) and other arthralgias and tendinopathies (20%).

All patients received medical treatment, 38.5% underwent ultrasound examination and 19.2% received joint injections.

The pathologies with longest lengths of TD after the first visit to the rheumatologist were lumbar/sciatic pain (mean 40.6 days), neck pain (mean 33 days) and shoulder pain (mean 23.8 days). If we compare this data with the existent control group from San Carlos Hospital (Madrid), we can see a decrease of the days in sick leave of 29.5% in lumbar/sciatic pain (from 57.6 to 40.6 days), 11.7% in neck pain (from 37.4 to 33 days) and 36.3% in shoulder pain (from 37.4 to 23.8 days).

**Conclusions:** Early intervention by rheumatologists in patients with temporary work disability due to musculoskeletal disorders reduces the length of sick leaves. A quick diagnosis and assessment by specialists can improve the patient outcomes saving costs to health system.

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AB1071

### WHAT FACTORS AFFECT THE EFFECTIVENESS OF NSAIDS FOR ACUTE LOW BACK PAIN?

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**Background:** Nonsteroidal anti-inflammatory drugs (NSAID) are the main instruments for acute LBP (LOW BACK PAIN) treatment. However, up to now, factors that influence the effectiveness of NSAIDs have not been determined fully.

**Objectives:** To assess effects of some clinical and anamnestic factors on NSAIDs effectiveness in acute LBP.

**Methods:** The study group comprised 2078 patients (46.3±13.4 years, women 56.6%) with acute LBP treated in real clinical practice. 34.8% had first episode of LBP, 65.2% had second episode (an average of 2.6±1.4 episodes a year). Numerical rating scale (NRS) of 0–10 points estimated the level of pain. Initially, the pain level was 6.69±1.65, 57.0% of patients had severe pain ( $\geq 7$  NRS). Pain remained at rest in 32.0%, at night in 19.0%, stiffness was noted in 60.7%, radiating leg pain in 28.2%, sciatica at 9.6%. NSAIDs used 70.2% of patients in the history of LBP, 28.0% rated their effectiveness as good, 54.6% as moderate and 17.4% as low. Meloxicam 15 mg once daily was prescribed for a period of up to 2 weeks for all the patients. 86.1% of patients received meloxicam intramuscular injection (i/m) for 2 days, then per os, 13.9% only per os. 52.3% received muscle relaxants, 17.4% – B vitamins, per os or i/m. 21.6% of patients received PPI for the prevention of gastrointestinal complications. The study evaluated the frequency of LBP complete relief with NSAIDs for up to 2 weeks.

**Results:** The complete pain relief was in 75.2% of patients, the average NSAID use duration before pain ceased was 8.6±5.5 days. 83.7% of patients rated the effect of treatment as "good" or "excellent." Adverse reactions were noted only in 4.6% of patients, there were no serious complications. Female sex and the use of B vitamins did not influence the outcome of the treatment: odds ratio (OR, 95% confidential interval) 0.967 (0.795–1.177),  $p=0.763$  and 0.917 (0.804–1.1201),  $p=0.452$ . Age <65 years, the first episode of LBP and a good effect of NSAIDs in a history were associated with the best result of treatment: OR 2.053 (1.592–2.642),  $p=0.000$ ; 1.415 (1.09–1.836),  $p=0.009$ ; 1.937 (1.513–2.481),  $p=0.000$ . Severe pain ( $\geq 7$  NRS), pain at rest and at night, radiating leg pain and especially sciatica were associated with worse results: OR 0.599 (0.487–0.737),  $p=0.000$ ; 0.481 (0.393–0.588),  $p=0.000$ ; 0.559 (0.441–0.709),  $p=0.000$ ; 0.511 (0.413–0.631),  $p=0.000$ ; 0.346 (0.256–0.466),  $p=0.000$ . The combination of NSAIDs and muscle relaxants, in comparison with the monotherapy of NSAIDs, was associated with a lower incidence of pain: OR 0.827 (0.594–0.889),  $p=0.02$ .

**Conclusions:** Meloxicam 15 mg/day dosage is effective and safe for treating acute LBP. The sex of patients does not affect the outcome of treatment. Age <65 years, first episode of LBP and a good "response" to NSAIDs in history are associated with better treatment outcomes. Severe pain, the pain at rest and pain at night, radiating leg pain and sciatica are associated with the worst result. The combination of NSAIDs with muscle relaxants and B vitamins did not improve the outcome of the treatment.

**Disclosure of Interest:** None declared

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AB1072

### THE MEDIAN NERVE CROSS-SECTIONAL AREA MAY BE A PARAMETER OF FOLLOW- UP AFTER TREATMENT IN PATIENTS WITH CARPAL TUNNEL SYNDROME?

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**Objectives:** Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy in general population. Diagnosis of CTS depends on clinical symptoms, physical examination and electrophysiological findings. In recent years, diagnostic value of median nerve ultrasonography has increased particularly for the CTS. To aim of this study compare the electrophysiological and ultrasonographic findings at CTS patients who treated with splinting at night during three months.

**Methods:** The patients, who were diagnosed with mild or moderate CTS, received a fabricated night orthotic which held the wrist in a neutral position during three months. All patients were evaluated clinically, electrophysiologically, and ultrasonographically before treatment and at 3 months by blind physicians. Pain was evaluated using Visual Analogue Scale (VAS) Boston Carpal Tunnel Questionnaire was used to evaluate symptom severity and functional capacity. In electrophysiologic evaluation median nerve conduction studies was recorded. Median nerve cross-sectional areas (M-CSA) were measured by ultrasonography at the level of radio-ulnar joint, pisiform bone, and hook of hamate. After treatment, 68



patients were divided into two groups according to whether there was a 50% reduction in VAS.

**Results:** The study was completed with 68 patients and 114 hands. While in group 1, in which VAS reduction was less than 50%, there were 38 hands; in group 2, in which VAS reduction was more than 50%, there were 76 hands. There were no differences improvement of symptom severity, nerve conduction studies parameters, M-CSA at the level of radio-ulnar joint between groups. Improvement of functional capacity and decrease of M-CSA at the level of pisiform bone and hook of hamate were significantly better in group 2 ( $p < 0.05$ ).

**Conclusions:** After conservative treatment, while M-CSA was consistent with clinical findings, this consistency has not been observed with nerve conduction studies. M-CSA may be used to follow-up after receiving conservative treatment in patient with CTS.

**Disclosure of Interest:** None declared

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#### AB1073 THE EFFECTS OF LYMPHEDEMA SEVERITY ON DYNAMIC SCAPULAR CONTROL

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**Background:** Women with mastectomy are reported to have altered dynamic scapular control compared to the asymptomatic healthy individuals. However, the effects of breast cancer related lymphedema (LE) on scapular control has not been fully understood yet.<sup>1,2</sup>

**Objectives:** The aim of this study was to determine the impact of LE severity on scapular kinematics in breast cancer patients with moderate LE, severe LE and without LE.

**Methods:** 67 women who have undergone radical or modified radical mastectomy as part of the breast cancer treatment were included in the study. The study was approved by the local ethics committee of the university and all participants provided written informed consent. Individual's demographic and medical characteristics were recorded. By volumetric measurement, women were divided into 3 groups. Between the affected and non-affected extremities; the non-LE group (group 1,  $n=22$ ) had 0 and 200cc difference, the moderate LE group (group 2,  $n=18$ ) had 250–500cc difference, and the severe LE group (group 3,  $n=27$ ) had a difference of 500cc or more. 3-D analysis of the scapula was performed during the bilateral upper extremity elevation in the scapular plane with the 3D Motion Monitor-Electromagnetic System. Scapular kinematics in the scapular plane were recorded at 30°, 60° and 90° (during elevation and lowering phases) of the arm elevation in the affected side. Each measurement was repeated 3 times and the mean of 3 repetitions were recorded. Patient characteristics and scapular kinematics were analysed by Kruskal Wallis test and two-way repeated measures of ANOVA test, respectively.

**Results:** There was no significant difference between groups in terms of age (mean ages; group 1: 45.54±5.88, group 2: 52.05±6.63, group 3: 56.37±8.24 years) ( $p=0.08$ ). Regarding the Body Mass Index (BMI) (group 1: 25.57±2.92, group 2: 25.95±2.35, group 3: 28.93±1.02 kg/m<sup>2</sup>), it was found that group 3 had higher BMI scores than group 1 and 2 ( $p < 0.001$ ). The duration of LE (group 2: 22.38±23.1, group 3: 42.29±31.85 months) was higher in group 3 than the group 2 ( $p=0.004$ ). There were significant interactions for scapular upward rotation between groups ( $F_{4,11, 131,51} = 3.09, p=0.015$ ). It was observed that group 1 had higher scapular upward rotation at 60° and 30° of the lowering phase of the arm elevation trials than group 3 ( $p=0.013, p=0.004$ ). There was no significant interaction in terms of the scapular internal rotation ( $F_{4,37, 139,9} = 0.59, p > 0.05$ ) and posterior tilt ( $F_{5,05, 161,8} = 1.02, p=0.4$ ) among groups during the arm elevation in scapular plane.

**Conclusions:** The results of this study revealed that scapular upward rotation could be reduced by LE severity. LE severity might also be associated with BMI and LE duration. Further studies comparing LE patients with healthy individuals are needed to better understand the effects of LE severity on scapular kinematics.

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#### AB1074 IN DEGENERATIVE SPINE DISEASE REGULAR SHORT COURSES OF NSAIDS USE ARE ASSOCIATED WITH GREATER KIDNEY INJURY, COMPARED WITH CONTINUOUS NSAIDS INTAKE AND WITH ABSENCE OF NSAIDS TREATMENT

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**Background:** Nephrotoxicity in short-term or continuous NSAIDs administration is well-known problem of anti-inflammatory treatment. However, data about kidney injury in case of repeated short-term courses of NSAIDs treatment are limited. **Objectives:** of the present study was to evaluate the kidney functions in patients with degenerative spine disease (DSD), taking NSAIDs in repeated short courses, compared with kidney function of patients with constant NSAIDs intake and to the healthy individuals.

**Methods:** The study included 137 patients, taking NSAIDs for DSD. 97 patients used NSAIDs in repeated short-term courses (3–5 courses per year, 7–14 days each course). 40 patients had continuous NSAIDs intake (5 and more days per week during the 1 year before the study). In the control group were involved healthy persons, did not treated with NSAIDs during the last year ( $n=40$ ). Controls were sex- and age-matched with the DSD patients. Glomerular filtration rate (GFR) was calculated using CKD-EPI calculator. Albumin,  $\alpha$ 1-microglobulin and creatinine levels of urea were measured; albumin/creatinine and  $\alpha$ 1-microglobulin/creatinine ratios were calculated.

**Results:** Kidney function in DSD patients with NSAIDs intake and in healthy controls are presented in table 1.

**Abstract AB1074 – Table 1.** Kidney function in patients with short-term and continuous NSAIDs use and in healthy controls

Kidney function parameter	NSAIDs short courses, n=97	NSAIDs continuous intake, n=40	Controls, n=40
GFR, ml/min/1.73 m <sup>2</sup>	77.5 [68.0; 89.0]	86 [68.0; 92.2]	82.5 [70.8; 90]
Albumin/creatinine, mg/g	57.1 [33.8; 82.4]*#	32 [21.0; 44.4]*	25.0 [17.5; 32.9]
$\alpha$ 1-microglobulin/creatinine, mg/g	134.7 [77.5; 197.7]*#	66.0 [41.0; 112.3]*	12.9 [0.5; 18.1]

\* $p < 0.000$  for the difference with controls; # –  $p < 0.000$  for the difference with NSAIDs' continuous intake.

In patients with DSD and short NSAIDs' use a decrease in GFR of less than 90 ml/min/1.73 m<sup>2</sup> was evaluated in 61 (62.9%) of cases, GFR less than 60 ml/min/1.73 m<sup>2</sup> was detected in 11 (11.3%) patients. In patients with DSD and continuous NSAIDs use a decrease in GFR of less than 90 ml/min/1.73 m<sup>2</sup> was evaluated in 34 (85%) of cases, GFR less than 60 ml/min/1.73 m<sup>2</sup> was detected in 2 (12.5%) patients,  $p < 0.01$ , compared with controls and  $p > 0.05$  compared with short-term use. GFR less than 60 ml/min/1.73 m<sup>2</sup> was found in 11 (11.3%) patients with DSD and short NSAIDs intake and in 0 (0%) of healthy volunteers ( $p=0.026$ ). Albumin/creatinine ratio  $\geq 30$  mg/g was found in 74 (76.3%) patients with DSD with short-term NSAIDs use, in 22 (55%) patients with constant NSAIDs intake, and 9 (22.5%) healthy individuals ( $p < 0.01$  for all intergroup differences). An increased level of microglobulin/creatinine ratio was found in 66% patients with DSD (in 82.4% cases of short-term and in 25% of continuous NSAIDs use,  $p < 0.01$ ) and in 3 (7.5%) healthy individuals,  $p < 0.0001$ .

**Conclusions:** Decrease of the GFR less than 60 ml/min/1.73 m<sup>2</sup> and subclinical kidney injury in patients, treated with NSAIDs, was found frequently, than in healthy persons never treated with NSAIDs. The subclinical glomerular and tubular damage in patients with short-term courses of NSAIDs use exceeded glomerular and tubular changes in patients with constant NSAIDs use.

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#### AB1075 RELATIONSHIP OF SERUM CHOLECALCIFEROL (VITAMIN D3) LEVEL WITH MUSCULOSKELETAL SYMPTOMS

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**Background:** Patients suffering from generalised aches and pains, not adequately responding to treatment are usually considered as fibromyalgia, depression, chronic fatigue syndrome etc. But those patients need further

evaluation and low vitamin D is often the underlying cause. Both clinical and sub-clinical low level vitamin D is common.<sup>1</sup>

**Objectives:** To assess the relationship between musculoskeletal complaints and serum vitamin D<sub>3</sub>(cholecalciferol) level.

**Methods:** This prospective cross-sectional descriptive study was conducted during July 2017 to December 2017 in Chittagong, Bangladesh. Patients with common musculoskeletal complaints were enrolled. Each patient was screened to exclude common possibilities. Serum cholecalciferol was measured for each patient. Race, occupation, skin complexion, body mass index, sunlight exposure, covering of body with clothing's and use of sunscreen were taken under consideration in final analysis. Visual analogue scale (VAS; 1–10) was used to quantify all complaints. Correlation of serum cholecalciferol level with VAS score of individual complaints was analysed.

**Results:** A total of 110 patients (79 Female and 31 Male) were enrolled after screening 165. All of them were Bangladeshi of multi-ethnic Asian origin. Mean age was 46.5±12.8 years. Their skin complexions were pale white to white skin 45.5%, light brown 30%, moderate brown 11.8% and dark brown 12.7%. Most had (90.9%; n=100) inadequate sunlight exposure and 77.2% (n=61) women used Burkah (full covered dress). Mean vitamin D<sub>3</sub> level was 25.2±7.3 ng/ml. Vitamin D deficiency was (mean 17.3±2.8 ng/ml) observed in 30 (27.3%), insufficiency (mean 25.1±2.7 ng/ml) in 62 (56.4%) and normal level (mean 34.8±4.4 ng/ml) in 18 (16.4%). After classifying Vitamin D level in relation to symptoms it was found that majority of patients (81.2% to 90.3%; depending on complaints) had insufficient or deficient cholecalciferol level (table 1).

**Abstract AB1075 – Table 1.** Serum cholecalciferol status in different musculoskeletal complaints

Complaints Vit D <sub>3</sub>	Normal (≥30 ng/ml)		Insufficiency (20-<30 ng/ml)		Deficiency (<20 ng/ml)	
	n	%	n	%	n	%
	Myalgia (n=104; 94.5%)	16	15.4	60	57.7	28
Muscle cramp (n=104; 94.5%)	18	17.3	60	57.7	26	25.0
Generalised weakness (n=99; 90.0%)	18	18.2	56	56.5	25	25.2
Difficulty in climbing stairs (n=89;80.9%)	14	15.7	50	56.2	25	28.1
Fatigue (n=87; 79.1%)	13	8.1	51	58.6	23	26.4
Difficulty in squatting (n=84; 76.4%)	9	10.7	49	58.3	26	30.9
Pain in weight bearing joints (n=80; 72.7%)	11	3.7	49	61.2	20	25.0
Bone pain (n=73; 66.4%)	8	10.9	43	58.9	22	30.1

Significant negative correlation was found between the serum cholecalciferol level and VAS for difficulty in getting up from squatting position ( $r=-0.253$ ,  $p=0.008$ ) and positive correlation was found for muscle cramps ( $r=0.220$ ,  $p=0.021$ ). Correlations with remaining symptoms were not statistically significant.

**Conclusions:** Vitamin D status directly and indirectly influences musculoskeletal health. Hypovitaminosis D should consider in every patient with muscle cramp.

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#### AB1076 COMPLEX REGIONAL PAIN SYNDROME TYPE 1: WHICH TREATMENT?

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**Background:** The treatment of Complex Regional Pain Syndrome Type 1 (CRPS-I) is multidisciplinary.<sup>1</sup> It aims to minimise symptoms, pain, preserve functional ability and professional activity. Unfortunately, therapeutic possibilities are still very limited and there is no Gold standard.

**Objectives:** The purpose of our work is to evaluate the efficiency of four therapeutic modalities in the management of CRPS-I.

**Methods:** Retrospective study of 60 patients (21 men and 39 women) treated for CRPS-I. Four groups were identified according to therapeutic modalities used: rehabilitation alone (16 patients), Calcitonin associated with rehabilitation (15 patients), Bisphosphonates (BP) (Sodium Risedronate, 1 tablet per week, over an average duration of 1 month) associated with rehabilitation (20 patients) and Calcitonin in combination with BP and rehabilitation (9 patients).

**Results:** The mean age of the patients was 51±16.5 years. The average time of treatment was 2 months and the average duration of follow-ups was 7 months. Traumatic origin was found in 88.3% of cases. Distal radius fractures (DRF) were the most incriminated (40% of cases). The evolution was judged on pain reduction, vasomotor signs and on functional improvement.

For all etiologies combined, no statistically significant difference was found between the different groups ( $p=0.462$ ).

For patients with a DRF, a favourable outcome was noted in the BP group associated with rehabilitation in 85.7% of cases while it was only 42.9% for rehabilitation alone.

**Conclusions:** Our study concludes that the different therapeutic modalities evaluated for the treatment of CRPS-I had an efficiency close to each other with a superiority of BP. Oral Sodium Risedronate could therefore be proposed as a treatment for CRPS-I without marketing authorisation (MA).

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#### AB1077 INVESTIGATION OF FRAILTY, MOBILITY AND DAILY LIFE ACTIVITY IN ELDERLY

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**Background:** There are many factors that affect negatively mobility and daily life activity of older people. Frailty is one of these. frailty is a state of decline in physiologic reserve capacity and resiliency due to impairment in multiple physiologic systems, thereby causing vulnerability to death and adverse health outcomes.

**Objectives:** The aim of this study was to analyse gender differences in frailty, mobility and daily life activity score.

**Methods:** The study included 173 women, 124 men total 197 persons aged 65 years and older. The demographic information including age, height and weight, the individuals marital status, educational state, chronic diseases were taken. Elderly Mobility Scale (EMS), Edmonton Frail Scale (EFS) and KATZ were used to evaluate mobility, frailty and daily life activities level, respectively. Individuals were divided into groups according to their gender.

**Results:** There was significant difference between women and men in EMS ( $p=0.001$ ), EFS ( $p<0.001$ ) and KATZ scores (0.048). Frailty score were lower, mobility score and daily life activity score higher than women in men. In both men and women were found positively a relation between mobility and daily life activity ( $p<0.001$ ), were found negatively a relation between frailty and mobility, daily life activity ( $p<0.001$ ).

**Conclusions:** It was seen that female gender affected mobility, frailty and daily life activity. It is important that Strategies for preventing or delaying the predisposing factor of frailty need to address gender differences and determinants among women.

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## Paediatric rheumatology

AB1078

**APPLICABILITY OF THE CASPAR CRITERIA OF PSORIASIC ARTHRITIS IN A COHORT OF CHILDREN PATIENTS FOLLOWING IN A PAEDIATRIC RHEUMATOLOGY UNIT OF A TERTIARY HOSPITAL**

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**Background:** The ILAR consensus establishes classification criteria, dividing the JIA into 7 subcategories, with juvenile psoriatic arthritis (APsJ) being one of them. In the adult population, the CASPAR classification criteria are usually used to classify a patient with psoriatic arthritis. However, the two classifications have some differences that sometimes produce confusion

**Objectives:** To assess the applicability of the CASPAR classification criteria in a series of patients previously diagnosed in paediatric age of JPAs or undifferentiated arthritis by exclusion criteria to be male >6 years old and HLA B27 positive, comparing these with the ILAR classification criteria, through the study of clinical features

**Methods:** Retrospective cross-sectional observational study. Clinical, epidemiological, sociodemographic and analytical variables were collected from 30 patients previously diagnosed with JPAs (<16 years) or undifferentiated arthritis by exclusion criteria age >6 years in HLA B27-carrying male. It was assessed whether the patients met the ILAR classification criteria as well as the CASPAR classification criteria, which, unlike the previous ones, did not exclude HLA B27 positive patients, considered the family history of the 2nd degree and added a test radiographic

**Results:** The mean age at diagnosis was 11.23±4.6 years; 15 of them being women and 15 men. 15 (15/30) patients presented cutaneous psoriasis at some point during the follow-up, in 5/15 patients psoriasis began before arthritis while 7/15 patients were previously diagnosed with arthritis than cutaneous psoriasis; in 3/15 patients the diagnosis was simultaneous during the medical visit. 9 (9/30) patients presented a family history of 1st degree cutaneous psoriasis and 7/30 of them had a family history of 2nd grade psoriasis. Of the total number of patients, 10 of them would not meet the ILAR classification criteria, 8 because they presented as exclusion criteria being male, HLA-B27 positive and >6 years of age, among which, 7/8 would fulfil CASPAR criteria, and 2 other patients who were not classified according to ILAR criteria, did meet the CASPAR classification criteria, given the presence in these criteria of negative RF, family history of the 2nd degree and typical radiological alterations, which are not present in the ILAR criteria. 1 (1/30) patient did not meet CASPAR criteria, and belonged to the group of patients excluded from the ILAR criteria for being male >6 years HLA-B27 +.

If we did not take into account the negative FR of the CASPAR criteria, 14 patients would not meet these criteria and if we eliminated the 2nd grade AF, 5 patients would not be classified (among them 2 who meet CASPAR and do not ILAR)

**Conclusions:** In our series of patients despite the fact that the presence of current skin psoriasis contributes 2 points in the CASPAR criteria, only 1 patient would not meet the CASPAR criteria, since the majority of patients present other clinical or analytical manifestations, such as the presence of negative rheumatoid factor or 2nd degree family history. Patients who do not meet criteria for PsA by exclusion criteria, practically all of them would be diagnosed with psoriatic arthritis by CASPAR criteria.

**Disclosure of Interest:** None declared

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AB1079

**TRANSITION CARE OF PATIENTS WITH CHILDHOOD ONSET CHRONIC RHEUMATIC DISEASE IN A TERTIARY MEDICAL CENTRE IN TURKEY**

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**Background:** Transitional care is a purposeful, planned movement of adolescence and young adults with chronic condition from childhood- to adult-oriented health care systems. Well-organised, systematic transitional health care is of high importance for providing the continuous medical treatment and for reaching optimal outcomes. Up to date, there is no unique, consensus-based model for patients' transition from childhood- to adult oriented health care centres in Turkey.

**Objectives:** We aimed to assess the transitional care among patients with juvenile onset rheumatologic disease in referral tertiary centre in Turkey.

**Methods:** The transitional polyclinic is held once per month at the department for paediatric rheumatology, consisting of 2 adult and 4 paediatric rheumatologist. A total of 147 patients have undergone the transitional care in the time period from May 2014 to December 2017. Patients were called by telephone, by two different investigators (EP, OK). Thirty-three (22%) patients were not reached and 17 (11%) of them were excluded from the study due to short post-transitional period

(<6 months). Consequently, 97 (66%) patients have been reached and included in the study. Data on demographic, clinical and socio-economic features and experience with transitional practice were collected by using a structured questionnaire, which was fulfilled during the phone conversation between investigator and patient.

**Results:** A total of 147 patients (79 (54%) females) underwent transition process and 97 of them were included in the study. There was no statistically significant difference between different patients groups regarding the age of transition. The education levels of patients were as following: university 60 (61.9%), high-school 21 (21.6%), middle-school 13 (13.4%), primary school 3 (3.1%). Majority of patients was single at the time of study (79 (81.4%) patients) while only 18 (18.6%) patients were married; half of them being child owner. At the time of study, 44 (30%) patients were employed and mean age at employment was 19.06±3.1 years. Most of patients had health insurance at the time of study (94 (96.9%)). Seventy-one (73.2%) patients continued their regular follow up at adult department while 26 (25.8%) patients discontinued medical treatment. The most common reasons for cessation of follow up were the work/school absence (20 (76.9%)), followed by patients' personal reasons (2 (7.6%)) and dissatisfaction with adult clinic services (4 (15.5%)). Most of patients reported satisfaction with transition process: 96 (99%).

**Abstract AB1079 – Table 1**

	n=97
Female, n (%)	58 (59.7%)
Age at transition, mean±SD	21.4±1.4 years
Age at study mean±SD	22.8±1.8 years
JIA	26 (26.8%)
FMF	60 (61.8%)
Connective Tissue Disease	7 (7%)
Vasculitis	4 (4%)

**Conclusions:** This is the first Turkish model of transitional care among patients with chronic rheumatic disease. Well-organised transitional health care is of crucial importance for the continuous and optimal health care of adolescents and young adults with chronic rheumatic disease. Further studies with higher number of patients would reveal the relevance of described transitional care model.

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**Disclosure of Interest:** None declared

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AB1080

**NEUROLOGICAL EVALUATION OF CHILDHOOD-ONSET CRYOPYRIN-ASSOCIATED PERIODIC SYNDROMES-A PRELIMINARY REPORT**

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**Background:** The cryopyrin-associated periodic syndrome (CAPS) is a treatable autoinflammatory disease that encompasses familial cold autoinflammatory syndrome (FCAS), Muckle-Wells syndrome (MWS), and chronic infantile, neurologic, cutaneous, and articular syndrome (CINCA), which are quite different in severity. Early diagnosis of CAPS and prompt initiation of IL-1 blockers have significant effect on the neurologic prognosis of CAPS. Although neurologic complications of CINCA are well-known, there are scarce data regarding neurologic features of milder phenotypes.

**Objectives:** We aimed to review the neurologic features in detail and summarise the other CAPS-related manifestations in 9 children.

**Methods:** All children with CAPS that have been followed-up from paediatric rheumatology outpatient clinic, were enrolled to the study. In addition to the neurologic examination, magnetic resonance imaging (MRI) of brain, electroencephalography, eye examination, hearing test and neuropsychiatric tests were done. Demographic, clinical features, genetic analysis and laboratory tests were noted from patient records and hospital database.

**Results:** The median age of the subjects was 6 years (range 2–14 years), with a female-to-male ratio 4/5. Most frequently noted neurologic clinical manifestations during the disease course were papilledema (3/9) and epilepsy (3/9), followed by neurodevelopmental delay (2/9), aseptic meningitis (2/9), upper motor neuron



**Abstract AB1080 – Table 1.** Demographic, clinical, electroencephalography and neuroimaging features of CAPS patients

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Patient 9
Age (years)	10	2	6	4	3	13	6	12	14
NLRP3 gene analysis result	Q703K	Negative	G569R	Q705K	Negative	T433I	Negative	T436A	A242A
Sensorineural hearing loss	No	No	Yes (Bilateral)	No	No	No	No	No	No
Uveitis or conjunctivitis	No	No	No	No	No	No	No	Yes	Yes
Papilledema	Yes	No	No	No	Yes	No	No	No	Yes
Optic atrophy	No	No	No	No	Yes	No	No	No	No
Headache	Yes	No	No	No	No	Yes	No	No	Yes
Seizure	Yes	No	Yes	No	Yes	No	No	No	Yes
Mental retardation	No	No	Yes	No	Yes	No	No	No	No
Aseptic meningitis	No	No	Yes	No	Yes	No	No	No	No
EEG	Normal	Normal	Focal epileptiform activity	Normal	Generalised fast rhythm and sharp-wave activity	Normal	Normal	Normal	Neuronal hyperexcitability in left temporal lobe
Cranial MRI	normal	normal	Diffuse parenchymal atrophy, hydrocephalus	normal	Global cortical atrophy, sequela lesions	normal	normal	normal	Normal

findings (2/9), ocular symptoms/signs (2/9), sensorineural hearing loss (1/9), optic atrophy (1/9) (table 1). MRI of the brain was abnormal in two patients.

**Conclusions:** Increased understanding and awareness of this rare but treatable syndrome among neurologists is essential, since the disease could manifest with neurologic manifestations such as seizure, papilledema, sensorineural deafness and aseptic meningitis. If remains untreated and recognised, this autoinflammatory syndrome could lead to significant morbidity and mortality. Hence, early treatment with anti-interleukin-1 therapy provides complete resolution of symptoms and, also prevent progression of neurologic findings when initiated in the late stage of the disease.

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**Disclosure of Interest:** None declared

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#### AB1081 FIRST TRANSITION CLINIC OF ADOLESCENTS WITH RHEUMATIC DISEASES IN MÉXICO, A PILOT STUDY

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**Background:** The adolescence is a critical period when different process are made, as identity, cognitive changes, enhance of autonomy, etc. Besides that, an adolescent with rheumatic disease has to front facing the disease acceptance. Already, different Transition Programs are made around the world. In México does not exist this important project yet.

**Objectives:** Provide and uninterrupted, multi-disciplinary and coordinated, properly developed health system with a comprehensive and psychosocial background.

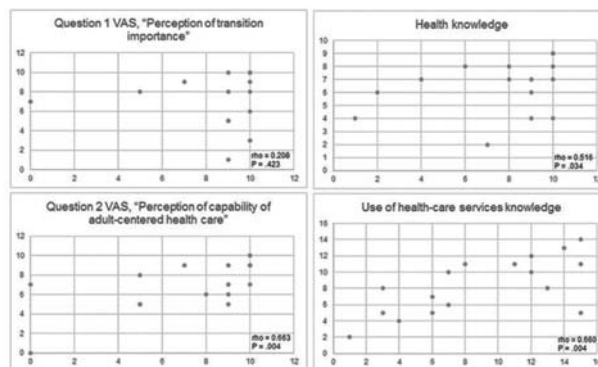
**Methods:** We included rheumatologist, rehabilitation specialists, psychiatrist, nutritionist, clinical psychologist, nurse and social services. Got Transition Questionnaire (GOT) in Spanish version was used to evaluated patients and parents to evaluated the knowledge in transition process. We implemented the beginning of the clinic last July. We included patients with established rheumatic diseases, older than 16 years old. We use descriptive statistics with measures of central tendency or frequencies depending on variable characteristics. We use Spearman's correlation test to evaluated concordance of answers in GOT between parents and patients.

**Results:** We made a systematic evaluation program of all patients. Nineteen patients had already seen at the clinic, most of them are female, the rest of clinical

variables are shown in Table 1. Even though we found a positive Spearman's coefficient ( $\rho$ ), and significant difference in answers related with "Perception of capability of adult-centred health care", "Health knowledge", and "Use of health-care services knowledge", GOT results demonstrate weak of correlation between answers from patients and their parents. Correlation plots from GOT results are shown in figure 1.

**Abstract AB1081 – Table 1.** Clinical and demographic characteristics

Variables	n=19
Age, years, mean±SD	18±1.4
Female gender (%)	15 (79)
Rheumatic diagnosis (%)	JIA SLE Inflammatory Myopathy Scleroderma Episcleritis
BMI, median (min – max)	20.3 (15.7–41.5)
BMI based classification (%)	Underweight Normal weight Overweight Obese
Any limited joint mobility and other musculoskeletal problems (%)	18 (95)
Psychiatric assessment abnormal (%)	14 (74)

**Abstract AB1081 – Figure 1.** GOT Transition correlations between parents and patients.

**Conclusions:** In this pilot study, we shown a high prevalence of psychiatric, nutritional, and mobility problems among adolescents, adding the non-concordance of transition abilities perception in GOT answers between parents and patients. These results encourage the need of an organised, specialised, multidisciplinary, and integrated clinic in which the patient could adapt to adult care centres.

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**Disclosure of Interest:** None declared

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AB1082

**CHARACTERISATION OF A GROUP OF PATIENTS WITH IGG4-RELATED DISEASE: SINGLE CENTRE EXPERIENCE**

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**Background:** Immunoglobulin G4-related disease (IgG4-RD) is a chronic systemic inflammatory condition with an unclear pathophysiology and IgG4-positive plasma cells infiltration of various organs and parts of the body. If untreated, the disease can lead to fibrosis and irreversible organ damage. IgG4-RD mostly has been described in adults, hence it is generally unknown among paediatricians.

**Objectives:** We conducted a retrospective analysis of clinical features and response to therapy of five patients (one female, four males, median age 13.6 years) with IgG4-related disease, treated in our Centre.

**Methods:** The diagnosis was confirmed by detection of lymphoplasmacytoid infiltration with >30% of cells expressing IgG4 in all, and elevated IgG4 serum concentration in 4 cases.

**Results:** Three patients had localised lesions (orbit, hip muscle, peripancreatic tissue, respectively), two – multi-organ disease with polylymphadenopathy, pulmonary, renal and hepatic foci, dacryoadenitis with oedema of the eyelids. Auto-immune thrombocytopenia ( $70 \times 10^9/l$ ), neutropenia ( $0,79 \times 10^9/l$ ) were present in one patient. Rituximab therapy was successful in 2 cases (one patient received monotherapy with rituximab, another one – Rituximab and Sirolimus). Two other patients received JAK inhibitor therapy (ruxolitinib) with good effect. No side effects were noted. One patient underwent surgery – the infiltration in the abdominal cavity was removed with positive effect without specific therapy.

**Conclusions:** IgG4-RD symptoms can be diverse and sometimes atypical, so dealing with this pathology requires physician's awareness. Rituximab was effective in patients with multi-organ manifestations, and JAK inhibitor (Ruxolitinib) was effective in patients with mono-focal disease. Steroids are routinely used in IgG4-RD as a first line of treatment with significant side effects. We propose that alternative drugs could be used in IgG4-RD, especially in paediatric patients to achieve fast remission with significant morbidity.

**Disclosure of Interest:** None declared

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AB1083

**CLINICAL AND DENSITOMETRIC CHARACTERISTICS IN PAEDIATRIC POPULATION WITH RISK FACTORS TO DEVELOP LOW BONE MASS/OSTEOPOROSIS**

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**Background:** Low Bone Mass (LBM)/Paediatric Osteoporosis (Ped OP) is a disorder of unknown prevalence, partly due to the lack of diagnosis, associated with the absence of clinical manifestations of the disease until patients develop complications such as fractures, deformities or pain

**Objectives:** To describe the clinical and densitometric characteristics of the paediatric population with risk factors to develop LBM/Ped OP

Abstract AB1083 – Table 1

Age group	N,% age group	Average calcium intake (mg/d)±SD	Recommended Daily Amount (RDA) (mg/d)	% that reach RDA
Preschooler (2–3 y)	8, 8.9%	847±271	700	50%
Scholar age (4–9 y)	29, 32.2%	671±238	1000	27.6%
Teenagers (10–17y)	47, 52.2%	660±348	1300	8.7%
Young (18–20 y)	6, 6.7%	726±156	1100	0%

**Methods:** We collected prospectively demographic and clinical data of patients aged 2 to 20 years, referred for bone health assessment due to the presence of a risk factors for LBM/Ped OP, including: inflammatory diseases, immunosuppressants and/or corticosteroids, malabsorptive diseases and chronic systemic

disorders. We evaluated daily calcium intake and Bone Densitometry (DXA) was performed. We did also a vertebral morphometry

**Results:** Data were collected from 90 patients, with an average age of 9.9 years, 53% female, 82% Caucasian. The age distribution and calcium intake by age can be seen in table 1.

There was a significant decrease in the compliance of the RDA with calcium with increasing age ( $p=0.01$ ). No differences were found in the average daily calcium intake between the different diagnostic groups.

The most frequent diagnoses were: Malabsorption:44.4%, JIA:20%, Nephropathies:17.8%, Haematological diseases:7.8% and Vasculitis: 4.4%.

18% of the sample had had a fracture (Fx), 44% of them had more than one, being the adolescents the group of greater prevalence. 3 cases met the criteria for fragility Fx (vertebral Fx).

20% of the patients were on systemic corticosteroids, with an average dose of 5.9 mg of prednisone (or equivalent)/day, and another 20% had previously received them. The total cumulative average corticosteroid dose in both groups was: 7 grams of prednisone, with an average exposure of 37 months. 29 patients (32%) received immunosuppressive treatment, of which 20% were methotrexate (alone or in combination with biological DMARD).

Only 7% had supplements with Calcium and 14% with Vitamin D.

100% had a normal calcium, 82% a normal phosphate (rest slightly increased) and 11% were deficient in Vitamin D

13% of the sample had a LBM for their age assessed by DXA. The densitometric results can be seen in Table 2.

Abstract AB1083 – Table 2

DXA results	Max Z score	Min Z score	% with Z score≤-2
Vertebral Z score	-3	2	13.3%
Whole body Z score	-3	1.8	9.2%
Total femoral Z score	-4.8	2.3	10.7%
Femoral neck Z score	-4.8	3	12%

**Conclusions:** Calcium intake in children and young with at least 1 risk factor for LBM/Ped Op is lower than recommended, especially in the groups with the highest requirements.

Up to 13% of this population have a BMO for their age and a 3'3% meets Ped OP criteria.

Larger studies are needed to help us to identify paediatric patients who are candidates for bone health screening

**Disclosure of Interest:** None declared

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AB1084

**PRELIMINARY RESULTS OF THE USE OF SERUM CALPROTECTIN (MPR8/MPR14) IN CLINICAL PRACTICE IN PAEDIATRIC RHEUMATOLOGY**

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**Background:** Serum Calprotectin is a new biomarker of clinical activity in Rheumatology, especially in Juvenile Idiopathic Arthritis (JIA)

**Objectives:** To assess the use of serum Calprotectin in paediatric patients with inflammatory/Rheumatic diseases in clinical practice

**Methods:** We retrospectively collected Demographic and Clinical data from patients of our Paediatric Rheumatology Clinic, in which serum Calprotectin levels were determined.

The determination of serum Calprotectin was carried out using the ELISA technique.

Diagnostic and Inflammatory activity data were also collected: RCP, ESR and Clinical Assessment of the patients

**Results:** We present 28 patients, 61% females, with an average age of 11 (3–23 years)

The diagnoses were as follows: 16 JIA (57% of the total), of which 8 were of the Oligoarticular type, 3 were Polyarticular, 3 were Arthritis related to Enthesitis, 1 was Psoriatic and 1 Systemic. Other diagnoses were: Behçet, <sup>1</sup>Autoinflammatory Diseases: 4 (2 ADA2 Deficit, 1 Familial Mediterranean Fever, 1 PFAPA) and 7 patients had suspected rheumatological/inflammatory diseases in study

17 patients were considered clinically inactive, 6 with inflammatory activity and 3 doubtful at the time of blood test. The mean values of Calprotectin, RCP and ESR can be seen in Table 1.

Abstract AB1084 – Table 1

	Calprotectin (µg/mL) (range)	PCR (mg/dL) (range)	ESR (mmHg) (range)
Active	3,43 <sup>1.80</sup> – 5.31	4,27 (0,7–11,6)	16,86 <sup>3–51</sup>
Inactive	2,15 (0,78–4,06)	1,83 (0,7–4,6)	13,11 <sup>3–43</sup>

Calprotectin was statistically correlated with Clinical Activity ( $p=0.018$ ), however, neither ESR ( $p=0.539$ ) nor RCP ( $p=0.059$ ) did, although in RCP there was a clinical trend, (ANOVA)

Calprotectin, RCP and ESR were negative in 91%, 80% and 76% respectively of Inactive patients; and positive in 43%, 100% and 33% of the Active ones

The analysis of the ROC curves in our sample showed that the value that allows to discriminate between active and non-active disease with a Sensitivity of 80% and a Specificity of 69% is 2'07 µg/mL

Serum Calprotectin was 2 points higher in the group of patients with Autoinflammatory diseases than in the group of JIA, with a mean of 4.91 compared to 2.90 ( $p=0.002$ ). However, since it is a retrospective study, we must bear in mind that this can be influenced by the reasons for the test request, being in the group of Autoinflammatory Disease the suspicion of active disease, and in the AIJ simply monitoring or assessment of treatment optimisation.

It should be noted that, in the patients in diagnostic process that did not present any rheumatological disease (final diagnoses of: arthralgias in 3 cases and glomerulonephritis not associated to rheumatologic/autoimmune disease in 1), serum Calprotectin did not exceed in any case the 1.15 µg/mL

**Conclusions:** Serum Calprotectin is emerging as a useful marker, not only in the field of JIA, but also in other diagnostic groups such as Autoinflammatory Diseases.

Prospective and larger studies are needed to determine its role

**Disclosure of Interest:** None declared

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#### AB1085 THE FACTORS AFFECTING REMISSION IN JIA PATIENTS, SINGLE CENTRE RESULTS

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**Background:** Juvenile idiopathic arthritis (JIA) is the most common rheumatic disease in childhood. Nowadays, in the management of JIA, clinical remission is the accepted goal. However, remission is much associated with the JIA subtype and inversely with suggested predictors for poor outcome.

**Objectives:** The aim of the study is to evaluate the predictors of clinical outcome in patients with juvenile idiopathic arthritis

**Methods:** This was a single-centre, an observational study including children diagnosed with JIA at Health Sciences University Istanbul, Umraniye Education and Research Hospital, Turkey, between June 2016 and January 2018. All patients were evaluated at the time of diagnosis, and at 3 months of their disease. We routinely collected the patients' baseline profile which included the age of disease onset, gender, number of active joints, patients' and physicians' global assessment of disease activity (PGA, range from 0 to 10 mm; 0 is the best score), the JADAS 27 score, and therapy. Patients were identified through the divisional database which includes all patients seen in the rheumatology clinic.

**Results:** A total of 141 JIA patients were included in the analysis. The mean follow-up duration of these patients was 23.36 months (range from 12 to 156 months). We examined 71 joints in all patients. At the time of diagnosis, it was seen that they were frequently in knee joint (61.7%) and sacroiliac joints (34.8%). The rate of improvement of joints in the last visit was found to be metatarsophalangeal joints (100%), sacroiliac joints (79%) and knee joints (44.8%), respectively. The non-systemic group ( $n=133$ ) was evaluated for initial steroid use, among the patients, 54 (% 41) had steroid therapy at the time of diagnosis. There was seen that 29 of the 141 patients (20.6%) were in the remission in 3 months of follow-up. According to subtype of JIA patients, systemic patients (62.5%) were frequently in remission at 3 months. At the end of the study, of the 141 patients, 72 (51.1%) achieved remission and were assigned to the remission group. Among the patients in the remission group, 44 (49.4%) had episodes of disease flares. The other 30 (40.5%) patients did not have disease flares. Comparing the baseline

data in the remission group and non-remission group, there was no difference between these two groups in disease onset age, gender, JIA subtypes, number of active joints at disease onset and JADAS 27 scores and used steroid therapy.

We also analysed whether each group used biological drugs and analysed the duration of starting biologic therapy. Among 72 patients achieved remission, 17 (23.6%) patients had at least one biological drug. There was no difference between two groups. The median time of biologic drug starting was 12 (interquartile range (IQR), 12) months. There was longer time of biologic drug starting in non-remission group than remission group ( $32.3\pm 36.2$  vs  $25.0\pm 31.4$ ,  $p>0.05$ ). We determine that in systemic and poli JIA patients who were used biological therapy were found to have a high percentage of achieved to remission

**Conclusions:** JIA is a heterogeneous disease with significant variability in course and long-term outcome. No parameter could be used as a single predictor of long-term outcomes. Standardised baseline work-up, disease activity evaluation and a definition of a treat to target approach will result in better health outcomes for JIA patients

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.4234

#### AB1086 A 6-MONTH, MULTICENTER, OPEN-LABEL, EXPLORATORY STUDY OF FIXED DOSE NAPROXEN/ESOMEPRAZOLE IN ADOLESCENT PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS (JIA)

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**Background:** JIA is an inflammatory arthritis of unknown etiology, which lasts for greater than 6 weeks with onset before 16 years of age.<sup>1</sup> Per the ACR guidelines, JIA is the most common chronic rheumatic disease in children.<sup>3</sup> NSAIDs have been the mainstay of initial management with naproxen being commonly used, but they can cause serious side effects such as gastritis. Herein, we report the results of a clinical trial in JIA patients receiving one of 3 fixed doses of naproxen/esomeprazole magnesium (nap/eso) given BID (table 1).

**Objectives:** To evaluate the signs/symptoms of JIA, safety and tolerability of nap/eso in adolescents age 12 to 16 years.

**Methods:** Forty-six children and adolescents with JIA by ILAR criteria, mean age of 13.6 years, from 18 US sites were prospectively enrolled over 2 years and treated for up to 6 months. Mean number of active joints at baseline was 3.1. Doses were based on baseline weight (table 1). Disease activity was assessed with the ACR Pediatric-30, -50, -70, -90 Response and the Childhood Health Assessment Questionnaire (CHAQ) discomfort and functional scores at months 1, 3, and 6 as change from baseline. Occurrence and causality were assessed for treatment emergent AEs (TEAEs) and discontinuations were monitored monthly.

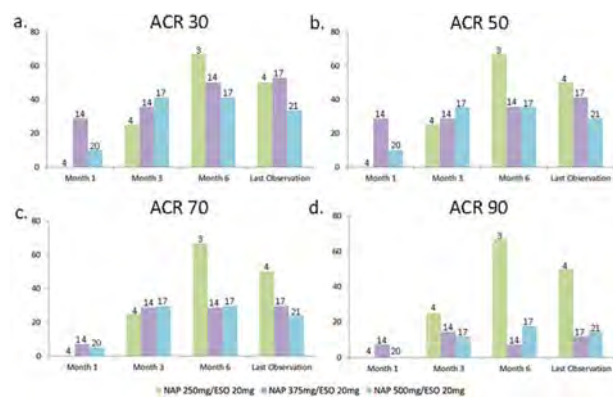
**Results:** Forty-six patients received at least 1 dose of study drug and 36 completed the trial. The % of patients achieving ACR Paediatric response increased over time (figure 1). CHAQ discomfort improved at each assessment and functional scores improved at all assessments for 'Arising, Walking, and Activities' with several improved for 'Dressing and Grooming, Eating, Hygiene, and Grip'. There was no indication of a dose-related efficacy effect. Thirty-seven (80.4%) had at least 1 TEAE. Frequent TEAEs ( $\geq 5\%$ ) were upper respiratory tract infection, upper abdominal pain, sinusitis, diarrhoea, headache, nausea, and ligament sprain. Eleven (23.9%) had at least 1 TEAE considered to be related to study drug. Most frequent study drug-related TEAE ( $\geq 5\%$ ) was upper abdominal pain. Four (8.7%) discontinued due to a TEAE.

Abstract AB1086 – Table 1. Minimum and Maximum Study Drug Dose (nap/eso) by Weight Group

Weight at Enrollment (kg) <sup>1</sup>	Minimum Dose <sup>2</sup>	Maximum dose <sup>2</sup>
<38	250 mg/20 mg	250 mg/20 mg
38 –<50	250 mg/20 mg	375 mg/20 mg
50 –<75	375 mg/20 mg	500 mg/20 mg
$\geq 75$	500 mg/20 mg	500 mg/20 mg

<sup>1</sup> Based on typical day-to-day fluctuations in body weight,  $\pm 3\%$  window was permitted and used at the discretion of the Investigator when assigning the initial dose group. <sup>2</sup> Study drug dose, given twice daily.





Abstract AB1086 – Figure 1

Note: the number above each bar represents the number of patients at that dose. The ACR Pediatric-30, -50, -70, and -90 responses were defined as an improvement of at least 30% (or 50%, 70%, 90% respectively) from baseline in at least 3 of the 6 signs and symptoms variables, with no more than 1 of the remaining variables worsening by >30%. JIA signs and symptoms variables: physician's global assessment of disease activity, CHAQ disability index score, CHAQ global assessment of well-being, number of joints with active arthritis, number of joints with limited range of motion, serum CRP or ESR.

**Conclusions:** Improvement in JIA signs and symptoms occurred at most assessments and by month 6, the percentage of patients with an ACR Pediatric-30, -50, -70, and -90 Response was 47.1%, 38.2%, 32.4%, and 17.6%. No new safety signals were identified for the well-characterised components of this fixed dosed JIA treatment, which was developed to reduce the risk of gastric ulcers.

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#### AB1087 PROLONGED RESPONSE WITH TUMOUR NECROSIS FACTOR ALFA INHIBITION IN A 5 YEAR OLD BOY WITH SEVERE MANIFESTATIONS OF IL-36 RECEPTOR ANTAGONIST DEFICIENCY (DITRA)

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**Background:** Deficiency of the interleukin (IL)–36 receptor antagonist (DITRA) is an autosomal recessive autoinflammatory syndrome caused by mutations in the IL36RN gene. Clinical manifestations of DITRA include recurrent episodes of generalised skin postulation, fever, systemic inflammation and leukocytosis. An uniformly effective treatment for DITRA has not yet been identified.

**Objectives:** We present a case of a 5 year old patient with DITRA with prolonged response with tumour necrosis factor alfa inhibition with adalimumab.

**Methods:** A five-year-old came to our dermatology clinic after worsening of a previous diagnosed plaque psoriasis, with an erythematous scaly dermatitis that extended throughout the trunk. Treatment with acitretin and cyclosporin were not effective and patient developed in few weeks a generalised erythroderma with

pustules covering almost every part of his body, including palms and soles. He was admitted for the onset of fever and irritability due to painful rubbing of the skin. Family history of recurrent fevers or psoriasis were not revealed. Parents were not consanguineous.

Complete blood count showed leukocytosis with neutrophilia and thrombocytosis, with an erythrocyte sedimentation rate (ESR) of 6 mm/hr and a C-reactive protein (CRP) of 8,4 mg/dl. Biochemistry panel revealed a mild elevation of liver enzymes without other abnormalities. Antinuclear antibody (ANA) and rheumatoid factor were negative with normal serum immunoglobulin and complement. Blood culture grew *E. Coli*, *S. Maltophilia* and *S. epidermidis*. Skin biopsy showed acanthosis and papillomatosis with perivascular polymorphous inflammatory cells. Genetic analyses showed a homozygous mutation in the IL36RN gene (pSer113Leu). No mutations were detected in IL1RN and CARD 14 genes.

**Results:** Treatment was initiated with intravenous methylprednisolone 2 mg/kg/day and subcutaneous anakinra 2 mg/kg/day. Cefotaxime and co-trimoxazole were added until blood cultures were negative. Although skins lesions improved during the following days and patient was finally discharged, symptoms reappeared when decreasing the steroid dose. Three months later adalimumab and methotrexate were started, allowing the patient to end treatment with corticoids without evidence of activity of the disease.



Abstract AB1087 – Figure 1

**Conclusions:** After incomplete response with anakinra, inhibition of tumour necrosis factor alfa resulted in a prolonged response in our patient with deficiency of the interleukin (IL)–36 receptor antagonist (DITRA).

**Disclosure of Interest:** None declared

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#### AB1088 CAPILLARY HEMOSIDERIN DEPOSITS OR EXTRAVASATIONS: A SUBTYPE OF HAEMORRHAGETHAT ACQUIRES SEPARATE ATTENTION IN QUANTITATIVE ANALYSIS OF NAILFOLD CAPILLAROSCOPY IN CHILDHOOD-ONSET SLE

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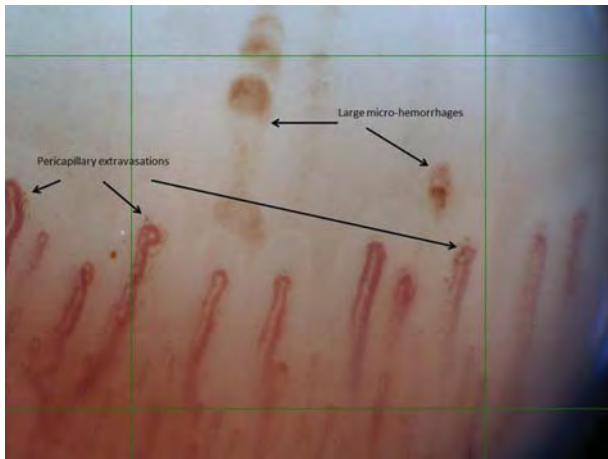
**Background:** Quality of images in nailfold capillaroscopy has improved in the last years by introduction of videocapillaroscopy. Microangiopathy, as observed in capillaroscopy of SLE-patients,<sup>1–3</sup> can now be described by more detailed quantitative analysis. Recently, in a small cohort (n=22) of childhood-onset SLE (cSLE), we described capillary bleedings by two different subtypes: large haemorrhages and small point-shaped haemorrhages with a total count of resp. 0.2/1.5 per

analysed image per patient.<sup>4</sup> These small point shaped haemorrhages have also been described as hemosiderin deposits.<sup>5</sup>

**Objectives:** To describe the reliability of assessment of two subtypes in capillary haemorrhages by inter-observer agreement.

**Methods:** Three observers, DS (paediatric rheumatologist with experience in capillaroscopy), AN (fellow paediatric rheumatology without experience in capillaroscopy) and MB (trainee in adult rheumatology with experience in capillaroscopy), scored capillaroscopy images from patients with Raynaud's phenomenon and with cSLE. The observers were blinded for patient name and diagnosis. The number of haemorrhages were scored per subtype. Hemosiderin deposits were defined as small point-shaped extravasations surrounding the capillary apex (see image). Large haemorrhages were defined according to the Atlas of Capillaroscopy.<sup>6</sup> Reliability was calculated by the intra-class correlation coefficient (ICC) with 95% confidence interval (CI). Statistical analyses was performed by IBM SPSS Statistics version 24.

**Results:** Two-hundred images from 50 patients (diagnosed with Raynaud's phenomenon and/or cSLE) were scored by the three independent observers. ICC for the number of capillaries with hemosiderin deposits was 0.77 (95% CI 0.69–0.82). ICC for the number of large capillary haemorrhages was 0.97 (95% CI 0.96–0.98).



Abstract AB1088 – Figure 1

**Conclusions:** Reliability of the observation 'hemosiderin deposits' in nailfold videocapillaroscopy was good with an ICC of 0.77. This study shows that capillary haemorrhages can be described in 2 subtypes: 'large haemorrhages' and 'hemosiderin deposits' which are small point-shaped extravasations surrounding the capillary apex.

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AB1089

#### INVESTIGATION OF THE EFFICACY AND SAFETY OF SECUKINUMAB TREATMENT IN JUVENILE IDIOPATHIC ARTHRITIS SUBTYPES OF JUVENILE PSORIATIC AND ENTHESTITIS-RELATED ARTHRITIS: DESIGN OF A RANDOMISED, DOUBLE-BLIND, PLACEBO CONTROLLED, MULTICENTER STUDY

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**Background:** Secukinumab (AIN457), a fully human anti-interleukin-17A monoclonal antibody, has demonstrated a significant clinically meaningful efficacy on signs and symptoms, structure and function in adults with ankylosing spondylitis (AS)<sup>1</sup> and psoriatic arthritis (PsA)<sup>2</sup>, both approved indications. These data support the proposed study in children with enthesitis-related arthritis (ERA) and juvenile psoriatic arthritis (JPsA).

**Objectives:** This phase 3 study will investigate the efficacy and safety of secukinumab in children  $\geq 2$  to  $< 18$  years with active JPsA or ERA. The primary objective is to demonstrate that the time to flare in a double-blind placebo control treatment withdrawal part of the trial is longer with secukinumab than placebo.

**Methods:** Eighty biologic-naïve children with active ERA or JPsA (active  $\geq 3$  active joints and  $> 1$  site of enthesitis at baseline or documented by history) will enrol into treatment period 1 and receive weekly open label s.c. secukinumab 75 or 150 mg, based on their body weight ( $< 50$  kg or  $\geq 50$  kg) to maintain secukinumab blood levels equivalent to the adult 150 mg dose, for the first month then every 4 weeks thereafter. At week 12, responders (minimum JIA ACR Pedi 30 response) enter treatment period 2 and will be randomised to receive secukinumab or a matching placebo every 4 weeks. Patients enter treatment period 3 if they experience a disease flare or when the treatment period 2 closes for the entire study because the target number of flares has been reached. Upon entering treatment period 3, patients receive open-label secukinumab every 4 weeks until week 100 and then followed until week 112.

**Results:** The primary efficacy endpoint will be time to flare in treatment period 2. Key secondary endpoints include JIA ACR 30/50/70/90/100 response rate, total dactylitis and enthesitis counts at week 12. Safety and tolerability will be assessed throughout the study.

**Conclusions:** The efficacy of Secukinumab in the approved adult indications of PsA and AS support the current study design to evaluate the efficacy and safety of secukinumab treatment in children with active JPsA or ERA. The primary efficacy endpoint will be time to flare in treatment period 2. Key secondary endpoints include JIA ACR 30/50/70/90/100 response rate, total dactylitis and enthesitis counts at week 12. Safety and tolerability will be assessed throughout the study.

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AB1090

#### ANALYSIS OF A COHORT OF PATIENTS ATTENDING A COMBINED OPHTHALMOLOGY- RHEUMATOLOGY CLINIC IN A TERTIARY REFERRAL CENTRE IN EGYPT

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**Background:** Paediatric rheumatologic diseases may have sight-threatening ocular complications including uveitis, scleritis, and retinopathy. Conversely, children presenting with uveitis, scleritis, episcleritis, or optic neuritis may have an underlying rheumatologic disease. Combined ophthalmology-rheumatology clinics can facilitate the comprehensive management of these patients.

**Objectives:** To describe the demographic characteristics, paediatric rheumatologic diseases distribution, paediatric ocular manifestations distribution, and active treatments in a combined ophthalmology- rheumatology clinic in a tertiary referral centre in Egypt.

**Methods:** We included all new patients who attended a combined ophthalmology–rheumatology clinic at a tertiary referral hospital from the 1st of October 2015 to the 30th of November 2017. We analysed their demographic, clinical, laboratory, and treatment characteristics. Patients were considered to have activity according to the joint opinion of the ophthalmic and rheumatologic consultants.

**Results:** We included 538 new patients. 331 were female (61.5%) and the median age (range) was 8.1 years (1.1–17.3). 59.5% of the patients had juvenile idiopathic arthritis (JIA), whereas patients with SLE, Behçet's disease, dermatomyositis, scleroderma, and juvenile ankylosing spondylitis represented 8.6%, 8.1%, 7.2%, 4.7%, and 4.3% of the studied cohort respectively.

Of the patients with juvenile idiopathic arthritis, 56.7% had not developed ocular manifestations by the end of the study, while 27.3% suffered from uveitis that was controlled by methotrexate, 7.4% suffered from uveitis that was controlled by both methotrexate and adalimumab, and 8.6% suffered from uveitis that was still active by the end of the study period.

72.3% of the patients with Behçet's disease had uveitis, of which 34.6% suffered profound diminution of vision in the affected eye(s) despite receiving anti TNFs. Other medications that were given were prednisolone, azathioprine, cyclosporine, and cyclophosphamide.

Smaller percentages of patients with dermatomyositis, scleroderma, and juvenile ankylosing spondylitis, developed ocular manifestations, and the vast majority were systemically and ophthalmologically quiescent by the end of the study duration.

**Conclusions:** More than half the patients attending the combined clinic during the period of the study had JIA. A greater percentage of patients with uveitis due to JIA could be controlled medically than of patients with uveitis due to Behçet's disease. A multidisciplinary clinic can save patients with rheumatologic diseases and uveitis precious time.

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#### AB1091 TOLERABILITY OF VACCINATION OF 13 PCV IN PATIENTS WITH JIA, WITHOUT SYSTEMIC MANIFESTATIONS

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**Background:** Juvenile idiopathic arthritis (JIA) is one of the most frequent and most disabling rheumatic diseases in children. Children with JIA receiving immunosuppressive and genetically engineered biologic drugs belong to the high-risk group for the development of bacterial and viral infections, including those administered by preventive vaccines.

**Objectives:** Our aim was to evaluate the tolerability of the pneumococcal 13-valent conjugate vaccine (PCV) in children with JIA.

**Methods:** In a prospective cohort study, 3 groups were formed: children with JIA in the remission phase on methotrexate or etanercept (group I), with JIA in the active phase prior to the appointment of methotrexate or etanercept (group II), control group (conditionally healthy children). 0.5 ml of the 13-valent PCV was administered once subcutaneously during therapy in patients in the remission phase or 3 weeks before the appointment of methotrexate or etanercept in patients in the active phase.

**Results:** At this stage of work, the tolerability of the 13 PCV vaccine was evaluated in patients with JIA, without systemic manifestations. In our study, the post-vaccination period was asymptomatic in 58% of the children in Group I, 66% in children in Group II, and in 60% in the control group. Most often in the postvaccinal period, local reactions were noted, which were painful at the place of administration of the vaccine in 6% of the children in group I, 8% in group II, and 24% in the control group, respectively. Less developed oedema and hyperemia at the

injection site – in 12% of children in group I, 6% in group II, in 8% of children in the control group. There was no significant difference in the incidence of local reactions to vaccination of 13 PKV in patients with JIA and in children of the control group. Analysis of the time of occurrence and duration of local and systemic reactions to vaccination of 13 PKV showed that the maximum severity of symptoms was noted in the first day, by the 2–3 day of observation, complaints and fever disappeared. The increase in local reactions was noted 2 days after immunisation, followed by extinction to 3–4 days of follow-up. There were no serious adverse events in the post-vaccination period.

**Conclusions:** Vaccination with the 13-valent PCV in children with JIA is safety and is not accompanied by the development of serious adverse events.

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#### AB1092 AN AUDIT ON PAEDIATRIC UVEITIS IN THE GREATER GLASGOW AND CLYDE (GGC) SERVICE: GUIDELINE ADHERENCE AND IMPACT ON PATIENT OUTCOMES

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**Background:** 2010 guidelines from the Scottish Paediatric and Adolescent Rheumatology Network (SPARN) and the Scottish Uveitis Network (SUN) outlined management pathways for paediatric uveitis. Given the time since its establishment and last review, an audit on the GGC service's adherence to the guidelines as well as patient outcomes was conducted.

**Objectives:** To determine the service's compliance to the SPARN/SUN guidelines for the management of paediatric uveitis, in addition to establishing patient outcomes and identifying current shortcomings and areas for improvement in future practice. We also aimed to provide data to inform the revision and updating of the guideline for the year 2018.

**Methods:** This retrospective audit was conducted by collecting data from patients within the GGC's Royal Hospital for Children's joint rheumatology and ophthalmology service who were diagnosed with uveitis between the 1st of January 2008 and the 31st of December 2017. The data was then compared to the guidelines set by SPARN/SUN, in addition to a study conducted by this service prior to the guideline's development.

**Results:** 39 suitable patients were identified from the list of 253. From these patients, 92 separate events of uveitis were recorded – 84 of which ended in remission within the audit period. 17 events (20%) remained active after 7 months and required ongoing treatment, falling out with the guideline's standards. Time to remission was further stratified by modality of treatment. Of the 78 eyes evaluated, 7 eyes in 5 patients were found to have had cataracts. This comprises 12.8% of patients, an improvement from the 29% of the previous study. Notably, 5 of the 7 eyes had cataracts detected at the first appointment with the service. An additional 7 eyes across 6 patients (15%) were recorded to have had cystoid macular oedema, which is comparable to the previous study's 11%. A majority of these (4 of 7 eyes, or 57%) were again discovered to already be present at the first appointment.

**Conclusions:** Guideline adherence was commendable, though improvement is needed in treatment escalation to decrease the time taken for patients to achieve remission. There exists a tendency to maintain patients on topical steroid therapy due to relapsing and remitting disease activity, though given the high risk of glaucoma, consideration should be given to quickly progressing these patients up the treatment ladder. A large proportion of patients with severe complications of uveitis appear to have developed these prior to their first attendance at the service, suggesting a need for more stringent screening processes for early detection. Overall, outcomes in terms of the number of patients affected by complications of uveitis appear to have improved when compared to the study previously conducted by the service, implying a beneficial effect from adherence to the implemented guidelines.

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AB1093

#### CAN DMARDS THERAPY MODIFY CLINICAL HISTORY OF OLIGOARTICULAR JUVENILE IDIOPATHIC ARTHRITIS (JIA)?

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**Background:** Therapy of oligoarticular JIA is based on intra-articular injections of steroids, methotrexate and biotechnological therapy. ANAs-positive oligoarticular JIA patients with an early onset of disease have a consistent risk to develop uveites.

**Objectives:** The primary aim of this study is to evaluate longitudinally the effect of non-systemic therapy and of systemic immunomodulating drugs (e.g MTX) on ANAs in JIA patients; secondary occurrence of iridocyclitis was evaluated.

**Methods:** Monocentric retrospective not randomised study of 40 patients affected by oligoarticular JIA (ILAR classification) with ANA positivity at the baseline (T0, time of diagnosis). Patient of Group 1 received only intra-articular infiltrations or NSAID. Patients of Group 2 were treated with DMARDs (most of them with subcutaneous MTX 15 mg/m2/week) or MTX +biotechnological therapies. The assay for ANAs (I.I.F.) was assessed in all patients at T0, at T1 (12 months) and T2 (24 months). At 24 months was also recorded the occurrence of uveitis during the follow up. Exclusion criteria were the ANAs negativity at T0 and other subgroups of JIA.

**Results:** Twenty-one patients (52.5%) were treated with non-systemic therapy (Group 1), and nineteen (47.5%) with systemic immunomodulating therapy (Group 2). In Group 2 fifteen subjects were treated with MTX, one with MTX plus cyclosporine, one with only cyclosporine, two with MTX plus biotechnological agent (etanecept and adalimumab). At T1, in Group 1 only one patient out of 20 (4.8%) became ANAs negative versus 42.1% (8/19) of patients in Group 2 (p 0.0033). At T2 the incidence of ANAs positivity did not change in Group 1 (only 1/21 ANAs negative), while 42.1% of patients treated with systemic therapies were ANA negative (p 0.006). Three patients were lost at the follow up. The two patients who received bDMARDs in addition to MTX remained ANAs-positive both in T1 and T2. At the end of follow-up period eight uveitis have occurred, six in ANAs positive patients of Group 1 (6/21, 28.5%) and two in ANA negatives patients in Group 2 (2/19, 10.5%).

**Conclusions:** ANAs-positive patients treated with methotrexate seems to have higher possibility to become ANAs-negative versus patients treated with non-systemic immunomodulating therapy. It's known that MTX might prevent onset of uveitis in JIA, as shown in our results. Demonstrating a negativization of antinuclear antibodies using MTX therapy could help to add a role of this drug in the disease history of the oligoarthritiis.

**Disclosure of Interest:** None declared

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AB1094

#### ACUTE RHEUMATIC FEVER: NEW ASPECTS OF AN OLD DISEASE

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**Background:** Acute rheumatic fever is a nonsuppurative sequela that occurs two to four weeks following group A beta-hemolytic Streptococcus (GABHS) pharyngitis. Despite its decline in incidence in Europe, rheumatic fever still represents a serious healthcare concern. The most common manifestations are arthritis and carditis, followed by chorea, erythema marginatum, and subcutaneous nodules. The diagnosis of ARF is clinical and requires satisfaction of revised Jones criteria as well as evidence of a recent streptococcal infection.

**Objectives:** Aim of this study was to highlight new emerging features of disease clinical presentation.

**Methods:** Data regarding patients who fulfilled the Revised Jones Criteria for acute rheumatic fever were retrospectively collected from January 1996 and July 2017. The following clinical and demographic data were obtained: patient sex, birth date, age at presentation, clinical manifestations, evolution of cardiac involvement after therapy.

**Results:** 35 patients (19 males, 16 females) were included. The mean age at diagnosis 7.9±4 years (range 2–17). Carditis was the most frequent manifestation, occurring in 31 patients (89%). Other common symptoms were fever (91%), arthritis (43%) or arthralgias (54%) and chorea (20%). In 6 out of 7 patients chorea occurred together with carditis. Cardiac auscultation revealed new pathologic

murmurs only in 49% of cases. Echocardiography detected cardiac involvement in the absence of auscultatory findings (subclinical carditis) in 11 patients at the time of diagnosis. In 3 cases ultrasound examination became positive within 4 weeks. Throat cultures were negative in 37% of cases. Anti-streptolysin O (ASO) and anti-desoxyribonuclease B (ADB) antibodies titers did not bear correlation with the severity of cardiac involvement.

**Conclusions:** In our casistic, carditis was the most common and worrisome manifestation of ARF. Detection of cardiac involvement is still challenging and echocardiography testing should be performed even in the absence of abnormal auscultation findings. If the initial ultrasound is negative but clinical suspicion remains high, US investigation should be repeated, given that rheumatic carditis can evolve over weeks to months. Early detection and treatment of manifestations improves outcome as in all the cases of this series.

Streptococcal serology is most helpful in the diagnosis of ARF because culture or detection of the organism is usually no longer possible by the time ARF presents. The severity of clinical manifestations, particularly of carditis, does not correlate strictly with ASO and ADB titer.

Sydenham chorea, which usually has a longer latent period (up to 6 months), tends to occur earlier in the disease course, presenting in the acute phase in this series.

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AB1095

#### LONG-TERM IMPACT OF JUVENILE IDIOPATHIC ARTHRITIS ON QUALITY OF LIFE OF ADULT PATIENTS IN GREECE

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**Background:** Juvenile Idiopathic Arthritis (JIA) is the most common rheumatic disease in childhood and affects negatively both physical and psychosocial functioning.

**Objectives:** To explore the long-term impact of JIA on quality of life of adult patients in Northern Greece.

**Methods:** Adult patients with a definite diagnosis of JIA were assessed by the SF-12v2 questionnaire in the outpatient transition (from Paediatric to adult Rheumatology) clinic of Hippokratio Hospital of Thessaloniki. SF-12 questionnaire is a quality of life assessment tool and consists of a Physical Component Summary (PCS) and a Mental Component Summary (MCS). PCS and MCS of the patient group were compared to an age-matched control group, using *t-test* or *Mann-Whitney U test*, as appropriate. Moreover, percentages of patients and controls who were severely affected (<45 points in PCS or MCS) were compared, using *Chi-squared test*. Finally, correlation between the two summary components of SF-12 of patients was measured, using *Spearman's rho*. Statistical analysis was done using SPSS software. Level of statistical significance is p<0.05.

**Results:** A total of 50 patients and 135 controls were enrolled in the study. The median (IQR) patient age was 32<sup>10</sup> years and disease duration was 24<sup>9.5</sup> years. PCS scores of patients group were statistically significantly lower compared to control group (p=0.021) and more patients than controls scored low values (<45) in PCS (22% versus 6.7%, odds ratio, 4.0 [95% CI, 1.5, 10.2]; p=0.007). MCS scores of patients were slightly better than scores of controls (mean difference, 3.67 [95% CI, 0.44, 6.90]; p=0.026), but the severely affected were similar in both groups (odds ratio, 0.6 [95% CI, 0.3, 1.2]; p=0.174). No correlation between PCS and MCS was found (p=0.48).

**Conclusions:** There is an apparent impact of JIA on many patients' quality of life, specifically in terms of their physical health, that persists for many years after disease onset, which is in line with studies from other countries. This could be related to disease severity, disease subtype and duration, socioeconomic status and availability of treatment options. Interestingly, JIA wasn't found to affect the patients' mental health. A more specific psychometric test would be appropriate for in-depth analysis and confirmation of this result. Study design did not allow subgroup analysis according to JIA subtype, disease severity or duration, highlighting the need for long-term outcome studies focusing on the risk factors which may be involved.

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**AB1096** **OBSERVATIONAL SAFETY STUDY OF GOLIMUMAB IN TREATMENT OF POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS USING THE GERMAN BIOLOGICS JIA REGISTRY**

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**Background:** Golimumab (GLM) received European marketing authorisation for treatment of polyarticular JIA (pJIA). The long-term safety of GLM in clinical practice has not been characterised.

**Objectives:** The aim of the present project is to conduct a post-authorisation safety study to monitor long-term safety of subcutaneous GLM in the treatment of pJIA in routine clinical practice setting.

**Abstract AB1096 – Table 1**

Cohort	<sup>1</sup> GOL	<sup>2</sup> concurrent TNFi (ETA/ADA)	<sup>3</sup> concurrent MTX	<sup>4</sup> historic TNF	<sup>5</sup> historic MTX
<b>n</b>	18	53	13	2103	1517
<b>Age, median [IQR]</b>	13.9 [12.8;15.2]	11.6 [7.9;14.8]	10.5 [4.6;12.6]	12.7 [8.9;15.5]	10.2 [5.6;13.9]
<b>Disease duration, median [IQR]</b>	8.0 [2.5;11.4]	2.6 [0.9;6.5]	0.2 [1.1;0.6]	3.0 [1.1;5.8]	0.9 [0.4;2.8]
<b>Pretreatment</b>					
NSAID, n(%)	16(89)	44(83)	11(85)	1886(90)	1293 (85.2)
Steroids systemic, n(%)	10(56)	27(51)	5 (38)	1030 (49)	315 (20.7)
MTX, n(%)	18(100)	49(92)		1794(85)	
other DMARDs, n (%)	7 (39)	4 (8)	0	636 (30)	143 (9.4)
Biologics	14 (78)	17 (36)	0	226 (11)	0
<b>Concomitant Treatment</b>					
NSAID, n(%)	8 (44)	38 (72%)	12(92)	1544(73)	1394 (91.9)
Steroids systemic n(%)	0	11 (21%)	4 (31)	619 (29)	359 (23.7)
MTX, n(%)	13(72)	39(74)	13(100)	1389(66)	1517 (100)
other DMARD,s n (%)	0	0	0	233 (11)	57 (4)
<b>Baseline Disease Activity</b>					
Active joints, median [IQR]	5 [2;6]	4 [2;9]	9 [7;13]	3 [1;7]	3 [2;7]
Phys Global, median [IQR]	37 [19;56]	33 [24;49]	59 [43;75]	48 [26;71]	43 [24;67]
JADAS <sub>10</sub> , median [IQR]	12 [6;16]	12 [8;16]	21[18;24]	13 [8;18]	13 [8;18]

**Methods:** Monitoring of GLM in 200 pts with polyarticular JIA (cohort 1) in clinical practice will be performed by the German BiKeR Registry compared to a concurrent cohort 2 with 400 pts newly treated with alternative (approved) TNF-inhibitor, a concurrent cohort 3 with 500 pts newly starting methotrexate, a historic cohort 4 of patients treated with TNF-inhibitors and a historic cohort 5 never exposed to biologics but treated with methotrexate. Efficacy will be assessed by single disease activity markers and JADAS10, safety will be assessed by adverse event reporting and monitoring with a special interest on serious infections including opportunistic infections and TB, malignancies, autoimmune processes and exposure during pregnancy.

**Results:** Recruiting of three new cohorts 1–3 started in July 2017. Historic control cohorts 4 and 5 were obtained from the BIKER data base. Cohort 4 was recruited from 2006 to 2016, cohort 5 from 2005 to 2011. Baseline patients' characteristics

are outlined in table 1. So far, patients of the GLM cohort 1 were older, had a much longer disease duration and received pre-treatment with other biologics more often. All patients in this cohort received combination with methotrexate. Since so far GLM is approved for children with body weight of at least 40 kg and in combination with methotrexate, differences were expected. Baseline disease activity indicators are within the range of alternative TNF inhibitors and the historic cohort 4 while patients of the concurrent methotrexate cohort receiving their first treatment approach had the highest baseline disease activity.

**Conclusions:** The BiKeR registry has been collecting data from JIA patients treated with approved biologics in routine clinical practice since 2001. To provide context for interpreting long-term safety and effectiveness of data for GLM, analysis will also include data from contemporary pJIA patients treated with alternative TNF inhibitors and methotrexate.

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**AB1097** **PROGRESSIVE PSEUDORHEUMATOID DYSPLASIA (PPRD) IN SIBLINGS MIMICKING INFLAMMATORY ARTHROPATHY**

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**Background:** Progressive pseudorheumatoid dysplasia is a rare condition with an incidence of 1 in 1 million.

**Objectives:** Keeping in mind rare disorders when dealing with children in rheumatology clinics.

**Methods:** A 12 years old girl was referred to rheumatology by general practitioner. Her main complaint was difficulty walking, standing up from sitting position, short stature and nodulosis of interphalangeal joints. Initially she had muscle weakness which was thought to be contributing to her gait problem and difficulty standing.

Investigation revealed myopathic changes on electromyography though her CK was entirely normal. Other investigations including routine bloods and inflammatory markers were normal. Immunology was negative. X-rays revealed reduced joint spaces in interphalangeal joints and epiphyseal dysplasia in elbows and hips. On examination there was no evidence of any synovitis. The child was of short stature i.e less than the 3rd percentile on growth chart. She had a waddling gait. There was nothing in the history to suggest previous or current inflammatory arthropathy.

Interestingly this child had another younger sibling, 7 years old girl who had similar changes in her hands.

**Results:** Based on history, investigations, examination and familial characteristic we felt that these two kids (siblings) had PPRD. It usually happens at the age of 3 to 8 years. Walking pattern, fatigue, weakness and intermittent episodes of stiffness are the common symptoms. Other feature is reduced joint spaces in knees and hips. At birth kids are usually of normal height but by adulthood they are short statured. They also can have calcium deposition around the joints. PPRD is caused by mutation in WISP3 gene which is responsible for bone growth and cartilage maintenance and is inherited in an autosomal recessive pattern.



**Abstract AB1097 – Figure 1**

**Conclusions:** Kids can have a variety of musculoskeletal disorders. We feel that management of rheumatological conditions in kids need to be approached in a multidisciplinary way. Genetic disorders mimicking inflammatory conditions need to be considered all time. In those places particularly where paediatric rheumatologists are not available, involvement of paediatricians may be useful. In terms of PPRD, it is commonly mistaken as juvenile rheumatoid arthritis, however there is no inflammatory process going on in PPRD.

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AB1098

#### EARLY PROSTHESIS IMPLANTATION IS POSSIBLE IN PATIENTS AFFECTED BY JUVENILE IDIOPATHIC ARTHRITIS, TREATED WITH BIOLOGICS: A MONOCENTRIC EXPERIENCE OF 160 PROSTHESIS FROM THE LAST TWENTY YEARS

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**Background:** The main reasons for prosthesis implantation in a young patient are post-traumatic osteoarthritis, congenital dysplasia and autoimmune diseases involving joints, like Juvenile Idiopathic Arthritis (JIA). Often, related to particular anatomic conditions and severe grade of deformity, there may be a need for special (custom made or revision) components of prosthesis. Biologic therapy in severe, refractory JIA has permitted to obtain a better control of the disease so as to proceed with prosthesis implantations (hip, knee, ankle).

**Objectives:** The aim of the study was to present a monocentric experience of a transitional care centre for JIA and the outcome of early prosthesis implantation in patients treated with biologics.

**Methods:** 160 prosthesis implantation (72 Hip arthroprosthesis, 71 Knee arthroprosthesis and 17 Ankle arthroprosthesis) were performed between 1999 and 2017. It was defined a wash-out period from the biologic therapy depending on the half-life of the medication. The survival of the implant was evaluated for a period of 10 years. We evaluated the different type of implants and it was proposed a radiographic classification for every type of implant.

**Results:** All patients included in the study were treated with biologics. A long-term analysis of the following ten years of follow-up proved an average survival of 95.5% of the prosthesis and good results in term of function and comfort for the patients. Complications in 2% (two trochanter detachment, two sepsis and one peri-operative haemorrhage).

**Conclusions:** Prosthesis implantation for JIA patients is a complicated and difficult procedure in comparison with the traditional approach used in patients affected by osteoarthritis. This is related to the management of the biologic therapy, the low quality of the bone, the remarkable stiffness and deformity of the joints. Long-term results were good, even in patients with severe arthritis. There was a drastic reduction of articular pain and an improvement of functionality. Prosthesis implantation in patients with active disease and mild or bad response to the biologics had a worse outcome. The use of not cement-retained implants doesn't influence the long-term survival at ten years, similar to that of the adult patients affected by osteoarthritis.

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AB1099

#### AN AUDIT ON THE SCREENING GUIDELINES FOR UVEITIS IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS WITHIN THE ROYAL HOSPITAL FOR CHILDREN, GLASGOW

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**Background:** Juvenile Idiopathic Arthritis (JIA) defines many arthropathies occurring in children which persist for at least 2 weeks. All JIA patients are at risk of developing uveitis, an inflammatory condition of the eye which poses a risk to visual impairment. The British Society of Paediatric and Adolescent Rheumatology outline guidelines for the screening of these patients. Given the time since publication, an audit on the adherence to said guidelines, as well as patient outcomes, was conducted.

**Objectives:** Our aim was to identify adherence to the screening guidelines within the RHC, Glasgow; and to what extent adherence to these guidelines prevented the occurrence of uveitis. We aimed to identify areas which could be improved within the Glasgow service itself, as well as providing data for the revision of the guidelines.

**Methods:** We performed a clinical audit of all JIA patients diagnosed between 1st January 2008 and 31st December 2017, analysing the frequency and adherence of appointments, as well as medication use. Data was gathered from patient medical files and collected into a database for analysis.

**Results:** 97 of 115 JIA patients entered the screening programme. 72 patients had their initial eye screen within the appointed guidelines of 6 weeks, and 13 of the patients were examined under anaesthetic, with a mean time to examination of 3.31 weeks (0–7.14).

15 patients were seen according to the two-monthly guidelines for the first 6 months of diagnosis. Following this 6 month period, it is suggested patients are screened every three to four-months. 463 out of 641 (72.2%) appointments met this guideline.

After stopping immunosuppressive therapy, it is advised to screen at two-monthly intervals. 97 patients were treated with immunosuppressants, with 10 patients stopping whilst still in the screening service. 9 continued to be seen on a three to four-month basis as before, 1 patient was not screened at all, but no patients were screened according to the guidelines.

**Conclusions:** Adherence to the screening service could be improved, with 75% of patients having had their first screen within the guideline criteria, and 72% seen within the guidelines following the initial 6 months. It seems that improvement mainly needs to be focussed on the methods of appointment rearrangement.

There is believed to be a 6 month high-risk period of developing uveitis following cessation of immunosuppressants, thus increased screening is suggested. This was not adhered to well in the Glasgow service, but there was no increased risk of uveitis development found, suggesting the need for alteration to the guidelines.

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AB1100

#### EPIDEMIOLOGY AND MANAGEMENT PRACTICES FOR CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: A SURVEY IN LATIN AMERICA

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**Background:** Two groups have reported data focused on epidemiology, clinical and laboratorial features of childhood-onset systemic lupus erythematosus (cSLE) patients in Latin America (LA): BRAC-SLE (Brazilian Childhood-onset SLE Registry Group) and GLADEL (Grupo Latino Americano De Estudio del Lupus). However, to the best of our knowledge, epidemiology and management of cSLE based on LA Paediatric Rheumatologists (LAPR) were not carried out.

**Objectives:** Therefore, the objective of the present cross-sectional survey study was to assess LAPR reports of cSLE patients regarding epidemiology, classification criteria, disease activity and other instruments used in clinical practices, laboratory and other exams availability, general supportive care, drugs availability, infections, non-live vaccines, issues observed in adolescents, reproductive health issues and transition-focused program to adult care.



**Methods:** A cross-sectional study was performed in 288 LAPR based on online survey about cSLE practices, which included 21 countries. All physicians are members of Pan-American League of Association for Rheumatology (PANLAR).

**Results:** The response rate of web-based survey by LAPR was 170/288 (59%) and the majority worked in University Hospitals (63%). The ACR and/or SLICC classification criteria (99%) and disease activity tools (97%) were almost universally used by LAPR, whereas damage index (70%) and CHAQ (58%) instruments were less frequently used. Laboratory exams, diagnostic imaging and biopsies were generally available (>75%), however low availability for densitometry (66%). Drug access was excellent for the most common prescribed medications (>75%), except for belimumab (11%). Endemic illnesses were reported by LAPR in at least one cSLE patient during the previous year: tuberculosis (16%) and Hansen disease (2%). Emerging mosquito-borne diseases were also reported: dengue (20%), Chikungunya (11%) and Zika (8%). Groups were further divided in two, according to the number of cSLE patients followed by LAPR in the last year: group A ( $\geq 25$  patients) and group B (<25 patients). Frequencies of condom in combination with other contraceptive methods were significantly higher in group A than B (69% vs. 48%,  $p=0.01$ ). The frequencies of reported pregnancy (50% vs. 16%,  $p<0.001$ ) and non-adherence to therapy were significantly higher in group A (100% vs. 93%,  $p=0.023$ ). Alcohol intake (42% vs. 21%,  $p=0.004$ ) and illicit drug use (19% vs. 5%,  $p=0.007$ ) were also reported more frequently by LAPR of group A in at least one cSLE patient.

**Conclusions:** This first large web-based survey demonstrated an overall excellent access for diagnosis and therapy by LAPR, probably related to their high rate of practices in tertiary care of University Hospitals. Adherence to therapy, pregnancy and substance abuse were identified as major challenges in this population, particularly in larger centres.

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## AB1101 THE DEVELOPMENT OF A PALATABLE, STABLE ORAL METHOTREXATE SOLUTION

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**Background:** Methotrexate is used in the treatment of Rheumatoid Arthritis, Juvenile Idiopathic Arthritis and other conditions such as Acute Lymphoblastic Leukaemia and psoriasis. It can be administered orally or by injection. With oral administration, methotrexate's bitter taste may not be masked, particularly when tablets are crushed to facilitate dosing in paediatrics or patients who have difficulty swallowing tablets.<sup>1</sup> This can lead to long term treatment adherence issues and inaccurate dosing, putting patients at risk of adverse reactions or inadequate efficacy. A palatable oral liquid presentation of methotrexate would facilitate more accurate dosing and potentially improve treatment adherence; however, methotrexate is difficult to formulate as an oral liquid due to taste, solubility and stability challenges. Despite these difficulties, a palatable, stable oral methotrexate solution has been developed.

**Objectives:** To develop a palatable, stable, oral methotrexate solution, which complies with EU requirements for development of paediatric products,<sup>2</sup> to aid accurate dosing and treatment adherence.

**Methods:** During each of two single-dose (10 mg and 2.5 mg) bioequivalence studies of the test 2 mg/ml methotrexate oral solution with licenced tablets, 24 healthy male subjects were asked to comment on the oral solution's taste, indicating whether it was: Bitter, Sour, Salty, Sweet, or No Obvious Taste and they could also leave a remark. In parallel to clinical studies, long term ICH stability studies at ambient conditions (25°C/60%RH) and in-use shelf life studies were conducted.

**Results:** All subjects in the 10 mg dose study reported the oral solution as sweet tasting. One subject also reported an aftertaste and strange smell. In the 2.5 mg dose study, all subjects except one reported the solution as sweet tasting. The remaining subject reported a 'soothing' taste. One subject reported it was also sour and another reported an aftertaste. Two subjects additionally commented that they liked the taste. Both studies demonstrated bioequivalence and a similar safety profile between the oral solution and tablets. The stability studies illustrated that the oral methotrexate solution utilised in these clinical studies was stable at ambient conditions for up to 20 months, including a 3 months in-use period. The oral solution has recently been granted a European Union marketing authorisation and is the first methotrexate oral solution to be authorised for treatment of polyarthritic Juvenile Idiopathic Arthritis in Europe.

**Conclusions:** A 2 mg/ml oral methotrexate solution, developed to improve treatment adherence and dose accuracy, is reported to have a palatable, sweet taste and can be stored long term at ambient conditions with a 3 months in-use period.

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## AB1102 KAWASAKI DISEASE AND GIANT ANEURYSM IN MEXICAN CHILDREN: EVOLUTION AND CLINICAL CHARACTERISTICS: A 5-YEAR EXPERIENCE

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**Background:** Kawasaki disease (KD) is an acute, self-limited, systemic vasculitis, predominantly involving medium-sized arteries. It mainly affects children younger than five years and it is the leading cause of acquired heart disease in children in developed countries. Of unknown pathogenesis, KD severe complication is the occurrence of coronary artery lesions. Without early treatment, there is a 15% to 25% incidence of coronary artery lesions. Management with intravenous immunoglobulin (IVIG), combined with aspirin, effectively decrease the incidence of this lesions to a 4%. The long-term prognosis is determined by the initial and current level of coronary artery involvement. Methods to predict which children are at higher risk for coronary aneurysms have been sought to determine prognosis and select patients for more rigorous treatment and follow-up.

**Objectives:** To describe the clinical presentation and evolution in addition to laboratory findings in Mexican paediatric population who developed giant aneurysms diagnosed with KD during the past 5 years. By identifying mayor risk factors in our population, an effective score could be used to select children for evaluation of additional therapies to prevent coronary artery aneurysms that occur despite treatment with IVIG.

**Methods:** Retrospective cohort study of the Children's Hospital of Mexico Federico Gomez, last 5 years. We reviewed the data from the clinical archives of the patients who developed giant aneurysms after the diagnosis of KD from 2011 to 2016. A total of 84 patients with KD, 7% developed giant aneurysms. The variables analysed, apart from the typical clinical and laboratory findings of KD, include size and Z score of the aneurysms, involution through follow up, cardiac morbidity and mortality, and treatment strategy.

**Results:** Results: The mean age of patients at diagnostic was 17 months, and 84% were males. Only 33% of the patients developed complete KD, while 66% were diagnosed as incomplete. All patients presented with a positive Harada score. IVIG was administered in 83% of the patients, and a second dose was needed in 33%. Infliximab was used in 33% of the patients. One patient died due to cardiogenic shock. Results from echocardiography in the follow-up show that 33% of the patients have evolved to even larger aneurysms and 50% present no changes. Of the patients with a longer follow-up, 4 years after diagnostic, 33% have developed arrhythmias and 16% myocardial infarction. All are at high risk of sudden death.

**Conclusions:** The late diagnosis is the characteristic present in all patients which developed giant aneurysms, making imperative to identify clinical and laboratory findings that will help identify KD in Mexican paediatric population to avoid cardiac complications.

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**AB1103 SEVERE PULMONARY ARTERIAL HYPERTENSION AS THE INITIAL MANIFESTATION OF SYSTEMIC LUPUS ERYTHEMATOSUS IN A 7-YEAR-OLD MALE PATIENT: A CASE REPORT**

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**Background:** Pleural pulmonary manifestations in patients with systemic lupus erythematosus are reported in approximately 5% of cases. Presenting as pleural effusion, alveolar haemorrhage, diffuse interstitial lung disease, pulmonary infections and pulmonary arterial hypertension, among others, they are a manifestation difficult to diagnosis. Pulmonary arterial hypertension is a rare condition, usually occurring 3 to 5 years after the diagnosis of systemic lupus erythematosus.

**Objectives:** We report the case of a 7-year-old male patient who presented with pulmonary arterial hypertension as the initial manifestation of systemic lupus erythematosus.

**Methods:** Case report

**Results:** A 7-year-old male patient who was admitted to the Pneumology Department at Children's Hospital of Mexico Federico Gómez due to respiratory distress. In emergency assessment, pulmonary arterial hypertension of 66 mmHg was identified, of unknown cause. The patient did not have significant medical background, having enjoyed of good health up to 6 months prior to his admission. He presented with a history of non-quantified fever, as well as episodes of fatigue and dyspnea. Two months before admission, chest pain was added, exacerbated with inspiration. On admission, transthoracic echocardiography revealed severe dilatation of right cavities, moderate tricuspid insufficiency, with left ventricular ejection fraction of 56% and arterial pulmonary pressure of 66 mmHg. The diagnostic approach is initiated. Due to a history of pulmonary tuberculosis in the patient grandmother, the patient was studied with BAAR and cervical lymph node biopsy, ruling out the diagnosis. Infectious process causing the manifestations was also ruled out. The patient was discharged with medical treatment, requiring readmission in for 7 days, with facial oedema and in lower extremities, generalised pallor, asthenia, adynamia and 4 days before a decrease in urinary volumes and frequency. On admission, right heart failure, secondary to increase of pulmonary hypertension for discontinuation of diuretic administration. A renal biopsy was performed, which was reported as class IV lupus nephropathy, with an index of activity and chronicity of 0. The diagnosis of systemic lupus erythematosus is integrated based on the ACR criteria. Induction of remission of lupus nephropathy based on the CARRA protocol. As treatment was administered the patient showed important clinical improvement.

**Conclusions:** Pulmonary arterial hypertension is a rare condition, usually occurring 3 to 5 years after the diagnosis of systemic lupus erythematosus. In paediatric population, it is reported as a lupus complication in 5% to 14% of patients, and less than 1% as an initial manifestation. It is a clinical complication that gives the patient a high risk of morbidity and mortality. It is important to acknowledge that pulmonary arterial hypertension can be the initial manifestation of lupus in paediatric population. A prompt identification assures a prompt treatment and a better prognosis.

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**Disclosure of Interest:** None declared

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**AB1104 MALIGNANCY-RELATED ARTHROPATHIES IN PAEDIATRIC PATIENTS SEEN IN A TERTIARY HOSPITAL**

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**Background:** Along with constitutional symptoms such as fever, fatigue, and weight loss, childhood malignant diseases often also present with various musculoskeletal symptoms and findings, prompting consult or referral to a paediatric rheumatology clinic.

**Objectives:** The study described the characteristics of patients seen at the paediatric rheumatology clinic who were eventually diagnosed with malignancy.

**Methods:** Medical records of 35 children diagnosed with hematologic or solid malignancy who were seen at the paediatric rheumatology clinic from August 2013 to December 2017 because of with joint pains or difficulty in ambulation were reviewed.

**Results:** Twenty of the 35 patients (57.1%) were males and 15 (42.9%) were females. The mean age at diagnosis was 7.3 years old  $\pm 4.1$  (range 2.5–17.0). The time of diagnosis from the onset of symptoms has a mean of 4.5 months  $\pm 7.4$ . Fever was the most common constitutional symptom (82.8%), followed by pallor (45.7%) and weight loss (37.1%), while the most common musculoskeletal symptom or finding was joint pains (100%), followed by difficulty in ambulation (40%), joint swelling (37.1%) and nocturnal pains (31.4%). Mean haemoglobin level was 93.9 g/L  $\pm 18.9$ . Mean white cell count was 11.9  $\times 10^9/L \pm 7.1$ , mean segmenters was 41.6%  $\pm 21.7$ , and mean lymphocytes was 53.0%  $\pm 24.2$ . Mean platelet count was 294.0  $\times 10^9/L \pm 220.5$ . Mean ESR was 99.6 m/h  $\pm 33.7$  at baseline. Radiographic evaluation done were all normal. Peripheral blood smears and bone marrow aspiration study were done in all patients. Thirty-three patients (94.2%) were diagnosed with acute leukaemia, 18 of which was acute lymphocytic leukaemia, 14 acute lymphocytic leukaemia pre-B, and 1 acute myelogenous. One patient had Non-Hodgkins Lymphoma and 1 patient had hemoblastoma.

**Conclusions:** Children with joint pains associated with findings atypical of a rheumatologic disorder presentation should be further investigated for the possibility of malignancy.

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**Disclosure of Interest:** None declared

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**AB1105 INFLUENCE OF JUVENILE IDIOPATHIC ARTHRITIS ON THE QUALITY OF LIFE OF YOUNG ADULTS IN THE TRANSITION PERIOD TO ADULT RHEUMATOLOGIC CARE IN UKRAINE**

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**Background:** Young adults with juvenile idiopathic arthritis (JIA) often have an active disease with significant functional impairment in adulthood that can affect their physical and mental functions.

**Objectives:** The aim of the study was to determine the impact of JIA on quality of life, mental and physical health in young adults with JIA during the transition healthcare in Ukraine.

**Methods:** The cross-sectional study of 89 young adults aged 16 to 22 years with a history of JIA and 25 age- and sex-matched controls (without rheumatic disease) were included. The study was performed at the Aleksandrivsky Central Clinical Hospital, Kyiv, Ukraine in the period between April 2015 and February 2017. There was performed an evaluation of the disease activity by JADAS, received therapy, quality of life by the SF36, the functional activity (HAQ), long-term JIA damage indices JADI-A and JADI-E, PHQ-9, Beck depression scale.

**Results:** Patients with JIA had worse ( $p < 0.001$ ) physical health in comparison with the control group. Physical ( $p < 0.001$ ) and role ( $p < 0.05$ ) functioning and bodily pain ( $p < 0.001$ ) in JIA patients were decreased, compared with the controls. However, the indicators responsible for psychological function in patients with JIA did not differ from the controls. The analysis of functional activity revealed a strong negative effect of the disease on physical role functioning ( $p < 0.001$ ), bodily pain ( $p < 0.001$ ), general health ( $p < 0.001$ ), vitality ( $p < 0.001$ ), social role functioning ( $p < 0.001$ ), and mental health ( $p < 0.001$ ), which are included in physical ( $p < 0.001$ ) and mental ( $p < 0.05$ ) health. HAQ had strong negative effects on physical functioning ( $r = -0.56$ ,  $p < 0.001$ ), role function ( $r = -0.33$ ,  $p < 0.001$ ), bodily pain ( $r = -0.60$ ,  $p < 0.001$ ), general health ( $r = -0.40$ ,  $p = 0.01$ ), vitality ( $r = -0.46$ ,  $p < 0.001$ ), social functioning ( $r = -0.48$ ,  $p < 0.001$ ) and mental health ( $r = -0.42$ ,  $p < 0.001$ ). Articular long-term damages (JADI-A) have a predominantly negative effect on the patient's physical health ( $r = -0.27$ ,  $p < 0.05$ ) and on the indices associated with it: physical functioning ( $r = -0.24$ ,  $p < 0.05$ ), bodily pain ( $r = -0.24$ ,  $p < 0.05$ ), general health ( $r = -0.24$ ,  $p < 0.05$ ), vitality ( $r = -0.19$ ,  $p < 0.05$ ), social functioning ( $r = -0.27$ ,  $p < 0.05$ ), mental health ( $r = -0.22$ ,  $p < 0.05$ ). While the extra-articular long-term damages – JADI-E also have a predominantly negative effect on the patient's physical health ( $r = -0.22$ ,  $p < 0.05$ ) and on the indexes associated with it: physical functioning ( $r = 0.28$ ,  $p < 0.05$ ), bodily pain ( $r = -0.20$ ,  $p < 0.05$ ), general health ( $r = -0.23$ ,  $p < 0.05$ ), mental health ( $r = -0.23$ ,  $p < 0.05$ ), as well as a positive association with Beck depression scale ( $r = 0.28$ ,  $p < 0.05$ ) and PHQ-9 ( $r = 0.28$ ,  $p < 0.05$ ).

**Conclusions:** In our transitional cohort of Ukrainian patients at the era of biological therapies, juvenile idiopathic arthritis had a larger effect on the physical than mental SF-36 subscale. Pain was the main factor influencing quality of life. Extra-articular long-term JIA damages have impact on physical and mental health of young adults. Additional evaluation of mental health by PHQ-9 and Beck depression scale is recommended for evaluation signs of depression in Ukrainian young adults in transition period.

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**Disclosure of Interest:** None declared

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**AB1106 DEPRESSION AND ANXIETY IN PAEDIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS. A SYSTEMATIC REVIEW**

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**Background:** Depression and anxiety are common and treatable childhood mental health disorders that have been reported to impact outcomes for individuals with childhood-onset Systemic Lupus Erythematosus (cSLE)<sup>1</sup>. Research into the prevalence of depression/anxiety and cSLE comorbidity has reported conflicting results, and to our knowledge, no previous review of these data has been undertaken.

**Objectives:** To synthesise current knowledge regarding the association of depression and anxiety disorders with cSLE among paediatric patients.

**Methods:** Studies were identified through a comprehensive search of MEDLINE, EMBASE, PsychINFO, LILACS and Web Of Science (from database inception – July 2017) using MESH headings and Keywords for 'lupus erythematosus', and 'depression' or 'anxiety'. Included studies measured depression and/or anxiety symptoms prospectively among children and youth 8 to 21 years of age with a diagnosis cSLE. Data were extracted by two independent coders and where discrepancies occurred, agreement was reached by consensus.

**Results:** Sixty-two studies met criteria for full text review, and of these, 13 studies were included in the final analysis. The majority (80%) of studies were of cross-sectional design, with sample sizes ranging from 14 to 100 (mean=47) participants. The mean age of participants was 15.6 years and participants were predominantly female. Prevalence rates for depression ranged from 6.7% to 54%. Anxiety symptom prevalence was 20% to 34%. All studies employed self-report instruments to assess depression and anxiety; none of the studies utilised semi-structured diagnostic interview to make psychiatric diagnoses. Significant heterogeneity precluded meta-analysis of the data.

**Conclusions:** Depression and anxiety may be common comorbidities of cSLE however current research is limited by a paucity of studies, small sample sizes and an inability to confirm psychiatric diagnoses. Future research addressing these limitations is needed.

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**Disclosure of Interest:** None declared

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**AB1107 TRANSITION FROM PAEDIATRIC TO ADULT RHEUMATOLOGY SERVICES IN NEWCASTLE TRUST HOSPITALS**

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**Background:** Transitional care is defined as “the purposeful, planned movement of adolescents and young adults with chronic physical and medical conditions from child-centred to adult-oriented healthcare systems.”<sup>1</sup>

In 2016, EULAR produced recommendations on how this transition process should occur within rheumatology.<sup>2</sup>

**Objectives:** To audit the Newcastle-Upon-Tyne Hospitals rheumatology transitional care service against EULAR recommendations.

**Methods:** EULAR recommendations were adapted into a questionnaire, which was reviewed and edited by several Young Adults (YAs) with Juvenile Idiopathic Arthritis (JIA) attending clinics.

Patients attending specialist YA/JIA clinics between November 2017 and January 2018 were asked to complete the questionnaire; responses were audited against EULAR recommendations.

**Results:** 28 YAs with JIA completed the audit questionnaire (10 males and 18 females, age range 16–25). Not all questions were answered by all YAs.

Of the 17 patients with 'childhood-onset disease' (onset ≤age 10) 12% (2/17) had their transition started by age 14 ('essential' recommendation) and none by age 11 (the 'ideal' recommendation). Of the 11 patients with 'adolescent-onset

disease' (onset >age 10) 18% (2/11) had their transition started at the time of diagnosis (EULAR recommendation 2).

63% (17/27) of patients had ≥1 'direct' contacts with adult and paediatric rheumatology via a joint appointment (EULAR recommendation 3).

11% (3/28) of patients were aware of a documented individual transition plan (EULAR recommendation 4).

40% (6/15) were able to list ≥3 multidisciplinary team (MDT) members that had positively impacted their care. 54% (15/28) were able to provide the name of a transition coordinator (EULAR recommendation 6).

81% (21/26) of respondents 'agreed or strongly agreed' that they had been signposted to information on their condition, 48% (12/25) to peer support groups, mentoring schemes and charities, and 25% (6/24) to information sources on careers and finance. 64% (of patients were consulted on how they would like their parent/carer to be involved in their care during and after their transition (EULAR recommendation 7).

82% (23/28) of respondents reported having copies of letters concerning their care and transition (EULAR recommendation 8).

**Conclusions:** Newcastle-upon-Tyne hospitals transition services are in line EULAR recommendations in terms of MDT involvement in the transition process and addressing the medical needs of patients during transition, whilst signposting them to other agencies and ensuring they have copies of communication.

The audit also identified areas for improvement including: the need for a single named coordinator for all patients; ensuring discussions with patients about the transition process begin at an earlier age, and making sure patients are aware of and able to contribute to their documented and individualised transition plan.

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**Disclosure of Interest:** None declared

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**AB1108 THE EFFICACY AND SAFETY OF TREATMENT OF 152 NON-SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS PATIENTS WITH ETANERCEPT: FACTORS ASSOCIATED WITH ACHIEVEMENT REMISSION AND RISK OF FLARE**

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**Background:** Juvenile idiopathic arthritis (JIA) is the most frequent chronic inflammatory joint disease in childhood, required biologics administration if the previous therapy fails. Etanercept is the most worldwide biologic using in JIA patients.

**Objectives:** The aim of our study was to evaluate the efficacy and safety of etanercept in children with non-systemic categories of JIA and determine predictors of achievement of the remission and risk of flares.

**Methods:** In the retrospective observational study were included 152 children with non-systemic categories of JIA, treated with etanercept. Standard JIA measures and outcomes were utilised, remission was based on C. Wallace criteria (2004). We used descriptive statistics,  $\chi^2$ -test, Fisher's exact test, Mac-Nemar test, Mann-Whitny, Wilcoxon, Friedmann and log-rank tests, AUC-ROC analysis, odds ratio and relative risk calculation with Cox regression models.

**Results:** The cumulative remission was achieved in 58.8% patients during the trial. The maximum remission rates (80%) were in children with treatment duration near the 5 years and increased from year to year. Patient who achieved remission had less JIA onset age ( $p=0.015$ ), age of inclusion in the study ( $p=0.004$ ) and age of etanercept administration ( $p=0.00007$ ). The main predictors of achievement remission were JIA onset age  $\leq 7.8$  years (OR=4.3 (95%CI: 1.9–9.8),  $p=0.0003$ ), age of inclusion in the study  $\leq 14.0$  years (OR=2.85 (95%CI: 1.4–5.9),  $p=0.00007$ ), age of etanercept administration  $\leq 10.0$  years (OR=3.5 (95%CI: 1.7–7.2),  $p=0.0007$ ), time before etanercept administration  $\leq 2.4$  years (OR=2.7 (95%CI: 1.3; 5.5),  $p=0.0007$ ). In Cox regression model ( $p=0.007$ ) HLA B27 positivity (RR=2.15 (95%CI: 0.98; 4.75),  $p=0.06$ ) and time before etanercept administration  $\leq 2.4$  years (RR=2.4 (95%CI: 1.4; 4.4),  $p=0.003$ ) were main predictors of remission achievement. Polyarticular JIA increased the risk of flare compare to oligoarticular (RR=2.7 (95%CI: 0.9; 8.2),  $p=0.08$ ), then concomitant methotrexate decreased the risk of flare (RR=0.32 (0.1; 1.15),  $p=0.05$ ) in Cox regression model. During the



study etanercept was discontinued due to primarily or secondary inefficacy (9.2%), new onset of uveitis (5.2%) and other reasons (4.0%), including injecting site reaction. No serious adverse events, including severe infections, required hospitalisation were observed during the study.

**Conclusions:** Etanercept enables of induction of remission in JIA patients less than 10 years, with JIA duration less than 2.4 years, and whome have HLA B27-antigene. More stable effect was observed in oligoarticular JIA patients and who received concomitant methotrexate treatment.

**Acknowledgements:** Etanercept enables of induction of remission in JIA patients less than 10 years, with JIA duration less than 2.4 years, and whome have HLA B27-antigene. More stable effect was observed in oligoarticular JIA patients and who received concomitant methotrexate treatment.

**Disclosure of Interest:** None declared

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AB1109

### MISSED CASES OF MACROPHAGE ACTIVATION SYNDROME IN JUVENILE IDIOPATHIC ARTHRITIS (RETROSPECTIVE STUDY)

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**Background:** Macrophage activation syndrome (MAS) is a complication of JIA which elevates morbidity and mortality. Early recognition, differentiation from activity of JIA itself and the subsequent introduction of aggressive treatment contributes to better prognosis.

**Objectives:** A retrograde study to investigate the occurrence of missed MAS among JIA patients to assess the extent of the problem among those patients.

**Methods:** The study included 100 JIA patients registered in paediatric departments over 2 years in urban areas of Cairo. All JIA subtypes where included. MAS was diagnosed according to preliminary diagnostic guidelines for MAS complicating sJIA.<sup>Ravelli et al., 2005</sup> JIA patients who had history of recent infection, hepatitis or other liver disease, malignancy and pancytopenia were excluded. The hospital registry for JIA patients was scanned for medical history with special attention for records of history suggestive of MAS. Clinical examination, Laboratory investigations and radiological data. Complementary investigations were done when needed.

**Results:** Among the studied 100 JIA patients, 14% of patients fulfilled the criteria and were diagnosed awith MAS. Mortality rate was 2% of all JIA patients and 14% of JIA cases with MAS. Regarding gender, there were 10 females (71%) and 4 males (35%). Their age ranged from 3.5 to 18 years old (median 8 years). The disease duration ranged from 0.1 to 6 years (median 1.5 years). Ferritin level was elevated in all MAS patients. Renal affection was present in 10 MAS patients (71%) in the form of elevated serum creatinine level. In contrast to uncomplicated JIA where there was no significant renal involvement.

**Table 1** Frequency of clinical manifestations of MAS among the studied patients

Clinical manifestations	JIA with MAS (n=14)	JIA without MAS (n=86)
Fever	14 (100%)	2 (2.3%)
Central nervous system manifestations	3 (21%)	-
Haemorrhage	1 (7.1%)	-
Hepatomegaly	9 (64%)	3 (3.4)%
Splenomegaly	6 (42%)	1 (1.1%)
Generalised lymphadenopathy	5 (35%)	-
Cardiovascular system manifestations	1 (7.1%)	7 (8.1%)

**Table 2** Laboratory results among studied patients

Parameter	JIA with MAS	JIA without MAS
	Mean±SD	
R red blood cells (10 <sup>9</sup> /mm <sup>3</sup> )	3.4±0.6	4.66±0.73
Haemoglobin(gm/dl)	9.04±1.39	11.8±1.87
Platelets (10 <sup>9</sup> /mm <sup>3</sup> )	124.29±85.8	299±90.053
WBCS (10 <sup>9</sup> /mm <sup>3</sup> )	6361.43±3937.7	11989.6±6056.3
Aaspartate transaminase(u/l)	90.14±93.1	29.5±23.084
Creatinine (mg/dl)	2.19±0.91	0.73±0.2
International normalised ratio	2.04±0.6	1.07±0.14
Fibrinogen(mg/L)	203.5±86.02	317.86±67.39
Eerythrocyte sedimentation rate(mm/h)	28.29±13.12	17.56±2.83
C – reactive protein(mg/dl)	60.71±52.21	7.49±7.48

**Conclusions:** MAS is a potentially fulminant disorder whose incidence has increased due to raised manifestations awareness. It may be a complication of any JIA subtype but primarily systemic onset subtype. The diagnosis of MAS should be considered in presence of continuous fever, CNS, renal or haemorrhagic manifestation in JIA.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.2439

AB1110

### LIPID ABNORMALITIES IN CHILDREN AND ADOLESCENTS WITH JUVENILE IDIOPATHIC ARTHRITIS JIA

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**Background:** Atherosclerosis and its complications are known that one of the causes of lethality in rheumatic diseases. The risk of cardiovascular catastrophes increases not only with the prolongation of pathological process, but also in young patients, who are seropositive to rheumatoid factor and antinuclear antibodies in the early years of the disease.

**Objectives:** The study of lipid blood spectrum in patients with JIA with the definition of its clinical significance for the course of the disease was conducted.

**Methods:** 97 children (5–18 years) of patients with JIA were examined. The first group consisted of 38 children (39.2%) without symptoms of comorbidity, the second group, with signs of comorbidity, included 59 children (60.8%). The age of the debut of the disease in the first group was 6.3 years, and in the second group – 5.9 years. The duration of the disease at the time of the survey was 71 and 61 months. General clinical trials included the complex included autoantibodies, disease activity, drugs. Total cholesterol (TCh), triglycerides (TG), high density lipoprotein cholesterol, low-density lipoprotein cholesterol, apolipoprotein B, ApoA-I and lipoprotein-α were evaluated. The state of the blood coagulation system was also studied: fibrinogen of the blood, prothrombin index (PTI), thrombin time (TrT), active partial thrombin time, d-dimer, international normalised ratio.

**Results:** It was established that the parameters of the lipid blood spectrum changed in the presence of an increase in the level of fibrinogen. Patients with comorbidity had higher rates of low-density lipoprotein cholesterol (2.55 mmol/L versus 3.16 mmol/L; p<0.03), TG (0.99 mmol/L versus 1.04 mmol/L, p<0.03); the coefficient of atherogeny (3,10 mmol/L versus 3.24 mmol/L, p<0.03).

In the group of children with signs of comorbidity, there was a certain increase in the PTI and probable prolongation of the TrT (p<0.03), compared with the group without comorbid diseases. Children with JIA coagulation system parameters were also studied in a group of patients with signs of kidney damage. There is a probable increase in the PTI (p<0.05), which may indicate a predisposition to thrombosis.

It was found that in children with JIA with the presence of atherogenic changes in the lipid blood spectrum, there are signs of the hypercoagulation with parameters of the PTI (89,70±0,74% vs. 94,05±3,11%, p<0.05); fibrinogen (3.55±0.25 vs. 3.96±0.21 g/L, p<0.05) and the level of d-dimer (0.25±0.08 units versus 0.82 ±0.13 units), p<0.01).

Thus, in children with JIA, with signs of comorbidity, signs of hypercoagulation are established, especially in the presence of violations of the lipid profile of the blood. Regression analysis has shown that the greatest interaction exists between atherogenic dyslipidemia (the coefficient of atherogenicity) and d-dimer.

**Conclusions:** The obtained results confirm that the formation of comorbid pathology in children with JIA takes place against the backdrop of a close relationship between atherogenic changes in the lipid blood spectrum (the coefficient of atherogenicity) and signs of hypercoagulation (TG, d-dimer).

**Disclosure of Interest:** None declared

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**AB1111 ARTHRITIS IS NOT A PREREQUISITE DISEASE MANIFESTATION FOR THE DIAGNOSIS OF SYSTEMIC JIA: RESULTS OF A PROSPECTIVE COHORT TRIAL USING RIL-1RA AS FIRST LINE TREATMENT WITH LONG TERM FOLLOW-UP**

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**Background:** Systemic onset juvenile idiopathic arthritis (sJIA) is a multifactorial disease, characterised by arthritis, spiking fever, skin rash, lymphadenopathy, hepatosplenomegaly and/or serositis, in combination with increased inflammatory parameters as erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and ferritin. sJIA is nowadays seen as a complex autoinflammatory disorder. However, in the current ILAR classification, sJIA is still classified under the umbrella of JIA. The past decade has learned that the mechanisms underlying the systemic inflammation in sJIA differ in important aspects from the other subtypes like polyarticular JIA.

**Objectives:** Here we compare disease characteristics, manifestations and response to treatment of ILAR-criteria fulfilling sJIA (n=30) and 'sJIA without arthritis' (n=12), in order to evaluate whether arthritis should still be a prerequisite for the diagnosis of sJIA.

**Methods:** We included 30 consecutive diagnosed and prospectively followed new onset sJIA patients as well as 12 'sJIA without arthritis' from our paediatric rheumatology clinic from 2008 until 2017. The 'sJIA without arthritis' patients underwent extensive diagnostic procedures to exclude infections (PCR, blood cultures, serology etc), malignancies (bone marrow punctures, PET scans etc) and other diagnoses.

All patients followed a standardised treatment protocol, starting with rIL-1RA (2 mg/kg) as 1st line treatment (without steroids), as previously described.<sup>1</sup> In case of partial response, rIL-1RA dose was raised to 4 mg/kg with a maximum of 200 mg/day. If that failed, corticosteroids were added and/or patients switched to alternative biologicals as canakinumab or tocilizumab. If patients had inactive disease at 3 months after start of rIL-1RA treatment, rIL-1RA was tapered for a month (alternate day regimen) and subsequently stopped.

Peripheral blood samples were taken before initiation of rIL-1RA and at all follow-ups for routine lab measurements. For biomarker analyses, serum was isolated at disease onset and at three months after initiation of rIL-1RA.

**Results:** There were no differences in disease manifestations like skin rash, serositis, hepatosplenomegaly or symptoms like arthralgic (painful) joint count between sJIA and 'sJIA without arthritis' patients at diagnosis. Nor was there a difference in the levels of CRP, ESR, ferritin or IL-18 at start of therapy.

Importantly, also the response to rIL-1RA treatment did not differ between sJIA and 'sJIA without arthritis' patients in our cohort. At last follow-up (median 5.8 years, IQR 2.9–7.6 years), 95% of patients had inactive disease, of which 72% off medication.

**Conclusions:** Based upon disease manifestations and inflammatory parameters in patients with confirmed sJIA and 'sJIA without arthritis' at disease onset and on excellent treatment responses to a standardised treatment protocol with rIL-1RA as 1st line treatment, we conclude that arthritis should not be a prerequisite disease criterion in the next classification criteria of sJIA.

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**Disclosure of Interest:** None declared

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**AB1112 AUTOANTIBODIES IN CHILDREN WITH JUVENILE ARTHRITIS ON BIOLOGICAL THERAPY**

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**Background:** Antinuclear antibodies (ANA) are described as initial serological findings in juvenile idiopathic arthritis (JIA). SLE-like syndromes with ANA seroconversion have been described in the patients on biological therapy, including JIA children. Biologicals have been used in Ukraine since 2011. In 459 of 2,542 JIA cases registered in 2016, patients were on biologicals. According to the data of the Ukrainian Registry of Patients Receiving Biologicals, autoimmune diseases as complications of biological therapy have not been registered in Ukraine so far.

**Objectives:** To study the ANA dynamics in JIA children on biologicals.

**Methods:** There was conducted a retrospective observational study which involved 138 JIA patients, including 44 children with the biologicals as follows: TOZ 12, ADA 29, ETA 3. JIA markers (HLA B27 (PCR), RF (ELISA), aCCP

(immunosorption), ANA (IFT and ELISA (10 subtypes) were determined in patients at the disease onset and after 1, 2, 5 years of biologicals medication.

**Results:** Among all JIA patients, ANA were detected in 54% of oJIA, 47% of pJIA, 7% of all spondyloarthropathy (spA) cases. At the beginning of biologicals, only 22% children were ANA-positive, 66% of them being female, mean age at the disease debut was 6.9±3.81 y. The median of the time from the disease onset to the initiation of biologicals was 4.2±3.2 y. The mean age at biologic therapy start was 10.3±4.18 y. At the time of the examination, the mean duration of biologicals was 2.4±1.46 y. In pJIA onset ANA were detected in 62% of patients, in oJIA with uveitis in 75%, in spA in 14.2%; in sJIA ANA were not identified. RF and aCCP were found in 2 pJIA children; HLA B27 was detected in 1 child with uveitis and in 64.2% of patients with spA. The data obtained showed that ANA were found more often in patients on biologicals than in general JIA population (pJIA, p=0.04, oJIA, p=0.02), RF was lower (4.5%) (p=0.001). The relationship with the sex was not seen (r=0.19). 21.4% of patients had been ANA positive before ADA therapy initiation. Reverse seroconversion was seen in most patients after a year of ADA therapy (3.5% remained ANA+, reduced ANA titer). After 2 year medication, ANA were detected by IFT in 3 seronegative at the disease debut patients (7.1%). They had negative antibodies to histones and aDNAII (ELISA). After 5 y, 2 patients on ADA remained ANA+. Among patients on ADA, who had ANA as a new phenomenon there were 2 female and 1 male teens in disease remission. They had no clinical manifestations of secondary autoimmune pathology. All the patients continued methotrexate, corticosteroids were discontinued in 2 of them. All patients were on isoniazid medication for over a year. In RF +patients on ADA, the RF was not detected a year later, after 2 y it was revealed in 1 pJIA patient who was RF-neg (aCCP neg). There was 1 RF +case at pJIA debut with TOZ, after the therapy it was not detected. Two paediatric patients on TOZ (16.6%) were ANA +at the debut, but the subsequent dynamics studies did not detect ANA (TOZ vs ADA, p=0.04). Patients treated with ETA were observed for less than 1 year.

**Conclusions:** ANA types which are detected at JIA debut and after initiation of biologic treatment may differ. It is suggestive of the biologicals potential to modify the immune response, thus increasing the risk of overlap-syndromes. Therefore, it is advisable to monitor autoantibody titers in JIA children on biologic treatment.

**Disclosure of Interest:** None declared

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**AB1113 PREVALENCE OF GENERALISED JOINT HYPERMOBILITY IN THE CHILDREN POPULATION OF ORDU; TURKISH STUDY**

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**Background:** Generalised Joint hypermobility (GJH) is a clinical conditions that may cause common musculoskeletal pain during childhood. In our study, we aim to show the prevalence of GJH in children of 11–18 age group, and to provide guiding information for rheumatologists and paediatricians who are interested in this subject.

**Objectives:** Our study aimed to evaluate the frequency of GJH in children aged 11–18 years in the province, Ordu.

**Methods:** This cross-sectional study was performed with 410 students aged 11–18 years who receive education in the province, Ordu. Questionnaire forms were filled in, and each student was examined. The children, who reported to have any disease, were excluded from the study. GJH was diagnosed according to criteria of Beighton diagnosis.

**Results:** A total of 410 students, 210 of whom were girls (51.3%) and 200 (48.7%) of whom were boys, participated in the study. The subjects' mean age was 13.7±1.7 years for girls and 13.1±1.79 years for boys. The body mass index (BMI) of the girls was 21.5±3.4 kg/m<sup>2</sup> and of the boys were 22±3.8 kg/m<sup>2</sup>. 160 (39%) of the students participated from the city centre and 250 (61%) from the district centres. The presentations of the students to the health institution due to any complaint in 1 year were examined. The students participating in the study were questioned in terms of presence and time of previous joint complaints. Accordingly, the number of participants who previously had a joint-related complaint was found to be 155 (37.8%). 40 (10.7%) of these participants had a joint-related complaint 3 months ago, 18 (4.3%) had it 6 months ago, 40 (9.7%) had it 1 year ago, and 47 (11.4%) had it more than one year ago. The frequency of GJH was 8.7%. 24 of 36 participants in whom GJH was detected and had a Beighton score of 5 and above consisted of girls; and this was 11.4% of the girls. The number of male participants in whom GJH was detected, was found to be 12; and this was 6% of the boys. There was a significant difference between female and male participants in terms of the frequency of GJH (p=0.021). A statistically significant and highly negative correlation was found between age and Beighton score (r=-0.182, p<0.001). A statistically significant and highly negative correlation was found between body mass index and Beighton score (r=-0.092, p<0.05).

**Conclusions:** One of the most common complaints seen during the childhood is musculoskeletal system pain. As shown by various studies performed, one of the significant reasons of extremity pain is GJH.<sup>1</sup> In our study, no significant correlation was found between GJH and joint pain. GJH is a disease that may cause musculoskeletal system pain during childhood. In our study which investigates the frequency of GJH in our region, we detected the GJH prevalence as 8.7. GJH is a clinical syndrome that is characterised with the fact that the joints have a range of motion above normal levels without a correlation with any systemic rheumatismal disease. The specific definition of GJH was shown by Kirk et al. in 1967.<sup>2</sup>

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#### AB1114 SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS: A SINGLE CENTRE EXPERIENCE

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**Background:** Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease in childhood, divided into several subgroups. The sJIA could be presented by monocyclic, polycyclic or persistent polyarticular clinical course. Macrophage activation syndrome (MAS) represents the most devastating complication that could appear during the disease course. Studies on follow up, treatment response and disease complications of the sJIA patients are sparse and rare.

**Objectives:** To evaluate demographic and clinical characteristics and to explore the long-term treatment response and disease complications in a large cohort of sJIA patients from the single centre.

**Methods:** Demographic and clinical features of the sJIA patients were reached from the patients's archives. The frequency of disease flares, treatment response and side effects were recorded for each patient.

**Results:** A total of 168 sJIA patients were included in the study: 87 (51.8) female, 81 (48.2) male. The clinical features are shown in table 1. Fifty-three (31.5) patients had monocyclic while 23 (13.7) patients had polycyclic clinical course (mean recurrence of attacks 2.5±2 (IQR:1–4)); in 38(.42) Polyarticular course was present in 92 (54.8) patients. Initially diagnosis of patients were: infection in 86 (51.1), sJIA in 34 (20.4), acute rheumatic fever in 19 (11.3), urticaria in 10 (5.9), Kawasaki disease in 4 (2.4) and juvenile systemic lupus erythematosus in 2 patients.

The most common disease complications were: MAS in 20 (11.9), growth retardation in 19 (11.3) and vertebral fracture due to osteoporosis in 3 (1.9) patients. Gastrointestinal symptoms secondary to methotrexate intolerance that led to cessation of treatment were present in 9 (7.1) patients. Among 5 (2.9) patients that developed tuberculosis, 4 (2.3) were under etanercept treatment.

All of the patients were treated with corticosteroids: a doses of 2 mg/kg/day in 118 (70.2) patients and pulse steroids in 50 (29.8) patients with severe clinical presentation. The methotrexate was used in 126 (75), leflunomide in 5 (3), cyclosporine A in 29 (17.3), intravenous immunoglobulin in 19 (11.3), anakinra in 27 (16.1), canakinumab in 27 (16.1), tocilizumab in 18 (10.7), etanercept in 50 (29.8) and adalimumab in 7 (4.2) patients. The median time to remission after the initial treatment with corticosteroids was 4 (IQR:2–4) months. The remission off medications was achieved in 82 (48.8) while remission on medications was achieved in 83 (49.4) of patients.

Table: Demographic, clinical features of sJIA

Female/male	87 (51.8)/81 (48.2)
Mean age at disease onset	76.7±54.5 months (IQR: 28–118)
Mean age at diagnosis	79.7±54.5 months (IQR: 33–121)
Clinical features, n(%)	
- Typical fever	160 (95.2)
- Typical rash	99(59)
- Lymphadenopathy	45 (26.8)
- Hepatosplenomegaly	70 (41.7)
- Arthritis/arthralgia	143 (85.1), 25 (14.9)

**Conclusions:** Systemic JIA is a subtype of JIA characterised by significant morbidity and mortality rate with macrophage activation syndrome being the most severe disease complication. Corticosteroids represent the main treatment modality. Biological agents should be considered in the steroid-resistant patients.

The clinical remission could be achieved and chronic arthritis sequelae could be prevented in a majority of patients with biological agents.

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#### AB1115 SYSTEMIC LUPUS ERYTHEMATOSUS IN PAEDIATRIC POPULATION- A SINGLE CENTRE STUDY FROM INDIA

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**Background:** systemic lupus erythematosus is an autoimmune disease that can be manifest in paediatric population in various ways. It is characterised by widespread inflammation of the blood vessels and connective tissues with positive autoantibodies. Though it is a chronic disease it can be fatal at times.

**Objectives:** 1. To study the diversity in clinical and laboratory profile in paediatric systemic lupus erythematosus patients at a tertiary care centre in Kolkata.

2. To identify the poor prognostic factors at the time of admission to the hospital.

3. To quantify the drug related adverse effects in follow up.

**Methods:** Both old known cases and newly diagnosed cases of paediatric SLE who presented to our rheumatology follow up clinic over last 18 months were retrospectively reviewed for their clinical and immunological presentation. SLICC diagnostic criteria has been applied to define a positive case.

**Results:** A total number of 64 patients were evaluated, among which 54 were girls and 10 were boys with a sex ratio of 5.4:1 favouring girls. Mean age on presentation was 9.9 years with a range of 2.5 to 16 years. Among the clinical presentation fever (72%) was the most common symptom, followed by skin manifestation (68.8%), musculoskeletal involvement (53.1%), haematological involvement (37.5%). Renal involvement was seen in 35.9%, among which 59.1% had stage IV lupus nephritis, and central nervous system involvement was observed in 10.9%. Among immunological profile, ANA was positive in 95.3%, anti-double-stranded DNA was positive in 92.1% and low complement levels were seen in 92.1%. Antiphospholipid antibody was seen in 7

patients (n=21) and anti-Smith antibody in 3 (n=4). All the patients required therapy with steroids and hydroxychloroquine. Steroid sparing agents like azathioprine (54.7%), cyclophosphamide (28.1%), mycophenolate mofetil (23.4%), methotrexate (18.7%), and rituximab (10.9%) were also used.

**Conclusions:** Paediatric SLE has got a varied presentation, and a high index of suspicion is needed for early diagnosis and timely management with multiple drugs of this dreadful disease

**Disclosure of Interest:** None declared

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#### AB1116 MACROPHAGE ACTIVATION SYNDROME: AN EXPERIENCE FROM A TERTIARY PAEDIATRIC CARE SETTING IN EASTERN INDIA

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**Background:** Macrophage activation syndrome (MAS) is a rare but potentially fatal complication of systemic inflammatory disorders occurring most commonly in Systemic arthritis(SJIA) but also being increasingly reported in SLE, Kawasaki disease and Periodic Fever Syndromes. We present a series of 29 cases of MAS encountered in the last 9 years in a tertiary paediatric care setting in eastern India.

**Objectives:** The objective of this study is to evaluate the clinical features, laboratory findings and outcome in MAS; to assess the treatment response to different therapies and to identify the poor prognostic factors.

**Methods:** It is a prospective analysis of data of patients diagnosed as having MAS, between July 2008 and April 2017, admitted in the Department of Paediatrics at Institute Of Child Health, Kolkata.

All patients with Haemophagocytic Lymphohistiocytosis (HLH) secondary to autoimmune or inflammatory connective tissue diseases were included whereas HLH secondary to infections were excluded. Diagnosis of HLH was based on the HLH 2004 criteria. MAS diagnostic criteria for SJIA was laid down in 2014. <sup>Post 2014</sup> we used those criteria in SJIA patients.

The data noted were the clinical and laboratory features, treatment details, the response to therapy and outcome.

**Results:** Twenty nine (n=29) patients were found to have MAS with the primary illness being SJIA in 24 (83%), SLE in 4 (14%) and Kawasaki Disease in 1 (3%). The mean age at presentation was 5 years 3 months. The male female ratio was 1.2:1. Neurological, cardiac, renal and pulmonary involvement was seen in 21 (72%), 14 (48%), 6 (20%) and 5 (17%) patients respectively. Pulse methyl



prednisolone (30 mg/kg) for 3 days was given in 27 patients. Two patients received hydrocortisone in SJIA MAS secondary to infections (chickenpox, Hepatitis A). In patients unresponsive to steroids IVIG and/or cyclosporine was used. 19 (65%) patients survived whereas 10 (35%) died. Of the 10 who succumbed, the HLH 2004 protocol (including etoposide) was used in 2 who were refractory to pulse methylprednisolone +cyclosporine +IV Ig, but without any success. 2 patients on Tocilizumab had silent MAS.

Ferritin >50000 ng/ml was seen in 11 patients of which 8 died. Chi square test of significance was done and p value (0.001) was significant for mortality in patients with ferritin >50000 ng/ml, with a positive correlation (0.613).

Patients with cardiovascular involvement especially pericardial effusion in SJIA was observed to have higher mortality but no statistical correlation could be made. **Conclusions:** MAS is a fatal complication with a high mortality rate of 35% in our series. Ferritin levels >50,000 ng/ml was associated with high mortality. Early and aggressive intervention with optimal intensive care support maybe life saving.

**Disclosure of Interest:** None declared

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### AB1117 ISOLATED CERVICAL ARTHRITIS AS THE SOLE MANIFESTATION OF FAMILIAL MEDITERRANEAN FEVER: A CASE REPORT

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**Background:** Familial Mediterranean Fever (FMF) is an autosomal recessive disease affecting mainly eastern Mediterranean populations. Fever and Abdominal pain are the 2 most prevalent features. The most common arthritic manifestation of FMF is acute self-limiting monoarthritis. 5% of FMF patients develop chronic erosive arthritis. FMF mutation M694V has been associated to an increased risk of spondylarthropathy.

**Objectives:** We report the case of a child with cervical spine inflammation as the sole presentation of FMF.

**Methods:** A boy born to non-consanguineous parents presented at the age of 4 with complete blockage of his neck. He was described to have experienced progressive neck stiffness since the age of 3 years. His history is notable for intermittent limp at the age of 1 with complete spontaneous remission, and possible recurrent fever in the first 2 years of life. Family history is negative.

His physical exam revealed a painful and completely blocked neck in all movements, and stubby fingers. He had failure to thrive and a big belly without hepatosplenomegaly. Cognitive development was normal.

Laboratory tests revealed increased inflammatory markers. Other biological tests were insignificant. ANA, RF, anti-CCP and HLA B27 were negative. Lysosomal enzyme activities were normal ruling out mucopolysaccharidosis, mucopolidoses and multiple sulfatase deficiencies. Work-up for failure to thrive was noncontributory. Ophthalmic screening showed no abnormalities.

Cervical spine plain radiographs were normal. Cervical MRI showed global contrast enhancement of cervical vertebrae and joints with blurring of the osseous contours and synovial inflammation; bone oedema was noted and involved some posterior arcs, spinous processes and pedicles. Sacro-iliac MRI was normal.

The child was treated with oral steroids along with methotrexate and etanercept secondarily due to steroid dependence. Inflammatory markers normalised and clinical improvement was noted as the range of motion of neck increased and pain subsided. Repeated MRI after 6 months showed an almost normal image.

**Results:** Given this atypical isolated inflammation of the cervical spine, genetic testing for FMF was conducted. We identified 2 typical mutations (M694V and M694I) confirming the diagnosis of FMF. Colchicine treatment was started.



Abstract AB1117 – Figure 1

**Conclusions:** To the best of our knowledge, this is the first report of FMF masquerading as neck arthritis. Early spondylarthropathy is a possibility, but this

unusual neck inflammation might be an isolated arthritis associated to FMF. Based on this clinical presentation, in the setting of atypical arthritis, diagnosis of FMF is to be raised in at-risk ethnicities, even in the absence of familial history and common clinical signs.

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### AB1118 PROCALCITONIN DIFFERENTIATES INFECTION FROM ACTIVE DISEASE IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS (JIA)

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**Background:** Patients with JIA often present with signs and symptoms suggestive of infection. However, differentiation of infectious from non-infectious presentation in routine clinical care is challenging. Procalcitonin (PCT) is a serum biomarker elevated in the setting of bacterial infection, but whether it can reliably differentiate infection from disease flare in patients with JIA is unknown. [1]

**Objectives:** To test the hypothesis that PCT levels will differ between active JIA, quiescent JIA, bacteremic patients and healthy controls.

Abstract AB1118 – Table 1. Patient Characteristics

	Active Untreated JIA (n=12)	Quiescent JIA (n=15)	Healthy Controls (n=16)	Bacteremic Patients (n=5)
Age, years (median, IQR range)	9.0 [2.4–12.8]	14.5 [9.9–17.4]	14.4 [13.9–15.5]	1.1 [0.8–1.8]
Male Gender	5 (41.7%)	3 (20.0%)	6 (37.5%)	3 (60.0%)
Race				
Caucasian/White	7 (58.3%)	14 (93.3%)	12 (75.0%)	2 (50.0%)
AA/Black	1 (8.3%)	0 (0.0%)	3 (18.8%)	1 (25.0%)
Asian	3 (25.0%)	1 (6.7%)	0 (0.0%)	1 (25.0%)
Other	1 (8.3%)	0 (0.0%)	1 (6.3%)	0 (0.0%)
Hispanic Ethnicity	2 (16.7%)	2 (13.3%)	1 (6.3%)	1 (20.0%)
Private Insurance	7 (58.3%)	14 (93.3%)	14 (87.5%)	4 (80.0%)

Abstract AB1118 – Table 2. Laboratory Data

	Active Untreated JIA (n=12)	Quiescent JIA (n=15)	Healthy controls (n=16)	Bacteremic patients (n=5)	p-value
WBC (mean, SD)	8.9±4.4	7.7±1.6	6.7±1.7	13.1±12.1	0.06
ESR (median, IQR)	6.0 [4.0–46.0]	8.0 [5.0–10.0]	8.0 [5.0–10.0]	43.0 [20.0–66.0]	0.18
CRP (median, IQR)	0.27 [0.12–6.48]	0.31 [0.16–2.65]	0.44 [0.12–1.85]	16.63 [7.76–25.68]	0.067
PCT (median, IQR)	0.00 [0.00–0.00]	0.00 [0.00–0.00]	0.00 [0.00–0.00]	5.78 [4.26–52.00]	<0.001

**Methods:** From 10/16–4/17, consecutive children 6 months – 18 years with a) active untreated JIA b) quiescent JIA and c) healthy pre-surgical candidates were recruited from a musculoskeletal specialty hospital. JIA was defined according to ILAR criteria. Patients with active JIA despite treatment were excluded, to avoid

confounding by treatment. Consecutive bacteremic patients were identified from an associated paediatric intensive care unit over the same period. Descriptive statistics and univariate logistic analyses were performed as appropriate.

**Results:** Patient characteristics are summarised in Table 1; bacteremic patients were younger. PCT was elevated in bacteremic patients, and was undetectable in all other subjects (Table 2). There were trends towards higher ESR and CRP in bacteremic patients, but these were not statistically significant.

**Conclusions:** Serum PCT levels appear to be a reliable biomarker to distinguish infection vs. active JIA at presentation, and can aid in directing therapy. However, PCT does not appear useful to assess disease activity in JIA. Further studies are needed to assess utility of serum PCT measurement in differentiating JIA flares from less severe infections.

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AB1119

#### CLINICAL, THERAPEUTIC CHARACTERISATION AND TIME TO ACHIEVE REMISSION ANALYSIS OF A COLOMBIAN COHORT WITH JUVENILE IDIOPATHIC MYOPATHY

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**Background:** The clinical characteristics of paediatric patients with idiopathic inflammatory myopathies differ from adults in several aspects. Its clinical presentation can include amyopathic onset and the skin involvement has different characteristics

**Objectives:** To describe a Colombian cohort with Juvenile Myositis (JM) recruited in a rheumatology facility.

**Methods:** A cross-section retrospective research with data collected between 2014 and 2017 from a population diagnosed before 16 years of age with Idiopathic Myopathy according to Peter and Bohan criteria and followed up for at least six months. Kaplan-Meier curves were performed to analyze time to achieve remission.

**Results:** Out of 37 patients, one was excluded for having a dystrophy myopathy gene, 73% fulfilled definitive and 16% probable Bohan and Peter criteria; most patients were female 75.8%,<sup>26</sup> with mean age of onset 7.2 years, and clinical remission was achieved on average at 4 years of disease. There was high prevalence of Gottron's sign and papules (89%), Heliotrope rash (62%) and Calcinosis (37%). Other involvements are described in Table 1. Antinuclear antibodies were positive in 52%. Electromyography (EMG) was positive for myopathy in 39% of the patients. Biopsy was compatible with myopathy in 10% and was negative in 32% of the patients. The most common treatment was methotrexate (91%) followed by antimalarials (72%) and corticoids (56.7%). Medication used in severe forms included Cyclophosphamide (5%), Rituximab (16%) and IV Immunoglobulin (5%). Kaplan-Meier curves showed an earlier time to remission in patients with Gottron sign compared to patients without them (HR:8.25 HR CI95%IL:1.076–63.3;p=0.042 and in childrens younger than 15 years compared to older patients (HR: 2,529 HR95%IL: 1,084–5,901, p: 0,039).

**Abstract AB1119 – Table 1.** Clinical characteristics of Colombian patients with JM.

Characteristics in JM n=37	N	%
Symmetrical muscle weakness	27	72,97
Gottron's papules	33	89,19
Heliotrope rash	23	62,16
Calcinosis cutis	14	37,84
Gastrointestinal involvement	6	16,22
Pulmonary involvement	4	10,81
Articular involvement	9	24,32
Amyopathic	9	24,32
ANA(+)	14/ 27	37,84
EMG Myopathic changes	9/23	24,32
Biopsy-proven myopathy		
Positive	4	10,81
Negative	12	32,43

**Conclusions:** Our results agreed with those obtained in other multi-centred studies including latin america that evaluated clinical and therapeutic characteristics in children with myopathy, Gottron's sign and papules being the most common findings and with high rates of calcinosis and joint involvement. There was a significant difference between remission lapse in patients younger than 15 years compared to older ones.

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**Disclosure of Interest:** None declared

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AB1120

#### THYROID HORMONE CONCENTRATIONS IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS FROM A SINGLE TERTIARY REFERRAL CENTRE

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**Background:** Despite mounting evidence linking both endocrine disorders and rheumatic diseases, there is a lack of studies investigating any association between the prevalence and clinical characteristics of thyroid disorders and juvenile idiopathic arthritis (JIA).

**Objectives:** The aim of this study is to assess the prevalence of abnormalities in thyroid function in patients with JIA, and to investigate the possible association between this endocrine disorders and specific disease activity markers.

**Methods:** Thirty patients diagnosed with JIA according to the International League of Association for Rheumatology were screened for thyroid diseases. We performed stratified analyses by sex, age, subtype of JIA, disease duration, the Juvenile Arthritis Disease Activity Score (JADAS-71), clinical peculiarities, laboratory values and ultrasound examination of thyroidal gland.

**Results:** Our results revealed that 67% of patients were girls. The mean age of the studied group was 127,56±8,8 months, the median age at diagnosis was 74,33±8,49 months and the median disease duration was 50,83±9,33 months. The most frequent types of JIA were oligoarticular (40%), polyarticular negative RF (34%) and systemic (20%). The median JADAS-71 score was 16,91±1,64 [range values from 5 to 34]. The status of the thyroid function in those patients was euthyroidism. Contrary to other findings in the literature, a high free triiodothyronine was recorded in 33% of cases. However, specific antibodies as antithyroglobulin and antithyroid peroxidase were not detected in any patients. The ultrasound examination of thyroidal gland revealed abnormalities in 30% cases, most of them cystic changes (26,6%) and hypo-echogenicity (23,33%). In 2 cases were detected 2 thyroid nodules. Furthermore, 2 patients presented mean thyroid volume above 2SDS according their age reference values. An increased vascular flow pattern on Doppler examination of thyroidal gland was found in 10% cases. Correlation and regression analysis showed low age at diagnosis and JADAS-71 score (more than 20) to be predictors for those thyroid disorders.

**Conclusions:** The goal of early identification of endocrine comorbidities in rheumatic diseases is to prevent and limit the clinical disease impact. The identification of autoimmune diseases in preclinical stage secondary to juvenile idiopathic arthritis allow a better disease control and quality of life.

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**Disclosure of Interest:** None declared

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AB1121

#### EVALUATION OF CASES DIAGNOSED WITH CRMO; SINGLE CENTRE EXPERIENCE

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**Background:** Chronic recurrent multifocal osteomyelitis (CRMO); is a rare auto-inflammatory bone disease characterised by recurrent, sterile inflammatory

lesions occurring primarily in children and adolescents. Symptoms of presentation may range from mild unspecific bone pain, local swelling and warmth to severe pain, malaise, fevers and even fractures.

**Objectives:** In this study, we aimed to evaluate our patients who had a diagnosis of CRMO, retrospectively.

**Methods:** Six patients who were diagnosed with CRMO between 2010–2017 years were included in the study. The CRMO diagnosis was based on characteristic clinical features and magnetic resonance imaging findings. The clinical data were obtained from the records of electronic files.

**Results:** The female to male ratio of the cases was 4/2 and the median age was 11.15 years.<sup>6–12</sup> The age of diagnosis was 10.35 years (4–12.5), the median period for diagnosis delay was 3 years (0.75–8). The most common complaint was localised pain (n=6, 100%). Accompanying diseases were detected in 3 patients; 1 case had inflammatory myositis, 1 case had PFAPA syndrome and 1 case had selective IgA deficiency. Multifocal bone involvement was present in 4 (66%) cases and unifocal bone involvement in 2 (33%) cases. The most common site of disease was femur. Acute phase reactants were high most of the cases; elevated erythrocyte sedimentation rate (ESR) in 5 cases (83.3, n=6), elevated c-reactive protein level in 4 cases (66.6%, n=6), elevated serum amyloid A level in 3 cases (60%, n=5), and elevated fibrinogen in 2 cases (50%, n=4) were present. ANA was found positive at low titer in only 1 case, whereas rheumatoid factor was negative in all cases. Non-steroidal anti-inflammatory drugs were prescribed in all cases and anti TNF drugs in 3 (Etanercept in 2 cases and adalimumab in 1 case). Clinical characteristics of the patients are given in Table 1.

**Abstract AB1121 – Table 1.** Clinical findings of the cases

Initial complaints of cases	n	%
Pain	6	100
Walking abnormality	4	66.7
Swelling on bone	1	16.7
Weight loss	1	16.7
<b>Distribution of involved bones</b>		
Femur	4	66.7
Iliac bone	2	33.3
Tibia	2	33.3
Calcaneus	1	16.7
Vertebral column	1	16.7
Acetabulum	1	16.7
<b>Treatment</b>		
Ibuprofen	3	50
Naproxen Na	2	33.3
Aspirin	1	16.7
Indomethacin	1	16.7
Adalimumab	1	16.7
Etanercept	2	33.3

**Conclusions:** The diagnosis of CRMO is difficult and no consensus exist on diagnosis and treatment. Multifocal bone lesions with characteristic radiological findings are very suggestive of CNO. The first line treatment is usually NSAIDs, however, anti TNF treatment are needed in some patients to achieve for remission. Our case is the second one who had inflammatory myositis and CRMO according the literature.

**Disclosure of Interest:** None declared

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#### AB1122 DIALYSIS TREATMENT OF SYSTEMIC VASCULITIS IN PAEDIATRIC PATIENTS

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**Background:** Childhood-onset systemic vasculitis is a rare but serious condition with high mortality rate even with proper treatment. Renal involvement at presentation is a high risk for end stage renal disease (ESRD).

**Objectives:** The aim of our study was to review the results of the dialysis treatment in paediatric patients with systemic vasculitis in a single dialysis centre for children in Bulgaria.

**Methods:** For a period of 20 years we observed 9 clinical cases of systemic vasculitis – 5 cases of Goodpasture syndrome (GPS) – 4 girls and 1 boy from 6 to 17 years old; one 6 year old girl and one 12 year old boy with Granulomatosis with polyangiitis (GPA); an 8 month old boy with microscopic polyangiitis (mPAN), and one 8 year old girl with Takayasu arteritis. Seven of the children were treated by hemodialysis because of progressive kidney failure leading to ESRD, one of them was treated by continuous ambulatory peritoneal dialysis (CAPD) and one conservatively.

**Results:** In the GPS group one of the girls still continues on hemodialysis with no pulmonary symptoms for more than 14 years follow-up. The second girl was treated with immunoadsorption after which reminded antibody negative. On the follow-up she is managed conservatively for chronic kidney disease. Two of the girls died because of severe pulmonary bleeding caused by exposure to fragrant smoke during incense. The boy was treated conservatively because of mild pulmonary and kidney involvement and died from pulmonary bleeding caused by smoke. In the GPA group the girl underwent kidney transplantation and died one month later, and the boy died because of severe pulmonary bleeding. The 8 month old boy with mPAN was treated by dialysis with some clinical improvement but after six months died because of thrombus in the right atrium. The girl with Takayasu arteritis was treated with CAPD but died because of cardiopulmonary complications.

**Conclusions:** End stage renal disease is poor prognostic factor for survival in paediatric patients with systemic vasculitis. 75% of the children died in a period of 5 months after initiation of dialysis treatment.

**Disclosure of Interest:** None declared

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#### AB1123 DO CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS PLAY AN ACTIVE ROLE IN THEIR TREATMENT ADHERENCE? FIRST RESULTS OF THE RUMAJI STUDY

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**Background:** Adherence to DMARDs such as methotrexate and biologics is critical for patients with Juvenile Idiopathic Arthritis (JIA). Notwithstanding, few studies exist on that topic and we lack information to understand the grounds for adherence.

**Objectives:** The RUMAJI study aims, among others, to understand and decipher the parents and children adherence mechanisms and practices.

**Methods:** Qualitative methods were chosen in order to investigate parents' and children's everyday life with JIA and its treatment. An ethnographic study was designed by a multidisciplinary team including rheumatologists, paediatricians, patient associations members and anthropologists. The study involved 15 families (enough to reach saturation), recruited from 5 centres by diversity of clinical and sociological profiles. The panel included 17 children with JIA, 11 girls and 6 boys, median age 10,<sup>3:17</sup> median disease duration 2.5,<sup>1:15</sup> 4 children were treated with conventional DMARDs in monotherapy, 4 with biologic DMARDs in monotherapy, 5 with cDMARD-bDMARD association and 4 with NSAIDs only.

Interviews were conducted by anthropologists at family's home using in-depth semi directive and biographic methods. 3 fields were explored: organisation of everyday life with JIA, treatment practices, impact on school and social activities. Interviews were recorded and transcribed for analysis.

**Results:** Adherence results from an appropriation process of the JIA and treatment that require both an active role from parents and children, even before the transition. This active role played by children could be either stimulated or inhibited at home according to the family's structure, social background and parents' attitudes toward their child (participation to the decision, explanation of the disease).

Children's active role includes in particular: 1) negotiations with parents and physician, 2) experiments with the treatment (forgetting or involuntary switch from the parents, changing the dosage on their own initiative) and 3) participation to the treatment administration and ritualization.

The manner children consider and manage their DMARDs is the result of an arbitration depending on the positive (a) and side effects (b) they felt in their body and the effects noted by the doctors (c) during the examinations and test results. Dealing with these 3 dimensions requires to link together both a theoretical and practical knowledge of JIA. Thus, children build their own and singular knowledge of their disease and treatment, which is a source of control of their body and their life.

**Conclusions:** Qualitative methods, through an ethnographic study starting from children's point of view, underline the active role they play in their care. Adherence to DMARDs could be improved by supporting children's implication as soon as the beginning of JIA.

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**AB1124 A UK STUDY: VOCATIONAL EXPERIENCES OF YOUNG ADULTS WITH JUVENILE IDIOPATHIC ARTHRITIS**

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**Background:** Little is known about the experiences of young adults living with Juvenile Idiopathic Arthritis (JIA) preparing for employment and career development.

**Objectives:** The purpose of this study was to understand the impact JIA has on career planning and early employment experiences of young adults (16–30 years).

**Methods:** Using existing literature (including grey literature), an online survey (consisted of 152 questions, 29 items related to young adults two of which were free text questions) was developed and sent to UK National Rheumatoid Arthritis Society (NRAS) members and distributed to non-members via social media tools including Facebook, Twitter and HealthUnlocked. Data collected included views and experiences in career planning and employment. The data pertaining to young adults are presented here.

**Results:** Of 1241 respondents 19 were young adults with JIA (range 16–30 years), 89% were female and 84% had university or equivalent qualifications. Due to incomplete responses there is missing data on all 19 young adults. 4/13 young adults were studying at university, 9/13 were in paid employment. 9/17 respondents reported their school did not offer additional work-related activities to students with disabilities and/or additional needs. 10/14 young adults felt their school did not provide advice about coping with possible limitations on placements/traineeships due to their arthritis. 11/14 respondents did consider their condition when thinking about future career plans e.g. "I wanted to work as a ranger or similar for the National Trust but it's a fairly physically demanding job and I knew my joints would suffer so I changed track slightly". However, 8/14 felt their career advisors at school/university did not take their arthritis into account e.g. "I had to cease my physiotherapy master's degree as my arthritis got too bad to continue and change career choice. I wish there would have been more discussion about it not being a reasonable choice for me at the time as we just didn't have the information then". 8/14 young adults changed their career plans because of their arthritis with managing JIA symptoms and a physically demanding role, as well as wanting to stay healthy, being the main reasons for changing career. Important aspects of employment included: "good relationships with your line manager, work you like doing and a job you can use your initiative".

**Conclusions:** Despite small numbers these results highlight potential current unmet vocational needs of young adults with JIA in the UK and the need for further research with this age group. There appears to be a lack of structured support within schools and universities offered to students with disabilities and/or additional needs, about work-related activities and careers. Young adults with JIA actively consider their condition whilst thinking about career opportunities and value a productive and challenging job with a good working environment, including relationships with colleagues and supervisors.

**Disclosure of Interest:** None declared

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**AB1125 URINARY SOLUBLE CD25 AS A BIOMARKER OF ACTIVE LUPUS NEPHRITIS IN EGYPTIAN CHILDREN WITH JUVENILE SYSTEMIC LUPUS ERYTHEMATOSUS**

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**Background:** Lupus nephritis (LN) is more prevalent and severe in children than adult and considered a major predictor of poor outcome. Thus, early diagnosis and treatment is associated with better outcome. Soluble CD25 (sCD25), also known as Interleukin-2 receptor alpha chain, is a type I transmembrane protein present on activated T lymphocytes that play important role in the pathogenesis LN.<sup>1</sup>

**Objectives:** This study aimed to measure urinary levels of sCD25 in children with juvenile systemic lupus erythematosus (JSLE) and to investigate its role as a potential biomarker of activity in LN.

**Methods:** We measured sCD25 using enzyme-linked immunosorbent assay in urine samples from 53 JSLE patients and in urine samples from 30 healthy controls and these levels were normalised to creatinine excretion in urine. All JSLE patients underwent thorough clinical examination and disease activity assessment using Systemic Lupus Erythematosus Disease Activity Index (SLEDAI).

Systemic Lupus International Collaborating Clinics (SLICC) renal activity score<sup>2</sup> was used to assess activity of LN.

**Results:** Urinary sCD25 normalised levels were highly significantly increased in JSLE patients (278.38±133.68 pg/mg) compared to urinary level in the healthy controls (187.33±83.59 pg/mg), p<0.001. Also, patients with active LN had significantly higher normalised urinary sCD25 levels (402.69±139.58 pg/mg) compared to urinary level in active JSLE patients without LN (262.18±98.35 pg/mg), p=0.002 and inactive JSLE patients (192.7±66.4 pg/mg), p<0.001. In JSLE patients, urinary sCD25 normalised levels significantly correlated with SLEDAI (r=0.48, p<0.05), renal SLEDAI (r=0.61, p<0.001), SLICC renal activity score (r=0.68, p<0.001) and C3 (r=-0.48, p<0.001).

**Conclusions:** JSLE patients have significantly increased urinary levels of sCD25 especially in those with active LN. Urinary sCD25 levels are remarkably correlated with the renal disease activity scores suggesting that it could be a useful marker to reflect active renal involvement in JSLE patients.

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**AB1126 NO RADIOGRAPHIC WRIST DAMAGE AFTER TARGETED TREATMENT IN JUVENILE IDIOPATHIC ARTHRITIS**

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**Background:** Juvenile idiopathic arthritis (JIA) is characterised by chronic inflammation of the joints which can lead to structural bone damage.

**Objectives:** The objective of this study was to evaluate the response of new onset JIA patients to an early targeted treatment by conventional radiography.

**Methods:** JIA patients participating in the BeSt for Kids study (NTR 1574) were eligible in case of wrist involvement at inclusion and if conventional radiographs were available at baseline or within 6 months before or after study inclusion. Follow-up radiographs of hands and wrists after 12–36 months were available for comparison. Radiographic bone damage as reflected by carpal length was assessed using the Poznanski score<sup>1</sup>, providing 'Z' as indication of the deviation from a healthy population as measured by radiometacarpal length relative to the second metacarpal length (RM/M2). BoneXpert method<sup>2</sup> was used to automatically determine bone age and bone mineral density (BMD) of the wrist.

Abstract AB1126 – Table 1

	Baseline Z-score (95% CI)	Compared to healthy population	Follow-up Z-score (95% CI)	Compared to healthy population	Change in Z-score
<b>Poznanski score</b>	0.047 (-0.32 to 0.41)	p=0.795	0.055 (-0.28 to 0.39)	p=0.744	p=0.937
<b>BMD</b>	-0.71 (-1.12 to -0.30)	p=0.001	-0.44 (-0.75 to -0.12)	p=0.008	p=0.032
<b>Bone age</b>	-0.08 (-0.44 to 0.28)	p=0.651	-0.25 (-0.59 to 0.09)	p=0.574	p=0.092

**Results:** Forty JIA (27 female) patients were evaluated for Poznanski score and BMD (mean age 7.2±3.4 years), 26 patients (15 female) were evaluated for bone age (mean age 9.3±2.2 years). Assessed by the mean Z-score of RM/M2, we did not detect wrist damage at baseline nor at follow-up. Assessed by the mean Z-score of the bone age, we did not detect deviating bone age at baseline nor at follow-up. At baseline BMD was significantly diminished compared to healthy

controls (Z-score  $-0.71$ , 95% CI  $-1.12$  to  $-0.30$ ). BMD at follow-up improved significantly (Z-score  $-0.44$ , 95% CI  $-0.75$  to  $-0.12$ ,  $p=0.032$ ). Results are summarised in table 1.

**Conclusions:** In this cohort of JIA patients treated early and targeted at inactive disease, we have detected no radiographic wrist damage at baseline or follow-up as detected by Poznanski score. BMD was significantly diminished at baseline but improved significantly after follow-up.

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## Other orphan diseases

### AB1127 PULMONARY ARTERIAL HYPERTENSION AND POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME (PRES) IN A PATIENT WITH ADULT ONSET STILL'S DISEASE

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**Background:** Pulmonary arterial hypertension is a rare complication of AOSD and there are only a limited number of case reports in the literature.

PRES is a rare acute neurological condition characterised by rapid onset of headache, seizures, altered consciousness, visual disturbances and usually very high blood pressure. Brain imaging characteristically shows high signal change in the subcortical white matter, predominantly in the posterior lobes which normalises within days to weeks. There are rare case reports of seizures and other neurological manifestations associated with AOSD but no published case reports of classic PRES.

**Objectives:** To share this interesting case with our rheumatology colleagues.

**Methods:** We present a case of 24 year old Afro-Caribbean lady, diagnosed with AOSD in December 2015, presenting with recurrent fevers, weight loss, polyarticular synovitis, small volume lymphadenopathy, evanescent urticarial rash, hyperferritinemia (3700 ug/L) and raised CRP (146 mg/L). Rheumatoid factor, ANA, CCP, ENA and ANCA were negative. Infection screen was negative including blood-borne viruses and whole-body imaging was normal.

She was initially treated with pulsed Methylprednisolone 1 g IV for 3 days followed by 40 mg oral prednisolone. She had a good initial response (ferritin 1700 ug/L, CRP 36 mg/L), but subsequently we were unable to reduce her prednisolone below 35 mg due to recurrence of symptoms.

She had quite a stormy course over the rest of the year with a number of hospital admissions and her ferritin running as high as 35,000 ug/L and CRP more than 200 mg/L.

In February 2017 she had a further severe flare and was started on Anakinra. She initially responded well (Ferritin 400 ug/L, CRP 3 mg/L), but four months later started to flare again, requiring a further admission, treated with IV Methylprednisolone.

She was switched from Anakinra to Tocilizumab but was stopped after 4 doses due to poor response.

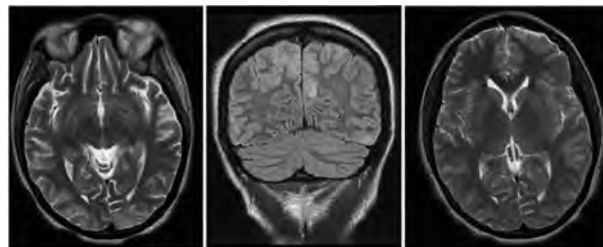
Following development of exertional dyspnoea, echocardiography and right heart catheter studies demonstrated a raised mean pulmonary artery pressure of 42 mmHg with severe TR, right sided volume overload and a BNP of 8741 ng/L warranting referral to the regional PAH centre.

She also developed peripheral sensorimotor neuropathy in her lower limbs confirmed by NCS.

**Results:** In December 2017 she was admitted with severe shortness of breath, hypoxia and a ferritin of over 15,000 ug/L. She developed seizures with status epilepticus, very high blood pressure and ended up requiring mechanical ventilation. MRI and CT brain were suggestive of PRES with subcortical high signal change and symmetrical vasogenic oedema in occipital and parietal lobes. She was treated in Neuro ITU with anti-epileptics, anti-hypertensives, IV hydrocortisone and Anakinra was restarted. She made a rapid and full neurological recovery with resolution of changes on her brain scans.

She continues Anakinra, and Cyclosporine 2 mg/kg body weight has been added since. She has also been started on Tadalafil 20 mg BD for her pulmonary arterial hypertension.

Prednisolone has been tapered to 15 mg and she is clinically well with a CRP of 26 mg/L and ferritin of 2600 ug/L.



**Abstract AB1127 – Figure 1**

**Conclusions:** We present a case of life threatening AOSD complicated by pulmonary arterial hypertension, PRES and peripheral neuropathy.

She has unusually severe disease, which is quite refractory to treatment and has been associated with rare manifestations.

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### AB1128 EVALUATION OF SERUM VERSICAN LEVELS IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER (FMF)

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**Background:** Familial Mediterranean fever (FMF) is an autoinflammatory disease which has self-limiting inflammatory attacks placing in polyserositis.<sup>1</sup> Versican is an extracellular proteoglycan which interacts with receptors that regulate immune system.<sup>2</sup>

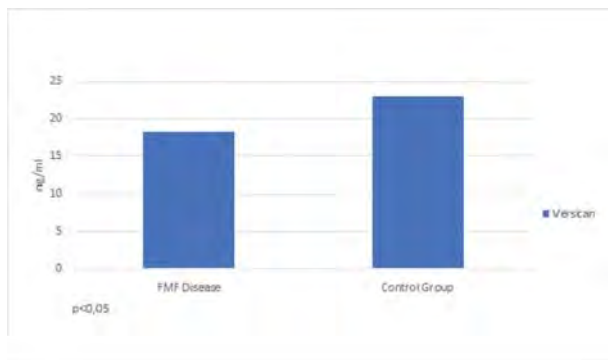
**Objectives:** The aim of this study is to measure serum versican levels between FMF and control group.

**Methods:** Between June 2017 – , September 2017 thirty-seven FMF patients with attack-free period that following-up at Cumhuriyet University Faculty of Medicine Department of Internal Medicine Rheumatology and thirty-five healthy volunteers without any rheumatic, systemic and metabolic diseases were enrolled in this study. Clinical findings of all patients were recorded. Blood tests were examined by Elisa method in Cumhuriyet University Department of Biochemistry.

**Results:** The median age of the FMF patients was 33<sup>(19–64)</sup> years. Of the FMF patients, twenty-one (56.8%) were female and sixteen (43.2%) were male. The median age of control group was 26<sup>(18–38)</sup> years. Of the control group fourteen (40%) were female and twenty-one (60%) were male. The median versican level was measured as 18.3 ng/ml in FMF group and 23 ng/ml in healthy group ( $p<0.05$ ). There was no correlation between eritrosit sedimentation rate (ESR), CRP, fibrinogen, serum amyloid-A (SAA) protein other clinical manifestations, medications and versican levels (table 1).

**Abstract AB1128 – Table 1.** Subgroup analysis in patients with FMF.

	Serum Versican Levels ng/ml (median)	P value
ESR>20 mm/h n=25	20.03	
ESR<20 mm/h n=2	16.5	.597
CRP>10 mg/L n=25	19.2	
CRP<10 mg/L n=12	16.5	.713
Fibrinogen>200 mg/dl n=9	18.2	
Fibrinogen<200 mg/dl n=28	18.7	.986
>40 years n=15	18.2	
<40 years n=22	19.5	.591



**Abstract AB1128 – Figure 1.** Serum Versican levels between FMF and Control groups

**Conclusions:** Serum versican level was statistically significant lower in FMF group than in control. On the other hand, there was no statistically significant correlation between versican levels and other parameters in FMF patients with attack-free period. Clinical trials including FMF patients with attack-period, attack-free period and amyloidosis would be designed in order to investigate the possible role of versican.

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**Disclosure of Interest:** None declared

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#### AB1129 EPIDEMIOLOGICAL AND CLINICAL PROFILE OF PATIENTS WITH PARANEOPLASTIC RHEUMATOLOGIC SYNDROMES IN A SPANISH TERTIARY HOSPITAL

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**Background:** Paraneoplastic rheumatic syndromes (PRS) are defined as rheumatic symptoms caused by a malignancy, but which are not caused directly by the tumour or metastasis. PRS are characterised by a close temporal relationship with an underlying malignancy and fast regression of the symptoms after the treatment of the primary tumour.

**Objectives:** To describe the epidemiological and clinical profile of patients diagnosed with PRS in a Spanish tertiary hospital.

**Methods:** A retrospective observational study was performed, which included all patients who were diagnosed of PRS in our centre during the period 1985–2017. The demographic, clinical and outcome data were obtained from their medical records.

**Results:** During the study period 48 patients with suspected paraneoplastic syndrome were identified, but diagnosis was confirmed in 14 of them, 7 women (50%), with a mean age at diagnosis of 69.8±14.5 years. 42.9% of patients were smokers, 14.3% reported alcohol consumption, 35.7% and 7.1% had personal and family history of neoplasia, respectively; no patient reported personal or family history of autoimmune disease. The comparison between patients with and without PRS is shown in the table, but no significant differences were identified. The most common neoplasm was breast cancer (28.6%). 21.4% of the cases of PRS appeared as a consequence of a tumour recurrence. In 42.9% of patients the diagnostic of the tumour was concomitant to PRS, while the remaining 57.1% SPR was previous. The most frequent paraneoplastic syndrome was polymyalgia rheumatica (42.9%), followed by dermatomyositis (28.6%) and paraneoplastic polyarthritis (28.6%). The most common musculoskeletal manifestation was shoulder girdle pain and stiffness (35.7%) followed by polyarthritis and proximal

muscular weakness (28.5%). 85.7% of the patients had high erythrocyte sedimentation rate and C-reactive protein levels with a mean value of 60.2±39.4 mm/h and 77.6±9.5 mg/L, respectively. Antinuclear antibodies were positive in 7 patients (50%), while rheumatoid factor, anti-CPP and anti-RNP were positive in 1 patient each (7.1%). The response of PRS to the treatment of the tumour was available in 9 patients, of which 6 (66.7%) presented remission of the PRS. Regarding mortality, 5 patients (35.7%) died due to complications associated with the primary tumour.

**Abstract AB1129 – Table 1**

	PRS (n=14)	NO PRS (n=34)	P-value
Age (years)	69,78±14,57	73,23±10,81	0534
Sex (Male)	7 (50%)	14 (41,17%)	0575
Personal history of malignant neoplasm	5 (35,71%)	16 (47,05%)	0471
Personal history of autoimmune disease	0 (0%)	4 (11,76%)	0180
Family history of malignant neoplasm	1 (7,14%)	0 (0%)	0115
Family history of autoimmune disease	0 (0%)	1 (2,94%)	0115
Smoking	6 (42,86%)	13 (38,24%)	0766
Alcoholism	2 (14,29%)	4 (11,76%)	0810

Comparison of the demographic characteristics of patients with and without a diagnosis of paraneoplastic rheumatic syndrome.

**Conclusions:** Polymyalgia rheumatica was the most frequent PRS in our study, in contrast to several published series where other PRS are more common such as hypertrophic osteoarthropathy, polyarthritis and dermatomyositis/polymyositis. The laboratory data and response to treatment of the tumour were similar to those reported in the literature. The mortality in our series was high, but in none of the cases was related directly to PRS.

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**Disclosure of Interest:** None declared

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#### AB1130 LATE ONSET TUMOUR NECROSIS FACTOR RECEPTOR (TNFR)–ASSOCIATED PERIODIC SYNDROME (TRAPS) CAUSED BY SOMATIC TNFRSF1 MOSAICISM

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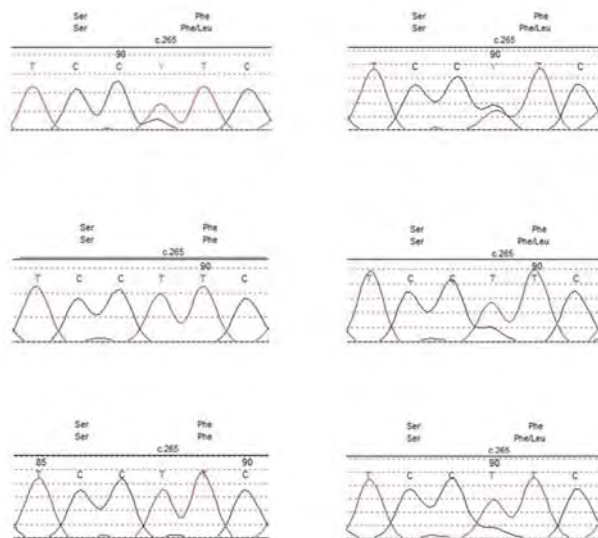
**Background:** Tumour necrosis factor receptor (TNFR)–associated periodic syndrome (TRAPS) is an autosomal-dominant disease caused by gain-of-function mutations in the TNFRSF1A gene, which encodes the 55-kd TNFR type I (TNFRI) protein. Mosaicism has been identified in a single patient. A 60 year old male presented with a 6 year history of intermittent fever as high as 103.5, lasting 3–4 weeks with associated peritoneal symptoms, arthralgias, myalgias, lymphadenopathy, bilateral episcleritis, erythematous rash in his torso. Prednisone up to 60 mg daily and colchicine was ineffective where he responded fully to canakinumab at a dose of 150 mg every 4 weeks.

**Objectives:** To identify the extent of mosaicism in a patient with adult onset TRAPS phenotype.

**Methods:** DNA was extracted from the patient's whole blood, saliva and hair root. The TNFRSF1A gene was analysed by Sanger sequencing in all tissues, whole blood and fractionated cell subsets. *In silico* molecular modelling was performed to predict the structural and functional consequences of the tumour necrosis factor receptor (TNFR) type I protein mutation.

**Results:** Sanger sequencing revealed differential tissue and hematopoietic cell presence of a missense mutation at c.265 T>C p.Phe89Leu (F89L) Chr12 (GRCh37):g.6442960A>G ex3 rs104895245. The mutant allele was present in whole blood and buccal mucosa and absent in hair root, supporting the presence of somatic TNFRSF1A mosaicism. Additionally, quantitative analysis revealed allele frequency of 50% in B cells, 30% in NK cells and 30% in neutrophils. The mutation was absent in T cells and monocytes. *In silico* prediction modelling with SIFT and PolyPhen2 suggested that this mutation led to numerous structural rearrangements which resulted in changes in the protein surface profile.





Abstract AB1130 – Figure 1

**Conclusions:** This is the second reported case of TNFRSF1A mosaicism in a patient with TRAPS, which was attributable to a *de novo* mosaic missense mutation in the TNFRSF1A gene. (c.265 T>C) p.Phe89Leu (F89L). Our results point to a late-onset mutational event at the level of a multipotent hematopoietic stem cell.

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**Disclosure of Interest:** None declared

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#### AB1131 IL-33, A NOVEL CYTOKINE FOR FMF? HOW IS IT RELATED WITH DISEASE PATHOGENESIS?

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**Background:** Familial Mediterranean Fever (FMF) is an autosomal recessive inherited autoinflammatory disease characterised with unpredictable attacks of fever, polyserositis and arthritis. The disease is associated with MEFV gene mutation causing dysfunction of pyrin protein. This dysfunction of pyrin is related with aberrant production of proinflammatory cytokines, especially IL-1 $\beta$  and IL-18. IL-33 is a novel proinflammatory cytokine that belongs to interleukin (IL)-1 superfamily. When released from epithelial, endothelial and fibroblasts, it binds to its specific receptor ST2 and induces the production of inflammatory cytokines. IL-33/ST2 pathway has been recently shown to be related with several rheumatological diseases such as rheumatoid arthritis, systemic lupus erythematosus.

**Objectives:** As it is well known that inhibition of IL-1 pathway is the cornerstone of FMF treatment, the aim of this study was to evaluate the role of IL-33, a member of IL-1 family, in the pathogenesis of FMF.

**Methods:** Seventy-six FMF patients and 30 sex-age matched healthy controls were enrolled in the study.

**Results:** The demographic data of FMF patients and healthy controls are demonstrated in Table 1. Serum IL-33 and its soluble receptor ST2 (sST2) were analysed with ELISA. There was no statistically significant difference between IL-33 and sST2 levels in FMF and control groups ( $p=0.687$  and  $p=0.054$ , respectively) (table 1). FMF patients were grouped as active and inactive disease according to Autoinflammatory Disease Activity Index (AIDAI) for the past 31 days and  $\geq 9$  was accepted as active disease. The serum IL-33 and sST2 levels were similar in both active and inactive groups ( $p=0.362$  and  $p=0.706$ , respectively). In active group, C-reactive protein and serum-amyloid A levels were significantly higher than inactive group. ( $p=0.01$ ,  $p=0.015$  respectively) (table 2).

**Abstract AB1131 – Table 1.** The table that shows the characteristics of FMF patients and healthy controls

	FMF (n=76)	Control (n=30)	p
Age (years)	33.8 $\pm$ 11.8	37.0 $\pm$ 8.4	0.123
Female, n (%)	56 (73.7)	18 (60)	0.167
IL-33	3.88 $\pm$ 2.04	3.71 $\pm$ 1.36	0.687
sST2	2756.8 $\pm$ 411.0	2828.0 $\pm$ 118.8	0.054

**Abstract AB1131 – Table 2.** The table that shows the characteristics of active and inactive FMF patients

	Active <sup>24</sup>	Inactive (52)	p
Age (years)	31.8 $\pm$ 10.8	34.8 $\pm$ 12.2	0.310
Female, n (%)	17 (70.8)	39(75)	0.701
IL-33	4.26 $\pm$ 2.73	3.70 $\pm$ 1.64	0.362
sST2	2730.4 $\pm$ 426.8	2769.0 $\pm$ 407.1	0.706
Attackno/year (IQR)	4 (5)	2 (4)	<b>&lt;0.001</b>
AIDAI score(IQR)	16 (16)	0 (3)	<b>&lt;0.001</b>
ESR	17.7 $\pm$ 12.1	12.8 $\pm$ 8.1	0.108
CRP	22.5 $\pm$ 31.3	4.4 $\pm$ 7.7	<b>0.01</b>
Fibrinogen	3.5 $\pm$ 1.3	3.6 $\pm$ 3.3	0.896
SAA	29.9 $\pm$ 41.7	5.4 $\pm$ 8.2	<b>0.015</b>

**Conclusions:** In this study, significant differences were not found in serum IL-33 and sST2 levels neither in FMF vs control nor active vs inactive FMF groups. This may be because of, unlike the other members of IL-1 superfamily, IL-33 mainly induces T helper (Th)2 immune responses. On the other hand, the pathogenesis of FMF is mainly dependent on Th17 cell activation and Th1 cell differentiation via IL-18 induction. As a result, it can be concluded that even if IL-33 is a component of IL-1 family, it has no role in the pathogenesis of FMF. As far as we know, this is the first study in the literature. Therefore, further studies with larger sample size are needed to confirm this result.

**Disclosure of Interest:** None declared

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#### AB1132 PANNICULITIS IN RHEUMATOLOGY PRACTICE: SPECIFIC FEATURES OF CLINICAL COURSE AND OUTCOMES

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**Background:** Panniculitis (Pn) is a heterogenic group of inflammatory diseases with predominant involvement of subcutaneous adipose tissue and may occasionally be seen in clinical practice by many specialists. Although, fever, skin symptoms and joints involvement alongside with pronounced rise of acute phase inflammation reactants are the reasons for referral to a rheumatologist. At the same time absence of clear diagnostic algorithm would result in delayed diagnosis and, consequently, inadequate treatment.

**Objectives:** To assess clinical course and clinical outcomes of panniculitis in current rheumatology practice.

**Methods:** The study included 209 pts on the record at VA Nasonova Research Institute of Rheumatology during 2009–2016 yy. (185 females and 24 males, aged 17–80 years) with referral diagnosis “Erythema nodosum. Non-differentiated panniculitis» and disease duration from 1 week to 25 years. Patients' assessment included general clinical examination, serological and immunological tests, histological and immunohistochemical analyses, chest CT scan, Doppler ultrasonography of the lower extremity veins, and tuberculin skin test. Outcomes were evaluated in 1–6 years.

**Results:** Secondary to underlying non-rheumatic condition Pn was identified in 23 pts. The most prevalent Pn types in remaining 186 cases were: erythema nodosum (EN) (121pts), lipodermatosclerosis (LDS)<sup>38</sup> and Weber-Christian disease (WCD).<sup>18</sup> Symmetrical distribution of nodules over upper and lower extremities (ULE) was characteristic for 93% of all EN cases. In LDS populations 68% cases had increased mean body mass index (BMI), 79% – chronic venous insufficiency (CVI), 60% – asymmetric distribution of lesions, mostly over medial leg (92%). In WCD patients the nodules were covering all ULE surfaces, and in 14 nodules were found on the trunk. The three Pn types had certain differences in the clinical course: high clinical and lab activity was documented in *Löfgren syndrome* and WCD pts. Asymmetric distribution of nodules on the legs was characteristic for LDS, nodules on the trunk were specific for WCD. The highest recurrence rate was documented in WCD pts (39,7 per 100 patient-years), the lowest—in *Löfgren*

*syndrome pts* (15,3 per 100 patient-years). The probability of EN recurrence in *Löfgren syndrome pts* was significantly higher in subjects older than 40 y (OR 3,81;  $p=0,03$ ), in subjects with late ( $\geq 3$  months from EN onset) initiation of treatment (OR 8,94;  $p=0,0008$ ) and in subjects with indurations  $>5$  cm in size (OR 3,65;  $p=0,03$ ). The probability of LDS recurrence was significantly higher in pts with confluent nodules, forming conglomerate masses (OR 4,33;  $p=0,037$ ), and pts taking hydroxychloroquine at  $\leq 200$  mg/day during  $\geq 6$  months (OR 5,25;  $p=0,019$ ).

**Conclusions:** Comprehensive examination is needed to identify the clinical type of Pn. Symmetrical involvement of all extremities is characteristic for EN in young subjects. Asymmetric nodular rash over lower extremities in subjects with abnormal BMI and CVI is specific for LDS. CWD usually presents with nodular rash on the trunk. Identified risk factor for EN and LDS recurrence should be taken into consideration while writing a treatment plan.

**Acknowledgements:** The study had no sponsorship.

**Disclosure of Interest:** None declared

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#### AB1133 ROLE OF THE RHEUMATOLOGIST IN A REGIONAL REFERENCE HAEMOPHILIA UNIT

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**Background:** Haemophilia is an X-linked hereditary bleeding disorder caused by deficiency in coagulation factor VIII (FVIII), in haemophilia A (HA), and factor IX in haemophilia B (HB).

They are classified as severe, moderate or mild, depending on the level of coagulation factor deficiency. Men are affected clinically by the disease, and women, who are carriers, usually remain asymptomatic.

HA is more common than HB (from 80% to 85% of all cases).

Their bleeding complications primarily affect the musculoskeletal system. Hemarthrosis is the major haemophilia-related complication, responsible for a particularly debilitating chronic arthropathy, in the long term, affecting mainly the load joints (knees, ankles and elbows).

In addition to clotting factor concentrates, usually prescribed by the haematologist, The management of acute hemarthrosis and chronic arthropathy requires a close collaboration with rheumatologists. This collaboration is the key to effectively preventing hemarthrosis, managing acute joint bleeding episodes, assessing joint function, and actively treating chronic arthropathy.

**Objectives:** To analyse the clinical characteristics, extent of joint involvement and associated comorbidity of a cohort of patients with hemophilic arthropathy.

**Methods:** This is a retrospective study, carried out in the Haemophilia Unit of our hospital (regional reference), in patients with moderate to severe haemophilia A and B, with hemophilic arthropathy, seen in consultation with episodes of joint bleeding (2007–2017). Severity of haemophilia was defined based on determined by the percentage of FC activity (VIII and IX), moderate from 1% to 5%, severe  $<1\%$ . The number of episodes of hemarthrosis was collected in the 3 months before and after the radioisotopic synoviorthesis (intra-articular injection of a colloidal suspension of particles marked with a radioisotope, whose objective is the destruction of the synovial membrane).

**Results:** We included 88 patients (87 men and 1 symptomatic carrier woman with decreased levels of factor VIII), mean age  $31 \pm 17$  years. HA (severe 56%, moderate 26%), HB (severe 14%, moderate 1%). The target joint: knee 51%, followed by ankle 26%, elbow 13% and other 7% (5 shoulders and 2 wrists). In 61 patients, magnetic resonance imaging (MRI) was performed: synovial hypertrophy 9%, hemosiderin deposits (in acute stage of joint bleeding) 2% and structural alteration (erosions and subchondral cysts, loss of focal cartilage) 68%. A radioisotope synoviorthesis was made to 18 patients: 12 with sulfide 186 Re colloidal (5 ankles, 4 knees, 2 elbows) and 6 with 90 Y coloidal citrate (4 knees, 3 ankles), having a decrease of 74% (range 59%–100%) in the number of hemarthrosis in the 3 subsequent months. Total knee replacement was needed in 13% of the patients (7 with HCV liver disease and in 6 HCV liver disease and coexistence with HIV). They have infection due to HCV 33%, HIV 25% and HBV 6%.

**Conclusions:** This study highlights the extent of joint damage in haemophilic patients as well as the high comorbidity of HCV and HIV infections.

The experience of a monographic Haemophilia consultation, with the participation of different specialties (being fundamental the rheumatologist), benefits the multidisciplinary approach of these patients, being the results obtained in our series concordant with the described in the literature.

**Disclosure of Interest:** None declared

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#### AB1134 DETERMINING FACTORS OF SEVERITY IN HEMOPHILIC ARTHROPATHY

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**Background:** In patients with haemophilia, the development of inhibitors to factor VIII/IX (Haemophilia A and B, HA/HB), prevents adequate replacement therapy and results in increased risk of serious bleeding episodes, poor control of joint bleeding, and progressive, debilitating joint disease.

**Objectives:** To describe, according to the Arnold-Hilgartner scale (AHRS), the radiological findings in a cohort of hemophilic arthropathy (HArth) patients and to analyse the relationship that may exist between the degree of joint involvement and HA/HB, severity, age and presence or absence of inhibitor.

**Methods:** This is a retrospective study, carried out in the Haemophilia Unit of our hospital, in patients with HArth (2007–2017). Severity of haemophilia: percentage of coagulation factor (CF) activity, moderate (1%–5%) and severe  $<1\%$ . The AHRS includes 5 levels.

For the study of the association of the type and degree of haemophilia; and the presence of inhibitor, with the level in the AHRS, a linear model was used. The significance in this regard of the linear contrasts of interest was studied using F tests, defining the first species error at 0.05.

**Results:** We included 88 patients. Characteristics of the patients in the attached chart. No significant association was detected between the type and severity of haemophilia with the development of inhibitor.

The results of the linear model only showed association ( $p=0.01$ ) between the severity of haemophilia and AHRS, patients with moderate haemophilia presented a least square mean for the AHRS of 2.6 (0.3), whereas the serious ones had a value of 3.4 (0.2). The least squared means for patients with HA and HB were 2.9 (0.2) and 3.1 (0.4) respectively, the contrast did not reach statistical significance ( $p>0.1$ ), and the same occurred between patients who had generated or not inhibitor 2.8 (0.2) Vs 3.1 (0.3). Apart from the severity of haemophilia, the other factor that showed a significant and significant effect ( $p<0.001$ ) on the AHRS values was age. The estimated value for the regression coefficient of age on the radiological status was 0.05 (0.009).

#### Abstract AB1134 – Table 1

Type of Haemophilia	
Haemophilia A n (%)	73 (82%)
Haemophilia B n (%)	14 (15%)
Severity of Haemophilia	
Haemophilia A severe n (%)	50 (56%)
Haemophilia A moderate n (%)	23 (26%)
Haemophilia B severe n (%)	13 (14%)
Haemophilia B moderate n (%)	1 (1%)
Age m (SD)	31 (17)
Development of inhibitors to factor VIII/IX n (%)	16 (18%)
Haemophilia A severe with inhibitors n (%)	10 (11%)
Haemophilia A moderate with inhibitors n (%)	3 (3%)
Haemophilia B severe with inhibitors n (%)	3 (3%)
AHRS scale 1 n (%)	18 (20%)
AHRS scale 2 n (%)	17 (19%)
AHRS scale 3 n (%)	18 (20%)
AHRS scale 4 n (%)	15 (17%)
AHRS scale 5 n (%)	19 (21%)

**Conclusions:** Contrary to what has been observed in other studies, in our cohort it does not seem that the presence of inhibitor or the type of haemophilia has a negative effect on the severity of the radiological findings. The age and severity of haemophilia do seem to influence the radiological stage.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.3542

#### AB1135 CARDIAC MAGNETIC RESONANCE FINDINGS IN PATIENTS WITH BIOPSY-PROVEN VIRUS-NEGATIVE LYMPHOCYTIC MYOCARDITIS

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**Background:** Cardiac magnetic resonance (CMR) is considered to be useful for non-invasive myocarditis diagnosis. Lake Louise Criteria (LLC) has been proved to have moderate accuracy in the diagnosis of acute or chronic myocarditis.

**Objectives:** to describe the CMR findings in patients with virus-negative lymphocytic myocarditis (VNLN) from a large monocentric Italian cohort.

**Methods:** CMR findings in 40 patients (mean age 45.43±14.7 years; male:female ratio 1:1) diagnosed with endomyocardial biopsy-proven VNLM at our Centre from January 2015 to December 2017, were retrospectively evaluated. CMR was performed at time of clinical presentation and before EMB. At contrast-enhanced CMR we analysed: ventricular function, T2-weighted sequences, short inversion time inversion recovery sequences (STIR), early (EGE) and delayed gadolinium enhancement (LGE). Demographic, clinical and histological data were correlated with CRM findings.

**Results:** Mean left ventricular (LV) ejection fraction (EF) was 52.5%±10.8%. 50% of patients had reduced LVEF (<55%). Mean right ventricle EF was 55.25%±7.2%. Akinetic or hypokinetic areas were detected in 3 (7.5%) and 17 (42.5%) patients, respectively. LLC were identified in 39 patients (92.5%). LGE was the most common CMR finding. 20 patients (50%) met one LLC, 16 patients (40%) 2 LLCs. 1 patient met all 3 LLCs. STIR abnormalities were identified in the LV lateral wall in 8 (19%), septal wall in 9 (21.4%), LV inferior wall in 9 (21.4%), in the apex in 3 (7.1%), LV posterior wall in 3 (7.1%) and LV anterior wall in 2 (4.8%) patients. Myocardial oedema on T2 images was detectable in 21 (52.5%), EGE in 1 (2.5%) and LGE in 36 (90%) patients. LGE was intramural in 22 (55%), subepicardial in 23 (57.5%) and subendocardial in 4 (10%) patients. Multiple LGE patterns were disclosed in 10 (25%) patients. Pericardial effusion was detected in 9 patients (22.5%). 2 patients did not meet any LLC at CMR. When comparing CMR findings with Holter-ECG tape, clinical presentation, histology, biochemistry and autoimmunity results we found CRM oedema positively correlated with the detection of active myocarditis on EMB (11 vs 4, p=0.027). Serum anti-heart antibodies positively correlated with the detection of pericarditis at CMR (3 vs 1, p=0.050). Patchy/intramural LGE positively correlated with rhythm abnormalities at Holter-ECG tape (12 vs 6, p=0.037).

**Conclusions:** VNLM is an overlooked disease defined by EMB established histological, immunological and immune-histochemical criteria. Although the diagnostic power of CMR needs to be further investigated, it seems to correlate with EMB results and arrhythmic burden.

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**Disclosure of Interest:** None declared

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#### AB1136 CLINICAL FEATURES OF ADULT CHINESE PATIENTS WITH PERIODIC FEVER, APHTHOUS STOMATITIS, PHARYNGITIS, AND ADENITIS: REPORT FROM AN SINGLE CENTRE

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**Background:** Periodic fever, aphthous stomatitis, pharyngitis, and cervical adenopathy (PFAPA) syndrome is a polygenic or multifactorial autoinflammatory disease (AUIDs) with unknown etiology. It mainly affects children, though recently it has been also recognised in adulthood. PFAPA syndrome has not been reported in the Chinese population up till now.

**Objectives:** We aimed to investigate the clinical features, treatment and prognosis of the first cohort of adult Chinese patients with PFAPA syndrome.

**Methods:** We prospectively evaluated clinical data of adult patients (≥14 years) with recurrent fever of unknown origin who were suspected monogenic AUIDs in the period April 2015 to December 2017, at the adult AUIDs centre, Department of Rheumatology, Peking Union Medical College Hospital. Gene tests of AUIDs associated pathogenic genes were examined to exclude monogenic AUIDs. The clinical features were evaluated for patients with PFAPA syndrome, and were compared with a newly reported large Italian cohort of adult patients with PFAPA syndrome.<sup>1</sup>

**Results:** During the study period, a total of 7 adult patients with PFAPA syndrome were diagnosed (table 1), and the male to female ratio was 6:1. All these patients had a disease onset in adulthood, and the mean age of onset was 27±10 years, and the mean time of delay of diagnosis was 4.9±4.0 years. Clockwork periodicity fever was the main feature of PFAPA syndrome, and the median duration of attacks was 3.5 days, and the median interval between attacks was 4 weeks. Pharyngitis, adenitis and aphthous stomatitis were present in 85.7%, 57.1% and 42.9%, respectively. Other common symptoms included fatigue (100%), headache (71.4%), and myalgia (71.4%). The presence of arthralgia/arthritis was less frequent compared to the Italian cohort (p=0.012) (table 2). Corticosteroids given during attacks were effective in 3 patients. NSAIDs were partially effective but tonsillectomy was of no effect. Colchicine was rarely used compared to the Italian cohort (p=0.046).

**Abstract AB1136 – Table 1.** Summary of the clinical characteristics of our patients.

No. of patients	7
Male	6 (85.7%)
Female	1 (14.3%)
Age at onset (years)	27 ± 10 (16-46)
Age at diagnosis (years)	31 ± 11 (17-53)
Delay in diagnosis (years)	4.9 ± 4.0 (1.0-11.0)
Adult onset	7
Positive family history	0
Duration of febrile attacks (days)	3.5 (0.5-7.0)
Duration of attack intervals (days)	4 (1-12)
Frequency of attacks per year	10 (4-20)
Peak temperature (°C)	39.2 ± 0.6 (38.5-40)
Periodic Fever with 3 major clinical features	2 (28.6%)
Periodic Fever with only 2 major clinical features	2 (28.6%)
Periodic Fever with only 1 major clinical features	3 (42.9%)

Clinical features	Ours (n, %) (n=7)	Italian (n, %) (n=30)	p value
Pharyngitis	6 (85.7)	23 (76.7)	0.601
Cervical adenopathy	4 (57.1)	22 (73.3)	0.399
Aphthous stomatitis	3 (42.9)	15 (50)	0.734
Fatigue	7 (100)	19 (63.3)	0.056
Headache	5 (71.4)	13 (43.3)	0.181
Myalgia	5 (71.4)	16 (53.3)	0.384
Conjunctivitis	2 (28.6)	4 (13.3)	0.325
Arthralgia/arthritis	1 (14.3)	20 (66.7)	<b>0.012</b>
Nausea and vomiting	1 (14.3)	5 (16.7)	0.878
Chest pain	0 (0)	6 (20)	0.196
abdominal pain/diarrhea	0 (0)	8 (26.7)	0.123
Periorbital edema	0 (0)	5 (16.7)	0.245
Rash	0 (0)	5 (16.7)	0.245
Treatment			
Glucocorticoid	3/3 (100)	15/17 (88.2)	0.531
NSAIDs	1/3 (33.3)	10/12 (83.3)	0.080
Colchicine	0/1 (0)	3/3 (100)	<b>0.046</b>
Tonsillectomy	0/2 (0)	1/3 (33.3)	0.361

**Abstract AB1136 – Table 2.** Comparison of with an Italian cohort of adult patients with PFAPA syndrome

**Conclusions:** PFAPA syndrome is one of the main causes of adults Chinese patients with recurrent fever of unknown origin and might be misdiagnosed. Clinicians, not only paediatricians, should take into account this clinical entity, especially for patients with pharyngitis, cervical adenopathy and aphthous stomatitis.

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**Disclosure of Interest:** None declared

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#### AB1137 INFLAMMATORY AND EROSIVE ARTHRITIS, A COMMON UNKNOWN MANIFESTATION OF VOGT-KOYANAGI-HARADA DISEASE (VKHD)

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**Background:** VKHD is a rare cause of bilateral granulomatous panuveitis leading to significant visual loss in patients who present it. VKHD is a multisystemic, autoimmune, inflammatory disease that usually displays extraocular manifestations that include meningismus, vitiligo, poliosis, and hearing loss. Arthritis is an unknown manifestation of the disease. In Mexico, VKHD affect mainly young women and is responsible for 13% to 27% of all uveitis.

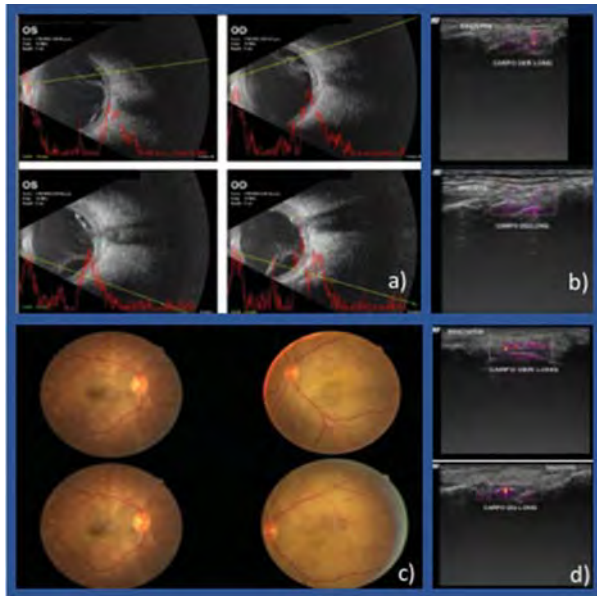
**Objectives:** To describe the presence of inflammatory and erosive arthritis in patients with VKHD.

**Methods:** Observational study of patients with established VKHD that fulfilled the 2010 revised diagnostic criteria for VKHD was rolled out. Articular ultrasonography was performed to all patients by a trained rheumatologist in carpal, metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints evaluating



presence of sinovitis, power Doppler (PD) signal, bone erosions, and cartilage changes; serology and hand x-ray were requested and evaluated.

**Results:** We included 5 women and 1 man, mean age was  $36.2 \pm 10.3$  years, and they all had characteristics of acute (4 patients) or chronic (2 patients) VKHD. They received treatment with intravenous methylprednisolone 1 g/day for 3 days combined with cyclophosphamide and thereafter methotrexate (12.5–17.5 mg/week) for maintenance therapy, scheme with which no ocular recurrences have been presented. Two patients had synovitis on physical examination. All patients had PD signal on the ultrasound and they had involvement of both wrists, MCPs and PIPs joints consistent with polyarthritis pattern; additionally bone erosions were detected in 2 patients. Rheumatoid factor and anti citrullinated peptide antibody were negative in all patients



**Abstract AB1137 – Figure 1.** a) Ocular ultrasonography of patient 1, showing bilateral exudative retinal detachment b) Articular ultrasound of patient 1, showing synovitis with PD signal in both wrists. c) Fundus photographs of the right and left eyes of patient 2 showing exudative retinal detachments d) Articular ultrasound of patient 2, showing synovitis with PD signal in both wrists.

**Conclusions:** The presence of inflammatory and erosive arthritis in patients with VKHD has only been described in one case recently. We propose that polyarthritis is common manifestation of this rare disease, including erosive arthritis, representing part of the spectrum of the disease, processes that share some features of the genetic susceptibility with rheumatoid arthritis as HLA-DR4, CTLA-4 and STAT4.

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#### AB1138 HIGH LEVELS OF ANTI-U1RNP AND ANTI-SM IN MIXED CONNECTIVE TISSUE DISEASE PATIENTS

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**Background:** The mixed connective tissue disease (MCTD) is an autoimmune systemic disease characterised by clinical manifestations that are included in systemic lupus erythematosus (SLE), scleroderma (SSc) or rheumatoid arthritis (RA). Moreover the MCTD exhibits anti-U1RNP high-titer antibodies. However, anti-U1RNP antibodies are not specific or exclusive from MCTD, because of can be detected in other systemic autoimmune diseases as SLE, SSc and RA.

**Objectives:** To verify the differentiation of MCTD patients from other systemic autoimmune diseases using anti-U1RNP titers. The secondary objective is to characterise anti-U1RNP titer in other systemic autoimmune diseases with clinical manifestation.

**Methods:** An observational retrospective study of patients with inflammatory autoimmune disease evaluated in the Rheumatology Department from 2012 since 2016 was performed. In all cases a blood-test with anti-U1RNP, anti-Sm, anti-Ro, and anti-La analysis was conducted. Clinical data was registered according to the patients' medical history, with special emphasis being placed on renal affection, vascular affection, pulmonary hypertension, arthritis-synovitis, tendonitis-tenosynovitis, dry eye syndrome and Raynaud's phenomenon. Biostatistical analysis was performed using R.

**Results:** We collected data from 355 patients with a mean age of 50.84 (15.49) years, 98.55% of them were female. 13.8% of patients showed anti-U1RNP high titers (up to 20 pg/mL), and a significant increase of anti-U1-RNP in MCTD patients in contrast to other connective pathologies ( $p < 0.0001$ ) was observed.

Anti-Sm antibody also exhibit significantly higher values in MCTD patients than in RA ( $p = 0.025$ ) or scleroderma ( $p = 0.003$ ). No differences in anti-Ro and anti-La levels among all diagnosis were observed. Patients with the high anti-U1-RNP levels, regardless of the diagnosis, showed more Raynaud's phenomenon and vascular affection. ( $p < 0.001$  y  $p = 0.008$ ). Related to Anti-Ro and anti-La, high titer of these antibodies in patients with Dry eye syndrome was observed ( $p < 0.001$ ).

Specifically in SLE patients, those with the highest levels of anti-U1-RNP exhibit Raynaud's phenomenon ( $p < 0.001$ ), highest levels of anti-La was shown in those patients with renal affection ( $p = 0.02$ ) and the highest levels of anti-Ro and anti-La was shown in those patients with Dry eye syndrome ( $p = 0.002$  and  $p = 0.006$ ).

**Conclusions:** In our patient series anti-U1RNP were significantly elevated in MCTD diagnosis, and in lesser extent anti-Sm antibodies. Anti-Ro and anti-La antibodies are increased in dry eye syndrome patients. In SLE patients, anti-La increased levels were associated to renal affection.

**Disclosure of Interest:** None declared

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#### AB1139 RITUXIMAB FOR SCLERITIS AND PERIPHERAL ULCERATIVE KERATITIS ASSOCIATED WITH RHEUMATOLOGIC DISEASE

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**Background:** Some types of ocular surface inflammatory diseases are often related to rheumatic conditions: 37% of scleritis (especially diffuse and necrotizing forms) and 60% of peripheral ulcerative keratitis (PUK). Rheumatoid arthritis (RA) and ANCA-associated vasculitis are the most frequently related conditions. Significant loss of visual acuity can be observed if these ocular diseases are not properly treated. To date, no approved therapies are available. Consequently, the management of these ocular diseases are based on published evidence coming from clinical trials (scarce and often with a low sample size), observational studies and case reports. There are positive efficacy data of rituximab (RTX) for ocular surface inflammatory disease.<sup>1-4</sup>

**Objectives:** To describe our experience with RTX as a therapy for severe ocular surface inflammatory diseases associated to rheumatic conditions.

**Methods:** This is a retrospective observational study. It includes patients with severe scleritis or PUK associated to rheumatic diseases diagnosed and managed at our Multidisciplinary Uveitis Clinic between January 2006 and November 2017. We recorded demographic and clinical variables. As outcome variables we used the

**Abstract AB1139 – Table 1.** RTX for scleritis and PUK

	Age (ys)	Gender	Ocular disease	Rheumatic disease	Comorbidities	Previous treatment	RTX cycles	Δ VA	Inflammatory activity	AE	Follow up (ms)
1	55	F	PUK	RA	Amiloidosis	MTX, CS-A, IFX, MPLN ev	1	+0.1	No	No	132
2	58	F	Scleritis	GPA	HBV chronic carrier, LTI	MPLN ev, PDN	1	+0.1	No	No	19
3	59	F	Scleritis	RP	DM	MTX, CS-A, PDN, DXM io	1	0	Diffuse nodular scleritis	No	17
4	75	M	Scleritis	RP	DM, Sweet's syndrome, myelo displasic syndrome	MTX, CS-A, ETN, PDN	1	+0.5	No	No	11
5	75	F	PUK	RA	Previous thyroid CA, asthma	MTX, PDN	1	+0.5/ +0.1	No	No	25
6	60	F	PUK	RA	No	MTX, AKR, IFX, PDN	2	+0.1	No	No	128
7	70	M	PUK	RA	LTI	MTX, CS-A, TCZ, PDN	1	+0.1	No	No	10
8	53	F	PUK	RA	CSC	MTX, LFN, PDN	1	+0.1/0	No	No	7

change in visual acuity and the presence of inflammatory activity by biomicroscopy.

**Results:** VA: visual acuity, AE: aduers events, RA: rheumatoid arthritis, GPA: granulomatosis with polyangiitis, RP: relapsing polychondritis, LTI: latent tuberculous infection, DM: diabetes mellitus, CSC: central serous choroidopathy, MPLN: metilprednisolone, PDN: prednisone, DXM: dexametasone, MTX: methotrexate, CS-A: cyclosporine, LFN: leflunomide, IFX: infliximab, ETN: etanercept, AKR: anakinra TCZ: tocilizumab.

**Conclusions:** As previously described we consider rituximab as an effective therapy for severe ocular surface inflammatory diseases related to rheumatic conditions when other immunosuppressant drugs fail or are contraindicated.

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AB1140

#### COMPARISON OF CUT-OFF VALUES FOR FERRITIN TO DISCRIMINATE ADULT ONSET STILL'S DISEASE FROM OTHER CAUSES OF FEVER OF UNKNOWN ORIGIN: RESULTS OF A PROSPECTIVE STUDY

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**Background:** Adult onset Still's disease (AOSD) is a rare, auto-inflammatory disease that commonly presents as fever of unknown origin (FUO). As AOSD can cause complications as reactive lymphohistiocytosis that can be mortal, discriminating AOSD from FUO is important. Ferritin, an acute phase reactant, is commonly high in patients with AOSD as a part of systemic inflammation.

**Objectives:** To determine a cut-off value of ferritin that favours AOSD over FUO.

**Methods:** Data from patients who admitted to Hacettepe University Hospitals, inpatients sections of department of internal medicine with the complaint of FUO collected prospectively during 30 months. Patients with uncertain diagnosis after all diagnostic procedures excluded. AOSD patients followed at Hacettepe University department of rheumatology were included. Of AOSD patients whose initial test ferritin levels were not available also excluded. For determination of cut-off values, receiver operator curve (ROC) analysis were done for each predetermined value. Upper normal level in our laboratory for ferritin is 336 ng/ml.

**Results:** Total 150 patients (n=63, for AOSD; n=87, for FUO) were included. Median ferritin level was significantly higher in AOSD group [1705 (657–6417) ng/ml vs. 424 (141–1188) ng/ml, p<0001]. FUO group were also divided into three subgroups: rheumatologic (n=31, 35.6%), infectious (n=28, 32.2%) and malignant (n=28, 32.2%) causes. Median ferritin levels for these subgroups were 222 (104–1020), 527 (145–1057), 599 (166–2766) ng/ml, respectively. Area under curve

(AUC) 95% confidence intervals, sensitivity and specificity for predetermined cut-off values are given in Table-1. ROC curve for all ferritin levels are given in Figure 1.

**Abstract AB1140 – Table 1**

Cut/off value (ng/ml)	Area under curve (AUC)	Sensitivity, %	Specificity, %	p value	95%, Confidence Interval (CI)
>UNL	0,73	98	49	<0001	0,65–0,81
>3xUNL	0,66	64	68	0001	0,56–0,74
>5xUNL	0,67	52	82	<0001	0,58–0,74
>750	0,69	75	63	<0001	0,60–0,77
>1250	0,66	59	76	0001	0,57–0,75
>2500	0,66	43	85	0001	0,57–0,75

\*UNL: Upper normal limit (for ferritin: 336 ng/ml)

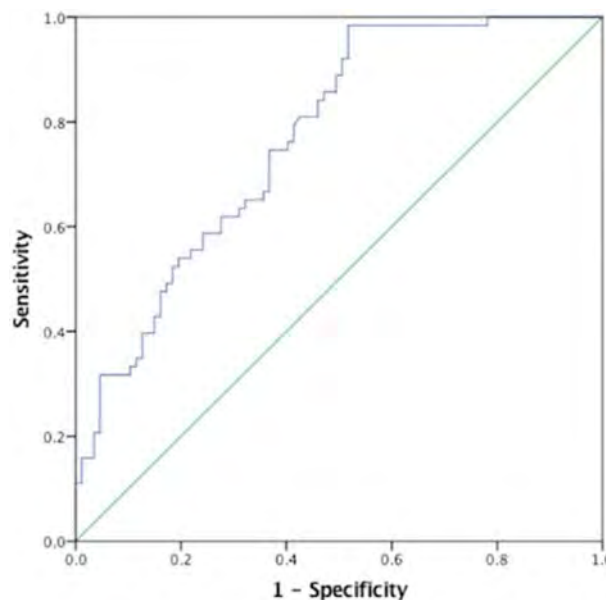


Figure-1: ROC analysis for each ferritin level (AUC 0,77%;95 CI: 0,70–0,84, p<0.001)

**Conclusions:** For each cut-off values for ferritin, test performances were quite well to differentiate patients with AOSD from FUO. While ferritin levels higher than upper normal level have 98 percent sensitivity, ferritin levels higher than 5 times of upper normal level have 82 percent specificity. Large number of patients in each FUO subgroup is needed to determine ferritin test performance for each particular group of patients to differentiate from AOSD.

**Disclosure of Interest:** None declared

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**AB1141 UTILITY OF MUSCLE BIOPSY WITH NEEDLE IN A RHEUMATOLOGY SERVICE. A 12 YEARS EXPERIENCE**

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**Background:** Muscle biopsy with needle is presented as a faster and less invasive alternative than conventional open biopsy for the diagnosis of some myopathies. However, its use as a diagnostic technique is still very limited in the Rheumatology services.

**Objectives:** To describe the experience of 12 years and the diagnostic usefulness of needle biopsy in a Rheumatology service.

**Methods:** Descriptive study including all patients who, since 2005, had undergone a needle biopsy in the Rheumatology service of the Parc Taulí University Hospital in Sabadell, as a diagnostic technique for suspected myopathy.

The technique was performed in all cases on the lateral aspect of the thigh, about 10 cm above the knee. After disinfection and local anaesthesia, an incision of 1 cm longitudinal to the thigh was made until reaching a depth of about 3–4 cm, then introducing the Bergstrom needle for the muscle biopsy (about 4–5 muscle fragments of 2–3 mm taken in different directions) from the vast lateral. Finally, the incision was sutured with a single stitch.

In obese patients, a previous ultrasound was performed to exactly knowing the depth at which the muscle sample should be taken.

The collected samples were sent fresh to the Pathology service, wrapped in a gauze moistened with 0.9% physiological saline solution.

**Results:** In these 12 years we have performed a needle biopsy on 49 patients (29 women). Age 52±10 years (range 25–70). The reason for performing the biopsy was always the increase of muscle enzymes, mainly creatine kinase (CK), which in 9 of the cases was isolated, without any underlying disease, myotoxic drugs or other symptoms. Eight patients presented myalgia or weakness as the only symptomatology. Twelve patients had a rheumatic or autoimmune disease, and in 7 of these 12 cases there was a suspicion of antimalarials myopathy. In 6 cases the suspicion was dermatomyositis and in 5 cases of vasculitis. The biopsy was performed in 4 patients with fibromyalgia and in a patient with diabetes. In 4 of the cases, the suspicion was a lipid-lowering drug myopathy.

In 48/49 cases (98%) sufficient muscle sample was obtained. The technique had only to be repeated in one patient due to insufficient or inadequate tissue. Only in 2/49 cases (4%) the histological diagnosis was not concordant with the definitive clinical diagnosis (dermatomyositis), which was confirmed in one patient with open muscle biopsy.

In 31 cases (63%) the biopsy was normal. Among the pathological biopsies, the most frequent histological diagnosis was polymyositis, in 12 cases. In 3 cases a dermatomyositis was confirmed, in 3 cases a vacuolar myopathy by antimalarials and in 1 case a necrotizing myopathy.

As complications, it should be noted that only 2/49 (4%) patients presented moderate pain, which subsided in less than a week with analgesia, and one patient presented a hematoma in the area. No case of wound infection was observed.

**Conclusions:** Muscle biopsy with a needle is a quick, simple, low invasive and safe technique that can be very useful in a Rheumatology department. The incorporation of this technique as a diagnostic tool should be extended to the majority of Rheumatology departments.

**Disclosure of Interest:** None declared

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**AB1142 REDUCTION OF ABSOLUTE NUMBER OF CD4+CD25+FOXP3+ TREG CELLS IS ASSOCIATED WITH PATHOLOGICAL FEATURES OF PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHY**

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**Objectives:** To explore the alterations and their significance of peripheral CD4<sup>+</sup>CD25<sup>+</sup>FOXP3<sup>+</sup>regulatory T cells (Tregs) and Th17 cells in Idiopathic inflammatory myopathy.

**Methods:** Clinical indicators of IIM cases (n=85) and healthy controls(n=60) were enrolled. The absolute number of peripheral Tregs and Th17 cells were analysed by flow cytometry. The clinical features were collected retrospectively. Since the data was disregarded from the normal distribution, the median four quantile method was used for statistical description. Two samples were compared with Mann-Whitney U test, and the correlation between variables was Spearman rank correlation analysis.

**Results:** (1) The absolute number of Treg cells in the patients was significantly lower than that in the control group ( $P<0.05$ ); the ratio of Th17/Treg was also significantly higher than that in the control group ( $P<0.05$ ); (2) Peripheral Treg cells levels were negatively correlated with CRP ( $r=-0.279$ ,  $p<0.05$ ); (3) According to the involvement of important organs was classified into two groups: organ group and non-organ group. The absolute number of Treg cell in organ group is fewer than

that in non-organ group ( $p<0.05$ ), and the ratio of Th17/Treg in organ group was significantly higher than that in non-organ group.<sup>4</sup> The peripheral Th17 cell absolute number in patients with skeletal muscle inflammatory oedema was significantly higher than that of non inflammatory oedema patients ( $p<0.05$ );<sup>6</sup> The levels of Th17, Tregs and ratio of Th17/Treg did not correlated with pathological features of inflammatory infiltration ( $p>0.05$ ).

**Conclusions:** The absolute number of peripheral Treg cells decreased significantly in IIM, and correlated with CRP. Patients with organ involvement had fewer Treg cells, and imbalance between Th17 and Treg. When muscle MRI appeared inflammatory oedema, it has a higher level of Th17 cells. Our results suggest that Treg cells plays an important role in the pathogenesis of IIM and increasing the number of Treg cells and maintaining Th17/Treg immune balance will become a new therapeutic strategy for IIM.

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**AB1143 AUTOIMMUNE CHARACTERISTICS IN A COHORT OF 89 PATIENTS WITH PRIMARY BILIARY CHOLANGITIS**

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**Background:** Primary biliary cholangitis (PBC) is associated to other autoimmune diseases with an unknown prevalence. Their treatment can prevent progression to liver cirrhosis and other systemic complications

**Objectives:** To describe the clinical and analytical autoimmune characteristics in a cohort of patients with PBC diagnosed and followed in a specific unit of Hepatic Diseases. All patients were also studied in the Autoimmune and Systemic Diseases Unit of our hospital to check for the presence of extrahepatic autoimmune diseases.

**Methods:** We have studied patients with PBC diagnosed in our Service since 1994 who are currently under follow-up. The diagnosis of PBC was made taking into account: the presence of colostasis enzymes with positive anti-mitochondrial antibodies (AMA) and/or compatible liver biopsy

**Results:** We studied 89 patients with PBC. 81 of them were women (female/male ratio 10/1) with a mean age at diagnosis of 56 years (range 23–84 years). The mean follow-up was 106 months (range 9–286). IgM was elevated in 70% of the patients in whom it was found (56/80). The ANA were positive in 71% (61/86) and the AMA in 75% (67/89). 43% of patients AMA-negative PBC had other suggestive antibodies: 7 anti-centromere, 2 AMA-2 and 1 anti-sp-100. A liver biopsy was performed on 75 patients (87%), resulting in a diagnosis of 58% and useful to exclude other pathologies in the rest. In 18 patients (20%) an overlapping condition was diagnosed: PBC +Autoimmune hepatitis. In 11 patients (12%) a Reynolds syndrome was diagnosed: PBC +Scleroderma, in all of them Raynaud phenomenon was present. On another 11 of 41 (27%) Raynaud phenomenon was also present. In 17 patients (19%) there was a history or new diagnosis of autoimmune thyroiditis and in 13 patients (15%) of Sjögren syndrome. None of them was diagnosed of IgG4-related disease. Serum IgG4 was measured in 56 patients (63%) with a mean value of 36.6 mg/dL.<sup>2,8–125</sup>

The patients with pure PBC were treated only with urodeoxycholic acid, with a complete response of 41%, a partial response of 51% and an absence of response of only 6 (7%). There was no difference regarding liver response to treatment among patients with pure PBC and patients with overlapping autoimmune hepatitis, Reynolds syndrome, Raynaud phenomenon, Sjögren syndrome nor autoimmune thyroiditis. Only 3% of patients with complete response and 12% of



those who responded partially evolved to liver cirrhosis, with a similar follow-up time in both groups (105 vs 113 months). 5 of the 6 patients who did not have a biochemical response developed liver cirrhosis. 7 of the 13 patients with cirrhosis (54%) already presented clinical or histological data of cirrhosis in the initial evaluation

**Conclusions:** PBC patients have frequently other autoimmune diseases such as Autoimmune Hepatitis, Sjögren syndrome or Scleroderma so we must actively seek the presence of these pathologies. The treatment with ursodeoxycholic seems to be useful in all patients but it is important to make an early diagnosis

**Disclosure of Interest:** None declared

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**AB1144 HISTOLOGY OF ROSAI-DORFMAN DISEASE IN A SUBSET OF PATIENTS WITH ERDHEIM-CHESTER DISEASE: A DISTINCT ENTITY MAINLY DRIVEN BY MAP2K1**

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**Background:** Diagnosis of Erdheim-Chester disease (ECD) is based on characteristic imaging of bone, retroperitoneal and/or cardiovascular involvement.<sup>1</sup> Biopsy is mandatory to exclude other diagnoses and confirm infiltration of histiocytes, but histology is not specific.<sup>2</sup> By contrast diagnosis of Rosai-Dorfman disease (RDD), a rare histiocytosis, is based on histology, which is characterised by infiltration by CD68 +CD1 a- S100+ histiocytes with large nuclei and abundant lesions of emperipolesis.<sup>2</sup> Up to 70% of ECD have *BRAF* or *MAP2K1* mutations,<sup>3</sup> which are rare in RDD.

**Objectives:** We investigated patients harbouring an ECD phenotype but RDD histology.

**Methods:** We reviewed records of ECD patients followed in Pitié-Salpêtrière hospital (Paris, France) and Memorial Sloan Kettering Cancer Centre (New-York, NY, USA) between 2007 and 2018. Biopsy samples of the patients were systematically investigated for mutations of genes of MAP kinase pathway.

**Results:** Among 209 patients with ECD, we found 10 (4.7%) patients who had RDD histology. These 10 patients had typical ECD clinical and radiological presentation, in particular bones (n=7), vascular (n=5) and peritoneal (n=6) involvements. Patients also had typical neurological involvement of ECD (n=6). All patients except one had at least one biopsy with a compatible histology of ECD at diagnosis. ECD biopsies showed non-specific fibrosis (n=5), foamy CD 68 +CD1 a- histiocytes (n=3) and/or Touton cells (n=1). Biopsies disclosing RDD histology were performed during the course of the disease involving testes (n=5), stomach (n=1), tibia (n=2), cheek (n=1) and omentum (n=1). All tissues showed lympho-plasmocytic infiltrate with large histiocytes infiltration. Histiocytes were CD68 +CD1 a- S100 +with large nuclei and abundant lesions of emperipolesis. Five patient harboured *MAP2K1* mutation and one patient had *PIK3CA* mutation. None of the patients had *BRAF* mutation.

**Conclusions:** Some patients with ECD may also present the iconic histological lesions described by Rosai and Dorfman. Overlap forms of such distinct histiocytoses between ECD and RDD is mainly driven by *MAP2K1* but not by *BRAF*.

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**AB1145 ACUTE POSTERIOR MULTIFOCAL PLACOID PIGMENT EPITHELIOPATHY: CLINICAL PATTERN AND MANAGEMENT OF 79 PATIENTS**

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**Background:** Acute Posterior Multifocal Placoid Pigment Epitheliopathy (APMPPE) is an uncommon inflammatory disease causing acute-onset chorioretinal bilateral disease. It typically affects the posterior pole of both eyes leading to visual blurring or scotomas. Although it is thought to be benign, APMPPE has been associated with central nervous system (CNS) manifestations: cerebral vasculitis, meningoencephalitis and cerebral vascular disease.

**Objectives:** The aim of this study was to define clinical features, systemic manifestations, treatment and outcomes of a review of 79 patients with APMPPE.

**Methods:** We retrospectively analysed the epidemiology, potential triggers, prodromes, clinical data, ophthalmological study, extraocular manifestations, treatment and outcomes of 79 patients collected through an extensive review of the literature from the first description of Gass JD up to the present time.

**Results:** A total of 79 patients were reviewed (47 male). Mean age at diagnosis was 30 years (with a range of 8 to 58 years old). 27 patients (34.2%) presented with a previous triggering being flu-like illness the most frequent.<sup>15</sup> However, the complete serological study was only requested in 28 patients (and the immunological study just in 22) Median time from trigger to overt APMPPE was 9 days. Main clinical symptoms were: decreased visual acuity/blurred vision (100%), headache (51.8%) and photophobia (12.2%). Average decreased visual acuity was 13/20. APMPPE is defined by the presence of multiple white-yellowish plaques in funduscopy, and early hypofluorescent areas with late hyperfluorescence in fluorescein angiography. The fundus was pathological and compatible with APMPPE in all cases (100%), as was fluorescein angiography in those that had been performed (59). CNS involvement appeared in up to 50.6% (40 patients). The CNS manifestations were divided into language disorders (11 patients), motor deficit,<sup>20</sup> sensory deficit<sup>20</sup> and other CNS manifestations.<sup>23</sup> The mean time from visual deficit to neurological manifestations was approximately 2 weeks. Cerebrospinal fluid was studied in 37 patients, with a predominance of lymphocytic pleocytosis (mean of 46 cells/mm<sup>3</sup>) and elevated proteins (mean of 111 mg/dl). Within the neuroimaging studies carried out (58) up to 69.7% were pathological. 67 patients (84.8%) received treatment with corticosteroids. 14 patients (17.7%) also received other immunosuppressants (mainly azathioprine and cyclophosphamide), especially if CNS involvement. Regarding the evolution, 55 patients (69.6%) presented improvement, 12 (15.2%) relapsed and 6 (7.5%) died due to APMPPE.

**Conclusions:** APMPPE is a rare inflammatory disease which primarily affects the retina. However, the CNS involvement could be more frequent than what is classically described. Also, it seems that there might be a trigger effect either inflammatory or infectious. Steroids and immunosuppressants should be considered in patients with CNS involvement from the beginning.

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**AB1146 THE ASSOCIATION OF COMMON MEFV GENE MUTATIONS WITH AXIAL SPONDYLARTHROSIS IN FMF PATIENTS: A RETROSPECTIVE STUDY**

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**Background:** Familial Mediterranean fever (FMF) is an autoinflammatory disease seen with autosomal recessive inheritance and is characterised by recurrent and self-limiting attacks with peritonitis, pleuritis, arthritis or fever alone. The association of spondylarthrosis and FMF is reported in some studies. There are few studies evaluating the association of MEFV gene mutations with axial spondylarthrosis in FMF patients.

**Objectives:** The aim of this study is to identify patients with FMF associated spondylarthrosis retrospectively and to compare the frequency of common MEFV gene mutations in FMF patients with and without axial spondylarthrosis.

**Methods:** We have reviewed 138 charts of FMF patients. The data of 116 patients (70 female, 46 male) who met the diagnosis of FMF with Tel Hashomer classification criteria and have the results of MEFV gene mutation were examined. Patients' age, sex, MEFV gene mutations were recorded. The presence of

inflammatory back pain (IBP) obtained from rheumatological system questionnaire in the patients' charts were recorded. The x-ray and MR images of sacroiliac joint registered in the PACS system were evaluated by a Rheumatologist. Patients with inflammatory low back pain and sacroiliitis detected by X-ray or MR were included in the FMF with axial spondylarthritis (FMF-SPA) group and others to FMF group. The frequency of MEFV gene mutations were compared between two groups.

**Results:** The frequency of M694V, M680I, V726A, E148Q and R202Q are 82.4%, 19.6%, 16.7%, 10.8% and 16.7% respectively in FMF group and 78.6%, 21.4%, 14.3%, 21.4% and 28.6% respectively in FMF-AS group. There was no significant difference between groups ( $p=0.716$ ,  $p=1.000$ ,  $p=1.000$ ,  $p=0.373$  and  $p=0.279$  respectively). The frequency of M694V homozygotes and heterozygotes mutations were 27.5% and 21.6% respectively in FMF group and 35.7% and 7.1% respectively in FMF-SPA group and difference between groups was not significant ( $p=0.537$ ,  $p=0.296$  respectively).

**Abstract AB1146 – Table 1.** The characteristics and MEFV gene mutations of FMF patient with spondylarthritis

	Age, years	Sex	IBP	Sacroiliitis X-ray/MR	MEFV mutations
1	34	F	+	-/+	M694V/M680I
2	41	F	+	-/+	M694V/M694V
3	31	F	+	+/ND	E148Q/R202Q
4	56	M	+	+/ND	M680I/E148Q
5	49	M	+	+/ND	M694V/-
6	47	M	+	+/ND	M694V/E148Q
7	22	M	+	+/ND	M694V/M680I
8	22	F	+	+/ND	M694V/M694V
9	39	F	+	+/ND	M694V/M694V
10	30	M	+	+/ND	M694V/M694V
11	37	M	+	+/ND	M694V/M694V/R202Q/R202Q
12	41	F	+	+/ND	M694V/R202Q/A744S
13	24	F	+	-/+	V726A/K695R
14	31	F	+	+/ND	M694V/V726A/R202Q

ND: Not done, IBP: inflammatory back pain

**Conclusions:** The frequency of common MEFV gene mutations in this study is not different between FMF patients with and without axial spondylarthritis. Increased frequency of axial spondylarthritis in FMF patients may not be associated with MEFV gene mutations.

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#### AB1147 EVOLUTIONARY STUDY OF 45 CASES OF UNDIFFERENTIATED NEGATIVE HLA B27 SERONEGATIVE OLIGOARTHRITIS

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**Background:** The prognosis of patients with undifferentiated arthritis may vary from self-limited to severe destructive rheumatoid arthritis. Early diagnosis is important, specially in seronegative oligoarthritis in order to start a treatment as early as possible.

**Objectives:** To describe the evolution of patients older than 16 years diagnosed with negative HLA B27 seronegative oligoarthritis without axial involvement.

**Methods:** We retrospectively studied 45 patients (23 women, 22 men) with negative HLA B27 seronegative oligoarthritis without axial involvement who debuted between 1985 and 1990 and who did not meet the criteria for any of the rheumatic diseases at the time of debut: rheumatoid arthritis (AR), psoriatic arthropathy (PsA), spondyloarthropathy, enteropathic arthritis, reactive arthritis, microcrystalline arthritis or connective tissue disease.

**Results:** The mean age at onset of oligoarthritis was 42.2 years (range 17–66). The mean follow-up time was 13.7 years (range 1–32). In its evolution, a definitive diagnosis was reached in 21 (46.6%) patients, with the mean time between debut and diagnosis being 5.47 years (range 1–25): 8 AR, 4 APs (3 with involvement) peripheral and 1 mixed), 2 undifferentiated spondyloarthritis, enteropathic arthritis, 5 gouty arthropathies and one SLE. In the case of RA, the diagnosis was made on an average of 4.8 years after the debut (range 1–16); the RF was positive in 4 patients a mean of 7.6 years (range 3–11) after the debut, and the anti-CCP were positive in 3 of the patients with positive RF. Within PsA, one developed skin psoriasis, another psoriatic onychopathy at 4 years after debut and 2 continue without skin involvement but with a family history of psoriasis, all met CASPAR criteria. From the other 24 patients (53.3%), only 3 patients (12.5%) continued to be followed up, with an average of 21.3 years (range 18–26) without meeting the criteria that allow us to define diagnosis. With the rest of the patients (40.8%), followed for an average of 4.5 years, a diagnosis was not achieved by resolution of the clinical picture or loss of follow-up.

**Conclusions:** In our series, 46.6% of the patients with a diagnosis of negative HLA B27 seronegative oligoarthritis began to meet diagnostic criteria for rheumatic disease after a mean time of 5.47 years, with RA being the most frequent diagnosis (38%) after an average of 4.8 years after the arthritis onset.

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#### AB1148 BIOLOGICAL TREATMENT OF NON ISCHAEMIC OPTIC NEURITIS ASSOCIATED TO IMMUNE-MEDIATED INFLAMMATORY DISEASES. MULTICENTER STUDY

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**Background:** Non ischaemic optic neuritis (NION) is a severe inflammation of the optic nerve that may lead to blindness. It can be primary or associated to immune-mediated inflammatory diseases (IMIDs). The treatment of the NION is based on systemic corticosteroids and conventional immunosuppressive drugs.

**Objectives:** To assess the efficacy of the biological treatment in refractory NION to conventional treatment.

**Methods:** Multicenter study of 8 patients diagnosed with NION refractory to systemic corticosteroids and at least one conventional immunosuppressive drug.

The main outcomes were visual acuity (VA) and OCT of the optic nerve and the ganglionar cells. Comparisons were made between baseline and the 1st week, 1st and 6th month and 1st year. (STATISTICA, StatSoft Inc. Tulsa, Oklahoma, USA).

**Results:** We studied 8 patients (12 affected eyes) (4♀/4♂); mean age of 34.37 ±13.30 years. The underlying diseases were SLE (n=1), neuromyelitis optica (n=1), neuroretinitis (n=1), relapsing polychondritis (n=1), idiopathic (n=2) and Behçet's disease (n=2).

Before biological treatment and besides oral corticosteroids patients had received intravenous (IV) methylprednisolone boluses (n=6), cyclosporine A (CyA) (n=1), ciclophosphamide (n=2), micophenolate (n=2), hydroxychloroquine (n=1), methotrexate (MTX) (n=4) and azathioprine (AZA) (n=2).

Biological treatment was based on rituximab (n=2) (2 IV. doses of 1 g/very 2 weeks and every 6 months), adalimumab (n=2) 40 mg/week, tocilizumab (n=2) 8 mg/kg/2–4 weeks and infliximab (n=2) 5 mg/kg at 0, 2 and 6 week and then every 8 weeks.

The characteristics of the 8 patients are shown in the **TABLE**

After biological treatment we observed an improvement in the ocular parameters: VA [0.60±0.33 to 0.76±0.41,  $p: 0.04$ ], OCT of the optic nerve [130.63±60.54 to 102.60±8.17,  $p: 0.1$ ] and OCT of the ganglionar cells [404.60±184.73 to 243 ±18.38,  $p: 0.17$ ] at one year. After a mean follow-up of 27±14.47 months there were no severe adverse effects.

Abstract AB1148 – Table 1

Case	Sex / Age (years)	Underlying disease	Laterality	Immunosuppressive drugs before biologic therapy	Biologic therapy
1	♂ / 25	Behçet's disease	Right	MTX, CyA	ADA
2	♂ / 43	Neuromyelitis optica	Bilateral	AZA	RTX
3	♂ / 14	Neuroretinitis	Bilateral	MTX	ADA
4	♂ / 56	SLE	-	HYDROXYCHLOROQUINE, MMF, CFM	RTX
5	♂ / 29	Idiopathic	Right	AZA	TCZ
6	♂ / 26	Idiopathic	Bilateral	AZA	TCZ
7	♂ / 43	Relapsing polychondritis	Bilateral	MTX, CFM	IFX, TCZ
8	♂ / 39	Behçet's disease	Right	MTX, MMF	IFX

MTX: methotrexate, CyA: cyclosporine A, AZA: azathioprine, CFM: cyclophosphamide, MMF: mycophenolate, ADA: Adalimumab, RTX: rituximab, TCZ: tocilizumab, IFX: infliximab.

**Conclusions:** This study shows that treatment with biologic drugs, including anti-TNF drugs, in NION associated to IMIDs, refractory to conventional treatment, seems to be effective. These results must be confirmed in prospective and randomised trials.

**Disclosure of Interest:** None declared

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### AB1149 CYSTIC FIBROSIS AND INFLAMMATORY ARTHRITIS REQUIRING IMMUNOSUPPRESSION: A WORRYING COMBINATION?

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**Background:** Inflammatory arthritis is a recognised complication of cystic fibrosis (CF) with an estimated prevalence of 2.3<sup>[1]</sup> to 8.5%<sup>[1]</sup> of CF patients. Cystic fibrosis associated arthritis (CFA) constitutes the majority of this, but other there may be other co-morbid rheumatic disease. Concerns about use of immunosuppression in the context of chronic pulmonary infection, and consequent risk of destabilisation, may limit use of these medications when clinically indicated. Immunosuppressive therapy is used in patients with CF lung disease who have inflammatory rheumatic disease, inflammatory bowel disease, or who have had a liver transplant for CF-related liver disease. Some data on those receiving immunosuppression post-transplant has been published and reassuringly reported fewer courses of intravenous antibiotics following transplant.<sup>[1]</sup> Reports of immunosuppressants being used in other contexts, including arthritis, are more sporadic.

**Objectives:** To assess prior use and safety outcomes of immunosuppressant therapy in adults with CF.

**Methods:** A retrospective case note review of patients with CF receiving disease modifying anti-rheumatic drugs from 2 large adult CF centres (total >700 patients) from electronic records spanning 3–10 years.

**Results:** 41 patients were identified: 7 post liver transplant, 1 with inflammatory bowel disease, 1 with IgA nephropathy; 32 with inflammatory arthritis.

Abstract AB1149 – Table 1

Medication	Number of patients	Cumulative months of treatment	Stopped due to side effects
Azathioprine	4	239	0
Hydroxychloroquine	27	726	3
Sulfasalazine	7	98	3
Tacrolimus	7	900	0
Methotrexate	6	192	1
Cyclophosphamide	1	1	0
Etanercept (with methotrexate, sulfasalazine, hydroxychloroquine)	1	7	0

There was one possible case of increased pulmonary exacerbation associated with methotrexate; they remained on treatment at the time of the study. There was no evidence that immunosuppression resulted in a fall in lung function necessitating cessation of treatment in any of these cases. Three patients stopped hydroxychloroquine and 1 patient stopped methotrexate due to non-respiratory side effects. Four of 7 patients responded to treatment with sulfasalazine for inflammatory arthritis, 3 stopped due to non-respiratory side effects.

**Conclusions:** No patients had immunosuppression stopped because of deterioration in lung disease. Steroids were not included in this analysis because duration and dose varied widely. However, it is important to note that they are frequently used in CF (particularly for allergic bronchopulmonary aspergillosis). Indeed 14% of all CF patients in these centres have had steroids in the last 6 months, of whom nearly half received a course of more than 6 months duration.

Whilst our results are reassuring, the numbers remain small. Decisions must be made in conjunction with the multidisciplinary team, but CF in itself should not delay or stop treatment with immunosuppression where it is indicated.

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### AB1150 THE EUROPEAN REFERENCE NETWORK ON RARE AND COMPLEX CONNECTIVE TISSUE AND MUSCULOSKELETAL DISEASES: ERN RECONNET

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**Background:** Set up under the European Union (EU) directive on patients' rights in cross-border healthcare (2011/24/EU), European Reference Networks (ERNs) on rare and complex diseases are aimed at connecting healthcare providers (HCPs) across different EU Countries to tackle complex and rare medical conditions that require highly specialised treatment. ERN ReCONNET, endorsed by EULAR, and approved for rare and complex connective tissue diseases (CTDs), aims at developing a framework for the delivery of high quality, innovative, sustainable and equitable standard of care and practice for better access to care of European patients.

**Objectives:** To report the activities of ERN ReCONNET during the first 10 months of work

**Methods:** ERN ReCONNET is composed of 26 HCPs from 8 EU Countries: Belgium, France, Germany, Italy, Netherlands, Portugal, Romania and Slovenia. Patients involvement is ensured by the ERN ReCONNET European Patients Advocacy Group, included in the activities of the ERN. The diseases covered are divided into 3 main thematic areas: rare CTDs (systemic sclerosis, mixed CTD, idiopathic inflammatory myopathies, antiphospholipid syndrome, undifferentiated CTD, IgG4 related diseases, relapsing polychondritis), complex CTDs (SLE, Sjogren's Syndrome), hereditary connective tissue diseases (Ehlers-Danlos syndrome). Senior and Junior Coordinators for each disease were selected. The scientific activities of ERN ReCONNET officially started in Vilnius in March 2017, where the 24 ERNs have been formally launched.

**Results:** The scientific activities of the first year were mainly focused on existing clinical practice guidelines (CPGs). The first phase was aimed at identifying the scientific publications, selecting them by evaluation of titles and abstracts, and by reviewing the full texts. More than 6.000 publications have been screened. The second step was to review critically the articles according to the principles of the AGREEII flow-chart. This work allowed to identify CPG for the majority of the diseases covered by ERN ReCONNET, as well as unmet needs, in particular for the rarest diseases (IgG4 related diseases, relapsing polychondritis, mixed CTD). Good progress has also been made in the field of IT, in which ERN ReCONNET was mainly focused on the use of the Clinical Patients Management System web-platform, designed for the interactive discussion of difficult clinical cases. Notably, the creation of ERN website is being co-designed by all Networks stakeholders.

**Conclusions:** The ERN ReCONNET will significantly improve the clinical approach to rare and complex CTDs, promoting an improvement of the quality of the specialised care provided to patients, of the activity of the physicians, the empowerment of the patients sharing expertise and promoting the interaction among EU HCPs. All these activities are addressed to create a highly specialised network, in which the knowledge travels rather than the patient.

**Disclosure of Interest:** None declared

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**AB1151 POLYMYALGIA RHEUMATICA. NEW THERAPEUTIC STRATEGY BASED ON LOW DOSE OF METROTEXATE PLUS LOCAL INFILTRATION WITH CORTICOSTEROIDS**

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**Background:** The polymyalgia rheumatica is a rheumatic inflammatory disease more frequent in the eldest population. The classic therapy is based on medium doses of corticosteroids followed by a maintenance phase of low doses, generally lasting from 1–2 years. Recurrences frequently require an escalation of dose, thus lengthening the treatment time, and that entails important comorbidity. Methotrexate (MTX) has been tested in 3 randomised clinical trials, showing in two of them the efficacy as a steroid sparing agent, but it has never been tested as monotherapy.

**Objectives:** To analyse the results of an alternative therapy in order to avoid the oral corticotherapy through the use of low dose of MTX and joint infiltration with a total duration of 24 months.

**Methods:** A prospective observational study in which patients that had been diagnosed with 2012 EULAR/ACR criteria were evaluated in outpatient medical consultations of Rheumatology at "Doce de Octubre" Hospital between 2015–2017, with the restriction of not having received previous steroid treatment. Right after diagnosis, the treatment with MTX 5–7.5 mg/w plus the infiltration of triamcinolone acetonide in both shoulders begins, being repeated if necessary after 15 or 30 days, or in case of subsequent relapse.

**Results:** 26 patients were included, with an average follow-up 19±5 months.<sup>12–24</sup> The age average at diagnosis was 74±7 years,<sup>55–83</sup> being 56% women. 73% had symmetrical hand arthritis and 27% structural pathology of the rotator cuff. 96% had moderate-severe pain (VAS) in shoulders, 73% in hips and 54% in hands. These percentages after a month of treatment were 15%, 11.5% and 7.7%. From the onset of symptoms until the start of treatment 104±54 days passed,<sup>30–180</sup> applying an initial dose of 5 mg of MTX in half of cases and 7.5 mg in the other half. There are no significant differences between precocity of the treatment or initial dose regarding a faster remission. The average of infiltrations in the shoulder per year is 2±1.4 (1–4). 25% of patients showed reactivation with good response to the MTX dose increase [maximum dose 8±1.7 (5–12.5)] plus/or joint infiltration. The average time until the revision (subjective clinical evaluation, HAQ and APR) was 2.7±1 months,<sup>1–6</sup> being significantly higher ( $p<0.05$ ) in patients with peripheral arthritis 3.3±1.9 vs 1.3±0.7. The change of HAQ, CRP and other variables are indicated in the table.

The treatment was stopped in 12% because of adverse effects (digestive intolerance, alopecia and respiratory infection in a patient with COPD). A patient showed mild plaquetopenia in which not necessary to suspend the treatment with MTX.

8 patients were monitored during ≥2 years, in 87% of them MTX has been removed with an average follow-up after the suspension of 3±1.7 months<sup>1–6</sup> with no need to restart it in any case.

Abstract AB1151 – Table 1

	Start	1 Month	3 Months	6 Months	12 Months
Morning stiffness>1 hour	69%	38%	4%	4%	4%
HAQ	2	0.750	0.300	0.500	0.125
ESR	43,2	20	20	15	13
CRP mg/dl (0–0,5)	4,1	0,81	0,44	0,48	0,47
Peripheral arthritis	77%	23%	7%	11%	7%
Shoulder limitation	100%	69%	26%	23%	20%

**Conclusions:** The use of low dose of MTX and local joint infiltration with corticosteroids (initial and on demand) is an efficient therapeutic strategy with a low complication rate in PMR. All these results must be confirmed with controlled studies and a longer period of follow-up after the suspension of treatment.

**Disclosure of Interest:** None declared

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**AB1152 MUSCULOSKELETAL MANIFESTATION OF DIABETES MELLITUS IS HIGHLY PREVALENT AND IS ASSOCIATED WITH POOR DIABETIC CONTROL**

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**Background:** Diabetes mellitus is one of the most common medical conditions all over the world. A variety of musculoskeletal (MSK) conditions have been associated with diabetes mellitus (DM). These MSK symptoms are important to recognise because these can respond to treatment. Estimates of the prevalence of MSK problems in patients with DM vary depending upon the definitions used for the problems and the study population with diabetes, which can range from a primary care cohort to patients with severe diabetes in a specialised referral setting.

**Objectives:** The objectives of our study were: 1) to investigate the prevalence of musculoskeletal complications of diabetes in a consecutive cohort of patients attending a secondary care endocrinology clinic; and 2) to identify clinical associations of such musculoskeletal complications by examining likely contributing features including patient characteristics, life style factors and features of underlying diabetic disease.

**Methods:** The study participants were all consecutive patients attending endocrinology clinics of University Hospital Kerry for the management of their DM. Patients with chronic inflammatory arthritis or chronic autoimmune diseases were also excluded. This was a questionnaire-based study and was carried out in two steps. The first step involved having a short interview and assessment of the patient, and in the second step their clinical records were reviewed to populate clinical parameters. The clinical variables studied were gender, smoking habits, body mass index (BMI), units of alcohol intake per week, smoking habits, type of DM, duration of DM, medications used for DM, employment status and also their current HbA1c blood results. End organ complications of DM were also included. Moreover, personal history of cardiovascular risk factors and diseases were also recorded. Since there is a long list of rheumatologic manifestations which are potentially associated with DM and many of them are less sensitive and specific for DM, we choose to study the 4 common DM-associated rheumatologic presentations (Stiff hands, Carpel Tunnel Syndrome, Charcot joint, bilateral shoulder rotator cuff tendinopathy). Moreover, importantly, only patients with the musculoskeletal symptoms lasting for >3 months were included in the analysis. These 4 DM-associated musculoskeletal diseases are labelled as DM-MSK diseases.

**Results:** A total of 250 patients [mean age 66±16 years; 58% male; mean duration of DM 13±10 years; mean BMI of 27.5±6] were evaluated. DM-MSK diseases were present in 37.6% (n=94) of the entire cohort.

On univariate analysis, patients with older age, type-2 DM, using hypoglycaemic agents, hypertension, ischaemic heart disease, peripheral vascular disease, cerebrovascular accident, congestive heart disease, and patients with renal involvement had significantly higher prevalence of DM-MSK symptoms. However, on multivariate analysis (table-3), poor diabetic control as reflected by higher HbA1c levels, presence of diabetic kidney disease and advancing age were associated with the presence of DM-MSK symptoms.

**Conclusions:** We conclude that MSK manifestations of DM are very common but unfortunately these remain poorly recognised and continue to cause significant disabilities. Similar to the microvascular and macrovascular complications, MSK manifestations are associated with poor diabetic control.

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**AB1153 IDIOPATIC LOBULAR PANNICULITIS (DISEASE WEBER-CHRISTIAN): CURRENT ASPECTS**

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**Background:** Idiopathic lobular panniculitis (ILP) (syn. Weber-Christian disease) is the least studied condition from the group of systemic connective tissue diseases, which is characterised by predominant involvement of subcutaneous fat (SCF) tissue.

**Objectives:** To evaluate the interrelation between clinical signs and lab parameters in ILP patients.

**Methods:** The study evaluated 67 patients (9 males and 58 females) aged 20–76 years with verified ILP diagnosis and mean disease duration of 78.91<sup>48;540</sup> months who were on the record at V. A. Nasonova Research Institute of Rheumatology during 2007–2017 yy. Alfa-1 antitrypsin, liver fractions, amylase, lipase, trypsin, ferritin, creatine phosphokinase (CPK), leptin and TNF- $\alpha$  levels were measured, chest CT and histopathological study of skin and SCF lesions biopsy specimens were made in addition to conventional clinical examination.

**Results:** ILP was found to affect all age groups, with 57% of cases falling on able-bodied adults aged 45–60 yy. Based on clinical manifestations including location, distribution, spatial extent of lesions, and clinical course of the disease, the following 4 clinical forms of ILP were identified: nodular (30 patients), plaque-like,<sup>10</sup> infiltrative<sup>15</sup> and mesenteric.<sup>12</sup> ILP population demonstrated significant ESR ( $p=0,01$ ) and CRP ( $p<0,0001$ ) elevation. ESR elevation correlated with palpatory nodular pain intensity, assessed by visual analogue scale (VAS ( $p<0,05$ ,  $r=0,29$ ), with the amount of affected body surface area (BSA) measured using the hand area surface (HAS) to equal 1% BSA ( $p<0,05$ ,  $r=0,50$ ), with elevation of body temperature ( $p<0,05$ ,  $r=0,68$ ) and CRP ( $p<0,05$ ,  $r=0,68$ ). CRP elevation correlated with pain intensity measured by VAS ( $p<0,05$ ,  $r=0,46$ ), affected BSA ( $p<0,05$ ,  $r=0,61$ ) and presence of stage II nodules ( $p<0,05$ ,  $r=0,41$ ). Histopathologic features of skin and SCF biopsy specimens were studied in 65 patients (97,01%), including antero – and retroperitoneal fat tissue biopsy specimens from 3 patients out of 5 (5,97%)

with mesenteric panniculitis without skin and SCF involvement; the remaining 2 were not biopsied in hard to access areas. Histopathological study ruled out the probability of neoplasms and confirmed the diagnosis of lobular panniculitis in all specimens.

Therapy included such common in rheumatology practice agents as glucocorticosteroids, NSAIDs, cytotoxic drugs, hydroxychloroquine, and oths). Therapeutic success was documented in 62,68% cases, therapeutic failure and disease progression – in 17,91% (12 patients), requiring dose escalation and modification of therapeutic regimen.

**Conclusions:** Identified correlation between clinical features and lab parameters measuring disease activity confirms ILP as a systemic inflammatory disease of the connective tissue. There's a flagrant necessity to improve physicians awareness of ILP, as well as need in future studies to enable earlier ILP diagnosis and identify more effective treatment of the disease.

**Disclosure of Interest:** None declared

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AB1154

#### INCREASE GENERATION BUT DEFECTS OF SECRETING INF- $\alpha$ PLAY A ROLE IN THE PATHOGENESIS OF IGG4-RD

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**Background:** IgG4 related disease (IgG4-RD) is a multi-organ involvement, fibro-inflammatory disease of unknown etiology. Both innate and adaptive immunity played vital roles in the pathogenesis of IgG4-RD. Plasmacytoid dendritic cells (pDC) had major roles in antigen presentation and secreting INF- $\alpha$  upon infection. However, the characteristics and relevant function of this cell population in IgG4-RD was poorly understood. So we aim to study the expression and function of pDC in IgG4-RD.

**Objectives:** To study the expression and function of Plasmacytoid dendritic cells (pDCs) in IgG4-RD

**Methods:** Flow cytometry was performed to analyse the expression of pDC cells in untreated IgG4-RD patients (n=12) and healthy controls (n=12). The immunohistochemistry technique was used to assess the location of pDC in the involved tissues of IgG4-RD patients. Furthermore, by cells culture *in vitro*, the abilities of pDC secreting INF- $\alpha$  and the activation of NF- $\kappa$ B signal in IgG4-RD were explored.

**Results:** The frequencies of pDC in the IgG4-RD patients were significantly higher in the peripheral blood and involved tissues compared with healthy controls. The cell surface marker of CCR7 in pDC was lower in untreated IgG4-RD patients, but after treatment, the expression of CCR7 increased. There was on significance of the expression of pDC maturation marker (CD83), activation marker (CD80, CD86), CCR1, CCR2, CCR3, CCR4, CCR5, CCR6, CCR8, CCR9, CCR10, CXCR2, CXCR3 and CX3CR1 compared with healthy controls. Interestingly, the frequencies of CD123hiCD303+cells were also higher in untreated patients, and reduced after treatment, and the cell surface marker CD83 was also elevated. By cell culture *in vitro*, pDC had defects in secreting INF- $\alpha$  of IgG4-RD patients than healthy controls.

**Conclusions:** The excessive infiltration of pDC in peripheral blood and tissue but less CCR7 Defects of secreting INF- $\alpha$  of pDC in IgG4-RD may indicate less function of eliminating infection which may induce constant infection. pDC may played vital roles in the pathogenesis of IgG4-RD,

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AB1155

#### IMMUNOGLOBULIN G4 – RELATED DISEASE, A DIAGNOSTIC CHALLENGE

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**Background:** The IgG4-related disease (IgG4-RD) is a chronic, inflammatory, multi-organic, systemic disease. The pathological assessment is the gold standard for the diagnosis, hallmarked by the lymphoplasmacytic tissue infiltration of mainly IgG4-plasma cells, the storiform fibrosis and the obliterative phlebitis.

**Objectives:** The aim of this study was to analyse the features of IgG4- RD cases followed in a specific autoimmune diseases unit, since 2013.

**Methods:** Descriptive, retrospective study, through the review of clinical charts. Medical records were reviewed for demographics information, clinical

presentation, underlying conditions, laboratory and radiological data, medical and surgical treatments and clinical outcomes. All patients diagnosed by biopsy were included (international consensus pathological criteria of 2012). We excluded the possible cases of IgG4-RD when biopsy was not available or did not meet the criteria previously mentioned.

**Results:** Eight patients with characteristic clinical, histological and laboratory features of IgG4-RD were included. The patients were predominantly male (87.5%), the mean age at diagnosis was 66±11 years.<sup>48–80</sup> 87.5% of the cases were consulted from other hospital Services, mainly surgical: Urology 25% (hydrocele and urinary retention), General Surgery 25% (obstructive jaundice and forearm tumour), Vascular Surgery 25% (abdominal aortic aneurysm), Cardiac Surgery 12.5% (thoracic aortic aneurysm) and Neurology 12.5% (hypertrophic pachymeningitis). The most commonly involved organs were vascular 87.5% (6 aorta, 1 pulmonary veins) and retroperitoneum 75%, followed by renal 37.5%, pancreatic 12.5%, and central nervous system 12.5%. It was found isolated organic involvement in only one patient (autoimmune pancreatitis). Two patients had previous malignancy: renal cells and prostate. Magnetic resonance imaging, computed tomography and FDG-PET were made in 62.5% each of them. Serum IgG4 was determined in all cases, 62.5% of patients had normal IgG4 serum levels (the upper limit of normal for serum IgG4 is 135 mg/dl). Three patients (37.5%) had elevated serum IgG4, the mean level was 188±38 mg/dL (152–266). The pathological findings were dense lymphoplasmacytic infiltrate in 6 cases (75%) with obliterative phlebitis in 5 of them, storiform-type fibrosis in 4 cases (50%) and IgG4/IgG ratio >40% in 75% of the samples. Glucocorticoids treatment was initiated in 75% of patients, 25% were untreated for predominantly fibrotic involvement. There were treatment response in 60% of cases. 25% had a relapse after corticoid withdrawal. Only one patient received a second drug due to lack of response to Prednisone (rituximab).

**Conclusions:** According to the literature, IgG4-RD patients were predominantly male in their sixth and seventh decade of life. The predominant involvement in our serie was vascular and retroperitoneal, with no cases of glandular manifestations. Highlight the high number of cases with normal serum IgG4. Most of our patients responded to corticosteroid therapy.

**Disclosure of Interest:** None declared

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AB1156

#### DRESS (DRUG REACTION WITH EOSINOPHILIA AND SYSTEMIC SYMPTOMS): LOOKS MAY BE DECEPTIVE!

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**Background:** Drug reaction with eosinophilia and systemic symptoms(DRESS) is a rare, potentially life threatening multisystem disorder with fever, skin eruptions, lymphadenopathy, eosinophilia and systemic involvement most commonly after a drug exposure. These cases may mimic various rheumatological conditions. We report a series of 14 cases of DRESS who presented to Rheumatology Clinic as suspected connective tissue disease or sepsis in Northern India.

**Objectives:** To highlight DRESS as a common mimic of common rheumatologic conditions and sepsis and report its etiology, characteristics, treatment and prognosis

**Methods:** We manually searched the inpatient records of Immunology Department in SGPGI 2007–18 for the cases discharged with a diagnosis of probable/ probable/definite DRESS. The records of the patients with probable and definite DRESS according to regiSCAR criteria<sup>1</sup> were reviewed.

**Results:** All the 14 patients fulfilled clinical criteria for diagnosis (4 probable, 10 definite). The age of patients ranged from 9–53 years with majority in their 3rd decade. Majority of the patients were referred to us when their counts were rising in the setting of fever and skin rashes with a suspicion of rheumatic disease/sepsis. The clinical and laboratory features of these patients are as follows (table 1):

TLC: Total Leucocyte Count, AEC: Absolute Eosinophil Count, ED: Exfoliative dermatitis, F: facial oedema, M: maculopapular rash, L: Liver, K: Kidney, P: Lung, G: GI, SSZ: Sulphasalazine, HRZE: Isoniazid, Rifampicin, Pyrazinamide, Ethambutol, FU: Follow up

All the patients were treated with oral steroids showing signs of clinical improvement within 4–5 days. Rashes and leucocyte count were first to respond. Transaminitis responded within a week. Mean Followup is 9.3 months. They were gradually tapered off steroids over next 3–4 months except for two patient who were lost to follow up.

Abstract AB1156 – Table 1

Age/ Sex	Drug	Late-ncy (weeks)	Type of rash	Systemic involve- ment	TLC/AEC /cu.mm	ALT/AST IU/L	Score <sup>1</sup>	Initial Suspected Diagnosis	Followup (months)
14/F	Phenobarbitone	6	F, ED	L, K	23100/693	252/407	5	Lupus	4
33/F	Cefuroxime	2	F, ED	L	27600/ 9936	203/460	6	Acute viral hepatitis, sepsis or Lupus	11
9/M	Carbamazepine or HRZE	2	M, F, ED	L, K	19800/ 2300	2752/ 1385	7	ATT induced hepatitis (for TBM), sepsis	24
53/M	Gabapentin	7	F, ED	L, P	21400/ 3424	63/135	7	Vasculitis, Lupus	Lost FU
50/F	Alternative medicine	3	M	L, P	39630/ 2830	150/202	5	Lupus	24
15/M	SSZ	1	ED	L, G	28300/ 3100	133/92	7	AGE with Sepsis	3
21/M	HRZE	5	F, ED	L, G, K	51900/ 3114	491/478	8	Lupus or Vasculitis	8
20/F	SSZ	3	F, M, ED	L	60820/NA	137/233	6	Lupus Malignancy	3
20/F	Valproate	8	M	L, G,	13500/NA	148/177	5	Lupus	24
53/M	SSZ	6	F, M, ED,	L, K	31300/ 5634	516/436	7	Lupus or Vasculitis	Lost FU
46/M	HRZE	2	M	L, K	24000/NA	135/118	6	Sepsis, ATT induced hepatitis	1
27/F	SSZ	12	M, ED	L, K	38900/850	94/96	6	Sepsis	3
32/F	Leflunomide	4	M	L, P	10500/210	543/297	4	Drug induced transaminitis	4
38/F	SSZ/Leflunomide	20	M,	L, G	36400/ 7200	112/142	8	Sepsis	3



Abstract AB1156 – Figure 1

**Conclusions:** – Skin rash, arthritis, multi-organ failure of DRESS closely mimic rheumatologic disorders or sepsis (especially with rising TLC)

- As early diagnosis is imperative for successful outcome, low threshold of suspicion is necessary.

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#### AB1157 CLINICAL IMPLICATIONS OF ULTRASONOGRAPHY (US) IN MONITORING DISEASE ACTIVITY OF RELAPSING POLYCHONDRIITIS (RP) AND COMPARATIVE INVESTIGATION BY US BETWEEN AURICLE OF RP, REPEATED TRAUMA AND HEALTHY SUBJECT

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**Background:** Relapsing polychondritis (RP) is a rare systemic inflammatory disorder and might often be refractory. Therefore, the discovery of more convenient imaging modality than contrast-CT, MRI and FDG-PET/CT would be required on diagnosis and treatment.

**Objectives:** To assess the clinical implications of ultrasonography (US) in monitoring disease activity and diagnosis of relapsing polychondritis (RP).

**Methods:** Firstly, auricular chondritis of patients with RP (n=5) were assessed by US before and after treatments. Second, the relationship between US findings and other serum inflammatory markers were evaluated. Moreover, the comparisons of US findings between the auricle of patients with RP (n=5), repeated trauma (n=5) which is similar to auricle of RP, and healthy subjects (n=5) were also assessed.

**Results:** US finding before treatment showed low-echoic swollen auricular cartilage with increased power Doppler signals (PDS) in all cases of RP. US findings corresponded to biopsy findings. After treatment with prednisolone (PSL) combined with methotrexate, the swollen ear completely resolved. Then, US findings also showed dramatic reductions in swollen cartilage with the decrease in PDS. When serum inflammatory markers completely improved, but US finding remained in 1 of 5 cases, and this case showed flare due to PSL tapering. Finally, RP could be differentiated from the damage of repeated trauma with producing subperichondrial serous effusion.

**Conclusions:** US of auricular cartilage in RP possibly facilitates evaluation of auricular lesions and monitoring of disease activity, especially when we consider the treatment response and the timing of drug tapering.

**Disclosure of Interest:** None declared

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#### AB1158

#### MALIGNANCY IN PATIENTS WITH SARCOIDOSIS: A RETROSPECTIVE COHORT STUDY FROM TURKEY

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**Background:** The relationship between sarcoidosis and malignancy is not clear yet. There is debate with different speculations in the literature in this regard, that this association may be just a coincidence and/or common pathogenetic link.

**Objectives:** The goal of our study was to evaluate the incidence and characteristics of malignancies in patients with sarcoidosis follow-up in a single centre.

**Methods:** Our study is a retrospective analysis of patients diagnosed with sarcoidosis at the single Rheumatology centre from Turkey. Electronic patient records from the years 2010 to 2016 were screened, and 131 patients with the diagnosis of sarcoidosis were included in the study. Diagnosis of sarcoidosis was either a clinical diagnosis in patients with Löfgren's syndrome or confirmed by tissue biopsy in all other patients. The incidence of malignancies were evaluated in this cohort. Malignant diseases were diagnosed by histopathology. The clinical data of patients with sarcoidosis and malignant diseases were further analysed.

**Results:** A total of 6 patients with malignancy were identified in our cohort of 131 patients with sarcoidosis, representing an incidence of 4.6%. Among them, Hodgkin lymphoma (HL) were detected in three patients, followed by one patient with breast cancer, one patient with thyroid cancer and one patient with testicular cancer. All patients had chronic sarcoidosis with pulmonary involvement, and only 1 patient (with thyroid cancer) had acute sarcoidosis with Löfgren's syndrome. HL developed concomitantly with sarcoidosis in one patient while other two patients developed disease before and after sarcoidosis diagnosis. Two patients with solid tumours (breast Ca, testicular Ca) developed malignancy years before sarcoidosis diagnosis (1 year and 2 year respectively), while one patient developed thyroid cancer during sarcoidosis follow-up. All 6 sarcoidosis-malignancy patients were survived during six year follow-up.

**Conclusions:** We found low incidence of malignancy in patients with sarcoidosis in our small cohort. Malignancy may develop in patients with sarcoidosis. Its may occur before, after, or concurrent with the diagnosis of sarcoidosis. The sarcoidosis-malignancy relationship can only be a coincidence and/or can be explained by



a common pathogenesis. New prospective studies involving large patients series are needed in this regard.

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AB1159

#### VIRUS-NEGATIVE LYMPHOCYTIC MYOCARDITIS: CLINICAL AND DIAGNOSTIC FEATURES FROM A MONOCENTRIC ITALIAN COHORT

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**Background:** Virus-negative lymphocytic myocarditis (VNLM) is defined by endomyocardial biopsy (EMB) established histological, immunological and immune-histochemical criteria; it may occur as a distinct disease or in the context of systemic autoimmune or inflammatory disorders.

**Objectives:** To describe the demographic, clinical, histological and immune-histochemical features of VNLM from a monocentric Italian cohort.

**Methods:** 42 patients (mean age 45.57±14.9 years; male to female ratio 1:1) were diagnosed with EMB-proven VNLM at our Centre from January 2015 to December 2017. In all patients, comprehensive demographic, clinical and histological data were collected.

**Results:** The most common initial clinical feature was chest pain (40.5%), followed by palpitations (26.2%) and syncope (23.8%). Aborted sudden cardiac death (SCD) was the first manifestation in 3 cases, while arrhythmias were overall present in 47.6% of patients, being life-threatening in 10 of them. Interestingly, 4 patients had only few constitutional symptoms and 2 patients were completely asymptomatic. The distribution of traditional cardiovascular risk factor reflected that of the general population, apart for a more common familiarity for SCD (31.7%) and for autoimmunity (31.7%). Serum levels of troponin T and NT-proBNP were increased in 40.5% and 30.9%, respectively. Both echocardiography and standard ECG were unremarkable in half of the patients, while nearly all patients (92.5%) had at least one Lake-Louise criterion at cardiac magnetic resonance (CMR) evaluation. The most common CMR finding was delayed enhancement in 90% of cases, while T2-oedema was found in 21 patients (50%). Left ventricular ejection fraction was reduced in 50% of patients; a concomitant pericardial effusion was detected in 22.5% of cases. Abnormalities on 24h-ECG-Holter tape were overall detectable in 20 patients (47.6%), with ventricular ectopic beats and non-sustained ventricular tachycardia being the most common findings.

Despite positivity for ANA in 42.8% patients, only 4 patients could be diagnosed with a systemic autoimmune disease. Anti-heart antibodies (AHA) and anti-intercalated disks antibodies (AIDA) were positive in 21 patients (50%) and 12 (28.6%) patients, respectively.

On EMB, myocarditis was classified as active in 23 cases (54.8%) and as chronic in 18 (42.3%), while 7 patients (16.7%) had evidence of both features. CD3 +T-lymphocytes >7/mm<sup>2</sup> were detectable in 27 patients (64.3%), necrosis in 20 patients (47.6%), oedema in 28 patients (66.7%), while only 4 patients showed signs of vasculitis or thrombotic microangiopathy. At time of diagnosis, myocardial fibrosis was evident in 73.8% of EMBs and dilated cardiomyopathy in 6 patients (14.3%). All patients were treated with steroids and azathioprine as first line therapy, and 17 patients (40.5%) were initially referred for device implantation.

**Conclusions:** VNLM is an overlooked disease characterised by a broad spectrum of clinical features and peculiar immune-mediated hallmarks. The early recognition of myocarditis, allowing a prompt therapeutic intervention, should be a major goal for rheumatologists.

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AB1160

#### A SYNDROME OF RECURRENT IDIOPATHIC HYDROPS FETALIS, RESPONDING TO ANTI-PLATELETS/ANTI-COAGULANT PROPHYLAXIS. IS IT A NEW ENTITY OR A PART OF MATERNAL HYPERCOAGULATION STATE; THROMBOPHILIA OR ANTI-PHOSPHOLIPID SYNDROME (APS)?

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**Background:** Anti-phospholipid (aPL) syndrome (APS) is defined in the presence of anticardiolipin (aCL), anti-β<sub>2</sub> glycoprotein-I antibodies, or lupus anticoagulant (LAC) with hypercoagulability, including arterial/venous thrombosis episode (s), or pregnancy morbidity; early spontaneous abortions, stillbirth or prematurity with (pre)eclampsia. Beside these classification criteria the increased awareness for seronegative APS and non-criteria clinical manifestations, necessitate additional laboratory diagnostics for aPL's. Use of preventive treatment protocol; low-dose (100 mg/d) aspirin (ASA) and/or daily subcutaneous (SC) heparin, is highly effective and improves fetal vitality and pregnancy outcome. Beside APS, stillbirth and fetal loss may result from thrombophilia and Hydrops fetalis (HF). HF is described as fetal pathological fluid accumulation in serous cavities and soft tissues. It is accompanied with placental thickening and hydramnios. Most of the cases refer to non-immune (NIHF), not caused by red cell alloimmunization. Almost third of NIHF are idiopathic (iNIHF). The pathogenesis of tissue hypoxia with capillary leakage remains unclear. With advanced in-utero therapy mortality is still high (50%–95%).

**Objectives:** To describe the entity of recurrent idiopathic NIHF, resulting in habitual miscarriages. To document the use of APS prophylactic regimen for fetal loss, and its effect on iNIHF occurrence.

**Methods:** Data from medical files of women with previous iNIHF, who were treated in the rheumatology clinic, Hadassah Mount Scopus Hospital in Jerusalem, between years 2002–2017 were summarised (table 1).

**Results:** The present series illustrates the impact of the prophylactic regimen of APS in preventing obstetrical morbidities, including miscarriages and fetal death due to Hydrops fetalis (table 1). Thrombophilia and aPL profiles were normal. Five women who had multiple early abortions and 8 pregnancies with iNIHF, following treatment had a total of 12 successful pregnancies with uneventful delivery to healthy babies.

ANA:anti nuclear antibodies, IUFD:intra uterine fetal death, IVF:in vitro fertilisation, CLX:Clexan=Enoxaparin (SC 40 mg/d), HCQ:Hydroxy-Chloroquine (200 mgx 2/d), PRD:Prednisone (10–20 mg/d)

Abstract AB1160 – table 1. summary of cases

patient	Age (yrs)	Pregnancies before prophylaxis	Outcome (mother age, outcome, gestation age wks)	Treatment (Prophylaxis during pregnancy)	Pregnancies on prophylaxis (maternal age)	Outcome	Positive findings
1	38	10(x7 IVF)	x1(21, preterm, 30), x2(22, 23, iNIHF/IUFD, 31), x7 abortions,<10)	CLX, ASA, HCQ	x3 <sup>(25, 27, 29)</sup> Spontaneous (no IVF), on HCQ, PRD 5 mg/d	Uneventful	ANA+, aCL+, LAC+, Raynaud's, Livedo Reticularis
2	43	2	x2(20, 21 IUFD/iNIHF, 27,23)	ASA, PRD	x3 <sup>(23, 26, 29)</sup>	1-mild HF, live birth 34 wks. 2+3 uneventful	Migraine, low platelets
3	31	2	x1(22, abortion, 8), x1(23 IUFD/iNIHF, 24)	ASA, CLX	x2 <sup>(25, 27)</sup>	Uneventful	None
4	27	3	x1(20, IUFD/iNIHF, 25), x1(21, abortion,<10), x1(22 IUFD/iNIHF, 26)	ASA, CLX, PRD	x2 <sup>(23, 25)</sup>	Uneventful	Raynaud's, Alopecia
5	48	4	x1(25 normal, term), x2(26, 27, abortions,<10), x1(29, IUFD/iNIHF, 30)	CLX 60 mg/d	x2 <sup>(30, 33)</sup>	Uneventful	None

**Conclusions:** Idiopathic NIHF, is a very serious condition with high fetal mortality and limited effective therapy, so prevention is very crucial. APS prophylaxis regimen, based on anti-platelets and anti-coagulant therapy during pregnancy, may have promising effects.

**Disclosure of Interest:** None declared

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**AB1161** **FAMILIAL MEDITERRANEAN FEVER AS AN OUTCOME OF UNDIFFERENTIATED ARTHRITIS**

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**Background:** The term «undifferentiated arthritis» (UA) was proposed to emphasise the heterogeneity of unclassifiable arthritides and their potential into a definable form of arthritis. A patient with UA have an early stage of defined arthritis that will meet criteria in time, a forme fruste or partial form of a classifiable disease, an overlap of more than one disease entity, or an arthritis of unknown or in that may (or may not) become differentiated in the future. The heterogeneity associated with the term «UA» emphasises the need for continued follow-up and reassessment of the diagnosis and management of these patients.

**Objectives:** The aim of this study was revelation of MEFV gene mutations in patients with UA.

**Methods:** We have examined 80 patients (34 male, 46 female, mean age 36,4 ±3.4 years) with UA. The patients were observed every 6 months in follow-up period of 5 years. The anamnestic and treatment data were obtained. Joint disease activity scores and presence of extra-articular manifestations were determined. The CBC, urinalysis, serum concentrations of creatinine, bilirubin, transaminases, glucose, CRP were determined every 6 months, X-ray examination and ultrasonography of joints were performed once a year. Molecular-genetic analysis of 12 MEFV-mutations, common for Armenians, were carried out in Medical Genetic Centre of Armenia.

**Results:** From 80 investigated patients with UA 10 had repeated episodes of mono- and oligoarthritis of ankle and/or knee joints with local skin hyperemia and hyperthermia, without subsequent joint deformities, 45 – sacroiliitis (26 bilateral, 19 unilateral), accompanied by enthesopathy, 2 – joint syndrome, resembling rheumatoid arthritis. In 23 patients joint syndrome was accompanied by erythema rash, livedo reticularis, photosensitivity and alopecia. The latter group of patients was diagnosed as SLE-like syndrome. All patients didn't fulfil accepted classification criteria of any autoimmune or autoinflammatory disease. The 80% of investigated patients had no classic febrile attacks of abdominalgia and/or thoracalgia, specific for FMF. In remaining 20% of patients febrile attacks hadn't preceded joint syndrome, but appeared during 5 year follow-up period.

All investigated patients had MEFV gene mutations, which's compositions (homozygous or compound heterozygous) were enough to confirm Familial Mediterranean Fever (FMF). The most common mutations were: M694V–41.2%, V726A–18.8%, M680I–10%. The most common compositions were M694V/M694V, M694V/V726A, M694V/M680I.

**Conclusions:** As FMF is widely distributed in Mediterranean region, and it had changed its phenotype in last decades, as well as taking into account the increasing rate of migration worldwide, every single case of UA, which doesn't fulfil classification criteria of any disease, should be tested for presence of MEFV-mutations. The diagnosis of FMF changes the approach to follow-up, management, outcome and prognosis of UA.

**Disclosure of Interest:** None declared

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**AB1162** **DIAGNOSTIC UTILITY OF LYMPH NODE BIOPSY IN DIFFERENTIAL DIAGNOSIS OF IGG4-RELATED DISEASE, IDIOPATHIC MULTICENTRIC CASTLEMAN'S DISEASE AND PRIMARY DISSEMINATED MALT-LYMPHOMA**

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**Background:** Lymphadenopathy (LA) is a frequent and challenging syndrome in rheumatic patients. It requires comprehensive clinical and expert pathological evaluation. IgG4-related disease (IgG4-RD) combines a group of fibroinflammatory conditions characterised by formation of tumor-like lesions with unique morphological features and hyper-IgG4 secretion in different organs and tissues. LA is frequent in IgG4-RD and doesn't have a unique morphology. Idiopathic multicentric Castleman's disease (iMCD) is a rare lymphoproliferative disorder of a hyper-IL-6 spectrum with obligate lymph nodes (LN) affection and less frequent

extranodal lesions. Pathologic features of the LN in iMCD overlap with IgG4-LA and there can be IgG4 hypersecretion in iMCD patients as well. Primary disseminated MALT-lymphomas (DMALT) are also in the spectrum of differential diagnosis because of the involvement of salivary and lacrimal glands.

**Objectives:** To evaluate the diagnostic utility of LN biopsy in differential diagnosis of IgG4-RD, iMCD and DMALT.

**Methods:** Retrospective study. We reviewed medical records from 2009 to 2017 and identified 13 pts. who were examined in our clinic due to some rheumatological diagnosis suspicion and whose leading symptom at the onset of the disease was LA. All patients had prior multiple LN biopsy (25 LN biopsies in total) which was reviewed by an expert pathologist during our examination. 11 pts. had extranodal lesions and underwent extranodal biopsy.

**Results:** Eight pts. were men, 5 women with average age at the onset 34,7 years (15–71 years). The directional diagnoses established on the LN pathology were as following (in some cases a few diagnosis): iMCD (4 pts), non-Hodgkin lymphoma (3 pts), reactive LN (12 pts). 11 pts. had some extranodal lesions (3,9 per patient, from 1 to 8): orbit – 8, major salivary glands – 8, hepatosplenomegaly – 5, lungs – 5, thyroid – 5, kidneys – 3, sinusitis – 3, skin, cholangitis – 2 each, retroperitoneum, mediastinum, pancreas and soft tissues – 1 each. Due to orbital and major salivary glands involvement some patients had directional diagnosis of Sjogren's syndrome or IgG4-RD. In all 13 pts. the directional diagnosis was changed to some other based on the extranodal biopsy pathology results (in 11 pts) and/or clinical presentation (in 2 pts with isolated LA). LN pathology was not conclusive in all cases. In all cases LN pathology fell into I-IV type of LN morphological picture as reported by J. Ferry et al.<sup>1</sup> Clinical presentation in 13 pts see in table 1. The final diagnosis were: IgG4-RD in 7 pts, iMCD in 2 pts and DMALT in 4 pts.

**Abstract AB1162 – Table 1.** Clinical-laboratory features of patients

	IgG4-RD (n=7)	iMCD (n=2)	DMALT (n=4)
Median age at the onset, years	26	17	49
Constitutional symptoms, N (%)	1 (14)	2 (100)	1 (25)
Orbit involvement, N (%)	4 (57)	0 (0)	4 (100)
Major salivary glands involvement, N (%)	4 (57)	0 (0)	4 (57)
Atopic, N (%)	4 (57)	0 (0)	0 (0)
Extranodal lesions, N (%)	7 (100)	1 (50)	4 (100)
Blood eosinophilia, N (%)	4 (57)	0 (0)	0 (0)
Blood thrombocytosis, N (%)	0 (0)	2 (100)	0 (0)
Elevation of IL-6 > 2N, N (%)	0 (0)	2 (100)	1 (25)
Elevation of CRP > 2N, N (%)	0 (0)	2 (100)	0 (0)
Serum IgG4 > 200 mg/dl, N (%)	7 (100)	2 (100)	0 (0)
Autoantibodies (ANA, RF, anti-SSA/Ro), N (%)	3 (43)	0 (0)	1 (25)
Hypocomplementemia, N (%)	3 (43)	0 (0)	1 (25)
Serum monoclonal secretion, N (%)	1 (14)	0 (0)	3 (75)
B-cell clonality in the tissue, N (%)	0 (0)	0 (0)	4 (100)
Tissue IgG4+/IgG+ plasma cells > 40%, N (%)	7 (100)	0 (0)	0 (0)

**Conclusions:** It seems to be very challenging to set a reliable differential diagnosis based on the LN pathology thus extranodal biopsy is preferable. Orbital and major salivary glands involvement is a feature of IgG4-RD or DMALT, but not iMCD. Prominent constitutional symptoms with high laboratory inflammatory markers (CRP, IL-6) are characteristic of iMCD.

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**AB1163** **MY BEHCET'S DISEASE AND MY MENSTRUATION CYCLE: OBSERVATION FROM AN IRISH COHORT**

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**Background:** The menstrual cycle is regulated by the rise and fall of sex hormones in the body. Literature has demonstrated anti-inflammatory properties in both progesterone and oestrogen hormones.<sup>1</sup> There has been recent interest to determine the association between Behçet's Disease (BD), a poorly understood autoinflammatory disorder and menstruation.

**Objectives:** The objective of this study was to evaluate the effect of menstruation in triggering exacerbations of Behçet's disease in a Northern European cohort.

**Methods:** 18 female patients from our rheumatology department satisfying the International Study Group for Behçet's Disease (ISGBD) criteria were recruited. A questionnaire was conducted via telephone to determine whether their exacerbations of BD were correlated to their menstrual cycle.

**Results:** All 18 patients responded to the questionnaire, with the mean age of 38.8 years and mean age of menarche of 13 years. Four (22.22%) patients were in menopausal state. Half (nine) of the patients reported that their BD flare ups were correlated to their menstrual cycle. Exacerbations experienced include oral aphthosis (88.9%), arthralgia (55.6%), genital ulcerations (44.4%), lethargy (44.4%), skin lesions (11.1%) and headaches (11.1%). Six of the seven patients (86%) who were on contraception were on a progesterone containing contraception. Four out of nine (44%) who did not notice any exacerbations during menstruation stated that they were on progesterone containing contraceptives. It is noteworthy that 10 patients (55.56%) had previous pregnancies while three patients experienced an episode of miscarriage and 1 had a stillbirth.

**Conclusions:** Our results demonstrated that the disease activity in BD is related to the menstrual cycle, which is contributed by the female sex hormones. The study supports previous hypothesis that the abrupt decline in progesterone during onset of menstruation is associated to disease flare in BD.<sup>2</sup> Studies comprising larger cohorts should be conducted to further support and strengthen this evidence.

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#### AB1164 IMMUNOGLOBULIN USE IN GRANULOMATOUS MYOSITIS WITH BACKGROUND OF THYMOMA AND SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Contracting granulomatous myositis is rare in clinical practice.

**Objectives:** To report a case with systemic lupus erythematosus presented with contracting granulomatous myositis and previous history of thymoma which responded to intravenous immunoglobulin (IVIG).

**Methods:** A case report from a local hospital in asia

**Results:** A forty-two year old gentleman presented with polyarthralgia, raynaud's phenomenon, photosensitivity with elevated ANA and anti-dsDNA was diagnosed to have SLE in 2014 in rheumatology clinic. His lupus activity was stable on hydroxychloroquine (HCQ) and low dose steroid for the arthritis control. In May 2015, an anterior mediastinal mass was noted on CT thorax for symptoms of chronic cough and chest pain. Operation was performed in Aug 2015 with incomplete excision with invasion into lung, pericardium and nodal metastases. Pathology showed thymoma. Adjuvant radiotherapy 60 Gys in 30frs was given and completed in Dec 2015. He had stable lupus activity all along until Aug 2017. He was hospitalised with sudden onset of proximal muscle weakness which rendered patient unable to walk. Elevated CK level was up to 5354 IU/L. There was no evidence of concurrent infection. Myositis panel showed Strongly positive anti-PM/SCL, borderline positive Anti Mi2 alpha and PM Scl 100. Dysphagia was documented by speech therapist. Muscle biopsy of right quadriceps was performed by neurologist and showed granulomatous myositis. Electromyography (EMG) showed myopathic changes. Lupus myositis was diagnosed with dysphagia. Patient was started on IVIG (0.4 gm/kg/day) for 5 days and high dose steroid (prednisolone 30 mg daily orally) was initiated concurrently. CK showed good response and normalised with improvement in the lower limb power within one month. Patient was able to walk and discharged home. However he was re-admitted one month later for generalised tightening of 4 limbs and contractures over elbows and knee joints with intense pain and limited range of movement. CK level was normal in this admission. PET-CT showed a small (2.2 × 1.4 cm SUV Max5.5) right anterior mediastinum lesion near to surgical site. It was suspicious of local recurrence. Cardiothoracic surgeon was consulted and suggested not for further surgery since of high operative risk. In view of worsening of contractures and weakness over lower limbs, despite normalisation of CK level and quiescent lupus serology,

further courses of IVIG monthly were commenced. Steroid dosage was able to titrate down to prednisolone 9 mg daily orally gradually with improvement in 4 limbs power and halting of further contractures. No more dysphagia was documented afterwards. With the incomplete excision of thymoma, further discussion with oncologist and neurologist on future treatment plan ensued. Role of IVIG in controlling the underlying autoimmune phenomenon attributed by the underlying malignancy was unknown. IVIG was stopped after 6 courses and oncologist proceeded with palliative chemotherapy.

**Conclusions:** IVIG use in contracting granulomatous myositis in a lupus patient with underlying thymoma may be useful.

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#### AB1165 MONOCLONAL GAMMOPATHY IN RHEUMATIC DISEASES AND ITS ROLE IN PREDICTING MALIGNANT TRANSFORMATION

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**Background:** The monoclonal gammopathy (MG) constitutes a group of diseases characterised by the proliferation of a single clone of plasma cells or B-lymphocytes. The spectrum of conditions capable of producing MG mainly includes a premalignant state known as monoclonal gammopathy of undetermined significance (MGUS) and a group of malignant hematologic disorders. In previous studies, significantly increased risk of MG was seen in patients with a history of various rheumatic diseases. We analysed 41 hospitalised patients with underlying rheumatic diseases who were diagnosed with MG at our institute from 2010 to 2017, in order to identify clinical clues for early diagnosis, as well as the risk factors for MG and malignant hematologic neoplasias in patients with rheumatic diseases.

**Objectives:** To analyse the clinical spectrum, laboratory characteristics and outcomes of monoclonal gammopathy (MG) in patients with rheumatic diseases.

**Methods:** Screening for the presence of MG was performed in 872 inpatients with rheumatic diseases from January 2010 to July 2017. A total of 41 patients were enrolled. Their clinical and biological features in addition to outcomes were described. For each patient with primary Sjögren syndrome (pSS), 2 age- and sex-matched pSS patients without MG were selected as controls. Risk factors for the presence of MG and malignant haematological neoplasias were assessed.

**Results:** MG was observed in patients with various rheumatic diseases, with SS the most frequent type. Serum M protein was detected in 37 patients. M components were observed in urine in the other 4 patients. High ESR, albumin/globulin inversion, rheumatoid factor positivity, hypergammaglobulinemia, hypocomplementemia were common features, presented in more than half of the 41 patients. Patients with pSS, when complicated with MG, showed a higher rate of abnormal urine NAG (71.4% vs 15.8%,  $p=0.025$ ), higher levels of ESR [55.0 (53.5) mm/h vs 21.0 (31.8) mm/h,  $p=0.001$ ], ESSDAI [26.0 (25.0) vs 12.0 (9.0),  $p=0.006$ ] and ClinESSDAI scores [24.0 (25.0) vs 10.5 (10.0),  $p=0.011$ ]. Multivariate analysis revealed that the disease activity, assessed by either ESSDAI [adjusted OR 1.127 (95%CI 1.015–1.251),  $p=0.025$ ] or ClinESSDAI [adjusted OR 1.121 (95%CI 1.011–1.242),  $p=0.030$ ], was the only independent risk factor for the presence of MG. During the follow-up, 2 patients had transient serum M protein, 2 had isotype switch, 1 progressed to multiple myeloma (MM) and another 2 experienced renal injuries attributed by monoclonal or polyclonal plasma cell interstitial infiltration. Seven (17.1%) of the 41 MG patients presented haematological neoplasias, 4 with MM, 2 with smouldering multiple myeloma and 1 with B-cell lymphoma of mucosa-associated lymphoid tissue (MALT) type. The presence of light-chain MG was associated with the development of MM [OR 17.5 (95%CI 1.551–197.435),  $p=0.041$ ], but not with an increased risk of lymphoma or SMM.



**Conclusions:** MG was observed in patients with various rheumatic disorders, with SS being the most common type. The presence of MG might associated with higher disease activity. The development of haematological neoplasias including MM and lymphoma was seen in this setting. Therefore, we recommend the screening for MG and close monitoring for potential malignant transformation in patients with rheumatic diseases as needed.

**Disclosure of Interest:** None declared

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**AB1166 THE ASSOCIATION OF THE EARLY ONSET OF REMITTING SERONEGATIVE SYMMETRICAL SYNOVITIS WITH PITTING OEDEMA (RS3PE) SYNDROME WITH DIPEPTIDYL PEPTIDASE-4 (DPP4) INHIBITOR**

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**Background:** Remitting seronegative symmetrical synovitis with pitting oedema (RS3PE) syndrome is a rare inflammatory arthritis, characterised by absence of rheumatoid factor, symmetrical distal synovitis, pitting oedema of the hands and feet.

In recent years the use of dipeptidyl peptidase-4 (DPP4) inhibitor has increased and some reports have described the association of RS3PE syndrome with DPP4 inhibitor.

**Objectives:** : We have tried to investigate the association of RS3PE syndrome with DPP4 inhibitor in our hospital.

**Methods:** : In Japan DPP4 inhibitor was released in December 2009, so we retrospectively analysed background, treatment and clinical course of 25 patients with RS3PE syndrome diagnosed between <sup>December 2009</sup> and December 2016 in our hospital. We divided them in two groups according to DPP4 inhibitor prescription and compared two groups.

**Results:** : Our cases included 18 males and 7 females, and the mean age of RS3PE syndrome onset was 76 years old. The mean follow-up period was 32.5 months. Six patients had diabetes mellitus and DPP4 inhibitor was prescribed in five of six patients (83.3%). (sitagliptin 3 cases, teneligliptin 1 case, alogliptin 1 case). The duration of RS3PE syndrome onset after DPP4 inhibitor prescription was mean 22.9 months, and two cases developed within a half year, two cases after two years.

Compared with non DPP4 inhibitor group, the mean age of RS3PE syndrome onset was significantly low (70 vs 78.5,  $p=0.023$ ), and HbA1c (NGSP) was high (7.3% vs 6.02%,  $p=0.00022$ ) in DPP4 inhibitor group.

The occurrence of flare was four cases in non DPP4 inhibitor group and zero in DPP4 inhibitor group, but was not statistically different ( $p=0.275$ ). Other clinical features were not significantly different.

**Abstract AB1166 – Table 1.** Clinical characteristics of the patients

Characteristics	DPP-4 inhibitor (N=5)	non DPP-4 inhibitor (N=20)	P value
Mean age – yr	70 (±7.91)	78.5 (±6.61)	0.023
Male sex – no.(%)	5 (100%)	13 (65%)	0.119
CRP, mg/dl	7.97 (±5.08)	7.45 (±5.86)	0.86
HbA1c (NGSP), %	7.3 (±0.68)	6.02 (±0.57)	0.00022
<b>Medications</b>			
<b>MTX</b>			
Patients, no.(%)	2 (40%)	9 (45%)	
Dose, mg/week	8 (±0)	7.33 (±1)	0.081
<b>Oral prednisolone</b>			
Patients, no.(%)	5 (100%)	18 (90%)	
Dose, mg/day	12 (±4.47)	10.8 (±4.62)	0.625
Malignancies – no.(%)	0 (0%)	1 (5%)	0.61
Flare – no.(%)	0 (0%)	4 (20%)	0.275

**Conclusions:** : DPP4 inhibitor group was significantly younger than non DPP4 inhibitor group, and the possibility that DPP4 inhibitor contributed to the early onset of RS3PE syndrome was suggested.

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**Diagnostics and imaging procedures**

**AB1167 METHOD COMPARISON OF AESKUSLIDES ANCA FOR THE DIAGNOSIS OF ANCA-ASSOCIATED VASCULITIS**

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**Background:** AESKUSLIDES ANCA is an indirect immunofluorescence assay used to detect anti-neutrophil cytoplasmic autoantibodies (ANCA) in human serum. This *in vitro* diagnostic assay is used as an aid for the diagnosis of ANCA-associated vasculitis (AAV) in conjunction with other clinical and laboratory findings.

**Methods:** A method comparison of ethanol and formalin fixed granulocytes was carried out between AESKUSLIDES ANCA (AESKU. Diagnostics) and the NOVA Lite ANCA of INOVA. 507 clinical serum samples (comprising 135 serum samples from patients with AAV and 375 samples from patients with other diseases) were analysed by standard IFA protocols. Results were obtained by manual processing and reading.

**Results:** In this cohort, AESKUSLIDES ANCA Ethanol slides show higher sensitivities (48.5% vs. 36.4%) and specificities (69.3% vs. 55.2%) compared to INOVA. AESKUSLIDES ANCA Formalin slides show higher sensitivities (50.0% vs. 37.9%) and similar specificities (90.7% vs 91.5%) compared to INOVA.

**Conclusions:** AESKUSLIDES ANCA Ethanol showed higher diagnostic sensitivity (48.5%) and specificity (69.3%) compared to the predicate assay NOVA Lite provided by INOVA (36.4%, 55.2%). This is due to the fact, that AESKU assay detects more positives in the AAV cohort, and less positives in the other disease groups. AESKUSLIDES ANCA Formalin showed a diagnostic sensitivity (50.0%) compared to the predicate assay NOVA Lite provided by INOVA (37.9%). However, the diagnostic sensitivity was comparable between the two (90.7% vs 91.5%).

**Disclosure of Interest:** None declared

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**AB1168 IS MY CLINICAL EXAMINATION ADEQUATE TO EVALUATE DISEASE ACTIVITY IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS (JIA)? A COMPARATIVE ASSESSMENT OF CLINICAL AND ULTRASOUND (US) EXAMINATION OF 40 KNEES AND ANKLES IN 10 CHILDREN WITH JIA**

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**Background:** JIA is the commonest rheumatologic disease of childhood with a quoted prevalence of 1:1000. Assessment of children with JIA includes: Clinical, laboratory and more recently US evaluation of joints. Rapid attainment of inactive disease is critical for a good long term outcome. There is a debate in the rheumatology community about added advantage of US examination over clinical assessment of joints. This study was done to compare clinical versus US evaluation of knees and ankles in children with JIA.

**Objectives:** 1. To clinically examine and scan knees and ankles of 10 children with JIA

2. To determine sensitivity and specificity of clinical examination of knees and ankles vis a vis US scan findings

3. To compare results of knee and ankle examination both clinical and US

**Methods:** 1. 10 consecutive children with JIA were evaluated for active arthritis of knees and ankles and documented on a pre designed proforma.

2. Children were then examined with US on same day by same observer and joint effusion and or synovitis was captured using an E9/S7 GE machine with a linear transducer 6–15 MHz.

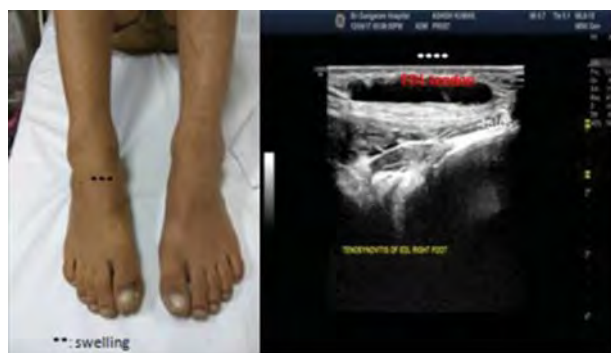
**Results:** 10 children aged 6–16 years, (6F and 4M) who attended the out-patient paediatric rheumatology clinic at our hospital with JIA were clinically evaluated and US examination performed on same day by same examiner with prior consent. Using the standard ESSR protocols, US knee and ankle joints were examined in longitudinal view and if any effusion or synovitis detected was confirmed on transverse view. The presence of grey scale synovial proliferation or anechoic effusion was taken as a positive US finding.

Knee-Sensitivity of clinical examination-100%, specificity-91.7%.

Ankles-Clinically 8 had swollen ankle, On US only 5 children had swollen ankle (tibio talar TT) joint. 3 who had a swollen ankle clinically had no synovial hypertrophy or effusion in the TT joint but had tenosynovitis(TS) of adjacent tendons: 1 each has a TS of the Extensor Digitorum Longus, Tibialis Anterior, Tibialis Posterior. Sensitivity-60% and specificity-66.7%.

**Abstract AB1168 – Table 1.** Clinical & US examination details on knees & ankles of 10 children (40 joints)

Patients	Diagnosis	Rt Knee Clinical	Rt Knee US	Lt Knee Clinical	Lt Knee US	Rt Ankle Clinical	Rt Ankle US	Lt Ankle Clinical	Lt Ankle US
Pt 1	SJIA	+	+	+	+	-	+	+	+
Pt 2	SJIA	-	-	-	-	+	+	-	-
Pt 3	ERA	-	-	-	-	-	-	+	-
Pt 4	ERA	-	-	-	-	-	-	+	-
Pt 5	PJIA	-	-	-	-	-	+	-	-
Pt 6	PJIA	+	+	+	+	-	-	-	-
Pt 7	ERA	+	+	-	-	+	-	-	-
Pt 8	ERA	-	-	-	-	+	-	-	-
Pt 9	PJIA	+	+	+	+	-	-	+	+
Pt 10	PJIA	+	+	+	-	+	-	-	-

**Abstract AB1168 – Figure 1**

**Conclusions:** With gold standard as US for detection of synovitis, sensitivity of clinical examination-100% for knee, specificity-91.7%. For clinical examination of ankles, sensitivity-60% and specificity-66.7% suggesting possibility of mistaking an adjacent tendon sheath swelling for a TT joint disease. This has important implications for systemic therapies and intervention. The US is a valuable addition to clinical examination of the joints. Clinical examination alone in this pilot study of 10 children with JIA is inadequate to assess disease of the ankles. Evidence shows US to be superior to the clinical examination alone, but the lack of validated US findings, scoring systems and treatment algorithms exposes the need for further research.

**Disclosure of Interest:** None declared

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#### AB1169 CAN ULTRASOUND-DETECTED SYNOVITIS PREDICT RADIONUCLIDE SYNOVECTOMY EFFICACY IN CHRONIC INFLAMMATORY RHEUMATISM?

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**Background:** The better management of inflammatory joint diseases, including biological treatments, has not eliminated in the clinical practice the persistence of chronic inflammatory monoarthritis despite local glucocorticosteroids (GC) injection and optimal systemic treatment. No therapeutic consensus was proposed in this clinical situation. In addition, radionuclide synovectomy (RS) was proposed with no clear benefit-risk effect. However, it has been shown that ultrasound-detected residual synovitis is frequent and predictable to relapse and structural progression in rheumatoid arthritis patients.

**Objectives:** We explored ultrasound-detected synovitis predictive value of response to RS in chronic inflammatory monoarthritis.

**Methods:** A monocentric prospective study was performed including unclassified monoarthritis, rheumatoid arthritis, spondyloarthritis, and lupus between January 2012 and December 2017. All patients already received GC intra-articular injections (GCI) and were treated in particular by cs or bDMARDs. On the day of the RS performed by a radiologist under radioscopy control, all patients had an articular power Doppler (PD;0-3) with greyscale (GS;0-3) ultrasonography with a MyLab 60 – EASAPOTE, by 2 experimented sonographers.

Primary endpoint (EP) was subjective overall improvement  $\geq 50\%$  without of any GCI and/or surgical management at 6 months (M).

Chi-square test was used to check the difference between groups.

**Results:** Data from 23 patients, 17 women and 6 men, with mean age 54 $\pm$ 14 years were analysed. Eleven RA (45.5% RF +or ACPA+), 3 pSpA, 2 axSpA HLA B27+, 1 Lupus, and 6 unclassified monoarthritis (FR and ACPA-). Histological analysis of the synovium in 7 patients concluded to chronic nonspecific synovitis. Twenty eight joints were treated. Of them, 25 were coted US GS  $\geq 2$  and/or DP  $\geq 2$ . None had US GS=0 and DP=0. Effusion on US exam was reported in 24 joints.

On X-ray, 46.4% of patients had joint space narrowing and/or erosion. ESR or CRP increased in 43.5%. Forty five previous GCI were declared (Cortivazol or triamcinolone hexacetonide), with a median at 2.<sup>1-6</sup>

Patients were treated with methotrexate, n=16 (69.6%), hydroxychloroquine, n=1, bDMARDs, n=11 (48%), oral GC, n=8 (35%) and non-steroidal anti-inflammatory drug, n=6 (26%).

At M6 and M12, 64.6% of patients reached the EP. One patient reached the EP only at M12 and another one only at M6. No significant differences were observed between groups in terms of PDUS (DP  $\geq 2$  vs DP  $\leq 1$ ), unclassified monoarthritis, and joint space narrowing and/or erosion.

Only one patient had pain exacerbation 24 hour after RS followed by a quick recovery.

**Conclusions:** In chronic inflammatory monoarthritis, PDUS was not predictive of clinical outcome after RS. However, this intra-articular procedure appeared effective in either unclassified or classified monoarthritis or in presence of radiographic joint lesions.

**Disclosure of Interest:** None declared

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#### AB1170 FIRST RESULTS OF THE RHEUMATOID ARTHRITIS HANDSCAN REGISTRY LEEUWARDEN

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**Background:** The handscan is a new technologic device which uses diffuse optical transmission in combination with blood flow modulation. It is a non-invasive measurement of joint inflammation potentially more sensitive than the clinical evaluation of the joints by a rheumatologist.<sup>1</sup> However, more clinical data is necessary before this new device can be implemented in the daily clinical practice.

**Objectives:** This study investigates the additional value of the handscan in decision making in the daily practice for patients with rheumatoid arthritis.

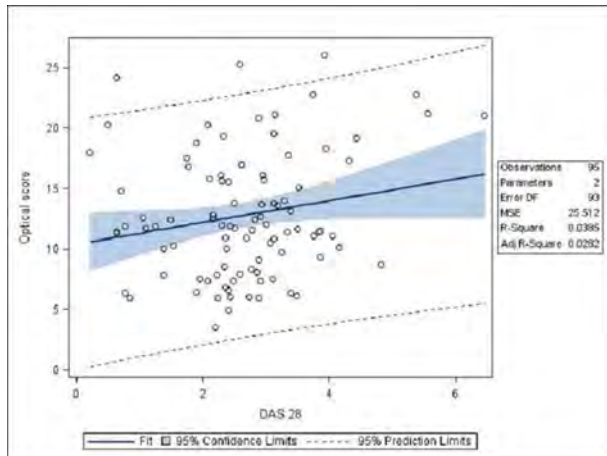
**Methods:** At our outpatient clinic we started a registry for rheumatoid arthritis patients with a disease duration of at least two years. During this period, a handscan will be made for all patients before every regular visit. Both the patient and the treating rheumatologist will be blinded to the handscan outcome. Primary outcome is the association between DAS28 score and the total optical score (TOS) of the handscan per visit.

**Results:** The study started in December 2017, until now 100 patients are included. The mean age was 61.1 years, the mean disease duration at time of inclusion 11.2 years, 67% were rheumatoid factor positive, 51% were anti-CCP positive. In figure 1 we show the association between DAS28 and the TOS in a linear model.

Currently there is no validated cut off point for the TOS (negative or positive score for inflammation). In our group of 100 patients the median TOS was 10, the most discriminating TOS was found to be 17 using chi-square test as depicted in table 1.

**Abstract AB1170 – Table 1.** Crosstab for total optical score of the handscan versus DAS28

DAS28	TOS<17	TOS≥17	Total	P-value
Mean	2.54	3.07	2.56	<b>0.068</b>
Std	0.90	1.72	1.12	
Median	2.55	3.13	2.61	
N	76	19	95	
	(4missings)	(1missing)	(5missings)	

**Abstract AB1170 – Figure 1**

**Conclusions:** In this preliminary evaluation of the first 100 patients, we observed a limited positive correlation between the total optical score of the handscan and the DAS28. The TOS above 17 associates with moderate to severe disease activity. The definite clinical value of the handscan needs to be determined with longitudinal measurements and its predictive value versus the DAS28. The ongoing current registry aims to answer these questions.

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**AB1171** **ULTRASOUND ASSESSMENT OF THE KNEE IN ELDERLY JAPANESE POPULATION**

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**Background:** Osteoarthritis (OA) is known as degenerative arthritis. Knee OA is a common disease among aged population and one of the leading causes of disability. Many modalities are used to evaluate bony abnormalities and joint space narrowing for knee OA.

Ultrasound is one of the imaging modalities for evaluating knee joint structures such as cartilage, meniscus, osteophyte and synovium. There are few large-scale

studies focused on ultrasound findings of the knee of the elderly in general population.

**Objectives:** The aim of our study is to evaluate relationship between clinical and ultrasound findings of the elder population.

**Methods:** Two hundred and twenty two participants were recruited from Nagahama residents aged 60 years or older. We evaluated the both knees of participants with ultrasound with a 5MHz transducer. Ultrasound scans were performed and assessed by a standardised protocol of the Outcome Measures in Rheumatoid Arthritis Clinical Trial Guidelines. The symptoms were clinically assessed by using Knee Society Score 2011 (KSS). We statistically examined whether the KSS (symptom) correlated with other clinical parameters and each ultrasonographical findings.

**Results:** Participants were 65 men and 137 women with a mean age of 67±5 years old. The mean body mass index (BMI) was 21.8±2.76 kg/m<sup>2</sup>. The symptom subscale of KSS were significantly associated with age, BMI, knee maximum extension and flexion angle, suprapatellar effusion, medial meniscus protorusion, medial recess synovial hypertrophy, and femoral and tibial medial osteophytes. Multiple regression analysis showed that medial osteophytes was most closely related to the symptom subscale of KSS among the ultrasound findings and demographic data evaluated.

**Conclusions:** The present study showed a strong association between the symptoms of the knee and the medial osteophytes in Japanese elder population.

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**Disclosure of Interest:** None declared

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**AB1172** **DOES ULTRASOUND-SCORED SYNOVITIS DEPEND ON THE PHARMACOKINETICS OF INTRAVENOUS INFLIXIMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS?**

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**Background:** Musculoskeletal ultrasound (US) was developed more than four decades ago and gradually made its way to daily rheumatological practice. This dynamic, non-irradiating and relatively inexpensive technique allows detection of synovitis/tenosynovitis as well as quantification of joint inflammation. However, several external factors, such as, joint position, machine settings, sonographer expertise and certain medications can influence the results of the US examination.

**Objectives:** The aim of this study was to investigate whether the pharmacokinetics of intravenous (*i.v.*) infliximab (IFX) influences the grade of US detected synovitis, measured by gray-scale (GS) and colour Doppler (CD) in rheumatoid arthritis (RA) patients.

**Methods:** Inclusion criteria were RA patients with at least one swollen joint, being treated with *i.v.* IFX, who had neither, changes in DMARD therapy nor local corticosteroid injections in the previous 3 months. Patients underwent clinical, laboratory and US assessment at three time points: at trough, peak plasma drug concentration and at mid-cycle. US assessments were performed blindly to the clinical and laboratory data. Twenty-four joints were assessed for the presence and grade (0–3) of GS synovitis and synovial CD signal: elbows, wrists, 2nd-5th metacarpophalangeal (MCP) joints, knees, ankles, 2nd-5th metatarsophalangeal (MTP) joints. A global OMERACT-EULAR synovitis score (GLOESS) as well as the sum of GS and CD scores were calculated for the 24-joint set, for the 12-joint set (Naredo score) and for wrists-MCP-ankles-MTP joints. Several disease activity scores (DAS) [28-joint DAS (DAS28-CRP), Simplified Disease Activity Index (SDAI)] and health assessment questionnaire (HAQ) were assessed in all patients. Trough plasma IFX concentrations were available in 20 patients.

**Results:** Twenty-two RA patients were prospectively recruited from the biologic therapy unit of our hospital. Two thirds of patients were female and mean age was 61 years. The majority of them had long-standing seropositive RA and over 90%



had radiographic damage. The median of IFX treatment duration was 9 years. There were no significant differences between the GS, CD and GLOESS scores at IFX peak time and trough time. US-joint count, GS, CD and GLOESS scores did not significantly differ between peak time and trough time. Patients with long-lasting RA treated with IFX had relatively stable US-detected synovitis and slightly lower clinical scores at 4 weeks after IFX administration as compared to baseline. The DAS28CRP, 28 and 44 swollen joint counts did not correlate with trough serum IFX concentrations. US scores (GS and GLOESS) significantly correlate with trough serum IFX concentrations (Spearman correlation coefficient,  $r=-0.55$ ,  $p<0.01$ ,  $n=20$ ). Patients with low trough IFX levels, especially  $\leq 1 \mu\text{g/ml}$ , had higher US joint count as well as US scores ( $p<0.01$ ).

#### REFERENCE:

- [1] US-scored synovitis is not significantly influenced by pharmacokinetics of IFX in RA patients. US examination can be conducted independently of time of IFX administration i.e. before or after IFX administration in clinical trials. Although there was no correlation with clinical scores, low trough IFX concentration correlated with the degree of US-detected synovitis.

**Disclosure of Interest:** None declared

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#### AB1173 CORRELATION BETWEEN TRABECULAR BONE SCORE (TBS) AND NAILFOLD VIDEOCAPILLAROSCOPY IN SYSTEMIC SCLEROSIS PATIENTS

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**Background:** Systemic sclerosis (SSc) is associated with an increased risk of altered bone and fractures as a result of multiple factors, including treatment-related side effects, low vitamin D serum concentrations and reduced physical activity.<sup>1</sup> Trabecular Bone Score (TBS) is an index extracted from dual-energy X-ray absorptiometry (DXA) analysis, that provides an indirect measurement of axial bone microarchitecture and bone quality.<sup>2</sup>

**Objectives:** The aim of this study was to evaluate possible correlation between bone quality, by TBS, and different levels of microvascular damage, as evaluated by nailfold videocapillaroscopy (NVC) patterns<sup>3</sup> in SSc patients and to compare the results regarding bone quality with RA patients and healthy subjects (CNT).

**Methods:** Eighty-eight SSc patients, 98 rheumatoid arthritis (RA) patients and 60 CNT were studied. Bone Mineral Density (BMD,  $\text{g/cm}^2$ ) of the lumbar spine (L1-L4) was analysed by dual-energy X-ray absorptiometry (DXA) scan. Lumbar spine bone quality was derived from each spine DXA examination using the TBS analysis. NVC patterns were analysed as previous reported.<sup>3</sup> All patients were subjected to 25 hydroxyvitamin D (25(OH)D  $\text{ng/ml}$ ) serum dosage.

**Results:** TBS values were found statistically higher in SSc with a "Early" NVC pattern, compared to the "Active" or "Late" pattern ( $1.182\pm 0.1$ ,  $1.101\pm 0.8$ ,  $1.074\pm 0.1$  respectively,  $p<0.001$ ). No statistical significant difference was observed in the three groups about DXA values ( $p=0.13$ , for all areas). A total of 56/84 SSc patients (66%) as well as in 78/98 RA patients (80%) showed bone loss at DXA and BMD was found significantly lower than in the CNT ( $p<0.001$ ). Similarly, lumbar spine TBS was found significantly lower in SSc and RA patients than in CNT ( $p<0.001$ ). There was no statistically significant difference in the mean lumbar spine TBS between SSc and RA patients ( $p=0.238$ ). Serum levels of 25 (OH) D were statistically significantly higher in patients with "Early" SSc pattern than in those both "Active" and "Late" pattern ( $19.1\pm 7.5$ ,  $15.1\pm 5.3$ ,  $12.1\pm 7.1$  respectively,  $p=0.002$ ).

**Conclusions:** The bone quality seems lower in SSc patients with more altered microvasculature ("Late" NVC pattern). The data obtained showed also a significantly lower bone quality (lower TBS and BMD) in SSc and RA patients compared to CNT. The association between bone damage and the "Late" advanced NVC

pattern of microvascular damage, may suggest that tissue hypoxia/ischemia related to the diffuse microangiopathy might be a further promoting factor for osteoclastogenesis and bone loss. Our results support the development of a combined approach using both TBS and BMD for the assessment of bone microarchitecture/quality in SSc patients during their disease progression.

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**Disclosure of Interest:** None declared

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#### AB1174 THE INFLAMMATORY CHANGES AT JOINTS AND ENTHESIS IN A COHORT OF PATIENTS AFFECTED BY OCHRONOSIS: AN ULTRASONOGRAPHIC STUDY

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**Background:** The pathogenesis of Ochronosis, the musculoskeletal manifestation of alcaptonuria (AKU) is still unclear. The joint damage usually described is similar to osteoarthritis, but in some cases the spinal involvement could resemble spondyloarthritis (SpA). These findings suggest that inflammatory changes could be prevalent in some cases while degenerative aspects could be dominant in others.

**Objectives:** To evaluate the prevalence of inflammatory changes in peripheral joints and entheses of a cohort of patients affected by AKU.

**Methods:** Consecutive patients with definite diagnosis of AKU referred to our clinic from 2014 to 2017 were enrolled. All patients underwent an ultrasound (US) exam of the metacarpo-phalangeal joints (MCP), proximal interphalangeal joints (PIP), radiocarpal/mid carpal joints, elbow, gleno-humeral, hip, knee, ankle and metatarso-phalangeal (MTP) joints bilaterally; flexor and extensor tendons of fingers and wrists and the ankle tendons were also examined. Further, the entheses of the rotator cuff of the shoulder, triceps, quadriceps, patellar and Achilles tendons were assessed. Joints and tendons with a synovial sheath were assessed for effusion, synovial hypertrophy and power Doppler (PD) signal while entheses were evaluated for the presence of PD signal, enthesophytes and calcifications. All the US lesions were scored using a dichotomous scale (presence/absence). All US exams were performed by an expert sonographer blind to clinical history, using an Esaote MyLab70 scanner equipped with high resolution linear probes.

**Results:** We enrolled 19 patients (11 women) with a mean age of 53 yo (SD  $\pm 14.69$ ). Only 2 patients didn't show inflammation at any joint or tendon. The most involved joint was the knee (11/19), while regarding entheses, the Achilles tendon (4/19) and the distal patellar tendon insertion were the most frequently involved (6/19). The mean number of joints with effusion or synovial hypertrophy was respectively equal to 2,47 (median 2, range 1–8) and 1,84 (median 2, range 1–7), while 0,21 joints (median 0, range 0–2) presented also PD. The mean of the exudative tenosynovitis was 0,47 (median 0, range 0–3), while for proliferative tenosynovitis was 0,42 (median 0, range 0–2). The PD signal in tendons with sheaths was rare (mean 0,16, median 0, range 0–2). Finally, the mean number of entheses with PD was 0,95 (median 0, range 0–7) while the mean value was 0,37 (median 0, range 0–3) for enthesophytes and 2,63 (median 1, range 0–9) for calcifications.

**Conclusions:** The pathological processes that lead to the typical joint damage in ochronosis are not yet completely clarified. The results of this study showed that articular inflammation is common in these patients, sometimes associated with entheses involvement. The role of inflammation should be further addressed as could be a new therapeutic target for this disease.

**Disclosure of Interest:** None declared

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**AB1175 DEVELOPMENT AND PRELIMINARY VALIDATION OF AN OMERACT MRI ENTHESITIS SCORING SYSTEM FOR THE ANKLE IN SPONDYLOARTRITIS**

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**Background:** Enthesitis is regarded the primary lesion in spondyloarthritis (SpA) and MRI allows sensitive visualisation of enthesal inflammation/damage, but no validated, internationally accepted scoring system exists.

**Objectives:** To develop and perform preliminary validation of a novel OMERACT MRI scoring system for assessing ankle enthesitis in SpA patients, and to improve this through iterative multi-reader scoring exercises and calibration sessions.

**Methods:** A systematic literature review of MRI studies on enthesitis in SpA identified key inflammatory and structural pathologies. Definitions were agreed by consensus within the OMERACT MRI in arthritis working group. Then, in a first internet-based multireader exercise the Achilles tendon and plantar fascia entheses in 10 ankle MRIs (sagittal T1W, sagittal and Axial T2W fat suppressed) were scored by 15 readers (3 radiologists and 12 rheumatologists), with varying expertise in ankle MRI, for tendon/fascia thickness/signal change, tendon/peritendon signal alteration, retrocalcaneal bursitis, bone spur, erosion and bone marrow oedema, using semi-quantitative scores (0–3: no/mild/moderate/severe pathology). After a subsequent calibration session leading to minor modifications of assessed parameters, 16 ankle MRIs (specifications as above), were scored by 15 readers in exercise 2 with a modified score sheet. Rules were agreed for scoring pathologies. In both exercises, scores for each reader for individual variables were compared and discussed, and mean scores for each variable were determined using descriptive statistics, as were sum scores. Inter-reader agreement was calculated using two-way consistency single measures intra-class correlation coefficient (ICC 3,1) for inflammatory and structural lesions.

**Results:** Exercise 1: Mean pairwise inter-reader ICC for combined score of inflammatory and structural variables was 0.65 (range 0.10–0.94), with 75% of values being good/very good ( $\geq 0.50$ ). Discussion of results led to minor modifications of parameters to be assessed.

Exercise 2: Inter-reader agreement (ICC) for all inflammatory variables combined ranged from 0.26–0.93 among reader pairs (mean 0.64; median 0.66; IQR 0.46–0.79). For structural variables combined ICC ranged from 0.05–0.91 among reader pairs (mean 0.45; median 0.45; IQR 0.2–0.6).

**Conclusions:** Initial steps in developing an OMERACT MRI heel enthesitis scoring system have demonstrated overall moderate reliability of the proposed variables. Further modification, refinement, calibration and validation (ongoing) are needed before this system is ready for use in SpA clinical trials.

**Disclosure of Interest:** None declared

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**AB1176 ULTRASOUND EVALUATION OF ADHESIVE CAPSULITIS OF THE SHOULDER. DESCRIPTION OF A NEW AND SIMPLE DIAGNOSTIC SIGN**

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**Background:** Adhesive capsulitis of the shoulder (ACS) is a common disease that is characterised by a global and progressive loss of mobility of the glenohumeral joint. It is the result of a capsular inflammation, thickening, and fibrosis with subsequent retraction of the joint capsule. Although it is a frequently self-limiting process, it may persist for years and be resolved with a permanent limitation of

glenohumeral mobility. Its diagnosis is based on clinical presentation because the glenohumeral capsule is not visible in simple radiology and the MRI does not offer specific diagnostic findings for ACS.

**Objectives:** To evaluate the specific ultrasound signs to diagnose ACS in patients with clinical suspicion of ACS.

**Methods:** Prospective, non-interventional observational study in consecutive patients with clinical suspicion of ACS referred for an ultrasound evaluation. All patients signed an informed consent before the study. Adult patients with a painful shoulder less than 2 years of evolution with clinical suspicion of ACS were included. We excluded patients with surgery or severe articular trauma in the symptomatic shoulder and patients with ultrasound findings that could explain the painful symptoms of the shoulder due to other causes such as rotator cuff tendinopathy, synovitis or glenohumeral osteoarthritis.

The ultrasound examination was systematically performed by an expert sonographer, using an Esaote MayLab 70 with a linear probe. In the ultrasound examination, the measurement of the joint capsule was performed in the axillary recess in the longitudinal plane (maximum passive abduction of the shoulder). The statistical analysis was carried out comparing the capsule means with the Mann-Whitney test (the variable did not follow a normal distribution verified with the Kolmogorov-Smirnov test).

**Results:** A total of 35 patients were included, with a mean age of 58.27 years, 46–77 17 men and 18 women. Nine patients had both shoulders affected, so a total of 70 shoulders (44 affected shoulders and 26 control shoulders) were studied. The mean time of evolution of the ACS clinic was 5.6 months.<sup>1–18</sup> The 28.57% of the patients were diabetic and 14% had a history of severe cardiovascular disease before the onset of symptoms. The 44% of bilateral ACS cases were diabetic. The totality of the affected shoulders presented in the clinical exploration limitation of the degrees of mobility of the glenohumeral joint; on the other hand, all control shoulders had a preserved mobility. Regarding the sonographic findings, the mean axillary capsular measurement of the affected shoulders was 4,414 mm (SD 0.177) compared to a mean measurement of 2,203 mm (SD 0.165) in the controls with a statistically significant difference between both groups ( $p < 0.001$ ).

**Conclusions:** The glenohumeral capsule is easily visible in the axillary approach by ultrasound and allows thickness measurement, being a feasible test for the diagnosis of ACS.

**Disclosure of Interest:** None declared

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**AB1177 A COHORT OF PATIENTS WITH ANTISYNTHEASE SYNDROME EVALUATED IN A MULTIDISCIPLINARY CONSULTATION**

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**Background:** Antisynthetase syndrome (AS) is an uncommon connective tissue disease characterised by the presence of antibodies to anti-aminoacyl t-RNA synthetase (anti-ARS) along with features of interstitial lung disease (ILD), myositis, arthritis and Mechanic's hands.

**Objectives:** To analyse the most common demographic, clinical, radiological, spirometry and capillaroscopic findings in a cohort of patients with AS. As a secondary objective, the association between capillaroscopic findings and diffusion lung capacity for carbon monoxide (DLCO) and the radiologic pattern in the high-resolution computed tomography of the chest (HRCT) was evaluated.

**Methods:** A ten-year (2007–2017) retrospective analysis of patients diagnosed with AS followed in a multidisciplinary consultation with a pulmonologist and a rheumatologist. The nailfolds from 2nd to 5th fingers in both hands were examined in all subjects by using videocapillaroscopy (Mediscope-Optilia).

**Results:** Twenty patients were included, 15 (75%) females and 50% (10/20) non-smokers. Mean age at the clinical debut was 47,5±16 years. Throughout their evolution, 90% of patients (18/20) presented Interstitial Lung Disease (ILD); 70% (14/20), arthritis and 75% (15/20), myositis. Furthermore, 40% (8/20) associated fever, 45% (9/20), Raynaud's Phenomenon and 55% (11/20), Mechanic's hands. Three patients only had ILD and Raynaud's Phenomenon at presentation. In the immunologic assessment, 73,7% (14/19) were positive for anti – Jo-1 antibodies and 26,3%, for anti PL-12. As non-anti-ARS antibodies, 6 had positivity for rheumatoid factor; 3, for ACPA and 5, for antiRo-52 antibodies. Of those 18 diagnosed of ILD, spirometry tests at baseline were available for 13. It was remarkable that 69,23% (9/13) of patients presented a diminished value of DLCO (low in 23% (3/13), moderate in 46% (6/13) and normal in the rest of subjects). The most common ILD pattern was non-specific interstitial pneumonia (55%, 10/18) followed by usual interstitial pneumonia (33,3%, 6/18) and organising pneumonia (11,1%, 2/18). Nailfold capillaroscopy was performed in 16 patients: Scleroderma pattern was observed in 5 (all of them associating Raynaud's phenomenon) and 6 patients showed microangiopathic changes. The most frequent capillaroscopic findings were neoangiogenesis (93,8%) and microhaemorrhagias<sup>68,8</sup> followed by avascular areas (37,5%) and megacapillaries (31%). An association between capillaroscopic findings and reduction of DLCO or the radiologic pattern was not observed,

possibly influenced by the number of patients included. One subject associated Sjögren Syndrome, another one cutaneous Lupus and another patient, morphea. All of the patients included, received steroids and immunosuppressants. Azathioprine was the most frequently used (18/20), followed by Methotrexate (7/20), Rituximab (5/20), Mycophenolate (4/20), Cyclophosphamide (3/20) and Abatacept (1/20).

**Conclusions:** In our cohort with AS, the most common clinical manifestation was ILD, and an important part of the patients showed a decreased DLCO. Capillaroscopy was pathogenic in most of them and could be useful for the diagnosis of AS, specially in those patients presenting solely with ILD at the clinical debut, although its prognostic value is still unknown. Multidisciplinary consultations are useful in the management of these truly challenging patients.

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### AB1178 IS ANTI NUCLEAR ANTIBODY TEST REQUIRED CORRECTLY IN DAILY PRACTICE? A CHOOSING WISELY ANALYSIS

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**Background:** The most sensitive and gold-standard test used for the detection of antinuclear antibody (ANA) is accepted as the indirect immunofluorescence (IIF) test.<sup>1</sup> International proposals, including the choice of rational examination, referred to as "choosing wisely", include significant efforts to reduce overuse of examinations such as the ANA.<sup>2</sup>

**Objectives:** Our aim was to retrospectively analyse the distribution of the ANA test samples for clinical reasons according to the clinical departments and to determine the most frequently requested reasons and to draw attention to the rational ANA request.

**Methods: Detection of ANA samples.** Between January 2014 and August 2016, the results of the requested ANA test samples were screened for various reasons. The results of the first 4 divisions with the most common ANA test request and the reasons for the test were also analysed in detail (paediatric diseases were excluded). The ANA test was evaluated using the IIF method and the interpretation of the results was done according to the fluorescence intensity observed in the samples (+1 positive, +2 positive, +3 positive and +4 positive).

**Results:** 11407 ANA samples were evaluated. The first 5 sections requiring ANA test most were as follows: Neurology 1917 (24.7%), dermatology 1825 (23.6%), rheumatology 1574 (20.3%), paediatric nephrology 1404 (18.1%) and haematology 1027 (13.3%). In all the sections dealing with children, the ANA test number was 2461 and the mean age of the patients was 12.7 years, while the number of ANA samples required in the entire adult patient group was 8946 and the mean age of the patients was 46.8 years. ANA positivity rates for neurology, dermatology, rheumatology and haematology departments are 14.9%, 15.4%, 32.6% and 14.1%, respectively. The interclinical positivity rate was statistically significant ( $p < 0.0001$ ). Positive +1, +2, +3 and +4 positivity rates were 33.5%, 27.8%, 22.2% and 16.3%, respectively, when all positive ANA results were evaluated in terms of titre. When positivity was evaluated in terms of ANA positivity rates/titre, +4 positivity was found to be the most common in the patients from the rheumatology department (135/262=51.5%) ( $p < 0.0001$ ).

The reasons for ANA requests were determined according to ICD diagnostic codes. According to this; in neurology, headache, cerebrovascular event and multiple sclerosis; in dermatology urticaria, psoriasis and dermatitis; in rheumatology, SLE, arthritis and fibromyalgia; in haematology, anaemia and thrombocytopenia were the most common reasons for ANA requests.

**Conclusions:** Based on specific recommendations and "choosing wisely", the ANA test should be requested in patients with a high pre-test probability for autoimmune diseases. Raising awareness in terms of wisely choosing ANA test is needed in departments outside the rheumatology.

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### AB1179 MUSCULOSKELETAL PATTERN OF 18F-FDG UPTAKE IN PATIENTS WITH POLYMYALGIA RHEUMATICA

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**Background:** Polymyalgia rheumatica (PMR) is a common inflammatory rheumatic disease of the elderly whose diagnosis is usually based on clinical and ultrasound findings. Recently, <sup>18</sup>F-FDG PET/CT has been proposed as a promising one-step tool for assessing extent and severity of PMR. However, the pattern of <sup>18</sup>F-FDG uptake in PMR is not well established and there is a lack of imaging guidelines.

**Objectives:** Our aim was to describe the musculoskeletal pattern of <sup>18</sup>F-FDG uptake in PMR patients and assess if there were any differences between classic and atypical PMR.

**Methods:** Retrospective study of 75 patients with PMR and their respective PET/CT scans from a referral centre. We considered two groups: **a)** Classic PMR: patients who fulfilled the 2012 EULAR/ACR criteria; and **b)** Atypical PMR: patients with symptoms resembling PMR but did not fulfil the 2012 EULAR/ACR criteria. Distributions of categorical variables were compared by Pearson Chi2 or Fisher exact test as appropriate.

**Results:** We evaluated 75 patients (27 men and 48 women) with a mean age  $\pm$ SD of 68.2 $\pm$ 10.7 years. A PET/CT was performed in all of them. Forty-two (56%) patients classic PMR and 33 (44%) atypical PMR. FDG-PET uptake was observed in the following musculoskeletal regions: in shoulders (n=45), sternoclavicular joints (n=33), hips (n=32), cervical interspinous bursae (n=8), lumbar interspinous bursae (n=29), pubic symphysis (n=4), subtrochanteric bursae (n=20), ischial tuberosities (n=19) and knees (n=33). The comparative study between both groups is shown in the **TABLE**, without observing any statistical significance.

Abstract AB1179 – Table 1

	PMR (N=75)	Classic PMR (N=42)	Atypical PMR (N=33)	P <sup>a</sup>
Sex (women), n (%)	46 (64.0)	29 (69.0)	19 (57.6)	0.30
Age (years), mean $\pm$ SD	68.2 $\pm$ 10.7	73.9 $\pm$ 8.5	61.6 $\pm$ 9.5	0.60
F-FDG uptake		25 (59.5)	20 (60.6)	0.92
Shoulders	45 (60.0)	20 (47.6)	13 (39.4)	0.48
Sternoclavicular joints	33 (44.0)	19 (45.2)	13 (39.4)	0.76
Hips	32 (43.7)	5 (12.0)	3 (9.1)	0.98
Cervical interspinous bursae	6 (10.7)	12 (28.6)	11 (33.3)	0.40
Lumbar interspinous bursae	29 (38.8)	1 (2.4)	3 (9.1)	0.31
Pubic symphysis	4 (5.3)	12 (28.6)	6 (24.3)	0.67
Subtrochanteric bursae	20 (26.7)	12 (28.6)	7 (21.3)	0.47
Ischial tuberosities	19 (25.4)	16 (38.1)	17 (51.5)	0.25
Knees	33 (44.0)	25 (59.5)	20 (60.6)	0.92

# Comparisons between classic and atypical PMR.

**Conclusions:** In patients with PMR, <sup>18</sup>F-FDG uptake seems to be more frequent in shoulders, sternoclavicular joints, hips and knees. In addition, <sup>18</sup>F-FDG uptake can be also detected in lumbar interspinous bursae and less frequently in subtrochanteric bursae, ischial tuberosities, cervical interspinous bursae and pubic symphysis. No differences between classic and atypical PMR patients were seen.

**Disclosure of Interest:** None declared

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### AB1180 THE INFLUENCE OF MECHANICAL STRESS ON THE HANDS ON ULTRASOUND RESULTS: A PROSPECTIVE STUDY WITH VOLLEYBALL PLAYERS (US-VOLLEY) – PRELIMINARY DATA

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**Background:** Various imaging studies have found an influence of physical exercise on joint and tendon pathology in ultrasound. It is not clear<sup>1</sup> how specific grey scale and power Doppler changes are in a context of mechanical stress and<sup>2</sup> if a distinction to findings in acute arthritis exists.

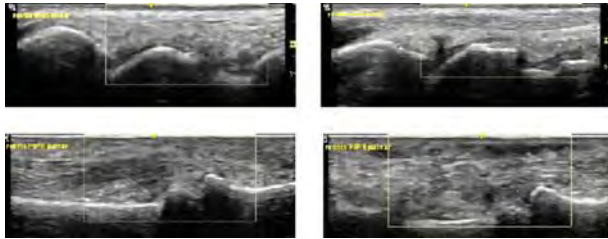
**Objectives:** To examine via grey scale and power Doppler ultrasound the acute physiological effects of increased physical stress on the fingers and wrists and their surrounding structures through volleyball training in amateur healthy subjects as a reference to the known pathological findings (effusion, increased perfusion) in acute arthritis.

**Methods:** Examination of 18 healthy amateur volleyball players via musculoskeletal ultrasound before and directly after their routine volleyball practice. Ultrasound assessment included a grey scale and power Doppler examination of the dominant hand (longitudinal planes of the dorsal wrist and dorsal and palmar



planes of MCP II-III and PIP II-III joints). Findings were graded semi-quantitatively from 0 to 3 both in grey scale (effusion) and power Doppler (perfusion). The results of the joint assessment were aggregated in a composite index for grey scale and power Doppler (range 0–54 points). All ultrasound images were graded by two independent raters who were blinded to image acquisition.

**Results:** Volleyball training showed statistically significant effects in the composite index for grey scale and power Doppler scores ( $p=0.004$ ). 16 of 18 players showed a change in their composite index with a median change of 1 and a maximum change of 3 points. Subanalysis revealed that changes were related to grey scale exclusively, with no statistical difference in power Doppler scores.



Abstract AB1180 – Figure 1

**Conclusions:** The results of our study suggest that mechanical stress on the hands leads to changes in grey scale ultrasound in healthy subjects in at least one joint. However, the composite index for changes in grey scale and power Doppler changed 3 points at the most in one subject over various joints. To add, no changes in power Doppler score were observed. While changes in grey scale ultrasound appear to be minor, power Doppler ultrasound appears to be a more robust method and less prone to environmental factors. Power Doppler appears to be able to discriminate between physiological changes due to mechanical stress and acute arthritis and thus, is highly specific.

**Disclosure of Interest:** None declared

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AB1181

#### ANTI-RO60 SEROPOSITIVITY DETERMINES EPIPOPE SPECIFICITY OF ANTI-RO52 ANTIBODIES IN PATIENTS WITH AUTOIMMUNE RHEUMATIC AND MALIGNANT DISEASES

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**Background:** Epitope mapping of anti-Ro52 antibodies (abs) has been extensively studied in patients with Sjögren's syndrome (SjS) and systemic lupus erythematosus (SLE). Comprehensive epitope mapping in systemic sclerosis (SSc) or malignant diseases (MD), also associated with anti-Ro52 abs, has not been performed.

**Objectives:** To fully characterise Ro52 epitopes in anti-Ro52 ab-positive SSc and MDs.

**Methods:** Testing was performed in sera from 95 anti-Ro52 positive patients with various autoimmune diseases (32 SSc, 20 SjS, 28 SLE) and 15 with malignant diseases (MD). Five recombinant Ro52 fragments [Ro52-1 (aa 1–127), Ro52-2 (aa 125–268), Ro52-3 (aa 268–475), Ro52-4 (aa 57–180, partly overlapping Ro52-1 and Ro52-2), and Ro52-5 (aa 181–320, partly overlapping Ro52-2 and Ro52-3)] were tested by line-immunoassay. Anti-Ro60 was tested by ELISA.

**Results:** Overall, reactivity to Ro52-1, Ro52-2, Ro52-3, Ro52-4 and Ro52-5 were present in 35.8%, 100%, 0%, 32.6%, 50.5%, respectively. Patients with SLE more frequently recognised Ro52-1, Ro52-4 and Ro52-5 than patients with SSc and malignant diseases. When epitope mapping was analysed in accordance to Ro60 reactivity, patients were subdivided in 50 Ro52pos/Ro60pos (13 patients with SSc, 14 with SjS, 18 with SLE and 5 patients with MD) and 45 Ro52pos/Ro60neg patients (19 with SSc, 6 with SjS, 10 with SLE and 10 patients with MD) and the following findings were noted: Abs to Ro52-1 were present in 26/50 (52%) Ro52pos/Ro60pos compared to 8/45 (18%) Ro52pos/Ro60neg patients ( $p<0.001$ ); antibodies to Ro52-2 were present in all patients; antibodies to Ro52-3 was totally absent; antibodies to Ro52-4 were present in 23/50 (46%) Ro52pos/Ro60pos compared to 8/45 (18%) Ro52pos/Ro60neg patients ( $p=0.003$ ); antibodies to Ro52-5 were present in 33/50 (66%) Ro52pos/Ro60pos compared to 15/45 (33.3%) Ro52pos/Ro60neg patients ( $p=0.001$ ). Ro52 epitope recognition did not differ between Ro52pos/Ro60pos and Ro52pos/Ro60neg in patients with SLE, SjS and patients with MD. In SSc anti-Ro52-1 reactivity was present in 8/13

(62%) Ro52pos/Ro60pos compared to 0/19 (0%) Ro52pos/Ro60neg patients ( $p<0.001$ ); In SSc, anti-Ro52-5 reactivity was present in 9/13 (69.2%) Ro52pos/Ro60pos and 5/19 (26.3%) Ro52pos/Ro60neg patients ( $p=0.029$ ). Ro52 epitope recognition in Ro52pos/Ro60pos patients did not differ amongst diseases.

**Conclusions:** Ro52-1 (aa 1–127) and Ro52-4, partially overlapping with Ro52-1, (aa 57–180) are dominant epitopes in Ro52pos/Ro60pos patients but not in Ro52pos/Ro60neg patients with autoimmune rheumatic diseases, suggesting that amino acids 57–127 may contain an epitope specifically recognised by the Ro52pos/Ro60pos group. Whether Ro60 is responsible for the unmasking of Ro52 (aa57–127) neoepitope remains to be investigated.

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AB1182

#### THE STABILITY OF RHEUMATOID FACTOR AND ANTI-CCP ANTIBODY IN ARCHIVED SAMPLES OF BLOOD

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**Background:** Recently, there has been an increasing demand for analysing a large amount of specimen at the same time and for stably storing those specimens for clinical research. Therefore, the role of the biobank that collects and preserves the samples for research and supplies them stably is very important.<sup>1</sup> Anti-CCP antibody and RF predated the onset of RA by several years, which indicates that citrullination and the production of anti-CCP and RF autoantibodies are early processes in RA.<sup>2</sup> In addition, RA patients with anti-CCP antibody had more swollen joints and more severe radiological destruction.<sup>3</sup>

**Objectives:** The purpose of this study is to evaluate the stability of RF and anti-CCP antibody after preserving the remaining samples for a long time and to determine the usefulness of the remaining samples that were kept for future research.

**Methods:** Serum samples used in this study were collected from 50 patients with RA in Eulji university hospital in 2011. The patients had baseline measurement at the time the samples were obtained and had more than one serum aliquots stored for archived samples. At baseline measurement, rheumatoid factor was quantified with turbid immunometry and anti-CCP was measured by an ELISA analyzer. All specimens were kept in a freezer where temperature monitoring was carried out for 24 hours to keep the temperature below  $-70^{\circ}\text{C}$ . 6 years later, the samples were slowly thawed at  $4^{\circ}\text{C}$  and measured by the same method of the baseline measurement.

**Results:** The mean age for 50 patients from which the samples were collected is 51.22 years. It was an average of 6.0 years (range: 5.6–6.1 years) for the samples to be stored at the biobank. We observed a slight decrease in concentration of RF and anti-CCP. There were significantly difference in concentration of RF and anti-CCP ( $Z=-5.10$ ,  $p\text{-value}<0.001$ ;  $Z=-3.81$ ,  $p\text{-value}<0.001$ ). The correlation between baseline sample and archived sample is strong (RF:  $\rho=0.973$ ,  $p\text{-value}<0.001$ ; anti-CCP:  $\rho=0.938$ ,  $p\text{-value}<0.001$ ).

**Conclusions:** This study assessed the stability of RF and anti-CCP antibody in archived samples of blood. Our results showed that serum concentration of RF and anti CCP antibody remain stable for up to 5 years at  $-70^{\circ}\text{C}$ . There was a slight decreased in the level overtime that was correlated with baseline value. These data indicated that the archived human samples in human cohorts could be used to examine for research and could be estimated according to the regression analysis.

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**Disclosure of Interest:** None declared

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**AB1183** **DIAGNOSTIC VALUE OF SALIVARY CRP AND IL-6 IN PATIENTS UNDERGOING ANTI-TNF-ALPHA THERAPY FOR RHEUMATIC DISEASE**

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**Background:** Saliva has been increasingly used as a diagnostic medium for disease detection and monitoring. Since saliva contains many of mediators of inflammation, collagen breakdown and/or bone remodelling, they may be of potential use for the rheumatic disease monitoring.<sup>1,2</sup>

**Objectives:** The aim of this pilot study was to investigate whether and how well salivary concentrations of CRP and IL-6 correlate with those in serum and with the clinical course of a rheumatic disease.

**Methods:** The nineteen consenting patients with rheumatoid arthritis or ankylosing spondylitis, newly scheduled for anti-TNF $\alpha$  therapy, were analysed. CRP and IL-6 were measured with high-sensitivity immunoassays before and after 12 weeks of anti-TNF $\alpha$  therapy, according to standard regimens. Disease activity and oral health parameters were also assessed.

**Results:** The patients' baseline characteristics were summarised in Table 1.

**Abstract AB1183 – Table 1.** Patients' baseline characteristics

Demographic and clinical features	
Age (years)	46 (36–61)
Men (%)	10 (53%)
Oral health parameters	
Plaque Index (PLI)	0.7 (0.4–1.0)
Approximal Plaque Index (API) (%)	75.0 (42.9–100.0)
Sulcus Bleeding Index (SBI)	0.0 (0.0–0.3)
Gingival Index (GI)	0.4 (0.0–1.0)
Probing Pocket Depth (PD) (mm)	0.8 (0.6–1.3)
Clinical Attachment Level (CAL)	1.4 (0.6–2.0)
DMFT index	18.5 (15.0–26.0)

The treatment resulted in a significant improvement in the clinical status and standard biochemical parameters in the majority of patients (table 2).

**Abstract AB1183 – Table 2.** Selected parameters before and after treatment.

	Before treatment (n=19)	After 12 weeks of treatment (n=19)	P-value (Wilcoxon-test)
DAS28 <sub>(ESR)</sub> (for RA; n=10)	6.2 (5.5–6.4)	3.5 (2.8–4.5)	<b>0.005</b>
BASDAI (for AS; n=9)	7.9 (6.6–8.6)	2.8 (2.0–4.2)	<b>0.008</b>
ESR (mm/h)	30 (8–70)	6 (4–24)	<b>0.002</b>
WBC (10 <sup>9</sup> /l)	9.3 (8.2–9.9)	8.0 (6.4–9.7)	<b>0.015</b>
Serum CRP (mg/l)	10.24 (4.65–24.31)	1.52 (0.54–4.13)	<b>0.010</b>
Serum IL-6 (pg/ml)	14.23 (5.03–34.61)	2.32 (1.49–25.14)	<b>0.044</b>
Salivary CRP (mg/l)	0.30 (0.02–3.72)	0.05 (0.00–1.87)	0.098
Salivary IL-6 (pg/ml)	1.91 (0.94–2.43)	1.48 (0.98–2.78)	0.811

Concentrations of CRP in saliva correlated significantly with those in serum ( $R=0.62$ ;  $p<0.001$ ) and decreased markedly after successful response to treatment ( $n=15$ ) ( $1.7\pm 0.2$  mg/L vs.  $0.8\pm 1.4$  mg/L;  $p<0.001$ ). In patients with a limited or no response to treatment ( $n=4$ ) salivary CRP levels increased ( $0.4\pm 0.8$  mg/L vs.  $2.6\pm 2.4$  mg/L;  $p=0.250$ ).

In contrast to CRP, the salivary concentrations of IL-6 did not change significantly over the course of therapy and they did not correlate with serum IL-6 concentrations. Salivary levels of neither CRP nor IL-6 corresponded to parameters of oral health and hygiene.

**Conclusions:** These data indicate, that salivary CRP but not IL-6 could be of potential use for monitoring the rheumatic disease activity.

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**AB1184** **CORRELATION BETWEEN CLINICAL DISEASE ACTIVITY AND SACROILIAC MRI DETECTION IN AXIAL SPONDYLOARTHROPATHY**

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**Background:** Ankylosing spondylitis (AS), a chronic rheumatic disease affecting young adults, is the prototype of the seronegative spondyloarthropathies (SpA). Magnetic resonance imaging (MRI) has an established role in the diagnosis and monitoring of patients with axial spondyloarthropathies (axSpA). Changes in MRI have shown some correlation with changes in clinical disease activity scores in the setting of biologic trials. MRI of the sacroiliac joints (SIJ) is currently widely used to assess inflammatory activity in AS patients. In general, agreement of status scores was somewhat better than agreement of change scores, and agreement of the comprehensive Spondyloarthritis Research Consortium of Canada scoring system (SPARCC) was somewhat better than agreement of the more condensed systems.

**Objectives:** The aim of this study is to evaluate the correlation between clinical disease activity of axSpA and MRI findings of sacroiliac joints.

**Methods:** Patients who were diagnosed as axSpA according to the Assessment of SpondyloArthritis international Society (ASAS) classification criteria in the our outpatient clinic and followed up routinely between November 2015 and August 2017 were included in this study. 32 patients between 18 and 55 years of age had been referred for routine blood tests and sacroiliac MRI. In this cross-sectional study, VAS, BASDAI, MASES, BASFI, ASDAS-ESR, ASDAS-CRP, ESR and CRP were used as the indicators of clinical activity. MRI of the sacroiliac joint was performed and the SPARCC score was evaluated by a radiologist who was blind to the clinical and laboratory parameters of the patients.

**Results:** The mean age of the patients was  $39.3\pm 9.2$ . 11 of the patients participating in the study were female (34.4%), 21 were male (65.6%). The mean duration of symptom onset was  $9.3\pm 7.7$  years and the mean duration of diagnosis was  $3.6\pm 2.8$  years. HLA-B27 is positive in 16 patients (50%). There is no correlation between SPARCC score and VAS, BASDAI, MASES, BASFI, ASDAS-CRP, ASDAS-ESR, ESR, CRP values ( $p>0.05$ ). In the HLA-B27 subgroup analyses, a statistically significant correlation was found between HLA-B27 negative patients and SPARCC score ( $p=0.008$ ).

**Conclusions:** As a result of this study, we could not find any relationship between other clinical disease parameters and sacroiliac joint imaging findings except for SPARCC score relationship with BASDAI in HLA-B27 negative patients with axSpA. We think that this relationship can be better revealed in future studies.

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**AB1185** **ANTINUCLEAR ANTIBODIES (ANA) IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE): ASSOCIATIONS WITH CLINICAL MANIFESTATIONS AND CYTOKINE PROFILES**

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**Background:** SLE is a multisystem heterogeneous autoimmune disease characterised by production of antibodies to cellular components, innate and adaptive immune alterations and dysregulation of cytokine production. Multiplex immunoassay is a useful tool for the detection of ANA associated with different clinical phenotypes and cytokine profiles in SLE.

**Objectives:** To evaluate the relationship between ANA subpopulations, clinical subtypes and cytokine profiles in SLE.

**Methods:** We studied 61 patients with SLE (2012 SLICC classification criteria) (8M/53 F), median and interquartile range (25th–75th percentile) of age 30.0 (27.0–45.0) years, disease duration 90.5 (12.5–168.0) months, SLEDAI 2K score 8.0

[4.0–16.0]; SLICC damage index score 1.0 (0–2.0) and 28 healthy donors. Serum samples were analysed for SLE-associated ANA (anti-dsDNA, anti-Sm, anti-chromatin, anti-SS-A/Ro 52 kDa and 60 kDa, anti-SS-B/La, anti-RNP-70, anti-ribosomal P – anti-RibP) using multiplex bead-based immunoassay system BioPlex 2200 (ANA Screen; Bio-Rad Laboratories Inc., USA). The levels of cytokines were determined with Bio-Plex 200 technology (Human Grp I Cytokine 27-plex panel; Bio-Rad Laboratories Inc., USA).

**Results:** Serum levels of anti-dsDNA, anti-chromatin, anti-Sm and anti-RibP antibodies were positively correlated with SLEDAI-2K scores ( $r=0.6$ ,  $r=0.7$ ,  $r=0.4$ ,  $r=0.3$ ,  $p<0.05$ ). Antibodies to dsDNA, chromatin, Sm and SS-A/Ro was most often detected in patients with dermatologic (59%, 57%, 32%, 43%), renal (64%, 66%, 36%, 38%) and neuropsychiatric (61%, 61%, 28%, 39%) manifestations of SLE. Increased serum concentrations of IFN-inducible chemokines: IP 10 and MCP1 were associated with high anti-dsDNA ( $r=0.3$ ), anti-chromatin ( $r=0.5$ ), anti-Sm ( $r=0.5$ ), anti-SS-B/La ( $r=0.3$ ), anti-RibP ( $r=0.4$ ) ( $p<0.05$ ) and anti-Sm ( $r=0.3$ ), anti-SS-B/La ( $r=0.3$ ), anti-RibP ( $r=0.3$ ) ( $p<0.05$ ) antibodies levels. Hyperproduction of chemokines RANTES and IL-8/MIP-1 $\alpha$  negatively correlated with anti-dsDNA ( $r=-0.3$ ), anti-chromatin ( $r=-0.3$ ) ( $p<0.05$ ) and anti-SS-A/Ro ( $r=-0.3$ ) ( $p<0.05$ ) antibodies levels, respectively. Low levels of pro-inflammatory cytokines IL-1 $\beta$ , IL-15 were negatively associated with the presence of antibodies to dsDNA and RibP ( $r=-0.3$ ) ( $p<0.05$ ), but a positive correlation was found between the levels of anti-inflammatory cytokines IL-10, IL-1ra and anti-Sm ( $r=0.3$ ), anti-SS-B/La ( $r=0.3$ ), anti-SS-A/Ro ( $r=0.3$ ) ( $p<0.05$ ) antibodies titers. Elevated concentration of GM-CSF was negatively correlated with serum level of antibodies to Sm ( $r=-0.3$ ) ( $p<0.05$ ).

**Conclusions:** These data suggest that the presence of ANA clusters may identify patients with distinct clinical subtypes and cytokine profiles and can reflecting different pathways of immune dysregulation in SLE.

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AB1186

#### DYNAMIC CONTRAST ENHANCED MR IMAGING IN EARLY STAGE KNEE OSTEOARTHRITIS: A TEST-RETEST REPEATABILITY STUDY IN HEALTHY AND MODERATELY DISEASED SUBJECTS

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**Background:** Osteoarthritis(OA)in the knee exhibits signs of synovial activation in early phase of disease.<sup>1</sup> DCE-MRI provides quantitative measurement of vascular disruption associated with synovitis<sup>2,3</sup>and has been shown to be sensitive to early treatment-induced changes in small group sizes in multicentre trials.<sup>4</sup>

**Objectives:** 1. Determine the reproducibility of DCE-MRI parameters in the knee. 2. Compare DCE-MRI parameters between participants with mild/moderate OA and aged matched controls.

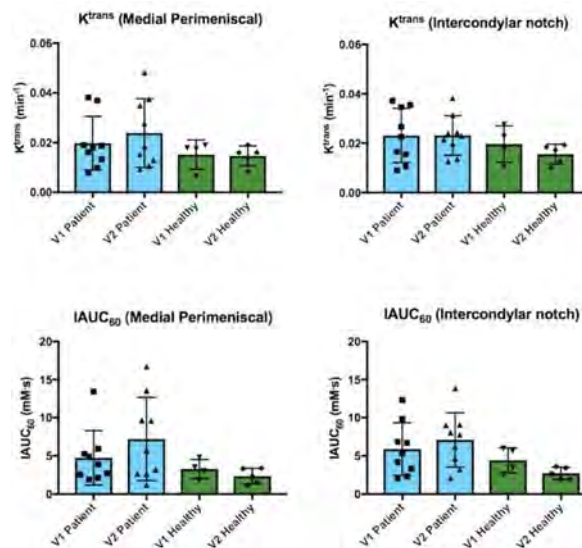
3. Enable effect and sample size calculations for further studies.

**Methods:** 9 knee OA patients and 4 controls underwent two MRI scans with a month separation. All patients had diagnosis of knee OA as per ACR criteria, with medial compartment predominant disease and Kellgren-Lawrence grade 2/3 on radiographs. 3 pre-contrast injection series were obtained with flip angles 2°,6° and 14°for T1 calculation.35 consecutive phases formed the DCE-MRI series (temporal resolution:14 s). Contrast agent(CA)(Dotarem(0.4 mL/kg))was administered on the 6th phase at the rate 3 mL/s followed by 50 mL saline. All Images were registered together. Here 2 DCE parameters are reported: $K^{trans}(\text{min}^{-1})$ , volume transfer constant for CA between blood plasma and extravascular extracellular space; estimated using the extended Tofts model<sup>5</sup> with population arterial function,<sup>6</sup> and  $\text{IAUC}_{60}(\text{mM}\cdot\text{s})$ , initial area under CA concentration curve over 60 s post-arrival. Manual segmentation was performed by radiologist.

**Results:** Test-retest coefficient of variation(CoV) was lower in controls.  $K^{trans}$  had CoVs of 26/16% in OA patients/controls. An effect size of 30% reduction in  $K^{trans}$ <sup>4</sup> indicates a treatment effect would be observed in a group of 11 patients with 90% power. DCE parameters were generally higher in OA patients than in controls. 4 out of 9 patients (All with KL score 3)demonstrated parameter values outside the healthy volunteer range at  $p<0.01$  level (one sample t-test).

Abstract AB1186 – Table 1

	Age (mean $\pm$ SD)	BMI (mean $\pm$ SD)	#KL-grade 2/3	#MOAKS effusion synovitis grade 0/1/2	#MOAKS Hoffa synovitis grad 0/1
Patient (n=9, 4F)	52 $\pm$ 5.2	30 $\pm$ 4.15	5/4	5/1/3	7/2
control (n=4, 3F)	55 $\pm$ 3.0	30 $\pm$ 3.50	NA	3/1/0	3/1



Abstract AB1186 – Figure 1

**Conclusions:** Higher  $K^{trans}$  and  $\text{IAUC}_{60}$  in patients indicates the potential of revealing microvascular function differences. The fact that this is not observed in all patients could suggest phenotypical variation. High CoV values in patient relative to healthy may be explained in part by fluctuation in disease status. Manual delineation also contributes to this variation.

DCE-MRI measures of vascular disruption associated with synovitis in knee OA are practical and feasible for imaging trials. These measures offer greater insight and sensitivity into the inflammatory component of OA that is not captured using other radiological methods.

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AB1187

#### WHAT IMAGING DETECTED PATHOLOGIES ARE ASSOCIATED WITH SHOULDER SYMPTOMS AND THEIR PERSISTENCE? A SYSTEMATIC LITERATURE REVIEW

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**Background:** Shoulder pain is a very common musculoskeletal complaint and a significant contributor to disability and morbidity. Recovery can be slow and over 50% continue to have pain at 18 months. Shoulder pain has a significant negative impact on quality of life and poses a significant economic burden, with costs estimated to be € 345 million per year in the UK alone. Modern imaging modalities can accurately detect soft-tissue pathologies and are increasingly used, but the relationship of imaging findings to patient symptoms remain unclear.

**Objectives:** Our aim was to systematically review the literature to determine what imaging features are associated with symptoms and their progression.

**Methods:** A systematic review using Medline, EMBASE, Cochrane and grey literature was conducted to April 2017. The cross-sectional and longitudinal relationships between imaging-detected abnormalities and symptoms were analysed and associations qualitatively characterised by a best evidence synthesis based on study design, covariate adjustment and the Grade of Recommendations



Assessment, Development and Evaluation (GRADE). Modalities included ultrasound, magnetic resonance imaging (MRI), radiographs, positron emission tomography (PET), bone scintigraphy and computerised tomography (CT).

**Results:** 6569 abstracts were screened and 56 papers were included. 50 studies did not adjust for covariates. The majority of studies showed conflicting findings. There was no significant association between most imaging features (rotator cuff tears, tendinopathies, subacromial bursal pathologies, osteoarthritis, calcification, acromial pathologies and adhesive capsulitis) and symptoms amongst high quality, cross-sectional studies. There was low-quality evidence suggesting that enhancement of the joint capsule on MRI and increased uptake of the rotator cuff interval, anterior joint capsule or axillary recess on PET was associated with symptoms in adhesive capsulitis. Based on high-quality, unadjusted longitudinal studies, enlarging rotator cuff tears was associated with an increased incidence of pain. 20 out of 56 studies evaluated more than one pathology, but only one study examined the association of symptoms with a combination of pathologies.

**Conclusions:** There were conflicting results on the association of imaging features with shoulder symptoms and its persistence and the existing evidence was very low in quality. There may be some imaging features associated with adhesive capsulitis symptoms and increasing RC tear may be associated with incident shoulder symptoms. Further high quality studies are required to understand the relationship between imaging and symptoms.

**Disclosure of Interest:** None declared

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#### AB1188 NAREDO AND BACKHAUS ULTRASOUND SCORES IN TUNISIAN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Ultrasound becomes increasingly important in the diagnosis and management of rheumatoid arthritis (RA).

**Objectives:** Our purposes are to evaluate Naredo (NS) and Backhaus (BS) ultrasound scores of synovitis, performed in daily practice in RA and to study their correlations with clinical assessment and SHARP radiological score modified by Vander Heijde (SS).

**Methods:** This is a cross-sectional study, conducted at the Rheumatology Department of Monastir Teaching Hospital, Tunisia, in 69 consecutive patients with RA. For each patient, clinical and biological evaluation (DAS 28 score), radiological assessment (SS) and ultrasound evaluation (by TOSHIBA machine) to determine NS and BS, were performed.

**Results:** The mean age of our patients was 52.01±10.1 years.<sup>27-78</sup> The women accounted for 89% of patients. The average of disease duration was 121±86 months [1-333]. The mean tender joint count (TJC) was 5.9±5.6 [0-27]. The most frequently hands tender joints were the 5th MCP right, 3rd MCP right and the 1st MCP left and right. The mean swollen joint count (SJC) was 3 [0-22]. The most frequently swollen joints at both hands were the wrists and the 2nd MCP. The overall mean SS score was 105±59 [17-272], the overall mean score for joint erosion was 52±38 [0-166] and narrowing score was 53±26.<sup>3-136</sup> The mean NS was 17±15 [0-64] and BS was 21±10.<sup>2-44</sup> The mean duration of ultrasound assessment for calculating NS and BS was 21±7 min and 17±5 min, respectively. NS was significantly associated with SJC (p<0.000) and DAS 28 (p<0.01) but was not significantly associated with SS nor with its components. The BS was significantly associated with TJC (p<0.000), SJC (p<0.04) and DAS 28 (p<0.02). It was not significantly associated with SS. The number of erosions found by the BS was significantly associated with the erosion score of both hands and overall erosion score found by the SS (p<0.001). Ultrasound shows superiority in detecting erosions than standard radiographs: the number of erosions found by the BS was superior in 91% of cases to the number of erosions found by SS in the same joints.

**Conclusions:** NS and BS are significantly associated with RA disease activity. Ultrasound detects better osteoarticular erosions than radiological assessment. BS, which needs on average 17 min, can be used in daily practice.

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**Disclosure of Interest:** None declared

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#### AB1189 ROLE OF DIFFUSION WEIGHTED IMAGING IN DIABETIC FOOT MAGNETIC RESONANCE IMAGING

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**Background:** Differentiation of acute diabetic osteoarthropathy from acute osteomyelitis is one of the most challenging issues in the evaluation of diabetes related foot complications. Early differentiation between these conditions is crucial, as early management of acute diabetic osteoarthropathy could prevent permanent deformity and resultant morbidity and initiation of appropriate treatment for osteomyelitis can reduce the risk of amputations. Acute diabetic osteoarthropathy may mimic osteomyelitis clinically and at different imaging modalities. The current imaging modalities used for assessment for diabetic foot have several limitations

**Objectives:** evaluate the role of diffusion weighted echoplanar MR imaging in differentiation of diabetic osteoarthropathy from osteomyelitis of diabetic foot.

**Methods:** Prospective study was conducted on 37 consecutive patients with diabetic foot. They underwent diffusion weighted MR imaging of the foot using a single shot echo planar imaging with a b-factor of 0,500 and 1000 sec/mm<sup>2</sup>. The scanning parameters were: TR=10000 ms, TE=108 ms, NEX=8-16, bandwidth=125 kHz, slice thickness=4 mm. Apparent diffusion coefficient (ADC) map was reconstructed. The ADC value was calculated and correlated with surgical findings or biopsy. Statistical analysis was done.

**Results:** The mean ADC value of diabetic osteoarthropathy was 0.97±0.13 × 10<sup>-3</sup> mm<sup>2</sup>/sec and of osteomyelitis was 0.121±0.12 × 10<sup>-3</sup> mm<sup>2</sup>/sec. There was statistically difference in mean ADC values between diabetic osteoarthropathy and osteomyelitis (p<0.01). When apparent diffusion coefficient value of 0.77 × 10<sup>-3</sup> mm<sup>2</sup>/sec was used as a threshold value for differentiating of diabetic osteoarthropathy from osteomyelitis, the best result was obtained with an accuracy of 90%, sensitivity 92%, specificity 89%, positive predictive value 88% and negative predictive value of 86%.

**Conclusions:** we concluded that apparent diffusion coefficient value is a new non-invasive imaging parameter that can be used for differentiation of diabetic osteoarthropathy from osteomyelitis. Application Diffusion weighted MR imaging can be added to routine MR imaging of diabetic foot.

**Disclosure of Interest:** None declared

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#### AB1190 ULTRASONOGRAPHY IN SPANISH RHEUMATOLOGY: A CROSS SECTIONAL SURVEY

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**Background:** Ultrasonography (US) is the rheumatologists' best tool that must be taught and learnt correctly. The ultrasound school of the Spanish Society of Rheumatology has trained many rheumatologists for more than twenty years. Approximately 75% of the rheumatology departments in Spain use US. However, we lack current views of features related with competency, teaching rheumatology residents, US usage and implementation.

**Methods:** A cross sectional survey was performed using an online standardised questionnaire sent to all members of the SSR in January 2017. The questionnaire was developed by the four authors, corrected for size, style, syntaxes and was piloted on four different aged rheumatologists. Six aspects were studied; general data, US training, rheumatology residents training in US and main uses and applications of US. The questionnaire used either closed or Likert scale answers and took about 20 min to answer. Herein we describe the main results on usage and applications of US.

**Results:** 113 responses: 60% women, 45±12 years old, 73% working in public university hospital with one or more US machines. US is usually used at the time of clinical consultation or at appointment for US. 43% have a specific agenda for US diagnosis and monitoring inflammatory arthritis patients. The 3 principals for using US are: as a problem solving tool in the clinical context; as a diagnostic tool in inflammatory arthritis and; as a tool to guide injections. The table shows the percentage of the responses always and almost always for 10 clinical contexts. As diagnostic tool in rheumatoid arthritis (RA), 66% use US to confirm arthritis when clinical exam is unclear and 33% in patients with inflammatory arthralgia plus high ESR, CRP, RF or anti-CCP. 36% monitor disease activity using a reduced joint assessment; one target joint plus 2,3 MCP and 2,3, 5 MTP joints and 32% use a validated joint count. 66% use US to assess remission in RA all patients (22%), only in those treated with biologic drugs (28%) and in RA patients with poor

prognostic factors (18%). Most use US to confirm clinical enthesitis when a spondyloarthropathy (SpA) is suspected and half consider that a positive enthesal Doppler signal supports more aggressive management. 76% perform real-time guided injections for the following disorders/sites: Baker's cyst, subacromial-subdeltoid bursa, tibionavicular joint, anterior coxofemoral joint, retrocalcaneal bursa and extensor wrist tenosynovitis.

#### Abstract AB1190 – Table 1

	% (Likert 4 +5)
To detect articular or periarticular inflammation when there is a clinical doubt	94
To detect enthesopathy, tendinosis or tendon ruptures when there is a clinical doubt	79
To detect crystal deposits when microcrystalline arthropathy is suspected	48
To detect bone erosions when radiology is obscure	39
To assess skin fibrosis	35
To assess palpable nodules or masses	34
To detect temporal artery vasculitis when it is clinically suspected	20
To detect salivary gland involvement in patients with xerostomy	17
To detect arteriosclerosis in chronic inflammatory patients	13
To assess interstitial lung disease	2

**Conclusions:** Rheumatologist- ultrasonographers in Spain use ultrasonography in a wide spectrum of diseases and clinical contexts mainly to facilitate diagnosis and improve treatment of rheumatic patients.

**Disclosure of Interest:** None declared

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#### AB1191 VITAMIN D AND CD34+ CELLS AS BIOMARKERS OF SUBCLINICAL ATHEROSCLEROSIS AND MYOCARDIAL DYSFUNCTION IN INFLAMMATORY JOINT DISEASES

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**Background:** increased cardiovascular (CV) risk in inflammatory joint diseases (IJD) such as rheumatoid (RA) or psoriatic arthritis (PsA) is linked to an impaired vascular homeostasis. Chronic inflammation and immune dysregulation prompt endothelial damage and impair reparative mechanisms. Among them, circulating CD34 +bone marrow-derived progenitors are known to participate in endothelial turnover and improve myocardial neovascularization and ventricular remodelling, likely delaying CV disease development. Among factors related to CD34 +cells mobilisation, a role for vitamin D has emerged in other scenarios. Whether impaired CD34 +cells or vitamin D levels underlie endothelial and myocardial dysfunction in IJD patients remains unknown.

**Objectives:** to evaluate the associations between CD34 +cells and vitamin D levels with markers of subclinical atherosclerosis and myocardial functionality in IJD patients.

**Methods:** CD34 +cells counts were assessed by flow cytometry in peripheral blood samples from 41 RA (2010 EULAR/ACR criteria) and 35 PsA (CASPAR criteria) patients recruited at onset and 58 matched healthy controls (HC). Vitamin D levels were quantified in serum by HPLC. PWV and cIMT were evaluated as markers of subclinical atherosclerosis, whereas myocardial dysfunction was assessed by speckle-tracking echocardiography (STE).

**Results:** vitamin D was decreased in RA (23.68±6.42) and PsA (23.53±4.84) compared to HC (31.75±5.05 ng/ml, both p<0.001). Vitamin D was negatively associated with cIMT in HC (r=-0.308, p=0.026) and in PsA patients with low disease activity (DAS28 <2.9, n=11) (r=-0.636, p=0.035), but not in their high disease activity or RA counterparts. CD34 +cells were decreased in RA compared to HC (1.58±0.58 vs 2.35±1.14 cells/ul, p=0.002). CD34 +cells frequency was associated with total- and LDL-cholesterol levels in HC (r=-0.295, p=0.031 and r=-0.354, p=0.011, respectively) but not in IJD. CD34 +cells negatively paralleled DAS28 in PsA (r=-0.338, p=0.047) and RA (r=-0.303, p=0.057). Multivariate regression analyses revealed that vitamin D levels (B=0.019, p=0.009) and DAS28 (B=-0.152, p=0.050) were independently associated with CD34 +counts in PsA, whereas vitamin D (B=0.010, p=0.028) and duration of the symptoms (B=0.016, p=0.010) did in RA. CD34 +cells counts were correlated with GCS (r=-0.291, p=0.068) and GLS (r=-0.301, p=0.057) in RA.

**Conclusions:** vitamin D was negatively associated with cIMT and risk factors in HC and PsA patients with low disease activity, but not in those with active disease or RA. Vitamin D was an independent predictor of CD34 +cell depletion in IJD.

CD34 +cells, negatively associated with risk factors in HC, were altered in RA in relation to disease activity and the duration of symptoms. CD34 +cells were associated with myocardial dysfunction in RA.

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#### AB1192 DIAGNOSTIC YIELD OF MUSCLE BIOPSIES PERFORMED OVER A 10 YEAR PERIOD

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**Background:** Patients with suspected inflammatory myopathy (IM) are often referred to Rheumatology, where the diagnostic process may include a biopsy of skeletal muscle. A new service was set up in 2007 at Sunderland Royal Hospital, whereby a trained consultant performs open muscle biopsies of vastus lateralis muscle under local anaesthetic within the Rheumatology outpatient department. Samples are sent to a histology laboratory at another hospital site for analysis, which can include electron microscopy. Referrals most commonly come from other consultant Rheumatologists within the team.

**Objectives:** To evaluate the diagnostic yield amongst muscle biopsies performed over a 10 year period. To review the correlation between final clinical diagnosis and investigation results. To identify any complications caused by the biopsy procedure.

**Methods:** Retrospective analysis of medical notes of all patients who were referred for muscle biopsy within the Rheumatology department during 2007 – 2017.

**Results:** The mean patient age was 51 years; 28 patients were female. All procedures were performed or directly supervised by one trained rheumatology consultant. 45 patients were referred for muscle biopsy. 41 patients had elevated creatinine kinase. 2 were unable to tolerate the procedure. 3 samples were either too small for analysis or did not contain skeletal muscle. A total of 40 muscle samples were reviewed.

16 muscle biopsy samples showed histological features of IM (3 polymyositis, 3 dermatomyositis, 6 inclusion body myositis and 4 undifferentiated CTD). 15 samples showed other diagnoses including genetic, neurological and storage disorders. In 9 samples no definite diagnosis could be made on biopsy, despite this 3 patients were diagnosed with IM based on clinical features and other investigations.

Of the 19 patients with a final diagnosis of inflammatory myopathy (clinical and histological), 15 had positive ANA, 3 had negative ANA (1 of which had positive Ro antibodies).

EMG/NCS performed prior to muscle biopsy had a high positive predictive value: all 7 with an IM pattern on EMG had a histological diagnosis of IM. 2 patients with normal EMG had eventual diagnosis of IM.

Complication rates were low. 3 patients had subsequent numbness around the biopsy site and 1 required a compression dressing for increased bleeding during the procedure.

**Conclusions:** Muscle biopsy was successful in achieving a diagnosis in 64% of all patients referred. Out of biopsies taken, 40% of biopsies performed showed IM. 37.5% showed other diagnoses. The total diagnostic yield is therefore calculated as 77.5%. It appears to be a useful diagnostic investigation in patients with suspected myopathies and helps with correct diagnosis and appropriate treatment. Muscle biopsy is relatively safe and can be performed in the outpatient setting. Despite delays in the transfer of 3 specimens, histological analysis was still possible, suggesting that having an off-site histopathology laboratory does not adversely affect outcomes. Further review could focus on the increasing use of MRI scanning in the diagnostic evaluation of these patients, which may in some cases prevent the need for open biopsy.

**Disclosure of Interest:** None declared

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#### AB1193 AN IMMUNE REFERENCE ATLAS FROM BIRTH TO ADULTHOOD IDENTIFIES KEY DEVELOPMENTAL MILESTONES

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**Background:** A developmental atlas of the immune system is key to understanding its normal maturation process and identifying the disease-associated cell subsets. The absence of a holistic developmental immune normogram is a critical unmet need.

**Objectives:** To address this need and our hypothesis that age-related immune effector and regulatory cell subsets changes are present, we employ a multi-dimensional approach using mass cytometry to identify the cell subsets that shape the developing immune landscape from birth to adulthood.

**Methods:** We interrogated the peripheral blood mononuclear cells from 126 healthy individuals (cord blood, newborn to adult) with mass cytometry using two extensive antibody panels embracing the most important cell lineages and their function. Quality control and batch effect correction were performed with outliers excluded before dimensional reduction and clustering to identify the unique immune cell subsets. Their frequencies across the age categories were presented as 3-D frequency histograms. Subsequent manual gating was done to further describe these immune cell subsets changes with age using Pearson correlation coefficient.

**Results:** Distinct developmental gradients involving multiple effector and regulatory cell subsets shaped the maturing immune landscape. The naïve TNF $\alpha$ +CD4 +T cells were enriched in the early childhood period and declined with age (Pearson correlation coefficient,  $r=-0.3503$ ,  $p<0.001$ ). In contrast, the memory TNF $\alpha$  +CD4+T cells increased with age ( $r=0.4149$ ,  $p<0.0001$ ). A transitional milestone from naïve to memory TNF $\alpha$ +CD4+T cells was observed after 2 year old. This indicates that an intact CD4 +T cells TNF $\alpha$  effector mechanism is present at birth which progressively mature to involve the memory CD4 +T cells. For another cytokine IL17A, it was secreted solely by the memory CD4 +T cells with its population increasing with age ( $r=0.3753$ ,  $p<0.001$ ). Another distinct maturation milestone was observed in the naïve CD8 +T cell subset where a transition from IL8 to IFN $\gamma$  secretion after 10 year old was observed. The IL8 +and IFN $\gamma$ +naïve CD8+T cell subsets correlated negatively and positively with increasing age respectively ( $r=-0.2661$ ,  $p<0.01$  and  $r=0.2835$ ,  $p<0.01$ ).

For the T regulatory cells, the age related changes were more gradual. The early thymic T regulatory cells (CD3+, CD4+, CD31+, CD45RA+, CD25+, Foxp3+, CD152+) demonstrated a gradual decline with age ( $r=-0.2966$ ,  $p<0.01$ ) while the memory T regulatory cells gradually increased with age (CD3+, CD4+, CD45RO +, CD25+, Foxp3+, CD152+) ( $r=0.2444$ ,  $p<0.05$ ).

**Conclusions:** Key developmental milestones in the T cell compartment were identified and with the other subsets identified, a holistic description of the developing immune landscape was obtained. This atlas has the potential dual translational role of defining the stage of immune maturity and distilling the pathological cell subset in both paediatric and adult immune mediated diseases. The database and the related pipeline to analyse it will be provided as a free reference.

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#### AB1194 ARE THERE NEW PARAMETERS TO BE CONSIDERED IN SPECTRAL DOPPLER TO EVALUATE THE NAIL BED IN PSORIASIS AND PSORIASIS ARTHRITIS?

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**Background:** Other spectral Doppler parameters can assess joint impairment caused by psoriatic arthritis and psoriasis<sup>1</sup>.

**Objectives:** To detect and compare Doppler velocimetric indexes changes in 3 groups of patients.

**Methods:** Thirty – eight patients were evaluated: 8 in the control group – healthy (52 nail beds); 15 in the psoriasis group (134 nail beds); and 15 in the group with psoriatic arthritis (147 nail beds). "CASPAR" criteria were used to classify the patients. The ultrasound (US) was performed in all patients using Esaote MyLab 50, with high resolution linear probe with a frequency of 18 MHz, it was positioned longitudinally to the nail bed.

**Results:** The psoriasis group of patients included 7 males (46.6%) and 8 females (53.4%); 66.6% were white, 33.4% black.

**Abstract AB1194 – Table 1.** Mean and standard deviations of US, clinical and laboratory variables by clinical group:

	Psoriatic Arthritis	Psoriasis	Control
RI (Resistance Index)	0.58 (0.09)	0.59 (0.10)	0.60 (0.07)
PI (Pulsatility Index)	1.05 (0.31)	1.06 (0.45)	1.12 (0.25)
Acceleration (A=m/s <sup>2</sup> ;	0.37 (0.29)	0.39 (0.47)	0.51 (0.44)
Acceleration Time (AT=ms)	107.30 (37.10)	114.64 (41.14)	113.10 (40.10)
Angle of Insonation ( $\alpha=^{\circ}$ )	18.21 (25.8)	14.76 (24.71)	27.28 (30.10)
Nail bed thickness (T=mm)	1.60 (0.78)	1.68 (0.50)	1.44 (0.40)
VHS	27.5 (24.9)	20.4 (14.9)	-
PCR	0.75 (1.1)	0.54 (0.7)	-

**Abstract AB1194 – Table 2.** Distribution and percentage of individuals according to clinical group and to the PASI, NAPS1 variables:

	Psoriatic Arthritis N(%)	Psoriasis N(%)	Control N (%)
<b>NAPS1</b>			
Normal (=0)	0 (0)	0	8 (100)
Mild (<20)	4 (28.6)	10 (71.4)	0
Severe (>20)	11 (68.7)	5 (31.3)	0
<b>PASI</b>			
Mild (<15)	14 (51.8)	13 (48.2)	0
Moderate <sup>15-25</sup>	1 (50.0)	1 (50.0)	0
Severe (>25)	0	1 (100.0)	0

Statistically significant: Mean age and SD of the psoriasis, psoriatic arthritis and control groups, respectively: 57.13 $\pm$ 14.3 years; 54.66 $\pm$ 10.6 years; 24.87 $\pm$ 2.03 years ( $p<0.05$ ). A statistically significant difference was found in the **NAPS1** variable among all groups ( $p<0.05$ ); in the variable **PASI**, a difference was only found in the control group ( $p<0.05$ ) (Kruskall-Wallis) (table 2); the **A** variable between the psoriasis group and control ( $p<0.001$ ); between the psoriatic arthritis group and control ( $p=0.001$ ), the variable **T** between the psoriasis and psoriatic arthritis groups ( $p=0.006$ ) and between the psoriasis and control groups ( $p=0.001$ ) and the  $\alpha$  variable between control and psoriasis groups ( $p=0.017$ ) (table 1). **Spearman and Pearson correlations** between US variables per group, psoriasis, psoriatic arthritis and control were: **RlxPI**  $r=0.744$  ( $p<0.001$ ), **PD (power Doppler) xT**  $r=0.301$  ( $p<0.001$ ), **RlxPI**  $r=0.914$  ( $p<0.001$ ), **PlxA**  $r=0.46$  ( $p<0.001$ ); **RlxPI**  $r=0.889$  ( $p<0.001$ ), **PDxT**  $r=0.490$  ( $p<0.001$ ) respectively.

**Conclusions:** There are other parameters in spectral Doppler to be validated in order to characterise changes in nail beds.

#### REFERENCE:

- [1] Mendonça JA. High Specificity of Spectral Nail Assessment in Psoriatic Arthritis Patients [abstract]. *Arthritis Rheumatol.* 2015;67(suppl 10).

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#### AB1195 DEVELOPMENT AND VALIDATION OF AN ULTRASONOGRAPHIC ACTIVITY SCORE (USAS) FOR RHEUMATOID ARTHRITIS

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**Background:** Composite scores developed in Rheumatoid arthritis (RA) not include all dimensions of disease activity. An index based on essential clinical plus a ultrasound (US) measures, focused on simplicity, with appropriate validation, would allow a better classification at different levels of disease activity than a clinical only or US only index.

**Objectives:** To develop and validate a mixed clinical-US inflammation score in RA for use in clinical practice.

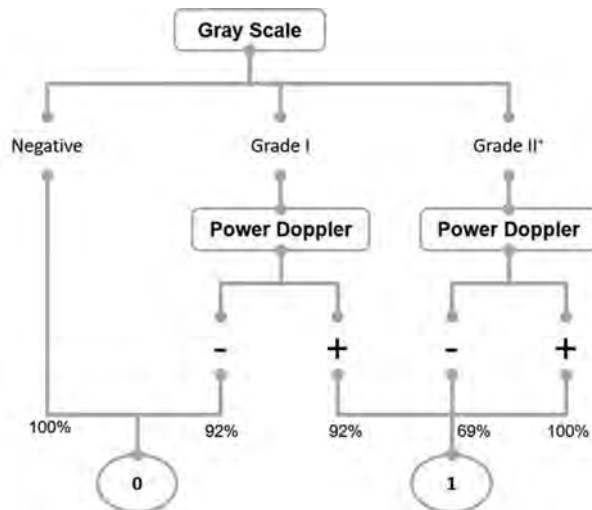
**Methods:** Mixed methods. Experts elicited items reflecting inflammation which were prioritised by Delphi. Patients with RA with various grades of activity underwent clinical [28 swollen and tender joints counts, patient and physician global assessment (PhGA), erythrocyte sedimentation rate, and C-reactive protein (CRP)] and US assessments [synovitis or tenosynovitis by grey-scale (GS) and Power Doppler (PD) of 42 structures], blinded to the clinical assessment. An index was created after supported selection of US structures and scoring method. Construct validity was tested by correlation with DAS28, SDAI, CDAI, and PhGA. Reliability was evaluated in a subgroup of patients with the intraclass correlation coefficient (ICC).

**Results:** US of joints and tendons, CRP, and swollen joints were the items that passed the prioritisation phase. Then, 281 patients were randomly divided into design (n=141) and validation analysis (n=140). The combination of US sites chosen detected the maximum proportion of GS and PD present. Were elected



wrist, 2–3 MCP, Knee, tibio-talar and 2–3 MTP joints, and the following tendons: carpal extensor and flexor tendons, tibial posterior and peroneal. For scoring structures, three methods were tested: semiquantitative (0–3 GS +0–3 PD), dichotomous (0/1 GS +0/1 PD), and qualitative (0/1 based on algorithm [image 1]). All showed strong correlation with activity measures ( $\rho \geq 0.60$ ), and reliability (ICC 0.89 to 0.93). The most feasible index, qualitative, was chosen.

The proposed formula for USAS was: **USAS=N° swollen joints+US score+CRP**



Abstract AB1195 – Figure 1

**Conclusions:** USAS is a valid and reliable measure of inflammation in RA equal to the sum of 28 swollen joint count, a simplified (0/1) US assessment of 11 structures and CRP.

**Disclosure of Interest:** None declared

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#### AB1196 ROLE OF CAPILLAROSCOPY IN THE STUDY OF THE RAYNAUD PHENOMENON IN CONDITIONS OF CLINICAL PRACTICE

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**Background:** The Raynaud phenomenon (RP) is very common throughout the world, especially in cold climates, affecting approximately 3%–5% of the population. Most RPs are primary. The risk of the onset of autoimmune disease associated with RP (ADRP) is between 6% and 12%, and the diagnosis is usually made within 2 years of its onset. Capillaroscopy is a simple, innocuous and inexpensive technique that is very useful in the study of RP

**Objectives:** The primary goal was to evaluate the capillaroscopic findings in patients with RF as the only symptom and establish their relationship between the subsequent development of ADRF.

**Methods:** We conducted an observational, descriptive, cross-sectional study of a random sample of 98 patients with RP as the main manifestation, selected from within the capillaroscopy consult of our Unit. The capillaroscope used was a stereomicroscope (Stereoscope), with a triocular head, zoom range from 1x to 4x magnification, with cold light illuminator and high resolution ocular camcorder. Periungual capillaroscopy was performed in 3rd, 4th and 5th finger of the right and left hands in each patient and always by the same rheumatologist. We described the sociodemographic variables of patients, and analytical results of the antinuclear antibodies (ANA). After an initial statistical exploration of the data, the same are described. The quantitative variables are expressed as means and standard deviations and if the distributions are asymmetric with medians and quartiles. The qualitative variables with percentages. To assess the validity of capillaroscopy as a diagnostic test, we determined the sensitivity, specificity, and positive and negative predictive value of the test.

**Results:** 73.5% were women, with an average age of 45.7 years. The median time of evolution of the RP until the capillaroscopy was 2.5 years. 76% of the patients were ANA negative.

The evaluation of the predictive capacity of capillaroscopy for the development of EARP yields the following results:

Abstract AB1196 – Table 1

Sensitivity	83,3% <sup>(62.6–95.2)</sup>
Specificity	78% <sup>(66.8–86.9)</sup>
Predictive positive value	34,1% <sup>(24.5–45.3)</sup>
Predictive negative value	97,1% <sup>(93.3–98.8)</sup>

When analysing the relationship between the presence of ANA and the association with ADRF we found that it was independent ( $p=0.002$ ) of the result of capillaroscopy, being the risk of developing the disease in a patient with positive ANA 8.5 times higher than in an ANA negative patient.

**Conclusions:** Capillaroscopy in patients with RP has a high predictive negative value, which allows us to estimated, with high reliability, the association of this phenomenon with autoimmune disease in patients with normal capillaroscopic patterns. Given the results of our study, capillaroscopy should be protocol in the RP study

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#### AB1197 MULTIPARAMETRIC ANALYSIS OF CONNECTIVE TISSUE DISEASE SPECIFIC AUTOANTIBODIES USING A SPOT IMMUNOASSAY (SERASPOF<sup>®</sup>ANA)

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**Background:** Because autoantibody profiling compared to single autoantibody determination is more relevant for diagnostics, differential diagnostics and even prognostics of the different kinds of connective tissue diseases (CTD), cost and time saving multiplex assays are more and more used in routine practice.<sup>1</sup>

**Objectives:** Evaluation of the diagnostic relevance of the *SeraSpot<sup>®</sup>* ANA assay (Seramun Diagnostica GmbH, Heidesee, Germany), a novel spot immunoassay for multiplex analysis of the main connective tissue disease (CTD) specific autoantibodies (AABs) against dsDNA, histone, nucleosome, Scl-70, U1-RNP, Sm, PCNA, RibP, Ro52/TRIM21, Ro60, La/SS-B, CENP-B, Jo-1, PM/Scl-100, and Ku) based on autoantigens immobilised in microtiter plates.

**Methods:** AAB profiles using the *SeraSpot<sup>®</sup>* ANA assay were determined in sera of 381 patients with CTD and 202 apparently healthy individuals (AHI). The CTD patients comprises 105 SLE, 117 systemic sclerosis (SSc), 32 Sjögren's syndrome (SjS), 58 idiopathic inflammatory myopathies (IIM), 5 mixed connective tissue disease (MCTD), and 64 undifferentiated connective tissue disease patients (UCTD).

**Results:** At least one CTD associated AAB was positive in 88.2% of the tested CTD patients. A high diagnostic specificity for CTD above 95% compared to AHI were found for antibodies to dsDNA, RibP, Sm, Ro60, Ro52, CENP-B, Scl70, PM/Scl-100, Ku and Jo-1. Excluding low-titre reactivity, the specificity of U1-RNP, nucleosome, histone and La/SS-B antibodies was also very high (96.5%–98%) regarding CTD diagnosis. The highest specificities vs. AHI were found for anti-Sm, -Ro60, -RibP and -Jo1 antibodies (99.5%), followed by anti-CENP-B (99%), -dsDNA (98.5%), -Ku (98.5%) and -Ro52 antibodies (98%). Regarding SLE, 104 (99%) were positive for SLE-associated AABs. Anti-dsDNA antibodies were most frequently found (88.6%). The highest specificities (98.5%–99.5%) for SLE compared to AHI were found for anti-dsDNA, -RibP, -Sm, and -Ro60 antibodies. SjS relevant AABs against Ro60, Ro52 and La/SS-B were seen in 81.3%, 84.4% and 46.9% of the SjS patients, respectively. The diagnostic specificity of Ro60 antibodies for SLE and SjS compared to other SARD (excluding UCTD) is 96.8% and 99.5%–100% compared to AHI. SSc associated AAB against Scl-70, CENP-B, PM/Scl-100 and -U1-RNP were found in 53.0%, 20.5%, 8.6%, and 13.7% of the included SSc cases, respectively, with diagnostic specificities between 96% and 99%. AABs against Jo-1, PM/Scl-100, U1-RNP, Ro52 and Ku were positive with high specificity (98.4%–99.5%) in 29.3%, 10.3%, 19% (100% of MCTD), 27.6% and 10.3% of IIM patients, respectively.

**Conclusions:** In combination with the HEP-2 cell assay, the *SeraSpot*<sup>®</sup> ANA assay can be used as a novel cost-effective multiplex assay for the serological confirmation of CTDs.

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AB1198

#### THE DIFFERENCES OF THE DISTRIBUTION OF FEEDING VESSELS AND BONE SURFACE IRREGULARITY BETWEEN YOUNG AND ELDERLY ADULTS IN WRIST JOINTS OF HEALTHY VOLUNTEERS BY MUSCULOSKELETAL ULTRASOUND (MSKUS)

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**Background:** Synovial vascularity as measured by power Doppler (PD) of MSKUS is correlated to rheumatoid arthritis disease activity, and PD signal reveals the prevalence of subclinical synovitis overlooked on physical examination. It is often difficult to distinguish bone erosion from normal concave surface of the bone, and it is necessary for us to be familiar with these normal structures well in evaluating disease activity by using MSKUS. Here we examine the age-specific differences of normal feeding vessels and bone surface irregularity between in wrist joints.

**Objectives:** To elucidate the differences of distribution of feeding vessels and bone surface irregularity in wrist joints both young and older adults among healthy volunteers.

**Methods:** The dorsal side of wrist joints was scanned with 2D-probe in healthy volunteers (young <50 y.o., elder ≥50 y.o). The distribution of feeding vessels in the capsule and the extensor(E.) tendon sheath(TS), and the evaluation of bone surface irregularity at lunate(Lu) were examined. The comparative review between young and elderly adults was validated.

**Results:** The distribution of feeding vessels in younger healthy volunteers (n=30: mean age 32.2±8.0 y.o.) vs elderly healthy volunteers (n=21: mean age 66.0 ±7.2 y.o.) were near-Trapezoid (Rt100.0% vs 100.0%, Lt100.0% vs 100.0%: p=1.00), E.digitum TS (Rt86.7% vs 81.0%:p=0.59, Lt66.7% vs 76.2%:p=0.47), E. digiti minimi TS (Rt30.0% vs 52.4%:p=0.11, Lt30.0% vs 66.7%:p=0.0089), near-Capitate (Rt23.3% vs 42.9%:p=0.14, Lt30.0% vs 47.6%:p=0.21), near-TFCC (Rt16.7% vs 19.0%:p=0.83, Lt30.0% vs 38.1%:p=0.56), distal radial side of radio-carpal joint (Rt20.0% vs 42.9%:p=0.08, Lt23.3% vs 28.6%:p=0.68), distal end of Ulna (Rt10.0% vs 42.9%:p=0.006, Lt16.7% vs 28.6%:p=0.31), feeding vessels from vascular channels were depicted at Lu (Rt53.3% vs 52.4%:p=0.95, Lt46.7 vs 66.7%:p=0.16), Radius (Rt20.0% vs 33.3%:p=0.29, Lt16.7% vs 23.8%:p=0.54), Triquetrum (Rt10.0% vs 42.9%:p=0.0057, Lt16.7% vs 33.3%:p=0.17) and Capitate (Rt6.7% vs 33.3%:p=0.013, Lt10% vs 33.3%:p=0.0395). The bone surface irregularity as a transverse diameter (Mean ±S.D.) at Lu of dominant hand in both groups were 1.26±0.33 vs 1.14±0.2 mm: p=0.21, respectively.

**Conclusions:** The frequency of feeding vessel's distributions in elderly adults were significantly higher at E.digiti minimi TS, distal end of Ulna and Triquetrum/Capitate vascular channels compared to those of younger adults. It is suggested that these differences are crucial to evaluate the age-specific synovitis with ultrasound.

**Disclosure of Interest:** None declared

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AB1199

#### DYNAMIC ULTRASOUND FOR MULTILEVEL EVALUATION OF MOTION AND POSTURE IN LOWER EXTREMITY AND SPINE

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**Background:** Evaluation of motion and posture is a crucial task in management patient with rheumatic diseases and pain. Integrative protocol including multilevel assessment of intrinsic/extrinsic muscles postural imbalance for disease staging and treatment efficacy control has not been finally developed.

**Objectives:** The aim was to study feasibility of multilevel motion and posture analysis using dynamic M-mode ultrasound in foot, ankle, gluteus region, pelvis and spine.

**Methods:** We included 21 patients (13 females, aged 18–52 y.o.) with clinically diagnosed reduced motility in spine, pelvis and lower extremity levels due to detected back leg, pain, muscle spasticity, joints effusion, tissue swelling, etc. Another healthy 20 patients (aged 18–50 y.o.) without movement restriction and pain were controls. We conducted precise physical tests, extensive neuromuscular ultrasound (US) using M-mode to evaluate muscle thickness, CSA and motion in intervertebral spaces, pelvis, intrinsic/extrinsic muscles in foot and ankle gluteus region and pelvis, central and peripheral trigger points identification.<sup>1</sup>

**Results:** We obtained sufficient quality panoramic scans on leg using convex 5–8 MHz probe in 2 approaches to evaluate structure and motion of extrinsic/intrinsic portion of muscles during one session. Thickness measurements of peroneal portion, plantar intrinsic foot muscles on the plantar surface in two transverse positions and one longitudinal using linear probe; contractility using M-mode tested in walking were most representative data. We evaluated different patterns of decreasing motility, contractility (muscle contracted/rested thickness) on M-mode during functional tests and walking in all levels in group 1 (p<0.05). We observed the preliminary correlation between the changes (muscle hypertrophy) in contralateral extrinsics and intrinsic muscles at the same levels, due to biomechanical instability; local areas of spasticity (trigger points) were successfully detected on distal/proximal leg, pelvis and spine. Documented pictures were collected and accessible for telemedical consulting.

**Conclusions:** Extensive evaluation of motion posture in foot, ankle, and gluteus region, pelvis and spine is feasible and informative protocol for patient with pain and rheumatic diseases. Further studies needed to evaluate reliability studies, comparative RCT using US, CAREN, static and dynamic balance tests, pressure analysis, and extensive molecular profiling, to study crosslinks with immune phenotype of the patients; and to develop educational programs.

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AB1200

#### FROM THE CALCANEUS QUANTITATIVE ULTRASONOGRAPHY (QUS) TO THE FEMORAL RADIOFREQUENCY ECHOGRAPHIC MULTI SPECTROMETRY (REMS): NON-INVASIVE APPROACHES TO DIAGNOSIS OSTEOPOROSIS PROPOSED BY F.I.R. M.O. FOUNDATION

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**Background:** The high prevalence of osteoporosis and its insidious development, often silent until a fracture occurs, make it necessary to resort to prevention by promoting early diagnosis and educational programmes for a healthy life style.

**Objectives:** To develop screening campaigns of the Italian population for the osteoporosis prevention thanks to the collaboration with F.I.R.M.O. Foundation (Fondazione Italiana Ricerca Malattie Ossee).<sup>1</sup>

**Methods:** An experienced medical staff administered to the afferent people the IOF "One minute risk test" questionnaire, (to detect the presence of clinical risk factors), together with a densitometric examination performed by a portable device aboard a mobile unit, in several Italian cities between 2011 and 2017.

The technique employed to assess bone status in 2011 and 2012 was calcaneus Quantitative Ultrasonography (QUS), applied to a peripheral skeletal site, which has been shown as effective in identifying osteoporotic men or post-menopausal women.<sup>2</sup> Although representing a low-cost and accessible approach, the heel measurement of speed of ultrasound (SOS) can be influenced by foot positioning, oedema and temperature.<sup>3</sup>

Since 2017, a novel non-invasive densitometric technique is available, which allows to evaluate the axial fragile bone sites (spine and femur). It is Radiofrequency Echographic Multi Spectrometry (REMS), that a multicentric clinical study has been shown to provide parameters highly correlated with DXA ones.

**Results:** As measured by calcaneus QUS in 7305 subjects, the prevalence rate of osteoporosis was approximately 18.7%, while the 42.6% had a T-score compatible with osteopenia. People with a QUS T-score <−2.5 was recommended to early undergo a DXA at lumbar and femoral sites and a specialist visit.

On the other hand, REMS examinations at femoral neck, performed on 397 people, revealed that osteoporosis resulted in 25% of the sample and osteopenia in 54%. Also in this case, people with a T-score  $< -2.5$  was suggested to perform a DXA, considering that the accuracy and operator-independent automatic analysis performed by REMS, make more reliable the obtained data.

**Conclusions:** Nowadays, with REMS introduction, F.I.R.M.O. foundation and the health system could avail themselves of a new non-invasive, rapid, easy-to-use and automatized technology for the prevention of osteoporosis.

§ Equal contributors listed in alphabetical order

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AB1201

#### ULTRASONOGRAPHY POWER DOPPLER(PDUS) IN EARLY ARTHRITIS. DOES 44 JOINT COUNT PREDICTE MORE ACCURETLY THE DEVELOPMENT OF RA THAN OTHER ULTRASOUND COUNTS?

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**Background:** Early rheumatoid arthritis is a diagnostic challenge for the rheumatologist since early treatment may be crucial for reaching remission and low rate of structural damage. Previous correlation studies between different ultrasonographic (US) scores suggested that few joint examination may be equivalent to more comprehensive ones about the inflammatory activity in established rheumatoid arthritis.

**Objectives:** To determine if the presence of basal power doppler US signal in patients with early arthritis by three different US joint counts (12, 28 or 44 joint count) may be equally useful in order to establish the risk of final diagnosis of rheumatoid arthritis (RA) according ACR criteria 1987 at a year of follow up.

**Methods:** We studied the presence of US Power Doppler (PD) signal on 28 joints (shoulders, elbows, wrists, MCPs, PIPs, knees), 44 joints (28 joints and in addition hips, ankles, tarsus and MTP joints) and in 12 joints (elbows, MCFs 2 and 3, wrists, knees and ankles), with a mid-range equipment GE L5 in 70 pacientes with suspected RA. The patients met at least one of the following inclusion criteria: a) Swelling in 2 or more joints b) pain in MCPs, MTPs and/or the wrists c) morning stiffness of more than 30 min with  $< 12$  months of duration of the symptoms and no previous steroid nor DMARDs treatment. At one year of follow-up was established whether patients met ACR 1987 classification criteria for RA or not. PD signal was scored 0–3, and PD score sum index (IPD) was the total sum of scores in each joint for 44, 28 and 12 joint counts. Correlations between 44, 28 and 12 joint US IPDs were studied as well. Statistical study: Chi-square, Fisher exact test, p univariate, Odds Ratio, Spearman correlation.

**Results:** The presence of basal power doppler signal in  $\geq 1$  joint of 44 (PD44) is associated to RA diagnosis at 12 months by ACR 1987 criteria,  $p=0.003$ ,  $OR=5.43^{1.71-17.24}$  but the presence of  $\geq 1$  joint with power doppler signal of 28 joints (PD28) did not ( $p=0.051$ ). The presence  $\geq 1$  joint with basal power doppler signal of 12 joints (PD12) was associated to RA diagnosis at 12 months with  $OR\ 3.11^{1-12-8.6}$   $p=0.026$  as well, so may predict development of RA. However, we missed 6/44 (14%) of patients that were not diagnosed of RA when we evaluate only 12 joints. We found high correlations between IPD44 and IPD28 (0.845), IPD44 and IPD12 (0.807) and between IPD28 and IPD12 sum scores (0.913).

BASAL VARIABLES n=70		RA YES	p (univariate)	OR	95% CI
PD 44	YES	38/52 (73,1%)	0,003	5,43	(1,71-17,24)
	NO	6/18 (33,3%)			
PD 28	YES	35/50 (70%)	0,051	-	-
	NO	9/20 (45%)			
PD 12	YES	32/44 (93,9%)	0,026	3,11	(1,12-8,60)
	NO	14/26 (53,7%)			

Abstract AB1201 – Figure 1

**Conclusions:** The presence of at least one joint with power doppler signal of 44 joints (PD44) on baseline visit may help to predict the RA diagnosis at 12 months of follow up according ACR 1987 criteria in patients with early RA, but PD28 did not. PD12 reduced joint count may help to predict RA as well but missed 14% of RA patients. Odds ratio rendered better information for different PD joint count about early identification of RA, whereas correlations were high between all different US joint scores. Further studies are required to decide the best US joint set for early identification of patients with early rheumatoid arthritis, but inclusion of ankle/foot joints may be important.

**Disclosure of Interest:** None declared

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AB1202

#### IS FLUORESCENCE OPTICAL IMAGING ASSESSMENT ASSOCIATED WITH ULTRASONOGRAPHY SYNOVITIS IN THE WRIST AND HAND OF RHEUMATOID ARTHRITIS PATIENTS?

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**Background:** Fluorescence optical imaging (FOI) has been used for assessment of inflammation (i.e. synovitis) in the hands and has in several cross sectional studies been compared with ultrasonography (US) and magnetic resonance imaging (MRI), using different, but not validated scoring systems.

**Objectives:** The primary objective was to examine the association between FOI and US for assessment of synovitis in the rheumatoid arthritis (RA) hands, in a longitudinal study, using a new validated and clinically feasible FOI scoring system.

**Methods:** 46 RA patients, eligible for induction or intensification of conventional synthetic or biological disease modifying anti-rheumatic drugs and with  $\geq 1$  clinically swollen joint in the hand, were included. FOI image-sets of both wrists and hands were obtained at baseline and 6 months' follow-up using a Xiralite system unit (nanoPET Pharma GmbH, Berlin, Germany). The patients received a bolus of i.v. indocyanine green (ICG) pulsion 10 s after starting the examination, which obtained 1 image/second for 6 min.

All FOI images were scored by two readers for synovitis at the wrist, 1st-5th metacarpophalangeal, 1st interphalangeal and 2nd-4th proximal interphalangeal joint levels in both hands, using the novel semiquantitative scoring system. Each joint was scored 0–3 (range 0–66) for synovitis. The readers were blinded to patient data, but not chronology and had previously showed a high intra- and inter-reader agreement (intra-class correlation coefficient (ICC):0.70–0.92).

For ultrasound assessment, a GE Logiq E9 US unit with a high frequency linear 6–15 ML probe and with Doppler settings according to published recommendations was used. Synovitis was scored from 0–3 for grey scale (GS) and Doppler (DP) using the OMERACT US synovitis scoring system by two trained assessors who had previously demonstrated high intra- and inter-reader agreement ( $wKappa:0.88-0.95$ ).

DAS28-CRP and swollen joint count (SJC) in the hand were assessed at both time points.

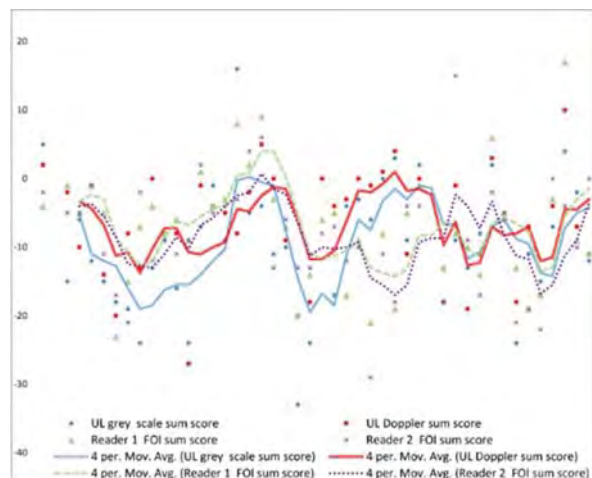
Descriptive statistics and the Wilcoxon signed-rank test were used to assess change in score over time. Agreement for status and change scores were assessed using single measure ICCs and spearman's correlation (SP). Responsiveness was assessed using standardised response mean (SRM).

**Results:** Median (IQR) total score at baseline was FOI 11.0 (6;19), GS 14.5 (8;22.), DP 8 (3;14), DAS28 5 (4.4;5.4) and SJC 6 (3;8) and improved with  $-7.8$  (-13;-3.5)  $-9$  (-15;-3.5),  $-5.5$  (-11;-0.5),  $-2$  (-2.9;- 0.8) and  $-4$  (-7;-2) at 6 months' follow up, respectively ( $p<0.01$ ). Figure 1 presents the change score and a trend line based on 4 patients' average score.

ICC and SP between FOI and US (GS and DP) total scores were low for both readers at baseline (range 0.3–0.4) ( $p<0.05$ ), and low to moderate (range 0.31–0.54) ( $p<0.01$ ) for change scores. The mean SRM for total change scores between baseline and 6 months' follow-up were good for all parameters (FOI:0.9,



GS:1.0, DP:0.8, DAS28:0.9 and SJC:1.0). The average sum time required to score one patient was 140 s.



**Abstract AB1202 – Figure 1.** Scatterplot for FOI and US changes sum score and 4 patient averages trendlines

**Conclusions:** This study shows a significant correlation and corresponding trendlines between FOI and US for change over time, and good responsiveness using the new FOI scoring system. FOI may therefore be used as an alternative to known imaging modalities for monitoring RA patients in clinical trials, and potentially in the daily clinical practice.

**Disclosure of Interest:** None declared

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#### AB1203 USE OF MAGNETIC RESONANCE IMAGING OF THE PELVIS TO DESCRIBE INFLAMMATORY CHANGES AT DIFFERENT ANATOMICAL SITES IN THE PELVIS WHICH ARE POTENTIALLY SPECIFIC FINDINGS IN PATIENTS WITH POLYMYALGIA RHEUMATICA

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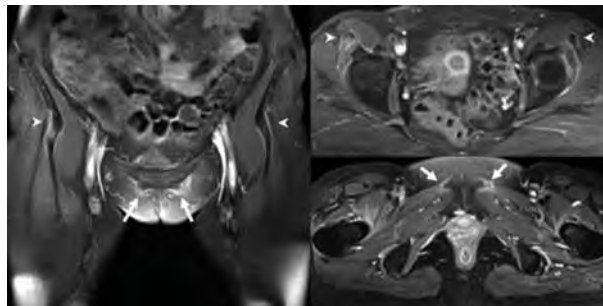
**Background:** Pelvic girdle pain is a common clinical symptom of patients with polymyalgia rheumatica (PMR). It also occurs in patients with rheumatoid arthritis (RA). The origin of this characteristic pain is not really clear, even though some imaging findings have been reported. However, this has neither changed pathophysiological thinking nor clinical practice related to diagnosis.

**Objectives:** To describe pelvic structures in PMR patients in detail which show signs of inflammation by magnetic resonance imaging (MRI) in order to find a disease specific pattern.

**Methods:** In a retrospective study we used MRIs of patients who had presented with clinical symptoms suggestive of PMR in our centre between 2015 and 2017. Only patients with complete MRI examinations, including contrast enhanced scans in coronal and transversal planes were included to be carefully examined by an experienced musculoskeletal radiologist (MF). After having first described all findings in much detail we developed a preliminary semiquantitative scoring system that assesses a total of 12 sites which appeared to be frequently involved. A total of 40 patients with pelvic girdle pain and complete data were identified from the hospital records. The median (25th/75th percentiles) age of the patients was 67 (55/73) years, the median symptom duration was 13 (6/22) weeks, 55% were female, the median C-reactive protein measured close to the day of the MRI examination was 1.9 (0.7/4) mg/dl, and the median erythrocyte sedimentation rate was 30 (17/43) after the 1st hour. Only 3 patients were rheumatoid factor positive, and 2 patients had anti-CCP antibodies. Ten patients had a diagnosis of RA (25%) in addition to the leading PMR like symptom.

**Results:** The MRI signal of interest for PMR is a post-gadolinium signal in T1 weighted pelvic images. The most frequently involved anatomic sites were: the hamstring tendon and the M.gluteus medius and minimus tendon near the greater trochanter in all cases, which were found to be bilaterally involved as was the proximal M.rectus femoris in all cases, and the insertion of the adductor muscles, especially the M.adductor longus at the inferomedial pubic symphysis in 90% of cases. Other sites were also, but less frequently, involved. We think that the involvement of 4 sites including either the M.rectus femoris or the M.adductor

longus is rather specific for PMR, see exemplary images below. There was no major difference between patients with and without RA.



**Abstract AB1203 – Figure 1**

**Conclusions:** This study suggests that there may be a MRI pattern specific for PMR. The target structure of the characteristically inflamed anatomic site seems to be the paratenon which implies that the pattern observed in PMR differs from the enthesitis seen in patients with spondyloarthritis. Prospective randomised trials are needed to further test and prove the clinical usefulness of this approach.

**Disclosure of Interest:** None declared

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#### AB1204 QUANTITATIVE MRI AND DYNAMOMETERS CAN DISTINGUISH MYOSITIS FROM HEALTHY CONTROL MUSCLE

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**Background:** Myositis is an autoimmune disease which can decrease quality of life and increase mortality. Clinical presentation includes muscle weakness, changes in muscle microstructure, myosteatosis, raised muscle enzymes and myalgia. Diagnosis is reliant on subjective clinical examinations, blood tests and invasive muscle biopsies. Quantitative MRI techniques such as diffusion tensor imaging (DTI) and fat fraction (FF) measurements offer non-invasive measurements, which could improve the understanding of muscle pathology and potentially inform diagnosis. DTI measures water diffusion within tissues which is sensitive to changes in muscle microstructure<sup>(1)</sup>. FF provides a quantitative measure of myosteatosis in muscles<sup>(2)</sup>. The use of these techniques could provide new imaging biomarkers in the diagnosis and management of myositis.

**Objectives:** To evaluate whether fat fraction, mean diffusivity and dynamometer measurements are sensitive enough to detect muscle differences in myositis patients compared to healthy controls.

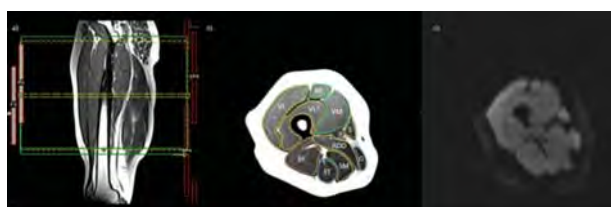
**Methods:** 10 active myositis patients (6 female, mean age 55±18) diagnosed according to the Bohan and Peter myositis criteria (mean CK 2,015±10,787) and 16 healthy controls (10 female, mean age 44±17), were imaged using STEAM-EPI diffusion and 2-point Dixon to obtain FF measurements. Myositis patients included 5 polymyositis, 3 dermatomyositis and 2 inclusion body myositis. Mean measurements of FF and mean diffusivity (MD) were obtained from regions drawn manually within the individual muscles of the quadriceps and hamstrings (image 1). No distinction was made between affected and unaffected muscles. In addition to MRI, all participants had knee extension and flexion power and torque measured on an isokinetic dynamometer and handgrip measurements on an isometric dynamometer. Differences were assessed using independent T-tests.

**Results:** FF and diffusion measurements were higher in myositis patients compared to healthy controls, whereas muscle power and torque were reduced (table 1). These results were consistent across both quadriceps and hamstrings.

**Abstract AB1204 – Table 1**

		Mean		Mean difference (95% CI)		Significance (p value)	
		Hams	Quads	Hams	Quads	Hams	Quads
FF (%)	Myositis	15.09	14.33	10.08	11.2	<0.001	<0.001
		(-9.21, 39.39)	(-16.95, 45.6)	(5.12- 15.05)	(5.79- 16.61)		
	Healthy	5.0	3.13				
		(-4.89, 14.82)	(-0.28, 6.54)				

		Mean	Mean difference (95% CI)	Significance (p value)			
MD (x10-3mm <sup>2</sup> /s-1)	Myositis	1.31 (1.15-1.47)	1.26 (1.05-1.47)	0.087 (0.00-0.17)	0.02 (-0.05, 0.09)	0.046	0.02
	Healthy	1.22 (0.69-1.75)	1.23 (0.75-1.72)				
Leg power (Watts)	Myositis	34.92 (-14.42, 84.25)	58.2 (-29.39, 145.77)	-25.05 (-43.71, 6.39)	-47.53 (-92.14, 12.92)	0.011	0.010
	Healthy	59.97 (18.88-101.07)	105.72 (18.48-192.96)				
Leg torque (N m)	Myositis	19.66 (-16.29, 55.62)	30.45 (-27.47, 88.36)	-18.01 (-31.7, 4.33)	-33.36 (-56.12, 10.57)	0.013	0.006
	Healthy	37.68 (6.8-68.55)	63.80 (6.98-120.63)				
Handgrip (kg)	Myositis	15.6 (-0.05, 31.25)		-18.74		<0.001	
	Healthy	34.34 (14.94-53.73)		(-25.4, -12.1)			



Abstract AB1205 – Figure 1

a) Sagittal (localiser) image of the thigh used in the planning of the Vibe-Dixon imaging volume (shown by the box). b) Regions of interest were drawn corresponding to the individual muscles of the thigh. c) Stimulated echo acquisition mode-Echo planar imaging (STEAM-EPI) diffusion image

**Conclusions:** MRI based FF and DTI measurements and dynamometer measurements can detect muscle differences between myositis and healthy control groups. These differences are consistent with increased myosteatosis, increased oedema and the effects of muscle fibre plasticity. These measures show potential as novel imaging biomarkers in the diagnosis and management of myositis.

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#### AB1205 PRECISION OF SERUM AND PLASMA TESTING IN ANTI-CARDIOLIPIN AND ANTI-B2 GLYCOPROTEIN-1 ANTIBODIES

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**Background:** Anti-cardiolipin (aCL) and anti-β2 glycoprotein-1 (β2GP1) antibody ELISA testing may be performed on serum, plasma, or both in accordance to the manufacturers' suggested protocols. There exists some variability in manufacturers' preference for serum or plasma. Various societal guidelines have published a preference for serum over plasma; however, there is scarcity of data assessing reproducibility between serum and plasma in aCL and β2GP1 testing.

**Objectives:** To determine reproducibility of aCL and β2GP1 testing between serum and plasma samples obtained in a routine clinical setting.

**Methods:** Patients with clinical serum draws for IgG/IgM aCL and β2GP1 antibodies were identified, and same-day, citrated plasma samples were obtained for repeat ELISA testing (QUANTA Lite, INOVA Diagnostics, San Diego, CA). Quantitative levels were determined for each isotype and further stratified into Negative (<15.0 GPL/MPL or U/mL), Weakly Positive (15.0–39.9 GPL/MPL or U/mL), or Positive (≥40.0 GPL/MPL or U/mL) reference categories. Differences were

compared using paired t-tests. Agreement between the reference categories were compared by kappa coefficients.

**Results:** Fifty patients were identified for study with 50 and 40 samples eligible for repeat aCL and β2GP1 plasma testing, respectively. Mean age was 49±18 years. 70% were female, 86% were Caucasian, 22% with systemic lupus erythematosus and 22% with antiphospholipid syndrome. As shown in Table 1, quantitative levels tended to be slightly higher in serum than plasma. Although a statistically significant difference was found for most of the antibodies tested, the difference between serum and plasma values were generally small. There was good agreement in reference category between serum and plasma. Kappa coefficients ranged from 0.70 to 1.00.

Abstract AB1205 – Table 1. – Reproducibility of anti-Cardiolipin and anti-β2 Glycoprotein-1 Testing in Serum versus Plasma

	Quantitative Levels		Agreement to Reference Category	
	N Samples	Mean Difference (sd) <sup>1</sup>	p-value	κ Coefficient (95% CI)
IgG aCL	50	0.4 (14.8) GPL	0.84	0.81 (0.64–0.98)
IgM aCL	50	3.3 (8.5) MPL	0.008	0.73 (0.56–0.91)
IgG	40	1.4 (4.2) U/mL	0.038	1.00 (1.00–1.00)
β2GP1				
IgM	40	4.6 (8.9) U/mL	0.002	0.74 (0.54–0.94)
β2GP1				

1: Serum-Plasma. **Abbreviations:** aCL=anti cardiolipin, β2GP1=anti-β2 glycoprotein 1, sd=standard deviation

**Conclusions:** There appears good reproducibility of IgG/IgM aCL and β2GP1 antibody ELISA results between serum and plasma.

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#### AB1206 DYNAMIC CONTRAST ENHANCED (DCE)-MRI IN RELATION TO INFLAMMATORY MARKERS IN SERUM AND JOINT FLUID: INITIAL DATA AND VALIDATION IN FOUR MOST COMMON KNEE ARTHRITIC DISEASES

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**Background:** Biomarker science has advanced to aid in distinguishing between different forms of arthritis: inflammatory arthritides such as rheumatoid arthritis (RA) and psoriatic arthritis (PsA) and osteoarthritis (OA). Biomarkers are also used to assess disease activity. Diagnostic serum biomarkers such as rheumatoid factor (RF) and cyclic-citrullinated peptide (CCP) and assays of disease activity such as C-reactive protein (CRP), and multi-biomarker assays have utility but lack complete sensitivity and specificity. Increasingly quantitative imaging biomarkers may fill an important gap in disease identification and assessment.

**Objectives:** 1) To investigate the association between imaging measures of inflammation in the synovium of the knee joint and systemic levels of CRP in patients with RA, PsA and OA. 2) Investigate how imaging and clinical markers correlate to IL-6 levels from joint fluid in different patient cohorts.

**Methods:** 38 patients with a flare of pain in the knee were recruited. 12 were diagnosed with RF positive (+) RA, 6 with RF negative (-) RA, 6 PsA, and 14 OA, according to ACR/EULAR criteria. CRP in blood and IL-6 levels from joint fluid were determined. Patients underwent MRI, including Dynamic Contrast Enhanced (DCE)-MRI exam prior to an ultrasound-guided arthrocentesis.

MRI were scored for synovitis<sup>1</sup> and DCE-MRI were quantified using Dynamic Enhanced MRI Quantification (DEMRIQ) method, extracting the volume of enhancing voxels (Nvoxel), Initial Rate of Enhancement (IRE), Maximum Enhancement (ME). Inflammation was quantified as IRExNvoxels and

MExNvoxels.<sup>2</sup> Correlation between all clinical scores and all imaging parameters was done using Spearman rho, with significance levels of  $p < 0.05$ .

**Results:** The imaging markers of perfusion in the synovium of the knee (MExNvoxels and IRExNvoxels) were the only imaging measures, which showed a very high association with CRP in both RF +RA ( $r=0.92/0.97$ ,  $p < 0.05$ ) and PsA patients ( $0.93/0.99$ ,  $p < 0.05$ ), whereas all other imaging markers of inflammation showed no statistical association with blood levels of CRP in these diseases. We found no association between CRP and any imaging assessed scores of inflammation in either RF- RA or OA. In addition, only RF +RA patients showed a positive moderate to high association between MExNvoxels and IL-6 ( $r=0.66$ ,  $p < 0.05$ ) in the knee joint aspirate.

**Conclusions:** Quantitative imaging and blood biomarkers of inflammation, such as DCE-MRI parameters and CRP, appear to relate differently to each other in the four most common knee arthritic diseases, RF +RA, RF- RA, PsA and OA. DCE-MRI may have specific utility in differentiating these conditions and their disease activity.

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AB1207

#### CORRELATION BETWEEN CLINICAL FINDINGS AND ULTRASONOGRAPHY IN EVALUATING PAINFUL RHEUMATOID SHOULDER

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**Background:** Shoulder pain is one of the most common complaints encountered in patients with rheumatoid arthritis (RA) <sup>1</sup>. In recent years ultrasonography (US) became an essential tool in diagnosing rheumatic diseases <sup>2</sup>. As clinical examination often does not allow an exact diagnosis, the agreement between both methods needs to be discussed to know how much the US add benefits to clinical examination.

**Objectives:** To determine the agreement between clinical examination and ultrasound in evaluating shoulder pain in rheumatoid.

**Methods:** A cross-sectional study including thirty RA patients, meeting the ACR/EULAR classification criteria for RA complaining of shoulder pain. They were recruited from rheumatology outpatient clinic in Mansoura University Hospitals. The sixty shoulders of the thirty patients were examined clinically by inspection, palpation and special tests, then fully examined by ultrasound including biceps tendon, subacromial bursa, rotator cuff tendons and acromioclavicular joint.

**Results:** Agreement among clinical examination and US was examined using Cohen's kappa. There was slight agreement between clinical examination and US regarding biceps tenosynovitis with  $k=0.206$ , fair agreement regarding acromioclavicular osteoarthritis with  $k=0.392$  and SASD bursitis with  $k=0.233$ . There was also moderate agreement between clinical examination and US examination of the shoulder in case of supraspinatus tendinopathy with  $k=0.464$ . Data were statistically significant ( $p < 0.001$ ). The overall agreement between clinical examination and ultrasound was poor.

**Conclusions:** Clinical examination of shoulder pain in rheumatoid arthritis is not accurate, insufficient. It should be confirmed with US examination during the initial evaluation of the shoulder to give reliable data and differentiate between different pathologies.

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AB1208

#### THE ROLE OF ULTRASOUND IN THE DISCOVERY OF INTERSTITIAL CHANGES IN THE LUNGS IN PATIENTS WITH SYSTEMIC CONNECTIVE TISSUE DISEASE

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**Background:** Interstitial lung disease (ILD) is one of the most serious lung complications in patients with connective tissue disease (CTD), most commonly in patients with systemic sclerosis (SSc). High-resolution Computed Tomography is a gold standard for assessing ILD. Ultrasound examination of the lungs has been increasingly used lately to evaluate the existence of interstitial changes (B lines) in the lungs.

**Objectives:** To determine whether there is a significant difference in the presence of B lines on lung ultrasound examination in patients with SSc compared to patients with other CTD and healthy controls. Also, to investigate if there is a significant difference in the presence of B lines on lung ultrasound examination in patients with diffuse SSc compared to patients with limited SSc.

**Methods:** The study included 150 people of both sexes, aged between 19 and 81, who were examined at the Institute of Rheumatology in Belgrade. In the first group there were 55 patients with SSc (28 with diffuse and 27 with limited form of SSc), in the second group 45 patients with other CTD (16 with rheumatoid arthritis, 16 with systemic lupus erythematosus lupus and 13 with Sjogren syndrome) and in the third group 50 healthy subjects who were matched by gender and age with other two groups. At the ultrasound examination, the number of B lines was determined in all segments of the lungs. A positive ultrasound finding was considered to be one with 3 or more B-lines in at least two adjacent ultrasound scanning fields or one with more than 5 B-lines in any single field of ultrasound scanning.

**Results:** There was statistically significant difference in positive findings between the group of subjects with SSc and the group of healthy subjects (65,5% vs. 2%;  $p < 0.001$ ) and between the group of subjects with SSc and the group with other CTD (65,5% vs. 13,3%;  $p < 0.001$ ). Also, it was shown that there was statistically significant difference in positive findings between the group of subjects with diffuse SSc and the group with limited SSc (85,7% vs. 44,4%;  $p < 0.001$ ).

**Conclusions:** The conducted study confirmed that the presence of B lines on lung ultrasound examination is significantly more frequent in patients with SSc, especially in the patients with diffuse SSc.

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AB1209

#### USEFULNESS OF IMAGENOLGY TO DIFFERENTIAL DIAGNOSIS IN PATIENTS WITH PRESUMED SERONEGATIVE RHEUMATOID ARTHRITIS AND OTHER ARTHROPATHIES

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**Background:** It is difficult to make a differential diagnosis between seronegative RA and other inflammatory arthropathies. Many patients could be wrong diagnosed followed of expensives treatments.

**Objectives:** To assess the usefulness of X-rays of hands and feet (X-rays), Ultrasound (US) and Magnetic Resonance Imaging (MRI) to discard false positive diagnosis of seronegative RA from real-world evidence.

**Methods:** An analysis from medical records of patients with presumptive seronegative RA diagnosis reportedly seronegative for both rheumatoid factor and anti-cyclic citrullinated peptide antibodies and clinical criteria of RA, in the period between July 2016 and ; June of 2017 who were assessed by imagenology (X-rays, US or MRI) in a centre of rheumatoid arthritis to confirm diagnosis or discard it. Laboratory, and imagenology data was retrospectively analysed and multivariate analysis was performed to determinate the usefulness of imagenology.

**Results:** 360 patients were received in the centre with presumptive diagnosis of RA in the period, mean of age was 58 years, 80,9% females and 19,1% males. X-



rays shows only 3,59% of patients with erosions, 38,6% were positive for Osteoarthritis (OA), and 58,6% of patients without erosions. From patients without erosions, 36% were confirmed for RA and 13,4% for OA by US; on the other hand 37% was confirmed for RA and 20% for OA by MRI. A total of 94 patients (26,1%) had a final diagnosis of seronegative RA, while (261) patients 72,5% were confirmed for Osteoarthritis,<sup>5</sup> 1,4% were classified in other arthropathies.

**Conclusions:** According with our findings the screening by imagenology is a useful tool with low cost to make a differential diagnosis of seronegative RA and other arthropathies. In order to improve outcomes through well-defined treatments and to save high cost treatments for pathologies with more precise diagnoses.

**Disclosure of Interest:** None declared

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AB1210

#### ANKLE BRACHIAL INDEX FOR THE DIAGNOSIS OF SUBCLINICAL ATHEROSCLEROSIS USING CAROTID INTIMA MEDIA THICKNESS IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENT IN SANGLAH HOSPITAL

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**Background:** Atherosclerosis and its complications in Systemic Lupus Erythematosus (SLE) patients occurred more rapidly than the general population. Early detection of atherosclerosis is currently a challenge for clinicians. Angiography as a gold standard diagnosis of atherosclerosis is invasive, has a limitation. The surrogate marker carotid intima media thickness (CIMT) examination with B-mode ultrasonography has been used widely and validated. The limitation of this examination is operator dependence. Ankle brachial index (ABI) examination is simpler, cheaper, objective and widely available and is expected to be used for the diagnosis of subclinical atherosclerosis.

**Objectives:** to determine the sensitivity, specificity, positive predictive value and negative predictive values of the ABI to establish the diagnosis of subclinical atherosclerosis in SLE patients.

**Methods:** A cross sectional study was enrolling 56 subjects and was conducted from September 2016 to July 2017 at Sanglah Hospital, Denpasar, Bali, Indonesia. We used 2 × 2 cross table to determine the sensitivity, specificity, positive predictive value and negative predictive values of ABI to establish the diagnosis of subclinical atherosclerosis.

**Results:** Of the 56 samples, 48 people (85.7%) were female. The area under ROC curve was 0708 (70,8%), p=0041. ABI examination to diagnose subclinical atherosclerosis in patients with SLE with a cutoff value of 0.95 has a sensitivity of 70%, specificity of 76.1%, 38.9% positive predictive value, and negative predictive value of 92.1%. The best cut-off value of ABI as a diagnostic tool for subclinical atherosclerosis in SLE patients is <0.95.

**Conclusions:** Examination with ABI can be considered as an alternative diagnostic when CIMT is not available. The diagnostic value of ABI is reliable enough for screening and diagnostic confirmation of subclinical atherosclerosis in patients with SLE.

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AB1211

#### UTILITY OF PET/CT FOR THE DIAGNOSIS AND DISEASE MANAGEMENT: A STUDY OF 88 PATIENTS FROM AN AUTOIMMUNE DISEASES HOSPITAL UNIT IN A 2-YEAR PERIOD

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**Background:** 18F-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography (18F-FDG PET/CT) is a non-invasive imaging technique commonly used in clinical oncology. 18 F-FDG accumulation is recognised as useful for diagnosing and monitoring the response to therapy in patients with some inflammatory disorders, but the role of the PET/TC in the management of these diseases is debated.

**Objectives:** The aim of this study was to investigate the role of 18F-FDG PET/CT in the diagnosis of the disease and assessing disease activity in an autoimmune diseases unit, and to evaluate if the results of this image technique imply a change in clinical management.

**Methods:** We retrospectively reviewed all 18F-FDG PET/CT requested since August 2015 to August 2017 by our unit. Data collected were: patient demographics, reason for PET request, PET results and change in therapy.

**Results:** PET/CT were performed in 88 patients and were positive in 68 (77,3%) cases. Patients (49 women/39 men) had a mean age of 58,1±15,7 years (range, 27–92 years). The clinical diagnosis at the moment of ordering the PET/CT were: sarcoidosis (n=45), large-vessel vasculitis (LVV) (n=16), immunoglobulin G4-related disease (IgG4-RD) (n=9), collagen-vascular diseases (CVD) (n=7), mesenteric panniculitis (n=4), myopathy (n=4), polymyalgia rheumatica (PMR) (n=2) and ANCA-associated vasculitis (n=1). (See **table 1**).

**Abstract AB1211 – Table 1**

	Sarcoidosis	LVV	IgG4-RD	CVD	Mesenteric panniculitis	myopathy	PMR
n	45	16	9	7	4	4	2
women	27 (60%)	13 (81,2%)	1 (11,1%)	4 (57,1%)	1 (25%)	2 (50%)	1 (50%)
age	50,9 (27–83)	72,5 (29–92)	63,7 (48–80)	53 (30–80)	60,5	66,2	72,5
PET to the diagnosis	9 (20%)	2 (12,5%)	1 (11,1%)	3 (42,9%)	3 (75%)	2 (50%)	2 (100%)
PET to disease activity	36 (80%)	14 (87,5%)	8 (88,9%)	4 (57,1%)	1 (25%)	2 (50%)	0
Positive PET/TC	36 (80%)	11 (68,7%)	6 (66,7%)	6 (85,7%)	3 (75%)	3 (75%)	2 (100%)
Change of therapy	31 (68,9%)	11 (68,7%)	6 (66,7%)	7 (100%)	2 (50%)	3 (75%)	2 (100%)

PET results supported a change in therapeutic management in 71.6% of the cases. In the group of sarcoidosis there was a change in treatment in 68.9% of cases. PET/TC revealed extrapulmonary manifestations in 57,8%. All patients with extracranial manifestations of giant cell arteritis (GCA) showed uptake in PET/TC. That result supported the clinical diagnosis, although negative temporal artery biopsy. PET was useful in the diagnosis and treatment of IgG4-RD in 66,7% of cases. PET scan did not find malignancy in inflammatory myopathies nor mesenteric panniculitis.

**Conclusions:** PET/TC is an increasingly utilised in our patients with inflammatory disorders as a support for the diagnosis and management. PET/TC detection extrapulmonary sarcoidosis may have therapeutic and prognostic clinical implications. PET may be useful in patients with GCA suspicion with negative biopsy and extracranial symptoms. More studies will be necessary to establish the real role of PET/TC in autoimmune and inflammatory diseases.

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AB1212

#### ANALYTICAL VALIDATION OF AN INTERFERON-INDUCIBLE GENE EXPRESSION KIT AS A POTENTIAL DIAGNOSTIC TEST FOR ANIFROLUMAB

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**Background:** Anifrolumab, a fully human monoclonal antibody that binds to the type I interferon receptor, is in Phase III development for moderate to severe systemic lupus erythematosus (SLE). Patients with greater interferon-inducible gene signatures (IFNGS) have enhanced response to anifrolumab treatment.<sup>1</sup>

AstraZeneca and QIAGEN developed an *in-vitro* diagnostic test for interferon-inducible gene expression (IFIGx). Efficacy of anifrolumab will be evaluated in patients with high and low IFNGS.

**Objectives:** We aimed to analytically validate the IFIGx kit for use in a pivotal clinical study and potentially to support future regulatory submission.

**Methods:** The IFIGx kit measures expression of four interferon-inducible genes (IF127, IF114, IF114L and RSAD2) compared with three housekeeping genes. Measurements were performed on mRNA extracted from whole blood from adults with SLE. A score was generated that identified patients as "IFNGS test-high" or "IFNGS test-low." Analytical validation involved six studies measuring lot interchangeability, linearity, repeatability, reproducibility, cross contamination, and system verification.

**Results:** Repeatability was 100%. Reproducibility was >96%. No cross contamination was observed. Results of all studies validated the IFIGx kit (table 1).

#### Abstract AB1212 – Table 1

##### Summary of Analytical Validation of Anifrolumab IFIGx Test

Study	Description	Results
Lot interchangeability	Verification that scores and assay Ct values were robust when different lots of kit components were used Acceptance criterion was <0.58 Ct	<b>Lot interchangeability verified</b> Largest observed change=0.16 Ct
Linearity	Verification, using linear and quadratic regression analyses, that mRNA input concentration (10 ng/μL) is in assay's linear range	<b>Linearity verified</b> Change in score over the concentration range on either side of 10 ng/μL=0.0043 Ct
Repeatability	Verification of Dx result repeatability when the same operator tested 60 random samples using the same kit lot and instrument	<b>Repeatability verified</b> Observed repeatability=100%
Reproducibility	Verification of Dx result reproducibility when multiple operators tested 48 random samples using multiple kit lots and instruments at different sites For verification, overall rate of correct calls must be ≥95%	<b>Reproducibility verified</b> Overall rate=99.7% After six samples with values close to the cut-off were added for further confirmation, overall rate=96.5%
Cross contamination	Investigation of inter- and intra-run cross contamination	<b>No cross contamination</b> No cross contamination found in reverse transcription or PCR steps
System verification	Verification of functionality and utility of the IFIGx software and IFIGx assay package	<b>System verification confirmed</b> Software flags produced as expected

Ct, cycle threshold (PCR cycle at which fluorescence rises above background level); Dx, diagnostic; IFIGx, interferon-inducible gene expression; PCR, polymerase chain reaction; mRNA, messenger ribonucleic acid.

**Conclusions:** The IFIGx kit was shown to be a robust, reproducible diagnostic test for IFNGS. The IFIGx kit has demonstrated value in prior anifrolumab studies,<sup>1</sup> and will be used both for patient stratification in Phase III studies and to support anifrolumab regulatory filings.

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#### AB1213

##### ULTRASONOGRAPHIC EVALUATION OF THE HIP JOINTS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS AND PSORIATIC ARTHRITIS: ASSOCIATED WITH CLINICAL AND LABORATORY MARKERS, IMAGING AND FUNCTIONAL OUTCOMES

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**Background:** The hip joints are frequently involved in spondyloarthritis (SpA). Should ultrasonography (US) be additionally used for clinical assessment of disease in patients (pts) with SpA.

**Objectives:** to detect by US synovitis of the hip joints and to analyse the correlation between US finding and magnetic resonance imaging (MRI) and/or X-ray sacroiliitis, clinical and laboratory markers and functional status in pts with axial SpA (axSpA) and psoriatic arthritis (PsA).

**Methods:** 13 pts (7M/6F) with definite axSpA (7 with ankylosing spondylitis (AS) and 6 with non-radiographic nrSpA:ASAS) and 7 pts (4M/3F) with PsA (CASPAR) of similar age [median (IQR), 44<sup>35–55</sup> vs 42<sup>34–56</sup> years] and disease duration [7 (1–10) vs 9<sup>7–10</sup> years] were enrolled. US examination (Mindray DC-N6, C5–2 MHz probe) included bilateral of the hip joints according to the EULAR US Scanning App ([www.eular.org](http://www.eular.org); <http://ultrasound.eular.org>). MRI of sacroiliac joints (SIJ) was performed on Signa HDxT GE, 1.5 T. The bone marrow oedema on MRI (STIR) considered as active MRI sacroiliitis (MRI-SI).<sup>1</sup> X-ray of SIJs (modified New York criteria), functional status (BASFI), disease activity indices (ASDAS-CRP, DAPSA), laboratory tests (CRP, ESR, HLA-B27) were assessed.

**Results:** History of hip involvement was present in 7/20 (35%) pts who had ≥1 tender hip joint. 9/20 pts (45%) had US – synovitis of the hip joints. All pts were divided into two groups: g1(n=9) – US synovitis «+» (at least one hip joint), g2(n=11) – US -synovitis «-». Pts from g1 had higher CRP and BASFI compared to g2 (table 1). Elevated CRP ≥25 mg/L and ESR ≥30 mm/h, as well as MRI- and X-ray -SI were detected more often in g1pts than g2. But other parameters did not differ between the groups (table 1). US – synovitis of the hip joints was positively correlated with CRP (r=0.489, p<0.05), MRI-SI (r=0.688,p<0.05), X-ray-SI (r=0.634, p<0.05) and BASFI (r=0.541, p<0.05).

#### Abstract AB1213 – Table 1. Association between the US- synovitis of the hip joints and clinical and laboratory markers, imaging and functional outcomes

Parameters	US-synovitis "+" (n=9)	US-synovitis "-" (n=11)	P*
Age, years	44 (26–49)	46 (40–57)	.294
Duration since diagnosis, years	5 (1–10)	9 (7–10)	.551
AS/nrSpA/PsA	4 (57)/3 (50)/2 (28.5)	3 (39)/3 (50)/5 (71)	.411
Male sex	6 (67)	5 (45)	.456
HLA-B27	6 (67)	5 (45)	.456
CRP, mg/l	38 (6.7–51)	7.7 (3–19.2)	.031
Elevated CRP≥25	6 (67)	1 (9)	.031
ESR, mm/h	30 (16–39)	11 (6–25)	.080
Elevated ESR≥30	5 (55.5)	1 (9)	.027
ASDAS-CRP	3.4 (2.1–4.5)	2.7 (1.7–4.2)	.294
DAPSA	33 (19.6–46.4)	12.4 (12.3–12.4)	.190
BASFI (0–10)	5 (4–6)	3 (1.7–4)	.015
BASFI>4	6 (67)	2 (18)	.030
MRI-SI	9 (100)	5 (45)	<0.001
X-ray SI	9 (100)	5 (45)	<0.001

Numbers are medians (IQR) and n (%); \* Mann-Whitney U-test.

**Conclusions:** US – synovitis of the hip joints was associated with CRP, MRI- and X-ray- SI and severe functional disability in SpA pts. US evaluation of the hip joints may be used for identifying SpA pts with high risk of the disease progression at an early stage.

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**Disclosure of Interest:** None declared

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#### AB1214

##### BONE MINERAL DENSITY AND T-SCORE EVALUATION IN A GROUP OF PATIENTS WITH RHEUMATOID ARTHRITIS USING A NEW ULTRASOUND METHOD: ECHOS – GENODYNAMIC - A PILOT STUDY –

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**Background:** There is a great need of a screening programme for osteoporosis in the general population and even more amongst the rheumatologic patients, with additional risk factors. Although DXA is the gold standard for diagnosing osteoporosis, it is not appropriate for screening, because of its' limitations regarding ionising radiation, but also the massive machine, that needs dedicated spaces and specialised operators, all in all, involving high costs.

**Objectives:** To apply a new method that integrates ultrasonography with radiofrequency signals from an echographic scan, in order to evaluate the bone mineral

density (BMD) and T-scores in patients with rheumatoid arthritis (RA), compared to a control group.

**Methods:** We enrolled 150 menopausal women, 75 diagnosed with RA and 75 age matched controls. The controls were selected considering the lack of both an inflammatory disease and history of corticotherapy.

All patients in the study group were under monotherapy with a conventional synthetic DMARD and they are or have been under corticotherapy during the evolution of RA.

The BMD and T score were evaluated using a quantitative ultrasound Echolight machine. There were two evaluators for both lots, on order to minimise the inter-observer variability.

**Results:**

Abstract AB1214 – Table 1

	Study group	Control group
Age distribution (years)	63,24 <sup>49</sup> – 85	64,19 <sup>41</sup> – 85
Menopause age (years)	46,9 (34–60)	45,78 <sup>30</sup> – 55
BMI (kg/m <sup>2</sup> )	25.97 (15.63–34.86)	26.83 (18.36–33.67)
Period since dg of RA (years)	7.26 (5–12.5)	–

13% of the patients in the study group were under corticotherapy at the moment they were recruited in the study and 87% were treated with cortisone before, at some point during the evolution of RA. The average dose followed for more than 2 weeks was 8.8 (5–15) mg prednisone/day. The average corticotherapy period of 2.6 (0.5–14) months.

For the lumbar vertebrae (L1-L4), the average T score in the study group was –1.81, while the control group had a T score of –1.11. For the femoral neck, the average T score for both hips was –1.73 for the study group and –1.04 for the controls.

The spine average BMD was 0.92 g/cm<sup>2</sup> in the study group, compared to 1.16 g/cm<sup>2</sup> in the control group. For the femoral neck, the study group average BMD was 0.72 g/cm<sup>2</sup>, while in the control group it was 0.94 g/cm<sup>2</sup>.

**Conclusions:** The differences between the two groups were significant, but still in the osteopenia interval. The significance of these results translates into an increased fracture risk and a longer treatment duration in the study group.

At this point, this is a preliminary study, but we plan to continue it by comparing these results to DXA results for the same patients, in order to evaluate the cost-effective superiority of this portable, radiation-free technique, in a screening programme.

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**Disclosure of Interest:** None declared

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AB1215

#### MINIMAL INVASIVE ULTRASOUND-GUIDED PAROTID GLAND BIOPSY IN CADAVERS DONE BY RHEUMATOLOGISTS

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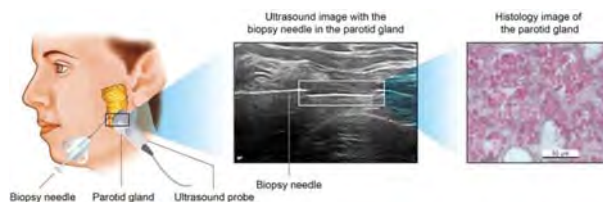
**Background:** In daily practice, surgical biopsy of minor salivary glands is routinely performed for the diagnosis of Sjögren's syndrome. The classification criteria for Sjögren's syndrome imply specific positive labial salivary gland biopsy findings. Surgical biopsies of the minor labial glands may result in up to 6% of patients in various complications, e.g. numbness of the lower lip. On the other hand, adverse events following core needle biopsies of the parotid gland in non-rheumatological settings were reported as very rare. Even so parotid gland biopsies require a more demanding surgical expertise mainly to protect the facial nerve.

**Objectives:** The objective of this study was to assess the feasibility and to determine the presence of parotid gland tissue in minimally invasive ultrasound-guided

parotid gland biopsies in cadavers performed by rheumatologists using histology as a gold standard.

**Methods:** Two senior rheumatologists obtained under direct ultrasound visualisation in in-plane technique biopsies of 8 parotid glands from 4 different cadavers using a core biopsy needle (core biopsy needle 18G). One biopsy per gland was taken and was subsequently stored. The direction of the bioptic access is shown in Figure 1. The specimen underwent histological examination by an experienced pathologist.

**Results:** All histological exams showed typical parotid gland tissue. Notably, no facial nerve tissue or major vessels could be detected in the biopsy material.



Abstract AB1215 – Figure 1

**Conclusions:** In this cadaveric feasibility study, we demonstrated that minimally invasive ultrasound guided parotid core biopsy is a highly precise and easy method to obtain salivary gland tissue.

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AB1216

#### QUANTITATIVE EVALUATION OF THERAPEUTIC CHANGES IN DIGITAL PSORIATIC ARTHRITIS WITH CONTRAST ENHANCED DUAL ENERGY COMPUTED TOMOGRAPHY IODINE MAP

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**Background:** Dual Energy Computed Tomography (DECT) iodine map is highly sensitive in depicting the inflammatory changes of psoriatic arthritis (PsA). A modified PsA Magnetic Resonance Imaging Scoring System (mPsAMRIS) was developed to assess the severity of PsA on DECT iodine map<sup>1,2,3</sup>. DECT iodine map also enables the calculation of iodine uptake in the lesion, which provides a more direct measure of disease activity<sup>4</sup>. However, the usefulness of DECT in evaluating the therapeutic effect of PsA by using iodine quantification, is still undetermined.

**Objectives:** To assess the validity of DECT iodine map in evaluating the therapeutic effect of PsA by iodine quantification.

**Methods:** The study included symptomatic PsA patients who underwent two consecutive contrast-enhanced DECT of hand or foot, prior and post medical intervention. All images were independently evaluated by two radiologists. Each symptomatic joint and matched non-symptomatic control joint were scored with mPsAMRIS. To measure the iodine uptake, the region of interest was selected at the level where the joint was most affected. The treatment effect of mPsAMRIS and iodine uptake was calculated by subtracting the results of the matched non-symptomatic joints.

**Results:** The demographics and clinical characteristics of enrolled patients are shown below.

Abstract AB1216 – Table 1

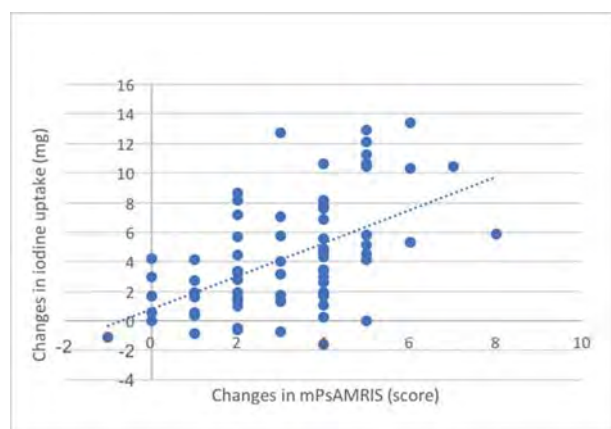
Demographic and patient Characteristics			
Characteristic	All patients	Men	Women
Number of patients	26	17	9
Mean age (yr)	50.6 (22–89)	54.2 (25–89)	45.2 (22–68)
Mean psoriasis duration (yr)	13.1 (0–41)	12.3 (0.5–35)	14.1 (0–41)
Mean current joint symptom duration (mo)	26.9 (1–192)	40.3 (1–192)	4.5 (1–120)
Fulfilled CASPAR criteria	26	17	9
Mean interval between two DECTs (mo)	7.0 (4–12)	7 (4–12)	6.4 (4–11)



Inter-reader agreement for mPsAMRIS was moderate or sufficient (weighted  $\kappa(w)$  =0.57 for pre-treatment; weighted  $\kappa(w)$ =0.70 for post-treatment, respectively). Inter-reader agreement for iodine quantification for pre- and post-treatment showed significant correlation (Spearman's  $\rho$ =0.93  $p$ <0.005, Spearman's  $\rho$ =0.95  $p$ <0.005, respectively).

Both mPsAMRIS and iodine uptake showed significant improvement after treatment for both readers (Wilcoxon signed-rank test:  $z$ =7.37,  $z$ =5.98 for reader 1,  $z$ =7.38,  $z$ =6.20 for reader 2,  $p$ <0.005 for all  $z$ ).

The treatment effect of mPsAMRIS and iodine uptake showed significant correlation (Spearman's  $\rho$ =0.56  $p$ <0.005 for reader 1, Spearman's  $\rho$ =0.57  $p$ <0.005 for reader 2). Graph shows the correlation between change of mPsAMRIS score and iodine uptake.



Abstract AB1216 – Figure 1

**Conclusions:** A significant improvement of inflammatory changes in PsA was confirmed by iodine uptake post-treatment, which was in-keeping with mPsAMRIS, and there was a strong correlation between the mPsAMRIS scoring system and iodine quantification. Therefore, iodine quantification may be useful in evaluating the treatment effect of PsA. Furthermore, changes in iodine uptake were observed even with small changes of mPsAMRIS, thus iodine uptake may provide a more sensitive and detailed measure of inflammatory activity in PsA.

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**Disclosure of Interest:** None declared

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#### AB1217 FLUOROMETRIC IMAGING FOR EARLY DIAGNOSIS AND PROGNOSIS OF RHEUMATOID ARTHRITIS

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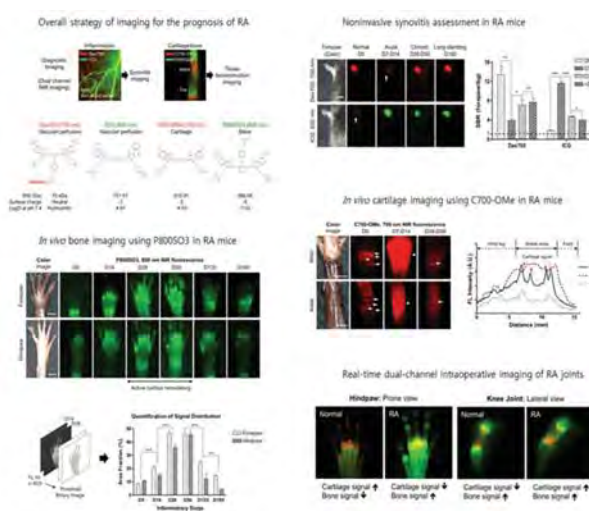
**Background:** Early diagnosis and monitoring of disease progress are of significant importance in the effective treatment of rheumatoid arthritis (RA), because the continuing inflammation can lead to irreversible joint damage and systemic complications. However, using imaging modalities for the prognosis of RA remains challenging, because no tissue-specific guidelines are available to monitor the progressive course of RA

**Objectives:** We report fluorometric imaging of RA for early diagnosis and prognosis, using structure-inherent targeting of the blood vessel, bone, and cartilage

**Methods:** we conducted dual channel near-infrared (NIR) fluorescence imaging, by using NIR light in the wavelength range of 700–800 nm and NIR fluorophores, to monitor the pathophysiologic processes of RA. In RA mice, we intravenously injected two NIR fluorophores—indocyanine green (ICG, 800 nm) and DEX700 (700 nm)—that have the characteristics of vascular perfusion agents in order to identify the severity of joint inflammation and the corresponding changes, on the

basis of differences in fluorescence intensity. In addition, for monitoring the changes in cartilage and bone on the basis of the progression of arthritis, we also intravenously injected C700-OMe (700 nm), a cartilage-targeting NIR fluorophore with an affinity for hyaluronic acid and glycosaminoglycan and P800SO3 (800 nm), a bone-targeting agent that has a strong binding affinity for bone minerals such as hydroxyapatite and calcium phosphate.

**Results:** In the acute inflammatory stage of arthritis, ICG with a lower molecular weight showed a significantly higher signal-to-background ratio (SBR) than DEX700 ( $p$ <0.05). But, in the chronic inflammatory stage, DEX700 showed a higher SBR value than ICG ( $p$ <0.05). The changing tendency of SBR value obtained from ICG showed similar to those of the clinical arthritis score in RA mice. In the fluorescence images of the mouse cartilage with C700-OMe before arthritis induction, very clear and distinct lines were observed in the fore paw and ankle joints. In the images obtained after arthritis was induced, these lines were lost, indicating cartilage destruction due to the progression of arthritis. A fluorescence image of the bone was obtained 24 hour after the injection of P800SO3; in this image, it was difficult to view the bone shape of joints especially in the fore paw before arthritis induction, because of a very low fluorescence intensity, in contrast to the cartilage. However, with the progression of arthritis, the fluorescence image of the bones was dramatically appeared and the SBR value of them increased significantly to clearly display the altered morphology of the joints ( $p$ <0.05). In particular, as it was confirmed that bone-specific NIR fluorophore, P800SO3 went only into the osteoclast cells, it was determined that monitoring of bone remodelling caused by arthritis-induced osteoclastogenesis is possible by using NIR fluorescence images.



**Conclusions:** The fluorometric imaging of RA by using tissue-specific contrast agents plays a key role in the systemic treatment of RA by monitoring structural damage and disease progression

**Disclosure of Interest:** None declared

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#### AB1218 DIAGNOSIS OF PRIMARY RAYNAUD'S PHENOMENON AND CAPILLAROSCOPY

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**Background:** Raynaud's phenomenon (RP) is a clinical expression of recurrent reversible vasospasm of small peripheral arteries and arterioles. It is a common pathology in clinical practice and is classified into two main categories – primary RP in the absence of an underlying disorder and secondary RP that is in the context of another disease. The differential diagnosis is of crucial importance for the practising rheumatologists because the patients with primary RP are with benign course while those with secondary RP require further differentiation and establishment of the precise diagnosis and treatment. Differentiation between primary and secondary RP is based on clinical features, laboratory including immunological investigations and capillaroscopic findings.

**Objectives:** The nailfold capillaroscopy is a key imaging tool for monitoring the RP patients because of the high predictive value of the abnormal capillaroscopic pattern for future development of connective tissue disease. Patients with primary

RP have younger age at onset (<30 years), there are no clinical features of a secondary disease, no trophic changes or abnormal capillaroscopic pattern.

**Methods:** Literature data on quantitative analysis of capillaroscopic parameters in primary RP are limited.

**Results:** In an own study that included 31 patients with primary RP patients, significantly wider arterial and venous capillary diameters as compared with healthy controls was found in 96.6% of cases. The mean arterial capillary diameter (0.018 ± 0.004 mm) in primary RP patients was significantly larger in comparison healthy volunteers (0.012 ± 0.001 mm,  $p < 0.005$ ). The mean venous capillary diameter was also significantly higher in primary RP (0.026 ± 0.006 mm vs 0.017 ± 0.002 mm in healthy controls,  $p < 0.005$ ).<sup>1</sup> Similarly, Bukhari *et al.* (2000)<sup>2</sup> also observed greater diameters of arterial, venous limb and apical loop in comparison with control subjects in 15 primary RP patients, but the difference was not statistically significant.<sup>2</sup> Anderson *et al.* (2005)<sup>3</sup> also found greater capillary diameters in 21 patients with primary RP vs healthy volunteers but the difference was statistically significant only for the arterial capillary limb and the apex loop but not for the venous capillary diameter.<sup>3</sup>

**Conclusions:** These capillaroscopic observations in primary RP patients suggest that the absence of an abnormal capillaroscopic pattern is diagnostic for primary RP but minor capillaroscopic dilation is a frequent microvascular feature in these patients.

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**Disclosure of Interest:** None declared

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#### AB1219 CONTRIBUTION OF MRI TO CERVICAL INVOLVEMENT IN RHEUMATOID ARTHRITIS: PROSPECTIVE STUDY OF 30 CASES

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**Background:** Cervical spine involvement is common during RA and is characterised by its potential severity.

**Objectives:** To determine the prevalence of cervical involvement in RA, to clarify the contribution of MRI to diagnosis and to identify predictive factors for cervical rheumatoid involvement.

**Methods:** Our study included 30 RA patients with a duration of more than 2 years.

**Results:** 16 patients (53%) were assessed on the two imaging methods (standard radiographs in 37% and MRI in 53%), of which 2 cases (7%) were asymptomatic. This cervical involvement was dominated by the C1-C2 pannus objectivated in 50% of cases and AAS. Of the AAS, aAAS was the most frequent with a prevalence of 23%, followed by the pAAS found in 10% of the cases, the vAAS present in 7% of the cases then the IAAS and the rAAS objectivated in 3% each. The ASS was found in 3 cases (10%), odontoid erosion in 11 cases (37%), C1-C2 arthritis in 5 cases (16%) and inflammatory spondylodiscitis in 6 cases (20%). MRI resulted in a better study of the C1-C2 pannus and odontoid erosions as well as the evaluation of the impact of rheumatoid lesions on the neural axis: a medullary imprint was noted in 4 cases (13%). Several factors were associated with cervical rheumatoid involvement: the presence of cervicobrachial neuralgia or bulbomedullary signs, duration of PR ≥ 5 years, HAQ score ≥ 1.1 and positive RF. The search for factors associated with AAS has revealed the duration of the disease, DAS 28 > 3.2 and the presence of a biological inflammatory syndrome.

**Conclusions:** Cervical involvement accompanies the active and destructive forms of RA. It can be asymptomatic, it is the interest to seek it in a systematic way in RA. The standard radiography with dynamic views is to be realised first-line. The MRI must be indicated in order to make an early diagnosis, to carry out an accurate lesional assessment and to guide the therapeutic decision.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.5730

#### AB1220

#### STUDY OF THE RELATIONSHIP BETWEEN TOE DEFORMITIES IN THE FOREFOOT REGION AND THE FLEXOR TENDONS IN RHEUMATOID ARTHRITIS USING 3D VOLUME RENDERING

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**Background:** Multi-slice computed tomography (CT) is frequently used to evaluate the morphology, arrangement, and other characteristics of bone. Three-dimensional volume rendering (3D-VR) has made it possible to three-dimensionally visualise tendons and other structures by arbitrarily changing CT values. In deformities of the forefoot region in rheumatoid arthritis (RA), dislocation of the metatarsophalangeal (MTP) joints results in the formation of painful calluses that require surgery; however, the toes can sometimes be displaced inwards or outwards by this dislocation. MTP joint dislocation also causes the flexor tendons to dislocate from their original positions, although the relationship with toe displacement is unclear.

**Objectives:** We therefore used 3D-VR to examine the relationship between the flexor tendons and toe displacement in the dislocated toes of RA patients.

**Methods:** Thirty-one feet (10 right and 21 left) of 24 patients (5 men and 19 women) were examined. The Tsuboi classification was used to classify MTP joint dislocation into subluxation (Grade 2) or dislocation (Grade 3). CT images taken with no load applied to the feet were used for preoperative evaluation. The mean age of the patients at the time of imaging was 59.0 (36–76) years. A Fujifilm volume analyzer (SYNAPSE VINCENT) was used for 3D-VR reconstruction and CT values were adjusted to visualise the flexor tendons and examine their relationship with the heads of the metatarsal bones. When the flexor tendons were displaced inward or outward from the base of the metatarsal bone head, this was classified as flexor tendon dislocation. Toe displacement was identified when the proximal phalanx was displaced inward or outward from the extended line of the metatarsal axis.

**Results:** MTP joint dislocation was seen in 80 toes (63 cases of dislocation and 17 cases of subluxation). The flexor tendons were dislocated in 27 s toes (15 inward and 12 outward), 27 third toes (21 inward and 6 outward) and 16 fourth toes (15 inwards and 1 outward). Of the cases of MTP joint dislocation, toe displacement was seen in 12 s toes (1 inward and 11 outward), 12 third toes (12 outward) and 2 fourth toes (1 inward and 1 outward). The flexor tendons were dislocated towards the displaced toes in all cases. No flexor tendon dislocation was seen in any of the cases of subluxation.

**Conclusions:** RA is often accompanied by hallux valgus and toe displacement is affected by retraction of the first toe. The results of this study demonstrate that the toes are displaced inwards in some cases and can become dislocated independent of the influence of the first toe. All the toes were displaced towards the dislocated flexor tendons and MTP arthritis had resulted in loosening of the joint capsule and ligaments and dislocation of the flexor tendons, which was likely to cause displacement.

**Disclosure of Interest:** None declared

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#### AB1221

#### THE ASSOCIATION BETWEEN SYNOVITIS IN THE FOOT ON JOINT ULTRASONOGRAPHY AND CLINICAL PARAMETERS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Treatment of rheumatoid arthritis (RA) has improved dramatically with the widespread use of biological disease-modifying antirheumatic drugs. In this context, the number of RA patients who undergo orthopaedic surgery is reportedly decreasing. However, the number of RA patients who undergo foot surgery is increasing. Joint ultrasonography has been used for early diagnosis and

disease activity assessment in RA, allowing visualisation of synovitis. However, few detailed studies or evaluations of clinical parameters related to synovitis in the foot have been performed.

**Objectives:** This study investigated the association between synovitis in the foot as observed on joint ultrasonography and the degree of disability on the health assessment questionnaire (HAQ) in RA patients.

**Methods:** The study included 79 outpatients (101 feet) with RA. Patients who had undergone surgery were excluded. The mean age was 66.0 years (24–92 years), and the mean disease duration was 13 years and 5 months (ranging from 1 month to 49 years). Joint ultrasonography was performed by the same examiner using the same diagnostic instrument in the same room. Synovitis was defined as a power Doppler score of  $\geq$  Grade 1. The scanning sites were forefoot (metatarsophalangeal joints of toes 1–5), metatarsus (calcaneocuboid and talonavicular joints), and hindfoot (talocrural and subtalar joints, peroneal tendon, posterior tibial tendon). The presence or absence of synovitis was evaluated at each site, and the association with the HAQ score was examined.

**Results:** Synovitis was detected in the forefoot of 40 feet (39.6%), in the metatarsus of 34 feet (33.7%), and in the hindfoot of 63 feet (62.4%). Patients with synovitis in the forefoot (PD+:  $0.41 \pm 0.1$ , PD-:  $0.80 \pm 0.1$ ,  $p=0.018$ ) and hindfoot (PD+:  $0.52 \pm 0.1$ , PD-:  $0.86 \pm 0.1$ ,  $p=0.043$ ) had significantly lower HAQ scores.

**Conclusions:** Given that assessment of foot impairment is not included in the disease activity index for RA, there may be a delay in diagnosis of foot lesions. Our results showed that patients with synovitis in the forefoot and rearfoot had lower HAQ scores (disability measure), suggesting that increased physical activity may be associated with increasing incidence of synovitis in the foot. The ability of RA patients to perform activities of daily living may have improved with advances in pharmacotherapy, leading to increased physical stimulation, resulting in an increased incidence of synovitis of the foot.

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#### AB1222 COMPARISON OF QUANTITATIVE MRI FAT-FRACTION MEASUREMENT IN SIJ JOINT ON DIFFERENT SCANNER PLATFORMS

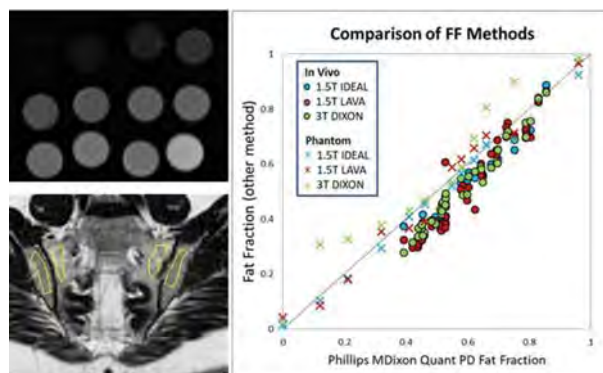
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**Background:** Quantitative MRI Proton Density Fat Fraction (PDFF) measurement can objectively identify areas of active inflammation and structural damage in spondyloarthritis by identifying oedema and fat metaplasia in bone marrow.<sup>1</sup> PDFF is typically implemented as a 3D multi-echo Gradient-echo protocol and all of the major MRI equipment manufacturers have PDFF imaging products available that combine a complex multi-peak fat-spectrum model with simultaneous determination and correction for T2\* signal decay. However, if the appropriate specialist imaging option has not been purchased, as is commonly the case, then the user may have to rely on simpler base-level protocols for fat-fraction measurement. An important step to implementing quantitative fat-fraction measurement as a clinical tool is to demonstrate that measurements are robust to both scanner platform and measurement technique.

**Objectives:** We aimed to compare quantitative FF measurements obtained using 3 scanners supplied by different manufacturers, and using a range of techniques.

**Methods:** The sacroiliac joints (SIJ) of 10 healthy volunteers (mean age 42 years, range 23–63) were scanned on 3 scanners: a) 3T Philips Ingenia, using MDixon Quant (MDQ) – a specialist PDFF package; b) 1.5T GE Optima MR450W, using IDEAL and LAVA – both base-level options; and c) 3T Siemens Skyra, using DIXON – a base-level option. We also scanned a fat-water phantom constructed using tubes of emulsions of peanut oil and 3% agar. MDQ uses data from 6 different echo-times; IDEAL from 3; and LAVA and DIXON from 2. The excitation flip angle was set to 3 degrees for all acquisitions to minimise the T1 weighting. Each technique yields Fat-only (F) and Water-only (W) images. FF images were calculated using the formula:  $FF = F / (W + F)$ . Regions of interest (ROIs) were drawn in the SIJ as shown in the figure 1. MDQ PDFF was used as the 'gold-standard' measurement for comparison to IDEAL, LAVA and DIXON.

**Results:** The figure shows the results of the ROI analysis. For the phantom measurements, both LAVA and IDEAL correlated well with MDQ, but Siemens DIXON deviated away from the expected linear relationship. The *in vivo* data showed good linear relationships with MDQ for all 3 base-level techniques for FF in the range 0.4–0.8, although all 3 slightly underestimated FF compared to MDQ.



**Abstract AB1222 – Figure 1**

**Conclusions:** A clinically useful quantitative image-analysis tool should be applicable to results obtained from several platforms. FF measurement in the bone marrow of the SIJ is robust to both technique and platform. The slight underestimation of FF values on base-level FF measurements is probably due to the influence of T2\* weighting. However, these variations are smaller than the FF changes observed in areas of oedema or fat metaplasia.<sup>1</sup> FF measurement is a quantitative and widely applicable method for the diagnosis and assessment of spondyloarthritis.

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#### AB1223 ULTRASONOGRAPHY EXAMINATION OF ELBOWS IS USEFUL WHEN COMBINED WITH EXAMINATION OF PIP AND WRIST JOINTS

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**Background:** Because elbows are important joints for the function of upper limbs, the daily activity of the patients with rheumatoid arthritis (RA) may be impaired by synovitis of elbows. Although elbows are included into the 28 essential joints for evaluation of the disease activity of RA, ultrasonography (US) examination of elbows is not routinely performed and there have been a few surveys on the correlation between US scores of elbows and disease activity.

**Objectives:** To reveal whether there is a correlation between US scores of elbows and disease activity in the patients with RA.

**Methods:** We recruited 198 patients with RA from KURAMA cohort, which is the database of the patients with RA treated in the Kyoto University Hospital, and performed US examination of proximal interphalangeal (PIP) joints, metacarpophalangeal (MP) joints, wrist joints and elbow joints. Synovial hypertrophy is scored semiquantitatively on a scale of 0–3. We analysed correlations between the total scores of each component (PIP, MP, wrist and elbow) and clinical parameters.

**Results:** We found weak correlations between DAS28-ESR and the US scores of PIPs, MPs and wrists ( $\rho=0.25$ ,  $0.21$  and  $0.29$ , respectively) whereas there was little correlation between DAS28-ESR and the US score of elbows ( $\rho=0.16$ ). However, multivariable analysis showed that the US scores of PIPs, wrists and elbows were independently associated with DAS28-ESR ( $p=0.021$ ,  $0.0027$  and  $0.025$ , respectively). US scores of elbows showed little or weak correlations with US scores of PIPs, MPs and wrists ( $\rho=0.23$ ,  $0.16$  and  $0.11$ , respectively).

**Conclusions:** US examination of elbows may be useful to assess the disease activity of patients when combined with US examination of PIPs and wrists although US scores of elbows alone has a weak correlation with DAS28-ESR. US examination of elbows may detect the disease activity which is overlooked by the US examination of joints of hand.



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**AB1224 CT PET SCANS IN SUSPECTED LARGE VESSEL VASCULITIS AND GIANT CELL ARTERITIS – AN AUDIT IN THE BELFAST HEALTH AND SOCIAL CARE TRUST (BHSC)**

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**Background:** British Society of Rheumatology (BSR) guidelines, due to be updated in April 2018, recommend consideration of CT PET when there is suspicion of large-vessel GCA (LV-GCA) in patients with prominent systemic symptoms, limb claudication or persistently high-inflammatory markers despite adequate glucocorticosteroid therapy. Vascular Ultrasound is unhelpful in assessment of the aorta.

**Objectives:** We investigated the use of CT PET in suspected cases of LV-GCA and its impact on management of patients in the BHSC from August 2016 to August 2017.

**Methods:** The IT support team in Royal Victoria Hospital provided a list of CTPET scans requested under the specific code for vasculitis and/or Pyrexia/infection and another code for general. Of the 250 scans identified under these codes, 34 scans were requested by Rheumatology for possible vasculitis following a review of the electronic care records. A proforma was used to aid data collection.

**Results:** Female:Male ratio was 3.25:1, with a mean age of 65. 88% of the scans were requested due to a suspected diagnosis of vasculitis and 12% were for follow up of known vasculitis. 24% of CT PET scans were positive for large vessel vasculitis (LVV). The ESR was greater than 50 mm/hr in 75% of positive scans. Of those patients with a positive CT PET scan, 88% were treated with steroids. Of those patients with a negative CT PET scan, 42% were treated with steroids. It is noteworthy that 29% of patients were on steroids at the time of CT PET which may impact results. 60% of patients who were on steroids at the time of CT PET were on 60 mg of prednisolone daily. 31% of patients with negative scans were on steroids at the time of CT PET. 46% of patients with negative CT PET scans remained on steroid treatment. Steroid treatment was continued in patients with negative scans on basis of active aortic valve histology ±clinical criteria for diagnosis of GCA ±cerebral vasculitis on neuroimaging ±polymyalgia rheumatica evident on CTPET. CT PET changed management in 65% of patients with positive results supporting steroid treatment and negative results guiding withdrawal of steroids.

**Conclusions:** We are fortunate to have access to CT PET in Northern Ireland. CT PET scans changed management in 65% of our patients, despite 29% of patients being on steroid treatment prior to CT PET. We wish to increase awareness of the role CTPET in the diagnosis and management of LVV. We are liaising with radiology colleagues to refine and maximise appropriate referrals for CT PET scans for patients with suspected vasculitis.

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**AB1225 ANTIBODIES AGAINST HETEROGENEOUS NUCLEAR RIBONUCLEOPROTEINS (RA33) MAY HAVE A DIAGNOSTIC AND PROGNOSTIC VALUE IN RHEUMATOID ARTHRITIS, PARTICULARLY WHEN OTHER SEROLOGICAL TESTS ARE NEGATIVE**

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**Background:** The high frequency of detection of antinuclear antibodies in rheumatoid arthritis (RA), although predominantly in low titres, allows us to consider the possibility of using varieties of these antibodies (primarily antibodies to RA-33) markers of RA especially in the early stages of the disease.

**Objectives:** To study the frequency of occurrence and determine the prognostic significance of antibodies to RA-33 in RA patients.

**Methods:** 57 RA patients were examined (mean age 50.5±10.1 years).

The patients with the developed stage of the disease (47.4%) prevailed, the average activity (DAS28=3.2–5.1) of the pathological process (86%); with the second radiographic stage (42%) and functional class 2 (77%).

The antinuclear factor was determined in the indirect immunofluorescence reaction on the HEp-2 cell line (norm <1:80), IgM-rheumatoid factor by the latex agglutination method (up to 20 IU/ml), antibodies (norm up to 20 U/ml) and antibodies of IgG class to RA33 antigen (norm up to 25 U/ml) by ELISA test.

**Results:** ANF was detected in 18 patients with RA (32%), and in 94.4% of cases (17 patients) a diagnostic titer of 1:80 and a diffuse type of glow of the nucleus were noted. The ANF titres did not correlate either with the activity of the disease or with extra-articular manifestations of RA ( $p>0.1$ ). Anti-RA33 was detected in 20 (35%) RA patients: 18 positive people (90%) had low positive anti-RA33 values (25 to 75 U/ml). In 35 (61.4%) of RA patients, anti-CCP was detected: 19 (33.3%) had low positive values (20 to 60 U/ml), 16 (28%) had highly positive values (more 60 U/ml). IgM-RF was detected in 26 (45.6%) patients in the values>48 IU/ml, as well as in 17 (30%) patients with RA in the values from 24 to 48 IU/ml. 14 people (54%) of patients with high IgM-RF levels had systemic manifestations of RA. It should be noted that anti-RA33 was detected in 9 patients with seropositive for anti-CCP and in 11 patients with seronegative both for anti-CCP and IgM-RF. Thus, when the results of standard serological tests are negative, an additional study of anti-RA33 is recommended to diagnose seronegative RA.

When assessing the prognostic significance of the available clinical and laboratory and instrumental data we have analysed the results of the study of anti-CCP, anti-RA33, as well as all data on the presence of X-ray erosions in patients with RA with magnetic resonance imaging or ultrasound examination of affected joints. The presence of erosion was noted in 23 (40.4%) RA patients. The frequency of detection of anti-CCP in RA patients was significantly higher in the presence of erosive lesions of joints (19 of 35 patients were positive by anti-CCP, compared with 4 of 22 patients, negative for anti-CCP,  $\chi^2=5.89$ ,  $p=0.015$ ). In the RA group of patients positive for a wide range of antibodies (IgM-RF, anti-CCP, anti-RA33), the signs of joint erosion were identified in 22 of 46 patients, and in isolated increase only anti-RA33 – in 1 patient out of 11 people in this group  $\chi^2=4.04$ ,  $p=0.044$ .

**Conclusions:** In the presence of highly positive anti-CCP values, RA patients have a more unfavourable prognosis, while an isolated increase in anti-RA33 is associated with a "milder progression" of the disease and inversely proportional to erosive processes in the joints.

**Disclosure of Interest:** None declared  
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**AB1226 THE DIAGNOSTIC VALUE OF SERUM KL-6 IN CONNECTIVE TISSUE DISEASE ASSOCIATED INTERSTITIAL LUNG DISEASE**

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**Background:** The connective tissue diseases is a group of inflammatory, immune-mediated diseases. CTD often leads to autoimmunity and subsequent tissue injury. It is an important contribute to thoracic changes, particularly interstitial lung disease, is are the main causes of mortality and morbidity among patients with connective tissue diseases. Prognosis and response to therapy are the most pressing challenges for connective tissue disease-associated ILD (CTD-ILD).

At present, the basic methods for the diagnosis of various types of ILD includes high-resolution computed tomography, bronchoscopy, and surgical lung biopsy. In addition, continuous lung function tests are commonly used to monitor disease activity and predict the outcome of patients with ILDs. But these tests require specific inspection machines and Repeatability is not good. At present, many biomarkers have been developed to detect ILDs, and the most important biomarkers is KL-6 and lung surface active protein A (SP- A) and surfactant protein D (SP – D) witch secreted by alveolar epithelial type II cells. But Relevant studies have shown that the sensitivity, specificity and accuracy of KL-6 are higher than SP-A and SP-D.

**Objectives:** To evaluate the diagnosis of the serum Krebs von den Lungen-6 (KL-6) for the interstitial lung disease(ILD) associated with connective tissue diseases(CTD).

**Methods:** We retrospectively analysed the medical records of 50 patients with CTD associated ILD,46 CTD patients without ILD. Measurement of serum KL-6 levels and pulmonary function tests performed in parallel were reviewed.T test,  $X^2$  test, non-parametric test, SPSS and correlation analysis were used for data analysis.

**Results:** The significantly higher levels of KL-6 were determined in the CTD-ILD group than in either the CTD without pulmonary involvement group( $P<0.05$ ). Serum KL-6 correlated negatively with forced vital capacity(FVC%) (%predicted), forced expiratory volume in one second (FEV1)(%predicted) and diffusing capacity of the lung for carbon monoxide (DLCO) (% predicted). By the ROC curves of serum KL-6 levels in 96 patients. The optimal cutoff value of serum KL-6

for a diagnosis of CTD-ILD was 500 mg/L, and the sensitivity and specificity were 82.0% and 89.1%, respectively. The area under the curve (AUC) was 0.877. By multivariate analysis, we found only the reduced DLCOsb%, and elevated serum KL-6

**Abstract AB1226 – Table 1.** single factor and multifactor analysis of the risk factors of ILD

Variables	Univariate analysis		Multivariate regression analysis	
	(OR 95% CI)	P	(OR 95% CI)	P
Age	0.956	(0.924, 0.988)	0.008	
VC%	1.051	(1.018, 1.084)	0.002	
FVC%	1.030	(1.004, 1.057)	0.022	
FEV1%	1.032	(1.004, 1.062)	0.026	
TLCOsb%	1.081	(1.042, 1.120)	0.000	1.097 (1.031, 1.168) 0.004
KL-6	0.998	(0.997, 0.999)	0.000	0.997 (0.996, 0.999) 0.000

**Conclusions:** The serum KL-6 is a valuable biomarker for CTD-ILD diagnosis and even as a predictive factor could be used to identify the clinical development of ILD.

**Disclosure of Interest:** None declared

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**AB1227 INFLAMMATORY FINDINGS ON ULTRASOUND AND MRI CAN PREDICT FUTURE DEVELOPMENT OF RHEUMATOID ARTHRITIS IN PATIENTS WITH SERONEGATIVE, UNDIFFERENTIATED ARTHRITIS**

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**Background:** The 2010 rheumatoid arthritis (RA) classification criteria has been verified to classify patients early as having RA more efficiently than the 1987 criteria. However, sensitivity of this criteria decreased remarkably in patients whose rheumatoid factor (RF) and anticitrullinated antibodies (ACPA) were both negative. Modern imaging technique including ultrasound (US) and magnetic resonance imaging (MRI) are more sensitive than physical examination for detecting joint inflammation objectively, however, US may offer only slight additional value when assessing patients with positive ACPA and RF. Reliability and value of inflammatory findings detected by US and MRI in seronegative, undifferentiated arthritis (UA) patients are still unclear.

**Objectives:** To clarify benefits of US and MRI for predicting futuristic diagnosis of RA in UA patients with neither ACPA nor RF.

**Methods:** Consecutive, untreated, early arthritis patients who underwent both US and contrast enhanced MRI of 22 sites including bilateral wrists, MCP and PIP joints were enrolled. Synovitis and tenosynovitis were defined as inflammatory findings of US and MRI. Concordance between swollen joint counts (SJC) by experienced physician, inflammatory findings of US and MRI were assessed. We defined UA as non-fulfillment of the 2010 RA classification criteria and the clinical diagnosis of RA as the initiation of disease modifying anti-rheumatic drugs.

**Results:** Seventy one patients were included in the analysis. Fifty eight (82%) were female, the median age was 63 years old, and the mean symptom duration 3 months. Forty eight (67.6%) did not fulfill the 2010 criteria being defined as UA, among which thirty six were seronegative. In all patients, the concordance of detecting inflammation was quite high between MRI and US ( $\kappa$ : 0.67–0.70). In 36 seronegative UA patients, SJC detected by physical examinations were fewer than US or MRI (2.2 vs 3.9,  $p < 0.05$ ) and discrepancy between clinical SJC and inflammatory findings by US/MRI were more frequent in seronegative UA patients ( $\kappa$ : 0.18) compared to the patients who fulfilled the 2010 RA criteria ( $\kappa$ : 0.32). Although only 4 of the seronegative UA patients would have fulfilled the 2010 criteria if inflammation findings by US/MRI were used instead of physical examinations, 21 seronegative UA were diagnosed with clinical RA (sensitivity 19% and specificity 100%). One or more inflammatory arthritis in wrists and MCP joints detected by US or MRI in seronegative patients significantly predicted the development of RA with a good sensitivity of 62% and specificity of 87% (Odds ratio, 10.5).

**Conclusions:** Our study suggested that both US and MRI inflammation findings are reliable with a good concordance and can be useful as predictor for futuristic development of RA in UA patients without ACPA and RF.

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**AB1228 SONOELASTOGRAPHY OF QUADRICEPS IS MORE ACCURACY THAN GRIP STRENGTH TO PREDICT LOW MUSCLE MASS**

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**Background:** Reduced muscle mass had associated with higher mortality. So it is mandatory for simple techniques to early detection of sarcopenia. However, some patients with low grip strength had normal muscle mass, especially those with rheumatoid arthritis.

**Objectives:** Our objective was to examine the validity of sonoelastography to predict sarcopenia in osteoporotic patients.

**Methods:** We conducted an observational study in Kaohsiung Chang Gung Memorial Hospital. Low muscle mass was determined using a dual-energy X-ray absorptiometry. Sonoelastography was performed over mid thigh over quadriceps muscle. We measure grip strength and hardness and elastography ratio of quadriceps over subcutaneous fat tissue. Logistical regression was used to find the factors to predict low muscle mass. While ROC analysis was used to find best cut-off point.

**Results:** A total 122 (68 low muscle mass, 54 normal muscle mass) patients were enrolled. The mean age was 79.26±6.77 years in low muscle mass group and 74.7±13.49 in normal muscle mass group ( $p=0.017$ ). Most patients (86.9%) were women. Sonoelastography showed low muscle mass patients had more soft than normal muscle mass patients, furthermore the elastography ratio of quadriceps over subcutaneous tissue was lower than normal muscle mass patients. Using logistical regression, grip strength, sex and age cannot be used to predict low muscle mass, while the hardness and ratio had statistically significant to predict low muscle mass ( $p=0.001$ ). When the cut points determined by receiver operating characteristic (ROC) curve analysis were applied, The best cut-point of hardness was 64.79% (sensitivity, 0.741; 1-specificity, 0.147), while the best cut-point of quadriceps over subcutaneous tissue was 0.81 (sensitivity, 0.815; 1-specificity, 0.118).

**Abstract AB1228 – Table 1**

	Regression coefficient	S.E.	P value	OR
Gender	1.976	1.063	0.063	7.216 (0.899–57.939)
Age	0.043	0.041	0.297	1.043 (0.963–1.132)
Hardness	–4.015	0.897	0.001	0.018 (0.003–0.105)
Ratio	–3.927	0.856	0.001	0.019 (0.004–0.105)
Grip strength	0.218	0.640	0.734	1.243 (0.355–4.356)

**Conclusions:** Our findings indicate that sonoelastography is more accurate to predict low muscle mass. The measurement include quadriceps over subcutaneous tissue and hardness of the quadriceps. Although, grip strength is less expensive for evaluation of muscular weakness, from this findings, it is not a reliable method for evaluation of low muscle mass. The possible reason is that sarcopenia initial occur at thigh muscle and then spread up to upper limb. So grip strength is not an accurate method to screen sarcopenia.

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**Disclosure of Interest:** None declared

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AB1229

### ASSESSMENT OF ENTHESITIS BY ULTRASONOGRAPHY IN PATIENTS WITH SERONEGATIVE RHEUMATOID ARTHRITIS

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**Background:** In patients with seronegative rheumatoid arthritis (RA) there is a difficulty to make the differential diagnosis with the spondyloarthropathies.

**Objectives:** To assess the presence of enthesitis in patients with seronegative RA in comparison with the healthy controls (HC), patients with seropositive RA and ankylosing spondylitis (AS).

**Methods:** In this cross-sectional study, seronegative and seropositive RA patients, who fulfilled the 2010 ACR/EULAR criteria, patients with AS and HC have been assessed by grey scale and power doppler ultrasonography for the presence of enthesopathy at the achilles tendon, plantar fascia, proximal patella, distal patella, quadriceps, tibialis anterior, triceps, common flexor and extensor tendons. Clinical assessment of the patient groups included demographic findings, health assessment questionnaire and DAS28.

**Results:** In our study, we recruited age and sex matched 27 seronegative RA, 19 healthy controls, 24 seropositive RA and 23 ankylosing spondylitis patients. We evaluated and analysed both right and left sides of the entheses regions separately which have been indicated in the methods section. The mean DAS28, mean ESR and mean CRP of the patients with seronegative RA were 3.6±1.28, 32.2±21.2 and 12.37±27.77 respectively (table 1).

Median of Madrid sonographic enthesitis index (MASEI) was 5 in patients with seronegative RA. 4 patients have severe scores (MASEI score ≥20). There were significant differences between seronegative RA and healthy controls (MASEI score:3), (p=0.014) but no differences has been observed between seronegative RA with seropositive RA (MASEI score:6) and ankylosing spondylitis (MASEI score:7) in MASEI scores.

In comparison, hypoechoogenicity of quadriceps tendon (16 (29.6%) vs 6 (12.5%), p=0.037), bone erosion at the quadriceps tendon attachment (9 (16.6%) vs 0, p=0.003), calcification at achilles tendon (17 (31.4%) vs 6 (12.5%), p=0.023) have been observed more frequently in patients with seronegative RA than seropositive RA. Significantly higher number of patients with bone erosion at the common extensor tendon (26 (48.1%) vs 3 (6.5%), p<0.001), calcification at achilles tendon (17 (31.4%) vs 2 (4.3%), p=0.024), erosion at triceps tendon (13 (24%) vs 1 (2.1%), p=0.035) have been detected in patients with ankylosing spondylitis than seronegative RA (table 2).

Abstract AB1229 – Table 1

	Seronegative RA	Healthy control group	Seropositive RA	Ankylosing spondylitis
Age, years	51,85±11,49	46,2±6,6	53,12±10,95	43,75±4,1
Women, n (%)	48 (88,9)	38 (100)	44 (91,7)	38 (82,6)
RA duration, year	9,8±6,75	NA	12,29±9,3	NA
RF titre, median	10,77±3,21	NA	323,68 ±372,72	NA
AntiCCP titre, median	3,99±4,13	NA	300,16 ±264,93	NA
DAS28, median	3,6±1,28	NA	3,73±1,45	NA
ESR, median	32,2±21,2	NA	38,73±26,88	38,72±9,16
CRP, median	12,37±27,77	NA	12,73±18,57	10,38±9,3

Abstract AB1229 – Table 2. Assessing patients with seronegative rheumatoid arthritis about enthesopathy by ultrasound- Pathological findings

Pathological finding	Seronegative RA	Healthy control group	Seropositive RA	Ankylosing spondylitis
Bone erosion at the quadriceps tendon, n(%)	9 (16,6) (p=0,003)	0 (p=0,003)	0 (p=0,003)	3 (6,5) (p=0,25)
Hyper-echogenicity in quadriceps tendon, n(%)	38 (70,6) (p=0,006)	2 (5,4) (p=0,006)	8 (13,5) (p=0,017)	2 (4,6) (p=0,12)
Calcification of achilles tendon, n(%)	17 (31,4) (p<0,001)	0 (p<0,001)	6 (12,5) (p=0,023)	0 (0,0) (p=0,238)
Bone erosion at the common extensor tendon, n(%)	26 (48,1) (p=0,001)	0 (p=0,001)	3 (6,5) (p=0,296)	3 (6,5) (p=0,001)
Calcification of achilles tendon, n(%)	17 (31,4) (p=0,001)	0 (p=0,001)	6 (12,5) (p=0,023)	2 (4,6) (p=0,12)
Erosion of triceps tendon, n(%)	13 (24) (p=0,005)	0 (p=0,004)	9 (18,75) (p=0,004)	1 (2,1) (p=0,025)

**Conclusions:** We observed that enthesitis involvement was not seldom in patients with seronegative RA. Furthermore there were also similar frequency of entesis involvement in seropositive patients with RA. The value of enthesitis sites evaluation for the differential diagnosis of patients with seronegative RA should be further investigated and the assessment of enthesitis sites in seronegative and seropositive RA patients can be important to detect active and chronic changes at the enthesitis region.

**Disclosure of Interest:** None declared  
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### Public health, health services research and health economics

AB1230

### PATIENT EMPOWERMENT THROUGH THE USE OF A MOBILE PHONE APPLICATION: THE EXPERIENCE OF RHEUMABUDDY IN ITALY

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**Background:** Patient education and empowerment are cornerstones in the management of rheumatic and musculoskeletal diseases (RMDs). In fact, they improve the physician-patient relationship and ensure a successful shared decision making process. In recent years, the exponential growth of interactive media and the progress of technology led to the parallel development of digital health-care and the evaluation of how tools like mobile applications (app) can contribute to patient empowerment. Rheumabuddy has been developed thanks to the collaboration of the Danish association of young patients with RMDs (FNUG) and a Danish agency specialised in digital healthcare (Daman). RheumaBuddy is designed for young patients (18–35 years old) with chronic arthritis and integrates the function of a diary to monitor the main features of the disease (e.g. pain, stiffness, fatigue) and a forum to interact with other users and provide mutual help.

**Objectives:** We aimed at developing the Italian version of RheumaBuddy to make it available to Italian patients with RMDs.

**Methods:** The Italian Society of Rheumatology Committee for young rheumatologists (SIRyoung) translated the content of the app from English to Italian adapting when needed because of language incompatibility.

**Results:** The Italian version of RheumaBuddy was launched on the 12th October 2017 (World Arthritis Day) in partnership with national patient associations (ANMAR and APMAR). The app was also presented via a press release from the Italian Society of Rheumatology. To date, RheumaBuddy was downloaded by 1182 users with 822 of them currently using the app on a regular basis. The feedback collected so far highlighted the usefulness of the app and pointed out potential weaknesses and issues to be tailored to the Italian population. The gathering of feedback from users is still ongoing.

**Conclusions:** We developed the Italian version of RheumaBuddy, which is currently used by a consistent number of young patients with chronic arthritis. A board including patient representatives, rheumatologists and the app developers will be established to specifically tailor the app according to the needs and priority of Italian users and based on the feedback collected.

**Disclosure of Interest:** None declared  
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AB1231

### EFFICACY AND COST ANALYSIS OF A SYSTEMATIC SWITCH FROM ORIGINATOR INFILIXIMAB TO BIOSIMILAR CT-P13 OF ALL PATIENTS WITH INFLAMMATORY ARTHRITIS FROM A SINGLE CENTRE

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**Objectives:** The aim of this study was to analyse efficacy, safety and cost savings of switching from infliximab originator (IFXor) to the biosimilar (BS) CT-P13 in single centre.

**Methods:** Eligible patients were those older than 18 years old with the diagnosis of rheumatoid arthritis (RA), spondylarthritis (SpA) and psoriatic arthritis (PsA) on treatment (Tx) with IFXor for at least 6 months and with stable disease activity. In December 2016 all eligible patients were proposed to switch to CT-P13. At the day of the last Tx with IFXor, informed consent, data and blood samples were collected. On the next Tx day, CT-P13 was administered after standard evaluation of efficacy and safety. Efficacy was measured considering change from baseline in Disease Activity Score in 28 joints (DAS28) for RA and PsA and in Ankylosing Spondylitis Disease Activity Score (ASDAS) for SpA. Disease worsening was



considered when an increase of 1.2 from baseline in DAS28 or an increase of 1.1 in ASDAS occurred. A cost analysis was done based on the purchasing prices of the 2 drugs at our centre.

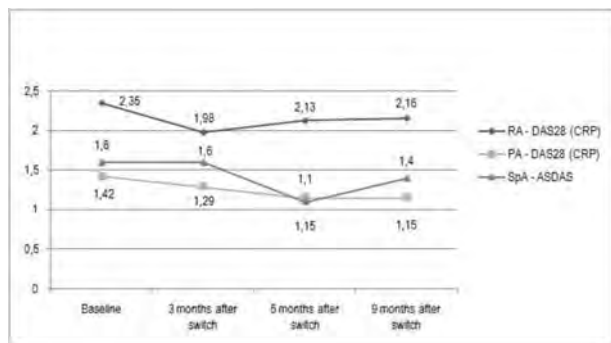
**Results:** In a 12 months period switch to CT-P13 was performed in 60 patients for non-medical reasons. Disease activity (DA) was stable over the observation period and similar to the values observed with IFXor. Median follow-up time was 261 days during which disease worsening occurred in 3 (5%) patients. 1 patient had a minor adverse event (oedema of the lip). These 4 (6.7%) patients stopped the BS. One returned to IFXor and the other 3 switched to another drug. The switch to CT-P13 represented a 26.4% reduction of costs in the use of IFX Tx in these patients.

**Abstract AB1231 – Table 1.** Numbers are medians unless otherwise stated.

	Total (n=60)	SpA (n=36; 60%)	RA (n=16; 27%)	PA (n=8; 13%)
Age (years)	53 (48–64)	50 (41–59)	59 (52–70)	56 (48–64)
Gender (n,% male)	39 (65%)	30 (83%)	2 (13%)	7 (88%)
Disease duration (years)	17 (10–23)	16 (10–22)	18 (13–24)	16 (10–22)
Patients on methotrexate	41 (68%)	20 (33%)	15 (25%)	6 (10%)
Patients with previous biologic therapy	4 (6.7%)	1 (2.8%)	3 (18.8%)	0 (0%)
Time on IFX originator before switch (years)	7.9 (6.5–11.9)	7.7 (6.4–12.3)	8.4 (6.7–12.4)	7.6 (6.7–9.6)
Time on CT-P13 since switch (months)	9 (7–11)	9 (7–11)	10 (9–10)	9 (4–10)

**Abstract AB1231 – Table 2.** Variables median from baseline to 9 months after switch to CT-P13. ESR – Erythrocyte Sedimentation Rate; CRP – C-Reactive Protein; PtGA – Patient global assessment of DA; PhGA – Physician global assessment of DA.

	Baseline	3 Months after switch	6 Months after switch	9 Months after switch	Variation from baseline to 9 Months after switch
ESR (mm/h)	15 (10–21)	17 (9–29)	15 (9–24)	15 (9–24)	0
CRP (mg/dL)	0.18 (0.80–0.57)	0.17 (0.06–0.50)	0.19 (0.10–0.46)	0.25 (0.10–0.72)	0.07
PtGA (0–100)	30 (20–50)	20 (30–50)	30 (3–50)	30 (15–50)	0
PhGA (0–100)	20 (10–30)	20 (10–30)	20 (0–30)	20 (10–30)	0



**Abstract AB1231 – Figure 1**

**Conclusions:** The switch in routine care of a group of RA, SpA and PsA patients from IFXor to CT-P13 did not affect efficacy and safety and reduced costs in 26.4%.

#### REFERENCE:

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**Disclosure of Interest:** None declared

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AB1232

#### ESTIMATING THE ECONOMIC VALUE OF A PATIENT SUPPORT PROGRAM IN RHEUMATOID ARTHRITIS IN THE UNITED KINGDOM

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**Background:** A Patient Support Program (PSP) offered by AbbVie to adalimumab-treated patients assists them with issues pertaining to medication costs, nurse support, injection training, pen disposal, and medication reminders. A number of studies have reported the benefit of enrollment in this PSP from different perspectives, including clinical, patient-reported, and adherence outcomes.<sup>1–2</sup> There is limited information available on the economic value of the PSP.

**Objectives:** To estimate the incremental economic value associated with enrollment in the PSP for adalimumab-treated patients with rheumatoid arthritis (RA) from a UK societal perspective.

**Methods:** An Excel-based economic model was developed to describe adalimumab-treated PSP enrollees over non-enrollees in terms of a) improvement in clinical status as measured by the Health Assessment Questionnaire Disability Index (HAQ-DI), which resulted in reduced healthcare resource utilisation (HRU), and b) improvement in work productivity as measured by the Work Productivity and Activity Impairment Questionnaire (WPAI). The associated incremental direct and indirect cost savings were estimated over a 12 month period. Scores on HAQ-DI, work productivity impairment, and employment rate were obtained from a prospective, observational Phase IV study assessing patient satisfaction and outcomes in the context of the PSP (AbbVie Care) among RA patients (NCT01383421, PASSION)<sup>1</sup>. Inputs from literature and UK-specific publically available sources were used to model the association between HAQ-DI score categories (0 –<0.6, 0.6 –<1.1, 1.1 –<1.6, 1.6 –<2.1, 2.1–3) and HRU among RA patients, and to obtain unit costs of HRU (i.e., hospitalizations, specialist visits, imaging assessments) and weekly work compensation.

**Results:** In PASSION, a greater proportion of PSP enrollees were in the lower HAQ-DI categories (i.e., better outcomes) and enrollees had greater reduction in total work impairment than non-enrollees after treatment with adalimumab. Assuming a population of 10 000 adalimumab-treated RA patients in the UK, this was associated with an incremental annual cost saving of £2,320,809 should all these patients enrol in the PSP. The largest proportion of incremental cost saving resulted from the reduction in RA-related hospitalizations (£1,550,637; 66.8%). Cost saving due to improved work productivity accounted for the second largest proportion (£686,963, 29.6%). Specialist visits and imaging assessments accounted for 1.9% (£44,564) and 1.7% (£38,645) of the total incremental cost saving, respectively.

**Conclusions:** Enrollment in AbbVie's PSP was shown to be associated with incremental cost saving among adalimumab-treated RA patients due to reduced resource utilisation and improved work productivity.

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AB1233

#### DOES TIME MATTER? A SYSTEMATIC REVIEW TO ASSESS THE RELATIONSHIP BETWEEN DELAY IN DIAGNOSIS AND COSTS IN DMARD-NAÏVE RA PATIENTS

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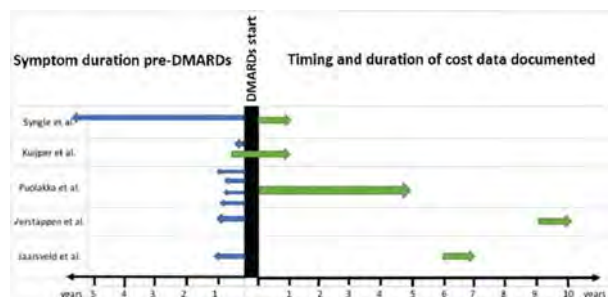
**Background:** Early diagnosis is crucial to enable timely DMARDs initiation in RA patients. Although, early treatment improves clinical outcomes, it is unclear whether this has a similar impact on health economic outcomes. Early DMARDs

intervention may avert the requirement of expensive biological therapy as second-line treatment, which leads to improved overall cost-effectiveness. As a first step to address this issue, we performed a systematic literature review to appraise existing evidence relating to delay in diagnosis and cost-of-illness in DMARD-naïve newly-diagnosed RA patients.

**Objectives:** To identify whether disease duration before initiation of first DMARD therapy is a determinant of subsequent direct and indirect costs in DMARD-naïve RA patients.

**Methods:** We systematically searched Pubmed, EMBASE, CINAHL and Medline databases for published literature relating to rheumatoid arthritis, and direct and/or indirect costs. We included studies with DMARD-naïve patients who fulfilled the 1987 ACR or 2010 ACR/EULAR classification criteria for RA. We excluded: <sup>1</sup> studies on non-rheumatoid arthritis patients; <sup>2</sup> conference abstracts, systematic reviews or review articles; <sup>3</sup> studies with no documented symptom duration prior to diagnosis; <sup>4</sup> studies which did not report direct and/or direct costs and/or health utilisation. All studies were required to report their methods and sources of respective cost measurements. We extracted the following data from each study; <sup>1</sup> study design; <sup>2</sup> potential determinants of RA cost; <sup>3</sup> health economic outcomes and <sup>4</sup> source of unit cost for the health-resources.

**Results:** A total of 173 records were identified in the systematic search, five of which included in the analysis. Two were cost-of-illness studies within the context of observational studies and the remaining were cost-of-illness studies alongside clinical trials. The health outcomes reported were heterogeneous: 1) Direct medical costs were reported in three studies; 2) Indirect non-medical costs were reported in one study and 3) Health-care utilisation was reported in one study. Only one study reported indirect costs from the societal perspective e.g. work disability. The definition of symptom duration was not specified in any studies. Three studies reported disease duration of one year or less and two studies reported symptom duration of six months and <two years. The timing and duration of the reported health economic outcomes varied widely (figure 1). The direct medical costs for three papers were adjusted for purchasing power parities and consumer price index for 2017 US Dollars.



Abstract AB1233 – Figure 1

**Conclusions:** Data on the relationship between symptom duration and costs in DMARD-naïve RA patients is limited. Comparability between studies is hampered due to heterogeneity of the definition for symptom/disease duration and the health economic outcomes reported. An inception cohort of suspected/early RA should include data in resource utilisation and costs studies to identify the relationship between symptom duration and health economic outcomes.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.3967

**AB1234** **WHAT HAPPENS IF IT ISN'T EARLY INFLAMMATORY ARTHRITIS? A RETROSPECTIVE CASE NOTE REVIEW OF PATIENTS REFERRED TO OUR EIA SERVICE WHO DID NOT HAVE EIA**

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**Background:** Early inflammatory arthritis (EIA) has been a flagship subject for Rheumatology in the last few years. There has been a lot of interest in the patients diagnosed with EIA but less is known about those who enter the EIA pathway and are subsequently found not to have EIA.

**Objectives:** This study looks at the diagnoses and management of those discharged from the EIA pathway and what impact this has on resources, management and time. Croydon University Hospital Rheumatology Department has been running an Early Inflammatory Arthritis service incorporating ultrasound since 2014. In this study we are looking at patients that were referred to the EIA Pathway from August 2014 to August 2015.

**Methods:** To collect the data we looked at the patient records from our clinical system, Cerner Millennium. We recorded the clinical impression on first appointment, final diagnosis, additional investigations, referrals to therapies and other specialists and those that were discharged within the 6 weeks of referral. The data was analysed using <sup>Microsoft Excel 2010</sup>

**Results:** Of the 368 patients who were referred to the EIA pathway 140 (38%) were not diagnosed with EIA. The final diagnosis of these patients was osteoarthritis 29 (26%), no rheumatological diagnosis 16 (14%), soft tissue abnormality 11 (9.8%), gout 7 (6.3%), fibromyalgia/hypermobility 7 (6.3%), SLE 5 (4.5%) and polymyalgia rheumatica 4 (3.6%). The remainder, 29 (26%), had miscellaneous rheumatological diagnoses. Of the 140 patients, 28 were thought to have possible EIA on the first consultation. The final diagnosis in this group was osteoarthritis 7 (25%), no rheumatological diagnosis 7 (25%), soft tissue/musculoskeletal injury 3 (11%) and fibromyalgia 2 (7%). The remainder had miscellaneous diagnosis 9 (32%). All patients had routine bloods and x-rays. In addition, musculoskeletal ultrasound was carried out in 22, MRI in 12, CT in 3, EMG in 4 and 3 patients underwent bone density scanning. 13 were referred on to physiotherapy (8 were to hand therapy). 5 were referred to other medical specialities. 30 patients were discharged within 6 weeks.

**Conclusions:** This is the first study looking at those who did not have EIA. The Best Practice Tariff for EIA states that those without EIA should be discharged back to the GP within 6 weeks. We have shown that these patients have a variety of rheumatological diagnoses that require investigation, referral and treatment with the majority (79%) remaining under our care at 6 weeks. This study highlights the resources needed to manage the patients attending rheumatology via the EIA pathway who do not have EIA and this should be taken into account when such a service is developed.

**Disclosure of Interest:** None declared

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**AB1235** **WORK PRODUCTIVITY AMONG WORKERS WITH AXIAL SPONDYLOARTHRITIS**

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**Background:** Axial Spondyloarthritis (axSpA) usually starts in early adulthood and the lifetime impact of the disease can be considerable. Pain, stiffness, sleep disturbances contribute to health-related quality of life reduction with significant impact in work productivity. Absenteeism and presenteeism are still responsible for high costs associated with the disease.

**Objectives:** Assess absenteeism, presenteeism, work and daily-activities impairment and their related associated factors in patients with axSpA.

**Methods:** Cross-sectional postal, unicenter, non-interventional study. Patients fulfilling the Assessment of Spa International Society Classification criteria for axSpA under working age were included. Two groups were defined: A) patients under current anti-TNF; B) patients under conventional therapy. Quantitative and qualitative surveys were performed: Work Productivity and Activity Impairment Questionnaire in SpA (WPAI); participants' experiences of working and their perceptions of how their condition had affected their work capacity and workplace relationships were recorded. The questionnaires were applied through a telephone call, after consent of the participant and respecting anonymity.

**Results:** 60 patients were included (table 1). No significant differences were found between the two groups. They worked on average 42±14.7 hours per week (h/w) and missed 2.3±4.1 h/w due to axSpA. Mean absenteeism, presenteeism, work and activities impairment due to axSpA were 6.8%, 32%, 35% and 41%, respectively. The univariable analysis showed correlations between absenteeism and Visual Analogue Scale physician (pVAS) (p=0.027); presenteeism and Anquilosing Spondylitis disease activity score – C reactive protein (ASDAS-CRP) (p=0.002), Bath AS Disease Activity Index (BASDAI) (p=0.03), Bath AS Functional Index (BASFI) (p=0.02), VAS patient (pVAS) and phVAS (p=0.01, p=0.006), erythrocyte sedimentation rate (ESR) (p=0.03), CRP (p=0.024); percent overall work impairment and ASDAS-CRP (p=0.002), BASDAI (p=0.019), BASFI (p=0.026), pVAS and phVAS (p=0.016, p=0.01), ESR (p=0.03) and CRP (p=0.03); percent activity impairment and BASDAI (p=0.006), BASFI (p=0.004), pVAS (p=0.0004) and phVAS (p=0.007). No correlation was found between work productivity and anti-TNF medication, education or marital status. Regression analysis revealed that BASDAI, BASFI, pVAS, phVAS and CRP accounted for 63% of the variance of presenteeism, with 10 points increase in pVAS resulted in an increase of 17% in presenteeism (p=0.046). Over time, 95% had already gone to work sick: economic reasons (60%), not liking staying at home even sick (43%) and importance of work (35%) were the major reasons to presenteeism. Overall, 63% considered that the disease can limit their projects or career progression; 56% had already cancelled or postponed work; 20% had already changed jobs and 15% stated that had already felt discriminated.

**Abstract AB1235 – Table 1.** Patient demographics and clinical variables.

		Group A under current biological therapy (for at least 6 months n=31)	Group B conventional therapy n=29	p- valu e
Patients	Male, female: n (%)	16 (52%); 15 (48%)	21 (72%); 8 (28%)	0.1
	Age: median (min-max)	40 (29-66)	43 (22-66)	0.6
Education	Primary education (5-11 ages)	8	4	0.5
	Secondary education (11-18 ages)	13	15	
	Tertiary education (> 18 ages)	10	10	
Clinical characteristics	Number of anti-TNF: median (min-max)	1 (1-4)	NA	
	Anti-TNF duration (months): mean (min-max)	30 (6-63)	NA	
	ASDAS CPR (mean, SD)	1.59 ± 0.97	1.95 ± 1.04	0.1
	BASDAI (mean, SD)	2.95 ± 2.13	2.41 ± 2.11	0.3
	BASFI (mean, SD)	3.04 ± 2.92	1.82 ± 2.43	0.3
	VAS patient (0-100) (mean, SD)	31.04 ± 24.53	27.13 ± 28.88	0.4
	VAS physician (0-100) (mean, SD)	13.35 ± 15.99	15.96 ± 16.81	0.5
	ESR (mm/h) (mean, SD)	13.35 ± 9.05	14.21 ± 11.11	0.9
	CRP (mg/d) (mean, SD)	0.56 ± 0.56	0.74 ± 0.82	0.4
	CRP (mg/d) (mean, SD)	0.56 ± 0.56	0.74 ± 0.82	0.4
Work Productivity and Activity Impairment Questionnaire in Spa (WPAI)	Absenteeism (Percent work time missed due to problem) (%)	7.6%	5.8%	0.6
	Presenteeism (Percent impairment while working due to problem) (%)	30.9%	34%	0.7
	Percent overall work impairment due to problem (%)	34.2%	35.9%	0.9
	Percent activity impairment due to problem (%)	43.5%	37.9%	0.4

**Conclusions:** Presenteeism, impairment of work productivity and activity were correlated with disease activity and physical functioning, with the increase of VAS physician resulting in increase in presenteeism. Economic reasons were the major factors to presenteeism and the majority of patients considered that the disease can limit their projects or career progression.

**Disclosure of Interest:** None declared

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#### AB1236 THERAPEUTIC ADHERENCE AND SATISFACTION IN A RHEUMATOLOGY CONSULTATION

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**Background:** The lack of treatment adherence to is considered the main reason for therapeutic failure. It entails a high health care cost, both direct and indirect, affecting the patient's morbidity and mortality. In order to measure this adherence, there are different methods, which can be both objective and subjective. The ideal is the combination of both types in order to ensure that the data are as close as possible to reality.

**Methods:** We carried out an anonymous voluntary survey in October 2017 concerning the degree of satisfaction and therapeutic adherence of patients under follow-up in outpatient Rheumatology Consultations, selecting demographic data from them and using a MARS questionnaire for chronic diseases, which is validated in Spanish. This questionnaire consists of 30 questions that include items about beliefs, experiences and behaviour in terms of health. A score higher than 25 indicates good compliance, while a score lower means a suboptimal compliance.

**Results:** 201 surveys were collected, excluding those patients whose consultation was the first one and those who rejected their participation. The data analysis was performed descriptively with Microsoft Excel. 61% of the surveys collected were carried out by women, with an age range between 55 and 70 years (35%). 45% of the patients surveyed had a basic level of education and 28% had an average level of education, representing both of them three quarters of our sample. When we analyse the treatments that our patients receive, the most prevalent are the DMARDs, which represent 35% of the treatments, followed by the corticotherapy and biological drugs (25% and 16% respectively). Approximately 50% of the survey respondents stated that they had no problems with their medication, and in a small percentage (14%), they claimed they had problems, mostly digestive in relation to the administration of subcutaneous Methotrexate. A 14.92% of questionnaires that were not correctly completed were discarded. Out of the 171 surveys, only one respondent was considered to have a good compliance, being the compliance of the remaining respondents suboptimal. This can be influenced by the limitations of understanding due to the language used, taking into account the characteristics of our population, mainly aged and with a primary level of education, as well as the place where the survey was completed. We obtained 74% of satisfaction with the information shared in the consultation, 73% considered that enough time was devoted to said consultation and 98% said they followed the treatment regimens. However, 11% and 21% said they changed the regimen according to their lifestyle and according to how the treatment made them feel and only 55% had clear treatment options available.

**Conclusions:** The lack of therapeutic adherence is one of the fundamental factors of therapeutic failure. There is no a single method for its assessment. Our patients show a suboptimal therapeutic compliance, although we have to take into

account the limitations of the survey carried out. We must bear in mind the sociological aspects that can hinder adherence and re-assess it periodically for possible changes, as well as individualise each patient.

**Disclosure of Interest:** None declared

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#### AB1237 PATIENTS' PERSPECTIVES AND EXPERIENCE OF PSORIASIS AND PSORIATIC ARTHRITIS: A SYSTEMATIC REVIEW AND THEMATIC SYNTHESIS OF QUALITATIVE STUDIES

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**Background:** Patients with psoriasis and psoriatic arthritis have a lower health related quality of life than the normal population and experience high rates of treatment dissatisfaction<sup>1</sup>. The complexity of unmet needs in diagnosis and treatment<sup>2</sup> necessitate a deep understanding of the experience of people with both conditions to guide development of outcomes important to patients and improve patient centred care.

**Objectives:** To describe the perspectives and experiences of patients with psoriasis and psoriatic arthritis.

**Methods:** Databases (MEDLINE, Embase, PsycINFO, CINAHL) were searched to October 2016. Thematic synthesis was used to analyse the findings.

**Results:** From 46 studies (n=37 psoriasis and n=9 psoriatic arthritis) involving 1290 adult patients with psoriasis (n=1105) and psoriatic arthritis (n=185) we identified six themes (with subthemes): suffering uncontrollable and ongoing upheaval (dictating life choices and course, disrupting role functioning, limited by debilitating symptoms, unstoppable and far reaching fatigue); weighed down by mental load (struggling with unrecognised distress, anxiety provoked by the volatility and constancy of symptoms, depleting motivation and pleasure); harbouring shame and judgement (marked as unhygienic and contagious, rejected and isolated, resenting own appearance, pain and embarrassment in intimacy); demoralised by inadequacies and burden of therapy (disappointed by unmet expectations of treatment benefit, daily drudgery, deterred by unpalatable or inconvenient treatments, disempowered by lack of personalised care, fearing long term side effects); gaining control (making sense of the condition, shutting the disease out, accepting a new health status, attuning to the body); and making confident treatment decisions (trading off perceptible benefits against safety and convenience, relying on family input, reassured by clinician acknowledgement of fears, seeking empowering relationships with clinicians).

**Conclusions:** Patients with psoriasis and psoriatic arthritis contend with profound disruption in their functioning, roles and life course; fear deterioration of their health; and have unmet expectations about their treatment and care. Patients with psoriasis feel marked by their disease, stigmatised and rejected by others while patients with psoriatic arthritis experience social withdrawal and depleted motivation due to fatigue, joint impairment and pain. Establishing therapeutic relationships, addressing treatment expectations, and supporting psychosocial needs may help to improve satisfaction and outcomes in patients with psoriasis and psoriatic arthritis.

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#### AB1238 THE SELF-MANAGEMENT MODEL IN THE AGENDA OF SUCCESSIVE CONSULTATIONS IN RHEUMATOLOGY

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**Background:** The rheumatology service of Ciudad Real Hospital, located in an autonomous community of that same name that is nearly in the centre of Spain, implemented a self-management model of successive appointments more than



10 years ago. Since then, the physicians of the department schedule follow-up visits for their patients depending on the disease, its course and ancillary tests.

**Objectives:** The purpose of this study is to evaluate and compare the self-management model for successive appointments in the rheumatology service of Ciudad Real Hospital versus the model of external appointment management implemented in 8 of the hospital's 15 medical services.

**Methods:** A comparative and multivariate analysis was performed to identify variables with statistically significant differences, in terms of activity and/or performance indicators and quality perceived by users. The comparison involved the self-management model for successive appointments employed in the rheumatology service of Ciudad Real Hospital and the model for external appointment management used in 8 hospital medical services between January 1 and May 31, 2016.

**Results:** In a database with more than 1 00 000 records of appointments involving the set of services included in the study, the mean waiting time and the numbers of non-appearances and rescheduling of follow-up visits in the rheumatology department were significantly lower than in the other services. The number of individuals treated in outpatient rheumatology services was 7,768, and a total of 280 patients were surveyed (response rate 63.21%). They showed great overall satisfaction, and the incidence rate of claims was low.

**Conclusions:** Our results show that the self-management model of scheduling appointments has better results in terms of activity indicators and in quality perceived by users, despite the intense activity. Thus, this study could be fundamental for decision making in the management of health care organisations.

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**Disclosure of Interest:** None declared

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#### AB1239 THE BRAZILIAN RHEUMATOLOGY TRIAGE: AN ASSESSMENT OF THE PRIMARY HEALTHCARE SYSTEM

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**Background:** There are more than 100 rheumatic diseases involving 10% of the population. Their clinical manifestations and treatment vary but generally progress to disability. Recently, new technologies in rheumatology are available for diagnosis and treatment. However, the timely diagnosis and access to treatment are essential to prevent disability. Many barriers for the access to the rheumatologist have been identified, namely: population lack of knowledge regarding rheumatic diseases, lack of prioritisation in the reference process from primary care to rheumatologists, and scarcity of rheumatologists. Therefore, it is fundamental to address all the barriers and present facilitators in the healthcare system to ensure that rheumatic patients have timely access to rheumatologists.

**Objectives:** To assess the primary healthcare triage system in Maringá, a countryside city in the state of Parana-Brazil. Mainly, identifying barriers (waiting time from symptoms to primary care visit, to timely access to rheumatologists and beginning the treatment).

**Methods:** This is a cross-sectional study. The population of Maringá in 2016 was 399.605 people. There were 1200 patients in the waiting list for rheumatologists (2016). Medical records were analysed to describe the format and content of referrals, the duration of symptoms, exams ordered, and diagnosis agreement with rheumatologists.

**Results:** Medical records of 774 women and 147 men were analysed. The mean (SD) age was 55,1 (16)yrs. old. The median (IQR) time from symptoms to the rheumatologic visit was 16 mo. (9 to 28). About 10% of the referrals did not mention any detail about physical examination or diagnosis. 207 (22%) had diagnosis of gout, osteoporosis, rheumatoid arthritis, spondyloarthritis, and systemic lupus erythematosus. 111 patients (10%) cancelled their visits.

**Conclusions:** The period from the symptoms to the visit with rheumatologists was large. The format and content of the referrals were incomplete. There were many patients that cancelled the visits with unknown prognosis. Educational

initiatives should be implemented in Maringá-Brazil to enhance the skills of the primary care physicians to establish referral priorities and to start timely treatment.

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#### AB1240 EFFECT OF A MULTIDISCIPLINARY APPROACH IN THE PHARMACOLOGICAL THERAPY PROCESS FOR PATIENTS WITH RHEUMATOID ARTHRITIS IN A SPECIALISED RHEUMATOLOGY CENTRE

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**Background:** Rheumatoid arthritis (RA-9 is an inflammatory autoimmune disease with a prevalence of 0.2% to 1%.<sup>1</sup> Although the advances in pharmacological treatments offered to manage the disease have achieved many goals, the disappearance of symptoms and disabilities are accomplished by a small proportion of patients with RA.<sup>2</sup> However, patients need a follow up where a multidisciplinary team care programs for patients with RA take into consideration not only the disease activity but psychosocial, adherence and other aspects that conventional care does not take into account, showing a positive effect in all life aspects of a patient with RA.<sup>2,3</sup>

**Objectives:** To evaluate the effectiveness regarding, treatment, safety and rehabilitation in patients with a complex disease activity through a multidisciplinary care management.

**Methods:** Once a rheumatologist identified a patient with RA with indication to begin biological therapy or switching from one biological to another, a checklist and an evaluation was performed, then the patient was presented in a multidisciplinary team meeting where a rheumatologist, pharmaceutical chemist, psychologist, physiatrist and a nurse assessed the particular case of the patient. Additionally, an ultrasound was performed in every patient in order to evaluate disease activity. Based on the patient's disease activity, adherence to treatment, psychosocial and economic factors the pharmacological therapy and management of the patient was prescribed.

**Results:** During 18 months 551 patients were evaluated by a multidisciplinary team, 90% to define the pharmacological therapy, and 10% for biologic switching. Mean DAS28 of patients was 3.79±1.37, once the patients were evaluated the choices made by the team were: 60% continued in follow-up receiving conventional DMARDs therapy because ultrasound didn't show any disease activity; finally biological therapy was initiated in 21% and switching among biologicals was made in 11%. conventional therapy was adjusted in 5% of patients, and discontinuation of therapy due to non-adherence of patients or other reasons was ordered in 3%.

**Conclusions:** As other studies have shown, a multidisciplinary assessment of the patient with RA from different viewpoints allows taking into consideration aspects that are not linked only to the pharmacological therapy but to other aspects in a patient's life. Also we avoided high costs therapies for the management of rheumatoid arthritis, therefore we contribute not only to the health outcomes of patients but the health economic aspects in the management of RA.

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**Disclosure of Interest:** None declared

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### AB1241 HIGH LEVELS OF PATIENT SATISFACTION IN A PUBLIC HOSPITAL STREAMED RHEUMATOID ARTHRITIS CLINIC COHORT

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**Background:** Many Australian public rheumatology services have now adopted streamed clinics for RA and specific rheumatic diseases to promote best practice care. Our RA clinic has been operating for a decade and serves a large population in Southeast Victoria. Patient attitudes to such streamed clinics have not been extensively examined, despite the integral role patient satisfaction plays in decisions about how health care is delivered<sup>[1,2]</sup>.

**Objectives:** To evaluate the level of patient satisfaction in an established tertiary hospital streamed RA clinic.

**Methods:** A cross-sectional study of 106 patients was undertaken at a public RA outpatient's clinic. Eight domains included questions which evaluated clinic administration, the consultation itself, and overall experience using a Likert scale ranging from 1–5 (1=very poor, 5=very good). Qualitative comments were also recorded.

**Results:** Patient attitudes toward the clinic were predominately positive. 90.5% of patients scored their overall experience as good<sup>4</sup> or very good<sup>5</sup> (mean=4.46), with 69.8% of these patients scoring 5. Questions regarding the consultation itself received the highest satisfaction scores. Patients were highly satisfied with the explanations given about their condition or treatment (mean=4.59), addressing of patient concerns (mean=4.56) and length of consultation (mean=4.52). Waiting time received the lowest satisfaction score (mean=3.25), and a further 36.4% of qualitative comments expressed dissatisfaction with the long wait times. 15.2% of qualitative comments regarded limited parking at the hospital, and 9.1% to difficulty locating the clinic within the hospital. 6.1% of patients wanted more information regarding complementary medications or lifestyle modifications. Despite this, 94.7% of all patients surveyed would recommend the clinic to friends or family.

**Abstract AB1241 – Table 1**

Category	Question	Mean
Clinic administration	Ease of booking appointments	4.36
	Waiting time	3.25
Consultation	Explanations given by doctor/nurses	4.59
	Questions and concerns answered to your satisfaction	4.56
	Amount of time	4.52
Overall Experience	Rating of overall experience	4.46
	Would you recommend clinic to friends/family	Yes=94.74% No=5.26%

**Conclusions:** High levels of patient satisfaction with the streamed RA clinic consultation outweighed frustrations with wait times and parking. This is demonstrated by the high overall rating and most patients being likely to recommend the clinic, and highlights the priority and importance of good communication for patient satisfaction. These findings can guide areas of future improvement to the quality of patient experience. From the perspective of patients, streamed disease clinics like this RA clinic appear to be highly acceptable in the provision of specialised care, and have garnered extremely positive patient satisfaction and feedback.

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### AB1242 COMPARING ADHERENCE TO TREATMENT IN LUPUS AND VASCULITIS PATIENTS

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**Background:** Good adherence to prescribed pharmacotherapy is often over-estimated by physicians. Although in Systemic Lupus Erythematosus (SLE) non-adherence is well-researched,<sup>1</sup> less research exists for vasculitis.

**Objectives:** We compared cohorts of patients with SLE and vasculitis to identify emerging patterns, behaviours and differences that could introduce barriers to adherence.

**Methods:** With patient input, we designed and undertook an anonymised questionnaire-based survey on the assessment of self-reported adherence and influencing factors in lupus and vasculitis clinics at University College Hospital (UCLH) and Royal Free Hospital (RFH). Both serve a largely urban and ethnically diverse population.

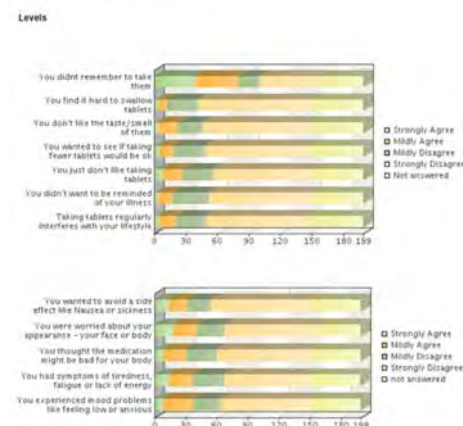
**Results:**

**Abstract AB1242 – Table 1**

	Lupus (n=110)	Vasculitis (n=75)	P value
Female	99/109 (91%)	43/73 (59%)	<0.001
Age>60 years	14/104 (14%)	34/68 (50%)	<0.001
Disease duration>10 years	61/106 (58%)	18/74 (24%)	<0.001
Self-rate Disease activity≥7/10	17/106 (16%)	16/70 (23%)	0.324
Kidney function Moderate or severe	32/96 (33%)	22/73 (30%)	0.659
Self-medicating	103/108 (95%)	69/72 (96%)	1.00
"Always taking tablets as prescribed"	70/102 (67%)	50/62 (81%)	0.104
"Managing well with medication"	52/103 (51%)	63/66 (96%)	0.0001
≥7/10 on Self rate Likert scale			
Attending>75% of clinic appointments	99/107 (93%)	72/72 (100%)	0.022

A total of 199 patients completed the questionnaire. 110 (55%) had lupus and 75 (38%) vasculitis. 14 (7%) patients reported having other conditions and thus excluded. 52% were Caucasian and 37% were born outside the UK. The majority (78%) were female and 28% were aged >60 years. Half were university graduates. Both centres had similar number of responses reducing bias. As shown in table 1, lupus patients were more females (p<0.001), younger (p<0.001), with longer disease duration (p<0.001) and commented that adherence decreased with time (p=0.011) compared to vasculitis patients. Conversely, the vasculitis patients had higher attendance at clinic appointments (p=0.022) and were more confident they could manage taking tablets correctly. 67% of lupus patients and 81% of vasculitis patients reported that they always took tablets as prescribed (p=0.104). Concerns of weight gain and osteoporosis worried patients on steroids. Changes in weight, appearance, nausea and fatigue were common side-effects for missed medications. A small number of patients cited religion or alternative therapies as a reason (<5%). Furthermore, as shown in fig 1, non-deliberate forgetfulness was the most common reason for non-adherence, in both groups. Overall, the majority of patients (96%) were self-medicating and reported taking an average of 5 different types of tablets, half of this for their Lupus/Vasculitis. Patients were well-informed about their condition and medications.

**Reasons relating to the Tablets/Medication**



**Abstract AB1242 – Figure 1**

**Conclusions:** Self-reported adherence was high in our cohort with differences between the two groups. "Forgetfulness" regarding medication and keeping track of hospital appointments were the commonest reasons for non-adherence rather than deliberate non-adherence. Therefore novel behavioural or electronic cues for medication, including mobile app use, and appointment alerts could lead to improvement. Further work is required to identify whether a different personalised approach in the lupus and vasculitis patients can improve adherence.

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**Disclosure of Interest:** None declared

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AB1243

#### GETTING A HEEADSSS IN PSYCHOSOCIAL SCREENING: USE OF STANDARDISED CLINIC NOTE TEMPLATES FOR PSYCHOSOCIAL SCREENING IN A PAEDIATRIC RHEUMATOLOGY CLINIC

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**Background:** Children and adolescents with rheumatic diseases are at risk for psychosocial challenges related to illness, treatment, and normal development and should receive psychosocial screening. Psychosocial assessments have been successfully utilised in other paediatric specialties, including oncology and gastroenterology. A common psychosocial screening tool is the HEEADSSS (home environment, education/employment, eating, activities, drugs, sexuality, suicide/depression, and safety). This tool is easy to remember, quickly administered, and modifiable for younger children.

**Objectives:** We conducted a quality improvement project aimed to increase psychosocial screening by providers in a single paediatric rheumatology clinic by instituting standardised follow up templates for juvenile idiopathic arthritis (JIA) and systemic lupus erythematosus (SLE) including the HEEADSSS assessment.

**Methods:** The quality improvement intervention evaluated in this study involved the creation of disease specific follow up note templates inclusive of the HEEADSSS assessment and introduction of the templates to the paediatric rheumatology fellows clinic. Charts of patients with an ICD-10 diagnosis of JIA or SLE were reviewed during a 3 month window prior to (February-April 2017) and after (October-December 2017) the intervention. Charts were reviewed for presence of 2 elements of the HEEADSSS assessment documented within the previous 12 months: smoking exposure (all patients) and sexual activity (ages 11 years and up). The proportion of patients with completed HEEADSSS assessment components pre- and post-intervention were compared using Fisher's exact test.

**Results:** Chart review included 36 patients pre- and 42 post-intervention (table 1). There was an increase in assessment of both measures in the period immediately following the intervention. Assessment of smoking exposure increased from 0.0% to 21.4% ( $p=0.003$ ) with greater but not significant improvement in SLE versus JIA patients (29.4% versus 16.4%,  $p=0.45$ ). Assessment of sexual activity in

patients 11 years and older increased from 13.0% to 37.5% ( $p=0.09$ ), although this comparison may be underpowered due to decreased sample sizes.

**Abstract AB1243 – Table 1.** Documentation status pre- and post- implementation of standardised follow up templates for providers.

	Pre-Intervention	Post-Intervention	p-value
Smoking assessed			
Overall	0/36 (0.0%)	9/42 (21.4%)	0.003
JIA	0/20 (0.0%)	4/25 (16.0%)	0.12
SLE	0/16 (0.0%)	5/17 (29.4%)	0.04
Sexual Activity (11+) assessed			
Overall	3/23 (13.0%)	9/24 (37.5%)	0.09
JIA	1/9 (11.1%)	2/8 (25.0%)	1.00
SLE	2/14 (14.3%)	7/16 (43.8%)	0.14

**Conclusions:** Introduction of standardised note templates with the HEEADSSS assessment has resulted in preliminary improvement in psychosocial screening by providers in a single paediatric rheumatology clinic as demonstrated by improved rates of screening for smoking exposure and a trend towards improved screening rates for sexual activity. Additional studies are needed to confirm these findings, and future studies will assess whether the improvement seen is sustained and whether usage of this template can be expanded to other paediatric patient populations.

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AB1244

#### QUALITY LIFE IN PATIENTS WITH RHEUMATIC DISEASE, NON-RHEUMATIC DISEASES AND HEALTHY POPULATION

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**Background:** Within public health strategies, the quality of life is a fundamental factor of intervention. The EQ-5D-3L is one of the most used instruments worldwide.

**Objectives:** To describe the change in quality of life and functional limitation of patients with rheumatic diseases compared to a healthy population and patients with other systemic diseases.

**Methods:** The EQ-5D-3L survey was used in 6693 people from 6 cities in Colombia. An analytical study was developed.

**Results:** In general, the healthy population ( $n=1104$ ) reported not to have problems according to the EQ-5D-3L (median: 98,34). Of the non-rheumatic patients ( $n=642$ ), 20% showed a moderate compromise because of pain and discomfort, as well as anxiety and depression. Twenty percent of patients with cardiovascular

**Abstract AB1244 – Table 1.** Dimensions of EQ-5D-3L in patients with non-rheumatic diseases

		HBP n=201	Venous insufficiency n=190	Migraine n=158	Mental diseases n=137	Obesity n=95	Diabetes n=55	CVD n=53	Cancer n=13	Stroke n=11
MOBILITY	No problems	93,5	95,8	98,1	97,1	93,7	96,4	90,6	100	81,8
	Some problems	6,5	4,2	1,9	2,9	6,3	3,6	9,4	0	18,2
	Confined to bed	0	0	0	0	0	0	0	0	0
SELF-CARE	No	97,5	97,9	98,7	100	98,9	98,2	94,3	100	90,9
	Moderate	2	2,1	0,6	0	1,1	1,8	3,8	0	9,1
	Extreme	0,5	0	0,6	0	0	0	1,9	0	0
USUAL ACTIVITIES	No problems	95,5	97,4	99,4	99,3	97,9	100	92,5	100	90,9
	Some problems	4	2,6	0,6	0,7	2,1	0	7,5	0	9,1
	Unable to	0,5	0	0	0	0	0	0	0	0
PAIN/ DISCOMFORT	No	87,1	89,5	86,1	84,7	88,4	92,7	84,9	92,3	81,8
	Moderate	11,9	9,5	12	14,6	11,6	5,5	13,2	7,7	18,2
	Extreme	1	1,1	1,9	0,7	0	1,8	1,9	0	0
ANXIETY/ DEPRESSION	No	91	93,7	92,4	76,6	94,7	96,4	84,9	92,3	90,9
	Moderate	8,5	6,3	7,6	22,6	5,3	1,8	15,1	7,7	9,1
	Extreme	0,5	0	0	0,7	0	1,8	0	0	0



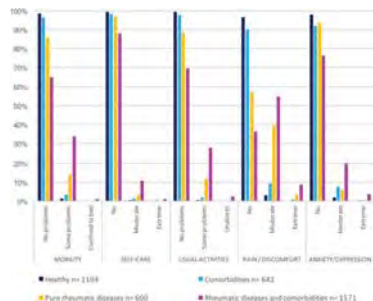
disease (n=53) reported moderate limitation for mobility. Patients with cardiovascular diseases reported moderate difficulties in carrying out daily activities.

\* The values of each of the dimensions of the instrument are expressed in%

\*\* HBP: high blood pressure, CVD: cardiovascular disease, TB: tuberculosis

\*\*\* Mental disorders: anxiety, nervousness or depression.

Patients with rheumatic diseases (n=2274) manifested different degrees of limitation in mobility and daily activities. Patients with rheumatic diseases and comorbidities had greater compromise in quality of life predominately by pain and physical discomfort (more than 50% of the patients) figure 1.



**Abstract AB1244 – Figure 1.** EQ5D-3L in patients with comorbidities, rheumatic diseases and healthy patients

**Conclusions:** In comparison with general population, rheumatic patients had a lower quality of life, and it is even worse in patients with rheumatic diseases and comorbidities. Comprehensive care of rheumatic patients should include strategies to improve standards of quality of life such as mobility, to perform daily activities and management of problems such as pain and discomfort. There are specific factors of intervention to reduce long-term disability of patients with rheumatic diseases.

**Disclosure of Interest:** None declared

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#### AB1245 EFFECTS OF A WORKPLACE-CENTRED COUNSELLING OF INDIVIDUALS WITH MUSCULOSKELETAL COMPLAINTS: A PROSPECTIVE COHORT STUDY

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**Background:** Actively employed people with musculoskeletal complaints frequently seek medical advice only when symptoms have become chronic and have led to loss of workability.

**Objectives:** In this study, a brief examination was offered in the workplace setting in order to detect and to counsel individuals with symptoms of Rheumatic and musculoskeletal diseases (RMDs).

**Methods:** Employees of four companies were sent a screening questionnaire regarding musculoskeletal problems. In case of a positive screening, consultation by RMD specialists was offered which took place close to the workplace. If necessary, participants were referred to a practice/clinic specialised in RMDs (Orthopaedics, Rheumatology, Physical Medicine). Employees' work was categorised into physically highly demanding (HD) and less demanding (LD).

From participants consenting to follow-up, additional data were acquired: demographics, known pre-existing RMD, pain intensity, affected region(s), current treatment, number of sick leave-days due to musculoskeletal complaints, and out of pocket costs for treatments during the preceding year. General wellbeing and depression were measured by Euroqol-5d (EQ-5d) and Hospital Anxiety and Depression Scale (HADS). After one year, information about general wellbeing, pain intensity, treatment, individual costs, and days of sick leave during the intervening year was collected by telephone-interview.

**Results:** 6170 employees were invited. 413 participated in the counselling program, 344 were enrolled in the study. 56.6% of the participants had no previously diagnosed RMD, after the specialists' assessment, this percentage decreased to 35.7%. Men with LD workload had significantly higher wellbeing (EQ-5d scale):  $77.3 \pm 15.1$  compared to women with both LD ( $71.0 \pm 20.1$ ,  $p=0.034$ ) and HD ( $64.6 \pm 21.3$ ,  $p=0.001$ ). LD and HD differed significantly regarding percentage with painful upper ( $28.6$  vs.  $45.3$ ,  $p=0.006$ ) and lower ( $49.6$  vs.  $65.3$ ,  $p=0.016$ ) limbs.

Back pain was distributed equally among all groups. HD women reported significantly higher use of NSAIDs (55.1% vs. 27.7% in female LD, 21.7% in male HD, 23.5% in male LD,  $p=0.001$ ). HD men showed the lowest ( $4.1 \pm 2.9$ ), HD women showed the highest HADS anxiety-score ( $6.3 \pm 3.8$ ,  $p=0.042$ ).

235 individuals participated in telephone follow-up. There was significant improvement in wellbeing (mean  $77.2 \pm 17.4$  vs.  $73.6 \pm 18.2$  at baseline,  $p=0.006$ ) and in rating of RMD pain (mean  $27.8 \pm 24.9$  vs.  $40.8 \pm 24.6$  at baseline,  $p=0.001$ ). Participants who were suspected by the specialist to suffer from RMDs had significantly increased out of pocket costs after one year (mean in €  $441.8 \pm 861.6$  vs.  $254.1 \pm 407.0$ ,  $p=0.026$ ). Use of NSAIDs decreased significantly from 29.1% to 17.4%,  $p=0.02$ . Conversely, rates of use of physiotherapy (7.6 vs. 24.7,  $p=0.001$ ), gymnastics (2.7 vs. 23.4,  $p=0.001$ ), physical therapy (12.8 vs. 43.3,  $p=0.027$ ) and complementary/alternative methods (7.4 vs. 13.2,  $p=0.003$ ) were significantly increased.

**Conclusions:** In our study we found most physical and psychological problems related to RMDs in HD working women. After one year, participants reported improved quality of life, reduction of RMD pain, higher utilisation of medical services and of gymnastics, less use of NSAIDs, and, if suspected to suffer from RMDs, higher out of pocket costs. Thus, this brief workplace-centred intervention appears to have had beneficial effects on both subjective well-being and on objective parameters suggesting improvements in physical/physiological health.

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#### AB1246 PROVISION OF RHEUMATOLOGY SERVICES TO 30 MILLION PEOPLE IN NORTH-WESTERN PAKISTAN (A NAÏVE DEPARTMENT WITH HUGE CHALLENGES)

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**Background:** Practicing rheumatology needs multidisciplinary team work and also good funding. This becomes difficult in places where proper structure of healthcare is lacking.

**Objectives:** To share experience of establishing a Rheumatology unit in Khyber Pukhtunkhwa (KP) Pakistan.

**Methods:** KP is the Northwestern province of Pakistan. The population of KP is 30 million. The per capita income of Pakistan was 1180 US \$ in 2016.

Modern day treatments are expensive in rheumatology. Difficulties are in areas of expertise and biologics.

The first ever Rheumatology unit was established in Lady Reading Hospital (LRH) Peshawar in July 2017 which started its regular outpatient services. Problems at the start were absence of specialist nurses, junior doctors, special immunology and MSK Radiologists. Regular MSK ultrasound was started along with routine procedures. This had an enormous impact on the quality of care. Lack of awareness about rheumatic diseases in general population has been an issue which was addressed through newspapers, television and social media. The response was excellent. The outpatient numbers have raised, referral pathway was established and more patients are now seen in outpatients. Team was further built up by acquiring a trainee registrars and a consultant rheumatologist. Another problem was lack of proper patients education system due to lack of specialist nurses and non-availability of literature in local languages. Biologics are costly and very few people can afford these. Pakistan Baitul Maal, a charitable organisation is the only way to provide biologics to patients on need basis. Currently only few biologics are available in the market i.e Etanercept, Rituximab and Tocilizumab. Adalimumab will come to market sometime in 2018.

Kids with Juvenile Idiopathic arthritis, Systemic Lupus Erythematosus and other rheumatic problems are difficult to manage as there is no Paediatric Rheumatologist available in the entire province. We now have established a rapport with our paediatric colleagues which is working well.

Pakistan has only seven hospitals where training is offered in rheumatology but all are based in other provinces and none in KP. For this purpose we are in the process of establishing a dedicated rheumatology department where full training will be given to trainees according to international standards.

The data on rheumatic diseases is non-existing so we are now working on data collection on our local population.

**Results:** Working as a rheumatologist is a big challenge in under resourced areas. We have been having worst case scenario in almost all aspects. However someone has to be at the forefront as millions of people have rheumatic diseases and they cannot be left alone with these conditions untreated.



Abstract AB1246 – Figure 1

**Conclusions:** The idea is to persevere and continue efforts for the betterment of our patients. More specialists are needed to fill in the gaps along with appropriate funding to develop rheumatology services in our part of the country. We feel that situation in other countries with low socio-economics will be more or less the same or even worst for patients with rheumatic diseases. International communities and leagues such EULAR, BSR, ACR and APLAR etc should discuss this on their forums to see if in anyway they can improve lives of millions of people with rheumatic disorders in under-resourced countries.

**Disclosure of Interest:** None declared

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AB1247

#### IMPACT OF A SELF-CARE EDUCATION PROGRAM FOR PATIENTS WITH OSTEOARTHRITIS

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**Background:** Osteoarthritis (OA) has a prevalence rate that reaches 29% in people older than 60 years<sup>1</sup>. Treatments available are limited. The costs of OA in Spain are about 4.800 million euros/year<sup>2</sup>.

**Objectives:** To create a self-care program for OA patients in order to improve their quality of life (QoL) and therefore to reduce the socioeconomic cost.

**Methods:** The design of the program was carried out by 2 PC physicians, 1 rheumatologist, 1 rehabilitator, 1 nurse and 2 psychologists. The program included a total of 9 sessions of 1.5 hours once a week. There were 2 sessions for each of the following topics: general information, physical activity, nutrition, coping with the disease, and 1 summary session. Three OA patients were trained and afterwards they were in charge of imparting the program to other patients with the assistance of a nurse. Before and after the program some data was collected relating the patients' knowledge, food and physical activity habits, social networks and hours of rest. They were asked to complete WOMAC, EuroQoL-5D, and HAD Scale questionnaires. The statistical analysis was performed using package SPSS v16.

**Results:** 60 Knee OA patients were recruited from Hospital del Mar and Vila Olímpica PC centre, and divided into 6 different groups. Only the results of the first two groups are shown. Group1 (11 patients) and 2 (10 patients). First we analysed differences between the basal data and the ones collected after the last session. The analysis of the data from all the patients (groups 1 and 2) showed that in knowledge about OA management the average value obtained in the basal visit was  $6.31 \pm 2.798$ , and  $7.81 \pm 1.94$  after the last session ( $p=0.024$ ). Analysis of pain by VAS showed that the average value in the basal visit was  $3.91 \pm 1.82$ , and  $2.44 \pm 2.03$  after the last session ( $p=0.014$ ). We observe a tendency, although it doesn't reach significant differences in QoL, where the average value in the basal visit was  $2.31 \pm 1.81$ , and  $1.63 \pm 1.54$  after the last session ( $p=0.052$ ). In the HADS scale the average value in the basal visit was  $9.86 \pm 6.02$ , and  $8.36 \pm 5.40$  after the last session ( $p=0.052$ ). Regarding the analysis of differences between two groups, categorical items were analysed. In the total questionnaire at the end of the sessions the average for group 1 was 6.89 and for group 2 was 8.75 ( $p=0.038$ ). Meeting with friends frequency at the beginning and at the end of the study was also different among groups ( $p=0.014/p=0.019$ ).

**Conclusions:** This self-care education program had a positive effect on the OA patients pain perception, and it could also be observed an improvement in QoL and the anxiety and depression. As differences among groups were also observed, socioeconomic and education aspects must be considered in the future.

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AB1248

#### VACCINATION RATE IN PATIENTS WITH RHEUMATIC DISEASES: A CROSS-SECTIONAL STUDY IN MEXICAN PATIENTS

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**Background:** Patients with rheumatic diseases have an increased risk of infections, which can be prevented with vaccination schemes. The vaccination rate in rheumatic patients is low in Mexico (17%–25%), mainly because of the lack of physician recommendation. Vaccination strategies have been shown to improve adherence to the application.

**Objectives:** The objectives of the study was to determine the vaccination rate in patients with rheumatic diseases and the main reasons of failed vaccination.

**Methods:** We questioned 84 patients from the rheumatology clinic of the Univesitary Hospital "José E. González", Mexico, from June to July 2017. The vaccination status and the reasons for failed vaccination were recorded.

**Results:** The majority of patients were women (89.3%), average age 50 years (17–81 years). Most of the patients had rheumatoid arthritis (45.3%), followed by other autoimmune diseases (27.4%) and non-autoimmune diseases (27.4%). The highest rates of vaccination were for tetanus-diphtheria (44%), influenza (39.3%) and pneumococcus (31%). They were lower for hepatitis B virus (9.8%), human papilloma virus (4.8%), hepatitis A virus (2.4%) and herpes zoster virus (0%). The main reason for failed vaccination was the lack of indication from the physician (34.5%). If indicated, 89.3% of the patients would accept to be vaccinated.

Abstract AB1248 – Table 1

Vaccination rate	Influenza	Pneumococcus	Hepatitis B	Human Papillomavirus	Herpes Zoster
Rheumatoid Arthritis	15 (39%)	16 (42%)	3 (7.9%)	1 (2.6%)	0 (0%)
Systemic Lupus Erythematosus	2 (25%)	1 (12.5%)	1 (12.5%)	1 (12.5%)	0 (0%)
Spondyloarthritis	1 (33%)	1 (33.3%)	0 (0%)	0 (0%)	0 (0%)
Systemic sclerosis	2 (25%)	2 (25%)	0 (0%)	0 (0%)	0 (0%)
Other autoimmune diseases	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
<b>Reason of failed vaccination</b>					<b>N%</b>
Lack of medical recommendation					29 (34%)
Fear of vaccine side effects					8 (9.5%)
Previous vaccine side effects					2 (2.4%)
Disbelief in vaccination					7 (8.3%)
Other reasons					35 (41%)

**Conclusions:** We found a low vaccination rate in the rheumatology clinic. We found an insufficient promotion and indication of vaccination by the rheumatology staff. Constant fomentation and updated knowledge about vaccination recommendations in autoimmune diseases is necessary for the prevention of infections and to improve the comprehensive care of patients with rheumatic diseases.

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AB1249

**AN ANALYSIS OF INPATIENT REFERRALS TO RHEUMATOLOGY IN AN IRISH TERTIARY REFERRAL HOSPITAL**

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**Background:** Reviewing patients under other services is an important part of the service we deliver in our hospital's rheumatology department.

**Objectives:** In order to improve quality of the inpatient consult service and relevance of teaching delivered to rheumatology trainees, we wanted to examine the nature of referrals to our service.

**Methods:** All available consults (n=81) were reviewed. The age, gender, urgency and referral source were recorded. The most likely reason for referral as decided by our specialist registrar (research fellow) were determined.

**Results:** 49% of patients were 70 years of age or older. 30% of patients were 70–79 years old. 68% were female. There was a wide range of referrals, 21% were vasculitides (including polymyalgia and giant cell arteritis), 20% inflammatory arthritides, 19% crystal arthropathies, 16% connective tissue disease, 14% osteoarthritis, 3% septic arthritis, 3% fibromyalgia, 3% pyrexia of unknown origin, 1% sarcoid, 1% antiphospholipid syndrome and 1% osteoporosis. 59% of consults came from general medical teams, 14% from acute medicine, 14% from surgery, 3% from psychiatry and 11% from other inpatient services (including haematology, oncology etc).

36% of consults were considered urgent (to be seen within 24 hours) by the referring team, 64% were routine (to be seen within 48 hours).

**Conclusions:** Almost half of referrals were over 70 years of age. Most referrals came from medical teams. The majority of consults were women and referred due to a vasculitis, inflammatory arthritis or connective tissue disease. 3% were septic arthritis. Our trainee teaching will now focus primarily on these topics.

3% of referrals were for fibromyalgia, which could perhaps be managed on an outpatient basis. This may improve utilisation of limited inpatient hospital resources.

**Disclosure of Interest:** None declared

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AB1250

**VACCINATION AWARENESS AND UPTAKE IN INFLAMMATORY ARTHRITIS PATIENTS**

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**Background:** Inflammatory arthritides (IA) increase infection risk. The Centre for Disease Control and Prevention recommends influenza vaccination for all adults and pneumococcal vaccine for >65 years old and under 64 years receiving certain immunosuppressive therapies, including TNF inhibitors.

**Objectives:** We examined patients' knowledge, uptake and attitudes to influenza and pneumococcal vaccination and opportunities to increase vaccination rates in our IA clinic.

**Methods:** Patients attending the IA Clinic completed an anonymous 23 question worksheet recording demographic details, medical history, medications, knowledge about vaccinations, vaccination status, reasons for non-vaccination and availability and willingness to use smartphone for healthcare records.

**Results:** 329 patients completed the survey. Respondents were predominantly female (78%). 69% were >50 years old. 82% had completed secondary education. 59% of patients had rheumatoid arthritis, 11% had psoriatic arthritis and 30% other conditions. 29% of patients were taking a biological DMARD, 27% using methotrexate and 19% oral steroids.

52% knew some rheumatological conditions increase infection risk. 54% knew some rheumatological medications can increase infection risk.

66% knew influenza vaccination was recommended, most commonly via their general physician (GP) (70%). 50% of patients were up to date with their 'flu' vaccination, mainly (75%) via their GP. Reasons for non-vaccination included lack of awareness (45%) and fear of side effects (25%).

29% knew pneumococcal vaccination may be indicated, 78% of whom were informed by their GP. 33% of patients were up to date with their pneumococcal vaccine. 80% cited lack of awareness for non-vaccination.

70% of patients had smart phone access. 74% of these were willing to use this for their healthcare record and reminders re vaccination.

**Conclusions:** These data show low awareness amongst IA patients of the risk of immunosuppression associated with their disease and treatments and the need for regular vaccinations. Mobile technology may help increase vaccination rates.

**Disclosure of Interest:** None declared

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AB1251

**QUALITY OF INPATIENT REFERRALS TO RHEUMATOLOGY IN AN IRISH TERTIARY REFERRAL HOSPITAL**

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**Background:** A previous audit of inpatient referrals to our service found 21% were vasculitides, 20% inflammatory arthritides, 19% crystal arthropathies, and 16% connective tissue disease. It was felt that many of these referrals lacked appropriate investigations (such as inflammatory markers) prior to rheumatology review.

**Objectives:** Prior to transitioning from handwritten to electronic consults, we wanted to examine the data given in inpatient referrals to our service.

**Methods:** All available consults (n=81) were reviewed. We assessed whether the age/date of birth, gender, location, duration of symptoms, medications, clinical examination findings, reason for consult, urgency and suspected diagnosis had been written on the consult request form. We examined what investigations were detailed (any blood result, C Reactive Protein (CRP) value and any imaging result) and what referrer details were given (name, contact details, consultant responsible).

**Results:** In 99% of cases, patients age or date of birth was given by the referring team. 84% detailed gender. 78% contained ward. 68% contained bed number. 56% listed urgency.

96% indicated reason for consult. 30% listed duration of symptoms. 21% detailed whether patient known to rheumatology service. 57% gave suspected diagnosis. 33% gave medications. 42% detailed clinical examination findings. 41% reported any blood test. 27% gave a CRP. 44% detailed imaging findings.

49% contained referrer name. 80% had referrer contact details. 70% gave referring consultant.

**Conclusions:** Overall, it was felt many of the inpatient referrals to our service lacked potentially important details. Less than half of consult requests included duration of symptoms, medications, examination findings, blood test results or referrer name.

We will soon be transitioning to an electronic referral system and all of these data points must be entered prior to submission of the consult. Hopefully, this will improve the quality of care we deliver to our patients.

**Disclosure of Interest:** None declared

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AB1252

**PREVALENCE OF ANALGESIC USAGE IN PATIENTS WITH RHEUMATOID ARTHRITIS AND RELATIONSHIP WITH DISEASE ACTIVITY**

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**Background:** Rheumatoid arthritis (RA) is a systemic, autoimmune disease in which chronic pain is a persistent symptom,<sup>1</sup> additionally pain management remains as a serious public health issue. Pain is often disabling and can reduce the quality of life of a patient.<sup>2</sup>

**Objectives:** To describe prevalence of analgesic usage in patients with rheumatoid arthritis and relationship with disease activity.

**Methods:** We collected data from the medical charts in a specialised RA centre conducted during 2017, we performed a descriptive analysis, we collected socio-demographic information, DAS28, and the prevalence of prescription of analgesic medications divided in three groups non opioid analgesics, opioid analgesics and NSAIDs. We calculated means, and standard deviations for continuous variables and categorical variables were presented as rates. We estimated the prevalence of comorbidities and evaluate independent associations calculating prevalence ratios.

**Results:** We included data from 6700 patients, 80% were women and 20% were men. Mean age was 59 years±13, 47% of all patients were between 60 and 80 years; The prevalence of use pain medications was 63.41%. Most of patients received non opioid analgesics 52% (paracetamol or dipyron) followed by opioids 23% (codein or tramadol), 10% of patients had pain medication combination of non opioids plus opioids. See table 1. The prevalence of pain medications usage was associated with sex but not with disease activity see table 2.



**Abstract AB1252 – Table 1.** Characteristics of patients with RA and comorbidities

Pain medication	n	%
Non-opioids	2234	52
Opioids	990	23
NSAID	67	2
<b>COMBINATIONS</b>		
Non opioids +Opioids	430	10
Non opioids +NSAID	309	7
Opioids+NSAID	209	5
All	70	2

**Conclusions:** Rheumatoid arthritis is a pain associated condition; two thirds of patients are using of pain medications mainly women; the most prescribed medication was paracetamol or opioids, coinciding with other studies.<sup>2</sup> This descriptive study is useful for further studies to develop in Latin America.

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### AB1253 ANALGESIC DRUGS AND RISK OF ISCHAEMIC STROKE IN PATIENTS WITH OSTHEOARTRITIS: A REAL WORLD DATA CASE-CONTROL STUDY

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**Background:** Pharmacological treatment of osteoarthritis (OA) usually include analgesics, non-steroidal anti-inflammatory drugs (NSAID) and symptomatic slow-acting drugs in OA (SYSADOA). The association between these groups of drugs and the risk of ischaemic stroke has not been properly addressed.

**Objectives:** To analyse the risk of stroke in patients using analgesics, NSAID and SYSADOA drugs.

**Methods:** We used a population-based patient hospital registry to identify all patients with a first-ever stroke discharge diagnosis between 2009–2015. Cases were matched to controls obtained from the Information System for Research in Primary Care (SIDIAP) database. Information on drug exposure was obtained from invoice data from pharmacies. Crude and adjusted odds ratios (OR, OR<sub>adj</sub>) and their 95% confidence interval (95% CI) were calculated using multivariate models of conditional logistic regression for the next pharmacological groups and individual agents of each group: acetic acid derivatives, oxicams, propionic acid and derivatives, coxibs, SYSADOA and analgesics (opioids, metamizole and paracetamol). A cardiovascular risk score was calculated for each subject based on comorbidities.

**Results:** 12 616 cases were matched to 1 25 264 controls by gender, age and geographic area. Among cases, 43% were women. The mean age was 72.6 (IQR 65–82) years and more cases were classified as high cardiovascular risk patients (n=2,511, 19.9%) than controls (n=12,467, 10.0%). Mortality in the following year after the index date was higher for cases (n=2,633, 20.9%) than for controls (n=8,168, 6.5%). A higher percentage of cases had a previous diagnostic of ischaemic heart disease, 13.8% (n=1,745) vs 7.7% (n=9,656) of the controls. OA diagnosis was present in 2823 (22.4%) cases and in 29 098 (23.2%) controls. Paracetamol was the most used drug (n=106,515, 77.3%) followed by ibuprofen (n=84,790, 61.5%).

Current users of acetic acid derivatives showed an increased risk of stroke [OR<sub>adj</sub>, (95% CI) 1.10 (1.01–1.19)], so did diclofenac [OR<sub>adj</sub>1.14 (1.04–1.25)]. Among the propionic acid derivatives, current users showed an increased risk [OR<sub>adj</sub>1.24 (1.27–1.32)], dexametopfen showed the highest risk [OR<sub>adj</sub>1.42 (1.25–1.60)] and naproxen the lowest [OR<sub>adj</sub>1.18 (1.02–1.37)]. The SYSADOA group did not show any increased risk for any type of exposure, with a decreased risk of 17% [OR<sub>adj</sub>0.83 (0.77–0.91)] for lifetime glucosamine exposure and a 22% [OR<sub>adj</sub>0.84 (0.78–0.90)] for chondroitin sulfate. Analgesics were the most consumed drugs,

and cases were more exposed to all subgroups of analgesics than controls. While the non-adjusted OR showed an increased risk of stroke for lifetime exposure for all agents in this group, this association was not observed with the adjusted OR<sub>adj</sub> for fentanyl, neither buprenorphine, but it showed a risk for current users of metamizole [OR<sub>adj</sub> of 1.67 (1.56–1.80)], tramadol [OR<sub>adj</sub>1.15 (1.06–1.24)] and paracetamol [OR<sub>adj</sub>1.43 (1.37–1.51)].

**Conclusions:** Current exposure to NSAIDs, tramadol, metamizole and paracetamol is a risk factor for ischaemic stroke. Exposure to chondroitin sulphate and glucosamine are associated with a lower risk of ischaemic stroke.

**Disclosure of Interest:** None declared

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### AB1254 IMPROVING RHEUMATOLOGIC CARE AND EDUCATION IN THE REPUBLIC OF MACEDONIA: A MODEL FOR PROMOTING RHEUMATOLOGIC EDUCATION IN A DEVELOPING COUNTRY

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**Background:** In 2011 ILAR supported a pilot project in training a rheumatologist in an underserved area in Macedonia. The pilot took place in the clinical centre of Bitola. Previously, rheumatologic care was provided by visiting rheumatologists from the rheumatology clinic in the capital city.<sup>1</sup>

**Objectives:** The primary goal of this project was to pilot a model in rheumatologic training and improve rheumatologic care in an underserved area in Macedonia.

**Methods:** An internist from the clinical centre in Bitola was enrolled in a two-year training by the Rheumatology clinic at Ss Cyril and Methodius University in Macedonia, and the rheumatology division at the University of Michigan. Pre intervention metrics of quality of care as measured by access, standard therapy, and DAS 28 scores were compared with post intervention metrics.

**Results:** The primary goal of the project enabled training of a rheumatologist. A local internist completed her training in rheumatology (2014), and established a rheumatology clinic within the clinical centre in the city of Bitola in 2014, providing daily access to patients with rheumatic conditions in a region with a population of 3 000 000. Patient access changed from 120 visits/month to 800 visits/month. The service provided consultations to hospitalised patients.

The secondary endpoints: quality of care as measured by standard therapy for rheumatoid arthritis and DAS-28 scores are as shown on table 1.

**Abstract AB1254 – Table 1**

Rheumatoid Arthritis patients	Pre-intervention 2011 (n=115)	Post-intervention 2017 (n=86)	Statistical Significance
Patients taking methotrexate	44%	53%	
Methotrexate dose	11.5 mg (10–15 mg)	13.9 mg (10–25 mg)	p<0.00001
Combination therapy*	39%	38.5%	NS
Dual therapy*	31%	35%	NS
Triple therapy*	3.5%	5%	NS
DAS-28 average	4.8	4.41	NS

MTX=methotrexate; \*methotrexate, sulfasalazine, leflunomide, antimalarial (chloroquine, hydroxychloroquine)

Post intervention, more patients were taking methotrexate and at higher doses. Despite this trend, its average dose was less than 50% of its maximal dose (25 mg/week) commonly used in standard practice. The frequency of combination therapy remained unchanged. Likewise, no significant change in the DAS-28 scored was observed.

**Conclusions:** Prior to launching the pilot, the rheumatologic care in this region was provided by visiting rheumatologists from the university clinic in the capital city. Initial assessment pointed to several obstacles: poor access and substandard therapy that likely contributed to the prevalence of high disease activities. Our pilot succeeded in training a rheumatologist, thus reaching our primary goal of improving local access to rheumatic care. The secondary goals of improving the quality of care as measured by the DAS-28, standard of therapy for rheumatoid arthritis- reflected by appropriate use of DMARDs (use of methotrexate, combination therapy) showed a modest improvement While higher doses of methotrexate were used, combination therapy and better control of rheumatoid arthritis (DAS-28) remained unchanged, thus posing a challenge for ongoing need and future intervention goals.

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education and care in a developing country—ILAR Initiative. *Clin Rheumatol* 2013 Nov;32(11):1669–71

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AB1255

### A REVIEW OF CASE-MIX AND CENTRE EFFECT ADJUSTMENT IN EARLY RHEUMATOID ARTHRITIS COHORTS

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**Background:** Observational cohort studies have been utilised extensively in early Rheumatoid Arthritis (RA), regularly conducted across multiple centres spanning regional and national boundaries. Case-mix and centre effect are considerations essential for determining comparability of results, and likely prevalence of bias. There is currently no standardised approach for case-mix and centre effect adjustment in early RA observational cohorts.

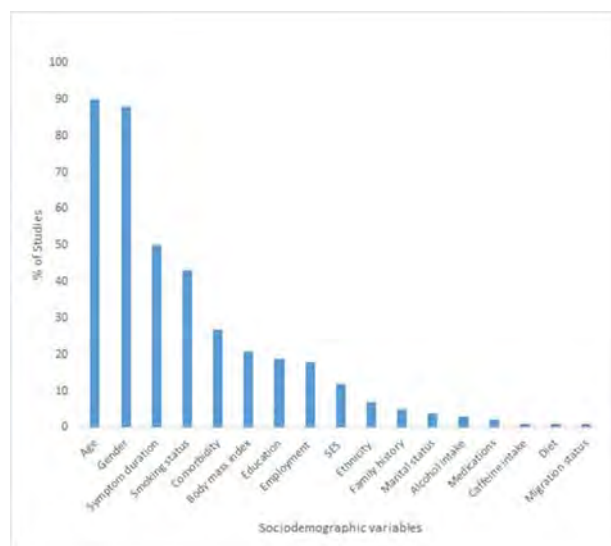
**Objectives:** Describe the spectrum of methodologies used to address case-mix and centre level effects on outcomes in multi-centre early RA observational cohort studies.

**Methods:** Inclusion criteria were cohorts recruiting from 2 or more centres with 100 or more subjects, with a Rheumatologist diagnosis of RA or EIA within the last 24 months. A systematic electronic search of publications was undertaken. Papers were reviewed by two researchers independently. Reference lists of included papers were reviewed for further relevant publications. A search of all included papers' authors was also conducted. Detail on cohort characteristics, case-mix data collection and adjustment, and consideration of centre-level effect in analyses were collected.

**Results:** 1047 papers were identified from the initial search. A total of 20 unique cohorts were identified. Reference review and author search produced 14 more, to make a total of 34 unique observational cohorts drawn from 205 papers. The cohorts were mainly conducted in Europe (24/34, 71%), With 2 (6%) from less economically developed regions. The period of data collection was between 1955 and 2017.

**Case-mix:** All cohorts considered case-mix in some form (e.g. age and gender), but with heterogenous approaches. The figure displays the relative frequencies of sociodemographic variable consideration across all included papers.

**Centre effect:** 18/205 (9%) of the included papers accounted for centre in their results, utilising a range methodologies. Where reported, centre had a significant impact.



Abstract AB1255 – Figure 1

**Conclusions:** The degree of case-mix reporting varied widely, and few studies addressed centre effect. Where analysed, a centre level impact was clearly apparent. A failure to incorporate centre into analyses can lead to unrecognised bias as a result of confounding by centre. It must be acknowledged that including case-mix variables and adjusting for centre substantially reduces power, and it is likely that many of the reported observations may have lost statistical significance had case-mix and centre effect been addressed more completely. This is the first

systematic review of centre effect and case-mix in early RA, and highlights a challenging field deserving further research.

**Disclosure of Interest:** None declared

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AB1256

### DEVELOPMENT OF A NATIONAL SERVICE FOR BIOLOGIC DRUG MONITORING

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**Background:** Monitoring serum levels of biological drugs has well recognised benefits for patients and health services. These include appropriate dosing, avoidance of overtreatment, identification of drug failure due to immunogenicity, cost and facilitation of switching therapy.<sup>1</sup>

**Objectives:** To establish a national service for monitoring serum levels of biological drugs.

**Methods:** National Services Scotland established a working group comprised of clinicians, lead pharmacist and Director of Public Health to help optimise biological drug prescribing. (Effective Prescribing Programme Biologics -EPPB). It was recognised that ad-hoc biologic drug monitoring (BM) posed a risk of variation in standards and inequity of access. Existing test volume and cost was established and a business case submitted to the CEO's of each Health Board in Scotland for a national service, testing adalimumab and infliximab twice yearly in 2265 patients. Potential cost savings based on drug withdrawal of 2.5%, 5%, 10%, and 15% in gastroenterology patients ranged from 400,000Euro to 3.5 million Euro. Additional savings for dose reduction in rheumatology patients were not costed but likely to incur further financial advantage.

**Results:** The case was accepted and service tendered. A single site in Glasgow will run the assays (purchased from Grifols) commencing December 2017. The cost modelling predicts a 50% reduction in cost per test compared to existing arrangements. Cost for the whole service will be divided between the commissioning Health Boards with outlay proportional to patient population. The EPPB developed specialty specific advice and an ordercomm with minimum dataset accessible from all Health Boards with the option of retrospective interrogation. A national educational event is scheduled to improve clinician confidence and awareness.

**Conclusions:** To our knowledge this is the first national fully funded biologic drug monitoring service with access to all users of biological drugs. Its introduction will:

1. Support the implementation of national standards of care to ensure the effective and cost effective use of biologic medicines
2. Ensure equity of access to BM across Health Boards.
3. Provide a stronger position for procurement of biologic drugs (uncomplicated by additional service offerings)
4. Provide a sustainable service for Scotland, independent of the drug manufacturer.

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**Disclosure of Interest:** None declared

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AB1257

### IMPACT OF A SYSTEMATIC SCREENING OF MULTIMORBIDITIES IN PATIENTS WITH CHRONIC INFLAMMATORY RHEUMATIC DISEASES

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**Objectives:** EULAR proposes to screen multimorbidities in chronic inflammatory rheumatic diseases. The aim of the study was to assess i) multimorbidities in patients with chronic inflammatory diseases, ii) how patients follow recommendations given after a systematic standardised multimorbidity screening.

**Methods:** Exams were performed during a 1 day multimorbidity clinic. Diabetes, hypertension, CVD damage, chronic respiratory diseases, osteoporosis and preventive measures were assessed. Advice, complementary exams and prescriptions were provided to patient and general practitioner after this check-up if needed. Patients were called 3 months later to assess the applications of the given recommendations.

**Results:** Among the 541 patients screened, hypertension was present in 28.1% patients, dyslipidemia in 19.2%, chronic respiratory tract diseases in 12.8% and diabetes in 9.6%. Screening led to the following recommendations: blood pressure monitoring (22.6% patients), dietary advice (56.8%), cardiologist referral (35.5%), intensification of physical activity (27.0%), cancer screening (50.5%), vaccinations (60.6%) and vitamino-calcium supplementation (30.3%). On the 237 patients called back, 72.3% underwent blood pressure monitoring, 58.6% followed dietary advice, 64.4% took vitamino-calcium supplementation, 55.2% had vaccinations done, 52.1% saw a cardiologist, 42.7% increased physical activity and 31.4% performed cancer screening. No specific gender, age, pathology, or psychological factors were associated with adherence to recommendations.

**Conclusions:** This study underlines the relevance of a systematic screening of multimorbidities in chronic inflammatory rheumatic diseases, and the good patient's adherence rate to the recommendations.

**Disclosure of Interest:** None declared

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**AB1258 EARLY ARTHRITIS SERVICE IS COST EFFECTIVE, IMPROVES OUTCOMES AND REDUCES BIOLOGIC USE**

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**Background:** There is good evidence that dedicated early arthritis clinics (EACs) improve referral lag time and reduce delay in establishing disease-modifying therapy. However it remains arguable whether such clinics improve relevant disease outcomes. Nationally, only 57% of units have dedicated EACs.

**Objectives:** We established Early Arthritis Service (EAS), centred on NICE RA quality standards, to reduce the time to diagnosis and the start of definitive therapy with an aim to accomplish good outcomes by the introduction of dedicated Early Arthritis Clinics (EACs).

**Methods:** The department set up an early arthritis service with introduction of six clinics (EACs) every week. An agreed treatment protocol incorporating ultrasound was developed to ensure standardised approach to early initiation of treatment, drug education and timely review. This is a retrospective study of all patients presenting to the service in the first year.

**Results:** Our catchment area covers a population of 3 50 000 with 40% ethnic minorities. Of 1884 patients referred, 482 (25.5%) were triaged into EACs based on set criteria. All were reviewed within 3 weeks. 247 (51%) were confirmed to have early arthritis. Mean age was 52.4 years (17–86y). 157 (63.5%) were women. 177 (71.6%) were White, 58 (23.5%) of Asian and twelve of other background. 159 (64.3%) had RA, 57 (23%) with PsA and 31 had other inflammatory arthritides. 25 (10%) had erosions at presentation. There was median 26 weeks delay (0.4–1043 weeks) from symptom onset to GP presentation. Median time for GP referral to the department was 4.0 days (0–84 days). Mean DAS28 at first visit was 4.65 (0.6–8.0, n=166).

95% commenced their DMARDs within 3 week of initial review. Other 5% who missed the target was owing to patient factors. Treating to target achieved DAS28 remission for 84 (53.5%) and low disease activity for a further 44 (34%). Median time to achieve remission or LDA was 20 weeks (0–52 weeks, n=128). Similarly, 40/57 (70%) of PsA patients achieved good PsARC response in median 24 weeks. Of 247, only 21 (8.5%) patients required escalation to biologic therapy.

**Conclusions:** Dedicated EACs help achieve good clinical outcomes in majority of patients. Nearly 87% of our cohort attained remission or low disease activity in

less than six months. This was despite a significant delay in patients presenting to their GPs and moderately-high disease activity. 100% of our patients were treated to target facilitated by protocol driven escalation of therapy in these clinics. This is in contrast to the national audit findings whereby only 68% of patients were treated with disease modifying drugs within 6 weeks of referral and 89% had treatment to target. Patient experience also improved (94% would now recommend the service compared to 76% prior to the initiative).

The project was a financial success with total savings for the year, accounting for most generous cost estimates, were £1 36 973. In addition, there was a 42% reduction in biologic use in this group compared to 2015. These savings are on top of wider economic and societal benefits achieved by inducing low disease activity or remission.

**Disclosure of Interest:** None declared

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**AB1259 IS DOSE BANDING OF INFlixIMAB COST EFFECTIVE – RESULTS FROM REAL WORLD IMPLEMENTATION**

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**Background:** Infliximab dose is based on the patient's body weight (3–5 mg/kg) and requires the use of multiple 100 mg vials to reconstitute the individualised dose. As the product is expensive, there is a significant cost associated with unused and wasted infliximab in any part-used vials. "Dose banding" is one solution so that patients receive a pre-prepared dose produced in advance in batches where wastage from part vials is minimised. There is some encouraging data that reconstituted infliximab is stable for long enough to allow batch production of pre-prepared doses. The theoretical risk of course is over or under treatment while respectively rounding up or down the administered dose.

**Objectives:** We undertook a retrospective analysis of our experience of dose banding in rheumatology unit.

**Methods:** All patients prescribed infliximab for rheumatic indication at our centre were included in the analysis. Case notes were retrospectively reviewed to look at dose variance following implementation of this initiative, resultant disease control and the consequent cost savings.

**Results:** 10 patients prescribed infliximab biosimilar and two bio-originator were identified for the analysis. Median age was 55.5 years (range 25–80 years). Nine had the drug for RA, two for AS and one for myositis.

Three had no change in dose as a result of implementing dose banding program. Three had dose increased by 3%–5%. Remaining six had dose reduced by range of 4%–6%. Their disease scores before and after dose banding remained largely unchanged (table 1). This equated to £1,184.58 annual savings in addition to the economic benefit of successfully switching the ten patients to biosimilar. No patient suffered loss of efficacy or adverse events in any of the three groups.

**Conclusions:** Our data confirms the utility of dose banding program for infliximab in rheumatology practice with no concerns about efficacy or safety of the initiative. There are potential opportunities to achieve considerable reductions in medicines discarded and improving finances by adopting dose banding for infliximab. It also helped curb over £10 000 expense to our Trust in infliximab waste cost alone. There are some important caveats to consider as well. True savings will depend on list price of each product and varies with originator versus biosimilar. The variance increases as the width of the dose bands increases i.e. the variance is greater at lower body weights. Consequently, depending on patient population both clinical and cost considerations could alter. Finally, assurance of the product

**Abstract AB1259 – Table 1**

Age	Sex	Ethnicity	Indication	Prior dose (mg)	Pre banding Disease score	New dose (mg)	Post banding Disease score	Variance	Dose vials	Saving (12 month)
48	M	Mixed	AS	400	3.2	400	3.9	0%	4	£0.00
58	F	White	RA	210	2.3	200	2.8	-5%	2	£87.00
54	F	White	RA	300	3.6	300	1.7	0%	3	£0.00
44	F	White	RA	210	2.2	200	1.8	-5%	3	£87.00
78	F	Asian	RA	170	4.1	175	3.3	3%	2	-£43.50
56	F	White	RA	300	2.5	300	2.1	0%	2	£0.00
73	F	White	RA	210	3.9	200	3.9	-5%	2	£87.00
80	F	White	RA	190	3.8	200	3.8	5%	3	-£87.00
49	F	White	RA	210	2.3	200	3.4	-5%	3	£87.00
55	M	White	AS	320	0.2	300	0.4	-6%	2	£174.00
<b>Bio-originator Patients</b>										
25	F	White	RA	120	4.1	125	4.1	4%	0	£0.00
49	F	White	Myositis	470	Well controlled	450	Well controlled	-4%	0	£793.08
<b>Total saving</b>										<b>£1,184.58</b>



integrity and stability is reliant on efficient pharmacy processes necessary to accommodate the use of new formulations for dose banding.

**Disclosure of Interest:** None declared

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AB1260

#### BASELINE CHARACTERISTICS AND PATIENT SATISFACTION DATA FROM COACH@HOME: THE GERMAN SUPPORT PROGRAM FOR PATIENTS WITH RHEUMATIC DISEASES TREATED WITH CERTOLIZUMAB PEGOL

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**Background:** Certolizumab pegol (CZP)-treated patients (pts) with rheumatoid arthritis (RA), axial spondyloarthritis (axSpA, including ankylosing spondylitis [AS] and non-radiographic [nr-]axSpA), and psoriatic arthritis (PsA) may be recommended the patient-coaching program, coach@home (c@h) in Germany to manage their disease. Eight coaching calls are offered over one year, scheduled around 'critical' milestones along the therapeutic journey. These calls are made by professionally-trained nurses, who offer support and information about both the disease and its treatment with CZP.

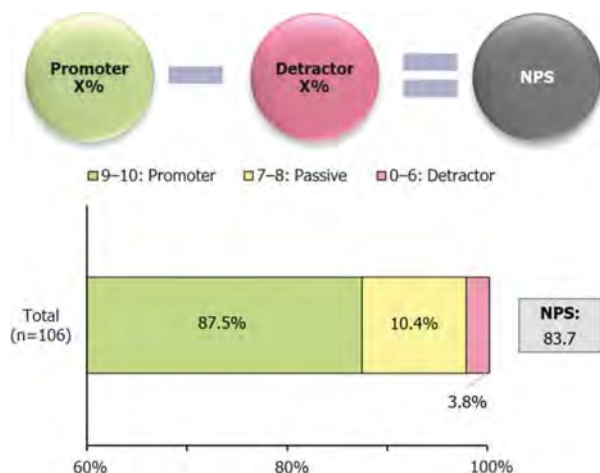
**Objectives:** The purpose of this observational analysis was to assess the baseline characteristics of pts subscribed to c@h, and the level of pt satisfaction with the program.

**Methods:** c@h was launched in June 2014 and is available to pts who are prescribed CZP according to the local product label. Pts must be CZP-naïve when subscribed to the program, and pt consent is required prior to subscription by the treating physician. There are no additional criteria for enrolment, although the program must be recommended to the pt by the treating physician.

Pt satisfaction was measured either at the end of the program or at discontinuation using the net promoter score (NPS), which has previously been used for this purpose.<sup>1</sup> The NPS is derived by asking pts to state how likely it is that they would recommend c@h to others (on a 0–10 scale). Rankings of 9–10 are considered 'promoters', 7–8 'passives', and 0–6 'detractors'. Subtracting the percentage of detractors from that of promoters yields the NPS (figure 1).

**Results:** A cumulative total of 655 pts had been registered to the program as of 5 Oct 2017. Of the total number of reported indications (n=683; multiple indications per pt possible), 55.9% were RA, 16.5% AS, 7.6% nr-axSpA, and 19.9% PsA. The mean age at baseline was 55 (RA), 54 (AS), 53 (nr-axSpA), and 52 (PsA), and the proportion of female pts was 80%, 58%, 65%, and 69%, respectively. Prior biologic DMARD exposure was 32.8%.

The most common topics discussed on phone calls were therapy compliance (in 1339 calls), CZP maintenance dose (in 1333 calls) and syringe disposal (in 870 calls). The average length per call was 15.9 min at the end of Week 0 (total: 28 calls), and 14.0 min at the end of Week 52 (total: 1796 calls). A cumulative total of 272 pts had either completed the 1 year coaching period (n=70) or discontinued (n=202) by 28 Sep 2017 of whom 106 rated the program. Of these, 87.5% gave promoter scores, 10.4% passive, and 3.8% detractor, yielding an NPS of 83.7 (figure 1). The program was still ongoing at the time of this data cut.



**Abstract AB1260 – Figure 1.** Patient ratings and Net Promoter Score for the coach@home program (as of September 2017)

Patients were asked to rate the coach@home program on a scale of 0–10, where 0="I would certainly not recommend this program" and 10="I would most probably recommend this program". Scores of 9–10 were considered 'promoters', 7–8 'passives' and 0–6 'detractors'. Percentages shown are out of the total number of responders by the end of September 2017 (n=106). NPS: Net Promoter Score.

**Conclusions:** The c@h program offers guidance and support to pts treated with CZP in Germany. Feedback from pts who were willing to provide a rating indicates a high level of satisfaction with the program.

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AB1261

#### DEVELOPMENT OF A LOCAL NEEDS-BASED GP CURRICULUM FOR SHARED CARE IN RHEUMATOLOGY

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**Background:** There is a role for shared care between rheumatologist and primary care for Musculoskeletal (MSK) disorders. General practitioners (GPs) are involved in monitoring of clinical status of patients and their management, in addition to psychosocial aspects of chronic pain and disability. We are going to look at the rheumatology knowledge and skills needed by local GPs and based on their needs we plan to develop an initiative to improve the service provided to our patients. Here are the results of the initial survey of local GPs.

**Objectives:** We aim to identify knowledge and skill gaps in primary care related to MSK disorders and to develop a need-based curriculum to address these gaps. Develop an implementation plan to deliver the curriculum components.

**Methods:** Initially we identify the needs and gaps in the current practice using survey in a small group of local GPs. There are two rounds of questionnaires to reach a list of important areas to develop the curriculum. The second round will include large number of GPs. Also, there will be meetings with GPs to reach agreement and to adopt method of delivering these training and skills.

**Results:** In the first survey, 31 out of 36 GPs (86%) returned questionnaires. One GP (3.2%) refer to rheumatology department twice a week, 4 GPs (13%) refer weekly, 23 GPs (74%) refer every month and three GPs (9.7%) rarely refer to rheumatologist. Reasons for referral were diagnosis and long-term management,<sup>21</sup> diagnosis and discharge back to GP<sup>15</sup> and patient's request.<sup>4</sup> Thirteen GPs (42%) have interest in rheumatology conditions management. Regarding GPs' concerns with rheumatology service, 22 of them (71%) mentioned the long wait time for rheumatology appointment. Other issues were delayed clinic letter, need for clear instruction, patients not aware of appointment time, whether there is an urgent clinic and which clinic patient should be referred to (outpatient versus procedure clinics). Nineteen GPs (61%) received undergraduate rheumatology training, 16 (52%) during GP training programme and 4 (13%) attended postgraduate courses. Topics of interest by GPs were variable rheumatology conditions in addition to joint injections,<sup>3</sup> referral guidance<sup>2</sup> and update on DMARD. Preferred teaching methods to deliver the syllabus were small group tutorials,<sup>12</sup> face-to-face lectures<sup>5</sup> and protocols and guidelines.<sup>5</sup>

**Conclusions:** From this initial survey, we could identify that the major concern of local GPs is the long waiting time for rheumatology clinic. Some of GPs (42%) expressed their interest to have further training in rheumatology. When we reach an agreed curriculum with GPs, we aim to deliver the syllabus through preferred methods by GPs. Shared care between rheumatologists and GPs would improve quality standard of care in community, provide patient care close to home and reduce referral rates.

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AB1262

### TAPERING OF BIOLOGICAL ANTIRHEUMATIC DRUGS IN RHEUMATOID ARTHRITIS PATIENTS IS ACHIEVABLE AND COST EFFECTIVE IN DAILY CLINICAL PRACTICE: DATA FROM THE BRUSSELS UCL RA COHORT

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**Background:** Several studies demonstrate that Rheumatoid Arthritis (RA) patients achieving low disease activity or remission are able to taper biological (b) DMARDs.

**Objectives:** The aim of this study is to determine the number of patients suffering from RA in whom tapering of bDMARDs is achievable in daily practice and to evaluate the patient characteristics. Another objective is to analyse the budget impact and determine which bDMARDs are more adapted to dose reduction.

**Methods:** Inclusion criteria were RA patients from our Brussels UCL cohort treated with a bDMARD for at least one year. A dose reduction was proposed by the senior physician when sustained low disease activity or remission was observed. Data from 357 eligible RA patients (247 women and 110 men) were collected. Patient characteristics and baseline features before the current bDMARDs and flares if happened were collected. Annual drug dosage and cost were calculated.

**Results:** In 131 patients (35.7%), the dose of the bDMARD could be tapered. Patients in the decreased dose group were older (60.6 vs 55.9 years,  $p=0.005$ ) and started bDMARDs earlier in their disease course (6.8 vs 8.4 years,  $p=0.025$ ). As expected, the current DAS28-CRP was lower (2.26 vs 2.55,  $p=0.018$ ) and interestingly, more patients were treated with a combination of Methotrexate (84% vs 73%,  $p=0.019$ ). No differences between groups was observed for gender, disease duration, baseline HAQ, DAS28-CRP, erosion, ACPA, number of previous bDMARDs and use of Glucocorticoids. In our cohort, Anti-TNF agents were the most commonly prescribed medications (see Table). Annual drug cost was largely decreased for Rituximab and anti-TNF agents. Only 11 patients experienced a flare during the follow-up.

Abstract AB1262 – Table 1

bDMARD	Number of Pts	Stable dose (%)	Annual cost/ Pts (€)	Dose decreased (%)	Annual cost/ Pts (€)
ABA	23	12 (52)	12 979	11 (48)	8643,5
ADA	46	21 (46)	12 525	25 (54)	6908,8
CERTO	7	7 (100)	11740,2	0 (0)	Not available
ETN	69	41 (59)	9328,6	27 (39)	6101,6
GOL	24	22 (92)	12703,08	2 (8)	Not available
IFX	99	74 (75)	7290	25 (25)	6067
RTX	37	22 (59)	8784	17 (46)	4691,6
TOC	52	35 (67)	12773,7	17 (33)	9371,9
	357	234		124	

**Conclusions:** In daily practice, tapering of bDMARDs in RA patients with low disease activity or remission is an achievable goal, thereby reducing annual drug cost, especially for Rituximab, Infliximab, Etanercept and Adalimumab.

**Disclosure of Interest:** None declared

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AB1263

### FINNISH HEALTHVILLAGE.FI-RHEUMATICDISEASES.FI: A SPECIALISED CARE SERVICE UNIT DEVELOPED TOGETHER WITH PATIENTS TO OFFER ON-LINE INFORMATION AND TREATMENT FOR PATIENTS IN A MODERN WAY

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**Background:** Finnish on-line Health village environment, so-called HUS-MAP®, was used to develop on-line information for rheumatic patients.

**Objectives:** To face the challenge of increasing demand for rheumatological care without additional resources a new virtual client-orientated service was developed.

**Methods:** In Finland, an on-line Health village environment, so-called HUS-MAP®, has been developed to offer virtual digital information to citizens, patients, and healthcare professionals. By using this HUS-MAP® environment, we provide information and support to citizens and patients who need information on different rheumatic diseases and various unspecified aches and musculoskeletal pains. The study group consisted of participants from every university hospital in Finland, from local authorities; rheumatologists, other specialists, general practitioners, nurses, special professionals such as physical therapists, and patients. Information provided was based on updated international and Finnish guidelines on rheumatic diseases. After the information was reviewed and accepted by our study group, it was fed into a special program and published on-line in the Health village environment.

**Results:** E-service for citizens and patients was opened in March 2017. Detailed description of symptoms, diagnosis and therapy of various rheumatic diseases, such as rheumatoid arthritis, spondyloarthritis, connective tissue diseases and vasculitis are available. Early diagnosis and treatment to remission when possible is emphasised. The service aids to identify, by using symptom navigator and questionnaires for back pain, as well as swollen and painful joints those who may have a rheumatic disease and guide patients to find medical services without delay. Already 60 500 persons have visited our website.

**Conclusions:** Finnish e-service, rheumaticdiseases.fi, offers an easy way to reach people and increase citizen's awareness on their own health. By guiding people to search for care the service may reduce delays in diagnosis of rheumatic diseases and the onset of therapy

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AB1264

### BARRIERS AGAINST TESTING ANTI-TNF DRUG LEVELS AND ANTI-DRUG ANTIBODIES IN ROUTINE CLINICAL PRACTICE

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**Background:** There is growing interest in using tests to measure anti-TNF drug levels and anti-drug antibodies (ADAb) in routine clinical practice for patients with rheumatic diseases. Testing may provide rheumatologists with additional information when considering a decision to adjust biologic treatment; for example, a decision to increase the interval between injections of an anti-TNF or to change treatment to a biologic that has a different target. However, it is not clear whether rheumatologists consider drug level and ADAb testing to be a useful technology within their routine clinical decision-making. Testing may be implemented imperfectly if rheumatologists perceive barriers against measuring drug levels and ADAb which, in turn, can affect the effectiveness and cost-effectiveness of care.

**Objectives:** To explore the potential barriers against testing anti-TNF drug levels and ADAb in routine clinical practice.

**Methods:** Semi-structured telephone interviews were conducted individually with a purposive sample of consultant rheumatologists from different hospitals across England. The telephone interviews were recorded and transcribed verbatim. Pilot interviews were undertaken to develop the interview schedule. The rheumatologists were invited to discuss their perceptions and experiences of anti-TNF drug

level and ADAb testing within their own clinical practice. The transcripts were analysed by thematic framework analysis where themes comprised perceived barriers to testing. Ethical approval was obtained from The University of Manchester's Research Ethics Committee.

**Results:** Eleven rheumatologists provided informed consent to participate in the study. All rheumatologists demonstrated an awareness of tests that were available to measure anti-TNF drug levels and ADAb. However, the majority (n=10) did not use these tests in their routine clinical decision-making. Five potential barriers against testing were identified as themes: <sup>1</sup> recognising the clinical problem within their own patients; <sup>2</sup> understanding the purpose of testing drug levels and ADAb; <sup>3</sup> a lack of robust evidence to support testing; <sup>4</sup> insufficient capacity to implement testing locally, and <sup>5</sup> the additional cost associated with testing.

**Conclusions:** The potential barriers against measuring anti-TNF drug levels and ADAb suggest that introducing these tests into practice for rheumatology may be challenging. Authoritative guidance for measuring anti-TNF drug levels and ADAb in specific rheumatic diseases may reduce the uncertainty over the purpose of testing in routine clinical settings. The generation and dissemination of robust evidence for the accuracy, effectiveness, and cost-effectiveness of testing is likely to be informative to rheumatologists and decision-makers that allocate resources for health care. Decisions to introduce testing in clinical practice may benefit from considering the implications of capacity constraints when analysing samples and the mechanisms to pay for the additional cost of testing. These barriers against testing are not unique to the health care system in England and may generalise to the delivery of care for rheumatic diseases within health care systems internationally.

**Disclosure of Interest:** None declared

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#### AB1265 LOSS OF SPECIALTY MEDICAL CARE FOR ELDERLY RHEUMATOID ARTHRITIS PATIENTS WHO DISCHARGED FROM HOSPITAL

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**Background:** As the ageing of the population progresses, the proportion of the population over the age of 65 reaches 27.3% in 2016, in Japan. Even elderly rheumatoid arthritis (RA) patients often require immunosuppressive agents or biological disease modifying antirheumatic drugs (DMARDs) due to their high disease activity. Therefore, they need to continuously receive treatment by specialty rheumatologists. Due to the deterioration of the ability of daily living activities, some patients may drop out of specialty medical care.

In recent years, the age of RA patients who need to be hospitalised has also increased. However, it is unclear whether elderly patients discharged from the hospital are able to continue receiving specialty medical care.

**Objectives:** To clarify whether a patient who has been discharged from a rheumatology specialty hospital can continue receiving rheumatology specialty medical care.

**Methods:** RA patients who discharged from our rheumatology unit from January 1, 2016 to December 31, 2016, were included. We investigated the backgrounds and outcomes of those patients retrospectively. We compared the background characteristics of patients who are receiving treatment by specialty rheumatologists at the final follow-up (specialty group) and those who are not (non-specialty group). For the statistical analysis, a chi-squared test and Student's t-test were used.

**Results:** We identified 147 patients. The mean  $\pm$ SD age of patients at discharge was 72.2 $\pm$ 9.1 years and 74.8% was female. The reasons for hospitalisation were 87 patients (59.2%) for treatment of RA and 60 (40.8%) for treatment of complications (sepsis, fracture and so on).

After discharge, 134 patients (91.1%) had returned to follow up in our department for RA treatment. The remaining 13 patients were treated at other hospitals, five of whom were treated by a primary care physician who was not specialised for rheumatology. Overall, we compared 142 patients in the specialty group and 5 in the non-specialty group.

The age, the use ratio of immunosuppressive agents/biological DMARDs/prednisolone and the dose of prednisolone in the specialty group and the non-specialty group were 71.9 and 79.0 years old (p=0.09), 50.0% and 20.0% (p=0.37), 29.6% and 20.0% (p=1.00), 78.7% and 80.0% (p=1.00), 6.5 and 5.6 mg/day (p=0.83), respectively.

**Conclusions:** In elderly RA patients, some patients drop out of RA specialty medical care. The background of such patients is not different from those of patients who are receiving treatment by specialty rheumatologists. In order to provide specialty medical care for RA patients throughout the community, a co-management medical collaboration system between specialty rheumatologists and primary care doctors should be established.

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#### AB1266 AUTOIMMUNE DISEASES INDUCED BY BIOLOGICAL AGENTS USED IN PATIENTS WITH ADVANCED CANCER: A NATIONWIDE MULTICENTER REGISTRY OF CASES DIAGNOSED IN DAILY PRACTICE (cBIOGEAS-SEMI)

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**Objectives:** To characterise the development of autoimmune diseases triggered by the new biological therapies used as immunotherapy in patients with advanced cancer in a real-life clinical setting.

**Methods:** In 2006, the Study Group on Autoimmune Diseases (GEAS) of the Spanish Society of Internal Medicine created the BIOGEAS project, a multicenter study devoted to collecting data on the use and safety of biological agents in adult patients. In December 2016, the cBIOGEAS-SEMI multicenter registry was formed with the aim of collecting patients with cancer treated with biological immunotherapies who developed autoimmune diseases.

**Results:** By January 2018, the cBIOGEAS-SEMI Registry includes 40 patients (26 men and 14 women, mean age of 59.7 years) who developed 54 triggered autoimmune diseases, including interstitial lung disease (n=11), enterocolitis (n=8), hypophysitis (n=6), polyarthritis (n=4), thyroiditis (n=3), vasculitis (n=3), severe cutaneous involvement (n=3), adrenalitis (n=2), Sjögren syndrome (n=2), cardiomyopathy (n=2), pancreatitis (n=2), Guillain-Barre syndrome (n=2), hepatitis (n=2) and CNS involvement, sclerosing cholangitis, glomerulonephritis and sarcoidosis (one case each). Underlying neoplasia consisted mainly in pulmonary neoplasia (n=16), melanoma (n=11) and breast cancer (n=3). The main pharmacological groups of cancer immunotherapies included PD1 inhibitors (n=26), CTL4 inhibitors (n=7), growth factor/adhesion molecules inhibitors (n=4), combined PD1/CTLA4 blockade (n=2) and TK inhibitors (n=1); biologics included nivolumab (n=20), ipilimumab (n=9), pembrolizumab (n=8), trastuzumab (n=3), catumaxomab (n=1) and vemurafenib/combinetinin (n=1). Glucocorticoids were used in all cases but 4, and 9 patients required intravenous methylprednisolone pulses; 5 patients required additional immunosuppressive therapies (intravenous immunoglobulins in 4, methotrexate in one). All cases responded to treatment with glucocorticoids except 4 patients who died (3 due to ILD and one due to neurological disease).

**Conclusions:** A wide variety of systemic and organ-specific autoimmune diseases triggered by the new cancer immunotherapies is emerging. In this nationwide real-life Registry, immune checkpoint inhibitors are the biologics involved in nearly 90% of cases. We found an excellent response to glucocorticoids, with a poor prognosis in those patients who developed pulmonary and neurological autoimmune diseases.

**Disclosure of Interest:** None declared

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#### AB1267 BIO-SIMILAR TO BIO-ORIGINATOR SWITCHBACK: NOT A RELIABLE QUALITY INDICATOR

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**Background:** SB4 in an etanercept biosimilar which was licensed by the EMA in January 2016 for clinical use. Switching etanercept treated patients from reference etanercept (ETN) to SB4 can deliver substantial saving in drug costs. The SB4 to ETN switchback rate is often scrutinised by commissioners and clinicians, as it may be a quality indicator for the switch process.

**Objectives:** To evaluate SB4 drug survival and the SB4 to ETN switchback rate in our cohort of patients with Rheumatoid Arthritis, Axial Spondyloarthritis and Psoriatic Arthritis.

**Methods:** This was a retrospective observational study of 56 patients who were switched from ETN to SB4 in December 2016 at Kings College Hospital. Clinical data was collected 8 months post-switch to establish the number of patients in whom SB4 had been discontinued, the reasons for discontinuation, and the switchback rate.

**Results:** 84% (n= 47) of patients remained on SB4 at 8 months following the switch. Of the 9 patients who discontinued SB4, 89% (n=8) was due to loss of efficacy, whilst 11% (n=1) reported side effects. Of these, 78% (n=7) were switched over to a 3rd biologic agent, whilst 22% (n=2) were switched back to ETN. The



median pre-SB4 switch DAS score for patients with RA who were switched to a 3rd biologic agent was 4.23 (Range: 2.59–7.65), whilst that of those switched back to ETN was 4.08 (Range: 3.35–4.81).

Abstract AB1267 – Table 1

Demographics (n=56)	No. of patients remaining on SB4 at 8 months (n=47)	No. of patients switched to a 3rd biologic agent at 8 months (n=7)	No. of patients switched back to ETN at 8 months (n=2)
Mean Age	57.2	55.4	39.5
% Female	64%	71%	100%
% Disease RA	70%	71%	100%
AS	15%	14%	0
PsA	15%	14%	0
% Etanercept Monotherapy	43%	71%	100%
Median Time on SB4 prior to switch (days)	N/A	251 (Range: 79–357)	122.5 (Range: 114–131)

**Conclusions:** This switch back rate to ETN is considerably lower than what has been reported in the literature.<sup>1–3</sup> There appears to be a preference for switching patients to an alternative biologic agent, rather than switching patients back to the bio-originator. This could be explained by inadequate disease control on etanercept, which has been unmasked under the scrutiny of the biosimilar switch process. An alternative explanation could be that our local clinical commissioning group offers financial incentives if the department maintains a high percentage of etanercept treated patients on SB4. Hence, as prescribing practice can be influenced by both clinical factors and external targets, utilizing the switchback rate from biosimilar drugs to bio-originators is not a reliable indicator of the quality of biosimilar switch process.

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#### AB1268 NO DIFFERENCES BETWEEN HOSPITAL AND CLINIC IN PATIENTS WITH RHEUMATOID ARTHRITIS BASED ON REAL-WORLD DATA FROM THE AORA OBSERVATIONAL COHORT STUDY IN JAPAN

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**Background:** In Japan, orthopaedic surgeons, rather than internists, are often involved in the management of rheumatoid arthritis (RA), including drug treatment. However, the paradigm shift in the RA management has changed, and orthopaedic surgeons have often faced challenges in treating RA. The proportion of RA patients treated by orthopaedic surgeons is high in Akita Prefecture, located in Tohoku region in Japan. Akita Prefecture has the 6th largest area in Japan and the highest ageing rate. As many elderly patients have difficulty commuting to distant clinics or hospitals, specialised centres are desirable for advanced treatment of RA. However, in Akita Prefecture, the focus has been on improving treatment of RA by orthopaedic surgeons in the community. In 2010, the Akita Orthopaedic Group on RA (AORA) was established. Currently, 18 hospitals and 10 clinics are participating in the group, and cover all medical districts throughout the prefecture. In addition to a regular study meeting, a workshop on joint ultrasonography and a

case conference with internists have been held. We established a case registration system (AORA registry) 8 years ago. This system has enabled us to share treatment experiences.

**Objectives:** This study examined whether the AORA clinics have provided consistent community-based care comparable to that provided by hospitals.

**Methods:** Data from the 2017 AORA registry (including 2238 registrations [1300 in hospitals and 938 in clinics]) were used.

**Results:** Patients treated in clinics were younger (68.1 years in hospitals vs. 64.4.1 years in clinics), and had shorter duration of disease (157.4.0±4.0 months in hospitals vs. 143.5±4.5 months in clinics). The frequency and amount of methotrexate use were not significantly different between the two groups, while those of prednisolone use were greater in patients treated in hospitals than in those treated in clinics. There were no significant differences in the frequency or amount of biological disease-modifying antirheumatic drug use (19.9% in hospitals vs. 18.9% in clinics). There were also no significant differences in disease activity (Disease Activity Score-28-erythrocyte sedimentation rate) in the total cohort (2.91±0.04 in hospitals vs. 2.90±0.04 in clinics) or in patients aged 80 years or older (n=341) (3.35±0.08 in hospitals vs. 3.37±0.11 in clinics). The frequency and amount of drug use for treatment of osteoporosis were significantly higher in patients treated in hospitals than in those treated in clinics.

**Conclusions:** The results of this study showed that RA treatment outcomes were not significantly different between hospitals and clinics, indicating that the treatment level provided at orthopaedic clinics in the community was high and in accordance with the treat-to-target strategy. Given that orthopaedic surgeons are better able to examine joints and are able to treat osteoporosis, they are expected to treat more RA patients. We believe that the AORA plays an important role in maintaining the quality of clinical services for RA patients in Akita Prefecture.

**Disclosure of Interest:** None declared

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#### AB1269 QUALITY STANDARD FOR THE MANAGEMENT OF PATIENTS WITH PSORIATIC ARTHRITIS: QUANTUM PROJECT

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**Background:** In the context of complex diseases like psoriatic arthritis (PsA), in which patients are often followed by different professionals, it is important for health professionals, providers and patients to have tools for delivering and demanding optimal care. One way to organise and evaluate health care quality is by the use of validated standards of care and quality indicators.

**Objectives:** To develop nationally accepted standards of care and quality indicators for care in PsA.

**Methods:** Qualitative methodology was followed that included: 1) Two focus groups (one with patients with PsA and another with non-rheumatologists specialists involved in the care of patients with PsA); 2) A narrative literature review of published documents related to the quality of care in PsA (including the QUANTUM Report<sup>1</sup>); 3) A nominal group meeting in which 15 expert rheumatologists generated and consensuated, a series of quality criteria as well as formulas or quantifiable objective measures to evaluate them; 4) A Delphi to establish the feasibility, priority and agreement with the quality criteria; 5) A final generation of standards of care and their attributes (including quality indicators). A descriptive analysis of the results was carried out.

**Results:** A total of 59 standards of care were generated, 19 of mandatory compliance, grouped into 4 blocks according to specific objectives: 1) Early diagnosis (n=6); 2) optimising the management of the disease (n=26), 3) multidisciplinary collaboration (n=9); 4) monitoring improvement (n=18). To assess the compliance of these standards of care, in many cases the medical records will be reviewed. Other sources will be the memory of the service and hospital and bibliographic databases. Regarding to the level compliance, for some of the standards of care this is yes/no, for others the compliance will range are from 50% to 100%, and in this range for many this will be by 80%.

**Conclusions:** This set of standards of care should help improve quality of care in APs patients.

**Abstract AB1270 – Table 1.** – Regression analysis on indirect cost

	Univariate Analyses			Multivariate Analyses*					
	$\beta$	95% CI	p	$\beta$	95% CI	p			
Age	-32.5	-242.4 to 5351.7	0.211	-6.4	-66.2 to 53.3	0.830	-11.4	-68.0 to 45.2	0.688
Gender, female	-119.6	-1491.0 to 1251.9	0.862	66.4	-1601.9 to 1734.8	0.937	63.6	-1597.7 to 1725.0	0.939
Disease duration (months)	44.5	-7.5 to 96.7	0.093	17.7	-42.4 to 77.4	0.561	14.2	-48.8 to 77.2	0.632
Baseline VAS pain score	300.8	88.3 to 513.2	0.006	280.5	72.5 to 488.5	0.009	271.4	62.2 to 480.6	0.012
Baseline HAQ	893.8	-15.7 to 1083.3	0.054	-223.5	-1760.2 to 1313.2	0.772	-397.6	-1641.4 to 846.2	0.525
Baseline FACIT	-63.9	-114.9 to -12.8	0.015	-19.6	-0.4 to 0.6	0.635	-40.7	-127.2 to 45.762	0.350
Baseline SF36 PCS	-30.0	-660.0 to -0.017	0.050	17.7	-27.3 to 62.8	0.434	12.4	-38.1 to 62.9	0.625
Baseline SF 36 MCS	-42.6	-72.8 to -12.4	0.006	-26.9	-63.4 to 9.63	0.146	-27.9	-64.3 to 8.6	0.131
Month 6 DAS CRP Score	695.4	137.4 to 1253	0.015	634.8	96.1 to 1175.4	0.022	-	-	-
Cannot achieve early remission/ LDA	1465.3	318.1 to 2612	0.013	-	-	-	1287.5	164.3 to 2410.7	0.025

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**Conclusions:** Early intensive treatment with early disease control yield lower indirect cost. Health care system shall consider reallocating adequate resource for managing early arthritis patients to reduce indirect cost related to disease.

**Acknowledgements:** This is to acknowledge the Hong Kong Society of Rheumatology Education and Research Foundation for supporting this project.

**Disclosure of Interest:** None declared

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**AB1270** **ACHIEVING EARLY DISEASE CONTROL AND REDUCING INDIRECT COST – THE CRYSTAL REGISTRY IN HONG KONG RHEUMATOID ARTHRITIS PATIENTS**

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**Background:** Rheumatoid arthritis is associated with irreversible joint erosion, jeopardising patients' work ability and incurs substantial indirect cost to the society. While early treatment yield clinical efficacy, its economic outcome remains uncertain in Hong Kong.

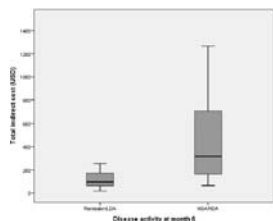
**Objectives:** To ascertain the effect of early disease control in early RA subjects on indirect cost.

**Methods:** This was a multi-centre, prospective cohort study involved 13 hospitals in Hong Kong. Subjects underwent intensive treatment scheme aiming at remission. Early disease control was defined as achieving remission or low disease activity (LDA) at month 6 indicated by DAS-28 score.

**Results:** Seventy early RA patients [53 (75.7%)Female, mean age: 53±11 years, mean disease duration 30±11 months] were included in this analysis. Forty-two (60%) subjects achieved early disease control. Subjects with or without early disease control were comparable at baseline. Twenty-two(31.4%) subjects had non-zero indirect cost[median(IQR) indirect cost: USD162(76–317)]. Among them, early disease control non-achievers(n=11) had significantly higher indirect cost than achievers[median(IQR) indirect cost: USD317(133–934) vs USD95,<sup>48–163</sup> p=0.008](figure 1). Using multivariate linear regression, after adjusting for age, gender, baseline pain score, fatigue level, physical and mental condition, every 1-unit increase in DAS score at month 6 was associated with USD82 increase in indirect cost [95% CI: 12–151, p=0.022]. When disease activity was categorised, not achieving remission/LDA was associated with USD165 increase in indirect cost [95% CI: 21–310, p=0.025] (table 1).

Model 1 – DAS score as continuous variable

Model 2 – DAS score categorised as early disease control or not



**Abstract AB1270 – Figure 1**

**AB1271** **SEVERE OUTCOMES OF AFRICAN PATIENTS FROM PALOP EVACUATED FOR MEDICAL ASSESSMENT IN PORTUGAL – RHEUMATOLOGY AS A CASE STUDY**

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**Background:** Portugal has made an official commitment for improving health in Portuguese speaking African countries (PALOP) by allowing an annual quota of patients evacuated from these countries for medical reasons. The agreements pretend to compensate difficulties in health care access and medical resources of these populations. However, the bureaucratic process that mediates the displacement of patients to Portugal is invariably complex and delayed, so these aims are commonly not achieved.

**Objectives:** to report our experience dealing with PALOP rheumatic patients and evaluate their outcomes.

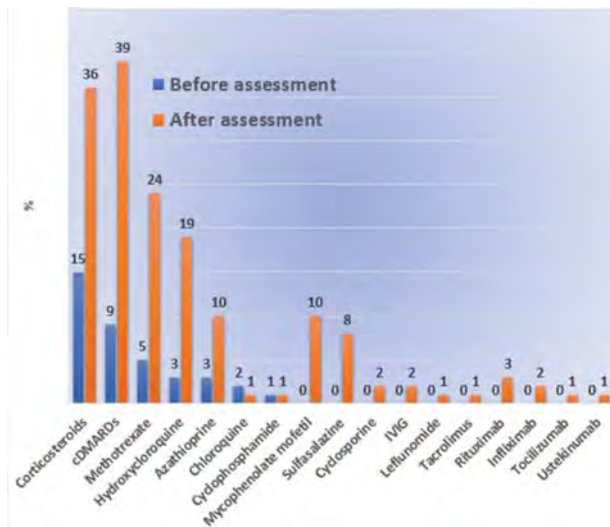
**Methods:** a retrospective analysis of patients evacuated from PALOP and referred due to rheumatic diseases or potentially related conditions, followed-up in our Department for the last 7 years. Clinical data was collected until September 2017.

**Results:** a total of 58 patients (77.6% female), with an average age of 33.5 years (±SD 15.2; range 2–78 years) were included, representing Guinea-Bissau 44.8%, Cape Verde 27.6%, São Tomé and Príncipe 17.2% and Angola 10.3%. Of all these patients, only 44.8% were primarily referred to our Department. The majority (55.2%) had no previous diagnosis, 19% were considered to have a wrong diagnosis and 25.9% were well diagnosed. After assessment in our Department, we ended up with the diagnoses listed, mainly SLE (17.2%) and Rheumatoid Arthritis (17.2%).

**Abstract AB1271 – Table 1**

Disease	N
SLE	10
Rheumatoid Arthritis	10
Vasculitis	6
Dermatomyositis	3
Other CTD	4
Osteoarticular infections	3
Psoriatic Arthritis	2
Ankylosing Spondylitis	2
Reactive Arthritis	2
JIA	1
SAPHO Syndrome	1
Non-inflammatory rheumatic diseases	6
Non-confirmed rheumatic diseases	8

The mean duration of symptoms was 62.4 months (minimum 1 month; maximum 40 years). From the evacuation request until effective journey patients waited a mean of 13.9 months (missing data in 37 patients). At arrival, only 25.9% of patients were or had been on corticosteroids and only 15.5% on conventional disease modifying antirheumatic drug (DMARD) treatment, versus 62% and 67.2%, respectively, after assessment in Portugal (graphic). Even common and cheap drugs, like prednisolone and hydroxychloroquine were underprescribed before our assessment. Twelve percent of patients required biologics. Hospitalizations related to disease activity or complications were required in 43.1%. Severe damage, measured by indication for orthopaedic, cardiothoracic or vascular surgery, need of chronic dialysis or long-term oxygen therapy and permanent neurologic deficits was present in 34.5% of the patients. Three patients died. Regarding infectious comorbidities, 12.1% of patients were diagnosed with tuberculosis, 8.6% had chronic hepatitis B infection and 12.1% had evidence of previous contact with hepatitis B virus.



Abstract AB1271 – Figure 1

**Conclusions:** PALOP patients present with long-lasting and severe rheumatic diseases with chronic damage, due to lack of precise diagnosis, ineffective referrals and lack of appropriate treatment. They also frequently present with important infectious comorbidities and social needs that may delay treatment. Despite the obvious advantages of the evacuation of patients to a more resourceful country, we believe there is a need for identification of onsite barriers and improvement of local awareness on Rheumatic diseases and Rheumatology speciality.

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AB1272

#### INCREASING STRENGTHS OF EVIDENCE FOR ROLE OF NURSES IN THE MANAGEMENT OF CHRONIC INFLAMMATORY ARTHRITIS: RESULTS OF A SYSTEMATIC LITERATURE REVIEW

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**Background:** In 2011 EULAR first published European recommendations for the potential role of nurses in the management of patients with rheumatic diseases.<sup>1</sup> Since then, the EULAR recommendations were well disseminated and positively evaluated both across Europe and the United States (US).<sup>2</sup>

**Objectives:** To assess new evidence for the role of nurses in the management of chronic inflammatory arthritis (CIA) obtained since the 2011 EULAR recommendations.

**Methods:** A systematic literature search was performed for the time between 1/2010 and 9/2016 based on the PRISMA guidelines, using the search strategies and eligibility criteria and categorising evidence as did the EULAR taskforce.

**Results:** A total of 44 articles and 10 abstracts were identified fulfilling the eligibility and exclusion criteria. Strong new evidence exists for recommendation 3 with nurse-led telephone services to enhance continuity of care and to provide ongoing support (evidence level 3), and – at least in part – for recommendation 6, that nurses should promote self-efficacy (evidence level 1B) and empowerment (evidence level 2B), but sense of control was not studied. Some new evidence also exists for recommendations 7 and 8 (level 2B).

**Conclusions:** This literature review reveals new evidence for a role of nurses in managing CIA-patients especially with RA and in stable and low disease activity, and thus further supports the existing 2011 EULAR-recommendations.

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**Acknowledgements:** -

**Disclosure of Interest:** None declared

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AB1273

#### UPTAKE OF PNEUMOCOCCAL AND INFLUENZA VACCINATION IN PATIENTS RECEIVING BIOLOGICAL DMARDS (bDMARDs) IN IRELAND

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**Background:** Biological disease-modifying antirheumatic drugs (bDMARDs) have made significant positive outcomes in the lives of patients with rheumatic disease. This treatment has proven efficacy in delaying joint destruction and inducing disease remission.<sup>1</sup> Studies have shown that pneumococcal vaccination is cost effective while the influenza vaccination significantly prevents morbidity and mortality in the elderly and in patients with chronic disease.<sup>1</sup>

**Objectives:** To evaluate the pneumococcal and influenza vaccination status in patients receiving biological disease-modifying antirheumatic drugs (bDMARDs). **Methods:** Patients on bDMARDs attending the rheumatology infusion unit were asked about their vaccination status on pneumococcal and influenza using a questionnaire. The patients' diagnosis, current bDMARD and reasons for not having had vaccination were recorded.

**Results:** 92 patients were recruited. Mean age of 53.2 years with 63 (68.5%) female and 29 (31.5%) male. A total of 30 (32.6%) patients received both pneumococcal and influenza vaccination, 1 (1.1%) received pneumococcal vaccination alone, 22 (23.9%) received influenza vaccination alone and 39 (42.4%) had neither. Of the 18 (19.6%) patients age >65 years, 5 (27.8%) received influenza vaccination alone and 8 (44.4%) received both. Patients who did not receive vaccinations were given an educational booklet.

The most common diagnosis from our cohort was rheumatoid arthritis(37%), followed by spondyloarthritis(13%), Behçet's disease(9.8%), myositis(7.6%), vasculitis(5.4%), systemic lupus erythematosus(5.4%), psoriatic arthritis(4.4%) and others(17.4%). 48 (52.2%) were on rituximab, 37 (40.2%) on infliximab, 6 (6.5%) were on tocilizumab and 1 (1.1%) was on abatacept.

Of the 61 (66.3%) patients who did not receive the pneumococcal vaccine, 44 (72.1%) were unaware of its availability, 6 (9.8%) were not interested in receiving it, 4 (6.6%) were afraid of the side effects, 4 (6.6%) declined vaccination and 3 (4.9%) were unaware it was recommended. 40 (43.5%) who did not receive the influenza vaccine stated that they were either unaware(45%), not interested (25%), declined vaccination(10%), forgotten(5%), unaware it was recommended (5%) and afraid of the side effects(2.5%). 3 (7.5%) had previous bad experiences from influenza vaccination.

**Conclusions:** This is the first study in Ireland looking at vaccination uptake in patients on bDMARDs. The vaccination rate in our cohort was less than satisfactory. Patients on immunosuppressants are recommended to have these vaccinations and preferably to receive them before commencing on the immunosuppressants.<sup>2</sup> The lack of awareness is the main reason for failure to be vaccinated. Hence, primary care physicians and the rheumatology team should take active roles in increasing awareness amongst patients about the recommendation for pneumococcal and influenza vaccination.

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AB1274

### THE EFFECT OF IMPLEMENTING AN ONLINE PATIENT HEALTH RECORD AIMING TO PROMOTE PATIENT PARTICIPATION IN RHEUMATOID ARTHRITIS PATIENTS ON THE USE OF DISEASE-MODIFYING ANTIRHEUMATIC DRUGS AND OUTCOME IN DAILY CLINICAL PRACTICE

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**Background:** Current guidelines say that there should be a prominent place for patient participation and shared decision making in rheumatic care.

To achieve this Bernhoven introduced an online patient health record (OPHR) for patients with rheumatoid arthritis (RA) aiming to facilitate self management and giving insight in the individual disease course in April 2014. This platform enables patients to monitor their disease by completing questionnaires about for instance pain, fatigue and quality of life. It also gives access to their medication history and offers patients information in the form of an online library.

**Objectives:** This study analyses how the introduction of an OPHR, aiming to promote patient participation, influences the prescription of DMARD's and the disease activity (DAS28) in daily clinical practice. A distinction was made between the effects of the PHR on patients recently diagnosed with RA (study A) and the RA population as a whole (study B).

**Methods:** In April 2014 anan OPHR for patients with RA was introduced at the rheumatology department of Bernhoven.

Using data from the rheumatology department registry, two analyses were performed to evaluate this implementation.

Study A compared the treatment and course of DAS28 of patients diagnosed in the period three years prior to the implementation ("prior group") with those diagnosed in the period three years after the implementation ("after group").

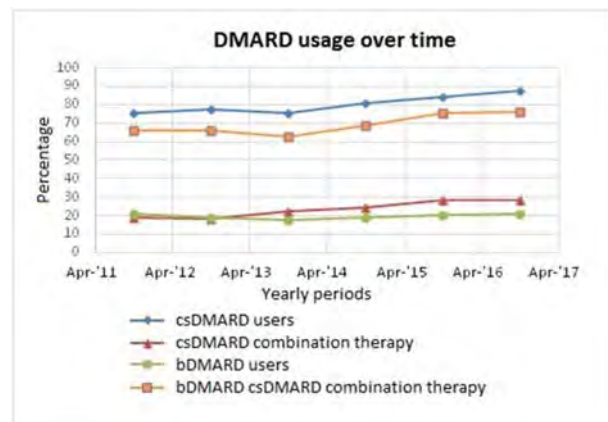
Study B was an observational study that examined yearly trends for DMARD use and DAS28 for the whole RA population between April 2011 and April 2017

**Results:** Study A

A total of 287 patients were diagnosed with RA of which 127 were in the prior group and 171 in the after group. CsDMARD's were given 160 days [95%>CI 123–198] after diagnosis in the "prior group" versus (vs.) 32 days [95%>CI 22–43] in the after group. Next to that there was an increase in cumulative time csDMARD's were used during follow-up, 54% vs. 74% (p-value<0.001). Also, more patients received csDMARD combination therapy, 49% vs. 64% (p-value=0.001). There was no difference in number of patients that started a bDMARD, 7% vs. 14% (p-value=0.059). However, a significant larger group started with a bDMARD in the first year after start of csDMARD therapy in the after group, 3.1% vs. 9.9% (p-value 0.024). 39% of the prior group vs. 69% in the after group achieved either remission or LDA within the first year of DMARD therapy (p-value<0.001).

Study B

The trend analysis of DMARD use in the RA population is plotted in figure 1. Between 2011 and 2017 a change in trend can be observed for the use of csDMARD's, the use of csDMARD combination and the use of bDMARD csDMARD combination therapy. The usage of bDMARD therapy did not change.



**Abstract AB1274 – Figure 1.** Trends in DMARD prescription, per yearly period

**Conclusions:** After the introduction of the OPHR patients recently diagnosed with RA got earlier and more intense treatment, with a more prominent role for biologicals. Next to that a bigger proportion of patients recently diagnosed with RA achieved remission and LDA within the first year of DMARD therapy. When looking for trends in the total RA population, an increase of the use of csDMARD's, the use of csDMARD combination and the use of bDMARD csDMARD combination therapy was observed after April 2014.

**Disclosure of Interest:** None declared  
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AB1275

### RESEARCH CONTRIBUTION TO THE JOURNAL OF ANNALS OF THE RHEUMATIC DISEASES FROM 2012 TO 2016: A BIBLIOMETRIC ANALYSIS

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**Background:** Rheumatology, a subspecialty of medicine, is devoted to diagnosis and therapy of rheumatic diseases, including clinical problems in joints, soft tissues, and autoimmune diseases. "Annals of the Rheumatic Diseases" is one of the most read and prestigious journals in the field of rheumatology. Bibliometric studies concerning the quantity and quality of articles published in rheumatology journals are scarce. The scientific production in the field of rheumatology from 1996 to 2010 was compared by Cheng.<sup>1</sup> On the other hand, as to our knowledge, there is no study investigating research contribution to Annals of the Rheumatic Diseases since 2012.

**Objectives:** This study aims to investigate countries' research contribution in the field of rheumatology by classifying scientific papers according to their countries between 2012 and 2016 in Annals of the Rheumatic Diseases, official journal of EULAR.

**Methods:** All scientific papers which were published from 2012 to 2016 in Annals of the Rheumatic Diseases were screened. Some scientific papers such as editorial, viewpoint notes, or letters were excluded. In addition, supplementary issues were excluded as well. Rest of the papers were separated in two different part: "clinical and epidemiological research" and "basic and translational research". The papers were investigated one-by-one to determine their countries. All papers were classified according to their corresponding author.

**Results:** A total of 1616 scientific papers were investigated. Totally 1092 papers were included. While *clinical and epidemiological research* included 753 articles, *basic and translational research* contained 339 articles. There are 211, 188, 260, 235, 198 published articles in 2012, 2013, 2014, 2015, 2016, respectively. In 2012, 2014 and 2015 the top countries to publish articles in Annals of the Rheumatic Diseases are England, Netherlands and USA. In 2013 and 2016, France is in the list of top countries instead of Netherlands. While, 46, 37 and 37 articles were published from England, Netherlands and USA, respectively in 2012, 53, 35 and 18 articles were published from England, USA and France, respectively in 2016.

**Conclusions:** According to our results, Western Europe and USA clearly dominate the production of scientific papers in Annals of the Rheumatic Diseases, official journal of EULAR. Our results are in accordance with the literature. We conclude that research resources, financial and other some issues may contribute the publishing process.

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**Disclosure of Interest:** None declared  
**DOI:** 10.1136/annrheumdis-2018-eular.6856

AB1276

### ECONOMIC IMPACT OF NON-MEDICAL SWITCHING FROM ORIGINATOR BIOLOGICS TO BIOSIMILARS – A SYSTEMATIC LITERATURE REVIEW

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**Background:** Biosimilars, often priced at a discounted rate of originator biologics, may prompt switching patients from originator biologics to biosimilars for non-medical reasons. However, other relevant costs (e.g., non-medical switching (NMS) program setup, costs of concomitant therapies, additional healthcare resource utilisation [HRU]) associated with NMS are not well understood.

**Objectives:** A systematic literature review (SLR) was conducted to review and summarise economic consequences of NMS from a biologic originator to its biosimilar.

**Methods:** English publications reporting HRU or costs associated with biosimilar NMS were searched in PubMed and Embase over the past 10 years, and from selected scientific conferences over the past 3 years, along with grey literature (e.g., organisational reports). Search strings for keywords (e.g. biosimilar, HRU, cost, switch etc.) were combined using Boolean operators for all relevant agents with an approved biosimilar (e.g., tumor-necrosis factor inhibitors, erythropoiesis-stimulating agents, insulin, hormone therapies).

**Results:** A total of 244 publications were retrieved for review, where 122 were identified from the database search, 117 from conference abstracts and 5 from grey literature. Of these publications, 23 reported costs or HRU associated with biosimilar NMS, including 10 center-based cohort studies (all except one were single arm), 10 budget impact models/simulation studies, 2 national registry studies, and 1 policy review. Only three studies reported real-world HRU: a single-centre, two-cohort study found that switching to biosimilars was associated with higher inpatient readmission rate (80% vs 5%,  $p<0.001$ ), surgery rate (29% vs. 0%,  $p=0.02$ ), and steroid use (60% vs. 8%,  $p<0.001$ ); a single-centre, single-arm study reported extra visit/phone consultation with a provider among patients experiencing injection-site pain; a national registry-based study found that comparing 6 months before vs. after NMS, post-NMS had increased outpatient visit days (5.7 vs 5.4,  $p<0.001$ ) and increased rates in 6/16 service categories. Among the other 20 studies, most of them focused on potential cost savings with approximately half considering drug cost only. Estimation/simulation in cost savings varied substantially due to heterogeneity in study design and assumptions (e.g. disease areas, drug price discount rates, cost components, population size, study period etc.). Among these, discontinuing/switching or switching back to the originator was reported in four studies (rate range: 6%–29%) and biosimilar dosing increase (35%) was reported in one study. A policy review study pointed out that biologic rebates (commonly at 50%) should be taken into account in the context of NMS.

**Conclusions:** Few real-world studies reported economic consequences of biosimilar NMS and found increased HRU in patients with biosimilar NMS. Studies of cost estimation have been largely limited to drug prices. Comprehensive evaluation on the economic impact of NMS should incorporate all important elements of economic outcomes such as drug price, biologic rebates, HRU, NMS program setup, administration, and monitoring costs.

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AB1277

#### VACCINATION STATUS AND KNOWLEDGE AND ATTITUDE ON VACCINE AMONG PATIENTS WITH RHEUMATIC DISEASE IN CHINA

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**Background:** Rheumatic diseases are associated with an increased susceptibility to infections.<sup>1</sup> Specific inactivated vaccinations are recommended for patients with autoimmune diseases.<sup>2–4</sup> However, vaccination coverage among patients with rheumatic disease is extremely low in China.

**Objectives:** Our study was to discover infection and vaccination status in patients with rheumatic diseases in recent five years. and then to determine knowledge and attitude on vaccine among patients with rheumatic diseases.

**Methods:** A questionnaire-based survey was conducted in a total of 242 patients. The Statistical Package for Social Sciences (SPSS) software version 21 was used for all data management and analysis.

**Results:** Of 242 patients, mean age was 39.84±4.42. Mean disease duration was 30.00±4.42. 55% had connective tissue disease. 7 patients had herpes zoster infection. 4 had influenza. 5 had pneumonia, 1 had dengue fever. And 1 had herpes genitalis infection in recent 5 years.

Only 15 patients (6.2%) had vaccination in recent 5 years. 2 female patients had inoculation of human papillomavirus (HPV) vaccine. 3 patients took shots of hepatitis B virus (HBV). 2 were vaccinated for tetanus, 4 for rabies vaccine and 1 for influenza.

159 (65.7%) of the patients had heard of influenza vaccine. Only 62 (25.6%) had heard of pneumococcal vaccine. 103 (43.6%) of the participants knew where to take vaccine. Only 9 patients had reported of former doctors' advice to taking vaccine (influenza, 2). 144 (59.5%) believed influenza could turn to serious infection.

47.5% had correct knowledge of vaccination function. Only 42.1% believed vaccine was safe and valid. 8.3% of the patients thought vaccination was useless. 57.4% of the patients would like to take vaccine if medical insurance could cover vaccination. Only 37.6% of the patients preferred to take vaccine with doctors' recommendation.

**Conclusions:** There is a need for educational intervention and awareness campaigns over the importance of vaccination in patients with rheumatic diseases.

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AB1278

#### MOBILE DEVICE-AIDED HEALTH CARE: ADMINISTRATION OF NEW HEALTH CARE IN CHINA

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**Background:** ,<sup>1</sup> <sup>2016</sup> the total population of mainland China has reached 1.38 billion, while there are only 2.21 licensed/assistant physicians per thousand people.<sup>1</sup> Another serious problem is uneven geographical distribution of medical resources. Less than 3% of general hospitals are responsible for more than 40% of medical service. Limited medical resources and distribution imbalance lead to countless of trans-provincial medical behaviours, resulting in an increase of economic cost and time cost. Meanwhile, China's mobile Internet communication is booming. By the end of 2016, there were 1.32 billion mobile phone users nationwide.<sup>2</sup> Based on these advantages, a new type of digital medical care has been developed rapidly in China.

**Objectives:** Our aim was to describe current situation of medical care and mobile medical care in China, and then to analyse medical big data to help manage chronic diseases such as rheumatic diseases.

**Methods:** Distribution and number of medical resources were acquired by the website of National Bureau of Statistics of the People's Republic of China and National Health and Family Planning Commission of the People's Republic of China. 7 biggest digital medical services and other healthcare websites or applications were compared in the aspects of application function, numbers and distribution of registered doctors and patients, and chronic disease management.

**Results:** According to different stages of medical interventions, operation modes of digital medical services can be divided into different types. Major functions encompass reservation, payment and medical consultancy. 3% of applications involve the management of chronic diseases. Many mobile medical platforms rely on doctors from comprehensive hospitals. Patients with definitive diagnosis and initial treatment could be managed and followed-up via the platform. This Internet management mode of chronic diseases currently attracts 3 89 407 specialists from comprehensive hospitals and 8 95 921 patients with chronic diseases. Although the number of registered doctors in the southeastern areas is absolutely higher, many doctors are more accepting Internet-based medical practice in relatively poor western regions. The proportion of physicians and patient with chronic diseases is very large. The top 5 departments of registered users are related to chronic diseases.

**Conclusions:** Limited medical and health resources and distribution imbalance is a serious problem in China. A new mode of digital medical service may help manage chronic diseases.

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AB1279

#### EFFICACIOUS TRANSITION FROM REFERENCE PRODUCT INFLIXIMAB TO THE BIOSIMILAR IN DAILY PRACTICE

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**Background:** The biosimilar of infliximab, approved in September 2013 for the treatment of rheumatic diseases. The biosimilar is non-inferior to the reference product of infliximab based on safety, quality and efficacy.<sup>1</sup> In order to enable health care cost saving and efficient treatment, a transition to the biosimilar was deemed necessary.

**Objectives:** To evaluate the transition from the reference product to the biosimilar in patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA).

**Methods:** Consecutive patients treated with reference product were switched to the biosimilar in the period July 2015 to June 2016 at the Amsterdam Rheumatology and immunology Center, Reade. Patients were informed by a letter about the transition to the biosimilar and were subsequently contacted by a nurse or the pharmacist for additional questions and whether they agreed upon the switch. Patients were advised to contact their treating rheumatologist when in doubt. Once agreed, the biosimilar was administered at the same dosage and interval as previous treatment with the reference product. Patients were followed until January 2018. The primary outcome was to evaluate the transition from the reference product to the biosimilar, secondary outcome was the change in disease activity measured with the Disease Activity Score in 28 joints using erythrocyte sedimentation rate (DAS28-ESR). Last available DAS28-ESR before switching and first available DAS28-ESR approximately 12 months after switching was used. In addition, the reason for discontinuation with infliximab or the restart with the reference product was recorded.

**Results:** In total 45 patients switched from the reference product to the biosimilar, 2 patients disagreed upon the switch and continued the reference product. The median treatment duration within fliximab in patients with RA and PsA was 17 (SD=11) years (table 1). During the follow-up period, 3 patients (7%) restarted the reference product due to subjective reasons, increase in disease activity was not objectified by the rheumatologist. The biosimilar was continued by 42 patients (93%). Furthermore, 1 patient switched to another biological due to lack of effect and in 2 biological therapy was stopped because of malignancy. The DAS28-ESR remained comparable before and after the switch, with a mean (SD) of respectively 2.34(±1.02) and 2.31 (±1.11).

**Abstract AB1279 – Table 1.** Baseline characteristics of the 45 patients who switched from the reference product to the biosimilar

RA/PsA no.	41/4
Age, mean (SD) years	65 (14)
Female no. (%)	32 (71)
Disease duration, median (SD) years	17 (11)
DAS28-ESR, mean (SD)	2.34 (1.02)
Duration infliximab use, median (SD) years	19 (11)
Methotrexate use; no.(%)	31 (69)

**Conclusions:** In our population, a high amount of patients (n= 42, 93 %) continued the biosimilar during the follow up period of two years. A very low number of the patients (n=3) restarted the reference product, due to subjective reasons, whilst retaining stable DAS28-ESR.

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#### Epidemiology, risk factors for disease or disease progression

AB1280

#### PREDICTING WORK DISABILITY, PENSION CLAIM, ABSENTEEISM AND PRESENTEEISM IN RA PATIENTS

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**Background:** Despite advances in treatments for Rheumatoid Arthritis (RA) a high prevalence of unemployment and work disability (WD) is reported; almost one third of affected patients leave the work force within two years of diagnosis. However, historic studies focused upon work disability as a dichotomous outcome, whereas more recent research has shifted the focus to work productivity, absenteeism and presenteeism.

**Objectives:** We undertook a systematic review of observational studies to identify the known predictors of work productivity from work disability and identify the gap in between.

**Methods:** A systematic search of Medline and Embase and PsychINFO since 2000 was undertaken using search terms: "Rheumatoid arthritis", "Disability", "Employment", "Work", "Occupation", "presenteeism", "absenteeism", "productivity" and "indirect cost". Original publications, all observational studies, reporting on predictors of work outcomes in RA were eligible. Clinical trials of drug therapies were excluded. All article titles were manually reviewed by 2 reviewers (AH and MY) and relevant abstracts was discussed and agreed, for which full text articles were sourced. Selected articles were assessed for quality using: QUality In Prognosis Studies (QUIPS) for observational studies. The heterogeneity in study designs meant meta-analysis was not appropriate. Therefore, To account for variation across studies in outcome measures used, an albatross plot was used to confirm predictors that were significantly associated with adverse work outcome.

**Results:** In total 57 observational studies were included in the review, with data collectively on 83 686 patients. The studies were from 19 different countries, predominantly including developed countries. There was substantial heterogeneity across studies in terms of predictors evaluated as well as how work productivity was estimated. More contemporary studies were more likely to capture information on mental health as a predictor. Consistent significant predictors of work outcome could be divided into<sup>1</sup> demographic factors: older age, obesity, lower educational level, job type, commuting difficulty;<sup>2</sup> disease factors: higher disease activity, longer disease duration, joint erosions, longer morning stiffness, higher disability;<sup>3</sup> comorbidity: concomitant mental health disorder, fibromyalgia or cardiovascular disease.

**Conclusions:** The review highlights the lack of consistency in the use of validated work outcome measures in research. The key determinant of work disability extends beyond disease severity measures, and in particular mental health is emerging as a pivotal component of health that predicts ability to remain within the work force.

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AB1281

### INCIDENCE AND CHARACTERISTICS OF HEALTHCARE-ASSOCIATED INFECTION (HCAI) IN HOSPITALISED PATIENTS WITH RHEUMATOLOGIC DISORDERS AT ALEXANDRIA MAIN UNIVERSITY HOSPITAL

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**Background:** Healthcare-associated Infection (HCAI) is an important cause of morbidity and mortality in autoimmune diseases<sup>(1)</sup>. The increased susceptibility to infections in such patients is explained by abnormalities of the cellular and humoral immune responses, as well as the use of immunosuppressive drugs. Infection in these patients can present with minimal signs and symptoms or with atypical features in unusual locations that considerably can delay the diagnosis and worsen the outcome. There are few detailed systematic reports on HCAI in rheumatology; most previous reports investigated HCAI in the setting of systemic lupus erythematosus (SLE) but lack other connective tissue diseases<sup>(2)</sup>.

**Objectives:** To determine the incidence and characteristics of HCAI in patients with rheumatologic diseases admitted to the Rheumatology Unit at the Alexandria Main University Hospital (AMUH) on 2017.

**Methods:** A One-year duration prospective observational study to elucidate the incidence and characteristics of HCAI in patients with underlying rheumatologic diseases who were admitted to the Rheumatology Unit of the Internal Medicine Department at AMUH between January 1st and December 31st 2017.

**Results:** A total of 516 patients (423 female (82%) and 93 male (18%)) with underlying rheumatologic diseases and disease duration of 6.03±4.18 years were admitted between January 1st and December 31st 2017. The mean age was 32.18±9.54 years, and the mean length of hospitalisation was 10.04±5.76 days. HCAI occurred in 14.9% (n=77) of patients with a total number of infections of 81 (15.69%) (four cases had more than one episode of infection in more than one site with a different organism during the same admission). Gram -ve bacilli were the most commonly isolated organisms (46.3%; n=38) followed by Gram +ve cocci (25.6%; n=21). The urinary tract was the most commonly documented site of infection (39.5%; n=32) followed by blood stream (18.5%; n=15), and *Klebsiella spp* (17.9%; n=15) was the most frequently identified infectious agent, followed by *Methicillin-resistant Staphylococcus Aureus* (MRSA) (14.3%; n=12). Of the total cases with HCAI (n=77), 85.7% (n=66) treated, 7.8% (n=6) deteriorated and shifted to the ICU with multiorgan failure, 5.2% (n=4) died, and 1.3% (n=1) (a case with meningitis) were referred to another specialised hospital.

**Conclusions:** Despite the improvement in healthcare services, the incidence of HCAI infection in our inpatient population is still high and represents a burden on our resources. Although most cases were treated with appropriate antimicrobials, HCAI is still the cause of deterioration and death in a considerable percentage of patients with rheumatologic diseases.

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AB1282

### TYPE OF PATIENT REFERRAL TO EARLY ARTHRITIS CLINIC (FLOW AND FATE)

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**Background:** Early Arthritis clinic (EAC) has a major contribution in Rheumatology outpatient services. Clinically, it gives a unique opportunity to assess, diagnose and classify various Rheumatic and Musculoskeletal diseases (RMD) during the initial phase of the disease process. Studying the patient's profile of EAC population aids in better management from the epidemiologic point of view. The average referral to EAC in Dubai hospital is 2 weeks over the last 5 years.

**Objectives:** The current study was conducted to explore the characteristics and common diagnoses of patients referred to EAC Rheumatology clinic in Dubai Hospital.

**Methods:** A review of the Electronic Medical Record of 117 patient presented to EAC between August 22nd 2017 and December 31st 2017. The following data were extracted from EMR and patient's files: Type of patient referral to EAC, initial visit diagnosis as well as concordance between initial diagnosis and established diagnosis.

**Results:** Autoimmune Rheumatic Diseases (ARDs) represents 41.1% of new cases diagnosed in the EAC. The number and percentage of the whole new cases

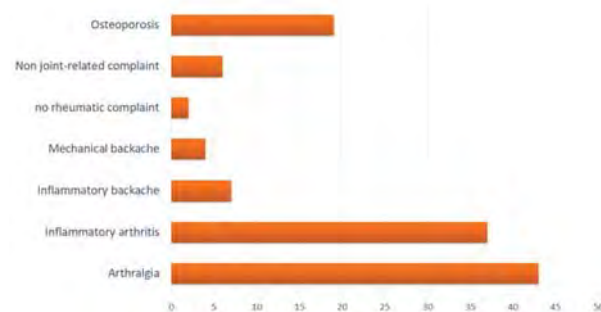
diagnosis is as shown in the following table while the type/percentage of patient presentation to EAC is shown in the graph.

Abstract AB1282 – Table 1

Disease category	Number	Percent (%)
Mechanical and soft tissue rheumatism	31	26.5
Fibromyalgia	10	8.6
Rheumatoid arthritis	19	16.2
Systemic lupus erythematosus	7	6
Spondyloarthritis	9	7.7
Vasculitis	3	2.6
Other	19	16.2
Osteoporosis	19	16.2

Occasionally, patients' clinical features were inconclusive at the initial presentation. Knowing that most patients presented within two weeks of symptoms onset to EAC, hence classification at initial visit was difficult in 16.2% (others or undifferentiated inflammatory arthritis).

on review of the initial visit diagnoses and the final established diagnoses after 3 months, we have found 97 of 117 has the same diagnosis, i.e. 82.9% concordance.



Abstract AB1282 – Figure 1. Type of patient presentations to EA in %

**Conclusions:** Early Arthritis Clinic grants an efficient access to patients with inflammatory and inflammatory back pain. However, a need of a standardised tool to triage patients with different musculoskeletal diseases to prevent delayed appointments to EAC.

We suggest adding Osteoporosis (Bone metabolic disorders), Undifferentiated (arthritis, CTD, SPA) and non-Rheumatic diseases to initial diagnosis to increase the current concordance.

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AB1283

### THE PREVALENCE AND COMORBIDITIES ASSOCIATED WITH PSORIATIC ARTHRITIS IN PATIENTS WITH PSORIASIS: AN OBSERVATIONAL COHORT STUDY

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**Background:** The prevalence and comorbidities of psoriatic arthritis (PsA) varies in different parts of the world and there is little clinical and epidemiological data from the Egyptian

**Objectives:** : To investigate the prevalence of psoriatic arthritis (PsA) in patients with psoriasis (PsO), and to identify comorbidities associated with it.

**Methods:** : The study was designed as an observational cohort study involving patients with psoriasis. Information was collected about lifestyle, habits, comorbidities, and psoriasis activity. Patients were classified as having PsA if they fulfilled the criteria of the Classification of Psoriatic Arthritis Study group (CASPAR).

**Results:** : The data was obtained from the 371 psoriasis patients. The mean age was 40.0±16.6 years, 42% were women, and 58% were men. A diagnosis of PsA was found in 104 patients (28%), of whom 34.6% had peripheral involvement, 15.4% had isolated axial involvement, and 50% had both peripheral and axial involvement. The PsA onset was preceding psoriasis in 48%, together with psoriasis in 40% and following psoriasis in 12%. Family history of PsO and PsA was positive in 21.6% and 8.4% respectively. PASI score of our patients ranged from 1–30 with a mean of 8.77±6.33, which were relatively higher in PsA patients. Comorbidities in form of diabetes mellitus, hypertension, liver disease, HIV and dyslipidemia

were found in 14.6%, 10.5%, 10.2%, 0.3% and 0.5% respectively. Smoking was found in only 10 patients (2.7%).

**Conclusions:** The prevalence of PsA in Egyptian patients with psoriasis appears to be within the range reported in other studies. Whereas, most of PsA onset was found to precede the psoriasis.

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AB1284

**PRELIMINARY DATA OF VACCINATION STATUS, POST VACCINATION IMMUNITY AND LATENT TUBERCULOSIS IN PATIENTS WITH CHRONIC INFLAMMATORY DISEASE IN A RHEUMATOLOGY CONSULTATION IN ST RAFAEL'S HOSPITAL IN BARCELONA**

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**Background:** Chronic inflammatory diseases (CID)(Rheumatoid arthritis(RA), Psoriatic arthritis(PsA) and ankylosing spondylitis(AS) are treated with disease modifying antirheumatic drugs(DMARDs). The most common adverse events are infections so an adequate vaccination is necessary before starting these treatments

**Objectives:** Determine the vaccination status, post-vaccination response and presence of latent tuberculosis(TB) in patients(pts)with CID

**Methods:** Before treatment with DMARDs, hepatitis C virus(HCV) antibodies, hepatitis B(HBV)surface antigen are determined. Following the guideline of Spanish Society of Rheumatology, before start a biological treatment(BT), latent tuberculosis(TB)screening is done by PPD and booster test. We and Preventive Medicine Department(PMD) of Vall Hebron Hospital(VHH) established vaccination protocol for pts with CID treated with DMARDs or/and BT:anti pneumococcal vaccination, virus serological status(varicella zoster IgG, measles IgG, anti-hepatitis A IgG, HBV surface antigen, HBV anti-surface antigen, HBV anti-core antigen and anti-HCV) and quantiferon(QT) test by assessment latent TB. Vaccines were administered depending on the above tests such as the determination of the post-vaccination HBV serology. Positive QT pts were referred to Infectious Diseases Department of VHH and received Isoniazid for 6 months

**Results:** From October 2016 to November 2017,123 pts with CID(including new onset and chronic disease) were referred to PMD. The pts were classified:81 RA (16 BT/65 DMARDs);25 PsA(9 BT/16 DMARDs),13 AS(10 BT/3 DMARDs),5 others(2 BT/3 DMARDs);2 juvenile idiopathic arthritis,1 reactive arthritis,1 monoarthritis and 1 polymyalgia rheumatica. Pts with BT were treated:14 RA with combined therapy(CT) and 2 with monotherapy;9 AS with monotherapy and 1 with CT,2 PsA with monotherapy and 7 with CT.19 pts had QT(+);2 had previously PPD(-);3 had previously PPD(+) and it was unknown in 14. Pts with PPD(+) and QT(+)(n=4), all of them who received BT(n=3) had been treated with isoniazid. The patient treated with DMARDs didn't received it. Pts QT(+) and previous PPD(-)(n=2):1 with BT for years and never before had been treated with isoniazid, so this treatment was started. The other with DMARDs started treatment with isoniazid as she was going to start BT in a short time. The rest of the pts QT(+)(n=14) didn't have a previous PPD(all DMARDs).11 received prophylaxis with isoniazid and 3 didn't, because they didn't require BT soon.19% of pts had positive HBV's serology, so they didn't receive HBV vaccination. 81%(n=100) had a negative anti-Ag surface HBV.92% of them received the vaccination, and from them, 9% didn't develop immunologic response so they needed revaccination(3 received TC BT-DMARDs and 5 DMARDs in monotherapy).42% developed immunologic response and in 49% we are waiting for the results.16% had a negative HAV's serology and all of them received the vaccination

**Conclusions:** The quantiferon can detect latent TB in patients with negative PPD and booster. Most patients need vaccination to HBV. Check the immunity from HBV is necessary after vaccination to know if they need revaccination. In our preliminary data we have observed absence of immunity to HBV in patients who are treated with BT (with CT) and also in patients who are treated with synthetic DMARDs.

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AB1285

**SERUM INTERLEUKIN 33, A POSSIBLE NEW MARKER PREDICTING THE DEVELOPMENT OF VASCULITIS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS**

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**Background:** Systemic lupus erythematosus (SLE) is an autoimmune disease characterised by abnormal production of autoantibodies and proinflammatory cytokines. Although interleukin-33 (IL-33), a novel member of the IL-1 family, has

been reported to have proinflammatory effects, the association of IL-33 with SLE has not been fully investigated<sup>1</sup>

**Objectives:** To estimate serum levels of IL- 33 in Egyptian patients with SLE and in controls, and to find out any relation between IL-33 serum levels in SLE patients and disease activity in addition to other clinical and laboratory criteria.

**Methods:** 60 SLE Egyptian patients (53 females and 7males) diagnosed according to systemic lupus international collaborating clinics (SLICC); new classification criteria 2012 and 20 healthy controls matched for age and sex were included. Patients with diseases suggesting the possibility of increased serum IL-33 were excluded<sup>2</sup> 27 SLE patients were diagnosed clinically as having vasculitis and this was confirmed by laboratory and imaging studies. Serum IL-33 was measured by sandwich ELISA Kit. Disease activity was assessed using SLE disease activity index (SLEDAI) score.<sup>3</sup>

**Results:** Using Mann-Whitney U test, median serum level of IL-33 (30.3 pg./ml) was significantly higher in patients with SLE than that of healthy controls (24.80, p=0.003). Using logistic regression analysis, SLE patients with high IL-33 serum levels have 3.8 times higher risk of developing vasculitis (OR 3.8 (1.1–13.6, 95% CI: p=0.01) and 3.2 times higher risk of developing oral ulcers (OR 0.3.2 (1.2–11.7, 95% CI: p=0.033.) than those with lower IL-33 serum Levels. No significant correlation was found between serum levels of IL-33 and total SLEDAI score or any of the other clinical or laboratory criteria.

**Conclusions:** Our findings suggest that IL-33 may be considered as a possible new inflammatory marker predicting the development of vasculitis and/or mucosal ulcers in SLE patients. Neutralisation of IL-33 may hopefully result in a new therapeutic option for these patients. Further studies are warranted to get more conclusive results.

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AB1286

**ANKYLOSING SPONDYLITIS (AS), PSORIATIC ARTHRITIS, UNDIFFERENTIATED (U) SPONDYLOARTHRITIS (SPA) IN INDIA: RESULTS FROM WHO ILAR COPCORD INDIA PROGRAM STAGE I SURVEY 2000–2010**

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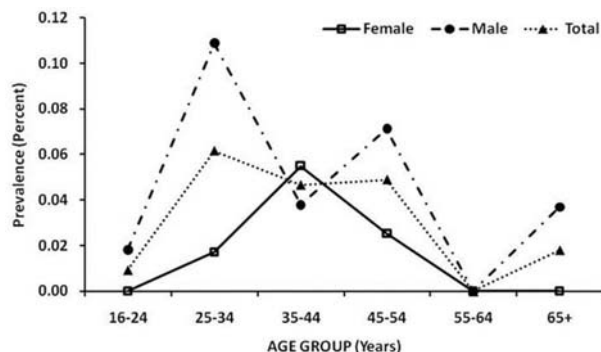
**Background:** Using a low cost low infrastructure model, the WHO ILAR COPCORD (Community Oriented Program for Control of Rheumatic Diseases) surveys have covered several population in Asia and Latin America. The reported prevalence of AS based on large sample surveys was 0.2–0.3 in China and 0.12 in Iran. We used the Bhigwan COPCORD model to complete comprehensive surveys at several urban and rural site in India.

**Objectives:** To describe the prevalence of SpA in India with a focus on AS

**Results:** 51 741 population (66% rural) in 11 sites all over India was screened using a suitable COPCORD core questionnaire and protocol. Stage I survey was carried out in 3 concurrent overlap phases. House to house visit identified respondents with current/past musculoskeletal pain (last 7 days). Paramedics interviewed respondents to map MSK pain and record patient centric outcome including an Indian version HAQ (Phase 2). Clinical evaluation was carried out by rheumatologists with minimal investigations (Phase 3). The diagnosis was clinical. Survey sites and samples were chosen by convenience. Data was centrally processed and analysed using standard software; significant p<0.05. Data standardised (age-gender) as per; India census 2002 adjusted prevalence reported.

Abstract AB1286 – Table 1

Disorder	Male (%)	Mean age (Range) years	Prevalence (95% confidence interval)
Spondyloarthritis	44.8	43 (19–80)	0.24 (0.20–0.29)
Ankylosing Spondylitis	72.2	39 (19–65)	0.03 (0.02–0.06)
Psoriatic Arthritis	64	54 (40–80)	0.02 (0.00–0.03)
Undifferentiated SpA	38.4	42 (21–80)	0.19 (0.16–0.23)



Abstract AB1286 – Figure 1

**Conclusions:** The burden of SpA in India (1.2 billion population) is enormous. Compared to global statistics, the prevalence of clinical AS and psoriatic arthritis in the Indian population appears low.

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AB1287

#### A POPULATION-BASED STUDY ON THE PREVALENCE AND INCIDENCE OF VASCULAR PRIMARY ANTIPHOSPHOLIPID SYNDROME: A NEW RARE DISEASE

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**Background:** Antiphospholipid Syndrome (APS) is a systemic autoimmune disease characterised by the presence of thrombotic and/or obstetrical manifestations and antiphospholipid antibodies (aPL). In 2006 the updated Sapporo criteria for APS were published but by now no epidemiological study on this disease were performed. Incidence and prevalence of primary APS (PAPS) in the general population are still unknown.

**Objectives:** The aim of this study was to evaluate the prevalence during the year 2013 and incidence for the period 2011–2015 of vascular PAPS in the adult population of a defined area, Valtrompia valley, using multiple sources. Valtrompia is a 40 kilometers-long prealpine valley in northern Italy. The population in 2013 was 101.477 inhabitants. The only easy access to the valley is from Brescia, the main city of the province. This valley is a cul-de-sac area without any other comfortable and practicable access. Therefore, this valley is ideal for epidemiological studies. In addition, the only Rheumatology referral tertiary Centre of the province is located in Brescia. This project was approved by the local Ethical Committee.

**Methods:** We identified adult subjects of 18–50 years old living in Valtrompia. Patients with thrombotic events were identified by two sources: 1) hospital

discharge code using keywords (deep vein thrombosis, pulmonary embolism, myocardial infarction, ischaemic stroke); 2) patients with defined diagnosis of vascular PAPS already followed by the Rheumatology tertiary Centre in Brescia.

**Results:** The prevalence of PAPS in 2013 was calculated to be 35.4 (CI 95% 20.6–59.6) per 100.000 inhabitants. Table 1 shows the incidence rates of vascular PAPS. We identified 47 patients with venous events during 2011–2015. 27/47 (57%) were tested for aPL, 4/27 (15%) positive. Regarding arterial events, 36 patients had stroke and 33/36 (92%) were tested for aPL, 4/33 (12%) positive. Finally, 64 patients with myocardial infarction (IMA): only 14/64 (22%) were tested for aPL, 2/14 (14%) positive.

**Table 1** Incidence rates of antiphospholipid antibody syndrome per 100.000 inhabitants in Valtrompia in adult population (18–49 years) between 2011 and 2015. The 95% confidence intervals (CIs) are reported in parenthesis.

	INCIDENCE	
	Number of cases	Incidence (95% CI) per 100,000
<b>OVERALL</b>		
Males + Females	9	3.7 (1.7-7.1)
Males	5	4.0 (1.3-9.4)
Females	4	3.4 (0.9-8.8)
<b>VENOUS THROMBOSIS</b>		
Males + Females	4	1.7 (0.5-4.3)
Males	1	0.8 (0.0-4.5)
Females	3	2.6 (0.5-7.5)
<b>STROKE/ICTUS</b>		
Males + Females	4	1.7 (0.5-4.3)
Males	3	2.4 (0.5-7.1)
Females	1	0.9 (0.0-4.8)
<b>IMA</b>		
Males + Females	1	0.4 (0.0-2.3)
Males	1	0.8 (0.0-4.5)
Females	0	-

Abstract AB1287 – Figure 1

**Conclusions:** Preliminary results of this population-based study showed that PAPS is a rare disease. A critical point emerged from this study is that aPL were not routinely tested in young subjects with vascular events, especially in patients with myocardial infarction. The study will be implemented by contacting patients who never tested for aPL during the hospital admission.

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AB1288

#### PREDICTION OF AMENORRHEA IN FEMALE RHEUMATOID ARTHRITIS PATIENTS WITH TRIPTERYGIUM WILFORDII HOOK F

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**Background:** The Chinese anti-inflammatory and immunosuppressive herbal remedy *Tripterygium wilfordii* Hook F (TwHF) is a widely used and effective treatment for rheumatoid arthritis (RA). Ovarian failure is one of the most important adverse effects among pre-menopausal women with TwHF therapy.

**Objectives:** To construct a statistical model for pre-treatment prediction of amenorrhea after TwHF therapy.

**Methods:** In this retrospective study, potential predictors of amenorrhea including demographic and clinical data were retrieved. Multivariate logistic regression models were used to evaluate the association between pre-treatment variables and amenorrhea. The probability of amenorrhea was calculated for combinations of pre-treatment variables.

**Results:** Post-TwHF therapy amenorrhea rate was 10.9% (70 of 641). The mean age was 36.2±5.5 years, mean body mass index 22.5±7.5 kg/m<sup>2</sup>. Age was the



strongest determinant of this adverse effect. In the final model, age >36 years, cumulative dose >4000 mg, and WBC<4.1 × 10<sup>9</sup>/L, were predictive of amenorrhea with adjusted odds ratios of 1.7 for TwHF therapy vs disease modifying anti-rheumatic drug (95% CI,1.2–3.2, p=0.017), 3.1 age >40 years (95% CI,1.8–4.7, p<0.001), 2.8 cumulative dose >6000 mg (95% CI,1.6–4.3, p<0.001), and 2.7 for WBC<3.5 × 10<sup>9</sup>/L (95% CI,1.4–6.3, p=0.012). The probability of amenorrhea can be as high as 76% or as low as 9% depending on the age, cumulative dose, WBC and the type of combination treatments employed.

**Conclusions:** This is first study to identify pre-treatment factors predictive of amenorrhea following TwHF therapy. Our model allows for optimum patient counselling and will help clarify expectations for the probability of amenorrhea following TwHF therapy.

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AB1289

#### SYSTEMIC FACTORS THAT AFFECT THE PROGRESSION OF PERIODONTAL DISEASE IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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**Background:** An association between Rheumatoid arthritis(RA) and Periodontal Disease(PD) has been reported. However, predicting factors of PD progression in patients with eRA are lacking

**Objectives:** To establish the predictive factors for progression of PD in patients with eRA including clinical and serological active scores of RA and status of PD

**Methods:** This cohort study evaluated the progression of PD at 280 inter-proximal dental sites in 28 patients within 2 years of diagnosis with eRA and they were evaluated to establish their progression through one year of follow-up. Adult patients were classified according to the 2010 ACR and the EULAR criteria. Periodontal diagnosis was established based on the AAP and the CDC and Prevention criteria. Serum markers of RA (rheumatoid factor, erythrocyte sedimentation rate (ESR), C reactive protein (CRP), and anticitrullinated protein antibodies (ACPAs) were evaluated, disease activity was assessed by disease activity score (DAS28-ESR) AND the simplified disease activity index (SDAI). Plaque index, gingival index, pocket depth, and clinical attachment loss (CAL) were evaluated at baseline and at one year follow-up. Data were analysed to establish predictive generalised linear mixed models (GLMM) for clinical attachment loss progression at each site with  $\geq 2$  or  $\geq 3$  mm CAL

**Results:** The patients included had an average age of 47.5±12.69 and 75% were women. The comorbidity given by the habit of smoking actively occurred only in 1% of patients. The 35.71% had levels of ESR >20 mm3/h and 39% APCA positive while in 60.71% had CRP  $\geq 3$  mg/L and 67.86% of patients had a positive FR. Regarding the indices of activity of the disease, DAS28-PCR>2.6 was found in 67.86% of the patients and SDAI scale >3.3 in 75%. 71.43% of the patients were being treated with DMARD and corticoid therapy. 71.43% of patients had a diagnosis of periodontitis. CAL $\geq 2$  mm and  $\geq 3$  mm was observed at 15% and 7.5% of dental sites, respectively. Factors associated with CAL in dental sites were: age, ESR, RF, DAS28, treatment with DMARD-Corticoids, periodontal pocket, CAL and percentage of CAL>5 mm, plaque index, gingival index and haemorrhage. Variables RA associated with activity such as CRP, DAS28, and SDAI showed a similar behaviour and they were more frequently associated in periodontal progressive sites. The principal predictive periodontal factors were the percentage of sites with CAL>5 mm and high gingival inflammation at baseline. Patients receiving combined treatment with disease-modifying antirheumatic drugs (DMARD) and corticosteroids exhibited less CAL. The predictive values of the GLMM for CAL of  $\geq 3$  and  $\geq 2$  mm were 98% and 82%, respectively

**Conclusions:** Systemic factors as disease activity score and serum biomarkers such as baseline periodontal status are associated with periodontal disease progression in early RA patients. It is known that the very low daily dose prednisolone in combination DMARD therapy substantially decreased radiographic progression and it could influence periodontal disease progression too in patients with RA in early stages of the disease

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AB1290

#### ANTI CARBAMYLATED PROTEIN IN HEALTHY SYSTEMIC FIRST-DEGREE RELATIVES OF RHEUMATOID ARTHRITIS INDIVIDUALS: RELATION WITH CLINICAL SIGNS OF ARTHRITIS

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**Background:** Association studies in rheumatoid arthritis (RA) have been focused in the pre-clinical phases of the disease in asymptomatic individuals with higher risk to develop RA such as first-degree relatives (FDR). A new group of autoantibodies directed against carbamylated proteins (anti-Carp) have been discovered in RA.

**Objectives:** To investigate the levels of anti-Carp in FDR and establish their association with the state of rheumatic condition and compare these variables with a control group of healthy individuals from general population

**Methods:** In total, 118 FDR and 118 healthy controls matched by age and gender were included. Rheumatologic (clinical and markers) and periodontal assessment was performed. Individuals selected were over 18 and less than 65 years old were studied in Bogota-Colombia. A complete medical history related to RA was obtained by rheumatologist. They were assessed by two periodontists calibrated. Cancer, autoimmune disease, recent infection, lactation or pregnancy, use of antibiotics in the last three months, diabetes, edentulous, periodontal and orthodontic treatment in the last six months, were exclusion criteria. Anti-carbamylated-fetal calf serum protein by ELISA (RUO, Inova Diagnostics, San Diego), RF (Rheumatoid Factor, Spinreact), ACPAs IgG/IgA (Inova, Diagnosis), Enzyme-linked immunosorbent assay for leptin, Adiponectin based on Luminex xMAP technology, high-sensitivity CRP and IL-6 (Siemens) by chemiluminescence and ESR were evaluated. An association analysis was performed to evaluate the relationship between anti-Carp levels and rheumatologic conditions using Chi square and Fisher test. Logistic regression model was performed to confirm these associations. All the analyses were performed with a level of significance of 95%

**Results:** In the FDR-group, seventy three percent were female with a mean age of 40.19±12.47 years, 22.2% were current smoker, leptin high in 26.27% and 4.23% and 16.9%, had positive RF and ACPAs respectively. Anti-Carp in 26.3%; Among the controls, 70.97% were women, with an average age of 41.0±12.2 years, leptin high in 12.7% (p=0.004), positive RF in 2.5% (p=0.71), ACPA 6.8% (p=0.013) and anti-Carp 15.3(p=0.027); in the general group 20.8% were positive (49/236) for anti-Carp, of which 63.3% are FDR (OR=2.02 IC 95% 1.03–3.96, p=0.04). Likewise, a greater frequency of painful joint (62.2%) p=0.008 and swollen joint (79.2%) (OR=4.35 CI 95% 1.5–12.36,p=0.006) were observed. The model designed for FDR showed a significant association between anti-Carp positive with of at least 1 swollen joint adjusted to the presence of leptin levels above the moderate range (OR=2.84, CI 95% 1.20–6.71,p=0.017)

**Conclusions:** The Research effort aimed at the "risk" phases of RA has increased. That is, before the development of clinical signs of arthritis, to identify those individuals and modify environmental factors and pharmacological intervention. The findings show us a significantly higher frequency of anti-Carp in a cohort of FDR of RA patients compared to healthy controls no associations were found with other autoantibodies but a very interesting way with signs of early inflammation

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AB1291

### CAROTID INTIMA-MEDIA THICKNESS IS INCREASED IN MEXICAN-MESTIZO PATIENTS WITH RHEUMATOID ARTHRITIS: A CASE-CONTROL STUDY

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**Background:** Patients with rheumatoid arthritis (RA) have a significantly increased risk for cardiovascular (CV) morbidity and mortality when compared to general population. Traditional risk factors do not explain the increased CV risk, which appears to be linked to chronic inflammation.<sup>1</sup> The leading cause of death in RA-patients is atherosclerotic cardiovascular disease (ASCVD).<sup>2</sup> Carotid artery evaluation by ultrasound is a useful tool for the detection of subclinical atherosclerosis. The presence of increased carotid intima-media thickness (CIMT) significantly raises the risk of ASCVD, mainly stroke and myocardial infarction.<sup>3</sup>

**Objectives:** To compare CIMT between Mexican-mestizo RA-patients and matched controls.

**Methods:** Design: observational, cross-sectional, case-control study. Patients 40 to 75 years old who fulfilled the 2010 ACR/EULAR and/or the 1987 ACR classification criteria for RA were consecutively enrolled. Patients with previous ASCVD or any other rheumatic disease were excluded. Carotid artery wall hypertrophy (CAWH) was defined as a CIMT $\geq$ 0.9 and <1.2 mm whereas carotid plaque (CP) was defined as a CIMT $\geq$ 1.2 mm or a $\geq$ 50% focal increase of CIMT compared to the surrounding wall.

**Results:** A total of 100 RA-patients and 49 matched control subjects were included in the final analysis. Their characteristics are shown in Figure 1. RA-patients had a median disease duration of 10.3 years and a median DAS-28-CRP of 3.2. Regarding carotid ultrasound findings, there was a significant difference in CAWH and average CIMT between groups (p<0.001).

	RA-Patient Group (n = 100)	Control Group (n = 49)	P
Female gender, n (%)	96 (96)	42 (85.7)	0.04
Age, mean $\pm$ SD	56.6 $\pm$ 9.1	53.6 $\pm$ 6.4	0.6
DM2, n (%)	14 (14)	4 (8.1)	0.42
Current Smoking	9 (9)	12 (24.4)	0.03
Lipid-lowering drug use	16 (16)	7 (14.2)	0.78
CAWH, n (%)	27 (27)	1 (2)	<0.001
Carotid Plaque, n (%)	27 (27)	16 (32.7)	0.564
Average CIMT (mm), median (p25 – p75)	0.82 (0.71 – 1)	0.62 (0.52 – 0.85)	<0.001
Disease duration (years), median (p25 – p75)	10.3 (4.2 – 17.9)	–	–
DAS-28-CRP, median (p25 – p75)	3.2 (1.9 – 4.1)	–	–

Abstract AB1291 – Figure 1. Demographic Characteristics

SD: Standard deviation, DM2: Type 2 diabetes mellitus, CAWH: Carotid artery wall hypertrophy, CIMT: Carotid intima-media thickness.

**Conclusions:** There was significantly increased CIMT and presence of CAWH in RA-patients compared to matched controls. These findings might be major contributors to the increased CV morbidity and mortality of RA-patients. Further research is needed to determine the relationship between RA-specific factors such as disease duration and activity and the presence and magnitude of carotid ultrasound abnormalities.

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AB1292

### METABOLIC SYNDROME AND ITS COMPONENTS AMONG HISPANIC RA PATIENTS: A CASE CONTROL STUDY

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**Background:** Metabolic syndrome (MetS) comprises a group of risk factors for type 2 diabetes and cardiovascular diseases. MetS is responsible for a three-fold increase in the risk of atherosclerotic cardiovascular diseases (ASCVD) and increased mortality compared to general population.<sup>1</sup> The frequency of MetS in RA patients is 14% to 56%. However, although many studies have reported a higher prevalence of MetS among RA patients, a number of studies have reported a higher prevalence of MetS in healthy controls.<sup>2</sup> Despite the importance of detection of MetS and its role in RA patients, information is scarce.

**Objectives:** To compare the prevalence of MetS among Mexican-mestizo RA-patients and matched controls.

**Methods:** Design: observational, cross-sectional, case-control study. Patients of 40 to 75 years old who fulfilled the 2010 ACR/EULAR and/or the 1987 ACR classification criteria for RA were consecutively enrolled. Patients with any other rheumatic disease were excluded. Our study used ATP III Criteria (Abdominal obesity: Men<102 cm Women<88 cm; Triglyceride level  $\geq$ 150 mg/dL; HDL:<40 mg/dL for men<50 mg/dL for women; Blood pressure  $\geq$ 130/ $\geq$ 85 mmHg; Fasting glucose  $\geq$ 100 mg/dL) to classify patients with MetS.

**Results:** There were no differences in any independent variable of these patients. However there was a higher prevalence of high blood pressure in controls than RA patients (See Table 1).

A. Demographic Characteristics			
Variable	RA n=299	Control n=125	P
Age (years), mean $\pm$ SD	55.3 $\pm$ 13.2	53.5 $\pm$ 7	0.282
Women, n (%)	287 (96)	112 (90)	0.340
Weight, mean $\pm$ SD	68.2 $\pm$ 13.5	73.1 $\pm$ 15.0	0.055
Height (meters), mean $\pm$ SD	1.5 $\pm$ 0	1.3 $\pm$ 0.07	0.001
BMI, mean $\pm$ SD	25.5 $\pm$ 4.9	28.6 $\pm$ 6	0.859
Waist circumference (cm), mean $\pm$ SD	95.8 $\pm$ 8.8	96.2 $\pm$ 4.4	0.432
Type 2 diabetes mellitus, n (%)	47 (16)	20 (16)	0.369
Hypertension, n (%)	114 (38)	35 (28)	0.288
Dyslipidemia, n (%)	108 (36)	20 (16)	0.023
Active smokers, n (%)	18 (6)	15 (12)	0.482

B. Metabolic Syndrome, ATP III Criteria				
Variable	RA n=299	Control n=125	P	OR (I.C. 95%)
Metabolic syndrome, n (%)	100 (33)	46 (37)	0.570	0.85 (0.55-1.33)
Large waist circumference, n (%)	250 (77)	95 (74)	0.695	1.04 (0.66-1.65)
High triglyceride level, n (%)	198 (66)	40 (32)	0.417	1.29 (0.77-1.87)
Reduced high-density lipoprotein, n (%)	141 (47)	66 (53)	0.289	0.79 (0.52-1.21)
Increased blood pressure, n (%)	52 (17)	59 (48)	0.00001	6.31 (6.13-6.50)
Elevated fasting blood glucose, n (%)	85 (28)	30 (24)	0.425	1.20 (0.75-1.87)

Abstract AB1292 – Figure 1. Metabolic Syndrome among RA patients. A. Demographic Characteristics. B. Metabolic Syndrome by ATP III Criteria

**Conclusions:** There is no difference in the diagnosis of MetS in RA patients than control population. However, the role of the diagnosis of MetS in patients with RA represents an important task in the management of the disease in order to reduce its high cardiovascular risk.

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AB1293

### INCIDENCE OF SACROILIITIS IN INFLAMMATORY BOWEL DISEASE: A SINGLE-CENTRE STUDY FROM TIANJIN, CHINA

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**Background:** Time trend studies have shown a rising incidence and prevalence of inflammatory bowel diseases (IBD) in China. IBD is a complex disease, which can present with a large number of extraintestinal manifestations (EIMs), such as skin, eye and joint lesions. Among these EIMs, spinal involvement is often silent and do not correlate with IBD activity. So the prevalence of spinal involvement in IBD is poorly understood.

**Objectives:** To estimate the incidence of sacroiliitis and other extraintestinal complaints among patients with IBD in Tianjin Union Medical Centre.

**Methods:** From September 2017 to January 2018, for all patients who came to our hospital do endoscopic examination, we picked out patients who had a diagnosis of IBD (include ulcerative colitis, crohn's disease and colitis). All IBD patients who agreed to participate in the study completed a questionnaire. To investigate the incidence of spondyloarthritis, part of patients took screening test. Radiologic examination of pelvic to screen sacroiliitis, blood sample to test erythrocyte sedimentation(ESR), C-reactive protein(CRP) and human leukocyte antigen B27 (HLA-B<sub>27</sub>).

**Results:** 87 patients were enrolled; 93.1% had ulcerative colitis (UC), 1.1% had Crohn's disease (CD), and 5.7% had colitis. Among them, 54% were female. The mean age of onset in female and male was 47.6 years (range from 28 to 81) and 41.3 years (range from 18 to 72) respectively. Of the 87 patients, 56 patients (64.4%) had a history of articular pain, some of which were involved in axial articular (45/56), peripheral articular (2/56), and both axial and peripheral articular (9/56). 20 patients (22.98%) had history of enthesitis (e.g. plantar fasciitis, tendinitis achillea, anterior chest wall pain). 4 patients (4.6%) had history of skin impairment (e.g. nodule erythema, psoriasis, urticaria). 6 patients (6.9%) had history of ocular lesions (e.g. red eye, sore eye, epiphephsitis, cataract, vitreous opacity). 5 patients (5.7%) had oral ulcer. 3 patients had family history of gastrointestinal disease (2 bowel cancer, 1 UC). 25 patients conducted radiologic examination of pelvic (14 X-ray, 10 CTs and 1 MR). 8 patients (32%) revealed sacroiliitis. Among these 8 patients, 2 of them showed asymptomatic radiological involvement of sacroiliac joint. The texts of HLA-B<sub>27</sub> were performed in 29 patients (include patients who conducted radiologic examination of peivic), and all revealed negative results. 52 patients tested ESR and CRP, 30 patients showed higher results than normal bias.

**Conclusions:** This study displayed the incidence of sacroiliitis, among patients with IBD in our centre, it showed that patients with IBD have a higher incidence of sacroiliitis. In order to evaluate the patients comprehensively, IBD patients with articular pain should be evaluated by rheumatologist. Besides, among our patients with IBD, the occurrence of HLA-B<sub>27</sub> is low, and there were no correlation between IBD activity and articular symptoms or inflammatory indicators.

#### REFERENCE:

[1] inflammatory bowel disease, extraintestinal manifestations, sacroiliitis

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AB1294

### IMPACT OF WORK STATUS ON HEALTH-RELATED QUALITY OF LIFE (HRQOL) IN RA

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**Background:** Compared to the general population, RA patients (pts) are less likely to be employed and have lower HRQoL.<sup>1,2</sup> However, data on impact of work status on HRQoL in RA pts are limited.

**Objectives:** Evaluate association between work status and HRQoL in RA pts.

**Methods:** We analysed data from adult pts enrolled in a large sequential RA registry. Physicians assessed pt demographics, clinical characteristics, disease activity and laboratory parameters at baseline (BL) and then annually. Follow-up questionnaires to assess pt-reported outcomes were administered every 6 months and included HRQoL measures (12-Item Short-Form Health Survey physical and mental component summary [SF-12 PCS, MCS], EuroQoL-5 Dimension [EQ-5D]) and work status; higher score indicates better health for all 3 HRQoL measures. General linear mixed models with repeated measures were used for SF-12 analysis and finite mixture models for the EQ-5D analysis, controlling for BL covariates.

**Results:** A total of 974 RA pts with HRQoL information were included: 49.3% (n=480) 'employed for pay', 38.9% (n=379) 'employed not for pay' (retired,

homemaker or student), 11.8% (n=115) 'not employed or on disability'. Pts employed for pay were younger and had lower disease activity compared with other groups (table 1). Compared with pts 'not employed or on disability', pts employed had significantly higher PCS (mean [SE] 7.17 [0.82]; p<0.001), MCS (5.39 [0.80]; p<0.001) and EQ-5D (0.48 [0.16]; p=0.0031) scores. Similar results were observed comparing pts 'employed not for pay' to pts 'not employed or on disability' (Table 2).

**Abstract AB1294 – Table 1.** BL Characteristics by Work Status

Variable	Employed (n=480)	Employed not for pay* (n=379)	Not employed or disabled (n=115)
Age, years	52.66 (0.53)	66.21 (0.60)	56.69 (0.90)
RA disease duration, years	12.78 (0.46)	18.40 (0.67)	17.09 (1.05)
DAS28 (CRP)	2.94 (0.07)	3.51 (0.08)	4.03 (0.16)
Multidimensional HAQ	0.36 (0.02)	0.60 (0.03)	0.99 (0.05)
SDAI	13.34 (0.65)	18.83 (0.89)	24.75 (1.84)
TJC (28 joints)	7.47 (0.47)	11.67 (0.66)	14.64 (1.41)
Female, n (%)	395 (82.29)	310 (81.79)	106 (92.17)
Biologic DMARDs, n (%)	239 (49.79)	174 (45.91)	64 (55.65)
Seropositive, n (%)	230 (60.53)	211 (67.2)	59 (64.13)
Household income <\$50,000, n (%)	86 (18.90)	146 (45.63)	65 (60.74)
Household income ≥\$50,000, n (%)	369 (81.10)	174 (54.38)	42 (39.25)
Stopped work due to RA, n (%)	9 (1.88)	101 (27.15)	80 (70.18)

Data are mean (SE) unless otherwise indicated; \*Retired, homemaker or student

**Abstract AB1294 – Table 2.** Multivariate Analysis of Impact of Work Status on HRQoL

Effect	SF-12 PCS general linear model		SF-12 MCS general linear model		EQ-5D mixture model	
	Estimate (SE)	Pr > t	Estimate (SE)	Pr > t	Estimate (SE)	Pr > t
Employed for pay (vs not employed or disabled)	7.17 (0.82)	<0.0001	5.39 (0.80)	<0.0001	0.48 (0.16)	0.0031
Employed not for pay (vs not employed or disabled)	3.75 (0.82)	<0.0001	6.78 (0.81)	<0.0001	0.42 (0.16)	0.0104
Income <\$50,000/year (vs ≥\$50,000/year)	-1.04 (0.56)	0.0655	-2.56 (0.55)	<0.0001	-0.19 (0.12)	0.1084

Other covariates included in the model were age, sex, disease duration, disease activity, acute-phase reactant (CRP), BMI, serostatus and time points

**Conclusions:** Work status and household income in RA are independently associated with HRQoL. More studies are needed to evaluate impact of work on changes in HRQoL in RA pts.

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**Abstract AB1298 – Table 1.** Prevalence of rheumatic diseases distributed by city

	Men	Women	Bogotá	Medellín	Calí	B/quilla	B/manga	Cúcuta
Non-specific musculoskeletal disease	15,99%	16,50%	14,67%	14,64%	17,16%	21,88%	20,43%	26,15%
Osteoarthritis	11,13%	20,31%	17,98%	17,07%	11,06%	10,60%	14,22%	16,78%
Mechanical Low Back pain	8,58%	8,19%	10,15%	4,39%	5,23%	11,91%	3,82%	11,68%
Rheumatoid arthritis	0,95%	2,89%	2,60%	0,69%	2,22%	1,19%	0,80%	1,04%
Rheumatic Regional Pain Syndromes	0,96%	1,96%	2,67%	0,32%	0,10%	0,26%	0,23%	-
Fibromyalgia	0,05%	2,27%	1,29%	1,09%	1,41%	1,07%	0,44%	1,34%
Inflammatory Low Back Pain	1,08%	0,72%	1,29%	0,49%	0,47%	0,43%	-	0,83%
Gout	1,28%	0,05%	1,09%	-	-	-	0,27%	1,34%
Undifferentiated spondyloarthritis	0,42%	0,62%	0,82%	-	0,37%	0,38%	-	0,29%
Ankylosing spondylitis	0,96%	0,08%	0,08%	2,20%	0,47%	-	-	-
Undifferentiated arthritis	0,14%	0,46%	0,09%	0,56%	0,19%	0,48%	0,78%	1,97%
Systemic lupus erythematosus	-	0,41%	0,22%	0,29%	0,16%	0,36%	-	-
Sjogren's syndrome	0,04%	0,28%	0,24%	-	0,16%	0,23%	-	-
Systemic sclerosis	-	0,04%	0,04%	-	-	-	-	-

### AB1295 ASSOCIATION OF SHARED EPITOPE AND POOR PROGNOSTIC FACTORS IN RA

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**Background:** Strong genetic association has been reported between RA and human leukocyte antigen (HLA) regions, particularly HLA-DRB1 alleles with the shared epitope (SE). SE alleles are associated with seropositivity, erosions and higher disease activity (DA) in RA.

**Objectives:** To evaluate the association between SE alleles and the presence of multiple poor prognostic factors (PPFs) of seropositive (anti-citrullinated protein antibody [ACPA] and/or RF) and erosive RA; as well as changes in DA.

**Methods:** We analysed patients (pts) enrolled in a large sequential RA registry established in 2003; most had established RA and annual clinical evaluations. Pts with baseline (BL) data on SE status were included. A commercially available kit (Qiagen, USA) was used for HLA genotyping. HLA-DRB1 serotypes were assessed from DNA sequences using allele-specific polymerase chain reaction methods and categorised as pts with no, 1 or 2 SE alleles. Changes from BL were compared in pts with vs without SE alleles. The association of multiple PPFs and SE status was evaluated using multinomial logistic models. The association between change in DA and SE status was analysed using linear regression models with age, sex, disease duration (DD), co-morbidities and biologic DMARDs as covariates.

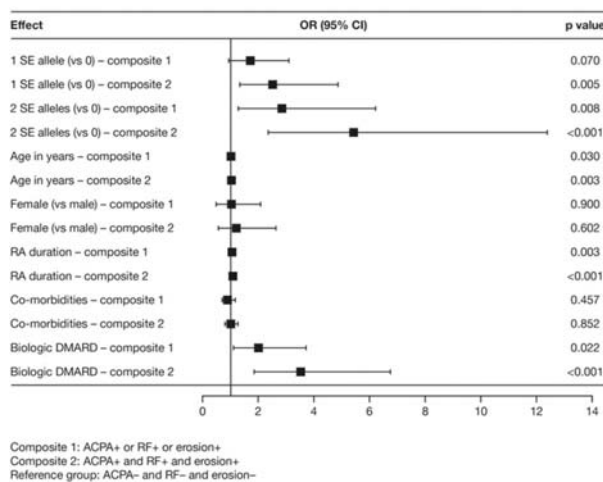
**Abstract AB1295 – Table 1.** Baseline Characteristics by SE status

	No SE alleles (n=241)	1 SE allele (n=275)	2 SE alleles (n=173)
Mean (SD) age, years	57.7 (13.6)	58 (13.9)	57.8 (13.6)
Female, n (%)	202 (83.8)	219 (79.6)	141 (81.5)
Mean (SD) RA duration, years	12.9 (12.1)	17 (13.3)	16.1 (12.2)
Biologic DMARDs, n (%)	83 (34.4)	145 (52.7)	83 (48.0)
ACPA+, n (%)	118 (49.0)	196 (71.3)	137 (79.2)
Erosions, n (%)	116 (48.1)	168 (61.1)	114 (65.9)
RF+, n (%)	120 (49.8)	195 (70.9)	128 (74.0)
Double positive, n (%)	100 (41.5)	174 (63.3)	121 (69.9)
DAS28 (CRP), mean (SD)	3.8 (1.5)	4.2 (1.6)	4.3 (1.6)

**Abstract AB1295 – Table 2.** Multivariate Analysis of Impact of SE Status on Change in DA

	DAS28 (CRP) model		CDAI model		SDAI model	
	Coefficient	p value	Coefficient	p value	Coefficient	p value
1 or 2 SE alleles (vs no SE)	0.24	0.031	2.71	0.027	3.25	0.013
Baseline DA	-0.41	<0.001	-0.46	<0.001	-0.48	<0.001
Age, years	0.01	0.271	0.04	0.367	0.04	0.406
Female (vs male)	0.11	0.435	2.52	0.099	2.12	0.198
No. of co-morbidities	0.11	0.003	1.25	0.003	1.42	0.002
Biologic DMARD (yes vs no)	0.41	<0.001	3.79	0.002	4.09	0.001
Adjusted R-square	0.23		0.27		0.29	

**Results:** Of 689 RA pts included, no, 1 and 2 SE alleles were reported in 241 (35.0%), 275 (40.0%) and 173 (25.1%) pts, respectively. At BL, pts with SE alleles (vs no SE) were more likely to have PPFs, and had longer DD and higher DA (table 1). The odds ratio (OR) for seropositive erosive RA in pts with 2 and 1 SE alleles (vs no SE) was 5.44 (95% CI 2.39, 12.39) and 2.87 (1.32, 6.23; Fig), respectively. The OR for double seropositivity in pts with 2 and 1 SE alleles (vs no SE) was 4.27 (95% CI 2.51, 7.28) and 2.56 (1.66, 3.94), respectively. A total of 551 pts had DA measures at BL and 1 year follow-up. After controlling for BL covariates, pts with SE (vs no SE) had an average increase in DAS28 (CRP) of 0.24 (p=0.031), CDAI of 2.71 (p=0.027) and SDAI of 3.25 (p=0.013; Table 2).

**Abstract AB1295 – Figure 1.** Multinomial Model for Multiple PPFs (Seropositive and Erosions)

**Conclusions:** Pts with (vs without) SE alleles are more likely to have multiple PPFs; pts with 2 SE alleles are 5 times more likely to be seropositive with erosive RA and 4 times more likely to be double positive. Pts with (vs without) SE alleles also experienced an increase in DA over time with standard-of-care treatment.

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**AB1296 GENETIC POLIMORPHISMS AND METHOTREXATE SAFETY IN RHEUMATOID ARTHRITIS**

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**Background:** Methotrexate (MTX) is the DMARD of choice in the treatment of rheumatoid arthritis (RA). Despite an acceptable efficacy, its use is limited by side effects. The most known adverse events (AE) are gastrointestinal, hepatic, and haematological.

**Objectives:** To study the effect of clinical characteristics and of different genetic single nucleotide polymorphisms (SNPs) related to the transport and metabolic pathways of MTX, on the toxicity of this compound, in a cohort of RA patients treated with MTX in monotherapy.

**Methods:** Observational study. Toxicity was defined as the occurrence of AE, global and of haematological, hepatic, and gastrointestinal nature. Factors under study: SNPs of transport (ABCB1 C3435T), glutamation (GGH T16C and FPGS G2782A), transmethylation (MTHFR C677T and MTHFR A1298C) and adenosine (AMPD1 C34T, ADA A534G, ITPA C94A). The association between SNPs and MTX toxicity was analysed using logistic regression models, assessing allele independence (Hardy-Weinberg equilibrium) and interaction with sex. Different models of inheritance of SNPs were analysed. The models were adjusted by the characteristics of the patient, of disease and of treatment. The haplotypes of the MTHFR SNPs (C677T and A1298C) were also analysed.

**Results:** Bivariate analysis showed that AE, globally considered, are related to lower age at diagnosis (OR=0.98), female sex (OR=1.95), disease activity (OR=1.38), extra-articular manifestations (OR=1.84) and comorbidity (OR=1.14). For the SNPs, the A/G genotype of the ADA A534G decreases the probability of AE (OR=0.55); the G/G of the ADA A534G increases the hepatic AE (OR=10.1) and the genotypes C/T and T/T of the ABCB1 C3435T decrease the risk of haematological AE.

According to the adjusted analysis, the probability of global AE increased with the C/T genotypes of MTHFR C677T (OR=1.85) and C/C of GGH T16C (OR=2.53) and decreased with the A/G of ADA A534G (OR=0.49). Gastrointestinal AEs were less frequent in patients with A/G genotype of ADA A534G (OR=0.49) and in men with G/A of FPGS\_2782GAc (OR=0.29). The G/G genotype of the SNP ADA\_534AG was associated with a significant increase in hepatic AE (OR=12.7), which was also observed in men with the MTHFR A1298C (OR=8.34). The T allele of the ABCB1 C3435T decreases the probability of haematological AE, especially in women (OR=0.06). All the effects were independent of the characteristics of patient, disease and treatment. The C/C haplotype of the combination MTHFR C677T and MTHFR A1298C increases the probability of global (OR=4.35) and hepatic AE (OR=11.9) in men, but not in women.

**Conclusions:** SNPs related to the transport and metabolism of MTX are associated with liver toxicity of MTX.

**Disclosure of Interest:** None declared

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**AB1297 HIGH PREVALENCE OF SERONEGATIVE RHEUMATOID ARTHRITIS IN A MAYA-YUCATECO INDIGENOUS POPULATION: A COHORT COMMUNITY-BASED STUDY**

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**Background:** Eighty percent of people living with rheumatoid arthritis (RA) are seropositive. Recent studies show that seronegative RA is associated with a more aggressive clinical presentation; however, this association has not been studied in indigenous populations.

**Objectives:** To compare the clinical and radiographic characteristics, functioning and quality of life in a group of Maya-Yucateco indigenous patients with RA, based on their seropositivity Rheumatoid Factor (RF- IgM).

**Methods:** A community-based cohort was formed in 2014 with the aim of detecting and performing a community intervention in a Mayan Municipality in Mexico. Patients who fulfilled ACR/EULAR criteria 1987/2010 for RA were included and rheumatologists evaluated them every 3 months. All evaluations were conducted in the community with the support of trained translators and included: 1. Clinical examinations. 2. Laboratories (i.e. RF, ESR, CRP). 3. Radiographic evaluations. 4. Functioning (HAQ-DI) and quality of life (EQ5D-3L) assessments. 5.

Pharmacological treatment. 6. Non-pharmacological treatment: individual and group exercises.

A quantitative comparative analysis was conducted by dividing the cohort in seropositive and seronegative and comparing all variables measured using a  $\chi^2$  test, Student's *t*-test or Mann-Whitney *U* test, as well as Kruskal-Wallis test for the non-parametric variables.

**Results:** Twenty eight of 430 participants were diagnosed with RA (1.8%, CI95%: 1.2 to 2.6), for an incidence 0.72% (CI95% 0.3 to 1.2) in 4 years. Seventy-eight% were women, the mean age was 53.9 years (standard deviation (SD)=13.2) and the level of education was on average 2 years (0–5.5).

We observed high prevalence of family history of rheumatic disease (75%), exposure to woodstove (96.1%), and a Chikungunya virus infection (10.7%) and RF- (65.3%).

The treatment given was methotrexate in 64.2% as monotherapy, and 21.4% in combination therapy. NSAIDs were prescribed in 98.2%. Prednisone was prescribed at low doses (<7.5 mg/day) in 14.2%.

The level of pain/discomfort assessed through EQ-5D3L dimension was significantly higher in the seropositive group in comparison with the seronegative group. No other differences were detected between these groups (see Table).

**Abstract AB1297 – Table 1**

Variable	Seronegative (n=17) n(%)	Seropositive (n=9) n (%)	p value
Family history of RD*	16 (94.1)	5 (55.5)	0.01
Work	16 (94.1)	6 (66.6)	0.06
DAS28, median (IQR)	3.7 (2.9–3.9)	3.9 (3.3–4.4)	-
Van der Heijde- modified Sharp score, mean (SD)	93.4 (13.0)	110.2 (7.8)	-
<b>EQ5D-3L</b>			
<b>Pain/discomfort*</b>			0.04
No problems	2 (12.5)	1 (11.1)	
Some problems	11 (68.7)	2 (22.2)	
Extreme problems	3 (18.7)	6 (66.6)	
<b>Disability (HAQ&gt;0.8)</b>	3 (17.6)	4 (44.4)	0.1

\*ps<0.04

RD rheumatic diseases; DAS-28 disease activity score; HAQ Health Assement Questionnaire.

**Conclusions:** The prevalence with negative RF is high in the community studied, however, no differences were observed in the variables studied, except in pain.

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**AB1298 PREVALENCE OF RHEUMATIC DISEASES IN COLOMBIA BY CITY**

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**Background:** Knowledge of the prevalence of rheumatic diseases allows us to design public health strategies for their comprehensive care and reduction of the costs derived from the potential complications of these diseases.

**Objectives:** To describe and compare the prevalence of rheumatic disease between six cities from Colombia.

**Methods:** The study was developed according the COPCORD epidemiological strategy designed for the identification, prevention and control of rheumatic diseases in developing countries.

A cross-sectional analytical study including individuals older than 18 years was designed with a calculated sample size of 6528 people (2336 from Bogotá, 1220 from Medellín and Cali each, 746 from Barranquilla, from Bucaramanga and Cúcuta each one). Prevalence of each rheumatic disease was compared between the evaluated cities from Colombia.

**Results:** A total of 6693 individuals from six cities of Colombia were evaluated. The average age was 46,40±18,35 and 4283 (64%) individuals were women. The cities with the highest frequency of positive COPCORD population were Bogotá 36,6% (n=1813), Cali 19,1% (n=945) and Medellín 15,9% (n=789). **Abstract AB1298 – Figure 1**

The majority of musculoskeletal pain manifested by the population correspond to non-specific muscular discomfort (MMNE). Osteoarthritis (OA) is the most prevalent rheumatic disease (10,81%, 95% CI, 9,68–12,06%). Mechanical low back pain was the most frequent disease in Barranquilla, with a prevalence of 11,91%, mainly in men 15,9% (95% CI, 11,24–21,92%). Regarding to rheumatoid arthritis (RA) it was more prevalent in women, between 40 and 59 years. It was found to

be more prevalent in Bogotá (2,8%, 95% CI, 1,8%–4,1%), Cali (4,2%, 95% CI, 2,4–7,3%) and Barranquilla (1,5%, 95% CI, 0,65–3,23%). **Table 1.**



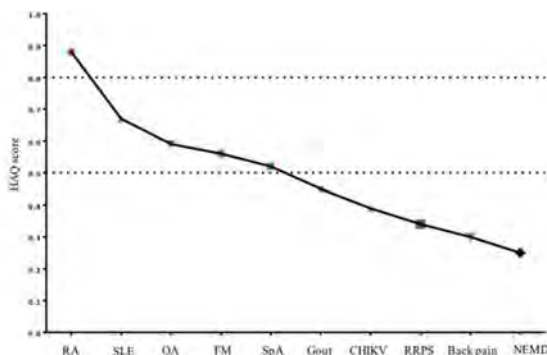
**Abstract AB1298 – Figure 1.** Diagram of cities surveyed as COPCORD\* positive

**COPCORD\*:** Community Oriented Program for Control of Rheumatic Diseases  
**Conclusions:** Prevalence of rheumatic diseases is higher in the cities of Bogotá, Cali and Medellín. In Bogotá, Cali and Barranquilla, RA was more prevalent. Low back pain was found to be more prevalent in Barranquilla. The hypothesis is that ethnic diversity of Colombia could explain the difference in prevalence of the rheumatic disease among separate regions.  
**Disclosure of Interest:** None declared  
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**AB1299 FUNCTIONAL CAPACITY MEASURED BY HAQ IN PATIENTS WITH RHEUMATIC DISEASES IN COLOMBIA**

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**Background:** Functional capacity is an important indicator of quality of life that is affected in different pathologies and is susceptible to intervention in early stages once it is recognised. In rheumatic diseases, functional limitation has a great impact that is evidenced by multiple degrees of long-term disability.  
**Objectives:** To evaluate the functional capacity in different rheumatic diseases by HAQ (Health Assessment Questionnaire) instrument.  
**Methods:** In the context of the prevalence study of rheumatic disease in Colombia, the assessment of functional capacity was measured by using the HAQ score, where functional limitation is scored in a range from 0 to 3 points according to the severity of limitation. The major functional limitation is scored 3 and not limitation 0.  
 A total of 4020 individuals answered the questionnaire.  
**Results:** Patients with rheumatic diseases (n=2274) reported a greater degree of limitation compared with disease-free people (n=1104) or non-rheumatic patients (n=642) (p<0.001). Especially patients with rheumatoid arthritis (RA) had the worst score (0.88±0,72) compared to 0.06±0,22 and 0.01±0,14 of the population with non-rheumatic and healthy population, respectively (p<0.001). The HAQ score in the remaining diseases was 0,67 (SD ±0,62) for systemic lupus erythematosus (SLE), followed by patients with osteoarthritis (OA) 0,59 (SD ±0,58), fibromyalgia (FM) 0,56 (SD ±0,57) and spondylarthritis (SpA) 0,52 (SD ±0,43).  
**Abstract AB1299 – Figure 1**



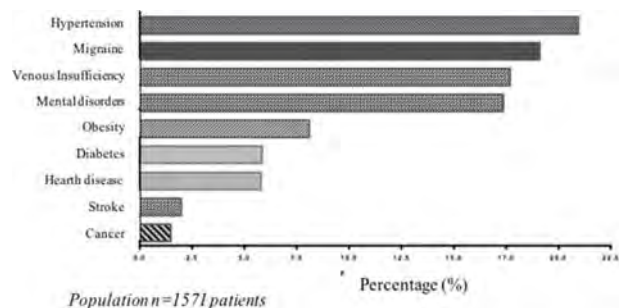
**Abstract AB1299 – Figure 1.** Functional capacity of patients with rheumatic diseases

Functional capacity evaluated by HAQ, the points represent the mean of the instrument. \* RA: Rheumatoid Arthritis; SLE: Systemic Lupus Erythematosus; OA: Osteoarthritis; FM: Fibromyalgia; SpA: Spondylarthritis; CHIKV: Chikungunya fever; RRPS: Rheumatic Regional Pain Syndromes (Rotator cuff tendinopathy, shoulder bicipital tendinopathy, lateral and medial epicondylalgia, Quervain's tendinopathy, carpal tunnel syndrome, Dupuytren's contracture, trochanteric syndrome, anserine bursitis, achilles tendonopathy, plantar talgalgia); NEMD: non-specific musculoskeletal disease.  
**Conclusions:** In comparison with disease-free population and non-rheumatic patients, the rheumatic patients had a lower functional capacity measured by HAQ. Patients with RA had more disability followed by patients with SLE and OA.  
**Disclosure of Interest:** None declared  
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**AB1300 COMORBIDITIES IN PATIENTS WITH RHEUMATIC DISEASES IN COLOMBIA**

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**Background:** Patients with systemic autoimmune conditions often develop concomitant disease contributing to a higher mortality than in the general population. An early diagnosis and treatment is fundamental to improve the life expectancy of this population.  
**Objectives:** The objective of this study was to describe the frequency of comorbidities in patients with rheumatic diseases.  
**Methods:** Based on data from the population studied under the COPCORD strategy, in the prevalence of rheumatic disease in Colombia, the frequency of non-rheumatic diseases in patients with rheumatic diseases was described in 6 cities of Colombia (Bogotá, Medellín, Cali, Barranquilla, Bucaramanga and Cúcuta).  
**Results:** From a total of 4020 individuals, 2274 rheumatic patients were identified. Sixty nine percent of the Colombian patients with rheumatic disease (n=1571) had some comorbidity. The most frequent was hypertension (HBP) in 20,95% (n=330), followed by migraine 19,11% (n=300) and venous insufficiency 17,69% (n=278). Seventeen percent had any mental disorders, of which anxiety and depression were the most common (n=273). Other comorbidities like obesity (8,1%), diabetes (5,85%), heart disease (5,79%) and cerebrovascular disease (1,99%) were less common among rheumatic patients. The frequency of cancer was low 1.48% (n=23).  
**Abstract AB1300 – Figure 1**



**Abstract AB1300 – Figure 1.** Most frequent comorbidities in rheumatic patients

**Conclusions:** Hypertension is the most common comorbidity in patients with rheumatic diseases in Colombia. Screening and diagnosis in early stages of HBP is important, since it is the main modifiable cardiovascular risk factor. The goals of pharmacological and non-pharmacological treatment are essential to reduce the risk of coronary heart disease, stroke and end-stage renal disease. Additionally, migraine is the second most frequent disease that affects the patient's quality of life. And venous insufficiency should be taken into account by primary care physicians in order to assure a complete health care assessment.  
**Disclosure of Interest:** None declared  
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AB1301

### CARDIOVASCULAR RISK AGE AND VASCULAR AGE ESTIMATIONS IN PREDICTING CARDIOVASCULAR EVENTS IN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Rheumatoid arthritis (RA) patients are at high risk of cardiovascular disease (CVD). Risk age estimations are recommended as adjuncts to assessment of absolute 10 year risk of fatal CVD events. Two risk age models based on the Systematic Coronary Risk Evaluation (SCORE) algorithm have been developed; the cardiovascular risk age and the vascular age.

**Objectives:** We aimed to compare the discriminative ability of cardiovascular risk age and vascular age among RA patients and in subgroups of RA patients.

**Methods:** Patients with RA were included from an international consortium, aged 30–70 years at baseline. Those with prior CVD, diabetes and/or users of lipid-lowering and/or antihypertensive therapy at baseline were excluded. Cardiovascular risk age was estimated based on chronologic age, smoking status, total cholesterol and systolic blood pressure at baseline. Vascular age was derived from the 10 year risk of CVD according to the SCORE algorithm, with or without high density lipoprotein cholesterol, using the equations for low and high risk countries. Performance of each risk age model in predicting CVD events was assessed by c-statistics.

**Results:** Among 1867 patients included, 74% were female, median (inter-quartile range) age and disease duration were 52.0 (44.0, 59.9) and 0.6 (0.1, 6.4) years, 72.5% were rheumatoid factor positive, 24.7% were using glucocorticoids and 10.3% were using biologics at baseline. Overall, 144 CVD events occurred. Median follow-up time was 5.0 (2.6, 9.3) years. C-indices across risk models ranged from 0.71 to 0.73 with standard errors of 0.03. Across prediction models, the lowest observed concordance was found among women and in glucocorticoid users and in those with new-onset disease ( $\leq 1$  year). Additional analyses including RA patients on cardio preventive therapy yielded slightly lower c-indices. Since SCORE was developed for use in Europe, we performed analyses on European RA patients, which yielded similar results. Certain characteristics were associated with low concordance, but standard errors were high (data not shown).

**Conclusions:** The cardiovascular risk age and vascular age models have comparable performance in predicting CVD in RA patients. The influence of RA disease characteristics on the predictive ability of these prediction models remains inconclusive.

**Disclosure of Interest:** None declared

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AB1302

### RESULTS FROM THE PROSPECTIVE NATIONWIDE NORWEGIAN PREGNANCY QUALITYREGISTER REVNATUS

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**Background:** To establish a register to determine disease activity, pregnancy surveillance and safety of medication during pregnancy and lactation, and monitoring this group as a quality register.

**Methods:** The Norwegian pregnancy register RevNatus is designed as a nationwide, web-based longitudinal observational cohort study with 17 participating centres. Pregnant patients or patients planning a pregnancy with confirmed diagnosis of inflammatory rheumatic disease are eligible to be enrolled. The women are preferred enrolled before conception and with registrations each trimester, 6 weeks, 6 and 12 months postpartum. At baseline diagnosis, sociodemographic parameters, disease activity, anti-rheumatic medication, obstetric history, comorbidities and antibody status are reported. The register has been approved by the Norwegian Data Inspectorate and is run by The Norwegian National Advisory Unit on Pregnancy and Rheumatic Diseases.

**Results:** From February 2016 – January 2018 597 women were included in RevNatus, mean age at inclusion was 30.8 (17–44). Among these patients 4% had only completed primary school, 24% secondary education and 72% had completed a university education. At inclusion 4% were smoking (general population 11%) and 6% used snuff (general population 12%). At registration 6 weeks after delivery 3% were smoking and 2% used snuff. Altogether 346 women were registered with a control 6 weeks after delivery. Of these, 31 women experienced spontaneous abortion and one therapeutic abortion. Among the remaining, 314 had live born infants including 7 twin births and one triplet birth. Among the women with registration 6 week postpartum, 260 (75%) women were diagnosed with chronic inflammatory arthritis including rheumatoid arthritis, spondylarthritis, juvenile idiopathic arthritis and unspecified arthritis. Correspondingly, 79 (23%) women were registered with inflammatory connective tissue disease (SLE, MCTD, poly-dermato myositis, systemic sclerosis), 3 with vasculitic disease (Takayasu's arteritis, Mb Behcet), and 5 with primary anti-phospholipid antibody (APS) syndrome. Mean disease duration (SD) for all diagnoses was 6.5 years.<sup>6,8</sup> Corresponding, mean disease duration in women with RA was 6.7 (4.1) years, in women with SLE 9.4 (6.1) years and in women with JIA 20.7 (7.3) years. Mean gestational age at birth for all diagnoses was 38.7 (2.5) weeks. The gestational age was lowest in SLE women 37.9 (2.59) weeks. Mean gestational week for spontaneous abortion was at 11 weeks. Mean birthweight (SD) was 3268<sup>758,7</sup> gram in offspring of women with RA and 3133 gram in women with SLE. Overall 71 (22%) women had caesarean deliveries, 14% were acute and 9% planned caesarean deliveries. Six weeks postpartum 258 women (82,7%) were breastfeeding their babies.

**Conclusions:** The Norwegian pregnancy register RevNatus was established to study the course and outcomes of pregnancies in women with inflammatory rheumatic diseases as well as increased knowledge on the use and safety of treatments during pregnancy and lactation. The results of the register gives data to monitor the quality of the treatment for this group of patients.

**Disclosure of Interest:** None declared

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AB1303

### ANALYSIS OF SYMPTOMS IN VERY EARLY PHASE IN PATIENTS WITH ADULT-ONSET STILL'S DISEASE

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**Background:** The initial symptoms of Adult-onset Still Disease (AOSD) are non-specific and confusing with those of common cold, which can lead to the delay of diagnosis and treatment.

**Objectives:** To clarify characteristic features in AOSD in very early phase and to find the key symptoms and markers to an earlier diagnosis and treatment.

**Methods:** We retrospectively reviewed consecutive AOSD patients in our hospital from April 2012 to July 2017. Symptoms and laboratory data before treatment were collected from their charts and analysed.

**Results:** A total of 62 patients were enrolled. The mean age at diagnosis was 45.9 and female was 81%. The duration from the first symptoms to the first visit to a medical facility was 18.7 days, from the first visit to the first blood test was 5.8 days, from the first blood test to the fulfilment of Yamaguchi's Criteria was 11.0 days, and from the fulfilment of Yamaguchi's Criteria to the treatment was 22.2 days. During the course of developing the disease, fever was found in all patients, skin lesion in 91.9%, arthralgia in 87.1%, sore throat in 66.1%. Laboratory and imaging tests demonstrated liver enzyme elevation in 82.2%, white blood cell count (WBC) increase in 80.6%, lymphadenopathy/splenomegaly in 72.6%, negative RF and ANA in 56.5%, ferritin elevation in 82.3%. Laboratory tests before treatment demonstrated that the mean WBC count 15272.3/ $\mu$ L, AST 101.8 U/L, CRP 15.1 mg/dl, and ferritin 10103.1 ng/ml. Patients who presented with sore throat as the first symptom fulfilled Yamaguchi's Criteria in 13.6 days after the onset, which was shorter than patients with any other symptoms (fever, 24.0 days; arthralgia, 45.7 days; skin lesion, 31.5 days). Before treatment, patients with sore throat as the first symptom showed highest AST of 139.6 U/L (fever, 95.3 U/L; arthralgia, 100.7 U/L; skin lesion, 71.6 U/L) and highest ferritin of 19791.8 ng/ml (fever, 9508.2 ng/ml; arthralgia, 13071.5 ng/ml; skin lesion, 8438.1 ng/ml). However, the duration from the Yamaguchi's Criteria fulfilment to treatment initiation in patients with sore throat as the first symptom was 38.5 days, which was no less

**Abstract AB1307 – Table 1.** Prevalence and direct medical costs of AIRDs in South Korea

Category of diseases	Number of patients (N/100,000)					Change of prevalence between 2012 and 2016 (%)	Total direct medical cost (USD) in 2016	Direct medical cost per person (USD) in 2016
	2012	2013	2014	2015	2016			
Seropositive RA	70 276 (139.6)	76 441 (151.2)	83 322 (164.2)	90 280 (177.2)	96 330 (188.5)	35.0	107,255,471.1	1,113.4
SLE	15 287 (30.4)	16 304 (32.2)	17 484 (34.4)	18 245 (35.8)	19 441 (38.0)	25.3	27,694,324.4	1,424.5
AS	20 132 (40.0)	22 362 (44.2)	24 794 (48.8)	27 311 (53.6)	30 006 (58.7)	46.8	78,133,501.3	2,603.9
Polymyositis	763 (1.5)	810 (1.6)	896 (1.8)	935 (1.8)	1036 (2.0)	33.7	2,553,296.9	2,464.6
Dermatomyositis	935 (1.9)	1012 (2.0)	1089 (2.1)	1159 (2.3)	1275 (2.5)	34.3	3,369,996.6	2,643.1
Systemic sclerosis	2648 (5.3)	2873 (5.7)	3126 (6.2)	3271 (6.4)	3606 (7.1)	34.1	5,191,029.1	1,439.6
Sjögren syndrome	6727 (13.4)	7687 (15.2)	8756 (17.2)	10 255 (20.1)	12 018 (23.5)	76.0	7,730,515.4	643.2
Psoriatic arthritis	655 (1.3)	783 (1.5)	1005 (2.0)	1256 (2.5)	1457 (2.9)	119.1	5,250,520	3,603.7
Polymyalgia rheumatica	1133 (2.3)	1370 (2.7)	1582 (3.1)	1770 (3.5)	2112 (4.1)	83.6	1,731,316	819.8
Behçet disease	13 254 (26.3)	13 754 (27.2)	14 444 (28.5)	14 562 (28.6)	14 943 (29.2)	11.1	11,026,314	737.9
Wegener granulomatosis	260 (0.5)	305 (0.6)	338 (0.7)	364 (0.7)	376 (0.7)	42.4	1,061,500	2,823.1
Microscopic polyangiitis	114 (0.2)	147 (0.3)	204 (0.4)	259 (0.5)	323 (0.6)	179.1	2,010,130	6,223.3

than that in patients with the other symptoms (fever, 15.4 days; arthralgia, 31.0 days; skin lesion, 27.0 days).

**Conclusions:** Although symptoms of AOSD developed rapidly with symptoms of sore throat, fever, liver enzyme elevation and ferritin elevation, the diagnosis was frequently delayed. Our study suggests that the delayed diagnosis can be attributed in part to non-assessment of the disease. Paying attention to the combination of these symptoms can lead to an earlier diagnosis.

**Disclosure of Interest:** None declared

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**AB1304**

### ASSOCIATION BETWEEN CONCOMITANT USE OF SULFASALAZINE AND DECREASE OF ANTI-CCP ANTIBODY LEVELS IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH TUMOUR NECROSIS FACTOR INHIBITOR OR ABATACEPT

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**Background:** Anti-citrullinated protein antibodies (anti-CCP) has been found to be associated with not only the development of rheumatoid arthritis (RA), but also treatment response of RA. A recent study revealed that biologics targeting adaptive immunity, such as abatacept and rituximab, significantly decreased anti-CCP levels.<sup>[1]</sup> However, anti-cytokine therapy, such as tumour necrosis factor inhibitor (TNFi), and methotrexate (MTX) did not significantly lower anti-CCP levels. However, whether concomitant use of sulfasalazine (SSZ) is associated with a decrease of anti-CCP levels in RA patients treated with TNFi or abatacept is unknown.

**Objectives:** To investigate the influence of sulfasalazine on the decrease of anti-CCP IgG levels among RA patients treated with TNFi or abatacept.

**Methods:** After exclusion of those whose baseline anti-CCP levels (CCP0) were above the level that could be accurately measured, we enrolled biologic-naïve, anti-CCP-positive RA patients who initiated treatment with TNFi (n=76), including etanercept (n=20), adalimumab (n=40), and golimumab (n=16), or abatacept (n=23). We followed anti-CCP levels (CCP1) 12 months after the initiation of biologics. A decrease of anti-CCP levels after therapy was identified if CCP1 minus CCP0 was less than 0. A multivariable logistic regression analysis was used to examine the influence of age, sex, biologic agents, disease duration, MTX, SSZ, hydroxychloroquine (HCQ), and leflunomide (LEF) on the risk of anti-CCP decrease, as shown by odds ratios (ORs) with 95% confidence intervals (CIs).

**Results:** Sixty-one (80.3%) of the 76 TNFi users and 18 of the 23 abatacept users were female (p=0.834). The mean ±SD age was 49.8±15.2 years and 56.0±12.4 years for TNFi users and abatacept users respectively (p=0.079). The mean ±SD disease duration was not different between TNFi users and abatacept users (4.7 ±5.1 vs. 6.7±4.9, p=0.098). Thirty-eight (50.0%) of 76 TNFi users and 7 (30.4%) of 23 abatacept users concomitantly used SSZ (p=0.099). Of the 74 TNFi users and 23 abatacept users, 59 (77.6%) and 14 (60.9%) had a decrease of anti-CCP levels (p=0.110). Using multivariable logistic regression analysis to examine factors associated with a decrease of the anti-CCP level after 12 months, we found that only concomitant use of SSZ had a significant correlation (OR, 3.54; 95% CI, 1.06–11.89; p=0.041). In subgroup analysis, this positive correlation remained consistently significant in the TNFi group (OR, 5.19; 95% CI, 1.16–23.29; p=0.031), but not in the abatacept group.

**Abstract AB1304 – Table 1**

	Univariate		Multivariable	
	OR(95% CI)	P value	OR(95% CI)	P value
Concomitant DMARDs				
SSZ	2.95 (1.11–7.86)	0.031	3.54 (1.06–11.89)	0.041
MTX	2.23 (0.85–5.85)	0.104	2.13 (0.58–7.77)	0.254
LEF	0.86 (0.29–2.53)	0.787	0.79 (0.22–2.93)	0.728
HCQ	1.55 (0.55–4.41)	0.409	0.64 (0.15–2.76)	0.546

**Conclusions:** In RA patients who initiated treatment with TNFi or abatacept, concomitant use of SSZ was associated with a decrease of anti-CCP levels, especially among TNFi users.

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**Disclosure of Interest:** None declared

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**AB1305**

### RISK OF AUTOIMMUNE RHEUMATIC DISEASES IN PATIENTS WITH PALINDROMIC RHEUMATISM: A NATIONWIDE, POPULATION-BASED, COHORT STUDY

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**Background:** Although the association between palindromic rheumatism (PR) and rheumatoid arthritis (RA) development has been widely reported, no research has estimated the magnitude of the risk of progression of PR to RA or to other autoimmune rheumatic diseases, such as systemic lupus erythematosus (SLE), systemic sclerosis (SSc), Sjögren's syndrome (SS), dermatomyositis (DM) and polymyositis (PM).

**Objectives:** This study aimed to examine the relative risk of development of RA, SLE, SSc, SS, DM, or PM among patients with PR compared with that in non-PR individuals using a nationwide, population-based, administrative dataset.

**Methods:** The study utilised 2003–2013 claims data from the Taiwanese National Health Insurance Research Database. We identified 4421 cases of PR from 2007 to 2012 and randomly chose 44 210 non-PR individuals who matched (1:10) for age, sex and the year of index date without prior history of RA, SLE, SSc, SS, DM, or PM. After adjusting for age, sex, and the Charlson comorbidity index, we calculated the hazard ratios (HRs) with 95% confidence intervals (CIs) using the Cox proportional hazard model to quantify the risk of RA, SLE, SS, DM and PM in PR patients compared with that in matched non-PR individuals.

**Results:** The mean age ±SD was 46±15 years, and 70.4% of the study subjects were female. The proportion of patients with one or more CCI was higher in the PR group than in the non-PR group (33.0% vs. 14.8%, p<0.001). Among the 4421 patients with PR, 569 (12.87%) developed RA, 269 (6.08%) developed SS, 113 (2.56%) developed SLE, 5 (0.11%) developed SSc, 8 (0.18%) developed PM, and 1 (0.02%) developed DM. After adjusting for potential confounders, the patients

with PR had an increased risk of RA (HR, 118.76; 95% CI, 89.81–157.04), SS (HR, 59.57; 95% CI, 43.87–80.88), SLE (HR, 51.56; 95% CI, 32.96–80.66) PM (HR, 57.38; 95% CI, 6.90–476.83), and SSc (HR, 13.42; 95% CI, 3.79–47.55) but not of DM (HR, 3.44; 95% CI, 0.34–34.59).

**Conclusions:** Patients with PR had an increased risk of developing RA, SS, SLE, PM, and SSc.

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AB1306

#### EPIDEMIOLOGY OF ACUTE ANTERIOR UVEITIS, PSORIASIS, INFLAMMATORY BOWEL DISEASE, PALINDROMIC RHEUMATISM AND SJOGREN'S SYNDROME IN TREATED ANKYLOSING SPONDYLITIS PATIENTS IN TAIWAN

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**Background:** The population-based epidemiology of extra-articular manifestations of ankylosing spondylitis (AS), including acute anterior uveitis (AAU), psoriasis (PsO), inflammatory bowel disease (IBD) in Taiwan had not been investigated. Whether or not the incidences of palindromic rheumatism (PR) and Sjogren's syndrome (SS) are higher than non-AS individuals is also unknown.

**Objectives:** This study aimed to investigate the incidences of AAU, PsO, IBD, PR, and SS in a population-based AS cohort compared with a matched non-AS cohort in Taiwan.

**Methods:** Using 2003–2012 claims data from the Taiwanese National Health Insurance Research Database, we firstly identified 30,900 AS patients newly diagnosed from 2006 to 2012 who received at least 3 courses of AS-related therapy (i.e., non-steroidal anti-inflammatory drugs, methotrexate, salazopyrine or corticosteroid) and defined the first date of AS diagnosis as the index date of the AS cohort. Then we randomly selected 3 09 000 non-AS individuals matching (1:10) AS cases for age, sex and the year of the index date as the comparison cohort and defined the first ambulatory visit date of the index year as the index date of the non-AS cohort. We calculated the proportions of having AAU, PsO, IBD, PR, and SS before the index date in both cohorts. After excluding subjects with the corresponding prior diseases, we calculated the incidence rates (IRs) of AAU, PsO, IBD, PR and SS for the AS and non-AS cohorts, and estimated the incidence rate ratios (IRRs) with 95% confidence intervals (CIs) of AAU, PsO, IBD, PR, and SS for AS patients as compared to non-AS individuals.

**Results:** The proportion of men was 62.9%, and the mean  $\pm$ SD age was 42 $\pm$ 17 years. Before the index date, AS patients had higher proportions of having AAU (8.6% vs. 0.7%), PsO (1.8% vs. 0.5%), IBD (0.061% vs. 0.007%), PR (1.7% vs. 0.1%) and SS (0.33% vs. 0.042%) compared with non-AS individuals. AS patients also had higher incidence rates of AAU (IR, 992 per 10<sup>5</sup> years vs. 128 per 10<sup>5</sup> years; IRR, 7.74, 95% CI, 7.16–8.38), PsO (IR, 167 per 10<sup>5</sup> years vs. 73 per 10<sup>5</sup> years; IRR, 2.30; 95% CI, 1.97–2.70), Crohn's disease (IR, 2.7 per 10<sup>5</sup> years vs. 0.2 per 10<sup>5</sup> years; IRR, 16.44; 95% CI, 2.75–98.4), ulcerative colitis (IR, 6.1 per 10<sup>5</sup> years vs. 0.1 per 10<sup>5</sup> years; IRR, 76.03; 95% CI, 9.35–617.98), PR (IR, 591 per 10<sup>5</sup> years vs. 29 per 10<sup>5</sup> years; IRR, 20.33 95%; CI, 17.87–23.12), and SS (IR, 84 per 10<sup>5</sup> years vs. 6 per 10<sup>5</sup> years; IRR, 13.61; 95% CI, 10.05–18.43).

**Conclusions:** Consistent with prior studies, our data showed that the incidence of AAU, PsO, and IBD were higher in AS patients than non-AS individuals. We also found that AS patients had a higher incidence of PR and SS compared with non-AS individuals.

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AB1307

#### DISEASE BURDEN OF AUTOIMMUNE INFLAMMATORY RHEUMATIC DISEASES IN SOUTH KOREA

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**Background:** Little is known about the epidemiology and disease burden of autoimmune inflammatory rheumatic diseases (AIRDs) in South Korea.

**Objectives:** To investigate the prevalence and direct medical cost of AIRDs in South Korea.

**Methods:** The prevalence of AIRDs including seropositive rheumatoid arthritis (RA), ankylosing spondylitis (AS), systemic lupus erythematosus (SLE), vasculitides, and other connective tissue diseases was calculated, and their trends between 2012 and 2016 were observed using nationwide claims database and the Rare Intractable Disease registration program. Direct medical costs of each AIRD in 2016 were estimated on the basis of claims charged for specific ICD-10 diagnostic codes.

**Results:** Among the all AIRDs, seropositive RA was most prevalent in Korea with prevalence of 188.5/100,000 persons in 2016, followed by AS (58.7/100,000), SLE (38.0/100,000), Behçet disease (29.2/100,000), Sjögren syndrome (23.5/100,000), and systemic sclerosis (7.1/100,000). Relatively low prevalence was observed in inflammatory myositis (4.5/100,000), polymyalgia rheumatica (4.1/100,000), psoriatic arthritis (PsA, 2.5/100,000), and each vasculitis (0.6–3.1/100,000). Prevalence of most AIRDs had been increased from 2012 to 2016, while their sex and age distribution were not changed significantly. Total direct medical costs in 2016 of overall AIRDs were \$263,136,087, which were mostly composed of direct medical expenditures for seropositive RA, AS, and SLE. For the direct medical cost per person, microscopic polyangiitis (\$6,223.3) was the highest, followed by PsA (\$3,603.7), Wegener granulomatosis (\$3,002.6), dermatomyositis (\$2,643.1), and AS (\$2,603.9).

**Conclusions:** Most prevalent AIRD in Korea was seropositive RA, followed by AS, Sjogren's syndrome, SLE, Behçet's disease, and systemic sclerosis. Direct medical cost per person was high in microscopic polyangiitis, PsA, Wegener granulomatosis, dermatomyositis, and AS.

**Disclosure of Interest:** None declared

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AB1308

#### FACTORS ASSOCIATED WITH THE DEVELOPMENT OF ESRD IN A RECENT LARGE SINGLE CENTRE COHORT OF PATIENTS WITH LUPUS NEPHRITIS

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**Background:** Lupus nephritis (LN) remains a major cause of morbidity in systemic lupus erythematosus. Worldwide, at 5 years about 19% (Class IV) and 4% (class V) of patients with LN develop end-stage renal disease (ESRD), depending upon the disease severity, ancestral and socio-economic factors as well as response to initial treatment. ESRD is an unusual direct cause of death in this disease but is associated with premature mortality.

**Objectives:** The aim of this study was to retrospectively review our large cohort of LN patients, predominantly treated with MMF and rituximab based steroid sparing regimens, who required renal biopsy for new presentation between 2010 and 2017 to analyse the factors associated with the development of ESRD.

**Methods:** We identified 176 patients with LN from a renal biopsy database, at our tertiary Lupus Centre presenting between 01/2010 and 09/2017. The 21 patients (11%) who progressed to ESRD were included, and using propensity score matching, were matched for age, gender and ethnicity with 63 patients who did not develop ESRD. Patients who required dialysis at presentation were excluded.

**Results:** Baseline characteristics were similar with regard to gender, age and ethnicity between both groups. Mean follow-up was 4 $\pm$ 17 years overall (2.1 $\pm$ 1.4 years in the ESRD group and 3.8 $\pm$ 1.5 years in the non-ESRD group, p=0.0002). The ESRD group had significantly higher serum creatinine at baseline (184.2  $\pm$  143.6 vs 89.0 $\pm$ 48.0, p=0.031) and at 12 m (256.2 vs 79.5, p=0.001) and significantly lower baseline eGFR (44.6 vs 68.1, p=0.003) and eGFR at 12 m (27 vs 73.1, p=0.001). The absence of remission at 1 year was also associated with a higher risk of ESRD (71.7% vs 9.5%, p=0.001), as well as the presence of positive



MPO-ANCA ( $p=0.040$ ), the ANCA titre ( $p=0.031$ ) and persistent low levels of complement (50% vs 21.5%,  $p=0.035$ ). Using multivariable regression analysis, independent factors predictive of ESRD were baseline serum creatinine and no response to treatment at 12 months. There was no significant difference in outcome between groups regarding the type of induction treatment.

**Conclusions:** The rates of ESRD in our LN cohort are comparable with the published literature despite. In our patient population with high use of rituximab and low steroids, the features that predict poor long term outcome are baseline serum creatinine and the failure to attain a remission at 1 year. These data highlight the importance of a) early diagnosis of lupus nephritis and b) defining the features which determine non response at 1 year and being able to identify earlier what would be the right treatment regimen for each individual patient.

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AB1309

#### RADIOGRAPHIC PROGRESSION OF WEIGHT-BEARING LARGE JOINT DAMAGE IN PATIENTS WITH RHEUMATOID ARTHRITIS DURING TNF-BLOCKING THERAPIES – MAXIMUM 12-YEAR FOLLOW UP –

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**Background:** We have demonstrated that TNF-blocking therapies are effective in inhibiting the radiographic progression in weight-bearing large joints with pre-existing Larsen grade 0-II during short term follow-up<sup>1,2</sup>. However, it is not clarified that the observed effect is persistent during long-term TNF-blocking therapies.

**Objectives:** The purpose of this study is to assess radiographic progression of weight-bearing large joint damage in patients with rheumatoid arthritis during long-term TNF-blocking therapies.

**Methods:** Sixty two consecutive patients (7 male, 55 women, mean age of 59.5 years old) were evaluated at baseline and after TNF-blocking therapy (infliximab, etanercept, adalimumab and golimumab). Joints that had undergone surgical intervention or ankylosis before the initiation of TNF-blocking therapy were excluded from the radiographic analysis. We assessed the radiographic progression of 327 weight-bearing large joints (109 hip joints, 99 knee joints, 119 ankle joints) at baseline and every year after TNF-blocking therapy. The structural damage in the weight-bearing large joints was evaluated using the Larsen grade (LG) at baseline. Radiographic progression of joint damage was defined as ARASHI change score<sup>3</sup> except bone quality score  $\geq 1$ . Survival rate was analysed using Kaplan-Meier method and the end point was defined as progression of joint damage.

**Results:** Average follow-up period was 7.0 years (rang, 1–12 years). Analysis of hip and knee joints with baseline LG 0/I indicated that 12 year survival rates were 93.4% and 84.1%, respectively. Radiographic progression was limited to cases with poor clinical response. All of the hip and knee joints with pre-existing damage of LG III/IV showed rapid progression at 1 year. Hip joint with baseline LG II showed gradual progression of damage. Two and 5 year survival rates of hip joint with LG II were 60.0% and 0%, respectively. Knee joint with baseline LG II also showed slow progression. Two, 5- and 9 year survival rates of knee joint with LG II were 81.3%, 48.2% and 0%, respectively. On the other hand, the radiographic progression of ankle joint damage was not significantly related to pre-existing damage. Twelve-year survival rates of ankle joint with baseline LG 0/I, II and III/IV were 81.6%, 75.0% and 82.4%, respectively.

**Conclusions:** In hip and knee joint, it was sometimes difficult to inhibit the progression when the baseline Larsen grade had been at II-IV. Therefore, it is essential to pay attention to the occurrence of early radiographic damage to avoid progression of hip and knee joint destruction.

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AB1310

#### ANTI-MÜLLERIAN HORMONE AND VITAMIN D SERUM LEVELS IN WOMEN WITH RHEUMATOID ARTHRITIS

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**Background:** Anti-Müllerian hormone (AMH) is a marker for ovarian reserve, whose levels when found decreased suggest compromise of the fertility. The AMH gene promoter contains a vitamin D response element that may cause vitamin D status to influence serum AMH levels, vitamin D has an influence in the activity of Rheumatoid Arthritis (AR) since it has been found that patients with autoimmune diseases show lower serum levels of this vitamin in comparison of normal controls. The current study examined the vitamin D status and AMH levels in women with RA.

**Objectives:** Evaluate serum levels of vitamin D and AMH in women with RA and in control group.

**Methods:** Observational, cross-sectional, study conducted between May and July 2017 at the University Hospital "Dr. José E. González " in Mexico. We included 38 women between 18 and 39 years of age, they met diagnostic criteria for RA established by the ACR in 2010, excluding pregnant patients, with primary amenorrhea or known risk factors for diminished ovarian reserve. A control group of 38 healthy age-matched women was integrated. Serum AMH level was measured using ELISA method in commercial kit (AMH Gen II, Beckman Coulter, Brea, CA, EU) as well the 25-hydroxyvitamin D [25(OH)D] status using chemiluminescence immunoassay. To analyse differences between the groups, we used Mann-Whitney U test; Spearman correlation coefficients were calculated between AMH level and Vitamin D level. Values are shown as the mean  $\pm$ SD. Two-sided *P* values less than 0.05 were considered significant. The statistical package used was SPSS Statistics, V17(Chicago: SPSS Inc.)

**Results:** It was found a mean age of 34.42 ( $SD=5.43$ ) and 31.47 years ( $SD=5.72$ ) in the control group and in women with RA, respectively. Regarding the mean serum levels of Vitamin D it was reported 20.04( $SD=7.81$ ) in control group and 23.55 ( $SD=8.2$ ) in women with RA. In control group, it was reported a mean of AMH of 2.83( $SD=0.47$ ) and in women with RA a mean of 2.63( $SD=0.50$ ). Serum levels of Vitamin D of patients with RA were statistically significant compared with the control group ( $p=0.015$ ) and AMH were statistically significant in women with RA compared with the control group ( $p=0.052$ )(Table1). There was no significant correlation between serum levels of vitamin D and AMH ( $p=0.795$ ).

Abstract AB1310 – TABLE 1

	Control	RA	<i>P</i>
Age (years)	34.42 $\pm 5.43$	31.47 $\pm 5.72$	
Serum 25 (OH) D (ng/ml)	20.04 $\pm 7.81$	23.55 $\pm 8.2$	0.015a
Serum AMH (ng/ml)	2.83 $\pm 0.47$	2.63 $\pm 0.50$	0.052a

Control: healthy patient; RA: rheumatoid arthritis; AMH: anti-Müllerian hormone. The values are expressed in mean  $\pm$ SD. A Differences between the 2 groups as calculated by the Mann-Whitney U test. Values of 25 (OH) D <10 deficient, 10–30 insufficient, 30–100 normal.

**Conclusions:** The current study shows that AMH and Vitamin D levels are lower in RA patients compared with controls. However, results do not indicate significant correlation between serum levels of vitamin D and AMH. So, it is suggested more studies.

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AB1311

#### ULTRASOUND EVALUATION OF ENTHESIS IN PSORIATIC ARTHRITIS: A SYSTEMATIC LITERATURE REVIEW

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**Background:** Enthesis involvement is considered as a key pathological lesion in psoriatic arthritis (PsA) patients. Recently, ultrasound (US) became an important

tool to evaluate the enthesis involvement in PsA. Power Doppler (PD) is able to identify vascular abnormalities which are known to be associated with inflammation.

**Objectives:** To perform a systematic literature review on how entheses are evaluated by US in PsA.

**Methods:** The objective was reformulated according to the PICO approach. Several synonyms for the main components (i.e. ultrasound and entheses) were used. No search limits were applied. The literature search was performed in Medline and Embase from databases inception to 1st October 2017. References identified were imported into a bibliographic manager. Firstly, duplicates were removed. Then, to identify eligible studies the remaining articles were assessed by title and abstract. Only articles in English and Latin languages were retained.

From the selected studies, data about the examined structures, pathological findings and definition used to identify pathology were retired using a predefined data collection form.

**Results:** The literature search resulted in 411 articles, of which 101 were captured in Medline and 310 in Embase. Figure 1 shows the study flow-chart for article selection. After removing duplicates and scanning titles and abstracts, 41 articles remained for the detailed review. After full-text review, 12 articles were excluded. The main reason for article exclusion after full-text review was the lack of explanation of US evaluation.

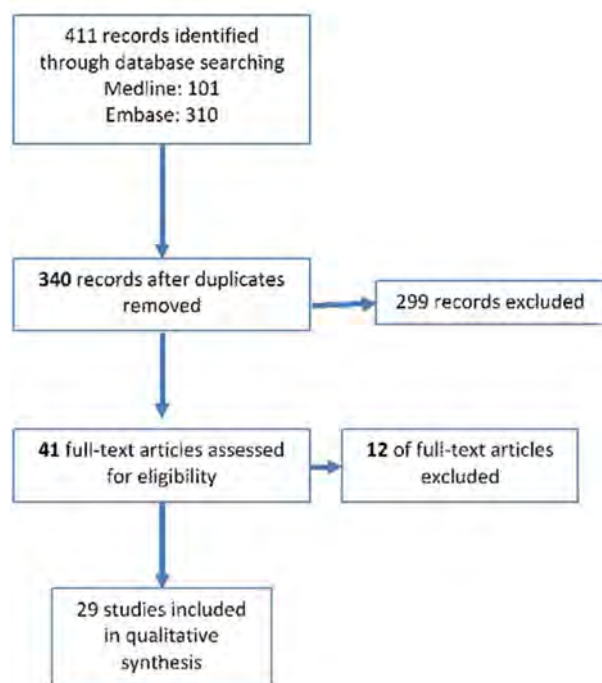
29 articles were included in qualitative analysis. The mean (range; SD) number of patients evaluated was 66.3 (7–141; 41.9).

The US was used for diagnostic in 26 (89.7%) articles and for monitoring in 7 (24.1%) articles. 4 (13.8%) evaluated also the US nail involvement. All articles used B mode evaluation and 26 (89.7%) used also Doppler mode, all of them using PD.

Thickening was evaluated in 27 (93.1%) articles, hypoechogenicity in 21 (72.4%), the presence of enthesophytes in 21 (72.4%) articles, the presence of calcifications in 11 (37.9%) articles, the presence of erosions in 21 (72.4%) articles, irregularities in 8 (27.6%) articles and bursitis in 15 (51.7%) articles, peri-enthesal soft-tissue oedema in 2 articles.

Triceps was evaluated in 8 (29.6%) articles, elbow extensors in 8 (29.6%) articles, quadriceps in 14 (51.9%) articles, proximal patellar in 12 (51.9%), distal patellar in 15 (55.6%), Achilles in 22 (81.5%), plantar fascia in 18 (66.7%) and finger extensor in 2 (7.4%), elbow flexors 3, medial collateral ligament in femur condyle 3, supraspinatus tendon in 1 articles, gluteus tendons in 1 article, first and seventh costo-sternal joints, anterior superior iliac spine, and iliac crest, the posterior superior iliac spine, and the fifth lumbar spinous process, rotator cuff in one article.

OMERACT definitions were used in 6 (20.6%) articles. Qualitative evaluation was used in 12 (41.3%) articles, semi-quantitative evaluation in 4 (13.7%) articles. As global score, GUESS score was used in 5 (17.2%) articles and MASEI score was used in 4 (13.7%) articles.



Abstract AB1311 – Figure 1

**Conclusions:** Although the majority of the articles evaluated the same enthesis and the same US findings, we found a lack of consensus regarding the global score.

**Disclosure of Interest:** None declared

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**AB1312 EFFECTS OF VITAMIN D ON DISEASE ACTIVITY, FUNCTIONAL DISABILITY AND SERUM INTERLEUKIN-6 IN RHEUMATOID ARTHRITIS**

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**Background:** Vitamin D may have a potential role in rheumatoid arthritis (RA) pathogenesis by inhibiting the expression of pro-inflammatory cytokines including interleukin-6 (IL-6)<sup>1-2</sup>.

**Objectives:** The aim of this study is to determine the clinical factors of vitamin D deficiency in a multi-ethnic Malaysian RA patients and its association with disease activity, functional disability and serum IL-6 level.

**Methods:** One-hundred RA patients and 50 healthy controls, age- and sex-matched were recruited. DAS28 and HAQ score were assessed. Baseline serum vitamin D and IL-6 were measured in all subjects. RA patients who were vitamin D deficient were given loading dose of vitamin D3 and repeated assessments were done.

**Results:** Vitamin D deficiency (<50 nmol/L) was found in 63% of RA patients and 76% of healthy controls. Chinese RA patients and healthy controls had significantly more sufficient vitamin D levels compared to Malays and Indians (p=0.002) and (p=0.006), respectively. Only BMI was significantly associated with vitamin D deficiency in RA patients (p=0.012) after adjustment for potential confounding variables. 21 patients received and were compliant to 8 weeks of loading dose 50,000 IU/week vitamin D. Serum vitamin D levels improved from 24.10±7.78 to 91.57±23.70 nmol/L (p<0.001) during this period, whereas no improvement was seen in serum IL-6 levels (16.33±24.58 to 16.38±22.56 pg/ml). No significant association was seen between vitamin D level and disease activity or serum IL-6 level in both pre- and post-treatment groups. A negative association was observed between vitamin D levels and functional disability, including a 33% improvement post-treatment (mean ±SD 0.30±0.46 to 0.20±0.18). The table below shows the independent factors association with serum vitamin D level in RA patients (n=100).

		Mean ± SD	P value	
Vitamin D	Age (years)	45.9 ±3.48	0.202	
	Race	Malay (35%)	30.73 ± 18.19	0.002
		Chinese (34%)	68.64 ± 23.76	
		Indian (31%)	38.11 ± 22.40	
	BMI (kg/m <sup>2</sup> )	26 ± 5	0.002	
	Post-menopausal (%)	yes	45 %	0.784
		no	55 %	
	ESR (mm/hr)	37.4 ±19.6	0.206	
	CRP (mg/L)	1.37 ±1.53	0.779	
	Prednisolone (%)	yes	51.5%	0.083
		no	47.5%	
	Low dose vit D (%)	yes	61.4%	0.791
		no	37.6%	
Serum IL-6 (pg/ml)	14.1 ±18.56	0.330		
DAS28 (n)	Inactive (remission/low)	31	0.802	
	Active (mod/high)	69		
HAQ (n)	Mild to mod disability	94	0.033	
	Mod to severe disability	6		

Abstract AB1312 – Figure 1

**Conclusions:** Vitamin D deficiency is prevalent in Malaysian RA patients. This study suggests that vitamin D does not have a role in disease activity or serum IL-6 but it may have a role in functional disability in RA patients.

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AB1313

**SYSTEMATIC SCREENING OF COMORBIDITIES IN CHRONIC INFLAMMATORY RHEUMATIC DISEASES IN DAILY PRACTICE: A RETROSPECTIVE MONOCENTRIC FRENCH STUDY ACCORDING TO RECENT EULAR GUIDELINES**

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**Background:** In chronic inflammatory rheumatic diseases, comorbidities such as cardiovascular diseases and infections are more frequently observed than in general population and are suboptimally prevented, screened and managed.<sup>1-4</sup> A nurse-led programme demonstrated the short-term benefit on management of comorbidities in rheumatoid arthritis patients.<sup>5</sup> EULAR recently published points to consider for reporting, screening, and preventing specific comorbidities in chronic inflammatory rheumatic diseases in daily practice.

**Objectives:** Our objective was to screen and report comorbidities in chronic inflammatory rheumatic diseases patients in daily practice according to recent EULAR guidelines.

**Methods:** We included patients with rheumatoid arthritis, spondyloarthritis, and psoriatic arthritis from November 2016 to November 2017 in a retrospective monocentric study in the rheumatology department of the Grenoble Alpes Teaching Hospital. Data regarding comorbidities were collected in a standardised multidisciplinary consultation with a rheumatologist, a specialised nurse and a hospital pharmacist, according to EULAR and French Society of Rheumatology guidelines. Data concerning cardiovascular diseases, infectious comorbidities, cancer screening, and osteoporosis were collected. Data about the rheumatic disease including treatment and disease activity were recorded. Adherence was analysed in consultation by the pharmacist. Recommendations were notified to the patients, his general practitioner, and rheumatologist on a standardised letter. Data were analysed as mean/SD if appropriate and percentage.

**Results:** We included 101 patients, 43 patients had rheumatoid arthritis, 45 had spondyloarthritis, and 13 were diagnosed with psoriatic arthritis. The mean age was 49,6 years old.<sup>14,9</sup> 50 patients were followed in the hospital, 39 were followed by private practitioners and 12 were followed by both. All patients were treated with bDMARDs. In average, patients received 2,3 (SD 1,6) different biologic treatments. In our total population, 55,5% had influenza vaccination >1 year ago, 42,6% had an appointment to the dermatologist >1 year ago, 25% of the women between 50 and 75 years old had a mammography >2 years ago and 27,3% of women >50 years old with FRAX above threshold were not treated for osteoporosis. Moreover, 60,5% of patients with rheumatoid arthritis had a Heart Score >1% and 45,6% in the total population.

**Conclusions:** Our monocentric study confirmed that comorbidities are frequent and suboptimally prevented and managed according to the EULAR point to consider. An evaluation of the efficiency of our standardised consultation and intervention is necessary.

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AB1314

**LACK OF ASSOCIATION BETWEEN ABO BLOOD GROUPS AND RHEUMATIC DISEASES IN CHINA: A SINGLE-CENTRE EXPERIENCE**

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**Background:** Various genetic and environmental risk factors have been shown to be associated with the incidence of rheumatic diseases. Several studies have shown associations of ABO blood groups with various diseases.

**Objectives:** Our study aimed to determine whether there is an association between the types of rheumatic diseases and ABO blood groups.

**Methods:** The study included the patients, followed up at the Immunology-Rheumatology clinic between January 2010 and December 2017 for diagnosis of rheumatic disease, who had an ABO Rh blood data. Age, gender, type of rheumatic disease, ABO Rh blood groups were recorded.

**Results:** A total of 1551 patients were included in the study, such as 392 AS patients, 297 RA patients, 752 SLE patients and 110 pSS. The patients were assessed for blood types, 40.2% had O type, 26% patients had A type, 26.8% had B type, and 7.0% had AB type. AS, RA, SLE and pSS were more common in the patients with O blood type. The blood type where all the diseases are observed the least commonly was AB. There was no significant difference in the distribution of blood types in rheumatic diseases.

**Conclusions:** In our study, we thought that there was lack association between types of different rheumatic diseases and ABO blood groups.

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AB1315

**MEDICATION USE AMONG PREGNANT WOMEN WITH RHEUMATIC DISEASES IN KOREA BASED ON THE NATIONAL HEALTH INSURANCE SERVICE-NATIONAL SAMPLE COHORT**

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**Background:** Many rheumatic diseases (RD) predominantly affect women in their reproductive ages. Medication use during pregnancy is an important issue in women with RD since it may affect the health of both fetus and the mother.

**Objectives:** This study aimed to characterise the status of medication dispensed for Korean women with RD in pre-gestational period and during pregnancy.

**Methods:** Women aged between 20–44 years and diagnosed as RD and had delivery after the diagnosis of RD were identified from National Health Insurance Service-National Sample Cohort (NHIC-NSC) (2009–2013). Rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and ankylosing spondylitis (AS) were included as RD. We analysed prevalence of RD related medication including disease-modifying antirheumatic drugs (DMARDs), NSAIDs, and corticosteroids (CSs) dispensed between the pre-gestational periods of 3 months before pregnancy until delivery. We also analysed prevalence of other medications and supplements which are commonly dispensed during pregnancy in women with RD and the age and sex matched controls.

**Results:** There were 71 deliveries among 1059 women with RD. In RD pregnancies, 54.9% had taken at least 1 RD related medications. The prevalence of DMARDs dispensing during pregnancy was 23.9%, CSs 43.7%, and NSAIDs 38.0% in RD population. Although usage of antibiotics and medication for thyroid diseases during pregnancies were not different between the women with RD and the control, use of vitamin and iron supplements were significantly higher in the women with RD (38.0% vs 13.4%,  $p < 0.0001$ ).



**Abstract AB1315** – Table 1RD-related. medication dispensing prevalence by pregnancy period (N=71)

	Pre-pregnancy	1st Trimester	2nd Trimester	3rd Trimester
<b>cdMARDs</b>	17 (23.9)	15 (21.1)	14 (19.7)	12 (16.9)
Azathioprine	1 (1.4)	1 (1.4)	1 (1.4)	1 (1.4)
Cyclosporin	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hydroxychloroquine	17 (23.9)	14 (19.7)	13 (18.3)	10 (14.1)
Sulfasalazine	0 (0.0)	0 (0.0)	1 (1.4)	2 (2.8)
Tacrolimus	1 (1.4)	1 (1.4)	0 (0.0)	0 (0.0)
Others	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
<b>bdMARDs</b>	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
<b>Corticosteroids</b>	31 (43.7)	24 (33.8)	24 (33.8)	22 (31.0)
<b>NSAIDs</b>	27 (38.0)	13 (18.3)	3 (4.2)	1 (1.4)

**Conclusions:** Medications are frequently required during pregnancies of women with RD. RD are a significant burden for pregnant women requiring increased number of medication use.

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#### AB1316 HOSPITAL ADMISSION TRENDS AND SHORT-TERM OUTCOME FOR IGA VASCULITIS IN CHILDREN AND ADULTS IN WESTERN AUSTRALIA

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**Background:** Immunoglobulin A vasculitis (IgAV), formerly called Henoch-Schönlein purpura, is an immune complex mediated small-vessel vasculitis that preferentially affects the skin, intestines and kidneys. While more common in children, IgAV is not unusual in adults, where it has been associated with worse outcomes.

**Objectives:** To compare hospital admission rates and outcomes over time between adult and paediatric inpatients with IgA vasculitis

**Methods:** Data were extracted from a state-wide registry for all hospital admissions in Western Australia (WA) between 1980 to 2015 for patients with a primary or secondary diagnosis of IgAV (ICD-9-CM code 287.0/ICD-10-AM code D69.0). Paediatric cases were defined as those ≤19 years at first diagnosis.

**Results:** From a total 764 patients admitted to hospital with an IgAV diagnosis 508 (66%) were paediatric and 256 (34%) adult cases. IgAV was the primary diagnosis in 463 (91.1%) paediatric and in 123 (48%) adult patients (p<0.01). In children, mean age at primary diagnosis was 5.6 years of (range 0–19) versus 50.2 years (range 20–91) in adults. Both groups had similar proportions of Indigenous (3.5 vs 1.6%, p=0.4) and male patients (59 vs 51.2%, p=0.3). Over the observation period, the annual rates per 100,000 for a first admission for IgAV declined from 4.2 to 0.4 for children and from 0.42 to 0.2 for adults, while length of stay in days decreased from 5.8 to 1.8 for children and increased from 10.5 to 21.1 for adults. Three adults (2.4%) but no child required ICU admission, while one adult (0.7%) and no child died in hospital. Readmission rates for IgAV were considerable and higher in children than adults (25.6% vs 18.7%, p=0.1).

**Conclusions:** Admission rates for IgAV in children in WA have declined steeply over the last decades and now almost equate admission rates for adults. The reduction in length of stay and absence of in-hospital mortality support an increased willingness or necessity to manage children with IgAV outside the hospital setting despite a significant readmission rate. In contrast, hospital admission for IgAV in adults associates with prolonged length of stay and a slight risk for ICU admission and in-hospital mortality.

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#### AB1317 IDENTIFICATION OF CARDIOMETABOLIC ABNORMALITIES IN THE FIRST VISIT TO A PREVENTIVE CARDIO-RHEUMA CLINIC

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**Background:** Rheumatoid arthritis (RA) is a chronic, systemic and autoimmune disease with articular and extra-articular manifestations. RA is associated with increased prevalence of comorbidities and higher cardiovascular risk when compared to general population. Atherosclerotic cardiovascular (CV) events are the leading cause of death in RA. In a recent meta-analysis, hypertension, type 2 diabetes mellitus (T2DM) and hypercholesterolemia were shown to increase the risk of CV disease in this population.<sup>1</sup> A study reported a prevalence of hypertension 29.8%; dyslipidemia 27.1% and T2DM 12.4% in Mexican-mestizo RA patients.<sup>2</sup> The cardio-rheuma clinics were designed to provide healthcare for CV diseases in patients with rheumatic conditions. Specific guidelines recommendations have been published to enhance detection and management of specific comorbidities associated to RA.<sup>3</sup>

**Objectives:** To identify the prevalence of unknown cardiometabolic risk factors in a Mexican-mestizo cohort with RA.

**Methods:** Cross-sectional, observational study. Patients who fulfilled the 1987 ACR and/or the 2010 ACR/EULAR classification criteria were consecutively recruited. Patients were divided in two groups, with and without history of cardiovascular comorbidities. Clinical history and physical exam were performed by a general physician in a cardio-rheuma clinic. Fasting blood glucose and lipid profile were performed on all subjects. Categorical variables are expressed as percentages and numerical variables as means±standard deviations.

**Results:** A total of 296 patients were included. Demographical characteristics are shown in Figure 1. Hypertension was the most frequent comorbidity (27.7%), followed by dyslipidemia (26.7%) and T2DM (13.5%). Many of the patients without history of cardiometabolic risk factor had important findings on baseline visit: 18.7% had altered blood pressure without history of hypertension, 76.5% had an abnormal lipid profile without history of dyslipidemia, and 21.5% had an altered fasting glucose without history of T2DM.

A. Demographic data		
Characteristic	N= 296	
Age (years), mean ± SD	55.8 ± 8.5	
Female, n (%)	275 (92.9%)	
Active or former smoker, n (%)	27 (9.1%)	
T2DM history, n (%)	40 (13.5%)	
Hypertension history, n (%)	82 (27.7%)	
Dyslipidemia history, n (%)	79 (26.7%)	
Steroids use	174 (58.8%)	
bdMARDs, n (%)	20 (6.8%)	
Methotrexate, n (%)	249 (84.1%)	
Leflunomide, n (%)	61 (20.6%)	
DAS 28-CRP, mean ± SD	3.36 ± 1.4	
Disease duration (years), mean ± SD	10.91 ± 13.3	
B. Cardiometabolic abnormalities		
	Previous history	No previous history
<b>Hyperglycemia (n)</b>	<b>40</b>	<b>256</b>
<b>Fasting plasma glucose levels (mg/dL)</b>		
≤99 mg/dL, n (%)	13 (32.5 %)	201(78.5%)
100-125 mg/dL, n (%)	13 (32.5 %)	43 (16.8 %)
126-199 mg/dL, n (%)	6 (15 %)	12 (4.7 %)
≥ 200 mg/dL, n (%)	8 ( 20 %)	0
<b>Hypertension (n)</b>	<b>82</b>	<b>214</b>
<b>Blood pressure (mmHg)</b>		
Blood pressure ≤ 140/90 mmHg, n (%)	52 (63.4 %)	174 (81.3 %)
Systolic blood pressure ≥ 140 mmHg, n (%)	15 (18.3 %)	26 (12.2 %)
Diastolic blood pressure ≥ 90 mmHg, n (%)	5 (6 %)	13 (6.1 %)
Blood pressure ≥ 140/90 mmHg, n (%)	10 (12 %)	1 (0.5 %)
<b>Dyslipidemia (n)</b>	<b>79</b>	<b>217</b>
Normal lipid profile, n (%)	14 (17.7 %)	51 (23.5 %)
Altered lipid profile*, n (%)	65 (82.3 %)	166 (76.5 %)

Abstract AB1317 – Figure 1

\*Altered lipid profile was defined as TC  $\geq$ 200 mg/dL, HDL-C  $<$ 50 mg/dL, TG  $\geq$ 150 mg/dL, LDL-C  $\geq$ 100 mg/dL. SD=Standard deviation; T2DM=Type 2 diabetes mellitus; bDMARDs=biological agents; DAS 28-CRP=Disease Activity Score 28 joints C-reactive protein.

**Conclusions:** In our cohort of Mexican-mestizo RA patients there is a high prevalence of cardiometabolic risk factors. An important amount of these were discovered in patients without previous diagnosis at their first visit to a cardio-rheuma clinic.

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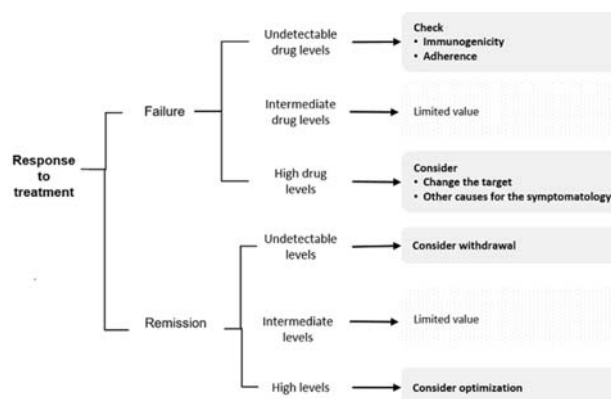
#### AB1318 PRACTICAL ASPECTS OF BIOLOGICAL-DRUG MONITORING IN RHEUMATOID ARTHRITIS AND SPONDYLOARTHRITIS

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**Objectives:** To prepare recommendations on practical aspects of biological-drug monitoring that may be useful for rheumatologist

**Methods:** A systematic review of the literature was carried out to determine in which patients and in what clinical circumstances may be most beneficial to monitor the levels of biological drugs and their antibodies in patients suffering Rheumatoid Arthritis (RA) and/or Spondyloarthritis (SpA). With the results of the review, a group of experts produced a series of clinical questions, to be answered through the available scientific evidence, and then, subsequently, to make the recommendations and clinical algorithms for instructing the decision-making process.

**Results:** Results from the systematic review showed that the biological-drug monitoring might be especially useful in two clinical situations; in case of a treatment failure (primary or secondary) and in sustained remission (see figure 1). It was also reviewed which laboratory technique might be better and the optimal time for blood withdrawal. Specific recommendations are given on the interpretation of drug levels and on factors that should be taken into account are given (i.e. body mass index and concomitant medication).



Abstract AB1318 – Figure 1

**Conclusions:** Informed algorithms have been developed regarding the optimal time for requesting drug levels and anti-drug antibodies in patients with RA and

SpA. This recommendations may help in the decision-making process and could be useful as part of future guidelines in the field.

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#### AB1319 DRUG RESISTANCE IN BACTERIA ISOLATED FROM URINE OF RHEUMATOID ARTHRITIS PATIENTS AND INDUCTION OF RESISTANCE BY CHLOROQUINE

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**Background:** Rheumatoid arthritis (RA) was connected with bacterial infections.<sup>1</sup> Usage of antibiotics generate resistance in pathogens as well as natural microflora.<sup>2</sup> Some anti-rheumatic drug (chloroquine) probably is associated with selection of quinolone resistant bacteria.<sup>3</sup>

**Objectives:** To isolate bacteria from urine of rheumatoid arthritis patients, determine antibiotic resistance profiles for isolated bacteria and induce ciprofloxacin resistance by exposition to chloroquine.

**Methods:** Two consecutive samples of morning urine was obtained from 26 RA patients without urinary infection tract symptoms. Patients were treatment-naive or treated with different anti-rheumatic drugs. Bacteriuria was determinate on UTI chromogenic medium (HIMEDIA). Resistance against 38 commonly used drugs (MAST) was determined according EUCAST standards. For OXA-48 carbapenemase detection, a temocillin disc was used. Isolated bacterial strains were cultivated on LB broth supplemented with chloroquine (625 and 1875 µg/ml) for 2 weeks, than incubated on medium with ciprofloxacin (32, 15, 8, 4, 2, 1, 0.5 µg/ml). Growth was measured with spectrophotometer ( $\lambda=600$  nm) against non-inoculated medium.

**Results:** Bacteria were cultivated from almost 88% of patients, but only in 26% of them in titer higher than  $10^5$  cfu/ml of urine. Bacteriuria were more often in treated individuals. Isolated bacteria belonged to *Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter cloacae*, *Proteus mirabilis*, *Morganella morganii*, *Staphylococcus* sp. Among tested bacteria 23% were determined as MDRs and one strain were XDR. Screening test detecting OXA-48 revealed that 35% of strains probably possess this resistance mechanism.

Selected 10 ciprofloxacin sensitive strains (*E. coli*, *P. mirabilis*, *E. cloacae*, *M. morganii*) were exposed to increasing concentration of chloroquine. After 2 weeks of passing, 80% of bacteria become resistant to antibiotic (with ciprofloxacin MIC up to 8 µg/ml).

**Conclusions:** Asymptomatic bacteriuria is general phenomenon in RA patients. This research showed that many of Polish RA patients may be carriers of drug resistant bacteria, including MDR. This phenomenon may be connected with poor comply of antibiotic policy by patients as well as health service in Poland. Exposition on chloroquine induce bacterial resistance against ciprofloxacin. In RA treatment procedure, a risk of induction of quinolone resistance in bacterial flora should be considered.

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AB1320

### CLINICAL, IMMUNOLOGICAL AND EXPOSITIONAL FACTORS IN A COLOMBIAN POPULATION WITH SYSTEMIC LUPUS ERYTHEMATOSUS ASSOCIATED WITH LUPUS NEPHRITIS

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**Background:** Systemic lupus erythematosus (SLE) is an autoimmune disease characterised by multiple organ involvement, lupus nephritis (LN)<sup>1</sup> being one of the most serious manifestations

**Objectives:** To establish associated factors with lupus nephritis development in patients with SLE

**Methods:** Cross-sectional study taken from a cohort of 1175 patient with SLE who met criteria for classification for ACR<sup>1997</sup> or SLICC<sup>2012</sup> between 2007 and 2015. Bivariate analysis of multiple characteristics was performed between patients with presence and absence of LN at through chi squared and U Mann Whitney. Multivariate analysis was performed by logistic regression to adjust for significant associations

**Results:** The cohort of patients with SLE 90% was female gender, had an average of 44 years with a duration of the disease of 10.6 years. Joint and haematological involvement was present in more than 80% of patients. The presence of antibodies against DNA and low complement was found in 53% and 60% respectively. The exposure to dyes was 44% and tobacco 21%.

It was found 455 patients with SLE and LN with an average age of 41 years and a time of evolution of SLE of 11 years. The male gender proportion was higher in those who presented LN with 11.6% compared to 7.1% who did not have LN. The immunological profile of patients with NL was characterised by a higher proportion of positivity for Anti-DNA, anti-SM and low complement. Male gender has a greater association with LN (OR 1.98 CI 95% 1.20–3.27). Having a disease duration greater than 10 years increases the association with LN (OR 1.48 95% CI 1–2.16) as well as the presence of anti-DNA (OR 1.34 CI95% 1.03–1.75) and antiSM (OR 1.45 95% CI 1.04–2.02). Never smoker was a protective factor for LN (OR 0.52 CI95% 0.34–0.81).

**Abstract AB1320 – Table 1.** Factors associated with Lupus nephritis in a cohort of patients with systemic lupus erythematosus, in Colombia from 2007 to 2015

Lupus nephritis	OR	CI (95%)	OR adjust*	CI (95%)
<b>Gender</b>				
Male	1,27	1,04–1,55	1,98	1,20–3,27
<b>Time progress SLE<sup>a</sup></b>				
≥10 years	1,37	1,08–1,74	1,48	1,01–2,16
<b>Anti SM</b>				
Positive	1,46	1,10–1,95	1,45	1,04–2,02
<b>Anti DNA +</b>				
Positive	1,34	1,05–1,72	1,34	1,03–1,75
<b>Past or current cigarette consumption</b>				
Yes	1,66	1,22–2,25	1,75	1,14–2,69
<b>No previous or current cigarette consumption</b>				
Yes	0,56	0,41–0,77	0,52	0,34–0,81

**Conclusions:** This study shows a greater association of LN in men. Although there are disparities in the findings worldwide, we believe that other factors typical of this current population such as ancestry and racial mixing may be influencing this finding. No smoking seems to be a protective factor. Awareness of the disclosed risk factor should encourage preventive strategies for LN in SLE patients such as suppression of cigarette smoking.

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AB1321

### THE EXPANSION OF MYELOID-DERIVED SUPPRESSOR CELLS IN PATIENTS WITH RHEUMATIC DISEASES

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**Background:** Myeloid-derived suppressor cells (MDSCs) are a heterogeneous population of immature myeloid cells with a remarkable ability to suppress the immune system. Although MDSCs were found to suppress the T cell response of some cancer patients and tumour bearing mice, the role of those cells have been revealed in patients with RA, SLE, and IBD. Nevertheless, most rheumatic diseases have a common pathological process, such as inflammatory arthritis and systemic tissue damage. Whether or not MDSCs and their subsets are abnormally expressed in patients with inflammatory-associated rheumatic diseases is still unclear.

**Objectives:** To investigate the proportion of MDSCs and their subsets in patients with different rheumatic diseases and clarify the association between those cells and patients clinical data including the disease activity index and the inflammation of joints.

**Methods:** One hundred and nine patients with various rheumatic diseases and twenty-five healthy controls were recruited. The common clinical characteristics and the special clinical indexes for each rheumatic disease were obtained from patients. The MDSCs and their subsets were marked with fluorescently labelled antibodies and were then analysed with flow cytometry. All statistics were calculated with SPSS 20.0. A p<0.05 was considered to be statistically significant.

**Results:** The patients included 31 with RA, 21 with AS, 14 with OA, 11 with SLE with arthritis, 13 with SLE without arthritis, 9 with Gout, 10 with HUA, and 25 healthy controls. The proportions of MDSCs, M-MDSCs, and G-MDSCs were higher in patients with RA than in healthy controls (6.56%±6.77% vs. 1.46±0.96%, 2.52±3.81% vs. 0.35±0.35%, 1.13±1.64% vs. 0.18±0.14%; p<0.001). The same increase in the number of MDSCs and their subsets was also found in patients with AS, OA, SLE with arthritis, and Gout. The proportions of MDSCs and M-MDSCs were mostly correlated with the patient's joint inflammation indexes (such as CRP and total joint pain) and the disease activity. Additionally, an increased risk of arthritis was found from MDSCs, M-MDSCs, and G-MDSCs (OR=2.417, 13.257, 6.204; 95% CI=1.625–3.597, 3.974–44.223, 1.798–21.406; p<0.01). When other cell subsets were adjusted, the same risk was also obtained for the expansion of M-MDSCs (adjusted OR=5.772; 95% CI 1.174–28.369; p=0.031).

**Conclusions:** The expansion of MDSCs and their subsets were found to be correlated with the disease activity and joint inflammation in patients with different rheumatic diseases. Further analysis revealed that the proportion of M-MDSCs was associated with the risk of arthritis in those populations.

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AB1322

### TREATMENT RESPONSE AS A PREDICTOR FOR REFRACTORY DISEASE AND/OR TRANSITION TO RHEUMATOID ARTHRITIS IN PATIENTS WITH POLYMYALGIA RHEUMATICA

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**Background:** Polymyalgia rheumatica (PMR) is a common inflammatory rheumatic disease that affects elderly people and predominantly causes shoulder and pelvic girdle pain. PMR is sometimes refractory (1), and some cases are finally diagnosed with rheumatoid arthritis (RA) (2). Predictive factors for clinical course of PMR are not fully elucidated.

**Objectives:** The purpose of this study is to elucidate predictive factors for clinical course of PMR.

**Methods:** Newly diagnosed PMR patients at our hospital from July 2006 to June 2017 were enrolled. All patients fulfilled the EULAR/ACR<sup>2012</sup> Provisional Classification Criteria for PMR but not the EULAR/ACR<sup>2010</sup> Classification Criteria for RA.



Patients who had GCA, other rheumatic disorders like SLE or were newly diagnosed with cancer within 2 years of diagnosis were also excluded. The primary endpoint was the remission by one month after commencement of treatment. Remission was defined as the absence of PMR symptoms and the elevation of erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP). For evaluation of the composite outcome of refractory PMR and final diagnosis of RA, the secondary outcome was defined as requirement of additional treatment and/or relapse during the observation period. Relapse was defined as a flare of PMR symptoms and the elevation of ESR or CRP. Categorical variables with a possible relation to the outcomes such as clinical characteristics, criteria items, articular symptoms and laboratory data were compared by using the nonparametric chi-square test.

**Results:** The mean age of enrolled 61 patients was 70.6 years and 67% were female. 38 (62%) patients failed to achieve remission by one month. The proportion of patients showing elevated ESR (>100 mm/h) at baseline was higher in patients without remission than those with remission (62% vs. 30%,  $p=0.017$ ) though there were no differences in sex, articular symptoms. Patients without remission also showed a lower reduction rate of CRP after a week (76% vs. 89%,  $p=0.026$ ) compared to those with remission. Furthermore, 30 (49%) patients required additional treatments and/or had relapses during the observation period. These patients showed higher platelet counts at baseline ( $42.9 \pm 1.9$  vs.  $36.3 \pm 2.0 \times 10^4/\text{mm}^3$ ,  $p=0.023$ ) and lower proportion of achievement of CRP levels less than 1.0 mg/dl after a week (44% vs. 80%,  $p=0.009$ ).

**Conclusions:** ESR and platelet counts at baseline and early treatment response might be useful for prediction of refractory PMR and/or transition to RA.

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#### AB1323 DOES OBESITY REPRESENT A RISK FACTOR FOR A POOR REMISSION RATE IN JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH ANTI-TUMOUR NECROSIS FACTOR-ALPHA THERAPY?

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**Background:** Despite increased interest in the association between obesity and rheumatoid arthritis,<sup>1</sup> evidence remains sparse in the Japanese population due to the fact that Asians have different associations between the body mass index (BMI), percentage of body fat, and health risks compared with the Western population. To address this problem, a World Health Organisation (WHO) consultation report proposed appropriate BMI cut-off points for the Asian population and redefined obesity as BMI of  $\geq 27.5 \text{ kg/m}^2$ .<sup>2</sup>

**Objectives:** From the perspective of exploring the association of obesity and rheumatoid arthritis, it is necessary to precisely define obesity for appropriate ethnic groups. Hence, this study aimed to assess whether obesity represents a risk factor for a poor remission rate in Japanese patients with rheumatoid arthritis requiring anti-tumour necrosis factor-alpha (TNF- $\alpha$ ) therapy using appropriate BMI cut-off points for the Asian population.

**Methods:** Participants were identified from our hospital in Shizuoka, Japan, and followed up from 2009 to 2017. Based on WHO guidelines, we classified participants using an appropriate BMI for the Asian population as follows: underweight,  $< 18.5 \text{ kg/m}^2$ ; normal weight,  $18.5\text{--}23.0 \text{ kg/m}^2$ ; overweight,  $23.0\text{--}27.5 \text{ kg/m}^2$ ; and obese,  $\geq 27.5 \text{ kg/m}^2$ . The primary outcome was to define whether obesity affects the clinical response to anti-TNF- $\alpha$  therapy. The response variable was defined as the simplified disease activity index (SDAI) remission after 12 months. In addition, we estimated multivariate odds ratios and their 95% confidence intervals (CIs) for nonremission after 12 months of initiating anti-TNF- $\alpha$  therapy or censored as nonresponders to the therapy after adjusting for sex, age, smoking status, anticyclic citrullinated peptide antibody status, rheumatoid factor status, and disease duration.

**Results:** We monitored 295 outpatients with rheumatoid arthritis who received anti-TNF- $\alpha$  therapy for at least 12 months or censored as nonresponders to the therapy. The mean  $\pm$ SD for SDAI at the baseline was  $24.20 \pm 14.47$ . The BMI was  $\geq 27.5 \text{ kg/m}^2$  (obese) in 16 (4.2%) of 295 patients. At the 12 month follow-up, 62.0% of patients with rheumatoid arthritis had reached SDAI remission. The multivariate odds ratio for nonremission at 12 months or nonresponsiveness of obese patients referred to normal weight was 2.24 (0.53–9.43), which tended to be higher for poor response, albeit not significantly.

**Conclusions:** Obesity may represent a risk factor for a poor remission rate in Japanese patients with rheumatoid arthritis treated with anti-TNF- $\alpha$  therapy. Thus, weight-loss programs might be a feasible solution for improving the condition of obese Japanese patients with rheumatoid arthritis.

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#### AB1324 STUDYING THE RELATIONSHIP BETWEEN BODY MASS INDEX, BMI, AND BONE MINERAL DENSITY, BMD, OF LUMBAR VERTEBRAE AND FEMORAL NECK

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**Background:** There is a well known association between BMI and BMD in as much that patients with higher BMI have higher BMD, secondary to factors including muscle mass and fat mass<sup>1</sup>. However it is not clear whether this relationship is equal in all areas of the body assessed for bone mineral density (BMD) estimation, which traditionally are the lumbar vertebrae, and different areas of the femur. Our study sets out to establish if this association exists in the lumbar vertebrae and femoral neck, since Dual Energy X-ray Absorptiometry (DEXA) scans measure BMD of both.

**Objectives:** To explore the relationship between BMI and BMD in a cohort of patients referred for DEXA scan.

**Methods:** Data was used from patients referred for DEXA scan to Royal Lancaster Infirmary between (2006 and 2010). The following were recorded: age, sex, height, weight, BMI, BMD at L1-L4, BMD at femoral neck (left and right) and BMD at hip (left and right).

Male and female patients were analysed separately. A Linear regression model was fitted using BMI with BMD at L1, L2, L3, L4, total right hip, total left hip, right neck of femur and left neck of femur as explanatory variables. Adjusted r-squared ( $r^2$ ) values were used to compare the fit of the models, both with and without age-adjustment.

**Results:** 35759 patients were used in the study, of which 84% were female. Mean age was 62.2 years (SD 12.8), mean height was 161.9 cm (SD 8.3), mean weight was 70.4 kg (SD 15.3), mean BMI was 26.8 kg/cm<sup>2</sup> (SD 5.2).

**Abstract AB1324 – Table 1** Adjusted.  $r^2$  values for each group were as follows:

Site	Adjusted $r^2$ Male	Adjusted $r^2$ Female	Adjusted $r^2$ Male (age-adjusted)	Adjusted $r^2$ Female (age-adjusted)
L1	0.0986	0.0909	0.1002	0.1747
L2	0.0708	0.0678	0.0718	0.1488
L3	0.0581	0.0603	0.0695	0.1127
L4	0.0611	0.0548	0.0921	0.0740
Total Right Hip	0.1480	0.1345	0.1806	0.2983
Total Left Hip	0.1532	0.1518	0.1767	0.3180
Neck of Femur, Right	0.0997	0.0616	0.1768	0.2536
Neck of Femur, Left	0.0898	0.0715	0.1603	0.2695

**Conclusions:** Our study identifies that there is a positive correlation between increasing BMI and BMD at lumbar vertebrae and at the hips, in both male and female patients. We also identified age as a contributing factor. The relationship between BMI and BMD appears to be more significant in the hip and neck of femur than the lumbar spine. When studying the lumbar spine we found that the association is greater the higher up the lumbar spine, with most positive correlation being in L1 of female patients. This would indicate that using the lower lumbar spine might not be appropriate to assess bone health.

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AB1325

**THE FREQUENCY OF ANTI-DFS70 AUTOANTIBODIES IN JAPANESE WOMEN WITH PERI- AND POST-MENOPAUSAL ARTHRALGIA**

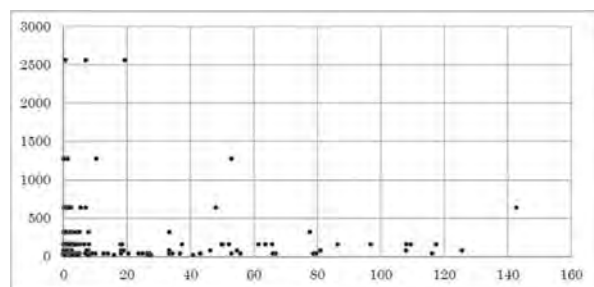
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**Background:** The antinuclear antibody (ANA) test is often used as a screening test to aid in the diagnosis of systemic lupus erythematosus (SLE) and other systemic autoimmune rheumatic diseases (SARD). However, recently it was reported that a certain autoantibody referred to as anti-dense fine speckled 70 (DFS70) are much more common (up to 25%) of non-SARD and healthy individuals but rare (<5%) in SLE and certain SARD. The frequency of anti-DFS70 is even lower (i.e. <1%) if monospecific anti-DFS70 antibodies are found. Some reports suggested that anti-DFS70 are more common in younger females, suggesting that hormonal factors may be responsible for the cognate B cell response.

**Objectives:** The primary objective of our study was to determine the frequency of anti-DFS70 in menopausal women who were referred for evaluation of undifferentiated arthritis (UA).

**Methods:** 282 women including 105 with UA and an age range of 27~91 years (mean=60.3) were enrolled. Menopausal women were divided into pre-, peri-, and post-menopausal stages according to menstrual regularity. (E2), Follicle stimulating hormone (FSH), rheumatoid factor (RF), ANA (by indirect immunofluorescence (IIF) (MBL) anti-cyclic citrullinated peptide antibody (ACPA: MBL ELISA) and C-reactive protein (CRP) were included in the serology workup. Postmenopausal arthralgia was designated PoMA and perimenopausal arthralgia PeMA.

**Results:** In PoMA women who received HRT for two months estradiol levels increased, FSH levels decreased and the joint pain visual analogue scale was reduced by 70%, as compared to baseline. Similarly in PeMA women, administration of 600 mg tocopherol N daily had the same efficacy as that observed in PoMA. The overall frequency of anti-DFS70 of 26.7% (28/105) in PoMA and PeMA women was significantly higher than that in UA females who were diagnosed with rheumatoid arthritis (RA) (7/65:10.8%) or primary Sjogren's syndrome (SjS) (3/31: 9.7%) (p<0.05). In addition, anti-DFS70 Ab was observed primarily in low titer (1:40 – 1:160) ANA positive sera. On the other hand, higher titer ANAs (titer >1/320) were observed in the females that were diagnosed as systemic lupus erythematosus (SLE) (30%) or primary SjS (48.4%), the majority of whom had lower titers of anti-DFS70, although several sera contained both high titer ANA and anti-DFS70 (see figure).



**Abstract AB1325 – Figure 1.** Relationship of ANA titers and anti-DFS70 levels in peri- and post-menopausal women. The majority of anti-DFS70 positive sera had only low to modest ANA titers. ANA titer in vertical axis and anti-DFS70 titers by ELISA on the horizontal axis

**Conclusions:** Anti-DFS70 was found in higher frequency in PeMA and PoMA women than in women who developed a defined systemic autoimmune rheumatic disease such as SLE, SjS or RA. This is the first study to suggest that the presence of this autoantibody may reflect oestrogen fluctuations or deficiency. A negative association between ANA titer and anti-DFS70 levels by ELISA remains to be confirmed in larger studies.

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AB1326

**NICOTINAMIDE PHOSPHORIBOSYLTRANSFERASE MAY BE NEW FACTORS CONTRIBUTING TO OSTEOARTHRITIS**

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**Background:** Obesity is a condition that prolongs chronic inflammation and promotes synthesis and secretion of pro-inflammatory factors by adipose tissue including adipokines<sup>1</sup> and can be one of the significant factors in the progression of osteoarthritis (OA).<sup>2</sup> Nowadays many studies have shown that level nicotinamide phosphoribosyltransferase (Nampt) increases in obesity and can also affect the inflammation in local tissues and together with other adipokines influences the development of OA.<sup>3</sup>

**Objectives:** To study the effect of weight loss over 5 kg on the clinical manifestations of OA, indicators of water, lipid metabolism and Nampt serum levels in patients with OA.

**Methods:** We observed 110 people: 80 patients with OA and 30 healthy individuals in the control group with body mass index (BMI) of 25 to 35 kg/m<sup>2</sup>, aged 18 to 79 years participated in the study.

Nampt level in serum was determined by indirect solid phase ELISA using a commercial test systems (RaiBiotech, cat № EIA – VIS – 1).

**Results:** As overweight patients were recruited in the study, hypocaloric diet low in animal fats and physiotherapy has been recommended to all participants. The first group consisted of patients who were able to reduce body weight by 5 kg and more (18 pers.), the second group – patients with weight reduction of less than 5 kg and patients without any weight loss (62 pers.). Nampt concentration were evaluated in these patients I groups 4,33±0,39 before treatment to 2,40±0,23 ng/ml (t=5,85, p<0,001). In analysing the parameters before and after treatment, it should be noted that we observed significant decrease in the severity of the clinical manifestations of OA, visfatin level, CRP, and glucose levels and lipid profile in the 1st group of patients. These data proves that obesity may be an important risk factor for OA progression. As a result, weight loss results in decreasing metabolic disorder severity. In the second group of patients we have seen a decrease in all the parameters, but a significant difference has been observed only in the level of CRP, level of pain at rest and during walking according to VAS scale and total index on the WOMAC.

**Conclusions:** As a result of our study patients with OA with weight loss of more than 5 kg had more obvious pain relief than patients with the original weight. At the same time a significant improvement has been seen in carbohydrate and lipid metabolism. These findings suggest that there is a possible role of Nampt in the pathogenesis of OA.

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AB1327

**CARDIAC MANIFESTATIONS IN SPONDYLOARTHRITIS: PREVALENCE AND PREDICTIVE FACTORS**

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**Background:** Cardiac involvement is a well-recognised complication of spondyloarthritis (SpA). The spectrum of this condition is large and includes mitral valve disease, conduction disorders and pericarditis, but the aortic disease remains the most characteristic lesion.

**Objectives:** The aim of this study is to determine the prevalence of cardiac manifestations and to assess their predictive factors in a population of Moroccan patients suffering from SpA.

**Methods:** We have conducted a cross-sectional study over two months in our department of rheumatology. All SpA patients fulfilled <sup>ASAS 2009</sup> criteria. They all have had a cardiac check up with research of clinical cardiac manifestation, 12-lead electrocardiogram and trans-thoracic echocardiography.

Data analysis was carried out using the SPSS Statistics 20 software. A univariate analysis as well as multivariate regressions were carried out to identify the factors associated with cardiac manifestations.

**Results:** We have included 61 men and 31 women with a mean age of 37.34 ±12.77 years old. The mean disease duration was 10.59±7.63. The median CRP was 9.60 mg/L (IQR 0–180), the mean ASDAS CRP 2.24±1.30 and the mean BASDAI 2.7±1.99.

Traditional cardiovascular risk factors in our series included dyslipidemia in 15 patients (18.3%), hypertension in 10 patients (10.9%) and type 2 diabetes in 7 patients (7.6%). Mean BMI was 23.88±5.83 Kg·m<sup>-2</sup>. Twenty nine patients (31.9%) were overweight and 10 patients (11%) were obese. Eight patients (8.7%) smoked and 3 patients (3.3%) used alcohol whereas 19 patients (20.7%) had a history of smoking and 6 patients (6.5%) had a history of alcohol use.

Cardiac manifestations were found in 12 patients (13.6%): 3 (3.3%) had aortic regurgitation (AR), 1 (1.1%) had aortic dilatation, 1 (1.1%) had aortic thickening, 2 (2.2%) had mitral thickening, 1 (1.1%) had mitral regurgitation (MR), 1 (1.1%) had mitral stenosis (MS), 3 (3.4%) had pericarditis and 2 (2.2%) had bundle branch block.

In comparison with the group without cardiac manifestations, axial involvement, current enthesitis and extra-articular manifestations were common in patients with cardiac involvement. Furthermore, uveitis was frequent in patients with aortic dilatation and MR. Patients with AR and MS had higher ESR and disease activity compared to the group without heart disease. Patients with pericarditis had an accelerated ESR unlike the group without cardiac involvement.

In univariate analysis, AR was significantly associated with ESR and ASDAS VS (OR=1.03 [1.003–1.063], p=0.028; 2.75 [1.062–7.123], p=0.037, respectively). Pericarditis was significantly associated with ESR (OR=1.03 [1.003–1.062], p=0.029).

In multivariate analysis, cardiac manifestations were significantly associated with current enthesitis and extra-articular manifestations (OR=4.48 [1.078–18.683], p=0.039 and 6.35 [1.156–34.893], p=0.033, respectively).

**Conclusions:** Heart disease was common in our study and was associated with the enthesitis involvement and the severity of SpA.

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#### AB1328 FLARES IN SPONDYLOARTHRITIS: PREVALENCE AND RELATED FACTORS

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**Background:** Spondyloarthritis is a chronic condition characterised by alternated periods of flares and stable disease.

**Objectives:** The aim of this study is to assess the prevalence of patient-reported flares and the validity of this concept through its related factors.

**Methods:** We have conducted a cross-sectional study over two months in our department of rheumatology. All SpA patients fulfilled <sup>ASAS 2009</sup> criteria.

Current and past flares over the last 3 months were recorded. Disease activity and functional status were assessed by the BASDAI score (0–10) and the Bath Ankylosing Spondylitis Functional Index (BASFI; 0–100), respectively. Data analysis was carried out using the SPSS Statistics 20 software. Univariate and multivariate regressions were performed to identify the factors associated with current flare.

**Results:** We included ninety tow patients with SpA, 61 (66.3%) were men. The mean age was 37.34±12.77 years old. The mean disease duration was 10.59 ±7.63 year. The mean BASDAI was 2.7±1.99 and the median BASFI was 14 (IQR 0–100). Thirty-five patients (38%) received antitumor necrosis factor alpha (anti-TNF-α). Twenty-nine patients (31.5%) were currently in flare, and 6 patients (6.5%) reported only past flares.

In univariate analysis, patients reporting current flares had a current enthesitis (OR=3.14 [1.250–7.923], p=0.015) and higher values of BASDAI, ASDAS VS and

ASDAS CRP (OR=2.17 [1.085–4.362], p=0.029; 2.20 [1.448–3.359], p=0.0001; 2.23 [1.495–3.340], p=2.235, respectively). These patients had also more extra-articular manifestations (OR=3.37 [1.326–8.601], p=0.011).

In multivariate analysis, the following factors were associated with current flare: higher BASFI (OR=1.05 [1.013–1.098], p=0.010), protein c-reactive (OR=1.087 [1.016–1.163], p=0.016), ASDAS VS (OR=10.99 [1.921–62.873], p=0.007), current enthesitis (OR=25.00 [2.185–286.146], p=0.01), the presence of extra-articular manifestations (OR=30.66 [1.709–550.049], p=0.02) and the use of non steroidal anti-inflammatory drugs during the last 3 months (OR=125.064 [3.33–4491.0], p=0.009).

**Conclusions:** Our study shows that assessment of flares may provide a good estimation of disease activity.

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**Disclosure of Interest:** None declared

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#### AB1329 BIOLOGIC AGENTS AND RISK OF SERIOUS INFECTIONS IN RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS AND ANKYLOSING SPONDYLITIS: RESULTS BY INTEGRATING TEN-YEAR (2006–2015) ADMINISTRATIVE DATABASES IN THE ITALIAN REGION OF FRIULI VENEZIA GIULIA

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**Background:** Serious infections are a major concern for patients considering biologic agents for rheumatoid arthritis (RA) or psoriatic arthritis (PsA) or ankylosing spondylitis (AS). Evidence from meta-analyses is consistent with an increased risk of serious infections with biologic disease-modifying antirheumatic drugs (bDMARDs);<sup>1</sup> however, long-term real-life studies are scarce and controversial.

**Objectives:** To determine the risk of serious infections (i.e., need of hospitalisation) in patients affected by RA, psoriatic arthritis (PsA) or ankylosing spondylitis (AS), treated by bDMARDs in the Italian region of Friuli Venezia Giulia, approximately 1,200,000 inhabitants.

**Methods:** The regional health information system was used as the source of data. Administrative data from the hospital discharge records database, the medical prescription database, and the database of exemptions from medical charges were linked at the individual patient level through an anonymous univocal stochastic key. A cohort of patients diagnosed for RA, PsA or AS from 2006 to 2015 was identified from specific national exemption codes (006, 045, 054) and followed up to either the end of 2015, or hospitalisation with the main discharge diagnosis of infection, as ICD-9-CM codes, or death, or change of residency out of the Region. Multivariate Cox regression was used to estimate the hazard ratio (HR) of hospitalisation associated with bDMARDs and adjusting for age, sex, Charlson's comorbidity index, calendar year, prescription of steroids and of csDMARDs. Use of bDMARDs was treated as a time-dependent variable.

**Results:** Overall, the cohort consisted of 5596 subjects: 3216 (57.5%) with RA,<sup>1702</sup> (30.4%) with PsA, and 678 (12.1%) with AS. Of them, 940 patients (16.8%) had received at least one prescription of a bDMARDs during the study period. During follow-up, 193 (3.4%) subjects were admitted to the hospital with a primary diagnosis of infection. The most frequent infections were upper and lower respiratory tract infections (86/193, 44.5%), followed by sepsis (19/193, 9.8%), and soft tissue and skin infections (16/193, 8.3%). After adjusting for the abovementioned variables, when starting a bDMARD, the risk of infections was significantly increased, with an observed increased risk of almost 2-fold by the time of the bDMARD prescription (HR 1.694, 95% CI 1.158–2.478, p=0.0066). Compared with patients <40 years if age, the elderly (>=65 years) showed a much higher risk of infections (HR 3.919, 95% CI 2.286–6.716, p<0.0001). Analyses stratified by disease indicated that RA, PsA, and AS patients starting biologic medications have increased risk of infection.

**Conclusions:** By integrating the information coming from ten-year administrative databases, RA, PsA and AS patients starting bDMARDs are at high risk of serious infections. This risk is much higher in the elderly. Upper and lower respiratory tract



infections are the most common infections, supporting the prevention policies by vaccination for influenza viruses and *Str. pneumoniae*, in particular in the elderly population.

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**Disclosure of Interest:** None declared

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#### AB1330 A PRELIMINARY STUDY ON THE BASELINE HRCT SCORING CRITERIA FOR PREDICTING THE FIBROSIS PROGRESSION OF RA-ILD

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**Background:** Interstitial lung disease (ILD) is the most common pulmonary manifestation of RA. The progression of fibrosis in RA-ILD varied differently, and effective predictors of progression were absent.

**Objectives:** To explore the baseline HRCT scoring criteria that can predict progressive fibrosis and provide reference for clinical diagnosis and treatment.

**Methods:** The chest HRCT of RA-ILD patients from 2009 to 2017 were retrospectively analysed, including 102 patients with progressive fibrosis and 50 patients without progressive fibrosis. Progressive fibrosis was defined as honeycombing development or an increase in extent of reticulation on follow-up HRCT. The baseline HRCT evaluation was performed by two thoracic radiologists blinded to all patient data, which including routine interstitial lesion evaluation and fibrosis predictive score. We proposed the baseline HRCT fibrosis predictive score to differentiate progressive fibrosis from the stable patients. The score included two parts, subpleural lesion score and bronchovascular bundle thickening score, with a total score of 0–9 points.

**Results:** In the routine evaluation, peripheral distribution was more common in the progressive fibrosis group (78.43% VS 52%,  $p < 0.05$ ), traction bronchiectasis and traction bronchiolectasis both were more common in the progressive group (41.18% VS 8%,  $p < 0.01$ ; 93.14% VS 46%,  $p < 0.01$ ; respectively). Compared with non-progressive fibrosis group, subpleural reticulation and subpleural linear opacities were more common in the progressive fibrosis group (79.21% VS 28%,  $p < 0.0$ ; 41.80% VS 14%,  $p < 0.01$ ; respectively), subpleural honeycombing was more common in the progressive fibrosis group (41.17% VS 20%,  $p < 0.05$ ), subpleural ground-glass opacity showed no difference between the two groups (52.94% VS 66%,  $p > 0.05$ ). Notably, subpleural honeycombing in the progressive group were all accompanied by the presence of subpleural reticulation and subpleural linear opacities on baseline HRCT. The AUC curve of fibrosis predictive score was 0.87 (95% confidence interval, 0.81, 0.93), indicating that baseline HRCT score had a better judgement value for progressive fibrosis. The cut-off value was 5.5 points (sensitivity was 64%, specificity 94%), that is, baseline HRCT score  $\geq 6$  points was more likely to develop progressive fibrosis. Drug interventions (glucocorticoids, cyclophosphamide) were relatively deficient in the progressive fibrosis group, (26.47% VS 44%,  $p < 0.05$ ; 9.80% VS 22%,  $p < 0.05$ ; respectively). Further analysis showed that treatment situations (glucocorticoids, cyclophosphamide) were similar between the baseline HRCT score  $\geq 6$  points group and the baseline HRCT score  $< 6$  points group (34.78% VS 30.12%,  $p > 0.05$ ; 10.14% VS 16.87%,  $p > 0.05$ ; respectively), suggesting that patients with potential fibrotic tendencies had not been treated actively in the early stage.

**Conclusions:** The baseline HRCT score has a better predictive value for the progressive fibrosis of RA-ILD, traction bronchiectasis and traction bronchiolectasis are helpful to identify progression. The baseline HRCT evaluation may provide a reference for the choice of time for treatment.

**Disclosure of Interest:** None declared

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#### AB1331 SERUM DRUG LEVELS IN THE MANAGEMENT OF RHEUMATOID ARTHRITIS AND SPONDYLOARTHRITIS: A SYSTEMATIC REVIEW

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**Background:** Several studies in rheumatic and other inflammatory diseases treated with tumour necrosis factor-alpha inhibitors (TNFi) support the association between clinical response and trough drug levels (DL). The utility of monitoring DL in rheumatoid arthritis (RA) and spondyloarthritis (SpA) patients on biological

therapy is not clear, so it is important to identify clinical situations in which, the knowledge of DL, would allow an individualised therapeutic decision in the patient, more cost-effective.

**Objectives:** To answer the most relevant clinical questions related to the usefulness of DL measurement in clinical practice: 1) whether, in patients in remission who are candidates for optimisation, DL predict relapse or survival to dose-titration; 2) whether, in patients with primary or secondary failure to biological agents, DL influence prognosis; and 3) whether concomitant use of methotrexate (MTX) influences the association between DL and response.

**Methods:** An electronic search of the major databases was performed, Medline, Embase and Cochrane Library, from inception to December 2016. We included articles published in English or Spanish on patients with RA, SpA or both, treated with TNFi, tocilizumab or abatacept, and related to answer any of the three questions of the target research. Overall characteristics and outcomes of the studies were collected in a table of evidence and the quality of the studies was assessed with a scale based on the Oxford levels of Evidence.

**Results:** The electronic search strategy yielded 1749 articles, twelve of which were included in this systematic review. 2 studies responded the first question, 5 the second, and 7 the third. These studies were mainly observational studies, 6 retrospective and 4 prospective cohort studies, and 2 randomised clinical trials. Sample sized varied from 24 to 395 patients, for a total of 1482 patients analysed. A total of 1281 RA patients were included (64 in the first question, 243 in the second and 1038 in the third) and 201 SpA patients (32 in the first and second questions, 169 in the third). Studies were small and with limitations, but suggest that measurement of DL may be useful in patients in remission, that higher DL predict a longer relapse-free optimisation, and in patients with failure to a biological agent, treatment may need individual adjustment according to the presence of DL or anti-drug-antibodies. In addition, MTX influences the association between response and DL in most studies, with greater controversy in tocilizumab and SpA patients.

**Conclusions:** Monitoring DL would allow optimal use of current biological therapies, but more studies and of better quality are needed to draw definitive conclusions. In addition, future research should be performed to determine therapeutic ranges of DL, so that the proposed algorithms can be used in a standardised and reliable manner.

**Disclosure of Interest:** None declared

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#### AB1332 FACTORS ASSOCIATED TO PERSISTENCE ON GOLIMUMAB IN PATIENTS WITH INFLAMMATORY ARTHRITIS OF THE BIOBADASER REGISTRY

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**Background:** Persistence to treatment may be used as a surrogate marker for long-term treatment success

**Objectives:** To assess the probability of persistence on golimumab (GOL) up to 5 years after treatment initiation and the factors associated to longer persistence

**Methods:** BIOBADASER is the Spanish registry of biological drugs of the Spanish Society of Rheumatology and the Spanish Medicines Agency. A data-base analysis was done in October 2017 on all the patients who had initiated GOL for one of the approved indications (rheumatoid arthritis [RA], axial spondyloarthritis [SpA] or psoriatic arthritis [PsA]). The probability of persistence was calculated with a Kaplan-Meier test. Factors related to persistence were analysed with a Cox-regression model.

**Results:** 353 patients were included (105 [29.8%] RA, 147 [30.6%] axial SpA and 101 [28.6%] with PsA), mean age 52<sup>11</sup> years, 55% women). Median duration of disease at the onset of GOL was 8.0 [2.8–15.0] years. GOL was the first biological drug in 40.1% of the patients, second in 30.1% and third or further biological in 29.8%. Concomitant medication at GOL initiation was methotrexate (MTX) (33.7%), sulphasalazine (SSZ) (6.1%), leflunomide (LEF) (12.7%), steroids (CS) (26.0%). At the last observation on GOL, 32.0% were on MTX, 5.8% on SSZ, 12.8% on LEF, 16.3% on CS. The probability of persistence on GOL since treatment initiation was 85.9% at year 1 (95% CI 81.4–89.5), 73.7% at year 2 (67.1–79.1), 68.5% at year 3 (60.5–75.1), 60.6% (50.2–69.5) at year 4 and 57.1% (44.9–67.5) at year 5. Persistence was similar for RA, axial SpA or PsA patients (p log-rank 0.070), and higher when GOL was used as first biological agent (p log-rank  $< 0.001$ ). As first biological drug the probability of persistence was 94.5%

(year 1) and 85.4% (year 2), (insufficient number of cases to assess persistence at year 3 or further). As second biological drug, it was 89.8% (year 1), 75.2% (year 2), 67.4% (year 3) and 59.2% (year 4) and as third biological drug the figures were, respectively, 69.6%, 58.4%, 54.5% and 46.1%. Cox-regression analysis (table 1) showed that the probability of persistence on GOL therapy was higher in first vs second or third biological line patients (Hazard Ratio for discontinuation [HR]: 2.30 [95% CI: 1.16–4.55] for second and 3.92 [2.07–7.39] for third line), and in patients with concomitant MTX (HR discontinuation=0.55 [0.33–0.91]), and lower in those needing CS (HR discontinuation=2.83 [1.72–4.66]).

**Abstract AB1332 – Table 1.** Factors related to persistence of golimumab treatment

	Hazard Ratio of Discontinuation	95% Confidence Interval	p
<b>Initial Model</b>			
Gender (women vs men)	1.23	(0.62-2.44)	0.56
Age at golimumab initiation	1.01	(0.99-1.04)	0.25
Disease duration	0.99	(0.95-1.02)	0.38
Smoking habit	1.67	(0.85-3.26)	0.13
Overweight (vs normal)	1.61	(0.74-3.52)	0.23
Obesity (vs normal)	1.53	(0.64-3.66)	0.33
Second vs first biological drug	3.06	(1.28-7.32)	0.01
Third vs first biological drug	5.22	(2.18-12.49)	<0.01
Axial SpA vs RA	0.79	(0.36-1.73)	0.55
PsA vs RA	0.59	(0.27-1.29)	0.19
Methotrexate	0.41	(0.21-0.80)	0.01
Steroids	4.26	(2.26-8.04)	<0.01
<b>Final Model</b>			
Gender (women vs men)	1.38	(0.84-2.27)	0.21
Age at golimumab initiation	1.01	(1.00-1.03)	0.14
Second vs first biological drug	2.30	(1.16-4.55)	0.02
Third vs first biological drug	3.92	(2.07-7.39)	<0.01
Methotrexate	0.55	(0.33-0.91)	0.02
Steroids	2.83	(1.72-4.66)	<0.01

**Conclusions:** In patients with RA, axial SpA or PsA, the probability of persistence on GOL after initiation was high. The retention rate was higher both in patients with GOL as first biological drug and in those with concomitant therapy with MTX, and lower in those needing CS.

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**AB1333 RETENTION RATES OF ADALIMUMAB, ETANERCEPT, AND INFLIXIMAB AS BIOTHERAPIES FOR RHEUMATOID ARTHRITIS, SPONDYLOARTHRITIS, OR PSORIATIC ARTHRITIS PATIENTS IN DAILY PRACTICE IN AUVERGNE (FRANCE)**

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**Background:** The use of TNF- $\alpha$  inhibitors, has considerably improved the treatment of rheumatoid arthritis (RA), spondyloarthritis (SpA), and psoriatic arthritis (PsA). The most widely used anti-TNFs are infliximab (IFX), adalimumab (ADA), and etanercept (ETN). Their efficacy and safety have been demonstrated in randomised controlled trials, though of short duration and involving a selected patient population differing from those seen in daily practice.

**Objectives:** To compare, in real-life settings, the retention rates of anti-TNF treatments (ETN, ADA, or IFX) initiated as first-line biotherapy following their approval in the three clinical indications.

**Methods:** Monocentre retrospective cohort involving patients on initial anti-TNF therapy for RA, SpA, or PsA since 2006.

**Results:** Anti-TNF treatment was initiated on 228 RA (ETN 160, ADA 45, or IFX 23), 208 SpA (ETN 91, ADA 62, or IFX 55), and 81 PsA (ETN 40, ADA 26, or IFX 15) patients. Treatment retention rates at 1, 3, and 5 years were 82%, 53%, and 44% in RA; 75%, 57%, and 49% in SpA; 75%, 64%, and 51% in PsA, with no differences detected among the pathologies ( $p=0.96$ ). Retention rates at 1, 3, and 5 years did not differ among the 3 anti-TNFs either for all pathologies included (ETN: 80%, 57%, and 43%; ADA: 80%, 58%, and 51%; IFX 72%, 56%, and 52%;  $p=0.75$ ) or each pathology alone (RA: ETN: 83%, 55%, and 41%; ADA: 83%, 51%, and 51%; IFX: 76%, 44%, and 44%,  $p=0.84$ ; SpA: ETN: 78%, 57%, and 48%; ADA: 78%, 59%, and 46%; IFX: 68%, 55%, and 52%,  $p=0.81$ ; PsA: ETN: 70%, 60%, and 36%; ADA: 79%, 69%, and 69%; IFX: 80%, 66%, and 53%,  $p=0.65$ ). Overall, 89 RA, 85 SpA, and 28 PsA patients discontinued treatment for inefficacy (32%) or side effects (SE, 9%). In RA, predictors for treatment discontinuation were: Disease activity (DAS 28 ESR HR: 1.27 [1.05–1.55]); DAS28-CRP HR: 1.27 [1.03–1.60]), (CRP HR: 1.01 [1.01–1.02]), and corticosteroid intake (HR: 2.05 [1.027–3.32]). Concomitant methotrexate intake tended to decrease the

treatment discontinuation risk (HR: 0.64 [0.41–1.01]). Predictors for treatment discontinuation due to inefficacy were similar (DAS28 ESR, HR: 1.31 [1.05–1.63]; DAS28 CRP, HR: 1.33 [1.04–1.72], CRP HR: 1.02 [1.01–1.03]), corticosteroid intake HR: 3.79 [2.02–7.11]). We were unable to identify any predictors for treatment discontinuation due to SE, though corticosteroid intake was found to be protective (HR: 0.23 [0.07–0.71]). In SpA, the sole predictor for treatment discontinuation identified was increased BASDAI score (HR: 1.02 [1.01–1.04]), while the sole predictor for treatment maintenance was inflammatory syndrome (CRP HR: 0.97 [0.95–0.99]). Similar findings were seen for treatment discontinuation due to inefficacy (BASDAI HR: 1.03 [1.01–1.05]); CRP HR: 0.98 [0.96–0.99]). We were unable to identify any predictors for treatment discontinuation due to SE. In PsA, active smoking was revealed to be a predictor for treatment discontinuation due to inefficacy (HR: 2.234 [1.02–4.91]).

**Conclusions:** ETN, ADA, and IFX display similar treatment retention rates in RA, SpA, or PsA without between-agent differences.

**Disclosure of Interest:** None declared

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**AB1334 EVALUATION OF DYNAMICS OF MORTALITY FROM DISEASES OF THE BONE-MUSCULAR SYSTEM IN KARAKALPAKSTAN**

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**Background:** Karakalpakstan is now mostly desert and is located in western Uzbekistan near the Aral Sea, in the lowest part of the Amu Darya basin. The desertification of the Aral Sea has brought a lot of dust in the air, and respiratory diseases – bone-muscular diseases – have become the largest local health problem among the population of Karakalpakstan, a region in the North Western part of Uzbekistan.

**Objectives:** To assess the dynamics of mortality trends from diseases of bone-muscular system (BMS) in the Karakalpakstan region in 2010–2015

**Methods:** To study mortality from BMS, databases on mortality of residents in Karakalpakstan for 2010–2015, obtained with the help of an automated mortality registration system, were used to automatically code and select the original cause of death in accordance with the rules of ICD-10.

**Results:** In the Karakalpakstan region, there has been a trend of a significant increase in mortality from BMS from 3.0 in 2010 to 5.6 per 1 000 in 2015 (1.9 times), with a slight decrease in the death rate from the BMS in Uzbekistan from 1.7 in 2010 to 1.6 in 2015 per 100 thousand people (the rate of decline is 5.9%). So that Decrease in the mortality rate from diseases of the musculoskeletal system in Uzbekistan from 1.7 to 1.6 per 100 thousand of population (the rate of decrease is 5.9%) and the growth of mortality rates from diseases of the musculoskeletal system was 1.9 times from 2001 to 2015

**Conclusions:** The growth of mortality rates from musculoskeletal system diseases in the Karakalpakstan region is not related to the rates of overall mortality of the population, but is more reliable due to the use of the automated system for recording mortality, as well as training physicians to codify medical and statistical diagnoses.

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**AB1335 SERUM MMP-3 IS CLOSELY RELATED TO KNEE JOINT SYMPTOMS IN RHEUMATOID ARTHRITIS PATIENTS: A CROSS-SECTIONAL STUDY FROM KURAMA COHORT**

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**Background:** Joint damage progression occurs within the first 2 years of rheumatoid arthritis (RA).<sup>1</sup> Large joints are often involved in RA patients. The knee joint, in particular, is affected in about 30% of RA patients.<sup>2</sup> Knee joint disability in RA is thought to be one of the most important prognostic factors decreasing quality of life. However, few studies have focused on what would influence knee joint function in RA patients. Therefore, a cross-sectional study on this subject was

conducted using a RA patient cohort: the Kyoto University Rheumatoid Arthritis Management Alliance (KURAMA) cohort.

**Objectives:** The purpose of this study is to clarify risk factors related to functional disability in knee joint from a RA cohort.

**Methods:** A total of 447 female RA patients (mean age; 63.7 years) were recruited in KURAMA cohort. Clinical data included age, disease duration (DD), Steinbrocker stage and class, anti-cyclic citrullinated peptide antibody (anti-CCP), rheumatoid factor (RF), C-reactive protein (CRP), matrix metalloproteinase-3 (MMP-3), Disease Activity Score 28 using CRP (DAS28-CRP), and visual analogue scale for pain (Pain-VAS). Knee function was assessed by the scores of the Japanese Knee Osteoarthritis Measure (JKOM) questionnaire.<sup>3</sup> The correlations between the total JKOM score and each factor were evaluated by univariate and multivariate regression analyses.

**Results:** A total score of JKOM had a median value of 17 points, an interquartile range of 5.5 to 43.5 points. Univariate analyses showed that age, DD, stage, class, anti-CCP titer, CRP, MMP-3, DAS28-CRP, and Pain-VAS were significantly correlated with total JKOM score (table 1). Multivariate regression analysis with JKOM as the objective variable revealed that Pain-VAS ( $\beta=0.63$ ,  $p<0.01$ ), age ( $\beta=0.23$ ,  $p<0.01$ ), and MMP-3 ( $\beta=0.16$ ,  $p<0.01$ ) were extracted as significant factors (table 2).

**Abstract AB1335 – Table 1.** Pearson's correlation coefficients (r) between each risk factor for knee disability and total JKOM score.

Parameter	r	p
Age	0.32	< 0.01
Disease duration	0.22	< 0.01
Steinbrocker stage	0.24	< 0.01
Steinbrocker class	0.29	< 0.01
Anti-CCP	0.13	0.01
CRP	0.20	< 0.01
MMP-3	0.33	< 0.01
DAS28-CRP	0.54	< 0.01
Pain-VAS	0.66	< 0.01

Parameter	$\beta$	p
Age	0.23	< 0.01
MMP-3	0.16	< 0.01
Pain-VAS	0.63	< 0.01

**Abstract AB1335 – Table 2.** Multivariate regression analyses of risk factors for knee disability and total JKOM scores.

**Conclusions:** Pain has the most significant influence on knee joint symptoms in RA patients. Serum MMP-3 is closely related to knee joint disability, and attention should be paid to knee joint dysfunction in RA patients with high serum MMP-3.

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AB1336

#### MUSCULOSKELETAL DISORDERS IN HEMODIALYSIS PATIENTS: DIFFERENT DISEASE CLUSTERING ACCORDING TO AGE AND DIALYSIS VINTAGE

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**Background:** The number of patients suffering from stage 5 Chronic Kidney Disease is constantly increasing and their life expectancy has improved due to the hemodialysis technique. Musculoskeletal disorders remain a major problem in long term hemodialysis patients. Frequency and severity of these manifestations increase with the length of the dialysis.

**Objectives:** To identify diseases clustering profiles of musculoskeletal disorders in hemodialysis patients.

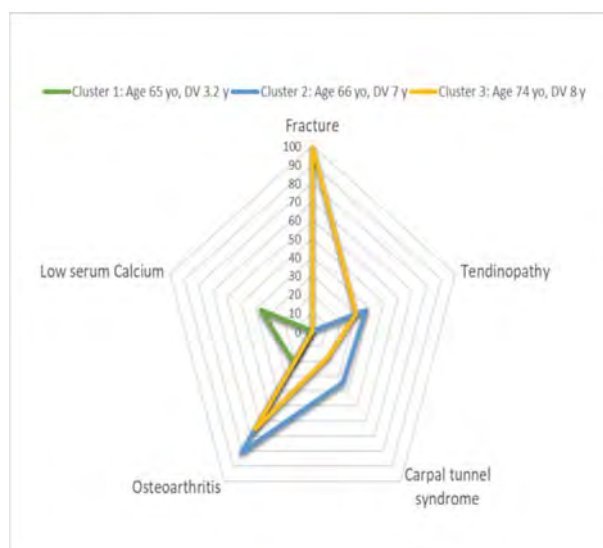
**Methods:** All adult patients in the hemodialysis centre were included in this cross-sectional study. For each patient, we filled a data collection sheet including basic demographic characteristics, musculoskeletal symptoms, biologic parameters and treatments. Musculoskeletal disorders were classified by a rheumatologist into pre-defined diagnostic categories: Osteoarthritis, Fractures, Tendinopathies, Carpal Tunnel Syndrome, Crystal deposition disease and Others. Prevalences were presented and a cluster analysis was performed.

**Results:** Eighty-nine patients were included (table 1). Mean age was 67.5±12 years. 43.8% were female. Dialysis vintage was 5.7±5.37 years. Musculoskeletal symptoms were reported by 76.4% of the patients. Pain was the most frequent symptom (44.9%). The main disorders were osteoarthritis (53.9%), fracture (27%), tendinopathy (22.5%), carpal tunnel syndrome (18%), and chondrocalcinosis (9%). Musculoskeletal symptoms were significantly related to the dialysis vintage and age ( $p=0.044$ ,  $p=0.035$  respectively). All disorders categories were significantly associated with dialysis vintage, particularly increasing after the seventh year of dialysis. Cluster analysis identified three patient profiles: younger with low calcium levels, younger but long dialysis vintage with osteoarthritis and carpal tunnel syndrome, older and long dialysis vintage with fractures (figure 1).

**Abstract AB1336 – Table 1**

#### Population characteristics

N	89
Age (years±SD)	67.5±12.6
Sex ratio (M/F)	49/39
Age at the start of hemodialysis year(±SD)	61.5±14.6
Dialysis vintage (years±SD)	5.7±5.37
Diagnostic nephropathy	
Diabetes	27 (30.3%)
Hypertension	26 (29.2%)
Chronic glomerulonephritis	13 (14.6%)
Polycystic kidney disease	10 (11.2%)
Chronic interstitial nephropathy	7 (7.9%)
Others	6 (6.7%)



**Abstract AB1336 – Figure 1**



**Conclusions:** The prevalence of the musculoskeletal manifestations is high (76.4%) in the hemodialysis population. Musculoskeletal disorders seem to cluster differently according to age and dialysis vintage.

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### AB1337 CELIAC DISEASE AND RISK OF SARCOIDOSIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

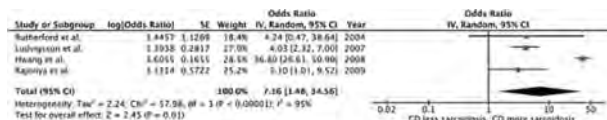
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**Background:** Several epidemiologic studies have demonstrated that patients with celiac disease may be at an increased risk of developing sarcoidosis. However, the data on this risk remain inconsistent.

**Objectives:** To compare the risk of developing sarcoidosis between patients with celiac disease and individuals without celiac disease.

**Methods:** A literature review was performed using MEDLINE and EMBASE database from inception to December 2017. Studies that compared the risk of sarcoidosis among patients with celiac disease versus those without celiac disease were included. The inclusion criteria were as follows: <sup>1</sup> case-control, cross-sectional or cohort studies that investigated the risk of sarcoidosis among patients with celiac disease compared with individuals without celiac disease and <sup>2</sup> odds ratios (OR), relative risks (RR), hazard ratios (HR) or standardised incidence ratios (SIR) with 95% confidence intervals (CI) or sufficient raw data to calculate these ratios were provided. Study eligibility was independently determined by 3 investigators. Differences in the determination of study eligibility were resolved by mutual consensus. Pooled odds ratio (OR) and 95% confidence interval (CI) were calculated using a random-effect, generic inverse variance method of DerSimonian and Laird.

**Results:** Of 375 retrieved studies, 4 studies (2 case-control studies and 2 cohort studies) with 6 93 639 participants met our eligibility criteria and were included in analysis. We found a higher risk of sarcoidosis among patients with celiac disease compared with individuals without celiac disease with the pooled OR of 7.16 (95% CI, 1.48–34.56). The statistical heterogeneity of this study was high ( $I^2=95\%$ ). Funnel plot was relatively symmetric and did not suggest the presence of publication bias in favour of positive studies.



Abstract AB1337 – Figure 1. Forest plot of this meta-analysis

**Conclusions:** This systematic review and meta-analysis found a significantly higher risk of sarcoidosis among patients with celiac disease.

**Disclosure of Interest:** None declared

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### AB1338 COHORT OF PARAGUAYAN PATIENTS WITH EARLY ONSET ARTHRITIS

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**Background:** The PANLAR-EOA (early-onset-arthritis) project includes panamericanrheumatologists to determine regional characteristics of patients with early onset arthritis.

**Objectives:** To describe the cohort of Paraguayan patients included in PANLAR-EOA project.

**Methods:** Longitudinal, prospective, multicentric study. Patients were included according to the PANLAR-EOA project and registered in REPANARC (www.panlareoa.org) database. At baseline and annual visits, a large number of demographic, clinical and analytical variables were recorded. Quantitative variables were characterised by their means and standard deviations, while the qualitative

variables were characterised according to the percentage of patients. The comparison of epidemiological and clinical variables was performed using the chi-squared test and the Wilcoxon test respectively for qualitative and quantitative variables, respectively.

**Results:** 136 patients with early onset arthritis were included, out of which 88 completed the 12 months follow up and 58 the 24 months one. In these, 86% were female with a median age of 43.9±13.2 years. The most frequent race was mestiza in 80.1%. According to GRAFFAR index, middle class was the predominant social stratum (9.8±3.1). The average number of years of schooling was 12.8±3.8. Polyarticular onset was registered in 61% patients. During follow-up, 43.1% had positive rheumatoid factor and 56.5% positive anti-CCP. The diagnostic delay was 3.9±3.0 months. Initially, 63.2% (86/136) were diagnosed with rheumatoid arthritis (RA) and 36.8% (50/136) with undifferentiated arthritis (UA). The most frequent treatment was methotrexate (85.3%, 90.9%, and 89.3% at baseline, 1 and 2 years of follow-up respectively). During follow-up, a significant diagnostic change was observed in patients with UA (p=0.004, OR=2.9 [95%CI, 1.4–6.5]). The variables associated with RA diagnosis were presence of anti-CCP (p=0.000, OR=15.8 [95%CI, 5.4–51.1]), rheumatoid factor (p=0.000, OR=9.2 [95%CI, 3.4–27.0]), smoking (p=0.032, OR=8.8 [95%CI, 1.1–404.7]), high body mass index (p=0.041, OR=1.94 [95%CI, 0.2–4.1]) and high activity measured by the DAS28 index (p=0.01). After one year of follow-up there was a significant decrease in disease activity according to DAS 28 (p=2.2e-09 [95% CI, -1.5, -0.9]), SDAI (p=1.2e-11 [95% CI, 18.2, -11.2]) and HAQ (p=7.2e-08 [95% CI, -0.7, -0.4]). Similar results were found at the 2nd year of follow-up, DAS28 (p=8.8e-06 [95% CI, -1.6, -0.7]), SDAI (p=2.1e-07 [95% CI, -20.0, -10.3]) and HAQ (p=3.4e-08 [95% CI, -0.9, -0.5]).

**Conclusions:** In this cohort of early onset arthritis, diagnostic delay was lower than that observed in other series and the rate of change from diagnosis of UA to RA was statistically significant during the first year of follow-up. A good control of the inflammatory activity of the disease was observed, with a significant improvement of all the variables analysed during its evolution.

**Disclosure of Interest:** None declared

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### AB1339 ASSOCIATION OF ANTI-THYROID ANTIBODIES AND MUSCULOSKELETAL PAIN IN PATIENTS WITH AUTOIMMUNE THYROIDITIS

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**Background:** Autoimmune thyroiditis is closely associated with autoimmune diseases and can exhibit musculoskeletal pain as a clinical manifestation; the exact pathogenic mechanism of coexistence with other autoimmune disorders has not been clearly defined. There are very few studies that describe the association of anti-thyroid antibodies and musculoskeletal pain in patients with controlled autoimmune thyroiditis without rheumatologic disease

**Objectives:** To Determine the association of anti-thyroid antibodies and musculoskeletal pain in euthyroid patients with autoimmune thyroiditis who doesn't meet any criteria of a rheumatic disease

**Methods:** Fifty consecutive euthyroid (TSH test in a range of 0.34–5.6 μU/mL and Ft4 0.54–1.64 ng/dL) patients with a diagnosis of autoimmune thyroiditis (positive anti peroxidase antibodies [TPOAb] ≥10 IU/mL and/or anti thyroglobulin antibodies [TGAb] ≥5 IU/mL), who attended the endocrinology clinic in an one-year period were included. At the moment of enrollment the patients didn't meet any classification criteria of a rheumatic disease. The presence of musculoskeletal pain was assessed using the survey "Program of modified community orientation for rheumatic diseases" (COPCORD) phase II, validated for the Mexican population, and used as a tool to determine the prevalence of rheumatic and musculoskeletal diseases [6]. COPCORD questionnaire consists of several sections such as number of affected joints, anatomic sites and pain severity measured by Visual Analogue Scale (VAS) with values ranged from 0 to 10. Descriptive statistical analyses were performed using the mean, range and standard deviation of variables. Correlations of statistical significance between groups were carried out using Spearman's rank correlation. P values <0.05 were considered to be significant.

**Results:** 26 patients were TPOAb positive (830.76 IU/mL ± 1169.33 IU/mL); 41 patients were TGAb positive (257.126 IU/mL ± 629.344 IU/mL). There was a positive correlation between the presence of TPOAb with the number of affected joints (Spearman  $r=0.9618$ ,  $p=0.00001$ ) and with pain intensity (Spearman  $r=0.9552$ ,  $p=0.00001$ ). Similarly, there was a positive relationship between TgAb with the number of joints affected ( $r=0.07800$ ,  $p=0.00001$ ) and with pain intensity ( $r=0.7268$ ,  $p=0.00001$ ).

Correlation, (n)	Spearman <i>r</i>	<i>p</i> value
TPOAb versus intensity of pain, 26	0.9552	0.00001
TPOAb versus number of joints affected, 26	0.9618	0.00001
TPOAb versus age, 26	-0.3007	0.1328
TPOAb versus body mass index (BMI), 26	0.0024	0.9904
TgAb versus intensity of pain, 41	0.7268	0.00001
TgAb versus number of joints affected, 41	0.7800	0.00001
TgAb versus age, 41	-0.1615	0.6959
TgAb versus body mass index (BMI), 41	0.2172	0.1694

Abstract AB1339 – Figure 1

**Conclusions:** Our results suggests that in patients with controlled autoimmune thyroiditis, anti-thyroid antibody titers have a positive correlation with the presence of musculoskeletal pain and its severity; these findings deserve further study and research to establish the relationship of different autoantibodies present in autoimmune thyroid disease and musculoskeletal pain, as well as their role in rheumatic diseases, with a clinical importance not yet well established in this latter group.

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AB1340

#### DIFFERENTIAL CHARACTERISTICS IN A COHORT OF COLOMBIAN PATIENTS WITH THREE AUTOIMMUNE/AUTOINFLAMMATORY DISEASES: A NATIONAL REGISTRY UNDER A RISK MANAGEMENT MODEL

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**Background:** Latin American (LA) population with autoimmune/autoinflammatory (AID/AI) diseases is considered as a minority, with special characteristics of ancestry, socioeconomic status (SES) and cultural among others, with particular manifestations and prognosis outcomes

**Objectives:** To describe the largest cohort of patients with rheumatoid arthritis (RA), spondyloarthropathies (SpA) and systemic lupus erythematosus (SLE), in Colombia, evaluated through the social health care security system (SHCSS) and under a risk management model highlighting shared characteristics, as well as differences

**Methods:** A national register-based retrospective cohort study of the SHCSS since 2015 assessing three AID/AI diseases (RA, SLE, SpA) treated in a centre of excellence in rheumatology, under a risk management program in six cities of Colombia. Data about covered population was obtained from the integral information system of SHCSS (SISPRO). Clinical records of patients with AID/AI ICD-10 codes were selected. Adult patients fulfilling international validated diagnoses criteria for the three AID/AI were included. A survey data collection instrument was implemented. Analyses (SAS software V9.4) with standard statistical methods (Polytomous logistic regression, Chi-squared test Fisher's exact test, and Kruskal-Wallis test) were done. Odds ratio (OR) and 95% percent CIs were computed ( $p < 0.05$ )

**Results:** Of 1 62 487 population covered from national security system (SISPRO data) having AID/AI diseases, 71 515 were evaluated in the 6 cities and 12 323 records were selected of patients by population census attended in the institution. A total of 5372 records meet international validated criteria and were included (RA=3576, SLE=1175, SpA=621). RA patients were older, had lower educational level and SES, longer duration of the disease and late age at onset. Cardiovascular compromise was high in RA and SLE. Polyautoimmunity was predominant in SLE. A total of 89% of patients were under steroids treatment (SLE and RA) and 35% in SpA. Biologics were indicated in 59% (SpA), 23% (RA) and 7,1% (SLE). EuroQoL five dimensions scores were significantly better in the SLE group (time of admission). Additional clinical characteristics are described in Table 1

Abstract AB1340 – Table 1. Main Clinical characteristics in the three groups

Clinical compromise	RA n=3576		SLE n=1175		SpA n=621	
	N	%	N	%	N	%
Cardiovascular*	1397	39,1	371	31,6	13	2,1
Pulmonary *	112	3,1	65	5,5	6	0,96
Central and peripheral nervous system*	67	1,8	63	5,4	5	0,8
Cutaneous*	170	4,7	881	75	298	47,9
Ocular*	415	11,6	130	11,1	112	18
Haematological*	90	2,5	970	82,5	10	1,6
Hepatic*	141	3,9	54	4,6	51	8,2
Renal*	11	0,3	473	40,2	4	0,64
Polyautoimmunity**	137	3,8	248	21,1	15	2,4

\*p-value<0.0001 \*\* p-value<0,0001

**Conclusions:** This is the largest cohort evaluated through the SHCSS and under a risk management model in Colombia (LA). This population share special characteristics, highlighting differences between these three AID/AI diseases that are frequently evaluated in the same scenario in real life conditions by the rheumatologist. It is worth noting the specific poor prognosis factors of RA and the high percentage of patients under biological treatment in SpA group, which implies a high cost for the health system

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AB1341

#### PROFILE AND IMPORTANT CHARACTERISTICS OF RHEUMATOLOGICAL DISEASES MANAGED OVER ONE YEAR IN A URBAN UNIVERSITY BASED RHEUMATOLOGY CLINIC IN KUALA LUMPUR, MALAYSIA

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**Background:** The Rheumatology Unit of University Malaya in Kuala Lumpur is cases that are managed as outpatient over a period of 1 year. The data is analysed to provide the required information Details regarding therapy with biologics and small molecules are collected and analysed.

**Objectives:** The main objective is to create a database and registry of all the cases that are managed as outpatient over a period of 1 year. The data is analysed to provide the required information Details regarding therapy with biologics and small molecules are collected and analysed.

**Methods:** A case report form was designed for each patient, which include fields capturing first time visit and subsequent visits. Information captured were demographic data, disease diagnosis and duration, clinical features, laboratory values, co-morbidity and current medications. Longitudinal data was captured. All information were entered into RedCap software with an institutional license. SPSS statistical analysis software was used.

**Results:** Total number of patients in 2017 was 2329. The total number of patient visits was 8255. There was preponderance of females (1,856, 79.7%) compared to males (473, 20.3%). For ethnicity, Chinese patients constitute the most (1,041, 44.5%), followed by Malay (697, 29.8%), Indian (565, 24.2%) and others ethnicities (34, 1.5%). In this population, 3 most common rheumatological diseases seen are Rheumatoid arthritis (760, 32.6%), osteoarthritis (610, 26.2%) and Systemic Lupus Erythematosus (514, 22.1%). Following in descending order are gout (158, 6.8%), soft tissue rheumatism (153, 6.6%), psoriatic arthritis (118, 5.1%), Sjogren syndrome (102, 4.4%), scleroderma (58, 2.5%), mixed connective tissue diseases (49, 2.1%), vasculitis (44, 1.9%), ankylosing spondylitis (36, 1.5%), overlap syndrome (29, 1.2%), Adult onset Still's disease (26, 1.1%), dermatomyositis/polymyositis (25, 1.1%), and fibromyalgia (20, 0.9%). Most recent management activity after clinical assessment, majority of patients (1391, 60.8%) were noted to have no change in management (same therapy continued, but not in remission), followed by those in remission (544, 23.6%). 215 (9.3%) patients require escalation therapy. 13 patients (0.6%) required hospitalisation. 112 (4.9%) had de-escalation therapy. There were 13 deaths (0.6%). Most patients on biologics or small molecules are diagnosed with either Rheumatoid arthritis, SLE, Ankylosing Spondylitis and Psoriatic Arthritis. 44.7% of the patients on biologics have moderate disease activity while 33% of them have mild disease activity. 13.8% of them had achieved remission and 8.5% of them continued to have severe disease activity. The overall assessment of disease activity noted that 57 (2.5%) had severe

disease activity, 550 (23.9%) had moderate disease activity, 1139 (49.5%) considered as mild disease activity and 557 (24.2%) were considered to be in remission.

**Conclusions:** This study has created a database and registry from which important data has been derived. Majority of the patients are being managed sub-optimally, most likely due to limited access to advanced therapies in prominent rheumatological diseases that are intrinsically active and respond modestly to conventional DMARDs and therapy. Further analysis is ongoing

**Disclosure of Interest:** None declared

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**AB1342 RHEUMATIC DISEASES PREVALENCE AND QUALITY OF LIFE IN SARAGURO INDIGENOUS POPULATIONS OF ECUADOR: A CROSS-SECTIONAL COMMUNITY-BASED STUDY**

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**Background:** Rheumatic diseases are more prevalent and aggressive in indigenous population groups, in which providing medical attention poses a challenge for the rheumatologist.

**Objectives:** To estimate the prevalence of musculoskeletal (MSK) disorders and rheumatic diseases in the Saraguro indigenous people and their impact on the quality of life.

**Methods:** Cross-sectional analytical study carried out in the community of Saraguro using the COPCORD methodology. Mixed and randomised sampling techniques were employed. The following validated questionnaires were administered: 1. Screening for musculoskeletal (MSK) disorders and rheumatic diseases. 2. A sociodemographic questionnaire. 3. A functional capacity questionnaire (HAQ-DI) and an instrument to measure workload and repetitive movements. 4. Quality of life (EQ-5D3L). Cases with MSK disorders were reviewed by rheumatologists within the community.

**Results:** A total of 2687 individuals over 18 years of age participated, with an average age of 44 (SD 19.9) years; 1690 (62.9%) were women, 872 (32.4%) were Kwichua speakers; 2108 (78.4%) were employed, of these 32.5% were farm workers. MSK pain was reported in 1244 (46.3%); pain was severe in 448 (36%); 868 (69.7%) used some medical treatment and 1013 (81.4%) used traditional medicine. The most prevalent self-reported comorbidities were anxiety (55.5%) and depression (46.8%). Rheumatic diseases were diagnosed in 861/1244 (69.2%), with the following most prevalent conditions: Low back pain 9.3%, hand osteoarthritis 7.2%, knee osteoarthritis 6.5%, RRPS (rheumatic regional pain syndrome) 5.8%, fibromyalgia 1.8%, rheumatoid arthritis (RA) 1.3%. Disability (HAQ >0.8) was observed in 356 (28.6%), whereas loading and pushing objects heavier than 20 kg and shaking hands was significantly associated with MSK pain. The regression models showed a significant association with a lower quality of life in those with lower education levels (OR=0.89; 95% CI 0.88 to 0.91, p<0.001), physically demanding jobs (OR=0.54; 95% CI 0.42 to 0.69, p<0.001), cooking with firewood (OR=1.55; 95% CI 1.05 to 2.30, p=0.02), high blood pressure (OR=2.31; 95% CI 1.73 to 3.10, p<0.001), and rheumatic diseases, especially RA (OR=5.52; 95% CI 2.48 to 12.27, p<0.001) and hands OA (OR=2.05; 95% CI 1.44 to 2.91, p<0.001). One finding is that having RA was associated with cooking with firewood, and that smoking was almost nonexistent in this population. This suggests that wood smoke pollutants play a similar role to that described with tobacco smoke.

**Conclusions:** A high prevalence of MSK disorders, rheumatic diseases and RA was found. The prevalence of rheumatic diseases was associated with a lower education level, cooking with firewood, and physically demanding jobs. The greatest impact on the quality of life in all dimensions was on the individuals with RA and hand OA.

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**Disclosure of Interest:** None declared

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**AB1343 PREVALENCE OF AUTOIMMUNE DISEASES IN CATALONIA: A POPULATION BASED STUDY USING A PUBLIC BIG DATA ANALYTICS (PADRIS)**

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**Objectives:** To analyse the prevalence of autoimmune diseases (ADs) in Catalonia by using a public big data program (Public Data Analysis for Health Research and Innovation Program, PADRIS)

**Methods:** We used the health insurance database of the Catalan National Health Insurance (CNHI) which includes all catalan population registered as insured population in 2016. The sample included 7,483,761 inhabitants. ADs were identified according to the corresponding International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes. A total of 33 autoimmune diseases were analysed classified in 4 main categories: rheumatic, systemic, organ-specific and immunodeficiency/autoinflammatory. The prevalence of ADs was calculated as the number of ADs patients divided by the total CNHI beneficiaries in the same year (rate per 1 00 000 persons, 95% confidence intervals -CI-)

**Results:** The overall prevalence of ADs was 1202 per 1 00 000 persons (95% CI 1,194–1,209); the prevalence was 1455 (95%CI 1,443–1,467) in women and 939 (95%CI 929–949) in men. ADs were classified as organ-specific (43%), systemic (33%), rheumatic (23%) and immunodeficiency/autoinflammatory (1%) autoimmune diseases. The ADs with the highest prevalence rates included psoriasis (282 cases per 100,000, 95% CI 278–286), rheumatoid arthritis (RA) (178 cases per 100,000, 95% CI 175–181), polymyalgia rheumatic (98 cases per 100,000, 95% CI 96–101), spondyloarthropathies (92 cases per 100,000, 95% CI 90–94), systemic lupus erythematosus (SLE) (68 cases per 100,000, 95% CI 66–70) and Sjögren's syndrome (59 cases per 100,000, 95% CI 57–61). In 26 (79%) of the 33 ADs, the female:male ratio was higher than 1; the highest ratios were reported for Sjögren's syndrome (10.5:1), primary biliary cholangitis (5.8:1), SLE (5.4:1), systemic sclerosis (3.4:1) and rheumatoid arthritis (2.6:1). An enhanced prevalence of ADs was reported in Southern regions (1225 cases per 1 00 000 persons in Barcelona/Tarragona regions -CI95% 1,216–1,233- vs 1075 cases per 1 00 000 persons in Girona/Lleida regions -CI95% 1,056–1,093-, p<0.001).

**Conclusions:** Nearly 90 000 catalans are classified as having an autoimmune disease, representing a prevalence of 1.2% of the total catalan population, a rate which reaches 1.5% in women. The highest frequencies are reported for psoriasis (0.28%), rheumatoid arthritis (0.18%), polymyalgia rheumatica (0.10%), spondyloarthropathies (0.09%), lupus (0.07%) and Sjögren syndrome (0.06%).

**Disclosure of Interest:** None declared

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**AB1344 PRESENCE OF ECHOCARDIOGRAPHIC CRITERIA FOR HFPEF MULTIPLIES THE RISK FOR DEATH AND CARDIOVASCULAR EVENTS IN PATIENTS WITH RHEUMATIC DISEASES**

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**Background:** Patients with rheumatic diseases (RD) have an increased risk for cardiovascular (CV) disease and heart failure (HF). Clinical assessment of HF signs and symptoms in RD is often limited by functional impairment.

**Objectives:** We investigated the prognostic value of echocardiographic and neurohormonal criteria for HF with preserved ejection fraction (HFpEF) in patients with RD.

**Methods:** This prospective, single-centre study included consecutive RD outpatients considered at increased risk for CV events according to ESC score ( $\geq 3\%$ ), pathological ECG, or elevated NTproBNP ( $>200$  pg/mL) as published by this group\*. Clinical assessment and transthoracic echocardiography according to



ESC criteria was performed. Presence of HFpEF was assumed if patients had NTproBNP >125 pg/mL, and either left ventricular hypertrophy (LVH; averaged septal-posterior wall thickness >11 mm) or left atrial dilation (LAD; LA Diameter >43 mm), regardless of presence of dyspnea. Kaplan-Meier plots were generated, and hazard ratios (HR) with 95% confidence intervals were computed using Cox regression with adjustment for age.

**Results:** Out of 764 patients (mean age 51 years, 70% female) 46% had rheumatoid arthritis (RA), 34% systemic autoimmune diseases (SAI; connective tissue disease or vasculitis), and 20% spondylo-arthritis (SpA); 248 of these patients (mean age 61±13 years, 62% female, RA 46%; SAI 32%; SpA 22%) had valid echocardiographic data (4 patients with LV ejection fraction <50% were excluded; follow-up data was missing in 3 cases). After a median follow-up time of 5.4 years, 20.6% of patients (group 1–4: n=19/5/8/1 respectively) had died or suffered a CV event (myocardial infarction 4.1%; stroke 1.8%; decompensated HF 1.8%; resuscitation 0.9%).

In univariable analysis NTproBNP >125 pg/ml (HR 3.6; 1.9–6.8, p=0.0001), LAD or LVH (HR 2.3; 1.1–4.5, p=0.02), and age per 5 years (HR 1.4, 1.2–1.6, p<0.0001) were significant predictors for an increased risk for death or CV event. Compared to the referent group consisting of patients with no signs of LVH or LAD in the presence of normal NTproBNP (group 4; n=59, 23.8%), patients with echocardiographic criteria for HFpEF (group 1; n=84, 33.9%) had a 7-fold increased risk for death or CV event: HR 7.2 (1.6–31.9; figure). The event risk for both patients with elevated NTproBNP but absent LVH or LAD (group 2; n=49, 19.8%) as patients with normal NTproBNP but presence of LVH or LAD (group 3; n=56, 22.6%) was also 5- to 6-fold increased: HR 5.5 (1.2–25.8) and 5.5 (0.9–18.2), respectively.

**Conclusions:** In patients with RD with an increased baseline CV risk, echocardiographic criteria suggestive of HFpEF are highly relevant indicators of worse outcome (7-fold increased risk for death or CVE), in particular in conjunction with an elevated NTproBNP value, irrespective of clinical presentation.

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**Disclosure of Interest:** None declared

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#### AB1345 EVALUATION OF MACROPHAGE ACTIVATION SYNDROME IN HOSPITALISED FEBRILE PATIENTS WITH KIKUCHI-FUJIMOTO DISEASE BASED ON THE 2016 EULAR/ACR/PRINTO CLASSIFICATION CRITERIA

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**Background:** The incidence and the risk of MAS in Kikuchi-Fujimoto disease (KFD) have been poorly understood, probably because of the rarity of the disease.

**Objectives:** To evaluate the 2016 classification criteria for MAS in hospitalised febrile patients with KFD and compare the clinical features of MAS in KFD with those of systemic lupus erythematosus (SLE) and adult-onset Still's disease (AOSD).

**Methods:** The records of febrile patients with KFD, hospitalised between November 2005 and April 2017, were reviewed. Patients were evaluated for MAS using the 2016 classification criteria. Clinical and laboratory features between patients with KFD with and without MAS, as well as those of patients with MAS in KFD, AOSD, and SLE were compared.

**Results:** Among 78 patients hospitalised with KFD, 24 had MAS during admission. Patients with MAS had longer hospital stays than patients without MAS and only patients with MAS required intensive unit care and experienced in-hospital mortality. Patients with MAS had higher C-reactive protein, aspartate aminotransferase, alanine aminotransferase, lactate dehydrogenase, and ferritin levels and lower lymphocyte count, platelet count, and total protein and albumin levels. MAS patients with KFD, AOSD, and SLE exhibited different clinical characteristics

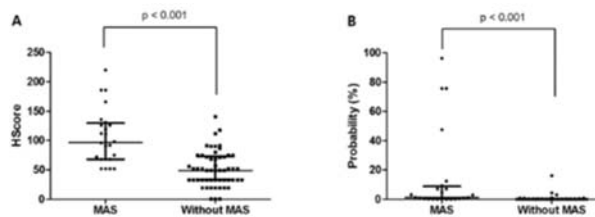
according to the underlying disease; however, MAS patients with KFD required less intensive immunosuppressive treatment than those with AOSD and SLE.

**Abstract AB1345 – Table 2.** Comparison of baseline laboratory findings of patients with MAS and without MAS

Variable	Without MAS (n=54)	With MAS (n=24)	p-value
<b>General laboratory variables</b>			
WBC count (/ $\mu$ L)	3475.0 (2350.0–5000.0)	3285.0 (2335.0–5905.0)	0.996
Haemoglobin (g/dL)	12.5 (11.7–13.4)	11.7 (10.3–13.2)	0.102
Neutrophil count (/ $\mu$ L)	1925.0 (1310.0–3050.0)	2206.5 (1375.0–4833.5)	0.378
Lymphocyte count (/ $\mu$ L)	1045.0 (860.0–1370.0)	600.0 (490.0–940.0)	<0.001
ESR (mm/h)	48.5 (27.0–64.0)	52.5 (39.5–72.5)	0.242
CRP (mg/L)	15.0 (7.5–37.1)	52.6 (27.7–97.1)	<0.001
Creatinine (mg/dL)	0.7 (0.6–0.8)	0.7 (0.5–1.1)	0.349
ALT (IU/L)	21.5 (14.0–38.0)	44.5 (23.0–153.0)	0.003
Albumin (mg/dL)	4.0 (3.7–4.3)	3.4 (3.1–3.7)	<0.001
LDH (IU/L)	439.5 (291.0–611.0)	771.5 (460.0–1213.5)	0.003
<b>Laboratory variables selected for MAS classification</b>			
Platelet count ( $\times$ 1000/ $\mu$ L)	195.5 (155.0–260.0)	139.0 (94.5–184.0)	<0.001
AST (IU/L)	29.0 (22.0–39.0)	93.5 (62.5–191.0)	<0.001
Ferritin (ng/mL)	242.8 (112.0–405.2)	1449.7 (812.9–4463.1)	<0.001
Triglyceride (mg/dL) <sup>†</sup>	89.0 (60.0–106.5)	133.0 (90.3–161.3)	0.076
Fibrinogen (mg/dL) <sup>§</sup>	342.0 (338.0–346.0)	317.5 (227.5–401.0)	0.695
<b>Bone marrow biopsy findings*</b>			
Presence of hemophagocytosis	0/7 (0.0)	2/12 (16.7)	0.509

Data are expressed as median (interquartile range) or n (%).

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; LDH, lactate dehydrogenase; MAS, macrophage activation syndrome; WBC, white blood cell



**Abstract AB1345 – Figure 1.** Comparison of HScore and the probability of having hemophagocytic syndrome in patients with KFD with and without MAS

Comparison of HScore (A) and the probability of having hemophagocytic syndrome (B) in KFD patients with MAS and without MAS

HScore, hemophagocytic syndrome score; KFD, Kikuchi-Fujimoto disease; MAS, macrophage activation syndrome.

**Conclusions:** The 2016 classification criteria were useful in identifying KFD patients with poor clinical outcome. Although treatment for patients with MAS in KFD, AOSD, and SLE differed according to the underlying disease, the 2016 classification criteria for MAS might aid in stratifying high-risk patients and provide guidance for treatment.

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AB1346

### THE CLINICAL COURSE OF PATIENTS WITH BIOLOGICS-TREATED RHEUMATOID ARTHRITIS COMPLICATED WITH NONTUBERCULOUS MYCOBACTERIAL LUNG INFECTION

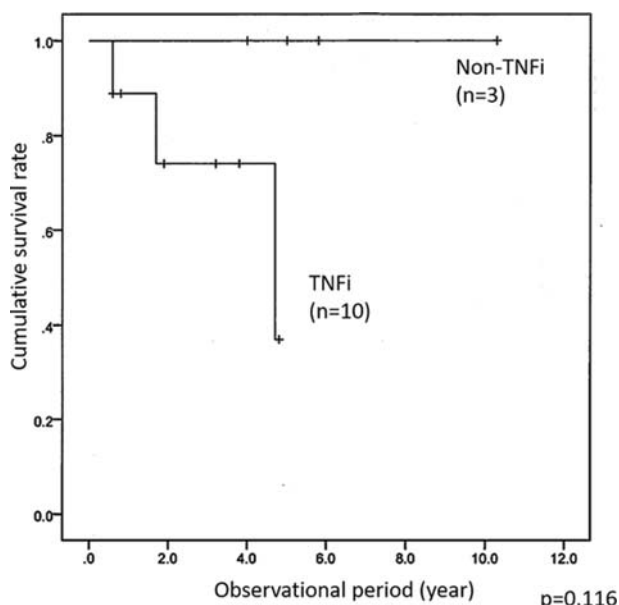
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**Background:** For now, it has been difficult for rheumatoid arthritis (RA) patients with lung nontuberculous mycobacterial infection (LNTMI) to achieve therapeutic goal of RA because of insufficient treatment considering the risk of NTM deterioration by immunosuppressive therapy. Although use of biologics in RA with LNTMI is not recommended based on results of an epidemiological study from USA,<sup>1,2</sup> prognosis analysis considering confounding factors, including the species of NTM, remains to be studied. On the other hand, some Japanese case series of RA with LNTMI after biological treatment had shown the acceptable outcomes.<sup>3</sup>

**Objectives:** This study was performed in order to investigate clinical course of patients with biologics-treated RA complicated with LNTMI.

**Methods:** This study is descriptive study. All the patients diagnosed with RA and proved the positivity of acid fasting culture were extracted. We retrospectively collected the clinical data between 1<sup>Jan 2011</sup> and 31<sup>Mar 2017</sup> including age, sex, date of RA onset, onset of NTM infection, species of NTM organisms, biologic drugs used, the clinical course, the findings of high resolution computed tomography (HRCT) and the outcome after commencement of biologics, at Tokyo Metropolitan Tama Medical Centre. The diagnosis of LNTMI was made by satisfying both of the two following conditions;<sup>1</sup> either positivity of bronchoalveolar lavage fluid culture at least once or sputum culture twice or more and<sup>2</sup> the compatible findings with LNTMI on HRCT.

**Results:** During investigation period, 13 LNTMI-RA patients were administered biologics, of which 76.9% were female. Their mean age at NTM diagnosis was 71 years old. The duration between the RA diagnosis and the occurrence of LNTMI ranged widely from 1 to 40 years. The species of NTM were *Mycobacterium avium* (12 cases) and *M. intracellulare* (1 case), which did not include rapid growing species. Twelve cases had treated with glucocorticoid. Of 10 cases who underwent biologics therapy after NTM diagnosis, 6 had continued biologics after diagnosis of LNTMI. All the 4 of the 13 cases who first received biologics after diagnosis of LNTMI were treated with abatacept, which improved their RA activity and did not exacerbate LNTMI. Of the 13, there were no patients requiring home oxygen therapy. During the average observational period after LNTMI of 3.6 years (0.8–10.3 years), 10 of the 13 were alive and 3 died, whose causes of death were not directly associated with LNTMI. When each period upon every biologics was independently calculated, the Kaplan-Meier survival curve illustrated the tendency of survival difference of between LNTMI-RA cases treated with non-TNF inhibitors and those with TNF inhibitors (figure 1).



Abstract AB1346 – Figure 1

**Conclusions:** Even when patients with RA have LNTMI of not rapid growing species, RA may be safely and sufficiently treated by abatacept with careful monitoring of the respiratory condition, which may improve their joint prognosis.

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**Disclosure of Interest:** None declared

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AB1347

### ELEVATED NESFATIN-1 LEVELS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Recent studies indicate that adipokines affect tissues and cells involved in rheumatoid arthritis (RA), including synovium, cartilage, bone, and immune cells.<sup>1,2,3</sup> Nesfatin-1, a member of the adipokine family, was identified in 2006 as a potent anorexigenic peptide involved in the regulation of homeostatic feeding. Nesfatin-1 concentrations in serum and synovial fluid were closely correlated with disease occurrence and severity of knee osteoarthritis.<sup>4</sup> We did not find any data about Nesfatin-1 levels in sera of rheumatoid arthritis (RA) patients.

**Objectives:** To investigate the serum nesfatin-1 level in RA patients.

**Methods:** At baseline we measured Nesfatin-1 level in sera of 110 RA patients (mean age 54,07±11,32; hereinafter M±Std.dev.) and 60 healthy controls (52,09±14,12). The diagnosis of RA was set according to the ACR/<sup>EULAR Classification Criteria for RA (2010)</sup>. Serum C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were measured to assess inflammation severity. Nesfatin-1 in serum was determined by enzyme-linked immunosorbent assay (RaiBiotech, cat№ EIA-NESF).

**Results:** We revealed that nesfatin-1 levels in RA patients were equal 50,49±34,05 ng/ml and was higher than of healthy controls – 31,61±3,17 ng/ml. We divided 120 RA patients into 2 subgroups – 1st (n=44) with normal nesfatin-1 concentration in sera, and 2nd (n=66) – with increased nesfatin-1 level. We noted that 2nd group's patients had higher DAS28 activity index, functional joints disability, higher levels CRP and ESR.

**Conclusions:** The present study shows that RA patients have increased serum Nesfatin-1 levels which strongly correlated with systemic inflammation and functional impairment in RA. These data sustained the pathogenic role of Nesfatin-1 in RA progression.

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**Disclosure of Interest:** None declared

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AB1348

### PREVALENCE, GENDER-PREDOMINANCE AND CLINICAL PRESENTATION OF BEHÇET'S DISEASE IN EGYPT: PRELIMINARY FINDINGS FROM A MULTICENTER NATIONWIDE STUDY

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**Background:** Behçet's disease is a chronic, relapsing multisystemic vasculitis that is common in the Mediterranean basin region with a diverse spectrum of clinical manifestations. A previous single-centre study from Alexandria conducted 20 years ago reported a prevalence of 7.6/100.000 population and a M:F ratio of 5.4:1.

**Objectives:** The aim of this multicenter study was to present the prevalence and pattern of Behçet's disease (BD) in adult Egyptian patients.

**Methods:** This study included 1098 BD patients from 14 highly specialised centres over <sup>Egypt during 2017</sup>. The demographic, clinical characteristics, laboratory findings, BD current activity form (BDCAF) and medications received were reported.

**Results:** The mean age of the patients was 36.3±10.2 years (16–73 years), disease duration was 6.7±5.2 years and they were 776 males and 322 females (2.4:1) and was 1.9:1 from Alexandria. Their mean age at disease onset was 29.8±8.7 years. 24.9% were diabetic and 30.7% hypertensive. The frequency of presenting cases was highest from Alexandria (41.3%) followed by Cairo (35.3%), Beni-Suef (6.4%), Assuit (6.1%), Sharkia (3.9%), Fayoum (3.2%), Minia (2.7%) and 1.1% from Ismailia. The total prevalence from those 8 major cities after adjusting for adults according to the 2017 population consensus was 4.35/100.000 inhabitants; 13.76 for Alexandria, 6.3 for Cairo and the highest prevalence in upper Egypt from Beni-Suef was 3.48 and the least from Minia (0.85). The prevalence from Sharkia was 0.93, Fayoum 1.51 and was 1.41 from Ismailia. All patients had oral ulcers while genital ulcers were present in 80%. The eyes were involved in 78.9%, cutaneous manifestations were present in 59.8%, arthritis in 34.7%, neuropsychiatric manifestations in 13.9%, gastrointestinal tract involvement in 11.5% and deep venous thrombosis in 23.1%. Their mean BDCAF was 4.6±4.6. The mean erythrocyte sedimentation rate was 29.1±19.9 mm/1sthr, C-reactive protein 11.3±15.2 mg/dl, haemoglobin content 13.3±6 g/dl, total leucocytic count 8.6±14.5 × 10<sup>3</sup>/mm<sup>3</sup>, platelets 262.6±76.9 × 10<sup>3</sup>/mm<sup>3</sup> and serum uric acid 4.8±1.6 mg/dl. 90.7% were receiving steroids, 81.1% were receiving colchicine, while only 8.1% were receiving biologic therapy.

**Conclusions:** The prevalence of BD in Egypt is high and higher in Alexandria than previously reported. The male-to-female ratio is lower than previously found being more in harmony with the globally reported ratios. The pattern of clinical presentation is unique for this country yet comparable to the universally stated frequencies.

**Disclosure of Interest:** None declared

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AB1349

#### SAFETY AND EFFECTIVENESS OF COSMETIC MINIMALLY INVASIVE PROCEDURES AMONG PATIENTS WITH SYSTEMIC AUTOIMMUNE DISEASE

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**Background:** Noninvasive or minimally invasive cosmetic dermatologic procedures are considered safe with low percentage of reported adverse events. However, reliable prevalence data regarding adverse event of such cosmetic procedures among patients with systemic autoimmune diseases are insufficient.

**Objectives:** To assess the occurrence of adverse events and disease exacerbation associated with noninvasive or minimally invasive cosmetic dermatologic procedures, including those involving hyaluronic acid fillers, botulinum toxins and laser application among patients with systemic autoimmune diseases.

**Methods:** Consecutive cases of patients suffering from autoimmune diseases and attending the rheumatology clinic for regular follow-ups, were asked about receiving cosmetic procedures during the last two years. Medical history, including clinical and laboratory signs of disease exacerbation after the date of the procedure, was retrospectively obtained from medical files of the patients included in the study. Patients were also asked about subjective disease exacerbation and local adverse events after the procedure.

**Results:** During the three months of study period, 148 patients were inquired. Nineteen patients (89% females) underwent 23 cosmetic procedures in total. Thirty-nine percent had Rheumatoid arthritis (RA), 39% had Ankylosing spondylitis (AS) and 22% had other systemic connective tissue disease. Sixty seven percent were treated by Disease-modifying antirheumatic drugs (DMARDs), 28% by Biologic treatment and 5% did not receive any specific treatment. All patients were in remission during the cosmetic procedures. Forty three and a half percent of patients underwent hyaluronic acid injection, 21.7% botulinum toxin injection, 21.7% laser application, 8.7% mesotherapy and 4.3% silicon injection. None of

the patients suffered from subjective disease exacerbation after the procedure. No changes in antibody titer and level of acute phase reactants (C-reactive protein and erythrocyte sedimentation rate) were noticed. Two patients (10.5%) experienced local oedema after filler injections. Both patients received Hydroxychloroquine treatment (one patient with RA and one with AS).

**Conclusions:** Our results suggest that noninvasive or minimally invasive cosmetic dermatologic procedures, including energy, neurotoxin, and filler procedures, may be safe among rheumatological patients, and do not cause autoimmune systemic disease exacerbation when performed in periods of remission. Hydroxychloroquine may predispose to a higher occurrence rate of local site injection adverse events. Further studies are desired to investigate this phenomena.

**Disclosure of Interest:** None declared

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AB1350

#### IS THE RADIOGRAPHIC DAMAGE A RISK FACTOR FOR NEUROPATHIC PAIN IN RHEUMATOID ARTHRITIS?

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**Background:** Features suggestive of neuropathic pain (NP) have been described in Rheumatoid Arthritis (RA) patients. The structural damage assessed on radiographs is a direct consequence and reflection of cumulative of disease activity and its association with NP has not been studied in RA.

**Objectives:** To determine whether existence and intensity of NP is associated with radiographic damage in RA patients.

**Methods:** Cross-sectional study was performed with RA patients followed at our Rheumatology department. Patients with diagnosed neuropathy or non-RA risk factors for NP were excluded. Selected patients were evaluated in a medical visit. Two questionnaires were applied to assess NP: the Leeds Assessment of Neuropathic Symptoms (LANSS) and the painDETECT (PDQ). Wrist, hands and feet radiographic studies from the previous 12 months before were classified according to the modified van der Heijde Sharp's method by one trained reader, blinded for patient clinical variables and treatment allocation. Correlation studies (spearman coefficient analysis) and univariate and multivariate logistic regression were performed. Significance level was set as <0.05.

**Results:** Ninety one RA patients were included. Seventy (77%) were women, with a mean age of 55.6±10.8 years and median disease duration of 12 years;<sup>2-41</sup> 84% patients were seropositive for Rheumatoid Factor and/or ACPA; 85 (93%) were treated with conventional synthetic Disease-Modifying Antirheumatic Drugs (DMARDs) and 41% with a biological DMARD (bDMARDs). The mean DAS28 4V CRP was 3.15±0.77 and the mean HAQ score was 1.04±0.6. The median joint erosion score (JE) was 28<sup>3-143</sup> and the median joint space narrowing (JN) was 46.<sup>10-133</sup> Forty-two (46%) patients had LANSS NP (≥12), 29% had a possible/likely NP in the PDQ (>12), and 13% had likely NP in the PDQ (>18). JN and global score (GS) had a negative weak correlation with LANSS (r=-0.21 and r=-0.25, respectively, p<0.05) and JN correlated with PDQ (r=-0.23, p=0.03). No significant correlations were observed with JE. Disease duration significantly correlated with all the radiographic scores (r=0.48 for GS, r=0.43 for JN, r=0.44 for JE, p<0.05) and negatively correlated with LANSS (r=-0.28, p=0.01). Lower median GS values were observed in LANSS positive group (62 vs 79, p=0.01). Patients under bDMARDs had significant higher median GS (80 vs 61, p=0.03) but also higher disease duration (14 vs 10, p=0.01). No statistically significant differences were observed for other variables. Disease duration was a negative predictor of LANSS NP (OR: 0.98, p=0.03). JN was inversely associated with LANSS NP (OR: 0.978, p=0.02) and remained significant after adjustments for bDMARDs treatment, but not for disease duration. JN was also a negative predictor of PDQ likely NP and remained significant after adjustment for bDMARDs (OR: 0.979, p=0.03), but not for disease duration.

**Conclusions:** In this cohort, JN score had a weak negative association with NP. Higher structural damage and disease duration do not seem to increase the risk of non-nociceptive RA pain. Further studies are needed to confirm these results.

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**AB1351 SYSTEMIC RHEUMATIC DISEASES AND CUMULATIVE CHILDHOOD STRESS**

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**Background:** It has been suggested that the adaptative stress response may be disrupted by life adverse events. Childhood maltreatment has been linked to increased inflammatory markers such as C reactive protein levels and increased prevalence of autoimmune disorders in adulthood. The mechanisms that underlie such association are not clear but it has been postulated that a dysregulated hypothalamic adrenal axis, accelerated immune cell ageing and altered immune cell gene expression pattern may play a role.

**Objectives:** To study the prevalence of adverse childhood experiences (ACEs) in a sample of patients with systemic lupus erythematosus (SLE), spondyloarthritis (SpA), scleroderma (SSc) and rheumatoid arthritis (RA) comparing them with controls.

**Methods:** After approval from the local Committee of Ethics in Research, we interview 315 patients with rheumatic disease (100 SLE; 40 SSc; 60 SpA; 115 RA) and 272 controls applying the ACEs Study questionnaire with questions on childhood abuse, negligence, domestic violence and household dysfunctions. This questionnaire score ranges from zero (best result) to 8 (worst scenario). Controls were paired for age ( $p=0.39$ ), gender ( $p=0.64$ ), monetary income ( $p=0.20$ ), religiosity ( $p=0.19$ ) and years of formal education ( $p=0.62$ ).

**Results:** In the whole group of rheumatic patients the median number of ACEs was 3 (IQR 2.5–5); in the controls was 3 (IQR=2–5) with  $p=0.45$ . About 201/315 (63.8%) of patients had ACEs score  $\geq 3$ ; the controls had 163/272 (59.9%) with  $p=0.31$ . In the SLE group 64/100 (64%) of the patients have had at least 3 ACEs; in SSc group 24/40 (60%); in SpA 36/60 (60%); in RA 77/115 (66.9%) and in controls 163/272 (59.9%). Studying the prevalence of ACEs according to the rheumatic disease it was found that patients did not differ from controls in SLE ( $p=0.47$  for ACEs scale and 0.87 in the number of ACEs $\geq 3$ ); in SSc ( $p=0.67$  for ACEs scale and 0.72 in the number of ACEs $\geq 3$ ); in SpA ( $p=0.92$  for ACEs scale and 0.21 in the number of ACEs $\geq 3$ ); neither in RA ( $p=0.06$  for ACEs scale and 0.14 in the number of ACEs $\geq 3$ ).

**Conclusions:** In this sample, it was not possible to associate the occurrence of ACEs with the appearance of rheumatic diseases in adulthood.

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**Disclosure of Interest:** None declared

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**AB1352 EVALUATION OF MRI RAMRIS SCORE AND CLINICAL RESPONSE IN PATIENTS WITH ACPA POSITIVE UNDIFFERENTIATED ARTHRITIS TREATED WITH INFILIXIMAB VERSUS PLACEBO**

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**Background:** Patients (Pts) with Undifferentiated Arthritis (UA), positive for ACPA antibodies are at high risk of progressing to Rheumatoid Arthritis (RA). TNF play a key role in the pathogenesis of RA. Very early treatment with the combination of Methotrexate and Infliximab (IFX) in a small cohort of UA showed a benefit in clinical symptoms and reduction of MRI evidence of synovitis and erosions.

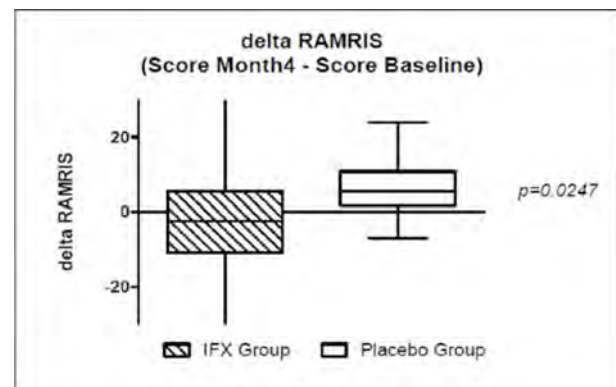
**Objectives:** To assess whether IFX as a monotherapy is more effective than placebo (Pbo) in UA pts positive for ACPA. Here we evaluate the clinical response, the MRI RAMRIS score MRI and the risk to develop RA.

**Methods:** This was a randomised, double-blind, Pbo-controlled, two-arm parallel design study of 12 months to the primary endpoint (proportion of pts who developed RA by ARA 2007 criteria). Pts with UA and symptomatic clinical synovitis of  $\geq 1$  joints and ACPA positivity were randomised 1:1 to IFX (3 mg/kg) or Pbo at week

0, 2, 6, 14 and 22, after which treatment was terminated. NSAIDs/stable low-dose oral corticosteroid ( $\leq 5$  mg/day prednisone or equivalent) were permitted but no DMARDs.

Disease activity measures (DAS28-CRP) were evaluated at BL, Wks 2 and 4, and every 4 wks until Wk 52. OMERACT RAMRIS scores (components: erosion, osteitis, synovitis, tenosynovitis) and peritendinitis scores were evaluated at BL and Mth 4. Pts who developed RA at any time were discontinued and could receive standard of care.

**Results:** 28 pts were randomised (mean age:  $48 \pm 12$  years; mean duration of arthritis:  $0.34 \pm 0.53$  year; mean CRP level:  $1.67 \pm 2.23$  mg/dL). By 1 year, 11/15 (73%) pts treated with IFX developed RA vs 10/15 (67%) Pbo-treated pts (Kaplan Meier, log rank  $p=0.868$ ). At wk 14, ACR 20, 50, 70 responses were observed respectively in 71.4%, 42.9%, 28.6% pts treated with IFX vs 21.4%, 0%, 0% treated with Pbo. Remission DAS28CRP rate was observed in 50% in the IFX group vs 21.4% in the Pbo group. Pts in the IFX arm experienced significantly greater improvements in RAMRIS score versus pbo at wk 16 (see graph). No severe safety issues was observed except one case of severe hepatotoxicity induced by Isoniazid.



Abstract AB1352 – Figure 1

**Conclusions:** In this small randomised cohort of UA ACPA positive pts, we noted a significant difference in the RAMRIS scoring after 4 months in the IFX group vs PBo. This is the first study to report a worsening of disease activity based on the RAMRIS scores in the PBo group but changes were minimal and not observed in all pts. IFX has higher efficacy but did not prevent the progression to definite RA. Further analyses are ongoing to determine MRI predictors for severity.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.3504

**AB1353 HOW MUCH TEMPERATURE CAN TRULY IMPACT ON RAYNAUD'S PHENOMENON SECONDARY TO SYSTEMIC SCLEROSIS?**

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**Background:** Raynaud's phenomenon (RP) is considered a prominent feature of systemic sclerosis (SSc).<sup>1</sup> SSc-RP is related to considerable disease-related morbidity including pain, impaired hand function, reduced social participation, body image dissatisfaction, increased reliance on others and reduced quality of life.<sup>2</sup> In most cases RP is triggered by low environmental temperature or sudden variation of it. According to EULAR recommendations, intravenous (IV) iloprost (ILO) should be used to control severe RP, after oral therapy failure.<sup>3</sup> Unfortunately no validated IV ILO regimens have been so far published.

**Objectives:** Aim of our study was to estimate the impact of environmental temperature on RP in patients with SSc treated with two different IV ILO regimens and in patients not treated with IV ILO.

**Methods:** We conducted a monocentric, prospective, pragmatic and non-randomised study, after the local ethical committee approval, between September 2016 and February 2017. In the present study, we enrolled all consecutive SSc patients not requiring therapy with IV ILO (group A), or requiring therapy with IV ILO once monthly (group B) or therapy with IV ILO for 5 consecutive days every 3 months

(group C). RP severity was evaluated through a visual analogue scale (VAS) from 0 to 10. Group A and C patients were evaluated at baseline and after 3 months. Group B were evaluated at every infusion for 3 months. Environmental temperature for each patient was calculated as the mean temperature during the week before the evaluation in the place of residence (data supplied by Meteo Operations Italia (MOPI) Srl – Centro Epson Meteo). Moreover for each participations demographic and disease characteristics were collected at baseline.

**Results:** 96 patients were enrolled in the study: 52 in group A, 24 in group B, and 20 in group C. Of these 35, 21 and 16 respectively completed the study.

RP VAS was related to the average temperature observed the week before the evaluation at place of residence. In group A, VAS RP decreases of  $-0.072$  for a growth of one grade of the temperature (IC 95%:  $-0.206-0.061$ ,  $p$ -value=0.297). In group B, VAS RP decreases of  $-0.278$  for a growth of one grade of the temperature (IC 95%:  $-0.397 - -0.160$ ,  $p$ -value<0.001). In group C, VAS RP decreases of  $-0.053$  for a growth of one grade of temperature (IC 95%:  $-0.201-0.095$ ,  $p$ -value=0.483).

**Conclusions:** RP severity, as assessed by VAS, showed a correlation with the environmental temperature. This information could support the seasonal administration of IV ILO only during the coolest periods of the year.

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**Disclosure of Interest:** None declared

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#### AB1354 RHEUMATOID ARTHRITIS IN ADULTS IN AN URBAN AREA: TRENDS FOR INCIDENCE, PREVALENCE AND HOSPITALISATION RATES FOR A 10-YEAR PERIOD

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**Background:** Rheumatoid arthritis (RA) is the most common inflammatory polyarthropathy. According to the previously published data its prevalence was 0.3%–1.5% and incidence – about 0.01%–0.02%<sup>1,2</sup> with some variations due to genetic and ethnical factors.<sup>3</sup> During last decades significant progress has been achieved in early diagnostic and treatment of RA. Nevertheless a tendency for the increase of both incidence and prevalence of RA was reported lately by some national registers.<sup>4</sup>

**Objectives:** We estimated incidence, prevalence and hospitalisation rates for RA in Minsk (the Republic of Belarus) for a 10 year period.

**Methods:** Minsk is a typical urban area which is considered to be representative for the urban population of the whole country. The data on the new onset RA and the first visit for RA in a corresponding year were collected from all rheumatologic services of Minsk for the period 2005–2015. Only patients older than 18 years old with the diagnosis of RA according to the ICD-10 (M05-M06) were included. Demographic data on the population of the Republic of Belarus were obtained from the annual Statistical bulletins of the National Statistical Committee. Hospitalisation rates were calculated on the base of statistical reports on discharges for the corresponding years.

**Results:** Population size for adults in Minsk in 2005 was 1467390 with 135 new onset RA cases revealed and corresponding RA incidence was 9.2 (CI<sub>95%</sub>8.6–9.8) per 100 000 adults. Population size in 2010 increased to 1529470, 131 new onset RA cases were revealed and RA incidence was 8.6 (CI<sub>95%</sub>8.4–8.7) per 100 000 adults. Population size in 2015 also increased at the same rate and amounted to 1598120, 206 new onset RA cases were revealed and corresponding RA incidence increased to 12.9 (CI<sub>95%</sub>12.7–13.1) per 100 000 adults ( $p$ <0.001).

There were registered 2745 first visits for RA in 2005 with corresponding RA prevalence 187.1 (CI<sub>95%</sub>186.4–187.7) per 100 000 adults. There were registered 3373 first visits for RA in 2010 and 4315 visits in 2015. RA prevalence rates were 220.5 (CI<sub>95%</sub>219.9–221.2) and 270.0 (CI<sub>95%</sub>269.3–270.7) per 100 000 adults, correspondingly. These data suggest a steady increase of RA prevalence for the last 10 years ( $p$ <0.001).

There were 7147 hospitalizations in Minsk for RA for the period 2010–2015. Hospitalisation rates for RA increased from 75.4 (CI<sub>95%</sub>73.8–77.1) to 79.2 4 (CI<sub>95%</sub>77.5–80.9) per 100 000 adults ( $p$ <0.001) with the same provision of the population with the specialised rheumatologic beds – 15.7 (CI<sub>95%</sub>14.9–16.5) and 15.0 (CI<sub>95%</sub>14.3–15.8) per 100 000 adults (NS) in 2010 and 2015,

correspondingly, while hospitalisation rates among RA patients decreased from 34.2% to 29.3% ( $p$ <0.001).

**Conclusions:** We revealed the significant increase (1.4 times) in incidence and prevalence of RA in adults in Minsk (Belarus) for the period 2005–2015. Hospitalisation rates for RA in the population had the same trend for the study period.

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**Disclosure of Interest:** None declared

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#### AB1355 BONE MINERAL DENSITY, T-SCORE AND Z-SCORE IN YOUNG MEN WITH JUVENILE IDIOPATHIC ARTHRITIS

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**Background:** Juvenile Idiopathic Arthritis (JIA) is term used to classify a group of heterogeneous paediatric rheumatic diseases. Many of these conditions remain active until adulthood. Presences of chronic inflammatory disease together with glucocorticoid treatment are the risk factors of development of osteoporosis in young adult males.

**Objectives:** Aim: to study the bone mineral density (BMD), T-score, Z-score in young adult males with JIA.

**Methods:** The study included 50 adult men aged 19 to 25 years, divided into two groups: I – 25 practically healthy young males; II – 25 young men from different regions of Ukraine with a history of JIA in childhood regardless of the presence or absence of active inflammation at the time of the observation. Two-energy X-ray densitometry (Prodigy, GE Lunar, Madison, USA) was performed on the basis of the Institute of Gerontology, Ukrainian Research Centre of Osteoporosis Problems with analysis of BMD, T- and Z-scores in different skeletal areas.

**Results:** Young men with JIA and healthy individuals did not differ in age, height, weight and BMI. In assessing the number of fractures in patients with JIA were identified 4 patients (16%), while in the control group were no fractures. Negative impact of the JIA on the BMD was found in the I group compared with II group. Lumbar spine BMD in I group was lower ( $p$ <0.01) than in healthy subjects, as well as the Z-score ( $p$ <0.001) in the L1-L4 lumbar spine region. BMD, T-score and Z-score in femoral neck region were lower in I group than in II ( $p$ <0.001,  $p$ <0.001,  $p$ <0.01 correspondingly). Reliable differences between the two groups were found in total body BMD ( $p$ <0.001), T-score ( $p$ <0.01), Z-score ( $p$ <0.05). Patients with JIA had lower ( $p$ <0.01) BMD and T-score ( $p$ <0.05) in ultradistal area of forearm. Reduction of BMD up to the level of osteopenia (Z-score <2 SD) was found in 5 out of 25 (20%) patients at the level of L1-L4 lumbar spine, in 2 (8%) patients at the level of femoral neck, in 3 (12%) patients at total body and in 2 (8%) patients at the level of ultradistal area of forearm.

**Conclusions:** Young men with JIA aged 19–25 years had reduced total body BMD, T-score, Z-score, which indicates the negative impact of the disease on the bone tissue compared with healthy men of the corresponding age.

**Disclosure of Interest:** None declared

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#### AB1356 AGE PECULIARITIES OF BONE MINERAL DENSITY IN YOUNG FEMALE WITH JUVENILE IDIOPATHIC ARTHRITIS

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**Objectives:** Aim: to study the bone mineral density (BMD) in young adult females with juvenile idiopathic arthritis (JIA) depending on the age.

**Methods:** 99 females aged 19–39 (40 patients with JIA and 59 practically healthy persons) were examined. All surveyed were divided into 2 groups by age: I group–20–29 years old and II group–30–39 years old. The age of disease onset, delay in diagnosis, disease duration, ILAR-variant of JIA, BMD, T-score and Z-score were estimated.

**Results:** The onset of JIA was at the age of 11.16±4.34 years, delayed diagnosis–23.52±21.37 months, the disease duration–11.9±9.4 years, persistent

oligoarthritis was detected in 25% of patients, RF-negative polyarthritis—in 22.5%, extended oligoarthritis—in 10%, RF-positive polyarthritis—in 10%, systemic-onset JIA—in 12.5%, enthesitis-related JIA—in 15%, undifferentiated arthritis—in 2.5%, psoriatic arthritis—in 2.5% of patients. BMD ( $p < 0.000001$ ) in the lumbar spine (LS) were lower in female with JIA than in healthy people. Femoral neck (FN) BMD ( $p < 0.000001$ ), total body (TB) BMD ( $p < 0.000001$ ) were lower in patients with JIA than in healthy people. The BMD was significantly lower at the LS ( $p < 0.001$ ) and at the TB ( $p < 0.01$ ) in both groups, and at the FN ( $p < 0.001$ ) in patients aged 20–29 years in comparison with healthy group. Z-score  $< -2$  SD in young females was detected in 40% of patients in the LS, in 25% of patients in the FN, in 35% of patients in the TB and 52.5% of patients in ultradistal forearm, and T-score  $< -2.5$ —in 2.5% in LS, 2.5%—FN, 37.5%—TB, 22.5%—ultradistal forearm. Osteopenia by T-score at the LS was found in 42.5%, of the FN—42.5%, TB—37.6%, ultradistal forearm—22.5% of patients.

**Conclusions:** The presence of JIA in childhood had negative effects on the formation of peak bone mass and BMD at young female.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.6255

### AB1357 RISK FACTORS FOR CYTOMEGALOVIRUS REACTIVATION IN PATIENTS WITH CONNECTIVE-TISSUE DISEASE; SINGLE-CENTRE PROSPECTIVE COHORT STUDY

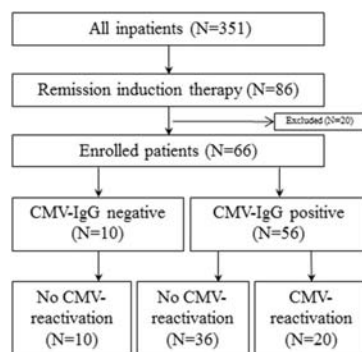
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**Background:** Cytomegalovirus (CMV) reactivation is one of serious opportunistic infections for immunosuppressed patients, therefore, identifying patients at risk for CMV reactivation is of importance. However, no prospective study about CMV reactivation in connective tissue disease (CTD) has been reported.

**Objectives:** To identify risk factors relevant with CMV reactivation in patients with CTD during remission-induction therapy.

**Methods:** Consecutive CTD cases who started immunosuppressive therapy from February until December 2017 were enrolled. Serum CMV-IgG was measured before the induction therapy, and subsequently, CMV pp65 antigen was monitored weekly. Patients were divided into 2 groups according to the presence or absence of CMV reactivation, and risk factors for CMV reactivation were analysed.

**Results:** Sixty six cases were enrolled. Mean age was 59.9±17.9 y/o, and female was 68.2%. The underlying diseases were following; anti-neutrophil cytoplasmic antibody-associated vasculitis 18, systemic erythematosus 11, polymyositis/dermatomyositis 9, IgG4-related disease 7, giant cell arteritis 6, and others 15. The initial dose of glucocorticoid (GC) was 50.8±11.5 mg/day (0.92±0.15 mg/kg/day) as prednisolone (PSL) with additional methylprednisolone (mPSL) pulse therapy being conducted in 17 (25.8%). Concomitant immunosuppressive therapies were intravenous cyclophosphamide (IVCY) in 25, mycophenolate mofetil 9, and calcineurin inhibitor 7, tocilizumab 2, infliximab 1, abatacept 1, and rituximab 1. None of 10 CMV-IgG negative patients developed CMV reactivation. Among 56 CMV-IgG positive patients, CMV reactivated in 20 patients (35.7%). Among those, CMV infection occurred in 2 patients (hematopoietic injury and hepatitis). Previous history of GC administration ( $p = 0.032$ ), initial GC dose ( $p = 0.033$ ), mPSL pulse therapy ( $p = 0.018$ ), IVCY ( $p = 0.003$ ), and low lymphocyte count 1 week after treatment initiation ( $p = 0.023$ ) were significantly related with CMV reactivation.



**Abstract AB1357 – Figure 1.** Patient flow of this study.

**Conclusions:** While no CMV reactivation occurred in CMV-IgG negative cases, treatment regimen and low lymphocyte count were associated with CMV reactivation in CMV-IgG positive CTD cases.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.4391

### Validation of outcome measures and biomarkers

#### AB1358 INFECTIOUS ANTIBODIES REPERTOIRE IN RHEUMATOID ARTHRITIS

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**Background:** The incidence of infectious diseases in the RA ADAPThera study by ELISA antibody screening and the differences in infectious distribution in active or low active disease patients was explored.

**Methods:** Sera from 88 naive RA patients out of the ADAPThera study cohort, disease duration  $< 6$  months, were tested for antibody titers against: Herpes simplex virus 1 and 2 (HSV1 +2, IgG and IgM) Helicobacter pylori (HP, IgA and IgG), Cytomegalovirus (CMV, IgG and IgM), Toxoplasma gondii (Toxo, IgG), Adenovirus (IgG and IgM), Epstein Barr virus (EBV, IgG and IgM), and Parvovirus B19 (P-B19, IgG) were determined by using NovaLisa from NovaTec Immunodiagnostica GmbH, GERMANY. Borrelia (IgG and IgM) titers were determined by AESKULISA and confirmed by Western blot (AESKUBLOTS) by AESKU.DIAGNOSTICS GmbH and Co. KG, GERMANY.

**Results:** 82% RA patients were found to be positive for HSV1 +2 IgG (2% IgM positive), 8% for Adenovirus (IgA), 77% (IgG), and 1% (IgM). 99% for EBV-IgG (no IgM positive). 53% (IgG), and 26% (IgM) for CMV. 38% for HP-IgG and 15% for IgA and 79% for P-B19-IgG (3% IgM). 6% for Borrelia-IgM and 14% for IgG. A slightly increase was found for EBV sera positivity (99% IgG), compared to the normal population.

**Conclusions:** Limited evidence exists regarding the impact of the disease activity on the susceptibility for infections, possibly due to the close association of RA disease activity and therapy dependent dosage of immunosuppressive treatment. Still, some infections may present memory contact, presenting an epiphenomenon. On the contrary, they might play an active role in RA pathophysiology.

**Disclosure of Interest:** None declared

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#### AB1359 TRANSLATION, CULTURAL ADAPTATION AND VALIDATION OF THE ITALIAN VERSION OF THE BILD: THE BILDIT

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**Background:** Evaluation of organ damage is one of the most important assessments in SLE patients; the SLICC/DI is a physician-driven instrument widely used to assess organ damage in SLE. Patient-reported outcomes (PROs), self-assessments that are not being interpreted by a clinician, are gaining a central role as outcome measures. Among these, the Brief Index of Lupus Damage (BILD) is a patient-reported instrument for the assessment of organ damage in SLE.<sup>1</sup>

**Objectives:** The aims of the present study are translation, cultural adaptation and validation of an Italian version of the BILD.

**Methods:** The process of translation and cultural adaptation followed published guidelines.<sup>2</sup> The final version of the questionnaire (BILDit) was pretested in a group of 30 SLE patients to evaluate acceptability, comprehension and feasibility. The validity of the BILDit was evaluated by its administering to consecutive patients attending the outpatients clinic or the inpatients wards. The external validity was tested toward the SLICC/DI scored by a physician blinded to the BILDit results. Correlation with other PROMs (FACIT, SF-36) was also tested. In a subgroup of 30 patients the questionnaire was administered twice at 2 weeks interval to assess their reliability.



**Results:** A total of 166 SLE patients participated to the study (93.4% female, 97% Caucasian); mean age ( $\pm$ standard deviation) at enrollment was 45.4 years $\pm$ 13, mean disease duration resulted 14.3 $\pm$ 10 years. Overall, disease activity at enrollment as expressed by the SLEDAI score resulted quite low (median SLEDAI 2, IQR 0–4) and 27.3% of patients presented an active disease (SLEDAI >4). At least one organ damage according with the SLICC/DI was present in 111 patients (56.35%) with a median score of 2 (IQR1–4). In the pilot test, 80% of patients answered to all the questions; 93% of the patient declared no difficulty in completing the questionnaire and the median time required resulted 5 min.<sup>3–5</sup> BILDit showed very high reliability (test-retest  $\alpha$  >0.8). The BILDit scores in our sample showed a strong positive correlation with SLICC/DI ( $\rho$ =0.69;  $p$ <0.001); by comparing the single BILDit and SLICC/DI items, we found a significant concordance for all but retinopathy and cerebrovascular disease that resulted underestimate by patients. BILDit scores showed a positive linear relation with age ( $p$ <0.01) and disease duration ( $p$ <0.01); in a multivariate analysis, a significant inverse correlation was found between BILDit scores and FACIT scores ( $p$ <0.01) and with both physical and mental components of the SF-36 ( $p$ <0.01).

**Conclusions:** BILDit demonstrated to be acceptable, comprehensible, feasible and reliable in our routine clinical setting; it also showed good correlation with physician's driven instruments and quality of life measures. The BILDit can be considered a useful screening tool for the assessment of organ damage as perceived from the patient's point of view before the standard visit.

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#### AB1360 RANGE AND CONSISTENCY OF OUTCOME MEASURES REPORTED IN RANDOMISED TRIALS IN DERMATOMYOSITIS: A SYSTEMATIC REVIEW

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**Background:** Dermatomyositis – an idiopathic inflammatory myopathy- can be resistant and unresponsive to initial treatments and require chronic therapy. Symptoms including muscle weakness and skin rash can lead to severe complications and impair quality of life. There are a paucity of randomised trials in dermatomyositis, which may not consistently report outcomes that are important to patients and their clinicians.

**Objectives:** To assess the scope and consistency of outcomes reported in randomised trials in dermatomyositis.

**Methods:** MEDLINE, Embase, CINAHL, PsycINFO were searched to February 2017 for randomised trials in children and adults with dermatomyositis. The frequency and characteristics of the outcome domains and measures reported were then analysed. Similar outcomes were grouped into outcome domains and classified as surrogate, clinical or patient-reported outcomes. The frequency and characteristics of the outcome domains and measures reported were then analysed.

**Results:** We included 18 trials ( $n$ =844 participants), reporting 680 outcome measures. These were grouped into 27 different outcome domains; including 12 (44%) clinical outcomes, 9 (33%) surrogate/biochemical outcomes, and 6 (22%) patient-reported outcomes. The 5 most frequently reported outcome domains were: physical function (13 trials, 72%), muscle strength (12, 67%), muscle inflammation (12, 67%), biomarkers (11, 61%), and composite i.e. myositis disease activity (10, 56%).

**Conclusions:** The majority of outcomes reported in trials in dermatomyositis are clinical outcomes and few are patient-reported. Establishing a core set of patient-important outcomes may improve the consistency and relevance of outcomes reported in trials in dermatomyositis to inform decision-making.

**Disclosure of Interest:** None declared

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#### AB1361 SEASONAL SENSITIVITIES OF DISEASE ACTIVITY INDICES IN RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is a chronic and progressive autoimmune disease which is primarily characterised by the inflammation of synovial joints. In rheumatoid arthritis, evaluation of the disease activity is very important in monitoring the disease progression and effectiveness of the treatment

**Objectives:** The aim of this study was to evaluate the seasonal sensitivity of disease activity indices (DAS28-ESR, DAS28-CRP, SDAI and CDAI) in rheumatoid arthritis. In addition, we investigated the presence of seasonal variation in disease activity in rheumatoid arthritis and its relation to vitamin D levels.

**Methods:** This is a prospective study. This study included female RA patients, who were diagnosed/verified according to 2010 ACR/EULAR criteria, with a diagnostic history of 5 years or older. The seasons were identified as spring (March, April, May), summer (June, July, August), autumn (September, October, November) and winter (December, January, February), and the study was completed with 85 patients. We assessed the disease activation with DAS28-ESR, DAS28-CRP, SDAI and CDAI scales, functional status with HAQ questionnaire, quality of life with the 36-Item Short Form Health Survey (SF-36), and presence of depression with beck depression inventory (BDI). Blood samples from patients were kept at appropriate storage conditions at  $-80^{\circ}\text{C}$ , and serum levels of 25-OH vitamin D were analysed by the chemoluminescence assay method at the end of each season.

**Results:** The assessment of mean of DAS28-ESR and DAS28-CRP scores found that the disease activity showed statistically significant seasonal differences ( $p$ <0.05). Although the assessment of mean of SDAI and CDAI scores showed that the disease activity was higher in the autumn season, this difference was not statistically significant ( $p$ >0.05). There was no statistically significant correlation between the mean vitamin D levels and mean of DAS28-ESR, DAS28-CRP, SDAI, CDAI scores in any season ( $p$ >0.05).

**Conclusions:** These results suggest that there may be seasonal variation in disease activity in RA and that DAS28-ESR and DAS28-CRP may be more sensitive than CDAI and SDAI in establishing this variation. There was no correlation between seasonal changes in disease activity and changes in serum 25-OH Vitamin D levels

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#### AB1362 SPECIFIC FEATURES OF THE CLINICAL COURSE AND OUTCOMES OF ERYTHEMA NODOSUM, ASSOCIATED WITH INFECTION

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**Background:** Erythema nodosum (EN) is the most common type of septal panniculitis (Pn) without vasculitis. The prevailing identifiable cause of EN in paediatric population is bacterial infection (*Streptococcus*), while in adults sarcoidosis and streptococcal infection are considered to be the most common etiological factors.

**Objectives:** The aim of the current study is to evaluate specific features of the clinical course and outcomes of EN, associated with infection, in rheumatology practice.

**Methods:** The study included 121pts (112 females—92,6%, 9 males—7,4%, mean age 38,9 $\pm$ 12,6 y) who were on the record at VA Nasonova Research Institute of Rheumatology during 7 years with referral diagnosis «erythema nodosum». The disease duration varied from 1 week to 20 years. Patient's assessment included general clinical examination, immunological and serological tests for *Chlamidia* (*Chl. Pneumoniae*, *Chl. trachomatis*), *Mycoplasma* (*M. pneumoniae*, *M. hominis*), *Ureaplasma*, Herpes viruses type I and II, Cytomegalovirus, Epstein-Barr virus, *Yersinia*, HBV and HCV, HIV, anti-streptolysin O (ASO) using ELISA and immunoturbidimetry. The outcomes were assessed in 1–6 years.

**Results:** EN association with infection was identified in 32 pts (30 females, 2 males, mean age 39,6 $\pm$ 13 y). Chronic conditions prior to EN onset were found in 12 pts (37%): tonsillitis—in 8 pts (25%), endometriosis—in 1 (3%), bronchitis—in 1 (3%), colpitis—in 1 (3%), toxoplasmosis—in 1 (3%). Elevated ASO titers were documented in more than half cases (18 (56,25%) pts). "Blooming bruise" symptom was characteristic for this population ( $p$ <0,0001). Clear clinical and laboratory

signs of active inflammation were not found. Based on etiological agent all pts were divided into 3 groups: Group I—with bacterial infection (5 pts (15%)), Group II—with viral infection (11 pts (35%)), Group III—with mixed bacterial and viral infection (16 pts (50%)). Rapid nodule regression was strongly associated with elevated ASO titers at baseline ( $p=0,02$ ) and presence of bacterial agents ( $p=0,0007$ ). Recurrences were documented in 13 pts (40,6%), among them 7 (54,1%) cases were triggered by ARVI/common frigorigism, 2 (15,3%) cases—by stress, 2 (15,3%) cases – by non-compliance or treatment failure, 2 (15,3%) – by exacerbation of chronic tonsillitis. There was no statistically significant association between intake of individual medications and full reversal of the disease. There was 1 (8% from total number) recurrence episode in Group I, 7 (54%) episodes—in Group II, and 5 (38%)—in Group III. Recurrent disease inversely correlated with affected surface area (affected leg surfaces) ( $p=0,03$ ). Pts who achieved nodular regression had elevated ASO at EN onset ( $p=0,00008$ ), in contrast to pts with recurrent disease.

**Conclusions:** Streptococcus spp (56,3%) seem to be the leading cause of EN associated with infection. Lab verification of streptococcal infection with subsequent adequate antibacterial therapy facilitates the favourable clinical course of EN.

**Acknowledgements:** The study had no sponsorship.

**Disclosure of Interest:** None declared

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AB1363

#### ARE YOU ABLE TO CUT YOUR MEAT? – EXPLORING THE CHALLENGES DURING THE CULTURAL ADAPTATION OF THE HEALTH ASSESSMENT QUESTIONNAIRE DISABILITY INDEX (HAQ-DI) INTO 130 LANGUAGES

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**Background:** The disability assessment component of the Health Assessment Questionnaire, the HAQ-DI,<sup>1</sup> developed in US English, assesses a patient's level of functional ability and includes questions of fine movements of the upper extremity, locomotor activities of the lower extremity, and activities that involve both upper and lower extremities. There are 20 questions in eight categories of functioning which represent a comprehensive set of functional activities – dressing, rising, eating, walking, hygiene, reach, grip, and usual activities. The stem of each item asks over the past week "Are you able to ..." perform a particular task. The patient's responses are made on a scale from zero (no disability) to three (completely disabled).

**Objectives:** To explore the challenges faced during the cultural adaptation of the HAQ-DI, focusing on one simple task, i.e., "Are you able to cut your meat?" in the eating category.

**Methods:** The archives of Mapi Language Services were searched and 130 translations were retrieved, representing 13 language families. The translation methods followed either the standard linguistic validation process [i.e., conceptual analysis, dual translation process (forward, backward translation into English), test with patients and clinician review] or the adjusted process in case of countries using national variants of the same language (i.e., Australian English or English used in India).<sup>2</sup>

**Results:** In most of the target languages, cutting a whole piece of meat presented in one plate was not a cultural issue. However, in vegetarian-driven cultures or countries where cutting meat was performed while cooking, the item had to be adapted and changed to comply both with the local culture and the concept explored by the item (i.e., fine movement of the upper extremity). For instance, an equivalent of "to cut meat while cooking" was chosen in Korean; "to cut meat (when eating or preparing food)," in Bahasa (Indonesia); "to cut raw vegetables," in Gujarati (India); or "make bite size pieces of your food (e.g., chapatis)" in English for India.

**Conclusions:** The close collaboration between the developer and the translation teams was essential in finding appropriate conceptual equivalents of the simple task of cutting meat in 13 different language families.

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AB1364

#### ADAPTATION AND VALIDATION OF THE RHEUMATOID ARTHRITIS QUALITY OF LIFE (RAQOL) SCALE FOR PORTUGAL

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**Background:** Rheumatoid Arthritis (RA) is a chronic inflammatory disease that has a major impact on patients' quality of life. The Rheumatoid Arthritis Quality of Life Questionnaire (RAQoL) is a patient-centric outcome measure, specific to RA. The measure has not previously been available for use with Portuguese RA patients.

**Objectives:** To produce a Portuguese version of the RAQoL that is acceptable to Portuguese patients and demonstrates sound psychometric properties.

**Methods:** The dual panel methodology was used to translate the UK RAQoL into Portuguese. This involved conducting a bilingual panel (providing the initial translation into Portuguese) followed by a lay panel (where items are assessed for comprehension and acceptability). Cognitive debriefing interviews were conducted with Portuguese RA patients to determine the face and content validity of the translated scale. A large-scale postal validation survey was carried out to establish the psychometric properties of the Portuguese RAQoL. The measure was administered on two occasions to RA patients, alongside a comparator instrument – the Nottingham Health Profile (NHP).

Internal consistency was assessed using Cronbach's alpha coefficient. Spearman's Rank correlation coefficient was employed to assess test-retest reliability. Convergent validity was tested by correlating RAQoL scores with those on the NHP sections. Known group validity was assessed using non-parametric tests for independent samples. This involved determining the ability of the RAQoL to distinguish between patients that differed according to their self-perceived severity of RA and general health.

**Results:** The translation panels produced a Portuguese version of the RAQoL that was easily understood and considered natural by native speakers. Interviewees considered the new language version to be relevant and appropriate. One hundred and seventy-eight RA patients (82% female) took part in the postal validation survey with a mean age of 56.6 (range 25 to 79) years. The Portuguese RAQoL demonstrated excellent internal consistency (Cronbach's  $\alpha=0.95$ ) and test-retest reliability ( $r=0.92$ ), indicating that the measure produces low levels of random measurement error.

RAQoL scores correlated most strongly with scores on the NHP Physical mobility scale ( $r=0.77$ ) and showed moderately strong correlations with the Emotional reactions, Pain and Energy level section scores.

Non-parametric tests for independent samples demonstrated significant differences in RAQoL scores between patients who differed according to their self-perceived RA severity ( $p<0.001$ ) and general health ( $p<0.001$ ).

**Conclusions:** The Portuguese version of the RAQoL was found to be a comprehensive, reliable and valid questionnaire. The new language version is recommended for use in routine clinical practice and for research purposes, to assess quality of life in Portuguese RA patients.

**Disclosure of Interest:** None declared

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AB1365

#### PROTEIN CONVERTASE SUBTILISIN/KEXIN TYPE 9 (PCSK9) IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS/LUPUS NEPHRITIS

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**Background:** SLE patients have a tendency of accelerated atherosclerosis (AS) which can only partly be explained by traditional risk factors for cardiovascular disease. Proprotein convertase subtilisin/kexin type 9 (PCSK9), which is a protease associated with cardiovascular risk that regulates both cholesterol metabolism and inflammatory reaction, had been regarded as a highly promising therapeutic target for cardiovascular disease.<sup>1</sup> Recent study had demonstrated that SLE patients with lupus nephritis (LN) had much higher risk of atherosclerosis.<sup>2</sup>

**Objectives:** To assess serum PCSK9 concentrations and the possible factors linked with PCSK9 variation in SLE/LN patients.

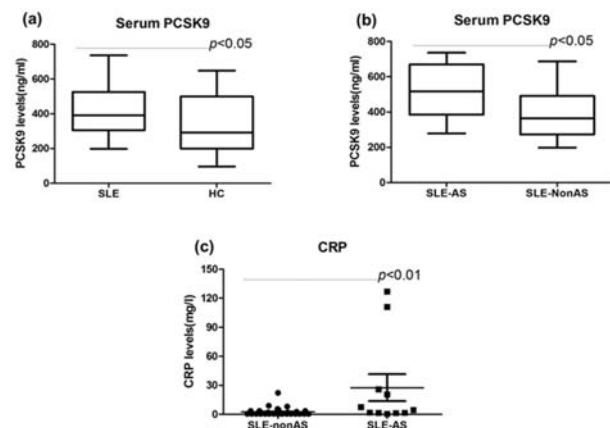
**Methods:** 47 SLE patients and 30 healthy controls were included. Traditional cardiovascular risk factors were compared. According to cIMT, SLE patients were divided into two subgroups (SLE-AS subgroup and SLE-NonAS subgroup, cut-off point is 1.0 mm). PCSK9 concentrations were compared between:<sup>1</sup>SLE patients

and controls;<sup>2</sup>SLE-AS subgroup and SLE-NonAS subgroup;<sup>3</sup>SLE patients with and without lupus nephritis(LN). The correlational analyses between PCSK9 levels and disease parameters were undergone.

**Results:** The differences of lipids parameters, body mass index (BMI), uric acid (UA) between SLE group and controls had no statistical significance. Even so, the ratio of cIMT thickening were higher in SLE patients, when compared with healthy controls (23.40% versus 6.67%,  $p=0.05$ ). Serum PCSK9 levels were also significantly elevated in SLE patients than controls (median of PCSK9 level: 390.53 ng/ml versus 292.44 ng/ml,  $p<0.05$ ). Patients in SLE-AS subgroup had even higher PCSK9 and C-reactive protein(CRP) levels than those in SLE-NonAS subgroup (median of PCSK9 level: 516.41 ng/ml versus 364.47 ng/ml,  $p<0.05$ ; median of CRP level: 4.56 mg/L versus 1.05 mg/L,  $p<0.01$ ) (figure 1). PCSK9 levels correlated with CRP levels, but not with age, disease activity, lipids characteristics, BMI or UA levels, particularly in female patients (table 1). Despite of no statistical significance, the ratio of lupus nephritis were higher in SLE-AS subgroup than those in SLE-NonAS subgroup (63.64% versus 44.44%,  $p>0.05$ ). SLE patients with LN had higher PCSK9 concentrations than those without LN evidence(509.53  $\pm$ 131.69 ng/ml versus 332.02 $\pm$ 92.72 ng/ml,  $p<0.001$ ).

**Abstract AB1365 – Table 1.** Correlational analysis of PCSK9 levels and disease parameters in SLE patients.

Variables	$r_s$	$p$ -value
Age(years)	-0.014	0.927
SLEDAI	0.092	0.539
BMI(kg/m <sup>2</sup> )	-0.120	0.420
Cholesterol(mmol/l)	-0.012	0.935
LDL cholesterol(mmol/l)	0.002	0.989
ApoA1(g/l)	0.011	0.943
ApoB(g/l)	0.181	0.223
Triglycerides(mmol/l)	-0.020	0.896
HDL cholesterol(mmol/l)	-0.112	0.453
Fasting blood glucose(mmol/l)	-0.193	0.193
Uric acid( $\mu$ mol/l)	-0.079	0.599
CRP(mg/l)	<b>0.351</b>	<b>0.016</b>
CRP(mg/l) in female patients	<b>0.487</b>	<b>0.001</b>



**Abstract AB1365 – Figure 1**

**Conclusions:** Elevation of PCSK9 concentrations can be observed in SLE patients, especially in those with LN or atherosclerosis. PCSK9. PCSK9 is probably linked with low-grade inflammation participating in the pathogenesis of atherosclerosis in SLE/LN patients.

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#### AB1366 RADIOISOTOPIC SYNOVIORTHESIS IN THE CONTROL OF REFRACTORY SYNOVITIS IN CASTILLA-LA MANCHA (A REGION OF SPAIN). AN EXPERIENCE OF 10 YEARS

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**Background:** Our hospital is the reference hospital in Nuclear Medicine for the realisation of radioisotopic synoviorthesis for all of Castilla-La Mancha (a region of Spain).

**Objectives:** To describe the experience in the performance of radioisotopic synoviorthesis in arthritis refractory to other treatments in our hospital.

**Methods:** Observational, descriptive and cross-sectional study protocolised through the review of the database of radioisotopic synoviorthesis performed between 2007 and 2017. Previous clinical data were collected (age, sex, pathology, previous treatments, previous infiltration and affected joint) and evolutive at 6 months after administering the isotope. An Excel database was created for a frequency analysis with SPSS 21.

**Results:** 30 radiosynovitis were performed with the most frequent pathologies, in this order: pigmented villonodular synovitis (40%), rheumatoid arthritis (23.3%), spondyloarthritis (13.3%), osteoarthritis (10%) and nonspecific arthritis (6.7%), followed by systemic lupus erythematosus and gout. After 6 months, 56.7% of patients improved compared to 36.7% who remained the same. Likewise, none of them presented complications related to the procedure. A 6.6% of patients were lost to follow-up.

**Conclusions:** In patients with episodes of recurrent arthritis with associated joint effusion in one or two joints, refractory to systemic treatments, to local infiltrations with corticosteroids and in those patients in whom other treatments may be contraindicated, we must consider the possibility of performing an isotope radiosynoviorthesis, as it is a simple, safe technique with a success rate of more than 50%.

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AB1367

### DIAGNOSTIC ASSOCIATION BETWEEN ELASTIN AND ELASTASE ANTIBODIES WITH CARDIOVASCULAR SYSTEM INVOLVEMENT IN SYSTEMIC SCLERODERMA PATIENTS

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**Background:** Large amounts of elastin are contained in vascular walls and in the cardiac valves. Elastin and elastase antibodies are predictors, *sui generis*, of vascular disease development in systemic scleroderma. The mechanism of direct proatherogenic effect of antibodies consists in stimulation of adhesion molecules and cytokine synthesis, oxLDL capture, induction of serine proteinase cascade by the coagulation system. In systemic rheumatoid disease, autoimmune inflammation is nowadays regarded as one of risk factors for the development of early atherosclerosis, disturbance of the structure and elasticity of vascular wall and of related cardiovascular conditions.

**Objectives:** Studying the effect of elastin and elastase autoantibody production on the cardiovascular system in systemic scleroderma (SSD) patients.

**Methods:** 42 patients hospitalised at municipal hospital 25 with diagnosis of SSD verified by <sup>ARA</sup> diagnostic criteria (1980) the diagnosis was considered firm if the patient showed one major and two minor criteria in any combination, simultaneously or consecutively, regardless of the time of their onset. The systemic scleroderma patients included 11 men and 31 women aged 22–72. The mean age of patients was 44.1±15.4 years. 30 healthy donors from the Volgograd hemotransfusion centre served as controls. Antibodies to elastin and elastase were determined in the blood serum using indirect enzyme immunoassay with magnetocontrolable adsorbents based on polyacrylamide granules according to the original technique by Gontar et al (1990)

**Results:** SSD patients showed considerable increase in the rate of elastase (52%) and elastin (38%) antibodies formation, in comparison with the controls. The upper normal limit of elastin antibody was within the range of 0.131 optical density units, elastase antibodies – 0.131 optical density units. In SSD patients elastin antibodies amounted to 0.125±0.068 optical density units. The titer of elastase antibodies was 0.143±0.071 optical density units. Healthy individuals did not show any elastin or elastase antibodies. An elevated antibody titer was associated with heart and vessels lesion in 47% of patients with SSD. In 20 patients of the studied group we revealed cardiovascular disease (IHD, macrofocal cardiovascular sclerosis with false infarction changes, chronic cardiac failure, and aorta atherosclerosis).

**Conclusions:** Among the patients we examined, 47% showed cardiovascular lesion associated with elevated elastin and elastase antibodies. This fact indicates that in systemic rheumatic disease, autoimmune inflammation is a risk factor for the development of early atherosclerosis, and of related cardiovascular conditions. Elastin and elastase antibodies are predictors, *sui generis*, of the development of vascular disease in patients with SSD.

**Disclosure of Interest:** None declared

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AB1368

### THE COMPARATIVE RESPONSIVENESS OF HOSPITAL UNIVERSITARIO PRINCESA INDEX AND OTHER COMPOSITE INDICES FOR ASSESSING RHEUMATOID ARTHRITIS ACTIVITY

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**Background:** HUPI was developed with data from the PEARL study (Princess Early Arthritis Register Longitudinal study) as an easy to calculate index, which avoided the gender bias affecting DAS28 and SDAI. In addition, it can be calculated either with erythrocyte sedimentation rate (ESR), C reactive protein (CRP) or both. Response criteria based on HUPI have also been developed<sup>1</sup>.

**Objectives:** To evaluate the responsiveness of the Hospital Universitario La Princesa Index (HUPI) comparatively to the traditional composite indices to assess disease activity in rheumatoid arthritis (RA), and to compare the performance of HUPI-based response criteria with that of the EULAR response criteria.

**Methods:** Post-hoc analyses were performed using data from the following studies: ACT-RAY (clinical trial), PROAR (early RA cohort) and EMECAR (pre-biologic era long term RA cohort). Responsiveness was evaluated by: 1) comparing change from baseline ( $\Delta$ ) of HUPI with  $\Delta$  in other scores by calculating correlation coefficients; 2) calculating standardised effect sizes. The accuracy of response by HUPI and by EULAR criteria was analysed using linear regressions in which the dependent variable was change in global assessment by physician ( $\Delta$ GDA-Phy).

**Results:**  $\Delta$ HUPI correlation with change in all other indices ranged from 0.387 to 0.791; HUPI's standardised effect size was larger than those from the other indices in each database used. In ACT-RAY, depending on visit between 65% and

80% of patients were equally classified by HUPI and EULAR response criteria. However, HUPI criteria were slightly more stringent, with higher percentage of patients classified as non-responder, especially at early visits. HUPI response criteria showed a slightly higher accuracy than EULAR response criteria when using  $\Delta$ GDA-Phy as gold standard.

Table 1

Comparison of sensitivity to change HUPI with other composite indices.

	Standardised size effect					Response (% EULAR vs HUPI)		
	HUPI	DAS28-VSG	DAS28-PCR	SDAI	CDAI	None	Moderate	Good
3 months	2'3	2'18	2'2	1'99*	1'67*	9 vs 22	53 vs 42	38 vs 36
6 months	3'13	2'93	2'85	2'56*	2'27*	3 vs 9'5	34 vs 29	63 vs 60'5
12 months	3'69	3'45	3'28*	2'87*	2'65*	2 vs 6'5	23 vs 20	75 vs 73'5

\*p<0.05 respect HUPI

**Conclusions:** HUPI shows good responsiveness in each studied scenario (clinical trial, early RA cohort, and established RA cohort). Response criteria by HUPI seem more stringent than EULAR's.

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**Acknowledgements:** We are indebted to the Roche laboratory for the transfer of the ACT-RAY trial data and to the Spanish Rheumatology Society for the transfer of data from the EMECAR and PROAR projects. Without the work of all the researchers who participated in these three projects, this work could not have been developed. This work has been supported by project P114/00442 to IG-A from the Ministry of Economy and Competitiveness (Carlos III Health Institute) and co-financed with the European Fund for Regional Development (FEDER).

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AB1369

### ELEVATED CA-125 IN IGG4-RELATED MESENTERIC DISEASE: A RED HERRING? A SYSTEMATIC LITERATURE REVIEW

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**Background:** Mesenteric panniculitis (MP), a rare fibrotic inflammatory disease of the bowel mesentery, can be a rare manifestation of IgG4-related disease (IgG4-RD). IgG4-RD is a chronic inflammatory disease most commonly affecting the pancreas, characterised by infiltration of IgG4-positive plasma cells and lymphocytes into various organs.<sup>1</sup>

We recently encountered a male patient with IgG4-related MP who was incidentally found to have a very high level of CA-125, which correlated with CRP levels and normalised after steroid treatment. This prompted a systematic literature review (SLR) to better understand this unexpected phenomenon.

**Objectives:** To investigate for associations between CA-125, MP and/or IGG4-RD, understand possible common pathophysiological mechanisms and explore potential clinical implications.

**Methods:** The SLR was performed using MEDLINE, EMBASE, Web of Science, and Scopus, looking for literature on either MP and CA-125 or IgG4-RD and CA-125 up to January 8 2018, using a comprehensive search strategy with relevant mesh terms and keywords linked to the above broad categories. Literature screening was performed by two independent reviewers.

**Results:** 24 unique citations were found, of which 13 were unanimously identified as relevant by the two reviewers. The final selected articles included: 8 case reports, 3 conference abstracts of case reports, 1 cohort study of 22 patients, and a retrospective study of 7 patients (table 1). CA-125 was raised in 22/40 patients in the identified reports (shown in red), including males, and was often the only elevated tumour marker (yellow). We also report on the presence of effusions (blue), as this may be linked to the causal mechanism.

Table 1 The clinical and laboratory characteristics of cases of IgG4-RD and MP

Article	Patient demographics	Main diagnosis	Serum CA-125 (U/mL)	Other tumour markers	Presence of effusions
Tong et al. (2017)	43 F	IgG4-RD	↑ (1/6)	CA 19-9 ↑, AFP ↑, CEA ↔	Ascites, pleural and pericardial effusions
Khosla et al. (2016)	72 M	AIP	↑ (1/6)	CA 19-9 ↔, CEA ↔	N/A
Thomas et al. (2015)	46 F	AIH, AI myositis	↑ (1/1)	CA 19-9 ↑	Ascites
Zhou, Zeng (2014)	24 F	IgG4-RD (lung)	↔	CA 19-9 ↔, CEA ↔, CA-153 ↔	Pleural effusion
Fengping et al. (2014)	Cohort study of 22 patients	IgG4-RD	↑ (15/22)	CA 19-9 ↑ in 6/22	N/A
Cheng et al. (2013)	45 M	AIP	↑ (2/3)	CA 19-9 ↔	Ascites, pleural effusions
Liu et al. (2012)	41 M	IgG4-RD (lung)	↔	CA 19-9 ↔, CEA ↔, PSA ↔, NSI ↔	No
Graham, Harvin (2016)	66 F	IgG4-RD (SM)	↔	CA 19-9 ↔, CEA ↔	Ascites
Ghadir et al. (2012)	70 M	AIP	↔	CA 19-9 ↔, CEA ↔	N/A
Dogan et al. (2015)	60 F	SM	↑ (2/5)	CA 19-9 ↔, AFP ↔, CEA ↔	N/A
Buyukbayrak et al. (2011)	38 F	SM	↑ (4/5)	CA 19-9 ↔, AFP ↔, CEA ↔, CA 153 ↔	Ascites
Maiter et al. (2017)	57 F	MP	↑ (1/1)	N/A	Ascites
Kiaoting et al. (2017)	Retrospective study of 7 patients (3 F, 4 M)	IgG4-RD (lung)	↑ in 1/7 F (45.5%), 4/5 M (80%)	CA 19-9 and CEA ↑ in 1/3 F	No
Current report	56 M	IgG4-related MP	↑ (1/1)	CA 19-9 ↔, AFP ↔, CEA ↔	Pleural effusion in 1/4 M

## Abstract AB1369 – Figure 1

**AI:** Autoimmune, **AIH:** Autoimmune Hepatitis, **AIP:** Autoimmune Pancreatitis, **SM:** Sclerosing Mesenteritis, **↑:** Raised, **↔:** Normal

**Conclusions:** To our knowledge, this is the first SLR exploring the association between CA-125 and IgG4-RD and MP. Despite the small sample, our results do indicate that CA-125 was raised in more than 50% of reported cases, the majority of which also had some kind of effusion. Although traditionally a marker of ovarian cancer, this report highlights that a raised CA-125 can be found in other, non-malignant, inflammatory conditions, and potentially correlates with inflammatory burden. CA-125 in this setting may thus represent a useful biomarker and have a role in monitoring treatment response.

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**Disclosure of Interest:** None declared

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### AB1370 PATIENT REPORTED OUTCOMES MEASURES FOR FIBROMYALGIA: A REVIEW

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**Background:** Persons with fibromyalgia (FM) suffer from numerous symptoms with various levels of intensity, such as widespread pain, fatigue, cognitive dysfunction, non-restorative sleep, depression, and anxiety among others. The patient's perspective has been recognised by Outcome Measure in Rheumatology (OMERACT) as a key assessment in FM. For that reason, some patient reported outcomes measures (PROMs) have been developed. PROMs allow the comparison of a specific component of the disease in a patient through time, and also provide the opportunity to health professionals to compare patients between them in clinical trials. However, some PROMs are used over others despite a limited validation process. In addition, different versions of the same PROMs can co-exist, what can lead to uncertainty when selecting the adequate instrument.

**Objectives:** To identify the existing PROMs for FM and analyse their psychometric properties.

**Methods:** The authors performed a comprehensive search in electronic databases (Medline, Embase, and Cochrane) in order to identify validation studies of PROMs for FM. Studies published between January 1990 and November 2017 were included. Generic PROMs and validation of diagnostic criteria and related screening tools were not considered as PROMs and were excluded. Information was gathered based on the Consensus-based Standards for the selection of health Measurement Instruments (COSMIN) checklist manual.

**Results:** The electronic search produced 1832 records. After screening, a total of 48 studies containing 16 PROMs for FM were included. The PROMs included address different constructs of the disease, Fibromyalgia Impact Questionnaire (FIQ), Revised Fibromyalgia Impact Questionnaire (FIQR), Combined Index of Symptom Severity, Combined Index of Severity of Fibromyalgia, Comprehensive Rating Scale for Fibromyalgia Symptomatology, Fibromyalgia Assessment Status, Fibromyalgia Bladder Index, Fibromyalgia Burden Assessment, Fibromyalgia Health Assessment Questionnaire, Fibromyalgia Impact Questionnaire+Visual Analogue Scales, Fibromyalgia Participation Questionnaire, Fibromyalgia Sleep Diary, Multidimensional Inventory of Subjective Cognitive Impairment, Multidimensional Patient Reported Outcome Measures Questionnaire, PROMIS Fatigue FM Profile, and Multidimensional daily diary of fatigue-fibromyalgia-17 items.

Almost all PROMs have adequate content validity. Three PROMs do not report construct validity; seven do not report reliability, and six do not report internal consistency. Only three PROMs evaluate criterion validity and three responsiveness. The FIQ and the FIQR are the PROMs more widely cross-cultural validated with 18 and 13 adaptations respectively.

**Conclusions:** PROMs for FM have, in general, only partial validation of their psychometric properties. Validation of an instrument is a continuous process in which quality is more important than quantity. Instead of creating new PROMs for FM, future works should focus on completing missing parts of the validation process of existing ones. In addition, cultural adaptations and translations of the available PROMs should be prioritised in order to offer researchers across the globe a toolbox of options in where they can choose the best PROMs to address their objectives in a highly subjective syndrome as FM.

**Disclosure of Interest:** None declared

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### AB1371 CLINICAL SIGNIFICANCE OF KL-6 AND SP-D AS SERUM MARKERS FOR INTERSTITIAL LUNG DISEASE IN PATIENTS WITH CONNECTIVE TISSUE DISEASE

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**Objectives:** To evaluate the association between serum levels of Krebs von den Lungen-6 (KL-6) and surfactant protein-D (SP-D) and the clinical manifestations and severity of interstitial lung disease (ILD) in patients with connective tissue disease (CTD).

**Methods:** Eighty patients with various CTDs were included, as follows: 33 with rheumatoid arthritis (RA), 19 with systemic lupus erythematosus (SLE), 10 with systemic sclerosis (SSc), 9 with Sjogren's syndrome (SS), and 9 with inflammatory myositis. KL-6 and SP-D levels were measured using an enzyme-linked immunosorbent assay and defined as abnormal if KL-6  $\geq 500$  U/mL and SP-D  $\geq 110$  mg/mL. All patients were simultaneously evaluated for parameters related to disease activity using laboratory tests and a pulmonary function test, and interstitial lung abnormalities (ILA) using chest computed tomography (CT). Patients were subclassified according to ILA score: 0 for no ILD, 1 for indeterminate ILD, 2 for mild ILD, and 3 for advanced ILD based on chest CT scans.

**Results:** In all, 29 patients had radiologically advanced ILD, 18 had mild ILD, 18 had indeterminate ILD, and 15 had no ILD. A higher ILA score was associated with more severe dyspnea, and decreased volume and percent of functional vital capacity, forced expiratory volume in 1 s, and diffusion capacity of carbon monoxide. As clinical manifestations, a higher ILA score was associated with a higher GAP index but not with the parameters of disease activity. A higher ILA score was associated with higher levels of KL-6 and SP-D and a higher percentage of subjects with abnormal levels, and this was more pronounced in SLE, SSc, and SS than in RA.

**Conclusions:** Serum levels of KL-6 and SP-D are associated with the radiological severity of ILD. Hence, these can serve as markers for ILD severity, especially in SLE, SSc, and SS.

**Disclosure of Interest:** None declared

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### AB1372 TOWARDS REFORMING THE TAXONOMY OF HUMAN DISEASE: THE PRECISESADS CROSS SECTIONAL STUDY

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**Objectives:** The PRECISESADS project aims at using OMICs, and bioinformatics to identify new classifications for systemic autoimmune diseases (SADs) known to share common pathophysiological mechanisms in view of personalised treatments. Multi OMICs parameters collected in addition to routine clinical data in a cross-sectional study involving patients suffering from systemic lupus erythematosus (SLE), systemic sclerosis (SSc), Sjogren's syndrome (SjS), rheumatoid arthritis (RA), primary antiphospholipid syndrome (PAPs), mixed connective

tissue disease (MCTD), undifferentiated connective tissue disease (UCTD) and healthy controls (HC) will be analysed to identify clinically relevant clusters.

**Methods:** A European multi centre, non-randomised, cross-sectional clinical study was conducted in 18 sites and 9 countries. Collection of OMIC data including genetic, epigenomic, transcriptomic (from peripheral blood and from isolated cells), flow cytometry, metabolomics and proteomic in plasma and urine, exosome analysis and classical serology (antibodies and autoantibodies) was organised. Novel and innovative methodologies including fine flow cytometry were conducted. Quality procedures were established to ensure standardisation of samples collection, processing, transportation and storage. Techniques were validated to ensure reproducibility of analyses. Unsupervised bioinformatics and biostatistics approaches will be applied.

**Results:** Recruitment started in <sup>December 2014</sup> and ended in October 2017. A total of 2656 participants were recruited: 377 RA, 470 SLE, 402 SSs, 385 Sjs, 99 MTCD, 106 PAPs, 166 UCTD patients and 651 HCs. Median age was between 46 and 59 years and was consistent with each disease onset peak. 97% of the population was Caucasian. Most of the patients were treated with standard of care therapies and less than 10% were on biologics. OMICs and bioinformatics analyses are on-going.

**Conclusions:** We have established one of the largest collaborative multi-OMICs studies from patients with SADS. The most important challenge is now the integration of all these novel data to support hypothesis-free, machine learning-led analytical protocols. It is expected that the integration of data from affected patients, in comparison with well-matched controls, will provide new biomarker-led descriptions of clusters of potentially etiologically distinct disease entities.

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#### AB1373 URINARY PROTEIN PROFILE COMPARISON BETWEEN SLE PATIENTS WITH AND WITHOUT RENAL INVOLVEMENT

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**Background:** Lupus nephropathy (NL) is an important cause of morbidity and mortality in patients with Systemic Lupus Erythematosus (SLE). The objective of the renal biopsy is to determine the type of glomerulonephritis that the patient presents to direct treatment. Considering that it is a specialised technique and not risk free, a proteomics study is proposed to determine biomarkers that help us to differentiate patients diagnosed with SLE with and without renal involvement.

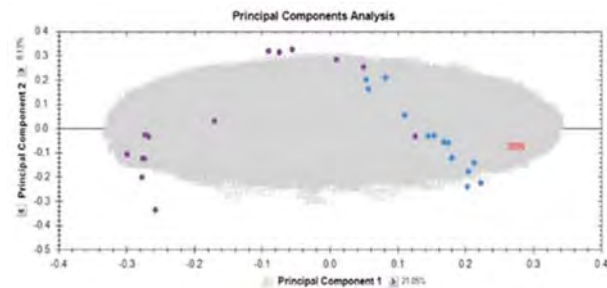
**Objectives:** To determine if there is a different pattern of proteins between patients diagnosed with SLE with and without renal involvement.

**Methods:** We selected 12 patients diagnosed with SLE with renal involvement and 14 patients diagnosed with SLE without renal involvement. There were no differences between groups according to race, gender and age. The patients were classified as high, low or negative level of proteinuria in the urine. A 24 hour urine sample was obtained for analysis.

**Results:** We have done a Principal Component Analysis (PCA) where we can see differences between samples from patients who have high level of proteinuria in 24 hours and patients who have not renal involvement. Patients with positive proteinuria but not high level are a little confuse figure 1.

A total of 292 proteins (identified with at least two peptides with a FDR<1%) were quantified and further considered in the analysis. The Student's T-test analysis reflected the differential presence of 147 proteins ( $p<0.01$ ). Of these, 130 were less abundant in the urine of the patients with renal damage, whereas 17 showed the opposite pattern, being more abundant in the patients with affected renal function.

Consistent with the nature of the sample, the Gene Ontology (GO analysis) of the whole list of identified proteins revealed the presence of extracellular (277 proteins,  $p=2.25E-171$ ) and secretion-related proteins (49 proteins,  $p=1.1E-09$ ), among others. Proteins related to defensive processes were prominent among them. Interestingly, the subset of proteins whose abundance increases upon renal damage is comprised of typical highly-abundant serum proteins. These proteins render a large number of peptides, suggesting they are very abundant. This protein pattern may reflect the higher albuminuria characteristic of patients with affected renal function. On the other hand, a number of proteins became significantly less abundant upon renal damage. The presence of highly abundant serum proteins in the urine of patients with compromised renal function may explain this phenomenon, since this will provoke a dramatic reduction in the relative abundance of the proteins already present in their urine.



Abstract AB1373 – Figure 1

**Conclusions:** A different protein pattern is observed between the two groups of patients, so in a more detailed study we can indicate if some of these can serve as prognostic markers for this type of patients.

**Disclosure of Interest:** None declared

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#### AB1374 PERFORMANCE OF EQ-5D, RAPID-3 AND HADS SCALES IN THE ASSESSMENT OF QUALITY OF LIFE AND FUNCTIONAL STATUS IN PATIENTS WITH ERYTHEMA NODOSUM

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**Background:** Erythema nodosum (EN) is the typical example of a mostly *septal panniculitis* with no vasculitis. Sarcoidosis and streptococcal infection are considered to be the most common etiological factors. There are no special scales available for practitioners to assess the efficacy of EN treatment in spite of high disease prevalence in general population. Sensitivity, specificity and validity of EQ-5D, RAPID-3 and HADS questionnaires have been demonstrated in other rheumatic diseases.

**Objectives:** The aim of this study is to evaluate the psychometric properties of EQ-5D, RAPID-3 and HADS scales in EN patients.

**Methods:** The study included 47 patients (45 females, 2 males) aged 37,6 ± 11,2 y with mean EN duration 2,5<sup>1</sup>; 6 months who were on the record at V. A. Nasonova Research Institute of Rheumatology during 2013–2017 yy. All patients filled in EQ-5D, RAPID-3 and HADS questionnaires at baseline (first visit) and 12 months later. The sensitivity of the questionnaires was assessed by comparing obtained scores with patient's response to therapy until achievement of nodular regression at the time of dynamic examination. The construct validity was determined using a correlation analysis with "external criteria", such as presence of artralgia/arthritis, palpatory tenderness of nodules assessed with VAS scale, ESR and CRP levels.

**Results:** Complete nodular regression was achieved in 39 patients. Positive post-treatment changes (nodular regression) correlated with improved EQ-5D (EQ-5D-index –  $p=0,005$ , EQ-5D-VAS –  $p=0,009$ ) and HADS-anxiety subscale –  $p=0,02$ . No significant association was found for other questionnaires with  $p$  value=0,11 for RAPID-3 and  $p=0,69$  for HADS-depression scale. Moderate correlation was established at control visit after 12 months (Mo12) between EQ-5D-index and nodular tenderness to palpation ( $r=-0,49$ ,  $p=0,0001$ ), between EQ-5D-index and ESR value ( $r=-0,55$ ,  $p=0,0016$ ), as well as between general health status assessed by VAS and nodular tenderness to palpation at baseline visit ( $r=-0,56$ ,  $p=0,0001$ ), indicating close association of data obtained by these assessment tools with objective physical and laboratory findings. There was also moderate correlation between functional RAPID-3 scores and nodular tenderness to palpation at Mo12 ( $r=0,37$ ,  $p=0,0172$ ) and ESR level ( $r=0,52$ ,  $p=0,0002$ ). These data demonstrate close association of assessment scales performance with objective health status. Moderate correlation was established for HADS-depression subscale scores with nodular tenderness to palpation in 12 month after initiation of treatment ( $r=0,41$ ,  $p=0,0077$ ) and CRP value ( $r=0,34$ ,  $p=0,025$ ). There were no additional statistically significant correlations for RAPID-3 and HADS subscales with clinical and laboratory findings.

**Conclusions:** EQ-5D questionnaire is a valid and sensitive tool for assessment of quality of life in EN patients.

**Acknowledgements:** The study had no sponsorship.

**Disclosure of Interest:** None declared

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AB1375

### RELIABILITY AND VALIDITY OF TURKISH VERSION OF SHORT FORM OF THE SOCIAL ROLE PARTICIPATION QUESTIONNAIRE (S-SRPQ) IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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**Background:** Ankylosing spondylitis (AS) is a chronic inflammatory rheumatic disease with a usual onset in the third decade of life, when persons are committed to various social roles that adults fulfil.<sup>1</sup> When evaluating the outcomes of clinical care, social role participation is an increasingly important outcome, especially when considering diseases with substantial limitations in physical functioning such as inflammatory rheumatic diseases.<sup>2</sup> The Short Form of the Social Role Participation Questionnaire (s-SRPQ) is a questionnaire which was developed to assess effect of ankylosing spondylitis (AS) on participation.<sup>2</sup>

**Objectives:** This study aims to evaluate the reliability and validity of the Turkish version of the s-SRPQ in Turkish patients with AS.

**Methods:** The Turkish version of s-SRPQ questionnaire was obtained after a translation and back translation process. The study sample included 100 AS patients (59 males, 41 females; mean age 42.00±11.00 years; range 19 to 69 years). To assess the test-retest reliability of the Turkish s-SRPQ, the questionnaire was reapplied 15 days after the first interview (interclass correlation coefficient, ICC). Cronbach's alpha (α) was used to evaluate the internal consistency. The s-SRPQ was compared with Short Form-36 survey (SF-36), Ankylosing Spondylitis Quality of Life questionnaire (ASQoL), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI), and Satisfaction With Life Scale (SWLS) for convergent validity. The internal structure of s-SRPQ was examined by factor analysis.

**Results:** For s-SRPQ/experienced physical difficulties; the individual item ICC ranged from 0.78 to 1.00 and Cronbach's alpha value ranged from 0.88 to 1.00. For s-SRPQ/satisfaction with role performance; the individual item ICC ranged from 0.93 to 0.98 and Cronbach's alpha value ranged from 0.96 to 0.99. KMO values was determined as 0.90 and 0.89 in the s-SRPQ/experienced physical difficulties and s-SRPQ/satisfaction with role performance, respectively. Bartlett's test of sphericity had a p<0.001. The Turkish version of s-SRPQ/experienced physical difficulties scores negatively correlated with the SWLS and SF-36 sub-parameters scores (p<0.01). There were also strong positive correlations between s-SRPQ/experienced physical difficulties scores and BASDAI, BASFI, and ASQoL scores (p<0.01). The SRPQ/satisfaction with role performance scores positively correlated with the SWLS and SF-36 sub-parameters scores (p<0.01). There were also strong negative correlations between s-SRPQ/experienced physical difficulties scores and BASDAI, BASFI, and ASQoL scores (p<0.01).

**Conclusions:** Turkish version of s-SRPQ has good comprehensibility, internal consistency, and validity and is an adequate and useful instrument for the assessment of participation in Turkish patients with AS.

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**Disclosure of Interest:** None declared

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AB1376

### URINARY MONOCYTE CHEMOATTRACTANT PROTEIN 1 CANNOT DIFFERENTIATE BETWEEN HISTOLOGICAL CLASSES OF LUPUS NEPHRITIS

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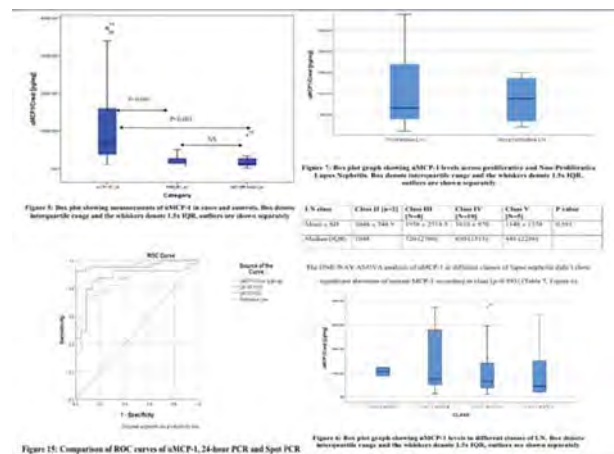
**Background:** Lupus Nephritis, one of the commonest manifestation of SLE, seen in 60% of adult SLE patients at some point of time, carries poor prognosis when compared to those with no renal involvement. The natural course of the LN has recurrent flares, necessitating the need for early detection and treatment. Despite being the gold standard in diagnosing Lupus nephritis and its severity, renal biopsy is an invasive procedure with potential complications, and difficult to repeat. Hence, a novel biomarker, reflecting the disease activity and severity is needed to predict flare. Monocyte chemoattractant Protein 1, a chemokine

produced locally during Lupus Nephritis flare, was shown in many previous studies as a promising biomarker

**Objectives:** We studied the role of Urinary MCP-1 as a biomarker of disease activity in LN and compare its value among different histological classes of Lupus nephritis

**Methods:** This is a case-control study conducted at a tertiary care centre in North India from July 2016 to December 2017. Cases were those patients undergoing renal biopsy satisfying the inclusion criteria set for SLE with LN (n=36). Controls were patients of SLE without active LN [Control I-prior LN (n=11) and Control II-never had LN (n=15)]. Urinary MCP-1 measurement was done using Sandwich ELISA kit

**Results:** The mean age in cases was 31.1±10.2 years and mean age in control-I was 34.6±8.0 and in control II was 36.3±10.4. Urinary MCP-1 values in cases (1214±1467.1 pg/mg) was significantly higher compared to Controls (184.5±186.8). However, no significant difference was observed between Control I (170.5±150.8) and Control II (194±214). Urinary MCP-1 levels show significant correlation when compared with classical disease markers like 24 hour proteinuria, 24 hour PCR, Spot PCR and SLEDAI. Cut off value (339 pg/mg, p<0.001) obtained from ROC curve has sensitivity and specificity of 80% and 92% respectively. However, there was no significant difference of Urinary MCP-1 levels was observed among different classes of LN (p=0.593). ROC curve comparison of urinary MCP-1 (AUC=0.879) with 24 hour urine protein to creatinine ratio (AUC=0.964) and spot urine protein to creatinine ratio (AUC=0.872) showed that it is not a better marker of disease activity than both of them. Urinary MCP-1 levels didn't show significant correlation with Renal activity index calculated on renal biopsy.



**Conclusions:** In this study we found higher Urinary MCP-1 levels in active LN compared to Inactive LN and its level was correlated well with the presently used disease markers. However there was no significant difference among different histological classes of LN.

**Disclosure of Interest:** None declared

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AB1377

### IS THE PATIENT GLOBAL HEALTH ASSESSMENT RELIABLE IN JUVENILE IDIOPATHIC ARTHRITIS (JIA)?

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**Background:** JIA is a chronic autoimmune disease that poses many challenges. There is increasing recognition of the importance of patient-reported outcomes (PROs) and newer PROs are being developed and more widely utilised both in clinical care and in research. However, their performance and reliability remain unclear.

**Objectives:** This study seeks to evaluate:<sup>1</sup> performance of the patient global health assessment (PGA) compared to standard disease activity measures in children with JIA,<sup>2</sup> correlations of the PGA with socioeconomic status (SES) in JIA, and<sup>3</sup> relationship between PGA and physician global health assessment in JIA.

**Methods:** A convenience sample of patients with JIA (n=47) aged 2–18 were recruited from a single centre. Patients aged ≥10 years completed the questionnaire, and parents of patients aged 2–9 completed a proxy questionnaire for their child. Correlations between<sup>1</sup> the PGA and disease activity, as measured by the Juvenile Disease Activity Score-71 (JADAS-71),<sup>2</sup> the PGA and physician global health assessment, and<sup>3</sup> the physician global health assessment and the JADAS-71 were evaluated using Spearman correlation coefficients. PGAs were compared by age, sex, insurance status, race, and ethnicity; and differences between

PGA and physician global health assessments were compared using Wilcoxon rank-sum tests.

**Results:** 16 parents and 31 patients completed the assessments (table 1). There was a moderate correlation between PGA and JADAS-71 ( $r=0.503$ ,  $p<0.001$ ), and PGA and physician global health assessments ( $r=0.503$ ,  $p=0.002$ ). There was a stronger correlation between physician global health assessments and JADAS-71. PGA median scores and IQRs appeared to be higher among patients with Medicaid insurance, non-white race, and Hispanic ethnicity, with the greatest difference seen in the category of race (Table 2). There were no differences between patient and physician assessments across all groups except among patients with Medicaid (difference median=-1.25) and Hispanic patients (difference median=2).

**Abstract AB1377 – Table 1.** Patient Characteristics

	Patients and Parents (n=47)	Patients (n=31)	Parents (n=16)
<b>Age, years</b>	12.4	14.2	4.3
<b>(median, IQ range)</b>	[8.6–15.0]	[12.4–15.8]	[3.3–9.0]
<b>Male Gender</b>	17 (36.2%)	14 (45.2%)	3 (18.8%)
<b>Race</b>			
<b>Caucasian/White</b>	38 (80.9%)	24 (77.4%)	14 (87.5%)
<b>Asian</b>	3 (6.4%)	3 (9.7%)	0 (0.0%)
<b>Other</b>	6 (12.7%)	4 (12.9%)	2 (12.5%)
<b>Hispanic Ethnicity</b>	8 (17.0%)	5 (16.1%)	3 (18.8%)
<b>Insurance</b>			
<b>Medicaid</b>	8 (17.0%)	4 (12.9%)	4 (25.0%)
<b>Private</b>	39 (83.0%)	27 (87.1%)	12 (75.0%)

**Abstract AB1377 – Table 2.** Comparison of Patient Global Assessments by age, sex, insurance status, race and ethnicity

	Patient global median [IQR]	P-value
<b>Age</b>	2 [0–5]	0.892
<b>Patient completed</b>	2 [0.05–4.5]	
<b>Parent completed</b>		
<b>Sex</b>	2 [0–5]	0.679
<b>Male</b>	2 [0–4]	
<b>Female</b>		
<b>Insurance</b>	2.5 [1, 5]	0.313
<b>Medicaid</b>	2 [0–4]	
<b>Private</b>		
<b>Race</b>	1.5 [0–4]	0.266
<b>White</b>	4 [2–5]	
<b>Non-white</b>		
<b>Ethnicity</b>	2.5 [2.5–5]	0.134
<b>Hispanic</b>	1 [0–4]	
<b>Non-Hispanic</b>		

**Conclusions:** Our results demonstrate that physician global health assessment had a stronger correlation with standard disease activity measures than the PGA. These scores were higher in patients who were non-White race, Hispanic, and had Medicaid insurance; however, these were not statistically significant. These data indicate that the PGA is fairly stable across groups, and can be used reliably for disease monitoring.

**Disclosure of Interest:** None declared

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**AB1378** **CLINICAL COMPARISON OF NEW CRITERIA FOR INFLAMMATORY MYOPATHY IN A COLOMBIAN COHORT**

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**Background:** Idiopathic inflammatory Myopathies are a group of diseases characterised by weakness due to muscle inflammation, with or without dermatological involvement, that classically includes pathognomonic findings like Gottron sign. There have been different criteria used to classify these diseases, being Peter and Bohan the most used in time, but recently the ARC/EULAR group proposed a new way to approach the classification.

**Objectives:** To compare ACR/EULAR 2017 versus Peter and Bohan criteria for Idiopathic Inflammatory Myopathy in a Colombian cohort

**Methods:** A cross-section retrospective research was done with data collected between 2014 and 2017 from a population diagnosed with Idiopathic Myopathy according to Peter and Bohan criteria and followed up for at least six months. The new ACR/EULAR criteria were applied to each individual using the online tool

(<http://www.imm.ki.se/biosstatistics/calculators/iim>). Both sets of criteria were compared using Cohen's kappa coefficient and concordance was evaluated.

**Results:** Data of 149 patients were obtained. Anti-Jo1 results were not available for 75% of the patients. Biopsy was available in 44,3% of patients. Biopsy results were compatible with inflammatory myopathy in 66,7% and non-compatible in 33,3%. According to Peter and Bohan criteria the diagnosis of idiopathic inflammatory myopathy was definite in 63,1% of the patients, and probable in 27,5%. Using ACR/EULAR 2017 criteria instead the diagnosis was definite in 63,1%, probable 10,1% and non-possible in 20,8%. According to the new criteria, 31 patients had polymyositis, 47 dermatomyositis, 4 amyopathic dermatomyositis, 35 juvenile myositis and 1 inclusion body myositis. The concordance analysis between the two sets of criteria showed agreement of 54% (kappa 0,22  $p<0,001$ ) in the whole group, 59% (kappa 0,21  $p<0,001$ ) in adults, 32% (kappa 0,18  $p=0,05$ ) in children, 44% (kappa 0,05  $p=0,3$ ) in polymyositis and 42% (kappa 0,16  $p=0,1$ ) in dermatomyositis.

**Conclusions:** Data of 149 patients were obtained. Anti-Jo1 results were not available for 75% of the patients. Biopsy was available in 44,3% of patients. Biopsy results were compatible with inflammatory myopathy in 66,7% and non-compatible in 33,3%. According to Peter and Bohan criteria the diagnosis of idiopathic inflammatory myopathy was definite in 63,1% of the patients, and probable in 27,5%. Using ACR/EULAR 2017 criteria instead the diagnosis was definite in 63,1%, probable 10,1% and non-possible in 20,8%. According to the new criteria, 31 patients had polymyositis, 47 dermatomyositis, 4 amyopathic dermatomyositis, 35 juvenile myositis and 1 inclusion body myositis. The concordance analysis between the two sets of criteria showed agreement of 54% (kappa 0,22  $p<0,001$ ) in the whole group, 59% (kappa 0,21  $p<0,001$ ) in adults, 32% (kappa 0,18  $p=0,05$ ) in children, 44% (kappa 0,05  $p=0,3$ ) in polymyositis and 42% (kappa 0,16  $p=0,1$ ) in dermatomyositis.

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**Disclosure of Interest:** None declared

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**AB1379** **POTENTIAL DIAGNOSTIC SERUM IMMUNOLOGICAL MARKER PANEL IN PRIMARY AND SECONDARY OSTEOARTHRITIS IN SRI LANKAN PATIENTS**

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**Background:** Osteoarthritis (OA) is commonly perceived as a degenerative joint disease but it is now established that inflammation contributes to OA. Though OA is categorised into primary and secondary osteoarthritis, most clinicians manage patients of both categories in a similar manner.

**Objectives:** The current study aimed to identify potential diagnostic markers of primary and secondary OA. Two cohorts of Sri Lankan patients, one with primary OA and another with secondary OA were assessed for a selected panel of immunologic mediators i.e. cytokines (TNF- $\alpha$ , IL-1 $\beta$ , IL-6, IL-10) and nitric oxide derivatives (NOx).

**Methods:** A case control study was conducted with 40 OA patients (Primary, n=30; Secondary, n=10), and 60 age and gender matched controls (normal healthy, n=30; Systemic Lupus Erythematosus (SLE) disease control, n=30). The socioeconomic and demographic data were accrued via an interviewer administered questionnaire. Sandwich ELISAs assayed serum cytokine levels, while the 'Griess assay' measured serum NOx levels.

**Results:** In comparison to healthy controls, OA patients showed significantly higher serum concentrations of all five analytes tested ( $p<0.05$ ). Patients with primary OA had significantly higher levels of TNF- $\alpha$  and IL-1 $\beta$  and lower level of IL-6 in serum compared to disease controls (SLE) ( $p<0.05$ ). Secondary OA patients exhibited a significant increase in serum TNF- $\alpha$  and IL-1 $\beta$  and lower serum IL-10 levels compared to disease controls ( $p<0.05$ ). In the two test groups, the serum levels of TNF- $\alpha$  and IL-6 were significantly elevated in secondary OA patients ( $p<0.05$ ). The NOx concentrations between the two test groups was not significantly different. The Th1:Th2 cytokine ratio (TNF- $\alpha$ :IL-10) was significantly higher in secondary OA compared with primary OA ( $p<0.05$ ).

The Receiver operating characteristic (ROC) curves identified TNF- $\alpha$  and IL-10 as potential diagnostic biomarkers of both primary OA and secondary OA compared with healthy controls. IL-1 $\beta$  and IL-6 may be used specifically as diagnostic

biomarkers for primary and secondary OA, respectively, when compared with healthy individuals. TNF- $\alpha$  is a suitable biomarker for the diagnosis of both primary and secondary OA when compared to SLE patients, whereas IL-6 and IL-1 $\beta$  were apparent explicit markers of primary OA, while IL-10 was exclusive for secondary OA.

**Abstract AB1379 – Table 1.** lists the values obtained from the ROC curves for the cytokine panel and NOx for patients clinically diagnosed with primary and secondary osteoarthritis against normal healthy controls.

	Primary OA				Secondary OA			
	AUC (%)	Cut-off value*	Sensitivity	Specificity	AUC (%)	Cut-off value*	Sensitivity	Specificity
TNF- $\alpha$	88.3	>10.8	93.33	80.00	97.0	>28.2	100.00	96.67
IL-10	88.6	>32.67	85.71	92.59	93.1	>32.67	90.00	92.59
IL-6	59.3	>3.98	89.66	40.74	81.2	>12.02	66.67	96.15
IL-1 $\beta$	85.2	>1.18	96.43	68.42	61.4	>0.88	77.78	57.89
NOx	72.0	>18.89	93.33	60.71	73.0	>18.89	100.00	60.71

\*For the cytokines, in pg/ml and for NOx in  $\mu$ mol/l

**Conclusions:** This preliminary study suggests that higher levels of inflammatory cytokines are present in secondary OA compared to primary OA. Furthermore, distinct markers for primary and secondary OA were identified, indicative of the potential for developing different therapeutic agents for the different types of OA.

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## AB1380 PERIPHERAL NEUROPATHY IN INFLAMMATORY JOINT DISEASES

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**Background:** For frequent extra-articular (systemic) manifestations of joints inflammatory diseases are various damage of the nervous system,<sup>2</sup> and the presence and severity of peripheral neuropathy (PNP) have significance in the clinical course, which incidence among these patients is 5%–10%.<sup>1</sup> Nevertheless, many clinical and pathogenic aspects of this peripheral neuropathy (PNP) remain obscure.

**Objectives:** to evaluate the rate and clinical features of PNP in rheumatoid arthritis (RA), chlamydia urogenital reactive arthritis (ReA), psoriatic arthritis (PA) and ankylosing spondylitis (AS), to examine the issues of pathogenetic constructions such changes of the nervous system, define risk factors.

**Methods:** The study included 416 patients with inflammatory joint diseases, among them 131 RA patients, 101 ReA, 76 PA and 108 AS. The average age of the examined was respectively 45, 32, 42 and 38 years, disease duration – 10, 4, 12 and 11 years, male to female ratio – 1.5, 1.1, 1.2 and 10.1.

**Results:** The frequency of the PNP in RA, ReA, PA and AS was 13%, 19%, 24% and 34%, while its severity in patients with PA <ReA < RA < AS, and the same type ratio of motor, sensory and mixed disorders of inflammatory joints diseases, trophic, visceral and vascular vegetative changes, the connexion with the male sex, the activity of arthritis and the presence of tendovaginitis, participation of immune disorders, endothelial dysfunction of blood vessels and changes in physical and chemical rheological viscoelastic properties of blood in the pathogenesis constructions of the nervous system lesions are united around. ReA and PA are different by frequency of hands and feet distal pathology, the AS – by the beginnings of tunnel syndrome. RA tends to impact on the PNP digital arteritis, myositis, eye disease, and Sjogren's syndrome, ReA – on sacroiliitis, PA – on exudative form of cutaneous psoriasis, AS – on eye disease, at that, the risk factors for severe course of neuropathy in RA is considered to involve in the process of elbows, ReA – intervertebral and facet joints, PA – wrist, AS – sacroiliac. Guillain-Barré syndrome develops respectively in 3%, 4%, 5% and 9% of patients with RA, PA, ReA and AS, or in 24%, 17%, 26% and 27% cases of PNP, which is closely linked to the presence of tendovaginitis in all inflammatory diseases and severity of articular syndrome, in RA it depends on the presence of hypothyroidism, in ReA – on nephropathy and violations of the heart's electrical conduction, in AS – on osteoporosis, and seropositive for anti-cyclic citrullinated peptide antibody is a risk factor for such peripheral nervous system disorders.

**Conclusions:** PNP is a relatively common manifestation of inflammatory diseases of the joints, which correlate with clinical and laboratory signs of the disease, and in the future such active detection of the nervous system pathology will be useful for timely follow-up rehabilitation.

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## Education

### AB1381 FOUR ANNUAL INTERNATIONAL DIFFERENT MEETINGS OF RHEUMATOLOGY: COMPARISON OF THE CONTENTS, ANALYSIS, CHALLENGE AND OPPORTUNITIES

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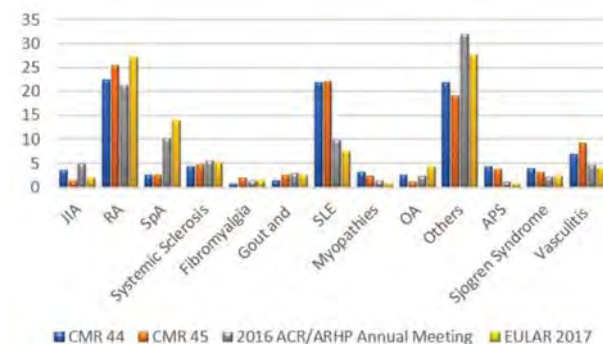
**Background:** The medical meetings are a tool to help us be able to escalate and actualize the medical knowledge and their quality is a responsibility of Colleges and Institutions.

**Objectives:** To assess the academic level of four types of different annual Meeting of Rheumatology

**Methods:** We used as support information the summaries published in the supplements of the journal *Reumatologia Clinica*, SE1 Vol. 12 of February 2016, the supplement SE 1 Vol. 13 of February 2017, the application for electronic media of the ACR/ARHP 2016 of the American Congress of Rheumatology 2016 and the website for abstracts of EULAR 2017 dedicated to the surveys presented in the XLIV Mexican Congress of Rheumatology, XLV Mexican Congress of Rheumatology and the 2016 ACR/ARHP Annual Meeting, and EULAR 2017 respectively, of each survey we was obtained information about of the diverse pathologies, the type of trial, content and population referred (adults versus children).

**Results:** 275, 340, 3275 and 4129 were presented in the XLIV Mexican Congress of Rheumatology, XLV Mexican Congress of Rheumatology, the 2016 ACR/ARHP Annual Meeting and EULAR 2017 respectively. Rheumatoid arthritis (RA) was the most common pathology with 23%, 26%, 21% and 27% in CMR 44, CMR 45, ACR 2016 and EULAR 2017 respectively, followed by systemic lupus erythematosus, third place was vasculitis, beside in international congress was the spondyloarthritis. Highlighted, RA the items about of clinic manifestations were accounted for almost 30% in the Mexican congress and almost 20% in ACR and EULAR. Observational studies accounted for almost 40% in Mexican congresses vs. 33% in ACR 2016 and 55% in EULAR 2017 beside surveys about of basic research were minimal in Mexican congress, but in ACR 2016 accounted for 21% and 12% in EULAR 2016

The trials about of Paediatric Rheumatology were 12.3%, 5.5% and 4.9% in CMR 44, CMR 45 and ACR 2016 respectively.



**Abstract AB1381 – Figure 1.** percentage of rheumatic disease

**Conclusions:** Rheumatology Meeting constitutes a support to obtain the adequate medical knowledge based in evidence, in this important branch of



Medicine. We require of the collaborative efforts to achieve best goals with controlled studies, clinical and basic assays, increasing the Meeting's quality.

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AB1382

#### HOW EFFECTIVE IS POSTGRADUATE TRAINING IN THE RHEUMATOLOGY DEPARTMENT OF A TEACHING HOSPITAL?

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**Background:** Rheumatological disorders are very common in primary<sup>1</sup> and secondary care.<sup>2</sup> Each year, 20% of the general population consult their General Practitioner (GP) due to a musculoskeletal problem.<sup>3</sup> With demands on musculoskeletal service likely to rise further, there is a growing concern that new doctors of tomorrow may not be equipped with necessary competencies to deal with this burden.<sup>4, 5</sup>

**Objectives:** To explore the effectiveness of rheumatology departmental induction training. To explore the confidence of post-graduate trainees in assessing and managing patients with rheumatological conditions. To evaluate the confidence of post-graduate trainees to do knee aspiration and injection. To explore the satisfaction of post-graduate trainees and trainers with various teaching activities in the department. To make recommendation for further improvement of the quality of on-the-job teaching of junior doctors posted in the department of rheumatology.

**Methods:** An online questionnaire survey was administered to all current and previous four years' rheumatology trainees. Subsequently trainees were interviewed divided in to two focus groups for Specialty Trainees and non-specialist (General Practice and Foundation Year 2) trainees. Consultants, Allied Health Professionals and nurses were also interviewed divided in to two focus groups. The data from questionnaire survey and qualitative data from focus group interviews was then analysed and collated.

**Results:** Induction was suboptimal with only two-thirds of trainees rating its quality as excellent or good. Most trainees were confident in the assessment and management of rheumatological conditions but felt less confident in prescribing rheumatological drugs. Most trainees were confident in performing knee injection and aspiration. The trainees were satisfied with educational and clinical supervision, learning environment and availability of training opportunities. However both trainees and trainers were dissatisfied with inadequate formal teaching and under-utilisation of specialty and multidisciplinary clinics. Rota gaps and excessive workload were thought to be the main barriers.

**Conclusions:** In a climate of increasing service demands, limited time and manpower shortage, training junior doctors effectively has become more challenging. An effective induction, supportive learning environment, structured training with incorporated formal teaching would help optimise the learning opportunities.

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**Disclosure of Interest:** None declared

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AB1383

#### RHEUMATOLOGY NURSES KNOWLEDGE AND CONFIDENCE IN THE EVER-CHANGING RHEUMATOLOGY -A REGIONAL SURVEY AMONG EAST MIDLANDS RHEUMATOLOGY SPECIALIST NURSES

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**Background:** Rheumatology as a specialty moving rapidly due to the advent of novel therapeutic agents. Rheumatic Disease management concepts are also changing with a treat to target approach and early escalation of therapies. Role of Rheumatology specialist nurses should not be underestimated in the tight control and achieve treat to target goals. The expectation of Specialist Nurse role has been changed over the years. NHS pressure in service delivery compromised teaching and training opportunities for Specialists Nurses which may result in the knowledge gap. Education and training for Rheumatology nurses are key in delivering high-quality service to rheumatology patients. We attempted to explore the current knowledge and skills among Rheumatology specialist nurses regionally.

**Objectives:** 1To explore the knowledge perception of different disease management

2. To identify the difference in two disease management RA and Spondyloarthritis (SpA).

3. To evaluate the confidence level in assessing different Rheumatic diseases

**Methods:** This is a Questionnaire based prospective study among east midlands Rheumatology Specialist Nurses. The initial questionnaire was piloted and improved 17 questionnaires were distributed among the specialist nurses working in our region via email and in person. The questions were designed to gauge the nurses level of confidence in assessing different rheumatology conditions and also their confidence in making treatment decisions for different conditions.

**Results:** 26 out of 40 nurses in East Midlands responded with response rate of 65%. 77% Responses are from nurses working in University hospitals and 23% working from DGH. The level of experience in current role is variable from 2 to 20 Year and clinical session performed by nurses varies from 2–8 per week. The nurses are mostly supervised by consultant and some do independent clinic. The awareness of delay in diagnosis of SpA is about 80% with average reported delay as 6 years. Confidence in assessing RA is very good however not confident in assessing SLE. Confidence level in counselling biologic therapy varies with different diseases with SLE been very low. SpA assessment with extra articular management is low and less confidence in advising therapy in Pregnancy. Interesting note the awareness concept of Non-Radiographic SpA and MRI protocols in SpA Confidence is exists. Variable level of confidence in the in assessment of various diseases. Confidence in assessing Fibromyalgia in a patient with Rheumatic disease is at a low level.

**Conclusions:** we noted the very good level of confidence in RA and PSA assessment and management however low levels of confidence in the assessment of SLE and SpA. More education and training is needed particularly focused on assessment. This is the first study among Rheumatology Specialist Nurses with limitations. Education and training through continuous Medical education for Rheumatology nurses are key to achieve tight control of Rheumatic diseases, reduce the morbidity and Mortality.

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AB1384

### ARE THE SPANISH HOSPITALARIAN EMERGENCY UNITS PREPARED FOR THE DIAGNOSTIC AND THERAPEUTIC CARE OF URGENT RHEUMATOLOGICAL PATHOLOGY?

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**Background:** The rheumatological emergencies are considered a pathology of low complexity by the classification and triage systems of the Emergency Departments (ED). However, their frequency ranks first in reasons for consultation. Although the majority of these reasons for consultation do not imply immediate urgency, some autoimmune diseases and their manifestations in the locomotor system are underdiagnosed, causing a delay in the referral to the specialist and the initiation of appropriate treatment.

**Objectives:** To determine the baseline knowledge level of the medical staff of the EDs in the diagnosis and treatment of rheumatological emergencies.

**Methods:** A survey was designed and distributed in 18 Spanish EDs. The choice of centres was made exclusively by availability and logistical access. In all cases, only medical personnel were surveyed. The survey was distributed through an electronic link to an online form created on the Google Forms platform. The first section of the questionnaire collected demographic data from the surveyed and the SU in which he performs his clinical activity. The second part compiled several aspects of general knowledge, training in diagnostic techniques and therapeutic behaviours.

**Results:** Of a potential 290 recipients, the survey was answered by 267 physicians. 68% of the surveyed were specialists in Family and Community Medicine, 25% in Internal Medicine and 7% were from other specialities. 25% declared having more than ten years of experience, 61% between 5 and ten years, and 14% less than five years. 91.7% of the people polled stated that the management of the non-traumatic pathology of the locomotor system was part of their usual work, while 8.3% indicated that this activity was within the responsibility of the Emergency Traumatologist. The proportion of surveyed who declared themselves capable of performing the following procedures were: knee arthrocentesis, 91.7%; Shoulder infiltration, 75%; Shoulder bursae puncture and fluid aspiration, 16.7%; Joint ankle infiltration, 2.3%; Infiltration in the carpal tunnel, 3.5%; drainage of a patellar bursa, 14.3%; drainage of an olecranon bursa, 12.1%; Infiltrate the elbow, 21.2%; Drain a popliteal cyst, 2.3%. In the last three months, 38.5% of the polled said they had never obtained a joint or bursal fluid for diagnostic purposes, while 30.8% said they had done so only once. In the last three months, 61.5% of the assessed suspected once, giant cell arteritis. More than 60% of the surveyed felt confident of suspecting an outbreak of gout, rheumatoid arthritis, spondyloarthritis, rheumatic polymyalgia, giant cell arteritis, vertebral crushing and chondrocalcinosis based on the clinical signs. Less than 20% of the surveyed reported being able to suspect a connective tissue disorder or a vasculitis.

**Conclusions:** It is our understanding that the teaching priorities are in the field of training in diagnostic techniques, infiltrations other than those of large joints, clinical suspicion of autoimmune systemic diseases and diagnostic management of soft tissue pathology. Those topics must be included in further teaching initiatives to improve the quality of emergency units healthcare in the field of rheumatological urgencies.

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AB1385

### #RHEUMJC: 3 YEAR ANALYSIS OF A TWITTER BASED RHEUMATOLOGY JOURNAL CLUB

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**Background:** Twitter is an increasingly popular platform for discussion and engagement amongst healthcare professionals. #RheumJC is a Twitter-based international rheumatology journal club which has occurred approximately once a month for the past 3 years. Here we describe participant analysis and survey results from the past 36 months of this initiative.

**Methods:** A #RheumJC development team, consisting of academic and private practice rheumatologists as well as rheumatology Fellows in Training (FIT), was created to help define the structure and moderate the online discussions. Based

on results from an initial needs assessment survey, a structured journal club format was developed. A total of 23 different online journal clubs were conducted between January 2015 and December 2017, each consisting of both "live" one hour chats, as well as a full 24 hours to allow for asynchronous participation for each session. An analysis of the different sessions was performed to assess participant demographics and participation rates. Additionally, follow up surveys were conducted after the 4th, 10th and 23rd journal club sessions to assess metrics of satisfaction and identify additional strengths or barriers to participation.

**Results:** Over the 36 month observation period, a total of 646 individuals from 36 different countries tweeted with the hashtag #RheumJC. Over 90% of these tweets occurred during the live chat sessions. While the majority of participants were rheumatologists, over 10 different medical fields were represented. The Twitter account @RheumJC currently has almost 2700 followers from 36 different countries, with the USA and UK representing the largest numbers of followers (36.4% and 15.7% respectively), and 31.9% of all accounts originating from the European continent. The affiliated mailing list for #RheumJC has over 235 subscribers. The most recent survey (done after the 23rd journal club session) recorded responses from 37 individuals from 13 different countries who indicated they had participated or followed along in at least one of the journal clubs. 74% of the respondents indicated they had participated in at least 2 or more different sessions. The majority (86%) indicated they were either satisfied or very satisfied with the #RheumJC initiative. 31% of respondents admitted that they had only observed some of the sessions and not joined in the actual discussion suggesting that the total number of #RheumJC participants could be greater than the participation data presented here. Of interest, 9% of respondents indicated they had joined Twitter solely because of #RheumJC, and another 29% stated that #RheumJC had increased their use of Twitter as a tool for medical education. The results from this survey closely mimic the responses from prior surveys suggesting an enduring satisfaction with the initiative.

**Conclusions:** #RheumJC is a novel and popular approach to the traditional medical journal club, bringing together people from around the globe and across specialities to discuss current rheumatology literature utilising Twitter as a medium for medical education. Given its continued success for over 3 years now, the #RheumJC initiative has proven itself a valuable addition to the rheumatology medical education community.

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AB1386

### PHYSICIAN AWARENESS OF RHEUMATIC IMMUNE-RELATED ADVERSE EVENTS IN CANCER PATIENTS TREATED WITH IMMUNE CHECKPOINT INHIBITORS

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**Background:** Immune checkpoint inhibitors (ICI) are novel and promising therapies for the treatment of a range of cancer types, acting through stimulation of the patient's immune system to engage on tumour cells. This enhanced immune system may potentially cross-react against any organ system, and reporting of rheumatic immune-related adverse events (irAE) has been growing.

**Objectives:** To evaluate awareness of treatment with ICI and rheumatic irAE among Portuguese rheumatologists and oncologists.

**Methods:** A web-based questionnaire was sent in November 2017 to members of the Portuguese Society of Rheumatology and Portuguese Society of Oncology. Aside from demographic variables, assessed domains included awareness and clinical experience with ICI and irAE, as well as educational needs on the topic and interest in participating in multidisciplinary approaches.

**Results:** Response rates were 61/221 (27.6%) for rheumatologists and 13/653 (2.0%) for oncologists. Demographics were similar in both groups, including mean age (39.9 and 41.1 years) and female gender (59% and 53.8%), respectively; the majority were consultant physicians (67.2% and 69.2%) working at public hospitals (86.9% and 92.3%), respectively. Regarding ICI, most rheumatologists had heard of but were unfamiliar (63.9%) while most oncologists were at least moderately familiar (92.3%) with such therapies. Almost all physicians were aware but more oncologists reported having patients with rheumatic irAE (46.2 vs 4.9%); the most frequent were arthralgia and arthritis. These physicians were all moderately or very confident in managing these irAE. Most physicians considered that Rheumatology-Oncology multidisciplinary approaches would be of benefit and were interested in participating. Education on pathophysiology, epidemiology, clinical assessment and treatment was deemed necessary. Table 1 summarises the main results.

	Rheumatology n=61	Oncology n=13	Total n=74
<b>How familiar are you with ICI used for the treatment of cancer (for instance, anti-CTLA-4, ipilimumab, and anti-PD-1, nivolumab)?</b>			
Totally unfamiliar, n(%)	7 (11.5)	0 (0.0)	7 (9.5)
I have heard of them, but am not familiar, n(%)	39 (63.9)	0 (0.0)	39 (52.7)
Somewhat familiar, n(%)	11 (18.0)	1 (7.7)	12 (16.2)
Moderately familiar, n(%)	4 (6.6)	7 (53.8)	11 (14.9)
Totally familiar, n(%)	0 (0.0)	5 (38.5)	5 (6.7)
<b>Are you aware that ICI can cause rheumatic irAE?</b>			
Yes, n(%)	52 (85.2)	13 (100)	65 (87.8)
No, n(%)	6 (9.8)	0 (0.0)	6 (8.1)
No answer, n(%)	3 (4.9)	0 (0.0)	3 (4.1)
<b>Do you have any patient treated with ICI (namely, anti-CTLA-4, ipilimumab, or anti-PD-1, nivolumab) who developed a rheumatic irAE?</b>			
Yes, n(%)	3 (4.9)	6 (46.2)	9 (12.2)
No, n(%)	36 (59)	6 (46.2)	42 (56.7)
I have no patient treated with such drugs, n(%)	19 (31.1)	1 (7.7)	20 (27)
No answer/do not know, n(%)	3 (4.9)	0 (0.0)	3 (4.1)
<b>If you answered "yes" to the previous question, what type of rheumatic irAE was it?</b>			
Arthralgia, n(%)	2 (66.7)	3 (50.0)*	5 (50.0)
Arthritis, n(%)	1 (33.3)	1 (16.7)	2 (20.0)
Myositis, n(%)	0 (0.0)	1 (16.7)	1 (10.0)
Sicca syndrome, n(%)	0 (0.0)	1 (16.7)*	1 (10.0)
Vasculitis, n(%)	0 (0.0)	0 (0.0)	0 (0.0)
Other, n(%)	0 (0.0)	1 (16.7)	1 (10.0)
<b>Do you believe there is benefit in a multidisciplinary Rheumatology-Oncology approach allowing timely assessment and referral of patients who develop rheumatic irAE?</b>			
Yes, n(%)	56 (91.8)	11 (84.6)	67 (90.5)
No, n(%)	1 (1.6)	1 (7.7)	2 (2.7)
No answer/do not know, n(%)	4 (6.6)	1 (7.7)	5 (6.8)
<b>What are your educational needs on rheumatic irAE?</b>			
Pathophysiologic and immunologic principles, n(%)	7 (11.5)	0 (0.0)	7 (7.9)
Epidemiology and clinical features, n(%)	8 (13.1)	0 (0.0)	8 (9.1)
Assessment and treatment, n(%)	19 (31.1)	5 (38.5)	24 (27.3)
All of the above, n(%)	41 (67.2)	8 (61.5)	49 (55.7)

ICI: Immune checkpoint inhibitors; irAE: Immune-related adverse events  
 \* Postgraduate clinical experience, including residency.  
 † Predominant workplace (> 50% of weekly schedule).  
 \* One patient developed concurrent arthralgia and sicca syndrome.  
 \* More than one answer was allowed.

Abstract AB1386 – Figure 1

**Conclusions:** Most rheumatologists had limited knowledge of ICI and limited experience with rheumatic irAE, compared to oncologists. Both groups considered that the development of multidisciplinary teams would be beneficial to allow timely assessment and referral of these patients. Despite limited by the response rate (particularly low for oncologists) and response bias, this study emphasises the need for specific education on ICI and irAE, especially for Portuguese rheumatologists.

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AB1387

#### ACKNOWLEDGED BIostatistical HELP AND THE QUALITY OF STATISTICAL ANALYSES IN RANDOMISED CONTROLLED TRIALS IN RHEUMATOLOGY

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**Background:** The quality of statistical analysis and reporting are wanting even in our most prestigious journals.<sup>1</sup> It stands to reason that active participation of biostatisticians in data analysis and reporting would improve the situation.

**Objectives:** We aimed to test the hypothesis that more close cooperation with biostatisticians would improve the quality of reporting randomised clinical trials in rheumatology. We defined a *close cooperation* as the inclusion of a formal biostatistician among the co-authors and/or a declaration of formal statistical help in the study reports.

**Methods:** Two independent observers screened both by reading and, when applicable, electronic scanning the texts of all randomised controlled trials (RCT) in *Annals of the Rheumatic Diseases*, *Arthritis Care and Research*, *Arthritis and Rheumatology*, *Rheumatology Oxford* published in 2015 and 2016. Using a prepared worksheet, the observers specifically tabulated, the presence of a biostatistician among the co-authors and/or formal acknowledgement of statistical help in the methods, the inclusion of effect sizes (whether they were specifically indicated as such, could be calculated or not given at all) and the corresponding confidence intervals. The instances in which an effect size was given as a number needed to treat (NNT) and number needed to harm (NNH) were separately sought. In addition at the number of times separate p values were reported for interdependent comparisons (like DAS28-CRP and DAS28-ESR), and the presence of a Bayesian analysis in the methods.

**Results:** The total RCT number in these four journals was 134. In 26 trials, there was a biostatistician or an epidemiologist as a co-author and in 3, statistical help

was acknowledged in the text. In the remaining 105 papers (78%) no statistical help was declared. The tabulation of effect sizes, confidence intervals and giving separate p values for interdependent variables are given in the table 1. In giving the effect sizes it is to be noted that the presence of a statistician made did not improve the explicit announcement of an effect size but made it more calculable. None of the trials used Bayesian methods for analysis. Only in one trial NNT and in another NNH (both with no acknowledged biostatistical help) were given.

Abstract AB1387 – Table 1. The differences of the parameters between two groups

	Group 1 (n=29) (with statistician)	Group 2 (n=105) (without statistician)	Calculated effect size between the Groups 1 and 2
Effect size reporting, n (%)	26 (90)	61 (58)	32% (95% CI 13.1–43.3) p=0.001
Given directly, n (%)	2 (7)	5 (5)	
Can be calculated (given HR, OR, RR, B coefficient), n (%)	24 (83)	46 (44)	
Confidence intervals reporting, n (%)	16 (55)	43 (41)	14% (95% CI –6–32.7) p=0.18
Calculating p values for interdependent variables, n (%)	14 (48)	46 (44)	4% (95% CI –14.9– 23.9) p=0.67

**Conclusions:** The inclusion of a biostatistician improved the reporting of effect sizes, at least rendering them calculable. The same cannot be said for reporting confidence intervals and separate p values for interdependent variables. It was interesting that Bayesian analyses and giving NNT and NNH, rather intuitive ways of expressing effect sizes, were not popular. There were 2 main limitations. The sample size was relatively small and many authors could have obtained statistical help without acknowledging it.

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AB1388

#### LIFESTYLE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND METABOLIC SYNDROME. INTERVENTION TO EXPLORE SELF-KNOWLEDGE, PERCEPTION AND IMPROVEMENT

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**Background:** Lifestyle in patients with systemic lupus erythematosus and metabolic syndrome. Intervention to explore self-knowledge, perception and improvement.

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**Summary:** Systemic lupus erythematosus (SLE) has been associated with cardiovascular disease and metabolic syndrome (MS). A supportive educational intervention to modify lifestyle could improve morbidity and mortality in SLE patients with MS.

**Objectives:** To measure the impact of an educational intervention that improves the knowledge about disease and lifestyle in SLE patients with MS.



**Methods:** A quasi-experimental study was conducted among SLE patients with SM according to the ATP III criteria at Systemic Autoimmune Diseases Research Unit of the Regional General Hospital No. 36 of the Mexican Institute of Social Security, Puebla. Clinical educational intervention in emotional and cognitive domains in the experimental group included classroom activities and outpatient consultation, evaluating healthy lifestyle knowledge that included physical activity, feeding habits and stress management with FANTASTIC instrument. Basal and final measurements were analysed with the Wilcoxon test with SPSS v21.

**Results:** Eighty nine patients were included. Age  $46.1 \pm 12.6$  years,<sup>17-70</sup> weight  $64.2 \pm 14.5$  kg,<sup>42-137</sup> 20.2% overweight and 38% obesity, 50% education over 12 years, 49.4% housewife, 39% employed, 67% lived with a partner, SLE disease evolution  $12.1 \pm 6.9$  years and prednisone dose  $10.2 \pm 10.8$  mg/day (0–50).

In the retest, disease and comorbidities knowledge was modified. The domains of lifestyle such as physical activity, family-friends and nutrition showed statistical significant changes after the intervention  $p < 0.05$ .

**Conclusions:** The educational intervention modified the conceptual perception of SLE and MS as well as some domains of lifestyle.

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AB1389

### HOW DO WE LEARN TO COMMUNICATE TO OUR PATIENTS? AN INVENTORY STUDY AMONGST RHEUMATOLOGISTS IN TRAINING IN THE NETHERLANDS HOW THEY TRAIN COMMUNICATION SKILLS

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**Background:** Effective doctor-patient communication, more specific 'Shared Decision Making (SDM)', is essential in high-quality health care. Physicians value the principles of SDM, but the practice is disappointing. Difficult subjects are avoided, options are not equally explained or patients' values remain unclear. As a rheumatologist, communication is an essential and powerful competency. Guidelines endorse SDM for the management of various rheumatic diseases. What we do not know is how we acquire the right communication skills for the task. As rheumatologists we learn a lot about pathophysiology, diagnostic approach and treatment options, but not how to explain these aspects in comprehensible language to our patients.

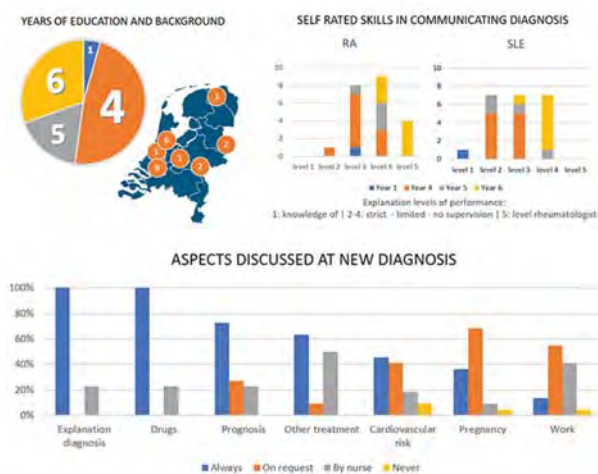
**Objectives:** Objective of this study is to investigate how rheumatologists in training acquire communication skills, more specific skills in SDM. How do they rate their communication competency and what can be done to improve.

**Methods:** An online survey was developed with questions dedicated to evaluate the posed questions. The survey was distributed amongst aspirant members of the Dutch Society for Rheumatology by email with a link to the survey. The survey consists of questions asking for self-reflection and rating on various communication skills regarding different aspects of communication.

**Results:** These are preliminary results based at the first 23 responses, which is 33% of the total number of rheumatologists in training. From the received responses eleven fellows were in their fourth year, four in their fifth year and seven were in their final year of education. Fellows believe communication is the most important CanMEDS competency after 'Medical Expert'. Self-assessment of communication competency shows an average score of 3.7 on a five-point scale (5=most experienced). When a new diagnosis is explained, fellows rate their skills at levels to be expected for their years of education, except for the diagnose SLE, Systemic Sclerosis and M. Sjögren. Items that are always discussed are the diagnosis and the treatment, but other aspects such as implications for pregnancy, work, social life and sexual intercourse are only discussed on request. Regarding the explanation of treatment options the right words to explain different biological DMARDs seem to run short. When presenting details about treatment fellows always communicate possible treatment effect and side effects, but do not always mention frequency of side-effects. Furthermore, alternatives and preferences of the patient are not always discussed but only on request by 68% of the respondents. Fellows indicate that they think communication and SDM are very important and are interested to acquire further skills. They prefer videos with examples of how to explain certain diagnoses, treatment options and how to deal with various patient types. A specific request was made for a training in Somatic Unexplained Complaints.

### HOW DO WE LEARN TO COMMUNICATE TO OUR PATIENTS?

AN INVENTORY STUDY AMONGST RHEUMATOLOGISTS IN TRAINING IN THE NETHERLANDS HOW THEY TRAIN COMMUNICATION SKILLS



Abstract AB1389 – Figure 1

**Conclusions:** Rheumatologists in training highly value good doctor-patient communication. In daily practice the explanation of certain diseases and treatment options seems difficult. Diagnoses and drugs with possible (side) effects are always explained, but social implications and patients' preferences are only discussed on request. Therefore, additional training of SDM seems important.

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AB1390

### OSTEOPOROSIS ASSOCIATED MORBIDITY ANALYSIS CAN REVEAL TARGETS FOR BETTER DISEASE DIAGNOSIS AND MANAGEMENT

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**Background:** Osteoporosis accounts for more disability and life years lost than rheumatoid arthritis. It brings an elevated risk of mortality, morbidity and re-hospitalisation due to fractures and a significant financial and social burden.

A rationale use of diagnostic and therapeutic resources is useful and should be encouraged at all intervention levels. For admitted patients, clinical risk factors for fractures and conditions that are causes for secondary osteoporosis should trigger either the diagnosis approach or the referral to a (Rheumatology/Endocrinology) specialist and treatment should be started during hospitalisation.

**Objectives:** We aimed to identify targets for educational or protocol interventions in order to improve inpatient osteoporosis diagnosis and subsequent management.

**Methods:** A retrospective three years (2014–2016) cross-sectional prevalence analysis of comorbidities in all hospitalised patients with osteoporosis in our general hospital was conducted. We used the medical records database of our hospital.

**Results:** Osteoporosis as a principal diagnosis was found in 46 cases, mostly from the Endocrinology Department (65%). Osteoporosis as a secondary diagnosis was found in 2464 cases, and only 11% were diagnose-associated with fractures. 23% of all comorbidities are of endocrine or diabetic etiology. A small percent of osteoporosis cases have simultaneous skeletal disease, mostly vertebral fractures, osteomalacia or degenerative disease. Only 8,77% of secondary osteoporosis was diagnosed in the Orthopaedic Department. No osteoporosis was mentioned in association with COPD or oncologic disease. Only 65% of patients leaving the hospital had specific recommendation for anti-osteoporotic medication.

**Conclusions:** Osteoporosis should be mentioned in all cases in the patients medical records that are further sent to the general practitioner. Osteoporosis may be better diagnosed in diabetic, oncologic, COPD, Parkinson disease patients and in a large percent of fracture patients if internal referral protocols will be implemented. Appropriate therapy should be recommended from the hospital specialists.

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AB1391

### OBSTACLES FACING EVIDENCE BASED MEDICINE IN PHYSICAL MEDICINE AND REHABILITATION: FROM OPINION AND KNOWLEDGE TO PRACTICE

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**Background:** Evidence-based medicine (EBM) is a new approach to medicine. Up to now, there have been few available articles about specialists' EBM status, specifically the status of physiatrists in the area of EBM.

**Objectives:** To determine the present status of physiatrists' attitudes, knowledge and skill in the area of EBM and the existing obstacles

**Methods:** The cross-sectional study was performed among physiatrists in Iran. The valid and reliable questionnaire contained 25 questions in 8 fields including demographic and professional information, point of view regarding EBM, familiarity with databases, educational history and information about EBM, use of scientific resources, scientific evidence usage, and the amount of access to resources.

**Results:** One hundred twenty-eight questionnaires were completed (response percentage 52.2%). In total, 48.4% specialists had attended EBM workshops and 89.6% of people were familiar with medical search engines. The amount of familiarity with databases was mostly with MEDLINE/PubMed (52.3%). Respondents mainly had a positive point of view towards EBM. Those who had access to databases at work or somewhere out of home had a more positive attitude ( $p=0.002$ ). Those who had attended EBM workshops and members of faculty also had more positive attitudes ( $p=0.003$  and  $p=0.01$ , respectively). Around 70% of responders had adequate knowledge regarding EBM. Physicians, members of faculty and participants who had spent more time on research, reviewed articles and attended workshops had more knowledge ( $p=0.001$ ).

**Conclusions:** Results from our study revealed that although there is a significant number of physiatrists who are familiar with the practicality of EBM, they are still not familiar enough with its concepts and applications.

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AB1392

### EFFECT OF UNIVERSITY STRUCTURE ON MEDICAL STUDENTS' KNOWLEDGE DURING EXAM PREPARATION

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**Background:** In 2016 the German Society of Rheumatology found out that only seven faculties out of 37 could be classified as an independent rheumatological teaching unit. Amount of lecture hours and type varied largely between

universities and was usually the most in universities with academic freedom. Besides the lack of lectures in rheumatology, all students have to pass a medical state examination ("Staatsexamen"), which is carried out by the IMPP ("Institut für Medizinische und Pharmazeutische Prüfungsfragen"). The written exam consists of 320 Multiple-Choice IMPP-Questions with only one correct answer out of five possible choices. Approximately five to ten questions, varying from exam to exam, also contain rheumatological content. After each exam questions are published and used by younger students for exam preparation. The e-Learning platform "Amboss" is frequently used by medical students for this reason in Germany.

**Objectives:** To investigate the effect of university structure on correct answering former IMPP-Questions during exam preparation.

**Methods:** We analysed former IMPP-Questions answered by students over a four-year period recorded on "Amboss" (Oct. 2012 – Oct. 2016). First time answered questions with rheumatological content from students during exam preparation were identified and extracted from the total record. Students with only a single or very few questions answered were not considered as being in exam preparation and excluded. A sensitivity analysis was done after exclusion. Students from independent (Group A) and non-independent (Group B) medical faculties were divided into two groups and investigated for the rate of correct answering IMPP-Questions. Statistical Analysis was done with the Statistical Software R (The R-Foundation for Statistical Computing; Version 3.4.1).

**Results:** A total of 176 questions with rheumatological content were identified. 32.166 students answered those questions or a subset of these (in total 2.610.217 questions). After excluding students not being in exam preparation 14.739 students were left, answering those questions 2.148.801 times. On an average 68,3% of the questions were answered correctly. The sensitivity analysis did not show a significant difference. 3330 students from Group A answered 495.614 questions, on an average 69,4% correct. 11.409 students from Group B answered 1.963.066 questions, on an average 68% correct. The difference between both groups was significant ( $p<0.01$ ).

**Conclusions:** Students from independent faculties answered more questions correct than from non-independent faculties. The difference was significant, but taking into account the few questions asked in the real exam the difference would have no relevance.

**Disclosure of Interest:** None declared

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AB1393

### EFFECT OF AN EDUCATIONAL INTERVENTION BASED ON CLINICAL SIMULATION IN THE DIAGNOSIS OF RHEUMATOID ARTHRITIS IN LATIN AMERICAN NON-RHEUMATOLOGISTS PHYSICIANS

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**Background:** Previously our group demonstrated the effectiveness of an educational intervention based on clinical simulation to improve the diagnostic approach to RA (Rheumatoid Arthritis) <sup>(1)</sup> so we wanted to apply this same principle in the learning of RA among a group of Latin American non-Rheumatologists

**Objectives:** This paper wants to quantify the rate of improvement in the diagnosis of Rheumatoid Arthritis (RA) among a group of Latin American non-Rheumatologists (general practitioners, internists, physiatrists, orthopedists, neurosurgeons, dermatologists) who received an educational intervention based on clinical simulation.

**Methods:** Observational study before and after

**Results:** 286 Latin American non-rheumatologists physicians received an educational intervention based on clinical simulation. The topic of this educational intervention was based on Rheumatoid Arthritis. They reviewed a workshop that includes clinical simulation models of 5 hands and each hand, had various semiological findings of RA (synovitis, pannus, joint deformities). The workshop lasted 5 hours and it was divided into two parts: the first was about the clinical approach of joint pain and relevant aspects of RA. The second part focused on clinical cases applied to clinical simulation models, applying the knowledge acquired during the theoretical phase. Participants made a several stations where they could appreciate for periods of 20 min each simulator and improve their visual and tactile sensitivity in each semiological findings for the diagnosis of RA. The participants filled out a pre and post test, which included 6 (six) clinical cases with simulators and photographs of hands of patients with suspected RA. 286 non-rheumatologists (general practitioners, internists, physiatrists, orthopedists, neurosurgeons, dermatologists) from 3 Latin American countries (Colombia, Costa Rica and Dominican Republic) participated in the study, 71% women, average age 40,3 years (SD 7,5 years). Non-rheumatologists physicians obtained an improvement in the correct diagnosis of RA of 45,6% (the correct diagnosis increased from 44,5% to 90,1%). The total number of exams requested in the cases presented decreased significantly, from an average of 7 to 3 exams requested by each clinical case presented. 95% of participants would recommend to other colleagues to make this



workshop. 97% believe that this educational intervention will improve the diagnostic approach to patients with suspected RA.



Abstract AB1393 – Figure 1

**Conclusions:** The present research is a pioneer and innovator in the field of rheumatology education. We have shown the usefulness of clinical simulation by an improvement in the diagnostic sensitivity towards the diagnosis of RA, highlighting the semiology as a key element at the time of making the diagnosis. A significant decrease in the total number of exams requested for each of the clinical cases analysed was documented, which can have a positive effect on costs for the national health systems.

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- [1] Fernández-Ávila DG, Ruiz AJ, Gil F, Mora SA, Tobar C, Gutiérrez JM, Rosselli D. The effect of an educational intervention, based on clinical simulation, on the diagnosis of rheumatoid arthritis and osteoarthritis. *Musculoskeletal Care*. 2017;1–5. DOI: 10.1002/msc.1228

**Disclosure of Interest:** None declared

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#### AB1394 DEVELOPMENT OF A SERIES OF SIMULATORS AND DESIGN OF A COURSE BASED ON CLINICAL SIMULATION, FOR TEACHING DIAGNOSTIC APPROACH TO PATIENTS WITH JOINT PAIN AND SUSPECTED RHEUMATIC DISEASES

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**Background:** The teaching of clinical approaches to patients with RA (Rheumatoid Arthritis) and SpA (Spondyloarthritis) requires both a practical and a theoretical component, and there are difficulties in having real patients for teaching. Previously our group has shown the use of clinical simulation in rheumatology, an area in which it had not been used. We demonstrated the effectiveness of an educational intervention based on clinical simulation to improve the diagnostic approach to RA1. Thus, the idea emerged to apply clinical simulation in the field of RA and SpA teaching. An exhaustive search of the scientific literature through May 2017 revealed no works on clinical simulation for rheumatic diseases. The simulation models received a patent for intellectual property and utility for education, with a 10-year protection.

**Methods:** Design and installation a life-sized mannequin and separate anatomical parts (five hands, six fingers, three feet) with a set of semiological findings for SpA and RA

**Results:** We have designed unique simulation models –a life-sized mannequin and separate anatomical parts (five hands, six fingers, three feet) with a set of semiological findings for SpA and RA. Each simulator (artificial hands, finger or feet) has natural size and was made of epoxy resin. The simulators ligaments, muscles and support tissues were made of silicone rubber, and the simulator was covered by polyurethane skin on an acrylic support. Each hand, feet or finger has various semiological findings of SpA and RA (synovitis, pannus, enthesitis,

dactylitis, joint deformities, classical findings of psoriatic nails and psoriatic plaques) made from materials that generated textures very similar to those found in real patients. Learning is transferred from interacting with the models by using the sense of touch to feel and perceive how the clinical manifestations of the diseases are. The workshops comprise a six-stage rotation where the anatomical models are accompanied by a brief video describing a clinical case. After viewing the video participants interact with the models to understand and recognise each of the clinical features of SpA and RA, as if in a real patient. Whereas in regular workshops where knowledge is transfer through a keynote speaker and visual images, this one is a total learning by the experience of touching and feeling.



Abstract AB1394 – Figure 1

**Conclusions:** The present research is a pioneer and innovator in the rheumatology education. In this vein, we hope that this research is the first in the context of a new way of teaching rheumatology, educational process and eventually will have a global projection that allows the creation of a course for early diagnosis and initial treatment of rheumatic diseases, similar to what is currently done in cardiology with ACLS and in trauma with ATLS

#### REFERENCE:

- [1] Fernández-Ávila DG, Ruiz AJ, Gil F, Mora SA, Tobar C, Gutiérrez JM, Rosselli D. The effect of an educational intervention, based on clinical simulation, on the diagnosis of rheumatoid arthritis and osteoarthritis. *Musculoskeletal Care*. 2017;1–5. DOI: 10.1002/msc.1228

**Disclosure of Interest:** None declared

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#### AB1395 EFFECT OF AN EDUCATIONAL INTERVENTION BASED ON CLINICAL SIMULATION IN THE DIAGNOSIS OF SPONDYLOARTHRITIS (SPA) FROM GENERAL PRACTITIONERS, A STUDY BEFORE AND AFTER

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**Background:** Previously our group has shown the use of clinical simulation in rheumatology. We demonstrated the effectiveness of an educational intervention based on clinical simulation to improve the diagnostic approach to RA1, so we wanted to apply this same principle in the learning of SpA (Spondyloarthritis).

**Objectives:** This paper wants to quantify the rate of improvement in the diagnosis of Spondyloarthritis (SpA) among a group of general practitioners who receive an educational intervention based on clinical simulation.

**Methods:** Intervention study before and after

**Results:** 102 general practitioners received an educational intervention based on clinical simulation. The topic of this educational intervention was Spondyloarthritis (SpA). A workshop that includes clinical simulation models of feet, fingers and a mannequin created for this purpose was created, based on the strategy of problem-based learning. The workshop lasted 5 hours, it was divided into two parts: the first was about the of the clinical approach of joint pain and lumbar pain diagnosis and relevant aspects of SpA. In this first part, besides the theoretical support



for the diagnosis of SpA, participants viewed pictures of patients with spondylitis and peripheral involvement (enthesitis, dactylitis, arthritis) seeking to achieve awareness of their sense of sight with respect to the diagnostic approach to patients with suspected SpA and sought to strengthen the logical approach to be implemented when approaching this type of patients. The second part focused on clinical cases applied to clinical simulation models, applying the knowledge acquired during the theoretical phase. Participants made a several stations where they where they could appreciate for periods of 15 min each simulators of 3 feet, 6 simulators simulated fingers and a mannequin where they can identify entheses and psoriasis lesions, improving visual and tactile sensitivity in each semiologic findings for the diagnosis of SpA. The participants filled out an pre and post test, which included clinical cases with simulators and photographs of hands and feet of patients with suspected SpA. 102 participants (59% women), average age 32.3 years (SD 7.1). Improvement in the correct diagnosis of SpA of 47% (the correct diagnosis increased from 39% to 86%). laboratories application in the cases presented decreased significantly, from an average of 8–4 exams requested by each clinical case presented. 98.5% of participants would recommend to other colleagues to make this workshop. 97.7% believe that this educational intervention will improve the diagnostic approach to patients with suspected SpA



Abstract AB1395 – Figure 1

**Conclusions:** We have shown the usefulness of clinical simulation given by an improvement in the diagnostic sensitivity towards the diagnosis of SpA. A significant decrease in the total number of exams requested for each of the clinical cases analysed was documented, which can have a positive effect on costs for the national health systems.

#### REFERENCE:

- [1] Fernández-Ávila DG, Ruiz ÁJ, Gil F, Mora SA, Tobar C, Gutiérrez JM, Rosselli D. The effect of an educational intervention, based on clinical simulation, on the diagnosis of rheumatoid arthritis and osteoarthritis. *Musculoskeletal Care*. 2017;1–5. DOI: 10.1002/msc.1228

**Disclosure of Interest:** None declared

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AB1396

#### TEACHING THE MILLENNIALS: USING YOUTUBE FOR TEACHING RHEUMATOLOGY IN THE STANDARD EDUCATIONAL SETTINGS

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**Objectives:** To assess learning potential and educational value of online videos made freely available via a dedicated YouTube channel for undergraduate and post-graduate students studying musculoskeletal medicine.

**Methods:** The YouTube video database was systematically searched using 5 search terms related to "Joint": examination, anatomy, regional anatomy, OSCE and Ultrasonography. Two independent clinical reviewers assessed videos for procedural technique and educational value using a 5-point global score, ranging from 1=poor quality to 5=excellent educational quality. To be included in the teaching process the clip must score  $\geq 4$ . Permission for sharing the video was sought from the publisher. 59 undergraduate 55 postgraduate trainees were included in this educational activity. The students were sent the YouTube channel link to the students for viewing prior to the class-time active learning session. The teaching session adopted an interactive learning environment and the course instructor served as a facilitator rather than a dominator and offered timely feedback/guidance to students. Evaluation of the teaching session was assessed using a scenario based learning and an evaluation check list. The students were asked to complete a survey based on a 5-point Likert scale: to assess for their perceived effectiveness and satisfaction. The outcomes of the evaluation sheet and students' survey, were compared to 55 undergraduate and 52 postgraduate trainees, a control group, who were taught in former years on the same topics in a lecture-based model using the standard teaching protocols.

**Results:** 25 videos met the inclusion criteria and were considered useful for teaching purposes. The average length was  $5.31 \pm 2.28$  min. The mean global score for educational value was  $4.3 \pm 0.3$ . There was no significant difference regarding socio-demographics between the 2 students' groups included in this work. In the study group 93% of the students viewed the videos prior to the class session, and 95% attended the education sessions in comparison to 86% attendance in the traditional teaching group. Students reported an increase in knowledge, a positive learning experiences and perceptions of the online teaching model. Student perceived effectiveness and satisfaction was significantly high among the online flipped learning in contrast to the traditional teaching comparative group (4.88 Vs 4.31,  $p < 0.05$ ). Similarly, analysis of the students' assessment scores after the scenario based learning sessions was higher in the online learning group compared to the students taught by traditional methods ( $p < 0.01$ ).

**Conclusions:** Making videos on Joint anatomy and OSCE joint examination freely available on a dedicated channel on the YouTube appeared to be suitable and valuable for medical students, fellows, and residents learning. YouTube is a great example for web-based modern musculoskeletal teaching tailored to the students' needs/time, and this educational approach seems to be very well received by the students. However, though the learning potential of the internet is incredible, finding the best content can be a challenge.

**Acknowledgements:** Omar El Miedany for setting up the YouTube channel

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**Health Professionals in Rheumatology  
Abstracts**

THURSDAY, 14 JUNE 2018

**HPR Patients' perspectives, functioning and health (descriptive: qualitative or quantitative)****THU0710-HPR QUALITIES OF PARTICIPATION AS DESCRIBED BY PEOPLE WITH EARLY RA IN WORKING AGE**

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**Background:** Early diagnosis and medication has been effective but impairments, activity limitations, and participation restrictions are still evident in RA. To be able to participate despite RA is a recurrent goal for persons with early RA as well as in standards of care. Nevertheless, patients' perceptions of what kind of situations constitute an experience of participation are seldom explored in research. Though, participation ladders illustrating people's influence on matters that concern them have earlier been described in social sciences in relation to citizens' rights, and children's rights.

**Objectives:** To describe when and how people with early RA describe a positive sense of participation in everyday life, including to categorise the qualities of these experiences.

**Methods:** This study is part of the Swedish early RA project "TIRA". Critical incidents technique was used in the design of the semi structured interviews. In all, 59 patients (age 18–63 years) were interviewed; 25 men and 34 women. The study has been approved by the local ethics committee and has followed the ethical standards of the Helsinki Declaration. Content analysis was used to identify meaning units with descriptions related to the aim, which were sorted based on type of situations described, and later on categories based of quality aspects of participation were developed.

**Results:** The qualities of participation as described by people with RA were arranged as a ladder with the following steps; 1. Being part of a group, 2. Carry out activities in company, 3. Share everyday chores and responsibilities, 4. Have influence on actions, 5. Give direction of goals, 6. Share decision making. Participation was experienced with others at specific moments when the positive feeling described was *being part of a group* in relations with family, friends, in working life and in recreation and social life. For instance, both women and men described the experience of participation in the work group, especially when given the possibility to *have influence on actions*, or the possibility to *give direction of goals* in the management of work or in organised activities. They described a positive feeling of participation if *sharing everyday chores and responsibilities* with someone and when just *carrying out activities* in company with others at work, in domestic life, and in sports and leisure activities. The interviewees also described how the sense of participation was particular intensive when *sharing decision making*.

**Conclusions:** Participation from an individual's perspective is about belonging and having influence that mediates a positive feeling of being included and that you matter as a person. The results are important when using participation as a goal in the clinical care.

**Disclosure of Interest:** None declared

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THURSDAY, 14 JUNE 2018

**HPR Measuring health (development and measurement properties of PROs, tests, devices)****THU0711-HPR WIDESPREAD PAIN IN AXIAL SPONDYLOARTHRITIS: CLINICAL IMPORTANCE AND GENDER DIFFERENCES**

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**Background:** Cardinal clinical signs and symptoms of axSpA include inflammatory pain, stiffness and impaired mobility in the axial region and to a lesser extent the peripheral joints. Although these features are thought to reflect local disease processes, bottom-up or top-down amplification of nervous system signalling may

alter this relationship and may induce widespread pain.<sup>1</sup> There is a remarkable lack of detailed knowledge on pain areas in axSpA and its clinical relevance is unknown. Also, gender differences in pain area may exist in axSpA and may confound disease activity outcomes.

**Objectives:** Firstly, pain locations in axial axSpA were detailed and gender differences were assessed. Secondly, the relationship of regional pain definitions as well as widespread pain with clinical outcomes was evaluated. Finally, the role of pain area in the assessment of disease activity was explored, taking gender into account.

**Methods:** Body charts informed on axial, peripheral articular and non-articular pain in 170 (108 men, 62 women) patients with axSpA. Multivariate odds ratios compared genders. General linear models explored clinical differences in disease activity (BASDAI, Bath Ankylosing Spondylitis Disease Activity Index), activity limitations (BASFI, Bath Ankylosing Spondylitis Functional Index), fear of movement (TSK-11, Tampa Scale for Kinesiophobia 11-item version), anxiety (HADS-A, Hospital Anxiety and Depression Scale subscale anxiety) and depression (HADS-D, HADS subscale depression) between four subgroups classified by widespread non-articular pain (WNAP±) and physician-reported global disease activity (PGDA±). Principal component analysis explored gender differences in the structure of disease activity outcomes.

**Results:** Axial thoracic pain was least prevalent (lumbar: 74.4%, cervical: 47.6%, cervicothoracic: 47.6%, thoracic: 32.4%), but about three times more likely in women (OR: 2.92, p=0.009). Axial cervicothoracic junction pain spread more diffusely in women (OR: 2.48, p=0.018). Women exhibited a two to three-fold increased likelihood of widespread axial (OR: 3.33, p=0.007) and peripheral articular (OR: 2.34, p=0.023) pain. A subgroup of WNAP+/PGDA- combined with low PGDA (27% of all patients) was associated with worse BASFI, BASDAI, HADS-A and HADS-D in men and worse TSK-11 and HADS-A in women (p<0.05). Disease activity outcomes showed a two-factor structure in women, but not in men.

**Conclusions:** In patients with axSpA, the location and spread of pain was different between genders and is related to worse clinical status. Based on pain area and physician-reported global disease activity, meaningful clinical subgroups were identified with a remarkably distinct health status. Outcome instruments such as BASDAI should acknowledge gender differences to ensure structural validity.

**REFERENCE:**

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.6683

THURSDAY, 14 JUNE 2018

**HPR Epidemiology and public health (including prevention)****THU0712-HPR TRAJECTORIES OF PAIN AND PHYSICAL FUNCTION IN PATIENTS WITH SYMPTOMATIC KNEE AND HIP OSTEOARTHRITIS: RESULTS FROM THE FRENCH POPULATION-BASED KHOALA COHORT**

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**Objectives:** The aims of this study were to identify homogeneous subgroups with distinct trajectories of pain and physical function in patients with symptomatic knee and/or hip OA and to identify the baseline predictive factors associated with these trajectories.

**Methods:** The KHOALA cohort is a French population-based multi-center cohort of 878 patients with symptomatic knee and/or hip OA, aged between 40 and 75 years old. Pain and function were measured annually with the WOMAC questionnaire. Baseline comorbidities were assessed by the Functional Comorbidity Index (FCI), perceived vitality was measured with SF-36 and psychosocial distress with the General Health Questionnaire (GHQ). Using the follow-up data over 5 years, latent class growth analyses (LCGA) were used to identify homogeneous subgroups with distinct trajectories of pain and function. The selection of the optimal models was based on maximisation of the Bayesian information criterion, the proportion of patients in each trajectory group (>5%) and the statistical significance of the equation modelled (intercept only, linear, quadratic or cubic). Multinomial logistic regressions were performed to identify the predictive baseline characteristics associated with each trajectory and were adjusted for socio demographic and clinical factors.

**Results:** Among the 878 patients, 609 (69.4%) were women, 222 (25.3%) had hip OA, 607 (69.1%) knee OA and 49 (5.6%) both hip and knee OA.



LCGA revealed 4 distinct linear and stable trajectories of pain: "no pain" (n=131, 16.2%), "mild pain" (n=269, 33.3%), "moderate pain" (n=247, 30.5%), and "severe pain" (n=162, 20.0%). Compared with the "no pain" group, subjects belonging to the subgroup "severe pain" were more likely to be female (Odds ratio [OR]=5.13, 95% confidence interval [CI]=2.46–10.70), with a high body mass index (BMI) (OR=1.13, 95%CI=1.07–1.20), a high number of comorbidities (OR=1.42, 95% CI=1.13–1.78), a low vitality score (thus a high level of fatigue; OR=0.94, 95% CI=0.91–0.96), a high disease duration (OR=1.06, 95%CI=1.02–1.10), and a low GHQ score (thus a high psychosocial distress; OR=0.94, 95%CI=0.91–0.98). For physical function, 4 distinct stable trajectories were identified: "no functional limitations" (n=239, 29.6%), "low functional limitations" (n=266, 32.9%), "moderate functional limitations" (n=208, 25.7%), "severe functional limitations" (n=95, 11.8%). In multivariate analyses, female sex (OR=5.11, 95%CI=2.04–12.81), increasing age (OR=1.13, 95% CI: 1.08–1.18), a high BMI (OR=1.15, 95% CI=1.08–1.21), a high number of comorbidities (OR=1.28, 95%CI=1.12–1.61), a low vitality score (thus a high level of fatigue; OR=0.91, 95%CI=0.88–0.93), and a low GHQ score (thus a high psychological distress; OR=0.96, 95%CI=0.93–0.99) were associated with the trajectory of "severe functional limitations".

**Conclusions:** Based on the 5 year follow-up data, we identified 4 distinct trajectories of pain and 4 trajectories of physical function. None of the trajectories demonstrated worsening or improvement over time, confirming that OA is a chronic persistent disease that does not inevitably worsen.

**Disclosure of Interest:** None declared

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THURSDAY, 14 JUNE 2018

## HPR Interventions (educational, physical, social and psychological)

### THU0713-HPR BEHAVIOUR CHANGE INTERVENTIONS TARGETING PHYSICAL ACTIVITY IN ADULTS WITH FIBROMYALGIA SYNDROME: A SYSTEMATIC REVIEW

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**Background:** Recent EULAR guidelines for the management of fibromyalgia syndrome (FMS) strongly recommend aerobic and strengthening exercise programmes, which demonstrate positive effects on symptoms and physical function.<sup>1</sup> Despite these benefits, physical activity (PA) and exercise promotion remains a significant clinical challenge. Behaviour change theories and techniques are recommended as part of complex health interventions to change health behaviours<sup>2</sup>; their integration into interventions aimed at PA behaviour in people with FMS is not known.

**Objectives:** To review behaviour change interventions targeting PA and exercise behaviour of adults with FMS.

**Methods:** A systematic review of quasi-randomised and randomised controlled trials targeting PA behaviour in people with FMS was conducted. Studies were retrieved by searching MEDLINE (OVID), EMBASE, PEDro, PsychINFO, CINAHL, Scopus, Web of Science, and The Cochrane Central Register of Controlled Trials for keywords and medical subject headings relating to FMS, PA and exercise, and behaviour change. Two reviewers independently determined study eligibility. The Cochrane Risk of Bias tool was used to assess risk of bias and data extraction was completed using a standardised template. Due to heterogeneity of interventions and outcome measures, a planned meta-analysis was deemed inappropriate.

**Results:** The search strategy produced 2117 records, after removal of duplicates. Of these, 6 studies were ultimately deemed eligible for inclusion. Overall, the risk of bias of included studies varied from unclear to high. Median (IQR) study size was 114.5 (91.5) participants, with mean (SD) participant age ranging from 42.5 (7.6) to 53.1 (9.9) years. PA and exercise behaviours were the primary focus of three interventions and were components of broader interventions in three studies. Specific behaviour change theories informed two interventions. The number of behaviour change techniques (BCTs) included in studies ranged from 9 to 21; all interventions included elements of goal setting, problem solving, instruction, demonstration and practice of PA or exercise, and use of credible sources. Two studies reported objective measures of PA (pedometry and accelerometry); no significant improvements were sustained at 6 month follow-ups, although a significant post-intervention increase in steps-per-day favouring a behaviour change intervention compared to an education intervention was reported. Outcomes of self-reported measures of PA were conflicting.

**Conclusions:** To date, the small number of behaviour change interventions targeting PA in people with FMS have had limited success. This may be partly due to the varying application of behaviour change theories and techniques in interventions. If the potential benefits demonstrated in exercise trials are to be realised,

future studies should incorporate behaviour change theories at the core of PA interventions and describe BCTs comprehensively so that the most effective techniques may be identified.

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## HPR Professional education, training and competencies

### THU0714-HPR INTERPROFESSIONAL COLLABORATION IN RHEUMATOLOGY REHABILITATION – THE CLASH BETWEEN IDEOLOGY AND PRACTICE

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**Background:** Interdisciplinary collaboration in rheumatology rehabilitation is pivotal in order to meet the complex and multifaceted needs of the patients.<sup>1</sup> However, in practice, an interprofessional approach is hard to achieve.<sup>2</sup>

**Objectives:** To explore how health professionals working with inpatient rehabilitation at a Danish hospital for rheumatic diseases, experience the interdisciplinary collaboration in practice compared to their ideals. Further, to explore what fosters or prevents interprofessional collaboration.

**Methods:** In total six focus groups and two individual interviews were conducted with 32 health professionals (HPs) working with rehabilitation. The HPs included occupational therapists, physiotherapists, rheumatologists, nursing staff, a social worker and a dietician. The composition of the focus groups were monodisciplinary, except from one group where nurses and doctors from the outpatient unit were interviewed together. The individual interviews were conducted with a social worker and a dietician, as they were sole employers within these disciplines.

The interviews were transcribed ad verbatim and a thematic condensation and indexing was used in the analysis of the data.<sup>3</sup>

**Results:** The analysis revealed a clash between ideals about interdisciplinary teamwork and the dominant monodisciplinary work practice. Physical, organisational and cultural factors were perceived as important barriers. Lack of common physical facilities hindered both informal and formal interdisciplinary cooperation. The organisational set up with only one interdisciplinary team meeting before the patients were admitted to hospital and with a lack of rheumatologists' involvement during admission did not support interdisciplinary teamwork. The existing monodisciplinary work culture acted as a barrier towards both formal and informal collaboration. All these factors led to a lack of knowledge about the contributions from other HPs.

Common physical work and meeting facilities and informal networking fostered interprofessional collaboration.

**Conclusions:** To support the development of interprofessional teamwork in rehabilitation practice, it is important to consider both common physical work facilities and to change the organisational and cultural factors acting as barriers towards collaboration. Further knowledge about the contributions from other HPs is a prerequisite to interprofessional collaboration.

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**HPR Interventions (educational, physical, social and psychological)****THU0715-HPR STRATIFIED EXERCISE THERAPY BY PHYSICAL THERAPISTS IN PRIMARY CARE IS FEASIBLE IN PATIENTS WITH KNEE OSTEOARTHRITIS**

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**Background:** There is strong evidence that exercise therapy is effective in reducing pain and activity limitations in knee osteoarthritis (OA), but effect sizes are low to moderate. Stratified exercise therapy tailored to clinically relevant subgroups of patients is expected to optimise treatment effects in a cost-effective manner.

**Objectives:** This study aimed to explore the feasibility of a newly developed model of stratified exercise therapy in primary care.

**Methods:** A mixed method design was used, consisting of an uncontrolled pre-test-posttest design and a process evaluation. Eligible patients visiting a participating primary care physical therapist (PT) were included. Based on our model, participants were allocated to the 'high muscle strength subgroup', 'low muscle strength subgroup', 'obesity subgroup' or 'depression subgroup', and received subgroup-specific, protocolised, 4 month exercise therapy. Feasibility of stratified exercise therapy according to this model was evaluated by a process evaluation (process documentation, semi-structured interviews and focus group meeting) and outcome (physical functioning (KOOS-ADL) and knee pain (NRS), assessed at baseline and 4 months follow-up).

**Results:** We included 50 patients, of which 3 patients dropped out. The process evaluation suggests that our model is feasible for patients and PTs, with some adaptations for further optimisation. We found clinically relevant improvements on physical functioning ( $p < 0.001$ ; 20%) and knee pain ( $p < 0.001$ ; 37%) for the total group. PTs provided on average 10 sessions, ranging from 2 to 24. The average number of sessions was 6 for the 'high muscle strength subgroup', 12 for the 'low muscle strength subgroup', 13 for the 'obesity subgroup' and 16 for the 'depression subgroup'.

**Conclusions:** Our model of stratified exercise therapy is feasible in primary care. Minor adaptations could further optimise the feasibility. Future research should determine the (cost-)effectiveness of this model, compared to usual, non-stratified exercise therapy.

**Disclosure of Interest:** None declared

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**THU0716-HPR THE IMPACT OF EXERCISE ON SLEEP IN PEOPLE WITH RHEUMATOID ARTHRITIS: A PILOT RANDOMISED CONTROLLED TRIAL**

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**Background:** Reduced sleep duration and poor sleep quality are prevalent complaints in rheumatoid arthritis (RA). These in turn may further deteriorate functional ability and reduce the person's exercise levels. Current rheumatology guidelines recommend exercise as a key component in the management of RA however, what is lacking is its impact on sleep.

**Objectives:** To obtain reliable estimates regarding recruitment rates; retention; protocol adherence; adverse events, in addition to producing estimates of the potential effect sizes of the intervention on changes in outcomes of sleep duration; sleep quality and disturbances; RA related pain; depression; anxiety; functional limitation; disease activity and fatigue.

**Methods:** Participants were recruited in person at weekly rheumatology clinics at a University Hospital and through self-selected social networking. They were randomised to either a walking based exercise intervention consisting of 28 walking sessions, with 1 per week being supervised by a trained physiotherapist, spread over 8 weeks (2–5 times/week), or a control group who received advice on

the benefits of exercise for people with RA. Ethical approval was received. Descriptive statistics and t-tests were used to analyse the data with SPSS v22.

**Results:** One hundred and one (101) people were identified through the rheumatology clinics, with 36 contacting the primary investigator through social networking. Of these, 24 met the eligibility criteria, with 20 being randomised (18% recruitment; 100% female; mean age 57 (SD 7.3 years). Ten exercise participants (100%) and 8 controls (80%) completed final assessments, with both groups being equivalent for all variables at baseline. Exercise participants completed 87.5% of supervised sessions and 93% of unsupervised sessions. No serious adverse events were recorded and through semi-structured interviews the intervention was highly acceptable to exercise participants. Pittsburgh Sleep Quality Index (PSQI) global score showed a significant mean improvement between the exercise group  $-6.6$  (SD 3.3) compared to control  $-0.25$  (SD 1.1) ( $p = 0.012$ ); PSQI subcomponent sleep duration showed a significant improvement in mean hours between the exercise group 1.65 (SD 0.39) and control 0.56 (SD 0.46) ( $p = 0.021$ ); PSQI subcomponent sleep quality indicated those in the exercise group improved their sleep quality from fairly bad/poor to fairly good/very good, while those in control reported no change at fairly bad/poor. Global rating of change indicated exercise participants reporting their sleep was minimally/much improved, while control participants reported no change/minimally worse, post intervention.

**Conclusions:** The walking based exercise intervention designed to improve sleep was feasible, safe and highly acceptable to study participants, with those participants in the exercise group reporting improvements in sleep duration and sleep quality compared to the control group. Adverse events were predominantly mild. This pilot provides a framework for larger intervention studies and based on these findings a fully powered trial of walking as an exercise based intervention is recommended, preceded by focus groups to investigate methods to improve recruitment of males.

**Disclosure of Interest:** None declared

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**HPR Patients' perspectives, functioning and health (descriptive: qualitative or quantitative)****THU0717-HPR IMPAIRED MUSCLE FUNCTION AND SHOULDER-ARM MOVEMENT IN PATIENTS WITH SYSTEMIC SCLEROSIS**

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**Background:** A few studies report limitations in upper and lower extremity mobility and muscle function in patients with systemic sclerosis (SSc). Little is known about to what extent skin involvement (lcSSc/dcSSc) and lung function (no-mild vs moderate-endstage lung disease) influence active range of motion (AROM) in the shoulder-arms and muscle function in patients with SSc.

**Objectives:** We aim to examine shoulder-arm AROM, shoulder and hip muscle endurance as well as lower extremity muscle function in patients with SSc in comparison with reference values and also to explore possible differences in function depending on lung function and skin involvement.

**Methods:** 205 patients, fulfilling the EUSTAR/ACR criteria for SSc, were recruited from the Karolinska University Hospital. AROM in shoulder-arms (Functional Shoulder Assessment, FSA), muscle endurance in shoulder and hip flexion (Functional Index 2, FI-2), and muscle function in the lower extremities (Timed-Stands Test, TST) were assessed and compared with reference values. Patients were classified as to lung disease severity using sub-items from the SSc disease severity score for lung involvement. Patients with a score of 0–1 were classified as no-mild lung disease and a score of 2–4 as having moderate-endstage lung disease.

**Results:** SSc-patients had overall more reduced muscle endurance (FI-2, % of predicted) in shoulders 53(27–100) and hips 40(23–90) when compared with reference values, 100(100–100) and 100(72–100) ( $p < 0.001$ ) and patients with moderate-endstage lung disease were more impaired, 39(21–71) and 35(20–70) than no-mild, 57(33–99) and 48(28–100) ( $p < 0.05$ ). No differences were found between dcSSc/lcSSc. All patients, regardless of subgrouping, had lower muscle strength when measured with TST, 21(17–29) seconds, when compared to reference values, 17(15–18) ( $p < 0.001$ ). The FSA-scores were overall lower on both right, 22(20–24) and left, 23(20–24) compared with reference values 23(22–24) and 23(22–24) ( $p < 0.05$ ), especially in patients aged 60 years or more. DcSSc-patients had lower FSA-score than lcSSc-patients ( $p < 0.05$ ). No differences were found between patients with no-mild and moderate-endstage lung disease.

**Conclusions:** SSc-patients have markedly reduced muscle endurance and muscle function compared with reference values and patients with moderate-end-stage lung disease have reduced lower extremity muscle function compared to patients with no-mild lung disease. SSc-patients have slightly less AROM than controls and dcSSc-patients are more restricted than lcSSc. This study highlights the importance of identifying patients with an enhanced risk of developing severe muscle impairments. We suggest that physiotherapists regularly assess muscle function using standardised tests and when needed initiate exercise to improve function

**Disclosure of Interest:** None declared

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### THU0718-HPR THE PSYCHOSOCIAL IMPACT OF JOINT HYPERMOBILITY SYNDROME AND EHLERS-DANLOS SYNDROME (HYPERMOBILITY TYPE): A QUALITATIVE INTERVIEW STUDY

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**Background:** Existing research examining those with Joint Hypermobility Syndrome (JHS) and Ehlers-Danlos Syndrome (Hypermobility Type) (EDS-HT) has predominately focused on factors such as pain, range of movement and physical function. However psychosocial factors have received much less attention.

**Objectives:** This study sought to 1. Identify the psychosocial impact of JHS/EDS-HT by examining participants' lived experiences, and; 2. Identify characteristics of effective coping with JHS/EDS-HT, using qualitative methods.

**Methods:** Adults with JHS/EDS-HT took part in semi-structured telephone interviews to discuss their own lived experiences and the impact of the condition on their lives. All met the Hakim and Grahame (2003) five-item criteria for clinically significant joint hypermobility, and had a self-confirmed diagnosis of JHS/EDS-HT. The transcripts were coded using NVivo 10 and analysed using inductive thematic analysis.

**Results:** 17 participants (14 women, 3 men) took part (age range 22–70, mean 38 years). The sample was purposively selected from across the UK to broadly represent different genders, ages and ethnicities. Inductive thematic analysis indicated five main themes:

**Healthcare limitations:** All participants reported a lack of awareness of JHS/EDS-HT among healthcare professionals, and diagnosis typically took several years. Examples were given where local anaesthetics had either partly or completely failed, leaving patients aware of severe pain during surgical or dental procedures.

**A restricted life:** Participants experienced a range of symptoms including joint pain and instability, fatigue, gastrointestinal issues, frequent dislocations and subluxations. Due to difficulty completing daily activities, some relied on their partners or family for support, but this led to feelings of guilt and shame.

**Social stigma:** The invisible nature of their condition led to participants facing criticism and confrontations with others as they 'looked fine'. Fears of being judged led some to hide their symptoms. Many felt frustrated and angry that due to fatigue or injury they could not keep up with friends, family or colleagues.

**Fear of the unknown:** Not knowing when the next injury was going to occur, and how JHS/EDS-HT would affect them over time made participants especially fearful of declines in their physical ability. Many cited a lack of reliable information about their condition, other than in published books or research journals. Psychological support to better cope with the enduring impact of JHS/EDS-HT on their lives was lacking.

**Ways of coping:** Several coping approaches were identified by participants, including acceptance of their condition, building social networks, finding out more about JHS/EDS-HT and adapting their activities. Physiotherapists were instrumental in supporting participants to exercise regularly.

**Conclusions:** The results of this qualitative study highlight the significant psychosocial impact of JHS/EDS-HT on participants' lives. Further research should consider potential interventions to improve information provision, address psychological support and increase awareness of JHS/EDS-HT among healthcare professionals.

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### THU0719-HPR NON-PHARMACOLOGICAL CARE IN SYSTEMIC SCLEROSIS: ROOM FOR IMPROVEMENT?

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**Background:** Although health professional (HP) treatment is considered to be a corner stone in the management of systemic sclerosis (SSc), little is known about the referral process to and the content of non-pharmacological care in SSc.

**Objectives:** To describe the contribution of HP to SSc care from the perspective of SSc patients, including the referral process, use of care provided by HP, treatment targets and outcome satisfaction.

**Methods:** Dutch SSc patients from different hospitals were invited through their rheumatologists (RT) to complete an still ongoing online survey provided by the ARCH (Arthritis Research and Collaboration Hub) working group, containing questions on a wide range of issues within SSc care. Items concerning access to care (referral versus direct access), use of HP services, and quality of care perceived by patients assessed by the CQ Index were extracted to answer the research question. Reasons for referral/direct access and treatment targets were examined by means of open questions.

**Results:** On January 10th, 2018, 433 SSc patients, 73% women (n=317), with a median age of 61 (SD=10,81) completed the survey. 38% of the patients had limited and 23% diffuse cutaneous SSc. The mean time since diagnosis was 4,1 years.

In total, 10 different HP disciplines were reported and 76% (n=331) of the patients ever had contact with one or more HP; 50% (n=215) had contact with a HP in the past year. Compared to the other 9 disciplines named, physiotherapists (PT) were the most often referred to; 57% (n=245) had PT treatment since SSc onset, 41% (n=177) in 2017, whereas only 35 were referred to occupational therapists and 9 to hand therapists (figure 1).

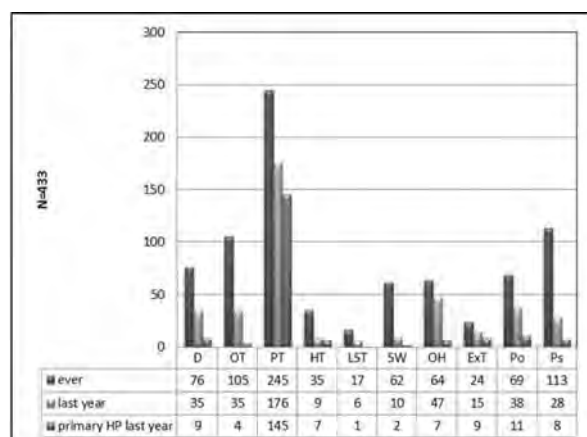
Rheumatologists (RT) were the main referrers to HP care with 49% (n=106); 27% (n=59) sought care by one or more HP through direct access in the past year. A total of 52% (n=111) of the 215 patients that received HP treatment in 2017 perceived the collaboration between their RT and the treating HP as insufficient and 68% (n=146) reported that RT and HP did not make good agreements with each other. Further, 45% (n=97) of the patients felt that there was no coordination between the referrers and the HP about advices issued.

76% (n=164) of respondents found their HP sufficiently competent for SSc treatment. 73% (n=156) could cope better with their complaints after the treatment and reported improvement in their daily activities. Qualitative analysis of the data on the PT as main HP treatment provider in 2017 yielded 36 different referral reasons and 42 treatment targets, of which the most frequently mentioned (>4) are shown below.

Most frequent reasons for referral and therapeutic objectives physiotherapy

**Referral reasons:** pain, joint problems, shoulder problems, decreased mobility, back problems, muscle weakness/stiffness/ pain and general stiffness.

**Treatment targets:** improvement of general mobility, joint mobility, condition, muscle function, skin flexibility and hand function, pain relief, stiffness avoidance and fatigue reduction.



D=dietist, OT=occupational therapist, PT=physio therapist, HT=hand therapist, LST=language and speech therapist, SW=social worker, OH=oral hygienist, ExT=exercise therapist, Po=podiatrist, Ps=psychologist

Abstract THU0719HPR – Figure 1. Frequency of referrals to health professionals

**Conclusions:** HP treatment is a meaningful part of SSc care, as reflected in the satisfaction of SSc patients. The results describe a suboptimal communication



between RT and HP. In view of other published studies on hand problems in SSc, a surprisingly small amount of referrals to occupational- and hand therapists. Further research should focus on the optimisation of professional communication.

**Disclosure of Interest:** None declared

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## HPR Interventions (educational, physical, social and psychological)

### THU0720-HPR FACTORS ASSOCIATED WITH POOR SLEEP QUALITY IN PATIENTS WITH CHRONIC WIDESPREAD PAIN: RESULTS FROM THE AMSTERDAM PAIN COHORT

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**Background:** Reduced sleep quality is a major concern in patients with chronic widespread pain (CWP).<sup>1,2</sup> Poor sleep quality in CWP has received relatively little attention in both multidisciplinary treatment and clinical research in multidisciplinary treatment.<sup>3,4</sup>

**Objectives:** (i) To investigate the prevalence of poor sleep quality and (ii) to explore the associations between clinical, cognitive and emotional factors and quality of sleep in patients with CWP indicated for multidisciplinary treatment.

**Methods:** Baseline data were used from 163 CWP patients referred for multidisciplinary treatment. Linear regression models, adjusted for age and gender, were used to assess the relationship of clinical (pain, fatigue, pain interference and disability), emotional (anxiety, depression and psychological distress) and cognitive factors (catastrophizing, acceptance, self-efficacy, kinesiofobia and illness beliefs) with sleep quality, as measured with the Pittsburgh Sleep Quality Index (PSQI).

**Results:** Poor sleep quality was found in 92% of the patients. The multivariate model showed that a higher level of fatigue, psychological distress and more concerns about the illness were independently associated with poorer quality of sleep. The model explained 27.9% of the variance of sleep quality.

**Conclusions:** The high prevalence of poor sleep quality in patients with CWP referred for multidisciplinary treatment emphasises the need to target sleep during the treatment program. Poorer quality of sleep is related to a higher level of fatigue, psychological distress and more concerns about the illness. Attention to these factors during multidisciplinary treatment could contribute to improvement in quality of sleep.

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**Disclosure of Interest:** None declared

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### THU0721-HPR THE EFFECTS OF UPPER AND LOWER LIMB EXERCISE ON THE MICROVASCULAR REACTIVITY IN SYSTEMIC SCLEROSIS PATIENTS

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**Background:** Vascular endothelial injury is one of the early hallmarks in systemic sclerosis (SSc). High intensity interval training (HIIT) is known to improve vascular function in a range of clinical conditions. Ramos et al., 2015 HIIT in particular has demonstrated improvements in clinical outcomes, in conditions that have a strong macroangiopathic component. Nevertheless, the effect of HIIT on microcirculation in SSc patients is yet to be investigated.

**Objectives:** Therefore, the purpose of the study was to compare the effects of two HIIT protocols (cycle and arm cranking) on the microcirculation of the digital area in SSc patients.

**Methods:** Thirty four SSc patients (65.3±11.6 years old) were randomly allocated in three groups (cycling n=11, arm cranking n=11 and control group n=12). The exercise groups underwent a twelve-week exercise program twice per week. All patients performed the baseline and post-exercise intervention measurements where the physical fitness, functional ability, transcutaneous oxygen tension ( $\Delta\text{tcpO}_2$ ), body composition and quality of life were assessed. Endothelial-dependent as well as -independent vasodilation were assessed in the middle and index fingers using LDF and incremental doses of acetylcholine (ACh) and sodium nitroprusside (SNP). Cutaneous flux data were expressed as cutaneous vascular conductance (CVC).

**Results:** Peak oxygen uptake increased in both exercise groups ( $p<0.01$ ,  $d=1.36$ ).  $\Delta\text{tcpO}_2$  demonstrated an increase in the arm cranking group only, with a large effect, but found not statistically significant ( $p=0.59$ ,  $d=0.93$ ). Endothelial-dependent vasodilation improvement was greater in the arm cranking ( $p<0.05$ ,  $d=1.07$ ) in comparison to other groups. Both exercise groups improved life satisfaction ( $p<0.001$ ) as well as reduced discomfort and pain due to Raynaud's phenomenon ( $p<0.05$ ). Digital ulcers and hospitalizations reported in four patients (36%) of the control group and one of them proceeded for amputation. Arm cranking seems to be the preferred mode of exercise for study participants as compared to cycling ( $p<0.05$ ). No changes were observed in the body composition or the functional ability in both exercise groups compared to the control group.

**Conclusions:** Our results suggest that the arm cranking has the potential to improve the microvascular endothelial function in SSc patients and to prevent digital ulcers and further related complications. Also notably, our recommended training dose (e.g., a 12 week HIIT program, twice per week), appeared to be sufficient and tolerable for this population. Future research should focus on exploring the feasibility of a combined exercise such as aerobic and resistance training by assessing individual's experience and the quality of life in SSc patients.

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### THU0722-HPR PHYSICAL THERAPY IS EFFECTIVE IN PATIENTS WITH ANKYLOSING SPONDYLITIS: A RANDOMISED CONTROLLED TRIAL

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**Background:** Ankylosing spondylitis (AS) is a chronic inflammatory disease that predominantly affects the spine and may cause serious functional impairment. The prevalence of AS is approximately 0.1% of the Caucasoid population. Treatment of AS includes use of anti-inflammatory drugs to reduce pain and stiffness. In addition, patients are advised to exercise daily and to engage in weekly group physical therapy to maintain mobility of the spine and peripheral joints.

**Objectives:** To evaluate the effects of physical therapy on pain, disease activity, functional and emotional status and quality of life in patients with AS.

**Methods:** Thirty one patients diagnosed with AS and followed up in outpatient clinic were conducted into the study. Routine physical examination of musculoskeletal and neurological system of all patients has been performed. Patients divided into two groups (physical therapy group and control group) as random. 15 seance physical therapy (hotpack, ultrasound, TENS and hydrotherapy) exercise and medical treatment performed for the physical therapy group and only home exercise programme and medical treatment for control group. All patients received medical therapy which was not changed during the study. We evaluated all patients with visual analogue scale (VAS) at night and rest for pain, Bath Ankylosing Spondylitis Functional Index (BASFI) for functional status, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) for disease activity and modified Schober, finger floor distance (FFD), lateral flexion of the lumbar spine, cervical rotation, intermalleolar distance, tragus wall distance, chest expansion, cheek manubrium distance and Bath Ankylosing Spondylitis Metrology Index (BASMI) for spinal mobility measurements at the beginning, 2nd and 6th weeks. Also Beck Depression Inventory (BDI) and short form 36 (SF-36) were fulfilled by all patients at the beginning and 6th week.

**Results:** Between the groups there was no difference in demographic data. We showed significant improvement in all parameters except lateral flexion, tragus wall distance measurements for spinal mobility and beck depression index scores at second week ( $p<0.05$ ) in physical therapy group. This improvement in all parameters was discontinued for intermalleolar distance, cheek manubrium distance, cervical rotation, finger floor distance and BASFI at 6th week measurements. We also showed significant improvements mental capacity and social function subgroups of SF-36 at 6th week when compared with beginning ( $p<0.05$ ). We detected significant improvement in second week and sixth week for VAS rest and general health subgroup of SF-36 at physical therapy group when comparing two groups.

**Conclusions:** Physical therapy may have beneficial effects on pain, spinal mobility and quality of life in patients with AS.

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#### THU0723-HPR NICE GUIDANCE ON SPONDYLOARTHRITIS: RECOMMENDATIONS SUPPORTING RECOGNITION AND REFERRAL BY PHYSIOTHERAPISTS & PODIATRISTS

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**Background:** Physiotherapists and podiatrists are key to earlier diagnosis of spondyloarthritis (SpA) and have an essential role in assessing for signs, symptoms and risk factors in people with joint, tendon or back pain. Spondyloarthritis can be a challenge to recognise and often mistaken as chronic back pain or unrelated tendon and joint problems. Symptoms can move around, flare and settle, and links between back pain, peripheral problems and extra-articular conditions can be missed.

**Objectives:** This presentation raises awareness of recent NICE guidelines on Spondyloarthritis<sup>1</sup> and provides an overview of recommendations on recognition and referral relevant for physiotherapists and podiatrists.

**Methods:** The guideline was developed using standard NICE guideline methodology. Quality ratings of evidence applied GRADE methods based on quality of available evidence for assessed outcomes. When standard methodology could not be applied, customised quality assessments provided narrative summaries or customised GRADE tables. Recommendations were developed by a multispecialty development group which included people with SpA and review by stakeholder organisations informing the final version.

**Results:** NICE guidance offers recommendations for suspecting axial and peripheral presentations and when to refer to rheumatology for assessment. These are based on the evidence for signs, symptoms and risk factors that increase the likelihood that a person may have SpA. The guidance highlights that SpA can occur with negative HLA B27, normal inflammatory markers and not to exclude SpA based on any one sign, symptom or test result.

Referral is recommended for suspected axial spondyloarthritis with back pain lasting >3 mths with onset before 45 years of age plus four or more additional features: Onset before 35 years; Woken second half of night by symptoms; Buttock pain; Improves with movement; Improves within 48 hours of taking NSAIDs; First-degree relative with SpA or psoriasis; Current/past enthesitis; Current/past psoriasis; Current/past uveitis plus psoriasis or if HLAB27 positive).<sup>1,2</sup> Morning stiffness lacked specificity as a referral criterion for axial SpA however prolonged morning stiffness remains important in suspecting inflammatory disease.

Referral is recommended for suspected peripheral SpA if a person presents with dactylitis; or with persistent or multiple-site enthesitis (inflammation at tendon/ligament attachment to bone) without apparent mechanical cause plus if any of the following: back pain without apparent mechanical cause; current/past psoriasis, inflammatory bowel disease or uveitis; first degree relative with SpA or psoriasis; or symptom onset following gastrointestinal or genitourinary infection.

**Conclusions:** Recognising possible signs, symptoms and risk factors of spondyloarthritis is an essential aspect of clinical practice for clinicians assessing musculoskeletal problems. Recent NICE guidance offers advice on suspecting SpA and when to refer to rheumatology for assessment to support earlier diagnosis, treatment and reduce the significant impacts of these conditions.

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#### THU0724-HPR INVESTIGATION OF IMMEDIATE EFFECT OF CERVICAL STABILISATION EXERCISES ON PROPRIOCEPTION IN PATIENTS WITH NECK PAIN

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**Background:** Reduced ability to maintain and upright posture, may reflect impaired muscle endurance and proprioceptive accuracy required to control the postural position in patients with neck pain. A recent study investigated the effect of cervical stabilisation exercises on proprioception of neck pain patients. But in mentioned study the joint position change was evaluated for only cervical flexion movement.

**Objectives:** The aim of our study is determine the acute effect of cervical stabilisation exercises on joint position sense in all ranges of neck movement in patients with idiopathic chronic neck pain.

**Methods:** 20 patients (27–45 ages, 80% female and 4 men 20% male) with neck pain for more than 3 months were participated in this study. Exercise training was performed only one session. Patients with any neurological deficits, any recent injuries to neck and were excluded from the study. Training included craniocervical flexion, deep cervical extensor muscle activation, isometric flexion-extension exercises in upright position and shoulder flexion with neutral cervical position in upright position. Each exercise were performed five times. The measured variables included joint repositioning errors in the sagittal and horizontal directions. Visual Analogue Scale (VAS), Neck Disability Index (NDI) were implemented for determining the personal characteristics of patients. Cervical joint repositioning error was evaluated by laser pointer in flexion, extension, rotation and lateral flexion of cervical movement directions at sitting position before and after exercise session. Wilcoxon test was used to compare to differences between repeated assessments

**Results:** VAS values for pain intensity were (mean  $\pm$ SD) 5.56 $\pm$ 3.17, NDI values were 14.06 $\pm$ 6.83 and HADS scores were 18.27 $\pm$ 2.23. In comparison to baseline values, joint position error was significantly lower in flexion, extension, rotation and lateral flexion directions at horizontal and sagittal planes ( $p<0.001$ ) except right lateral flexion at sagittal plane ( $p>0.05$ ) (table 1).

**Abstract THU0724HPR – Table 1.** Comparison of joint position errors

Variable (degree)	Before exercise Median $\pm$ SD	After exercise Median $\pm$ SD	p value
JPE in flexion horizontal	1.71 $\pm$ 0.66	0.57 $\pm$ 0.80	<0.001
JPE in flexion sagittal	1.14 $\pm$ 0.43	0.68 $\pm$ 0.40	<0.001
JPE in extension horizontal	0.85 $\pm$ 0.48	0.57 $\pm$ 0.42	<0.001
JPE in extension sagittal	0.85 $\pm$ 0.55	0.28 $\pm$ 0.22	<0.001
JPE in right rotation horizontal	1.05 $\pm$ 0.53	0.57 $\pm$ 0.31	<0.001
JPE in right rotation sagittal	0.76 $\pm$ 0.73	0.28 $\pm$ 0.30	<0.001
JPE in left rotation horizontal	1.14 $\pm$ 0.39	0.28 $\pm$ 0.42	<0.001
JPE in left rotation sagittal	0.95 $\pm$ 0.49	0.29 $\pm$ 0.28	<0.001
JPE in right side bend horizontal	1.05 $\pm$ 0.56	0.57 $\pm$ 0.28	<0.001
JPE in right side bend sagittal	0.19 $\pm$ 0.36	0.19 $\pm$ 0.22	0.209
JPE in left side bend horizontal	1.19 $\pm$ 0.54	0.47 $\pm$ 0.37	<0.001
JPE in left side bend sagittal	0.19 $\pm$ 0.39	0.38 $\pm$ 0.23	<0.001

JPE=Joint position error, p values are based on Wilcoxon Signed Ranks Test



**Conclusions:** The immediate effects of neck stabilisation exercises on proprioceptive function of neck may reflect that these exercises, may enhance postural awareness and control while in motion.

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**Disclosure of Interest:** None declared

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#### THU0725-HPR EULAR POINTS TO CONSIDER/RECOMMENDATIONS FOR THE HEALTH PROFESSIONALS' PREVENTION AND MANAGEMENT OF OSTEOPOROTIC FRACTURES

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**Background:** Interventions delivered by non-physician health professionals, such as physiotherapists, occupational therapists and nurses play an important role in effective management of patients with osteopenia or osteoporosis.

**Objectives:** To establish EULAR Points to Consider/Recommendations for the prevention and management of osteoporotic fractures by non-physician health professionals.

**Methods:** Points to consider/recommendations were developed according to EULAR standard procedures<sup>1</sup> using six stages: i) establishment of an international expert panel/task force including patients, rheumatologists, orthopaedic surgeons and health professionals; ii) a first Delphi-round to set up clinical questions; iii) a literature review; iv) a task force meeting to review the results of the literature search and to formulate points to consider/recommendations; v) development of consensus and assessment of the level of agreement with the points to consider/recommendations using second Delphi round; vi) a field test.

**Results:** Eight clinical questions and two overarching principles were formulated, subject to the literature search (the clinical questions only) and discussed and refined during the task force meeting. The two overarching principles focused on the importance of shared decision making between patients and professionals and the involvement of different health professionals. Two clinical questions were merged and the task force finally agreed on seven recommendations/points to consider: 1) Health professionals should start with fall risk evaluation in patients at risk of primary or secondary fracture. Patients with high risk should be evaluated by a health professional using multi-component screening, or referred to another health professional competent in multi-component screening. 2) Health professionals should ensure that after osteoporotic fracture, patients are given

opportunities to participate in adequate exercise and are supported in adequate nutritional intake. Calcium and vitamin D intake should be discussed with the patients. 3) Smoking and overuse of alcohol should be discouraged. 4) Tailored multicomponent interventions including, for example: exercises, environmental adaptations, nutrition, life-style and education, should be offered to patients at high risk of primary osteoporotic fracture and/or high risk of falls. 5) Health professionals should be included in Fracture Liaison Services (FLS) and/or a coordinated, multidisciplinary post-fracture prevention program. Patients with fragility fractures should be referred to a FLS or an adequate, coordinated, multidisciplinary post-fracture prevention program. 6) Health professionals should address, monitor and support medication adherence in a structured follow up. 7) Health professionals should identify patients at risk of bone fragility, ensure they are offered opportunities for adequate treatment, and address bone fragility through patient education.

**Conclusions:** These points to consider/recommendations should be applied by health professionals in the prevention and management of osteoporotic fracture to ensure high quality care.

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**Disclosure of Interest:** None declared

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#### THU0726-HPR ADHERENCE TO BIOLOGICAL THERAPY IN CHRONIC INFLAMMATORY RHEUMATISM: RESULTS OF A RETROSPECTIVE STUDY IN AUVERGNE, FRANCE

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**Background:** The arsenal of treatment options for Chronic inflammatory rheumatism (CIR) has considerably grown over recent years with the biological therapies. Poor patient adherence to treatment is a major barrier to proper disease management. Patient education enhances drug adherence by improving the knowledge and skills needed to manage the disease and treatments.

**Objectives:** This study aimed to assess adherence to subcutaneous biological therapy using the Morisky Medication Adherence Scales (MMAS-4) in patients with CIR: rheumatoid arthritis (RA), ankylosing spondylitis (SA) and psoriatic arthritis (PsA), who received education in our department.

**Methods:** This was a retrospective single-centre observational study of routine care. All patients on subcutaneous biological therapy who received at least one education interview between 2009 and 2013 were included. Adherence was assessed using the Morisky questionnaire (MMAS-4). A comparison of adherence was made based on the BIOSECURE questionnaire (knowledge and skills relating to biological therapy) and type of educational model received by patient (model 1: providing information; model 2: performing one-on-one education; model 3: performing head to head and group-based education). Adherence was also compared based on population characteristics, type of care (mixed or solely hospital), type of CIR, number of education interviews, injection frequency and type of biological therapy.

**Results:** A total of 193 patients were included in the study, 124 of whom were women. The population's mean age was 53.3±14.8 years. Patients had had CIR for 10 years, 5-18 with 113 patients suffering from RA, 73 from SA, and 7 from PsA. Of the 193 patients, 192 (99.5%) were on TNF inhibitors (of whom 107 [55.4%] were on etanercept, 58 [30.1%] on adalimumab, 10 [5.2%] on certolizumab and 17 [8.8%] on golimumab) while 1 (0.5%) was on abatacept. About 75.7% (n=146) of the patients reported good adherence (Morisky=0), 17.6% (n=34) moderate adherence (Morisky=1 or 2), and 6.7% (n=13) poor adherence (Morisky=3 or 4). No significant association was observed between knowledge and skill levels as evaluated by the BIOSECURE questionnaire and adherence as evaluated by the Morisky questionnaire (respectively, 76±13, 77±11, 76±18, p=0.91). A total of 92 patients received model 1, 80 received model 2, and 21 received model 3. Adherence was poorer in the group that received model 3 compared with the other two models (79% Morisky score of 0 for model 1, 76% for model 2 versus 57% for model 3; p=0.04) and poorer in young patients (p=0.005). No difference existed based on gender, education level, marital status, type of care (mixed or solely hospital), type of CIR, number of education interviews, frequency (1, 2 or 4 weeks) of biological injections.

**Conclusions:** Adherence to biological therapy was quite good in this study. No link existed between adherence and knowledge levels. Combining head to head and group-based patient education did not improve adherence compared with simply providing information or performing head to head patient education alone.

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**THU0727-HPR** **COMPARISON OF KINESIO TAPE APPLICATION AND MANUAL LYMPHATIC DRAINAGE ON LOWER EXTREMITY OEDEMA AND FUNCTIONS AFTER TOTAL KNEE ARTHROPLASTY**

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**Background:** Significant trauma and muscular tightness often result during Total Knee Arthroplasty (TKA) surgery and thus act to restrict tissue fluid movement resulting with lower extremity oedema. Kinesio Taping is applied directly on the skin for restoration of normal fluid perfusion, removing congestion of lymphatic fluid or haemorrhages. In addition manual lymphatic drainage (MLD) enhances blood circulation and stimulates the lymphatic movement and unblocks lymphatic territories.

**Objectives:** The aim of the study was to investigate the effectiveness of Kinesio Taping and MLD in reducing postoperative oedema, pain and lower extremity functions in the early stage after TKA.

**Methods:** Forty patients who underwent unilateral TKA were randomised as Kinesio Taping group (n=12), MLD group (n=13) and control group (n=15). For all patients, postoperative rehabilitation program included early mobilisation and physical therapy twice a day during the stay in orthopaedic traumatology department. On the second day after surgery, lymphatic correction method was used on the Kinesio Taping group patients and a standardised 30 min MLD treatment was applied to the MLD group patients. Control group received only physiotherapy treatment. Circumference measurements were applied on preoperatively and the second, third, fourth day and 6th weeks after surgery. Knee Injury and Osteoarthritis Outcome Score (KOOS) was used to determine the functional outcomes on the 6th weeks after surgery. Repeated measures analysis was used to determine the group by time differences between groups.

**Results:** A significant group effect was observed for oedema difference ( $F_{(4,42)}=2.44$ ,  $p=0.047$ ) and pain levels ( $F_{(3,54)}=4.56$ ,  $p=0.006$ ) and post hoc testing demonstrated a significantly lower oedema and pain levels in the both Kinesio Taping and MLD compared to control group. There was no difference found between Kinesio Taping and MLD groups ( $p=0.933$ ). KOOS results were better in Kinesio Taping and MLD groups when compared to control group ( $p=0.021$ ). There was no difference in KOOS results between Kinesio Taping and MLD groups ( $p=0.851$ ).

**Conclusions:** Applications of both Kinesio Taping and MLD to remove congestion of lymphatic fluid at the early stage after TKA surgery were found affective in enhancing blood circulation and stimulating the lymphatic movement. In addition, Kinesio Taping and MLD were both effective on relieving pain and improving functional outcomes after TKA surgery.

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**THU0728-HPR** **A MIXED METHODS STUDY OF A GROUP PHYSIOTHERAPY PROGRAMME INCORPORATING EXERCISE AND EDUCATION IN FIBROMYALGIA PATIENTS**

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**Background:** Research on non-pharmacological treatments for fibromyalgia patients has demonstrated that exercise and education have positive effects on pain and disability<sup>1</sup>. However, the traditional approach of studying treatment effectiveness based exclusively on quantitative measures has been questioned. There is growing recognition of the importance of integrating patients' perspectives into clinical research. Outcome measures focused on patients' perceptions of improvement have been increasingly used, however they do not offer expanded definitions of what constitutes a "successful" outcome<sup>2</sup>. The further exploration of patients' perspectives about treatment benefits may contribute to the development of treatments that better match patients' needs.

**Objectives:** The aim of this study was twofold: firstly, to examine the effectiveness of a group physiotherapy programme (incorporating exercise and education) on pain intensity, disability and global impression of change in fibromyalgia

patients; and, to explore how patients, who achieved success in pain and/or disability (according to the score from the Patient Global Impression of Change Scale - PGIC), understand and make sense of the results.

**Methods:** A sequential explanatory mixed methods approach, combining quantitative (1 st phase) and qualitative methods (2nd phase), was carried out. In the 1 st phase, the participants underwent an 8 week (3 times weekly) standardised group programme. Participants were assessed at baseline, 4 and 8 weeks later. Outcome measures included the Numeric Pain Rating Scale (NPRS), the Revised Fibromyalgia Impact Questionnaire (FIQR) and the PGIC. Participants who had scored  $\geq 5$  in the PGIC were invited to participate in a focus group. In the 2nd phase, 2 focus groups meetings were carried out to collect data. A semi-structured interview schedule was used and the sessions were audiotaped and transcribed verbatim.

**Results:** Thirty-seven participants (females; 49.3±10.2 years) completed the 1 st phase. Analysis using SPSS revealed statistically significant improvements on pain intensity (mean SD change:  $-1.38\pm 2.363$ ,  $p=0.001$ ) and disability ( $-21.577\pm 21.02$ ,  $p<0.001$ ). In what concerns to participants' impression of change, 26 participants (70.3%) perceived substantial improvements on pain and disability (PGIC  $\geq 5$ ). From these, 12 accepted to participate in the focus groups. The qualitative analysis indicated that "doing more daily-life activities" and "taking less medication" were identified as the main reasons for the participants' improvements. According to these participants, the knowledge about strategies for self-management played a key role in their success.

**Conclusions:** The combination of data from both phases provided detailed information about the participants' perceptions regarding the key elements for achieving success with a physiotherapy programme. Further research on patients' perspectives regarding treatment effectiveness is recommended since it may contribute to the design of more effective and patient-centred treatments.

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**THU0729-HPR** **PATIENT WITH RHEUMATOID ARTHRITIS ARE STILL NOT SUFFICIENTLY PHYSICAL ACTIVE. TIME FOR A PERSONALISED PHYSICAL ACTIVITY PROGRAMME!**

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**Background:** For individuals with rheumatoid arthritis (RA), it is important to be sufficiently physically active. The international recommendation for physical activity states that each adult should perform moderate-intensity aerobic physical activity for at least 30 min, five days a week. In recent years, attention and awareness of the importance of being physically active has increased, including the development of exercise programmes for people with rheumatic diseases. However, it is unknown whether patients with RA actually became more physically active in daily practice in the past years.

**Objectives:** Primary, this study will estimate whether the percentage of RA patients that meet the recommended level of physical activity has changed in recent years. Secondary, this study aims to identify RA patients of the outpatient clinic who are physical inactive and motivated to improve their level of physical activity.

**Methods:** In 2014, 740 RA patients from seven outpatient clinics across the Netherlands filled out a questionnaire which contained items about self-reported physical activity and sport habits. In 2017, the same items were assessed again by sending a questionnaire to all 727 RA patients of the outpatient clinic in Bernhoven, a hospital in the south of the Netherlands. In addition, questions about motivation to increase the level of physical activity were added.

**Results:** In 2014, 52% of the RA patients met the recommendation for physical activity. In 2017, 33% of the 514 RA patients of the outpatient clinic in Bernhoven who filled out the questionnaire reported that they met the recommendation. Walking, cycling, aerobic and strength fitness training and swimming were mentioned as the most popular sports among RA patients in 2014 as well as in 2017. 133 of the 233 (57%) inactive RA patients of the outpatient clinic in Bernhoven reported that they were convinced to be able to improve their physical activity level and 51% reported that they were motivated to become more physically active in the upcoming months.

**Conclusions:** Despite the increased attention and awareness of the benefits of being physically active, the percentage of RA patients who meet the recommended level of physical activity did not increase between 2014 and 2017. This could be caused by the fact that the effect of the developed exercise programmes typically wear off after the exercise interventions have stopped. Another reason could be that patients with RA need to be more assisted to overcome barriers to implement physical activities in their daily life. A more personalised approach, based on coaching and shared-decision making to set personal physical activity goals, could increase compliance and reduce barriers to being physically active. Half of the inactive RA patients of the outpatient clinic are motivated to become more physically active. Therefore a new study will examine whether a personalised physical activity programme is effective to increase and sustain the level of physical activity in inactive RA patients.

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#### THU0730-HPR A SYSTEMATIC REVIEW OF ONLINE INTERVENTIONS FOR ADDRESSING PSYCHOLOGICAL DISTRESS IN RHEUMATOID ARTHRITIS AND OTHER LONG-TERM CONDITIONS

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**Background:** Psychological distress in rheumatoid arthritis (RA) is associated with severity of disease activity and poor treatment outcomes. Online interventions have the potential to reach large numbers of patients.

**Objectives:** The aims of this study were to identify online interventions for psychological distress and determine their effectiveness in RA and other long-term conditions.

**Methods:** The following databases were searched: MEDLINE, EMBASE, CINAHL and PsychINFO (Jan 2007-Jul 2017). Inclusion criteria were randomised controlled trials (RCTs) of effectiveness of interventions to address psychological distress in adults. Titles and abstracts were screened independently by 2 reviewers. Methodological quality was assessed by 3 reviewers using Cochrane's Risk of Bias tool. Data were extracted independently by 4 reviewers. Meta-analysis was not possible due to clinical heterogeneity of the included studies.

**Abstract THU0730HPR – Table 1.** Presents the studies and evidence of their effectiveness.

Study	Condition	Effectiveness
Boeschoten 2017	Multiple sclerosis	Not effective BDI: Effect size d=0.01; p=0.953
Bond 2010	Diabetes	Effective CESD: Effect size d=0.7; p<0.05 PAID: Effect size d=0.6; p<0.05
Cohn 2014	Type 2 diabetes	Mixed CESD: Effect size d=-0.44; p=0.05 Diabetes Distress Scale: Effect size not shown
Ferwerda 2017	Rheumatoid arthritis	Effective BDI: Effect size d=0.54; p=0.001 IRGL-Negative mood: Effect size d=0.38; p=0.01 IRGL-Anxiety: Effect size d=0.48; p=0.001
Fischer 2015	Multiple sclerosis	Effective BDI: Effect size d=0.53; p=0.01
Hunt 2009	Irritable bowel syndrome	Effective Anxiety Sensitivity Index -GI: Effect size d=0.63; p<0.01 Anxiety Sensitivity Index -non GI: Effect size d=0.70; p<0.01
Lorig 2008	Rheumatoid arthritis, osteoarthritis and fibromyalgia	Effective Health Distress Scale RA: d=0.5 Health Distress Scale OA: d=0.4 Health Distress Scale FM: d=0.03
Newby 2017	Type 1 and type 2 diabetes	Effective Patient Health Questionnaire: Effect size g=0.78; p<0.001 PAID: Effect size g=0.80; p=0.01
Nobis 2015	Type 1 and type 2 diabetes	Effective CESD: Effect size d=0.89; p<0.001
Rondags 2016	Type 1 and type 2 diabetes	Not effective Hypoglycaemia Fear Survey: RR=0.80; 95% CI 0.64 to 1.01; (p=0.059).
Van Bastelaer 2011	Type 1 and type 2 diabetes	Effective CESD: Effect size d=0.70; p<0.001.

Effectiveness of interventions is reported with effect sizes based on between-group differences in the primary outcomes at the end of each study.

**Results:** The review included 11 RCTs in the following conditions: arthritis,<sup>2</sup> multiple sclerosis,<sup>2</sup> diabetes<sup>6</sup> and irritable bowel syndrome.<sup>1</sup> The quality of most RCTs was poor due to attrition, selective reporting and limited follow-up. Eight disease-specific and 3 generic interventions were identified. Cognitive behavioural therapy was the most common intervention type. All interventions were online but support delivery and outcome measures varied significantly. Nine of the 11 interventions were shown to be effective, including 2 for RA. Most interventions were not available outside of the trial.

**Conclusions:** The findings are inconclusive due to the overall bias of the included studies and insufficient evidence in RA. More good quality RCTs are required to determine effectiveness of online interventions in RA.

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#### THU0731-HPR THE ABDOMINAL HYPOPRESSIVE TECHNIQUE CAN BE USED TO TREAT LOW BACK PAIN?

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**Background:** In 1980, Dr. Marcel Cauriez created the abdominal hypopressive technique (AHT) with the goal of reprogramming the core muscles. The term hypopressive refers to the decrease of the pressure related to the thoracic, abdominal and pelvic cavities. However most traditional exercises are hyperpressive – they increase the internal pressure. In addition, conventional core exercises train conscious control, but the core is designed to cope at a subconscious level. Publications testing AHT are surprisingly low and are mostly published in not indexed journals. Despite the lack of scientific evidence to support its benefits, AHT is gaining popularity among European physiotherapists as a recommended treatment for a wide spectrum of disorders.

**Objectives:** To test the effect of a structured AHT program on low back pain intensity and disability in women and the retention of effect after two-month.

**Methods:** A cross-over intervention trial with random assignment and blind assessments was carried-out. The experimental sequence included a first period of intervention or control (rest), and a second period in which the initial groups were switched to the complementary. The exercises included in the AHT program were standardised by two Doctors in Physiotherapy trained in this technique. Measures were taken by a trained physiotherapist blinded to the group allocation at baseline, after finishing the first period, and after completing the entire sequence. Efficacy was defined as changes between groups in low back pain intensity and disability, measured with a visual analogue scale (VAS) and the Oswestry Disability Index (ODI) respectively.

**Results:** Overall, 42 participants were randomly assigned to a sequence (n=21 for each group). From the initial sample, 88% have been diagnosed by a physician with low back pain at least once in their lives and 100% of them self-reported low back pain at baseline. Baseline low back pain intensity measures did not differ between groups. The VAS for the group that started as control was 4.0 (2.5 to 5.4) vs 4.3 (2.8 to 5.7) for the group that started with the AHT program (p=0.774). However, the difference ( $\Delta$ ) after two months was statistically significant between groups (group that started as control, 0.3 (-0.1 to 0.6) vs the group that started with AHT, -2.7 (-3.9 to -1.6); p<0.001). Improvements decayed by 0.87 after a two-month follow up (p=0.094).

Regarding low back pain disability, similar results were found. ODI baseline measures between groups were not significantly different with 10.3 (5.7 to 14.9) for the group that started as control and 7.7 (4.1 to 11.3) for the group that started with the AHT program (p=0.368). The  $\Delta$  after two months showed that both groups improved (started as control, -0.2 (-2.7 to 2.4)) but the improvement in the AHT group was greater (-3.5 (-7.1 to 0.3)); p=0.120. Improvements were maintained after a two-month follow.

Is important to highlight that a sequence effect was noted, with residual effect of AHT; therefore, only results from the first sequence were analysed.

**Conclusions:** A structured AHT program produce benefits on low back pain intensity (short-term) and disability (long-term). However, further research is needed to test its effectiveness in comparison with conventional core exercises.

**Disclosure of Interest:** None declared

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**THU0732-HPR** **INDIVIDUAL RESPONDER ANALYSIS OF THE EFFECTIVENESS OF MANUAL THERAPY AND EXERCISE VERSUS USUAL CARE IN PATIENTS WITH CHRONIC NONSPECIFIC NECK PAIN: PRELIMINARY RESULTS OF A RANDOMISED CONTROLLED TRIAL**

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**Background:** Chronic nonspecific neck pain (CNP) is a common health problem worldwide. The physiotherapy approach is the second line of treatment and a large variety of modalities are frequently used. However, the mean effect of interventions is small and it is unknown if the patients achieving clinically important change. Individual responder analyses provide researchers with complementary information about the patterns of recovery and the proportion of patients achieving clinically important treatment responses.

**Objectives:** The aim of this study was to compare the effectiveness of a combined intervention of manual therapy and exercise (MET) versus usual care (UC), on pain intensity and global perceived recovery.

**Methods:** A randomised controlled trial was conducted on 62 participants with CNP lasting  $\geq 3$  months, assigned to MET and UC groups. Participants in the MET group (n=31) received 12 sessions of passive articular mobilisation and exercise (coordination, strength, endurance), whereas the UC group (n=31) received 15 sessions of usual physiotherapy care, combining electrotherapy, massage and stretching exercises. Patients were assessed at baseline, and then at 3 and 6 weeks (final of intervention). The Minimal Clinically Important Difference (MCID) in treatment response for pain intensity was defined as a decrease of  $>2$  point in the Numeric Rating Scale of Pain compared to the baseline score and for global perceived recovery a value of  $\geq 5$  in Patient's Global Impression of Change Scale.

**Results:** A significant difference between-groups was observed at 6 weeks on pain intensity ( $p \leq 0.001$ ), favouring the MET group. No significant differences were found between-groups in pain intensity at the baseline ( $p \geq 0.626$ ) and at 3 weeks ( $p \geq 0.777$ ). At patient-level response, in the MET group, 58% of the participants experienced an MCID in the first 3 weeks of treatment and this proportion was increased to 94% at 6 weeks on pain intensity, and rose from 68% to 81% on global perceived recovery. In the UC group the proportion of patients that experienced an MCID rose from 55% to 61% on pain intensity, at 3 and 6 weeks, respectively, and 68% in global perceived recovery in both moments. The patients in MET group were 10% (RR=1,1) and 50% (RR=1,5) more likely to achieve the MCID on pain intensity than the UC group, at 3 and 6 weeks, respectively. In global perceived recovery, the MET group were 20% (RR=1,2) more likely to achieve an MCID response at the 6 weeks. No differences were found in chances of recovery at 3 weeks.

**Conclusions:** These findings suggest that participants of MET group had a pattern of recovery over 6 weeks and achieved a higher response rate to treatment, on pain intensity and a better global perceived recovery, compared to those receiving UC.

**Disclosure of Interest:** None declared

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**THU0733-HPR** **EFFECT OF CUSTOM-MADE FOOT ORTHOSES VERSUS PLACEBO IN PATIENTS WITH RHEUMATOID ARTHRITIS: RANDOMISED CLINICAL TRIAL**

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**Background:** Rheumatoid Arthritis (RA) affects among 0.3% and 1.5% of people.<sup>1</sup> Foot involvement occurs in more than 85% of people with RA.<sup>2</sup> One of the most prevalent deformities is rearfoot valgus.<sup>3</sup>

**Objectives:** To study whether the use of custom made foot orthoses improves pain, foot function, and quality of life in RA patients.

**Methods:** This randomised clinical trial was carried out in the University of Seville and of A Coruña. Inclusion criteria: to be over 18 years and to have diagnosis of RA with involvement in the foot. Exclusion criteria: Acute phase, neurological problems or cognitive impairment. Participants were given an informational form. They had to use physiological footwear and assigned foot orthoses during at least 8 hours/day, for 3 months. Participants were randomly assigned to one of the two groups: Experimental Group (A) (foot orthosis with a Rovafoam upper sheet and polypropylene) and Control Group (B) (5mm-thick Rovafoam sheet, without adaptation). The SF-12, the Visual Analogue Pain Scale (EVA), the Manchester

Questionnaire and the Foot Function Index (FFI) are administered at the first visit and at the last review.

**Results:** The final sample consisted of 47 participants with RA, 53.2% were group A and 46.8% were group B. This

**Abstract THU0733HPR – Table 1.** shows the results of the different questionnaires for both groups.

		Group A		Group B	
		Baseline	End	Baseline	End
EVA		6.52±2.34	4.16±2.82	6.23±1.88	5.47±2.89
Manchester	Functional	12.32±5.77	10.72±7.17	12.19±4.53	10.71±5.58
	Personal Appearance	1.2±1.44	0.68±1.21	1.62±1.56	1.38±1.57
	Pain	7.00±2.61	5.52±3.28	6.52±3.06	5.47±2.63
	Work	2.56±1.78	2.12±1.83	2.33±1.46	2.19±1.75
	Total	22.60±9.58	19.04 ±11.93	21.86±8.54	19.76±9.79
FFI	Pain	69.26	45.97	61.85	53.36
		±18.67	±29.11	±19.59	±25.95
	Disability	58.97	45.55	57.71	46.67
		±28.95	±34.43	±24.09	±30.97
	Activity Limitation	24.75	13.24	14.14	10.54
	Limitation	±23.76	±14.67	±12.43	±10.55
	Total	54.70	39.08	51.12	42.69
	±20.55	±26.26	±15.98	±24.17	

At the initial moment between groups, there were no statistically significant differences.

Data obtained baseline and end of the follow-up period were compared within the control group, and showed significant differences in some FFI domains (days with pain, disability and total). In the experimental group there was a statistically significant decrease in EVA scale, some Manchester questionnaire domains (pain and total sections) and in some FFI domains (activity limitation and total; there was a very statistically significant in EVA scale and in some FFI domains (pain and total). There was no significant difference in the SF-12 scale between these two moments.

**Conclusions:** Custom made foot orthoses improved foot pain and function in people with RA who participate in this study. However, this treatment did not have a positive effect on their quality of life.

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**THU0734-HPR** **NOVEL EXPERIENCE EQUIPMENT FOR RHEUMATOID HAND-FINGERS**

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**Background:** RA patients are prone to ulnar deviation and swan-neck deformity even early after onset of the disease. Limitation of finger joint range of motion due to hand-finger deformation brings restriction to ADL in the workplace as well as in the home. Patients and caretakers of patients are often burdened by these limitations; however, RA hand-finger deformation experience equipment have not been developed to experience these limitations. We have developed a novel RA hand-finger deformation experience equipment with opened fingertips (RSE; RA hand/finger simulation equipment).

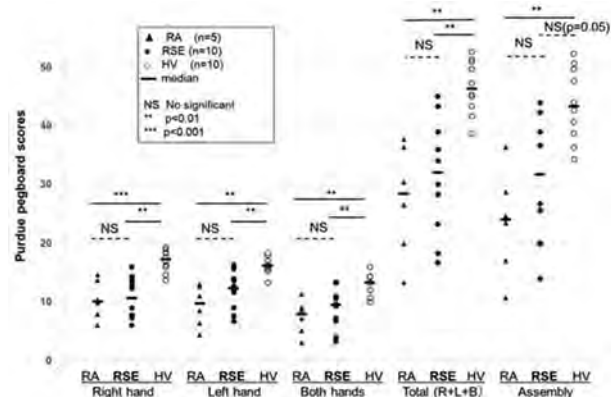
**Objectives:** To assess the utilisation of RSE in healthy volunteers (HV) to experience RA hand-finger dysfunction using DASH (Disabilities of the Arm, Shoulder



and Hand), STEF (Simple Test for Evaluating Hand Function), and Purdue Pegboard.

**Methods:** We developed the following equipment: Type U to imitate extension limitation of metacarpophalangeal (MCP) joints seen in ulnar deviation; Type B which imitates flexion deformity of the distal interphalangeal (DIP) joints by seen in boutonniere deformity; and Type S which imitates flexion limitation of proximal interphalangeal (PIP) and interphalangeal (IP) joints by reversing the upper and lower ends of the Oval-8 Finger Splint (Fukui Co. Ltd, Japan). Types U and S were fitted on HV (index to pinky). RSE was evaluated using DASH, STEF and Purdue Pegboard in hand-finger function evaluation. Twenty-four RA patients with hand-finger deformation and Forty-one HV were included in this study to evaluate the equipment.

**Results:** Mean  $\pm$ SD ages for RA patients was  $67.4 \pm 8.0$  years (95.8% female) and  $38.2 \pm 17.7$  for HV (63.4% female), respectively. Total hand-finger deformities for RA patients were 23 hands for ulnar deviation, 66 fingers for swan-neck deformity, and 33 fingers for boutonniere deformity. Randomization for RA patients was as follows: 13 DASH, 5 (10 hands) STEF, and 6 Purdue Pegboard. 10 HV were assigned to DASH, 10 to Purdue Pegboard, and 14 (28 hands) to STEF. HV were evaluated with RSE and without RSE. For DASH, STEF, and Purdue Pegboard, RA patients showed significant functional loss compared to HV. Significant function loss in RA patients was also observed with the RSE. However, no differences were seen between the RA group and the HV with RSE group (figure 1).



Abstract THU0734HPR – Figure 1 Purdue. pegboard scores of RA, RSE and HV groups

**Conclusions:** We developed the RSE, which allows for one to experience the decrease in function with RA hand-finger deformity. Our study showed that RSE use can indeed allow this experience. By using RSE, health care workers, patient caretakers and early RA patients can experience joint limitation of RA for educational purposes, personalised rehab programs, and development of self-help tools.

**Disclosure of Interest:** None declared

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#### THU0735-HPR HOW RHEUMATOLOGY SPECIALIST NURSE DETECTS SMOKING HABIT IN RHEUMATOID CHRONIC INFLAMMATORY DISEASE PATIENTS

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**Background:** Inflammation plays a significant role in the development of atherosclerosis and cardiovascular disease (CVD). Patients with chronic inflammatory disease (CID) have an increased risk of CVD. Smoking is one of the main risk factors for CVD and a predictor of poor response to treatment and poor prognosis.

**Objectives:** We aimed to describe the role on a rheumatology specialist nurse in the detection of smoking habit and dependence to nicotine in CID patients before the start of an interventionism plan to avoid it in CID patients.

**Methods:** All CID patients attended in a nurse rheumatologist unit, during one month, were asked for smoking habit. We determined the characteristics, onset of smoking and number of cigarettes per day. The Fagerström test was used to establish the nicotine dependence (ND) (score >5) and the Richmond test for predicting abstinence following intervention to stop smoking (score >5). Exhaled CO level Coximetry was also recorded. We planned an interventionism consenting in health advice provided by a nurse and the derivation to a smoke unit.

**Results:** 22 patients were identified. 12 (50.0%) were female and mean age was 46.0 (SD 10.5). 14 (63.6%) suffered Rheumatoid Arthritis, 6 (27.3%) Ankylosing Spondylitis and 2 (9.1%) Psoriatic Arthritis. 5 (22.7%) subjects were under

biological treatment. Mean number of cigarettes smoked per day and smoking years were 16.0 (SD 8.9) cigarettes and 27.2 (SD 11.7) years respectively. Up to 5 out of 22 (22.7%) subjects had high ND. Patients with ND had higher exhaled CO levels than non ND subjects (24.6 [SD 6.0] vs. 17.9 [SD 12.2] p-value 0.160). We observed no differences in age, sex, rheumatoid diagnosis, years smoking or cigarettes per day between both groups. Active treatment with biological drugs was significantly associated with ND (60.0 vs. 14.3%, p-value 0.046). One out of five patients with ND had good abstinence prediction according to Richmond test

**Conclusions:** Nearly one out of five smoking CID subjects had severe ND. Treatment with biological drugs was related to ND. Interestingly, most of the ND subjects had good prediction for smoking cessation. Therefore, the development of a nurse program to detect smoking and our interventionism plan to avoid smoking habit are of enormous interest.

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#### THU0736-HPR THE EFFECTIVENESS OF SHORT TRAINING IN PSYCHOLOGICAL SUPPORT FOR NURSES IN RHEUMATIC CARE

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**Background:** Patients with rheumatoid arthritis (RA) often suffer from psychological concerns.<sup>1</sup> There is a lack of psychology specialists in many hospitals and clinics. According to EULAR, nurses should undertake a significant portion of providing psychological support to patients.<sup>2</sup> However, in Japan nurses involved in clinical practice often do not have sufficient time and opportunity to receive adequate education on psychological support.

**Objectives:** The aim of this study is to evaluate nurses' understanding of basic psychological concepts and the efficacy of a short psychology workshop for nurses in RA clinical care.

**Methods:** A clinical psychotherapist provided a lecture on psychological support once for a period of 30 min, followed by 1 hour of role-play groupwork. The lecture focused on basic psychological support including concepts of "listening", "acceptance", "empathy", "open question", "closed question" and "patient-centred perspective". Group work focused on applying the aforementioned concepts. Nurses were asked before and after workshop regarding their understanding and opinions on the necessity and feasibility of psychological support, as well as their motivation for implementation. Nurses' opinions were evaluated on a 1-7 rating scale (1=not at all, 7=full). Client Satisfaction Questionnaire-8 (CSQ-8J) was utilised to assess satisfaction with the workshop. Data analyses were performed with Wilcoxon signed rank test.

**Results:** 53 nurses (M/F: 1/52) participated in this study. The average of ages, clinical experience and clinical experience in RA care were 45.5 years old, 21.0 and 7.9 years, respectively. Nurses' opinions regarding the necessity and feasibility of psychological support in general, as well as their motivation for providing psychological support statistically significantly increased post-workshop (necessity: p=0.0052, feasibility: p<0.0001, motivation: p=0.0033).

Nurses' answers regarding their current application of these concepts in clinical practice were as follows: mean  $\pm$ SD; listening: 5.15 $\pm$ 1.20, empathy: 5.06 $\pm$ 1.18, acceptance: 4.71 $\pm$ 1.18, open question: 4.80 $\pm$ 1.31, closed question: 4.49 $\pm$ 1.47. The understanding of these concepts was statistically significantly higher after the workshop (p<0.0001 for each concept). Moreover, the feasibility of all the above concepts was rated as statistically significantly higher post-workshop. (p<0.001 for each concept). The necessity of adopting a patient centred perspective was also judged as statistically significantly higher post-workshop (p<0.001). Based on CSQ-8J, satisfaction with the workshop was overall high.

**Conclusions:** This is the first report evaluating the effectiveness of brief psychological workshops for nurses in rheumatic care in Japan. This preliminary study

demonstrated that even a brief workshop appears effective for assisting and encouraging nurses in providing psychological support to patients. Further studies of training methods and of nurses' application of the skills acquired in such training are ongoing.

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#### THU0737-HPR THE EFFECTIVENESS OF RELAXATION EXERCISES ON PAIN, FUNCTIONAL LEVEL AND MUSCLE STRENGTH IN PATIENTS WITH TOTAL KNEE ARTHROPLASTY: A PRELIMINARY RESULTS

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**Background:** Total Knee Arthroplasty (TKA) is a common procedure performed mainly due to advanced osteoarthritis (OA), pain, physical disability and reduced quality of life. However, approximately 20% of the patients respond poorly to the surgery and chronic pain and disability following TKA remains a major health burden for many patients. Among the most well documented predictors of poor outcome following TKA is pain catastrophizing. Inadequate pain relief can cause impaired functional performance, increased skeletal muscles tension which are close to surgery related incision site, longer length of hospital stay, unnecessary psychological distress and decreased patient satisfaction. There is high need of developing treatments aimed at improving self-management for patient with TKA at early postoperative period.

**Objectives:** The aim of this study is to investigate the effectiveness of progressive muscle relaxations exercises (PMR) on pain coping, physical function and muscle strength among patients with TKA due to OA.

**Methods:** The study group consisted of 22 patients (33 knees), who underwent primary TKA because of OA were consecutively allocated to an intervention group (n=11, with mean age; 66.18±13.29 years), and were allocated to a control group (n=11, with mean age; 62.45±7.28 years). After surgery, all patients underwent the same rehabilitation program. The intervention group also was instructed pre-operative patient education about PMR exercises, and the intervention group received PMR exercises focusing on reducing overall body tension, anxiety and pain managed by a physiotherapist. Patients were evaluated regarding the pain (Numeric Pain Rating Scale (NPRS)), muscle strength, knee function score (Hospital for Special Surgery (HSS) score), pain-related fear (Tampa Scale for Kinesiophobia (TSK)), anxiety and depressive symptoms (Hospital Anxiety and Depression Scale (HADS)) and quality of life (Short-Form 12 Health Survey (SF-12)). Functional activities were evaluated using the Iowa Level of Assistance Scale and walking speed was evaluated using the Iowa Ambulation Velocity Scale. Also functional outcomes were evaluated with timed up and go (TUG) test and 10-metre walk test (10 MWT). Patients were evaluated preoperatively and at discharge.

**Results:** At baseline, demographic characteristics were similar in groups and there was no statistically difference between groups (p>0.05). It was determined at postoperatively that; the intervention group had better results in terms of reduction of pain severity (p=0.001), improvement of HADS anxiety level (p<0.030), pain-related TKS level (p<0.035) and SF-12 mental component score (p<0.011). When the HSS knee scores and quadriceps muscle strength were compared, there was statistically difference between groups and the two outcomes scores were lower in control group after surgery (p<0.040, p<0.012, respectively). There were no statistical differences between groups for other outcomes after TKA (p>0.05).

**Conclusions:** The current results suggest that the PMR exercises at early stage after TKA might be an effective method for patient rehabilitation outcomes. However, in this comparison to obtain more comprehensive results studies on larger series are needed. In this way, a more uniform and objective data can be achieved.

**Disclosure of Interest:** None declared

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#### THU0738-HPR COMPARISON OF THE FUNCTIONAL PROFILE OF THE FOOT BETWEEN THE PATIENTS WITH PATELLOFEMORAL OSTEOARTHRITIS AND TIBIOFEMORAL OSTEOARTHRITIS

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**Background:** The biomechanics of the patellofemoral (PF) joint are distinct from the tibiofemoral (TF) joint and hence, interventions that have been designed to reduce pain and improve function in those with tibiofemoral disease may be inappropriate for those with Patellofemoral OA (PFOA). Therefore, patients with PFOA have been recently considered a subgroup different from patients with Tibiofemoral OA (TFOA). Loading asymmetries of the foot, discrepancy in foot contact area, and excessive increase in plantar pressure are associated with knee OA patients but there is lack of information that how PFOA or TFOA affect the foot profile.

**Objectives:** The purpose of this study was to investigate the foot profile differences between PFOA and TFOA patients and also compare these foot profiles with healthy individuals.

**Methods:** Twenty-nine patients with unilateral knee OA and 14 age-matched controls (median age=42.5 years, median BMI=23.8 kg/m<sup>2</sup>) were included in the study. The patients were divided into two groups; PFOA group (n=16, median age=52.5 years, median BMI=26.7 kg/m<sup>2</sup>) if they had a radiographic Kallgren and Lawrence (KL) score grade 2 or 3 in the PF joint, which was greater than KL score for the TF compartments; TFOA group (n=13, median age=54 years, median BMI=26.6 kg/m<sup>2</sup>) if they had a radiographic KL score grade 2 or 3 in the TF joint, which was greater than KL score for the PF compartments. Plantar pressure distribution was recorded by Digital Biometry Scanning System and Millettix software (DIASU, Italy). The static test was used to determine the maximum foot pressure (N/cm<sup>2</sup>) of the foot, forefoot weight ratio, rarefoot weight ratio, total load and foot angle axis (FAA). Kruskal Wallis test was used to compare the affected side of TFOA and PFOA groups with the control group. After application of the Bonferroni correction, Mann Whitney-U was used to compare the two-group differences.

**Results:** The age (p=0.179) and BMI (p=0.150) were similar between the groups. There were no differences on the affected side maximum foot pressure (p=0.603), forefoot weight ratio (p=0.247), rarefoot weight ratio (p=0.240) and total load (p=0.599) between TFOA, PFOA and control groups. FAA was higher in TFOA group [median-IQR: 17.0°(13.3°–35.4°)] when compared to PFOA (p<0.001) and control group (p<0.001). In addition, foot angle axis was lower in PFOA groups [median-IQR: 9.4°(1.5°–19.5°)] than control group [median-IQR: 13.4°(10.0°–15.8°)] (p=0.005). A reference value is appreciable if found to be between 12°–16°.

**Conclusions:** The angle of the foot plays an important role on optimal weight distribution during walking. Changing the angle of the foot may affect all other joints and create a modifying effect on the moment around the lower extremity. PFOA patients presented lower foot angle axis than normal values while TFOA patients presented higher angles. This may indicate that the intervention should be design for the joint involvement in the knee OA patients.

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**Disclosure of Interest:** None declared

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#### THU0739-HPR EFFECTIVE PREVENTION AND MANAGEMENT OF OSTEOPOROTIC FRACTURES: A SYSTEMATIC LITERATURE REVIEW OF NON-PHYSICIAN HEALTH PROFESSIONALS' INTERVENTIONS FOR A EULAR POINTS-TO-CONSIDER PROJECT

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**Background:** Osteoporotic fractures are a global concern due to associated patient mortality, morbidity and health service expenditure. Optimal care provided

by non-physician health professionals, such as dieticians, nurses, occupational therapists, pharmacists and physiotherapists, to adults at high risk of primary or secondary osteoporotic fracture, is integral in the prevention and management of minimal trauma fracture, but may not be sufficiently realised in all European countries. To address this, a commissioned task force has developed the first collaborative EULAR points to consider/recommendations for non-physician health professionals in the prevention and management of osteoporotic fractures, underpinned by a systematic literature review (SLR).

**Objectives:** To identify and review the scientific literature to inform the development of evidence-based EULAR points to consider/recommendations for non-physician health professionals in the prevention and management of osteoporotic fracture.

**Methods:** A SLR for each of eight clinical questions that were previously formulated and consensually agreed by the task force members was undertaken by a research fellow (NW), with guidance from the task force convenors and the methodologist. Four electronic databases (Medline, Embase, Cinahl and PubMed) were searched over the period 13th - 31 st October 2017. The search strategies combined MeSH terms and keywords to identify studies related to two key concepts: (i) adults  $\geq 50$  years of age at high risk of primary or secondary osteoporotic fracture and (ii) interventions delivered by non-physician health professionals to prevent, treat and manage osteoporotic fractures. Exclusion criteria included articles not in English and without online access. Evidence was categorised using the Oxford Centre for Evidence-based Medicine Levels of Evidence. For critical appraisal of systematic reviews, AMSTAR 2 was used. Risk of bias was assessed by the Cochrane Collaboration's tool.

**Results:** The eight primary searches returned a total of 15 917 citations; duplicates were removed and the remaining 11 195 citations screened for relevance by title, abstract, design and year of publication (recently published reviews and/or RCTs were prioritised). Thirty-two studies were finally selected. Overall confidence in the findings of included systematic reviews ( $n=13$ ) ranged from low to high. Risk of bias also varied across other included studies. Strongest evidence of benefit was found for exercise in the management of osteoporotic fracture [level 1a].

**Conclusions:** There is a lack of high quality evidence for the role of health professionals in the prevention and management of adults at high risk of primary or secondary osteoporotic fracture. We recommend the instigation of an education and research agenda for non-physician health professionals.

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#### THU0740-HPR DETERMINATION OF EXERCISE BEHAVIOUR IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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**Background:** Juvenile idiopathic arthritis (JIA) is one of the most common rheumatic diseases in childhood, affecting at least 1 in 1000 children. Children with JIA experience joint inflammation and swelling, pain and tenderness, morning stiffness, limited mobility. Children with JIA complain pain and have lower functional ability and decreased quality of life compared with their peers. Many studies have reported that patients with JIA have low physical activity levels and also exercise therapy is considered an important component of the treatment of JIA. Nowadays, studies for evaluating exercise behaviours in order to cope with physical inactivity for many chronic diseases are becoming increasingly important.

**Objectives:** The objective of this study was to determine exercise behaviour in patients with JIA.

**Methods:** 34 patients with JIA (23 female and 11 male), age range 5–18 years, home exercise program being recommended, participated in this study. The survey that was created with Google Forms was sent via WhatsApp to patients after 1 week-10 days than setting home based exercise program for each patient. In the survey, disease duration, involvement joint(s), Childhood Health Assessment Questionnaire (CHAQ) for functional ability, 11-point Numeric Analogue Scale

(NRS) for satisfaction of exercising, Exercise Stages of Change Scale-Short Form (ESCS), Exercise Self-Efficacy Scale (ESES), and Decisional Balance Scale (DBS) for exercise behaviour were inquired for the patients with JIA.

**Results:** The mean age and disease duration were 11.38 $\pm$ 4.68 and 5.36 $\pm$ 4.16 years, respectively. The mean of the number of affected joints was 5 $\pm$ 4.41. According to the five behavioural processes by ESCS, the patients were enrolled 38.2% of them in the stage of maintenance, 26.5% of them in the stage of action, 14.7% of them in the stage of preparation, 14.7% of them in stage of contemplation, 5.9% of them in stage of pre-contemplation. 67.5% of them was satisfaction for exercising ( $\geq 5$  for NRS). When comparison of the patients' CHAQ scores due to satisfaction level with NRS, the mean of CHAQ scores was significantly lower in patients with high satisfaction than patients with low satisfaction ( $p=0.014$ ). The mean of scores ESES and DBS were 17.06 $\pm$ 6.13 and 12 $\pm$ 4.61, respectively. All of the patients represented "positive perception of exercise" due to DBS. Only a significant correlation with age of patient and DBS was found ( $r=0.375$ ,  $p=0.029$ ).

**Conclusions:** This study demonstrated that patients with JIA were in high stages participated in exercising and have high self-efficacy of exercise, decreasing of functional ability may affect the satisfaction level of exercising and as age increases, decisional balance for exercising also increases. Therefore, future researchers should investigate potential facilitators of and barriers to exercise for larger population in patients with JIA by following up long term.

**Disclosure of Interest:** None declared

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#### THU0741-HPR MAPPING THE BEHAVIOUR CHANGE TECHNIQUES USED IN A PRACTICE-BASED FIBROMYALGIA SELF-MANAGEMENT PROGRAMME: A QUALITATIVE STUDY

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**Background:** Fibromyalgia (FM) is a complex long-term condition affecting up to 5.4% of the UK population. It is associated with chronic widespread pain, fatigue, sleep and cognitive difficulties. FM can cause high levels of functional and work disability; with individuals making frequent use of healthcare resources. There is limited robust evidence for effective pharmacological treatments for FM, and current guidelines all recommend non-pharmacological interventions.

Allied health professionals at the Royal National Hospital for Rheumatic Diseases (RNHRD), Bath developed the Fibromyalgia Self-Management Programme (FSMP); a non-pharmacological, multidisciplinary exercise and education group.

**Objectives:** Main aims of the FSMP are to provide condition-specific, patient centred, education and exercise advice, to support development of core, self-management skills. The FSMP comprises of 16 hours of group treatment, spread over four or six weekly sessions. Core components include education about FM, sleep, diet and lifestyle advice, hydrotherapy and stretches.

The FSMP was developed clinically, with little opportunity for the clinical team to explore the mechanisms by which it is effective. To inform successful implementation beyond the RNHRD, this evaluation aimed to map the FSMP to the NICE recommended Michie Behaviour Change Taxonomy (BCT) to determine key behaviour change components.

**Methods:** Non-participatory observations were conducted of the four and six week FSMP. Detailed notes on course content, therapist delivery, and additional content not included in the manual were recorded. Semi-structured interviews were conducted with therapists ( $n=4$ ) and patients ( $n=9$ ). Observations and review of the therapist manual data were deductively coded in NVIVO to the Michie Behaviour Change Taxonomy using Framework Analysis. Interview data were analysed using Theoretical Thematic Analysis.

**Results:** Review of the course manual and course observations show the FSMP coded onto 12 of the 16 main areas of the Michie Behaviour Change Taxonomy, encompassing 22 behaviour change techniques. Patients' interviews indicated significant behaviour changes as a result of attending the course; including increased activity levels, pacing, better quality sleep, and improved communication with family members. Patients reported positive changes to symptoms as a result of attending the course.

Therapists highlighted four key challenges in delivering the course; fidelity between therapists, patient readiness and acceptance of FM, group management and patient fatigue while attending the programme.

**Conclusions:** The FSMP utilises a range of behaviour change techniques. Patients who attend the course make changes to their behaviour which enables them to manage their symptoms of FM more effectively.



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**THU0742-HPR** HOW TO OPTIMISE EXERCISE BEHAVIOUR IN AXIAL SPONDYLOARTHRITIS: RESULTS OF AN INTERVENTION MAPPING STUDY

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**Background:** Regular exercise has many health benefits for people with axial spondyloarthritis (axSpA).<sup>1</sup> However, most patients do not engage in frequent exercise.<sup>2</sup> In order to improve exercise behaviour of axSpA patients, a well-founded intervention is needed.

**Objectives:** To identify effective intervention methods to optimise exercise behaviour in axSpA.

**Methods:** The first three steps of the Intervention Mapping (IM) protocol, which is a six-step framework for intervention development, were used to determine effective intervention components. This study comprised 1) a needs assessment, to examine the discrepancy between current and desired exercise behaviour of axSpA patients, 2) a determinant analysis, to identify barriers and facilitators (determinants) to overcome this discrepancy, and 3) an intervention method analysis, to select effective methods that target these determinants. All three steps included literature reviews: PubMed and Web of Science were systematically searched for articles up to August 2017 using a well-defined search strategy. Additionally, semi-structured interviews with axSpA patients (n=2) and physiotherapists specialised in axSpA (n=2) explored the literature search findings of IM steps 1 to 3 qualitatively and ranked the determinants and methods identified in steps 2 and 3 in order of relevance.

**Results:** The literature searches resulted in 28 (64), 23 (257) and 15 (209) included articles (hits) for IM steps 1, 2 and 3, respectively. IM step 1 revealed that only one third of axSpA patients engage in (frequent) mobility, strengthening and/or cardiorespiratory exercises, while especially these components appear beneficial in axSpA. IM step 2 showed that the determinants self-efficacy, attitude, skills, therapists' skills, knowledge, intentions, planning and exercise group support positively influence exercise behaviour in axSpA (ordered by relevance). IM step 3 identified effective methods to stimulate exercise behaviour in axSpA by targeting aforementioned determinants: guided practice, action planning, goal setting, education (on disease, coping, exercise and available resources), feedback, tailoring, motivational interviewing, monitoring, therapists' education and encouragement of exercising in a group (ordered by relevance).

**Conclusions:** This study showed that in order to optimise exercise behaviour in axSpA, patients should be offered an intervention including education, motivational interviewing, goal setting and action planning and they should be stimulated to exercise in a group. In addition, therapists should be educated how to tailor, practice and monitor exercise and how to base this on thorough assessment.

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**THU0743-HPR** SUPPORTED SELF-MANAGEMENT INTERVENTIONS FOR FAMILIES AND CHILDREN AGED 4 TO 11 YEARS OLD LIVING WITH ARTHRITIS, ASTHMA AND TYPE ONE DIABETES: AN INTEGRATIVE REVIEW

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**Background:** The Shared Management Model implies that as children with chronic conditions like rheumatic and musculoskeletal diseases (RMDs) mature, they should increasingly take on responsibility for self-managing their health, in partnership with those involved in their care and education.<sup>1</sup> An initial search of the literature suggested that there was a reduced emphasis on the supported self-management of chronic conditions like RMDs in children aged 4 to 11 years, inspiring a more rigorous and systematic search of the empirical literature.

**Objectives:** The aim of this integrative review were to understand the evidence base regarding supported self-management of chronic conditions by children and their families, including interventions that promote supported self-management skills development.

**Methods:** Studies published since 2012 were identified through a search of eight bibliographic databases. Given the extensive nature of chronic conditions in children, the review focused on three groups of chronic conditions sharing similar self-management characteristics: asthma, RMDs, and type one diabetes mellitus (T1DM). The methodological quality of quantitative studies was assessed using the Cochrane Risk of Bias scale. Non-randomised studies were assessed using the Methodological Index for Non-randomised Studies (MINORS) instrument. Review articles and qualitative studies were assessed using Critical Appraisal Skills Programme (CASP) Systematic Review Checklist and CASP Qualitative Checklist, respectively.

**Results:** The review identified 29 relevant articles, reporting on 22 primary research studies and three review articles. Study participants were children with asthma (n=17) and T1DM (n=4). No studies were identified for children with RMDs. Seventeen studies reported an underlying theoretical basis, the most common of which was social cognitive theory. Interventions promoting supported self-management skills appeared to be effective in improving a range of self-reported and clinical outcomes, including health status, health knowledge, and self-efficacy. However, there was limited evidence of the effect of interventions on the psychosocial wellbeing of children. It also became clear that education-based interventions alone are insufficient in improving self- and shared-management skills. In addition, most studies failed to contextualise chronic conditions in children and their families, who shift between interacting with interventions and living their everyday lives over time.

**Conclusions:** Given the complexity of childhood chronic conditions and intervention components and contents, further investigation is required to specify the mechanisms by which supported self-management interventions operate. Most studies were also aimed at parents and carers, and appeared to neglect the importance of including and engaging children in decisions involving their health-care. Finally, the review clearly highlighted the need for research on the supported self-management of RMDs in children, since no evidence-based interventions were identified for these individuals.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.2994

**THU0744-HPR** EFFECTIVENESS OF PROFIBRO MOBILE APP ON QUALITY OF LIFE, SYMPTOMS AND SELF-CARE AGENCY IN PATIENTS WITH FIBROMYALGIA: A RANDOMISED, SINGLE-BLIND TRIAL

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**Background:** ProFibro is the first free mobile Android application in Brazilian Portuguese for fibromyalgia (FM). It was developed as a complementary Mobile Health resource in FM management for the promotion of self-care. Its main functions are educational animation, self-monitoring, sleep strategies, scheduling, exercise, hints through notifications, practice of gratitude with a diary and family adjustments.

**Objectives:** to assess the effectiveness of ProFibro in the improvement of health-related quality of life, symptoms and self-care agency of patients with FM.

**Methods:** Forty subjects with FM, aged 19–59 years, were randomised into ProFibro and a control group. ProFibro group received a smartphone with the mobile app and subjects were instructed to use it for 6 weeks, while control group

	Control group			ProFibro group			Intergroup analysis p-value
	Baseline Mean ±SD	Post-intervention Mean±SD	Intra-group analysis p-value	Baseline Mean ±SD	Post-intervention Mean±SD	Intragroup analysis p-value	
WPI	13,6±3,7	12,3±4,5	0323	13,6±4,0	12,5±4,6	0442	0670
SS	9,2±1,9	7,6±2,4	0,024*	9,4±1,5	7,6±2,9	0,025*	0912
FIQR							
Function	18,5±6,9	15,8±7,6	0248	16,5±6,8	14,9±6,8	0588	0808
Impact	12,3±5,8	9,5±5,1	0112	13,0±4,2	9,8±5,3	0,041*	0777
Symptoms	34,6±7,8	30,3±8,2	0090	33,1±8,1	29,0±7,1	0090	0968
Total score	65,4 ±18,0	55,5±18,2	0093	62,6 ±16,8	53,7±17,1	0105	0745
VAS	5,7±2,2	5,3±2,3	0555	5,9±2,2	5,1±2,6	0291	0593
Self-care	53,5 ±11,0	54,3±11,0	0839	51,9±9,7	56,8±10,2	0127	0132

SD: standard deviation. \*significant.

received a paper booklet of similar content. Subjects were assessed at baseline and after 6 weeks with the Revised Fibromyalgia Impact Questionnaire (FIQR), Widespread Pain Index (WPI), Pain Visual Analogue Scale (VAS), Symptom Severity (SS) Scale and Revised Appraisal of Self-Care Agency Scale.

**Results:** Control group showed significant improvement only in SS compared to baseline. ProFibro group showed significant improvements in SS and FIQR overall impact domain. In intergroup comparison, no differences in change scores were found.

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**Disclosure of Interest:** None declared

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#### THU0745-HPR USE OF WEARABLE ACTIVITY TRACKERS TO IMPROVE PHYSICAL ACTIVITY BEHAVIOUR IN RHEUMATIC CONDITIONS – A SYSTEMATIC REVIEW

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**Background:** Patients with rheumatic conditions, such as low back pain (LBP), lower limb osteoarthritis (OA) and chronic inflammatory rheumatic diseases (CIRDs) are vulnerable regarding physical inactivity, although they derive specific benefits from regular physical activity.<sup>1, 2</sup> Wearable activity trackers (WATs), including simple pedometers and more advanced WATs (e.g. Fitbit), could be a promising strategy to improve physical activity levels.

**Objectives:** To obtain an overview regarding the adherence and effectiveness of WATs to increase physical activity levels and to reduce sedentary behaviours in rheumatic patients.

**Methods:** This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement (PROSPERO CRD42018083532).

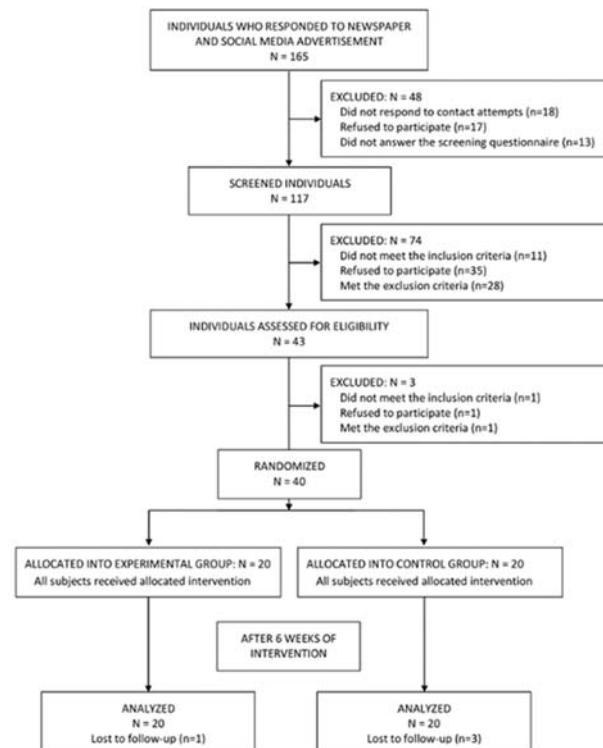
All articles available in English, published between 2000 and 2018 (January), in MEDLINE, EMBASE, PsycINFO and Central Register for Controlled Trials were screened as well as extensive hand search. Study selection and data collection were performed by two independent reviewers. Studies were included if they assessed WATs in patients with OA, LBP or CIRDs. Data collected pertained to (a) adherence (i.e.% days with the WAT worn), (b) efficacy on physical activity (i.e. increase in step counts or moderate to vigorous physical activity), (c) efficacy on symptoms (function, pain, quality of life). Standardised mean differences were calculated and reported as null (<0.2) small (0.2–0.5) moderate (0.5–0.8) or large (>0.8).

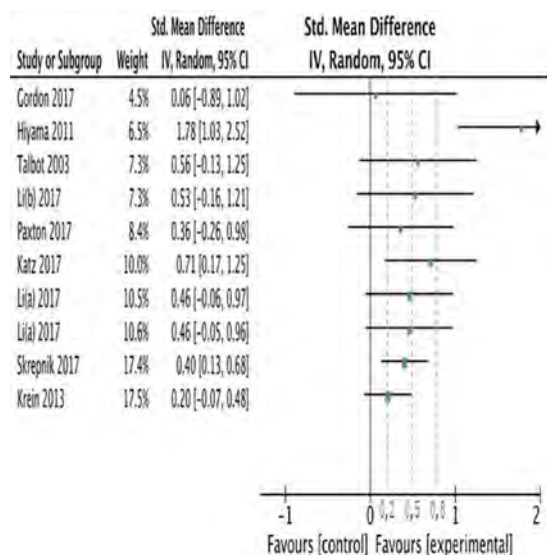
**Results:** Of 2378 abstracts, 15 studies were included in the review (of which, 7, 47%, published in 2017) with a total of 1344 patients: 42% men, range of mean age 16–64 years. Among the 15 studies, 7 (47%) were related to OA, 5 (33%) to LBP and only 3 (20%) to CIRDs. In all, 7 (47%) reported on advanced WATs and 8 (53%) on simple pedometers. (a) Adherence: 4/15 studies (27%) reported adherence, in a total of 416 patients. The weighted mean duration of the studies was 12.6 weeks and adherence was excellent (weighted mean time worn: 92.7% (SD 4.6)). (b) Efficacy on physical activity was reported in 11/15 (73%) studies (ie 876 patients). The mean increase in steps per day was 1579 (SD 770) in the intervention group over a weighted mean duration of 22.6 (SD 13.6) weeks. Effect sizes were null (2/10 studies), small (4/10 studies), moderate (3/10 studies) or large (1/10 studies) (figure 1). (c) For impact on symptoms, 14/15 (93%) studies reported on function, pain or quality of life (or several of these leading to 20 analyses). Overall, effect sizes were null (14/20, 70%) or small (6/20, 30%).

**Conclusions:** Findings suggest that both ProFibro app and the booklet are effective for reducing symptom severity. ProFibro may also reduce the overall impact of FM in the quality of life. More studies with larger sample sizes and longer periods of intervention are needed to confirm the findings of the present study.

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**Conclusions:** Short term adherence to WATs was high in published studies of LPB, OA or CIRDS but the efficacy to increase physical activity levels was small to moderate. There were no modifications of symptoms. The incorporation of WAT in patient care remains challenging. Further studies are needed, especially for CIRDS.

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#### THU0746-HPR EFFICACY OF SURGICAL TREATMENTS FOR PAIN ASSOCIATED WITH TRAPEZIOMETACARPAL (THUMB BASE) OSTEOARTHRITIS: A SYSTEMATIC REVIEW

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**Background:** Trapeziometacarpal osteoarthritis (TMO) is a highly prevalent, painful, and debilitating disorder. Unfortunately, TMO management remains sub-optimal and this is in part due to the lack of knowledge on evidence-based care management. The aim of this systematic review (SR) is to document the efficacy of existing surgical interventions for reducing TMO pain.

**Methods:** We performed this SR according to the Cochrane intervention review methodology. Trials and SRs assessing surgical intervention efficacy on TMO were identified via 16 databases and hand search via the included references. Studies selection, data extraction and methodological quality assessment were conducted by two independent reviewers. Effect estimates of interventions were extracted from SRs when available, otherwise estimated from randomised controlled trials (RCTs). If RCTs were not available, non-RCTs (NRCTs) were referred to. Characteristics and efficacy of interventions were quantitatively analysed. In addition, we rated the level of evidence quality by using the GRADE tool.

**Results:** A total of 8 SRs, 16 RCTs and 41 NRCTs were identified. Most of these studies had unclear to high risk of biases which may have compromised their results. More than 40 comparisons of different surgical interventions were identified, including arthroscopic debridement (AD) (n=2 studies); 1 st metacarpal osteotomy (n=3); resection of 1 st metacarpal/trapezium (R) (n=3); arthrodesis (A) (n=14); trapeziectomy (T) (n=16); hematoma distraction arthroplasty (n=5); ligament reconstruction (LR) (n=5); tendon interposition (TI) (n=13); LRTI (n=17); and manufactured implants - Arex (n=1), Artelon (n=7), chondrocostal autograft (n=4), De la Caffinière (n=5), Elektra (n=5), Graftjacket (n=1), Gore-Tex (n=6), Guepar (n=3), Ledoux (n=2), Maia (n=1), Marlex (n=5), porcine dermal collagen xenograft (n=2), pyrocarbon Pi<sub>2</sub> (n=5), PyroDisk (n=1), Pyrocardan (n=1), and Swanson (n=11). The effect sizes of most of the interventions were small (standardised mean differences 0.04–4.81, risk ratios 1.05–11.1) and/or their 95% confidence intervals included null value. Nonetheless, the superiority of the following interventions was supported by the evidence of very low to moderate quality: AD

over conservative interventions; R+GraftJacket over R; A over R, T+TI and T+LRTI; partial T+chondrocostal autograft over T; T over T+porcine xenograft; T+TI over Artelon; T+LRTI+ bone tunnel over T+LRTI without tunnel for a short-term period; T+LRTI over T+LRTI+ Mitek anchor suture; T+Elektra over T+TI; PyroDisk over Pyrocardan.

**Conclusions:** This SR allowed collating comprehensive evidence on the efficacy of surgical interventions for TMO pain. Based on the available scientific evidence, arthrodesis appears superior to other interventions (R, T+TI and T+LRTI) to alleviate pain, however, adverse effects (e.g., nonunion) have been reported. Thus, it goes without saying that when choosing a proper surgical intervention for TMO, not only its analgesic effects but also the risk and gravity of adverse effects must be taken into consideration.

**Disclosure of Interest:** None declared

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#### THU0747-HPR THE EFFECT OF CLINICAL PILATES EXERCISES ON DISEASE SPECIFIC INDICES, CORE STABILISATION AND BALANCE IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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**Background:** The Pilates method has been widely used to improve physical fitness and rehabilitation in general. Although Pilates method gives precedence to the spine and focuses on controlled movement, posture, and breathing, which are obviously the basic goals of Ankylosing Spondylitis(AS) treatment there is limited literature on the effectiveness of the Pilates method as treatment for patients with AS.

**Objectives:** The aim of this study was to investigate the efficacy of clinical pilates exercises on on disease-specific indices, core stabilisation and balance in patients with AS.

**Methods:** The study included 21 AS patients(11 male, 10 female). Demographic and physical characteristics(age, height, weight, body mass index) were recorded. Evaluations were performed before clinical pilates treatment and after 8 weeks clinical pilates treatment. Bath Ankylosing Spondylitis Disease Activity Index(BASDAI) for disease activity, Bath Ankylosing Spondylitis Functional Index (BASFI) for functional capacity, Bath Ankylosing Spondylitis Mobility Index (BASMI) for spinal mobility were used. Balance was evaluated with Biodex Balance System SD. Overall postural stability indices obtained with bilateral stance (stable and unstable platform), single leg stance(stable platform) and overall limits of stability scores were recorded. Static and dynamic endurance tests were used to evaluate core stabilisation. Modified sit-ups test for dynamic core endurance and static core endurance tests recommended by McGill were used to evaluate core stabilisation. Patients attended group clinical pilates exercise sessions three times a week, during 8 weeks with physiotherapist.

**Results:** The mean age of patients was 43,9±8,93 years and the mean body mass index(BMI) was 27,37±3,68 kg/m<sup>2</sup>. Pre and post treatment measurements were shown in table 1. Statistically significant improvement was observed in all parameters except stable platform bilateral stance and single leg stance postural stability results(p<0,05).

**Abstract THU0747HPR – Table 1.** Comparison of pre and post treatment measurements

	Pre-Treatment Median(IQR)	Post Treatment Median(IQR)	p value
BASDAI	1,70 <sup>(1,01–3,27)</sup>	0,8 (0,56–1,75)	0,000*
BASFI	1,8 (0,35–3,13)	1 (0–1,83)	0,001*
BASMI	2,4 (1–3,7)	2 (0,7–3,1)	0,002*
Flexor endurance(s)	30,0 (20,5–60,35)	54,50 <sup>(42,85–86,00)</sup>	0,000*
Extensor endurance(s)	44,6 (20,75–63,00)	76,5 (54,25–91,77)	0,000*
Lateral side bridge(right)(s)	39 <sup>(21,86–60,00)</sup>	59,00 <sup>(43,61–80,00)</sup>	0,000*
Lateral Side Bridge(Left)(s)	42,40 <sup>(27,35–55,90)</sup>	65 <sup>(34,65–89,00)</sup>	0,001*
Sit-up test(reps)	16 <sup>(3,50–25,50)</sup>	20 <sup>(13–26,50)</sup>	0,001*
Bilateral stance (stabil)	0,30 (0,2–0,45)	0,3 (0,2–0,40)	0,907
Bilateral stance (unstable)	1,5 (1,25–2,10)	1,40 <sup>(1,10–1,75)</sup>	0,007*
Single leg stance(Right)	0,7 (0,6–0,95)	0,7 (0,6–0,85)	0,298
Single leg stance(left)	0,7 (0,6–1,05)	0,7 (0,6–0,80)	0,463
LOS (overall)	51 <sup>(46–62)</sup>	64 <sup>(52,5–70,5)</sup>	0,007*

Mann Whitney U test. IQR: Interquartile Range

**Conclusions:** Clinical pilates exercises is beneficial and safety method in patients with AS to improve functional capacity, disease activity, spinal mobility, core stabilisation and balance. Clinical pilates is an enjoyable and effective way to exercise for Ankylosing Spondylitis patients.

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**Disclosure of Interest:** None declared  
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**THU0748-HPR** EVALUATION OF ADHERENCE TO BIOLOGIC DISEASE MODIFYING ANTI-RHEUMATIC DRUGS IN PATIENTS WITH INFLAMMATORY ARTHRITIS

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**Background:** In recent years, bDMARDs have revolutionised IA treatment in improving IA symptoms, as well as slowing down structural damage. However, efficacy observed in the controlled settings of clinical trials may not always translate to effectiveness in clinical practice.<sup>1,2</sup> Currently, there are no published studies assessing adherence to bDMARDs and its associated factors among IA patients in Singapore. Knowledge of the extent of poor adherence to bDMARDs and its risk factors can facilitate efficient implementation of interventions to improve adherence and IA outcomes.

**Objectives:** The primary objective of the study was to assess adherence to bDMARDs among patients with IA in Singapore. The secondary objective was to identify factors associated with poor adherence to bDMARDs.

**Methods:** A retrospective observational study was conducted at Singapore General Hospital, a 1600-bed academic medical centre. Electronic records of patients diagnosed with rheumatoid arthritis (RA), spondyloarthritis (SpA) or psoriatic arthritis (PsA) who had received at least six consecutive months of bDMARDs between 1 st January 2010 and 31 st December 2015 were reviewed. Adherence was calculated by proportion of days covered (PDC) using the following formula:  $PDC = \frac{\sum(\text{number of doses} \times \text{prescribed frequency})}{(\text{total duration}) \times 100\%}$ . Patients with  $PDC \geq 0.80$  were considered adherent.<sup>3</sup> Factors associated with adherence to bDMARDs were identified using multivariate logistic regression using the entire dataset and then by type of IA.

**Results:** Among 115 patients included in the analyses, majority of the patients were Chinese (n=77, 67%) and females (n=61, 53%). Other pertinent demographics and clinical characteristics are detailed in table 1. The mean PDC was 0.82 ( $\pm 0.18$ ) and 69 (60%) patients were adherent (i.e.  $PDC \geq 0.8$ ). Multivariate logistic regression did not identify any factors significantly associated with adherence. Patients with SpA who previously received a bDMARD (OR=5.12; 95% CI 1.02–25.8;  $p=0.048$ ) and who did not receive subsidy (OR=0.21; 95% CI 0.50–0.89;  $p=0.034$ ) were found to be significantly associated with adherence.

**Abstract THU0748HPR – Table 1.** Patient demographics and clinical characteristics

Characteristics (n=115)	n, (%) unless indicated
Mean age at bDMARD initiation, years ( $\pm$ SD)	45.5 ( $\pm 12.0$ )
Gender	
Male	54 (47.0)
Female	61 (53.0)
Race	
Chinese	77 (67.0)
Indian	17 (14.8)
Malay	9 (7.8)
Others	12 (10.4)
Diagnosis	
RA	45 (39.0)
SpA	44 (38.0)
PsA	26 (23.0)
Biologic Naïve	
Yes	79 (68.7)
No	36 (31.3)
Current Biologic	
TNFi	101 (87.8)
Non-TNFi	14 (12.2)

**Conclusions:** The findings of this study suggest that IA patients have suboptimal adherence to bDMARDs. Determinants of poor adherence remain elusive and further research into the social, psychological and environmental aspects is warranted. Measures to improve affordability of bDMARDs such as obtaining government subsidies and offering patient access schemes may improve adherence as seen in patients with SpA.

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FRIDAY, 15 JUNE 2018

**HPR Patients' perspectives, functioning and health (descriptive: qualitative or quantitative)**

**FRIO702-HPR** TREATMENT SATISFACTION IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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**Background:** Limited information exists regarding treatment satisfaction in patients with Juvenile Idiopathic Arthritis (JIA).

**Objectives:** The aim of this study was to investigate satisfaction with synthetic and biologic disease-modifying anti-rheumatic drugs (sDMARDs and bDMARDs) in adults with JIA.

**Methods:** Patients with JIA who attended Oslo University Hospital from 1995–2000 with <18 months disease duration were invited to participate. From a cohort of 96 patients, 52 (54%) used DMARDs. Patients treated with Methotrexate (MTX) or biologics were assessed with the 14-item Treatment Satisfaction Questionnaire for Medication (TSQM, one questionnaire for each medication). The TSQM covers 4 domains (effectiveness, side effects, convenience and global satisfaction) with a score range from 0 – 100 and with higher score representing higher satisfaction on the domain.

**Results:** The mean age of the 52 participants was 25.1 (4.6) years, 75% were female and 33 (63%) patients had polyarticular course JIA. The following DMARDs were used; MTX (n=29), biologics [n=37 (etanercept, n=13; adalimumab, n=8; tocilizumab, n=6; infliximab, n=3; certolizumab, n=3; golimumab, n=2; anakinra, n=1 and rituximab, n=1)] and sulfasalazine (n=5). 19 patients used a combination of sDMARDs and bDMARDs or 2 sDMARDs.

Clinical characteristics	All patients (N=96)	Patients on DMARDs (n=52)
Disease duration, years, mean (SD)	18.9 (1.5)	18.7 (1.6)
Age at disease onset, years, mean (SD)	6.1 (4.0)	6.3 (4.4)
ILAR classification, n (%)		
Systemic arthritis	7(7)	2 (4)
Polyarticular RF negative	24 (25)	16 (31)
Polyarticular RF positive	1 (1)	1 (2)
Oligoarticular persistent	36 (38)	13 (25)
Oligoarticular extended	10 (10)	7 (13)
Enthesitis-related arthritis	5 (5)	2(4)
Psoriatic arthritis	4 (4)	4 (8)
Undifferentiated arthritis	9 (9)	7 (13)

TSQM domains, mean (SD)	MTX (n=29)	Biologics (n=37)	P-value
Effectiveness	59.8 (19.6)	74.2 (15.5)	0.002
Side effects	62.(30.1)	90.1 (20.5)	<0.001
Convenience	64.3 (22.1)	69.1 (13.3)	0.282
Global satisfaction	48.5 (23.1)	70.4 (18.9)	<0.001

A correlation was found between the domain side effects and age in patients using MTX (rs 0.368,  $p=0.049$ ). No other associations were found between TSQM domains and age, gender, disease duration or polyarticular disease course.

**Conclusions:** Patients reported higher treatment satisfaction with biologics compared to MTX in the domains effectiveness, side effects and global satisfaction. An association was found between age and the TSQM domain side effects in patients using MTX. Other domains of TSQM were not related to patient or disease characteristics in JIA. In order to ensure good health care, information of patients' treatment satisfaction should be incorporated in the process of treatment decision-making.

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**FRI0703-HPR** **EVALUATION OF AN INDIVIDUAL TARGETED INTERVENTION WITH THE PURPOSE OF REDUCING SEDENTARY TIME IN PEOPLE WITH RHEUMATOID ARTHRITIS – A MIXED METHODS STUDY BASED ON QUESTIONNAIRES AND FOCUS GROUP INTERVIEWS**

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**Background:** People with rheumatoid arthritis (RA) spend a high proportion of their waking time in sedentary behavior (SB). Reduction of SB and increase in light intensity physical activity has been suggested as a means to improve health in people with mobility problems. RCT study was conducted aiming to investigate the efficacy of an individually tailored, theory-based behavioral intervention for reducing daily sitting time, pain and fatigue, as well as improving health-related quality of life, general self-efficacy, physical function and cardio-metabolic biomarkers in people with RA[1]. The 16-week intervention included 1) three individual motivational counseling sessions and 2) Tailored Short Text Message Service (SMS) reminders. The intervention was effective for reducing daily sitting time, improving patient reported outcomes and reducing total cholesterol in the intervention group (n=75) compared to the usual lifestyle control group (n=75) [1]. It is relevant to know the participants' attitude towards the intervention prior to implementation.

**Objectives:** To evaluate participants' perspective on an individually tailored intervention in the RCT study "The efficacy of motivational counselling and SMS reminders on daily sitting time in people with rheumatoid arthritis".

**Methods:** A mixed methods study including both quantitative and qualitative data was applied. In a convergent parallel design, quantitative data (N=69) was collected by the end of the intervention using a questionnaire designed to evaluate experiences with participation and the intervention. 18 out of those 69 responding to the questionnaire were invited to take part in one of three focus group interviews, involving an evaluation of the intervention through discussion and dialogue. Criteria: maximum of variation in gender, age, duration of RA, employment and the time of conclusion in the RCT study. Data from quantitative and qualitative studies were analyzed and reported separately and then merged at the final stage of the mixed methods study.

**Results:** Participants were generally satisfied with the content and the course of the intervention. In particular, they were satisfied with the individual tailoring of the intervention and the ongoing feedback and follow-up throughout the intervention period. Participants indicated that they had changed their habits regarding sedentary behavior as a direct result of the intervention, and had managed to maintain these changes after their participation. Furthermore, participants reported that their participation in the RCT study indirectly affected their family, friends and colleges, who also gained knowledge about the risk and consequences of sedentary behavior and participation led to changed habits especially at work.

**Conclusions:** Participants in the intervention group in the RCT "The efficacy of motivational counselling and SMS reminders on daily sitting time in patients with rheumatoid arthritis" were satisfied with the content and delivery of the intervention and had managed to change behavior in relation to sedentary time.

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**Disclosure of Interest:** None declared

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**FRI0704-HPR** **SESAME QUIZ: A PLAYFUL ONLINE QUESTIONNAIRE TO ASSESS PATIENTS' KNOWLEDGE ABOUT SJOGREN'S SYNDROME**

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**Background:** We needed to assess the impact of our patient education program on Sjogren's syndrome (SESAME) in order to continuously improve it.

**Objectives:** A playful online questionnaire was designed and implemented to assess patients' knowledge about Sjogren's syndrome.

**Methods:** A interprofessional team (3 rheumatologists, 3 pharmacists) and a 4-patient group who participated in the education program together proceeded to the questionnaire design: 1) definition of a competency framework for patients with Sjogren's syndrome; 2) from literature review, identification of quality requirements for a questionnaire (scientific quality, opportunity to interact, means of expression, logical chaining of questions, simplicity, utility, shortness, bias prevention, playfulness, variety, online diffusion). To fulfill these criteria, we used a clear vocabulary and concise questions, included open-ended questions on patient experience, focused on the artwork, randomized the order of answer choices, and shared the questionnaire online. Once the SESAME quiz was established, a scoring system was defined by the expert group. Face validity, feasibility and reproducibility were assessed to validate the questionnaire. 25 patients were contacted to complete the questionnaire twice. Patients also evaluated the content, structure and feasibility using 12 items (understandable language, unambiguous sentences, length of the questionnaire, difficulty, web access). Reproducibility was calculated using intraclass correlation coefficient (ICC) on patient answers separated by 48 hours.

**Results:** The questionnaire includes 28 questions divided into 4 parts: Sjogren's signs, Sjogren's causes, treatment, daily life with the disease. The 25 patients filled in the questionnaire twice (96% women, 54 years min-max[23;74], 4 years since the diagnosis min-max[1;20]). The questionnaire was filled in from a computer (n=38), a tablet (n=3) or a smartphone (n=9). The average response time was 19 minutes. The median score was 34 points min-max[22;46] out of 50. 18 patients evaluated the questionnaire. 15 patients or more regarded its content, organization and feasibility as "very good". 5 patients found it difficult. The reproducibility was very high (total ICC=0.87 IC95% [0.74–0.94], ICC on each part between 0.61 et 0.87).

**Conclusions:** The SESAME quiz is now freely available (<https://etp-rhumato.typeform.com/to/qsVhr1>) and all the Hospital centers caring for Sjogren patients can use it for their follow up.

**Disclosure of Interest:** None declared

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**FRI0705-HPR** **COMPARISON OF PAIN BEHAVIOR OF INDIVIDUALS WITH DIFFERENT RHEUMATIC DISEASE**

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**Background:** Pain is an important symptom in rheumatic diseases. Chronic pain is strongly associated with cognition, anxiety and depression levels in these patients.<sup>1,2</sup> Pain behavior can be related to the patient's response to the disease and the use of painkillers.

**Objectives:** The aim of this study is to compare the pain behavior of patients with different rheumatic diseases.

**Methods:** Patients with Ankylosing Spondylitis (AS), Fibromyalgia (FM), and Rheumatoid Arthritis (RA) were included in the study and their demographic data were recorded. The Hospital Anxiety and Depression Scale (HADS) was used to determine the anxiety and depression levels of patients. Health Assessment Questionnaire (HAQ) was used to determine functional status and Cognitive Exercise Therapy Approach Scale (the authors request that the abbreviation stays as "BETY" as the original in Turkish) was used to assess bio-psychosocial status of the patients.<sup>3</sup> The first and fourth questions of BETY were used to investigate pain behavior.

**Results:** The mean age of 329 patients were 45,5±11,5 years and the body mass index was 27,8±5,9. The patient's HAQ score was 12,5±10,5, the HADS anxiety score was 8,7±5,2 and the HADS depression score was 7,50±4,6. The BETY total score was 62.6±26.3. According to BETY scale's 1st question, although the patients felt pain, the rate of continuing activity was 42.6% and the non-continuity rate was 13.4%. According to BETY scale's 4th question, the painkiller using rate was 27.8% and the non-painkiller rate was 25.3% (table 1).

**Conclusions:** Although patients knew that their pain would increase, it was determined that the patients had continued their activities. It was also found that the use of painkillers was higher in AS patients compared to the others. It was concluded that these groups should be trained in regarding to restricting their activities when they felt pain.

Table 1 Findings related to questionnaires

	RA (n=126)	AS (n=100)	FMS (n=103)	ALL (n=329)
HAQ	13,3±11,9	12,6±9,9	11,7±9,5	12,6±10,6
HADS-A	7,1±5,4	9,9±4,8	9,7±4,8	8,8±5,2
HADS-D	5,7±4,5	8±4,2	9,2±4,4	7,5±4,6
BETY	60,6±29,7	59,9±24,3	67,1±22,7	62,7±26,3
<b>1st question</b>				
(I can't stop myself doing activities even though I know it will increase my pain.)				
Yes always (%)	46	50	33	43,2
Yes often (%)	8,7	21	21,4	16,4
Yes sometimes (%)	23	12	26,2	20,7
Yes rarely (%)	4	2	13,6	6,4
No never (%)	18,3	15	5,8	13,4
<b>4th question</b>				
(I don't feel comfortable unless I take painkillers.)				
Yes always (%)	21,4	38	29,1	28,9
Yes often (%)	9,5	11	9,7	10
Yes sometimes (%)	22,2	15	22,3	20,1
Yes rarely (%)	16,7	13	19,4	16,4
No never (%)	30,2	23	19,4	24,6

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**FRI0706-HPR** **VALUES UNDERLYING DISEASE-MODIFYING ANTIRHEUMATIC DRUG PREFERENCES OF PATIENTS WITH RHEUMATOID ARTHRITIS**

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**Background:** Disease-modifying antirheumatic drugs (DMARDs) are the cornerstone of treatment in rheumatoid arthritis (RA). Each DMARD has its own characteristics (e.g. onset of action, route of administration and dosing frequency). Treatment decisions should ideally be made through a shared decision making (SDM) process between clinicians and patients, taking account of patient preferences (1,2). This requires an understanding of patient preferences. A number of studies have explored DMARD preferences of patients with RA (3). However, insight into values underlying DMARD preferences that may drive patients' treatment decisions is still lacking. Such information is relevant for clinicians in order to better understand patient preferences. Ultimately, this will facilitate the SDM process.

**Objectives:** To provide insight into values underlying DMARD preferences of patients with RA.

**Methods:** A secondary analysis of transcripts from three focus groups in patients with RA. Two researchers independently analysed the transcripts, using thematic analysis with an inductive approach.

**Results:** Twenty-three patients participated in the focus groups. They had a median age of 62 years (range: 36–78 years), 87% were female and the median disease duration was 11 years (range: 2–42 years). Three values were identified: certainty, independency and safety. Certainty: patients wanted to be certain that the DMARD would work for them. DMARD characteristics that represented this value were onset of action and efficacy. Independency: a DMARD that could easily be fitted into patients' everyday lives was considered important. Route of administration, dosing frequency, location of administration and storage conditions were DMARD characteristics that represented this value. Safety: patients wanted to prevent health damage related to their DMARD use. DMARD characteristics that represented this value were chance of side effects, severity of side effects and consequence of long term use.

**Conclusions:** Certainty, independency and safety are important values to patients with RA. These values underlie DMARD preferences that may drive patients' treatment decisions. This deserves attention in the SDM process.

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**FRI0707-HPR** **PATIENTS' EXPERIENCES OF HEALTH IN EARLY RHEUMATOID ARTHRITIS – A QUALITATIVE STUDY**

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**Background:** The World Health Organization defines health as "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity". Health changes dramatically when a person becomes ill in a chronic disease as rheumatoid arthritis (RA). RA is a disease with great impact on all aspects of life. Living with RA affects patients' health including physical, emotional, psychological and social aspects. The purpose of a person-centered care is to see patients as experts; sharing decisions with them and helping them manage their health. Therefore it is important to understand how patients in early disease stage of RA experience the concept of health.

**Objectives:** The purpose of this study was to describe patients' experiences of health in early RA.

**Methods:** The study had a descriptive design with a qualitative content analysis approach. Individual interviews were conducted with 24 patients with early RA. In this study the patients had disease duration less than 12 months. A manifest qualitative content analysis was used to analyze the question: "What does health mean to you?"

**Results:** In the early stage of RA, patients experienced health as the most important goal in their life. They described health as well-being, independence, life satisfaction and vitality. Health as well-being meant to feel good, be painless and



have a good sleep to feel rested. Health as independence meant to have both physical and financial prerequisites to perform everyday activities, to exercise and being able to travel. Health as life satisfaction meant to feel joy in life, enjoy the family and to believe in the future. Health as vitality meant to have the energy, power and strength to cope with everyday life. The patients expressed that their health had been adversely affected by the RA disease and they had a strong desire for full health including well-being, independence, life satisfaction and vitality.

**Conclusions:** Patients in an early stage of RA describe a strong desire to regain health in terms of well-being, independence, life satisfaction and vitality. The concept of health at early RA is similar to health at established RA in terms of well-being, independence and life satisfaction. Unique findings for patients with early RA are the description of health as vitality, and the emphasis of having energy, power and strength to cope with everyday life. Health professionals should have these different ways of experiencing health in mind when providing person-centred care to patients with early RA. Depending on the patients' perception of health, different support strategies are needed.

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#### FRI0708-HPR THE USE OF TECHNOLOGY FOR SYMPTOM MEASUREMENT IN RHEUMATOID ARTHRITIS: A QUALITATIVE INVESTIGATION

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**Background:** Rheumatoid Arthritis (RA) outcome measurement is limited by infrequent appointments, triggered by symptom flares, linking blood test data with retrospective recall of symptoms. Remote measurement technologies (RMT), such as wearable sensors or smartphone apps, provide opportunity for ongoing measurement of symptoms such as pain, fatigue, and depression, which may vary throughout the day, offering new insight into the lived experience of chronic illness [1]. However, implementation of such data collection strategies requires careful development with the service-user an integral part of co-design to maximise real-world acceptability [2].

**Objectives:** This study aimed to gather qualitative information about service-user priorities for using RMT for symptom measurement.

**Methods:** Two focus groups were conducted in people with RA, using a semi-structured topic guide designed to elicit thoughts about RA symptoms considered important and acceptable for measurement via RMT. The focus groups were moderated by an expert service user (RW) and research lead (FM). A systematic thematic analysis was applied to the data, using a coding framework to extract themes and sub-themes by two researchers independently.

**Results:** A total of 9 participants attended the two focus groups. Participants were aged 23–77 (mean=55.8, SD=18.1), with a mean disease duration of 20.2 (SD=15.2). All 9 were female, with 44.4% identifying as White British. Symptoms prioritisations and the perceived benefits and risks of technology were categorised into several themes including: personal empowerment; communication with healthcare teams; routine/convenience; and under-prioritised symptom experiences.

**Conclusions:** The results of these focus groups highlight several areas to focus RMT development in this area, including identifying the symptoms patients feel are under-prioritised by healthcare providers, and establishing methods to ensure RMT can be embedded in daily activities despite fluctuating symptom severity. Future work testing specific app prototypes and wearable usability can ensure RMT projects are developed with optimised user experience.

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#### FRI0709-HPR LEVELS OF SATISFACTION WITH PSORIATIC ARTHRITIS (PSA) TREATMENT AND ASSOCIATED ALIGNMENT BETWEEN RHEUMATOLOGISTS AND THEIR PATIENTS ACROSS LATIN AMERICA

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**Objectives:** To assess levels of rheumatologist and patient satisfaction with PsA treatment across Latin America and any disconnects that may exist between the two in real world clinical practice.

**Methods:** Data from the 2015 PsA Disease Specific Programme (DSP), a cross-sectional, multi-national survey of patients and rheumatologists conducted in Argentina, Mexico, Colombia and Venezuela were analyzed. Rheumatologists (n=141) completed forms containing patient demographics, patient disease severity and treatment satisfaction. Patients self-reported their level of treatment satisfaction and disease severity.

**Results:** A total of 293 PsA patients from across Latin America were included in this analysis. Current mean age was 49.9 years and 48.1% were female. Proportions of rheumatologists and patients reporting satisfaction with treatment were both similarly high (84% and 92% respectively), however current disease severity reporting differed more markedly between rheumatologists and patients (mild 78%/moderate-severe 22% rheumatologists vs. 63% mild/37% moderate-severe patients; p=0.002). When assessed for alignment, 19% of all rheumatologists and patients disagreed on the level of treatment satisfaction; 13% of this was due to rheumatologists stating greater dissatisfaction than their patients, with the remaining 6% due to patients stating greater dissatisfaction than their rheumatologists (p=0.0543). For current disease severity, 32% of all rheumatologists and patients disagreed; 25% due to patients stating greater severity than their rheumatologists, with 7% due to rheumatologists stating greater severity than their patients (p<0.001). Of those patients for whom their rheumatologist was satisfied with treatment, 14% were classified as having moderate to severe PsA by that same physician.

**Conclusions:** Despite many rheumatologists and their patients in Latin America reporting high levels of satisfaction with treatment, PsA patients can remain moderate to severe and disconnected from their physician. There is a need to improve physician/patient engagement as a means to improving clinical control.

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#### FRI0710-HPR OBJECTIVE AND SUBJECTIVE MEASURES OF PHYSICAL FUNCTIONING IN WOMEN WITH FIBROMYALGIA: WHAT TYPE OF MEASURE IS ASSOCIATED MOST CLEARLY WITH SUBJECTIVE WELL-BEING? THE AL-ÁNDALUS PROJECT

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**Background:** In fibromyalgia there is a discordance between performance-based (i.e., objective) and patient-reported (i.e., subjective) physical functioning (1,2). However, it is unknown whether the association of physical functioning with health outcomes is different between objective and subjective measures.

**Objectives:** To analyse the associations of the objective and subjective dimensions of physical activity, sedentary behaviour, and physical fitness with subjective well-being in women with fibromyalgia.

**Methods:** This population-based cross-sectional study included 375 women with fibromyalgia from southern Spain. Physical activity, sedentary behaviour, and physical fitness were measured by questionnaires, accelerometers, and performance testing. Participants self-reported their levels of positive affect, negative affect, and satisfaction with life. Conservative multivariate analyses were used to

analyse the association between these physical functioning measures and the assessment of affect and life satisfaction.

**Results:** We found independent associations of the objective measures but not the subjective assessments of physical activity with positive affect and satisfaction with life (both,  $p < 0.01$  and adjusted  $R^2 > 0.06$ ) and of sedentary time with positive affect ( $p < 0.02$  and adjusted  $R^2 > 0.03$ ). Moreover, we observed consistent and independent associations of both the objective and subjective dimensions of physical fitness with all the components of subjective well-being (all,  $p < 0.01$  and adjusted  $R^2$  ranged from 0.02 to 0.05).

**Conclusions:** Both objective and subjective measures of physical activity and sedentary behaviour independently impact affect and subjective well-being. Strategies to enhance both dimensions of physical fitness may be a promising approach for improving the subjective well-being in fibromyalgia.

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### FRI0711-HPR KINESIOPHOBIA IN ADULT PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER: ASSOCIATION WITH PHYSICAL ACTIVITY, DEPRESSION AND ANXIETY

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**Background:** Familial Mediterranean fever (FMF) characterized by pain and inflammation with fever which requires a lifelong treatment<sup>1</sup>. All of this causes psychosocial influences and also causes kinesiophobia, which is defined as avoidance of physical activity and fear of repetition of the pain. As it may affect the levels of physical activity and functional capacity, it is important to identify factors related to kinesiophobia in patients with FMF.

**Objectives:** The aim of this study was to investigate the existence of kinesiophobia and related factors such as depression, anxiety and physical activity in adult patients with FMF.

**Methods:** 38 subjects with FMF (15 male) from Society of Behçet & FMF Diseases included in the study. The demographic characteristics of the participants were recorded. The 'Tampa Scale for Kinesiophobia (TSK)<sup>2</sup>', 'International Physical Activity Questionnaire (IPAQ)<sup>3</sup>', 'Hospital Anxiety and Depression Scale (HADS)<sup>4</sup>' and 'Fatigue Severity Scale (FSS)<sup>5</sup>' were used to assess associated factors.

**Results:** Demographic and disease characteristics of the participants were presented in the table 1. Only 9 subjects reported regular exercise. 86% of the subjects had a score over 37 in TSK representing high kinesiophobia<sup>6</sup>. TSK scores were positively correlated with HAD-D ( $r=0,530$ ;  $p=0,001$ ) and FSS ( $r=0,340$ ;  $p=0,035$ ). On the other hand, age, disease duration, body mass index, HAD-A and IPAQ scores were not correlated with TSK. Gender or exercise routine had no effect on TKS.

Table 1 Demographic and disease characteristics

	Mean±Std	Min.	Max.
Age (year)	37.05±8.71	19	57
Disease duration (years)	13.11±11.14	1	46
BMI (kg/cm <sup>2</sup> )	24.5±4.43	16.65	38.05
IPAQ	6942.5 ±2520.4	3018	14580
TSK	44.16±5.06	33	54
HAD-A	9.84±4.43	2	20
HAD-D	8.82±4.70	1	20
FSS	56.45±13.05	23	70

**Conclusions:** Kinesiophobia is very common and associated with depression and fatigue in patients with FMF. Limited number of participants reported regular exercise habit which should be added to treatment programs to increase physical activity and functional capacity in patients with FMF.

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### FRI0712-HPR THE EXPERIENCE OF PATIENTS WITH DIFFERENT CHRONIC DISEASES WITH HEALTH CARE. A SURVEY WITH THE IEXPAC INSTRUMENT

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**Background:** Insights from patients are important for health care planning

**Objectives:** In this study we describe the perception of patients with 4 different chronic conditions with health care in Spain through the IEXPAC scale ("Instrument to Evaluate the Experience of Patients with Chronic diseases"), a scale developed and validated in Spain.

**Methods:** The IEXPAC scale (<http://www.iemac.es/iexpac/>) was developed and validated in Spain by health care professional and social organizations, experts in quality of health care and chronic patients. The scale is structured in 12 items with Likert responses from "always" to "never", yields a score from 0 (worst experience) to 10 (best experience), and identifies aspects of health care needing improvement. A survey was handed to patients needing care in at least two different levels (i.e. primary care and hospital) and with one of the following chronic conditions A) Rheumatic diseases, B) Inflammatory bowel disease (IBD), C) Human immunodeficiency virus infection (HIV) and D) Diabetes mellitus (DM) plus cardiovascular or renal chronic disease. Patients completed the survey at home and responded by pre-paid mail.

**Results:** 2474 patients received the survey, 1618 (65.4%) returned it (359 with rheumatic disease, 341 with IBD, 467 with HIV infection, 451 with DM, mean age 56 years, 41% women). Only 6.1% were affiliated to a patients association. Patients declared a median of 8 visits (IQR 25–75: 4–15) to primary care or specialty clinics in the last year and 29% had visited an emergency room. In the last 3 years 48% had been hospitalized. Up to 61% reported to search for information on diseases, therapies, lifestyle or diet in webpages, general or social media. Responses to the IEXPAC items (percentages that responded "mostly" + "always" to each item) are displayed in the table. In general, these % were higher in HIV patients, which represents a better experience with health care. In some items, patients with rheumatic diseases scored lower (table 1). Mean IEXPAC score was 6.0 (SD1.8) and was higher in HIV patients (table 1). Worst scores were seen in items related to access or guidance for getting reliable information on health and on social resources, contact with other patients and follow-up after hospital discharge.

IEXPAC item	Percentage (%) who responded "mostly" + "always"					p
	All patients	Rheumatic Disease	IBD	HIV	DM	
They respect my lifestyle	81.5%	76.5%	75.1%	89.6%	81.9%	<0.001
They are coordinated to offer good health care to me	69.3%	60.6%	69.1%	76.8%	73.3%	<0.001
They help me to get information from the Internet	15.0%	12.8%	19.0%	19.8%	8.3%	<0.001
Now I can take care of me better	81.0%	74.5%	79.3%	89.7%	78.3%	<0.001
They ask me and help me to follow my treatment plan	79.8%	73.5%	77.8%	87.6%	78.2%	<0.001
We set goals for a healthy life and better control my	70.1%	63.4%	62.6%	74.7%	76.1%	<0.001
I can use Internet and my mobile phone to consult my medical records	7.2%	7.3%	5.5%	8.6%	7.1%	0.529
They make sure that I take medication correctly	76.0%	72.4%	73.7%	83.5%	72.9%	<0.001
They worry about my welfare	84.3%	79.1%	80.4%	91.5%	83.8%	<0.001
I have been informed on the health and social	41.3%	33.8%	32.3%	52.6%	42.3%	<0.001
They encourage me to talk to other patients	14.9%	10.3%	15.7%	30.4%	12.0%	<0.001
Respond to the following statement only if you have been admitted to the hospital in the last 3 years.						
They care about me when I come home after being in the hospital	30.6%	25.7%	28.9%	33.0%	32.8%	0.205
Global IEXPAC score, mean (SD)	6.0 (1.3)	5.3 (2.0)	5.9 (2.0)	6.6 (1.7)	5.9 (1.9)	<0.001

**Conclusions:** The IEXPAC questionnaire identified areas of improvement in chronic patients health care in Spain, especially those related with access to reliable information and services, interaction with other patients and continuity of health care after hospital discharge. Patients with HIV infection scored higher, maybe consequence of a more personalized care. In several items, patients with rheumatic diseases scored lower

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**FRI0713-HPR THE PATIENTS' PERSPECTIVES TOWARDS THE PROVISION OF INFORMATION DURING TRANSITION TO A BIOSIMILAR**

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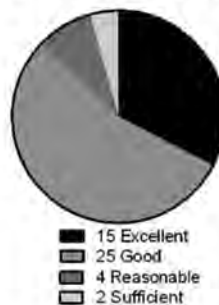
**Background:** In July 2015, at the Amsterdam Rheumatology and Immunology Centre, location Reade, 93% of the patients with rheumatoid arthritis, treated with reference product infliximab switched to the biosimilar infliximab. This transition was needed to enable cost savings. Patients gained information via several ways, where the rheumatology nurses had a central role in informing the patients. Patients' perspectives are warranted to investigate the effect of the transition to the biosimilar.

**Objectives:** To investigate patients' perspectives towards the provided information regarding the switch to the biosimilar.

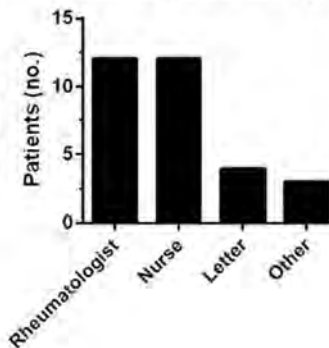
**Methods:** Consecutive patients treated with reference product infliximab were switched to the biosimilar in the period July 2015 to June 2016 at the Amsterdam Rheumatology and immunology Center, Reade. Patients were informed by a letter about the transition to the biosimilar and were subsequently contacted by a nurse or the pharmacist for additional questions and whether they agreed upon the switch. All patients who were switched from the reference product to the biosimilar were approached at the day care to fill in a questionnaire. In this qualitative questionnaire, patients were asked to evaluate the information provision process and how they gained information about the transition to the biosimilar initially. This was done by the nurses of the day care.

**Results:** All patients who switched to the biosimilar (n=46) filled in the questionnaire, of which 15 patients scored the information provision as excellent (33%), 25 patients as good (54%), 4 patients as reasonable (9%) and 2 patients found the information sufficient (4%). Furthermore, the majority of patients was initially informed by nurses and rheumatologist prior to the letter that was sent to all patients. In total, 12 patients were initially informed by rheumatology nurse (26%), 12 patients by the rheumatologist (26%). Four patients were informed via the letter that was sent at first (9%) and 3 patients gained the information about the transition otherwise (7%). Fifteen patients gave more than one answer to the question by whom they were informed initially.

**A. Patient's perspective**



**B. Initially informed by:**



**Conclusions:** Patients were satisfied about the information provision process, there were no patients who experienced the information provision insufficient. Next to the rheumatologist, rheumatology nurses played an important role in informing the patients about the transition.

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**FRI0714-HPR THE PATIENT'S JOURNEY FROM ONSET OF BACK PAIN TO DIAGNOSIS OF AXIAL SPONDYLOARTHRITIS: RESULTS FROM A QUALITATIVE STUDY**

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**Background:** People with axial spondyloarthritis (SpA) wait an average of 9 years between onset of back pain and time to diagnosis by a rheumatologist (Feldkeller 2000). During this time, patients often experience significant pain and dysfunction, while waiting for appropriate diagnosis and intervention. Understanding patients' perspectives of this diagnostic process is essential in order to optimize early detection and promote appropriate management for axial SpA.

**Objectives:** The purpose of this study was to understand patients' perspectives of referral and screening practices for axial SpA from onset of back pain to diagnosis by a rheumatologist.

**Methods:** Semi-structured key informant interviews were conducted with patients diagnosed with axial SpA, based on ASAS criteria, attending a tertiary academic spondylitis clinic. Interviews addressed patients' experiences with screening and referral practices for adults with chronic back pain and suspected axial SpA from symptom onset to diagnosis. All interviews were recorded, transcribed verbatim and evaluated using a compare and contrast analysis by coding groups of words that addressed the research objectives. Two members of the research team undertook this exercise independently and then met to reconcile emergent overarching categories and their respective themes. NVIVO V9 was used to assist with organization of codes.

**Results:** A total of 10 patient interviews were conducted. 90% of participants were male, mean age 42.8 years (± 12.6). The mean duration of back pain prior to diagnosis of axial SpA was 8.9 years (± 6.0). The majority of patients (90%) had post-secondary education. Three overarching categories were identified regarding patients' experiences with screening and referral practices for axial SpA from symptom onset to diagnosis and included: 1) "system factors"; 2) "healthcare provider factors" and 3) "patient factors". Themes related to "system factors" included timely and appropriate access to care. Perceived lack of clinical skills and healthcare provider interpersonal skills were allocated to the category of "healthcare provider factors". Themes identified under the category of "patient-related factors" included: coping with uncertainty; the role of health literacy; the notion of hope, and the belief of stoicism.

**Conclusions:** The results of this study indicate that care provided by knowledgeable, caring, empathetic and receptive healthcare providers is critical to patients with axial SpA as they navigate the healthcare system from symptom onset to



diagnosis. Furthermore, access to the right specialist, at the right time, in the right place may improve patients' experience of screening and referral practices for chronic back pain. Models of care and targeted patient and medical education strategies aimed at reducing the gap between onset of back pain and diagnosis of axial SpA may have the potential to improve existing screening and referral practices of axial SpA.

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**Disclosure of Interest:** None declared

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#### FRI0715-HPR PATIENTS', RELATIVES AND HEALTH PROFESSIONALS VIEWS ON GOALSETTING IN RHEUMATOLOGY REHABILITATION.

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**Background:** Patient-centered goals are important for successful rehabilitation because they focus on the direction and process of rehabilitation. Scarce knowledge exists about goalsetting in rheumatology rehabilitation.

**Objectives:** To explore views on the goalsetting process in rehabilitation during admission among health professionals (HPs), patients with rheumatic diseases and their relatives.

**Methods:** Two focus group interviews, with 11 HPs (physiotherapists, occupational therapists and nursing staff) were conducted as well as eight individual interviews with patients. Relatives participated in two of the patient interviews. The analysis of the transcribed interviews focused on meaning condensation. (Kvale, Brinkmann, 2014)

**Results:** The analysis resulted in three overarching themes. The first theme focused on *the many aspects of communication before and during the goalsetting process*. The HPs expressed that the patients need to be well-informed. Several of the patients expressed the need for information about what the hospital can provide to ease the goalsetting process for them. The HPs pointed out the need for a uniform approach and to be able to communicate with the patients in a clear and understandable way. Some of the patients' experienced unclear communication, as some were not sure what the long-term goal was until halfway through the actual admission. The second theme was *considerations regarding goals*. The HPs considered patient-centered goals to be important, and patients also expressed that the goals should reflect what they prioritized to work with during admission. Both HPs and patients found that the goals needed to be realistic in order to be beneficial. The HPs considered that goals should be measurable. They saw it as a requirement that they should demonstrate that goals were reached, although this was sometimes difficult to demonstrate. Some of the patients expressed a need to be able to relate to and understand the goal in order to see themselves work towards it during admission. The HPs also pointed out that the patients had to take ownership of the goals. The last theme was *the roles in the goalsetting process*. Both the HPs and the patients expected the HPs to have a guiding role in the goalsetting process. The HPs found that patients needed to participate actively in the goalsetting process to reach a patient-centered goal. Both the HPs, patients and relatives believed that participation of a relative in the goalsetting process was positive since they could complement on what the patients said.

**Conclusions:** The goal-setting process is complex, and several aspects need to be taken into consideration to achieve successful patient-centered goals. Clear communication and an overall agreement on the content and importance of the goals are important. Each stakeholder has their role to play in the goalsetting process; the patients need to take an active role, relatives complement the patients views and the HPs guide the goalsetting process.

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#### FRI0716-HPR ASSESSING THE BURDEN OF TREATED AND UNTREATED OSTEOARTHRITIS PAIN IN EUROPE

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**Background:** Osteoarthritis (OA) is a chronic, progressive musculoskeletal condition, estimated to affect >40 million people across Europe. OA is a major challenge for health care systems worldwide and is a leading contributor to years lived with disability (YLD) globally.<sup>1</sup> Current pharmacological treatment options may provide limited pain relief or may not be appropriate for long-term use in all patients because of adverse events.<sup>2</sup> There are few studies on the burden of chronic pain due to OA in Europe and whether this burden varies for those being treated with prescription (Rx) treatments compared with those who are not Rx treated.

**Objectives:** To assess the burden of OA in Europe and to determine whether burden differs by pain severity and treatment status.

**Methods:** A retrospective, cross-sectional study was conducted using data from the 2016 and 2017 National Health and Wellness Survey (NHWS) from five European Union countries (5EU): France, Germany, Italy, Spain, and United Kingdom. NHWS respondents with a self-reported OA diagnosis who completed the pain module were identified. Neuropathic and phantom limb pains were excluded. OA respondents were categorized into 4 groups by severity of pain and treatment: moderate/severe Rx-treated [M/S-Treated]; moderate/severe Rx-untreated [M/S-Untreated]; Mild Rx-treated; and Mild Rx-untreated (reference group). Outcomes of interest included health-related quality of life (HRQoL) (SF-12v2: mental and physical component summary scores [MCS, PCS]), health status (EQ-5D), productivity loss (Work Productivity and Activity Impairment [WPAI] questionnaire), and healthcare utilization in past 6 months. Multivariable analyses adjusted for baseline differences between groups (e.g., demographic and health characteristics).

**Results:** 2,417 OA patients reported a mean age of 61.8 (SD=10.8) years and the majority was female (64.5%). Sixty-percent of OA patients had M/S pain (n=1,440). Stratification by pain and treatment groups resulted in the following: M/S-Treated=27.4%, M/S-Untreated=32.2%, Mild-Treated=22.3%, and Mild-Untreated=18.2%. Those with M/S pain severity, both Rx treated and untreated, showed significantly worse HRQoL, health status and work impairment compared with the reference group (table 1). Further, both Rx treated groups had significantly more health care provider visits compared with OA patients without a Rx.

Table 1 Adjusted mean levels per outcome according to disease severity and prescription treatment status<sup>a</sup>

Outcome	M/S-Treated (A) (n=663)	M/S-Untreated (B) (n=772)	Mild-Treated (C) (n=338)	Mild-Untreated (D) (n=439)	95% CI	p-value	95% CI
					Group A	Group B	Group C
Mental Component Score (MCS)	41.2	44.3	44.9	45.9	<0.001	<0.001	<0.001
Physical Component Score (PCS)	38.7	44.8	43.4	50.0	<0.001	<0.001	<0.001
Health Status (EQ-5D)	0.48	0.66	0.65	0.77	<0.001	<0.001	<0.001
Absenteeism <sup>b</sup>	19.9	15.0	22.0	8.1	0.116	0.143	0.102
Presenteeism <sup>b</sup>	49.4	36.2	34.9	15.9	0.001	<0.001	<0.001
Overall Work Impairment <sup>b</sup>	54.4	38.1	37.9	17.3	0.001	<0.001	<0.001
Activity Impairment	41.5	30.6	33.2	20.0	<0.001	<0.001	<0.001
General Practitioner Visits	1.8	2.7	1.6	2.4	0.007	0.085	0.008
Total Traditional Healthcare Provider Visits	9.3	6.8	8.6	6.0	0.004	0.066	0.005

<sup>a</sup>All models controlled for age, sex, marital status, education, income, employment status, smoking status, alcohol use, exercise, body mass index, Charlson Comorbidity Index, and country using generalized linear regression models.

<sup>b</sup>Among employed respondents only: M/S-Treated n=163; M/S-Untreated n=214; Mild-Treated n=155; Mild-Untreated n=143

<sup>c</sup>Among employed respondents only: M/S-Treated n=138; M/S-Untreated n=222; Mild-Treated n=146; Mild-Untreated n=141

**Conclusions:** The majority of European patients with OA in this study reported moderate-severe pain irrespective of prescription treatment. Whether treated or untreated, those with moderate to severe OA pain demonstrated a substantial burden on quality of life, health status, and productivity compared with those with mild pain.

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### FRI0717-HPR | ASSESSING THE BURDEN OF TREATED AND UNTREATED CHRONIC LOW BACK PAIN IN EUROPE

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**Background:** Chronic low back pain (CLBP) is estimated to affect about 20% of adults<sup>1</sup> and is the greatest contributor to disability globally.<sup>2</sup> Current pharmacological treatment options may provide limited pain relief or may not be appropriate for long-term use in all patients because of adverse events.<sup>3</sup> Despite the large burden of CLBP, few studies have evaluated the humanistic and economic impact of this condition in Europe, or whether this burden varies for those being treated with prescription (Rx) treatments compared with those who are not Rx treated.

**Objectives:** To assess the burden of CLBP in Europe and to determine whether burden differs by pain severity and treatment status.

**Methods:** A retrospective, cross-sectional study was conducted using data from the 2016 and 2017 National Health and Wellness Survey (NHWS) from five European Union countries (5EU): France, Germany, Italy, Spain, and United Kingdom. NHWS respondents with a self-reported CLBP diagnosis, current pain lasting  $\geq 3$  months, and who completed the pain module were identified. Neuropathic and phantom limb pains were excluded. CLBP respondents were categorized into 4 groups by severity of pain and treatment: moderate/severe Rx treated [M/S-Treated]; moderate/severe Rx untreated [M/S-Untreated]; mild Rx treated; and mild Rx untreated (reference). Outcomes of interest included health-related quality of life (HRQoL) (SF-12v2: mental and physical component summary [MCS, PCS]), health status (EQ-5D), productivity loss (Work Productivity and Activity Impairment [WPAI] questionnaire), and health care professional (HCP) visits in past 6 months. Multivariable analyses adjusted for baseline differences between groups (e.g., demographic and health characteristics).

**Results:** A total of 2,086 CLBP patients were identified from the NHWS. CLBP patients reported an average age of 56.4 (SD=13.2) years and most were female (61.2%). Two-thirds of CLBP patients had M/S pain (n=1,403). Stratification by pain and treatment groups resulted in the following groups: M/S-Treated=29.8%, M/S-Untreated=37.4%, Mild-Treated=19.5%, and Mild-Untreated=13.2%. Increased pain severity among both treated and untreated patients showed significantly worse HRQoL, health status, work and activity impairment, and greater HCP visits compared with the reference group (Mild-Untreated) (table 1).

Table 1 Adjusted mean levels per outcome according to disease severity and prescription treatment status<sup>a</sup>

Outcome	M/S-Treated (A) (n=422)	M/S-Untreated (B) (n=791)	Mild-Treated (C) (n=497)	Mild-Untreated (D) (n=276)	Mild-Untreated (Reference) n=276		
					% Group A	% Group B	% Group C
Mental Component Score (MCS)	39.9	42.1	42.4	44.2	<0.001	0.001	0.024
Physical Component Score (PCS)	38.2	43.8	42.2	48.9	<0.001	<0.001	<0.001
Health Status (EQ-5D)	0.51	0.71	0.66	0.79	<0.001	<0.001	<0.001
Absenteeism <sup>b</sup>	5.8	1.8	3.3	2.9	<0.001	0.118	0.075
Presenteeism <sup>c</sup>	11.6	21.4	28.4	12.2	<0.001	<0.001	<0.001
Overall Work Impairment <sup>d</sup>	11.7	23.2	28.2	13.6	<0.001	<0.001	<0.001
Activity Impairment	36.8	38.1	43.9	25.3	<0.001	<0.001	<0.001
General Practitioner Visits	3.1	1.9	2.6	1.8	<0.001	0.043	<0.001
Total Treatment Healthcare Provider Visits	7.1	4.8	6.0	3.7	<0.001	0.009	<0.001

<sup>a</sup>All models controlled for age, sex, marital status, education, income, employment status, smoking status, alcohol use, exercise, body mass index, Charlson Comorbidity index, and country using generalized linear regression models.

<sup>b</sup>Among employed respondents only. M/S-Treated n=192, M/S-Untreated n=321, Mild-Treated n=144, Mild-Untreated n=135.

<sup>c</sup>Among employed respondents only. M/S-Treated n=163, M/S-Untreated n=304, Mild-Treated n=131, Mild-Untreated n=132.

**Conclusions:** Results suggest the majority of European patients with CLBP in this study had moderate to severe pain irrespective of treatment. Whether treated or untreated, those with moderate to severe pain demonstrated a substantial burden related to HRQoL, health status, overall work and activity impairment, and HCP visits compared with those with mild pain.

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### FRI0718-HPR | ARE PAIN, ACTIVITY LIMITATIONS AND QUALITY OF LIFE ASSOCIATED WITH OBJECTIVELY MEASURED PHYSICAL ACTIVITY IN PATIENTS WITH END-STAGE OSTEOARTHRITIS OF THE HIP OR KNEE?

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**Background:** Hip and knee osteoarthritis (OA) are a major cause of disability, yet relatively little is known on the relationship between OA and the total amount of physical activity.

**Objectives:** We investigated if OA-associated pain, functional disability and quality of life (QoL) are associated with objectively measured physical activity in patients with end-stage hip/ knee

**Methods:** Preoperative data from the Longitudinal Leiden Orthopaedics Outcomes of Osteoarthritis Study (LOAS) were used. All patients were scheduled for primary total hip or knee arthroplasty. Patients wore an accelerometer (Activ8 Remedy Distribution Ltd) which assessed levels of physical activity (LPA) in activity counts and %time spent on physical activity (%PA, i.e. time spent on walking, cycling or running) and sedentary behaviour (%SB, i.e. time spent in lying/sitting). Pain, functional disability and health related QoL were assessed with the Hip Disability and Knee Injury Osteoarthritis Outcome Scores (HOOS/KOOS) and Short-Form 12 (SF12). Multivariate linear regressions models adjusted for confounding were conducted. The physical activity outcomes were transformed to Z-scores.

**Results:** 9 hip OA and 48 knee OA patients were included. When awake, mean LPA was 18.787 $\pm$  7.247 for hip OA patients and 21.193 $\pm$  6.164 for knee OA patients. In hip OA patients %PA was on average 14 $\pm$ 6.4, while %SB was 66 $\pm$ 10.5. In knee OA patients these percentages were 15 $\pm$ 5.0 and 68 $\pm$ 8.7, respectively. In hip OA, the HOOS-QoL and SF12-PCS were positively associated with more LPA, ( $\beta$ 0.028; 95%CI:0.007 – 0.048,  $\beta$ 0.041; 95%CI:0.010 – 0.071) and better SF12-PCS scores also with PA ( $\beta$  0.040, 95%CI:0.007 – 0.073). No other associations were found.

**Conclusions:** Whereas QoL was associated with physical activity in end-stage hip OA patients, no associations between pain or functional disability and physical activity were observed in either hip or knee OA.

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### FRI0719-HPR | SELF-ASSESSMENT OF QUALITY OF LIFE OF PATIENTS WITH RHEUMATIC DISEASES AND OTHER CHRONIC DISEASES IN THE IEXPAC PROJECT

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**Background:** Improving quality of life is a goal in the treatment of patients with rheumatic diseases.

**Objectives:** In this work, we describe the self-assessment of quality of life made by patients with rheumatic diseases and with other chronic diseases through an anonymous survey in the context of a wider project on quality of care.

**Methods:** In the context of a quality of care project, focused in the perceptions of chronic patients with health care in Spain (assessed with the IEXPAC scale ("Instrument to Evaluate the EXperience of PATients with Chronic diseases", <http://www.iemac.es/iexpac/>), a survey was handed patients with 4 different profiles of chronic diseases needing care in at least two different levels (i.e. hospital clinic and primary care): A) Patients with rheumatic diseases (rheumatoid arthritis or spondyloarthritis) from hospital clinics, B) Inflammatory bowel disease (IBD) patients from hospital clinics, C) Patients with human immunodeficiency virus (HIV) infection from HIV units and D) Patients with diabetes mellitus (DM) plus

cardiovascular or renal chronic disease from primary care or endocrinology clinics. Patients were handed the survey and completed the survey at home, returning it by pre-paid mail. As part of the survey, they completed the quality of life questionnaire EQ-5D-5L.

**Results:** 2474 patients received the survey, 1618 (65.4%) returned it (359 with rheumatic disease [mean age 55 years, 63% women], 341 with IBD [mean age 47 years, 48% women], 467 with HIV infection [mean age 52 years, 27% women], 451 with DM [mean age 70 years, 32% women]). Patients with rheumatic diseases more frequently described moderate or severe problems with mobility, self-care and usual activities and reported more pain (table 1). Patients with rheumatic disease and IBD more frequently reported anxiety or depression (table 1). Scores in the Visual Analogic Scale "Your Health Today" (from 0 worst health to 100 best health) were lower in patients with rheumatic diseases (mean score 61.9 [SD 19.5]) than in patients with IBD (68.8 [17.8]), HIV infection (73.3 [19.1]) or DM (67.0 [17.1]), all multiple comparison tests rheumatic disease versus other,  $p < 0.001$ .

		Rheumatic Disease	IBD	HIV	DM	P
MOBILITY	I have no problems in walking about	48.4%	74.7%	73.3%	59.3%	<0.001
	I have slight problems in walking about	27.8%	17.3%	12.0%	21.3%	
	I have moderate problems in walking about	15.0%	6.3%	8.3%	13.0%	
	I have severe problems in walking about	8.3%	1.2%	3.1%	5.8%	
	I am unable to walk or use a cane	0.3%	0.0%	1.1%	0.4%	
SELF-CARE	I have no problems washing or dressing myself	70.1%	90.8%	92.4%	86.3%	<0.001
	I have slight problems washing or dressing myself	19.2%	7.4%	5.3%	7.0%	
	I have moderate problems washing or dressing myself	9.3%	1.8%	1.3%	3.4%	
	I have severe problems washing or dressing myself	0.8%	0.0%	0.0%	0.7%	
	I am unable to wash or dress myself	0.6%	0.0%	0.9%	0.4%	
USUAL ACTIVITIES	I have no problems doing my usual activities	44.6%	66.7%	77.3%	70.1%	<0.001
	I have slight problems doing my usual activities	24.9%	17.9%	13.8%	17.8%	
	I have moderate problems doing my usual activities	25.4%	12.5%	8.1%	8.3%	
	I have severe problems doing my usual activities	5.1%	1.3%	2.0%	2.7%	
	I am unable to do my usual activities	2.0%	1.5%	0.8%	1.1%	
PAIN / DISCOMFORT	I have no pain or discomfort	9.4%	28.6%	50.3%	31.9%	<0.001
	I have slight pain or discomfort	33.8%	42.3%	27.5%	31.9%	
	I have moderate pain or discomfort	40.3%	23.2%	16.5%	27.2%	
	I have severe pain or discomfort	14.3%	5.4%	4.3%	6.1%	
	I have extreme pain or discomfort	2.0%	0.6%	0.9%	0.9%	
ANXIETY / DEPRESSION	I am not anxious or depressed	43.8%	44.5%	51.2%	57.2%	0.042
	I am slightly anxious or depressed	32.9%	25.4%	27.6%	24.8%	
	I am moderately anxious or depressed	16.6%	15.4%	15.0%	13.2%	
	I am severely anxious or depressed	5.4%	3.4%	3.1%	3.6%	
	I am extremely anxious or depressed	1.2%	1.3%	1.2%	1.2%	

**Conclusions:** Self-evaluation by patients showed that quality of life of patients with rheumatic diseases (rheumatoid arthritis, spondyloarthritis) is worse than that of patients with IBD, HIV infection or DM. Improving quality of life is an essential goal to achieve in the care of patients with these rheumatic diseases.

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#### FRI0720-HPR THE EFFECT OF OVERWEIGHT ON KNEE PROPRIOCEPTION INPATIENTS WITH KNEE PROSTHESIS DUE TO KNEE OSTEOARTHRITIS

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**Background:** Total knee arthroplasty (TKA) has been established as a valuable procedure for the management of patients with disabling knee osteoarthritis, and the rates of elective TKA are increasing steadily each year. Being overweight is a risk factor for osteoarthritis of weight-bearing joints, such as the knee joint. In literature some studies about obesity and lower limb biomechanics found that obesity will change a person's gait model to adapt weight loading. Also it is stated that obese people have to reorganize their neuromuscular function to reduce the total load on the knee joint. Therefore, the ability to reorganize neuromuscular function may be a more insightful risk factor for knee osteoarthritis. There is not any study research on the effect of overweight on knee proprioception in patients with TKA due to osteoarthritis.

**Objectives:** The aim of this study was to determine the effect of the overweight on knee joint proprioception in patients with TKA due to osteoarthritis.

**Methods:** The study group consisted of 61 patients, who underwent primary TKA because of arthrosis were stratified by obesity status using pre-operative

BMI. Non-obese (n=23, mean age; 67.60±8.48 years) subjects were those with BMI <30 kg/m<sup>2</sup> and obese (n=38, mean age; 63.81±9.21 years) subjects were those with BMI ≥30 kg/m<sup>2</sup>. Patients were evaluated regarding knee proprioception (in knee joint angle 15°, 30° and 60°), knee function score (Hospital for Special Surgery (HSS) score), pain (Numeric Pain Rating Scale (NPRS)), knee range of motion, length of hospital stay, the day of knee flexion angle achieved 70 degrees, quality of life (Short-Form 12 Health Survey (SF-12)). Functional activities were evaluated using the Iowa Level of Assistance Scale and walking speed was evaluated using the Iowa Ambulation Velocity Scale. Patients were evaluated preoperatively and at discharge. All patients underwent the same rehabilitation program.

**Results:** When the patients' proprioceptive acuity in knee joint angle 30° were compared between groups, while there were statistically differences preoperatively (p=0.007), there were not differences after surgery (p>0.05). When the proprioceptive acuity measured before and after surgery were compared in knee joint angle 15°, 60°, there were not differences (p>0.05) between groups. It was determined that; the non-obese group had better results in terms of length of hospital stay, the day of knee flexion angle achieved 70 degrees and both pre-/postoperative knee flexion degree (p<0.05, for all). There were no statistical differences in the pain degree, HSS score, Iowa help level and Iowa walking speed, SF-12 score between groups before and after TKA (p>0.05).

**Conclusions:** There were not differences in knee proprioception between groups after surgery (p>0.05). The deficits in joint position sense in patients with TKA may be due to factors other than the BMI level (being overweight). On the other hand, obesity had negative effects on inpatient rehabilitation outcomes following TKA due to osteoarthritis. These results suggest that the rehabilitation after TKA focused on reducing hospital stay, the day of knee flexion angle achieved 70 degrees and improving knee flexion degree could be important to enhance the potential benefits of the patients' outcomes, and could be important to reduce the payment in rehabilitation hospitals.

**Disclosure of Interest:** None declared

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#### FRI0721-HPR WE ARE IN IT TOGETHER: EXPLORING RHEUMATOLOGY PRACTICE WITH PATIENTS AS RESEARCHER PARTNERS

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**Background:** Rheumatological conditions are often complex requiring careful history-taking, discussion of options, and plans for treatment and ongoing monitoring. Accordingly, similar to many areas in health, the importance of good communication with patients and with colleagues is well recognised. Issues such as adherence, safety, patient satisfaction and workplace thriving are often cited as supporting evidence for good communication. However communication comes with different intentions (e.g. developed as a one-size-fits-all or personalised to individual situations), in different forms (e.g. verbal, non-verbal, written), occurs within and across different spaces (e.g. face-to-face and technologically enabled) and uses time in different ways (e.g. synchronous and asynchronous, structured or unstructured)<sup>1</sup>. While the literature relating to colleague communication is vast, covering different aspects of communication, literature relating to patient communication tends to focus on one-size-fits-all styles of written communication, such as web resources and printed patient handouts, and verbal and non-verbal communication styles during consultations. We identified scope to contribute to understandings about patient communication by focusing on personalised written communication for patients, as both a product of the consultation and a tool for ongoing dialogue. In taking a patient-centred approach we sought to involve patients as co-researchers and dialogue partners. Together we explored the value of patients' personalised written consultation summaries.

**Objectives:** The purpose was to (i) to enhance patient communication within a rheumatology practice, and (ii) to develop insights into collaborating with patients in research.

**Methods:** Collaborative dialogical inquiry provided an appropriate research method for exploring the complex practice of communication, transforming such practice and being authentic to the topic by involving patients. The research team was composed of a rheumatologist, a practice nurse, a medical registrar, a researcher and two patients. Using a lens of appreciative inquiry, data were collected through documenting and recording formal and informal discussions between co-researchers, observing practice and undertaking semi-structured interviews with 20 patients. Each researcher kept a reflective journal about their



experiences. Data and experiences were iteratively analysed and discussed to identify and further explore themes.

**Results:** The personalised written consultation summary was interpreted to be a *living* document, *shared* document, *valued* document, *dialogued* document and *stored* document. Our research experiences echoed these themes, in that they were *lived*, *shared*, *valued*, *dialogued* and *recorded*. The five themes, and their echoes, will be illustrated with quotes. Implications for patient-centred practice and research will be discussed.

**Conclusions:** A set of reflective questions will be posed for the consideration of patients, their families and carers and their clinicians, as well as researchers. These questions have scope to inform dialogue about patient-centred communication in rheumatology practice, and guide collaborative research in this space.

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**Disclosure of Interest:** None declared

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### FRI0722-HPR POSTURAL PROBLEMS AND PAIN IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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**Background:** Juvenile idiopathic arthritis (JIA) is a chronic autoimmune condition of unknown etiology. JIA combine with joint pain and inflammation that affects children who are less 16 years of age and continue more 6 weeks. JIA is a chronic inflammatory disease resulting in joints arthritis, pain and deformities. Disturbances in the posture may occur before deformities in patients with JIA. In some cases, pain can also lead to postural deterioration. Postural control is the ability to maintain equilibrium in a gravitational field by keeping or returning the center of body mass over its base of support.

**Objectives:** The first purposes of this study was to assessed postural problems in patients with JIA and compared with healthy peers. The other objective was to examine the pain relationship with postural problems.

**Methods:** 19 patients with JIA aged 5–17 years (13 girls and 6boys) diagnosed according to ILAR classification criteria and 19 healthy controls were enrolled in this cross-sectional study. "PostureScreen Mobile<sup>®</sup>" was used to evaluate static posture, "11-point Numeric Analogue Scale (NRS)" was used to evaluate the pain (during rest, activity and exercise). The PostureScreen Mobile<sup>®</sup> an application facilitates the assessment of posture in a variety of settings. Anterior (Head, Shoulders, Ribcage, Hips) and lateral translation (Head, Shoulders, Hips, Knees) were recorded and calculated as a total score for anterior and lateral. For statistical analysis SPSS Version 21.0 program was used.

**Results:** The mean age and body mass index of patients and healthy control were 10.79±3.59 and 10.68±2.86 years, 17.05±3.88, and 18.50±2.49 kg/m<sup>2</sup>, respectively. The mean of NRS-rest, activity and exercise scores were 1.18±1.42, 3±2.64 and 1.91±2.02, respectively. As a result of postural assessment for patients and healthy control, the mean of anterior translation scores was significantly higher in patients with JIA than healthy control (p=0.014) (table 1). Two significant correlations with NRS-rest between hip anterior translation (r=0.375, p=0.029) and ribcage anterior translation (r=-0.534, p=0.027) were found.

**Table 1** Anterior and lateral translation in patients with JIA and healthy controls

	JIA mean ±SD	Healthy controls mean ±SD	t	p
Anterior translation	4.16±1.91	2.82±1.16	2.602	<b>0.014</b>
Lateral translation	9.03±4.35	8.41±3.35	0.490	0.627

**Conclusions:** We found that children with JIA have minimal postural problems according to their healthy peers. At the same time, pain during rest is associated with anterior postural deterioration. Therefore in future researches, translations in the posture should be evaluated comprehensively in children with JIA for larger sample size. If it is not intervened in the early period, it may lead to overloading of joints and increased pain in later periods.

**Disclosure of Interest:** None declared

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### FRI0723-HPR PHYSICAL ACTIVITY AWARENESS AND PREFERENCES IN RHEUMATIC DISEASES: A QUALITATIVE STUDY.

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**Background:** Physical inactivity is the fourth leading cause of death (1) and a risk factor for cardiovascular disease (CVD). Patients with rheumatic diseases (RDs), especially rheumatoid arthritis (RA), report low cardiorespiratory fitness levels (2), placing them at an increased risk of premature mortality and CVD.

**Objectives:** The aims of the present study were: a) to evaluate if patients with RDs [RA, ankylosing spondylitis (AS), systemic lupus erythematosus (SLE), osteoarthritis (OA), psoriatic arthritis (PSA), systemic sclerosis (SSC), fibromyalgia (FM), enteropathic arthritis-Crohn's disease (CD), Sjögren's syndrome (SD), Raynaud's disease (RD)] were aware of the physical activity (PA) benefits, and b) to examine their preferences in terms of PA mode and principles (i.e. intensity, duration, frequency).

**Methods:** We designed a questionnaire consisted of dichotomous, open-ended and multiple-choice questions. Patients registered with the Hellenic League Against Rheumatism (EL.E.A.N.A), participated by filling in the questionnaire a) online, or b) through phone calls. Content analysis approach was performed for data analysis.

**Results:** Out of the 625 RDs patients registered with the EL.E.A.N.A, 197 (31.5 % response rate) returned the questionnaire [137 online and 60 via phone calls (69.6% and 30.4% of the sample, respectively)]. 93 patients had RA (47.3% of the sample, age=54.9±14.5) and 104 (52.7% of the sample, age=50.2±13.9) were diagnosed with other RDs [AS (n=29, 14.7%), SLE (n=25, 12.6%), OA (n=15, 7.6%), PSA (n=10, 5%), SSC (n=8, 4%), FM (n=7, 3.5%), CD (n=4, 2%), SD (n=4, 2%) and RD (n=2, 1%)]. In all patients, subjective beliefs about the benefits of PA, concerned three main themes: a) functional ability, b) mental health and c) overall health. Swimming, was revealed as the most frequent PA mode (n=63, 38.1%). Regarding the principals of PA, patients reported that they preferred moderate intensity (n=76, 41.7%), a duration of "about an hour" (n=81, 49.3%), a frequency of "2–3 times per week" (n=71, 45.2%) and a blended intervention consisted of group-based, individualised and supervised programmes (n=56, 29.4%). The questionnaire was judged by the patients to be very or fairly understandable in almost all cases (n=196, 99.5%).

**Conclusions:** According to subjective beliefs from the self-reported data of this study, PA is considered from patients to improve physical and mental health in RDs. Additionally, individualisation and supervision of PA programmes were considered amongst the most important parameters of a program for participation. In planning successful PA regimes in RDs, more qualitative studies with representative sample sizes and demographic data are required to address patients' PA needs and preferences and help them adhere to a more physically active lifestyle.

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### FRI0724-HPR DISEASE ACTIVITY AFFECTS FAT MASS INDEX AND FUNCTIONAL CAPACITY OF RA PATIENTS OVER 12 MONTHS

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**Background:** Rheumatoid cachexia (RC) is a condition characterized by adverse changes in body composition, specifically in muscle mass and fat mass components [1]. RA patients have life quality and expectative impacted by RC [2], but there are very few prospective data analyzing the evolution of this condition.

**Objectives:** To assess body composition, RC, clinical features and functional capacity in RA patients followed for 12 months.

**Methods:** 81 patients with RA, aged between 40 and 70 years, were recruited. Body composition was assessed by total body dual-energy x-ray absorptiometry (DXA) for measurement of fat mass index (FMI;Kg/m<sup>2</sup>) and fat free mass index (FFMI;Kg/m<sup>2</sup>).The patients were categorized as rheumatoid cachectic if FFMI was below the 10th percentile and FMI above the 25th percentile[1],and if FFMI was below the 25th percentile and FMI above the 50th percentile[2].Disease features assessed were disease activity score 28 (DAS28). Functional capacity was assessed by muscle strength (hand grip test;Kg) and gait speed (Time up and Go (TUG;m/s)). Frequency analysis, McNemar test and GEE analyses were used and statistical significance was considered as p<0.05.

**Results:** Of the 81 patients analyzed, most were women (88.9%;72/81), with mean age of 56.8±7.3, mean disease duration time of 11.9±9.6 years. At baseline, the prevalences of RC using both diagnostic criteria were similar to the prevalences described in literature (table 1), and they did not change during the 12 month follow-up(p>0.05).FMI increased after 12 months and patients with moderate disease activity showed higher FMI when compared with other DAS28 categories (p<0.05).Thus, over 12 months, DAS28 affected FMI, and had no impact on FFMI (p>0.05).Muscle strength decreased significantly after 12 months, and patients with high disease activity showed less muscle strength when compared with other DAS28 categories(p<0.05).Gait speed increased after 12 months(p<0.05).

Table 1

	Baseline	12 months
FMI(kg/m <sup>2</sup> )	10.8±4.3	11.1±4.2*
FFMI(kg/m <sup>2</sup> )	16.3±1.9	16.4±1.8
RC [1]	12(13.3%)	12(13.3%)
RC [2]	27(30.0%)	22(24.4%)
DAS28	3.7±1.3	4.0±1.3*
Muscle strength(kg)	16.6±10.4	9.7±8.7*
Gait speed (m/s)	0.5±0.1	0.6±0.1*

\*p<0.05 between baseline and 12 months.

**Conclusions:** In this study, RC prevalence was similar to the prevalence described in literature. DAS28 score of our patients increased over 12 months, and it affected FMI, muscle strength and gait speed of RA patients. However, no effect was observed on FFMI. Our results show that the patients that are not in remission by DAS28 have decreased muscle strength and increased fat mass, possibly due the inflammatory process and the reduced physical activity level, creating a vicious circle.This vicious circle may negatively impact on life quality of RA patients.

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#### FRI0725-HPR UNDERSTANDING THE BURDEN OF RHEUMATOID ARTHRITIS USING QUALITATIVE RESEARCH: WHICH IMPACTS ARE NOT CAPTURED BY PATIENT-REPORTED MEASURES?

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**Background:** Existing measures of disease burden in rheumatoid arthritis (RA) include patient-reported measures (PRMs) of physical and mental functioning, symptoms and work disability. However, these measures may be inaccurate if interpreted by respondents in unintended ways and may not capture some impacts of RA of importance to patients.

**Objectives:** To explore the perspectives of RA patients on PRMs used in The National Data Bank for Rheumatic Diseases (Forward) registry and to identify impacts of importance to patients that may not be captured by commonly used measures.

**Methods:** Semi-structured ethnographic interviews were conducted with adult RA patients in the United States participating in Forward. Interviewees were asked to discuss the impact of RA on their lives and their perspectives on PRMs used in Forward. Interviews were audio-recorded and transcribed verbatim. Transcripts were analyzed for themes related to: 1) perspectives on PRMs, and 2) important impacts of RA.

**Results:** We interviewed 18 patients aged 27–80 years, with RA durations of 4–40 years and Forward participation of 1–19 years. Participants' perspectives on PRMs fell into 4 categories (table 1). Several patients doubted that the PRMs adequately captured the severity of their symptoms. Important impacts of RA not measured by Forward included: expenditures on adaptive devices and measures,

impact on life goals and activities (educational and career plans, family responsibilities, and valued activities) and interaction with stressful life events (such as family deaths).

Table 1 Patient Perspectives on PRMs

Category	Perspectives
<b>Ease of responding to questions</b>	<ul style="list-style-type: none"> <li>- Numerical measures are easy to comprehend</li> <li>- Anchors for scale endpoints are too vague</li> <li>- Difficulty remembering severity of past symptoms</li> <li>- Difficulty understanding questions</li> <li>- Questions could be emotionally disturbing</li> </ul>
<b>Communication of symptoms</b>	<ul style="list-style-type: none"> <li>- Numerical measures were preferred to open-ended survey questions because communicating symptoms in words can be difficult</li> <li>- Difficulty quantifying symptoms and feelings</li> <li>- Infrequent assessments cause gaps in measurement</li> </ul>
<b>Factors biasing responses</b>	<ul style="list-style-type: none"> <li>- Patients may interpret questions in unintended ways</li> <li>- Adaptation and high tolerance for symptoms may lead patients to underreport the severity of symptoms</li> <li>- Patients may underreport the severity of past symptoms not clearly remembered</li> </ul>
<b>Interpretation of responses</b>	<ul style="list-style-type: none"> <li>- PRMs do not assess shifts in expectations for health that may affect responses</li> <li>- Responses from 1 patient at different times/from different patients may not be comparable</li> </ul>

**Conclusions:** Challenges in interpreting and answering questions may reduce the accuracy of PRMs of RA symptoms. The PRMs discussed by participants may not fully capture the impact of RA on patients' financial burdens and on their pursuit of life goals and activities. Future efforts to improve the accuracy and comprehensiveness of burden of disease measurement in RA should help to address these issues. Use of qualitative methods (such as ethnography) may also help to illuminate aspects of living with RA that are not captured by existing PRMs.

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#### HPR Service developments, innovation and economics in healthcare

#### FRI0726-HPR STUDY ON THE EFFICACY OF CURCUMIN THERAPY IN EARLY STAGES OF JUVENILE OLIGOARTHRITIS

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**Background:** Juvenile arthritis is one of the most common rheumatic diseases in childhood. With all remission drugs, a high percentage of patients continue to have an active disease as young adults and sometimes locomotor and ocular sequelae. Turmeric originated in South Asia is used as spice in these regions and has in its structure a polyphenolic compound called Curcumin, very well known for its anti-microbial, anti-inflammatory, anti-oxidative effects and anti-cancer action. Pleiotropic effects are demonstrated by inhibition of transcriptional-kappa B nuclear factor and subsequently of tumor necrosis factor, IL-12 and IL-2 cytokines involved in the inflammatory cascade. Curcumin has been successfully administered in rheumatoid arthritis, but less investigated in juvenile arthritis.

**Objectives:** Aim of study was to evaluate the effects of curcumin administration in patients with Oligoarticular Juvenile Idiopathic Arthritis (OJIA) as an integrated therapy at the onset of the disease.

**Methods:** Thirty-two children aged 8–16 years with OJIA were included in a randomized placebo controlled trial from May 2014 – May 2017. All patients were initially hospitalized at the "St. Mary" Emergency Hospital for Children, Iasi and met the criteria of the American College of Rheumatology (ACR). Patients and their parents/legal guardians signed an informative consent on the treatment with curcumin at Laser Clinic. Patients were randomly assigned to one of the two groups: Group 1 (16 patients) received UltraCur 600 mg of Protein Curcumin Complex (15,000-fold bioavailability supplement), 1.8 g per day (in 3 doses, during meals) for 9 months and Group 2 (16 patients) received *placebo*; all patients were under their standard treatment. Disease activity was evaluated at 0, 3, 6 and 9 months using ACR Pedi30 score. This score defines the improvement of at least 30% from baseline in three of the six variables in the base set, while no more than

one of the remaining variables may worsen by >30%. Core set criteria were: physician global assessment of disease activity (0–10 cm VAS); parent/patient global assessment of overall well-being (0–10 cm VAS); functional ability; number of joints with active arthritis; number of joints with limited range of motion; and ESR.

**Results:** All patients completed the study. After 3 months from the initiation of Curcumin therapy, patients in group 1 had an improvement of 75% ACR Pedi30, compared to only 37.5% ( $p=0.0353$ ) in control group. In the end, ACR Pedi30, 50, 70 and 90 scores improved by 87.50%, 81.25%, 68.75% and 43.75%; compared to only 56.25% ( $p=0.0508$ ), 50% ( $p=0.0670$ ), 37.5% ( $p=0.0813$ ) and 12.75% ( $p=0.0553$ ) in the control group. Curcumin at 1.8 g/day associated with standard therapy was well tolerated, did not induce major reactions and ultimately reduced rheumatic disease activity scores statistically significant ( $p<0.05$ ) compared to placebo.

**Conclusions:** Results proved that curcumin in combination with standard therapy is safe, well tolerated, available at a low cost and has significantly improved the outcome in early stages of OJIA.

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#### FRI0727-HPR IMPLEMENTATION OF A MODEL FOR THE MEDICATION RECONCILIATION PROCESS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Medication reconciliation is defined as “the process of identifying the most accurate list of all medications a patient is taking, including the name, dosage, frequency, and route of each medication, and using this list to provide the correct medications for the patient anywhere within the health care system”. It has been demonstrated that inadequate prescribing due to inaccurate medication histories and reconciliation can lead to medication errors, which have been associated with increased morbidity, mortality, and healthcare costs.

**Objectives:** The aim of study was to design an intervention model led by pharmaceutical personnel in order to implement the reconciliation medication process in patients with RA in a specialized center.

**Methods:** We included patients with RA; we analyzed their particular situation regarding their pharmacological therapy, dosage, frequency among others. Additionally, we applied checklists to find out about the pharmaceutical processes previously established in the RA center and applied a SWOT analysis (strengths, weaknesses, opportunities, and threats) to plan according to the needs diagnosis.

**Results:** In our specialized RA center we found as strengths 1. the existence of analysis committee for the evaluation of patient's therapy, 2. the open mind of the managers in order to implement the reconciliation process 3. The continued education opportunities that the health professionals receive in the specialized RA center. As weaknesses we found: 1. The absence of processes regarding the reconciliation process. 2. In the medical charts there was no registry of the chemical pharmaceutical professional procedures into the patient's therapy. We performed 900 consultations as a pilot to implement the reconciliation medication process, as a result we found 73 patients with a clear need of medication reconciliation the reasons were therapeutic failure or adverse events related to medications. Probably attributed to the existence of multiple pathologies in 81% of patients. Regarding the pharmacological therapy 83% had a conventional DMARD primarily methotrexate in any pharmacological presentation, and biological therapy and, 12% had prescribed only biological DMARDs.

**Conclusions:** With these results we will implement a new model where there will be a process to perform a medication reconciliation in patients with RA, we will review the medical charts in order to identify patients that have needs with the medication process interactions among others. Additionally, we will start new research projects in order to provide evidence of the usefulness of these types of interventions.

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#### FRI0728-HPR COST-REDUCING AND IMPROVING QUALITY OF LIFE IN JUVENILE ARTHRITIS BY BLUE LASER AND ULTRABIOAVAILABLE CURCUMIN

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**Background:** Juvenile idiopathic arthritis (JIA) is associated with significant disease- and treatment-related morbidity, despite all modern management efforts. Photo biomodulation counts today more than 5,000 peer-reviewed published papers, including randomized controlled clinical trials. A review of the literature shows that Curcumin has the potential to be a safe, effective and an affordable alternative in the treatment of chronic inflammation. Its anti-inflammatory mechanism is a molecular response to the down-regulation of enzymatic activity of COX-2, lipoxygenase, and inducible nitric oxide synthase. Photobiomodulation at the maximum absorption spectra of curcumin is an innovative approach due to its complex immuno-modulatory effect.

**Objectives:** Aim was to investigate the effects of sublingual photo biostimulation with blue laser in association with ultrabioavailable curcumin in extensive oligoarticular and polyarticular forms of JIA.

**Methods:** 48 children with an average age of 13.8 years, diagnosed with JIA were included in a randomized placebo controlled trial from January 2014 to December 2017. Patients together with the legal owners signed an informed consent. Group 1 (28 patients) was administrated along with the standard treatment, Ultra Bioavailable Curcumin (15,000-fold bioavailability) 1200 mg/day p. o. and after 30 minutes was applied sublingual blue laser (447 nm), 5 mW maximum output power continuously, 10 minutes each session. Patients received one session every two days, 5 sessions per month, repeated monthly, for 6 months. Group 2 (20 patients) as control, received only conventional therapy and placebo.

Disease activity was evaluated at 0, 4, 12 and 24 weeks with JADAS-71 scores, including: physician's global assessment and parent's global assessment of well-being, both measured on 0–10-cm VAS, normalized ESR (0–10) and active joint count. Childhood Health Assessment Questionnaire (CHAQ) – Disability Index was calculated as a mean of the eight functional areas, on a 4 point scale of difficulty, scored from 0–3 each. Pain level was quantified on 0–10-cm VAS (0-no pain, 10-severe pain).

**Results:** In the end of study, median JADAS-71 significantly improved ( $p=0.0228$ ) in Group I (from 13.8 to 2.8), comparatively with Group II, where the evolution was less favourable (from 14.2 to 7.4). Pain level initially estimated at 7.5 significantly decreased to 2.5 in Group I (66.7%), comparatively to the evolution from 7.4 to 5.2 in placebo group (29.7%) [ $p=0.0125$ ]. Daily functional activity assessed by the CHAQ score improved with 62.7% in Group I, comparatively with only 13.93% in Group II ( $p=0.0003$ ). In the end of study the most important economic aspect was that the percentage of patients receiving remissive medications and the corresponding costs per patient have decreased for methylprednisolone by 72.25% in Group 1, comparatively with only 35.04% in placebo group ( $p=0.0111$ ); methotrexate decreased by 66.7% in Group I, comparatively to only 31.25% for placebo group ( $p=0.0165$ ).

**Conclusions:** Blue laser and curcumin proved to be a safe, efficient and money saver integrative therapeutic intervention with direct impact on JIA patient's quality of life.

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**Disclosure of Interest:** None declared

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**FRI0729-HPR RHEUMATOLOGY ADVANCED NURSE PRACTITIONERS TREAT TO TARGET PERSON CENTERED CARE: IRELAND'S POLICY FRAMEWORK.**

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**Background:** Advanced practice refers to a registered nurse, educated to master's degree level, with the expert knowledge base, complex decision-making skills and clinical competencies for expanded practice beyond that of the first level nurse. Advanced practice characteristics are shaped by the speciality, local context and/or country of practice. Countries, as well as speciality areas are at different stages in the development of legislation, scope of practice, roles, responsibilities, education and clinical preparation. Rheumatology nursing development continues apace internationally.

**Objectives:** To bring rheumatology advanced nurse practitioners (ANPs) to the forefront in the delivery of quality person-centered care, working to enhance patient outcomes and reduce the personal and societal burden of rheumatic musculoskeletal diseases.

**Methods:** The Irish Rheumatology Nursing Forum proposed a business case for the development of advanced nurse practitioner posts to implement, as a standardised approach to care nationally, the therapeutic strategy of treat to target for patients with inflammatory arthritis. This was endorsed by the Irish Society for Rheumatology and approved by the Rheumatology National Clinical Programme in 2015. Subsequently this proposal was chosen by the Chief Nursing Office as a demonstrator project for the Department of Health (DOH) draft policy to raise the critical mass of ANPs in healthcare delivery.

**Results:** In late 2017, the DOH allocated 22 new ANP posts to rheumatology services countrywide, aligned to the national integrated care programme for the prevention and management of chronic disease. These 22 candidate ANPs are now completing advanced practice education at MSc level run by a consortium of Irish universities (University College Dublin, Cork, Galway, and Trinity College Dublin). Supervision of the requisite 500 clinical hours at advanced practice level is being provided by local consultant rheumatologist in partnership with the universities. Local teams of key service, nursing, medical, and academic personnel have been established across all centres to oversee project development; implementation; utilisation of robust evaluation criteria to capture clinical impact and cost-effectiveness. Initial evaluation will focus on key performance indicators related to patient access such as i) ratio of new patients seen to ANPs, ii) new: return attendance ratio, iii) percentage of referrals seen within three months, iv) percentage of non-attended appointments. Intermediate-long-term evaluation will encompass patient care and health care outcome through evaluation of all nursing interventions such as health assessments; medication prescribing and optimisation; patient education; health promotion; comorbidity screening; referral to other professionals; ordering of investigations; patient and staff satisfaction survey data. Quality of care will be evaluated guided by published quality care indicators. Patient outcome will be evaluated using appropriate nursing sensitive and validated disease activity scores and patient reported outcome measures. Real-time data collection using a specifically commissioned epr will ensure cANPs are supported by the appropriate technology to treat to target.

**Conclusions:** ANP-led care underpinned by evidence based practice and guidelines, continues to grow as a model of care delivery in rheumatology.

**Disclosure of Interest:** None declared

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**FRI0730-HPR THE CONCEPT OF PATIENT CENTERED CARE IN SPONDYLOARTHRITIS BASED ON A MULTIDISCIPLINARY MODEL**

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**Background:** Spondyloarthritis (SpA) is one of the most prevalent musculoskeletal disease in the Americas, with an estimated prevalence of 0.5%. This group of patients presents a number of unmet needs for accessibility to the consultation, diagnosis and adequate treatments. That for this reason it is necessary to develop a program of Centers of Excellence (CoE), which allows answer to these needs and at the same time to add values for our health systems.

**Objectives:** The aim was to create a program with pilot SpA centers initially in some countries that operate under the scheme of CoE, as they are already delineated in projects like REAL-PANLAR for rheumatoid arthritis. In a second phase and under the auspices of PANLAR (Panamerican league of associations for rheumatology) create a Pan American Network of Centers of Excellence in SpA (CESPA).

**Methods:** We performed a systematic review of the literature in global and regional databases (Pubmed, Medline, Scopus, Lilacs), in order to search

information on this research question-hypothesis. Subsequently and under a Delphi-modified methodology and consensus of involved rheumatologists lay the conceptual bases on this particular subject – the Centers of Excellence in SpA (CESPA). As a result of the above was defined as should be a CESPA.

**Results:** In accordance with the principles of creation and operation of the CoE in particular, specific themes were developed by a coordinator who, after a review of the literature, presented a specific proposal on every particular topic that was discussed and then voted on and implemented within the CESPA concepts. A CESPA must have: 1. Screening Clinic and Early Diagnosis of SpA: the purpose is to rule out false positives of disease and to diagnose early SpA; 2. Model of patient-centered care: a model of frequencies of care should be implemented for SpA patients from the perspective of the different specialities involved in the multi-disciplinary team; 3. Laboratories and images: conventional laboratory tests as having a minimum of 3–4 times a year and each patient will have conventional X-ray images of cervical and lumbosacral column at the beginning and then once a year. Ultrasound of entheses: upon admission to the program and then with a certain periodicity (annual) or depending of sensitivity to change (OMERACT). The same applies to the subject of MRI of sacroiliac joints and column for both diagnosis and follow-up; 4. Clinical guideline on SpA should be adapted and customized to the particular realities of some of our countries; 5. There must be a management (disease management) program that must include Structure, Process and Result Indicators to define CESPA as Standard, Optimal and Model; 6. There must be standardized education and research programs for patients and physicians at the center

**Conclusions:** There is a global need to develop CESPAs, in order to define treatment targets type T2T-SpA, which would improve clinical outcomes and avoid so much disability and health economic costs.

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FRIDAY, 15 JUNE 2018

**HPR Professional education, training and competencies**

**FRI0731-HPR SWITCH MANAGEMENT BETWEEN SIMILAR BIOLOGICAL MEDICINES, A COMMUNICATION INFORMATION GUIDE FOR NURSES**

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**Background:** Biologics are used in the field of rheumatology but are also important in other fields such as oncology and gastroenterology. Over the last few years, biosimilar versions of many biologicals have been launched. Patients may be switched depending on local rules and appointments. To provide support and information for nurses working with patients who are switching between similar biological medicines ESNO has taken the initiative to develop an information guide for nurses.

Nurses can take the lead in implementing the transition between branded and bio-similar biologic medicines. This includes managing the process before, during and after the switch.

**Objectives:** The guide was developed to provide support and information for nurses working with patients who are switching between similar biological medicines

The guide provides examples of projects and best practices based on different specialities to increase trust in biological medicines including biosimilars. Its aim is to contribute to the safe use of and trust in biologic medicines, and give nurses the tools to implement switching decisions in a clinical context and deal with patient concerns, drawing on the learnings from real-life experiences.

**Methods:** We collected previous experiences from nurses with switching biologics. We also developed a roadmap for how to inform patients, a set of frequently asked questions (FAQ) and points to consider when switching.

**Results:** The guide is written in English and will be translated into the 23 different languages of the EU.

With information about:

- The definitions of biological and biosimilar medicines.
- Switching and substitution.
- The benefits of biosimilars

The document also includes flow charts for switch implementation, follow up and support.

**Conclusions:** Switching between similar biologicals opened new chapter in which nurses play a crucial role in communicating with patients and providing support and reassurance, before, during and particularly after the switch. This is build on nurses' many years of education, and their experience with patients in different situations. It is a process that requires time, patience and care.

Patients may be concerned about changes in biologic medicines, and will have a lot of questions. Positive language is important in answering these questions, to provide confidence and reassurance. Patients need to know that their healthcare professionals understand the reasoning behind the change and are confident that it is the right thing to do. To avoid confusion, the team of nurses and other healthcare professionals should have a consistent explanation that is used by all.

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**Disclosure of Interest:** J. Voorneveld-Nieuwenhuis: None declared, L. Moortgat: None declared, M. Pavic Nikolic: None declared, P. Crombez: None declared, B. Oomen Grant/research support from: This document has been created with funding from Medicines for Europe and EFPIA.

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#### FRI0732-HPR RHEUMATOLOGY NURSE SPECIALISTS AND CORTICOSTEROID PRESCRIBING – DOES IT CONFORM TO EULAR GUIDELINES

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**Background:** The rheumatology nurse specialist (RNS) plays a central role in the multi-professional rheumatology team. Delivering corticosteroid (CS) therapy to patients is an area where there is little understanding of RNSs confidence in managing them.

**Objectives:** Considering CSs are a cornerstone of treating rheumatic diseases where RNSs are invariably involved, we undertook a pilot survey to understand the present climate of RNSs prescribing of corticosteroids in their practice.

**Methods:** A focus group discussion was held at South West regional meeting to ascertain the minimum level of understanding required to successfully deliver CS therapy to patients. It was centred on EULAR recommendations. Nine items were identified based on three main themes – safe prescribing, optimal dosing and prevention of complications. A questionnaire was created based on this discussion and all participants of the meeting were surveyed.

**Results:** There are 21 centres providing rheumatology services in the South West England. All were represented in 30 participants of the survey. Median age of the nursing establishment was 48 years (mean 47 year, range 27–60 years). Only 6/30 (20%) were nurse prescribers.

14 (47%) did not feel comfortable advising patients on adjusting their CS dose. Only four (13%) had any patient group directive in place at their trust to enable them to amend CS dose for non-medical prescribers. 11 (36%) considered CS to be disease modifying therapy in inflammatory arthritis. 17 (56%) employed CS therapy as part of early arthritis management protocol. 4/30 (13%) considered prednisolone equivalent dose of  $\geq 10$  mg/day safe in long term and seven (23%) would be happy to utilise 120 mg IM depomedrone monthly as necessary. 10 (33%) were unaware of therapeutic co-intervention for CS related osteoporosis risk and 21 (70%) were not employing any fracture risk stratification tools.

**Conclusions:** This pioneering initiative highlights a wide variation in the prescription standards of a key job provision. Very few units have independent nurse prescribers. Others lack patient group directive to at least enable non-medical

prescribers i.e. RNSs to safely amend CS therapy prescribed by a rheumatologist. Less than a quarter of those surveyed actually consider CSs to have any disease-modifying role. Rather worryingly, some do not even recognise the safe long-term CS dose and willing to offer high doses periodically. Though most know the concomitant therapeutic options to mitigate against osteoporosis, few are actually assessing fracture risk thereby unlikely to offer the appropriate interventions.

In conclusion, there is wide variation in the service provision of RNSs. This can potentially have a negative impact on effort to promote safer use of CSs in the management of inflammatory rheumatic diseases. There is a need for improving training standards to help deliver good quality rheumatology professionals of the future and ensure safe and effective drug interventions.

**Disclosure of Interest:** None declared

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#### FRI0733-HPR AN INTERACTIVE COURSE ON EXERCISE THERAPY FOR KNEE OSTEOARTHRITIS AND COMORBIDITY: A FEASIBILITY STUDY

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**Background:** A structured, tailored exercise therapy strategy was found to significantly improve physical functioning, reduce pain and was safe for patients with knee OA and severe comorbidity. The intervention was performed in a specialized, secondary care center. Before the intervention can be implemented in primary care, appropriate education of physiotherapists (PTs) as well as insight into barriers and facilitators for using the protocol in primary care is needed.

**Objectives:** This study aimed to 1) evaluate the effect of an interactive course on the exercise therapy strategy for patients with OA and comorbidity for PTs working in primary care; and 2) map facilitators and barriers for applying the protocol in primary care.

**Methods:** A pre-posttest study was performed among PTs who were working in primary care. PTs were offered a postgraduate blended educational course consisting of an e-learning lecture (7 hours study load) and two interactive workshops (each 3 hours study load). Measures of effectiveness included a questionnaire on knowledge (60 multiple choice questions) before (T0) and two weeks after the course (T1) and a patient vignette to measure clinical reasoning (nine open questions) before the course (T0) and six months after the course (T2). Facilitators and barriers for using the protocol were measured at T2 by means of a 27 item questionnaire (each item was scored on a 5-point Likert scale, ranging from 0 totally agree to 4 totally disagree).

**Results:** Thirty-four PTs were included. Fourteen out of 34 PTs had treated at least one patient with knee OA and comorbidity according to the protocol. Statistically significant improvements were found, both for knowledge levels between baseline and T1 (N=34) (p<0.00), and for clinical reasoning between baseline and T2 (N=34) (p<0.00). With regard to facilitators to implement the protocol, the majority of PTs found the protocol feasible in daily practice (68%) and to be supportive regarding clinical reasoning and clinical decision making (77%). Perceived barriers for implementation included the small number of patients with OA and severe comorbidity being referred or referring themselves. Of the therapist who actually treated patients according to the protocol, 86% indicated that the protocol was applicable in their daily clinical practice and that they perceived to have sufficient knowledge (71%) and skills (64%) to apply the protocol. Other barriers indicated by PTs were the limited number of treatment reimbursement by the insurance companies (65%) and a suboptimal collaboration with general practitioners and physicians (65%).

**Conclusions:** An interactive educational course on exercise therapy for knee OA patients with comorbidity proved to be effective in improving knowledge and clinical reasoning skills of primary care PTs. Main barriers for protocol use included limited referrals of patients with knee OA and severe comorbidity to PTs, and limited number of treatment reimbursement by insurance companies. For larger scale implementation these barriers should be solved.

**Disclosure of Interest:** None declared

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### FRI0734-HPR PHYSICAL ACTIVITY AND AEROBIC CAPACITY ASSESSMENT – A SURVEY AMONG RHEUMATOLOGY HEALTH PROFESSIONALS IN FOUR EUROPEAN COUNTRIES.

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**Background:** Regular physical activity (PA) is associated with improvements in health outcomes, such as quality of life, aerobic fitness, pain, stiffness and inflammation in people with inflammatory joint disease (IJD) (1,2). Current practice in the management of patients with inflammatory arthritis emphasises the importance of health professionals (HPs) in assessing PA and aerobic capacity.

**Objectives:** The objectives of this study were to identify how HPs working with IJDs measure PA and aerobic capacity.

**Methods:** Rheumatology HPs in Denmark, Sweden, Ireland and Belgium participated in an online survey. Descriptive statistics was undertaken (SPSS v21 and SASv9.4) to describe data aggregates and range and to identify sub-classes of groups with respect to use of PA measures.

**Results:** Three hundred and twenty two (n=322, 75% female) HPs responded from Denmark (n=50, 15.5%), Sweden (n=66, 20.5%), Ireland (n=28, 8.7%), and Belgium (n=178, 55.3%). The majority of respondents (n=286, 92%) reported it was important to measure PA in people with IJDs. The mean number of years qualified was 20.08 (SD 9.37) and years working in Rheumatology was 12.29 (SD 8.27), with 32.3% reporting half of their workload coming from people who have inflammatory arthritis. Only 28.2% of HPs used simple body worn sensors to measure PA levels in their patients. Moderate levels of confidence were reported in using a simple body-worn sensor (mean 6.15/10; SD 3.63) and paper questionnaire (6.85/10; SD 3.62) to measure PA, with lower levels of confidence in using a complex body-worn sensor (3.80/10; SD 3.55) and digital diary (4.22/10; SD 3.67). When assessing aerobic capacity 58% were very familiar/somewhat familiar using a bicycle ergometer, 44% a treadmill and 56% other aerobic capacity tests. Low levels of confidence were reported in instructing their patients in performing aerobic capacity tests (4.54/10; SD 3.74) and in interpreting the results (4.79/10; SD 3.58). A large majority were interested in further education around measuring PA (83%) and aerobic capacity measurement (74%), with an online module favoured for both.

**Conclusions:** The majority of respondents reported that they considered measuring PA as important in people with IJDs; however, the majority lacked confidence in how to measure it. There is strong interest in further education around measuring PA.

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### FRI0735-HPR KNOWLEDGE, CONFIDENCE AND EDUCATIONAL NEEDS OF PRIMARY CARE NURSES' ON PATIENT EDUCATION AND CONTINUITY CARE IN RHEUMATIC DISEASES

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**Background:** Primary care health professionals (HPs) are essential for continuity of care, especially for chronic conditions like rheumatic diseases. Therefore, knowledgeable and skilled HPs are needed in both settings, with close contact, to

improve quality and safety. Primary care nurses may be pivotal to assure this continuity and liaison between care players. However, there is a lack of postgraduate rheumatology education for HPs working in this field<sup>1</sup>, a lack expected to be even greater in primary care.

**Objectives:** We aimed to: 1) determine the knowledge on Disease Modifying Anti-Rheumatic Drugs (DMARDs) of nurses working in primary care in Portugal; 2) determine their confidence in providing patient education (PE) on (i) the rheumatic diseases they contact most, (ii) biological DMARDs and (iii) Methotrexate (MTX); 3) explore professional factors influencing these confidence levels; 4) explore their educational needs in rheumatology.

**Methods:** A national online survey was performed among nurses working in primary settings for ≥6 months. The survey assessed their certifications, experience in primary care, and their practice, knowledge, and confidence (from 0 to 10) in providing PE to these patients. Their educational needs and communication with their colleagues in rheumatology were also assessed. Educational leaflets were provided at the survey's end for didactic purpose. Spearman's correlation and Mann-Whitney tests were used to test nurse's confidence levels on PE.

**Results:** There were 290 individuals accessing the survey, but only 129 (44.5%) completed it [mean age (SD)=42.6 (7.8) years, experience in primary care=13.7 (8.2) years; 47.3% having a post-graduate specialization].

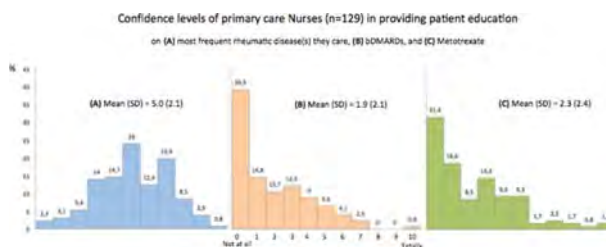
Osteoarthritis (69.0%), low back pain (68.2), and rheumatoid arthritis (62.8%) were the diseases that nurses contact the most. Only 5.4% of nurses recognized an image with five sc bDMARDs pens, reporting frequent contact with them; 18.6% reported rare contact. Knowledge on bDMARDs was poor (table 1). More than half of nurses reported not knowing what PE to provide (55.0%) and when these drugs should be suspended for patient's safety (63.6%); 55% never contacted with MTX and only 6.2% reported to know its side effects.

Table 1 Nurse's knowledge on bDMARDs (n=129)

bDMARDs	% yes
<b>are:</b>	27.1
Immunosuppressant's	10.1
NSAIDs	9.3
Corticosteroids	1.6
Powerful analgesics	0.8
Hormone therapy	51.1
I don't know	
<b>most common side effects are:</b>	15.5
Local reactions	20.2
Infections	7.0
Kidney insuf.	6.2
Cytopenia	3.1
Worsening of heart failure	6.2
Neoplasms	1.6
Respiratory insuf.	14.7
Tuberculosis	3.1
Gastritis and peptic ulcers	16.3
Hepatotoxicity	2.3
Demyelinating disease	58.9
I don't know	

Confidence levels in providing PE were low (figure 1) and not correlated (p>0.05) with years of experience on primary care or with post-graduate specializations.

Nurses' doubts are answered mainly via internet (68.2%) or by local colleagues (51.2%). Only 2 nurses (1.6%) had formal, although minor, rheumatology education but 88.4% would like to have it (delivery preferences were expressed).



**Conclusions:** Knowledge and confidence in key areas of rheumatology care seem to be very low in Portuguese nurses working in primary care. Unmet education and training needs exist and provide useful directions for the development of future training programmes.

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**Disclosure of Interest:** None declared

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### FRI0736-HPR | A STUDY AIMING FOR THE IMPLEMENTATION OF THE EULAR RECOMMENDATIONS FOR THE ROLE OF THE NURSE IN THE MANAGEMENT OF CHRONIC INFLAMMATORY ARTHRITIS IN CHINA

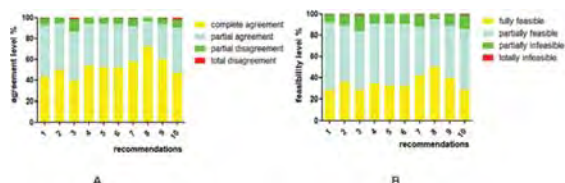
L. Ma<sup>1</sup>, Y. Liang<sup>1</sup>, S.N. Yu<sup>1</sup> on behalf of Ying Wang, Susan M Oliver, Yan-ling Chen, Yi Zhao, Yu-qiong Cao, Xue-mei Liu, Zi-yun Zhang, Li-hong Chen, Yi Liu, National Collaborative Group of Rheumatic and Immunological Disease Management. <sup>1</sup>the department of rheumatology and immunology, West China Hospital, Sichuan province, Chengdu city, China

**Background:** Chronic inflammatory arthritis(CIA) is considered the leading cause of disability that places severe limits on daily activity and quality of life for over 100 million Chinese. Nurse-led CIA management reveals tremendous benefits for CIA patients. European League Against Rheumatism(EULAR) developed the recommendations for the role of the nurse in the management of CIA in 2011, however, whether or not the recommendations could be fully implemented in China is unknown.

**Objectives:** The aim was to test the EULAR recommendations among registered Chinese rheumatology nurses in terms of its agreement level, practicality, and adverse conditions to the implementation.

**Methods:** We conducted an anonymous online questionnaire among registered clinical nurses in the department of rheumatology and immunology nationwide based on convenience sampling. The agreement and feasibility of the recommendations were assessed by visual analogue scale(VAS 0=total disagreement/completely infeasible, VAS 1–4=partial disagreement/partially infeasible, VAS 5–9=partial agreement/partially feasible, VAS 10=complete agreement/completely feasible). The respondents needed to select the reasons they agreed or disagreed and if they thought the recommendations were feasible or not.

**Results:** 485 subjects were included, and 438 valid questionnaires were retrieved(valid recovery rate=90.3%). The subjects were from 49 national medical centers with the average age of 31.65±6.65. The average years of working experience were 6.41±5.438. With each and every piece of the recommendation, approximately 50% of the subjects completely agreed(VAS 10), about 40% partially agreed(VAS 5–9), under 10%(VAS 1–4) partially disagreed and around 1% (VAS 0) totally disagreed(shown in figure 1A). As for the feasibility, around 30% of the subjects thought the recommendations were fully feasible(VAS 10), about 50% considered partially feasible (VAS 5–9), 10% partially infeasible(VAS 1–4), and less than 1% totally infeasible(shown in figure 1B). Factors made the subjects disapprove of the recommendations include busy clinical loading(39.98%), lack of professional knowledge and nursing skills(25.7%), patients did not accept the extended role of nurses(17.35%). In the meantime, lack of working time(16.33%), shortage of professional nurses(12.74%), lack of training and education(10.59%), lack of professional knowledge(9.22%), attitude of patients toward nurses (8.28%), and lack of financial support(7.53%) were the reasons that made subjects think the recommendations infeasible in China.



**Figure 1** the agreement and feasibility analysis of the EULAR recommendations in China

**Conclusions:** The role and tasks of nurses should be clearly described in the framework in China. Professional training and educational nursing programs at both basic and advanced levels need to be well developed with the aim of providing better care and bringing added value to patients at a lower cost.

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FRIDAY, 15 JUNE 2018

### HPR Patients' perspectives, functioning and health (descriptive: qualitative or quantitative)

#### FRI0737-HPR | WOMEN'S EXPERIENCES OF COPING WITH CHRONIC WIDESPREAD PAIN – A QUALITATIVE STUDY

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**Background:** Approximately ten percent of the population report chronic widespread pain (CWP), the condition is more common among women than men. For most people, the pain interferes with many aspects of every-day life and implies large consequences. However, the group reporting CWP is heterogeneous and there is a need for better understanding of the different strategies used for coping with pain in every-day life.

**Objectives:** The purpose of this study was to describe women's experiences of how to cope with CWP.

**Methods:** The study had a descriptive design with a qualitative content analysis approach. Individual interviews were conducted with 19 women, 31–66 of age, who had reported CWP in a survey 2016. CWP was defined according to the 1990 ACR criteria for fibromyalgia. To be considered chronic, the pain should have persisted for more than three months during the last 12 months. A manifest qualitative content analysis was used to analyze the main question "How do you cope with your chronic widespread pain?" The analysis resulted in four categories.

**Results:** Women described their coping with CWP in four different ways; to take control, to continue as usual, to follow instructions and to rest. *To take control* meant to make deliberate decisions to handle everyday day life. It also meant to take care of oneself, to think positive and to exercise at an adequate level. *To continue as usual* meant not to listen to body signals and either to ignore or accept the pain. *To follow instructions* meant listening to the health professionals and following advices, but without taking any part of the responsibility for the treatment outcome. *To rest* meant to perceive an unreasonable need for recovery, to resign and let the pain set the terms for the daily living.

**Conclusions:** Women expressed different ways of coping with CWP including both active and passive strategies. The coping strategies included two dimensions, where one ranged from *actively taking control over the pain*, to *passively following instructions* and the other from *actively continue as usual* by either accepting or ignoring the pain to *passively rest* and being mastered by pain.

**Disclosure of Interest:** None declared

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FRIDAY, 15 JUNE 2018

### HPR Epidemiology and public health (including prevention)

#### FRI0738-HPR | NURSE-LED SCREENING: CHANGES IN CARDIOVASCULAR RISK PROFILE AND ASSOCIATION TO SOCIO-ECONOMIC STATUS IN OUTPATIENTS WITH INFLAMMATORY ARTHRITIS

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**Background:** Persons with inflammatory arthritis have an increased risk for cardio-vascular (CV) disease and screening is therefore recommended (1)

**Objectives:** To investigate changes in the patient's risk for CV disease and whether risk reduction was associated with socio-economic status in a hospital population of outpatients with inflammatory arthritis (IA) (rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS))

**Methods:** Outpatients with IA ≤85 years of age connected to King Christian X's Hospital for Rheumatic Diseases in Graasten, Denmark, who had participated in a 30-minute nurse-led screening consultation (SC) (2) based on the EULAR recommendations between July 2012 and July 2015 were included. During the SC the patients' risk for cardiovascular death was calculated according to the SCORE system (3). Elements of motivational interviewing were used. Data was entered in a national rheumatology quality database, DANBIO, and combined with national registers. Whether socio-economic status influenced changes in risk factors from first to second screening consultation was explored in simple logistic regression analyses for each risk factor including the socio-economic variables sex, age, marital status, education, and income separately one at a time

**Results:** A total of 1266 patients, 18–85 years of age, were included; 72.5% with RA and 27.5% with AS or PsA. 447 patients had high risk (≥5% risk) for CV death in 10 years and 819 had low to moderate risk (<5%). Number of patients achieving relevant changes from the first to the subsequent yearly or biannual screening consultation, are reported for high and low risk patients in table 1.

For all the patients, female gender significantly decreased the odds for increased exercise frequency (OR, [CI], p-value) (0.40[0.17; 0.92], 0.0320), being single decreased the odds of reduced BMI (0.57[0.32; 0.99, 0.0472] and age ≥65 years

increased the odds of a normalization of SBP (2.13[1.30; 3.50], 0.0027). In high risk patients, higher education (1.94[1.05; 3.57], 0.0338) and higher income (2.07 [1.00; 4.28], 0.0508) increased the odds of a normalization of SBP although not significant, we include this effect based on the confidence interval not including any values indicating a decreased odds

Table 1 Changes in CV risk profile from first to subsequent screening consultation for high and low risk patients

Risk factor	Patients with high risk (SCORE≥5%) Number with changes out of number affected (%)	Low to moderate risk (SCORE<5%) Number with changes out of number affected (%)
Changes in exercise habits: from < 5 times a week to ≥5 times a week	73/153 (48%)	27/136 (20%)
Smokers changed to non-smokers	12/60 (20%)	10/66 (15%)
Elevated blood sugar (fasting Blood sugar or HbA1C): changes to normal level	69/72 (96%)	94/95 (99%)
LDL-cholesterol: changes from elevated level to normal level (<3 mMol/Mol)	4/18 (22%)	0/0 (0%)
Systolic blood pressure ≥ 145: changes from elevated level to normal level (≤140 mmHg)	73/153 (48%)	0/0 (0%)
BMI≥30: reduction with at least 1	21/68 (31%)	36/90 (40%)

**Conclusions:** Clinically relevant reductions in CV risk factors were seen after SC for CV risk in both high and low risk patients. Surprisingly female patients improved their exercise habits less often than male patients did. Older age increased the odds to reach a normal SBP. In high-risk patients, education and income positively influenced the odds to reduce SBP to normal

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## HPR Interventions (educational, physical, social and psychological)

### FRI0739-HPR EXPERT RECOMMENDATIONS ON PSYCHOLOGICAL NEEDS OF PATIENTS WITH RHEUMATOID ARTHRITIS

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**Objectives:** To generate recommendations in order to: 1) Optimize the management of psychological needs of RA patients, their family and caregivers; 2) Promote and improve communication and decision making with patients; 3) Establish referral criteria to mental health professionals.

**Methods:** A nominal group meeting of RA experts, rheumatologists and psychologists was held, in which the most important psychological and emotional needs and related aspects in RA were addressed. With an extensive review of the literature, a set of preliminary recommendations was generated that the experts discussed and modified. The definitive recommendations were voted in a Delphi which was extended to 20 more professionals. Participants voted from 1 (strongly disagree) to 10 (totally agree). Agreement was considered if at least 70% voted ≥7 (GA). Each recommendation was assigned a level of evidence (LE) and a grade of recommendation (GR) according to the Center for Evidence Based Medicine of Oxford.

**Results:** A total of 13 recommendations were generated (see table 1).

#	RECOMMENDATIONS	LE*	GR*	GA†
1	One of the objectives of the treatment of RA should be the psychological well-being of the patient	5	D	80%
2	The panel recommends to perform, along with the usual clinical actions, a psychological approach of patients with RA at the diagnosis and during the course of the disease	5	D	80%
3	It is recommended to analyze the impact that the information on the diagnosis of RA may cause in the patient	4	D	93%
4	It is recommended to adapt the information we give, to patient knowledge of their own illness, their concerns and characteristics, and to offer it sequentially, using all the available resources	5	D	100%
5	Information about RA should avoid medical technicalities as much as possible, as well as words and expressions that may negatively impact on the patient	5	D	87%
6	The panel recommends to use a constructive messages when we inform the patient about RA	5	D	100%
7	It is recommended to encourage and motivate the patient regarding to the treatment plan of the RA	2a	B	100%
8	During the course of the disease special attention must be paid to the psychological needs of the patient and their family and caregivers	4	D	100%
9	It is recommended to generate an atmosphere of trust, to share treatment decisions, and to avoid paternalistic attitudes or reprimands	5	D	87%
10	It is recommended to use open questions, an active listening, and to let the patients express themselves freely, as well as time for reflection	5	D	93%
11	Empathy should be practice in daily consultation, allowing discussion to seek consensus, and avoiding confrontation	5	D	100%
12	In patients with negative attitudes, it is recommended to promote self-efficacy, to promote the solution of problems and to offer other therapeutic options	5	D	87%
13	In patients with emotional lability, the panel recommends to use the HADS screening questions in order to detect depression	5	D	73%

**Conclusions:** These recommendations will help health professionals address psychological needs of the patient in daily practice, in order to manage them and improve patient's quality of life.

**Disclosure of Interest:** None declared

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## HPR Patients' perspectives, functioning and health (descriptive: qualitative or quantitative)

### FRI0740-HPR RESPONDING RESILIENTLY TO CHRONIC DISEASE: RHEUMATOID ARTHRITIS PATIENTS' DISCOURSE ON COPING STRATEGIES AND CHALLENGES

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**Background:** Little is known about how rheumatoid arthritis (RA) patients build and maintain resilience, or their ability to recover from, and adapt successfully to, stressful situations.<sup>1</sup> As symptoms and limitations caused by RA are often beyond patients' control, it is important to understand how patients develop and maintain resilience throughout fluctuations in their condition.

**Objectives:** We qualitatively explored patient narratives of coping with RA to examine their strategies for building/maintaining resilience in the context of RA.

**Methods:** Semi-structured interviews were conducted with adult RA patients in the United States. Interviewees were asked to discuss their experiences with diagnosis, living with RA, coping with challenges, treatment, and healthcare providers. The interviews were audio-recorded and transcribed verbatim. Transcripts were analyzed to identify patients' strategies for building/maintaining resilience (including examples, patterns in how and when strategies were used, and changes in use as patients gained experience with RA). Patients were categorized as 'high resilience' and 'low resilience' based on how confidently they coped with symptoms, physical limitations, the prospect of future life with RA, taking treatments, and communicating with healthcare providers. The characteristics of the high-resilience and low-resilience groups were qualitatively described.

**Results:** Eighteen patients were interviewed, with ages of 27–80 years and RA durations of 4–40 years. Patients used 10 strategies to build/maintain resilience

(table 1): perseverance, avoiding threatening thoughts, social support connection, pursuing valued activities, positive reframing, maintaining a sense of control, acceptance, humor, equanimity, and flexibility. Nine patients were categorized as high-resilience and 9 patients as low-resilience cases. High-resilience patients tended to have more years' experience of living with RA compared with low-resilience patients. Although low-resilience patients sometimes struggled to cope, they made efforts to improve their capacity to face their personal challenges.

Table 1 Strategies described by RA patients for building/maintaining resilience

Strategy	Definition
<b>Perseverance</b>	Habitually enduring difficult situations
<b>Avoiding threatening thoughts</b>	Avoiding emotionally threatening thoughts and information
<b>Social support connection</b>	Receiving or giving emotional or instrumental social support
<b>Pursuing valued activities</b>	Deep engagement in valued activities
<b>Positive reframing</b>	Finding positive meaning in difficult experiences
<b>Maintaining a sense of control</b>	Adopting actions or thoughts to promote a sense of control over one's condition
<b>Acceptance</b>	Acknowledging the realities of living with RA
<b>Humor</b>	Joking about stressful situations due to RA
<b>Equanimity</b>	Staying calm in stressful situations
<b>Flexibility</b>	Adjusting to changes in physical limitations

**Conclusions:** Participants used a combination of behavioral and emotion management strategies to build and maintain resilience when facing challenges of living with RA. Awareness of these strategies may benefit patients, healthcare providers and researchers developing behavioral interventions and social support programs in the context of RA and other chronic diseases.

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**FRI0741-HPR DISCUSSIONS OF LIFESTYLE HABITS AS AN INTEGRAL PART OF CARE MANAGEMENT IN PATIENTS WITH ESTABLISHED RHEUMATOID ARTHRITIS.**

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**Background:** Rheumatoid arthritis (RA) is associated with an increased risk of developing comorbidities which are known to be associated with lifestyle-related habits; such as having a sedentary lifestyle, having an unhealthy diet, smoking, and over-consumption of alcohol. In 2010, the European League Against Rheumatism (EULAR) published general guidelines on risk management in patients with RA, with an update 2017 (1,2) in which health professionals are encouraged to prioritize discussions with patients regarding their lifestyle and it is of interest to study the extent to which these discussions actually occur.

**Objectives:** To study if lifestyle habits; physical activity, diet, smoking and alcohol had been discussed with patients having RA during health care visits.

**Methods:** A cross-sectional postal survey in 2017 included 1542 eligible patients from the BARFOT (Better Anti-Rheumatic Pharmacotherapy) study. All patients received a questionnaire including lifestyle habits (physical activity, diet, smoking, and alcohol), and whether these habits had been discussed during health care visits. There was also a question regarding if they would have wanted such a discussion.

**Results:** 1,061 patients (68%) responded to the survey (mean age 67 years (SD 13); 73% women). Physical activity was discussed with 49% of the patients (figure 1A). Those who reported that they were active on a health-enhancing level were more likely to have discussed physical activity with health professionals. Diet had been discussed with 23% of the patients (figure 1B). Patients who reported a non-traditional mixed diet were more likely to have discussed diet. Smoking was discussed with 25% of the patients (figure 1C). Current smokers had more often

discussed smoking habits with healthcare professionals compared with never smokers (32% vs. 17%; p=0.000). Alcohol had been discussed with 17% of the patients (figure 1D). Of the patients with hazardous drinking habits, 77% had not had a discussion regarding alcohol.

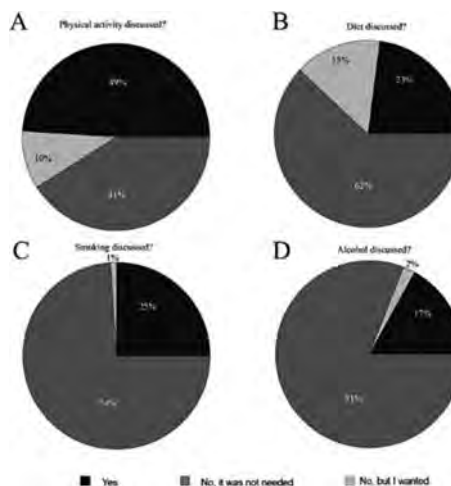


Figure 1 Rate of patients reporting that they had a discussion regarding life-style-related habits and whether they had wanted to have a discussion. Panel A relates to physical activity, panel B relates to diet, panel C relates to smoking, and panel D relates to alcohol consumption.

**Conclusions:** Physical activity had been discussed at least once with every second patient with established RA. Diet, smoking, and drinking habits had been discussed with about a quarter of them. There is a need for improvement, since lifestyle habits are especially important in a long-standing disease such as RA. Discussions concerning lifestyle habits should be an integral part of care management and an interactive process.

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FRIDAY, 15 JUNE 2018

**HPR Service developments, innovation and economics in healthcare**

**FRI0742-HPR EULAR RECOMMENDATIONS FOR THE ROLE OF THE NURSE IN THE MANAGEMENT OF CHRONIC INFLAMMATORY ARTHRITIS: 2018 UPDATE**

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**Background:** During the past years an increasing number of papers regarding rheumatology nursing have been published, which may contribute to a higher level of evidence and increased insight into the nurses' roles.

**Objectives:** To update the EULAR recommendations for the role of the nurse in the management of chronic inflammatory arthritis (IA) (1).

**Methods:** The EULAR standardised operating procedures were followed to integrate available higher level of evidence and new insights of nursing care in the



treatment of patients with IA. The EULAR Task Force comprised 15 nurses, 2 patient research partners, 1 physiotherapist, 1 psychologist, 1 occupational therapist, 1 medical student and 2 rheumatologists of whom one was also methodologist. A total of 17 European countries were represented. The systematic literature review included available literature from 2010 until December 2017 and was performed in the databases Medline, EMBASE, Cochrane Central, CINAHL, PsycINFO and in the 2016/2017 ACR and EULAR conferences abstracts. The original search strategy was used with no limitations applied with regard to publication type, research type or language. Titles, abstracts and full texts were screened for eligibility independently by the fellow and the convenor. Results were shared with the task force to check for comprehensiveness. Subsequently, the steering committee prepared proposals for update and rewording of the ten recommendations. The proposals were discussed with the Task Force in a one day consensus meeting and final agreement was obtained by voting.

**Results:** A total of 51 studies was included. Some studies added to existing evidence with a higher level of evidence to nurses' contribution regarding patients' satisfaction with care, cost-effectiveness, and self-efficacy, and also for the benefit of nurses' extended roles to patient outcomes as well as structured training aiming at improving nurses' skills. Additional evidence was found for needs-based patient education and telemonitoring. Two recommendations remained unchanged, six were reworded, two were merged and one recommendation was deleted and reformulated as an overarching principle together with the formulation of two additional overarching principles (figure 1). The level of agreement from each Task Force member will be retrieved by email.

Overarching principles		
Rheumatology nurses are part of a healthcare team		
Rheumatology nurses provide evidence based care		
Rheumatology nursing is based on shared decision making with the patient		
Recommendations	Level of evidence*	Strength of recommendation*
1 Patients should have access to a nurse for needs-based education to improve knowledge of CIA and its management throughout the course of their disease	1B	A
2 Patients should have access to nurse consultations in order to enhance satisfaction with care	1A	A
3 Patients should have the opportunity of timely access to a nurse for needs-based support; this includes telehealth	1B	B
4 Nurses should participate in comprehensive disease management to control disease activity, reduce symptoms, and improve patient preferred outcomes; this leads to cost-effective care	1A	A
5 Nurses should address psychosocial issues to reduce patients' symptoms of anxiety and depression	1B	A
6 Nurses should support self-management skills to increase patients' self-efficacy	1A	A
7 Nurses should have access to and undertake continuous education in the speciality of rheumatology to improve and maintain knowledge and skills	2C	B
8 Nurses should be encouraged to undertake extended roles after specialized training and according to national regulations	1A	A

\*According to the Oxford Centre for Evidence-based Medicine, CEBM Levels of Evidence 1

**Figure 1** EULAR recommendations for the role of the nurse in the management of CIA: 2018 Update

**Conclusions:** A total of three overarching principles and eight evidence- and expert opinion-based recommendations have been formulated, that provide an up-to-date guidance of nursing care in rheumatology.

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**Disclosure of Interest:** None declared

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#### FRI0743-HPR NURSE-LED OUTPATIENT MANAGEMENT FOR IMPROVED TREATMENT OF GIANT CELL ARTERITIS (GCA) AND POLYMYALGIA RHEUMATIC (PMR) IN A RHEUMATOLOGY OUTPATIENT CLINIC

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**Background:** GCA and PMR are challenges with regard to diagnosis and effective treatment because of varied and vague symptom presentations and overlapping pathologies that often require specialist for diagnostic investigations and specific treatment. Long-term glucocorticoids (GC) dependency is common, and

GC side effects occur in approximately 50% of patients emphasizing the need for continued monitoring and symptom control (1).

**Objectives:** To present the development and the implementation of a nurse-led, rheumatologist-supported model of care in the outpatient management of adults diagnosed with GCA or PMR.

**Methods:** Initially, available evidence about symptom regulated GC tapering in the treatment of GCA and PMR was identified. Subsequent, a fixed phase-out schedule for high dose GC therapy following either of three pathways (GCA with/without eye symptoms and PMR) was agreed on in a multidisciplinary working group. Furthermore, the group developed a nurse-managed protocol for nurse-led outpatient consultations to ensure systematic treatment and proper response to relapse. Prior to the implementation rheumatology nurses were taught and trained by rheumatologists in pertinent regulation of medication and identification of adverse signs and symptoms essential for providing appropriate support and patient education. Overall patient satisfaction was assessed on-site by an anonymous iPad questionnaire.

**Results:** An individual, initial GC dose are set by the rheumatologist based on clinician diagnosis, supported by currently available diagnostic and classification criteria. Subsequently, a nurse-led protocol reassures patient education and support during approximately one year of steroid therapy. The protocol includes close and continues observation and assessment by planned rheumatology nursing consultations followed by reassuring telephone calls. A rheumatologist can be consulted if doubt arises. Further, the rheumatology nurse is responsible for allocating final tapering (approximately 24 weeks) in the individualized PMR-management-plan for general practitioner. Patient overall self-reported satisfaction first nine month was high indicated by patients' experience of confidence, being heard and having questions resolved. Within the first 18 months, n=190 patients (GCA, n=82/PMR, n=108) with a mean aged of 73.2 (SD 8.4) years have been enrolled into nurse-led managed protocols for GC tapering.

**Conclusions:** A nurse-managed protocol for systematic and individualized GC tapering and patient support was developed as well as implemented successfully for individualized treatment of GCA and PMR. The extensive supportive patient education and involvement in symptom management secured by the rheumatology nurse provided high satisfaction. Also, the protocol executes rapid and direct access to advice for patients as recommended by EULAR for the management of PMR (2).

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**Disclosure of Interest:** None declared

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#### HPR Patients' perspectives, functioning and health (descriptive: qualitative or quantitative)

#### FRI0744-HPR THE ASSOCIATION OF LOCAL DISEASE ACTIVITY AND FOREFOOT DEFORMITIES WITH PLANTAR PRESSURE IN PATIENTS WITH RHEUMATOID ARTHRITIS AND FOREFOOT SYMPTOMS: A CROSS-SECTIONAL STUDY IN THE AMSTERDAM FOOT COHORT

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**Background:** In patients with rheumatoid arthritis (RA), both high and low forefoot plantar pressures have been reported in the literature (1-3). Understanding of contributing factors to forefoot pressure alterations can help to better formulate and specify goals for treatment with foot orthoses or therapeutic footwear.

**Objectives:** Investigate the association of local disease activity and forefoot deformity with plantar pressure in RA patients with forefoot symptoms.

**Methods:** A cross sectional study was conducted in the Amsterdam Foot (AMS-foot) cohort, using data of 172 consecutive patients with RA and forefoot symptoms. Peak pressure (PP) and pressure time integral (PTI) in the forefoot were measured with a pressure platform. Forefoot deformity was measured with the Platto score. Forefoot disease activity was defined as swelling and/or pain measured by palpation of the metatarsophalangeal (MTP) joints. The forefoot was

divided in a medial, central and lateral region, in which the following conditions could be present: 1) no abnormality, 2) disease activity, 3) deformity or 4) deformity and disease activity. A multilevel analysis was performed using condition per forefoot region as the independent variable and PP or PTI in the corresponding region as the dependent variable.

**Results:** Statistically significant higher PP and PTI were found in forefoot regions when deformities were present (RR 1.2, CI 1.1–1.3,  $P < 0.0001$ ), compared to forefoot regions without forefoot abnormalities. No significant differences in PP and PTI were found when solely local disease activity was present in forefoot regions (RR 1.0, CI 0.9–1.2,  $p = 0.749$  and RR 1.0, CI 0.8–1.2,  $p = 0.850$  respectively).

**Conclusions:** Deformities in the medial, central and lateral forefoot regions are related to higher plantar pressures measured in these regions. The absence of an association between local disease activity and plantar pressure might be explained by the low prevalence of MTP pain or swelling as detected by palpation. Future research with ultrasound measurements to detect disease activity is recommended to reveal the effect of forefoot disease activity on plantar pressure.

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#### FRI0745-HPR IMPLICIT AND EXPLICIT ATTITUDES AND ASSOCIATIONS OF RHEUMATOID ARTHRITIS PATIENTS TOWARDS CONVENTIONAL DISEASE MODIFYING ANTI-RHEUMATIC DRUGS AS POSSIBLE TARGETS FOR IMPROVING MEDICATION ADHERENCE

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**Background:** Medication adherence to conventional disease modifying anti-rheumatic drugs (cDMARDs) is suboptimal in patients with rheumatoid arthritis (RA) with medication adherence rates ranging from 30 to 80% [1]. Since existing interventions are only partially effective, identifying (modifiable) factors associated with non-adherence might help to find targets for more effective adherence-improving interventions. There is growing evidence that not only explicit attitudes (conscious responses) are responsible for behaviour, but also implicit attitudes (unconscious responses) might be involved [2].

**Objectives:** The aim of this study is to examine implicit and explicit attitudes of RA patients towards cDMARDs, and their association with medication adherence.

**Methods:** A multicenter observational cohort study in two rheumatology specialized centres was initiated to examine implicit and explicit attitudes of 254 consecutive adult RA patients (ACR 2010 criteria) treated with at least one cDMARD for a minimum period of one year. Prior to their regular consultation, patient's implicit attitudes were measured with the Single Category Implicit Association Test and explicit attitudes were evaluated with a bipolar evaluative adjective scale and the validated Beliefs about Medicines Questionnaire (BMQ-specific). Primary outcome was self-reported medication adherence measured with the validated Compliance Questionnaire on Rheumatology.

**Results:** Implicitly, more patients displayed negative attitudes (49.0%) and sickness related associations (60.9%) than explicitly (21.3% and 23.5% respectively). Only significant correlations between explicit attitudes and associations of RA patients and beliefs about medicines were found. The lowest levels (48.8%) of self-reported adherence were found in patients who displayed congruent negative (implicit and explicit) attitudes. The highest levels (71.4%) of self-reported adherence were found in patients who displayed congruent (implicit and explicit) health (versus sickness) related associations.

**Conclusions:** Implicit attitudes and associations of RA patients were not always congruent with explicit attitudes and associations. Slightly higher adherence rates were found in patients who displayed positive explicit attitudes and associations.

However, implicit and explicit attitudes and associations of RA patients towards cDMARDs and their adherence should be further investigated with MEMS (medication event monitoring system) devices.

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FRIDAY, 15 JUNE 2018

#### Public health, health services research and health economics

#### FRI0746 NURSING CONSULTATION VERSUS RHEUMATOLOGIST FOLLOW UP FOR PATIENTS WITH STABLE RHEUMATOID ARTHRITIS: A RANDOMIZED CONTROLLED TRIAL

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**Background:** Conventionally, patients with RA have been managed by scheduled routine consultations by rheumatologists every 3 to 6 months. However, the burden of RA has been increasing globally. Although rheumatology nursing consultation was shown to be an effectiveness management strategy in western countries, its feasibility has not been evaluated in Chinese population. Therefore, we would like to compare the efficacy of rheumatology nursing consultation with usual rheumatologist follow-up in Hong Kong.

**Objectives:** To evaluate the efficacy of rheumatology nursing consultation in patients with stable RA over 1 year.

**Methods:** Study design and patient selection: This is a single centre, randomized controlled, non-inferiority trial conducted in Queen Mary Hospital. Patients with RA were recruited from the rheumatology clinic in Queen Mary Hospital. Subjects have to fulfill the 2010 ACR-EULAR classification criteria for RA, with DAS28-CRP  $\leq 3.2$  for at least 6 months with no increase in dose of conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs). Subjects with systemic manifestation of RA, current malignancies or current use of biologic therapies were excluded.

**Intervention:** Subjects were randomized in a 1:1 ratio to the following treatment groups.

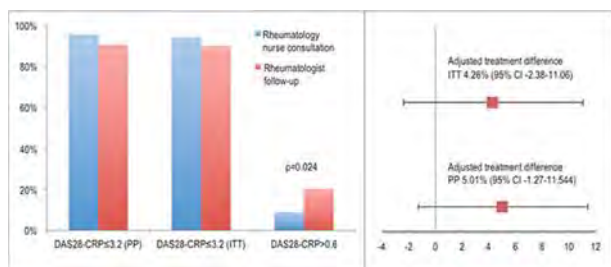
Usual rheumatologist follow-up (control): Subjects were followed up by rheumatologists or registrars every 4 months. The treatment target was to maintain the DAS28-CRP  $\leq 3.2$ .

Rheumatology nursing consultation: Subjects were followed up by the rheumatology nurses every 4 months. At 12 months, all subjects will be reviewed by a senior rheumatologist. The treatment target was to maintain the DAS28-CRP  $\leq 3.2$ .

**Outcomes:** The primary outcome was the difference in proportion of subjects who remained to have DAS28-CRP  $\leq 3.2$  at 12 months. Secondary outcomes included the difference in proportion of subjects with DAS28-CRP  $> 0.6$  at 12 months; the change in modified Sharp score, health assessment questionnaire (HAQ) score, patients' drug compliance from baseline and patients' satisfaction at 12 months.

**Statistical analysis:** SPSS v.22 was used to performed the statistical analyses according to intention to treat and per protocol analysis. The comparisons between 2 groups was performed by Student's t-test for continuous variables and chi-square test for categorical variables. A one-way repeated measures ANOVA was conducted to determine if there was a difference in DAS28-CRP between treatment groups during the study period.

**Results:** 276 subjects were randomized to receive rheumatology nurse consultation or usual rheumatologist follow-up. At 12 months, 95.5% and 90.5% of subjects in the nurse consultation and rheumatologist follow-up remained to have low disease activity respectively, with an adjusted treatment difference of 5.0% (CI -1.27–11.54) and showed non-inferiority with a pre-defined margin of -10%. However, more subjects in the rheumatologist follow-up experienced DAS28-CRP  $> 0.6$  at 12 months. One-way repeated measures ANOVA test showed significant difference in DAS28-CRP between 2 treatment group over time. No statistically significant differences were seen in other outcome measures.



**Conclusions:** Rheumatology nurse consultation is not inferior to regular rheumatologist follow-up for rheumatoid arthritis patients with low disease activity.

**Disclosure of Interest:** None declared

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Saturday, 16 JUNE 2018

## HPR Measuring health (development and measurement properties of PROs, tests, devices)

### SAT0716-HPR PATIENTS PREFERENCE GOES TO METHOTREXATE AUTOINJECTORS OVER PREFILLED SYRINGES: RESULTS FROM A PHASE III TRIAL, SELFI

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**Background:** The offer of injectable MTX in Europe expanded during past few years with different types of enhanced devices such as prefilled syringes and autoinjector pens.

**Objectives:** SELFI trial intended to compare historical MTX prefilled syringes vs a new MTX autoinjector in terms of treatment adherence, functional capacity and patients' preference at 6 months in RA patients.

**Methods:** SELFI was a phase III, randomised open-label trial, conducted in France between Sept. 2015 and March 2017. It included RA patients, treated by oral or injectable MTX for  $\geq 3$  months (monotherapy or association). Patients were randomised in two arms: MTX in prefilled syringes (PS) or MTX in autoinjectors (AI) at the dosage decided by the investigator. Primary objectives of the trial were to prove the 4% non-inferiority of AI vs PS in terms of patients' adherence and functional capacity (HAQ-DI) at 6 months. Secondary objectives included the evaluation of satisfaction and patients' preference.

**Results:** Between Sept. 2015 and ,Sept. 2016 50 rheumatologists, mostly in private practice, included 271 patients, 197 of which composed the *per protocol* population. Patients baseline characteristics were [mean ( $\pm$ SD)]: age: 59.2 ( $\pm$ 12.3) yrs; BMI: 26.0 ( $\pm$ 4.9) kg/m<sup>2</sup>; RA duration: 5.35 ( $\pm$ 6.70) yrs; DAS28: 3.1 ( $\pm$ 1.2); HAQ-DI: 0.6 ( $\pm$ 0.6). All patients were treated by MTX (1/3 oral; 2/3 parenteral) at a mean dose of 15.4 ( $\pm$ 4.1) mg/wk. There were no significant differences at baseline between PS and AI arms. At 6 months, the treatment adherence was over 95% for both arms, and HAQ-DI was improved by a mean of 0.05 in both arms. The AI 4% non-inferiority as compared to PS was shown for both primary criteria.

Patients' reported satisfaction was very significantly higher ( $p \leq 0.001$ ) in AI arm vs PS for the following criteria: easy to use, pleasant, satisfying, willingness for further utilisation and significantly higher ( $p < 0.05$ ) for reassuring and not constraining. Of the 132 patients who experienced both devices (during the study or before it), 127 (96%;  $p < 0.001$ ) preferred the auto injector over the historical prefilled syringe. No unexpected safety issues were observed during this trial and injection point safety tolerance satisfaction was higher for AI vs PS.

**Conclusions:** SELFI trial showed that although the new MTX autoinjector is comparable to historical prefilled syringe in terms of treatment adherence and functional capacity improvement, it is significantly superior in terms of patients'

satisfaction. Over 95% of patients who have tried both devices report preferring the pen.

**Disclosure of Interest:** A. Saraux Consultant for: Nordic Pharma, C. Hudry Consultant for: Nordic Pharma, E. Zinovieva Employee of: Nordic Pharma, H. Herman-Demars Employee of: Nordic Pharma

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### SAT0717-HPR PSYCHOMETRIC TESTING OF A GERMAN VERSION OF THE EVALUATION OF DAILY ACTIVITY QUESTIONNAIRE IN RHEUMATOID ARTHRITIS

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**Background:** The Evaluation of Daily Activity Questionnaire (EDAQ) is a patient reported outcome (PRO) of activity limitations. The English EDAQ is reliable, valid and a comprehensive measure of the commonest problems experienced by people with rheumatoid arthritis (RA) and musculoskeletal conditions.<sup>1,2</sup> It includes 138 items in 14 'domains' (Eating/Drinking; Personal Care; Dressing; Bathing; Cooking; Moving Indoors; House Cleaning; Laundry; Moving and Transfers; Moving Outdoors; Gardening/Household Maintenance; Caring; Leisure/Social Activities). All items are scored on a 0–3 scale (no difficulty to unable to do). There is no similar measure available in German. PROs must be tested in target languages and conditions, prior to use, to ensure validity and reliability.

**Objectives:** To linguistically validate a German EDAQ and test its reliability and validity in German-speaking people with RA.

**Methods:** The English EDAQ was forward-backward translated to German. Cognitive debriefing interviews were conducted and the German EDAQ developed. Participants from a Rheumatology clinic (Switzerland) and arthritis patient organisations (Switzerland, Germany, Austria) then completed postal questionnaires including: demographic questions, German EDAQ, Health Assessment Questionnaire (HAQ), SF36v2, RA Quality of Life scale (RAQOL), and a hand pain numeric rating scale (NRS). Three weeks later, the EDAQ was mailed again. Test-retest reliability of domain scores, and validity of the 14 German EDAQ domains against the other measures, were evaluated using nonparametric correlations. Internal consistency was tested using Cronbach's alpha.

**Results:** Six German-speaking people with RA were interviewed, recommended changes reviewed by the expert panel and the German EDAQ agreed. 163 people then completed questionnaires: 145 women and 18 men; mean age=52.84 (SD14.94) years; mean RA duration=15.73 years (SD12.12). 85 (45%) were employed; 21 had children<18 y at home. Median pain score=4 (IQR 2–6) and fatigue=5 (IQR 3–7).

107 (65%) completed a second questionnaire. Test-retest reliability of total domain scores was excellent for all domains ( $r_s = 0.80–0.93$ ). Internal consistency was high in all domains: Cronbach's alpha=0.84–0.96. All EDAQ domains (except Caring) correlated significantly ( $p < 0.001$ ) with: HAQ  $r_s = 0.73–0.87$ ; SF36v2 (Physical Function)  $r_s = -0.61$  to  $-0.84$ ; SF36v2 Bodily Pain  $r_s = -0.53$  to  $-0.65$ ; SF36v2 (Vitality)  $r_s = -0.27$  to  $0.31$ ; RAQOL  $r_s = 0.55–0.68$ ; and hand pain  $r_s = 0.43–0.52$ . Correlations were lower in the 'Caring' domain due to the smaller sample size ( $n=77$ ), although mostly still significant ( $p < 0.01$ ;  $r_s = 0.25$  to  $0.42$ ; except SF36v2 Vitality= $-0.10$  non-significant).

**Conclusions:** The German EDAQ is a valid and reliable measure of daily activity in people with RA. Either the whole EDAQ or individual domains can be used in clinical practice to identify clients' daily activity problems and help find solutions, or as an outcome measure in research and audit. A User Manual is available.<sup>3</sup>

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Patients' reported satisfaction (Likert Scale)	Easy to use	Pleasant	Satisfying	Motivating for further utilisation	Reassuring	Not constraining	Not stressful	Not painful
Strongly agree (AI/PS)	60%/21%	7%/0%	63%/21%	61%/35%	30%/14%	51%/36%	55%/41%	51%/38%
Agree (AI/PS)	32%/42%	20%/11%	31%/50%	23%/34%	52%/60%	18%/17%	23%/26%	21%/31%
Neither agree nor disagree (AI/PS)	4%/23%	32%/26%	2%/19%	9%/17%	9%/15%	19%/24%	14%/17%	25%/24%
Disagree (AI/PS)	1%/6%	26%/30%	2%/6%	6%/10%	4%/5%	10%/15%	4%/8%	1%/6%
Strongly disagree (AI/PS)	4%/8%	14%/33%	1%/4%	1%/4%	5%/6%	2%/8%	8%/9%	1%/1%
<b>Significance level</b>	<b>p&lt;0.001</b>	<b>p&lt;0.001</b>	<b>p&lt;0.001</b>	<b>p=0.001</b>	<b>p=0.02</b>	<b>p=0.02</b>	<b>p=0.05</b>	<b>p=0.15</b>



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**Disclosure of Interest:** None declared

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**SAT0718-HPR ARE THERE SYMPTOMS DISTINGUISHING FIBROMYALGIA FROM CHRONIC PAIN THAT ARE MISSING FROM THE 2016 CRITERIA?**

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**Background:** Fibromyalgia (FM) patients have a wide range of symptoms. **Objectives:** Herein we analysed 20 common symptoms to determine those that best discriminate between FM patients and chronic pain patients without FM (Chronic Pain).

**Methods:** 352 patients (mean age 50+/16.3 years, 70% female) scheduled for a routine examination in two primary care practices were studied. 50 patients (14.2%) had FM (based on 1990 ACR) and 108 patients (30.7%) had Chronic Pain. All subjects completed a survey of 20 symptoms commonly found in FM patients – 10 were from the Symptom Impact Questionnaire (SIQR).

**Results:** Table 1 presents the 20 symptoms ranked by magnitude of Somers' D. This is a statistic that provides an estimate of predicting a diagnosis of fibromyalgia versus no fibromyalgia (OR: 1.87–8.00; p<0.001). The top 10 symptoms showed strong correlations with diagnosis (D=0.49 to 0.64) and large mean differences between the 2 groups (Means: 2.8–4.3). Notably, there was a 4.3 score difference in Persistent Deep Ache and only a 1.4 difference in SIQR Pain (p<0.001). Using a 4-point criterion as a clinical cut-off (0–10), symptoms best discriminating patients with FM from Chronic Pain were: Persistent Deep Aching (86% vs. 36%), Environmental Sensitivity (82% vs. 38%), Poor Balance (82% vs. 35%), Tenderness to Touch (84% vs. 39%) and Pain after exercise (96% vs. 54%). The symptoms of Pain, Unrefreshing Sleep, Muscle Stiffness and Low Energy were high in both groups, thus they are not good discriminators.

**Abstract SAT0718HPR – Table 1.** Twenty common fibromyalgia symptoms ranked by Somers' D. The top 10 symptoms are shaded. SIQR symptoms are italicised.

Symptom	Somers'D (rank)	FM Mean (%)	Chronic Pain Mean (%)	Mean difference
Persistent Deep Aching	.641 (1)	7.40 (86)	3.14 (36)	4.26
Intolerance to Noise	.592 (2)	6.98 (86)	3.27 (34)	3.71
Environmental Sensitivity	.574 (3)	6.82 (82)	3.04 (38)	3.78
Poor Balance	.552 (4)	6.26 (82)	3.06 (35)	3.20
Pain after Exercise	.534 (5)	8.08 (96)	4.07 (54)	4.01
Muscle Weakness	.524 (6)	6.92 (88)	3.77 (42)	3.15
Tenderness to Touch	.511 (7)	6.82 (84)	3.61 (39)	3.21
Muscle Stiffness	.505 (8)	7.68 (94)	4.86 (57)	2.82
Intolerance to Bright Lights	.492 (9)	6.58 (72)	3.41 (33)	3.17
Tender Muscles	.491 (10)	7.90 (94)	4.94 (56)	2.96
Non-refreshing Sleep	.452 (11)	7.54 (84)	4.60 (52)	2.94
Poor Memory	.421 (12)	5.66 (66)	3.03 (37)	2.63
Intolerance to Cold	.414 (13)	6.62 (74)	3.82 (40)	2.80
Irritable Bowel Symptoms	.412 (14)	5.68 (64)	3.05 (31)	2.63
Swollen Joints	.409 (15)	6.16 (76)	3.78 (41)	2.39
Depression	.398 (16)	5.44 (64)	3.17 (42)	2.27
Stiffness	.396 (17)	6.92 (88)	4.54 (53)	2.38
Chronic Headaches	.390 (18)	5.62 (66)	3.45 (38)	2.17
Low Energy	.349 (19)	6.82 (84)	4.92 (61)	1.90
Pain Level	.320 (20)	6.54 (94)	5.12 (69)	1.42

**Conclusions:** In this sample from 2 primary care practices, Persistent Deep Aching, Tenderness to Touch, Environmental Sensitivity, Poor Balance and Pain after Exercise were the best discriminators between FM patients and patients with Chronic Pain. Notably: Depression, Headaches, Poor Memory and Irritable Bowel symptoms were weak discriminators; in fact, none of the top 10 discriminators appear in the 2016 Fibromyalgia Diagnostic Criteria.

**Disclosure of Interest:** None declared

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**SAT0719-HPR PERFORMANCE-BASED PHYSICAL FUNCTION MEASURE WAS MORE SENSITIVE TO DETECT RESPONDERS THAN SELF-REPORTED MEASURE AFTER A PHYSICAL THERAPY EXERCISE INTERVENTION IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS**

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**Background:** Physical function is regarded as an important outcome in axial spondyloarthritis (axSpA) and the self-reported questionnaire Bath Ankylosing Spondylitis Functional Index (BASFI) is recommended for the evaluation. However, it is shown that BASFI may not be sufficiently sensitive to detect changes after physical therapy. Based on BASFI a disease-specific performance-based measure has been developed; the Ankylosing Spondylitis Performance-based Improvement (ASPI).

**Objectives:** To compare the proportion of patients with axSpA considered as responders in the performance-based function measure ASPI and the self-reported BASFI after a physical therapy exercise intervention.

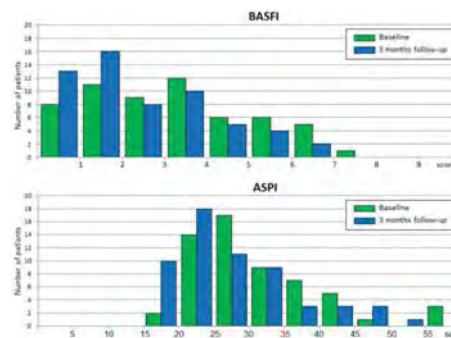
**Methods:** This study was part of the ESpa-study (Exercise for SpondyloArthritis) which examines the effect of 12 weeks, supervised high intensity exercise intervention. Patients with axSpA were included from 4 centres in Scandinavia. Physical function was assessed with ASPI and BASFI at baseline and after 3 months. The ASAS20 response criteria were used to categorise patients as intra-individual responders or non-responders. In BASFI, patients were classified as responders if they showed an improvement of ≥20% and ≥1 unit. In ASPI, patients were classified as responders if they showed an improvement of ≥20% on 1 or more subtest(s) and the absence of deterioration on the potential remaining test. Deterioration was defined as a worsening of ≥20% in 1 or more subtest(s). The proportion of patients categorised as intra-individual (non-) responders was examined with Chi square test.

**Results:** A total of 58 patients (intervention n=30, control n=28) with complete data on ASPI and BASFI were included in the analyses, 41% were male, mean age (SD) was 45 (10.7) years, 55% had radiographic axSpA and mean disease activity (ASDAS) (SD) was 2.6 (0.7). In BASFI, a score of <1 was present in 14% at baseline and in 22% at 3 months, indicating a ceiling effect (figure). The proportion of responders in the total group was 53% in ASPI and 36% in BASFI, p=0.13 (table 1). In the intervention group, 70% were responders in ASPI and 43% were responders in BASFI, p=0.02.

Table. Number of responders measured with performance-based function test (ASPI) and self-reported physical function (BASFI) according to study sub-group

	All patients (n=58)	Intervention (n=30)	Control (n=28)
ASPI Responder	31 (53%)	21 (70%)	10 (36%)
ASPI Non-responder	27 (47%)	9 (30%)	18 (64%)
BASFI Responder	21 (36%)	13 (43%)	8 (29%)
BASFI Non-responder	37 (64%)	17 (57%)	20 (71%)
p-value*	0.13	0.02	0.45

Values are number (percentages). \*Chi square test between (non-) responder in ASPI and BASFI within groups



**Abstract SAT0719HPR – Figure 1.** Distribution of BASFI scores and time in seconds in ASPI assessed at baseline and at 3 months follow-up (n=58). Lower values indicates better physical function in both measures

**Conclusions:** The performance-based physical function measure ASPI was more sensitive to detect responders than the self-reported measure BASFI according to the ASAS20 response criteria in patients with axSpA after a high intensity exercise intervention. Our findings suggest that the performance-based physical function (ASPI) measure is preferable when evaluating physical function after exercise interventions with physical therapy.

**Disclosure of Interest:** None declared

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### SAT0720-HPR MORE PRECISE MEASUREMENTS OF SPINAL MOBILITY WHEN ASSESSED WITH A SENSOR IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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**Background:** Rotation of the spine is one of the principal movements of spinal motion. Cervical rotation (CR) is included in the assessment for monitoring axial spondyloarthritis (axSpA). Thoracolumbar rotation (TLR) is also known to be a valid measure for axSpA specific changes, but is seldom used due to lack of easy feasible measures. Goniometer or myrinometer (compass) is traditionally used to evaluate rotation. A sensor with excellent criterion validity and reliability for rotation in the range of motion from 10 to 120 degrees, that are able to detect changes of  $\leq 1$  degree, has recently been developed<sup>1</sup>.

**Objectives:** To examine the concurrent validity between the sensor and compass in CR and TLR and to evaluate the usability and satisfaction with the sensor.

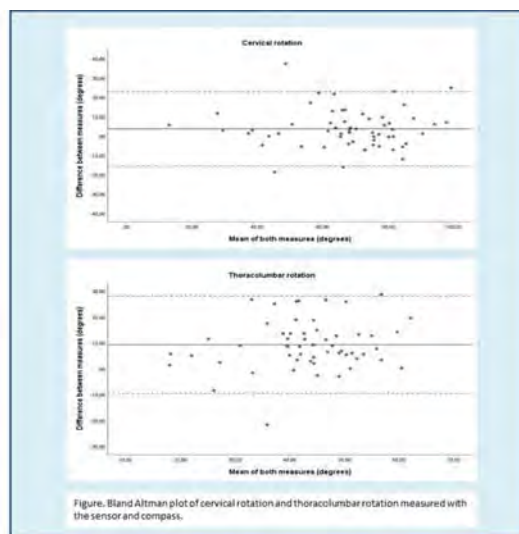
**Methods:** This study was part of the MOSKUS-study (Mobile mosculo Skeletal User Self-management). Patients with axSpA were included from two rheumatology outpatients' clinics and examined by experienced physiotherapists. CR and TLR were assessed three times with both the sensor and compass; mean score are used in the analyses. The measuring order was randomised. The sensor was considered gold standard. Group differences were assessed with paired sample t-test or Wilcoxon signed rank test, and agreement with Bland Altman plot. Time to conduct the test (instruction, conducting and note of results) was recorded for the 10 last included patients. Satisfaction was assessed both by the patients and assessors with numeric rating scale (NRS), (0–10, 10=highest satisfaction).

**Results:** A total of 60 patients with axial SpA and 2 assessors participated. Of the included patients 60% were male, median (min-max) age was 39<sup>20–73</sup> years and 77% had radiographic axSpA. There were statistically significant differences in measure of rotation between the sensor and the compass of 3.7° in CR,  $p=0.01$  and 9.2° in TLR,  $p<0.001$  (table 1). The Band Altman plots show that the compass systematically measured lower rotation than the sensor in both CR and TLR (figure). There was no difference in time used to conduct the measurements. Patients satisfaction in CR measured with the sensor was mean (SD) 7.8 (2.4) and compass 6.7 (2.6),  $p<0.001$  and in TLR 7.8 (2.4) and 7.3 (2.3),  $p=0.08$  respectively. Assessors satisfaction in CR measured with the sensor was 9.0 (1.2) and compass 5.6 (2.8)  $p<0.001$  and in TLR 8.1 (2.2) and 3.6 (2.2)  $p<0.001$ , respectively.

**Abstract SAT0720HPR – Table 1.** Characteristics of rotation measures, agreement and time to conduct measurements

Mobility	Measure	n	Mean (SD)	Mean difference (SD)	p-value	Time in sec, median (min-max), n=10	p-value
Cervical	Sensor	59	69.2 (18.2)			96 (44–216)	
	Compass	59	65.4 (18.2)	3.7 (10.0)	0.01	96 <sup>62–150</sup>	0.36
Thoraco-lumbar	Sensor	56	47.8 (11.8)			107 (36–200)	
	Compass	56	38.6 (10.3)	9.2 (9.5)	<0.001	86 <sup>46–158</sup>	0.92

**Conclusions:** Measure of CR and TLR were significantly lower when measured with a traditional compass compared to a digital sensor. There were no difference in time use and both patients and assessors were more satisfied with the sensor. The results suggest that the sensor gives more precise measurements of rotation and allow a feasible way to assess TLR in daily clinical practise.



**Abstract SAT0720HPR – Figure 1.** Bland Altman plot of cervical rotation and thoracolumbar rotation measured with the sensor and compass.

#### REFERENCE:

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**Disclosure of Interest:** None declared

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### SAT0721-HPR IMPROVEMENT IN CLINICAL RESULTS BY ENHANCING ADHERENCE TO A HEALTHCARE MODEL IN RHEUMATOID ARTHRITIS

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**Background:** A Centre of Excellence (CoE) healthcare model aims to obtain a high quality results from the appropriate and minimal use of resources in rheumatoid arthritis (RA); Enhancing adherence of patients to healthcare model and treatment using a Treat to Target approach and patient education has demonstrated the improvement of patient conditions and clinical results.<sup>1</sup>

**Objectives:** To describe the adherence patterns to a centre of excellence model and clinical outcomes in patients with RA in a specialised centre. For this study researchers defined adherence as the attendance to an appointment with our healthcare team for more than three times during 12 months.

**Methods:** We reviewed the clinical records of patients with RA in a specialised centre during a 12 month period. We included socio demographic variables and the attendance to consultations to rheumatology, psychiatry, physical therapy, occupational therapy, nutrition, and psychology consultations. Descriptive epidemiology was done, percentages and averages were calculated We analysed bivariate association with Pearson's  $\chi^2$ .

**Results:** We included 5413 patients, where 83% were female and 17% were male; mean age was 59 years $\pm$ 12. Mean DAS28 of patients was 2.82 $\pm$ 0.84, where 46% of patients were on remission, 27% in low disease activity, 24% in moderate disease activity and 3% in severe disease activity. The specialty where the adherence was higher was in rheumatology 98%, followed by psychiatry 33%, psychology 29%, physical therapy 28%, occupational therapy 20% and nutrition 13%. In our study 47% of patients were considered as adherents; from all patients who were adherent 75% were in remission or low disease activity. When we compared disease activity with the attendance to all specialties there was statistical association between disease activity and the patients who attended to more than four visits.

**Conclusions:** Patients who attend satisfactory to a multidisciplinary healthcare approach team can achieve better results compared to those who doesn't attend to all medical specialties; thus it is relevant to implement patient education

processes in order to create awareness about the importance and value of each medical specialty, mainly in patients with moderate or severe disease activity.

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**Disclosure of Interest:** None declared

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#### **SAT0722-HPR** THE VALIDITY AND TEST-RETEST RELIABILITY OF THE TURKISH PATIENT SPECIFIC FUNCTIONAL SCALE IN CHRONIC NECK PAIN PATIENTS

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**Background:** Current clinical guidelines recommend to use both clinical and self-reported measurements for evaluation of chronic neck pain. Among the self-reported outcomes, Neck Disability Index (NDI) and Patient Specific Functional Scale (PSFS) are the most widely used and recommended instruments.<sup>1</sup> Although, NDI was validated in Turkish language before, but no validation study related to the PSFS was detected in the literature.

**Objectives:** The purpose of our study was to determine the validity and reliability of PSFS which was not validated in Turkish language previously.

**Methods:** The PSFS has been translated into Turkish (PSFS-T) according to "translation-backward translation" method as recommended in the guidelines. Demographic data, PSFS-T, and NDI were recorded at the initial assessment. For the test-retest reliability analysis, the first 30 patients were called by phone. Intra-class correlation coefficient (ICC) was established for reliability analyses. The correlations between PSFS-T and NDI was examined for the validity analysis.

**Results:** The final form was completed by 110 chronic neck pain patients (F:77, M:33). The mean age of patients was 44±14 and the average duration of pain was 43±49 months. Test retest reliability of PSFS-T was found good level (ICC: 0.85). The relationship between PSFS-T and NDI was found moderate level ( $p < 0.05$ ,  $\rho = -0.578$ ). Furthermore, reading books/newspapers, cleaning and carrying heavy things were reported by Turkish neck patients as the first three activities which are the most problematic for their daily activities of life.

**Conclusions:** PSFS-T is a valid and reliable method of measuring outcome in patients with neck pain. Future studies should focus on the validity and reliability of PSFS-T in different populations.

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**Disclosure of Interest:** None declared

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#### **SAT0723-HPR** COMPARISON OF PHYSICAL ACTIVITY, FATIGUE, HEALTH-RELATED QUALITY OF LIFE, ANXIETY AND DEPRESSION BETWEEN ANKYLOSING SPONDYLITIS AND RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Rheumatoid arthritis (RA) and ankylosing spondylitis (AS) are chronic progressive inflammatory diseases, leading to joint damage and reducing the physical fitness of patients. They are among the most common rheumatic diseases. Physical inactivity, fatigue, low health-related quality of life (HRQoL), higher anxiety and depression levels are common problems reported in patients both ankylosing spondylitis (AS) and rheumatoid arthritis (RA) although the clinical manifestations differ in many ways. These low outcomes have been found to be associated with functional limitations in both AS and RA serves as mediators in the link between disease activity and functional limitations in spite of NSAIDs and DMARDs therapies. Although many studies have assessed the outcomes of a single disease state, either RA or AS, few studies have focused on a direct comparison between those both diagnostic groups.

**Objectives:** The aim of this study to assess and compare physical activity, fatigue, HRQoL, anxiety and depression levels between AS and RA patients.

**Methods:** Twenty-six RA patients and 18 patients with AS were recruited from the outpatient clinic. Physical activity was assessed using the International Physical Activity Questionnaire-Short Form (IPAQ-SF), a validated instrument comprising of four items that estimates the levels of vigorous activity, moderate activity, walking and time spent sitting during the previous 7 days. The Fatigue Severity Scale (FSS) was used to measure the severity of fatigue. Disease-specific instruments to measure (HRQoL) in patients with RA and AS (RAQoL and ASQoL) were used. The Hospital Anxiety and Depression Scale (HADS) were used to assess anxiety and depression. The patient groups were compared using the Kruskal-Wallis test and the Chi-square test.

**Results:** Disease durations were similar between RA (mean age=48.92±12.50 years, disease duration=10.81±7.68 years) and AS (mean age=43.44±12.36 years, disease duration=11.39±8.87 years) patients ( $p=0.867$ ). There was no statistically difference between FSS (RA=45.27±16.95; AS=41.00±12.95;  $p=0.173$ ), IPAQ-SF (RA=1289.65±839.75; AS=2110.06±1210.86;  $p=0.062$ ) and HADS scores (RA=18.31±2.93; AS=17.00±2.87;  $p=0.123$ ) in both patient groups.

**Conclusions:** Our results support that physical inactivity due to impaired mobility as well as fatigue, anxiety/depression and low (HRQoL) are common and similar features of both RA and AS. In conclusion, management of disease activity with drug therapies should be targeted not only to improve physical function for RA and AS but also to improve physical activity levels, restore fatigue, anxiety and depression levels and preserve HRQoL.

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**Disclosure of Interest:** None declared

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#### **SAT0724-HPR** TECHNOLOGICAL ASSISTED REHABILITATION FOLLOWING TOTAL KNEE JOINT REPLACEMENT. A RANDOMISED CONTROLLED NON-INFERIORITY TRIAL

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**Background:** Supervised rehabilitation after total knee arthroplasty (TKA) has been suggested effective for quicker recovery. The effect of Technological Assisted Rehabilitation (TAR) in the participant's home compared to supervised rehabilitation has been investigated in trials and results suggest it being equal to supervised rehabilitation on short time follow-up (6 weeks to 4 months). No studies have been found that evaluate the effect of TAR on follow-ups longer than 4 months.

**Objectives:** The aim of this study was to evaluate the effect of TAR compared to supervised rehabilitation (usual care) on participants with TKA after 6 and 12 months.

**Methods:** This was a single-blinded, randomised controlled, non-inferiority study. 155 participants were randomised to either TAR (ICURA) or usual care. Intervention time was 6 weeks, follow-ups were after intervention, at 6 and 12 months. This study only concluded on 6 and 12 months. Primary outcome was 10 m walk test. Secondary outcomes were 2.45 m up and go, 30 s. Sit to Stand, active knee flexion and extension and the KOOS questionnaire. All outcomes were measured at all time points by a blinded assessor. Non-inferiority margin was no statistical significant- and less than 10% between group difference at 6 and 12 months, estimated by a repeated measurement analysis, adjusted for relevant baseline variables.

**Results:** Overall, the groups did not differ at baseline. No statistical between group difference was detected after 6 and 12 months for primary and secondary outcomes. A power analysis suggested severe lack of power to detect a statistical between group difference, due to high numbers of participants lost to follow-up after 6 and 12 months. The between group difference at 6 and 12 months was less than 10% for all outcomes except KOOS Quality of Life at 6 months, were a difference of 12.2% was detected, in favour of ICURA

**Conclusions:** The results show that the effect of ICURA is equal to usual care after 6 and 12 months. Because lack of power after 6 and 12 months, the statistical significance should be interpreted with caution, but overall between group difference after 6 and 12 months was less than 10% for primary and secondary outcomes.



**Disclosure of Interest:** None declared  
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**SAT0725-HPR** **COMPARATIVE ANALYSES OF RESPONSIVENESS BETWEEN THE RHEUMATOID ARTHRITIS IMPACT OF DISEASE (RAID) SCORE, OTHER PATIENT REPORTED OUTCOMES AND DISEASE ACTIVITY MEASURES: SECONDARY ANALYSES FROM THE ARCTIC STUDY**

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**Background:** The RAID score is a patient-derived patient reported outcome measure (PROM), developed by a EULAR task force, that assesses the impact of RA on seven important domains. Responsiveness of the RAID score was assessed in the preliminary validation,<sup>1</sup> but more data is needed on the sensitivity to change, especially compared to other PROMs and other conventional outcome measures.

**Objectives:** The objective of this study was to assess the changes in the RAID score in patients with early RA during the first six months of intensive DMARD treatment, and to evaluate the responsiveness of RAID after 3 months compared to other PROMs and conventional measures of disease activity.

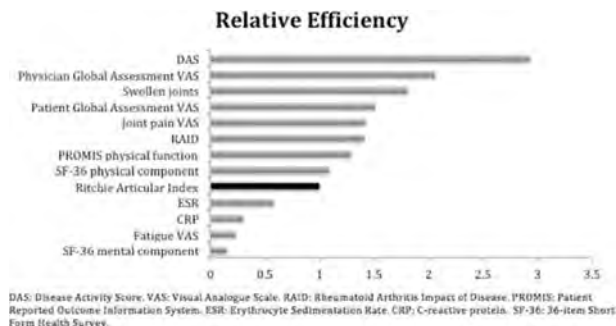
**Methods:** RA patients with short disease duration were followed in the 24 month treat-to-target strategy ARCTIC trial.<sup>2</sup> The responsiveness of the RAID score was evaluated by calculating the Standardised Response Mean (SRM) followed by the Relative Efficiency (RE) with respect to the Ritchie Articular Index. SRMs and RE were also calculated for other PROMs and clinical outcome measures. An SRM with absolute value above 0.80 was considered high.

**Results:** 230 RA patients were included. The mean symptom duration was 7.09 ±5.40 (±SD) months, the baseline mean RAID score was 4.49±2.14. At the 3 month follow-up, the mean change score for RAID was -2.25±1.98 and the SRM was -1.13 (-1.33 to -0.96) (table 1).

Table Mean change±SD and standardised response mean (SRM) with 95% confidence intervals for patients reported outcomes and conventional disease activity measures at 3 and 6 months

	3 months		6 months	
	Change, mean±SD	SRM (95% CI)	Change, mean±SD	SRM (95% CI)
RAID	-2.25±1.98	-1.13 (-1.33 to -0.96)	-2.39±1.98	-1.21 (-1.38 to -1.06)
DAS	-1.71±1.04	-1.63 (-1.89 to -1.42)	-1.95±1.09	-1.80 (-2.04 to -1.60)
ESR	-10.9±15.0	-0.73 (-0.83 to -0.63)	-11.7±16.5	-0.71 (-0.84 to -0.59)
CRP	-9.68±18.4	-0.53 (-0.62 to -0.43)	-10.8±19.5	-0.55 (-0.63 to -0.48)
Swollen joint count	-8.86±6.89	-1.28 (-1.46 to -1.14)	-9.63±7.41	-1.30 (-1.46 to -1.17)
Ritchie Articular Index	-5.75±6.03	-0.95 (-1.12 to -0.80)	-6.33±6.30	-1.01 (-1.15 to -0.88)
Patient global assessment VAS	-28.3±24.2	-1.17 (-1.35 to -1.02)	-30.2±25.2	-1.20 (-1.38 to -1.05)
Physician global assessment VAS	-26.2±19.2	-1.37 (-1.54 to -1.22)	29.2±20.7	-1.41 (-1.58 to -1.27)
PROMIS physical function	14.8±13.7	1.08 (0.96 to 1.22)	15.5±14.0	1.11 (0.97 to 1.26)
Fatigue VAS	-13.3±29.3	-0.45 (-0.60 to -0.32)	-16.0±29.8	-0.54 (-0.68 to -0.40)
Joint pain VAS	-27.7±24.4	-1.14 (-1.31 to -0.98)	-29.5±25.2	-1.17 (-1.35 to -1.02)
SF-36 Physical component	8.99±9.02	1.00 (0.84 to 1.18)	9.19±9.47	0.97 (0.83 to 1.14)
SF-36 Mental component	3.89±10.6	0.37 (0.23 to 0.52)	3.02±10.8	0.28 (0.15 to 0.43)

The RAID score was more efficient in detecting change than the Ritchie Articular Index and also demonstrated relatively high efficiency in detecting change compared to other PROMs and clinical outcome measures (figure 1).



**Abstract SAT0725HPR – Figure 1.** Relative efficiency to tender joint count (Ritchie Articular Index) of the various outcomes reflecting disease activity at 3 months follow-up (Ritchie Articular Index = reference with a relative efficiency of 1.00).

**Conclusions:** The RAID score proved to be highly responsive to change in RA patients with short disease duration who followed a treat-to-target strategy. The RAID score was efficient in detecting change compared to other PROMs and conventional disease activity measures.

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**Disclosure of Interest:** K. Holten: None declared, J. Sexton: None declared, T. K. Kvien: None declared, E. A. Haavardsholm Grant/research support from: Pfizer, UCB, Roche, MSD and AbbVie, A.-B. Aga: None declared

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**SAT0726-HPR** **IMPROVEMENT OF HAND FUNCTION, PHYSICAL CAPACITY AND QUALITY OF LIFE OF SYSTEMIC SCLEROSIS PATIENTS AFTER AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION**

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**Background:** Systemic sclerosis (SSc) is characterised by skin thickening and visceral involvement, leading to impairment of physical function, daily life activities and quality of life. Severe cases usually have poor prognosis, despite conventional immunosuppressive treatment. Autologous hematopoietic stem cell transplantation (AHST) has been investigated as treatment for patients with severe SSc and promotes reduction of skin thickening and at least stabilisation of visceral involvement. There are no reports in the literature addressing the influence of AHST on hand function and physical capacity of SSc patients.

**Objectives:** To evaluate the impact of AHST on skin involvement, hand function, physical capacity and quality of life (QoL) of SSc patients.

**Methods:** This is a prospective longitudinal study of a cohort of 27 SSc patients who underwent AHST at a University Hospital in the state of São Paulo, Brazil. Patients were evaluated before, and at 6, 12 and 24 months after transplant. The evaluations included modified Rodnan skin score (mRSS), hand function (hand-grip strength, finger-to-palm distance – FTP, range of motion measures, DASH and COCHIN questionnaires), mouth opening, six-minute walk test (6MWT) and quality of life questionnaire (SF-36). Results were subjected to statistical analyses and significance levels were established at p<0.05.

**Results:** Twenty-seven patients were evaluated before and at 6 months after transplant, 22 of which were additionally evaluated at 12 months, and 13 patients at 24 months post-transplant. At 12 months after AHST, patients presented significant improvement of mRSS (p<0.01), hand grip strength (p<0.01), range of motion of hands (p<0.01, except for 1 metacarpophalangeal joints of both hands), FTP distance (p<0.01), DASH (p<0.01), COCHIN (p<0.01), mouth opening (p<0.01), 6MWT distance (p=0.01), and physical (p<0.01) and mental (p=0.02) components of the SF-36, when compared to pre-transplant evaluations. Significant correlations were observed between skin involvement and range of motion measures (dominant hand: R=-0.65, p<0.01; non-dominant hand: R=-0.59,

p<0.01), and between the 6MWT distance and quality of life (R=0.62, p<0.01), and between DASH and quality of life (R=-0.48, p=0.03).

**Conclusions:** AHSCT enhances the functional status of SSc patients, significantly improving skin involvement, hand function, physical capacity and quality of life. These results can be interpreted as positive outcomes of AHSCT for SSc.

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**Disclosure of Interest:** None declared

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**SAT0727-HPR CRITERION VALIDITY AND RELIABILITY OF A SUBMAXIMAL TREADMILL TEST IN JUVENILE IDIOPATHIC ARTHRITIS PATIENTS**

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**Background:** For both research purposes and daily clinical practice, a feasible exercise test with acceptable measurement properties is needed to measure exercise capacity in juvenile idiopathic arthritis (JIA) patients.

**Objectives:** To evaluate the criterion-validity, test-retest reliability and inter-rater reliability of an eight-minute submaximal treadmill test, which can be used to estimate VO<sub>2peak</sub><sup>1</sup>, in JIA patients.

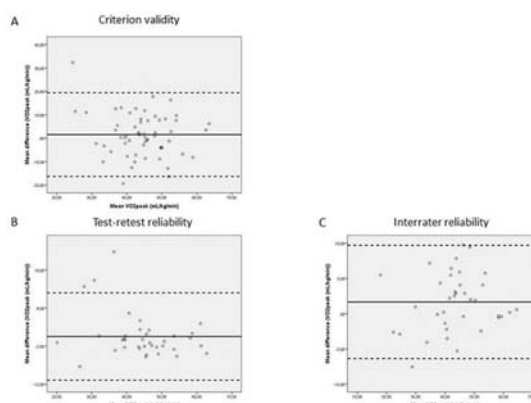
**Methods:** 59 patients with oligo- (n=30) and polyarticular (n=29) JIA (mean age (SD) 13.6 (2.2), 50 girls) participated in this study. They performed a maximal treadmill test until exhaustion to measure the VO<sub>2peak</sub> directly and the eight-minute submaximal treadmill test to estimate the VO<sub>2peak</sub>. A standardised formula was used to estimate the VO<sub>2peak</sub><sup>1</sup>. To evaluate the reliability, 37 patients also performed the submaximal treadmill test twice on the same day 1–4 weeks after the initial test. Paired t-tests were used to test potential differences between the tests. Criterion validity and reliability were evaluated with two ways mixed interclass correlation coefficient<sub>agreement</sub> (ICC). Limits of agreement (LoA) (Bland and Altman method), standard error of measurement (SEM<sub>agreement</sub>) and smallest detectable change (SDC<sub>95</sub>) were calculated to evaluate the measurement error of the submaximal treadmill test.

**Results:** No significant difference was found between the observed and estimated VO<sub>2peak</sub> (mL·kg<sup>-1</sup>·min<sup>-1</sup>), 44.8 (8.8) vs 43.2 (10.3) respectively, p=0.18. The single ICC (95% CI) value at individual level between the estimated and measured VO<sub>2peak</sub> was moderate; ICC 0.55 (0.34–0.70) while the ICC at group level was good; 0.71 (0.51–0.82). The measurement errors were large (SEM 6.5 and SDC<sub>95</sub> 18.0). The single ICC value for test-retest reliability and interrater reliability were good to excellent, 0.84 (0.71–0.91) and 0.92 (0.83–0.96), respectively. The ICC value at group level for test-retest reliability and interrater reliability were excellent, 0.91 (0.83–0.96) and 0.96 (0.91–0.98), respectively. There were no significant differences between estimated VO<sub>2peak</sub> (mL·kg<sup>-1</sup>·min<sup>-1</sup>) when comparing the results from the three performed submaximal treadmill tests. The measurement errors were moderate/large for both test-retest reliability and interrater reliability (table 1). The Bland Altman plots showed no systematic differences, but confirmed the large variability for both the validity and reliability (figure 1).

Table. Reliability and measurement error of the submaximal treadmill test

	Test*	Retest*	Difference*	SEM <sub>agreement</sub>	LoA	SDC <sub>95</sub>
Est VO <sub>2peak</sub> (mL·kg <sup>-1</sup> ·min <sup>-1</sup> )	44.9 (9.4)	44.3 (11.0)	0.6 (5.9)	4.1	-11.0–12.0	11.4
	Tester 1*	Tester 2*	Difference*	SEM <sub>agreement</sub>	LoA	SDC <sub>95</sub>
Est VO <sub>2peak</sub> (mL·kg <sup>-1</sup> ·min <sup>-1</sup> )	44.3 (11.0)	42.7 (10.5)	1.6 (4.1)	3.1	-6.4–9.7	8.6

\*Values are mean (SD).



**Abstract SAT0727HPR – Figure 1.** Limits of agreement for VO<sub>2peak</sub> (mL/kg/min) for criterion validity (A), test-retest (B) and interrater reliability (C).

**Conclusions:** The submaximal treadmill test is valid for use in JIA patients on group level, but showed only moderate validity on an individual level. The test-retest and intra-rater reliability is good to excellent; however, the measurement errors are large. Our findings indicate that the submaximal treadmill test is not optimal for use in daily clinical practice to estimate VO<sub>2peak</sub> in individual patients and it is important to be aware of the large measurement errors.

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**Disclosure of Interest:** None declared

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**SAT0728-HPR EVALUATION OF THE EFFECTIVENESS OF AN EDUCATIONAL PROGRAM IN PATIENTS WITH OSTEOARTHRITIS OF THE KNEES**

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**Background:** Osteoarthritis (OA) is the most common chronic joint disease, affecting about 50% of the population aged 65 or over, its incidence tends to increase according to the age.

Educational intervention is considered an important part of treatments for chronic diseases. However, in the literature, for OA there is still no standard of educational program to be followed.

**Objectives:** To evaluate the effectiveness of the educational intervention in patients with knee osteoarthritis regarding to pain, function, anxiety and quality of life

**Methods:** Sixty patients with knee OA, both genders and age between 40 to 80 years, were included. The patients were randomised into 2 groups: Experimental Group (EG) received an educational intervention, composed of 5 consecutive sessions held once a week, with a duration of 60 min each session. At the end of the last class, a booklet was given to each patient with all the content of the classes. In addition to the educational program, this EG also received a TENS (Transcutaneous Nerve Electrical Stimulation) treatment performed twice a week for 5 weeks for 40 min each session. Control group (CG) received the same TENS treatment as EG group.

The evaluations were performed at baseline, 4 and 12 weeks after baseline with the following instruments: numerical pain scale (NPS) for pain; WOMAC questionnaire and 6 min walk test for function; IDATE questionnaire for anxiety and SF-36 questionnaire for quality of life.

**Results:** Regarding the variables pain, function, anxiety and quality of life, no statistically significant difference was found between groups over time. (table 1)

The intragroup comparisons show no improvement in both groups between T0 and T4 and T0 and T12for: pain; function total and pain score of WOMAC and domains physical role functioning and social role functioning of SF-36 (table 1)

Abstract SAT0728HPR – Table 1. – Intergroup and intragroup comparisons

	Control group n=30			Experimental group n=30			p interaction	
	T0	T4	T12	T0	T4	T12		
Numerical pain scale (cm)	6.3761.39	4.8922.27*	5.0661.73*	6.2321.62	4.7621.12*	5.5652.24*	0.377	
WOMAC questionnaire	Total	35.2215.4	31.9217.1*	30.8216.9*	35.6119.1	30.2219.6*	32.4217.60*	0.623
	Pain	9.1023.82	8.4724.07*	8.6023.69*	8.5024.68	8.6724.46*	8.7724.14*	0.391
	Stiffness	3.9324.09	2.9721.13	2.9721.33	3.2722.20	3.0722.12	2.9721.87	0.79
	Physical function	21.7211.33	22.9212.9	21.3213.0	24.1114.0	21.4214.2	22.6713.4	0.438
GATE questionnaire	Trace	30.9218.3	31.8218.3	31.4214.5	43.1114.3	42.7210.3	45.4211.7	0.529
	State	48.4211.7	48.9214.2	47.9215.6	51.8213.6	52.7212.2	51.8210.7	0.406
SF-36 questionnaire	Physical functioning	50.0222.9	48.9229.1	60.9225.9	45.7229.2	53.1228.9	51.2228.5	0.12
	Physical role functioning	35.7232.4	44.2234.5*	52.8236.4*	38.3241.	51.2235*	49.7228.5*	0.529
	Bodily pain	44.0220.7	50.3221.1	52.7223.1	31.224.5	48.0225.5	47.4222.2	0.885
	General health perceptions	50.4224.1	59.1227.3	65.9227.2	58.2222.0	63.7221.2	59.4221.2	0.192
	Vitality	49.1223	54.9224.3	59.224.6	51.9221.2	54.224.1	44.7222.1	0.125
	Social role functioning	33.4225.9	35.1224.1*	33.3216*	38.3214	38.3224.3*	37.10223.8*	0.052
	Emotional role functioning	52.2230.0	63.3249.1	72.4244.7	42.2247.9	63.3249.0	46.7250.7	0.211
	Mental health	52.8225.3	66.3247.2	66.2248.8	60.7228.4	59.1245.5	62.7248.7	0.561
	5-Minute walking test (meters)	356.92110.1	376.2296.0	370.92105.1	360.12112.3	369.02102.9	394.2116.6	0.454

\* = p &lt; 0.05 in the intragroup analysis compared to baseline.

**Conclusions:** This educational intervention was not effective in improving pain, function, anxiety and quality of life in patients with osteoarthritis of the knees.

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#### SAT0729-HPR FIRST EXPERIENCES WITH ONLINE REMOTE MONITORING IN PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASES

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**Background:** Inflammatory rheumatic diseases (IRDs) such as Rheumatoid Arthritis (RA) and Psoriatic Arthritis (PsA) are characterised by a fluctuating disease course. Because of these fluctuations, the disease activity in between outpatient visits can be different from the disease activity objectively measured at outpatient visits. In order to capture the in between disease activity and to encourage patients to take an active role in their disease management, iMonitor<sup>1</sup> was developed. This online self-monitoring tool allows patients to complete Patient-Reported Outcome Measures (PROMs) in order to get insight in their disease activity.

**Objectives:** To gather patient experiences regarding online remote monitoring in IRDs and to provide recommendations in order to efficiently arrange and optimise self-monitoring.

**Methods:** This mixed-method study was conducted at a teaching hospital (Bernhoven, Uden, the Netherlands) from April 2016 until August 2017. Adult patients with RA or PsA were eligible to participate and were recruited by means of purposive sampling. Four instruction classes were organised in which patients received instructions regarding how to use iMonitor. Patients indicated which PROM(s) they preferred to complete (HAQ, RAID, and/or RADAI-5) and at which frequency (one-, two-, four-, six-, or eight-weeks). The system generated an alert email accordingly, adherence was determined by checking whether the PROM was completed within the time interval. Level of congruence between DAS28-scores and PROM-values (very poor – very good) were independently determined by two researchers (LR and PvR). Facilitators and barriers with regard to using iMonitor were collected by means of a focus group discussion and four telephone interviews.

**Results:** Seven patients with PsA and 32 with RA participated in this study. Most were female (n=23, 59%). Mean (±SD) age was 56.6 (10.7) years. RAID was chosen most often (29 times). Most patients (n=25) chose a four-week PROM-frequency. Mean adherence was 52.9%, patients with a one-week frequency were most compliant (73.8%). Regarding the congruence between DAS28 and PROMs, RAID scored best. Overall, patients were positive about iMonitor. They felt more aware about their disease and its consequences, felt supported in

handling their disease, and gained more knowledge about their disease (activity). Based on our first experiences, recommendations for optimal self-monitoring are: 1) Patients need to be actively recruited 2) Tailored education (e.g. instruction class) is useful for some patients in order to get familiar with the program. 3) Patients need to get feedback from their healthcare provider regarding their outcomes. 4) Working with a stand-alone system such as iMonitor is not feasible, it should be integrated in an existing (hospital) system.

**Conclusions:** Self-monitoring is a first step towards personalised healthcare. Patients become more aware about their disease and gain more knowledge about their disease (activity), which can result in increased self-management. Future research should investigate the possibility of skipping outpatient visits for those patients with stable disease activity.

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- [1] iMonitor, developed and funded by Pfizer <http://www.imonitor-med.co.uk>

**Disclosure of Interest:** None declared

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#### SAT0730-HPR DEVELOPMENT OF PSYCHOMETRICALLY EQUIVALENT SHORT FORMS TO MEASURE DISEASE AND TREATMENT ASSOCIATED KNOWLEDGE IN RHEUMATOID ARTHRITIS: APPLICATION OF ITEM RESPONSE THEORY (IRT)

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**Background:** Patient education can be used to support and enable people with Rheumatoid Arthritis (RA) to optimise health and wellbeing. It has been recommended as an integral part in management of RA in order to undertake self-management activities or to adhere to treatments. Disease-specific knowledge can be measured with a Patient Knowledge Questionnaire (PKQ). Because PKQs in RA are outdated, de Jonge et al. developed the Disease and Treatment Associated Knowledge in Rheumatoid Arthritis (DataK-RA) item bank and provided preliminary evidence to support its construct validity. It was developed with input from patients and rheumatology experts. DataK-RA contains 42 multiple choice items with 2–4 response alternatives per item and was calibrated using the two parameter item response model for dichotomous responses. IRT scores are corrected for item characteristics, which allows scores to be compared between measures that include different items. IRT models also provide detailed information about the precision of scores at different levels of knowledge. Various methods are available that can help select optimal items to be administered to patients, given certain criteria.

**Objectives:** The objective of this study was to develop two DataK-RA short forms using linear optimal test design.

**Methods:** The open source excel add in “solver” was used to program a linear optimisation algorithm to develop two short forms. The algorithm was instructed to optimise precision (i.e. reliability) of the scores for both short forms, subject to the constraints that: 1) each item could only be included in one short form 2) each short form should include 15±1 items, 3) reliability for each short form should be >0.70 for all patients who are within 1 SD of the mean of knowledge scores, and 4) scores on each short form should be similarly precise, defined as maximum allowable difference in information of 0.15.

**Results:** Two short forms were derived from the DataK-RA item bank that satisfied all content constraints. The short forms include respectively 15 and 16 unique items. Reliabilities across different score levels ranged from 0.71–0.80 for both short forms, and the maximum difference in information between the short forms was 0.13.

**Conclusions:** DataK-RA is a new and promising tool that can be used by healthcare providers to measure disease and treatment related knowledge in patients with RA. The short forms can be used in pre/posttest intervention studies in which disease related knowledge is one of the outcomes. Because each short form includes unique items and IRT scores are adjusted for item characteristics, the application of these short forms will allow users of DataK-RA to avoid learning effects commonly associated with using the same items at two occasions. Furthermore, the equal and high reliabilities of both forms ensure that the observed score distributions for both versions will have similar variances.

**Disclosure of Interest:** None declared

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**SAT0731-HPR** EARLY POSTOPERATIVE OUTCOMES OF UNILATERAL VERSUS BILATERAL TOTAL KNEE ARTHROPLASTY

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**Background:** Many patients in need of total knee arthroplasty (TKA) have bilateral symptoms and require surgery to both extremities. Performance of a bilateral procedure under a single anaesthetic provides a reduced hospitalisation time, an isolated anaesthesia risk, a single rehabilitation, and substantial cost savings. However, previous studies' reports vary from unilateral TKA producing better outcomes than bilateral TKA, the 2 procedures producing no significant difference, and bilateral TKA producing a better outcome than unilateral TKA. There is a need for new studies to examine the differences between unilateral and bilateral TKA in terms of the early postoperative outcomes.

**Objectives:** The aim of this study was to compare the effect of the unilateral and bilateral TKA on the early postoperative outcomes.

**Methods:** The study group consisted of 71 patients (106 knees), who underwent primary TKR because of arthrosis were stratified either unilateral or bilateral TKA status. The mean age of unilateral (n=36) subjects were 66.00±10.71 years, and the mean age of bilateral (n=35) subjects were 64.17±7.61 years. Patients were evaluated regarding the knee function score (Hospital for Special Surgery (HSS) score), pain (Numeric Pain Rating Scale (NPRS)), knee range of motion, length of hospital stay, the day of active straight leg raise, the day of knee flexion angle achieved 70 degrees, quality of life (Short-Form 12 Health Survey (SF-12)). Functional activities were evaluated using the Iowa Level of Assistance Scale and walking speed was evaluated using the Iowa Ambulation Velocity Scale. Patients were evaluated preoperatively and at discharge. All patients underwent the same rehabilitation program.

**Results:** At baseline, demographic and anthropometric characteristics were similar in groups and there was no statistically difference between groups (p>0.05). When the patients' knee range of motion were compared, there were statistically differences (p=0.027) between groups after surgery. The unilateral group had better results in terms of postoperative knee flexion degree. There were no statistical differences in terms of the pain degree, HSS score, length of hospital stay, the day of active straight leg raise, the day of knee flexion angle achieved 70 degrees, IOWA help level and IOWA walking speed, SF-12 score between groups before and after TKA (p>0.05).

**Conclusions:** According to our results, the unilateral group had better result in terms of postoperative knee flexion degree. On the other hand, the bilateral method may provide an advantage in terms of a single rehabilitation, and substantial cost savings. Therefore, in this comparison to obtain more comprehensive results studies on larger series are needed. In this way, a more uniform and objective data can be achieved.

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**SAT0732-HPR** RATING OF PERCEIVED EXERTION IN PATIENTS WITH RHEUMATOID ARTHRITIS – WHICH ARE THE CORRELATES?

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**Background:** People with rheumatoid arthritis (RA) are recommended to participate in physical activity to improve or maintain their health. The intensity of the physical activity is important to gain the health benefits. One way for the individual to monitor the intensity of physical activity is to use the Borg scale for rating of perceived exertion (RPE), which is claimed to be strongly correlated to heart rate (HR). While this is true for healthy individuals, RPE in people with RA might however be influenced by a range of additional factors.

**Objectives:** To analyse correlates of RPE assessed at the end of an aerobic capacity test in patients with RA.

**Methods:** Data from 192 people with RA participating in the <sup>PARA</sup> 2010 study were analysed. Their mean age was 59 years (SD 9.7), 159 (83%) were women, mean disease duration was 12 years (SD 9.4), mean DAS28 score was 2.95 (SD 1.25) and median Health Assessment Questionnaire (HAQ) score 0.375 (range 0–1.875). Submaximal tests of aerobic capacity on bicycle ergometers were performed according to the Åstrand protocol and perceived exertion was rated on the Borg RPE scale.<sup>9–20</sup> Data on the potential correlates pain (VAS, 0–100), fatigue (VAS, 0–100), general health perception (GHP, VAS, 0–100), lower extremity function (Timed Stands Test, TST, s), healthy physical activity levels (yes/no),

activity limitation (HAQ, 0–3), fear avoidance beliefs (Fear avoidance beliefs questionnaire, FABQ, 0–24), exercise self-efficacy (Exercise Self Efficacy Scale, ESES, 6–60), and depression (EQ5D, question # 5, 1–3) were collected. Generalised linear models (GLM) with normal log models were used to calculate each variable's correlation with the RPE. Correlates with p-value<0.10 were entered in a forward stepwise model.

**Results:** The correlation between RPE and working HR at the end of the aerobic capacity test was  $r_s=0.15$  (p<0.05). Analysis using GLM identified general health perception, lower extremity function, activity limitation, depression, resting HR and working HR as correlates of RPE with p-value<0.10. A forward stepwise model including these variables, together with age and gender, identified lower extremity function (OR: 1.0044/s, p=0.0001), resting HR (OR: 0.9977/beat, p=0.0071) and working HR (OR: 1.0030/beat, p<0.0000) as correlates of RPE.

**Conclusions:** As expected, RPE correlated with working HR, but only weakly. Although our study participants were instructed to focus on perceived central exertion in their ratings, it seems that they were not able to distinguish that from peripheral exertion. Considering this bias in ratings, wearable HR monitors should be recommended to people with RA for accurate feedback on physical activity intensity.

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**SAT0733-HPR** DUTCH RECOMMENDATIONS FOR PHYSICAL THERAPY IN AXIAL SPONDYLOARTHRITIS (AXSPA)

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**Background:** According to the ASAS/EULAR recommendations, physical therapy (PT), especially exercise therapy, is an essential element within the management of axSpA.<sup>1</sup> In the Netherlands considerable variation in the delivery of PT was observed,<sup>2</sup> suggesting suboptimal care delivery. This practice variation is likely to be related to the lack of specific recommendations regarding referral, assessment, content, and monitoring of its effectiveness and safety.

**Objectives:** To develop practice recommendations on PT in axSpA.

**Methods:** A taskforce of 31 experts was responsible for the recommendations. It consisted of patients,<sup>2</sup> rheumatologists,<sup>7</sup> physical therapists,<sup>13</sup> policy makers,<sup>3</sup> researchers<sup>2</sup> and representatives of patient organisations.<sup>4</sup> These were based on scientific evidence, expert opinion and patient values and were formulated following a combination of literature review and three expert-group meetings. Clinical questions were formulated in the first expert-group meeting. Then, a systematic literature review was performed to answer the clinical questions. It focused on systematic reviews, meta-analyses and (inter)national guidelines recommendations and consensus statements published after 2010 in English or Dutch. When this approach did not yield sufficient information, relevant RCTs or other types of research designs addressing (one of) the clinical questions were selected. Subsequently, draft recommendations based on the literature, expert opinion and patient values were formulated and discussed in a second meeting. In the third expert group meeting the recommendations were finalised and the level of agreement was determined by a written voting (rating from 1 (total disagreement) to 10 (total agreement)). We defined agreement if at least 80% voted ≥8.

**Results:** In the first meeting 18 clinical questions were formulated. Six questions pertaining to the content and safety of PT were merged and integrated. In total 12 practice recommendations were formulated on indication,<sup>2</sup> referral,<sup>2</sup> assessment/monitoring,<sup>2</sup> treatment,<sup>5</sup> reporting<sup>1</sup> and safety.<sup>2</sup> (Figure 1) Three recommendations were (partly) based on level 1 evidence (Dutch Evidence Based guidelines, EBRO); others were based on lower levels combined with the opinion of experts written in literature. Agreement was reached for 11 out of 12 recommendations. Mean levels of agreement were high and varied between 8.5–9.1.

Indication and referral	
1	Describes indications and reasons for referral to a PT
2	Describes the information that a referral to a PT should contain
Assessment and monitoring	
3	Describes selection of domains, personal and environmental factors that should be assessed at intake and monitoring
4	Describes recommended and optional measuring instruments in the PT assessment
Analysis, objectives, treatment plan, and treatment	
5	Describes on which factors the choice for the duration and form of a PT intervention should be based
6	Describes how a personalized plan should be made and which elements are included (information, education, supervised exercise therapy and planning)
7	Describes the intensity, duration and frequency of the exercise therapy and exercise plan, including monitoring
8	Describes when land or water-based exercise therapy is preferred.
9	Describes which interventions are not recommended in treatment.
Reporting	
10	Describes the information a report from a physiotherapist should contain to give insight in the treatment-effects
Safety	
11	Describes that consideration should be taken to certain comorbidities and axSpA specific aspects that can influence the daily functioning and the therapeutic process and what the contra-indications and PT modalities are
12	Describes information relevant to patients in relation to an increased fracture risk

**Abstract SAT0733HPR – Figure 1.** Short description of the content of the Dutch recommendations for physical therapy in axial Spondyloarthritis (axSpA)

**Conclusions:** Using a standardised process of professional guideline development, 12 practice recommendations for PT management of patients with axSpA were developed. They can guide clinicians and physiotherapists dealing with patients with axSpA, ultimately leading to a delivery of a better care. Next steps are the ratification by relevant professional societies as well as dissemination and implementation.

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#### **SAT0734-HPR** CORRELATES OF PAIN AND PREDICTORS OF PAIN RELIEF IN A CONTROLLED RA STUDY IN INDIAN PATIENTS

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**Background:** Potassium (K) enriched vegetarian diet (PEVT) significantly reduced pain (primary hypothesis and efficacy) compared to ad libitum diet in RA patients on standard drugs. We had earlier validated Indian version of RA Pain Scale/RAPS. EULAR 2014

**Objectives:** To determine correlates of pain (VAS) and RAPS and predictors of 'pain relief' in RA in a dietary intervention study

**Methods:** In the primary study, 172 consenting symptomatic patients ( $\geq 4$  cms pain VAS) were randomised into a 3 arm 16 week study [2 active PEVT arms, 1 control routine diet] with ongoing background medication [72% methotrexate, 60% prednisolone]; 155 patients completed study. Evaluation included ACR core set and other measures (plus dietary) and RAPS (4 domains- physiological, affective, sensory discriminative, cognitive; 24 questions, score 0–144). The study (80% power,  $\alpha < 0.05$ ) sample size was based on improvement in pain VAS (0–10 cms, with no pain at 0). Reduction in pain VAS of at least 1 cm on VAS was considered 'responder'. A Pearson correlation matrix was computed. A linear logistic regression model was used (good fit after 5 iterations). The dependent variable was number of 'respondents' (pain). 28 independent variables included clinical (+patient functional), laboratory (+steroid assay), drug use and dietary analytics

(+micronutrients) at baseline. From the latter, 13 qualified variables (a priori significance) were run in a forward stepwise model.

**Results:** Data below shows significant correlation of pain measures ( $p < 0.05$ ). Other measures with significant correlation  $\geq 0.3$  were: patient global assess-DAS 28, C-reactive protein (CRP)-Erythrocyte Sed rate (ESR), Haemoglobin-ESR, health assessment questionnaire score (HAQ)-medical outcome short form 36 physical (SF 36-phy), DAS 28-painful tender joint count, HAQ-general health on 100 mm VAS (GH). Significant ( $p < 0.05$ ) predictors in the first regression run were allocation to K intervention, female gender, and disease duration (less than 5 years). In the subsequent run, the significant predictors [Odds's Ratio, 95% confidence interval] were: K allocation arm (1.13, 5.27), disease duration less 5 years (1.98, 9.67), female gender ( $p = 0.01$ ), serum K (1.44, 6.29), body mass index (0.99, 4.76)

Correlates of RAPS: Swollen joint count (0.16), general health assessment 100 mm VAS (–0.18), morning stiffness (0.16), SF 36 phy (–0.35), SF36-mental (–0.21), serum potassium/K (0.16), C-reactive protein (0.25)

Correlates of PAIN VAS: Painful joint count (0.16), general health assessment 100 mm VAS (–0.43), C-reactive protein (0.2), dietary K (–0.22)

**Conclusions:** Despite a complex questionnaire, RAPS shared significant correlates with the popular and seemingly simplistic pain VAS. The association between dietary K and pain VAS was inverse and modest ( $p < 0.01$ ) and consistent with the primary study hypothesis. The predictors of pain response included patient 'allocation to the PEVD' in support of the efficacy result in the primary study.

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#### **SAT0735-HPR** SEX DIFFERENCES IN ILLNESS PERCEPTIONS AND SELF-MANAGEMENT IN PATIENTS WITH GOUT

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**Background:** Illness perceptions are important and can influence all aspects of management in chronic diseases. Differences in gender aspects of illness perceptions have been shown for other diseases, but have scarcely been examined in gout. Lifestyle and dietary adjustments are principal components of self-management of gout.

**Objectives:** to examine illness perception, self-management strategies and advice from healthcare professionals in Swedish patients with gout by sex.

**Methods:** All patients above 18 with diagnose of gout were identified from 12 primary centres (serving a population of 1 00 000 inhabitants) and one rheumatology clinic within western Sweden. Patients were sent a questionnaire including gout characteristics, demographics, illness perception questionnaire (B-IPQ), questions about diet, alcohol and advice from health care professionals. Age-adjusted differences between sexes were analysed in logistic regression models

**Results:** Of 1589 individuals with a gout diagnosis, 868 (69.3%) responded to the survey. The proportion of men was 80%. Mean age was 70 years for men and 75 years for women. Women reported modest but significant worse illness perception with regard to severity of disease, identity, concerns and emotional response (see table 1). Women had made more dietary food changes, whereas there was no difference regarding changes in alcohol reduction. Advice from health personal regarding dietary changes had more often been given to men (53% vs 22%) and among obese patients (BMI  $> 30$  kg/m<sup>2</sup>) more men (65% vs 47%) had been given advice about weight reduction.

**Conclusions:** Men with gout perceive their illness as less serious and are less likely to make dietary adjustments compared to women, despite been given more lifestyle advice from health care personal. There may be a need to focus more on how advices regarding disease and life style changes are given from a gender perspective for achieving optimal results.

**Disclosure of Interest:** None declared

Brief-Illness Perception Questionnaire	Men (n=653)	Women (n=154)	p-value*
	mean±SD	mean±SD	
<b>Consequences</b> (10=severely affects life)	2.8±2.6	3.8±3.0	<0,01
<b>Timeline</b> (10=will continue forever)	6.9±3.7	6.8±3.7	0,87
<b>Personal control</b> (10=extreme amount)	5.8±3.3	5.3±3.5	0,19
<b>Treatment control</b> (10=extremely helpful)	6.8±3.0	6.2±3.2	0,08
<b>Identity</b> (10=many severe symptoms)	3.3±2.9	4.0±3.1	<0,01
<b>Concerns</b> (10=extremely concerned)	3.1±3.0	3.8±3.3	<0,01
<b>Understanding</b> (10=very clearly)	5.9±3.2	5.4±3.2	0,26
<b>Emotional response</b> (10=extremely affected)	2.5±2.8	3.1±3.1	<0,01
<b>Questions: dietary changes, health care advice</b>	Yes (%)	Yes (%)	
Have you reduced your intake of seafood?	13%	23%	<0,01
Have you reduced your intake of meat?	19%	41%	<0,01
Have you reduced your intake of organ meats?	45%	69%	<0,01
Have you reduced your intake of alcohol?	44%	48%	0,47
Have you been advised by health care professionals about dietary changes?	53%	22%	<0,01
Have you been advised by health care professionals about weight loss? **	65%	47%	0,04

\* Adjusted for age \*\* In those with BMI >30 kg/m<sup>2</sup> (men: 25%, women: 40%)

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### SAT0736-HPR COMPARISON OF CORE STABILISATION AND BALANCE IN HEALTHY CONTROLS AND PATIENTS WITH ANKYLOSING SPONDYLITIS

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**Background:** Ankylosing spondylitis is thought to cause balance problems. One component of balance is core stability. Core stability can be defined as the ability of the lumbopelvic-hip complex to control the trunk in response to disturbances generated by movement of the limbs, or other perturbations. There is limited literature about balance problems in AS. However there is no study investigating the effect of AS on core stability.

**Objectives:** The aim of this study was to investigate whether there is a difference in balance and core stabilisation between patients with ankylosing spondylitis(AS) and healthy individuals.

**Methods:** 64 patients(40 male, 24 female) with AS and 64 healthy controls(39 male, 25 female) were included in this study. Demographic and physical characteristics(age, height, weight, body mass index) were recorded. Static and dynamic balance was evaluated with Biodex Balance System SD. Anteroposterior(AP), mediolateral(ML) and overall(OA) postural stability indices were obtained with bilateral stance(stable and unstable platform), single leg stance(stable platform). Also overall, forward, backward, right and left limits of stability were evaluated. For evaluation core stabilisation static and dynamic core endurance tests and hip strength assessment were used. Modified sit-up test for dynamic core endurance and four static endurance tests (flexor endurance, extensor endurance and lateral side bridge tests) recommended by McGill et al for static core endurance were used. Hip strength measurement were assessed by hand-held dynamometer.

**Results:** There were no significant differences between groups regarding to gender, age, weight, height, body mass index(p<0,05). Overall, anteroposterior and mediolateral indices for bilateral stance(stable platform) and left leg stance(stable platform) were statistically better in control group(p<0,05). Overall, forward, backward and right limits of stability scores were significantly higher in control group (p<0,05). All of the core endurance tests were statistically better in control group (p<0,05) table 1. Although all of the hip strength measurements were higher in control group than AS group, only statistically significant difference was found in hip abduction strength(p<0,05).

Abstract SAT0736HPR – Table 1. Comparison of the core endurance test results

	AS group(n=64) Median(IQR 25–75)	Control group(n=64) Median(IQR 25–75)	p value
Trunk flexion	34,10 <sup>(20,00–53,50)</sup>	56,50 <sup>(40,92–82,50)</sup>	0,00*
Trunk extension	43,30 (22,06–69,75)	86,00 <sup>(71,25–106,62)</sup>	0,00*
Right side bridge(s)	40,70 <sup>(23,12–59,95)</sup>	61,00 (43,5–84,38)	0,00*
Left side bridge(s)	40,00 <sup>(25,70–58,92)</sup>	61,5 (45,20–82,25)	0,00*
Sit-up test	17,50 <sup>(7,00–26,75)</sup>	24 <sup>(15,25–30,00)</sup>	0,004*

Mann Whitney U test. IQR: Interquartile Range \*p<0,05

**Conclusions:** To our knowledge this is the first study that investigating core stability in AS patients. The findings of this study showed AS patients have reduced core endurance and hip abductor strength. According to our results AS has negative effect on bilateral stance, left leg stance postural stability and limits of stability.

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### HPR Epidemiology and public health (including prevention)

#### SAT0737-HPR MEASURES OF PHYSICAL ACTIVITY AND FEAR AVOIDANCE IN PEOPLE WITH CHRONIC PAIN

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**Background:** Lifestyle factors such as physical activity (PA) has the possibility to contribute to improved health and quality of life in the population as well as in



chronic diseases. Most often PA is self-reported while measures of the aerobic capacity are more seldom measured in subjects with chronic pain.

**Objectives:** To describe physical activity levels (self-reported and aerobic capacity) in people with chronic pain classified as regional or widespread and to compare the findings with a group that report no pain.

**Methods:** From the 2016 follow-up of the Swedish population based Epipain cohort (n 1321), 146 subjects were invited to a clinical assessment where the aerobic capacity was assessed by using a submaximal bicycle test, the Ekblom-Bak test, together with assessment of the Borg scale for perceived exertion (RPE). Aerobic capacity was also classified as low, average or high according to data from the general population. Self-reported physical activity was coded as MVPA<sub>rec</sub> if recommended levels of PA was reported (physically active on a moderate level  $\geq 150$  min/week (MPA) or on an vigorous level  $\geq 75$  min/week (VPA) or not). The Fear Avoidance Beliefs Questionnaire for PA (FABQ-PA, 0–24 best to worst) and for work (FABQ-W, 0–48 best to worst) were also assessed. The participants were classified as having chronic widespread pain (CWP), chronic regional pain (CRP) or no chronic pain (NCP) based on a pain mannequin presenting 0–18 pain regions and if pain had lasted for 3 months or more. Chi2 and Kruskal-Wallis tests were performed to study differences between the three pain groups.

**Results:** 141/146 (97%) subjects (mean (SD) age 59.4 (8.2) years) whereof 61% were women, could be classified into pain groups; 43 as CWP (84% women), 43 as CRP (42% women) and 55 as NCP (58% women). The group with CWP was slightly older than those with CRP (mean (SD) age 57.0 (7.6) years vs. 61.9 (6.9) years,  $p < 0.02$ ). The CWP group also had lower aerobic capacity (mean (SD) 2.2 (0.5) l/min vs. 2.6 (0.6) l/min,  $p < 0.03$ ), and a larger proportion was classified as having low aerobic capacity (CWP 21%, CRP 7% and NCP 10%,  $p < 0.04$ ). The proportion of MVPA<sub>rec</sub> did not differ between the groups: CWP 70%, CRP 81% and NCP 74% ( $p > 0.5$ ). There was neither a difference between the groups in BMI, RPE or in sitting hours/week ( $p > 0.6$ ). However, differences were found in the FABQ where in the PA scale those with CRP had worse scores compared with NCP (mean (SD) 11.2 (7.3) vs. 6.0 (6.0),  $p < 0.001$ ), the difference between CWP (mean (SD) 8.9 (6.7)) and NCP was  $p < 0.06$ . In the work subscale of FABQ, CWP had worse scores compared with CRP (mean (SD) 18.9 (15.7) vs. 10.0 (12.5),  $p < 0.002$ ) and CRP had worse scores compared to those with NCP (mean (SD) 10.0 (12.5) vs. 6.5 (9.1),  $p < 0.001$ ).

**Conclusions:** In this sample of subjects with chronic pain or no pain, having widespread pain tended to affect the aerobic capacity negatively while self-reports of reaching recommended levels of physical activity did not differ between groups. Fear avoidance in relation to physical activity and especially in relation to work was more noticeable in subjects with chronic pain compared to those with no pain. Measures of aerobic capacity and information of fear avoidance beliefs might help health professionals to better tailor the non-pharmacological treatment for subjects with chronic pain.

**Disclosure of Interest:** None declared

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#### SAT0738-HPR FACTORS ASSOCIATED WITH RISK OF FALLING IN ADULTS WITH KNEE OSTEOARTHRITIS: A CROSS-SECTIONAL STUDY

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**Background:** There is evidence of increasing number of falls in adults with knee osteoarthritis (OA). However, the contributing factors for falling in adults with knee OA has not been substantially investigated.

**Objectives:** This cross-sectional study aimed to explore the relationship between falling in adults with knee OA and clinical characteristics of knee OA such as balance, pain, instability, muscle strength, and physical function.

**Methods:** Participants with knee OA were recruited from the community (Dunedin, New Zealand). The protocol of the study was registered in Australia New Zealand Clinical Trial Registry (ACTRN 12617000154303). Falls characteristics in the preceding year were collected to distinguish between those with and without history of falling. All participants completed the following measures: Sensory Organisation Test (SOT) using NeuroCom SMART Equitest system, version 8.4.0 which produced Composite Score; Knee injury and Osteoarthritis Outcome Score for knee OA related symptoms; Knee outcome survey for self-reported knee instability (buckling); Nicholas MMT hand-held dynamometer for quadriceps and hamstrings isometric muscle strength measured at 20 and 70 degrees; and Timed-Up and Go (TUG) test for physical function.

**Results:** Sixty-three participants with knee OA (30 female, 33 male), with a mean age (SD) of 53.78 (16.17) years were included in the study. Thirty-one (49%) participants reported at least one fall in the previous 12 months. The independent t-test suggested that the SOT Composite Score in fallers was significantly less (mean  $\pm$ SD: faller=72.16 $\pm$ 3.26, non-faller=74.84 $\pm$ 4.77;  $p < 0.012$ ) and the TUG test was significantly longer (mean  $\pm$ SD: faller=7.64 $\pm$ 1.29, non-faller=6.74 $\pm$ 0.78;

$p < 0.001$ ) when compared with the non-faller group. Also, lower muscle strength of knee flexors and extensors were significantly less in the faller group ( $p < 0.05$ ). Falling in the previous 12 months was associated with Composite Score (OR 0.85, 95% CI 0.74–0.97,  $p = 0.017$ ), knee extensors strength [20 degrees (OR 0.76, 95% CI 0.66–0.82,  $p = 0.025$ ) and 70 degrees (OR 0.71, 95% CI 0.55–0.91,  $p = 0.008$ )], and TUG test (OR 2.65, 95% CI 1.32–5.31,  $p = 0.006$ ) using univariate logistic regression analysis. There were no changes in these results with multivariable analyses adjusting for age, gender, and body mass index.

**Conclusions:** The study demonstrated that balance, knee muscle strength, and performance of physical function significantly differed between those with and without the history of falling. An understanding of these risk factors may help in implementing an appropriate evaluation and intervention strategy to reduce falls in this patient population. Given the prevalence of falls in knee OA, this study suggests that falls assessment should be part of the clinical practice routine when evaluating patients with knee OA.

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#### SAT0739-HPR OCCUPATIONAL EXPOSURE TO PESTICIDES INCREASES THE RISK OF RHEUMATOID ARTHRITIS: RESULTS FROM THE MALAYSIAN POPULATION-BASED CASE-CONTROL STUDY

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**Background:** Several studies have suggested farming occupation with exposure to pesticides as risk factor for rheumatoid arthritis (RA).

**Objectives:** We investigated the association between pesticides exposure and risk of RA subsets in the Malaysian population.

**Methods:** Data from the Malaysian Epidemiological Investigation of Rheumatoid Arthritis (MyEIRA) population-based case-control study involving 1055 early RA cases and 1057 age, sex and residential area matched controls were analysed. All study subjects answered a structured questionnaire on a broad range of issues including occupational exposures to pesticides. The self-reported information on ever/never occupationally exposed to pesticides was used to estimate the risk of developing ACPA-positive and ACPA-negative RA. Association between pesticides exposure and the HLA-DRB1 shared epitope (SE) was evaluated.

**Results:** The proportion of ACPA positivity in the RA patients was 64.4% and 1.9% in the normal controls. The presence of HLA-DRB1 SE alleles in RA patients was 40.2% and 15.8% in the normal controls. Our data demonstrated that occupational exposure to pesticides was significantly associated with an increased risk of developing RA in the Malaysian population (OR 2.31, 95% CI 1.12–4.73,  $p = 0.03$ ). The association between occupational exposure to pesticides and risk of RA was observed with ACPA-positive RA (OR 3.10 95% CI 1.49–6.47,  $p = 0.003$ ), but not with ACPA-negative RA. A dramatically increased risk for ACPA-positive RA was seen in individuals who both exposed to pesticides occupationally and carried SE alleles (OR 28.06, 95% CI 3.58–220.09,  $p < 0.0001$ ).

**Conclusions:** This study demonstrates that occupational exposure to pesticides is associated with an increased risk of ACPA-positive RA in Malaysian population.

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**SAT0740-HPR** **PARITY AND THE RISK OF DEVELOPING RHEUMATOID ARTHRITIS: EVIDENCE FROM THE MALAYSIAN EPIDEMIOLOGICAL INVESTIGATION OF RHEUMATOID ARTHRITIS CASE-CONTROL STUDY**

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**Background:** Recent evidence from epidemiological studies has suggested that reproductive factors may play an important role for rheumatoid arthritis (RA) development. An inverse association was reported in several studies between parity and risk of RA.

**Objectives:** We investigated the association between parity and risk of anti-citrullinated peptide antibody (ACPA)-positive RA and ACPA-negative RA in the Malaysian population.

**Methods:** Data from the Malaysian Epidemiological Investigation of rheumatoid Arthritis (MyEIRA) population-based case control study involving 902 female early RA and 906 age and residential area-matched female controls were analysed. Parity history was assessed through a questionnaire. Parous women were compared with nulliparous women, by calculating odds ratio (OR) with 95% confidence intervals (CI).

**Results:** Our findings demonstrated that parity was significantly associated with decreased risk of developing RA in the Malaysian population (RA versus controls, 82% vs. 89%, OR 0.58, 95% CI 0.44–0.77,  $p < 0.001$ ). The association between parity and risk of RA was uniformly observed for ACPA-positive RA (OR 0.58, 95% CI 0.43–0.80,  $p < 0.001$ ) and ACPA-negative RA (OR 0.58, 95% CI 0.40–0.84,  $p < 0.01$ ) subsets, respectively. Compared with nulliparous women, the decreased risk was pronounced at the level of three and more live births for both ACPA-positive (OR 0.48, 95% CI 0.34–0.66,  $p < 0.001$ ) and ACPA-negative RA (OR 0.46, 95% CI 0.31–0.68,  $p < 0.001$ ) subsets.

**Conclusions:** Our data demonstrated that parity and level of three and more live births was associated with decreased risk of developing RA in the Malaysian population. The associated decrease risk was observed in both ACPA-positive and ACPA-negative RA subsets.

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**SAT0741-HPR** **COGNITIVE-BEHAVIOURAL AND SOCIAL FACTORS DO NOT PREDICT RECURRENT SECONDARY HEALTH CARE USE IN PATIENTS WITH FIBROMYALGIA: A LONGITUDINAL STUDY**

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**Background:** Health care use in fibromyalgia (FM) is relatively high. Besides disease-related variables, cognitive-behavioural factors have been concurrently associated with health care use. It is unknown whether cognitive-behavioural and social factors also predict future health care use.

**Objectives:** To identify cognitive-behavioural and social factors predicting recurrent secondary health care use in FM.

**Methods:** Data were drawn from a prospective cohort of recently diagnosed patients with fibromyalgia (n=199), spanning 18 months. Patients were recruited after receiving their diagnosis and protocolled treatment advice by a rheumatologist. Using self-report questionnaires, health care use, cognitive-behavioural (i.e. illness cognitions, pain coping, coping flexibility), social (i.e. invalidation by family, spousal responses to pain and well behaviour), sociodemographic and disease-related variables including comorbidities, severity of FM, and depressive and anxiety symptoms were collected. Primary outcome was recurrent secondary health care use at 18 months follow-up defined as the use or non-use for each of the following four categories of secondary health care: consultation with medical specialists, diagnostic procedures, admission to health care institutions, and multimodal treatment program. A patient was considered a recurrent secondary health care user, if secondary health care from at least one of the four categories was used in the past six months. Univariate and multivariate logistic regression models examined whether and which variables were predictors for recurrent secondary health care use. Internal validation was performed to correct for over-fit of the final multivariate model.

**Results:** Recurrent secondary health care use was lower than initial secondary health care use. Univariate analysis showed that having at least one comorbidity, depressive feelings, severe consequences of fibromyalgia, low personal control and a high severity of fibromyalgia predicted recurrent secondary health care use. In the multivariate model, having at least one comorbidity was the only remaining predictor for recurrent secondary health care use.

**Conclusions:** Our results suggest that the existence of comorbidities as communicated by the patient is the strongest warning signal for recurrent secondary health care use in FM. There seems no value in using cognitive-behavioural and social factors for early identification of patients with FM at risk for recurrent secondary health care use.

**Disclosure of Interest:** None declared

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**SAT0742-HPR** **EUROPEAN LEAGUE AGAINST RHEUMATISM RECOMMENDATIONS FOR THE ROLE OF THE NURSE (EULAR-RN) IN THE MANAGEMENT OF CHRONIC INFLAMMATORY ARTHRITIS (CIA): RESULTS OF PATIENTS IN NORDIC COUNTRIES**

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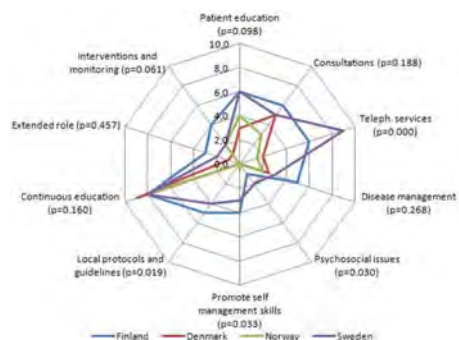
**Background:** The dissemination of the EULAR-RN in the management of CIA<sup>1</sup> have been completed in Europe and in the USA.<sup>2</sup> The treatment is supposed to be carried out based on shared decision making (SDM).<sup>3</sup> Lay versions of the recommendations and input from the patient organisations are essential in the integration of the recommendations and SDM.<sup>4</sup>

**Objectives:** The aims of this study were to assess agreement with and application of, and identify barriers against implementing the EULAR-RN in the management of CIA and to assess differences between individual Nordic countries.

**Methods:** A web-based survey was distributed using snowball sampling. Levels of agreement and application were assessed using a 0–10 rating scale (0=none, 10=full agreement/application). Reasons for disagreement with and barriers against applying each recommendation were sought. Differences between groups were assessed using the Kruskal-Wallis Test.

**Results:** A total of 318 patients from Finland participated in the survey. Their mean age was 52.1 years (SD 15.6). 47% had completed secondary education, 25% only primary and one third tertiary education. The mean duration of the disease was 17.7 years (SD 13.0), with a diagnosis of RA (63.5%), AS or PsA (29.8%, 6.7% respectively) and treated in general (45%), university (32%) or other hospitals. The median level of agreement was high, ranging from 8 to 10 in Finland

and from 7 to 10 in the other countries. Levels of agreement with the four recommendations differed between countries. Reasons for non-complete agreement in Finland included fear of losing contact with the rheumatologist and do not accept the nurse; barriers were if service is not offered or available and nurses were too busy. The application range was 0–9 in the four countries, with some individual differences (figure 1).



**Abstract SAT0742HPR – figure 1.** Application levels of the EULAR-RN in the Nordic countries

**Conclusions:** Further work and participation of patient organisations is needed for applying the EULAR-RN and removing the barriers against it.

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#### **SAT0743-HPR** RELATION BETWEEN SERUM ALBUMIN AND PHYSICAL PERFORMANCE AND MOBILITY IN A COMMUNITY-BASED ELDERLY PEOPLE WITH OSTEOPOROSIS

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**Background:** Osteoporosis is a disease related to ageing and to other interacting variables, including genetic, metabolic, physical and nutritional factors. Several studies have reported that the serum albumin level in the elderly is significantly associated with muscle mass, muscle strength and functional capacity.<sup>1</sup> Even among a nondisabled older persons, lower albumin concentrations have been shown to be independently associated with poorer performance as assessed by objective physical performance tests.<sup>2</sup>

**Objectives:** The purpose of this study was to investigate the association of serum albumin with physical performance (muscle strength and mobility ability) in patients with osteoporosis.

**Methods:** For the study, 168 patients with OP (98 women and 70 men) underwent an interview, physical performance testing and blood analysis. A total of patients followed by Hacettepe University Faculty of Medicine Department of Internal Medicine, Division of Geriatric Medicine Department and Geriatric Rehabilitation Unit. We excluded those who Mini Mental State score is under 24 points, Mini Nutritional Assessment Test score is under 11 and have advanced kidney disease. Physical performance was evaluated with Five Times Sit to Stand (FTSS) and Six Metre Walk Test (SMWT). Hand grip strength was measured with dynamometer. Pearson's correlation coefficients were calculated for serum albumin, FTSS, SMWT and handgrip strength.

**Results:** Participants mean age of 72.73±6.34 years and BMI 22.56±2.98 kg/m<sup>2</sup> mean serum albumin concentration ±standart deviation was 41.9±3.5 g/L for women and 41.9±2.9 g/L for men. Serum albumin was associated significantly with physical performance (mobility and walking speed) and muscle strength (hand grip) were in men and women with OP (p<0.005).

	FTSS	Walking Speed	Hand Grip
Serum albumin (men)	0.001	0.001	0.022
P r	-0.322	-0.358	0.255
Serum albumin (women)	0.001	0.001	0.026
P r	-0.314	-0.243	0.205

**Conclusions:** Our study demonstrated that a decrease in the serum albumin level is associated with a decrease in physical performance and muscle strength, although causality is still unclear.

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#### **SAT0744-HPR** PREVALENCE OF COMORBIDITIES IN PATIENTS WITH RHEUMATOID ARTHRITIS AND CORRELATION WITH DISEASE ACTIVITY AND TYPE OF THERAPY

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**Background:** Rheumatoid arthritis (RA) is a common systemic autoimmune disease characterised chronic joint inflammation. Patients with RA are also reported to have higher prevalence of comorbidities such as cardiovascular disease, osteoporotic among others.<sup>1</sup> These comorbidities can be associated with higher mortality, poor life quality, and the increasing of costs for the health system.

**Objectives:** To describe the prevalence of comorbidities and characteristics of a Colombian population that assist to a RA specialised centre.

**Methods:** We performed a descriptive analysis; our main goal was to provide real-life data regarding characteristics of patients with RA. We collected sociodemographic information, DAS28, and prevalence of comorbidities regarding hypertension, cerebrovascular disease, diabetes mellitus, osteoporosis, renal chronic disease, or Sjogren's syndrome. We calculated means, and standard deviations for continuous variables and categorical variables were presented as rates. We estimated the prevalence of comorbidities and evaluate independent associations calculating prevalence ratios.

**Results:** 6376 patients were included in the analysis; mean age was 59 years ±12, 81% were woman and 19% were men. Mean DAS28 was 2.8±1.07. From all patients the prevalence of comorbidities was 42% hypertension, cerebrovascular disease, diabetes mellitus, osteoporosis, renal chronic disease, or Sjogren's syndrome. Most of these patients 60% reported to have hypertension with any of the others comorbidities mentioned above, or osteoporosis with other comorbidities



46%. Regarding pharmacological therapy a higher proportion of patients received conventional DMARDs 90% see table 1. The prevalence of comorbidities was associated with sex and disease activity but did not have any association with pharmacological therapy see table 2.

**Abstract SAT0744HPR – Table 1** Characteristics. of patients with RA and comorbidities

CHARACTERISTICS n (%)	WITHOUT COMORBIDITY		WITH ANY COMORBIDITIES	
	n	%	n	%
SEX				
FEMALE	2865	45%	2289	36%
MALE	795	12%	427	7%
DAS 28				
REMISION	1975	31%	1499	24%
LOW DISEASE ACTIVITY	581	9%	554	9%
MODERATE DISEASE ACTIVITY	929	15%	565	9%
SEVERE DISEASE ACTIVITY	175	3%	98	2%
MEDICATIONS				
Conventional DMARDs	2352	37%	3072	48%
Biological DMARDs	359	6%	580	9%

**Abstract SAT0744HPR – Table 2.** Assoc of comorbidities, sex, and disease activity.

Variable	PR*	IC 95%	P VALUE
Sex	7.21	6.58–7.89	0.000
DAS28	1.18	1.10–1.27	0.000
Therapy	0.91	0.86–0.96	0.000

PR: prevalence ratio

**Conclusions:** As other studies conducted in Asian or Australian populations high blood pressure is the most common disease among patients with RA followed by osteoporosis.<sup>1</sup> Sex is associated with higher comorbidities. According to these results it is important to consider the patient's context, medical conditions, and the number of comorbidities in order to understand the complexity of the management of patient with RA.

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#### **SAT0745-HPR** TIME TO DIAGNOSIS, BUT NOT DISEASE DURATION, IS ASSOCIATED WITH POOR QUALITY OF LIFE IN SPONDYLOARTHRITIS: RESULTS FROM THE ASAS-COMOSPA STUDY

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LIRMM, University of Leeds, Leeds, UK

**Background:** Spondyloarthritis (SpA) is a group of related chronic inflammatory conditions associated with impaired quality of life.

**Objectives:** To explore the potential associations between both "Time to Diagnosis" and "SpA Disease Duration" and current quality of life in SpA.

**Methods:** Using ASAS-COMOSPA, a large international cross-sectional study comprising 3984 patients with SpA, we investigated the association between either "Time to Diagnosis" (time from symptom onset to diagnosis) or "SpA Disease Duration" (time from symptom onset to study visit) and current quality of life at the single study visit. Data collected from 5 domains of quality of life in EQ-5D-3L were summarised as an index (ranging from -0.59 to 1.00). In separate models of linear regression, the association between the aforementioned chronology parameters with the quality of life index were investigated before and after adjustments for age, sex, education, HLA-B27, BMI, smoking, alcohol, and medication (NSAIDs, steroids, DMARDs, biologics) history.

**Results:** Data for 3923 patients (35.1% female; mean age 43.21 (SD: 13.89) years) were available for this analysis. The median (IQR) quality of life index was 0.64 (0.36–0.89) for the entire cohort. In multivariate analysis, "Time to Diagnosis" was significantly associated with poorer quality of life ( $p=0.005$ ). Other factors and covariates associated with adverse quality of life were higher BMI ( $p<0.001$ ), smoking ( $p=0.003$ ), ever use of NSAIDs ( $p<0.001$ ), ever use of steroids ( $p<0.001$ ) and ever use of biologics ( $p=0.002$ ). Factors associated with favourable quality of life were male gender ( $p<0.001$ ), higher education ( $p<0.001$ ) and HLA-B27 positivity ( $p=0.006$ ) (Table). In contrast, "SpA Disease Duration" was not associated with the current quality of life index when corrected for confounders, including age.

Table: Association between Quality of Life index and "Time to Diagnosis" in Spondyloarthritis, adjusted to all potential confounders

Factors	p value	Coefficients (B)	95% CI for B
Time to Diagnosis (1 year blocks)	0.005	-0.002	-0.004,-0.001
Age	0.134	-0.001	-0.002, 0.000
Sex (M vs F)	<0.001	0.070	0.045-0.096
Current BMI	<0.001	-0.008	-0.010,-0.005
Smoking (pack-year)	0.003	-0.001	-0.002, 0.000
Alcohol intake (higher)	<0.001	0.026	0.015-0.037
Education (higher)	<0.001	0.036	0.019-0.054
HLA-B27 (+)	0.006	0.037	0.011-0.064
Ever NSAIDs	<0.001	-0.122	-0.147,-0.096
Ever Steroids	<0.001	-0.138	-0.163,-0.113
Ever DMARDs	0.489	-0.009	-0.034, 0.016
Ever Biologics	0.002	-0.037	-0.061,-0.013

**Conclusions:** In this global cohort of patients with SpA, time to diagnosis but not the duration of SpA appears to be associated with current quality of life, as assessed by the EQ-5D-3L index. Future work should explore geographic variation and whether this association is the same for axial and peripheral SpA disease.

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#### **SAT0746-HPR** COFFEE DECREASES METHOTREXATE INTOLERANCE AND INCREASES ITS COMPLIANCE IN RHEUMATOID ARTHRITIS (RA): A STUDY BY RHEUMATOLOGY NURSE COUNSELLORS

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**Background:** Methotrexate (MTX) is universally regarded as the 'anchor drug' for the treatment of Rheumatoid Arthritis (RA). Intolerance to MTX is the common cause of non-compliance that leads to poor disease control. The addition of coffee in the treatment regimen for MTX intolerance increases the patient compliance<sup>1</sup>. Therefore, awareness about the effect of coffee and counselling for strict adherence to the recommended coffee schedule should be an essential part of patient's education.

**Objectives:** To assess the effect of coffee on MTX intolerance in patients with RA.

**Methods:** RA patients attending the Rheumatology clinic, willing to participate in the survey were enrolled in this study. All the patients were asked to take weekly MTX dose along with coffee as per schedule. The coffee schedule advised was as follows: 2 strong cups of coffee early in the morning on the day of the week on which the MTX was scheduled. This was repeated in the late evening 1–3 hours before the dose of MTX. The 3rd dose of 2 cups of strong coffee was repeated the next morning. This schedule was repeated every week synchronised with the weekly dose of MTX. All the patients were counselled and explain to follow the coffee schedule. All the information was collected in a pre-designed form.

**Results:** 600 patients were enrolled in this study. All the patients were treated with the weekly dose of MTX. Among 600 patients 285 (47.5%) did not have any MTX intolerance; 315 (52.5%) had MTX intolerance. In the latter category, 200 (63.5%) patients had minimal intolerance not requiring any intervention. The remaining 115 (36.5%) patients had moderate or severe MTX intolerance. Among these, 52 (45.2%) had complete relief of symptoms with the addition of coffee and were able to continue taking the advised dose of MTX; 17 (14.8%) had partial improvement and continued taking MTX but only with antiemetic; 14 (12.2%) were minimally better but were somehow managing; 14 (12.2%) did not get any relief and discontinued MTX. Another as 18 (15.6%) patients did not agree to take coffee and continued with the symptoms of MTX intolerance.

The result of persistent counselling and explaining the coffee schedule with the help of audio-visual aids help the patients to manage MTX intolerance and increases the MTX compliance to ~60% of those with MTX intolerance.

If the intolerance symptoms disappeared completely over time, the patients were advised to discontinue coffee unless the patient liked coffee and preferred to continue taking it.

**Conclusions:** Coffee relieved the symptoms of MTX intolerance in 45.2% and partial relief in 14.8% of the patients. A significant number of patients did not like to take coffee. By intense regular counselling by the specialist rheumatology nurses about the benefits of coffee intake in MTX intolerant patients, helped in decreasing the intolerance and increased its compliance in patients with RA.

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#### SAT0747-HPR THE IMPACT OF NON-PERSISTENCE ON THE DIRECT AND INDIRECT COSTS IN PATIENTS TREATED WITH SUBCUTANEOUS TUMOUR NECROSIS FACTOR-ALPHA INHIBITORS IN GERMANY

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**Background:** No recent data is available about the association between non-persistence with subcutaneous TNFi and costs in Germany.

**Objectives:** The goal of the present study was to estimate the direct and indirect treatment costs in immune-mediated rheumatic disease (IMRD) patients initiating treatment with a subcutaneous biologic agent based on treatment persistence.

**Methods:** This is a retrospective cohort study based on the German statutory health insurance funds database. Patients aged  $\geq 18$  with a diagnosis of ankylosing spondylitis, psoriatic arthritis, or rheumatoid arthritis treated with subcutaneous TNF-alpha blockers (sc-TNFis) were included. Persistence was estimated as the duration of time from sc-TNFis therapy initiation to discontinuation, which was defined as at least 60 days without therapy. We performed 1:1 matching based on a propensity score that was constructed as the conditional probability of being persistent as a function of age, gender, index year, physician specialty, and Charlson comorbidity index. Finally, the differences in direct costs, indirect costs, and services between the matched pairs were estimated using the Wilcoxon test.

**Results:** After 1:1 matching, 678 persistent and 678 non-persistent patients were available for cost analyses. Both cohorts were similar in terms of age, gender, year of therapy initiation, CCI, and indication. Using a two-year time period, the costs for office based visits per patient were € 2319 in the persistent cohort, as compared to € 3094 in the non-persistent cohort ( $p < 0.001$ ). Co-medication costs were € 2828 in the persistent cohort, as compared to € 5498 in the non-persistent cohort ( $p < 0.001$ ), hospitalisation costs were € 3551 in persistent cohort, as compared to € 5890 in non-persistent patients, and sick leave costs were € 717 in persistent cohort, as compared to € 1241 in non-persistent patients.

**Conclusions:** The results of this study indicate that persistence with SC-TNFis treatment can be associated with several cost offsets for IMRD patients. For healthcare providers/payers, these findings reinforce the value of persistence, given the additional economic burden associated with non-persistent patients.

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#### HPR Measuring health (development and measurement properties of PROs, tests, devices)\_\_\_\_\_

#### AB1397-HPR RELIABILITY, VALIDITY AND CROSS-CULTURAL VALIDITY OF THE TURKISH VERSION OF THE ABILHAND QUESTIONNAIRE IN RHEUMATOID ARTHRITIS INDIVIDUALS, BASED ON RASCH ANALYSIS

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**Background:** 80%–90% of Rheumatoid Arthritis (RA) individuals are thought to be affected by the hands and wrists. Patients complain of various symptoms that cause more difficulty while performing daily activities such as joint pain and stiffness, loss of joint range of motion, reduction of grip strength. Abilhand is a Rasch-built questionnaire and evaluates manual ability.

**Objectives:** This study aimed to evaluate reliability, validity and the cross-cultural validity of the Turkish version of the Abilhand questionnaire for Rheumatoid Arthritis individuals, based on Rasch Analysis.

**Methods:** A total of 90 participants who were diagnosed as RA according to the American College of Rheumatology (ACR) 2010 criteria with a mean age of  $51.8 \pm 10.9$  years were included in the study. Manual ability was evaluated by use of Abilhand Questionnaire; disease activity by Disease Activity Score 28 (DAS28), upper limb impairment by Jamar dynamometer, pinchmeter, Nine Hole Peg Test (NHPT); disability by Duruöz Hand Index (DHI) and quality of life by Nottingham Health Profile (NHP). Abilhand results were evaluated using Rasch analysis.

**Results:** The Abilhand-Turkish, consisting of 27 items, provided the invariance of item difficulty hierarchy in general. Item fit statistics, person-item residual correlation matrix and principal component analysis of the residuals was examined and 8 items were removed. As a result of the deletion of 8 items in the questionnaire, it was determined that the remaining 19 items provided Rasch model compatibility and the invariance of item difficulty hierarchy. DAS28, bilateral grip strength, dominant side, NHPT, DHI ve NHP were significantly correlated with the Abilhand measures.

**Conclusions:** The Abilhand-Turkish in individuals with rheumatoid arthritis is clinically valid and reliable. We recommend using the Abilhand-Turkish in clinical evaluations, in rehabilitation interventions, and in evaluating improvements due to its sensitivity.

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**Disclosure of Interest:** None declared

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**AB1398-HPR THE EFFECTS OF KINESIOPHOBIA ON PAIN, FATIGUE SEVERITY, FUNCTIONAL EXERCISE CAPACITY, FUNCTIONAL STATUS AND QUALITY OF LIFE IN FIBROMYALGIA**

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**Background:** Kinesiophobia play an important role in the development of chronic pain in Fibromyalgia (FM) patients. This condition lead to increase clinical symptoms and reduce quality of life.

**Objectives:** The aim of the study is to examine the effects of kinesiophobia on pain, fatigue, functional exercise capacity, functional status and quality of life in FM patients.

**Methods:** Twenty-one FM patients were evaluated. We used Tampa Scale of Kinesiophobia (TSK) for perception kinesiophobia, Visual Analogue Scale (VAS) for pain intensity, Fatigue Severity Scale (FSS) for fatigue, six-minute walk test (6MWT) for functional capacity, Fibromyalgia Impact Questionnaire (FIQ) for the functional status, and Short-Form Health Survey (SF-36) for quality of life.

**Results:** The results of this study, there was a strong correlation between TSK and VAS, FSS, physical and mental components of SF-36 ( $r=0.754$ ,  $r=0.762$ ,  $r=0.780$ , and  $r=0.843$ , respectively;  $p<0.05$ ). There was a moderate correlation between TSK and FIQ and 6MWT ( $r=0.695$ ,  $r=0.510$ , respectively;  $p<0.05$ ).

**Conclusions:** The results of the present study indicate that kinesiophobia can adversely affect pain, fatigue, functional status and functional exercise capacity, which is result in impaired quality of life in FM. Further, it demonstrates kinesiophobia can be a clinically appropriate assessment to evaluate patients and to determine the effectiveness of treatments in FM.

**Disclosure of Interest:** None declared

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**AB1399-HPR CONCURRENT VALIDITY AND STABILITY OF SUBGROUP ASSIGNMENT TO THREE LEVELS OF PAIN CONDITION SEVERITY IN PATIENTS WITH MUSCULOSKELETAL PAIN**

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**Background:** Pain screening instruments have been used to identify risk factors for poor prognosis and are recommended for the stratification of treatment for musculoskeletal pain.

**Objectives:** The aim of this study was to investigate the concurrent validity of subgroup assignment based on the Örebro Musculoskeletal Pain Screening Questionnaire compared with reference instruments: The Pain Disability Index, the Tampa Scale for Kinesiophobia, and the Pain Catastrophizing Scale. A secondary aim was to investigate the stability of the subgroup assignment over a defined period of time.

**Methods:** Participants ( $n=40$ ) aged 18–65 years were recruited from five primary health care centres in Sweden. Data were collected using self-reported questionnaires. The subgroups based on the Örebro Musculoskeletal Pain Screening Questionnaire were pre-defined to low, moderate or high pain condition severity. The reference instrument data were dichotomized into low or high level based on previously used cut-off scores. Concurrent validity was analysed with Fisher's exact test. Stability was calculated using quadratic-weighted kappa analysis.

**Results:** The results indicated acceptable psychometric properties of the subgroup assignment based on the Örebro Musculoskeletal Pain Screening Questionnaire regarding concurrent validity, and the stability ( $K_w:0.51$ , 95% CI: 0.22–0.81) over two to three weeks. To further increase validity, it is suggested that subgroup assignment is complemented with other measures assessing e.g. pain catastrophizing.

**Conclusions:** In conclusion, assignment to subgroups with low, moderate and high levels of pain condition severity based on the Örebro Musculoskeletal Pain Screening Questionnaire, could be used as a valid basis for stratified treatment for patients with musculoskeletal pain.

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**AB1400-HPR MUSCLE QUALITY INDEX IN OBESE SUBJECTS WITH HIP OSTEOARTHRITIS**

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**Background:** Obese older adults with hip osteoarthritis suffer a progressive loss of neuromuscular function affecting their activities of daily living.

**Objectives:** The objective of this study is to determine the behaviour of the muscular quality index in obese subjects with osteoarthritis and to compare the manifestations of strength and anthropometric variables with control subjects.

**Methods:** Thirty-two subjects (4 men and 28 women, 66.2±5.2 years of age, 159.2±7.5 cm, 71.5±11.7 kg) were evaluated. 14 subjects suffered osteoarthritis. Muscle circumference, limb length, body mass and sit and stand test were evaluated, in addition to the maximal voluntary isometric contraction in hip flexion and extension movements.

**Results:** The osteoarthritis group presented obesity ( $p=0.037$ ). The muscle quality index of the osteoarthritis group correlated with the weight ( $p=0.776^{**}$ ), with maximum peak strength in flexion ( $p=0.552^*$ ) and average maximal strength ( $p=0.574^*$ ). In the control group the muscle quality index correlated with: weight ( $p=0.689^{**}$ ), muscle circumference ( $p=0.571^*$ ), maximum peak strength in extension ( $p=0.534^*$ ), average peak strength in extension ( $p=0.523^*$ ), average maximal strength in extension ( $p=0.509^*$ ) and maximum impulse in extension ( $p=0.508^*$ ).

**Conclusions:** The muscle quality index is a useful tool to measure muscle quality in the healthy population, but is not clear enough for obese subjects with osteoarthritis, so it is necessary to perform future studies to determine their behaviour.

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**AB1401-HPR AN EXPLORATORY STUDY EVALUATING FEASIBILITY AND EFFECTIVENESS OF TWO DIFFERENT EXERCISE PROGRAMS IN SYSTEMIC SCLEROSIS ASSOCIATED MICROSTOMIA**

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**Background:** Systemic sclerosis (SSc) is a severe chronic connective tissue disease with a high disease burden. Oral involvement with impaired oral aperture (microstomia) is frequent and associated with impaired food intake, oral hygiene and secondary dental problems. Preventive measures through mouth-stretching and oral augmentation exercises have been shown to reverse the progression of microstomia.

**Objectives:** This exploratory study assesses the effectiveness and feasibility of two different exercise approaches designed to increase oral aperture.

**Methods:** Two groups had to exercise for 10 min, 3 times/day for 3 months. Group A exercised with a passive jaw motion device (Therabite), and Group B did mouth-stretching exercises. Patients were contacted 4 times by telephone to address encountered problems. The subjects used an exercise diary to document compliance. Patients were evaluated at baseline, 3 months (period without intervention), 6 months (at the end of the treatment after 3 months of intervention) and 9 months (follow-up).

**Results:** At present, 9 patients (Therabite n=4, mouth-stretching exercises n=5) were included and recruitment is ongoing. Seven patients completed the study and increase of oral aperture was observed in all patients in both groups. In the Therabite group, after 3 months of exercise, increase of oral aperture was 9, 2, 9 and 10 mm. In the mouth-stretching exercise group the increase of oral aperture was 11, 10 and 4 mm after 3 months. The compliance, measured as the ratio of executed exercises relative to the planned number of exercises was 95,2%, 85,7%, 98,9% and 63,7% in the Therabite group and 97,4%, 48,6% and 68,3% in the mouth-stretching exercise group.

**Conclusions:** An increase of oral aperture is observed in all patients after 3 months of exercising with the Therabite device as well as after mouth-stretching exercises. No clear differences are observed between both groups, but the study was not designed nor powered for this. Remarkably, a high compliance for the treatment regime was observed in most patients.

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**AB1402-HPR VALIDITY OF BIODEX BALANCE SYSTEM IN FIBROMYALGIA PATIENTS**

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**Background:** Fibromyalgia (FM) patients are commonly suffer from balance problems and increased fall frequency. However, validity of any measurement tool has not been determined in clinical trials. Modified Clinical Test of Sensory Interaction and Balance Test (M-CTSIB) is a simple and easily administered test.

**Objectives:** The aim of the study was to investigate the validity and reliability of the M-CTSIB in FM patients.

**Methods:** Twenty-one FM patients and 15 age matched controls were evaluated M-CTSIB. M-CTSIB was evaluated by Biodes-BioSway<sup>TM</sup> (Biodes Inc., Shirley, New York). M-CTSIB evaluates the relationship between balance and visual, somatosensory and vestibular system. Tests carried out were 4 conditions, condition-1: eyes open-firm surface, condition-2: eyes closed-firm surface, condition 3: eyes open-foam surface, and condition 4: eyes closed-foam surface, for 30 s intervals with two repetitions. Body oscillations of the participants were calculated by the system and Sway Index scores obtained. High scores indicate high postural sway of the test subject.

**Results:** The results of this study, FM patients had significantly impaired balance in all conditions of M-CTSIB compared to controls ( $p<0.05$ ). Discriminatory power of all subcomponents of M-CTSIB between groups was excellent. The ROC areas under the curves were 0.803 for condition-1, 0.757 for condition-2, 0.833 for condition-3, 0.776 for condition-4 (AUC=0.803, AUC=0.757, AUC=0.833, AUC=0.776, respectively).

**Conclusions:** These results suggest that FM may lead to increase balance problems. M-CTSIB has been proved to be valid, objective and clinically useful method to detect balance impairments in FM patients.

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**AB1403-HPR INVESTIGATION OF THE VALIDITY OF BETY SCALE IN PATIENTS WITH RHEUMATOID ARTHRITIS**

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**Background:** The Cognitive Exercise Therapy Approach is a biopsychosocial model for the patients with rheumatic diseases.<sup>1</sup> Cognitive Exercise Therapy Approach Scale (the authors request that the abbreviation stay as "BETY" as the original in Turkish) is a scale that evaluates the biopsychosocial status of the patients with rheumatic diseases. This scale needs validation studies in different rheumatic diseases.<sup>2</sup>

**Objectives:** The aim of this study is to investigate the validation of the BETY scale in patients with Rheumatoid Arthritis (RA).

**Methods:** 120 RA patients were included in this study. To determine the functional status of the patient Health Assessment Questionnaire (HAQ) was used. Rheumatoid Arthritis Quality of Life Scale (RAQoL) and 36-Item Short Form Survey (SF-36) were used to measure quality of life. Hospital Anxiety and Depression Scale (HADS) was used to determine anxiety and depression levels. BETY scale was used to in addition to this questionnaires for the validation.

**Results:** 120 RA patients including 13 men and 107 women were participated in the study. The average age of the participating patients was 28,47±11,39 years and the body mass index was 28,4±6,56. There was a very high correlation between the BETY scale and RAQoL ( $r=0,817$ ,  $p<0,001$ ). There was high correlation between the BETY scale and

**Abstract AB1403HPR – Table 1.** Correlations

	RAQoL	SF-36 PF	SF-36 RL	SF-36 RLE	SF-36 P	SF-36 GHP	xHAQ	HADS Anxiety	HADS Depression	
BETY	r	0817	-0,576	-0,525	-0,598	-0,610	-0,420	0606	0617	0597
p		0000	0000	0000	0000	0000	0000	0000	0000	0000

PF: Physical Functioning, RL: Role Limitations, RLE: Role Limitations Due to Emotional, P: Pain, GHP: General Health Perception

subscale of the HADS-Anxiety, HAQ and subscale of the SF-36 Pain ( $r=0.617$ ,  $p<0.001$ ;  $r=0.606$ ,  $p<0.001$ ;  $r=-0.610$ ,  $p<0.001$ , respectively). There was moderate correlation between the BETY scale and subscale of the HADS-Depression, subscales of the SF-36 form Physical Functioning, Role Limitations, Role Limitations Due to Emotional and General Health Perception ( $r=-0.597$ ,  $p<0.001$ ;  $r=-0.576$ ,  $p<0.001$ ;  $r=-0.525$ ,  $p<0.001$ ;  $r=-0.598$ ,  $p<0.001$ ;  $r=-0.420$ ,  $p<0.001$ , respectively) (Table 1–2).

**Conclusions:** There were high or moderate correlations between the BETY scale and valid and reliable scales that are developed for these parameters. The BETY scale can be considered as a valid scale in patients with RA.

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#### AB1404-HPR PRELIMINARY NORMATIVE DATA OF ULTRASONOGRAPHIC MUSCLE THICKNESS AND CROSS-SECTIONAL AREA OF THE THENAR MUSCLES

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**Background:** Muscle thickness and cross-sectional area (CSA) of the thenar muscles can vary depending on different pathologies (such as neuropathies, arthritis etc.). It is important to evaluate these muscles throughout the diagnosis and treatment processes to understand the pathophysiology of diseases and to identify new treatment strategies. Ultrasonographic imaging has been shown to be valid and reliable tool for the measurement of the muscle thickness and CSA of the particular thenar muscles,<sup>1–2</sup> however there are no studies demonstrating normative values of all thenar muscles.

**Objectives:** The purpose of this study is to obtain normative thickness and CSA values for the thenar muscles in healthy individuals by ultrasound and to assess the inter-rater reliability of sonographic muscle assessments.

**Methods:** The thenar muscles were examined ultrasonographically in eleven healthy volunteers. The assessment was carried out using Shimadzu SDU 1200-Pro US system working with 8–10 MHz linear probe. A custom-made foam cast was used for standardised positioning of the probe. The thickness and CSA parameters of FDI, OP, APB, flexor pollicis brevis (FPB), adductor pollicis (AdP) muscles were examined by two different investigators on the same image. Measurements were made from the palm side of the hand for APB, FPB, OP muscles and from the dorsal side of the hand for AdP and FDI muscles, using five different positions.<sup>3</sup> To analyse inter-rater reliability, the examinations of both raters were compared.

**Results:** Eleven healthy female subjects (mean age: 24.45±2.77 years; BMI: 21.43±2.48 kg/m<sup>2</sup>) were included in this study. Nine subjects had right hand dominance and 2 had left hand dominance. The reliability between two assessors, expressed as an interclass correlation coefficient (ICC), was excellent for all muscles (ICC range min:0.759, max:0.993  $p<0.05$ ).

The mean thickness values of muscles were ordered from thick to thin in longitudinal assessment as AP, FDI, FPB, OP, APB. The mean thickness values of muscles were ordered from thick to thin in transverse assessment as AP, FDI, FPB, OP, APB. The mean CSA values of muscles were ordered from thick to thin as AP, FPB, FDI, APB, OP.

**Abstract AB1404-HPR – Table 1**

Muscle		Longitudinal Thickness (cm)	ICC(p)	Transverse Thickness (cm)	ICC(p)	CSA (cm <sup>2</sup> )	ICC(p)
APB	D	0.54	0.976(<0.001)	0.43	0.877(<0.001)	1.0	0.969(<0.001)
	ND	0.54	0.943(<0.001)	0.38	0.872(<0.007)	0.90	0.836(<0.004)
OP	D	0.58	0.993(<0.001)	0.44	0.964(<0.001)	0.74	0.759(<0.017)
	ND	0.56	0.909(<0.001)	0.40	0.872(<0.002)	0.75	0.851(<0.003)
FPB	D	0.63	0.883(<0.001)	1.0	0.891(<0.001)	2.20	0.891(<0.001)
	ND	0.63	0.795(<0.011)	0.95	0.928(<0.001)	2.16	0.944(<0.001)
AP	D	1.26	0.997(<0.001)	1.28	0.981(<0.001)	2.68	0.900(<0.001)
	ND	1.25	0.967(<0.001)	1.26	0.986(<0.001)	2.42	0.886(<0.001)
FDI	D	1.03	0.977(<0.001)	0.95	0.956(<0.001)	1.96	0.948(<0.001)
	ND	1.0	0.968(<0.001)	0.93	0.959(<0.001)	1.97	0.896(<0.001)

D: dominant, ND: non-dominant

**Conclusions:** Ultrasonography can be used to reliably assess the thenar muscle architecture. This study is important to reveal the normative thickness and CSA values of the thenar muscles in healthy subjects. This data may provide a more comprehensive understanding of musculoskeletal problems and underlying pathophysiological mechanisms which consequently may have an impact on clinical decision making.

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#### AB1405-HPR THE COMPARISON OF POSTERIOR SHOULDER TIGHTNESS IN PATIENTS HAVING CHRONIC NECK PAIN AND IN HEALTHY SUBJECTS

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**Background:** Chronic neck pain (CNP) causes the disruption of the thoracic region and the shoulder girdle biomechanics besides the cervical region. The shoulder capsule is often thickened in shoulder problems, which causes shoulder tightness. In the literature, the effect of CNP on shoulder tightness was not investigated.

**Objectives:** The purpose of this study is to investigate the posterior shoulder tightness (PST) in patients having CNP and to interpret the effect of patients functional level and posture.

**Methods:** Non-specific CNP patients (n=16, female) and healthy subjects (n=16, female) were included and no shoulder problem was identified. The severity of the pain with Visual Analogue Scale (VAS); PST with bubble inclinometer; functional disability level with Neck Disability Index (NDI); influence of posture with New York Postural Rating Scale (NYPRS), upper limb muscle strength evaluated with handgrip. The Mann-Whitney U test Pearson correlation analysis was used to determine the relationship between PST and functional disability levels.

**Results:** Age and BMI values of healthy subjects and patients with CNP were similar ( $p>0.05$ ). The mean duration of disease in patients with CNP was 60.63±35.37 months. Patients with CNP had lower PST values than healthy subjects, namely shoulder tightness is more than healthy subjects ( $p<0.001$ ). The functional disability level score was higher in patients with CNP than in healthy subjects ( $p<0.001$ ). NYPRS scores were lower in patients with CNP than in healthy subjects, namely the posture was more adversely affected in these patients ( $p<0.001$ ). Handgrip values were lower and the pain severity at rest and activity was

significantly higher in patients with CNP than in healthy subjects ( $p < 0.001$ , Table 1). PST correlated well with the NYPS value ( $r = -0.56$ ,  $p = 0.03$ ) and functional disability level ( $r = -0.63$ ,  $p < 0.001$ ) in patients with CNP.

**Abstract AB1405HPR – Table 1.** The comparison of clinical parameters in patients having chronic neck pain and healthy subjects

	Healthy Subjects mean ±SD	Patients with CNP mean ±SD	p
Age (years)	40.63±11.86	45.06±11.04	0.20
BMI (kg/m <sup>2</sup> )	26.25±6.57	25.81±4.06	0.76
Pain <sub>rest</sub> (VAS, cm)	0.13±0.52	2.77±2.51	<0.001
Pain <sub>activity</sub> (VAS, cm)	0.31±0.60	6.00±2.08	<0.001
PST (°)	66.89±13.15	43.6±9.27	<0.001
NDI	0.94±1.23	19.94±6.29	<0.001
NYPRS	60.38±4.60	43.13±8.34	<0.001
Handgrip Strength (kg)	28.48±4.08	23.00±5.65	0.003

SD: Standard Deviation, BMI: Body Mass Index, CNP: Chronic Neck Pain, PST: Posterior Shoulder Tightness, NYPRS: New York Postural Rating Scale, NDI: Neck Disability Index.

**Conclusions:** Pain and upper limb muscle strength loss due to problem in patients with CNP, adversely affect patients' posture and reduce their functional levels. For these reasons, it is suggested that the shoulder girdle should be evaluated besides the neck area in the treatment of patients having CNP and treatment should be included with appropriate physiotherapy and exercise program from the early period.

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#### AB1406-HPR RELATIONSHIP BETWEEN KNEE MUSCLE STRENGTH, PAIN AND FUNCTIONAL OUTCOMES IN PATIENTS WITH PATELLOFEMORAL OSTEOARTHRITIS

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**Background:** Knee Osteoarthritis (OA) is one of the most common musculoskeletal disorders that adversely affect the functional levels of the patients. Traditionally, knee OA is considered as a problem at the medial compartment of the tibiofemoral (TF) joint. However, OA in patellofemoral (PF) joint can be seen around 25% of the patients. Since the biomechanics of PF joint are distinct from TF joint, the functional assessments specific to PF joint should be considered for PFOA patients.

**Objectives:** The aim of the study was to investigate the relationship between quadriceps femoris strength differences between PFOA patients and control group. Another aim was to define the relationship between pain, knee muscle strength, and functional outcomes in PFOA.

**Methods:** Twenty-five patients with PFOA (age=52.1 years, BMI=26.2 kg/cm<sup>2</sup>) and 20 age-matched controls (age=54.1 years, BMI=26.1 kg/cm<sup>2</sup>) were included in the study. The patients diagnosed with PFOA if they had a radiographic Kallgren and Lawrence score grade 2 or 3 in the PF joint, which was greater than KL score for the TF compartments. Pain level was measured with Visual Analogue Scale. The quadriceps femoris and hamstring isometric muscle strengths at 20° and 60° of knee flexion were measured with a hand-held dynamometer. The functional levels of the patients were determined with Kujala Patellofemoral Score and Western Ontario McMaster Universities Osteoarthritis Index (WOMAC). Student t-test was used for the comparison of quadriceps strength between PFOA and control groups. Spearman correlation test was used to determine the relationship between pain, muscle strength and functional outcomes.

**Results:** The quadriceps strength at 20° ( $p = 0.03$ ) and 60° ( $p = 0.01$ ) of knee flexion were lower in PFOA group when compared to control group. Hamstring strength at both angles was similar between groups ( $p > 0.05$ ). There were negative correlations between quadriceps muscle strength at 60° knee flexion and pain levels ( $r = -0.54$ ,  $p = 0.02$ ) and total WOMAC score ( $r = -0.33$ ,  $p = 0.01$ ). The quadriceps muscle strength at 20° knee flexion was only correlated with Kujala score ( $r = -0.47$ ,  $p = 0.01$ ). There

were no correlations between hamstring strength with pain and functional outcomes ( $p > 0.05$ ).

**Conclusions:** PFOA patients had significantly lower quadriceps strength than control group. Pain level, quadriceps muscle strength and functional outcomes were associated with each other in patients with PFOA. These findings suggest that interventions that have been designed to reduce pain and to improve function should be specific to the affected compartment in knee OA.

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#### AB1407-HPR ADVERSE DRUG REACTIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** adverse drug reactions (ADRs) are events that may seriously affect the health of people who use drugs for therapeutic purposes.<sup>1</sup> In the case of patients with rheumatic diseases the existence of comorbidities, the use of DMARDs, or polymedication may increase the risk of developing any type of adverse drug reaction.<sup>2</sup>

**Objectives:** We aim to describe the adverse drug reactions in patients with rheumatoid arthritis.

**Methods:** A cross sectional study was performed during 2017; we collected data from the patients who reported an adverse drug reaction in the consult with a multidisciplinary health care team. We collected the ADR characteristics, medication group and severity. Descriptive epidemiology was done.

**Results:** A total of 6793 patients were diagnosed with rheumatoid arthritis and comorbidities in our specialised centre where 1.8% (123) patients reported any adverse drug reaction, 82% were women. The main diagnosis was rheumatoid arthritis 88% followed by rheumatoid arthritis plus osteoarthritis 12%; less than 1% was other diagnoses. The drug that had a higher proportion of ADRs was methotrexate 33% followed by leflunomide 14%, Certolizumab 7% and acetaminophen combined with hydrocodone 6%; see table 1. The dermatological adverse events were the most common followed by gastrointestinal events and errors in self-medication 11%, these adverse events were classified as mild or moderate; see

**Abstract AB1407-HPR – Table 1**

ADVERSE EVENT	N	%
DERMATOLOGIC	31	25.2
GASTROINTESTINAL	20	16.26
SELF-MEDICATION	14	11.38
THERAPEUTIC	10	8.13
FAILURE		
PAIN	9	7.32
HEADACHE	8	6.5
BREATHING	7	5.69
DIFFICULTY		
GENERAL	5	4.07
DISCOMFORT		
DIZZINESS, DYSPNEA	4	3.25
HERPES ZOSTER - VIRUS	4	3.25
INFECTIOUS		
INFECTIOUS	2	1.63
HAIR-LOSS	2	1.63

**Conclusions:** The proportion of adverse events in our centre is low; other studies had shown, the frequency of patients with ADRs is common, mainly in patients who use anti rheumatic medications. This real life data can support the evidence for future studies in order to prevent ADRs.

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**AB1408-HPR** **CONTENT VALIDITY OF A SWEDISH VERSION OF THE SATISFACTION WITH APPEARANCE SCALE IN SYSTEMIC SCLEROSIS – THE HEALTH PROFESSIONALS' PERSPECTIVE**

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**Background:** Systemic sclerosis (SSc) can lead to visible changes in appearance such as varied skin texture, pigmentations, facial changes, and hand contractures which could generate concerns among patients. Valid questionnaires that capture these concerns are of great value.

**Objectives:** To assess content validity of a Swedish translation of the Satisfaction with Appearance Scale (SWAP) from the perspective of health professionals (HPs).

**Methods:** The Swedish SWAP (SWAP-Swe) was originally translated into the context of burn injuries. The multi-disciplinary research team applied it to the context of SSc by changing burn injury to SSc, changing part of the lay out, and using a version with two subscales: A) *Social discomfort* and B) *Dissatisfaction with appearance*. Initially, the validity was tested by individual interviews with 10 HPs with varied occupational background, who had 5.5 years (median, range 2–30) experience of SSc patient care. The interview guide included questions concerning comprehensibility, relevance, and suggestions of items to include and exclude. The interviews were sound recorded, transcribed verbatim, and analysed by manifest, partly deductive, content analysis.

**Results: Comprehensibility** Most HPs stated that items were not difficult to understand, nevertheless, concerns were highlighted in subscale A, and suggestions for improvements were made. In subscale B words that were connected to the disease was thought to be missing. **Relevance** The items were overall considered to cover relevant aspects of appearance in SSc. **Include/exclude items** Inclusion of items concerning appearance of mouth, lips, nose, fingers, and feet was suggested. Other aspects such as stiffness when moving or limping were found to be lacking. **Suggestions for exclusion covered** "...appearance of my scalp" and items that was thought to be too harsh for the patients, such as "I don't think people would like to touch me". **Fear of hurting the patients** Most HPs felt that it might be inappropriate to focus on patients' appearance and they feared hurt reactions. Negatively formulated subscale labels and emotionally demanding items in subscale A contributed to these thoughts. **When and how to use** Thoughts were expressed about when to use the questionnaire, how they would handle the results, and the importance of discussing appearance issues.

**Conclusions:** SWAP-Swe was, considered by HPs to be comprehensible and covering relevant aspects of appearance in SSc. However, further development of SWAP-Swe is suggested to better cover disease specific appearance topics and to limit potential risk of negative emotions among patients. Interviews with patients with SSc will further contribute to the content validity of SWAP-Swe.

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**AB1409-HPR** **GAIT STABILITY IN INDIVIDUALS WITH CHRONIC IDIOPATHIC NECK PAIN**

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**Background:** Gait stability ratio (GSR) is represented by step counts per metre during walking. Higher GSR value means to increase in time spent on double support period and decrease in dynamic components of gait, which refers to more stable gait pattern. Recent studies showed that individuals with chronic idiopathic neck pain (CINP) demonstrate altered balance and gait parameters. However, it is not clear whether GSR is affected in individuals with CINP.

**Objectives:** We have hypothesised that GSR could be altered in individuals with CINP because of their altered gait pattern. Therefore the aim of the study was to compare GSR, gait speed, step length and cadence between individuals with CINP and healthy controls and investigate the relationship between disability and spatiotemporal gait parameters in individuals with CINP.

**Methods:** Twenty-five individuals with CINP (17 female – 8 male, mean age: 37,28±13,47) and 25 healthy controls (17 female – 8 male, mean age: 36,6±14,2) recruited into this study. Participants with CINP completed the Turkish version of Neck Disability Index (NDI). All participants performed the 10-metre walking test in three walking conditions: Preferred walking (PW), walking with head rotation (HRW), walking at maximum speed (MAXW). Video analysis method involving slow motion camera (120 fps) was used to measure spatiotemporal gait parameters. GSR was calculated by dividing cadence (step/s) to gait speed (m/s). Independent samples t-test was used to compare groups for GSR and other gait parameters. Pearson correlation coefficients were computed to find associations between NDI and gait parameters.

**Results:** Individuals with CINP exhibited slower gait speed and cadence in all walking conditions (p<0.05). In individuals with CINP, step length was found to be shorter in only HRW (p<0.05), however, GSR was higher in HRW and MAXW (p<0.05). GSR values calculated in three walking conditions were found to be moderately correlated with NDI (r=507 for PW, r=533 for HRW, r=516 for MAXW, p<0.05). A negative and moderate correlation was found between preferred walking speed and NDI (r=-473, p<0.05).

**Conclusions:** Our results suggested that neck pain have a negative impact on gait parameters. Also, individuals with CINP had a more stable gait pattern involving less dynamic components. Assessment of GSR and related gait parameters in different walking conditions may be addressed in clinical assessment of CINP and may provide additional information for management of such disability.

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**AB1410-HPR** **HEALTH PROFESSIONALS' PERSPECTIVE ON BENEFITS AND RISKS OF LOW DOSE GLUCOCORTICOIDS IN RA – AN INITIATIVE UNDER THE GLORIA PROJECT**

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**Background:** The Glucocorticoid Low-dose Outcome in Rheumatoid Arthritis Study (GLORIA) is an international investigator initiated pragmatic

randomised trial designed to study the effects of low dose glucocorticoids (GC) in elderly patients with Rheumatoid Arthritis (RA). The research team is also committed to promoting a better understanding of the risks and benefits of these drugs among health professionals and patients. In order to achieve these goals, it is important to assess the current concepts and concerns of health professionals (HP) regarding GCs.

**Objectives:** In this study, we evaluated the beliefs about GC benefits and risks of HP who regularly use and monitor them in the treatment of RA.

**Methods:** These surveys were disseminated to HP who have experience dealing with RA patients in their daily clinical practice. These surveys mainly enrolled physicians, but also nurses or physiotherapists who considered themselves experienced in this field. The surveys were made available in Portuguese and English, and disseminated through the GLO-RIA investigational team. National medical societies contributed by inviting clinicians to participate.

Regarding the questions on GC efficacy, HP could signal (dis)agreement on a 5 point scale: disagree, slightly disagree, neutral, slightly agree, and agree. Agreement was defined as the proportion of HP answering slightly agree or agree. Survey Monkey software was used to disseminate the online surveys.

**Results:** Responses provided by 130 HP are summarised in table 1. The results are presented taking all participating countries in account as the rates are similar between them. Most responses came from The Netherlands (57%) and Portugal (34%). Almost all participants were physicians (97%).

Efficacy of GC was highly endorsed. Close to 90% of HP considered low dose GC were very effective in the control of signs and symptoms of RA, and agreed that GC improve RA symptoms within days. Almost 80% agreed that GC reduce structural damage, and 85% disagreed that GC lose their efficacy after a few months.

The opinions of health professionals regarding frequency of GC adverse events are presented in table 2.

Regarding GC AE events, most of the respondents considered that low dose GC adverse events were very rare or rather rare, except for glycaemic control in patients with diabetes and osteoporosis. Acne and cardiovascular events were evaluated as very rare adverse events by approximately one third of HPs. However, there was significant heterogeneity in the responses.

**Abstract AB1410HPR – Table 1.** Health professional's characteristics (n=130) and data on GC's efficacy.

Country of participants, number (%)	
Netherlands	70 (57)
Portugal	41 (33)
Others	11 (9)
Physicians, number (%)	122 (97)
Level of agreement for statements, number (%)	
At a dose ≤ 7.5 mg prednisolone/day, GC:	
- are very effective in the control of signs and symptoms of RA	88 (90)
- improve RA symptoms within days	86 (88)
GC reduce the probability of articular damage caused by RA	77 (79)
In RA these doses of GC lose efficacy after a few	
- months of therapy	15 (15)
- years of therapy	18 (18)

GC – Glucocorticoid; RA – Rheumatoid Arthritis.

**Abstract AB1410HPR – Table 2.** Frequency of low dose GC's adverse events according to health professionals who attended this survey (% of HP per frequency category).

	None	Very rare (<1%)	Rather rare (1-3%)	Rather frequent (4-10%)	Frequent (11-20%)	Very frequent (>21%)	Don't know
Acne	13	33	29	19	2	1	4
Mood disturbances	8	19	40	28	4	0	2
Poor DM control	1	6	15	42	27	9	1
Cardiovascular events	6	34	33	16	3	0	9
Osteoporosis	1	7	21	43	19	7	3
Serious infections	13	33	42	11	1	0	1

**Conclusions:** GC are widely used drugs in RA. The vast majority of participating HPs are convinced that GCs are efficacious in the treatment of RA, including DMARD effects, and retain this efficacy long term. However, concerns about severe side-effects are also very prevalent.

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## AB1411-HPR HYPERMOBILITY AND FIBROMYALGIA: COEXISTENCE OR MISTAKEN IDENTITY?

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**Background:** The 2010 classification of fibromyalgia (FM) has many overlapping features with hypermobility-Ehler Danlos Syndrome (hEDS) such as chronic widespread musculoskeletal pain, sleep disturbances, fatigue and anxiety.<sup>2, 4, 5</sup> Indeed hEDS may be misdiagnosed as FM because of diffuse pain with a strong myofascial component.<sup>1</sup> Chopra<sup>1</sup> believes these should be considered as two distinct conditions which may co-exist. By classifying as one and ignoring the other are we doing our clients a disservice?

The five point questionnaire (5PQ) is a simple questionnaire used to detect hypermobility and is claimed to have good reproducibility in addition to satisfactory sensitivity and specificity.<sup>3</sup> This audit examined the numbers of FM clients that also fulfilled the hEDS criteria according to the 5PQ.

**Methods:** 66 clients with a consultant diagnosis of FM who attended the multidisciplinary FM education session were invited to fill in the 5PQ along with their fibromyalgia impact questionnaire (FIQ). 57 of the 66 completed both questionnaires over a 13 month period.

The cut off points of 2 out of 5 for the 5PQ and 50 on the FIQ were used.

The higher numbers on the 5PQ indicate increased likelihood of hypermobility.

Around 50 on the FIQ is typical for FM with higher values indicating increased severity.

The individual scores for the FIQ question on anxiety were also examined. Question 19 rates anxiety on a visual analogue scale from 0–10, the higher values indicating increased levels of anxiety.

**Results:** 54 females and 3 males aged between 18 and 76, mean age 51.

15 of the 57 (26%) scored 2 or above on the 5PQ suggestive of hypermobility.

Of those 15, 10 (66%) scored greater than 50 on the FIQ thus meeting the criteria of FM also.

7 of the 15 (47%) scored 8 or above on the anxiety scale.

**Conclusions:** From this audit 26% of FM clients also scored positively for hEDS as per the 5PQ. hEDS may account for some or all of their FM symptoms.

The 5PQ is a quick and easy tool to use. It may improve hEDS detection rates and could be used in a busy rheumatology clinic.

Further research is required to ascertain whether those with positive scores meet the physical criteria for hEDS.

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## HPR Epidemiology and public health (including prevention)

### AB1412-HPR IS DIFFUSE ALVEOLAR HAEMORRHAGE IN ANCA-ASSOCIATED VASCULITIS PREDICTIVE OF POOR PROGNOSIS?

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**Background:** Diffuse alveolar haemorrhage (DAH) is a serious complication of anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV). Detailed characteristics of patients with AAV and associated DAH have been limited to case reports and a few case series, due to the rarity of the condition.<sup>1</sup> Prompt diagnosis is required as early treatment is crucial.

**Objectives:** To compare clinical manifestations, laboratory and immunological values, morbidity and mortality in patients with ANCA-associated vasculitis (AAV) with and without Diffuse Alveolar haemorrhage (DAH)

**Methods:** Retrospective cohort study. Data from the medical records of patients over the age of 18 were evaluated between the years 2000–2017. Ninety patients with diagnosis of AAV who met the criteria of ACR 1990 Classification or Chapel Hill Consensus Conference 2012 were included. DAH was diagnosed based on minor or major hemoptysis and/or respiratory insufficiency together with at least 1 positive result on x-ray and/or computed tomography scan. The sample was divided in two groups: with DAH (group 1) and without DAH (group 2) along the disease. We compared demographic data, Birmingham Vasculitis Activity Score (BVAS) and Five Factor Score (FFS) at the onset of the disease, hemogram, creatinine and ANCA antibodies by immunofluorescence and/or ELISA, clinical manifestations as renal, neurological, mucocutaneous, articular, cardiological, ophthalmological and ear, nose and throat (ENT) damage and mortality between groups.

Chi-square or Fisher's exact test was used for dichotomous variables as appropriate. P-value < 0.05 was considered statistically significant. Logistic regression analysis was used to identify predictors of survival.

**Results:** Group 1 included 24 patients (66% male, mean age at onset of the disease 54 years). Most frequent type of vasculitis was Granulomatosis with polyangiitis (GPA) 54%. Mean BVAS 21 points and FFS 1 point. Group 2 included 66 patients: 36% male, mean age of the disease 52 years, GPA 45%, BVAS was 17 points and FFS de 0 points. Table 1 shows demographic, clinical data and mortality of each group. Logistic regression analysis showed statistically significant difference between DAH and male sex (p: 0.017 OR 6.08 CI 95% 1.37–26.92).

Abstract AB1412-HPR – Table 1

	With HAD n=24 (26.6%)	Without HAD n=66 (73.4%)	p-value	OR (CI 95%)
Male sex	16 (66.7%)	24 (36.4%)	0.011	3.50 (1.30–9.38)
BVAS	21 points	17 points	0.009	
FFS	1 point	0 point	<0.001	
Anaemia	21 (87.5%)	30 (45.5%)	<0.001	8.4 (2.28–30.91)
Mucocutaneous disease	1 (4.2%)	19 (28.8%)	0.018	0.11 (0.01–0.91)
ENT disease	7 (29.2%)	35 (53%)	0.045	0.36 (0.13–0.99)
Neurological disease	4 (16.7%)	31 (47%)	0.009	0.22 (0.07–0.73)
Renal damage	24 (100%)	31 (47%)	<0.001	1.70 (1.40–2.23)
RPGN	13 (54.2%)	12 (18.2%)	0.001	5.31 (1.92–14.71)
Dialysis	8 (33.3%)	4 (6.1%)	0.003	6.8 (1.69–27.35)
Mortality	5 (22%)	12 (21%)	0.930	1.05 (0.32–3.44)

**Conclusions:** DAH was associated with increased morbidity but not modified the mortality in this group of patients. The results seem to be agree on the Five Factor Score<sup>2</sup> that does not include DAH within parameters.

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### AB1413-HPR ADVANTAGES OF RHEUMATOLOGY NURSING VACCINATION OF PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASES OF AUTOIMMUNE ORIGIN. ANALYSIS OF THE FIRST 3 YEARS

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**Background:** Patients with systemic autoimmune diseases (SAD) have higher incidence of infections. In our Service, until 2014 about 50% of patients did not complete vaccination for pneumococcus or hepatitis B virus (HBV).

**Objectives:** To know the characteristics of vaccinated patients and advantages of vaccination by Rheumatology nurse (Nurse-RHEU).

**Methods:** Observational study of patients in follow-up in rheumatology, vaccinated from 2015–2017, by SAD in treatment with biological therapy and/or immunosuppressive, by Nurse-RHEU, following the recommendations from SVR and the Valencian Society of Preventive Medicine and Public Health Consensus Document for the vaccination of patients with SAD, published in 2014. Nurse-RHEU, assumed from 2015 the vaccination of all rheumatology patients with SAD. The vaccines to be administered were: pneumococcal (13 V and/or 23 V) and hepatitis B virus (HBV).

Pneumococcal vaccination should be initiated with the conjugate/13 V type and at least 8 weeks later with a dose of polysaccharide/23 V vaccine. A single 23 V booster dose is recommended 5 years after the first dose. Only if patient have received a previous dose of 23 V, it is advisable to administer type 13 V, one year later. For the HBV vaccine, it is necessary previously check the immune status of the subject. If it is not immune, 3 doses will be administered (0–1–6 months).

Since 2015, our Section has: refrigerator, electronic access to the Vaccinated Nominal Registry of the Valencian Community (it collects data of the patient, date, type, batch of vaccine administered), specific database (epidemiological data of the patients, future dose programming, access to electronic medical records) and Nurse-RHEU trained. Previously, the nurse details possible side effects, and how to act or contact.

**Results:** Of the 261 patients vaccinated during 2015 to 2017, 65% were women, with mean age 53.57±15.50 years (10–81 years). The diagnosis was: rheumatoid arthritis: 48%, ankylosing spondylitis: 23%, psoriatic arthritis: 13%, systemic lupus erythematosus: 7%, uveitis: 4%, and others 5%. The reason for vaccination was: initiation treatment with a biological drug (51%), or immunosuppressive (49%). A total of 621 vaccines were administered, which were: 13-valent conjugate antineumotococcal: 259 (42%), 1 st VHB dose: 94 (15%), 2nd VHB dose: 85 (14%), 3rd VHB dose: 72 (12%), pneumococcal 23-valent polysaccharide: 111 (17%). All vaccines were registered in the Vaccinated Nominal Register of the Valencian Community.

**Conclusions:** 1. Patients with SAD in biological treatment and/or immunosuppressant, vaccinated by Nurse-RHEU, achieve a completeness of all doses of vaccination, close to 100%. 2. In a large part of the patients, vaccination is scheduled at the beginning of the diagnosis of the disease, at the first consultation or immunosuppressive treatment, the same day of the visit to the Rheumatologist, avoiding unnecessary visits to the patient. 3. An adequate electronic registry allows immediate access to information from any point in the Valencian Community, through access to the computer program of the Health department.

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**AB1414-HPR** LONG TERM EFFECTIVENESS OF A TREAT TO TARGET APPROACH AND IMPACT IN OVERALL HEALTH IN PATIENTS WITH RHEUMATOID ARTHRITIS – A 3 YEAR FOLLOW-UP

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**Background:** Rheumatoid arthritis (RA) is a common chronic inflammatory disease. It is characterised by progressive, irreversible joint damage, impaired joint function and pain, the disease causes disability and reduced quality of life. Treat-to-target (T2T) is an acknowledged management strategy for RA. It proposes that the therapeutic target in RA should be a state of remission, or an alternative goal could be a low disease activity, additionally it looks to achieve long-term health quality of life for the patient.<sup>1,2</sup>

**Objectives:** To describe the effectiveness of a T2T strategy regarding Disease Activity Score 28 (DAS28) in a 36 month period in patients who receive conventional or biological DMARDs and attend at least at four consults per year in a specialised in RA centre.

**Methods:** A descriptive cohort study was conducted. Medical records of patients from specialised in RA centre were reviewed between 2015–2017; those patients were followed-up under T2T standards and a multi-disciplinary approach. Each patient had a minimum of 4 follow-up visits per year. Clinical follow-up was designed by the authors according to DAS28 as follows: every 3–5 weeks (DAS28 >5.1), every 7–9 weeks (DAS28 ≥3.1 and ≤5.1), and every 11–13 weeks (DAS28 <3.1). Therapy had to be adjusted with DAS28 >3.2 unless patient's conditions don't permit it; We divided patients in four groups: remission (REM), low disease activity (LDA), moderate disease activity (MDA) and severe disease activity (SDA) patients and the aim of the study was to look at what percentage of patients reached a LDA or REM. Descriptive epidemiology was done, we calculated means, and standard deviations for continuous variables and categorical variables were presented as rates. We analysed normality for DAS28, in order to compare disease activity at beginning and the end of follow-up.

**Results:** During three years 1146 patients had confirmed RA and attended to a specialised centre with a minimum of 4 visits per year, 86% were female and 14% were men, mean DAS28 at baseline was 3.69±1.10 with a median of 3.1 while at 3 years mean DAS28 was 2.94±0.87 with a median of 2.79. At baseline 46% were in LDA, 40% in MDA and 13% were in SDA. Regarding pharmacological therapy 63% were receiving conventional DMARDs while 37% were receiving biological DMARDs. When we evaluated the effectiveness of T2T approach in terms of disease activity at the end of 36 months 42% achieved remission and 26% LDA (in total 68.5% of patients improved clinically) see table 1. We performed a Wilcoxon test in order to compare the mean DAS28 at baseline and at the end showing statistical significance (p<0.05).

Abstract AB1414-HPR – Table 1

ACTIVITY LEVEL	AT BASELINE		3 YEARS FOLLOW-UP	
	n	%	n	%
REM			488	42.6
LDA	532	46.42	297	25.9
MDA	462	40.31	336	29.3
SDA	152	13.26	25	2.2

**Conclusions:** This real-world data demonstrates the effectiveness of a T2T multidisciplinary approach in patients with rheumatoid arthritis who remained in conventional or biological therapy during three years.

Abstract AB1415-HPR – Table 1

	Mean	SD		CI 95%		Mean	SD		CI 95%		p values
		Control Group	Rheumatoid Arthritis Group	Control Group	Rheumatoid Arthritis Group		Control Group	Rheumatoid Arthritis Group			
Age(years)	53.8	13.3	14.86	49.55	58.05	56.78	14.86	51.83	61.74	0.689	
BMI(Kg/m2)	26.9	3.87	2.46	28.48	25.49	27.1	2.46	28.74	25.33	0.879	
FFI TOTAL	11.08	15.57	6.1	16.05	39.03	39.03	26.44	30.21	47.85	>0,001	
FFI Pain	14.75	18.8	22.54	8.71	20.79	41.16	22.54	33.65	48.68	>0,001	
Manchester	52.5	35	10.8	10	2.5	54.1	32.4	10.8	2.7	0.986	
Hallux Scale	None	Mild	Moderate	Moderate	Severe	None	Mild	Moderate	Severe		

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**AB1415-HPR** DIFFERENCES ON PAIN AND STRUCTURAL ANORMALITIES BETWEEN PATIENTS WITH RHEUMATOID ARTHRITIS AND THOSE WITH INESPECIFIC FOOT PAIN: CROSS SECTIONAL STUDY

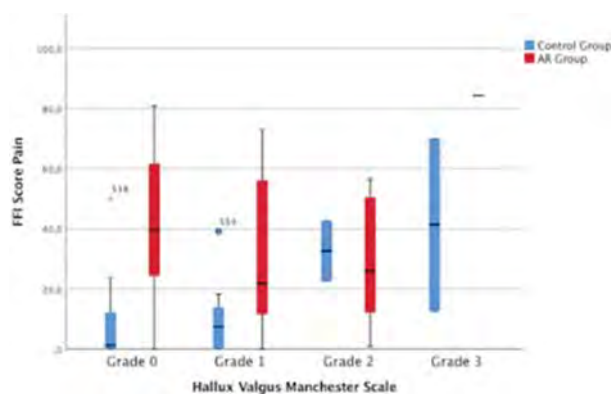
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**Background:** The presence of foot pain and deformity is ubiquitous in Rheumatoid Arthritis (RA). Epidemiological studies consistently suggest a prevalence of foot pain of 90%.<sup>1</sup> Weight gain, high levels of fatigue and deformities such as hallux valgus and metatarsus primus varus, are very frequent too.<sup>2</sup>

**Objectives:** The aim of this study was to analyse pain levels and structural abnormalities among subjects with foot pain and patients with RA.

**Methods:** A sample comprised of 40 subjects was studied. Participants were recruited from a private podiatry clinic and from the Department of Rheumatology (Granada, Spain). The inclusion criteria were subjects with RA with a duration of at least 10 years according to the American Rheumatism Association criteria for RA, while patients with foot pain seeking podiatry services from April 2017 to January 2018 were used as control group. Outcome measures were as follows: foot pain, activity limitation, disability and foot health status by Foot Function Index questionnaire<sup>3</sup> and Hallux Valgus by Manchester Hallux Valgus Scale.<sup>4</sup>

**Results:** As shown in Table 1, we found statistical significant differences for the pain scale(p>0.001) and in total score(p>0.001) in the FFI scale between AR group and the control group, but not between group in the Manchester Hallux Scale (p=0.986)



Abstract AB1415-HPR – Figure 1

**Conclusions:** We found higher levels of pain in subjects with RA compared to the control group. Furthermore, although there are clinical

differences subjects with RA and with foot pain, we can not conclude strongly that RA increases the possibility of having deformities such as Hallux Valgus.

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#### AB1416-HPR RISK FACTORS ASSOCIATED WITH FRACTURE RISK IN WOMEN WITH BREAST ADENOCARCINOMA IN A SEVILLE COHORT

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**Background:** Introduction: Women with breast cancer have a higher risk of osteoporotic fractures than the rest of the population of the same sex and age. This problem is due to multiple factors among which are the treatments to which they are subjected. Among them, chemical castration, chemo and/or radiotherapy, corticosteroids, surgery, monoclonal antibodies against HER-2 and aromatase inhibitors are related to increased bone resorption.

**Objectives:** Objectives: To assess the prevalence of and factors associated with fragility fractures in women with breast adenocarcinoma.

**Methods:** Patients and methods: Prospective, cross-sectional study in progress. In a multidisciplinary consultation of OP and Oncology of two third-level centres in Seville, women diagnosed with breast cancer are treated. The factors associated with the presence of vertebral and peripheral fragility fractures in these patients at the time of the first evaluation were analysed.

**Results:** Results: 409 women were included in this analysis, evaluated between September 2014 and December 2017. The median age (Q1-Q3) was 63 55–68 years. 38 (9%) fragility fractures were observed, 22 (5.4%) vertebral and 18 (4.4%) peripheral. Three patients presented peripheral and vertebral fractures. Factors such as smoking, family history, menopause age, exercise, sun exposure, milk consumption or BMI were not associated with fragility fractures. The t-score in the femoral neck or spine was also not associated with fragility fractures. Of the 88 patients treated with tamoxifen, 6 (6.8%) had fragility fractures compared to 32/320 (10%) of those who did not receive tamoxifen (p=0.367). They presented fragility fractures 22/215 (10%) women with letrozole compared to 16/194 (8%) that were not treated with letrozole (p=0.490). At the time of the first evaluation, the mean (SD) of the FRAX was 6.1 (5.3) in women without fractures and 11.7 (7.7) in those with fragility fractures (p<0.001). In the logistic regression, the only variable associated independently was the FRAX [FRAX >10, adjusted OR 8.9 (3.9–20.4), p<0.001]. The best logistic regression model explained 12% of fragility fractures

**Conclusions:** Conclusion: In women with breast cancer, FRAX is the only clinical variable associated independently with the presence of fragility fractures in our

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#### AB1417-HPR PREDICTORS OF COGNITIVE DYSFUNCTION IN PATIENTS WITH LUPUS

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**Background:** Cognitive Dysfunction (CD) is one of the most common neuropsychiatric manifestations in systemic lupus erythematosus (SLE).

CD occurs independently of structural damage<sup>1,2</sup> or disease activity<sup>3</sup> impacts life quality.<sup>4</sup> Cardiovascular comorbidities, lower educational level and physical inactivity are risk factors for dementia in elderly worldwide<sup>6</sup> and are frequently found in SLE patients. Identifying the factors involved with CD in SLE can clarify physiopathological processes and preventive measures.

**Objectives:** To verify if cardiovascular comorbidities and physical inactivity are predictors of CD in Brazilian patients with SLE.

**Methods:** a 168 patients and healthy controls between 18 and 59 years were allocated into three groups: CON (n=57), SLEG (n=63) and NPSLE (n=48). Epidemiological information, laboratory results, medication use, cardiovascular comorbidities (hypertension, diabetes, dyslipidemia, previous myocardial infarction), SLICC and SLEDAI scores were compiled from charts. Variables were compared using ANOVA, Kruskal-Wallis, Mann-Whitney and Qui-square, and p<0.05.

**Results:** There were no differences between groups regarding age, educational level. There was also no difference in prevalence of diabetes, myocardial infarction, tobacco use and disease duration. SLEG and NPSLE had more hypertension (CON 18.9%; SLEG 55.6%; NPSLE 39.6%) and dyslipidemia than controls (CON 9.4%; SLEG 36.5%; NPSLE 39.6%). SLE patients presented more depression (p<0.001), anxiety (CON 9.5±8.3; SLEG 16.3±13.3; NPSLE 14.1±10.9; p=0.008) and lower levels of physical activities than controls. NPLES group presented more CD (CON 21.1%; SLEG 34.9%; NPSLE 62.5%) when compared to CON (p<0.001) and SLEG (p=0.012). Major neuropsychiatric manifestations (OR 2.460; 95% CI 1.007–6.008; p=0.048); low educational level (OR 0.870; 95% CI 0.756–1.000; p=0.050), anxiety (OR 1.031; 95% CI 0.994–1.069; p=0.096), and disease damage (OR 1.691; 95% CI 1.175–62.435; p=0.005) were independently associated with CD.

**Conclusions:** Neuropsychiatric manifestation, low educational level, anxiety and disease damage are predictors of CD in patients with SLE. Although cardiovascular comorbidity and sedentary lifestyle are a risk factor for dementia in general population, those variables might play a minor role in SLE patients.

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#### AB1418-HPR LOW BACK PAIN AND INFLUENCE ON THE FUNCTIONAL DISABILITY OF THE ELDERLY POPULATION OF MANAUS – AMAZONAS, BRAZIL: A CROSS – SECTIONAL STUDY

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**Background:** Low back pain (LBP) is the primary cause of disability and absenteeism in the workplace, it is a complex multidimensional phenomenon with staggering social costs. These symptoms reduce functional capacity and limit both physical and psychosocial aspects of elderly life.

**Objectives:** To identify the influence of LBP on the functional disability in elderly subjects.

**Methods:** The study was approved by Research Ethics Committee of Medical School at University of Sao Paulo, Protocol. CAAE.56709716.5.1001.0065. This a cross-sectional study, 700 community-dwelling elderly participated, both genders, ≥60 years old, and functional

disability was measured using the Rolland Morris Disability Questionnaire – Brazil version (RMDQ–BR).

**Results:** The punctual prevalence of LBP was 42.09%, age 68.61±6.06 years old, women 78.14%, and the functional disability score assessment was 11.26±6.07. About responses frequently items (RMDQ–BR) were: I change position frequently to try to get my back comfortable (84%); I avoid heavy jobs around the house because of my back (75%); Because of my back, I try not to bend or kneel down (73%); Because of my back, I go upstairs more slowly than usual (62%); I walk more slowly than usual because of my back. (57%); Because of my back, I use a handrail to get upstairs (55%).

**Conclusions:** The data demonstrates that there is a relationship between DL and functional disability in the elderly. It has been verified that the constant change to the maintenance of the posture, the decrease of the walking speed, to climb stairs with assistance, and the accomplishment of the activities of the daily that require movements of flexion trunk or knee have been reported to be difficult to perform. These data may be useful in the development of preventive strategies by health professionals that aim to encourage changes in routine care of daily living activities.

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**Disclosure of Interest:** None declared

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#### AB1419-HPR CLINIC OF PREGNANCY AND RHEUMATIC DISEASES: EPIDEMIOLOGIC CHARACTERISATION

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**Background:** Pregnancy in women with Rheumatic Diseases (RD) is of high risk and requires a close communication between the rheumatologist, obstetrician, and all other specialists involved. It may have an effect on the natural history of autoimmune disease, a phenomenon that is particularly relevant in Systemic Lupus Erythematosus (SLE) and Rheumatoid Arthritis (RA). Additionally, there are consequences that autoimmune disease may yield throughout the course of conception and gestation.

**Objectives:** To describe the epidemiological characteristics of patients seen at the Clinic of Pregnancy and Rheumatic Diseases (Clínica de Embarazo y Enfermedades Reumáticas, CEER) located in the Jose E. Gonzalez University Hospital in Mexico.

**Methods:** We conducted a descriptive transversal study of a cohort of 50 adult patients that attended CEER; which were categorised within three consultation groups (reproductive age, with a present or future desire to become pregnant, pregnant or in postpartum period). All patients were evaluated by the Maternal-Fetal Medicine and Rheumatology department. CEER was created in August 2017 and provided medical follow up for newly pregnant patients, those already pregnant, and patients in the immediate postpartum period. Epidemiological data was collected.

**Results:** Of the 50 patients, 8 (16%) with a present or future desire to become pregnant, 24 (48%) pregnant, just only one presented gestational diabetes; and 18 (36%) were in the immediate postpartum period. The median age was 32 years ( $SD=6.16$ ). The 18 births were live births obtained by caesarean section, 8 (55.8%) were pre-term (<37WG) and none presented eclampsia or preeclampsia. Of the patients, 22 (44%) had a diagnosis of RA, 10 (20%) had SLE, 10 (20%) had Antiphospholipid Syndrome, and the remaining 8 (16%) had other diagnoses (table 1). Only 18 (36%) had previous abortions.

**Abstract AB1419HPR – Table 1.** Association between current status and diagnosis

Current status	Systemic Lupus Erythematosus	Rheumatoid Arthritis	Antiphospholipid Syndrome	Other	Total
Reproductive age	0 (0%)	5 (10%)	2 (4%)	1 (2%)	8 (16%)
Pregnant	7 (14%)	6 (12%)	6 (12%)	5 (10%)	24 (48%)
Postpartum	3 (6%)	11 (22%)	2 (4%)	8 (16%)	18 (36%)

Note: n=50

**Conclusions:** The evaluation of patients with RD requires a close follow-up, which is why the population of reproductive age with RD must be seen early on. Considering that our results revealed a high percentage of preterm live births medical attention must be provided from the pre-conception to the postpartum period.

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#### AB1420-HPR PATIENT DELAY IN RHEUMATOID ARTHRITIS. A SURVEY ON SYMPTOM INTERPRETATION BEFORE FIRST VISIT TO GENERAL PRACTITIONER

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**Background:** Early initiation of effective treatment of rheumatoid arthritis (RA) leads to improved clinical and radiological status in the patients. Thus, there is a need to decrease the time from patients experience their first joint symptoms to initiation of treatment. The patient's social context may influence the period from the patients experience their first joint symptoms until they present their symptoms to their general practitioner (GP) (patient delay (PD))

**Objectives:** Firstly, to explore whether socioeconomic and other factors influence PD in persons referred to a rheumatologist due to suspicion of RA. Secondly, if socioeconomic factors affected whether the patients subsequently received a diagnosis with inflammatory arthritis (IA)

**Methods:** We developed a survey based on previous Danish<sup>1,2</sup> and UK<sup>3</sup> studies regarding symptom interpretation and PD together with two patient research partners. We asked consecutive patients, referred to a rheumatology outpatient clinic or a private rheumatologist in the Region of Southern Denmark, with a suspicion of RA, to complete the survey online or in a paper version before examination by a rheumatologist. We used STATA/IC 15.0 for descriptive statistics, univariate, and multivariate logistic regression analyses.

**Results:** From December 2016 to July 2017, 144 patients completed the survey. In total 86 (60%) were female, mean age 55 (SD 15.3). In total 76 (53%) had short PD (0–3 months), 51 (35%) intermediate or long PD (≥4 months) (12% missing answers); 71 (49%) totally or partially agreed that their symptoms had a gradual onset. Three to seven months after the survey, 45 (22%) had received a diagnosis of some sort of inflammatory arthritis (IA). In the following analyses age was dichotomized (<or≥50 years). Age, sex, cohabitant status, educational level and whether patients undertook paid work or not, did not significantly affect



the duration of PD. Female sex reduced the odds for an IA diagnosis compared to male sex (OR 0.35,  $p=0.05$ ), but this did not reach significance in the multivariate analyses. Whether patients' totally or partially agreed that they had: confidence to their general practitioner, felt they had support from others, whether their symptoms were obvious to others or significantly affected their work or leisure time, did not affect PD. Only gradual onset of symptoms significantly increased the odds for longer PD (OR 2.20,  $p=0.04$ )

**Conclusions:** In Denmark, socioeconomic factors did not seem to affect PD, but gradual onset of symptoms significantly increased the odds for median or longer PD

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#### AB1421-HPR IS THERE ANY CHANGE IN THE DEMOGRAPHICS OF RA PATIENTS CANDIDATE FOR bDMARD THERAPY?

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**Background:** There are an increasing number of data that rheumatoid arthritis (RA) patients who are candidates for bDMARD (biologic disease modifying drug) therapy have nowadays a milder disease and lower disease duration than 10 years ago. The T2T strategy aims to achieve remission. Percentage of patients achieving the treatment goals seems to be a good quality indicator.

**Objectives:** To verify among our RA patients treated with bDMARD since 2006, whether they have lower disease activity (DAS28) and shorter disease duration and younger age nowadays than at the beginning of the biologic era. As a measure of quality: how many patients treated with bDMARD achieved remission.

**Methods:** This is a cross sectional study. Among 455 patients RA treated with 9 different bDMARD we selected those who were treated with the most widely used at the time of the study (12.01.2017). The 103 ADA treated patients' data were collected by means of a tablets with the help of study nurses. Descriptive statistics were used for analysis of data (age and disease duration at the start of bDMARD, DAS28 at start and last visit, percentage of patients on remission).

**Results:** 103 (incl. 15 men) biologic naive patients (age: 56±13,1) are treated with ADA at time of the study. In 3 years cohorts (2006–2008;2009–2011, 2012–2014, 2015–2017) we found no change of age, but a slight decrease of disease duration as well as DAS28 at bDMARD initiation.

**Abstract AB1421-HPR – Table 1**

Cohort	n	Age at bDMARD initiation	Disease duration at bDMARD initiation	DAS28 at bDMARD initiation
2006–2008	24	50±10.1	10±7.1	6.1±0.84
2009–2011	10	42±15.1	14±15.1	5.2±0.72
2012–2014	20	49±13.1	6±6.7	5.5±1.09
2015–2017	49	55±13.5	7±7.8	5.0±1.35

51%(53) of the 103 RA patients on ADA therapy were in remission.

**Conclusions:** In our study population on ADA treatment we didn't find significant shift toward younger patients, but the disease duration and activity of disease at the start of the ADA treatment slightly decreased. By means of bDMARD's half of the patients achieved remission.

**Disclosure of Interest:** None declared

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#### AB1422-HPR PREVALENCE AND RISK FACTORS OF LOW BACK PAIN IN THE INDIGENOUS POPULATION OF GALIBI IN SURINAME: A CROSS-SECTIONAL COMMUNITY-BASED STUDY

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**Background:** Musculoskeletal disorders are regarded as the fourth greatest burden on world health. Among these disorders, low back pain (LBP) ranks first for disability and sixth for overall burden. However, there is a large range in prevalence in the general population (1.0% to 58.1%) due to environmental and individual factors. There is limited data on prevalence and risk factors for LBP in developing countries, especially for vulnerable groups. This includes indigenous populations. Therefore a study was done regarding LBP in an indigenous population in Suriname, a South-American middle-income country.

**Objectives:** The objective of the study was to determine prevalence of self-reported LBP and possible relationships with several risk factors (gender, age, education level, body mass index (BMI), and smoking) in an indigenous community.

**Methods:** Data on LBP in Galibi was acquired through the COPCORD (Community Oriented Program for the Control of Rheumatic Diseases) stage 1 method. Galibi is located in the rural eastern coastal area of Suriname and consists of two indigenous villages: Langamankondre and Christiaanankondre. The Ministry of Health provided ethical approval. Indigenous persons above 15 years, who were present in the village at the time of the study, were eligible for participation. After informed consent all participants were interviewed, and their anthropometric measurements were taken (height, weight, waist circumference). Association between LBP and risk factors were analysed with the chi square test. Significance level was set at  $p \leq 0.05$ .

**Results:** From 4–11 December 2016, a total of 153 persons participated in the study. There were 79 (52%) male and 74 (48%) female respondents. Mean age was 50.9 years (standard deviation 18.1 years; age range 16–92 years). A total of 80 respondents (52.2%) indicated that they had experienced at least one episode of LBP during their life time. Prevalence for males was 53.2% and 51.4% for females. The highest prevalence was among persons in the age group 55–74 years (60.3%). The lowest prevalence was found among persons who at least finished secondary school (41.2%). Smokers had a higher prevalence for LBP (60.7%) compared to non-smokers (50.4%), and LBP prevalence increased as BMI increased. None of the variables were significantly associated with LBP.

**Conclusions:** The life time prevalence of LBP among the study population was 52%. No significant difference in prevalence between genders was found. There was a higher prevalence for smokers, persons with a lower education level and those with an increased BMI. However, significant associations between LBP and risk factors were not found in this study. Further research in a larger population is recommended.

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#### AB1423-HPR IMPACT OF OSTEOARTHRITIS ON WORK PARTICIPATION: A SYSTEMATIC REVIEW

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**Background:** Osteoarthritis (OA) is a common musculoskeletal condition in working age adults and linked to substantial reduction in work productivity and increased risk of work loss.<sup>1,2</sup>

**Objectives:** This systematic review aimed to investigate the impact of OA on the individual's work participation to identify targets for interventions and reduce the risk of future work loss.

**Methods:** Database searches included the Cochrane Library, Medical Lit-

erature Analysis and Retrieval System Online, Excerpta Medica Database, Cumulative Index to Nursing and Allied Health literature, King's Fund, Allied and Alternative Medicine, Psychological Information Database, Applied Social Sciences Index and Abstracts, Ageline, Social Services Abstracts and British Nursing Index from earliest to November 2017. The PRISMA statement was used to guide the process. Observational, interventional and qualitative studies were included in the review and their methodological quality was assessed by two researchers using the Johanna Brigg Institute Checklists.

**Results:** Twenty-two studies, which were published in 2007 to 2016 (12 cross sectional; 5 cohort; and 5 qualitative) were included. Measurement of workplace limitation varied largely amongst the studies. High pain intensity, decreased physical functioning, physically demanding jobs, lack of opportunities to re-train, and lack of co-worker support were identified as important workplace factors associated with loss of productivity, and both presenteeism and absenteeism were predictive of job disruption and premature work loss. Function was identified as an important mediator of the impact of pain on work productivity, with physiotherapy and exercise classes that target pain and physical function<sup>3</sup> and maximising work place support<sup>4</sup> being recommended to prevent or reduce loss of work productivity. Qualitative studies emphasised the significance of physical environments, and social networks and support, recommending interventions to target individual needs to prevent future work loss.<sup>5</sup>

**Conclusions:** There is a wide range of scientific literature to suggest working people with OA are experiencing work instability due to pain, reduced physical functioning, activity limitation, and lack of co-worker and workplace support, placing them at increased risk of work disability. However, the measurement of workplace limitation varies greatly in this literature, making it hard to conduct empirical comparisons. Due to the temporal and biopsychosocial nature of work disability, there is a need for longitudinal studies to investigate the links between workplace factors and the onset and persistence of work instability in people with OA. Additionally, future qualitative studies should explore the role of personal and psychological factors, such as an individual's self-efficacy and coping skills, and the employer's perspectives on the provision of workplace support, to establish whether these potentially modifiable factors could influence work outcomes in people with OA.

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#### AB1424-HPR CORRELATES OF SLEEP IN RHEUMATOID ARTHRITIS: A SYSTEMATIC REVIEW

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**Background:** Over 50% of those with a diagnosis of Rheumatoid Arthritis (RA) experience poor sleep quality,<sup>Scott 2010</sup> This may result in altered health-related quality of life in addition to decreased daytime function.

**Objectives:** The aim of this systematic review is to identify and compile an account of the correlates of poor sleep in those with RA.

**Methods:** Two reviewers carried out literature searches of nine electronic databases. Literature was chosen based on the application of eligibility criteria, implementation of quality assessment and in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Moher *et al* 2009

**Results:** Fifteen full-text studies were included in the review – fourteen of cross-sectional design, and one randomised controlled trial (RCT). This included 3283 participants with a diagnosis of RA in accordance with the American College of Rheumatology criteria. The outcome measures included in the literature were largely heterogeneous in nature and therefore a meta-analysis was deemed to be unsuitable.

**Conclusions:** There is evidence within the literature to suggest that interactions between pain, fatigue, depression and functional ability play a role in sleep quality in those with RA. However, longitudinal data is

required in order to determine the directionality of these relationships. The most prominent correlate of poor sleep is pain, with twelve studies identifying a positive association between the two variables. Conflicting evidence exists with regard to the association between sleep quality and disease activity, RA medications and patient demographics.

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**Disclosure of Interest:** None declared

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#### HPR Interventions (educational, physical, social and psychological)

##### AB1425-HPR THE EFFECTS OF AEROBIC EXERCISE TRAINING ON PAIN AND DISABILITY FROM OSTEOARTHRITIS OF THE KNEE IN POSTMENOPAUSAL WOMEN

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**Background:** The prevalence, incidence and severity of osteoarthritis (OA) increases in women after menopause. It was indicated that, loss of oestrogen at menopause period was related to the increase in the risk of OA development. It was well documented that aerobic exercise training has positive effects on knee osteoarthritis symptoms and menopausal symptoms however we did not found study on the effects of aerobic training in postmenopausal women with knee osteoarthritis.

**Objectives:** Objective of this study was to evaluate the effects of aerobic exercise training on pain and disability in postmenopausal women with knee osteoarthritis

**Methods:** The study was approved by the Kirikkale University Ethic Committee. 50 voluntary postmenopausal women aged 48–78 years, with stage 2–3 knee OA according to the Lawrence classification were recruited to the study. The clinical information (age, menopause age, duration of OA, etc.) of the patients were questioned.

The cases were randomly divided into two groups as control which was performed combine physiotherapy and treatment group. Combine physiotherapy lasted three weeks and included hot pack, short wave diathermy, transcutaneous electrical nerve stimulation (TENS) and home exercises. After completed treatment, physiotherapist asked the patients to perform home exercises two times every day in three weeks period.

In the treatment group, in addition to combine physiotherapy, walking training on the treadmill performed 5 days/week during 6 weeks. The training intensity was%50–70 maximal heart rate (220-age). 40 min total exercise duration, consisted of a five minute warm-up and cool-down, 30 min brisk walking.

Both groups were evaluated before and after 6 six weeks the treatment. Visual Analogue Scale (VAS) was used to the pain evaluation. Functional ability was assessed by Western Ontario and McMaster Osteoarthritis Index (WOMAC).

Statistical analyses were performed using SPSS version 16 software.

**Results:** It was not observed significant difference on age, body mass index, menopause age, menopause duration and VAS value, WOMAC scores (subscales of pain, stiffness and physical function) before the treatment. ( $p>0.05$ ).

After the treatment, VAS value, WOMAC all subscales' scores were significantly different in favour of treatment group ( $p<0.05$ ). It was found that, VAS value and WOMAC all subscales' scores improved in both groups after the treatment ( $p<0.05$ ).

Subscales of WOMAC' scores and VAS value showed a significant increase that corresponds to a large effect ( $d>0.8$ ) in the treatment group. In the control group, only VAS value showed a significant increase that corresponds to a large effect ( $d>0.8$ ), other increases on WOMAC subscales that corresponds to small and moderate effects ( $d=0.38–0.58$ ).

**Conclusions:** Aerobic exercise training which added to the combined physiotherapy may contribute to decrease of pain and disability in postmenopausal women with knee osteoarthritis.

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**AB1426-HPR IMPLEMENTATION OF NURSE LED CLINIC IN RHEUMATOLOGY DEPARTMENT LJUBLJANA, SLOVENIA**

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**Background:** Nurse-led clinics in Rheumatology Department in Ljubljana have been established in September 2011 after nurses finished education module. The main goal was to provide good care and improved monitoring of patients with rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis which are treated with biologics. In this way nurses started to contribute and shape new ways in helping patients to better manage their disease. With this new approach the nurses have applied some of the recommendations regarding the role of the nurse in treatment of patients with inflammatory rheumatic diseases.

**Objectives:** The aim of this study is to describe the organisation, purposes and activities of a nurse-led rheumatology clinics.

**Methods:** Nurse's intervention data was collected from January 2012 to December 2017. The data is allocated according to individual intervention which has been implemented. We used excel table to represent data.

**Results:** The patients have opportunity for telephone counselling with the dedicated nurse about issues with their anti-TNF therapies. Between January 2013 and May 2014 we collected data in which we recorded 101 calls from patients who were seeking information about biologics. We recorded how many patients had come to the nurse led-clinics. We sorted them in four groups; nurse led follow up clinics, education about self-administration of biologics or some other medicine, blood or skin tests and daily care unite (table 1).

**Abstract AB1426HPR – Table 1.** Number of patients after intervention

Intervention/ Year	2012	2013	2014	2015	2016	2017
<b>Nurse led follow up</b>	478	780	1009	1101	1303	1455
<b>Education</b>	74	117	153	130	141	156
<b>Other intervention</b>	265	316	374	395	448	476
<b>Daily care unit</b>	309	390	446	501	570	664

**Conclusions:** The number of interventions has increased and show importance of nurses in patient management. This is most evident in the area of patient education and monitoring.

**Disclosure of Interest:** None declared

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**AB1427-HPR THE ROLE OF PARENTS' AWARENESS IN PHYSICAL ACTIVITY IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS**

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**Background:** Whilst Juvenile Idiopathic Arthritis (JIA) is one of the most common chronic diseases amongst children, the impact of physical therapy on affected children's life-quality and the importance of an appropriate and regular physical activity get less attention than they ought to. In addition, there are no such studies about the role of parents' awareness in connexion with the regular physical activity for children with JIA available yet.

**Objectives:** The purpose of the survey was to evaluate the awareness of parents in connexion with the Juvenile Idiopathic Arthritis' diagnose, its treatment options, the importance of regular physical activity and how it affects children's life-quality. Everyday experiences say that children with JIA take part in less physical activities than their healthy mates do. Our aim was to detect how important regular physical activity is for parents.

**Methods:** This is a descriptive analysis of our self-compiled questionnaire which has 41 questions. It is being filled in both online and in paper forms since the February of 2017 in the National Institute of Rheumatology and Physiotherapy on the Department of Clinical Immunology, Adults' and Children's Rheumatology. Participants of the study are parents whose child has the diagnose of Juvenile Idiopathic Arthritis and ages between 2–18. Parents whose child has not differentiated diagnose or is under 2 years are excluded.

**Results:** 48 answers met the criteria, 6 answer sheets were excluded. In case the children's condition get worse, 20,8% of parents marked wrong parental measures. All parents acknowledge the importance of physical activity, but only 63% of children do regular physiotherapy at home. Parents could not choose from or rank the appropriate and useful ways of physical activities. Beside the medical team (doctor, physiotherapist, nurse) parents get information from media and internet. They would like to get further information personally in words, in written forms or pamphlets. Parents of children with JIA miss psychic support, alternative treatment options and customised, complex information from the general treatment.

**Conclusions:** The findings of this study support the fact that parents of children with Juvenile Idiopathic Arthritis are well informed about the JIA's inflammatory nature and its symptoms, but they have few and wrong information in connexion with regular physical activity. They have a lack of knowledge about the different kinds of physical activities and sports' effects on the disease, due to which they choose ergonomically wrong kinds of activities in schools or pre-schools. Based on our results, we would like to develop a complex educational program including physical therapy as well.

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**AB1428-HPR TWO-YEAR FOLLOW-UP OF THE THERAPEUTIC EXERCISE PROGRAM FOR PATIENTS WITH ROTATOR CUFF TENDINOPATHY: A SINGLE GROUP STUDY TO INVESTIGATE THE EFFECTS ON PAIN AND DISABILITY**

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**Background:** Although exercise training is accepted as one of the important and active treatment approach for the shoulder-related musculoskeletal problems,<sup>1</sup> the scientific rationale and long-term results for the inclusion of specific progressive exercises are less clear.

**Objectives:** This longitudinal, single group study aims to investigate the effects of a therapeutic exercise program on pain and disability in patients with the rotator cuff tendinopathy.

**Methods:** Twenty-eight participants with chronic non-traumatic unilateral shoulder pain diagnosed with rotator cuff tendinopathy (28.6±5.4 years old, symptoms duration 3.2±1.5 months) were included. The appropriate patient education and criteria-based, supervised exercise program including scapular and rotator cuff neuromuscular control exercises were performed. We evaluated self-reported shoulder pain and disability status by using Shoulder Pain and Disability Index (SPADI)<sup>2</sup> at baseline, after 6 week, 12 week training, at one-year-follow-up, and two-year-follow-up. Repeated measures ANOVA used for statistical analysis.

**Results:** Comparisons showed that there was significantly less SPADI-pain and SPADI-disability score reported starting from six-week after baseline and at two-year-follow-up (p<0.05).

**Conclusions:** The findings of the study showed that pain and disability gains can be achieved with 6 week progressive exercise training for participants with rotator cuff tendinopathy. Therefore, the progressive exercise training should be recommended to apply starting from early shoulder rehabilitation program.



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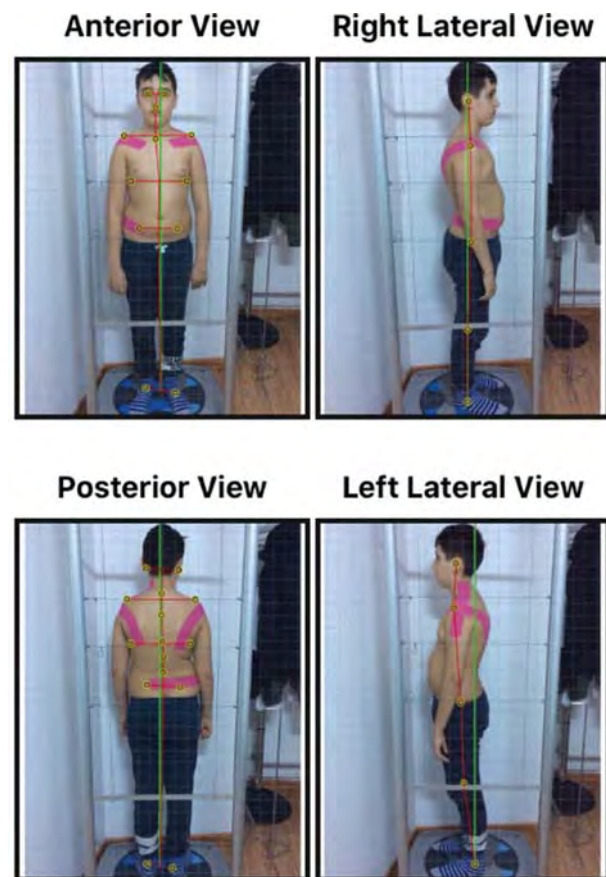
**AB1429-HPR KINESIOTAPING MIGHT HELP TO IMPROVE POSTURAL DISPLACEMENTS IN ADOLESCENTS**

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**Background:** The optimal posture plays an important role for preventing musculoskeletal problems. The therapeutic effects of kinesiotaping have been shown in forward head posture and rounded shoulder posture in adults previously.<sup>1,2</sup> However, as to our knowledge, the effect of kinesiotaping on total posture has not been evaluated before in adolescents.

**Objectives:** To investigate the effect of kinesiotaping application on total posture in adolescents.

**Methods:** Twenty children (11 M/9 F) with postural displacements were enrolled in the study. The postural displacements were evaluated with a mobile application (PostureScreen) which was validated for postural assessment previously. The total scores which were obtained from the anterior view was used for the analysis. Assessments were performed at baseline and 45 min following the kinesiotaping application. The kinesiotaping application was performed as seen in Figure 1.



**Abstract AB1429-HPR – Figure 1**

**Results:** The median age was 12.5 years (IQR: 11.0/15.0 years), the median height was 145.5 cm (IQR: 142.5/166.5 cm) and the median

weight was 38.0 kg (IQR: 33.5/51.0 kg). A significant improvement was observed in anterior angulation degrees. While the baseline score was 8.70° (IQR: 4.10°/14.55°), the score improved following kinesiotaping application to 4.35° (IQR: 2.35°/6.30°) (p=0.009). No significant changes were detected in anterior translation, lateral translation and lateral angulation parameters (p>0.05).

**Conclusions:** According to our results kinesiotaping has a potential to improve postural displacements in adolescents. The improvement in the posture might be resulted from a sustained feedback on the trunk by the kinesiotaping. However, future longitudinal studies which are mainly focused on the chronic effect of kinesiotaping are needed to reveal the real potential of kinesiotaping on the postural displacements in adolescents.

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**Disclosure of Interest:** None declared

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**AB1430-HPR EFFECTIVENESS OF FUNCTIONAL RIGID TAPING ON PAIN, FUNCTION AND KINESIOPHOBIA IN PATIENTS WITH LOW BACK PAIN**

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**Background:** A small number of studies in the literature suggest that rigid bands applied with different techniques in different regions are effective treatment techniques. On the other hand, there is no study of how rigid bands are effective in the treatment of acute and subacute lumbar pain.

**Objectives:** Purpose of this study is to determine the efficiency of functional tape application to patients with acute or subacute low back pain.

**Methods:** 40 patients with acute-subacute low back pain were divided into two groups: control and experimental group. To control group, McKenzie exercises, Transcutaneous Electrical Nerve Stimulation (TENS), Hot Pack (HP) and pulsed ultrasound treatments were applied. To experimental group, functional taping were applied in addition of these treatments. Range of Motion (ROM), Visual Analogue Scale (VAS), Tampa Scale of Kinesiophobia (TSK) and The Oswestry Disability Index (ODI) were evaluated pre- and post-treatment and datas were analysed with statistical methods. In analysis; p value was accepted p<0,05 for t test and Mann Whitney U test process.

**Results:** In the measurements that compared the improvement of both groups, based on pre- and post-treatment evaluations; improvement in the experimental group was significantly higher in all of these parameters of ROM, VAS, TSK and ODI than in the control group (p<0,05).

**Abstract AB1430-HPR – Table 1**

Difference		N	D ±	SD	U	p
Lumbar flexion angle	control	20	10,70 ±	4,18	346,50	<b>0,000*</b>
	intervention	20	20,30 ±	7,25		
Lumbar extantion angle	control	20	2,25 ±	1,65	282,50	<b>0,024*</b>
	intervention	20	3,95 ±	2,42		
VAS-rest	control	20	-1,86 ±	1,53	109,50	<b>0,014*</b>
	intervention	20	-3,37 ±	2,26		
VAS mobility	control	20	-1,87 ±	1,10	48,00	<b>0,000*</b>
	intervention	20	-3,87 ±	1,47		
TSK	control	20	-5,55 ±	3,95	46,00	<b>0,000*</b>
	intervention	20	-14,25 ±	5,89		
ODI	control	20	-18,07 ±	10,63	69,00	<b>0,000*</b>
	intervention	20	-30,89 ±	16,51		



Abstract AB1430-HPR – Figure 1

**Conclusions:** The use of functional rigid taping in patients with acute and subacute low back pain provided a statistically significant improvement in all measured values of patients and provide better results than the control group. However, there is a need for comparative new studies in order to measure the effectiveness of rigid taping in a more accurate way.

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#### AB1431-HPR DEVELOPING AN EVIDENCE-BASED GROUP PROGRAMME FOR OCCUPATIONAL THERAPY MANAGEMENT OF OSTEOARTHRITIS

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**Background:** Patients with Hand OA form a significant proportion of Rheumatology referrals to Occupational Therapy. Occupational Therapy (OT) interventions for patients with Hand OA can reduce hand pain, and improve grip strength, hand function and quality of life. Under-resourcing of staff can mean that patients with Hand OA are waiting a long time for OT intervention. Providing OT interventions in a group setting for patients with arthritis has been used in Ireland and the UK with good results.

**Objectives:** To review the process of developing and piloting a group-based Occupational Therapy programme for patients with Hand Osteoarthritis. The programme would include self-management education, splinting and a hand exercise programme.

**Methods:** The group programme was developed and piloted with 4 different patient groups between December 2016 and September 2017. The programme was delivered by two OTs and one OT Assistant, with between 3 and 9 patients per group. Outcome measures were taken at week 1 and at the end of the programme, week 13.

**Results:** Initial results are very positive, with the majority of patients who attended the group sessions showing improved grip strength, reduced hand pain, better hand function and they also reported increased confidence of how to manage their arthritis.

**Conclusions:** The development and commencement of a pilot group programme for OT management of Hand OA in Our Lady's Hospital, Navan, Ireland, has provided effective intervention, and also provides patient access to therapy in a more timely manner.

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#### AB1432-HPR MINDFULNESS-BASED STRESS REDUCTION (MBSR) PROTOCOL APPLIED TO SYSTEMIC SCLEROSIS (SSC) PATIENTS: A PILOT INTERVENTIONAL STUDY FOCUSED ON NURSING ASSESSMENT AND PERCEIVED STRESS

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**Background:** MBSR is a protocol, developed by John Kabat-Zinn, which fosters awareness by focusing on the present experience. Basing on scientific evidences, the numerous benefits of MBSR on diseases symptoms have been widely demonstrated.<sup>1-2</sup> No studies have used MBSR on SSC. SSC is characterised by skin and systemic involvement: patients may complain for pain, psychological distress, concerns about disfigurement and reduced self-esteem.<sup>3</sup> Thus, nurse's role is pivotal not only in improving SSC patients global health and quality of life (QoL) but also in ameliorating their self-management strategies.

**Objectives:** to assess the effect of MBSR protocol on sleep quality, QoL and perceived stress in SSC.

**Methods:** 28 SSC patients were enrolled and randomly assigned to experimental group or to control group, and were assessed at baseline and after 8 weeks of MBSR program for the experimental group compared to the control group. The following clinimetric outcomes were measured: QoL with SF-36, sleep quality with a NRS (0–10 range) and Likert scale on night awakenings, perceived stress scale (PSS) and Likert Scale on the way they cope with the stress. Data are presented as differences of Mean and Percentage (%), between and within the groups.

**Results:** QoL presented an improvement for Mental Index Subscale for the experimental group (44.3 to 49.06) while the control group did not show any modification (40.73–40.75). For the impact of sleep quality, MBSR obtained an improvement from 53.3% at baseline to 26.7% at the end of the study: these patients still felt a bad sleep quality but were from far better in respect to controls that did not show any change. In MBSR group night awakenings were reduced from 73% to 60%, while in the control group were increased from 54% to 67%. Satisfaction of sleep quality was slightly improved in MBSR group (6.8 to 7.6) while controls did not experience any change (5.25 to 5.45). MBSR patients at baseline classified stress as a "high" health problem (53%) while after MBSR training only 20% kept the same answer.

**Conclusions:** MBSR program, applied for the first time to SSC patients, showed a very good tolerability and a positive impact on aspects of life like sleep quality, stress perception and self-management strategies. The present study has limitations, nevertheless this is the first time that an alternative approach, such as MBSR, is used. Obviously, MBSR is a supportive approach which can provide to patients a self-management strategy against stress and disease perceptions and in the future it can be integrated to pharmacological therapy and clinical rehabilitation.

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#### AB1433-HPR IMPROVING NURSING CARE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Systemic Lupus Erythematosus (SLE) is a systemic inflammatory autoimmune disease with a heterogeneous presentation in which almost every organ can be affected<sup>1</sup>. SLE patients experience a lower health-related quality of life, due to variation of disease severity over time, arthritis, arthralgia, skin abnormalities, myalgia and general fatigue<sup>2</sup>. The treatment and support of patients with SLE is carried out by a multi-disciplinary team, composed of rheumatologists, clinical immunologists, nurse practitioners and rheumatology nurses. Although nurses have a major task concerning providing information, support, and education in SLE care<sup>3</sup>, little is known about how patients experience nursing care and what needs and expectations they have.

**Objectives:** To investigate the patients' needs for nursing support in order to optimise and standardise nursing care in a SLE clinical pathway.

**Methods:** To identify specific factors regarding nursing care for SLE patients, a literature search was performed. Subsequently, semi-structured interviews were held among patients with SLE from the department Rheumatology and Clinical Immunology of the University Medical Centre Utrecht (tertiary care referral centre with approx. 300 SLE pts/year). The interviews focused on patients' needs, quality of life and nursing care. The questions regarding quality of life were partially derived of the SLE QoL Questionnaire<sup>4</sup> and focused on; daily-, social- or occupational activities, symptoms, medical treatment, and negative emotions. Interviews were recorded, transcribed and analysed with thematic analysis by the researchers and patient partners.

**Results:** Several tools to explore individual needs among patients with SLE, such as the Dutch version of the Educational Needs Assessment Tool (D-ENAT), were identified<sup>5</sup>. Eight SLE patients were interviewed (female n=6, average age 37.5 years). All were using a DMARD and/or biological. Patients indicated a need for help with problems in daily life, information regarding SLE, peer support, and psychosocial help. Pain and fatigue were the most commonly reported symptoms. Most patients saw their nurse on an irregular basis. They appreciated the accessibility, accuracy, clarity, and patience of nurses.

**Conclusions:** There is a need for individualised nursing support in dealing with SLE. To assess individual needs among patients, a needs assessment tool could be used. Further research on the usefulness and effectiveness of a needs assessment tool in daily clinical practice is needed.

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#### AB1434-HPR EFFECTS OF CORE STABILITY EXERCISES ON GRIP STRENGTH AND MANUAL DEXTERITY IN PATIENTS WITH CHRONIC NECK PAIN

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**Background:** It is known that chronic neck pain causes sensorimotor disturbances. A reduction occurs in upper extremity functions due to pain and sensorimotor disturbances in chronic neck pain patients. Core stability exercises were thought to be effective in order to improve stability and muscular strength. However, there is insufficient information on whether core stability training improve grip strength and/or manual dexterity in chronic neck pain patients.

**Objectives:** The aim of this study was to investigate the effect of core stability exercises on grip strength and manual dexterity in patients with chronic neck pain.

**Methods:** Thirty-six patients with chronic neck pain were enrolled. Grip strength and manual dexterity were evaluated by hand held dynamometer and Nine Hole Peg Test, respectively. Patients were randomly divided into supervised core stability exercise and home exercise group. Patients underwent twelve-week exercise training. All assessments were repeated at the 12th week.

**Results:** Grip strength and manual dexterity were significantly increased in both groups ( $p < 0.05$ ). While both treatment methods had positive effects on grip strength and manual dexterity, core stability exercises were found to be more effective than home exercises to improve grip strength ( $p < 0.05$ ) and manual dexterity ( $p = 0.003$  for right side,  $p = 0.008$  for left side).

**Conclusions:** Core stability exercises were more effective than home exercises to improve manual dexterity and grip strength. Core stability training should be added to rehabilitation approaches in order to enhance upper extremity functions in patients with chronic neck pain.

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#### AB1435-HPR EFFECTS OF FLAT CUSHIONING INSOLE ON GAIT PARAMETERS OF INDIVIDUALS WITH CHRONIC IDIOPATHIC NECK PAIN

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**Background:** Shock waves caused by ground reaction force dissipate through the body during walking, which brings about dynamic loading on bones and soft tissues. It was showed that individuals with neck pain walk with a stiffer spine due to protective movement strategy against pain. Degenerative changes, pain and increased stiffness decrease the shock absorption capacity of the spine and cause an increase in dynamic loading affecting the spine. It was known that chronic idiopathic neck pain (CINP) causes alternations in gait parameters, but it is still unclear if using flat cushioning insole affects gait parameters in individuals with CINP.

**Objectives:** The aim of the study was to investigate the effects of flat cushioning insole on neck pain during walking and gait parameters in individuals with CINP.

**Methods:** Twenty-one individuals with CINP (15 female – 6 male, mean age: 35,67±12,64) and 21 healthy controls (15 female – 6 male, mean age: 35,33±12,51) recruited into this study. Assessment of gait



parameters and pain were carried out in two sessions, standard shoe only and standard shoe with flat cushioning. In both sessions, all participants performed the 10-metre walking test in two walking conditions: normal walking (PW), walking at maximum speed (MAXW). The order of sessions and walking conditions were randomised. Plantar pressure parameters were assessed using pressure sensitive insoles and spatio-temporal parameters were assessed using video analysis method involving slow motion camera (120fps). Pain severity was assessed using Visual Analogue Scale at the beginning of both sessions and immediately following the end of the walking conditions in individuals with CINP. Paired sample t-test was used to determine the effects of flat cushioning insole on gait parameters for both groups and on neck pain for the only neck pain group.

**Results:** Our findings indicated that the flat cushioning insole results in a decrease in the maximum force, peak pressure, force-time integral, pressure-time integral and an increase in the contact area in both groups ( $p < 0.05$ ). In individuals with CINP, flat cushioning insole increased walking speed and step length in both walking conditions ( $p < 0.05$ ), however, it had no impact on cadence ( $p > 0.05$ ). Flat cushioning insole reduced the severity of neck pain during MAXW ( $p < 0.05$ ), but there was no difference in neck pain at beginning of both sessions and during PW conditions ( $p > 0.05$ ). In healthy individuals, no difference was found in spatiotemporal gait parameters between two sessions ( $p > 0.05$ ).

**Conclusions:** The study suggested that the flat cushioning insole reduces neck pain severity during walking and has positive effects on gait parameters in individuals with CINP. Flat cushioning insole may be used to decrease neck pain during walking and improve spatiotemporal gait parameters in individuals with CINP.

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#### AB1436-HPR COMPARISON OF PHYSIOTHERAPY GAINS OF THE PATIENTS WITH AND WITHOUT OSTEOPENIA IN DISTAL RADIUS FRACTURES

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**Background:** It is known that osteopenia was correlated with severity of forearm fractures.<sup>1</sup> Since there is an increased risk of long-term impairment due to the involvement of wrist joint after distal radius fractures, physiotherapy is an integral component of the complete concept for the treatment.<sup>2, 3</sup> However, there are no recommendations supported by studies regarding which patients might possibly benefit more or less from physiotherapy.<sup>4</sup>

**Objectives:** The aim of this study was to compare physiotherapy gains of the patients with and without osteopenia in distal radius fractures.

**Methods:** 31 patients (13 with normal bone quality, 18 osteopenic) surgically treated with volar plating after distal radius fracture were included. Bone mineral density (BMD) was assessed by using Dual-energy X-ray absorptiometry (DEXA). A BMD T-Spine value higher than  $-1$  were considered as normal bone quality and the value between  $-1$  and  $-2.5$  were considered as osteopenia. A physiotherapy program, beginning at first day postoperatively, was applied for all patients, twice a week, through 12 weeks. Wrist and forearm range of motions (wrist flexion, wrist extension, ulnar deviation, radial deviation, forearm supination, forearm pronation), severity of pain, oedema and grip strength were assessed at 3rd week and 12th week postoperatively after ending of physiotherapy program. Physiotherapy gains of patients with normal bone quality (group 1, n=13) and patients with osteopenia (group 2, n=18) were compared.

**Results:** Median (min-max) BMD-T spine value was  $-0.3$  ( $-0.7$ – $-1.0$ ) for group 1 and  $-1.75$  ( $-1.3$  –  $-2.3$ ) for group 2. At baseline, there were no statistically significant differences between groups in terms of evaluated parameters ( $p > 0.05$ ). In-group analyses showed that all evaluated parameters except forearm pronation were significantly improved in both groups ( $p < 0.05$ ). Changes of the measurements in both groups were

similar and no significant differences were found in between-group analyses ( $p > 0.05$ ).

**Conclusions:** Physiotherapy gains of osteopenic patients with distal radius fractures were similar to patients with normal bone quality after 12 week treatment program. Wrist and forearm range of motions, severity of pain, oedema and grip strength of osteopenic patients can be improved like that of patients with normal bone quality after distal radius fracture by implementing physiotherapy program.

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#### AB1437-HPR THE EFFECTS OF SHORT FOOT EXERCISE ON PAIN, KNEE AND FOOT BIOMECHANICS IN PATIENTS WITH PATELLOFEMORAL PAIN

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**Background:** It was well known that patellofemoral pain (PFP) has multifactorial aetiology. Increased navicular drop measures and especially more pronated foot posture in stance phase have been reported as distal factors.<sup>1,2</sup> Foot orthosis are recommended as distal interventions but remained passive.<sup>3</sup> For this reason, short foot exercise (SFE),<sup>4</sup> as an active approach, may be of significant benefit in patients with PFP.

**Objectives:** The aim of this study was to investigate the effects of SFE on pain, knee and foot biomechanics in patients with PFP.

**Methods:** Twenty-two patients with PFP, mean age was  $40.91 \pm 10.73$ , included in this study. They were randomly divided into two groups. The first group (KHE) was followed under the exercise program including knee and hip exercises, and the second group (SFE) was followed under SFE in addition to the same exercise program 2 days per a week for 6 weeks. At the beginning and the end of the study, for pain at walking, sitting, squatting, climbing stairs Visual Analogue Scale (VAS) and Kujala Patellofemoral Symptom Scale (KPSS); for knee and foot biomechanics measurement of Q angle, Navicular Drop Test (NDT), Calcaneo-tibial angle (CTA) and Foot Posture Index (FPI) were performed.

**Results:** As a result of this study, it was found that all parameters were improved in both groups, whereas the improvements in the pain intensity (VAS) of sitting and stair activities, values of Q angles, NDT, CTA and FPI were statistically significant in SFE group compared to KHE group ( $p < 0.05$ ).

**Conclusions:** In conclusion, it was shown that SFE has positive effects on pain, knee and foot biomechanics in patients with PFP. At this point, SFE is an exercise approach in order to increase the success of the rehabilitation program in patients with PFP.

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#### AB1438-HPR THE ASSESSMENT OF IMAGERY ABILITY IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER

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**Background:** Studies have shown that individuals with FMF are more restricted in terms of physical function than the normal population and that depression and anxiety are more common in these individuals. Catastrophizing is the strongest psychological factor associated with pain. Imagery is a cognitive process fundamental to motor learning and performance. It is also a mental technique that can be utilised in many ways. A main function of imagery is to aid self-regulation of thoughts, feelings, and behaviours. Studies have shown to be more effective for individuals displaying a higher level of imagery ability when using imagery to improve motor and motivational outcomes, including self-efficacy. Several studies suggest that pain-related imagery may help to reduce distress and increase behavioural flexibility in individuals suffering from chronic pain. However, there is no published imagery research in FMF patients.

**Objectives:** The aim of this study was to assess imagery ability and pain catastrophizing in patients with familial mediterranean fever.

**Methods:** Between October and December 2017, 30 participants diagnosed with FMF were recruited through the Division of Rheumatology Department of Internal Medicine Cerrahpasa Medical Faculty University of Istanbul. The Istanbul Medipol University Ethics Committee approved the study. Demographic and participant characteristic information were recorded. Clinical data collected were: Age onset of FMF, age of diagnosis were inquired. Pain catastrophizing was assessed with Pain Catastrophizing Scale (PCS) and imagery ability was assessed with Movement Imagery Questionnaire-3 (MIQ-3). A total PCS score of 30 represents clinically relevant level of catastrophizing. MIQ-3 is a 12-item questionnaire to assess individuals ability to image four basic movements: a knee lift, jump, arm movement, and waist bend. Ease of imaging is measured in both visual and kinesthetic modalities. For each item, participants read a description of the movement. Then, they physically perform the movement before assuming the same starting position to either visually or kinesthetically image the movement. Following this step, participants rate their ease of imaging on a 7-point Likert-type scale ranging from 1 to 7 (*very hard/easy to see/feel*). After the items for each subscale are averaged, a higher score represents a greater ease of imaging.

**Abstract AB1438HPR – Table 1.** Demographic and clinical characteristics of study population

Variables	Mean ± SD
	Median (min-max)
Age	32.37 ± 11 (19-56)
BMI (Kg/m <sup>2</sup> )	24.39 ± 6.1 (17.3-40.3)
Age of Diagnosis	22.20 ± 14.7 (2-54)
Disease Duration	10.17 ± 7.6 (2-28)
Kinesthetic Imagery Ability	14.99 ± 4.5 (3.1-21.1)
Internal Imagery Ability	13.84 ± 5.3 (3.16-20.0)
External Imagery Ability	12.41 ± 4.7 (3.8-19.0)
Pain Catastrophizing Scale	23.27 ± 12.5 (6-44)

**Results:** The study included 27 female, 3 male. Mean age was 32±11 years, mean BMI was 24±6.1 kg/m<sup>2</sup>; (table 1). Kinesthetic imagery ability

was higher than internal and external visual imagery. There was no significant relationship between imagery and pain catastrophizing severity.

**Conclusions:** According to previous studies people with chronic pain had pain-related imagery, catastrophizing, and distress related in proportion with each other but in our study, we didn't find any significant relationship between imagery and catastrophizing. This may be due to small sample size or the pattern of pain in FMF which is periodic, intermittent, differently from chronic pain. Each patient with rheumatic disease should be addressed as a composite biopsychosocial being with unique characteristics and needs. Previous study have shown that imagery is an effective treatment for neuropathic and chronic pain. We suggest that imagery may be an effective method for management of pain in patients with FMF.

**Disclosure of Interest:** None declared

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#### AB1439-HPR THE EFFECTS OF DIFFERENT EXERCISE PROTOCOLS ON FUNCTIONAL STATUS AND AEROBIC CAPACITY IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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**Background:** Although there is the emphasis on the importance of life-long regular exercise to improve the efficacy of medication in the treatment of ankylosing spondylitis (AS) patients, there is a lack of information about the safe exercise dosage in clinical practice.

**Objectives:** In this study, we aimed to investigate the effects of different exercise protocols on functional status and aerobic capacity in patients with ankylosing spondylitis.

**Methods:** Thirty-one ankylosing spondylitis patients were evaluated and grouped according to their arrival order. Patients' spinal mobility (Bath Ankylosing Spondylitis Mobility Index), disease activity (Bath Ankylosing Spondylitis Disease Activity Index), flexibility (back scratch test), pulmonary functions (forced vital capacity with pulmonary function test, maximal inspiratory and expiratory pressures with respiratory muscle strength test), aerobic capacity (oxygen consumption test with submaximal modified Bruce protocol), fatigue level (Fatigue Severity Scale) and sleep quality (Pittsburgh Sleep Quality Index) were assessed. Group 1 (n=16) did both aerobic training and clinical pilates exercises, while group 2 (n=15) only did aerobic training. Patients did exercises for 8 weeks, 3 days a week under the supervision of a physiotherapist and then measurements were repeated.

**Results:** According to the measurements, it was found that disease activity level, respiratory muscle strength was improved (p<0.05) in both groups. When clinical pilates exercise was given additionally to aerobic training spinal mobility (BASMI score), upper extremities flexibility, forced vital capacity, fatigue severity and sleep quality (p<0.05) was also improved.

**Conclusions:** As a result of the study, it was noted that when clinical pilates exercises applied together with the aerobic exercise training in ankylosing spondylitis patients, effectiveness on functional status and aerobic capacity was increased.

**Disclosure of Interest:** None declared

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#### AB1440-HPR YOGA-THERAPY FOR RHEUMATOID ARTHRITIS: RAPID IMPROVEMENT IN PROMS

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**Background:** Rheumatoid Arthritis (RA) is associated with mood disorders and poor quality of life (QOL) Chorus et al., 2003 Yoga therapy (Y-T) has been used in several Long Term Conditions. Khalsa et al, 2016.

**Objectives:** This study investigated: a) impact of a 16 week Y-T intervention on functional outcomes and QOL in 10 adult-onset RA patients, b) acceptability and experiences of the intervention.

**Methods:** Ten adult RA patients (Ages: 29–71 Y; RA duration: 1–15 years) consented to 10 individual Y-T sessions (weekly ×4; biweekly ×6) with a yoga therapist in a standard consulting room. The intervention was tailored to the needs and abilities of each patient and included: breath-centred physical yoga postures, breathing and visualisation techniques, mantras and meditation, and Lifestyle/behavioural strategies. All participants completed measures to assess changes in health pre- and post-intervention (EQ-5D and HADS) and took part in a semi-structured

interview in a mixed methods design. Thematic analysis was applied to interview data.

**Results:** 98/100 sessions were attended by participants.

**Abstract AB1440HPR – Table 1.** Pre-Post 10 sessions Y-T metrics

Pre-Post Y-T Change:	PRE	POST	CHANGE
Mean Depression	6.70	2.30	-65%
Mean Anxiety	9.40	4.80	-48%
Mean HAQ	1.10	0.85*	-23%
Mean Pain Score (HAQ)	5.66	2.40	-58%
Mean Health Score (HAQ)	5.10	1.72	-66.3%
Mean health Utility (EQ-5D)	6.01	8.40**	+39.6%

\*8/10 HAQ reduced >0.35 =>MID (minimal important difference);

\*\*6/10 participants achieved EQ5D maximum score=1

Qualitative findings indicated that considerable value was placed on the therapeutic function of the consultation, of being listened to and receiving advice on concerns. Therapeutic mechanisms appeared to reflect tailored physical practices alongside psychosocial techniques which promoted psychological wellbeing and increased perceptions of control and self-efficacy. Several reported reductions in their medication and broader benefits such as improved sleep, mood and energy. All but one participant reported positive changes to their RA symptoms, including pain reduction, greater mobility and joint flexibility.

**Conclusions:** This novel pilot YT intervention was positively received by patients with RA, with high levels of adherence to both the course of treatments and the tailored home practice. The results suggest that yoga therapy has potential as an adjunct therapy to improve RA symptoms, increase self-care behaviours and address negative mood. Whilst promising, a larger multi-centre study is required to evaluate the therapeutic and cost-effectiveness of Y-T.

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## HPR Patients' perspectives, functioning and health (descriptive: qualitative or quantitative)

### AB1441-HPR DOES THE INCIDENCE OF INFECTIONS INCREASE IN PATIENTS WITH CHRONIC ARTHRITIS AND OSTEOPOROSIS TREATED WITH DENOSUMAB AND BIOLOGICAL THERAPY?

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**Background:** Biological therapies (BT) have changed the prognosis of chronic arthritis (CA); however, they have associated the increased risk of infections. Denosumab (DNS) is the first biologic approved for the treatment of osteoporosis (OP) and is also associated with an increased risk of infections.

**Objectives:** To evaluate the incidence of infections in patients with CA and OP treated with DNS alone or associated to another biological treatment.

**Methods:** A prospective observational study was designed in which all patients with OP who received treatment with DNS between January 2013 and December 2017 were included. The group of patients with CA (RA, EA, PsA) were treated, in addition to DNS as treatment for their OP, with BT. Follow-up was carried out in the rheumatology nursing examination room every 6 months. Demographic data, disease

characteristics, infections and associated comorbidities were collected. Serious infections were defined as those that required admission, suspension of therapy or death.

**Results:** 200 patients were included (81.1% women). The main diagnoses were OP 112 (51%) and AC 76 (34.5%) [RA 58 patients (26.3%), SpA 8 (3.6%), PsA 10 (4.5%)] and other rheumatologic diagnoses 32 (14.5%). Demographic data are shown in Table 1. Both groups were similar except for the higher GC consumption and the higher lumbar bone mass of the CA group. Of the patients with CA, 41 patients received a synthetic DMARD (MTX mainly, 90%), and 40 patients (53.9%) received GC. The average dose of DNS injections was 4.5 (1–10), with average treatment duration (range and DS) of 23.03 months (6–66, 13.3). The incidence of infections was 74 (39.3%), 31 patients had repeated infections. The most frequent were urinary tract infections (UTI), respiratory, mouth and other infections. There were 4 serious infections, 2 UTI and 2 pneumonias (both concluded in death, in patients with RA). The incidence of infections among patients with OP and with CA was similar in both groups (40 (35.7%) vs. 34 (44.7%), p<0.209). Multiple regression including age, synthetic DMARD, GC and duration of treatment with DNS showed that the duration of treatment with DNS [Exp (B)=1.058, p<0.001] and GC [Exp (B)=2.484, p=0.010] were the only predictors of increased risk of infections.

**Abstract AB1441-HPR – Table 1**

	OP (n=112)	CA (n=76)	p
Women, n (%)	99 (88.3)	66 (86)	0.822
Age, mean (SD)	66.9 (10.27)	67.7 (11.11)	0.622
BMD LS, mean (SD)	-2.9 (0.98)	-2.3 (1.5)	<b>0.003</b>
EPOC, n (%)	12 (10.7)	11 (14.4)	0.499
Smoking ever, n (%)	23 (20.5)	10 (13.1)	0.242
Diabetes mellitus, n (%)	13 (11.6)	14 (18.4)	0.209
Infections n (%)	40 (35.7)	34 (44.7)	0.227
Corticosteroid dose, mean (SD)	0.79 (4.1)	4 (5.59)	<b>&lt;0.0001</b>

**Conclusions:** Patients with CA and OP who receive DNS and TB have a similar incidence of infections. However, the risk of infection is higher in CA patients related with the use of GC. The most frequent infection was UTI followed by respiratory infections, but they did not suppose the suspension of the treatment in the majority of the cases.

**Disclosure of Interest:** None declared

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### AB1442-HPR A MISUNDERSTOOD BURDEN – LIVING WITH SLE IN SOUTH AFRICA

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**Background:** Systemic lupus erythematosus (SLE) has a profound impact on health related quality of life (HRQOL). There has been no qualitative research to the explore patients' perspectives and unmet needs in SLE in sub-Saharan Africa.

**Objectives:** To examine the experiences and perceptions of SLE women.

**Methods:** In-depth interviews of 25 South African women with SLE were conducted to explore a range of HRQOL experiences including pain, fatigue, emotional health, sexual well-being, fertility and aesthetic concerns.

**Results:** Most patients (72%) were black Africans, the remaining were of mixed race ancestry, and only a quarter were employed. Living with pain was the commonest complaint, negatively impacting on activities of daily living, coping with family expectations, social life, sleep and intimacy with partners. Patients struggled to explain the pain to their families, employers, community and health care providers. Seventeen participants expressed the challenge of living with fatigue, described as "emotionally draining" and as "always tired, a person who doesn't have the energy." One patient believed that witches in church had supernatural powers that took all her energy away. Many felt their fatigue was misconstrued, and that they were labelled as 'simply lazy' by health professionals and family members. This pernicious fatigue had negative consequences on many facets of daily life, including caring for dependents, holding down steady job and sexual wellbeing. All patients experienced low emotional states ranging from anger, bitterness, anxiety, confusion, and sadness, which frequently resulted in suicidal ideation. Many patients experienced difficulties with conception, complicated pregnancies and miscarriage. The



pessimism of doctors regarding the prognosis of pregnancy in SLE left many patients feeling confused and depressed. Changes in physical appearance such as alopecia, rashes and weight fluctuations were also a major concern affecting self-image and libido, often leading to strained relationships and breakups. Coping mechanisms included intense spiritual beliefs giving them the courage to 'push through the difficult times'. Use of alternative therapies was common, which they believed helped contain the symptoms of SLE. These included drinking 'blessed' water, traditional herbal remedies, and soothing leaf or pressure applications to painful joints. A poor understanding of SLE by the patients themselves, family and the community, coupled with the unpredictable course of the disease, exacerbated frustration and uncertainty. For many patients, limited income, lack of basic services like public transport, dependency of family members, and comorbid diseases, such as HIV and tuberculosis, exacerbated the negative daily experiences of living with SLE. Patients felt that patient-led support groups, better education by health professionals, and public awareness of SLE would help them cope with the disease.

**Conclusions:** Indigent South African women with SLE in SA have complex, chronic and challenging life experiences. A poor understanding and acceptance of SLE by patients themselves, compounded by a background of poverty and a perception of being misunderstood by family members, health professionals and the community at large had negative impact on multiple dimensions of patient's lives.

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**AB1443-HPR** **EXPLORING THE RELATION BETWEEN IMPAIRMENT RATING BY DAS-28 AND BODY FUNCTION, ACTIVITY-PARTICIPATION AND ENVIRONMENTAL FACTORS BASED ON ICF IN THE PATIENT WITH RHEUMATOID ARTHRITIS**

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**Background:** Rheumatoid Arthritis (RA) is the cause of functional loss and disability of individuals. It also results in negative effects on the emotional components as well as physical components related to health. If specific domains of medical condition criteria are systematically linked with relevant parts of ICF, we will have a common conceptual understanding of ICF and patient-oriented health criteria. It may also make clinical practices easy.

**Objectives:** The aim of this study was to link and allocate items of disability questionnaires with body function, activity participation and environmental factors based on ICF Hand Core Set. The other objective of this study is to examine the relationship between the impairment and the ICF components determined on the basis of disability questionnaires in participants with Rheumatoid Arthritis.

**Methods:** Impairment was evaluated by use of DAS28 and disability by Disabilities of Arm, Shoulder and Hand Questionnaire (DASH), Michigan Hand Outcomes Questionnaire (MHQS), Duruöz Hand Index (DHI), Arthritis Impact Measurement Scales 2 (AIMS 2) in participants with rheumatoid arthritis (n=100). Items of DASH, MHQS, DHI and AIMS 2 were linked and allocated with the ICF Hand Core Set as a result of three expert opinions. The data was analysed using Kappa index and Pearson's correlation coefficient.

**Results:** Based on expert distinction on DASH, MHQS, DEI and AIMS 2 items, MHQS covered the highest number of body function categories of ICF Hand Core Set with 8 and AIMS 2 covered the highest number of ICF Hand Core Set with totally 25 (body function=3, activity participation=20, environmental factors=2). While impairment (DAS28) had moderate correlation with subjective impairment (body function scores considered as subjective impairment) and activity participation for all assessment questionnaires (r=0.50–0.69); subjective impairment had high correlation with activity participation for DASH and MHQS (r>0.70) and also had moderate correlation with activity participation for AIMS 2 (r=0.50–0.69). Furthermore, subjective impairment had weak correlation with environmental factors (r=0.10–0.49).

**Conclusions:** We suggest that AIMS 2 is the most appropriate for clinicians and researchers who aim to perform a more comprehensive biopsychosocial assessment in patients with RA. In addition, the clinician's assessments and the impairment levels reported by the patients are inter-related and the impairment levels reported by patients is also affected by environmental factors.

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**AB1444-HPR** **UNDERSTANDING FATIGUE BURDEN AND COPING STRATEGIES IN RHEUMATOID ARTHRITIS USING QUALITATIVE RESEARCH**

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**Background:** Fatigue is a major symptom of RA but is under-represented when considering an appropriate treatment and in the measurement of disease activity. At the same time, patients' perspectives on fatigue in the overall context of their RA and life have not been studied in detail before. To understand that perspective, we aimed to explore patients' lived experience with RA-related fatigue.

**Objectives:** We explored the narratives of patients with RA and their discourse on RA-related fatigue to assess the burden of disease and coping strategies.

**Methods:** Semi-structured interviews were conducted with adult patients with RA living in two geographical regions in the United States. Interviewees were asked to discuss their experiences with diagnosis, symptoms, physical and social limitations, coping with challenges, treatment and healthcare providers. The interviews were audio-recorded and transcribed verbatim. Transcripts were analysed for themes related to the burden of RA-related fatigue and coping strategies.

**Results:** Eighteen patients were interviewed, with ages ranging from 27 to 80 years and RA duration ranging from 4 to 40 years. Four themes emerged around the impact of RA-related fatigue, fatigue in context of RA symptoms, coping strategies and coping success (table 1).

**Abstract AB1444HPR – Table 1.** Burden of RA-Related Fatigue and Coping Strategies Themes

Theme	Details
Fatigue limits RA patients' ability to live their lives	<ul style="list-style-type: none"> <li>– Patients with RA have limited energy reserves to perform common activities of daily living</li> <li>- Fatigue creates 'brain fog' that reduces RA patients' ability to focus and diminishes academic and job performance</li> <li>- Patients with RA adjust their future career choices based on these limitations</li> </ul>
Fatigue and pain are intertwined	<ul style="list-style-type: none"> <li>– Fatigue is strongly connected with pain and it is difficult for patients with RA to separate the two symptoms. Pain and active RA symptoms increase fatigue. Fatigue also amplifies pain</li> <li>- Fatigue can be a bigger concern than pain. Patients with RA find it harder to manage fatigue compared with pain</li> </ul>
Coping with fatigue is an internal struggle	<ul style="list-style-type: none"> <li>– Patients with RA are faced with the tough choice of giving in to the fatigue or pushing through and risk exceeding energy reserves</li> <li>- Patients with RA who have difficulty coping with fatigue feel frustrated, embarrassed and inadequate</li> </ul>
Acceptance of limitations leads to more effective coping strategies	<ul style="list-style-type: none"> <li>– Patients with RA use a variety of coping strategies, often in combination</li> <li>- Coping strategies include pushing through the fatigue, using distractions, pacing oneself, sleeping, drinking coffee and using medication</li> <li>- Patients with RA who accept their limitations are more likely to pace themselves, as opposed to pushing through their limits, and have fewer negative emotions when they give up</li> </ul>

**Conclusions:** Fatigue is a major concern for patients with RA and can be more debilitating than pain. A patient's constant battle with fatigue can have physical, mental and emotional consequences.

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#### AB1445-HPR PATIENT SATISFACTION IN A RHEUMATOID ARTHRITIS OUTPATIENT CENTRE

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**Background:** Patient experience (PX) can be conceptualised as “the sum of all interactions, shaped by an organisation’s culture, that influence patient perceptions, across the continuum of care” nowadays patient satisfaction is considered as one of the quality for performance in health systems.<sup>1</sup> Rheumatology is mainly an outpatient, multidisciplinary medical specialty, therefore care does not stop at the diagnosis it continues during a long-term with frequent monitoring and patient participation.<sup>2</sup>

**Objectives:** Describe the results of a patient satisfaction survey in a specialised centre in Colombia during 2017

**Methods:** In our RA specialised centre during a 12 month period we performed a satisfaction survey in order to evaluate the health services provided. We evaluated the waiting times, timing on attention, appointment assignment, and information provided, the treatment received by the healthcare team, facilities among others. Patients evaluated the services provided in a scale from 1 to 5 were 1 was very bad, 2 bad, 3 regular 4 good and 5 very good. Descriptive epidemiology was performed for each variable presented.

**Results:** We performed 4756 surveys during 2017, 4550 surveys were completed with a 95% rate response, out of total 80% of respondents were female and 20% male. 80% of patients reported to receive their appointments on time; regarding the service provided by our health care professionals 99% of patients understood the indications regarding their treatment, 98% understood about the administrative procedures to program future appointments and to how to access to their medications, also 98% had clearly understood the date and time of their consultation (rheumatologist, physical therapist, nutritionist, psychologist, infusion therapy, among others.) The mean score for the overall assessment of the services was 4.2/5.0 (table 1). The average time of stay at our centre was 60 min±33. The main aspects to improve our patient satisfaction were the telephone programming of appointments, and the compliance regarding the delivery of medications.

**Abstract AB1445-HPR – Table 1**

Question	MEAN (SD)	MEDIAN (MIN – MAX)
How was the quality of the service provided?	4.25 (0.51)	4 (3–5)
How was the service provided by our health care team?	4.31 (0.49)	4 (1–5)
How was the service provided y in the waiting room?	4.27 (0.49)	4 (1–5)
Facilities	4.31 (0.49)	4 (1–5)
Overall experience	4.32 (0.53)	4 (3–5)

**Conclusions:** This survey describes well-functioning multidisciplinary services for all patients who visit to our specialised centre. On the other hand although we found that our patients are highly satisfied, there is a large opportunity to improve our services and generate evidence regarding other aspects that involve the patient’s health determinants.

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#### AB1446-HPR INVESTIGATION THE EFFECT OF KINESOPHOBIA AND NECK DISABILITY LEVELS ON THE NECK AWARENESS IN CHRONIC NECK PAIN PATIENTS: PILOT STUDY

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**Background:** Chronic neck pain can cause patients to limit their activities due to kinesophobia. Patients may experience more disability during rest because of staying in the same position while restricting their activities, lacking exercise and muscles spasms. For these reasons, they may not be aware of many factors related to the position, movement, and shape of their necks.

**Objectives:** The aim of this study is to examine the effect of kinesophobia and neck disability levels on neck awareness in individuals with chronic neck pain.

**Methods:** Forty-two patients who have chronic neck pain and aged 18–65 years were participated in this study. The demographic characteristics of the patients were recorded, kinesophobia levels with Tampa Kinesiophobia Scale (TKS), neck disability level with Neck Disability Index (NDI) and neck awareness with Fremantle Neck Awareness Questionnaire (FNAQ) were evaluated. Correlation analysis were performed with Pearson correlation coefficients for parametric conditions and the Spearman correlation coefficients for nonparametric conditions.

**Results:** The mean age of the patients participating in the study was 42.4±13.47 years (7 men and 36 women). There was a moderate statistically significant positive correlation ( $r=0.462$ ,  $p<0.01$ ,  $p=0.002$ ) between FNAQ and NDI, indicating that individuals with chronic neck pain had kinesophobia reduced neck awareness. It was found that there was a very good relationship between FNAQ and NDI ( $r=0.602$ ,  $p<0.001$ ) and neck awareness decreased as the neck disability level increased. There was a moderately significant relationship between TKS and NDI ( $r=0.567$ ,  $p<0.001$ ), levels of kinesophobia increased as neck disability increased.

**Conclusions:** It has been shown that the high level of kinesophobia and neck disability results in a negative effect on neck awareness and that these three variables are interrelated as a result of our work on neck awareness, which has been rarely studied in the literature. Therefore, increasing the activity and movement will reduce the level of neck disability and increase awareness. For this reason, patients with chronic neck pain need to be directed in terms of activity and movement.

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#### AB1447-HPR BIOPSYCHOSOCIAL STATUS OF JIA PATIENTS: PERSPECTIVES OF DAILY LIVING ACTIVITIES, DISEASE ACTIVITY AND FAMILY IMPACT

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**Background:** Juvenile Idiopathic Arthritis (JIA) is the most frequent chronic rheumatic disease during childhood. It can result in disabilities, loss of quality of life and mood changes.<sup>1</sup> Furthermore, literature reviewing the effects of arthritis on children and family is inconsistent, with studies showing significant difference or not, compared to healthy children.<sup>2</sup>

**Objectives:** The purpose of this study is to present results regarding the functional status, psychosocial status and disease activity of children with JIA and their effects on the child’s family. The second aim is to present the correlations between these parameters.

**Methods:** The study included children diagnosed with JIA who applied to Hacettepe University İhsan Doğramacı Children's Hospital Rheumatology Department. After demographic data was collected, all children were assessed with Child Health Assessment Questionnaire (CHAQ) for daily living activities, with the Juvenile Arthritis Disease Activity Score (JADAS) for disease activity and with a newly developed scale from Hacettepe University Faculty of Health Sciences Department of Physiotherapy and Rehabilitation for children with rheumatism by Edibe Ünal<sup>3</sup> for functional and psychosocial status. Cut-off point was accepted as  $\leq 2.7$  for disease activity.<sup>4</sup> The Family Impact Scale (FIS) was used to assess perspective of parents.

**Results:** A hundred and ninety-six children were included in the study. The mean age of children was  $12,44 \pm 3,97$  and female/male ratio was 55,6/44,4. Although the mean JADAS score was  $3,33 \pm 4,21$ , it only detected active disease in 81 children. There was a moderate correlation between CHAQ (Pain) and functional scores of Ünal's scale and JADAS score. CHAQ total score was well correlated with function and psychosocial scores. The correlation between FIS and other scales was very low.

Abstract AB1447HPR – Table 1. Descriptives

	Mean±SD
JADAS	3,33±4,21
CHAQ (Total)	0,32±0,38
CHAQ (Pain)	2,31±3,01
CHAQ (General VAS)	3,52±2,99
Function (range: 0–30)	4,09±5,85
Psychosocial (range: 0–30)	13,25±5,76
FIS	43,6±10,12

Function; Psychosocial; Functional and Psychosocial subscales of Ünal's scale.<sup>3</sup>

Abstract AB1447HPR – Table 2. Correlations

	CHAQ Pain	Function	Psychosocial
JADAS	r 0,499	0,423	0,216
	p 0,000	0,000	0,003
CHAQ (Total)	r 0,384	0,757	0,507
	p 0,000	0,000	0,000
CHAQ (Pain VAS)	r	0,438	0,308
	p	0,000	0,000
CHAQ (General VAS)	r	0,360	0,358

**Conclusions:** Our results show that pain and function alter disease activity in children with JIA. It is seen that psychosocial states of children and their functional states expressed by their own knowledges also affect their daily life. These changes did not affect the viewpoint of the family.

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#### AB1448-HPR PATIENTS EXPERIENCE WITH A NURSE-LED TELEPHONE SERVICE IN AN OUTPATIENT CLINIC

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**Background:** According to "EULAR recommendations for the role of the nurse in the management of chronic inflammatory arthritis"<sup>1</sup>, patients with rheumatic diseases should get access to nurse-led telephone service. Patients call if they have a flare and need an appointment with the rheumatologist, have questions regarding their disease, medical treatment, infections or side-effects.

Patients experience with calling a nurse need further investigation.

**Objectives:** The objective for this study was to explore and describe the patients' experience with the nurse-led telephone service in an outpatient clinic at a rheumatology department.

**Methods:** The helpline is open 2 hours daily during the week, and served by 2–3 nurses. Patients at the outpatient-clinic between 01.10.17 and 29.12.17, were invited to answer a questionnaire about the nurse-led telephone service.

The questions were about access to a nurse, if they got the help they needed, if they had confidence in the nurse's knowledge, understanding her information, if the helpline was important in their lives with a chronic disease and if the nurse-led telephone service gives comfort or makes them feel secure.

They could choose between 5 different answers: not at all, to a small degree, to some degree, to a large degree or to a very large degree. It was also possible to write comments.

All the answered phone calls were registered.

**Results:** The nurse-led telephone service answered mean (min–max) 30<sup>19–48</sup> phone calls every day, and in total 1875 calls during the period of 3 months. Only 29% of these patients needed and got an appointment with a rheumatologist.

341 patients answered the questionnaire.

68 commented regarding long time to wait, or a need for extended time for the telephone service. However, concerning how easy the access to a nurse on helpline was, 70% answered to a large or a very large degree, as shown in table 1.

89% answered that they to a large or a very large degree got the information or help they needed from the nurse.

90% answered that they to a large or a very large degree trusted the nurse's professional skills.

The nurse spoke to them so they could to a large or a very large degree understand her according to 92% of the respondents.

There was some variation in the answers about the helpline's importance in their life with a chronic disease, but 44% answered to a very large degree and only 4.7% answered not at all.

66% answered that access to a nurse on helpline provides a very large degree of security.

Abstract AB1448HPR – Table 1. Results from the questionnaires with response shown in% (N)

Question	Not at all	To a small degree	To some degree	To a large degree	To a very large degree
Was it easy to get in touch with the nurse on the helpline?	2.9 (10)	4.4 (15)	20 (68)	41.4 (141)	28.5 (97)
Did you get the information/help you needed from the nurse at the helpline?	1.2 (4)	2.1 (7)	5.6 (19)	32.5 (111)	56.3 (192)
Did you trust that the person was professionally skilled?	0.6 (2)	1.5 (5)	4.1 (14)	31.4 (107)	59.2 (202)
Did you experience that the nurse talked to you so you could understand her?	0.3 (1)	0 (0)	3 (10)	27.4 (93)	64.6 (219)
Is the helpline important to you in your life with a chronic disease?	4.7 (16)	8.8 (30)	12.4 (42)	24.2 (82)	44 (149)
How much security is there for you to have access to a nurse on helpline?	1.2 (4)	1.8 (6)	5.3 (18)	20.7 (70)	66.4 (225)

**Conclusions:** This study shows that calling a nurse-led telephone service is valuable for patients with a rheumatic disease. Although there can be some time to wait, almost 90% got the help they needed, understood the nurse and had confidence in the nurse's knowledge.

Only 13.5% answered that nurse-led telephone service has not at all or a small degree of importance in their lives with a chronic disease.

The nurse-led telephone service was important to a large or very large degree to feel secure and confident for 87% of the participants in this study.

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- [1] van Eijk-Hustings Y, et al. *Ann Rheum Dis* 2012

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**AB1449-HPR** **PATIENT FACTORS CONTRIBUTING TO AND SHARED DECISION MAKING IN STARTING/SWITCHING BIOLOGICS SPONDYLOARTHRITIS**

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**Background:** Biologics are effective for treating symptoms in patients (pts) with active spondyloarthritis (SpA) and a number of drugs are available with different working mechanisms, and mode and interval of administration for this indication. Starting/switching a specific biologic occurs for various reasons. It is increasingly advocated to involve pts in treatment decisions. Pts can have various needs and expectations when involved in shared decision making.

**Objectives:** To explore which pts factors contributed to starting or switching biologics in SpA, how pts experienced shared decision making in this process, and the needs of pts starting biologics.

**Methods:** Pts with SpA were recruited from the rheumatology department, Maastricht University Medical Centre. In semi-structured focus group interviews pts were asked to elaborate on when and why biologics were started and switched and if they were involved in the treatment decision. A decision aid for rheumatoid arthritis (RA) biologics was shown and pts were asked if they consider a similar decision aid for SpA as valuable. Interviews were audiotaped, transcribed and analysed in NVIVO11 software.

**Results:** In total, 14 pts with SpA participated in 4 focus group interviews. Three pts were diagnosed with axial SpA, 5 pts with peripheral SpA and 6 pts were diagnosed with axial- and peripheral SpA, with or without concomitant extra-articular manifestations. Mean age was 62 years (range 41–77 years), 10 were female (62.5%). Average time since diagnosis was 28 years. Pts started on average 7.3 years (range 1–14 years) ago with their first biologic. Six pts used 1 biologic, 5 pts had switched once or twice, and 3 pts switched more than 3 times. Factors contributing to starting a first biologic were disease activity, fatigue, intolerance to prior medication, and ineffectiveness of prior medication. Two pts were included in a biological trial. Factors contributing to switching were adverse effects and ineffectiveness of prior biologic.

Most pts were not involved in decision making when biologics were started or could not remember this. Some pts mentioned that only one or limited options were available at the time of start, and that the decision to start was made by the rheumatologist. However, also when more agents became available, decision for a specific biological was often made by the rheumatologist without discussing treatment options.

Pts underlined the importance of how care providers offer a treatment decision. When the decision was offered as a suggestion, "Shall we do.", it was experienced more pleasurable than when the decision was offered as a command, "Let 's do."

All pts expressed their wish to develop a decision aid in which clear information about each biologic is provided on mode of administration, interval, and effect on different SpA features. One pt explicitly stated that he did not want to be actively involved in decision making, but preferred that the care provider decides.

**Conclusions:** When involving SpA pts in shared decision making on start/switching of a biological, information on effectiveness on disease activity, fatigue, adverse events as well as expected duration of effectiveness should be provided, in addition to modes of administration and interval of each agent. A decision aid can support pts in this.

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**AB1450-HPR** **COMPARISON OF BIOPSYCHOSOCIAL STATUS OF RHEUMATOID ARTHRITIS AND FIBROMYALGIA PATIENTS**

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**Background:** Rheumatic diseases have biopsychosocial effects on individuals.<sup>1</sup> This affection includes the combination of anxiety, depression, and participation in daily living activities. It can be thought that individuals can be affected from different diseases in different ways.

**Objectives:** The aim of this study is to compare the biopsychosocial status of patients with Rheumatoid Arthritis (RA) and Fibromyalgia (FMS).

**Methods:** Individuals diagnosed with Rheumatoid Arthritis (RA) and Fibromyalgia (FMS) who applied to the Rheumatology Department of the Medical Faculty of Hacettepe University were included in the study. After the

demographic characteristics of the individuals were recorded; daily living activities were assessed with the Health Assessment Questionnaire (HAQ), quality of life with Short Form 36 (SF-36) scale, anxiety and depression levels with Hospital Anxiety and Depression Scale (HADS) and disease related biopsychosocial status with the Cognitive Exercise Therapy Approach Scale (BETY) which is a newly developed scale in rheumatic patients (the authors request that the abbreviation stay as "BETY" as the original in Turkish).<sup>2</sup>

**Results:** 120 RA and 99 FMS patients were included in the study. The scores of individuals on scales are shown in Table 1. When analysed in terms of differences according to RA and FMS, the anxiety and depression scores of the HADS scale and the SF-36 quality of life scale of the individuals were found to differ between the Physical Functioning, Social Functioning, General Mental Health, Role Limitations Due to Emotional Problems, Vitality Energy or Fatigue and General Health Perception sub-parametric scores.

**Abstract AB1450HPR – Table 1.** Comparison of two groups.

	RA (n=120)	FMS (n=99)	p
Age	51,91 ±11,39	43,03±8,42	0,00
BMI	28,47±6,55	27,46±5,67	0227
HAQ	13,48 ±11,86	11,7±9,47	0229
HADS-A	7,07±5,4	9,59±4,82	0000
HADS-D	5,62±4,39	9,23±4,46	0000
BETY	60,64 ±29,74	67,14±22,7	0075
SF36-FF	45,12 ±26,09	38,44 ±22,45	0046
SF36-FR	28,54 ±43,63	20,95 ±34,57	0162
SF36-A	39,87 ±25,76	42,06 ±20,25	0492
SF36-SI	36,67 ±45,82	50,63±25,9	0008
SF36-RS	73,15 ±19,82	53,87 ±20,25	0000
SF36-ER	55,1±24,91	30,03 ±41,83	0000
SF36-EC	70,41±30,4	27,27 ±19,99	0000
SF36-GS	50,08 ±24,76	38,38 ±16,61	0000

PF: Physical Functioning, RL: Role Limitations, RLE: Role Limitations Due to Emotional, VEF: Vitality, Energy or Fatigue, GMH: General Mental Health, SF: Social Functioning, P: Pain, GHP: General Health Perception

**Conclusions:** Physical function, mental health, emotional role strength, energy vitality and general health perception, anxiety and depression levels in RA patients were found to be better than FMS patients. The activities of daily living were thought to be unaffected by the changing parameters of pain and biopsychosocial status.

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**AB1451-HPR** **BURDEN AMONG CAREGIVERS IN RHEUMATOID ARTHRITIS – A PILOT STUDY**

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**Background:** Rheumatoid arthritis (RA) is a chronic, inflammatory disease of the joints affecting more than 1% of global population, it is a long term condition that causes pain and disability.<sup>1</sup> Evidence had shown that

most of the patients are moderately disabled, and about 10% of the patients suffered from severe disablement which brings the necessity of a caregiver to become the patient's companion due to its chronic disease.<sup>2</sup> The caregiving role can have an impact in the psychological and physical spheres of the caregiver's life.<sup>3</sup>

**Objectives:** The aim of this study was to explore demographical characteristics and caregiver burden through the Zarit Scale.

**Methods:** We conducted a cross sectional study in a meeting where caregivers in a rheumatoid arthritis specialised setting. We collected sociodemographic information, and applied the Zarit caregiver burden interview (ZBI) adapted to Spanish. The ZBI includes 22 questions which has 5 responses from 0 (never) to 4 (nearly always), where scores lower than 47 indicated little to no burden, 47 to 55 low burden and >55 intense burden. We calculated means, and standard deviations for continuous variables and categorical variables were presented as rates. We categorised age of caregivers and compared to it to ZBI score, we used X<sup>2</sup> to perform bivariate analysis.

**Results:** 115 caregivers were included in the study, 63% were female and 37% were male. Mean age was 49 years±18 and 35% were single. Regarding educational level 44% had college degree, most of caregivers 30% had a full time job, and also 45% had other family members as their responsibility. See table 1. Zarit mean score was 44±14, additionally 71% had a score lower than 47. See table 1. Regarding age groups 35% of patients were older than 60 years and 15% of them were considered with intense burden disease, there was no statistical association between age and disease burden, see table 2.

**Abstract AB1451HPR – Table 1.** Zarit score

Zarit Score		
<47	82	71
47–55	14	12
>55	19	17

**Abstract AB1451HPR – Table 2.** Zarit scale classification according to age groups

Variable	15–39 years n=36	40–60 years n=38	Older than 60 years n=41	P value
No burden	20	28	30	0.108
Low burden	8	5	5	0.375
Intense burden	8	5	6	0.436

**Conclusions:** Although a high proportion of caregivers reported to have not burden, it is important to develop strategies and activities in order to attend the necessities of the caregivers in order to reduce the overload of responsibilities among them. Also further research is needed in order to identify the risk factors or protector factors that can prevent disease burden in caregivers.

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#### AB1452-HPR WHICH ONE HAS A GREATER EFFECT ON FUNCTION AND THE PSYCHOSOCIAL STATUS IN JIA?: DISEASE TYPE OR THE PRESENCE OF PAIN

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**Background:** Juvenile idiopathic arthritis (JIA) is a chronic inflammatory childhood disease with symptoms such as joint inflammation, pain and

loss of quality of life.<sup>1</sup> Types of disease and the presence of pain can impact the child psychosocially, as well as affecting functional activity.<sup>2</sup>

**Objectives:** The aim of this study is to examine the results of functional and psychosocial status according to the disease type and the presence of pain symptoms in children with JIA.

**Methods:** The study included 71 children diagnosed with JIA who applied to the Hacettepe University İhsan Doğramacı Children's Hospital Rheumatology Department. Following the collection of demographic information, functional status was assessed with the Child Health Assessment Questionnaire (CHAQ) and psychosocial and functional status was assessed with the scale developed in Hacettepe University Faculty of Health Sciences Department of Physiotherapy and Rehabilitation for functional and psychosocial status of children with rheumatism by Edibe Ünal.<sup>3</sup> Children were divided into groups according to disease type as oligoarthritis or polyarthritis and the presence or absence of pain.

**Results:** Table 1 shows the mean age and numbers of children. There was no difference between the groups according to disease type (p>0,05). On the other hand, comparing scores for the CHAQ total, CHAQ general VAS assessment, functional and psychosocial status according to the presence or absence of pain revealed significant differences (p<0,05).

**Abstract AB1452HPR – Table 1.** Assessment values and comparison statistics

	Disease Type			Pain		
	Oligoarthritis (n=51)	Polyarthritis (n=20)	p	Present (n=21)	Absent (n=50)	p
Age (years)	10,88±3,81	13,50±3,92	0016	11,71 ±3,77	11,58 ±4,12	0885
CHAQ Total	0,28±0,29	0,46±0,41	0127	0,51±0,4 ±0,27	0,26 ±0,27	0012
CHAQ (General VAS)	2,49±2,43	3,93±3	0068	4,46 ±2,86	2,24±2,3	0002
Function (range 0–30)	4,72±4,85	5,05±6,32	0766	7,85±6,6 ±4,02	3,54 ±4,02	0004
Psychosocial (range 0–30)	23±5,67	14,5±5,82	0363	16±5,74 ±5,4	12,34 ±5,4	0012

Function; Psychosocial; Functional and Psychosocial subscales of Ünal's scale.<sup>3</sup>

**Conclusions:** We conclude that pain has a greater effect on functional, psychosocial and overall disease assessment in children with JIA when compared to the disease type. Thus, it must be taken into consideration that child's ability to cope with pain should be improved.

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#### AB1453-HPR ARE DMARD THERAPIES EFFECTIVE ON QUALITY OF LIFE, ANXIETY AND DEPRESSION LEVELS IN PATIENTS WITH RHEUMATOID ARTHRITIS?

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**Background:** Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease with persistent joint inflammation manifesting as joint pain, stiffness, and swelling. Treatment of rheumatoid arthritis (RA) should be aimed at achieving the lowest possible disease activity. Conventional DMARDs (eg, methotrexate [MTX], hydroxychloroquine, and sulfasalazine) are still widely used in newly diagnosed RA patients. On the other hand, the rate of biologic therapy use in clinical practice is rising as more agents become available in spite of efficacy of these treatments is broadly comparable. Depression is a common under-recognised co-morbidity in patients with RA accompanying with substantial disability, reduced quality of life.

**Objectives:** The aim of this study was to determine whether depression level is effected by response to therapy and compare the effectiveness of DMARD therapies in terms of quality of life, anxiety and depression levels in patients with RA.

**Methods:** A total of 105 patients (Conventional DMARDs, n=67; Biological Therapy, n=38) with RA participated to the study. Disease activity was assessed using the Disease Activity Score in 28 joints (DAS28). Remission was defined as the absence of disease activity (i.e. tender joint count [TJC]=0+ swollen joint count [SJC]=0+ESR <10 mm/hr). The Hospital Anxiety and Depression Scale (HADS) was used to measure both anxiety and depression level. The Rheumatoid Arthritis Quality of Life (RAQoL) questionnaire was applied to assess quality of life. The drug therapy groups were compared using the Kruskal-Wallis test and the Chi-square test. Correlation between the scales was evaluated by Spearman's correlation coefficient.

**Results:** There was no statistical difference in terms of RAQoL scores, disease activity and anxiety/depression scores between conventional DMARDs (RAQoL=16.78; DAS Remission=%46.3; Anxiety score=9.31; Depression score=7.34) and biological therapy (RAQoL=13.87; DAS Remission=%36.8; Anxiety score=8.24; Depression score=9.13) (p=0.096; p=0.816). RAQoL scores were significantly higher in patients with higher disease activity treated with conventional DMARDs (conventional DMARDs, DAS Activity=%43.3; biological therapy, DAS Activity=%39.5; RAQoL=17.54; p=0.006). RAQoL scores were statistically lower in patients with lower disease activity (p<0.001). Depression levels were statistically higher than anxiety levels (p=0.008).

**Conclusions:** Our results demonstrated that the presence of depression coexisting with RA independent from disease activity may result in poorer clinical response to standard therapies. According to recent ACR recommendations, RA patients who may be candidates for biologics (eg, infliximab, etanercept, adalimumab) include patients with high disease activity, and those who have previously failed to respond adequately to conventional DMARD therapy. However, the results of the study suggest that different pharmacological therapies are not enough to improve quality of life in patients with RA. There is a need for certain non-pharmacological treatments integrated with medication management based on bio-psychosocial approaches to cope with depression in RA patients.

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#### AB1454-HPR INTERACTIONS BETWEEN WOMEN WITH RHEUMATOID ARTHRITIS AND NURSES IN NURSING CONSULTATIONS – BALANCING ILLNESS, MOTHERHOOD AND WORK LIFE

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**Background:** Patients with rheumatoid arthritis (RA) are offered outpatient follow-up in nurse-led consultations.<sup>1</sup> RA affects almost every aspect of daily life.<sup>2</sup> Many women with rheumatoid arthritis find it challenging to be mothers and simultaneously participate in paid work.<sup>3</sup>

**Objectives:** To investigate how women's understanding of RA, motherhood and working life are parts of the interactions with nurses during nursing consultations.

**Methods:** Participant observations were conducted during 10 women's attendance in nursing consultations and subsequently the women were interviewed about their experiences. Data generation and analysis were carried out according to the principles of constructivist grounded theory.<sup>4</sup>

**Results:** A core category was developed: "Cooperation through mutual recognition" which describes how women and nurses through verbal and non-verbal communication confirm their common understanding of the

content and form of nursing consulting. Furthermore, three sub-categories were identified:

1) "On safe ground" illuminates, that biomedical aspects of the disease such as blood tests results, examination of the joints and pharmacological treatments represent the foundation of the dialogue. This interaction has elements that may be characterised as ritualised behaviour.

2) "Taking risks" documents how both parties are more aware of the counterparts' reaction when it comes to dialogue concerning how the women manage illness in everyday life along with motherhood and paid work.

3) "Gentle correction" shows how the nurses gently express when they find the women's talk is too far out.

**Conclusions:** The biomedical aspects of the disease (disease perspective) constitute the starting point for a discussion and allow both parts to initiate conversations on the women's subjective understanding (illness perspective) of how illness, motherhood, and work are managed.

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#### AB1455-HPR THE EXPERIENCE OF LIVING WITH FATIGUE AMONG PEOPLE WITH RHEUMATOID ARTHRITIS – A QUALITATIVE META-SYNTHESIS

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**Background:** People with Rheumatoid Arthritis (RA) experience fatigue as the most significant symptom of their illness. Despite a substantial body of knowledge about fatigue, there is a need for an overall comprehensive understanding of the experience of living with fatigue among people with RA

**Objectives:** To identify, appraise and synthesise qualitative studies on experiences of living with fatigue in people with RA

**Methods:** We conducted a qualitative meta-synthesis, inspired by Sandelowski and Barroso<sup>1</sup>. This included a systematic literature search conducted in February 2017, for studies published in the past 15 years, in the databases PubMed, Cinahl, Embase, SveMed, PsychInfo and Web of Science. To be included the studies had to include findings regarding the experience of adults with RA living with fatigue. The international Critical Appraisal Skills programme was used to assess the quality. The analysis and synthesis were inspired by Malterud's systematic text condensation<sup>2</sup>

**Results:** Eight qualitative articles were included. The synthesis resulted in an overall theme 'fatigue: the vicious cycle of an unpredictable symptom'. In addition, the analysis derived five subthemes, 'being alone with fatigue', 'necessary prioritising in everyday life', 'when time gets a different meaning', 'language as a tool for increased understanding' and 'strategies to manage fatigue'. Fatigue affects all areas of everyday life for people with RA. They strive to plan and prioritise, pace, relax and rest. In addition, they try to make use of a variety of words and language to help others understand that the RA-related fatigue they experience is not 'normal' fatigue. People with RA-related fatigue experience feeling alone with their symptom, but they develop their own strategies to manage fatigue in their everyday life

**Conclusions:** The unpredictability of RA-related fatigue is dominant, pervasive and is experienced as a vicious cycle, which can be described in relation to its physical, cognitive, emotional, social and behavioural impact.



Acknowledgement and support from health professionals can make a difference to people with RA-related fatigue

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#### AB1456-HPR SHARED DECISION MAKING IN PRACTICE AND NEEDS OF RHEUMATIC PATIENTS ON NURSING SUPPORT

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**Background:** Value Based Health Care entails creating value for the patient by providing meaningful care. Meaningful care can be given with focus at the perspective of the patient. Nurses play a role in measuring and monitoring care outcomes, but also have an important role in providing information about, treatment options and counselling of patients with their illness and treatment. Nurse consultation is part of the clinical pathway for rheumatoid arthritis patients.

**Objectives:** What are the needs and expectations of a patient at a consultation with the rheumatology nurse?

What do rheumatology nurses discuss with patients and their relatives during the nursing consultation and does this fit with the nursing competences from the generic self-management model?

**Methods:** Beside literature research two focus groups with patients about nursing care in the out-patient clinic were held. Also 10 nurse consultations were analysed from 3 different nurses. Qualitative data from both focus groups and observations were analysed and encoded with Atlas.ti.

**Results:** Patients were positive about the time spending for education and information. They expect the nurse to be a guide and give reliable information. They wanted emotional support especially when medication change and in the begin period when diagnose is set. Suggestions for subjects for follow up consultation like medication check, co-morbidity screening were positively received. Talking about self management is also a well received subject. A specific tool for self management like the self management web could support both patients and nurses.

Observation in practice showed that nurses give education and advice, but coaching is a less used skill.

**Conclusions:** Patients want emotional support, education about illness and self management support. Nurses are well equipped in give information and advice but must be educated in using there coaching skills and support patients to talk about their experienced problems in daily live.

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#### AB1457-HPR AGGRESSION, DEPRESSION LEVEL AND GOUT-RELATED CHARACTERISTICS AMONG FILIPINOS DIAGNOSED WITH GOUTY ARTHRITIS: A CROSS-SECTIONAL, MULTI-CENTRE STUDY

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**Background:** Uric acid (UA) is the end-product of purine metabolism in humans. Hyperuricemia or the elevated levels of serum UA have been implicated in the development of multiple health problems, including gout. Several studies show that UA predicts changes in behaviour over-time.

The importance of these behavioural changes can affect implementation of psychotherapeutic intervention and rehabilitation. However, there is a dearth of literature to support the relationship between gout-related characteristics and the aggressive and depressive behaviour of individuals with gouty arthritis.

**Objectives:** The primary aim of this study was to determine the predictors of aggression and depression tendencies through exploring the association of gout-related characteristics with the level of aggression and depression among adults aged 30–79 years old diagnosed with gouty arthritis within the healthcare facilities of Manila.

**Methods:** This study employed an observational, cross-sectional multi-centre design that was conducted in various healthcare facilities within the city of Manila. The participants were composed of 75 Filipino individuals diagnosed with gouty arthritis.

**Results:** Using logistic regression with significance level of  $p \leq 0.05$ , findings revealed that there were significant associations between the aggression and gout-related characteristics, specifically the average gout pain level ( $p=0.013$ ), gout duration ( $p=0.022$ ) and serum UA ( $p=0.018$ ). Furthermore, results also showed that there were significant correlations between the depression and gout-related characteristics such as self-reported comorbidities ( $p=0.020$ ), average gout pain level ( $p=0.032$ ), serum UA ( $p=0.045$ ), number of joints with gout ( $p=0.016$ ), and number of gout attacks ( $p=0.029$ ).

**Conclusions:** Findings revealed that the higher the values are in the gout-related characteristics, the higher the level of aggression and depression among gout patients. These significant associations can be considered as predictors of aggression and depression tendencies which validates the necessity to address the biopsychosocial aspect of an individual and to consider an effective approach on psychotherapeutic intervention and rehabilitation.

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#### AB1458-HPR WORK PARTICIPATION OF PEOPLE WITH MUSCULOSKELETAL DISORDERS IN IRELAND: A QUALITATIVE MULTI-STAKEHOLDER ANALYSIS

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**Background:** Musculoskeletal disorders (MSD's) are a leading cause of work disability. Good work offers many potential benefits to employees with MSDs. Understanding the perspectives of all the players involved in helping people with MSD's to stay at, return to and remain in work will advance understanding of work related interventions and services. Given the varying health and social insurance systems across international contexts there is a need to develop contextually specific knowledge.

**Objectives:** To explore in-depth the perspectives of multiple stakeholders involved in helping people with MSD's stay at, return to or remain in work.

**Methods:** In-depth qualitative interviews were completed with people with MSD's, health professionals, and employers to explore their perspectives on what factors support people with MSD's to stay in, return to, or remain in work in Ireland. Data were analysed using thematic analysis.

**Results:** Across all stakeholder groups biological factors were most implicated as the reason for work absences and the resolution of symptoms

was identified as the single greatest enabler of return to work. Although pockets of good practice were identified, in the main, health professionals and employers describe uncertainty about their role and responsibilities and describe a narrow scope of practice. Patients report a mostly adversarial experience of vocational supports.

**Conclusions:** Irish vocational rehabilitation stakeholders do not report awareness of the complex interplay of biological, psychological and social factors influencing work participation for people with MSD's. Vocational supports and services are hampered by role uncertainty and consequentially adversarial experiences for service users.

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### AB1459-HPR PATIENTS WITH RHEUMATOID ARTHRITIS HAVE LATERALITY ON THE UPPER LIMBS RANGE OF MOTION

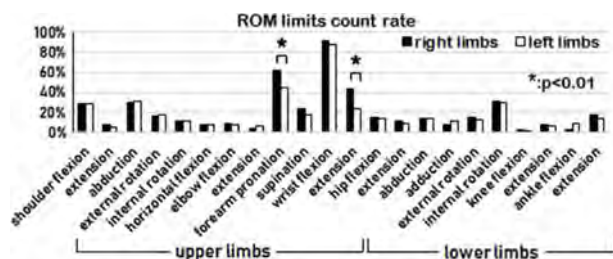
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**Background:** Biological disease-modifying antirheumatic drug (bDMARD) has been introduced since 2003 in Japan. In many patients, bDMARD has made it possible to control the disease activity of rheumatoid arthritis (RA), and has led to the structural remission and the functional remission. As for the structural damage, the relationship between mechanical stress and radiographic damage in RA has been recently reported. Koh reported that radiographic damage was worse and progressed more rapidly in the dominant hand in individuals with early RA<sup>1</sup>. Nakazaki reported that the eroded joint count was significantly more in the dominant than the non-dominant upper extremity<sup>2</sup>. Incidentally, there are few studies as for the relationship between mechanical stress and functional impairment, while joint range of motion (ROM) plays a important role on the physical function of the patients with RA.

**Objectives:** The aim of this study is to examine whether patients with RA have difference between right and left on the upper limbs and to see whether mechanical stress influences on ROMs.

**Methods:** We assessed 103 RA female patients aged less than 75 years old with their disease onsets after 2003 and their disease durations within 10 years. Exclusion criteria were the patients with past history of any apoplexy or fracture. We measured the ROM of joints including the shoulder, elbow, wrist, hip, knee, and ankle. The ROMs were measured by criteria of the Japanese Orthopaedic Association and the Japanese Association of Rehabilitation Medicine, and then the joints with restricted ROM were counted to see if any difference between right and left limbs. Data were analysed by using McNemar's test and judged as statistically significant when p value was less than 0.01.

**Results:** The mean age was 57.1 (26~74) years, the mean disease duration was 64.0 (7~120) months, the rate of bDMARD was 33.3%, the right limb was dominant in 99.0% among the patients. As for the ROM of upper limbs, the forearm pronation and the wrist flexion of the right limbs demonstrated significantly more restricted ROM compared with the left limbs (p<0.001). The ROM of lower limbs showed no significant laterality.



Abstract AB1459-HPR – Figure 1

**Conclusions:** The ROM limit count in the upper limbs was significantly more in the right limbs than the left limbs and the right limb was dominant in 99% of the patients, therefore it was suggested that the mechanical stress influenced the ROM of upper limbs and physical function in patients with RA even in the era of the bDMARD.

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**Disclosure of Interest:** None declared

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### AB1460-HPR PSYCHOLOGICAL VARIABLES PREDICTOR OF SLEEP DISORDERS IN PATIENTS WITH ANKILOSING SPONDYLITIS AND PSORIASIC ARTRITIS. MULTICENTER STUDY

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**Objectives:** To study the variables associated with the severity of insomnia and hypersomnia according to the Oviedo sleep questionnaire (COS) in patients with ankylosing spondylitis (AS) and psoriatic arthritis (PsA).

**Methods:** Design. Transversal descriptive study. PATIENTS: Patients with follow-up AS or PSA were selected by consecutive sampling in rheumatology units of 4 Spanish cities. Selection criteria: age  $\geq 16$  years old) with AE (New York criteria) or PSA (CASPAR criteria) able to understand and willing to carry out the questionnaires. Protocol: they were explained and the patients were given to meet the selection criteria and the informed consent signed a battery of questionnaires; his doctor performed the evaluation of disease activity and recorded comorbidities and current medication. Main outcomes: the 3 dimensions of COS:<sup>1</sup> Subjective satisfaction with sleep,<sup>2</sup> Insomnia and<sup>3</sup> Hyperinsomnia. Other variables: current medication for AE or PsA, comorbidities, use of sleeping drugs and/or CPAP according to the COS questionnaire, disease activity: axial AS (BASDAI) and PSA (DAS28), quality of life related to health (HRQL) through SF-36, pain perception (Brief Pain Inventory BPI questionnaire), AE (BASDAI) and PSA (DAS28) and fatigue through FACIT, emotional intelligence through TMMS, resilience with the resilience questionnaire, anxiety screening and depression through HADs. Statistical analysis: Descriptive analysis of the main variables. Bivariate using T-Student, Mann Whitney U and  $\chi^2$  followed by binary logistic regression (RLB) (Vd: Insomnia: value greater than 22 of the insomnia scale).

**Results:** 302 patients participated: 152 patients with AE and 149 patients with PA (47.8% women, 48.97 $\pm$ 10.26 years) with an average of 8.35 $\pm$ 6.8 years of disease. They used 47.8% biological therapy. The most frequent comorbidities were: disc disease 143 (47.5%), visual impairment 60 (19.9%), anxiety 49 (16.3%), obesity 47 (15.6%) and depression 45 (15%). In the bivariate analysis it was observed that patients with AE suffered more insomnia than patients with PSA (57% vs 43%, p=0.029), they took more drugs to sleep (30.3% vs 22.9%, p=0.001) and suffered a higher activity of the disease measured by BASDAI (mean [SD] 4.7 [1.8] vs 3.8 [1.9], p=0.005). In insomnia in PsA, it was not associated with the degree of activity measured by DAS28 but it was associated with depression. In the binary logistic regression analysis (RLB), insomnia was associated with BASDAI and depression. Therefore, patients with greater BASDAI and depression have almost twice the risk of presenting insomnia in patients with spondyloarthropathies. There are no associations of insomnia with the resilience and emotional intelligence with results above the cut, that is, patients with good resilience and emotional intelligence.

**Conclusions:** There is an association between insomnia, disease activity and depression in the group of AE, in the case of PSA there is a relationship with depression. Insomnia is a problem related to depression, so education in sleep hygiene in nursing consultation could be of help for insomnia.

**Disclosure of Interest:** None declared

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**AB1461-HPR** **FREQUENCY OF RHEUMATOID FACTOR ISOTYPES IN PARAGUAYAN PATIENTS WITH RHEUMATOID ARTHRITIS**

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**Background:** Rheumatoid Arthritis is a chronic rheumatic disease characterised by polyarticular inflammation. The rheumatoid factor is one of the most known prognostic markers, not only its presence, but also the levels. It also presents different isotypes (IgG, IgM, IgA), which can affect the course of the disease.

**Objectives:** To analyse the presence of different rheumatoid factor (RF) isotypes in Paraguayan patients with rheumatoid arthritis (RA) and to study their association with clinical and analytical characteristics.

**Methods:** Descriptive, cross-sectional study. A large number of clinical and serological variables were recorded. The anti-CCP 3.1 and Rheumatoid factor (RF) isotypes IgA, IgG, and IgM were measured in serum samples by ELISA (enzyme-linked immunosorbent assay) (NV<17 U/ml). Statistical analysis was performed using SPSS v.23. Quantitative variables were characterised by their means and standard deviations, while the qualitative variables were characterised according to the percentage of patients. The comparison of clinical and serological variables was performed using the chi-squared test and the student test respectively for qualitative and quantitative variables.

**Results:** 103 patients with RA were included, 86.4% were female, with a median age of onset of 44.7±13.6 years, and the mean disease duration was 7.13±7.03 years. The oligoarticular onset was the most frequent (46.6%). 13.7% were smokers. Extra-articular manifestations were present in 13.5%. The most frequent treatment was methotrexate (84.3%). Erosions were observed in 43.2% of patients. 28% were in remission of the disease measured by the DAS28 index. The average of HAQ was 0.47% ±0.58. 91.3% had anti-CCP positive, the mean anti-CCP levels were 290.5±152.8 U/mL. RF isotypes was observed in 75.7%, 53.4% and 38.8% for IgM, IgA and IgG respectively. Mean levels were as follow, IgA 85.62±56.6 U/mL, IgM 96.7±30.9 U/mL, IgG 70.98±72.42 U/mL. 32% of the patients had 2 isotypes of RF, while 25.2% had the 3 isotypes. The 57.3% had ≥2 isotypes of RF. We did not find significant differences when comparing gender, age, disease duration, form of onset, extra-articular manifestations, smoking status, erosions, disease activity, HAQ, treatment, between the different RF isotypes, and levels, except in the presence of anti-CCP with the RF-IgM isotype (p<0.000).

**Conclusions:** This is the first study of RF isotypes in Paraguayan patients with RA. The most frequent isotype of RF was IgM. More than 50% of patients had 2 or more RF isotypes. The majority of patients with positive RF had high levels of different isotypes, being the highest IgM.

**Disclosure of Interest:** None declared

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**AB1462-HPR** **ACTIVITY LIMITATIONS AND PERCEIVED HEALTH-RELATED QUALITY OF LIFE IN PEOPLE WITH INCLUSION BODY MYOSITIS – A CROSS-SECTIONAL STUDY**

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**Background:** Inclusion body myositis (IBM) is a slowly progressive inflammatory myopathy with muscle weakness around thighs, knees and finger flexion muscles. Most people are 50 years or older at onset and there are more men than women with ratio of 2–3: 1. The diagnosis leads to activity limitations in daily life.

**Objectives:** The aim of this study was to describe how individuals with IBM describe their activity limitation and how they estimate their perceived health-related quality of life as well as to describe the correlation between activity limitation and experienced health-related quality of life.

**Methods:** A quantitative cross-sectional study involving a total of 29 people with IBM participated. Data collection was performed in Stockholm Sweden. The Myositis Activities Profile (MAP) were used to measure activity limitation and the Short Form-36 (SF-36) were used to measure experienced health-related quality of life.

**Results:** Activity limitations were estimated from no difficulty to impossible to do. The activity with the highest value (very difficult) was movement.

There was a significant difference between individuals with IBM and Swedish normative references measured with SF-36 in physical function, physical role function, general health and social function (p≤0.01).

There were high correlations between SF-36 physical and social function with MAP's movement, household activities, social activity, work/school and leisure (−0.872 ≥r<sub>ss</sub>−0.702; p≤0.001).

**Conclusions:** Participants estimated activity limitations in many areas, of which movement was estimated as very difficult. The study demonstrated correlation between activity limitations and the experience of impaired health-related quality of life. In order to make positive impact on the health-related quality of life, it is important to focus on social areas such as family, friends and leisure activities, as well as optimising everyday living with proper mobility tools.

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**AB1463-HPR** **IS THERE ANY DIFFERENCE IN JOINT POSITION SENSE AMONG DIFFERENT KNEE ANGLES IN PATIENTS WITH KNEE OSTEOARTHRITIS?**

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**Background:** The joint related structures such as joint capsule, menisci, ligaments, muscles, skin provide the sensory input for the knee proprioception. Individuals with knee osteoarthritis (OA) have poor proprioceptive sense when compared with the same ages healthy individuals. Due to OA, the joint structures such as menisci, ligaments, and joint capsule rapidly undergo degeneration, and the deficiency of the knee proprioception progresses. Daily activities such as stair climbing, rise from a chair, walking require different knee joint angles. Therefore, the evaluation of the knee position sense at different joint angles is necessary for a better understanding of the knee proprioceptive sense deficit and for planning rehabilitation program in patients with knee OA.

**Objectives:** The purpose of this study was to analyse the knee joint position sense in different knee joint angles and to compare the results.

**Methods:** The study group consisted of 80 patients (62 female/18 male, 124 knees), with unilateral or bilateral knee OA and with a mean age 65.5±9.1 years were included in the study. Patients were evaluated regarding knee proprioception in knee joint angle 30°, 60° and 75°. The starting position was in knee joint angle 90° flexion, and the target angles was attempted to replicate using active knee extension movements. Patients performed active joint angle replication test in sitting position at a standard back supported chair. The average of the 3 repetitions of active joint repositioning test was recorded position sense score. The angular displacements from the target angles (in knee joint angle 30°, 60°, 75°) at the end of the active reproduction tests were recorded as position sense deficit scores.

**Results:** When the patients' knee position sense deficit at different joint angles (in knee joint angle 30°, 60° and 75°) were compared, there were statistically differences between at joint angle 75° and 60° (p=0.002), and also there were statistically differences between at joint angle 75° and 30° (p=0.001). However, there were not statistically differences between the patients' knee position sense deficit at joint angle 30° and 60° (p>0.05).

**Conclusions:** According to our results, the patients with knee OA have better proprioceptive acuity at knee joint angle 30°, 60° than at knee joint angle 75°. Specifically, the detection of active knee movement occurred with lower target angle displacement at a starting knee angle close to terminal extension (30°) than at knee angles closer to midrange (75°). These results can be reasonably speculated that proprioceptive input arose primarily from hamstring muscle stretching, posterior capsule tautness, and possibly ligament strain. It could be argued that the observation of the greater motor responses at decreased angles likely have been facilitated from enhanced sensitivity of these sensory terminals. Also, the results of this study may provide guidance for future proprioceptive sensory evaluations and provide guidance for planning rehabilitation programs in patient with knee OA.

**Disclosure of Interest:** None declared

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**AB1464-HPR ACUTE EFFECTS OF COLD – PACK APPLIED IN DIFFERENT WAYS FOLLOWING FATIGUE ON POSTURAL STABILITY, PROPRIOCEPTION AND MOTOR PERFORMANCE**

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**Background:** There is a lack of literature examining local cooling on postural stability, proprioception, and motor performance following fatigue.

**Objectives:** The purpose of this study was to examine the effects of cold-pack applied on knee joint following fatigue on postural stability, proprioception, and motor performance in healthy subjects. It was hypothesised that fatigue might cause deficits in measurements of postural stability, proprioception, and motor performance and cold-pack treatment applied on knee joint in different ways might prevent this deficit.

**Methods:** Sixty healthy subjects (33 female, 27 male; age=22.00±1.37 years, height=169.62±9.21 cm, weight=63.48±12.61 kg) were participated in the study. Subjects had no history of lower extremity injury, vestibular or postural stability problems, proprioception problems, hip, knee, and ankle instability. Postural stability, knee proprioception and motor performance were assessed by Pedalo Sensamove System, Biodex System Pro 4, and Stair Climbing Test, respectively.

The subjects were received a clinically-used fatigue protocol on a cycle ergometer. The Modified Borg's Rate of Perceived Exertion Scale has been used for fatigue determination. All assessments were performed three times at rest, immediately after fatigue and cold-pack treatment.

**Results:** There were no significant changes in terms of postural stability and knee proprioception after fatigue and cold-pack treatment compared to the condition at rest in all groups ( $p>0.05$ ). However, motor performance was significantly decreased following fatigue compared to the condition at rest ( $p<0.05$ ).

**Conclusions:** The hypothesis of this study, that fatigue could cause a deficit in measurement of motor performance was supported. On the other hand, postural stability and proprioception did not decrease following fatigue. According to the results of our study, we concluded that the subjects do not benefit from the use of cold-pack for compensating deficit in measurement of motor performance following fatigue.

**Disclosure of Interest:** None declared

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**AB1465-HPR IMPACT OF ULCERS IN QUALITY OF LIFE AND FOOT FUNCTION IN SYSTEMIC SCLEROSIS PATIENTS**

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**Background:** Systemic Sclerosis (SSc) is a progressive, highly disabling pathology associated with pain, functional limitation, loss of ability at work and high social costs. Recent studies have proved that quality of life is worst in SSc patients than in healthy people, however there is lack in literary works investigating ulcers and lower limb complications.

**Objectives:** The aim of the present study is to investigate health-related quality of life and foot function in patients affected by SSc with or without ulcers.

**Methods:** 215 patients (mean age 48,6 years SD ±12,3) completed four questionnaires: Short-Form 36 (SF-36) and Health Assessment Questionnaire (HAQ) for quality of life, Foot Function Index (FFI) for foot function, Cardiff Wound Impact Scale (CWIS) for patients with ulcers only (88). Demographic data were also investigated such as sex, occupation and living place. In addition, further information about type of SSc, age at diagnosis of SSc, age at first Raynaud phenomenon, podiatric assessment and orthopaedic insoles or shoes wear was inquired.

**Results:** SF-36 scores were significantly lower in patients with ulcers than in patients without ulcers ( $p=0,001$ ) as regards the physical component score (PCS). PCS was also positively correlated to its own sub-domain Physical Function ( $R=0,81$ ), Role Physical ( $R=0,72$ ) and Body Pain ( $R=0,71$ ). SF-36 Mental component score (MCS) was positively correlated to its own sub-domain Mental Health ( $R=0,85$ ) and Role Emotional ( $R=0,77$ ). HAQ scores were significantly higher in patients with ulcers than in patients without ulcers ( $p<0,001$ ). PCS was negatively correlated to the HAQ ( $R=0,75$ ). FFI scores were significantly higher in patients with ulcers than in patients without ulcers ( $p=0,001$ ). CWIS scores were pretty high (50,6% SD ±26,6). Chi-square-test wasn't statistically significant ( $p=0,926$ ): ulcers and age are not correlated. Only 17 patients out of 215 were used to wear orthopaedic footwear, 38 wore foot orthoses and 71 were informed about the figure of the podiatrist.

**Abstract AB1465-HPR – Table 1.** Questionnaire scores and P-value

Group	SF-36		HAQ	FFI	CWIS
	PCS	MCS			
All patients	35.78±10.3	39.40±11.1	0.90±0.6	23.16%±24.7	-
Patients with ulcers	33.0±9.4	37.7±11.6	1.11±0.6	28.9%±27.5	50.6%±26.6
Patients without ulcers	37.73±10.5	40.6±10.5	0.74±0.6	19.1%±21.6	-
P-value	0.001	0.07	<0.001	0.001	-

**Conclusions:** According to the literature,<sup>1-2</sup> patients with SSc show an impaired quality of life compared to healthy subjects. The majority of patients are unemployed or stay at home due to disability. Furthermore, in case of ulcers, the more pain grows, the more foot function is reduced as well as quality of life gets worse. Wounds could be considered as a biomarker of pathology progression; therefore, clinicians should pay more attention in prevention improving lower limb assessment and treatment.

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**AB1466-HPR EFFECTS OF SHORT-TERM NEUROMUSCULAR ELECTRICAL STIMULATION ON PAIN, QUADRICEPS MUSCLE STRENGTH, PHYSICAL PERFORMANCE AND KINESIOPHOBIA IN PATIENTS WITH OSTEOARTHRITIS OF THE KNEE (A PRELIMINARY STUDY)**

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**Background:** Osteoarthritis may cause fear of movement, increased pain, detention, reduced muscle strength, and range of motion. Quadriceps muscle strengthening is a common goal in the management of knee osteoarthritis. Neuromuscular electrical stimulation (NMES) is considered to be an effective technique for strengthening the quadriceps muscle. It has been used to treat patients with knee osteoarthritis.

**Objectives:** The aim of the study is to determine the effect of short-term neuromuscular electrical stimulation on pain, strength, physical performance and kinesophobia in patients with knee osteoarthritis.

**Methods:** 20 patients (9 women 11 men, who were 40–75 years, diagnosed as stage 2 or stage 3 knee OA according to Kellgren-Lawrence criteria, participated to the study. Socio-demographic data of all individuals were recorded. The cases were randomly divided into two groups as control group (n=10) and study group (n=10). Control group treatment consisted of conventional physiotherapy program (hot pack, transcutaneous electrical nerve stimulation (TENS), ultrasound and home exercises). In the study group, NMES application was added to conventional physiotherapy program. Both groups were treated five days/week for two weeks. The patients were assessed; before and after treatment. The pain was assessed by Visual Analogue Scale (VAS). Muscle strength was assessed by manual muscle test. Stair-climb test was performed to evaluate physical performance. Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) was used to assess functional disability. Kinesiophobia was evaluated by Tampa Kinesiophobia Scale.

**Results:** There was no significant difference between control and study groups in terms of age, Body Mass Index, the scores of VAS value, Quadriceps Muscle strength, Stair-climb test, WOMAC and TAMPA scores at baseline ( $p>0.05$ ). Post treatment VAS value decreased significantly in both groups compared with pretreatment values ( $p<0.05$ ). However the scores of Quadriceps Muscle strength, Stair-climb test, WOMAC and TAMPA did not change significantly in both groups after the treatment. When compared the two groups, all the outcomes were similar ( $p>0.05$ ) after the treatment.

**Conclusions:** Because of the preliminary report and less number of patients; drawing definitive conclusions is not possible. It seems that, short-term conventional physiotherapy program decreased only pain, but did not improve strength, physical performance, functional disability and kinesiophobia. Also, we thought that short-term NMES application which added to conventional physiotherapy program did not provide superiority over treatment outcomes.

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**Disclosure of Interest:** None declared

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#### AB1467-HPR MEASUREMENT OF CERVICAL PROPRIOCEPTION IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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**Background:** Axial spinal inflammation and spinal posture disorders in axial spondyloarthritis (axSpA) may deteriorate proprioception which may be caused by pathologic involvement of spinal entheses containing proprioceptive afferents.<sup>1</sup> Cervical spine is one of the main inflammation area in axSpA.<sup>2</sup> Impaired cervical proprioception has negative effects on postural control system.<sup>3</sup> The cervicocephalic relocation measure by laser pointer is found a reliable method to measure cervical sensory function in healthy participants in a recent study.<sup>4</sup> And there is limited data that regarding cervical proprioception in axSpA.

**Objectives:** To examine the differences in cervical joint proprioception between patients with axSpA and healthy subjects.

**Methods:** The cervical joint position errors (JPE) were measured to evaluate proprioceptive function accuracy in patients with 29 axSpA and 21 healthy subjects by laser pointer with cervical application. Neutral head position method was used to evaluate proprioception in flexion, extension, rotation and lateral flexion in right and left movement directions at sitting position (figure 1).<sup>5</sup> Three measures were performed, and the average of the three trials was used for analysis. The distance between zero spot and joint position which patient had been reconstructed was measured by centimetre. Spinal mobility evaluated by BASMI, function evaluated by BASFI and HAQ-S; disease activity defined by BASDAI, pain and fatigue were evaluated by VAS.



Abstract AB1467HPR – Figure 1

**Results:** There were 29 patients (21 men, mean ( $\pm$ SD) age; 41.4 $\pm$ 10.9 years) and 21 healthy subjects (15 men, mean age 41.1 $\pm$ 11.3 years). BASMI, HAQ-S and fatigue score were significantly higher in patients (BASMI values were 3.9 $\pm$ 2.3 vs 1.3 $\pm$ 0.7,  $p$ <0.001; HAQ-S values were 2.1 $\pm$ 0.8 vs 0.8 $\pm$ 0.2,  $p$ <0.001; fatigue values were 37.2 $\pm$ 23.3 vs 16.2 $\pm$ 14.9,  $p$ =0.001). The comparison of cervical JPE showed significantly larger errors ( $p$ <0.05) in patients with axSpA, except right rotation ( $p$ =0.166) (table 1).

#### Abstract AB1467HPR – Table 1

Comparison of joint position errors between patients with axSpA and healthy subjects			
Variable (cm)	AxSpA patients (n=29) (mean $\pm$ SD)	Healthy subjects (n=21) (mean $\pm$ SD)	P value
JPE in flexion	9.88 $\pm$ 6.70	4.66 $\pm$ 3.57	<b>0.001</b>
JPE in extension	12.99 $\pm$ 8.99	5.55 $\pm$ 2.98	<b>0.001</b>
JPE in right rotation	11.10 $\pm$ 6.56	8.62 $\pm$ 4.41	0.166
JPE in left rotation	10.59 $\pm$ 6.51	7.02 $\pm$ 5.78	<b>0.011</b>
JPE in right side bend	11.32 $\pm$ 6.53	6.39 $\pm$ 3.54	<b>0.001</b>
JPE in left side bend	9.62 $\pm$ 6.18	6.14 $\pm$ 4.46	<b>0.036</b>

JPE=Joint position error,  $p$  values are based on Mann-Whitney U test.

**Conclusions:** Cervical joint position sense is impaired in subjects with axSpA. Proprioceptive training may help to boost the effectiveness of rehabilitation.

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#### AB1468-HPR SATISFACTION WITH THE BDMARD ETANERCEPT BIOSIMILAR (SB4) PRE-FILLED PEN AMONG RHEUMATOID ARTHRITIS AND SPONDYLOARTHROPATHY PATIENTS; A GERMAN OBSERVATIONAL STUDY

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**Background:** The TNF $\alpha$  inhibitor etanercept was the first targeted biological disease modifying anti-rheumatic drug (bDMARD) approved for treatment of RA; the first etanercept biosimilar (SB4) was authorised in the EU in January 2016. Various administration devices have been developed for convenient subcutaneous self-injection of bDMARDs including pre-filled pens.

**Objectives:** This study aims to document general patient satisfaction in day-to-day use of the SB4 pre-filled pen. Patients' experience regarding handling, convenience, other features and the associated training on self-injection is also evaluated.

**Methods:** This non-interventional, cross-sectional study is enrolling patients who are treated according to usual medical practice. Patients had experience with the SB4 pre-filled pen in accordance with the prescribing information for at least 3 months prior to completing the onetime standardised patient questionnaire. This study started in August 2017, is ongoing and plans to enrol 500 patients in total from 50 centres across Germany. Subgroup analyses by previous therapy, modality of administration and by indication group are pre-planned.

**Results:** By November 2017, completed surveys from 142 patients were available for interim analysis. Mean age was 55 years, 61% were female

and the median duration of the disease was 6 years. The indications were rheumatoid arthritis in 63% (median disease activity score DAS28: 2.4), psoriatic arthritis in 19% (median DAS28: 2.5) and axial spondyloarthritis in 18% of patients (median BASDAI: 3.0). 68% of patients were new to bDMARD therapy. Previous therapies included conventional synthetic DMARDs (67% of patients), steroids (49%), non-steroidal anti-inflammatory drugs (43%) and bDMARDs (32%). Patient satisfaction response rates are shown in table 1.

**Abstract AB1468HPR – Table 1.** Patient-assessed satisfaction with SB4-pre-filled pen by previous treatment (Full Analysis Set)

	New to bDMARD (n=96)	Switch from syringe (n=22)	Switch from pen (n=21)	Switch from intravenous bDMARD therapy (n=2)	Total* (n=142)
General satisfaction: (very) satisfied	79 (82%)	19 (86%)	17 (81%)	2 (100%)	118 (83%)
Ease of execution: (very) simple	90 (94%)	18 (82%)	17 (81%)	2 (100%)	128 (90%)
Satisfaction with training on injection with the training pen**:	81/85 (95%)	20/21 (95%)	16/19 (84%)	2/2 (100%)	120/128 (94%)

\*Missing responses are not included in calculations; total includes one patient with unknown previous therapy.

\*\*Number of (very) satisfied patients/total number of patients who received injection training

**Conclusions:** High level of patient general satisfaction as well as satisfaction with the ease of use were reported with the etanercept biosimilar (SB4) pre-filled pen for patients who were new to bDMARDs or who had switched from other bDMARDs.

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**AB1469-HPR A STUDY TO INVESTIGATE WHETHER IF ANY BARRIERS IN ETHNIC MINORITY PATIENTS MAY IMPACT ON RESEARCH PARTICIPATION IN A DISTRICT GENERAL HOSPITAL (2011)**

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**Background:** A literature review of the current evidence suggests that research barriers exist within a diverse and ethnic population and that these barriers are often perceived to be cultural, behavioural, structural, organisational or clinical. Though a number of studies have been done showing the impact the above, these cannot be generalised at a local level. Hence, it is of vital importance that those involved in undertaking clinical studies locally are aware of the factors which may be preventing them from recruiting ethnic patients in their respective specialist area. There is a need to evaluate systems currently in place and to investigate whether factors such as attitudes, beliefs, health care professionals approach and patient experience may have an impact on recruitment.

**Objectives:** The aim of this study is to investigate whether any barriers exists within a small sample of ethnic minority patients who have been previously approached to participate in a clinical trial in a local hospital.

**Methods:** A qualitative study involving semi-structured interviews with both consultants active in research and patients with a background of inflammatory conditions invited to participate in a study locally. Purposive sampling was applied in all three groups. Participant information sheets and invitation letters was sent to all participants with a two week follow up by telephone for patients. Consent was taken from all participants, open-ended questions used during the interviews, the data collected by hand notes and then analysed using the five stages of the framework approach. Data was analysed in 3 groups:<sup>1</sup> investigators,<sup>2</sup> consented patients and<sup>3</sup> unconsented patients.

**Results:** A total of 24 patients were invited and twelve agreed to attend for individual interviews. Out of twelve investigators approached, eight responded to the invitations. Investigators' displayed positive attitudes towards recruitment, reported language and some cultural barriers along

the informed consent pathway and a gap in support systems within research. Patients from both groups reported a lack of awareness in clinical trials. Fears of study drug and a lack of trust to commit were the main themes that emerged from the unconsented group. Cultural barriers did not have an impact on the informed consent process in both groups.

**Conclusions:** This study is among the first that has been conducted in our trust and focused on main areas of qualitative research looking at patients' responses when invited to participate in a trial and complexities of recruitment from a healthcare professional perspective. The findings provide evidence of research barriers that exist within the trust perceived by investigators and patients Unfortunately, few studies have focused on various background of ethnicity within different specialties. This could be because it is difficult to carry out studies without focusing specifically on a certain area of disease or a particular group of patients. These findings can only be generalised to areas of research locally upon further exploration of these barriers, which may have a significant impact on the recruitment of ethnic minority patients.

**Disclosure of Interest:** None declared

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**AB1470-HPR BELIEFS AND SATISFACTION WITH GOLIMUMAB AS SECOND ANTI TNF-ALPHA OF PATIENTS WITH SPONDYLOARTHRITIS. GO-BEYOND**

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**Objectives:** In patients with spondyloarthritis (SpA: axial SpA or psoriatic arthritis [PsA]), treated with golimumab as second biological therapy (after failure or withdrawal of a first anti TNF- $\alpha$  drug), we describe patients' insights with regard to their beliefs and their satisfaction with golimumab therapy.

**Methods:** Patients on golimumab from GO-BEYOND, a retrospective study undergone in 20 Spanish rheumatology clinics, were requested to respond to the *Beliefs About Medicines Questionnaire* (BMQ). Statements of the BMQ include a 5-item necessity and a 5-item concern scale with Likert response options from "strongly agree" to "strongly disagree". Patients also responded to questions on their satisfaction and experience with golimumab self-injection. Descriptive data are displayed, and responses to the BMQ in axial SpA vs PsA patients were compared with the chi-square test.

**Results:** 123 patients on golimumab as second anti TNF- $\alpha$  responded (81 axial SpA and 42 PsA, mean age 49 years [SD=11], 40% women). Patients showed strong beliefs in the necessity of golimumab for the treatment of their SpA (percentages of "agree" or "strongly agree" to the necessity statements: 50%–80%), but also concerns: half the patients agreed/strongly agreed to be worried about long term effects of golimumab, and  $\approx$ 30% about becoming too dependent on the drug (table 1). Responses were similar in axial SpA and PsA patients (table 1). 111 patients declared to self-inject golimumab. Of these, 22.7% considered the experience with self-injection as very positive, 66.4% as positive, 10.0% neutral and only 0.9% unfavourable, and the use of the device very easy (37.3%), easy (57.3%), neutral (3.6%) and only 1.8% difficult. Finally 36.4% and 49.1% were very satisfied or satisfied with the interval of administration of golimumab, 11.8% were neutral and only 1.8% and 0.9% declared to be dissatisfied or very dissatisfied.



**Abstract AB1470HPR – Table 1.** Percentage of patients who responded “strongly agree” or “agree” to the BMQ statements

	All (n= 123)	Axial SpA (n= 81)	PsA (n= 42)
<b>Necessity scale</b>			
My health, at present, depends on golimumab*	72.7%	71.8%	75.0%
My life would be impossible without golimumab*	51.5%	49.3%	57.1%
Without golimumab*, I would be very ill	63.6%	60.6%	71.4%
My health, in the future, will depend on golimumab*	42.4%	46.5%	32.1%
Golimumab* protects me from becoming worse	89.7%	88.7%	85.7%
<b>Concerns scale</b>			
Having to inject golimumab* worries me	29.3%	29.6%	28.6%
I sometimes worry about the long-term effects of golimumab*	49.5%	49.3%	50.0%
Golimumab* is a mystery to me	35.7%	35.2%	37.0%
Golimumab* disrupts my life	7.1%	9.9%	0.0%
I sometimes worry about becoming too dependent on golimumab*	30.3%	32.4%	25.0%

All p-values>0.1. \*For a better understanding, the commercial name was used in the patients' questionnaire

**Conclusions:** Patients with SpA currently using golimumab as second anti TNF-alpha describe strong beliefs in the necessity of golimumab and good experience and satisfaction with self-administration. The BMQ also identified concerns that should be addressed in the clinic. The study is limited to the subset of patients still on golimumab at the study visit.

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**AB1471-HPR INVESTIGATION OF THE EFFECT OF MANUAL THERAPY AND CERVICAL STABILISATION EXERCISES ON DISABILITY, KINESIOPHOBIA, DEPRESSION AND ANXIETY IN CHRONIC NECK PAIN PATIENTS: A PILOT STUDY**

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**Background:** Neck pain is a common pain after low back pain and becomes chronic in most of the individuals (43%). Due to the severe pain experienced in chronic neck pain (CNP) individuals, the level of disability, depression and anxiety increases and kinesiophobia develops. Cervical stabilisation exercises in individuals with CNP are one of the most effective treatment methods applied recently and the main purpose is to provide training of deep cervical muscles. Manual therapy approaches such as suboccipital release and post-isometric relaxation techniques provide relaxation of the fascia and superficial muscles. These techniques are rarely applied compared to cervical stabilisation exercises and the number of studies done in the literature is very limited. The effects of these three approaches in the treatment of pain severity, disability, kinesiophobia, depression and anxiety are not known in the patients with CNP.

**Objectives:** The aim of this study is to investigate the effect of physiotherapy program consisting of suboccipital relaxation technique, post-isometric relaxation technique and cervical stabilisation exercises on pain severity, disability, kinesiophobia, depression and anxiety in individuals with CNP.

**Methods:** Ten patients who have CNP aged 18–65 years (mean age 37.11±4.26) were included in this study. Pain intensity at rest, activity and night with visual analogue scale (VAS), levels depression with Beck Depression Scale (BDS), anxiety with Beck Anxiety Scale (BAS), kinesiophobia with Tampa Kinesiophobia Scale (TKS) and disability with Neck Disability Index (NDI) were assessed. All participants in the study were included in a 10-session physiotherapy program that included suboccipital relaxation, post-isometric relaxation to the upper part of the trapezius muscle, and cervical stabilisation exercises.

**Results:** It was found that pain intensity at rest, activity and night were significantly decreased after treatment (p=0.008). Disability (p=0.008) and kinesiophobia (p=0.01) level were also significantly dropped. Depression (p=0.015) and anxiety levels (p=0.024) were statistically significantly improved after treatment.

**Conclusions:** As a result of our study, pain, depression and anxiety levels decreased, kinesiophobia and disability were improved after physiotherapy applied to individuals with CNP. The suboccipital relaxation and post-isometric relaxation techniques applied before cervical stabilisation exercises increased the adaptation to the exercise by providing relaxation of the painful and tense region in the patients. We think that the activation of the deep cervical muscles is facilitated when the tension of the superficial muscles and the fascia are relaxed. Soft tissue loosening does not

result in pain during and-exercise, which may have reduced the tendency for kinesiophobia, anxiety and depression in patients.

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**AB1472-HPR INFLAMMATORY OR RHEUMATOID ARTHRITIS PATIENTS' PERSPECTIVES ON THE EFFECT OF ARTHRITIS GLOVES ON THEIR HAND PAIN AND FUNCTION (A-GLOVES TRIAL): A QUALITATIVE STUDY**

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**Background:** Arthritis (compression) gloves are frequently provided to people with inflammatory (IA) or rheumatoid arthritis (RA) in the NHS, to help reduce swelling and alleviate hand pain by providing compression and improving circulation. However evidence for their effectiveness is limited.<sup>1</sup>

**Objectives:** Nested within a randomised controlled trial (RCT) testing the effectiveness of intervention (compression) gloves with control gloves (fitted at least one size too big) in people with RA and IA, this qualitative study aimed to explore patients' perspectives on the effect of the arthritis gloves on their hand pain and function.

**Methods:** Once randomised, participants were provided joint protection and hand exercise booklets and fitted with either the intervention or the control glove(s) by a trained occupational therapist.<sup>2</sup> Both gloves had similar thermal qualities but control gloves did not apply compression. Semi-structured interviews were conducted with 10 participants, purposively selected from each group (n=20) following 12 weeks of glove wear. Interviews were audio-recorded, transcribed and analysed by three researchers using thematic analysis with a critical realist perspective.

**Results:** Participants' perspectives on the effects of the arthritis gloves had three emergent sub-themes. These were<sup>1</sup> Usage: both groups predominantly used the gloves for activities such as wearing them outdoors to keep hands warm, night-time wear to help with sleep, and doing light domestic activities (e.g. dusting). Gloves were not used for cooking or washing-up or for personal activities of daily living (e.g. toileting, grooming) “*What didn't help as such, obviously was with washing etc. and toileting because I had to keep taking them off and putting them back on again*”.<sup>2</sup> Symptomatology: while some reported that gloves helped to keep their “*hand pain in check*” others said that gloves had no effect on their hand pain or that they'd found “*it's made them worse*”. Participants from both groups frequently mentioned the warmth element of the gloves, as a positive attribute to help with their symptoms.<sup>3</sup> Aesthetics: participants had opposing views on the appearance of the arthritis gloves. Some felt that the intervention gloves “*look a bit ugly with the seams outside*” or stated that they “*would not want to wear that colour*” but did not think they were obtrusive. Most noticeably, patients seemed to view the arthritis gloves as ordinary everyday gloves, rather than a medical device “*if it was cold I wore them outside*”.

**Conclusions:** Trial participants reported experiencing similar effects from wearing either the intervention or control gloves, with varied perspectives on whether or not gloves affected hand pain and/or function. Overall, patients did not reflect on the compressive but rather the thermal qualities of the gloves, as warmth was the main effect perceived.

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## HPR Service developments, innovation and economics in healthcare

### AB1473-HPR QUALITY OF REFERRAL LETTERS RECEIVED IN RHEUMATOLOGY

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**Background:** The referral letter is an essential tool in the relationship between Primary Care and other specialties with Rheumatology. In our area, in 2010, a computer system called SELENE was introduced at hospital level and, in Primary Care, O.M.I. was set up more than 20 years ago

**Objectives:** To assess the quality of referral letters received in the Rheumatology Unit during the first four months of 2017

**Methods:** Retrospective and descriptive study, in which referral letters received in the Rheumatology Unit between January and April 2017 were analysed. The following variables were collected: medical specialty that sent the document, computerization of the document, reference to medical history, chronic treatments, current disease, physical examination, complementary tests, presumption diagnosis, treatment for the current process, and number of reasons for consultation per document. The quality of the document was assessed using the recommendations of Irazábal and Gutiérrez modified by Morera et al, which classified them as: good, acceptable and bad (table 1).

**Abstract AB1473HPR – Table 1.** Quality of referral letters.

**Good:** It includes medical history, familiar medical history, chronic treatment, current disease, complementary tests, presumption diagnosis, differential diagnosis and reason for consultation

**Acceptable:** It includes reason for consultation and enough information about current disease, although not all those included in the previous one

**Bad:** Unreadable, without enough information to assess the current disease or absence of information

In the descriptive statistical analysis of quantitative variables, the mean and standard deviation were used. Frequencies were used to analyse qualitative variables

**Results:** 1234 referral letters were included and 90.3% were computerised. The specialties that referred patients more frequently were: Primary Care (84.7%), Traumatology (3.4%), Neurology (1.9%) and Emergency (1.6%). 14.5% of the documents included more than one reason for consultation. The variables related to the fulfilment of quality criteria in the referral letters are shown in Table 2. Regarding the quality level, 4.1% of the documents were good, 95.2% acceptable and 0.6% bad.

**Abstract AB1473HPR – Table 2.** Quality criteria in the referral letters

Reference to medical history, n (%):	242 (21.7)
Reference to chronic treatment, n (%):	67 (6)
Reference to symptoms, n (%):	1050 (94.3)
Reference to physical examination, n (%):	170 (15.3)
Reference to complementary tests, n (%):	740 (66.4)
Reference to treatment for the current process, n (%):	373 (33.5)
Reference to presumption diagnosis, n (%):	712 (64.3)

**Conclusions:** The quality of the referral letters was mostly acceptable. Therefore, there is much room to improve, especially in the sections referencing medical history, chronic treatment, physical examination and treatment for the current process

**Disclosure of Interest:** None declared

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### AB1474-HPR ARE CLINICAL PATHWAYS USEFUL IN CLINICAL PRACTICE?

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**Background:** The aim of clinical pathways is to improve the care of patients with chronic diseases, ensuring continuity of care through a better coordination and communication between Primary and Hospital Care. Even though clinical pathways have proved to be effective, their

publication and dissemination does not necessarily lead to the systematic use of them in clinical practice.

**Objectives:** To assess the fulfilment of clinical pathways in area III of Murcian Health Care System.

**Methods:** Retrospective and descriptive study in which the fulfilment of clinical pathways in musculoskeletal pathology was analysed in the Rheumatology Unit the first four months of 2017. The variables collected were: reason for consultation, waiting time for an appointment and fulfilment of clinical pathways in the following clinical processes: back pain, shoulder pain, knee pain and fibromyalgia.

In the descriptive statistical analysis of quantitative variables, the mean and standard deviation were used. Frequencies were used to analyse qualitative variables

**Results:** 1234 referral letters were received in Rheumatology during the first four months of 2017, 85.1% were mechanical pathology, 8.2% inflammatory pathology and 4.1% bone metabolism pathology. 628 were susceptible to follow the clinical pathways implemented in musculoskeletal pathology: 462 (73.56%) were back pain, 87 (13.85%) knee pain, 73 (11.62%) shoulder pain, and 6 (0.95%) fibromyalgia. The clinical pathways were fulfilled in 252 (40.12%) of the cases.

**Abstract AB1474HPR – Table 1.** Fulfilment of clinical pathways

Back pain, yes (%)	206 (44.6)
Shoulder pain, yes (%)	26 (35.6)
Knee pain, yes (%)	19 (21.1)
Fibromyalgia, yes (%)	1 (14.3)

**Conclusions:** The fulfilment of clinical pathways in musculoskeletal pathology in our health care area was carried out in less than half of the cases. Therefore, it is necessary to implement procedures to make easier their use in clinical practice

**Disclosure of Interest:** None declared

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### AB1475-HPR COST EVOLUTION OF BIOLOGICAL AGENTS FOR THE TREATMENT OF SPONDYLOARTHRITIS IN A SPANISH TERTIARY HOSPITAL: INFLUENTIAL FACTORS IN PRICE DEVELOPMENT

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**Background:** Spending on biological agents has risen dramatically in Spanish hospitals due to the drugs' high cost and the increased prevalence of spondyloarthritis.

**Objectives:** To calculate and compare the annual cost per patient with spondyloarthritis and for each biological drug according to clinical practice from 2009 to 2016 and to analyse the factors that influence consumer pricing, such as biological therapy optimisation (by monitoring drug and anti-drug antibody serum levels), the use of tumour necrosis factor inhibitor biosimilars, and drug discounts, refunds, and rebates.

**Methods:** We conducted a retrospective observational study that analysed patient demographic parameters, disease activity, and annual cost per patient and per drug and determined the economic factors that affected on consumer pricing.

**Results:** A total of 129, 215, and 224 patients were treated in 2009, 2013, and 2016, respectively; 77 (59.69%), 133 (61.86%) and 139 (62.05%), respectively, were men aged 46.04 (±12.57), 47.76 (±12.35) and 48.27 (±13.49) years, respectively. Nonstatistically significant differences were observed.

The annual cost per patient decreased during the study period (from €11.604 in 2009, €8.513 to €7.464 in 2016). There was an increase in the number of marketed biological drugs and in the total savings per drug, with discounts and bonus units in 2016 reaching 12%–18% for etanercept, adalimumab, certolizumab, and golimumab and up to 25% for the recently released secukinumab, while rebates for biosimilar infliximab reached 69% in 2016. Biological therapy optimisation reached 47.5% in 2016, which resulted in cost savings of 23.89%, in addition to the savings from refunds and rebates (11.06%) in 2016.

**Conclusions:** The resulting treatments after the rebates, invoice discounts, and optimizations were more cost-effective, leading to a significant decrease in the annual cost per patient and an overall reduction in expenditure for these drugs.

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**Disclosure of Interest:** None declared

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#### AB1476-HPR EFFECTS OF WEARABLE TECHNOLOGY AS VIRTUAL REHABILITATION ON FUNCTIONAL OUTCOMES IN PATIENTS WITH ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION

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**Background:** Virtual rehabilitation systems play an increasing role in rehabilitation. They provide an interactive environment and increased motivation for patients during the session.<sup>1</sup> In recent years, intervention methods based on virtual reality have been studied. However, existing studies are limited because most of them focused on the balance ability of the elderly or studied in stroke patients with same systems.<sup>2</sup> Thus, it is necessary to investigate the effects of virtual rehabilitation in patients with Anterior Cruciate Ligament (ACL) Reconstruction.

**Objectives:** The purpose of this study was to investigate the effects of a wearable technology as virtual rehabilitation which provides visual and auditory stimulus aimed for educating and controlling the joint on proprioception, postural stability and fear of re-injury in patients with ACL reconstruction.



Abstract AB1476-HPR – Figure 1

**Methods:** Nineteen patients (age=28.47±6.18 years, height=176.31±6.06 cm, weight=79.47±14.38 kg) with ACL reconstruction were participated in this study. In addition to conventional physiotherapy, a virtual rehabilitation treatment applied with visual and auditory stimulus three times in a week for 8 weeks. Knee proprioception, postural stability and fear of re-injury were measured with Biodex System Pro 4 Isokinetic Dynamometer, Pedalo Sensamove System, Tampa Kinesiophobia Score, respectively.

**Results:** There were statistically significant improvements in measures of proprioception (p=0.003), postural stability (p=0.001), and fear of re-injury (p=0.001) between pre- and post – treatment.

**Conclusions:** According to the results, wearable technology as virtual rehabilitation may be beneficial on proprioception, postural stability, and fear of re-injury to treat patients with anterior cruciate ligament reconstruction. We conclude that devices used as wearable technologies should be used as treatment modalities in clinical services because of providing feedback, easy to carry and interactive treatment.

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**Acknowledgements:** This study was supported by Marmara University, Scientific Research Research Projects Committee (Project Number: SAG-C-DRP-200716–0374) and TÜBİTAK, The Scientific and Technological Research Council of Turkey (Project Number: 115E351).

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#### AB1477-HPR ADHERENCE TO RCOPHTH GUIDELINES IN MONITORING OF HYDROXYCHLOROQUINE BY RHEUMATOLOGISTS AT LNWH CMH

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**Background:** The Royal College of Ophthalmologists (RCOPHTH) published in 2017 revised recommendations regarding screening for hydroxychloroquine (HCQ) toxicity. Recent data reported the prevalence of retinopathy to be around 7.5% and depending on dose and duration can rise to 20%–50% after 20 years of therapy. Much higher than the 0.5% reported previously in the 2009 guidelines. Risk is increased in patients taking more than 5 mg/kg/day, and those with renal dysfunction, pre-existing retinopathy or also taking tamoxifen. Retinopathy appears as damage to the photoreceptors, followed by degeneration of the retinal pigment epithelium (RPE). This can produce visual loss and a "Bull's eye maculopathy".

Current guidelines state patients looking to take HCQ long term should have a baseline screening (10–2 Humphrey visual test) in a hospital eye department, and then be referred for annual screening after 5 years of therapy. Dosage should ideally be kept ≤5 mg/kg/day.

Previous guidelines recommend a maximum dose of ≤6.5 mg/kg/day, and baseline optometrist review. Referral to ophthalmologist only if a visual impairment or eye disease is detected at the baseline assessment or the patient notices reduced vision whilst on treatment. Long term HCQ patients, were advised to agree and individual screening arrangement with the local ophthalmologist.

**Objectives:** This single point of care audit was to assess real world practice at Central Middlesex Hospital against the new 2017 guidance as a gold standard.

**Methods:** HCQ questionnaires were collected from patients attending regular appointments over one month October–November and recorded:

- 1) date commenced HCQ,
- 2) est. total dose,
- 3) weight and
- 4) last retinal screen;

Hospital EPR database was used to confirm or assist documentation of therapy data.

**Results:** In one calendar month 152 of 414 patients were prescribed HCQ.

94/152 of the patients had been on HCQ for >5 years.

63/152 patients were high risk with doses of >5 mg/kg/day.

55/152 patients had either failed to attend a baseline screening, or had no record of having had a baseline screen.



Of the 21 patients that had started HCQ after the introduction of the new guidelines (2017); only 5 had failed to have a baseline hospital screen (3/5 instead had optometrist/high street screen instead). No cases of HCQ related retinopathy had been reported.

**Conclusions:** Real world OHC retinal screening was poor compared to new Guidance. These figures imply a huge medico-legal responsibility for the previously considered rare risk of retinal damage from OHQ. The logistics of the workload in Eye Clinics will necessitate local solutions including nurse screening clinics and closer monitoring and documentation of outcomes. This rare but serious complication of a very well tolerated and effective agent will not come at a cheap price today. A repeat audit following 12 months of an agreed screening policy is recommended.

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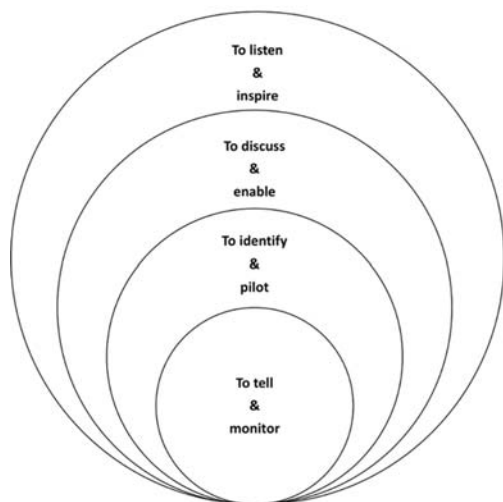
## HPR Professional education, training and competencies

### AB1478-HPR PROMOTING EXERCISE IN RHEUMATIC DISEASES: PHYSICAL THERAPISTS' UNDERSTANDING

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**Background:** Physical therapists have unique expertise in planning, prescribing and supporting exercise programs for patients with chronic diseases. Promoting exercise can be a challenge and include a range of strategies, but descriptions of physical therapists' experiences within the field of rheumatology are limited.

**Objectives:** The purpose of this study was to explore and describe ways of understanding exercise promotion among physical therapists working with patients having rheumatic diseases.



Abstract AB1478-HPR – Figure 1

**Methods:** A phenomenographic approach was used to analyse semi-structured interviews with 25 physical therapists, working primarily within the

field of rheumatology, from eight different physical therapy departments at hospitals in various cities of Sweden.

**Results:** Four categories related to the promotion of exercise were identified: *to tell and monitor; to identify and pilot; to discuss and enable; and to listen and inspire*. Key aspects were responsibility, setting and supervision, tools to support change and the role as an educator. The findings are interpreted as a hierarchically organised structure, where the understandings of the PTs differ in respect to comprehensiveness regarding some aspects of interaction and collaboration with the patients.

**Conclusions:** Physical therapists working with patients having rheumatic diseases understand exercise promotion in different ways and these understandings differ in respect to comprehensiveness, which might lead to unequal promotion. A more comprehensive repertoire would probably make physical therapists more prepared to meet patients' needs for different strategies in the adoption and maintenance of exercise behaviours.

**Disclosure of Interest:** None declared

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### AB1479-HPR MULTIFACETED INTERVENTION TO IMPROVE MEDICATION UNDERSTANDING AND COMPLIANCE AMONG PATIENTS WITH AUTOIMMUNE INFLAMMATORY RHEUMATIC DISEASES

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**Background:** Non-compliance with treatment in patients with autoimmune inflammatory rheumatic diseases are directly associated with relapse, deformities and higher treatment cost. Many of times it can be related to poor understanding of complex drug regimen. Consistent reports of sub-optimal treatment adherence among patients with autoimmune inflammatory rheumatic disease underscore the importance of understanding how adherence can be promoted and supported.

**Objectives:** To evaluate the efficacy of various methods of drug explanation to AIRD patients in rheumatology OPD.

**Methods:** It is a retrospective study of 100 DMARD naive first visit patients in rheumatology OPD. Demographic and clinical information were noted in pre-designed performa. After prescription of DMARDs regimen by rheumatologists, various methods are used to explain the advised prescription such as using permanent markers on medication strips, making envelopes, using different medication performa in their local language, as well as counselling regarding importance of medication; done by rheumatology nurse. Adherence rate and reasons of non adherence was measured by different methods like interview, pill counts, review of prescription on their routine follow up visits.

**Results:** 1. 79.8% of patients fully understood and had adherence with their prescribed medication.

2. 20.2% were non-adherent with the prescribed treatment, varying from occasional to complete failure. The factors for non-adherence were identified.

- 25% patients stopped when no symptoms.
- 22.5% got influenced by alternative therapy.
- 20% family pressure and financial constrains.
- 12% of myths about side effects of medication.
- 15% lost follow up.
- 5% had doubts could not understood properly.

On stactical analysis of all methods of drug explanation, use of permanent marker on medicine strips were found to be most effective.

**Conclusions:** As per results non-adherence to treatment due to poor understanding of drug regimen is very low. But another factors were identified which have influence over adherence rate. In a busy OPD a single sitting counselling is not adequate. To summarise patients need more intensified and focused counselling to improve adherence.

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**People with Arthritis and Rheumatism in Europe  
Abstracts**



## Poster Presentations

PARE0001

### #DOESNTSHOWDOESNTEXIST/#SYNSINTEFINNSINTE – AN AWARENESS CAMPAIGN FOR PUBLIC TRANSPORT BY SWEDISH NATIONAL ORGANIZATION FOR YOUNG RHEUMATICS

K. Nordlund, M. Beermann. *Swedish National Organization for Young Rheumatics, Stockholm, Sweden*

**Background:** "Rheumatism amongst young people, is that really a thing?" "Isn't rheumatism something that only old people have?" "You seem so happy and so active, surely you can't be in pain?" These are all questions that young people with rheumatism have to listen to, and answer every day. Yes, it's possible to have rheumatism even as a young person, and to be in pain, even though we're not letting it show. We know adjustment is possible, and that we can live our life to the fullest and follow our dreams, despite rheumatism. But sometimes it demands some extra understanding from the people around us. That's what we wanted to recognize, for the second year in a row, but with another approach, and created a campaign together with AbbVie.

**Objectives:** It can be hard to understand and fully grasp something you can't see, something that is invisible. But as young people with rheumatism, we have to live and deal with our swollen joints, with the pain and the fatigue, and with the side effects of our medication. None of which should be questioned. We recognized that this was an issue for most people with rheumatism, especially young people, and especially in the public transport. Therefore, we wanted to start a conversation about that we, young people with rheumatism that doesn't show, can also need to sit down at the priority seats. The main purpose with our campaign was to acknowledge the fact that you can't always tell whether or not a person has a diagnosis, or is in pain. We also wanted to show young people with rheumatism that they are not alone in their situation.

**Methods:** We wanted to make a quiz. Each pair of person with and without rheumatism in the campaign is presented in a photo taken on a bus next to each other with a quiz question. For example: "Who of us needs to sit on the bus so we can hang out in the skate park this afternoon?" The whole idea of the quiz is to make people realize that it is impossible to see if a person needs to sit on the bus or not, that you have to trust us when we asks for a seat. Every answer is put together with the person's story about their passion in life and what it's like to live and deal with an invisible disability in public transport. The quiz was released on October 9th 2017, together with a new decal for public transport that all of our members helped us put on buses and trains all over Sweden, pins to wear all week for all our members, debate articles in local and national papers, interviews in radio and television, letters and decals to all public transport companies, and a social media campaign with photo and personal story each day. People were also told to share their own stories under the hashtag #synsintefinnsinte

**Results:** The campaign ended up being our organization's most successful campaign to this date, we reached over 4.5 million people – more than we could ever dream of. The campaign had more likes and shares on both Facebook and Instagram than any of our other campaigns has had so far. The debate articles in local and national papers were really important for the campaign and started a lot of discussions, debate and awareness. The photos combined with the personal stories make a powerful statement. We managed to show that young people with rheumatism some days also need access to the priority seats and we look forward to the conversation continuing on at #synsintefinnsinte.



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PARE0002

### ADHERENCE TO THERAPY AND PATIENTS ENGAGEMENT IN ITALY: A CLOSE LINK

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**Background:** In the last years ANMAR Italia and the federated Regional Association worked hard to educate people with Rheumatic diseases (RMDs) to an appropriate adherence to the therapy prescribed, as the Mosaico project confirmed that even patients in bio-technological therapies reveal unwillingness to assume their drugs within the schedule prescribed by the rheumatologist (timing and doses).

"ANMAR we care", study by the Italian Association of patients with Rheumatic diseases (ANMAR) in 2017 thanks to an unrestricted grant from ABBVIE and the precious collaboration of the Engage Minds Hub Research Center of Università Cattolica del Sacro Cuore di Milano directed by prof. Guendalina Graffigna, intended to analyze the problem again after the campaigns acted in the last two years and to link adherence to therapies with the degree of patient engagement.

**Objectives:** to verify the percentage of adherent patients and their degree of adherence to the therapy.

To appraise the relationship among adherence and engagement of people with rheumatic diseases.

**Methods:** in the study we administered to patients a specifically pursued questionnaire containing a fair number of questions on adherence to therapies.

This sub-analysis was made using the answers to those questions and data have been interpolated with those related to the level of engagement of the patients.

**Results:** overall data confirm that in Italy also in 2017 the percentage of people with RMDs adherent to therapies settles in dissatisfying degrees (54%) and that such includes patients partially adherent.

Looking at the relationship within adherence and engagement, if divided in the four groups anticipated by the PHE Model the percentage are: Blackout (cognitive blindness, deny, freezing) 47%, Arousal (superficial knowledge, alert, behavioral disorganization) 46%, Adhesion (cognitive adhesion, acceptance, formal adherence) 61%, Eudaimonic Project (sense making, elaboration, situated practices) 78%.

Notice that patients with Psoriatic Arthritis are the most adherent, followed by those with Fibromyalgia, Spondylitis and finally with Rheumatoid Arthritis.

**Conclusions:** this analysis highlights that the information and awareness campaigns made in the last years were useful, but results are still far away from the optimum.

As we expected, the engagement degree hardly affects the adherence process, but totally unexpected is that patients in "Arousal" are more confused and less adherent than those in "Blackout".

**Disclosure of Interest:** None declared

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PARE0003

### PROVIDING PATIENT AND FAMILY EDUCATION AND SUPPORT FOR CHILDREN WITH RHEUMATIC DISEASES AND THEIR FAMILIES: CASSIE AND FRIENDS ANNUAL FAMILY DAY IN BC

J. Wilson<sup>1</sup>, L. Tucker<sup>2</sup>, on behalf of Tucker, Petty, Setton, Houghton, Morishita, Guzman, Brown, Green, Tekano, Davidson, Best, Eccles, Cabral.. <sup>1</sup>Executive Director, *Cassie and Friends Society for Children with Juvenile Arthritis and other rheumatic diseases*; <sup>2</sup>*Pediatric Rheumatology, BC Children's Hospital, Vancouver, Canada*

**Background:** Family Day, an annual patient education event starting in 2009, is organized and funded by Cassie and Friends, a registered BC charity dedicated to transforming the lives of children with rheumatic diseases and their families. It is a full day, multi-track conference held outside the hospital environment, organized collaboratively by the pediatric rheumatology team members at BC Children's Hospital and the Cassie and Friends' volunteer conference committee.

**Objectives:** To describe the growth and impact of an annual Family Day event on children with rheumatic diseases and their families in BC.

**Methods:** The program includes lectures, round table discussions, and patient panels for parents and caregivers, with both age-related recreational and educational activities for children and youth (i.e. peer to peer support). Content and format of the program is informed annually by feedback from previous Family Days and advice from pediatric rheumatology team members. Formal feedback from attendees (parents) is provided by a post-event survey.

**Results:** Registration has increased annually from just a handful of families in 2009 to 141 attendees in 2015, and 372 attendees in 2017( with a waitlist). In 2017, attendees were 81 children and youth with rheumatic diseases, 68 siblings, and 150 parents and caregivers. A total of 72 speakers and volunteers

participated. 186 participants had attended Family Day the previous year; 148 participants were first time attendees. Families came from 29 communities throughout British Columbia. 59% of attendees completed the post-event survey. The event was rated as very good or excellent by 98% of respondents, with most stating they would recommend Family Day to other families, and planned to attend the event next year. Parents enjoyed opportunities to meet other parents and health professionals in small interactive groups, and asked for more actionable strategies to help them with their children. The post-meeting questionnaire identified what families perceived as their greatest challenges in dealing with their child's rheumatic disease: day-to-day family life, pain, well-being, school, medications and treatments, and fear.

Please also see our Family Day video with kids and teens sharing what the day means to them: <https://vimeo.com/234426339>



**Conclusions:** A family-centered interactive educational and recreational day offers the opportunity for peer-to-peer connections, education and support for families of children, and youth with rheumatic diseases, and promotes the formation of a strong community addressing family and child needs.

**Disclosure of Interest:** None declared

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#### PARE0004 LET'S MOVE WITH ARTHRITIS! – NORDIC WALKING FOR PEOPLE WITH RMDs

*P. Balazova, J. Dobsovicova Cernakova. Slovak League Against Rheumatism, Piestany, Slovakia*

**Background:** Slovak League against Rheumatism (SLAR) identified a need among its members to provide support when it comes to physical exercise and rheumatic diseases. Nordic Walking is fitness walking with specially designed poles. It uses 90% of the skeletal muscles. Nordic Walking is ideal for neck, shoulder and back problems while it also reduces pressure on knees and joints. Poles propel the walker along, making it easier to move faster than normal without feeling the effort. With the cooperation with the Slovak Nordic Walking Association, SLAR provides trainings in local branches and encourages individuals to do physical activities while monitoring their progress.

**Objectives:** The aim of the project Let's Move with Arthritis! is to improve treatment, prevention and rehabilitation of RMDs, to support healthy lifestyle and thus lower the impact of RMDs on individuals and society through a structured training on the correct Nordic Walking techniques.

**Methods:** The project Let's Move with Arthritis! started in September 2017 when SLAR obtained 5 pairs of Nordic Walking poles for each of our 17 local branches and clubs. SLAR provided trainings with the cooperation of the Slovak Nordic Walking Association. Individuals were tracking their progress using excel sheets. The goal was to achieve 1 000 000 steps for people with RMDs by 14 October when SLAR held its World Arthritis Day event. Steps of all individuals in local branches were summed up and the goal was not only achieved, it was overcome.

**Results:** A total of 506 individuals participated in the Nordic Walking trainings from September until 14 October 2017. They walked 1 144 km and made 3 386 517 steps. Each of the participating branches provided SLAR with a final report that showed that the cooperation with the instructors of the Slovak Nordic Walking Association was excellent. The activities showed that people with RMDs walked with enthusiasm. The local branch in Kosice made the most steps – over 800 000. Participants were keen on continuing Nordic Walking trainings also without instructors and beyond October 2017.

**Conclusions:** The project Let's Move with Arthritis! proves that even people affected by RMDs are able to do physical exercise, in our case Nordic Walking. Importantly, the project provided simplified and step-by-step instructions to Nordic Walking with the aid of the Slovak Nordic Walking Association. The instructors provided individuals with warm-up techniques, correct Nordic Walking techniques and cool-down techniques after each session. The aim of the project was to reach at least 1 000 000 steps for people with RMDs but it also proved that people with RMDs benefit from physical activities like Nordic Walking when using correct techniques. It can improve their quality of life, increase mobility, improve coordination and strengthen the ligaments. Each participant expressed the will to continue with the project beyond October 2017.

**Acknowledgements:** We would like to acknowledge the Slovak Nordic Walking Association for their guidance and support.

**Disclosure of Interest:** None declared

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#### PARE0005 DEVELOPMENT & DISSEMINATION OF A RESOURCE ABOUT METHOTREXATE USE FOR AND BY PATIENTS WITH INFLAMMATORY ARTHRITIS

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**Background:** In managing inflammatory arthritis, methotrexate is often one of the first therapies prescribed.<sup>1,2</sup> Methotrexate is a therapy used long-term and often in combination with other medications.<sup>3,4</sup> As people who live with arthritis, we know that for a variety reasons, people do not use methotrexate as prescribed by their healthcare provider and as a result, they may not experience its maximum benefits.

**Objectives:** We set out to build and disseminate a resource about methotrexate and its use from the patient perspective. It is our aim to help patients find ways to deal with taking their methotrexate by sharing other patients' experiences and tips with them.

**Methods:** We surveyed people who live with arthritis about their attitudes and coping mechanisms related to taking methotrexate, seeking tips and tricks to share. A Board member/project manager created an online survey that was medically reviewed (English, French) and collected responses (circulated via newsletter, social media, patient organizations). Following the analysis of survey responses, a resource was developed and reviewed by 2 rheumatologists and a pharmacist. The resource was disseminated using similar methods to the survey.

**Results:** The survey response was global (363 responses, 77% with rheumatoid arthritis, 22% with psoriatic arthritis, 63% in Canada). Almost half of the survey respondents indicated they "do not like taking methotrexate, but it helps me manage my arthritis." Along with 5 top adaptations made to better tolerate taking methotrexate, a major gap was that 80% of respondents indicated not talking to their physician or pharmacist about finding an appropriate solution with respect to taking methotrexate. A web-based resource was developed and its dissemination plan are currently being completed and will be presented.

**Conclusions:** CAPA created a web-based, medically reviewed resource about taking methotrexate informed by patients' experiences who live with inflammatory arthritis. This resource aims to help people better manage taking methotrexate and is being disseminated.

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**PARE0006** **A SUMMARY OF KEY FINDINGS FROM THE SJÖGREN'S SYNDROME FOUNDATION'S NATIONAL PATIENT SURVEY RELATED TO TREATMENTS AND MEDICATIONS USED**

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**Background:** Sjögren's is a systemic autoimmune disease that affects the entire body. The purpose of this major national patient survey was to gain an understanding from adults who have been diagnosed with Sjögren's about the impact of the disease on their quality of life, including information on the treatments and medications used to manage the disease.

**Methods:** The Sjögren's Syndrome Foundation (SSF) conducted the *Living with Sjögren's* survey between May 11 and July 11, 2016. Participants were recruited by Harris Poll from a pool of 9,252 active SSF patient members. The survey was conducted among adults aged 18 years or older who reported having been clinically diagnosed with Sjögren's by a physician or other medical professional. The survey asked closed-ended questions about patient experiences with Sjögren's and the impact it has on their quality of life.

**Results:** There were 3,072 survey responses (33% response rate), 2,963 of which were included in the analyses. Survey respondents were 96% female and 4% male; 32% were aged 60 years or less. On average, respondents reported using 8.8 medications and treatments to help manage their Sjögren's symptoms, with an average of more than four prescription medications and treatments. When comparing patients living with Sjögren's between 0–4 years and 5–9 years, respondents in the latter group reported using slightly more treatments, on average (8.7), compared to those living with Sjögren's for a shorter period (8.2 mean). Nearly all respondents (97%) reported using eye drops, artificial tears, or non-prescription eye ointments. Other medications reportedly used by a majority of respondents include ibuprofen or other anti-inflammatory agents (81%), disease-modifying anti-rheumatic drugs (DMARDs) (67%), over-the-counter or prescription fluoride (67%), and corticosteroids (62%). Notably, patients 60 years and younger were significantly more likely than patients older than 60 years to have used health food supplements or remedies (90% vs. 87%), exercise (88% vs. 83%), and alternative therapies (70% vs. 58%) in attempt to treat their Sjögren's. Nearly all respondents (96%) indicated they wished that additional treatments for Sjögren's were available. Specifically, respondents indicated a need for new treatments for fatigue (63%), brain fog/forgetfulness (53%), sleep problems (51%), joint pain or swelling (48%) and muscle pain (43%).

**Conclusions:** Patients reported relying on a large number and variety of treatments to manage their Sjögren's as well as the need for new treatment options to treat the various manifestations of the disease. The findings from this survey will help to inform and support future SSF efforts to increase public and professional awareness of Sjögren's and encourage research into new treatments and a cure.

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**PARE0007** **FAMILY DAY BY THE SWISS LEAGUE AGAINST RHEUMATISM: A NETWORKING EVENT FOR CHILDREN AFFECTED BY JIA AND THEIR FAMILIES**

M. Roffler, V. Krafft. *Swiss League Against Rheumatism, Zurich, Switzerland*

**Background:** In Switzerland 0,7 out of 1'000 children is affected by juvenile idiopathic arthritis (JIA). The incidence of JIA is 11:100'000 (1). The families affected by JIA are spread over three different language regions (the German, French and Italian regions). It is difficult for these families to get in touch with other affected

families since there is no support group for JIA. A support group has never been established due to the uneven distribution in Switzerland.

**Objectives:** The aim is to offer continuing education for parents of affected children concerning their chronic disease, as well as their dealing with the illness as a family. Furthermore parents and children shall attain the opportunity to exchange information about their experiences and problems with peers in an informal setting.

**Methods:** The Swiss League Against Rheumatism has established the so-called "Family Day" (German: Familientag) which features a program for affected children/youths and their siblings as well as a separate program for their parents on the same day. In order to enable families from all Swiss language regions to participate in the "Family Day", it takes place separately in German and French in both language regions. Since most Italian speaking families in Switzerland either speak German or French, the "Family Day" is equally open to them. The Swiss League Against Rheumatism collaborates with the task group "Paediatric Rheumatology Switzerland" in order to develop relevant contents. The program for the parents aims at imparting medical therapeutic knowledge about their child's disease. Several additional main topics (e.g. uveitis, developmental paediatrics) are chosen and presented by certified experts. All are made in layman language and explain medical terms thoroughly. The parents additionally get the opportunity for formal and informal exchange within their group. The children and youth program (0–16 yrs.) is dedicated to a specific non-medical topic (e.g. magic tricks). The children are divided into several age-specific subgroups and are assisted by staff from the Swiss League Against Rheumatism. Teenagers (11–16 yrs.) may attend a specialized program during half a day.

The "Family Days" are easily financed by foundation endowments.

**Results:** From 2011 to 2017 329 families (1157 individuals) participated in the "Family Day", of which 27% were in the French-speaking part of Switzerland. For participating parents this event became essential in order to educate themselves concerning their child's disease and to exchange experiences with other affected families. For most families the "Family Day" has become a fixed event in their yearly calendar. Many families participate on a regular basis for several years.

**Conclusions:** The "Family Day" has been taking place for 7 years and remains an objective for the future. Demand from parents of affected children continues to be strong and continues to increase. Since support groups have not yet been possible to implement due to demographics, this one-day-event remains a unique resource for affected families.

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**Disclosure of Interest:** None declared

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**PARE0008** **SURVEY RESULTS FROM A NATIONWIDE ONLINE AWARENESS CAMPAIGN SUGGEST A CLEAR DIFFERENCE IN TREATMENT AND PERCEPTION OF QUALITY OF HEALTHCARE FOR PATIENTS DIAGNOSED WITH PSORIASIS ARTHRITIS, PSA, VERSUS PATIENTS WITH SYMPTOMS SIMILAR TO PSORIASIS ARTHRITIS I.E. PSORIASIS AND JOINT PAIN**

N. Unesi, E.-M. Dufva, L. Håkansson. *Swedish Rheumatism Association, Stockholm, Sweden*

**Background:** Psoriasis arthritis (PsA) is a chronic inflammatory joint disease closely linked to psoriasis in the skin. The need for increased knowledge of PsA is extensive in both the public and in healthcare in Sweden. For that reason Swedish Rheumatism Association, Swedish Psoriasis Association and health portal company NetDoktor, with support from Novartis, initiated a web-based awareness campaign, which included a survey, in April 2017.

On December 17, approximately 12,500 people, of which about 4,000 with the diagnosis PsA and 8,500 with psoriasis and joint pain, had taken part of the material. Of these, approximately 2,400 people participated fully and provided detailed information on how they view their disease and the care they are offered.

**Objectives:** Raise awareness and educate about to PsA aimed specifically to people with PsA or with symptoms consistent with the diagnosis – but also relatives, healthcare professionals and the interested public.

**Methods:** The awareness campaign consisted of five lessons that provided participants with increased knowledge about PsA, and a survey about their experience of healthcare. The survey gave us a foundation to address the deficiencies in healthcare, and in patient needs. The lessons highlighted the following issues: background, causes, symptoms, comorbidity, diagnostics, drug treatment and prognosis.

**Results:** The average waiting time for a diagnosis among the survey participants was 3,5 years. Every fourth person had waited 5 years or more, and over 10 percent waited more than 10 years for a diagnosis. The survey showed remarkable



differences in life quality between people who have a diagnosis and people who do not have a PsA diagnosis or who have not yet received one:

### 1. Many are without diagnosis and treatment

High proportion of undiagnosed patients have symptoms indicating PsA. Many have suffered a long time from joint related pain and sought out treatment from a number of doctors.

3 out of 4 with joint pain have negative or very negative experiences of healthcare related to their joint pain. The survey participants indicated that they suffer from waiting a long time for healthcare.

### 2. Major differences in perception of care and treatment

Statistics on overall satisfaction with healthcare show remarkable differences that can be linked to getting a diagnosis. People with joint pain but without a PsA diagnosis indicate a great dissatisfaction with the care they receive. People who have been diagnosed with PsA are overall quite satisfied with the care and treatment they receive after getting a diagnosis.

### 3. High use of opiate remedies for pain

The use of pain reliever opiate drugs is remarkably high in the group with joint pain but without the diagnosis of PsA. Also very high use of non-steroidal anti-inflammatory drugs, NSAIDs.

**Conclusions:** Given that the prevalence for psoriasis arthritis in Sweden is between 10 000 -30 000 people, it is likely that the awareness campaign reached a considerable number of people with the diagnosis or with symptoms similar to it. The longer the patient goes without adequate healthcare the worse the disease gets. If untreated it could lead to permanent joint damage. Early diagnosis and treatment are important to slow down the disease.

**References:** www.HarDupSoriasisarthritis.se

**Disclosure of Interest:** None declared

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## PARE0009 CANADIAN ARTHRITIS PATIENT ALLIANCE: UNDERSTANDING MEMBER PROFILES AND NEEDS

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**Background:** Established in 2002, the Canadian Arthritis Patient Alliance (CAPA) is a grass-roots, patient-driven, independent, national organization with members across Canada. CAPA believes the first expert on arthritis is the individual who has the disease. We assist members to become advocates not only for themselves but all people with arthritis. CAPA works with other organizations, representatives from all levels of government, and researchers to ensure the patient voice is both heard and present. We communicate the latest news on health policy developments, research, technology and emerging issues relevant to members through our newsletter, website, Facebook, Twitter and YouTube channels. CAPA welcomes all of those who support CAPA's goals, especially Canadians with arthritis, to become members.

**Objectives:** CAPA underwent a strategic renewal in 2013, re-establishing its focus and operations. Since that time, CAPA has produced an annual strategic plan, and reported on yearly achievements in relation to the plan. In 2017, CAPA decided to conduct a membership survey.

The survey was designed with three objectives in mind: (1) Understand our membership's profile and interests, (2) Understand member awareness and support for CAPA projects and strategic direction, and (3) Seek membership input on CAPA's website.

**Methods:** A survey was created using Survey Monkey (in both English and French, Canada's official languages) and sent to members. Results of the survey were sent to the members and made available on CAPA's website ([http://www.arthritispatient.ca/files/5315/1128/7211/CAPA\\_Survey\\_-\\_Spring\\_2017.pdf](http://www.arthritispatient.ca/files/5315/1128/7211/CAPA_Survey_-_Spring_2017.pdf)). As an additional incentive, two C\$50 VISA gift cards were drawn from among Canadian respondents. The survey was open from May 1 to 21, 2017.

**Results:** The response rate to the survey was 23% (that is, 85 respondents out of a possible 369). Of those who responded, the majority were women, with over 75% aged 55 years of age or over. Respondents came from all across Canada. Members generally came to CAPA to find information and stay abreast of events in the arthritis community; only a small portion, 17%, joined to become more involved. Members supported CAPA's strategic direction, which aligned with their stated interests.

Members also provided feedback on the website. For the most part, members appreciated the information, providing some recommendations moving forward, including supporting a mobile friendly website (i.e., responsive design).

**Conclusions:** CAPA is using the information from this membership survey as confirmation of its strategic direction moving forward; continued focus will be on providing information, connecting with key stakeholders in the arthritis community (Canadian and abroad), and undertaking focused projects as they arise.

Member feedback has been critical in guiding the website redevelopment, which is currently underway. We expect it to be complete in early summer 2018.

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**Disclosure of Interest:** None declared

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## PARE0010 NATURALLY HEALING THE CHRONIC PAIN AND HEALTH MAINTENANCE

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**Background:** Everyday life is not easy for people with RMDs. Chronic Pain is the "roommate" usually on patient's life. Patients usually try to find other ways of confronting their symptoms, beyond drugs or other classic options such as physiotherapy. One of these ways that often people with RMD's are discussing is the treatment with Natural Healing Sources based on water which is used in various cultures from ancient times. Cyprus League Against Rheumatism gives these opportunities to the members every year; by organizing excursions in Natural healing resorts at least two times per year.

**Objectives:** The aim of organizing therapeutic trips to therapeutic treatment centers – Natural Healing Resorts, was to give members the opportunity to get acquainted with and experience this mode of therapy, with team approached on rehabilitation treatments, for patients who cannot afford to visit as individuals because of the cost or to travel as individuals tourists and they need extra services and attention. In addition to therapeutic qualities, it would also give psycho-social affiliation to people who would participate, which CYPLAR gives a lot of insight into all of its programs

**Methods:** In 2012 CYPLAR approach the Ayioi Anaryiroti Natural Healing Resort & Spa which is situated in Miliou, a small village in Paphos area, and their thermal waters are from ancient times, organized the first trip to this healing Resort.

In 2014 CYPLAR approached a Cypriot travel agency, and asked for help to organize a trip in Sandanski, in Bulgaria, as after a research find that it is a very good and famous thermal water springs and not too far from Cyprus so was easy to access and not too expensive.

**Results:** The trip to Ayioi Anaryiroti Natural healing Resort & Spa was very successful so every year at least one time is organized a trip for a weekend. The difference for the people with RMDs participated in this trip instead of going alone, is that CYPLAR is having better rates for members for this special weekend, and also the therapeutic treatments during this weekend are targeted on RMD's. Another ad is that people are coming close to each other, bonding, and sharing their experiences. Every time around 20 people with RMD's are participating on these trips. CYPLAR members have all year around discount. Future Goal is to be organized twice times per year.

The trip to Sandanski is organized every year in July (3 times until now). It is a ten days program and includes examination, target treatments based on each participant and his/her needs, also include sightseeing tours in the area, entertainment dinners, and many other amenities. It is a very succeed therapeutic excursion that 40 people are participating and has a lot of good results. CYPLAR conducted a survey among the participant of the last trip in July 2017 and the results are very encouragingly to continue and have these excursions for more and more years. At the question "Do you want to go again in Sandanski with Cyplar?" The answer was **Yes** for the **95%** of the participants. Results showed also the need for people with RMDs to have this kind of therapies in their life and the beneficial effects on their health status.

**Conclusions:** Patients with RMD's need these types of therapy for their body health but also for their psychosocial improvement. CYPLAR will continue to support the members with these two excursions but also is trying to find new resorts to enrich the program and give more opportunities for members.

**References:** Survey – Participants Sandanski 2017 -CYPLAR

**Disclosure of Interest:** None declared

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## PARE0011 FUNKA UTAN SKAM TO FUNCTION WITHOUT SHAME

T. Diaq. The Swedish Rheumatism Association, The Swedish Rheumatism Association, Stockholm, Sweden

**Background:** Introduction:

Kids, youngsters and adults with an immigrant background are more vulnerable in the new country of arrival. It is quite hard to learn a new language and the rules and regulation in the new country.

In several cultures, people with a visible or invisible disability can experience guilt and Shame because of their diagnoses. Due to the cultural background, most of the time the families are also feeling the same. This feeling could be conscious or unconscious due to the cultural background.

Therefor did the Swedish National Assyrian Organization (SNAO) take the initiative to start a knowledge-sharing project together with the Swedish Rheumatism Association and the Swedish Neuro-Association to inform and educate the kids and their parents with the Assyrian background.

**Objectives:** The aim of this project is to empower the persons and families suffering of an RMD or/and neurological disease among the immigrants from Syria and to break barriers within the immigran's society as well as saving on the national welfare system.

**Results:** To achieve such a project the SNAO applied for funds from the Swedish General Inheritance fund nad worked closely with the Swedish Rheumatism Association as well as the Swedish Neuro-Association.

The project included other stakeholders that could embrace the goal and use unconventional methods to mark the point and reach out to the target group.

- Organizing weekend seminars open for to the target group
- Working with *Läsa för integration* (Reading for integration) <http://www.lasaforintegration.se/index.html>
- Opratat is a theater group that lifts difficult subjects to the surface and make a pedagogic scen of the subject. <http://anhoriga.se/opratat/>
- The Swedish Disability Rights Federation: that enable the project to reach a broader target but also to reach the decision makers.

**References:** The project reach a great number of immigrant with an Assyrian background and could inform the attendees about their right and how the Swedish society works. This was of a great help to the families as well as the kids.

**Disclosure of Interest:** None declared

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**PARE0012 THE FRENCH PATIENT'S ASSOCIATION AFLAR: HAS GENERATED THE FRENCH NATIONAL ALLIANCE AGAINST OSTEOPOROSIS AND THE FIRST GENERAL CONVENTION FOR OSTEOPOROSIS, THAT IS A CAMPAIGN TO CREATE A NATIONAL PROMOTING TOOL TO IMPROVE THE MANAGEMENT OF OSTEOPOROSIS.: 7 PRIORITIES TO BETTER TREAT PATIENTS I**

L. Grange<sup>1,2</sup>, B. Cortet<sup>3</sup>, T. Thomas<sup>4</sup>, F. Srour<sup>5</sup>, P. Guggenbuhl<sup>6</sup>, C. Roux<sup>7</sup>, P. Monod<sup>8</sup>, J. M. Feron<sup>9</sup>, F. Alliot-launois<sup>10</sup>, F. Tremollières<sup>11</sup>, G. Chalés<sup>2</sup>, J. Giraud<sup>12</sup>, E. Senbel<sup>13</sup>, G. Thibaud<sup>14</sup>, P. Niemczynski<sup>15</sup>, D.R. Bertholon<sup>16</sup>, C. F. Roques<sup>17</sup>, D. Buchon<sup>18</sup>, C. Bonnet<sup>19</sup>, H. Blain<sup>20</sup>, C. Rolland<sup>21</sup>, D. Lafarge<sup>22</sup>, L. Carton<sup>2</sup>, On behalf of French National Alliance Against Osteoporosis.

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**Background:** Osteoporosis is a major public health issue with 5 million of French affected. Overall, she seriously underestimated, and costs are barely covered in France. Considering this situation, AFLAR were urged to create the so-called National Osteoporosis Alliance made up of 15 various stakeholders and patients.

**Methods:** National consultations on osteoporosis rely methodologically on 2 pillars: First the bottom-up reporting on patient needs and expectations. Second the conduct of coordination meetings with various osteoporosis key stakeholders and patients as part of regional panel-discussions. The aim is to provide an overview of real obstacles contributing to the lack of government subsidies for osteoporosis and write consensual proposals compiled into a white paper.

**Results:** An online survey along with a citizen's panel were key to provide feedbacks on difficulties, knowledges and believes but also patient needs. From November 2016 to June 2017, 10 days of dialogue and debate covering 5 various topics were convened in 10 different cities: Consultation and consolidation work regarding proposals made during various panel-discussions allowed synthesis around one call: the creation of a real public health plan against osteoporosis-related fractures relying on 7 key axis.

**Conclusions:** The human and medico-economic rational considering dramatic fallouts caused by osteoporosis has been illustrated many times over. The policy makers mobilization made by stakeholders through white paper release, a real manifesto for public health plan against osteoporosis-related fracture, remain a significant challenge to face.



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**PARE0013 SOURCES OF INFORMATION AND KNOWLEDGE ABOUT RHEUMATIC DISEASES AMONG PEOPLE WITH RHEUMATIC DISEASES IN POLAND AND IN OTHER EUROPEAN COUNTRIES**

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**Background:** Knowledge on rheumatic and musculoskeletal diseases (RMDs) is an important factor in helping patients live independent lives as long as possible. The internet and easy access to all sorts of information make it seem that delivering appropriate information to patients is one of the key objectives of health promotion.

**Objectives:** The aim of this study was to evaluate patients' knowledge on RMDs and find out how and when they seek and retrieve relevant information. The results provide an opportunity to increase efforts in proper education of patients and health care professionals, reduce adverse effects of incorrect information and increase self-awareness as well as personal health responsibility among patients.

**Methods:** We used questionnaires for patients with RMDs and carried out focus group interviews. The Computer-Assisted Web Interview Questionnaire was divided into 2 sections: one describing characteristics of respondents and evaluating importance of various information and its sources and the latter which tested knowledge on RMDs. The respondents were asked to rate their own knowledge and information provided by their physician. All the data were collected in 2017. We used two language versions of the questionnaire – Polish and English for international patients. The results from both groups were compared.

Both versions were distributed with the help of patient organizations. The link to the English version was distributed with the kind support from EULAR.

**Results:** We received 207 on-line responses – 140 in Polish and 67 in English. Both language groups had similar characteristics, however the English-speaking

respondents (EG) had a university degree more often (82% vs. 64%). The largest group of respondents were experienced patients with more than 10 years from diagnosis (47% in Polish group (PG) and 54% in EG). The EG was more diversified in terms of a diagnosis.

The information about a disease and methods of treatment were the most important pieces of information for the respondents (83% of PG rated it very important and 78% in EG) followed by finding a doctor (79% vs. 76% respectively). The three most important sources of information were: PG-Internet 46%, rheumatologist 35%, medical books 15%; EG- Internet 43%, rheumatologist 21%, lectures for patients – 15%.

**Conclusions:** The Results of Polish and English surveys were similar. The English group was more often interested in facilitating everyday life and finding support in living with a disease.

The test of knowledge on RMDs results confirmed that myths are still present among some patients. As much as 25% of Polish and 49% of international respondents associate occurrence of inflammatory rheumatic disease with weather conditions. Majority of people (94% in both groups) are aware that moderate physical activity is recommended in rheumatic diseases. The results also suggest insufficient knowledge about treatment methods and curability of RMDs. It is important to increase efforts in dissemination of appropriate knowledge among patients and health professionals using different methods. Such attitude should help in minimizing adverse effects that result from lack of knowledge or self-awareness.

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#### PARE0014 GETTING THE PULSE ON WORKPLACE EXPERIENCES AND ACCOMMODATIONS

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**Background:** As a patient-driven and managed non-profit organization, the Board members of the Canadian Arthritis Patient Alliance (CAPA) have experienced many of the workplace challenges of arthritis first-hand. Recognizing the importance of being able to contribute in the workplace, CAPA recently initiated a project focused on broadening the understanding of the challenges faced by people living with arthritis in the workplace; and, to develop workplace tools and appropriate advocacy activities to address these challenges.

**Objectives:** A survey concerning arthritis in the workplace was developed with the goal of enhancing the understanding of the workplace challenges faced by people with arthritis, including the type and effectiveness of personal and workplace accommodations and the effectiveness of available resources.

**Methods:** A Board member/project manager developed the survey in consultation with people living with arthritis. The survey was available in English and French and targeted to people who live with various forms of arthritis, including inflammatory arthritis as well as Systemic Lupus Erythematosus, osteoarthritis, etc. The survey was distributed to membership in December 2017 through the newsletter and social media channels. Further promotion of the survey was completed through outreach to French and English patient and non-profit groups. The results were collected online through a survey platform and analyzed using basic statistical techniques.

**Results:** At the date of submission, 218 survey responses were received (127 English responses, 91 French responses) and the majority of respondents (over 90%) live in Canada. Over 80% of respondents live with inflammatory arthritis and 86% reported that arthritis affected them moderately or significantly in the workplace. Although 49% of respondents indicated that working had a positive effect on their lives, 66% indicated that working took energy away from other life activities. The most highly helpful workplace accommodations were: flexible hours of work (58%), breaks to give joints/body time to recover (55%), paid time away from work to attend medical appointments (47%), and working from home one or more days per week (39%). The most highly used personal accommodations were: reduction of social activities (77%), pacing during the work day (70%) and spreading out non-work activities (64%). The survey responses will be further summarized for the presentation, along with ideas for development of resources based on the gaps identified.

**Conclusions:** CAPA developed a workplace survey to broaden the understanding of the challenges faced by people living with arthritis in the workplace. Early analysis of the survey indicates a number of implications such as the significant impact of arthritis on the workplace and the impact on other life activities. CAPA will develop appropriate workplace tools and plan advocacy activities in order to address the survey findings.

**Acknowledgements:** CAPA would like to thank the organizations that collaborate with us as well as various pharmaceutical companies whose funding enables our operation.

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#### PARE0015 LARGE-SCALE SURVEY OFFERS GENERAL INSIGHT AND BASIS FOR POLICY DRAFTING

S. De Jong, I. Koopmans, M. Feith. *Patient advocacy, Dutch Arthritis Foundation, Amsterdam, Netherlands*

**Background:** The Dutch Arthritis Foundation (DAF) commissioned a large-scale survey to gain a broad insight into the various aspects of living with RMDs in the Netherlands. The results offer an insight into the prevalence of RMDs, as well as into living with RMDs and the use and standard of relevant healthcare and social care in our country. This was the first survey of this scale in the Netherlands.

**Objectives:** The survey aimed to generate data about the prevalence and the impact of RMDs on people's every-day lives in the Netherlands. The DAF will use the results to better inform parties involved in caring for people with RMDs and to help them with policy drafting, such as authorities, healthcare insurers and healthcare providers.

**Methods:** The bulk of all data consists of statistical data from the NIVEL Healthcare Registrations (from 355 GP clinics, which register 1.1 million RMD patients). The survey also built on statistical and qualitative data from Vektis (business intelligence centre for the healthcare industry) and the National Institute of Public Health and Environmental Protection. Patients were contacted through the National Panel for Chronical Patients and asked to score their quality of life, the impact RMD has on their lives, and the standard of care. Rheumatologists, health professionals in rheumatology and orthopaedics were also represented in the monitoring group. The survey was carried out for four key disorders – chronic inflammatory rheumatism, osteoarthritis, gout and osteoporosis. These disorders are registered by both GPs and specialists. Fibromyalgia is not registered as a specific disorder by GPs and was therefore outside the scope of the survey.

**Results:** The report generated the following results for the more than two million people with RMDs in the Netherlands:

1 in 9 people have a RMD; More than 2 million people have a RMD; Every day, 700 people are diagnosed with a form of RMD; There are 1.3 million people with osteoarthritis; 400,000 people with osteoporosis; 370,000 people with gout; 220,000 people with inflammatory rheumatism such as RA, ax-SpA, SLE, Sjögren syndrome and scleroderma.

69% of people with RMD are restricted by their symptoms in their day to day life; 50% of people with RMD between the ages of 40 and 65 are not in paid employment;

54% of people with RMD indicate they suffer from loneliness;

50% of people with RMD deal with incomprehension;

65% uses medication, 37% physiotherapy.

**Conclusions:** The report shows the extent of the impact of RMDs, not only medically, but also with regard to social effects. This was the first study to adequately reveal the sense of loneliness among RMD patients, laying bare the incomprehension they face in others. It also studied the impact of RMDs on employment, the great reliance on voluntary carers, and the fact that many people with a RMD also suffer other symptoms. The report was able to pinpoint the most vulnerable patients, and therefore provides a clear indication as to where improvements can be made. It also clearly shows that there is room for improvement when it comes to the registration of specific disorders such as fibromyalgia, but also disorders classed as a form of inflammatory arthritis, to enable the generation of objective data from the registration systems.

**Disclosure of Interest:** None declared

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#### PARE0016 THE ROLE OF EMPATHY QUOTIENT IN PATIENT-PHYSICIAN COMMUNICATION: A TOOL TO IMPROVE MEDICATION ADHERENCE

A. Celano. *Italian National Association for People with Rare and Rheumatic Diseases – APMAR Italia, Lecce, Italy*

**Background:** Brain circuits governing the identification with others and those regulating the care feeling towards suffering people form wide distinct brain networks and are essential elements of empathy. This last is ruled by the "circuit of



empathy" involving ten interconnected brain areas, operating on a personal base. This explains why some people have little or no empathy, and consequently, high or low propensity to communicate effectively: lower "empathy quotient" leads to inadequate social competence. The circuit of empathy is a very sophisticated and complex system, and its erosion is due to both genetic (deficiencies) and environmental (life experiences) factors.

**Objectives:** The EQ increase is essential to improve patient-physician communication and enhance medical adherence. It is easy to achieve it by promoting the ability to understand others' feelings and thoughts and to interpret signals and experience (beyond the symptoms), as well as by using effective communication. Being open improves quality and effectiveness of the patient-physician relationship, as well as medical adherence.

**Methods:** Observation, EQ measurement on patients and health personnel—APMAR carried out an observation activity to evaluate possible EQ improvement in patients and health personnel, and enhance medication adherence. Interventions were classified based on target (patient/health personnel), focus (educational/behavioural/affective), implementation (general/customized), complexity (one or more aspects) and the operator involved, followed by specific evaluation on adherence and disease outcomes. Patients suffering from rheumatological diseases and health personnel were interviewed to collect psychosocial information and indicatively measure their EQ. This allowed to act directly on parameters determining empathy improvement. Effective engagement was achieved through diagnostic alliance\*, therapeutic alliance\*, disease self-awareness, medication adherence and self-administration. 78 patients and 10 health personnel followed a training to improve EQ and ability to relate effectively through communication, narrative and psychodynamic. Health personnel followed an experiential and practical training, with cognitive, emotional and behavioural elements inspired by psychodynamic, Gestalt, AT, NLP, to learn how to use situational logic, modulate tone of voice, speech quality and speed, gestures, also using NBM principles. 30-minute individual monthly consultations and cognitive-behavioural therapy were conducted.

**Results:** Interventions showing some impact on medication adherence were direct, personalized on the patient and mediated by the health personnel. Disease outcomes, patients' self-care education and decision-making were considered, and a gym program was included. Follow-up occurred every 2 months (total 10 months); 86% of patients were adherent and the program significantly improved disease outcomes such as DAS28, pain, exacerbations, functional disability and quality of life.

**Conclusions:** The EQ increase is essential to improve patient-physician communication and to enhance medical adherence.

#### REFERENCE:

- [1] Antonella Celano, APMAR President Rosario Gagliardi, Professor of Socio-medical Management and Medical Communication, MIAS Master – Università La Sapienza, Rome

**Disclosure of Interest:** None declared

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#### PARE0017 SUPPORTING YOUNG PEOPLE WITH RMDs IN MANAGING ISSUES AROUND RELATIONSHIPS, PREGNANCY AND SEXUALITY

*W. Olsder, L. van Nieuwkoop, A.A.J. Haenen. Youth-R-Well.Com, Lisse, Netherlands*

**Background:** Young people with rheumatic and musculoskeletal diseases (RMDs) experience issues considering relationships, pregnancy and sexuality (Kedde, 2012). The report of the PARE Youth Research Project shows that in the Netherlands 42% of the young people with RMDs report an impact on their sexual life (Poldemaa, Tammaru & de Wit, 2014). Furthermore, 24% of the respondents want to receive information about managing sexual health issues. During past events organised by Youth-R-Well.com (the Dutch organisation for young people with RMDs), the young people indicated that they had questions about managing relationships and getting pregnant. For instance, they had questions about the hereditary of the disease, the impact of medication when getting pregnant, and how they could improve their sexual life. This shows a clear need for more information about managing relationships, pregnancy and sexuality from young people with RMDs.

**Objectives:** To respond to this need of young people with RMDs, Youth-R-Well.com organised an event around managing issues that are faced with relationships, pregnancy and sexuality. The main objective was to inform and empower the patients and their partners around these three topics. Informing patients and helping them managing issues around these three themes, aims to improve their social life, increase their self-management and in turn increase their quality of life.

**Methods:** Young people with RMDs might encounter a barrier for discussing issues around relationships, pregnancies and sexuality with their health care providers. Therefore, Youth-R-Well.com organised an informal event to inform the young people about these topics. The event consisted of three speakers: a rheumatologist speaking about pregnancies, a sexologist speaking about sexual issues and a young person with an RMD speaking about her personal experience with (sexual) relationships and getting pregnant. The event was interactive, such that young people had the chance to ask questions about all topics.

**Results:** In total, 30 young people between the age of 20–30 attended the event. The attendees evaluated the event with an average of 8,2/10. During the event, there was an informal, safe atmosphere. The attendees were not afraid to ask their questions and discuss the topics with others. From the three presentations, the attendees most highly valued the presentation of the rheumatologist about pregnancy (8,6/10).

**Conclusions:** An event from a patient organisation decreases the barrier to discuss issues around relationships, pregnancy and sexuality for young people with RMDs. Combining information from health care professionals with peer support, can help in managing issues around these three topics, empower young people with RMDs, and eventually increase their quality of life.

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**Acknowledgements:** The event was financially supported by UCB and AbbVie.

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## Speaker Abstracts

### Patient information and education

#### AB1480-PARE MOTIVATION OF RHEUMATOID ARTHRITIS PATIENTS FOR SMOKING CESSATION

*I. Holc, A. Pahor, M. Božič, M. Dobnik. Dept. Of Rheumatology, UMC Maribor, Maribor, Slovenia*

**Background:** The intensive nursing care algorithm in the individual treatment of a rheumatoid arthritis patient includes the "treat to target" treatment approach while predicting the extended role of a nurse in patient care. Nurse's responsibility for patients suffering from rheumatoid arthritis includes a deeper knowledge of the patient's health status (14 activities – Virginia Henderson), implementation of customised nursing care, education, consultation, as well as offering support to patients and their families. Smoking is a major global health issue due to increasing tobacco use and problems associated with cessation of smoking.

**Methods:** The study group comprised of 90 patients (34 male, 56 female) aged 56 to 72 years, (mean 64.29 years) treated in an outpatient clinic of Department of Rheumatology, University Medical Centre Maribor, Slovenia. All patients suffered from rheumatoid arthritis. 34 (44%) of them were smokers, 54 (44%) non-smokers and 11.11% of them used to smoke, 45 patients were treated with biological disease modifying anti-rheumatic drugs (bDMARDs) The research is based on quantitative methodology. Questionnaire was used as the research method. For statistical analysis, a t-test and Spearman correlation was used.

**Results:** The analysis did not show any statistically significant correlations between gender, age, or level of patients' education and desire to quit smoking. Nor we found any statistically significant correlations with patients' awareness to smoking – among those who are treated and those who are not treated with bDMARDs.

**Conclusions:** Every nurse should offer advice to rheumatoid arthritis patients to quit smoking as this is the best decision rheumatoid arthritis patients can make in order to improve their health. This mission carried out by a nurse is of great importance not only for the patient but also for public health. Nurses need to understand the motives and obstacles in association with smoking cessation. In addition, they need to be aware of the options that are available to help patients quit smoking. The most important factor for an effective smoking cessation is motivation. Important

negative factor that impact smoking cessation is the pleasure while smoking.

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**Disclosure of Interest:** None declared

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## Building patient led organisations

### AB1481-PARE CANADIAN ARTHRITIS PATIENT ALLIANCE: WHO ARE WE? WHAT HAVE WE BEEN UP TO?

C. Reece, N. Robertson, L. Wilhelm, L. Proulx, D. Richards, A. McKinnon, J. Gunderson, A. Sirois. *Canadian Arthritis Patient Alliance of Canada, Ottawa, Canada*

**Background:** The Canadian Arthritis Patient Alliance (CAPA) is a grass-roots, patient-driven, independent, national advocacy organisation with volunteer members from across the country. CAPA's fundamental belief is that the first expert on arthritis is the individual who lives with the disease and who provides a unique perspective that is all too often absent in health care, health policy and research.

**Objectives:** Here we will present a poster with the intent to give an overview of what CAPA is, the resources that are available to individuals living with arthritis, our involvement in research as well as our collaboration with other health organisations and government.

**Methods:** CAPA continues to promote its Arthritis Patient Charter and provide print outs to organisations that request it. It has conducted various surveys to better understand the needs of its members and develop support materials to help address these needs. CAPA also worked with Health Canada on various initiatives in regards to health policy development, drug review policy and patient engagement initiatives as well as participated as collaborators on research teams.

**Results:** The following key accomplishments and continued projects will be highlighted:

- 1) Arthritis Patient Charter was developed with other groups in the Canadian arthritis community that outlines the rights and responsibilities that arthritis patients should expect in their care.
- 2) Collaboration on research teams – for example, as a Member of the Canadian Institutes of Health Research (CIHR) Strategy for Patient-Oriented Research (SPOR) as well as on CIHR's Institute of Musculoskeletal Health and Arthritis Research (IMHA) Ambassadors. Individual CAPA members also work with researchers to contribute to their projects and have co-authored research publications.
- 3) A methotrexate resource – A survey on the topic of Methotrexate was developed by CAPA Board members with the advice from a rheumatologist was as circulated through its wide network in English and French via social media, newsletters and an email blast to our membership. Patient resources will be developed based on the survey response.
- 4) Pregnancy with Arthritis – a web-based resource created with patient input to help those contemplating a step into parenthood.
- 5) Biosimilar and medical cannabis resources – along with its position papers, CAPA has created a video to help patients understand this type of medication. CAPA has also written a position paper on Medical Cannabis.
- 6) Other forms of input – CAPA provides the patient perspective via official submissions to Health Canada, and the Canadian Agency for Drugs and Technologies in Health.

**Conclusions:** CAPA will present highlights of its key achievements and continued collaboration within the arthritis community. CAPA continues to engage with various organisations in order to identify gaps within the community with the intent to develop needed resources for patients and caregivers and direct our advocacy efforts.

**Acknowledgements:** CAPA would like to thank the organisations that collaborate with us as well as various pharmaceutical companies whose funding enables its operation.

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## Arthritis research

### AB1482-PARE PARTICIPATION IN CLINICAL TRIALS HAS A POSITIVE IMPACT ON THE PSYCHOLOGICAL AND EMPLOYMENT WELL-BEING OF PATIENTS WITH INFLAMMATORY ARTHRITIS

H. Alkomy, C. Tierney, V. Ramasamy, P. Knight, E. Ingram, S.-E. Aconstaninesei, A. Pakozdi, Y. Abbye-Nayake, H. Tahir. *Rheumatology, Barts health, London, UK*

**Background:** Biologic therapies have improved the physical well-being of patients with Inflammatory arthritis. However, there remains a lack of emphasis on addressing patients' psycho-social needs in routine rheumatology practice.

**Objectives:** The aim of this study was to explore the unmet psychological, emotional and social needs of inflammatory arthritis patients (Rheumatoid Arthritis (RA), Psoriatic Arthritis (PsA), Axial Spondyloarthritis (AS)) entering clinical trials, and to evaluate the factors leading to improvement in physical and psychological wellbeing during the clinical trial.

**Methods:** A cross sectional survey was distributed to all inflammatory arthritis patients having completed a minimum of 12 weeks of treatment within phase II and III clinical trials, in Whipps Cross University Hospital, between Nov 2017 and Jan 2018. The anonymous survey included satisfaction scales with scores ranging from 0 to 10 (0=extremely dissatisfied and 10=extremely satisfied) to rate physical (ie: improvement in joints pain and swelling) and psychological satisfaction during the clinical trial. Factors contributing to patients' physical and psychological improvement were also explored. Employment status and changes were also explored.

**Results:** A total of 46 questionnaires were completed with 5 excluded from analysis due to missing data. Of the 41 patients, 26 (63%) had PsA, 3 (7%) AS, and 12 (29%) RA. 22 (54%) patients were male. 26 (63%) patients were white caucasian, 9 (21%) were Asian and 6 (15%) were from other ethnic backgrounds. 71% of the patients were aged between 36–60.

37 (90%) of patients were satisfied with their physical improvement (joint pain and swelling) during the clinical trial. 34 (83%) said their inflammatory arthritis had a negative impact on their psychological well-being, however 39 (96%) were satisfied with the emotional support received from the clinical research staff.

The most frequently reported factors contributing to their psychological improvement included, in all patients (41, 100%), the involvement of the clinical research staff and the frequency of regular follow ups. In 40 (98%) patients, the clinical research doctor and the clinical research environment and in 36 (88%) patients the study drug itself.

Regarding employment status, 29 (71%) were employed prior to participating in the clinical trial, and 18 (44%) reported improvement in their employment situation after entering the clinical trial. These included new job positions,<sup>5</sup> reduction in sick leave days,<sup>5</sup> and the capability of working more hours.<sup>1</sup>

**Conclusions:** Inflammatory arthritis is associated with a high prevalence of psychological burden. Addressing the physical needs solely and ignoring the psychological wellbeing of patients can adversely affect their quality of life. The current survey highlighted that by participating in clinical trials, the majority of inflammatory arthritis patients, gained additional satisfaction with regards to their psychological and emotional needs and received invaluable support within the trial setting. This led to improved well-being and employment satisfaction. We would therefore, encourage health care professionals to invest in the psychological and emotional wellbeing of patients in routine clinical practice.

**Disclosure of Interest:** None declared

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## Innovations in arthritis health care

### AB1483-PARE DEVELOPMENT AND ADAPTATION OF RHEUMABUDDY FOR YOUNG PEOPLE WITH JIA, THEIR FAMILIES AND PEOPLE WITH RA RESIDING IN THE UK

A Gilbert<sup>1,2</sup>, <sup>1</sup>The National Rheumatoid Arthritis Society, Maidenhead, UK; <sup>2</sup>Daman, Copenhagen, Denmark

**Background:** The number of children and young people (CYP) with JIA needing support is on the increase as available allied services continue to face cuts and are under more pressure than ever. A valuable life skill for any CYP with a long-term condition is self-management, the ability to control emotions, learn resilience, communicate, work toward goals and ultimately improve their physical and emotional wellbeing.

**Methods:** Rheumabuddy is a Danish app developed for children (aged over 12) adults in Denmark with RA. We were approached by the developers, Daman, in June 2016 and meetings and discussions followed regarding NRAS launching and distributing this innovative app in the UK. For a JIA audience, our main concerns were online child safety issues and whether the app could be used by younger children with JIA with their parents as well as by adults with RA. A survey of parents and young people with JIA and RA followed and after discussions with pilot users some adaptations were made, and child safety protection protocols were put in place between NRAS and Daman.

**Results:** Daman appointed NRAS as its UK partner and NRAS undertook a soft launch of Rheumabuddy in November 2017.

**Conclusions:** Since its launch, to date we have 2000 active users who are a mixture of children with JIA and their parents, adults with JIA and adults with RA. Here are some quotes from users:

"Rheumabuddy has been so helpful and I am now able to track my progress which I can show my consultant. I would often forget how I felt 3 or 4 months ago"

"The Rheumabuddy app was a way for my daughter to let me know how she felt each day, normally she doesn't like discussing it"

We know that CYP are growing up in a challenging and fast changing world. The ability to use self-management strategies effectively is a skill that becomes very important for success as children grow into adulthood yet is hard to acquire through the NHS alone. Rheumabuddy encourages the self-monitoring and regular recording of key patient reported outcomes. Changes in symptoms over time can be displayed in graph format and can be shared with HCP's, family, and school. The collation of cumulative data around mood, pain and fatigue can, for example, lead to empowerment of the individual or family resulting in ability to effect positive lifestyle change in the person with JIA or RA.

**Acknowledgements:** Anne Gilbert, Phil Baker, Ailsa Bosworth, Clare Jacklin, The National Rheumatoid Arthritis Society, Maidenhead and Daman Denmark

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## Best practice campaigning

### AB1484-PARE FORMING PROGRESSIVE PATIENT ALLIANCES FOR PROGRESSIVE THINKING

E Kritza<sup>1</sup>, E. Tsigki<sup>2</sup>, V. Romero Pazos<sup>3</sup>, B. Boteva<sup>4</sup>, S. Micallef<sup>5</sup>. <sup>1</sup>Chair, Agora, Heraklion, Greece; <sup>2</sup>Agora Secretariat, Agora, Groningen, Netherlands; <sup>3</sup>Vice-Chair, Agora, La Coruna, Spain; <sup>4</sup>Board Member, Agora, Sofia, Bulgaria; <sup>5</sup>Treasurer, Agora, Msida, Malta

**Background:** The role and scope of influence of patient organisations has been undeniably increasing. Wilson 1999 Patients are in the lead of influencing the decision-making processes in healthcare and in doing so, forming strategic and constructive alliances through umbrella organisations can be of great value. This article discusses the benefits of forming progressive alliances between RMDs patient organisations using the example of the partnership between Agora and the Global Alliance for Patient Access (GAfPA). The data presented has been drawn from the first joint project between Agora and GAfPA (2017) in an effort to raise awareness about access to Biosimilar and Biologic medicine, in combination with developing self-management skills in the sense of a holistic model for treating and managing RMDs.

**Objectives:** The objectives of the joint project were to provide patient groups with a greater understanding of the current policy landscape for Biologic and Biosimilar medicines in Europe; equip patients with effective tools to inform policymakers about patient concerns; kick-start the

establishment of an advocacy platform for the Agora organisations; and to examine the role of self-management programmes in supporting patients with RMDs along with the use of technology (HTA). The main objective of this article is to examine the role of strategic alliances in creating a strong patient front that seeks to become part of the decision-making processes and influence policy changes on national and EU levels. Auch alliances offer patients a new perspective and a progressive way of thinking healthcare matters.

**Methods:** Keynote presentations and group discussions were carried out. The patients who participated in the workshop were exposed to the fundamental information about the use of Biologic and Biosimilar medication and related policy issues and were engaged in a discussion that eventually led to the composition of a position paper with concrete principles on the use of this treatment.

**Results:** Agora and GAfPA have published the "Patients Principles around the use of Biologics and Biosimilars", which was disseminated amongst the Agora members and has been used to raise awareness about the specific topic in each country-member.

**Conclusions:** The alliance between Agora and GAfPA has enabled Agora to strengthen its advocacy efforts and focus towards becoming more active in monitoring policy changes. There was a strong consensus that the patient voice should be central to all discussions about commencing or switching treatments and that shared decision making should always be an integral part of the process. The collaboration between national and umbrella organisations has created a strong network of patients, who share similar ideas, principles and support each other towards advocating for patients' rights to a higher quality of life. These principles would certainly be of interest to EULAR PARE members and other patient organisations beyond the immediate AGORA/GAfPA network, who could consider using them in their own advocacy work and/or when supporting individual patients in their organisations.

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### AB1485-PARE REUMANIFEST: JOINING FORCES FOR POLITICAL URGENCY

N Lopuhaä, M. Feith. *Patient Advocacy, Dutch Arthritis Foundation, Amsterdam, Netherlands*

**Background:** In 2012, health insurance provisions for people with RMDs were cut drastically when reimbursement of physical therapy under the Dutch basic health insurance package was scrapped for reasons including lack of scientific evidence, the economic crisis and rising healthcare costs. The effect has been counterproductive. Costs have gone up as more patients use more medication and visit their rheumatologist and other specialists more often. It has also led to patients not getting the care they need. Because the Dutch Arthritis Foundation (DAF) believes that patients with RMDs should have access to the care they need, it launched a lobby to influence key governmental and political stakeholders.

**Objectives:** According to the DAF, patients with RMDs need access to the physical therapy they need. Efforts made in this area, such as the introduction of a registration point and impact research to demonstrate the effect of decreased accessibility, remained unsuccessful. We needed to adopt a different approach to instil in the government and political stakeholders a sense of urgency and to raise general awareness of the issue.

**Methods:** Parties in the field of RMD have now joined forces by:

- consulting patients and care providers in a national survey: "Why is physiotherapy important to you?"
- drafting a Reumanifest in which patients, doctors and researchers lobby for reinstatement of physiotherapy in the basic medical insurance package.
- having the Reumanifest signed by patients, caregivers, professional organisations, professors, and other patient organisations (more than 25 000 responses).

**Results:** The Reumanifest was presented to political parties as a petition, and appeared in newspapers as an advertisement. This led to critical questions being asked to the Dutch Minister of Health, and put the issue



and its urgency firmly back on the political agenda. With renewed political pressure on the issue, we expect that this will eventually lead to a solution for people with RMDs who need physiotherapy, but who now have to pay for this privately. The campaign has increased awareness among the cabinet and other political stakeholders.

**Conclusions:** By joining forces, you can make your voice heard in politics, as support from various perspectives lends credibility and relevance to the urgency.

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